A patient with recurrent sweating

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A 60-year-old retired baker was referred to out-patients with a 6-year history of intermittent sweating. The sweats occurred without warning approximately once per month, and were accompanied by anxiety. Each episode would last up to 10 minutes, and would drench his clothes. There was no associated flushing or palpitations and no headaches. There was no change in bowel habit. He had a history of rheumatoid arthritis treated with prednisolone and weekly methotrexate. On examination he was plethoric and mildly Cushingoid, but had no telangiectasia. Blood pressure was 140/80 mmHg in the right arm and 145/80 in the left with no postural drop, and there were no cardiorespiratory abnormalities. The liver was palpable 2 cm below the costal margin. No other abnormalities were found on examination. Routine investigations showed normal urea and electrolytes, liver function tests, thyroid function tests and full blood count, an erythrocyte sedimentation rate of 6 mm/h and a normal chest radiograph. Four separate 24-h urine collections for catecholamines were undertaken (table). Abdominal magnetic resonance imaging (MRI) showed two lesions (arrowed) on a T2-weighted scan (figures).

Table 24-Hour urinary catecholamine results on four occasions

	Normal (nmol/l)	1	2	3	4
Noradrenaline	70–550	1312	889	771	877
Adrenaline	10–100	70	59	59	48
Dopamine	350–2900	2921	2356	1691	2031

Figure 1

Figure 2

Questions

- 1 What is the probable diagnosis?
- 2 Where is the site of the primary lesion?

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Answers

QUESTION 1

Persistently raised urinary noradrenaline is highly suggestive of phaeochromocytoma. Classical symptoms of paroxysmal palpitations and headache occur in 60% of patients, although sweating may be the only symptom in approximately 12%. Sustained hypertension is seen in 50% of patients.

QUESTION 2

The MRI scans show no abnormality of the adrenal glands. The arrowed areas show a bright signal adjacent to the lower edge of the liver. This is in the area of the Organ of Zuckerkandl, which is a sympathetic ganglia at the origin of the inferior mesenteric artery. A second bright area is seen in the right lobe of the liver, which was thought to be a secondary deposit. After adequate blockade with phenoxybenzamine and propranolol, the patient underwent a laparotomy where a 2-cm lesion between the upper inferior vena cava and the right crus of the diaphragm was isolated and removed. Frozen section suggested a neuroendocrine tumour although malignancy could not be excluded, and hence the lesion in the liver was also removed by partial hepatectomy. Histological examination of the lesion in the abdomen showed a benign paraganglioma of the Organ of Zuckerkandl, while the lesion in the liver was a cavernous haemangioma unrelated to the endocrine tumour. The patient was subsequently asymptomatic and further urinary catecholamine estimations 2 months post-operatively were in the normal range.

Discussion

Phaeochromocytoma is a rare tumour of chromaffin cells, which are of neuroectodermal origin. It is estimated that phaeochromocytoma is present in 0.1% of patients with hypertension, although up to half of patients with phaeochromocytoma may be normotensive between paroxysms.¹ Approximately 10% of these tumours in adults are extra-adrenal (also called paragangliomas), although in children 35% are extra-adrenal. Most extra-adrenal phaeochromocytomas are intra-abdominal, and common sites include the urinary bladder, liver or kidney, sympathetic ganglia in the para-aortic area of the abdomen, and the Organ of Zuckerkandl at the origin of the inferior mesenteric artery. Rarer sites include sympathetic ganglia in the aorticopulmonary, carotid, jugulotympanic, intravagal, laryngeal, coronary, pulmonary and orbital areas. Extra-adrenal phaeochromocytomas are also described in association with Carney's multiple neoplasia triad (extra-adrenal phaeochromocytoma, gastric epithelioid leiomyoma and pulmonary chondromas).²

Learning points

- around 10% of phaeochromocytomas are extra-adrenal
- a common extra-adrenal site is the Organ of Zuckerkandl
- elevated 24-h urinary noradrenaline alone is suggestive of an extra-adrenal phaeochromocytoma
- extra-adrenal phaeochromocytomas are more likely to be malignant than their adrenal counterparts

Extra-adrenal phaeochromocytomas appear to exhibit slightly different behaviour to their adrenal counterparts. There is some evidence to suggest that extra-adrenal phaeochromocytomas are more likely to be malignant compared to adrenal disease; approximately 30% of extra-adrenal phaeochromocytomas are malignant compared to 10% of adrenal tumours. Furthermore, extra-adrenal phaeochromocytomas may be more likely to recur following excision.³ A higher index of suspicion for extra-adrenal phaeochromocytoma is suggested by an elevated noradrenaline compared to adrenaline. This is due to lack of expression in extra-adrenal phaeochromocytoma of the glucocorticoid regulated enzyme, phenylethanolamine N-methyl transferase (PNMT), which is responsible for the conversion of noradrenaline to adrenaline (tumours of the Organ of Zuckerkandl may secrete both noradrenaline and adrenaline as they may possess PNMT). In keeping with adrenal phaeochromocytoma, feedback inhibition of the tyrosine hydroxylase enzyme by noradrenaline is lost, thus the high catecholamine synthesis with defective storage in chromaffin granules results in a large increase in catecholamine turnover.⁴

Localisation of extra-adrenal phaeochromocytoma has been made considerably easier by the advent of MRI scanning, where lesions greater than 1 cm are seen as a bright signal on a T2-weighted image.⁵ ¹²³I-MIBG (metaiodobenzylguanidine) scanning can also be used, although smaller extra-adrenal tumours may not be easily observed. Follow-up after resection of the original tumour is important because of the risk of recurrence, and also the possibility of malignancy which may have been missed on original histological assessment. This can be adequately done by yearly 24-h urinary catecholamine estimations.

Final diagnosis

Extra-adrenal phaeochromocytoma of the Organ of Zuckerkandl.

Keywords: phaeochromocytoma; Organ of Zuckerkandl; catecholamines

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