Injection Augmentation for Chronic Cough

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Summary: Objectives/Hypothesis. Chronic cough (CC) is a pervasive and expensive health problem in the United States. Almost as diverse as its etiologies are the available therapeutic options. When vocal fold paresis and CC coincide, injection augmentation may provide an alternative to standard medical and behavioral treatments for CC. Our objective was to assess the effect of injection augmentation in a selected group of patients with CC who had failed multiple medical and behavioral treatments.

Study Design. The study design is a retrospective case review.

Methods. Our study group included six subjects (1 male and 5 females; aged 24–84 y) who presented for laryngologic evaluation with a chief complaint of CC unresponsive to conventional medical and behavioral management. The cough severity index (CSI), reflux symptom index (RSI), dyspnea severity index (DSI), and voice handicap index-10 (VHI-10), as well as subjective evaluation were assessed before and after the injection augmentation of the vocal folds was undertaken.

Results. Five of six patients reported subjective improvement in cough. CSI scores improved in all six (average change 7.3, range 2–13). RSI and DSI scores also improved significantly after injection, whereas VHI-10 scores did not significantly change. One patient reported transient hoarseness after injection that completely resolved. One patient received injection augmentation three times, as the material resorbed and symptoms returned.

Conclusions. Injection augmentation effected relief from CC in a select group of patients with CC refractory to previous medical and/or behavioral treatments. This intervention is a novel option for such patients and offers an alternative approach to medical treatment.

Key Words: Chronic cough–Vocal fold paresis–Laryngeal neuropathy–Vocal fold injection–Neurogenic cough.

INTRODUCTION

Chronic cough (CC) is a pathologic state consisting of persistent, unproductive, and irritating upper airway-related cough lasting at least 8 weeks.[1] CC is estimated to occur in 9–30% of the population and is associated with significant comorbidities including anxiety, depression, sleep disturbance, and decreased quality of life.[2–4] Available treatment regimens reflect the myriad causes of CC: sinonasal-directed therapy, antireflux medications and behavioral changes,[5] asthma medication regimens,[1] voice therapy,[6,7] and botulinum toxin A.[8] Recently, clinical connections have been drawn between sensory neuropathy and chronic refractory cough after upper respiratory infection (URI), and medical therapy for neuropathy has been applied to some effect.[9–12] The very diversity of these remedies underscores their lack of universal success and the complexity of the clinical problem.

Of the patients with CC who presented to our center, a subset displayed some degree of laryngeal asymmetry on examination, suggestive of laryngeal nerve paresis. Although these patients rarely had vocal complaints typical of glottic insufficiency, such as weak voice or breathiness, such findings drove us to consider whether a motor paresis may be significant in the pathophysiology of CC. Current concepts of neurogenic cough assume the presence of sensory dysfunction. This assumption is validated when the presentation or modification of chemical, thermal, or proprioceptive sensory stimuli prevents or exacerbates cough.[13–16] Although neurogenic cough is commonly thought of as a solely sensory neuropathy, sensory and motor neuropathy are unlikely to be separate in reality. Considering the close association of sensory and motor fibers of the vagus nerve, an inflammatory or infectious process likely affects both afferent and efferent nerves. The notion of distinct afferent and efferent neuropathy of the larynx may be as artificial as the historically obsolete distinction between adductor and abductor paralysis.

We then hypothesized that injection augmentation, an effective treatment for glottic insufficiency from motor paresis, might be effective in the relief of cough. The purpose of this article was to report treatment results in a small cohort of carefully selected patients with CC unresponsive to conventional treatment and pharmacologic measures directed at CC.

METHODS

This study was approved by the Institutional Review Board of Weill Cornell Medical College. The study group consisted of six patients with CC who had failed pharmacologic and behavioral treatments and who had been diagnosed with vocal fold paresis on laryngeal videostroboscopic examination by an otolaryngologist. Paresis is a qualitative diagnosis for which no established criteria exist. At our center, diagnosis of paresis is considered in the presence of specific findings. In order of importance from greatest to least important, these are atrophy, as demonstrated by vocal fold thinning and/or dilatation of the ventricle; unilateral ventricular fold hyperfunction; presence of a contact lesion; impaired adduction; phase difference/asymmetry of the mucosal wave; and glottic axis deviation.[17] Patients underwent injection augmentation via peroral approach if performed in the operating room and cricothyroid approach

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if performed in the office; the latter technique has been described elsewhere.[18]

Age, gender, comorbidities, and smoking histories were extracted from the medical record. The history and duration of the cough and each patient's studies and treatments before injection were recorded. We also noted the laterality of the vocal fold paresis perceived on clinical evaluation. Pretreatment and posttreatment voice handicap index (VHI-10),[19] reflux symptom index (RSI),[20] dyspnea severity index (DSI), and cough severity index (CSI)[21] data were collected. Posttreatment data were collected at the patients' first follow-up visit at 1 month after procedure. The number and type of procedures undertaken were documented as were their results, adverse effects, and duration of follow-up.

RESULTS

Five of six patients were females with ages ranging from 24–84 years (mean 55.7). None were active smokers, although two quit more than 20 years before presentation, well before symptom onset. Four reported a respiratory infection associated with the onset of their symptoms. Comorbidities included depression in five patients and a history of pulmonary complaints (pneumonia, bronchiectasis, asthma, and bronchitis) in three. All had seen at least two specialists for the complaint of cough. Notably, one had consulted four pulmonologists, a gastroenterologist, an allergist, a rheumatologist, two otolaryngologists, a speech pathologist, and a hypnotist. Table 1 summarizes the inventory of patients' treatments before injection. No lasting improvement was achieved with any these regimens.

Each patient received an initial injection of methylcellulose (Radiesse Voice Gel; Merz Aesthetics, San Mateo, CA) as a trial treatment according to the principles outlined by Carroll and Rosen.[22] Four injections were performed in the office and two in the operating room, these last by patient request. Preinjection and postinjection patient-reported VHI, RSI, DSI, and CSI scores are presented in Figures 1–4. In addition to index data, five of six patients reported a satisfactory reduction in cough after the injection. The only adverse effects were dissatisfaction with the degree of relief (patient 3) and transient hoarseness (patient 1). Three patients underwent subsequent calcium hydroxylapatite (CaHA; Radiesse Voice; Merz Aesthetics, San Mateo, CA) injections based on the success of the initial injection, one on three occasions (8/30/12, 9/27/12, and 5/30/13). In each case, relief was replicated, and the duration of relief was consistent with the expected duration of the injectable material.

Case study

Patient 1 was a 53-year-old woman with a history of hypothyroidism, metabolic syndrome, and migraines. She presented with 2.5 years of chronic unproductive cough after an upper respiratory infection. She denied dysphagia, but noted intermittent hoarseness and dyspnea.

She did not identify any specific cough triggers. She had seen several specialists and was treated for upper airway cough syndrome, pulmonary pathology, allergies, and gastroesophageal reflux disease (GERD). She tried several proton-pump inhibitors, steroid nasal sprays, oral steroids, amitriptyline, and gabapentin. Although she intermittently attained transient relief with new medications, her symptoms always returned, usually in a matter of days. She ascribed a 65-pound weight gain to her course of amitriptyline. She completed a remarkable 6 months of speech therapy, which reduced her nighttime coughing but did not appreciably improve her daytime coughing. She had never smoked or used angiotensin-converting enzyme (ACE) inhibitors, denied alcohol use, and her surgical history was noncontributory. The head and neck examination was unremarkable, with the exception of mucosal wave phase asymmetry and mildly impaired left vocal fold adduction on stroboscopy. Glottic closure was not obviously impaired (Figure 5A and B). Based on the laryngoscopic findings, the patient underwent bilateral methylcellulose injections. At her follow-up visit, she reported a dramatic improvement in her cough and stated that speaking and breathing seemed easier. She continued her behavioral therapy but returned in 3 months, complaining that her cough was beginning to return. She underwent bilateral repeat injections with calcium hydroxyapatite (CaHA), which gave her partial relief. Residual symptoms were successfully

TABLE 1.
Therapeutic Interventions Before Injection Trial

Patient	Gabapentin	Amitriptyline	Tramadol	Lyrica	LPR*	Steroids†	Allergy Medication‡	Pulmonary/ Asthma§	Botox	Behavioral Therapy	Surgery‖
1	x	x			x	x	x	x		x	
2	x				x					x	
3¶	x	x	x	x	x				x	x	
4			x		x	x	x			x	x
5	x	x		x	x		x	x			
6					x		x	x		x	x

* Laryngopharyngeal reflux therapy.
† Oral PPI and H2-blocker.
‡ Oral or topical nasal, desensitization therapy.
§ Oral or inhaled.
‖ Nissen, septoplasty/turbinate reductions.
¶ Patient 3 reported minimal benefit after injection augmentation.