Myasthenia gravis, Hashimoto's disease and pernicious anaemia

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THE ASSOCIATION of myasthenia gravis with Hashimoto's disease and pernicious anaemia was described in a patient by Singer & Sahay (1966). Another patient with myasthenia gravis and pernicious anaemia who showed post-mortem evidence of Hashimoto's disease was reported by Simpson (1964). A further case history in which the patient had overt manifestations of these three conditions is described here.

Case report

Mrs F.G., a 48-year-old housewife, presented in 1960 with 1 year's history of intermittent diplopia and ptosis relieved by rest. Her symptoms and signs were abolished temporarily by intravenous edrophonium and were then controlled by oral prostigmine and pyridostigmine. There was no family history of myasthenia, pernicious anaemia or endocrine disorder.

The initial investigations showed a hypochromic anaemia (Hb 11.9 g/100 ml). The white cell count was normal and ESR 15 mm/hr (Westergren). Chest radiographs were normal.

In 1961, her symptoms worsened and examination showed bilateral ptosis with paresis of the right superior oblique and of the left lateral rectus, superior oblique and inferior oblique muscles. There was still a hypochromic anaemia (Hb 10 g/100 ml). The ESR had risen to 28 mm/hr. Clinical improvement was achieved by increasing the dose of anticholinesterases.

By 1963 she had again deteriorated and complained of dyspnoea on effort and tiredness. Again ptosis was seen and all external ocular movements were impaired in both eyes. Her thyroid gland was diffusely enlarged, her skin dry and her eyelids puffy.

Investigations showed the hypochromic anaemia was still present (Hb 10 g/100 ml). The ESR had remained at 28 mm/hr and the serum electrophoretic pattern was normal. The chest radiograph showed that her heart had increased in size compared with the film of 1960 and the aortic arch had dilated. Tomography of the mediastinum was normal. The

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serum protein-bound iodine was low (3.6 µg/100 ml) and the cholesterol elevated (564 mg/100 ml). The thyroid antigen complement fixation test was positive (1 : 16) and the thyroglobulin tanned red cell test also positive (1 : 250).

Treatment was started with oral L-thyroxine sodium and her clinical condition improved.

The patient was reassessed in 1967 following the development of myasthenic weakness in all her limbs and pitting oedema of her ankles. Vibration sensation was markedly diminished over both medial malleoli.

An ECG was normal and no change was seen in chest radiographs or tomograms of the mediastinum. Although the haemoglobin concentration was 12.2 g/100 ml and the white cell count normal, the blood film was macrocytic and the bone marrow megaloblastic. The ESR was 30 mm/hr and serum electrophoresis showed increased α_2 -, β - and γ -globulins. Gastric juice analysis after maximal histamine stimulation showed complete achlorhydria and the serum vitamin B₁₂ was low (131 µg/ml). The serum cholesterol was now normal (180 mg/100 ml).

The results of serum autoantibody studies done in May 1967 were as follows:

Thyroid antibodies

Thyroglobulin tanned red cell agglutination titre = 1 : 160.

Colloid antibody immunofluorescence, strongly positive.

Cytoplasmic antibody immunofluorescence, positive.

Cytoplasmic antibody complement fixation titre = 1 : 8.

Gastric antibodies

Parietal cell antibody immunofluorescence, strongly positive.

Parietal cell antibody complement fixation titre = 0.

Gastric intrinsic factor antibody, positive.

Muscle antibodies

Skeletal, positive.

Cardiac, positive.

Smooth, negative.

Non-organ-specific antibodies

Antinuclear factor, negative.

Mitochondrial immunofluorescence, negative.

Mitochondrial complement fixation titre, negative.

By August 1968 the thyroglobulin tanned red cell agglutination titre had risen to 1 : 640, the cytoplasmic immunofluorescence test had become strongly positive and the cytoplasmic complement fixation titre had risen to 1 : 32. In 1968 no antibodies to skeletal or cardiac muscle were detected but antibodies to pancreatic and suprarenal tissue were found. Latex fixation and direct Coombs' tests were negative.

Treatment with intramuscular cyanocobalamin was started and there was symptomatic improvement although there was no marked anaemia when vitamin B₁₂ deficiency was diagnosed. By 1968 the haemoglobin concentration was 12.2 g/100 ml and the blood film normal. The myasthenic symptoms, however, have remained difficult to control.

Comment

The association of various clinical syndromes with autoimmune phenomena has been frequently recorded. Evidence of thyroid dysfunction and the finding of thyroid antibodies have been described in patients with myasthenia gravis (Simpson, 1960; Adner *et al.*, 1964; Sahay, Blendis & Greene, 1965). The finding of gastric antibodies or pernicious anaemia in patients with myasthenia gravis and the association of pernicious anaemia or defective vitamin B₁₂ absorption with Hashimoto's disease and thyroid antibodies have all been reported (Simpson, 1960, 1964; Downes, Greenwood & Wray, 1966; Tudhope & Wilson, 1960, 1962; Williams & Doniach, 1962; Doniach, Roitt & Taylor, 1963; Ardeman *et al.*, 1966). Autoimmune phenomena have also been invoked in certain cases of Addison's disease and diabetes mellitus (Anderson *et al.*, 1957; Blizzard *et al.*, 1962; Turner & Bloom, 1968).

Myasthenia gravis, hypothyroidism, hypoadrenalism, diabetes mellitus and pernicious anaemia may all present as muscular weakness. It is suggested, therefore, that full antibody testing should be performed as part of the initial investigation of any of these conditions in anticipation of the development of related syndromes. Weakness may also be caused by overdosage of anti-cholinesterases or thyroxine,

thus increasing the factors which have had to be considered in the management of the patient described.

The association of autoimmune phenomena with myasthenia gravis supports the hypothesis of Simpson (1965) that this condition may be itself due to the development of antibodies to motor end-plate protein.

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