Familial Congenital Bilateral Vocal Fold Paralysis - A Novel Gene Translocation

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INTRODUCTION
Bilateral true vocal fold (TVF) paralysis is a common cause of neonatal stridor and airway obstruction. A number of different etiologies have been described including neurologic, iatrogenic, and idiopathic. Patients with congenital TVF paralysis should have a magnetic resonance imaging scan to rule out a central etiology, as correction of a central lesion could potentially lead to improvement in vocal fold function. In patients without a central etiology, the case of bilateral TVF paralysis often remains unknown. The occurrence of familial propagation of bilateral TVF paralysis implies a genetic origin. The additional association with other congenital anomalies has significant implications for the phenotype of these genetic alterations. However, few genetic abnormalities have been discovered to date. A case series of familial congenital bilateral TVF immobility with genetic analysis is presented.

RESULTS
All three patients presented with respiratory distress at birth. Tracheotomy was required in 2 out of 3 patients. Some return of vocal fold mobility was seen in the 2 patients who required tracheotomy, and to date one of the patients has been successfully decannulated. An improvement in airway symptoms was seen in all three patients.

Blood samples were taken from the mother, the two daughters, and the maternal grandparents for genetic analysis. A karyotype analysis revealed the same balanced translocation between chromosomes 5 and 14, t(5:14) (p15.3, q11.2) in both the mother and her two daughters (Figure 3). No other genetic abnormalities were identified. Neither the maternal grandmother nor the maternal grandfather has the translocation. The translocation appears to be a spontaneous mutation in the mother with an autosomal dominant mode of inheritance and variable penetrance.

DISCUSSION
Congenital bilateral true vocal fold paralysis is second only to laryngomalacia as a cause of neonatal stridor, and it is the leading cause of neonatal respiratory distress. Patients typically have respiratory symptoms with normal voice and swallowing function. Stridor and respiratory distress may present at delivery or in a delayed fashion as a result of vocal fold edema associated with infection or reflux. Respiratory symptoms may necessitate acute airway management, including endotracheal intubation or tracheotomy in severe cases. Many patients have spontaneous improvement in vocal fold function, with rates of recovery related to etiology of TVF immobility1,2.

Neonatal TVF paralysis can be classified as acquired or congenital. Causes of acquired TVF paralysis include traumatic delivery, infection, and cardiothoracic surgery3. Congenital TVF paralysis can be caused by central neurologic disorders or anatomic anomalies that affect the recurrent laryngeal nerve or larynx. Congenital TVF paralysis is frequently associated with other congenital anomalies. However, it may also occur as an isolated abnormality with no identifiable cause. In idiopathic cases such as these, a familial pattern of involvement is sometimes seen. Small series of families with autosomal dominant, autosomal recessive, and X-linked inheritance patterns of TVF paralysis have been described4-6. However, few genetic abnormalities have been identified4,7.

We identified a chromosomal translocation shared by three family members with congenital vocal fold immobility and no other associated abnormalities. The translocation has an apparent autosomal dominant mode of inheritance with variable penetrance, as one of our patients did not have severe enough symptoms to require tracheotomy. To our knowledge, this represents the first description of a chromosome 5 and 14 translocation associated with congenital bilateral vocal fold paralysis.

REFERENCE