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Case Report

Tracheal Atresia/Agenesis Syndrome and a Protocol for Perinatal Management Associated with Indications of Oesophageal Intubation for Oxygenation and Ventilation

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ABSTRACT

Background: Tracheal atresia/agenesis syndrome (TAAS) is an infrequent congenital disorder consisting of tracheal atresia/agenesis that is usually associated with other anomalies. It may be confronted as a challenging emergency for airway management and diagnosis. The mortality rate is high due to associated congenital anomalies and unfamiliarity with surgical procedures for tracheal reconstruction. Outcomes may be improved by proper airway management protocols and plans for multidisciplinary perinatal care.

Case presentation: We present the case of a neonate with severe respiratory distress, non-audible cry, and inability to pass an endotracheal tube via the vocal cords. Bag-mask ventilation was possible, and inadvertent oesophageal intubation provided oxygenation and stabilization.

Conclusion: TAAS may not be as rare as previously described, and it is amenable to tracheal reconstruction. Increased awareness and a clear initial indication for intentional rather than inadvertent oesophageal intubation for oxygenation may be lifesaving. A proper protocol for early diagnosis and perinatal management may facilitate surgical correction.

Keywords: Tracheal atresia/agenesis; Tracheoesophageal fistula; Congenital malformation

BACKGROUND

Tracheal atresia/agenesis (TAA) was first described by Payne in 1900 [1], and since then, more than 200 cases have been reported. It is known as an extremely rare and uniformly lethal congenital anomaly [2-4]. TAAS may be associated with other congenital anomalies, such as VATER (vertebral defect, anal atresia, tracheoesophageal fistula, oesophageal atresia, radial, or renal anomalies). It may present with VACTERL (VATER plus cardiovascular and limb defects). TAA may be part of TARCD (tracheal atresia or agenesis, radial anomaly, cardiac abnormality, and duodenal atresia) [5]. TAA may be associated with congenital high airway obstruction syndrome (CHAOS) [6]. We prefer the term syndrome rather than disease or anomaly due to its common association with multiple congenital anomalies [4]. Case reports have described tracheal agenesis, but there may be no agenesis at all and only atresia of part of the trachea [7], which may be the middle part of the trachea [8].

CASE PRESENTATION

A male neonate was born at 33 weeks by emergency caesarean section with an Apgar score of 4, 4, and 8 at 1, 5, and 10 minutes, respectively. His birth weight was 1625 grams (gm). The mother was a 34-year-old, known to have gestational diabetes, and prenatal ultrasound showed polyhydramnios. The neonate had a bilateral absence of radial bones and thumbs (Figure 1), non-audible cry, respiratory distress, and cyanosis, and endotracheal intubation was difficult.

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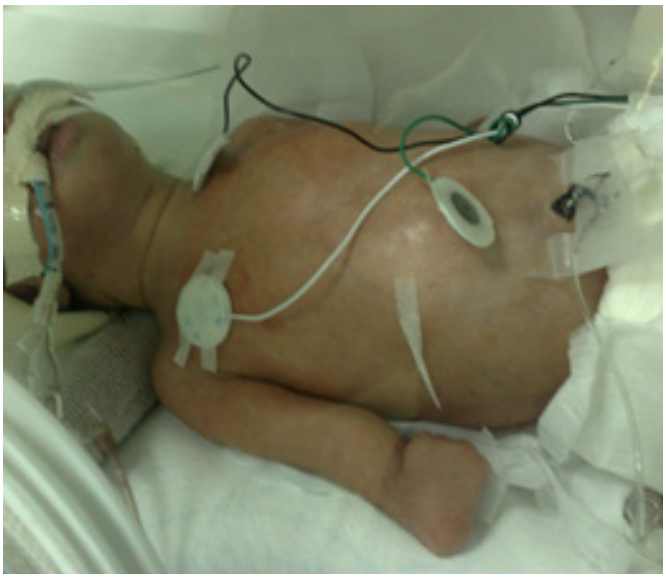

Figure 1: The neonate with bilateral absence of both radial bones and thumbs.

Bag-mask ventilation was possible, and the endotracheal tube (ETT) was inadvertently inserted into the oesophagus. The ETT position was confirmed by auscultation, bilateral chest rise, increased peripheral oxygen saturation (SpO_2), and relief of cyanosis. At the age of eight days, direct laryngobronchoscopy (DLB) was planned due to the inability to wean the patient from mechanical ventilation. The neonate arrived at the operating room intubated for ventilation, and the SpO_2 was 95%.

On 0.4 inspired oxygen, capnography revealed a distorted waveform, the heart rate was 128/min, the blood pressure was 84/51 mmHg, and the patient was afebrile. Sevoflurane was administered, and then total intravenous anesthesia was initiated by midazolam/fentanyl/cisatracurium because of the large leak around the ETT. Pressure-controlled ventilation (PCV) was applied, and DLB was performed by the paediatric ear, nose, and throat (ENT) surgeon. DLB showed a subglottic membrane just below the level of the vocal cords (Figure 2), and the endotracheal tube was in the oesophagus (Figures 3) ventilating the lungs through a carino-oesophageal fistula through which both main bronchi were visible.

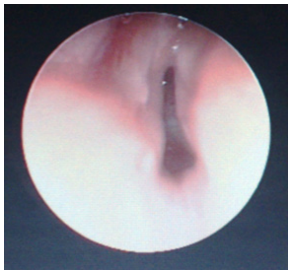

Figure 2: DLB shows bilateral folds of vocal cords and subglottic obstruction.

Computed Tomography (CT) of the chest with contrast showed absence of the subglottic laryngeal and tracheal air column and showed that the ETT was in the oesophagus. In neonatal intensive care, the patient was on synchronized intermittent mandatory ventilation, which was facilitated by continuous gastric

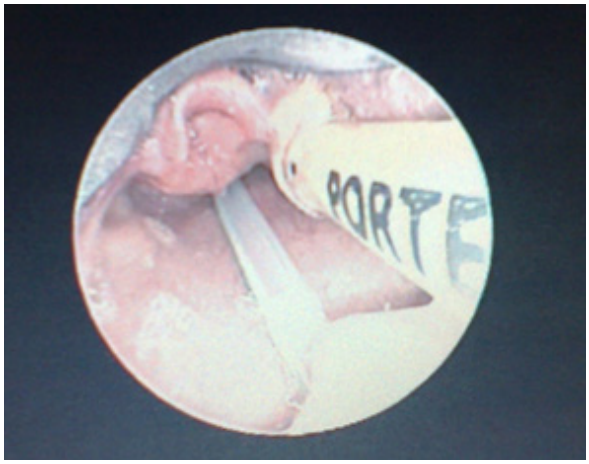

Figure 3: TDLB shows endotracheal tube and nasogastric tube are sharing same passage, epiglottis can be seen with bilteral vocal cords and subglottic obstruction.

decompression through a nasogastric tube. Renal ultrasound was normal, and echocardiography showed a patent ductus arteriosus that was closed later. The initial decision after the meeting with the paediatric surgeon, paediatric ENT, and the father was to insert a gastrostomy tube, ligate the lower oesophagus, and plan further treatment later on. The father refused surgical intervention due to the poor expected prognosis, and the infant died at the age of 35 days due to pulmonary infection.

DISCUSSION

TAAS has an estimated incidence of 1 per 50,000 newborns and affects more males than females, with a 2:1 ratio [5]. A concomitant malformation is found in 94.2% of cases [9]. Polyhydramnios is present in 79% of cases, oligohydramnios in 5.9%, foetal ascites in 2.3%, and CHAOS in 2.3% [10]; 72% of affected neonates are born weighing less than 2500 gm, and 60% are born at less than 36 weeks of gestation [11]. In our case, the patient was born at 33 weeks, weighed 1625 gm, and exhibited the bilateral absence of the radial bones and thumbs.

TAAS represents a variety of tracheal malformations with or without TEF. Floyd and his colleagues, in 1962, made the first classification system, which included 3 types [7]. Our case was type 2, with a carino-oesophageal fistula. Floyd's classification was based on 13 cases that were published from 1900-1962. Floyd's report recorded the first attempt of surgical reconstruction and inadvertent oesophageal intubation (IEI). IEI was performed in our case by the neonatologist and was also reported recently [11-13]. This issue indicates that the diagnosis may be missed, capnography is unreliable, and oesophageal intubation is the initial lifesaving manoeuvre. In 1978, Faro and colleagues proposed a more comprehensive classification with 7 different groups [14]. Although there were only 37 reported cases until 1978, Faro et al identified 2 cases in their centre. Later, in many other countries, 3 cases were reported several times by the same centres, although neither a linking factor nor prenatal exposure to any teratogens was identified [2,5,15]. Six cases of TAA were identified at a single hospital in the Netherlands during the period from 1988-2005 [16]. A report from India described 4 cases of TAA among 1152 perinatal autopsies performed over a 13-year period [17] (Table 1).

Table 1: Review articles that include more than 3 cases from one center. From this table we concluded that TAAS may be more frequent than previously described and miss diagnosed or under reported.

Serial	Authors	Time	Number of Cases	Location	Specialty
1	Veenendaal, et al.[5]	2000	3 Cases	Netherland	Otolaryngology
2	Heimann, et al. [15]	2007	3 Cases	Germany	Pediatric
3	Mohamed, et al. [2]	2016	3 Cases	UK	ENT Surgeons
4	Aneel, et al. [17]	2019	4 cases	India	Clinical Pathology
5	Felix et al. [16]	2005	6 Cases	Netherland	Otolaryngology

This raises the possibility of a missed diagnosis or underreporting and confirms the value of increasing awareness. It may be worth refining the surgical techniques of tracheal reconstruction. Identified review articles are shown in Table 2, and the timeline since the first case was reported in 1900 until 2017 is shown in Table 3.

Table 2: Review Articles that were involved in our research.

Serial	Authors	Time	Number of Cases	Location	Specialty
1	Floyed, et al. [7]	1962	13 Cases	USA	Pediatric Surgeons
2	Faro, et al. [14]	1978	39 Cases	USA	Pediatric Surgeons
3	Hirakawa, et al. [11]	2002	59Cases	Japan	Pediatric Surgeons
4	De Groot-van der Mooren, et al. [3]	2012	49 Cases	Netherland	Neonatology, Obstetrics and Gynecology Clinical Genetics Pathology Otolaryngology
5	Mohamed, et al. [2]	2016	186 Cases	UK	ENT Surgeons
6	Smith, et al. [9]	2017	149 Cases	Canada	Otolaryngology

Identifying the type of TAA is essential for reconstructive surgery. The presence or absence of the trachea and the length of the remaining part influence the surgical outcome. Patients with a longer residual trachea have higher long-term survival rates. Among patients with a short but present trachea, 21.7% survived more than 1 year, but if the trachea was absent and both bronchi communicated directly with the oesophagus, only 2.2% were long-term survivors. When there is a TEF between the carina and the oesophagus, the proportion of long-term survivors increased slightly to 4.4% [9]. The mortality rate is 87.2% within the first week of life and 92.6% at 1 year of age [18]. There are 12 cases (7.4%) of long-term survival [18-29]. We present our conception versus the current conception regarding TAAS in Table 4.

Standard neonatal resuscitation guidelines do not specify the course of action for failed intubation in suspected TAA [30], and the mortality rate remains high due to a lack of definite airway management protocols [31]. We present a protocol that outlines the perinatal diagnosis and management of TAAS (Table 3).

Table 3: Timeline of Review Articles of TAAS Since First Case Reported by Payane in 1900.

1st Case	13 Cases	39 Cases	150Case	49Case	186Cases	149Cases
1900	1962	1978	2002	2012	2016	2017
Payane et al	Floyed et al	Faro et al	HiraKawa et al	Mooren et al	Mohammed et al	Smith et al

Antenatal diagnosis

Antenatal ultrasonography may detect TAAS if there is no fistula as in CHAOS; these findings are as follows:

- Polyhydramnios.
- Enlarged hyperechogenic lungs.
- Dilated trachea and bronchi.
- Compression of the heart.
- Flattened diaphragm.
- Massive ascites.
- Visualization of the obstructed site.

The above findings are indications on magnetic resonance imaging (MRI) [32]. Amniotic phospholipids may be absent in amniotic fluid, which is normally secreted by the respiratory tract. Confirmation of the diagnosis may indicate an ex utero intrapartum therapy (EXIT) procedure [33]. If there is a fistula, the finding of polyhydramnios and associated anomalies may indicate MRI [34].

Postnatal diagnosis

Cardinal signs of TAAS and indications for oesophageal intubation:

A: Aphonic, or non-audible cry, although there may be a strong effort [5].

B: Bag-mask ventilation improves SpO_2.

C: Cyanosis and respiratory distress [30].

D: Difficult ETT passage.

Intentional oesophageal intubation allows resuscitation and neonatal stabilization through controlled mechanical ventilation (CMV) [35]. The preferred mode is PCV, aiming at a peak inspiratory pressure (PIP) of [30-35] cm H2O and peak end-expiratory pressure (PEEP) of 5-10 cmH2O to compensate for both the leak around the cuffed ETT and collapsibility of the oesophageal wall and maintenance of a tidal volume of 8-10 ml/kg and $EtCO_2$ of [30-35] mmHg [36].

Direct laryngo-bronchoscopy (DLB) should be performed to confirm the diagnosis [11], followed by CT with contrast to delineate the anatomy of the trachea and the associated congenital anomalies [4]. Echocardiography and hepatic, renal, and haematological investigations are mandatory.

Table 4: Summery of our conception versus the current conception regarding TAAS.

Item to be defined	Current conception	Proposed conception
Definition	Tracheal agenesis/atresia	Tracheal Atresia/Agenesis Syndrome (TAAS) Associated anomalies: VATER VACTERL TARCD CHAOS Laryngeal anomalies are common
Incidence	Extremely rare	Unknown, but may be infrequent! Miss diagnosed and unreported
Mortality	Uniformly lethal	85%, Amenable to surgical correction
Fistula(Position and Presence)	Tracheo-Esophageal fistula (TEF)	* Present: Laryngo-Esophageal Fistula Tracheo-Esophageal fistula Bronco-Esophageal Fistula Carino-Esophageal Fistula *Absent (CHAOS)
Capnography ($EtCO_2$)	Sure- sign of endotracheal intubation	Only sure-sign of ventilation and oxygenation, unreliable in TAAS (false positive $EtCO_2$)
Intubation	Unique case of difficult intubation37	Indication of esophageal intubation
Surgical correction	Not to be tried	Cases must be categorized and may be successful
Protocol for management	Not available	Available now

Neonatal management

The results of radiological and laboratory investigations should be available for neonatologists, paediatric ENTs, cardiothoracic physicians, paediatric surgeons, and anaesthesiologists to scrutinize all associated anomalies. A multidisciplinary meeting is recommended, and then parents should be involved in the discussion of possible options and the prognosis for decision making.

Isolation of the lower oesophagus by oesophageal banding and gastrostomy is mandatory to prevent the regurgitation of gastric fluid and abdominal distention during CMV [21]. Higher oesophagostomy may be performed to allow for salivary drainage [19,20]. Extracorporeal membrane oxygenation provides an excellent environment for complex tracheal reconstruction and promotes postoperative healing by minimizing trauma to the reconstructed airway [38]. Tissue engineering may create new possibilities for definitive surgical repair in TAAS [9]. At this moment, no form of tracheal replacement appears to be satisfactory, and although oesophageal trachealization and stenting have been reported to be successful [29], homologous tissue will offer a good option for tracheal prostheses.

CONCLUSION

TAAS is amenable to tracheal reconstruction, which depends on an early diagnosis and the severity of the associated anomalies, and it may not be as rare as previously described. We aim to increase awareness, and provide a protocol that may improve the initial diagnosis and management and provide an indication for initial and intentional rather than inadvertent oesophageal intubation for oxygenation and ventilation.

ABBREVIATIONS

TAAS: Tracheal Atresia/Agenesis Syndrome; TAA: Tracheal Atresia/Agenesis; VATER: Vertebral Defect, Anal Atresia, Tracheoesophageal Fistula, Oesophageal Atresia, Radial, or Renal Anomalies; VACTERL: Vater Plus Cardiovascular and Limb Defects; TARCD: Tracheal Atresia or Agenesis, Radial Anomaly, Cardiac Abnormality, and Duodenal Atresia; CHAOS: Congenital High Airway Obstruction Syndrome; ETT: Endotracheal Tube; SpO2: Peripheral Oxygen Saturation; DLB: Direct Laryngobronchoscopy; PCV: Pressure-Controlled Ventilation; CT: Computed Tomography; IEI: Inadvertent Oesophageal Intubation; TEF: Trachea-Oesophageal Fistula; MRI: Magnetic Resonance Imaging; EXIT: Ex Utero Intrapartum Therapy; CMV: Controlled Mechanical Ventilation; PIP: Peak Inspiratory Pressure; PEEP: Peak End-Expiratory Pressure

CONSENT FOR PUBLICATION

All authors have seen and approved the final version of the manuscript.

AVAILABILITY OF DATA AND MATERIAL

All data related to this case report are contained within the manuscript.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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None.

AUTHORS' CONTRIBUTIONS

AE conducted the anesthesia, created the protocol, wrote the manuscript, and critically reviewed the literature, SB made DLB, discussed, shared, and reviewed the protocol. MD; prepared and shared the manuscript. FA made a critical revision and supervision of the protocol and the manuscript. AH shared and reviewed the protocol and made literature review. SY, RA and FB critically reviewed the manuscript, BI conducted the anesthesia and reviewed the manuscript, YA, AK, YAW, MT and BB collected, organized the

literature, and reviewed the manuscript. All authors have read and approved the manuscript.

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