Clinical Reports

Myasthenia gravis and Schmidt syndrome

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Summary  We describe a 47 year old woman with a 30-year history of generalized myasthenia gravis whose condition had been stable and well controlled on a combination of pyridostigmine and ephedrine until she presented. At this time she gave a 2 month history of weakness, nausea, vomiting and more recently intermittent confusion. Investigations confirmed both primary hypothyroidism and primary adrenal failure (Schmidt syndrome). The autoimmune aetiology of these three conditions was confirmed by positive acetylcholine receptor, adrenal and thyroid microsomal antibodies.

Introduction

The association of organ-specific autoimmune diseases is well recognized. A defect of T cell function and immunoregulation helps to explain the observed associations. Very few cases of myasthenia gravis with Addison's disease and only one previous case of the combination of myasthenia gravis, primary hypothyroidism and primary adrenal failure with autoimmune aetiology have been reported.

Case report

A 47 year old woman with a 30-year history of generalized myasthenia gravis presented with a 2 month history of weakness, nausea, vomiting and mild diarrhoea and more recently confusion. In spite of these symptoms she had been able to do her housework until a few days prior to admission when she had become bedbound. Until this point her myasthenia had been well controlled on a combination of pyridostigmine and ephedrine.

On admission examination revealed poor concentration but correct orientation in time, place and person, no dehydration or pigmentation, the blood pressure lying was 110/60 mm Hg, but unrecordable on standing, pulse 72/minute regular, intermittent left convergent strabismus but full muscle power.

Investigations showed plasma sodium 99 mmol/l, potassium 4.9 mmol/l, chloride 76 mmol/l, bicarbonate 18 mmol/l, urea 6.7 mmol/l, creatinine 80 μmol/l, glucose 5.6 mmol/l, plasma osmolality 212 mosm/kg, urine osmolality 613 mosm/kg, haemoglobin 10.6 g/dl with a normochromic normocytoc blood film. Liver function tests, plasma proteins and calcium were normal.

Further investigations revealed: total thyroxine 38 nmol/l, total triiodothyronine under 0.5 nmol/l, thyroid stimulating hormone (TSH) over 60 mU/l. Short tetracosactrin (Synacthen) test – plasma cortisol 323 and 278 nmol/l at zero and 30 minutes; after 3 days of Depo-Synacthen a short Synacthen test on day 4 gave plasma cortisol 458 and 490 nmol/l at zero time and 30 minutes (normal cortisol range 08.00 h 280–720 nmol/l; normal increment >200 nmol/l with peak >500 nmol/l). These results indicate primary hypothyroidism and primary adrenal insufficiency (Addison's disease).

The patient's hypovolaemia was corrected over some days with an intravenous infusion of normal (0.9%) saline. In addition thyroxine, hydrocortisone and fludrocortisone were commenced with appropriate adjustments in dosage.

One year later thyroxine was temporarily withdrawn and her TSH level monitored. In fact her TSH rose over several weeks to more than 60 mU/l. The patient was also re-admitted to exclude isolated ACTH deficiency. Twenty-four hours after stopping hydrocortisone her ACTH level was 168 mU/l which is grossly elevated (upper limit of normal 20). A repeat long Synacthen test gave cortisol measurements of less than 30 nmol/l at zero time and 30 minutes both on day 1 and day 4.
The following investigations confirm the autoimmune basis for this patient’s multiple organ involvement: acetylcholine receptor, thyroid microsomal (1/6400), adrenal, gastric parietal cell and intrinsic factor antibodies all positive. Antinuclear factor was weakly positive with negative rheumatoid factor, mitocondrial, smooth muscle, steroid producing cells (ovary), pituitary and thyroglobulin autoantibodies. Vitamin B₁₂ levels 956 ng/l and Schilling test confirmed normal B₁₂ absorption. The patient had experienced the menopause at age 45 and her follicle stimulating and luteinizing hormone levels were consistent with her post-menopausal status. HLA typing revealed A₁ A₂₆ B₈ B₁₆ DR₃ DR₄.

Discussion

The association of organ-specific autoimmune disease is common and Schmidt syndrome (primary hypothyroidism and primary adrenal failure) is well recognized. A classification of polyglandular autoimmune syndromes has been developed. Our patient with early onset generalized myasthenia gravis, primary hypothyroidism and Addison’s disease fits into type II polyglandular autoimmune syndrome which has an HLA association with B₈ DW₃ DR₃. Our patient was shown to have this haplotype.

There has only been one previous report of the association of myasthenia gravis, primary hypothyroidism and Addison’s disease with an autoimmune aetiology in a single patient. In that particular case the authors did not exclude the possibility of reversible hypothyroidism in adrenal insufficiency, and the acetylcholine receptor antibody assay was negative using radioimmuno-precipitation and only equivocally positive using a cultured myotube assay.

After our patient had been well and stable on hydrocortisone, fludrocortisone and thyroxine for one year with normal electrolytes and thyroid function tests we temporarily withdrew her thyroxine replacement.

This manoeuvre demonstrated that her abnormal thyroid function tests at presentation were not a secondary phenomenon to glucocorticoid deficiency but truly represented primary hypothyroidism.

Conclusions

If one accepts the case report by Bosch et al., our patient appears to be only the second reported case of the association of myasthenia gravis, primary hypothyroidism and Addison’s disease.

After diagnosing any autoimmune disease, the clinician must remind himself and remain alert to its wide associations both for the present and the future.

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References