Operative technique in laryngeal paraganglioma: A case series and literature review

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Abstract

Background: Laryngeal paragangliomas (LP) comprise a rare subset of head and neck neoplasms and are an important differential in the patient with a submucosal laryngeal mass.

Methods: We discuss an operative technique using coblation assisted excision via laryngofissure in the cases of four confirmed LPs and discuss the current literature with respect to diagnosis and management of these patients.

Results: Our case series of four patients demonstrate the laryngofissure approach for LP is safe, provides oncological cure and preserves laryngeal function. This technique with coblation has not been previously discussed in the surgical management of LPs. Patient-reported postoperative voice and swallowing outcomes were excellent in all patients. Whole body imaging techniques were utilized in all patients, with octreotide scintigraphy demonstrating synchronous lesions in two of the four patients—one had a retroperitoneal lesion, whilst another patient had multiple lesions in the skull base, paravertebral region, liver, and adrenal gland.

Conclusions: Our cases also highlight the changing clinical paradigms in the diagnostic approach of LPs and an emerging role for octreotide scintigraphy in the workup of these patients. Coblation assisted excision via laryngofissure is efficient and effective in the surgical resection of LP. In patients with multicentric forms of LP, the size, side, and anatomic location of synchronous lesions should be considered in surgical planning to determine feasibility and safety of operative management.

Level of Evidence: IV

KEYWORDS

case series, laryngofissure, larynx, operative technique, paraganglioma

Abbreviations: 2SC, 2-succinocysteine; CT, computed tomography; FNE, flexible nasendoscopy; LP, laryngeal paraganglioma; MRI, magnetic resonance imaging; PET, positron emission tomography; SDH, (succinate dehydrogenase).

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Paragangliomas are rare neoplasms derived from neural crest derivatives arising from autonomic paraganglion. Head and neck paragangliomas are usually derived from parasympathetic structures and commonly involve the carotid body, Jacobson’s nerve on the tympanic promontory, and the adventitia surrounding the jugular bulb inferior to the tympanic cavity and the vagus nerve.\(^1\) Laryngeal paragangliomas (LP) comprise a minor subset of head and neck paragangliomas, arising from the superior or inferior paraganglia, with the overwhelming majority of these located in the supraglottis. They are usually nonfunctional, unifocal, and sporadic, though associations with hereditary conditions occur in 30–40% of these cases.\(^1\)

Multicentric forms of LP have been reported, with synchronous lesions discovered in the head and neck, typically in the carotid body,\(^2\) jugulotympanic cavity,\(^3\) or skull base.\(^4\) The diagnostic workup involves biochemical testing to exclude catecholamine hypersecretion, genetic testing, and multimodal imaging of the lesion. Transcervical and microlaryngoscopy with transoral biopsies are unfavorable due to the risk of bleeding with vascular lesions.\(^5\,6\) The emergence of whole-body screening with octreotide scintigraphy allows detection of smaller tumors and synchronous lesions, as paragangliomas express somatostatin receptors.\(^7\) It enables differentiation between paragangliomas and other differential diagnoses including other neuroendocrine tumors of the larynx, nerve sheath tumors, hemangiomas, chondroma and chondrosarcomas, and laryngoceles.

Definitive treatment of LP involves conservative surgical excision with complete resection of the lesion with aim to preserve laryngeal structures.\(^5\) An external cervical approach is favored as it provides a good surgical field with the advantage of easy vascular control. Current approaches involve lateral pharyngotomy, lateral thyrotomy, and laryngofissure. The aim of this study is to describe an approach to resection of LP with coblation, which has not been previously reported in the literature. Coblation wands may offer advantages in laryngeal surgery by minimizing thermal damage to surrounding tissue (which aids postoperative voice outcomes), achieving better intraoperative hemostasis to facilitate a bloodless surgical field when operating on vascular tumors, reducing operating times, and providing easier access to difficult to reach areas including working around corners.\(^8\,9\) In addition, we present a case series of four patients with LP, providing a comprehensive review of current diagnostic paradigms and management strategies. LP with multicentric lesions are rare, and we present two such cases, including the first synchronous lesion outside the head and neck region and one case with metastatic paraganglioma affecting the bilateral skull base, paravertebral region, liver, and adrenal gland. In the context of these cases, we discuss the approach to surgical planning in LP with synchronous disease.

## 2 | CASE 1

### 2.1 | Case presentation

A 62-year-old man presented with progressive symptoms of dysphagia to solids, odynophagia, throat pain, and dysphonia over a 3-year period. He was a lifetime nonsmoker. Examination with video laryngoscopy revealed a submucosal mass involving the left aryepiglottic fold mass and false cord, which obscured visualization of the left glottis and true vocal cord (Figure 1). There were no palpable neck masses.

### 2.2 | Investigations

Concurrent CT and MRI imaging demonstrated a vascular supraglottic lesion, strongly suggestive of LP (Figures 2 and 3). A 68-Gallium Dotatate...
case presentation

A 34-year-old nonsmoker presented with a 2-year history of dysphonia without throat pain, deglutition symptoms, or dyspnea. He was otherwise fit and well with no medical comorbidities. FNE revealed a vascular, pulsatile mass in the right supraglottis with sparing of the false and true vocal cords. Effacement of the right pyriform fossa was noted.

3.2 | Investigations

A CT neck showed a well-defined 28 × 26 × 35 mm hypervascular right supraglottic mass with extension through the piriform fossa and sparing of bilateral vocal cords (Figure 7). No cervical lymphadenopathy was noted. A PET FDG scan showed an avid lesion (SUVmax 7.1) that extends slightly beyond the midline. A preoperative balloon occlusion study and formal digital subtraction angiogram was performed, identifying the right superior laryngeal artery as the feeding vessel. Biochemical screening with plasma and urinary metanephrine panels excluded secretory paraganglioma.

4 | CASE 3

4.1 | Case presentation

A 33-year-old male nonsmoker presented with an 8-month history of left sided neck mass without dysphonia, dyspnea, or deglutition symptoms. Physical examination was unremarkable. FNE showed a supraglottic lesion with involvement of the left false cord.

4.2 | Investigations

An MRI neck showed a small, T2 enhancing lesion within the left thyroid cartilage measuring 9 × 6 mm, corresponding with CT images (Figure 8). Reactive edematous change of the left inferior belly of the neck was noted.
FIGURE 5  Intraoperative photos showing the (A) presence of the left supraglottic paraganglioma, (B,C) a view of the endolarynx post complete en bloc resection, and (D) the resected laryngeal paraganglioma specimen.

FIGURE 6  Surgical technique showing the (A) left supraglottic paraganglioma after laryngofissure, (B, C) paraganglioma dissected off of paraglottic soft tissue and slowly removed from the endolarynx, and (D) use of coblation wand to assist dissection of the lesion.
omohyoid was noted on MRI. A PET FDG scan showed low grade avidity (SUVmax 2.1) within this region.

5 | CASE 4

5.1 | Case presentation

A 48-year-old female nonsmoker presented with a known history of metastatic paraganglioma, over 15 years, with FNE showing a submucosal vascular lesion of the left supraglottis with bulging of the false vocal cords (Figure 9). Multiple somatostatin-rich foci were noted on serial 68-gallium DOTATATE PET scans, including the larynx (Figure 10). Octreotide avid lesions were noted in the right and left skull base (SUVmax 87.5 and 53, respectively), the left paravertebral region at C2 (SUVmax 142), the left supraglottis (SUVmax 68.5), the left lobe of the liver (SUVmax 30.7), and the right adrenal gland (SUVmax 46.7). The patient had a preoperative transcervical biopsy of the supraglottic lesion, which confirmed the diagnosis of paraganglioma, however was complicated by postprocedural stridor and supraglottic edema. She was admitted briefly to ICU for close monitoring and a weaning course of steroids.

6 | RESULTS

The four cases are summarized in Table 1. Histopathology of the lesions in each case confirmed the diagnosis of LP with characteristic Zellballen pattern with central chief cells and peripheral sustentacular cells. The lesions were unencapsulated and highly vascular with lobules of congested blood vessels. In case 1, immunohistochemistry confirmed positive synaptophysin and chromogranin staining of chief cells and S-100 of sustentacular cells. CAM5.2 staining was negative and Ki67 staining showed low proliferative index. Genetic testing with
immunohistochemistry showed negative staining for SDHA and SDHB, with dual loss strongly consistent with a germline SDHA mutation. Further testing showed positive staining for fumarate hydratase and negative staining for 2SC, which is the normal pattern and excludes fumarate hydratase mutation. In case 2, immunohistochemistry confirmed positive synaptophysin and chromogranin staining of chief cells and S-100 staining of sustentacular cells. Genetic testing was consistent with SDHB germline mutation. In Cases 3 and 4, immunohistochemistry showing positive of chief cells with CD56, synaptophysin, and chromogranin, and of sustentacular cells with S-100.

7 | OPERATIVE TECHNIQUE

Perioperative airway management is of utmost importance in the surgical treatment of patients with LP. Patients underwent awake fibreoptic oral intubation, with video assistance ensuring trauma is avoided. Each patient underwent an external cervical approach via laryngofissure technique with complete resection of the paraganglioma using coblation assistance.

A horizontal anterior cervical incision was created within a natural skin crease and subplatysmal flaps elevated. The thyroid isthmus and strap muscles were identified and divided, and the thyroid cartilage was freed from muscle attachments with exposure of the thyrohyoid membrane. A perichondrial flap was elevated. The feeding vessels, often the superior laryngeal or superior thyroid vessels, were identified, ligated, and divided, with preservation of accompanying superior laryngeal nerves. In some patients, preoperative angioembolization of the feeding artery was performed to minimize intraoperative bleeding. A laryngofissure with midline thyrotomy was performed, allowing visualization of the endolarynx and identification of the paraganglioma. In some cases, preplating of the thyroid cartilage was used to aid symmetrical closure. The internal branch of the superior laryngeal nerve was identified and protected. A combination of coblation (EVAC Xtra HP coblation wand EIC5874-01, Smith+Nephew) and blunt dissection with adrenaline-soaked neuro patties was used, essentially peeling the lesion off of the underlying mucosa, thyroid cartilage perichondrium, and paraglottic soft tissue using meticulous technique. This helped to provide a bloodless surgical field. The lesion is then mobilized and excised en bloc with preservation of the true vocal cords (Figures 5 and 6). The mucosal defect at the site of the

| TABLE 1 | Summary of case presentation of laryngeal paraganglioma in a series of four patients |
|----------|----------------------------------|
| Characteristics | Study cohort (n = 4) |
| Average age | 44 ± 14 |
| Male gender | 3 |
| Laryngeal paraganglioma | |
| Supraglottic | 4 |
| Left sided | 3 |
| False cord involvement | 3 |
| True cord involvement | 0 |
| Functional (secretory) | 0 |
| Diagnostic modalities | |
| CT | 4 |
| MRI | 2 |
| Octreotide scan 68-Gallium DOTATATE | 2 |
| PET FDG scan | 2 |
| Preoperative biopsy | 1 |
| Synchronous lesions | 2 |
| Management of LP | |
| Preoperative angioembolisation | 1 |
| Surgical resection by laryngofissure | 4 |
| Radiotherapy | 0 |
| Octreotide therapy | 0 |
| Management of synchronous lesion | |
| Laparoscopic resection of para-aortic mass | 1 |
| Conservative management with serial imaging | 1 |
| Histopathology | |
| Paraganglioma | 4 |
| Genetic etiology | 2 |
| SDHA mutation | 1 |
| SDHB mutation | 2 |
| Postoperative outcomes | |
| Voice deficit | 0 |
| Swallowing deficit | 0 |
| Recurrence at 6 month follow-up | 0 |
excised lesion was repaired with absorbable sutures. Hemostatic matrix agents can be used as an adjunct due to the vascular nature of these lesions; in Case 2 Floseal was utilized. The laryngofissure is then closed and good approximation of the vocal cords is ensured. Low profile titanium plating was used to close the laryngofissure in two of the cases, where the thyroid cartilage was sufficiently ossified. Alternatively, nonabsorbable monofilament was used in the other cases to close the laryngofissure. The strap muscles were reapproximated. A tracheostomy is optional and dependent on patient, airway and tumor factors as well as surgical and anesthetic team preference—this was used in cases 1, 2, and 4. The patients with tracheostomies were admitted to ICU postoperatively. Decannulation was achieved early in the postoperative course once FNE showed resolution of postoperative laryngeal edema. The patient’s diet was slowly upgraded with input from speech pathologists.

OUTCOME AND FOLLOW UP

All tracheostomized patients were successfully decannulated during their hospital admission and discharged without complications. All achieved excellent patient-reported voice and swallow outcomes with resolution of dysphonia, comprehensible speech, and maintenance of a full diet without issues such as aspiration. FNE at 1 month, 3 months, and 6 months showed no recurrence of disease. The patient in Case 1 was referred to a general surgeon for opinion and management of the para-aortic lesion. He underwent laparoscopic excision of the mass, which was confirmed as a synchronous paraganglioma. The patient in Case 2 had a mild glottic insufficiency with a well-compensated 2 mm glottic gap and no obvious submucosal recurrence. A postoperative 68-gallium DOTATATE scan and MRI showed no persisting disease. He was referred to an Endocrinologist and geneticist for counseling. In Case 3, the patient had no further symptoms at follow-up with normal FNE at 6 months. The patient in Case 4 is planned for close surveillance with yearly whole-body scintigraphic imaging to monitor the size of the synchronous skull base lesions. Due to difficult surgical access, risk of iatrogenic cranial nerve injury, and lack of symptoms, a discussion between patient and surgeon reached a consensus for conservative management. All patients require close monitoring with serial examinations and FNE to monitor for recurrence of disease.

DISCUSSION

The surgical approach to the management of symptomatic laryngeal paraganglioma is conservative, due to its benign characteristics, with complete excision of the lesion and conservation of surrounding structures. A neck dissection or permanent tracheostomy is not indicated in these patients. In our case series, we performed a voice-sparing surgery with maintenance of laryngeal speech and preservation of swallow function. The indication for surgical intervention in patients with LP should be carefully considered and discussed with the patient. As these lesions are benign, close monitoring for tumor growth with serial imaging and FNE is a consideration. Our patient cohort was symptomatic with discomfort or deficits in speech or swallowing, with surgical resection providing a curative option. Clinical and radiographic features should be considered in the decision-making process, with the goal of functional preservation of the larynx with relief of symptoms associated with tumor presence.

We describe an operative technique involving excision of LP using a laryngofissure approach with coblation assistance. Coblation involves low-temperature radiofrequency ablation to create a controlled plasma field between the two electrodes of the coblation wand, allowing for precision excision of soft tissues. The technique has been widely implemented in head and neck surgery, and has been described previously for the endoscopic resection of intranasal and sinus and base of tongue paragangliomas. We present a case series of transcervical resection of a laryngeal paraganglioma using laryngofissure, with assistance from coblation. Our technique was performed successfully, without complications, and postoperative laryngoscopy showed no remaining tumor. An external cervical approach with laryngofissure was adopted in all cases as we find improved postoperative swallow and voice outcomes and optimal vascular control. The technique provided excellent exposure and access to the lesion, with better visualization allowing for full tumor clearance without the need for postoperative adjunctive therapies. Tracheostomy provides a definitive airway in the patient with expected postoperative laryngeal edema. The coblation wand allowed access to difficult-to-reach areas within the surgical field and work around corners. Other benefits we found with coblation were easier dissection of the lesion off of the surrounding paraglottic soft tissue and minimal thermal damage to the adjacent structures, which was particularly important for voice-preservation surgery. The coagulation function in coblation was beneficial for vascular control and provided an essentially bloodless surgical field. The need for tracheostomy following excision of LP is dependent on patient and tumor factors, including disruption of laryngeal mucosa, anatomical location of the lesion, and involvement of the arytenoid. The lateral thyrotomy approach, if feasible, can also be used to minimize airway edema and reduce the need for tracheostomy.

An alternative approach is transoral endoscopic approach, which is technically complicated by decreased access and difficulty controlling hemorrhage, which can obscure the narrow field of view. It is associated with greater recurrence rates and has been largely replaced by the external cervical approach.13 The endoscopic technique is further limited to the endolarynx and is not feasible in paragangliomas that demonstrate extension into the extralaryngeal spaces. Additional techniques that have been described include microlaryngoscopy with laser excision and transoral robotic resection, though neither have garnered favor over the external cervical approach. The conventional external approach is advantageous as direct access and visualization of the tumor is beneficial in controlling bleeding and working around tumor margins.

Isolated external radiotherapy has been described in few studies, though this modality only halts further tumor progression and has no role in inducing regression of the mass. Hence, there are
higher rates of recurrence in these patients. Surgical resection is advantageous over radiotherapy in terms of providing tumor clearance, allowing definitive airway management, and avoiding complications such as reduced cervical mobility, swallowing disorders, and chondronecrosis. There is no role for postoperative adjuvant radiotherapy as paragangliomas do not demonstrate malignant behavior. Octreotide-based therapy has been described in unresectable head and neck paragangliomas and metastatic neuroendocrine tumors of the gastrointestinal and bronchopulmonary tracts. It has a role in limiting tumor growth and ameliorating symptoms associated with catecholamine hypersecretion. However, paragangliomas of the larynx are typically nonsecretory, well localized and amenable to surgical resection via the external cervical approach.

Preoperative angioembolization of the feeding artery is a consideration in patients with LPs and can minimize intraoperative bleeding and create a more favorable surgical field. In Case 2, angiography was performed without decision to embolize. In an external cervical approach vascular control is good and we find that these vessels can be readily ligated. The need for supraselective embolisation is generally not needed unless the tumor is massive (>30 mm), herniating through the thyrohyoid membrane and presenting as a neck mass, or causing airway obstruction. In these cases, there is clinical concern with significant anticipated blood loss.

Our cases further highlight the evolving paradigm in the diagnostic approach to laryngeal paragangliomas due to advances in imaging modalities and surgical techniques. Earlier studies emphasized the importance of confirming a preoperative diagnosis with biopsies as the main diagnosis of exclusion is a neuroendocrine tumor of epithelial origin, which includes typical and atypical carcinoid tumors and small cell neuroendocrine carcinomas. These lesions are aggressive with high malignant potential, often requiring an aggressive surgical approach with radical resection and neck dissection. Recent studies have endorsed a biopsy-sparing approach as seen in Case 1. In the cases described above, there was strong clinical suspicion to suspect a non-epithelial neuroendocrine tumor of the larynx as the patients were young and nonsmokers without risk factors for aggressive malignancies. Furthermore, FNE showed normal mucosal appearance with submucosal fullness. Identification of a major feeding vessel and the presence of synchronous somatostatin-avid lesions further substantiates the diagnosis of paraganglioma compared to neuroendocrine carcinoma.

Paragangliomas have distinctive imaging characteristics on contrast-enhanced CT/MRI and, like other neuroendocrine tumors, express somatostatin receptors that can be detected with octreotide scintigraphy. Incorporating multimodal cross-sectional and functional imaging techniques obviates the need for biopsy, allowing a presump-tive preoperative diagnosis to be obtained. Biopsies are typically performed via a transoral microlaryngoscopy approach and involve the unnecessary risk of bleeding from the highly vascular lesion and difficulty achieving hemostasis using endoscopic approach. The risk of postprocedural laryngeal edema and threatened airway is a possibility as well.

Octreotide scintigraphy with 68-gallium DOTATATE scanning is useful in both the diagnosis and postoperative monitoring of patients with LP, as shown in our cases. A 2016 systematic review of 58 reported cases of LP between 1996 and 2016 reported the incidence of multicentric disease, with extra-laryngeal synchronous lesions, to be 13%. Previous studies report multicentric lesions only within the head and neck, often involving the carotid body, jugulotympanic cavity, or skull base. The high spatial resolution of DOTATATE scanning allows smaller lesions to be visualized, with superiority in detecting head and neck paragangliomas compared to conventional CT/MRI neck imaging, as shown in a study of 26 patients. Scintigraphic imaging allows whole-body screening for synchronous or metastatic disease. Hence, it is likely that the incidence of multicentric forms of LP have been underestimated in earlier studies.

To the best of our knowledge, Case 1 represents the first reported incidence of LP with a synchronous lesion outside the head and neck region. It is probably that prior to the emergence of octreotide scintigraphy, previous studies had restricted imaging to the head and neck area of interest, resulting in distant synchronous lesions being undiagnosed. The presence of multicentric lesions should also raise suspicion for hereditary disease, which warrants further genetic investigations and more stricter follow-up due to greater risk of recurrence. Naswa et al. showed that DOTATATE scanning altered management in three out of five patients with known head and neck paragangliomas due to the detection of additional synchronous or metastatic disease. Case 1 further reinforces this point. This can involve referral to other surgical teams for management or, in the case of metastatic paragangliomas, alter the intent of treatment from curative to palliative or highlight the need for adjuvant radiotherapy. In Case 2, we demonstrated how DOTATATE scanning can be utilized to exclude recurrent disease. Synchronous lesions in LP have currently been reported in the head and neck region, and surgical planning must account for the size and anatomic location, unilaterality versus bilaterality, association with cranial nerve deficits at presentation, and presence or absence of symptoms. Carotid body tumors are the most common head and neck paraganglioma and similar to LPs are readily amenable to surgical resection via the external cervical approach. However, skull base paragangliomas such as vagal and jugulotympanic lesions have difficult surgical access with increased risk of injury to major neurovascular structures. As paragangliomas are generally slow growing and non-secretory within the head and neck, asymptomatic lesions of the skull base can be monitored with serial imaging as with the patient in Case 4. Some authors have considered stereotactic radiotherapy to halt tumor progression in skull base paragangliomas that were deemed high risk to resect. Synchronous tumors should be identified as multifocal disease is more commonly associated with genetic etiology, with mutation-positive patients having increased incidence of bilateral or functional lesions and greater risk of treatment failure. The risk of treatment failure in multicentric forms of LP may be due to synchronous acting as a nidus for recurrence or an underlying genetic mutation. Bilaterality in head and neck paragangliomas is important in surgical decision making and requires a staged approach to resection to avoid the risk of bilateral cranial nerve injury. Due to the paucity of such cases, guidelines are based on experiences from cases reports and series in the literature. Current recommendations include resection of...
10. Amiraraghi N, Syed M, Syed S, et al. Paraganglioma of the skull involved in the study and all presented information is de-identified. Informed written consent was obtained from all patients exemption from formal institutional review for this retrospective study. The Nepean Hospital Human Research Ethics Committee provided ethical approval for the study. Informed written consent was obtained from all patients involved in the study and all presented information is de-identified.

CONFLICT OF INTEREST
The authors no declare conflicts of interest.

ETHICS STATEMENT
The Nepean Hospital Human Research Ethics Committee provided exemption from formal institutional review for this retrospective study. Informed written consent was obtained from all patients involved in the study and all presented information is de-identified.

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