Head and Neck Pathology–Radiology Classics: Vagal Paraganglioma

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Received: 20 April 2007 / Accepted: 20 July 2007 / Published online: 27 November 2007
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Paragangliomas are tumors arising from extra-adrenal paraganglia and are present throughout the body.

Paragangliomas—also called chemodectomas—of the head and neck are the most common of all paragangliomas. They are rare with an incidence of 0.2–1/100,000. They may originate from carotid body, vagal body, middle ear, and larynx. The ones of vagal origin represent less than 5%.

Vagal paragangliomas originate within the first 2 cm of the extracranial stretch of the vagus nerve and are associated with the inferior ganglion.

Vagal paragangliomas, as other paragangliomas of the head and neck most commonly present as masses, but may cause other symptoms, such as tinnitus or hoarseness or cranial nerve paralysis. They may present as singular tumors or multiple paragangliomas. Most multiple cases are associated with a family history (MEN IIA and MEN IIB, von Hippel-Lindau syndrome and other, rarer entities). Although they might have a secretory product, usually they are hormonally inactive.

Radiographically the tumor appears as a well-circumscribed, homogeneously- and intensely-enhancing mass on CT. On MRI, the mass is iso- to slightly hyperintense to

muscle on T1-weighted imaging, and slightly hyperintense to muscle on T2-weighted imaging. Multiple, branching flow voids are typically seen within the tumor on both T1- and T2-weighted images. On T2-weighted imaging, the punctate black flow voids in cross section within the relatively bright tumor create a characteristic “salt and pepper” appearance in tumors over 2 cm in maximal diameter. Additionally, flow voids of large feeding arteries are seen at the periphery of the mass. Angiography demonstrates the characteristic appearance of a vascular tumor with large feeding arteries, intense tumor stain, and early draining veins (Fig. 1A–D).

Grossly the tumor is encapsulated ovoid mass with tan to red-brown cut surface. Histologically, the tumors have a characteristic organoid growth pattern, consisting of two cell populations: chief cells arranged in a ball-like fashion (zellballen—German for cell balls) and sustentacular cells surrounding them (Fig. 2). Chief cells are of neural crest origin. They have abundant amphophilic, slightly granular cytoplasm and central nuclei. Nuclear pleomorphism is variable, occasionally striking; however, its presence is not indicative of aggressive behavior. The cytoplasm contains neurosecretory granules, consequently the cells react with neuroendocrine markers, such as chromogranin, synaptophysin and CD 56. Sustentacular cells are inconspicuous, spindle shaped cells surrounding the “zellballen”. They are believed to be modified Schwann cells, have a supporting role and react with S-100 (Fig. 3). As other neuroendocrine tumors, paragangliomas are highly vascular neoplasms.

Most paragangliomas are benign; however, there are no definite criteria for malignancy other than the presence of metastatic disease. The presence of capsular or vascular invasion and necrosis may be indicative of malignancy.

Differential diagnosis includes hemangiopericytoma, neuroendocrine carcinomas, alveolar soft part sarcoma, metastatic medullary carcinoma of the thyroid and

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Fig. 1 (A) Angiography. Lateral view (patient's face is on left side of image) of the arterial phase of a digital subtraction angiogram with left common carotid artery injection shows early, intense enhancement of a vascular mass (arrow) that is causing anterior deviation of the carotid artery (arrowhead). (B) Intravenous contrast-enhanced axial CT. Large enhancing mass in the left carotid space, deep to the sternocleidomastoid muscle (tailed arrow), causing lateral deviation and compression of the slit-like left jugular vein compared to normal right jugular vein (arrowheads). In addition, the mass deviates the internal and external carotid arteries (arrows) anteriorly on the left

compared to the normal position seen on the right. (C) Sagittal reformat of intravenous contrast-enhanced CT. Anterior deviation of the carotid arteries (arrow) by the large mass containing many irregular, nontapering tumor vessels (arrowheads). (D) MR, T1-weighted coronal image of the neck. Intermediate signal mass in the left neck displacing the flow void of the left common carotid artery which would normally be in the same plane as that on the right (tailed arrows). Irregular flow voids in high-flow tumor vessels are also seen within the mass (arrowheads)

Fig. 2 Histology, H&E, 20 $\times$. Note the organoid growth pattern with zellballen and the rich vasculature in the delicate septa between them

metastatic renal cell carcinoma. The vascular component of the tumor occasionally shows wide, branching, staghorn-like architecture, reminding of hemangiopericytoma. Hemangiopericytoma lacks the organoid growth pattern with zellballen and the immunohistochemical characteristics are different. Metastatic medullary carcinoma is a logical option on the neck, moreover the growth pattern may be similar and both react with neuroendocrine markers. However, medullary thyroid carcinoma often produces amyloid, which is not a characteristic of paraganglioma and reacts with calcitonin that is not expressed by paragangliomas. The alveolar growth pattern of alveolar soft part sarcoma and some renal cell carcinomas may mimic the zellballen, but the latter are much smaller units and have two distinct types of cells. Neuroendocrine

Fig. 3 (A) Chromogranin immunostain, 40×. Chief cells forming the zellballen react with Chromogranin A, while the surrounding sustentacular cells are negative (left). (B) S100 immunostain, 40×. As a mirror image, sustentacular cells react with S100 highlighting the contour of the zellballen (right)

carcinomas may have an organoid growth pattern, but they are usually malignant looking neoplasms with high mitotic rate and lack the S100 positive sustentacular cell component.

Therapeutic options include surgery, radiotherapy and stereotactic radiosurgery. The vascular nature of the tumor makes surgery difficult sometimes—this can be reduced with preoperative chemoembolization.

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