When BAIT Masquerades as Pigment Dispersion Syndrome

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CASE PRESENTATION

A 44-year-old white woman with a history of pigment dispersion and myopic shift of unknown etiology was referred to us for IOP management. She first presented to her primary care physician 10 months before our initial examination with symptoms of laryngitis, headache, and a “boring” pain behind the right eye. The working diagnosis included infectious etiology, and the patient was prescribed clarithromycin (Biaxin; AbbVie) and a methylprednisolone (Medrol; Pfizer, Inc.) dose pack. One week later, she developed a fever, and moxifloxacin (Avelox; Pfizer, Inc.) was substituted for clarithromycin. The subsequent week, she developed redness and blurred vision in both eyes and worsening eye pain in her right eye, which prompted a visit to the ER. Computed tomography scans of the patient’s face and orbits were normal, and she was referred to an ophthalmologist.

At her initial visit to a comprehensive ophthalmologist she was noted to have
- anisocoria (4 mm OD, 5 mm OS)
- minimally reactive pupils
- distance visual acuity of 20/20 OD, 20/25 OS, with -1.75 D wear OU
- hyperemia (4+)
- pigment and cells in the anterior chamber (OD > OS)
- posterior synechiae OD
- diffuse transillumination defects OU
- an IOP of 9 mm Hg OD and 15 mm Hg OS

The patient was diagnosed with scleritis and uveitis and started on homatropine 5% b.i.d. OD, prednisolone acetate 1% q.i.d. OD, ibuprofen (Motrin; Johnson & Johnson) 600 mg p.o. t.i.d, and ranitidine 150 mg p.o. b.i.d. Two days later, her pain had lessened, the hyperemia decreased, and most of the synechiae had broken.

At a follow-up visit 1 week later, the patient’s visual acuity decreased to 20/80 OD and 20/60 OS. There was a 1.50 D myopic shift and significant pigment in both anterior chambers. Her IOP was 40 mm Hg OD and 38 mm Hg OS. She was started on timolol maleate 0.5% b.i.d OU, the prednisolone was decreased to b.i.d., the ibuprofen was decreased to 400 mg t.i.d., and the homatropine and ranitidine were stopped.

Two days later, the patient’s IOP was 13 mm Hg OD and 17 mm Hg OS. One week later, her IOP was elevated (29 mm Hg OD, 21 mm Hg OS), her pupils were nonreactive, and she experienced a loss of accommodation and difficulty reading without her glasses, as noted by the examining ophthalmologist (manifest refraction, -2.25 D sphere OD, -1.75 D sphere OS). The timolol was switched to brimonidine tartrate 2%-timolol maleate 0.5% (Combigan; Allergan, Inc.), and the patient was prescribed bifocals and tinted contact lenses for photophobia and referred to a glaucoma specialist for evaluation. Visual field and optic nerve examination were not reported by the comprehensive ophthalmologist.

The patient’s IOP in both eyes remained controlled on medications, and the pain in her right eye completely subsided. Her pupils were still middilated and nonreactive to one-eighth percent pilocarpine. There was also a persistent
loss of accommodation (1.00 D) and decreased corneal sensation in her right eye. Immunoglobulin G and anti-GQ1B antibody titers ruled out atypical Miller-Fischer syndrome, and magnetic resonance angiogram and a magnetic resonance imaging scans were unremarkable.

One month later, the patient’s IOP remained controlled on brimonidine tartrate 2%-timolol maleate 0.5% and travoprost 0.4% (Travatan; Alcon Laboratories, Inc.), and her visual acuity had improved to 20/25 OD and 20/20 OS. Internal ophthalmoplegia persisted, and she had 2 mm of ptosis in her left eye that had increased over the preceding 3 weeks. A neuro-ophthalmic evaluation that included serological studies was unremarkable. The patient was diagnosed with pigment dispersion syndrome of an atypical nature and myopic shift of uncertain etiology.

The patient was referred to our facility for continued management of her IOP 10 months after the initial onset of symptoms. Her past medical history was significant for Lyme disease in 1992, Hashimoto’s thyroiditis in 2003, sinus surgery in 2005, medullary sponge kidneys, and vertigo. Her family and social history were unremarkable.

HOW WOULD YOU PROCEED?

1. Has sufficient testing been performed to determine a diagnosis, or would you recommend additional testing?

THERAPEUTIC COURSE

The constellation of internal ophthalmoplegia, elevated IOP, marked pigment dispersion in an atypical pattern, and a possible preceding viral infection is different from a typical pigment dispersion/pigment glaucoma presentation. In patients presenting similarly to the one described, the approach to management is a question of whether or not the disease is progressive and for how long and how aggressively is it necessary to lower the IOP. Examinations at our center were initially performed 10 months after the onset of symptoms. At this time, the IOP appeared well controlled on brimonidine tartrate 0.2% b.i.d. OU and travoprost q.h.s. OU. Visual field and optic nerve examinations revealed no glaucomatous damage. Anterior chambers were without cell or flare. Thus, it appeared that the acute episode had resolved, and despite elevated IOP early in the course of this condition, that glaucomatous optic nerve damage had not occurred. As a result, a reverse therapeutic trial of glaucoma medications

Figure 1. Iris with broad, diffuse transillumination defects as well as posterior synechiae.

Figure 2. Grade 3+ open angles with dense pigment inferiorly, as reflected in superior mirror on gonioscopy.
was recommended. The patient has been observed for 14 months after our initial visit, with an unchanged examination, well-controlled IOP, and no glaucomatous damage. Her reduced accommodation is managed with progressive lenses, and the photophobia is controlled with tinted lenses.

**OUTCOME**

On examination, the patient’s BCVA was 20/25 OU. Her pupils were fixed, middilated, and nonreactive with posterior synechiae in her right eye. Goldmann applanation IOPs measured 16 mm Hg OD and 15 mm Hg OS, and Humphrey Visual Fields (standard 24-2 Swedish interactive threshold algorithm; Carl Zeiss Meditec, Inc.) were full in both eyes. A slit-lamp examination was significant for minimal endothelial pigment granules (OD > OS) and broad diffuse transillumination defects (Figure 1). Gonioscopy revealed grade 3+ open angles in both eyes with dense pigment inferiorly (Figure 2). A dilated fundus examination revealed healthy discs with cup-to-disc ratios of 0.3 bilaterally and normal retinas.

**DISCUSSION**

Depigmentation of the iris is seen in many conditions, such as pigment dispersion syndrome (PDS), viral iridocyclitis, Fuchs uveitis syndrome, and bilateral acute iris transillumination, to name a few.

Primary PDS is a condition that results from iridozonal friction when the midperipheral iris contacts the lens zonules, causing disruption of the iris pigment epithelium and deposition of dispersed pigment granules throughout the anterior segment. Classic features of PDS are corneal endothelial pigmentation (Krukenberg spindle), slit-like radial midperipheral iris transillumination defects in a radial pattern, concentric iris pigmentation, and dense trabecular pigmentation. Posterior bowing of the iris also primarily affects individuals of European descent most commonly between the ages of 30 and 50 years. Men are slightly more susceptible than women. Myopia is an important risk factor. Patients are usually asymptomatic at presentation but may occasionally experience blurred vision during pigment showering. Eyes are affected in a bilateral fashion. There are no inflammatory cells in the anterior chamber. Pupillary response to light and accommodation are preserved.

Viral iridocyclitis is caused by viruses, the most common of which are herpes simplex virus and varicella zoster virus. The typical features of viral iridocyclitis are anterior uveitis with sectoral iris atrophy and unilaterality. Patients present with red, painful eyes and complaints of photophobia. The cornea and skin in the region of the V1 dermatome are usually involved. Despite the so-called classic presentation, many cases have been described in which there is no associated keratitis or skin involvement. A rare case of zoster sine herpete with bilateral ocular involvement has been reported.

Internal ophthalmoplegia with nonreactive pupils and loss of accommodation have also been described in patients with viral iridocyclitis. Internal ophthalmoplegia is thought to arise from direct viral invasion or occlusive vasculitis. Fluorescein angiography has been useful in demonstrating the occlusive angiitis of iris vessels. The resulting ischemia produces a full-thickness sectoral atrophy, distortion of the pupil, and patchy transillumination defects. Involvement of the ciliary vessels and nerves can lead to corneal anesthesia and loss of accommodation.

Although not classically associated with diffuse iris transillumination or pigment particles in the anterior chamber, a case of herpes simplex virus associated with acute iris depigmentation was recently described by Dastrup et al, and these two features were present. IOP rise can occur secondary to the presumed trabeculitis and is usually acute and transient.

The classic diagnostic features of Fuchs uveitis syndrome are the absence of acute symptoms such as red eyes, ocular pain, and photophobia; the absence of posterior synechiae; diffuse stellate; small or medium-
sized keratic precipitates; chronic low-grade anterior chamber reaction; diffuse iridal stromal atrophy with blunting of iris crypts with or without heterochromia; and anterior vitritis. This syndrome is typically unilateral, and Krukenberg spindles and pigment particles in the anterior chamber are usually not seen. Pupillary changes (anisocoria) can occur but are quite rare, and transillumination, if it does occur, is peripupillary. IOP rise is a frequent complication that develops over the course of years. The etiology of Fuchs uveitis syndrome is unknown, but recent studies have shown a relationship with the rubella virus.14-17

Bilateral acute iris transillumination (BAIT) is a recently described clinical entity that is being increasingly recognized. This condition was initially reported as an ocular complication of oral moxifloxacin.18 Patients were found to have developed a uveitis-like episode that lasted an average of 10 days after taking oral moxifloxacin for respiratory tract infections. This was coupled with severe iris transillumination and persistent mydriasis of the pupil with no reaction to light and no near reflex. Although our patient has a history of moxifloxacin use, similar ocular findings have also been found in patients with no history of the drug.19

The common thread that seems to bind these cases is the history of antecedent respiratory virus-like illness. It is our impression that our patient’s history and constellation of findings on clinical examination are consistent with this condition. BAIT commonly follows a flu-like illness or upper respiratory tract infection as in the case of our patient. The IOP spike occurs acutely, over weeks to months, unlike in PDS, where pigment is shed gradually, and ocular hypertension develops over years. In BAIT, the severe diffuse iris transillumination occurs suddenly from the iris pigment epithelium and is not in the classic midperipheral radial spoke-like pattern that typifies PDS (Figure 3). Pupillary response to light and accommodation is not affected in PDS, but it is affected with BAIT and is thought to be related to sphincter paralysis. Although the cause of BAIT has yet to be identified, a recent series of 26 patients with similar findings suggests a possible viral etiology, although the authors said that the etiology and pathogenesis are uncertain.19

It is important that clinicians be sensitized to the existence of BAIT, as it often masquerades as other conditions. Initially, it masquerades as acute iridocyclitis, and later it develops findings that resemble PDS. Persistent mydriasis with compromised pupillary reaction to light and near stimuli is a feature. IOP rise is an early complication, and its duration varies (1 month-3 years in the series mentioned above). The time taken for resolution of pigment dispersion in the anterior chamber is also variable (1-18 months has been reported).19 The condition seems to respond to symptomatic and supportive medical treatment; none of the patients in the series described developed glaucomatous optic neuropathy or visual field defects. Trabeculectomy was only required in two patients for IOP control.

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