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Case Report

Bilateral Acute Iris Transillumination Syndrome after Topical Moxifloxacin/ Dexamethasone Initially Misdiagnosed as Uveitis: Case Report

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Keywords
Bilateral cute iris transillumination syndrome · Iris transillumination · Moxifloxacin/ dexamethasone · Pigment dispersion · Atonic pupil

Abstract
Bilateral acute iris transillumination (BAIT) syndrome is a rare condition of unknown etiology, characterized by acute onset of pigment dispersion in the anterior chamber, depigmentation of the iris, and heavy pigment deposition in the anterior chamber angle, with bilateral involvement in most cases. We present a case of a 46-year-old healthy woman, who developed BAIT in both eyes, following the use of topical moxifloxacin/dexamethasone for bilateral bacterial conjunctivitis, followed by a nonarteritic anterior ischemic optic neuropathy in the left eye.

Introduction

Bilateral acute iris transillumination (BAIT) is a rare condition characterized by bilateral acute loss of the iris pigment epithelium, pigment dispersion in the anterior chamber, severe iris transillumination defect, mydriatic atonic pupil, and occasional increased intraocular pressure (IOP) [1]. The etiology of this condition is unclear; however, an association with the use of antibiotics – in special systemic moxifloxacin – and/or viral illness has been proposed [2]. We report a case of a middle-aged woman who developed BAIT after using topical

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moxifloxacin/dexamethasone for a bacterial conjunctivitis in both eyes (OU), evolving to nonarteritic anterior ischemic optic neuropathy in the left eye (OS).

Case Report

A 46-year-old healthy woman of Turkish ancestry was referred to our clinic for a second opinion. She had a history of seeking emergency assistance in another hospital 1 month before with redness, purulent discharge, and discomfort in her OS, with contralateral involvement after 4 days. At this time, she was diagnosed with bilateral bacterial conjunctivitis, being aggressively treated with topical 0.5% moxifloxacin/0.1% dexamethasone every 2 h, for a week.

Three weeks later, she developed ocular hypertension, ocular pain, severe photophobia, mild hyperemia, and decreased vision in her OS, being diagnosed with autoimmune hypertensive uveitis in both eyes. For this reason, treatment with topical prednisolone acetate 1% every 2 h, atropine 1% twice-daily, topical carbonic anhydrase inhibitor/β-blocker combination, and oral steroids (1 mg/kg/day, tapered during 3 weeks) was prescribed, with no improvement of the symptoms. Past family and personal ocular history were negative, including for glaucoma.

During our initial examination, her best correct visual acuity was 20/25 in the right eye (OD) and 20/200 in OS, with normal color vision. Slit-lamp revealed severe pigment dispersion in the anterior chamber, iris transillumination defect, and mydriatic atonic pupils OU (Fig. 1). There were no inflammatory keratic precipitates and no inflammatory cells in the anterior chamber. Corneal sensibility was normal, with no hypoesthesia. Gonioscopy revealed wide-open angles (Shaffer IV), heavy pigment deposition in the trabecular meshwork, and no appearance of posterior iris bowing and/or peripheral anterior synechiae in OU (Fig. 2).

Even though she was not using steroids anymore, her IOP was 30 mm Hg in OD and 45 mm Hg in OS, despite the use of topical and oral antiglaucomatous medications described above. Fundus examination revealed tilted discs and increased cup-disc ratio in OU. In the OS, an edematous optic nerve, associated with peripapillary retinal hemorrhage, suggestive of nonarteritic optic neuropathy (NAION) was noticed (Fig. 3), and confirmed by optical coherence tomography, and high-frequency B-scan-ultrasonography. Fluorescein angiography did not show any signs of inflammation.

A routine laboratory workup was performed including complete blood cell count, erythrocyte sedimentation rate (11 mm/h), infectious – including VDRL, FTA-ABS, herpes simplex virus and cytomegalovirus serology – and inflammatory tests, quantiFERON-TB gold test, homocysteine, anticardiolipin antibody, lupus anticoagulant, antinuclear antibody, human leukocyte antigen-B27 (HLA-B27), all with negative results. Chest, orbit, and brain magnetic resonance imaging, as well as magnetic resonance angiography were unremarkable.

Since ocular hypertension persisted despite maximal medical therapy, and as the patient was not using any more steroids, a tube shunt was implanted in OU 3 weeks after her first appointment with us. After the procedure, the IOP gradually decreased, hence, topical hypotensive medications were reduced. Anterior chamber pigment was also significantly reduced in the second postoperative week.

After 6 months of follow-up, best correct visual acuity was still 20/25 in OD and 20/200 in OS. IOP was 12 mm Hg OU with topical use of carbonic anhydrase inhibitor/beta-blocker twice a day. Pigment dispersion in the anterior chamber resolved in OU, and optical coherence tomography of retinal nerve fiber layer showed a localized temporal inferior defect in the OD

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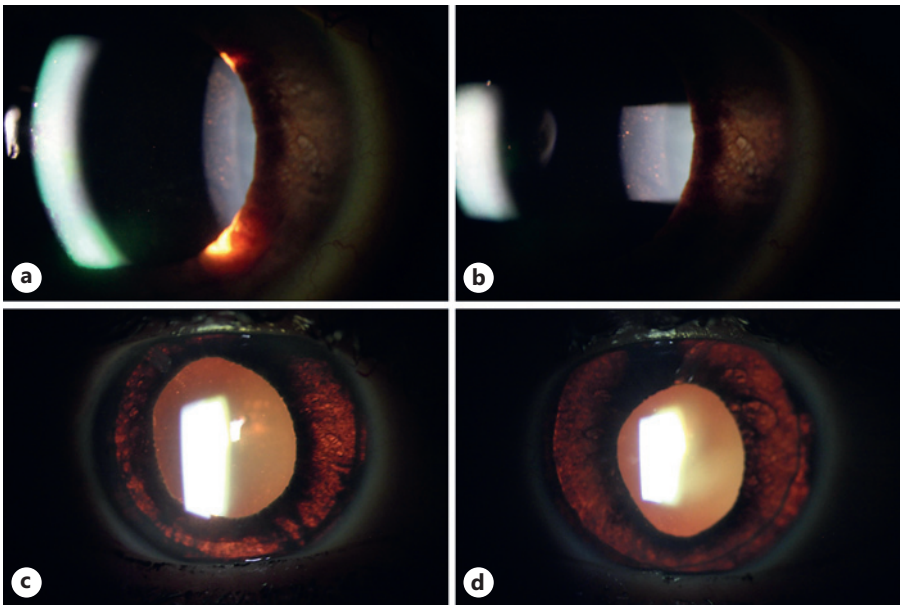

Fig. 1. Slit-lamp photograph of the right (**a**) and left (**b**) eyes showing intense pigment dispersion in the anterior chamber, a typical picture of BAIT syndrome. Iris transillumination and pupil deformation with associated mydriasis of the right (**c**) and left (**d**) eyes. The photographs were taken without pharmacological dilatation of the pupils.

and a diffuse loss in the OS (Fig. 4). Visual field tests revealed a superior paracentral scotoma in the OD and a diffuse reduction in sensitivity in the OS. The presence of bilateral iris atrophy, heavy pigment dispersion in the anterior chamber and trabecular meshwork, in the absence of inflammatory cells and keratic precipitates, associated with high IOP, with no improvement with maximum medical therapy, in a patient with history of using topical moxifloxacin/dexamethasone drops led us to the diagnosis of BAIT syndrome.

Discussion

BAIT syndrome is a relatively new entity, first described in 2004 by Bringas Calvo [3]. It is characterized by acute and diffuse bilateral transillumination defects, pigment dispersion (which leads to pigment deposition in the anterior chamber angle and in the corneal endothelium), variable pupillary sphincter paralysis and distortion (usually presenting with persistent mydriasis), and occasional increased IOP [4]. Another condition in the same spectrum of this disease is BADI syndrome, considered less severe, in which only atrophy and depigmentation of the iris stroma occur – while BAIT is characterized by loss of iris pigment epithelium, leading to iris transillumination.

Its exact etiology remains unknown. Several studies reported associations between this condition and prior antibiotic therapy, most frequently with systemic fluoroquinolones – particularly moxifloxacin [4–7]. Fluoroquinolones are a large group of broad-spectrum bactericidal, which act by blocking replication and transcription of bacterial DNA by inhibiting DNA gyrase and topoisomerase II and IV. They are indicated for a large number of bacterial conditions, including pulmonary, urinary, and digestive infections. In ophthalmology, they are frequently used in topical form – as drops, ointments, or even as anterior chamber injections, in the treatment of ocular surface conditions or prophylaxis for endophthalmitis,

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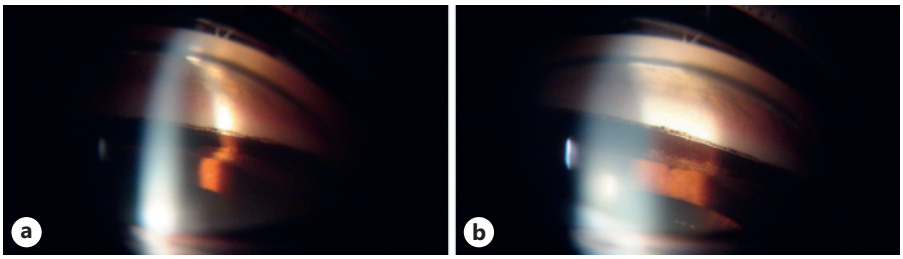

Fig. 2. Gonioscopy of the right (**a**) and left (**b**) angles showing heavy trabecular meshwork pigmentation.

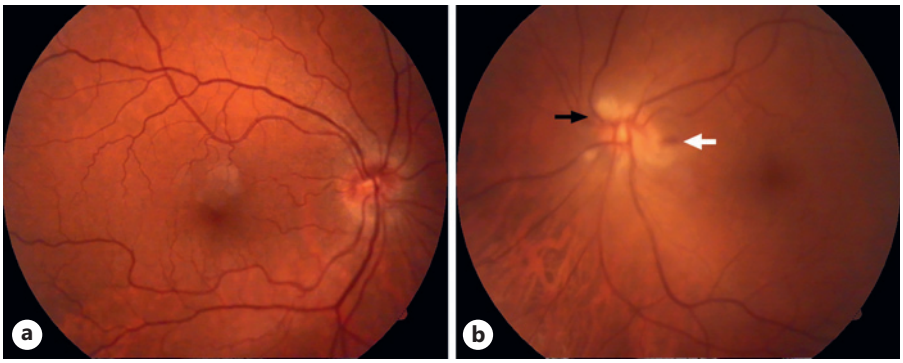

Fig. 3. Fundus photographs of the right (**a**) and left (**b**) eyes showing optic disc edema (white arrow) with peripapillary retinal haemorrhage (black arrow) in the left eye.

and postoperative infection [8]. Although it is known that quinolone can cause dermal melanocytic toxicity [9, 10], the exact mechanisms by which moxifloxacin can lead to BAIT syndrome have not been fully understood. Some authors evoke that this drug has an affinity for ocular and meningeal structures containing melanin, which could induce phototoxicity of the iris pigment in sensitized patients [4]. The pigment is liberated from the iris pigment epithelium, and may deposit on the surface of the lens, iris stroma, the zonules, and along Wiegert's ligament.

At first, BAIT syndrome was usually described as a bilateral condition in patients with a history of systemic moxifloxacin administration. More recently, cases of unilateral BAIT were described in patients who underwent intraoperative intracameral moxifloxacin for endophthalmitis prevention [11–14]. BAIT syndrome after the use of topical moxifloxacin, such as in our cases, is rarer. Kawali [15] published a review of 22 patients (31 eyes of 17 patients with BADI and 10 eyes of 5 patients with BAIT) in which 17 of them had a history of topical fluoroquinolone before the onset of symptoms. Another study proved that topical moxifloxacin could cause toxicity to iris melanocytes [16]. The use of clarithromycin in the days preceding ophthalmic symptoms [17], fumigation therapy [1], and mostly upper respiratory tract infections [4, 18] have also been described as possible etiologies for this condition.

Regarding epidemiology, Perone [4] performed a literature review showing that 91% of the cases with BAIT were described in Europe (mainly Turkey – our patient's ancestry – Greece and Belgium), 75% were women, the mean age was 46 ± 9 years, and 69% of them had an upper respiratory infection in the days or weeks preceding the BAIT syndrome – 81% of them treated with oral or parenteral antibiotherapy, mainly moxifloxacin. Furthermore,

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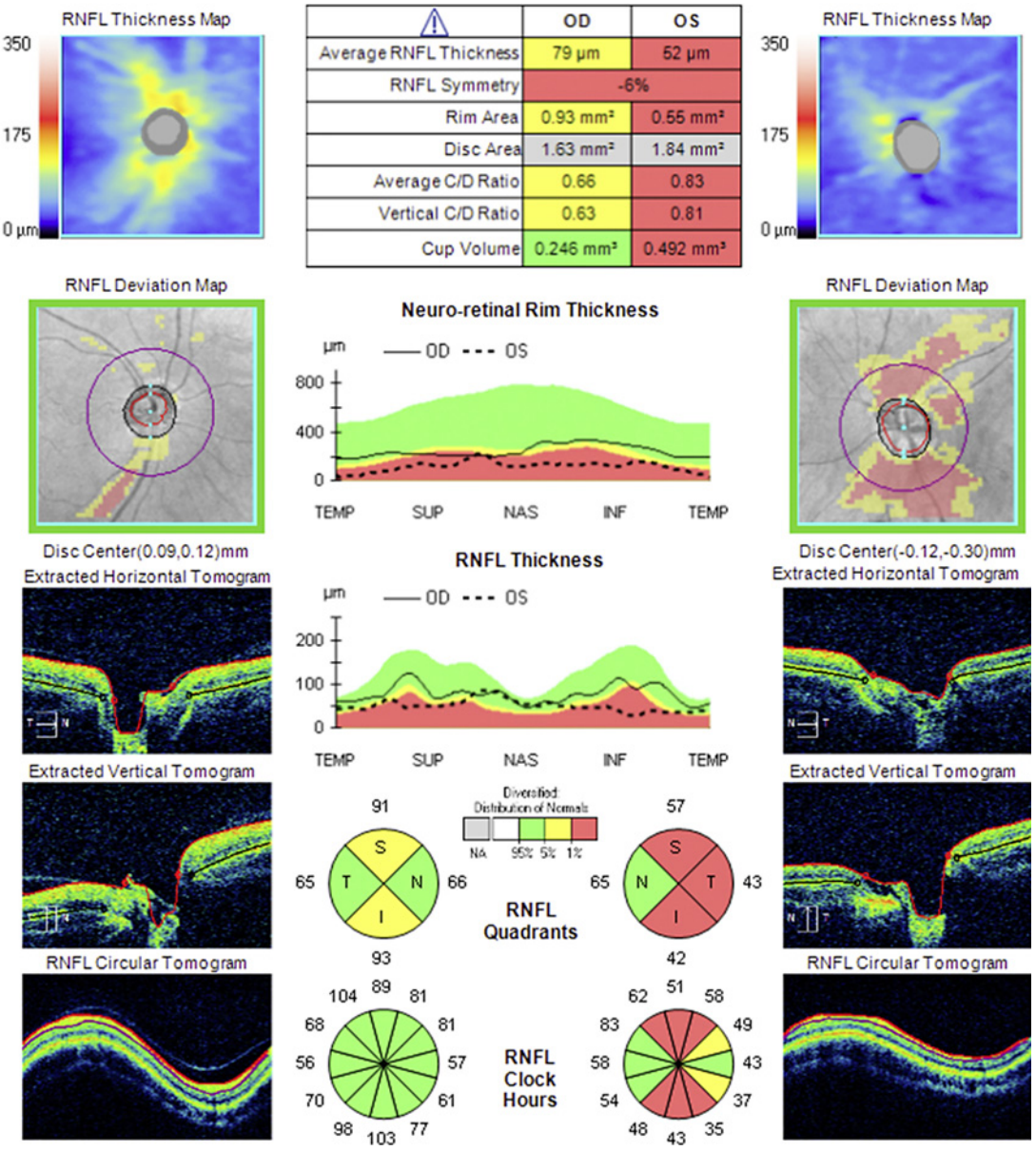

Fig. 4. Optic nerve OCT of both eyes, demonstrating loss of the retina nerve fiber layer, especially in the left eye, as it can be noticed in the graphs on this report.

according to the European Center for Disease Prevention and Control, Belgium is the leading European country in terms of moxifloxacin consumption [9].

Patients usually complain of conjunctival hyperemia, photophobia, ocular pain, and blurred vision, such as in our case. The diagnosis is clinical: facing a patient with bilateral irregular depigmentation, ocular hypertension, and iris transillumination should lead the ophthalmologist to the diagnosis of BAIT. Differential diagnosis includes: pigment dispersion syndrome, in which iris depigmentation is less diffuse, and usually has a radial shape on iris midi periphery; pseudoexfoliation syndrome, in which the depigmentation is usually peri-pupillary, and associated with microfibrillar deposits [4]; viral iridocyclitis, which usually does not show bilateral involvement, and is also associated with inflammatory signs – absent

in BAIT – although some physicians may confuse the dispersed pigment in the anterior chamber as Tyndall effect, and treat patients with BAIT syndrome as anterior uveitis [4]; fuchs uveitis syndrome, which is unilateral in more than 90% of cases and has a chronic course with inflammatory keratic precipitates and inflammatory cells in the anterior chamber and the vitreous [5]. The absence of various ocular and systemic signs and symptoms also helps exclude other diseases like Vogt-Koyanagi-Harada.

An early rise in IOP is also part of the BAIT syndrome. Sometimes it can be refractory to medical therapy, and its etiology remains unclear. Pigment dispersion with heavy pigment deposition in the trabecular meshwork and topical corticosteroid therapy seems to be a possible mechanism for IOP elevation [4]. In our case, IOP did not decrease after the cessation of topical corticosteroid therapy, and glaucoma valve implant surgery was required in OU. Therefore, we believe that the blockage of trabecular outflow by acute pigment dispersion from the iris is the main mechanism of IOP increase in our case.

NAION is a common cause of acute vision loss, especially among patients with vascular risk factors. Perfusion of the optic disc is directly proportional to the mean arterial pressure and inversely proportional to IOP [19]. In our case, NAION was caused by a decreased perfusion to the optic disc secondary to a significant and persistent increased IOP. Elevated IOP has already been identified as a cause of NAION in patients with primary angle-closure and neovascular glaucoma [19–21]. As we are concerned, NAION secondary to BAIT had not been previously reported.

This is the first patient reported in Brazil of secondary glaucoma due to BAIT syndrome following topical moxifloxacin/dexamethasone eye drops, complicated with NAION. Pharmacological studies show that topical administration of moxifloxacin results in a concentration up to ten times higher in the aqueous humor (2.28 ± 1.23 μg/mL), when compared to vitreous administration (0.11 ± 0.05 μg/mL), and oral intake gives equivalent concentrations between aqueous humor and vitreous [22].

BAIT syndrome is a relatively new condition, which the ophthalmologist should have in mind in the differential diagnosis of iridocyclitis and pigment dispersion. This way, one can avoid unnecessary diagnosis and treatment, due to misdiagnosing as anterior uveitis. Early diagnosis of this condition is also important, due to the risk of increases in IOP. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000529014).

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Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors declare that they have no competing interests.

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Author Contributions

Daniella Socci da Costa: conceptualizing, analyzing images, writing the manuscript, and approved final manuscript. Aluisio Rosa Gameiro Filho: analyzing images, writing the manuscript, and approved final manuscript. Andrea Lima Barbosa: analyzing images, writing the manuscript, and approved final manuscript. Maria Vitória Moura Brasil: analyzing images, writing the manuscript, and approved final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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