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Myasthenic Crisis in Thymoma: A Clinical Case Report

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Abstract: Thymoma is an anterior mediastinal tumor commonly associated with paraneoplastic syndromes, notably myasthenia gravis. This case report describes a 40-year-old man presenting with progressive dysphagia, cranial and limb muscle weakness, and severe dyspnea. Thoracic imaging revealed an anterior mediastinal mass suspected to be thymoma. The patient developed a myasthenic crisis requiring intubation and mechanical ventilation. Treatment included intravenous anticholinesterase, intravenous immunoglobulin, and thymectomy. Prompt radiological assessment and clinical diagnosis are crucial in managing such cases to prevent life-threatening respiratory complications.

Keywords: Thymoma, Myasthenic crisis, Paraneoplastic syndrome

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Introduction

The thymus is a gland that plays a vital role in the development of the adaptive immune system. Thymoma is a tumor originating from the epithelial cells of the thymus gland. At birth, the thymus measures approximately 5 mm in length, 4 mm in width, and 6 mm in thickness. Each lobe consists of multiple lobules separated by areolar tissue. The gland comprises two main regions: the cortex and the medulla. The cortex, located on the outer part of the gland, is composed of lymphocytes and reticular epithelial cells, which are associated with the medulla—the site of T-cell maturation. In the medulla, the reticular epithelial cells are more prominent, and the number of lymphocytes is significantly lower. The medulla is the primary site for the further differentiation of T cells. Thymoma is the most common anterior mediastinal tumor, accounting for approximately 20% of malignancies in the mediastinum. However, thymoma is a rare neoplasm when considered in the context of all malignancies, representing less than 0.5% of all cancer cases. Globally, the incidence of thymoma is about 0.15 per 100,000 population per year. There is no significant sex predilection, and the average age at diagnosis is between 40 and 60 years. Naturally, the thymus undergoes involution with age, resulting in a decrease in both size and function (Mira Itani, 2023; Ritesh Kumar, 2015).

Thymomas are associated with various autoimmune disorders. Approximately 30–40% of patients with myasthenia gravis are found to have thymomas. Alfred Blalock first identified the association between thymoma and myasthenia gravis in 1939. The 15-year survival rate is approximately 12.5% for invasive thymomas and 47% for non-invasive thymomas. Mortality related to thymoma is often due to complications such as cardiac tamponade or cardiorespiratory failure (Shawn P. Robinson; Hossein Akhondi, 2023).

Nilke et al. conducted a retrospective cohort study on 815 patients diagnosed with myasthenia gravis to identify independent risk factors for exacerbation and crisis. They found that the presence of thymoma and tyrosine kinase antibodies were independent predictors of myasthenic crisis (Nilke et al., 2022).

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The World Health Organization (WHO) classifies thymomas into five histological subtypes based on epithelial cell morphology: Type A, AB, B1, B2, and B3, as summarized in the table below

Table 1. Classification of thymoma according to WHO

Type	Histology Description
Type A	Medular thymoma
Type AB	Mixed thymoma
Type B1	Predominantly cortical thymoma
Type B2	Cortical thymoma
Type B3	Well-differentiated thymic carcinoma

Approximately 50% of patients with Type B2 thymomas present with myasthenia gravis (MG) symptoms, whereas Type A is the least frequently associated subtype (Kumar R, 2015).

The clinical manifestations of thymoma vary and are largely related to tumor size and local mass effect on adjacent structures, presenting with symptoms such as chest pain, cough, and phrenic nerve palsy. Some patients may exhibit signs of superior vena cava (SVC) syndrome. Pleural and pericardial effusions may also occur as a result of disease spread. Patients with thymoma often experience paraneoplastic syndromes, the most common of which is myasthenia gravis. MG is an autoimmune disorder in which the immune system targets nicotinic acetylcholine receptors at the neuromuscular junction (NMJ), resulting in impaired postsynaptic transmission. In thymoma-associated MG, studies have shown that the thymoma retains epitopes capable of cross-reactivity with skeletal muscle proteins, including the ryanodine receptor (RyR), titin, and acetylcholine receptors (AChR)—with the anti-AChR antibodies being most clinically relevant (Mira Itani, 2023). Symptoms include diplopia, ptosis, dysphagia, muscle weakness, and dyspnea. Thymectomy has been shown to alleviate severe MG symptoms (Shawn P. Robinson; Hossein Akhondi, 2023).

Another autoimmune manifestation is pure red cell aplasia (PRCA), characterized by non-proliferative erythroid precursors in the bone marrow. It occurs in 5%–15% of thymoma patients, more commonly in elderly women. Clinical features include recurrent infections, diarrhea, and lymphadenopathy. Unlike MG, thymectomy does not alleviate immunodeficiency in PRCA. Another syndrome, thymoma-associated multiorgan autoimmunity (TAMA), presents with skin rashes, chronic diarrhea, and elevated liver enzymes (Shawn P. Robinson, 2023).

Diagnosis of thymoma or thymic carcinoma begins with thoracic CT or MRI. Thymic carcinoma often presents with necrotic, cystic, or calcified areas. With contrast administration, thymomas typically appear as well-defined, smoothly contoured masses. CT imaging is useful for evaluating the tumor and its relationship with mediastinal structures, while MRI is superior in differentiating solid from cystic lesions. Management strategies for thymic tumors include chemoradiation, immunotherapy, tyrosine kinase inhibitors, and surgical resection (thymectomy). Kim et al. demonstrated a significant reduction in anti-AChR antibody titers following thymectomy (Kim et al., 2018).

The prognosis for thymoma-associated MG is generally favorable if treated promptly. The 5-year recurrence rate after complete resection ranges from 5% to 17%, depending on the thymoma subtype, with subtypes B2 and B3 being most frequently associated with recurrence (Anna De Rosa, 2021).

According to Nelke et al., poor prognosis was observed in patients of advanced age, those with high MGFA scores, or with reduced vital capacity on pulmonary function tests. Additional poor prognostic indicators included the need for intubation, prolonged ventilatory support, and infections triggering MG crises. There was no significant difference in outcomes between IVIG therapy, plasma exchange, or their combination (Nelke et al., 2022).

Cases and Operation Technique

A 40-year-old male presented to the Emergency Department of the West Nusa Tenggara Provincial General Hospital with complaints of shortness of breath and dysphagia, which had progressively worsened over the past three weeks. Initially, the patient was able to swallow solid foods such as rice, but later developed increasing difficulty with solids and could only tolerate liquids. There was no odynophagia. The patient also reported dysarthria, which gradually progressed to aphonia, along with a sensation of lower jaw weakness, particularly after prolonged speaking or chewing.

Over the past week, he developed progressive limb weakness, particularly in the lower extremities, making it difficult to walk without assistance. He required a cane or help from family members to rise from bed and ambulate. These symptoms improved with rest. The patient also experienced bilateral ptosis with difficulty opening his eyes, and reported diplopia when focusing on nearby objects.

He had previously been admitted for five days at a local hospital, where he was suspected of having myasthenia gravis. During that admission, a nasogastric tube was inserted, and he was administered pyridostigmine (Mestinon). His condition improved and he was discharged. However, three days after discharge, the nasogastric tube dislodged, resulting in the patient

being unable to take pyridostigmine. Subsequently, he developed progressive dyspnea, unrelated to body position and without wheezing or other specific triggers. Previous symptoms also began to recur and worsen. He denied fever, cough, coryza, diarrhea, nausea, or vomiting. He was brought to the provincial hospital where, in the Emergency Department, he experienced desaturation and a decline in consciousness, necessitating intubation and mechanical ventilation. A chest X-ray and contrast-enhanced CT scan were performed before transfer to the Intensive Care Unit (ICU). Imaging revealed an anterior mediastinal mass, raising suspicion of thymoma.

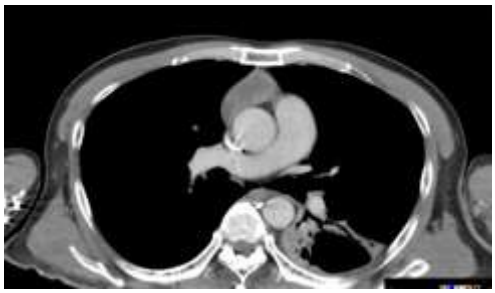

Figure 1. A well-defined mass measuring 4x4x2 cm was identified in the anterior mediastinum, which is indicative of thymoma.

The patient was treated with intravenous anticholinesterase agents for 24 hours, followed by oral pyridostigmine and corticosteroids (IV and oral). On the fifth day of ICU care, he underwent thymectomy and tracheostomy. Intraoperatively, a 6×4×4 cm thymic mass was resected. Histopathological examination confirmed a Type B3 thymoma. Postoperative treatment included intravenous immunoglobulin (IVIG), which led to significant clinical improvement.

Discussion

Thymoma is frequently associated with paraneoplastic syndromes, with studies indicating that 50–70% of patients exhibit such manifestations (Zhao et al., 2020). Among these, myasthenia gravis (MG) is the most common, observed in 30–40% of thymoma cases (Padda et al., 2018). Thymomas are more often discovered in patients with MG than in non-MG individuals, as the symptoms of MG typically precede mediastinal imaging (Chen et al., 2020).

In the present case, the diagnosis of thymoma was made after the patient presented with myasthenic crisis. MG affects the neuromuscular junction, and in approximately 85% of cases, it is associated with autoantibodies targeting the acetylcholine receptor (AChR) (Nabe et al., 2021). The underlying mechanism involves a humoral immune response to epitopes expressed by thymoma cells, which mimic those found at the neuromuscular junction. Neoplastic thymic epithelial cells, surrounded by T lymphocytes, may express cross-reactive antigens that trigger the production of AChR antibodies (Melzer et al., 2016).

Nearly all patients with thymoma-associated MG test positive for anti-AChR antibodies, which bind to the postsynaptic endplate and impair neuromuscular transmission, resulting in muscle weakness (Chen et al., 2020). In this patient, typical MG symptoms included progressive dysphagia (initially tolerating solids, later only liquids), dysphonia, jaw weakness, ptosis, and diplopia (Melzer et al., 2016). Proximal limb weakness and gait disturbance were also present, which are commonly reported (Padda et al., 2018).

The patient progressed to a myasthenic crisis, a life-threatening condition characterized by severe respiratory distress, desaturation, and the need for mechanical ventilation (Daum et al., 2021). To investigate the underlying cause, a chest X-ray was performed—often insufficient to detect anterior mediastinal masses—followed by contrast-enhanced thoracic CT scan, which revealed a 4×4×2 cm mass in the anterior mediastinum (Klug et al., 2024).

The gold standard for diagnosing thymoma is histopathological examination. In this case, the mass was confirmed as a Type B3 thymoma (Erşen et al., 2018). To confirm MG, measurement of serum AChR antibody titers is standard, although this test was unavailable at the facility (Narayanaswami et al., 2020).

Surgical resection (thymectomy) remains the cornerstone of treatment. Both transsternal and video-assisted thoracoscopic surgery (VATS) approaches yield similar clinical outcomes and allow for proper staging (Erşen et al., 2018). For advanced-stage tumors with pleural or pericardial invasion, adjuvant radiotherapy or chemotherapy may be indicated (Narayanaswami et al., 2020; Robinson & Akhondi, 2021). In this patient, an extended thymectomy was performed on day 5 of ICU care, with resection of a 6×4 cm mass.

The standard therapy for myasthenic crisis includes plasmapheresis or intravenous immunoglobulin (IVIG) prior to surgery to rapidly eliminate pathogenic antibodies (Daum et al., 2021). In settings where these options are unavailable, immunosuppressive agents such as corticosteroids, azathioprine, cyclosporine, tacrolimus, cyclophosphamide, methotrexate, mycophenolate mofetil, or rituximab may be utilized (Narayanaswami et al., 2020).

In this case, high-dose corticosteroids (methylprednisolone 125 mg/day) were administered while awaiting IVIG availability. Subsequently, intravenous immunoglobulin (IVIG, Gammaras) was

initiated on day 9 of hospitalization, administered over five consecutive days, consistent with recommendations for myasthenic crisis management (Daum et al., 2021). Treatment also included intravenous acetylcholinesterase inhibitors, specifically neostigmine, followed by oral pyridostigmine (Mestinon) for maintenance therapy (Thomsen & Andersen, 2020).

The prognosis for thymoma-associated myasthenia gravis is generally favorable when prompt diagnosis and treatment are achieved. This patient demonstrated a positive clinical response following combined medical and surgical interventions and is scheduled for regular outpatient follow-up to monitor for recurrence or complications (Thomsen & Andersen, 2020).

Conclusion

The initial manifestation of myasthenia gravis often begins with mild symptoms, such as extraocular muscle weakness. Myasthenia gravis frequently presents as a paraneoplastic syndrome associated with thymoma. The management of thymoma requires a multimodal approach and close coordination among thoracic surgery, radiology, anesthesiology, pathology, oncology, and other relevant specialties depending on the complications encountered. The use of acetylcholinesterase inhibitors, intravenous immunoglobulin (IVIG), and plasmapheresis plays a key role in the treatment of thymoma-associated myasthenia gravis. In cases of myasthenic crisis leading to respiratory failure, immediate intubation and mechanical ventilation are life-saving measures. Thymectomy serves both diagnostic and therapeutic purposes. The prognosis depends on factors including the tumor stage, thymoma subtype, the clinical condition at presentation, and the timeliness of intervention.

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