THYROTOXICOSIS AND ADDISON'S DISEASE IN SAME PATIENT

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The association of Addison's disease and thyrotoxicosis in the same patient is uncommon. A case was described by Rupp and Paschkis (1957), but they could find only eight previously reported cases in which such a double diagnosis appeared to be acceptable. A case showing this combination of diseases is described below and illustrates the influence of the thyroid gland on adrenal cortical function.

Case Report

A married woman aged 53 was involved in a motor-car accident in February, 1957, sustaining no injury. In August of that year she began to "shake like a dancing doll," so that at times she was unable to dress herself and became very irritable. Six months later her eyes became prominent and she noticed a swelling in her neck. During the year before admission she noted increasing pigmentation of the skin, loss of appetite, and severe nausea; and over the last four months she lost 2 st. (12.7 kg.) in weight.

On admission to hospital in January, 1959, she was agitated; blood-pressure 130/60; weight 7st. 6 lb. (47.2 kg.); temperature 100.8° F. (38.2° C.); pulse 140. Increased pigmentation was present, especially over the face, chest, and axillary folds, and patches were visible on the buccal surface of the cheek and soft palate. A diffuse smooth enlargement of the thyroid gland, a well-marked exophthalmos, and a fine tremor of the hands were present.

Investigations.—Haemoglobin, 10.8 g./100 ml.; white blood count, 11,500/c.mm. (neutrophils 42%, lymphocytes 48%, monocytes 5%, eosinophils 5%); E.S.R., 25 mm. in one hour (Wintrobe). An electrocardiogram showed sinus tachycardia with ST depression in leads II, III, aVF, V5-7. Radiological examination of the lungs revealed a calcified primary complex but no other evidence of tuberculosis, and examination of the abdomen showed no evidence of calcification in the adrenal area.

The patient remained febrile, and two days after admission she was moved into a single room, but complained that she could not sleep owing to a noisy heating installation. She became progressively more restless and agitated, mentally confused, and resentful of any interference, and threatened to take her own discharge from the hospital. She then began to vomit small quantities of bile-stained material, the pulse became very weak, and the systolic blood-pressure suddenly fell to 70 mm., the diastolic pressure being unobtainable. At this time the serum sodium was 132 mEq; potassium 6.0 mEq; bicarbonate 25 mEq; serum cholesterol 163 mg./100 ml.; and blood-sugar 98 mg./100 ml. A diagnosis of Addisonian crisis precipitated by severe thyrotoxicosis was made, and she was treated with intravenous dextrose-saline, hydrocortisone hemisuccinate intravenously to a total of 400 mg. in 12 hours, and 5 mg. of deoxycortone intramuscularly. Within a few hours of starting treatment she was much improved, was again rational though still restless, and the blood-pressure had risen to 140/60. Intravenous therapy was subsequently replaced by oral cortisone, 25 mg. b.d., fludrocortisone,

0.25 mg. daily, and propylthiouracil, 200 mg. t.d.s., for the next two weeks, during which she continued to improve though remaining febrile. In order to continue investigations of thyroid and adrenal function all treatment was then discontinued apart from fludrocortisone, 0.25 mg. b.d.

Ten days later the following tests were performed. **Thyroid function:**—B.M.R. +38%; plasma protein-bound radioactive iodine, 1.4% of administered dose per litre at 48 hours (normal <0.4%). **Adrenal function:**—*Before corticotrophin:* urinary 17-ketosteroids, 0 (normal 5-15 mg./24 hours); urinary 17-ketogenic steroids, 4 mg./24 hours (normal 8-18 mg./24 hours); plasma free 17-hydroxycorticoids, 3 µg./100 ml. (normal 6-20 µg.). *After corticotrophin* (corticotrophin-zinc 40 units intramuscularly b.d. for two days): urinary 17-ketosteroids, 0 each day; urinary 17-ketogenic steroids, 4 mg. and 1 mg./24 hours; plasma free 17-hydroxycorticoids, 0 (on two successive days four hours after corticotrophin).

Treatment was resumed with cortisone acetate, 37.5 mg. daily, and fludrocortisone, 0.1 mg. daily. Carbimazole, 10 mg. t.d.s., was substituted for propylthiouracil; there was no recurrence of the pyrexia. One month after discharge from hospital she was very well, having gained 14 lb. (6.4 kg.) in weight. The pulse rate was 80 and the blood-pressure 170/90.

Discussion

The diagnosis of hyperthyroidism in this patient was made clinically and was confirmed by a raised basal metabolic rate and increased protein-bound radioactive iodine. The diagnosis of Addison's disease was suggested by the presence of increased pigmentation and anorexia, and confirmed by the low steroid levels in plasma and urine.

In uncomplicated hyperthyroidism urinary 17-hydroxycorticoids are either normal or slightly raised (Levin and Daughaday, 1955), and plasma 17-hydroxycorticoids are normal (Levin and Daughaday, 1955; Wallace *et al.*, 1955). In this patient the low or absent 17-hydroxycorticoids and 17-ketosteroids in urine and plasma, together with a failure of the steroid levels to rise after the administration of corticotrophin, indicated primary adrenal insufficiency.

It has long been known that the administration of thyroxine to patients with Addison's disease may precipitate adrenal crisis (Lerman and Stebbins, 1942), and recent investigations into the influence of the thyroid on adrenal cortical function have thrown further light on these clinical observations. Levin and Daughaday (1955) and Peterson (1958) have shown that in cases of hyperthyroidism there is a greatly increased metabolism of hydrocortisone, and this is normally accompanied by an increased production by the adrenal cortex, since plasma levels of hydrocortisone remain within the normal range.

This relationship, however, may be disturbed either in the event of the metabolism of hydrocortisone being so great as to overwhelm the productive capacity of a normal adrenal, such as may be postulated to occur in a thyroid crisis, or, more certainly, when coexistent disease of the adrenal cortex is present.

In the above case signs of Addison's disease appeared to develop after the onset of thyrotoxicosis. During an exacerbation of the hyperthyroidism the adrenal cortex was presumably unable to meet the demand for an increased output of hydrocortisone, and an adrenal crisis occurred which responded rapidly to the intravenous administration of hydrocortisone. Since the hyperthyroidism has been treated by antithyroid drugs the adrenal insufficiency has been controlled by steroid therapy in conventional dosage without difficulty.

Summary

A case is described in which both hyperthyroidism and Addison's disease were present. Exacerbation of hyperthyroidism resulted in an adrenal crisis.

The relationship between thyroid and adrenal cortical function is discussed.

We thank Dr. J. R. Nassim for permission to publish details of this case, admitted under his care.

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Medical Memoranda**Response of Favus to Griseofulvin**

Favus of the scalp is an intractable disease due predominantly to *Tricophyton schoenleini*, though *T. quinckeanum* may also be responsible for the infection. In the past the choice in therapy has been x-ray epilation and vigorously applied local medicaments, but the advent of griseofulvin and its success in the management of other fungous infections of skin, hair, and nails has caused speculation about whether favus, too, will respond. Sulzberger and Baer (1959) refer to this gap in our knowledge, and Pardo-Castello *et al.* (1959), while hailing the drug as the treatment of choice in all superficial mycoses, omit all mention of favus. It seemed to us that an account of the progress we have observed in two cases of favus under treatment with griseofulvin might be of interest.

CASE 1

A married woman aged 38 attended as an out-patient with a view to obtaining a wig. She complained of having had baldness for 36 years. This was diffuse, with crusting and scarring mainly round the sides of the scalp and on the occipital region, where typical yellowish scutula were also present (Fig. 1). Bright-green fluorescence was noted under Wood's light, most vivid on the occiput. Direct microscopy revealed the presence of fungus in hairs, and *T. schoenleini* was grown on culture.

Blood counts, liver-function tests, serum electrolytes, and urinalysis, repeated at weekly intervals, remained normal throughout, with the exception of serum alkaline phosphatase, which was raised to 28 K.A. units on the first estimation (before treatment started) but was normal on the next and all subsequent estimations.

Griseofulvin in divided dosage of 0.75 g. daily—that is, 15 mg./kg. body weight—was begun on April 1, 1959, and has been maintained since then. Three weeks later definite loss of fluorescence was noted in the proximal part of the hairs. After five weeks microscopical examination revealed fungus in the distal part of the hair, with a clear portion extending up to 2.5 cm. from the bulb and a fairly sharp line of demarcation (Fig. 2). Since then the clear region of the hair has continued to extend, recently at a slower rate, and the contrasting shades are now so marked as to be obvious to the naked eye (Figs. 3 and 4).

The patient's weight showed a gain of 11 lb. (5 kg.) while in hospital but returned to near its previous level before discharge. No untoward effects of treatment were noted, and she was discharged for out-patient observation after a stay of 35 days in hospital. In view of the above findings on microscopical examination and examination with Wood's light, fungistasis was considered to be complete at this stage.

CASE 2

A girl aged 12, daughter of the above patient, complained of scaling of the scalp of 10 years' duration. Confluent crusting and scarring were present over the vertex and occiput with scattered lesions on the frontal and parietal regions. Bright-green fluorescence was obtained under Wood's light. Direct microscopy revealed the presence of fungus in hairs, and *T. schoenleini* was grown in culture.

Blood counts, liver-function tests, serum electrolytes, and urinalysis, repeated at weekly intervals, remained normal throughout.

Griseofulvin in divided dosage of 0.625 g. daily—that is, 15 mg./kg. body weight—was begun on April 1, 1959, increasing to 0.75 g. on June 12 (owing to an increase in weight by 16 lb. (7.3 kg.) since her admission) and has been maintained.

Since treatment started, her progress has been similar to that in Case 1 apart from the fact that fluorescent and

FIG. 1.—Case 1.

FIG. 2.—Case 1. Photomicrograph of fresh potassium hydroxide preparation of hair, showing arrest of fungal invasion of hair shaft. ($\times 84$.)