Original Article

Laryngeal cleft—case series from a surgical neonatal intensive care unit

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Background: Laryngeal clefts are rare congenital anomalies of the upper aerodigestive tract with a persistent connection between the posterior laryngotracheal airway and the oesophagus. The purpose of this study was to review the clinical presentation, management and outcomes of a cohort of infants presenting with laryngeal clefts to a tertiary surgical neonatal intensive care unit in the newborn period.

Methods: A single centre retrospective case review was conducted on infants with a diagnosis of types I to IV laryngeal cleft.

Results: Eight infants with laryngeal clefts were identified. The median age at presentation was 1.5 days (1–118 days) and median age to diagnosis was 6.5 days. Seven out of eight neonates were male and five were born prematurely. Seven out of eight had a significant comorbidity and four infants died.

Conclusions: Patients with laryngeal clefts in this study had a high morbidity and mortality despite various forms of surgical intervention.

Keywords: Laryngeal cleft; laryngotracheoesophageal cleft; infant; newborn; neonatal intensive care unit; outcome

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Introduction

Laryngeal clefts are rare congenital anomalies of the upper aero-digestive tract in which a persistent connection between the posterior laryngotracheal airway and the oesophagus exists (1). The incidence ranges from 1 in 10,000 to 20,000 live births, with a male predominance (2). Upper airway clefts range in severity from asymptomatic soft tissue defects in the inter-arytenoid region to complete clefts of the larynx, trachea and oesophagus. The most accepted classification system of laryngeal clefts proposed by Benjamin and Inglis (3) is anatomically based and remains widely used today. This system classifies laryngeal clefts as: type I, supra-glottic inter-arytenoid cleft, in which the cleft is above the level of the vocal cords; type II, a partial cricoid cleft wherein the laryngeal cleft extends below the level of the vocal cords (but does not involve the posterior cricoid lamina completely); type III, encompasses a total cricoid cleft and may further extend into the cervical tracheoesophageal wall; type IV is a laryngo-oesophageal cleft extending into the intra-thoracic tracheoesophageal wall. Several studies have highlighted an increasing diagnosis of this rare condition in tertiary paediatric institutions (4,5).

Many children with laryngeal clefts have other congenital abnormalities, with the most common being tracheoesophageal fistula (6,7). Other common malformations include oesophageal atresia, imperforate anus, microgastria and intestinal malrotation. Congenital malformations of the cardiovascular system and

genitourinary tract have also been reported (1,6,8). A higher incidence of laryngeal cleft is reported in Pallister-Hall syndrome and Opitz-Frias syndrome (9-12).

Presentation of laryngeal cleft depends on the type (13). Infants with isolated types I and II laryngeal clefts present a diagnostic challenge, with non-specific symptoms such as stridor, feeding difficulties, chronic cough and choking with feeds. Types I and II clefts can go undiagnosed for a prolonged period of time. Non-specific symptoms may eventually prompt laryngo-broncho-oesophagoscopy (LBO) which remains the gold standard for diagnosis.

The presence of comorbidities, such as congenital heart disease generally prompts close medical scrutiny of these neonates. Comorbidities can have a significant clinical impact either facilitating earlier diagnosis or conversely, delaying diagnosis while respiratory symptoms are ascribed to other systems. This highlights the need for treating clinicians to consider the diagnosis and recognize the spectrum of severity in the context of the broader clinical picture (4,5,8,14).

Infants with a type III cleft usually present with significant aspiration and respiratory tract infections, while infants with a type IV cleft have significant early respiratory distress and difficulty in maintaining mechanical ventilation (15-17). In this situation, the cleft may be diagnosed during endotracheal intubation by an astute clinician. Early diagnosis can potentially reduce irreversible pulmonary damage and other associated morbidities that may occur due to repeated aspiration (6).

The management of laryngeal cleft ranges from medical therapy to surgical intervention. Conservative medical management aims to maintain optimal respiration, prevent pulmonary complications and ensure adequate nutrition. It is appropriate only when respiratory function is stable and to facilitate investigation of comorbidities (8). The decision to proceed to surgical intervention is dependent on both anatomy and presentation. Types III and IV clefts often require early surgical intervention, although they are not always readily diagnosed at birth (15-17). Surgical repair can be via an endoscopic or an open surgical approach (18,19).

The objective of this paper is to review the clinical presentation, management and outcomes of a cohort of infants that presented with a laryngeal cleft to a tertiary neonatal intensive care unit in the new-born period.

Methods

Infants admitted between January 2003 and August 2016 to a tertiary neonatal intensive care unit with a diagnosis of types I to IV laryngeal cleft were eligible for inclusion. Infants were identified from a neonatal database using ICD-9 and -10 coding. The classification of laryngeal cleft was based on the Benjamin and Inglis classification system (3). Data was compiled through a manual chart review. Ethics approval was obtained from the relevant institutional board.

Results

Eight infants with a laryngeal cleft were identified (*Table 1*), of which three infants had a type I laryngeal cleft, one type II, two type III and two type IV. The median age at presentation was 1.5 days (range 1–118 days) and median age at diagnosis was 4.5 days (1–119 days). Seven infants were male and five were born prematurely (28–36 weeks gestation). Of the eight infants, four survived.

Case 1

A preterm male infant born at 28 weeks gestation with a birth weight of 1,270 g was admitted at four months of age for assessment of feeding difficulties and gastroesophageal reflux disease. Persistence of these non-specific symptoms at 'corrected term' age led to an LBO where the diagnosis of type I laryngeal cleft was made, Mild tracheomalacia and right bronchomalacia was also noted. A repeat LBO with gel foam injection into the interarytenoid notch to lift the arytenoid folds was performed four days later. The procedure was uncomplicated and he was discharged on full enteral nutrition via nasogastric tube due to lack of oral motor coordination.

Case 2

A term male infant was admitted shortly after birth weighing 2,730 g with a hypoplastic left ventricle, hypoplastic aorta with a large ventricular septal defect. After a surgical procedure for the congenital heart disease, soft cry was noted. A flexible nasoendoscopy showed left vocal cord palsy. An LBO performed at four days of age showed a type I laryngeal cleft. Insertion of gel foam was performed with subsequent improvement in oral feeding.

Case 3

A 28-day-old male term infant with a birth weight of 2,862 g was admitted for assessment of episodes of oxygen desaturation during feeding. Continuous positive airway

Table 1 Demographics

Case	Gestation (weeks)	Birth weight (g)	Gender	Type of cleft	Comorbidities	Age at admission	Age at diagnosis	Length of hospital stay (days)	Repair	Died
1	28	1,270	Male	I	Gastroesophageal reflux, tracheomalacia, bronchomalacia	4 months	4 months	13	Gel foam	No
2	38	2,730	Male	I	Congenital cardiac disease, vocal cord palsy	Day 1	Day 4	38	Gel foam	No
3	40	2,862	Male	I	Nil	4 weeks	5 weeks	79	Endoscopic repair	No
4	36	2,670	Male	II	Pulmonary artery atresia, hypoplastic left lung, small upper thoracic cage, cutis laxa, facial dysmorphism features, cleft palate	Day 1	Day 1	2	No repair	Yes
5	31	2,010	Female	III	VACTERL association	Day 1	Day 1	66	Surgical repair	Yes
6	37	2,520	Male	III	Smith-Lemli-Opitz syndrome	Day 10	Day 5	108	Surgical repair	No
7	32	1,800	Male	IV	Diaphragmatic hernia and Tetralogy of Fallot	Day 1	Day 5	16	No repair	Yes
8	29	1,452	Male	IV	Omphalocele	Day 1	Day 1	2	No repair	Yes

pressure was required to maintain a patent airway. An LBO performed at 35 days of age confirmed a type I laryngeal cleft. A week later, endoscopic repair of the cleft and epiglottoplasty were performed. In view of the high risk of aspiration with thin fluids, thickened oral feeds were commenced. No comorbidities were identified.

Case 4

A preterm male infant, born at 36 weeks gestation with a birth weight of 2,670 g was admitted with an abnormal upper airway identified at laryngoscopy for endotracheal intubation at birth. Postnatal evaluation confirmed the presence of pulmonary artery atresia, a hypoplastic left lung, small upper thoracic cage, cutis laxa, multiple facial dysmorphic features and a cleft palate. An LBO identified a type II laryngeal cleft. Given the multiple congenital abnormalities life-sustaining measures were withdrawn.

Case 5

A preterm female infant, born at 31 weeks gestation with a birth weight of 2,010 g was admitted with an antenatal diagnosis of oesophageal atresia. A difficult endotracheal intubation at birth raised the suspicion of a laryngeal cleft. On postnatal assessment, a diagnosis of VACTERL association with oesophageal atresia & tracheoesophageal fistula, ventricular septal defect, atrial septal defect, and imperforate anus was made. Repair of oesophageal atresia and tracheoesophageal fistula were performed on day 2 and an LBO confirmed a type III laryngeal cleft. The post-operative course was complicated by oxygen desaturations from persistent occlusion of the bronchi and difficulty in maintaining a secure airway prior to the cleft repair.

Open surgical repair of the laryngeal cleft with creation of a tracheostomy and gastrostomy was performed at 12 days of age. Episodes of airway obstruction with difficulty in achieving adequate ventilation persisted after the repair of the cleft. Repeat LBO showed a blind pouch near the carina with persistent occlusion of the bronchi. Tracheoplasty to remove the blind pouch and closure of the tracheostomy was performed at four weeks of age. In view of reopening of the repaired laryngeal cleft and significant multi-site sepsis life sustaining measures were withdrawn on day 67.

Case 6

A term male infant with a birth weight of 2,520 g, had a surgical repair of coarctation of the aorta. An LBO performed due to poor feeding, diagnosed a type III laryngeal cleft. On day 22, open surgical repair of the cleft was performed. An LBO a month later, showed trachea-oesophageal fistula at the lower end of the repaired cleft. The fistula was repaired at 10 weeks of age. Comorbidities included Smith-Lemli-Opitz syndrome, facial dysmorphic features, bilateral vocal cord palsy, tracheomalacia and hypospadias. The infant was discharged to his local hospital for continued management on day 118 of life, self-ventilating in room air and tolerating full enteral feeds via a jejunostomy tube.

Case 7

A preterm male infant born at 32 weeks gestation with a birth weight of 1,800 g was admitted with an antenatal diagnosis of congenital diaphragmatic hernia and Tetralogy of Fallot (TOF) which was confirmed on postnatal assessment. Facial dysmorphism was also noted. A laryngeal cleft was visualised on laryngoscopy during a difficult resuscitation at birth. On LBO a diagnosis of laryngeal cleft type IV with small and abnormal bronchi was made. Surgical repair of the cleft was not possible and the infant died on day 17.

Case 8

A preterm male infant born at 29 weeks gestation with a birth weight of 1,452 g had an antenatal diagnosis of omphalocele. A difficult intubation at birth with a large air leak led to suspicion of laryngeal cleft. An LBO confirmed a type IV cleft that could not be repaired surgically. The infant was subsequently transferred back to the referring hospital and died the following day.

Discussion

Laryngeal cleft is a rare anomaly which was first successfully surgically reconstructed and a classification system reported in 1955 (20). The current, widely used system was developed by Benjamin and Inglis (3) in which a hierarchal of classification of laryngeal cleft is described. A high index of suspicion is required for early diagnosis of laryngeal cleft to prevent problems associated with airway compromise (21).

The age at diagnosis of laryngeal cleft in our series was early, with 6 of 8 infants diagnosed within the first week of age, however all six infants had significant comorbidities. Conversely, a large case series reporting the experience from two paediatric tertiary care centres identified the age at diagnosis from 15 days to 12 years with a mean age of 21 months (6). Adil *et al.* (19) reported a mean age of diagnosis in infants with type III cleft to be 4 months, while in our series, the two infants with a type III cleft were diagnosed at 1 and 5 days of age.

The existence of other congenital anomalies may lead to earlier recognition of symptoms and investigation of airway anomalies. In three instances within our study, there was a strong suspicion of a laryngeal cleft shortly after birth that was subsequently confirmed on LBO. In two of the three infants with a type 1 cleft, the reason for admission was investigation of feeding and airway issues. For the remaining three infants a laryngeal cleft was diagnosed at LBO in the setting of other congenital anomalies.

Seventy five percent of infants (6 out of the 8) in our series had other significant congenital anomalies. This finding is higher than that of current literature where comorbidities in association with this pathology were reported as 56% (6,7) or a range of 16–68% (15). Though a small number, infants in our series seem to fall in two clinical groups. In the first, presence of comorbidities and/or significant severity of cleft led to earlier diagnosis of the laryngeal cleft. The second group with less severe cleft in presence of non-specific symptoms were diagnosed later.

Advances in medical care and surgery have improved the prognosis for laryngeal cleft in some instances. In 1983 a large study of 85 infants with laryngeal cleft showed an overall mortality rate of 46% (1). In our study, all infants with a type 1 cleft survived, with one infant with a type II cleft died, however this infant had multiple comorbidities. More recently, mortality has been reported to be between 0 and 25% for types I–III clefts (14,19,22,23). In a case series that looked at types III and IV clefts (16) mortality rates were similar to our series. Simpson reported a mortality rate of 50% in a small series of six cases (24) however none were in the neonatal period. In contrast, three of the four infants in our study died in the neonatal period, suggesting a neonatal diagnosis could be associated with an increased risk of mortality.

Surgical management was offered in 5 out of 8 cases. Significant congenital co-morbidities affected the timing of surgery and the decision to proceed with surgical intervention. Two infants with type I cleft received a gel

foam injection. Kennedy (25) describes a series of cases with marked improvement in symptoms using this technique. In our series, one infant received a repair of their type 1 cleft via endoscope. Numerous articles have described successful endoscopic technique for the closure of types I and II laryngeal clefts with many benefits (3,17,26,27). Recently, this technique has advanced to type III cleft, with the success of a series of repaired type III cleft being published by Strychowsky *et al.* (18). The two infants in our series with type III cleft had an open reconstruction, with the aim of repair to achieve complete and functional separation of the airway from the digestive tract and maintain a functioning larynx (16).

One of the well-known complications of laryngeal cleft surgery is the risk of a post-operative breakdown at the site of surgical repair, with an incidence of up to 50% (19,23). Two of our infants suffered a cleft breakdown. Interestingly, Walner (10) found a much higher incidence of breakdown of cleft repair in infants with a history of TOF. In our experience, one infant who suffered a cleft breakdown had a history of TOF and the second suffered a trachea oesophageal fistula at the distal end of the repair site with acute associated respiratory deterioration. Tracheomalacia also appears to be a common occurrence in the postoperative management of types III and IV clefts (28). One infant in our series with a type III cleft experienced tracheomalacia post-surgical repair, while another with type I laryngeal cleft was diagnosed simultaneously with the cleft.

This case review highlights the importance of skilled laryngoscopy by experienced clinicians familiar with the neonatal airway. A diagnosis of laryngeal cleft with serious comorbidities requires complex surgical decision making with multi-disciplinary collaboration and involvement of the family as not all laryngeal clefts are survivable.

There are many case series describing the management of laryngeal clefts in the paediatric population. This is the first case series to our knowledge highlighting the specific experience of infants diagnosed with laryngeal cleft in the early neonatal period. These infants have a high mortality and morbidity with the severity of underlying co-morbidities playing a large factor.

Conclusions

Laryngeal clefts are rare congenital anomalies which a high morbidity and mortality. We report a high incidence of additional congenital abnormalities of 75% and a survival rate of 50%. Neonatal presentation with a more severe cleft and additional comorbidities had high mortality. This case series adds to the body of knowledge describing the experience of infants with congenital laryngeal clefts. Although, there are other case series that include both paediatric and neonatal populations, our study is reporting the experience of infants diagnosed with laryngeal cleft exclusively in the neonatal period.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ajo.2018.01.12). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethics approval was obtained from the relevant institutional board. Informed consent was waived due to the retrospective nature of the study.

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