Case report

Hypothyroidism associated with mixed connective tissue disease and its response to steroid therapy

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SUMMARY The case is reported of a 49-year-old housewife who presented with arthralgia and severe Raynaud's phenomenon. A diagnosis of mixed connective tissue disease (MCTD) was made on the basis of the clinical picture and serological findings. During the course of her disease she developed hypothyroidism. She was started on prednisolone to control the symptoms of the MCTD, and after this her thyroid function returned to normal despite her never having had any thyroid replacement therapy. There is reported evidence that Hashimoto's thyroiditis responds to systemic steroid preparations, but we can find no report of hypothyroidism in MCTD having a similar response.

Thyroid disorders have a recognised association with other diseases which manifest autoantibodies. Moreover in a clinical study of patients with Hashimoto's thyroiditis Becker *et al.*¹ found an increased incidence of rheumatic disease. Further studies of similar patients suggest a link between Hashimoto's thyroiditis and rheumatoid arthritis (RA)^{2,3} and possibly with systemic lupus erythematosus (SLE).³ In their original description of mixed connective tissue disease (MCTD) Sharp *et al.*⁴ noted that 4 of their 25 patients had antithyroglobulin and/or thyroid disease. We can find no further detailed evaluation of thyroid disease in this syndrome. We wish to report a patient with MCTD who developed hypothyroidism and whose thyroid function then returned to normal on prednisolone therapy.

Case report

A 49-year-old housewife presented with a 2-month history of pains in the shoulders, arms, and knees. During the previous 18 months she had developed marked Raynaud's phenomenon. There was no history of skin rash, muscle tenderness, or dysphagia, and she had no relevant past or family history. On examination she had blue, swollen hands with

dystrophic nails. There was no evidence of an arthropathy and no goitre. The course of her disease over the subsequent 2 years has been complicated by two episodes of neutropenia (associated with phenylbutazone and azathioprine respectively) and severe vasculitis, mainly affecting the extremities. These vasculitic lesions have led to necrotic areas on the fingers and toes. Her renal function and urinary sediment have been normal throughout. A diagnosis of MCTD was made on the basis of the clinical picture and the following investigations: antinuclear factor (ANF) positive to a titre 1:2560 with a speckled pattern; DNA binding 18% (normal 0-20%); precipitating ribonucleoprotein (RNP) reactive extractable nuclear antigen (ENA) antibodies positive to a titre of 1:128. C3 = 50% (normal 75-125%); C4 = 36% (normal 60-140%). Circulating immune complexes were demonstrated by the C1q binding assay and by polyethylene glycol precipitation.⁵ The serological findings have varied during observation, and in particular the DNA binding was borderline raised at 25% on only 2 occasions from numerous readings.

At her initial presentation the thyroxine level was normal (Table 1). Fifteen months later her thyroid function was again measured and the results at this time were indicative of hypothyroidism (Table 1). This was confirmed by an abnormal thyrotrophin releasing hormone (TRH) stimulation test (Table 2). Shortly after this she was started on prednisolone 30 mg daily to control the MCTD. It was planned to initiate thyroid replacement therapy when the

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Table 1 *Thyroid function tests*

Date	Thyroxine nmol/l (70–160)	Thyroid stimulating hormone (TSH) mU/l (1.0–3.5)
February 1977	158	—
May 1978	69	12.3
October 1978	98	9.0
January 1979	108	1.0

Table 2 *TSH levels (mu/l) in TRH stimulation test*

TSH level	August 1978	January 1979
Basal level	4.6	3.4
20 min after TRH	33.0	13.5
60 min after TRH	38.5	9.6

MCTD had clinically improved. Subsequent tests showed an increasing improvement in thyroid function until she was biochemically euthyroid (Table 1), a state confirmed by a second TRH stimulation test (Table 2). The following thyroid antibodies were detected: thyroglobulin tanned cell agglutination titre of 1:640 and cytoplasmic antibody haemagglutination titre of 1:80². These antibody levels remained unchanged after the thyroid function returned to normal. However, the titre of precipitating RNP reactive ENA antibodies was 1:10 at the time of the second TRH stimulation test.

Discussion

Sharp *et al.*⁴ described a group of patients with overlapping features of SLE, scleroderma, and polymyositis which they called MCTD. The clinical pattern is usually characterised by arthralgia or arthritis, diffuse swelling of the hands and tapering of the fingers Raynaud's phenomenon, oesophageal hypomobility, and inflammatory polymyositis. There are no strict clinical criteria for the diagnosis, but high titres of precipitating RNP reactive ENA antibodies must be demonstrated.⁴ Although there is uncertainty that MCTD constitutes a separate entity,⁶ our patient would fit into the clinical pattern described, and she did have high titres of precipitating RNP reactive ENA antibodies. Her hypothyroidism may be associated with her MCTD. She had significant titres of thyroid antibodies, though

these interestingly remained unchanged when her thyroid function returned to normal. In Hashimoto's thyroiditis the damage to the thyroid gland is thought to be mediated through infiltration of lymphocytes and locally produced antibodies. Steroids have been shown to reduce the goitre⁷ and reverse hypothyroidism.^{8,9} It has been postulated that the response is related to a decrease in the lymphocyte infiltration rather than an effect on the circulating antibody levels. Since our patient has had no thyroid replacement therapy, the resolution of her hypothyroidism may be related to an effect of prednisolone. The exact mechanism is unclear, though it may be influencing lymphocyte infiltration of the thyroid gland. We cannot find any reported cases of hypothyroidism associated with MCTD which resolved on steroid therapy.

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