

## Congenital corneal clouding: A case series

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### ABSTRACT

Congenital corneal clouding often causes diagnostic dilemma; hence, detailed evaluation and timely intervention are required to decrease the morbidity. Various genetic, developmental, metabolic, and idiopathic causes of congenital corneal clouding include Peters anomaly, sclerocornea, birth trauma, congenital glaucoma, mucopolysaccharidosis, and dermoids. We report a case series of four neonates with congenital corneal clouding admitted in our neonatal intensive care unit, over 5 years. Two cases were of Peters anomaly, one each of primary congenital glaucoma and glaucoma secondary to congenital rubella.

**Key words:** *Buphthalmos, Corneal clouding, Glaucoma, Peters anomaly*

The prevalence of congenital corneal opacities (CCO) is estimated to be 3 in 100,000 newborns. This number increases to 6 in 100,000, if congenital glaucoma patients are included. Corneal opacifications of infancy are caused by several different disorders such as anterior segment dysgenesis disorders (Peters' anomaly, sclerocornea, and congenital anterior staphyloma), metabolic disorders (mucopolysaccharidoses and mucopolipidoses), and corneal dystrophies (congenital hereditary endothelial dystrophy [CHED], congenital hereditary stromal dystrophy, and posterior polymorphous dystrophy). Other causes include posterior corneal defects (posterior keratoconus), corneal dermoids, trauma (forceps trauma), infections (congenital rubella, herpes simplex, and bacterial infections), and congenital glaucoma [1].

Some studies have shown Peters anomaly to be the most common cause of congenital corneal clouding. This is followed in frequency by sclerocornea, corneal dermoids, congenital glaucoma, microphthalmia, birth trauma, and metabolic diseases [2]. Many of the CCOs have recently been linked to genetic defects; hence, identifying mutations for specific disorders may lead to better understanding of the underlying pathogenesis and may help with diagnosis and prognosis. Corneal opacity obstructs the visual axis, leading to sensory deprivation, amblyopia, and severe visual impairment. Early surgical intervention has been advocated in patients to prevent deprivation amblyopia and irreversible glaucoma [3,4].

### CASE REPORT

We report here four neonates with congenital corneal clouding/opacities admitted in our neonatal intensive care unit over

5 years (Table 1). Two cases were of Peters anomaly, the third neonate was of primary congenital glaucoma, and the fourth had glaucoma secondary to congenital rubella. The two cases of Peters anomaly were siblings and the first case was a full-term female child with Peters Type 2 (Figs. 1 and 2), while the second case (Fig. 3) was full-term male child with Peters Type 1. The mother of the siblings also had similar complaints at birth. Our third case was a preterm male child with primary congenital glaucoma (Fig. 4) and the fourth case was preterm male child with congenital rubella and he had secondary glaucoma (Fig. 5).

Antenatal anomaly scans were normal for all the babies. Detailed ophthalmic evaluation was done for all the babies and B-scan ultrasonography was suggestive of Peter's anomaly for the first and second case (anterior segment dysgenesis). All our cases were presented as bilateral corneal clouding. The first case had additional bilateral lenticular cataract and on follow-up at 3 years, he had developed anterior staphyloma of the left eye (Fig. 2). Postnatal 2D echo was suggestive of ventricular septal defect (VSD) (first case), atrial septal defect (ASD) with patent ductus arteriosus (PDA) (second case), and ASD with large PDA in case 4. Toxoplasma, syphilis, rubella, cytomegalovirus, and herpes simplex titers were positive for the baby with congenital rubella (fourth case) and normal in other three cases. Surgical treatment was done for the first three cases (trabeculotomy+trabeculectomy) with additional lensectomy for the first case. The fourth case expired before surgical intervention due to other associated medical conditions. The other three operated patients were discharged and were advised regular follow-up.

Table 1: Clinical profile of cases

Patient Details	First case: Peters type 2	Second case: Peters type 1	Third case: Primary congenital glaucoma	Fourth case: Secondary congenital glaucoma with congenital rubella
Sex	Female	Male	Male	Male
Gestational age	Full term (38 weeks)	Full term (39 weeks)	Preterm (36 weeks)	Preterm (32 weeks)
Birth weight (kg)	2.6	3.1	2.3	1.2
Gravida	P1L1	P2L2A1	P2L2	P1L1
Antenatal history	Uneventful	Uneventful	Uneventful	Uneventful
Family history	Mother had congenital corneal clouding at birth	Mother had congenital corneal clouding at birth	Not significant	Not significant
Facial dysmorphism	No	No	No	No
Examination	Systolic murmur	Continuous murmur	Normal	Icterus present, systolic murmur, hepatosplenomegaly
Ocular examination	Bilateral central corneal opacity, with bilateral buphthalmos (Rt>Lt)	Bilateral central corneal opacification with 360-degree superficial vascularization, and bluish discoloration of both sclera with buphthalmos	Bilateral congenital corneal clouding with buphthalmos with megalocornea	Bilateral buphthalmos with megalocornea with corneal haziness
Ocular tonometry	Raised intraocular pressure of the right eye	Normal intraocular pressure	Raised intraocular pressure	Raised intraocular pressure
B-scan of eyes	Bilateral marked thickening of cornea, iridocorneal adhesions with lamellar cataract, features s/o peters type 2 anomaly.	Bilateral marked thickening of cornea, thick iris – stuck to the cornea, closed angles and normal lens and zonules – features s/o Peters anomaly type-1.	–	Could not be done
2D echo	VSD	ASD with PDA	Normal	4 mm OS-ASD with large PDA
TORCH titers	–	–	–	Positive for rubella IgM
Treatment	Trabeculectomy+trabeculectomy+lensectomy of the right eye, with antiglaucoma medications. At 3 months full thickness penetrating keratoplasty of the right eye was done	Trabeculectomy+trabeculectomy+peripheral iridectomy done in B/L eyes and corneal keratoplasty planned	Bilateral trabeculectomy+trabeculectomy. Baby was discharged with antiglaucoma medications	Expired before surgery

TORCH: Toxoplasma, syphilis, rubella, cytomegalovirus, and herpes, VSD: Ventricular septal defect, ASD: Atrial septal defect, PDA: Patent ductus arteriosus



Figure 1: First case: At birth, Peters anomaly type 2 showing central corneal opacity



Figure 4: Third case: Bilateral corneal clouding with buphthalmos and megalocornea in a case of primary congenital glaucoma



Figure 2: First case 1: Follow-up at 3 years showing anterior staphyloma of the left eye



Figure 5: Fourth Case: Bilateral buphthalmos with megalocornea with corneal haziness in a neonate with congenital rubella



Figure 3: Second case: Peters anomaly type 1 showing central corneal opacification with 360-degree superficial vascularization and bluish discoloration of the left sclera

## DISCUSSION

The mnemonic STUMPED is helpful for remembering the differential diagnosis for CCOs: Sclerocornea, tears in Descemet membrane

(usually due to forceps trauma or congenital glaucoma), ulcers (infection), metabolic (e.g., mucopolysaccharidosis), Peter's anomaly, edema (e.g., CHED), and dermoid [5]. The corneal opacities can be classified as follows: (a) Central opacity – Peters anomaly, forceps injury, and posterior corneal defects; (b) peripheral opacity – sclerocornea and dermoid; and (c) diffuse opacity – infantile glaucoma, congenital hereditary stromal dystrophy, CHED, and mucopolysaccharidosis/mucopolipidosis.

Sclerocornea, in which, the normal translucent cornea is replaced by scleral-like tissue. White feathery ill-defined and vascularized tissue develops in the peripheral cornea. It can be unilateral/bilateral, non-progressive with sporadic inheritance.

Tears in endothelium and Descemet membrane can be secondary to birth trauma or congenital glaucoma. Primary infantile glaucoma, commonly termed congenital glaucoma or trabeculodysgenesis, is an unusual, inherited anomaly of the trabecular meshwork and anterior chamber angle which leads to obstruction of aqueous outflow, increased intraocular pressure, and optic nerve damage. Several genes are implicated, prominently CYP1B1 [6]. Classic symptoms at presentation include tearing, photophobia, blepharospasm, eye rubbing,

and irritability. Examination may reveal elevated intraocular pressure, corneal edema, increased corneal diameter, and Haab striae. Angle surgery remains the first-line treatment for primary congenital glaucoma with a recent advance being circumferential trabeculotomy. Secondary glaucoma can result from multiple etiologies including trauma, neoplasms, and infections including congenital intrauterine infections [7].

Corneal ulcers that are present at or develop around birth are rare and may be caused by herpes simplex virus keratitis, bacterial keratitis, or neurotrophic keratitis. Congenital rubella is acquired during the first trimester of gestation, and corneal opacity may result from an endotheliitis, elevated intraocular pressure, or keratolenticular adhesions. Metabolic, which is rarely present at birth, bilateral, progressive, autosomal recessive, mucopolysaccharidosis (hurler syndrome), mucopolipidosis (Scheie syndrome), tyrosinemia, and cystinosis, can also present as corneal opacities.

Peters anomaly is a disease that causes central corneal opacity due to anterior segment dysgenesis, which is as a result of defective neural crest cell migration during development. Peters anomaly can be caused by many different diseases including genetic conditions (e.g., Axenfeld-Rieger syndrome) and non-genetic conditions (e.g., congenital rubella) [5]. Unilateral cases are usually isolated, but bilateral cases are often associated with systemic disorders and warrant a complete genetic workup. Genes controlling differentiation of primordial cells are thought to be responsible for abnormal neural crest cell migration to the posterior cornea. Specifically, mutations within the PAX6 gene, PITX2 gene, and FOXC1 gene have been found to be responsible [8]. The majority of cases are sporadic; however, autosomal recessive and dominant patterns of inheritance have been found in consanguineous marriages.

The two clinical variants of Peters anomaly are Peters Type I characterized by a central corneal opacity with iridocorneal adhesions and Peters anomaly Type II characterized by a central corneal opacity with cataracts or corneolenticular adhesions. Peters plus syndrome is characterized by Peters anomaly in association with cleft lip/palate, short stature, abnormal ears, and mental retardation [9]. High-frequency ultrasound biomicroscopy is well established as a useful tool for the examination of the anterior segment, especially in eyes with opaque corneas [10]. Patients with Peters anomaly should undergo penetrating keratoplasty or optical iridectomy within the 1<sup>st</sup> year of life by a corneal specialist [3,4].

Bilateral and autosomal dominant, the cornea is diffusely and uniformly edematous due to a defect of the corneal endothelium and Descemet membrane. The edema involves both the stroma

and the epithelium and is typically a bilateral process. The hallmark of CHED is increased corneal thickness.

An epibulbar (limbal) dermoid is a choristoma composed of fibrofatty tissue covered by keratinized epithelium. It is present from birth and little if any postnatal growth occurs. Dermoids may contain hair follicles, sebaceous glands, or sweat glands. They can be up to 10 mm in diameter and usually straddle the limbus. Corneal opacities in neonates can obstruct the visual axis, leading to sensory deprivation, amblyopia, and severe visual impairment. Hence, treatment should be initiated as early as possible, to prevent sensory amblyopia and irreversible glaucoma [3].

## CONCLUSION

Early diagnosis is essential so that appropriate treatment can be initiated as early as possible and the child can obtain the best possible vision. A detailed evaluation and timely intervention are required to decrease the morbidity.

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