Paragangliomas of the Head and Neck

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KEYWORDS

• Computed tomography • DOPA-PET • FDG-PET • MR imaging • In 111-DTPA-D-Phe1-octreotide • I-123 Metaiodobenzylguanidine (MIBG) • Paraganglioma • Pheochromocytoma

KEY POINTS

- The most common paraganglioma locations of the head and neck are the carotid body, jugular, tympanic, and vagal paragangliomas.
- Syndromes associated with a high incidence of paragangliomas include multiple endocrine neoplasia type II, von Hippel-Lindau disease, and neurofibromatosis type I.
- All patients, including those with a sporadic tumor, should be referred for a genetic consultation.
- Jugular and tympanic paragangliomas commonly present with tinnitus and hearing loss, whereas carotid body and vagal paragangliomas usually present with nonpainful palpable neck mass.

INTRODUCTION

Paragangliomas make up a family of neoplasms that develop from the paraganglia tissues, which are themselves of neural crest origin and have similar functions and histologic appearances.[1] They may occur along the ganglia's pathway of embryologic migration extending from the skull base to the pelvic floor.[2] Paraganglia play an important role in organismic hemostasis by acting directly as chemoreceptors or by the secretion of catecholamines in response to stess.[1] Paragangliomas of the head and neck are rare vascular skull-base tumors derived from the paraganglionic system with an estimated incidence of 1:30,000, accounting for 3% of all paragangliomas.[2–4]

The most common paraganglioma locations of the head and neck in descending order are the carotid body, jugular, tympanic, and vagal paragangliomas.[5] Tympanic paragangliomas are the most common primary neoplasms of the middle ear.[6] Jugular paragangliomas are the most common tumor of the jugular foramen.[7] Of the different paraganglioma locations, jugulartympanic are the most common paraganglioma causing tinnitus with incidence of 1 per 1.3 million people per year.[4]

Paragangliomas can be sporadic or familial, with genetic mutations occurring in the SDHB, SDHC, or SDHD genes.[8–10] It is now known that at least 30% of patients with a paraganglioma and no other know risk factors harbor a genetic mutation that increases their risk for these tumors and for other neoplasia.[11] Moreover, other genes discovered within the past 5 years: SDHAF2, TMEM127, MAX, EGLN1, HIF2A, KIF1B, and SDHA, add to the genetic complexity of hereditary paraganglioma-pheochromocytoma syndrome.[11] Sporadic paragangliomas are more common in women, with the average age at presentation of 40 to 50 years, as familial present earlier and more commonly in men.[12] Classic tumor syndromes associated with a high incidence of

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paragangliomas included multiple endocrine neoplasia type II (MEN II), von Hippel-Lindau (VHL) disease, and neurofibromatosis type I (NF I).[13] Multicentric paragangliomas occur in 10% to 20% of sporadic cases and in up to 80% of hereditary cases.[2]

Paragangliomas are benign neoplasms in most cases; overall, less than 10% of all paragangliomas have been cited to be malignant.[2] In the head and neck, malignancy seems to be more common in vagal paragangliomas (16% to 19%) when compared with carotid body tumors (6%) and jugulartympanic tumors (2% to 4%).[2] There are no accepted histopathological criteria for malignancy, although the diagnosis of a malignant paraganglioma can only be made when there is metastasis to nonneuroendocrine tissue.[2] In head and neck paragangliomas, metastases are most frequently found in cervical lymph nodes; distant sites, which include lung, liver, bone and skin, are very rare.[2,14]

The clinical presentation of a paraganglioma varies based on the tumor location. Jugulartympanic paragangliomas (**Fig. 1**) present with pulsatile tinnitus (84%) and hearing loss (76%) and frequently cause dysfunction of the cranial nerves VII–XII with large tumors.[15,16] Tympanic (**Fig. 2**) and jugular paragangliomas often present to the otolaryngologist as a bluish, pulsating mass behind the eardrum.[17]

In contrast, carotid body paragangliomas (**Fig. 3**) present as a painless, slowly enlarging mass lateral to the tip of the hyoid bone.[14] On physical examination, the tumor typically reveals a rubbery, nontender mass along the anterior border of the sternocleidomastoid. The tumor is mobile from side to side, but limited vertically because of the tumor's attachment to the carotid artery (Fontaine sign).[14] A carotid bruit or pulsatile character of the tumor strengthens the diagnosis. Neurologic deficits of cranial nerves VII, IX, X, XI, and XII can be found in some cases.[14] A painless neck mass is also the most frequent symptom in patients with a vagal paraganglioma (**Fig. 4**).[18] The tumor most commonly arises from the inferior (nodose) ganglion; however, it can arise from any point along the course of the nerve. Miller and colleagues[18] described their experience with a group of 19 vagal paraganglioma patients. The most frequent presenting symptoms were the presence of a neck mass (n = 14) and hoarseness (n = 7), followed by pharyngeal fullness (n = 5), dysphagia (n = 4), dysphonia (n = 4), pain (n = 4), cough (n = 3), and aspiration (n = 1).

In order to establish a diagnosis of a head and neck paraganglioma, imaging is essential.[19] Depending on the location and extent of the tumor, the following imaging modalities are frequently used: B-mode ultrasonography in combination with color-coded Doppler ultrasonography, computed tomography (CT), MR imaging, and digital subtraction angiography.[19] The most common radioligand for imaging of paragangliomas is In 111-DTPA-D-Phe1-octreotide (**Fig. 5**).

The different treatment options for paragangliomas include surgical excision, endovascular embolization, conventional radiotherapy, and stereotactic radiosurgery.[20] In selected cases, a watchful approach with repeat imaging may be warranted.

This article discusses normal anatomy and imaging techniques, imaging protocols, imaging findings/pathology, diagnostic criteria, differential diagnosis, and pearls/pitfalls/variants as they relate to paragangliomas involving the skull base. Finally, a brief bulleted list is presented describing what the referring physician needs to know.

NORMAL ANATOMY AND IMAGING TECHNIQUE

Normal Anatomy

The 3 most common paragangliomas of the head and neck are the carotid body, jugular, and tympanic tumors.[5] These tumors are located in the following areas: the carotid body paraganglioma is located at the carotid bifurcation; the jugular paraganglioma is located at the jugular foramen/bulb; and the tympanic paraganglioma is located at the cochlear promontory.[21] Therefore, paragangliomas of the head and neck require extensive anatomic knowledge of the jugular foramen, middle ear, and anterolateral neck.

Jugular fossa (JF) anatomy is important for understanding glomus jugular and tympanic paraganglioma pathology and imaging. The JF is a deep depression located in the temporal bone and cradles the jugular bulb. The JF is located directly behind the entrance of the carotid canal, lateral to the anterior half of the occipital condyle, medial to the stylomastoid foramen, posteromedial to the styloid process, and posteroinferior to the middle ear cleft. The foramen can be divided into anteromedial as well as posterolateral compartments. The anteromedial compartment contains the glossopharyngeal nerve, inferior petrosal sinus, and meningeal branch of the ascending pharyngeal artery. The posterolateral compartment contains the vagus and spinal accessory nerves. Tympanic paragangliomas typically arise from the tympanic plexus formed by tympanic nerve (Jacobson nerve), a branch of the glossopharyngeal nerve. The plexus of nerves lies on the cochlear promontory of the middle