Thymic Extranodal Marginal Zone Lymphoma of Mucosa-associated Lymphoid Tissue with 8q24 Abnormality

Akihito Momoi¹, Koichi Nagai¹, Noriatsu Isahai¹, Takeshi Sakai², Koichi Ohshima³ and Sadao Aoki⁴

Abstract

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) of the thymus is reported to have characteristic features that distinguish it from MALT lymphoma of other organs; it is proposed to be a distinct clinicopathological subgroup of MALT lymphoma. We herein present a case of thymic MALT lymphoma accompanied by Sjögren’s syndrome, involving the first report of a thymic MALT lymphoma patient carrying a chromosomal abnormality of 8q24. No c-myc gene translocation or c-Myc protein overexpression was observed, suggesting that c-myc was not involved in lymphomagenesis or progression. Although we did not examine the mechanisms by which the lymphoma developed, this chromosomal structural change in 8q24 may be associated with the pathogenesis in our case.

Key words: thymic MALT lymphoma, 8q24 abnormality, no c-myc translocation

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Introduction

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is a low-grade B-cell lymphoma arising from various organs, such as the stomach, salivary gland, lung, head and neck, ocular adnexa, skin, thyroid gland and breast (1), and is often associated with chronic inflammation and autoimmune diseases. Chromosomal abnormalities, such as trisomy 3, trisomy 18 or t(11;18)(q21;q21), are frequently seen in patients with MALT lymphoma. MALT lymphoma of the thymus, first reported by Isaacson et al. in 1990 (2), is a rare subtype, of which around only 50 cases have been reported. In 2002, Inagaki et al. investigated 15 cases of thymic MALT lymphoma and showed that it is a distinct clinicopathological subgroup of MALT lymphoma, characterized by a predominance in Asia, marked predominance in women, strong association with autoimmune diseases, especially Sjögren’s syndrome, epithelium-lined cysts, the presence of neoplastic plasma cells of the IgA phenotype and the absence of t(11;18)(q21;q21) (3). However, there are only a few reports of chromosomal abnormalities in cases of thymic MALT lymphoma and it has not been studied in detail. We herein present for the first time a case of thymic MALT lymphoma in a patient carrying a chromosomal abnormality of 8q24, which showed no c-myc gene translocation or c-Myc protein overexpression. This chromosomal aberration may be involved in the pathogenesis in our case.

Case Report

A 58-year-old woman with a persistent cough and dyspnea visited our hospital. She had been diagnosed with Sjögren’s syndrome six years previously. The laboratory findings showed leukocytopenia, anemia and hypergammaglobulinemia with IgA predominance. Anti-SS-A antibodies were positive, and IgA-kappa monoclonal proteins were

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Table. Laboratory Findings.

<table>
<thead>
<tr>
<th>Hematology</th>
<th>Biochemistry</th>
<th>Anti-IgM</th>
<th>Anti-IgG</th>
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<tbody>
<tr>
<td>WBC 3,000/μL</td>
<td>TP 8.5 g/dL</td>
<td>CRP 0.3 mg/dL</td>
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<tr>
<td>Seg 58%</td>
<td>Alb 3.1 g/dL</td>
<td>IgA 2.347 mg/dL</td>
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<tr>
<td>Lymph 32%</td>
<td>BUN 16.0 mg/dL</td>
<td>IgA 1.600 mg/dL</td>
<td></td>
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<tr>
<td>Mono 6%</td>
<td>Cre 0.7 mg/dL</td>
<td>IgM 40 mg/dL</td>
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<tr>
<td>Eosino 4%</td>
<td>UA 3.4 mg/dL</td>
<td>sIgG 287 U/mL</td>
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<tr>
<td>RBC 321 × 10^6/μL</td>
<td>Na 149 mEq/L</td>
<td>ANA × 1280</td>
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<tr>
<td>Hb 10.3 g/dL</td>
<td>K 4.0 mEq/L</td>
<td>Anti-SS-A &gt;240 U/mL</td>
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<tr>
<td>Ht 34.8%</td>
<td>Cl 106 mEq/L</td>
<td>Anti-SS-B 1.7 U/mL</td>
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<tr>
<td>Plt 29.8 × 10^12/μL</td>
<td>Ca 8.3 mEq/L</td>
<td>IgAK k type M protein (+)</td>
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<tr>
<td>Urinalysis</td>
<td>protein (-)</td>
<td>ALT 17 IU/L</td>
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<tr>
<td>occult blood</td>
<td>ALT 24 IU/L</td>
<td>LDH 242 IU/L</td>
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<tr>
<td>glucose (-)</td>
<td>ALP 154 IU/L</td>
<td>TB 0.3 mg/dL</td>
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</tr>
<tr>
<td>Bence-Jones Protein (-)</td>
<td>TB 0.3 mg/dL</td>
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</table>

**Discussion**

MALT lymphoma of the thymus is suggested to have characteristic features that distinguish it from MALT lymphoma of other organs, as reported by Inagaki et al. (3). Our case also involved the typical features of thymic MALT lymphoma: occurrence in an Asian woman, the presence of underlying Sjögren’s syndrome and the IgA-kappa phenotype histologically. Several chromosomal abnormalities have been identified in patients with non-thymic MALT lymphoma, including t(11;18)(q21;q21), t(3;14)(q27;q32), t(1;14)(p22;q32) and t(14;18)(q32;q21), trisomies of chromosomes 3, 7, 12 and 18 and structural anomalies with breakpoints in 1q21 and 1p34 (4). In cases of thymic MALT lymphoma, trisomy 3 (5-7) and trisomy 18 (5, 6, 8) have been reported using FISH analyses, but not MALT1-associated or IGH-associated translocation, including t(11;18) forming the API2-MALT1 fusion using karyotyping, FISH and reverse-transcription polymerase chain reaction (RT-PCR) methods (3, 5, 9, 10). Moreover, only two cases of thymic MALT lymphoma showing abnormal karyotypes with G-banding have been reported: 46,X,dup(X)(p11p22) (11) and 46,XX,add(8)(q24.1)[4]/46,XX[1] (Fig. 4a). To detect c-myc gene-associated translocation, a fluorescence in situ hybridization (FISH) analysis was performed using a dual-color split probe. Split signals were detected in only 11 out of 1,000 cells, equal to the value of the negative control (Fig. 4b). The copy number of c-myc was also normal. Immunohistochemical staining for c-Myc proteins showed that the tumor cells were negative for c-Myc (Fig. 3f).

Because the left supraclavicular lymph nodes became enlarged to up to 15 mm in diameter after mediastinal tumor resection, the patient was treated with six courses of R-CVP (rituximab, cyclophosphamide, vincristine and prednisolone) and achieved complete remission (CR). She has maintained CR for more than one year.
Figure 2. Gallium-67 citrate scintigraphy showed an increased uptake in the anterior mediastinal mass (arrows). No other regions with an abnormally intense uptake were found.

Figure 3. Pathological features of the thymic tumor. (a) Monocytoid B cells with centrocyte-like cells diffusely infiltrated the thymus (Hematoxylin and Eosin staining). (b) Immunostaining of AE1/AE3 showed disruption of the epithelium by the infiltrating cells. (c) An immunohistochemical study showed IgA positivity in neoplastic cells with plasmacytic differentiation. (d) Immunostaining for kappa and lambda immunoglobulin light chain. Neoplastic cells showed light chain restriction for kappa chain. (e) Immunostaining for MIB-1. The MIB-1 labeling index was low. (f) Immunostaining for c-Myc. Neoplastic cells were negative for c-Myc. Scale bars: a-d: 50 μm. e, f: Original magnification ×40.
of (2;8) or (8;22) have been indicated to involve translocation 8q24. Some cases of Burkitt’s lymphoma with translocation codes a long non-coding RNA and maps to chromosome NSMCE2 (8q24.13) and NSMCE2 (8q24.13), and a fusion gene between NSMCE2 (8q24.13) and CCDC26 (8q24.21) (14). PVT-1 encodes a long non-coding RNA and maps to chromosome 8q24. Some cases of Burkitt’s lymphoma with translocation (2;8) or (8;22) have been indicated to involve translocation of PVT-1 (15). PVT-1 amplification has been reported in ovarian cancer, breast cancer, colorectal cancer and hepatocellular carcinoma (16-18), and it has been suggested that PVT-1 serves as an anti-apoptotic phenotype in studies of ovarian cancer, breast cancer and colorectal cancer cell lines (16, 17). Genes except for c-myc on 8q24, such as PVT-1, might be candidates for contributors to the development of thymic MALT lymphoma. Disappointingly, we were unable to examine more details of genetic alterations, including PVT-1. Kominato et al. suggested that the numerical chromosome abnormality of trisomy 3, detected in 7/14 (50%) of patients in their study, might be associated with thymic MALT lymphoma development; however, no significant differences in the clinicopathological features were found between the patients with or without trisomy 3 (5). Candidate genes responsible for the development of thymic MALT lymphoma have not been identified. Although we did not examine the mechanisms by which lymphoma developed in the current case, this chromosomal structural change in 8q24 may be associated with the pathogenesis in our patient. Further studies to clarify these points will be needed in the future.

The authors state that they have no Conflict of Interest (COI).

References


