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Case Report

Thymectomy during Myasthenic Crisis under Artificial Respiration

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A 34-year-old man was diagnosed with thymoma, which was evaluated preoperatively as stage II or III, with myasthenia gravis (MG). The size of the tumor was 70 × 44 × 80 mm. No invasion to neighboring organs was observed. Prednisolone was prescribed for stabilization of MG. However, a myasthenic crisis (MC) occurred, and intensive care, including emergent endobronchial intubation followed by artificial ventilation, pulse steroid therapy, high-dose intravenous immunoglobulin, and tacrolimus hydrate, was initiated. A chest computed tomography on day 6 revealed tumor reduction to 50 × 30 × 60 mm. An extended total thymectomy by median sternotomy was performed, and artificial ventilation was continued after that. Scheduled artificial ventilation and steroid therapy together can, therefore, enable complete resection of thymoma in patients undergoing treatment for MC. While ventilation helps avert a respiratory failure, the steroid therapy temporarily reduces the tumor size, making resection easier.

Keywords: thymectomy, myasthenic crisis, artificial ventilation

Introduction

Myasthenia gravis (MG) is a rare autoimmune neuromuscular disease. MG is often accompanied by thymoma. Nationwide studies have reported that the prevalence of MG in the Japanese is 23%–25%.[1,2] Myasthenic crisis (MC) is the most critical complication of MG. The sudden weakness of the respiratory and bulbar muscles caused by MG result in acute respiratory failure. Patients in MC must receive intensive care with artificial ventilation followed by pulse steroid therapy and immune-suppressive therapy. Scheduled surgical interventions, such as total thymectomy, are typically postponed until remission of MC.

This report describes a case of an individual who underwent extended total thymectomy for thymoma and MG during a period of MC with the help of artificial ventilation. Additionally, the pulse steroid therapy for MC led to a temporary tumor regression which made complete resection of the tumor easier.

Case Report

The patient described in this report provided informed consent for publication of anonymized data and images, and the study design was approved by the appropriate ethics review board.

A 34-year-old, non-smoking Japanese man, with no remarkable disease history became aware of a cough at the beginning of 201X. He presented to the respiratory medicine clinic of our hospital complaining of a continuous

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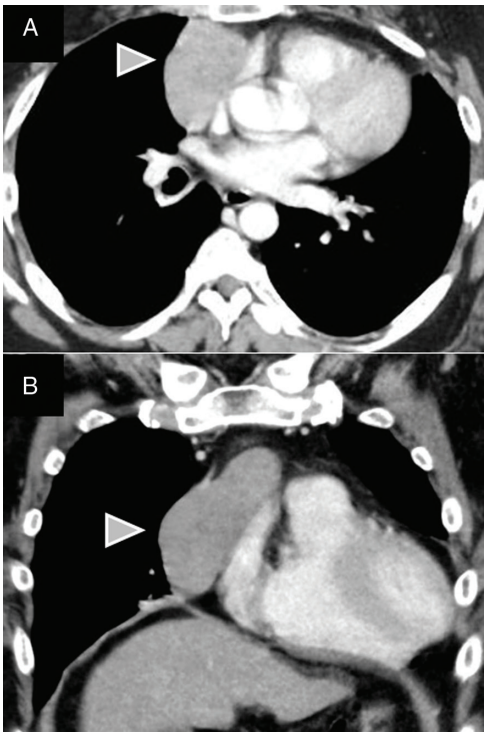

Fig. 1 Initial computed tomography imaging before oral prednisolone and pulse steroid therapy for myasthenia gravis and thymoma. The arrowhead indicates the anterior mediastinal tumor, measuring 70 × 44 × 80 mm. Coronal (**A**) and frontal (**B**) images are presented.

cough in June of the same year. After several consultations, around August, he was diagnosed with chronic bronchiolitis. He also presented with bilateral ptosis and dysarthria, indicative of MG. A chest X-ray and chest computed tomography (CT) examination in August revealed the presence of a tumor on the right side of the anterior mediastinum (**Fig. 1**). The tumor measured 70 × 44 × 80 mm, had smooth margins, and did not directly invade the neighboring organs. The patient's serum anti-acetylcholine receptor (AChR) antibody level was 51 nmol/L in mid-September. Based on the coexistence of an anterior mediastinal tumor and high levels of serum AChR,[3] a clinical diagnosis of invasive thymoma with MG was made. Physicians suspected that his cough and dysarthria were the symptoms of MG-related bulbar paralysis. He was referred to neurologists and a general thoracic surgeon within the hospital in late September. The neurologists prescribed 20 mg/day of prednisolone for MG (day 1). An extended total thymectomy for thymoma was scheduled after stabilization of MG. However, the patient complained of severe dyspnea and dysphagia

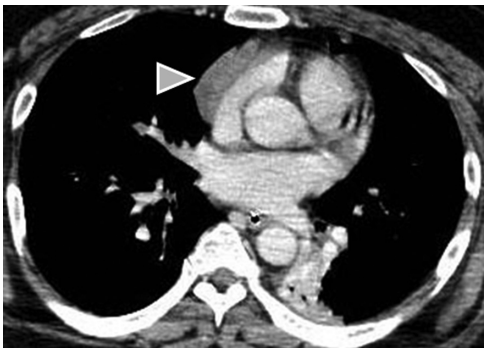

Fig. 2 Computed tomography imaging on day 6. Tumor size is reduced (arrowhead).

on day 3, and his arterial blood gas analysis (under oxygen administration [3 L/min]) revealed the following: pH 7.3; partial pressure of oxygen 82.5 mmHg; partial pressure of carbon dioxide 53.7 mmHg; bicarbonate 26.3 mmol/L; and base excess −0.6 mmol/L. The patient was diagnosed with MC, and emergent endotracheal intubation and artificial ventilation were initiated. Simultaneously, he was given pulse steroid therapy followed by prednisolone (30 mg/day), high-dose intravenous immunoglobulin (35 g/day [days 3–7]), and tacrolimus hydrate (4 mg/day [day 6]). The patient's neurologists opted for these therapies instead of plasmapheresis. The decision was based on their experience which showed that plasmapheresis tends to perturb circulation, leading to alterations in blood pressure. The intensive care measures adopted gradually stabilized his spontaneous respiration around day 6, and the patient was out of MC. However, these treatments are usually required for an additional 2 or 3 weeks before the withdrawal of artificial respiration, which meant that the extended total thymectomy was possible only on or past day 40. A chest CT on day 6 revealed a reduction in the tumor size, which now measured 50 mm × 30 mm × 60 mm (**Fig. 2**). At this time, it was decided to perform an extended total thymectomy by median sternotomy under artificial ventilation on day 12. The major reasons for this decision were as follows: a) his MC had almost stabilized under artificial ventilation, b) thymoma remission caused by the pulse steroid therapy being temporary, the tumor was likely to regrow in a few weeks,[4] and c) there was a risk of infection at the surgical site as the blood concentration of tacrolimus hydrate stabilized. The tumor and thymus were resected completely and smoothly by median sternotomy, without the need for resection of neighboring organs. Artificial ventilation was safely continued up to day 19 with no major complications although steroid-induced diabetes mellitus was noted. On day 32, his respiratory

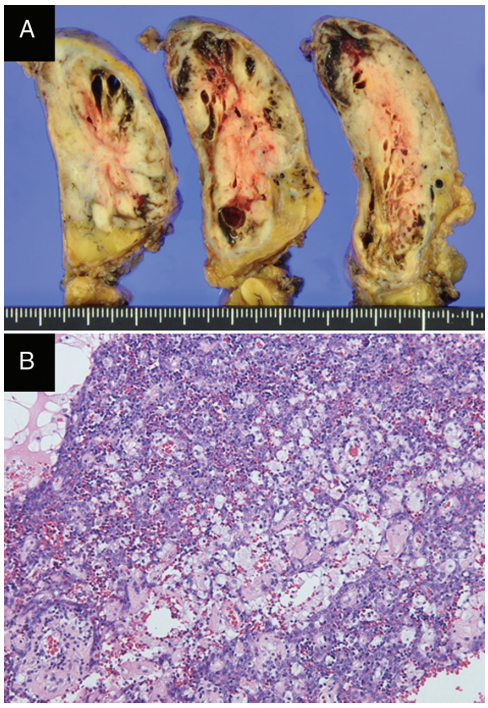

Fig. 3 Pathological findings from the tumor. (**A**) Macroscopic image of tissue sections and tumor revealing extensive cavities. (**B**) The microscopic image reveals a few lymphocytes alongside tumor epithelial cells. Also seen are a significant number of macrophages and cholesterol crystals (hematoxylin and eosin stain, original magnification × 100).

functions showed great improvement. While his vital capacity had been restored from 73.6% to 100.8%, the FEV1% (forced expiratory volume in 1 second) had improved from 63.91% to 73.15%. The MC stabilized, and the patient was able to walk with little dysarthria when he was discharged on day 41.

Surfaces of the sectioned tumor contained many extensive cavities resembling a coarse sponge. Microscopic evaluation revealed few lymphocytes alongside tumor epithelial cells. A large number of macrophages and cholesterol crystal precipitates were observed (**Fig. 3**). Since the pulse steroid therapy induced considerable necrotic changes, an original World Health Organization (WHO) histological classification[5] of the tumor could not be determined. The tumor was diagnosed as an invasive thymoma, Masaoka-Koga stage IIa, and TNM classification T1N0M0 stage I.[6,7]

The patient is currently receiving neurological therapy for MG at our hospital as an outpatient.

Discussion

A Japanese nationwide survey in 2006 reported that 13.3% of MG patients experience MC,[8] which tends to occur within the first or second year after diagnosis.[9] Steroid administration is reported to be one of the precipitating factors for MC. In our study, prednisolone could, therefore, have induced the MC.[10] However, calcineurin inhibitors, such as cyclosporine or tacrolimus, that are administered along with prednisolone on day 1 can help prevent steroid-induced MC. These immunesuppressive drugs improve the MG symptoms, thereby restricting the use of prednisolone only for early stage MG and thymoma-associated MG.[11] Mitsui et al.[12] reported that MG with thymoma tends to be more sensitive to tacrolimus than MG without thymoma. The tumor in this case was considered to be completely resectable and postoperative recurrence was less likely. Therefore, there had been a requirement for a calcineurin inhibitor, we could have safely administered it. Some studies and guidelines have stated that thymectomy should be performed only in MG-stabilized cases to maintain postoperative respiratory function.[13,14] Therefore, most thoracic surgeons schedule surgical interventions only after stabilization of MG, which is a month or later after the onset of MC.

Our patient benefited from the extended total thymectomy during MC under artificial ventilation. Surgeons usually fear postoperative MC, since it needs emergent artificial ventilation. Our study demonstrates that ventilation can be continued for more than 1 week after surgery. Recent reports published after 2000 indicate that postoperative MC after extended thymectomy occurs at a low rate of 11.5–18.2%,[13–17] and cannot be prevented completely by any preoperative treatments or surgical procedures. Acute respiratory failure caused due to MC can be directly linked to death.[14] While the occurrence of MC before surgery is rare, it is an epoch event, and postoperative acute respiratory failure can usually be avoided.

In our case, tumor reduction resulting from pulse steroid therapy for MC also facilitated surgical intervention. Thymomas, regardless of the WHO classification, express high levels of glucocorticoid receptors,[18] and therefore respond well to steroid therapy.[17,18] Funakoshi et al.[18] have reported that glucocorticoids induce G1 cell cycle arrest and apoptosis in epithelial cells of thymoma. Additionally, steroid pulse therapy reduces the number of lymphocytes in patients with thymoma,[19,20] as observed in our case. The WHO type

B1 thymomas show a higher reduction in tumor size in response to steroid therapy, compared to types AB or B3.[19] In our study, due to the histological degeneration of the tumor in response to pulse steroid therapy, we could not assign a WHO histological classification to it although we suspected it to be a type B1 case.[19] Steroid-induced reduction in tumor size is temporary, and the tumor grows back in a few weeks.[4] The thymoma in our case too would have regrown had we prolonged the surgery irrespective of whether MC had stabilized or not. Therefore, if the tumor reduction is seen after steroid therapy, clinicians should make a quick decision regarding surgical intervention.

Conclusion

Thymoma patients being treated for MC can greatly benefit from surgical resection of the tumor, which can be achieved by a) steroid therapy to reduce the tumor size and b) scheduled artificial ventilation to avert a respiratory failure.

Disclosure Statement

The authors have no conflicts of interest to declare regarding the content of this article.

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