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Case Series of Stickler Syndrome Presenting with Acute Angle Closure

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Précis

Angle closure is a potential feature of Stickler syndrome.

Abstract

Purpose—Stickler syndrome is associated with open angle glaucoma, but no reports exist of adults presenting with acute angle closure. Here, we report the clinical associations and short-term outcomes in two patients with Stickler syndrome who presented with acute angle closure at a single tertiary referral center.

Observations—A 36-year-old female with Stickler syndrome presented with acute onset of red and painful left eye with cloudy vision. Initial intraocular pressure (IOP) was measured to be 54 mmHg. Gonioscopy revealed no angle structures or peripheral anterior synechiae in the left eye. Two laser peripheral iridotomies (LPI) were created five days apart without adequate IOP lowering. Left eye cataract extraction with intraocular lens implantation and Ahmed glaucoma drainage device implantation were performed with resolution of ocular hypertension.

A 35-year-old male with Stickler syndrome presented with intermittent right eye pain and blurry vision. IOP was 42 mmHg and gonioscopy revealed 270 degrees of angle closure in the right eye. The patient underwent LPI in the right eye with resolution of ocular hypertension by the next day.

Conclusions—Recognizing angle closure as a potential feature of Stickler syndrome can help providers adequately screen and manage patients with Stickler syndrome presenting with acutely elevated IOP.

Keywords

Stickler syndrome; acute angle closure; angle dysgenesis; collagen type 2; collagen type 11

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Introduction

Stickler syndrome is a typically autosomal dominant^{1,2}, arthro-ophthalmopathy due to mutations most commonly in collagen type 2 alpha 1 (COL2A1, Type 1 Stickler syndrome) or collagen type 11 alpha 1 (COL11A1, Type 2 Stickler syndrome), resulting in abnormal collagen fibril formation³. The incidence of Stickler syndrome is approximately 1 in 7500 births, systemically manifesting with craniofacial abnormalities, hearing loss, and hypermobile joints³. Known ocular manifestations of Stickler syndrome include high myopia, open-angle glaucoma, retinal detachment, pediatric glaucoma³, anomalous or hypoplastic vitreous¹, ectopia lentis, and other lenticular abnormalities.⁴ Non-glaucomatous axial lengthening with associated high myopia and predisposition for retinal detachments is the most common ocular abnormality in Stickler syndrome⁵. Both acquired and congenital ectopia lentis have been described in Stickler syndrome.⁴ Infantile-onset³ and open-angle glaucoma in adults has been described in patients with Stickler syndrome⁶, but there is only one prior report of associated acute angle closure in the setting of concurrent persistent hyperplastic primary vitreous in a child.⁷ The purpose of this case series is to report the clinical associations and short-term outcomes in adult patients with Stickler syndrome who presented with acute angle closure at a single tertiary referral center.

Findings

Case 1

A 36-year-old female with a history of hearing impairment, chronic joint pain, and Stickler syndrome diagnosed at age 2 presented to the emergency department with acute onset of red and painful left eye with cloudy vision. There was no history of retinal detachment or eye surgery. Positive family history included her mother. On exam, her uncorrected visual acuities were counting fingers at five feet in the right eye and hand motion in the left eye, which improved with pinhole occlusion to 20/400 in the right eye and 20/800 in the left eye. Initial tonometry measurements of intraocular pressures (IOP) were 18 mmHg in the right eye and 54 mmHg in the left eye. Gonioscopy revealed the right eye was open to trabecular meshwork but occludable, while no angle structures or peripheral anterior synechiae were visible in the left eye with indentation. The left pupil was unreactive to light and mid-dilated without reverse afferent pupillary defect. Slit lamp exam of the left eye demonstrated conjunctival injection, corneal edema, with moderate anterior chamber cell and flare. No neovascularization of the iris or angle was noted. The lens was clear with trace glaukomflecken but without visible phacodonesis. Her optic nerve appeared staphylomatous but with intact rims in both eyes. She was placed on maximal medical therapy, including topical dorzolamide-timolol combination twice daily, brimonidine twice daily, latanoprost every evening, and oral acetazolamide 250mg four times daily. The next day, left IOP remained elevated at 54 mmHg. A laser peripheral iridotomy (LPI) was created inferiorly at the area of greatest chamber depth and the pressure started to improve. The patient was started on topical prednisolone acetate four times daily and continued on maximum medical therapy for IOP lowering. The next day, IOP had improved to 24 in the left eye. However, four days later, the left IOP was elevated again to 57 mmHg. The LPI appeared clogged with blood products, and a second LPI was created and the pressure started to decrease in clinic at

the 1-hour IOP check. However, the following day, the IOP in the left eye was elevated again above 50 mmHg and gonioscopy showed 360 peripheral anterior synechia. At this point, cataract extraction with intraocular lens implantation with capsular tension ring and Ahmed glaucoma drainage device implantation were performed on the left eye. Axial lengths, lens thickness, and anterior chamber depths (OD/OS) were 29.14/29.29 mm, 4.83/4.86 mm, and 2.36/2.00 mm respectively on pre-operative biometry. The next day, IOP had decreased to single digits. Over subsequent visits, IOP remained normotensive. Corrected visual acuities 11 weeks after presentation were 20/50 OD and 20/25 OS with intraocular pressure of 13 mmHg in the left eye on topical dorzolamide-timolol combination daily. The appearance of her optic nerves remained unchanged in both eyes.

Case 2

A 35-year-old male with genetic confirmation of Stickler syndrome (*de novo* mutation in COL2A1 gene) presented with intermittent right eye pain and blurry vision. Past medical history included cleft palate, hearing loss, and chronic joint pain. Past ocular history included glaucoma suspicion due to ocular hypertension and optic nerve appearance, narrow angles in both eyes, bilateral lattice degeneration treated with retinopexy, LASIK surgery, and left eye rhegmatogenous retinal detachment repaired by scleral buckle. Ocular medications included topical dorzolamide-timolol combination twice daily and latanoprost every evening in both eyes. At presentation, visual acuities with contact lens correction and pinhole were 20/50 OD and 20/20 OS. IOP was 42 mmHg in the right eye, and 15 mmHg in the left eye. Gonioscopy revealed 270 degrees of angle closure the right eye, and 180 degrees in the left without peripheral anterior synechiae in either eye. Slit lamp exam showed no conjunctival injection or corneal edema, and optic discs exhibited moderate glaucomatous thinning bilaterally (Figure 1). The patient underwent LPI in the right eye with improvement in IOP to 10 mmHg the next day.

Discussion

Although open angle glaucoma has been well reported in Stickler syndrome⁶, there exists only a single report of angle closure in this population, in a child with a novel missense mutation in COL11A1, unilateral retinal dysplasia, persistent hyperplastic primary vitreous, and microphthalmia⁷. Our case series is the first to describe acute angle closure in adults with Stickler syndrome.

The mechanism by which glaucoma typically manifests in patients with Stickler syndrome is unknown, though is generally diagnosed as open angle disease. Stickler syndrome has been associated with anatomic and physiologic alterations that suggest a mixed mechanism.⁵ Angle dysgenesis has been associated with genetic defects in collagen synthesis.⁵ Transgenic mice with mutations in the COL2A1 gene show anterior segment alterations including abnormal trabecular meshwork and shallow anterior chambers.⁵ The reported incidence of long and thick iris processes extending to the trabecular meshwork, ciliary body face, and scleral spur in Stickler syndrome is 26%.⁴ In addition, type 2 collagen interacts with hyaluronic acid to mediate aqueous outflow resistance, and is decreased in the trabecular meshwork in eyes with adult-onset glaucoma⁵.

Ectopia lentis is a known complication of Stickler syndrome⁴, other type 2 collagenopathies⁸, and in other hereditary conditions that affect components of the zonular fibers and attachments.⁹ COL2A1 and COL11A1 products have been identified in the human zonule in trace amounts, particularly in hyaloid zonules,⁹ possibly contributing to decreased zonular integrity in Stickler syndrome. Though type 2 collagen represents the major structural component of the secondary vitreous⁸, collagen products are present in lower concentrations in the vitreous than in the hyaloid zonules⁹. The distinct phenotypes of “membranous” and “beaded” vitreous in types 1 and 2 Stickler syndrome, respectively, suggest an integral role of collagen in the structure that supports the anterior face of the vitreous.⁹

Angle closure is a rare finding in myopic eyes given their long axial lengths and naturally deeper anterior chambers. The patient in case 1 had an axial length of 29mm, though her anterior chamber depth was more shallow than expected. Additionally, her lens with thicker than usual for her age. This may suggest that pupillary block may be accompanied by other factors (including phacomorphic angle narrowing) in acute angle closure presentations in patients with Stickler syndrome. Due to the extensive PAS in Case 1, the pressure was not improved after LPI, and thus required incisional surgery, while the elevated pressure was successfully lowered with LPI alone in case 2 due to less extensive PAS.

Conclusions

Although rare, it is important to recognize angle closure as a potential complication of Stickler syndrome. While more research is required to understand the exact mechanisms of angle closure in Stickler patients, understanding this association can help providers adequately screen and manage acute angle closure in patients with Stickler syndrome.

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Patient Consent

Both patients underwent informed consent prior to laser and incisional surgeries. This report does not contain any personal information that could lead to the identification of the patients.

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Figure 1. Fundus photographs of the patient in Case 2 three months prior to presentation. (A) The right eye demonstrates superior and inferior disc erosion, temporal vitreous veil, and mid-peripheral lattice with surrounding laser scars. (B) The left eye demonstrates superior and inferior disc erosion and peripheral lattice degeneration with scleral buckle and laser scars.