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. The mother was 34 years old, known to have gestational diabetes, and prenatal ultrasound showed polyhydramnios. The neonate had bilateral absence of radial bones and thumbs (Figure 1), non-audible cry, respiratory distress, and cyanosis, and endotracheal intubation was difficult.
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.

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 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).
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.

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] mmHg [36]. Assisted ventilation limits the volume of 8-10 ml/kg and EtCO₂ of 3-5% 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 EtCO₂ 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 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 missed diagnosed or under reported.

<table>
<thead>
<tr>
<th>Serial</th>
<th>Authors</th>
<th>Time</th>
<th>Number of Cases</th>
<th>Location</th>
<th>Specialty</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Veenendaal et al.</td>
<td>2000</td>
<td>3 Cases</td>
<td>Netherlands</td>
<td>Otolaryngology</td>
</tr>
<tr>
<td>2</td>
<td>Heimann et al.</td>
<td>2007</td>
<td>3 Cases</td>
<td>Germany</td>
<td>Pediatric</td>
</tr>
<tr>
<td>3</td>
<td>Mohamed et al.</td>
<td>2016</td>
<td>3 Cases</td>
<td>UK</td>
<td>ENT Surgeons</td>
</tr>
<tr>
<td>4</td>
<td>Ameel et al.</td>
<td>2019</td>
<td>4 Cases</td>
<td>India</td>
<td>Clinical Pathology</td>
</tr>
<tr>
<td>5</td>
<td>Felix et al.</td>
<td>2005</td>
<td>6 Cases</td>
<td>Netherlands</td>
<td>Otolaryngology</td>
</tr>
</tbody>
</table>

This raises the possibility of a missed diagnosis or under-reporting 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.

<table>
<thead>
<tr>
<th>Serial</th>
<th>Authors</th>
<th>Time</th>
<th>Number of Cases</th>
<th>Location</th>
<th>Specialty</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Floyed et al.</td>
<td>1962</td>
<td>13 Cases</td>
<td>USA</td>
<td>Pediatric Surgeons</td>
</tr>
<tr>
<td>2</td>
<td>Faro et al.</td>
<td>1978</td>
<td>39 Cases</td>
<td>USA</td>
<td>Pediatric Surgeons</td>
</tr>
<tr>
<td>3</td>
<td>Hirakawa et al.</td>
<td>2002</td>
<td>59 Cases</td>
<td>Japan</td>
<td>Pediatric Surgeons</td>
</tr>
<tr>
<td>4</td>
<td>De Groot-van der Mooren et al.</td>
<td>2012</td>
<td>49 Cases</td>
<td>Netherlands</td>
<td>Neonatology, Obstetrics and Gynecology, Clinical Genetics, Pathology, Otolaryngology</td>
</tr>
<tr>
<td>5</td>
<td>Mohamed et al.</td>
<td>2016</td>
<td>186 Cases</td>
<td>UK</td>
<td>ENT Surgeons</td>
</tr>
<tr>
<td>6</td>
<td>Smith et al.</td>
<td>2017</td>
<td>149 Cases</td>
<td>Canada</td>
<td>Otolaryngology</td>
</tr>
</tbody>
</table>

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 SpO₂.
- 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 EtCO₂ 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.
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: Tracheo-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.

FUNDING

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

<table>
<thead>
<tr>
<th>Item to be defined</th>
<th>Current conception</th>
<th>Proposed conception</th>
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</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Tracheal agenesis/atresia</td>
<td>Tracheal Atresia/Agenesis Syndrome (TAAS)</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>Extremely rare</td>
<td>Unknown, but may be infrequent!</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td>Uniformly lethal</td>
<td>85%, Amenable to surgical correction</td>
</tr>
<tr>
<td><strong>Fistula (Position and Presence)</strong></td>
<td>Tracheo-esophageal fistula (TEF)</td>
<td>Laryngo-esophageal Fistula</td>
</tr>
<tr>
<td><strong>Capnography (EtCO₂)</strong></td>
<td>Sure-sign of endotracheal intubation</td>
<td>Only sure-sign of ventilation and oxygenation, unreliable in TAAS (false positive EtCO₂)</td>
</tr>
<tr>
<td><strong>Intubation</strong></td>
<td>Unique case of difficult intubation?</td>
<td>Indication of esophageal intubation</td>
</tr>
<tr>
<td><strong>Surgical correction</strong></td>
<td>Not to be tried</td>
<td>Cases must be categorized and may be successful</td>
</tr>
<tr>
<td><strong>Protocol for management</strong></td>
<td>Not available</td>
<td>Available now</td>
</tr>
</tbody>
</table>

Table 4: Summery of our conception versus the current conception regarding TAAS.
literature, and reviewed the manuscript. All authors have read and approved the manuscript.

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REFERENCES