• **Letter to the Editor** •

Iridoschisis misdiagnosed as acute angle-closure glaucoma: a case report and literature review

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Dear Editor,

We present the case of a patient with iridoschisis complicated with cataract, peripheral anterior synechiae (PAS), secondary glaucoma, and corneal endothelial damage. The patient was initially misdiagnosed with acute angle-closure glaucoma. Iridoschisis is a rare condition characterized by the splitting of the iris into two layers: the anterior layer breaks down into fibers, floating freely in the anterior chamber with a "shredded wheat" appearance. In addition, the former layer of decomposed fibers may also come into contact with the corneal endothelium forming PAS, while the posterior layer attaches to the dilator muscle and pigment epithelium. Iridoschisis was first described by Schmitt in 1922[1], and the term "iris splitting" was first proposed by Lowenstein and Foster in 1945[2]. Iridoschisis occurs mostly in patients of 60 to 70 years of age, and its etiology is still unclear. Angle-closure glaucoma is a common problem associated with iridoschisis, whereas corneal endothelial decompensation is relatively rare, as previously reported[3-6]. Other complications include cataracts, lens dislocation, keratoconus, and syphilitic interstitial keratitis[3-6]. Generally, iridoschisis without complications does not need treatment. Sometimes, improper treatment may result in the aggravation of the disease. Because this disease is uncommon in clinics and rarely reported, some ophthalmologists have inadequate knowledge about it, resulting in insufficient measures to treat it. We report the case of a patient with iridoschisis complicated with cataract, PAS, secondary glaucoma, and corneal endothelial damage. The patient was initially misdiagnosed with acute angle-closure glaucoma. Phacoemulsification with bag-in-the-lens implantation and a peripheral iridectomy were performed. We compared the manifestations of iridoschisis under different pupil states. For the first time, we investigated possible gene mutations related to iris dysplasia using peripheral blood gene testing. This study followed the principles of the Declaration of Helsinki, and it was approved by the Ethics Committee of West China Hospital of Sichuan University (2019, No.53). All subjects fully understood the purpose of the study and provided written informed consent.

A 71-year-old male was admitted with a complaint of painless decreased vision in the left eye during the last year. His right eye had been enucleated because of ocular trauma that had occurred 30y before admission. The patient was scheduled for cataract surgery in the left eye at a local hospital. However, the surgery was canceled because of increased intraocular pressure (IOP) and corneal edema during pupil dilation. After the administration of pilocarpine, mannitol (250 mL) and pyrimine to reduce IOP, the left cornea regained transparency, and the IOP returned to normal. The patient was diagnosed with acute angle-closure glaucoma in the left eye and was transferred to our hospital. A full ophthalmologic examination of the left eye was performed. The vision acuity (VA) was 20/600, and the IOP was 9.7 mm Hg. The periphery of the cornea was clouded. The central anterior chamber depth was 4.73 mm, and the anterior chamber angle was N IV (Scheie classification; Figure 1). Gonioscopy demonstrated PAS in all quadrants. The nasal portion of the iris was loosened, and cable-like tissue was visible in the upper, temporal, and lower iridoschisis. Figure 2A1 showed upper, temporal, and lower iridoschisis with PAS and cataract. Both ends of the cleavage matrix bands were connected to the iris center, one end of the cleaved matrix band was connected to the iris center and the other end adhered to the anterior cornea, or one end of the cleavage matrix band was connected to the iris center and the other end floated in the anterior chamber.

Figure 2A2 showed the ultrasound biomicroscopy (UBM): anterior chamber angle, disorganization of the iris separation, iris, and corneal endothelium adhesion. Figure 2A3 showed the anterior-segment optical coherence tomography (AS-OCT): enhanced reflection can be seen in the superficial stroma, epithelium, and endodermis of the peripheral cornea. Separation of the anterior iris stromal layer and contact of iris fibrils with the posterior cornea open angle at 10 and 5 o'clock can be observed. The fundus was not clearly visible because of the cataract. The corneal endothelium could not be evaluated, and the thickness of the central cornea was 515 μm. The eye axial length was 22.35 mm. The patient was diagnosed with iridoschisis (OS), senile cataract (OS), and secondary angle-closure glaucoma (OS). A rapid plasma reagin test for syphilis was negative. DNA was extracted from the patient's blood samples for whole-exome sequencing and Sanger sequencing. Genetic testing revealed a heterozygous variation (chr4:111544132–111544132) on the intron of the paired like homeodomain 2 (PITX2) gene. After administering antibiotic eyedrops and pilocarpine (Figure 1B), Figure 2B1–2B3 shows the preoperative shrinkage of the pupil of the left eye. Loose improvement of the pre-iris matrix fiber was showed in Figure 2B1. The separation of the anterior iris stroma is improved and the contact area between iris fibers (Figure 2B2 and 2B3), phacoemulsification with bag-in-the-lens implantation and peripheral iridectomy were performed on the left eye under local anesthesia. Mannitol (250 mL) was administered during preoperative pupil dilation to avoid an acute attack of glaucoma. The posterior margin of the cornea is reduced (Figure 2C1–2C3). Figure 2C1 showed the upper, temporal, and lower PAS with lens opacity. Figure 2C2 and 2C3 showed the iris built up in the anterior chamber angle, blocking the anterior chamber angle. Anterior chamber angle narrowed at 10 and 5 o'clock. The operation was uneventful. Peripheral iris adhesion was separated as far as possible (approximately 90°), and the split iris was removed for pathological examination. On the first day after surgery, an ophthalmological examination revealed that VA and IOP of the left eye were counting finger (CF)/30 cm and 15.6 mm Hg, respectively. Slit-lamp examination revealed widespread corneal edema with inferior bullous lesions in the left eye. Patent peripheral iridotomies were observed at the 1 o'clock position. The intraocular lens was in place. Anterior-segment photographs showing corneal edema and bullous keratopathy, and unblocked peri-iris incision at one point. The intraocular lens is in place (Figure 3A1). AS-OCT image showing that the cornea was thickened, the anterior iris adhesion was significantly improved, and the anterior chamber angle was essentially open (Figure 3A2). One week after surgery, the central cornea regained transparency. Transparent cornea and temporal PAS are evident. The intraocular lens

was in place (Figure 3B1). Corneal thickness was significantly improved, and the anterior iris adhesion was also significantly improved (Figure 3B2), and the VA increased to 15/25. Best-corrected VA was 20/25, and the IOP in the left eye was 10 mm Hg. Fundus color photography and optical coherence tomography yielded normal results.

Iridoschisis is typically bilateral and is often located in the inferior quadrants. The pigment epithelium can be seen in the defective posterior stromal fiber, and the reflection of pigment epithelium is continuous. The pathogenesis of iridoschisis is currently unclear. It might develop because of age-related changes, blunt trauma, syphilis, or secondary glaucoma. Mansour[7] reported on families with iridoschisis, narrow chamber angles, and senile cataract and speculated that iridoschisis might exhibit autosomal dominant inheritance. Our patient had iridoschisis, a short ocular axis, a narrow anterior chamber angle, extensive PAS, cataract, corneal endothelial dysfunction, and other manifestations in the eyes. Therefore, we conducted genetic testing on the patient; however, no definite pathogenic variation related to disease phenotype was found. Interestingly, we found a heterozygous variant in an intron in chr4 of PITX2 (111544132-111544132), but this variant is not considered to be disease-causing. PITX2 is a homologous domain transcription factor that regulates the development of the anterior segment, branchial arch, heart, and pituitary gland[8-11]. Studies on PITX2 in animal models have confirmed its key role in ocular and craniofacial development[8]. Sequence variations in PITX2 are associated with iris dysplasia type 2, Axenfeld-Rieger syndrome type 1, annular dermoid of the cornea, and other diseases[12]. Considering the patient's condition, the disease may have been caused by changes associated with old age. Diagnoses should be differentiated from Axenfeld-Rieger syndrome type 1 based on clinical manifestations and genetic testing results. Extensive PAS caused by iridoschisis, secondary glaucoma, or corneal endothelial dysfunction are rare. Extensive PAS may be caused by iris fibers floating in the anterior chamber, combined with a short ocular axis and shallow peripheral anterior chamber. Due to mechanical injury caused by contact between iris fibrils and the fragile corneal endothelium, corneal endothelial cells die, resulting in a decrease in corneal endothelial cells and compensatory enlargement of surrounding corneal endothelial cells, resulting in a decrease of total corneal endothelial cells. Therefore, the removal of the adhesive iris is necessary to prevent further damage to the corneal endothelium. Most patients with iridoschisis are older and often have cataracts. The corneal endothelial cell count for our patient was not determined in the preoperative examination; however, the cornea in the anterior region with the adhesion of the peripheral iris was thickened and clouded, and corneal
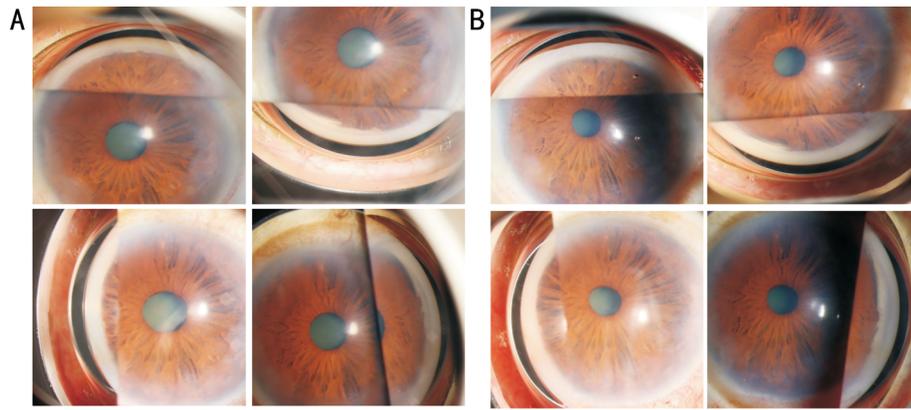
Figure 1 Gonioscopy images showing peripheral anterior synechiae in four quadrants (A) that exhibited no change after miosis (B).
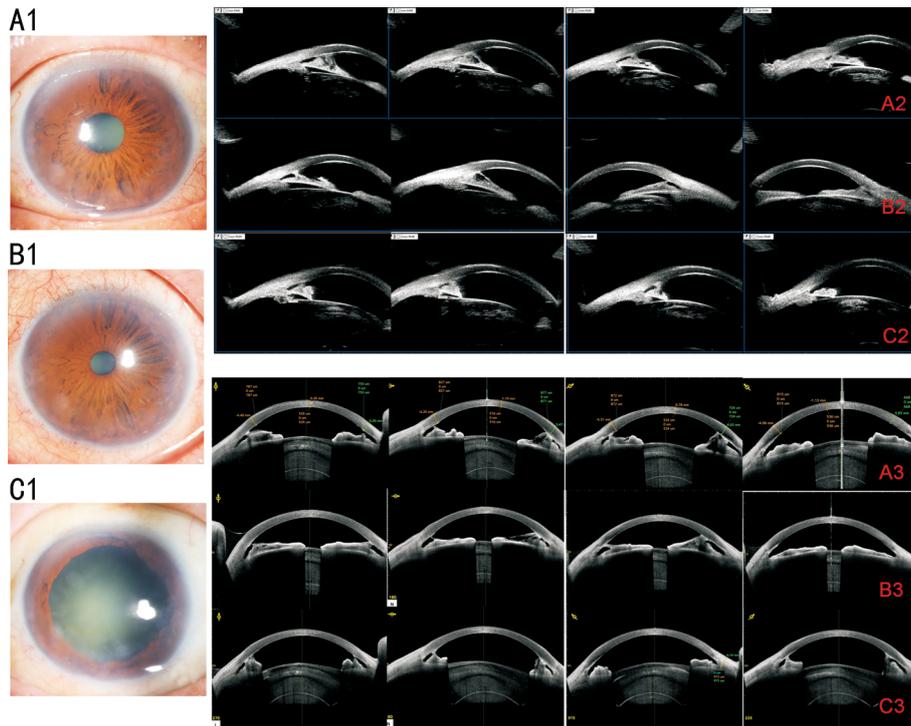
Figure 2 Preoperative imaging of the left eye The patient's left eye before (A1) and after pupillary constriction (B1), and after preoperative pupil dilation (C1). Ultrasound biomicroscopy of the same eye before (A2) and after pupillary constriction (B2), and after preoperative pupil dilation (C2). Anterior-segment optical coherence tomography of the same eye before (A3) and after pupillary constriction (B3), and after preoperative pupil dilation (C3).
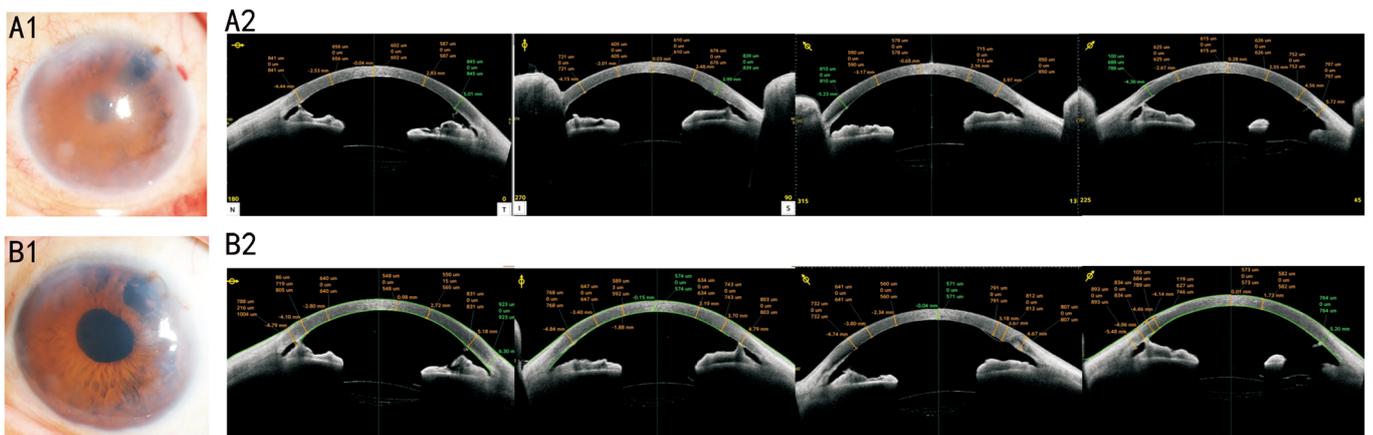
Figure 3 Anterior-segment photographs and optical coherence tomography images corresponding to postoperative days 1 (A) and 7 (B).

endothelial function was impaired. In patients undergoing phacoemulsification, corneal endothelial decompensation may occur after surgery, requiring corneal transplantation[13]. Previous studies suggest that bullous keratopathy secondary to iridoschisis can be successfully managed by corneal transplantation, including endothelial keratoplasty, non-Descemet's stripping automated endothelial keratoplasty, or Descemet's membrane endothelial keratoplasty[5,13-14]. Fortunately, corneal transparency was restored in our patient, and VA improved a week after surgery. This suggests that postoperative corneal endothelial decompensation may disappear a few days or weeks after surgery, and it is difficult to determine the timing of endothelial keratoplasty again[13]. Patients with iridoschisis and a shallow anterior chamber should be closely followed up for iridotrabecular and iridocorneal contacts. The iridotrabecular contact index or iridocorneal contacts can be assessed by AS-OCT in patients with iridoschisis[5]. To avoid further corneal endothelial injury and secondary glaucoma caused by PAS, cataract surgery should be performed as soon as possible when such contacts are accompanied by reduced endothelial cell density in the cornea. During cataract surgery, loose iris tissue can easily obstruct the superlactation suction head, resulting in iris tissue damage. At present, the free stromal fibers can be fixed using an ophthalmic viscosurgical device[15], and the microcautery or vitrector trimming techniques can eliminate or contract the fibers[16]. The vitreocutter can excise loose anterior iris fibers[17]. A flexible iris hook[18] and a Graether pupil expander[19] can be applied, and long free iris strands can be cut using Vannas scissors[20]. Our patient underwent cataract surgery without a pupillary device. During surgery, the opening of the ultrasonic emulsifying head should be as far as possible to split the iris from the back to avoid further damage to the iris.

This study evaluated the manifestations of iridoschisis in different pupil states and suggested that phacoemulsification with bag-in-the-lens implantation and a peripheral iridectomy may be an effective treatment for iridoschisis complicated with cataract, PAS, and secondary glaucoma. In iridoschisis, pupil dilation may lead to the anterior chamber angle and increased IOP; however, corneal edema is more likely to occur because of poor corneal endothelial function. Therefore, mydriasis must be fully evaluated, and abnormal iris tissue in contact with the cornea should be surgically released, with regular postoperative follow-up. In cases of corneal endothelial decompensation, corneal endothelial transplantation should be performed. To the best of our knowledge, this has not been previously reported. Moreover, genetic tests were carried out on a patient with iridoschisis for the first time. Further, ocular observation and genetic testing of the family members are needed to identify potential genetic causes of iridoschisis.

Patients with iridoschisis require long-term regular follow-up of the corneal endothelium, IOP, UBM examination, and iridotrabecular contact index or iridocorneal contacts, while the associated complications should be actively treated.

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