Myasthenia Gravis, Hashimoto's Thyroiditis, and Pernicious Anaemia

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In view of the reported increased incidence of multiple auto-antibodies occurring together, we wish to report the finding of myasthenia gravis, Hashimoto's thyroiditis, and pernicious anaemia in one patient—an association not previously reported.

CASE REPORT

A 48-year-old English woman was first seen in January 1964 with a three-month history of unilateral ptosis, diplopia, and difficulty in walking and performing fine finger movements. One month previously she noticed difficulty in mastication and swallowing. All these symptoms were more noticeable in the evening or after exercise.

On examination she had a typical myasthenic facies with bilateral ptosis and generalized weakness of limb and trunk muscles, more marked in the proximal group of limb muscles. She had a non-explosive cough and difficulty in swallowing her saliva. She showed a good response to intravenous edrophonium and intramuscular neostigmine. Ergometry (Greene *et al.*, 1961) showed a response diagnostic of myasthenia gravis. She appeared clinically euthyroid.

The results of investigations were as follows: a pneumo-mediastinogram (Kreel *et al.*, 1964) showed the presence of a tumour 5 cm. in diameter in the left lobe of the thymus. Haemoglobin 88%, white cell count 5,100/c.mm., E.S.R. 6 mm. in 1 hour (Westergren). Red and white cell morphology was normal. Serum protein-bound iodine 5.4 $\mu\text{g.}/100$ ml. Antibodies to skeletal muscle (fluorescein method) were present in her serum (Dr. D. Doniach).

The patient's myasthenic symptoms were largely controlled with neostigmine 15 mg. and pyridostigmine 300 mg. daily in divided doses. Deep x-ray irradiation to the superior mediastinum was performed. Thymectomy (Mr. J. E. Piercy and Mr. M. J. Lange) on 25 July 1964 revealed a small tumour in the left lobe of the thymus. Histology showed this to be a lympho-epithelioma with fatty replacement of the remainder of the gland. Her myasthenic symptoms rapidly improved post-operatively and she was satisfactorily maintained on 240 mg. of pyridostigmine daily.

In November 1964 she complained of lack of energy, increased sensitivity to cold, and an increase of 10 lb. (4.5 kg.) in weight. On examination the pulse rate was 64/min., her face was puffy, and her skin was cool and dry. Her thyroid was not palpable. Her ankle jerks were absent but the other deep tendon reflexes were present and showed no delay in relaxation. There was no sensory impairment.

Investigations gave the following results: haemoglobin 75%, M.C.V. 92 $\mu\text{m.}$, M.C.H.C. 31%, E.S.R. 20 mm. in 1 hour (Westergren). Red and white cell morphology was normal. Serum protein-bound iodine was 0.8 $\mu\text{g.}/100$ ml. Serum cholesterol 475 mg./100 ml. The thyroid "microsomal" complement-fixation test was positive in a titre of 1/128. Colloid and cytoplasmic antibodies and thyroglobulin tanned red cell agglutinins were present in moderate titres (Dr. D. Doniach). Gastric parietal cell antibodies were also present in moderate titres. Serum intrinsic factor antibodies were found. Serum vitamin B₁₂ was 190 $\mu\text{g.}/\text{ml.}$ The patient had a histamine-fast achlorhydria with absence of intrinsic factor in the gastric aspirates. A Schilling test showed 0.7% excretion of ⁵⁷Co-labelled vitamin B₁₂, which rose to 20% after ingestion of hog intrinsic factor.

A diagnosis of Hashimoto's thyroiditis and Addisonian pernicious anaemia was made. The patient was treated with L-thyroxine, 0.3 mg. daily, and vitamin B₁₂, 250 $\mu\text{g.}$ intramuscularly monthly. In August 1965 her myasthenic symptoms had somewhat worsened and anticholinesterase medication had to be increased. Since then her condition has remained satisfactory.

COMMENT

The presence of multiple auto-antibodies in autoimmune disease has been frequently reported. The presence of several autoimmune disorders in the same patient is also a relatively

common finding. The incidence of thyroid dysfunction in myasthenia gravis was estimated at 3% to 8% (Sahay *et al.*, 1965), and at 14% (Simpson, 1960). Daly and Jackson (1964) reported a case of myasthenia gravis and Hashimoto's thyroiditis, and Simpson (1964) also reported a myasthenic patient in whom Hashimoto's thyroiditis developed seven years after the removal of a thymoma. He also reported a further similar case and one where Hashimoto's thyroiditis was found at necropsy. In the latter case pernicious anaemia was also present. Adner *et al.* (1964) reported a 35% incidence of thyroglobulin antibodies in 48 myasthenic patients; two of these patients had thyrotoxicosis but none had an antibody titre high enough to warrant the diagnosis of Hashimoto's thyroiditis.

The association of myasthenia gravis and pernicious anaemia does not appear to be well documented. Simpson (1960; 1964) cites a total of nine cases of pernicious anaemia in 491 patients with myasthenia gravis—an incidence of 1.8%. Downes *et al.* (1966) found gastric antibodies in 12% of over 74 myasthenic patients—an incidence similar to that of a group of matched controls, though the myasthenic patients had higher complement-fixation titres. None of their cases had intrinsic factor antibodies. Doniach and Roitt (1964) report an increased incidence of pernicious anaemia in Hashimoto's thyroiditis. Williams and Doniach (1962) showed in a necropsy study that extensive focal thyroiditis was three times more prevalent in patients with pernicious anaemia than could be expected by chance. Over 50% of patients with pernicious anaemia had detectable thyroid antibodies (Irvine *et al.*, 1962; Markson and Moor, 1962; Doniach and Taylor, 1964), moderate to high titres being found in 30%. Conversely, patients with primary myxoedema or Hashimoto's thyroiditis showed a 12% incidence of pernicious anaemia (Tudhope and Wilson, 1960) and nearly 20% showed partial defects of vitamin-B₁₂ absorption (Tudhope and Wilson, 1962). Ardeman *et al.* (1966) found a 3% incidence of pernicious anaemia in a study of 250 patients with various thyroid disorders.

Our case appears to be the first one reported showing the association of myasthenia gravis, Hashimoto's thyroiditis, and Addisonian pernicious anaemia in one patient, apart from one case reported by Simpson (1964), where the diagnosis of Hashimoto's thyroiditis was made at necropsy. In view of the increased frequency with which these diseases occur in association with each other, investigations for their exclusion should be carried out whenever they are diagnosed.

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