Treatment of Laryngeal Contact Ulcers and Granulomas: A 12-Year Retrospective Analysis

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Summary: Multiple etiological factors including gastroesophageal reflux, hyperfunctional voice use, and endotracheal intubation have been implicated in the development of posterior laryngeal ulcers and granulomas. The optimal approach to treatment of these lesions remains controversial. The mainstay of treatment at Vancouver General Hospital has been aggressive medical management of gastroesophageal reflux, with complimentary voice therapy offered to patients suspected of having significant hyperfunctional phonation. The authors reserve Botulinum toxin injection or surgical excision for patients who fail initial therapy. They conducted a retrospective analysis of their voice clinic records from 1985-1997 to examine the efficacy of this approach. They identified 76 patients with the diagnosis of contact ulcer or granuloma. Fifty-two patients had follow-up data available for review. Ninety-four percent of patients were treated nonsurgically: 35 patients were treated solely by dietary and medical therapy to control gastroesophageal reflux, 10 patients were treated by a combination of medical gastroesophageal reflux control and voice therapy, 3 patients had Botox injections, 2 patients had surgical excision of granuloma, 1 patient had a Kenalog injection, and 1 patient underwent laparoscopic fundoplication. Overall, 77% of patients had complete resolution, whereas 11% had partial resolution and another 11% had no significant improvement. The data supports control of gastroesophageal reflux as a central component in treatment of posterior laryngeal ulcers and granulomas. Key Words: Contact granuloma—Contact ulcer—Larynx—Laryngeal ulcer—Laryngeal granuloma.

Since Jackson described posterior laryngeal ulceration in 1928,1 reports have associated their development with etiological factors such as vocal abuse, endotracheal intubation and chronic gastroesophageal reflux (GER).1-12 Vocal process granulomas are thought to occur as inflammation and repeated injury produce granulation tissue at the site of ulcerations.3,4 These lesions are usually located at the level of the medial surface and vocal process of the arytenoid where cartilage is covered by a tight mucoperichondrium and a thin layer of mucosa. The lack of soft tissue protection leads to frequent ulceration of the area with minimal trauma. Santos et al demonstrated ulcerations in this area in 76% of patients orotracheally intubated for longer than 3 days.12 Jackson, Feder, Watterson, and others have associated development
of contact ulcers and granulomas with voice abuse and harsh glottal attacks. In 1968, Cherry et al introduced GER as a causative process in formation of contact granulomas. Since then many other investigators have added supportive data to the role of GER in development of contact ulcers and granulomas. Several authors have suggested that the etiology of these lesions is likely multifactorial with elements of laryngeal trauma, voice abuse, and GER present in various degrees in each patient.

Treatment of these lesions has focused on 4 primary areas: prevention, voice therapy, medical therapy, and surgical excision. Avoidance of long-term orotracheal intubation, use of smaller endotracheal tubes, and use of histamine-2 receptor blockers in patients intubated for prolonged periods have all been reported as helpful in decreasing laryngeal trauma. Various voice therapy techniques have been reported in the literature with varying degrees of success. Bloch reported complete resolution of granulomas in 64% of patients treated with voice therapy. Compliance with voice therapy, however, has been a problem according to several reports including that of Jaroma who reported that only 41% of his patients participated in voice therapy. Medical treatment has included antibiotics, steroids (systemic, inhaled, or locally injected), antacids, histamine-2 receptor blockers, proton pump inhibitors, and Botulinum toxin (Botox) injections. Surgical excision, although still commonly performed, has been shown to have a high incidence of recurrence. The method of choice in most centers is endoscopic removal with the carbon dioxide (CO2) laser.

At Vancouver General Hospital, treatment has focused on control of GER with concomitant use of voice therapy in well-motivated individuals identified as having significant hyperfunctional phonation. Other modalities, such as inhaled or locally injected steroids and Botox injections, are used in resistant cases. Surgical excision with CO2 laser was used in patients with significant symptoms despite prolonged medical therapy.

METHODS

The patient data base at the Vancouver General Hospital Voice Clinic from January 1, 1985, to December 31, 1997, was reviewed. Written clinic records for all patients with the diagnosis of “contact ulcer/ granuloma” were reviewed. The diagnosis was made by rigid or flexible videostrobolaryngoscopy at the clinic in all cases. Patients with granuloma formation post microlaryngeal surgery were excluded. Data included age, gender, history of intubation, chief complaint, location of lesion(s), therapeutic modalities, outcome of therapy, duration of therapy, and recurrence.

Patients at the voice clinic undergo a team evaluation by a laryngologist, a speech pathologist, and sometimes laryngology fellows as well as otolaryngology residents. Initial evaluation includes history, head and neck examination, and video-strobolaryngoscopy in all patients. At follow-up, patients are asked about their primary complaint and repeat videostrobolaryngoscopy compared to the initial video: a subjective interpretation of change in the size and appearance of the lesion is recorded on the chart.

All patients in the review were given verbal and written instructions for reduction of GER. Patients treated medically for GER before 1992 were given either cimetidine or ranitidine BID or TID. After 1992, omeprazole, and later lansoprazole or pantoprazole were used as firstline agents; cimetidine or ranitidine were used after 1992 in patients who could not tolerate the firstline agents. Patients were typically started on a 2-month trial of medication initially; further medical therapy was then based on repeat interview and videostrobolaryngoscopy.

Voice therapy was provided by the Voice Clinic or by consultant community speech pathologists. The therapy is designed to reduce laryngeal and supralaryngeal tension by improving speech, breathing, and resonance as well as providing specific exercises to relax jaw, tongue, neck, and face. The voice therapy program also incorporated vocal abuse awareness and reduction.

Botox was injected into the ipsilateral thyroarytenoid muscle via the EMG guided percutaneous method. The dose ranged from 10 to 12 units. Kenalog was injected in the region of the thyroarytenoid joint transcutaneously with EMG guidance. Surgical management of GER was performed via laparoscopic Nissen fundoplication by the General Surgery service. Granulomas were excised with CO2 laser microsuspension laryngoscopy at the outpatient surgical center.

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Patients with complete or near complete resolution of their primary complaint(s), as well as the endoscopic findings, were defined as “resolved.” Patients who had improvement in their primary complaint, as well as reduction in the size of their endoscopic findings, were defined as “partially resolved.” Patients who exhibited no improvement or worsening of their primary complaint were termed “nonresolved”: none of these patients exhibited appreciable resolution of their endoscopic findings.

RESULTS

Of 76 patients identified with the diagnosis of contact ulcer/granuloma, the 52 (42 men and 10 women) patients who had both initial and follow-up data available for review form the study cohort. Mean age was 47 (range 20-74). Although 17 (33%) patients had a history of orotracheal intubation, only 6 (12%) patients had onset of symptoms immediately or shortly after extubation; mean duration of intubation was 6 days (range 9 hours to 14 days) in these 6 patients.

The most common chief complaint was pain/discomfort; second most common was hoarseness (Table 1). Other findings included previous external laryngeal trauma (1 patient), rheumatoid arthritis (1 patient), history of cervical radiotherapy (1 patient), unilateral vocal fold paralysis (1 patient), and psychiatric disorder (1 patient).

Videostrobolaryngoscopy showed that 5 patients (10%) had bilateral lesions: 3 in the nonintubation-related lesions and 2 in the intubation-related group. Other significant findings were sulcus vocalis (1 patient) and scarring of vocal folds (1 patient). Thirteen patients (21%) were identified as having significant hyperfunctional phonation. Of this group, 10 patients enrolled in and 9 were compliant with their voice therapy.

<table>
<thead>
<tr>
<th>TABLE 1. Most common complaints of 52 Adult Subjects</th>
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<tr>
<td>Chief Complaint(s)*</td>
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<tr>
<td>Pain</td>
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<tr>
<td>Hoarseness</td>
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<tr>
<td>Cough</td>
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<tr>
<td>*11 patients had more than one chief complaint</td>
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</table>

Therapeutic modalities used are shown in Table 2. Of 35 patients treated solely by GER control, 27 (77%) had resolution, 4 patients (11%) had partial resolution, and 4 patients (11%) had no response. In the 23 patients treated by proton pump inhibitors alone, 17 (74%) had resolution (mean duration of treatment: 5.7 months), whereas 3 patients (13%) had partial resolution and another 3 patients (13%) had no response. Mean duration of follow-up was 6.4 months (range 2-30 months). Three patients had recurrence of granuloma while off medication: 2 on the same side and 1 on the opposite side. All 3 responded to a repeat course of proton pump inhibitor therapy.

Three patients received Botox injection in addition to GER control; 2 resolved, whereas 1 patient had partial resolution. One patient had Kenalog injection near the thyroarytenoid joint in addition to GER control, with near complete resolution. Of the 9 patients who completed a voice therapy program in addition to GER control, 7 (78%) resolved, whereas 1 patient (11%) had partial resolution and 1 patient (11%) had no response. Of the 4 patients who were offered but did not complete voice therapy, 3 (75%) resolved and 1 (25%) had no response.

One patient had severe GER despite proton pump inhibitor treatment. She underwent laparoscopic Nissen fundoplication with complete resolution of her granuloma 8 months postoperation. Two patients had excision of granuloma by CO₂ laser. Both operations were performed before availability of proton pump inhibitors. Both patients were started on histamine-2 blockers postoperation and did not have recurrence.

Overall, 40 patients (77%) had resolution, 6 patients (11%) had partial resolution and 6 patients (11%) had no significant improvement. Forty-nine of 52 patients were treated nonsurgically.

DISCUSSION

Jackson is credited with the first description of contact ulcers in 1928.¹ He proposed that these injuries were caused by vocal abuse, and advocated voice rest and surgical excision as treatment options.¹,² Over the years other etiological factors such as endotracheal intubation and GER have been recognized in the literature. In 1984, Feder described a classification system based on three etiologic factors: intubational, hyperfunctional and hyperacidic.⁸ De-
Development of contact ulcers and granulomas has been estimated in as many as 76% of patients intubated for longer than 3 days. However, most of these lesions resolve spontaneously and do not come to the attention of otolaryngologists. In the Vancouver study, 12% of patients could be categorized as intubational. It has been the authors' experience that these lesions respond to therapy in a similar fashion as those not related to intubation.

Hyperfunctional phonation has been identified in multiple series as quite prevalent in these patients. Men to women ratios of 2:1 to 9:1 have been reported for contact ulcers and granulomas (3:1 in the present study). Men are well known to have a lower habitual pitch and hard glottal attacks as well as more complete posterior glottic closure patterns that may predispose the posterior portion of the vocal folds to injury. Psychological factors, such as anxiety and tense personalities have also been noted to contribute to hyperfunctional phonation. However, the most damaging vocal activity in these patients appears to be frequent and forceful throat clearing that may be secondary to underlying and often unrecognized GER.

The role of GER in development of laryngeal mucosal injury was suggested over 30 years ago. In 1968 Cherry et al proposed that bathing of the mucosal surfaces of the larynx by acidic material from the stomach caused inflammation in the tissue that predisposed the mucosa to ulceration and granuloma formation. Laboratory support for this postulate was presented by Delahanty and Cherry in an animal study, showing ulceration of canine laryngeal mucosa resulting from daily exposure to "gastric juice." The role of GER in the development of chronic laryngitis was well articulated by several authors over the ensuing years. Ward and Berci described a whole spectrum of laryngeal pathology associated with GER, with mild inflammation of the posterior larynx at one end of the spectrum, and contact ulceration and granulomas at the other end. Koufman further detailed the association between GER and laryngeal abnormalities with extensive use of ambulatory pH monitoring. Radiological GER has been documented in as many as 72% of patients with contact ulcers and granulomas. Finally, Morrison, Ward and Hanson as well as other authors have postulated a relationship between long standing GER and development of laryngeal carcinoma.

Although multiple motility modifying agents are available, the cornerstone of treatment of GER remains the reduction of acidity of gastric secretions. Dietary changes in treatment of hyperacidity were recognized as early as 1915. The current recommended dietary regimen includes: avoidance of infrequent large meals, eating late in the evening, caffeine and nicotine intake, tomato-based sauces, and fatty foods. Additional measures such as head of bed

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**TABLE 2. Therapeutic Interventions for 52 Adult Subjects***

<table>
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<tr>
<th>Treatment Type</th>
<th>Interventions</th>
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<tr>
<td>GER Control Only (35)</td>
<td>Diet &amp; life style (6)</td>
</tr>
<tr>
<td></td>
<td>Diet &amp; life style &amp; H-2 blockers (6)</td>
</tr>
<tr>
<td></td>
<td>Diet &amp; life style &amp; PPI* (23)</td>
</tr>
<tr>
<td>GER Control &amp; Voice Therapy (10)</td>
<td>Voice &amp; diet (4)</td>
</tr>
<tr>
<td></td>
<td>Voice &amp; diet &amp; H-2 blockers (2)</td>
</tr>
<tr>
<td></td>
<td>Voice &amp; diet &amp; PPI (4)</td>
</tr>
<tr>
<td>GER Control &amp; Localized Injections (4)</td>
<td>Botulinum toxin (3)</td>
</tr>
<tr>
<td></td>
<td>Steroid (1)</td>
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<tr>
<td>Surgical Intervention (3)</td>
<td>Fundoplication (1)</td>
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<tr>
<td></td>
<td>CO2 Laser excision (2)</td>
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*Proton pump inhibitors.
elevation (6-8 in) is also recommended. Pharmacotherapy of hyperacid conditions was revolutionized by the introduction of histamine-2 receptor blockers in the mid 1970s. These agents, however, had several drawbacks including suboptimal acid suppression and development of tolerance. In 1992 with the introduction of proton pump inhibitors, near complete suppression of gastric acid production became plausible. The first generation agent, omeprazole, is usually prescribed once daily, but for 24-hour complete acid suppression BID dosage may be used. The newer proton pump inhibitors (lansoprazole and pantoprazole) have higher gastric stability and are given once daily for complete 24-hour acid suppression. Since 1992, the authors’ policy has been to treat patients with contact ulcers or granulomas with an initial 2 month course of BID omeprazole or QD lansoprazole or pantoprazole. In the authors’ experience, however, these patients often require an additional 2 to 3 months of therapy to reach a complete response. They are then cautioned to remain cognizant of dietary and behavioral modifications indefinitely.

Application of ambulatory pH monitoring and esophageal manometry studies in clinical practice has become increasingly popular. Comparative studies have shown 24-hour pH monitoring to be superior to both barium and nuclear medicine studies in detection of GER. Patient time and comfort issues continue to be the primary drawback of this procedure and most patients prefer a therapeutic trial of proton pump inhibitors. The authors have generally conducted 24-hour ambulatory pH studies only on patients who have demonstrated little or no response to the initial course of therapy. Most patients do in fact respond to the initial course of therapy and thereby avoid having an ambulatory pH study. Once a pH study is obtained, patients with persistent symptoms and no evidence of GER can have measures such as voice therapy or thyroarytenoid Botox injection instituted. If these fail and the patient remains symptomatic then surgical excision may be considered. On the other hand, if there is suspicion of malignancy then excisional biopsy can be performed, and GER pharmacotherapy initiated immediately postoperatively in order to minimize the risk of recurrence. With the availability of high resolution videolaryngoscopy units and the characteristic appearance of these lesions, this situation is likely to occur rarely if at all in experienced hands. The authors’ preferred technique for removal of all granulomatous lesions in the larynx has been the CO₂ laser. It must be noted that with the availability of proton pump inhibitors and botulinum toxin, the authors have not had to excise any contact granulomas.

In summary, the Vancouver General Hospital experience demonstrates that treatment of laryngeal contact ulcers and granulomas with medical and behavioral measures aimed at control of gastroesophageal reflux is effective and well tolerated in a large majority of patients. Proton pump inhibitor therapy for 2-4 months is the authors’ current treatment modality of choice. In well motivated patients with hyperfunctional phonation, voice therapy may be instituted as adjunctive treatment. Use of Botulinum toxin also appears to be helpful in selected patients. Primary excision of these lesions is not indicated unless suspicion of malignancy or other unusual diagnoses ex-
ists; use of high resolution videostrobolaryngoscopy is helpful in correctly identifying these lesions and reducing the need for microlaryngoscopy and biopsy.

REFERENCES