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Case Report of Subclinical Myasthenia Gravis Associated with Castleman Disease

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 31-year-old
Final Diagnosis: Castleman's disease
Symptoms: Exertional dyspnea
Medication: —
Clinical Procedure: Thymectomy
Specialty: Surgery

Objective: Rare co-existance of disease or pathology

Background: Castleman disease is a lymphoproliferative disorder of uncertain origin that is most commonly found in the mediastinum. It is classified based on pathological features into hyaline-vascular, plasma cell, and mixed variants. An association between Castleman disease and myasthenia gravis very rarely has been reported, except of the hyaline variant type, because it is associated with various clinical abnormalities. Castleman disease typically is diagnosed based on an incidental radiology finding of enlarged local lymph nodes, which result in compression symptoms.

Case Report: Here, we report the case of a 31-year-old Saudi woman who presented with a 2-year history of exertional dyspnea associated with mouth and eye ulcers. She had no other associated symptoms, such as muscular weakness, rapid fatigue, or drooping eyelids. She was referred to our institution for further investigation and management and was diagnosed with myasthenia gravis after testing positive for acetylcholinesterase antibodies. A computed tomography (CT) scan then was performed, which showed an enlarged thymus gland. The patient eventually underwent a bilateral thoracoscopic thymectomy.

Conclusions: The aim of the present report was to add to the literature by presenting a rare case of asymptomatic subclinical myasthenia gravis associated with Castleman disease. The findings underscore the importance of considering Castleman disease in an asymptomatic patient who has a mediastinal mass and avoiding an unusual intraoperative occurrence such as massive bleeding by performing a preoperative biopsy and angiography.

Keywords: Giant Lymph Node Hyperplasia • Myasthenia Gravis • Thymectomy • Thymoma

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Background

Castleman disease was first described in 1956 by Dr. Benjamin Castleman as a lymphoproliferative disorder of uncertain origin. It is most commonly found in the mediastinum [1]. Enlargement of localized lymph nodes associated with Castleman disease is usually asymptomatic or results in nonspecific compression symptoms, such as cough, dyspnea, and chest and back pain [1,2]. Castleman disease is classified based on either pathology or clinical features. Pathologically, it is divided into hyaline-vascular, plasma cell, and mixed variants; clinically, the presentation can be either unicentric or multicentric, depending on the number and region of lymph nodes affected [1-3]. The hyaline-vascular variant is the type that is commonly associated with myasthenia gravis [3]. It is associated with various clinical abnormalities, including HIV, Hodgkin and non-Hodgkin lymphoma, Kaposi sarcoma, paraneoplastic pemphigus, and polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome [1,2]. Castleman disease typically is diagnosed based on incidental radiological findings related to enlargement of lymph nodes around the thymus gland, which results in compression symptoms [2]. Lymphoproliferative disorders are considered inflammatory conditions because they reflect high levels of both interleukin-6 and vascular endothelial growth factor [4]. Myasthenic crisis is one of the most serious complications of surgery [1].

Case Report

A 31-year-old Saudi woman presented with a 2-year history of exertional dyspnea associated with mouth and eye ulcers. She had no other associated symptoms, such as muscular weakness, rapid fatigue, or drooping eyelids. She was initially diagnosed with Bechet disease and was started on immunosuppressive therapy, with no improvement. The patient then was referred to our institution for further investigation and management. She was diagnosed with myasthenia gravis after testing positive for acetylcholinesterase antibodies. A computed tomography (CT) scan was performed, which showed an enlarged thymus gland, for which she subsequently underwent a bilateral thoracoscopic thymectomy. The patient's history was remarkable for an abdominal desmoid tumor 4 years previously, but she was otherwise healthy and medically stable. She did not smoke nor was she exposed to second-hand smoke and she had no history of drug abuse. Her travel history was insignificant and the rest of her history was unremarkable. Results of physical examination were all within normal limits.

Further evaluation with chest positron emission tomography and CT scans showed a large anterior mediastinal mass filled with collaterals and a maximum standardized uptake value of 2.9, which corresponded with a 10×4×10.4-cm mediastinal mass on diagnostic CT; no other abnormalities were detected (**Figure 1A, 1B**). The patient was admitted electively for a bilateral thoracoscopic thymectomy. The procedure was started on the left side but was complicated by blood loss from massive blood vessels and collaterals attached to the thymus, which required an intraoperative transfusion. The procedure was eventually converted to a left anterolateral thoracotomy and the patient was transferred to the Intensive Care Unit for close observation and monitoring. On the sixth day after surgery, she was discharged on antibiotics and analgesics.

The pathology report showed that the 11.5×10×4-cm specimen, which weighed 219 g, consisted of a homogeneous, soft, white mass with a small rim of fibroadipose tissue. Microscopically, the sections showed lymphoid follicles with small germinal

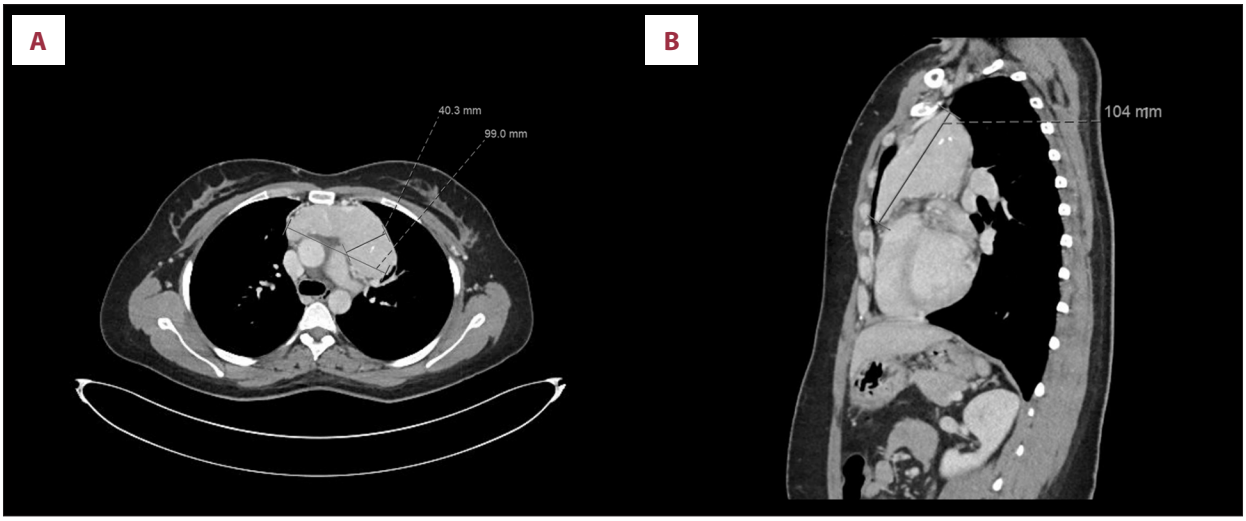

Figure 1. Computed tomography scans of an anterior mediastinal mass that measured 10×4×10.4 cm. (**A**) Coronal view. (**B**) Sagittal view.

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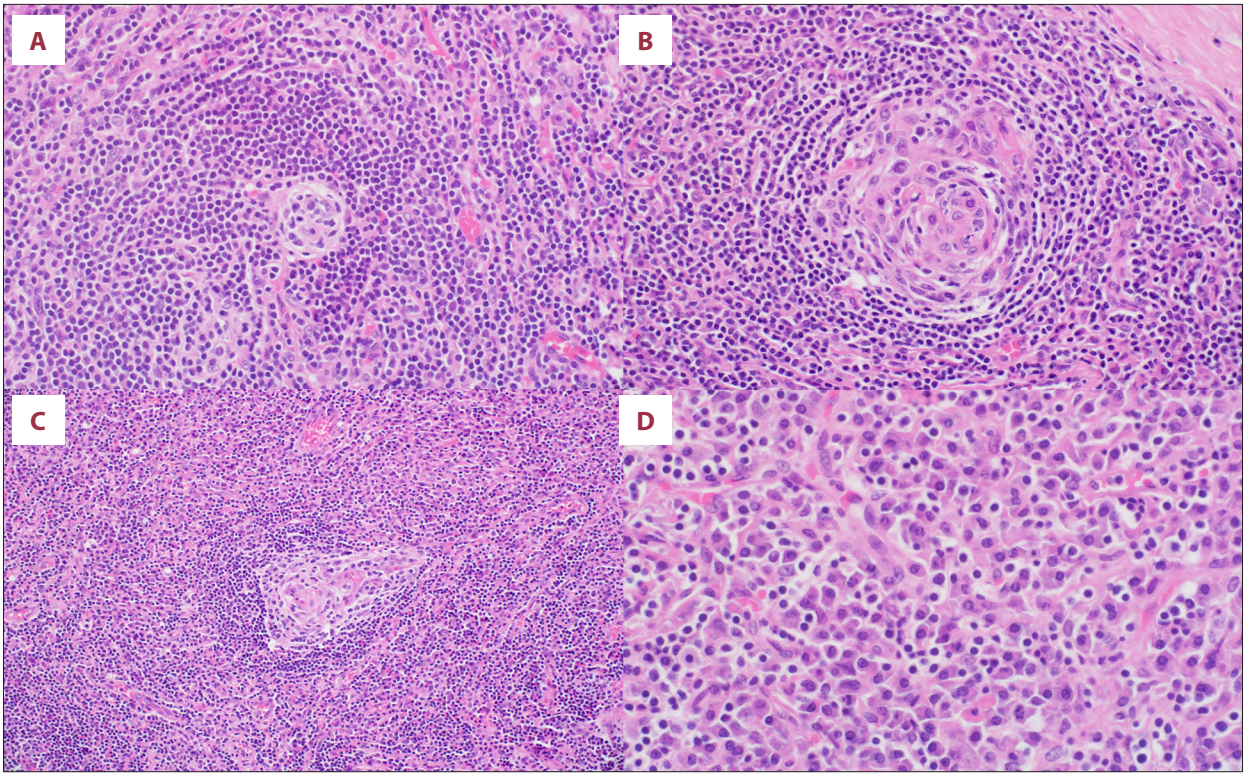

Figure 2. Hematoxylin and eosin-stained biopsy specimens. (**A**) Lymphoid follicle with small germinal center that is lymphocyte-depleted. Hyaline-vascular variant Castleman disease. Hyaline deposits are present within the germinal centers. (**B**) The germinal center of this follicle is partially lymphocyte-depleted and some of the follicular dendritic cells are mildly atypical. The follicle is surrounded by a mantle zone of concentric rings of small lymphocytes ("onion-skin" sign). (**C**) The follicle is radially penetrated by a prominent blood vessel ("lollipop" sign). (**D**) In the interfollicular region, blood vessels are lined by plump endothelial cells and are associated with cytologically mature plasma cells and small lymphocytes.

centers that were lymphocyte-depleted and contained hyaline deposits. An onion-skin pattern of regressed follicles with mildly atypical follicular dendritic cells and mantle zone showing concentric rings was noted, which was associated with sclerotic blood vessels that radially penetrated the germinal centers forming the HV lesions (lollipop lesion). Interfollicular areas showed blood vessels lined with plump endothelial cells, which were associated with cytologically mature plasma cells, and small lymphocytes. In one section, the residual thymus gland was seen, with fat infiltration and thymic follicular hyperplasia. The overall findings were in keeping with hyaline-vascular or mixed-type Castleman disease, which confirmed the clinical diagnosis (**Figure 2A-2D**).

Discussion

Castleman disease is a benign lymphoproliferative disorder of uncertain origin that most commonly is found in the mediastinum [1]. It is classified based on either pathology or clinical features. Pathologically, it is divided into hyaline-vascular, plasma cell, and mixed variants; the clinical presentation is unicentric or multicentric [1-3]. The hyaline-vascular variant is the type of Castleman disease that is commonly associated with myasthenia gravis [3]. The association between Castleman disease and myasthenia gravis has been very rarely reported, except for the hyaline variant type, because that is associated with various clinical abnormalities [1,2].

Development of Castleman disease in patients with myasthenia gravis has been intensely studied but the association remains incompletely defined. Very few case reports exist in the literature. Between 2003 and 2013, 4 cases were reported discussing the association between Castleman disease and myasthenia gravis [2-5]. In 2014, another case report was published that discussed the outcome of and prognosis for Castleman disease in association with myasthenia gravis and paraneoplastic pemphigus (PNP); the conclusion was that the association with PNP resulted in a poor prognosis [6].

Between 2010 and 2020, 2 cases of Castleman disease were documented, one of which was associated with myasthenia gravis [7,8]. That patient underwent resection of a mediastinal tumor, which was complicated by a follicular dendritic cell

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sarcoma. Treatment with an anticholinesterase agent and corticosteroids was successful. The second report showed that the presence of Castleman disease in patients with myasthenia gravis increases the risk of developing a myasthenic crisis, which is considered a serious postoperative complication [7,8].

Conclusions

The co-occurrence of Castleman disease and myasthenia gravis is rare [2]. The aim of the present case report was to add to the literature by reporting a rare case of asymptomatic subclinical myasthenia gravis associated with Castleman disease. It underscores the importance of considering Castleman disease in patients who are asymptomatic and has an unusual intraoperative finding in the differential diagnosis. The authors suggest performing a biopsy to rule out lymphoma or Castleman disease and angiography to avoid massive intraoperative bleeding in patients who have unusual thymomas and evidence of arterial collaterals on CT scan.

Acknowledgments

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Conflict of Interest

None.

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