


CASE REPORT

Amyloid deposition in thymic extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue in a patient with myasthenia gravis: A case report

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B-cell; lymphoma; marginal zone; myasthenia gravis; thymus neoplasm.

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Thoracic Cancer **11** (2020) 781–784**Abstract**

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) in the thymus is a rare disease. Furthermore, amyloid deposition in thymic MALT lymphoma has not been previously described. Here, we report a case of a 35-year-old man with thymic MALT lymphoma with amyloid deposition and myasthenia gravis. Chest computed tomography revealed an anterior mediastinal mass with internal cystic component and extensive calcification. Total thymectomy was performed and histopathologic findings were compatible with a diffuse amyloid deposition in extranodal marginal zone MALT lymphoma. The results indicate that thymic MALT lymphoma should be considered as a possible diagnosis in patients with a solid and cystic thymic mass and autoimmune disease, including myasthenia gravis.

Introduction

Thymic extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) is a rare disease first described by Isaacson *et al.*¹ Clinically, thymic MALT lymphoma is associated with autoimmune diseases and chronic inflammation, in particular Sjögren's syndrome.² Amyloid deposition in MALT lymphoma is unusual and few cases have been reported.^{3–6} However, there have been no reports on amyloid deposition in thymic MALT lymphoma. This report describes a case of thymic MALT lymphoma with amyloid deposition in a patient with myasthenia gravis. An unusual manifestation of extensive calcification of an anterior mediastinal mass on computed tomography (CT) can lead to difficulties in a differential diagnosis.

Case report

A 35-year-old man presented to our clinic with dyspnea on exertion for two years with no previous medical history.

His serum acetylcholine receptor (AChR) antibody level was initially measured at 7.83 nmol/L (normal, 0.0–0.5 nmol/L); therefore, he was diagnosed with myasthenia gravis. There were no symptoms of Sjögren's syndrome. Apart from the AChR antibody test, no other laboratory tests for autoantibodies were performed.

The patient's initial chest radiograph revealed a bulging countoured right mediastinal mass (Fig 1). Chest CT demonstrated a 7.4 cm solid mass at the anterior mediastinum with internal dense calcification. The mass showed mild enhancement of approximately 10 HUs and contained low-density lesions, thought to have a necrotic or cystic component. There was no evidence of invasion into adjacent structures (Fig 2). Based on the clinical diagnosis of myasthenia gravis, the anterior mediastinal mass was considered to be a thymoma, and total thymectomy was subsequently performed. The specimen was poorly demarcated and firm and the longest dimension was 7.5 cm. The cut surface was hard, whitish-yellow, and calcified (Fig 3a). Histopathologic examination showed that numerous

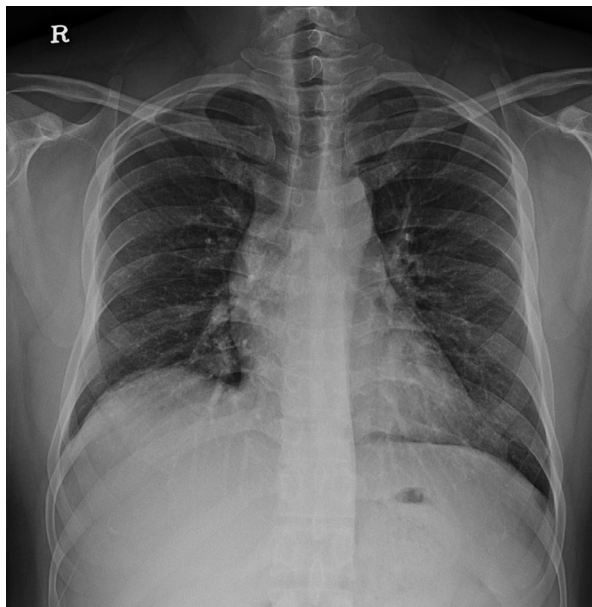


Figure 1 Chest radiograph showing a bulging contoured mediastinal mass with internal high density, suggesting calcification.

lymphoid cells diffusely infiltrated the thymic tissue with expansion of marginal zones and centrocyte-like cells invading Hassall's corpuscles, forming lymphoepithelial

lesions (Fig 3b). The tumor cells were immunoreactive for CD 20 (Fig 3c). Congo red stain confirmed amyloid deposition (Fig 3d). The tumor cells also showed cytoplasmic staining for kappa light chain (Fig 3e), but were negative for lambda light chain (Fig 3f). The pathologic diagnosis was compatible with thymic marginal zone MALT lymphoma with extensive amyloid deposition. Positron emission tomography/computed tomography (PET/CT) scan was performed for clinical staging and there was no hypermetabolic lesion on other sites of the body. His clinical stage was IE using an adaptation of the Ann Arbor staging system.⁷ After thymectomy, the patient's symptoms improved but the level of AChR antibody had not decreased following laboratory tests performed two months after surgery.

Discussion

Marginal zone MALT lymphoma is a mature B-cell neoplasm that occurs in various extranodal tissues. Thymic MALT lymphoma is very rare,^{2,8,9} although it is more common in Asian populations.^{2,8} Most patients with thymic MALT lymphoma also have autoimmune disorders, most commonly Sjögren's syndrome.⁸

A thymic mass with internal cystic components is a well known imaging finding of thymic MALT lymphoma.^{9,10}



Figure 2 (a) A 7.4 cm soft tissue mass was visible in the anterior mediastinum on computed tomography (CT). There was dense calcification within the mass. The mass abutted the pericardium, but there was no evidence of definite invasion to adjacent structures (a–b). On contrast-enhanced CT (c–d), the mass showed mild enhancement. There was a focal low-density lesion (arrow) within the mass, suggesting necrosis or cystic component.

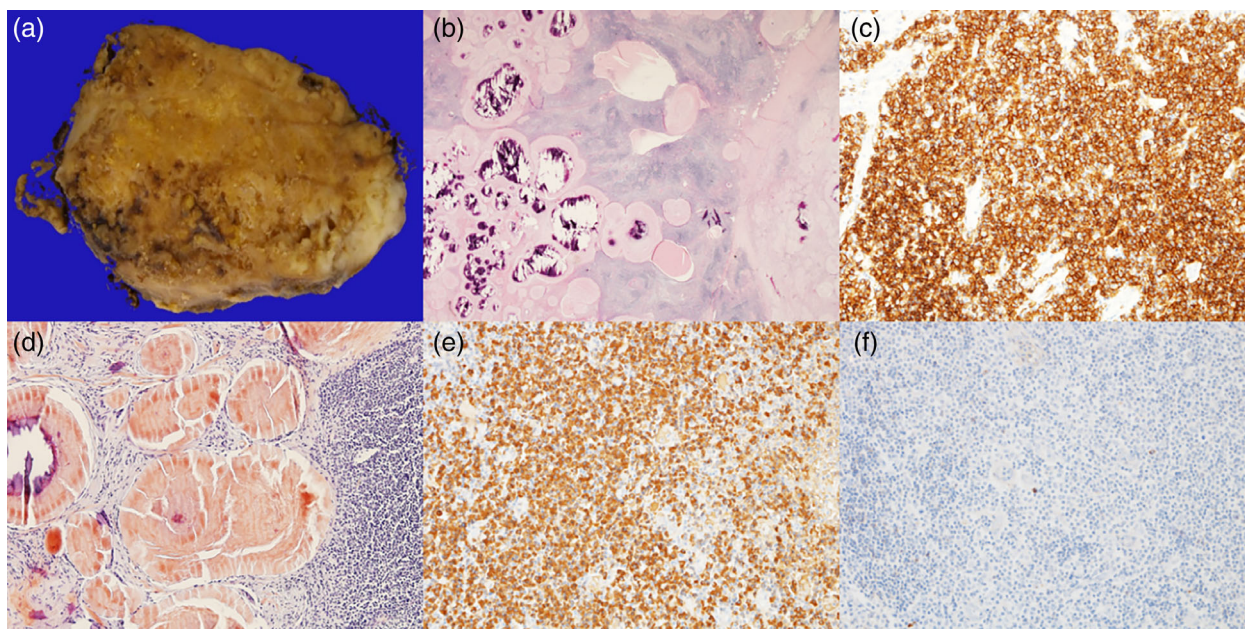


Figure 3 (a) The resected thymic mass measured 7.5 cm at its longest dimension. The cut surface was hard, whitish-yellow and diffusely calcified. Centrocyte-like cells invaded Hassall's corpuscles with expansion of mucosa-associated lymphoid tissue (MALT). (b) There were diffuse amyloid depositions with calcification (hematoxylin and eosin, $\times 12.5$). (c) The cells were positive for CD20. (d) The amyloid was positive for Congo red stain. (e) Plasma cells show were positive for kappa light chain, (f) but negative for lambda light chain.

An intratumoral cyst may be related to the tendency for cystic transformation of medullary duct-epithelium-derived structures (including Hassall's corpuscles) when the tumor grows in the thymus.¹¹ Shimizu *et al.* reported that thymic MALT lymphoma should be considered as a differential diagnosis in Asian patients who have a cystic thymic mass and an autoimmune disease.² In our case, there was a suspicious cystic component within the mass. When there is an anterior mediastinal mass with a cystic component in patients with autoimmune diseases other than Sjögren's syndrome, thymic MALT lymphoma should be suspected.

Approximately 2%–4% of cases of amyloid deposition in tissue arise in the setting of non-Hodgkin B-cell lymphoma, especially in lymphoplasmacytic lymphoma.^{12–14} Amyloid deposition in MALT lymphoma is rare,^{3,5} and most reported cases of MALT lymphoma with amyloid deposits showed indolent clinical courses.³ Amyloid deposition in MALT lymphoma is associated with peritumoral amyloid deposits, single organ involvement, and low or undetectable levels of circulating IgM monoclonal protein.¹⁵ It is thought that immunoglobulin light chains, produced by neoplastic plasmacytoid cells, are not sufficient to deposit amyloid in low-grade MALT lymphoma patients.¹⁵ Cases of MALT lymphoma with amyloid deposition have been reported in organs such as the orbit,³ lung,⁴ soft tissue⁵ and breast.⁶ However, there has been no report of MALT lymphoma with amyloid deposition in the thymus. In our case, extensive amyloid deposits showed

extensive calcification on CT images, making differential diagnosis difficult.

Thymic MALT lymphoma in a patient with myasthenia gravis patient has not been previously reported. Parrens *et al.* reviewed slides of 14 patients (including 12 patients with myasthenia gravis) originally diagnosed with lymphofollicular thymic hyperplasia and found three patients with early MALT lymphoma lesions. One of the three patients with early thymic MALT lymphoma had myasthenia gravis.¹⁶ This implies the potential for underdiagnosed MALT lymphoma in patients with myasthenia gravis. In our case, the level of AChR antibody did not decrease within two months after thymectomy. AChR antibody titers decrease slowly over time,¹⁷ and they do not always fall after thymectomy.¹⁸ Therefore, it is not clear if there is a true association between thymic MALT lymphoma and myasthenia gravis and further research on the relationship between these diseases is necessary.

In summary, thymic MALT lymphoma is a rare disease. Here, for the first time, we report a case of extensive amyloid deposition in thymic MALT lymphoma in a patient with myasthenia gravis. Based on the observation in this case, we emphasize the importance of considering thymic MALT lymphoma as one of the possible diagnoses in patients with a solid and cystic thymic mass and autoimmune disease, including myasthenia gravis.

References

- 1 Isaacson P, Wright DH. Malignant lymphoma of mucosa-associated lymphoid tissue. A distinctive type of B-cell lymphoma. *Cancer* 1983; **52** (8): 1410–6.
- 2 Shimizu K, Yoshida J, Kakegawa S *et al.* Primary thymic mucosa-associated lymphoid tissue lymphoma: Diagnostic tips. *J Thorac Oncol* 2010; **5** (1): 117–21.
- 3 Zhang Q, Pocrnich C, Kurian A *et al.* Amyloid deposition in extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue: A clinicopathologic study of 5 cases. *Pathol Res Pract* 2016; **212** (3): 185–9.
- 4 Nakamura N, Yamada G, Itoh T *et al.* Pulmonary MALT lymphoma with amyloid production in a patient with primary Sjogren's syndrome. *Intern Med* 2002; **41** (4): 309–11.
- 5 Ryan RJ, Sloan JM, Collins AB *et al.* Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue with amyloid deposition: A clinicopathologic case series. *Am J Clin Pathol* 2012; **137** (1): 51–64.
- 6 Kambouchner M, Godmer P, Guillevin L, Raphael M, Droz D, Martin A. Low grade marginal zone B cell lymphoma of the breast associated with localised amyloidosis and corpora amylacea in a woman with long standing primary Sjogren's syndrome. *J Clin Pathol* 2003; **56** (1): 74–7.
- 7 Naeim F, Rao P, Song S, Phan R. *Atlas of Hematopathology*, 2nd edn. Academic Press, Massachusetts 2018.
- 8 Inagaki H, Chan JK, Ng JW *et al.* Primary thymic extranodal marginal-zone B-cell lymphoma of mucosa-associated lymphoid tissue type exhibits distinctive clinicopathological and molecular features. *Am J Pathol* 2002; **160** (4): 1435–43.
- 9 Kang LY, Ho SP, Chou YP. Primary thymic mucosa-associated lymphoid tissue lymphoma with multiple thin walled lung cysts: Case report and literature review. *Chin J Cancer Res* 2013; **25** (3): 354–7.
- 10 Yi JG, Kim DH, Choi CS. Malignant lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) arising in the thymus: Radiologic findings. *AJR Am J Roentgenol* 1998; **171** (3): 899–900.
- 11 Chan JKC. *Diagnostic Histopathology of Tumors*, 2nd edn. Churchill Livingstone, London 2000; 1306–1307.
- 12 Gertz MA, Kyle RA, Noel P. Primary systemic amyloidosis: A rare complication of immunoglobulin M monoclonal gammopathies and Waldenstrom's macroglobulinemia. *J Clin Oncol* 1993; **11** (5): 914–20.
- 13 Cohen AD, Zhou P, Xiao Q *et al.* Systemic AL amyloidosis due to non-Hodgkin's lymphoma: An unusual clinicopathologic association. *Br J Haematol* 2004; **124** (3): 309–14.
- 14 Sanchorawala V, Blanchard E, Seldin DC, O'Hara C, Skinner M, Wright DG. AL amyloidosis associated with B-cell lymphoproliferative disorders: Frequency and treatment outcomes. *Am J Hematol* 2006; **81** (9): 692–5.
- 15 Telio D, Bailey D, Chen C, Crump M, Reece D, Kukreti V. Two distinct syndromes of lymphoma-associated AL amyloidosis: A case series and review of the literature. *Am J Hematol* 2010; **85** (10): 805–8.
- 16 Parrens M, Dubus P, Danjoux M *et al.* Mucosa-associated lymphoid tissue of the thymus hyperplasia vs. lymphoma. *Am J Clin Pathol* 2002; **117** (1): 51–6.
- 17 Okumura M, Ohta M, Takeuchi Y *et al.* The immunologic role of thymectomy in the treatment of myasthenia gravis: Implication of thymus-associated B-lymphocyte subset in reduction of the anti-acetylcholine receptor antibody titer. *J Thorac Cardiovasc Surg* 2003; **126** (6): 1922–8.
- 18 Fujii Y, Monden Y, Hashimoto J, Nakahara K, Kawashima Y. Acetylcholine receptor antibody-producing cells in thymus and lymph nodes in myasthenia gravis. *Clin Immunol Immunopathol* 1985; **34** (1): 141–6.