



Multimodality Treatment for the Contact Granuloma of the Vocal Folds

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ABSTRACT

Introduction: This study aims to show the response of contact granuloma (CG) to Botulinum toxin type A injection (BTXA), proton pump inhibitors (PPI) and voice therapy (VT).

Materials and methods: A non-randomized prospective analytical study was done at a tertiary care hospital, in which 70 patients with CG were seen over a 2 years period. Depending on the size of the CG, the patients were divided into three groups and treated as below:

Group A: VT + BTXA+ PPI for farewell grade I and II CG

Group B: VT + BTXA + PPI + Microlaryngeal surgery (MLS) for Farewell Grade III and IV CG

Group C: VT + PPI (a group which did not agree for BTXA).

Statistical analysis: Data were analyzed and stored using Microsoft Excel 2010 file and qualitative data was represented in the form of frequency and percentage.

Results: Of the 70 patients in our study, we included 30 patients in group A, 19 in group B and 21 included in group C. All Group A patients (100%) resolved; however 1 patient needed a reinjection of BTXA. In group B, 18 patients (94.7%) resolved, 1 patient (5.3%) had recurrence. In Group C, 18 patients (85.7%) resolved, and three patients (14.3%) had persistent CG.

Conclusion: In our study, patients of farewell grade I and II treated with BTXA, PPI and VT had a 100% resolution rate. Surgery along with BTXA, PPI and VT is an acceptable treatment modality for farewell grade III and IV CG, as our study indicated a 94.7% success rate and 5.3% recurrence rate. The patients who did not receive BTXA had a decreased rate of resolution (85.7%).

Keywords: Botulinum toxin type A injection (BTXA), Contact granuloma, Microlaryngeal surgery, Proton pump inhibitor, Voice therapy.

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INTRODUCTION

Contact granulomas (CGs) are benign and inflammatory lesions of the vocal fold, often attached to the vocal processes of the arytenoid cartilage,¹ resulting from the continuous hammering of one vocal cord process against the other vocal cord process during phonation, especially during loud phonation and during hard glottal attacks.² CGs are mostly due to vocal abuse, laryngopharyngeal reflux, habitual throat clearing,² excessive glottic attack during initiation of speech and intubation (prolonged or traumatic).³ Other etiological factors thought are perichondritis of the arytenoid cartilage, infection, psychosomatic disorders, allergy and individual susceptibility.² CGs are observed more commonly in men than in women and have a high propensity to recurrence in spite of many treatment alternatives.² Patient's symptoms are foreign body sensation, need to repeatedly clear throat and hoarseness.

Based on appearance, Farewell et al. have proposed a grading system for CG.⁴ In grade I, CG appears as a sessile lesion, without ulceration and is limited to vocal process. In grade II, CG which were ulcerated or pedunculated and which is limited to the vocal process was taken. In grade III, granuloma which was extending up to vocal process but not crossing of the midline of an airway in a fully abducted position of the vocal fold. Grade IV included granulomas past vocal process and also the midline of the airway in a fully abducted position.⁴

Many treatment options have been suggested by various authors for CG, probably because no one treatment is extremely successful. The treatment plan of voice therapy is aimed to decrease the hammering action of vocal folds by teaching the patient to speak with a softer phonation and avoiding a hard glottal attack. Voice therapy should be the initial step in treating a patient with contact granuloma as the lesion generally develops due to hard glottal attack and voice misuse. Laryngopharyngeal reflux is one of the factors causing contact granuloma, hence contact granuloma is treated with antireflux medication and lifestyle modifications, like avoiding the spicy and high-fat diet, reflux-provoking foods and beverages, promotion of eating small volume meals, avoiding immediate sleeping after meals, and elevating the bed during sleep at the head end.²

Botulinum toxin injection type A (BTXA) is very effective and safe therapy in resolving contact granulomas in patients whose disease is resistant to the traditional therapy given in doses which range from 2.5 to 30 U and is injected into the thyroarytenoid and lateral cricoarytenoid muscles to relax adduction of the arytenoid vocal process thus decreasing trauma of one vocal process to the other vocal process. The resulting temporary paresis of the vocal cord will allow for a window of time so that vocal process can heal and resolve contact granulomas and avoiding exposure of ongoing intermittent contact and friction with the opposing arytenoid.²

Microalaryngoscopic excision with laser or coldsteel technique, cryotherapy and electrocautery are other treatment alternatives for contact granuloma. The mucosal graft can also be used to cover the mucosal defect after surgical excision to prevent recurrence of contact granuloma.²

MATERIALS AND METHODS

Our study was conducted in Tertiary Care Hospital as a prospective non-randomized, analytical study of 70 patients diagnosed with CG of the vocal folds from February 2014 to February 2016.

All patients were above 18 and below 65 years of age, of either gender divided into three groups A, B and C as *Group A*: Patients with farewell grades I and II CG treated with botulinum toxin type A (Botox company name Allergan) [BTXA + (PPI + VT)].

Group B: Patients with farewell grades III and IV CG treated with MLS + BTXA + (PPI + VT)

Group C: Patients treated with VT + PPI only (for the patients) who did not consent for BTXA.

The exclusion criteria consisted of patients below 18 and above 65 years of age, pregnant woman, patients with the neurological disorder like motor neuron diseases, amyotrophic lateral sclerosis, myasthenia gravis, parkinson's disease, patients with severe swallowing problems and patients who refused to be a part of the study.

All patients were followed at 1, 3 and 6 months.

We gave VT to all the patients, by using a phonoscopic approach which modified patient's vocal fold contact pattern; thus a small gap remained between the two vocal cords while talking.⁵ PPI, Lifestyle and dietary modification such as avoiding spicy and oily food, the gap between duration of food intake and sleep, increasing water intake, reducing tea, coffee intake along with PPI twice in a day was given to treat gastroesophageal reflux for all groups.

All patients in Group A were injected BTXA 3.75 mu into the ipsilateral thyroarytenoid muscle (TAM) through the cricothyroid membrane under laryngeal electromyography (EMG) control.

In group B patients, MLS was performed under general anesthesia using a laser safe tube, CO₂ laser acublade at 10 watts, super pulse repeat mode with two depth. The granuloma was not excised flush to its base, and a small stump of granuloma attached to the vocal process was left behind in an attempt to prevent exposure of the perichondrium. After excision of the CG, BTXA (3.75 mu) was injected into the ipsilateral TAM by using 25 gauge laryngeal needle.

All patients (of groups A, B, and C) were given PPI (40 mg twice a day) and VT for 6 months and were followed up for 6 months.

STATISTICAL ANALYSIS

Data were analyzed and stored using Microsoft Excel 2010 (Microsoft Corp) file for descriptive statistical evaluation. Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed by using Chi-Square test with continuity. Correction and Fisher's exact test was used for all 2 × 2 tables. A p-value <0.05 was taken as the level of significance.

Ethical and Humane Considerations

Ethical Approval

The Institutional Ethical Committee approved the study.

Informed Consent

Consent was taken from all the patients after informing them about the study chance to discuss in detail about the study was given to all patients and they were also aware that their participation is voluntary.

RESULTS

Most of our patients were above 40 years of age (74.3%), and male to female ratio is 5.3:1. The most common risk factors among our study subjects were the history of reflux (71.4%) followed by consumption of excessive tea, more than four cups (61.4%) and vocal abuse (voice use more than 8 hours) (55.7%). Other important risk factors in our patient groups include a history of smoking (45.7%) and habitual throat clearing (24.3%). History of alcohol and intubation was given by 34.3% and 2.9% patients respectively. The most typical symptom was changed in voice seen in 92.9% of patients, throat pain 27.1% of patients followed by foreign body sensation (12.9%) and breathlessness on exertion (8.6%) of patients. Other symptoms were the dry cough 10% of patients and difficulty in swallowing 4.3% of patients. In our study group, 28.6% of patients were in farewell grade I, 44.3% of patients in

farewell grade II, 24.3% of patients in Grade III and 2.9% in grade IV.

After first follow-up (1 month) in group A 36.7% lesion resolved, 60.0% partially resolved, 3.3% not resolved. In group B, 36.8% lesions were resolved, 63.2% lesions partially resolved. In group C, 9.5% lesions resolved, 81.0% partially resolved and 9.5% not resolved

After second follow-up (3 months), in group A, 86.7% lesions resolved, 13.3% partially resolved. In group B, 78.9% lesions were resolved, 15.8% lesions partially resolved, 5.3% not resolved (recurrence). In group C, 76.2% resolved, 9.5% partially resolved and 14.3% not resolved.

After third follow-up (6 months), in group A, all 30 patients (100%) CG were resolved one patient needed reinjection of BTXA (Figs 1 and 2). In group B out of 19 patients, 18 patients (94.7%) CG were resolved, one patient (5.3%) had a recurrence (Figs 3 and 4). In group C out of 21 patients, 18 patients (85.7%) CG were resolved, 3 patients (14.3%) CG were not resolved. The dose of 3.75 mouse units (mu) was utilized in all cases, and a repeat injection was required in one patient (group A). One patient showed recurrence in group B while no recurrence was observed in group A. No complication was observed in group C, one patient had a soft voice in group A (Table 1).

DISCUSSION

Vocal process granulomas were first described by Jackson and Jackson,⁶ in 1935. Despite ensuing developments in investigative and management techniques in laryngology, their etiology and appropriate treatment remain contentious. This uncommon lesion is also known as vocal cord granuloma, contact pachydermia, and contact granuloma. The proposed major causative factors include intubation, voice abuse, and gastroesophageal reflux disease (GERD).

Other causative factors suggested are smoking, infections, allergy, postnasal drip, and psychosocial traits.^{3,7,8}

Most common risk factors among our patients in our study were a history of reflux (71.4%) followed by consumption of excessive tea (61.4%) vocal abuse (55.7%), and other important risk factors were smoking (45.7%) and habitual throat clearing (24.3%). History of alcohol consumption and intubation was given by 34.3% and 2.9% of our patients respectively.

Thomas et al. in their study have found that 22.9% of granulomas occurred after intubation while 16.1% were professional voice users. The complaint of gastroesophageal reflux disease was reported in 76% of patients.⁹ In a similar study, following risk factors were obtained by Augusto et al.: 15 (22.7%) for post-intubation, 22 (33.3%) for vocal abuse, 20 (30.3%) for gastroesophageal reflux disease and 9 (13.7%) from idiopathic cause.¹⁰ The concept of acid reflux having a role in vocal process granuloma formation was highlighted by many authors.¹¹⁻¹³

In our study, most of the patients were above 40 years of age (74.3%) and the male to female ratio is of 5.3:1. The most common observed symptom was changed in voice seen in 92.9% of patients. Other symptoms were throat pain (27.1%) foreign body sensation (12.9%) and breathlessness on exertion (8.6%). On voice assessment, significantly more breathy voice was observed in patients with severe grades (farewell grade III and IV) of CG. Lower pitch and decreased loudness were also observed in these subjects. Decreased amplitude of mucosal wave on stroboscopy was observed in 77.5% of subjects.

In a study of 55 patients of CG by Thomas et al.⁹ 39 were men, and 16 were women. The age range was 30 to 86 years with a mean age of 53 years for men and 53.4 years for women. The male preponderance was also observed by Augusto et al. with mean age of 51.1 years.¹⁴ Out of 76 patients diagnosed with contact ulcer granu-



Fig. 1: Contact granuloma pre-botulinum injection



Fig. 2: Contact granuloma post-botulinum injection

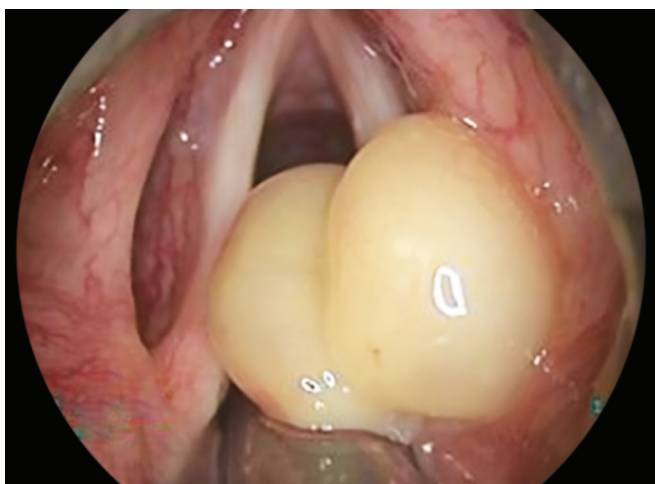


Fig. 3: Farewell grade IV contact granuloma

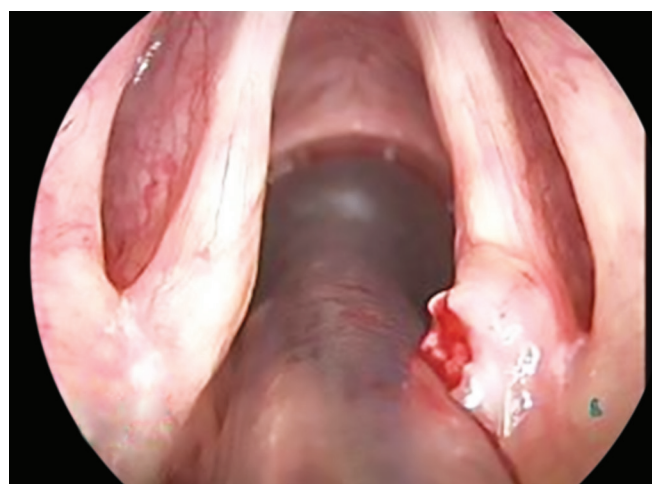


Fig. 4: A small stump of granuloma attached to the vocal process was left behind after excision

Table 1: Outcome profile of contact granuloma as published by various authors

Name of author	Treatment modality	Outcome	Recurrence	Repeated treatment
Our Study 70 patients	PPI + VT	85.7%		
	PPI + VT + BTXA	100%		1BTXA
	PPI + VT + BTXA + MLS	94.7%	5.3%	
Emami A.J. et al. (1999) 52 patients	GER control	77%		
	GER control + PPI	78%	13%	3
	GER control + BTXA	67%		
	Kenalog injection + GER control	100%		
Lee SW et al. (2013) 590 patients	Laposcopic fundoplication	100%		
	Micro laryngeal surgery	100%		
	Speech therapy (ST)	44.3%	4.9%	
	Proton pump Inhibitor	44%	6.9%	
	Botulinum toxin injection	74.2%	6.5%	
	Micro laryngeal surgery	60%	7.1%	
	Steroid inhalation	31.6%	10.5%	
Observation	20.5%	10.3%		

Botulinum toxin type A injection (BTXA), Proton pump inhibitors (PPI), Voice therapy (VT), Micro laryngeal surgery (MLS), Gastroesophageal reflux disease (GERD)

loma by Emami et al. 42 were men and women were 10 with the mean age of 47 years (ranging from 20 to 74). The main symptoms observed were: throat pain/discomfort followed by hoarseness of voice.¹⁵

Vocal fold granulomas are the result of several additive insults; hence, their treatment should be multidimensional. The most important step to treat granulomas is to identify, eliminate the causes and preventing their recurrence. Treatment of contact granuloma primarily includes prevention, voice therapy, medical therapy, and surgical excision. Various voice therapy techniques with varying degrees of success reported have been discussed by various authors.¹⁵ Bloch reported about the complete resolution of granulomas in 64% of patients who were treated with voice therapy.¹⁶ However, compliance with

voice therapy is a problem according to many reports including that of Jaroma who reported that only 41% of patients participated in his study of voice therapy.¹⁷ Medical treatment includes antibiotics, steroids (systemic, inhaled, or locally injected), antacids, histamine-2 receptor blockers, proton pump inhibitors, and Botulinum toxin injections. Surgical excision has shown a high incidence of recurrence.¹⁵

Nasri et al. were the first to suggest Botulinum toxin injection as a form of treatment for patients with contact granuloma.^{1,18} Damrose and Damrose¹⁹ suggested that percutaneous injection of Botulinum toxin injection is a safe and effective therapy in treating vocal cord process granulomas in patients whose disease was resistant to traditional therapy given in doses which range from

2.5 to 30 U, injected into the region of the thyroarytenoid and lateral cricoarytenoid muscles to relax adduction on the arytenoid vocal process thus decreasing trauma of one vocal process to the other vocal process. It can be used as the only treatment or can be combined with microlaryngoscopic excision. Botulinum toxin can be injected as an office procedure via the oral cavity, via the thyrohyoid membrane, via the thyroid cartilage, via the cricothyroid membrane, or using general anesthesia thus causing temporary paresis of the vocal folds allowing for a window of time to heal vocal process and resolving contact granulomas avoiding exposure to ongoing intermittent contact and friction with the opposing arytenoids.¹⁴

In our study, After third follow up (after 6 months), in group A all 30 patients (100%) CG were resolved one patient needed reinjection of BTXA. In group B out of 19 patients, 18 patients (94.7%) CG were resolved, one patient (5.3%) had a recurrence. In group C out of 21 patients, 18 patients (85.7%) CG were resolved, three patients (14.3%) CG were not resolved. A dose of 3.75 mouse unit was utilized in all cases and a repeat injection was required in one patient of group A. In group B, one patient (5.3%) had a recurrence (patient had denied repeat botulinum injection and repeat surgery), no recurrence was observed in group A. ST, and PPI was given for 6months. So our study evidence that adding botulinum toxin to microlaryngeal surgery for larger CGs improves healing rates significantly.

In the study of Thomas et al. antireflux therapy, lifestyle modifications, and adjuvant speech therapy achieved resolution and preventing recurrence of most of the contact granulomas. However, 6.1% of patients still required antireflux surgery for the total resolution of the granulomas.⁹

In a study of 20 patients, Yilmaz et al. treated recurrent contact granuloma were with the help of microlaryngoscopic excision and botulinum toxin injection. Seventeen patients out of 20 were healed of their contact granuloma, and patients experienced recurrences. Out of these three recurrent cases, two cases who received botulinum toxin injection only as outpatients recovered but one patient required reexcision and reinjection under general anesthesia. All these three patients were healed on their last follow-up. They thus concluded that after the failure of conservative treatment, microlaryngoscopic excision and BTXA injection is successful in the treatment of recurrent contact granuloma and also recurrent rate is low, when BTXA is added at the time of excision.²

Lee et al. conducted a retrospective study of 590 cases having contact granuloma in which they evaluated the efficacy of treatment modalities and determined predictors of treatment outcome. The outcomes of good

response rates after each treatment were 20.5% for observation, 31.6% for steroid inhalation, 44.0% for PPI, 44.3% for voice therapy, 60.0% for surgical removal, and 74.2% for botulinum toxin injection. It was observed that voice therapy, PPI, and botulinum toxin showed better responses than simple observation for the long-term outcome. However, surgical removal showed a significantly higher recurrence rate (37.1%) than simple observation (10.3%) ($p < 0.05$).²⁰

Joanne et al. performed a prospective study on six patients with vocal cord granulomas who failed prolonged antireflux treatment, speech therapy, and surgical excisions, BTXA injection was given into the affected thyroarytenoid muscle to reduce adduction trauma. On video-stroboscopy, 50% reduction in the size of the granulomas in 2 weeks and complete permanent response within 8 weeks in five patients out of total six was seen. One patient developed obstructing pyogenic granuloma required removal but recurred after excision however responded well repeat injection of Botulinum toxin was given. They thus concluded that by adding a single injection of botulinum toxin A to the standard treatment eliminated persistent and recurrent vocal cord granulomas.²¹

CONCLUSION

In our study, patients of farewell grade I and II treated with BTXA, PPI and VT had a 100% resolution rate. Surgery along with BTXA, PPI and VT is an acceptable treatment modality for farewell grade III and IV CG as our study indicated a 94.7% success rate, 5.3% recurrence rate. The patients who did not receive BTXA had a decreased rate of resolution (85.7%).

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