ORIGINAL ARTICLE

Factors responsible for the development of carbon granuloma post transoral laser cordectomy

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Abstract

Our study was performed with an aim to analyse the factors responsible for the formation of a carbon granuloma (CG) following transoral laser microlaryngeal cordectomy (TLMC) for early glottic carcinoma. Our study comprises of retrospective data analysis of 78 patients who underwent TLMC for early glottic carcinoma between 2012 and 2017 with the laser settings of an acublade with scanning system, size 1–2 mm, depth 1–3 (250–750 μm), power 10 watts in a repeat mode with time off 0.25 s. A total of 19 patients had undergone type 1 cordectomy, 38 patients a type 2 cordectomy, 20 patients a type 3 cordectomy and 1 type 4 cordectomy. In the follow-up period, patients were divided into two groups—group A, who healed well and group B, who developed a CG. Both groups were analysed based on surgical factors (type of cordectomy, postoperative surface of vocal fold and cautery use) and healing factors (presence of diabetes mellitus and laryngopharyngeal reflux). Of 81 cordectomies, 15 (18.5%) developed a CG at an average period of 4 weeks postoperatively. All 15 patients were managed medically and by 4–8 weeks, 13 carbon granulomas resolved. Surgical excision in 2 patients who did not improve revealed granulation tissue. Of 40 type 2 cordectomies, 9 developed a CG (22.5%); of 20 type 3 cordectomies, 5 developed a CG (25%) and the 1 patient of type 4 cordectomy developed a CG (100%). Patients with cautery use, diabetes mellitus (DM) and laryngopharyngeal reflux (LPR) had a higher rate of CG formation. To summarise, in our study, a CG developed in 18.5% of our TLMC patients at an average postoperative duration of 4 weeks. An algorithm for treating and preventing this type of lesion is recommended.

Keywords Voice/dysphonia · Laryngology · Larynx · Head and neck · Glottic cancer · Carbon granuloma · Healing granuloma · Laser cordectomy

Introduction

Laryngeal cancer is the seventh most common cause of cancer in males in India with the incidence being 1.26–8.18 per 100,000 population [1]. About 95% of laryngeal carcinomas are squamous cell carcinoma with verrucous, neuroendocrine carcinoma and adenocarcinoma rarely seen [2, 3]. Early glottic carcinoma comprises of a spectrum of disease from high-grade dysplasia to T2N0M0 tumours [4]. The treatment of glottic cancer continues to evolve with emphasis remaining on maximising cure rates along with preservation of voice. Currently, the mainstay of treatment for early glottic carcinoma includes either radiotherapy or TLMC, with open partial laryngectomies becoming rarer by the day. Management of early glottic carcinoma has seen a paradigm shift in the last few decades, with TLMC becoming a popular modality of treatment which has gained sufficient acceptance as an oncologically safe and functionally equivalent modality to conventional radiotherapy [5]. Initially reported by Stuart Strong in 1975 [6], but popularised by Steiner [7, 8], this modality has made rapid strides in both the extent and complexity of tumours treated. The short treatment time and minimal loss of workdays compares favourably in a cost-benefit analysis for most patients [9, 10].

Endolaryngeal cordectomies were classified in the year 2000 by the European Laryngological Society as type 1 (subepithelial cordectomy), type 2 (subligamentous cordectomy), type 3 (transmuscular cordectomy), type 4 (total cordectomy), type 5a (extended cordectomies encompassing the contralateral cord), type 5b (extended cordectomies encompassing the arytenoid), type 5c (extended cordectomies

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encompassing the ventricular band) and type 5d (extended cordectomies encompassing the subglottis). The type 6 cordectomy (extended cordectomies encompassing the anterior commissure) was added to the above classification in 2007 [11].

Laser is a tool which permits the precise and controlled haemostatic cutting across tissue planes when warranted. This is not possible to achieve efficiently using cold steel instruments. Thus for type 2 to type 6 cordectomies, use of a laser is essential. However, a type 1 cordectomy can be performed efficiently even with cold steel instruments. The limitations of TLMC include inadequate exposure of the lesion on suspension microlaryngoscopy with a consequent inability to achieve tumour free margins, intraoperative bleeding especially in the case of patients who need to stay on blood thinners, development of postoperative granulation tissue and adhesion formation and occasional aspiration post operatively especially when the disease is excised from the posterior larynx including the arytenoid (type Vb) [12].

Over the last 10 years, we have observed some of our TLMC patients developing a lesion suggesting a CG. With TLMC becoming a standard modality of treatment worldwide, the identification and management of CG that may develop in the healing phase is important. These lesions are pale with a smooth surface, have a spherical shape with no remarkable vascularity around the lesion and have the size of which varies from 1 to 4 mm. We have over time formulated a protocol of managing these lesions. Our study was aimed at the hypothesis that certain high risk factors (surgical and systemic) predispose a patient to develop a CG, and by controlling those factors, the rate of carbon granuloma formation can be reduced. We audited the rate of CG formation in the last 5 years and its response to our treatment. Based on our results over the last 5 years, we have formulated a treatment management protocol and extrapolated this as a preventive regimen for patients who have a higher risk of CG formation.

Materials and methods

Our study is a retrospective analysis of hospital records of 81 cordectomies performed for early glottic carcinoma in 78 patients between January 2012 and January 2017 (5 years), where long-term follow-up records were available. Our study included a total of 78 patients of early glottic carcinoma who had been treated by TLMC and had regularly followed up as identified from the hospital database. Patients with early glottic carcinoma who were treated with radiotherapy were not included in the study. Out of the 78 patients, 76 were male and 2 were females. These 78 patients were then divided into two groups (Fig. 1) based on the stroboscopy findings (Olympus CLL–S1 Strobe system, Olympus Medical Systems Corporation, Tokyo, Japan) in the postoperative
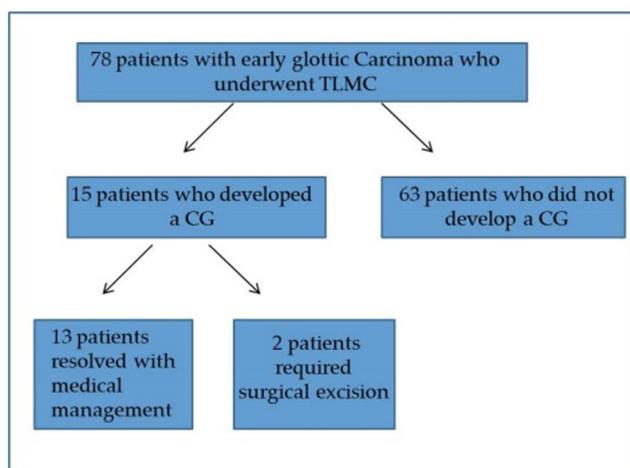

Fig. 1 Diagrammatic representation of patients included in the study

period as per records. Group A comprised of patients who healed well post laser cordectomy (63 patients) and group B included patients who had developed a carbon granuloma (Fig. 2) post laser cordectomy (15 patients). Medical records of these 78 patients were reviewed to identify the presence of comorbid conditions like diabetes mellitus or other immunocompromised states, history of smoking or tobacco use and also to review the intraoperative notes pertaining to cautery use (Valleylab- Force FX Electrical Unit Cautery machine, Medtronic, Minneapolis, USA) to achieve haemostasis during surgery and the type of cordectomy performed. The analysis of the types of endolaryngeal surgery performed on these 78 patients is as follows: in 19 patients, a type 1 cordectomy (1 patient had undergone bilateral type 1 cordectomy), in 38 patients, a type 2 cordectomy (2 patients had undergone bilateral type 2 cordectomy), in 20 patients, a type 3 cordectomy and only 1 patient (female) had undergone a type 4

Fig. 2 A left vocal fold 3–4 mm smooth, pale, spherical and evenly contoured carbon granuloma seen post transoral laser microlaryngeal cordectomy

cordectomy. This patient had previously received radiation therapy for cancer of the same vocal fold 10 years back at another institute. No other patient in our study group had received pre- or postoperative radiation therapy. The endolaryngeal cordectomies were all performed by the first author with a CO_2 laser AcuBlade with a scanning system (Lumenis Limited, Yokneam, Israel) along with a plume evacuator. The settings used were an acublade size of 1–2 mm at 10 watts in repeat superpulse mode (time on—0.03 s and time off—0.25 s) with depth penetration between 250 and 500 μm. The recordings of these surgeries along with the postoperative photo records were reviewed to note the surface of vocal folds at the end of surgery, intraoperative cautery (coagulation—15 watts) use and exposure of the thyroid cartilage. Patients with DM were all cases of secondary DM and were controlled before surgery by the endocrinologist. During the postoperative period, all patients were administered oral antibiotics (Tablet Ceftum, 500 mg, GlaxoSmithkline Pharmaceuticals Ltd., Nashik, Maharashtra, India) twice a day for 3 days, proton pump inhibitors (Tablet Pan40, Alkem Laboratories Ltd., Taloja, Maharashtra, India) before breakfast for 1 month, paracetamol (Tablet Dolo 650 mg, Micro Labs Ltd., Hosur, Tamil Nadu, India) thrice a day for 5 days and trypsin-chymotrypsin tablets (Tablet Chymoral forte, 100,000 units, Torrent Pharmaceuticals Ltd., Dahej, Gujarat, India) thrice a day for 10 days. Postoperatively, in the first year, the patients were followed up at 1 week, 1 month, and 3 months and then at 4-monthly interval. However, if the patient developed a CG, the patient was put on a medical line of treatment consisting of tapering doses of oral methylprednisolone (Tablet Predmet 8 mg, Sun Pharma Laboratories Ltd., Halol, Gujarat, India) three times a day for 5 days followed by twice a day for 5 days, followed by once a day for 5 days and finally 4 mg once a day for 5 days after meals, PPIs (Tablet Pan-40, 40 mg twice a day before meals) for a month, 15 ml of alginate (Syrup Gaviscon, Reckitt Benckiser Group, Baddi, Himachal Pradesh, India) after dinner for a month and nebulisation of 2–5 ml of steroid (Budesal 0.5 mg respules, Cipla Ltd., Pune, Maharashtra, India) followed 20 min later by sterile water nebulisation (Amanta healthcare Ltd., Hariyala, Gujarat, India) for 3 min. The sterile water nebulisation was advised to prevent fungal laryngitis post steroid nebulization. They were also advised to talk for a maximum of 15–20 min per hour in a confidential voice and guided accordingly by the voice therapist. Confidential voice is when the patients talk in a soft voice as if speaking confidentially but not a whispered tone and is designed to reduce laryngeal tension and facilitate relaxation in the laryngeal musculature. The patients were called for follow-up every month till the CG resolved.

Results

Of the 81 cordectomies performed for early glottic carcinoma, 15 patients presented with a lesion suggestive of a CG, usually at around 4 weeks postoperatively. Of these 15 patients who developed a CG, 9 had undergone type 2 cordectomy, 5 had undergone type 3 cordectomy and 1 a type4 cordectomy (Fig. 3). Thus, of the 40 type 2 cordectomies, 9 developed CG (22.5%) and of the 20 type 3 cordectomies, 5 developed CG (25%), suggesting that irregular healing margins in type 3 cordectomy (transmuscular) probably lead to a slightly higher CG formation rate as compared to type 1 and type 2 cordectomies. Cartilage exposure may probably be the underlying cause for the formation of a CG in type 4 cordectomy; in our series, we had only 1 type 4 cordectomy (100%).

In patients where intraoperative cautery usage was more, there was a higher rate of CG formation in the postoperative period. Cautery was not used in any patients undergoing type 1 cordectomy and no patient of type 1 cordectomy developed a CG. In patients undergoing a type 2 cordectomy, of the 9 cases that developed a CG, cautery was used in 6 (66.66%), of the other 31 cases who did not develop a CG, cautery was used in 12 (38.7%). Similarly in patients with type 3 cordectomy, in all the 5 patients that developed a CG, cautery was used during surgery to control the bleeding while dissecting through the muscle (100%) and of the remaining 15 cases that did not develop a CG, 13 had intraoperative cautery usage (86.6%). These results reveal that in patients where cautery was used during surgery, chances of developing a CG were higher.

Patients with DM and LPR also had a higher rate of developing CG than patients who did not have DM or LPR. Of the 15 patients of CG, 6 had DM (40%), and 12 (80%) patients had signs and symptoms of LPR (symptoms: lump sensation the throat, clearing of throat, coughing after lying down, troublesome cough, choking episodes, heartburn, indigestion and stroboscopic findings of diffuse vocal fold oedema, erythema, posterior commissure hypertrophy, thick endolaryngeal mucus). We used the Belafsky Grading system to identify patients with features of LPR [13]. Of the 63 patients who did not develop a CG, 15 (23.8%) patients had DM and 38 patients (60.3%) had LPR, thus suggesting that patients with DM and LPR were more prone to develop a CG.

Out of the 15 patients who developed a CG, the lesion resolved completely with medical management (Fig. 4) in 13 patients (86.6%) within 4–8 weeks. In patients with DM, the same treatment regimen was followed along with an increased dose of oral hypoglycaemic agents/insulin, if needed, after consulting the concerned endocrinologist. In the 2 patients in whom the CG persisted in spite of medical management for more than 2 months, both the patient and their referring physician were apprehensive and wanted a histopathological diagnosis to rule out tumour recurrence. A bronchoscopic

Fig. 3 Diagrammatic table representation of the cases in the study that developed a CG

TYPE OF CORDECTOMY	TYPE 1	TYPE 2	TYPE 3	TYPE 4
Total No. Of Cases	20	40	20	1
No. of Patients who developed CG	0	9	5	1
Percentage of patients who developed CG	0	22.5%	25%	100%

excision was performed for one patient who had a small polypoidal CG under local anaesthesia, and in the other patient who had a multilobed broad-based CG, we performed a microlaryngoscopic excision under general anaesthesia so as to enable complete excision with precision and haemostasis and also achieving a smooth surface post excision. The histopathological examination of both the lesions revealed benign polypoidal tissue with granulation and nonspecific inflammatory changes which is the same as a reparative or a healing granuloma [14]. No patient in our study developed a CG after 1 month of undergoing TLMC.

Discussion

The last two decades has seen a marked rise in the use of laser for the management of early glottic carcinoma. The CO_2 laser has been considered as the workhorse in laryngeal surgeries, more so with the acublade and scanning system enabling a char-free surgery. The user of medical lasers should appreciate the mechanism of action of lasers especially with regard to the representative zones of injury created, with the layer of carbonisation due to the interaction of the laser beam with tissue surface, layer of vaporisation due to explosive conversion of water to steam, layer of coagulation due to denaturation of proteins and collagen and layer of hyperaemia [15]. One of the principal advantages of CO_2 laser over other types is that there is very little evidence of the thermal damage extending below the surface of the wound created. Minimising the extent of such tissue damage is essential as extensive damage impairs tissue healing and pre disposes to inflammation [16]. Despite the use of the CO_2 Acublade laser with the settings in repeat mode with a depth of 250–500 μm, we noticed a relatively large number of patients developing a CG in our series, and this warranted an audit of our results and this forms the rationale behind our study.

Betlejewski et al. first described laser carbon granulomas in 2005. In their study of 167 cases of SCC of the larynx in which laser cordectomies were applied, they found 3–5 mm spherical, evenly contoured granulomas in the central area in 14 patients (8.3%) during 1–6 month follow-up [17]. In a study done by Burak et al. in 2016, 4 out of a total of 35
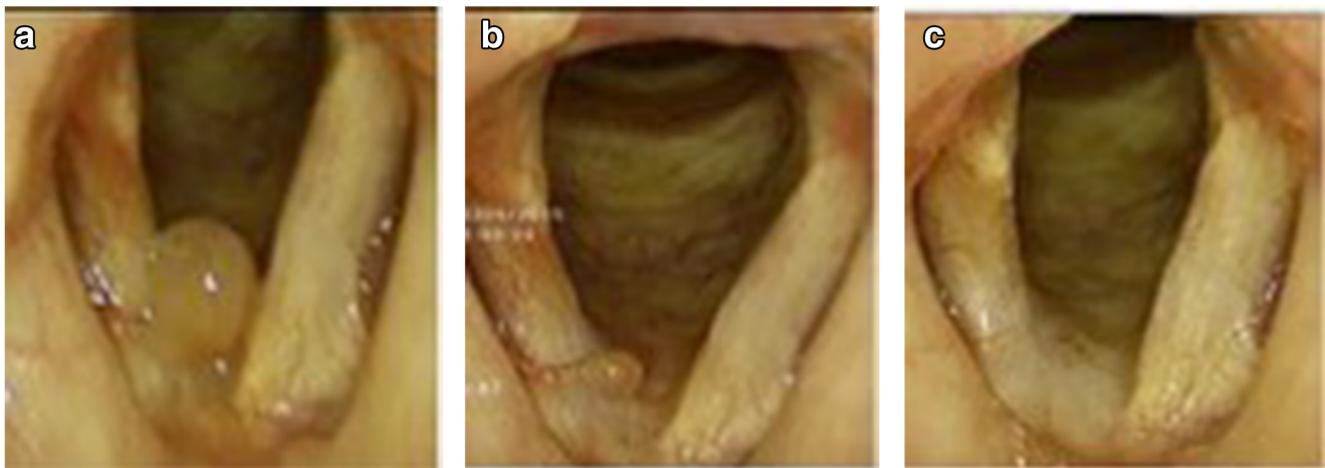

Fig. 4 A right vocal fold carbon granuloma following a type 4 cordectomy is seen in different phases of resolution with medical management. **a** Before medical management. **b** After 1 month of instituting medical management. **c** After 2 months of instituting medical management

patients (11.4%) developed a spherical and evenly contoured lesions located in the rear and central zone [18]. Caused by the thermal effects of laser or as a defect in the healing process during postoperative period, spherically structured carbon granulomas in the healing phase can be confused with tumour recurrence (Fig. 5) [18]. The development of a CG is unique to the surgery performed with laser as such lesions were not observed in other than laser microlaryngeal cordectomies [17].

In our study of 78 patients of laser cordectomy for early glottic carcinoma, 14 patients developed a lesion in the membranous part of the vocal fold and 1 in the posterior part of the healing vocal fold, at an average time of 4 weeks postoperatively. Our overall rate of CG formation was 18.5%, which was higher than the rate reported by Burak et al. (11.4%) and Betlejewski et al. (8.4%) [17, 18].

Thus, we did a retrospective analysis of the possible factors responsible for the development of a CG and divided them into surgical factors and healing factors. The first factor analysed was the type of cordectomy performed. Of the 40 type 2 cordectomies, 9 developed a CG (22.5%), of the 20 type 3 cordectomies, 5 cases (25%) developed CG and the only type 4 cordectomy performed developed a large multi-lobed CG (100%). This suggested that irregular healing margins, which are often the result of cutting through the muscle in type 3 cordectomies, lead to higher CG formation as compared to types 1 and 2 cordectomies. This is probably because of the fact that the plane of cleavage for surgery is well defined in both type 1 and type 2 cordectomy. In type 1 cordectomy, we removed the epithelium and SLP leaving the vocal ligament intact, and in type 2 cordectomy, we removed the epithelium and vocal ligament leaving the vocalis muscle intact, whereas in a type 3 cordectomy, the plane of cleavage was not well defined, and the dissection is arbitrarily through the muscle layer, thus leaving behind an irregular surface (Fig. 6) which probably predisposes to irregular healing of wounds and hence granuloma formation. When we compared the surface of the vocal fold at the end of the surgery, all our type 2 cordectomy had a relatively smoother surface (Fig. 7) as compared to type 3 which had an irregular carpet of muscle layer
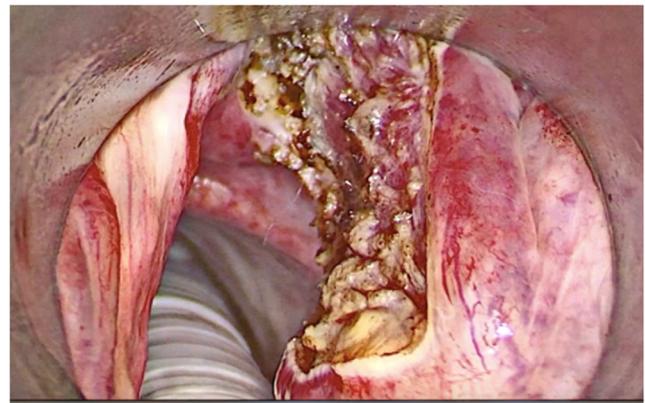

Fig. 6 Irregular muscular surface at the conclusion of a type 3 (transmuscular) cordectomy performed on the right vocal fold

left behind. This irregular surface possibly affects the healing process and was consistent with our study results, where patients with type 3 cordectomy had a higher rate of developing CG as compared to type 2 cordectomy. Another surgical factor studied was the use of cautery during the intraoperative period. While performing a laser cordectomy, one can encounter diffuse bleeding which needs to be controlled occasionally using a surgical cautery. This increases the risk of thermal damage and thus predisposes to CG formation, as was seen in our study.

Study conducted by Burak et al. revealed a higher rate of carbon granuloma formation in type 4 cordectomies, thus suggesting that the contact between the cartilage and the laser increases the probability of CG formation [18]. In our study, we had only 1 patient of type 4 cordectomy who did develop a large carbon granuloma. It is known that patients with DM have impaired healing process as they are more prone to develop postoperative infection and inflammation and have immune-deficiency and impaired blood circulation [19–21, and]. All these factors can alter the healing process post cordectomy and predispose to CG formation. Similarly, in laryngopharyngeal reflux, the acid, pepsin and bile acids can cause inflammation and impair healing [22]. This was consistent with our study as patients with DM and LPR had a higher rate of carbon granuloma formation. Smoking can also be a risk factor as it impairs

Fig. 5 **a** A right vocal fold carbon granuloma seen on strobe light with overlying keratosis giving an appearance of possible tumour recurrence. **b** narrow-band imaging evaluation of the same lesion suggesting benign nature
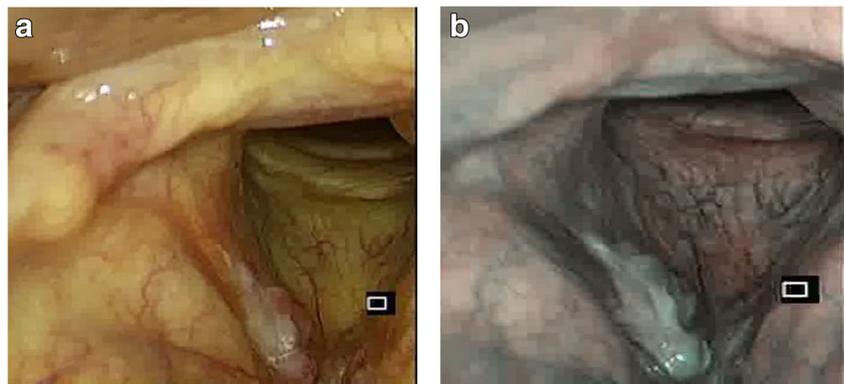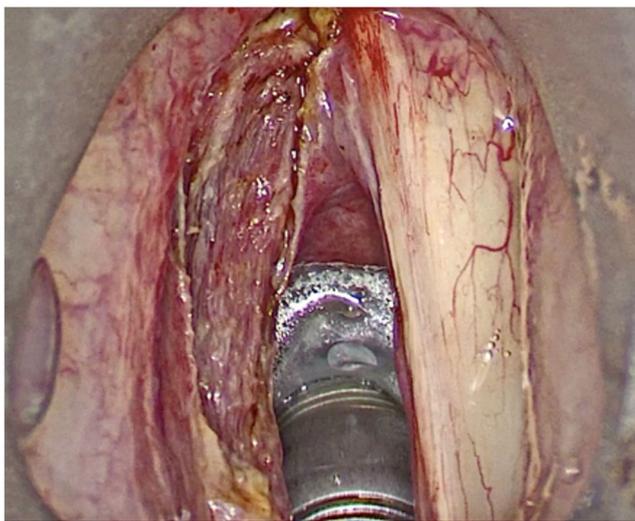
Fig. 7 Smooth surface seen at the conclusion of a type 2 (sub-ligamental) cordectomy performed on the left vocal fold

healing, but most of our patients had prior history of smoking and use of tobacco, so we did not consider it in our study. This suggests that our hypothesis, stating certain surgical and healing factors increase the risk of CG formation is true.

Of the 15 patients who developed a CG, 13 (86.6%) resolved with medical management. Of the 15 patients, 2 patients did not respond and were keen to undergo a surgical excision at 3 months postoperatively. Of the 2 patients that required surgical excision, 1 patient was a known diabetic who developed a CG after undergoing type 2 cordectomy, and although the size of the granuloma regressed with medical management, it did not resolve completely. The patient was apprehensive and wanted it excised, so a bronchoscopic excision was performed under local anaesthesia. The second patient had developed a multilobed polypoidal CG post type 3 cordectomy and was operated under general anaesthesia, so as to achieve a complete excision with a smooth surface postoperatively. In both these patients, the granuloma was sent for histopathological examination which revealed benign polypoidal tissue with nonspecific granulation and inflammatory tissue.

Keeping our study factors in mind, we propose the following methods to reduce the rate of CG formation: achieving a smooth postoperative plane of the surface of the vocal fold, reducing the use of intraoperative cautery by pre- and intraoperative haemostatic local infiltration, which not only helps in achieving haemostasis but also helps in hydro dissection preoperatively. The frequent use of cotton balls soaked in haemostatic solution to control diffuse ooze also helps to reduce the cautery use. Finally, controlling the comorbid conditions such as diabetes and LPR preoperatively also plays a crucial role. LPR should be controlled with either lifestyle modifications or pharmacological intervention with PPI and

Alginates for 2–3 months duration as per the current guideline [23]. All our patients were advised moderate vocalisation (15–20 min per hour in a confidential voice) and relaxation therapy a week after surgery by a speech and language pathologist. This seems necessary to prevent wrong compensatory techniques of phonation developing in the patients.

On the basis of our study, when patients have high risk factors for developing a CG, such as cautery usage intraoperatively, irregular surface at the end of surgery (type 3 cordectomies), signs and symptoms of LPR and history of DM, we now suggest giving a prophylactic treatment regimen comprising of steroids (oral/ nebulization) and PPIs for a longer duration (minimum 3 months) in the postoperative period. We propose to now audit our results (prospectively) having instituted these new protocols to evaluate the rate of CG formation.

Conclusion

The high-risk factors responsible for a CG formation are irregular postoperative healing surface, intraoperative cautery use, diabetes mellitus and LPR. Carbon granulomas respond well to a medical line of treatment involving oral tapering dose steroids and inhalational steroids, PPIs and alginates. Ours is an on-going study, where we plan to prospectively audit our CG formation rate after having implemented all our study recommendations.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval Required ethical approval taken from Bombay Hospital Ethics Approval Committee.

Informed consent Application for waiver of consent form given to the Bombay Hospital Ethics Committee and approved since our study is a retrospective observational study.

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