

Immediate Improvement after Thymoma Resection in a Young Refractory Myasthenia Gravis Patient: A Case Report

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In the acute settings of generalized myasthenia gravis (MG) treatment options include plasma exchange (PLEX), intravenous immunoglobulin (IVIG), and pyridostigmines. A thymoma is associated with the disease in up to 20% of cases [1,2].

In cases where a thymoma is detected, surgical treatment to remove the tumor is recommended in certain age groups. At present, there are no clear guidelines regarding the optimal time to perform thymectomy after diagnosis of acute crisis or from the last treatment to thymectomy. Treatment is at the clinician's discretion.

MG patients exhibit fluctuating weakness in voluntary muscles, particularly those controlled by motor nuclei of the brainstem, which improves rapidly at rest. The affected muscles are mostly the eyelids and eye muscles, and to a lesser extent, the muscles of the face, jaws, throat, and neck. Eventually, the disease progresses insidiously to the limb muscles and axial muscles in most

patients [3]. The primary treatment, especially for mild cases and ocular restricted types of MG is anti-cholinesterase drugs (AChE-inhibitors). For patients with moderate to severe weakness who have inadequately responded to AChE-inhibitors, long-term steroid therapy and steroid sparing agents such as azathioprine and immunosuppressants are effective while patients pass the acute and sub-acute phases. PLEX and IVIG are reserved for acute treatment or unstable disease. Eculizumab is reserved for treatment refractory cases.

Thymic malignancies occur more often in MG patients. Lymphofollicular hyperplasia of the thymus medulla occurs in 65% or more of MG cases, and thymic tumors appear in 10–15% of cases. Thymomas with malignant properties may spread locally in the mediastinum as well as to regional lymph nodes, but they rarely metastasize outside these structures. Malignant thymoma was also associated with Morvan syndrome, frequently accompanied by MG [4]. Patients with thymoma are frequently male and usually older (50–60 years of age).

Thymectomy is considered adequate treatment in patients with gen-

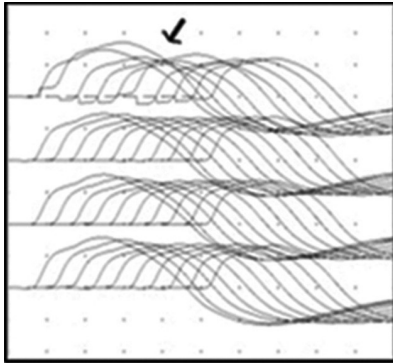
eralized MG without thymoma. It is best to postpone until after puberty in adolescent patients due to the importance of thymus in the development of the immune system [5]. There is a clear indication for thymus removal in all patients in whom thymoma is detected. There are established treatment guidelines regarding patients with non-thymomatous MG but not for those with thymic cancer.

PATIENT DESCRIPTION

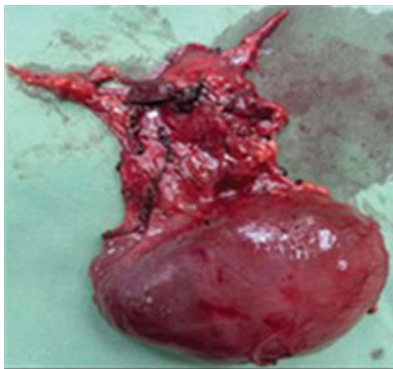
A 33-year-old female with seropositive generalized MG who did not respond to immune treatments such as plasma exchanges (7 cycles) and high doses of steroids (1 g/kg) presented with severe bulbar MG symptoms and a cystic thymic tumor. After undergoing thymoma resection, the patient showed improvement. She was admitted to the hospital with dysphagia and a Quantitative Myasthenia Gravis Score (QMGS) score of 23 (reference range 0–39). Acetylcholine receptor antibodies and baseline decrement (17%) of spinal accessory nerve [Figure 1A] were present on admission. Chest computed tomography showed a large 7 cm cystic

Figure 1. Patient data

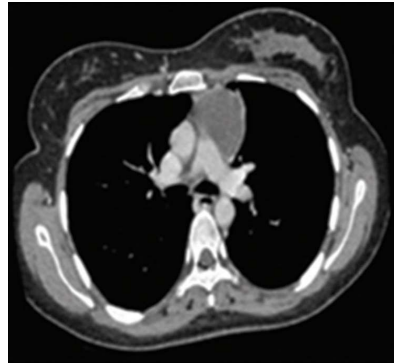
[A] Repetitive nerve stimulation at 2 Hz at baseline of the spinal accessory nerve demonstrates 17% decrement (arrow)



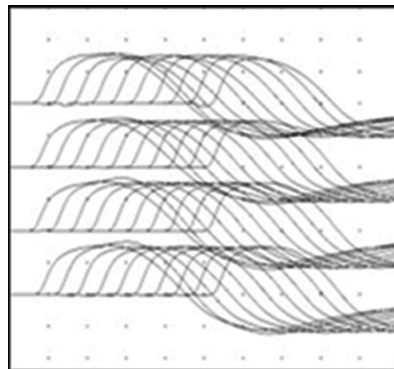
[C] Gross pathology of what was confirmed to be localized thymoma with growth into local fat (T1) without further metastasis



[B] Cystic mass (7 cm) seen on chest computed tomography



[D] Resolution of spinal accessory nerve decrement 1-week post-thymectomy



mass [Figure 1B]. Thymectomy resection was performed by open chest thoracotomy [Figure 1C]. By postoperative day 1, she showed dramatic improvements in fatigable weakness including swallowing and improved QMGs score (12), which improved over the week with normalized decrement 21 days post-surgery. [Figure 1D]. At a follow-up visit 3 months post-surgery, her QMGs score was 4. Our case demonstrates the potential of prompt clinical improvement after thymectomy in patients able to undergo thymoma resection.

COMMENT

We report a case treatment refractory MG patient with a mediastinal cystic thymoma. The neurological presentation included moderate to severe dysarthria and dysphagia with generalized muscle weakness. The QMGs includes 13-items and measures ocular, bulbar, respiratory, and limb function. The instrument grades each finding. Scores range from 0 (no myasthenic findings) to 39 (maximal myasthenic deficits). Her QMGs score on admission was 23, which improved

to 4 three months post-surgery.

To date, guidelines have been established regarding the need for thymic removal with no specific time for surgery in patients presenting with a MG crisis. Thymoma resection in MG is primarily focused on attempting to treat the cancer. Our young female patient with MG failed to improve after multiple plasma exchange treatments. However, she showed marked clinical and electrophysiological improvement after thymectomy [Figure 1D].

Our patient's rapid clinical improvement immediately after thymectomy raises the question of whether early removal of the tumor should be added as a soft recommendation if patients are capable of undergoing surgery. Furthermore, in addition to the clinical impression and neurological examination, PLEX or IVIGs should be considered when treating refractory MG patients with thymoma. Patient's understanding and operative complications need to be weighed against benefits, similar to other paraneoplastic syndromes in which a tumor triggers an abnormal immune-mediated pathogenesis.

Thymoma-related diseases, such as red cell aplasia, rarely resolve after thymectomy, and immunosuppression is usually required after surgery. Future prospective studies should be conducted to establish guidelines, especially due to the common occurrence of thymomas in patients with MG and due to the relationship of this tumor to the worsening of symptoms.

CONCLUSIONS

We demonstrated rapid recovery immediately after thymus removal in a young refractory patient. Our case highlights the necessity to fur-

ther investigate the optimal period for thymectomy in newly diagnosed young MG patients.

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Capsule

Not just random chromosome changes

Aneuploidies, which are changes in the numbers of whole chromosomes or chromosome arms, are common in cancer, but their contributions to cancer cell survival have been difficult to pinpoint. **Girish** and colleagues developed a chromosome-engineering tool to orchestrate the targeted loss of aneuploid chromosome arms and thereby compare isogenic cancer cell lines with and without selected trisomies. The authors

discovered that trisomy of chromosome 1q in particular is advantageous to cancer cells and phenocopies the loss of tumor suppressor *TP53* signaling. Tumors with this aneuploidy are sensitive to compounds activated by an enzyme encoded on chromosome 1q, suggesting a potential therapeutic approach.

Science 2023; 381: 848
Eitan Israeli

Capsule

How metastases hack the brain

Brain metastases are often associated with cognitive impairments. However, predicting how these metastases will affect brain function remains an unmet challenge. **Sanchez-Aguilera** and colleagues applied computational modeling and machine learning to predict the effect of brain metastasis on brain function. Using in vivo electrophysiology, ex vivo calcium imaging, and transcriptomic data obtained in three rodent models of brain metastasis, the authors

identified brain activity associated with specific subtypes of metastasis. Although the translational relevance remains to be seen, the results pave the way for the development of models able to predict the impact of brain metastasis on cognition based on electroencephalographic recordings.

Cancer Cell 2023; 41 (9): 1637
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Capsule

Aging gets on the heart's nerves

Changes in innervation of the heart can contribute to arrhythmias, and the risk of arrhythmias greatly increases with age. **Wagner** and colleagues uncovered a mechanism connecting these two phenomena. The authors studied young and aging mice and demonstrated that innervation of the heart decreases with age. Age-related accumulation of senescent cells promotes the release of semaphorin-3A, which reduces the density of neuronal axons in the heart.

At the same time, aging is associated with a decrease in a microRNA that counteracts the effects of semaphorin-3A, further tipping the balance toward decreased innervation. These age-related losses in innervation could be reversed by treating the mice with senolytic drugs, suggesting a potential therapeutic approach.

Science 2023; 381: 897
Eitan Israeli