Reversible hypothyroidism after steroid replacement for Addison’s disease

A. W. BURROWS
B.M., M.R.C.P.

Department of Medicine, Leeds General Infirmary, Leeds LS1 3EX

Summary

An insulin-requiring diabetic patient who developed Addison’s disease is described. At diagnosis, investigations revealed biochemical hypothyroidism and these abnormalities resolved after replacement therapy for the adrenal failure only. The possible mechanism of this change is discussed in relation to the presence of organ-specific antibodies.

Introduction

A previous report (Gharib et al., 1972) describes the occurrence of reduced thyroid function in 4 patients with Addison’s disease. The abnormal thyroid chemistry in these patients was corrected by adrenocorticosteroid replacement therapy alone. The case discussed here shows many of the features of those previously described. The endocrine abnormalities have been established more fully and in addition the HLA type of the propositus and his family have been determined.

Case report

A 24-year-old male diabetic patient presented with symptoms of malaise, lethargy and recurrent hypoglycaemia. He had received insulin therapy for 18 years. His thyroid gland was firm and slightly enlarged. He had florid background diabetic retinopathy, and new vessels were present in both fundi. Clinically there was no evidence of hypothyroidism.

Initial investigations showed plasma sodium 124 mmol/l, plasma potassium 5.8 mmol/l, plasma urea 14.6 mmol/l. Haemoglobin was 8.9 g/dl with a normochromic normocytic film. Bone marrow biopsy showed reduced iron stores. Plasma thyroxine was 40 nmol/l (normal range 60–140 nmol/l), plasma triiodothyronine (T3) was 1.2 nmol/l (normal range 1.6–3.0 nmol/l) and plasma TSH 90 mu./l (normal range < 8 mu./l). He was treated with thyroxine in a dose of 0.05 mg daily. Within 2 days of starting this therapy he experienced further hypoglycaemia and also an acute hypotensive episode.

Further investigations confirmed Addison’s disease – 9 a.m. plasma cortisol 150 nmol/l (normal range 150–600 nmol/l) with no increase in response to tetracosactrin depot injections over 6 days. Plasma ACTH at 9 a.m. was 514 ng/l (normal range < 80 ng/l) and 24-hr urine aldosterone was 3 nmol/24 hr (normal range 10–70 nmol/24 hr) with no rise in response to low sodium diet (20 mmol sodium/24 hr).

He was treated with replacement doses of hydrocortisone (20 mg in the morning and 10 mg in the evening) and 9α-fluorocortisone (0.1 mg daily). Thyroxine therapy was withdrawn. The patient has remained euthyroid over the course of the subsequent 18 months. At the end of this time he had normal plasma concentrations of thyroxine (84 nmol/l), T3 (2.4 nmol/l) and TSH (4 mu./l). The only biochemical abnormality that could be demonstrated initially was an exaggerated TSH response to TRH (plasma TSH value of 45 mu./l at 20 min after TRH injection). This test gave a normal response at 6 months after stopping thyroxine.

Within 4 months of the start of steroid replacement the patient’s diabetic retinopathy had dramatically improved. The background haemorrhages resolved and there was also regression of the new vessels.

The patient’s brother, also a diabetic on insulin, had a thyroidectomy for thyrotoxicosis 12 years previously. On investigation he proved to be biochemically hypothyroid (plasma thyroxine 32 nmol/l, plasma T3 1.2 nmol/l and plasma TSH 39 mu./l) and has started replacement therapy.

Organ specific antibodies were measured in the patient and the members of his family available to study. HLA typing was also performed and these results are shown in Table 1.

Discussion

The association of myxoedema and Hashimoto’s disease in patients with autoimmune Addison’s disease (previously termed Schmidt’s syndrome) has a reported incidence of about 5% (Nerup, 1974), although other groups have found a higher frequency. The hypothyroidism may not be clinically obvious, and the only biochemical abnormality may be elevated plasma TSH concentrations and an
impaired thyroidal response to TSH injection (McHardy-Young, Lessof and Maisey, 1972). The patient described here had clearly abnormal thyroid function which resolved completely after steroid treatment alone, and this may be a more unusual presentation. If this reversibility of thyroid function is not recognized, patients with Addison’s disease may be treated needlessly with thyroxine on a permanent basis.

The suppression of serum TSH and thyroidal iodine release by high dose glucocorticoids in euthyroid and primary hypothyroid subjects has been reported (Wilber and Utiger, 1969; Nicoloff, Fisher and Appleman, 1970). Withdrawal of maintenance doses of steroids for 48 hr in primary hypoadrenal patients was followed by elevation of both serum TSH and thyroidal iodine release. It was suggested that hydrocortisone may play a prime role in the diurnal rhythms of TSH and thyroid hormones. However, this action of glucocorticoids appears to be a relatively short-term effect. Such an action is not applicable to the patient described here, where restoration of thyroid hormones occurred despite the lowering of plasma TSH, and the effect seems permanent.

Resolution of the hypothyroid biochemistry in this patient occurred despite the presence of antibodies to thyroid microsomes in the serum. Once established, autoimmune thyroid disease is assumed to be a stable or slowly progressive condition, although spontaneous reductions in antibody titre and remissions of goitre can occur. Fluctuations in thyroid antibodies and goitre size related to the more short-term situations of pregnancy and steroid administration have been reported and are relevant to the present case. During pregnancy, circulating antithyroid antibodies decrease and then rise again after delivery (Amino et al., 1978). It is suggested that immune mechanisms are suppressed by increased steroid production during pregnancy. Large doses of oral cortisone also reduce thyroid antibodies in patients with established Hashimoto’s thyroiditis with remission of hypothyroidism (Blizzard et al., 1962). A decreased thyroid antibody production rate induced by corticosteroids, rather than a modification of the toxic activity of the antibody, seems the likely explanation of the improved thyroid function in these cases. Restoration of physiological corticosteroid concentrations in patients with Addison’s disease and concurrent thyroiditis would be expected to have the same result.

A striking clinical feature was the rapid change induced in the patient’s diabetic retinopathy after treatment for the hypo-adrenalism. Some of this improvement may be attributed to the response of the anaemia to iron therapy, but it is possible that hormonal influences may also have played a part.

The HLA studies show the presence of HLA B8 haplotype in the patient and 2 of the 3 members of his family investigated. HLA B8 is associated with several organ-specific autoimmune disorders including Addison’s disease and hypothyroidism. There is also an association with diabetes mellitus (Cudworth et al, 1979). In this family both the brothers positive for HLA B8 developed diabetes, although the onset in the propositus was some 14 years earlier. In the patient described above diabetes preceded the development of Addison’s disease and temporary thyroid failure, while in his brother diabetes followed Graves’ disease. It is difficult to determine whether the diabetes in this family is of the ‘primary autoimmune’ type (Bottazzo et al., 1978) and related to the polyendocrinopathy, for neither patient had persisting islet cell antibodies which have been suggested as the marker for this group of diabetics.

**Acknowledgments**

Assessments of the patient’s diabetic retinopathy were performed by Mr B. Martin, Consultant Ophthalmic Surgeon, Leeds General Infirmary.

Organ specific antibodies were measured with the help of Professor D. Doniach in the Department of Immunology, Middlesex Hospital Medical School.

**References**

Case reports


Reversible hypothyroidism after steroid replacement for Addison's disease.
A. W. Burrows

doi: 10.1136/pgmj.57.668.368

Updated information and services can be found at:
http://pmj.bmj.com/content/57/668/368

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/