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Clinical Record

Recurrent familial malignant carotid body tumour presenting with lymph node metastasis: case report, and review of diagnosis and management of familial carotid body tumours

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Abstract

Objective: We report the case of a recurrent familial malignant carotid body tumour presenting with metastasis to local ipsilateral lymph nodes; the rarity of both recurrence combined with nodal spread is emphasised in this article.

Method: We present a case report, and a review of the world literature concerning the diagnosis and management of carotid body tumours in the familial setting.

Case report: A woman with a family history of succinate dehydrogenase complex subunit B gene mutation presented with right vocal fold palsy. A causative carotid body tumour was excised. Fifteen years later, the patient developed a right-sided swelling in the jugulo-digastric region, together with shooting pains towards her right ear. Imaging revealed right posterior triangle lymphadenopathy. Fine needle aspiration cytology of the node was equivocal. Computed tomography of her neck revealed, in addition, a mass within the right side of the larynx. Excision biopsy of the lymph node demonstrated metastatic paraganglioma. A carotid angiogram revealed a right-sided carotid body tumour. This was embolised prior to neck exploration and excision of the carotid body tumour with en bloc resection of adjacent nodes. Histological analysis confirmed the presence of lymph nodes containing metastatic paraganglioma.

Conclusion: This case report demonstrates the need for extra vigilance to enable early disease detection in the familial setting of carotid body tumour, in order to reduce the surgical morbidity associated with disease progression. In addition, our report highlights the atypical aspects of presentation in the familial setting, together with the difficulty and lack of standardisation regarding monitoring of the disease.

Key words: Carotid Body Tumour; Recurrence; Paragangliomas; Lymph Nodes; Metastasis

Introduction

The carotid body tumour is a rare neoplasm of neural crest tissue origin. It is also known as a chemodectoma, nonchromaffin paraganglioma and paraganglioma. The incidence of malignant carotid body tumour is between 6 and 12.5 per cent.[1,2] This variation is due, in part, to the considerable discrepancies in defining malignancy in cases of carotid body tumour. Some authors describe locally aggressive or recurrent behaviour as malignant,[3] whilst others require the presence of metastasis as evidence of malignancy.[4]

Familial carotid body tumours represent 10 per cent of cases. Bilateral lesions are more common and the disease onset is usually earlier,[5] compared with non-familial cases.

Case report

A 50-year-old woman presented initially in 1992 with a right vocal fold palsy. Investigation revealed a causative carotid body tumour, which was excised. Interestingly, the patient's brother had died from an extra-adrenal phaeochromocytoma aged 33 years. In addition, the patient's two sons suffered from glomus tumour. She and her two sons were subsequently found to suffer from the effects of succinate dehydrogenase complex subunit B gene mutation. Paragangliomas associated with this gene mutation have a high rate of malignancy.[6]

The patient was referred to our department in May 2007 with a right-sided neck swelling in the jugulo-digastric region, which seemed to fluctuate in size. At this time, ultrasound of the patient's neck revealed appearances consistent with reactive lymphadenopathy. There was no suggestion of recurrence.

In February 2008, the patient was seen by the endocrinology team regarding her succinate dehydrogenase complex subunit B gene mutation. A magnetic resonance imaging (MRI) scan of her abdomen and thorax demonstrated prominent lymph nodes within the right deep cervical chain, corresponding to previous ultrasound findings. The scan also demonstrated a further prominent lymph node to the left of the upper abdominal aorta. The significance of these nodes was doubtful.

The following month, the patient was seen again in the ENT out-patients department complaining of shooting pains from the right side of her neck radiating towards her right ear. A repeated ultrasound scan demonstrated a previously undetected node in the right posterior triangle region with prominent capsular vessels and hilar vessels. Fine needle aspiration and cytological analysis were

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performed but results were equivocal. A computed tomography (CT) scan of the patient's neck revealed two moderately enlarged lymph nodes on the right side of the neck, one each in the high deep cervical and high posterior triangle regions. There was also a well defined, 16×12 mm mass within the right side of the larynx at the level of the true vocal folds, extending into the subglottic region. These findings were suggestive of either lymphoma or proteinaceous mucus retention cyst.

In August 2008, an excision biopsy of the patient's right level V lymph nodes revealed metastatic paraganglioma. Reviewing the previous MRI scan, it was thought that there was a similar lesion in the carotid sheath on the right, below the skull base.

At this point, the patient was referred to the vascular radiology department. A right carotid angiogram demonstrated good vascular blush of the right-sided paraganglioma arising from branches of the right external carotid artery (Figure 1).

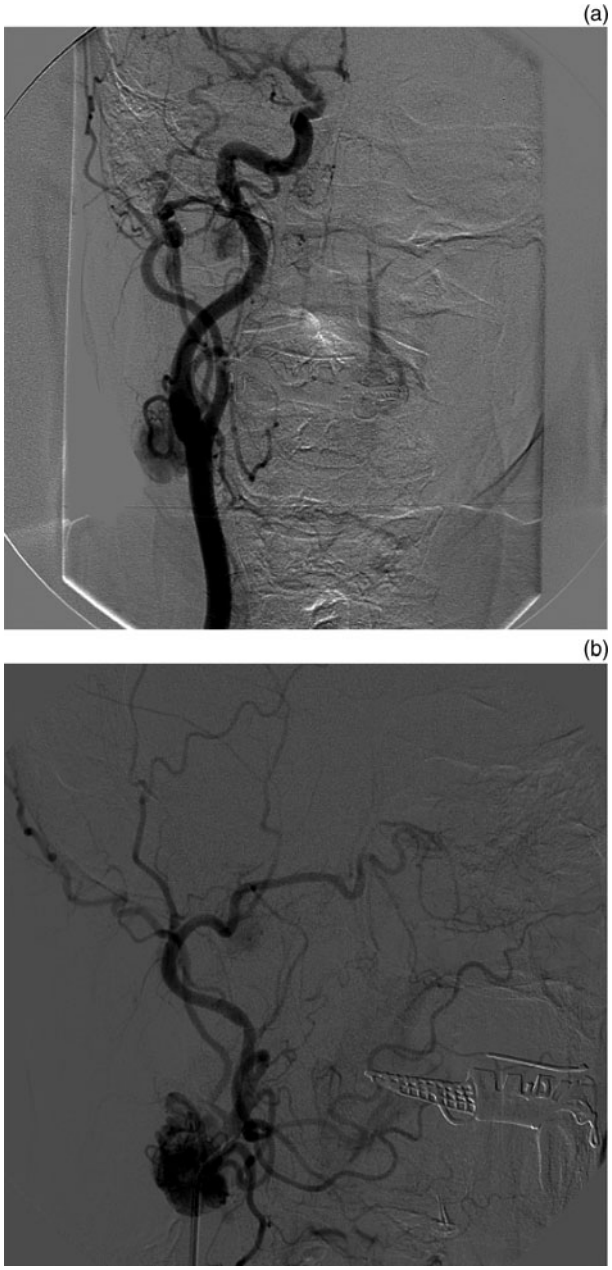

FIG. 1

Right carotid angiograms demonstrating good vascular blush of the right-sided paraganglioma arising from branches of the right external carotid artery.

Pre-operative cerebral angiography and embolisation of the right carotid body tumour were performed. The superior thyroid artery was demonstrated to be its principal vascular supply. Two smaller lesions thought to be paragangliomas were seen at the skull base, supplied by the ascending pharyngeal artery and measuring 10 and 5 mm.

A right neck exploration and excision of the carotid body tumour was undertaken. This was removed en bloc together with adjacent anterior triangle nodes. Intra-operatively, no masses were felt at the skull base.

Histopathological analysis of the resected specimens showed complete excision together with lymph nodes containing metastatic paraganglioma. It was thought that the two skull base lesions represented lymph glands rather than primary paragangliomas.

A six-month follow-up MRI of the patient's neck was reported as showing no detectable change in the size of these skull base lesions. In addition, there was no evidence of recurrent disease on either side of the neck. Interestingly however, a CT performed shortly prior to the MRI was suggestive of sclerotic lesions in the T7 and T9 vertebrae, and concern was raised as to whether these represented metastasis. Subsequent fluoroscopy-guided biopsy showed no evidence of paraganglioma metastasis or neoplasia.

Discussion

The vast majority of carotid body tumours are benign. However, metastases do occur, and have been reported in the regional lymph nodes, lungs, bones, liver and abdominal wall. A literature review revealed only one case report, from China, of recurrent malignant carotid body tumour presenting with lymph node metastasis.[7]

Pre-operative diagnosis can be obtained by digital spiral angiography, spiral CT angiography and colour Doppler imaging. Arteriography remains the 'gold standard' for diagnosing carotid body tumours, demonstrating a pathognomonic tumour blush together with its feeding vessels. Arteriography also serves as a screening tool for concomitant paragangliomas.

The differentiation of benign from malignant carotid body tumour is based on final pathological examination. Controversy remains over the histopathological diagnostic criteria for malignant carotid body tumour. In some cases of malignant carotid body tumour with regional or distant metastases, atypia of the primary tumour cells may not be prominent. Malignancy is usually defined by the existence of metastasis rather than by histological appearances, as there are no characteristic cellular changes.[7]

Hereditary carotid body tumour genes code for subunits B, C or D of succinate dehydrogenase, a mitochondrial enzyme. Our patient suffered from subunit B gene mutation; carriers of this specific mutation are more likely to undergo malignant change and to develop concomitant phaeochromocytoma (subunit D gene mutation carriers are also likely to develop this latter tumour). In comparison, the subunit C gene mutation is seldom associated with malignancy and generally occurs as an isolated mutation. Subunit D gene mutation carriers are more likely to present with multiple paragangliomas.

Carotid body tumour excision is recommended at the time of initial diagnosis in patients in good general health, in order to avoid the difficulty of subsequent excision of an enlarging and highly vascular tumour with possible encasement of the carotid arteries.[2] Neck dissection should be considered in cases with cervical lymph node metastases (as in our patient). Pre-operative embolisation of carotid body tumours aims to reduce operative blood

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loss, facilitate tumour excision and preserve the internal carotid artery flow. It contributes to devascularisation without complication,[8] but may lead to an inflammatory response. However, it has been suggested that such preoperative embolisation may make subadventitial plane dissection more difficult.[9]

Paragangliomas have historically been considered radioresistant. However, some authors now consider this belief to be false, based as it is on past experience in which only large, recurrent or inoperable tumours were treated with this modality. Several more recent studies have indicated good responses to super-voltage radiation, including some complete responses.[10]

- **Familial carotid body tumours represent 10 per cent of all carotid body tumour cases**
- **Familial carotid body tumours can present atypically**
- **Extra vigilance is needed in the familial setting, in order to enable early disease detection and to reduce morbidity**
- **There is currently a lack of standardisation of carotid body tumour monitoring**

The literature suggests that long term monitoring is essential in patients with familial carotid body tumour; screening of family members is also recommended.[11] Such screening comprises clinical examination (although reports suggest this can be unreliable),[11,12] CT, colour duplex imaging, MRI, whole body positron emission tomography, metaiodobenzylguanidine scintigraphy and genetic testing. All these tools have inherent strengths and weaknesses.

The presented case demonstrates the need for extra vigilance to enable early disease detection in the familial setting of carotid body tumour, in order to reduce the surgical morbidity associated with disease progression. In addition, our report highlights the atypical aspects of presentation in the familial setting, together with the difficulty and lack of standardisation regarding monitoring of the disease.

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Mr T C Hall takes responsibility for the integrity of the content of the paper.
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