Laryngeal Granulomas Associated with Superior Laryngeal Nerve Paresis

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Summary. The association between superior laryngeal nerve (SLN) paresis and laryngeal granuloma formation has not been described earlier. The aim of this study was to present a series of patients with isolated unilateral SLN paresis who developed contralateral vocal process granulomas. The study design was a retrospective chart review including all patients presenting to Indiana University from February 2006 to August 2007 with laryngeal electromyography (LEMG)-documented unilateral SLN paresis and evidence of laryngeal granuloma on videostroboscopy. Patient history, examination, LEMG findings, and response to treatment were recorded. Three cases of unilateral SLN paresis associated with contralateral vocal process granulomas were identified. In all patients, videostroboscopy examination demonstrated shortening of the ipsilateral vocal fold on adduction and asymmetric contact of the vocal processes at the site of granuloma formation. All patients failed to respond to aggressive antireflux therapy. One patient had spontaneous recovery of the SLN paresis, with subsequent resolution of the granuloma. Two patients were successfully treated with surgical laser excision of the granulomas and injection of botulinum toxin into the normal cricothyroid muscle to alter the vocal process contact points. Vocal process granulomas can be associated with unilateral SLN paresis, potentially related to altered contact points between the vocal processes of the arytenoids.

Key Words: Larynx—Vocal fold—Superior laryngeal nerve paresis—Granuloma.

INTRODUCTION

The etiology of vocal process granulomas is often multifactorial. Granulomas typically develop when an ulcerated squamous epithelium is underlaid by granulation tissue in a reactive-reparative process. After an isolated self-limited injury, such as a brief period of endotracheal intubation, a granuloma may resolve without intervention. However, with ongoing injury and inflammation, vocal process granulomas are likely to persist. Potential sources of chronic traumatic injury include throat clearing, coughing, and vocal overuse/misuse. Chronic inflammation of the larynx related to laryngopharyngeal reflux (LPR) has also been shown to play a major role in both the development and persistence of vocal process granulomas.

Koufman previously suggested that incomplete glottic closure related to vocal fold paresis can result in hyperkinetic compensation that leads to granuloma formation. However, as the superior laryngeal nerve (SLN) has been shown to have no influence on vocal fold adduction, an isolated SLN injury would not be expected to influence glottic closure. Tsai et al recently described the videostroboscopic findings in unilateral SLN paresis to include bowing and shortening of the ipsilateral vocal fold and height asymmetry of the vocal processes, among other findings. Such findings have not been previously described in association with vocal process granulomas. The purpose of the present study was to describe the presentation, treatment, and outcomes for a series of patients with unilateral SLN paresis and associated contralateral vocal process granulomas.

METHODS

The study was approved by the Institutional Review Board at Indiana University School of Medicine. All patients who presented to Indiana University Clinic for Voice, Swallowing and Airway Disorders from February 2006 to August 2007 with laryngeal electromyography (LEMG)-documented unilateral SLN paresis and evidence of laryngeal granuloma on videostroboscopy were included. Patient symptoms, age, gender, treatment, examination findings, LEMG findings, and outcomes were recorded for each patient. LEMG studies were performed with needle electrode placement by an otolaryngologist (S.L.H.), and interpreted by a neurologist at Indiana University School of Medicine. The studies were performed using a concentric needle electrode with a Nicolet Viking IV Electromyography Instrument (Nicolet Biomedical, Madison, WI). Routine LEMG testing included the bilateral cricothyroid and thyroarytenoid muscles to assess neural input via the SLN and recurrent laryngeal nerve (RLN), respectively.

RESULTS

A total of 28 LEMG studies were carried out between February 2006 and August 2007. Of these, 15 patients had evidence of neurogenic injury involving at least one SLN. In nine of these cases, the SLN injury was associated with ipsilateral RLN injury, suggesting unilateral vagal nerve injury. Six patients had evidence of isolated unilateral SLN paresis.

Of those cases with isolated unilateral SLN paresis, three demonstrated contralateral vocal process granulomas on videostroboscopy. Videostroboscopy examination for each of these patients demonstrated signs of right SLN, including the appearance of a foreshortened right vocal cord and asymmetric arytenoid contact on phonation. Each patient’s left vocal process had a granuloma where it appeared to contact the contralateral arytenoid on phonation (Figure 1).
**Case 1**
A 36-year-old Caucasian man who was a lead singer in his church choir presented with a 1-month history of sudden onset dysphonia with no known precipitating cause. He reported having abdominal cramping and diarrhea the week before he noted the voice changes, but otherwise, had no history of intubations/truma, and denied any previous history of LPR symptoms (cough, throat clearing, globus, heartburn, and others). He was a well-trained singer, with no change in vocal or singing demands before the onset of his dysphonia. He reported loss of his upper singing range, with voice breaks and vocal fatigue when attempting to sing high pitches. He also reported that he had progressive difficulty with throat discomfort and throat clearing, noted only over the past month. LEMG demonstrated the right cricothyroid muscle to have decreased recruitment with nascent polyphasic potentials, whereas the left cricothyroid muscle and bilateral thyroarytenoid muscles had normal activity. The patient was prescribed antireflux therapy with twice-daily omeprazole and began working with a speech-language pathologist. After 1 month, he noted no symptomatic improvement; hence, he stopped the antireflux medication and speech therapy. Over the next 2 months, his voice gradually returned to normal and his throat clearing/discomfort decreased. Follow-up videostroboscopy examination demonstrated absence of the right SLN paresis findings, with symmetric vocal folds on adduction and complete resolution of the vocal process granuloma.

**Case 2**
A 72-year-old Caucasian male presented with a 10-year history of mild dysphonia, recently noting a sudden worsening of his voice. Before this sudden change, he had no history of intubations, trauma, vocal abuse/overuse, or LPR symptoms (cough, throat clearing, globus, heartburn, and others). He was a well-trained singer, with no change in vocal or singing demands before the onset of his dysphonia. He reported loss of his upper singing range, with voice breaks and vocal fatigue when attempting to sing high pitches. He also reported that he had progressive difficulty with throat discomfort and throat clearing, noted only over the past month. LEMG demonstrated the right cricothyroid muscle to have severely decreased recruitment with spontaneous activity (p waves and fibrillations) and no evidence of ongoing recovery (no polyphasic waveforms), whereas other laryngeal muscles demonstrated normal activity. With a diagnosis of unilateral SLN paresis and presbylaryngis, he underwent direct laryngoscopy with CO2 laser removal of the granuloma, bilateral injection laryngoplasty with collagen, and EMG-guided injection of botulinum toxin into the left cricothyroid muscle. His voice demonstrated little to no improvement; however, the granuloma had not recurred at his last follow-up (4 months postoperatively).

**Case 3**
A 52-year-old Caucasian male presented with a 2-year history of mild dysphonia and LPR symptoms, including chronic throat clearing, globus sensation, and chronic cough. He had no history of intubations, vocal abuse, or laryngeal trauma. When videostroboscopy demonstrated evidence of a vocal process granuloma (Figure 1), he underwent dual pH probe study, which demonstrated moderate LPR. He was treated with twice-daily PPIs for 6 months and underwent speech therapy with no change in the granuloma. LEMG demonstrated the right cricothyroid to have severely decreased recruitment with no evidence of ongoing recovery, whereas the left cricothyroid and bilateral thyroarytenoids demonstrated normal findings. He underwent microdirect laryngoscopy with CO2 laser removal of the granuloma and EMG-guided injection of botulinum toxin into the left cricothyroid muscle. He was also maintained on perioperative antireflux medications. For several months, he had no recurrence of the granuloma. However, at his 9-month follow-up, fiberoptic laryngoscopy demonstrated improvement. Videostroboscopy examination demonstrated the aforementioned findings to be consistent with unilateral superior laryngeal neuropathy, with bilateral vocal fold bowing, incomplete glottic closure on phonation, and mild muscle tension patterns. LEMG demonstrated the right cricothyroid muscle to have severely decreased recruitment with spontaneous activity (p waves and fibrillations) and no evidence of ongoing recovery (no polyphasic waveforms), whereas other laryngeal muscles demonstrated normal activity. With a diagnosis of unilateral SLN paresis and presbylaryngis, he underwent direct laryngoscopy with CO2 laser removal of the granuloma, bilateral injection laryngoplasty with collagen, and EMG-guided injection of botulinum toxin into the left cricothyroid muscle. His voice demonstrated little to no improvement; however, the granuloma had not recurred at his last follow-up (4 months postoperatively).
interarytenoid contact on phonation (similar to his preoperative status), and he had developed a recurrence of the granuloma in the same position.

**DISCUSSION**

The patients in this review were evaluated with videostroboscopy and LEMG. Although SLN paresis was suspected based on videostroboscopy findings, the LEMG was critical to the assessment, because the clinical findings of SLN paresis and paralysis are often subtle.\(^8,9\) Tsai et al described videostroboscopic findings in unilateral SLN paralysis and paresis.\(^8\) Common features observed during phonation in their case series were bowing and shortening of the ipsilateral vocal fold, height asymmetry with the ipsilateral vocal process overriding the normal vocal process, and ipsilateral hyperadduction/hypertrophy of the false vocal fold. Similar findings were seen in the patients within this review.

In a very recent study, Roy et al demonstrated that flexible laryngoscopy findings after selective external SLN block with lidocaine results in deviation of the petiole of the epiglottis ipsilaterally (to the side of the block), posterior commissure rotation contralaterally (away from the blocked side), and improved glottic closure during high-pitched phonation.\(^10\) They specifically noted that most participants (67%) demonstrated a posterior glottic chink before the SLN block, with over half of the participants showing complete closure after the block. It is possible that this change in glottic closure is actually detrimental in some patients, resulting in increased contact between the vocal processes of the arytenoids.

It has long been noted that traumatic irritation to the vocal process and LPR play roles in vocal process granuloma formation. Jackson and Jackson were the first to report that granulomas could result from contact between the vocal processes during abusive phonation.\(^11\) Contact granulomas are prone to recurrence because of repeated injury from contact of opposite arytenoids during phonation or coughing.\(^1\) Cherry and Margulies were among the earliest investigators noting development of contact ulcers of the larynx from LPR.\(^2\) They were also among the first to show the benefit of antacids in treating contact ulcers. A later study showed reflux in 76% of patients with vocal process granulomas and suggested that LPR plays the most important role in granuloma etiology and propagation.\(^3\) Thus, although some researchers indicate that chronic irritation from vocal abuse is necessary with reflux for contact granulomas to persist, others state reflux alone causes contact granulomas.\(^1-3\)

In the patients in this review, we believe that the change in contact points of the vocal processes because of the SLN injury may be responsible for the persistent nature of their vocal process granulomas. In all patients, the vocal folds appeared shortened on the weaker side, and there was asymmetry of the vocal processes on phonation, which could contribute to chronic, repeated trauma at the level of one vocal process, thereby resulting in granuloma persistence. In all three cases, the SLN paresis was believed to be idiopathic. In case 1, symptoms were actually preceded by diarrhea/cramping (possibly a viral gastroenteritis), leaving one to speculate that the SLN paresis might have been postviral in nature. Based on the concept that alteration in vocal process contact was contributing to the granulomas, botulinum toxin injection to the contralateral (normal) cricothyroid muscle was included in the treatment plans for cases 2 and 3. This did not significantly impact swallowing or voice quality, although those patients were not professional voice users or singers, and therefore, may not have noted alterations in vocal range if this had been affected.

Although many granulomas are multifactorial, the first two cases actually lacked history of LPR symptoms, laryngeal trauma, or changes in voice use, suggesting that isolated SLN neuropathy may have been the greatest factor. Case 1 was especially interesting in that resolution of the SLN paresis findings on videostroboscopy was associated with resolution of the granuloma, even though the patient had failed to use antireflux therapy or work with a speech therapist. The authors considered a follow-up LEMG in this patient, but the cost and patient discomfort involved could not be justified, as it would not have changed his clinical management. Regarding case 2, there was an evidence of presbylaryngis and isolated SLN paresis on videostroboscopy, and his history did not suggest that LPR, trauma, or vocal abuse were factors in etiology of the granuloma. Although he did well after granuloma resection with collagen and botox injections, it is difficult to discern which factors were responsible for his outcome considering the multiple variables involved. Finally, case 3 had LPR symptoms and pH probe-documented LPR in addition to SLN paresis. Interestingly, this is the one case that did have granuloma recurrence at his 9-month follow-up, possibly being related to the loss of the botulinum toxin effect, LPR, or both.

Because LPR is such a major contributing factor to granuloma formation and persistence, all patients were initially started on aggressive antireflux treatment with twice-daily PPIs. Although it is recognized that it can take up to 6 months for the resolution of a granuloma on PPI therapy, case 2 was tried on PPI therapy for only 3 months, because, in the authors’ experience, granuloma resolution is preceded by at least a mild reduction in granuloma size within 3 months if a patient is responding to PPI treatment. Thus, although LPR likely played a role in granuloma development, these patients had granulomas that persisted unchanged with aggressive PPI treatment, thus suggesting a more complex mechanism.

There have been a few cases reports in the literature similar to the cases in this study. Koufman et al suggested that patients with glottal closure problems, such as paresis, may have vocal nodules, vocal process granulomas, or other lesions that result from hyperkinetic compensation for hypokinetical vocal fold paresis.\(^4\) One patient described in their study had a recurrent left vocal process granuloma with left RLN neuropathy shown on LEMG.\(^5\) It is interesting to note that this patient had the granuloma on the same side as his neuropathy, possibly indicating a slightly different mechanism causing the granuloma than in our patients. Hoffman et al identified granulomas occurring on the arytenoids after arytenoid adduction in patients with unilateral laryngeal paralysis.\(^1\) As the vocal processes are often at
different levels (height) on phonation after the arytenoid adduction surgery, this finding and granulomas detected with SLN paresis may have similar etiologies of mechanical trauma.

Because of the multifactorial etiology of vocal process granulomas, a multimodal treatment approach aimed at the underlying causes is often recommended. Hoffman et al concluded that managing LPR with PPIs and correcting vocally abusive behavior will treat most of the vocal process granulomas. Leonard and Kendall had success with combined voice therapy and PPIs. Havas et al demonstrated that a concurrent medical and speech therapy regimen for postintubation and hyperfunctional voice patients provided the best treatment outcome. When these conservative measures fail, laryngeal surgery (CO2 laser, pulsed dye laser, cold excision, or cautery) is sometimes effective, and antibiotics, vocal fold augmentation, and laryngeal botulinum toxin injection may also have important roles in treatment. Botulinum toxin has been used to successfully treat vocal process granulomas based on the hyperadduction/hypermobility theory. Augmentation of the vocal folds by injection laryngoplasty has also been used successfully in patients with vocal fold paresis and paralysis.

There are several factors that weaken this report. First, the strength of the association between the SLN paresis and vocal cord granulomas cannot be determined from this review because of the small sample size. Second, the multiple variables involved in granuloma formation and resolution, such as reflux and voice abuse/misuse, do not allow for a cause-and-effect relationship between SLN paresis and vocal cord granulomas to be established. Finally, although follow-up LEMG studies would be informative and potentially supportive of such a relationship, they were not performed because of the retrospective nature of this review and the lack of medical necessity. A larger prospective study may be helpful in the future to study the association.

CONCLUSION

The purpose of this review was to describe the presentation, treatment, and outcomes for a series of patients with unilateral SLN paresis and associated contralateral vocal process granulomas. The chronicity of these granulomas was likely, in part, related to altered contact points between the vocal processes of the arytenoids related to the SLN paresis. As most granulomas are multifactorial in nature, it is important to consider a full range of etiologies and treatment options for these patients.

REFERENCES