Paraganglioma neck – a neuroendocrine tumour revisited

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Paragangliomas are uncommon neck swellings, usually associated with hypertension and flushing. They occur in the neck and other

amine precursor uptake and decarboxylation cell rests, and are a challenge to the anesthetist at the time of excision.

Key Words: Carotid body tumour; Glomus jugulare; Paraganglioma

Paraganglia are rests of cells that arise from neuroendocrine or amine precursor uptake and decarboxylation cells. Paraganglia are divided into chromaffin and nonchromaffin subtypes. A tumour arising from the paraganglia is called a paraganglioma. The carotid body is a nonchromaffin paraganglion, classically situated at the bifurcation of the common carotid artery (CCA) into the external and internal divisions. It is a chemoreceptor involved in the regulation of pH in the body. A tumour arising from the carotid body is a challenge because of its location and the gross variations in pressure that occur during tumour handling.

CASE PRESENTATION

A 16-year-old girl presented to the outpatient clinic with complaints of a swelling just beneath the left ear for one year. Examination showed a 5 cm × 4 cm swelling just beneath the sternocleidomastoid that was well circumscribed, smooth and pulsatile (Figure 1). A biopsy was previously attempted and abandoned, according to the patient; no records were available for verification. There was no tachycardia, hypertension or variation of blood pressure with posture or on tumour palpation. There were no associated cranial nerve palsies.

Computed tomography with contrast showed a tumour in the region of the carotid bifurcation (Figure 2), but the true 'road map' was revealed on magnetic resonance (MR) angiography, which showed a well-defined tumour arising from the region of the external carotid artery with a well-defined feeder vessel (Figure 2). Shamblin grade II carotid body paraganglioma was the diagnosis. Vanillyl mandelic acid estimations were normal.

The patient was informed of the high risk of the surgery; consent was obtained and the tumour was approached through a vertical incision over the sternomastoid. Proximal control of the CCA was obtained with a vessel sling. The extremely vascular lesion had multiple feeders. Tumour handling produced gross

Figure 1) Examination showing a 5 cm × 4 cm swelling just beneath the sternocleidomastoid that was well circumscribed, pulsatile and smooth

blood pressure swings (variations between 200/140 mmHg and 60/30 mmHg). With support from the anesthetist, the tumour was subadventially excised in toto (Figure 3) and sent for histopathological examination. Postoperatively, the patient had mild ptosis that resolved with anti-inflammatory medication (Figure 4).

Histopathology showed characteristic Zellballen body formation, with type I and II cells. The immunohistochemistry was positive for neuroendocrine granules.

DISCUSSION

Carotid body tumours are referred to as paragangliomas, neuroendocrine tumours, amine precursor uptake and decarboxylation

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Figure 2) Computed tomography with contrast showing a tumour in the region of the carotid bifurcation (left). Magnetic resonance angiogram showing a well-defined tumour arising from the region of the external carotid artery, with a well-defined feeder vessel (right)

(APUD)-omas, glomus jugulare and glomus vagale (1-4). The carotid body, first described by von Haller in 1743, is a vascular reddish-brown structure approximately the size of a grain of rice, located within the adventitia posteromedial to the bifurcation of the CCA. Blood reaches the carotid body through a fibrovascular bundle – the ligament of Mayer – that runs from the posterior surface of the CCA to the inferior portion of the carotid body and supplies the normal carotid body with more blood by weight than the brain.

There may be an increased incidence of these tumours in high-altitude dwellers, and some reports show a female predominance – a ratio of women to men of 5:1 (5-7). Classically, carotid body tumours grow with progressive involvement of the internal and external carotid arteries, usually without constricting the arterial lumens. These lesions can extend into the base of the skull through a foramen or by bone erosion. Alternatively, they may grow medially or laterally, into the parapharyngeal space, or inferiorly to invade the clavicle.

The syndrome of bradycardia, hypotension and loss of consciousness may occur spontaneously, or secondary to head movement or direct pressure on the tumour in some patients, and is known as the carotid sinus syndrome. Additional reports of systemic abnormalities that resolved after tumour excision include alterations in gut motility with emesis on manipulation of the tumour, extensive skin alterations, constitutional symptoms such as weight loss and fever, and even one case of membranous glomerulonephritis (8,9). Finally, while exceedingly rare for extra-adrenal paragangliomas, patients with these tumours may present with a variety of symptoms or signs secondary to catecholamine production. If there are such symptoms, patients should undergo vanillyl mandelic acid estimations, adrenaline and noradrenaline assays, and take alpha- and beta-blockade medication before surgery (9).

Imaging

Patients thought to have a carotid body paraganglioma should undergo multiplanar, thin-section, T1- and T2-weighted

Figure 3) Excision of the tumour subadventially in toto

Figure 4) Mild postoperative ptosis that resolved with anti-inflammatory medication

gadolinium diethylenetriaminepenta-acetic acid-enhanced magnetic resonance imaging (MRI). Paragangliomas have an intermediate signal on T1-weighted and a high signal on T2-weighted images and enhance intensely. In addition, paragangliomas larger than 2 cm produce a characteristic salt-and-pepper appearance that results from the fast-flowing blood pools and large tumour vessels within these lesions. Although MRI clearly proves involvement of the carotid arteries and jugular vein in these lesions, bony landmarks in the skull base are poorly defined in MR images; parallel imaging with computed tomography may be necessary. On MR angiography, besides the characteristic tumour blush (lyre sign) in patients with a carotid body tumour, a characteristic distortion of the carotid bifurcation is also visible. The internal carotid artery is generally pushed laterally and posteriorly, while the external carotid artery is displaced anteriorly. Biopsy, including fine needle aspiration, is unnecessary, dangerous and contraindicated in the evaluation of paragangliomas (10,11).

A classification system based on size and difficulty of resection has been developed (12). Group I tumours are small and easily dissected away from the vessels. Group II includes

paragangliomas of medium size that are intimately associated with the vessels, but are separable with careful subadventitial dissection. Group III tumours are large and typically encase the carotid vessels, requiring partial or complete vessel resection and replacement.

Genetics in carotid body paraganglioma

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. It is multicentric in approximately 10% of cases, with bilateral carotid body lesions being the most common combination. Malignancy occurs in 6% to 12.5% of cases, which ranks carotid body paragangliomas as the most frequently malignant head and neck paraganglioma (13,14).

The hereditary form occurs in 7% to 10% of cases and is more frequently multicentric (30% to 40%). It is 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 activated during spermatogenesis and not during oogenesis. Because treatment of smaller tumours 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 (6). This costly approach may be eliminated in the future if a reliable genetic screening test can be developed. The succinate dehydrogenase subunit D (*SDHD*) mutation is the most common mutation in familial carotid body paraganglioma (15).

Treatment: There are three treatment modalities for carotid body tumours (16,17) – surgical excision, embolization and radiotherapy. Surgical excision is the best option and the

Shamblin grade indicates the degree of difficulty to be anticipated. However, because of the tumours' close approximation to important vessels and nerves, there is a very real risk of morbidity (mainly cranial nerve X to XII deficits and vascular injuries) and mortality, which is estimated to be 3% to 9% (1). Tumour size is important because those greater than 5 cm in diameter have a markedly higher incidence of complications – 67% versus 15% for tumours less than 5 cm in diameter (6).

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 tumour is then carefully dissected from the CCA in a subadventitial plane. This dissection is carried superiorly, making every effort to protect the internal carotid artery. If necessary, the external carotid artery can be sacrificed in most cases. If the CCA or internal carotid artery is encased in the tumour or damaged during resection, immediate shunting, grafting or reconstruction should be performed (18,19).

Tumour embolization is advocated preoperatively by some, but the disadvantage is that the inflammatory response makes subadventitial dissection difficult (18).

Radiotherapy causes edema, fibrosis, hemosiderin deposition and degeneration of the vessel wall, with intimal proliferation leading to thrombosis of the vessel. Radiotherapy is indicated for large tumours, recurrent tumours and in patients who are not indicated for surgery (20,21).

CONCLUSION

The carotid body paraganglioma is a rare vascular tumour of the neck that is diagnosed by imaging and not by biopsy (22,23). Surgical excision is advised after obtaining a good road map using angiography or MRI. Preoperative functional assessment is essential to avoid perioperative fluctuations in blood pressure.

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