A lump in the neck and in the petrous part of the temporal bone

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INTRODUCTION

Medullary thyroid carcinoma (MTC) accounts for 10% of all thyroid carcinomas and occurs either as a sporadic (80%) or an inherited condition (20%). Although MTC can occur as familial isolated MTC, a vast majority of the familial cases occur as a part of the multiple endocrine neoplasia syndrome type 2 (MEN 2). MEN syndromes describe the occurrence of tumours involving two or more endocrine glands and are classified into MEN 1 (parathyroid hyperplasia or adenomas, pancreatic endocrine tumours and pituitary adenomas), MEN 2a (familial MTC, phaeochromocytoma and parathyroid hyperplasia or adenomas) and MEN 2b (familial MTC associated with phaeochromocytoma and mucosal ganglioneuromatosis).

Diagnosis of MTC is based on raised plasma calcitonin values and typical pleiomorphic histological appearance with nests of polygonal, oval or spindle-shaped cells separated by varying amounts of fibrous stroma and demonstration of amyloid material. This article reports a case of MTC occurring as part of MEN 2a whose presentation, clinical course, investigations and management highlighted several interesting features of this condition.

CASE REPORT

In May 1998, a 49-year-old man was referred to the endocrine clinic with long-standing low back pain and asymptomatic hypercalcaemia. There was no history of renal calculi and family history was negative. Systemic examination and blood pressure were normal. Serum calcium was 2.79mmol/litre (normal range (NR) 2.10–2.50mmol/litre) and parathyroid hormone (PTH) level was 7.5mU/litre (NR 1.0–5.5mU/litre). Renal function was normal. X-rays of lumbar spine showed severe osteopenia, which was confirmed by a dual energy X-ray absorptiometry (DEXA) scan (z score = –2.1SD). In 1977, he had undergone sub-total thyroidectomy for a thyroid nodule and the histology had shown typical features of medullary thyroid carcinoma (MTC) including amyloid formation. Plasma calcitonin values from that time could not be traced from the hospital records. An observational policy had been pursued till 1989, when, in the absence of overt disease, he was discharged.

In view of the history of MTC and the subsequent presentation with primary hyperparathyroidism, a clinical diagnosis of multiple endocrine neoplasia (MEN) 2a was made. Urinary catecholamines were normal. Fasting plasma calcitonin was 1.5 mg/litre (normal <0.08 mg/litre) and pentagastrin test (pentagastrin 0.5mg/kg is injected intravenously over 10 seconds and calcitonin measured at 2 and 5minutes; a rise in calcitonin indicates MTC) was positive indicating residual or metastatic MTC (basal calcitonin 1.0 mg/litre peaking at 8.2 mg/litre). Computed tomography (CT) scans and an isotope bone scan did not reveal metastases in liver, lungs or bones. Residual disease was suspected to be in the thyroid remnant and he was referred for a combined parathyroidectomy and completion thyroidectomy. A single parathyroid adenoma was identified in the left lower parathyroid gland and was removed. However, the thyroid remnant could not be removed as it was adherent to the trachea and attempts to remove it resulted in significant bleeding. Histology confirmed a well-defined parathyroid adenoma and serum calcium and PTH levels normalized. Following surgery the patient was lost to follow up.

In June 2000, he presented with a sudden onset of diplopia on looking to the right and paraesthesia over the right half of face. A right sixth cranial nerve palsy was confirmed. There was no objective facial sensory loss and the rest of the neurological examination was normal. CT scan showed erosion of the petrous part of the temporal bone and a magnetic resonance imaging (MRI) scan showed a lesion in the right Meckel's cave, the appearances of which were suggestive of a schwannoma or neurofibroma. However, in view of the history of MTC and a plasma calcitonin of 4.0 mg/litre, the possibility of a secondary deposit was considered. The authors sought evidence for a neuroendocrine tumour using specific radionuclides. An octreoscan, an MIBG scan (iodine-131-meta-iodobenzylguanidine) and a pentavalent dimercaptosuccinic acid (DMSA) scan did not show any uptake in the area where the lesion had been demonstrated on the MRI scan.

Over the following 12 months there has been no clinical or radiological progression of the lesion and the patient has remained well. Diplopia has persisted and is being successfully managed by appropriate prism lenses. The authors believe that this patient has MEN 2a syndrome and the residual MTC is likely to be in the thyroid remnant. The intracranial lesion is most probably a neurofibroma, which is known in association with MTC. As the patient remains well, an observational policy will be followed for both the residual MTC and the intracranial lesion and the neurosurgical team would consider a biopsy or removal of the intracranial lesion in the event of its clinical and radiological progression.

DISCUSSION

MTC arises from the parafollicular cells of the thyroid. In its hereditary form it occurs as a part of the MEN 2 syndromes or as isolated familial MTC. MTC is the commonest clinical manifestation of MEN 2 and even patients who present with phaeochromocytoma or hyperparathyroidism usually have a positive pentagastrin test (Gagel et al, 1998). It usually presents as a thyroid swelling and uncommonly with systemic symptoms as a result of ectopic hormone production (Vitale et al, 2001). Diagnosis is based on histological features and a positive pentagastrin test.

The clinical course of MTC is variable, ranging from indolent to extremely aggressive (Kakudo et al, 1985). The 10-year survival varies from 55 to 95% depending on the stage of the disease (Girelli et al, 1998). The clinical staging systems correlate survival to size of the

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primary tumour, presence or absence of lymph node metastases, and presence or absence of distant metastases.

Several interesting features of this condition are demonstrated by this patient. Typically MTC was the first manifestation of the MEN 2a syndrome. Absence of family history is recognized in up to a third of cases. Although a distinct parathyroid adenoma, as seen in this patient, is a recognized cause of hyperparathyroidism in MEN 2, it is much less common than diffuse parathyroid hyperplasia (Carney et al, 1980). The clinical course of this patient suggests that the MTC was indolent, as the patient has survived for over 20 years even though he clearly harboured persistent disease. Attempts to localize the persistent disease were not successful which is another well-recognized feature of MTC (Van Heerden et al, 1990).

The management of such a patient is controversial. An aggressive approach using selective venous catheterization is recommended by some (Tisell et al, 1986), which is a laborious, invasive and expensive technique (Hansen et al, 1976). In view of the excellent 5- and 10-year survival rates (90% and 85%) seen in patients without this treatment being undertaken (Girelli et al, 1998), others recommend a conservative approach (Van Heerden et al, 1990) similar to the one the authors followed. The possibility of a metastatic disease was considered for the intracranial lesion but was excluded by radionuclide imaging and an absence of progression of the lesion over the next year. Radiological diagnosis of neurofibroma could not be confirmed histologically although this possibility is favoured by the known association of familial MTC and neurofibromas type 1 (Hansen et al, 1976).

The genetic link between these two types of tumours probably lies in the expression of ret proto-oncogene. Ret mutations have been identified in patients affected by familial MTC syndromes (Eng et al, 1996; Karga et al, 1998) and ret proto-oncogene product has been histologically localized in neurofibromas (Nakamura et al, 1994). It is tempting to speculate that a mutation in ret proto-oncogene is responsible for both the MTC and intracranial mass lesion in this patient. **HM**

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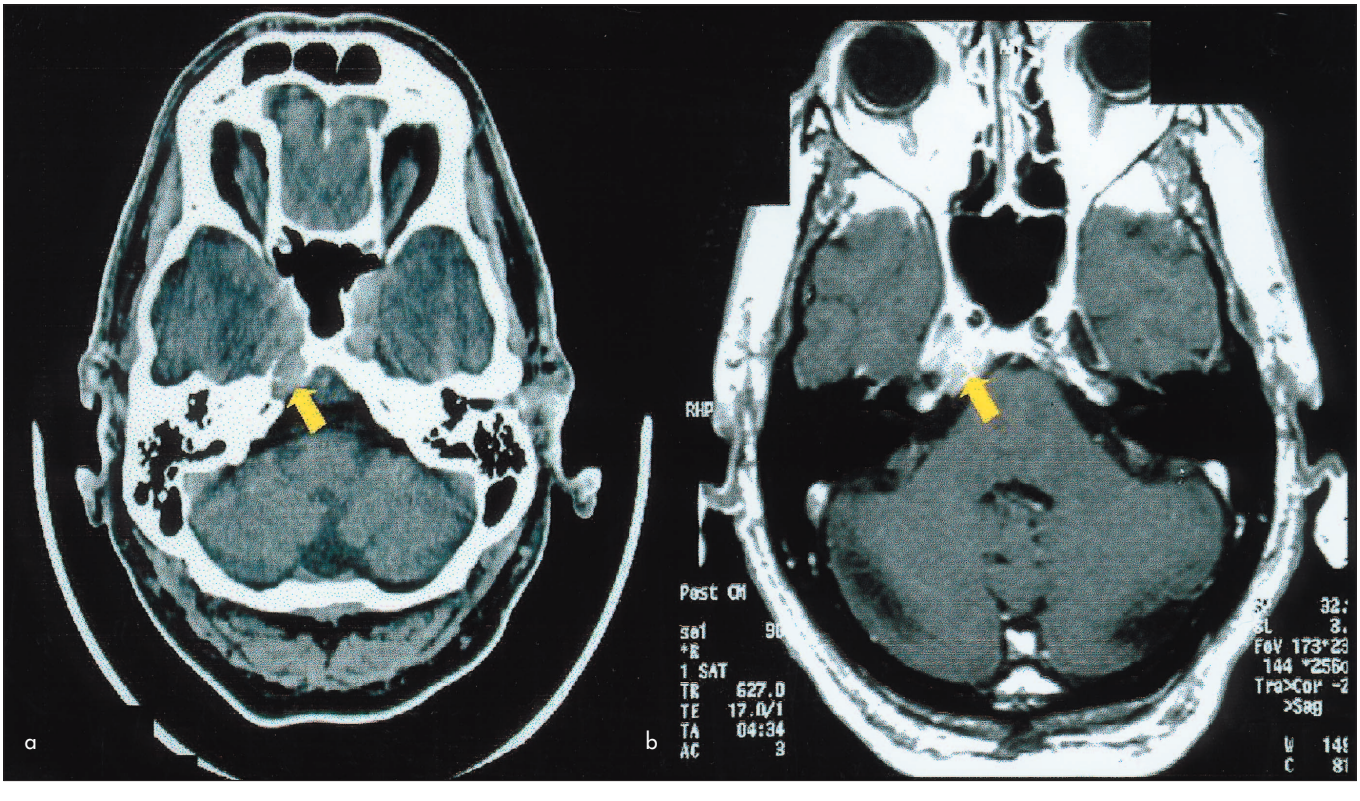

Figure 1. a. Computed tomography and (b) magnetic resonance imaging of the head.