Botulinum toxin A: A novel adjunct treatment for debilitating habit cough in children

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Abstract
Vocal fold injection with botulinum toxin type A (BTX-A) may be used as an adjunct treatment for habit cough in children. We conducted a retrospective review of 3 cases involving children aged 11 to 13 years with habit cough treated with vocal fold injection of BTX-A. Injections of BTX-A to the thyroarytenoid muscles were effective in breaking the cough cycle in all 3 children. Their coughs recurred but were controlled with 4 to 8 sessions of behavioral therapy. Behavioral therapy remains the first-line treatment, but BTX-A may be a useful complement to behavioral therapy in patients who fail standard treatments or in those with severe cough who have limited or delayed access to mental health professionals. This is the first report, to our knowledge, on the use of BTX-A in the treatment of a habit cough.

Introduction
Habit, or psychogenic, cough is a somatoform disorder that occurs in older children and adolescents. It presents as a stereotypic, nonproductive cough for which there is no underlying medical explanation. Often described as “honking” or “seal-like,” it can occur up to several hundred times an hour during waking hours; it is characteristically absent during sleep.¹ The patient history may reveal the recent introduction of an unusually stressful social situation. While the disorder is mild in some children, in others it is severe enough to cause them to miss several months of school.

Habit cough is not believed to be overly common in the general pediatric population. However, it was found to be the third most common cause of chronic cough in children aged 6 to 16 years with normal chest x-rays who were referred to one tertiary pediatric otolaryngology practice.² The principal treatment for habit cough is behavioral therapy, as well as addressing underlying psychiatric issues.³⁻⁵

We recently evaluated the cases of 3 children with habit cough in the pediatric airway and swallowing disorders clinic at Massachusetts Eye and Ear Infirmary (MEEI). Each child had a debilitating cough that had resulted in prolonged school absence. We found no identifiable organic cause. We hypothesized that vocal fold injection with botulinum toxin type A (BTX-A) might break the cough cycle. While waiting for the children’s first appointment for psychological evaluation, we tried this treatment in an attempt to improve their function so that they could return to school sooner. We felt that if the treatment were successful, this would also make psychological evaluation and intervention easier.

Patients and methods
This study was approved by the institutional review board at MEEI. Charts of patients were reviewed from January 2004 through July 2006. Charts of 3 children with habit cough treated with BTX-A were selected. We recorded details concerning how the diagnosis of habit cough was established and the outcomes after BTX-A injection.

The 3 patients in our study had missed between 2 and 6 months of school because of their incessant coughing. Each patient was evaluated individually by a pediatric otolaryngologist, gastroenterologist, and pulmonologist during the initial visit.

A frequent, dry cough causing embarrassment and prolonged school absence was the chief complaint of each patient and his or her family. The cough was present during waking hours and absent during sleep. None of the patients had a history of fever, wheezing, rhinorrhea, postnasal drip, heartburn, choking, gasping for air, facial pain, or fatigue. Each child had been healthy before the onset of the cough. Referring physicians had attempted empiric treatments with antibiotics, H₂-antihistamines...
or proton-pump inhibitors, and asthma inhalers in all 3 patients without success.

The physical exams were highlighted by a frequent, nonproductive cough with a honking or barking quality. No signs of respiratory distress or systemic illness were observed, and there was no stridor or wheezing. Verbal requests to control the cough were met with failure. Results of chest x-rays and pulmonary function tests were normal.

We told the parents that habit cough was the likely diagnosis and that the primary treatment was behavioral therapy. The patients were referred to a clinical child psychologist specializing in somatoform disorders. We also explained to the parents that to completely rule out an organic cause for their child’s cough, direct laryngoscopy, rigid and flexible bronchoscopy, and gastroesophagoduodenoscopy could be performed under general anesthesia. If the endoscopic findings were normal, we could inject BTX-A into the patient’s vocal folds. If this treatment proved successful, the cough could be expected to resolve for as long as 2 to 3 months, allowing the patients to return to daily activities more quickly than with behavioral therapy alone. We informed the parents that this was an unproven, off-label use of BTX-A and that risks of dysphonia, aspiration, and tracheotomy were possible.

No abnormalities were seen on endoscopy in any of the 3 patients. We sent pathologic specimens of duodenal, gastric, and esophageal biopsies for examination, and they all proved to be normal. Five units of BTX-A (2.5 U/0.1 ml normal saline) were injected into each of two locations on each thyroarytenoid muscle with a 25-gauge laryngeal injection needle at the time of direct laryngoscopy.

Results
All 3 patients had cessation of their cough after the injections, and all 3 reported decreased irritation in their throats at post-treatment visits.

Patient 1. This 12-year-old boy had presented with a 3-month history of incessant cough; he had missed 2 months of school. After he received a laryngeal BTX-A injection, his cough resolved immediately. The boy was of Korean ancestry and had Caucasian adoptive parents. His parents were asked specific questions about his adoption, which had taken place just prior to the onset of his cough. He did not keep his follow-up appointments at MEEI until after his cough returned 2.5 months postinjection. Behavioral therapy (4 sessions) was instituted, and an additional referral was made to a psychologist who specializes in treating children with adoption issues. He remains asymptomatic 10 months post-treatment.

Patient 2. A 10-year-old girl presented with 3 months of school absence due to a chronic cough. The cough would disappear when the patient was in the supine position. She was brought into the clinic on a stretcher. After the application of nebulized lidocaine, she was able to sit upright without coughing for 1 hour. Her cough resolved on the second day after she received the BTX-A injection. Behavioral therapy was initiated, during which it was revealed that her cough had started after her father moved to a different state. This issue was addressed by the psychologist. Now, 9 months after injection, there have been 2 evenings during which her cough has recurred, the first of which was 6 months after treatment. However, each time it resolved after the mother firmly told her that the cough had no medical cause.

Patient 3. This 13-year-old girl was originally referred for the evaluation of a “post-pertussis tic.” She had been treated for a chronic dry cough that began after she had received two separate courses of azithromycin for a high pertussis titer. Her initial cough had resolved, but a second cough began after a live singing performance. It lasted for more than 6 months, did not respond to a host of medical treatment regimens, and was significantly affecting her quality of life. Her cough resolved on the second post-treatment day but returned after 10 days. On further questioning, it was learned that the patient’s family had recently assumed care of two male foster children just before the return of the cough. Behavioral therapy was instituted, and the patient was able to keep her cough under control.

Discussion
Habit cough caused significant social disruption for our 3 patients and their families. All 3 patients stopped coughing after BTX-A injections and quickly returned to school. All of the patients reported being better able to suppress their urges to cough after injection. However, each patient had recurrences of the cough that resolved only after behavioral intervention.

Factors at the receptor, afferent, cortical, and efferent level contribute to the seemingly simple complaint of a cough. Psychological factors and habituation in conjunction with physical irritants have been proposed as other mechanisms. The patients in our cases series reported that irritation had triggered their coughs; the irritation disappeared with the administration of topical lidocaine in one of our patients. We hypothesized that laryngeal BTX-A injections could break the cough cycle in children with habit cough.

Pertussis is a common cause of chronic cough in adolescents and young adults. The initial catarrhal phase resembles an upper respiratory infection lasting 1 to 2 weeks. This is followed by paroxysmal coughing spells that last another 1 to 2 weeks. The convalescent stage is characterized by a residual cough that lasts weeks to months. Harnden et al reported that persistent cough was present 100 days after the serologic diagnosis of pertussis in 40 of 62 children. Serology studies are most useful late in the course of disease, and evaluation of pertussis in children with a
long-standing course should be considered. We chose not to test the children in this series for pertussis for several reasons: First, each child in this series presented with a barking or “seal-like” cough that was absent during sleep, which is stereotypic of habit cough. Also, each child had experienced the introduction or magnification of a significant psychosocial stressor during the onset of the cough. Habit, or psychogenic, cough is a clinical diagnosis, and it is very common for habit cough to appear after a respiratory illness. Finally, there is also little to no effect on the course of pertussis if treatment is delayed 1 week after onset of symptoms.

While the outcomes of these cases were satisfactory, sound scientific conclusions about the effectiveness of BTX-A in treating habit cough cannot be made. One patient had complete resolution of his cough immediately after injection with BTX-A—well before its pharmacologic activity is known to take effect. Kravitz et al reported that resolution of habit cough occurred after the simple suggestion that the patient undergo bronchoscopy. The effectiveness of treating habit cough with noninvasive techniques is discussed in 9 separate reports. In these reports, 95% of patients (111/117) with habit cough were successfully treated with reassurance in conjunction with various forms of hypnotic, behavioral, psychiatric, or speech therapy. Some of these patients were reported to experience a complete cure after one intervention.

Given the success of nonpharmacologic treatments, first-line intervention should be behavioral therapy performed by professionals familiar with behavioral medicine interventions. Laryngeal BTX-A injections could be considered for recalcitrant cases of habit cough in which a mental health professional feels it might be advantageous to lessen the symptoms as a component of a behavioral intervention.

Laryngeal BTX-A injections may play a role (1) in patients with habit cough in whom standard treatments fail, (2) as an adjunct to behavioral therapy, or (3) in patients with severe cough who have delayed or limited access to mental health professionals. This is the first report, to our knowledge, discussing the use of BTX-A in the treatment of a habit cough.

References