CASE REPORTS

ASSOCIATION OF MYASTHENIA GRAVIS AND HYPERTHYROIDISM, SHOWING RECIPROCAL RELATIONSHIP: REPORT OF A CASE AND REVIEW OF THE LITERATURE *

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Myasthenia, or muscle weakness, is not an uncommon symptom in toxic goiter, but the coexistence of myasthenia gravis and hyperthyroidism has rarely been reported. MacLean and Wilson,[1] adding one of their own, tabulate 11 cases previously reported. In view of the long duration of life in myasthenia gravis, and the frequency of hyperthyroidism, the concurrent appearance of the two conditions, on the basis of statistical probabilities alone, could be expected to be much higher than the literature suggests. However, Kane[2] states that, when patients with chronic thyrotoxic myopathy and exophthalmic ophthalmoplegia are eliminated, there are fewer than two dozen well documented cases.

Of considerable interest, both for providing a clue to the pathophysiologic mechanism involved in the two diseases, and as a guide to therapy, is the effect of thyrotoxicity and antithyroid therapy on the state of preëxistent myasthenia. Observations on this point vary considerably in the cases reported in the literature. Thorner in 1939[3] first called attention to a "see-saw" relationship between the two conditions, wherein occurrence of hyperthyroidism appeared to ameliorate the myasthenia, and radiotherapy of the thyroid gland made the myasthenia worse. Bauer[4] and others have reported the rapid deterioration and death of patients in myasthenic crisis following treatment of intercurrent hyperthyroidism. On the other hand, Thorn[5] observed no significant change in the state of the myasthenia following response to antithyroid therapy. Bartel[6] reported some improvement in one of his patients following partial thyroidectomy, but death in myasthenic crisis occurred following total resection. Two of his patients improved after surgery, but the effect of thyroidectomy is difficult to evaluate, since thymectomy was performed at the same time. MacLean and Wilson consider a reciprocal "relationship" as always present, and surgical intervention as dangerous.

It is the purpose of this communication to add to the well documented cases in the literature the following observations on a young woman who developed

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hyperthyroidism while under treatment for myasthenia, and to record the effects on the myasthenia gravis when she was treated with propylthiouracil.

Case Report

This 26 year old white female was first seen in 1957 during a prenatal examination in consultation for control of myasthenia gravis.

In 1953 the diagnosis of myasthenia gravis had been made at another institution and thymectomy performed. Since that time the patient had been maintained on from 10 to 14 tablets (15 mg.) of neostigmine per day. Whenever medication was withheld she experienced extreme fatigue and weakness, and slurring of speech and ptosis were noted. At the time of her first visit, and on subsequent examinations during the remainder of her prenatal period, the myasthenia gravis was under excellent control, and no change in therapy was considered to be necessary. Two months following full term delivery of her normal child she was referred by the obstetrical department because of a 30-pound weight loss and nervousness manifested by irritability and nightmares.

Physical examination at this time revealed a striking change in the patient's appearance. Whereas during previous examinations she had been a somewhat obese, placid young woman, she now showed evidence of weight loss, and was extremely agitated and apprehensive. Pulse rate was 104/minute; blood pressure, 120/60 mm. of Hg. Her eyes were prominent, but no true exophthalmos was observed. There was a fine tremor of the outstretched hands and of the protruded tongue. The thyroid gland was enlarged to three times normal size, and was smooth and firm. The scar of the thymectomy was well healed. Multiple small, nontender cystic masses were palpated in both breasts. There was a grade III harsh systolic murmur over the pulmonic area. Neostigmine requirements were from six to eight tablets daily. Laboratory studies on January 19, 1958, showed a basal metabolic rate of plus 39%, an initial 24-hour I^{131} uptake of 74% by the thyroid gland, a protein-bound I^{131} conversion ratio of 97%, and a 24-hour saliva protein-bound iodine I^{131} ratio of 14 to 1. After receiving tri-iodothyronine, 100 μg./day in divided doses for eight days (suppression test), the patient's studies were as follows: 24-hour I^{131} uptake, 82%; conversion ratio, 100%; saliva protein-bound iodine ratio, 2 to 1.

Clinical Course: On initial therapy of 300 mg. propylthiouracil in three divided doses the patient slowly gained weight, and her tremor and anxiety subsided. The thyroid gland at first enlarged and then gradually became smaller. On April 1, 1958, her 24-hour I^{131} uptake was 52%, and her 24-hour protein-bound I^{131} conversion ratio was 60%.

The patient's neostigmine requirements rose to 10–14 tablets per day, and by June, 1958, she had gained 15 pounds. Propylthiouracil was reduced to 150 mg., and was discontinued in August, 1958. The patient remained well until November, 1958, when weight loss and further anxiety and tremor returned. Her thyroid gland had again increased in size, and the 24-hour I^{131} uptake was 65%. At this time her requirements of neostigmine were eight tablets per day. Antithyroid medication was again administered. In March, 1959, her weight returned to normal (150 pounds), pulse rate was 80/minute, and no tremor of the outstretched hands was noted. Her neostigmine requirement was 12–14 tablets per day. She was taking propylthiouracil, 50 mg. every eight hours.

Comment

The diagnosis of myasthenia gravis had been well established in this patient at an outstanding medical center three years prior to her development

of hyperthyroidism. At that time, as well as when seen by us during repeated prenatal examinations, no evidence of thyroid dysfunction was noted. Following thymectomy, myasthenic symptoms were well controlled with from 10 to 14 tablets of neostigmine daily. Findings two months post partum were unequivocally those of hyperthyroidism as to symptomatology, clinical findings and laboratory studies. In view of the experience of MacLean and others, it was felt advisable to employ a reversible form of antithyroid therapy. Response of the thyrotoxic state was satisfactory, although a daily maintenance dose of 150 mg. propylthiouracil has been found necessary to date. Close observation during periods of euthyroidism and recurrent thyrotoxicosis when antithyroid medication was temporarily discontinued has tended to support the impression, referred to by a number of observers, of the existence of a "see-saw" relationship between the two diseases.

Up to the present time there has been no difficulty in controlling the myasthenic symptoms while the patient was on a maintenance dose of propylthiouracil.

Discussion

In view of the frequent occurrence of myopathy in thyrotoxicosis, proof of the coexistence of myasthenia gravis frequently presents a difficult problem in diagnosis. Where myasthenia occurs first, and the patient has been under observation for a number of years (as was our patient before emergence of thyrotoxicosis), resolution of the problem is not too difficult. However, in the circumstance where thyrotoxicosis predates or is found to be coexistent with myasthenic symptoms, clear-cut delineation of the two diseases is not so easily made. Many workers accept improvement following administration of neostigmine, and aggravation by curare, as criteria diagnostic of myasthenia gravis, but a similar if not so pronounced effect has been reported in thyrotoxic myopathy. Millikan [7] states that marked weakness of other than ocular muscles, and then only in the presence of exophthalmos, is practically nonexistent in myasthenia gravis. Laurent [8] and Brain [9] are firmly of the opinion that thyrotoxic myopathy can be cured by thyroidectomy, but thyroidectomy without thymectomy has never cured myasthenia gravis.

That the neuropathologic defect in myasthenia differs from that found in the myopathy of hyperthyroidism appears to be clear from both clinical and pharmacologic evidence. The defect in myasthenia gravis is considered to be either deficient production or excessive destruction of acetylcholine at the myoneural nerve junction. By protecting acetylcholine, neostigmine, an anticholinesterase, relieves the symptoms of muscle weakness and easy fatigability. What role, if any, thyroxine plays in this mechanism appears highly problematic, particularly in view of the frequent paradoxic improvement of myasthenia in the presence of hyperthyroidism. Moreover, no significant alteration of thyroid function or thyroxine blood levels has ever been demonstrated in uncomplicated myasthenia.

Summary

1. The twenty-third instance of the coexistence of hyperthyroidism and myasthenia gravis is reported.

2. A definite "see-saw" relationship between the two conditions was noted,

wherein appearance of the thyrotoxic state ameliorated the symptoms of myasthenia, and antithyroid therapy increased the neostigmine requirement.

3. Review of the literature indicates that this effect is by far the more common occurrence, although adequate therapy of the thyrotoxic state can usually be accomplished.

4. In view of this and of the many other reported instances where radical antithyroid therapy has been followed by marked aggravation of myasthenia and death in myasthenic crisis, a reversible form of therapy, such as antithyroid drugs, rather than I^{131} or surgery, appears to be the preferable treatment for hyperthyroidism.

SUMMARIO IN INTERLINGUA

Debilitate muscular es frequente in thyrotoxicosis. Le occurrentia de hyperthyroidismo in un patiente con pre-existente myasthenia grave rende probabile un aggravation del myasthenia, durante que le tractamento del hyperthyroidismo rende probabile le melioration de illo. Ben que iste relation non es un nove discoperta, le reportos in le litteratura nota le plus frequentemente un alternation del effectos de reciprocitate. Un numero de casos se trova in le litteratura in que le tractamento de hyperthyroidismo esseva sequite per morte in un crise myasthenic.

Un patiente feminin de 26 annos de etate con previemente establite myasthenia grave qui disveloppava hyperthyroidismo esseva tractate con doses moderate de propylthiouracil. Esseva notate un relation leve sed definitemente reciproc, evidentiate per le augmento del requirimento del parte del patiente de prostigmina quando le thyrotoxicosis esseva ben regulate e per le melioration del myasthenia quando le thyrotoxicosis recurreva.

Es proponite, per consequente, que un forma reversibile de therapia, del typo hic describite, es indicate in loco de radiotherapia o chirurgia quando le duo morbos occurre in association.

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