TITLE: Carotid Body Paraganglioma
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Introduction

Nomenclature

The term paraganglia was first used by Kohn in the early twentieth century and is the most appropriate nomenclature from an embryologic standpoint. These nests of cells appear to originate from neural crest cells that have migrated in close association with the autonomic nervous system ganglion cells. Other terms such as glomus tumors (general term used to indicate a cluster of specialized cells and more appropriately applied to tumors of the skin and superficial tissues of the extremities), chemodectomas (describing a tumor from chemoreceptor origin), and nonchromaffin tumor (related to staining characteristics) are less accurate terms and therefore should be avoided.

Anatomy, function and histology of the normal carotid body

The carotid body was first described by von Haller in 1743 and is a round, reddish-brown to tan structure found in the adventitia of the common carotid artery. It is located on the posteromedial wall of the vessel at its bifurcation and is attached by "Mayer's ligament" through which the feeding vessels run (primarily from the external carotid). The normal carotid body measures 3-5 mm in diameter but is often larger in people living at higher altitudes. Afferent innervation is provided through the glossopharyngeal nerve. The histologic appearance of the carotid body is identical to other paraganglia and includes two types of cells. Type I (chief) cells are APUD type cells with copious cytoplasm and large round or oval nuclei. Their cytoplasm contains dense core granules that store and release catecholamines. Chief cells are divided into three types: progenitor cells, light, and dark (mature) cells. It is hyperplasia of the dark chief cells that leads to enlargement of the paraganglia during chronic hypoxia. Type II (sustentacular) cells are
elongated cells that closely resemble schwann cells. Their function is not entirely clear. These cells are arranged into clusters with a core of chief cells surrounded by sustentacular cells embedded in a fibrous stroma.

The function of the carotid body is related to its role in the autonomic control of the respiratory and cardiovascular systems. It is responsible for detecting changes in the composition of arterial blood. The only other paraganglia with similar chemoreceptor function are the aortic bodies. Hypercapnia, hypoxia, or decreasing pH stimulate Type I cells to initiate an autonomic reflex which leads to increased respiratory rate and depth, sympathetic nervous system activation (increased heart rate, systemic vascular tone and blood pressure), and cerebral cortical activity. The carotid body is also stimulated by increased blood temperature and certain chemicals (cyanide and nicotine). It is this close association with respiratory drive and the sympathetic nervous system response that have prompted investigation of the carotid body's role in disease processes such as obstructive sleep apnea and sudden infant death syndrome. Although no clear conclusions can be drawn at this time, the carotid body and its response to intermittent hypoxia appear to be related to the systemic hypertension seen in OSA. It has also been shown that some SIDS children had either small carotid bodies or a decreased Type I cells (mature) to Type II cells ratio. It is hypothesized that this may attenuate the child's response to a hypoxic crisis.

**Anatomy and Histology of carotid paragangliomas**

Grossly the carotid paraganglioma is dark, tan to purple in color and is usually fairly well circumscribed although there may be only a very thin fibrous capsule. They tend to splay the carotid bifurcation as they enlarge and can extend along the internal carotid to skull base. Histologically, the paraganglioma is similar to the normal carotid body except that clusters tend to be larger (Zellballen formation). Also, there are often areas of spindle-shaped cells (“sarcomatoid foci”) and highly vascular areas that may resemble an angioma. Nuclear pleomorphism and cellular hyperchromatism are common and should not be considered evidence of malignancy. In fact, there are no clear histologic characteristics of malignancy. This diagnosis should be reserved for the presence of local, regional or distant metastasis. Carotid paragangliomas also resemble pheochromocytomas but are chemically active less often than this adrenal counterpart.

**Hereditary and Sporadic occurrence**

The sporadic form of carotid body paraganglioma is more common than the inherited variety and tends to occur slightly more often in women. It is seen more frequently in people living at high altitudes and is multicentric in approximately 10% of cases with bilateral carotid body lesions being the most common combination. Malignancy occurs in 6-12.5% of cases which ranks carotid body paragangliomas as the most frequently malignant head and neck paraganglioma.

The hereditary form occurs in 7-9% of cases and is more frequently multicentric (30-40%). These are seen with equal frequency in both sexes and the inheritance pattern is autosomal dominant modified by genomic imprinting. Although the allele can be passed from either parent, only those from the father will lead to the paraganglioma phenotype in the children. It is thought that
this occurs because the allele is only activated during spermatogenesis and not during oogenesis. Since treatment of smaller tumors carries a much lower risk of morbidity and mortality, and because of the autosomal dominant pattern of inheritance, routine examination and screening with MRI every two years for at risk individuals older than 16 to 18 years of age is recommended (McCaffrey, 1994). This costly approach may be eliminated in the future if a reliable genetic screening test can be developed.

**Presentation and diagnosis**

The vast majority of carotid body paragangliomas present as slowly enlarging (~5mm per year), non-tender neck masses located just anterior to the sternocleidomastoid muscle at the level of the hyoid. The classic finding is a mass in this location that is mobile in the lateral plane but limited in the cephalocaudal direction. Occasionally the mass may transmit the carotid pulse or demonstrate a bruit or thrill. As these tumors enlarge, progressive symptoms of dysphagia, odynophagia, hoarseness and other cranial nerve (IX-XII) deficits appear. The history should include questioning as to the presence of similar lesions in family members and symptoms associated with catecholamine production such as fluctuating hypertension, blushing and palpitations.

Although it is an invasive test, carotid angiography is by far the most useful diagnostic test for paragangliomas. This modality can establish the diagnosis, demonstrate multiple lesions, determine the size and vascularity, and evaluate the tumor blood supply. Additionally, it can be modified to include selective, controlled balloon occlusion of the internal carotid artery to evaluate the cerebral cross-flow. This information is extremely important in pre-operative planning and counselling of the patient as to the relative risk of surgery. The classic, pathognomonic finding on arteriogram is widening of the carotid bifurcation by a well-defined tumor blush ("lyre sign"). It should be emphasized that angiography of both carotid systems is required to rule out bilateral tumors. MRI with gad. (tumors as small as 5 mm) and contrast CT are also effective imaging modalities in this area and are non-invasive. Biopsy, including fine needle aspiration is unnecessary, dangerous, and contra-indicated in the evaluation of paragangliomas.

Routine screening for urinary metanephrines and VMA, and serum catecholamines is probably only indicated for multiple or familial paragangliomas or in the presence of catecholamine related symptoms (Johnson, 1991). However, considering the hazards associated with operating on a previously unsuspected, metabolically active tumor, an argument can be made for obtaining these studies in all cases.

**Treatment**

The treatment of choice for most carotid body paragangliomas is surgical excision. However, because of their location in close approximation to important vessels and nerves, there is a very real risk of morbidity (mainly cranial nerve X-XII deficits and vascular injuries) and mortality which is estimated as 3-9% (Kyriakos, 1987: Maves, 1993). Tumor size is important because those greater than 5 cm in diameter have a markedly higher incidence of complications-67% vs. 15% for
The approach is usually transcervical but occasionally a superiorly based carotid paraganglioma or one that reaches the skull base may require a skull base approach. Wide exposure is a must as is meticulous hemostasis. Early control of the proximal and distal vessels is then accomplished with vessel loops. Important neurovascular structures are identified and appropriately retracted. The tumor is then carefully dissected from the common carotid in a subadventitial plane. This dissection is carried superiorly, making every effort to protect the internal carotid. If necessary, the external carotid can be sacrificed in most cases. If the common or internal carotid is encased in tumor or damaged during resection, immediate repair/replacement should be performed. Again, the preoperative work up should indicate the likelihood of vascular involvement and give some indication as to how well the patient will tolerate temporary internal carotid compromise.

Radiotherapy, either alone or in conjunction with surgery, is a second consideration and an area of some controversy. Historically, paragangliomas were considered radioresistant. Some authors believe this is false and is based on past experience where only large, recurrent or inoperable tumors were treated with this modality. Several more recent studies indicate good responses to supervoltage radiation including some complete responses. They report only minimal acute complications(skin changes) and no long term complications. However, other studies have demonstrated persistence of disease in lesions whose growth was stabilized by radiotherapy. Most authors still recommend XRT only for very large tumors, recurrent tumors or for those patients who are poor surgical candidates(Sykes, 1986).

Summary

Carotid paragangliomas are rare tumors overall but are the most common form of head and neck paraganglioma. There are sporadic and familial forms that have distinct differences. They have characteristic physical exam findings and the diagnosis is made radiographically, not by FNA or biopsy. Surgical excision is the treatment of choice although radiation therapy is an option for patients who are not surgical candidates.

BIBLIOGRAPHY


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