A case of associated thyrotoxicosis and phaeochromocytoma. A diagnostic problem

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Summary

A case of phaeochromocytoma and thyrotoxicosis occurring in the same patient is described, in which the similarity between the signs and symptoms produced by the two conditions delayed full diagnosis until post mortem. The mechanisms involved in the production of these signs and symptoms are discussed.

Introduction

This case of thyrotoxicosis associated with a malignant phaeochromocytoma is reported to emphasize the similarity between the clinical features of the two diseases. The persistence of the sympathomimetic features of thyrotoxicosis, despite adequate antithyroid therapy, was attributed to inconsistent taking of medication, and the diagnosis of phaeochromocytoma was made only at post-mortem.

Case presentation

A 28-year-old housewife with two children had symptoms of anxiety for 1 year before she presented with features of thyrotoxicosis. These included recent weight-loss of 12.71 kg despite a normal appetite, palpitations, exertional dyspnoea and heat intolerance. There was no history of headaches and the only relevant family history was that her mother died of a cerebral haemorrhage in her forties.

Examination revealed hyperkinesis and fine finger tremor, slight generalized thyroid enlargement, bilateral lid retraction together with slight proptosis of the right eye, regular tachycardia, a warm skin and excessive sweating. Blood pressure was 130/75 mmHg, heart sounds were normal and there was no retinopathy.

The diagnostic index score was +36 (Crooks, Murray and Wayne, 1959), euthyroid patients scoring less than 11.

The clinical diagnosis was confirmed by a PBI of 11.0 mg/100 ml (normal range 4-8 mg/100 ml); T_3

resin uptake 125 (normal range 82-128) giving a free thyroxine index of 13.8 (normal range 2.2-7.1).

Twenty minute thyroid uptake of intravenous ^{132}I was high at 20% (normal less than 8%). Thyroid antibodies and long acting thyroid stimulator LATS were not detected in her serum and a TSH level was 2.4 m μ /ml (normal 0.5-4.0 m μ /ml).

Treatment was begun with carbimazole 40 mg daily in divided doses reducing after 2 months to 30 mg daily. She became clinically euthyroid only after continuing this relatively high maintenance dose for 6 months.

At this time she became pregnant, aborting in the first trimester and her blood pressure was recorded at 160/90 mmHg.

Six months later, whilst on the same antithyroid regime she began her fourth pregnancy, which was associated with a rapidly increasing exophthalmic ophthalmoplegia.

During the 22nd week of this pregnancy she was admitted with a small ante-partum haemorrhage and a blood pressure of 150/90 mmHg. The bleeding stopped and the hypertension settled with bed rest.

During the latter half of her pregnancy she reported a severe panic attack with headache and tachycardia but when seen her blood pressure was again only 150/90 mmHg and the attack was thought to have been psychogenic. Shortly before term a normal child was delivered vaginally and a few days later sterilization by tubal ligation was carried out.

During the recovery phase from this operation the blood pressure rose to 210/150 mmHg but settled rapidly following administration of a 'lytic cocktail' consisting of pethidine 100 mg, promazine 50 mg and promethazine hydrochloride 50 mg.

Following delivery her thyrotoxicosis was controlled on 20 mg of carbimazole but a relapse with tachycardia, heat intolerance and tremor, necessitated an increase to 40 mg daily. Despite this relatively large dose of carbimazole, with a normal PBI and T_3 resin uptake she continued to have apparent relapses which coincided with domestic crises and were attributed to inconsistent taking of her medication.

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FIG. 1. Right-sided pontine haemorrhage.

At this stage she required a myomectomy for the severe exophthalmic ophthalmoplegia; there were no complications during or after this operation.

Two and a half years after her initial presentation, the patient was admitted as an emergency with a right lower neurone facial weakness and a left hemiparesis of sudden onset.

Lumbar puncture revealed evenly blood stained cerebrospinal fluid and she was thought to have had a pontine haemorrhage.

Initially she was alert and orientated with a pulse rate of 96/min and a BP of 210/100. After 48 hr, she developed a pyrexia and an increasing tachycardia, with a pulse rate of 180/min. Thyrotoxic crises and septicaemia were considered as causes and she was given Lugol's iodine and propranolol together with antibiotics. The tachycardia was controlled, but circulatory collapse supervened and she died 72 hr after admission.

At post-mortem she was noted to have many pigmented naevi on the thorax and gross exophthalmos. A large, recent, right-sided pontine haemorrhage was present with cerebellar tonsillar herniation (Fig. 1).

A large haemorrhagic, brown tumour (145 g) replaced the left adrenal, and a single small metastasis was present in the liver (Fig. 2). Both tumours had the characteristic histological appearance and staining reactions of a pheochromocytoma. Extensive quantities of depleted brown adipose tissue were noted around the kidneys, adrenals and in the

mediastinum. The heart weighed 310 g and showed left ventricular hypertrophy. The thyroid (weight 13.5 g) showed some diversity of acinar size but no histological features of thyrotoxicosis or thyroiditis.

Discussion

Pheochromocytoma is known to occur in association with medullary carcinoma of the thyroid (Ljungberg, Cederqvist and Standnitz, 1967; Sipple, 1961; Williams and Pollock, 1966); but in this patient the association with thyrotoxicosis was probably fortuitous.

The clinical features of thyrotoxicosis can be explained partly by the direct action of the thyroid hormones on the tissues (Wollerburger, 1965; Buccino *et al.*, 1967), and in part by over-activity of the sympathetic nervous system.

The mechanism of this over-activity is uncertain; urinary catecholamine excretion products are normal in hyperthyroidism (Wiswell *et al.*, 1963). Although β -adrenergic blockade by propranolol reduces the heart rate and cardiac output at rest (Howitt and Rowlands, 1966), it has a quantitatively similar reaction in simple anxiety states (Turner, Granville-Grossman and Smart, 1965). Other features of thyrotoxicosis improved by this drug include palpitation, heat intolerance, tremor and warm skin (Shanks *et al.*, 1969), but it does not reduce the raised oxygen consumption (Howitt and Rowlands, 1966).

These sympathomimetic features are common to

FIG. 2. Large left phaeochromocytoma replacing the adrenal.

both thyrotoxicosis and phaeochromocytoma. In patients with a phaeochromocytoma, serum protein bound iodine, rate of release and uptake of ^{131}I , and rate of clearance of labelled T_3 or T_4 are usually within the normal range (Harrison, 1964) and it is therefore unlikely that the catecholamines have a significant direct effect on thyroid function in man.

The increased heat production and oxygen consumption in both thyrotoxicosis and phaeochromocytoma may be related to the increased metabolism of fat (Goodman and Bray, 1966; Engleman, Mueller and Sjoerdsma, 1964) which may be stimulated by the synergistic activity of noradrenaline and thyroid hormones (Leblanc, 1970). This synergistic effect is easily seen in the metabolism of the thermogenetic brown adipose tissue which in

this patient showed an almost complete loss of stored fat. This has been previously reported in both phaeochromocytoma (Sherwin, 1959) and in thyrotoxicosis (Hammond and Hamolsky, 1969).

It is well recognized that phaeochromocytoma requires a high index of suspicion for its diagnosis and that the presenting symptomatology is also varied. The diagnosis of phaeochromocytoma in a patient with thyrotoxicosis is particularly difficult because of their overlapping clinical features.

Thyroid swelling occurs in 6% of patients with a phaeochromocytoma and can be induced experimentally by infusion of noradrenaline (Herman and Momex, 1964). Moreover, only about 50% of patients (Gifford *et al.*, 1964) with a phaeochromocytoma exhibit continuous hypertension; indeed, rarely the patient may present with postural hypotension (Parkinson, 1964).

Phaeochromocytoma is not invariably considered in the clinical differential diagnosis of thyrotoxicosis (Werner and Ingbar, 1971); this case suggests that the continuing presence of the sympathomimetic features of hyperthyroidism, despite adequate anti-thyroid medication, should prompt the clinician to consider the possibility of an associated phaeochromocytoma.

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Arterial surgery in pseudoxanthoma elasticum

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Summary

A 25-year-old female with pseudoxanthoma elasticum was referred with disabling ischaemia in one lower limb. She had suffered from peripheral vascular disease from the age of 15. Reconstructive arterial surgery was successful.

Case report

A 25-year-old female was referred in 1973 with a history of ulceration of the left foot for 3 months, with severe pain at rest. Walking had become too painful to attempt. Pseudoxanthoma elasticum had been diagnosed at the age of 7 on the basis of classical skin changes. She had suffered from intermittent claudication in both calves for at least 10 years. A haematemesis had occurred in 1967. She became thyrotoxic in 1972 and was treated with carbimazole. On referral in 1973 she was euthyroid. Skin changes of pseudoxanthoma elasticum were present, particularly involving the sides of the neck. Angioid streaks were seen on fundoscopy. The lower limbs were wasted. The peripheral pulses were absent below the femorals. A painful ulcer, 3 × 2.5 cm, was present on the dorsum of the left foot, and a smaller

ulcer was noted on the medial malleolus of the same foot. She was normotensive and an electrocardiogram was normal.

A lumbar sympathectomy was performed but there was no improvement. A left femoral arteriogram showed small calibre vessels and occlusion of the left femoral artery in its distal third. There was good filling of the popliteal artery via collaterals (Fig. 1). Femoropopliteal by-pass grafting was therefore carried out. At operation the left femoral artery was very small but patent. It was dissected free below the origin of the profunda femoris artery and a length of reversed autogenous saphenous vein was sutured, end to side, proximally to the top end of the superficial femoral artery and distally to the popliteal artery which was of wider calibre than the femoral. Both arteries took sutures normally. Post-operatively there was a return of the peripheral pulses in the left leg. Pain was relieved and the ulcer gradually healed. Twelve months later full recovery in the limb was maintained.

Discussion

Pseudoxanthoma elasticum is a genetically determined, probably autosomal recessive, disorder. A number of recent studies (Moran and Lansing, 1958;

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