CLINICAL REPORTS

Autoimmune endocrinopathy associated with diabetes insipidus

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Summary

A case is described in which diabetes insipidus was associated with hypopituitarism, insulin-independent diabetes mellitus, pernicious anaemia and circulating antibodies to the thyroid gland, adrenal gland and the pancreatic islet cells.

Introduction

Certain individuals and families seem to be unusually prone to develop organ-specific autoimmune disorders. The conditions which appear most closely associated are thyroid disease (Hashimoto's thyroiditis, thyrotoxicosis or primary hypothyroidism), Addison's disease, hypoparathyroidism and pernicious anaemia. A number of other conditions may also be associated including diabetes mellitus, ovarian failure, male infertility and autoimmune haemolytic anaemia. The existence of autoimmune hypophysitis was suggested some years ago on histological grounds (Goudie and Pinkerton, 1962). More recently, antibodies reacting with prolactin-secreting cells (Bottazzo *et al.*, 1975) and growth hormone-secreting cells (Bottazzo *et al.*, 1980) have been observed in a number of patients although their clinical significance remains uncertain. In view of this uncertainty, it was thought of interest to report a patient who shows not only auto-immune reactions directed against pancreas, thyroid, adrenal and stomach but in addition has several abnormalities of hypothalamic-pituitary function.

Case report

A 70-year-old woman was admitted to hospital in March 1979 with complaints of extreme weakness and confusion of 3 weeks' duration. Past medical history included the diagnosis of pernicious anaemia in 1954, diabetes insipidus in 1957 and diabetes mellitus in 1971. In the recent past she had received treatment for hypertension with methyl dopa and for Parkinsonism with L-dopa.

On examination she was drowsy, apathetic and pale. Her speech was slow and slurred and there was a mild left-sided hemiparesis. The only other abnormal feature was the blood pressure of 90/60 mm Hg. Preliminary investigations showed Hb 11 g/dl; Na 137 mmol/l; K 5.8 mmol/l; urea 26 mmol/l; creatinine 200 µmol/l; albumin 27 g/l; total protein 76 g/l. X-rays of the chest and the abdomen did not reveal any abnormality.

Despite the initial supportive measures she continued to be apathetic and slow, and clinical suspicion of hypothyroidism was confirmed by a low level (8 nmol/l) of serum thyroxine (normal range: 55-155 nmol/l). The fact that the thyroid-stimulating hormone (TSH) level (6.3 mu./l) was not raised (normal range: up to 10 mu./l) suggested that the hypothyroid state might be secondary to hypopituitarism. Replacement therapy with thyroxine was started but the response was unsatisfactory. She continued to be lethargic, developed generalized aches and pains and had episodes of diarrhoea and vomiting.

During the next few months she collapsed several times at home and upon admission to hospital was found to be dehydrated and hyponatraemic. The lowest level of serum sodium recorded was 92 mmol/l. Each time, she improved symptomatically after rehydration with normal saline. In December 1979, plasma cortisol concentrations were found to be subnormal: 60 nmol/l at midnight and 159 nmol/l in the morning (normal range: 170-720 nmol/l). Treatment with prednisolone produced a dramatic improvement. She became asymptomatic, blood pressure rose to 140/90 mmHg and the blood urea and electrolyte levels returned to normal. Further investigations showed normal visual fields and a normal pituitary fossa radiologically. At a later stage, hormone therapy was temporarily withdrawn and adreno-corticotropin (ACTH) and thyrotropin (TRH) tests were carried out. Delayed production of cortisol after ACTH injection (maximum plasma

concentration 420 nmol/l) suggested that adrenal function was impaired but not absent. TSH showed only a minimal rise in response to TRH injection, consistent with the diagnosis of hypopituitarism. Serum autoantibody tests showed high titres to thyroid antigens, and positive tests for gastric parietal cell, adrenal cortex and pancreatic islet cell. Anti-gastric intrinsic factor and pituitary antibodies were not detected.

Discussion

This patient presents evidence of auto-immune reactions directed against the thyroid, adrenal cortex, stomach and pancreatic islet, combined with evidence of widespread hypothalamic-pituitary dysfunction. Her diabetes insipidus was of long standing and was clearly central in origin indicating hypothalamic damage. The combination of low ACTH and cortisol concentrations and the good cortisol response to exogenous ACTH administration suggests that her hypo-adrenalism resulted primarily from ACTH deficiency rather than adrenal destruction. Similarly, the normal TSH concentration in the face of a very low thyroxine concentration would suggest an abnormality of TSH secretion. The TSH response to TRH appeared somewhat blunted, but since the thyroid response to exogenous TSH was not tested one cannot say whether her hypothyroidism resulted mainly from pituitary or thyroid failure.

In addition to the strong evidence of an auto-immune tendency shown by direct tests on the patient's serum, there is also a strong family history of diabetes mellitus and auto-immune disorder.

Two brothers, her mother and a maternal aunt had suffered from diabetes mellitus, none of them, like her, having needed insulin. Her father and one brother had pernicious anaemia and another sister

who is clinically well has strongly positive circulating thyroid antibodies. In view of this, it is tempting to suggest that auto-immunity may have played a part in the development of hypothalamic-pituitary disease.

There is no positive evidence to suggest any other familiar cause of hypothalamic-pituitary failure. Goudie and Pinkerton (1962) found destructive lesions of the anterior pituitary with heavy lymphoid infiltration at post-mortem in a young woman who also had thyroiditis and adrenal atrophy. Bottazzo *et al.* (1975) found auto-antibodies to prolactin-secreting cells of the human pituitary in 19 of 287 patients with auto-immune endocrine disease. More recently, Bottazzo *et al.* (1980) have shown the presence of antibodies to growth hormone secreting cells in a patient with Turner's syndrome and partial growth hormone deficiency. This evidence indicates that autoimmune hypophysitis occurs although the present authors were unable to demonstrate the presence in their patient of antibodies to anterior pituitary cells.

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