Comment

This finding clearly shows that a raised plasma β-MSH level is not the cause of the pigmentation in systemic sclerosis. Although we did not measure the para-aminohippurate clearance in our patients, a decreased renal blood flow had been found in most of those in whom it was measured several years earlier; we therefore surmise that decreased renal blood flow does not impair renal metabolism of β-MSH. This supports our parallel evidence from post-transplantation studies[5] that access to the renal tubule of β-MSH undergoing catabolism is by tubular absorption after glomerular filtration of the peptide and not by delivery from the peritubular vasculature.

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Hypercalcaemic phaeochromocytoma

The occasional occurrence of hypercalcaemia in phaeochromocytoma is usually due to coexisting primary hyperparathyroidism as part of a multiple endocrine tumour. In four recent cases of phaeochromocytoma the hypercalcaemia, unlike that of patients with a polyendocrine neoplasia, subsided after the catecholamine-secreting tumour was removed.[1-4] We describe here a patient with a noradrenaline-secreting phaeochromocytoma whose associated hypercalcaemia was corrected by removal of the tumour.

Case report

A 45-year-old miner was admitted to hospital on 28 September 1975 for evaluation of severe hypertension and mild diabetes mellitus. An episode of macroscopic hematuria two months earlier had led to the discovery of a renal stone in the right pelvis. Over the past six months the patients had lost 11 kg in weight. Treatment on admission consisted of glipizide 2·5 mg/24 h and debrisoquine 20 mg/24 h. No diuretic had been given.

On examination the patient was pale and sweating. The pulse was 104/min and blood pressure was 200/123 mm Hg supine and 200/120 mm Hg standing. The severity of the hypertension was shown by left ventricular hypertrophy noted both on electrocardiogram and chest radiograph and by a Keith-Wagener stage-3 retinopathy.

Serum electrolytes and renal function were normal. Twenty-four hour proteinuria was raised at 1·09 g. Microscopical examination of the urine sediment disclosed 100-120 red blood cells and 100-120 white blood cells per high power field. Urine culture was sterile. Glucose tolerance was decreased; insulin response was raised and delayed. Serum calcium levels, determined on four different days, were slightly but consistently raised (see table). Serum alkaline phosphatase levels, 24-hour urinary calcium, bone radiography, and parathyroid hormone blood level were normal. Adrenocortical and thyroid function were normal. Urinary excretion of free catecholamines, noradrenaline, total metanefrines, and vanillylmandelic acid were about 10 times higher than normal, whereas adrenaline excretion was within normal limits (see table).

A right suprarenal tumour measuring 3 × 6 cm was disclosed by renal and adrenal arteriography and removed on 22 October 1975 (weight 30 g). Histological examination showed a benign phaeochromocytoma. The catecholamine concentration in the tumour was 1176 μg/g for noradrenaline and 53·1 μg/g for adrenaline.

Blood pressure and catecholamine excretion returned progressively to normal within eight days after surgery. The serum calcium level, determined on four different days, and glucose tolerance became normal. Serum albumin and total protein concentrations were normal both before and after operation. Urinary cyclic adenosine monophosphate excretion remained normal.

The patient was discharged on 8 November 1975. The blood pressure remained normal up to a month later, when the patient died suddenly at home after complaining for a few minutes of an excruciating transthoracic pain.

Discussion

The cause of hypercalcaemia associated with phaeochromocytoma but unrelated to coexisting primary hyperparathyroidism remains a moot point. Gray and Gillon[4] have suggested that catecholamines stimulate the release of parathyroid hormone. Alternatively, Finlayson and Casey[3] have proposed that hypercalcaemia results from a direct action of catecholamines on bone cyclic adenosine monophosphate production. These two hypotheses are tenable in the presence of adrenaline-producing phaeochromocytomas, as both parathyroid hormone release from parathyroids and bone adenylcyclase are stimulated mainly by adrenaline but little by noradrenaline.

Sufficient data to test this hypothesis are available in only one patient,[2] who excreted mainly noradrenaline whereas adrenaline output was only slightly raised. In our patient adrenaline excretion was normal and adrenaline concentration in the tumour was strikingly reduced, the main abnormality being confined to noradrenaline production. It thus seems unlikely that hypercalcaemia resulted from a direct or indirect action of adrenaline, a conclusion substantiated by the observation of Miller *et al*[5] that three patients with adrenaline-secreting phaeochromocytomas did not have hypercalcaemia. Other explanations, perhaps implicating increased prostaglandin secretion by the tumour,[4] should therefore be proposed.

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Blood pressure and urinary catecholamine, calcium, and parathyroid hormone levels before and after resection of phaeochromocytoma

	Blood pressure (mm Hg)	Free catecholamines (μg/24 h)	Noradrenaline (μg/24 h)	Adrenaline (μg/24 h)	Calcium (mmol/l)	PTH (ng/l)
Normal range:		10–90	10–80	2–15	2·2–2·6	0–400
3 October 1975	200/125	918·6	909·3	9·3	2·70 2·67 2·70 2·67	210
6 November 1975	120/80	81·1	75·0	6·1	2·35 2·48 2·53 2·45	

Conversion: SI to traditional units—Calcium: 1 mmol/l ≈ 4 mg/100 ml.