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Pigmented vagal paraganglioma

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Abstract
Paragangliomas are uncommon and those arising from the vagal trunk are rarer. Pigmented extra-adrenal paragangliomas are still rarer and reported sites of occurrence are the uterus, spine, retroperitoneum, bladder, mediastinum and orbit. The presence of abundant pigment in a cervical paraganglion has not been reported previously. We report one such unusual case of pigmented vagal paraganglioma that arose from the vagal trunk below the nodose ganglion, had massive central necrosis and showed hypovascularity on angiography. The unusual features and difficulties in the diagnosis of such cases are discussed.

Key words: Paraganglioma; Vagus Nerve; Diseases; Pigmentation

Introduction

Paraganglia are collections of neuroepithelial cells ('Chief cells') scattered throughout the body and are embryologically derived from the neural crest. Paraganglioma is the generic term applied to tumours of the paraganglia regardless of their location.[1] These tumours are named by their site of origin. In the neck vagal paragangliomas or glomus vagale are the second most common after carotid body tumours and arise from vagal ganglia or rarely from the trunk.[2] Cervical paragangliomas are uncommon entities whose surgical management is technically challenging. Histologically, they are characterized by cell nests (Zell-ballen pattern) with a prominent fibrovascular connective tissue stroma surrounding and separating the nests.[3]

Pigmented ('black') or melanotic paragangliomas are extremely rare and only a few cases have been reported. They are located in the uterus, retroperitoneum, lumbar spine, urinary bladder and mediastinum.[4–6] The presence of abundant pigment in a cervical paraganglioma has not been reported earlier in the English literature.

An unusual case of vagal paraganglioma is reported that depicted hypovascularity on angiography, abundance of melanin pigment within tumour cells and histopathologic features of an aggressive tumour. The patient was treated by surgical excision followed by a course of radiotherapy. The differential diagnosis of such tumours is discussed and the literature reviewed.

Case report

A 45-year-old male presented with a swelling in the right side of the neck for three years. It was insidious in onset and had gradually increased in size over the past few months. There was no history of pain or trauma. Wedge biopsy had been attempted three months ago by a private practitioner. Neither the details of the procedure nor biopsy were available for review. Examination revealed a 7×6 cm firm, non-tender and non-pulsatile swelling located just below the angle of the mandible. The surface of the swelling was smooth and carotid pulsations could be felt on its anterior surface. The lower cranial nerves were normal. No bulge was seen in the lateral pharyngeal wall. The swelling was mobile in the horizontal plane only. Contrast enhanced computed tomography (CT) scan of the neck showed a contrast enhancing mass with a large area of central necrosis. The great vessels were displaced anteriorly (Figure 1).

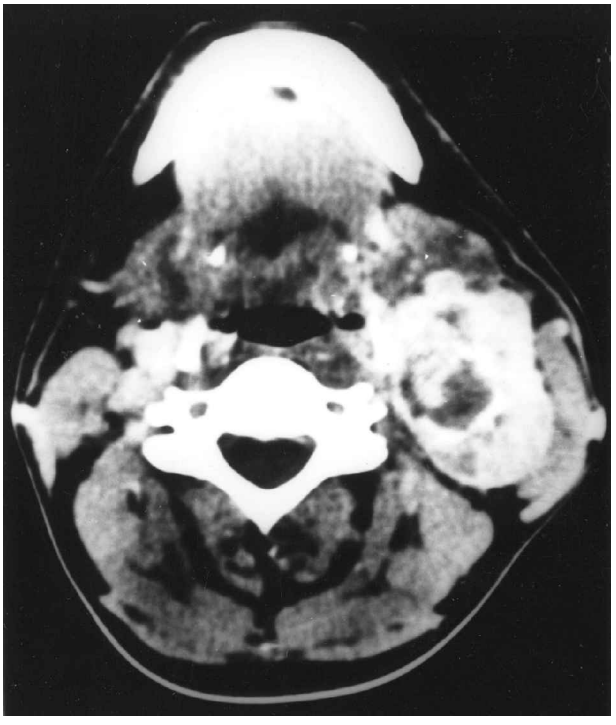

Fig. 1
CT scan showing the contrast enhancing mass with central necrosis.

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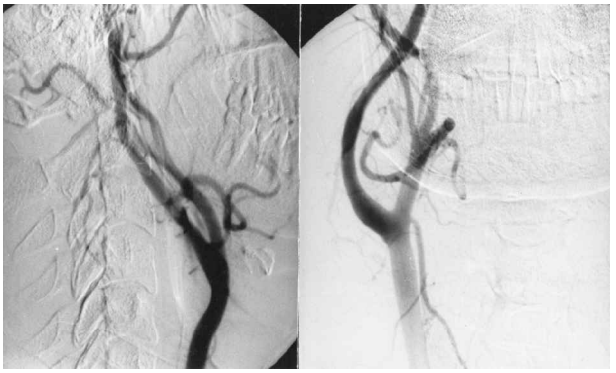

FIG. 2

Digital subtraction angiography. (a) Lateral view showing anterior displacement of common and internal carotid arteries. (b) Anteroposterior view showing splaying of internal and external carotid arteries.

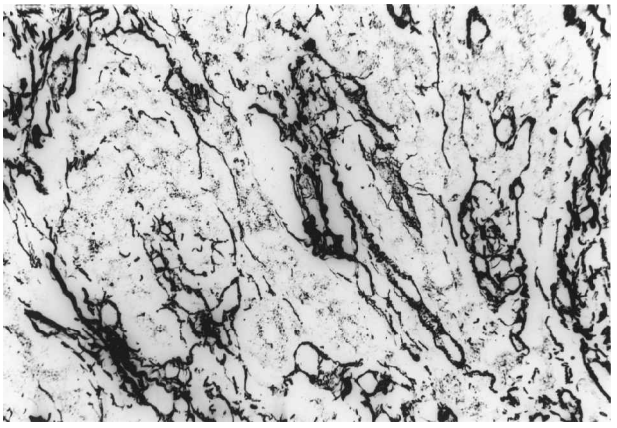

FIG. 4

Photomicrograph of reticulin preparation showing nests and trabecular arrangement of tumour cells (Reticulin; ×300)

Digital subtraction angiography showed the mass to be hypovascular, both the internal and external carotid artery were displaced anteriorly and there was splaying of the vessels at carotid bifurcation (Figure 2).

The patient was taken up for surgery with the aim of completely excising the mass. The vagus nerve and the internal and external carotid arteries were stretched over the anterior surface of the mass. The tumour was not vascular. The mass was firmly adherent to the posterior surface of the internal and common carotid artery at its bifurcation, and had to be separated by subadventitial dissection. The mass was removed in toto. It was dark brown in colour and its cut surface showed central necrosis and black pigmentation (Figure 3).

Histopathologic examination revealed cells arranged in diffuse sheets with focal nests and interconnected trabeculae separated by fibrovascular septae. The nests were surrounded by spindle-shaped sustentacular cells (Figure 4). The cells had moderate to abundant eosinophilic cytoplasm having abundant blackish brown pigment (Figure 5). The pigment was Schmorl's stain positive and negative for haemosiderin by Perl's stain indicating it to be melanin. Cellular detail could only be studied after bleaching the pigment with 25 per cent potassium permanganate followed by one per cent oxalic acid. The nuclei showed a moderate degree of pleomorphism with prominent nucleoli, but characteristic inclusions such as nucleoli of melanoma were not seen. Large areas of necrosis and capsular infiltration were present. Vascular emboli were noted. Mitotic activity was occasional. Immunostaining was carried out on paraffin sections after adequate bleaching. Antibodies used were obtained from Dako, Denmark. Immunostaining by the peroxidase anti-peroxidase method was carried out using neuron specific enclose (NSE dilution 1:100), HMB-45 (dilution 1:30) and S100 protein (dilution 1:500). Tumour cells showed focal cytoplasmic positivity with NSE (Figure 6) and a negative reaction with the other. However, the sustentacular cells were found to be positive for S100 protein. Based on the characteristic morphological appearance supported by the histochemistry and immunohistochemistry a diagnosis of paraganglioma was made. Postoperatively the patient developed right-sided vocal fold palsy. He was given 45 Gy megavoltage radiotherapy in 20 fractions over a period of four weeks. At 10 months' follow up, the patient was tumour free and his voice was near normal as the opposite fold had compensated well.

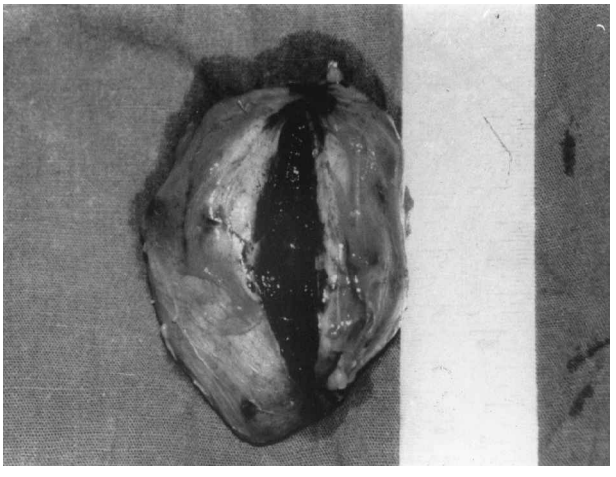

FIG. 3

Cut section of the mass showing the abundant pigment.

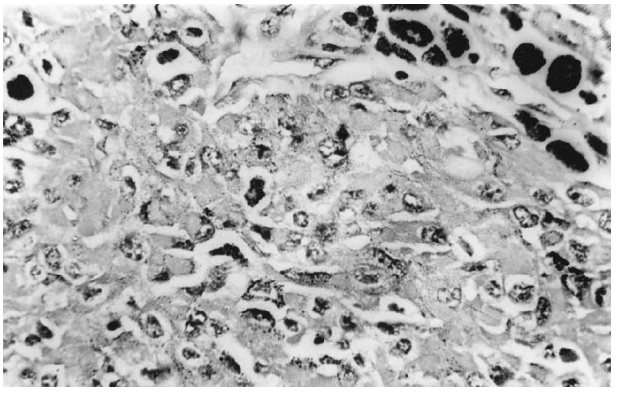

FIG. 5

Photomicrograph of the tumour showing cells with moderate amount of cytoplasm. The darkly stained cells contain abundant pigment. The lighter stained cells show moderately pleomorphic vesicular nuclei with conspicuous nucleoli. (H & E; ×300)

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FIG. 6

Photomicrograph of an immunostained section using NSE of the tumour showing cytoplasmic positivity in a few cells. The positive cells are indicated by black granular cytoplasmic positivity that has been highlighted with arrows (PAP; ×620).

- **This paper reports a pigmented vagal paraganglioma**
- **Pigmented paragangliomas in extra-adrenal sites are uncommon and no such case has been reported previously in the cervical region**
- **The paper reports the unusual features encountered and the difficulties in diagnosis that this caused**

Discussion

Vagal paraganglioma represents 2.5–4.5 per cent of head and neck paragangliomas and shows a higher incidence in females.[7] They arise from the paraganglia within, or adjacent to, the vagus nerve at the level of the inferior nodose ganglion, middle ganglion, superior ganglion or rarely at any part of the vagal trunk. Less than two per cent of head and neck paragangliomas are functional.[8] Multicentric and bilateral tumours are common.[9]

As in our case, cervical paragangliomas usually present as slowly enlarging and asymptomatic neck masses, which can be displaced laterally but not vertically because of adherence to the vagus nerve or carotid artery. Presence of bruit, pressure symptoms and cranial nerve involvement have also been reported.[7] In this case, the carotid artery was palpable over the anterior surface of the swelling with no cranial nerve palsy. Differential diagnoses of enlarged lymph nodes, branchial cleft cyst, schwannoma and carotid artery aneurysm were considered clinically.

Bilateral carotid angiography is a gold standard imaging modality for diagnosis of a cervical paraganglioma. Angiography demonstrates typical tumour blush and anterior displacement of the internal and external carotid arteries.[10] Vagal paragangliomas can produce widening of the carotid bifurcation.[2] An unusual feature of this case was the hypovascular nature of the tumour, which was uncharacteristic of a paraganglioma. Angiography revealed splaying of the internal and external carotid arteries along with anterior displacement of the common, internal and external carotid arteries.

Pre-operatively, the angiography findings and CT scan picture of a well delineated mass with central necrosis made it more likely to be a neurogenic tumour. As the tumour did not extend to skull base, the transcervical approach was selected. It showed adhesion to the carotid artery, which is a common feature. Such tumours are even known to invade the carotid artery.[7] Location of the present tumour suggests it to be arising from the vagal trunk, much below the nodose ganglion.

Other than melanomas, tumours in the neck, which can be pigmented, are schwannomas,[11] neurofibroma[12] and medullary thyroid carcinoma.[13] Although the presence of melanin pigment is relatively common in adrenal gland paragangliomas, a pigmented extra-adrenal paraganglioma is rare.[12] A cervical paraganglioma with abundant melanin pigment has not been reported before in the English literature. Reported cases are in sites where paragangliomas are rarely seen such as the uterus, bladder, mediastinum, spine and orbit.[4–6,14] In our case, the tumour cells contained coarsely granular pigment and showed the characteristic morphology of a paraganglioma. Coarsely granular pigment is unusual in a melanoma but could be seen in a pigmented schwannoma.[11] Pigmented tumour cells showing a negative reaction for S-100 protein but a positive reaction with NSE are suggestive of paraganglioma.[15] S-100 protein is nearly always present in a schwannoma.[11] Spindle cells were strongly S-100 positive indicating that they were indeed sustentacular cells of the paraganglioma.[15] Immunostaining for HMB-45, which is specific for malignant melanoma, was negative. Recently, some pheochromocytomas have shown positivity for HMB-45.[16] This strengthens the theory of divergent differentiation from the neural crest, which manifests different morphophenotypes and immunophenotypes.[17] The pigment was Schmorl's stain positive and Perl's stain negative (for haemosiderin) indicating it to be melanin. Recognition of the characteristic nesting pattern of the tumour cells and surrounding sustentacular cells with their immunohistochemical profile helped in the final diagnosis.

Hypovascularity of the tumour on angiography is difficult to explain because histological examination revealed capillaries in the fibrovascular septae. But the periphery of the tumour showed vascular emboli occluding the lumina of capillaries. This may partly explain the unique feature of hypovascularity in this paraganglioma.

The incidence of malignancy in vagal paragangliomas has been reported to be as high as 19 per cent, much higher than for any other paraganglioma.[18] The malignant form of the paraganglioma is diagnosed on the basis of clinical behaviour rather than on histological appearance. Although Lack *et al*.[8] described central necrosis, vascular invasion and mitosis as the features of malignancy, others consider metastases as the only acceptable proof.[19] In our patient the presence of vascular emboli, capsular infiltration and necrosis on histopathology and local infiltration prompted us to give radiotherapy. This would prevent recurrence and a second round of surgery which would be more difficult and associated with a higher rate of complications.

We report a rare case of vagal paraganglioma that was pigmented, had central necrosis, showed hypovascularity and angiography and arose from the vagal trunk.

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