

## OCULAR MYASTHENIA GRAVIS ASSOCIATED WITH AUTOIMMUNE THYROID DISEASE

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### ABSTRACT

The coincidence of thyroid ophthalmopathy and ocular myasthenia gravis is a defined but rather rare condition.

A 30-year-old female patient was admitted with complaints of weight loss, sweating, palpitation and tremor of both hands for about 4 months. She was diagnosed as having Graves' disease with elevated thyroid hormone levels, diffuse hyperplastic thyroid gland with increased iodine, <sup>131</sup>I uptake and positive antithyroid antibodies. Two months after the diagnosis of thyroid disease, she developed diplopia and in the following days, bilateral ptosis. Orbital magnetic resonance imaging showed that the lateral and inferior rectus muscles were thickened indicating the infiltration of those muscles. She had positive response to the prostigmine test and elevated acetylcholine receptor antibody levels supporting the diagnosis of myasthenia gravis. She had undergone thymectomy and the pathology specimen revealed thymic hyperplasia.

This case demonstrates the comorbidity of thyroid ophthalmoplegia and ocular myasthenia gravis. Ocular involvement by this two different

pathologies is a rare condition but should be taken into consideration.

**Key Words:** Myasthenia gravis, Graves' disease, Ophthalmopathy, Ocular involvement, Thyrotoxicosis, Thymectomy

### INTRODUCTION

Graves' disease and myasthenia gravis are both autoimmune diseases and the coexistence of these two diseases is well recognised. Myasthenia Gravis is more frequent in patients with thyroid disease. It is seen in less than one percent of patients with Graves' disease, and approximately five percent of myasthenic patients are thyrotoxic at some time (1). Moreover thyroid diseases occur more frequently in close relatives of patients with myasthenia gravis than in the general population (2). Antithyroglobulin and antimicrosomal antibodies have been reported to be present in 11% and 27% of myasthenic patients, respectively (3). Conversely, 51% of thyrotoxic non-myasthenic patients have been shown to have circulating antibodies against thyroid, smooth muscle and

thymus gland (3). If these two clinical conditions coexist in a patient, both present with their characteristic signs and symptoms. Here we present a case of thyroid ophthalmopathy and isolated ocular myasthenia gravis.

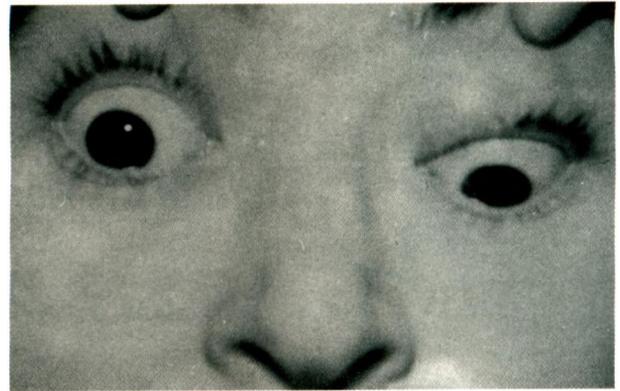
## CASE REPORT

A thirty-year-old, right-handed woman was admitted with the complaints of weight loss, sweating, palpitation and tremulousness continuing for about 4 months. The patient was diagnosed as having Graves' disease. The findings were: diffuse enlarged thyroid gland, elevated thyroid hormone levels, positive antithyroid antibodies, and increased iodine 131 uptake. Propylthiouracil 300 mg/day was started. Two months after the diagnosis of thyroid disease she developed diplopia on downward and lateral gazes. Three weeks later, bilateral ptosis was added to the symptoms. The severity of her ptosis fluctuated during day time. Her medical history revealed that, she had had a cesarian section 10 months before the appearance of the symptoms.

The patient was examined three days after the onset of ptosis. In physical examination, she had a diffusely palpable thyroid gland and exophthalmos of both eyes (right eye 24mm Hertel, left eye 22mm Hertel). The neurological examination revealed bilateral ptosis predominantly on the right side (Fig. 1). Diplopia occurred during horizontal and downward gazes. The right globe was restricted during downward gaze (Fig. 2). The severity of ptosis was increased after sustained upward gaze. Both lids



**Fig. 1** : Primary position showing bilateral ptosis



**Fig. 2** : Downward gaze showing the restriction of the right eye

exceeded the limbus 3mm and the pupilla was covered by the median line.

The routine laboratory investigations including blood glucose level, erythrocyte sedimentation rate, electrolytes, kidney and liver function tests were normal. Complete hemogram was consistent with mild iron deficiency anemia. Thyroid function tests revealed free T3: 10,19 pmol/L (Normal values:3,5-6,5), free T4: 31,84 pmol/L (Normal values:11,5-23,2), TSH: 0,01 mIU/ml (Normal values:0,35-5,5). Investigation of thyroid antibodies revealed Anti-M: 1020 IU/ml (Normal values:0-50), Anti-Tg: 17,7 IU/ml (Normal values:0-50), Tr Ab: 49 IU/ml (Normal values:0-15).

Magnetic resonance imaging (MRI) of the globes showed increased intensity and thickening of both lateral rectus, right medial rectus, right superior rectus and left inferior rectus muscles, indicating the infiltration of these muscles, which was consistent with thyroid ophthalmopathy.

Ptosis showed significant improvement after the intramuscular injection of 1,5 mg neostigmine methylsulphate, but the restriction of eye movements did not change. Repetitive stimulation of the right ulnar nerve-adductor digiti minimi muscle and facial nerve-nasalis muscle revealed no decrement. Acetylcholine receptor antibody level was found to be 1,30 nmol/L, which was more than two times higher than the normal levels (Normal values:0-0,50). Thorax computed tomography revealed a mass lesion of 6x3x2 cm located in the thymus zone.

After two months of propylthiouracil treatment, the patient became euthyroid. Pyridostigmine 60

mg four times daily was added for the treatment of ptosis. In spite of medication, exophthalmos and exophthalmic ophthalmoplegia were not relieved, but ptosis responded to the treatment. After two sessions of plasmapheresis, the patient was operated on. Total thyroidectomy and extended thymectomy were performed. Pathological examination was relevant with thymic hyperplasia. After the operation, the patient's medication included 60 mg pyridostigmine four times daily and 0,15 mg levothyroxine sodium daily. Under this medication, her ophthalmoparesis continued, but the ptosis was fairly controlled.

## DISCUSSION

Myasthenia gravis (MG) is an autoimmune disease characterized by impaired neuromuscular transmission due to circulating antiacetylcholine receptor autoantibodies. The clinical expression of MG varies, ranging from a mild localized disease such as ocular MG (OMG) to a severe generalized disease (GMG) (4).

Patients with MG may have evidence of coexisting autoimmune thyroid diseases (AITD), which include autoimmune thyroiditis and Graves' disease (5). Epidemiological studies showed that AITD occur in approximately 5-10% of MG patients, whereas a fairly low incidence of MG, (0.2%) has been reported in patients with AITD (6). The clinical presentation of MG associated with AITD is frequently restricted to the eye muscles. GMG was found to be more frequent in patients without thyroid disease. Also, thymic abnormalities were less frequent in MG associated with AITD than in MG without thyroid autoimmunity. Although this is not true for the patient who had thymic hyperplasia, a greater frequency of thyroid antibodies in OMG, when compared to GMG, has been reported (4).

The reason for the association of AITD with OMG is unknown, but several hypotheses may be considered. First, OMG and GMG might actually represent separate diseases (7) with different spectra of associated diseases. Second, an immunological cross-reactivity against epitopes or autoantigens shared by the thyroid and the eye muscles might be the basis of this association (8). A third explanation for the higher

frequency of OMG in AITD could be that these disorders have a common genetic background (9).

In three-quarters of patients with both conditions, thyrotoxic symptoms occur before or concurrently with those of myasthenia. Our patient had thyrotoxicosis symptoms seven months before her ptosis developed (10).

The ocular changes in Graves' disease may include exophthalmos, periorbital oedema, lid lag, chemosis and ophthalmoplegia. Exophthalmic ophthalmoplegia may be unilateral, but it is usually bilateral. The extraocular muscles most commonly involved are the superior and lateral recti (11). In our patient, the downward movement of the right eye was restricted and the patient was complaining of diplopia during downward and horizontal gazes. Her diplopia and ophthalmoparesis did not change after neostigmine injection, while her ptosis improved visibly. The MRI findings showing increased intensity and thickening of the extraocular eye muscles were consistent with thyroid ophthalmopathy.

Two thirds of the patients with both disorders show improvement in myasthenia gravis after treatment for thyroid disease. In other patients, however, the treatment of thyroid disease has no effect on myasthenic symptoms (1). The treatment of hyperthyroidism has not improved the myasthenic symptoms in our patient, since her need for anticholinesterase did not decrease. Some authors state that, thymectomy may have positive effects on the clinical condition of both myasthenia (12) and AITD (13). Our patient did not show an obvious improvement after thymectomy.

In conclusion, MG associated with AITD has a mild clinical expression characterized by preferential involvement of the eye muscles. This is consistent with the hypothesis that OMG and GMG are separate diseases with different spectra of associated diseases and different immunogenetic back-grounds. The association of OMG with AITD might also be due to common immunopathogenetic mechanisms acting through antigens shared by the eye muscles and the thyroid. Further immunological and genetic studies are needed to verify these hypotheses.

The important clinical implication of this report is that the coexistence of MG with thyroid autoimmunity might have prognostic relevance in the identification of a subgroup of MG patients with a mild form of the disease. It should be remembered that, ptosis is not an expected symptom in thyroid ophthalmopathy. If ptosis or paresis of the orbicularis oculi muscle develop in a patient with thyroid ophthalmopathy, superimposition of myasthenia gravis should be considered.

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