Over-dose Oral Moxifloxacin Related Bilateral Acute Iris Transillumination in a Short Period

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ABSTRACT

We aimed to report a case of bilateral acute iris transillumination and pigment dispersion related to oral moxifloxacin that used a higher dose than recommended. A 43-year-old woman who presented with redness, pain, blurred vision, and high intraocular pressure (IOP) 10 hours after taking six oral moxifloxacin tablets because of pneumonia was referred to our clinic for differential diagnosis. Slit-lamp examination revealed conjunctival hyperemia, endothelial dusting, floating anterior chamber pigments, and diffuse transillumination for both irises. IOP was in the normal range with both topical and systemic antiglaucomatous treatment. The patient experienced several flare-ups within three months, especially in the first month. The pigment cells decreased in both the anterior chamber and trabecular meshwork, however, diffuse transillumination is still continuing in both eyes. Although the relationship between oral fluoroquinolones and uveitis is still controversial, the presented case with severe signs and symptoms shortly after taking high dose oral moxifloxacin supports this relation.

Keywords: Oral fluoroquinolones, oral moxifloxacin, bilateral acute iris transillumination, uveitis

INTRODUCTION

Acute bilateral uveitis and pigment dispersion related to oral moxifloxacin was reported in 2004 for the first time in the literature[1] and several reports came after that.[2-6] In addition, there have been published some retrospective cohort studies and case-control studies to assess the relationship between uveitis and fluoroquinolones.[7-9] However, it has not demonstrated a causal relationship between them. In this paper, we report bilateral acute transillumination of iris (BAIT) related to oral moxifloxacin that used a higher dose than recommended.

CASE

A 43-year-old woman was admitted to an ophthalmology clinic with symptoms that included acute redness, pain, light sensitivity, and blurred vision. She was diagnosed with glaucoma and topical anti-glaucomatous and oral acetazolamide treatments were started. Intravenous mannitol was applied two times and then she was referred to our clinic for differential diagnosis.

In our initial examination, the best-corrected visual acuity was 20/25 for both eyes. The right pupil was round and the left was distorted with no light reaction. Slit-lamp examination revealed conjunctival hyperemia, endothelial dusting, and floating anterior chamber pigment (+4 right, +2 left eye) with no inflammatory cells. There is also diffuse transillumination defect for both irises. Gonioscopy revealed that there was heavy pigment deposition in the trabecular meshwork bilaterally. Intraocular pressure (IOP) was measured 10 mmHg in her right eye and 12 mmHg in her left eye under topical and systemic antiglaucomatous treatment. Fundus examination revealed a C/D ratio of 0.3 in both eyes.

Medical history revealed that she was taking oral moxifloxacin because of pneumonia. The patient mistakenly took a higher dose of moxifloxacin than recommended (one pill every hour, six times in the same day). She went to the emergency room because of dizziness and nausea within four hours after taking six pills.

The results of routine laboratory evaluation were in reference ranges. In the present case, it was thought that this might be moxifloxacin-related uveitis-like syndrome. Topical prednisolone acetate was initiated and the patient was called for follow-up closely.

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She applied to different hospitals with high IOP several times within three months, especially in the first month. The C/D ratio increased to 0.3 and 0.5 in the right and left eye, respectively.

In control visits, the pigment cells decreased in both the anterior chamber and the trabecular meshwork, however, diffuse transillumination was still continuing in both eyes (Figure 1 a-f). Optical coherence tomography shows the thinning of the retina nerve fiber layer in the superior and inferior quadrant in her right eye. There was not detected any functional loss in the visual field. Ultrasound biomicroscopy shows thinning and concavity of the iris (Figure 2).

Topical antiglaucomatous and steroid treatment was tapered slowly. The patient has been followed for eight months and there have been no flare-ups for the last five months. However, she has continued to experience extreme light sensitivity.

DISCUSSION

Besides some of the inflammatory and non-inflammatory syndromes like viral iridocyclitis, Fuchs's uveitis, Horner syndrome, and pigment dispersion syndrome, bilateral acute depigmentation of iris (BADI) and BAIT may cause atrophy or depigmentation of the iris.[10,11] Both of them have common features like acute onset, severe photophobia, bilaterality and floating pigments in the anterior chamber, however, BAIT seems more severe than BADI.

There are some case reports of uveitis/BAIT related to fluoroquinolones especially moxifloxacin. In most cases, there are floating pigment cells, transillumination, and pupillary changes rather than inflammatory uveitis. However, the exact mechanism of this condition has not been revealed yet. The phototoxic effect of fluoroquinolones may play a role in the pathogenesis of iris atrophy.[9,12] Fluoroquinolones have high tissue affinity especially for

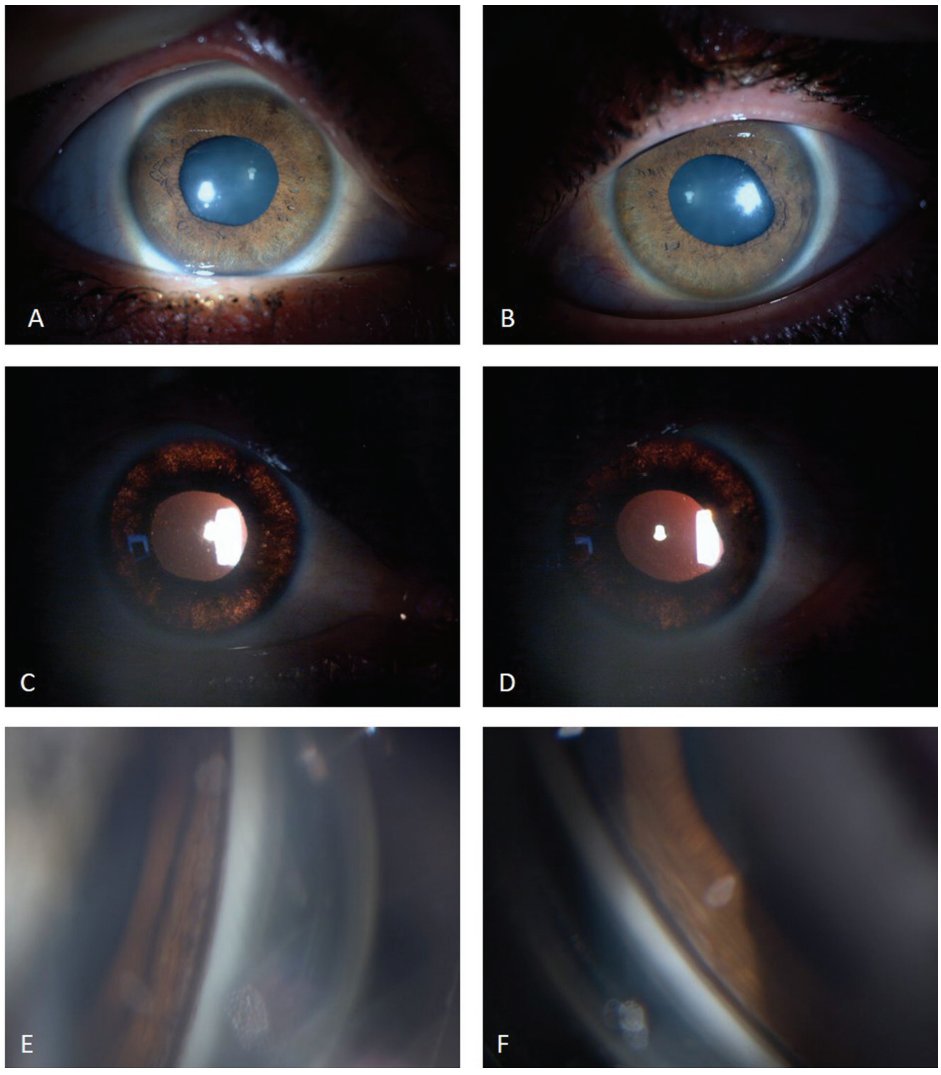

Figure 1. *Color photograph of the right eye (A) and left eye (B) shows diffuse iris atrophy and mid-dilated and distorted pupils. Diffuse iris transillumination is also significant in both eyes (C and D). Gonioscopic photograph of right angle (E) and left angle (F) shows pigmentation of the trabecular meshwork.*

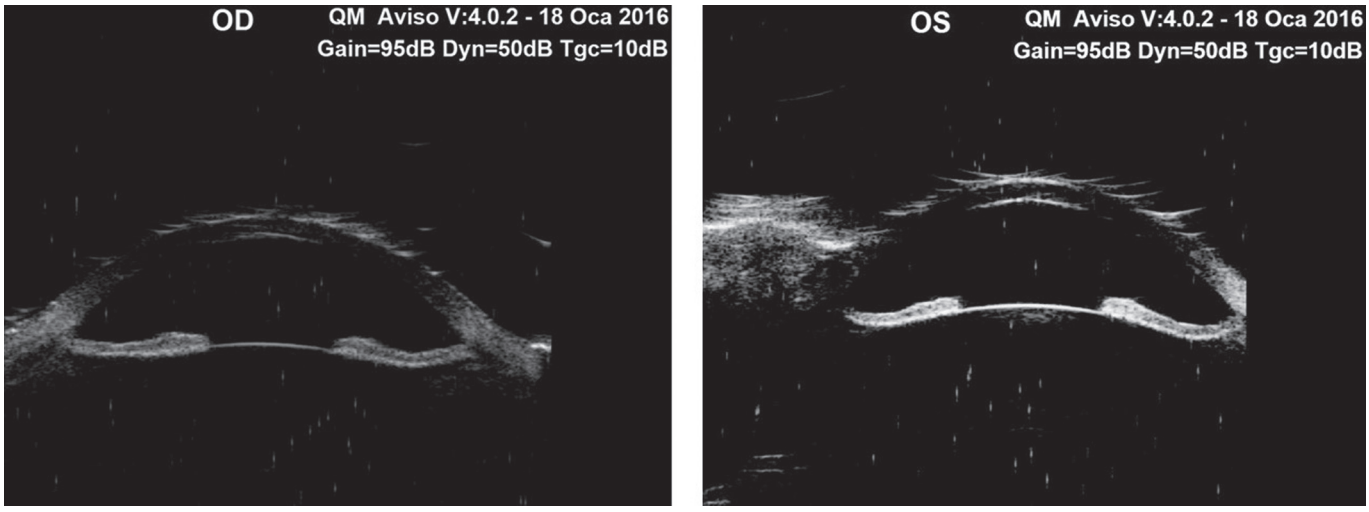

Figure 2. *Ultrasound biomicroscopy shows thinning and concavity of the iris.*

melanin-containing structures like meninges, skin, and eyes.[12] However, none of the reported uveitis cases had concurrent skin toxicity.

Tugal-Tutkun et al.[10] thought that a viral infection may trigger this condition, because, in their case series of BAIT, 35% of patients had been treated with moxifloxacin but 73% of the patients had antecedent respiratory illness. Besides, they argued that this complication has never been reported following topical, intracameral, and intravitreal moxifloxacin. Knape et al.[6] explained this by the pharmacokinetics of moxifloxacin, as its concentration in the vitreous does not reach aqueous levels after topical administration.[13] Additionally; it is known that systemic cidofovir treatment causes uveitis more frequently than intravitreal treatment. Knape et al.[6] proposed that it may be due to the more rapid clearance of drug via intravitreal administration than recirculating systemic way. Consequently, they argued that the serum and vitreous drug levels may remain steady during oral administration than both topical and intravitreal application.

Hinkle et al.[2] collected the data about fluoroquinolone-related uveitis from post-marketing surveillance systems and literature and added their own cases. They concluded that there was a possible relationship between fluoroquinolone treatment and uveitis according to the World Health Organization's causality assessment of suspected adverse drug reactions.

Two case-control studies and a cohort study were done to determine the risk of uveitis associated with the use of fluoroquinolones. Forooghian et al.[8] found that there is an increased risk of uveitis with not only fluoroquinolones but also oral macrolides and beta-lactams in their nested case-control study. Therefore, they thought the systemic illness requiring antibiotic therapy may cause uveitis rather than antibiotic itself. Another pharmacoepidemiologic case-control study found that oral moxifloxacin is associated with uveitis. Also ciprofloxacin may be related to this complication.[7] After these papers, a cohort study that did not find any association between oral fluoroquinolone and uveitis was published.[9] Despite the fact that these studies have some strong features like large sample size and long follow-up period, they also have some limitations like location of data collection. All the studies were retrospective and based on an administrative database. The diagnoses were made based on ICD-9 codes that do not have a specific code for BAIT. Also, it is impossible to say if the patients took prescriptions in the correct way.

Taking into account all of the case reports and studies, oral fluoroquinolones, especially moxifloxacin, appear to have a relationship with uveitis and pigment dispersion. In our opinion, this case is quite important to support this relationship, because it showed that taking a high dose of moxifloxacin caused severe signs and symptoms within a short period.

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