CASE REPORTS

Phaeochromocytoma and hypercalcaemia

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Summary

An example of possible pseudohyperparathyroidism associated with a non-endocrine benign tumour is reported. Some of the pertinent factors contributing to hypercalcaemia under these circumstances are reviewed, with particular reference to ectopic hyperparathyroidism and catecholamine-induced endogenous hyperparathyroidism.

Introduction

Phaeochromocytoma may occasionally induce hypercalcaemia. Case reports of correction of hypercalcaemia by surgical removal of the phaeochromocytoma indicate the importance of humoral mechanisms (Swinton, Clerkin and Flint, 1972; Kukreja *et al.*, 1973). Kukreja *et al.* (1973) noted a pre-operative elevation of serum immuno-reactive parathyroid hormone (i-PTH) implying that hypercalcaemia was either the result of ectopic parathyroid hormone secretion or of stimulation of endogenous parathyroid function by a product arising from the tumour. A similar case is presented in which raised levels of calcium and parathyroid hormone in the blood returned to normal after surgical removal of a benign phaeochromocytoma.

Case report

For 2 years a 14-year-old schoolboy had complained of weakness, fatigue on exertion, loss of energy and loss of weight. A dull pain beneath the right shoulder blade had been felt at daily intervals and it tended to last for about 30 min. The pain was not related to exercise, eating patterns, bowel habit, or to the passage of urine. He had not been ill previously and his family and siblings were all in excellent health.

The youth was tall, thin and slightly wasted. The pulse rate was 100/min and the blood pressure was 150/100 mmHg. The heart sounds were normal and

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no murmurs were heard over the precordium or abdomen. Jugular venous pulse was not raised. Radial artery pulses were synchronous with femoral arterial pulsations. The optic discs and fundi were normal. Slight abdominal tenderness was elicited in the right lumbar region anteriorly, but no associated guarding was detected.

Investigations

Hb, 11.5 g/100 ml; MCH, 24 pg; PCV, 35%; ESR 71 mm fall in 1 hr; serum iron, 40, and iron-binding capacity, 340 mg/100 ml; serum B₁₂, 230 pg/ml, serum calcium, 2.8 mmol/l; inorganic phosphate, 1.1 mmol/l; alkaline phosphatase, 10.5 KA units; sodium, 141 mmol/l; potassium, 4.3 mmol/l; chloride 104 mmol/l; urea, 4.5 and creatinine, 40 mmol/l; pH, 7.44; standard bicarbonate, 24 mmol/l; Pco₂, 35 mmHg.

Urine calcium excretion on ward diet varied from 8.1 to 15.3 mmol/24 hr: urine catecholamine excretion: vanillyl mandelic acid 486, conjugate metanephrines 56.5 and free catecholamines 49 µmol/24 hr.

Serum i-PTH was measured by immuno-radiometric assay (Addison *et al.*, 1971), using antibodies which react predominantly with the COOH-terminal portion of the hormone molecule. The normal range for this assay is up to 1 ng/ml when the patient is normocalcaemic. Hence the pre-operative serum i-PTH of 0.85 ng/ml was inappropriately elevated for a patient with hypercalcaemia.

Glomerular filtration rate (⁵¹Cr EDTA clearance) 93 ml/min/1.73 m². The urine concentrated to 820 mosmol/kg after water deprivation.

Gastro-intestinal absorption of calcium estimated by ⁴⁷Ca is shown before and after operation (Table 1).

Radiology

Chest X-ray was normal. Intravenous pyelogram demonstrated normal renal size and outlines with normal pelvicalyceal patterns. Hyperconcentration

TABLE 1. ^{47}Ca absorption from gut

	Peak plasma activity %/l	Urine excretion %	Faecal excretion %	Total absorption %
Before operation	2.7	0.9	10.6	88.5
After operation	1.0	1.7	5.1	47.3

of dye was observed in the right kidney. Aortography revealed a large vascular tumour in the right adrenal gland, and a right renal artery stenosis. Skeletal survey was normal.

Clinical progress

The hypertension was related to a large phaeochromocytoma in the right adrenal gland, accompanied by a right renal artery stenosis. Surgical removal of a benign 200 g phaeochromocytoma was successful, causing a prompt fall in blood pressure. The changes in serum calcium and i-PTH concentration after operation are charted (Fig. 1). Post-operative recovery was uneventful, but some months later the patient started to limp, and hip radiographs revealed aseptic necrosis of the right femoral head. Shortly after this, vision in the right eye was impaired owing to an angiomatic malformation.

FIG. 1. Serum calcium concentration and immuno-reactive parathyroid hormone following removal of phaeochromocytoma.

Discussion

Several mechanisms may be responsible for hypercalcaemia complicating a phaeochromocytoma. They include Sipple's syndrome, a genetic association of parathyroid hyperplasia, phaeochromocytoma, and medullary carcinoma of thyroid; primary

hyperparathyroidism; ectopic parathyroid hormone secretion from the tumour; secretion of calcium-mobilizing substances, other than parathyroid hormone, from the tumour; and catecholamine stimulation of endogenous parathyroid function. In Sipple's syndrome hypercalcaemia remains unchanged by removal of the phaeochromocytoma, and is lowered only by parathyroidectomy (Miller *et al.*, 1975).

In the present case significant hypercalcaemia was initially noted at a time when the serum i-PTH was not suppressed, suggesting that hypercalcaemia was induced by parathyroid hormone either endogenous or ectopic. Riggs *et al.* (1971) observed a relatively low serum i-PTH for a given increase in serum calcium concentration in ectopic as compared with primary hyperparathyroidism. Ectopic parathyroid hormone secretion was suggested by the fall in serum calcium concentration and i-PTH after tumour removal. Persistent low levels of serum i-PTH after operation presumably represent the slow turnover of COOH-terminal immune fragments of the parathyroid hormone molecule. Indirect evidence of parathyroid hormone effect in this case can be adduced from the study of calcium absorption from the gut which was high before operation and halved thereafter.

Both the pre-operative serum i-PTH and the peak in this value which occurred at the time of tumour mobilization could conceivably have been due to catecholamine influence in parathyroid function. Acute catecholamine infusion in the cow has revealed a rise in serum i-PTH, but serum calcium concentration has not risen concomitantly (Fischer, Blum and Binswanger, 1973). Enhanced parathyroid activity has been demonstrated in normocalcaemic patients with phaeochromocytoma, which has disappeared after tumour removal (Bouillon and De Moor, 1974). In a larger series of ten normocalcaemic patients with phaeochromocytoma no disturbance of serum i-PTH was recorded, suggesting that chronic catecholamine excess does not significantly increase parathyroid function (Miller *et al.*, 1975).

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A case of subacute bacterial endocarditis treated with parenteral clindamycin (clindamycin-2-phosphate)

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Summary

A case of subacute bacterial endocarditis which was due to an α -haemolytic streptococcus is described. A therapeutic dilemma arose when the patient developed a drug fever to penicillin and was found to be allergic to cephalosporine. Oral clindamycin was used, but had to be abandoned since severe exacerbation of an unsuspected duodenal ulcer resulted. The patient was finally successfully treated with clindamycin-2-phosphate, a new injectable form of the drug, and the success of this therapy is documented.

Introduction

Clindamycin-2-phosphate is a new derivative of clindamycin which has been formulated for parenteral use, and which has recently been available for clinical trial in the U.K. We report the following case of subacute bacterial endocarditis due to an α -haemolytic streptococcus which was successfully treated with this drug.

Case history

The patient was a 34-year-old man who had been admitted to another hospital complaining of weight loss, dyspnoea, malaise, anorexia and night sweats. The illness had slowly progressed over the previous month. There was no history of heart disease or of rheumatic fever, but the patient had undergone den-

tal scaling 2 months previously. Since heart disease was not suspected at that time no prophylactic antibiotics had been given. Admission took place on 26 December 1974.

On examination the patient had gross aortic incompetence, splinter haemorrhages and splenomegaly. He was in moderate left ventricular failure and was clinically anaemic.

Investigation confirmed the presence of anaemia (haemoglobin 9.0 g/100 ml) and revealed a neutrophil leucocytosis and a raised erythrocyte sedimentation rate (ESR) at 80 mm/hr. Blood cultures taken on admission yielded a pure growth of an α -haemolytic *Streptococcus* (*S. viridans*) which was reported as sensitive to penicillin.

The patient was treated with digoxin and frusemide to control the left ventricular failure and was given oral ferrous sulphate for his anaemia. Specific therapy was instituted with benzyl penicillin at a dose of 2 Mu (1.2 g) given 4-hourly intramuscularly (i.m.).

There was an initial good response, the fever which had been present on admission settling within 24 hr and the patient claiming to feel much better. The left ventricular failure was well controlled.

After 6 days the patient became febrile once more, although he claimed to be feeling much better, and it was thought wise to increase the penicillin to a dose of 4 Mu (2.4 g) 4-hourly, and to give this intravenously. The fever continued and after a further

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