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Use of Peripheral Nerve Stimulation to the Recurrent Laryngeal Nerves to Successfully Treat Refractory Globus Sensation: A Case Report

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Background: Globus sensation is a nonpainful sensation of a lump or foreign object stuck in the throat that is not associated with dysphagia. Persistent globus sensation is distressing for patients and often the result of no clear etiology.

Case Report: We present a case of a 71-year-old woman with persistent globus sensation following cervical spine surgery. Initial evaluations for etiology and treatment included hardware removal, endoscopy, pharmacological treatment, botulinum toxin injections, collagen injection laryngoplasty, speech therapy, anesthetic nerve blocks, and attempts at peripheral nerve stimulation. These interventions were not successful in relieving her sensation. After 60 days of peripheral nerve stimulation to her bilateral recurrent laryngeal nerves, she experienced a dramatic 90% reduction in her symptoms with subsequent improvement in quality of life.

Conclusion: Peripheral neuromodulation is a potential treatment option for refractory globus sensation.

Key words: Case report, globus sensation, neuromodulation, peripheral nerve stimulation, recurrent laryngeal nerves

BACKGROUND

The utility of peripheral nerve stimulation (PNS) as a treatment modality for chronic pain is established. More recently, PNS has been demonstrated as a potential option in some refractory, nonpainful conditions (1,2). With the growing use of this technology, its utility in previously clinically difficult-to-treat conditions may be explored. Globus sensation is a distressing condition defined as a persistent or intermittent nonpainful sensation of a lump or foreign body in the throat. Patients may describe the symptom as tightness, itching, or a tickling sensation between the thyroid cartilage and the sternal notch (1). Globus sensation is not uncommon, with a population survey of 6,300 individuals in the

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United States, United Kingdom, and Canada reporting a prevalence of 8.1% (3). Globus sensation accounted for 3.8% of new patient visits at an otolaryngology clinic (4). Globus sensation may be secondary to a space-occupying lesion, gastroesophageal reflux disease (GERD), abnormalities of the upper esophageal sphincter, eosinophilic esophagitis, heterotopic gastric mucosa in the cervical esophagus, major esophageal motor disorder, or laryngeal neuropathy (1,5). It has also been reported to occur a result of iatrogenic injury following head and neck procedures, including thyroidectomy, esophageal stent placement, neck liposuction, and cervical spine surgeries (6-8). There is an association with anxiety and depression, but no definitive causal link exists (6). Most often there is no clear identifiable etiology, in which case idiopathic or functional globus is diagnosed (9). In this report, we describe a refractory case of globus sensation that did not respond to conventional treatment standards but ultimately responded to PNS.

CASE

A 71-year-old woamn initially presented to an outpatient pain management clinic complaining of an uncomfortable sensation in her throat. She described this chronic sensation as "a lump in my throat as if a BrilloTM pad is stuck in my throat." The sensation was occasionally painful but was more so very distressing. The sensation was worse with swallowing, but she denied any difficulty with swallowing mechanics, coughing, or choking. Her appetite was reduced due to an aversion to the symptoms. She often had difficulty sleeping due to the sensation. Initial presentation of symptoms occurred 2 months following a C3-C7 anterior cervical discectomy and fusion. She had this surgery approximately 5 years prior to her presentation to the pain management clinic. Initially following the surgery, the patient lost her voice for several days. Her voice gradually returned with a hoarse quality. Several weeks afterwards, the globus sensation developed. The patient was reevaluated by the neurosurgeon who performed the surgery. Basic laboratory tests were unremarkable. Cervical magnetic resonance imaging (MRI) displayed concerns for postoperative inflammation attributed to possible allergic reaction to the titanium implant. Revision surgeries and allergy treatments were pursued but did not alter her symptoms. Ultimately, the titanium screws and plates were removed. The patient subsequently pursued a variety of treatment options from several specialists. She was evaluated by an otolaryngologist and an endoscopy revealed vocal cord dysfunction related to asymmetry of the cords. Botulinum toxin was injected into the muscles surrounding the vocal cords followed by laryngoplasty with collagen injection. Her voice quality improved significantly as a result of these treatments without improvement of her globus sensation. Gastroenterology evaluation of swallowing mechanics yielded no further answers and treatments with a proton pump inhibitor and various oral antidepressants were ineffective. The patient was diagnosed with globus sensation following these clinical evaluations. Additional treatment prior to her presenting to the pain clinic included anticonvulsants such as gabapentin with marginal benefit.

Several treatment options were pursued by pain management. A high-resolution 3.0T MRI did not identify any discernible pathology in the neck or larynx but noted some scarring at the former operative site. A treatment approach focused on anatomical and physiological etiologic factors was undertaken. Specifically, the vagus nerve became an initial target point given the proximity to the inflammation on previous imaging and its key role in voice production (10). An initial unilateral vagus nerve block was unsuccessful. The stellate ganglion was also in close proximity to the inflammation seen on imaging. A consideration was made for possible sympathetic hyperactivity manifesting in the current symptomatology (11). A stellate ganglion block also proved to be unsuccessful. Given the lack of success with anesthetic nerve blocks, we shifted our focus to nerve activation of the laryngeal sensory structures or musculature as a possible etiology for the globus sensation. Vagus nerve stimulation is known to result in laryngeal muscle activation and induces voice modifications (12). We then proceeded with bilateral vagus nerve stimulation with placement under ultrasound. This yielded a 10% to 30% reduction in the globus sensation and was removed at the end of therapy at 60 days. We continued to pursue our hypotheses of a nerve conduction-related etiology related to either the sensation or muscular function of the oropharynx or larynx. The patient was referred to speech therapy to help with phonation and laryngeal muscle relaxation, but this proved to be unsuccessful.

Following the removal of the vagus nerve leads, we considered a more targeted approach to the branches of the vagus nerve given the marginal improvement seen in response to stimulation of the main vagus nerve. The superior laryngeal nerves were considered due to their key role in sensation of the mucosa of the larynx, and

damage to these nerves has been known to cause both laryngeal hyposensitivity and hypersensitivity (12,13). The decision was made to pursue a bilateral superior laryngeal nerve peripheral stimulation. The patient completed a 60-day course with the peripheral nerve stimulator implant resulting in no further reduction of symptoms in comparison to the vagus stimulation at the time of implant removal. The decision was made to target the other major vagus branches, the recurrent laryngeal nerves, to assess if further relief might be obtained. The recurrent laryngeal nerves are responsible for innervating the muscles of the larynx with the exception of the cricothyroid muscles (14). Bilateral recurrent laryngeal nerve PNS was performed. The procedure was performed under ultrasound guidance (Fig. 1). The trachea and carotid artery were visualized bilaterally, and the recurrent laryngeal nerves were visualized lateral to the trachea (Fig. 2). The stimulator electrode leads were inserted in short axis to the ultrasound probe with direct visualization of the electrode adjacent to the recurrent laryngeal nerve. This procedure was performed using local anesthetic for incisional analgesia allowing for patient feedback during energy stimulation from the electrode. This allowed the provider to confirm proper placement of the electrode. The patient achieved a 90% reduction in symptoms within several hours after the implant. This alleviation of symptoms was maintained after lead removal 60 days later. She was followed longitudinally and maintained 90% relief 6 months after lead removal. She endorses significant improvement in quality of life, does not have any distressing limitations such as an aversion to swallowing or food, and denies sleep disturbances. She describes the intensity of the sensation as more of an afterthought in her day-to-day functioning. She no longer takes gabapentin and no longer wishes to pursue other treatments given her satisfaction with the results.

DISCUSSION

Evaluation of globus sensation involves exclusion of possible secondary causes. The currently accepted treatment algorithm involves a stepwise approach through these causes including clinical examination, laryngoscopy, proton pump inhibitor trial, endoscopy, manometry, and ambulatory reflux monitoring (1). In the absence of space occupying masses, esophageal motor dysfunction, or other apparent structural lesions, globus management can be redirected to other possible contributors such as stress, laryngeal tension, and concomitant voice problems (15). Speech therapy, relaxation techniques, and behavioral therapy may offer benefit without the risks associated with medications or procedures. Pharmacologic neuromodulators such as amitriptyline and paroxetine have also been successful. A randomized trial for refractory globus sensation showed paroxetine to be most effective, followed by amitriptyline and lansoprazole (16). Alternative therapy such as electroacupuncture has also been demonstrated to significantly improve globus symptoms compared to sham treatment (16,17). Globus symptoms generally have a benign prognosis but over 40% of patients continue to be symptomatic 8 years after diagnosis (18).

Our patient was not responsive to empiric treatment or speech therapy, and imaging yielded no clear pathology. Given the context of cervical surgery, postoperative inflammation/allergy, and vocal cord dysfunction, the possibility of nerve dysfunction of innervated structures associated with the larynx as a likely contributing factor was explored. The surrounding structures of the larynx include the vagus nerve, stellate ganglion, and branches of the vagus nerve, including the superior laryngeal nerves and recurrent laryngeal nerves (6).

Fig. 1. Model demonstration of the short axis ultrasound orientation at the level of the cricoid cartilage. The lead is inserted with visualization in this position.

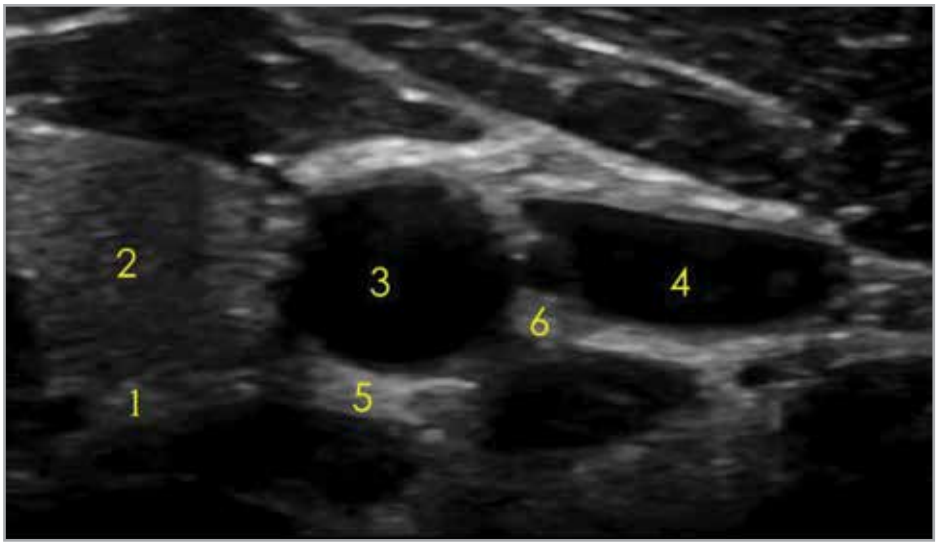

Fig. 2. Ultrasound image at the level of the cricoid cartilage. 1) Recurrent laryngeal nerve, 2) thyroid lobe, 3) carotid artery, 4) internal jugular vein, 5) stellage ganglion, 6) vagus nerve. The trachea is just medial to this image.

The patient had already displayed evidence of nerve dysfunction given the presence of vocal cord dysfunction and dysphonia after cervical spine surgery. This dysfunction was presumed to be the result of impaired nerve conduction to supporting laryngeal muscles. This is further supported by the successful treatment of the voice dysfunction with botulinum toxin injections. In a previous case report on the treatment of globus sensation, botulinum toxin injections to the cricopharyngeus muscle were used to resolve cricopharyngeal hypertonicity. The intervention was successful in resolving the globus sensation in that report, but our patient proved to be refractory to botulinum toxin (19).

Given the exhaustion of standard treatment approaches for globus sensation, the idea of PNS treatment as a method to restore proper nerve function and reset the coordination of the cricopharyngeus muscle and muscles from the same motor unit was pursued. Recurrent laryngeal nerve innervation to the cricopharyngeus muscle, in addition to many of the laryngeal muscles, allowed for a plausible PNS target (14,20). There is some literature demonstrating that muscle spasms of the cricopharyngeus muscle causing muscle tension and poor coordination of the laryngeal muscles function as a possible etiology for globus sensation (21-23). The sensation itself may be the result of impaired bolus transit and esophageal distension that can be maintained at rest (1). One such study by Chung et al (22) using videofluoroscopic evidence concluded that early closure of the cricopharyngeus muscle may contribute to the development of globus sensation.

Although recurrent laryngeal nerve stimulation has been used successfully for vocal cord paralysis, to our knowledge, this treatment approach for globus sensation has never been explored (24). A comprehensive review study on the history and progression of recurrent laryngeal nerve stimulation by Mueller and Pototschnig (24) discusses evidence regarding the use of this stimulation as a "laryngeal pacemaking system." When treated for vocal cord paralysis, 7 of 9 patients demonstrated normalized peak inspiratory and expiratory volumes and improvement in voice quality.

CONCLUSION

We describe a unique and successful treatment for globus sensation. We theorize that the success of this treatment gives stronger credence to impaired nerve conduction from the recurrent laryngeal nerves to the muscles of the larynx, including the cricopharyngeus muscle, as an etiology for globus sensation. We propose that nerve stimulation of the recurrent laryngeal nerves may be considered in patients with refractory globus sensation. Further studies will be needed to elucidate this association and treatment option.

Author Contributions

Nirguna Thalla (NT): This author helped with manuscript writing, literature review, data interpretation.

Eduardo J. Carrera (EC): This author helped with manuscript writing, literature review.

Ryan Russell (RR): This author helped with literature review, manuscript writing.

Mehul Desai (MD): This author helped with concept design, data collection, data interpretation and patient management.

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