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Primary Extranodal Marginal Zone B-cell Lymphoma of Mucosa-Associated Lymphoid Tissue-type in the Thymus of a Patient with Sjögren's Syndrome and Rheumatoid Arthritis

Primary thymic marginal zone B-cell lymphoma (MZBL) of mucosa-associated lymphoid tissue (MALT)-type is a very rare disease with distinct clinicopathologic features. I herein report a rare case of primary thymic MZBL of MALT-type arising in the thymus in a patient with Sjögren's syndrome and rheumatoid arthritis. A mediastinal mass was detected by computerized tomography in a 43-yr-old Korean woman with a history of Sjögren's syndrome and rheumatoid arthritis and the thymus was resected through median sternotomy. The solid and nodular tumor (7 × 6 × 3 cm) was confined in the thymus. Histologically, the lymphoid infiltrate comprised monotonous centrocyte-like cells with monocytoid cells, small lymphocytes, and plasma cells. Prominent lymphoepithelial lesions were formed by centrocyte-like cells infiltrating the Hassall's corpuscles. Immunohistochemically, the tumor cells were positive for CD20, CD79a, and bcl-2 and negative for CD3, CD5, CD10, CD23, and bcl-6. IgA and kappa light chain restriction were also found in plasma cells in the tumor. Sjögren's syndrome and rheumatoid arthritis are known to be associated with MALT lymphoma and were considered to play an important role in the development of malignant lymphoma in this patient.

Key Words : *Lymphoma, B-cell; Lymphoma Mucosa-Associated Lymphoid Tissue; Sjögren's Syndrome; Arthritis; Rheumatoid; Thymus Neoplasms*

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INTRODUCTION

Extranodal lymphoma of mucosa-associated lymphoid tissue (MALT) was first described by Isaacson and Wright in 1983 (1) and was recently reclassified as "extranodal marginal zone B-cell lymphoma (MZBL) of MALT-type" according to the REAL (2) and WHO classifications (3). Primary MZBLs of MALT-type have been described in a variety of sites, including gastrointestinal tract (1), thyroid gland (4) , lung (5), salivary gland (6), and ocular adnexa (7) associated with clinical setting of autoimmune diseases or chronic inflammation, usually Sjögren's syndrome, Hashimoto's thyroiditis, and *Helicobacter pylori* infection. Thymic MZBL of MALT-type is an extremely rare disease with only 22 cases having been reported in the literature to date and the largest series has included 15 cases (8-19). In this paper, I report a case of low-grade MZBL of MALT-type in the thymus of a patient with Sjögren's syndrome and rheumatoid arthritis.

CASE REPORT

A 43-yr-old Korean woman presented with a long history of Sjögren's syndrome and rheumatoid arthritis. She had complained of dry eyes, dry mouth, and arthralgia for about 16 yr and also complained of both parotid swelling that had developed 3 months before. The symmetrical swelling of the wrist, metacarpophalangeal, and proximal interphalangeal joints was accompanied by morning stiffness and pain. On admission, antinuclear antibody (ANA) revealed a speckled pattern and showed positive reaction for SS-A/Ro antibody and negative for the SS-B/La antibody. Rheumatoid factor was positive (147.3 IU/mL). A lobulated anterior mediastinal mass was detected by computerized tomography (Fig. 1) and the thymus was resected through median sternotomy. There were no symptoms of myasthenia gravis. The resected mass was confined within the thymus and did not show invasion to the surrounding structures. The specimen consisted of a solid, smooth, lobulated, encapsulated mass that measured 7 cm in maximum diameter and weighed 79 g. The cut surface was pale pink to tan, and showed homogenous appearance with some small cysts (Fig. 2). The tissue was fixed in 10% neutral buffered formalin and embedded in paraffin. Sections were stained with hematoxylin and eosin and periodic acid-Schiff. Histologically, the normal architecture of the thymus was diffusely effaced by a dense infiltration of lymphoid cells. Reac-

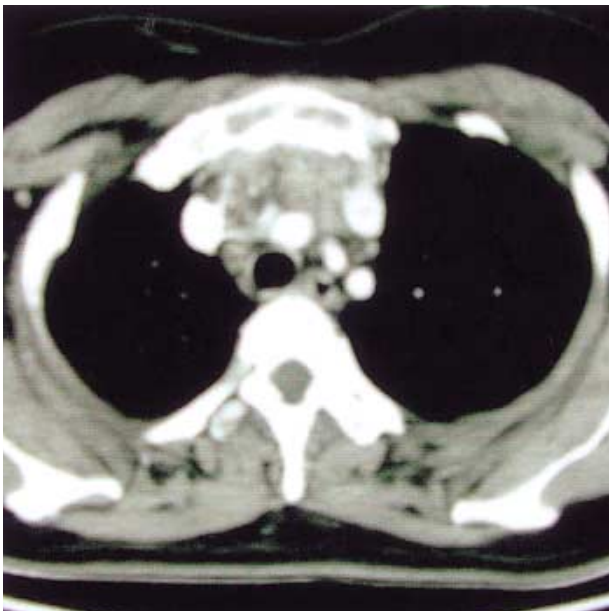

Fig. 1. CT scan shows a relatively well-demarcated lobulated solid mass in the anterior mediastinum.

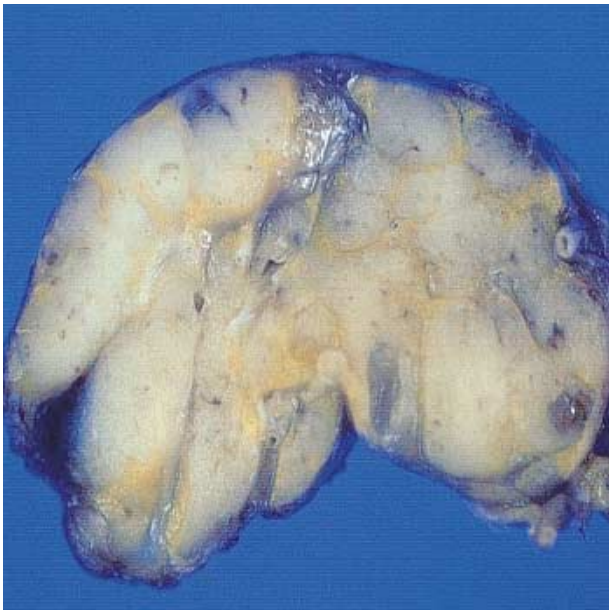

Fig. 2. The cut surface of the thymic tumor shows pale pink to tan, solid, homogeneous and lobulated tissue with some small cysts.

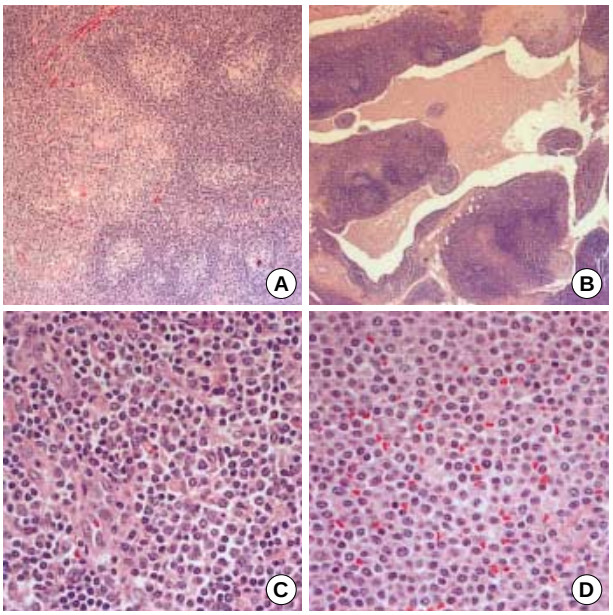

Fig. 3. The low-power view shows totally effaced architecture with diffuse lymphoid infiltration and interspersed reactive lymphoid follicles (A, H&E, ×200). Focal variable-sized cysts containing eosinophilic fluid (B, H&E, ×100). Neoplastic cells are predominantly composed of centrocyte-like (CCL) cells, small lymphocytes, and plasma cells (C, H&E, ×400). Sheets of CCL cells with monocytoid feature (D, H&E, ×400).

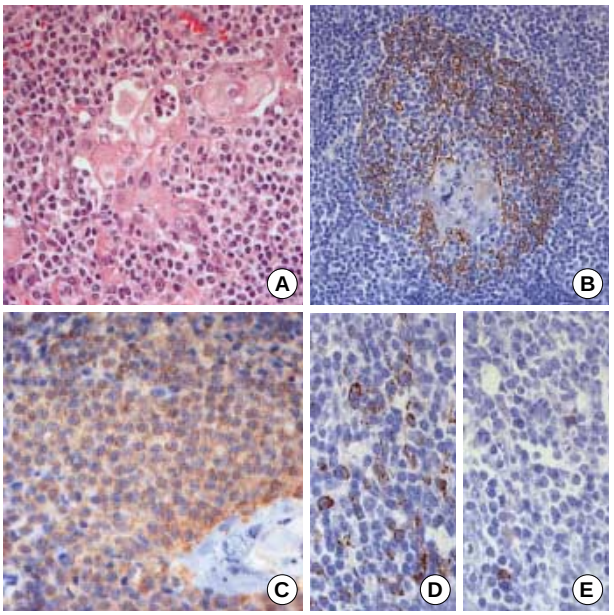

Fig. 4. Infiltration and expansion of Hassall's corpuscles by neoplastic cells forming a lymphoepithelial lesion is noted (A, H&E, ×400) and highlightened by an immunostaining for cytokeratin (B, ×400). Thymic lymphoma showing positive reaction for CD20 (C, ×400). Some plasma cells show cytoplasmic staining for kappa light chain (D, ×400), whereas lambda light chain is negative (E, ×400).

tive lymphoid follicles with germinal centers could be identified within the tumor (Fig. 3A). The microscopic cysts filled with eosinophilic proteinaceous fluid were lined by attenuated epithelium infiltrated by centrocyte-like (CCL) cells (Fig. 3B). The lymphoid infiltrate comprised monotonous CCL cells with monocytoid cells and plasma cells (Fig. 3C, D). There were considerable number of plasma cells and small lymphocytes. A few large transformed cells were also recognized (Fig.

3C). Prominent lymphoepithelial lesions (LEL), which were highlightened by cytokeratin staining, were formed by centrocyte-like cells infiltrating and expanding the Hassall's corpuscles (Fig. 4A, B). Immunohistochemical studies of paraffin sections were performed with the use of LSAB kit (DAKO, Carpinteria, CA, U.S.A.). The primary antibodies for the kappa light chain, lambda light chain, and CD3 were purchased from DiNona, Korea and primary antibodies for the CD20, CD79a, bcl-2, bcl-6, CD5, CD23, CD10, and cytokeratin were purchased from DAKO. Immunohistochemically, the CCL cells were positive for CD20, CD79a, and bcl-2 indicating B-cell phenotype (Fig. 4C) and negative for CD3, CD5, CD10, CD23, and bcl-6. Kappa light chain restriction was also found in plasma cells in the tumor confirming monoclonality of B-cell proliferation (Fig. 4D, E). The tumor cells showed IgA heavy-chain type. A variable number of CD3-positive T cells were admixed with CCL cells. Postoperative adjuvant chemotherapy or radiation therapy was not given. The patient has been followed up for 11 months without evidence of recurrent tumor.

DISCUSSION

I herein report a case of primary extranodal MZBL of MALT-type in the thymus associated with Sjögren's syndrome and rheumatoid arthritis. MZBL of MALT-type is characterized by an indolent clinical course and has been described in a variety of sites (1, 4-7) associated with clinical setting of autoimmune diseases and chronic inflammation, usually Sjögren's syndrome, Hashimoto's thyroiditis, and *Helicobacter pylori* infections which suggests proliferation of the lymphoma cells depend on the presence of antigen-driven T cells.

Thymic MZBL of MALT-type is an extremely rare disease with only 22 cases having been reported in the literature to date, including one Korean case (8-19). According to Inagaki et al. (19) who systematically investigated 15 cases of thymic MALT lymphoma, this tumor entity revealed prevalence in Asians, marked female predilection, strong association with autoimmune diseases, especially Sjögren's syndrome, mostly IgA phenotype, and consistent lack of *API2-MLT1* gene fusion, a recently reported MALT lymphoma-specific gene abnormality. They proposed that thymic MALT lymphoma is a distinct subgroup of MALT lymphoma. The association with rheumatoid arthritis was reported in only one case (11). No cases associated with both Sjögren's syndrome and rheumatoid arthritis as in my case were reported.

B-cell lymphomas other than MALT lymphoma arise in the thymus, especially mediastinal large B-cell lymphoma, which has been included in the REAL (2) and WHO classifications (3). In contrast to MALT lymphoma which shows an indolent course, this tumor is a highly aggressive lymphoma with a poor prognosis. The mixture of epithelial elements and small lymphocytes could be confused with more common thymoma. In type B thymomas, the lymphoid cells usually consist of small immature lymphocytes of T-cell immunophenotype, whereas in the thymic MALT lymphoma there is an admixture of small lymphocytes, CCL cells, a few blastoid cells, and plasma cells showing mostly B-cell immunophenotype.

In summary, I described herein is a thymic low-grade extranodal MZBL of MALT-type in a patient with both Sjögren's syndrome and rheumatoid arthritis. It is possible that the lymphoma arose on the underlying basis of long standing autoimmune diseases. Pathologists should be aware that MZBL of MALT-type may occasionally involve thymus. In a small biopsy, the presence of mixture of small lymphoid cells and epithelial cells may closely mimic a thymoma. Morphologic features of CCL cells, plasmacytoid cells, lymphoepithelial lesions as well as immunophenotype or molecular studies are helpful for a definitive diagnosis.

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