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Syngnathia and obstructive apnea in a case of popliteal pterygium syndrome

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Abstract

We describe an infant with popliteal pterygia, syngnathia, cleft lip and palate, and retrognathia diagnosed with popliteal pterygium syndrome (PPS). The neonatal course was complicated by severe obstructive apnea necessitating tracheostomy.

Conclusion—This report illustrates the potential for airway compromise in PPS patients and the need for thorough neonatal airway assessment.

Keywords

Intraoral adhesions; lip fistula; cleft palate

Introduction

Popliteal pterygium syndrome [PPS, OMIM # 119500] is an autosomal dominant syndrome with characteristic dense bands of tissue extending from the ischial tuberosities to the heels

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Authors' Summary

Infants with popliteal pterygium syndrome (PPS) have several congenital anomalies including craniofacial defects such as cleft lip and palate and retrognathia. There is no known association between the diagnosis of PPS and risk of airway compromise in the neonatal period. In this report, we describe a PPS neonate with significant airway compromise and discuss the features of PPS that may contribute to a risk for obstructive apnea in this population.

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[5]. PPS is part of a spectrum of disorders associated with mutations in *IRF6*, which plays an important role in keratinocyte and lingual development [11,6].

Characteristic features include bilateral popliteal pterygia and cleft palate [2]. Additional features, including cleft lip, congenital lower lip fistulae, syngnathia, ankyloblepharon filiform adnatum, syndactyly, talipes equinovarus (TEV), bifid scrotum, cryptorchidism, or hypoplasia of the labia majora, are seen with variable expressivity [2]. A unique pyramidal fold of skin overlying the nail of the hallux is a hallmark of the diagnosis [2]. Syngnathia seen in nearly 40% of PPS patients are usually fibrous in type, limiting jaw excursion and creating difficulties in breathing and feeding [2,3].

We describe a neonate with a prenatal diagnosis of PPS whose early course was complicated by severe obstructive apnea. This report illustrates the potential for severe airway compromise in PPS patients. Suspicion of a diagnosis of PPS should prompt a thorough neonatal airway assessment and careful monitoring for apnea.

Case Report

The patient was the second product of a non-consanguineous union between two unaffected parents. Antenatal ultrasound at 24 weeks gestation showed intrauterine growth restriction (IUGR), bilateral TEV, a unilateral cleft lip, and bilateral popliteal pterygia, raising suspicion of PPS (Figure 1). Subsequent fetal MRI revealed syndactyly of the toes, a small scrotum, and a duplicated right renal collecting system. Postnatal *IRF6* mutation analysis demonstrated a previously reported heterozygous missense mutation, p.Arg84His, confirming a diagnosis of PPS (Prevention Genetics, Marshfield, WI) [7]; parental testing was declined.

The patient was delivered by C-section at 35 weeks gestation for absent end diastolic flow and IUGR. The birth weight was 1.87 kg (3rd centile); length, 40 cm (below 3rd centile); and fronto-occipital circumference, 31.5 cm (10–50th centile). Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. Physical exam demonstrated ankyloblepharon, a left incomplete cleft lip, micro- and retrognathia, fibrous syngnathia, mild hypospadias, and an underdeveloped scrotum. Bilateral popliteal pterygia limited extension of the left and right knees to 90 and 135 degrees, respectively (Figure 2). Bilateral TEV with a pyramidal skin fold over each hallux, hypoplastic nails, and asymmetric syndactyly were also present (Figure 2). A maxillofacial CT revealed retrognathia and a Veau II midline cleft palate without involvement of the alveolus. Moderate respiratory distress in the setting of prematurity and syngnathia prompted prophylactic nasopharyngeal intubation with a flexible laryngoscope under general anesthesia (GA). Following an unplanned extubation on day 3, the infant showed resolution of respiratory distress. On day 4 of life, excision of oral fibrous adhesions was performed under GA with a 24-hour endotracheal intubation for peri-operative airway protection (Figure 2). Despite improved jaw excursion, post-operative recovery was significant for recurrent episodes of apnea and bradycardia, prompting a sleep study that demonstrated severe obstructive and mild central sleep apnea. MRI of the brain was normal. The infant underwent tracheostomy placement for airway protection and gastrostomy tube placement for feeds at 21 days of age, and he was discharged home at 39

days. He has had one brief re-admission for apnea secondary to a viral upper respiratory infection. Cleft lip was repaired at the age of 4 months. Jaw excursion continues to improve with daily range-of-motion exercises and oral stimulation. Palatoplasty and pterygium release are scheduled at 12 months.

Discussion

Popliteal pterygia may herald the diagnosis of a pterygium syndrome such as PPS, Bartosocas-Papas syndrome, or lethal multiple pterygium syndrome. PPS is the least severe of these and is characterized by cleft lip and/or palate, congenital lip fistulae, fibrous syngnathia, popliteal pterygium, syndactyly, abnormal external genitalia, ankyloblepharon, and a triangular fold of skin overlying the hallux [2]. Findings of facial clefting and popliteal pterygia on prenatal imaging should raise suspicion of this diagnosis, particularly in the setting of a history of lip fistulae or facial clefting in a first-degree relative [8]. Patients with PPS typically have a normal intellect, and management should focus on measures to optimize growth and development, including lysis of oral and eyelid adhesions and cleft repair [4]. Surgical correction of pterygia should proceed with caution as nerves or vessels may be present in the leading edge of the pterygia [2].

Syngnathia in patients with PPS has raised concerns regarding oral feeds and airway compromise. A majority of cases reported in the literature undergo lysis of these adhesions shortly after birth. While the use of GA during these procedures has prompted many to secure the airway with intubation during and immediately after the procedure [3], we are aware of only one report of airway compromise in a PPS patient. Steinberg *et al.* reported a 5-day-old infant with PPS who underwent surgical release of intra-oral adhesions under GA; the infant developed respiratory distress shortly after completion of the procedure, and he briefly required an oral airway for respiratory support [10]. This patient's respiratory distress was attributed to a hypoplastic mandible with weakness of the associated musculature that improved after introduction of oral feeds [10].

Though reports of PPS patients with airway compromise are uncommon, there is precedent for an association between neonatal respiratory distress and the types of craniofacial anomalies common in PPS. Simpson *et al.* described a preterm infant with micrognathia, cleft palate, and bony fusion of the mandible and maxilla who developed respiratory distress immediately after birth, requiring emergent tracheostomy placement [9]. Similarly, patients with Pierre Robin Sequence, who have features of cleft palate, mandibular hypoplasia, and glossoptosis, have an increased risk of airway obstruction, prompting consideration of polysomnography in the neonatal airway assessment for these at-risk patients [1]. The paucity of reports of PPS patients with neonatal respiratory distress suggests a lack of ascertainment, and a subsequent under-diagnosis of airway compromise. Though many infants with PPS might not manifest distress at basal conditions, they are at risk of major airway compromise during illnesses and even during emesis. Our patient had craniofacial features of cleft lip and palate, retrognathia, and soft-tissue syngnathia, and he demonstrated moderate respiratory distress after birth. Operative release of fibrous bands improved jaw excursion, but polysomnography later confirmed obstructive sleep apnea, necessitating tracheostomy placement.

Conclusion

A diagnosis of PPS should be considered when the combined features of popliteal pterygium and cleft palate are seen. Physicians should maintain a low suspicion for airway compromise in the neonatal period.

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Abbreviations

GA	general anesthesia
IUGR	intrauterine growth restriction
PPS	popliteal pterygium syndrome
TEV	talipes equinovarus

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Figure 1. Fetal MRI

(a) Arrow indicates popliteal pterygium; (b,c) Arrows indicate bilateral TEV

Figure 2. Patient at 6 weeks of age (a–d) and during adhesion release on day of life 4 (e,f) (a,b) Bilateral popliteal pterygium; (c,d) Bilateral syndactyly, hypoplastic nails, and pyramidal fold of skin over first digit; (e) Anterior thin intra-oral fibrous syngnathia; (f) Posterior thick intra-oral fibrous syngnathia