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Case Report

Vagal Paraganglioma: Surgical Removal with Superior Laryngeal Nerve Preservation

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Vagal paragangliomas (VPGLs) represent <5% of all head and neck paragangliomas (PGLs) and show a 17% to 20% risk of malignancy. We present a rare case of a 50-year-old gender with a left VPGL in her neck. To date, approximately 200 cases have been reported. The tumor showed web-like adhesions and arterial supply from the external carotid artery. We performed en bloc resection including a part of the vagus nerve. The superior laryngeal nerve was preserved with the "human communicating nerve" which maintains neural communication in >70% of humans, providing motor fibers to the larynx. The patient recovered uneventfully and was discharged on the 3rd postoperative day. These tumors are therapeutically challenging owing to their proximity to vital neck and skull base structures. Early detection decreases surgical morbidity and mortality. Preservation of viable neural tissue is important in advanced disease.

Key Words: Vagus nerve, Paraganglioma, Vagus paraganglioma, Superior laryngeal nerve, Human communicating nerve

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INTRODUCTION

Paragangliomas (PGLs) of the head and neck are rare, and although the exact incidence is difficult to estimate, they represent <0.5% of all head and neck tumors. They may originate from the carotid body the vagal, the tympanic, or the jugular paraganglia [1]. Notably, <5% of head and neck PGLs originate from the vagus nerve [2]. The vagus nerve (cranial nerve X) is the dominant nerve of the parasympathetic division of the autonomic nervous system, and a vagal PGL (VPGL) is a prime example of an endocrine tumor associated with the vagus nerve [3].

We present the case of a woman with a mass on the left side of her neck, which was diagnosed as a VPGL and was surgically excised. Furthermore, we have described the clinical findings, imaging investigations, differential diagnosis, and surgical treatment. This report highlights the importance of early diagnosis and surgical treatment.

CASE

A 50-year-old woman with an unremarkable medical history observed gradual growth of an asymptomatic mass in the left cervical region. Clinical examination revealed a firm, adherent painless mass, medial to the left sternocleidomastoid muscle with minimal lateral and vertical mobility, located close to the carotid artery pulse. She denied a family history of PGLs or other neuroendocrine tumors. Neurological examination was unremarkable, and we initially suspected a branchial cleft cyst. The patient underwent neck ultrasonography (U/S), which revealed a firm, well-defined, solid, hypoechoic oval mass measuring 3×1 cm, located in the left carotid triangle. Power Doppler imaging revealed that the mass was highly vascular, resembling a

carotid body PGL (CBPGL). Magnetic resonance angiography (MRA) (Fig. 1A), revealed a mass displacing the cervical vessels. Subsequently, digital subtraction angiography (DSA) was performed and revealed a tumor with a vascular "blush" compressing the internal and external carotid arteries just over the carotid bifurcation, displacing the latter towards the midline (Fig. 1B). We proceeded with an operation for the tentative diagnosis of a VPGL based on the absence of the classical "lyre" sign associated with a CBPGL on imaging studies.

The patient was electively admitted to our Vascular Unit and underwent surgical excision of the tumor under general intratracheal anesthesia. We used the typical left lateral cervical incision that extended to the skull base. The mass and the carotid bifurcation were covered by a peculiar arachnoid web-like structure with strong adhesions and a venous web (Fig. 2). The tumor received its arterial supply from the external carotid artery that crossed the carotid bifurcation in the frontal plane (Fig. 3). This artery supplying the tumor was ligated. The tumor nearly extending to the skull base was resected en bloc with the vagus nerve. All attempts to separate the tumor from the vagus nerve failed;

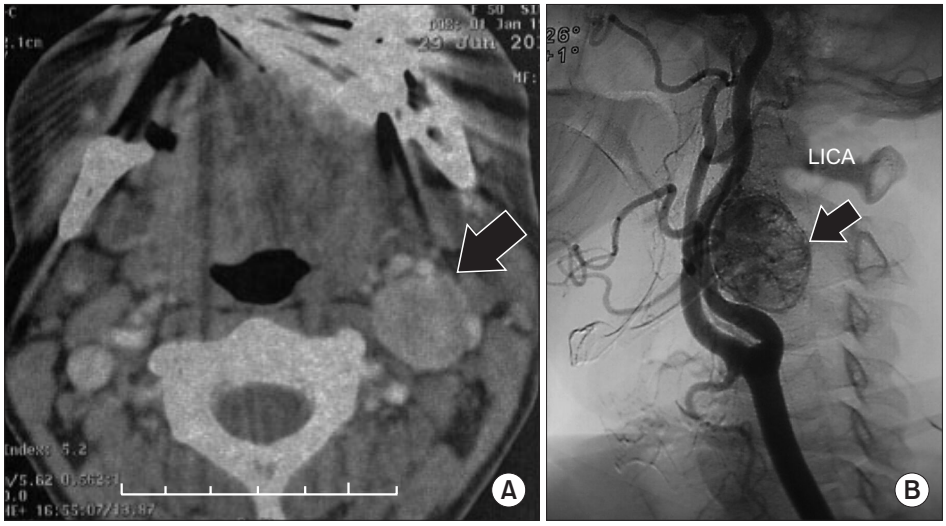

Fig. 1. (A) Magnetic resonance angiography image showing a mass, which wrings the cervical vessels (arrow). (B) Digital subtraction angiography image showing a left vagal paraganglioma (arrow). LICA, left internal carotid artery.

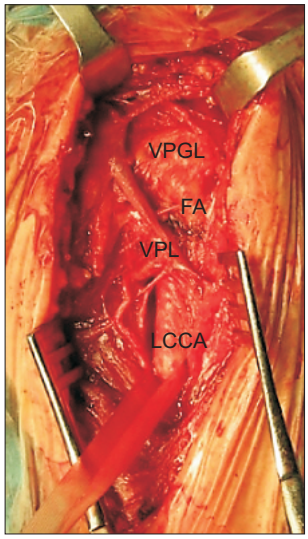

Fig. 2. Intraoperative photograph of tumor, prior to the preparation of vagal nerve and carotid bifurcation. The mass and the carotid bifurcation were covered by an arachnoid web-like structure and rich venous web. VPGL, vagal paraganglioma; FA, feeding artery; VPL, venous plexus; LCCA, left common carotid artery.

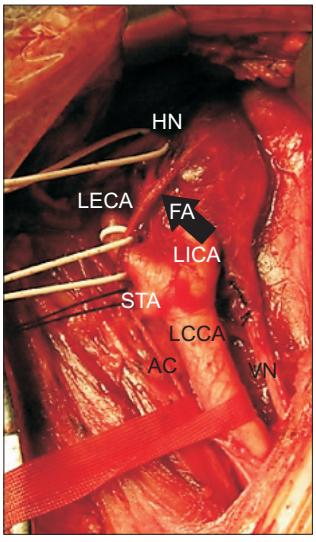

Fig. 3. Image showing exposure of the left carotid bifurcation. Arrow indicates FA. HN, hypoglossal nerve; LECA, left external carotid artery; FA, feeding artery; LICA, left internal carotid artery; STA, superior thyroid artery; LCCA, left common carotid artery; AC, ansa cervicalis; VN, vagal nerve.

thus, we decided to remove it with the part of the vagus nerve to which it was strongly adherent. Notably, owing to the cranially directed growth of the tumor, the superior laryngeal nerve (SLN) was not affected, both ends of the vagus nerve were ligated (Fig. 2-7). The patient experienced temporary hoarseness immediately postoperatively; however, the hoarseness subsided after approximately a month. Further investigations using neck U/S and brain magnetic resonance imaging (MRI) revealed normal findings. Histopathological examination of the resected specimen showed a VPGL measuring 3 cm in size. She was discharged on the 3rd postoperative day following an uneventful recovery. Regular follow-up over 7 years after surgery did not reveal any functional abnormality nor abnormal imaging studies, and she showed no evidence of recurrence.

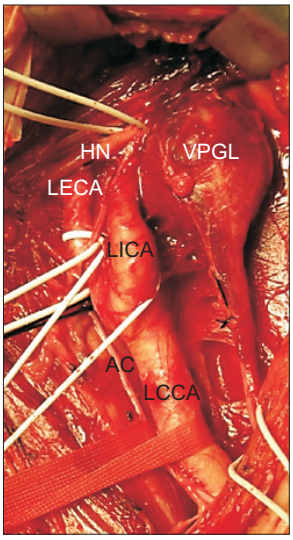

Fig. 4. Intraoperative photograph, during preparation of the tumor from carotid bifurcation. VPGL, vagal paraganglioma; HN, hypoglossal nerve; LECA, left external carotid artery; LICA, left internal carotid artery; AC, ansa cervicalis; LCCA, left common carotid artery.

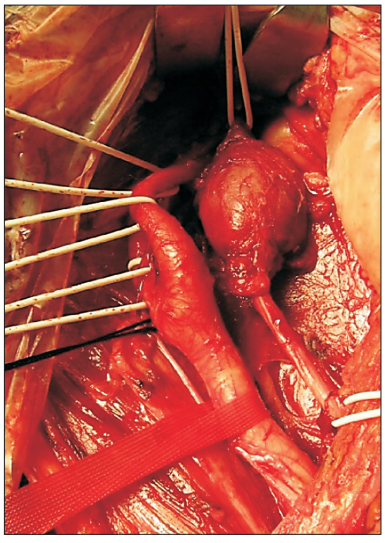

Fig. 5. Image showing the vagal nerve surrounding the tumor.

DISCUSSION

PGLs of the head and neck are rare, and although the exact incidence is difficult to estimate, they represent <0.5% of all head and neck tumors. Overall, a 3:1 woman predominance is observed, and two-thirds of all cases are diagnosed in patients aged 40 to 60 years [4].

PGLs may originate from the carotid body, the vagus nerve, or the tympanic and jugular paraganglia. They are associated with the parasympathetic nervous system and

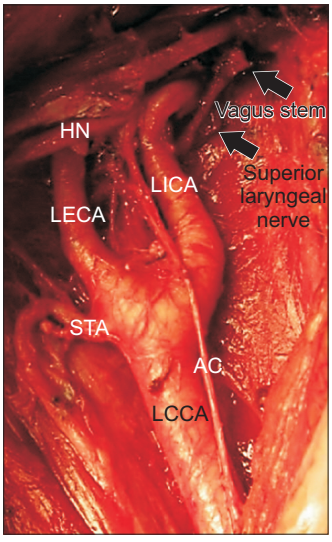

Fig. 6. Image showing the final view of the operative field following tumor removal. HN, hypoglossal nerve; LICA, left internal carotid artery; LECA, left external carotid artery; STA, superior thyroid artery; AC, ansa cervicalis; LCCA, left common carotid artery.

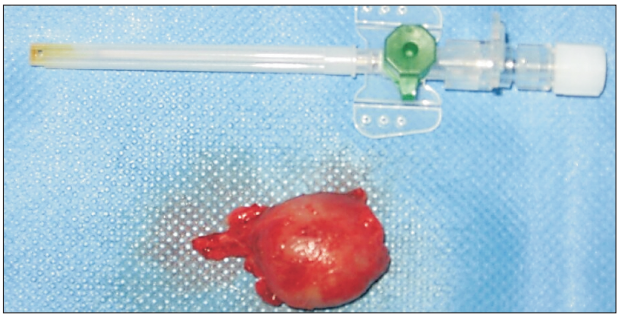

Fig. 7. Resected specimen showing the tumor with no vagal nerve preservation.

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are typically non-secretory tumors. In contrast, thoracic and abdominal PGLs are secretory in nature and thus differ from PGLs of the head and neck, primarily with respect to this feature [3-5]. Notably, <5% of head and neck PGLs originate from the vagus nerve [2]. The vagus nerve (cranial nerve X) is the dominant nerve of the parasympathetic division of the autonomic nervous system. VPGLs are a prime example of an endocrine tumor associated with the vagus nerve.

Embryologically, preganglionic somatic motor and sensory neurons, and supporting cells of the cranial ganglia originate from neural crest cells. The vagus nerve descends vertically through the neck within the carotid sheath and within the mediastinum following different pathways on the left and the right sides. cell bodies of fibers that transmit visceral stimuli and regulate "rest and digestive" functions of the parasympathetic system are located in the inferior ganglion of the vagus nerve, and this nerve constitutes the pathway of communication between the central nervous system and the viscera and transmits >80% of sensory input [6].

VPGLs may develop anywhere along the course of the vagus nerve, but usually they originate from the inferior ganglion of the vagus nerve or the plexiform ganglion that is more cranial and medial in location than the carotid body [7].

In the case presented in this report, the tumor was located laterally and protruded into the carotid bifurcation with forward and medial compression of the carotid bifurcation resulting in clear deviation of the internal carotid artery (Fig. 1B, 4).

VPGLs occur more commonly in women [3]. They present as a painless, rubbery, compressible slow-growing mass in the upper neck, with limited vertical but free lateral mobility in 60% of the cases. The tumor may transmit the carotid pulse, and if it enlarges around the carotid vessels and cranial nerves X to XII, patients may present with symptoms including odynophagia, dysphagia, and hoarseness. The growing mass causes compression of the carotid sinus or the internal carotid artery, occasionally resulting in syncope. Another symptom observed in patients is Horner's syndrome, which is a rare disorder characterized by a constricted pupil, drooping of the upper eyelid, and absence of sweating on the face. This condition occurs as an aftereffect of compression or invasion of the cervical sympathetic chain. The tumor may be pulsatile, and it can express a constellation of symptoms. Among all cranial nerves, the vagus is the nerve that is most commonly paralyzed. This may occur during operations and is observed in 30% of patients [1].

The patient described in this report presented with mild clinical manifestations with a palpable mass on the left side of the neck without any other significant symptoms. She experienced temporary hoarseness immediately postoperatively, which recovered after a month. We concluded that preservation of the SLN enabled the patient to tolerate excision of the vagus nerve caudal to the origin of the SLN. Cranial division of the left vagus nerve led to loss of function of the left recurrent laryngeal nerve (RLN). However, the "human communicating nerve" (present in >70% of humans), which functions as an interconnection between the fibers of the SLN and RLN was preserved and supplied functional motor fibers to the larynx in this patient [8,9].

Notably, 65% of PGLs occur sporadically and the remaining are inherited. However, the expression of mutations in the succinate dehydrogenase subunit D (SDHD) gene is unclear. Familial PGL syndromes commonly occur in young patients [5,6].

Genetic tests are recommended in patients with any of the following risk factors: age >50 years, family history, extra-adrenal tumors, multiple and/or metastatic tumors, and/or elevated dopamine and methoxytyramine levels [10-13]. In the patient described in this report, genetic testing was not performed owing to a negative personal medical and negative family history of PGLs or other neuroendocrine tumors.

The paraclinical investigations for VPGLs include U/S, computed tomography (CT), CT angiography (CTA), MRI, MRA, and DSA. Functional molecular imaging examination includes somatostatin receptor scintigraphy, [^{18}F]-2-fluoro-2-deoxy-D-glucose-positron emission tomography (PET), [^{18}F]-6-L-fluorodihydroxyphenylalanine-PET, and ^{68}Ga-labelled somatostatin agonist PET [7].

CTA and MRA provide valuable information for accurate diagnosis and for preoperative planning because the lesions present as highly vascular masses using contrast. The tumor presents with a ''salt-and-pepper'' appearance using the classic MRI flow voids, and ^{123}I-metaiodobenzylguanidine scintigraphy can be used to distinguish metastatic or convert VPGLs [4].

Owing to the progress in MR and CT technology, although DSA can evaluate tumor vascularity or identify multiple vascular tumors in the head and neck, its current role is limited and it may be useful for embolization of the tumor before surgery [14].

Conventional arteriography is commonly performed for large-sized VPGLs or skull base PGLs, given the fact that these tumors show a propensity for skull base or even intracranial extension through the jugular foramen [7]. The Netterville–Glasscock classification evaluates the expansion of the lesion in relation to its distance from the skull base and categorizes these tumors into 3 groups as follows: A:

confined to the neck, B: tumor in contact with the jugular foramen, and C: the tumor enters the jugular foramen [15].

PET should be performed to assess multiple tumors or associated thoracoabdominal tumors; ^{68}Ga-labelled somatostatin agonist PET is preferred regardless of the patient's genetic background [7].

Usually, VPGLs should be suspected and optimal surgical treatment should be planned in patients with a hypervascular mass in association with the major cervical vessels causing anterior/medial displacement of the carotid bifurcation and posterior displacement of the internal jugular vein, on neck CT or MRA [16].

Differential diagnosis includes neuroma, jugular meningioma, schwannoma, meningioma, CBPGL, as well as jugular or tympanic PGLs [7,13-16].

Early excision is proposed because VPGLs are potentially malignant, and it is hypothesized that VPGLs may progress with local advancement over time even in benign settings [17]. Malignant VPGLs are diagnosed exclusively on the basis of metastases invading non-neuroendocrine tissue.

Surgical excision is the classical and only therapeutic option for most VPGLs including symptomatic and malignant tumors. The level of difficulty of dissection differs between the cranial nerves (IX, X, XI, XII); however, distinguishing the nerve from the tumor capsule can be difficult in all cases. Unfortunately, the vagus nerve may often need to be sacrificed causing speech, swallow, and sensory deficits [18]. Cranial nerve preservation is unlikely in cases with advanced tumors.

The functional complications of VPGLs depend upon tumor size; tumors <2 cm in diameter can be removed with functional injury limited to the vagus nerve. In cases with multiple nerve lesions, postoperative repair is complicated in that restoration of speech and swallowing functions may be delayed. Notably, speech therapy is an important strategy to restore speech. Immediate postoperative swallowing disorders associated with paralysis of multiple cranial nerves (X, XII, IX) and the SLN occur in 60% to 80% of cases and persist in 50% of cases, requiring feeding gastrostomy. Patients with severe swallowing disorders need redo surgery such as thyroplasty, vocal cord injection, gastrostomy, or even tracheotomy. Airway protection is necessary to protect the airway and reduce mortality. Other complications include respiratory complications such as severe aspiration pneumonia, cardiac arrhythmias, sinus tachycardia, and/or positional blood pressure instability with disabling orthostatic hypotension [18].

The aforementioned functional disorders may occur after bilateral laryngeal nerve palsy during excision of bilateral VPGLs; therefore, accurate cranial nerve (IX, X, XII) examination is important before treating contralateral tumors [19].

Similarly, when a carotid bulb tumor and a vagal tumor coexist but on contralateral sides, the carotid bulb tumor should be resected before the vagal tumor to minimize the risk of bilateral vagus nerve palsy [17].

In the case presented in this report, we attempted to separate the mass from the nerve; however, the mass remained inseparable. Although previous reports have described that the mass could be successfully separated from the nerve, this was not feasible in our patient. However, perhaps owing to the preservation of the vagal stem (Fig. 6) containing the origin of the SLN, no further neurological or vocal complications were detected clinically.

VPGLs are commonly malignant, and preoperative criteria predictive of malignancy have not been identified. The risk of malignancy is difficult to estimate because the only recognized criterion is cervical lymph node and/or distant metastases.

Surgical resection followed by radiation therapy is the most common treatment described for malignant VPGLs, even if their rare occurrence is not clear. The 5-year survival rate is approximately 80% in patients with lymph node metastases and 12% in patients with distant metastases [7].

Conventionally, nonsurgical treatment for malignant nonresectable VPGLs includes radionuclide therapy and the administration of alkylating agents or tyrosine kinase inhibitors [17].

More recent methods of radiotherapy (which ensure minimal irradiation of healthy tissues), are single-fraction gamma knife radiosurgery (in contrast to conventional stereotactic radiosurgery based on fractionation over 25 to 30 sessions) and cyberknife radiosurgery, which is a new modality involving whole-body stereotactic radiotherapy for treatment of extracranial sites with 0% complications [15]. The optimal treatment strategy for VPGLs is a high index of suspicion to prevent tumor overgrowth, not permitting surgical excision. Surgeons should ensure minimal-to-no injury to the cranial nerves, which however occurs in 10% to 30% of patients [20]. Therefore, early detection using modern imaging methods and prompt surgical resection are important to decrease surgical complications.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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