CLINICAL CASE

SURGICAL APPROACH IN A CASE OF GENERALIZED MYASTHENIA GRAVIS

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Abstract

Myasthenia gravis (MG) is an antibody mediated, T cell dependent autoimmune disease characterized by a disorder of neuromuscular junction with progressive inability to sustain a maintained or repeated contraction of striated muscle. It is represented by antibodies directed against the nicotinic acetylcholine receptors (nAchR) of the post junctional membranes. We present the case of an 82-year-old patient, who was admitted to the hospital for plasmapheresis due to an aggravation of her auto-immune generalized myasthenia. The clinical examination at admission revealed ptosis, dysphagia, a medium effort dyspnea, difficulties in closing the mouth, dysphonia with a nasal voice and limited walking with a bent head and camptocormia, with Osserman score 46/100 (diplopia and bilateral ptosis). The thoracic scanner describes a tissue lesion in the thymus region with a diameter of 35 mm corresponding to a thymoma. The Magnetic Resonance Imaging confirmed the possible thymoma. A thymectomy using video-assisted thoracoscopic surgery (VATS) technique was performed according to the age and general status of the patient. Post-operative histological examination revealed a B2 type thymoma and the TNM staging system classifies the thymoma as being T1bNx.

Keywords*: myasthenia gravis, autoimmune disease, thymoma, thymectomy*

Introduction

Myasthenia gravis (MG) is the most thoroughly understood of all human autoimmune diseases and has served as a model for the elucidation of mechanisms underlying other autoimmune disorders [1]. It is a chronic autoimmune disorder of the postsynaptic membrane at the neuromuscular junction (NMJ) in skeletal muscle.

Patients usually present with muscle weakness and abnormal fatigability. Severity varies from isolated eye muscle weakness to generalized muscle weakness and respiratory failure requiring mechanical ventilation [2]. It is associated with thymoma and with other autoimmune diseases such as hyperthyroidism and Hashimoto's disease. Myasthenia gravis is associated with thymic abnormalities in about 85% of cases. This may be thymoma or thymic hyperplasia [1].

This disorder is caused by the presence of antibodies against components of the muscle membrane localized at the neuromuscular junction. In most cases, the autoantibodies are against the nicotinic acetylcholine receptor

(nAChR). Recently, other targets have been described such as the MuSK protein (muscle-specific kinase) or the LRP4 (lipoprotein related protein 4) [3].

It is now widely accepted that thymus gland has an important role in the pathogenesis of MG by T-lymphocyte education and self-tolerance [4] and therefore in addition to medical therapy, thymectomy has been accepted as a therapeutic option by both surgeons and neurologists. Myasthenia gravis is associated with thymic abnormalities in about 75% of cases out of which 15% have thymoma [1].

Historical background

Thomas Willis (1621-1675), English physician, published a book De anima brutorum in 1672 in which he wrote about "a woman who temporarily lost her power of speech and became 'mute as a fish'". This has been interpreted as being the first written description of myasthenia gravis [1].

In the Lancet of June 2, 1934, the remarkable discovery of physostigmine treatment by Dr. Mary Walker (1888-1974) was published, which was to become the mainstay of symptomatic treatment [5].

In the next five years, Dr. Walker and colleagues provided clinical evidence for the weakness of myasthenia gravis being caused by a "disturbance of transmission of excitation from motor nerve to voluntary muscle presumably caused by a deficiency of acetylcholine" [6].

Case presentation

We present the case of an 82-year-old patient, who was admitted to the hospital for plasmapheresis due to an aggravation of her auto-immune generalized myasthenia.

The most significant antecedents are represented by right kidney nephrectomy in 1986 (due to an adenocarcinoma), an auto-immune myasthenia with positive antibodies anti-acetylcholine receptor diagnosed in 2007. The latter was discovered during the pre-operative evaluation for a right knee total replacement surgery, initially with the presence of remnant thymus tissue but without any abnormality associated. The patient did not undergo thymus resection.

The patient was stable for a long period of time (Osserman score 90/100) due to the treatment with corticosteroids (prednisone), mycophenolate mofetil as immunosuppressive therapy and pyridostigmine.

After an aggravation of her general status, a treatment with 3 series of immunoglobulins was initiated, that at the beginning determined a clinical improvement. But the patient was hospitalized due to further complications.

Another worsening determined the appearance of ptosis, dysphagia, dysphonia, and important fatigue with walking difficulty treated with 4 series of plasmapheresis, with initially promising response, but ineffective as an end result.

It is important to note that despite all these treatment lines, the general condition of the patient continues to worsen.

The clinical examination at admission revealed ptosis, dysphagia, a medium effort dyspnea, difficulties in closing the mouth, dysphonia with a nasal voice and limited walking with a bent head and camptocormia, with Osserman score 46/100 (diplopia and bilateral ptosis).

The thoracic scanner describes a tissue lesion in the thymus region with a diameter of 35 mm corresponding to a thymoma (Figure 1).

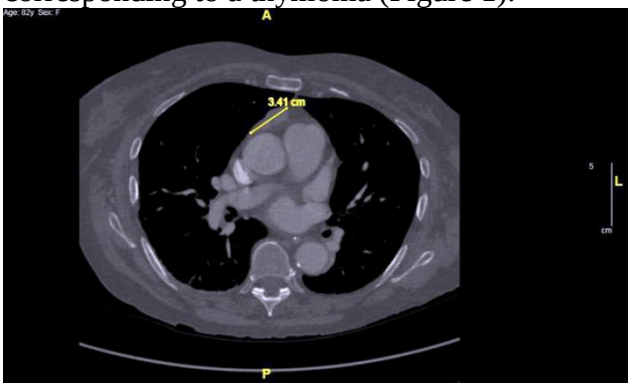

Figure 1 – Computer Tomography of the chest revealing a large mass in the anterior mediastinum (marked with the yellow line). Histology later established the diagnosis of a thymoma.

The thoracic Magnetic Resonance Imaging confirmed the possible thymoma (Figure 2).

After the analysis of the scanner and MRI a thymectomy was decided. The preoperative

evaluation showed that the respiratory function is normal with a saturation of 94 %, with a peak flow impossible to determine due to an insufficient closing of the mouth, but without any sign of respirator insufficiency.

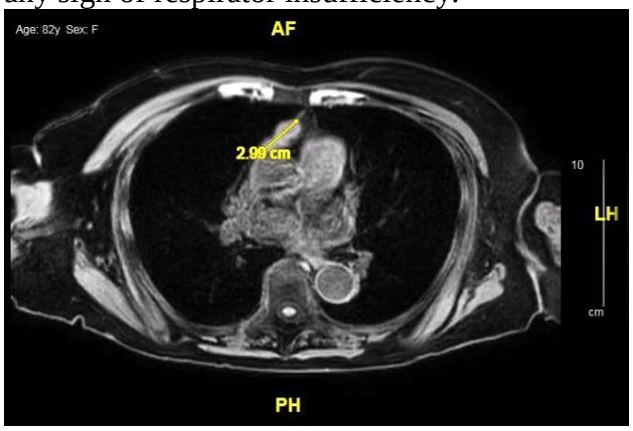

Figure 2 – Magnetic Resonance Imaging (MRI)

A thymectomy using video-assisted thoracoscopic surgery (VATS) technique was performed according to the age and general status of the patient (Figure 3).

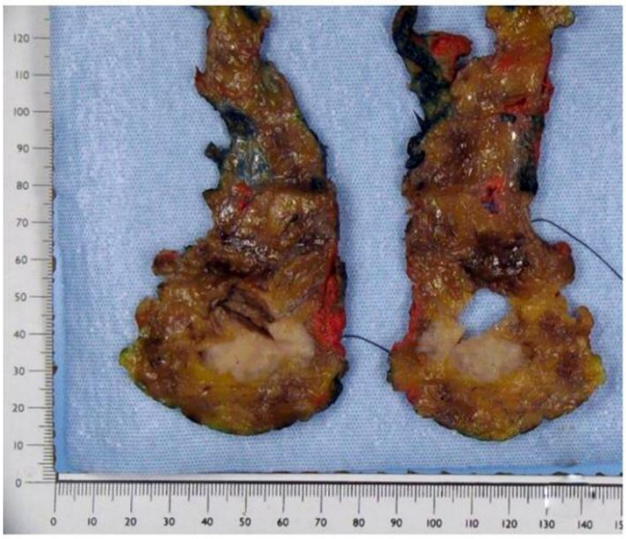

Figure 3 – Resected piece

Post-operative histological examination revealed a B2 type thymoma of 2.9 cm diameter, infiltrating the right mediastinal pleura and also the surrounding fat tissue without vascular emboli and peri-nervous infiltration. The TNM staging system classifies the thymoma as being T1bNx (Table-Thymic Epithelial Tumors).

The patient will continue to realize series of plasmapheresis. A consultation by vascular surgeon was scheduled to determine if an arterial venous fistula can be created. According to the Doppler echography the patient will undergo an operation to create a fistula (Figure 4).

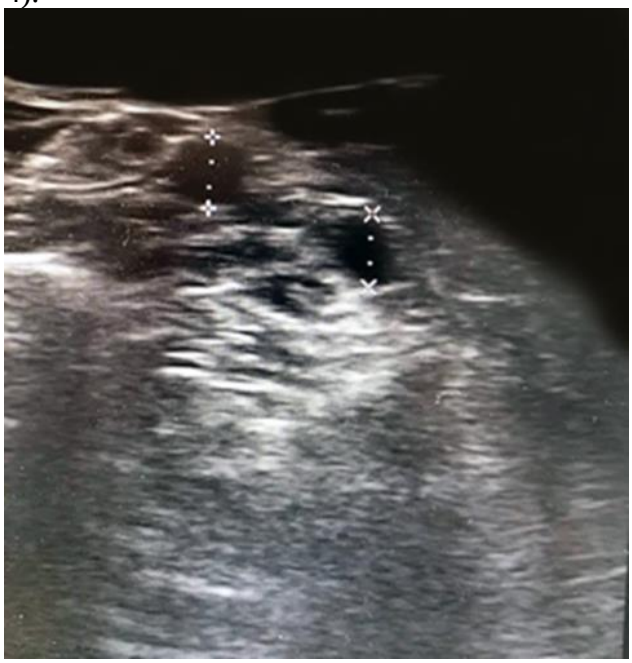

Figure 4 – Echo Doppler

Discussions

Sussman et al. indicated that thymic radiology is recommended for all patients with MG regardless of antibody status or specific clinical features. The primary value of chest radiology is in identifying patients with thymoma because thymoma has serious management implications [7].

Patients with MG undergoing VATS (Video-assisted thoracoscopic surgery) thymectomy achieved better surgical outcomes and fewer complications than those who received OT (open thymectomy) [8].

This minimally invasive technique involves several tiny incisions in the chest. A camera is inserted through one of the incisions, and surgery is performed with video guidance. The surgeon removes the thymus by using special surgical tools inserted into the other incisions. The goal is to provide the same result as the more invasive transsternal approach with less post-operative discomfort and a quicker recovery [9].

Rückert et al., Showed that after VATS thymectomy, the pain experienced by the patient had a lower intensity compared to that experienced after median sternotomy, quantified in relation to the amount of analgesic drugs needed. At the same time, pulmonary

complications had lower incidence in patients with VATS thymectomy [9].

It is also believed that thymectomy early after the diagnosis of MG would be associated with a higher rate of improvement and remission and so it is recommended to perform thymectomy early after the diagnosis is made regardless of age, stage, thymic pathology and preoperative clinical status [10].

In non-thymomatous MG, thymectomy can also be performed as an option to potentially avoid or minimize the dose or duration of immunotherapy, or if patients fail to respond to an initial trial of immunotherapy or have intolerable side-effects from that therapy. Because of the long delay in onset of effect, thymectomy for MG is an elective procedure.

Conclusions

Computer Tomography of the chest is imperative in suspected cases of myasthenia. The goal of thymectomy as a treatment for myasthenia gravis is to induce remission, or at least improvement, permitting a reduction in immunosuppressive medication. Therefore, assessing thymus histology is very important for myasthenia gravis prognosis.

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