

Application of local flipped pedicle microflap combined with botulinum toxin A injection in the treatment of refractory laryngeal contact granuloma

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Abstract

Objective Laryngeal contact granuloma (LCG) is a kind of benign lesion that related with improper use of voice, habitual throat clearing and laryngopharyngeal reflux. Under 3 months standardized treatment, those who have no improvement or disease recurrence are called refractory LCG. The purpose of this study was to explore an advanced surgical method with local flipped pedicle microflap combined with botulinum toxin A injection in the treatment of refractory LCG. **Design** A retrospectively analysed of totally 11 patients with refractory LCG from January 2018 to December 2020. After CO₂ laser granuloma resection with local flipped pedicle microflap combined with botulinum toxin A injection, the patients were followed up at 1, 3, 6 and 12 months after operation to evaluate the effect of the surgery. Descriptive statistical methods were used to analyze and summarize the improvement of postoperative symptoms and signs of laryngoscope. **Results** During follow-up, 4 of 11 patients had residual pseudomembrane under the electronic laryngoscope, and had smooth mucosa when subsequent follow-up. The remaining 7 cases of electronic laryngoscope granuloma disappeared. Up to now their symptoms disappeared, and there were no systemic and local complications. **Conclusion** CO₂ laser granuloma resection with local flipped pedicle microflap combined with botulinum toxin A injection can achieve the lesion clearance, restore the integrity of vocal fold cover-body, preserve the perichondrium, and reserve a time window for microflap recovery. It is based on the principle of preserving normal mucosa, with high cure rate and no recurrence. It is worthy of clinical promotion.

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Running title: The application of flipped pedicle microflap in refractory laryngeal contact granuloma

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Objective Laryngeal contact granuloma (LCG) is a kind of benign lesion that related with improper use of voice, habitual throat clearing and laryngopharyngeal reflux. Under 3 months standardized treatment, those who have no improvement or disease recurrence are called refractory LCG. The purpose of this study was to explore an advanced surgical method with local flipped pedicle microflap combined with botulinum toxin A injection in the treatment of refractory LCG. **Design** A retrospectively analysed of totally 11 patients with refractory LCG from January 2018 to December 2020. After CO₂ laser granuloma resection with local flipped pedicle microflap combined with botulinum toxin A injection, the patients were followed up at 1, 3, 6 and 12 months after operation to evaluate the effect of the surgery. Descriptive statistical methods were used

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KEY POINTS

- In recent years, a complete cure of the disease is still a huge challenge for ENT doctors.
- This advanced surgical method are more suitable for the those refractory LCG who have no response to the standardized medical treatment and voice correction for 3 months.
- Application of local flipped pedicle microflap combined with botulinum toxin A injection in the treatment of refractory LCG is effective and safe.
- Based on the principle of preserving normal mucosa, the surgery can achieve the lesion clearance, restore the integrity of vocal fold cover-body, preserve the perichondrium, and reserve a time window for microflap recovery.
- Precision operability with great patience and caution is needed in the surgery. The microflap tension should be appropriate, the torsion or fenestration should be prevented from necrosis of the mucosa, and the fully mucosal coverage of the surgical wound is the key to the success of the operation.

KEY WORDS granuloma; larynx; CO₂ laser; microflap; botulinum toxin

INTRODUCTION

LCG, is a kind of benign lesion that occurs around the vocal fold mucosa and presents ulcer and granulation tissue hyperplasia, which is easy to relapse and difficult to cure radically. After standardized treatment for more than 3 months, those who still have no improvement or disease recurrence are called refractory contact granuloma¹. LCG usually associated with several etiological factors such as laryngopharyngeal reflux, habitual throat clearing and improper use of voice. Though the disease is not completely clear, it is usually considered that mucosal inflammation and ulceration that occur the posteromedial aspect of the vocal cords followed by granulation tissue hyperplasia². Intubation granuloma is self-limited, caused by endotracheal intubation, and totally different from laryngeal contact granuloma. Very few of the intubation granuloma could not heal spontaneously, and surgery may resolve it well with low recurrence rate.

Conservative treatment and surgical treatment have been widely used in contact granuloma, but almost both treatments cannot form consensus to overcome the persistence and recurrence contact granuloma. Granulomas cause psychological trauma and anxiety in patients, leading to loss of interest in peripheral events³. In this article advanced surgical methods with mucosal-flap and botulinum toxin A injection are applied in the treatment of refractory LCG, with significant efficacy and extremely low recurrence rate.

MATERIALS AND METHODS

1 Material

A retrospective analysis of a totally 11 patients with confirmed LCG admitted to the Department of Otolaryngology Head and Neck Surgery of our hospital from January 2018 to December 2020, and no significant improvement after 3 months of standard treatment with proton pump inhibitors (PPI). Among them including 10 males and 1 female, aged from 24 to 63 years, with an average of 39.6 years. The course of disease ranged from 5 to 48 months, with an average of 25.5 months. 5 patients had one operation history and 1 patient had two operation history. The main symptoms were hoarseness in 6 cases, cough in 3 cases, foreign body sensation in throat in 1 case and dysphonia in 1 case.

2 Operation method

All 11 patients underwent general anesthesia and endotracheal intubation. In the supine position, the operative cavity was exposed under the supporting laryngoscope (Karl Storz, Germany). Under the microscope, the lesions were removed along the pedicle of granuloma with 2W CO₂ laser, and the carbon scab was completely removed and the bleeding was fully stopped by cold instruments or CO₂ laser. Local infiltration anesthesia with 2% epinephrine saline was applied to the affected ventricular band. The diameter of the wound was measured and the 1.5 times of the diameter of the pedicled mucosal flap was obtained from the affected ventricular band with scissors. The pedicle was left behind the ventricular band and rotated 90 degrees to cover the wound of granuloma. 7-0 vicryl absorbable suture was used to intermittently suture 3-5 needles between the free merge of the mucosal flap and the normal mucosa around the vocal fold wound to make sure that the surface of the mucosal flap is smooth without warping, the wound is completely covered, the pedicle is not twisted, and the tension is moderate (Figure 1). 2U Botulinum toxin A was injected into the middle part of bilateral vocal cords at the end of operation. The excised granuloma lesions were sent for pathological examination. After the operation, antibiotics and aerosol inhalation were given for 3 days, and the sound was silenced for 2 weeks, and correct the bad living habits. All 11 patients were treated with PPI for 8 weeks postoperatively.

3 Effect evaluation and Statistical analysis

At 1, 3, 6, and 12 months after the operation, the symptom improvement of the subjects was tracked and recorded, and the physical signs of the electronic laryngoscope or dynamic laryngoscope were recorded. Descriptive statistical methods were used to analyze and evaluate postoperative effects.

Result

All 11 patients underwent surgery and perioperative education without any local or systemic complications. During the follow-up, there were 4 cases of residual pseudomembrane observed under the electronic laryngoscope, of which 2 cases appeared in 1 month postoperatively, and 2 cases in 3 months after surgery. After 8 weeks of oral PPI treatment, 3 cases of mucosa recovered smooth when follow-up again, 1 case became smooth mucosa when the third follow-up. There were no relapse in the next follow-up. The remaining 7 cases of granuloma disappeared under the electronic laryngoscopy. After an average of 6.2 months, all patients preexisting symptoms such as hoarseness, foreign body sensation in the throat, and coughing, and laryngoscopic signs were eventually clinically cured (Figure 2).

DISCUSSION

Contact granuloma, also called larynx contact ulcer or vocal process granuloma⁴. It is reported that the incidence of the contact ulcer is approximately 0.9%-2.7% in voice disorders⁵. It is more common in man than woman, more precisely, man suffer 2~9 times large than woman among the disease⁶. The lesions usually appear in unilateral vocal folds and sometimes bilateral vocal folds, and typically in term of nodulation and epithelial ulceration of varying degrees. The diagnosis of granuloma is very easy, generally based on symptoms and laryngoscopy without biopsy, which is different from laryngeal cancer. Pathologically, contact granuloma is not true granuloma that because of lacking in cluster of mononuclear and multinucleated histiocytes. They usually manifested as infiltration of inflammation cells, capillary proliferation and fibrosis, and sometimes as epithelial hyperplasia and perichondrium keratosis⁷. According to a grading system by Farwell et al⁸, clinical manifestations of the patient may be asymptomatic or have varying degrees of voice disturbance, throat edema, and varying levels of laryngeal discomfort and breathing difficulties.

Contact granuloma is always considered idiopathic when the common causes like laryngopharyngeal reflux and anesthesia intubation are eliminated, and some other causes are no-good habits of voice like incorrect phonation and habitual throat clearing. That's to say, The mechanical irritation caused by bilateral vocal fold collision and the inflammation caused by gastric acid reflux cause direct damage to the vocal fold mucosa⁹. meanwhile, Smoking, inflammation, allergic reaction, postnasal drip and social psychological pressure are also important inducing factors of granuloma¹⁰. Only a few patients can determine the reasons through

application of reflux symptom index and reflux finding score, and pharyngo-oesophageal 24-h pH monitoring. The complexity of the causes makes the treatment difficult and controversial. The current treatment for LCG mainly includes voice correction, medication, surgical treatment and vocal fold injection. Empirically, voice therapy and PPI is its first-line treatment¹¹. During the treatment cycle, patients are instructed to silence their voices, try to avoid unconscious throat clearing and coughing, and change incorrect phonation. At the same time, patients need to improve their lifestyles to reduce laryngopharyngeal reflux, including losing weight, reducing the amount of meals, and avoiding lying down within 3 hours after eating, adhering to a low-fat and low-acid diet, and avoiding intake carbonated or caffeinated beverages and spicy stimulation food.

PPI are efficiency in contact granuloma even though the patient do not combined with laryngopharyngeal reflux¹². However, the treatment cycle of internal medicine is very long, and the average treatment period is about 4.7 months¹³. Some patients may experience gastrointestinal disorders such as diarrhea, nausea, abdominal pain, or lack of gastric motility such as flatulence and constipation or other symptoms. The recurrence rate up to 12.12% when recurrent patient received PPI, and 3% even though combined with injection corticosteroids into granuloma¹⁴.

Surgical treatment is usually considered in the case of drug treatment failure or recurrence granuloma. Surgical removal were not recommended by some researchers because of it can shrink the size of the granuloma in the short term but has high rate of recurrence in the long term¹¹. An recent study indicate that The initial non-surgical treatment (67 percent) has a much higher cure rate than surgical treatment (30 percent) in contact granuloma patients⁹. Jingyi Wu reported that given postoperative radiotherapy within 24 hours can reduce the recurrence of laryngeal granuloma effectively¹⁵. Vojko Djukic have studied that Zinc supplementation for the treatment of granuloma of the larynx is one of the conservative treatment¹⁶. Zinc affects the healing process of wounds though the exact mechanism is unclear.

From Q Pham, botulinum toxin A injection threaten the powerful collision and adduction of posterior portion larynx via relaxing lateral cricoarytenoid muscle¹⁷. The collision of bilateral arytenoid cartilage can cause local cartilage inflammation, mucosal ulcers, and granulation tissue hyperplasia. Therefore, botulinum toxin A injection can temporarily act on the denervated vocal fold muscles, reducing the strong collision of the bilateral vocal folds and promoting the repair of the vocal fold mucosa. The team's previous research showed that surgery combined with botulinum toxin A injection is highly effective in voice disorders¹⁸. A series of studies also show that botulinum toxin A injection is safe and effective in the treatment of LCG^{17,19}. Botulinum toxin A injection broaden the structure of the granuloma strategy from a chemical point of view for the first time and transfer to innervated muscles and can be alternative therapy under patients' choice and institution's situation or applied to the failure on voice therapy or PPI^{17,20}.

The recurrence and refractory of LCG has always been the clinical focus of attention of otolaryngologists. Regardless of the surgery strategy, CO2 laser, angiolytic potassium titanyl phosphate laser or cold instrument resection, it is difficult to achieve the desired effect in the operation to remove the lesion alone. In this study, the pedicled mucosal flap of ventricular band was transferred to the wound after laser resection of granuloma, and the mucosa was anastomosed by microsurgery. This is an update of the traditional operation of Ni Xin et al²¹ and solves the problem that the released mucosal margin of the wound cannot completely cover the fresh wound, which may resulting in easy recurrence. In this study, no matter the size of granulomatous wound, we can take the pedicled mucosal flap to completely close the wound, which eliminates the potential pathological basis of granulomatous inflammation and achieves the purpose of one-time basic cure. The acquisition and transfer of mucosal flap follows the principle of voice surgery, staying in as a superficial plane as possible and preserving the normal mucosa. It not only completely excises the lesion, but also limits the lesion wound to the root of granuloma, and completely reconstructs the cover-body of vocal fold (epithelium plus superficial lamina propria), which is conducive to the recovery of vocal fold mucosal wave and the prevention of local scar or stenosis. At the same time, assisted microsurgery can avoid mucosal avulsion and displacement, accelerate fibrosis of the mucosal flap wound and granuloma wound. Secondly, the choice and acquisition of mucosal flap is minimally invasive, easy to obtain and survive, which avoids

open surgical trauma and increases the survival rate of mucosal flap. Recently, the combined treatment of vocal fold granuloma has significantly improved the efficiency compared with the single treatment, and has gradually become a trend^{14,13, 22}. This method combined with botulinum toxin A injection reserve a time window for the recovery of mucosal flap, also help to correct the phonation model and stabilize the surgical effect. Postoperative PPI therapy is an important step to consolidate the curative effect, control potential gastric acid reflux and avoid recurrence. It can be seen that the concept of combined treatment of LCG retains the advantages of various treatment methods, which is of great significance for the thorough treatment of the disease, and is an undeniable trend in the treatment of contact granuloma.

Precision operability with great patience and caution is needed in the surgery. The width of the pedicle should not be less than half of its length in theory, so that the flap can survive. When suturing, the surgeon should pay attention to the position of the needle and the control of the wrist strength, the tension should be appropriate, the torsion or fenestration of the pedicle of the microflap should be prevented from necrosis of the mucosa, and the fully mucosal coverage of the surgical wound is the key to the success of the operation. Furthermore, experienced anesthesiologists will use a smaller diameter endotracheal tube to expose the surgical field more clearly. At the same time, when the glottis is exposed by endotracheal intubation, surface anesthesia will be combined to reduce the fluctuation of vital signs and hemodynamics during the operation.

After standardized medical treatment and voice correction for 3 months, there was no significant improvement in refractory LCG. It was suggested that local pedicled mucosal flap transfer combined with botulinum toxin A injection should be performed. As a preliminary study, there were no systemic or local complications, high cure rate and low recurrence rate. The cure of the disease also inspired the treatment of vocal fold scar, adhesion, laryngeal stenosis, etc. we will continue to further clinical observation and including more patients.

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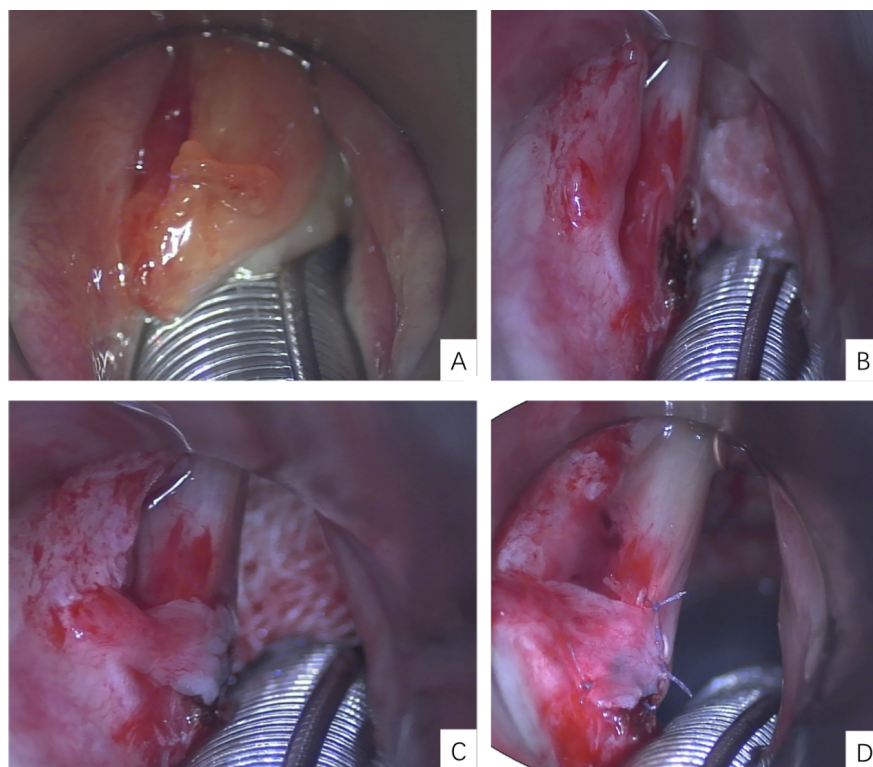


FIGURE 1 Intraoperative condition. A. Contact granuloma under the microscope of laryngoscope; B. After CO2 laser resection of granuloma; C. The pedicle microflap covered the wound; D. After mucosal flap sutured

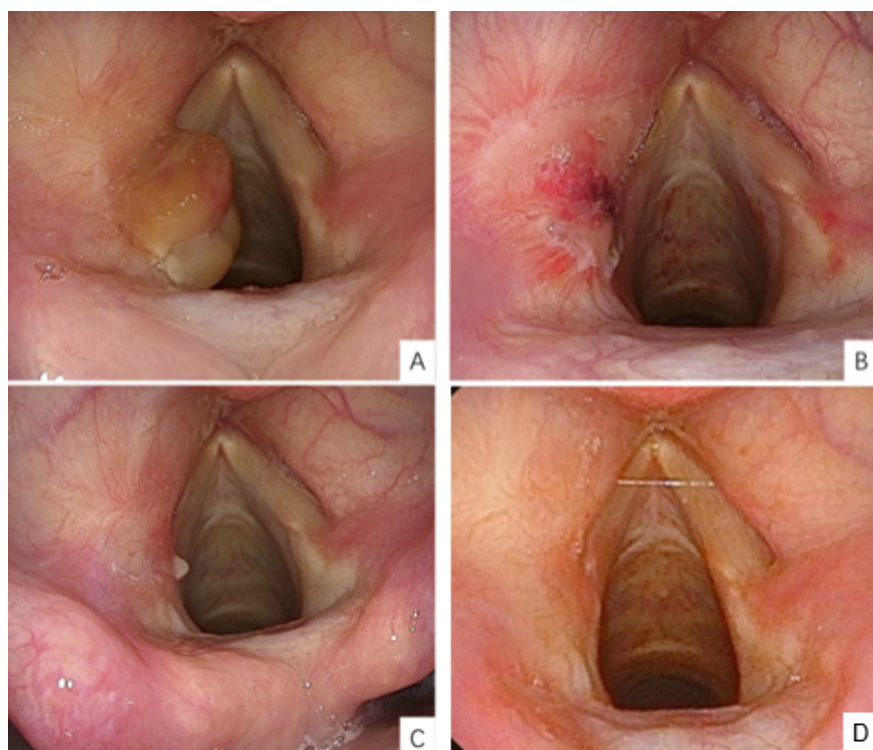


FIGURE 2 The vocal folds were observed by electronic laryngoscope. A. There was contact granuloma in the left vocal fold before operation; B. At 1 day after operation, the vocal folds showed that the pedicle microflap covered the wound well; C. 1 month after operation, the wound was smooth with residual pseudomembrane; D. At 12 months after operation, the mucosa of bilateral vocal folds were smooth under electronic laryngoscope

