Vocal Fold Paralysis in Infants With Tracheoesophageal Fistula

Yael Oestreicher-Kedem, MD; Ari DeRowe, MD; Hagit Nagar, MD; Gad Fishman, MD; Josef Ben-Ari, MD

Objectives: We describe the clinical characteristics and management of vocal fold paralysis in infants who were born with a tracheoesophageal fistula (TEF).

Methods: This retrospective case series included all infants born with TEFs who presented to our pediatric otolaryngology unit and intensive care unit because of dyspnea or aphonia in the years 2005 and 2006, and who were found to have vocal fold paralysis.

Results: Five boys and 1 girl were studied. One infant had stridor before TEF repair, and 5 after it. All children underwent flexible laryngotracheobronchoscopy and were treated in the pediatric intensive care unit before diagnosis of the vocal fold paralysis (5 bilaterally and 1 unilaterally) was made. The ages at diagnosis of paralysis ranged between 14 days and 14 months. Five infants required tracheostomy.

Conclusions: Vocal fold paresis in infants is difficult to diagnose. The risk for recurrent laryngeal nerve injury associated with TEF and TEF repair should be emphasized in these children. We recommend that all newborns with TEF should be examined by an otolaryngologist before operation to confirm the mobility of the vocal folds and to rule out other associated airway malformations, and examined after operation if respiratory difficulties develop.

Key Words: tracheoesophageal fistula, vocal fold paralysis.

INTRODUCTION

The esophagus (dorsal) and trachea (ventral) derive from the primitive foregut between 4 and 6 weeks of gestation. Failure of separation of the esophagus from the laryngotracheal tube at the tracheoesophageal septum will result in esophageal atresia (EA) with a tracheoesophageal fistula (TEF). Incomplete perforation of the esophagus at the eighth week of gestation will result in EA. Five types of TEF are described in the literature; type C has the highest prevalence (84%), and type B has the lowest (1%; see Figure).

Tracheoesophageal fistula and EA occur in 1 in 3,000 to 1 in 5,000 births. Between 10% and 17% of cases of congenital TEF and EA are associated with other congenital anomalies: VACTERL (defined as at least 2 of the following congenital anomalies: vertebral defects, anal atresia, cardiac defects, TEF, EA, renal anomalies, and limb anomalies, without other malformations); trisomies 13, 18, and 21; DiGeorge syndrome; and mitochondrial respiratory chain deficiency. Tracheoesophageal fistula and EA can also be associated with other congenital airway anomalies, among them laryngotracheobronchomalacia and laryngeal cleft. Infants with TEF and EA are also prone to aspiration, recurrent lung infections, and irreversible lung damage.


From the Pediatric Otolaryngology Unit (Oestreicher-Kedem, DeRowe, Fishman), the Department of Pediatric Surgery (Nagar), and the Intensive Care Unit (Ben-Ari), Dana Children's Hospital, Tel-Aviv Sourasky Medical Center, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel.


Correspondence: Yael Oestreicher-Kedem, MD, 28 He'Beiyar St, Tel-Aviv, Israel; e-mail: dkyo@013.net.
The pathogenesis of congenital EA and TEF remains unclear. The sonic hedgehog (Shh), a morphogene (a gene coding for an extracellular signaling glycoprotein and implicated in vertebrate axial organogenesis), and its transcription factors Gli2 and Gli3 have been shown to play a role in esophageal and tracheal development and correct separation of the two tracts in rodent models. Spilde et al8 demonstrated the absence of Shh protein in the fistula tract of neonates with TEF.

The first successful TEF and EA repair was reported by Haight and Towsley9 in 1943. Tracheoesophageal fistula and EA are traditionally managed by division of the fistula and primary anastomosis of the esophageal segments. The standard operation is done via an open thoracotomy by either the transpleural approach to the posterior mediastinum (in which the parietal pleura is incised and the pleural cavity is entered) or the extrapleural approach (in which the dissection plane is between the thoracic wall and the parietal pleura). The transpleural approach is time-saving, but at the cost of the risk of mediastinitis should the esophageal anastomosis fail. On the other hand, the extrapleural approach bears a risk for parietal pleura tears, especially in very low-birth weight infants (less than 1,500 g) because of tissue weakness. A staged repair (initial gastrostomy for drainage and feeding with fistula closure, followed later by a second operation for esophageal anastomosis) is performed for high-risk infants, ie, those with preoperative ventilator dependence or associated anomalies or when the distance between the two esophageal segments is long. Lobe et al11 reported the first successful thoracoscopic EA repair in 1999, and Rothenberg12 the first thoracoscopic TEF and EA repair in 2000. Since then, centers around the world have been gaining experience in this highly challenging and skill-demanding technique.13-15 The operative results seem to be comparable to those achieved with the open approach, combined with the benefits of less postoperative pain, reduction of the musculoskeletal sequelae associated with a thoracotomy, and possibly superior visualization of the anatomy of the thoracic cage. About one third of type E TEFs (ie, those cases with a fistula below vertebra T2) can be closed via thoracoscopy.16 Type E TEF and recurrent TEF can be managed endoscopically by injecting an obliterating agent (fibrin adhesive, tissue adhesive, or a sclerosing agent) into the fistula via rigid bronchoscopy.17 Interestingly, none of the series reporting these techniques mention vocal fold paralysis as a complication of TEF and EA repair.

Vocal fold paralysis is the second most common cause of stridor in newborns (after laryngomalacia).18 Vocal fold paralysis can be unilateral or bilateral.19 Causes of neonatal vocal fold paralysis are surgical or birth trauma, neurologic disorders, familial syndrome, and idiopathic causes. The diagnosis is made by awake flexible laryngoscopy, or by direct laryngoscopy under spontaneous respiration, the latter being a procedure that also facilitates a complete evaluation of the upper airway. The treatment of vocal fold paralysis depends on the patient’s symptoms, particularly the extent of airway compromise. Unilateral vocal fold paralysis does not usually necessitate surgical intervention for airway compromise. Bilateral vocal fold paralysis is traditionally managed by tracheostomy. Selected cases (specifically, children with no other medical conditions affecting respiration or children with an adequate growth rate and who have close access to a medical facility) may be managed expectantly and with close and frequent follow-up in the anticipation of vocal fold function recovery. Miyamoto et al20 reported a tracheostomy rate of 68% in a series of 36 infants with bilateral vocal fold paralysis. Fifty-three percent of the infants in their report were decannulated within an average of 31 months. Of those who did not require a tracheostomy, 85% regained an adequate airway within 1 to 82 months of diagnosis. Arytenoidectomy, arytenoidopexy, vocal fold lateralization, cordotomy, posterior grafting, and reinnervation procedures may be undertaken to facilitate decannulation. Hartnick et al21 used some of these procedures and managed to decannulate 85% of 56 infants with bilateral vocal fold paralysis. The timing of these procedures is debatable; many advocate waiting periods of months to years for spontaneous recovery of vocal fold motion. Daya et al19 reported a 56% recovery rate in a group of 64 infants with vocal fold paralysis of different causes. Recovery of function took up to 11 years; 69% of those children recovered vocal fold function within 2 years.

In this report we describe the clinical characteristics and management of vocal fold paralysis in infants who were born with TEF and/or EA and treated at the Pediatric Otolaryngology Unit of Dana Children’s Hospital, Tel-Aviv Sourasky Medical Center (Israel).

METHODS
We reviewed the files of all infants born with TEF and/or EA and referred to our pediatric otolaryngology unit and pediatric intensive care unit for evalu-
TABLE 1. DEMOGRAPHIC DETAILS, TEF TYPE, REPAIR TYPE, AND ASSOCIATED ANOMALIES

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Gestational Age at Birth (wk)</th>
<th>Birth Weight (g)</th>
<th>TEF Type*</th>
<th>Repair Type and Age</th>
<th>Associated Anomalies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>41</td>
<td>2,485</td>
<td>C</td>
<td>AE + FC at 1 d, dilation at 1 mo, FC again at 6 mo</td>
<td>Mitochondrial respiratory chain deficiency</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>32</td>
<td>1,183</td>
<td>C</td>
<td>Gastrostomy + FC at 1 d, AE at 2 mo, FC again at 20 mo</td>
<td>VSD, SVT, PS, inguinal hernia</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>40</td>
<td>2,100</td>
<td>C</td>
<td>AE + FC at 2 d</td>
<td>Dysmorphism, ptosis, facial paralysis, ophisthotonos</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>40</td>
<td>2,900</td>
<td>D</td>
<td>AE + FC at 1 d</td>
<td>Bicuspid AV, PS, inguinal hernia, hypogonadotrophic hypogonadism</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>34</td>
<td>1,950</td>
<td>A</td>
<td>Gastrostomy at 1 d, AE at 3 mo</td>
<td>ASD, polycystic kidney</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>34</td>
<td>1,664</td>
<td>C</td>
<td>AE + FC at 1 d</td>
<td>VSD</td>
</tr>
</tbody>
</table>

*Defined in Figure.

TEF — tracheoesophageal fistula; AE — anastomosis of esophagus; FC — fistula closure; VSD — ventriculoseptal defect; SVT — supraventricular tachycardia; PS — pulmonary valve stenosis; AV — aortic valve; ASD — atrioseptal defect.

RESULTS

Six infants, 5 male and 1 female, were included in the study (Table 1). Three were born at term, and 3 were preterm. The birth weights were between 1,183 and 2,900 g (average, 2,046 g). Four infants received diagnoses during the first postnatal day of a type C TEF, 1 of a type A TEF, and 1 of a type D TEF. All 6 children had other associated congenital anomalies (Table 1).

The surgical procedures for TEF closure were performed by different surgeons in 4 medical centers. Three were performed in our institution. All TEF repairs were via an open thoracotomy. A retropleural approach was used in 4 cases, and the approach for the other 2 was not known to us. Four infants — 3 with type C TEF and 1 with type D TEF — underwent primary fistula closure and an esophageal anastomosis 24 to 48 hours after birth (Table 1). One of these infants also underwent esophageal dilation for an esophageal stricture at the age of 1 month. Two of these infants had a recurrent TEF that was re-closed via open thoracotomy at ages 6 and 20 months. Two infants — 1 with type C TEF and 1 with type A TEF — underwent staged procedures consisting of gastrostomy 24 hours after birth and an esophageal anastomosis at 2 and 3 months of age, respectively.

Five children were referred to us for stridor, and 1 for aphonya. Their ages at the diagnosis of vocal fold paralysis ranged between 14 days and 14 months (Table 2). Five of the children were less than 3 months of age when referred to us. The diagnosis of vocal fold paralysis was made by flexible bronchoscopy in 4 cases, by flexible laryngoscopy in 1 case, and by direct laryngoscopy in 1 case. One infant underwent 1 flexible laryngoscopy and 2 flexible bronchoscopies before the final diagnosis of vocal fold paralysis was made via direct laryngoscopy. Five infants were found to have bilateral vocal fold paralysis, and 1 infant (who received a diagnosis at the age of 14 months) had a unilateral paralysis. Five received the diagnosis of vocal fold paralysis after...
the esophageal anastomosis, and 1 infant with a type A TEF had received the diagnosis of bilateral vocal fold paralysis before the esophageal anastomosis.

The infants had concomitant airway anomalies: tracheomalacia in 5 cases, laryngomalacia in 1 case, and posterior glottic stenosis in 1 case. The 5 children with bilateral vocal fold paralysis underwent tracheostomy for respiratory distress. The children were followed between 0 to 24 months (Table 2). Three of the children had been transferred to our hospital for emergent care and later returned to their primary hospital, so we do not have long-term follow-up data on them. One of the infants recovered the movement of one vocal fold at the age of 9 months. The 1 infant with unilateral vocal fold paralysis presented at 14 months of age because of aphonia but not stridor and did not require any airway intervention procedure.

Three of the infants underwent brain imaging, and no brain stem anomaly was found.

DISCUSSION

Dyspnea and stridor after TEF repair is not a rare event. Although there could be a number of reasons for the dyspnea in infants with TEF (eg, recurrent pneumonia, gastroesophageal reflux disease, aspiration, laryngomalacia, tracheomalacia, and bronchomalacia), the association of stridor with vocal fold paralysis is a known complication. Vocal fold paralysis after TEF repair is difficult to estimate. Robertson and Birk reported vocal fold paralysis after TEF repair in a series of 36 infants with vocal fold paralysis. Hartnick et al reported 2 cases of vocal fold paralysis after TEF repair in a series of 36 infants with vocal fold paralysis. Hartnick et al²¹ reported 3 cases of bilateral vocal fold paralysis after TEF repair in a series of 52 neonates with bilateral vocal fold paralysis, and Daya et al¹⁹ reported 3 cases in a series of 102 children with vocal fold paralysis.

It is difficult to determine whether the vocal fold paralysis in our case series resulted as a complication of the surgical interventions for TEF repair, because there had been no preoperative evaluation of their vocal fold movement and stridor was not reported in their records. However, in all cases some form of surgery was done within the first 48 hours of life; therefore, stridor and dysphonia could have been missed. In our series, vocal fold paralysis in 5 cases was diagnosed after the patients had undergone a surgical procedure for final repair of the TEF (end-to-end anastomosis) — a procedure in which dissection in the mediastinum is performed and in which the vagus nerve and RLNs are at risk of injury.

One case of bilateral vocal fold paralysis was diagnosed after gastrostomy in which there had been no intervention in the mediastinum, and so the vocal fold paralysis in this case cannot be considered a surgical complication of the TEF repair. We suspect that a congenital peripheral anomaly of the vagus nerve might have been the cause for vocal fold paralysis in this case. Qi et al²⁷ have shown fewer branches of the RLNs, deviation of the left vagus nerve behind the TEF to join the right vagus nerve to a common trunk, fewer branches from the fused vagus nerve to the esophagus, and aberrant RLNs in a rat model of Adriamycin-induced EA and TEF.

The bilaterality of vocal fold paralysis in our cases is also difficult to explain by surgical trauma alone, although we suspect that a bilateral injury can occur when surgery is performed in the vicinity of aberrant vagus nerves or RLNs. Another explanation for the bilaterality of vocal fold paralysis in infants with TEF might be a congenital central nervous system anomaly, since this is the most common cause for congenital bilateral vocal fold paralysis. One infant with bilateral vocal fold paralysis in our series was also born with unilateral facial nerve paralysis and unilateral ptosis, supporting the possibility of a central nervous system cause for his bilateral vocal
fold paralysis.

Three modalities are available for RLN monitoring and vocal fold function monitoring during surgery in an attempt to prevent paralysis. These include intraoperative direct flexible laryngoscopy (usually via a laryngeal mask), electromyographic recordings of evoked action potentials of the internal laryngeal muscles (vocalis muscle or posterior cricoarytenoid muscle) using needle electrodes, or registration of vocal fold movement using an electromyogram surface electrode over the endotracheal tube. However, RLN monitoring is still not routinely used during thoracic surgery. Odegard et al have shown that RLN monitoring (utilizing compound electromyographic recordings from the RLNs at the level of the cricothyroid ligament) during video-assisted thoracoscopic surgery for patent ductus arteriosus was effective in identifying the RLN. They also found that the RLN had an unexpected course in 13% of their patients and that RLN localization had altered their resection route and subsequent clip positioning in 62% of cases. Although intraoperative RLN monitoring cannot always prevent nerve injury, we believe that RLN monitoring may be of benefit during TEF repair, especially considering the possibility of an aberrant course of the vagus nerve in these cases. The use of the thoracoscopic repair technique may provide some advantage in vagus nerve and RLN identification by improving the visualization in the thoracic cage.

In our series, the infants underwent TEF and EA repair in 2 tertiary pediatric care centers, in 1 secondary care center, and in 1 primary care center. An open thoracotomy is still the main approach for TEF and EA repair in all of these centers. Four of the infants underwent primary fistula closure and esophageal anastomosis. Two of the infants, one with a low birth weight and one with an EA with a long gap between the esophageal segments, underwent staged procedures with primary gastrostomy and later esophageal anastomosis. Two of the infants had recurrent fistulas. The incidences of a recurrent fistula and an esophageal stricture in the literature are 2% to 12% and 4% to 32%, respectively. We cannot estimate the incidence of vocal fold paralysis or of fistula recurrence in our series, since we have data only on infants referred to us for vocal fold paralysis.

As described in the literature, TEF and EA are often associated with other congenital anomalies. In our series, all of the children had at least 1 other congenital anomaly (cardiac and/or renal). One of the children was discovered to have a mitochondrial respiratory chain deficiency that can also be associated with TEF, EA, and vocal fold paralysis.

CONCLUSIONS

Vocal fold paresis in infants is difficult to diagnose. The risk for RLN injury in association with TEF and EA repair should be borne in mind in performing surgery on these children. We strongly recommend that all newborns with TEF be examined by an otolaryngologist to confirm the mobility of the vocal folds and to rule out other associated airway malformations before TEF repair, and in all cases after repair if respiratory difficulties develop. Care should be taken during the repair procedures to identify and preserve the RLNs. The use of nerve monitoring should be considered.

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REFERENCES

6. van den Brink GR. Hedgehog signaling in development and homeostasis of the gastrointestinal tract. Physiol Rev 2007;87:1343-75.
11. Lobe TE, Rothenberg S, Waldschmidt J, Stroedter L. Thoracoscopic repair of esophageal atresia in an infant: a surgi-


