

Multimodal Imaging in Other Intraocular Inflammations

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Purpose: Multimodal imaging has become essential in the understanding of posterior segment uveitis.

Methods: Provide clinical examples of the use of multimodal imaging in the diagnosis and management of uveitis and uveitis masquerades including OCT, OCTA, autofluorescence, near infrared, fluorescein and indocyanine green angiography.

Results: Variable involvement of the posterior segment by many forms of uveitis or uveitis masquerades means that multimodal imaging may not be appropriate for all cases, however, all cases with posterior segment involvement should be explored to the extent possible.

Conclusion: Diagnosis and comprehension of inflammatory diseases improves with new ways of seeing old diseases.

AUS symposium – Imaging in the Diagnosis and Management of Uveitis: Imaging of the posterior segment by angiography: fluorescein and indocyanine green angiography

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Fluorescein (FA) and indocyanine angiography (ICGA) constitutes the mainstay of posterior segmenty imaging in uveitis. FA is an indispensable imaging modality in the diagnosis and management of patients with intermediate, posterior and panuveitis. The pattern and type of retinovascular and chorioretinal involvement may be useful diagnostically and in the assessment of structural abnormalities associated with visual loss. ICGA has also emerged as having an important role in the diagnosis and follow up of uveitic diseases, as well as in evaluating the full extent of choriocapillaris and choroidal stromal involvement in these diseases. Both approaches increadingly utilize widefield imaging technologies and studies suggest that widefield imaging are helpful for many inflammatory and infectious ocular diseases. A variety of commercially available imaging products offer widefield capability for FA and ICG, and each system has distinct advantages and disadvantages.

The Role of Multimodal Imaging in Monitoring Vogt–Koyanagi–Harada Disease Activity

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The goal of this presentation is to review and verify the role of multimodal imaging in Vogt–Koyanagi–Harada (VKH) disease, especially with regards to monitoring disease activity. Multimodal imaging including color photography, fundus autofluorescence, fluorescein angiography, indocyanine green angiography (ICGA), and enhanced depth imaging OCT (EDI-OCT) has been very useful for diagnosis in early cases, atypical presentations and for differentiating with other serous choroidopathies. Though VKH can be monitored by ICGA, which in the early phase reflects choroidal inflammatory changes, there are obvious difficulties with serial follow-up due to its invasiveness and costs. Recently, OCT-A has been reported to show choriocapillaris defects in VKH disease corresponding to ICG findings. In our experience, however, the accuracy and reproducibility of OCTA are not yet enough to be clinically used. On the other hand, EDI-OCT clearly revealed choroidal thickness changes that were well correlated with not only the severity of visual symptoms but also the degree of vitritis. In patients who were observed without intervention, a significant increase in choroidal thickness was observed consistently 3 to 6 months prior to the recurrence of serous detachment. When prompt treatments were performed based on the increase in choroidal thickness with systemic corticosteroids, non-steroidal immunosuppressants or with intravitreal dexamethasone implants, visually-threatening disease exacerbations were effectively prevented and long-term good visual prognosis was maintained. Therefore, multimodal imaging is required for the early diagnosis of VKH; for monitoring posterior uveitis activity and for determining treatment timing, EDI-OCT appears to be more sensitive and specific than other examinations.

Session 2 “Updates in infectious and non-infectious endophthalmitis” IOIS Section -
Endophthalmitis and Other Ocular Infections

Endogenous bacterial endophthalmitis

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Exogenous bacterial endophthalmitis

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Endophthalmitis is an intraocular inflammatory disorder affecting the vitreous cavity. It could be caused by spread of organisms into the eye exogeneously or endogeneously. The most common causes of exogenous endophthalmitis include post operative and post traumatic endophthalmitis. The etiology of the infection varies according to the geographic location. According to the EVS study 94% of the culture proven endophthalmitis was caused by gram positive organisms and Gram negative organisms contributed to 6%. However a study in India reported 53% of isolates to be gram positive, 26% to be gram negative organisms and 17% were fungus. Though the most common source of infection is the conjunctival flora, cluster endophthalmitis is a serious concern especially where large volume surgeries are performed. The signs and symptoms of endophthalmitis are pain, drop in vision, redness, hypopyon, cells in the anterior chamber and vitreous cavity. Endophthalmitis is an ocular emergency and the diagnosis is usually clinical. The treatment involves an aqueous or vitreous biopsy, to identify the causative organism and the immediate instillation of intravitreal antibiotics. The vitreous biopsy specimen is subjected to grams stain, KOH stain, culture for bacteria and fungus and PCR for eubacterial and panfungal genome. The commonly used intravitreal antibiotics are vancomycin(1mg/0.1ml) to cover gram positive organisms and amikacin(400ug/0.1ml) or ceftazidime(2.25mg/0.1ml) to cover gram negative organisms. When fungal infection is suspected amphotericin B(5-10ug/0.1ml) or voriconazole(100ug/0.1ml) is the preferred intra vitreal antibiotic. In severe cases a primary vitrectomy with intravitreal antibiotics may be indicated.

Non-infectious Endophthalmitis

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As intravitreal injection is getting popular, the incidence of noninfectious endophthalmitis is also abruptly increasing. The presenting symptoms are usually mild with less pain and normal IOP, but sometimes severe with hypopyon. So, an infectious cause of an unusual presentation of postprocedural inflammation should be carefully excluded. Noninfectious endophthalmitis can be treated with topical steroid alone but it takes over a month to recover the vision. Again, careful and close follow up during initial presentation period will lead to proper management on early postprocedural ocular inflammation caused by both non-infectious and infectious etiologies.

Overview of Infectious and Non-Infectious Endophthalmitis

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Endophthalmitis is one of the most devastating and sight threatening forms of intraocular inflammation. We describe there the presenting signs and symptoms, differential diagnoses, prevalence, etiology, pathophysiology, and management principles of endophthalmitis. Early recognition and timely, appropriate management are key to maximizing the chances for optimizing visual outcomes.

Pathogenesis and Pathology of Endogenous Fungal Endophthalmitis

Narsing Rao¹.

Purpose: Mycotic endogenous endophthalmitis are important cause of a visual loss with ocular morbidity. In this clinicopathological study 13 patients with endogenous *Aspergillus* endophthalmitis, 12 with endogenous *Candida* intraocular infections and 4 with *Coccidioidomycosis* were evaluated. Both clinical features and intraocular spread of the fungi were studied to determine which clinical and/or histopathologic features could help distinguish *Aspergillosis* from *Candida* infections.

Methods: Clinical information was sought from each case and patients with AIDS were excluded. The fungal elements, inflammatory response, and vascular invasion by the fungi were analyzed.

Results: *Candida* species endophthalmitis was noted in patients with a history of gastrointestinal surgery, hyperalimentation, or diabetes mellitus, whereas *Aspergillosis* was present in patients who had undergone organ transplantation or cardiac surgery. The vitreous was the primary focus of infection for *Candida*, whereas subretinal or sub-retinal pigment epithelium infection was noted in eyes with *Aspergillosis* and in *Coccidioidomycosis*, the organismal were localized to subretinal space. Retinal and choroidal vessel invasion by fungal elements was noted in cases of *Aspergillosis*. There was cerebral and cardiac infection with high mortality in patients with *Aspergillus* endophthalmitis.

Conclusions: The above results indicate that unlike *Candida* endophthalmitis, *Aspergillosis* is seen in organ transplant or cardiac surgery patients. In *Aspergillus* endogenous endophthalmitis, initial clinical presentation includes extensive areas of deep retinitis/choroiditis. This endophthalmitis is usually associated with a high rate of mortality caused by cerebral and cardiac complications. Contrary to the findings in *Candida* endophthalmitis, vitreous biopsy may not yield positive results in *Aspergillosis*.

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Pathogenesis and Pathology of Endogenous Fungal Endophthalmitis

Narsing Rao¹.

Mycophenolate mofetil combined with systemic corticosteroids prevents progression to chronic recurrent inflammation and development of “sunset glow fundus” in initial-onset acute uveitis associated with Vogt-Koyanagi-Harada disease

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Purpose: To evaluate the effectiveness and safety of mycophenolate mofetil (MMF) as first-line therapy combined with systemic corticosteroids in initial-onset acute uveitis associated with Vogt-Koyanagi-Harada (VKH) disease.

Methods: This prospective study included 38 patients (76 eyes). The main outcome measures were final visual acuity, corticosteroid-sparing effect, progression to chronic recurrent granulomatous uveitis, and development of complications, particularly “sunset glow fundus”.

Results: The mean follow-up period was 37.0±29.3 (range 9-120 months). Visual acuity of 20/20 was achieved by 93.4% of the eyes. Corticosteroid-sparing effect was achieved in all patients. The mean interval between starting treatment and tapering to 10 mg or less daily was 3.8 ±1.3 months (range 3-7 months). Twenty-two (57.9%) patients discontinued treatment without relapse of inflammation. The mean time observed off of treatment was 28.1±19.6 months (range 1-60 months). None of the eyes progressed to chronic recurrent granulomatous uveitis. The ocular complications encountered were glaucoma in 2 (2.6%) eyes, and cataract in 5 (6.6%) eyes. None of the eyes developed “sunset glow fundus” and none of the patients developed any systemic adverse events associated with the treatment.

Conclusions: Use of MMF as first-line therapy combined with systemic corticosteroids in patients with initial-onset acute VKH disease prevents progression to chronic recurrent granulomatous inflammation and development of “sunset glow fundus”.

Immunology and uveal melanoma: good or bad?

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Immunotherapeutic approaches such as the blocking of immune checkpoints are widely used in the treatment of malignancies. Regrettably, patients with uveal melanoma metastases hardly ever respond to anti-CTLA4 or PD1/PD-L1 antibodies. In contrast with well-responding cutaneous melanoma, uveal melanoma contain very few mutations, which may provide neo-antigens. Another relevant factor may be the presence of immune tolerance: the eye is an immune privileged site, and antigen shedding from the tumor may lead to ACAID (anterior chamber associated immune deviation).

Primary uveal melanoma that develop in the choroid may thus induce tolerance or not be recognized by the immune system. However, T cell responses against melanoma antigens have been observed in patients with a uveal melanoma, and primary uveal melanoma do contain CD3, CD4 and CD8 T cells. Especially tumors with high T cell numbers have a high chance to develop metastases. These tumors also contain many macrophages, which may play a role in angiogenesis. A recent study from our lab showed that genetic changes are associated with infiltrate: addition of chromosome 8q is associated with a higher presence of macrophages, while the loss of one chromosome 3 is associated with a higher influx of T cells. (G. Gezgin, Cancer Immuno Immunother 2017, 66, 903)

Conclusion: uveal melanoma contain macrophages and T cells; the presence of local inflammation may help to stimulate angiogenesis and metastasis formation. The local T cell response is insufficient to inhibit tumor growth.

Sjogren's Syndrome Myths and Facts

Esen Akpek¹.

One-quarter of patients with clinically significant dry eye have an underlying rheumatic condition, most commonly Sjögren's syndrome (SS). SS is a common cause of dry eye with multisystem involvement. Approximately 1/10 patients with dry eye have underlying SS. The immunological background of SS involves activation of both innate and acquired immune systems. The American College of Rheumatology/European League Against Rheumatism classification criteria are based on the weighted sum of five items: anti-SSA/Ro antibody positivity and focal lymphocytic sialadenitis with a focus score of ≥ 1 foci/4 mm², each scoring 3; an abnormal ocular surface staining score of ≥ 5 (or van Bijsterveld score of ≥ 4), a Schirmer's test (without anesthesia) result of ≤ 5 mm/5 min and an unstimulated salivary flow rate of ≤ 0.1 mL/min, each scoring 1. Individuals who have a total score of ≥ 4 for the above items meet the criteria for primary SS. More than third of patients with SS have extraglandular systemic findings such as interstitial nephritis, interstitial lung disease, autoimmune hepatitis, vasculitis etc. Extraglandular ocular manifestations are present in about quarter of patients with SS including paracentral interstitial keratitis, anterior uveitis, scleritis. Half of the patients with vision-threatening ocular findings do not carry the SS diagnosis on presentation. Importantly, patients with vision-threatening ocular findings are 4 times more likely to have systemic involvement. Dry eye precedes these findings on average by a decade. Therefore, ophthalmologists should consider assessing for SS in all patients with clinically significant dry eye.

Inflammation and inflammatory biomarkers in dry eye

ANDREA LEONARDI¹.

It is well established that inflammation has a significant role in the pathophysiology of dry eye disease (DED), promoting symptoms of irritation and ocular surface damage. Whether inflammation is a primary phenomenon in DED or is the consequence of repetitive abrasion of the ocular surface after tear film deficiency and hyperosmolarity has suggested the concept of the vicious circle. Tear hyperosmolarity by itself stimulates the production of inflammatory mediators on the ocular surface without the need for additional triggers. These inflammatory mediators promote the activation of immature antigen-presenting cells (APCs) responsible for priming naive T cells in the lymphoid compartment, leading to the expansion of autoreactive CD4+ TH1 and TH17 cell subsets. T-cells subsequently infiltrate the ocular surface, where they secrete additional pro-inflammatory cytokines. Some of these factors and other proteins, such as S100A proteins, lipocalin-1, secretory phospholipase A2, annexin, could be considered also as candidate biomarkers of either diagnosis, prognosis or activity of the disease. Metalloproteinase-9 tear level is confirmed as a good but not specific biomarker whereas cell parameters, such as HLA-DR, have been used to assess the efficacy of topical treatments. New technologies such as transcriptome analysis may further identify new and more specific biomarkers for ocular surface diseases. Therefore, protein or peptide analysis can be used as a possible fingerprint for disease biomarkers and pathological molecule identification.

Clinical characteristics and risk factors for symptomatic MGD in China. Results of a large multicenter study

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Purpose:To detect the clinical characteristics and risk factors for meibomian gland dysfunction (MGD) in the Chinese population.

Methods:We undertook a multicenter study on the clinical characteristics and risk factors of MGD in China using the same diagnostic criteria. All participants were aged 18 years or older. Patients completed a symptoms questionnaire and underwent a comprehensive slit-lamp examination. MGD was diagnosed when one or more of the following was present: absent, viscous, or waxy white secretion upon digital expression; presence of two or more lid margin telangiectases; and/or plugging of two or more gland orifices. There are 6 study parameters measured. The relationship between symptoms and signs was evaluated and the risk factors were detected.

Results:The study included 1286 patients (584 men and 702 women). Mean participant age was 45.3 ± 8.5 years (range, 18-72 years). The prevalence of symptomatic and asymptomatic MGD was 21.6% and 53.7%, respectively. The prevalence of total MGD increased significantly as participant age increased ($P < 0.005$). The dry eye symptoms are poorly correlated with dry eye signs. For the symptomatic MGD group, fluorescein score was higher, tear film breakup time was shorter, and meibo-score was larger, compared to asymptomatic patients. The presence of chronic pain syndrome, depression, and atopic disease was the risk factors.

Conclusions:This multicenter study has shown that dry eye symptoms are poorly correlated with dry eye signs. the risk factors included chronic pain syndrome, depression, and atopic disease.

New therapeutic strategies for Meibomian Gland Dysfunction

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The treatment of Meibomian Gland Dysfunction (MGD) is based on lid hygiene, oral antibiotics and topical anti-inflammatory drugs. However, efficacy may be poor in severe cases.

New therapeutic strategies for MGD include topical anti-infectious drugs, thermal pulsation and intense pulsed light therapy.

Azithromycine eye drops are available for the treatment of bacterial conjunctivitis. However, the anti-inflammatory effect of azithromycine may explain the efficacy of this treatment in MGD and in blepharitis. Due to its long tissular half life, discontinuous patterns of administration are possible.

The thermal pulsation device (Lipiflow[®]) is an automated single use system that heats the meibomian glands from inside the eyelids and simultaneously applies pressure from the outside to drain the meibum. One single treatment is more potent than daily manual lid hygiene, and its effect on symptoms may last more than one year.

Intense pulsed light therapy is widely used in dermatology for treating skin telangiectasia. Devices have been developed for MGD. Flashes of intense white light are applied on the periocular region, every 2 to 4 weeks. Although the exact mechanism of action is unknown, the effect on signs and symptoms seems to be interesting.

Anti-inflammatory Properties of Omega Fatty Acids and Coenzyme Q10 in the Treatment of Dry Eye Disease

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Inflammation seems to play a major role in the pathogenesis of Dry Eye Disease (DED) with an increase in tear film osmolarity, release of pro-inflammatory cytokines as well as matrix metalloproteinases, and inhibition of regulatory T-cells. Significantly increased inflammatory biomarkers including HLA-DR and MMP-9 can be detected at the ocular surface or in the tear film in about 50% of DED patients. Systemic and topical anti-inflammatory therapies such as topical corticosteroids, cyclosporine A, and lifitegrast as well systemic doxycycline are part of the basic treatment plan for DED.

Omega 3/6 fatty acids (FA) have been shown to reduce levels of pro-inflammatory IL-1 β , IL-6, IL-10 and HLA-DR, and increase levels of anti-inflammatory prostaglandin E1 in tears of patients with DED. Moreover, tuna fish intake with high levels of omega-3 FA was indirectly proportional to DED in a large epidemiological study. Systemic and topical Omega FA use was associated with subjective and objective improvement of DED.

Coenzyme Q 10 (CoQ10), an endogenous lipid soluble molecule also known as ubiquinone is involved in oxidative metabolism. Decreased CoQ10-levels with age play a role in aging and in the pathogenesis of many chronic or degenerative diseases. CoQ10 was shown to inhibit nuclear factor-kappa B activation, an important pathway in DED pathogenesis. Moreover, it is known to have anti-apoptotic capacity.

Thus, topical and oral omega fatty acids as well as topical and oral CoQ10 may support the anti-inflammatory action of DED therapy.

Small-molecule drugs to target complement activation and inflammation in macular degeneration

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Abnormal complement activation is associated with inherited and age-related macular degenerations (AMD). Here, we investigated innate mechanisms that protect the retinal pigment epithelium (RPE), a key site of damage in AMD, from complement attack. The final step of the complement cascade is the formation of membrane attack complex (MAC) pores on cell membranes. Sustained calcium influx through these pores causes aberrant signal transduction. Using primary RPE and *Abca4*^{-/-} Stargardt disease mice, we show that the RPE rapidly mobilizes two mechanisms to prevent complement-mediated mitochondrial injury. First, accelerated recycling of the membrane-bound complement regulator CD59 to the RPE cell surface inhibits MAC formation. Second, fusion of lysosomes with the RPE plasma membrane immediately after complement attack limits calcium influx and subsequent mitochondrial damage. Cholesterol accumulation in the RPE induced by vitamin A dimers in *Abca4*^{-/-} mice inhibits these mechanisms by activating acid sphingomyelinase (ASMase), which increases tubulin acetylation and derails organelle traffic. Defective CD59 recycling and lysosome exocytosis after complement attack lead to mitochondrial fragmentation and oxidative stress in the RPE. FDA-approved drugs that decrease RPE cholesterol or inhibit ASMase restore both these critical safeguards in the RPE and avert complement-induced mitochondrial injury in *Abca4*^{-/-} mice, indicating that they could be effective therapeutic approaches for macular degenerations. Epidemiological studies show that desipramine, the FDA-approved ASMase inhibitor that we used in our studies, significantly decreases the risk of developing AMD. Our data suggest that “drug repurposing”, or finding novel uses for approved drugs, holds great promise for intractable diseases like AMD.

The AMD genetic-risk promotes pathogenic subretinal inflammation.

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Mononuclear phagocytes (MP) comprise a family of cells that include microglial cells (MC), monocytes, and macrophages. The subretinal space, located between the RPE and the photoreceptor outer segments, is physiologically devoid of MPs and a zone of immune privilege mediated, among others, by immunosuppressive RPE signals. Age related macular degeneration (AMD) is a highly heritable major cause of blindness, characterized by a breakdown of the subretinal immunosuppressive environment and an accumulation of pathogenic inflammatory MPs. Studies in mice and humans suggest that the AMD-associated APOE2 isoform promotes the breakdown of subretinal immunosuppression and increased MP survival. Of all genetic factors, variants of Complement factor H (CFH) are associated with greatest linkage to AMD. Using loss of function genetics and orthologous models of AMD, we provide mechanistic evidence that CFH inhibits the elimination of subretinal MPs. Importantly, the AMD-associated CFH402H isoform markedly increased this inhibitory effect on microglial cells, indicating a causal link to disease etiology. Pharmacological acceleration of resolution of subretinal inflammation might be a powerful tool for controlling inflammation and neurodegeneration in late AMD.

Nuclear receptors: New therapeutic targets for AMD?

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Nuclear receptors are transcription factors that control a myriad of biological and disease processes. A subset of these receptors are activated by lipids and have been shown to play a vital role in chronic diseases such as diabetes, atherosclerosis, coronary heart disease, inflammatory skin disorders and obesity. These diseases share common pathogenic mechanisms with retinal diseases including age-related macular degeneration (AMD) and diabetic retinopathy. Recently we completed a nuclear receptor atlas of human retinal pigment epithelial cells, cells vulnerable in all clinical sub-types of AMD. We identified several candidate receptors that may be important in disease initiation and progression. In this presentation, we will review the impact of these signaling pathways on retinal function, morphology and AMD-related pathogenic pathways such as lipid metabolism, inflammation, angiogenesis and fibrosis. Furthermore, we will discuss the therapeutic potential of targeting these signaling pathways on pathobiology associated with the different clinical sub-types of AMD.

Molecular consequences of blood flow in the inner choroid

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Purpose: Atrophy of the choroid is a hallmark of age-related macular degeneration. Hemodynamic wall shear stress (WSS), the mechanical drag imparted on vascular endothelium arising from blood flow, has profound effects on the physiology of endothelial cells from different vascular beds, including retinal endothelial cells. However, the magnitude of WSS in the choroid and extent to which endothelial cells of the choroid respond to physiologic WSS are unknown.

Methods: Choroidal shear stress was quantified by computational fluid dynamic modeling of 3D reconstructions of normal human inner choroid. Physiologic WSS (0-11 dyne/cm²) was applied to primary and immortalized choroidal endothelial cells with an orbital shaker and parallel plate cell culture system for durations ranging from 10 min to 72 h.

Results: The human inner choroidal endothelium experiences a wide range of hemodynamic WSS. In response to shear stress stimulation, choroidal endothelial cells exhibited profound alterations in morphology, proliferation, and susceptibility to oxidative stress. WSS also reduced surface CD59 expression and increased susceptibility to MAC deposition. MAC deposition in human inner choroidal tissue correlated with computed shear stresses.

Conclusions: These findings suggest that WSS is a biologically relevant stimulus that elicits morphological and homeostatic changes in choroidal endothelial cells, and may be an important parameter to understand the biology of the choroidal endothelium in health and disease.

Neuro-ophthalmologic manifestations of syphilis

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Rates of infectious syphilis have been increasing globally since the year 2000. This has been accompanied with an increased number of neurosyphilis and ocular syphilis cases. Ophthalmologic manifestations of syphilis are common, as illustrated by our large case series of 119 patients (174 eyes) with ocular syphilis diagnosed and treated at two tertiary-care centers in Montreal between 2000 and 2015. Eighty percent were male and mean age of onset was 55 years. Mean presenting logMAR visual acuity was 0.70 (20/100 Snellen) and unilateral ocular involvement occurred in 54%. HIV status was available (previously known positive or requested at syphilis diagnosis) in 80 (66%) patients; 38 (48%) were HIV infected. The variable ocular manifestations included interstitial keratitis (24 eyes), anterior uveitis (33 eyes), intermediate uveitis (21 eyes), posterior uveitis (31 eyes), panuveitis (27 eyes), optic nerve involvement (26 eyes) and others (12 eyes) including VI nerve palsy (2 eyes), skew deviation (1 eye), scleritis, episcleritis and ocular ischemic syndrome. Overall, 22 patients (18%) had neuro-ophthalmologic involvement, most frequently optic neuropathy (26 eyes) followed by oculomotor involvement (3 eyes). The clinical manifestations and treatment outcomes of syphilitic optic neuropathy will be discussed.

VOGT KOYANAGI HARADA SYNDROME WITH NEUROLOGICAL INVOLVEMENT: CASE HISTORY & LITERATURE REVIEW

Mili Roy¹.

Vogt Koyanagi Harada (VKH) syndrome is a rare and complex autoimmune multisystem disorder which remains incompletely understood. The ocular, integumentary, auditory and nervous systems may be involved to various extents as reflected in the classification system of cases as complete, incomplete or probable. While some neurological manifestations are more common in VKH such as cerebrospinal fluid pleocytosis, as well as headache and meningismus as reflected in the classification criteria, other aspects of neurological involvement are noted only uncommonly. A case based presentation of various forms of neurological involvement followed by a literature review highlighting some of the lower frequency neurological manifestations described in VKH will be discussed

APMPPE and CNS vasculitis

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Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE) is a well described clinical form of posterior uveitis which can be accompanied by inflammatory pathology in other organ systems including skin, thyroid, kidney, central nervous system (CNS) and others. It typically affects young healthy individuals. While neurological symptoms or signs have been reported in as many as 60% of patients, demonstrated CNS vasculitis or stroke are uncommon. Some 28 cases of APMPPE with CNS vasculitis or stroke, occasionally occurring months after the onset of the uveitis, have been described in the literature. We are presenting the case of a 29 year old male with severe bilateral APMPPE who also presented CNS vasculitis resulting in death despite aggressive systemic therapy. The autopsy revealed occlusive vasculitis in the CNS and choroid with some granulomatous elements. Therapy of APMPPE is controversial but involvement of the CNS is a potentially life threatening complication which should be investigated and aggressively treated with immunosuppressive therapy when clinical signs or symptoms are present.

IgG4 mediated uveitis: Case report and review of the literature.

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Purpose: To review the clinical presentation, epidemiology, systemic associations and treatment of IgG4-related ophthalmic disease (IgG-ROD).

Materials and methods: A unique case of panuveitis associated with transient cranial nerve palsies due to IgG4-related ophthalmic disease will be described and a review of the literature on IgG4-related ophthalmic disease (IgG4-ROD) will be presented.

Conclusions:

IgG4 related disease is a multi-organ fibro-inflammatory disease first described in 2001, with characteristic histopathology showing lymphoplasmacytic infiltration and increased IgG4+ plasma cells and elevated IgG4/IgG ratios (>40%). IgG4- related ophthalmic disease was first described in 2007 and most often presents in the lacrimal gland and ocular adnexal structures. The lacrimal gland is the most common ocular site of involvement. *Several case reports and case series since 2012 have described simultaneous involvement of scleral and intraocular tissues. This presentation will describe a first case of panuveitis without scleritis and emphasizes the importance of including IgG4-ROD in the differential diagnosis of intraocular inflammation and cranial nerve palsies.* IgG4-related ophthalmic disease is an emerging cause of scleritis and uveitis and should be considered in any patient with multisystem inflammatory disease. Targeted immune therapies can lead to improved outcomes and disease remission.

Clinical And Imaging Features Of Posterior Uveitis Related To Nontuberculous Mycobacteria In Immunocompetent Patients

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Purpose: To describe clinical and imaging features of immunocompetent patients diagnosed with ocular nontuberculous mycobacterial (NTM) infection

Methods: Retrospective analysis of history and examination, fluorescein angiography (FA), fundus autofluorescence (FAF), and spectral-domain optical coherence tomography (SD-OCT) of cases with polymerase chain reaction (PCR)-proven NTM infection was done

Results: We report four cases (3 males; mean age: 38.75 ± 10.99 years) with recurrent episodes of posterior uveitis. Mean presenting visual acuity was 1.2 ± 0.91 LogMAR. Three patients had healed chorioretinitis in the fellow eye. All patients had previously received oral steroids with/without long-term immunosuppression. Two patients were already on anti-tubercular therapy (ATT) and 2 had received ATT in the past. Clinical features included yellowish subretinal elevated lesions (n=4) with raised voluminous edges (n=2), overlying retinal hemorrhages (n=3), significant vitritis (n=4), exudative retinal detachment (n=4) and disc edema (n=2). SD-OCT showed outer retinal hyper-reflective deposits, massive focal choroidal thickening with retinal pigment epithelial elevation and subretinal fluid. PCR from vitreous revealed *M.avium* (n=2), *M.abscessus* (n=1) and *M.fortuitum* and *M.bovis* co-infection in one patient. All patients also had PCR-proven co-infection with *M.tuberculosis*. Management included additional oral clarithromycin (n=2), oral levofloxacin (n=1) and intravitreal levofloxacin (n=2) with ATT and oral steroids. All but one patient responded favorably to treatment with final visual acuity of 0.43 ± 0.32 .

Conclusions: NTM infections are rare causes of posterior uveitis in immunocompetent patients. Atypical clinical features and poor response to ATT are important clues. High index of suspicion and appropriate molecular tests help in establishing accurate diagnosis.

Correlation of panorama optical coherence tomography angiography characteristics of active and healing serpiginous like choroiditis with indocyanine green angiography

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Purpose : To analyze the panorama optical coherence tomography angiography (OCTA) imaging characteristics of serpiginous like choroiditis and to compare these findings with indocyanine green angiography (ICGA) features.

Methods : Prospective cross-sectional study. Multimodal imaging was performed in subjects with serpiginous-like choroiditis using panorama OCTA (NIDEK RS-3000), OCT (Heidelberg Spectralis), fundus autofluorescence fluorescein angiography, and ICGA. Morphologic features at the sites of choroiditis lesions were analyzed using panorama OCTA imaging and compared with ICGA with minimum six months follow up.

Results : Twenty eyes were included in the study. In the active stage, the en face panorama OCTA images demonstrated discrete areas of flow void beneath the retinal pigment epithelium–Bruch membrane layer suggestive of choriocapillaris hypoperfusion that corresponded well with hypofluorescence in ICGA. In advance stages of healing preserved capillaries were observed corresponding to the healed areas in ICGA. It gave wider field of view than conventional OCTA.

Conclusion : The Panorama OCTA images is a useful non invasive tool to study areas of activity in eyes with serpiginous like choroiditis. The changes observed during healing stage in panorama OCTA corresponded well with ICGA images.

Effect of Anti-Tuberculous Therapy on Uveitis Associated with Latent Tuberculosis

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Purpose: To examine the clinical features of patients with uveitis associated with latent tuberculosis (TB) and examine the effect of anti-TB treatment (ATT) on uveitis outcome.

Design: Retrospective cohort study.

Subjects: Patients with uveitis associated with latent TB and no evidence of active TB.

Methods: Information was gathered from the clinical notes of all subjects.

Main outcome measures: Best corrected visual acuity (BCVA), rate of disease recurrence.

Results: This study included 199 eyes of 129 patients diagnosed with uveitis associated with latent TB. Eighty-nine patients (69%) received ATT. The mean change in BCVA following treatment was 4.5 ± 1.4 letters over the follow-up period, with no difference between eyes of patients receiving ATT and those who did not. Sixty-eight eyes (34.9%) had a recurrence of uveitis (0.64 ± 0.08 recurrences per-year), with eyes of patients receiving ATT less likely to develop a recurrence compared to those not receiving ATT (29.5% vs. 48.2%, OR 0.47, 95% CI 0.29-0.77, $p=0.003$). Eyes treated with ATT recurred at an estimated median of 120 months compared with 51 months in eyes with no treatment ($p=0.005$).

Conclusions: Among eyes with uveitis associated with latent TB, treatment with ATT halved the risk of uveitis recurrence and delayed the onset of the first recurrence.

The Role of QuantiFERON®-TB Gold and Tuberculin Skin Test as Diagnostic Tests for Intraocular Tuberculosis in HIV-positive and HIV-negative Patients in South Africa

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Purpose: To compare QuantiFERON®-TB Gold (QFT) and tuberculin skin testing (TST) as diagnostic tests for intraocular tuberculosis (IOTB) in HIV positive and negative patients.

Methods: A prospective study evaluating two different tests to help diagnose intraocular tuberculosis

Results: Thirty-five of 106 patients (33.0%) were diagnosed with IOTB including 11 (31.4%) with HIV infection and a median CD4+ cell count of 249 x 106/L. HIV- cases were more likely than HIV+ cases to have a positive QFT result ($p=0.04$). The median CD4+ count of HIV+ cases with negative QFT results (93 x 106/L) was lower than that of HIV+ cases with positive QFT results (415 x 106/L) ($p=0.005$). Patients were 6.95 times more likely to have IOTB if TST alone was positive ($p<0.001$) versus 2.19 times more likely if QFT alone was positive ($p=0.04$). TST showed superior specificity (60.3% vs 33.3%) ($p=0.001$) but similar sensitivity (90.3% vs 85.7%), positive (54.9% vs 40.5%) and negative predictive values (92.1% vs 81.5%) compared to QFT. If both the QFT and TST were positive patients were 3.92 times more likely to have IOTB (RR=3.29; 95% CI 2.04-7.52) ($p<0.001$) than if both were negative. If both the QFT and TST were positive the specificity (73.2%) and diagnostic accuracy (74.0%) were better than if TST alone was positive but these differences were not statistically significant.

Conclusions: In South Africa with its high HIV burden and limited public health resources QFT should not replace TST as it provides little additional value in diagnosing IOTB.

The Role of Polymerase Chain Reaction and Goldmann-Witmer Coefficient Testing in the Diagnosis of Infectious Uveitis in HIV-positive and HIV-negative Patients in South Africa

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Purpose: To describe the utility of polymerase chain reaction (PCR) and Goldmann-Witmer Coefficient (GWC) testing of aqueous humor (AH) in the diagnosis of infectious uveitis in patients with and without HIV infection.

Design: Prospective cross-sectional study

Methods: AH samples from 100 consecutive patients were investigated by multiplex PCR for herpesviruses 1 – 6, rubella virus (RV) and *Toxoplasma gondii* (Toxo). In addition, paired AH and serum samples from 82 patients were examined for intraocular antibody production against herpes simplex virus (HSV), varicella-zoster virus (VZV), cytomegalovirus (CMV), RV and Toxo.

Results: Positive results were obtained in 38 of 182 samples (21%): 19 (50%) each from HIV+ and HIV- patients. In the HIV+ group, 13 samples were PCR+ and 6 samples GWC+ while in the HIV- group 11 samples were PCR+ and 8 samples GWC+. Samples tested positive as follows: HSV=3 (7.9%; 1=PCR+, 2=GWC+), VZV=8 (21%; 4=PCR+, 4=GWC+), CMV=5 (13.1%; 2=PCR+, 3=GWC+), EBV=12 PCR+(31.6%), HHV6=1 PCR+(2.6%), RV=4 (10.5%; PCR & GWC 4), Toxo=1 (2.6%; 0=PCR+, 1=GWC+). More than 1 organism was identified in 9 patients, 7 (77.7%) of whom were HIV+. Anatomically, all 5 cases with herpetic posterior uveitis were PCR+ GWC- while all 8 cases with herpetic anterior uveitis were GWC+ PCR-. Only the 4 rubella cases were PCR+ and GWC+ for the same virus.

Conclusions: Polymicrobial infection occurs in HIV+ patients where PCR is more often positive than GWC. In herpetic uveitis PCR is mostly positive in posterior uveitis while GWC is mostly positive in anterior uveitis.

Lyme disease: a ten-year retrospective study of a North-Western Italian uveitis referral centre.

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Lyme borreliosis is an increasing tick-transmitted infectious disease. Ocular manifestations are rare and occur during every stage of the disease, but mainly in late stage and present with a wide variety of symptoms and signs.

The North Western Italian area (mainly Liguria, our region) is recognized as a *Borrelia*-infected ticks area; in last ten years, our uveitis referral centre collected 86 patients (49 males and 37 females, mean age 47 +/- 3.2 years) suffering from different ocular manifestations of Lyme disease.

Real-Time PCR (RT-PCR) was positive in blood and/or in aqueous humour of all patients.

Our study aims to show the polymorphous ophthalmological manifestations of Lyme disease and the antibiotic/steroid treatment outcome.

Main findings were: diplopia, oculomotor/accomodative palsy and periocular pain (13.9%), episcleritis or scleritis (24.4%), anterior acute/chronic uveitis (32.5%), intermediate uveitis (4.6%), papillitis or optic nerve pseudo-edema (12.8), retinal vasculitis (20.9%), retino-choroiditis or choriocapillaritis (11.6%).

The acute phase treatment protocol was: Ceftriaxon i.m. or i.v. 1 gr/twice a day for 3 weeks and if needed, Prednison 1 mg/kg/day x 5 days then low tapering.

Relapses were present in 26.7% subjects and a chronic relapsing -remitting course was the characteristic of anterior granulomatous uveitis in 9.3% patients.

Conclusions: This is the first report of ten years follow-up of ocular Lyme disease. In our experience, the management and treatment of these infrequent cases has to be performed in a tertiary referral centre and a benign course will follow an early recognized and treated disease.

Optical coherence tomography findings in infectious necrotizing retinitis: a comparison among different etiologies

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Purpose: To compare Optical Coherence Tomography (OCT) features of active necrotizing infectious retinitis (NIR) due to toxoplasmosis or viral-related disease and to find distinctive tomographic signs of these two entities.

Methods: OCT scans from eyes with active NIR due to Varicella Zoster Virus (VZV), Herpes Simplex Virus (HSV), Cytomegalovirus (CMV), and Toxoplasmosis (TOXO) were reviewed. All images were evaluated for the presence of previously described OCT findings in TOXO-NIR and compared with the viral group. New OCT findings were also recorded and compared. Retinal and choroidal thickness were measured at the site of the NIR and compared.

Results: 10 eyes diagnosed with TOXO-NIR and 13 eyes affected by viral-NIR (9 CMV and 4 VZV) were analyzed. All eyes showed full thickness hyper-reflectivity and disruption of the retina and variable degree of vitritis. Among the previously described OCT signs, only hyper-reflective oval deposits and hypo-reflectivity of the choroid had a higher prevalence in TOXO ($p=0.018$ and $p<0.0001$ respectively). Among the new signs, clots of cells along the posterior hyaloid, retrohyaloid hyper-reflective spots and a disruption of the choroidal architecture were more frequent in TOXO (all $p<0.01$). On the contrary, intraretinal edema and hyper-reflective vertical strips within the outer nuclear layer were suggestive of viral etiology ($p=0.045$). Retinal thickness at the site of NIR did not differ among the 2 groups. Choroidal thickness was significantly higher in TOXO ($p=0.01$).

Conclusions: Although the diagnosis remains based on clinical and laboratory findings, OCT may represent a helpful tool in the differential diagnosis of NIR.

Long-term Safety and Efficacy of Adalimumab in Patients with Non-infectious Uveitis in an Ongoing Open-label study: VISUAL-III

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Purpose: To evaluate the long-term safety and efficacy of adalimumab in patients with non-infectious intermediate, posterior, or panuveitis.

Methods: Adults who successfully completed/met treatment failure criteria in VISUAL-I/VISUAL-II studies and opted to enroll in VISUAL-III received adalimumab 40-mg every other week for the study duration. Corticosteroids and/or immunosuppressive therapy were permitted as needed. Interim follow-up data from VISUAL-III baseline through week-78 are described. Efficacy endpoints included new inflammatory chorioretinal and/or inflammatory retinal vascular lesions, anterior chamber (AC) cell grade, vitreous haze (VH) grade, best corrected visual acuity (BCVA), and corticosteroid dose. As-observed and non-responder imputation (NRI) were used. Adverse events (AE) are reported from first adalimumab dose up to the data cut-off date of 31-October-2016.

Results: Of the 424 patients enrolled, 371 were included in the intent-to-treat analysis. At week-78, 72%, 70%, and 70% of patients had no active inflammatory lesions, AC cell grade $\leq 0.5+$ in both eyes, and VH grade $\leq 0.5+$ in both eyes, respectively (NRI). At week 78, 88% of eyes showed maintenance/improvement (<5 letters deterioration) in BCVA (as observed). The mean observed uveitis-related systemic corticosteroids dose decreased from 9.3mg/day at week 0 to 2.1mg/day by week-78. AE rates of 424 events/100 patient-years were comparable with previous VISUAL trials.

Conclusions: Prolonged use of adalimumab maintained/improved BCVA and substantially reduced uveitis-related corticosteroid burden in patients with non-infectious intermediate, posterior, or panuveitis. No new safety signals were detected with AE rates consistent with previous VISUAL trials.

Limited efficacy of Methotrexate as first line therapy in JIA-related Uveitis

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BACKGROUND. Methotrexate (MTX) is the most used immunomodulator in JIA-related uveitis as biologic agents are recommended only in MTX-refractory cases. Time between onset of uveitis and MTX start as well as time to switch between first and second-line therapies are controversial.

OBJECTIVES. To evaluate the efficacy of MTX as first-line therapy in a monocentric inception cohort of children with JIA-related uveitis.

METHODS. Data on uveitis activity and need for second-line therapy from a cohort of JIA-related uveitis patients treated with MTX have been analyzed.

RESULTS. 84 children have been included (71 F, 13 M); mean age at MTX start: 5.58 y; mean f/u since MTX start 8.94 y. 68 patients (group A) began MTX for uveitis (disease duration 1.77 y), 16 (group B) introduced MTX for arthritis (disease duration 0.54 y). The mean interval between arthritis and uveitis was 0.83 y in group A and 2.08 y in B. After treatment start, 25% relapsed within 5 months, 50% within 9.8 and 75% within 36 mo (median: 9.67). 28/68 (41%) patients in group A and 12/16 (75%) in group B needed anti-TNF therapy. 16/84 pt (19.7%) discontinued MTX for uveitis remission, 9 (all in group A) were off therapy at the last visit (mean f/u: 39.4 mo).

CONCLUSIONS. MTX is not effective in the medium-long term. When started before uveitis, it delays the uveitis onset but does not prevent its severe course.

Clinical features of Tuberculous Serpiginous-like Choroiditis versus Autoimmune Serpiginous Choroiditis

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Purpose: To compare demographic, clinical and imaging characteristics of autoimmune serpiginous choroiditis (SC) and presumed tubercular serpiginous-like choroiditis (SLC).

Methods: Retrospective study of 38 patients diagnosed with SC, from the Ocular Inflammation Unit of Centro Hospitalar e Universitário de Coimbra, Portugal. The mean age of this patients was 50.4 years with a mean follow-up of 63.8 months. Patients were subsequently divided into two groups, based on interferon-gamma release assay (IGRA) result: Group I (SLC) IGRA+ and Group II (autoimmune SC) IGRA-. Patients were evaluated using a multimodal approach with conventional and wide-angle fundus photography and fundus autofluorescence, OCT, FA and ICG angiography.

Results: There were 10 males and 12 females in Group I, with mean age of 48.4 years. Initial BCVA was 70.9 letters and final BCVA 86.0 letters. Lesions were mainly perimacular in 17 eyes (51.5%) and peripapillary in 16. In group II (16 patients), half of the patients were male and half female, with a mean age of 52.6 years. Initial BCVA was 48.3 letters and final BCVA 75.2 letters. Lesions were predominantly perimacular in 14 eyes (53.8%) and peripapillary in 12.

Conclusion: No statistically significant differences were found between groups regarding the clinical parameters evaluated. Despite previous literature description of clinical differences between the two entities, our patients were virtually indistinguishable in what concerns clinical presentation.

Dynamic predictions of visual acuity in uveitis

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Objectives: Uveitis is the leading cause of legal blindness in the working population in the western world. Physicians utilize different types of information to predict patient visual acuity (VA). With the help of novel statistical approaches, it is now possible to fit and evaluate dynamic prediction models, employing longitudinal VA and inflammation (IN) data, that capture the dynamic adjustment of treatment and prognosis by ophthalmologists.

Methods: Dynamic predictions of patient VA were based on different types of patient characteristics that are collected at each visit. We employed a two-stage approach: (1) IN model including patient information: treatment, surgery, indicating whether the complications started before week 7, (2) VA model including patient information: complication and age. For the evaluation, we used 5-fold cross validation (CV), where prediction accuracy was deemed acceptable when the predicted VA was within 0.3 (logMAR scale) of the observed VA. To evaluate the predictions in terms of patient safety, we calculated the percentage with worse predicted VA. The dataset includes 365 patients with mean follow-up years 2.5.

Results: Figure 1 illustrates the dynamic predictions of a randomly selected patient and Figure 2 the results of the CV. In the CV, within the 0.3 range we obtained 90% of predictions and 60% worse than the observed VA. Outside the 0.3 range, 5% were worse than the observed values.

Conclusions: By modeling clinical characteristics, VA and IN of the patients it is possible to construct an individualized dynamic evidence-based tool that provide us with accurate and safe predictions.

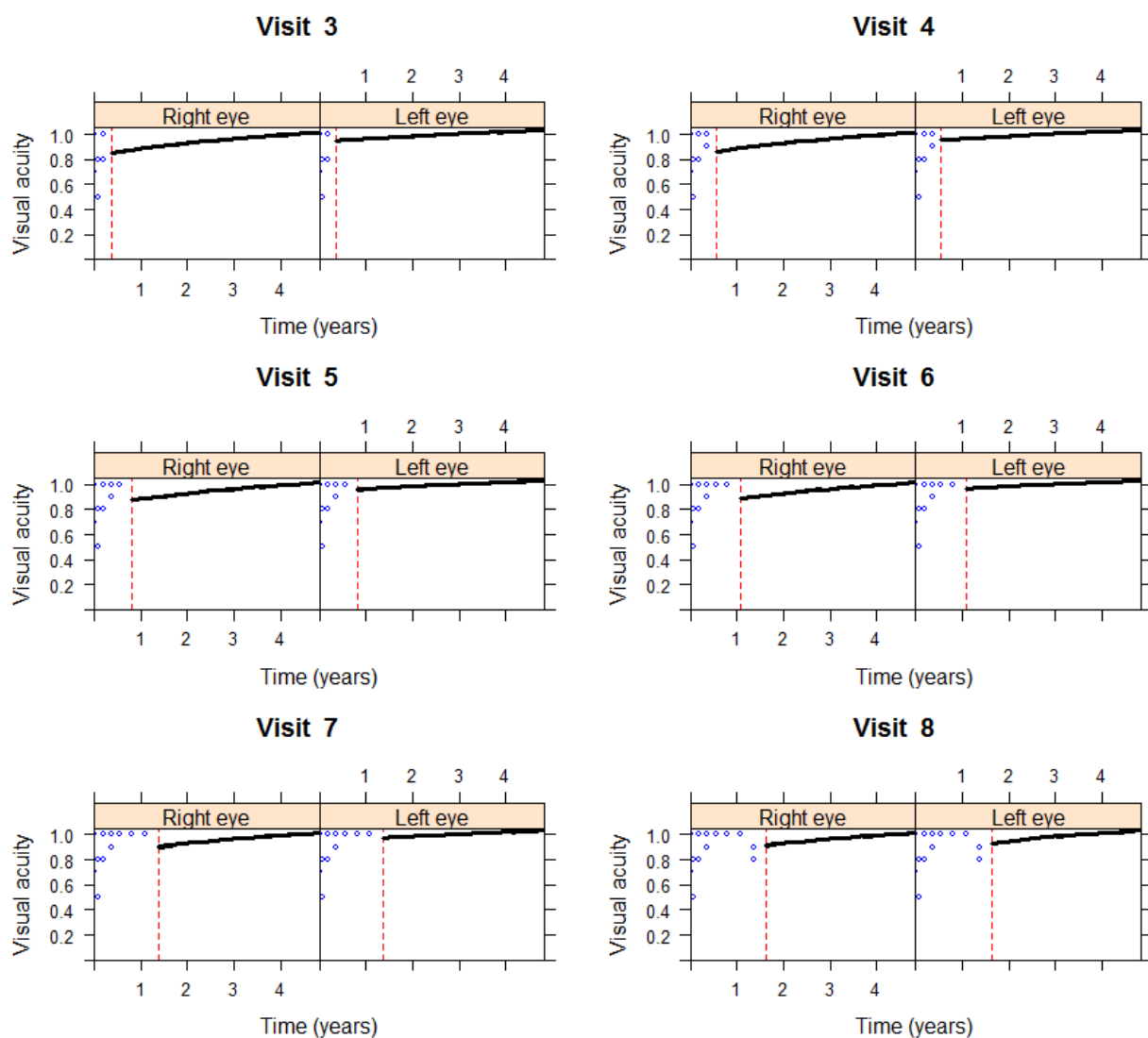


Figure 1: Dynamic predictions of a randomly selected patient that are updated at each visit. The blue dots present the true VA values up the last visit, the dotted red lines represent the time at the last visit and the solid black lines the predicted values of VA.

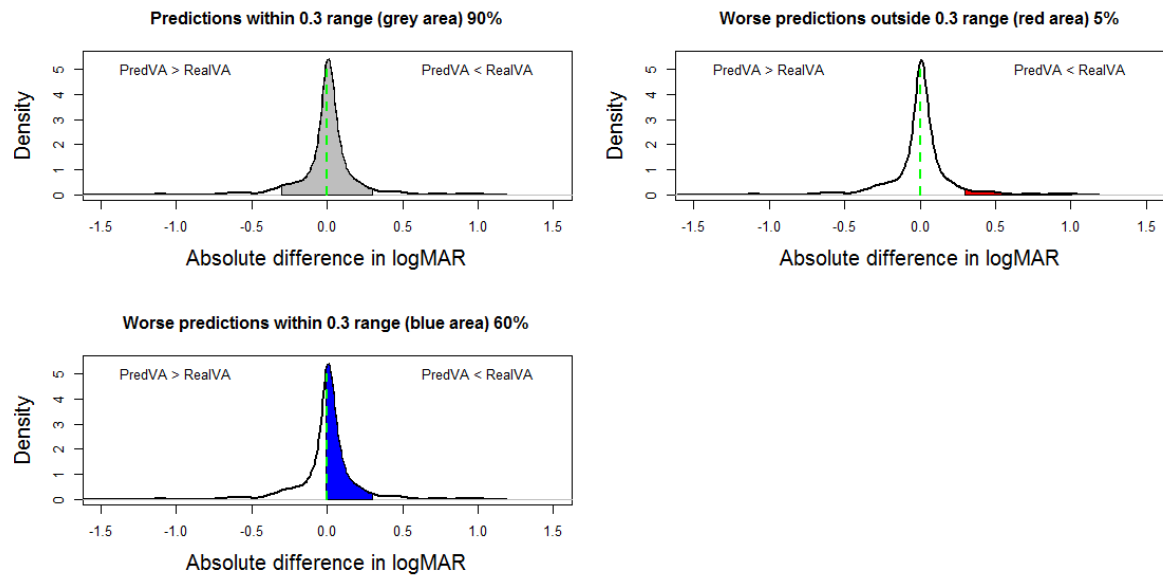


Figure 2: Graphical representation of the evaluation results.

Efficacy and safety of adalimumab in Behçet's disease-related uveitis: a multicenter retrospective observational study

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The study aim was to evaluate the efficacy of adalimumab (ADA) in a large series of Behçet's disease (BD)-related uveitis. We performed a retrospective observational study including 40 selected patients (66 eyes) receiving ADA. Clinical data were analyzed at baseline, at 3 and 12 months of treatment. Primary end point: reduction of ocular inflammatory flares. Secondary end points: improvement of BCVA, reduction of macular thickness measured by OCT, reduction in the occurrence of vasculitis assessed by fluorescein angiography (FA), and evaluation of statistically significant differences between patients treated with ADA monotherapy and those undergoing ADA plus DMARDs and in patients firstly treated with ADA compared to patients previously administered with other biologics; ADA steroid sparing effect was also evaluated. During the first 12 months of ADA therapy, the number of flares significantly decreased from 200 flares/100 patients/year to 8.5 flares/100 patients/year ($p < 0.0001$). Similarly, BCVA improved if compared to baseline (7.4 ± 2.9 versus 8.5 ± 2.1 , $p = 0.03$). OCT findings significantly improved showing a mean reduction of central macular thickness (CMT) of $27.27 \pm 42.8 \mu\text{m}$ at the end of follow-up ($p < 0.006$). FA identified retinal vasculitis in 22 cases at baseline (55%), 8 (20%) cases after 3 months, and in only one (2.5%) case at 12-month follow-up. FA improvement was highly significant at 3- and 12-month follow-up if compared to baseline ($p < 0.0001$ and $p = 0.006$, respectively). ADA is highly effective and safe for the treatment of BD related uveitis, providing a long-term control of ocular inflammation.

Electroretinogram abnormalities in non-anterior childhood uveitis

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Purpose: Irreversible retinal changes after prolonged inflammation are a major point of concern in uveitis. The purpose of this study was to assess the effect of non-anterior childhood uveitis on retinal function using full field electroretinography (ERG).

Methods: Cross-sectional. Sixty-three uveitis eyes (33 children) were analyzed. ERGs were measured using extended ISCEV (International Society for Clinical Electrophysiology of Vision) protocols. ERGs were investigated in relation to the following clinical parameters: uveitis- and patient characteristics, best corrected visual acuity (BCVA), severity of inflammation based on Standardization of Uveitis Nomenclature criteria, fluorescein angiography activity score, and treatment.

Results: Thirty-six eyes had an abnormal ERG. Most frequently seen were a prolonged b-wave implicit time of dim photopic flashes (n=25/63) and/or abnormal 30Hz flicker implicit times or amplitudes (n=22/63). Factors associated with these specific ERG abnormalities, at the time of ERG measurement (without correction for paired sampling), were cystoid macular edema (CME) (p-value<0.001), optic disc swelling (p-value=0.035) and 3+ cells in the vitreous (p-value<0.001). A history of CME was also associated with these ERG abnormalities (p-value=0.030), as well as younger age (p-value=0.009). BCVA did not differ between groups and remained relatively good (median 0.05LogMAR, IQR 0.00-0.15LogMAR).

Conclusion: Retinal function as measured by ERG is frequently affected in childhood uveitis, mostly resulting in a prolonged photopic implicit time of b-wave and/or abnormal 30Hz responses. These ERG abnormalities seem, among others, associated with the severity of posterior segment inflammation. These new findings indicate that childhood uveitis causes generalized retinal dysfunction.

An amino acid motif in HLA-DRβ1 distinguishes patients with uveitis in juvenile idiopathic arthritis

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Approximately 1 in 3 children that suffer from oligoarticular or polyarticular rheumatoid factor negative juvenile idiopathic arthritis (JIA) develop chronic anterior uveitis. Both JIA and uveitis are multifactorial autoimmune disorders with a genetic predisposition. However, genetic markers that predict development of uveitis in JIA remain elusive.

Here, we performed genotyping of 2 cohorts with in total 214 uveitis cases and 362 JIA patients without uveitis, with the aim of identifying those genetic variants that segregate more commonly in JIA-uveitis patients compared to those with JIA (and without uveitis).

Genotyping data underwent standard data quality control, and imputation, including MHC imputation, was performed.

Of all SNPs, amino acids, and classical alleles examined, the strongest association was observed for amino acid residues at position 11 in HLA-DRβ1 (presence of serine or aspartic acid, mega-analysis OR = 2.59, $p = 4.8 \times 10^{-10}$). This position appeared to be in perfect linkage disequilibrium (LD=1) with tyrosine at position 10 and threonine at position 12, what is together known as the YST-motif. The YST-motif is shared by six classical alleles, HLA-DRB1*03,*08,*11,*12,*13 and *14. Ninety-six percent of uveitis cases (185/192) had at least one copy of a classical DRB1 allele that contains the YST-motif, compared to 78% (259/330) of non-uveitis patients.

These findings suggest that JIA-uveitis patients are genetically different from JIA non-uveitis patients. Future prospective studies should point out whether we can use the YST-motif as a diagnostic test, to prevent unnecessary screening by an ophthalmologist in some JIA patients.

Long-term Efficacy and Safety of Immunomodulatory Therapy for Patients with Juvenile Idiopathic Arthritis Associated Uveitis: The MERSI Experience

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Purpose: JIA-associated uveitis is an indolent yet serious condition with poor visual prognosis. Our purpose is to present long-term clinical outcomes in patients treated with IMT in the long-term.

Methods: A retrospective analysis of JIA-associated uveitis patients presenting between 2005 to 2016 with a minimum of 3 years follow-up was conducted.

Results: A total of 61 patients with JIA-associated uveitis were identified, 88.5% were female. Mean age at presentation of 38 of patients not in remission (NR) was 16.2 years, and mean follow-up was 106.1 months. Of the 23 patients in the remission group, mean age at presentation was 13.5 years, and mean follow-up 105.4 months. VA differed minimally amongst the two groups, with 81.6% of 76 eyes of NR patients presenting with VA better than 20/80, compared to 84.8% of 46 eyes of remission patients. At final follow up, these proportions remained stable. NR patient eyes had a higher occurrence of cataracts. Development of glaucoma occurred in 27 eyes of the NR group and 14 of the remission group affected. The number of IMTs used differed between the two groups with 39.1% of the remission group requiring monotherapy compared to 7.9% of the NR group, conversely, 47.4% of the NR group required therapy with 4-10 IMTs.

Conclusion: IMT-free remission in JIA-associated uveitis may be difficult to achieve, long-term preservation of visual acuity emphasizes the benefit of IMT. The number of IMTs used to control inflammation appears to be a negative predictive factor for achieving drug-free remission in the long-term.

Longitudinal Cohort Study of Patients with Birdshot Chorioretinopathy. Quality of Life during 10 Years of Follow-up.

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PURPOSE: To describe vision-specific quality-of-life (QOL) for a cohort of individuals with birdshot chorioretinopathy (BSCR) during 10 years of follow-up, and to identify risk factors for change in QOL.

METHODS: In a prospective, observational study, 79 participants underwent an annual standardized evaluation that included the NEI Visual Function Questionnaire-25 (VFQ-25). The following visual function measures were determined for all eyes: best corrected visual acuity (BCVA [logMAR]); color confusion score (CCS); mean deviation (MD) from automated perimetry; and presence/absence of eight defined symptoms. Vasculitis was assessed by fluorescein angiography; macular edema was assessed by optical coherence tomography. Relationships between potential risk factors and longitudinal continuous VFQ-25 composite scores were analyzed using a fixed-effects model with robust standard errors accounting for serial correlation.

RESULTS: VFQ-25 data were available for 47 participants at year 10. Deterioration of scores occurred in 11 participants (23.4%); improvement occurred in 6 participants (12.8%; range of change in scores, -43.6 to +37). Incidence of VFQ-25 deterioration was 7.9/100 patient-years. In time-dependent analyses, change for each of the following measures (better eye) was associated with decline of VFQ-25 scores: BCVA (slope, -13.40; $p < 0.0001$); MD (1.17; $p < 0.0001$); macular edema (-3.61; $p = 0.0096$). Development of the following symptoms was associated with decline in VFQ-25 score: blurry vision (-1.75; $p = 0.0128$); poor color vision (-2.76; $p = 0.0125$); poor contrast (-2.86; $p = 0.0024$); poor peripheral vision (-3.69; $p = 0.0023$).

CONCLUSIONS: Change in QOL during 10 years of follow-up varies widely between individuals with BSCR. Macular edema and deterioration of visual function predict decline in QOL.

Ocular Behçet's Disease: Visual Prognosis after 20 years of follow-up.

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¹CHLC (Lisboa, PT); ²CHUC.

Purpose: To investigate demographic, clinical and ocular features correlated with long term visual prognosis in Portuguese patients with ocular Behçet's disease.

Material and Methods: Retrospective study of 100 patients with a minimum follow-up of 20 years. The population was divided into two groups according to visual acuity (VA), determined after remission (favorable prognosis: VA \geq 5/10; unfavorable prognosis: VA $<$ 5/10). The correlation between evaluated factors and the long-term visual prognosis was studied. Statistical analysis was done using the statistical software SPSS®, through a multivariate analysis of factors possibly related to vision loss, calculating the Odds Ratio and using logistic regression ("Back Logistic Stepwise Regression").

Results: Of the 200 eyes observed, 175 (87.5%) had a favorable visual prognosis and 25 (12.5%) had an unfavorable visual prognosis. Statistically significant differences were found between the two groups: male gender ($p=0.001$), panuveitis ($p<0.001$) and a positive pathergy test ($p=0.006$), were more frequent in the group with unfavorable prognosis. Uveitis as the first sign of eye disease ($p=0.001$) predominated in the group with favorable prognosis. Regression analysis demonstrated that use of non-Cyclosporine A (CSA) immunomodulators ($p<0.001$) was more frequent in the group with unfavorable visual prognosis.

Conclusions: Male gender, panuveitis and a positive pathergy test were associated with a long term loss of vision. Uveitis as first ocular manifestation is a predictive factor for an unfavorable visual prognosis. In patients with involvement of the posterior eye segment, therapy with non CSA immunomodulators was associated with a long term loss of visual acuity.

Ocular involvement in biopsy-proven sarcoidosis: clinical features at presentation and long-term follow-up.

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Ocular involvement occurs in 30-35% of Sarcoidosis (S) patients and ¼ of them show it before the systemic disease has been diagnosed.

An early diagnosis of the underlying S disease is requested to control intra-ocular inflammation. Main findings are: anterior granulomatous uveitis, intermediate uveitis with snow balls and dense vitreous peripheral opacities, multifocal choroiditis and retinal vasculitis.

Our work shows from a retrospective point of view, the 15 years experience of our centre; during this period, 235 cases of ocular S were followed. 172 patients (73.2%) had a biopsy-proven systemic S, the remaining are considered as ocular suspected S.

Main presentation is anterior granulomatous uveitis. Intermediate uveitis and vitreitis are infrequent findings. Posterior involvement in our case-series increased in last 5 years to more than 30% (retinal phlebitis, multifocal choroiditis, papillitis). Cystoid macular edema (in 32%) is a sight-threatening and not easy-to-manage complication.

Anterior uveitis can be well controlled with topical steroids and mydriatics. In our experience, only 30% of patients respond to systemic steroids and the others require immunosuppressive or biologic agents.

A delay in diagnosis and treatment of 1.8 (+/- 1.3) years is a frequent (42%) finding in our cases.

S management is rapidly improving in last years, thanks to new diagnostic tools, such as PET imaging which avoid the previous invasive techniques, and to a more effective systemic immune-modulating therapy.

Biologics switch during a long-term follow up of patients with Juvenile Idiopathic Arthritis-related Uveitis

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BACKGROUND. Systemic treatment for JIA-related uveitis is still controversial and its management needs a complex decision-making process.

OBJECTIVES. To compare the clinical features of patients with JIA-related refractory uveitis treated with biologics for at least five years and who maintained a single biological agent with those that needed a therapeutic switch.

METHODS. Data on uveitis activity, type and dosage of biologic agents, switches and withdrawals have been consecutively collected and analyzed from a single centre cohort of consecutive patients with JIA-related uveitis.

RESULTS. 41 children (37 F, 4 M) with at least 5 years follow-up from the start of biologic treatment have been included; mean age at arthritis diagnosis was 3.41 years and at uveitis diagnosis 4.19 years. Mean interval between the onset of arthritis and uveitis was 9.12 months. Mean age at biologic start was 7.6 years. 32 patients (78%) maintained a single agent and 9 (22%) underwent a therapeutic switch, after a median of 2.43 years (3.14 years in patients treated with adalimumab). Median interval time between uveitis onset and methotrexate start was 2.89 years in switchers and 1.46 years in non-switchers. Median interval time between methotrexate and biologic was 2.66 years in not-switchers and 3.41 years in switchers. First uveitis flare appeared at mean 1.23 years in switchers and 2.39 years in not-switchers after biologic start ($p=0.04$).

CONCLUSIONS. In patients requiring biologic switching the interval time between uveitis onset and methotrexate and then biologic start were delayed. Indeed, the first uveitis flare, after biologic start, occurred significantly earlier.

Five-year trends in multifocal electroretinogram for patients with birdshot chorioretinopathy

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Objective: To investigate temporal trends in multifocal ERG (mfERG) parameters and analyze their relationships with anatomical and functional tests in patients with BSCR.

Methods: Prospective longitudinal study of 16 BSCR patients who underwent two standardized follow-up (FU) visits within 5 years following a baseline examination between 2008 and 2010, including mfERG (N1, P1 amplitudes, and implicit times), visual acuity (VA, ETDRS chart), visual field (mean defect and foveal sensitivity), Lanthony desaturated panel D-15 test for color vision (calculation of the total error score), quality of life (NEI VFQ-25), fluorescein and indocyanine green angiography, and optical coherence tomography (OCT).

Results: A significant trend toward higher N1 amplitude values was observed over the follow-up period, while N1 implicit time remained unchanged. In contrast, P1 amplitude decreased and P1 implicit time increased over the same period. No significant temporal change was found for VA, color vision score, foveal threshold, mean deviation of visual field, and quality of life score. After adjusting for time to FU, lower N1 amplitude values were associated with venous vasculitis and peripheral capillaropathy, whereas lower P1 amplitude values correlated with alteration of the outer retina in OCT. Wave amplitudes correlated with visual field parameters, whereas longer implicit times correlated with quality of life, VA, and visual field parameters.

Conclusion and relevance: This study showed progressive deterioration in mfERG parameter values for BSCR patients during a 5-year period, whereas classical functional test results remained unchanged. This study suggests that mfERG has better sensitivity in monitoring BSCR patients.

President's Symposium- Progress and Perspectives in Understanding and Treating Ocular Inflammation or Infection

A new kind of inflammation in age-related macular degeneration

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The atrophic form of age-related macular degeneration (AMD), characterized by dysfunction and death of the retinal pigmented epithelium (RPE) is termed geographic atrophy (GA). Great strides have been made in delineating the role of innate immunity in the pathogenesis of GA. In particular, recent work has revealed the NLRP3 inflammasome as a critical driver of RPE cell death in GA. This talk will highlight the evolving understanding of the cellular and mechanistic processes of inflammasome biology in GA that are bringing us to the cusp of a novel therapeutic for this unmet medical need that causes vision loss in millions of people worldwide.

Molecular tools applied to ocular fluids for diagnostic purposes

Manabu Mochizuki¹, Manabu Mochizuki².

¹Tokyo Medical and Dental University (Tokyo, JP); ²Miyata Eye Hospital.

Polymerase chain reaction (PCR), a new molecular tool, has opened a new era of uveitis. PCR provides quick, specific and sensitive diagnosis of pathogenic microorganisms using only a small volume of intraocular tissues or liquid. Since PCR was applied in the clinical practice of intraocular inflammation, pathogenic microorganisms in a number of cases with unknown etiology have been identified. In addition, new diseases have been established by the investigation. More importantly in clinical practice, prompt differential diagnosis between infectious uveitis or non-infectious uveitis becomes possible.

In the symposium, the principle of PCR assay, various PCR assay systems including our current PCR system, and diseases established by the molecular diagnosis will be discussed.

Clinical and imaging prognostic factors in Ocular Behcet's disease

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Behcet's disease is a chronic and relapsing systemic vasculitis that may affect mucosa, skin, and the eyes. The eyes may be involved in about 70% of cases. Ocular involvement in Behcet's disease is associated with poor visual prognosis, even though the visual outcome is improving with the use of biological agents. There are some factors that are considered as prognostic factors for visual outcome in ocular Behcet disease. Risk factors that may be correlated with visual prognosis include sex, type of uveitis, laterality of ocular involvement, disease duration, race, and use of biologic agents. Some imaging modalities are beneficial for predicting the visual prognosis. Spectral-domain optical coherence tomography (OCT) is helpful to determine the visual prognosis. Newer techniques of OCT, enhanced depth imaging OCT, are used to visualize choroidal pathology, and have better measurement of choroidal thickness. We reviewed cases of ocular Behcet's disease for the last 5 years from our outpatient clinics and describing clinical factors that may be correlated with the visual prognosis. There were 9 eyes from 5 patients that were all male. Four patients presented with panuveitis, and 1 patient manifested as anterior uveitis with transient mobile hypopyon. Visual acuity at presentation was worse than 20/40 in 4 eyes. No abnormalities were found from OCT examination. All patients received conventional immunomodulatory agents and 2 patients relapsed during treatment.

Session 10 "Prognostic factors in granulomatous uveitis and Behçet's intraocular inflammation" Global Inflammation Workshop and Uveitis society of IDN

Prognostic Significance of International Workshop nomenclature of ocular sarcoidosis

Manabu Mochizuki¹, Manabu Mochizuki².

¹Tokyo Medical and Dental University (Tokyo, JP); ²Miyata Eye Hospital.

International criteria for ocular sarcoidosis was published in 2009 based on the discussion of 1st International Workshop on Ocular Sarcoidosis (IWOS). The diagnostic criteria was validated by an international validation study group and the study revealed several limitations of the international diagnostic criteria for ocular sarcoidosis.

An attempt to revised the IWOS criteria was made in the 1st Global Ocular Inflammation Workshop in Bali in 2017. Prior to the workshop, questionnaire regarding the revised criteria was sent to panelists and discussed in the workshop.

The process, discussion and conclusions of the revised international diagnostic criteria for ocular sarcoidosis will be presented in the session.

Prognostic value of OCT imaging of the choroid in new-onset acute Vogt-Koyanagi-Harada disease

Hiroshi Keino¹.

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Enhanced-depth imaging optical coherence tomography (EDI-OCT) has been used to evaluate the choroidal thickness non-invasively and reproducibly. It has been reported that choroidal thickness increases at acute phase in patients with new-onset Vogt-Koyanagi-Harada (VKH) disease and markedly decreases after starting high-dose corticosteroid treatment, suggesting that EDI-OCT is useful for detecting and monitoring choroidal changes in patients with VKH disease. We have reported that choroidal thickness > 550 μ m at 1 week after initiating corticosteroid therapy is associated with the development of peripapillary atrophy at 12 months. In this presentation, the potential of EDI-OCT imaging in the choroid to predict the visual prognosis in patients with new-onset VKH disease would be discussed. Vogt-Koyanagi-Harada (VKH) disease is an autoimmune disorder directed against melanocytes in choroid and elsewhere in the body. Enhanced-depth imaging optical coherence tomography (EDI-OCT) has been used to evaluate the choroidal thickness non-invasively and reproducibly. It has been reported that choroidal thickness increases at acute phase in new-onset VKH patients and markedly decreases after starting high-dose corticosteroid treatment and gradually decreases further over follow-up, suggesting that EDI-OCT is useful for detecting and monitoring choroidal changes in patients with VKH disease. We have reported that choroidal thickness > 550 μ m at 1 week after initiating corticosteroid therapy is associated with the development of peripapillary atrophy at 12 months (Nakayama et al. Retina, 2012). In this presentation, the potential of EDI-OCT imaging in the choroid to predict the visual prognosis in patients with new-onset VKH disease would be discussed.

Herpetic anterior uveitis – Visual Acuity and Recurrences

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¹Maccabi Health Care Services (Ramat Hasharon, IL); ³Tel-Aviv Medical Center; Sackler School of Medicine TAU.

Purpose: To evaluate clinical features, treatment modalities in clinically and/or PCR diagnosis of herpetic anterior uveitis (HAU).

Methods: Retrospective review of medical records of 28 patients with clinically and PCR proven diagnosis of HAU who were treated at Maccabi uveitis consultant clinic and the uveitis service at Tel Aviv Medical Center from 2001 to 2017.

Results: Sixteen (59.3%) were female. Mean age at presentation was 51.07 ± 18.34 years. Mean follow-up was 49.78 months (range 3-156 months). Six (22.2%) were PCR proven (5 HSV1, 1 VZV). The most common ocular findings were keratic precipitates (81.5%), iris atrophy (74.1%), high intra ocular pressure (63%), posterior synechiae (51.9%), corneal scarring and cataract (22.2%, respectively), dilated pupil (18.5%), epiretinal membrane (ERM, 11.1%) and cystic macular edema (CME, 7.4%). Recurrences were observed in 14 (51.9%) of the eyes and the mean number of recurrences was 3. Topical corticosteroids and oral antiviral (acyclovir) therapy were applied to all patients during active episodes. Long-term (> 6 months) oral acyclovir was used in 33.3% of the patients. Most of the patients (56%) had good visual acuity (VA) (> 20/40) at presentation, and overall VA maintained during follow up. Visual impairment was mainly due to corneal scarring and ERM (11.1%). Complication rates and visual outcome were similar between patients with recurrent disease and those with a single acute attack.

Conclusion: HAU has distinct clinical features, but in some cases PCR is critical for disease diagnosis. Recurrences may not significantly affect the complication rate and visual outcome

CMV Retinitis

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Purpose: CMV retinitis (CMVR) is a potentially blinding disease that occurs in patients with diminished T- cell immunity such as those with AIDS and those receiving immunosuppressive therapy. We aim to report on the clinical characteristics and ophthalmologic manifestations in patients with CMVR.

Methods: This is a retrospective cohort study of a single-center in an academic practice. Patients with active CMVR evaluated between 2007 and 2017 were included.

Results: Included were 11 patients (7 males) with a mean age at presentation of 37.7 years (median 32, range 14-84). All patients were immunocompromised: 7 had hematologic disease (6 were post bone marrow transplantation and post chemotherapy) and 4 had AIDS. In all patients there was evidence of past or current CMV infection by positive blood PCR. In six patients it was a bilateral disease (resulting in a total of 17 eyes). Mean visual acuity at presentation was 0.4 and it was 0.34 at last follow-up visit. CMVR was diffuse in 9 eyes, peripheral in 4 eyes and affecting the mid and far peripheral retina in 2 eyes. In 2 eyes, dense vitritis precluded fundus examination. Mean follow-up period was 5.8 months (median 3 months, range 1-27 months). Six patients passed away, in a median period of 6.5 months after being diagnosed with CMVR, all with an underlying hematologic disease.

Discussion: CMV retinitis is primarily a disease of immunocompromised hosts. It may be an ominous sign in hematologic patients as it indicates failing immune recovery in contrast to HIV patients receiving HAART.

Cat Scratch Disease: ocular manifestations and treatment outcome

Zohar Habet-Wilner^{1,2}.

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Purpose: To characterize cat scratch disease (CSD) ocular manifestations and visual outcome and evaluate treatment effect on final visual acuity (VA).

Methods: Multicenter retrospective study. Eight six patients (107 eyes) / 3,222 patients identified in a national CSD surveillance study were included.

Results: Mean age was 35.1±14.2 years. Median follow-up was 20 weeks (range 1-806 weeks). Of 94/107 (88%) eyes with swollen disc, 60 (64%) had neuroretinitis at presentation, 14(15%) developed neuroretinitis during follow-up and 20 (21%) were diagnosed with inflammatory disc edema. Optic nerve head lesion, uveitis, optic neuropathy, and retinal vessels occlusion were found in 43 (40%), 38 (36%), 34 (33%), and 8 (7%) eyes, respectively. Good VA (better than 20/40), moderate vision loss (20/40-20/200) and severe vision loss (worse than 20/200), were found in 26/79 (33%), 35/79 (44%), 18/79 (23%) eyes at baseline and in 63/79 (80%), 11/79 (14%), and 5/79 (6%) eyes at final follow-up, respectively ($p<0.001$). Significant VA improvement (defined as improvement of ≥ 3 Snellen lines at final follow-up compared to baseline) occurred in 12/24 (50%) eyes treated with antibiotics compared with 14/16 (88%) eyes treated with antibiotics and corticosteroids ($p=0.02$). Multivariate logistic regression was suggestive of the same association (odds ratio 7.0; 95% CI 1.3–37.7; $p=0.024$).

Conclusions: Optic nerve head lesion is a common and unique manifestation of ocular CSD. Most patients improved and had final good VA. Combined antibiotics and corticosteroid treatment was associated with a better visual outcome.

Cat Scratch Disease: ocular manifestations and treatment outcome

Zohar Habet-Wilner^{1,2}.

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Conclusions: Optic nerve head lesion is a common and unique manifestation of ocular CSD. Most patients improved and had final good VA. Combined antibiotics and corticosteroid treatment was associated with a better visual outcome.

Chorioretinal Toxoplasmosis clinical presentation, treatment results and long term follow up in a single tertiary center in Israel

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The hallmark of ocular toxoplasmosis is primary or recurrent necrotizing retinochoroiditis.

The purpose of this study is to retrospectively evaluate our experience with the treatment of the disease.

Methods:

22 consecutive patients were treated in a single tertiary center for active disease between the years 2007-2016.

Patients medical records were evaluated for: demographics, clinical presentation, treatment results and recurrence.

Results:

64% of patients were females. The average age at presentation was 29. 14% of patients presented with bilateral disease. The disease was congenital in 14%, Primary in 50% and a recurrent in 32%.

Clinical presentation included a white–yellow necrotizing chorioretinal lesion in all patients. Other clinical features included : vitreitis 85%, Vasculitis 45% and anterior uveitis 18%

Indications for treatment were lesions threatening the macula (73%),the optic nerve head(70%) or both (40%).

Visual acuity at presentation ranged from 6/6 to 1/15 depending on the lesion location, and size.

Treatment with classical Triple therapy and steroids was used in 86% of the patients. Other regimens included: oral Resprim (14%), oral Clindamycin (14%) and Intravitreal clindamycin(4.5%).

The mean follow up time was 37 months.

Treatment tolerance was good yet 22% developed drug reaction that needed treatment adjustment.

Disease control was achieved in all patients. All lesions scared with various degrees of pigmentation.

Recurrence occurred in 32% of cases . Mean time to recurrence was 42 months.

Visual acuity improved in 50%, did not change in 40% and decrease in 10%

Conclusion: Chorioretinal Toxoplasmosis can be successfully treated with favorable visual acuity results.

Intravitreal Administration of Antiviral Agents in Silicone oil-filled Human eyes

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²*Department of Ophthalmology, Jacobs Retina Center, Shiley Eye Institute, San diego; ³ ; ⁴ .*

Purpose: To report our experience with intrasilicone oil injection of antiviral agents for treatment of viral retinitis and to review the relevant literature.

Design: Two case reports and literature review.

Participants: Two patients with viral retinitis and silicone oil (SO) tamponade.

Methods: Two patients with viral retinitis were treated with intravitreal injections of low-dose ganciclovir (2 mg/0.05 ml) and/or foscarnet (1.2 mg/0.05 ml) after retinal detachment repair with SO tamponade, in addition to systemic antiviral therapy in 2014-2015. The literature on the use of intraocular antiviral agents in the setting of SO vitreous substitute was reviewed.

Main Outcome Measures: Clinical outcomes after administration of intrasilicone oil antiviral therapy.

Results: A patient with progressive outer retinal necrosis received 5 intrasilicone oil injections of low-dose ganciclovir and foscarnet post-operatively, over 6 weeks. Another patient with acute retinal necrosis received weekly low-dose foscarnet injections into his SO-filled eye for 8 weeks after surgery. Significant retinitis regression with long-term retinitis control was achieved in both patients throughout follow-up. No papers reporting the administration of soluble antiviral agents into SO-filled human eye were identified.

Conclusions: Our preliminary findings indicate that administration of low-dose ganciclovir and foscarnet into a SO-filled eye may be used as adjunctive treatment for viral retinitis. Further studies are needed to confirm these results.

ACTH Analogue as Novel Treatment Regimen in Three Cases of Panuveitis and One Case of Ocular Cicatricial Pemphigoid

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Purpose: To describe the potential role of subcutaneous repository adrenocorticotrophic hormone (ACTH) gel in the treatment of non infectious panuveitis and ocular cicatricial pemphigoid (OCP).

Observations: Novel treatment strategy with ACTH gel was initiated in a total of 4 patients; three patients, age range of 36-64 years, with diagnosis of non infectious panuveitis and a 75 years-old patient, diagnosed with OCP. All patients had in common a bilateral chronic ocular inflammatory disease, difficult to control, with multiple relapses. Various therapies, including topical and systemic corticosteroids and numerous immunomodulatory therapies had been tried, with no complete remission and side effects development. Therapy with twice weekly, subcutaneous ACTH gel was initiated, with systemic steroids tapering down. During mean treatment period of 12 months, all patients demonstrated significant improvement in ocular inflammation, visual acuity was stable and no adverse effects were observed. Systemic steroids dosage was successfully reduced from mean of 15 mg/day at start to 5 mg/day at last follow up.

Conclusions and Importance: ACTH gel may be an effective alternative treatment in the management of two vision-threatening diseases with a common inflammatory basis; panuveitis and OCP. Due to the treatment resistance nature of diseases with chronic inflammation that relapses under immunomodulatory treatment and steroids dependence, there is need for a safe and potent therapy and ACTH gel may be a good alternative. Presenting these cases may raise awareness and facilitate conduction of clinical trials, with use of ACTH gel as a therapeutic agent in non infectious panuveitis and OCP.

Correlation between cytomegalovirus retinitis and cytomegalovirus viremia

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Purpose: Cytomegalovirus (CMV) retinitis is one of opportunistic infections for immunocompromised patients. The aim of this study is to assess a correlation between CMV retinitis and viremia.

Material and Methods: This retrospective study included 37 eyes of 26 cases with CMV retinitis who visited Hokkaido University Hospital from 2007 to 2015. The average age was 47.4 years, ranging from 5 to 75 years. Fifteen cases were bilateral and 11 cases were unilateral. The mean follow-up period was 23 months.

Results: Underlying diseases for immunodeficiency were malignant lymphomas in 10 cases, acquired immunodeficiency syndrome (AIDS) in 3 cases, aplastic anemia in 2 cases, marrow dysplasia syndrome in 2 cases, invasive thymus tumor in 2 cases, neuroblastoma in 2 cases, and others in 5 cases. All cases except for AIDS were at immunocompromised state with systemic treatments. CMV-DNA was detected from the anterior chamber in all the 16 cases examined. Only 50% of cases were positive for serum CMV-antigen at the onset of retinitis, whereas 96.2% were positive at some time during the entire course of the disease. Antiviral medication had been discontinued in most of the cases in which CMV-antigen was negative at the onset of the retinitis. Ganciclovir intravenous injection was performed in 17 cases, and intravitreal injection was performed in 18 cases (25 eyes).

Conclusions: The major cause of CMV retinitis was an immunocompromised state with systemic treatments for underlying diseases. Even after CMV-antigen turns to be negative, careful attention should be paid to the risk of developing retinitis.

Clinical characteristics and risk factors for symptomatic MGD in China. Results of a large multicenter study

Qingfeng Liang¹.

Purpose: To detect the clinical characteristics and risk factors for meibomian gland dysfunction (MGD) in the Chinese population.

Methods: We undertook a multicenter study on the clinical characteristics and risk factors of MGD in China. All participants were aged 18 years or older. Patients completed a symptoms questionnaire and underwent a comprehensive slit-lamp examination. Meibomian gland dysfunction was diagnosed when one or more of the following was present: absent, viscous, or waxy white secretion; margin telangiectases; and/or plugging of two or more gland orifices. There are 6 study parameters measured, including SPEED and OSDI Questionnaire, Medical and Ophthalmic history, BSCVA, tear Break-up Time (TBUT), corneal and conjunctival staining, meibomian gland assessment. The relationship between symptoms and signs was evaluated and the risk factors were detected.

Results: The study included 1286 patients (584 men and 702 women). Mean participant age was 45.3 ± 8.5 years (range, 18-72 years). The prevalence of symptomatic and asymptomatic MGD was 21.6% and 53.7%, respectively. The prevalence of total MGD increased significantly as participant age increased ($P < 0.005$). The dry eye symptoms are poorly correlated with dry eye signs. For the symptomatic MGD group, fluorescein score was higher, tear film breakup time was shorter, and meibo-score was larger, compared to asymptomatic patients. The presence of chronic pain syndrome, depression, and atopic disease was the risk factors.

Conclusions: This multicenter study has shown that dry eye symptoms are poorly correlated with dry eye signs. the risk factors included chronic pain syndrome, depression, and atopic disease.

Diabetes Mellitus-Associated Uveitis

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Purpose: To describe clinical features of patients with Diabetes Mellitus-associated uveitis (DMAU).

Methods: We reviewed the clinical records of patients with uveitis and Diabetes Mellitus (DM) at the Uveitis Department of Hospital Del Salvador in Santiago, and classified them into three categories: 1. Patients with uveitis and DM with an underlying cause for uveitis; 2. Patients with DMAU, defined as patients with uveitis where secondary causes were ruled out, and decompensated DM (Capillary glycaemia \geq 300mg/dL and/or HbA1c \geq 12%) and; 3. Patients with idiopathic uveitis and well controlled DM.

Demographic data, DM features, comorbidities, complete ophthalmic examination and treatments were recorded in Excel[®] and analysed using Prism7[®].

Results: We found 72 patients with uveitis and DM: 41 with secondary uveitis(57%), 16 with DMAU(22%), and 15 with idiopathic uveitis(21%).

56% were male in the DMAU group and 27% in the idiopathic. Anterior uveitis was seen in 100% in DMAU vs 80% in idiopathic.

The DMAU patients presented inflammation of +3 to +4 cells in 33% of cases, a fibrinous reaction in 28% and posterior synechiae in 83%, compared with 5%, 0% and 50% in the idiopathic group, respectively ($p<0.05$). Three patients presented hypopyon in the DMAU category. Diabetic retinopathy was significantly higher in the DMAU patients.

All DMAU patients responded well to topical or periocular steroids.

Conclusion: Patients with DMAU present a much more severe inflammation compared with patients with DM and idiopathic uveitis. The distinctive clinical picture of these patients, suggests an independent entity from idiopathic uveitis in diabetic patients.

Failure to use quantitative measurement methods hampers clinical studies in posterior uveitis such as posterior sarcoidosis: dual fluorescein/indocyanine green angiography versus SUN vitritis evaluation

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Purpose: Assess the respective scores of SUN (standard uveitis nomenclature) vitritis scaling system versus dual fluorescein (FA)/ indocyanine green angiography (ICGA) scoring in posterior sarcoidosis(PS) and their potential use for clinical studies.

Methods: Retrospective study on PS patients seen in the Centre for Ophthalmic Specialized Care, Lausanne, Switzerland. Angiography signs were quantified according to an established FA and ICGA scoring system for uveitis. Evaluation of vitritis was performed using the SUN scaling system for vitritis.

Results: 23 patients (4 men) fulfilling the diagnostic criteria were included in the study. The choroid was predominantly involved in 19 patients (82.6%) (40/46 eyes[87%]) and the retina in 2 (8.7.4%) (6/46[13%] eyes) and the mean angiographic score was 14.2 ± 5.1 (choroid) versus 7.3 ± 4.6 (retina)($p < 0.0001$). 5 of 46 eyes showed a SUN vitritis score ≥ 2 necessary for inclusion in a clinical trial.

Conclusion: For the first time the precise measurement of global posterior inflammation was achieved by a dual FA/ICGA scoring system in PS. It should represent one of the outcomes for posterior uveitis (PU) in clinical trials in future. In contrast, SUN vitreous haze scale, the qualitative/subjective criterion presently used in studies on PU, appears as utterly inadequate, as in PS, a major entity of PU, only a tiny percentage of eyes could have been included in a clinical trial. To evaluate correctly intraocular inflammation in PS and probably other PU entities, the use of dual FA & ICG angiography is strongly recommended.

Galectin-1, an angiogenic factor associated with diabetic retinopathy, is regulated by advanced glycation end products triggering inflammatory cues

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Purpose: Galectin-1, a carbohydrate-binding protein recently identified as a VEGF receptor (VEGFR) 2 ligand and endothelial cell mitogen, was shown to increase in eyes with proliferative diabetic retinopathy (DR) independently of VEGF and to co-localize with VEGFR2 in fibrovascular tissues excised from eyes with proliferative DR. In this study, to understand the contribution of galectin-1 to the pathogenesis of DR, we investigated regulatory mechanisms of galectin-1 *in vitro* and *in vivo*.

Methods: Human surgical samples were examined by enzyme-linked immunosorbent assay and immunofluorescence. Immunoblot analysis and real-time PCR were performed to measure protein and mRNA expression levels in several human cell lines and streptozotocin-induced diabetes in mice.

Results: Galectin-1 protein levels in aqueous humor samples increased with the progression of clinical stages of DR. Administration of advanced glycation endproducts (AGEs) to macrophages induced the proinflammatory cytokine interleukin (IL)-1 β production via toll-like receptor 4, and upregulated IL-1 β elevated galectin-1/*LGALS1* expression in Müller glial cells. Antibody-based IL-1 β blockade significantly attenuated retinal *Lgals1* expression in mice with streptozotocin-induced diabetes.

Conclusions: We propose that diabetes-induced AGE accumulation activates IL-1 β -related inflammatory cues in macrophages followed by Müller glial cells, linking to galectin-1 upregulation according to the severity of DR. Our findings reveal for the first time the significant involvement of galectin-1 in the pathogenesis of DR along with the degree of disease activity.

Longitudinal study of retinal status using optical coherence tomography after acute onset endophthalmitis following cataract surgery

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Purpose To analyse the macula imaged with optical coherence tomography (OCT) in patients treated for acute postcataract endophthalmitis.

Methods Patients presenting with acute postcataract endophthalmitis were included in this observational and multicentre study from January 2008 to December 2011. We recorded the following OCT data at the 3, 6 and 12-month visits: the central macular thickness, the perifoveal macular thickness, the central foveal point thickness and abnormalities of the outer retina, the macula and vitreoretinal interface.

Results 46 patients were included in the OCT analysis. From month 3 to 12, epiretinal membrane (ERM) prevalence increased from 26% to 39%, vitreomacular traction prevalence decreased from 12% to 6%, nontractional macular oedema (ME) prevalence varied between 7% and 13%. Only macular thinning remained stable at 10%. At month 12, a significant correlation was found between non-tractional ME and capsular rupture (at the time of cataract extraction, $p=0.03$). Eyes with an ERM exhibited increased central macular thickness ($p=0.001$) and lower visual acuity (VA) ($p=0.02$) at M12 in comparison to the group with normal macula. OCT analysis showed a significant association between ERM and the alteration of the ellipsoid band ($p=0.02$), as well as the external limiting membrane (ELM, $p=0.07$) at M12.

Conclusions ERM and ME were the main macular abnormalities diagnosed after 1 year of follow-up, associated with VA less than or equal to 20/40 in 50% of the cases. Ultrastructural abnormalities of the ELM and the ellipsoid band were frequently observed in those patients.

Laser flare photometry: a useful tool for monitoring children with juvenile idiopathic arthritis-associated uveitis

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Purpose: To evaluate laser flare photometry (LFP) values for monitoring patients with juvenile idiopathic arthritis (JIA) associated uveitis.

Methods: We retrospectively analyzed children with JIA-associated uveitis followed between 1994 and 2015 at La Pitié Salpêtrière Hospital (Paris France). We defined two groups of patients according to decrease of the LFP value one month after treatment intensification (LFP decrease > 50% in group 1 and < 50% in group 2). Ocular complications were compared in each group and in overall population at baseline and during follow up.

Results: Fifty four children (87 eyes) were included in this study (mean follow up 9.9+/-5 years). Complications of uveitis were present in 68 eyes (76%) at baseline and in 76 eyes (85%) at last visit. Group 1 was composed of 59 eyes and group 2 of 30 eyes (33%). Group 1 children developed significantly less complications as compared to group 2 children at 5 years (none (p=0.03), band keratopathy (p=0.003), cataract surgery (p=0.003), glaucoma (p=0.003) trabeculectomy (p=0.004), macular edema (p=0.001), papilledema (p=0.02)) and at last visit (none (p=0.004), band keratopathy (p=0.007), cataract surgery (p=0.008), glaucoma (p=0.003), trabeculectomy (p=0.007), papilledema (p=0.02)). They also kept a better visual acuity (p<0.0001 at both 5years and last visit) and required less systemic immunosuppressive treatments (sixth treatment line at last visit p=0.01).

Conclusion: Decrease of LFP value one month after treatment intensification is a good predictive value of complications and low visual acuity over long-term in children with JIA-associated uveitis.

Photoreceptor cell injury detected with SD-OCT and fundus autofluorescence in the initial stage of Vogt-

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Purpose: Photoreceptor injury was reported in experimental Vogt-Koyanagi-Harada (VKH) animal model as well as in patients. In this study, we aimed to demonstrate photoreceptor cell injury using spectral domain optical coherence tomography (SD-OCT) and fundus autofluorescence (FAF) in VKH disease.

Methods: Thirty-four eyes of 17 patients diagnosed with VKH disease that was followed up from the initial stage to the convalescent stage were reviewed. All the patients underwent SD-OCT and FAF tests, along with ophthalmological examination at the follow-ups.

Results: In the initial stage of VKH disease, seventeen (50%) eyes of the patients had hyperautofluorescence around the macular and retinal pigment epithelium undulation. In the convalescent stage of VKH disease, the SD-OCT scans revealed the outer nuclear layer attenuation, interruption of myoid zone, ellipsoid zone and outer segments of photoreceptors in convalescent phase, along with suspect interdigitation zone and RPE/Bruch's complex injury. FAF showed the peri-macular hyperfluorescence area persistent existed in the convalescent stage of the disease. The microstructure abnormality of outer retina observed in SD-OCT scans was corresponded to the peri-macular hyperfluorescence in FAF in the initial stage.

Conclusions: The photoreceptor injuries in VKH disease started at the first beginning of the disease and persisted until the convalescent phase of VKH. SD-OCT scan and FAF are effective and noninvasive tools for evaluating photoreceptor cell damage in an early phase in VKH disease. The comprehensive analysis of SD-OCT and FAF could provide us more useful information of VKH disease.

Pathological role of receptor-associated prorenin system and tumor necrosis factor- α for the development of proliferative retinopathy in type II diabetes mellitus

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PURPOSE: Receptor-associated prorenin system (RAPS) refers to the pathogenic mechanism whereby prorenin binding to (pro)renin receptor [(P)RR] dually activates tissue renin-angiotensin system (RAS) and RAS-independent signaling via (P)RR, and plays a crucial role in ocular inflammation and the development of proliferative diabetic retinopathy (PDR). In this study, we explored correlations between protein levels of RAPS components and inflammatory-associated proteins in the plasma obtained from patients with PDR in type II diabetes mellitus (DM).

METHODS: Total twenty plasma samples from patients with PDR in DM, and total twenty plasma samples from patients with non-DM as a control were collected. Prorenin, soluble (P)RR [s(P)RR] and fifteen inflammatory-associated proteins were measured by magnetic multiplex bead-based quantitative immunoassay. Real-time PCR was performed to measure mRNA expression levels in cultured human retinal microvascular endothelial cells (HRMECs).

RESULTS: The plasma protein levels of prorenin, s(P)RR and five inflammatory-associated proteins with PDR were significantly higher than those with non-DM. Increased plasma leucine rich alpha-2-glycoprotein 1, tumor necrosis factor (TNF)- α , adiponin, and interleukin-1 β correlated significantly with s(P)RR levels. Administration of TNF- α , but not other three proteins, induced ATP6AP2/(P)RR mRNA expression in HRMECs, whereas neither prorenin nor angiotensin II treatment altered the expression level of those upregulated proteins. Both ATP6AP2/(P)RR and REN mRNA expression levels in HRMECs under hyperglycemic condition were increased.

CONCLUSIONS: We demonstrated the elevated plasma levels of s(P)RR showing correlation with increased TNF- α levels in patients with PDR in DM, suggesting a potential role of the RAPS and TNF- α in the pathogenesis of PDR.

Systemic steroid sparing effect of intravitreal dexamethasone implant in chronic non-infectious uveitic macular edema

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Purpose: to evaluate the effectiveness and the systemic steroids' sparing effect of a single intravitreal dexamethasone (DEX) implant in patients with chronic non-infectious uveitic macular edema (UME). Methods: data from 22 eyes treated with DEX implant for UME related to systemic or ocular-confined non-infectious diseases were retrospectively analyzed. Results: The mean prednisone (or equivalent) dosage significantly decreased at 3- and 6-month follow-up evaluations compared to baseline ($p=0.002$ and $p=0.01$, respectively). Compared to baseline, central macular thickness (CMT) values significantly decreased at 1-, 3- and 6-month evaluations after the implantation ($p<0.0001$). The mean BCVA value gradually improved at 1-, 3-, and 6-month visits compared to baseline ($p=0.009$, $p=0.0004$, and $p=0.0001$, respectively). Leakage at fluorescein angiography (FA) was identified in 11 (50%) patients at baseline, 3 (13.6%) at 1- and 3-month follow-up and in 2 (9.1%) at the last visit. Regarding side effects, 3/22 (13.6%) patients presented a newly recognized intraocular hypertension at 1-month follow-up; however, intraocular pressure reverted to normal values within the 6-month follow-up in all cases. Conclusions: treatment with intravitreal DEX implant in non-infectious uveitis allowed a significant steroids' sparing effect, a significant improvement in BCVA, and a prompt resolution of UME and vasculitis. No safety issues were observed.

Tuberculous Sclerokeratitis

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Aim: To study the clinical findings and outcome of patients with tuberculous sclerokeratitis treated with antituberculous therapy without concomitant use of systemic steroids.

Methods: A total of 8 patients with the diagnosis of tuberculous sclerokeratitis were included retrospectively. Patients were unsuccessfully treated with topical and/or systemic steroids. Patients underwent complete ophthalmic examination, medical evaluation, and laboratory investigations and imaging. Tuberculin skin test was done with purified protein derivative (PPD) on all patients. The diagnosis of tuberculous sclerokeratitis was made based on clinical findings of scleritis with adjacent peripheral corneal stromal keratitis, positive PPD test of 15 mm of induration or more, response to antituberculous treatment (ATT) within 4 weeks and exclusion of other causes of sclerokeratitis. Antituberculous drugs were given for a minimum of 6 months without concomitant use of corticosteroids. The outcome measure was resolution of the ocular surface inflammation of the sclera and cornea.

Results: Eight consecutive patients with the diagnosis of tuberculous sclerokeratitis were included. There were 1 male and 7 female patients. The mean age was 29 years with an age range of 7 to 43 years. The involvement of the sclera was nodular in six patients and diffuse in two patients. The involvement of the cornea consisted of peripheral corneal stromal inflammation adjacent to the area of scleritis. Patients responded well to antituberculous medications with complete resolution of the sclerokeratitis without anti-inflammatory agents.

Conclusion: Antituberculous medications can lead to complete resolution of the sclerokeratitis without concomitant use of steroids, or other anti-inflammatory agents.

Ocular syphilis: case series (2000-2015) from two tertiary care centers in Montreal

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Background: In the past years, a recrudescence of syphilis was observed in Canada, reflecting the worldwide increase, along with a surge in ocular syphilis cases.

Purpose: To describe the demographics, clinical presentations, proportion of co-infection with HIV, treatments and visual outcomes.

Methods: Retrospective and descriptive study of patients with a positive syphilis serology between 2000 and 2015.

Results: Among the 119 patients (174 eyes) included in the study, 80% were male; mean age of onset was 55 years. Mean presenting logMAR visual acuity was 0.70 and unilateral ocular involvement occurred in 54%. HIV status was undetermined in 33%; among those whose serology was performed, 48% were HIV-infected. Ocular manifestations included: interstitial keratitis (24 eyes), anterior uveitis (37 eyes), intermediate uveitis (17 eyes), posterior uveitis (31 eyes), panuveitis (27 eyes), isolated optic nerve involvement (25 eyes) and others (12 eyes) including VI nerve palsy, scleritis, episcleritis and ocular ischemic syndrome. Cerebrospinal fluid (CSF) examination was performed in 55%. Of those, CSF Venereal Disease Research Laboratory (VDRL) test was positive in 22%. HIV-positive patients had higher rates of panuveitis and abnormal CSF exam. Treatment consisted of intravenous aqueous penicillin G in 58%, intramuscular benzathine penicillin in 21% or other antibiotics in 3%. The treatment allowed a visual improvement of -0.22 logMAR after a mean follow-up period of 19 months.

Conclusion: In the context of increasing rates of syphilis, it is primordial to consider this diagnosis and consider ocular syphilis as neurosyphilis with an appropriate treatment, a lumbar puncture and a HIV workup.

Epidemiology and clinical presentation of Susac syndrome in Austrain population

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OBJECTIVE:

Susac syndrome is characterized the clinical triad of branch retinal artery occlusion (BRAO), encephalopathy and hearing loss caused by inflammation and occlusion of arterioles. Our objective was to collect all cases of Susac syndrome in Austria as no epidemiological data are available for this disease.

METHODS:

All neurology and ophthalmology departments in Austria were addressed to report adult patients with the diagnosis of Susac syndrome who were on immunosuppressive treatment between 2010 and 2015. Clinical course, treatment regimens, prevalence rates, and annual incidence of Susac syndrome in Austria population are reported.

RESULTS:

Ten patients with Susac's syndrome were identified, and eight of them were newly diagnosed within these five years. Minimum five-year period prevalence of the disease is 0.148/100,000 (95% confidence interval (CI) 0.071-0.272), annual incidence is 0.024/100,000 (95% CI 0.010-0.047). Minimum point prevalence rates varied from 0.030/100,000 (95% CI 0.004-0.108) to 0.088/100,000 (95% CI 0.032-0.192). Of all 10 patients, 8 showed typical magnetic resonance imaging with callosal or internal capsule lesions at first presentation, 7 presented with BRAO and 5 had hearing loss or tinnitus at the beginning of the disease. Four patients developed the complete clinical triad of Susac syndrome during the observation period.

CONCLUSIONS:

We provide for the first time population-based data about the clinical course, prevalence and incidence of Susac syndrome in the Austrian population.

Session 13 “Pediatric uveitis in 2017 : major achievements and new challenges” IOIS Section - Pediatric Uveitis

TNF alpha Blockers in JIA-associated Uveitis

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Posterior uveitis in Children (pediatric uveitis session)

Ilknur Tugal-Tutkun¹.

The frequency of posterior uveitis varies from 4% to more than 50% in pediatric uveitis series reported from various geographic regions. The risk of visual impairment or blindness is higher than anterior or intermediate uveitis. Children mostly have unilateral infectious posterior uveitis, that may be congenital. Toxoplasma is the leading cause. Less frequent infectious etiologies include toxocariasis, tuberculosis, bartonellosis, Lyme disease, brucellosis, diffuse unilateral subacute neuroretinitis, herpetic retinopathies, and other viral infections. Noninfectious causes of posterior uveitis are much less common in children than in adults. Masquerade syndromes deserve special emphasis in children given their life-threatening implications.

Surgical Management of Pediatric Uveitis Complications

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Purpose: Describe the surgical management of complications of pediatric uveitis

Methods: Case reports and literature review

Results: Bandage contact lenses and amniotic membrane grafts may improve healing and comfort after chelation of band keratopathy. Intraocular lens implantation for childhood cataract remains controversial in children with severe uveitis involving the anterior segment. Glaucoma management benefits from angle surgery as a first step prior to implantation of a glaucoma drainage device. Pars plana vitrectomy may provide a means to remove vitreous opacities and ameliorate cystoid macular edema

Conclusion: Advances in surgical technique have improved the ability to manage uveitic complications in children.

Alternative biologics in severe cases of noninfectious anterior uveitis

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Juvenile idiopathic arthritis (JIA) is the most common systemic disorder associated with uveitis in childhood, accounting for approximately 75% of all pediatric anterior uveitis cases. Long-term ocular complications of uveitis such as cataract, band keratopathy, posterior synechia, glaucoma and maculopathy can lead to severe visual impairment in about 38% of patients. Visual outcome in long-term follow-up of patients suffering from JIA-associated uveitis have been described as poor, with one third of patients developing substantial visual impairment and 10% becoming blind. Aggressive immunomodulatory therapy is often introduced to improve the visual prognosis and reduce corticosteroid induced adverse events. With the advent of biologic agents, tumor necrosis factor α (TNF α) antagonists (Infliximab, Adalimumab, Golimumab) have been successfully used and have changed and markedly improved the treatment options for JIA. However, a subset of patients fails to respond to TNF α blockers or is unable to tolerate these therapies and may benefit from switching to another agent of this class or to a different biologic drug. Other biologic agents such as Rituximab, the anti-CD 20 B cell monoclonal antibody, Abatacept, a selective T cell costimulation modulator and Tocilizumab, an anti-IL 6 monoclonal antibody have been recently proven effective in the treatment of JIA associated uveitis and in refractory ocular inflammation.

Session 14 "The new dimensions of imaging in uveitis" In Memoriam of Dr. Friederike Mackensen IOIS section - Imaging

Follow-up of VKH patients with EDI-OCT

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MEWDS is a true choriocapillaritis and has to be distinguished from the different phenotype of primary disease of the outer retina-pigment epithelium complex.

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Background: Recently it was theorized that, allegedly, MEWDS primarily affected the outer retina/retinal pigment epithelium complex (OR/RPE) because OCT-angiography failed to show choriocapillaris perfusion disturbance. Aim of this study was to question this speculation and show that MEWDS indeed results from primary choriocapillaritis which should be distinguished from primary OR/RPE disease, a very rare condition with a completely different phenotype.

Material and methods: MEWDS cases seen in the Centre for Ophthalmic Specialised care (COS), Lausanne, Switzerland and the Department of Ophthalmology of the Valduce Hospital, Como, Italy, were reviewed. The presence of hypofluorescent areas on indocyanine green angiography (ICGA) were recorded. Photoreceptor outer segment damage was analysed using optical coherence tomography (OCT) as were OCT-angiography and fundus autofluorescence (FAF) findings, when available. Features were compared to those of a case of primary disease of the OS/RPE complex.

Results: 26 MEWDS patients were included and all showed characteristic ICGA hypofluorescent areas, corresponding to FAF-hyperautofluorescence and to OCT outer segment damage. On OCT angiography no disturbance of choriocapillaris circulation was seen. Primary OS/RPE disease only showed pure outer segment damage on OCT.

Conclusion: All patients showed characteristic ICGA lesions that can only be attributed to choriocapillaris hemodynamic disturbance, the latter not being detected by OCT-angiography as MEWDS is thought to affect the end-capillary portion characterized by low pressure/low flow circulation undetected by OCT-angiography. The phenotype of true primary OS/RPE disease was shown to be different from MEWDS allowing to exclude primary RPE damage for MEWDS.

Session 14 "The new dimensions of imaging in uveitis" In Memoriam of Dr. Friederike Mackensen IOIS section - Imaging

MULTIPLE EVANESCENT WHITE DOT SYNDROME: A MULTIMODAL IMAGING STUDY OF FOVEAL GRANULARITY AND EXTRAFOVEAL SIGNS"

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MULTIPLE EVANESCENT WHITE DOT SYNDROME: A MULTIMODAL IMAGING STUDY OF FOVEAL GRANULARITY AND EXTRAFOVEAL SIGNS

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Multiple evanescent white dot syndrome (MEWDS) is an inflammatory disease of unknown etiology, traditionally grouped under the term of primary inflammatory choriocapillaropathies (PICCPs), chorioretinal diseases characterized by inflammatory hypo or non-perfusion of the choriocapillaris. Funduscopy shows multiple faint white dots in the posterior pole and in the mid-periphery. Foveal granularity, which appears as an irregular yellowish lesion, is a common finding that can persist overtime and often represents the only detectable sign of the disease. In such challenging cases a proper diagnosis can only be confirmed by the use of a combined imaging, revealing areas of increased autofluorescence on fundus blue autofluorescence (BAF) and, on indocyanine green angiography (ICGA), dark hypo-fluorescent areas, better visible during the late phases of the exam. In presence of the foveal granularity, BAF is normal, or minimally altered in the foveal area, while near infrared fundus autofluorescence (NAF) shows a granular appearance that remains visible several months after MEWDS presentation. A possible explanation for this disagreement can be found in the different capability of the two wavelengths used to collect the images to penetrate the macular pigment. To conclude, BAF and ICGA remain the gold standard examinations for the identification of MEWDS lesions. However, foveal granularity can be present even in atypical cases lacking of widespread white dot lesions, and NIR-FAF should be considered in the evaluation and follow-up of foveal alterations in patients affected by MEWDS.

Ultrabiomicroscopic findings in acute uveitic, convalescent and chronic recurrent stage of Vogt-Koyanagi-Harada syndrome

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Purpose: To describe the ultrabiomicroscopic characteristics in patients with uveitic, convalescent and recurrent Vogt-Koyanagi-Harada (VKH) disease.

Methods: An observational, descriptive, case-series study was done.

Results: Ninety-one eyes were analyzed. Ciliochoroidal detachment, increased iris thickness at 2 mm from the iris root (ID2) and absence of ciliary processes were found in the uveitic phase. During recurrences, pars plicata and pars plana thickness increased significantly (four quadrants mean: 0.57 mm) and decreased one month after treatment (four quadrants mean: 0.45 mm). In the convalescent phase no reduction of pars plana or pars plicata thickness were found at 6-months follow up .

Conclusions: In uveitic phase ciliochoroidal detachment, increased iris thickness and absence of ciliary processes were characteristic UBM findings. In recurrent VKH phase, pars plicata and pars plana thickness increased again and then decreased significantly one month after treatment. These findings show the utility of UBM in VKH diagnosis and follow up.

Optical Coherence Tomography Angiography findings in patients with occlusive retinal vasculitis

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Purpose: Fluorescein angiography (FA) has been the gold standard for the evaluation and management of occlusive retinal vasculitis. Our purpose is to describe swept-source optical coherence tomography angiography (SS-OCTA) findings in eyes with occlusive retinal vasculitis.

Methods: This prospective study included 15 patients (25 eyes) diagnosed with occlusive retinal vasculitis involving the posterior pole or the periphery. All patients were evaluated using FA, spectral domain optical coherence tomography, and SS-OCTA.

Results: The causes of occlusive retinal vasculitis included Behcet disease in 12 patients (21 eyes), ocular tuberculosis in 1 patient (2 eyes), West Nile virus infection in 1 patient (1 eye) and rickettsiosis in one patient (1 eye). OCTA was superior to FA in evaluating perifoveal microvascular changes. It showed in twenty eyes (80%) areas of retinal capillary nonperfusion/hypoperfusion with or without associated rarefied, dilated, or shunting vessels. The deep retinal capillary plexus was more severely affected than the superficial capillary plexus.

Conclusions: SS-OCTA allowed better evaluation of macular ischemia than FA in eyes with occlusive retinal vasculitis. The deep capillary plexus appeared to be more severely involved than the superficial capillary plexus.

MEWDS is a true choriocapillaritis and has to be distinguished from the completely different phenotype of primary outer retina-pigment epithelium complex disease.

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Background: Recently it was theorized that, allegedly, MEWDS primarily affected the outer retina/retinal pigment epithelium complex (OR/RPE) because OCT-angiography failed to show choriocapillaris perfusion disturbance. The aim of this study was to refute this speculation and to show that MEWDS results from a primary choriocapillaritis which should be distinguished from primary OR/RPE disease, a very rare condition with a completely different phenotype.

Material and methods: MEWDS cases seen in the Centre for Ophthalmic Specialised care (COS), Lausanne, Switzerland and the Department of Ophthalmology of the Valduce Hospital, Como, Italy, were reviewed. The presence of hypofluorescent areas on indocyanine green angiography (ICGA) were recorded. Photoreceptor outer segment damage was analysed using optical coherence tomography (OCT) as were OCT-angiography and fundus autofluorescence (FAF) findings, when available. Features were compared to those of primary disease of the OS/RPE complex.

Results: 21 MEWDS patients were included and all showed characteristic ICGA hypofluorescent areas, corresponding to FAF-hyperautofluorescence and to OCT outer segment damage. On OCT angiography no disturbance of choriocapillaris circulation was seen. Primary OS/RPE disease only showed pure outer segment damage on OCT.

Conclusion: All our patients showed characteristic ICGA lesions that can only be attributed to choriocapillaris hemodynamic disturbance. the latter not being detected by OCT-angiography as MEWDS is known to affect the endcapillary portion characterized by low pressure low flow circulation not detected by OCT-angiography. The phenotype of true primary OS/RPE disease was shown to be different from MEWDS allowing to exclude this mechanism for MEWDS.

Non infectious non demyelinating optic neuritis: when and what to look for?

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Background: In most patients, autoimmune optic neuritis is associated with demyelinating diseases, mainly multiple sclerosis, with good visual prognosis, referred to as **typical** optic neuritis. On the other hand there are few patients who present with **atypical** optic neuritis when one or more of the following features are found: patients with recurrent or bilateral optic neuritis, when vision deteriorates after cessation/tapering of corticosteroid treatment, or does not respond sufficiently to corticosteroids, in patients with known autoimmune disease, and when the MRI findings are not suggestive of MS. Once Neuromyelitis Optica is ruled out in these patients, other types of autoimmune optic neuritis should be suspected such as: Chronic Relapsing Inflammatory Optic Neuropathy (CRION), Optic neuritis that is associated with connective tissue disorders, or granulomatous diseases. Rarely atypical optic neuritis could reveal a tumor. Extensive lab work up and neuro-imaging are usually required in order to make the diagnosis.

Visual loss due to ischemic optic neuropathy can be rarely confused with autoimmune optic neuritis when it occurs in the young.

Infectious optic neuritis is less common, occurs in a different clinical context and requires usually urgent specific treatment as in Herpes Zoster Virus, Lyme, Syphilis, Tuberculosis and Toxoplasmosis.

Few patients with atypical optic neuritis will be presented and discussed.

MIVS in infectious uveitis

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Purpose

To analyze the efficacy of treating infectious endophthalmitis by micro-incision pars plana vitrectomy and the visual outcome.

Methods

The retrospective, noncomparative, interventional case series was conducted from June 2014 to April 2017 at Department of Ophthalmology, China Medical University Hospital, China Medical University. All patients presenting with infectious endophthalmitis and receiving micro-incision pars plana vitrectomy were included. 23 or 25 gauge micro-incision vitrectomy was performed by retina surgeons. Variables collected for the study were patient demographics, preoperative visual acuity and predisposing factors. Outcome measures included average operative time, postoperative visual acuity, and pathogen culture reports.

Results

A total of 34 eyes (17 men and 17 women, 50% versus 50%) of 34 patients were included in this study. The average age was of 65 years old. Of these, 25 (73%) eyes were diagnosed of exogenous endophthalmitis, mostly with obvious history of recent intraocular procedures, such as phacoemulsification with intraocular lens implantation, intravitreal injection and vitrectomy. The mean operative time was 64.6 minutes. Positive culture rate was 20.5% with *Staphylococcus* spp. as the leading pathogen. Visual gain was noted in 18 eyes (53%) with average gain of 1.1 LogMAR. The improvement was statistically significant with P value < 0.001. There was no significant difference among operative time, onset to treatment time, and etiology.

Conclusions

Treating infectious endophthalmitis by micro-incision vitrectomy is a relatively rapid approach and provides a promising outcome.

MIVS in uveitis-related retinal complications

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Retinal and macular complications are one major visual threatening complication of uveitis. In this presentation, we will discuss the incidence of retinal or macular complications of uveitis in a tertiary referral center in Taiwan. We will also discuss the advantages of using micro incision vitrectomy surgery in dealing with these complications.

MIVS for recalcitrant uveitis/intraocular tumor

Shwu-Jiuan Sheu¹.

Owing to advancements in vitreoretinal technology, the indication of vitrectomy has extended a lot, including the diagnosis and treatment of recalcitrant uveitis and intraocular tumor. Compared to the traditional 20-gauge vitrectomy system, microincision vitrectomy surgery (MIVS) causes markedly less intra-operative bleeding and improves procedural efficiency. In addition, advanced illumination and wide-angle viewing systems allow clearer view of the fundus through opaque media caused by corneal edema and vitreous opacity in cases with severe inflammation. The diagnostic vitrectomy usually has to be done in active status in patients with atypical presentations, rapid progressive course with no conclusive tests, non- or suboptimal response with standard treatment and masquerade syndrome. Therapeutic vitrectomy has better be done in silent eyes for persistent vitreous opacity and retinal detachment. This talk will include case-based discussion on the role of MIVS for recalcitrant uveitis/intraocular tumor.

Session 16 “The Role Of Small Gauge Vitrectomy In The Diagnosis And Treatment Of Uveitis”
Taiwan Uveitis Study Group

MIVS in cataract surgery of juvenile idiopathic iridocyclitis

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Vitrectomy and handling of vitrectomy sample in the diagnosis of primary intraocular lymphoma -techniques for cytology

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Primary intraocular lymphoma (PIOL) is also known as primary vitreoretinal lymphoma (PVRL) that is a subset of primary central nerve system lymphoma (PCNSL). PIOL is a rare non-Hodgkin's lymphoma involves retina and vitreous. To make accurate diagnosis of PIOL is challenging. It requires differential diagnosis includes infectious and non-infectious etiologies and a highly clinical suspicion of PIOL. Laboratory tests and cytology using intraocular fluids are required to differentiate PIOL from uveitis of unknown origin. As usual, vitreous sample is performed cytology evaluation, immunocytochemistry, flow cytometry, cell clonality, and interleukin (IL) measurement for the diagnosis of intraocular lymphoma. Microincision vitreoretinal surgery is known to produce sufficient amounts of vitreous specimen with good preservation of cellular integrity necessary for cytopathological analysis and laboratory tests. But a recent study showed that the diagnostic power of conventional cytology was not as high as other laboratory tests including the ratio of IL-10/IL-6 and IgH gene rearrangement analysis. In other words, low sensitivity is a major problem of cytology for PIOL diagnosis. To improve the key flaw, vitreous infusion fluids obtained from vitreoretinal surgery had been used to promote positive yield rate recently. Besides, cell block method could provide high diagnostic sensitivity and a low pseudo-positive rate for the cytological diagnosis of PIOL. In this section, we would review how to handle the vitrectomy sample in the diagnosis of primary intraocular lymphoma for cytology.

Role of Interleukins as Biomarkers in the Management of Uveitis

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Infective, autoimmune and inflammatory stimuli can lead to changes in various systemic and local ocular cytokine levels. In response to antigenic stimuli, immune cells produce various pro-inflammatory cytokines such as interleukin (IL)-1, 6, 12 and 18, tumor necrosis factor (TNF)- α , interferon (IFN)- γ , and transforming growth factor (TGF)- β , among others. The pro-inflammatory cytokines such as IL-1, IL-2, IL-6, IFN- γ and TNF- α have all been detected within ocular fluids or tissues in the inflamed eye together with others, such as IL-4, IL-5, IL-10 and TGF- β . There may be a change in anti-inflammatory cytokines that oppose pro-inflammatory cytokines leading to heightened IL-10 responses in uveitis. In an ongoing study, it has been observed that serum levels of cytokines correlate well with disease activity in ocular tuberculosis. Interestingly, levels of tear cytokines appear to correlate well with serum levels and activity of the disease, paving way for non-invasive objective assessment of inflammatory cytokine signatures. Detection of such novel cytokine bio-signatures has the potential to develop path-breaking strategies in the management of infectious as well as non-infectious uveitis.

MYD88 Mutation: a valuable diagnostic test for vitreoretinal lymphoma

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Vitreoretinal lymphoma (VRL) is a rare form of intraocular malignancy that commonly masquerades as posterior uveitis and has a peculiar tropism for the retina and central nervous system (CNS).

The disease is highly aggressive and associated with an elevated mortality rate and significant morbidity secondary to ultimate involvement of the CNS. The gold standard for the definite diagnosis of VRL remains histopathologic examination of the ocular specimen, with demonstration of malignant B lymphocytes in the vitreous or retina, and immunohistochemistry to characterize lymphocyte type and clonality. Additional procedures that may support VRL diagnosis include flow cytometry and cytokines study with identification of an elevated IL-10/IL-6 ratio. However, the diagnosis is challenging due to several factors including the limited material of the vitreous biopsy, the low number of neoplastic lymphocytes, previous treatment with corticosteroids and the skill and experience of the cytopathologist, thus resulting in a high rate of false-negative vitreous biopsies.

In view of the need of establishing additional procedures to support the diagnosis of VRL, new techniques of mutational analysis have been validated for the diagnosis of VRL in recent years. MYD88 is a protein associated with the innate immune system and detection of MYD88 L265P mutation is a useful diagnostic tool for Waldenström macroglobulinemia. In recent studies, MYD88 L265P mutation was detected in the vitreous of 69% to 87% of patients with VRL. This diagnostic procedure may represent a helpful diagnostic tool for the detection of early cases of VRL, increasing the sensitivity of the vitreous biopsy.

Biomarkers in Scleritis

Maite Sainz de la Maza¹.

Progress has been made in the immunopathogenesis of scleritis. The sclera in scleritis, either diffuse or nodular, shows a nongranulomatous inflammatory reaction characterized by infiltration of mononuclear cells such as macrophages, B and T lymphocytes, and plasma cells. In some cases, however, especially in the most severe ones, mononuclear cells organize into granulomatous lesions; mast cells, neutrophils, and eosinophils also could be present. The sclera in necrotizing scleritis reveals a granulomatous inflammatory reaction, the center of which consisted of an area of fibrinoid necrosis surrounded by epithelioid cells, multinucleated giant cells, B and T lymphocytes, plasma cells, and less often neutrophils. Based on limited studies, B lymphocytes and macrophages are the predominant cell types in ocular tissue derived from patients with severe chronic scleritis. The deposition of immune complexes on the vessel wall induces vasculitis. Immunohistochemical studies on cytokines in scleritis show strong positive staining for IL-1a, IL-1b, IL-2, IL-3, IL-6, IFN γ , and TNF α . Furthermore, IL-22 (a Th17- and Th22- derived cytokine) serum levels are significantly elevated in active scleritis patients compared to controls and decrease significantly after remission. Adhesion molecules such as LFA-1 and their ligand ICAM-1 are expressed in scleritis. T cells, plasma cells, macrophages and dendritic cells release matrix metalloproteinases which may cause tissue destruction. These observations show an integrated model of chronic inflammation involving both the innate and the adaptive immune systems in scleritis. They also have important therapeutic implications, particularly for the use of biological therapy in the treatment of patients with severe scleritis.

Challenges in the Diagnosis and Treatment of TB Uveitis

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Tuberculous uveitis (TB uveitis), an extrapulmonary form of tuberculosis, is a treatable form of uveitis but is associated with devastating consequences if diagnosis and treatment is delayed. Prompt and proper initiation of therapy is sight-saving. However, diagnosing and treating TB uveitis is associated with several challenges. Among them, the varying clinical presentations of the disease, the difficulty in acquiring specimen for analysis, drug resistance and paradoxical worsening of inflammation during treatment. Ophthalmologists in third world countries where tuberculosis is endemic are further faced with additional challenges as will be discussed.

TB Uveitis: the Philippine Experience

Vicente Victor, Jr. Ocampo¹.

Objectives: To present the current situation of Tuberculous (TB) Uveitis in the Philippines

Methodology: The incidence of TB Uveitis in 3 hospitals in the Philippines will be presented and issues regarding the disease will be discussed.

Results: In 3 Philippine hospitals, the incidence of TB Uveitis ranges from 9.27-21.11%. Among the issues encountered are the (1) problems in diagnosis due to its various clinical presentations, and reliability of the Tuberculin Skin Test in the absence of chest x-ray findings and (2) dilemmas in treatment particularly in instituting Directly Observed Treatment, Short Course (DOTS) in extra-pulmonary TB.

Conclusion: There is a relatively high incidence of TB Uveitis in the Philippines which further amplifies the issues that go with the disease in terms of diagnosis and treatment. A high index of suspicion for TB Uveitis is warranted in cases of chronic and difficult uveitis in Filipino patients.

Updates on TB as a Worldwide Epidemic

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The Global Tuberculosis Report 2016 contains information regarding the increasing number of tuberculosis cases and how the world has progressed in diagnosing, treating and preventing the disease. Data was gathered from more than 202 countries comprising 99% of the world's population and cases of TB.

In 2015, there were an estimated 10.4 million new cases of TB worldwide, 56% were men, 34% were women and 10% were children. People living with HIV made up 11% of all new TB cases. India, Indonesia, China, Nigeria, Pakistan and South Africa were identified as accounting for nearly 60% of the new cases in 2015. The rate of decline in TB incidence is reported to be only 1.5% from 2014-2015.

New cases of multi-drug resistant TB were estimated to be 480,000 while 100,000 were Rifampicin-resistant TB. China, India and the Russian Federation contributed 45% to the combined total number of both MDR and RR-TB.

The number of TB deaths dropped by 22% between 2000-2015 but TB still ranks as one of the top killers worldwide in 2015. Efforts to treat TB prevented 49 million deaths globally between 2000-2015.

Part of the United Nations sustainable development goals (SDGs) adopted in 2015 is to see and end in the TB epidemic. It hopes to see a 90% decrease in TB deaths and an 80% reduction in the TB incidence rate by 2030 compared to 2015.

Presumed IntraOcular TB Scoring System

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Tissue diagnosis is not always possible in intraocular Tuberculosis. In the Philippines, therapeutic trials, more often than not, encourage the emergence of resistant strains. We propose a scoring system to assist in the diagnosis of presumed ocular TB so that anti TB therapy can be instituted on a more rational basis.

YAG capsulotomy: Comparison of laser parameters between normal and uveitic eyes

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Title: YAG capsulotomy: Comparison of laser parameters between normal and uveitic eyes

Aim: To compare laser parameters and number of sittings required for YAG capsulotomy performed in uveitic versus normal eyes

Methods: We analysed the medical records of fifty consecutive YAG laser capsulotomies performed for posterior capsule opacification(PCO) in uveitic eyes with 50 consecutive YAG laser capsulotomies performed for PCO in normal eyes. All capsulotomies were performed by a single surgeon on a single laser machine. Demographic information and details of laser settings (energy, power and number of shots) and need for repeat procedures were extracted from the records.

Results: The gender ratio for both the uveitic (M:F , 26:24)and normal group (M:F , 26:24)were similar($p=1.0$). The uveitic group was significantly younger (Mean age(SD) : 39.7 (14.0)) than the normal group (Mean age(SD) : 61.6 (14.3)) . The mean power(SD) used per shot was similar; Uveitic : 1.9mJ(.06), Normal 1.8mJ(.04). The mean number(SD) of shots required were significantly higher in the uveitic group 80(49) compared to the normal group 33 (17.9). The mean total energy (SD) required was also significantly higher in the uveitic group 83.5mJ(85.3) versus normal eyes 49mJ(28.4). None of the normal eyes required a repeat procedure or second sitting compared to 5 eyes in the uveitic group among whom 4 required 2 and 1 required 4 repeats ($p=0.2$).

Conclusion: With similar laser power settings YAG capsulotomy requires significantly a greater number of shots and higher energy levels in uveitic eyes.

Punctate Inner Choroidopathy: The impact of Anti-VEGF on outcomes

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Objectives:

To describe the clinical features and outcomes of a large group of patients diagnosed with punctate inner choroidopathy (PIC). To compare clinical outcomes from eras before and after the advent of anti-VEGF treatment.

Methods:

A retrospective consecutive case series of patients, presenting to Moorfields Eye Hospital over a 22 year period, with clinical features of PIC and a minimum of 12 months follow-up. Main outcome measures included visual acuity and development of choroidal neovascularisation (CNV).

Results:

A total of 250 patients were included with an average age of 34 years (range 19-60), 90% female and 90% myopic (mean refraction of -4.6 dioptres). The mean follow-up was 5.3 years. PIC lesions were bilateral in 50%. 197 patients (79%) developed CNV in at least 1 eye, 46 patients (18%) had bilateral CNV.

Of 153 eyes with CNV diagnosed before anti-VEGF became widely used, the mean logMAR visual acuity (VA) was 0.63 at baseline and 0.71 at final follow-up. Final VA in this group was less than 6/60 in 40 eyes (26%).

Of 106 eyes with CNV diagnosed since anti-VEGF became available, the mean VA was 0.41 at baseline and 0.31 at final follow-up. 88% of these eyes with CNV got anti-VEGF (Avastin or Lucentis) with on average 4 injections. Final VA in this group was less than 6/60 in 5 eyes (5%).

Conclusion:

Choroidal neovascularisation is a common complication of PIC but the advent of anti-VEGF treatment has dramatically improved clinical outcomes with less severely sight impaired patients as a result.

Epidemiology on uveitis in a Saint-Petersburg uveitis center, a pilot study.

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¹Academician I.P. Pavlov First St.Petersburg State Medical University (Saint-Petersburg, RU).

Background: In the national literature, the incidence of uveitis in Russia comprises 15-38 per 100,000 inhabitants per year. The epidemiological data on uveitis are still under discussion. Our aim was to conduct a pilot study on epidemiological trends in Saint-Petersburg premonitory of a larger project.

Methods: During the period from January 2014 to December 2016, all new patients seen in our uveitis center at the Department of Ophthalmology of the Academician I.P. Pavlov First St.Petersburg State Medical University were examined and classified.

Results: During the study period, 209 new uveitis patients (128 female and 81 male, mean age 43 years; range 16-82) were seen in our center. These 209 cases (327 eyes) were subdivided into anterior uveitis (71 patients - 34%), intermediate uveitis (2 patients - 1%), posterior uveitis (124 patients - 59%), and panuveitis (12 patients - 6%). A specific diagnosis was established in 173 cases (82.8%). The most frequently diagnosed entities were: HLA-B27 associated anterior uveitis (52 cases - 25%), sarcoidosis (33 cases - 5.9%), herpetic anterior uveitis (12 cases – 5.7%), toxoplasmosis (10 cases - 4.8%), Fuchs' uveitis (9 cases – 4.3%), and Behçet's disease (8 cases – 3.8%).

Conclusion: The main trends in uveitis epidemiology in our center correspond to the incidence and distribution of most causative disease entities in European and American series.

Epidemiology of choriocapillaritis in a tertiary referral centre

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Background: Choriocapillaritis is a group of diseases where the inflammatory pathology is situated at the level of the choriocapillaris. Classically this includes Multiple evanescent white dot syndrome(MEWDS), acute posterior multifocal placoid pigment epitheliopathy(APMPPE), idiopathic multifocal choroiditis(MFC), Serpiginous choroiditis(SC), and undefined choriocapillaritis entities. The aim was to repertoriate the frequency of these diseases and to establish their respective proportions.

Methods: Patients seen in the Centre for Ophthalmic Specialised care (COS), Lausanne, Switzerland, from 1995 to 2016 presenting with characteristic signs of choriocapillaris perfusion impairment on indocyanine green angiography (ICGA) were classified into MEWDS, APMPPE, MFC, SC and undefined entities showing characteristic choriocapillaris ICGA features but unclassifiable into one of the defined entities and their respective proportions were calculated.

Results: During the study period, 108(6.2%) of 1739 new uveitis patients presented the characteristic ICGA features of choriocapillaritis. 21 were diagnosed as MEWDS, 13 as APMPPE, 37 as MFC, 18 as SC and 19 patients presented a choriocapillaritis not classifiable into one of the well-defined phenotypes.

Conclusion: Choriocapillaritis, a relatively recent concept defined by ICGA inflammatory perfusion disturbance of the choriocapillaris, represented 6.2% of uveitis cases in our referral centre. Although the mechanism is common, inflammatory choriocapillaris vasculopathy, it gives rise to a spectrum of diseases from the benign end of MEWDS to the severe condition of SC. The different phenotypes are probably explained by the level of choriocapillaris vascular inflammation from larger vessels to endcapillary involvement in MEWDS explaining its benign course and the fact that OCT-angiography is not detecting perfusion disturbance.

Diltiazem co treatment with cyclosporine for induction of disease remission in sight-threatening non-infectious intraocular inflammation

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Purpose To investigate the effects of diltiazem co-treatment with microemulsified cyclosporine-A (CsA) on dosage, blood concentrations of CsA, as well as therapeutic and side effects in patients with sight-threatening non-infectious intraocular inflammation. **Methods** A prospective, randomized, placebo-controlled, open-label trial of 39 patients with sight-threatening noninfectious intraocular inflammation. The change in visual acuity (LogMAR), the grade of inflammatory activity, therapeutic concentration of CsA in the blood and systemic and renal toxicity were determined after comparing two groups, one treated with CsA and diltiazem (treatment group), and the other without diltiazem (control group). **Results** Compared with the control group, the concentration of CsA in the blood of the treatment group significantly

increased ($P \leq 0.05$) requiring a reduction in dosage of CsA ($P \leq 0.05$). **Conclusion** In patients with severe intraocular inflammation treated with CsA and diltiazem, blood concentrations

of CsA increased as the dosage decreased. This efficient combination therapy reduced patient's economic burden, at the same time decreasing systemic and renal toxicity which in turn may promote the use of CsA for longer periods

Correlation between Visual Acuity and Integrity of Outer Retinal Layers in Uveitic Macular Edema

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Purpose: To investigate the correlation between BCVA and the integrity of the ellipsoid portion of inner segments (EPIS) and interdigitation zone (IZ) layers in patients with uveitic macular edema (UME).

Methods: A three-year retrospective observational study was conducted on 103 eyes of 56 adults with a median age of 44.8 years (± 16.69) with UME. Baseline BCVA and foveal SD-OCT were obtained. The morphological pattern of macular edema, central foveal thickness (CFT), and integrity of EPIS and IZ layers were correlated with BCVA in cross tables using the chi-square test.

Results: Intermediate uveitis accounted for most eyes (30.4%, n=17) followed by anterior uveitis (28.6%, n=16). Most patients had bilateral affection (75%, n=14) and controlled inflammation (53.6%, n=30) at evaluation. Visual loss ($<20/30$) was present in (33%, n=34) eyes, and correlated with the presence of diffuse macular edema (DME), cystoid macular edema (CME), and increased foveal thickening ($p > 0.001$). The disruption of EPIS and IZ layers was associated with poor visual outcome ($p > 0.001$).

Conclusions: The disruption of outer retinal layers, EPIS and IZ, appears to be a strong predictor of visual loss in UME. Our findings highlight the evaluation of outer retinal layers in the analysis of SD-OCT of patients with uveitis-associated macular edema.

Baerveldt Tube implants for management of uveitic glaucoma: long-term experience at the Manchester Uveitis Clinic

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Aims

This study investigated the efficacy and safety profile of Baerveldt tube (BT) in patients with uveitic glaucoma at the Manchester Uveitis Clinic.

Methods

This was a retrospective case notes review of 42 patients with uveitic glaucoma (UG) who underwent BT between 2006 and 2015. Primary outcomes measures were the intraocular pressure (IOP) and the number of medications at 5-year follow-up visit. Two IOP criteria were chosen to measure success: IOP ≤ 21 mmHg and $\geq 20\%$ reduction from baseline (criteria one) and IOP ≤ 15 mmHg and $\geq 20\%$ reduction from baseline (criteria two).

Results

A total of 25 eyes completed 5 years follow-up. The mean age was 39.3 years with male:females of 2:1. At the time of surgery, 76.2% of eyes were on oral steroids and 78.6% required immunosuppression or biologics. The mean pre-operative IOP was 29.5 ± 9.5 mmHg on 3.9 drops with 81.0% of patients on oral acetazolamide, which reduced by 51.2% to 14.4 ± 7.0 mmHg ($p < 0.005$) at 5-year follow-up on 1.4 drops and only 3 patients were on acetazolamide. The cumulative probability of success at 5 years based on criteria 1 and 2 was 79.7% and 52.4% respectively. Two patients required rescue diode at one week post-operatively; one developed severe, sight –threatening inflammation following rescue diode; two patients required further glaucoma drainage Implant surgery; and one developed endophthalmitis leading to loss of light perception.

Conclusion

This study demonstrated that BT is safe and effective in refractory UG.

Clinical and epidemiological profile of pediatric episcleritis and Scleritis in a tertiary care center in India.

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Purpose: To describe the clinical and epidemiological profile of pediatric episcleritis and Scleritis in a tertiary care center in southern India.

Methods: Retrospective non-comparative interventional case series of 63 consecutive pediatric patients of age less than 16 years with confirmed diagnosis of episcleritis and Scleritis.

Results: Of 63 consecutive pediatric patients seen in a tertiary care center with the diagnosis of episcleritis and Scleritis, 39 patients had episcleritis and 20 had Scleritis. Among the patients with episcleritis (20 females, 19 males) 32 had unilateral involvement. Mean age of the patients was 10.9 ± 4.9 years. Among patients with scleritis, equal gender distribution was seen and 16 patients (80%) had unilateral disease. Mean age of onset was 12.25 ± 2.51 years. Most common subtypes of the scleritis was anterior non-necrotizing scleritis and posterior scleritis diagnosed in 10 eyes each. Necrotizing scleritis was seen in 4 eyes. Systemic association was seen in four patients, all four with tuberculosis. Oral corticosteroid was used in 18 patients and methotrexate was the commonly used immunosuppressive. Recurrences were seen in three patients, rest went for remission, and none developed perforation.

Conclusion: Pediatric episcleritis and scleritis remains a challenging disorder, due to its subtle clinical presentation. Methotrexate remains the drug of choice for immunosuppressant in pediatric patients with good remission and steroid sparing effect.

HAART associated ocular lesions in patients with HIV/AIDS – Structural and functional study

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Purpose: To study clinical features and ocular manifestations attributable to anti retroviral drugs in patients with HIV/AIDS

Methods: Retrospective study of HIV/AIDS patients on HAART with ocular manifestations. Patients with ocular opportunistic infections, IRU, diabetic/hypertensive retinopathy and/or ocular findings attributable to other systemic diseases like diabetes or hypertension, or on systemic medication including steroids were excluded. OCT, ERG, visual fields, colour vision and contrast sensitivity findings with clinical correlation were analysed

Results: Nineteen patients-males-15(88.24%), females-4(23.53%) with mean age-38.11±10.37 years, mean duration of HIV diagnosis-55.31 days and mean duration of HAART-7.73±29.11 days were included. Mean CD4 counts at presentation-323.78 cells/microm. Ocular lesions included pigment epithelial defects(PED) in 7(41%) patients, CSR in 4(24%), Steven Johnson syndrome associated ocular lesions in 5(29%) and RPE mottling in one patient. Three patients with normal fundus had night vision defects with typical ERG and one had additional colour vision abnormalities. All three were on lamivudine, efavirenz and tenofovir, two patients' ERG reverted to normal after drug regimen change while one was lost to followup. HVF showed cecocentral scotoma and constricted fields in 2 patients each. Reduced amplitudes by FVEP/PVEP and reduced contrast sensitivity were noted in 3 patients each. OCT showed minimal foveal thinning in 7, serous PED in 6 and CME with NSD in 4 patients.

Conclusions: HAART associated ocular lesions are predominantly retinal. They cause functional abnormalities of colour vision, contrast and night vision defects which reverts to normal with appropriate change in drug regimen

Interleukin (IL)-1 inhibition with Anakinra and Canakinumab in Behçet's disease related Uveitis: a Multicenter Retrospective Observational Study

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Objective: to evaluate the role of interleukin (IL)-1 inhibitors anakinra (ANA) and canakinumab (CAN) in the treatment of Behçet's disease (BD) uveitis. **Methods:** retrospective observational study including 19 consecutive BD patients (31 affected eyes) receiving treatment with IL-1 inhibitors. Data were analyzed at baseline, at 3 and 12 months. **Primary end-point:** reduction of ocular inflammatory flares (OIF). **Secondary end-points:** improvement of Best Corrected Visual Acuity; reduction of macular thickness defined by OCT and of vasculitis identified with fluorescein angiography (FA); evaluation of statistically significant differences between patients treated with IL-1 inhibitors as monotherapy, subjects also administered with disease modifying anti-rheumatic drugs (DMARDs) and/or corticosteroids as well as between patients administered with IL-1 inhibitors as first line biologic treatment and those previously treated with TNF- α inhibitors. **Results:** at 12 months OIF significantly decreased from 200/100 patients/year to 48.87/100 patients/year ($p < 0.0001$). The frequency of retinal vasculitis significantly decreased between baseline, 3-month and 12-month follow-up visits ($p < 0.0001$ and $p = 0.001$, respectively). OIF rate was significantly higher in patients co-administered with DMARDs (81.8/100 patients/year) than in patients undergoing IL-1 inhibitors as monotherapy (0.0/100 patients/year) ($p = 0.03$). No differences were identified on the basis of corticosteroid use and between patients administered with IL-1 inhibitors as first-line biologic approach or second-line. Steroid dosage was significantly decreased at 12-month visit compared to baseline ($p = 0.02$). **Conclusions:** treatment with IL-1 inhibitors is effective in the management of BD-related uveitis and provides a long-term control of ocular inflammation in refractory and long-lasting cases.

In the search of biomarkers for thyroid associated orbitopathy (TAO)

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Introduction: The production and composition of tears result from a dynamic system, which is dependent on various stimuli, including ocular diseases. We propose therefore tears as a potential relevant source of biomarkers for thyroid-associated orbitopathy (TAO) using proteomics-based strategies.

Materials and Methods: Schirmer's test was adopted to collect tears from 68 TAO patients (17 men, 45.8 years \pm 13.3) and 34 healthy subjects (13 men, 45.0 \pm 19.9). Among TAO patients, 25 had more active form of the disease, with a clinical activity score ≥ 3 . Independent quantitative proteomics experiments were done to identify lacrimal proteins presenting differential levels in TAO patients compared to subjects. Biological processes and pathways of the differential proteins were analysed using dedicated software. Verification of targets was performed by Western blot or immunoassays.

Results: 68 lacrimal proteins displayed differential level between TAO patients and controls. Interestingly, the acute phase response signalling emerged as the main interesting pathway disturbed in the disease. In parallel, our study showed a marked lacrimal elevation of cytokines in TAO patients compared to healthy subjects, but only the increase of IL-10, IL-12p70, IL-6, IL-13 and TNF- α was significant. Furthermore, IL-12p70, IL-10 and IL8 levels were higher whatever the subtypes of TAO, TNF- α , IL-6, IL-8 seemed particularly affected by the smoking status of patients.

Conclusion: These results confirm that tears are a suitable source to discover biomarkers for TAO disease. In addition, the variations of the levels of some cytokines could help to better understand this complex disease, therefore enhancing patient's management.

Observational analysis of patients on biologic therapies for the treatment of inflammatory eye disease in Northern Ireland.

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Title: Observational analysis of patients on biologic therapies for the treatment of inflammatory eye disease in Northern Ireland.

Aim: To evaluate the spectrum and efficacy of biologic drugs for the treatment of inflammatory eye disease.

Methods: Observational retrospective case series of all patients treated with a biologic therapy in a regional tertiary centre for uveitis over a 10yr period.

Results: 78 patients met the study criteria and were aged between 19 and 79 years (mean 43.5 years). The most commonly used biologics were adalimumab 41 (56.4%) and infliximab 18 (23%).

32 patients (41%) were under the care of ophthalmology alone, 37 (47%) under care rheumatologist and ophthalmologist and the remainder joint care with other specialities.

3 patients after being controlled on infliximab for 2, 5, 7 years respectively developed breakthrough inflammation. One developed anti infliximab antibodies and subsequently responded to 100mg golimumab monthly, the other 2 had no demonstrable antibodies and failed to respond to change in biologic.

Of the 139 biologics started during the study period, the biologic drug was discontinued on 9 (6.5%) occasions due to side effects.

Conclusion: Biologic drugs have had a significant impact on the effective management of uveitis allowing reduction in prednisolone dosage and concomitant immunosuppression. Patients may require long term treatment to control their inflammatory eye disease and failure can be primary or secondary requiring alternate biologics or strategies to be looked at.

Results from the SAKURA Program: Change in Central Retinal Thickness with Intravitreal Sirolimus Injection in Subjects with Non-infectious Uveitis of the Posterior Segment

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Purpose: The SAKURA Program consisted of two Phase III (one pivotal, one supportive), randomized, multinational, active control studies assessing the safety and efficacy of every-other-month intravitreal (IVT) sirolimus injection in the treatment of active non-infectious uveitis of the posterior segment (NIU-PS).

Methods: Eligibility criteria included vitreous haze (VH) $\geq 1.5+$ in the study eye. Subjects from both studies comprised the integrated Intent-to-Treat (ITT) population evaluating IVT sirolimus 440 μg vs 44 μg (n=208 for each group). The primary endpoint was VH=0 at Month 5. Change in CRT from baseline was assessed at Month 5 and safety through Month 6.

Results: In the integrated ITT population, 21.2% vs 13.5% of subjects (in 440 μg vs 44 μg , $p=0.0381$) achieved VH=0 at Month 5. Month 5 CRT data were available for 57 and 56 subjects with baseline macular edema (ME) (CRT $\geq 300 \mu\text{m}$) in the 440 μg and 44 μg groups, respectively. Median percent reduction from baseline CRT was 23.7% in the 440 μg and 16.1% in the 44 μg . Reductions were greatest among subjects in the 440 μg group without epiretinal membrane: 57.2% in the 440 μg (n=12) and 8.2% in the 44 μg (n=16) groups ($p=0.0473$). Occurrences of serious ocular adverse events were similar among treatment groups, and no unexpected events were reported.

Conclusion: The SAKURA Program, the largest study of NIU-PS to date, suggests IVT sirolimus 440 μg has the potential to reduce CRT in subjects with baseline ME and has a favorable benefit:risk profile over 44 μg .

The Grey Line Surgery for Eyelid Margin Reconstruction in Stevens Johnson Syndrome

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Purpose: To describe a new microsurgery to reconstruct severe keratinised eyelid margin in SJS patients using a partial thickness labial mucous graft.

To assess the improvement of the ocular surface after this procedure.

The outcome after 30 months follow-up.

Setting: Study developed at UNIFESP/Brazil under the External Disease and Oculoplastic departments. Ethical approval was obtained.

Methods: Six SJS patients with severe keratinised eyelid margin and conjunctiva grading 2 and 3, underwent "Grey Line reconstructive surgery" using partial thickness labial mucous graft. Post operative follow up including ocular surface fluorescent examination, record of patients' report of symptom improvement and medical photographs performed from day one to 30 months post operative.

Results: In all six cases operated upon, the partial thickness labial mucous graft had an excellent survival over the 30 months follow-up period. The graft integrates easily to the tissue maintaining a well-defined junction of the graft and the anterior lid margin. The examination of the ocular surface shows improvement of the chronic changes of the cornea and conjunctiva. All patients reported improvement of the comfort of ocular symptoms after surgery, which remained over the following 30 months.

Conclusion: This new microsurgery reconstructive surgery using partial thickness labial mucous graft in keratinised eyelid margin in SJS has been proven to be very effective in improving the status of the ocular surface. The thin graft was shown to be durable, maintaining stable over the 30 month follow-up period.

Spectral Domain Optical Coherence Tomography findings in Endogenous Candida Endophthalmitis and their clinical relevance

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Purpose: To describe vitreal, retinal and choroidal features of eyes affected by Endogenous Candida Endophthalmitis (ECE) analysed by spectral domain optical coherence tomography (SD-OCT) and to evaluate their clinical impact.

Methods: Medical records and SD-OCT images from eyes diagnosed with ECE at 4 tertiary referral centres were retrospectively evaluated. SD-OCT images were analysed to evaluate the structural changes occurring in the vitreous, the retina and the choroid in areas involved by ECE. Baseline and final Best Corrected Visual acuity (BCVA) were correlated with SD-OCT findings.

Results: Fifteen eyes from nine patients were enrolled. Vitreous involvement (vitreous cells, posterior hyaloid thickening) was detected in 13/15 eyes. Peculiar hyper-reflective preretinal aggregates obscuring the underlying retina due to a shadowing effect ("rain-cloud" sign) were noticed in all eyes with vitreous involvement. Two patterns of retinal and choroidal findings were identified: the first (6 eyes) confined within the inner retinal layers (Intraretinal Pattern), the second (9 eyes) involving both retina (full thickness) and choriocapillaris (Chorioretinal Pattern). None of the eyes showed both patterns. None of the eyes, regardless the pattern, showed choroidal thickening. Baseline BCVA was not associated with OCT pattern ($p=0.09$). On the contrary, final BCVA was significantly higher in patients showing Intraretinal Pattern ($\sim 20/25$, 0.06 ± 0.08 LogMAR) than in subjects with Chorioretinal Pattern ($\sim 20/50$, 0.44 ± 0.30 LogMAR), ($p=0.01$).

Conclusions: ECE showed peculiar features on SD-OCT. Two distinct patterns of chorioretinal involvement influencing the final BCVA were identified. SD-OCT could be useful in the diagnosis, management and outcome prediction in ECE.

Need for quantitative measurement methods for posterior uveitis: FA/ICGA & EDI-OCT choroid thickness versus SUN vitritis score in stromal choroiditis

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Purpose: Quantitative investigation for posterior uveitis are needed in clinical practice and trials. Aim was to assess fluorescein and indocyanine green angiography (FA/ICGA) and EDI-OCT and compare their pattern in two stromal choroiditis entities, birdshot retinochoroiditis (BRC) and Vogt-Koyanagi-Harada disease (VKH): their potential in clinical trials was compared to SUN vitreous haze score, primary outcome presently used.

Methods: Retrospective study on BRC and VKH patients, evaluated at initial onset disease and at stabilisation. Angiography signs were quantified, using an established FA & ICGA scoring system for uveitis, evolution of choroidal thickness was measured using EDI-OCT as well as SUN vitreous scoring.

Results: 4 diagnosed BRC and 4 VKH patients had sufficient data for study inclusion. Initial FA score were high in BRC (12.6 \pm 7.0) and low in VKH (5.4 \pm 2.1) ($p < 0.01$). Initial ICGA score were high and comparable in BRC (20 \pm 3.5) and VKH (19.5 \pm 9.1) as was initial choroidal thickness (425.8 \pm 138 microm for BRC and 499.9 \pm 43 for VKH). Response to treatment for ICGA was better in VKH (3.5 \pm 2.6) than BRC (7.7 \pm 4.2) ($p < 0.01$) as was the case of FA (1.5 \pm 1.5 (VKH) versus 6.31 \pm 3.4 (BRC)) ($p < 0.01$). Choroidal thickness decreased in both diseases after treatment, however less significantly than for ICGA and FA. Vitreous haze never exceeded score of 2 out of 4 in all 16 eyes.

Conclusion: VKH involves the choroid (ICGA) while BRC involves the retina (FA) and the choroid. Response to treatment is monitored by dual FA/ICGA scoring system while EDI-OCT is less sensitive. These numbered outcome parameters should represent the methods of choice to monitor inflammation in posterior uveitis while SUN vitreous haze score is of little use in stromal choroiditis.

High resolution imaging of retinal vasculitis by flood illumination adaptive optics fundus imaging: a follow-up study

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Purpose: To quantify perivascular sheathing during the course of retinal vasculitis by flood illumination adaptive optics (FIAO) imaging.

Material and Methods: Retrospective case series. Eleven eyes of 11 treatment-naïve patients with posterior uveitis of various etiologies associated with retinal venous sheathing. Perivenous sheathings and venous diameters were quantitatively analyzed by semi-automatic segmentation of FIAO images (rtx1, ImagineEye, Orsay, France). Change over time of the width of perivenous opacification, of vessel diameter and correlation to clinical course.

Results: At initial examination, the peak width (mean \pm SD) of perivenous opacification was 92.7 μ m (\pm 46). In 8 cases, the underlying vein showed focal narrowing (mean \pm SD relative narrowing, 13% \pm 10%). Systemic treatment was initiated in 10 patients. The median interval between FIAO sessions was 2.5 months (range: 0.2- 24 months), and the mean follow-up was 6.5 months (\pm 5.6). Overall, in parallel with clinical response, there was a significant thinning of vascular sheathing (average width 93 μ m \pm 56 versus 23 μ m \pm 15; $p=0.003$). Vessel diameters, on the opposite, showed no clear correspondence with the clinical severity of ocular inflammation. However, in 4 cases, it was observed that the thickness of perivascular sheathing temporally and spatially correlated with deformation of adjacent axons and vessels.

Conclusions: Focal venous or arterial narrowing at site of sheathing may be of compressive nature, suggesting that focal compression may participate to inflammatory occlusion of the retinal vessels. FIAO may therefore be of interest for understanding the local complications of retinal vasculitis and characterizing the response to therapy.

Evaluation of superficial and deep capillary plexus using optical coherence tomography angiography in vasculitis

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Purpose : To evaluate the FAZ superficial capillary plexus and deep capillary plexus in vasculitis by OCTA

Methods: In this retrospective study 39eyes of 24patients with vasculitis due to different etiologies including Bechet's, Sarcoidosis, TB, SLE, TINU , MS and undifferentiated , with no current or minimal parafoveal macular oedema had superficial capillary plexus (SCP)and deep capillary plexus (DCP) assessed by OCTA, and measured by 2 methods. First method was the average of the horizontal and vertical diameter and the second method was by surface area measurement . All eyes had fundus fluorescein angiogram to evaluate the macula, peripheral ischemia and vasculitis.

Results: The size of the DCP using the surface area ,mean = $1.233 \text{ mm}^2 \pm 0.46$ and the DCP average diameter, mean = $1271.17 \text{ um} \pm 321.85 \text{ um}$ was larger than the SCP with average diameter , SCP mean = $731.45 \text{ um} \pm 242.82$ and SCP area mean = $0.446 \text{ mm}^2 \pm 0.36$. Correlating with previous macular oedema the diameter of SCP ($P<0.01$), area of DCP ($P=0.07$), diameter of DCP ($P<0.01$) , was significant however peripheral ischemia did not show significant correlation with the DCP or SCP.

Conclusion: The data suggests that DCP was found to be more impaired as compared to SCP and previous macular oedema may have a role in affecting the DCP and SCP in vasculitis.

Evaluation of vascular changes in intermediate uveitis and vasculitis using OCT-A

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Purpose: To evaluate vascular changes in intermediate uveitis and retinal vasculitis using OCT-A.

Methods: This cross-sectional study included patients with intermediate uveitis and vasculitis, who were examined using swept-source OCT-A (SS-OCTA; PLEX Elite, Carl Zeiss). Raster scans (3x3 and 12x12 mm), covering approximately 70° of the posterior pole, were performed. OCT-A and en-face slabs were analyzed.

Results: 40 eyes with intermediate uveitis and 7 with retinal vasculitis (5 occlusive) were included (mean age 50±21 yrs.). The majority of eyes were inactive (intermediate uveitis: 80%, vasculitis: 71%). All eyes with vasculitis were treated with conventional-synthetic (cs) and/or biological (b) DMARDs, whereas only 43% with intermediate uveitis received cs/bDMARDs. In intermediate uveitis, the majority of eyes showed no capillary rarefaction in the superficial capillary plexus (SCP) (93%), deep capillary plexus (DCP) (90%), choriocapillaries (80%) and choroid (83%). Rarefaction of vascular plexi was not associated with disease activity (SCP: p=0.4, DCP: p=0.3). En-face slabs showed intact ellipsoid-zone layers in 85%, choriocapillaries layers in 93% and choroidal slabs in 93%. Although the majority of vasculitis eyes were occlusive, only 29% had significant capillary-dropout visible in SCP and DCP. 43% had capillary rarefaction on SCP and DCP. En-face slabs showed intact ellipsoid-zone layers in 71%, intact choriocapillaries layers in 86%, and intact choroidal slabs in 86%.

Conclusion: Only a minority of eyes with intermediate uveitis and vasculitis revealed OCT-A abnormalities. Currently, OCT-A seems not the modality of choice for these diseases and its potential role has to be further evaluated.

Evaluation of SUN vitreous haze score (VH) and dual fluorescein/indocyanine green angiography (FA/ICGA) as outcome measures for disease follow-up and for trials in tuberculosis chorioretinitis

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background: Vitreous haze score (VH) was recommended by SUN (Standardization of Uveitis Nomenclature) as the gold standard to evaluate inflammation in posterior uveitis for clinical trials. Our aim was to assess VH score and compare it to dual FA/ICGA in tuberculous chorioretinitis (TCR).

methods: retrospective study on patients with diagnosis of TCR seen in the Centre for Ophthalmic Specialized Care, Lausanne, Switzerland. Angiography was quantified with an established dual FA/ICGA scoring for uveitis: VH was measured following SUN criteria, comparing to patients' VH to a set of fundus pictures with score from 0 to 4.

results: of 1739 uveitis patients seen from 1995 to 2015, 27/53 patients diagnosed as TCR had data for inclusion. Choroid was predominantly involved in 39/54 eyes and retina in 14. Mean scores were 6.97 ± 5.08 for retina (FA) versus 13.48 ± 7.06 for choroid (ICGA). Follow-up scores decreased to 3.63 ± 3.14 for FA and to 7.47 ± 5.58 for ICGA after therapy. Mean VH score was 0.75 ± 0.72 with 6/54 eyes having score of 2 and 2 having score of 3. Remaining eyes (44/54) had score of 1 or less.

conclusion: for the first time precise measurement of global posterior inflammation was achieved by dual FA/ICGA in TCR, appearing as precise/quantitative method to assess and monitor inflammation in TCR. In contrast, SUN-VH scale, recommended in studies on posterior uveitis, appears as inadequate: 8/54 eyes had sufficiently high VH to be included in study with little prospect to show statistical significance after treatment.

Contribution of combined indocyanine green angiography (ICGA) and interferon gamma-release assay (IGRA) to the appraisal of ocular tuberculosis in a non-endemic area.

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Purpose: To assess the potential utility of the combination of indocyanine green angiography (ICGA) with interferon-gamma release assays (IGRAs) for the diagnosis of presumed tuberculous chorioretinitis in a non-endemic area.

Methods: Retrospective study on patients where the combined use of IGRA and ICGA lead to the diagnosis of presumed ocular tuberculosis (POT) at the Centre for Ophthalmic Specialized Care, Lausanne, Switzerland. Quantiferon Gold was used as the IGRA test. Angiography signs were quantified using an established dual fluorescein/indocyanine green (FA/ICGA) scoring system for uveitis.

Results: Among 1739 uveitis patients seen from 1995 to 2016, 7 of 53 POT patients were diagnosed (13 %) thanks to the dual contribution of ICGA and IGRA. All 14 affected eyes, showed predominant choroidal involvement with a mean FA/retinal angiographic score of 6.39 ± 3.82 versus 15.29 ± 5.31 for the choroid. The scores decreased from 6.39 to 2.39 ± 2.47 ($p=0.01$) for FA and from 15.29 to 9.5 ± 4.79 ($p=0.01$) for ICGA after antituberculous treatment alone or together with inflammation suppressive therapy. The combined use of ICGA/IGRA also reduced the delay to diagnosis from 70.24 ± 89.45 months in a previously published series to 22.86 ± 20.07 months in the present collective.

Conclusions: Combined ICGA/IGRA testing allowed to reach an unsuspected diagnosis of ocular tuberculosis in 7 of 53 cases. The combination of ICGA showing occult stromal choroiditis leading to IGRA testing or IGRA testing leading to perform ICGA, improved the appraisal of ocular tuberculosis in a non-endemic area and should be recommended in case of undiagnosed posterior uveitis compatible with ocular tuberculosis.

Choroidal and Central Foveal Thickness using Enhanced Depth Imaging Optical Coherence Tomography in Acute Anterior Uveitis

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Purpose: To evaluate the choroidal and central foveal thickness during acute attack of anterior uveitis.

Design: Retrospective observational study

Methods: The medical records of 120 patients diagnosed with unilateral acute anterior uveitis (AAU) who visited Seoul St. Mary's Hospital were studied. Age, sex, and spherical equivalent of refractive error-matched healthy subjects (n=120) were recruited from consecutive patients who were scheduled for routine ocular examination. Subjects were divided into 3 groups; Group 1 (eyes with AAU, 120), Group 2 (unaffected fellow eyes, 120), and Group 3 (healthy-control eyes, 120).

Results: In uveitis group, their mean age was 44.25 ± 15.30 years, and 66 (55.0%) were female. The etiologic diagnoses were as follows; HLA-B27 associated (n=71 [59.1%]), idiopathic (n=44 [36.7%]) and juvenile rheumatoid arthritis (n=5 [4.2%]). Mean subfoveal choroidal thickness was 322.6 ± 69.0 μm in Group 1, 299.9 ± 69.8 μm in Group 2, and 296.2 ± 42.9 μm in Group 3. Mean central foveal thickness was 273.4 ± 29.3 μm in Group 1, 264.4 ± 24.6 μm in Group 2, and 263.0 ± 30.8 μm in Group 3. The subfoveal choroidal and central foveal thickness were significantly thicker during the acute stage of the uveitis in comparison with the control groups. There were no relationship between the anterior chamber cell grade and subfoveal choroidal thickness and central foveal thickness.

Conclusions: In this study, we found a significant increase of subfoveal choroidal and central foveal thickness in AAU period. Therefore, we suggests that the importance of OCT examination in all types of AAU to detect subclinical choroidal and retinal change.

SOIE session: FA/ICGA scoring for quantitative assessment of retinal and choroidal inflammation

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Angiographic investigation of the posterior segment is essential in uveitis in order to confirm clinical findings, to detect occult inflammation, to document complications such as NVD, NVE, and to monitor response to therapy. Dual fluorescein and indocyanine green angiography (FA/ICGA) is performed to evaluate the magnitude of retinal vs choroidal involvement. A semiquantitative FA/ICGA scoring system has been developed for the grading of posterior segment inflammation and validated in studies using both conventional and ultrawide field (UWF) imaging. There are also recent studies that have described quantitative analysis of UWFA images. Quantitative angiographic data should be included in outcome measures in clinical trials of uveitis

IL-6 inhibition for the treatment of noninfectious uveitis

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Interleukin-6 (IL-6) is a key cytokine that is strongly up-regulated during infection and inflammation. Featuring pleiotropic activity, IL-6 is responsible for the induction of hepatic acute-phase proteins, trafficking of acute and chronic inflammatory cells, differentiation of adaptive T-cell responses, homeostatic regulation, and tissue regeneration. Macular edema (ME) is a leading cause of visual loss in uveitis patients. The pathogenesis of uveitic ME includes disruption of tight junction proteins and subsequent breakdown of the blood-retinal barrier (BRB) that leads to accumulation of fluid within the macular retina. IL-6 is a pro-inflammatory cytokine that has been implicated in uveitis and uveitic ME. Such a notion is supported by several international clinical cohort studies showing that IL-6R blockade is beneficial in the treatment of uveitis and its related ME. After studying the clinical efficacy of IL-6 inhibition in uveitis patients, our group aimed to interrogate the effect of IL-6 and its blockade with tocilizumab (TCZ), a monoclonal antibody targeting the IL-6R, on the barrier properties of an in vitro model of the inner and outer BRB. Our preliminary in vitro data support the hypothesis that IL-6 disrupts the BRB and contributes to the pathogenesis of ME. Indeed, IL-6-induced disrupted ZO-1 expression was accompanied by an increase in paracellular permeability, and decreased transepithelial electrical resistance (TEER) of ARPE-19 and human retinal microvascular endothelial cell (HRMEC) monolayers, whereas TCZ-treated cells could restore IL-6-induced barrier disruption.

Intravitreal drugs in development for the treatment of non infectious uveitis

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Intravitreal medication achieves a therapeutic level in the vitreous while minimizing systemic complications and is thus used as an exciting alternative. Corticosteroids, antivascular endothelial growth factors, immunomodulators such as methotrexate and sirolimus, and nonsteroidal anti-inflammatory drugs are currently available for intravitreal therapy. The presentation reviews the existing and drugs in development for efficacy and safety of these various options for intravitreal drug therapy for the management of noninfectious uveitis (mainly intermediate, posterior, and panuveitis).

NanoMedicine and Cell based therapies for the treatment of Ocular Inflammation

Samuel Yiu¹.

Ocular surface inflammation is one of the most common ocular conditions that we encounter in our daily clinics. Over the years, topical steroid is the main therapeutic option to control the inflammation. In recent years advances in our understanding of ocular inflammation has led to many new developments including cell based therapies, nano-drug delivery platform, and ocular devices. This presentation seeks to provide an update on the most recent advances in treatment options.

Combining immunosuppressive agents and biologics safely

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Posterior segment uveitis commonly requires long term immunosuppressive treatment. If a single steroid sparing agent fails to control disease, combination of antimetabolites with or without T-cell inhibitors is frequently done. When steroid sparing conventional immunosuppressive drugs (non-biologic DMARDs) fail, biologic therapy is started. However, there are no clear guidelines about whether biologics should or should not be used in combinations with antimetabolites or T-cell inhibitors. Tumor necrosis factor inhibitors (TNFi; adalimumab, certolizumab, etanercept, golimumab, infliximab, biosimilars) are essentially considered to have similar efficacy. Other biologics (i.e., abatacept, tocilizumab, rituximab) are typically reserved for patients who fail or who have contraindications to TNFi and may have differential safety depending on the comorbidities and risk factors for each patient. The risks and potential benefits of combining non-biologic DMARDs and biologics will be discussed.

Monitoring for side effects during treatment with systemic immunosuppressants.

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Effective monitoring of side-effects induced by chronic immunosuppressive therapy requires strategies for screening multiple types of events: toxicities/side-effects, infections, neoplasms. While some adverse effects of immunosuppressive agents such as reduced response to infections are shared by all immunosuppressants although in a dose dependant fashion, most other side-effects are drug-specific and monitoring strategies need to be adapted accordingly. Pertinent literature from the fields of rheumatology, organ transplantation, gastro-enterology, dermatology, and ophthalmology will be reviewed and proposed monitoring guidelines, when available, will be presented for each class of immunosuppressive agent.

Pre-treatment assessment in the management of severe uveitis

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The aim is to describe recommendations for the assessment and investigation of patients with severe uveitis before commencing systemic immunosuppressive and/or biologic therapy to minimise side effects of long term therapy and avoid iatrogenic complications.

The recommended approach is based on clinical experience and a review of the literature with regard to the use of corticosteroids, immunosuppressive drug and biologic therapy in the management of patients with severe sight threatening inflammatory eye disease.

A careful assessment and consultative approach by physicians experienced in the use of immunosuppressive agents is recommended before commencing immunosuppressive and/or biologic therapy to improve therapeutic efficacy; prevent infection; cardiovascular, metabolic and bone disease; and minimise the potential for iatrogenic side effects. Adherence to established clinical guidelines is an integral part of the clinical approach to therapy.

Assessing the relationship between intermediate uveitis and multiple sclerosis

Matthias Becker¹.

Uveitis associated with multiple sclerosis (MS) occurs in only about 1% of MS-patients and often manifests as chronic, bilateral, intermediate and/or granulomatous anterior uveitis complicated by cystoid macular edema (CME) which can limit visual prognosis considerably. Clinical features may vary and include retinal vasculitis as well as pars planitis. In most patients, uveitis precedes the diagnosis of MS by several years. Relating uveitis to MS may be challenging, since the initial MRI, at the time of first signs of intraocular inflammation, is often normal and/or does not meet official McDonald criteria to diagnose MS, even in those patients that ultimately develop MS. Conventional immunosuppressive therapy for inflammatory activity and/or CME may respond less successfully than for other uveitic entities. Superior results with interferon-beta have been reported.

DNA viruses and uveitis: herpes simplex, varicella, CMV

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Recent studies with PCR using intraocular fluids revealed that all human herpes viruses (type 1 to type 8) were detected in patients with various types of intraocular inflammation. Herpes simplex virus (HSV), varicella zoster virus (VZV) and cytomegalovirus (CMV) are most common DNA viruses as a causative agent of intraocular inflammation, in particular anterior uveitis (AU). This presentation is focused on herpes-induced AU.

HSV-AU, VZV-AU and CMV-AU share common clinical features in many aspects, such as unilateral acute inflammation, presence of high intraocular pressure (IOP), association of various types of keratitis, moderate inflammation in the anterior chamber, iris atrophy, and moderate anterior vitreous cells. However, it is also known that there are some differences in their clinical pictures among the three herpes-induced AU. CMV-AU is mildest in the anterior chamber inflammation but it causes highest IOP increase and corneal endothelial cell loss. VZV-AU causes sectorial iris atrophy which is not seen in other herpes-induced AU.

Investigations to explain why these DNA viruses present these clinical features are not available at the moment. Possible mechanisms for the clinical pictures of these DNA viruses-induced AU will be discussed based on the review of literatures.

Birdshot Chorioretinitis HLA KIR and Microenvironment

Ralph D. Levinson MD

Ralph Levinson¹.

It is likely that birdshot chorioretinitis (BCR) is the result of complex genetic and environmental interactions. The strong association with HLA-A29 and the implication of KIR in the pathogenesis based on genetic associations, particularly KIR-HLA-B44 interactions, suggest a role for Class I antigen presentation, which plays a role in the immune response to intracellular organisms and immune surveillance for neoplasia.

Other observations must also be explained:

1. The average age of onset in the 6th decade. The aging of the immune system may alter the response to the microbiome as might age related alterations in gastrointestinal vasculature. Also, neoplasia may be more common as environmental challenges could be cumulative (such as sun exposure).
2. The predominance of Caucasians A concurrence of disease with intraocular melanomas and skin cancers has been suggested. A role for activation by such cancers or activation via immune surveillance may explain the Caucasian predominance. Complex interactions between microbial and tumor antigens and the immune response may also play a role.

Is sarcoidosis an autoimmune disease?

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Is Sarcoidosis an Autoimmune Disease?

Professor Nicholas Jones, Manchester, UK

The question might as realistically (and as hopefully) be posed “What causes sarcoidosis? Each passing year identifies new characteristics of the immunogenetics and pathogenesis of the disease, yet the causes remain elusive. It has become clear that possible initiating antigens are numerous, each with its claim to authenticity, and that genetic predisposition is complex, polymorphic, variable between races and of low heritability. The ability of biologic therapies (such as BRAF-inhibitors, anti-PD1 Mabs or interferons) to induce sarcoidosis or sarcoid-like reactions may provide important insights into the immune pathways responsible for this dysfunctional state.

It may transpire that “The Sarcoidoses” prove to be a group of diseases with variable clinical expression at a number of anatomical sites, with a common, possibly phylogenetically archaic, granulomatous response to antigen(s) which both induce vigorous local inflammation and are very difficult to clear. The resultant lymphocyte hyper-activation, cytokine exhaustion and apoptosis may be responsible for peripheral blood lymphopenia and anergy. Granuloma resolution probably represents antigen clearance, but switching to a Th2-induced fibrotic response may be a last-ditch attempt at encapsulation of an antigen resistant to all other adaptive immune processes. Is sarcoidosis an autoimmune disease?: there may be a hyper-inflammatory local response associated with a substantially disordered adaptive immune system, but if the initiating foreign antigen remains present as the granuloma fibroses, then the answer must be no!

RNA viruses and uveitis: rubella, Ebola, chikungunya, zika, dengue

Vishali Gupta¹.

RNA viruses are known to affect retina causing several protean manifestations. Some of them can have a very aggressive course with necrosis and destruction of retina within few days. Pattern recognition is the key to diagnosis. This talk aims to demonstrate illustrative cases of such presentations including Subacute sclerosing pan encephalitis, chikungunya, dengue, ebola and zika and the course of these rare infections.

Behçet disease (IUSG session:Infection, Autoinflammation, and Autoimmunity)

Ilknur Tutkun¹.

Behçet disease has several autoinflammatory features including recurrent inflammatory manifestations overlapping with monogenic autoinflammatory disorders, significant genetic predisposition, and abnormally increased inflammatory response predominantly involving the innate immune system. Triggering factors including commensal microbes and invasive pathogens may induce disease expression in genetically susceptible individuals. HLA-B51 is the strongest association. Non_HLA susceptibility genes have also been identified, such as IL-10, ERAP-1, IL-23R, IL-12A, CCR1, STAT4, KLRC4, TLR4, and FUT2, several of which are shared with other complex autoinflammatory disorders, including Crohn’s disease, ankylosing spondylitis, and psoriasis. A new concept of MHC-I-opathies has been proposed unifying the immunopathogenesis of these disorders based on development of aberrant innate immune response at sites of mechanical stress and induction of secondary adaptive immune response with tissue specific dynamics.

Treatment Challenges: intravitreal chemotherapy and systemic medical therapies

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Vitreoretinal lymphoma is a rare diffuse large B cell lymphoma involving the retina, vitreous and/or optic nerve, which frequently is associated with central nervous system tumor. Medical treatment options for this intraocular lymphoma include locally injected chemotherapy with methotrexate and/or rituximab, a range of systemically administered polychemotherapeutic regimens, and peripheral blood stem cell transplantation. Unfortunately however, despite an increasing number of medical treatment approaches, ocular relapses are common, and vitreoretinal lymphoma has high morbidity and high mortality.

Treatment challenges - radiotherapy: an outmoded Rx or not?

MING-LEE LIN¹.

The optimum management of intraocular lymphoma remains a contentious area. This is due to the complexity of the disease and the scarcity of controlled studies. Modern radiotherapy techniques have improved to minimize ocular toxicity but improved patient survival also emphasizes concerns for long-term safety. This presentation will outline viewpoints and controversies in the use of radiotherapy for the treatment of intraocular lymphoma.

Diagnostic work up of ocular lymphoma specimens

SARAH E. COUPLAND¹.

The eye is a relatively rare site for malignant non Hodgkin's lymphoma (NHL). The intraocular lymphomas can be divided into the primary vitreoretinal lymphomas (PVRL), the primary uveal (mainly choroidal) lymphomas, and the secondary uveal lymphomas. PVRL are most commonly diffuse large B-cell lymphomas (DLBCL) and are considered a variant of the the high-grade malignant primary DLBCL of the central nervous system (CNS). In contrast, the primary choroidal lymphomas tend to be low-grade extranodal marginal zone B-cell lymphomas with no association with the CNS. Secondary uveal lymphomas represent secondary manifestations of underlying systemic NHL, and vary in their degree of aggressiveness. Diagnosis of the intraocular lymphomas usually is made by cytological, immunocytochemical and molecular analysis of vitreous or subretinal aspirates, and/or chorioretinal biopsies. Degenerative changes, limited material and the occurrence of pseudoclonality in molecular analysis of B-cell clonality can hamper diagnostic assessment, and delay the diagnosis. Novel techniques such as detection of *MYD88* mutations common in PVRL as well as use of miRNAs ratios can increase diagnostic sensitivity. Close cooperation with clinical colleagues together with rapid specimen processing and slide review by a dedicated eye path team are prerogatives for successful diagnostics.

Diagnostic challenges with intraocular lymphoma - When to biopsy, how to biopsy?

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The management of primary intraocular lymphoma is often far from straightforward - first, one must consider it as a possible diagnosis at presentation, and then histological confirmation is required in order for appropriate treatment to be planned.

But how, and when, should a biopsy be considered? Is a tap enough, or should one instead always proceed to a core vitrectomy? How has 25Gu vitrectomy changed this paradigm? When should a chorioretinal biopsy be considered? What if systemic, or intraocular steroids have already been administered - how long should one wait in order to maximise the yield?

Clinical scenarios illustrating each of these issues will be discussed, in addition to a overview of the current literature and evidence (if any) supporting each approach.

Clinical features including multimodal imaging in ocular lymphoma

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The clinical features of primary vitreoretinal lymphoma will be presented. A rarer group of metastatic choroidal lymphoma will also be discussed.

The value of ocular coherence tomography, fundus photography including infrared and autofluorescence imaging will be demonstrated along with the features on fluorescein retinal angiography and indocyanine green chorioangiography,

Primary intraocular and primary central nervous system lymphoma, epidemiology and survival

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Purpose

Primary intraocular lymphoma (PIOL) is a rare subtype of primary central nervous system lymphoma (PCNSL). We describe the demographics, incidence and survival in patients with PIOL and PCNSL in Victoria, Australia.

Method

A retrospective study of cases of PIOL and PCNSL reported to the Victorian Cancer Registry from 1 January 1996 to 31 December 2015. Cases were included where a histological diagnosis of primary lymphoma was confirmed on brain biopsy, vitreoretinal biopsy or CSF cytology. Incidence rate was calculated using a dynamic population model.

Results

13 cases of isolated PIOL and 422 cases of PCNSL were identified over the 20-year study period. Incidence rates were 1.26 cases per 1,000,000 person-years, and 40.87 cases per 1,000,000 person-years, respectively. The incidence of isolated PIOL appeared to increase over time. Mean age at diagnosis was 65 years. 48% of patients were female. 85% of cases were diagnosed as diffuse large B-cell lymphoma. The median survival of patients with PIOL was > 48 months. Overall (PIOL and PCNSL) median survival was 22 months over the study period. The median survival of patients with PCNSL improved from 12 months in 1996-2005 to 34 months in 2006-2015.

Conclusion

This first registry-wide study of PIOL and PCNSL in an Australian population demonstrates a similar incidence and survival to that reported in international studies. Isolated PIOL remains a very rare disease with poor prognosis. There has been, however an improvement in survival in patients with PCNS lymphoma diagnosed in the last 10 years.

Session 27 “Imaging of the Anterior Segment in Uveitis” Hellenic Society for the Study of Intraocular Inflammation and Infections

Imaging of the Anterior Segment in Uveitis (Introduction)

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Photography of the anterior segment

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Photography of the anterior segment

Photography of the anterior segment is the method of documentation of the findings of the anterior uveitis. On the other hand this imaging technique is the way to classify objectively the lesions of the eye.

The diagnostic orientation and the estimation of the severity of the disease can be enhanced by the careful interpretation of images. Additionally, the comparison of the lesions of anterior uveitis between different steps of the disease course and also the response to the treatment and follow-up are possible.

Therefore, photography of corneal lesions (i.e. precipitates), anterior chamber (i.e. cells or hypopyon), iris lesions (i.e. granulomas, sectoral atrophy, posterior synechiae) and angle findings (i.e. synechiae) can be documented and the clarity and resolution of photography is crucial for the purposes described.

Specular Endothelioscopy

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Specular endothelial microscopy consists a non-invasive method to examine the structural and functional integrity of corneal endothelium. Currently there are several specular microscope brands available, each capturing the cell images at different calibrations and magnifications. In specular microscopy the image of the corneal endothelium is acquired after a specular reflection of the light from the corneal endothelium facilitating its qualitative, quantitative and morphometric analysis.

Specular microscopy has multiple advantages in the clinical practice, enabling the study of the corneal endothelium in vivo and therefore the observation of clinical disorders. Interestingly, involvement of the corneal endothelium during uveitis has not been thoroughly explored, although it might play a substantial role in or constitute a target of ocular inflammatory processes. It appears that anterior segment inflammation affects the corneal endothelium and the relevant alterations have been observed by specular microscopy in various studies. Those alterations concern abnormal endothelium in the vicinity of keratic precipitates and returned to near normal values on remission of uveitis. Endothelium abnormalities (sometimes they contribute to the diagnostic orientation) include endothelitis (especially in herpetic anterior uveitis), reduction of percentage hexagonality and alterations of mean cell size and cell density. In eyes with recurrent uveitis endothelial blebs are noted as dark shadows or defects in the endothelial mosaic.

In conclusion, the clinical applicability of specular endothelioscopy in uveitic patients could be considered as a useful tool for the evaluation of the corneal endothelium, as it enables the detailed study of corneal endothelium during and after the remission of uveitis.

Session 27 “Imaging of the Anterior Segment in Uveitis” Hellenic Society for the Study of Intraocular Inflammation and Infections

Imaging of the Anterior Segment in Uveitis - Anterior Segment Optical Coherence Tomography (OCT)

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Optical Coherence Tomography in Anterior Uveitis

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Optical Coherence Tomography in Anterior Uveitis

Alexander Charonis, MD
Retina & Uveitis Service, Athens Vision Eye Institute

Purpose: To investigate the role of anterior and posterior segment optical coherence tomography (OCT) in the clinical management of anterior uveitis.

Methods: Analysis of pertinent literature.

Results: The role of posterior segment OCT is well substantiated in the literature in terms of the clinical management of any maculopathy related to anterior uveitis, namely cystoid macular edema. The role of anterior segment OCT, however, is not yet fully substantiated. We analyze herein its role in terms of quantifying anterior segment inflammation and evaluating its structural sequelae.

Conclusions: There is an emerging role of anterior segment OCT in the clinical management of anterior uveitis.

Intraocular and serum cytokines profile in children with endogenous uveitis and different severity of proliferative complications

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Purpose: to study the relationship between aqueous humor (AH) and serum cytokines profile and proliferative complications (anterior and/or posterior synechiae, pupillary membranes, vitreous bands, epiretinal membranes) in children with endogenous uveitis (EU).

Methods. 16 cytokines (IL1 β , IL2, IL4, IL5, IL6, IL8, IL10, IL12, IL17, IL18, TNF α , TNF β , IFN α , IFN γ , VEGF-A, TGF β 1) were studied using multiplex immunoassay (flow cytometer) in 28 samples of AH and serum, taken during cataract surgery from 26 children with anterior (81%), intermediate (15%) or panuveitis (4%) and different degrees of proliferative changes (mild – 3, moderate – 7 and severe – 18 according to proposed classification) and in 14 serum samples from healthy children.

Results. Children with EU had higher serum levels of TGF β 1 than controls ($p = 0.02$) and tendency to higher levels of VEGF-A ($p = 0.06$) and IL18 ($p = 0.09$) that was statistically significant for both cytokines, when we compared cases with proliferative changes of the 1st - 2nd degrees with controls ($p = 0.02$ and $p = 0.016$ respectively) as well as for TGF β 1 level ($p = 0.003$).

In the AH only IL-6 level was higher than in serum ($p = 0.04$). Tendency to higher levels of IL-18 ($p = 0.09$) and TGF β 1 ($p = 0.18$) in children with proliferative changes of 3rd degree than in cases with changes of the 1st - 2nd degrees was discovered.

Conclusion. The results witness a possible pathogenetic role of systemic and local hypersecretion of TGF β 1 and IL18 and systemic VEGF-A in the development of proliferative complications of EU in children.

Monocyte subpopulations and their underestimated role in pars planitis

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Purpose: To evaluate the role of monocytes in pars planitis pathogenesis in the context of different subpopulations of lymphocytes.

Methods: Samples of peripheral blood were collected from 15 patients suffering from pars planitis (PP) and 17 of a control group (CG). All participants underwent full ophthalmological examination and appropriate tests confirming the diagnosis. The flow cytometry readings were performed using previously prepared peripheral blood samples. Subpopulations were identified as follows: 1) monocytes: NCL+INT- CD14+CD16+, CL- CD14++CD16-, NCL- CD14+CD16++ and INT- CD14++CD16+; 2) MDSC- CD16+IDO+ and CD16-IDO+; 3) lymphocytes: Th1- CD194-CD183+IFN+ and CD3+CD8-IFN+, Th17- CD194+CD196+IL17+ and CD3+CD8+IL17+, Treg- CD4+CD25+CD127- and CD4+CD25highCD127-.

Results: We found increased frequencies of all subpopulations of monocytes in PP compared to CG ($p < 0.01$, $p < 0.01$, $p < 0.05$ and $p < 0.001$ respectively in NCL+INT, CL, NCL and INT). The MDSC were increased only when labelled as CD16+IDO+ ($p < 0.05$). Interestingly, the percentage of IL-17A-producing cells, described as CD3+CD8-IL-17A+ and CD194+CD196+IL-17A+, were increased in subjects with PP ($p < 0.001$). We found decreased frequencies of CD3+CD8-IFN- γ +, CD194-CD183+IFN- γ + ($p < 0.01$ and $p < 0.001$) and Treg subsets in subjects with PP (respectively $p < 0.01$, $p < 0.001$ and $p < 0.001$).

Conclusion: Different subpopulation of monocytes can play an important role in the pathogenesis of pars planitis. Increased frequencies of different monocytes subpopulations correspond with higher percentage of IL-17A-producing cells. Additionally, there is a negative correlation between CD4+/CD8+ regulatory T cells and Th1.

Elevation of Th17-related cytokines in the eye with proliferative diabetic retinopathy by intravitreal injection of bevacizumab

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Purpose : To evaluate an effect of intravitreal injection of bevacizumab (IVB) on proinflammation and Th17- cell related cytokines in the eye with proliferative diabetic retinopathy (PDR).

Methods: The study group consisted of 20 eyes of 20 patients with PDR who underwent cataract surgery and vitrectomy for vitreous hemorrhage and/or tractional retinal detachment. Eight patients received IVB at 2 days before surgery. Approximately 0.2 to 0.5 mL of undiluted aqueous humor was collected during cataract surgery when the anterior chamber was replaced by viscoelastic substance. After cataract surgery, vitreous fluid was obtained using a 25G vitreous cutter inserted into the mid-vitreous cavity at the beginning of vitrectomy before active infusion. IL-1 β , IL-4, IL-6, IL-10, IL-17A, IL-17F, IL-21, IL-22, IL-23, IL-25, IL-31, IL-33, IFN- γ , soluble CD40 ligand (sCD40L), and TNF α in the aqueous humor and vitreous fluid were measured by beads-array system.

Results: IL-6 level in both the aqueous humor and vitreous fluid and IL-17F, IL-25 IL-31, IFN- γ and sCD40L levels in the aqueous humor were higher in PDR eyes with preoperative IVB than in those without preoperative IVB. Furthermore, there was positive correlation in IL-6 level between the aqueous humor and vitreous fluid, and levels of IL-17F, IL-25 IL-31, IFN- γ and sCD40L in the aqueous humor were significantly higher than those of the vitreous fluid in eyes with preoperative IVB.

Conclusions: The present study indicates that IVB leads to proliferation of proinflammation and Th17-cell related cytokines in the aqueous humor of eyes with PDR.

Distinct single-cell immune signatures in non-infectious uveitis

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Purpose: To deeply phenotype circulating immune cell subsets in three archetypical and clinically distinct types of non-infectious uveitis.

Methods: We performed flow cytometry for over 40 surface and functional markers on peripheral blood mononuclear cells (PBMCs) in 30 uveitis patients with HLA-B27 associated acute anterior uveitis, idiopathic intermediate uveitis, or Birdshot Uveitis, and compared the results with 16 matched controls. All patients had active disease and were free from systemic immunosuppressive therapy for at least 3 months. Automated data-driven identification and high-dimensional analysis of stratifying cell populations was performed.

Results: Unsupervised hierarchical clustering clearly distinguished uveitis patients from unaffected controls. Identification of cell subsets in multidimensional flow cytometry data revealed that previously identified changes in dendritic and T cell populations in patients with uveitis are not unequivocal. For example, plasmacytoid dendritic cells, and T follicular helper cells and Natural Killers cells were decreased in all patients, but although T helper 17 cells (identified by both surface and functional markers) were increased in uveitis patients compared to unaffected controls, this increase was primarily driven by patient with Birdshot Uveitis. We also performed multivariate clustering to detect rare or common subsets for distinct forms of uveitis that could be missed by manual identification (ie. gating).

Conclusion: Deep phenotyping of circulating immune cell subsets revealed both common molecular fingerprints and disease specific alterations in different types of non-infectious uveitis. We explored previously described as well as newly identified alterations in circulating immune cell subsets in different types of non-infectious uveitis.

Chronic exposure to TNF α impairs retinal pigment epithelium barrier and immunosuppressive functions

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Purpose: The retinal pigment epithelium (RPE) is a monolayer of pigmented cells with important barrier and immuno-suppressive functions. We have previously shown that acute stimulation of RPE cells by Tumor Necrosis Factor (TNF) α down-regulates gene expression of OTX2 (Orthodenticle homeobox 2) and that of other major ocular genes. We here investigated the long-term effects of TNF α on RPE cell morphology and functions.

Methods: Primary porcine RPE cells were cultivated in presence of TNF α (at 0.8, 4 or 20ng/ml) for 10 days. RPE cell morphology and gene expression, barrier, phagocytosis and immunosuppressive functions were assessed.

Results: 1. Cell morphology and gene expression: stimulation by TNF α (i) decreased the number of RPE cells; (ii) increased cell size; (iii) increased the number of multinucleated cells; (iv) and decreased OTX2 expression in a dose dependent manner (all $p < 0.05$). Proliferation and fusion assays suggested that impaired cytokinesis might be involved in multinucleation. 2. Barrier function: stimulation by TNF α (i) disturbed Zonula Occludens 1 cellular distribution and cytoskeletal architecture (actin F) and (ii) significantly decreased RPE transepithelial resistance in a dose-dependent manner (all $p < 0.05$). 3. Immunossuppressive function: prestimulation with TNF α significantly decreased RPE capacity to induce monocyte death after 24h of co-culture ($p < 0.05$).

Conclusions: Chronic exposure to TNF α deteriorates major RPE functions that are essential to vision and might play a key role in the pathophysiology of inflammatory ocular conditions such as age-related macular degeneration or uveitis.

Functionally distinct combination of ERAP1 and ERAP2 are key risk factors for HLA-A29-associated Birdshot Uveitis.

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Purpose: Emerging high-impact studies revealed that polymorphisms in ERAP genes affect their enzymatic activities and predispose to autoimmune diseases that manifest with - or as - uveitis. We hypothesize that combinations of functionally distinct ERAP1 and ERAP2 allotypes confer risk for the development of HLA-A29-associated (Birdshot) Uveitis (BU).

Method: Genotypes of functional variants in ERAP1 and ERAP2 were determined in 83 Dutch BU cases and 890 Dutch controls to map the protein allotypes of ERAP1 and ERAP2 and their contributions to BU disease risk. Protein expression of ERAPs was evaluated in patient material. Fluorogenic and cell-based assays were used to measure enzymatic activities.

Results: Almost all BU cases (>96%) had at least one copy of the ERAP2-coding protein allotype compared to 71% of controls. Considering 10 amino acid positions in ERAP1 together, we identified 8 common ERAP1 protein allotypes in the Dutch population (>1%). After accounting for ERAP2, we observed an independent strong association for a single ERAP1 allotype with BU (OR = 2.3, P = 8.3×10^{-6}), which was replicated in an independent Spanish cohort. Increase in this ERAP1 allotype count was significantly associated with a progressive increased risk for BU. The associated ERAP1 allotype was found in >60% of patients and revealed significant reduction in protein expression and displayed relatively low enzymatic activity.

Conclusion: A functionally distinct combination of ERAP2 and ERAP1 are key pathogenic factors for developing BU and provide rationale for future studies on targeting ERAP1/2 for treatment of BU and genetically related autoimmune diseases.

Human Choroidal Melanocytes and Toll-like Receptors (TLRs)

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Purpose: Uveal melanocytes are heterogeneous melanin-containing cells, distinct from skin melanocytes, within the choroid, ciliary body and iris of the eye. Toll-like receptors (TLRs) are a complex family of receptors involved in pathogen recognition, innate immunity and inflammation. TLRs are reported to be expressed on corneal and conjunctival epithelium, sclera, retina (including RPE) and iris pigment epithelium, and on skin melanocytes. We investigated primary human choroidal melanocytes for TLR4 protein, and examined for effects of the TLR4 ligand, lipopolysaccharide (LPS), on melanocyte secretion of pro-inflammatory factors.

Methods: Primary cultures of choroidal melanocytes were immunolabelled for MART1 and tyrosinase (melanocyte markers) and TLR4 and 7. Melanocytes (n=7) were treated with LPS (0.1ug/ml and 10ug/ml) up to 48 hours. Viability was assessed using MTT assays. Supernatants were analysed with ELISA for IL-8 and MCP-1 (CCL2).

Results: MART1 and tyrosinase were expressed by >95% of melanocytes. Cells showed immunoreactivity for TLR4 and TLR7 (TLR4>TLR7). ELISA showed that stimulation of choroidal melanocytes with LPS (0.1ug/ml and 1ug/ml) induced a marked dose-dependent increase in secreted pro-inflammatory IL-8 (1.0ug/ml LPS; ~400 fold) and MCP-1 (CCL2) (1.0ug/ml LPS; ~4-fold), compared to control cells (48 hrs post-treatment). The viability of the control and LPS-treated cells was similar after 48 hrs treatment.

Conclusions: The findings show that choroidal melanocytes express TLR4 and can be stimulated by LPS (ligand for TLR4) to express pro-inflammatory cytokines (IL-8 and MCP-1). These observations suggest melanocytes may be potential effectors of local immune responses within the human choroid.

Applications and indications of topical cyclosporine

ANDREA LEONARDI¹.

Cyclosporine A (CsA) is a well-known immunosuppressant and anti-inflammatory agent. Its potential topical use was considered more than 20 years ago for the treatment of severe forms of immune mediated ocular surface diseases such as vernal keratoconjunctivitis (VKC) and dry eye disease (DED). Only recently a new formulation of CsA 0.1% cationic emulsion (CE) has been approved in EU to treat severe keratitis in DED patients. DED patients showed a better improvement after 6 months of treatment with CsA compared with vehicle. The clinically significant improvement of keratitis associated to the significant reduced expression of HLA-DR, confirmed the efficacy of CsA to improve inflammation and its damaging effect in DED patients. A recent, phase III, multicenter, double-masked, vehicle-controlled trial, evaluated the efficacy and tolerability of CsA 0.1% CE eye drops for treating patients with severe VKC in pediatric patients. VKC patients who received CsA QID and BID showed significant improvement in keratitis and less use of rescue medication (topical dexamethasone) vs patients receiving vehicle alone over 4 months. VKC symptoms and patient quality of life (assessed by VAS and the QUICK questionnaire) were also significantly improved with QID CsA vs. vehicle. Follow-up at 8 months suggested a good tolerability and efficacy profile, with maintenance of beneficial treatment effects. Altogether, CsA treatment is effective in the improvement of corneal damage associated severe ocular surface inflammation in DED and VKC suggesting that the clinically relevant effects of CsA not only may control the inflammatory process but also prevent the disease progression.

Autologous stem cell therapy for ocular surface thermal or chemical burns

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Limbal stem-cell transplantation is the procedure of choice for the treatment of Limbal Stem-Cell Deficiency (LSCD). Numerous ocular or systemic disorders can result in LSCD, including congenital diseases (e.g. aniridia), acquired diseases due to chemical injuries, immunological diseases, toxicity and infections. The destruction, or severe reduction, of limbal stem cells (LSCs) results in defective wound healing, and ultimate migration of the conjunctiva onto the cornea, which commonly induces visual reduction and chronic inflammation of the ocular surface. Lamellar and/or penetrating keratoplasty cannot be used successfully in these cases as donor corneal epithelium is replaced by that of the recipient within months. In the presence of corneal epithelial stem-cell compartment deficiency, donor graft reepithelialisation will not take place, with subsequent epithelial defects and the ultimate recurrence of conjunctivalization, and the risk of rejection and failure. Unilateral limbal stem-cell deficiency has been successfully treated for years by directly grafting a portion of the healthy limbal tissue taken from the contralateral eye but some concerns exist regarding potential donor-eye risks. To overcome risks for the donor eye, a technique to reduce biopsy dimension using cell expansion in culture has been developed. Autologous Cultivated Limbal Epithelial Transplantation (CLET) was approved by the European Medicine Agency (EMA) in February 2015 for the treatment of corneal burns (Holoclar®).

The unhealthy ocular surface

Stefano Barabino¹.

The tear film, lacrimal gland, cornea and conjunctival epithelia and Meibomian glands work together as a functional unit to provide an efficient system recognized as the ocular surface. Its integrity is necessary for the health and normal function of the eye and visual system. Nervous connections and systemic hormones are well known factors which maintain the homeostasis of the ocular surface and control the response to internal and external stimuli, but recently it has become clear that also immunological mechanisms play a pivotal role in regulating the ocular surface environment. In particular, our studies have demonstrated that anti-inflammatory factors, the expression of vascular endothelial growth factor receptor-3 (VEGFR-3) in corneal cells, immature corneal resident antigen presenting cells, and regulatory T cells play an active role to protect the ocular surface. Dry eye disease (DED) affects millions of people worldwide and negatively influences the quality of life of patients. Although the etiology and pathogenesis of DED remain largely unclear, the disruption of afferent and efferent immunoregulatory mechanisms are responsible for the chronicity of the disease and for its symptoms and clinical signs.

Cataract surgery in HIV+ patients

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Purpose: to study the epidemiologic and clinical findings of cataract, and the long-term results of cataract surgery in HIV+ patients

Methods: data from 32 HIV+ patients, 11 with uveitis or retinitis before surgery and 21 without, with a mean follow-up of 44.9 ± 36.6 months, and those from 114 HIV- patients, 57 with uveitis or retinitis before surgery and 57 without, were compared

Results: HIV+ patients showed a visual acuity improvement after surgery ($p < 0.001$), lower in those with uveitis prior surgery, who were younger ($p = 0.01$) and more frequently male ($p = 0.027$). Posterior synechiae were associated with uveitis prior surgery ($p = 0.038$). Anterior chamber inflammation does not change significantly from baseline in both groups of HIV+ patients. At the end of follow-up, HIV+ and HIV- patients with uveitis prior surgery presented a visual acuity increase ($p = 0.046$ and $p < 0.001$, respectively); the anterior chamber inflammation was similar to baseline in HIV+ patients, while HIV- displayed an increased number of cells ($p = 0.01$). HIV+ patients with senile cataract were more frequently males ($p = 0.005$), younger ($p < 0.001$), with dyslipidaemia ($p = 0.058$), HBV+ ($p = 0.037$) and unilateral cataract ($p = 0.001$) than HIV- ones, but showed the same post-operative course

Conclusion: cataract surgery in HIV+ patients is safe and useful. Uveitis prior surgery did not affect significantly the postoperative course, which is also comparable to that of HIV- patients with uveitis. Systemic co-morbidities are more frequent in HIV+ patients with senile cataract than in HIV- subjects.

Session 30 “Mosquito Borne Causes of Infectious Uveitis” Indochina Ocular Inflammation Study Group and Brazilian Uveitis Society

Mosquito borne infection with ocular manifestation

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Swept source optical coherence tomography in various causes of infectious retinitis

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Purpose: To report swept source optical coherence tomography(SS-OCT) findings in patients with infectious retinitis due to varied etiology and study their correlation with clinical outcome in immunocompetent and immunocompromised patients.

Methods: Retrospective study of patients with infectious retinitis who underwent SS-OCT were included. Comprehensive eye examination findings, SS-OCT characteristics such as foveal thickness (FT) and sub-foveal choroidal thickness (SFCT) and its correlation to clinical and visual outcome were analysed between different groups of retinitis and between HIV positive and negative patients.

Results: Thirty-three eyes of 23 patients were included. Mean age was 35.07±14.54 years(Males-16, Females-11). Of these, ocular toxoplasmosis was the etiology in 10(43.5%) patients, cytomegalovirus in 11(47.8%), herpetic and chikungunya in 1(4.35%) patient each. Sixty percent of patients were HIV positive. Mean SFCT of ocular toxoplasmosis group was 319.44 microns and viral group was 259.47 microns. Two independent t-test analysis revealed statistically significant difference in SFCT between different etiology($p=0.02$). However no statistically significant difference was noted in FT. Significant association($p=0.008$) was noted between presence of HIV and clinical outcome. Improvement in vision was significantly better in HIV negative patients when compared with HIV positive patients. Mean logMAR difference before and after treatment in HIV positive group was -0.1(worsened after treatment), whereas in HIV negative group was 0.26(improvement).

Conclusion: SS-OCT features are characteristic in patients with different causes of infectious retinitis. SFCT plays an important role in differentiating disease etiology over FT alone. SS-OCT can also help in differentiating active versus inactive retinitis and in followup with treatment.

Dengue Fever

Fernanda Porto¹.

Dengue fever is caused by four Flavivirus serotypes, and transmitted by the mosquito *Aedes aegypti*. Dengue is endemic in South East Asia, Central and South America. Globally, approximately 50-100 million cases of dengue fever and 500,000 cases of dengue hemorrhagic fever occur each year. The public health impact of dengue is of considerable international concern, with a growing global incidence owing to developing urbanization, tourism, and trade.

Ocular involvement in dengue fever is uncommon, and occurs one week after the onset of dengue fever (one day from the resolution of fever and at the nadir of the thrombocytopenia). Proposed mechanisms include direct viral infection as well as immunologic phenomena. The presentation of ocular manifestations is varied, including anterior segment abnormalities (subconjunctival hemorrhage, keratitis, corneal erosion, anterior uveitis), intermediate uveitis, posterior segment involvement (retinal hemorrhages, posterior uveitis, foveolitis, maculopathy, retinal vascular occlusions, serous retinal detachment), neuro-ophthalmic disorders (optic neuritis, cranial nerve palsies, neuromyelitis optica), panuveitis, periorbital ecchymosis, and other hemorrhagic complications. Main symptoms include blurring of vision, scotoma, metamorphopsia, and floaters.

Management is based on clinical presentation and includes active surveillance as well as various anti-inflammatory and immunosuppressive therapies. It is unclear if the disease is self-limiting or if treatment is actually beneficial. Prognosis varies, ranging from full resolution to permanent vision loss despite intervention.

Chikungunya in Brazil

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Chikungunya outbreaks occurred in the Northeast region of Brazil in the past year. Ocular findings such as acute anterior non granulomatous uveitis, optic neuritis and scleritis were encountered. We will describe the features of this new uveitis entity.

Controversies in the Management of Infectious Uveitis – Viral anterior uveitis, how long to treat?

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¹Singapore National Eye Centre (Singapore, SG).

Asymptomatic virus shedding occurs in immunocompetent individuals and the herpes viruses genome tends to persist in infected tissues, with lifelong latency and a risk of reactivation. Infection in immunocompetent individuals results in lifelong immunity in most immunocompetent hosts. Ocular damage may arise from both virus-induced cytopathology and the subsequent inflammatory response. Due to the recurrent nature of the disease and the inability of treatment to clear latent virus, herpetic ocular disease causes significant ocular morbidity and impact on visual outcome and quality of life. The chronic and/or recurrent disease course can lead to sequelae such as corneal scarring, posterior synechiae, vision-threatening secondary glaucoma and cataract formation. Although antiviral therapy is indicated in chronic sight threatening uveitis, its long-term benefit in chronic mild or recurrent anterior uveitis remains to be established. The duration of treatment is also unsolved.

Corneal Inflammation Modulation

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Inflammatory and autoimmune disorders of the cornea represent a clinically heterogeneous group of conditions where acute and chronic autoreactive mechanisms can cause significant damage to the eye. Consecutive ingrowth of new blood vessels results in inflammatory cell infiltration which will maintain continuous inflammation.

Therapeutic immunomodulation main goal is to counteract the effect of the disruption of homeostatic mechanisms.

We present a review of the current anti-inflammatory mechanisms, treatment and promising therapeutic strategies and tools.

Multimodal Imaging in Scleritis

Maite Sainz de la Maza¹.

Purpose: To investigate the scleral changes observed in patients with scleritis with a posterior segment swept source optical coherence tomography device (SS-OCT, Atlantis DRI OCT-1, Topcon, Japan). **Methods:** SS-OCT images were acquired in patients with active unilateral scleritis and followed up until remission with sequential scans. Quantitative analysis included measurement of scleral thickness (conjunctiva+sclera). Qualitative analysis included the presence of: 1) subconjunctival hyporeflective areas, 2) scleral hyporeflective areas, 3) collagen fiber separation, 4) collagen fiber aggregation, 5) scleral destruction/scleral thinning areas. The normal fellow eye was used as a control. **Results:** Twenty active scleritis eyes were included in the study. Mean scleral thickness was significantly higher during active phase compared to remission phase ($891.5 \pm 241.7\mu\text{m}$ vs $687.4 \pm 142.1\mu\text{m}$, $p < 0.001$). No significant differences were observed between the inactive phase and the normal fellow eye (659.3 ± 63.8 , $p = 0.63$). All eyes showed subconjunctival and scleral hyporeflective spaces in active phase, which resolved completely in remission (100% and 0%, respectively). Collagen fiber separation and aggregation was observed in 100% and 15% in active phase, and only 10% and 5% in remission. No differences in scleral destruction/scleral thinning were observed in active and inactive phase and were just seen in necrotizing scleritis eyes. **Conclusion:** SS-OCT can be employed to obtain direct images of the sclera, allowing adequate identification of conjunctival and scleral layers that might render useful in the assessment of the scleral inflammation. These findings may have implications for the treatment of scleritis.

Clinical features of infectious scleritis

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Infectious scleritis is a rare but potentially devastating condition associated with multiple aetiologies, including viruses, fungi, bacteria and even parasites. Diagnosis of infectious scleritis is frequently challenging, not only because of the usual low index of suspicion, but also due to difficulties in identification/culture of implicated microorganisms. Characterization of clinical features possibly distinctive of infectious scleritis may thus orient the clinician to pursue proper investigations for etiologic confirmation. This presentation will review the importance and clinical features of the most common etiologies of infectious scleritis. Techniques of scleral sampling and main diagnostic investigations in this context will be also briefly presented, illustrated with cases of clinicopathologic correlation.

Necrotizing Viral Retinitis

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Necrotizing viral retinitis is potentially devastating ocular infectious disease. Necrotizing viral retinitis is commonly related to herpetic viral retinitis that including Acute Retinal Necrosis (ARN), Progressive Outer Retinal Necrosis (PORN), and Cytomegalovirus (CMV) retinitis. It is representing a real ocular emergency and may lead to permanent visual loss in case that not recognize earlier. Necrotizing viral retinitis affects healthy and immunocompromised individuals. Diagnosis of Necrotizing viral retinitis is primarily based on typical clinical features and could be supported by laboratory tests of ocular fluids in atypical cases. Management of necrotizing viral retinitis depends in early recognition and immediate medical treatment .Treatment of these viral infections is complex and requires systemic as well intravitreal antiviral medications with careful monitoring.

Toxoplasma Retinochoroiditis

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Ocular toxoplasmosis is the most prevalent form of infectious posterior uveitis worldwide. Although congenital infections have long been considered to account for most ocular disease, there is now clear evidence that the majority of ocular toxoplasmosis infections are acquired after birth. Following either congenitally or postnatally acquired infection, *Toxoplasma gondii* may induce a latent disease wherein *T. gondii* tissue cysts establish residence in various organs, including the eye. These cysts may subsequently rupture, resulting in clinical recurrence. Active ocular toxoplasmosis may occur at any age but is most common during the second through fourth decades of life. The objective of this presentation is to describe the posterior pole manifestations of ocular toxoplasmosis as well as its pathogenesis, epidemiology, clinical findings, diagnosis, and current management.

Clinical Pearls in Diagnosis and Management of Uveitis Emergencies: Vogt-Koyanagi-Harada disease and sympathetic ophthalmia

Mohammed Al Shamrani¹.

Vogt-koyanagi-Harada syndrome is a multisystem autoimmune disease involve ocular, auditory, nervous and integumentary. In Saudi Arabia, it has been reported as the most common cause of non-infectious uveitis. It affects individuals in their second to fifth decades but it has been reported in children as young as 4 years of age. Initial presentation of the disease is with disc hyperemia and exudative retinal detachment few days after neurological (headache, meningism...) and auditory (tinnitus) symptoms. Usually the anterior segment inflammation isn't obvious at first presentation that leads to delay in the diagnosis and mismanagement. Diagnosis of the disease depends mainly on the history and clinical examination with the help of characteristic features on fluorescein angiography. Early and aggressive treatment of the acute stage within two weeks of the onset of the disease is associated with a better outcome. Treatment with pulse dose of intravenous methylprednisone for 3 days followed by slow tapering of oral prednisolone and starting immunosuppressants early in the course of disease reduce the chance of reaching the end stage picture of the disease with sunset glow fundus appearance and other complications.

Sympathetic ophthalmia is a bilateral granulomatous panuveitis that occurs following surgery or ocular trauma. It has been reported following minor ophthalmic procedures like paracentesis and reported after trans-scleral cyclophotocoagulation. The delay between trauma and developing disease is commonly two weeks to three months but can be years. Aggressive treatment by corticosteroids and immunosuppressants has improved the outcome of the disease.

Recognition of Uveitis Emergencies

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Abstract

Aim:

to help ophthalmologists to develop a systematic clinical approach in diagnosing emergent uveitis based on medical history, clinical findings and investigations.

Method:

A systematic review to provide general ophthalmologists and residents with clinical guidelines for the main uveitic entities that require immediate recognition and urgent intervention in the emergency room to prevent severe permanent visual loss.

Results:

Attendees will be able to recognize uveitis related emergencies and formulate an evidence based clinical approach to manage them.

Conclusions:

Cases of emergent uveitis require immediate systematic approach to prevent permanent visual loss. A high index of suspicion with accurate recognition of specific diseases and timely initiation of proper therapy are essential.

Current management of CMV anterior uveitis

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Recognizing CMV as the cause of the anterior uveitis is important as appropriate antiviral therapy given in a timely manner may aid in controlling the intraocular pressure and preserving the endothelium whilst mismanagement with steroids only will hasten its decompensation. The diagnosis is confirmed by obtaining a positive polymerase chain reaction or demonstrating local antibody production for CMV on aqueous analysis. Response to ganciclovir gel 0.15% is good and if maintained, may prevent relapse. Eyes that fail to respond to commercially available gel often respond to ganciclovir 2% eyedrops. Oral valganciclovir is highly effective but costly and should be used as a last resort.

CURRENT MANAGEMENT OF CMV RETINITIS

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Cytomegalovirus (CMV) retinitis continues to be an important complication of AIDS, although it occurs at a markedly lower incidence in the West since the introduction of combination antiretroviral therapies (cART); however, it is a growing problem in some areas of the developing world, especially in Southeast Asia. Populations at risk are now more heterogeneous than before antiretroviral drugs became available, because of different durations of cART exposure and different levels of immune recovery at diagnosis of CMV retinitis. Treatment strategies are therefore more complex than when anti-CMV drug regimens were initially formulated. This lecture will describe populations at risk for active CMV retinitis; characteristics of CMV retinitis in the cART era; and risk factors associated with immune recovery uveitis (IRU) among those who had CMV retinitis before beginning cART. The lecture will review current management strategies for AIDS-related CMV retinitis, including choice of anti-CMV agents, and will address treatment controversies, including whether or not to withhold cART until all CMV retinitis lesions are inactive, as a means of reducing the risk of IRU; local vs. systemic anti-CMV drug delivery, and the risks and benefits of each approach; and when to discontinue anti-CMV drug therapy in patients experiencing immune recovery. Strategies for managing CMV retinitis in resource poor areas of the world will be described. Also addressed will be risk factors for, and treatment of, disease reactivations; and management considerations in patients with complications of IRU. Outcomes associated with CMV retinitis among long-term survivors after immune recovery will also be described.

Diagnostic of CMV anterior uveitis

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Purpose: To evaluate diagnostic methods and clinical signs of CMV anterior uveitis (AU), a rare and newly diagnosed entity in western countries (Europe and USA).

Design: Retrospective observational case series including patients from 2 European referral centers with clinical characteristic signs of CMV AU.

Methods: Anterior chamber (AC) paracentesis was performed to obtain a positive polymerase chain reaction (PCR) and/or Goldmann-Witmer coefficient (GWc) for CMV in aqueous. Inclusion criteria: patients with clinical signs of CMV AU (Posner-Schlossman syndrome (PSS) or Fuchs uveitis (FU)). Exclusion criteria: all other causes of AU excluded by classical AU evaluation, signs of CMV posterior uveitis and severe immune-depression.

Results: We report 21 patients (Brussels: n=15, Utrecht n=6), including 15 (71.4%) males, mean age of 38.57±12.11 years, with unilateral uveitis (100%) and signs of PSS (n=20, 95.2%), FU (n=1, 4.7%), endotheliitis associated with AU (n=4, 19.04%), glaucoma complications in n=8 (38.1%) and glaucoma surgery n=2 (9.5%). PCR was positive in 15/21 (71.4%) and GWc in 8/9 patients (88.9%) in aqueous for CMV. GWc was the only positive test in 6/9 patients. PCR was negative in the 6 patients who had only keratic precipitates (KPs) but no cell anymore at the time of aqueous tap. In order to confirm the diagnosis of CMV AU, repeated aqueous taps were needed, twice in five cases and thrice in one case.

Conclusion: Combining PCR and GWc and repeated aqueous taps were found to be very helpful to confirm the clinical diagnosis of CMV AU.

Fuchs uveitis : recent data

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It is important to recognize Fuchs heterochromic iridocyclitis (FHI) in order to avoid useless systemic work up and the toxic effect of long term topical, or even, systemic treatment. FHI diagnosis rely on a series of clinical characteristics some of them being already described by Fuchs in 1926. However, recently, some novel clinical findings have been described, such as choroidal thinning. Similarly, FHI classification has evolved, as some authors have insisted on the vitreous inflammatory component and proposed to classify FHI as intermediate rather than anterior uveitis. Finally, tremendous progress has been made these last 10 years in the understanding of the link between FHI and viral infection, mainly rubella and CMV, the latter opening the door to a specific treatment. In conclusion, since its description in the early years of the 20th century, many new data have continued to precise the characterization of FHI helping the clinician to make the correct diagnosis.

Treatment of VKH and other non infectious uveitides

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The principles of therapy of VKH disease are to suppress the initial intraocular inflammation with early and aggressive use of systemic corticosteroids for prolonged periods, often initially administered either orally or intravenously and accompanied by systemic immunomodulatory therapy during months to years. This treatment may also be supplemented with intravitreal injections of triamcinolone. In patients with chronic ocular inflammation who require high maintenance doses of corticosteroids, conventional immunosuppressive therapy is recommended, including antimetabolites (methotrexate, azathioprine and mycophenolate mofetil), alkylating agents (chlorambucil and cyclophosphamide), and antibiotics (cyclosporine and tacrolimus). Biologic drugs are a modern treatment strategy, including anti-TNF (tumor necrosis factor) and anti-VEGF (vascular endothelial growth factor) agents. An expert panel of the American Uveitis Society generated guidelines for the use of TNF blockers, considering adalimumab and infliximab as potential second-line immunomodulatory agents against severe ocular inflammatory diseases, such as posterior and diffuse uveitis.

Unlike VKH disease, Behcet disease is only treated with corticosteroids for short periods of time. Immunosuppressive drugs play an important role in the treatment of this disease. In cases of multifocal choroiditis, the first line of treatment are corticosteroids. However in patients with Birdshot choroidopathy, since it is a chronic entity, the second line of treatment (immunosuppressive drugs) is essential to keep inflammation inactive and to avoid complications.

The majority of uveitis related to arthritis are anterior and many of them improve just with topical treatment as opposed to the systemic treatment of JIA-related uveitis.

Thyroid orbital disease: other issue

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Autoimmune thyroid disease (AITD) patients are predisposed to other autoimmune diseases such as Myasthenia Gravis (MG), Diabetes Mellitus type I, pernicious anemia, and Autoimmune Adrenal Insufficiency. The main ocular/orbital characteristics of AITD mainly Grave's are: proptosis, eyelid retraction, diplopia and visual loss due to compressive optic neuropathy. MG occurs in 0.2% of AITD patients compared to prevalence of 20 per 100,000 and incidence of 2-3 per 100,000 in general population. On the other hand 5-10% of myasthenic patients might have AITD, much more common than in general population. In most patients the AITD symptoms occur before or simultaneously with those of MG. Ocular type of MG is more common in AITD patients, usually with mild clinical symptoms. One of the most significant clinical signs of MG in patients with AITD is ptosis. Diplopia is a common symptom of both diseases, still good clinical examination might differentiate between restrictive diplopia of ocular AITD and external ophthalmoplegia seen in MG. Single fiber-EMG has high sensitivity for ocular MG and is a helpful diagnostic test. Anti Acetylcholine receptor antibodies are positive in 35-70% of ocular MG patients. Both conditions, AITD and MG, should be treated if they occur concurrently in the same patient, although treating thyroid disorder might have positive effect on MG in some patients.

The role of imaging in diagnosis of VKH

Nazanin Ebrahimiadib¹.

The role of imaging in diagnosis of VKH

Harada is a common panuveitis in Iranian population. In a patient with acute decrease in vision and serous retinal detachment suspicious to VKH, we need an available test to give a clue leading to the diagnosis of VKH. Indocyanine green or fluorescein angiography is not feasible in many centers of the country and the patient need to wait several days to perform the test. We benefit the EDI-OCT in these situations as an available and noninvasive test. Based on findings such as choroid homogeneity and disappearance of its vascular pattern, inward bulging of retina and RPE, folds in RPE and Bruch's membrane and serofibrinous serous retinal detachment with septate, ophthalmologist feel confident to start the treatment such as methylprednisone pulse and immunomodulatory therapy. Corticosteroid treatment may have adverse effects on central serous chorioretinopathy (CSC), which is sometimes hard to differentiate from VKH by conventional OCT, and fluorescein angiography, however it lacks the EDI-OCT features of VKH.

This imaging modality also helps in monitoring VKH activity, although in this scenario it is better to order an ICG which gives information from the whole choroid and is not limited to the macula. In addition, in some circumstances when the patient is receiving treatment, ICG looks normal, however the choroid is still thick. The importance of this finding remains to be elucidated.

Altogether, EDI-OCT is a non-invasive and helpful imaging modality in the diagnosis of acute VKH.

Longterm clinical outcome of Korean VKH patients

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Clinical records of 81 Korean VKH patients were retrospectively reviewed. Among them, 13 patients completed longer than 10 years of follow-up, and the mean age was 47.3 ± 17.8 years. The mean follow-up duration was 162.7 ± 40.0 months (range, 120.2 - 253.1 months). All patients were treated with systemic and topical corticosteroids, and 7 patients were also treated with immunosuppressive agents. The mean cumulative incidence of recurrence was 4.0 times. During follow-up, cataract, secondary glaucoma, epiretinal membrane, and choroidal neovascularization developed in 18 (69.2%), 14 (53.8%), 12 (46.2%), and 1 eye (3.8%) eye(s), respectively. Final best corrected visual acuity (BCVA) was 20/50 or better in 16 (61.5%) eyes, and 20/200 or worse in 4 (15.4%) eyes. BCVA at last visit was better than initial BCVA in 18 (69.2%), and 8 (30.8%) eyes maintained or deteriorated visual acuity. Subfoveal choroidal thickness (SFCT) at the last visit was not correlated with final BCVA ($R^2 = 0.03$, $P = .57$) and recurrence ($P = .27$). Although most of VKH patients preserved useful vision after longterm follow-up, some of them had irreversible severe visual loss. Secondary glaucoma was the most frequent complication associated with irreversible severe visual loss.

The spectrum of Vogt–Koyanagi–Harada disease in Iran

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Purpose: To report the spectrum of Vogt-Koyanagi-Harada (VKH) disease in Persians

Material and Methods: Retrospective chart review of patients diagnosed with VKH disease at four referral centers in Iran. Patients' demographics, ocular and extraocular manifestations, treatment modalities, complications and visual outcomes were collected and analyzed.

Results: Eighty eight patients with a mean age of 32.1±12.6 years (range 7-79 years) were studied. Fifty nine patients (67.0%) were female. Sunset glow fundus was seen in 40.9% and nummular peripheral chorioretinal scars in 55.7% of eyes. Integumentary findings were noticed in 14.8% of the patients. In patients with acute presentation, exudative retinal detachment was the most common ocular finding (87.8%) followed by optic disc swelling (71.4%). Anterior uveitis and vitritis, each were found in about half of the studied eyes. Auditory symptoms were reported by 38.8% of the patients. Overall, immunomodulatory agents were used in 72.7% of the patients. Ocular complications occurred in 36.4% of eyes (mean follow up 3.8 years, range, 6–228 months). Final visual acuity was 20/40 or better in 73.3% of eyes. Four patients (4.5%) were classified as having ‘complete’ type of the disease, 36 (40.9%) ‘incomplete’ type, and 48 (54.5%) ‘probable’ type.

Conclusion: In our series, there are clinical features that differ from those reported in other studies. While auditory symptoms occurred in more than one third of patients, integumentary findings were rather rare. Most patients exhibited the ‘probable’ type of VKH disease. The overall visual prognosis was favorable.

Modifying the gut microbiome to treat uveitis

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Purpose

The gut microbiota and the metabolites that they produce are integral in states of disease and health. The purpose of this study was to test the hypotheses that oral antibiotics could ameliorate autoimmune uveitis through the modification of gut microbial constituents and T cell subsets; and that gut bacterial metabolites of dietary fiber administered exogenously might attenuate disease.

Methods C57Bl/6 (Bl/6) or B10.RIII mice underwent immunization with IRBP and MTX to produce induced experimental autoimmune uveitis (EAU). Broad spectrum antibiotics given singly or combined (ampicillin, metronidazole, neomycin, ampicillin) or short chain fatty acids (SCFA)(propionate, butyrate, acetate) were given orally. Clinical scoring was performed in addition to immunofluorescence staining on retinas, and flow cytometry on lymphoid tissues in the body.

Results

Quadruple broad-spectrum antibiotics as well as the single antibiotics metronidazole and ampicillin markedly attenuated disease severity in EAU mice through an increase in regulatory T cells in the gut lamina propria and extraintestinal lymph nodes, and by modifying the gut microbial constituents away from potential uveitis-associated bacterial strains, Clostridia, Adlecreutzia, and Dorea spp. Moreover, exogenously administered oral SCFAs decreased disease severity in Bl/6 but not B10.RIII mice with EAU through a reduction in effector T cells subsets in multiple extraintestinal lymph nodes and through a stabilization of ileal mucosa.

Conclusions

Modifying the gut microbiota through oral antibiotics or through exogenous short chain fatty acids may be part of a therapeutic approach to treat autoimmune uveitis.

Surgical Treatment of CME

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Purpose: Describe the medical evidence supporting surgical management of cystoid macular edema in patients with uveitis

Methods: Case reports and literature review. Examination of the pathophysiology, imaging, and interpretation of uveitic CME.

Results: Best evidence for surgical management of uveitic CME is in cases with recalcitrant edema, controlled inflammation, and macular traction related to vitreous adhesions and/or epiretinal membrane. In some cases, pars plana vitrectomy used as a disease-modifying therapy will also ameliorate uveitis CME by down-regulating the ocular inflammation.

Conclusions: In selected cases, vitrectomy and membrane peeling will improve outcomes in uveitic CME. Caution is advised for surgery in eyes with uncontrolled inflammation or structurally weakened tissue from chronic edema.

Treatment of Uveitic Macular Edema

C, Stephen Foster¹.

The essential element in treating macular edema associated with uveitis is to be absolutely certain that all evidence of inflammation has been abolished; otherwise all therapy for the edema will fail. The following have a track record for facilitating resolution of macular edema in someone who has had uveitis which is now in remission:

1. Topical, regional injection, intraocular injection and systemic corticosteroids
2. Topical and systemic non-steroidal anti-inflammatory agents
3. Intraocular anti-VEGF agents
4. Systemic interferon
5. Intramuscular octreotide
6. Hyperbaric oxygen
7. Intravenous tocilizumab
8. Subcutaneous interferon

Paradoxical Hypersensitivity Reactions in Ocular manifestations in HIV infection

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The HAART therapy has completely changed the spectrum of ocular manifestations in HIV infection. There is the occurrence of syndrome of Immune Recovery Uveitis with its various manifestations occurring after HAART therapy. Also a new variety of the healed CMV retinitis is seen. Mixed opportunistic infections are recently seen in the era of HAART therapy. These can occur even in the setting of absence of any evidence of active or healed CMV Retinitis. Incidence of retinal detachment is on the rise. Ocular tuberculosis is also frequently seen.

Paradoxical reactions in ocular TB

Sudha Ganesh¹.

World Health Organization reports, 9.0 million people developed active tuberculosis (TB) in 2013 – an overall annual incidence of 126 / 100,000 persons. Diagnosis of ocular TB is often presumptive and its management lacks uniform guidelines. Establishing prior exposure to MTB through the use of TST, IGRA, or chest X-ray or CT is straightforward. Techniques such as culture and biopsy, have limited utility in ocular TB. Multiplex, multi-targeted PCR for one or more MTB DNA is useful for diagnosis. Management of ocular TB, requires combined ATT and anti-inflammatory therapy. Paradoxical reaction in TB occur in patients receiving ATT. It consists of clinical worsening of preexisting TB lesions or development of new lesions in patients who initially improved on treatment. Recognition of a paradoxical reaction from treatment failure, drug resistance, poor compliance or secondary diagnoses can be difficult. Paradoxical reactions may be due to an abnormal immune response like reconstitution and strengthening of host immune response and/or a hyper-sensitivity reaction to mycobacterial antigens released / decrease in immunosuppression mechanisms. Paradoxical reactions occur in HIV co-infected patients with reductions in viral load and increases in CD4+ counts after HAART. Intraocular TB presents as posterior uveitis, choroidal tubercles, subretinal abscess, serpiginous-like choroiditis, granulomatous anterior uveitis, panuveitis or intermediate uveitis. Paradoxical worsening in ocular TB occurs in immunocompromised and immunocompetent patients. Prompt recognition and timely institution of corticosteroids can lead to restoration of vision. ATT need not be altered or discontinued in such cases.

Session 41 “Paradoxical Hypersensitivity Reactions in Management of Infectious Uveitis”
Uveitis Society of India

Paradoxical reactions in ocular TB

Sudha Ganesh¹.

Paradoxical Hypersensitivity Reactions in Ocular Syphilis

Padmamalini Mahendradas¹, Ankush Kawali, Rohit Shetty.

Paradoxical Hypersensitivity Reactions in Ocular Syphilis

Systemic manifestation of Jarisch–Herxheimer reaction is commonly associated with treatment of syphilis. Paradoxical hypersensitivity reactions in ocular syphilis can occur following antimicrobial therapy. Proposed mechanisms include endotoxin release from the death of organisms, delayed hypersensitivity, and decreased suppressor mechanisms.

We reviewed the medical records of patients diagnosed with ocular syphilis from 2007-2017 at our hospital. Ocular syphilis was diagnosed on the basis of non-treponemal and treponemal antibody tests. 22 eyes of 16 patients diagnosed with ocular syphilis were included. Five patients were seropositive for HIV. Clinical presentations ranged from anterior uveitis to panuveitis. All patients showed clinical improvement in the level of ocular inflammation with intravenous/ intramuscular penicillin except two cases who developed paradoxical hypersensitivity reactions. Our experience on ocular syphilis data will be presented along with literature review.

What we have learned of HLA and pars planitis

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Pars Planitis, mexican patients compare with others countries

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To describe the incidence of Pars Planitis in mexican population and to report clinical features, complications and visual prognosis and compare theses results with other countries.

New molecular mechanisms of immune privilege

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Mesenchymal Stem Cell Therapy to Promote Corneal Allograft Survival – Current Status and Pathway to Clinical Translation

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Mesenchymal stem (stromal) cells (MSCs) are adult multipotent cells with the ability to differentiate into several cell types such as chondrocytes, adipocytes or osteocytes. However, much of the current interest in therapeutic applications of MSCs to various disease settings can be linked to their immunomodulatory and anti-inflammatory properties. Several groups have investigated the ability of MSC to modulate corneal allograft survival. Most reports showed positive results, however, as different MSC-application strategies (time point of injection, cell number/number of injections, route of injection, MSC source, MSC licencing) have been investigated in various animal models it is difficult to compare and validate the results. Upon administration, the ability of MSC to promote graft survival has been attributed to their interaction with the recipient immune system, altering the Th1/Th2 balance, expanding Foxp3+ regulatory T cells, polarizing macrophages and inhibiting intra-graft infiltration of antigen presenting cells. MSC have shown potential to modulate corneal allograft rejection in various models using MSC from different species. In particular for high-risk patients with poor prognosis MSC-therapy might be a promising approach to promote corneal allograft survival.

In this presentation the therapeutic potential of MSC to promote corneal transplant survival in both low- and high-risk pre-clinical models and its pathway to clinical translation will be discussed.

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Session 44 “Common uveitis obstacles in Southeast-Asia” Uveitis Society of Thailand

Challenges faced in treating uveitis in Myanmar

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Session 44 “Common uveitis obstacles in Southeast-Asia” Uveitis Society of Thailand

CMV retinitis: when systemic treatment is unaffordable

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Challenges in Management of Ocular Tuberculosis in Southeast-Asia.

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Objective: To report, review and opening discussion in management of ocular tuberculosis in Southeast-Asia.

Contents: Ocular tuberculosis is one of the most challenges infectious uveitis which can present in various from of uveitis. Thailand is a part of Southeast-asia which an endemic area of tuberculosis. Used of BCG vaccine in newborn are standard in this region. Clinical use of tuberculin skin test and/or interferon gamma essay as a part of diagnosis for ocular tuberculosis in previous BCG vaccinated is challenges. Screening, diagnosis and management of ocular tuberculosis in immunocompromised patients with HIV infection, uveitis patients who on immunosuppressive medication(s) are controversial. Late presentation caused from limit access to healthcare system and patient compliance to anti-tuberculosis medications are challenges in our region. Various response to systemic anti-tuberculosis drugs in presumed ocular tuberculosis and drug resistance tuberculosis will be discuss in this session.

Conclusion: Management of ocular tuberculosis in Southeast-Asia is challenges in many aspect such as screening, diagnosis, recurrent, adherence to anti-tuberculosis medications, various treatment response and drug resistance tuberculosis. Clinical evaluation, reasonable investigations and careful interpretation, cooperate with multidisciplinary specialists in management of ocular tuberculosis are essential.

Diagnosis of Behçet uveitis (Combined societies session: Behçet disease in 2017)

Ilknur Tutkun¹.

Currently the diagnosis of ocular Behçet disease is based on the association of rather nonspecific signs of uveitis with systemic manifestations of the disease. In all the diagnostic criteria sets developed to date eye lesions are nonspecific and do not allow the diagnosis of isolated ocular involvement or differential diagnosis of Behçet uveitis from other uveitic entities. A multicenter study is underway in order to develop ocular diagnostic criteria for Behçet uveitis.

The role of OCT and OCT-A in Behçet uveitis

SUMRU ONAL^{1,2}.

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OCT enables noninvasive diagnosis and monitoring treatment response of macular edema in Behçet uveitis (BU). It is also useful in diagnosis of other macular complications such as foveal atrophy. OCT can predict degree of visual acuity damage in patients with remission of BU. Decreased foveal and outer retinal thickness and disruption of IS/OS and OS/RPE lines are associated with poor visual function as a result of irreversible damage to macula. OCT provides information on pathogenesis of retinal infiltrates and neuroretinitis in BU. Non-glaucomatous retinal nerve fiber layer (RNFL) defects occurring as sequela of infiltrates at post pole can easily be detected by OCT. This finding is a helpful diagnostic clue in early BU. EDI OCT shows no significant change in subfoveal choroidal thickness in patients with early BU (≤ 4 years). There is however choroidal stromal expansion which is not associated with subfoveal choroid thickening (assumed to be due to inner stromal involvement). Central foveal thickness (CFT) correlates with FA and has high sensitivity and specificity in predicting active intraocular inflammation in BU. CFT may serve as a noninvasive measure to assess inflammatory activity in patients with early BU. OCT-A visualizes and characterizes perifoveal microvascular alterations better than FA in eyes with active BU. Perifoveal deep capillary plexus is more severely affected than superficial capillary plexus in eyes with perifoveal and diffuse retinal capillary leakage on FA. CME, foveal atrophy, retinal infiltrates, and RNFL defects are associated with localized or diffuse non- or hypo-perfusion in perifoveal retinal capillary plexuses.

Poor prognostic factors in ocular involvement due to Behçet's syndrome

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Ocular involvement of Behçet's syndrome (BS) is characterized by recurrent episodes of inflammatory attacks leading to severe visual loss. Severity and the frequency of inflammatory attacks involving the posterior segment determine the extent of permanent structural changes labeled as 'damage' and as a result, the degree of irreversible visual loss(1-4). Young male patients are known to carry the highest risk for poor visual outcome. Other risk factors that have been associated with poor visual outcome include posterior uveitis attacks, more than three uveitis attacks per year, strong vitreous opacity, exudates within the retinal vascular arcade, neovascularization of the disc and macular ischemia (1-4).

We designed a study to determine the factors associated with poor visual outcome. We aimed to analyze the demographic and clinical features of 50 patients with ocular involvement due to BS who developed the first ocular episode during our follow-up, and who had been followed continuously for at least 10 years in our center. In this retrospective study, we analyzed especially a. the role of inflammatory attacks leading to poor prognosis, b.clinical features observed during the recurrent attack period such as hypopyon, vasculitis, cystoid macular edema (CME), retinal branch vein thrombosis and vitreous haze and c. anatomical localization of the damage.

References:

1. Sakamoto M, et al. Ophthalmology. 1995.
2. Demiroglu H, et al. Ophthalmology. 1997.
3. Tugal-Tutkun I, et al. Am J Ophthalmol. 2004.
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Macular Edema and the MUST Trial: Lessons Learned

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Macular edema (ME) is the leading cause of visual loss in uveitis. The Multicenter Uveitis Steroid Treatment (MUST) trial, a 2-year randomized clinical trial which was followed by an extended follow-up of the cohort, provides valuable information on the outcomes of uveitic ME. The MUST Trial randomized patients to systemic therapy vs. fluocinolone acetonide implant. 117 patients (57 in the systemic therapy arm and 60 in the implant arm) had macular edema at baseline. At the primary endpoint of 2 years, 71% of ME improved (20% reduction in macular thickness) & 60% resolved. 62% of eyes treated with systemic treatment needed adjunctive regional corticosteroid injections for their ME. There was a greater decrease in macular thickness with the fluocinolone implant. Eyes with macular leakage on FA (76%) were more likely to have improvement in ME compared to eyes without leakage (58%). Fewer eyes had ME in the implant group than in the systemic therapy group at 6 months. The reverse pattern was observed at 6 years, with a reduction in macular thickness from baseline favoring systemic therapy. In summary, although the fluocinolone implant appeared to have some advantages in terms of outcomes of ME in the short-term, 6 year outcomes favored systemic therapy. Currently the MUST group is implementing two other clinical trials to compare treatments for uveitic ME. The POINT Trial compares different corticosteroid injections, and the MERIT Trial compares a corticosteroid implant to non-steroid alternatives. These studies will provide an evidence basis to guide treatment of uveitic ME.

Enlargement of foveal avascular zone in diabetes

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Optical coherence tomography angiography (OCTA) is a newly developed technology that makes it possible to visualize chorioretinal vessels without dye injection. Using OCTA, we have reported that the enlargement of foveal avascular zone (FAZ) were noted even in the diabetic eyes without retinopathy (Takase N, et al. Retina 2015). Other reports also confirmed that the enlargement of FAZ in the diabetic eyes (Choi W, et al. Retina 2017), and the FAZ size were correlated with the severity of diabetic retinopathy (Bhanushali D, et al. Invest Ophthalmol Vis Sci, 2016). The enlargement of FAZ in proliferative diabetic retinopathy would be developed from ischemic capillary dropout. However, the mechanism of FAZ enlargement in early diabetes are still unknown. Leukostasis is a phenomenon which is found in early diabetic retina (Miyamoto K et al. Proc Natl Acad Sci USA, 1999), and local transient capillary obstruction caused by leukostasis may lead to FAZ enlargement. On the other hand, neurodegeneration in early diabetes are also reported and ganglion cell loss may influence the size of FAZ. This presentation will explore the role of inflammation in early diabetic retina, and OCTA and en face OCT findings will be discussed.

High-fat diet induces retinal inflammation and visual function impairment.

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Metabolic syndrome is one of the major social issues. It will disturb not only individual quality of life, but also acquisition of labor power because it can cause disorders in various organs and tissues. Here, we report retinal phenotypes induced by constant intake of high fat diet in Balb/c mice. The high fat diet did not cause diabetes but caused visual function impairment in the mice. Local expression of inflammatory cytokines and macrophage recruitment were increased, and retinal and choroidal inflammation was induced. The mechanism most likely involved accumulation of the oxidized low-density lipoprotein in the retinal pigment epithelium and macrophages.

DUSN

Dipankar Das¹.

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Session: Asia-Pacific Intraocular Inflammation Study Group (APIISG symposium) - Infectious uveitis you cannot afford to miss

Topic- DUSN

Abstract:

Diffuse unilateral subacute neuroretinitis (DUSN) also called unilateral wipe out syndrome, caused by more than one type of motile and sub-neural, retinal nematode. Nematodes in DUSN may invade the skin and migrate hematogenously to retino-choroidal complex. These small worms are thought to induce toxic, inflammatory and autoimmune reaction to the retino-choroid and its adjoining structures. DUSN can present as early and late stage manifestations. There have been variable sizes of worms detected and reported with longer worms leaving a tract of coarse clumping of pigment epithelium. Ancillary multimodal imaging and electrophysiology tests are helpful to diagnose this rare parasitic disease. Laboratory diagnosis should include eosinophils count for the nematode infections. Other diseases that have to be rule out are syphilis, sarcoidosis, toxoplasmosis and any other infections mimicking DUSN. Optic neuritis, pars planitis and some of the white dot syndromes need to be excluded for making the diagnosis. Management of DUSN depends if the worm is visible or not. Visible live nematodes are treated with retinal photocoagulation. Systemic treatments with anti-helminthic and oral steroid are given in the patient in confirmed cases. This presentation will highlight the interesting clinical cases seen and documented subsequently for this condition with follow-ups.

Endogenous endophthalmitis

Shwu-Juan Sheu¹.

Endophthalmitis is a rare but severe form of ocular inflammation due to infection of the intraocular cavity that may lead to irreversible visual loss if not treated properly and timely. Exogenous endophthalmitis occurs when infecting organisms gain entry into the eye via direct inoculation, while endogenous endophthalmitis occurs when infectious agents are hematogenously spread into the eye from a distant focus of infection. The diagnosis of endophthalmitis depends mostly on the clinical findings on ophthalmological examination. Delayed diagnosis of endogenous endophthalmitis can lead to not only visual loss but also increased risk of mortality. Since ocular and systemic symptoms of endophthalmitis are usually non-specific, early diagnosis relies on the alertness of clinicians. Early diagnosis and proper treatment are keys to saving the eye. This talk will include case-based discussion on endogenous endophthalmitis of different origins.

Session 48 “Infectious uveitis you cannot afford to miss” Asia Pacific Intraocular Inflammation Study Group

DUSN

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Tuberculous uveitis

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Background: Re-emergence of tuberculosis (TB) has been facilitated by reservoirs of infection in neglected populations. Despite reports of TB uveitis being the first presentation of patients with pulmonary TB, the management approach to TB uveitis remains controversial along with possible geographical variation in phenotypic expression. This study utilises big data analytics to examine regional variation management practices and outcomes for TB uveitis.

Methods: 10-year retrospective multinational cohort study of patients from 25 ophthalmology referral centers diagnosed with TB uveitis between January 2004 and December 2014, and a minimum follow-up of 1 year.

Results: 962 patients had TB uveitis with a mean age of 41.3 (range 4-90), and a slight predominance of males (52.6%, n=506/962) and asian ethnicity (74.4%, n=690/927). Most patients had no symptoms (92.0%, n=655/712) or history (76.7%, n=604/787) of pulmonary TB. Treatment regimens and outcomes in these patients are analysed with stratification by geographic region.

Patients with western geographical origin ($p=0.010$), African or Hispanic ethnicity ($p < 0.001$), and positive immigrant status ($p = 0.027$) had poorer survival outcomes.

Conclusion: Findings from this analysis facilitate the designing of future collaborative studies together with respiratory and infectious disease experts to develop guidelines for this early opportunity to address this form of extrapulmonary TB.

Infectious uveitis you can't afford to miss - toxoplasmosis retinochoroiditis

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Toxoplasma retinochoroiditis remains the most common cause of posterior uveitis world wide, with varied clinical presentations. It is now recognised that primary toxoplasmosis ocular infections do occur in adults, in addition to the classic reactivations of pre-existing scars.

Multiple treatment paradigms have been described in the literature for acute infections/reactivations, with no consensus on what may be the best approach. However, good evidence now exists supporting prophylactic treatment to prevent future recurrences, particularly when such relapses are frequent or may be immediately sight threatening due to their anatomical location.

This talk will present a number of varied presentations of toxoplasmic retinochoroiditis, both classic and unusual, in addition to a review of the current literature on its management.

Updates on the Current Understanding and Management of Emerging Infectious Disorders with Ocular Manifestations: Dengue and Beyond

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Dengue fever is the most common mosquito-borne viral disease in humans transmitted by the *Aedes aegypti* mosquito. The ocular involvement, which may be serotype specific and varying from region to region, ranges from mild blurring of vision to catastrophic visual loss occurring within a month of dengue infection. Fundal manifestations typically occur one week after the onset of fever, just as the fever is settling and the platelet count is recovering. Ocular manifestations are variable and generally involve the retinal and/or choroidal vessels, predominantly over the macular. Immunosuppressive treatment is controversial. Prognosis is variable and when there is occlusive vascular involvement or the maculopathy involves large retinal vessels, the visual acuity and field loss tends to be greater. This talk will also briefly cover other arthropod borne viruses such as Chikungunya and West Nile virus ocular manifestations.

Toxoplasmic chorioretinitis in the immunosuppressed patient

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Ocular toxoplasmosis is the most frequent cause of posterior uveitis. Usually it occurs in otherwise healthy young adults. Typical manifestations in the posterior segment consist of an unilateral focus of retinitis near to an atrophic, pigmented retinochoroidal scar together with vitritis of variable severity. Vasculitis may also be present. Anterior uveitis, granulomatous or not granulomatous, is frequent and ocular hypertension may be also present. Immunosuppressed patients show atypical manifestations of ocular toxoplasmosis. This group include patients with the acquired immunodeficiency syndrome (AIDS), persons who are systemically immunosuppressed pharmacologically or as a result of an underlying disease and the elderly. Lesions in these patients may be large, multiple or bilateral. Sometimes, the clinical picture may mimic an acute retinal necrosis syndrome and the risk of complications including retinal detachment, epiretinal membrane, chronic cystoid macular edema is high. A matter to remark is the association of ocular toxoplasmosis and cerebral toxoplasmosis in HIV-positive patients. Management of ocular toxoplasmosis in immunosuppressed patients is challenging due to its atypical presentation, the extension of lesions and the risk of structural complications. When facing an atypical presentation of intraocular inflammation, intraocular fluid analysis is useful and may allow an early treatment, which consists of standard antimicrobial treatment together with systemic steroids.

Viral uveitis in the immunocompromised patient

Maite Sainz de la Maza¹.

Viral posterior uveitis is one of the most visually devastating causes of uveitis worldwide. Many viruses share in common a lifelong persistence of their genome in infected tissues and the risk of reactivation. Acute control of infection is mainly dependent on virus-specific T lymphocytes, which eliminate intracellular pathogens. However, the activity of these lymphocytes in individuals with diminished immune function decrease or even disappear leading to a particular risk of acute infection and recurrence. Both virus-induced cytopathology and the subsequent inflammatory response are responsible for ocular damage. Most common viral posterior uveitis in the immunosuppressed patient are caused by herpes simplex virus (HSV-1 and HSV-2), varicella-zoster virus (VZV), and cytomegalovirus (CMV). Acute retinal necrosis is an acute unilateral diffuse necrotizing retinitis with panuveitis progressing to retinal detachment. The vast majority (over 50%) is due to VZV, followed by HSV-2 (5.1%), and HSV-1 (3.5%). Progressive outer retinal necrosis is a form of viral retinitis in immunosuppressed patients that is characterized by posterior multifocal outer retinal to full thickness necrotizing retinitis with sparing of the perivascular retina, usually due to VZV. CMV retinitis, unlike isolated anterior uveitis, usually occurs in immunocompromised individuals; it presents bilaterally, with one of two presentations: a granular necrotizing retinitis or a hemorrhagic necrotizing retinitis, usually associated with an occlusive retinal vasculitis. Early identification leading to a prompt and specific treatment can be achieved with a combination of maintaining a high suspicion, recognizing certain clinical features, utilizing multi-modal imaging, and obtaining specimens for molecular diagnostic testing.

Syphilitic uveitis in immunocompromised patients.

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Objective: to compare clinical and serological features between immunocompromised (IC) and non-immunocompromised (NIC) patients with syphilitic uveitis.

Methods: single-center, retrospective, comparative study. IC group was defined as CD₄ lymphocyte counts <500 Cells/ μ L or T-Cells <26%. Variables were compared by non-parametric statistics.

Results: from 24 recorded patients in the last 7 years, 4 should be excluded. Twenty patients (29 eyes), all males, 39.5 (24-76) years old were analyzed, 9 IC and 11 NIC. No demographical differences were found between groups. HIV co-infection was more frequent in IC (88% vs. 45%), with significant higher viral loads in HIV IC patients than in HIV NIC ($p < 0.001$). No differences were found in syphilitic stage, presence of extraocular signs or symptoms, including neuro-syphilis. Anatomic and specific types of uveitis were also found not different between groups, except for optic disc swelling that was more frequent in the IC group (85% vs. 46%, $p = 0.050$). Visual acuity (VA) improved significantly in IC during follow up, from 0.70 (2.00-0.00) to 0.13 (0.80-0.00) logMAR, $p = 0.012$ and eyes with VA <0.5 (Snellen) decreased from 71% to 14% ($p = 0.006$). Improvement of VA in NIC, however, resulted non-significant. Serum VDRL titers were found significantly higher in the IC group (median 1/768 vs. 1/8, $p = 0.042$), no other serological differences were noted in serum nor CSF.

Conclusions: Optic disk swelling as the only differential clinical feature, higher serum VDRL titers and more intense VA improvement after treatment was found in this defined IC patients with syphilitic uveitis.

Intraocular fluid analysis; the old and the new.

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Intraocular fluid analysis for the diagnosis of intraocular disease and particularly infectious uveitis has been around for some time. Bacterial and fungal culture as such have been available for over a century now and still is the gold standard for identifying the causative agent of endophthalmitis. With the discovery of antibodies indirect means of diagnosing an infection became possible. In 1954 Goldmann and Witmer, Bern, Switzerland, published their famous article describing the work on the detection of specific antibodies in the aqueous humor of horses with ocular leptospirosis, and of rabbits and humans with tuberculous uveitis, providing the basis of the Goldmann-Witmer coefficient (GWC). With the discovery of PCR early 1980s a whole new area of possibilities opened up. PCR is now the most applied diagnostic tool for directly identifying a causative agent, particularly for viral infections where culture is not sensitive or not possible at all. Though for the diagnosis of infectious uveitis PCR is most widely used, the Goldmann-Witmer coefficient is still a valuable tool, as it proves more sensitive late in disease and in chronic infections. Whereas antibody detection is still applied similarly as it was more than 50 years ago, nucleic acid detection is continuously developing with next generation sequencing being the most recent technological step forward. In addition to detection of foreign DNA or RNA and specific antibodies, identification of other substances such as cytokines and chemokines and other protein biomarkers are increasingly becoming the focus of interest for the diagnosis of intraocular inflammatory diseases.

Longitudinal monitoring of ocular fluids in acute retinal necrosis

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Purpose: To monitor semi-quantitative Varicella zoster viral load dynamics in aqueous humor in acute retinal necrosis (ARN) during the course of disease and for duration of intravenous or intravitreal treatment.

Methods: Cycle threshold (CT) values, which correlate inversely with viral load, were determined in aqueous humour by real-time PCR at different time points in 12 eyes (11 patients) with the clinical characteristics of ARN. In addition, Goldmann-Witmer coefficient (GWC) was calculated. Furthermore, disease activity was scored based on fundus photographs.

Results: The CT values increased in all eyes when disease activity decreased and became negative in 10 of the 12 eyes in the convalescence stage. The CT values correlated significantly with disease activity ($P = 0.0006$; Spearman's ρ : -0.5421). GWC for VZV was initially negative in 5 cases but became positive during the course of disease in all, except for one eye of a bilateral case.

Conclusion: In general the viral load diminished during the course of the disease and seemed to correspond with the disease activity. Therefore, real-time PCR CT values can be helpful in treatment decisions of ARN.

Transthyretin as a potential aqueous humor biomarker in JIA-associated uveitis

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PURPOSE. To investigate the presence of biomarkers in aqueous humor (AH) from children with uveitis.

METHODS. AH (n = 73) and serum (n = 105) samples from 116 children were analyzed using surface enhanced laser desorption/ionization time of flight mass spectrometry (SELDI-ToF MS). The samples were divided into the following groups: JIA, silent chronic anterior uveitis (CAU), other uveitis entities, and noninflammatory controls. Statistical biomarker identification, multivariate statistical analysis and biochemical identification of potential biomarkers was performed followed by ELISA validation of 57 paired AH en serum samples not included before.

RESULTS. In the JIA group, one AH protein peak at mass/charge (m/z) 13,762 had qualitative and quantitative differences in expression compared with the other uveitis entities and the controls, but not to the group of silent chronic AU. Its quantitative expression in AH of patients with JIA and other silent chronic AU was positively associated with uveitis activity. This protein was identified as transthyretin (TTR). TTR concentration in the aqueous humor of independent 57 samples differed significantly between the study groups with highest levels in JIA-samples and lowest levels in control samples. (p=0.003). The difference between JIA and non-inflammatory controls was the biggest (p<0.001), while only a trend to significance could be seen between the JIA and other uveitis group.

CONCLUSIONS. TTR is a potential intraocular biomarker of JIA-associated uveitis. Its role in the pathogenesis of silent chronic AU with and without arthritis needs further investigation.

Autoantibody profiling in intraocular fluid of patients with uveitis

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Purpose: An autoimmune origin is presumed in many uveitis entities. A high prevalence of serum antiretinal antibodies (ARAs) in patients with uveitis has been previously described, however the intraocular proof of autoimmune processes in uveitis was so far lacking. Herein we investigate the prevalence of multiple specific ARAs in intraocular fluid of patients with uveitis.

Methods: Autoantibody profiling with 188 different retinal antigens was performed by a multiplex immunoassay with intraocular fluid samples of 76 patients with uveitis. Clinical data from uveitis patients were collected and statistical analyses were executed to evaluate associations between intraocular ARAs and clinical characteristics. Controls consisted of 19 intraocular fluid samples from cataract patients.

Results: A spectrum of 22 different ARAs was present in higher levels in patients with uveitis than in controls ($p \leq 0.05$), but in moderately elevated titres. High elevations of ARAs were observed in varicella zoster virus-induced uveitis, multiple sclerosis-associated uveitis and patients with unexplained uveitis but positive quantiferon test. Presence of macular edema was associated with high intraocular levels of tyrosinase antibodies.

Conclusions: Patients with uveitis were characterized by the presence of a broad spectrum of moderately elevated levels of intraocular ARAs. High intraocular ARA levels were found in several uveitis entities and in patients with macular edema. Our results favour secondary production of ARAs and not their inciting role.

Molecular analysis of Aqueous humor: liquid biopsy for classification of eye disease'

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Retinal diseases generally are vision-threatening conditions that warrant appropriate clinical decision-making which currently depends upon extensive clinical screening by specialized ophthalmologists. In the era where molecular assessment has improved dramatically, we recently provided proof of concept for molecular biomarker profiling in ocular fluids to classify archetypical ocular conditions affecting the retina (age-related macular degeneration, idiopathic non-infectious uveitis, primary vitreoretinal lymphoma, and rhegmatogenous retinal detachment) with one single test. Unsupervised clustering of ocular proteins could discern disease specific profiles, which we exploited to develop and independently validate models that were able to correctly classify patients with high overall accuracy, sensitivity and specificity. Current efforts combine proteomic and genomic approaches to optimize early and accurate disease detection as a diagnostic aid for ophthalmologists in the care for patients with eye conditions.

Treatment to target in intermediate uveitis

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Introduction: Intermediate uveitis is associated is characterized by the presence of snowbanking and/or snowballs in the vitreous. Cystoid macular edema occurs in about 30 – 60% of cases and is the main cause of decrease of visual acuity. **Materials and methods :** 61 consecutive patients with intermediate uveitis were prospectively recruited. Two subgroups of patients were identified on the basis of the need or not of systemic treatment. In a post hoc analysis a cut-off value of central foveal thickness for systemic treatment was determined. **Results:** BCVA (LogMar) was of 0.222 ± 0.249 in the treated patients and improved to 0.087 ± 0.125 6 months after therapy. Mean central foveal thickness (mm) was respectively of 325 ± 122 and improved to 209 ± 86 mm after therapy. Correlation between LogMar visual acuity and central foveal thickness was strong ($r=0.7436$, $p<0.0001$, Pearson correlation coefficient). The cut-off value of CFT for initiating systemic treatment was determined at 215.5 mm in a post hoc analysis (sensitivity 62.5% specificity 96.4%). CFT measured in Cirrus HD-OCT was correlated to mean Central Macular Thickness (CMT). **Conclusion:** A cut off value of CFT resulting from a post hoc analysis of collected data has a strong specificity and a moderate sensitivity.

Role of biologicals in the treatment of JIA associated uveitis

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In a step-by-step approach, topical and/or systemic corticosteroids and synthetic and/or biological disease-modifying antirheumatic drugs (DMARD) are often needed to achieve inactivity of uveitis associated with juvenile idiopathic arthritis (JIA). If ocular inactivity is not achieved with synthetic DMARD (mainly methotrexate), tumor necrosis factor-alpha (TNF- α) inhibitors are used. For severe uveitis that is refractory to TNF- α inhibitors, further treatment options are required. However, only limited data is available for newer biologicals (e.g., rituximab, abatacept or tocilizumab).

Optical coherence tomography angiography (OCT-A) as a new diagnostic tool in uveitis

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Today, conventional angiography (FA/ICG) and optical coherence tomography (OCT) are commonly used imaging modalities in the diagnostics of patients with intraocular inflammation and macular pathologies supplementing each other. OCT-A is a recently developed noninvasive, noncontact and dye-less technique to image all layers of the retinal vasculature. It is a technique based on de-correlation between the signals of two sequential OCT cross-sectional scans repeated at the same location caused by blood flow. OCT-A is a method that allows for indirect visualization of all major vascular layers of the retina through blood flow measurements. Compared to FA, OCT-A can better image the deep retinal capillary network. Since vascular abnormalities may be more pronounced in the deep layer, OCT-A may be superior to FA for the early detection of CME and for the evaluation of the foveal avascular zone (FAZ) in advanced stages. This presentation reviews the current knowledge of OCT-A in the diagnostics of uveitis patients.

Intravitreal Therapy in Endogenous Uveitis

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Background: Systemic biologics have found broad acceptance in the treatment of uveitis. The treatment of isolated ocular disease with a systemic therapy goes along with an increased systemic morbidity during their use, but, in contrast to corticosteroids, usually not thereafter. Local therapeutic strategies, on the other hand, have to be balanced against their possible local side effects, as known from intravitreal corticosteroids. Moreover, they do not control systemic disease and a possible partner eye affection.

Results: Published information on intravitreal immunomodulatory therapy for uveitis beyond corticosteroids is limited. Anti-VEGF agents have been used to treat secondary threats as vascular leakage and uveitic macular edema, secondary choroidal neovascularization, but without controlling the inflammatory activity. Intravitreal infliximab may lead to a severe intraocular inflammation requiring vitrectomy in more than 30% of cases and ERG abnormalities. Intravitreal adalimumab, in contrast, is well tolerated, but does not demonstrate a relevant morphologic or functional benefit. Rituximab, a chimeric monoclonal antibody targeting CD20, effectively eradicates primary intraocular lymphoma (PIOL). Since a large number of patients with PIOL eventually develop CNS lymphoma, it should – like Methotrexate - be considered an adjuvant to systemic chemotherapy or radiation.

Conclusion: Despite a better understanding of specific inflammatory pathways resulting in several potential targets for therapy, the role of biologics has as yet not been established. These may be indicated in patients not sufficiently responding to systemic therapy and to escape the need for intravitreal corticosteroid therapy and the corresponding risks of glaucomatous optic neuropathy and cataract development and progression.

Choroidal thickness in birdshot retinochoroiditis over time and effect of early sustained therapy

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EDI-OCT measurement of choroidal thickness in birdshot retinochoroiditis has been reported in two articles in 2015 (11 patients) and 2016 (8 patients) which both showed decreased thickness. In this study the decrease of choroidal thickness was observed over time in 18 patients with birdshot retinochoroiditis. Thickness was put in relation with treatment and it was shown that choroid is significantly thinner in undertreated patients. Patients adequately treated conserved a significantly thicker choroid and presented significantly less birdshot fundus lesions.

Choroidal Lesions in Disseminated *Mycobacterium chimaera* Infection

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Purpose: To describe characteristics of choroidal findings in patients with disseminated *Mycobacterium chimaera* infection subsequent to open-heart surgery.

Methods: Nine patients (18 eyes) with systemic *M. chimaera* infection were assessed. Choroidal lesions were evaluated by biomicroscopy, fundus autofluorescence (FAF), enhanced-depth OCT Imaging (EDI-OCT), fluorescein/indocyanine green angiography (FA/ICG) and OCT angiography (OCTA). Relationships between choroidal and systemic disease activity were sought.

Results: All 9 patients were male, aged between 49 and 66 years, all were diagnosed with endocarditis and/or aortic graft infection. Four patients had mild disease with inactive lesions. Five patients had progressive ocular disease with occurrence of new and active lesions. All 10 eyes with active lesions had hyporeflective choroidal lesion by EDI-OCT. Lesions by ICG outnumbered lesions found by photography. One eye developed choroidal neovascularization. OCTA showed areas with reduced perfusion at the level of the inner choroid. All patients with progressive ocular disease had evidence of systemic disease activity.

Conclusion: Multimodal imaging is helpful to recognize progressive ocular disease in patients with disseminated *M. chimaera* infection.

Characterization of the microbiome on the ocular surface

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The cultivable microbiota on the ocular surface has been extensively studied, and shown to be composed of Gram-positive bacteria, predominantly *Staphylococcus epidermidis* and *Propionibacterium*. The lids are more commonly colonised than the conjunctiva, and the cornea has been considered to be essentially sterile. Recently, non-culture techniques have been used to evaluate the microbiome of the conjunctiva. The microbiome of a niche such as the conjunctiva is defined as the type of microbial DNA found in that area. The most commonly used technique to study the microbiome is sequencing of the 16s rDNA gene and comparing the sequence in databases. This technique has revealed a different microbiome compared to the culturable microbes, with *Acinetobacteria*, *Corynebacterium*, *Sphingomonas*, *Pseudomonas*, *Neisseria* (all Gram-negative bacteria) and *Streptococcus* (Gram-positive) being the predominant microbiome. I will present the latest data from my laboratory on the microbiome of the eye, and compare between the conjunctival microbiomes of humans and animals.

Epidemiology and Nomenclature of Ocular Allergy

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The terms Ocular Allergy and Allergic Conjunctivitis are often used interchangeably to reference a constellation of allergic diseases of the ocular surface and eyelids. Agreement as to Nomenclature variously occurs among international consortiums, continent wide organizations such as EACCI, and through single country professional organizations. Correlation between clinical presentations and laboratory and diagnostic test findings are often used to distinguish between the different diseases. Threads woven through most nomenclature schemes include IgE mediated, non-vision threatening disease and IgE plus cell mediated sight threatening disease.

Surprisingly, the epidemiology of Ocular Allergy reported alone is uncommon. The vast majority of epidemiology reports of allergic eye disease focus on Seasonal Allergic Conjunctivitis as found in conjunction with Seasonal Allergic Rhinitis. Next most commonly reported is Vernal Keratoconjunctivitis. These reports are typically from a single country n areas of the world where the incidence is high.

The Prevalence of Tear Abnormalities in Asymptomatic Patients with Cataract and Its Associated Risk Factors: A Hospital-based Study

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Purpose:

To evaluate the prevalence and risk factors of tear abnormalities in asymptomatic patients with cataract in Jakarta Eye Center, as unrecognized preexisting dry eye disease (DED) carries a potential of ocular surface damage after cataract surgery.

Method:

We included 34 eyes from 19 patients (median age [range] 65.5 [56.0 – 83.0] years; 68.4% were female) without any symptoms of DED in this cross-sectional study. Asymptomatic DED is considered when Ocular Surface Disease Index (OSDI) score was 25 or less. We evaluated noninvasive tear breakup time (BUT) using Tearscope® and Schirmer test, and history of diabetes and hypertension.

Result:

Median BUT and Schirmer of all eyes were 11.1 (6.2 – 28.9) seconds and 10.0 (3.0 – 28.0) mm, respectively. Among 34 eyes, 16 eyes (47.1%) had one abnormal tear parameter, either shortened BUT or low Schirmer result. Furthermore, 7 out of 34 eyes (20.6%) even had both decreased tear quality and production. Female had tendency of having lower BUT ($p=0.15$). Hypertension was not associated with tear abnormalities, while diabetes was associated with lower BUT, 6.9 ± 0.9 seconds in diabetes compared to 11.5 (6.4 – 28.9) seconds in nondiabetes ($p=0.006$).

Conclusion:

More than two thirds of eyes with cataract that were asymptomatic showed abnormal tear film condition. Ophthalmologists should be aware of the presence of DED even in patients without any symptoms as it may affect the result of cataract surgery or even worsen the ocular surface condition. Patients with diabetes had lower initial BUT regardless of the symptoms of dry eye.

The Collaborative Ocular Tuberculosis Study (COTS)-1: A multinational description of the spectrum of choroidal involvement in 299 patients with tubercular uveitis

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Background: Tubercular uveitis is a heterogeneous disease. The objective of this report is to contribute a global description of the spectrum of choroidal involvement in Tubercular uveitis and treatment outcomes using big data analytics.

Methodology: Retrospective cohort study of Tubercular uveitis patients with choroidal involvement from 25 global centers between January 2004 and December 2014. Medical record of patients with a minimum follow-up of 1 year were reviewed.

Results: 299 patients with Tubercular uveitis and any form of choroidal involvement were included. Patients had a mean age of 39.4 (range 9-90 years), predominantly males (n=167/299, 55.9%), of Asian ethnicity (n=201/289, 69.6%) and geographical origin (n=180/299, 60.2%). The phenotypic variants include serpiginous-like choroiditis (SLC) (46%), choroidal tuberculoma (13.5%), and multifocal choroiditis (MFC) (9.4%). Other phenotypes not commonly associated with tubercular uveitis were also noted (n=54/299, 31%). 264 patients were treated with anti-tubercular therapy (ATT) (n=264/299, 88.3%), 272 patients with steroid therapy (n=272/299, 91.0%) and 28 patients with steroid-sparing immunosuppressive agents (n=28/257, 10.9%). Treatment failure was noted in 42 patients (n=42/299, 14.0%). Among patients that received ATT, those with ampiginous choroiditis (APC) and SLC appeared to have superior outcomes on survival analysis however this was not statistically significant ($X^2 = 10.487$, $p = 0.063$).

Conclusion: This study provides a comprehensive description of spectrum of choroidal involvement in Tubercular uveitis. Most patients achieve disease resolution on treatment with ATT. SLC is the most common phenotype, encompassing a higher proportion in Asia Pacific region as opposed to the West.

Photodynamic therapy of fungal inflammatory eye diseases: studies 'in vitro' and 'in vivo'

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Purpose: To determine the best methylene blue (MB) concentration and best laser exposure for carrying photodynamic therapy (PDT) against fungi. Then study the effectiveness of PDT with methylene blue on modified model of fungal keratitis in rabbit.

Methods: We compared effect of different MB concentrations on growth of *C.albicans* and established best laser exposure 'in vitro'. We modeled fungal keratitis in 15 rabbits. Control group received standard anti-inflammatory therapy, main group also received PDT.

Results: The most effective parameters of MB was 0,1%, and 3 min for the laser exposure. Rabbits: in the control group with moderate fungal keratitis duration of a disease was $14,25 \pm 1,0$ days (outcome - local stromal opacity with neovascularisation), and $21,1 \pm 1,7$ days with severe keratitis (outcome – intensive stromal opacity with active neovascularisation). In the main group with moderate fungal keratitis duration of a disease was $7,15 \pm 0,75$ days (outcome – dotted superficial opacity), and severe - $14,25 \pm 1,0$ days (outcome – local stromal opacity with inactive neovascularisation).

Conclusions: The most effective parameters for carrying photodynamic therapy were 0,1% methylene blue and 3 min for the laser exposure. PDT appliance with methylene blue in the treatment of fungal keratitis in the experiment can reduce treatment time and achieve healing of the cornea with better optical result.

International Preferred Practice Patterns for Syphilitic Uveitis

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Background: Syphilis is re-emerging worldwide, accompanied by advances in diagnostics and treatment. We investigated current practice for syphilitic uveitis amongst uveitis specialists internationally.

Methods: A 25-question survey, focused on presentation and management of syphilitic uveitis, was distributed to 268 members of the International Ocular Inflammation Society (IOIS).

Results: Responses were received from 108 IOIS members (40.3%), who managed 5.8 mean cases of syphilitic uveitis in 2016. 45 of 83 respondents with relevant experience (54.2%) report increased frequency from 10 years prior. For 80 of 108 (70.1%), referrals come from other ophthalmologists with a diagnosis of uveitis. The most common presentations are posterior uveitis (64/107, 59.8%) and panuveitis (26/107, 24.3%), and common complications include optic neuropathy (73/106, 68.9%), macular edema (54/106, 50.9%) and posterior synechiae (54/106, 50.9%). 66 of 108 (61.1%) order simultaneous treponemal and non-treponemal serological tests for diagnosis, and lumbar puncture is requested by 98 of 108 (90.7%). HIV testing is ordered by most (103/106, 97.2%). 67 of 108 (65.7%) refer patients to infectious disease physicians for treatment; patients of 71 of 108 respondents (65.5%) receive treatment with intravenous aqueous penicillin G or ceftriaxone. Systemic corticosteroids are prescribed by 86 of 105 (81.9%), and initiated with or immediately after antibiotics in 66 of 101 (65.3%). The clinical factor considered best predictive of poor outcome is optic neuropathy (93/107, 86.9%).

Conclusions: Increasing numbers of syphilitic uveitis are being managed by uveitis specialists. Our findings provide a guide for best practice within the ophthalmology community.

Chlamydia trachomatis Infection triggers epigenetic mechanisms associated with Epithelial-Mesenchymal Transition in conjunctival epithelial cells.

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Chlamydia trachomatis (Ct) can induce scarring disease of the ocular mucosa, known as trachoma, the most common infectious cause of blindness worldwide. We hypothesized that epithelial-mesenchymal transition (EMT) contributes to the fibrotic process in trachomatous scarring. Infection of human conjunctival epithelial cells (HCjE) with Ct activated signaling pathways involved in EMT induction, which was correlated with decreased expression of E-cadherin, guardian of the epithelial phenotype. In addition, Ct infection was associated with increased expression of two mesenchymal cell markers: fibronectin and α -SMA. The DNA methylation statuses of selected regions of E-cadherin, fibronectin, and α -SMA genes revealed that Ct infection was accompanied with changes in DNA methylation of the E-cadherin promoter, while the expression of the two mesenchymal markers was not related with this epigenetic event. Our data suggest that Ct infection of conjunctival epithelial cells induces EMT-like changes that go along with modification of the methylation profile of the E-cadherin promoter and could, as one of the earliest events, contribute to processes triggering conjunctival scarring.

The Cytokine Interleukin-6 and the Chemokines CCL20 and CXCL13 are Novel Biomarkers of Specific Endogenous Uveitic Entities

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Purpose: To determine levels of the cytokines IL-1b, IL-6, IL-21, IL-22 and IL-23 and the chemokines CXCL13, CCL19, CCL20 and CCL21 in aqueous humor (AH) samples from patients with specific uveitic entities.

Methods: Paired serum samples (n=13) and AH samples (n=111) from patients with active idiopathic granulomatous uveitis (IGU) or with uveitis associated with HLA-B27-related inflammation, Behçet's disease (BD), Vogt-Koyanagi-Harada (VKH) disease or sarcoidosis and control patients were analyzed in two different multiplex assays.

Results: IL-1b, IL-21, IL-22 and IL-23 were not detected in any AH sample. CCL21 concentrations in serum were significantly higher than in AH. CCL19 levels in AH and serum were not significantly different. CCL20 and CXCL13 levels in AH were significantly higher than in serum. IL-6 was not detected in serum samples. IL-6 AH levels were significantly higher in patients with HLA-B27-associated uveitis and BD patients than in patients with VKH disease, sarcoidosis and IGU ($p<0.0001$). CCL20 AH levels were significantly higher in HLA-B27-associated uveitis than in BD, VKH, sarcoidosis and IGU ($p=0.001$), whereas CXCL13 AH levels were significantly higher in VKH disease and IGU than in HLA-B27-associated uveitis, BD and sarcoidosis ($p=0.007$).

Conclusions: IL-6-driven immune responses are more potent in HLA-B27-associated uveitis and BD compared with VKH disease, sarcoidosis and IGU. CCL20 appears to be a specific biomarker of HLA-B27-associated uveitis, whereas CXCL13 appears to be a biomarker of VKH disease and IGU. Our findings suggest that IL-6, CCL20 and CXCL13 could serve as drug targets for treatment of specific clinical entities of endogenous uveitis.

The efficacy and safety of an extemporaneous preparation of 2% ganciclovir eye drops in CMV anterior uveitis

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Background: To evaluate the efficacy and safety of 2% ganciclovir topical eye drops in cases with a diagnosis of cytomegalovirus (CMV) anterior uveitis.

Design: Retrospective cohort design.

Methods: This monocenter study enrolled 11 eyes (11 patients) with CMV anterior uveitis. All cases were proved by positive polymerase chain reaction for CMV DNA from aqueous tapping and received topical 2% ganciclovir. Outcome measures were best-corrected visual acuity, anterior chamber cell, coin-shaped and other keratic precipitates, intraocular (IOP) pressure (Goldman applanation tonometry), the number of anti-glaucoma drugs used, the frequency of steroid eye drops used daily and side effects over a 12-month follow-up period. Side effects after applying topical 2% ganciclovir were recorded using questionnaires.

Results: Eleven patients were included. Mean age was 49.0 ± 17.8 years. IOP, number of antiglaucoma drugs used and keratic precipitates decreased significantly at first week ($p < 0.013$, $p < 0.024$, $p < 0.031$) followed by decreased anterior chamber cells and significantly reduced frequency of applying steroid eye drops at four weeks ($p < 0.034$, $p < 0.017$). Visual acuity significantly improved at five months. All clinical improvement was maintained to 12 months and keratic precipitates were eliminated in 90% of all cases. However, in 27% of discontinued medicine cases, inflammation was recurrent. No significance was observed in all factors between recurrent and non-recurrent groups. The most common side effect was eye irritation (27.27%). No severe complication from the medicine was detected.

Conclusion: Extemporaneous topical 2% ganciclovir was effective and safely controlled CMV anterior uveitis. The medication is noninvasive, economical and convenient for hospitals where commercial topical ganciclovir is unavailable.

Endogenous fungal endophthalmitis

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Purpose:

The main aim of this study was to evaluate the outcome of early intervention in immunocompromized patients with endogenous fungal endophthalmitis.

Methods:

A retrospective review of the clinical records of five patients with confirmed diagnosis of fungal retinitis has been conducted. The clinical diagnosis of fungal endophthalmitis was confirmed in all patients by culture and cytology of vitreous specimens or blood cultures. Three patients were treated with systemic antifungal agents, one patient was treated with intravitreal and systemic antifungal and one patient was treated with vitrectomy and intravitreal antifungal agent.

Results:

There were three male and two female patients with an age range of one month to 65 years and a mean age of 34 years. Intraocular inflammation was brought under control in all five patients. All patients had complete resolution of vitritis and the chorioretinal lesions. The visual acuity was improved in four patients and one patient lost his vision due to a delay in the initiation of proper antifungal treatment.

Conclusion:

Endogenous fungal endophthalmitis can affect any age group. Early diagnosis and prompt treatment may lead to control of the intraocular inflammation and good visual outcome.

Enbril associated optic neuritis

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Purpose: To report a uveitic challenging case

Methods: The patient is a 47-year-old male presenting sudden onset of blurring in his right eye 3 days prior to his clinic visit. It was accompanied by mild soreness with eye movements. Tracing back his medical history, he was diagnosed as ankylosing spondylitis in 2010. On examination, best corrected visual acuity (BCVA) was 0.4 od and 1.2 os. The IOP was 8 mmHg in his right eye and 15 mmHg in his left eye. The slit-lamp exam of right eye demonstrated few small Kps and about 2+ cells in the anterior chamber. There was right grade I relative afferent pupillary defect with right disc swelling. The left disc was normal. Ishihara color vision test showed mild dyschromatopsia in his right eye. Under the impression of optic neuritis, he was treated with intravenous methylprednisolone of 1g for 3 days then continued with oral prednisolone. However, the resolution of disc edema and visual function recovery were incomplete.

Results: After reviewing his chart carefully, we found that he was treated with enbril for his ankylosing spondylitis since 2 months ago. Due to the suspect of enbril-associated optic neuritis, the enbril was discontinued. After discontinuing enbril, his disc edema and macular edema resolved gradually. Eight weeks after discontinuation of enbril, the edema of disc and macula resolved complete and the BCVA of his right eye achieved 20/20.

Conclusions : Patients being treated with TNF α antagonist should be closely monitored for the development of ophthalmological or neurological signs and symptoms.

Secondary Ocular Metastasis To Neuro Endocrine Carcinoma, Acoustic Neuroma: Case Report.

Boris Bajaire¹, Sierra Haishel , Pardo Juan.

¹IPS Bajaire (Bogota , CO); ²IPS Bajaire; ³IPS Bajaire .

Objective:to describe one case with metastasis to a neuroendocrine tumor.

Purpose :To perform the teaching of ophthalmologists and physicians in general to take into account, patients with facial symptoms of low response to treatment, in addition the association between ocular metastasys and neuroendocrine tumors and auditory nerve tumors, due to the little existing bibliography.

Methods:Retrospective review of one case.

Results:Diagnosis of the primary neuroendocrine tumor and orbital metastasis in rigth eye after 5 years under chymotherapy and radiation treatment; Primary neuroendocrine tumor was in acustic nerve. fluorescein angiography revealed orbital tumor. Treatment was in oncology department, associate with radiotherapy. Now after that, the tumor it is lower but the patient develop optic neuritis in this eye and Decreased vision in another eye without signs of tumor or neuritis in the contralateral eye, is under diagnostic work out.

Conclusion : patients with neuroendocrine tumor had evidence of systemic and intraorbital metastasis. Even after surgical estereo surgery, chymoterapy and radiation.

Follow up and tests were helpful in allowing diagnosis and treatment.

To evaluate the possible safety and effectiveness of HP Acthar in patients with active uveitis

Grace Levy-Clarke¹, Andrew Taylor², Mireya Cartaya¹, David Yee², John Kempen³.

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OBJECTIVE:

To evaluate the possible safety and effectiveness of Acthar in patients with active uveitis

DESIGN:

Prospective, open-label pilot

PARTICIPANTS:

Five patients, active uveitis/concomitant glaucoma/contraindication to local corticosteroid therapies.

METHODS:

Primary outcome was protocol defined resolution of inflammation within 12 weeks. Protocol defined treatment: Acthar 40 units at baseline and then twice weekly x 8 weeks, followed by once weekly x 4 weeks. Serum samples were collected pre/post treatment and analyzed with multi-cytokine array.

RESULTS:

None of the 10 eyes developed either a rise in intraocular pressure (IOP) ≥ 10 mmHg; none of 3 phakic eyes had progression of cataract. One of 10 eyes, after an initial gain in visual acuity by 10 letters, transitioned from dry to wet macular degeneration, and lost 45 letters of visual acuity.

One of ten uveitic eyes met the pre-specified primary outcome with a two-step improvement in inflammatory signs (vitreous haze from 2+ to 0.5+ and a 50.2% reduction in initially pathologically increased macular thickness). Six additional eyes had a 1-step improvement in vitreous haze (one to grade 0 and two to grade 0.5+), for a total of 70% having improved haze; none got worse (except the wet AMD).

An observed trend downwards seen in post-treatment serum level of pro-inflammatory cytokines IL-17A and MPC1 (CCL2) compared to pre-treatment.

CONCLUSIONS:

This preliminary trial had favorable local ocular safety outcomes in a population with uveitis (anterior and intermediate) with concomitant glaucoma. Further study is needed with greater

Clinical profile and treatment outcome of 103 cases of Vogt Koyanagi Harada (VKH) disease in a tertiary eye care centre in Eastern India

AMITABH KUMAR¹.

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TITLE: Clinical profile and treatment outcome of 103 cases of Vogt Koyanagi Harada (VKH) disease in a tertiary eye care centre in Eastern India

METHODS: Retrospective study of 103 patients examined by a single Ophthalmologist classified into complete (4), incomplete (35) and probable VKH (64) (Revised Diagnostic Criteria) divided into Early (<3months) and Late groups (>3months of symptoms). Early group had 45 patients(90 eyes) and late 58 patients (116 eyes)

RESULTS: Mean age was 34.8 years (early group) and 34.08 years (late group). Female:male ratio was 1.81:1 (early) and 1.33:1 (late group). Mean duration of complaints was 30.84 days (early group) and 943 days (late group).

58.9% had granulomatous anterior uveitis, 75.6% disc hyperemia, 64.5% serous retinal detachment in early group.

56.9% had granulomatous anterior uveitis, 51.7% sunset glow fundus, 1.7% chorioretinal scars, 34.5% retinal pigment clumps in late group.

33 patients had neurological signs and 6 had integumentary signs.

Treatment included topical, periocular, systemic steroids and immunosuppressants. 45 eyes(early group – 21.1%, late group – 22.4%) had reactivation . 30 eyes (early group – 7.8%, late group – 19.8%) developed complicated cataract.

Change in visual acuity in early and late groups were 0.571 LogMar (p=0.00001) and 0.329 LogMar (p=0.00284) respectively. Difference in final visual acuity between groups was 0.26 LogMar (p=0.0024).

CONCLUSIONS: Commonest presentation in Eastern India was probable VKH. Intravenous methylprednisolone, oral steroids and immunosuppressants formed the mainstay of

treatment. Early presentation and adequate treatment had better outcome. Patients required more aggressive treatment probably because of late presentation.

Posters exhibition

Clinical profile of posterior scleritis in a tertiary eye care centre in Eastern India

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¹*SANKARA NETHRALAYA, KOLKATA, INDIA (KOLKATA, WEST BENGAL, IN).*

TITLE:

Clinical profile of posterior scleritis in a tertiary eye care centre in Eastern India

INTRODUCTION:

Posterior scleritis is a commonly misdiagnosed entity due to protean manifestations.

METHODS:

Retrospective observational non comparative case series over five years

RESULTS:

20 eyes of 18 patients (44.4% males, 55.6% females) , average age of 41.3 years (26-63 years). 2 (11.1%) had bilateral involvement. 10 patients (55.6%) complained of periocular pain. 7 eyes(35%) had anterior uveitis and 3 (15%) anterior non-necrotizing scleritis. Posterior segment findings included subretinal fluid pockets (35%), internal limiting membrane striae (35%), disc oedema (25%), choroidal folds (15%), exudative retinal detachment (15%), vitritis(10%), nodule(10%) and macular star (5%). Ultrasonography revealed T sign in 6 eyes. All patients had pin point leaks on Fluorescein angiography with disc staining in 10 eyes (50%). All patients received oral steroids. 11 patients received intravenous methylprednisolone. 6 patients received additional immunosuppressive therapy. Average duration of treatment was 8.6 months (2-72 months). 8 patients had recurrence on cessation of treatment(average 9.1 months). Pre and post treatment average visual acuities (LogMAR) were 0.492 and 0.117 respectively (p=0.007)

CONCLUSIONS:

Patients with posterior scleritis have subtle clinical signs with relatively good visual acuity. Intravenous methylprednisolone, oral steroids and immunosuppressants help in achieving a favourable outcome. A high recurrence rate mandates long term treatment.

CMV retinitis in an immunocompetent 12years old

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Purpose CMV retinitis following MMR vaccination in an immunocompetent .

Method: 12year old healthy male patient with left rapid severe decreased vision to hand motion.

Ocular exam- yellow retinal infiltrates ,intraretinal hges,vitreous haze . First colored photography Fig1. 10 days later the condition progressed Fig2. Patient had no present or past illness. He had received MMR vaccine 10 days before ocular manifestations.

Laboratory - CBC – Hb- 10.6, TLC 3.4 , Plts 401, ESR -18 Toxoplasma Ig G and IgM , Quantiferon TB gold , Syphilis antibodies ,HIV testing all negative ,CMV IgG - positive and IgM - equivocal, normal blood glucose, CD4 –154cells/ul, CD/CD ratio =0.9 , CT chest – normal . Primary immunodeficiency was excluded by labs and examination.

Aqueous fluid sent for PCR CMV and ganciclovir 2mg/0.05ml was injected intravitreal with oral valgancyclovir and oral steroids started.

Result : 4 days after treatment the retinal infiltrates and vitritis started to regress. The PCR was positive for CMV . Patient continued on same treatment with final BCVA 0.5, 2months later – Fig3 . CD 4 and CD4/CD8 continued to improve.

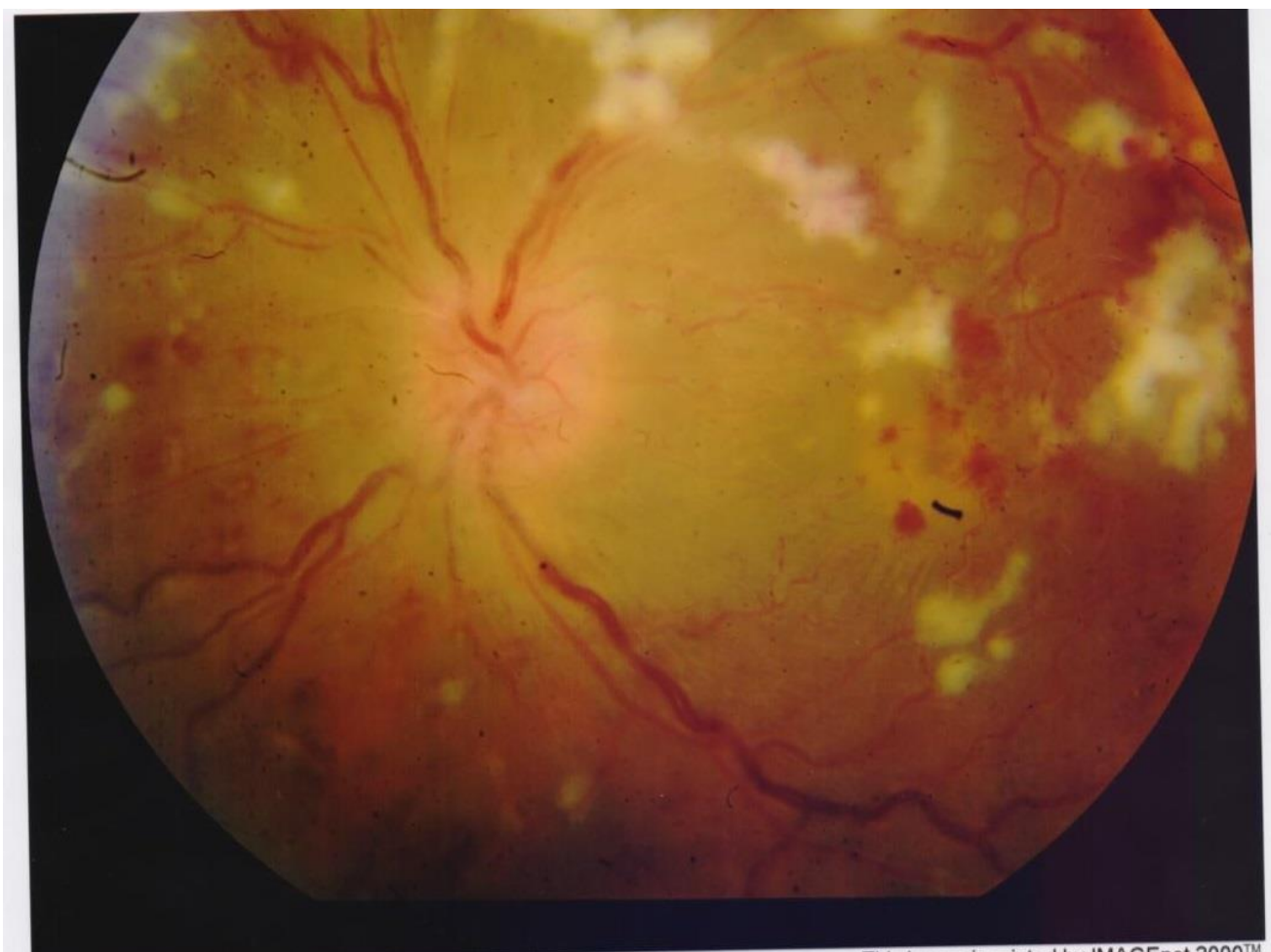
Conclusion: CDC earlier,reported 21 immunocompetents with transient depletion CD4 with opportunistic infections, but CMV retinitis was not reported. However, transient lymphopenia with decreased CD4 count following rubella vaccine was reported 1 . This may be the possible explanation for this patient's transient lymphopenia and decrease CD4, making him susceptible to CMV .

Reference:1-Mediators of Inflammation, 12(4),203-207(August 2003)

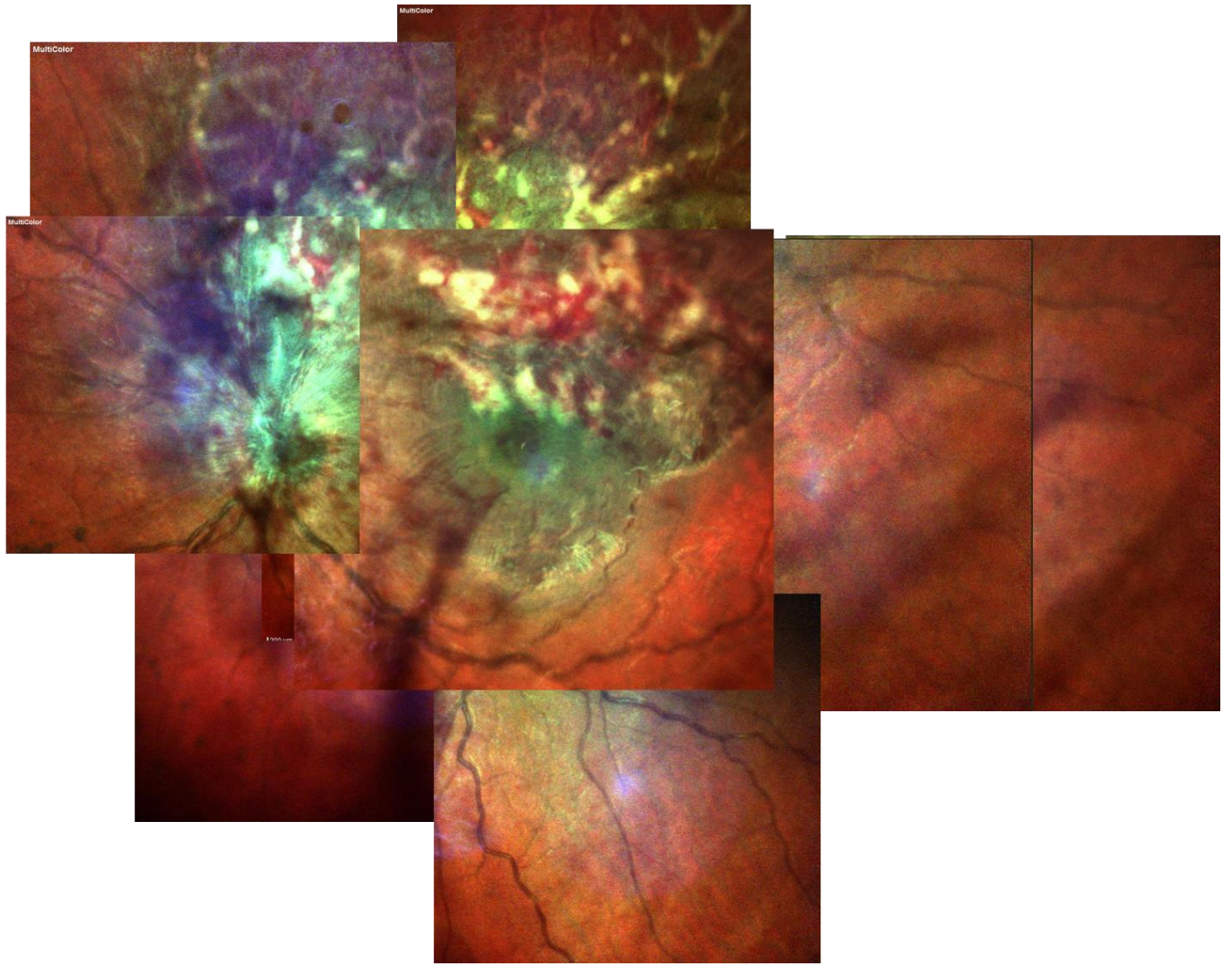
Fig1

Fig2

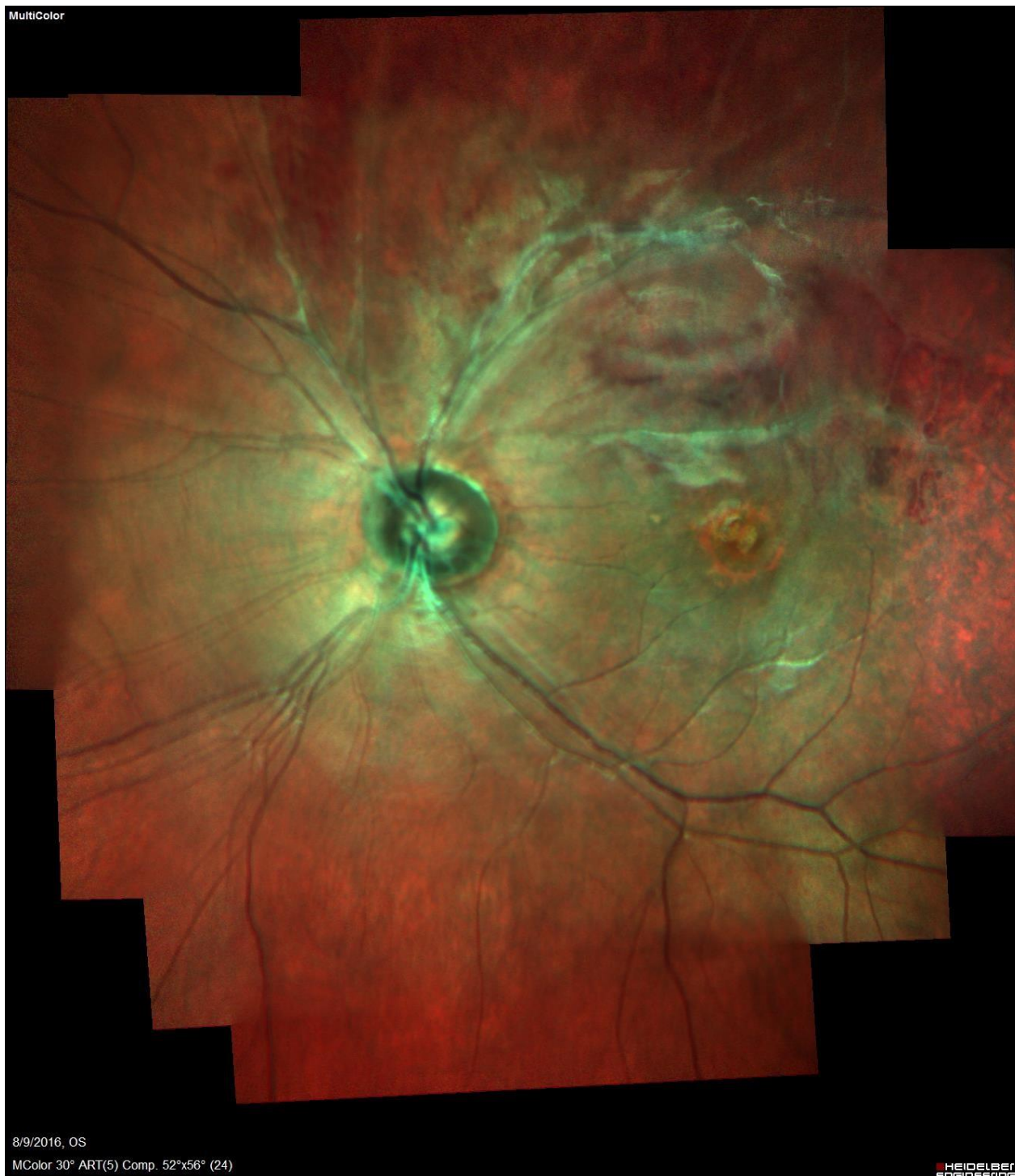
Fig3



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Intraocular manifestations of primary lymphoma of the central nervous system (clinical cases)

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Primary lymphoma of the central nervous system (PCNSL) is a rare form of non-Hodgkin lymphoma. In 15-25% of patients PCNSL starts with ocular manifestations, which are mistaken for intraocular inflammation and autoimmune, infectious, demyelinating vascular lesions. Over the past decades, there is an increasing number of patients with PCNSL which should be considered in the differential diagnosis of uveitis. Also, in the initial stages, PCNSL is sensitive to corticosteroid therapy, and this makes it difficult to diagnose early.

We observed 23 patients with acute retinal necrosis syndrome, in 2 of them in the course of treatment and examination was detected the primary CNS lymphoma.

These two cases are of interest due to the fact that patients had bilateral lesion of the type of acute retinal necrosis syndrome. Investigation of the humoral immune response to infectious antigens showed serological markers of reactivation of herpes virus group. Against the background of the assigned antiviral and corticosteroid therapy was obtained a positive effect. Joining neurological complaints and the subsequent examination, including brain MRI and stereotactic biopsy of the tumor allowed to diagnose primary CNS lymphoma. Assigned anticancer therapy in one case led to a remission of the disease, in the other - came death associated with the spread of the process.

Thus, ocular manifestations of primary CNS lymphoma clinical picture may resemble acute retinal necrosis syndrome; at the bilateral and atypical course of acute retinal necrosis syndrome patients should have a total survey involving chorioretinal biopsy and brain MRI.

Inflammatory Retinal vessel occlusion in a young Taiwan Chinese female alleviated by B cell depletion therapy.

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A 13-year-old girl was referred to our clinics due to blurred vision with progression over 4 days. Past history revealed intermittent episodes of dizziness and blackout in the past 6 months. However, brain CT showed negative findings in local hospital. On ophthalmic examination, visual acuity (VA) was hand motion 30 cm over her right eye (OD) and 6/60 over her left eye (OS). Significant swollen disc and retinal vessel occlusion was observed in both eyes (OU).

Fluorescein angiography (FA) demonstrated delayed filling of retinal vessels. Lab data showed elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Magnetic resonance angiography showed remarkable stenosis of bilateral common carotid arteries and their branches. Under the impression of Takayasu's arteritis, B cell depletion therapy with rituximab was prescribed. The ocular and systemic symptoms relieved. The vision revealed improvement to counting finger 30cm (OD) and 6/15 (OS), respectively. However, the retinal arterioles progressively attenuated and the optic disc turned pale.

Intermittent vision deterioration may result from Takayasu's arteritis. The B cell depletion therapy with rituximab is potential in the treatment of large-vessel inflammation such as Takayasu's arteritis.

Simultaneous Single Dexamethasone Implant and Ranibizumab Injection in a Case with Active Serpiginous Choroiditis and Choroidal Neovascular Membrane

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Intravitreal anti-vascular endothelial growth factor (VEGF) agents seem to be effective in choroidal neovascular membranes (CNV) in association with various entities of posterior uveitis. We herein report a 46-year-old woman who was treated with a simultaneous single intravitreal dexamethasone implant and ranibizumab administration for the treatment of unilateral extrafoveal CNV associated with an active serpiginous choroiditis. Simultaneously with the intravitreal therapy, oral mycophenolic acid (2×720 mg) was started, and oral cyclosporine (3×100 mg) was then added 2 months later. On the other hand, the fellow eye had been treated for subfoveal CNV but with an inactive disease 4 years previously and ended up with a final visual acuity of counting fingers despite treatment with a single session of photodynamic therapy and 3 subsequent intravitreal ranibizumab injections. Simultaneous administration of anti-VEGF agents and a dexamethasone implant can be a viable approach in eyes with CNV and active serpiginous choroiditis

Serum Cytokine Profile among Patients with Tubercular Multifocal Serpiginoid Choroiditis: A Longitudinal Analysis

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Purpose: To analyze the serum cytokines profile in patients with tubercular multifocal serpiginoid choroiditis (TB MSC) receiving anti-tubercular therapy (ATT) and oral corticosteroids.

Methods: In this prospective longitudinal study, patients with active TB MSC were included. Serum levels of interferon (IFN)- γ , interleukin (IL)-10, and tumor necrosis factor (TNF)- α were analyzed using bead-based immunoassay. The levels of transforming growth factor (TGF)- β were measured using cytokine bead array. Serial measurement was performed at baseline, 1, 3, and 6 weeks after initiation of therapy. Patients developing paradoxical worsening (PW) of TB MSC were identified and their serum levels of cytokines were compared to those patients who showed healing of lesions. Comparison of cytokine levels with baseline values was also performed.

Results: Twelve patients (3 females) were included in the study. 4 patients showed paradoxical worsening of TB MSC at 3.2 ± 1 weeks after initiation of therapy. Compared to patients who showed healing of lesions, patients with PW showed higher baseline IL-10 (not significant; $p=0.28$). Among patients developing PW, levels of IFN- γ peaked at 1 week ($p=0.01$) and levels of TNF- α peaked at 3 weeks ($p=0.02$) (coinciding with PW) compared to patients who showed healing. There was no significant difference in TGF- β levels at any time point in either group ($p>0.47$).

Conclusions: Baseline and serial levels of inflammatory serum cytokines may help in predicting the response to ATT and corticosteroids in TB MSC. Patients with paradoxical worsening may show rise in pro-inflammatory cytokines after initiation of ATT indicating higher bacillary load.

Optical Coherence Tomography and Microperimetry Findings in Ocular Behçet Disease

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PURPOSE: To evaluate optical coherence tomography and microperimetry findings as morphological and functional characteristics in patients with inactive posterior or panuveitis associated with Behçet disease.

METHODS: This retrospective study included 23 eyes of 12 patients. Age, sex, visual acuity, duration of follow-up, central macular thickness (CMT), disruption of retinal photoreceptor zone (PZ) and pigment epithelium (RPE) layer were analyzed. Macular integrity (MI) index, average threshold (AT) and fixation stability (FS) were also evaluated by Microperimeter-1 (MP-1) examination.

RESULTS: Visual acuity was negatively correlated with CMT ($p<0.001$), MI ($p=0.007$) values and positively correlated with AT ($p=0.001$), FS ($p<0.001$) values. None of the patients have macular edema. Statistically significant positive correlation was found between CMT and AT. Moreover, there was significant negative correlation between CMT and FS values. The optical coherence tomography (OCT) images of 6 eyes were not distinct enough to evaluate FZ and RPE disruption. In other patients, PZ/RPE disruption were compared with MI index, AT and FS values. In the eyes of which PZ and RPE layer integrity were good the mean AT and FS values were higher ($p=0.008$ and $p=0.02$, respectively). Although the mean MI index was higher in the eyes with PZ/RPE disruption, it was not statistically significant ($p=0.09$).

CONCLUSIONS: These results indicate that the visual acuity in patients with inactive posterior or panuveitis in Behcet disease correlated significantly with CMT, PZ/RPE zone disruption and MP-1 examination findings (MI, AT and FS). A high concordance was also found between OCT and MP-1 examination findings.

Long-term results of intravitreal dexamethasone implant in patients with non-infectious uveitis

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Purpose: To evaluate the long-term results of dexamethasone implant(DEX-implant) in non-infectious uveitis.

Material and Methods: 32 eyes (30 patients) with non-infectious uveitis injected with DEX-implant for macular edema and/or persistent vitreous haze and followed-up for at least one year were included. Best corrected visual acuity(BCVA), central macular thickness(CMT), vitreous haze score, pre/post-injection medications and recurrence rate, the number of injection and occurrence of complications were retrospectively reviewed.

Results: The mean age was 37.8 years and the mean post-injection follow-up period was 22.5±10.9 (12-62) months. Etiology of uveitis was Behçet disease in 14(46.7%), idiopathic uveitis in 11 (36.7%), HLA-B27 associated uveitis in 2(6.7%), multiple sclerosis in 2(6.7%) and sarcoidosis in 1(3.3%). Indications for DEX-implant were cystoid macular edema in 18(56.3%), persistent vitreous haze in 9(28.1%) and both in 5(15.6%) eyes. The mean BCVA improved from 0.89±0.54 logMar unit to 0.58±0.46, 0.46±0.46, 0.40±0.48 and 0.41±0.51 logMar at 1, 3, 6 and 12 months respectively(p<0.001). The mean CMT improved from 503±146 µm from baseline to 369±138 µm at 1, 368±165 µm at 3, 313±129 µm at 6 and 303±87 µm at 12 months(p<0.001). The vitreous haze score improved significantly during all follow-up period(p<0.001). A re-injection was not needed in 23(71.9%) eyes. Cataract requiring surgery developed in 28.1% and glaucoma in none.

Conclusions: DEX-implant is an effective and safe therapy providing long-term control of inflammation. Along with implantation, systemic treatment should also be intensified. In patients with unilateral uveitis without systemic association, DEX-implant monotherapy may be a good alternative to systemic therapy.

Association between Multiple Sclerosis and Fuchs' Heterochromic Iridocyclitis

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Purpose: To report the association of multiple sclerosis (MS) with Fuchs' heterochromic iridocyclitis (FHI).

Methods: A retrospective study.

Results: Medical records of 2642 patients with uveitis (in years 2003-2016) were analysed focusing on MS. Uveitis associated with MS was diagnosed in 78 patients (3.0 %): anterior uveitis (6), intermediate uveitis (20), retinal vasculitis (21) and panuveitis (31). The clinical examination revealed signs of FHI in the anterior segment in 8 out of 78 cases. Atypical manifestations of FHI included bilateral involvement (2), retinal vasculitis (2) and snowballs in vitreous (1). The diagnosis of FHI preceded the diagnosis of MS in 6 cases. In 4 patients, the demyelinating disease was determined within one year after the diagnosis of FHI. In 2 patients, the latency period was longer (8, respectively 15 years). We recommended neurological examination because of optic neuritis (1), paraesthesia (2), relapse with motor deficits (1), screening of etiology in cases with posterior segment involvement (3). In next 2 cases, the diagnosis of MS preceded the diagnosis of FHI (8, respectively 13 years).

Conclusions: We revealed clinical signs of FHI in 10.3 % of cases of uveitis associated with MS. This association has not yet been reported. Our observation might induce more research in this field.

Multimodal Imaging in Presumed Tuberculous Serpiginous-like Choroiditis

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Purpose: To describe multimodal imaging findings in a patient with presumed tuberculous serpiginous-like choroiditis (TB-SLC).

Method: We acquired and assessed multimodal imaging in a patient with peri-papillary TB-SLC using enhanced depth imaging optical coherence tomography (EDI-OCT), fundus autofluorescence (FAF), indocyanine green angiography (ICGA) and fundus fluorescein angiography (FFA) (all with Heidelberg Spectralis) as well as swept-source (SS)-OCT and optical coherence tomography angiography (OCTA) (DRI OCT Triton, Topcon). We analysed changes during active disease and transition to inactive state.

Results: Multimodal imaging provided a variety of useful clinical markers. In particular, non-invasive imaging with OCTA within the chorioretinal lesion demonstrated defined areas of altered flow and non-perfusion at the level of the choriocapillaris that corresponded with areas of hypofluorescence on ICGA. Both SS-OCT and EDI-OCT demonstrated retinal pigment epithelium elevation, focal choroidal thickening and outer retinal disruption in the active lesion. FAF demonstrated a hyperfluorescent lesion with hypofluorescent borders in the active phase. The hypofluorescent borders corresponded with areas of progressive lesion extension observed during follow-up. On administration of anti-tuberculous and systemic corticosteroid therapies the condition stabilised and transitioned to inactive disease. Progressive OCTA change with evidence of re-perfusion at the level of the choriocapillaris, evolution of FAF appearance, SS-OCT and EDI-OCT signs were seen.

Conclusion: OCTA delineates vascular non-perfusion to the level of the choriocapillaris in TB-SLC and suggests inflammatory vascular occlusive pathology in the acute stage followed by subsequent vascular remodeling. SS-OCT, EDI-OCT and OCTA are useful non-invasive diagnostic and follow-up imaging modalities for TB-SLC.

Bilateral diffuse uveal melanocytic proliferation (BDUMP): Nuances in pathological evidence

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¹*Sri Sankaradeva Nethralaya, Guwahati, Assam, INDIA (Guwahati, IN).*

Introduction: Diffuse uveal melanocytic proliferation (DUMP) can be unilateral or bilateral. This is a sequence of internal malignancy. It is characterized by proliferation of uveal melanocytes producing pigmented uveal tumours. We present two cases of enucleated eyeball with this condition.

Methods: A case series

Results:

Case 1: An 80 years old Indian lady presented with dimness of vision (DOV) in left eye (OS) for 1 month. Vision was perception of light negative in OS. Fundus examination revealed a choroidal mass in OS. Ancillary imaging gave the diagnosis of choroidal melanoma OS. Ultrasound of neck showed a colloid nodule in the thyroid with abnormal liver function test; Enucleated eyeball revealed evidence of DUMP with interesting changes of melanocytic proliferations in around retinal vessels, layer of retina with characteristic sparing of choriocapillaries. Immunohisto chemistry (IHC) was done with various markers. Other eye fundus examination had retinal pigment epithelial defect and she is currently under follow-up with oncologist for thyroid nodule.

Case 2: A 28 years old man with DOV in OD for 5 months. Previously, he was diagnosed to have ulcerative colitis (UC) with GIT polyps. Ocular imaging showed diffuse choroidal mass (OD). Enucleated eyeball revealed the evidence of DUMP with interesting gross, histopathology and IHCs findings. He is presently under the follow-up with gastroenterologist for UC and is on systemic immunosuppressive medication.

Conclusion:

Angiocentric melanocytic proliferations with IHC supported evidence in BDUMP were some of the newer observations that were seen in the study.

Clinical features of intraocular inflammation in Hokkaido University Hospital

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【Purpose】 We aimed to investigate the clinical features of intraocular inflammation (uveitis) in Hokkaido and to assess the current trend of etiology in comparison with that of our previous survey.

【Methods】 We retrospectively reviewed the medical records of 1617 uveitis patients (596 men, 1021 women) who newly visited Hokkaido University Hospital, Japan between 2004 and 2014.

【Results】 Mean age at the first visit was 35.7 ± 20.4 years in men and 49.9 ± 20.0 years in women. Sarcoidosis was the most frequent etiology (17.4%) followed by Vogt–Koyanagi–Harada (VKH) disease (8.1%), Behçet’s disease (4.5%), HLA-B27 associated uveitis (2.5%), cytomegalovirus retinitis (1.9%), and acute retinal necrosis (1.7%). The etiologies in 48.7% patients were unclassified. In this unclassified etiology, anterior, posterior, and combined anterior and posterior segment intraocular inflammation accounted for 44.2%, 4.3%, and 51.5%, respectively.

In our previous survey between 1994 and 2003, the etiologies were Sarcoidosis (14.9%), VKH disease (9.7%), Behçet’s disease (6.7%), and HLA-B27 associated uveitis (4.0%). Although the clinical features did not differ between these two decades, the rate of new patients decreased in Behçet’s disease and increased in sarcoidosis in the present survey. As for sarcoidosis, the rate of patients younger than 20 significantly decreased, whereas the rate of female patient over 70 significantly increased. These changes were consistent with the shift of population distribution in Japan.

【Conclusion】 These data suggest the trend of uveitis diseases has slightly changed in Hokkaido, Japan. However, the order of top 4 etiologies has been the same with that of our previous study.

Immunocytochemical analysis in cell block method using vitreous infusion fluids in patients with vitreoretinal lymphoma

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Purpose: Many vitreoretinal lymphoma (VRL) histologically reveals diffuse large B-cell lymphoma (DLBCL). The aim of this study is to analyze immunocytological findings in cell block (CB) preparations using waste cassette vitreous fluids in patients with VRL.

Methods: This is a retrospective observational study involving 13 eyes in 13 cases with VRL that presented vitreous opacity and underwent diagnostic vitrectomy. CB specimens were prepared in all 13 eyes from waste diluted fluids containing shredded vitreous. These specimens were then submitted for HE staining as well as immunocytological analyses with antibodies against the B cells marker CD20, and the T cell marker CD3. This study further examined immunoreactivity for MUM-1, Bcl-2, Bcl-6 and CD10 to determine systemic DLBCL cell type based on Hans algorithm (Blood 2004). Diagnosis with VRL was made based on the results of cytology, concentration of interleukin (IL)10 and IL6 in undiluted vitreous, and immunoglobulin heavy chain gene rearrangements.

Results: All CB specimens in VRL contained large lymphoma cells and small reactive lymphocytes with necrotic background. Immunoreactivity for CD20 was observed in the cell membrane of lymphoma cells in 12 VRL cases, whereas small lymphocytes were positive for CD3 but not CD20. Nuclear immunoreactivity for Bcl-2 and MUM-1 was detected in 4 out of 4, and 2 out of 4 cases examined, respectively. In contrast, no cases positive for Bcl-6 or CD10 were noted.

Conclusions: Based on immunocytological results, VRL can be classified as non-germinal center B-cell type indicating aggressive tumor burden with poor prognosis among systemic DLBCLs.

Inflammatory choroidal neovascularization imaged by optical coherence tomography - angiography.

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PURPOSE: To describe the optical coherence tomography - angiography (OCT- A) findings in patients with inflammatory choroidal neovascularization (iCNV). **DESIGN:** retrospective descriptive case series.

METHODS: We included all patients diagnosed with iCNV at the Pitie Salpetriere hospital between 2016/09/01 and 2017/01/17. All patients were assessed including best corrected visual acuity, clinical inflammatory parameters and multimodality imaging. All patients underwent OCT angiography with SS-OCT DRI Triton (Topcon, Japan) or/and Spectralis Angiography OCT (HRA, Heidelberg, Germany). OCT-A images were analyzed and compared with en face and B-OCT.

RESULTS: Eight patients (9 eyes), 3 women and 5 men, with a mean age of 55.5 years, were included. Three patients were diagnosed with ocular sarcoidosis and the rest of the patients with Birdshot retinochoroidopathy, sympathetic ophthalmia, punctate inner choroidopathy, HSV 2 chronic retinitis and presumed tuberculous chorioretinopathy. OCT-A revealed inflammatory CNV in all cases. CNV were subfoveal in five cases, papillomacular in two cases and eccentric in two cases. CNV as a complication of stromal inflammatory choroiditis seems to have higher voluminous signal, multiple thicker pedicles, less branching and less vessel termini. CNV as a complication of primary inflammatory choriocapillaropathies had a glomerule shape, a single pedicle, lot of branching. One month after anti VEGF injection, a second anti VEGF injection was necessary in five cases.

CONCLUSION: OCT-A is a new complementary imaging method for the diagnosis and the monitoring of inflammatory CNV. The features and the evolution of these lesions on OCT-A need to be investigated in further studies.

EARLIER USE OF INFLIXIMAB FOR THE UVEITIS OF BEHÇET'S SYNDROME APPEARS TO BE ASSOCIATED WITH BETTER OUTCOME

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BACKGROUND AND PURPOSE: The aim of this study is to compare the clinical characteristics and treatment responses of BS patients who started infliximab (IFX) for uveitis before and after 2013.

METHODS: The charts of 17 patients receiving IFX (5 mg/kg) for uveitis at our centre after 2013 (New Group) were reviewed retrospectively. The data were compared with those of 43 patients starting IFX before 2013 (Old Group).

RESULTS: The duration of previous immunosuppressive treatment was significantly shorter (median: 26 months) in the new group compared to that of the old group ($p=0.012$). There was no significant difference between groups regarding the baseline visual acuity (VA) at the time of initiation of IFX in the right eye ($p=0.8$) but the baseline VA of the left eye of the new group was significantly better compared to that of the old group ($p=0.005$). The percentage of patients with no useful vision in at least one eye was 47% in the new group and 67% in the old group ($p=0.23$). Information on outcome was available for 14 patients in the new group. The duration of IFX treatment was 13.8 ± 7.9 SD months. Ten patients (71%) had at least one attack in the right, left or both eyes before IFX, while all patients except one (93%) became attack free under IFX. The mean VA of the left eye improved significantly with IFX.

CONCLUSION: Earlier use of IFX for BS uveitis appears to be associated with better outcome.

Frequency of chronic infections with proven ocular tropism in patients with acute retinal necrosis

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Acute retinal necrosis (ARN) refers to a rare diseases, despite the widespread of chronic herpes virus infection.

We observed 235 patient with uveitis. Acute retinal necrosis was detected in 8.9% (21 people - 12 males and 9 females) with mean age 42.3 years. In 61.9% inflammatory process was at both eyes, what is more the fellow eye loss has evolved in a period of 7 days to 5 years.

Reactivation of herpes simplex virus types 1 and 2 was detected in 94.1% of patients, CMV in 35.3%, and Epstein-Barr virus only in 12.5%. All patients with ARN had chronic herpes virus infection which in 47% combined with Toxoplasma infection, in 23.5% with Chlamydia and in 35.3% with Mycoplasma. In the study of intraocular fluids and vitreous body was found that the overwhelming majority of patients (84.6%) had antibodies to herpes simplex virus type 1 and 2, and only 15.4% to to herpes simplex virus type 2.

Conclusion. Acute retinal necrosis in almost all patients occurs with symptoms of reactivation of herpes virus group, which confirms the necessity for systemic antiviral therapy.

The Use of Intravitreal Steroid Implant (Ozurdex) for Treatment of Refractory Cystoid Macular Edema Secondary to Retinitis Pigmentosa

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¹Dr. (Amman, JO).

Introduction: Retinitis pigmentosa is a clinically & genetically diverse group of diffuse retinal dystrophies that initially affecting rod with subsequent degeneration of cones, Maculopathy is one of the complications of RP that affecting vision.

Method: We retrospectively review a 24y old male patient that presented with bilateral refractory Cystoid macular edema secondary to RP which is not responding to topical carbonic anhydrase inhibitor and multiple anti VEGF injections of Lucentis in both eyes, the patient underwent bilateral 0.7 mg Intravitreal dexamethasone (OZURDEX) implant of 1 week apart, the spectral domain OCT was performed before and one month after OZURDEX injection and to assess the efficacy of Intravitreal steroid implants in treatment of refractory CMO in RP

Results: The Spectral Domain OCT after 1 month of injection showed a significant anatomical and functional improvements, CMT improved from 314 μ m to 233 μ m in the right eye and from 590 μ m to 207 μ m in the left eye. The BCVA improved from 6/18 to 6/9 in the right eye and from CF 1 meter to 6/60 in the left eye.

Conclusion: It seems that the refractory CMO in RP is mostly inflammatory driven, for this reason it shows a dramatic response to Intravitreal steroids, the results in our case was matching other small case series results. Further preferably randomized trials may establish the place of Intravitreal dexamethasone in the treatment of refractory CME related to RP.

Assessment of the Posterior Segment of Ocular Behçet's Uveitis with Opaque Ocular Media by Using Swept Source OCT

fawwaz almamoori¹.

¹Dr. (Amman, JO).

Introduction: Behçet's disease is a multisystem disorder named after the Turkish dermatologist, Hulusi Behçet (1889–1948), who in 1937 recognized and reported a triad of symptoms: recurrent intraocular inflammatory episodes with oral and mucosal ulcerations. The disease can affect both the anterior and posterior portions of the globe. Cataract formation is one of the anterior segment complication after recurrent inflammation, and it is considered as one of the main obstacles for viewing the posterior segment during ophthalmic examination.

Aim&objectives: We retrospectively review a 49 y old female patient, with history of bilateral chronic ocular Behcet Uveitis and dense cataract in both eyes that preventing a good view of the posterior segment by using Swept Source OCT Technology.

Results: Swept Source OCT images with 3D cuts showed severe hidden vitritis with increase in subfoveal choroidal thickness to ($448\ \mu\text{m} \pm 80\ \mu\text{m}$ in right eye) and ($649\ \mu\text{m} \pm 60\ \mu\text{m}$ in left eye) that reflects a high hidden activity of the disease in the posterior segment.

Conclusion: SS-OCT is a noninvasive reproducible imaging technique that allows enhanced visualization of the posterior segment of the eye with opaque media (especially in Uveitis cases) and in measurement of choroidal thickness that could be superior to B-scan ultrasound. The SS-OCT images were informative in detection of acute posterior segment complications of Behcet (Vitritis) and in evaluation of the choroidal thickness that increases in active and quiescent phases of posterior uveitis.

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Mixed retinopathies in post renal transplant patient

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Introduction:

Retinopathies are complications that we encounter in many organ transplant cases. There are various causes how these complications can occur and sometimes, there may be multiple reasons causing the retinopathies.

Method: A case presentation

Results:

A 24 year old man presented to tertiary Institute of north-east India with impaired vision in both eyes (OU) for past 20 days. He was diagnosed elsewhere as CMV retinitis. PCR from blood DNA was positive for CMV and HIV was negative; CD 4 cell count was 774 cell /mm³ and had ganciclovir intravitreal injection (OU) and was on oral ganciclovir medications. Patient had recent renal transplantation and was on Tablet Deflazacort, Tacrolimus(3mg) and Mycophenolate mofetil. He had hypertension and was on oral anti hypertensive. On examination, his vision was 6/60 in OU. Anterior segment and vitreous was normal OU. Fundus examination revealed symmetric ischemic retinopathy with hard exudates, multiple cotton wool spots, telangiectasia, perivascular hemorrhages and macular edema. Fluorescein angiography after nephrologist clearance revealed non-perfusion and drop-out at macula OU. OCT revealed cystoid spaces in outer retinal layers in OU. He was provisionally diagnosed as bilateral Tacrolimus associated thrombotic microangiopathy with hypertensive changes. His medications were modified with withdrawal of Tab Tacrolimus .He was on regular follow-up and by 4 month, his vision improved to 6/24 OU with significant decrease in the macular lesions.

Conclusions: Mixed retinopathies in post renal transplant are challenging one. The inciting factors need to be identified and initiation of appropriate measures can improve the outcome.

Impact of Uveitis on Quality of Life: a Prospective Study from a Tertiary Referral Rheumatology-Ophthalmology Collaborative Uveitis Center

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Purpose: we aimed at investigating the impact of non-infectious uveitis (NIU) on quality of life (QoL) using the 36-item Short-Form Health Survey (SF)-36. **Methods:** eighty consecutive NIU patients and 23 healthy controls (HC) prospectively completed the SF-36 questionnaire. The SF-36 subscores values were statistically analyzed in order to evaluate differences between patients and HC and to identify correlations between SF-36 subscores and clinical or demographic data. **Results:** NIU patients showed a significant decrease in the physical component summary score ($p < 0.0001$) compared to HC, while no significant difference was highlighted in relation to the mental component summary score ($p = 0.97$). Regarding each SF-36 subscore, NIU patients showed a significant decrease in physical functioning ($p = 0.008$), role-physical ($p = 0.003$), bodily pain ($p = 0.0001$), general health ($p < 0.0001$) and social functioning ($p = 0.01$). Physical functioning was significantly decreased in patients with acute anterior uveitis (AAU) than those with panuveitis ($p = 0.003$). No differences were found between patients with bilateral or unilateral ocular involvement, patients with isolated uveitis or uveitis associated with systemic diseases and patients with or without current or recent ocular activity. No correlations were identified between best-corrected visual acuity (BCVA) and SF-36 subscores. Physical functioning ($p = 0.02$), bodily pain ($p = 0.004$) and social functioning ($p = 0.02$) were significantly reduced in males compared to females with NIU. **Conclusion:** QoL is significantly impaired in NIU, particularly in the physical domains, general health and social functioning. AAU affects physical functioning more than panuveitis. NIU seems to affect per se QoL disregarding inflammatory activity, visual impairment and the presence of an associated systemic disease.

Vogt-Koyanagi-Harada disease in Children

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Purpose: To describe the prevalence, clinical characteristics, and role of immunosuppressive therapy in visual outcome of pediatric Vogt-Koyanagi-Harada disease (VKH) seen at a uveitis referral center in South India.

Method: Retrospective review of 17 patients below 18 years of age with VKH seen at a tertiary eye-care hospital from January 2004 to December 2014.

Results: Of 368 patients receiving a diagnosis of VKH during the study period, 20 patients (5.4%) were below 18 years of age. The study included 6 male and 11 female patients with mean age of 14.9 ± 2.9 (5-18) years. Mean age of first attack of VKH was 13.1 ± 3.8 years. The most common presenting complaint was diminution of vision (94.1%) and 23.5% of them had headache. Three patients (17.6%) had tinnitus. Anterior chamber inflammation was noted in 24(70.6%) eyes and two eyes presented with angle closure glaucoma. Exudative retinal detachment and optic nerve head edema were seen in 29.4% and 20.6% of the eyes respectively. Fifteen patients (88.2%) received long-term immunosuppressive therapy. Mean baseline best-corrected visual acuity (BCVA) improved from 0.7 ± 1.0 to 0.4 ± 1.0 ($P=0.014$). The patients receiving azathioprine showed better visual outcome than those receiving methotrexate. The most common complication encountered was cataract ($N=11, 32.4\%$) followed by glaucoma ($N=8; 23.5\%$). Protracted ocular hypotony was observed in two eyes.

Conclusion: Though the course of VKH tends to be aggressive, rapid control of inflammation with effective medications are useful. Use of immunosuppressives have been found to be associated with lesser side effects and favorable visual prognosis in children

Efficacy of Infliximab therapy evaluated by fluorescein angiography

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Purpose: We evaluated ocular symptoms of Behçet disease before and after infliximab therapy, using fluorescein angiography (FA) score and Behçet's disease ocular attack score 24 (BOS24) to assess Behçet disease activity, and analyzed the association between FA scores and ocular and extraocular symptoms of Behçet disease.

Material and Methods: Using medical records, we analyzed FA and BOS24 to evaluate the association between the efficacy of infliximab therapy and FA or BOS24 scores. Further, we evaluated the association between FA score or BOS24 and extraocular symptoms.

Results: Among 38 patients, extraocular symptoms resolved following treatment in 29 (76.3%). After 2 years of infliximab therapy, 6-month BOS24 was significantly reduced compared to that before treatment (PreBOS24-6M). After 4 years of infliximab therapy, 6-month BOS24 was also significantly reduced compared to preBOS24-6M. After 2 years of infliximab therapy, FA score decreased significantly compared to that before treatment (FA-2Y vs. pre-FA: 4.7 ± 3.6 vs. 9.1 ± 2.7 ; $P < 0.0001$; $n=38$). The FA-4Y score in subjects followed for at least 4 years was also significantly lower than the pre-FA score (3.4 ± 3.2 vs. 9.2 ± 2.8 ; $P < 0.0001$; $n=28$). No significant correlation was observed between the improvement in FA-2Y score and the occurrence or persistence of extraocular symptoms ($P=0.17$; $n=38$).

Conclusion: Infliximab therapy is effective for the treatment of ocular and extraocular involvements of Behçet disease. BOS24 and FA scores are useful for evaluating the efficacy of infliximab therapy.

Superficial and deep retinal foveal avascular zone OCT-A findings of non-infectious anterior and posterior uveitis compared to healthy controls

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Background: To compare the superficial (FAZ-S) and deep retinal foveal avascular zones (FAZ-D) of non-infectious anterior and posterior uveitis and healthy controls, using optical coherence tomography angiography (OCTA).

Methods: OCTA was performed on a total of 74 eyes, 34 eyes suffering from non-infectious posterior uveitis (26 eyes without macular edema (post-CME), 8 eyes with macular edema (post+CME)), 11 eyes with non-infectious anterior uveitis (6 eyes without macular edema (ant-CME) and 5 eyes with macular edema (ant+CME)). The control group included a group of 29 healthy eyes. The foveal avascular zones of the superficial (FAZ-S) and deep (FAZ-D) retinal vascular plexus were measured in mm² via the software's ruler tool on a Heidelberg HRA2 Spectralis OCTA. For statistical evaluation ANOVA-based linear mixed-effects models were performed with SPSS®.

Results: Eyes suffering from non-infectious posterior uveitis presented with significantly higher FAZ-D values when compared to healthy controls both, in the presence or absence of macular edema ($p < 0.001$, post-CME and post+CME subgroups). In the presence of macular edema eyes presenting with anterior uveitis (ant+CME) also showed significantly higher FAZ-S ($p = 0.03$) and FAZ-D ($p < 0.001$) values when compared to healthy controls. Meanwhile, in the absence of macular edema eyes with anterior uveitis cannot be distinguished from controls ($p > 0.6$).

Conclusion: Based on our preliminary results, the deep retinal foveal avascular zone seems to be enlarged in eyes presenting with non-infectious posterior uveitis, both in the presence or absence of macular edema. This finding could be used as a clinical marker in the future.

Post-operative ocular inflammation: A single sub-conjunctival injection of XG-102 compared to dexamethasone drops in a randomized trial

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Purpose: To evaluate the efficacy and safety of XG-102 (brimapitide) compared to dexamethasone eye-drops in the treatment of post-operative ocular inflammation.

Patients: Patients who underwent anterior and posterior segments combined surgery, or glaucoma surgery, or complex posterior segment surgery, were eligible to participate in a multicenter, randomized, double-masked clinical trial.

Methods: Patients were administered a single sub-conjunctival injection of 250 µl XG-102 90 µg (N=47) or 900 µg (N=48) or placebo (N=50) at the end of ocular surgery. Sub-conjunctival injection for each group, XG-102 90µg, XG-102 900µg or placebo, is followed by eye drops instilled 4 times/day for 21 days with placebo, placebo or dexamethasone solutions, respectively. The primary outcome measure was anterior chamber cells grade at day 28 comparing XG-102 900 µg with dexamethasone.

Results: The anterior cells grade for the XG-102 groups was non-inferior to dexamethasone (-0.054 anterior cell grade, 95% Confidence Interval (CI) -0.350 - 0.242, p <0.001) for XG-102 900 µg and -0.086 anterior cell grade, 95% CI -0.214 - 0.385, p =0.003 for XG-102 90 µg. Rescue medication was introduced for 10 (21%), 7 (15%) and 2 (4%) patients allocated to XG-102 90 µg, XG-102 900 µg and dexamethasone respectively. The number of patients for whom adverse events were reported and the nature of the events reported was similar between the three treatment groups.

Conclusions: A single sub-conjunctival injection of XG-102 (brimapitide) at the end of ocular surgery is non-inferior to dexamethasone eye drops in the treatment of post-operative ocular inflammation.

Acute Posterior Multifocal Placoid Pigment Epitheliopathy Following Human Papilloma Virus Vaccination

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Purpose: To report a case of acute posterior multifocal placoid pigment epitheliopathy (APMPPE) that developed after human papilloma virus (HPV) vaccination.

Methods: A 31-year-old woman experienced sudden bilateral blurred vision and paracentral scotomas four days before visiting the hospital. The symptoms occurred two weeks after the second vaccination with quadrivalent HPV vaccine (Gardasil[®], MSD Korea, Seoul, Korea), and she had no pain or cold symptoms. At initial visit, the anterior chamber cells were observed, and the anterior vitreous was found to be clear. On fundus examination, multiple placoid yellow-whitish lesions were observed at the posterior pole, and fluorescein angiography showed early hypofluorescence and late hyperfluorescence with staining.

Results: Under a diagnosis of bilateral APMPPE, oral corticosteroid was used as treatment for two weeks, after which symptoms were resolved, anterior chamber cells disappeared, and lesions at the posterior pole markedly decreased. After five weeks, multiple hyperreflective areas on the outer retinal layers as well as missing photoreceptor and retinal pigment epithelial layers were almost recovered upon optical coherence tomography.

Conclusions: Non-infectious uveitis such as APMPPE can rarely present after HPV vaccination. Further studies are necessary to understand whether HPV vaccine is a direct cause of uveitis.

Reactivation of Herpetic Keratitis in a Patient after Using Two Different Prostaglandin Analogues

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Purpose: To report a case of herpetic keratitis after administration of two different prostaglandin analogues.

Case summary: A 68-year-old female with a history of herpetic keratitis in her right eye after using latanoprost seven years

previous presented with redness, mild ocular pain and tearing in the same eye. She had also been prescribed travoprost

eye drops for both eyes for uncontrolled glaucoma one month earlier. The cornea in her right eye showed a dendritic epithelial

defect with focal epithelial erosions. Travoprost treatment was discontinued, and the herpetic keratitis recovered completely

in ten days with acyclovir ointment and oral agent. No further recurrence was observed in the following six months.

Visual Outcomes and Effecting Factors of 27-guage Vitrectomy for Endophthalmitis following Cataract Surgery

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Purpose: To report the clinical outcomes and influencing factors of 27-gauge transconjunctival sutureless vitrectomy (TSV) in patients with postoperative endophthalmitis following cataract surgery.

Methods: Medical records of 19 patients who underwent 27-gauge TSV due to postoperative endophthalmitis after cataract surgery were retrospectively reviewed. The following factors were analyzed: pre and postoperative best corrected visual acuities (BCVA), presence of posterior capsular rupture, induction of posterior vitreous detachment, results of bacterial culture, existence of systemic disease, and the interval between cataract surgery and TSV.

Results: The mean BCVA significantly improved from logMAR 1.69 ± 1.35 to logMAR 0.38 ± 0.97 ($p < 0.01$). Successful induction of posterior vitreous detachment during TSV and short interval between cataract surgery and TSV were related to better prognosis.

Conclusions: Small gauge TSV is effective and should be performed as soon as possible when endophthalmitis is diagnosed after cataract surgery. We recommend posterior vitreous detachment induction if possible during vitrectomy.

Characteristics and Clinical Course of Multiple Sclerosis-Associated Uveitis in Patients Presenting with Ocular Findings

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Purpose: To describe the demographic and clinical characteristics of patients with multiple sclerosis (MS) associated uveitis, in whom the diagnosis of uveitis preceded the diagnosis of MS.

Materials and Methods: Medical records of 30 patients (60 eyes) presented with ocular inflammatory signs suggestive of MS and had the definitive diagnosis after magnetic resonance imaging and neurological evaluation, were retrospectively reviewed.

Results: The mean follow-up period was 45.5 (1-186) months. The mean time interval between the diagnosis of uveitis and MS was 22.4 (1-144) months. Anatomically, uveitis was anterior in 4(13.3%), intermediate in 2(6.7%), posterior in 12(40%) and panuveitis in 12(40%) patients. Uveitis was granulomatous in 17(56.7%) patients. Vitritis in 23 (76.7%), retinal vasculitis in 22 (73.3%) and snowball opacities in 11(36.7%) patients were the most common ocular findings. The mean recurrence rate was 1.90 ± 1.52 . BCVA was ≥ 0.6 in 35 (58.3%) eyes at the first visit and 43 (71.7%) eyes at last visit. Cataract (22 eyes, 36.7%), cystoid macular edema (15 eyes, 25%), epiretinal membrane (8 eyes, 13.3%), and retinal vein occlusion (8 eyes, 13.3%) were the most common complications. Systemic (\pm topical) corticosteroids \pm immunosuppressive treatment was the most commonly used treatment approach.

Conclusion: Patients having ocular findings highly suggestive of MS should be followed closely. Our results showed that time interval for definitive diagnosis of MS may be as long as 12 years. Retinal vasculitis \pm granulomatous anterior uveitis is the most common ocular presentation of the disease and the visual prognosis is quite good despite the complications.

Improving team-based care for patients with non-infectious inflammatory eye disease

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We aimed to improve team-based care at Grady Memorial Hospital (GMH) as measured by a decrease in time to evaluation by specialty services for patients with non-infectious uveitis evaluated between November 2016 and March 2017.

Baseline data demonstrated patients with an average age of 52 years, 35% with glaucoma and 32% with cataracts. Fifty-four percent had a need for rheumatology with an average wait time of 7.31 weeks.

We performed a root cause analysis to understand limitations to timely access and identified and implemented four tests of change. We assessed the time to rheumatology appointment, changes in clinical metrics, performed a comprehensive needs assessment, and measured time until needs were met by the healthcare system (GMH). Needs assessment included labs, imaging, and specialty visits related to the management of their uveitis.

Results show uveitis patients fall into two utilization categories: “high” and “low”. Of the 58 patients followed through the study, 38% had two or more needs and 38% had zero needs identified. We identified 64 discrete patient needs (1-7 needs per clinic day). The following departments were frequently involved: Rheumatology, Infectious Disease, Gastroenterology, Neurology, DeKalb County Board of Health and Obstetrics.

Our study demonstrates that a large proportion of uveitis patients have complex needs and require a multi-disciplinary approach to care. We improved access to care and are implementing sustainable pathways for “high utilization” patients to enhance team-based care. We believe our model will be a useful tool for other medical systems.

Distinct profiles of soluble cytokine receptors between B-cell vitreoretinal lymphoma and uveitis

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Purpose.

To determine the profiles of soluble cytokine receptors and cytokines, including mostly their ligands, in the vitreous humor of patients with B-cell VRL and uveitis.

Methods.

Vitreous samples were collected from immunocompetent patients with VRL (n = 21), uveitis (n = 20), and idiopathic epiretinal membrane (n = 21) as controls. Cytometric beads assay were used to determine the vitreous concentrations of soluble receptors and cytokines.

Results.

Vitreous levels of soluble interleukin (IL)-2 receptor α (sIL-2R α), sIL-6R, soluble tumor necrosis factor receptor (TNFR) 1, sTNFR2, soluble vascular endothelial growth factor receptor (sVEGFR) 1, sVEGFR2, and IL-10 were higher in patients with VRL than in those with uveitis and controls, whereas those of sIL-1R1, sIL-1R2, and sIL-4R were higher in patients with uveitis than those with VRL and controls. In analyses in patients with VRL, elevation of sVEGFR1 and sVEGFR2 levels was more prominent in patients with systemic metastatic retinal lymphoma (SMRL) than in those with primary VRL/primary central nervous system lymphoma (PVRL/PCNSL). Furthermore, sIL-2R α levels were increased in patients with VRL who developed subretinal lesions compared to in those who mainly had vitreous cavity opacity, positively correlated with the density of CD3⁺ cells in the vitrectomy cell blocks.

Conclusion.

The profiles of soluble cytokine receptors and cytokines in patients with VRL were different from those with uveitis. In addition, sVEGFR1 and sVEGFR2 levels may be differential diagnostic markers between PVRL/PCNSL and SMRL, and sIL-2R α levels can anticipate infiltration of VRL cells into the subretina and/or retina.

Cytokine profiles in intraocular fluids of patients with acute retinal necrosis

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PURPOSE : Immune mediators play a critical role in the pathogenesis of acute retinal necrosis (ARN). A predominant Th1 cytokine profile characterized by high concentration of interferon- γ (IFN- γ) and low concentration of interleukin 4 (IL)-4 has been reported. However, limited data on cytokine concentrations in ocular fluids of patients with ARN are available, and are based on studies with small sample sizes. In this study, we measured a panel of cytokines in the ocular fluids of patients with ARN as well as controls.

METHODS : We performed a retrospective chart review of all patients diagnosed with ARN. Polymerase chain reaction (PCR) analysis was performed to determine the causative virus of ARN. Aqueous humor samples from 24 eyes with ARN (HSV: 5, VZV: 19) and 31 eyes with cataract, epiretinal membrane or macular hole were investigated. Vitreous humor samples obtained by vitrectomy from 29 eyes with VZV-ARN and 21 eyes with macular hole or epiretinal membrane were also analyzed. Twenty-four cytokines were measured using the Cytometric Bead Array Flex kit. All patients were immunocompetent.

RESULTS : Intraocular fluid concentrations of IFN- γ , IL-6, IL-8, IL-10, MCP-1, MIP-1 α , MIP-1 β , IP-10, Mig, RANTES, bFGF, angiogenin, Fas L, and VEGF were significantly increased in patients with ARN compared to controls.

CONCLUSION : This study suggests that increases of several cytokines in the aqueous and vitreous humor of eyes with ARN may indicate the activation state during inflammation. Further studies including correlation of cytokine profile with viral load and visual outcome will be planned.

Regression of retinal neovascularization after infliximab therapy in Behcet's disease

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Introduction: Chronic uveitis is considered a cause of neovascularization of the eye. Vitreous hemorrhage (VH), which occurs due to destruction of retinal neovascularization, causes visual impairment in Behcet's uveitis. We present 5 cases of improvement of retinal neovascularization and VH by administration of infliximab (IFX) in cases of Behcet's uveitis.

Patients: Five patients included 3 men and 2 women; the average age was 37 years (range, 16-58 years). All patients had retinal neovascularization and VH, 2 patients (40%) had neovascularization of the iris. Best-corrected visual acuity (BCVA) of 4 patients (80%) was < 1.0 logMAR unit. Average number of inflammation attacks was 2.6 attacks/6 months (range, 2-3 attacks), the average Behcet's disease ocular attack score 24 (BOS24) was 19.8 points (range, 12-24 points), and the evaluation of activity using fluorescence angiography (FA) (prescribed at Tokyo Medical University, 12 points total) was 10.2 points (range, 5-12 points) before IFX therapy. Improvement of VH and regression of neovascularization of the iris and retina were observed an average of 28.2 days (range, 4-90 days) after IFX treatment was begun. Three patients (60%) had improved visual acuity and a BOS24 of 0; the evaluation of activity using FA was 5.8 points (range, 0-8 points) and the average number of inflammation attacks was 0.2/6 months (range, 0-1) after IFX treatment. Two patients (40%) did not improve; however, improvement was observed after cataract surgery.

Conclusion: Infliximab is an effective treatment for retinal neovascularization in Behcet's uveitis.

Interferon alpha2a and systemic corticosteroid in monotherapy in chronic uveitis: results of the randomised controlled BIRDFERON study

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Purpose : Macular edema is the leading cause of vision loss in bilateral chronic non-infectious posterior uveitis, and is used to being treated using corticosteroids, immunosuppressive agents and biotherapies. The aim of this trial was to assess and compare the efficacy and safety of corticosteroids and IFN- α in adults with such conditions.

Study design : Randomized controlled trial

Subjects : Adult patients with bilateral posterior autoimmune non-infectious and non-tumoral uveitis complicated by macular edema in at least one eye, were recruited.

Intervention : Patients received either subcutaneous IFN- α 2a, systemic corticosteroids or no treatment for 4 months. The efficacy and safety were assessed for up to 4 months.

Main outcome : The main endpoint was the change of the central foveal thickness (CFT) obtained by optical coherence tomography.

Results : Forty-eight patients were included. In intention-to-treat analysis, the median CFT change showed no significant difference. However, the per-protocol analysis showed a significant difference between groups for both eyes (OD and OS), and for the worse and better eyes. Statistically significant difference was found between the control and corticosteroid groups for the OD ($p=0.0285$), and between the control and IFN- α groups for the OD ($p=0.0424$) and worse eye ($p=0.0354$). Serious adverse events occurred in two patients in IFN group, in one patient in corticosteroid group, in two patients in the control group and were completely resolved after switch.

Conclusions : IFN- α and systemic corticosteroids, compared to no treatment, were associated with significant anatomic and visual improvement shown in the per-protocol study.

VKH: an atypical presentation

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A 42 years old housewife presented to the local Hospital complaining of acute visual loss in OS associated to fever and headache. Acute phase retinography disclosed in OS an incomplete macular star associated to optic disc edema. Retinography in OD was unremarkable. Investigation for common and uncommon infectious causes of neuroretinitis were negative, as well as screening for non infectious causes. She was diagnosed with idiopathic neuroretinitis and was sent to our service for a second opinion. When examined, one month later, retinography in OS disclosed multiple serous retinal detachments in OS. Optical Coherence Tomography showed retinal septae in OS and mild chorioretinal folds in OD. On fluorescein angiography there was a moderate dye pooling in the areas of retinal detachments, while on indocyanine green angiography multiple hypofluorescent spots were detectable at the posterior pole and in retinal periphery in both eyes (OU). Systemic investigation was remarkable for pleocytosis on lumbar puncture. We made a diagnosis of Vogt - Koyanagi-Harada disease and treated the patient with high dose i.v. steroids followed by oral tapering. Vogt Koyanagi Harada disease has never been described before as a cause of neuroretinitis, nor neuroretinitis has been reported as a possible presentation of this disease. In our case indocyanine angiography was paramount in making a correct final diagnosis, showing a bilateral involvement in a case apparently unilateral as presentation.

Chronic herpetic retinitis: clinical features and long-term outcomes

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Introduction: Chronic uveitis treated with immunosuppressive agents may have unfavourable outcomes due to delays in diagnosis. The aim of this study was to review initial data from clinical and ocular assessments and patient outcomes following specific treatments for atypical herpes virus ocular infections.

Methods: The records of four consecutive patients with recurrent uveitis for at least five years treated in our department between 2001 and 2016 were retrospectively reviewed. They had atrophic retinal lesions resulting in an unfavourable outcome with lesion progression and vision loss under immunosuppressive treatment. Varicella zoster virus (1 case) and herpes simplex virus type 2 (3 cases) were detected in ocular samples. Best-corrected visual acuity, slit-lamp examination, intraocular pressure measurement, retinal studies including fundus photography and fluorescein angiography and anterior inflammation measurement by Laser Flare Meter were performed before and after administering specific treatments.

Results: Uveitis was granulomatous and bilateral (3 cases) or unilateral (1 case). Immunosuppressive treatments worsened the clinical situation whereas antiherpetic treatments improved the control of intraocular inflammation.

Conclusion: This description should be added to the broad repertoire of clinical polymorphisms associated with herpes virus infections. Recognising these cases should be useful due to their sensitivity to antiherpetic treatments.

Unilateral surgically induced Necrotizing Scleritis after trabeculectomy with Ologen in a patient with pigmentary glaucoma

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Purpose: In this report we record the first surgically induced Necrotizing Scleritis case related to trabeculectomy with the use of Ologen Collagen Matrix Implant. **Observations:** Surgically induced Necrotizing Scleritis is a rare pathological entity that complicates ocular (sclera) surgery. **Conclusions and importance:** Prompt management of surgically induced Necrotizing Scleritis related to trabeculectomy with the use of Ologen and close follow up is very important to prevent its destructive nature on the globe.

The address to uveitis diagnosis

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Uveitis case is one of the challenging tasks to the ophthalmologists who find its management is difficult in many aspects. Moreover, for the immune-privileged organ, like the eye, intra ocular inflammation carries the risk of destroying vital tissues and possibly causing irreversible damage to the sight. Therefore, the aim of management of such inflammation is, to immediately halt it, then, is to control the sight threatening inflammation on the Long-term. There is a great effort made by many uveitis specialists and organizations for classifying the disease, grading the inflammation, and putting specific lists of differential diagnosis to reach a better way for diagnosis. Nevertheless, the task of diagnosing uveitis is still complicated, so that the author attempts, in this short review, to provide a simple and practical algorithm for the diagnosis of uveitis, symbolizing this with the shortest way to safely reach a certain destination “The address to uveitis diagnosis”.

Optical Coherence Tomography Angiography in Punctate Inner Choroidopathy

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PURPOSE: To compare and describe retinal and choroidal vascular changes with SPECTRALIS® optical coherence tomography angiography (OCT-A) in comparison to current imaging techniques in eyes with punctate inner choroidopathy (PIC).

METHODS: In this single-centre-prospective-study, 40 eyes of 20 subjects with PIC underwent imaging with OCT-A (SPECTRALIS®, Heidelberg Engineering), spectral-domain OCT (SD-OCT; SPECTRALIS®, Heidelberg Engineering), fluorescein angiography, indocyanine green angiography and fundus autofluorescence. The clinical findings were also documented by fundus photography.

RESULTS: Mean age of the patients was 45 +/- 10 years and 18 patients were female (90%, 18/20). In more than half of the cases (60% of eyes, 24/40) a choroidal neovascularization (CNV) had been verified.

OCT-A showed in 55% of eyes abnormalities of capillary network which were seen in the superficial and deep capillary plexus. In the outer retina layer, the isolated punctate lesions displayed a “cluster of disturbance” while CNV lesions could be characterized as individual vascular formations.

In 60% of eyes with clinical recurrent CNV, a hypoperfusion with “lacy wheel shape” lesions could be seen on OCT-A while 50% of eyes with clinical stable CNV revealed a “dead tree aspect” in the outer retina. In the choriocapillaris, in 100% of affected eyes, other non-perfused areas were observed which had not been detected so far with the standard methods.

CONCLUSION: OCT-A imaging technique provides the possibility to visualize the microvascular structure of the retinal vascular layers and the choriocapillaris. It helps to detect and characterize secondary CNV's in PIC and to distinguish them from PIC lesions.

AQUEOUS HUMOR ELEVATED CD4/CD8 RATIO FOR THE DIAGNOSIS OF OCULAR SARCOIDOSIS

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Purpose:

Although it is usually not difficult to diagnose ocular sarcoidosis with typical clinical findings, a considerable number of cases present with a negative result in the systemic examination, challenging diagnosis.

A recognized immunologic feature in sarcoidosis is an increased CD4/CD8 T-cell ratio in bronchoalveolar lavage (BAL) fluid. Therefore, aqueous humor (AH) CD4/CD8 ratio analysis could provide an easier and inexpensive method for the diagnosis of ocular sarcoidosis.

Methods:

We performed flow cytometric lymphocyte analysis in 0.1–0.2 mL of AH from patients with acute anterior uveitis, in order to establish CD4/CD8 ratio. Six female patients were included, 3 patients with presumed ocular sarcoidosis (POS), 2 with idiopathic anterior uveitis (IAU) and one patient with hypertensive anterior uveitis from a viral etiology.

Results:

All patients with POS showed an elevated CD4/CD8 ratio (> 4.96). In 2 of the patients with POS, the CD4/CD8 ratio in the BAL was later performed and although elevated, it was still lower than the one found in the anterior chamber. In the 2 patients with IAU the ratio was close to 1 and in the patient with viral AU, the CD4/CD8 ratio was inferior to 1, suggesting an inversion of the ratio.

Conclusions:

Like in previous studies, AH tap for flow cytometric analysis is a simple and secure procedure that may yield a diagnostic value for patients with POS and, possibly, viral AU.

Further analysis of aqueous humor CD4/CD8 ratio, in viral etiology uveitis, might elucidate if the inverted ratio presents diagnostic significance.

Choroidal Neovascularization is nothing to sneeze at !

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A 75 years-old otherwise healthy chinese patient came to our observation for a sudden visual loss in the left eye (OS). His past medical history was significant for bilateral idiopathic peripheral chorioretinal neovascularization (CNV) treated with three bevacizumab intravitreal injections. Review of his previous fluorescein angiography showed peripheral retinal ischemia associated to peripheral CNV and subretinal haemorrhages. Vitreous was clear at that time. At our examination the patient presented a white cataract in the right eye (OD) and a massive vitreous hemorrhage in OS. Anterior segment examination was otherwise unremarkable with no signs of keratic precipitates or iris nodules. Visual acuity was light perception in OD and hand movement in OS; fundus oculi was undetectable in both eyes (OU). B-scan ocular echography disclosed vitreous hemorrhage and focal retinal hyperaecogenic lesions in OU. A prompt immunologic and infectivologic screening were performed that disclosed both positive quantiFERON-TB test and mantoux test. Chest CT resulted negative as well as PCR on aqueous for M. tuberculosis. A diagnosis of presumed bilateral ocular tuberculosis was made and treatment with triple antitubercular therapy and oral steroids was immediately administered. Ocular tuberculosis has the potential to cause variable clinical scenarios. Posterior segment involvement may happen without any signs of anterior segment inflammation and cause atypical retinal, vitreous and choroidal manifestations; hence, isolated ocular tuberculosis should be enlisted in the differential diagnosis of peripheral CNV and ruled out throughout appropriate tests.

The Challenge of Pediatric Uveitis

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The Challenge of Pediatric Uveitis

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Introduction

The purpose of the study is to describe clinical findings, visual outcomes, treatment and complications of patients affected by pediatric uveitis at a tertiary referral ophthalmic center in Waltham, USA.

Methods

A retrospective cohort study including patients with uveitis onset ≤ 16 years referred to Massachusetts Eye Research and Surgery Institution (MERSI) from January 2005 to July 2016 was performed.

Results

Two hundred eighty-six patients were included. Mean age of onset of uveitis was 8.4 ± 3.83 years. The age at first visit at MERSI was 9.58 ± 3.75 years. Anterior uveitis was the most frequent type (61.9%), followed by intermediate uveitis, panuveitis and posterior uveitis. Cataract was the most common complication in each group, accounting for 43.84% of the overall affected eyes.

Conclusion

Pediatric uveitis is a challenging issue for ophthalmologists in terms of diagnosis, treatment and management. Most children with uveitis have a bilateral chronic or recurrent course with insidious onset. Delay in diagnosis increases the number of complications. Good visual outcomes can be achieved more easily if patients receive appropriate steroid-sparing therapy in a specialized center.

Culture-proven *Candida albicans* endogenous endophthalmitis in a patient with onychomycosis.

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Purpose: We report a case of Candida albicans endogenous endophthalmitis with subretinal abscess in a patient with onychomycosis and with no predisposing risk factors.

Methods: Case report

Results: A 40-year-old man admitted the complaint of pain and redness in his left eye for 20 days. He denied ocular trauma, previous intraocular surgery, intravenous drug use or another predisposing factors for endogenous endophthalmitis. Oral prednisolone and co-trimoxazole had been started in elsewhere with the suspicion of ocular toxoplasmosis. At initial examination in our clinic, visual acuity was hand motions in the left eye. The slit-lamp examination revealed intense anterior chamber inflammation and fundoscopy showed an exophytic yellowish-white subretinal mass in the macula with vitreous cells and vitreous haze. Systemic steroids were discontinued. The patient underwent diagnostic vitrectomy followed by intravitreal injection of voriconazole. Culture and histopathological examination of vitreous specimen revealed *Candida Albicans*. *Candida albicans* was also detected in the scraping of his thickened toenails. Intravenous amphotericin B and fluconazole was also started and also intravitreal injection of amphotericin B was performed. Although combined antifungal treatment, inflammatory findings progressed and “string of pearls” appeared in the vitreous. Two weeks later, the patient underwent pars plana vitrectomy. One month after surgery, intraocular inflammation subsided gradually.

Conclusion: We present a proven endogenous fungal endophthalmitis in a patient with onychomycosis and with no predisposing risk factors. The use of systemic steroids in the past caused progression of the disease in this case.

Analysis of IL-10 in intraocular fluids of patients with infectious uveitis

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Purpose;

Measurement of vitreous interleukin-10 (IL-10) is critical for the diagnosis of intraocular lymphoma. On the other hand, IL-10 may have an inhibitory effect on infectious immunity. In this study, we measured and analyzed the concentrations of IL-10 in intraocular fluids obtained from patients with various forms of infectious uveitis.

Methods;

Aqueous humor or vitreous humor samples were collected from 31 eyes with acute retinal necrosis (ARN), 13 eyes with bacterial endophthalmitis, 6 eyes with fungal endophthalmitis, 9 eyes with VZV-related iridocyclitis, 3 eyes with toxoplasma chorioretinitis, 30 eyes with intraocular lymphoma, 26 eyes with epiretinal membrane or macular hole, and 22 eyes with cataract. The concentrations of IL-10 were measured using the Cytometric Bead Array Flex kitR.

Results;

The average vitreous humor IL-10 concentrations in eyes with bacterial endophthalmitis (17 pg/ml), fungal endophthalmitis (125 pg/ml), ARN (102 pg/ml) and toxoplasma chorioretinitis (197 pg/ml) were significantly higher than those in eyes with epiretinal membrane or macular hole, and significantly lower than that in eyes with intraocular lymphoma (2,359 pg/ml). IL-10 was detected in aqueous humor samples from eyes with ARN (mean 95 pg/ml) and VZV-related iridocyclitis (mean 58 pg/ml) but not in eyes with cataract.

Conclusion;

Elevated levels of IL-10 were detected in intraocular fluids of eyes with infectious uveitis irrespective of the causative microorganism, suggesting that IL-10 is related to the infectious immunity.

Posters exhibition

Interferon Alpha-2a Treatment for Refractory Behcet Uveitis in Korean Patients

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Purpose

To evaluate the treatment outcomes of interferon alpha-2a (IFN α 2a) treatment in patients with Behcet disease who were refractory to immunosuppressive agents. We report our treatment experiences in five refractory Behcet uveitis patients.

Methods

This study was a retrospective, interventional case series. We reviewed the medical records of refractory Behcet uveitis patients from Jan 2011 to Feb 2017. Relapse rates, clinical responses, and changes of visual acuity were evaluated.

Results

The mean age of patients was 39.60 ± 9.21 years and the mean treatment duration was 10.60 ± 10.38 months. The mean number of uveitis attack/year per patient during the treatment was 0.40 ± 0.89 . Four of 5 patients (80%) showed complete responses to IFN α 2a, in whom there was no uveitis attack during the treatment period. Visual acuity, however, did not show a significant improvement.

Conclusion

IFN α 2a is an effective therapy for Behcet uveitis refractory to conventional immunosuppressants in Korean patients.

Syphilitic Uveitis

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Introduction

Syphilis is a chronic bacterial infection with a high incidence in developing countries and increasing incidence in Europe and North America. Syphilis is called “the great imitator” of diseases due to heterogenous clinical manifestations. Ocular manifestation is rare. However, the early diagnosis and treatment may prevent irreversible neurological and cardiovascular complications and further transmission of this well treatable infection.

Purpose

The aim of our study is to present the clinical signs of syphilitic uveitis in our patients.

Methods

A retrospective study of 11 patients with ocular manifestation of syphilis (out of 2642 uveitis patients) that have been referred to our Centre for Diagnosis and Treatment of Uveitis in Prague in years 2004-2016.

Results

We examined 10 men and 1 woman of average age 41 years (25-55 years). The diagnosis of syphilis was determined on the basis of suspected ocular finding and positive serological tests in 9 patients, diagnosed prior to ocular manifestation in 2 patients. Simultaneous HIV infection was detected in 3 patients. Bilateral ocular manifestation was present in 6 patients. The main clinical manifestation in our patients was posterior uveitis: optic disc edema (5 patients), chorioretinitis (2 patients), vitritis (1 patient) and vasculitis (1 patient). Isolated anterior uveitis was present in 2 patients, associated with elevation of intraocular pressure in 1 patient.

Conclusion

The screening of syphilis should be considered in differential diagnosis of uveitis that does not respond sufficiently to the anti-inflammatory therapy. The actual serological diagnostics is highly sensitive. The systemic treatment is managed by venereologist.

The efficacy of dexamethasone implant in the treatment of cystoid macular edema secondary to non-infectious posterior uveitis.

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Purpose: To evaluate the efficacy of slow-release dexamethasone implant in the treatment of cystoid macular edema (CME) in patients with non-infectious posterior uveitis.

Methods: Thirteen eyes of 11 patients who did not respond sufficiently to standard uveitis therapy and had CME secondary to non-infectious posterior uveitis were included in the study. Patients were treated with single or repeat dose of intravitreal slow-release dexamethasone implant (DEX Implant 0,7 mg, Ozurdex, Allergan, Inc, Irvine, CA). Best-corrected visual acuity (BCVA), central retinal thickness and intraocular pressure were recorded at baseline, 1 and 3 months after the injections.

Results: Diagnosis included idiopathic uveitis (8 patients), Behcet Disease (2 patients) and vasculitis secondary to systemic lupus erythematosus (1 patient). Three eyes (23.1%) underwent repeated injections because of an increase in macular thickness after six months. At baseline mean BCVA was 0.53 logMAR and mean CMT was 527 μ m. One month after the injections, mean BCVA improved to 0.40 logMAR ($p=0.059$) and mean CMT decreased to 245 μ m ($p<0.05$). CME resolved in 12 eyes (92.3%). Only one eye had still CME with 100 μ m decrease in CMT (7.7%). Three months after the injections, mean BCVA decreased to 0.45 logMAR ($p>0.5$) and central macular thickness was 327 μ m ($p<0.05$). Only two eyes (15.4%) required topical anti-glaucomatous treatment.

Conclusion: Dexamethasone intravitreal implant reduced central retinal thickness in 92.3% of the eyes with CME secondary to non-infectious posterior uveitis in short term. Uveitic CME recurred in 23.1% of the eyes six months after the injection.

Biologic therapy in non-infectious inflammatory eye diseases: Experience in a group of Chilean patients

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Purpose: To describe the use of biologic therapy in a group of Chilean patients with non-infectious uveitis or scleritis, focusing on inflammation, visual acuity, adverse effects and associated therapies.

Methods: Retrospective, cross sectional, observational study. Medical records of patients with non-infectious uveitis and/or scleritis and biologic therapy were reviewed at 2 medical centres. Demographic data, degree of inflammation during follow-up, drugs used and complications were recorded in an Excel database and analysed using Stata®12 software.

Results: We found 41 patients with uveitis or scleritis and biologic treatment. The average age was 15 years at diagnosis (1.5-64). The most frequent aetiology of the inflammation was JIA-associated anterior uveitis. Adalimumab was the main drug used. In the subgroup of patients with ophthalmic indication of biologic therapy and a minimum follow-up of 1 year (1 to 5.6 years, 25 patients), we found a complete control of the inflammation in 72%, 84% and 92% at 3, 6 and 12 months, respectively. 44% had flares-up during follow-up (average 2.8 reactivations per-patient). In 6 patients the treatment was discontinued after 25 months (14-34) of quiescence, occurring reactivations in all but one.

Severe complications seen during treatment were one Varicella Zoster infection, one patient with Leukoencephalopathy, one with pustular psoriasis and one with a non-Hodgkin lymphoma.

Conclusions: Biologic treatment is effective in treating uveitis and scleritis in patients where conventional immunosuppressive drugs have failed. However, despite this high effectiveness, the withdrawal of treatment usually entails a reactivation of the disease and it is not exempted from complications.

Utility of smartphone application in assessing dry eye disease

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Purpose. We developed the iPhone application “DryEyeRhythm” for dry eye disease (DED) using ResearchKit® platform by Apple in Japan. We verified the function of DryEyeRhythm by comparison to slit-lamp microscope.

Methods. This study was a cross-sectional study. We observed 65 individuals (Male: n=43, Female: n=22, average age: 34.4±7.9 years old). We examined the Ocular Surface Disease Index (OSDI), maximal blink interval (MBI) and blink number in 30 seconds using DryEyeRhythm and slit-lamp microscopy. Corneal fluorescein staining score (CFS), tear film break-up time (BUT), Schirmer test1, MBI were also examined using slit-lamp microscopy. We diagnosed DED using the “Definition and Diagnosis of Dry Eye 2006” from the Japan Dry Eye Society. The OSDI, MBI and blink number were compared between DryEyeRhythm and slit lamp microscopy by the Spearman's rank correlation..

Result. The mean CFS score was 1.72, the mean BUT was 4.97 seconds and the mean tear volume by Schirmer test1 was 21.25 mm. We diagnosed 36 non-DEDs, 17 suspect DEDs (sDED) and 12 DED. The mean OSDI score was 16.6, the mean MBI was 17.6 seconds and the mean blink number was 8.2 using DryEyeRhythm. The mean OSDI score was 20.1, the mean MBI was 18.0 seconds and the mean blink number was 11.2 using slit-lamp microscopy. The correlation coefficient of Spearman between DryEyeRhythm and slit-lamp microscopy had a significantly positive correlation in OSDI, MBI and blink number (OSDI: $r=0.86$, MBI: $r=0.25$, blink number: $r=0.55$).

Conclusions. DryEyeRhythm is useful for monitoring subjective symptoms and blinking in DED.

Anti-CD80/86 injection prolongs the graft survival in murine corneal transplantation

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【Purpose】 To assess the immune responses and the effects on graft survival of anti-CD80/CD86 injection in murine corneal transplantation. **【Methods】** Three intrastromal sutures were placed in the recipient graft bed two weeks before allogeneic transplantation to induce angiogenesis. Control (LR) graft recipients did not undergo suture placement. Anti-CD80/86 was administered to transplanted mice by intraperitoneal injection immediately after, and 24 and 48 hours post transplantation (PBS was administered as control). Graft opacity scores were evaluated for 8 weeks by slit-lamp biomicroscopy. Ipsilateral draining lymph nodes (dLNs) were harvested 14 days after transplantation. dLNs were analyzed for CD4⁺CD25⁺Foxp3⁺regulatory T cells (Tregs), CTLA-4, CD11c⁺ dendritic cells (DC) and CD11b⁺ macrophage. The expression level of Foxp3, CTLA-4 in Tregs and MHC class II in CD11c⁺ DCs were analyzed by mean fluorescence intensity (MFI). **【Results】** Anti-CD80/86 injection prolonged graft survival in HR grafts (mean survival, HR-PBS; 24.5 days, HR-anti-CD80/86; 49 days, $p < 0.001$). Anti-CD80/86 administration reduced graft opacity score in HR-anti-CD80/86 compared to HR-PBS at day 56 post-transplantation (HR-PBS; 5.0, HR-anti-CD80/86; 1.3, $p < 0.05$). Anti-CD80/86 administration increased MFI expression level of CTLA-4 in dLNs of HR-anti-CD80/86 compared to HR-PBS (HR-PBS: 3462, HR-anti-CD80/86: 4229, $p < 0.0025$). The MFI expression of MHC class II in CD11c⁺ DCs of HR-anti-CD80/86 was reduced compared to HR-PBS (HR-PBS; 45748 vs. HR-anti-CD80/86; 34566, $p < 0.05$). **【Conclusions】** We found the blockade of CD80/86 at the time of transplantation induced long term allograft survival via CTLA-4 activation and MHC class II deactivation.

Anti-Bacterial Effects on Ocular Surface Pathology in Dry Eye Disease

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【Purpose】 To investigate effects of antibiotics and vaccine-induced antibodies on pathology and commensal bacterial levels on the ocular surface in the murine dry eye disease (DED) model. **【Methods】** DED was induced by exposure of 8-week-old female C57BL/6 specific pathogen-free (SPF), germ-free (GF) or GF mice co-housed with SPF mice for 2 weeks (GF/SPF) to a controlled-environment chamber (CEC). Immune (IGS) polyclonal antibody raised to the conserved microbial surface polysaccharide, poly-N-acetylglucosamine (PNAG) was administered to mice by intraperitoneal injection at day 1 before placing them into the CEC and at days 3, 5 and 8 (300 ul/mouse). Frequencies of CD4⁺CD25⁺Foxp3⁺Tregs, IFN- γ - and IL-17-producing T cells in draining lymph node cells (dLNs) were analyzed by flow cytometry.

【Results】 Corneal fluorescein staining (CFS) was increased in DED-GF compared to room air (RA) GF/SPF, RA-GF and DED-GF/SPF mice ($p < 0.001$). DED-GF had decreased frequencies of Tregs (DED-GF: 7.6%; DED-GF/SPF: 8.8%). IFN- γ - and IL-17-producing T cells were increased in DED-GF compared to DED-GF/SPF (IFN- γ : $p < 0.01$, IL-17: $p < 0.01$). DED with anti-PNAG had improved CFS com ($p < 0.001$). Anti-PNAG IGS injection significantly increased the frequencies of Tregs (DED: 6.9% vs. DED with anti-PNAG IGS: 9.9%). IFN- γ - and IL-17-producing T cells were decreased in DED with anti-PNAG compared to DED (IFN- γ : $p < 0.05$, IL-17: $p < 0.01$). **【Conclusions】** Our data suggest commensal bacteria contribute to pathology in DED and pathology can be reduced by treatment with anti-bacterial antibody to PNAG.

OCULAR MANIFESTATIONS ASSOCIATED WITH TAKAYASU ARTERITIS: A MULTIMODAL IMAGING STUDY

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Purpose : The goal of this study is to describe ophtalmological features of Takayasu disease on fundus exam, in fluorescein angiography and OCT angiography. Takayasu arteritis is a rare, inflammatory and systemic large-vessel granulomatous vasculitis of unknown etiology.

Methods : All patients with Takayasu disease followed in Pitié Salpêtrière from 2004 to 2016 were retrospectively included in this observational study. All underwent complete ophtalmological examination including fluorescein angiography and SDOCT. Most underwent OCTAngiography. The OCTA were analyzed to evaluate perifoveal anastomotic capillary arcade disruption, capillary perifoveolar density, microaneurysms. The foveal avascular zone (FAZ) was measured for Superficial (SCP) and Deep capillary complex (DCP).

Results : 13 patients (26 eyes) were included. Most frequent anomalies were retinal microaneurisms (6 patients). Stage I retinopathy (resp II, III, IV) was seen in 5 (resp 10, 2, 3) eyes. No hypertensive retinopathy observed. 7 patients (14 eyes) underwent OCTA. 11 eyes presented with ruptures of the perifoveal anastomotic capillary arcade in SCP. 5 had microaneurysms. 11 had rarefaction of the perifoveolar vascular density in SCP. The average SCP FAZ was increased to 0.34mm² in Takayasu compared to 0.27mm² in control patients.

Conclusion

Macular abnormalities are uncommon in Takayasu patients as retinopathy signs are mostly located in peripheral retina. This study reveals that most of our patients present an enlargement of the FAZ, even in the earliest stages of retinopathy with no macular abnormality on fluorescein angiography, then highlights the relevance of OCTA to evaluate macular ischemia as a complement to usual retina global study in fluorescein angiography.

Protective role of B7-H3/TLT-2 pathway in acceptance of corneal allografts

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Purpose: B7-H3 belongs to the B7 superfamily, a group of molecules that co-stimulate or down-modulate T-cell responses. Recently, triggering receptor expressed on myeloid cells-like transcript-2 (TLT-2) has been identified as a B7-H3 receptor. We have previously reported that B7-H3 is constitutively expressed in ocular tissue and B7-H3/TLT-2 pathway is necessary for corneal allograft survival. The purpose of the present study is to further investigate the mechanisms B7-H3-associated immune suppression.

Methods: We examined anterior chamber associated immune deviation (ACAID) *in vivo* and destruction of corneal endothelial cells (CECs) by allo- reactive CD4+ T cells *in vitro*. Allo-antigen-specific ACAID model was used.

Results: ACAID was abolished in the recipients treated with either anti-TLT-2 or anti-B7-H3 mAb. The number of dead CECs was significantly larger in anti-B7-H3 mAb-treated corneas than in control IgG-treated corneas after incubation with alloreactive CD4+T cells. The number of dead CECs was also significantly larger in anti-B7-H3 mAb-treated corneas than in control corneas after incubation with CD4+T cells activated against third-party allo-antigens.

Conclusions: B7-H3/TLT-2 pathway is involved in the induction of ACAID. B7-H3 expressed on CECs plays a role in protecting CECs from destruction by activated CD4+ T cells. Thus, B7-H3/TLT-2 pathway maintains acceptance of corneal allografts by inducing ACAID as a systemic effect and suppressing allo-reactive CD4+ T cells within the eye as a local effect.

Trabecular meshwork depigmentation and age of disease onset in Vogt–Koyanagi–Harada disease

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Purpose : Depigmentation of trabecular meshwork develops in some patients in the course of Vogt–Koyanagi–Harada (VKH) disease. We previously reported that this depigmentation (Ohno's sign) is significantly correlated with the development of sunset glow fundus, however, not with limbal depigmentation (Sugiura's sign) or skin lesions. We herein report the correlations between trabecular meshwork or limbal depigmentation and other parameters.

Methods : We performed retrospective review of 53 VKH patients (21 men, 32 women, average 41.0 years old) from 1991 to 2011 in the Hokkaido University Hospital, Japan. The age at disease onset ranged from 20 to 71 years. The average disease duration was 57.4 months (range 0-237). Trabecular meshwork and limbal depigmentation was investigated from June 2010 to September 2011. Each eighth of the trabecular meshwork pigmentation was scored from 0 to 4 based on Scheie classification, and all scores were summed up. In the same way, limbal pigmentation was scored from 0 to 2, and all scores were summed up. We then examined the correlations between trabecular meshwork or limbal depigmentation and age at disease onset or disease duration.

Results : Trabecular depigmentation was correlated with the intensity of sunset glow fundus ($p<0.05$). Significant negative correlation was observed between trabecular meshwork depigmentation and age at disease onset ($p<0.05$), whereas limbal depigmentation showed no significance. There were no correlations between trabecular meshwork or limbal depigmentation and disease duration.

Conclusions : Trabecular meshwork depigmentation is likely to be affected in young patients with VKH disease.

Vitreous Haze Improvement with Intravitreal Sirolimus in Subjects with Non-infectious Uveitis of the Posterior Segment: Results from the SAKURA Program

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Purpose: The SAKURA Program consisted of two Phase III (one pivotal, one supportive), randomized, multinational, active control studies assessing the safety and efficacy of every-other-month intravitreal (IVT) sirolimus in the treatment of active non-infectious uveitis of the posterior segment (NIU-PS).

Methods: Eligibility criteria included vitreous haze (VH) $\geq 1.5+$ in the study eye. Subjects from both studies comprised the integrated Intent-to-Treat (ITT) population evaluating IVT sirolimus 440 μg vs 44 μg active control (n=208 for each group). The primary endpoint was VH=0 at Month 5. Least squares (LS) mean change from baseline in VH were analyzed at Week 2 and monthly Months 1 to 5. Safety was assessed up to Month 6.

Results: In the integrated ITT population, 21.2% vs 13.5% of subjects (440 μg vs 44 μg , $p=0.0381$) achieved VH=0 at Month 5. At Month 5, the LS mean change in VH was -1.18 vs -0.96 (440 μg vs 44 μg , $p=0.0057$). In addition, 440 μg demonstrated a greater mean decrease in VH score from baseline vs 44 μg at each analysis visit. Occurrences of serious ocular adverse events were similar among treatment groups and no unexpected events were reported.

Conclusion: In the SAKURA Program, treatment with the novel mTOR inhibitor IVT sirolimus, administered 440 μg every other month, resulted in statistically significant improvements in VH at Month 5 in subjects with active NIU-PS when compared to 44 μg . Subjects who were treated with 440 μg also showed greater improvements in VH at each visit when compared to 44 μg .

PEDIATRIC UVEITIS: CLINICAL CHARACTERISTICS IN 96 CHILDREN

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Purpose: Uveitis is less common in children than in adults and its diagnosis and management can be challenging. Ocular complications may be encountered at presentation due to the occult nature of the inflammation. We aim to report on the clinical characteristics and visual outcome in a cohort of 96 children

Methods: Retrospective cohort study. Medical files of children (≤ 18 years) treated at the uveitis service of 2 tertiary referral centers were reviewed

Results: Ninety six children (156 eyes) were included in the study: 54 girls and 42 boys. The mean age at diagnosis of uveitis was 9.5 years. Non-infectious uveitis was found in 89 out of 96 children. Chronic anterior uveitis was the most common form of uveitis. Less common forms included intermediate uveitis, panuveitis, acute anterior uveitis and posterior uveitis. Idiopathic uveitis was found in 58 (60%) children, JIA - associated uveitis in 22 (23%) children, and Behçet's uveitis in 5 (5%) children. Infectious uveitis was secondary to toxoplasmosis, bartonella, herpes and CMV infections. The most common complications were macular edema, cataract and band keratopathy. Treatment modalities included: topical, periocular, intravitreal and systemic therapies. Visual acuity improved in most of the patients during follow-up

Conclusion: Non-infectious uveitis is the leading cause of uveitis in our cohort. Both genders were equally affected and most of the children had bilateral disease. Chronic anterior uveitis was the most common form of uveitis, with JIA being the most commonly associated underlying disease. Treatment resulted in visual acuity improvement in most of the eyes

Infectious uveitis: Is there a change in its spectrum?

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Infectious uveitis: Is there a change in its spectrum?

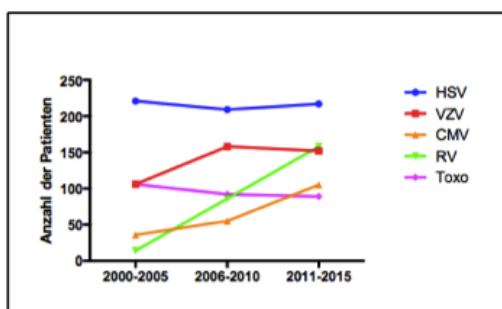
Purpose: To determine the pattern of infectious uveitis over the years 2000-2015.

Methods: We analyzed the findings in suspected infectious uveitis patients over the last 15 years. Specific etiologies were determined for Herpes viruses (H. simplex, -zoster and Cytomegalovirus) Rubella virus and Toxoplasma gondii. An infectious etiology was confirmed by a positive GW coefficient (≥ 3). To compare a potentially time related pattern we predetermined time frames for 2000-2005, 2006-2010 and 2011-2015.

Results: Between 2000 and 2015, 2777 aqueous humor samples were analyzed for a suspected infectious cause. The absolute numbers of samples for the given time period varied, but did not differ significantly.

Infectious agent	2000-2005	2006-2010	2011-2015	p-value	
HSV	221	209	217	0.3611	0.4468
VZV	106	158	152	0.0354	0.4371
CMV	36	55	105	0.0459	0.0007
RV	14	86	158	0.0010	0.0023
Toxoplasma gondii	106	92	89	0.4209	0.4414

Conclusions: Herpes (simplex/zoster) virus related uveitis remains a major cause of intraocular inflammation. We were not able to detect a significant shift over the given time frames. In contrast, the awareness and clinical importance for cytomegalovirus and rubella virus raised increasing attention and is most likely reflected in our findings. These data emphasize the value of a defined diagnosis based of intraocular inflammation and subsequent therapy.



Comparison of sociodemographic features between Behçet uveitis and other noninfectious uveitides.

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Purpose: To analyze and compare sociodemographic features between Behçet uveitis and other noninfectious uveitides.

Methods: The data of adults with noninfectious uveitis in the nationwide uveitis database were analyzed and sociodemographic features of patients with and without Behçet disease were compared.

Results: This study included data of 4978 eyes of 3363 patients from 33 centers. The mean age at presentation was 38.7 ± 13.3 (17–87) years. The mean age was 34.3 ± 10.5 years in Behçet uveitis group and 41.1 ± 14.0 years in other noninfectious uveitis group ($p < 0.001$). A male predominance was seen in Behçet uveitis group (67.7% vs 32.3%) while female patients had the majority in other noninfectious uveitis group (54.4% vs 45.6%) ($p < 0.001$). Regarding educational status, low educational status rate was higher in Behçet uveitis group than other noninfectious uveitis group (52.1% vs 45.5% for primary school graduates) ($p < 0.001$), (29.0% vs 25.8% for high school graduates) ($p < 0.001$). Having a low-income job or being currently unemployed, indicators of poor income, were more frequent in the Behçet uveitis group than in the other noninfectious uveitis group (31.5% vs 23.0%) ($p < 0.001$). When we compare places where patients live, the rate of patients who live in cities with low gross national product was 37.4% in the Behçet uveitis group and 31.2% in the other noninfectious uveitis group ($p < 0.001$).

Conclusion: Patients with Behçet disease had a low educational status and a poor socioeconomic status in comparison to the patients with other noninfectious uveitis entities.

Central serous chorioretinopathy in uveitis patients under corticosteroid therapy.

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Purpose: To report central serous chorioretinopathy (CSCR) in uveitis patients as complication of corticosteroid therapy.

Methods: A retrospective chart review of uveitis patients seen from 1995 to 2015 at the Centre for Ophthalmic Specialised Care, Lausanne, Switzerland. The ophthalmic and systemic features are presented.

Results: Out of 1793 uveitis patients followed at the Centre for Ophthalmic Specialised Care, 6 patients (0.3%) developed CSCR under corticosteroid therapy. The mean age of patients was 40 ± 13.4 years; disease incidence was not associated with gender (3 men; 3 women). 3 patients had idiopathic uveitis, 1 patient - birdshot retinichoroiditis, 1 patient - presumed tuberculosis, and 1 patient - Vogt-Koyanagi-Harada disease. The mean duration of corticosteroid therapy before CSCR occurred was 4.95 ± 4.0 months. At the moment of CSCR, the mean best-corrected visual acuity (BCVA) was 0.6 ± 0.26 ; after the discontinuation of corticosteroids, at the last follow-up BCVA was 0.73 ± 0.3 . The mean laser flare photometry was 44.7 ± 91.4 ph/ms showing a mild inflammation when CSCR occurred. The mean delay in diagnosis of CSCR was 6.8 ± 1.5 months.

Conclusion: Central serous chorioretinopathy should be suspected when the vision deterioration occurs among uveitis patients with no signs of active inflammation in whom corticosteroid therapy was administered. This complication is extremely rare but serious condition which needs a prompt tapering and discounting of corticosteroids.

Sarilumab, a Human Anti-IL-6 Receptor Monoclonal Antibody, in Posterior Segment Non-Infectious Uveitis (NIU): The SATURN study

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PURPOSE: To evaluate efficacy and safety of sarilumab in posterior segment NIU.

METHODS: SATURN, a 52-wk, double-masked, phase 2 trial, randomized (2:1) 58 patients with posterior segment NIU to subcutaneous sarilumab (200mg) q2 weeks or placebo. All patients had to be on a stable dose of systemic steroids ≥ 15 mg/day at baseline alone or in combination with methotrexate (≤ 25 mg/week).

RESULTS: At baseline, 94.7% (sarilumab) and 95.0% (placebo) of patients had active disease (presence of vitreous haze ≥ 4 , central retinal thickness ≥ 300 μm , and/or other signs of intraocular inflammation). At week 16, the proportions of sarilumab and placebo patients with a ≥ 2 -step reduction in vitreous haze (VH) or steroid dose < 10 mg/day was 46.1% vs 30.0% ($P=0.2354$) when VH was measured by the reading center (primary endpoint), and 64.0% vs 35.0% ($P=0.0372$) when VH was assessed by the investigator. At wk 52, mean CRT change in a subgroup of patients with baseline CRT ≥ 300 μm was -87.8 μm ($n=18$; baseline CRT = 432 μm) in the sarilumab group vs $+20.0$ μm ($n=11$; baseline CRT = 346 μm) in the placebo group, $P=0.0210$, with corresponding BCVA gain of 10.8 (baseline BCVA = 66.6) letters vs 2.6 (baseline BCVA = 77.8) letters, respectively. Ocular serious adverse events through wk 52 were uveitis (1 sarilumab patient [2.6%]) and increased intraocular pressure (1 placebo patient [5.0%])

CONCLUSIONS: Sarilumab may be efficacious in the management of posterior segment NIU.

Glucocorticoid biomarkers of steroid response and disease activity in Vogt-Koyanagi-Harada disease

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Purpose: To investigate the role of glucocorticoid receptor (GR) isoforms and MKP1 -a glucocorticoid (GC) inducible gene- in peripheral blood mononuclear cells (PBMC) as a biomarker of GC resistance and disease activity, in patients with Vogt-Koyanagi-Harada disease (VKH).

Methods: Prospective cohort study that included a total of twenty patients with VKH and fifteen healthy donors. A complete ophthalmologic evaluation was performed at recruitment. GC resistance was considered in patients having a reactivation with a dose of prednisolone of 10 mg or more, during the first cycle of treatment. *Quantitative* RT-PCR was performed to measure the mRNA levels of GR alpha isoform (GR α), beta isoform (GR β) and MKP1 in PBMC, after *in vitro* stimulation with dexamethasone (dex) and immune-cell activators (CD3/CD28, LPS and PHA).

Results: After six hours of stimulation with dex, PBMC from GC-sensitive patients had a greater increase in GR α levels in comparison with GC-resistant patients (1.99 and 1.27, respectively, $p=0.03$). No differences in GR β and MKP1 were found between both groups of subjects. While active patients presented no differences in the levels of MKP1 after *in vitro* stimulation with dex, inactive patients showed a significant dex-induced upregulation of MKP1 (1.05 and 5.12, respectively, $p= 0.005$). PBMC from healthy donors pre-stimulated with immune-cell activators had a significant lower dex-induced upregulation of MKP1 ($p=0.01$).

Conclusions: The evaluation of the expression of GR isoforms and MKP1 as potential biomarkers of treatment response and disease activity can contribute to the early identification of GC-resistance and sub-clinical inflammation in patients with VKH.

Miss

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Incidence, management and outcome of ocular hypertension and secondary glaucoma in children with uveitis: the Manchester experience

Aim: To investigate the incidence, management and outcome of uveitic children with secondary glaucoma treated at the Manchester Uveitis Clinic.

Methods: This was a retrospective, observational study of patients who presented with uveitis under the age of 16 to the Manchester Uveitis Clinic from July 2002 to June 2016.

Results: A total of 244 children were identified from the database. Out of these, 41 (16.8%) patients (64 eyes) were found to have raised intraocular pressure (IOP) requiring treatment. The mean age at diagnosis of uveitis and at first recorded raised IOP was 9.0 ± 4.0 and 10.0 ± 3.5 respectively. 35.9% of the eyes had juvenile idiopathic arthritis and 85.9% had chronic uveitis. 84.4% of the eyes were on topical steroids at the time of high IOP. The pre-treatment IOP was 32.3 ± 6.9 mmHg and the IOP at final visit was 15.6 ± 4.6 mmHg (mean follow-up period=45.2 months), on a mean number of 0.7 medications. Twenty-four patients (37.5%) required glaucoma drainage surgery and 8 (12.5%) had cyclodiode prior to that. The mean cup-disc-ratio at final follow-up was 0.4. The best-corrected visual acuity at diagnosis was 0.2 logMAR, which remained stable at 0.3 logMAR at final follow-up visit. One patient (1.6%) lost perception of light due to uncontrolled IOP.

Conclusion: Our cohort of young uveitic patients with high IOP appeared to have a good outcome overall through aggressive medical and surgical management. Early drainage surgery is recommended in eyes with uncontrolled high IOP.

Vitamin D Levels and Uveitis Activity: An Observational Case-Control Study

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Background: Experimental studies have demonstrated that calcitriol inhibits the development of experimental autoimmune uveitis (EAU), the animal model of uveitis, and has the potential to reverse already-developed EAU. Limited research currently exists regarding the clinical relationship between serum vitamin D levels and uveitis activity. We studied serum vitamin D levels in patients with active and inactive non-infectious uveitis and healthy controls.

Methods: This observational case-control study recruited patients with active and inactive non-infectious uveitis, as diagnosed by fellowship-trained ophthalmologists, from two Victorian tertiary hospitals and a private consulting room. Patients were recruited between February and September 2017. All patients had a serum 25-hydroxyvitamin-D measurement. These results were compared to age-matched and season/state-matched data from the Australian Bureau of Statistics in their Nutrition Survey 2011-2012.

Results: At this preliminary stage, 20 patients with active non-infectious uveitis and 15 patients with inactive non-infectious uveitis were identified, with a median (IQR) age of 43.5 (21.5). The median (IQR) level of serum vitamin D in active uveitis was 54nmol/L (49.5) as compared to inactive uveitis at 73nmol/L (29). The active uveitis group was significantly lower than the control median (IQR) of 66nmol/L (30). Age- and season-based sub-analyses yielded similar findings.

Conclusion: We found a relationship between low serum vitamin D levels and non-infectious uveitis, with significantly lower median vitamin D levels in active uveitis compared to inactive uveitis and controls. Further studies are recommended to determine the efficacy of vitamin D supplementation in decreasing uveitis relapses.

Ocular manifestations of SAPHO syndrome

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BACKGROUND: Synovitis–acne–pustulosis–hyperostosis–osteitis (SAPHO) is an acronym for various osteoarticular and dermatological manifestations that can appear in the same patient. Ocular presentation associated with SAPHO syndrome is relatively uncommon. We report ocular manifestations in four cases that developed ocular inflammation associated with SAPHO syndrome.

CASE REPORT: Three female and a male (age 46-63) developed painful red eyes. Slit-lamp examinations revealed bilateral anterior diffuse scleritis in the three female patients and unilateral acute anterior uveitis (non-granulomatous iridocyclitis) in the male patient. All cases had been diagnosed with palmoplantar pustulosis or psoriasis vulgaris before development of ocular findings. Three female cases have been diagnosed osteoarticular manifestations involve osteitis, hyperostosis, synovitis or arthropathy, before developing scleritis. The male case developed osteoarticular manifestations after acute anterior uveitis. All cases were diagnosed with SAPHO syndrome by rheumatologists after excluding other causative diseases. All cases were treated with topical steroid and/or tacrolimus eye drops, oral celecoxib, steroid, and methotrexate. Three cases (two female and a male) showed poor response to these treatments and resulted prolonged ocular inflammation. Treatment with anti-TNF mAb (Infliximab or Adalimumab) were effective for these three cases to improve ocular findings.

CONCLUSION: Ocular manifestations of SAPHO syndrome includes scleritis and non-granulomatous iridocyclitis, Anti-TNF therapy was effective for patients who showed poor response against immunosuppressive agents.

High resolution chest computerised tomography in the diagnosis of ocular tuberculosis: Clinical profile and tuberculin skin test results

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Objective: To report the clinical profile and tuberculin skin test (TST) results of patients with clinically diagnosed ocular tuberculosis and signs of systemic tuberculosis on high-resolution computerised tomography (HRCT) scans of thorax.

Methods: Retrospective review of clinical findings and Mantoux test results of 40 patients with clinically diagnosed ocular tuberculosis and signs of systemic tuberculosis on HRCT thorax.

Results: Out of the 40 cases, 16 were males and 24 were females. The mean age was 39.6 years with a range of 14 to 67 years. Twenty-eight (70.0%) patients belonged to 21-50 year age group. Twenty-two were bilateral and 18 showed unilateral ocular involvement. Eleven (27.5%) patients had intermediate uveitis, 9 (22.5%) had panuveitis, 9 (22.5%) had occlusive retinal vasculitis, 7 (17.5%) had multifocal choroiditis, 2 (5.0%) had serpiginous-like choroiditis, 1 (2.5%) had scleritis and 1 (2.5%) had a choroidal granuloma. HRCT of the thorax revealed calcified granulomas in 26 (65.0%) patients, calcified mediastinal lymphadenopathy in 10 (25.0%) patients and fibrosis with or without atelectasis and enlarged lymph nodes in 4 (10.0%) patients. Mantoux test with 5 tuberculin units was positive (≥ 10 mm induration) in 27 (67.5%) patients.

Conclusion: HRCT thorax can aid the diagnosis of ocular tuberculosis in patients with suggestive clinical findings, especially when TST is negative or inconclusive. Accurate diagnosis of this treatable condition is essential for the prevention of blindness from chronic and recurrent uveitis.

The role of toll-like receptor (TLR)-7 gene polymorphisms in development of Behçet uveitis

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Purpose: Behçet Disease is a multisystem inflammatory disorder characterized by recurrent inflammatory attacks. Genetic factors that predispose individuals to Behçet disease are considered to play an important role in the development of the disease. This study was conducted to determine whether Toll-like receptor (TLR)-7 gene polymorphisms are associated with Behçet uveitis in Turkish patients.

Methods: Eighty-nine patients with Behçet uveitis and 109 healthy controls were enrolled in the study. Genomic DNA obtained from blood samples of each participant. TLR-7 gene rs179009 and rs179008 genotypes were determined by using polymerase chain reaction with specific primers and DNA sequencing methods (ABI 3730). The allele/genotype diversity was evaluated between the patients and controls.

Results: As a result of the study, there was no statistically significant difference in the genotype and allele frequencies of the patients and controls for TLR-7 rs179009 (T>C) and rs179008 (A>T) polymorphisms ($p>0.05$).

Conclusions: In this study, it was found that the TLR-7 polymorphisms were not related to Behçet uveitis in a Turkish population.

Spectral-Domain Optical Coherence Tomography and Anterior Chamber Inflammation

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Introduction: The standard of care for recording the degree of anterior chamber (AC) inflammation in cases of uveitis is based on the Standardization of Uveitis Nomenclature (SUN) Working Group scale. However, this method is subjective. This study was designed to determine the viability of anterior segment optical coherence tomography (AS-OCT) to objectively image and quantify the degree of AC inflammation.

Methods: Observational study of patients admitted to emergency room with diagnostic of anterior uveitis. Clinical grading was based on SUN classification. Bidimensional AS-OCT (SPECTRALIS®, Heidelberg) scans were obtained and manually graded to evaluate for the presence or absence of cells in the AC. Clinical grading scores were correlated to the number of cells seen in AS-OCT analysis.

Results: The study included 4 men and 3 women with anterior uveitis. Ten eyes were analyzed clinically and by AS-OCT, with a total of 14 evaluations. The average number of cells on line scans was 0.15 for grade 0, 1.4 for grade 1/2+, 2.8 for grade 1+, 7.3 for grade 2+, 17.1 for grade 3+, and 39.2 for grade 4+. Spearman correlation coefficient comparing the manual and automated cell counts with the clinical grade was 0.997 ($P < 0.0001$).

Conclusion:

Anterior segment OCT can be used to image and grade the degree of AC inflammation. Clinical

grading strongly correlates with the number of cells on AS-OCT line scans. The development of an automated algorithm to measure cell count could be used to objectively grade response to treatment.

Worrisome increase in the incidence of ocular syphilis in a French reference center

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Syphilis is a re-emerging disease. The aim of this study was to describe the incidence, demographics, clinical ophthalmological features, and visual outcome of ocular syphilis over a 4-year period at a tertiary reference centre in Paris, France.

Over this period, twenty-one patients (29 eyes) with ocular manifestations of syphilis were identified who comprised 1.4% of 1493 new patients diagnosed with uveitis. Posterior uveitis was the commonest diagnosis (66%) followed by panuveitis (14%). The incidence of the disease increased ten-fold during the study period, from 2.22 to 25.21/1000 consultants. The most frequent presentation in the posterior segment of the eye was posterior placoid chorioretinitis (17 out of 29 eyes, 58%). While mean presenting best corrected visual acuity (BCVA) was 0.9 (range, 0 to 2.30 logMAR), 75% of patient had a good final visual outcome (BCVA \geq 0.3 logMAR). Visual outcome was worse for HIV-positive patient (final BCVA: 0.7 logMAR) compared with HIV-negative patients (final BCVA: 0.09 logMAR ($p=0.0139$)). One patient (4.7%) developed recurrence after treatment. Worse final VA outcomes (BCVA \geq 0.30 logMAR) were found in patients whose mean delay in consulting for visual symptoms was 61 days (SD \pm 53). Those who had the best final VA outcome (BCVA $<$ 0.30 logMAR) had a mean delay in consulting of 15 days (SD \pm 19).

The incidence of the disease increased ten-fold during the study period, from 2.22 to 25.21/1000 consultants. Physicians should be aware of ocular syphilis and screen any patient with visual complaints that could be related to Treponem.

LATE SPONTANEOUS IN-THE-BAG INTRAOCULAR LENS DISLOCATION IN PATIENTS WITH UVEITIS

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PURPOSE : analyze of 2 cases of late spontaneous in-the-bag intraocular lens dislocation in patients with uveitis. **DESIGN :** retrospective case serie with literature review. **MATERIALS AND METHODS :** All case records of eyes with chronic uveitis that had phacoemulsification with IOL implantation, at a referral uveitis clinic between were retrieved and analyzed. **RESULTS :** a total of 81 eyes of 62 patients with chronic uveitis underwent phacoemulsification with IOL implantation under steroid cover from February 2000 to December 2014, with a peroperative control of inflammation. Out of these 81 eyes, 2 eyes of 2 patients had experienced late in-the-bag IOL dislocation (2,84%). One patient had herpetic uveitis and one idiopathic panuveitis. Mean age at the time of cataract surgery was 22. The two cases underwent phakoémulsification with intraocular lens implantation with uneventful surgery. All had eye dislocation with mean time from initial cataract surgery to intraocular lens dislocation of 36 and 28 months, associated with a capsular contraction in the two cases. The two cases were managed conservatively by anterior capsular yag capsulotomy. After an initial good improvement, we observed a recurrence of the dislocation in the two cases. Best vision was count-finger at time of dislocation and 6/60 (case 1) and 6/20 (case 2)–2 at follow-up. **CONCLUSIONS :** In-the-bag dislocation of IOL is a rare late complication in uveitic eyes. The good options of restoring vision in these high-risk eyes should be individualized and based on clinical status of each case.

UNILATERAL HYPERTENSIVE UVEITIS AS THE PRESENTING SIGN OF GASTRO-INTESTINAL LYMPHOMA IN A YOUNG WOMAN

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Background : The uveitis masquerade syndromes (UMS) are a group of ocular diseases that may mimic chronic intraocular inflammation. UMS patients were generally older. We report a case in a 37-year –old woman due to lymphoma. **Observation :** A 37-year-old woman patient was followed for unilateral uveitis with 3 attacks in 9months, despite initial improvement with steroid therapy. The patient had visual acuity (VA) of 6/30 in right eye, with an hypopyon, an increased intrao-ocular pression and a vitritis with no chorioretinal lesions. The left eye was normal. The patient was evaluated for intraocular unilateral infection, intraocular foreign body, intraocular lymphoma and associated systemic disease, malignancy. Computed tomography of the abdomen showed a mass in the gastro-intestinal tractus. Biopsy confirmed lymphoma. After resection of the mass and appropriate chimiotherapy, intraocular inflammation improved completely and no attack was noted in the 2-years follow-up. In his last examination, VA was no light perception; seclusion pupilla and mature cataracts were seen on biomicroscopy. There was no sign of vitritis on ocular ultrasonography. Evidence is discussed that suggests a link and potential etiology between refractory hypertensive unilatéral uveitis with hypopyon and lymphoma. **CONCLUSION :** Differential diagnosis between chronic uveitis and UMS is challenging, more difficult in younger patient. The majority of patients with neoplastic masquerade syndromes had primary intraocular/vitreoretinal lymphoma.

Objective Measurement Of Vitreous Inflammation Using Optical Density Ratio In Recurrent Vogt-Koyanagi-Harada Disease

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Purpose : To quantify the vitreous inflammation and investigate the relationship between the uveitis severity and the optical density ratio obtained from vitreous using optical coherence tomography.

Methods: Patients with recurrent Vogt-Koyanagi-Harada disease after steroid pulse therapy were included in the study. Spectral-domain optical coherence tomography images of vitreous were analyzed. The optical density measurements were obtained by using Image J. The optical density ratios (ODR) were calculated from the optical density of total vitreous area to the optical density of the retinal pigment epithelium (RPE).

Results: 12 eyes with 7 patients diagnosed with recurrent uveitis as a chronic manifestation of Vogt-Koyanagi-Harada disease were analyzed in this study. Maximum ODR were 0.146 ± 0.09 (cell grade 0), 0.168 ± 0.10 (cell grade +0.5), 0.220 ± 0.06 (cell grade +1), and 0.344 ± 0.53 (cell grade +2). Average ODR were 0.27 ± 0.02 (cell grade 0), 0.32 ± 0.02 (cell grade +0.5), 0.36 ± 0.01 (cell grade +1), and 0.67 ± 0.10 (cell grade +2). There was significant relationship between anterior chamber cell grade and maximum ODR ($p=0.049$), but there was no relationship between anterior chamber cell grade and average ODR ($p=0.07$).

Conclusions: In this study, we found a significant increase of maximum ODR according to anterior chamber inflammation. This suggest the usefulness of ODR as an objective inflammation measurement tool in recurrent Vogt-Konayagi-Harada disease.

The Challenge of Uveitic Glaucoma: From Immunosuppression to Surgery

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Purpose: To describe surgical success ($6 \leq \text{IOP} \leq 18 \text{ mmHg}$), early (<1 month post-operative) and late complications in patients with refractory uveitic glaucoma (UG) submitted to Ahmed Glaucoma Valve (AGV) implant.

Methods: Prospective study of UG patients implanted with AGV with deep scleral graft at our center between January 2014 and January 2017. Full ophthalmological exam with BCVA, biomicroscopy, Goldmann applanation tonometry, fundoscopy and anterior segment photography was performed. Pré and post-operative glaucoma medications, type and duration of immunosuppression, early and late complications were registered. Post-operative visits took place on the 1st day, 1st week, 1st, 3rd and 6th months and biannually thereafter. Ultrasonic biomicroscopy (Ultrasonic B scanner Tomey UD-8000®) was performed to evaluate tube placement, distance to scleral bed and quantify conjunctival and device capsule thickness.

Results: 7 eyes of 7 women aged between 49 and 77 were included. Mean follow-up was 13.57 months. Mean pré-operative IOP improved from $37 \pm 12.53 \text{ mmHg}$ to $15.07 \pm 2.78 \text{ mmHg}$ (N=7), $18.43 \pm 5.97 \text{ mmHg}$ (N=7), $12.58 \pm 5.0 \text{ mmHg}$ (N=6), $13.33 \pm 1.53 \text{ mmHg}$ (N=3) and $12.67 \pm 2.52 \text{ mmHg}$ (N=3) at the 1st, 3rd, 6th, 12th and 18th post-operative months, respectively. Qualified success was 100% with 1.71 medications to maintain target-IOP. Complications registered were a hyphema on the 1st day and 2 transitory hypotonies solved after anterior chamber reposition with viscoelastic. One patient was lost to follow-up. Apart from recurrence of a cystoid macular edema, no other serious complications were reported.

Conclusions: In cases of traditional treatment failure in UG, AGV implant can present a safe and effective solution. Association of steroid/oral immunosuppression and close patient follow-up are crucial for surgical success.

Fluocinolone acetonide implant (Iluvien) in Birdshot cystoid macular edema

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INTRODUCTION: The development of cystoid macular edema (CME) in Birdshot chorioretinopathy (BSCR) occurs in up to 50% of patients and the mainstay of therapy are corticosteroids administered orally, by intravitreal injection or intravitreal implant. The authors present 2 cases of BSCR with chronic CME treated with fluocinolone acetonide implant (Iluvien[®]). Both cases were also under treatment with corticoid-sparing drugs.

DISCUSSION: Both cases of BSCR presented with a chronic CME refractory to oral immunosuppression. After 6 dexamethasone implants (Ozurdex[®]), 3 in each eye, with a 6 month interval between each implant, the first case was treated with the fluocinolone acetonide implant (Iluvien[®]) and cataract surgery in both eyes. The cataract development seemed to be secondary to previous treatment with intravitreal steroids. The second patient was treated initially with 2 dexamethasone implants (Ozurdex[®]), also with a 6 month gap, in the left eye, and then with a fluocinolone acetonide implant (Iluvien[®]). In both cases, there was no recurrence of CME after 6 months of fluocinolone acetonide implant (Iluvien[®]).

CONCLUSION: Treatment with intravitreal corticosteroid implants is effective in refractory CME associated to BSCR. The fluocinolone acetonide implant may be as effective as the dexamethasone implant with less frequent injections.

Cytomegalovirus retinitis detected by cerebrospinal fluid analysis in an immunocompetent woman

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Cytomegalovirus (CMV) retinitis is an opportunistic ocular infection usually observed in immunocompromised patients. We report a rare case of CMV retinitis in a healthy and immunocompetent 60-year-old woman. The patient complained of long-standing bilateral floaters and presented with visual acuity (VA) of 20/25 in the right eye (RE) and 20/20 in the left eye (LE). Slit-lamp examination revealed a quiet anterior segment in both eyes. Fundoscopy showed a severe bilateral vitreous cellularity and numerous yellowish retinochoroidal infiltrates in the posterior pole and mid-retina of the RE. In the LE, only rare small infiltrates and atrophic areas of RPE were detectable in mid-peripheral retinal. Fluorescein angiography showed hyperfluorescence because of fluorescein leakage and staining in the affected areas of RE and because of transmission defects in the LE. There was no macular edema, as confirmed by Optical Coherence Tomography scans. The clinical findings in RE progressed fast with extension of the retinal lesions reaching the macular region, appearance of retinal haemorrhages in the posterior pole and of retinal necrosis in the superior periphery. RE VA decreased to hand motion. All blood test were normal including ACE, lysozyme and markers of autoimmune, malignant and infectious diseases. Chest X-Ray and total body PET-scan were normal too. Head MRI showed areas of *nonspecific gliosis*. RE aqueous and vitreous taps were negative for HSV, VZV, CMV, EBV, Toxoplasma and Mycobacteria. Only cerebrospinal fluid analysis revealed the presence of CMV DNA. Prompt intravenous and intravitreal Ganciclovir administration significantly improved the CMV retinitis

Tocilizumab for the treatment of Behçet uveitis that failed interferon alpha and anti-tumor necrosis factor-alpha therapy

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Purpose: To report the safety and efficacy of tocilizumab (TCZ) treatment in patients with Behçet uveitis (BU) who had failed conventional, interferon alpha (IFN α), and anti-Tumor necrosis factor-alpha (TNF- α) therapy.

Methods: A retrospective case series of 5 patients with BU who were treated with TCZ between December 2014 and March 2017. All patients had failed interferon and anti-TNF treatment prior to TCZ administration. Patients received TCZ 8mg/kg every month. Clinical findings, central macular thickness (CMT), laser flare meter (LFM) values and fluorescein angiography (FA) scores were evaluated before and after the initiation of the treatment. The outcome measures were changes in visual acuity, anterior chamber cells, anterior chamber flare measured by LFM, vitreous haze, CMT, and FA score.

Results: Three female and 2 male patients, aged between 23 and 36 years, were treated with TCZ for 5 to 19 months. Clinical improvement was achieved in all. Mean LFM reading was 15.4 ± 2.7 photon/millisecond (ph/ms), 7.5 ± 4.0 after 3rd infusion and 5.0 ± 0.9 (ph/ms) at the last visit. Mean CMT was $324.7 \pm 36.6 \mu\text{m}$ at baseline, $311.8 \pm 60.6 \mu\text{m}$ after 3rd infusion and, $279.5 \pm 35.0 \mu\text{m}$ at the last visit. Mean FA score was 20.6 ± 5.4 at baseline, $15.8 \pm 2.2 \mu\text{m}$ after 3rd infusion, and 9.5 ± 4.5 at the last visit. The only side effect was a slight elevation of total cholesterol level in one patient.

Conclusions: Tocilizumab may be a safe and effective therapeutic option for refractory Behçet uveitis.

Choroid in different types of uveitis examined with AngioVue Imaging System and Spectralis Enhanced Deep Imaging - complementary not competitionary techniques

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Purpose: Description the morphology of choroid and choroidal blood flow in different types of uveitis. Evaluation of the changes of choroidal morphology in the respond of the treatment.

Methods: 12 patients with bilateral non-infectious uveitis (anterior -AAU, pars planitis -PP and posterior -PU respectively 4, 4 and 4 patients) and 6 control group (CG) were included in this study. Full ophthalmological examination were performed. The patients has been examined with AngioVue Imaging System (RTVue system) and Spectralis Enhanced Deep Imaging (EDI) in different disease activity status (without treatment, during treatment – recovery, stable on treatment). Analysis of raw data has been performed.

Results: The overall thickness of the choroid decreased nearly all eyes (except of AAU, $p < 0.05$) compared to CG. The differences in choroidal blood flow has been observed between active and non-active form of the disease in the PP and PU. This has been less prominent in AAU. Lesion observed in choroid in 2 patients has been masquerading the choroidal blood flow. The manufacturer setting are unable to properly distinguish different calibre of choroidal vessels, only raw data analysis enables to properly describe their morphology.

Conclusions: There is still a great need for improvement of choroidal visualisation techniques. Visualisation with different modalities enables the investigator to combine information and proceed with proper diagnosis and treatment.

EVALUATION OF CHOROIDAL PARAMETERS in BEHÇET'S DISEASE

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PURPOSE: To assess choroidal parameters with optical coherence tomography (OCT) in different ocular forms of Behçet's Disease (BD).

METHODS: Patients with BD were grouped as active uveitis (Group 1, 13 subjects, 26 eyes), uveitis in remission (Group 2, 24 subjects, 45 eyes), end-stage ocular (Group 3, 9 subjects, 15 eyes) and non-ocular (Group 4, 18 subjects, 36 eyes). Fifty eyes of 25 age and sex matched healthy persons were enrolled as controls (Group 5). Sd-OCT images, taken with Heidelberg Spectralis, were evaluated retrospectively. From the scans obtained with EDI mode, subfoveal choroidal area of 1500µm were analysed employing an image binarization tool. Central foveal thickness (CFT), central choroidal thickness (CCT), total choroidal area (TA), luminal area (LA), stromal area (SA), luminal area percent (also called CVI), stromal area percent (SAP) and luminal to stromal ratio (LSR) were calculated. Student's t test was employed in statistical analyses.

RESULTS: CFT was significantly thicker in Groups 1, 2 and 4, compared to group 5 ($p \leq 0.000$, $p = 0.015$, and $p \leq 0.000$ respectively). CCT, TA, LA, SA, LSR and CVI were significantly lower in Group 3 compared to Group 5 ($p \leq 0.000$, $p \leq 0.000$, $p \leq 0.000$, $p \leq 0.000$, $p = 0.003$, $p \leq 0.000$). SAP was significantly higher in group-3 ($p \leq 0.000$). CVI and LSR were significantly higher in Group 4 compared to Group 5 ($p = 0.016$, $p = 0.011$).

DISCUSSION: Choroidal parameters differed in BD. Choroidal stromal area was increased in end stage ocular disease, and luminal area was increased especially in the non-ocular form.

Multimodal imaging of posterior uveitis with vasculitis revealing a Hodgkin Lymphoma

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Aim : To describe an atypical form of posterior uveitis with vasculitis secondary to Hodgkin Lymphoma

case report

A 17 year old girl, was referred to the Ophthalmology Department of Lariboisière Hospital for a history of blurred vision over the past few weeks.

On presentation, visual acuity was 20/40 on the right eye, and 20/20 on the left eye. There was a mild bilateral vitreous inflammation, associated with bilateral optic disc swelling and diffuse vasculitis with multiple lesions located around the vessels. No macular edema was present on Optical Coherence Tomography.

Ultra Wide Field Fluorescein angiography showed papillitis, associated with vascular staining and leakage, with a peculiar appearance of round lesions located along the retinal vessels, predominantly around veins. No choroidal anomalies were detected on Indocyanin Green Angiography. Atrophic chorioretinal lesions located in the mid and far periphery was also noticed, responsible for a window defect, and could correspond to scars from former inflammatory lesions. OCT-A was performed and showed no relevant vascular findings in the macular area.

Neck lymphadenopathy was present, and further investigations diagnosed a Hodgkin Lymphoma. These para-vascular retinal lesions may represent lymphomatous cells deposit, secondary to acute vessel inflammation. To the authors' knowledge, no similar aspect of ocular findings associated with Hodgkin lymphoma was previously described in the literature. This posterior uveitis associated to Hodgkin lymphoma may be considered as a paraneoplastic syndrome.

Ultra-wide field acridine orange digital fluorography revealed that suppression of infiltrated macrophages by tissue plasminogen activator in laser-induced choroidal neovascularization model

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PURPOSE: We have reported that tissue plasminogen activator (tPA) suppressed choroidal neovascularization (CNV) in murine laser-induced CNV model (Ozone D et al, *Invest Ophthalmol Vis Sci*, 2016). The purpose of this study was to evaluate the influence of tPA in infiltrated macrophages in laser-induced CNV model using ultra-wide field acridine orange (AO) digital fluorography.

METHODS: CNV was induced by laser injury in C57BL/6J male mice, and the intravitreal injection of tPA (40 IU/ μ l) or PBS was performed right after laser injury. The infiltrated macrophages were evaluated on day 0, 3 hours, 1, 3, 5 and 7 days after laser using ultra-wide field AO digital fluorography (Optos 200Tx; Optos, Dunfermline, Scotland, United Kingdom). The number of AO positive cells/disc area were counted using the open-source image-analysis software FIJI. **RESULTS:** In PBS group, the number of AO positive cells/disc area were significantly upregulated on day 1 and 3 ($p < 0.01$).

CONCLUSIONS: Infiltrated macrophages were known as source of pro- angiogenic factor. Our results demonstrated that tPA suppress CNV via inhibitin macrophages infiltration in murine laser-induced CNV model.

Assessment of clinical course of Behçet patients with uveitis after discontinuation of infliximab treatment

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Purpose: Infliximab therapy of Behçet's disease (BD) uveitis requires the continuous administration with fixed-interval, and it is not established what cases could be discontinued. In this study, we evaluated clinical course of BD patients with uveitis after discontinuation of the infliximab therapy.

Methods: Medical records of 6 BD patients with uveitis, who had been treated with infliximab and were discontinued were retrospectively reviewed. Visual acuities, the mean numbers of uveitis attack per a year, and BD ocular attack score 24 (BOS24) before and after discontinuation of the infliximab therapy and the discontinuance reasons were investigated.

Results: The mean duration of infliximab treatment and the mean follow-up period after discontinuation of infliximab treatment were 23.50 ± 12.60 months and 20.67 ± 15.95 months, respectively. Reasons for discontinuation are infusion reaction in 4 cases, ovarian cancer in 1 case, and patient's request in 1 case. The mean of LogMAR, numbers of uveitis attack, and BOS scores were 0.19 ± 0.66 , 0, and 1.16 ± 0.83 at the last injection of Infliximab, and 0.22 ± 0.42 , 1.13 ± 1.75 , and 1.10 ± 1.37 ($p < .001^*$) at last visit. After discontinuation of infliximab, uveitis attacks occurred several times in 3patients, however remission of uveitis was maintained in other patients.

Conclusions: It was suggested that infliximab therapy might be discontinued in BD patients in whom the therapy was initiated early in the development of uveitis, and uveitis attack was sufficiently inhibited during the therapy more than 1year.

Correlation of laser flare photometry and FA/ICG angiography in posterior uveitis

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Background: Laser flare photometry (LFP) and dual fluorescein and indocyanine green angiography (FA/ICGA) are currently considered to be essential parameters to evaluate inflammatory eye diseases.

Purpose: To establish the correlation between LFP flare and FA and ICGA in active noninfectious posterior and panuveitis.

Materials and methods: 51 patients (100 eyes) with active noninfectious posterior and panuveitis were submitted to routine ophthalmological examination, as well as to B-scan, LFP (Kowa FM 600), optical coherence tomography and dual FA/ICGA (HRA2). All angiograms were assessed using scoring system, proposed by the Angiography Scoring for Uveitis Working Group (2007). The specific diagnosis was established in 67% of cases (sarcoidosis(18), Behçet's disease(3), multifocal choroiditis(4), poststreptococcal(3), ankylosing spondylitis(2), multiple sclerosis(1), VKH(1), APMPE(1), serpiginous choroiditis(1)).

Results: There is statistically significant correlation between LFP flare and FA and ICGA angiography score ($p < 0.05$), and the Spearman's rank correlation coefficient equaled 0.537 and 0.422, correspondingly. There is also a statistically significant correlation between LFP flare and optic disc hyperfluorescence established by FA or macular edema ($p < 0.05$). Spearman's rank correlation coefficient is 0.401 for optic disc hyperfluorescence and 0.658 for macular edema. The most significant difference in mean LFP flare was found for macular edema: the mean LFP flare in the absence of macular edema - 10.5 ± 8.7 ph/ms, and in its presence - 37.4 ± 48.7 ph/ms ($p = 0.000048$).

Conclusion: LFP flare reflects posterior involvement in active noninfectious uveitis. LFP flare could be used as an indicative index to predict the severity of FA inflammatory signs.

Efficiency and Safety of Ripasudil Hydrochloride Hydrate for Uveitis-associated Ocular Hypertension

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Purpose: Ripasudil hydrochloride hydrate (K-115) is an eye drop developed for the treatment of glaucoma and ocular hypertension in Japan. The aim of this study to evaluate the efficiency and safety of ripasudil hydrochloride hydrate for uveitis-associated ocular hypertension (OHT) and compare the outcomes of different uveitis.

Material and methods: Clinical records of 28 eyes of 20 patients with uveitis-associated OHT (18 eyes with granulomatous uveitis and 10 eyes with non-granulomatous uveitis) who were treated by K-115 combined with or without other anti-glaucoma agents were retrospectively reviewed. Intraocular pressure (IOP), aqueous flare, and posterior inflammation scores were compared before and after treatment with K-115.

Results: The mean observation period was 4.9 month. The mean IOP, aqueous flare, and posterior inflammation score were 22.6 ± 5.6 mmHg, 33.7 ± 40.7 , and 2.1 ± 1.2 at indication of K-115, and 17.4 ± 4.3 mmHg, 20.5 ± 11.7 , and 0.8 ± 0.4 after the treatment, respectively. There were significant decreases in all scores ($P < 0.000$, $P = 0.031$, and $P = 0.034$, respectively). The decreases were shown both in eyes with granulomatous uveitis and non-granulomatous uveitis. No remarkable adverse effect was occurred in the eyes of both groups during the observation periods.

Conclusion: K-115 was effective for OHT associated with both granulomatous and non-granulomatous uveitis.

Comprehensive analysis of the association between *IL10* gene variants and Vogt-Koyanagi-Harada disease in a Japanese population

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Purpose: Interleukin-10 (IL-10) is a potent suppressor of inflammatory cytokines, and *IL10* gene variants are reportedly associated with several immune-mediated diseases. IL-10 may play an important role in controlling Vogt-Koyanagi-Harada (VKH) disease. Here we investigated whether *IL10* variants were associated with VKH disease and its clinical symptoms among Japanese patients.

Methods: A total of 380 Japanese patients with VKH disease and 1,066 Japanese healthy controls were recruited. We genotyped 10 single-nucleotide polymorphisms (SNPs) in *IL10*. We also performed an imputation analysis to evaluate potential associations of un-genotyped *IL10* SNPs using the data of 10 genotyped SNPs, and the 33 SNPs were imputed.

Results: None of the genotyped and imputed SNPs were significantly associated with VKH disease itself. On the other hand, five SNPs in the 3'-UTR or 5'-UTR of *IL10* were significantly associated with the symptom of nausea ($P<0.01$, $P_c<0.05$, OR=4.21) and showed suggestive association with hypersensitivity to touch of hair and skin ($P<0.05$, $P_c>0.05$, OR=2.61). Additionally, other three SNPs in the intron or 5'-UTR were significantly associated with poliosis ($P<0.01$, $P_c<0.05$, OR=2.11). Moreover, another intronic SNP showed suggestive association with the symptom of vitiligo ($P<0.05$, $P_c>0.05$, OR=2.11). Expression analysis revealed that the risk alleles of these SNPs showed significant association with decreased *IL10* expression ($P<0.05$).

Conclusions: Our results suggest that the *IL10* variants contribute to the development of particular clinical symptoms of VKH disease. To confirm our findings, future validation studies with other independent populations are needed.

Association between HLA region and ocular involvement in Behçet's disease in a Japanese population: preliminary report

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Purpose: Behçet's disease (BD) is a chronic systemic inflammatory disorder characterized by recurrent ocular symptoms, oral and genital ulcers, and skin lesions. The etiology of BD is still uncertain, but currently some external environmental factors are thought to trigger BD in individuals with a particular genetic background. It is well established that BD is strongly associated with the human leukocyte antigen (*HLA*) class I allele, *HLA-B*51*, in many different ethnic groups. In this study, we performed a comprehensive association analysis between the *HLA* region and ocular involvement in BD.

Methods: We used a total of 877 single nucleotide polymorphisms (SNPs) in the *HLA* region genotyped in the genome-wide association study (Nat Genet 2010;42(8):703-6.) which enrolled 611 Japanese BD patients (including 469 patients with ocular involvement) and 737 Japanese healthy controls.

Results: We identified 65 SNPs, ascribed to three loci, showing significant associations with ocular BD ($P < 0.00001$, $OR \geq 1.40$) but not non-ocular BD ($P > 0.05$, $OR < 1.1$). Although these three loci are located in the *HLA* class I region, they were in weak linkage disequilibrium with each other ($r^2 < 0.10$) and were independently associated with ocular BD.

Conclusions: Preliminary results of the ongoing study point out to risk loci for ocular BD in the *HLA* region. To confirm the findings, future validation studies with other independent populations are needed.

Characteristics of unclassified uveitis in a tertiary hospital in Japan

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Purpose: To evaluate the characteristics and treatment outcomes of unclassified uveitis in a tertiary hospital in Japan.

Methods: We retrospectively reviewed the medical records of 52 eyes of 32 patients (9 males and 23 females) who were diagnosed as unclassified uveitis between January 2014 and March 2015 and were followed up for more than 12 months. The extracted data included age, gender, best corrected visual acuity (BCVA), intraocular pressure (IOP), intraocular inflammation (graded according to the Standardization of Uveitis Nomenclature Working Group criteria.) type of inflammation (granulomatous or non-granulomatous), treatment contents, and complications.

Results: The mean age was 51.7 years old, and there was a predominance of female (68%). the mean BCVA was 20/30, and the mean IOP was 15.6 mmHg at baseline. Of 52 eyes, 40% were granulomatous, 31% were non-granulomatous, and 29% were unclassified. Forty-four (85%) eyes were treated with corticosteroid: oral prednisolone (n=5), intravitreal triamcinolone injection (n=1), subtenon's triamcinolone injection (n=18), and eye drops (n=19). After 12-months treatment, anterior chamber cell and vitreous haze were significantly improved at 12 months ($p=0.0006$, 0.0107 , respectively). Forty-one (79%) eyes had a BCVA of equal or more than 20/40. The causes of poor BCVA (less than 20/40) included cystoid macular edema, cataract progression, and glaucoma, most of which existed before treatment. Four eyes (8%) needed anti-glaucoma eye drops for the treatment of increased IOP.

Conclusion: Most of unclassified uveitis was successfully treated with corticosteroid and attained good visual acuity unless severe ocular complications before treatment.

Semifluorinated alkanes enhance the lipid layer for dry eye therapy

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PURPOSE: Dry eye disease (DED) is one of the most prevalent ocular surface disorders causing significant pain and discomfort to patients. Recently, the semifluorinated alkane, Perfluorohexyloctane (F6H8, NovaTears®) has been introduced as a preservative-free tear substitute for treatment of DED symptoms. This study was performed to evaluate the mechanism by which F6H8 exerts a lubricating effect on the ocular surface.

METHODS: The influence of F6H8 on tear fluid dynamics was studied after instillation into healthy rabbit eyes twice daily for seven days and compared to the instillation of saline. Lipid layer grade (LLG), tear fluid evaporation rate (TFER) and tear volume were observed daily during the course of treatment. Tear osmolarity and clinical safety were also assessed.

RESULTS: A cumulative improvement in LLG was observed after application of F6H8, while no changes were seen after instillation of saline. No significant change in TFER, tear volume or tear osmolarity were observed over the seven day period. F6H8 were well tolerated on the ocular surface with no corneal or conjunctival adverse effects observed at any point.

CONCLUSION: F6H8 progressively improved the LLG or lipid layer thickness after topical application supporting its lubricating effect to provide symptomatic relief in dry eye patients. No significant difference in TFER or tear volume could be observed in healthy rabbit eyes after seven days.

Post-streptococcal uveitis syndrome in children: A case series

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Background

Beta-haemolytic streptococci are a common cause of acute infections and immune-mediated complications are most commonly seen 7-35 days post infection. Uveitis is an uncommon manifestation of post-streptococcal syndrome first reported in 1991 by Cokington. Despite further reports in the published literature, the condition is often not well recognized. We report a large case series of children with post-streptococcal uveitis.

Methods

We identified all cases of post-streptococcal uveitis from all new patients attending the Belfast specialist paediatric uveitis service from 2011. Demographics, disease characteristics, treatments and complications were recorded. Diagnosis was made on the basis of positive antistreptolysin O titres (ASOT) and/or anti-Deoxyribonuclease (anti-DNase) titres, and negative routine investigations for other causes of uveitis.

Result

There were eleven patients with post-streptococcal uveitis onset before the age of 16 years. All patients were Caucasian and 82% were female. The mean age at diagnosis was 11.7 months. The location of uveitis was anterior in 55% and intermediate in 45% of patients. 45% of patients had bilateral disease. 88% of eyes had a visual acuity ³ 6/12 at presentation improving to 100% at final visit. Complications occurred at presentation in 64% of patients and at any time point in 73% of patients. Systemic treatment was required in 27% of patients. Follow-up was 10.5 months.

Conclusion

We report a large consecutive series of patients under 16 years of age with post-streptococcal uveitis. With aggressive treatment and careful monitoring, we achieve VA outcomes better than published in the literature for this condition.

Reversible melanoma-associated retinopathy (MAR)

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Purpose:

To present the case of a patient with melanoma-associated retinopathy (MAR) that improved within a period of two years not only in symptoms, but also in visual acuity, visual field and electrophysiological diagnostics.

Background:

A female 51 years old patient with a history of metastasizing malignant melanoma was diagnosed with MAR in 07/2014. She featured subacute commencing typical symptoms like nyctalopia, shimmering photopsia and photosensitivity. Diagnostic findings included diminished visual acuity, paracentral visual field defects and electronegative electroretinogram (ERG). Diagnostics were repeated over a two years follow-up period.

The malignant melanoma had been excised in 08/2011 and dissection of a lymph node metastasis was conducted in 05/2014. An additional radiotherapy was performed in 08-09/2014. The patient did not receive any treatment for MAR except for a short-term therapy with oral prednisolone in a dosage of 60 mg per day, which was terminated because of progressive visual symptoms.

Results:

Within the period of observation, visual acuity rose from a minimum value of logMAR +0,5 / +0,4 to logMAR 0 / +0,1 and the patient's visual symptoms vanished. The initially substantial visual field defects reversed to a near to normal field of vision and the ERG b-wave improved considerably in both eyes. In parallel, no more evidence of melanoma activity was present.

Conclusion:

Melanoma associated retinopathy can be – at least partially – reversible. Not only the visual symptoms, but also visual acuity, visual field defects and a pathologic electroretinogram may improve over time.

FULL-THICKNESS CHOROIDAL THINNING AS A FEATURE OF FUCHS UVEITIS SYNDROME

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Purpose To perform a quantitative analysis of choroidal thickness in patients with Fuchs' Uveitis syndrome (FUS) using Enhanced Depth Imaging Optical Coherence Tomography (EDI-OCT). **Methods** All patients underwent comprehensive ophthalmic examination, including axial length measurements with a Swept Source biometer and macular 30° linear EDI- B-scan SD-OCT section in both eyes. Analysis of choroidal thickness was performed at 3 different locations: subfoveally, 750 µm nasally and 750 µm temporally to the fovea. Patients having received any surgery or intravitreal injections in the last 12 months and with axial length variance ≥ 1 mm between both eyes were excluded. **Results** Sixteen eyes of 8 consecutive patients with unilateral FUS were included. Segmented analysis of the choroid, separately considering Haller's layer and Sattler's-Choriocapillaris layers, showed statistically significant lower values ($p < 0.05$) in affected eyes (FEs) compared to fellow eyes (NFEs). In NFEs, total choroidal thickness mean values ranged from 305.62 ± 92.96 µm to 347.50 ± 91.55 µm; in FEs those values were significantly lower ($p < 0.05$), ranging from 232.62 ± 89.33 µm to 255.62 ± 89.33 µm. **Conclusion** Diffuse and full-thickness choroidal thickness in FEs was observed. Considering the absence of significant axial length differences between FEs and NFEs in our patients series, these data seem to suggest that the full-thickness choroidal thinning in FEs may be due to an inflammatory process. In that way FUS might be regarded as an inflammatory condition involving the whole uveal tunic, even the posterior part of it, definitively supplanting the early definition of "heterochromic iridocyclitis".

Deep Inside Multifocal Choroiditis: An Optical Coherence Tomography Angiography Approach

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Purpose

To report the clinical utility of optical coherence tomography angiography (OCT-A) in characterizing and differentiating inflammatory lesions and choroidal neovascularisation (CNV) in Multifocal Choroiditis (MFC).

Methods

Case report

Results

A patient affected by MFC complaining central visual loss and scotoma in his left eye was fully investigated with OCT, dye-based angiographies and OCT-A. A reactivation of macular CNV was initially suspected, while OCT-A revealed the absence of any decorrelation signal both over the RPE and between RPE and Bruchs' membrane.

Conclusions

OCT-A is a promising tool in detecting inflammatory CNV and in differentiating CNV from primitive inflammatory damage. Finely characterizing the aspect of a lesion allow us to choice the best therapeutic strategy for managing these potentially blinding diseases.

Collaborative Ocular Tuberculosis Study (COTS)-1: Role of Polymerase Chain Reaction in the Management of Intraocular Tuberculosis

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Purpose: Polymerase chain reaction (PCR) is being increasingly used in the diagnosis and management of ocular tuberculosis (OTB). In this study, correlation of PCR results with treatment outcomes in OTB was performed.

Methods: Patients with OTB from 25 centers worldwide were retrospectively analyzed (n=801) in the COTS cohort. In the index study, comparative analysis of management and outcomes of patients with OTB undergoing PCR testing of ocular fluids (n=59; 19 females; 50 Asian Indians) was performed.

Results: PCR was positive (PCR+) for Mycobacterium TB in 33 patients (23 males; all Asian Indians) (n=8 panuveitis; n=25 posterior uveitis). 23 patients were PCR negative (PCR-; 8 females) (n=4 panuveitis; n=19 posterior uveitis). 4 patients with PCR- had systemic TB and only 2 had negative immunology tests (Mantoux/interferon γ release assay). Anti-tubercular therapy (ATT) was given in 18 PCR- and 31 PCR+. At 1-year follow-up, 4 PCR+ and 2 PCR- had persistence/worsening of inflammation.

Conclusions: In this study, more than one-third patients showed negative PCR results but had positive immunological/radiological tests for TB. PCR serves as an adjunct to support the diagnosis of OTB. Treatment results with anti-tubercular therapy are not influenced by the results of PCR positivity. Results of TB PCR assays must be considered along with clinical and other laboratory features.

Evidence of choriocapillaris ischemia on Swept-source OCT Angiography in specific inflammatory maculopathies

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Purpose: To describe swept-source optical coherence tomography angiography (SS OCTA) findings in five patients with specific inflammatory maculopathies.

Methods: This study is a retrospective review of the chart of 5 patients (7 eyes) diagnosed with 5 different specific inflammatory maculopathies. All patients were evaluated using fluorescein angiography (FA), indocyanine green angiography (ICGA), spectral domain optical coherence tomography and SS OCTA.

Results: The patients were aged between 21 and 48 years. The inflammatory diseases included unilateral acute idiopathic maculopathy, relentless placoid chorioretinitis, multiple evanescent white dot syndrome (MEWDS), and acute posterior multifocal placoid pigment epitheliopathy and tuberculosis serpiginous-like choroiditis. SS OCTA showed areas of reduced flow within the choriocapillaris. These lesions were multifocal in 3 patients (5 eyes) and unique in 2 patients (2 eyes). Areas of choriocapillaris flow deficit correlated with hypofluorescent lesions on ICGA. At 6-month follow up, hypointense choriocapillaris lesions significantly decreased in the patient with MEWDS, and persisted in the patient with acute unilateral idiopathic maculopathy.

Conclusion: SS OCTA reveals areas of choriocapillaris flow reduction in specific inflammatory maculopathies. In these conditions, the inner choroid seems to be the primary site of a transient or persistent ischemic process.

Acute multifocal retinitis preceded by a flu-like illness: a retrospective review of 33 cases

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Purpose: To analyze clinical features and causes of acute multifocal retinitis preceded by flu-like illness.

Methods: Retrospective review of the charts of 33 patients (57 eyes).

Results: Retinal lesions ranged from 3 to 20 in number in at least one eye, and from 150 to 1500 μm in size. Associated clinical findings included mild vitritis in 39 eyes (68.4%), optic disc swelling in 9 eyes (15.8%), macular star in 4 eyes (7%), branch retinal artery occlusion in 6 eyes (10.5%), and exudative retinal detachment in 3 eyes (5.3%). Acute multifocal retinitis was found to be caused by *Rickettsia conorii* infection in 21 patients (63.6%), *Rickettsia typhi* infection in 7 patients (21.2%), and cat-scratch disease 4 cases (12.1%). Acute multifocal retinitis was idiopathic in one case (3%). Retinal lesions resolved without scarring in 3 to 12 weeks in all but two eyes (3.5%), where mild residual retinal pigment epithelial changes were noted.

Conclusion: Rickettsiosis was the most common cause of acute multifocal retinitis with flu-like illness. Less than one fifth of the patients were found to have cat-scratch disease or idiopathic acute multifocal retinitis.

Corneal endothelium changes in patients with uveitis

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Purpose: To study corneal endothelium changes in eyes with uveitis.

Methods: Prospective study including 3 groups: eyes with active anterior chamber inflammation (63 eyes, 38 patients), eyes with inactive uveitis (72 eyes, 41 patients), and a control group (84 eyes, 42 patients).

Results:

Endothelial cell density (ECD) was lower in eyes with uveitis than in the control group (2613 cells/mm² vs 2698 cells/mm²; p=0.01). Percentage hexagonality (HEX) was lower in eyes with uveitis (65% vs 68 %; p=0.01). The coefficient of variance (CV) and the central corneal thickness (CCT) were significantly higher than in the control group (30% vs 28%; p=0.002 and 541µm vs 525 µm; p=0.002). ECD was higher in the group of active uveitis than in the group of inactive uveitis, but the difference was not statistically significant (2642 cells/mm² vs 2587 cells/mm²; p=0.2). The CV and the CCT were higher (31% vs 29%; p=0.04 and 555 µm vs 535 µm; p=0.006), and the HEX was lower in the eyes with active uveitis (64.7% vs 67%; p=0.02). In eyes with initial severe anterior chamber inflammation (laser flare photometry value ≥ 50 ph/ms, or cells ≥ 2+), there was significant increase in ECD and HEX at one month follow-up. On the other hand, the CV and the CCT significantly decreased. Increase in ECD, and decrease in CCT correlated with initial anterior chamber flare.

Conclusion: Anterior segment inflammation may cause qualitative and quantitative endothelial changes. These changes may be responsible for endothelial dysfunction.

Bilateral Infectious Keratitis following Corneal Collagen Cross-linking

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Purpose:

To report a case of bilateral *Staphylococcus aureus* keratitis after corneal collagen cross-linking, in a patient with keratoconus.

Case report:

A 22-year-old female patient with bilateral progressive keratoconus underwent bilateral UVA-riboflavin corneal cross-linking and presented with painful red eyes three days later. At presentation, best-corrected visual acuity was limited to the light perception. Slit-lamp examination of the RE revealed severe keratitis with multiple scattered miliary infiltrates, diffuse corneal edema, and an epithelial defect in both eyes. Ultrasound B-scan showed no vitreous reaction. The patient was admitted to our department and received broad-spectrum fortified antibiotics. Cultures from corneal scrapping samples grew positive for *Staphylococcus aureus*. Topical corticosteroids were given after corneal lesions started to improve. At one-year follow-up, best-corrected visual acuity was 20/200 in the right eye and 20/32 in the left eye.

Conclusion:

Collagen cross-linking is considered a safe procedure aiming at halting keratoconus progression. However, sight-threatening bilateral keratitis may occur..

Acute Vogt-Koyanagi-Harada disease associated with retinal pigment epithelium detachment: a report of 2 cases

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Purpose: To report the cases of two patients who presented with acute VKH disease and associated inflammatory retinal pigment epithelium detachment (PED).

Methods: 2 case reports. Both patients had a complete ophthalmic examination and multimodal imaging including fundus photography, fluorescein angiography, spectral-domain optical coherence tomography, indocyanine green angiography, and B-scan ultrasonography. **Results:** **Case 1:** A 22-year-old male patient complained of acute bilateral decrease in vision. Initial BCVA was 20/63, OU. There was 1 + vitreous cells, OU. Fundus findings included exudative retinal detachment (ERD) in the right eye (RE), and a macular deep yellow lesion suggestive of PED in the left eye (LE). Multimodal imaging showed features of acute VKH disease with associated bilateral PED. The patient received prednisone and cyclosporine, with subsequent resolution of ERD and PED. **Case 2:** A 40-year-old female patient presented with bilateral vision blurring. Best-corrected visual acuity (BCVA) was 20/40 in the RE and 20/32 in the left eye LE. There was 1+ vitreous cells OU. Fundus examination showed bilateral optic disc swelling and choroidal and retinal folds. Multimodal imaging results were consistent with a diagnosis of acute VKH disease associated with PED. The patient was given oral prednisone and cyclosporine, with subsequent visual improvement and resolution of both ERD and PED. **Conclusion:** PED may rarely occur in acute VKH at presentation. A careful clinical examination and analysis of multimodal imaging findings are helpful in differentiating inflammatory PED from central serous chorioretinopathy-related PED.

Swept-source optical coherence tomography angiography in West Nile virus chorioretinitis and associated occlusive retinal vasculitis

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Purpose: To report swept source optical coherence tomography angiography (SS-OCTA) findings in a patient with West Nile virus (WNV) occlusive retinal vasculitis.

Methods: A 65-year-old diabetic man with a history of fever of unknown origin two weeks earlier complained of sudden decreased vision in the left eye. The patient was diagnosed with bilateral WNV chorioretinitis associated with occlusive retinal vasculitis in the left eye. He was evaluated with SS-OCTA.

Results : SS-OCTA of the left eye showed extensive well-delineated hypointense greyish areas of retinal capillary hypoperfusion and perifoveal capillary arcade disruption in the superficial capillary plexus, and larger greyish areas of capillary hypoperfusion, capillary rarefaction, and diffuse capillary network attenuation and disorganization in the deep capillary plexus.

Conclusion : SS-OCTA may be a valuable tool for assessing non-invasively occlusive retinal vasculitis associated with WNV infection. It allows an accurate detection and precise delineation of areas of retinal capillary hypoperfusion in both the superficial and deep capillary plexuses.

Swept-source Optical Coherence Tomography Angiography in Rickettsial Retinitis

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Purpose: To report optical coherence tomography angiography (OCTA) findings in a patient with rickettsial retinitis.

Methods: A 29-year-old man complaining of acute blurring vision in the right eye associated with *Rickettsia conorii* infection underwent a comprehensive ocular examination, fluorescein angiography (FA), spectral domain optical coherence tomography (SD-OCT), and swept source OCTA.

Results: Funduscopy showed two large areas of juxtavascular retinitis in the posterior pole with associated retinal hemorrhages, retinal edema, and serous retinal detachment. FA showed early hypofluorescence and late staining of white retinal lesions and associated adjacent retinal vascular leakage and optic disc hyperfluorescence. OCTA showed hypointense dark areas in the superficial capillary plexus and larger hypointense areas in the deep capillary plexus, outer retina, and choriocapillaris layer. The patient was treated with doxycycline and prednisone. Six weeks after presentation, retinal changes seen at the acute phase had resolved, leading to mild residual retinal pigment epithelial changes. FA showed retinal capillary nonperfusion within areas of resolved retinitis. SD-OCT findings included inner retinal atrophy, intraretinal cysts, and disruption of ellipsoid zone and interdigitation zone. Swept source OCTA showed well-delineated hypointense greyish areas of retinal capillary nonperfusion in both the superficial and deep capillary plexuses. Visual field testing revealed the presence of a corresponding paracentral defect.

Conclusions: OCTA may be a valuable noninvasive imaging technique for detecting and analyzing occlusive complications associated with rickettsial retinitis.

Optical coherence tomography angiography features of active versus quiescent inflammatory choroidal neovascularization in posterior uveitis

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Purpose: To study optical coherence tomography angiography (OCTA) imaging features of active and quiescent choroidal neovascularization (CNV) in posterior uveitis and response to anti-vascular endothelial growth factor (VEGF) therapy.

Methods: Two trained graders analyzed OCTA images of 12 patients (15 eyes) with posterior uveitis and their serial response to therapy.

Results: Ten eyes (7 patients) showed active CNV (fine anastomotic network with choriocapillaris flow deficit areas). Of these, 4 eyes showed intraretinal cystoid spaces on OCT. Five eyes (5 patients) showed quiescent CNV (tufts of thicker vessels in areas without choriocapillaris flow deficit). Anti-VEGF therapy led to reduction in CNV size on OCTA. Visual acuity improved (0.4 ± 0.3 to 0.3 ± 0.2) in all eyes following anti-VEGF therapy. One eye with active CNV on OCTA but no significant intraretinal cystoids spaces on OCT which was followed for 2 months without treatment, developed increase in CNV size on both OCT and OCTA with concurrent reduction in visual acuity. Visual acuity improved and reduction in size of CNV was documented both on OCT and OCTA after anti-VEGF therapy.

Conclusions: OCTA can help differentiate active and quiescent CNV in choroiditis where conventional multimodal imaging fails to make a definitive diagnosis and thereby guide the initiation of therapy.

Uveitis in Behçet's disease in Poland-diagnostic and therapeutic dilemmas

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Purpose: To present the problems in diagnosis and treatment of patients with uveitis in Behçet's disease in Poland.

Subjects and Methods: Retrospective review of 12 cases (8 males, 4 females; age 15-49) of uveitis in patients with Behçet's disease, treated at referral uveitis clinic in Poland in 1998-2017.

Results: Clinical data regarding age, sex, systemic symptoms and signs, anatomical location and management of uveitis were obtained. All patients were HLA-B51 positive and had systemic manifestations such as recurrent oral or genital ulceration, epididymitis, erythema nodosum, brain lesions, polyneuropathy. Medical treatment comprised prednisone, methotrexate, cyclosporine, mycophenolate mofetil, azathioprine, cyclophosphamide, adalimumab, rituximab, interferon-alfa. Four patients underwent pars plana vitrectomy, 1 intravitreal injection of aflibercept, in 2 cases enucleated eyeball was studied histopathologically.

Conclusion: Behçet's disease is rare in Poland and thus the implication is delay in diagnosis and proper treatment, especially in cases that initially do not fulfill international criteria for Behçet's disease and present with sole ophthalmic manifestations.

Vitreoretinal Lymphomas – one centre experience

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Introduction

Vitreoretinal lymphomas belong to the family of central nervous system (CNS) lymphomas. The optimal approach for the treatment of isolated primary vitreoretinal lymphoma (PVRL) is unclear because of the lack of large comparative clinical series. Combination of intravitreal and systemic chemotherapy is recommended in many reports.

Purpose

The aim of our retrospective study was to compare the survival rate and prognosis of patients with vitreoretinal lymphoma with and without CNS involvement.

Methods

Twenty patients with vitreoretinal lymphoma were diagnosed in our centre between 2004 and 2016. All patients underwent diagnostic pars plana vitrectomy.

Results

PVRL was determined in 10 patients, primary CNS lymphoma (PCNSL) with vitreoretinal involvement was detected in 10 patients. The 5-year survival rate of patients with vitreoretinal lymphoma was 71 % in our study. The 5-year overall survival was observed to be longer in PVRL patients compared to PCNSL (89 % v. 58 %). The relapse of lymphoma was frequent (50 % PVRL, 70 % PCNSL). Time to first relapse was almost equal in group of PVRL and PCNSL patients. Initial combined therapy in PVRL patients significantly extended the time until the first relapse when compared to initial local therapy alone.

Conclusion

Patients with vitreoretinal lymphoma without CNS involvement (PVRL) seem to have better prognosis compared to patients with CNS involvement (PCNSL). Local and combined treatment of PVRL show similar results, but combined treatment in our observation significantly postpones the relapse of lymphoma. However, most results are not statistically significant due to small number of patients.

Corneal involvement in tyrosinemia type II initially mistaken for herpetic keratitis in an adult: a case report

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Purpose: To report the case of a 40-year-old woman who presented with corneal lesions secondary to tyrosinemia type II that were initially mistaken for herpetic keratitis. **Case Report:** A 40-year-old woman, with a history of mild mental retardation, presented with a painful red right eye. Marginal inferior corneal infiltration and ulcer were found. The patient received valaciclovir (2g/day), and then topical *fluorometholone*. Three months later, the patient consulted with bilateral ocular complaints. Slit-lamp examination revealed two corneal marginal ulcers in the right eye and a pseudodendritic inferior keratitis in the left eye. Work-up showed a plantar hyperkeratosis and high serum tyrosine levels. A diagnosis of Richner Hanhart syndrome was made. The patient was prescribed tyrosine- and phenylalanine-restricted diet, and lubricants. Two months later, corneal lesions had healed. **Conclusion:** Richner Hanhart syndrome (Tyrosinemia type II) should be suspected in patients with bilateral pseudodendritic corneal lesions unresponsive to antiviral therapy, even in adults. Systemic manifestations including palmoplantar keratosis and mental retardation should be looked for.

Unilateral Optic nerve neuritis post influenza vaccination – a case report

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Purpose: We report on a case of unilateral optic neuritis following influenza vaccination.

Methods: A 62-year old male patient presented with visual field defects and a reduced visual acuity in his only eye. Two weeks prior to presentation he was vaccinated electively against influenza. Clinical examination showed a slightly hyperaemic optic disc swelling and a severe constricted visual field. Visual acuity and visual field improved after one week of high dose intravenous steroid therapy.

Conclusion: Optic neuritis is one of the rare complications associated with mumps, measles, rubella, herpes zoster and influenza vaccine. It may be a toxic reaction to the non viral components of the vaccine or anti-phosphatidylcholine antibodies that may play a role in the pathogenesis but the exact pathology remains unknown.

Clinical features of MOG Ig-positive Optic Neuropathies

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OBJECTIVE : To evaluate clinical features among patients with bilateral or recurrent optic neuropathy who are seropositive for Myelin Oligodendrocyte Glycoprotein (MOG) antibodies, and to compare them with patients with Neuromyelitis Optica Spectrum Disorder (NMO SD).

METHODS : Observational retrospective study. Cases of recurrent or bilateral optic neuropathy with MOG antibodies seropositivity were included, and compared with cases of Aquaporin-4 Ig-positive NMO SD and seronegative NMO SD.

RESULTS : Six MOG + patients and 9 patients with NMO SD (7 AQP4 Ig-positive and 2 seronegative with clinical or radiological criteria) were included. In the MOG group, optic neuropathy was bilateral in 5/6 patients and unilateral in 1/6 patients. 4/6 MOG patients experienced recurrent optic neuropathy. Vision loss was severe in both groups (counting finger or worse for at least one eye in 5/6 MOG + patients and in 7/9 NMO SD). After IV Methylprednisolone, visual recovery was excellent and quick for all MOG + patients (recovery better than 20/32 between 15 and 90 post-treatment for all patients). On the contrary, visual prognosis was poor for NMO SD patients (long term visual recovery worse than 20/32 for all the cases). All the patients in this study were started on immunosuppressive therapy.

CONCLUSION : Anti MOG seropositive optic neuropathies have a better visual prognosis than AQP4 Ig-positive and seronegative NMO SD. Testing for anti MOG antibodies may be useful in bilateral or recurrent optic neuropathy for diagnostic and prognosis purpose.

Posterior Segment Findings in Turkish Patients with Fuchs Uveitis

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Posterior Segment Findings in Turkish Patients with Fuchs Uveitis

Purpose: To describe posterior segment findings in Turkish patients with Fuchs Uveitis.

Method: Medical records of 208 patients with Fuchs Uveitis were retrospectively reviewed. The mean age, sex, number of affected eyes, follow-up period, initial and final visual acuities, fundus and fluorescein angiography findings and surgical treatments were recorded.

Results: The study included 227 eyes of 208 patients, of whom 112 (53.8%) were female and 96 (46.2%) were male. The mean age was 34.7 ± 11.2 years. Nineteen patients (9.1%) had bilateral involvement. The mean follow-up period was 22.9 ± 27.9 (6-130) months. Clinical findings included vitreous infiltration in varying grades in all the eyes (100%), chorioretinal scars (10.1%), mid-peripheral vascular sheathing (7%), epiretinal membrane (2.6%) and preretinal membrane at the peripheral retina (2.2%). Fluorescein angiography was performed in thirty-five patients (16.8%) and hyperfluorescence of the optic disc was detected in 10 eyes (4.4%) and mid-peripheral vascular leakage was detected in 5 eyes (2.2%). Vitreoretinal surgery was performed in 13 eyes (5.7%) due to dense vitreous infiltration.

Conclusion: As well as anterior segment findings, posterior segment findings may occur in eyes with Fuchs uveitis. Vitreous infiltration is the most frequent fundus manifestation. These results are not well known and may lead to misdiagnosis.

A rare presentation of Eales disease

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Purpose: To describe a rare case of a patient with Eales disease presenting as an anterior ischemic optic neuropathy.

Method: Patient case control

Results: 39-years-old male observed in the emergency department with complaints of an altitudinal defect in the right eye (RE). The patient had been treated in a private hospital with high dose EV and oral corticosteroids with no apparent recuperation. At observation, he had a best corrected visual acuity (BCVA) of counting fingers at 30cm, with a relative afferent pupillary defect and optic disc edema and was again started in methylprednisolone 1g EV. Brain MRI, doppler ultrasound, blood analysis including auto-immune, thrombophilia panel and infectious agents were negative except for a positive antinuclear antibody (1/160), hyperhomocysteinemia and factor VIII elevation. It was also detected hypercholesterolemia and hyperuricemia. Visual acuity improved to 3/10 and the patient was sent to the uveitis department to exclude a possible vasculitis. Fluorescein angiography showed a bilateral temporal peripheral ischemic retinopathy with vasculitis and a marked capillary peripheral non-perfusion but no neovascularization. New exams were requested which revealed a positive Mantoux test. A probable diagnosis of Eales disease was made and the patient is now on oral corticosteroids and started anti-bacillary therapy.

Conclusion: Although Eales disease patients often present with symptoms of floaters, blurring or vitreous hemorrhage we should be aware of other infrequent manifestations of this disease.

White dot syndromes: A report of 45 cases from Tunisia

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Purpose: To report etiologic profile, clinical features, and outcomes of white dot syndromes (WDS) in Tunisia, North Africa.

Methods: Retrospective study including 52 patients with WDS diagnosed and managed at the department of Ophthalmology, Fattouma Bourguiba University Hospital, Monastir, Tunisia between January 2007 and April 2017. Mean follow-up was 2.4 years (15 days-16 years).

Results: Mean age of our patients was 34.47 years. The following WDS entities were identified: Multiple evanescent white dot syndrome (MEWDS) (13 patients; 25%), punctate inner choroidopathy (9 patients; 17.3 %), idiopathic multifocal choroiditis (6 patients; 11.5 %), serpiginous choroiditis (6 patients; 11.5 %), Birdshot chorioretinopathy (6 patients; 11.5 %), acute posterior multifocal placoid pigment epitheliopathy (5 patients; 9.6 %), relentless placoid chorioretinitis (1 patient; 1.9 %), diffuse subretinal fibrosis (1 patient; 1.9%), presumed ocular histoplasmosis syndrome (3 patients; 5.7 %) and acute macular neuroretinopathy (AMNR) (2 patients; 3.8 %). All entities had female preponderance except serpiginous choroiditis. Both MEWDS and AMNR generally carried a good visual prognosis. The worst visual outcome was recorded in patients with serpiginous choroiditis and in those with multifocal choroiditis.

Conclusions: An array of WDS was observed in our referral center in Tunisia. Prognosis mainly depends on the type of clinical entity.

Clinical and multimodal imaging findings in posterior scleritis

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Purpose: To describe clinical and multimodal imaging findings in posterior scleritis.

Methods: Retrospective review of the charts of 14 patients (16 eyes) with posterior scleritis.

Results: Mean age of our patients was 35.3 years. Eleven patients (78.6%) were female and 3 patients (21.4%) were male. Mean initial visual acuity (VA) was 20/25. Fundus findings included retinal/choroidal folds in 8 eyes (50%), exudative retinal detachment (ERD) in 5 eyes (35.7%), optic disc swelling in 4 eyes (25%), and yellowish deep lesions in 5 eyes (31.25%). B-scan ultrasonography showed diffuse, high-reflective sclero-choroidal thickening with retrobulbar edema in all eyes. Of 10 eyes, OCT showed ERD in 7 eyes (70%), associated with subretinal septa in 2 eyes (20%), retinal pigment epithelial folds and bulge in 3 eyes (30%), and retinal folds in 3 eyes (30%). Of 15 eyes, fluorescein angiography (FA) disclosed delayed choroidal perfusion in 6 eyes (40%), pinpoint leakage in 8 eyes (53.3%) with dye pooling in 6 eyes (40%), choroidal folds in 3 eyes (20%) and optic disc hyperfluorescence in 10 eyes (66.7%). Indocyanine green angiography (ICGA) findings included delayed choroidal perfusion in 2 of 12 eyes (16.7%), hypofluorescent dark dots in 7 eyes (58.3%), and zonal hyperfluorescence in 2 eyes (16.7%).

Conclusions: OCT, FA, and ICGA, provide useful diagnostic clues in posterior scleritis. Findings may have similarities with those in acute Vogt-Koyanagi-Harada disease. However, unilateral involvement, ocular pain, and typical ultrasonography findings support the diagnosis of posterior scleritis.

Clinical features of inflammatory choroidal neovascularization in myopic patients

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Purpose: To describe the clinical features of inflammatory choroidal neovascularization (CNV) in myopic patients in a referral center in Tunisia.

Methods: Retrospectively review of the medical records of 9 myopic patients (10 eyes) diagnosed with inflammatory CNV.

Results: Mean age of patients was 34 years (8 females and one male). Two patients were referred to our department with a diagnosis of myopic CNV, and one patient with a diagnosis of central serous chorioretinopathy. Mean initial best-corrected visual acuity (BCVA) was 20/80. There were no cells in the anterior chamber or vitreous. Clinical and angiographic features at presentation were consistent with a diagnosis of punctate inner choroidopathy (PIC) in 6 patients (6 eyes) and presumed ocular histoplasmosis syndrome in 3 patients (4 eyes). CNV presented with characteristic hyperfluorescent lesions with late leakage on fluorescein angiography in all eyes. OCT B-scan showed the CNV in all eyes (10). Swept source OCT angiography was performed only in one eye and showed the CNV lesion. All patients were managed with intravitreal bevacizumab injection. Five patients received oral steroids and one patient azathioprine. Mean follow up was 24 months. Recurrence was observed in one patient (PIC) and bilateralization occurred in 3 patients. Mean final BCVA was 20/80.

Conclusion: Inflammatory CNV in myopic patients is a rare condition. A careful analysis of clinical and imaging findings can help differentiate such a choroidal neovascular condition for myopic CNV. This is essential for management and visual outcome.

To stop or not? Sight threatening bilateral panuveitis as side effect of Vemurafenib therapy for metastatic colorectal melanoma

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Background

Patients with metastatic melanoma can present a BRAF-gene mutation in 46% of the cases. Vemurafenib is a potent and specific BRAF v600-enzyme inhibitor, and uveitis its most common ocular side-effect. We report the case of a metastatic melanoma patient treated with vemurafenib who experienced a sight-threatening bilateral panuveitis.

Case presentation

A 51-year old male patient affected by gastro-intestinal melanoma with lung and lymphonodes metastasis complained of left eye blurred vision, 4 months after starting vemurafenib. Unilateral iridocyclitis was diagnosed and topical dexamethasone and mydriatics administered with a good initial response. Nevertheless in the following 16 months of follow-up, he experienced seven relapses of bilateral panuveitis with optic disc, macular edema, and cilio-choroidal effusion, treated with topical dexamethasone, methylprednisolone acetate 40 mg periocular injections and systemic prednisone (initial dose 0.5 mg/kg), combined with vemurafenib withdrawal for only two weeks. At the last examination no active uveitis was detected in both eyes, the left eye only showing epiretinal membranes and low-grade macular edema. Visual acuity was 1 and 0.8 in right and left eye, respectively. Systemic conditions were unchanged.

Discussion

In patients with metastatic melanoma vemurafenib significantly improves survival, but might cause uveitis, usually reversible within weeks after stopping drug. Nevertheless in many patients vemurafenib discontinuation is discouraged because of a possible tumor progression. A combination of topical, periocular and low-dose systemic steroids with a close follow-up and short-term vemurafenib withdrawal can lead to a satisfactory management of uveitis and of its sight-threatening complications, without leading to tumor progression.

Endogenous endophthalmitis: A review of 7 cases

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Purpose: To investigate the etiology, microbiological spectrum, and visual outcome of endogenous endophthalmitis.

Methods: Retrospective study of 10 eyes of 7 patients with endogenous endophthalmitis.

Results: Mean age of our patients was 52.3 years (range, 40-67). Six patients (85.7%) were male. Bilateral involvement was recorded in 3 patients (42.8%). Six patients (85.7%) had diabetes mellitus. There was a recent history of urinary tract infection with sepsis in 2 patients (28.6%), septicemia with liver and kidney abscesses in 1 patient (14.3%), a sepsis with psoas abscess in 1 patient (14.3%), and a dental abscess in 1 patient (14.3%). Mean initial best-corrected visual acuity (BCVA) was 20/200 (range, light perception-20/50). Clinical findings included vitritis in 100% of eyes, foci of chorioretinitis in 8 eyes (80%). Identified causative organisms included *Candida albicans* in 4 eyes (40%), *Staphylococcus aureus* in one eye (10%), and *Klebsiella pneumoniae* in one eye (10%). All patients were treated with systemic and intravitreal antibiotics and/or antifungal agents. Two eyes (20%) underwent vitrectomy. Final BCVA was 20/1000 in 6 eyes (60%), light perception in 2 eyes (20%) and hand motion in 2 eyes (20%). Complications included tractional retinal detachment in 2 eyes (20%), rhegmatogenous retinal detachment in one eye (10%), and phthisis bulbi in one eye (10%).

Conclusions: Endogenous endophthalmitis is a rare and severe intraocular infection that can be vision-threatening. Early diagnosis and appropriate management are mandatory to improve visual outcome.

Posters exhibition

Resolution of retinal vascular leak with oral JAK kinase inhibitor tofacitinib

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Purpose: To describe the resolution of retinal vascular leak in a patient treated with oral tofacitinib

Method: case report

Result: A 29 year old female with a known history of uveitis presented with symptoms of blurred vision. FFA showed retinal vasculitis. She had been recently put on tofacitinib for her seronegative arthritis. No additional treatment was given. After 3 months repeat FFA showed complete resolution of the vasculitis.

Conclusion: Oral JAK Kinase inhibitor tofacitinib may have a role in treating uveitis. Further studies will be needed to validate this finding.

RECENT ADVANCES IN IMAGING MODALITIES LEAD TO NEW MANAGEMENT AND PROGNOSIS OF FIVE CASES OF VOGT-KOYANAGI-HARADA (VKH) DISEASE.

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PURPOSE: *to analyze* clinical features, changes in imaging tests and response to treatment in patients diagnosed of VKH disease.

METHODS: we present a report of 5 patients diagnosed of VKH. We followed them through basic ophthalmologic exploration, OCT and fluorescein angiography.

RESULTS: during the follow-up, we measured the choroidal thickness with OCT, finding that it decreases with response to treatment and it increases in relapses of the disease. Initially, all the patients were treated using aggressive and long-term treatment with high-dose of oral or IV corticosteroids, followed by an oral taper (at least 6 months); we didn't find any difference between both routes of administration. We obtained good initial results in all cases, but in most patients, a biological or immunosuppressive agent had to be added to fully control of inflammation; in our experience, it could be related to the undulations of the retinal pigment epithelium in the acute phase of the disease. In the treatment with biological drugs, we found a lack of response with biosimilars in one patient who later responded to adalimumab and methothrexate. The long-term outcomes in visual acuity in all cases were 15/20 or better.

CONCLUSIONS: recent advances in imaging modalities have improved the understanding of VKH disease. This, added to the new pharmacological alternatives, has changed its management and prognosis. It would be interesting to carry out further studies with a greater number of patients.

Improvements in Signs and Symptoms of Severe Vernal Keratoconjunctivitis in Patients Treated With Ciclosporin A Cationic Emulsion 0.1%: Results from the VEKTIS Study

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Purpose: The phase III VEKTIS study evaluated the efficacy/tolerability of 0.1% ciclosporin A cationic emulsion (CsA CE) eye drops in pediatric patients with severe vernal keratoconjunctivitis (VKC; Bonini scale 3/4 with severe keratitis [4/5, modified Oxford scale]). **Methods:** 169 patients randomized to CsA CE QID, CsA CE BID+vehicle BID, or vehicle QID for 4 months, then 8-month follow-up (CsA CE used if needed). Primary endpoint was mean composite score reflecting corneal fluorescein staining (CFS), rescue medication use, and ulceration over 4 months. Changes in visual analogue scale (VAS) scores for 4 key VKC symptoms were assessed over 12 months. **Results:** Primary endpoint was superior in both active groups vs. vehicle ($p=0.007$, $p=0.010$ for CsA CE QID, BID respectively; mainly driven by CFS). VKC symptoms improved in each group from Months 1-4 (M1-4; largest decreases at M1). CsA CE QID provided significantly greater symptom improvement ($p<0.05$) vs. vehicle at M1, M2 and M4 for photophobia, M2, M4 for tearing, all timepoints for itching and mucous discharge. For CsA CE BID, significant improvements vs. vehicle were reported at M2 (photophobia, itching, tearing), M3 (itching). 8-month follow-up demonstrated stability of improvements, especially among patients treated beyond M4. CsA CE was well-tolerated. **Conclusion:** Both CsA CE doses significantly improved VKC signs vs. vehicle alone over 4 months. All 4 VKC symptoms showed improvements over time in each treatment group during the randomized period, with significant improvements for CsA CE QID vs. vehicle at most timepoints; improvements were stable over 8-month follow-up.

Presumed ocular sarcoidosis presenting with bilateral papilledema and disk haemorrhages

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This report aims to emphasize the importance of differential diagnosis via a complicated case of presumed sarcoidosis. The 34 year old man, referred from a primary care center for neuro-ophthalmology consultation, had lost vision in the last 15 days and was prescribed acetazolamide and topical nepafenac for macular edema. He described upper respiratory tract infection, sinusitis, weight loss of 6 kg in 1.5 months, nausea, and normal blood pressure. Cranial MR showed no space occupying lesion and no sinusitis. Vision was 0.1 and 0.2 Snellen on the right and left eye. Vitreous snowballs and disc elevation with haemorrhages were present in both eyes with no anterior chamber cells and flare. FA was not helpful. The visual fields were totally depressed. At the tertiary center, optic disc granulomas were noted and consulted with a rheumatologist and thoracic medical specialist with no yielding etiologic diagnosis, although chest X-ray revealed minimal enlargement of lymph nodes, CRP 10.6, sedimentation 33 mm/h, PPD 3 mm, mildly raised blood urea and creatinine. C-ANCA and P-ANCA were negative. Regarding occupational demands, the patient was put on systemic and topical steroids. After one week, the vision increased to 0.7 and 1.0 on the right and left eyes. The patient accepted to have an ICGA which revealed widespread hypofluorescent choroidal lesions in the initial phases which later faded. He was encouraged to consult another thoracic medicine specialist and the result was sarcoidosis suspect, also warned for close follow up.

Chlamydiaceae and Chlamydia-like organisms (CLOs) in the conjunctiva of children and adults from a trachoma endemic region in Sudan

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Several similarities have been demonstrated between CLOs and *Chlamydia trachomatis* (CT) concerning their developmental cycle, virulence factors, invading mechanisms and 16S rDNA identity. Considering the central role of CT in trachoma and CLOs as highly prevalent microorganisms in the environment, it is necessary to identify the frequency of CLOs in the eye surface and their association with trachoma. In this study, the frequency of CT and *Chlamydiales* families were examined in ocular samples from Sudanese children and adults.

Within a case-control study, 96 children (54 cases and 45 controls) and 93 adults (51 cases and 42 controls) were tested using a pan-*Chlamydiales* Real-Time PCR targeting the 16S rRNA gene of *Chlamydiales*. Positive samples were subjected to DNA sequencing.

The overall prevalence of *Chlamydiales* was 36%. Sequences have been classified into four families including *Chlamydiaceae* (55.6%), *Parachlamydiaceae* (29.6%), *Simkaniaceae* (13%) and *Criblamydiaceae* (1.9%). Infection with CT was significantly higher in children (31.5%) compared to adults (0%) with trachoma ($p<0.0001$). CT infection was associated with trachoma among children ($p<0.0001$). 21.5% of adults and 4.2% of children resulted positive for different CLOs ($p=0.0003$).

To our knowledge, this is the first study examining human eyes for the presence of various *Chlamydiales* families. These results are consistent with previous findings of the central role of CT in trachoma among children. Differences in the distribution of identified CLOs among trachoma patients and healthy controls cannot suggest a pathogenic role for these bacteria. Further studies are needed to understand the impacts of CLOs in pathogenicity and/or protection.

Efficacy of Adalimuab in treating severe non-infective posterior uveitis

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Introduction

Non-infective posterior uveitis is treated initially with local or oral corticosteroid with the introduction of steroid-sparing immunosuppressive agents as required. In recent times, the use of Biologic agents such as Adalimumab has been used when there is inadequate control on corticosteroid and immunosuppressive agents.

Purpose

This study details our experience of Adalimumab for the treatment of non-infectious posterior uveitis.

Method

A retrospective case study of 18 patients with non-infective posterior uveitis. The indication for starting Adalimumab in our patient group was intolerance to or inadequate disease control on immunosuppressive agents.

Results

Comparing visual acuity at the last clinic visit prior to commencement of Adalimumab to visual acuity after 6 months on treatment, 55% gained one or more lines on the snellen visual acuity lines with an average gain of 2 lines. 28% had no change in visual acuity. We compared the number of flare up in the 6 months leading to starting Adalimumab and number of flare up 6 months after. The average number of flare up pre- Adalimumab was 1.88 and post-Adalimumab was 0.833. There is a statistically significant difference in the number of flare ups pre and post- Adalimumab. (P value= 0.003).

Conclusion

Our study shows Adalimumab can improve disease control in severe non-infective posterior uveitis. National Institute of Clinical excellence recently recommended the use of Adalimumab as an option for treating non-infectious uveitis in the United Kingdom. We hope our results contributes to growing evidence of the efficacy of Adalimumab in severe non-infectious posterior uveitis.

Rare case of Rhabdomyosarcoma of ciliary body

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Rare type of masquerade uveitis. Case report.

Background: Uvea is extremely rare location of rhabdomyosarcoma (RMS). There are only three cases have been reported.

It accounts about 5% of pediatric cancer and can occur in any sites, including the ocular region (20% of all RMS, mostly orbital).

Case report.

5 y.o. Norwegian boy with granulomatous iritis and secondary glaucoma in the left eye from June 2013.

Clinical findings and investigations did't confirm any infections or tumors.

Radiological findings: first ultrasound then MRI caput/orbital had not confirm foreign bodies or tumors.

Clinical challenges: Because of high ACE, he was referred to genetic department and Blau syndrome was excluded.

His iridocyclitis and glaucoma did not respond to any treatment. Trabeculectomy, then Ahmed Valve operation were performed without effect. When precipitates become to be confluent new ultrasound was performed with suspected slightly thickening of the ciliary body and iris with white mass in the angle of camera anterior on gonioscopy. His eye (visus 0,5 LogMar) was enucleated because of strong suspicion of malignancy.

Histology: rhabdomyosarcoma of alveolar (most malignant) type.

Management: radiotherapy and chemotherapy. No local or distant metastasis were occur.

Discussion: Our work up took 9 month. We should never trust to negative single puncture of camera anterior . In case of non-response to any therapy it should be repeated with considering of malignancy. Lymphoma, leukemia, retinoblastoma and metastatic tumors are not ONLY tumors that follow to masquerade uveitis.

Bidirectional cross talk between uveal melanoma cells and hepatic myofibroblasts promotes inflammation-induced chemokines expression.

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Purpose

Uveal melanoma (UM) is the most common primary ocular neoplasm in adults. Its cause is largely unknown, and no risk factors have yet been identified. The metastatic disease develops in up to 50% of patients, usually involving the liver. Treatment only rarely prolongs survival, because metastases are highly resistant to most chemotherapeutic agents. Tumor cells may modulate the functions of surrounding cells to facilitate their own growth, survival, invasion, and metastasis. This study was conducted to investigate the role of hepatic microenvironment on UM cells (UMC).

Methods

Here, we utilized metastatic (Omm2.3) and non-metastatic (Mel270) UMC in coculture with hepatocyte-stellate cells (HSC) LX2. The transcriptomic study was performed by microarray assay. Expression of relevant genes was measured by qPCR. Cytokines were quantified by Elisa test. Cell proliferation was assessed by MTT staining. Extracellular matrix components were evaluated by quantitative cell adhesion assay.

Results

Hepatic microenvironment increased the expression of numerous genes. However, the number of genes overexpressed in metastatic co-cultures is three-times higher than in non-metastatic cocultures, demonstrating that hepatic microenvironment has more impact on metastatic UMC. Over-expressed genes in coculture were linked to inflammation and included several interleukins. In addition, UMC-HSC crosstalk generated expression of cell adhesion receptors, particularly by increasing fibronectin. In contrast, hepatic microenvironment had no effect on cell proliferation.

Conclusions

Our results provide evidence for an important role of inflammation in the progression of metastatic UM. Therefore, the inflammatory characteristics of the tumor microenvironment might offer therapeutic opportunities.

The role of enhanced depth imaging optical coherence tomography in the diagnostics of tuberculous chorioretinitis. The case series

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Purpose. To determine applicability of *enhanced depth imaging optical coherence tomography (EDI-OCT)* in the diagnostics of tuberculous chorioretinitis.

Methods: Study included eight patients with presumed tuberculous chorioretinitis. Carrying Mantoux test was impossible in 7 patients due to risk of central vision loss. All patients were examined by EDI-OCT in addition to standard ophthalmological examinations.

Results: We revealed choroidal thickening in inflammatory foci by EDI-OCT in 7 patients. We also determined RPE-choroid complex elevation. Secondary retinal alterations were also present over area of choroidal thickening. These patients were assigned to ex-juvantibus anti-TB drugs. On ex-juvantibus therapy positive dynamics had been reached, and patients were assigned to anti-TB therapy for 6–9 months. Upon further observation and treatment all these patients had chorioretinal scar formation. Complete remission with anti-TB therapy was achieved in 6 months in 2 patients. In 5 patients complete remission was achieved in 9 months. Choroidal thickening and RPE-choroid complex elevation was not observed by EDI-OCT after full chorioretinal scar formation. In 1 case with presumed tuberculous chorioretinitis choroidal changes were insignificant by EDI-OCT. But iso-hyperreflective intraretinal mass was determined. As known, isolated neuroretinal involvement extremely indistinctive for tuberculous chorioretinitis. Search for a possible etiology of chorioretinitis was continued, resulting in diagnosis ocular bartonellosis. On the specific therapy regression of inflammation and resorption of focus was achieved in the short term.

Conclusions. EDI-OCT can be effectively applied in diagnostics of tuberculous chorioretinitis, or even act as a key method of examination in cases of carrying the Mantoux test impossibility.

OCULAR INVOLVEMENT IN PATIENTS WITH AUTOIMMUNE DISEASES: 15 YEARS' EXPERIENCE IN COLOMBIA

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Purpose

To estimate the prevalence of ocular disorders in patients with autoimmune diseases (AD) from a Colombian rheumatology referral center.

Methods

Observational, descriptive prevalence-study from 2000 to 2015 in patients with AD. Randomized stratified sampling with proportional assignment using Epidat 3.4. Data analysis: SPSS v22.0. Categorical variables were subjected to univariate analysis. Measures of central tendency were performed for quantitative variables.

Results

From a total of 3600 patients with autoimmune diseases we analyzed a statistically representative sample of 1640 patients. Ocular involvement was present in 38.7% of patients; 83.3% were women. Rheumatoid arthritis (RA) was the most prevalent AD with ocular compromise (62.2%) and sarcoidosis was the less prevalent (10%). Keratoconjunctivitis sicca (KCS) was the most common finding (63.5%) in all AD except in spondyloarthropathies (19%). Cataract was presented in 4.1%, having the highest predominance of corticosteroid drug usage (88.8%). Ocular toxicity due to antimalarial drugs was developed in 7.2% of the total patients and in 18.7% of patients with Systemic Lupus Erythematosus (SLE). Antinuclear antibodies (ANA) were present in the whole vascular retinal disease group. The highest anti-DNA antibody serum positivity was found in patients with cataract; SLE rendered the highest episcleritis prevalence (12.5%); 22% of anti-RNP positive patients presented cataracts, 32.1% of uveitis patients were HLA-B27 positive. Eye manifestations preceded systemic involvement in 11.1 to 33.3% of patients.

Conclusions

RA had the highest prevalence of ocular co-morbidity; KCS was the most frequent ocular finding. Ocular adverse effects caused by rheumatic drugs should be monitored during the course of treatment.

GENETIC POLYMORPHISMS IN CYTOKINE GENES IN COLOMBIAN PATIENTS WITH OCULAR TOXOPLASMOSIS

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Toxoplasmosis is a major cause of uveitis in Colombian population, however, the association between genetic polymorphisms in cytokine genes and susceptibility to ocular toxoplasmosis has not been studied for this population. The present work will evaluate the association between polymorphisms in genes coding for cytokines TNF- α (rs1799964, rs1800629, rs1799724, rs1800630, rs361525); IL-1 β (rs16944, rs1143634, rs1143627), IL-1 α (rs1800587); IFN- γ (rs2430561); IL-10 (rs1800896, rs1800871), and the presence of ocular toxoplasmosis (OT) in a sample of Colombian population (61 patients with OT and 116 healthy controls). Genotyping was performed with the “ddNTP primer extension” technique. Functional effect predictions of SNPs were done using FuncPred.

Polymorphism in IL-10 gene-promoter (-1082G/A) was significantly more prevalent in OT patients than in controls ($P = 1.93E-08$; $OR=5.27E+03$; $95\%CI=3.18-8.739$; $pBONF =3.48E-07$). In contrast, the haplotype “AG” of IL-10 gene promoter polymorphism (rs1800896, rs1800871), was present with lower frequency in OT patients [$P= 7e-04$, $OR (95\%CI) 0.10 (0.03-0.35)$]. The polymorphism (+ 874 A/T) of IFN- γ was associated with OT ($P= 3.37E-05$; $OR=4.2$; $95\%CI=2.478-7.12$; $pBONF =6.07E-04$). The haplotype “GAG” of IL-1 β gene promoter polymorphism (rs1143634, rs1143627, rs16944), appeared to be significantly associated with OT ($p=0.0494$). The IL-10, IFN- γ and IL-1 β polymorphisms influence the development of OT in the Colombian population.

Scleritis Masquerading Posterior Choroidal Tumors

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Purpose: To present clinical characteristics of five eyes with scleritis masquerading choroidal tumors.

Methods: Five patients who were referred to our Ocular Oncology Unit for posterior uveal melanoma were included in our analysis.

Results: Three patients had multiple posterior elevated mass. These mass lesions were located on macular and perifoveal regions. Two eyes had serous retinal detachment. One case had bilateral involvement. While anterior uveal inflammation was noted in only one eye there was orbital pain and inflammation in two cases. Ocular Ultrasound showed medium internal reflectivity similar to a choroidal hemangioma. Orbital MR imaging was helpful only in two cases showing whole thickness scleral indentation, not a choroidal tumor. Orbital biopsies were performed in these two cases confirmed idiopathic orbital inflammation and scleral abscess formation in each. All patients responded well to systemic corticosteroids and oral immune suppressants.

Conclusion: Scleritis may represent as an intraocular tumor due to whole thickness eyewall inflammation or external scleral indentation due to co-existent orbital inflammation and scleral thinning. The clinical differential diagnosis of these cases is challenging and needs careful evaluation of the clinical and radiological findings.

Ocular involvement in Whipple disease: three challenging cases

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BACKGROUND

Whipple disease (WD) is a rare but underrated, chronic, multisystemic condition, caused by bacterium *Tropheryma Whipplei*. The most common symptoms are gastrointestinal and polyarthralgias. Ocular manifestations may result from direct ocular involvement. We report three cases of WD, with and without gastrointestinal symptoms, characterized by two different ocular involvements: surface and uveitis.

CASES

The first patient, HIV+, CD4-400cell/mm³, suffered from a chronic conjunctivitis with a fibrovascular pannus involving corneal periphery and diffuse limbic nodules in both eyes. Patient reported abdominal pain and weight loss, the diagnosis of ocular Whipple was confirmed by a positive PCR in conjunctival scraping, after positive PAS staining of bowel biopsies.

The second patient presented with gastrointestinal symptoms, abdominal lymphadenopathy and posterior uveitis, with intense bilateral vitritis. The diagnosis of WD was made by histopathological analysis of adenopathy, on suspicion of lymphoma. The patient was treated with systemic antibiotics with significant ocular improvement. The third patient suffered from gait unbalance, dysarthria and arthralgias associated with a ten-years-history of bilateral panuveitis. Reporting also sporadic oral ulcers, a diagnosis of neuro-Behcet's was first made. Considering the worsening of eye inflammation and progressive optic atrophy after local and systemic steroid therapy, a diagnostic vitrectomy was performed and a positive PCR for *T. Whipplei*-DNA was found in vitreo.

CONCLUSIONS

WD is underrated and it should be excluded in any atypical uveitis mimicking Behcet's disease or lymphoma, even in the absence of typical gastrointestinal symptoms. Uveitis is typical in WD, but also an isolated ocular surface involvement is possible.

Multidisciplinary study of systemic causes of 500 adults patients in a referral center in the North of Spain .

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Objective: To describe the main characteristics of a cohort of patients with uveitis in a referral multidisciplinary unit from northern Spain.

Methods: Retrospective analysis of clinical records of patients evaluated in the Multidisciplinary Unit of the Complejo Hospitalario of Navarra since January 2010 until March 2015. We analyzed the demographic characteristics, origin, types of uveitis, laterality, and etiology.

Results: We identified 500 patients, 50% women with a mean age of 47.9 ± 16.4 years. 87% of the patients were autochthonous and 13% were foreigners. The most frequent type of uveitis was anterior uveitis (AU) (61%), followed by posterior uveitis (PU) (23%), panuveitis (PAN) (14%), and intermediate uveitis (IU) (2%). Considering the etiology, 31.2% were unclassifiable, followed by non-infectious systemic disease in 29.2%. Ankylosing spondylitis were the most frequent etiology present in 10.8% of patients, followed by herpes infection in 9,2%, and toxoplasmosis in 7,8%, respectively. It was found that infectious cause was statistically significant superior in foreign patients than spanish –born patients (p value =0,002). There was a relationship between the type of uveitis and foreigner (p-value = 0.006), UA was less frequent than expected and PAN more frequent. There was a relationship between the laterality and foreigner (p-value = 0.435), being the unilateral form the most frequent.

Conclusions: The unilateral anterior and idiopathic uveitis were the most frequent in our series. The PAN type and infectious cause was the most frequent type of uveitis in the foreign population compared to the general population of our study.

TREATMENTS AND VISUAL ACUITY IN A REFERRAL MULTIDISCIPLINARY UVEITIS UNIT IN NORTHERN SPAIN

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Objectives: To analyze the treatments prescribed and loss of visual acuity in a cohort of patients with uveitis in a referral multidisciplinary unit from northern Spain.

Methods: Retrospective analysis of clinical records of patients evaluated in the Uveitis Multidisciplinary Unit of the Complejo Hospitalario of Navarra since January 2010 until March 2015. We analyzed the demographic characteristics, type of uveitis, etiology and treatments received in the following 3 months and loss of visual acuity after one year follow-up.

Results: We identified 500 patients, 50% women with a mean age of 47.9 +/- 16.4 years. The most frequent type of uveitis was anterior uveitis (65,4%), followed by posterior uveitis (17,6%), panuveitis (15,2%), and intermediate uveitis (1,8%). Considering the etiology, 31.2% were unclassifiable, followed by non-infectious systemic disease in 29.2%. During the 3-month follow-up, 904 treatments were prescribed. The most frequent treatment was ocular topical (39%), followed by immunosuppressive treatment (27%), antimicrobial (14%), other treatments (10%) and less biological (3%), surgical (3%) and finally periocular (2%) and intravitreal treatment (2%). The mean best corrected visual acuity at after one year follow-up in RE was 0.76±0.28 and LE was 0.75±0.28. It was observed that mean loss of visual acuity in RE was related to biological treatment (p-value=0,022), intravitreal treatment (p-value=0,028) and surgical treatment (p-value=0,008). There was no relationship with other type of treatments.

Conclusions: The majority of patients in our series received ocular topical treatment. Biological, surgical and intravitreal treatment were associated with loss of visual acuity.

Interferon-Gamma Release Assay (IGRA) and Ocular Tuberculosis: Implications for the diagnosis and management of tuberculosis-related ocular inflammation: Preliminary Results.

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Purpose:

To evaluate the various clinical features and management of presumed ocular tuberculosis and new approaches in diagnosis, such as Interferon-Gamma Release Assay (IGRA).

Methods:

Prospective ongoing research consisting in the analysis of the diagnostic value of IGRA tests and Real time PCR to confirm the diagnosis of ocular TB disease. The clinical findings of ocular disease will also be evaluated.

Results:

So far, we present a total of 36 patients with presumed ocular tuberculosis undergoing specific treatment. 91% of the cases show Positive IGRA test. TST was 10mm or higher in 91% of the cases. Eight percent (8%) of the cases (3/36) presented with positive IGRA test, in spite of negative TST (<10 mm) and has being treated as tuberculosis. Thirty six percent (36%) of the cases had TST values between 10-15mm. Mean TST value was 17 mm, range 1 to 32.

Regarding ocular inflammatory findings, retinochoroiditis or choroiditis were the main findings, observed in 36% of the cases. Other findings were: diffuse uveitis and/or vasculitis in 25%, scleritis (22%), anterior uveitis (14%) and interstitial keratitis (3%).

Conclusion:

Although the current gold standard for Ocular Tuberculosis diagnosis is a positive Tuberculin Skin Test (TST) combined with appropriate clinical findings, this test has somewhat limited accuracy. The introduction of new diagnostic techniques such as Interferon-Gamma Release Assays (IGRA) could be useful and further data is necessary so that they can be applied rationally in uTB.

Key Words: therapeutic approach, TBU diagnosis, IGRA, tuberculin intradermic test, uveitis, tuberculosis

Differences in the approach of Brazilian experts to diagnosis and treatment of tuberculous uveitis.

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Purpose: To describe the current approach of Brazilian uveitis experts for the diagnosis and treatment of tuberculous uveitis (TBU), and to compare it with the approach of experts from developing and developed countries. **Methods:** An online survey was sent to 169 Brazilian uveitis specialists. **Results:** In a period of 12 months, Brazilian experts evaluate a mean of 5.6 patients with TBU, while experts from India and North America evaluate about 76.3 and 2.2 patients respectively. Syphilis serology (88%), HIV serology (81%) and tuberculin skin test (TST, 81%) were the preferred tests of Brazilian experts to rule out another infectious uveitis. Brazilian experts use the IGRA and CR less frequently than experts from developing and developed countries. Unexpectedly, chest CT is used more frequent in Brazil than in the others two groups. A positive result of TST continues to be the principal test to prompt therapy in 81% of Brazilian experts. Results of IGRA and CR tests are less likely to be used by Brazilian experts to prompt anti-tubercular therapy (ATT) compared with the other 2 groups. Regarding the choice of TBU treatment, Brazilian and developing countries experts usually prescribed the standard ATT, while developed countries experts preferred to defer ATT to other clinician. Considering treatment time, 39% of Brazilian experts indicate 9 months of treatment, 34% indicate 6 months, and 14% indicates 12 months. A similar approach was found in both developed and developing countries. **Conclusions:** There is no general consensus about management of this disease. **Key Words:** therapeutic approach, TBU diagnosis.

Posters exhibition

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Pejvak Azadi¹, mohammad riaz esfahani.

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A 20 year-old man with history of right eye pars plana vitrectomy for corneoscleral laceration and retinal incarceration came to our center, complaining of left eye decreased vision since about 3 days ago. At the presentation in the left eye the vision was 1 LogMAR, and the fluorescein angiography (FA) and ocular coherence tomography (OCT) revealed multiple serous detachments with subretinal septations, mostly compatible with fibrinous reaction. After steroid therapy, the serous retinal detachments of the left sympathizing eye subsided and visual acuity improved to 0.045 LogMAR

Case Report: Cytomegalovirus Induced Unilateral Acute Retinal Necrosis with Contralateral Optic neuropathy in an Immunocompetent Adult

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Objective: To report an unusual case of cytomegalovirus induced unilateral acute retinal necrosis with contralateral optic neuropathy in a healthy patient.

Method: Retrospective case report. A 27-year-old healthy male presented with a 1-week history of blurred vision in the left eye. He was diagnosed with acute retinal necrosis in the left eye. The right eye was unremarkable.

Result: Aqueous polymerase chain reaction yielded cytomegalovirus. The anti-HIV test was negative. The retinal lesions resolved with ganciclovir treatment. The left optic disc became subsequently pale. On the 12th day of the admission, he developed an abrupt onset of profound visual loss in the right eye. Ocular examination showed 8 millimetres of fixed dilated pupils in both eyes. The retina and optic disc appeared initially normal in the right eye but subsequent development of optic atrophy was noted. Blood tests revealed transient elevation of lupus anticoagulant. Other investigations were unremarkable. We hypothesized that cytomegalovirus induced-transient elevation of lupus anticoagulant can be a cause of vascular thrombosis of the optic nerve, which led to contralateral optic neuropathy. Unfortunately, the right eye did not improve with anticoagulant therapy. Two months later, he developed rhegmatogenous retinal detachment in the left eye which was successfully treated with pars plana vitrectomy.

Conclusion: It should be emphasized that cytomegalovirus can be a cause of acute retinal necrosis even in immunocompetent patients. Ophthalmologists should remain vigilant that ocular cytomegalovirus infection can induce vascular thrombotic phenomenon in patients.

Two cases of presumed intraocular Tuberculosis

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Tuberculous uveitis is a vision-threatening disease that inevitably leads to blindness if not properly diagnosed and treated

We report two cases of ocular presumed tuberculosis with choroidal involvement not associated with clinical evidence of pulmonary tuberculosis.

In the first case we describe a 18 years old boy who presented a serpiginoid choroiditis with macular involvement in the left eye. We prescribed a standard four drugs anti tubercular therapy (ATT) and the lesions completely resolved with a good recovery of visual acuity .

In the second case an 8 years old boy from Vietnam showed a bilateral multifocal choroiditis appeared three years after a treatment for latent tuberculosis infection (LTBI).The patient showed an important vision loss in both eyes. We decided to start an anti tubercular treatment associated to a short course of oral steroid in order to reduce macular scarring . At the moment this patient who underwent only one month of ATT shows an improvement of visual acuity and a reduction of inflammatory reaction .

‘Molecular analysis of Aqueous humor: liquid biopsy for classification of eye disease’

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Abstract for session titled “utility of anterior chamber diagnostics”.

Molecular analysis of Aqueous humor: liquid biopsy for classification of eye disease

Retinal diseases generally are vision-threatening conditions that warrant appropriate clinical decision-making which currently depends upon extensive clinical screening by specialized ophthalmologists. In the era where molecular assessment has improved dramatically, we recently provided proof of concept for molecular biomarker profiling in ocular fluids to classify archetypical ocular conditions affecting the retina (age-related macular degeneration, idiopathic non-infectious uveitis, primary vitreoretinal lymphoma, and rhegmatogenous retinal detachment) with one single test. Unsupervised clustering of ocular proteins could discern disease specific profiles, which we exploited to develop and independently validate models that were able to correctly classify patients with high overall accuracy, sensitivity and specificity. Current efforts combine proteomic and genomic approaches to optimize early and accurate disease detection as a diagnostic aid for ophthalmologists in the care for patients with eye conditions.

Clinical Characteristics of Visually impaired patients with Uveitis

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BACKGROUND

Uveitis accounts for up to 10% of blindness worldwide, either directly or through complications of inflammation. This study aims to identify patients with uveitis who were registered sight-impaired or severely sight-impaired between 2007 and 2016, and to analyse the type, aetiology, duration, age at registration and complications encountered.

METHODS

Retrospective analysis of case records of uveitis patients attending a tertiary referral centre in Manchester, UK who were issued a Certificate of Vision Impairment (CVI) from 2007 to 2016.

RESULTS

63 patients were registered. Ages ranged from 5 to 84, of which 89% were in the working age group 20 to 65 . 38% were registered sight-impaired and 62% severely sight-impaired. The mean duration of uveitis from onset to registration was 8.6yrs (range <1 – 37yrs). 39 patients had extensive visual field loss. The remaining 24 were registered mainly because of poor vision. The most common complications were macular oedema (40%), direct retinal damage from inflammation or ischaemia (33%) and secondary glaucoma (24%).

The most common diagnoses were tuberculosis (13%), sympathetic uveitis (11%), Idiopathic panuveitis (8%), Behçet's ,sarcoidosis and chronic idiopathic anterior uveitis (6.3%, each);Twenty two CVIs (35%) followed infective uveitis.

Registrations dropped from 33 (2007-2010) to 17(2013-2016) in this period.

CONCLUSIONS

Uveitis is an important cause of visual impairment, especially in working-age adults. In this specialist clinic registration is uncommon and has decreased in frequency despite an increasing caseload. We attribute this mainly to earlier intervention with oral immunosuppression, intravitreal treatment of macular edema, and earlier glaucoma surgery.

Serologic Testing for Syphilis Among Patients with Uveitis

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Introduction. The prevalence of syphilis has increased recently, and no consensus exists among specialists about best testing protocols for diagnosing syphilitic uveitis. We reviewed serologic profiles and diagnoses for patients with suspected ocular syphilis to gain insights into appropriate testing procedures.

Methods. We reviewed records for all patients with at least one reactive test for syphilis seen by two uveitis specialists (IK, MKB) at a tertiary referral center since 2015. All underwent routine testing with both non-treponemal (RPR) and treponemal (TP-PA) tests. Diagnosis of syphilitic uveitis was made if the patient had (1) no known history of syphilis and a second treponemal test was reactive; (2) non-ocular manifestations of syphilis; or (3) a remote history of syphilis, unconfirmed treatment, and a reactive non-treponemal test.

Results. Among 14 patients with a reactive TP-PA test, 13 were diagnosed with syphilitic uveitis; 3 had non-reactive RPR tests, 2 of whom were HIV-infected. Only 1 patient had a concurrent non-ocular manifestation of syphilis (palmar rash). One patient with a reactive TP-PA and non-reactive RPR had been treated appropriately for a remote syphilis infection, and a diagnosis of syphilitic uveitis was not made.

Conclusion. Our findings support the following recommendations for diagnostic testing of patients with non-specific intraocular inflammation: (1) choice of serologic tests should be individualized, based on historical and medical factors; (2) “reverse-sequence testing” should be used for patients at low-risk for infection because of possible non-reactive non-treponemal tests; and (3) follow-up of all positive tests, to confirm diagnoses of syphilis, is critical.

Ocular toxicity of moxifloxacin: case report and review of the literature.

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Purpose: To describe a case of corneal melting with perforation after treating a corneal abscess with topical moxifloxacin + tobramycin and to review the cases of ocular toxicity after oral and topical moxifloxacin.

Patient and Methods: retrospective case report. A 56 year old patient presented 5 weeks after a retinal surgery with a central corneal abscess. Topical tobramycin + moxifloxacin 1/h + desomedine 8/d was initiated and tapered 3 days later to 1/h, 5/d and 5/d respectively. Four days later a large erosion appeared while the abscess had disappeared. Topical tobramycin 5/d and moxifloxacin 3/d were continued for 1 more week when the patient presented to our clinic with a large corneal melting in a clear cornea that perforated centrally with Descemet folds, fibrin, anterior cells ++, and, dilated iris vessels and posterior synechiae. Blood tests and medical history were unremarkable. Moxifloxacin and tobramycin were discontinued and replaced by preservative free ofloxacin 1/h tapered quickly therapeutic lens. All cultures for bacteria, virus, amoeba or fungi as well as PCR for HsV1, HsV2, VZV remained negative. Cornea healed quickly and therapeutic lens could be removed after a 3 days. Intraocular inflammation decreased progressively.

Discussion: Oral moxifloxacin and topical moxifloxacin have been previously reported to induce intraocular inflammation with iris depigmentation and corneal toxicity respectively. A review of the literature will be presented.

Conclusion: This case suggests that topical moxifloxacin (combined with tobramycin) may inhibit the healing of corneal ulcers and induce a corneal melting leading to perforation.

ocular inflammation and tuberculosis

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Background

Tuberculosis-related uveitis (TRU) is a multifaceted clinical manifestation. New diagnostic methods has emerged and it is worth studying their impact in diagnosing latent or active tuberculosis (TB) in TRU.

Methods

We present a retrospective chart analysis of 245 consecutive subjects diagnosed with presumed TRU at our institution, CHNO des 15-20 in Paris in 2012-2016.

All patients fulfilled the following study criteria : either exhaustive clinical records of confirmed active (TB) in internal medicine department, and or search for tuberculous contagion history, known infectious or non-infectious uveitic syndromes ruled out except for TRU, positive tuberculin skin test and/or QuantiFERON-TB Gold testing, pulmonary findings of TB on radiology.

In case of severe uveitis and when symptomatology was compatible with a herpes or toxoplasmosis, an anterior chamber puncture was performed with culture of mycobacterium tuberculosis.

We have recorded demographics data for potential factors are among the aspects influencing the prevalence of TRU wich can evolve on different anatomo-clinical forms of uveitis and can mimic systemic vasculitis.

Results

In 2012 ,TRU accounted for 5.1% of subjects with active intraocular inflammation referred to our uveitis clinics. This number increased to 5.7% in 2016.

The number of patients with presumed TRU with either anterior, intermediate, posterior uveitis or panuveitis and frequency of extraocular manifestations will appear.

Conclusion

The frequency of tuberculous uveitis over the period considered increased.

Screening for TB for uveitis of unknown etiology or not responding to conventional therapy, allows to start antituberculosis treatment and is of interest before immunosuppressive therapy.

The Collaborative Ocular Tuberculosis Study (COTS)-1: a multinational review of 251 patients with Tubercular Retinal Vasculitis (TRV)

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Background: Tubercular retinal vasculitis (TRV) is often described as a peripheral occlusive vasculitis possibly complicated by neovascularisation and vitreous haemorrhages. TRV can be difficult to diagnose due to non-specific presentation. Although TRV is associated with significant morbidity, near complete resolution of disease has been reported with prompt recognition and appropriate therapy. This is a descriptive study of TRV that provides analysis of phenotypes and treatment outcomes for TRV.

Methodology: Multicentre retrospective cohort study of patients diagnosed with TRV between January 2004 and December 2014, and a minimum follow-up of 1 year. Patients were treated according to individual institutional protocol.

Results: 251 patients with TRV were included. Patients had a mean age of 38.9 ± 14.4 years (range 9–86 years), and were predominantly males (n=167/251, 66.5%) of Asian ethnicity (n=174/246, 70.7%) and geographical origin (n=137/251, 54.6%). Most patients had features of occlusive type of RV (n=113/185, 61.1%). 228 patients (228/251, 90.8%) received anti-tubercular therapy (ATT). Treatment failure was less frequent in patients who received ATT (13.6%, n=31/228) as compared to patients who did not receive ATT (21.7%, n=5/23) although not statistically significant (p=0.252). Patients with occlusive type RV had superior outcomes if treated with ATT, however this was not statistically significant (p=0.057).

Conclusion: This study describes the largest multinational data set of TRV to date and supports the use of ATT in patients with TRV. Analysis of outcomes was limited by small numbers of patients who did not receive ATT.

Orbital Decompression In Recurrent and Difficult Cases of Thyroid Eye Disease

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Purpose: To explore clinical outcome of management strategies in severe or recurrent cases with thyroid eye disease.

Methods: A total of 12 patients, eight who had recurrent proptosis following decompression surgery and four patients with severe steroid resistant thyroid eye disease were included in our analysis. Six of eight patients with recurrent proptosis previously had two-wall orbital decompression and two patients had one-wall orbital decompression. Four patients had no previous surgery but resistant to iv steroid therapy. Eleven of 12 had some degree of diplopia. Six of 12 had elevated optic disk with some degree of visual field problems. Nine of 12 patients had additive orbital bone removal and 3 patients had only additional fat removal as an additive procedure in patients who had previous decompression. Three-wall orbital decompression was performed in steroid resistant cases.

Results: Five of 12 patients had persistent optic disk edema despite additional treatment. After postoperative rehabilitation, we added azathiopurine (50 mg) with lowering systemic steroids. All patients responded well with stable vision to combined usage of Azathiopurine and Surgery.

Conclusion: Additional surgery or additional azathiopurine are helpful in management of resistant and difficult cases with thyroid eye disease.

Mucosal Immunization via conjunctiva: Where do we stand?

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The ocular surface is recognized as part of the mucosal immune system as conjunctiva-associated lymphoid tissue (CALT). This lymphoid tissue consists of intraepithelial lymphocytes, subepithelial lymphoid follicles (conjunctival follicles) and adjacent lymphatic and blood vessels. Furthermore, together with lacrimal drainage-associated lymphoid tissue (LDALT), CALT forms the eye-associated lymphoid tissue (EALT). All these components have a key role in the protection of the ocular surface by initiating and regulating immune responses. In the context of needle-free delivery approach, the conjunctiva and its underlying CALT, with its possibility to detect antigens, taken up at the ocular surface, present them, and generate specific and nonspecific effector cells, would be an attractive choice for mucosal immunization, particularly against ocular infections. As the conjunctiva and CALT are interconnected with the nasal mucosa via the draining tear duct, antigens would additionally drain to nasal-associated lymphoid tissue (NALT).

Actual developments and outlooks for conjunctival immunization will be presented

Introduction

Uwe Pleyer¹.

Anterior uveitis is a potentially sight-threatening disease, which affects either one or both eyes. Important associations with systemic diseases and infections have been established and require a careful differential diagnosis. In the last decade multimodal diagnostic approaches have broadened our understanding and management of anterior uveitis. Advances in molecular biologic techniques have revealed an increasingly broader spectrum of infection-associated intraocular inflammation. In addition, imaging techniques such as in vivo confocal microscopy, anterior segment optical coherence tomography and laser flare photometry have improved our understanding and management of anterior uveitis. This session will therefore focus on recent advances on diagnostic approaches and options for disease monitoring.

Particular attention of this presentation will be paid to HLA-B27-associated acute anterior uveitis, which is the most common form. This overview will summarize current knowledge on clinical features, immunopathology and associations with HLA-B27 and its subtypes.

Milieu Intérieur: defining the boundaries of a healthy immune response for a better understanding of disease

Darragh Duffy¹, for The Milieu Interieur Consortium.

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Susceptibility to infections, disease severity, and response to therapies are highly variable between individuals. Medical practices and public health policies typically take a 'one size fits all' model for disease management and drug development ignoring individual heterogeneity in immune responses. Due to the complexity of immune responses at the individual and population level, it has been challenging thus far to define the borders of a healthy immune system as well as the parameters (genetic, epigenetic, and environmental) that drive its naturally-occurring variability. In particular, such assessments require large sample sizes, consensus for defining "healthy", and standardized protocols. In this context, the *Milieu Intérieur* Consortium initiated a cross-sectional healthy population-based study of 1,000 healthy volunteers with 1:1 sex ratio and stratified across five-decades of life. The overall aim of *Milieu Intérieur* is to assess the factors underlying immunological variance within the general healthy population. The primary objective is to define genetic and environmental factors that contribute to the observed heterogeneity in immune responses. This is being realized through the characterization and integration of (i) lifestyle and medical history (ii) genome-wide SNP genotyping and whole-exome sequencing (iii) metagenomic diversity (iv) induced transcriptional and protein responses (v) circulating immune cell populations based on flow cytometry. In parallel a number of disease specific studies have been launched including JIA and T1D which often present ocular inflammation or immunopathology. These results will lay the foundations for a better understanding of immune response variability helping to support new precision patient stratification strategies.

“Clinical Pearls in Diagnosis and Management of Uveitis Emergencies ”Behçet’s Disease

YAHYA ALZHRANI¹.

PURPOSE: To describe the features of Behçet disease over a 25-year period.

METHODS: A chart review of patients with Behçet disease who were evaluated from January 1986 to December 2011 at King Khaled Eye Specialist Hospital, Saudi Arabia. Demographic data, symptoms, type of uveitis, treatment, and complications were evaluated. The main outcome measures were presenting symptoms, types of uveitis, treatment, and complications.

RESULTS: There were 132 patients (232 eyes; 102 male [77.3%]) evaluated with age of onset of 36.9 ± 11.4 years. Panuveitis was the most common presentation, affecting 118 patients (89.4%). Episodes were bilateral in 100 patients (75.8%). Baseline best-corrected visual acuity (BCVA) was 20/125 in both eyes. Retinal vasculitis at presentation occurred in 61 eyes (26.3%), occlusive vasculitis in 59 eyes (25.4%), and macular edema in 42 eyes (18.1%). Common therapeutic management included oral corticosteroids in 123 patients (93.2%), intravenous steroid therapy in 35 patients (26.5%), cyclosporine in 98 patients (74.2%), and azathioprine in 65 patients (49.2%). Common anterior segment complications included glaucoma (44 eyes, 19%) and cataracts (34 eyes, 14.7%). The most common posterior segment complication was optic nerve atrophy. Cataract surgery was the most common surgery. At last visit, BCVA was better than 20/50 in 131 eyes (56.5%).

CONCLUSIONS: Behçet disease predominantly affects young men in Saudi Arabia. Bilateral panuveitis associated with retinal vasculitis was the most common manifestation. More than 50% of patients maintained 20/50 or better BCVA at final follow-up and were primarily managed with oral corticosteroids and other immunosuppressive agents.

PROFESSOR

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Common uveitis obstacles in Southeast-Asia; Challenging diagnosis and management of infectious uveitis

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Uveitis is a leading cause of blindness in developing countries. In contrast to common age-related eye disorders, uveitis has a significant socioeconomic impact because it often affects younger working-age patients. Infection is a leading cause of uveitis in developing countries, whereas idiopathic uveitis is more common in developed countries. *Toxoplasma gondii*, Cytomegalovirus and Herpes virus are common pathogens that cause infectious uveitis in Thailand. Since most infections can be prevented or treated, blindness resulting from uveitis in developing countries could be dramatically reduced by early etiologic diagnosis and proper treatment. Unfortunately, determining the accurate underlying etiology can be a challenge due to insufficient ancillary and laboratory investigation. Ocular tuberculosis is an example of a disease that is difficult to diagnose by clinical examination alone. A large proportion of infectious uveitis patients present with advanced-stage inflammation (severe vitritis), which makes it challenging to make an accurate diagnosis in order to save their vision. Patients lacking insurance coverage and being unable to afford to continue the treatment are major problems involved in cytomegalovirus treatment in Thailand. Thus, in most part of Thailand, intravitreal ganciclovir and topical ganciclovir eye drops were used instead of systemic ganciclovir.

Behçet Disease: Treatment options, when should we stop treatment?

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As visually incapacitating disease, Behçet uveitis (BU) warrants a powerful treatment once the diagnosis is made. It has been shown that early and aggressive treatment with either conventional immunosuppressive agents or biologics improves the visual prognosis significantly. The therapeutic decision is made based on the severity of ocular involvement and patient's general health status. Several other factors such as physician's experience, healthcare systems, economic status of the country and the cost of therapy may also influence the therapeutic strategy. Conventional treatment of BU consists of high-dose corticosteroids for the treatment of active intraocular inflammation and immunosuppressive agent(s) for the achievement of sustained remission and prevention of recurrences. Azathioprine and/or cyclosporine and their combination are still used as the first step. The second step of treatment consists of biologics. Interferon-alpha (IFN- α) is the first choice as biologic. In cases refractory to IFN- α , an anti-TNF- α agent, infliximab or adalimumab are considered. Golimumab, another anti-TNF- α agent; rituximab, a monoclonal antibody against CD20; and tocilizumab, an anti-IL-6 receptor antibody are also shown to be effective in few cases. In high-risk patients including acute and bilateral posterior segment involvement, severe macular involvement and severe visual loss at presentation, fast-acting biologics should be considered as first line.

Decision for stopping the treatment is critical and should be taken cautiously. We have to be sure that the disease is inactive. The disease activity should be monitored not only with clinical activity criteria but also with fluorescein angiography and laser flare photometry, if available.

Infectious uveitis you cannot afford to miss – CMV anterior uveitis

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Several cases will be presented and discussed in this talk that highlights the important clinical features of CMV anterior uveitis. In addition, these cases demonstrate the complications that may occur when the viral condition is initially missed and treatment is delayed.

Quality of Life Outcomes from a Randomized Controlled Trial Comparing Methotrexate to Mycophenolate Mofetil for Noninfectious Uveitis

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Purpose: To evaluate the changes in quality of life in uveitis patients treated with two commonly prescribed antimetabolite treatments.

Methods: Secondary analysis of an observer-masked clinical trial (ClinicalTrials.gov NCT01232920). Eighty patients at Aravind Eye Hospitals in Madurai and Coimbatore, India, with noninfectious intermediate, posterior, or panuveitis were randomized to receive oral methotrexate or oral mycophenolate mofetil. Best-corrected visual acuity, INDVFQ, and SF-36 were obtained at enrollment and at 6 months. Changes in quality of life scores were compared using Wilcoxon signed-rank testing. Associations with visual acuity and treatment outcome, as defined by corticosteroid-sparing control of inflammation, were assessed using linear regression models.

Results: IND-VFQ scores, on average, increased by 9.2 points from trial enrollment to 6 months (95% CI: 4.9, 13.5, $P < 0.001$). While the SF-36 physical component summary score did not differ over the course of the trial, the mental component summary score decreased by 2.3 points (95% CI: -4.4, -0.1, $P = 0.04$). The vitality subscale decreased by 3.5 points (95% CI: -5.6, -1.4, $P = 0.001$). Patients that achieved corticosteroid-sparing control of inflammation had an average 4.3 point higher increase in general health scores than patients who did not (95% CI: 0.3, 8.2, $P = 0.04$).

Conclusions: Although uveitis treatment was associated with a significant increase in vision and vision-related quality of life, patient-reported physical health did not change after 6 months of treatment and mental health decreased. Despite improved visual outcomes, uveitis patients receiving systemic immunosuppressive therapy may experience a deterioration in overall health-related quality of life

Therapeutic Potential of Exosomes

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Exosomes are nanometer-sized vesicles (30–100 nm in diameter) that are released by cells upon fusion of multivesicular bodies with the plasma membrane. Consequently, exosomes contain the proteins, lipids, and RNA, including mRNA and miRNA, of their parent cells. Unlike the fate of proteins trafficked for degradation to the lysosomal system, secreted exosomes are biologically active entities, and their biological information can be delivered into the cells which uptake the exosomes. Two major causes of visual disability are age-related macular degeneration (AMD) and autoimmune uveitis (AU). Vascular endothelial growth factor (VEGF) plays an important role in the development of choroidal neovascularization (CNV) and anti-VEGF treatment (such as ranibizumab, bevacizumab, and aflibercept) has been a major advance in the treatment of this complication of AMD. However, 65% of patients do not respond to treatment with improved vision, and regrowth of new vessels suggests that pathogenic factors other than VEGF are involved in the pathogenesis of this complication. Although the clinical presentation of AU is variable, experimental AU (EAU) has been demonstrated to be caused by CD4⁺ Th1 and Th17 cells. We observed that exosomes derived from retinal astrocytes (RACs) or mesenchymal stem cells (MSCs) of normal donors contain multiple anti-angiogenic and anti-inflammatory factors that inhibit the development of both laser-induced choroidal neovascularization (CNV) and EAU, whereas those derived from retinal pigment epithelium (RPE) do not.

Challenges in patients on biologics for systemic associated chronic uveitis

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The management of systemic disease associated chronic uveitis is challenging. Despite good stabilisation of the systemic disease, inflammatory activity in the eye may still occur and persist and may result in development of complications. Biologics have shown to be an effective mode of treatment for this condition. Despite carrying its own risks; where patients must be screened and monitored carefully before and during its use, in many cases, biologics have been the preferred choice of treatment for systemic associated chronic uveitis. However, unfortunately, in developing countries such as South East Asia, biologics are costly and not readily available. In addition to this, in South East Asia where infections are endemic, this tends to be one of the main complications of biologic use thus adding to the obstacles in the management of systemic associated chronic uveitis within this region.