

Myasthenia Gravis Appearing After Thymectomy: a Case Report and Review of the Literature

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A small proportion of thymoma patients without myasthenia gravis (MG) have been observed to develop MG after total removal of the thymoma. However, the underlying cause is not yet known due to the rarity of postoperative MG patients. We report a 39-year-old man in whom MG appeared after surgical removal of a thymoma. Computed tomography and magnetic resonance imaging showed no signs of recurrent or metastatic thymoma. Administration of pyridostigmine bromide resulted in the prompt improvement of myasthenic symptoms. Our observations indicate that postoperative follow-up care with monitoring of possible postoperative MG is necessary after resecting a thymoma.

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Myasthenia gravis (MG) is an autoimmune disease in which muscular weakness and fatigability of skeletal muscles are caused by an antibody against the acetylcholine receptor (AChR) at the neuromuscular junction. A thymoma, which is an epithelial tumor of the thymus gland that is usually benign, occurs in about 15% of adult patients with MG.¹ It has long been suspected that the thymus or a thymoma may play a role in the pathogenesis of MG. Although thymectomy may improve the myasthenic symptoms, MG can develop from months to years after the removal of a thymoma in previously nonmyasthenic patients.²⁻⁵ A nonresidual tumor or thymic tissues have been found in some patients, while MG heralded recurrent or metastatic thymoma in other cases.^{6,7} We defined cases of MG onset after total removal of the thymoma as 'postoperative MG'. We report a patient in whom MG appeared after total removal of the thymus for thymoma without tumor recurrence.

CASE REPORT

A 39-year-old man presented with diplopia and ptosis that was characterized by diurnal variation. Three years previously a mediastinal tumor was diagnosed on a chest X-ray during a routine medical examination. Chest computed tomography (CT) confirmed the presence of a demarcated anterosuperior mediastinal mass, leading to the diagnosis of a thymoma. Anti-AChR antibodies were not detected and an electromyogram was not performed. At that time the patient was asymptomatic, and there were no clinical signs of MG before surgery. He received a median sternotomy, and an anterosuperior, well-encapsulated tumor was found that was not adherent to the mediastinal structures. Total resection of the mass and the adjacent thymic tissue was performed. Histological examination findings confirmed the diagnosis of a noninvasive medullary thymoma. His

postoperative course was satisfactory.

On admission, bilateral ptosis and diplopia were present, but the physical examination was otherwise normal. Results from repetitive nerve stimulation and neostigmine tests were consistent with neuromuscular junction disorder. The titer of anti-AChR antibody was high, at 43.7 nmol/l. The diagnosis of MG was confirmed by the findings of both the anti-AChR antibody and electrophysiological test. Chest CT and magnetic resonance imaging showed no signs of recurrent or metastatic thymoma. Pyridostigmine bromide administration (180 mg per day) was started, which resulted in the prompt improvement of myasthenic symptoms. At a 2-year follow-up, the patient was doing well on pyridostigmine, with a chest CT revealing no evidence of a recurrent or metastatic tumor.

DISCUSSION

The thymus plays a key role in the immunologic status of an individual, and disease of the thymus can be associated with autoimmune disorders. MG first appearing many years following the removal of a thymoma reportedly occurs in 1.5-28% of cases.⁸ The interval between a thymectomy and the onset of postoperative MG has varied between studies. Two of the studies involving an adequate number of cases and obtaining detailed clinical data found that the mean interval between thymectomy and the onset of postoperative MG was 19 and 18 months. Namba et al. reported that patients with a shorter onset of postoperative MG had a better prognosis, but other study did not find this relationship.^{3,8} The rarity of postoperative MG cases has meant that it remains unclear whether the interval between thymectomy and the onset of postoperative MG influences the prognosis. We speculate that this discrepancy is due to different therapies being applied for MG. Most reports demonstrate that postoperative MG responds to anticholinesterase drugs and/or steroids, and that the prognosis is relatively good.^{5,8} Although a thymectomy does not prevent the onset of postoperative MG, this procedure is associated with a good prognosis.

One study found that 63%, 25%, and 12% of thymomas were of mixed histological type, predominantly lymphocytic type, and predominantly epithelial type, respectively,³ and the corresponding percentages in another study were 65%, 22%, and 13%.⁸ These distributions of the histological types were similar to that in patients with thymoma and preoperative MG. In the study of Kondo and Monden, the anti-AChR antibody at onset varied between 1.8 and 91 nmol/l.⁸ The majority of patients show a clinical severity of type I or type IIA on Osserman's classification. However, they found that the titer of anti-AChR antibody did not correlate with clinical severity, as was the case in our patient.

The mechanism underlying the onset of postoperative MG is unclear. The various time periods between a thymectomy and the onset of postoperative MG raise doubts as to whether a thymectomy directly triggers MG onset. Two useful studies were recently published. Hoffacker et al. found using T-cell-proliferation assays for a fragment of the AChR that the thymoma released mature auto-antigen-specific T-cells into the periphery.⁹ Buckley et al. found that T-cells in a thymoma were exported to the peripheral blood, and that these T-cells could persist in the periphery for many years.¹⁰ These studies suggest that a thymoma actively exports large numbers of mature T-cells into the peripheral blood, with these cells persisting in the periphery, potentially stimulating autoantibody production and subsequent autoimmune disease.

The late onset of MG and other autoimmune disorders should be kept in mind as possible complications of surgical treatment for thymoma. Therefore postoperative follow-up care with consideration of postoperative MG is necessary after resecting a thymoma. In postoperative MG cases, recurrent or metastatic thymoma should be ruled out because reoperation can be effective even in the treatment of MG.

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