

Recurrent Contact Granuloma

Experience With Excision and Botulinum Toxin Injection

Taner Yılmaz, MD; Nilda Süslü, MD; Gamze Atay, MD; Serdar Özer, MD; Rıza Önder Günaydın, MD; Münir Demir Bajın, MD

Importance: Contact granuloma is a difficult-to-treat laryngeal disorder associated with vocal abuse, habitual throat clearing, and laryngopharyngeal reflux. It has a high propensity for persistence and recurrence despite many treatment alternatives.

Objective: To present our experience with recurrent contact granuloma treated with microlaryngoscopic excision and botulinum toxin injection.

Design: Case series. The follow-up period had a mean (range) of 41 (11-88) months.

Setting: Tertiary referral university clinic.

Participants: Twenty patients with recurrent, grade 3 and grade 4 contact granuloma whose lesion was excised at least once after failure of conservative treatments.

Interventions: Microlaryngoscopic excision and botulinum toxin type A injection into the region of the bilateral thyroarytenoid and lateral cricoarytenoid muscles.

Main Outcomes and Measures: Disappearance of contact granuloma.

Results: Seventeen patients were cured of their contact granuloma. Three patients experienced recurrences: 2 received botulinum toxin injection only as outpatients and recovered. The other patient required reexcision and re-injection under general anesthesia. These 3 patients were free of granuloma at their last follow-up.

Conclusions and Relevance: After failed conservative treatment, microlaryngoscopic excision and botulinum toxin type A injection is successful in the treatment of recurrent contact granuloma. Removing recurrent granulomas can result in a low recurrence rate if botulinum toxin type A is added at the time of removal.


CONTACT GRANULOMA IS A relatively uncommon, difficult-to-treat laryngeal disorder with multifactorial causes. It arises from the vocal process of the arytenoid cartilage, and less commonly from the body of the arytenoid cartilage. This is why it is also called arytenoid granuloma. It is most commonly associated with vocal abuse, habitual throat clearing, and laryngopharyngeal reflux. It has a high propensity for persistence and recurrence despite many treatment alternatives.1-2

Intubation trauma associated with granuloma was once thought an important etiological factor; however, this lesion is called intubation granuloma and is a different disease entity from contact granuloma. Intubation granuloma is observed equally or more commonly in female patients than in male patients. It has a high rate of spontaneous resolution. If it does not resolve spontaneously, its surgical excision yields a low recurrence rate, in contrast to contact granuloma.1-2

Perichondritis of the arytenoid cartilage, infection, allergy, and psychosomatic disorders are suspected to be involved in the etiology of contact granuloma. Individual susceptibility is also mentioned as a possible etiological factor.1

In this article, we present our experience with patients with recurrent contact granuloma who received several different types of conservative treatments and underwent surgical excision elsewhere before being treated in our department.

METHODS

Participants consisted of 20 patients with recurrent contact granuloma whose contact granuloma was excised at least once after failure of conservative treatments. Eighteen patients were male and 2 were female, yielding a
The lateral cricoid lamina is palpated laterally and deep into the vocal process of the arytenoid. After palpation of the cricoid, the BTA is injected just lateral to the cricoid lamina. For the interarytenoid muscle, the injection is performed deep into the mucosa right between both arytenoids. For the aryepiglottic muscle, the injection is performed deep into the mucosa in the middle of the aryepiglottic fold.

The follow-up period had a mean (range) of 41 (11-88) months. Treatment of contact granuloma was successful for 17 patients. However, 3 patients experienced recurrences; 2 received another BTA injection as an outpatient procedure and recovered. The other patient required reexcision and reinjection under general anesthesia. These 3 patients were free of granuloma at their last follow-up appointment. Detailed information on patients is given in the Table.

Patient 4 had a right-sided grade 4 lesion (Figure 2A). He has been free of granuloma for more than 7 years (Figure 2B).

Contact granuloma results from continued hammering of 1 vocal process against the other during phonation, referred to as “hammer and anvil.” This is especially true for loud phonations and hard glottal attacks. Treatment strategy should be aimed at decreasing this hammering action by teaching the patient to speak with softer phonation and without hard glottal attack. This is the aim of the voice therapy. However, voice therapy is not always successful in alleviating granuloma because some patients cannot follow the recommendations of a voice therapist and are unable to diminish hard glottal attacks.

Contact granuloma has been observed 10 to 20 times more commonly in men than in women. In our series, it is 9 times more common in men than in women. The question of how women are protected against contact granuloma is answered by noting the presence of a posterior chink at their vocal process during phonation.

Contact granuloma is usually seen in people older than 30 years. The patients characteristically abuse their voice and habitually clear their throat. The lesions are mostly unilateral; however, bilateral cases are also seen. Seventy-five percent of contact granulomas are located at the medial face of the vocal process of the arytenoid, and the other 25% are seen posterosuperiorly on the body of the arytenoid.

The voice characteristics of patients with contact granuloma include intensity above 80 dB and low pitch. They frequently perform hard glottal attacks during phonation. Their mean flow rate is low and range is narrow. Their voice is usually strained, pressed, and loud. They demonstrate excess vocal fry.1

RESULTS

DISCUSSION

Figure 1. Botulinum toxin A injection sites within the larynx. A, Thyroarytenoid muscle; B, lateral cricoarytenoid muscle; C, interarytenoid muscle; D, aryepiglottic muscle.

Figure 2. Patient 4’s lesion did not respond to office BTA injection, so she underwent reoperation; because her lesion was located superiorly on the body of the arytenoid, we injected 2 × 5 U BTA into the region of the bilateral aryepiglottic muscle and interarytenoid muscle to relax the supraglottic sphincter.

Table

©2013 American Medical Association. All rights reserved.

Downloaded From: http://archotol.jamanetwork.com/pdfaccess.ashx?url=/data/journals/otol/927166/ on 06/25/2017
Diagnosis of contact granuloma is simple to perform by means of clinical examination alone, because of its characteristic location and peculiar appearance. No other tests are necessary. Biopsy is performed rarely—only if malignancy is suspected.

Despite its name, contact granuloma is not a granuloma in the pathological sense. On a specimen of contact granuloma, under light microscopy we may observe focal ulceration, epithelial hyperplasia, necrotic tissue with desquamating epithelium, acute and/or chronic inflammation, capillary proliferation, fibrosis, and partially necrotic arytenoid cartilage.2

Farwell et al3 have proposed a grading system for contact granuloma based on its endoscopic appearance. A grade 1 lesion is limited to the vocal process, there is no ulceration, and the lesion is sessile. A grade 2 lesion is limited to the vocal process and is ulcerated or pedunculated. A grade 3 lesion extends beyond the vocal process but does not cross the midline of the fully abducted vocal fold. A grade 4 lesion extends beyond the vocal process and crosses over the midline of the fully abducted vocal fold. Unilateral cases are designated as “A” and bilateral ones as “B.”

There are many treatment options available for contact granuloma. Such a high number of alternatives indicates lack of satisfaction from a single therapy modality. Furthermore, physicians are in search of better options. Wang et al4 claim that observation alone yields an 81% remission rate within a mean of 30.6 weeks (approximately 7 months). According to our experience, a high spontaneous remission rate is a characteristic of intubation granuloma, whereas contact granulomas rarely disappear without treatment. Contact granuloma is a benign lesion and does not have to be removed. However, all

### Table. Characteristics of Patients With Recurrent Contact Granuloma

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>PEs, No.</th>
<th>Lesion Grade</th>
<th>VTSs, No.</th>
<th>Preop Symptoms</th>
<th>Recurrences, No.</th>
<th>Additional Treatment, No.</th>
<th>Postop Symptoms</th>
<th>Follow-up, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>4</td>
<td>8</td>
<td>Dysphonia, dyspnea, throat irritation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Throat irritation</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>3</td>
<td>9</td>
<td>Dysphonia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>3</td>
<td>8</td>
<td>Dysphonia, throat irritation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>4</td>
<td>10</td>
<td>Dysphonia, dyspnea, lump in throat</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>3</td>
<td>10</td>
<td>Dysphonia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>3</td>
<td>12</td>
<td>Dysphonia, throat irritation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Throat irritation</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>4</td>
<td>12</td>
<td>Dysphonia, dyspnea, lump in throat</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td>4</td>
<td>11</td>
<td>Dysphonia, dyspnea, lump in throat</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>9</td>
<td>2</td>
<td>3</td>
<td>9</td>
<td>Dysphonia, throat irritation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>3</td>
<td>12</td>
<td>Dysphonia, lump in throat</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>4</td>
<td>12</td>
<td>Dysphonia, dyspnea, lump in throat</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>12</td>
<td>1</td>
<td>3</td>
<td>8</td>
<td>Dysphonia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>13</td>
<td>1</td>
<td>3</td>
<td>9</td>
<td>Dysphonia, throat irritation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Throat irritation</td>
</tr>
<tr>
<td>14</td>
<td>1</td>
<td>4</td>
<td>10</td>
<td>Lump in throat</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>15</td>
<td>1</td>
<td>3</td>
<td>12</td>
<td>Dysphonia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>16</td>
<td>1</td>
<td>3</td>
<td>11</td>
<td>Dysphonia, throat irritation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>17</td>
<td>2</td>
<td>4</td>
<td>12</td>
<td>Dysphonia, dyspnea, lump in throat, throat irritation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Throat irritation</td>
</tr>
<tr>
<td>18</td>
<td>1</td>
<td>3</td>
<td>10</td>
<td>Dysphonia, lump in throat, throat irritation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>19</td>
<td>1</td>
<td>3</td>
<td>12</td>
<td>Dysphonia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>20</td>
<td>1</td>
<td>3</td>
<td>8</td>
<td>Dysphonia, lump in throat, throat irritation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Throat irritation</td>
</tr>
</tbody>
</table>

Abbreviations: BTA, botulinum toxin A; PE, previous excision; postop, postoperative; preop, preoperative; VTS, voice therapy session.
of our patients complained of a change in their voice and feeling a lump in their throat. Patients with grade 4 lesions also reported dyspnea on exertion. Throat irritation, which is more commonly observed in patients with chronic pharyngitis, may persist after the granuloma has disappeared. These symptoms are given in the Table. Furthermore, once our patients see the mass on a video monitor, no matter what we say they want get rid of it one way or another. Although the prior pathology report indicates that it is benign, they still ask, “Why doesn’t it disappear?” or “Why does it come back again and again?” This attitude may be peculiar to our patients. Many years ago when endoscopic camera facilities were unavailable or underdeveloped, patients were unable to see their lesion and more readily followed their physician’s advice to treat it more conservatively. Today, however, having seen it with their own eyes, they are afraid of the mass and want it to go away, especially if it is a grade 3 or 4 granuloma. They seem to suspect cancer despite being informed of the benign results of pathologic analysis.

Voice therapy comprises the first step in treating a patient with contact granuloma because the lesion develops as a result of hard glottal attack and voice misuse.5 Because laryngopharyngeal reflux is thought to be a factor in causing contact granuloma, it is also treated with antireflux medication and lifestyle modifications, such as changing the diet, avoiding reflux-provoking foods and beverages, eating small volume meals, avoiding recumbency after meals, and elevating the head of the bed during sleep. Antireflux medications include single-dose or double-dose proton pump inhibitors with or without H₂ receptor blockers administered before bedtime, alginic acid, and prokinetics. However, the rarity of contact granuloma and frequency of laryngopharyngeal reflux makes us think that such an association, if it ever exists, is vague.

Botulinum toxin was suggested for the first time as a form of treatment for patients with contact granuloma by Nasri et al6 in 1995. Damrose and Damrose7 claimed that percutaneous injection of BTA is a safe and effective therapy in resolving vocal process granulomas in patients whose disease was refractory to traditional therapy. It is used in total doses ranging from 2.5 to 30 U. It is injected into the region of the thyroarytenoid and lateral cricoarytenoid muscles to relax their adducting action on the arytenoid vocal process to decrease trauma of 1 vocal process to the other one. This injection relaxes the glottic sphincter. It can be used as a sole treatment or combined with microlaryngoscopic excision. Injections of BTA can be performed as an office procedure via the oral cavity, via the thyrohyoid membrane, via the thyroid cartilage, via the cricothyroid membrane, or using general anesthesia. The resultant temporary paresis of the vocal folds allows for a window of time during which the vocal process can heal and the granulomas can resolve without being exposed to ongoing intermittent contact and friction with the opposing arytenoid.8 Our patients with recurrent contact granuloma responded well to our treatment protocol. Three of 20 patients had continued recurrence; however, their recurring lesions were also successfully managed with the same protocol. In a case resistant to regular BTA injection, injection into the region of the aryepiglottic muscle and interarytenoid muscle to relax the supraglottic sphincter may be an alternative method. This was successfully used for 1 of our patients.

The use of antibiotics against chondritis of the arytenoid and Helicobacter pylori–induced reflux may be beneficial in some patients with contact granuloma. Corticosteroids have been administered as topical spray, intralesional injection, and systemically to prevent inflammation in contact granuloma. However, inflammation is secondary to mucosal trauma and ulceration on the vocal process, and without acting on the primary cause, that is, mucosal trauma, corticosteroids are not likely to cure contact granuloma. Hillel et al9 treated 54 patients with granuloma with proton pump inhibitors and inhaled triamcinolone acetonide; 20 of their patients (37%) had intubation granuloma. They found a 69% complete response rate with a mean (range) follow-up of 21 (3.9–84.6) weeks. The main drawback of their study is the inclusion of patients with intubation granuloma in the study sample.

Vitamin and mineral supplementation has been tried to treat patients with contact granuloma. Recently, Sun et al10 claimed that zinc sulfate (ZnSO₄) supplementation was successful in contact granuloma treatment, either as an initial or compensatory treatment. However, zinc supplementation can cure vocal process granuloma only
in the presence of a zinc deficiency. If the patients have normal blood and tissue levels of zinc, zinc supplementation, even in large doses (the authors gave 22 times the daily requirement), is not expected to solve the problem.\textsuperscript{11} Microlaryngoscopic excision with or without laser, cryotherapy, and electrocautery are other alternatives for contact granuloma treatment. Mucosal graft was used to cover the mucosal defect after surgical excision to prevent granuloma recurrence. Low-dose botulinum therapy has been suggested for cases resistant to other forms of treatment.\textsuperscript{12}

Surgery alone should not be used as a first-line and sole treatment of contact granuloma because this leads to a mean of 3 removals per patient. Surgery alone yielded a 90% recurrence rate for contact granuloma.\textsuperscript{1} Some claim that surgery has no role in the treatment of this condition and should be used only for histologic diagnosis in case malignancy is suspected. However, Hirano et al.\textsuperscript{13} proposed fiberoptic laryngeal surgery as an office procedure to facilitate repeated surgical removals.

If there is glottal insufficiency due to paresis and paralysis, contact granuloma develops as a result of the compensatory stronger action of the healthy vocal process on the paretic one. In such cases, vocal fold augmentation in the form of injection laryngoplasty may alleviate the granuloma. Halum et al.\textsuperscript{14} pointed out the association of vocal process granulomas with unilateral superior laryngeal nerve paresis, potentially related to altered contact points between the vocal processes of the arytenoids.

Removing a part of the arytenoid cartilage, usually the vocal process, to stop trauma to the other side has been suggested; however, we believe that this is an unethical and unacceptable form of treatment for a benign disorder because it will lead to permanent dysphonia.

First-line therapy for contact granuloma is conservative, taking the form of voice therapy together with antireflux therapy. The recommended duration of this treatment, 3, 6, 9, or 12 months or longer, has not yet been determined. We have used this conservative treatment for 3 months and, if unsuccessful, have switched to BTA injection for grade 3 and 4 lesions. Thus far, we have been successful with this treatment regimen for recurrent or nonresponsive contact granuloma. In a case resistant to regular BTA injection to the thyroarytenoid and lateral cricoarytenoid muscles, injection to the aryepiglottic muscle and interarytenoid muscle to relax the supraglottic sphincter may be an alternative method.

In conclusion, removing recurrent granulomas can result in a low recurrence rate if BTA is added at the time of removal.

Submitted for Publication: January 7, 2013; final revision received February 21, 2013; accepted March 17, 2013.

**Correspondence:** Taner Yılmaz, MD, Department of Otolaryngology, Hacettepe University Faculty of Medicine, 06100 Sıhhiye, Ankara, Turkey (tyilmaz@hacettepe.edu.tr).

**Author Contributions:** All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Yılmaz. **Acquisition of data:** All authors. **Analysis and interpretation of data:** Yılmaz, Atay, Özer, Günaydı and Bajin. **Drafting of the manuscript:** All authors. **Critical revision of the manuscript for important intellectual content:** Yılmaz and Bajin. **Administrative, technical, and material support:** All authors. **Study supervision:** Yılmaz.

**Conflict of Interest Disclosures:** None reported.

**Previous Presentation:** This study was presented at the Fall Voice Conference; October 5, 2012; New York, New York.

**Additional Contributions:** We thank Ebru Oralli for creating Figure 1 for us.

### References