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CASE REPORT

Familial bilateral abductor vocal cord paralysis

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Summary Familial bilateral abductor vocal cord paralysis is a rare entity with few prior descriptions in the literature. Modes of inheritance include X-linked, autosomal recessive, and autosomal dominant. A case of this condition in a father and son is presented. Signs and symptoms at presentation, diagnosis, therapeutic considerations, and modes of inheritance are discussed.

1. Introduction

Vocal cord paralysis is the second most common cause of stridor in the neonate, following laryngomalacia. While unilateral paralysis occurs more frequently, bilateral paralysis can present with more severe symptomatology, most notably high-pitched inspiratory stridor and respiratory distress. Infants often require immediate intubation and eventual tracheotomy. Other presenting symptoms may include weak cry, cough, cyanosis, difficulty feeding, and aspiration. The majority of bilateral true vocal paralysis cases can be attributed to structural abnormalities of the central nervous system, such as Arnold-Chiari malformation, meningomyelocele, and meningocele [20]. Familial clustering of bilateral paralysis in the absence of other syndromes or features is rare. This case describes a father and son with isolated bilateral abductor vocal cord paralysis without other associated symptoms or syndrome.

2. Case study

A 5-week-old Caucasian male was referred for pediatric otolaryngology evaluation for persistent stridor since birth. The patient was born weighting 7lbs 11oz at term via Cesarean section given the mother's previous history of Cesarean section. There were no perinatal complications or hypoxic events. The patient had mild biphasic stridor at rest, which was exacerbated by agitation and crying. These symptoms became progressively worse in the first weeks of life. The patient's father described a personal history of bilateral vocal paralysis as an infant. He required tracheotomy until the age 5 years at which time he was successfully decannulated. The patient was noted to have high-pitched inspiratory stridor, tachypnea, suprasternal retractions, and intermittent respiratory dis-

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tress. Flexible laryngoscopy revealed bilateral vocal cord paralysis. The patient was admitted to the hospital and direct laryngoscopy, bronchoscopy, and tracheotomy performed. Intraoperatively, passive mobility of the true vocal cords was noted without evidence of active vocal cord motion. Anatomy of the supraglottis and glottis appeared normal, while minimal tracheomalacia was observed without evidence of endoluminal collapse. MRI of the brain revealed no intracranial abnormality. Gastroenterology consultation was obtained and pH probe was negative for reflux. Karyotype and fluorescent in situ hybridization (FISH) analysis revealed no chromosomal abnormality. The patient has an older female sibling without a history of airway problems.

3. Discussion

Congenital bilateral true vocal cord paralysis can be an acquired or inherited condition.

Acquired etiologies comprise the vast majority of cases and include primarily neurologic defects and trauma. In a series of 34 patients with bilateral paralysis, Rosin et al found 15 (44%) to have a neurologic etiology, primarily Arnold-Chiari malformation type II [16]. Abnormal development of the neural tube as a result of a teratogenic process in the first 4 weeks of gestation can result in this condition, which is characterized by cerebellar hypoplasia and subsequent brainstem herniation through the foramen magnum causing hydrocephalus, brainstem compression, vagal rootlet traction, and resultant vocal cord paralysis [10]. In patients with vocal cord paralysis secondary to hydrocephalus, Bluestone found bilateral vocal cord paralysis to occur two thirds of the cases, with all requiring tracheotomy [1]. Birth trauma accounts for 20% of congenital vocal cord paralysis cases. Forceps or complicated delivery can often result in traction upon the recurrent laryngeal nerve itself as it courses around the subclavian artery on the right and ductus arteriosus on the left, resulting in vocal cord paralysis. Cardiothoracic or esophageal surgeries can also be complicated by injury to the recurrent laryngeal nerves, either by stretch injury or lysis [20].

Bilateral vocal cord paralysis as an inherited disorder is a rare entity. Hollinger described only one familial case in a study that consisted of 149 infants and children [9]. Sex-linked, autosomal dominant, and autosomal recessive inheritance patterns have all been described in the literature [8,14,15,21]. Plott first described familial bilateral abductor vocal cord paralysis in four male siblings in 1964. The condition was associated with mental retardation in all cases and believed to be inherited in a sex-linked pattern. Only one sibling required a tracheotomy, which was removed by age one and a half years. Abnormal development of the nucleus ambiguus, which is responsible for vocal cord function, was believed to be the etiology of the paralysis [14]. While there exists only a single muscle responsible for vocal cord abduction (posterior cricoarytenoid), several exist for adduction, possibly explaining the increased incidence of abductor paralysis when brainstem dysgenesis is present. Watters and Fitch reported two male siblings and one male cousin with vocal cord paralysis and mental retardation in 1973. No females were affected in the family and the route of inheritance was again believed to be sex-linked [4]. In 1976, Gacek reported a father and two sons with vocal cord paralysis, with no evidence of mental retardation. Unlike cases in other studies, the onset of paralysis did not occur at birth, but rather between 6 months and 9 years of age. All subjects required tracheotomy. The presence of upper and lower extremity weakness in this family suggested the association of other motor neuron deficits in addition to those responsible for vocal cord abduction [6].

The autosomal dominant form of congenital bilateral vocal cord paralysis is known as Gerhardt syndrome, which was first described in 1863 [7]. It is an abductor paralysis that is also associated with mental deficiency, blank facial expression, speech and swallowing difficulty, and hypotonia. In 1978, Mace et al. first suggested linkage to the HLA complex on chromosome 6 in a pedigree including four males and one female [12]. This was studied and later confirmed by Brunner et al. in 1982 [2]. In 2001, a genome linkage analysis identified a locus for familial vocal cord paralysis on the q16 arm of chromosome 6 [13]. Grundfast and Milmoe found bilateral paralysis and swallowing difficulty in a father and his son and daughter. Tracheotomies were required for both children, but decannulation was successfully performed before age 14 months. Delay in neurologic maturation was suspected as the etiology [8]. Cunningham et al. reported two brothers and a sister with inspiratory stridor at birth secondary to bilateral vocal cord paralysis. Only one brother required tracheotomy. Based on ventilatory studies and subsequent improvement of the child's condition, the cause was believed to be immaturity of the chemoreceptive pathway between the carotid body, nucleus ambiguus, and posterior cricoarytenoid muscle [4]. In addition to these reports in humans, autosomal dominant mode of inheritance for vocal cord paralysis has been observed in dogs [3].

A variety of other genetic conditions are associated with hereditary vocal cord paralysis. Vocal

cord abnormalities have been described in William's Syndrome, as a result of de novo deletions in the elastin gene. These patients can have hoarseness secondary to bilateral vocal cord dysfunction from disorganized elastic fibers [19]. Other syndromes with potential vocal cord paralysis include Beck-with-Wiedemann syndrome (macroglossia, abdominal wall defects, and macrosomia) and cerebro-oculo-facio-skeletal syndrome [18]. Distal hereditary motor neuronopathy type VII (dHMN-VII) is an autosomal dominant disorder characterized by distal muscular atrophy and vocal cord paralysis and maps to chromosome 2q14 [11]. Charcot-Marie-Tooth disease type 2C is characterized by diaphragm and vocal cord paralysis. This disorder maps to chromosome 12q23-24, while the recessive form is caused by mutations in the ganglioside-induced differentiation-associated protein-1 gene (GDAP1) [17]. Vocal cord paralysis can also be associated with mutations in the MPD2 gene leading to distal myopathy of the hands and feet [5]. For these conditions, vocal cord paralysis is the initial sign at presentation, with additional neuromuscular symptoms developing much later. A higher level of suspicion and close follow-up of these patients is required for early referral to a neurologist and geneticist.

4. Conclusion

The case presented here is that of a father and son who have a history of bilateral abductor vocal cord paralysis. Probable modes of inheritance include autosomal dominant with variable penetrance or autosomal recessive. The father and son do not suffer from any other genetic syndrome, nor do they have a history of any other neurologic abnormality. The cause of paralysis can possibly be a delay in neural maturation in the area of the nucleus ambiguus, as Plott had previously hypothesized [14]. The father had spontaneous recovery of vocal cord function by the age 5 years, and underwent successful decannulation at that time. Given this history, the patient is being followed by interval flexible laryngoscopy and rigid tracheobronchoscopy to assess for potential spontaneous recovery of vocal cord function (Fig. 1).

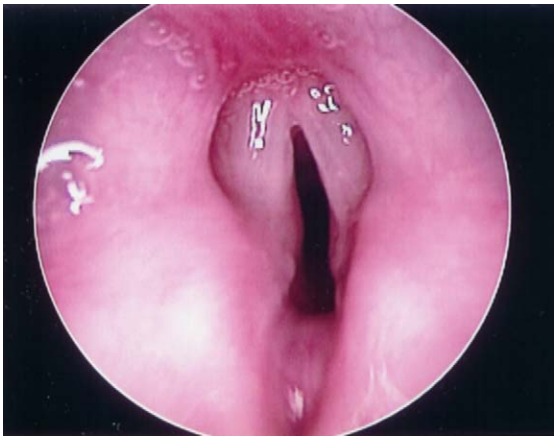

Fig. 1 Bilateral true vocal cord paralysis with vocal cords in a paramedian position. Taken at age 1 month 10 days.

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