Objective: To describe a series of patients with bilateral acute iris transillumination, pigment dispersion, and sphincter paralysis.

Methods: We reviewed the medical records and clinical photographs of 26 patients seen at 5 centers in Turkey and Belgium between March 16, 2006, and July 6, 2010. Observation procedures included clinical examination, anterior segment color photography, gonioscopy, laser flare photometry, and pupillometry.

Results: All 26 patients (20 women and 6 men; mean [SD] age, 43.2 [10.5] years) had bilateral involvement. Twenty-three patients (88%) had acute-onset disease with severe photophobia and red eyes. Nineteen patients (73%) had a preceding flulike illness and used systemic antibiotics, including moxifloxacin. Diagnostic laboratory workup was unremarkable. There was pigment dispersion into the anterior chamber, and flare was elevated in the absence of inflammatory cells. Most patients had severe diffuse transillumination of the iris and mydriatic distorted pupils. Pupillometry revealed a compromised reaction to light. The most serious complication was an intractable early rise in intraocular pressure. Gonioscopy revealed heavy pigment deposition in the trabecular meshwork. Although symptoms were relieved promptly by application of topical corticosteroid, the median duration of pigment dispersion was 5.25 months.

Conclusions: Bilateral acute iris transillumination with pigment dispersion and persistent mydriasis is a new clinical entity that is not an ocular adverse effect of oral moxifloxacin treatment, as previously suggested. The etiopathogenesis of this entity remains to be elucidated.

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KOWN CAUSES OF ACQUIRED iris atrophy with or without transillumination of the iris include herpetic iridocyclitis, pigment dispersion syndrome (PDS), pseudoexfoliation syndrome, Fuchs uveitis syndrome, Vogt-Koyanagi-Harada disease, trauma, and acute angle-closure glaucoma.1-10 Pigment discharge into the anterior chamber is a diagnostic feature of PDS and may also occur in pseudoexfoliation syndrome.1,2 Pigment dispersion is also one of the diagnostic features of the recently described entity bilateral acute pigmentary iris transillumination (BAIT). However, BADI is characterized by a nontransilluminating depigmentation of the iris (BADI). However, BADI is characterized by a nontransilluminating depigmentation of the iris stroma.11,12 More recently, an acquired bilateral diffuse iris transillumination with variable sphincter paralysis has been described as an ocular adverse effect of oral moxifloxacin treatment.13-15 We have seen patients with similar ocular findings with or without a history of moxifloxacin intake.

We herein describe the clinical features and course in 26 patients who developed bilateral acute iris transillumination (BAIT) associated with pigment dispersion and persistent mydriasis.

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pilometry and a laser flare photometer (KOWA FC-2000; Kowa Co Ltd, Tokyo, Japan) to measure anterior chamber flare only in patients seen at the Uveitis Service of the Department of Ophthalmology, Istanbul Faculty of Medicine, Istanbul University. The pupil diameters were measured under photopic and scotopic conditions. Pilometry was performed in age- and sex-matched control subjects for comparison with the retrospective data obtained from the study patients.

Diagnostic laboratory workup included erythrocyte sedimentation rate, complete blood cell count, and biochemistry. Serum IgG and IgM antibodies against herpes simplex virus types 1 and 2, varicella zoster virus, cytomegalovirus, and/or Epstein-Barr virus were measured in 10 patients. Patients were treated with topical corticosteroids when they had acute symptoms or ongoing high-grade pigment dispersion in the anterior chamber. Empirical oral acyclovir or valacyclovir therapy was given to the first 8 patients with pigment dispersion. In patients with an intraocular pressure (IOP) higher than 21 mm Hg, topical antiglaucomatous medications were used. If IOP exceeded 40 mm Hg, intravenous mannitol, 20%, infusions were given.

The main outcome measures were demographic features, initial ocular and systemic symptoms, ocular clinical findings, and pilometry and flare photometry measurements. In patients who had resolution of pigment dispersion during follow-up, time to resolution was also determined.

We used a commercially available statistical analysis program (SPSS, version 16.0 for Windows; SPSS Inc, Chicago, Illinois) for analysis of the data. The Mann-Whitney, Wilcoxon, and Kruskal-Wallis tests were used to test for differences between groups. The Dunn test was used as a multiple comparison post hoc test. Categorical data were analyzed by the χ² test. P < .05 was considered significant.

RESULTS

Twenty patients were women and 6 were men. The mean (SD) patient age when first seen was 43.2 (10.5) years (median, 42 years; age range, 25-69 years). Seven patients were seen only once or had follow-up of less than 1 month. The remaining 19 patients had mean (SD) follow-up of 13.2 (12.2) months (median, 9.7 months; range, 1.5-43.0 months). All the patients had bilateral involvement. The demographic and clinical characteristics of the patients at the first visit are given in Table 1 and in eTable 1 and eTable 2 (http://www.archophthalmol.com).

INITIAL OCULAR SYMPTOMS AND OCULAR HISTORY

All the patients had an acute onset of ocular symptoms. Twenty-three patients (88%) had or reported an acute onset of severe photophobia and red eyes. Three patients reported only red eyes. Both eyes were involved simultaneously; however, symptom severity could be asymmetrical. Seven patients were seen within 1 week of onset of ocular symptoms. The remaining 19 patients were referred with a diagnosis of iridocyclitis with unusual features. The median disease duration in the latter group was 2 months (range, 2 weeks to 14 months). All these patients had been treated with topical corticosteroids. Five patients reported systemic corticosteroid use, and 7 patients had been given oral antiviral medications. Twelve patients (63%) had a history of IOP rise, bilaterally in 10. All these patients had been treated with topical antiglaucomatous medication(s) and 6 with concomitant oral acetazolamide. One patient had undergone trabeculectomy in 1 eye 7 months after onset of the disease. Another patient had required intravenous infusion of mannitol, 20%, to control the IOP rise. Ocular history was otherwise unremarkable.

SYSTEMIC SYMPTOMS AND MEDICAL HISTORY

Nineteen patients (73%) reported a flu-like illness or upper respiratory tract infection preceding the onset of ocular symptoms. The mean (SD) interval between the on-
RESULTS OF THE LABORATORY WORKUP

Routine laboratory results were within the reference ranges. Viral serologic analysis in 10 patients showed that the IgM antibodies were negative and the IgG antibodies were not elevated. In patients tested for IgG antibodies against herpes simplex virus type 1 and Epstein-Barr virus, seropositivity was 83% and 75%, respectively. All patients tested for anti–varicella zoster virus and cytomegalovirus were found to have positive IgG antibodies. No patient was found to have IgG positivity against herpes simplex virus type 2.

INITIAL OCULAR FINDINGS

Median visual acuity was 1.0 OU (range, 0.3–1.0 OD and 0.4–1.0 OS). Reduced visual acuity was due to amblyopia in 2 eyes. Another eye with visual acuity of 0.3 had a preretinal hemorrhage at the posterior pole that had occurred after trabeculectomy.

 Conjunctival hyperemia was documented in the 7 patients (12 eyes) who were first seen within 1 week of the onset of ocular symptoms. Fine pigment precipitates on the corneal endothelium were recorded in 12 patients (21 eyes): in the form of Krukenberg spindle in 2 (4 eyes), diffusely scattered in 3 (6 eyes), and distributed in the lower half of the cornea in 7 (11 eyes). Inflammatory keratic precipitates were not seen.

None of the patients had inflammatory cells in the anterior chamber at the first visit or during follow-up. There was variable pigment dispersion in the anterior chamber in both eyes of 22 patients. Three patients who were first seen 4 months to 1 year after the onset of ocular symptoms had no circulating pigment in the anterior chamber but had diffuse transillumination of the iris and persistent mydriasis due to sphincter paralysis in both eyes. Another patient who was first seen on day 5 of the onset of ocular disease had + pigment in the left eye only. However, pigment dispersion occurred in the other eye during follow-up but did not exceed 0.5+. The iris of this patient exhibited diffuse transillumination in the left eye and only moth-eaten transillumination in the right eye.

Twenty-one patients (42 eyes) had severe diffuse transillumination of the iris and mydriatic pupils poorly responsive or unresponsive to light (Figure 1 and Appendix [eCase 1]). In 4 patients, there was asymmetrical involvement, with diffuse transillumination in 1 eye with a mydriatic pupil and less severe, moth-eaten transillumination without apparent mydriasis in the other eye. One patient had symmetrical bilateral moth-eaten transillumination with normal pupils. An irregular distorted pupil was also noted in 20 patients (32 eyes). Spiraling of the pupil was not apparent. Posterior synechiae were documented in 3 patients (4 eyes). The morphologic features of posterior synechiae were different from those of uveitic synechiae in that a thick layer of iris pigment seemed to be smeared on the surface of the lens and remained adherent with a broad base (Figure 2). In 10 patients (19 eyes), smeared iris pigment (Figure 1) or pigment dusting (Figure 3 and Appendix [eCase 2]) was seen on the surface of the lens. Scattered pigment particles were seen on the surface of the iris as well. One patient had unilateral mild posterior subcapsular lens opacity. The corneal sensation was intact, and the vitreous was clear in all the patients. The fundus was normal in all except 1 patient with preretinal hemorrhage at the posterior pole after trabeculectomy in 1 eye.

Mean IOP values are given in Table 1. An IOP higher than 21 mm Hg was measured in 8 patients (11 eyes). Nine patients were still taking topical antiglaucomatous medi-
Pupillometry was performed in 15 patients and 20 controls (Table 2). Sex and mean age did not differ between the 2 groups. Under scotopic conditions, no significant difference was noted in pupil diameter between patients and controls (P=.62 for right eyes and P=.85 for left eyes); however, under photopic conditions, patients’ mean pupil diameter was significantly larger (P<.001 for right and left eyes). Patients had significantly reduced amounts of miosis. Pupillary reaction to near stimuli was also compromised. Accommodation was not measured in any patient; however, none of the patients required additional plus lenses for near vision.

**TREATMENT AND FOLLOW-UP**

Treatment and follow-up are summarized in eTable 2. Seven patients who were first seen within 1 week of the onset of ocular symptoms were treated with hourly topical corticosteroid application, which resulted in prompt relief of their symptoms. Seven patients who were referred 1 to 14 months after disease onset and had less than 2+ pigment and low flare (<15 photon counts per millisecond [ph/ms]) were not given topical corticosteroids. Topical corticosteroid therapy prescribed elsewhere was maintained in 12 patients who were referred with a disease duration of 2 to 16 weeks and ongoing pigment dispersion. Four of them did not return for follow-up. Two of them with flare measurements exceeding 150 ph/ms were also given oral prednisolone (0.5 mg/kg/d), which was tapered and discontinued within 6 weeks. The mean (SD) duration of topical corticosteroid treatment was 3.51 (2.00) months (median, 3 months; range, 1-8 months). In 11 patients, topical corticosteroid therapy was discontinued with slow tapering, and no relapse was seen. Only 1 patient had 2 relapses during tapering, which were controlled with an increased dose and successful discontinuation of treatment at 5 months. Mean (SD) follow-up after withdrawal of treatment in these 12 patients was 13.6 (12.4) months (median, 9.12 months; range, 1-39 months).

Mean (SD) time from onset of ocular symptoms to complete resolution of pigment dispersion in the anterior chamber was 7.30 (5.68) months (median, 5.25 months; range, 1-18 months) in 14 patients (28 eyes). Resolution of pigment dispersion in the anterior chamber occurred simultaneously in both eyes in all except 2 patients. The mean (SD) flare was significantly reduced at the last visit (from 39.23 [73.44] to 5.18 [3.03] in right eyes, P=.02; and from 81.92 [132.66] to 4.52 [1.13] in left eyes, P=.002).

**COMMENT**

We described 26 patients with an unusual bilateral acute iris transillumination associated with symptomatic pigment showering after a flulike illness or an upper respiratory tract infection in most cases. Middle-aged women are more commonly affected. Despite the absence of inflammatory keratic precipitates or cells in the anterior chamber, pigment storm is associated with a flare rise,
and patients may be misdiagnosed as having acute bilateral iridocyclitis. Clinical findings that challenge conventional diagnosis include bilateral severe transillumination of the iris, pigment dispersion in the anterior chamber, and a mydriatic pupil that is unresponsive or poorly responsive to light due to variable sphincter paralysis. Symptoms are rapidly responsive to topical corticosteroid therapy; however, pigment dispersion may last months and even up to more than 1 year. An early rise in IOP is a common complication and can be refractory to treatment. The etiology remains unknown.

There are recent reports on the occurrence of acute pigment dispersion and iris transillumination after oral moxifloxacin treatment. Bilateral abundant pigment dispersion has been reported as a complication of moxifloxacin used for the treatment of pneumonia. More recently, Wefers Bettink-Remeijer et al. described 5 patients who had an acute onset of photophobia and pain followed by bilateral diffuse iris transillumination with variable sphincter paralysis and concluded that this was an ocular adverse effect of oral moxifloxacin use. Most patients in the present cohort had a preceding flulike illness or respiratory tract infection before the onset of ocular symptoms; although only approximately 35% reported moxifloxacin intake, 40% were exposed to other antibiotics. Therefore, we believe that the clinical picture described herein may represent a distinct condition probably triggered by a viral infection. Theoretically, such an ocular adverse effect would also be expected to occur with the topical application of moxifloxacin, which has been shown to have efficient ocular penetration. To our knowledge, there is no such reported ocular adverse effect of topical moxifloxacin treatment.

The differential diagnosis of BAIT is summarized in Table 3. Pigment dispersion syndrome is the most difficult to differentiate from the entity described herein. Se-
vere photophobia and markedly red eyes, as seen in the present series, are not characteristic of PDS. Patients described herein developed severe diffuse iris transillumination at a single episode and did not have a midperipheral radial spokelike pattern, which typically develops over a chronic progressive course in PDS. Ocular hypertension or pigmentary glaucoma develops over years in PDS, whereas the IOP rise occurred within weeks to months in the present series. Pupillary reactions to light and near stimuli are not affected in PDS. Compromised pupil-lary constriction to light was thought to be related to variable amounts of sphincter paralysis in the present patients. Posterior bowing of the iris is a characteristic feature of PDS. Willermain et al described a patient with bilateral symptomatic acute iris transillumination, pigment dispersion, and severe IOP rise after moxifloxacin use. Gonioscopy revealed heavy pigment deposition in the iridocorneal angle, and anterior segment optical coherence tomography showed iris concavity in their patient. Because iris concavity is a typical finding in PDS, their patient probably had PDS and an acute elevation in IOP due to the use of subconjunctival corticosteroids. Although we did not perform anterior segment optical coherence tomography or ultrasound biomicroscopy, we do not have any clinical observation of iris concavity or posterior bowing in any patient. This finding has not been reported by other researchers.

Table 3. Differential Diagnosis of BAIT

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Herpetic Iridoicytis</th>
<th>FUS</th>
<th>PXF</th>
<th>BADI</th>
<th>PDS</th>
<th>BAIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>No predilection</td>
<td>No predilection</td>
<td>Commonly female</td>
<td>Female predominance (2.7:1)</td>
<td>Mostly male</td>
<td>Female predominance (3.3:1)</td>
</tr>
<tr>
<td>Symptoms at onset</td>
<td>Symptomatic, with red eyes, ocular pain, and photophobia</td>
<td>Asymptomatic</td>
<td>Asymptomatic</td>
<td>Severe photophobia and red eyes</td>
<td>Usually asymptomatic; occasionally headache, blurred vision, and halos around light during pigment showering</td>
<td>Severe photophobia and red eyes</td>
</tr>
<tr>
<td>Laterality</td>
<td>Typically unilateral</td>
<td>Typically unilateral</td>
<td>Bilateral asymmetrical</td>
<td>Bilateral asymmetrical pigment</td>
<td>Bilateral, mostly symmetrical pigment</td>
<td>Bilateral, mostly symmetrical pigment</td>
</tr>
<tr>
<td>Keratic precipitates</td>
<td>Inflammatory, diffuse stellate, and medium sized</td>
<td>Inflammatory, diffuse stellate, and medium sized</td>
<td>Pigment</td>
<td>Pigment</td>
<td>Pigment</td>
<td></td>
</tr>
<tr>
<td>Krukenberg spindle</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Sometimes present</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Pigment particles in the AC</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Sometimes present</td>
<td>Present</td>
<td>Sometimes present</td>
</tr>
<tr>
<td>Inflammatory cells in the AC</td>
<td>Present during exacerbations</td>
<td>Chronic, low grade</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Iris transillumination</td>
<td>Patchy or sectoral</td>
<td>Rarely peripupillary</td>
<td>Peripupillary</td>
<td>None</td>
<td>Midperipheral spokelike</td>
<td>Diffuse</td>
</tr>
<tr>
<td>Change in the iris configuration</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Iris stromal changes</td>
<td>Patchy or sectoral stromal atrophy</td>
<td>Diffuse stromal atrophy with blunting of iris crypts with or without heterochromia</td>
<td>None</td>
<td>Bilateral symmetrical geographic or diffuse depigmentation and granularity with distinct margins</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Pupillary changes</td>
<td>Usually present, irregular distorted pupil with spiraling</td>
<td>Rarely anisocoria, with larger pupil on the affected side</td>
<td>None</td>
<td>None</td>
<td>Anisocoria in asymmetrical cases, with preserved light and near response</td>
<td>Present; usually symmetrical, dilated atonic pupil with compromised reaction to light and near stimuli</td>
</tr>
<tr>
<td>IOP rise</td>
<td>Acute and transient during exacerbations, related to trabeculitis</td>
<td>Frequent complication developing over years</td>
<td>Frequent complication developing over years</td>
<td>Uncommon, transient</td>
<td>Frequent complication developing over years</td>
<td>Early complication, resistant</td>
</tr>
<tr>
<td>Gonioscopy</td>
<td>Open angle</td>
<td>Open angle, new vessels, occasionally goniocneiectae</td>
<td>Pseudoexfoliation material</td>
<td>Pigment deposition</td>
<td>Pigment deposition</td>
<td>Pigment deposition</td>
</tr>
</tbody>
</table>

Abbreviations: AC, anterior chamber; BADI, bilateral acute depigmentation of the iris; BAIT, bilateral acute iris transillumination; FUS, Fuchs uveitis syndrome; IOP, intraocular pressure; PDS, pigment dispersion syndrome; PXF, pseudoexfoliation syndrome.
scribed herein include an acute onset of severe photophobia and red eyes after a flulike syndrome, pigment discharge into the anterior chamber, and exclusive involvement of the iris. Oral antibiotic drug use was reported in 38.5% of patients with BADI, including moxifloxacin use in 30.7% and amoxicillin-clavulenate use in 7.7%. Even if BAIT may be a more severe form of BADI and both conditions have a common etiology, the pigment discharge seems to be only from the iris pigment epithelium in the former and from the iris stroma in the latter. The most important differentiating feature between the 2 entities is that the pupil is not affected in BADI and a symmetrical geographic or diffuse depigmentation of the iris stroma causes a change in iris stromal texture and color without any transillumination defect. whereas patients described herein typically had atomic dilated pupils and diffuse iris transillumination without any visible change to the iris stroma. Furthermore, BADI has a more benign course with a shorter duration of pigment discharge, a lower incidence of IOP rise that is only transient, and reversibility of iris changes reported at least in some patients. Heavy pigment deposition in the trabecular meshwork was a consistent finding in the present series and explained the early severe IOP rise that could occur as early as 1 week and the need for trabeculectomy as early as 3 weeks after onset. On the other hand, a corticosteroid-induced IOP rise cannot be excluded in patients who developed this complication later on.

The present patients clearly differed from those with pseudoexfoliation syndrome, Fuchs uveitis syndrome, and herpetic anterior uveitis. Sectoral iris atrophy with chronic refractory glaucoma may rarely be seen in immunocompetent patients with cytomegalovirus anterior uveitis. Aqueous humor analysis for local antibody production or demonstration of viral DNA is needed for a definite diagnosis of viral etiology. Diffuse iris atrophy has been reported in 50% and elevated IOP in 100% of eyes diagnosed as having cytomegalovirus anterior uveitis. However, in those eyes, diffuse iris transillumination and spherincter paralysis have not been described. Anterior chamber tap was reported to be negative for herpes viruses in 5 of the 6 cases previously reported in the literature with findings similar to the present series, and the herpes virus genome was found in only 1 patient, who had a history of uveitis. The causative agent of the preceding systemic illness is not known in any of the present patients. With the emergence of new respiratory viruses, new disease entities may develop, and conjunctiva may not be the only ocular tissue affected by these infections. Although we presume that the entity described herein might represent an expanded spectrum of BADI. This may be a new entity or may represent an expanded spectrum of BADI. If the latter is true, prompt recognition of this condition is essential because of the high risk of early severe IOP rise.

Submitted for Publication: December 10, 2010; final revision received March 21, 2011; accepted March 24, 2011. Correspondence: Ilknur Tugal-Tutkun, Istanbul Tip Fakultesi, Goz Hastaliklari AD, 34390 Capa, Istanbul, Turkey (itutkun@yahoo.com). Financial Disclosure: None reported.


REFERENCES


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**From the Archives of the Archives**

Maher (348, On the treatment and prognosis of primary glaucoma). The author aims at a cystoid scar. He draws out a large loop of iris and allows the wound to heal before he excises the iris. . . .

In many cases an iris encleisis, even if it does not lead to septic infection, provides a bridge along which endothelial cells proliferate till they reach the iridic angle which they block and cause a glaucoma which is beyond treatment. Lagrange's and Herbert's methods are far preferable in every way. Most surgeons carefully avoid if possible any iris encleisis, which is recognized to be a potent cause of failure. The author only recommends his operation for chronic cases.