

Main Article

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Arytenoid granuloma: a single-institution experience of management of 62 cases

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Abstract

Objective. This retrospective study was undertaken to assess the outcome of the medical and/or surgical management of patients presenting with clinical features of arytenoid granuloma. **Methods.** The records of 53 males and 9 females were reviewed for predisposing factors, types of treatment received and recurrence following the treatment.

Results. Most of the patients (48 out of 62, 77.4 per cent) were treated conservatively with medical management and voice therapy, which resulted in complete resolution of arytenoid granuloma in over two-thirds of the patients treated (32 out of 48, 66.6 per cent). Overall, 28 patients (out of 62, 45.1 per cent) required surgery (14 failed medical treatment cases and 14 surgery as first-line treatment cases). Of these, five patients (out of 28, 17.9 per cent) had recurrence, and were managed with revision surgery and concurrent local injection of Botox.

Conclusion. Anti-reflux medication and voice therapy are effective first-line management options. Pre- and post-surgery adjuvant treatment improves the results of surgery. Local injection of Botox was successful in the treatment of failed surgical cases.

Introduction

Arytenoid granuloma is a benign exophytic inflammatory lesion that arises from the vocal process of the arytenoid cartilage. Arytenoid granulomas are also termed vocal process granulomas.^{1,2} On videolaryngostroboscopy, arytenoid granuloma appears as a fleshy pale or sometimes reddish pedunculated mass with an underlying erythematous ulcer base, or it may take the form of a nodular or exophytic mass lesion (often reddish or pale grey), as shown in [Figure 1](#).

Arytenoid granuloma is most commonly encountered in males.² Frequent throat clearing, globus sensation, chronic cough, difficulty in swallowing, pain in the throat and change in voice are the usual presenting symptoms.³ Laryngopharyngeal reflux (LPR), vocal abuse, continuous voice use in excess of 4–6 hours a day, and prolonged endotracheal intubation are the predominant factors associated with the development of arytenoid granuloma.⁴

The Reflux Symptom Index and Reflux Finding Score are used to quantify the symptoms of LPR.⁵ The Reflux Symptom Index is a clinical questionnaire administered to patients with LPR symptoms, such as excess throat mucus and repeated throat clearing. The Reflux Finding Score is an endoscopic scoring system for diagnosing mucosal changes caused by LPR, such as erythema or hyperaemia, and posterior commissure hypertrophy.

A wide variety of therapeutic methods, such as simple observation, voice therapy, voice rest, anti-reflux therapy, antibiotics, corticosteroids (injected, inhaled or parenteral) and local injection of Botulinum toxin, have been used for the treatment of arytenoid granuloma.^{6,7} In persistent and refractory cases, invasive procedures such as endoscopic cold steel removal, laser excision and low-dose radiotherapy have also been used.⁶ However, none of the treatment modalities has been uniformly successful. Likewise, there are also no randomised, controlled trials or large cohort studies to support the effectiveness of one modality over another.⁸

There is good evidence that aggressive and prolonged anti-reflux treatment, in conjunction with or without voice therapy, forms the main treatment strategy, and is associated with low recurrence rates.^{6,7} The role of surgical management in the treatment of arytenoid granuloma is controversial, as the majority of studies have reported low response rates and a high risk of recurrence following surgery.^{3,9–12}

However, surgical removal as the first-line treatment has been advocated for large granulomas, based on an endoscopic grading system proposed by Farwell *et al.* (grades 1–4; unilateral cases and bilateral cases are classified as ‘a’ and ‘b’, respectively).¹³ Surgery is also advocated for those granulomas causing airway obstruction (grade 3a or 4a), bilateral granulomas (grade 3b or 4b), and those with a short history, along with a history of tobacco or alcohol consumption, and clinical findings suggestive of malignancy needing histological confirmation. Surgery is also required for granulomas that fail to respond to conservative management.^{11,12}

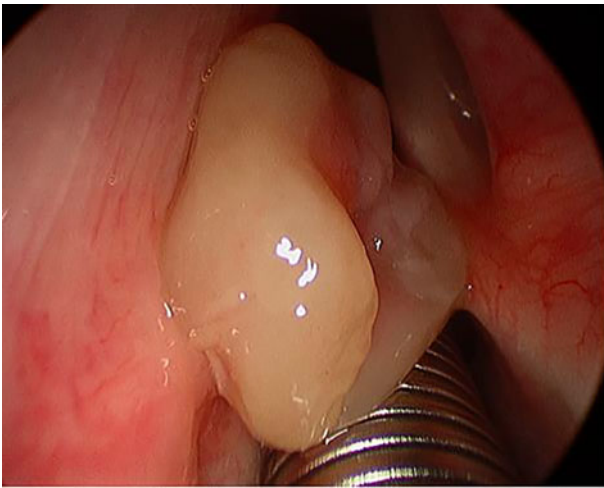


Fig. 1. Grade 3a right-sided arytenoid granuloma with a pale fleshy appearance.

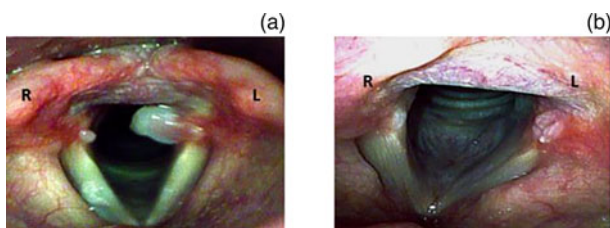


Fig. 2. (a) i-Scan image of right-sided grade 1 arytenoid granuloma and left-sided grade 4 arytenoid granuloma, showing contrast enhancement and sharpened view of blood vessels supplying the lesion. (b) i-Scan image of left-sided grade 1 arytenoid granuloma, showing contrast enhancement and sharpened view of blood vessels supplying the lesion. R = right; L = left

Surgical excision has been carried out with cold steel instruments, the carbon dioxide (CO₂) laser and the potassium titanium phosphate (KTP) laser.^{11,14,15} The CO₂ laser has been the preferred tool in recent times, as it offers precise cutting with a minimum of collateral thermal damage to the underlying tissue.⁷

This study aimed to assess the outcome of a combination of proton pump inhibitor (PPI) treatment, voice therapy and lifestyle modification. It also aimed to identify the indications for surgical management of arytenoid granuloma and the role of Botulinum toxin injection.

Materials and methods

This was a retrospective data analysis study conducted at a tertiary level care hospital in Pune, India. Institutional ethics committee approval was obtained.

The records of patients with clinically suggestive arytenoid granuloma, managed between July 2012 and June 2019, were retrieved and included in the study. The data retrieved included: age; sex; presenting complaints; history of symptoms suggestive of any systemic disease such as tuberculosis; history of intubation; history of smoking, alcohol intake or vocal abuse; Reflux Symptom Index; Reflux Finding Score; type and duration of treatment received; and histopathological examination reports of operated patients.

Videolaryngostroboscopy recordings and i-Scan[®] screening findings were reviewed (Figure 2a and 2b). The i-Scan tool is a dynamic software-based endoscopic image enhancement technology that provides an enhanced view of the texture of the

mucosal surface and blood vessels, allowing recognition of pathological lesions like dysplasia and malignancy that are otherwise not visible with conventional white-light endoscopy. This optical diagnostic software is available as a Pentax[®] system, and similar narrow-band imaging software is available via Olympus Medical[®].

Conservative management

The conservative treatment group included patients with LPR symptoms who were given anti-reflux medication (the PPI esomeprazole, 40 mg twice daily for three months). Those with a history of vocal abuse were given 8–10 sessions of voice therapy. In a few patients, both PPI treatment and voice therapy were given for the same duration. Intubation granulomas were treated conservatively with anti-inflammatories (i.e. oral and inhaled corticosteroids), anti-reflux medication, antibiotics and voice therapy.

During the course of treatment, patients were advised to attend for follow up every four to six weeks, for symptom assessment and endoscopic examination, until symptom resolution and normal endoscopy findings. Complete symptom resolution and arytenoid granuloma resolution after three months of conservative management was considered indicative of successful treatment.

Surgical management

Granulomas causing airway obstruction (grade 3a or 4a), bilateral granulomas (grade 3b or 4b), those with a short history, patients with a history of tobacco or alcohol consumption, and those who demonstrated clinical findings suggestive of malignancy needing histological confirmation were selected for surgical management with transoral CO₂ laser surgical excision. Patients for whom conservative treatment had failed were also managed with surgical excision.

Transoral CO₂ laser surgical excision was undertaken under general anaesthesia, with the patient in the supine position. The larynx was suspended using a Lindholm operating laryngoscope (Karl Storz, Tuttlingen, Germany) and was visualised through a Leica[®] microscope. Using microlaryngeal instruments, and an Acu-Blade[®] CO₂ laser at 2–3 W power in a continuous mode, the lesion was grasped and excised, along with its base, from the surrounding normal mucosa. Care was taken to prevent ‘ghost strikes’ on the exposed arytenoid cartilage. Excised tissue was sent for histopathological examination. Patients were given a course of broad-spectrum antibiotics, and continued on PPIs and vocal hygiene post-operatively.

Patients were advised to attend follow-up appointments every four to six weeks following surgery. Symptom assessment and endoscopic examination were performed during each visit. Complete symptom resolution and arytenoid granuloma resolution on endoscopy after three months of surgery was considered indicative of successful treatment. The cases that recurred after surgical excision were managed with revision surgery along with 10 units of Botox[®] injection into the ipsilateral thyroarytenoid muscle.

Results

The records of 62 patients diagnosed with arytenoid granuloma were retrieved and analysed. Fifty-three patients (85.5 per cent) were males; the male to female ratio was 5.9:1. The most common age at presentation was the fifth

Table 1. Age distribution of patients

Age group	Cases (n (%))
<20 years	1 (1.7)
21–30 years	6 (10.3)
31–40 years	16 (27.5)
41–50 years	22 (37.9)
51–60 years	11 (17.7)
>60 years	6 (10.3)

Table 2. Predominant symptoms of patients

Symptom	Cases (n (%))
Change in voice	28 (45.2)
Pain in neck	26 (41.9)
Foreign body sensation	4 (6.4)
Breathing difficulty	2 (3.2)
Throat irritation	2 (3.2)

Table 3. Risk factors for arytenoid granuloma

Predisposing factor	Cases (n (%))
Reflux	38 (61.2)
Vocal abuse	16 (25.8)
Smoking	10 (16.1)
Intubation	2 (3.2)
Unknown	8 (12.8)

decade, for both males and females; the age distribution of the patients is shown in Table 1. A change in voice (45.2 per cent) and pain in the neck (41.9 per cent) were the predominant symptoms in our patients; the distribution of symptoms among the patients is shown in Table 2.

Symptoms suggestive of LPR were found in 38 patients (61.2 per cent). Vocal abuse and vocal misuse history were found in 16 patients (25.8 per cent). Other risk factors, such as a history of smoking, were found in 10 patients (16.1 per cent). Two patients (3.2 per cent) had a history of intubation. In eight patients (12.8 per cent), no risk factors could be elicited, as shown in Table 3.

Videolaryngostroboscopy images of different grades of arytenoid granuloma are presented in Figure 3. Bilateral grade 4b intubation granuloma is shown in Figure 4.

Conservative management findings

Out of 48 patients, 32 (66.6 per cent) responded to conservative management, with complete and permanent resolution of symptoms and endoscopy findings. Twenty out of 32 patients (62.5 per cent) responded to PPI alone, 9 out of 12 (75 per cent) responded to a combination of PPI and voice therapy, and 3 out of 4 (75 per cent) responded to voice therapy alone, as shown in Table 4.

Sixteen patients in whom medical management failed (33.3 per cent) were recommended for surgery. Four of the 16 patients opted for continuation of conservative management.

They were recommended PPI and voice therapy for another three months. Two of these patients did not recover and were scheduled for surgery.

Surgical management findings

Twenty-eight patients underwent surgery. In 14 patients, it was the primary treatment modality; in the remaining 14 patients, conservative management had failed (Table 5). Of the 28 patients, 23 (82.1 per cent) had complete resolution of granuloma following surgery.

In 10 out of 28 operated patients, specimens were sent for rapid microscopic analysis because of doubtful features on clinical examination. The histopathology report revealed tuberculosis in three cases, which was treated with anti-tubercular therapy, and squamous cell carcinoma in two cases, for which the patients underwent radiotherapy. Surgical excision was completed in two cases of pyogenic granuloma, and in one case each of pleomorphic adenoma, moderate dysplasia, and moderate to severe dysplasia. Histopathology reports of the remaining 18 patients who underwent complete excision revealed 16 cases of inflammatory granuloma, and 1 case each of amyloidosis and mild dysplasia.

Pain in the throat and dry cough were the most common complaints in the post-operative period. None of the patients developed any major complications, such as posterior glottic stenosis, following surgery.

Eleven of 16 patients with inflammatory granuloma (68.8 per cent) had complete resolution of arytenoid granuloma following a single surgical procedure. Recurrence was seen in five patients (31.3 per cent), with inflammatory granuloma occurring within 6–12 weeks following surgery. All patients with recurrence underwent revision surgery after a trial of PPI and voice therapy. These patients were also injected with 10 units of Botox into the ipsilateral thyroarytenoid muscle. None of these five patients had recurrence on follow up after three months.

Analysing the outcome of conservative treatment, we found only two cases initially misidentified as arytenoid granulomas, and neither showed sinister disease (one amyloidosis and the other mild dysplasia). They were diagnosed after a failure of three months of conservative treatment.

Histopathology

The most common pathology identified was inflammatory granuloma, with hyperplastic epithelium and chronic inflammation in 16 out of 28 patients (57.1 per cent) (Table 6). Other pathologies included: tuberculosis (three cases); pyogenic granuloma (two cases); pleomorphic adenoma (one case); amyloidosis (one case); mild, moderate and severe dysplasia (one case of each); and squamous cell carcinoma (two cases).

Discussion

Arytenoid granuloma is most commonly seen in males, with a predominance in the fourth and fifth decades of life.^{16,17} A similar male predominance (85 per cent) was also observed in our study. Our study population compares favourably with most published work. A systematic review of arytenoid granuloma management identified 14 papers suitable for

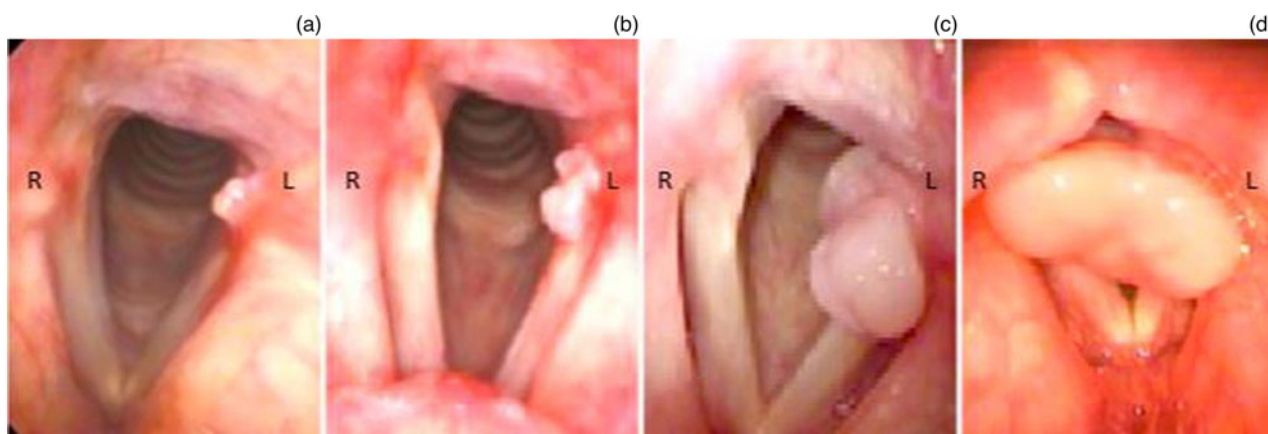


Fig. 3. Endoscopic images showing various grades of arytenoid granuloma: (a) grade 1a, (b) grade 2a, (c) grade 3a and (d) grade 4a. R=right; L=left

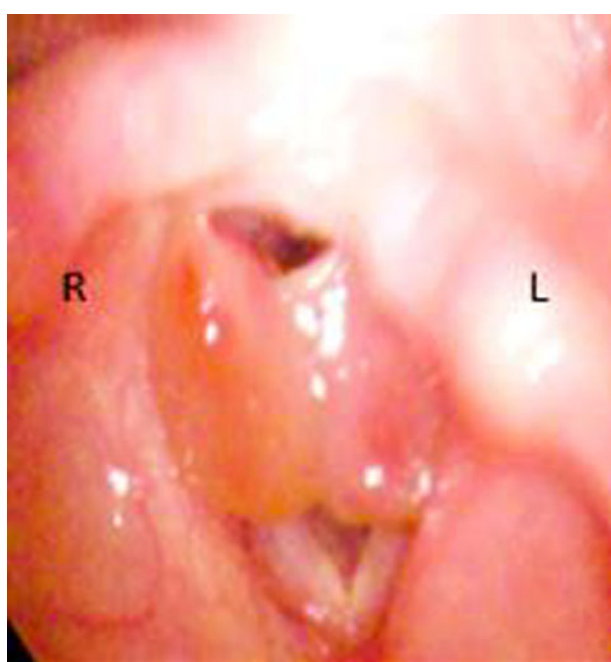


Fig. 4. Bilateral grade 4b intubation granulomas. R=right; L=left

Table 4. Patients who received conservative management

Type of treatment	Patients (n)	Response to treatment (n (%))
PPI treatment	32	20 (62.5)
PPI & voice therapy	12	9 (75)
Voice therapy	4	3 (75)
Total	48	32 (66.6)

PPI = proton pump inhibitor

analysis.⁸ Of these, only two presented larger numbers of patients than our study.

The causes of arytenoid granuloma are not well known, and there is no standard management protocol.¹⁶ History and findings suggestive of LPR (61 per cent) and vocal abuse (26 per cent) were the predominant risk factors identified in our patients with arytenoid granuloma, which is similar to other studies.^{16,18,19}

A systematic review by Karkos *et al.* concluded that aggressive and prolonged anti-reflux medication, with or without

Table 5. Patients who received surgical management

Histopathology for each surgical management type	Cases (n)
Primary surgical management	14
- Squamous cell carcinoma	2
- Inflammatory granuloma	4
- Tuberculosis	3
- Pyogenic granuloma	2
- Pleomorphic adenoma	1
- Moderate dysplasia	1
- Moderate to severe dysplasia	1
Secondary surgical management following failed conservative treatment	14
- Inflammatory granuloma	12
- Amyloidosis	1
- Mild dysplasia	1
Total	28

Table 6. Histopathological diagnoses

Diagnosis	Cases (n)
Inflammatory granuloma	16
Tuberculosis	3
Pyogenic granuloma	2
Pleomorphic adenoma	1
Amyloidosis	1
Mild dysplasia	1
Moderate dysplasia	1
Moderate to severe dysplasia	1
Squamous cell carcinoma	2
Total	28

voice therapy, forms the main treatment strategy, and is associated with fewer recurrences.⁷ Recent studies also emphasise these findings, and highlight the importance of continuing lifestyle modifications to prevent future recurrence.^{10,11}

We achieved resolution rates of 62.5 per cent with anti-reflux treatment and 75 per cent with voice therapy alone,

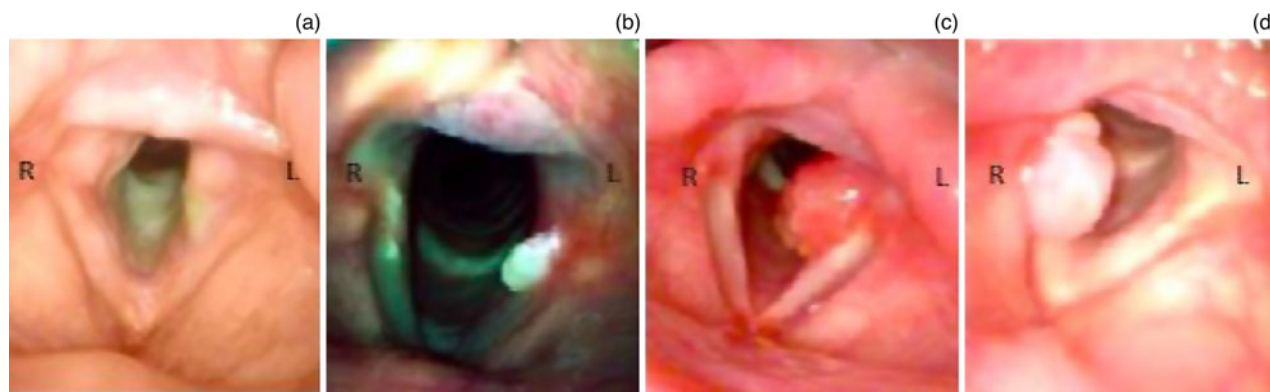


Fig. 5. Various pathologies mimicking arytenoid granuloma: (a) tuberculomas of the vocal process of the arytenoid bilaterally, (b) i-Scan image showing dysplasia of the vocal process of the left arytenoid, (c) pleomorphic adenoma of the left arytenoid, and (d) sarcomatoid carcinoma of the right arytenoid. R = right; L = left

which are similar to other studies.¹⁹ A resolution rate of 75 per cent with combination treatment was achieved in our study, which is similar to that reported in a study by Chen *et al.*, of 72.1 per cent.¹¹ The better resolution of granulomas following combination treatment instead of a single treatment in our study may be because of a better selection of patients, and possibly because of the prolonged treatment duration (i.e. three months). Combination treatment including voice therapy will change vocal behaviour and provide better circumstances for the healing process.³

A multicentre study by Lee *et al.* also claimed that PPI and Botox were effective treatments only in the short term, whereas voice therapy provided significant long-term improvement.⁶

Surprisingly, not many studies have described the duration of conservative treatment with PPI required for the complete resolution of granulomas. Despite conservative management with PPI for three months, 29 per cent of patients in our study had no resolution, which was similar to that reported in other studies.¹⁶ This proves the need for prolonged control of underlying reflux, combined with voice therapy and continuing lifestyle modifications, for the treatment of arytenoid granuloma.^{7,9–11}

The role of surgical management for arytenoid granuloma is unclear and remains controversial, with the majority of studies reporting a high recurrence rate following surgery.^{6,7,11,12} A recent systematic review by Tsai *et al.* reported that 98 per cent of patients treated conservatively and 84 per cent of patients treated with surgery alone improved or resolved.⁸ Surgical treatment is based on the removal of the mass burden, while conservative management is based on reducing inflammation and the alteration of vocal behaviour. Both approaches help in reducing granulomas.⁶ Surgical treatment shows a favourable outcome in the form of immediate improvement of voice parameters such as Voice Handicap Index-10 and maximum phonation time, but there is an increased likelihood of recurrence with surgical treatment alone.⁸ However, larger granulomas affecting voice and causing airway symptoms need to be removed surgically, but this should be followed by a conservative regimen to reduce the risk of recurrence.⁸ Finally, surgical management is also reserved for patients whose condition has not resolved with medical management, or in cases with risk factors for malignant changes, such as smoking and alcohol consumption.^{7,18}

Cold steel excision has been replaced by the use of the laser because of the latter's precise cutting, reduced tissue damage and lower recurrence rate. Different types of lasers, like the KTP laser, the pulsed dye laser and the CO₂ laser, have been

used in out-patient settings and in the operating theatre. The CO₂ laser has become the most popular choice because of its precise cutting and reduced injury to surrounding tissue.⁷ In comparison to CO₂ laser surgery, Hirano *et al.*¹⁴ and Dominguez *et al.*¹⁵ removed arytenoid granulomas using an in-office-based, pulsed KTP laser, and concluded that this is an effective treatment option for arytenoid granuloma. There are no comparative studies that describe the advantages of the CO₂ laser over the KTP laser, or vice versa.

In our study, 82.1 per cent of patients who underwent surgical excision had complete resolution, which is comparable to a study by Lemos *et al.* (90 per cent).¹⁶ Chen *et al.* reported a smaller response rate of 38.9 per cent following CO₂ laser surgery, and this could be because of a lack of adequate conservative treatment before surgery in their patients.¹¹

In our study, the recurrence rate following surgery was 17.9 per cent, which is lower when compared with the majority of studies. For example, Havas *et al.*⁹ reported a 50 per cent recurrence rate, Ylitalo and Lindestad³ reported a 92 per cent rate, and Kobayashi *et al.*¹⁰ reported a 75 per cent rate. The low recurrence rate in our study could be because of the use of the CO₂ laser, which has high precision and offers a bloodless operative field. The use of PPI pre-operatively as well as post-operatively is another factor supported by other studies.⁷

We combined laser surgery with Botox injection in five patients, and achieved complete resolution in all of them. Many studies have highlighted the use of Botox as an adjuvant treatment, as it causes temporary paralysis of the ipsilateral thyroarytenoid muscle, which gives sufficient time for healing.¹⁸ Percutaneous Botulinum toxin has been used as a safe and effective treatment for arytenoid granuloma in patients for whom conventional treatment has failed.^{4,6} There is no consensus regarding the dose and use of Botox injection either during conservative management or during primary or revision surgery.

The use of image enhancement technology, such as narrow-band imaging or i-Scan, in addition to white-light endoscopy, increases the sensitivity for detection of early neoplastic and preneoplastic glottic lesions.²⁰ We used i-Scan (Pentax Medical), and were able to detect a few cases of arytenoid granuloma with abnormal morphological features of dysplasia, as shown in Figure 5b. We advised surgical intervention in these cases. We encountered other pathologies with an appearance of arytenoid granuloma, including pleomorphic adenoma, tuberculosis, dysplasia and amyloidosis, as shown in Figure 5. It has been documented that failure to establish a proper histopathological diagnosis can misdirect definitive treatment.²¹

The cause of arytenoid granuloma is multifactorial and is the result of a complex inflammatory process. Trauma to the laryngeal mucosa is the initial insult, leading to ulceration of the vocal process. This causes chronic inflammation, resulting in the formation of granulation tissue. Surgical removal does not eliminate the underlying cause. Therefore, these patients need to be managed further, depending on their underlying risk factors.⁸ As reported by Tsai *et al.*, the recurrence rate following conservative management is lower compared with surgical management, but this difference did not reach statistical significance.⁸ We believe that surgery has a definite role to play in managing these patients, provided there is a proper combination of conservative management in the pre- and post-operative periods.

- Combination treatment with anti-reflux medication and voice therapy is effective first-line management for arytenoid granuloma
- Pre- and post-surgery adjuvant treatment with proton pump inhibitor and voice therapy improves transoral laser surgery results in selected cases
- Local injection of Botox used with revision surgery was successful in treatment of failed surgical cases
- Careful clinical history and examination should be employed to exclude other pathologies

It has been recently concluded that granulomas with minimal symptoms can be managed conservatively with a low chance of recurrence and a good response, whereas large and symptomatic granulomas require surgical excision followed by conservative management to reduce the chance of recurrence.⁸ Neither this nor the effects of smoking and alcohol consumption have been evaluated in this study. Finally, there is a need for future studies to define the timeline of conservative treatment for complete remission and to determine proper treatment guidelines for managing this rare entity.

Conclusion

Combination treatment with anti-reflux medication and voice therapy is effective first-line management for patients with arytenoid granuloma. Pre- and post-surgery adjuvant treatment with PPI and voice therapy improves the results of transoral laser surgery in selected cases. Local injection of Botox used with revision surgery was successful in the treatment of failed surgical cases. Careful clinical history and examination should be employed to exclude other pathologies.

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Competing interests. None declared

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