Functional Vagal Paraganglioma: A Case Report Illustrating Diagnosis and Management

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ABSTRACT

We report a case of functional vagal paraganglioma to illustrate the biochemical and radiological imaging tests important in diagnosis and to highlight the importance of a multidisciplinary team approach to manage the preoperative, perioperative, and postoperative effects of catecholamine secretion from these tumors.

KEYWORDS: Paraganglioma, carotid body tumor, pheochromocytoma, glomas vagale

Cervical paragangliomas are rare tumors of the head and neck of neurovascular origin arising from neural crest cells. Within the head and neck, they are generally defined and named according to the site of origin, including carotid body tumors, jugulotympanic, and vagal tumors.¹ These tumors generally exhibit a slow rate of growth and most often present as a neck mass noted clinically or radiographically. Diagnosis is usually made through a combination of clinical findings and radiographic imaging with computed tomography (CT) and magnetic resonance imaging (MRI).¹ Carotid angiography is usually unnecessary, unless the lesion requires tumor embolization.² Positron emission tomography (PET) scan and Octreoscan may be used to exclude multiple paragangliomas, which can occur in 10% of patients in sporadic cases and up to 40% of familial paragangliomas.¹ PET and Octreoscan are also helpful in excluding metastatic disease from suspected malignant paraganglioma. Catecholamine hypersecretion is rare in head and neck paragangliomas, occurring

in 1 to 3% of cases.¹ When present, patients may present with symptoms similar to that of adrenal-derived pheochromocytomas (i.e., hypertension, paroxysmal headaches, palpitations, and diaphoretic episodes). Benign cervical nonfunctional paragangliomas can be treated with surgery, radiation, or by observation, although definitive treatment for functional paragangliomas is complete surgical excision. We present a case of functional vagal paraganglioma (previously known as glomus vagale tumor) describing the diagnosis, biochemical profile, preoperative management, and surgical approach of this unique type of paraganglioma.

CASE REPORT

A 41-year-old African-American woman presented with a 1-year history of left neck swelling. She reported increasing episodes of flushing, dizziness, migraine-type headaches, voice changes, and pain, which interrupted her daily activities. On examination, she was

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Figure 1 Computed tomography (CT) and magnetic resonance imaging (MRI) scans showing the left carotid space mass. The tumor is contrast-enhancing on postcontrast CT and T1-weighted MRI scans. Tumor indicated by an arrow, and anteriorly displaced internal carotid artery and internal jugular veins indicated by arrowheads. T2-weighted MRI scan shows characteristic flow voids.

normotensive and had a left neck mass at level II; the superior border extended deep to the mandible. Complete head and neck examination, including flexible laryngoscopy and cranial nerve examination, was unremarkable. A contrast-enhanced CT scan showed a densely enhancing carotid space mass measuring $4 \times 2 \times 5$ cm (Fig. 1). The mass was in the poststyloid compartment of the parapharyngeal space (carotid space) and displaced the internal carotid artery and internal jugular vein anteriorly. A biochemical profile revealed an increase in plasma norepinephrine and normetanephrine levels of 1929 pg/mL (reference: 217 to 1009 pg/mL) and 613 pg/mL (reference: <148 pg/mL), respectively. A 24-hour urine collection confirmed an elevation in levels of norepinephrine and vanillyl mandelic acid. Both the serum and urinary epinephrine/metanephrine levels were undetectable. PET scan and Octreoscan showed no evidence of other paragangliomas or metastatic lymph nodes (Fig. 2). The clinical, biochemical, and radiographic presentation was consistent with a functional paraganglioma. Despite no cranial nerve deficit, it was suspected that the paraganglioma arose from either the vagus nerve or sympathetic trunk. Given the size of the lesion, the symptoms of catecholamine hypersecretion, and the age of the patient, surgical excision was recommended.

One week before surgery, the patient was first placed on α -adrenergic blockade with aggressive oral hydration followed by β blockade. Specifically, she was treated with phenoxybenzamine 10 mg twice a day for 4 to 5 days, increased to 20 mg twice a day for a further 3 days. She was subsequently started on atenolol 50 mg 2 days before surgery. Moreover, 24 hours prior to

surgery, she was admitted for intravenous hydration and blood pressure monitoring. Surgery was performed via a left cervicofacial approach. The tumor was located posterior to the carotid artery and internal jugular vein, pushing the artery anteromedially and the vein anterolaterally. The hypoglossal nerve was stretched across the lateral aspect of the tumor. To visualize the superior limit of the tumor, the digastric and stylohyoid muscles had to be divided (Fig. 3). The vagal nerve had to be transected as the tumor was intimately associated with the nerve, but the hypoglossal nerve, superior laryngeal nerve, and sympathetic chain were carefully preserved. The tumor, the distal segment of vagus nerve, and the sympathetic trunk are shown in Fig. 4. Intraoperative blood loss was minimal, and the patient experienced no major fluctuations in her blood pressure or heart rate. Postoperatively, the patient's symptoms resolved. She had mild hoarseness and minimal dysphagia secondary to a left vocal cord palsy. She was discharged to home on postoperative day 4, tolerating a regular diet after an uneventful recovery. Pathology showed a 6.5-cm paraganglioma, which was positive for chromogranin, synaptophysin, and s100 and negative for AE1/AE3 (Fig. 5).

DISCUSSION

Paragangliomas of the head and neck are rare tumors arising from neural crest cells. Most commonly, they arise from the carotid body (carotid body tumor or carotid paraganglioma) or jugular bulb (glomus jugulare or jugulotympanic paraganglioma). They can rarely arise from the vagus nerve (vagal paraganglioma) and the

Figure 2 (A) Positron emission tomography (PET) scan and (B) Octreoscan showing the same mass, which is fludeoxyglucose (18F) avid and takes up radiolabeled octreotide (axial and coronal sections). Tumor indicated by arrows.

sympathetic trunk. Although vagal paragangliomas are rare tumors (with fewer than 200 cases reported in the literature), 10 to 19% of these are malignant.³⁻⁵ Only 1 to 3% of cervical paraganglioma are hormonally active

with catecholamine hypersecretion.¹ Catecholamine secretions required for functional activity include epinephrine, norepinephrine, and dopamine. Functional paragangliomas (often referred to as extra-adrenal pheochromocytomas) lack the enzyme phenylethylamine-N-methyltransferase, which is required for the conversion

Figure 3 Surgical view showing tumor exposure after division of digastric and styloid musculature. Carotid artery is retracted medially with red vessel loops, and internal jugular vein is retracted laterally with blue vessel loops. Cut ends of the digastric and styloid musculature are indicated by arrows.

Figure 4 Surgical view showing tumor dissected completely free, except for inferior attachment to vagus nerve. The clamp points to the sympathetic trunk that was preserved.

Figure 5 Histopathologic images showing hematoxylin and eosin (H&E) stain (100 × magnification) and immunohistochemical staining for chromogranin, cytokeratin AE1/AE3 (40 × magnification), and CD56 (200 × magnification).

of norepinephrine to epinephrine. As a result, these tumors typically secrete norepinephrine and dopamine, which are responsible for the catecholamine activity, but not epinephrine, which is typically produced by the classical adrenal pheochromocytoma. Symptoms of functional paragangliomas vary in severity. Patients may experience paroxysmal hypertension, severe headaches, palpitations, and severe sweating from catecholamine excess. However, their presentation is highly variable and may mimic many other diseases. If unrecognized or untreated, it can be a life-threatening condition. This case describes a patient with a functional vagal paraganglioma, illustrating the imaging and biochemical investigations required to make the diagnosis and highlighting the importance of preoperative and perioperative adrenergic blockade.

Appropriate preoperative management involving a multidisciplinary team is essential for any catecholamine-secreting tumor, including functional paragangliomas, to minimize the risks of hypertensive crises and fatal arrhythmias intraoperatively. These adverse events are minimized with appropriate α -adrenergic blockade followed by β blockade. It is important to emphasize that adequate α blockade (dose titrated to achieve

orthostatic hypotension in the patient) must be achieved prior to β blockade due to the risk for unopposed α stimulation if β blockade is done first. In the case reported here, the α - and β -blockade process was not optimum as the patient was noncompliant with her treatment regimen, and hence these were performed over a shorter duration of time. Although there are no evidence-based studies comparing different pharmacological therapies, α antagonists,⁶⁻⁹ calcium channel blockers, and/or angiotensin receptor blockers have been shown to be useful.¹⁰ Tachyarrhythmias are best prevented and/or treated with β blockers or calcium channel blockers. To minimize signs and/or symptoms of orthostatic hypotension during adrenergic blockade as well as postoperatively following resection of the tumor, aggressive volume expansion commences with induction of α -adrenergic blockade, initially with increased oral fluid and salt intake followed by intravenous hydration 24 hours prior to surgery. Despite appropriate preoperative preparation, patients with functional paragangliomas may still experience hypertensive crises or arrhythmias during manipulation of the tumor due to increased catecholamine secretion. This requires the anesthesiologist and surgeon to have open communication throughout the

procedure to address changes in vital signs that occur during manipulation of the tumor. Technically, the intraoperative management should focus on preservation of the cranial nerves and the carotid artery. Care in the mobilization of the hypoglossal nerve away from the tumor aids in anatomic and functional preservation of the nerve. The glossopharyngeal nerve can usually be protected by elevation of the styloid musculature during superior tumor dissection. Invariably, division of the vagus nerve when resecting a vagal paraganglioma results in vocal fold paralysis, which is usually permanent.

Although radiotherapy—both fractionated radiotherapy and stereotactic radiosurgery (e.g., gamma knife surgery)—has been reported to give long-term control of tumor growth in benign cervical paraganglioma, its role in the management of functional paraganglioma is unclear.¹¹ Fewer than 10 cases of functional paraganglioma treated with radiation have been described in the literature. Earlier reports using external beam radiotherapy techniques have been disappointing. However, several recent reports using stereotactic radiosurgery suggest that there is a role in treating functional tumors, with complete local control, minimal morbidities, and functional resolution; however, these reports had very small patient numbers.¹²

In summary, functional paragangliomas are rare tumors of the head and neck. A complete history and physical examination should raise suspicion and enable an expedient diagnosis. CT scan and/or MRI are generally diagnostic of paragangliomas. Preoperative management involves sequential therapy with α blockade and aggressive hydration followed by β blockade to minimize intraoperative hypertensive crises. Treatment of choice for functional paragangliomas is complete surgical excision.

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