

Case report

A term neonate with cyanosis with crying

A term newborn with Holt–Oram syndrome (HOS) and absent thumbs was discharged from the newborn nursery without respiratory symptoms. He developed increased work of breathing and fevers at 2 weeks of age and was found to have respiratory syncytial virus requiring nasal cannula and supplemental oxygen *via* nasal cannula at a rate of 2 L·min⁻¹ (100% fraction of inspired oxygen ($F_{I_{O_2}}$)). The medical team was unable to wean his respiratory support.

Task 1

What is the differential diagnosis of progressively worsening effort of breathing over time in the neonate with failure to wean respiratory support?

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Given the observation that he had a weak cry in the setting of multiple congenital anomalies on examination, the decision was made to proceed with microlaryngoscopy and bronchoscopy (MLB). The MLB demonstrated pulsatile compression of the left, lateral portion of the lower third of the trachea that extended into the left mainstem bronchus, which was suspected to be extrinsic in nature. Computed tomography angiography (CTA)

of the chest was then performed, which confirmed that the aortic arch was compressing the left distal trachea and left mainstem bronchus in the setting of a high tracheal bifurcation and short tracheal length (figure 1). The carina was noted to be at the level of T2. Given that he had clinically improved and stabilised on 2 L·min⁻¹ of supplemental oxygen *via* nasal cannula, the decision was made to manage conservatively with supplemental oxygen at home.

At 5 weeks of age, he began to develop recurrent cyanosis episodes with associated respiratory distress. The cyanosis episodes were triggered by crying and by sitting in the car seat. It was noted on auscultation of the chest that there was significantly less air movement on the left side as compared to the right. The patient was started on high-flow nasal cannula (HFNC), which was gradually titrated up with associated resolution of the cyanosis episodes, even with crying, at 6 L·min⁻¹ ($F_{I_{O_2}}$ of 21%). These episodes returned if the HFNC was weaned below 6 L·min⁻¹ flow.

An echocardiogram during this hospitalisation demonstrated a large apical muscular ventricular septal defect and moderate secundum atrial septal defect, with Doppler evidence of elevated pulmonary vascular resistance. Diuretic therapy was started with furosemide and spironolactone, but symptomatic improvement was minimal, suggesting concurrent pulmonary hypertension.

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Congenital short trachea can be associated with bronchial compression with associated symptoms of apnoea, cyanosis, increased work of breathing, and/or respiratory failure in infancy. Operative intervention should be considered in symptomatic cases. <https://bit.ly/3gM6Vv9>



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Table 1 Differential diagnosis for progressively worsening effort of breathing over time in the neonate

Pulmonary aetiology	Examples
Airway disorders	Laryngomalacia Tracheobronchomalacia Tracheal stenosis Bronchial stenosis Tracheal haemangioma Tracheal papilloma Bronchogenic cyst
Pulmonary parenchyma	Childhood interstitial lung disease Pulmonary interstitial glycogenosis Neuroendocrine cell hyperplasia of infancy
Alveolar disorders	Surfactant dysfunction
Infectious disorders	Pneumonia/lower respiratory tract infection Sepsis
Disorders of lung development	Pulmonary hypoplasia Pulmonary aplasia Pulmonary agenesis Congenital lobar emphysema Congenital pulmonary airway malformation
Musculoskeletal disorders	Ribcage abnormality Skeletal dysplasias
Neurological disorders	Epilepsy Spinal muscular atrophy Recurrent laryngeal nerve dysfunction Phrenic nerve dysfunction Central dysfunction of the breathing control centre
Other pulmonary	Pneumothorax/air leak
Nonpulmonary	Congenital heart defects

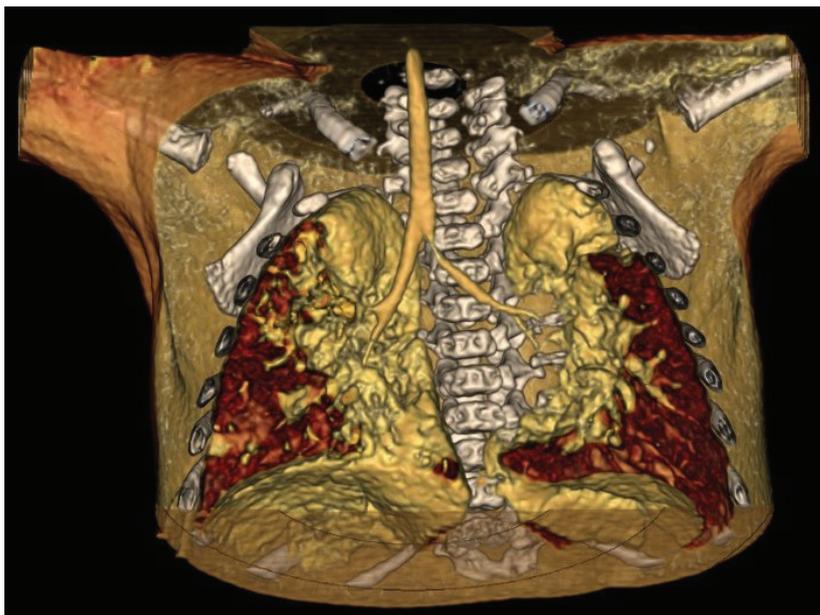


Figure 1 Computed tomography-derived three-dimensional reconstruction demonstrating abnormal elevation of the tracheal bifurcation at T2 level, with associated elongation and compression of the left proximal mainstem bronchus by the aortic arch.

Task 2

What is the most likely primary aetiology of the recurrent respiratory distress/cyanosis and the persistent HFNC requirement?

- a) Congenital heart disease with pulmonary overcirculation
- b) Congenital short trachea with extrinsic lower airway compression
- c) Bacterial pneumonia secondary to a viral respiratory infection
- d) Systemic infection with sepsis
- e) Disordered central control of breathing

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Task 3

What was the most likely cause of the cyanosis in this neonate with congenital short trachea and left mainstem bronchus compression?

- a) Induction of retractions
- b) Congenital tachypnoea
- c) Congenitally shortened large airways without compression
- d) Ventilation/perfusion mismatch
- e) Unilateral pulmonary hypoplasia

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Given the findings on history, physical examination and work-up, the decision for surgical management was made. At 3 months of age, the patient underwent operative intervention with the application of a flexible, bioresorbable external splint to the left mainstem bronchus and anterior aortopexy. During the same operation, patch atrial septal defect closure and patch ventricular septal defect closure were also undertaken to eliminate the intracardiac shunt. The patient recovered and his symptoms completely resolved without recurrence even after being weaned off all respiratory support. The decreased air movement previously noted on the left improved substantially post-operatively. The pulmonary artery Doppler pattern and interventricular septum position normalised on subsequent echocardiograms, suggesting resolution of the pulmonary hypertension. On follow-up 1 year post-operatively, the patient remained off all respiratory support without recurrence of respiratory distress or cyanosis.

Task 4

New dysphagia is a key risk associated with intrathoracic procedures: true or false?

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Discussion

Congenital short trachea is defined as the presence of fewer tracheal rings than normal (15 or fewer) [1, 2]. This results in abnormal elevation of the carina (above T4 for children <2 years of age and above T5 for children ≥ 2 years of age) and causes the bronchi to track abnormally [1, 2]. The longer course of the left mainstem bronchus increases its vulnerability to compression by either the ligamentum arteriosum or the aortic arch [1]. Our patient, specifically, had compression of the proximal left mainstem bronchus by the aortic arch.

HOS is associated with congenital heart defects, such as atrial and ventricular septal defects, upper extremity musculoskeletal defects, and pulmonary malformations such as right lung hypoplasia, right lung agenesis, and horseshoe lung with vascular anomalies [3, 4]. HOS is associated with a mutation in the TBX5 gene that is inherited in an autosomal dominant manner [3, 4]. TBX5 gene mutations can result in abnormal lower airway branching and development [5]. HOS is not reported to be associated with vascular extrinsic compression of the airways, however. The repair of the atrial and ventricular septal defects in our patient with resulting improvement in the concurrent pulmonary overcirculation was probably an important, though more minor, contributor to the patient's post-operative symptomatic improvement.

Anterior aortopexy has been reported in the past to relieve compression of the left mainstem bronchus in the specific setting of congenital short trachea [1]. Anterior aortopexy with external bronchial stenting resulted in the resolution of

the present patient's respiratory symptoms and the resolution of the patient's respiratory support requirement. The lower airways of an infant are very susceptible to clinically significant external compression, given the low airway conductance and structural immaturity of the infant airways at normal baseline [6]. Significant airway obstruction can cause stridor at rest, cyanosis, increased work of breathing, apnoea and/or cardiopulmonary arrest [7]. Uncorrected airway obstruction can result in recurrent or persistent positive pressure respiratory support need, including tracheostomy with chronic mechanical ventilation [6]. Given the presence of congenital short trachea, it is unclear whether the severity of the extrinsic compression of the left mainstem bronchus would have progressed over time if anterior aortopexy had not been undertaken. However, even if further progression had not occurred, continuous long-term use of noninvasive respiratory support would have been unsafe. The patient would thus have been likely to require tracheostomy placement with long-term invasive mechanical ventilation to prevent the recurrence of his respiratory symptoms if operative correction of the extrinsic bronchial compression had not been an option.

In conclusion, congenital short trachea is a rare congenital airway anomaly that is associated with extrinsic bronchial compression [1, 2]. Resulting unilateral hypoventilation can result in ventilation/perfusion mismatch and cyanosis, apnoea and/or respiratory failure. Operative intervention, such as anterior aortopexy and external bronchial stenting, can be extremely beneficial and should be considered in severe and symptomatic cases [7].

Answers

Answer 1

It is important to narrow/rank the differential as much as possible based on history and examination, so that selections for further evaluation and testing can be appropriately prioritised (table 1).

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Answer 2

b. Congenital short trachea with extrinsic lower airway compression. Significant extrinsic airway compression was suspected on bronchoscopy and confirmed on chest CTA with associated congenital short trachea. The inability to wean the flow rate on HFNC, the lack of need for increased F_{iO_2} above 21%, and the minimal improvement with diuretic therapy suggest that the patient's congenital short trachea with associated extrinsic lower airway compression was the key driver of the failure to wean respiratory support and that pulmonary overcirculation was not likely to be a significant contributor at this point. We hypothesised that the positive pressure from the HFNC was noninvasively stenting the lower airways open and that this was why the HFNC could not be weaned.

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Answer 3

d. Ventilation/perfusion mismatch. Unilateral compression of a mainstem bronchus can substantially decrease ventilation in the affected lung, causing a mismatch in perfusion in the affected lung relative to the ventilation. If the ratio of perfusion to ventilation is sufficiently elevated from normal, a significant fraction of haemoglobin can leave the lung in the deoxygenated state, resulting in cyanosis. Retractions and tachypnoea by themselves do not necessarily result in cyanosis, nor does unilateral pulmonary hypoplasia. Congenitally shortened airways will not, by themselves, cause cyanosis (unless there is extrinsic compression as in this case) as no air exchange occurs in the large airways.

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Answer 4

True. This patient had new-onset post-operative dysphagia after the procedure for which he required supplemental tube feedings for many months. The dysphagia had substantially improved without continued need for tube feeds by 1 year post-procedure. Accidental unilateral injury of a recurrent laryngeal nerve, which can affect vocal cord function and swallowing coordination, is a key risk and common complication of intrathoracic procedures, especially open chest procedures. Injury of the recurrent laryngeal nerves bilaterally, which did not occur in this case, can cause stridor/increased work of breathing, potentially requiring tracheostomy placement.

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Conflict of interest

None declared.

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