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Lesson of the week

Pitfalls in the diagnosis of phaeochromocytoma

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Phaeochromocytoma, a rare endocrine disorder causing arterial hypertension, is found in less than 0.1% of patients with hypertension.¹ The diagnosis is excluded by the repeated finding of normal catecholamine (for example, dopamine) concentrations in urine or blood. If catecholamine concentrations are increased in combination with an adrenal mass, phaeochromocytoma is usually confirmed by an increased uptake of a radiolabelled catecholamine precursor in the region of the adrenal tumour. We present a case in which the clinical presentation and the results of laboratory, radiological, and nuclear investigations led to an incorrect diagnosis of phaeochromocytoma.

Case report

A 73 year old woman presented with severe headache, tinnitus, and a blood pressure of 240/140 mm Hg. She had been treated for arterial hypertension and diabetes mellitus for over 10 years. During a search for secondary hypertension, abdominal ultrasonography showed an enlargement of the right adrenal gland of 3.5 cm. The dopamine level in a 24 hour urine was 25 252 nmol (upper normal limit 2500 nmol). This was confirmed by a second analysis (35 628 nmol). Adrenaline and noradrenaline concentrations were within normal ranges. Magnetic resonance imaging confirmed a 2.5×3.5×4 cm mass in the right adrenal gland, and a scan using metaiodobenzylguanidine labelled with iodine-123 showed isolated uptake of radionuclide in the same region (figure). A dopamine secreting, possibly malignant, right sided phaeochromocytoma was postulated, and the patient underwent right adrenalectomy. The procedure was uneventful. Histology, however, showed a large adenoma of the adrenal cortex; a phaeochromocytoma could not be detected. Postoperatively, the patient still required anti-hypertensive treatment. The urinary excretion of dopamine remained high at 43 068 nmol daily, and a

repeat ¹²³I-metaiodobenzylguanidine scan showed the same hot spot.

The patient was taking 125 mg levodopa with carbidopa twice a day for restless legs. This was stopped. A 24 hour urine sample three weeks later contained 4019 nmol dopamine, but this reverted to normal values four months later. Re-examination of the ¹²³I-metaiodobenzylguanidine scan and magnetic resonance imaging showed that the hot spot was located well below the adrenal mass and that it was caused by delayed excretion of the radionuclide due to a benign dilation of the right renal pelvis. The patient's blood pressure is now satisfactorily controlled with four antihypertensive drugs.

Discussion

This patient presented with poorly controlled blood pressure, which prompted the clinicians to search for secondary hypertension. Three classic pitfalls, however, led to the misdiagnosis of phaeochromocytoma. The first pitfall was that the finding of an adrenal tumour

Careful drug history and critical review of all tests are essential to diagnose phaeochromocytoma

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Suspected adrenal tumour (arrow) after magnetic resonance imaging (left) and scanning with ¹²³I-metaiodobenzylguanidine (right, dorsal view)

was related to hypertension. Adrenal tumours are incidentally found in 1.5% of computed tomograms; in a large survey, only 4.2% were found to be phaeochromocytomas. Thus the presence of an adrenal tumour together with hypertension is a coincidence in most of the cases.² The second pitfall was the assumption that the high urinary dopamine levels were related to the tumour, and other causes for false positive catecholamine concentrations were not considered.³⁻⁴ Our patient was taking a moderate dose of levodopa with carbidopa. After the drug was stopped, dopamine levels returned to normal over a period of several weeks, indicating that this drug was responsible for the increased levels. The specificity of urinary catecholamines in sporadic cases of phaeochromocytoma is only 75%. Recently, the determination of levels of plasma free metanephrines has been recommended, which have a higher specificity and sensitivity for detection of phaeochromocytoma.⁵ The third pitfall was that a positive ¹²³I-metaiodobenzylguanidine scan was thought to confirm the diagnosis of right sided phaeochromocytoma. The specificity of this scan is more than 95%, although accumulation of radionuclide in a dilated renal pelvis may give a false positive result.⁶⁻⁷

In this case, the sequence of positive tests misled the clinicians into suspecting a phaeochromocytoma. In a population of patients with therapy resistant hypertension and an adrenal mass, the prevalence of phaeochromocytoma is around 30%.⁵ The finding of increased levels of urinary catecholamines (sensitivity

91%, specificity 75%) double this probability.⁵ If 60% are taken as a pretest probability for next test, a positive ¹²³I-metaiodobenzylguanidine scan (sensitivity 100%, specificity of 95%) increases the probability to 97%.⁸ A correct diagnosis of phaeochromocytoma depends on a critical interpretation of each diagnostic test, a thorough review of anatomical and functional examinations, and careful history taking, including drugs.

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My most useful surgery instrument

What could it be that really makes a difference among the clutter of my room? Perhaps the clichéd badge of medical authority, the stethoscope? No, on reflection, I think not: "Mr chesty cough aged more than 60" will receive an antibiotic whatever I hear, and little "Miss croupy cough but well" will not, even if I do hear the odd crackle on a lung base. Perhaps it is the sphygmomanometer: think of all those strokes saved by judicious use of bendrofluazide. Yet again, perhaps not: "Mr ischaemic heart diseases on three antihypertensives at full dose" will have high blood pressure whatever I throw at his cardiovascular system. Perhaps then, it's the pocket spirometer, since I do like collecting patients' FeV₁ and FVC and entering the results in the little boxes on the COPD template, but does it alter my management? No? Perhaps the tape measure for measuring diabetic abdomens, or maybe the tendon hammer, but when last did a tendon reflex really matter? I can't claim it's the unused pulse oximeter purchased after much eloquent pleading with partners. The digital ear thermometer impresses parents, but feeling the heat from junior pink cheeks is probably more reliable and quicker. Still, the measurements give a veneer of competence.

No, what really matters is the pirate ship. It has perfect diagnostic precision: well children play pirates, sick ones ignore it. And this is the least of its benefits. Small children now contently jam pirates into the rigging instead of roaming the surgery floor. My room rings to little cries of delight at finding the pirate treasure instead of my frantic yelps as a toddler investigates the innards of the yellow waste bin that is too big to place out of reach. Perhaps doctors with pirate ships could negotiate cheaper surgery insurance.

I can hear parents now; I'm relaxed (though, curiously, the sound of wee pirates firing the ship's cannon or bashing buccaneers together seems to worry parents, whereas they cheerfully ignored their children's experiments with MSU bottles or syringes). And the little ones now cry as they are removed from the room and are separated from their new toy (parents' problem, not mine), which is much better than crying when they come in (definitely my problem).

There's also the curious fact that the cheeky wee chap with the white beard leaning out of the crow's nest and brandishing a cannon reminds me of a retired partner of mine wielding an electric drill, who even now might be roaming the North Sea on his own little ship.

And if I'm really having a hard time I can look at the rigging, and, with just a dash of imagination, I am sailing my own boat on Kielder Water far away from surgeries and sphygmomanometers.

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We welcome articles up to 600 words on topics such as *A memorable patient*, *A paper that changed my practice*, *My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. Please submit the article on <http://sdubmit.bmj.com>. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.