

## **The treatment of refractory angle-closure glaucoma in a patient with X-linked juvenile retinoschisis**

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X-Linked Retinoschisis (XLRs) is a common genetically determined form of macular degeneration affecting young males. Worldwide estimates of XLRs prevalence range from 1:5000 to 1:20000.<sup>1</sup> We report a thirty-nine-year-old man with refractory angle-closure glaucoma and genetically confirmed XLRs. The patient's retinal phenotype was atypical due to extensive exudative retinal detachments suggesting multiple mechanisms contributing to his glaucoma.

The patient presented with a two-day history of left eye pain and acutely reduced vision, on a background of a 9-month history of left sided hemicranial pain. His baseline visual acuity was counting fingers OD and 20/120 OS. On oresentations, visual acuity was hand movements OD and 20/300 OS. Prior IOP measuremets were 19mmHg OU, however, during this acute presentation IOP OS was 52mmHg and there was conjunctival injection, diffuse corneal oedema and a very shallow central and peripheral anterior chamber. Gonioscopy confirmed a completely closed angle. There was no iris or angle neovascularization, no posterior synechiae and no iris bombé. The crystalline lens was bulging anteriorly with visible glaucomflecken, but no frank phacodonesis. He patient was hypermetropic (OD +3.00/-1.00 x 120, OS +5.00/-1.25 x 25). The right eye was pseudophakic with inferior intraocular lens subluxation and he was treated for ocular hypertension. There was previously a dense white

cataract in the right eye before cataract surgery was performed, and no history of ocular trauma. The left eye was phakic and was his better-seeing eye. Ophthalmoscopy showed a 360 degree retinal fold OD with a nasal tractional retinal detachment and a cup-to-disc ratio of 0.3. There was no view of the left fundus due to the corneal opacification. Clinical and genetic analyses related to his XLR5 disease had previously been undertaken by an Institutional Review Board approved study. He carried the NM\_000330.3(RS1): c.574C>T (p.Pro192Ser) mutation.

The patient was managed medically with 1 gm of intravenous acetazolamide, and topical timolol/ dorzolamide, latanoprost, iopidine and dexamethasone drops in his left eye. IOP OS decreased to 46mmHg, with the corneal oedema clearing sufficiently to permit a YAG laser peripheral iridotomy. Following iridotomy, his IOP was 45mmHg and the iridocorneal angles remained closed. Anterior segment imaging and B-scan ultrasound excluded choroidal effusions. His chronic exudative retinal detachment, which had previously been noted in both eyes, remained unchanged. The axial lengths were 20.8mm (OS) with an anterior chamber depth (ACD) of 1.6mm (OS), compared to 20.9mm (OD) and ACD of 4mm with the subluxed lens (OD) suggesting possible zonular laxity in the right eye. Anterior segment imaging showed an anteriorly vaulted lens, hence the patient was instructed to lie supine and was given topical cyclopentolate 1%. Six hours following this, the IOP decreased to 36mmHg but the iridocorneal angle remained closed. Urgent cyclodiode ablation of the ciliary body was performed the same day and the IOP decreased to 24mmHg two hours post-laser.

A week later, the pressure in the left eye was 7mmHg with ongoing treatment with topical cosopt bid, latanoprost qhs, iopidine tid and dexamethasone qid. Two weeks

later, the IOP rose again to 43mmHg and he underwent a left lens extraction and IOL implantation without complications, and the patient was given a stat dose of atropine 1% post-operatively to reduce the risk of aqueous misdirection. Following surgery, his IOP decreased to 10mmHg to 14mmHg on without the need for glaucoma drops. His iridocorneal angle remained open. His vision improved to 20/100.

This case posed a difficult challenge given that this was a young patient with an 'only eye', whose acute rise in IOP was uncontrolled with medical treatment. Furthermore, he had a complex genetic retinopathy including XLRS but perhaps also another undiagnosed hereditary ocular condition that was responsible for his extensive bilateral exudative retinal detachments.

According to Ritch's anatomical classification of angle-closure (pupil block, plateau iris/ non-pupil block, lens-induced angle-closure and retro-lenticular causes)<sup>2</sup>, this patient is unusual as his mixed mechanism angle-closure glaucoma included all four levels of block. Our patient underwent systematic investigation and treatment to exclude each of these levels of angle-closure. After failure of initial medical treatment, he underwent a laser peripheral iridotomy to relieve any pupil block component. An anterior segment optical coherence tomography scan was able to rule out plateau iris configuration and confirmed the clinical finding that the crystalline lens was bulging anteriorly. The B-scan ultrasound showed heavy calcification in the area of chronic exudative retinal detachment.

At the molecular level, XLRS is due to mutations in the *RS1* gene located on chromosome Xp22<sup>3</sup>. *RS1* codes for retinoschisin, a protein known to play an important role in cellular fluid balance, cellular adhesion and cell–cell interactions across bipolar-photoreceptor synapses. Absence of retinoschisin in XLRS patients subsequently leads to pathological extracellular fluid accumulation and reduced bipolar-photoreceptor integrity<sup>3</sup>. XLRS patients are also at increased risk of developing ocular complications such as vitreous haemorrhage and retinal detachment<sup>4</sup> but angle-closure glaucoma has not been reported previously.

Our patient had the NM\_000330.3(*RS1*): c.574C>T (p.Pro192Ser) mutation. This *RS1* mutation has been reported in other families<sup>4,5,6</sup> but the specific phenotypic details relating to glaucoma such as axial length, refraction, and IOP were not available in the published reports. Interestingly, XLRS, is just one cause of macular retinoschisis, of which there are several known causes, such as retinitis pigmentosa, myopic degeneration and vitreo-macular traction. Of note, there are two case reports of angle-closure glaucoma in peripapillary schisis<sup>7</sup> and macular schisis<sup>8</sup>. In both these cases, and our own, the mechanism of interaction between the retinal disorder and angle-closure glaucoma is unknown.

Lens surgery in the treatment of primary angle-closure glaucoma<sup>9</sup> is gaining in popularity. There is an additional role for lens surgery in the treatment of secondary angle-closure glaucoma in the presence of an inherited retinal dystrophy. The present case demonstrates a systematic clinical and therapeutic approach to refractory angle-closure glaucoma, with good outcome following lens surgery. We suggest that patients with inherited retinal dystrophies presenting with headache or eye pain should

undergo gonioscopic examination, so as to prevent the devastating visual loss which can occur in undiagnosed angle-closure glaucoma.<sup>10</sup>

## References

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