

Tracheal Agenesis

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Tracheal agenesis is one of the rarest of congenital malformations of the airway. The case of a newborn infant who presented with immediate respiratory distress is described. Surgical and pathological examination confirmed a diagnosis of complete agenesis of the trachea, an elliptical cricoid cartilage, and several associated cardiac anomalies.

A 30-week gestational age female was born to a healthy 15-year old mother. Prenatal ultrasonography demonstrated polyhydramnios, for which she underwent a therapeutic amniocentesis. Cardiac anomalies were also noted, specifically, ventricular asymmetry. At delivery, Apgar scores were 2 and 6 at 1 and 5 minutes, respectively. She was ventilated by mask with 100% oxygen and subsequently developed bradycardia, followed by secondary apnea. The neonatal staff members were unsuccessful in passing an endotracheal tube past the immediate subglottis, and otolaryngology was consulted emergently.

The baby was noted to be in respiratory distress, with no audible cry. Transient saturations above 90% could only be accomplished while bagging the child with neck extension and full-seal mask ventilation. Arterial blood gas showed severe hypoxemia. The baby was brought emergently to the operating room. At laryngoscopy, the larynx appeared normal with mobile vocal cords, but a 2.5-mm endotracheal tube could not be passed beyond the subglottic region. Rigid bronchoscopy revealed a blind laryngeal pouch. Esophageal intubation with ventilation was also unsuccessful. Palpation of the neck revealed no tracheal rings, and after a vertical midline neck incision, no trachea could be identified. The esophagus was opened and an endotracheal tube was threaded distally, but the baby continued to desaturate and eventually died at 2 hours of age.

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An autopsy was obtained and showed complete agenesis of the trachea (Fig. 1). A common bronchus was noted connecting the right and left lungs, both of which appeared normal (Fig. 2). A 2-mm triangular bronchoesophageal fistula was discovered, which was oriented in a caudal-cephalad direction (Fig. 3). A Floyd's type II tracheal agenesis was diagnosed. On gross examination, the larynx appeared normal. Horizontal sectioning, however, revealed the cricoid cartilage to be somewhat elliptical in shape (Fig. 4). Cardiac anomalies were also noted, most notably a hypoplastic left ventricle and aortic arch. The remainder of the examination was otherwise unremarkable, as was the placenta. Chromosomal analysis revealed a normal female karyotype (46, XX).

EPIDEMIOLOGY AND CLASSIFICATION

Tracheal agenesis is one of the rarest of tracheal anomalies. Since first reported by Payne¹ in 1900, less than 100 cases have been reported to date.² Holinger and associates³ reviewed almost 73,000 admissions to the Children's Memorial Hospital in Chicago over a 15-year period and found an incidence of 0.002%. There is a male predominance (2:1 ratio),⁴ and an association with prematurity and polyhydramnios.

By strict definition, "atresia" refers to congenital absence or closure of a normal opening, and "agenesis" refers to complete, or almost complete, failure of the anlage of an organ to develop. Several classification schemes have been proposed for tracheal agenesis. At present, the classification of Floyd and colleagues⁵ remains the one most universally accepted, and the one referred to in this text. They classified tracheal agenesis into three variants (Fig. 5). In type I, a short segment of distal trachea arises from the anterior wall of the esophagus before dividing into the mainstem bronchi. In type II, there is complete agenesis of the trachea, with a fistula between the esophagus and carina from which the two mainstem bronchi originate. In type III, the two mainstem bronchi arise individually from the anterior esophageal wall. The relative incidence of these three types are 13%, 65%, and 22%, respectively.⁶



Figure 1. Dissected autopsy specimen, posterior view, including transected base of tongue, larynx, esophagus, heart, lungs, and great vessels. Note the complete absence of a trachea. The larynx ends in a blind pouch immediately beyond the cricoid cartilage.

EMBRYOLOGY AND ASSOCIATED ANOMALIES

The exact pathogenesis of tracheal agenesis is unknown. Several theories have been advocated, all of which suggest a vulnerable focus during the early embryologic differentiation of the respiratory tract.⁷ The respiratory system normally forms as a midline, ventral diverticulum, which itself arises from the proximal foregut at 26 days gestation. Within 10 days, the laryngotracheal grooves appear laterally and deepen to form the tracheoesophageal septum. It has long been taught that this process is thought to proceed in a cephalad direction to eventually separate the respiratory primordium from the esophagus.⁸ Recent experiments have suggested that preprogrammed cell death in the area designated as the tracheoesophageal septum is responsible for separation, rather than cellular proliferation.⁹ Meanwhile, the respiratory diverticulum bifurcates to form the lung buds and a

cartilaginous framework forms from surrounding mesenchymal tissue. From animal experiments, it has been shown that lung development depends on two main factors. First, there must be a sufficient quantity of fluid in the lungs, and second, the fetal breathing movements must be adequate.¹⁰ In the case presented here, there must have been sufficient leakage of fluid through the bronchoesophageal fistula during fetal life to prevent hypoplasia of the baby's lungs.

In contrast, the proximal larynx develops from the pharyngeal floor and branchial arches (primarily the IVth arch). The cricoid develops from the proximal trachea, which may explain the association of cricoid anomalies with tracheal agenesis.¹¹ Holinger and colleagues¹² studied two cases of tracheal agenesis using horizontal serial sections. An elliptic cricoid cartilage was found in both cases. They suggested that congenital laryngeal anomalies may have been present, but unrecognized, in previous reports of tracheal agenesis. A similar finding was seen in this case (Fig. 4). Laryngotracheoesophageal clefts, complete laryngeal agenesis, and webbing of the vocal cords have also been described in association with tracheal agenesis.⁶

The association of tracheal agenesis with other multiorgan congenital malformations has been a topic of interest. The high incidence of associated anomalies has led some authors to suggest that tracheal agenesis may be one of the components of the VACTERL association.¹³ VACTERL includes vertebral anomalies, anal atresia, cardiac anomalies, tracheoesophageal fistula or esophageal atresia, renal malformations, and limb defects. Although many of the reported cases of tracheal agenesis share anomalous features with the VACTERL association, Evans and colleagues¹³ suggested that tracheal agenesis is not a part of the association itself. Rather, they believed that tracheal agenesis is one manifestation of a different pattern of malformations that includes tracheal agenesis or laryngotracheal atresia, complex congenital cardiac anomalies, radial ray defects, and duodenal atresia (TACRD association). More recently they reviewed nearly 100 cases of tracheal agenesis with multiple congenital anomalies, and state that the complexity of the associated malformations may represent increasingly severe disruption of the fields encompassing the developing respiratory tract.¹⁴

Such distinctions become important in studies of pathogenesis, prevention, and prognosis. Categorization facilitates counselling of affected families. The patient

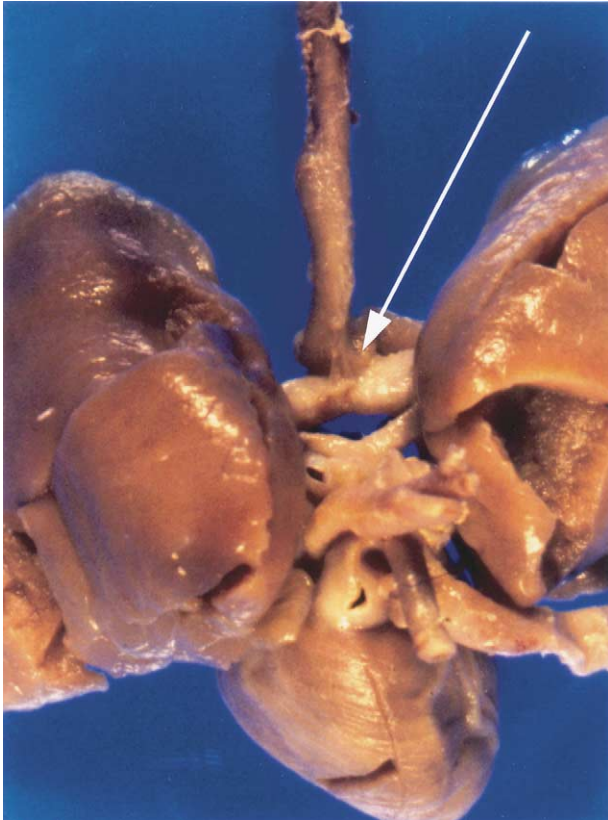


Figure 2. Dissected autopsy specimen, anterior view. Note the fistulous connection (arrow) between the common bronchus, and the distal esophagus.

presented here exhibited tracheal and cardiac anomalies, but lacked other features to clearly share either the VACTERL or TACRD associations.

DIAGNOSIS AND MANAGEMENT

In North America, prenatal ultrasonography is the standard of care in many obstetrics and gynecologic practices. Ultrasonographic normative data have been collected for fetal aerodigestive tracts,¹⁵ and have been used for prenatal diagnosis of certain tracheal anomalies.^{16,17}

Postnatal clinical diagnosis of tracheal agenesis should be suspected in cases of antenatal polyhydramnios, in an infant usually of less than 37 weeks gestation or weighing less than 2,500 grams, born with immediate respiratory distress and vigorous respiratory efforts, but with minimal air exchange detectable on auscultation. Although exceedingly rare, a high index of suspicion is required to make the diagnosis premorbidly. There is no audible cry, and endotracheal intubation is impossible. Ventilation is transiently achieved only if a tracheo-

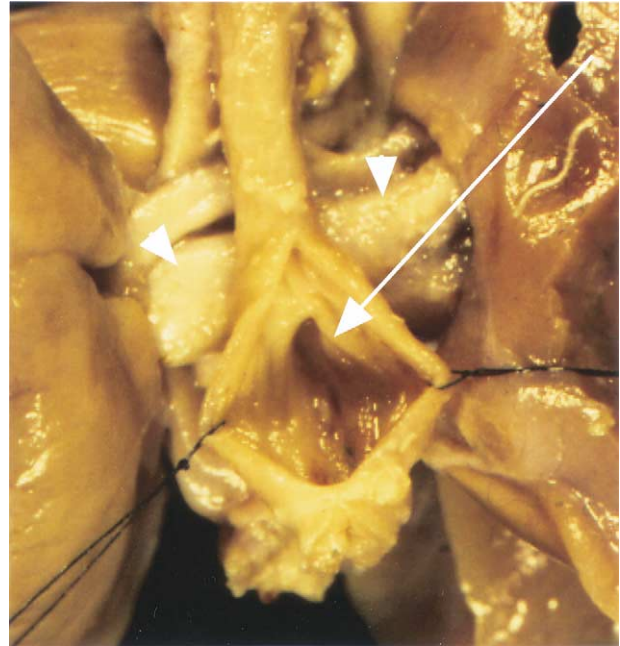


Figure 3. Dissected autopsy specimen, posterior view, opened (distal esophagus transected). Note the bronchoesophageal fistula (arrow), allowing temporary ventilation of the infant. The common bronchus is seen as well (arrowheads).

esophageal or bronchoesophageal fistula exists, and a tightly-sealed mask is applied.¹⁸ Esophageal ventilation produces gastric distension, and after sufficient back-pressure develops, air passes retrograde through the bronchoesophageal fistula and into the lungs. So marked abdominal distension will be apparent, and cycles of stabilization and deterioration will occur.

Radiographic findings may include posterior location of the endotracheal tube (esophageal intubation), and absence of the tracheal shadow. Contrast material may demonstrate a blind ingeal sac and a bronchoesophageal fistula.¹⁹ Helical CT scanning has been used to confirm the diagnosis.²⁰

Tracheal agenesis presents as a hierarchy of problems that necessitate immediate management. A high index of suspicion is of prime importance. Early stabilization of the infant's airway is mandatory while an adequate assessment can be made of other congenital anomalies. The decision to attempt salvage reconstructive measures is undertaken only after the first two issues have been addressed.^{21,22}

In most cases of tracheal agenesis, an oropharyngeal airway in conjunction with positive pressure ventilation will provide a grace period in which one can develop a strategy for the interim and definitive management of

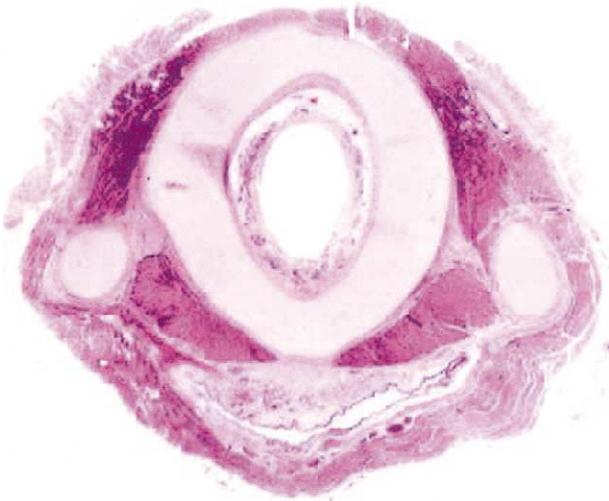


Figure 4. Horizontal section through cricoid cartilage (hematoxylin and eosin stain, 10x magnification). Note the elliptical shape of the cricoid cartilage.

the airway. In type I anomalies, an endotracheal tube may be threaded onto a 2.7-mm Hopkins rod telescope, allowing intubation of the distal tracheal stump under

direct visualization. In type II and III anomalies, esophageal intubation with a relatively large endotracheal tube to the level just above the bronchial communication will maintain the child's airway transiently, albeit tenuously. Under all circumstances, a nasogastric tube should be placed in order to aspirate the gastric contents and reduce the likelihood of airway soiling with gastric acid. The nasogastric tube is also useful for decompressing air from the stomach, which invariably collects with esophageal ventilation.

The two organ systems that require the most urgent evaluation once the airway has been stabilized are the central nervous system and the cardiovascular system. Major malformations, such as meningomyelocele or the tetralogy of Fallot, could preclude further consideration of therapeutic intervention, or radical reconstruction. If no other congenital anomalies are identified, some thought should be given to a surgical rearrangement of the anatomy to give the infant a chance to survive.⁶

Diaz and associates²³ point out that this malformation is universally fatal and advise against reconstructive surgery. Instead, they advocate strictly palliative measures.

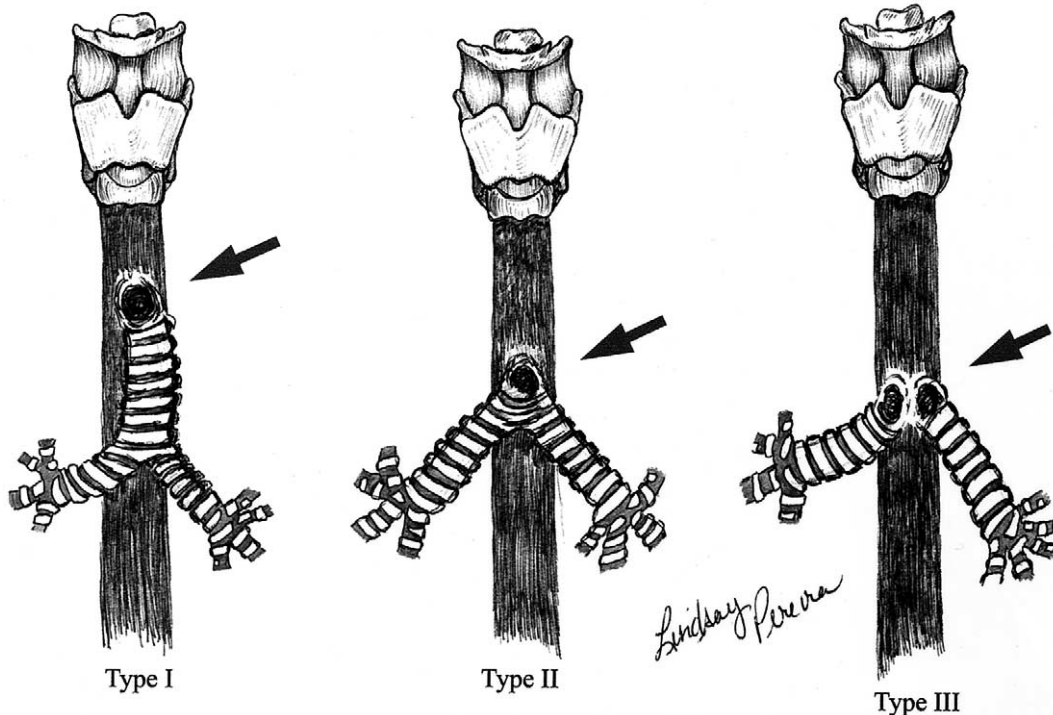


Figure 5. Floyd's classification of tracheal agenesis. In all three types a tracheoesophageal fistula exists (arrowhead). In type I, a short segment of distal trachea arises from the anterior wall of the esophagus before dividing into the mainstem bronchi. In type II, there is complete agenesis of the trachea, with a fistula between the esophagus and carina from which the two mainstem bronchi originate (commonest). In type III, the two mainstem bronchi arise individually from the anterior esophageal wall.

Nevertheless, it is worth reviewing selected cases in which attempts have been made at reconstruction.

In 1963, Fonkalsrud and colleagues²⁴ reported a case of an infant girl born at term with a type II tracheal agenesis. They divided the cervical esophagus in two places, the proximal end of which was made into an esophagostome for drainage of pharyngeal secretions. The intermediate esophagus was sutured to the skin to form a pseudotracheotomy, through which a ventilation tube was inserted into the common tracheoesophagus. The distal esophagus was divided below the insertion of the main stem bronchial segments in order to isolate the trachealized esophagus from gastric secretions. For nutrition, a gastrostomy tube was placed. The infant survived 6 weeks with this reconstruction, eventually succumbing to pneumonia.

To date, the longest surviving infant born with tracheal agenesis, surgically reconstructed, was reported by Soh and coworkers.²⁵ They performed a double barrel cervical esophagostomy with distal esophageal banding on a child born with a Floyd's type I tracheal agenesis. The child was ventilated by threading an endotracheal tube through the distal stoma, and was able to survive for 6 years and 10 months without artificial ventilatory support, until succumbing to acute esophageal hemorrhage. It is important to note that this was only possible because there existed a viable segment of trachea (Floyd's type I), with normal bronchi and lungs.

Definitive substitution of a large segment of the upper airway, or an entire trachea is hindered by lack of a suitable homologous tracheal replacement or prosthetic material that will provide ciliated epithelium for mucous clearance and withstand the normal pressure changes and movement of the tracheobronchial tree. These challenges are beginning to be met.²⁶ An ideal graft, if found, must also allow normal growth and development of the child. Recently, animal experiments using allografts and homografts²⁷⁻²⁹ have given hope that tracheal transplantation in humans may one day be clinically feasible.²⁷ The use of cryopreserved, irradiated tracheal homografts in human beings by Nakanishi and colleagues³⁰ and Kunachak and associates³¹, has also appeared in recent literature. It should be noted, however, that surviving surgical transplantation of the entire trachea has not been accomplished, even in an animal model. Free segmental tracheal autographs are being used successfully.³² There is a limit, however, to the extent of the trachea that may be replaced. Bechara and

coworkers³³ performed total tracheal reconstruction in a 3-month-old infant with tracheal stenosis using homologous left mainstem bronchus (the infant died 48 hours later).

Experimental tracheal reconstruction using a variety of materials have been attempted unsuccessfully, including the use of silicone elastomer and Dacron (Borrie and colleagues³⁴; Neville and associates³⁵), Marlex mesh (Beall and coworkers³⁶), urinary bladder wall (Rush and Clifton³⁷; Marshak and colleagues³⁸), and pericardium (Morghissi³⁹).

Most authors who attempt reconstruction tend to use the esophagus because a conduit to the lungs is already present through the bronchoesophageal fistula, as Fonkalsrud and colleagues²¹ showed. Or they may attempt a thoracic tracheotomy, as Hong and colleagues¹⁹ did.

Extracorporeal membrane oxygenation (ECMO), a form of cardiopulmonary life support, may be used temporarily in the acute setting as an alternative to ventilation. This provides the surgical team precious time to plan and execute a reconstruction. An infant can be sustained on ECMO for several days, if necessary. Unfortunately these facilities are generally limited to large, urban, tertiary care centers. The value of ECMO during the surgical correction of tracheal anomalies has been described, including its use during reconstruction of long segment congenital tracheal stenosis.⁴⁰

In conclusion, tracheal agenesis is fortunately a very rare anomaly, with less than 100 cases reported in the literature. Prompt diagnosis and establishment of ventilation is mandatory. The role for ECMO in these patients is still to be determined. Definitive airway stabilization is often impossible because reconstructive technology and materials are insufficient to date. At present, this anomaly is still considered to be incompatible with life.

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