The Yale Larynx Laboratory

A Clinical Review

Paraganglioma of the Head and Neck

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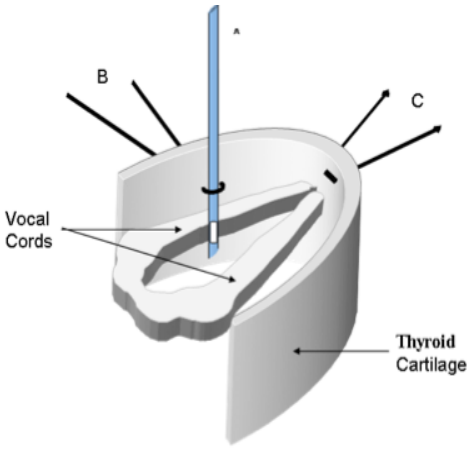

Laboratory Note

The purpose of this newsletter is to update our readers with the evidence-based management of certain Head & Neck disease presentations. In this issue we shall focus on head and neck paraganglioma.

The Yale Larynx Laboratory was founded by John A. Kirchner in 1967. Since 1975 this laboratory has been in continuous operation under the direction of Clarence T. Sasaki, the Charles W. Ohse Professor and has been funded by the National Institutes of Health and by endowments of grateful patients.

Case Presentation

A 40 year old healthy gentleman, never smoker, presented with a right neck mass, first noticed 2 months earlier. He denied pain, voice changes, difficulty speaking or swallowing, palpitations or excessive sweating. His brother and father were patients with a glomus vagale and glomus jugulare, respectively. Examination revealed a 2.0x1.5cm right level 2 neck mass, mobile in the horizontal plane without overlying skin changes. The mass was minimally pulsatile but did not exhibit a bruit. Otoscopic examination revealed normal tympanic membranes without middle ear masses. Neurologic examination confirmed normal cranial nerve function. Flexible laryngoscopy revealed fully mobile, symmetric vocal cords.

Further evaluation included a 24hr urine collection that resulted in normal catecholamine levels. Contrast enhanced CT scan showed a 2.0x1.5cm right neck mass at the right posterior carotid bifurcation, splaying the internal and external carotid arteries. Furthermore, an ocreotide scan confirmed the additional presence of an ipsilateral 2.5x3cm paraganglioma at the skull base likely representing a glomus vagale. The patient underwent pre-operative angiography and embolization with surgery the following day through a pre-auricular, submandibular approach. The tumor was peeled off the carotid bifurcation uneventfully with minimal bleeding using sequential bipolar cautery and blunt scissor dissection technique. The second lesion was similarly dissected at the skull base through the same surgical exposure. There was no hemodynamic instability. The patient maintained excellent voice and swallow function post-operatively

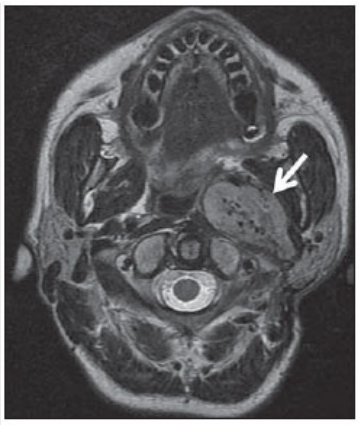

Figure 1 - salt and pepper sign

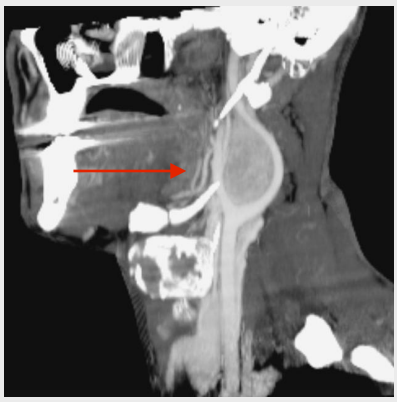

Figure 2 - lyre sign

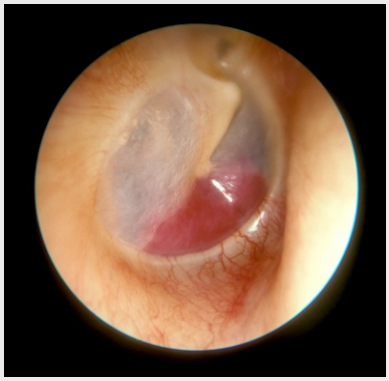

Figure 3 - glomus jugulare

without neurologic deficit.

Discussion

Paragangliomas are benign vascular neoplasms of neuroectoderm-derived chromaffin cells. During fetal development, prior to formation of the adrenal medulla, these cells are a vital source of catecholamines. Normal paraganglia consist of 2 cells types; type 1 chief cells and type 2 sustentacular cells. Paragangliomas contain both cell types.

These tumors are generally solitary, with exceptions in the setting of familial syndromes such as MEN 2A/2B, NF1, and von Hippel-Lindau Syndrome. Early literature also points to autosomal dominant genetic mutations in genes for succinate dehydrogenase (SDH) that can result in earlier onset of tumors and increased frequency of bilateral or multiple synchronous tumors. Recent literature, although sparse, reports 17%-40% of paragangliomas containing a SDH mutation. SDH subunit B mutations have the highest incidence of malignancy (38-70%) while subunit D is most commonly found in head and neck paragangliomas, carrying a 3-13% malignancy rate. However, there are no histologic criteria for malignancy, which is rather clinically diagnosed by detecting metastasis to regional nodes or distant sites.

The most common site of a paraganglioma is in the adrenal medulla (pheochromocytoma), with only 3% of paragangliomas found in the head and neck, comprising just 1/30,000 head and neck tumors. The most common subsites, in descending order, include the carotid body, jugulotympanic, and high vagal locations.

Presenting signs and symptoms will vary depending on the location of the tumor (see table). Signs of an actively secreting tumor include headaches, palpitations, episodic flushing and excessive perspiration.

After history and physical examination, evaluation includes 24hr urine collection for norepinephrine and its metabolites (vanillylmandelic acid and normetanephrine). Plasma metanephrine level may also be obtained.

CT scan will show a vascular mass with contrast enhancement, and MRI may show internal flow voids on T2 images resulting in a so-called ‘salt and pepper’ sign (Fig 1).

Octreotide scanning is a nuclear medicine technique

using indium-111-labeled somatostatin analogue ocreotide, useful in diagnosing primary tumors, synchronous lesions, or metastasis.
The primary treatment is surgical resection. Pre-operative embolization of the tumor (within 48hrs of resection) is often utilized to limit intra-operative bleeding and morbidity. In our practice, preoperative angiography is essential in determining vascularity of tumors as we have found tumor size and CT or MR imaging do not completely predict tumor vascularity. For catecholamine secreting tumors, pre-operative alpha and beta blockade is necessary due to possible catecholamine leak intra-operatively.
Radiation therapy is not considered curative as it is cytostatic to the tumor, not cytotoxic, thus arresting growth but not shrinking the tumor. In general, radiation may be considered primary treatment in the elderly but is less enthusiastically considered in healthy younger patients who may wish to avoid late onset radiation induced malignancies or carotid stenosis.
Further rationale for primary surgery is the invaluable opportunity to determine succinate dehydrogenase levels facilitating subsequent genetic counseling.

Lesion	Notable Findings
Carotid Body	-slow growing, painless neck mas -pulsatile, mobile in horizontal axis -hoarseness, vocal cord paralysis, dysphagia -Lyre sign - splaying of the internal and external carotid arteries (Fig 2)
Glomus Jugulare/Tympanicum	-pulsatile tinnitus, aural fullness, hearing loss, cranial neuropathies -vascular middle ear mass (Fig 3) -Brown sign - blanching of mass with positive pneumatocopic pressure
Glomus Vagale	-painless neck mass with tongue weakness, hoarseness, dysphagia and Horners syndrome -vascular lesion displacing the internal carotid artery anteromedially

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