A patient with co-existing bronchial carcinoid tumour and bilateral phaeochromocytoma

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Summary
We report a 31-year-old Chinese man with bronchial carcinoid tumour and bilateral phaeochromocytoma. His sister also gave a history of bilateral carotid body paraganglioma. This case demonstrates the importance of screening for other endocrine disorders in patients with foregut carcinoid tumours.

Keywords: bronchial tumour, carcinoid tumour, phaeochromocytoma

Introduction

Griffiths¹ first identified the association between duodenal carcinoid, phaeochromocytoma, and neurofibromatosis and proposed that this represented a specific multiple endocrine neoplasia syndrome which he classified as MEN type III a. We now report a patient in whom a bronchial carcinoid tumour coexisted with phaeochromocytoma. There was also a history of bilateral carotid body tumours in a sibling.

Case history

A 31-year-old Chinese man first developed episodic attacks of tremor, flushing, diarrhoea, and sweating in early 1988. These attacks came on several times a month and lasted 5–10 minutes. In February 1989, he developed haemoptysis and was seen in another hospital. Bronchoscopy indicated a tumour in the right upper lobe bronchus. Right upper lobectomy was performed. Histology showed a 15×10 mm carcinoid tumour which was neurone-specific enolase and Grimelins positive. The resection margin and three adjacent lymph nodes were clear of tumour. Spot urine for 5-hydroxy indole acetic acid (HIAA) checked after the procedure was not elevated. His symptoms, however, did not improve. Twenty-four hour urine for vanillylmandelic acid (VMA) was then checked and was found to be elevated at 156 nmol/day (normal range 7–85). Magnetic resonance imaging (MRI) of the abdomen revealed bilateral adrenal tumours. There was no sign of liver metastases, or thoracic or pelvic tumours. He was subsequently referred to our unit for further investigation and treatment. His sister had been diagnosed to have bilateral carotid body tumours which were removed in another hos-

pital in 1982 and 1985. Histology indicated non-functioning paraganglioma. His father died from oesophageal carcinoma. His mother and two brothers were well but refused further investigation or follow-up.

Clinical examination revealed a right thoracotomy scar. There was no palpable goitre nor skin nodule. Pulse was 80 beats/min. Blood pressure was 140/90 mmHg. There was no postural hypotension. The rest of the examination was unremarkable. The results of biochemical investigations are given in the box.

Thyroid ultrasound showed a 7-mm nodule at the lower pole of the right thyroid. Fine needle aspiration cytology was normal. Meta-iodo-benzylguanidine scan suggested a region of rather diffuse uptake which was only slightly increased above background in the right upper quadrant of the abdomen and appeared as low-grade liver uptake. MRI of his neck and upper thorax was normal. Venous catheterisation and sampling suggested a noradrenaline-secreting phaeochromocytoma of the right adrenal. The left renal vein could not be catheterized. He was treated with phenoxybenzamine and propranolol in preparation for adrenalectomy.

At operation a 5×2×4 cm tumour was found on the right adrenal and a 4.5×2×3.5 cm tumour on the left adrenal. Histology confirmed bilateral phaeochromocytoma. No capsular or vascular invasion was seen. He had an uneventful postoperative recovery and was given hydrocortisone and fludrocortisone replacement therapy. A pentagastrin-stimulation test performed subsequently showed normal calcitonin values. He remains well at regular follow-up.

Discussion

To our knowledge this is the first reported case of a Chinese patient with bronchial carcinoid,

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Investigations
<ul style="list-style-type: none">• 24-h urine VMA 130 nmol (normal 0–41)• 24-h urine adrenaline 46–82 nmol (normal 9–113)• 24-h urine noradrenaline 10 421–14 609 nmol (normal 63–146)• normal renal, liver and thyroid function• normal serum calcium and phosphate levels• normal dexamethasone suppression test

phaeochromocytoma, and a family history of paraganglioma. Interestingly, neither he nor any member of his family has evidence of neurofibromatosis. The coexistence of these neuroendocrine tumours is unlikely to be coincidental.

Lubarsch² first described a carcinoid tumour in 1888. In 1962, Williams³ classified carcinoid according to embryologic origin into derivatives of foregut (thymus, bronchus, stomach, and duodenum), midgut and hindgut (jejunum, ileum, appendix, colon, and rectum). Most reported carcinoid series⁴⁻⁶ indicate foregut carcinoids to be less common than midgut- and hindgut-derived carcinoids, accounting for less than 20% of all carcinoids. On the other hand, in patients with carcinoid tumours and other endocrine tumours, the carcinoid tumours are usually of foregut origin.^{4,5} Foregut carcinoids can produce a variety of hormones such as ACTH and somatostatin. In addition to the difference in anatomical distribution, there is also a difference in sexual predominance. Carcinoids not associated with other endocrine tumours are evenly distributed between men and women. In patients with other associated endocrine tumours, bronchial carcinoids are more common in women (79%) and tend to be benign while more men (88%) have thymic carcinoids which are usually malignant.⁶

Underdahl⁷ was the first to note the presence of a bronchial carcinoid in a patient with MEN type I. Since then other reports have emerged to support the linkage.⁸⁻¹⁰ In 1965, Barnard and Johnson reported a case of malignant pheochromocytoma and duodenal carcinoid.¹¹ More recently, Griffiths suggested that the association between duodenal carcinoid, pheochromocytoma and neurofibromatosis forms a distinctive neuroendocrine syndrome which he classified as type III a.¹² On the other hand, paraganglioma has been associated with carcinoid tumour and neurofibromatosis.¹³

Multiple endocrine neoplasia type I

Wermers' syndrome
autosomal dominant
parathyroid adenoma
+ pituitary adenoma (prolactin, growth hormone)
+ pancreatic endocrine tumour

Multiple endocrine neoplasia type II

Sipple's syndrome
autosomal dominant
parathyroid adenoma
+ pheochromocytoma
+ medullary carcinoma of the thyroid

The predominance of foregut carcinoid may be embryologically associated with the development of multiple endocrine neoplasia. Histological evidence suggests that bronchial carcinoid, pheochromocytoma, and paraganglioma are tumours of the peripheral nervous tissues. Although bronchial carcinoid derives from Kultchitsky cells of bronchial epithelium,^{14,15} histologically, it can be almost identical to pheochromocytoma and paraganglioma which arises from the chromaffin cells.¹⁶

The causes of these neuroendocrine tumours have not been well established. Stephen¹³ proposed the possibility of production of a local nerve-derived trophic factor in the pathogenesis of these tumours, whereas Griffiths¹² suggested a genetic defect leading either to a production of a circulating growth-stimulating substance or to an abnormality of the intracellular growth-control mechanisms rendering the cells more likely to develop neoplasia. There is, however, no evidence of racial differences in the incidence of these tumours.

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