Co-existence of Addison's disease and thyrotoxicosis

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THE occurrence of Addison's disease and thyrotoxicosis in the same individual is rare. In 1957 Rupp & Pasckis reviewed the literature and found only eight acceptable cases. Since then fourteen more cases have been reported (see Lazarits & Alant, 1961; Buttery, 1961; Stewart, Green & Lowe, 1962; Boshel *et al.*, 1963). Of the total, seven were males and fifteen were females, with an age range of 17–58 years. Sometimes the diagnosis of Addison's disease preceded that of thyrotoxicosis and vice versa.

These two conditions have several features in common, namely weight loss, pigmentation, weakness, gastro-intestinal symptoms and tachycardia. Whereas it is easy to distinguish typical thyrotoxicosis from Addison's disease, it is not surprising when they co-exist that some of the features might be wrongly attributed to the dominant disease, the co-existence of the other being overlooked. Such patients are particularly susceptible to Addisonian crises, and the physician must be aware of the possibility of this combination.

Case report

Miss D.P., a 39-year-old capstan operator was seen in March 1965 complaining of pigmentation and lack of energy. She had never suffered from tuberculosis or other illness. One sister died of pneumonia, and two others and four brothers are alive and well.

Five months previously she started feeling depressed and wanting to cry all the time. She noticed that her colour was getting darker, particularly in the hands, so much so that people at work remarked about it. She felt weak and lethargic and 'could not even sit up properly'. Over the next 3 months she was so weak as to be physically incapable of operating her machine. One month before admission she retired to bed completely, and when seen had nausea, vomiting and anorexia. She had lost 3 stones in weight in 6 months. Menstruation was normal, bowels regular.

On examination she looked ill, was apathetic, lethargic, afebrile and deeply pigmented over the face, hands, abdomen, axillary folds, dorsum of feet and buccal mucosa, and appeared to have lost weight. Pulse was 120/min, blood pressure 100/70 mmHg. Axillary hair was virtually absent

and pubic hair scanty. Examination of chest, heart, abdomen and nervous system revealed no abnormality.

The palpebral fissure was thought to be abnormally wide, and there was a fine tremor of the outstretched hands and lid lag. The extremities were warm, and on questioning she said she had never felt really cold for a year and wore fewer clothes in cold weather than her friends.

Investigations. Haemoglobin 10.2 g/100 ml, white blood cells 5000/mm³ with a normal differential. ESR 22 mm/hr (Wintrobe). Plasma urea 114 mg/100 ml, sodium 132, potassium 5.1, chloride 101 mEq/l. X-rays of chest and abdomen, ECG and urinalysis normal; urinary 17-hydroxy steroids 2.4 mg/24 hr. Two samples of blood taken at different times were sent for serum PBI.

Progress. Thirty-six hours after admission her temperature rose to 102.8°F, and she vomited. She was too weak to sit up.

Her BP fell to 80 systolic, with an imperceptible pulse; ECG was normal. Plasma electrolytes: Sodium 125, potassium 5.2, chloride 99 mEq/l, urea 157 mg/100 ml; a random urine sodium was 90 mEq/l. She was treated as an Addisonian crisis with i.v. saline and 500 mg hydrocortisone, in 24 hr. Two hours after beginning therapy she was much improved and the blood pressure was 140/90. After 24 hr, hydrocortisone was given orally in a dose of 37.5 mg daily. Her improvement was so marked that thyrotoxicosis was temporarily forgotten. The urine culture gave a growth of *E. coli* sensitive to tetracycline and this urinary infection was thought to be the cause of her adrenal crisis.

Subsequently the PBI was reported as 12.6 µg/100 ml and 11.2 µg/100 ml on the two specimens respectively; tests for thyroid antibodies were negative. She insisted on going home and was discharged on cortisone acetate, 37.5 mg daily. Four weeks later, despite her cortisone therapy, she had lost a further 10 lb in weight and still had tachycardia. She refused admission again, but an ¹³¹I uptake test was performed as an Out-patient and was 67% at 24 hr, confirming the diagnosis of thyrotoxicosis. She was put on carbimazole but still did not improve, and the PBI 10 weeks later was 9 µg/100 ml. She ulti-

mately agreed to be re-admitted. Cortisone was stopped for 3 weeks and then she was given 40 units of ACTH three times a day for 5 days. Urinary 17-OHCS excretion was 8 mg/24 hr before stimulation and 3.6, 6.3 and 5.9 mg/24 hr on the last 3 days of ACTH administration. The PBI was still 10 μ g/100 ml and she now admitted that she had never taken her carbimazole tablets.

Discussion

This case presented as a severe case of Addison's disease but the staring appearance of the eyes fortunately aroused the suspicion of thyrotoxicosis. Cortisol turnover is increased in thyrotoxicosis (Levin & Daughaday, 1955) and therefore symptoms of adrenocortical insufficiency might be expected to occur earlier during the development of Addison's disease in a patient with thyrotoxicosis than in Addison's disease without thyrotoxicosis. Severe symptoms of Addison's disease might appear while the urinary excretion of 17-hydroxycorticoids is maintained within the normal range, by maximal secretion by the functioning remnant. Therefore, if Addison's disease is suspected, the adrenocortical response to ACTH must be determined. The difficulty of managing such patients is well illustrated by reports in the literature. For example, the case reported by Stewart *et al.* (1962) repeatedly went into Addisonian crisis until thyrotoxicosis was diagnosed and treated, though our own case had no signs of crisis during the 6 months when she did not take her anti-thyroid drugs.

The simultaneous disorder of two or more endocrine glands that are normally dependent on the anterior pituitary gland raises the question of the role of the anterior pituitary. It has been suggested by Van Wyck & Grumbach (1960) that there might be a non-specific response of the hypothalamic-pituitary system to a failure of secretion by a target gland, leading to increased secretion of more than one trophic hormone. This was suggested as an explanation of galactorrhoea and precocious sexual development occurring in patients with hypothyroidism, one of whom was also pigmented, suggesting increased secretion of MSH. This hypothesis could explain cases of Addison's disease with thyrotoxicosis, the latter being due to non-specific secretion of TSH in

response to cortisol deficiency. No report has been found of studies of TSH in such cases, but in one case Frey (1959) attempted to suppress the pituitary with 9- α -fluorohydrocortisone, and found the 131 I uptake to be unaltered. The present patient was treated with 37.5 mg cortisone acetate daily for nearly 6 months during which time she never took her carbimazole tablets. There was clearly no suppression of thyrotoxicosis by this physiological dose because she continued to lose weight and the serum PBI and 131 I uptake remained elevated. While a cause-and-effect relationship cannot be excluded, it appears that at present there is nothing to indicate that this association is anything but coincidental.

Summary

A case of Addison's disease with thyrotoxicosis is described, with brief reference to other published cases. The possible aetiological role of the hypothalamic-pituitary axis is discussed.

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