• Letter to the Editor •

Clinical analysis of bilateral acute depigmentation of the iris: first reported case in China

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Dear Editor,

We are writing this letter to present a rare case of bilateral acute depigmentation of the iris (BADI). The case of BADI has not reported in China before, and this case report can help ophthalmologists to identify the clinical features of this disease. Written informed consent was obtained about the use of medical record for the case report from this patient. This case study adhered to tenets of Declaration of Helsinki.

On August 15, 2020, a 28-year-old man initially visited our outpatient department of ophthalmology with the complaint of sudden redness, pain, and photophobia in both eyes for two days, accompanied by lacrimation, foreign body sensation and slightly decreased vision. On July 16, 2020, the patient was treated with levofloxacin ear drops (1 drop, both ears, Tid) and oral moxifloxacin hydrochloride tablets (400 mg, Qd) because of diagnosed tympanitis of both ears. The symptoms were alleviated after 7d of treatment.

Ophthalmic examination: best-corrected visual acuity (BCVA) was 0.6 in the both eyes (no ametropia), and there was ciliary and conjunctival congestion in both eyes (Figure 1). Both corneas were transparent with visible dusty keratic precipitates (KPs). These KPs were formed by pigment granules and deposited on the infero-posterior surface of corneas. The anterior chamber (AC) had a normal depth and contained scattered, floating pigment granules. There was diffuse depigmentation in the anterior surface of the iris in both eyes (Figure 1), with normal pupil size and pupillary light reflex, without pupil conglutination. The lens, optic disc, and retina were normal. Intraocular pressure (IOP) was 9.0 mm Hg in the right eye and 7.7 mm Hg in the left eye [non-contact tonometer (NCT)]. Gonioscopy examination showed substantial pigment deposition in the inferior AC angle in both eyes (Figure 2). Ultrasound biomicroscopy (UBM; SUOER, SW-3200L, China) showed that the diffuse depigmentation was located in iris stroma, and a small number of enhanced spot echoes located in the AC (Figure 2). Optical coherence tomography (OCT, Carl Zeiss, Germany) revealed a normal optic disc and posterior pole of retina. He was treated mainly with dexamethasone eye drops and eye ointment (TobraDex, Novartis, China), of which eye drops were given 3 times a day and eye ointment was given once at bedtime in both eyes. After 10d of treatment, symptoms of both eyes were alleviated gradually. The BCVA of his bilateral eyes recovered to 1.0, the ciliary congestion was alleviated, and pigmental KP was still observed in the posterior surface of the cornea. The floating pigmentation in the aqueous humour was reduced, and no further depigmentation in the iris was observed by slit lamp examination. The IOP (NCT) was 13.2 mm Hg in the right eye and 14.5 mm Hg in the left eye.

On September 3, 2020, the patient complained of recurrent tympanitis and was treated with levofloxacin ear drops (1 drop, both ears, Tid) and moxifloxacin hydrochloride tablets (400 mg, Qd) again. There was no organism isolated by ENT specialist in this case because patient's symptoms were relieved significantly after empirical broad-spectrum antimicrobial therapy. On September 16, 2020, patient revisited outpatient department with a recurrence of redness, pain, and moderate photophobia in both eyes. Ophthalmic examinations were same as the first episode of attack. The laboratory tests performed on the patient showed that immunoglobulin G (IgG) antibodies against herpes simplex virus type I and II, rubella virus and human cytomegalovirus were elevated, but immunoglobulin M

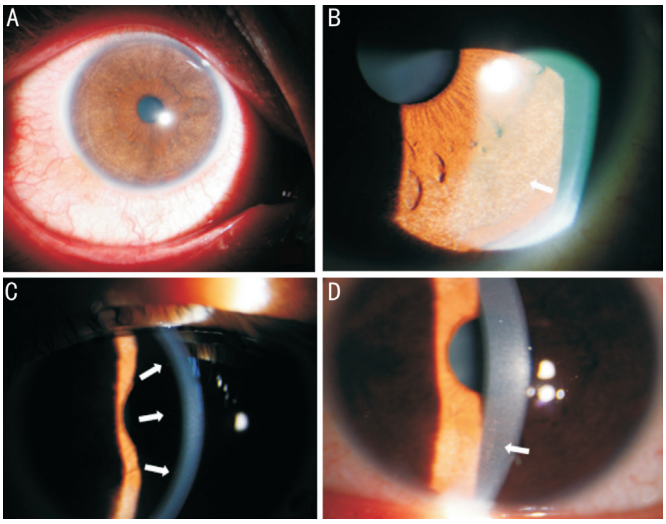

Figure 1 Slit lamp microscopy A: Ciliary and conjunctival congestion in the active stage of BADI (right eye). Massive pigment deficiency can be seen in the mid-peripheral iris. B: Due to a defect of part of the iris stroma, the underlying stroma is visible (left eye, white arrow). C: A few pigmented particles existing in the AC (white arrows). D: KPs deposited on the posterior surface of the inferior cornea was formed by pigment granules (white arrow). BADI: Bilateral acute depigmentation of the iris; AC: Anterior chamber; KP: Keratic precipitates.

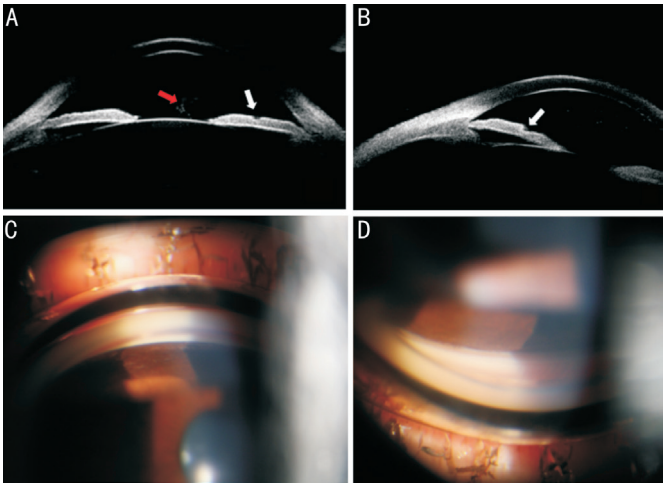

Figure 2 UBM and Gonioscopy A, B: The iris is thin in part of the mid-periphery, and a significant stromal defect in the iris can be seen (white arrow). Some high-density shades existed in the AC (red arrow). C: Massive pigment deposition in the inferior AC angle. D: A small amount of pigmentation in the superior AC angle. AC: Anterior chamber.

(IgM) antibodies were within the reference ranges. After 3wk of treatments by dexamethasone eye drops and eye ointment, the symptoms of both eyes were relieved gradually. Both eyes' BCVA recovered to 1.0, the ciliary congestion was alleviated. Less dusty KPs deposited on the posterior surface. The floating pigmentation granules in AC was reduced but the iris depigmentation was observed persistently. The ear and ocular symptoms did not recur at the 4-month follow-up. The patient felt satisfied with the effect of the treatment.

We believed that the patient's clinical symptoms and ophthalmological examinations were consistent with the diagnostic criteria of the rare disease, BADI, reported worldwide before. The first report of BADI was proposed by Turkish Tugal-Tutkun and Urgancioglu[1] in 2006, followed by scattered cases reported in Turkey, India, the Netherlands, Belgium, Spain, France, Brazil, and the United States. There is no relevant article reported in China according to the database query, and this case may be the first one reported in China. Current clinical case reports indicate that the symptoms of the disease mainly include acute attacks of severe photophobia, eye redness, eye pain, and decreased visual acuity in both eyes[2]. Ophthalmic examination revealed symmetrical diffuse or patchy depigmentation in the iris stroma, floating pigment granules in the AC, a small amount of pigmentary KPs depositing on the posterior surface of cornea, substantial pigment deposition in surface of trabecular meshwork, round and equal pupils in the bilateral eyes with normal light reflex, and often, fundus showed no significant abnormalities[2].

BADI needs to be differentiated from the bilateral acute iris transillumination (BAIT), which is also a new clinical condition. Patients with BAIT generally present with acute ocular pain, photophobia, and red eyes, with greater intensity than that in BADI. BAIT is characterized by severe transillumination of the iris and acute onset of melanin granules in the AC. Moreover, it is also characterised by mydriatic pupils, unresponsiveness or poor responsiveness to light, and temporary ocular hypertension. The melanin granules of BAIT seem to be shed from the iris pigment epithelium, but BADI is characterized by a depigmentation of the stroma[3-4]. The patient's symptoms seemed to be more in line with the diagnostic criteria of BADI. BADI needs to be differentiated from pigment dispersion syndrome (PDS). It is widely accepted that posterior bowing of the iris resulting in irido-zonular friction and subsequent pigment liberation is the underlying cause of PDS. With most of the trabecular meshwork blocked by melanin granules, the IOP of PDS patients may be elevated and develop pigmentary glaucoma[5]. In this reported case, UBM showed that the stroma of the iris was deficient, and without iris bowing, the anterior and posterior lens capsules had no pigmentation. Therefore, the clinical diagnosis in this case was not consistent with PDS.

Some researches supported the theory of viral hypothesis. Tugal-Tutkun *et al*[2] performed a viral serological examination in 10 of 26 cases of BADI. Antibodies against cytomegalovirus were positive in 10 cases. Maestrini *et al*[6] reported significant improvement in ocular symptoms after antiviral therapy in a patient diagnosed with BADI, which supported the viral

infection theory of the disease. The collection of aqueous humor samples by AC paracentesis for viral DNA/RNA analysis was considered. However, the patient declined the procedure because of his symptoms alleviated after effective treatment. The laboratory examination of the patient showed IgG antibodies against herpes simplex virus type I and II, and rubella virus and human cytomegalovirus were found to be elevated. We speculate that there may be a correlation between the occurrence of the disease and viral infection.

According to World Health Organization criteria, the relationship between fluoroquinolone (FQL) therapy and uveitis is "possible". Hinkle *et al*[7] put forward that clinicians should be aware of a possible bilateral fluoroquinolone-associated uveitis, particularly the finding of iris transillumination and pigment dispersion. In this case, patient presented symptoms of BADI on two separate occasions following the use of high doses of FQL for tympanitis. Integrating with other case reports worldwide, we speculated that the occurrence of BADI may be related to the use of FQL, especially moxifloxacin, but the specific mechanism has been not clear yet. Clinicians should warn the patient and other disciplines against the use of FQL in patients who have a history of BADI, which can reduce the risk of BADI occurrence and relapse.

According to the medical history of this patient, it can be speculated that the occurrence of the disease may be related to inflammation. The source of inflammation may be related to tympanitis, which has not been reported in the previous literature. However, the specific pathogenesis still needs further in-depth study.

Through a search of PubMed, CNKI, Wanfang, and other literature platforms, it was found that this case was the first BADI patient reported in China. There are few reports on the disease, and according to its clinical features, it is easily confused with some existing uveal diseases. With missed diagnosis in the clinic, the actual number of cases may be higher than that reported in the literature. Through the reporting and analysis of the clinical features and aetiology, we hope that the diagnosis of the disease can be standardized so that we can fully and correctly recognize it and reduce the misdiagnosis of BADI. At present, the causes and pathogenesis of the disease are not well understood, and increasingly in-depth studies on the pathogenesis of BADI are needed to clarify its real aetiology and pathogenesis in the future.

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