A Case of Primary Congenital Glaucoma

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CASE PRESENTATION

An 11-year-old girl and a case of primary congenital glaucoma (PCG) with negative family history of glaucoma, was referred to our glaucoma service for uncontrolled intraocular pressure (IOP). Maximum tolerable medications and multiple glaucoma operations had failed to control her IOP.

Review of the patient's chart revealed an IOP of 30 mmHg and horizontal corneal diameter of 11.5 mm in both eyes when she had been 3 days old, at the time which she underwent superior and inferior trabeculotomy in both eyes at a single session. One year later, she had IOP of 30 mmHg in both eyes without optic nerve head cupping; however, corneal diameters had increased to 14 and 13.5 mm in the right and left eyes, respectively. The patient continuously received two topical glaucoma medications for 8 years thereafter with IOPs remaining around 28 mmHg. At 9 years of age, she underwent mitomycin C (MMC) augmented trabeculectomy in both eyes.

Upon referral, the patient was on four topical agents including timolol, brimonidine, latanoprost and dorzolamide eye drops. Ten days after discontinuing all of these medications, IOP was increased from 35 to 56 mmHg and from 30 to 54 mmHg in the right and left eyes, respectively. Table 1 summarizes the results of her most recent ocular examination. The optic nerve heads of both eyes are displayed in figure 1, and figure 2 demonstrates the superior bulbar conjunctiva of both eyes.

- *What are the important points about her corneal thickness (CCT) and IOP?*
- *What would your target IOP be for this patient?*
- *What is the preferred management for this patient?*

Jonathan S. Myers, MD

This young girl has suffered elevated IOP for much of her life, but has healthy appearing optic nerves. Despite multiple procedures her IOP remains at 30 on medications and is extremely high without medications. She has much thicker than average corneas.

Thicker corneas lead to higher measured pressures. The relationship of CCT to artifactual IOP elevation on Goldmann tonometry is not linear, and is likely related to other biomechanical properties of the cornea beyond thickness, although currently there is limited understanding of these complex relationships. None of the alternative IOP measurement techniques are completely independent of corneal biomechanics.

If IOP elevation in this case was purely related to a stiff cornea, one would not expect cessation of medications to have such a dramatic

Table 1. The patient's current ocular examination

	OD	OS
IOP on 4 topical medications	35 mm Hg	30 mmHg
IOP without medications	56 mmHg	54 mmHg
CCT	660 µ	699 µ
Refractive error	-2.00 -2.50 × 16	-0.75 -0.25 × 37
BCVA	20/20	20/20
Keratometry	41.50× 14, 44.00× 104	41.5×39, 42.37× 129
Horizontal corneal diameter	14.00 mm	13.50 mm

IOP, intraocular pressure; OD, right eye; OS, left eye; CCT, central corneal thickness; BCVA, best corrected visual acuity

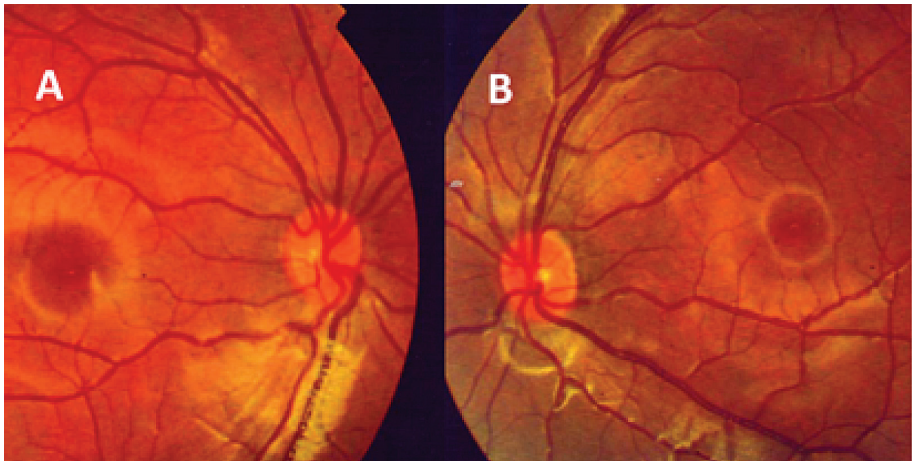

Figure 1. The optic nerve heads of the right **(A)** and left eyes **(B)** upon referral.

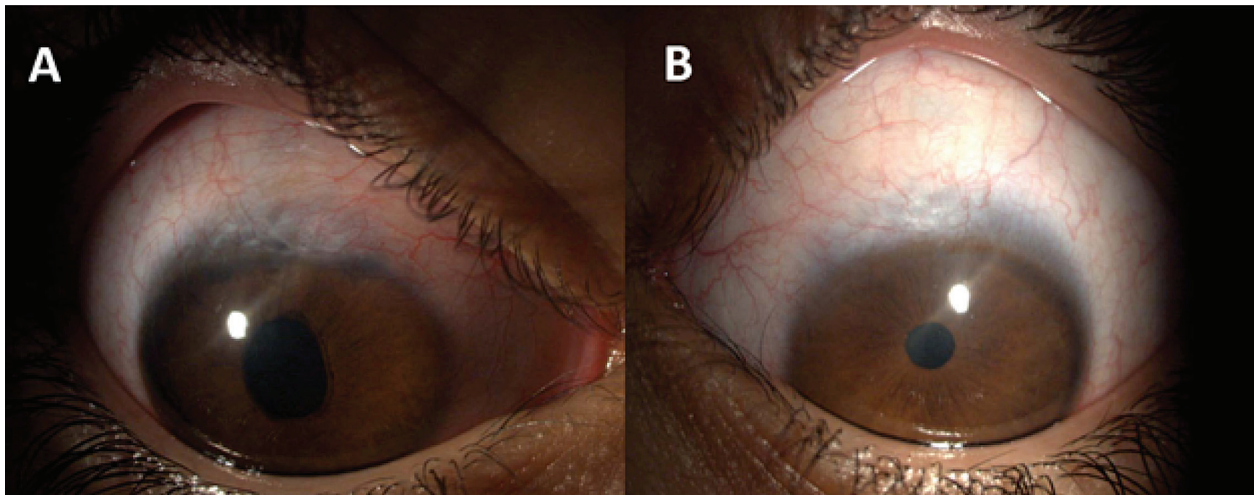

Figure 2. Slit lamp photographs of the right **(A)** and left **(B)** eyes showing the status of superior bulbar conjunctiva; no trabeculectomy bleb is visible in either eye.

effect. Indeed, stiffer corneas should partially blunt the measured changes when internal pressure is altered. In this case, though, the IOP rose dramatically when medications were stopped, suggesting that the outflow pathway is severely compromised. The Goldmann equation predicts that with reduced outflow, greater swings in IOP accompany changes in fluid production, as with aqueous suppressants.

Therefore this patient has two issues: an abnormal cornea and an abnormal outflow pathway. The congenital glaucomas may often involve the cornea and angle structures; examples include anterior segment dysgenesis such as the Axenfeld-Rieger syndrome. The photos here show an abnormal pupil in the right eye, but no other definitive findings, and the anterior chamber angle has not been described.

This patient has maintained a healthy appearing optic nerve through the years. Given the complicated issues surrounding accurate assessment of IOP in this case, it would be reasonable to follow this child on medications alone with frequent assessment of the nerve. At 11 years old, she is likely able to learn to perform a reliable visual field test. Serial stereoscopic optic nerve evaluation with drawings, disc photographs and spectral domain optical coherence tomography would all be helpful.

If the optic nerve or field should show clear change over time, or if the medical regimen proves too difficult for ideal compliance, I would favor tube shunt surgery. She has already failed trabeculectomy with mitomycin

C and trabeculotomy. She would be a good candidate for Ahmed S2 or FP-7 implants or a Baerveldt 250mm^2 or 350mm^2 implant. The two trials comparing Ahmed FP-7 and Baerveldt 350 implants suggest a slight advantage in IOP control with the Baerveldt 350 but a greater need for postoperative interventions, which may be challenging in a younger patient.

Arif O. Khan, MD

This is an interesting case of an 11-year-old girl with large corneas and high measured IOP, but initially no and currently minimal optic nerve head cupping. She had bilateral trabeculotomy soon after birth, but there is no documentation of corneal haze, edema, scarring, or Descemet breaks at that time. She was then treated with topical medications until 9 years of age and over that period had IOPs in the high 20's. When 9 years of age, she underwent bilateral MMC-augmented trabeculectomy. She is now referred at the age of 11 years with high measured IOPs and small central optic nerve head cups.

When children have increased measured IOP, buphthalmos, characteristic corneal haze/scarring, characteristic optic disc cupping, and characteristic myopia with astigmatism, the diagnosis of childhood glaucoma is easy. However, when these parameters are borderline or not at all present, the diagnosis can be challenging, particularly in infants. Also, there are ophthalmic conditions in which one or more of these parameters can be abnormal and thus mimic pediatric glaucoma. Therefore, it is particularly important in children with suspected glaucoma to collect as much clinical data as possible that together will provide evidence for or against the diagnosis of true pediatric glaucoma. The first thing to do is to carefully go over the documentation of her prior examinations and care.

Regarding the documentation we are provided of her care soon after birth, her large corneas and high measured IOP strongly suggest that she had glaucoma at that time; however, I would have liked to see further documentation of how IOP was taken and the corneal status at the time. Was the child crying when IOP was taken? I would have liked to see documented that IOP was taken while the child was calm and sleeping (or while struggling, if that was the case). If corneal edema and Descemet breaks were not present at that time, I would have liked to see that documented as a pertinent negative. Also, the cycloplegic refraction at the time would also have been useful in decision-making. Although a range of refractive errors can occur in infantile glaucoma, most affected newborns have myopia with astigmatism. The fact that there was no optic disc cupping at that time is unusual. Optic disc cupping in newborn glaucoma does not always have the same vertical configuration as occurs in adults, but it usually occurs early and therefore its absence raises suspicion for other conditions such as primary megalocornea. However, I have seen a few children with genetically proven primary congenital glaucoma who had gross corneal enlargement before any optic disc cupping during infancy.

There is no family history of glaucoma. We are not told about the ethnicity of the patient or if the parents were related. If the patient is from an area where *CYP1B1*-related pediatric glaucoma is common, I would be inclined to perform genetic testing for *CYP1B1* mutations. The results of such testing, whether positive or negative, may just provide further supporting evidence in the context of the clinical examination for decision making. I would like to stress that whether or not a decision for surgery is made is based on all clinical data taken together and not on the basis of genetic testing; there are children with congenital glaucoma who do not have *CYP1B1* mutations, and there are children with *CYP1B1* mutations who do not have glaucoma.

Regarding her current presentation at 11 years of age, the increased measured IOP is of course worrisome. However, the possibility exists that it is (and has been) artifactually elevated, particularly as it has been in the absence of significant optic disc cupping. CCT is a useful measurement in pediatric glaucoma assessment, as it often correlates with corneal rigidity such that thicker corneas tend to cause higher measured IOP readings. However, this is not always the case and exactly how to use CCT in pediatric glaucoma is not established. There

is no formula for using CCT to convert to an "actual" pediatric IOP, and other factors such as corneal hysteresis may affect the measured IOP more than CCT. In this patient, the relatively thick CCT is evidence that IOP may have been artifactually elevated. To crudely assess true IOP, I would digitally palpate the globes. If the IOP is truly above 50 mm Hg without medications, I would be able to feel an abnormally firm globe with my fingers.

There is no documentation as to whether or not there are Haab striae, so I assume there are none. I would like to see this documented as a pertinent negative, as this is useful clinical data. In corneal enlargement from pediatric glaucoma, the conjunctiva often inserts anteriorly on the cornea. I would like to know whether or not this finding is present as well.

If the measured IOP does truly reflect elevated IOP, the relative resistance of the optic nerve heads to glaucomatous cupping is unusual but not impossible. One possible explanation is optic disc drusen. There do not appear to be optic disc drusen in the clinical photographs. However, I would like to see the discs with stereoscopy and perform B-scan to assess for calcifications. Relative resistance of optic nerve heads to cupping in pediatric glaucoma theoretically could also be related to relatively rigid scleral canals, which might correlate with thicker CCT.

I think the most important test for this patient at this time is visual field testing. I prefer Goldmann visual fields. Given her situation, she needs to be followed at first monthly with Goldmann visual fields, and then less frequently if there are no defects characteristic of glaucoma or evidence of worsening. At the same time I would also perform serial optic nerve head photography to carefully follow the optic nerve heads for any evidence of glaucomatous changes. If the visual fields and optic nerve heads remain stable, I would not have any particular target measured IOP for this patient.

There may be a role for optical coherence tomography (OCT) in her case; however, I do not have experience with OCT in pediatric glaucoma as I do not routinely use it in young children.

If I decided that she did need surgery, at this point I would be inclined to implant a glaucoma drainage device. If I judged the superior conjunctiva to be problematic during intraoperative inspection, I would implant the device in the inferonasal quadrant where there are no extraocular muscles.

Suggested Readings

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Ramin Daneshvar, MD

Herein, an 11 year old girl with a presumptive diagnosis of PCG is described; however, the clinical dilemma is the absence of marked clinical worsening of the optic nerve appearance despite apparently high, uncontrollable IOP over a decade of follow-up. The discs are moderately sized, with healthy neuroretinal rims and vascular trunks. There is no obvious peripapillary changes and retinal nerve fiber layer defect. The corneas seem clear without obvious Haab's striae or edema and the eyes seem quiet. Indeed, the increase in corneal diameter over the first year of life is the mere clinical evidence of progression. Despite all medical and surgical interventions, IOP remained above 30 mmHg. To further complicate the picture, one could notice the higher than normal CCT. CCT in children with ocular hypertension is higher than normal, while in PCG cases it could be thinner[1-3] or thicker[4-7] than normal, depending on the degree of corneal stretching or edema, and probably racial factors.

It is well-established that thicker CCT could result in IOP overestimation with most tonometric methods. Damji and associates have

shown that although IOP underestimation in thin corneas are unlikely to be more than 4 or 5 mm Hg,[8] overestimations in thick corneas appear to have no limits.[9] The error could be as much as 24 mmHg with the Goldmann applanation tonometer.[10] Although some correction algorithms for IOP considering CCT values have been suggested,[11] these studies have been performed on adult eyes with normal corneal structure, and may not be generalizable to eyes of children with glaucoma. Collagen fibers are softer and more elastic in children less than 3 years of age as compared to older individuals. Indeed, a change in CCT in children has been demonstrated to be associated with greater difference in measured IOP than that in adults.[12] In addition, based on manometric investigations it has been suggested that one cannot predict "true" IOP based on applanation IOP readings.[13] While in an epidemiologic study higher CCT could on average be associated with IOP overestimation, on an individual basis, a thicker cornea could be associated with over- or underestimation of IOP based on many other biomechanical properties of the cornea. Actually, a thicker cornea could be 'softer' or 'harder' than normal. Feltgen and coworkers suggested that it is unsuitable to use any global recalculation formula to determine "true IOP" in clinical practice. They also suggested intracameral IOP measurement in challenging cases.[13]

Considering these and despite the strikingly high IOP in the fifties range, I seek some other clinical findings to make a decision for proper management:

1. First of all, I would try to have a better estimation of true IOP. As the method of tonometry is not described, I assume that it is performed using the current clinical gold standard, Goldmann applanation tonometry. So, I would check the IOP with a Pascal dynamic contour tonometer (DCT; Ziemer Ophthalmic Systems AG, Port, Switzerland) which has been shown, at least in adult eyes, to be less affected by corneal thickness and biomechanical properties.[14] Furthermore, knowing some corneal biomechanical parameters, using the ocular response analyzer (ORA; Reichert Inc., Depew,. NY, USA) or CorVis ST ("Corneal Visualization with Scheimpflug Technology" (CorVis ST), Oculus Inc., Wetzlar, Germany), could also be helpful.
2. I would do a gonioscopic evaluation: not only could this demonstrate how efficiently the previous interventions were done, it could also provide important diagnostic clues.
3. I need to check axial lengths of both eyes. The amount of anisometropia reported in this patient could be explained based on differences in her keratometric values and corneal distension. I wonder if there is any true axial lengthening of the eye as a result of PCG.
4. I would try to establish the visual field status. High quality automated perimetry could be obtained in most cooperative children with steady fixation starting at 9 or 10 years of age.[15] With some training, this child with excellent visual acuity may provide reliable automated visual fields. Regarding the lack of significant apparent structural changes despite high IOP over a decade of follow-up, it is reasonable to further observe the patient if there is no functional loss. If the patient could not perform reliable automated visual fields, one could try Goldmann perimetry as a friendlier alternative.
5. I would try to have some quantitative structural test, such as optic nerve head OCT along with high quality stereophotographs of the optic nerve head. Although the normative database of these instruments is not rich for pediatric patients, they could offer good baseline data for follow-up.
6. Last but not least, having some confocal microscopy or specular microscopy data could be helpful. It has been demonstrated that in contrast to non-glaucomatous megalocornea, in infantile glaucoma the number and density of endothelial cell are decreased.[16, 17]

If with proper follow-up and investigations I find convincing evidence that lower IOP is necessary, my first surgical option would be a repeated trabeculectomy augmented by MMC. The patient is aged enough to cooperate for

slit lamp examination and probably, timely removal of releasable sutures. Manometrically measuring IOP at the beginning of surgery could be highly yielding. If unsuccessful, I would proceed to a shunting procedure at a later stage. When deciding to proceed to surgery, one should consider the long life expectancy of the patient. On one hand this means that even slow progression could result in disabling visual loss during this patient's life span; on the other hand, even rare and late-occurring complications could deteriorate the patient's vision in the future.

Conflicts of Interest

None.

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