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Pseudophaeochromocytoma in two young Africans

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Patients with essential hypertension may present with a clinical syndrome mimicking phaeochromocytoma.

CASE HISTORIES

Case 1

An African man aged 36 was seen as an emergency with dysphasia, left facial weakness and a left hemiparesis. Hypertension had been detected by his general practitioner six months earlier and treated with bendroflumethiazide, but blood pressure control had been erratic, with frequent episodes of headache, palpitations and sweating. On admission he had a blood pressure of 240/120 mmHg, bounding tachycardia and a heaving displaced apex. Proteinuria was 2+ but there was no papilloedema. The chest radiograph, electrocardiogram and echocardiogram indicated left ventricular hypertrophy. CT of the brain revealed infarcts in the right caudate and thalamic nuclei.

Labetalol was prescribed for the hypertension but the blood pressure fluctuated widely, reaching peaks of 250/150 mmHg. A suspicion of phaeochromocytoma was supported by raised 24-hour urinary excretion of noradrenaline, metadrenaline, and hydroxymethoxymandelic acid (HMMA) (Table 1). However, when labetalol was stopped, the results of repeat tests were normal. Plasma renin activity (PRA) was 3.60 pmol/L (reference range 1.1–2.7) and aldosterone 120 pmol/mL/h (100–450). Abdominal CT was normal and on further investigations

no secondary cause of hypertension could be found. Subsequently, blood pressure control was achieved with an angiotensin-converting enzyme inhibitor and an alpha-blocker and he made a gradual neurological recovery.

Case 2

An African man of 30 was referred by his general practitioner for investigation of episodic dizziness, headaches, palpitations, sweating and tremors. Symptoms occurred in stereotypic fashion several times a day, sometimes lasting up to an hour and leaving him exhausted. There were no obvious precipitating stresses. A borderline raised blood pressure had been documented on several past surgery visits. Two of his sisters had hypertension. There was no proteinuria or papilloedema. The electrocardiogram was consistent with left ventricular hypertrophy but other investigations, including CT of the brain, yielded nothing of note.

He was admitted for exclusion of phaeochromocytoma. Inpatient monitoring revealed a pattern of symptomatic hypertensive episodes with blood pressure peaks of 200/140 mmHg. 24-hour urinary catecholamines on two separate days were normal (Table 1). PRA was within normal limits at 1.20 pmol/L, as was aldosterone at 310 pmol/mL/h. Other secondary causes of hypertension were excluded and his symptoms and blood pressure control improved on verapamil and atenolol.

COMMENT

Phaeochromocytoma should be considered in the evaluation of patients with symptomatic hypertensive episodes because it is potentially fatal if unrecognized. Confident exclusion of this condition can prove challenging. The diagnosis rests on demonstration of supranormal amounts of catecholamines or metabolites in urine or plasma. However, most of the widely used tests are prone to both false-negative and false-positive results. The most reliable biochemical screens for phaeochromocytoma are 24-hour urine estimations of catecholamines, metanephrines and vanillylmandelic acid (VMA) as well as plasma catecholamines and metanephrines.¹ Of these, VMA has the lowest sensitivity (64%) but its specificity is high (95%); 24-hour urinary catecholamines have better sensitivity (86%). The plasma metanephrines (sensitivity 99%, specificity 89%) have been advocated as the test of first choice but are not widely available.¹

In both our patients, phaeochromocytoma was excluded by the finding of normal urinary catecholamines. However, hypertensive patients with equivocal biochemical screens require further testing and the pentolinium suppression test is the preferred pharmacodynamic test. Pentolinium suppresses sympathetic overactivity in patients with

Table 1 Urinary catecholamines and metabolites on various days after hospital admission

Day	Noradrenaline (reference range 60–660 nmol/24 h)	Adrenaline (reference range 15–160 nmol/24 h)	Dopamine (reference range 540–4440 nmol/24 h)	HMMA (reference range <35 µmol/24 h)	Metadrenaline (reference range <6.5 µmol/24 h)
Case 1					
3	746	86	1747	39	9.7
6	243	52	1756	26	5
10	180	37	1195	7	–
14	150	26	1610	14	–
Case 2					
4	125	36	883	14	–
8	52	17	684	11	–

HMMA=hydroxymethoxymandelic acid. Urinary catecholamines were measured by high performance liquid chromatography with electrochemical detection, urinary HMMA by gas chromatography and urinary metadrenaline by the Pisano spectrophotometric method

primary hypertension, and a normal result effectively excludes a pheochromocytoma.² An abnormal result is an indication for diagnostic localization with MRI, CT or a metaiodobenzylguanidine (MIBG) scan. MIBG scanning is not sensitive enough to exclude pheochromocytoma (sensitivity 77–90%) but is useful in instances where CT or MRI have failed to localize a biochemically proven tumour.³

Certain clinical situations may further blur the distinction between essential hypertension and pheochromocytoma. In the first patient a suspicion of pheochromocytoma was enhanced by the finding of raised urinary catecholamines and metabolites but the patient was then taking labetalol, a known cause of false-positive results.⁴ Subsequent tests on stopping the medication were normal. In addition, this patient had a cerebral infarction, which itself can result in transient catecholamine increases.⁵ An unusual finding in this patient was the high renin activity. Though suggestive of the generalized sympatho-adrenal activation common to both pheochromocytoma and subsets of primary hypertension, this was not accompanied by a raised aldosterone. The reason for this is unclear but such renin/aldosterone dissociation has been described in critically ill patients.⁶ Conversely, renin activity in the second patient was low-borderline, with aldosterone in the upper range of normal. Low renin is not uncommon in black persons with primary hypertension; moreover, a recent study found a risk of primary hypertension in people with aldosterone levels in the upper-normal range.⁷

With the exclusion of secondary causes of hypertension both patients therefore have essential or primary hypertension. Primary hypertension as a pheochromocytoma imitator is well-recognized but seldom reported.⁸ Both our patients were young black males, a group in whom pseudopheochromocytoma has not been emphasized and who are particularly vulnerable to end-organ damage from hypertension.⁹

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