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Case report

# Angle closure glaucoma in congenital ectropion uvea

Grace M. Wang[a], Daniel Thuente[b], Brenda L. Bohnsack[a,*]

[a] Department of Ophthalmology and Visual Sciences, University of Michigan, United States
[b] Grand Traverse Ophthalmology Clinic, United States

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ABSTRACT

*Purpose:* Congenital ectropion uvea is a rare anomaly, which is associated with open, but dysplastic iridocorneal angles that cause childhood glaucoma. Herein, we present 3 cases of angle-closure glaucoma in children with congenital ectropion uvea.

*Observations:* Three children were initially diagnosed with unilateral glaucoma secondary to congenital ectropion uvea at 7, 8 and 13 years of age. The three cases showed 360° of ectropion uvea and iris stromal atrophy in the affected eye. In one case, we have photographic documentation of progression to complete angle closure, which necessitated placement of a glaucoma drainage device 3 years after combined trabeculotomy and trabeculectomy. The 2 other cases, which presented as complete angle closure, also underwent glaucoma drainage device implantation. All three cases had early glaucoma drainage device encapsulation (within 4 months) and required additional surgery (cycloablation or trabeculectomy).

*Conclusions and importance:* Congenital ectropion uvea can be associated with angle-closure glaucoma, and placement of glaucoma drainage devices in all 3 of our cases showed early failure due to plate encapsulation. Glaucoma in congenital ectropion uvea requires attention to angle configuration and often requires multiple surgeries to obtain intraocular pressure control.

## 1. Introduction

Congenital ectropion uvea is a rare, typically unilateral eye anomaly that is characterized by iris pigment epithelium on the anterior surface of the iris at birth.[1,2] While this condition is often an isolated finding, it can also be associated with other ocular anomalies (*e.g.* Riegers Anomaly, coloboma, and ptosis)[2,3] and systemic diseases (*e.g.* neurofibromatosis type 1, Prader-Willi Syndrome and facial hemihypertrophy).[1,2]

Glaucoma is a common complication of congenital ectropion uvea and the age of diagnosis ranges from infancy to early adulthood.[1–14] The mechanisms underlying elevated intraocular pressures may be multi-factorial. Gonioscopy of younger children affected with congenital ectropion uvea shows open, but dysplastic angles with anterior insertion of the iris at the level of the trabecular meshwork.[1,2] In addition, a membrane, which extends from the peripheral iris into and over the angle, is frequently described. Histologic studies reveal that this membrane consists of abnormal endothelial cells.[1,7] Further, enucleated eyes with end-stage glaucoma show complete angle closure both clinically and histologically.[1,4] It is unclear the stage at which angle closure develops in congenital ectropion uvea. Here we report three teenagers with congenital ectropion uvea with angle-closure glaucoma. In addition, to the best of our knowledge, we report for the first time the use of glaucoma drainage devices in multiple patients in the treatment of this rare form of glaucoma.

## 2. Observations

### 2.1. Case 1

A 19-year-old man initially presented at 8 years of age to an outside ophthalmologist after failing a vision screening. His parents noted that his left pupil had been larger and misshapen compared to the right pupil since birth. His intraocular pressures were ~30 mmHg in his left eye. Medical therapy consisting of travoprost, brinzolamide, and timolol was initiated, and he was referred for further treatment. At his initial visit at our institution, his best-corrected visual acuity was 20/20 in the right eye and 20/40 in the left eye with a cycloplegic refraction of plano sphere in the right eye and −2.75 + 7.50x075 in the left eye. Intraocular pressures were 12 mmHg in the right eye and 10 mmHg in the left eye after 2 weeks of ocular antihypertensive treatment. External exam was notable for left facial hemihypertrophy and mild, not visually significant ptosis of the left upper eyelid. Slit lamp examination showed that both corneas were clear without Haabs striae or edema. There was

* Corresponding author. Department of Ophthalmology and Visual Sciences, Kellogg Eye Center, University of Michigan, 1000 Wall Street, Ann Arbor, MI 48105, United States.
*E-mail address:* brendabo@med.umich.edu (B.L. Bohnsack).

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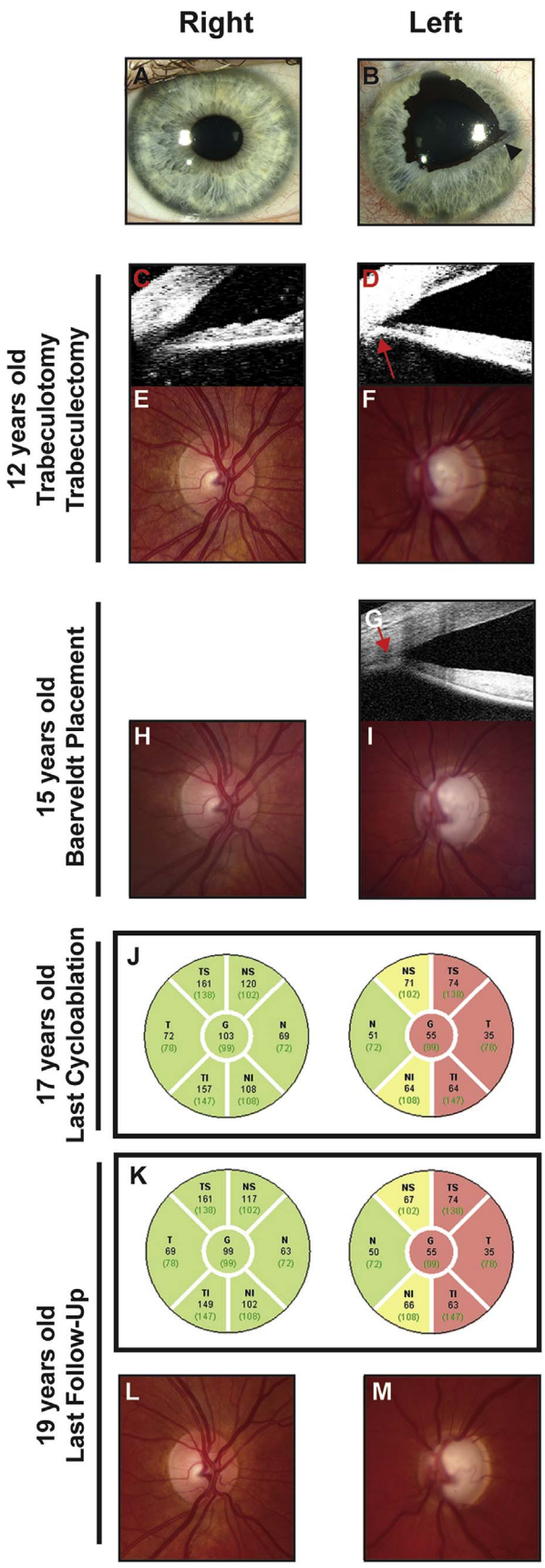


**Fig. 1. Case 1.**
Slit lamp photograph of the left eye (B) showed 360° of ectropion uvea and iris stromal atrophy compared to the right eye (A). The tube of the Baerveldt © glaucoma drainage device was in the temporal anterior chamber (arrowhead) of the left eye. When the patient was 12 years old, anterior segment optical coherence testing of the right eye (C) showed an open angle with a normal iris insertion. In the left eye (D), although the angle was open, there was anterior insertion of the iris pigment epithelium (arrow). The iris stroma lacked crypts and did not extend to the periphery of the iris pigment epithelium. Fundus photos of the right (E) and left eyes (F) showed a cup to disc ratio of 0.15 and 0.8, respectively. Three years later at time of placement of a Baerveldt © glaucoma drainage device, anterior segment optical coherence testing of the left eye showed that the angle was closed (G, arrow). Fundus photos showed no change in the right optic nerve (H) and progression to a cup to disc ratio of 0.95 (I). At last follow-up, the retinal nerve fiber layer thickness as measured by optical coherence testing remained stable (K) compared to 25 months prior at time of the last cycloablation treatment (J). Further, appearance of both optic nerves (L and M) were unchanged at last follow-up.

no difference in corneal diameters between the two eyes. The iris of the right eye was light blue with normal crypt architecture (Fig. 1A) while the iris of the left eye had 360° of ectropion uvea and showed stromal atrophy (Fig. 1B). Fundoscopic examination showed a cup to disc ratio of 0.15 in the right eye and 0.3 in the left eye at that time. Gonioscopy was not performed at that time due to the patient's age and lack of cooperation.

Four years later at age 12 years, his intraocular pressures were 41–48 mmHg in his left eye despite maximum medical management. Gonioscopy and anterior segment optical coherence testing of the unaffected right eye showed an angle open to the ciliary body 360° (Fig. 1C). In the left eye, the angle was open as the trabecular meshwork was visualized, but the iris inserted just anterior to the scleral spur. This was further confirmed by optical coherence testing which showed an open angle with a steep insertion of the iris pigment epithelium (Fig. 1D, arrow). The iris stroma lacked crypts and extended over the iris pigmented epithelium up to the angle. The cup to disc ratio in the right eye remained 0.15 (Fig. 1E) and in the left eye had increased to 0.8 with greatest preservation of the temporal rim (Fig. 1F). The patient underwent uncomplicated superior trabeculotomy with trabeculectomy (without antifibrotics) of the left eye.

In 2013, at 15 years of age, despite measured intraocular pressures of 15–20 mmHg, his left optic nerve showed progressive cupping (Fig. 1I). There was no change to the optic nerve in the right eye (Fig. 1H). Gonioscopy and anterior segment optical coherence testing now revealed 360° of complete angle closure in the left eye (Fig. 1G, arrow). There was no view of any angle structures. The patient underwent uncomplicated placement of a Baerveldt © 101–350 glaucoma drainage device with a 6-0 polyglactin ligature suture. Two months post-operatively, the intraocular pressure in the left eye was 11 mmHg, the tube had spontaneously opened, and there was a large amount of fluid over the plate. However, at 3 months post-operatively, the plate had encapsulated, and the intraocular pressure was 20–30 mmHg despite restarting timolol, dorzolamide, and travoprost. Over the next 20 months, the patient underwent three uncomplicated 180° treatment sessions (8 spots per 90°) of transcleral laser cycloablation (inferior 180°, nasal 180°, and superonasal 90°/inferotemporal 90°). At his most recent follow-up, which was 25 months after the last cycloablation and 45 months after glaucoma drainage device placement, his best-corrected visual acuity remained 20/20 in the right eye and 20/40 in the left eye. His intraocular pressures were 12 mmHg in both eyes. He was on timolol, dorzolamide, and travoprost in the left eye. Slit lamp examination showed a mild posterior subcapsular cataract in the left eye. The optic nerves were stable in appearance (Fig. 1L and M) and retinal nerve fiber layer thickness assayed by optical coherence testing had remained stable since the last cycloablation treatment (Fig. 1J and K).

### 2.2. Case 2

A 17-year-old woman initially presented at 3 years of age for

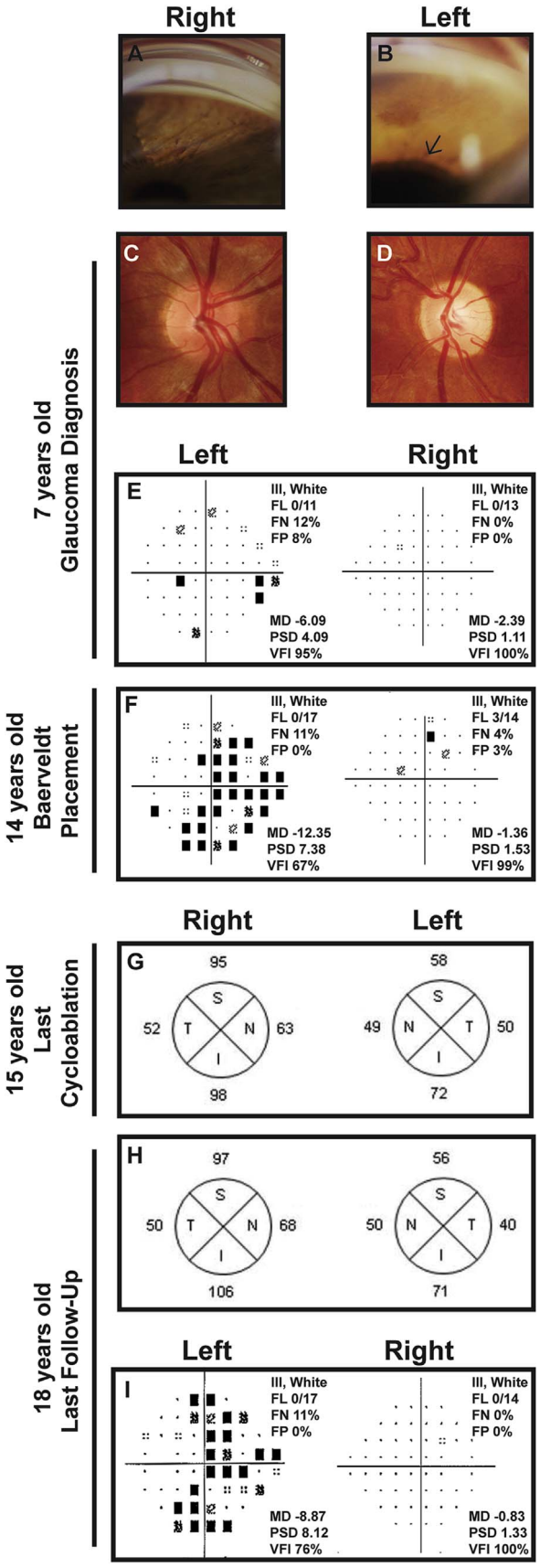


**Fig. 2. Case 2.**

Gonioscopy of the right eye demonstrated a normal iris (A) while the left eye had 360° of ectropion uvea (B). Fundus photos obtained when the patient was 7 years old showed a cup to disc ratio of 0.1 in the right eye (C) and 0.6 in the left eye (D). The pattern deviation of Humphrey visual field testing (24-2 Sita-Fast with III, white stimulus) at 7 years of age was normal in the right eye and showed an early inferior nasal step in the left eye (E). Seven years later, the pattern deviation at time of Baerveldt © glaucoma drainage device placement showed superior and inferior arcuate defects in the left eye (F). At last follow-up, retinal nerve fiber layer thickness (H) measured a decrease temporally compared to 35 months prior (G), but this did not correlate with changes in visual field testing (I). FL, fixation losses; FN, false negatives; FP, false positive; MD, mean deviation; PSD, pattern standard deviation; VFI, visual field index.

evaluation of ptosis and pupil abnormality. At her initial visit, her visual acuity without correction was 20/30 in the right eye and 20/40 in the left eye. Retinoscopy of both eyes was +0.50 sphere. External examination showed mild ptosis of the left upper eyelid, which did not impede the central visual axis. Slit lamp examination showed that the corneas were clear and equal in diameter. The right iris was brown with normal crypts (Fig. 2A). The left iris had 360° of ectropion uvea at the pupil margin (Fig. 2B, arrow). Fundoscopic examination was unremarkable, showing symmetric optic nerves without evidence of glaucoma.

At 7-years of age, the patient was diagnosed with glaucoma of the left eye and managed medically by an outside ophthalmologist. Intraocular pressures of the left eye increased into the 20s-30s mmHg and there was increased cupping of the left optic nerve (Fig. 2D) compared to the right (Fig. 2C). Gonioscopy was not performed at that time due to the patient's age and lack of cooperation. In addition, there was evidence of early enlargement of the blind spot and inferior nasal step with Humphrey visual field testing of the left eye (Fig. 2E).

In 2013, when the patient was 14 years of age, she was referred back to our institution for glaucoma progression. Visual field testing showed superior and inferior arcuate defects that involved the nasal half of central fixation (Fig. 2F). Her best-corrected visual acuity was 20/20 in the right eye and 20/30 in the left eye. Cycloplegic refraction was −3.00 + 1.00x102 in the right eye and −1.50 + 1.50x098 in the left eye. Intraocular pressures were 19 mmHg in the right eye and 14.5 mmHg in the left eye. She was on timolol, dorzolamide, brimonidine, and tafluprost in the left eye at that time. The cup to disc ratio in the right eye was 0.05 and in the left eye was 0.8. Gonioscopy in the unaffected right eye showed an angle open to the ciliary body band 360°. In the affected left eye, the angle was completely closed with no view of any angle structures 360°. In order to obtain intraocular pressure control, a Baerveldt © 101–350 glaucoma drainage device with a 6-0 polyglactin ligature was implanted. At 5 weeks post-operatively, the intraocular pressure in the left eye was 7 mmHg, the tube had spontaneously opened, and there was a large bleb over the superotemporal plate. At 3 months postoperatively, the intraocular pressure was elevated to 43 mmHg and the plate was encapsulated. Over the next 5 months, the patient underwent two uncomplicated 180° treatment sessions (8 spots per 90°) of transcleral laser cycloablation (inferior 180° and nasal 180°). At last follow-up, which was 40 months after glaucoma drainage placement and 35 months after the last cycloablation, the patient's best-corrected visual acuity was 20/20 in the right eye and 20/30 in the left eye. Her intraocular pressure was 16 mmHg in the left eye on timolol, dorzolamide, and latanoprost. Overall retinal nerve fiber layer thickness of the left eye was 54 μm at last follow-up compared to 57 μm at time of the last cycloablation. Quadrant analysis (Fig. 2H) showed decreased thickness temporally compared to 35 months prior (Fig. 2G), however optic nerve appearance and visual field testing were stable (Fig. 2I).

### 2.3. Case 3

A 13-year-old girl presented to an outside ophthalmologist with a

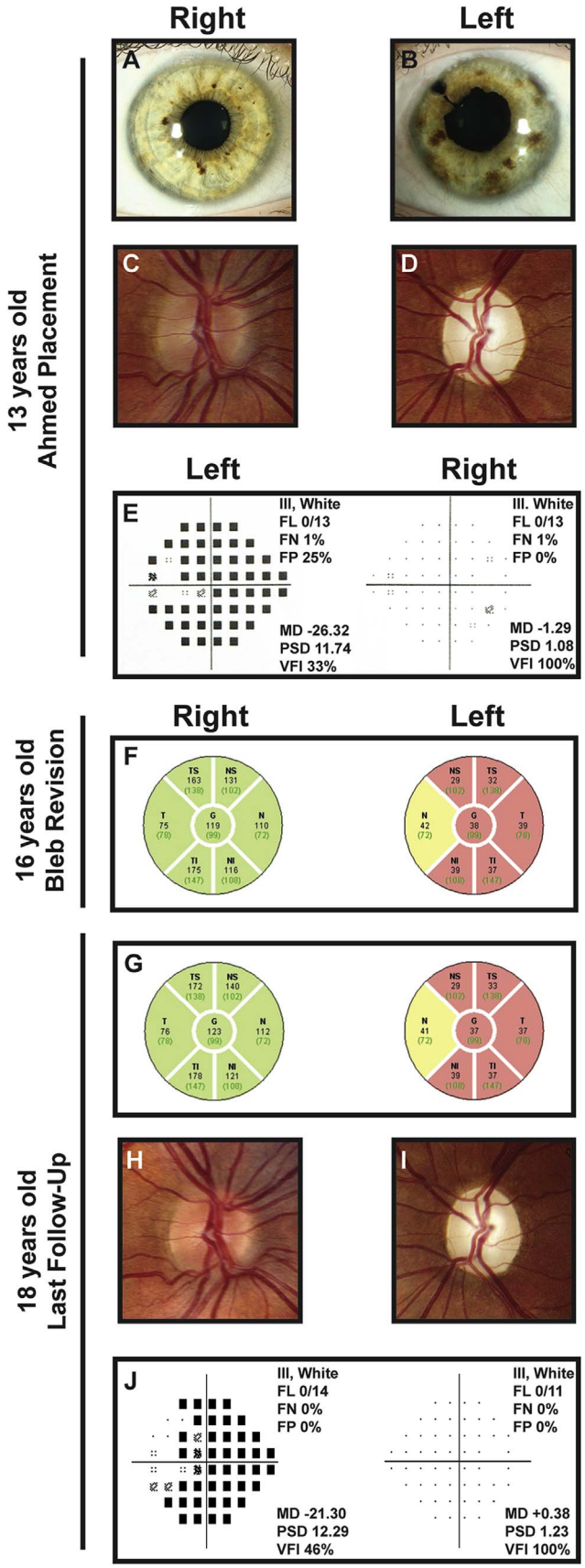


**Fig. 3. Case 3.**
Slit lamp photograph of the right eye showed a normal appearing iris (A) while there was 360° of ectropion uvea in the left eye (B). Fundus photos of the right (C) and left eyes (D) demonstrated a cup to disc ratio of 0.15 and 0.95, respectively. The total deviation of Humphrey visual field testing (24-2 Sita-Fast with III, white stimulus) was normal in the right eye and showed dense superior and inferior altitudinal defects in the left eye (E). At last follow-up, retinal nerve fiber layer thickness by optical coherence testing was stable (G) compared to 18 months prior at the time of the trabeculectomy bleb revision (F). Further, optic nerves (H, I) and visual fields (J) showed no progression at last follow-up. FL, fixation losses; FN, false negatives; FP, false positive; MD, mean deviation; PSD, pattern standard deviation; VFI, visual field index.

complaint of 6 months of blurry vision. She was found to have an intraocular pressure of 40 mmHg in her left eye. She was started on bimatoprost, brimonidine, timolol, and brinzolamide in the left eye, and referred to our institution for further treatment. At her initial evaluation with us, her best-corrected visual acuity was 20/20 in the right eye and 20/20 in the left eye with a cycloplegic refraction of plano sphere in the right eye and −3.00 + 1.75 x 105 in the left eye. Intraocular pressures were 15 mmHg in the right eye and 43 mmHg in the left eye. Slit lamp examination showed that the corneas were clear without edema or Haabs striae. The iris of the right eye was green-brown in color and had a normal crypt architecture (Fig. 3A). The iris of the left eye showed 360° of ectropion uvea along the pupil margin (Fig. 3B). On gonioscopy and anterior segment optical coherence testing, the right angle was open to the ciliary body band 360°. The left angle was completely closed with no view of any angle structures 360°. Fundoscopic examination showed a cup to disc ratio of 0.15 in the right eye (Fig. 3C) and 0.95 in the left eye (Fig. 3D). The remaining neural rim in the left eye was pale. By Humphrey visual field testing there were superior and inferior altitudinal defects that involved fixation in the left eye (Fig. 3E). An Ahmed © FP7 glaucoma drainage device was placed in the superotemporal quadrant in order to achieve immediate pressure lowering effect given the elevated pressure and severe cupping of the optic nerve. At 1 month post-operatively, the intraocular pressure in the left eye was 12 mmHg without ocular hypertensive medications. At 2 months post-operatively, the intraocular pressure in the left eye was 20 mmHg despite timolol, dorzolamide, and latanoprost treatment. For increasing intraocular pressures and medication intolerance, 3 months after glaucoma drainage device placement, the patient underwent a superonasal trabeculectomy with mitomycin C in the left eye. She required a bleb needling 12 months post-trabeculectomy and a bleb revision with tenonectomy and mitomycin C injection 16 months post-trabeculectomy. At her last follow-up, which was 18 months post-bleb revision, the patient's best-corrected visual acuity was 20/20 in each eye. Intraocular pressure was 12 mmHg in the left eye on timolol and dorzolamide. There was a diffuse superonasal trabeculectomy bleb. The retinal nerve fiber layer thickness (Fig. 3F and G), optic nerve appearance (Fig. 3H and I) and Humphrey visual field testing (Fig. 3J) were stable.

## 3. Discussion

Congenital ectropion uvea is a rare eye anomaly, although the prevalence and the incidence of glaucoma in this condition are not well-defined. To date, there are approximately 50 cases of glaucoma secondary to congenital ectropion uvea reported in the English literature.[1–15] A review of these cases shows that glaucoma occurs in 80–90% of affected individuals. However, the age of glaucoma diagnosis ranges from birth to middle age (0–42 years) with the majority occurring between 3 and 15 years of age.[1–15]

The majority of cases of glaucoma due to congenital ectropion uvea require surgical management. Although various case series and reports have been published, there is no consensus as to the best treatment of this form of glaucoma. Review of the literature shows that angle surgery, either in the form of goniotomy or trabeculotomy, is not highly

effective in obtaining long-term intraocular pressure control.[1,2] There is 1 case of continued intraocular pressure control at time of publication of that article, which was 2 and a half years after trabeculotomy.[8] Otherwise, all other reported cases required additional non-angle glaucoma surgery such as trabeculectomy and cycloabalation.[1,2,4] This was also true for patient 1 in our series who had undergone trabeculotomy with trabeculectomy without antifibrotics 3 years prior to glaucoma drainage device placement. Filtering procedures with antifibrotics are the most common successful glaucoma surgeries in congenital ectropion uvea.[1,2,4] There has been only 1 previous report of the use of a glaucoma drainage device in congenital ectropion uvea.[4] This was in an eye that presented with glaucoma at birth and eventually underwent enucleation. To the best of our knowledge, we are the first to report the use of glaucoma drainage devices in multiple cases of congenital ectropion uvea.

In our series, in all 3 cases the angles were closed and thus the options of trabeculectomy with antifibrotic medication or glaucoma drainage device implantation were discussed with the patient and their parents. Due to factors related to the increased life-long risk of trabeculectomy-related infections,[16–19] all three teenagers opted for glaucoma drainage device placement. Interestingly, in all of our cases, there was early encapsulation of the plates and the 3 eyes required additional glaucoma surgery (cycloablation or trabeculectomy with mitomycin C) within 4 months of tube implantation. In other forms of childhood glaucoma, plate encapsulation has been reported to cause long-term failure of intraocular pressure control in 2%–16% of cases.[20–33] Plate encapsulation is correlated with early flow of aqueous humor which carries inflammatory cytokines that incite fibrosis within the episcleral connective tissue.[20] In 2 of our cases, Baerveldt © 101–350 devices were ligated with absorbable polyglactin suture and gradually opened between 1 and 2 months after placement. Despite this approach, these plates encapsulated quickly, similar to the patient who had an Ahmed © device placed. The underlying mechanism of early plate encapsulation in congenital ectropion uvea is unclear. Further, this may be coincidental given the few cases presented here and the lack of additional reports within the literature. Additional studies are required to determine the utility of glaucoma drainage devices in congenital ectropion uvea.

Although congenital ectropion uvea is traditionally described as non-progressive, reports of changes in iris appearance over time and the development of glaucoma throughout childhood suggests changes in angle configuration. Previous studies of children with glaucoma secondary to congenital ectropion uvea have described open, angles with dysplastic structures. The predominant gonioscopic features include anterior insertion of the iris and a membrane that extends over the iris and angle.[1,2] The membrane consists of endothelial cells, although the origin whether from an embryonic remnant, corneal endothelial cells, or neovascularization of the iris is not clear.[1,4,7,8] Interestingly, enucleated eyes with end-stage glaucoma have been shown to have closed angles both clinically and histologically.[4] The mechanism of angle closure appears to be related to the abnormal endothelial cell membranes that extend from the iris over the trabecular meshwork. However, the time frame in which these blind painful eyes developed angle closure is not known. In addition, 5 of the 6 eyes in which there are pathology samples also had uveal neurofibromas in the context of systemic neurofibromatosis type 1, which confounds the finding of angle closure.[4] In the current series, we report 3 cases of angle closure glaucoma in teenagers with isolated congenital ectropion uvea. Thus, angle closure is not unique to end-stage eyes or patients with neurofibromatosis. Further, in one case (patient 1), we present evidence of progression from an open, dysplastic angle to complete angle closure over 3 years. This suggests that glaucoma in congenital ectropion uvea may be in part due to developmental abnormalities of the angle structures as well as progressive angle closure secondary to abnormal endothelial cell membranes. This progression could correlate with the overall long-term ineffectiveness of angle surgery in congenital ectropion uvea. Taken together, eyes with congenital ectropion uvea may show progressive changes that affect intraocular pressure control and continued monitoring of affected individuals is warranted.

## 4. Conclusions

Glaucoma in the setting of congenital ectropion uvea can be associated with angle closure. We report progression to angle closure in 1 case of congenital ectropion uvea and present 2 additional cases of angle closure glaucoma in children with congenital ectropion uvea. Further, glaucoma drainage device implantation in all 3 cases showed early failure due to plate encapsulation, necessitating either filtering surgery or cycloablation. This rare form of glaucoma often requires multiple surgeries and warrants close monitoring of intraocular pressures.

## Patient consents

Written consent to publish information and use photographs from each patient or his/her legal guardian was obtained for this case series. This study was approved by the University of Michigan Institutional Review Board and complied with the US Health Insurance Portability and Accountability Act of 1996 and the Declaration of Helsinki.

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*Authorship*

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

## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ajoc.2018.03.009.

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