Neonatal-Onset Congenital Ectropion Uveae: A Distinct Phenotype of Newborn Glaucoma

SUSHMITA KAUSHIK, DEEPIKA DHINGRA, BADRINATH VIBHA, ARSHIYA SAINI, GAURAV GUPTA, SAGARIKA SNEHI, NIRBHAI SINGH, FAISAL THATTARUTHODY, AND SURINDER SINGH PANDAV

• PURPOSE: To describe neonatal-onset congenital ectropion uveae (N-CEU) as a distinct clinical entity of newborn glaucoma (NG) and to study its significance toward the severity and outcome of NG.
• DESIGN: Prospective clinical cohort study.
• METHODS: The study took place at a tertiary care postgraduate teaching institute. It included consecutive patients with NG who presented between July 1, 2016 and September 30, 2017, with a minimum postoperative follow-up of 1 year. Infants with any ocular anomaly apart from CEU were excluded. Patients with N-CEU were compared with those with neonatal-onset primary congenital glaucoma (N-PCG). All infants underwent goniotomy or trabeculotomy, with trabeculectomy depending on corneal clarity. Clinical features at presentation and outcome 1 year after surgery were defined as good or satisfactory if intraocular pressure was ≤16.0 mm Hg under anesthesia without or with topical medications, respectively, and poor if the infant required additional surgery.
• RESULTS: Twenty eyes of 10 patients with N-CEU were compared with 16 eyes of 9 patients with N-PCG. Infants with N-CEU had significantly worse corneal clarity (mean grade 2.0 ± 0.7 vs 1.4 ± 0.8; $P = .026$) and poorer outcomes compared with those with N-PCG. Seven of 16 (43.7%) eyes with N-PCG had a cornea clear enough at presentation for a goniotomy compared with only 2 of the 20 (10%) eyes with N-CEU ($P = .026$). Thirteen of 16 (81.2%) eyes with N-PCG had a good or satisfactory outcome compared with 6 of 20 (30%) eyes with N-CEU ($P = .001$).
• CONCLUSIONS: N-CEU appears to be distinct from the unilateral CEU in older patients described in the literature and may be considered a poorer prognosis phenotype of neonatal-onset glaucoma. (Am J Ophthalmol 2021;223:83–90. © 2020 Elsevier Inc. All rights reserved.)

AJO.com Supplemental Material available at AJO.com.
Accepted for publication Oct 1, 2020.

From the Advanced Eye Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India.
Inquiries to Sushmita Kaushik, Advanced Eye Centre, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India; e-mail: sushmita_kaushik@yahoo.com

GLAUCOMA IN CHILDREN IS A POTENTIALLY BLINDing disease and poses difficult clinical challenges in both diagnosis and management. Blindness due to glaucoma may occur even with appropriate treatment.[1,2] Factors reported for poor outcome include earlier age of onset,[2,3] baseline intraocular pressure (IOP), secondary glaucoma as classified by the Childhood Glaucoma Research Network (CGRN),[4] and the presence of *CYP1B1* mutations.[5]

The CGRN[4] has a universally accepted system of classification of childhood glaucoma. Patients with isolated trabeculodysgenesis are deemed to have "primary glaucoma," which could be primary congenital glaucoma (PCG) or juvenile open angle glaucoma (JOAG). PCG, in turn, is classified according to the age at onset of disease as being neonatal PCG (onset within 1 month of age), infantile PCG (onset between 1 month and 2 years), and late-onset or late recognized PCG (onset after 2 years). Secondary glaucoma with nonacquired ocular anomalies is an umbrella term for a wide variety of entities grouped as anterior segment dysgeneses, such as aniridia, Axenfeld Rieger syndrome, congenital iris hypoplasia, ectropion uveae, and Peter anomaly.[6]

Congenital ectropion uveae (CEU) has been reported as a rare, nonprogressive condition characterized by the presence of iris pigment epithelium on the anterior surface of the iris, which is characteristically unilateral, often with ipsilateral blepharoptosis,[7–9] and sometimes associated with Rieger syndrome,[8] Prader-Willi syndrome,[10] and neurofibromatosis type 1.[10,11] Patients have been mostly in the second decade of life and have been associated with JOAG,[9,10,12] although there have been 2 reports of CEU in infancy.[8,13]

Newborn glaucoma (NG) is an umbrella term that includes patients who present with glaucoma before the age of 1 month. Although PCG is the most common phenotype, any of the anterior segment dysgeneses conditions could present in the neonatal period.[14]

In our patients with NG, we observed a phenotype that included bilateral ectropion uvea and varying degrees of iris hypoplasia, which appeared to have a poorer prognosis compared with neonatal-onset PCG (N-PCG). In an extensive literature search on the Medline database, we were unable to find any report of bilateral CEU presenting as NG.

We undertook this study to prospectively observe the incidence, presentation features, and outcome of CEU in

0002-9394/$36.00
https://doi.org/10.1016/j.ajo.2020.10.001

newly-diagnosed childhood glaucoma with an age of onset of younger than 2 years, to analyze whether it had any prognostic significance toward the severity and outcome of the disease.

METHODS

IN THIS PROSPECTIVE CLINICAL COHORT STUDY, CONSECUtive patients with childhood glaucoma who were younger than 2 years of age and presented to the Paediatric Glaucoma Clinic of the Advanced Eye Centre, PGIMER, Chandigarh, India, in the 15 months between July 1, 2016 and September 30, 2017, were prospectively recruited. Informed consent was given by parents of all infants to participate in the study and to use their photographs for educational purposes only. The study adhered to the tenets of the Declaration of Helsinki, and institutional review board approval was obtained from the Institute Ethics Committee of the Postgraduate Institute of Medical Education and Research (vide No. NK/6225/Study).

All infants underwent a comprehensive history and ocular examination. Birth history, maternal history during pregnancy, demographic data, laterality, history of ocular complaints (especially photophobia, blepharospasm, watering, corneal haze, enlargement of eyes), and any systemic complaints were recorded.

All patients underwent an examination with torchlight, and those with any 2 of the following features underwent a detailed examination under anesthesia: a large-sized eye; cloudy cornea; a cup/disc ratio >0.3 if visible; or cupping determined on ocular B-scan ultrasonography. Epiphora and photophobia were considered corroborating factors.

• **EXAMINATION UNDER ANESTHESIA:** A detailed examination was done under anaesthesia using sevoflurane. IOP and central corneal thickness were measured using a Perkins tonometer (Haag-Streit, Koeniz, Switzerland) and an ultrasonic pachymeter (Tomey, GmbH, Nuremberg Germany), respectively. Corneal clarity was graded objectively by a 4-stage system suggested by Gupta and colleagues,[15] with modification[16]: stage 0: clear cornea; stage 1: minimal opacity; stage 2: moderate stromal opacity (anterior chamber and iris both well visualized); stage 3: significant stromal opacity (pupil visible with haze), and stage 4: intense stromal opacity (pupil invisible).

The posterior segment was examined using indirect ophthalmoscopy. If the corneal haze did not allow fundus evaluation, optic disc cupping was evaluated on B-scan ultrasonography (HiScan Touch Unit, Optikon, Rome, Italy). Axial length was measured using A-scan ultrasonography (Tomey, GmbH, Nuremberg Germany).

A clinical diagnosis of glaucoma was made if 2 of the following criteria were present: 1) IOP >18 mm Hg on repeated testing or IOP <18 mm Hg in the presence of corneal changes (eg, Haab striae, limbal stretching, or corneal edema); 2) optic cup-disc asymmetry of ≥0.2, focal rim thinning, or optic disc cupping on ultrasonography; 3) corneal changes/findings: Haab striae or corneal diameter >12 mm; or 4) axial length more than that expected for age.

Subjective complaints of photophobia, watering or hazy cornea noticed by parents were considered corroborating findings, but were not necessary for diagnosis.

We specifically looked for CEU, diagnosed by the presence of pigment epithelium over the anterior surface of the iris stroma, with or without iris atrophy or hypoplasia (Figure 1).

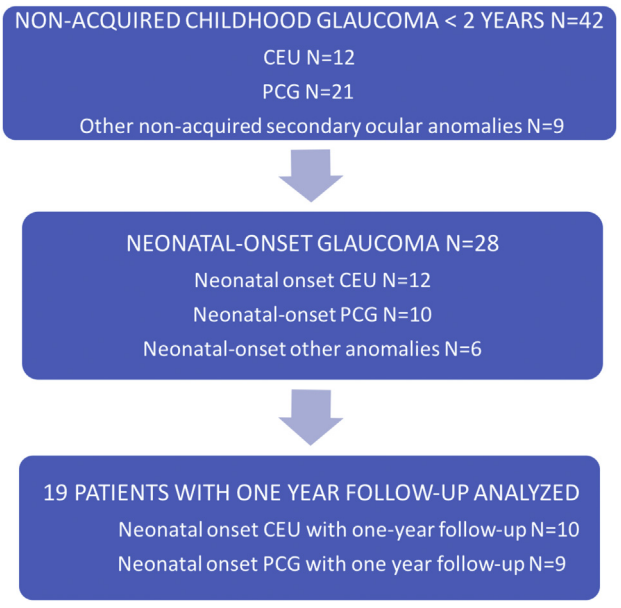

FIGURE 1. Flow of patients showing how the final cohort to be analyzed was selected. CEU = congenital ectropion uveae; PCG = primary congenital glaucoma.

• **INCLUSION CRITERIA:** Inclusion criteria were glaucoma in children younger than 2 years, as defined previously, with a minimum of 1-year follow-up after surgery.

• **EXCLUSION CRITERIA:** Any child with any ocular or systemic feature apart from CEU to account for the glaucoma was excluded. In case the anterior segment could not be visualized initially due to the hazy cornea, it was examined during the first postoperative examination under anesthesia. Patients were excluded from analysis in case there were features suggestive of other nonacquired ocular anomalies (eg, Axenfeld Rieger anomaly, Peter anomaly, or aniridia).

The following characteristics were recorded for each eye: corneal clarity graded as previously described; corneal diameter; IOP; central corneal thickness; anterior chamber details, including gonioscopy; optic disc evaluation if possible; axial length; and the presence or absence of CEU.

TABLE 1. Baseline Characteristics in Patients With Neonatal CEUongenital Ectropion Uveae and Neonatal PCGrimary Congenital Glaucoma

Parameter	CEU (n = 10 Patients; 20 Eyes)	All PCG (n = 21 Patients; 36 Eyes)	*p* Value[a]	Neonatal PCG (n = 9 Patients; 16 Eyes)	*p* Value[b]
Age at presentation (days)	37.3 ± 30.7 (15.3-59.3)	140 ± 134.7 (78.7-201.3)	.039	46.8 ± 21.7 (8.1; 16.3)	.453
IOP[#] (mm Hg)	22.5 ± 7.4 (19.3-25.9)	20.8 ± 7.1 (18.3-23.2)	.58	19.6 ± 6.5 (16.1-23.0)	.308
Corneal clarity grade	2.0± 0.79 (1.6-2.3)	1.3 ± 0.89 (1.0-1.6)	.006	1.4 ± 0.8 (0.9-1.8)	.026
Corneal diameter (mm)	12.1 ± 1.7 (11.3; 12.9)	12.9 ± 1.4 (12.4-13.4	.326	12.7 ± 1.5 (11.9; 13.5)	.315
Axial length (mm)	20.14 ± 2.7 (18.9-21.4)	21.5 ± 2.5 (20.6-22.3)	.04	20.3 ± 2.3 (19.1-21.6)	.82
CCT (μm)	801.5 ± 193.4 (698.4-904.5)	614.1± 90.3 (576.9-651.4)	<.0001	640.2 ± 81.6 (577.5-702.9)	.027

CEU = congenital ectropion uveae; IOP = intraocular pressure; PCG = primary congenital glaucoma.
Values are mean ± SD (95% confidence interval).
[a]Significance of difference between CEU and PCG.
[b]Significance of difference between CEU and newborn PCG.

Neonatal-onset glaucoma was defined as those patients who had an onset within 1 month of life and presented to us before 2 months of age, to avoid any poor outcome due to delayed surgery.

• **FOLLOW-UP:** Patients underwent a examination under anesthesia at 6 weeks, 3 months, 6 months, and then when required depending upon the clinical condition. Repeat glaucoma surgeries were done if needed.

Demographic data, clinical profile, surgical procedures performed, and outcomes at least 1 year after surgery were noted on prospectively filled forms.

• **MAIN OUTCOME MEASURES:** The outcome was assessed in terms of IOP control after surgery and the need for additional surgery.

Outcomes were described as: 1) good: when IOP was ≤16 mm Hg without drugs; 2) fair: when IOP was ≤16 mm Hg with up to 2 topical drugs; and 3) poor: when IOP was >16 mm Hg on 3 topical drugs, there was a need for systemic drugs for IOP control, or requirement of re-surgery for IOP control.

• **STATISTICAL ANALYSIS:** Descriptive statistics included demographic, presenting features, and outcomes. Qualitative variables were compared in the 2 groups using the Mann-Whitney U test for numerical variables with a skewed distribution. Categorical variables were compared using Fisher's exact test. Outcomes at 6 months and 1 year were analyzed. A P value <.05 was considered significant.

RESULTS

ONCE THE RECRUITMENT PERIOD WAS OVER, OUR PRELIMINARY analysis revealed that all infants in our cohort with CEU had NG (Table 1). Because the outcome in infantile-onset PCG is known to be more favorable compared with N-PCG,[2,3,17,18] it would not have been appropriate to compare neonatal-onset CEU with infantile PCG, which would, in any case, be expected to have had a better prognosis. Therefore, we believed it was best to exclude infantile-onset PCG from the analysis, and elected to analyze only neonatal-onset glaucoma with CEU (N-CEU) and N-PCG. The patient recruitment and final cohort selection is detailed in Figure 1.

A total of 42 children younger than 2 years with nonacquired childhood glaucoma without systemic disease presented in the 15-month period. Twelve children had CEU (32.4%), 21 had PCG, and 9 had other nonacquired ocular anomalies, who were excluded from subsequent analyses (Figure 1). All patients in the CEU group had neonatal-onset glaucoma with bilateral disease (N-CEU). Ten of the 21 patients with PCG had N-PCG.

In the study period, a total of 28 infants with neonatal-onset glaucoma presented to our clinic. Two of them had Peter anomaly, and 1 each had Axenfeld Rieger syndrome, Sturge-Weber syndrome, congenital primary aphakia, and congenital rubella syndrome, respectively. Of the remaining 22 infants, 12 had CEU and 10 had N-PCG; 10 infants with N-CEU and 9 infants with N-PCG completed 1-year follow-up. Twenty eyes of 10 patients with N-CEU were compared with 16 eyes of 9 patients with N-PCG.

Initial assessment revealed significant differences in the CEU and PCG groups. Table 1 shows the baseline characteristics of infants with CEU, the overall PCG group, and the N-PCG group to illustrate that the significant differences seen were likely because we compared a mixed group of infantile- and N-PCG group with a purely neonatal-onset group (CEU).

• **DEMOGRAPHICS:** There was no difference in the mean age of presentation (37.3 ± 30.7 days vs 46.8 ± 21.7 days; P = .45) between the 2 groups. Seven of 10

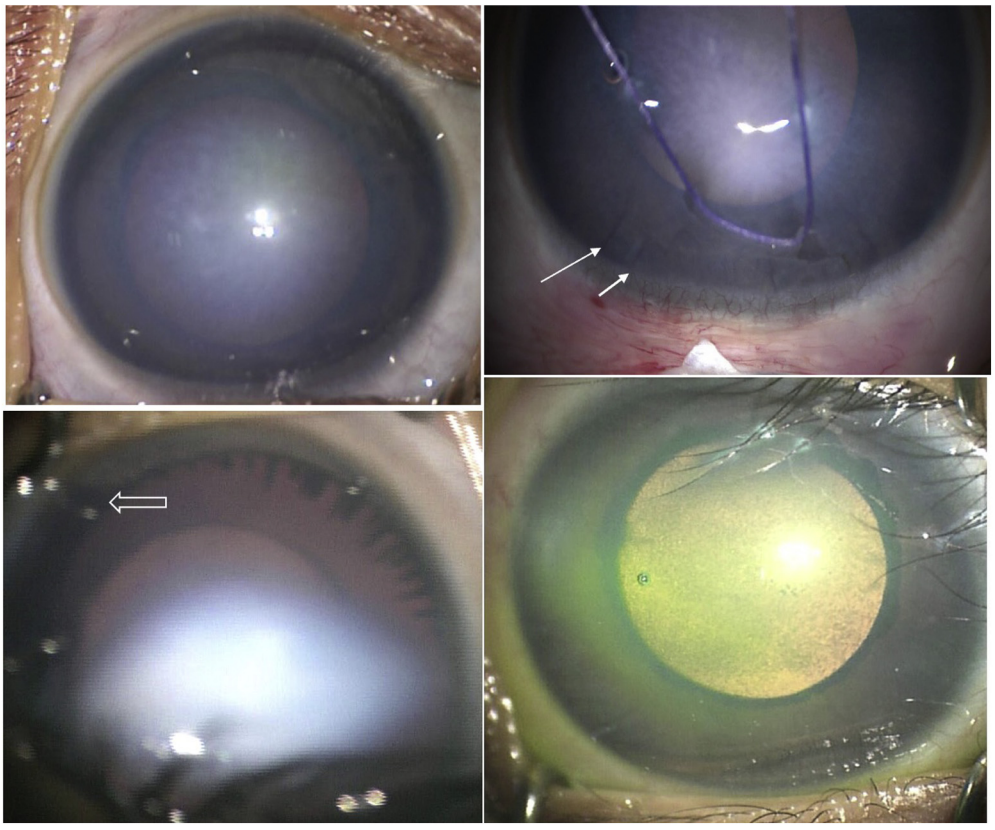

FIGURE 2. Advanced Eye Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India (Top left) Videograb photograph of neonatal congenital ectropion uveae (CEU) during surgery showing the presence of pigment epithelium over the anterior surface of the iris stroma at the pupillary margin, with significant iris hypoplasia leading to visibility of the iris vessels (white arrows). (Top left) Videograb photograph of neonatal CEU during surgery showing the significant iris hypoplasia leading to visibility of the iris vessels (white arrows). (Bottom left) Videograb photograph of another patient with neonatal-onset CEU showing the severe iris atrophy leading to an appearance of partial aniridia. Note the ciliary processes visible under the hypoplastic iris (open white arrow). (Bottom right) Videograb of a baby during examination under anesthesia. Note the corneal bedewing that has taken up the fluorescein stain used for measuring intraocular pressure.

infants (70%) with N-CEU and 5 of 9 (55.55%) infants with N-PCG were male ($P = .43$). All 10 patients with N-CEU and 7 of 9 patients with N-PCG had bilateral disease ($P = .21$).

• **BASELINE CHARACTERISTICS:** There was no significant difference in the IOP, corneal diameter, or axial length between the 2 groups (Table 1). Infants with N-CEU had significantly worse corneal clarity (mean grade: 2.0 ± 0.7 vs 1.4 ± 0.8; $P = .026$) and significantly thicker corneas (mean central corneal thickness: 801.5 ± 193.4 μm vs 640.2 ± 81.6 μm; $P < .001$) compared with those with N-PCG.

In the N-CEU group, there were varying grades of stromal iris hypoplasia. Four eyes had severe hypoplasia (Figure 2, left), akin to the partial aniridia (Figure 2, right) described by Khan and colleagues.[10]

• **SURGICAL INTERVENTION:** The initial surgery performed and the number of surgeries required are summarized in Table 2. Seven of 16 (43.7%) eyes with N-PCG had a cornea clear enough at presentation for a goniotomy compared with only 2 of the 20 (10%) eyes with N-CEU ($p = .026$).

• **FOLLOW-UP:** The IOP in eyes with CEU remained significantly higher than those without CEU throughout follow-up (Figure 3). The corneal clarity was also worse compared with eyes without CEU at every follow-up visit, although the difference did not reach statistical significance (Figure 3).

• **OUTCOMES:** Eyes with PCG had a significantly better outcome (Table 2). Six of 20 (30%) eyes with CEU eyes had a fair or good outcome compared with 13 of 16 (81.2%) eyes with PCG (Figure 4, Table 2) ($P = .001$). The IOP in 12 of 16 (75%) eyes with N-PCG was controlled without medications with 1 surgery compared with only 3 of the 20 (15%) eyes with N-CEU ($P = .001$).

TABLE 2. Surgical Procedures and Outcomes in Patients With Neonatal CEU and Neonatal PCG

	CEU (n = 10 Patients; 20 Eyes)	Neonatal PCG (n = 9 Patients; 16 Eyes)	*p* Value (Fisher's Exact Test)
Initial surgery			
Goniotomy	2 (10)	7 (43.7)	.026
Combined trabeculotomy with trabeculectomy	18 (90)	9 (56.3)	
Total	20	16	
Total no. of surgeries required			
1	6 (30)	13 (86.7)	.008
2	12 (60)	3 (13.3)	
3	2 (10)	0	
Total	20	16	
Outcomes			
Good (IOP <16 mm Hg without medication)	3 (15)	12 (75)	.001
Fair (IOP <16 mm Hg with up to 2 topical medications)	3 (15)	1 (18.75)	
Poor (IOP uncontrolled on 3 drugs or requirement of additional surgery)	14 (70)	3 (6.25)	
Total	20	16	

CEU = congenital ectropion uveae; IOP = intraocular pressure; PCG = primary congenital glaucoma.
Values are n and n (%).

DISCUSSION

IN OUR COHORT OF 25 INFANTS WITH NEONATAL-ONSET glaucoma, we observed CEU and iris hypoplasia, with no other ocular anomalies in 10 of 25 (40%) infants, other secondary nonacquired causes in 6 (24%) infants, and PCG in 9 (36%) infants. In our literature search for the term "congenital ectropion uveae" or "congenital iris ectropion," we did not find it reported previously with neonatal-onset glaucoma. The reported phenotypes were also different from what we observed.

The extent of ectropion uveae observed in our series was less extensive than has been described in some of the previously reported cases.[9,11,12] The corneas in our infants with CEU were hazy and thick. Our cohort also had severe iris hypoplasia, which was not seen in pictures of CEU described in the literature. The infants with N-PCG had better outcomes in terms of corneal clearing, IOP control, and required fewer repeat surgeries. Single surgery alone controlled IOP in 75% of patients with N-PCG without medication. This was better than that reported for neonatal-onset glaucoma,[17–19] but that might be because other nonocular anomalies were included in the earlier cohorts. Walton and associates[18] in a review of 35 newborn infants with PCG, reported a success rate of only 10% with goniotomy if the onset of disease was at birth but also reported better success rates for a trabeculectomy and a glaucoma drainage device. In a large series of 287 eyes with PCG, Shaeffer[19] reported success rates of only 30% if the onset was at younger than 1 month of age.

We had a more stringent criteria for success (16 mm Hg), which was lower than that of earlier studies (18 or 21 mm Hg). It was possible that our results would have been even better in PCG had we kept this criteria of IOP.

Most other references to CEU described JOAG as an associated condition, with clear corneas. Dowling and associates[8] described unilateral CEU, iris stromal hypoplasia, anterior insertion of the iris root, and glaucoma, with no underlying systemic abnormalities. One patient was a 4-month-old infant who had no glaucoma and was followed up. All patients had a clear cornea. Histopathology of 1 eye enucleated for intractable glaucoma revealed a normal central cornea. The iris-pigmented epithelium hyperplasia was postulated to be due to an embryological remnant that failed to completely regress in the anterior chamber.[6] Ritch and colleagues[9] described a similar appearance of CEU with a clear cornea in association with JOAG and underlying systemic abnormalities in 7 of 8 patients.

Harasymowycz and associates[20] reported glaucoma in a 3-year-old child, whose histopathologic specimen from the iridectomy showed a fibrovascular membrane covering the anterior surface of the iris stroma. They postulated that this membrane might have been responsible for pulling the posterior pigmented layer of the iris anteriorly, creating the ectropion. We found 1 isolated case report of glaucoma in an infant with CEU[21]; the clinical photograph of this eye

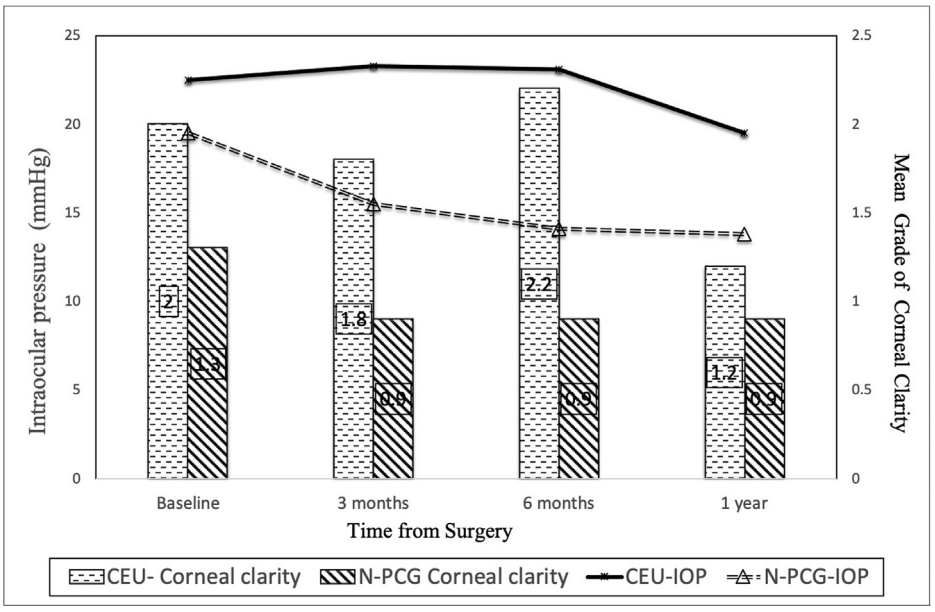

FIGURE 3. A combination graph showing the average intraocular pressure (IOP) and mean corneal clarity grade over time in neonatal-onset congenital ectropion uveae (N-CEU) and primary congenital glaucoma (N-PCG) groups. Note the significant difference in IOP at all time points. The corneal clarity was worse in N-CEU at all time points, although the differences did not reach statistical significance.

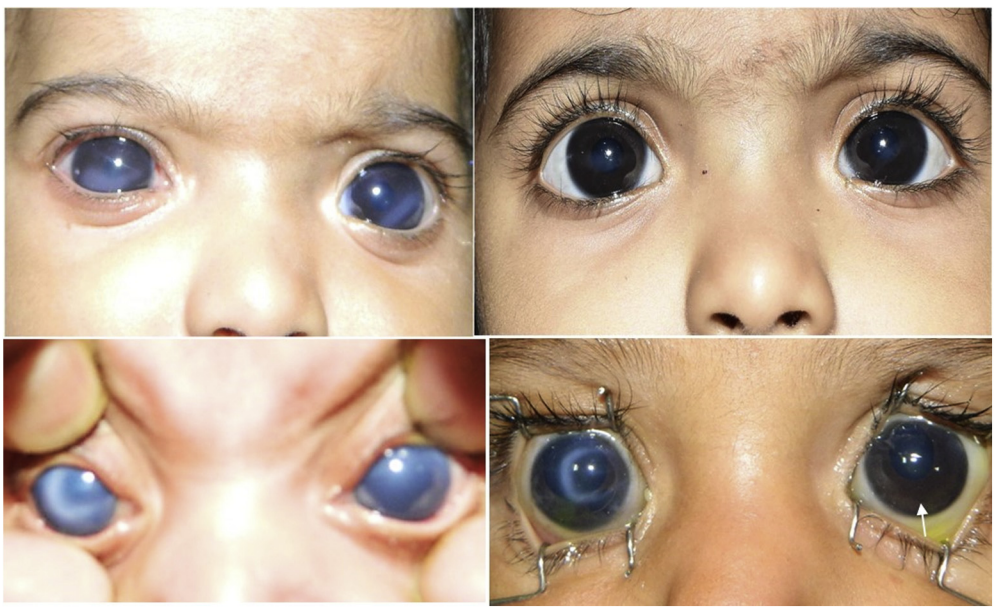

FIGURE 4. Presentation and follow-up clinical photographs of patients with (top panel) neonatal. -onset primary congenital glaucoma (PCG) and (bottom panel) neonatal-onset congenital ectropion uveae (CEU). (Top left) Clinical picture of neonatal-onset PCG at presentation. Note the normal iris and pupil visible through the steamy cornea and Haabs' striae. (Top right): Clinical picture 1 year after surgery. Note the clear cornea with minimal haze in the region of the Haabs' striae. The iris and pupil are normal. (Top left) Clinical picture of neonatal-onset CEU at presentation. Note the extreme corneal haze with no anterior chamber details visible. (Bottom left): Clinical picture 1 year after surgery. Note the clear peripheral cornea and persistent scar in the region of the Haabs striae. The ectroion uveae can now be visualized clearly (bottom right, white arrow).

was again like the ones described with JOAG. The affected eye also had mild ptosis with good levator function, also described in other reports.[8,9,12] This finding was postulated to be due to the neural crest origin of the Mueller muscle. No patient in our series had ptosis.

Willcock and associates[22] reported abnormalities in the *PAX6* gene seen typically in aniridia and suggested that congenital iris ectropion might be considered an indicator of variant aniridia. However, the pictures of the case they described were similar to the ones described earlier in association with JOAG.

We found the closest phenotype to those we reported in the images published by Khan and associates,[23] in which they termed the condition as a "partial aniridia" phenotype in neonatal-onset glaucoma. In their series, of the 67 patients with NG seen in 5 years, 8 probands had bilateral ectropion uveae with partial aniridia. They reported a large proportion of *CYP1B1* mutations in this cohort (91%) and suggested that this phenotype might be considered a marker for mutations in this gene. They found no mutation in *PAX6*, *FOXC1*, or *PITX2* in these patients with ectropion uveae and partial aniridia. They reported the p.G61E variant in their patients, which was previously reported as the most common CYP1B1 variant for the Saudi Arabian population.[24]

• **STUDY LIMITATIONS:** One limitation in our study was the lack of genetic information for all infants. We have now written this as an intramural project and hopefully will receive the grant to be able to screen all the infants for variants in the *CYP1B1* gene. We will expand our initial observations to include genetic testing in all of these infants, which is likely to throw more light on the underlying molecular biology of this distinctive condition.

The entity hitherto reported as CEU[8–10] has been described in older children or young adults, is characteristically unilateral, and is often associated with blepharoptosis, postulated to be related to an abnormality in structures derived from the neural crest.[7] It is possible that there is a spectrum of anterior segment anomalies that includes ectropion uveae and various degrees of iris hypoplasia, in which the worse case may present with neonatal-onset glaucoma, and the less severe cases are diagnosed later in life. However, because of the vast phenotypic difference in the 2 conditions (bilateral presentation in a neonate, severe glaucoma, no blepharoptosis), we feel that the 2 entities are not the same.

Our paper described a distinct entity of neonatal-onset CEU, which, to our knowledge, has not been described in reports of neonatal-onset glaucoma. Most other nonacquired glaucomas secondary to ocular or systemic anomalies described in the CGRN, such as Peter anomaly, Axenfeld Rieger anomaly, aniridia, and Sturge Weber syndrome, have been reported to occur in the neonatal period. The demonstration of *CYP1B1* mutations in both of the infants we tested might even point to this being an extremely severe form of PCG that had a early onset *in utero* and manifested these iris changes in the neonatal period.

CONCLUSIONS

WE BELIEVE THAT NEONATAL-ONSET CEU IS PHENOTYPIcally and genotypically distinct from CEU with glaucoma described in the literature. This condition should likely be considered a distinct phenotype of NG, and be described separately, rather than clubbing it with the more commonly reported unilateral entity that occurs in older children and young adults. Recognition of this condition is important because of its worse prognosis compared with PCG.

A. FUNDING/SUPPORT: NO FUNDING WAS RECEIVED FOR THIS STUDY. ALL AUTHORS ATTEST THAT THEY MEET THE CURRENT ICMJE criteria for authorship.

b. Financial disclosures: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

REFERENCES

1. Kargi SH, Koc F, Biglan AW, Davis JS. Visual acuity in children with glaucoma. *Ophthalmology* 2006;113:229–238.
2. Congenital glaucoma. In: Allingham RR, Damji KF, Freedman S, Mori SE, Shafranov G, eds. Shield's Textbook of Glaucoma. 5th ed. Philadelphia: Lippincott, Williams, and Wilkins; 2005:235–252.
3. Spaeth GL. Congenital glaucoma. *Pediatrics* 1991;88(5):1075–1076.
4. Beck AD, Chang TCP, Freedman SF. Definition, classification, differential diagnosis. In: Childhood Glaucoma: Consensus Series 9. Amsterdam: Kugler; 2013.
5. Al-Shahrani N, Khan AO. Observations regarding gender and response to initial angle surgery in CYP1B1-related primary congenital glaucoma. *Ophthalmic Genet* 2017;38(3):294.
6. Thau A, Lloyd M, Freedman SF, Beck AD, Grajewski A, Levin AV. Childhood glaucoma classification system: implications for clinical care and a research registry. *Curr Opin Ophthalmol* 2018;29(5):385–394.
7. Wilson ME. Congenital iris ectropion and a new classification for anterior segment dysgenesis. *J Pediatr Ophthalmol Strabismus* 1990;27(1):48–55.
8. Dowling JL Jr, Albert DM, Nelson LB, Walton DS. Primary glaucoma associated with iridotrabecular dysgenesis and ectropion uveae. *Ophthalmology* 1985;92(7):912–921.
9. Ritch R, Forbes M, Hetherington J Jr, Harrison R, Podos SM. Congenital ectropion uveae with glaucoma. *Ophthalmology* 1984;91(4):326–331.

10. Futterweit W, Ritch R, Teekhasaenee C, et al. Coexistence of Prader-Willi syndrome, congenital ectropion uveae with glaucoma, and factor XI deficiency. *JAMA* 1986;255(23):3280–3282.
11. Trovo-Marqui AB, Goloni-Bertollo EM, Teixeira MF, et al. Presence of the R1748X mutation in the NF1 gene in a Brazilian patient with ectropion uveae. *Ophthalmic Res* 2004;36(6):349–352.
12. Hatami M, Doozandeh A, Arumugam J, Feizi M. Glaucoma in ectropion uveae syndrome: A case report and literature review. *J Ophthalmic Vis Res* 2019;14(3):370–375.
13. Sethi HS, Pal N, Dada T. Bilateral juvenile glaucoma with iridotrabecular dysgenesis, congenital ectropion uveae, and thickened corneal nerves. *Eye (Lond)* 2005;19(12):1347–1349.
14. Mandal AK, Gothwal VK, Bagga H, Nutheti R, Mansoori T. Outcome of surgery on infants younger than 1 month with congenital glaucoma. *Ophthalmology* 2003;110(10):1909–1915.
15. Gupta N, Kalaivani M, Tandon R. Comparison of prognostic value of Roper Hall and Dua classification systems in acute ocular burns. *Br J Ophthalmol* 2011;95(2):194–198.
16. Choi H, Phillips C, Oh JY, et al. Comprehensive modeling of corneal alkali injury in the rat eye. *Curr Eye Res* 2017;42(10):1348–1357.
17. Anderson DR. Trabeculotomy compared to goniotomy of glaucoma in children. *Ophthalmology* 1983;90(7):805–806.
18. Walton DS, Katsavounidou G. Newborn primary congenital glaucoma: 2005 update. *J Pediatr Ophthalmol Strabismus* 2005;42(6):333–341.
19. Shaffer RN. Prognosis of goniotomy in primary infantile glaucoma (trabeculodysgenesis). *Trans Am Ophthalmol Soc* 1982;80:321–325.
20. Harasymowycz PJ, Papamatheakis DG, Eagle RC Jr, et al. Congenital ectropion uveae and glaucoma. *Arch Ophthalmol* 2006;124(2):271–273.
21. Laaks D, Freeman N. Congenital iris ectropion uveae presenting with glaucoma in infancy. *J AAPOS* 2013;17(2):214–216.
22. Willcock C, Grigg J, Wilson M, Tam P, Billson F, Jamieson R. Congenital iris ectropion as an indicator of variant aniridia. *Br J Ophthalmol* 2006;90(5):658.
23. Khan AO, Aldahmesh MA, Al-Abdi L, et al. Molecular characterization of newborn glaucoma including a distinct aniridic phenotype. *Ophthalmic Genet* 2011;32(3):138–142.
24. Bejjani BA, Lewis RA, Tomey KF, et al. Mutations in CYP1B1, the gene for cytochrome P4501B1, are the predominant cause of primary congenital glaucoma in Saudi Arabia. *Am J Hum Genet* 1998;62(2):325–333.