Presumed ocular sarcoidosis presenting with bilateral papilledema and disc haemorrhages

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Introduction:

Ocular Sarcoidosis is part of a multisystem disease of unknown pathogenesis that the ophthalmologist has to develop awarenes of (1,2,3). Although the diagnostic criteria for the eye are well defined (4), these do not manifest in an important percentage of patients (5). The systemic symptoms and investigations require interdisciplinary expert team work but the role of the ophthalmologist must not be underemphasized. Still, neuro-ophthalmic manifestations of the disease or neurosarcoidosis, may present with more complex findings and unresolved visual loss.

Objective:

This report is presented for emphasizing the importance of differential diagnosis of a complicated case of presumed ocular sarcoidosis presenting with optic nerve involvement.

Case report:

The case was a 34 year old man, referred from a primary center for neuro-ophthalmology consultation. He had lost vision in the last 15 days and was prescribed acetazolamide and nepafenac for subretinal serous collection. Subretinal fluid at the macula was then 499/460 µ centrally (Figure 1). The vision was 0.1 and 0.2 Snellen. No anterior chamber cells and flare were noted, but vitreus snowballs and chorioretinal inflammatory foci around the disk were present in both eyes. Fluorescein angiography was not contributing (Fig. 2,3). At the time of referral to the tertiary center after 4 more days, optic disc granulomas were noted and he was investigated for a granulomatous disease. He described upper respiratory tract infection, nausea and weight loss (8 kg in the last 1.5 month). Systemic blood pressure was 130/80 mm Hg. Chest X-ray revealed minimal enlargement of lymph nodes and dilation of the pulmonary artery. Non-contrast thoraxt BT revealed multiple mediastinal lymph nodes (Fig.4). Ecocardiogram was normal. C-ANCA and P-ANCA were both negative, CRP 10.6, sedimentation 33 mm/h, BCG vaccinated, PPD negative (3 mm), blood urea and creatinine were mildly raised. Cranial MR showed two nonspecific foci at centrum semiovale and corona radiata, with mucosal thickening and a retention cyst at maxillary sinus. Ten days after referral, + cells were noted in the anterior chamber of both eyes, with the emergence of subtle choroidal foci nasally, other findings persisting with no visible progression. Although the investigation was not completed, the patient, being a tailor, insisted on starting therapy and he was put on prednisolone 48 mg/day, oral Azythromycine 500/day for 6 days and topical dexamethasone. After one week, the vision increased to 0.7 and 1.0 Snellen in the right and left eyes respectively. Upon all the given data, the patient accepted to have an ICGA which revealed widespread hypofluorescent choroidal nodules on the initial phases that later faded, and became isofluorescent (Fig.5,6,7,8). The patient was convinced to see another pneumologist, the diagnosis was sarcoidosis suspect, he was warned for follow up and completion of the diagnostic tests, which he did not comply with.

After 3 months, the vision was still reserved and steroids were stopped by another consultant. Still the patient was warned for early cessation of steroids and the need for completing other diagnostic tests such as ACE, lysosyme, high resolution chest tomography and lymph node biopsy if necessary. The final examination showed resorption of disc haemorrhages and the subretinal fluid, and the faint visibility of the choroidal nodules (Fig 9,10). Vision was increased to 0.9 and 1.0 Snellen and the Visual fields were full.

Discussion:

Sarcoidosis is a multisystem disease, with the patogenesis obscure. Although the lungs are primarily involved, extrapulmonary sarcoidosis may be seen including the eye (%25-80) and the nervous system. The definitive diagnosis is the noncaseating granuloma of the biopsy specimen (1,2,3). Herbort CP et al presented the IWOS criteria in 2006*, a guide to international standards for diagnosing sarcoidosis based on ocular signs, laboratory findings and biopsy results (4).

Although these criteria are well known and of utmost importance for the diagnosis, Acharya et al (5) showed that % 37 of the patients did not meet the IWOS criteria and a new diagnostic consensus has to be established including new investigational tests. For example, in the diagnostic workup of sarcoidosis, assessment of HLA-DR(+) CD8(+) T cell and natural killer T-cell fractions in the bronchoalveolar lavage has shown to be highly conclusive(6).

Cases presenting with neuro-ophthalmologic findings can easily lead to misdiagnosis and can present with a wide spectrum of manifestations from optic neuritis mimicking other etiologies, to compressive lesions and lymphoma- associated neuro-sarcoidosis (7,8).

To the author’s opinion, the presented case had symptoms and signs complying with the IWOS criteria sufficient to be classified as presumed ocular sarcoidosis: Bilateral hilar adenopathy, negative PPD,

weight loss, bilaterality, optic disc and choroidal granulomas with vitreous pearls; although keratic mutton fat precipitates and vasculitis were lacking. ICG Angiographic findings were consistent with Type I lesions in sarcoidosis (9,10). Positive response to steroids was another clue supporting the diagnosis. The case is presented to emphasize the fact that findings of pulmonary, systemic and ocular signs and symptoms were not evaluated as important diagnostic criteria by the related disciplines putting the pieces of the puzzle together and the patient was directed to the neuro-ophthalmology section for intracranial hypertension due to disk haemorrhages and papilledema. Although this case cannot be accepted as a case of isolated neuro-sarcoidosis, optic nerve involvement in the form of papilledema and optic disc granulomas should alert the physician for a possible diagnosis of sarcoidosis.

Conclusion:

Ocular sarcoidosis may present with extremely complex signs as the eye is concerned and must always be considered as a diagnosis of exlusion. Systemic and ocular signs and symptoms, although prominent in this case, has been ignored by consulting disciplines, and the uveitis specialist has to be the one insistant on arriving at the etiologic diagnosis, thus salvation of the eye; also highlighting the systemic manifestations of the disease.

Literature:

1. Bonfioli AA, Orefice F. Sarcoidosis. Semin Ophthalmol. 2005 Jul-Sep;20(3):177-82.
2. Wu JJ, M.D., and Schif K R: Sarcoidosis, American Family Physician www.aafp.org/afp, 2004, 70 (2) : 312-322
3. Walscheid K, Tappeiner C, Heiligenhaus A. Ocular Manifestations in sarcoidosis Klin Monbl Augenheilkd. 2016 May;233(5):594-600. doi: 10.1055/s-0042-104063. Epub 2016 May 17.
4. Herbort CP, Rao NA, Mochizuki M; members of Scientific Committee of First International Workshop on Ocular Sarcoidosis. International criteria for the diagnosis of ocular sarcoidosis: results of the first International Workshop On Ocular Sarcoidosis (IWOS). Ocul Immunol Inflamm. 2009 May-Jun;17(3):160-9.
5. Acharya NR, Browne EN, Rao N, Mochizuki M; International Ocular Sarcoidosis Working Group Distinguishing Features of Ocular Sarcoidosis in an International Cohort of Uveitis Patients Ophthalmology. 2017, 16. pii: S0161-6420(17):31125-9.
6. Tøndell A, Rø AD, Åsberg A, Børset M, Moen T, Sue-Chu M.: Activated CD8(+) T cells and NKT cells in BAL fluid improve diagnostic accuracy in sarcoidosis. Lung. 2014, 192(1):133-40. doi: 10.1007/s00408-013-9527-8. Epub 2013 Nov 10.
7. Jacob J. Koczman, Jacinthe Rouleau, Morgan Gaunt, Randy H. Kardon, Michael Wall & Andrew G. Lee Neuro-ophthalmic Sarcoidosis: The University of Iowa Experience, Seminars in Ophthalmology ,2008, 23(3).157-168
8. Brandy-García AM, Caminal-Montero L, Fernández-García MS, Saiz Ayala A, Cabezas-Rodríguez I, Morante-Bolado I: Sarcoidosis-lymphoma syndrome. Reumatol Clin. 2016 Nov - Dec;12(6):339-341. doi: 10.1016/j.reuma.2015.11.010. Epub 2015 Dec 23.
9. Herbort CP, LeHoang P, Guex Crosier Y: Schematic interpretation of indocyanine green angiography in posterior uveitis using a standard angiographic protocol,Ophthalmology, 105:3,43-440
10. Wolfensberger T, Herbort CP: Indocyanine green angiographic features in ocular sarcoidosis. Ophthalmology 106:(2) 285-289

Figures:

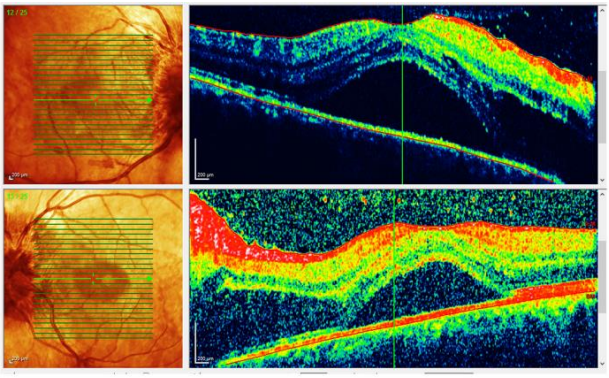

Figure 1- OCT findings on presentation. Subretinal fluid collection

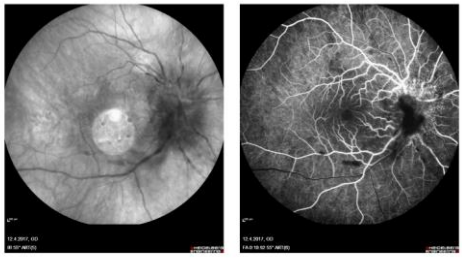

Figure 2- Infrared (IR) and fluorescein angiography (FA) right eye (RE) at presentation. Note haemorrhages and dotty fyperfluorescence on the disc.

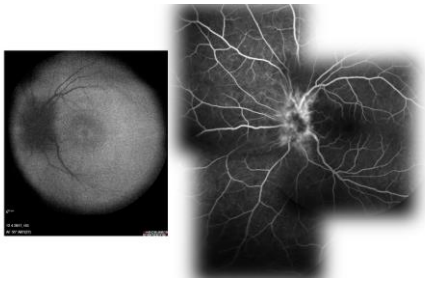

Figure 3- Fundus autoflorescence (FAF) and (IR) and fluorescein angiography (FA) left eye (LE) at presentation

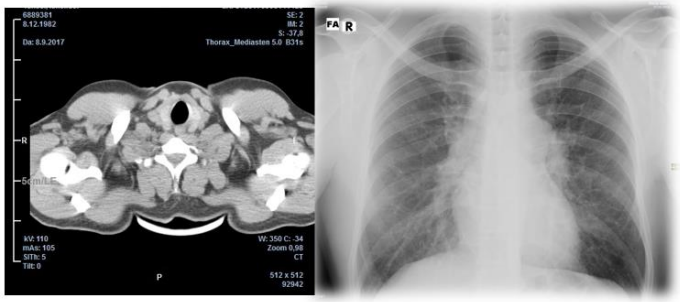

Figure 4- Chest CT and X-ray showing hilar arborization and prominant pulmonary artery with hilar micronodules

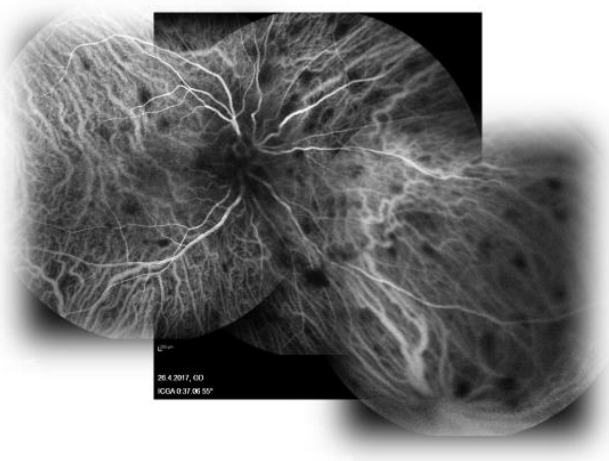

Figure 5- ICGA (RE) findings showing hypofluorescent choroidal involvement in the intermediate phase

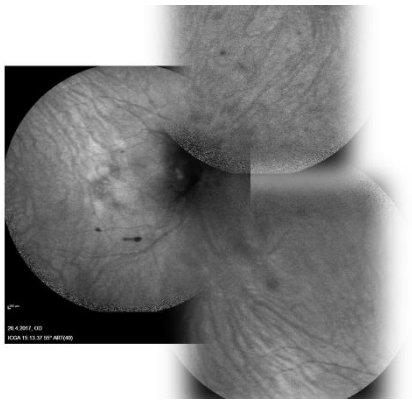

Figure 6- ICGA (RE) late phase. Hypofluorescence has faded, nodules being mostly isofluorescent. Note the haemorrhages still not resolved.

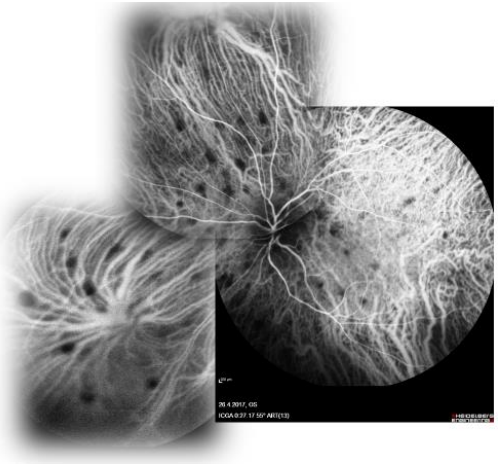

Figure 7- ICGA findings (LE) showing hypofluorescent choroidal involvement in the intermediate phase

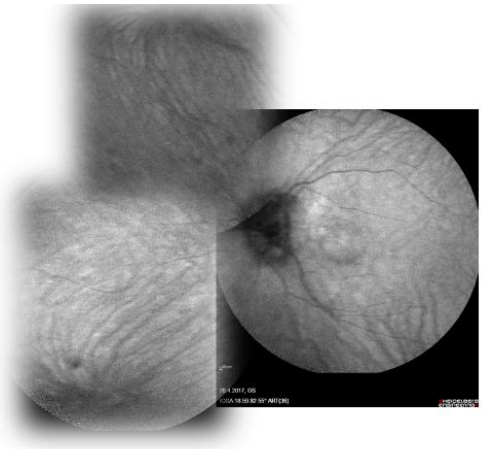

Figure 8- ICGA (LE) late phase. Hypofluorescence has faded, nodules being mostly isofluorescent.

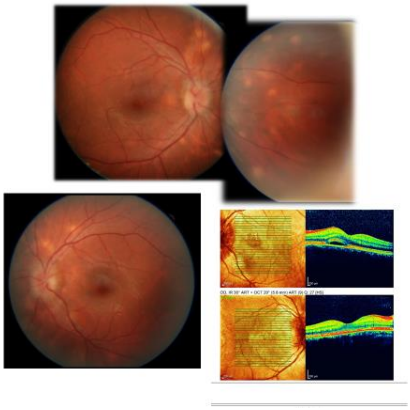

Figure 9- Fundus view after steroid therapy. Haemorrhages and macular fluid collection resolved. Hypopigmented nodules visible nasally on the right eye

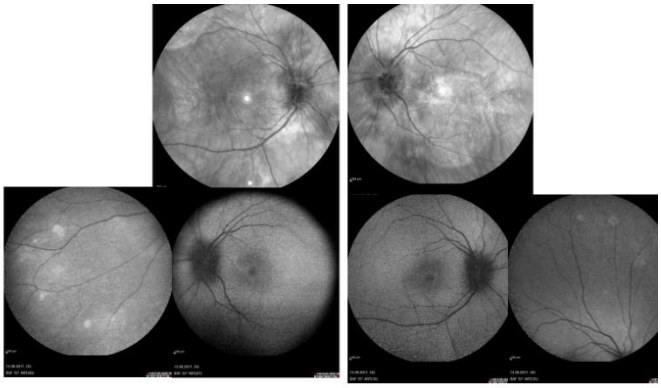

Figure 10- IR and FAF findings after steroid therapy. Mildly hyperfluorescent spots are seen at the midperiphery.