Cricothyroid Onabotulinum Toxin A Injection to Avert Tracheostomy in Bilateral Vocal Fold Paralysis

Sam J. Daniel, MD, MSc, FRCSC; Isabel Cardona, MD

Vocal fold paralysis (VFP) is the second most common congenital anomaly of the larynx. Bilateral VFP can occur secondary to neurologic conditions such as Arnold-Chiari malformation, cerebral palsy, spina bifida, leukodystrophy, and myasthenia gravis. It can be idiopathic in up to 38% of cases. Symptoms include a weak cry, biphasic or inspiratory stridor, labored breathing, feeding difficulties, and aspiration. With bilateral VFP secondary to abductor paralysis, as in the current case series, the vocal folds are located in a midline position, and thus, airway patency is compromised. It has been reported that up to 59% of children with VFP end up with a tracheostomy. We describe the successful use of onabotulinum toxin A injection (OTA) (Botox; Allergan Inc) in the cricothyroid muscles in a cases series of 6 pediatric patients with bilateral VFP that led to increased airway patency in all 6 children.

Case 1
A girl who had been born prematurely and undergone prolonged intubation was diagnosed as having bilateral VFP and moderate tracheomalacia. At age 7 months, she presented with respiratory distress and stridor. Flexible laryngoscopy revealed a glottic gap of 1 mm. As the patient’s condition was deteriorating, necessitating high-flow oxygen and pressure support, a tracheostomy was to be scheduled. However, at the insistence of the family, a less invasive procedure was performed. We injected 5 U of OTA into both cricothyroid muscles. The symptoms of stridor and respiratory distress started improving within 72 hours, and the stridor resolved within a month. Four months later, she was asymptomatic and made progress with her oral feeds. At last follow-up at age 4 years, the patient was free of any hospital admissions or respiratory complications.

Case 2
A boy born of full-term pregnancy was diagnosed as having bilateral VFP suspected to be secondary to a traumatic delivery. At age 3 weeks, he presented with labored breathing, and flexible endoscopy revealed 1-mm airway patency with bilateral VFP. We injected the cricothyroid muscles with 4 U of OTA each. His airway symptoms resolved fully until 15 months later, when he required reinjection for stridor associated with a respiratory infection. At 2-year follow-up from the second injection, he remained asymptomatic.

Case 3
A girl born of full-term pregnancy developed respiratory distress and stridor immediately after delivery requiring emergency intubation. She was extubated 12 hours later but continued to have stridor and respiratory distress at rest. She underwent a supraglottoplasty to palliate the laryngomalacia at age 16 days, and flexible laryngoscopy revealed bilateral VFP. Because she continued to have respiratory distress and oxy-
gen desaturation, a trial of OTA injection into her cricothyroid muscles was offered as an alternative to tracheostomy. The patient was extubated 2 days after the injection. At 18 months’ follow-up, the patient had a patent airway and mild, occasional stridor only when severely agitated.

Case 4
A 1-month-old girl was referred for persistent stridor, respiratory distress, and growth delay after repair of a tracheoesophageal fistula (type C) on the day she was born. Flexible laryngoscopy revealed bilateral VFP. Two months later, after unsuccessful attempts to extubate, we averted tracheostomy by injecting OTA into the cricothyroid muscles. The patient remained intubated for 24 hours after the procedure. At day 3 postinjection, she was breathing room air with normal oxygen saturation and no respiratory symptoms. At 10-month follow-up, she remained symptom free.

Discussion
Bilateral VFP as diagnosed on awake flexible laryngoscopy can be caused by either bilateral vocal fold fixation from scarring of the cricoarytenoid joint complex or neurogenic VFP. The entities can be distinguished via suspension laryngoscopy and palpation of the arytenoid and vocal fold. While many patients with bilateral VFP recover spontaneously, in the acute phase a number of them can present with life-threatening symptoms usually requiring an intubation followed by a tracheostomy or long-term mechanical ventilation. A tracheostomy places patients at increased risk of recurrent infections, speech and language retardation, and delay in starting oral feedings. The tracheostomy tube is usually left in place for a minimum of 1 year while potential vocal fold recovery is monitored.

Paralyzing the cricothyroid muscle with OTA injections led to an increase in the glottic airway opening in all of our patients, as documented on flexible endoscopy performed a few days following the procedure. The rapid improvement in all of these cases within days from the OTA injection points to a direct effect from the cricothyroid muscle paralysis rather than a coincidental recovery of function. In fact, all of these patients except patient 5 did not recover from their VFP but had averted a tracheostomy thanks to the increase in the glottic gap that occurred after cricothyroid muscle OTA injection (post-intervention follow-up range, 3 months to 5 years). Only 1 patient required reinjection 1 year later when he presented with stridor after viral infection.

Onabotulinum toxin A acts at the neuromuscular junction by inhibiting acetylcholine release, hence paralyzing the muscle. It was first used in the larynx for the treatment of spasmodic dysphonia, laryngeal dystonia or neurologic laryngeal dysfunction, in 1986. Further clinical studies revealed the relief of airway compromise when OTA was injected into the abductors of the larynx, weakening the force of laryngeal closure. This would rebalance the laryngeal muscles and adjust the arytenoid muscle by using the unopposed pull of the abductors.

Clinical pediatric studies have been scarce. In 2007, OTA injections were used bilaterally under general anesthesia into the thyroarytenoid muscle in 10 children with bilateral VFP and airway distress. Four of the 10 children had complete resolution of respiratory difficulty, and 3 continued with repeated injections 2 to 3 times annually. Only 2 children also had injections into their cricothyroid muscles, but the authors suggest no evident significant clinical results. The 6 patients for whom the treatment was unsuccessful had severe neurologic comorbidities. Laryngeal electromyography was not performed on these patients because it is difficult to document the cause of these disorders with laryngeal electromyography.

In 2008, El-Hakim reported the use of botulinum injection in the cricothyroid, sternothyroid, and sternohyoid muscles as a treatment option for bilateral VFP in a series of 7 patients. Six of these patients recovered fully from their laryngeal paralysis, and 1 partially. The author hypothesized that reinervation might have been responsible for the return of the laryngeal function.

Our technique is slightly different in that it is the first case series to our knowledge that uses OTA injection exclusively into the cricothyroid muscles, which were easily exposed through an external neck approach. Both bellies of the cricothyroid muscles were injected under direct vision. We used higher doses of OTA than reported in the literature (4-10 U per muscle). Endoscopy performed a few days after injection revealed an increase in the glottic gap in all patients. Our technique compares favorably with other procedures: it is minimally invasive, and there is no alteration in the laryngeal anatomy. Also, interestingly, none of our patients had worsening of their aspiration after the procedure despite the increase in the glottic gap.

Our group was the first to describe injecting OTA into the salivary glands to avoid a tracheostomy for severe recurrent
aspiration in a newborn with normal vocal folds and CHARGE association (coloboma and cranial nerve abnormalities; heart malformation; choanal atresia; retardation of growth after birth and retardation of development; genital hypoplasia [underdevelopment] in males and urinary tract malformations; and ear malformations, deafness, or both). Interestingly, we combined both techniques for patient 6 described herein, who had bilateral VFP and difficulty handling secretions.

In many patients with bilateral VFP, both folds are in a paramedian position secondary to the abductor paralysis.10 There are 2 main causes for bilateral VFP: neurogenic or scarring of the cricoarytenoid joint complex.4 None of our cases had vocal fold fixation, as confirmed by suspension laryngoscopy and palpation in all cases. We postulate that in several of our cases, the recurrent laryngeal nerve was compromised, with an effect on all laryngeal muscles except for the cricothyroid. The cricothyroid muscle is innervated by the external branch of the recurrent laryngeal nerve was compromised, with an effect on all laryngeal muscles except for the cricothyroid. The cricothyroid muscle is innervated by the external branch of the superior laryngeal nerve and is the only tensor muscle of the larynx, aiding with phonation by tensing of the vocal folds. As detailed by Blitzer et al,11 the Wagner and Grossman hypothesis proposes that in patients with recurrent laryngeal nerve injury, cricothyroid muscle activity will result in a median vocal fold position. This has been confirmed in piglet12 and mongrel dog13 models.

We hypothesize that at least initially, it is the denervation of the cricothyroid muscles with OTA that leads to an increase in the airway diameter, as we have demonstrated a widening glottic gap within few days after injection in all cases. We believe that the reason for airway improvement is directly related to an increase in glottic space between the folds resulting from the paralysis of the cricothyroid. Long term, as the child matures, bilateral VFP may resolve spontaneously, as seen in our patient 5. All other patients described herein will continue to be monitored twice a year for relapse. All 5 patients continue to have bilateral abductor paresis on flexible endoscopy without any airway compromise. Electromyography could be performed in the future should the patients become symptomatic again or require general anesthesia.

Conclusions
Onabotulinum toxin A injection in the cricothyroid muscles provides a noninvasive, safe, rapid, and successful treatment option for patients with bilateral VFP. This technique has been shown to widen the glottic gap and provide an adequate airway. A trial of OTA may therefore save the patient from multiple intubations and avert the need for a tracheostomy.

REFERENCES