Phaeochromocytoma
A CASE REPORT

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SUMMARY

A 52-year-old man presented with a 4-year history of paroxysmal attacks of anxiety, giddiness, palpitation, sweating, and severe headache. These symptoms were associated with sudden increases in his blood pressure; and a provisional diagnosis of phaeochromocytoma was made.

Collections of urine were submitted for catecholamine assay. One collection showed a slight increase in catecholamines but the rest were normal, including a collection made after a provocation test, using histamine 0,025 mg intravenously. The histamine test did, however, cause systolic and diastolic blood pressure to rise by 20 mmHg.

As he was mildly hypertensive between paroxysms, a phentolamine test was carried out, utilising 5 mg well diluted, intravenously, over 5 minutes under basal conditions. This, too, was negative. An aortogram failed to demonstrate convincingly tumour vascularisation, but there was a mild hypertensive crisis during this examination.

At laparotomy, a single phaeochromocytoma was found in the right adrenal gland, and was successfully removed. Recovery was uneventful and the patient was discharged, normotensive and not requiring hypotensive therapy, though mild hypertension has developed since. No residual catecholamine activity has been detected.

The preparation of the patient for surgery and the control of operative complications are described, and the salient diagnostic features of phaeochromocytoma are briefly discussed.

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Phaeochromocytomas occur in considerably less than 1% of hypertensives,[1] but they are important in that the associated hypertension is generally curable and there is a rational and specific approach to diagnosis and therapy.[2]

The case presented is of interest in that confirmatory diagnostic studies were equivocal, which led to a delay in planning definitive therapy, which was eventually almost entirely dependent upon a clinical diagnosis, confirmed only at laparotomy.

The patient exhibited such a highly characteristic clinical picture that embarking upon operative treatment despite the unsatisfactory results of our preliminary studies, was justified.

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CASE REPORT

A White farmer, aged 52, experienced severe paroxysmal headaches, towards the end of 1969. The paroxysmal nature of his symptoms and the associated dizziness led to investigation for an epileptiform disorder. He was in hospital for 2 short periods during which a lumbar puncture and an electro-encephalogram proved to be normal. He was admitted for painful cervical osteoarthritis in October 1972, and because of the paroxysmal symptoms, readings of his blood pressure were charted every 4 hours. While the readings remained for the most part between 110 and 160 mmHg systolic and 70 - 90 mmHg diastolic, there were sudden increases of brief duration, up to 240/120 mmHg about once or twice a day, when he complained of palpitations, headache, anxiety, and faintness, and his face and fingers became pale.

A 24-hour collection of urine showed the urinary catecholamine level to be slightly increased, and the laboratory requested elimination of the usual food substances and drugs before repeating the test. Thereupon, 3 further 24-hour collections were submitted, but in none were raised levels of catecholamines or vanillylmandelic acid found, nor did palpation of the abdomen and the renal areas produce any symptoms.

A rogitine (phentolamine) test was reported as negative, and the results of other investigations were as follows: intravenous pyelography, normal, with no apparent renal displacement; the urine was normal in all respects; haemoglobin level was 12 g/100 ml; white cell count 6 000/mm^3 with a normal differential count; ESR 10 mm in one hour; blood urea 21 mg/100 ml; serum sodium 139 mEq/litre, potassium 4,2 mEq/litre; chlorides 100 mEq/litre. The electrocardiogram was normal, apart from a left-axis deviation of -30°.

When on 24 November he reported as an outpatient, since all the subsequent tests for catecholamines were normal, he was admitted for further study. His blood pressure was stable at about 150/90 mmHg, with sudden increases as before. On a slow intravenous injection of 0,9% NaCl, the blood pressure was recorded at intervals of 1 minute until it stabilised. Phentolamine 5 mg, well diluted, was then injected intravenously during the next 5 minutes, but was without effect. Later, histamine 0,025 mg was injected, well diluted, with phentolamine ready at hand. The expected flush appeared, and the blood pressure rose from 160/90 to 180/110 mmHg for a few minutes.

Characteristic symptoms were not produced and the catecholamine content of a 24-hour urine collection was again normal. He was discharged and instructed to keep

a careful record of his symptoms, and to report regularly for follow-up examination. He reported twice, the second time being on 7 March 1973, when he brought with him a diary of his symptoms, which showed him to be having attacks almost every day. The worst attack occurred after driving a tractor, although some attacks appeared to be without a precipitating cause.

He experienced attacks of anxiety, giddiness, palpitation, sweating, pallor, and severe headache. The symptoms lasted for a few minutes usually, but sometimes up to several hours, leaving him exhausted. His previous medical history was unimportant except for a partial gastrectomy for peptic ulceration carried out a number of years before. He was admitted on 12 March with a view to surgery if spontaneous hypoglycaemia or the 'dumping syndrome' were excluded.

A fasting blood-sugar measurement was normal, and, using a 50 g load, a glucose tolerance test continued for 3 hours, at no time did the blood sugar level fall below 90 mg/100 ml. There was no relationship between attacks and meals.

A complete examination revealed a fit-looking, middle-aged man with a mildly elevated blood pressure and no other abnormalities, other than the upper abdominal scar of his gastrectomy. In particular, there was no significant hypertensive change in the ocular fundi. Blood urea, serum electrolytes, the blood count, thyroid function tests, creatinine clearance, and urinary excretion of 5-hydroxyindole-acetic acid (5-HIAA), were all normal.

Aortography was performed. Midstream, abdominal dye injection showed a faint flush in the right adrenal region, but selective, right renal arterial injection showed no abnormality. On injecting the dye into the lower thoracic aorta there was a mild hypertensive crisis during which the systolic blood pressure rose to 200 mmHg for a moment or two, but then settled spontaneously. A similar faint flush now appeared in the left adrenal region. The radiologist regarded the investigation as inconclusive, but since the clinical picture was now so definite, a decision to explore for a phaeochromocytoma was taken at a combined meeting of surgeon, physician, and anaesthetist, when a combined approach was planned for the control of any operative complications.

PREPARATION FOR SURGERY

In view of the negative catecholamine studies the regimen of pre-operative administration of α-adrenergic and β-adrenergic blocking agents, was not followed; instead, the patient was prepared with chlorpromazine. According to Bingham *et al.*,[3] chlorpromazine gives a measure of basal stability without the problems associated with complete blockade and resultant suppression of sympathico-adrenal activity, which deprives the cardiovascular system of its homeostatic mechanisms.

The patient was infused with a litre of 5% dextrose in water to counteract the possibilty of hypovolaemia, which sometimes occurs in this condition.

Premedication

This consisted of chlorpromazine 50 mg, promethazine 25 mg, and hyoscine 0,4 mg.

Induction

Two infusion lines and a central venous pressure manometer were connected. It was decided to administer the drugs to control any hypertensive or hypotensive episodes, and any cardiovascular instability, only when indicated. Cardiac monitoring was by oscilloscope and blood pressure readings. In the beginning the patient's blood pressure was 140/80 mmHg and the pulse rate was 84/min and regular.

The following drugs were held in readiness: phentolamine diluted 1 mg/ml for intravenous use; practolol, similarly diluted, prepared for tachycardia, or phentolamine tachyphylaxis; lignocaine 2%, for serious cardiac arrhythmia; and noradrenaline 2 mg in 1 litre 5% dextrose in water attached to one of the infusion lines for instant use should hypotension occur.

From the time of induction the blood pressure and the oscilloscope were continuously monitored by 2 observers. Induction was by drugs least likely to upset cardiovascular homeostasis. Propanidid 500 mg, followed by toxiferine 30 mg, were given.

There were no blood pressure changes nor cardiac irregularities at any time during induction.

Maintenance

Anaesthesia was maintained with methoxyflurane and nitrous oxide and oxygen, since most anaesthetists agree that halothane is less suitable because of its cardiovascular effects. A concentration of 5% methoxyflurane was used throughout and intermittent positive pressure ventilation was provided with a Manley ventilator.

Changes in blood pressure as the tumour was being handled, were violent, and required energetic control with phentolamine. During and immediately after removal of the tumour. The blood loss was estimated and replaced and accurate central venous pressure measurements made, since it is mandatory under these conditions to expand the blood volume to maintain cardiac output.

The blood pressure nevertheless dropped sharply with removal of the tumour, but this was readily controlled with the noradrenaline infusion.

The reversal of the relaxant effect with atropine and prostigmine, extubation, and the return to consciousness, were uneventful, but the monitoring regimen continued uninterrupted, since this is a critical time and hypotensive collapse is an ever-present danger in these patients.

The Operation

As the tumour had not been localised, a thorough abdominal exploration was necessary and made via a lengthy incision beneath the costal margins (Fig. 1).

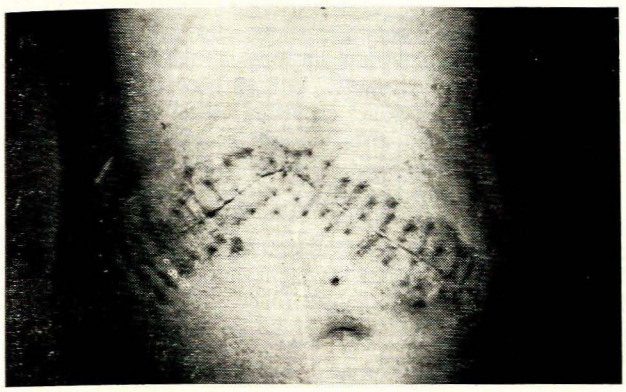

Fig 1. The operation scar, showing the wide exposure required to find the tumour.

As was anticipated, access was somewhat difficult because of the many adhesions from the previous laparotomy, and the obesity of the patient. No intra-abdominal masses were obvious, so a systematic search of the known sites for phaeochromocytoma was made. These sites were gently massaged to locate the tumour by a rise in blood pressure from the release of catecholamines.

No rise occurred on palpating the para-aortic region or the bladder. Palpation of the left adrenal gland showed the expected slight rise (Fig. 2). The left adrenal gland was exposed and found to be quite normal, macroscopically. The right adrenal gland was then exposed, and with gentle massage the blood pressure rose considerably (Fig. 2), but was rapidly controlled with phentolamine, as described, and careful inspection of the gland revealed a small tumour extending beneath the inferior vena cava. The adrenal vein was ligated at this stage, to prevent or minimise any further hypertensive crises, and then the whole right adrenal gland was removed. Further hypertensive crises were less explosive than the first and were readily controlled with phentolamine, and the tachycardia with practolol.

Histological examination of the tumour showed features typical of a phaeochromocytoma.

The cardiovascular events described are shown in Fig. 2, and Fig. 3 is a photograph of the tumour.

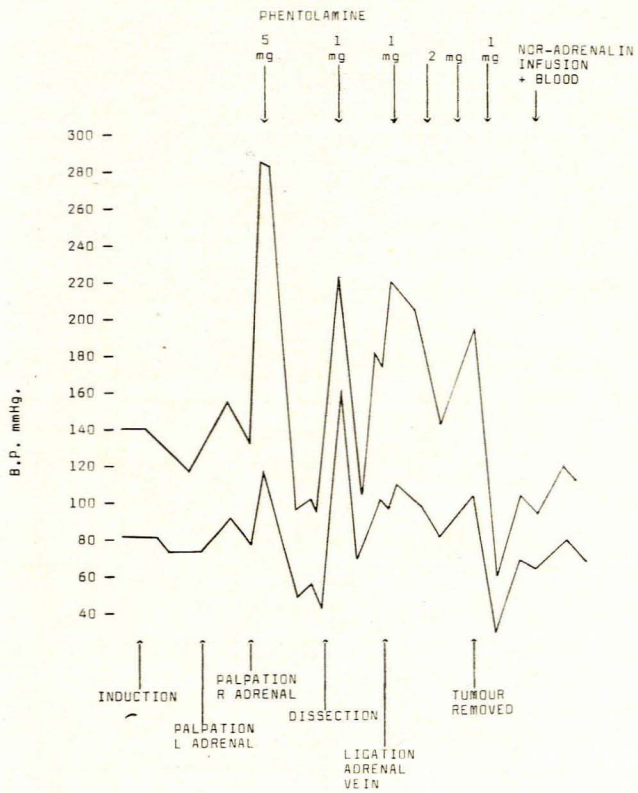

Fig. 2. Record of the blood pressure during surgery.

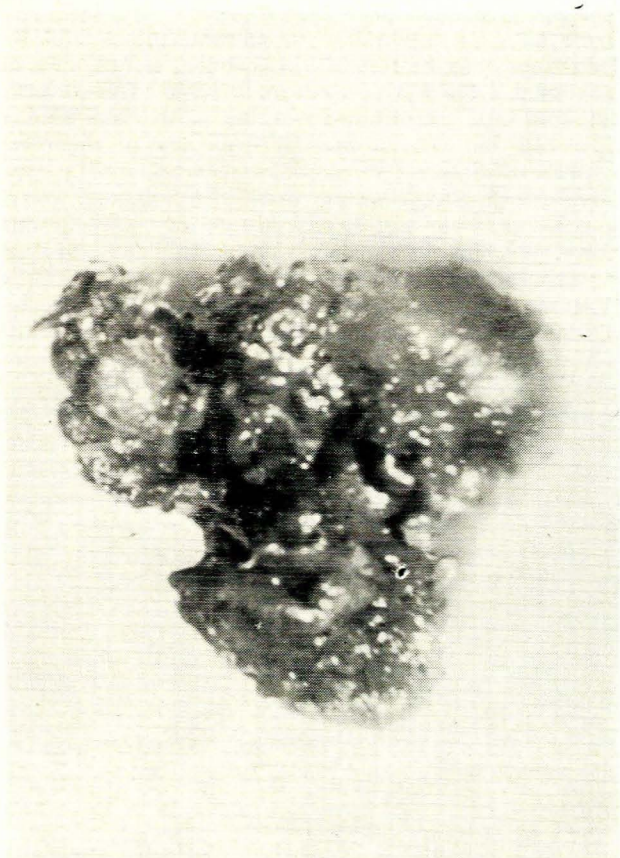

Fig. 3. The right adrenal gland, containing the tumour.

Postoperative Progress

Two hours after the operation it was possible to discontinue the noradrenaline infusion, after initial slowing. The blood pressure was maintained at about 120/90 mm-Hg; there were occasional, atrial, ectopic beats. The next day atrial fibrillation supervened and digitalisation was

commenced. Verapamil (Isoptin: Knoll) 5 mg, was given intravenously with a prompt reversion to sinus rhythm.

On the third postoperative day a purulent sputum and mild pyrexia developed without abnormal signs in the lungs. The response to ampicillin was prompt. The patient was discharged 16 days postoperatively, his wound soundly healed and his blood pressure consistently at, or below, 150/90 mmHg, without any medication and without any of his former paroxysmal symptoms. A postoperative urinary catecholamine estimation was normal. He has been followed up for 4 months and found to be mildly hypertensive, but this state is adequately controlled with a diuretic only, and he is not having any symptoms suggestive of catecholamine surges.

DISCUSSION

Most symptoms of phaeochromocytoma are explicable on the basis of a secretion of catecholamines, and the hypertension may be sustained if secretion is sustained, or paroxysmal if the secretion occurs in surges. Our patient's symptoms were characteristic of the paroxysmal clinical picture. He did not, however, display any of the other neurodermal disorders sometimes associated, such as neurofibromatosis, Sturge-Weber disease,[4] or tuberous sclerosis, nor was there any family history of phaeochromocytoma, in which an autosomal dominant inheritance has been described in some kindreds.

Tumours secreting excessive quantities of catecholamines have been found in the carotid body and the paravertebral regions of the neck, thorax, and abdomen as far as the organ of Zuckerkandl at the lower end of the aorta, but more than 80% are within the abdominal and pelvic cavities.[5] About 10% of tumours are bilateral and about 10% are said to be malignant, but this cannot be determined histologically, only by the presence or absence of metastases, or with no recurrence. Most tumours are very vascular and about 1 - 3 cm in diameter, though they may be very small or very big.

Both noradrenaline and adrenaline, and their major urinary metabolite, vanillylmandelic acid, are found in the urine in increased amounts at some time or other in the great majority of patients; but if secretion occurs in spurts the total 24-hour excretory level may be only slightly raised, or normal, though increased in a 4-hour collection immediately after the episode.

The ratio of adrenaline to noradrenaline has some localising value, since the *N*-methylating enzyme responsible for conversion of noradrenaline to adrenaline is present only in the organ of Zuckerkandl and the adrenal medulla, so that if adrenaline forms more than 20% of the total, the tumour is likely to be situated in one or other of these sites.

While at times they may be helpful, diagnostic studies such as the phentolamine and histamine tests, intravenous pyelography with or without tomography, abdominal X-ray examination with retroperitoneal gas insufflation, and selective arteriography, may be inconclusive or even misleading.

When we planned our surgical approach to this case, we hesitated to use the α-blocking agent phenoxybenzamine, partly because of the uncertainty occasioned by the equivocal nature of our investigations. We thought we could control reactions adequately with the drugs mentioned, and, indeed, a hypertensive reaction was of paramount localising and diagnostic importance, although the first of these proved to be so explosive and alarming.

This case emphasises once again the value of careful clinical observation, and we have also demonstrated the value of adequate personal consultation and interdisciplinary teamwork.

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