Bilateral acute depigmentation of the iris. First report on the american continent and 5 years follow-up of two patients

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PURPOSE: To report the first cases of Bilateral Acute Depigmentation of the Iris (BADI) in the American continent, the first iris angiography of one such case, and a follow-up of two cases over several years.

METHODS: Two patients were diagnosed in a routine eye exam, and two others were retrieved from our photo archives, called for an appointment and re-examined. One patient underwent iris angiography.

RESULTS: Two male and two female patients were diagnosed, with a median age of 47 yrs (range 16 to 75). Only one patient recalled having had an episode of bilateral red eye during the past year. All but one had bilateral asymmetrical depigmentation of the iris stroma, extending from the iris root but not reaching the pupillary border, normal pupillary function, no transillumination defects and no anterior chamber cellularity or flare; intraocular pressure was normal in all patients. Iris angiography was normal showing a window defect where the iris atrophy was present. In the 2 patients with years of follow-up, the depigmented iris became only partially re-pigmented and re-thickened.

CONCLUSION: Patients with BADI syndrome have bilateral, asymmetrical depigmentation of the iris stroma, without transillumination or pupillary deformities. The depigmentation and anterior stromal atrophy cedes partially over time. No etiology has been established.

INTRODUCTION

Acquired iris hypochromic heterochromia is an unusual finding and necessitates careful study of the patient to rule out serious and treatable entities such as herpetic keratouveitis, Fuchs’ heterochromic uveitis and Horner’s syndrome, among other.

Bilateral Acute Depigmentation of the Iris Syndrome (BADI) is a poorly known entity, first described by Tukal-Tutkun et al in 2005¹. To date, 28 patients with this syndrome have been described², all Turkish except for one French patient³, predominantly females in their third decade of life. This is a non-progressive bilateral, asymmetric entity of abrupt onset and short course, producing geographic atrophy of the iris stroma which eventually generates a very characteristic grayish granular appearance, without iris pigment epithelium involvement, compromising mainly the peripheral and superior iris¹-³. There is slow recovery showing partial repigmentation with the passage of years². All cases reported to date have been brown irises. There is no association with visual acuity alterations, segmental or diffuse pupillary abnormality, or iris transillumination defects.

To our knowledge, these are the first reported cases of BADI on the American continent, and the first case worldwide with an iris angiography.

METHODS

Two asymptomatic patients were diagnosed during a regular ophthalmological exam, prompting us to review our photo archives, where we identified two other patients.
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seen years previously complaining of spontaneous iris color change and on whom we had no diagnosis to date; these two latter patients were called and re-examined.

Laboratory tests on the two most recent patients included erythrocyte sedimentation rate, complete blood count, biochemistry, serum immunoglobulin G and M antibodies against Herpes Simplex virus I and II, Varicella-Zoster virus, Cytomegalovirus, Epstein-Barr virus, and chest x-rays. The two patients retrieved through the photo archive were not studied as they were considered to have a long standing process in resolution. An iris angiography was performed in one of the patients.

RESULTS

There were two female (35 and 62 yrs old) and two male (29 and 75 yrs old) patients. The two younger patients had consulted years previously after noticing an otherwise asymptomatic change in their iris color; in the two older patients this was an incidental finding during a routine ophthalmological examination; one of these latter patients recalled having an episode of bilateral red eye during the preceding year.

The iris aspect was surprisingly similar in all four patients: brown color, irregular geographic atrophy of the iris stroma, starting at the iris root with a sharply defined internal (pupillary) border and lesser compromise of the pupillary iris; the compromised iris had a grayish powdery aspect while the non-compromised iris looked absolutely normal (Figures 1-8); there was a sharp delimitation between the affected and healthy iris, with no pigment liberation to the anterior chamber, corneal endothelium or anterior chamber angle; pupil aspect and functionality were normal, with no distortion or motility alterations, and there were no transillumination defects. Intraocular pressure and corneal sensitivity were normal.

An iris angiography was performed in two patients (Figure 9), showing a normal circulatory timing and...
pattern, with radially oriented vessels, without pupillary or stromal leakage, and therefore with no signs of ischemia. The only novelty was that the iris vessels were more easily observed at the stromal iris atrophy areas due to a window defect.

Two of our patients were seen regularly for 3 and 5 years, observing a pattern of slow and gradual recovery of the initially involved iris sectors, although they never returned to complete normality (Figures 10 - 13). During this time frame, the initially unaffected area remained exactly the same (there was no enlargement of the initial insult), while the originally affected area slowly lost its grayish powdery aspect, with the iris becoming increasingly thicker and more normal in appearance.

**DISCUSSION**

BADI syndrome is a recently described entity, with unknown etiology and physiopathology. It predominantly affects women in their third decade with brown irises. It has a sudden onset, sometimes with red eye but otherwise asymptomatic, with bilateral and asymmetric involvement, slowly regressing without functional sequelae.

Twenty-eight cases have been reported to date worldwide, 27 in Turkey and one in France. To our knowledge, ours are the first cases reported on the American continent, and the first to undergo iris angiography worldwide. None of our patients attended our department complaining of red eye: the two younger
patients did so complaining of a color change in their irises, while in the two older patients, the condition was an incidental finding during a first time ophthalmological examination; one of these older patients is the only one with a strictly unilateral presentation, which we believe could be explained by the initial insult having occurred many years ago, during which time it has been slowly recovering until it has become unnoticeable in one eye.

The exclusive involvement of the iris stroma, in a capricious pattern not related to vascular or neurological distribution, the rare involvement of the pupillary iris, the absolute respect for the pupillary form and function and for the iris pigment epithelium, as well as the absence of any other sign of intraocular involvement (keratic precipitates, iris nodules, Tyndall, hypertension, etc.) are worth noting.

Figure 9. Right eye iris angiography, same patient as in Figure 1. Radially oriented, undisturbed, continent iris vessels, evident where there is stromal iris atrophy due to a window defect effect.

Figure 10. Same patient as Figure 1, 3 yrs after initial presentation. Right eye. There is considerable improvement of the affected iris, but still not complete; the originally involved iris is not grayish but more of a light brown color.

Figure 11. Same patient as in Figure 2, 3 yrs after initial presentation. Left eye.

Figure 12. Same patient as in Figure 3, 5 yrs after initial presentation. Right eye. Note how although the difference between the originally involved and healthy iris is still apparent, it is much less so. While the originally involved iris has an almost normal appearance, its contraction sulci are very apparent, and it looks thinner than the uninvolved iris.

Figure 13. Same patient as in Figure 4, 5 yrs after initial presentation. Left eye.
An ischemic etiology has been empirically suggested, but only now has an iris angiography been done and reported as completely normal, thereby excluding the ischemic hypothesis. Moreover, for an ischemic basis to be considered, one would expect progressive pupillary deformity and iris segmental atrophy with transillumination defects with the passage of time, which does not happen. On the contrary, in this report, as well as in a previous one, it has been observed that the initial iris stromal defect tends to slowly subside with the passage of time.

The reversibility of the iris pigment alterations suggest that it is not related to an active viral infection or iris inflammation, but could be the end result of some type of neuropathy.

A viral etiology (HSV, VZV) has been suggested, and some authors have empirically prescribed oral acyclovir, but this diagnosis has never been confirmed, and it would be very unusual to have simultaneous bilateral intraocular viral involvement.

Among the causes of acquired hypochromic heterochromia is Fuchs’ heterochromic iridocyclitis; however, it is unilateral in over 90% of cases, has characteristic fine PKs, involvement of the iris pigment epithelium, a chronic course over the years, and there is no regression of the hypochromia.

Pigmentary dispersion syndrome has a characteristic bilateral presentation with irreversible iris transillumination defects, pigment deposition on the corneal endothelium and anterior capsule, and has a slowly progressive and irreversible course.

Acute primary ischemic iris atrophy has an acute unilateral presentation with irreversible transillumination defects and pupil distortion, as a consequence of medium-sized iris vessel involvement of unknown etiology.

Ito’s Syndrome (Incontinentia Pigmenti Acromians) is a congenital entity comprising irreversible bilateral hypochromic nevi of the iris associated with multiple dermatologic, neurologic and musculoskeletal abnormalities.

Vogt Koyanagi-Harada syndrome causes iris hypochromia, but is progressive, irreversible and frequently accompanied by iris transillumination defects, pupil scission, chronic intraocular inflammation and choroidal involvement, among other signs.

Alterations in the sympathetic stimulation to the melanocytes of the superficial iris stroma can lead to ipsilateral hypochromia, a well known finding in Horner’s Syndrome, both congenital and acquired. However this is strictly unilateral, and accompanied by miosis, ptosis and anhidrosis, among other signs.

Finally, iris infiltration by metastatic non-pigmented tumors can produce asymmetrical bilateral hypochromia, but upon slit lamp examination the increase in the thickness of the iris involved is evident, and systemic workup will reveal the primary tumor location.

In conclusion, BADI syndrome is an entity whose etiology and physiopathology is still unknown seven years after being reported for the first time. We know it is a bilateral, asymmetric, non-ischemic, spontaneously reversible entity with no apparent ophthalmological sequelae.

Among the proposed physiopathological mechanisms, the neuropathic one seems more likely than infectious, inflammatory or ischemic mechanisms, as no evidence of microorganism involvement has been identified by PCR or other methods, there is no concomitant intraocular inflammation and the iris angiography is normal.

REFERENCES