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Spontaneous lens resorption in a patient with Marshall-Stickler Syndrome and glaucoma

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ABSTRACT

Purpose: The purpose of this case report is to describe the increased fragility of anterior capsule in patients with the rare genetic disease Marshall-Stickler syndrome.
Observations: We describe a 3-year old patient with Marshall-Stickler Syndrome and congenital glaucoma treated with glaucoma drainage implant placement who subsequently developed spontaneous lens resorption in one eye, which was noted incidentally during one follow-up appointment.
Conclusions and Importance: It is hypothesized that the lens material left the eye through the glaucoma drainage implant over time. This process was not associated with elevation of intraocular pressures or inflammation and did not require subsequent surgery to remove any residual lens fragments, which has not been reported before to the best of the authors' knowledge.

1. Introduction

The objectives of this case report are to describe the increased fragility of anterior capsule in patients with the rare genetic disease Marshall-Stickler syndrome, and its possible consequences. With this understanding, providers can complete a more thorough and careful examination for these patients. A few previous case reports have described lens resorption in patients with Marshall-Stickler; however, our study is relatively unique in that subsequent surgery was not needed, which is another important management consideration for providers to consider.

2. Case report

A 3-year old male with Marshall-Stickler syndrome was evaluated by the Pediatric Ophthalmology service at [study institution name redacted for review]. His medical history was notable for bradycardia and craniofacial abnormalities, including shallow orbits and mandibular distraction. Genetic testing confirmed a pathogenic heterozygous mutation on the *COL11A1* gene on chromosome 1 for Marshall-Stickler syndrome. His ocular history was notable for high myopia and bilateral congenital glaucoma. Cycloplegic refraction at initial presentation was −14.50 + 2.00 x 180 OD and −14.00 sph OS. There was no family history of glaucoma and both the patient's fraternal twin and older sister were healthy without ocular or medical issues. The left eye was noted to have more advanced disease (Fig. 1) and was treated with goniotomy at 2 months of age at an outside institution, trabeculotomy at 8 months of age, and finally Baerveldt glaucoma implantation (BGI) at the age of 21 months in July 2018. Of note, two months prior to the BGI surgery, the patient was involved in a motor vehicle accident. He was noted to be phakic in the left eye at the time of tube implantation. He was kept on topical hypotensive medications including timolol BID OU, dorzolamide BID OU, and latanoprost QHS OS.

The patient was lost to follow up from August 2018 until March 2019. He was subsequently seen in the Pediatric Ophthalmology clinic in March 2019, when the left eye was noted to be aphakic. It was confirmed by the parent that the patient had not received any ophthalmic care at an outside clinic during this interval; physical exam confirmed no paracentesis incision scars or any signs of intraocular surgery suggestive of lensectomy. The VA was central, unsteady, and maintained OD, and central, unsteady, and unmaintained OS with a preference for the right eye. The intra-ocular pressure (IOP) was 13 mmHg OD and 25 mmHg OS. Cycloplegic refraction at this visit was −14.00 + 2.00 x 180 OD and plano OS. Anterior segment exam of the right eye was unremarkable with a clear cornea and lens. Left eye findings were notable for corneal haze with buphthalmos. The tube was

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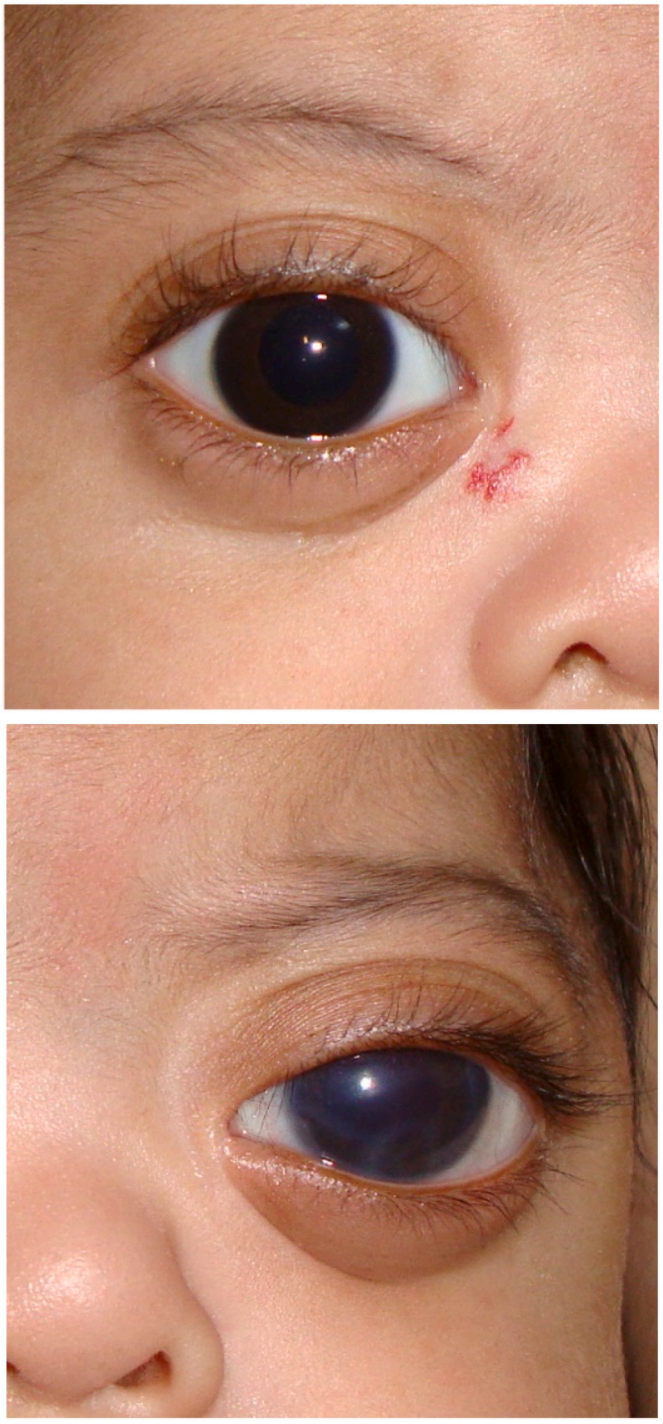

Fig. 1. Photos obtained prior to placement of a glaucoma drainage implant. The right eye (top image) had corneal diameters of 12.00 mm vertical x 12.75 mm horizontal, and an axial length of 28.00 mm. A capillary hemangioma is present on the medial right lower eyelid. The left eye (bottom image) had corneal diameters of 15.00mm vertical x 15.00mm horizontal, and an axial length of 32.77 mm. The left lens can be visualized without any opacity.

well-positioned in the anterior chamber with no tube-cornea touch and the plate was well covered. No lens material was observed, and ultrasound examination of the left eye confirmed that there was no lens dislocation to the posterior pole and that remnants of the capsule were still present (Fig. 2). Ultrasound also showed the retina was otherwise attached with fine vitreous strands. A retina consultation confirmed these retinal findings. Hence, it was concluded that the lens of the left

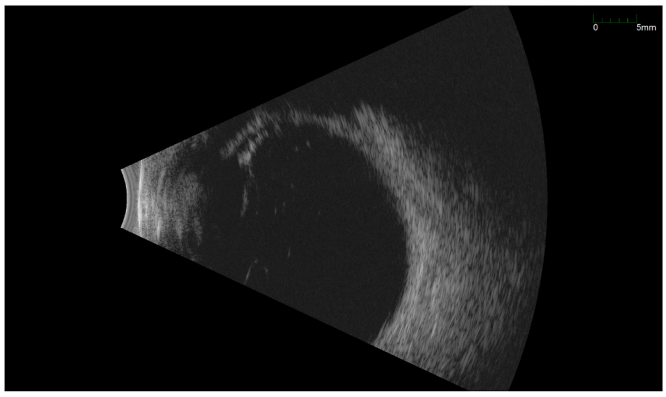

Fig. 2. B-scan ultrasound examination of the left eye confirmed that there was no lens dislocation to the posterior pole and that remnants of the capsule were still present. There are few small nonspecific vitreous opacities that do not appear to be lens fragments.

eye had shown spontaneous resorption. Subsequently, the patient rapidly developed a cataract in his right eye in February 2020, which was successfully removed with a limbal approach cataract extraction and anterior vitrectomy.

3. Discussion

Marshall-Stickler Syndrome is a rare genetic chondrodysplasia with significant ocular and extra-ocular manifestations that represents a spectrum of inherited connective tissue disorders with a variety of mutations, including in the *COL2A1*, *COL11A1*, and *COL11A2* genes. These syndromes are clinically variable and genetically heterogeneous, making genetic analysis important in the evaluation of this condition.[1] Marshall syndrome (MS), an autosomal dominant disorder first described in 1958, is caused by a splicing mutation in the *COL11A1* transcript.[2,3] Rare forms of this disorder inherited in an autosomal recessive pattern have been described.[4] It shares several clinical features with Stickler syndrome (SS), also known as hereditary arthro-ophthalmopathy, a more common connective tissue disorder which can be inherited in an autosomal dominant or autosomal recessive pattern.[5] MS and SS have been described as separate disorders, but the clinical pictures of the two syndromes have significant overlap.[6] There is still an ongoing debate as to whether they should be classified as two separate syndromes, or different clinical expressions of mutations in the same family of genes.[7] Ocular manifestations in both syndromes include high myopia, vitreoretinal degeneration, retinal detachment, cataracts, lens subluxation, amblyopia, nystagmus, glaucoma, and proptosis.[5,9]

Type XI collagen regulates the diameter of Type II collagen,[5] which is a fibrillar collagen that can be found in the lens capsule among other places in the body[7] (such as hyaline cartilage, the ocular vitreous, the nucleus pulposus of the intervertebral disc, and the inner ear). The fact that these collagen subtypes interact so closely may explain the overlapping symptomology.

In Marshall-Stickler syndrome, it is suggested that collagen mutations lead to an inherently weak lens capsule, causing rupture with minimal preceding trauma or even spontaneously.[7] Mutations in the *COL2A1* gene are associated with the early onset of distinctive cataracts.[8] We hypothesize that an anterior capsular break occurred either spontaneously, related to the motor vehicle accident, or iatrogenically during BGI implantation. It is possible that transient proximity of the BGI tube may have resulted in tube-capsule contact with resultant discontinuity on the lens capsule.[9] Regardless of the underlying cause, cataract formation may have been related either to this anterior capsular violation, or due to an underlying predisposition for early onset cataracts, evidenced by the subsequent development of a cataract in the

other eye. There was complete resorption of the lens material through the patent BGI gradually over the course of 6–8 months. Thus, no lens fragments were retained in the anterior chamber to incite inflammation or elevate IOP. Previous cases of lens resorption in patients with Marshall-Stickler have been documented.[7,10,11] In these cases, however, examination showed displacement of lens fragments into the anterior chamber and vitreous cavity. In these cases, the spontaneous rupture of the lens led to elevated IOP, prompting the need for either prolonged medical therapy, or subsequent cataract surgery and vitrectomy to remove the residual lens fragments and lens capsule. The authors would like to note that gradual lens resorption and accompanying inflammatory changes may have occurred during the period the patient was lost to follow-up. However, no sign of redness or pain was noted by the parents at any point during this period.

4. Conclusion

In conclusion, our case lends support to the increased fragility of anterior capsule in patients with Marshall-Stickler syndrome. It is recommended that a careful lens evaluation be undertaken in these patients at each visit as anterior capsular breaks may lead to cataracts, intraocular inflammation or, in rare cases, spontaneous lens resorption in the setting of a functioning tube implant, as demonstrated in our patient.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

Declaration of competing interest

The following authors have no financial disclosures: JG, EC, DE, MCM.

All authors attest that they meet the current ICMJE criteria for Authorship.

No other contributions to the present work.

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