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Secondary glaucoma induced by bilateral acute depigmentation of the iris

Glaucoma secundário à despigmentação bilateral aguda da íris

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Abstract

We report a case of a middle-aged woman who developed acute, bilateral, symmetrical, slightly transilluminating depigmentation of the iris and pigment discharge into the anterior chamber following the use of oral moxifloxacin for bacterial sinusitis. She had been misdiagnosed as having autoimmune uveitis, treated with steroids and tropicamide, and underwent severe ocular hypertension and glaucoma despite posterior correct diagnosis.

Keywords: *Iris diseases/diagnosis; Pigment epithelium of eye/pathology; Transillumination; Iridocyclitis/diagnosis; Diagnosis, differential; Anti-bacterial agents/adverse effects; Case reports*

Resumo

Relato de um caso de uma paciente do sexo feminino de meia idade que desenvolveu despigmentação bilateral simultânea aguda com dispersão de pigmentos na câmara anterior e discreta transiluminação após o uso de moxifloxacino oral para tratamento de sinusite bacteriana. Ela Havia sido diagnosticada com uveite autoimune e tratada com corticosteroide tópico e tropicamida e evoluiu com hipertensão ocular grave e glaucoma apesar de ,posteriormente, o diagnóstico ter sido correto .

Descritores: Doenças da íris/diagnóstico; Epitélio pigmentado ocular/patologia; Transiluminação; Iridociclite/diagnóstico; Diagnóstico diferencial; Antibacterianos/efeitos adversos; Relatos de casos

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Introduction

Bilateral acute depigmentation of the iris (BADI) and bilateral acute iris transillumination (BAIT) are recently described rare entities characterized by acute onset of pigment dispersion in the anterior chamber, depigmentation of the iris, and heavy pigment deposition in the anterior chamber angle.[1-5] Involvement is always bilateral, simultaneous, and associated with acute severe photophobia, ocular discomfort or pain and red eyes. Clogging of the trabecular meshwork with pigment may cause an acute rise of intraocular pressure (IOP).[1-3] In BADI depigmentation comes from the iris stroma,[1-3] whereas in BAIT it comes from the iris epithelium and is associated with acute iris transillumination defect.[4,5]

The exact etiology of both BADI and BAIT remains unclear; several publications have reported a relationship between BADI and flulike syndrome, herpes virus infection, upper respiratory tract infections,[1-3] and BAIT with a toxic effect of fumigation therapy[4] and systemic antibiotics such as cefazolin,[6] ampicillin/sulbactam, amoxicillin/ clavulanate, trimethoprim/ sulfamethoxazole, cefixime, and penicillin[4-7], and finally with moxifloxacin.[8-10]

We report a case of a middle-aged woman who developed bilateral iris depigmentation severe ocular hypertension and secondary glaucoma following the use of oral moxifloxacin for sinus infection treatment.

Case Report

A 40-year-old woman presented to Ocular Diagnosis and Treatment Institute (IDTO) Rio de Janeiro, Brazil, in June 2014 for a second opinion on the indication for tube shunt implant due to severe ocular hypertension unresponsive to antiglaucomatous medical therapy. She had been to many ophthalmologists on the past weeks and had no definite diagnosis. The last uveitis specialist she visited diagnosed her as having an autoimmune iridocyclitis and kept her on oral methotrexate use, topical steroids (1% prednisolone) four times a day (QID), tropicamide three times a day (TID) and topical antiglaucomatous treatment including 2% dorzolamide and 0.5% timolol association BID, 0.1% brimonidine twice a day (BID), and oral acetazolamide 750 mg/day. She has had Nd:YAG laser peripheral iridotomies (LPIs) performed in both eyes (OU) a few weeks previous to IDTO visit.

The patient had undergone a complete laboratory evaluation for uveitis that were unremarkable. She had no family history of glaucoma.

She reported an upper respiratory viral infection followed by a sinus infection initially treated with a 10 day course of oral amoxicillin followed by 14 days of oral moxifloxacin. One day after she completed moxifloxacin course she had acute onset of bilateral and simultaneous ocular pain, red eye, and severe photophobia. She went to the ophthalmologist who prescribed topical steroids and mydriatrics. She started her intraocular pressure (IOP) was normal until the end of the second week after the initial symptoms. After that, intraocular pressure raised up to 60 mmHg.

During our first exam her best-corrected visual acuity (BCVA) was 20/25 with +1.50 spherical correction OU. Examination revealed mild epithelium cornea edema, significant 3+/4+ fine pigments in the anterior chamber (AC) of right eye (OD) and 2+/4+ in left eye (OS). Her lens were clear, the AC was deep and there were no cells or keratic precipitates (KPs).

The pupil was mydriatic and irregular with posterior synechia OU (Figure 1 A and 1B), very slight central iris transillumination OU and pervious peripheral iridotomies OU. The iris had a peculiar loss of normal corrugated texture.

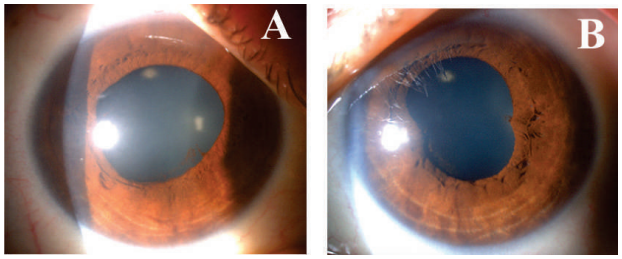

Figure 1: Biomicroscopy of right eye (A) and left eye (B) showing loss of normal corrugated iris texture, midryasis and posterior synechia.

Gonioscopy revealed a wide-open angle and a heavy pigment deposition at the trabecular meshwork 360 degrees (Figures 2A and 2B). Vitreous was clear, fundus was normal and the optic nerve head cup-disc ratio was 0.3 bilaterally. Her visual field and optic nerve Heidelberg Retina Tomograph (HRT) done 2 weeks before our first visit were within normal limits.

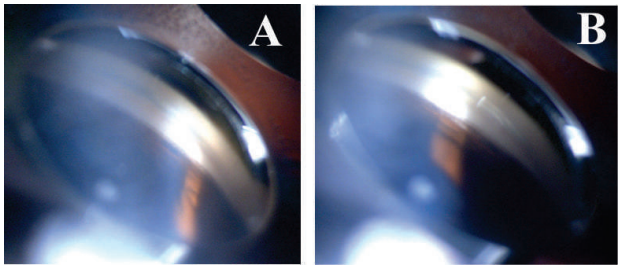

Figure 2: Gonioscopy of right eye (A) and left eye (B) demonstrating clogging of pigment in the anterior chamber angle.

Intraocular pressure was 55 mmHg in OU despite the use of topical and oral antiglaucomatous medications described above. The absence of cells and KPs, extremely high IOP and the sudden bilateral simultaneous symptoms following oral moxifloxacin led us to a research through scientific literature and the diagnosis of either bilateral acute depigmentation of the iris (BADI) or bilateral acute iris transillumination (BAIT) syndrome was considered.

Methotrexate and tropicamide were discontinued, 0,1% brimonidine was increased to TID, oral acetazolamide to 1g per day, and 2% dorzolamide and 0.5% timolol association BID were continued and bimatoprost was added. Topical prednisolone 1% was weekly tapered and completely discontinued after 4 weeks. Ten days after initial visit her IOP came down to 20 mmHg OU.

Despite the prompt IOP response to our treatment, she had been under extremely high IOP for 5 weeks before we saw her first and therefore her cup-to-disk ratio increased from 0.3 OU to 0.7 OD and to 0.5 OS, typical glaucomatous changes were observed in visual field, specially on OD (Figure 3A and B) and optical coherence tomography (OCT) of the right eye compared to her previous exams. (Figure 4)

Both pigment dispersion and IOP gradually decreased throughout the second, third and following months, systemic acetazolamide was discontinued and topical hypotensive medications were reduced.

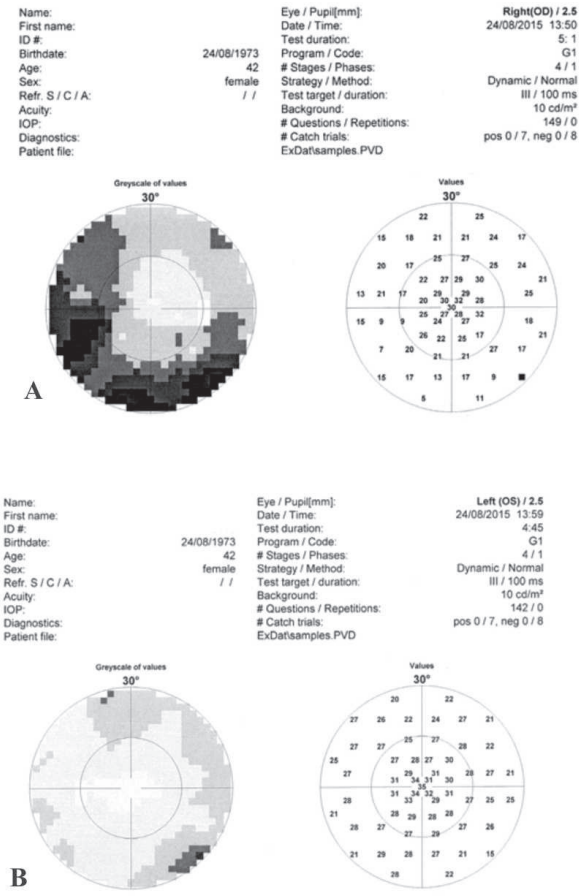

Figure 3: Campimetry with arcuate scotoma in the right eye (A) and mild nasal peripheral loss in the left eye (B)

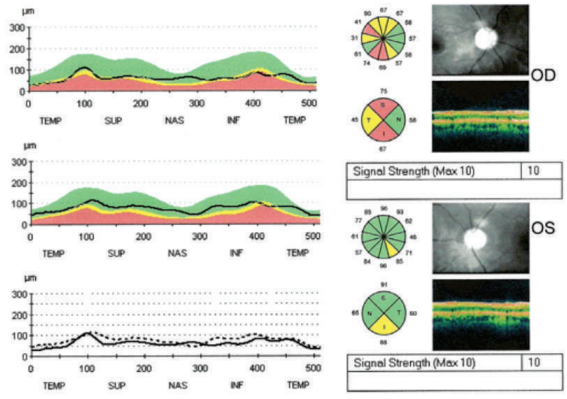

Figure 4: Coeherence computerized tomography of optic nerve OU demonstrating loss of nerve fiber layer specially in the right eye.

On her last visit, 2 and a half years after her initial presentation her anterior chamber angle were still pigmented, BCVA was 20/20 OU, pupils had normal sizes except for a slight posterior synechia and very slight iris transillumination OU and IOP was 15 mmHg OU. She was kept on 0.1% BAK-free brimonidine.

Discussion

Bilateral acute depigmentation of the iris (BADI) was first described by Tugal-Tutkun I in 2006 and by the end of 2009 twenty-eight cases had been reported in Turkey.[1,2]

Bilateral acute iris transillumination (BAIT) was then described in 2011 as being a new clinical entity that share main features with BADI: an acute onset of bilateral simultaneous severe photophobia and red eyes after a flulike syndrome, pigment dispersion into the anterior chamber, and pigment deposition in the AC angle, exclusive involvement of the iris, self-limited course and young women are more commonly affected.[1-7]

However, in BAIT depigmentation is from the iris epithelium leading to iris transillumination defects, posterior synechia and mydriatic/atonic pupil.[4-7] BADI has a more benign course, a shorter duration of pigment discharge and lower incidence of elevated intraocular pressure (IOP).[1-3] BAIT has been reported following systemic antibiotics such as fluoroquinolones use and is associated with an early, severely elevated IOP. A few cases of BAIT might even need a trabeculectomy to control an intractably elevated IOP. The iris changes are usually irreversible.[4-7]

Duncombe recently published a case of BAIT in France and the authors reported as severe pseudouveitis associated with moxifloxacin therapy.[8] Previous reports have noted fluoroquinolone-associated uveitis with oral fluoroquinolones not with the topical use of the drug. [5-7,9,10]

Pharmacokinetic data may explain why topical administration has not been associated with this clinical presentation. After topical administration, there is a greater-than-tenfold higher concentration of moxifloxacin in aqueous (2.28 ± 1.23 µg/mL) than in vitreous (0.11 ± 0.05 µg/mL)[11] whereas oral administration produces similar aqueous (1.34 ± 0.66 µg/mL) and vitreous concentrations (1.58 ± 0.80 µg/mL).[11,12]

The steady serum and vitreous reservoirs of moxifloxacin during oral administration may maintain drug levels in the tissue at risk better than intermittent topical therapy.[11-13]

The lens status of affected patients may also be relevant. Only phakic patients have been reported with fluoroquinolone-associated depigmentation. Less drug diffuses posteriorly in phakic eyes, and posterior-to-anterior clearance may also be impaired in phakic eyes.[11-14] Trapping of drug in the posterior chamber by synechia between an intact lens and the iris, may result in higher drug concentrations adjacent to the iris epithelium.[13] This may explain why BAIT is more commonly associated with moxifloxacin use compared with BADI.

Our main hypothesis in the present case was of BAIT triggered either by the use of systemic moxifloxacin or by viral upper respiratory tract infection. Her clinical findings of posterior synechia, mydriatic pupilla and severe unresponsive high IOP is expected for BAIT not for BADI. However she did not have significant iris transillumination as would be expected for BAIT and her pupil and most of her iris changes were slowly being reversible which would be expected for BADI and not for BAIT. UBM showed iris stromal thinning, which is typical in BADI patients.

Whether our patient had BADI or BAIT is not totally clear yet but this is the first case reported in Brazil of secondary glaucoma due to bilateral acute depigmentation following oral moxifloxacin. The fact that both BADI and BAIT share so many features gives strong support to the idea they are subtypes of the same disease rather than distinct entities.

The main differential diagnosis of BADI and BAIT are iridocyclitis[15,16] and pigment dispersion syndrome.[17] Ocular findings that helped us differentiate BADI from acute iridocyclitis included diffuse episcleral injection that was more pronounced than ciliary injection, presence of pigments but not inflammatory cells in the aqueous humor, heavy pigment deposition in the trabecular meshwork, and loss of normal corrugated iris texture. Tugal-Tutkun reported 52 patients so far and even in eyes with very high flare readings no inflammatory cells or KPs were observed. Except by heavy AC pigment dispersion, no other characteristic features of pigment dispersion syndrome was observed in the present case, including pigment deposition on the surface of the lens, zonules, iris stroma, and along Weigert's ligament, iris concavity, or slit-like, radial, midperipheral transillumination defect or myopia.[16]

Glaucomatous changes were observed one month after our first exam and remained stable until the patient's last visit. We decided not to do any glaucomatous surgery despite these changes because the IOP rapidly reduced within normal limits after discontinuation of tropicamide, addition of bimatoprost and steroid tapering. The main cause of the uncontrolled IOP was the heavy pigment clogging and intraocular pressure would improve as the load of pigment in the trabecular meshwork subsides.

Bilateral depigmentation secondary to BADI and BAIT are self –limited. Therefore treatment with tropicamide and corticosteroids for prolonged pigment dispersion in BADI and BAIT is unnecessary and may contribute to more pigment dispersion and glaucoma in steroid responders. Prostaglandin analogues may be necessary along with the other topical antiglaucomatous medications to control IOP and prevent secondary glaucoma.

The etiopathogenesis of BADI and BAIT remains to be elucidated. They probably have been under diagnosed and misdiagnosed as iridocyclitis, as it had previously occurred with our patient. An increased awareness of BADI and BAIT among worldwide ophthalmologists might result in the report of many new cases from different institutions as it occurred in Turkey. The increasing use of moxifloxacin as one of the first line choices of antibiotic for respiratory infections also has to be considered and physicians treating these patients should also be aware of the occurrence of this rare but severe adverse reaction of the drug so that depigmentation may be quickly recognized and managed.

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