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"TRACHEOESOPHAGEAL FISTULA" EMBRYOLOGICAL BASIS AND ITS CLINICAL SIGNIFICANCE

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ABSTRACT

Tracheoesophageal fistula is a life threatening condition. Patients not managed surgically ultimately die of their disease. Surgical management is the only treatment of choice. We present a case of a patient that developed a tracheoesophageal fistula after tracheostomy. Surgical repair was done which failed due to infection. The patient was managed with the help of an esophageal stent and Trichloroacetic Acid cautery. This approach can be used in selected patients, depending upon the size and site of TEF. Larger fistulae and those situated lower down e.g. supra cardinal cannot be managed by this technique.

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Keywords Tracheal fistula.

Subglottic opening, Rima Glottides, Oesophageal fistula, Nasal congestion, Dyspnea, Airway stenosis.

Introduction

The trachea or the windpipe carries air to the lungs whereas the esophagus carries food to the stomach. TEF has an abnormal connection between the trachea and the esophagus. It is a common congenital abnormality .When this happens, air within the trachea may pass into the esophagus or alternatively, food passes through the trachea [1]. There are three main types of TEF.TEF can also occur due to pressure necrosis by a tracheostomy tube in opposition to the nasogastric tube. In most of the tracheoesophageal fistulas, the upper part of the esophagus ends in a blind sac, and the lower part gets inserts into the trachea. The upper part of esophagus is directly connected to the second part, while the lower part ends in a pouch. In the H type which is a rare type fistula, both the esophagus and trachea are complete, but they are linked by a small passageway [2]. Neonates with TEF are unable to feed properly. It includes salivation associated with chocking, coughing, vomiting, and cyanosis coincident with the onset of feeding. After diagnosis surgery is required. TEFs often occur in babies with additional birth defects. TEF can be congenital or acquired. About 80% the acquired tracheoesophageal fistulae are malignant and rest non-malignant [3]. Due to trauma which can be internal or external, iatrogenic is nonmalignant. Internal trauma is due to cuffed endotracheal or nasogastric tube or a combination of both, whereas Pathogenic fistulae are mechanical ventilation [4]. TEF from cuffed endotracheal tube usually occurs between the sixth cervical and first thoracic vertebra and manifests after a week or more. In external trauma it is like penetration of the foreign bodies, open or closed aero digestive tract injuries [4]. Acquired TEFs resulting from esophageal malignancy are usually in the upper thoracic region. Time taken for acquired TEF to develop and become symptomatic depends on the precipitating causes. Chest wall crush injuries during road accidents cause majority of traumatic fistulae [3].

Laceration and disruption of blood supply is due to 1-3 compression of the esophagus and trachea between the sternum and thoracic spine. TEF formed at the cranial area have mortality rate of 15% because of the rapid spread of mediastinal infection. Congenital H type TEF is rare. Contamination of the tracheobronchial tree and interference with nutrition are the threatening aspects of post incubation [1-3]. This this date none of the records says that TEF has healed spontaneously and a large number of surgical techniques are required. These include direct closure of defects, esophageal diverticulum, closure of the defect with muscle flap and tracheal closure with dysfunctional esophagus [2-4]. **Incidence**

TEF is a common congenital anomaly with the incidence of 1 in 2000 to 4000 lives [5-8]. Acquired non-malignant TEFs occur in approximately 0.5% of tracheostomy undergoing patients. In malignant TEFs it is reported as 4.5% for primary malignant esophageal tumors and 0.3% for primary malignant lung tumor. TEFs secondary to esophageal carcinoma was noticed between the 4.3 - 8.1% populations [5-8].

Ontogenesis of the normal development of Trachea and Oesophagus

A. Development of Esophagus

Just caudal to the most posterior pharyngeal pouch of a 4week-old embryo, the pharynx becomes rapidly pointed, and a small ventral outgrowth appears[9-10]. The area of foregut just caudal to the lung bud is the esophagus. This part is firstly very short, with the stomach evident to reach almost to the pharynx. In the second month of development, during which the gut elongates very much, the esophagus assumes almost postnatal proportions in relation to the site of the stomach. even though the esophagus disgustingly resembles a simple tube, it undergoes a series of conspicuous differentiating changes at the tissue level [9-10].

In its initial stages, the endodermal lining epithelium of the esophagus is stratified columnar. By 8 weeks, the epithelium has partly occluded the lumen of the esophagus, and large vacuoles appear [11-14]. In succeeding weeks, the vacuoles are combined each other, and the esophageal lumen recanalizes, but with multilayered ciliated epithelium. During the fourth month, this epithelium finally is replaced with the stratified squamous epithelium that characterizes the mature esophagus. Stages in the histogenesis of the esophagus are at the 7th, 8th, 12th and 36th weeks of embryonic development. Deeper in the esophageal wall, layers of muscle also make different in response to inductive signals from the gut endoderm [14]. Very early (5 weeks' gestation), the primordium of the inner circular muscular layer of the esophagus is identifiable, and by 8 weeks, the outer longitudinal layer of muscle begins to take shape. The esophageal wall contains smooth and skeletal muscle. The smooth muscle cells differentiate from the local splanchnic mesoderm associated with the gut, and the skeletal musculature is derived from paraxial mesoderm [13-17]. All esophageal musculature is innervated by the vagus nerve (cranial nerve X). The cross-sectional structure of the esophagus, similar to that of the rest of the gut, is organized into distinct layers. The innermost layer (mucosa) consists of the epithelium, derived from endoderm, and an underlying layer of connective tissue, the lamina propria [18-20]. A thick layer of loose connective tissue (submucosa) separate the mucosa from the outer layers of muscle (usually smooth muscle, with the exclusion of the upper esophagus) [21]. This radial organization is regulated by the epithelial expression of sonic hedgehog, acting through its receptor, patched, and bone morphogenetic protein-4 (BMP-4) in the fundamental mesenchyme, but the mechanism remains indistinct [20]. The net effect is the lack of separation of the major outer layers of smooth muscle and enteric neurons in the mesenchyme close to the epithelium (the submucosa) [21]. Farther from the source of the endodermal, smooth muscle can differentiate in the outer wall of the intestine. How the developing smooth muscle layer of the mucosa (muscularis mucosa) escapes this inhibitory manipulate is also uncertain. Intestinal mesenchyme can instinctively differentiate into smooth muscle in the absence of an epithelium [20]. Because in humans the muscularis mucosa differentiate considerably later than the outer muscular layers, it is possible that inhibitory levels are reduced by that time.



Fig 1. Schematic representation of normal development of trachea and esophagus



Fig 2. Schematic representation of normal development of trachea and esophagus

B. Development of Trachea

At the early manifestation of the respiratory diverticulum, the Pair of bronchial buds appears at its end. And then it seems that the precursors of the windpipe and lung buds are derived from the different source of cells and that the lung buds give raise the bronchi and distal respiratory tree [22]. The straight portion of the respiratory diverticulum is the primordium of the windpipe. Then the bronchial buds ultimately become the primary bronchi, give rise to an additional buds -3on the right side and 2 on the left side. Then this bud develops and becomes the secondary, or stem bronchi, their number signify the formation of the 3 lobes of the right lung and 2 lobes of the left lung [23-24].

From that point each secondary bronchial buds undergoes a long series of branching during embryonic and fetal life. Then the mesoderm surrounds the endoderm controlling the extent of branching within the respiratory tract [25].

Abundant tissues recombination experiments have shown that the mesoderm surrounds the windpipe and inhibits its branching, the mesoderm surrounds the bronchial buds promotes branching. If the tracheal endoderm is joined with the bronchial mesoderm, anomalous budding is induced [25-27]. On the other hand, tracheal mesoderm placed around the bronchial endoderm which inhibits the bronchial budding. The mesoderm of the certain additional organ, such as the salivary glands, can promote the budding of the bronchial endoderm [28].



Fig 3. Schematic representation of normal development of trachea and esophagus

The pattern of branching characteristic of the mesoderm is induced. The mesoderm is capable of promoting or supporting budding must maintain a high rate of production of epithelial cells [29-30]. Generally, the pattern of epithelial organs is a large separation of the epithelium is a definite property of the epithelial cells, but the epithelial phenotype corresponding to the regions occupies by the mesoderm [30]. By week eight (28-30mm embryo), mesenchymal essential rudiments of the sixteen to twenty tracheal cartilages are seen and the next two weeks, the masses formation cartilage begins cranially and extending caudally [28].

At the same time fibroblastic tissue of the tracheal wall arising from the mesenchyme between the cartilage and then posteriorly between the ends of the embryonic rings of smooth muscles arises. Cilia appear at the tenth week of the development (51-53mm embryo) [29]. By the 12th week of development, the mucosal glands are seen and developed in a craniocaudal direction [24]. By the end of the 20th-week development, all major microscopic features of the trachea are visible. It is short and narrow while the larynx is relatively long.

By the end of 4th week the trachea divides as right and left primary bronchi. During this 4th week the respiratory diverticulum divides as left and right lung buds, which divides as two or three bronchi [29]. The tracheoesophageal septum is formed from the tracheoesophageal folds which fuse in middle. It further divides the esophagus from the trachea and divides the foregut tube into the laryngotracheal tube ventrally and esophagus dorsally [25].

Embryological basis of Tracheoesophageal Fistula

Abnormalities in separating of the esophagus and trachea by the tracheoesophageal septum result in esophageal atresia with or without tracheoesophageal fisula [19]. These faults occur in approximately 1/3000 births and 90% result in the upper portion of the esophagus terminating in a blind pouch and the lower section developing a fistula with the trachea. Isolated esophageal atresia and H-type tracheoesophageal fistula lacking esophageal atresia each description for 4% of these defects [17-19].

Other deviations each account for approximately 1% of these defects. These abnormalities are related with other birth defects, with cardiac abnormalities, which take place in 33% of these cases [19-20]. In this favor, TEFs are the component of VACTERL (Vertebral anomalies, Anal atresia, Cardiac defects, Tracheoesophageal fistula, Esophageal atresia, Renal anomalies, and Limb defects), a group of defects of unknown causation, but happens more commonly than predicted [17].

A complication of some TEFs is due to accumulation of excess fluid in the amniotic sac since in some types of TEF, amniotic fluid, when swallowed does not pass to the stomach and intestines [18]. The gastric contents or amniotic fluid at birth may go into the trachea through the fistula, causing pneumonitis and pneumonia.

 Table 1.Classification of congenital tracheoesophageal

 fistula and esophageal atresia.

Anatomic Characteristics	Percent of cases
Esophageal atresia with distal TEF	87
Isolated esophageal atresia without TEF	8
Isolated TEF	4
Esophageal atresia with proximal TEF	1
Esophageal atresia with proximal and distal TEF	1



Fig 4. Schematic diagram for tracheoesophageal fistula and esophageal atresia



Fig 5. Tracheoesophageal septum deviates posteriorly, results in esophageal atresia with a tracheoesophageal fistula develops

Discussion

Tracheoesophageal fistula can either be acquired or can be congenital. The acquired fistula can be malignant or can be non-malignant. The acquired non-malignant tracheoesophageal fistula occurs in almost 0.5% of the patients who has undergone tracheostomy [9]. This condition is unusual but serious and may possess challenging problem [7]. Contamination of the Tracheo- bronchial tree and interfering with nutrition are life threatening feature of this situation. After wide investigations and analyses it became clear that cuffed tubes were the most common reason of this problem and the fistula ensued while patients were getting positive pressure ventilation for respiratory failure [10]. The beginning of high volume, low pressure cuffs has reduced the incident but not rejected it [7]. High intra cuff pressure is the single most important factor in development of an acquired TEF. Cuff pressures above 22mm of Hg have been exposed to cause reduced capillary perfusion of the tracheal mucosa and pressure of 40mm of Hg may result in total obstruction of blood flow to tracheal epithelium [4-8]. Tracheoesophageal septum deviates posteriorly; esophageal atresia with a tracheoesophageal fistula develops [10].

Table 2. Risk factors for the development of tracheoesonhageal fistula

Risk factors for development of TEF	
•	High cuff pressure
•	Advanced age
•	Nasogastric tube
•	High way pressure
•	Excessive motion of tracheal tube
•	Prolonged duration of intubation
•	Steroids
•	Respiratory infections
•	Hypotension
•	Female sex

The nasogastric tube may also act as an rough against the anterior esophageal wall [11]. This leads to ulcerative tracheal inflammation and necrosis. Position of the head also changes amount of pressure exerted by the cuff on the tracheal wall. Flexion causes more pressure to the anterior wall of the trachea, where as extension causes more pressure on the posterior wall. There were numerous of these risk factors in patients [12]. Diagnosis of TEF is suggested by many symptoms. Among them is violent coughing after swallowing, food at the tracheostomy site, unusual passage of catheters or tubes and air escape into the hypopharynx despite suitable cuff inflation. Thomas' has outlined definite diagnostic criteria, A. Direct visualization with a special feature such as

• Ryle's tube or posterior wall of mucosa is seen on tracheostomy.

• Tracheal tube seen on esophagoscopy.

• Well defined edges of fistula seen moving on respiration.

- B. Radiology: Demonstration of contrast at the site of fistula
- C. Operative or autopsy confirmation.

Esophagoscopy is suggested in all patients having distrust of fistula [12-14]. Till date there is no report to propose that the fistula can heal instinctively and hence surgery is now believed as the treatment for those proven cases. This comprises of direct ending of defects, esophageal diversion, ending of the defect with muscle flaps and tracheal closing with dysfunctional esophagus [11]. However there is difference over the timing, some advocate immediate interventions whereas others advocate performed procedures. Esophageal stents have been broadly used for the treatment of strictures & malignant obstruction. We used a different technique to close the TEF by putting a stent in the esophagus & making the edges of fistula raw with chemical cautery to encourage granulation tissue and healing [14]. The stent prevents the salivary secretions from coming in interact with the fistula and meddling with healing. The nutrition of the patient, however, was managed with gastrostomy feeds [15]. The method can be used in particular patients only, depending upon the size and site of TEF [14]. Larger fistulae and those located lower down e.g. supra carinal cannot be achieved by this technique. Another vital thing to remember is the size and shape of the stent. If it is over sized then the stent will itself cause ischemia and necrosis leading to increase in size of the fistula. Anteriorly the tracheostomy tube and posteriorly the stent can cause the similar injury [17]. To avoid this injury once the stent is introduced the size of the tracheostomy tube is reduced and preferably an uncuffed tube is inserted. The shape of the stent is funnel shaped and it helps to recollect the stent superior to the site of fistula and at the same time not exerting pressure over the party wall [18].

Conclusion

Repair of EA and TEF in the neonate can be especially challenging for the anesthesiologist. Anticipation of potential perioperative problems and communication with the surgeon are essential in treating these congenital defects [32-35]. Although patients with associated VACTERL (vertebral anomalies, Anal antresia, Cardiac defect, Tracheoesophageal fistula and Esophageal atresia, Renal and Radial anomalies and Limb defects) anomalies have a poorer prognosis, their survival rate is greater than 90% after surgical repair [33-37]. Most children have a good long-term quality of life but are likely to return to the operating room later in life. Thus, the anesthesiologist must be familiar not only with the perioperative management of neonates undergoing TEF repair but also with the long-term sequelae after surgery [38-43]. Lifelong problems such as gastroesophageal reflux, tracheomalacia, obstructive and restrictive ventilator defects, airway reactivity, and recurrent pneumonia should be anticipated in patients with a history of TEF repair [43-46].

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