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RESEARCH REPORT

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Peters anomaly: A 5-year experience

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Abstract

Background: Peters anomaly is a rare, congenital eye malformation characterized by an opaque cornea and blurred vision. Central corneal opacification can lead to delayed progression of visual development caused by defects in Descemet membrane and the posterior stroma. These children require several anesthetics for multiple eye examinations under anesthesia and corneal transplantation.

Aims: We sought to review the anesthetic management of patients with Peters anomaly for ophthalmologic procedures at Westchester Medical Center, a major referral center for Peters anomaly.

Methods: A retrospective chart review was completed which included pediatric patients who underwent ophthalmologic procedures related to Peters anomaly from 2013-2018.

Results: The charts of 35 patients with Peters anomaly were reviewed: 14 patients with Peters anomaly Type I, 10 patients with Peters anomaly Type II, and 11 patients with Peters plus syndrome. Thirty patients required three procedures on average, two examinations under anesthesia pre- and post-transplant, and anesthesia for the corneal transplant itself. The youngest patient encountered for examination under anesthesia was 39-week postconceptual age. Anesthetic time for examination under anesthesia averaged 31 minutes using a laryngeal mask airway while corneal transplant averaged 104 minutes utilizing endotracheal intubation. Postanesthesia care unit stay averaged 51 minutes following examination under anesthesia and 65 minutes after corneal transplant. All examinations under anesthesia were successfully completed without adverse events with the use of a laryngeal mask airway. This case series includes two patients with Goldenhar syndrome and Al-Gazali syndrome accompanying Peters anomaly.

Conclusion: Although limited by its retrospective nature, this case series describes the cardiac and systemic implications of patients undergoing anesthesia with Peters anomaly. Our experience indicates that general anesthesia and airway manipulation are tolerated with minor postoperative concerns in these infants. Pediatric patients with Peters anomaly require multiple anesthetics for repeated ophthalmologic interventions. The laryngeal mask airway can be routinely utilized in infants less than 3 months of age for an eye examination under anesthesia with no airway complications noted. Perioperative providers should be aware of the multisystemic implications in patients with Peters plus syndrome.

KEYWORDS
age, airway, cardiac, congenital anomalies & syndromes, congenital heart disease, general anesthesia, ophthalmology

1 | INTRODUCTION

Peters anomaly was first described in 1905 by a German ophthalmologist, Dr Alfred Peters, as a condition characterized by an opaque cornea leading to blurred vision. Peters anomaly is a rare condition, and reports describing management are scarce. Westchester Medical Center is one of the few institutions where patients with this condition are commonly managed. This management includes anesthesia for ophthalmic procedures in children often younger than 3 months of age.

Although the exact prevalence of Peters anomaly is unknown, Kurilec et al have described the prevalence of disorders known as congenital corneal opacities as affecting 1 individual per 24 000.[1] While most cases of Peters anomaly are sporadic, it can be inherited in an autosomal dominant (FOXC1,[2] PAX6,[3] and PITX2[4]) or recessive (CYP1B1) manner via the aforementioned gene mutations. These genes are known as homeobox genes which direct the formation of numerous parts of the body during early embryonic development. FOXC1, PAX6, and PITX2 are involved in the development of the anterior segment of the eye, while the CYP1B1 gene encodes a member of the cytochrome p450 superfamily of enzymes, involved in the metabolism of a signaling molecule essential for corneal development. Abnormal neural crest migration to the posterior cornea may be caused by homeotic genes controlling differentiation of primordial cells.

Peters anomaly is categorized into three types: Type I, Type II, and Peter plus syndrome.[5] Type I results in an incomplete separation of the cornea and iris and leads to a mild to moderate corneal opacity. Type II also results in an incomplete separation of the cornea and the lens, but is typically more severe. In this syndrome, the lens adheres to the cornea causing keratolenticular adhesions. Individuals with Peters plus syndrome have short stature, shortened upper limbs and shortened fingers and toes (brachydactyly). The characteristic facial features of Peters plus syndrome include a prominent forehead; small, malformed ears; narrow eyes; a long philtrum, and a pronounced double curve of the upper lip known as Cupid's bow. A patient's neck may also be broad and webbed. A cleft lip with or without a cleft palate is present in about half the patients with this condition. Peters anomaly can also be associated with abnormal hearing and developmental delay in 80% of cases, although intellectual disability can vary from mild to severe.[5] Peters plus patients often manifest numerous systemic malformations, most commonly in children affected with bilateral opacities. These malformations include congenital cardiac abnormalities including atrial septal defect, ventricular septal defect, patent ductus arteriosus, intestinal malrotation, micrognathia, and short limb dwarfism.

Despite aggressive surgical and postoperative intervention, almost 40% of patients lose some visual perception secondary to glaucoma.[6] The wide spectrum of presentation of Peters anomaly must be considered when examining the patient. A thorough EUA must be performed to assess the severity of the corneal opacity and other associated ocular abnormalities to evaluate for successful corneal transplantation. A child's development can be devastatingly hampered if vision is not corrected early via a full thickness corneal transplant, or penetrating keratoplasty (PKP). We describe the anesthetic management of 35 children who were diagnosed with and treated for Peters anomaly between 2013 and 2018.

What is already known about the topic

- Peters anomaly is a rare, congenital ocular malformation characterized by corneal opacification that requires multiple anesthetic interventions for management.
- Systemic malformations commonly associated with Peters plus syndrome include cleft lip/palate, congenital cardiac abnormalities, micrognathia, intestinal malrotation, and short limb dwarfism.

What new information this study adds

- For an eye examination under anesthesia prior to corneal transplant, infants younger than 3 months of age can be routinely anesthetized with a laryngeal mask airway utilizing spontaneous ventilation with no airway complications noted.
- This case series documents the concomitant occurrence of Peters anomaly and Goldenhar syndrome.

2 | MATERIALS AND METHODS

A retrospective chart review of 35 patients at Westchester Medical Center from 2013-2018 was performed following institutional review board approval. Information obtained from the patient's medical record included affected eye, sex, age and weight at presentation, postconceptual age during the primary anesthetic, history of prematurity, co-existing cardiac complications, and existence of systemic abnormalities. Type of surgery, airway management, surgical duration, length of postoperative anesthesia care unit (PACU) stay, and anesthetic complications were identified. All patients included in this study underwent corneal transplantation. Patients were excluded if information about laterality of lesion, and ocular or systemic complications was missing, which consisted of five patients.

3 | CASE DESCRIPTION

The management of patients with Peters anomaly often requires several anesthetics. Patients are seen for an initial diagnostic workup and evaluation in the operating room for corneal opacities. The average EUA lasts 31 minutes. If appropriate, patients are then scheduled for corneal transplant under general anesthesia and subsequently for postoperative EUA. This necessitates at least three anesthetics utilizing a laryngeal mask airway (LMA) for shorter procedures and endotracheal intubation along with muscle relaxation for corneal transplantation. In addition to cardiac evaluation in patients with Peters plus syndrome, a complete workup included abdominal ultrasound for renal anomalies, neuroimaging (performed without sedation or general anesthesia) to rule out hydrocephalus and structural brain abnormalities, thyroid function tests, hearing assessments, and consultation with a genetic counselor.

Peters anomaly is often diagnosed by an infant's pediatrician and then referred to an ophthalmologist for further workup. For an EUA, patients were brought into the operating room and routine monitoring was applied- EKG, noninvasive blood pressure, pulse oximetry, temperature, and end-tidal carbon dioxide. Anesthetic management consisted of a mask induction with nitrous oxide/oxygen and sevoflurane. Intravenous catheter placement with a 22 or 24-gauge catheter was established, and patients were given propofol 1-2 mg/kg. Once a deep anesthetic plane was established, an LMA was inserted for airway management (typically size 1.5). Anesthesia was maintained with sevoflurane and air/oxygen as the patient maintained spontaneous respirations.

The EUA consisted of examination of each eye under the operating microscope. Intraocular pressure, corneal thickness, and presence or absence of astigmatism were evaluated in each patient. Ultrasonography of the front portion of the eye, known as UBM (Ultrasonic BioMetery), and ultrasonography of the back portion of the eye, known as B-scan ultrasonography, were then completed under anesthesia. Length of the eye, or the A-scan, was also evaluated. Following pupillary dilation, the retina was examined for corneal scars and the evaluation of cataracts. Following completion of the examination, once the patient was responsive, the LMA was removed, and the patient was given supplemental oxygen via a face mask and taken to the PACU with pulse oximetry.

Patients were subsequently brought back to Westchester Medical Center for PKP. If the transplant was for patients with bilateral Peters anomaly, corneal transplants were done individually 3-months apart. Patients were brought into the operating room and monitors were applied for induction. Mask induction with nitrous oxide/oxygen and sevoflurane was started, and an intravenous 22-24-gauge catheter was placed. Propofol 1-2 mg/kg was given and once adequate ventilation via mask was established, patients were paralyzed with 0.7-1 mg/kg of rocuronium. Endotracheal intubation with a cuffed oral endotracheal tube was performed, and the anesthetic was maintained with sevoflurane and air/oxygen. Pressure control ventilation was utilized to maintain normocarbia.

Pediatric corneal transplantation is often more technically challenging than the procedure in adults due to increased corneal and scleral elasticity, reduced rigidity, and smaller anatomical conformation. In the infant population, the cornea is more pliable and expulsion of the lens can be a more common complication. Due to the aforementioned factors, there are multiple efforts undertaken to reduce vitreous pressure. Paralysis with a nondepolarizing muscle relaxant reduces the risk of movement and extraocular muscle contraction. Posterior pressure is reduced via hyperventilation and placing the patient in a slight reverse Trendelenburg position. Intravenous mannitol (0.5-1.0 g/kg/dose) is given to reduce vitreous volume, with peak activity occurring approximately 45 minutes following administration.[7] Mannitol must be carefully administered in infants as it can lead to electrolyte imbalances and hemodynamic instability.

The average length of the corneal transplant procedure was 1-2 hours. Patients were given 1-2 mcg/kg fentanyl, and muscle relaxation was monitored. At the end of the procedure, patients were fully reversed with neostigmine and glycopyrrolate or sugammadex. Patients were extubated once they were awake and maintaining regular respiratory rate and adequate vital signs and transported to the PACU with oxygen facemask and pulse oximetry. They were discharged to the ward when appropriately recovered from anesthesia.

Post-transplant EUA was commonly performed between four and eight weeks after surgery to facilitate suture removal. This was the quickest surgical procedure because only the eye with a transplant was addressed. Once the child was anesthetized and an LMA placed, the eye was examined, less extensively than the original EUA, and the stitches were removed.

4 | RESULTS

Thirty-five cases of Peters anomaly were reviewed at our institution. Characteristics of each case including laterality, sex, postconceptual age at first encounter, co-existing cardiac complications, systemic abnormalities, and history of prematurity were charted (Table 1). In the cases reviewed, 57% of cases were male, while 43% were female. Twenty-two of 35 patients (62.8%) were unilateral, while 13/35 (37.2%) were bilateral. The youngest patient encountered for EUA in this sample was 39-week postconceptual age.

Based on the American College of Gynecologists description of term births being greater than 37-week gestational age, 8/35 patients, or 22.8% of patients in this sample, were born preterm. Of the 13 bilateral Peters anomaly patients, 6 had cardiac anomalies and 6 had systemic abnormalities. Of the 22 unilateral Peters anomaly patients, 4 had cardiac anomalies and 2 had systemic abnormalities (Table 1). A total of 10 of the Peters anomaly patients had congenital cardiac disease (28.6%), and 8 (22.8%) had systemic abnormalities. These frequencies are markedly greater than what would be expected in the normal population. In our sample, 14 patients presented with Peters anomaly Type I, 10 patients with Peters anomaly Type II, and 11 patients with Peters plus syndrome.

Surgical time for corneal transplant in these patients averaged 104 minutes and the airway was managed with endotracheal

TABLE 1 Cardiac and Systemic Findings in 35 patients with Peters anomaly at First Anesthetic Encounter

Patient Number	Affected Eye	Sex	Peters Type	Weight (Kg)	Gestational Age (Wk)	Postconceptual Age at First Encounter (Wk)	Co-Existing Cardiac Abnormalities	Systemic Complications
1	R	Male	Type I	5	40	47 Wk, 6 D	–	–
2	L	Female	Peters plus	4.1	40	46 Wk 3 D	–	Cleft Lip
3	R	Male	Type I	7.2	40	105 Wk 6 D	–	–
4	R & L	Male	Type II	12.4	40	127 Wk 3 D	–	–
5	R & L	Male	Type II	6.36	31	82 Wk	–	Jaundice, Obstructive sleep apnea, Hernia Repair, Anemia
6	R	Male	Type I	7.6	42	67 Wk 2 D	–	–
7	R & L	Female	Type II	9.6	40	105 Wk 4 D	–	–
8	R & L	Male	Type I	6.12	40	53 Wk 4 D	–	–
9	R & L	Male	Type I	6.2	36	60 Wk 6 D	–	Intestinal Volvulus
10	R & L	Female	Peters plus	6.9	40	51 Wk 2 D	–	Al-Gazali Syndrome
11	R	Male	Type I	7.5	40	59 Wk 4 D	–	–
12	L	Male	Type I	9.2	38	39 Wk 1 Day	–	–
13	L	Female	Type II	3.75	38	43 Wk 3 D	–	–
14	R	Female	Type I	8.7	40	60 Wk 2 D	–	–
15	R & L	Male	Type II	8	40	98 Wk 2 D	–	–
16	R	Female	Type II	6.7	40	63 Wk 1 Day	–	–
17	L	Male	Peters plus	4.7	40	49 Wk 5 D	Wolff-Parkinson-White syndrome	–
18	R	Female	Type I	11.4	40	153 Wk 2 D	–	–
19	L	Male	Type II	3.8	34	40 Wk 4 D	–	–
20	L	Male	Type II	8.5	38	52 Wk 3 D	–	Gastroesophageal Reflux Disease
21	R	Female	Type I	4.5	40	47 Wk	–	–
22	L	Male	Type II	9.4	40	59 Wk 2 D	–	–
23	L	Male	Type I	5.3	34	45 Wk 6 D	–	–
24	L	Male	Peters plus	5.3	42	47 Wk 5 D	Unstable Atrial fibrillation	
25	R & L	Male	Peters plus	6.23	40	59 Wk 3 D	Dilated Cardiomyopathy/ LV Dysfunction	–
26	R	Female	Peters plus	7.2	25	102 Wk	ASD	Intraventricular Hemorrhage/ Necrotizing Enterocolitis

(Continues)

TABLE 1 (Continued)

Patient Number	Affected Eye	Sex	Peters Type	Weight (Kg)	Gestational Age (Wk)	Postconceptual Age at First Encounter (Wk)	Co-Existing Cardiac Abnormalities	Systemic Complications
27	R	Female	Type I	12.1	40	130 Wk 1 Day	–	–
28	L	Female	Peters plus	5.8	40	51 Wk 1 Day	Left Pulmonary Artery Narrowing	–
29	R & L	Male	Peters plus	5.41	36	41 Wk 5 D	Hypertrophy of Ventricular Septum/ VSD	Macrosomia, Hypoglycemia
30	R & L	Female	Peters plus	5.86	38	63 Wk 2 D	ASD/VSD/PDA	Congenital Hydronephrosis/Lobar Holoprosencephaly/ Obstructive Hydrocephalus
31	R & L	Female	Type I	8	36	79 Wk	PDA	–
32	L	Female	Type II	4.3	40	55 Wk 4 D	–	–
33	R & L	Female	Peters plus	4.8	37	50 Wk 6 D	ASD/VSD/PDA	Digit Abnormality, Kidney Obstruction s/p nephrostomy tube/ Transverse Vaginal Septum
34	R	Male	Type I	5.7	40	47 Wk 2 D	–	–
35	R & L	Male	Peters plus	3.6	31	45 Wk 6 D	VSD, ASD	Goldenhar Syndrome, Cleft Palate, Mandibular Hypoplasia

intubation while EUA averaged about 31 minutes and primarily utilized a laryngeal mask airway. The longest EUA was completed in 82 minutes with an LMA in place, with no anesthetic complications. For all cases of EUA, LMA placement was chosen based on the patients' weight and performed successfully on the first attempt in <40 seconds. Physiologic parameters including heart rate and oxygen saturation were maintained with minimal fluctuation. Anesthesia providers remained near the head of the bed in case an emergency arose, but we found no incidence of such an occurrence. There were no inadvertent admissions to the hospital or intensive care unit among this patient population. Length of PACU stay averaged 65 minutes for corneal transplant surgery and 51 minutes for EUA. The only noted complication was a fever in PACU for a patient with unilateral corneal transplant.

One patient had a diagnosis of Al-Gazali syndrome associated with cherubism, optic atrophy and short stature, joint contractures, and skeletal abnormalities. Although careful positioning and padding of all joints was undertaken to avoid nerve injury in this patient, anesthetic management was otherwise unaltered during the case. Another patient in this sample was diagnosed with Goldenhar syndrome, with concomitant atrial septal defect, ventricular septal defect, cleft palate, and mandibular hypoplasia. Corneal transplant for this patient necessitated a fiberoptic intubation following mask induction with sevoflurane while maintaining spontaneous ventilation.

Peters plus patients in our sample manifested various systemic complications. Congenital heart defects included atrial and ventricular septal defects, patent ductus arteriosus, Wolff-Parkinson-White syndrome, unstable atrial fibrillation, ventricular septal hypertrophy, dilated cardiomyopathy with left ventricular dysfunction, and pulmonary stenosis. Genitourinary anomalies encompassed hydronephrosis, ureteropelvic junction obstruction, and a transverse vaginal septum. Structural neurologic malformations consisted of obstructive hydrocephalus, lobar holoprosencephaly, and cerebral intraventricular hemorrhage. Gastrointestinal anomalies involved jaundice, gastroesophageal reflux disease, umbilical hernia, intestinal volvulus, and necrotizing enterocolitis. One patient presented with macrosomia and hypoglycemia. Individual patients also manifested cleft lip, cleft palate, digit abnormalities, and obstructive sleep apnea. The infant with dilated cardiomyopathy and left ventricular dysfunction was optimized prior to surgical intervention on a diuretic and angiotensin-converting enzyme inhibitor.

5 | DISCUSSION

During normal physiologic development, the anterior segment of the eye separates into the lens, the iris, and the cornea. Peters anomaly is caused by incomplete separation of the anterior segment from the iris or lens, resulting in a corneal opacity that can be centrally or peripherally located in the cornea (Figure 1). Other conditions affecting the eye including glaucoma, cataracts, and microphthalmia are also associated with Peters anomaly patients. Visual deprivation during the early stages of life as a result of congenital corneal opacities can result in long-term changes to the central nervous system unless corrected prior to 3-6 months of age.[8] PKP has a significantly higher success rate in adults vs children, with the success rate being lowest for congenital corneal opacities.[9] An elastic cornea, scleral collapse, and anterior movement of the lens make PKP more challenging in infants. In addition, the rate of graft rejection is high and secondary glaucoma can occur due to chronic corticosteroid use and anterior segment abnormalities.[10]

Children with external features of Peters plus syndrome systematically underwent preoperative echocardiography prior to anesthetic induction for EUA. In our sample, these included one patient with dilated cardiomyopathy, another with ventricular septal hypertrophy, and a patient with left pulmonary artery narrowing. These patients with complicated congenital heart disease did not suffer from anesthetic complications with appropriate medical optimization preoperatively.

An LMA was utilized as the sole airway management technique for children <3 months of age undergoing EUA for Peters anomaly at our institution. Adequate depth of anesthesia was assured prior to LMA placement following mask induction, IV placement, and a bolus of propofol as infants were kept spontaneously breathing. Although the LMA has been described in the literature primarily for neonatal resuscitation in infants weighting greater than 2000 g or greater than 34-week gestation, it is not often utilized in the operating room environment in this age-group.[11]

There are a variety of anesthetic considerations in infants with Peters anomaly. Syndromic children have an increased incidence of potential difficult airway secondary to micrognathia, cleft lip, or palate. Only one patient with Goldenhar syndrome in this sample had a potentially difficult airway. LMA use for EUA reduces risk for coughing, bucking and elevated intraocular pressure. If measurement of intraocular pressure is foreseen, inserting an LMA is a better option than tracheal intubation as it causes less changes in intraocular

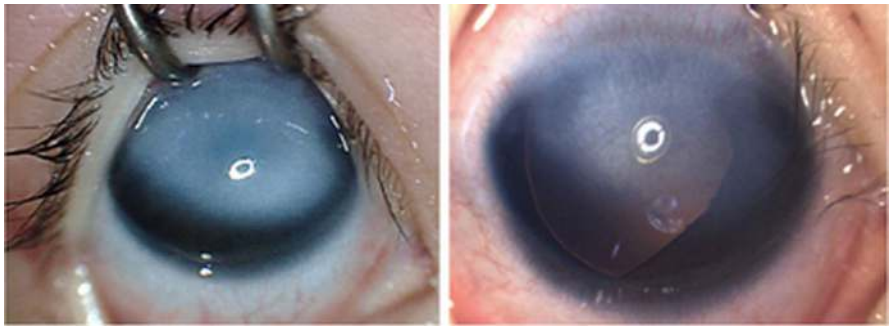

FIGURE 1 Image of corneal opacification seen in Peters anomaly [Colour figure can be viewed at wileyonlinelibrary.com]

pressure. Abnormal neural crest cell migration increases the risk of systemic anomalies in patients with Peters anomaly. Although bilateral Peters anomaly has a stronger association with systemic and cardiac anomalies in comparison to unilateral disease, patients with unilateral Peters anomaly should have a preoperative workup prior to anesthetic induction. Rare systemic malformations that can be associated with Peters anomaly include spontaneous corneal perforation, Wilms tumor[12] and Goldenhar syndrome identified in our sample population. Differential diagnosis for Peters anomaly includes Cornelia de Lange syndrome, Smith-Lemli-Opitz Syndrome, Robinow syndrome, Fetal alcohol syndrome, Rieger syndrome, and Walker-Warburg syndrome.[13]

Approximately 40%-50% of patients with Peters anomaly have associated glaucoma.[14]

This is likely due to the abnormal development of the trabecular meshwork or Schlemm's canal and due to a shallow anterior chamber. Glaucoma is more commonly seen in patients with cataracts or corneolenticular adhesions. Elevated intraocular pressure typically presents in infancy but can also arise later in life. The diagnosis of Peters anomaly is made clinically with the finding of corneal opacification.[15]

Children with corneal opacification or cataracts are at risk of developing amblyopia or vision loss. PKP may be indicated to reduce this risk. Visual prognosis is dependent on disease severity. Although there is no formal classification for disease severity in Peters anomaly, Chang et al[9] defined patients with severe disease as being characterized by dense central opacities covering more than half of the cornea, corneolenticular adhesions, or associated ophthalmic anomalies like microphthalmia, aniridia, or cataracts. Patients with mild disease characterized by corneal opacities covering less than half of the cornea and visual acuities of 20/100 or more had better visual outcomes with treatment.

Prognosis of patients with Peters anomaly is highly variable, based upon disease severity and comorbid ophthalmic and systemic abnormalities. We can provide anesthesia for young infants without serious complications utilizing an LMA with spontaneous ventilation for EUA procedures, while paralysis and endotracheal intubation is utilized for PKP procedures. Systemic abnormalities and their anesthetic implications should be taken into consideration when evaluating infants with Peters anomaly.

CONFLICT OF INTEREST

The authors report no conflict of interest.

ETHICAL APPROVAL

Retrospective chart review completed with IRB approval under Touro University Systems. IRB date of approval: October 30, 2017 with approval code: 12 188.

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