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CLINICAL RECORD

Successful treatment of a rare metastatic malignant carotid body tumour in a young adult, with conservative surgery and local radiotherapy

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Abstract

Objective: We report a patient with a malignant carotid body paraganglioma treated with surgery and adjuvant radiotherapy. We discuss her treatment and outcome in the light of the published literature.

Case report: A 26-year-old woman presented with a 12-month history of a painless, left-sided neck lump. Ultrasound, computed tomography and magnetic resonance imaging revealed a carotid body tumour, which at surgical excision was found to be adherent to the vagus and hypoglossal cranial nerves (X and XII). The tumour was resected from the surrounding structures. Two local lymph nodes were removed to allow access. The internal carotid artery was also involved and had to be repaired with a synthetic graft. Histology and immunohistochemistry confirmed malignant carotid body paraganglioma. There were positive resection margins, and cervical lymph node metastasis was reported in one of the two nodes. Post-operatively, she had left Horner's syndrome, left vocal fold palsy and right upper limb weakness, all of which resolved spontaneously. She underwent adjuvant radiotherapy and remained recurrence free after 30 months.

Conclusion: Malignant carotid body paraganglioma can affect young adults, with an insidious onset of symptoms. In this patient, local excision (without neck dissection) and adjuvant radiotherapy were well tolerated and resulted in satisfactory local disease control.

Key words: Carotid Body Tumour; Paraganglioma; Chemodectoma; Neoplasm, Malignant; Surgical Procedure, Operative

Introduction

Carotid body paragangliomas are rare, extra-adrenal, neuroendocrine tumours arising from the paraganglionic cells of the carotid body, at the bifurcation of the common carotid artery. The majority of these tumours are non-functioning, benign and slow growing; however, most studies suggest that between 5 and 10 per cent are malignant.[1] There are no published histological criteria upon which to base the diagnosis of malignant carotid body tumour. Establishment of malignancy is thus solely based on the presence of metastasis within loco-regional lymph nodes or distant sites such as the liver and skin.[1]

The management of these tumours has been on a case-by-case basis. Most cases are managed by surgical resection, with or without adjuvant radiotherapy. Small numbers of patients have also been treated with chemotherapy alone.[2]

Due to the rarity of this tumour, there are no published randomised controlled trials regarding the efficacy of various treatments, and therefore any guidance from the literature is restricted to reviewing a number of case series from multiple treatment centres.

We present a case of a malignant carotid body tumour in a 26-year-old woman, which was found to have metastasised to a cervical lymph node, when the post-operative histology was reviewed.

A literature search of the US National Library of Medicine, National Institutes of Health, was performed using the terms 'malignant carotid body tumour', 'paraganglioma' and 'chemodectoma'.

Case report

A 26-year-old woman was seen in the otolaryngology department of the Royal Gwent Hospital in December 2007, with a discrete left cervical swelling that had been present for the previous 12 months. The lump had first been noted by the patient at the time of wisdom teeth eruption, and thus had been ignored initially. When she presented, she reported that it had remained unchanged in size since its onset and was not painful or tender. During this time, she had been systemically well, with no weight loss or night sweats. She had no other medical problems and took no regular medications.

Examination at this time revealed a single, enlarged, 3 cm, level II cervical swelling, which was clinically diagnosed at this stage as a lymph node. The remainder of the otolaryngological and general examinations was normal.

An ultrasound scan of the neck showed circumferential thickening of the carotid vessels. A computed tomography (CT) scan of the neck revealed a vascular mass measuring

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35 × 27 mm at the carotid bifurcation and upper part of the common carotid artery, suggestive of a carotid body tumour (Figure 1). This was confirmed on magnetic resonance imaging (MRI). None of the three pre-operative radiological investigations at this point demonstrated cervical lymphadenopathy.

The patient was then referred to the vascular surgery department, in keeping with local protocol. After discussion with the patient, it was agreed to remove the lesion surgically. The tumour was staged as Shamblin type three, infiltrating into the carotid bifurcation.

During the operation, two lymph nodes were noticed in the tissue overlying the tumour, and these were removed to improve access to the carotid arteries. The nodes were 2.5 and 1.3 cm along their long axis, but were kidney bean shaped and not suspected of being metastatic. A neck dissection was therefore not carried out. The tumour was excised together with the carotid bifurcation and the external carotid artery and its branches. The tumour was dissected from cranial nerves X and XII; although there was adherence of the tumour to these nerves, it seemed that macroscopic clearance had been achieved. The vascular defect extended into the internal carotid artery, and this was reconstructed with a 6 mm polytetrafluoroethylene jump graft sutured end to end to the internal and common carotid arteries.

Histology showed a nested tumour (with 'Zellballen' growth pattern) comprising nests of round cells with hyperchromatic pleomorphic nuclei, voluminous eosinophilic cytoplasm and a vascular sclerotic stroma (Figure 2).

The tumour morphology was in keeping with a carotid body paraganglioma (chemodectoma). This diagnosis was supported by the immunohistochemical profile: chromogranin A positive (Figure 3), S100 positive (Figure 4) and epithelial membrane antigen negative.

Histological analysis confirmed that the tumour had invaded the vagus and hypoglossal cranial nerves (X and XII), which had been excised in part and were sent as separate specimens. The tumour was seen to extend to the resection margin in one area, and there was also histologically confirmed metastatic tumour spread to one of the adjacent lymph nodes. The tumour was therefore diagnosed as a malignant carotid body tumour (paraganglioma).

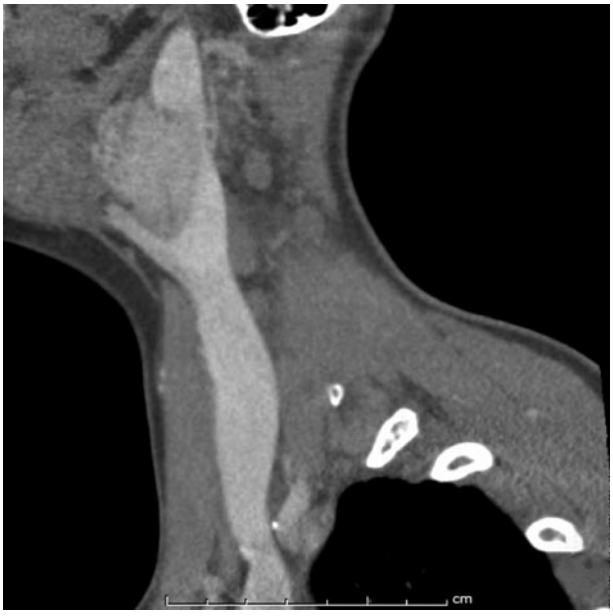

FIG. 1
Pre-operative, sagittal computed tomography showing vascular lesional mass involving common carotid and bifurcation.

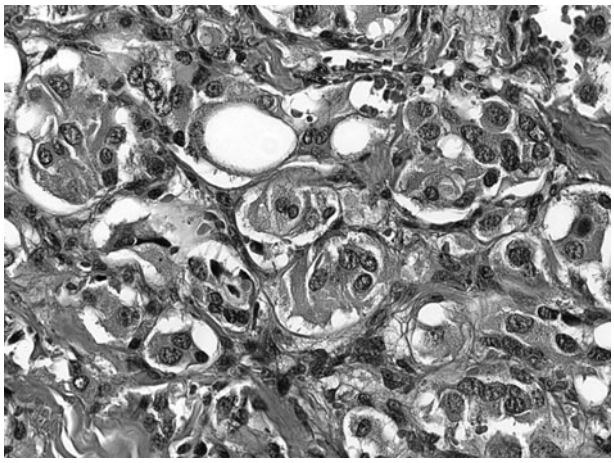

FIG. 2
Photomicrograph showing the characteristic nesting 'Zellballen' growth pattern of a paraganglioma (also known as carotid body tumour or chemodectoma). (H&E; ×400)

Post-operatively, the patient developed left Horner's syndrome, left vocal fold palsy and right upper limb weakness. There was no associated hypoglossal nerve palsy. A post-operative CT scan of the brain revealed no abnormality, and these symptoms resolved with conservative management.

The case was then referred to the head and neck multidisciplinary team for consideration of further management of the tumour, in the light of the positive surgical margin and cervical metastatic disease. A post-operative MRI was arranged, which showed no further lymphadenopathy. The patient stated that she wished to avoid further surgery if this would not have an impact on her prognosis, to minimise the risk of complications, including damaging the carotid artery repair. Because of the lack of literature to support the subsequent management plan, a further expert opinion was sought from Professor David Howard at Charing Cross Hospital, London.

After due discussion, a decision was made by the multidisciplinary team and the patient to avoid a completion neck dissection and further resection of the tumour bed. It was felt that a revised management plan of adjuvant localised post-operative radiotherapy to the neck and a post radiotherapy 'watch and wait' policy could be recommended, because of the paucity of published data regarding prognosis and neoadjuvant treatments. The patient gave written, informed consent for this treatment; (prior to this, the possible long-term secondary effects of irradiation were also discussed).

The patient received 60 Gray in 30 fractions over six weeks, which was the hospital unit's standard post-operative radiotherapy regime.

Following radiotherapy, she was reviewed monthly by the multidisciplinary team. There was no clinical suspicion of recurrence, and a post-treatment MRI scan at three months showed no lymphadenopathy.

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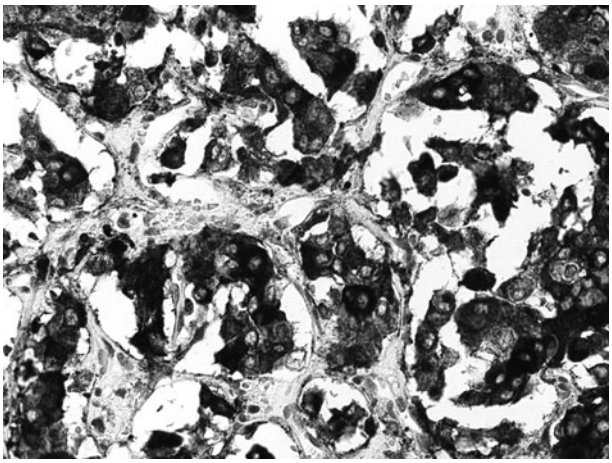

FIG. 3

Photomicrograph prepared with chromogranin stain (a specific marker for neuroendocrine differentiation), showing strong, diffuse cytoplasmic staining of the tumour cells. (×400)

After a 30-month follow up, the patient remained well with no evidence of recurrence.

Discussion

Malignant paraganglioma typically affects younger adults; the median age was 44 years in a recent case series of 59 patients taken from the American National Cancer Database between 1985 and 1996.[2] Only seven of these patients were under 30 years old. Our patient is one of the youngest cases of malignant carotid body tumour reported in the literature. The sex distribution has been approximately equal in most reports. The commonest presenting symptom is a painless, slow-growing, persistent neck mass, as in this case.[3] Signs and symptoms may be of insidious onset; a case series report by Zhang *et al.* described an average duration of 6.4 years.[4] Our patient had been aware of her neck lump for one year prior to diagnosis.

Diagnosis of carotid body paraganglioma is based upon clinical history, neurological examination, MRI scan of the neck, and histology.[3] Differentiating between benign and malignant carotid body paragangliomas is reliant on evidence of invasion into adjacent structures or lymph node metastases, as there are no reliable histological features upon which to determine their behaviour.[1]

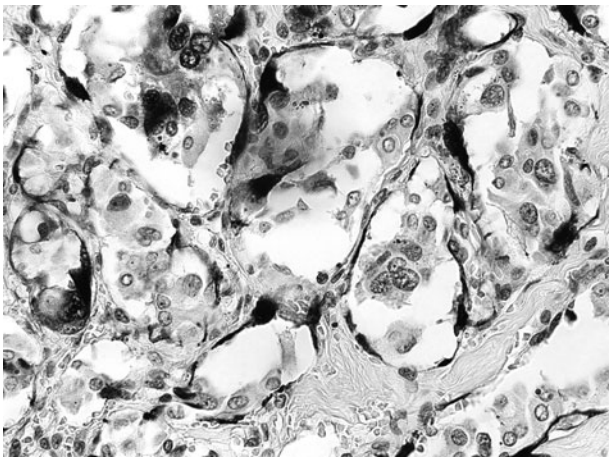

FIG. 4

Photomicrograph prepared with immunohistochemical S100 stain, showing strong staining of the sustentacular cells around the tumour nests. (×400)

Pre-operative histological diagnosis is recognised to be problematic due to the highly vascular nature of these tumours. Zhang *et al.* reported copious blood loss in one patient, and adenolymphitis in another following attempted fine needle aspiration.[4] Pettieri *et al.* suggested that biopsy of these lesions was unnecessary, and furthermore that cytological examination alone was insufficient to diagnose malignant status.[3]

These lesions have been treated surgically for over 100 years. Prior to the advancement of vascular grafting techniques, the mortality rate was up to 50 per cent.[5] More recently, the peri-operative mortality rate has been reported to be 1–2 per cent, with a morbidity rate of 40 per cent, mostly attributable to neurovascular damage.[6] Angiographic techniques now allow the possibility of radiological embolisation of the tumour prior to surgical excision or palliative radiotherapy.

Our patient had ipsilateral Horner's syndrome and vocal fold palsy post-operatively, due to adherence of the tumour to local neurological structures. A similar pattern was also noted by Morton *et al.*[7] These complications are difficult to avoid, and may indeed be part of the natural history of the disease. A recent case series noted that five out of nine patients had pre-operative Horner's syndrome, hoarse voice and glossal deviation.[4] Our patient also had a mild post-operative contralateral upper limb weakness for which no cause was found. This resolved spontaneously. There was no associated hypoglossal nerve palsy, despite the nerve being locally invaded and partially resected. This may be due to the fact that it was identified during surgery, and an attempt was made to preserve some of its fibres.

Unfortunately, surgical excision of our patient's lesion was incomplete, with positive resection margins histologically, invasion of cranial nerves X and XII, and cervical lymph node metastases. In such cases, the role of subsequent neck dissection has been debated in the literature. Lee *et al.* suggested that patients with metastasis confirmed by post-operative histological analysis may benefit from a subsequent, more comprehensive neck dissection.[2] Morton *et al.* described two cases in which selective ipsilateral neck dissection was performed at the time of primary excision, and both patients were found to have metastatic lymph nodal disease.[7] Both patients remained well at follow up, and the authors advocated this method as a means of detecting and controlling local metastasis. This may avoid the need to re-operate on an already scarred (fibrotic) neck. However, one reported case was found to have positive histological margins and lymph node metastasis, following excision of a carotid body paraganglioma.[8] This patient received a further carotid resection and neck dissection, but subsequent histology showed no evidence of residual tumour. Therefore, this patient may have received unnecessary surgery, which in the case of a radical neck dissection could have major sequelae regarding future morbidity. The authors advocated aggressive initial treatment to avoid this potential scenario.

Adjuvant radiotherapy is often used in cases of incomplete tumour excision, and radiotherapy alone is sometimes

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offered to patients for palliation and local control.[9] Due to the small number of cases and the differences in groups receiving various treatment modalities, direct comparisons are difficult. However, the use of adjuvant radiotherapy has been recommended in cases of incomplete tumour excision, as median survival may be significantly improved with adjuvant radiotherapy compared with surgical treatment alone, and is well tolerated.[2,10] This was the basis upon which we offered our patient adjuvant radiotherapy. At present, there is insufficient evidence to recommend chemotherapy in these cases.

- **A 26-year-old woman with a malignant carotid body paraganglioma was treated by primary surgery**
- **Surgery was associated with positive resection margins, a need for carotid artery graft repair, and cervical metastases**
- **Adjuvant loco-regional radiotherapy was also used**
- **The patient was in remission at 30 months' follow up**

In conclusion, our case highlights the fact that malignant carotid body tumours can occur in young adults. In this patient, despite the tumour's clearly malignant behaviour, with cranial nerve invasion and lymph node metastases, a surgical approach (without neck dissection or further carotid resection) and local radiotherapy was (at the time of writing) sufficient to achieve loco-regional control.

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Mr J Williamson takes responsibility for the integrity of the content of the paper
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