Thymoma exhibiting spontaneous regression with developing myasthenia gravis: A case report

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Abstract
Spontaneous regression (SR) of thymoma is rare. A 44-year-old man with right chest pain underwent computed tomography (CT), which showed an 11.0 cm mass in the anterior mediastinum and right pleural effusion. He refused surgery and was sent home without medication and additional treatment. One year later, the mass had regressed to 5.5 cm, and the right pleural effusion had disappeared. He was then lost to follow-up. Four years after the initial visit, he presented with diplopia and fatigue. An increase in anti-acetylcholine receptor antibody levels led to myasthenia gravis (MG) diagnosis. CT revealed a regressed mediastinal mass (3.0 cm). After extended thymectomy, histologic analysis confirmed a thymoma type B2, Masaoka stage IIa. The SR was due to intratumoral infarction. This report is the first to describe MG developing during SR. Anterior mediastinal tumors undergoing SR should be differentiated from thymomas and MG perioperative development should be considered.

Keywords
mediastinum, myasthenia gravis, neoplasm regression, spontaneous, pleural effusion, thymoma

INTRODUCTION
Thymoma is the most common neoplasm of the anterior mediastinum, accounting for 0.2%–1.5% of malignant tumors. Thymomas rarely spontaneously regress. Myasthenia gravis (MG), a common autoimmune disease, accounts for 20–30% of all thymomas and occurs as a paraneoplastic disorder. We report a rare case of a thymoma undergoing spontaneous regression (SR) due to intratumoral infarction with MG.

CASE REPORT
A 44-year-old man without surgery and trauma history had sudden right chest pain. Chest computed tomography (CT) revealed an 11.0 × 10.0 × 5.2 cm anterior mediastinal mass and right pleural effusion (Figure 1a). A hyperintense multilocular cystic component was evident on T2-weighted magnetic resonance imaging (Figure 2a). A thymoma was suspected, and a CT-guided needle biopsy was performed. Only fibrous connective tissue and adipose tissue were obtained. The patient’s anti-acetylcholine-receptor (anti-AchR) antibody level was normal, but C-reactive protein was elevated (2.1 mg/dl). He refused surgery and was sent home without any medication. One year later, the mass had regressed to 5.5 cm, and the right pleural effusion had disappeared. He was then lost to follow-up. Four years after the initial visit, he presented with diplopia and fatigue. A significant increase in his anti-acetylcholine receptor antibody levels led to myasthenia gravis (MG) diagnosis. CT revealed a regressed mediastinal mass (3.0 cm). After extended thymectomy, histologic analysis confirmed a thymoma type B2, Masaoka stage IIa. The SR was due to intratumoral infarction. This report is the first to describe MG developing during SR. Anterior mediastinal tumors undergoing SR should be differentiated from thymomas and MG perioperative development should be considered.
superior vena cava were removed easily. Wedge resection of the right middle lobe of the lung was performed to remove its attachment to the mediastinal tumor. The encapsulated tumor had a white cross-sectional outer surface and a well-circumscribed yellowish-white inner region (Figure 3a). Pathology examination revealed a central yellowish-white area with necrotic features, cholesterol clefts, and hematoidin deposits (Figure 3b, c) caused by ischemic infarction. Polygonal epithelial cells and abundant lymphocytes indicated a thymoma type B2 (Figure 3d). Partial microscopic invasion of the thymus was observed, with no pulmonary invasion. The diagnosis was thymoma, Masaoka stage IIa. The patient had an unremarkable postoperative course without tumor or MG recurrence for 6 months.

DISCUSSION

Our report is the first MG development in a patient with a thymoma undergoing SR. Neoplasm SR has been associated with ischemic infarction and thromboembolism caused by sclerosing arteriopathy or occlusive disorders. Most thymomas undergoing SR are encapsulated tumors with intratumoral necrotic features. Ischemic infarction induces an inflammatory reaction presenting as pleural effusion, fever, and chest pain. Here, thromboembolism was not observed, hence vascular occlusion caused by the rapid tumor enlargement resulted in ischemic infarction and inflammation. A relationship between multilocular cystic thymoma and inflammation has been reported. The multilocular cystic component observed during the patient’s initial visit was consistent with that report.

Thymoma SR is commonly reported in Japanese men aged 30–50 years. The predominant histologic subtypes are B2 and B3. Despite an aggressive subtype and large tumor size (median 65 mm, range 30–120 mm), thymomas exhibiting SR are diagnosed as early-stage tumors, specifically, Masaoka stage I or II. Because such thymomas are surrounded by a thick capsule, tissue invasion does not occur. The tumor was mostly encapsulated; only the thymus microscopic invasion was found.

Concomitant development of thymoma and MG has been observed in 30- to 50-year-old men, common subtypes being B2 and B3. The clinical presentation resembles a thymoma exhibiting SR. No previous reports have
described SR of a thymoma accompanied by MG. However, a thymoma exhibiting SR with elevated anti-AchR antibody was reported. The thymus pathology examination was unremarkable. Of thymomas with MG, 65–90% have germinal centers, likely related to MG development in the thymus. Although the relationship between SR and MG development in thymomas remains unclear, anterior mediastinal tumors undergoing SR should be differentiated from thymomas. Moreover, MG perioperative development should be evaluated.

In our case, marked tumor regression (97.2%) was confirmed due to 6.0 cm cystic component disappearance. The mechanism behind SR of thymic cysts reportedly involves the cystic wall breakdown due to inflammation and necrosis or absorption of intracystic components. Oral glucocorticoids sometimes induced radical thymoma regression; however, our patient did not take any medication during regression.

Our case also demonstrates pleural effusion resolution. Reports have described inflammation associated with intratumoral infarction-induced pleural effusion in thymomas undergoing SR. Pleural effusion was initially attributed to thymoma dissemination. However, no scars were evident, suggesting parietal and visceral pleura dissemination during surgery. The pleural effusion was probably caused by inflammation.

Solitary anterior mediastinal tumors suspected to be thymomas are resected for immediate diagnosis and treatment. The follow-up period for SR of a thymoma is ~1 month. This case demonstrates thymoma SR for 4 years without treatment.

Anterior mediastinal tumors undergoing SR should be differentiated from thymomas and the perioperative development of MG should be considered.

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CONFLICT OF INTEREST
The authors have no conflict of interest.

AUTHOR’S CONTRIBUTIONS
All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Conceptualization, K.N. and M.S.; data curation, K.N., A.N., R.S., T.S., and T.H.; visualization, K.N. and M.S.; writing – original draft, K.N. and M.S.; project administration, M.S.; writing – review and editing, M.S., R.S., T.S., M.H., T.H., and H.H; supervision, H.H.

PATIENT CONSENT
Informed consent was obtained from the patients for this publication.

DATA AVAILABILITY STATEMENT
Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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FIGURE 3 Pathology findings. (a) The tumor is encapsulated, with a white cut surface and a well-circumscribed yellowish-white internal area. (b) A low-power view: the tumor contains a broad necrotic area in the center (hematoxylin–eosin staining). (c) A high-power view: cholesterol clefts and hematoidin deposits are present in necrotic areas (hematoxylin–eosin staining). (d) A high-power view: polygonal epithelial cells and abundant lymphocytes suggest thymoma type B2 (hematoxylin–eosin staining).
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