

# Bilateral Acute Depigmentation of Iris (BADI) and Bilateral Acute Iris Transillumination (BAIT)-An Update

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## Abstract

Bilateral acute depigmentation of the iris (BADI) and bilateral acute iris transillumination (BAIT) are relatively new clinical entities characterized by acute pigment dispersion from the iris stroma or iris pigment epithelium, respectively. While BADI presents with diffuse or geographic areas of iris stromal depigmentation without transillumination, BAIT cases typically develop diffuse iris transillumination and mydriatic atonic pupils. Prolonged pigment dispersion and ocular hypertension are more common in BAIT. Although the exact etiopathogenesis is still unknown, moxifloxacin toxicity appears to be a probable/likely cause. The underlying cause of BADI or BAIT in patients who were not exposed to fluoroquinolone antibiotics remains unexplained. Systemic viral infections, including coronavirus disease 2019, may be the triggering event in several cases.

Keywords: Bilateral acute depigmentation of the iris, bilateral acute iris transillumination, ocular hypertension, moxifloxacin, pigment dispersion

# Introduction

Bilateral acute depigmentation of the iris (BADI) and bilateral acute iris transillumination (BAIT) are peculiar pigment dispersion syndromes first described in the early 2000s.<sup>1,2</sup> While these two entities have distinct clinical phenotypes and disease course, they may belong to the same spectrum, although the etiopathogenesis remains unclear.

#### **Clinical Features of BADI**

BADI was first described in 2006 by Tugal-Tutkun and Urgancioglu<sup>1</sup> in a series of 5 cases from Turkey. They described an acute episode of pigment discharge in the anterior chamber from the iris stroma, bilateral symmetrical diffuse or geographical areas of depigmentation and discoloration of the iris stroma, Krukenberg's spindles, and pigment deposition in the trabecular meshwork. In their subsequent series, Tugal-Tutkun et al.<sup>3</sup> described 26 new cases and long-term follow-up of 2 cases. Following these early publications, many cases have been reported from other countries.<sup>4,5,6,7,8,9</sup>

BADI affects predominantly young females. It presents as a sudden-onset redness, ocular pain, tearing, and photophobia in both eyes simultaneously or within a few days of each other. Severe photophobia is the most prominent symptom. The patients usually maintain normal visual acuity.<sup>1,3,4,5</sup>

Patients with BADI present with severe diffuse episcleral injection, more pronounced than ciliary injection. They do not have signs of intraocular inflammation, but they present with circulating pigment in the anterior chamber, which may

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be graded from 0.5+ to 4+, and endothelial pigment dusting or Krukenberg's spindle. The iris stroma shows a diffuse or patchy depigmentation typically starting at the iris root, with sharply defined margins, and has a granular appearance in the depigmented areas. Interestingly, diffuse depigmentation is seen from the iris root to the collarette, sparing the peripupillary iris (Figure 1). The superior peripheral iris is preferentially affected in patients with limited areas of depigmentation. Almost all of the cases reported in the literature originally had brown eyes and the depigmented areas caused a dull grayish discoloration. There are no iris transillumination defects or posterior synechiae. Pupils are round or slightly irregular and pupillary reactions are normal. In patients who are seen late, following the resolution of a mild episode of pigment discharge, iris stromal changes may be subtle and may escape detection. Therefore, BADI might be more frequent than reported. Furthermore, asymmetrical involvement of the two eyes has also been reported,<sup>4,6,7</sup> which may present a challenge in the diagnosis of BADI, originally described as a symmetrical bilateral entity.

In a study using anterior segment swept-source optical coherence tomography (OCT), it was confirmed that the stromal damage involved the iris from the collarette to the root of the iris, without affecting the pupillary area.<sup>8</sup> In the affected areas, the iris anterior border had lost its homogeneous hyperreflectivity. The stroma was thinned and showed a diffuse or patchy hyperreflectivity, while the pigmentary epithelium appeared unaffected.<sup>8</sup> Anterior segment OCT ruled out concave iris configuration in all 25 eyes with BADI in another study.<sup>7</sup>

Iris angiography showed normal circulation with no signs of leakage or ischemia in 2 cases examined late in the course, when they had no symptoms or signs of pigment discharge but still had stromal depigmentation.<sup>4</sup>



**Figure 1.** Slit-lamp photographs of the right (A) and left (B) eye of a 51-yearold man who presented with red eyes and photophobia and was diagnosed with BADI. The top row shows conjunctival hyperemia that is more severe in the right eye. The bottom row shows, at higher magnification, depigmentation of the iris stroma from the iris root to the collarette, sparing some sectors that retain normal iris color (arrows)

BADI: Bilateral acute depigmentation of the iris

On gonioscopy, there is heavy pigment deposition, especially in the inferior angle. Intraocular pressure (IOP) is usually normal but can increase in some patients due to clogging of the trabecular meshwork with pigment.

BADI is non-progressive and has a self-limited course. Topical corticosteroids can be used in symptomatic patients with circulating pigment in the anterior chamber. Topical corticosteroids should be slowly tapered and discontinued after resolution of pigment dispersion. Rapid tapering and early discontinuation of topical corticosteroids may result in a relapse of ocular symptoms and high-grade pigment discharge in the anterior chamber. Complete resolution of pigment dispersion in the anterior chamber takes around 8 (1-16) weeks from the onset of ocular symptoms. When there is an IOP rise, it can be rapidly controlled with topical antiglaucoma medications, and IOP remains at normal levels after discontinuation of antiglaucoma therapy.<sup>3</sup>

Tugal-Tutkun et al.<sup>3</sup> have reported that iris depigmentation was noticeable for up to 2 years, but repigmentation with normal stromal architecture was noted in two patients who were seen at 4 years. A pattern of slow and gradual recovery with repigmentation and rethickening of the iris stroma has been reported by others as well.<sup>4.9</sup> On the other hand, persistent depigmentation was seen at 4 and 5 years in two other cases reported in the literature.<sup>5,8</sup> There are no fundus changes throughout the disease course and visual acuity is not affected in BADI patients.<sup>3,7</sup>

## **Clinical Features of BAIT**

In 2004, Bringas Calvo and Iglesias Cortiñas<sup>2</sup> reported bilateral acute anterior uveitis with pigment dispersion in an older woman treated with moxifloxacin for pneumonia. Then in 2009 and 2010, six cases of a bilateral uveitis-like syndrome with pigment dispersion, iris transillumination, and sphincter paralysis were reported as an adverse effect of oral moxifloxacin.<sup>10,11</sup> Tugal-Tutkun et al.<sup>12</sup> named this entity BAIT in a series of 26 patients reported in 2011. In their series, however, moxifloxacin intake was reported in only 35%, while 73% had an antecedent respiratory illness.<sup>12</sup> This entity predominantly affects females around 40 years of age.<sup>12,13</sup>

Patients with BAIT present with similar but more severe symptoms compared to BADI patients. Both eyes are involved simultaneously with severe photophobia and red eyes, but symptom severity can be asymmetrical. Heavy pigment discharge into the anterior chamber, high flare, and low IOP (8-9 mmHg) are the typical presenting signs at onset. Pigment showering is severe during the first few weeks following symptom onset and declines over time.<sup>13</sup> As the pigment dispersion starts to clear, diffuse iris transillumination and irregularly mydriatic pupils that are poorly responsive or unresponsive to light become apparent and higher IOP levels are measured. Iris transillumination and mydriasis may increase with continued pigment circulation, pigment dusting on the corneal endothelium and on the surface of the lens is seen, posterior synechiae may develop, and IOP rise may become uncontrollable with antiglaucoma medications.<sup>12</sup> Posterior synechiae in BAIT are characterized by a thick layer of iris pigment smeared on the surface of the lens and remaining adherent with a broad base.<sup>12</sup> Scattered pigment particles can be seen on the surface of the iris as well. Gonioscopy shows a coat of thick pigment deposition obscuring the angle structures, especially in the inferior angle. Sectoral posterior iris bowing on anterior segment OCT has been reported,<sup>14</sup> but not confirmed by others.<sup>13,15,16</sup> Interestingly, pigment dispersion in the anterior vitreous is not seen and the fundus is typically normal.<sup>12,13</sup> However, a cotton-wool spot was reported in one case, and cystoid macular edema was reported in another case with a prolonged clinical course with recurrent episodes.<sup>14,17</sup>

Topical corticosteroids are used by adjusting the dose according to the severity of pigment dispersion, and gradually tapered. Symptoms are rapidly responsive to topical corticosteroid therapy. However, pigment circulation in the anterior chamber may last for months and even up to a year or longer. Recurrent symptomatic pigment discharge may occur with rapid tapering or early discontinuation of topical corticosteroids.<sup>12</sup>

Dense pigment deposition in the trabecular meshwork explains the earlier and more severely elevated IOP in BAIT compared to BADI patients.<sup>3,12,18</sup> In the original BAIT series reported by Tugal-Tutkun et al.,<sup>12</sup> 54% of the patients had IOP rise during the disease course, and two patients with 4+ pigment in the anterior chamber required bilateral trabeculectomy with mitomycin C (MMC) at 3 and 9 weeks after symptom onset. Kreps et al.<sup>19</sup> reported ocular hypertension (OHT) in 4 (33%) of 12 BAIT patients, which was controlled with antiglaucoma drops in all cases. Tranos et al.<sup>13</sup> reported that IOP elevation was recorded in all 32 eyes of 16 patients with BAIT and OHT persisted for more than 3 weeks in 47% of eyes. Severe anterior chamber pigment dispersion and higher IOP during the first week were significantly associated with longer duration of OHT in their study. Anterior chamber washout of one eye in an attempt to reduce the pigment burden did not lower the IOP, and 4 eves (12.5%) required filtration surgery, which was reported to successfully lower the IOP in all cases.13 Wey et al.20 reported that gonioscopy-assisted transluminal trabeculotomy could be used effectively in a BAIT case and suggested that this procedure could be tried before considering trabeculectomy. Bayraktar et al.<sup>21</sup> reported successful results of trabeculectomy with MMC in 9 eyes of 6 patients with BAIT-associated OHT or glaucoma. The time interval between BAIT symptom onset and trabeculectomy ranged between 42 and 128 days in their study.21 In a more recent series, 7 (29%) of 24 BAIT eyes required trabeculectomy.<sup>18</sup> The time from symptom onset to trabeculectomy ranged between 1 and 12 months and IOP was successfully controlled in all cases after surgery.<sup>18</sup> Absence of intraocular inflammation may be an important factor in the long-term success of trabeculectomy despite ongoing pigment dispersion in the aqueous humor.

BAIT patients should be monitored regularly with IOP measurements until complete resolution of pigment circulation and for several months thereafter. The duration of the pigment circulation was reported to be 1-18 months (median 5 months).<sup>12</sup>

Rarely, it can recur months after complete resolution and persist for more than 3 years.<sup>7,17</sup> Iris transillumination and mydriasis are not reversible (Figure 2) and persistent photophobia can cause long-term discomfort despite visual acuity being well preserved.<sup>22</sup> Kreps et al.<sup>19</sup> reported that phacoemulsification with two aniridia rings in the capsular bag was performed in 5 eyes of 3 BAIT patients and photophobia largely resolved postoperatively.

# Unilateral Cases and Overlapping Cases of BADI and BAIT

Early reports of moxifloxacin-induced BAIT were associated with oral administration of this antibiotic.<sup>10,13,14,19,23</sup> However, there are more recent reports of unilateral BAIT-like cases following intracameral administration of moxifloxacin.<sup>24,25,26,27,28</sup> These reports support the notion that BAIT can be considered as an adverse ocular reaction of fluoroquinolone antibiotic use, primarily moxifloxacin.<sup>29,30</sup>

Both BADI and BAIT patients may occasionally present with asymmetrical severity that can be misinterpreted as unilateral involvement.<sup>7</sup> It is noteworthy that there are also cases with mixed BADI and BAIT features in one or both eyes (Figure 3) or BADI in one eye and BAIT in the other eye.<sup>7,18</sup> These findings support the notion that BADI and BAIT may represent different phenotypes of the same disease process. It is not clear why iris stromal pigment is exclusively affected in some patients, causing only the BADI picture without any transillumination defects or pupillary abnormalities, whereas the iris pigment epithelium is exclusively affected in others, causing the typical BAIT picture with diffuse transillumination and paralytic mydriatic



**Figure 2.** Slit-lamp photographs of a 44-year-old woman who presented with BAIT one month after moxifloxacin treatment for bronchitis in 2007 (initial presentation of this case was included in a previous publication12). Top row photographs were taken during follow-up in 2011, showing diffuse iris transillumination in the right (A) and left (B) eye. Bottom row photographs taken in 2016 show persistence of iris transillumination and mydriasis in both eyes

BAIT: Bilateral acute iris transillumination



**Figure 3.** Slit-lamp photographs of a patient with combined BADI and BAIT features in both eyes. The top row shows iris transillumination defects in the right (A) and left (B) eye. The bottom row shows areas of stromal depigmentation in the superior iris in the right eye (C) and inferior iris in the left eye (D)

BADI: Bilateral acute depigmentation of the iris, BAIT: Bilateral acute iris transillumination

pupils. However, the accumulated data have established that heavy pigment discharge from the iris pigment epithelium has much more serious consequences, including early intractable OHT and persistent photophobia due to irreversible diffuse iris transillumination and dilated fixed pupils. By contrast, BADI has a more benign course with a shorter duration of pigment discharge from the iris stroma, a lower incidence of IOP rise that is only transient, and iris changes that can be reversible.<sup>3,4,5,7,12,18</sup>

#### **Differential Diagnosis**

The differential diagnosis of painful red eves with ocular pain, tearing, and photophobia includes viral conjunctivitis, episcleritis/scleritis, acute iridocyclitis, and angle closure glaucoma. In fact, in a series reported from India, the authors questioned the role of topical fluoroquinolone antibiotics in the induction of BADI or BAIT, because 17 of 22 patients with BADI or BAIT had a history of topical fluoroquinolone antibiotic use for conjunctivitis or red eyes before the correct diagnosis was made.7 Based on our own experience, BADI/BAIT cases are more likely to be initially misdiagnosed as conjunctivitis in general ophthalmology practice. Similarly, misdiagnosis as acute iridocyclitis is fairly common. Absence of inflammatory keratic precipitates, presence of pigment particles only in the anterior chamber, and heavy pigment deposition in the trabecular meshwork are diagnostic clues before the detection of the typical iris changes of BADI or BAIT.

Viral iridocyclitis is almost always unilateral, thus differential diagnosis may be a challenge only for the rare unilateral presentations of BADI or BAIT. Inflammatory keratic precipitates and cells in the anterior chamber, sectoral or patchy atrophy of the iris with transillumination defects, irregular or distorted pupil, and elevated IOP are the characteristic features of herpetic iridocyclitis.<sup>31</sup>

Acute symptomatic pigment showering in pigment dispersion syndrome (PDS) should also be included in the differential diagnosis.<sup>32</sup> Common features also include accumulation of pigment in the anterior chamber angle, pigment dusting on the corneal endothelium as well as on the surface of the iris and lens, and midperipheral iris transillumination defects.<sup>32</sup> However, pigment deposition along Scheie's stripe on the posterior lens capsule, a diagnostic feature of PDS, is not found in BADI or BAIT. Posterior bowing of the iris, another key feature of PDS, is not seen in BADI and is not a consistent finding in BAIT.

## Etiopathogenesis

Although it has been almost two decades since BADI and BAIT were first described, the etiology is still unclear. The accumulated evidence on the causality of fluoroquinolone antibiotics, especially moxifloxacin, suggests a category of "probable/likely".<sup>29</sup> A history of antecedent respiratory tract infection is commonly reported, 3,12,13,14,19 but treated with antibiotics other than fluoroquinolones in some of the patients.<sup>3,12,13</sup> There have also been reports of cases following moxifloxacin intake for other conditions7,13,19 and a case of BAIT with urinary tract infection but without antibiotic treatment.<sup>15</sup> Simultaneous onset of BADI in two siblings following upper respiratory tract infection suggests that there may be underlying genetic factors.6 One of the siblings had a history of oral moxifloxacin use, but it was unknown in the other.6 Other triggers have been reported as well, including accidental exposure to insecticide spray, fumigation therapy, and pitcher plant extract injections to the face for chronic migraine.<sup>5,9,33</sup>

Viral serology for varicella-zoster virus, cytomegalovirus, Epstein-Barr virus, and herpes simplex virus has proven unhelpful<sup>3,4,6,7,12</sup> and polymerase chain reaction analysis of aqueous humor for these pathogens has yielded negative results.<sup>3,10,13,19,34</sup>

During the recent COVID-19 pandemic, a total of 19 cases of BADI and BAIT were reported, 18 cases from Turkey and 1 from India.<sup>16,18,34,35</sup> In the recent series of 16 patients from Turkey (12 with BAIT and 4 with BADI), the mean interval between the COVID-19 infection and onset of ocular symptoms was 2.5 weeks.<sup>18</sup> Nine patients were treated with oral moxifloxacin and 4 patients with other antibiotics.<sup>18</sup> These data again leave the question unanswered of whether the viral infection itself, the moxifloxacin use, or both are the underlying cause of iris pigment dispersion in individuals who may have a genetic predisposition.

# Conclusion

Although BADI and BAIT have the common feature of sudden-onset symptomatic pigment dispersion in both eyes, iris stromal depigmentation with a benign course is seen in BADI, whereas BAIT is characterized by iris pigment epithelial depigmentation and has a more protracted course with persistent mydriasis and potentially severe OHT. There are recent reports of atypical unilateral cases as well as reports of both phenotypes being found in the same eye or both eyes of the same patient. Oral moxifloxacin intake has been held responsible for several cases of BAIT, and there are recent reports of unilateral BAIT-like syndrome after intracameral moxifloxacin injection. Yet there are still reports of patients without any history of antibiotic treatment, including those who developed BADI or BAIT following COVID-19 infection. An increased awareness of the presentation patterns of BADI and BAIT will ensure timely diagnosis and avoid unnecessary investigations. Ophthalmologists should remain vigilant when history-taking to avoid missing a history of past or present systemic illness and medication use which might be the trigger of acute pigment dispersion. Fluoroquinolone antibiotics should be avoided in patients with a history of BADI or BAIT, as a rechallenge may potentially exacerbate pigment dispersion.

# Ethics

Peer-review: Internally peer-reviewed.

## Authorship Contributions

Concept: İ.T-T., Design: İ.T-T., Data Collection or Processing: İ.T-T., Ç.A., Analysis or Interpretation: İ.T-T., Ç.A., Literature Search: İ.T-T., Ç.A., Writing: İ.T-T., Ç.A.

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