Ocular toxicity of moxifloxacin: case report and review of the literature

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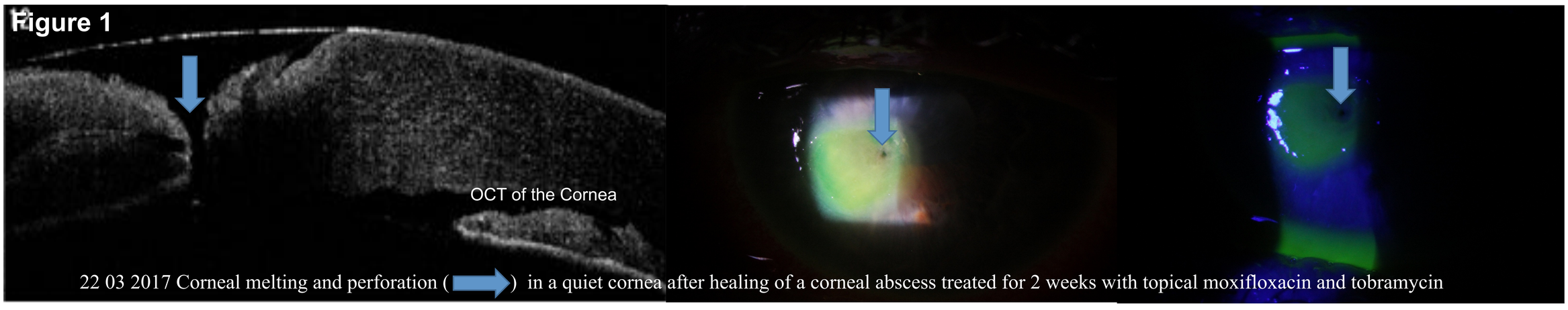
Background: Corneal toxicity of topical moxifloxacin has been reported in a few cases. [1-7] Toxicity of oral moxifloxacin has been reported more frequently. In 2006 bilateral acute depigmentation of the iris (BADI) characterized by an acute onset of pigment depigmentation of the iris was reported by Tugal Tutkun I et al. [8] The release of dispersed pigments from the iris into the aqueous humor is a possible ocular side effect of the systemic administration of Moxifloxacin, named bilateral acute iris transillumination (BAIT). Bilateral acute depigmentation of iris (BADI) is a similar condition, with iris pigment released into the aqueous. It has mostly been reported related to the systemic treatment of FQL and in particular moxifloxacin. [8-11]

Patients & Methods: retrospective case report. A 56 year old healthy patient presented 5 weeks after retinal surgery with a central corneal abscess. No corneal swab was performed. Topical tobramycin 0.3% with preservative + preservative free moxifloxacin 0.5% 1/h + desomedine 1% with preservative 8/d was initiated and tapered 3 days later to 1/h, 5/d and 5/d respectively. Four days later a large erosion (3.5x3.5 mm) appeared while the abscess had disappeared. Topical tobramycin 5/d and moxifloxacin 3/d were continued for 1 more week when the patient was addressed to our clinic with a large corneal melting (3x2 mm) in a clear cornea. The next day the cornea perforated centrally (1x1 mm with Descemet folds, fibrin, anterior cells ++, and, dilated iris vessels and posterior synechiae. Both blood tests and medical history were otherwise unremarkable**.** (Figure 1)



Therapy and Outcome: At presentation to our clinic gentle corneal swab was performed, cultures for bacteria, virus, amoeba or fungi as well as PCR for HSV1, HSV2 and VZV from corneal smear remained negative. Systemic treatment was consequently stopped. Moxifloxacin and tobramycin were discontinued and replaced by preservative free ofloxacin 0.3%1/h tapered quickly, tropicamide 3/d, oral valaciclovir (3g/day), oral levofloxacin 500 mg/d and therapeutic lens. Cornea healed very quickly and the therapeutic lens could already be removed after 3 days. No recurrence of the ulcer has been observed. Six months later, a cataract surgery was performed. Treatment was limited to tobramycin+ dexamethasone with preservative. VA improved to 2/10, slight superficial epithelial toxicity was observed in the nasal and temporal side of the cornea but not in front of the corneal scar. (Figure 2)

Comments:

Corneal toxicity of topical moxifloxacin

Several studies support the toxicity of topical moxifloxacin on corneal healing. Moxifloxacin has been demonstrated to induce an epithelial cell cytotoxicity. [1-3] It has been found to damage epithelial cell tight junctions. [1] Moxifloxacin have also been shown to decrease the production of type IV collagen preventing adherence of corneal epithelial cells to the underlining corneal stroma [1] and to stimulate the expression of metalloproteinases (MMP1,2,8 and 9) which degraded the extracellular matrix of the epithelium and the corneal stroma. [5] Topical fluoroquinolones have also been found to increase the incidence of corneal perforation. [4-6] Topical tobramycin appears to have a very low toxicity. [7] Benzalkonium chloride (BAC) used as a preservative in this patient might have increase the corneal cytotoxicity of moxifloxacin that have both been characterized by high productions of reactive oxygen species. [13] However the topical administration of tobramycin + dexamethasone with preservative (5x/d) used 6 months later, after cataract surgery, was well tolerated by the cornea**.**

Toxicity of systemic moxifloxacin: bilateral acute iris transillumination syndrome (BAIT).

Antibiotics such as fluoroquinolones are commonly used to treat ocular infections. The release of dispersed pigments from the iris into the aqueous humor has been considered to be a possible ocular side effect of the systemic administration of moxifloxacin. This condition mascarading uveitis is known as bilateral acute iris transillumination (BAIT). It is associated with a loss of the iris pigment epithelium and results in iris transillumination, and differs from the previously described bilateral acute depigmentation of the iris (BADI), which is associated with atrophy of the iris stroma without transillumination. [9] In 2010 we previously reported a case moxifloxacin associated with a BAIT Figure 3 and 4.[10] Anterior segment optical coherence tomography (OCT) findings suggest that both the iris stroma and iris pigment epithelium are affected with stromal thinning, iris concavity and posterior synechiae (Figure 4). [11] The exact mechanism of toxicity remains unclear but pharmacokinetic data might help to explain the toxicity of oral moxifloxacin. It was detected in aqueous humor as much as 18 days following the completion of oral treatment. [12] Treatment with corticosteroids for prolonged pigment dispersion after the initial inflammatory phase is likely unnecessary and may contribute to glaucoma in steroid responders. [11]

Conclusions: We report a case of topical toxicity of moxifloxacin leading to acute corneal melting. Such cases have only occasionally been reported and might be related to a toxicity of the extracellular matrix as well as oxidative stress that might be increased by the BAC used with tobramycin. Bilateral acute iris transillumination (BAIT) has been more frequently reported after systemic administration of moxifloxacin. The exact mechanism of toxicity of moxifloxacin is not yet completely elucidated.

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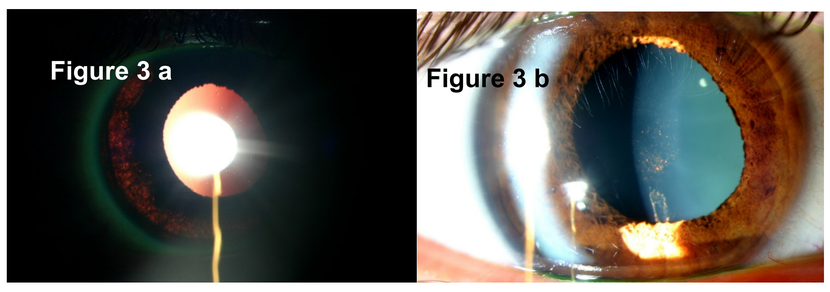

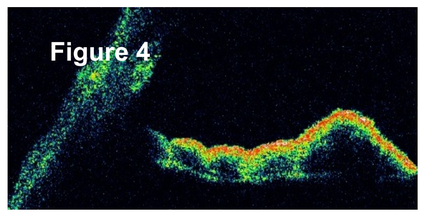

Figure 3 : case bilateral acute iris transillumination (BAIT) 3a : iris transilumination, 3b, iris depigmentation, pupil dilatation ans posterior synechiae, pigment deposits on the lens anterior surface

Figure 4 : OCT of the anterior segment. iris concavity and iris posterior

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