CASE REPORT

Mucosa-associated marginal zone B-cell lymphoma (MALT Lymphoma) of terminal ileum

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ABSTRACT

Extranodal mucosa-associated marginal zone B-cell lymphoma (MALT lymphoma) is extremely rare in ileum. A 35-year-old woman with traffic accident was found to have an ulcerated tumor (4 cm $\times$ 4 cm) in terminal ileum. Biopsies showed proliferation of atypical lymphocytes which were small or medium-sized, and resembled centrocytes. Germinal center-like nodular areas, plasma cell differentiation, and lymphoepithelial lesions (LELs) were seen. Immunohistochemically, the atypical lymphocytes showed high proliferative activity; the Ki-67 labeling was 82%. The atypical lymphocytes were positive for p53, vimentin CD45, CD20, CD79α, CD30, CD10, λ-chain, κ -chain and bcl-2, but negative for cytokeratin (CK) AE1/3, CK CAM5.2, CD45RO, CD3, CD23, CD43, CD68, CD56, CD10, TdT, CD4, CD5, CD8, and cyclin D1. Plasma cell differentiation was positive for CD38, CD79α, and CD138. Light chain restriction was present. The germinal center-like areas were negative for bcl-2. Since only B-cell markers were positive and histological features suggested a low grade neoplasm, the tumor was indolent low-grade B-cell neoplasms including MALT lymphoma, mantle cell lymphoma, lymphoplasmacytic lymphoma, follicular lymphoma, small lymphocytic lymphoma/CLL. A differential diagnosis was performed and discussed, and final diagnosis was ileal MALT lymphoma. After diagnosis, extensive examinations including CT, MRI, PET, endoscopies were performed; they revealed no tumors other than the ileal tumor. The patient is now treated by chemotherapy and radiation. The prognosis seems good.

Key Words: Ileum, Mucosa-associated lymphoid tissue lymphoma, Histopathology, Immunohistochemistry

1. INTRODUCTION

Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is defined as an extra-nodal lymphoma composed of morphologically heterogenous small B-cells including marginal zone (centrocyte-like) cells (CLCs), cells resembling monocytoid cells, small lymphocytes, and scattered immunoblasts and centroblasts-like cells.[1,2] There is a plasma cell differentiation in a proportion of cases. The infiltrate is in the marginal zone of reactive B-cell follicles and extends into the interfollicular regions. In epithelial tissues, the neoplastic cells typically infiltrate the epithelium, creating lymphoepithelial lesions (LELs).[2] The diagnosis of extra-nodal marginal zone B-cell lymphoma is difficult in tissues free from epithelium. MALT lymphoma should always be differentiated from low grade B-cell neoplasms including small lymphocytic lymphoma/CLL, lymphoplamacytic lymphoma, follicular lymphoma, and mantle cell lymphoma.[2–6]

In the gastrointestinal tracts, the MALT lymphoma occurs in stomach in almost all cases.[1–6] Helicobacter pylori play an important role in development of MALT lymphoma of stomach,[1–6] and eradication of helicobactor pylori can cure

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MALT lymphoma.[1–6]

MALT lymphoma of ileum is extremely rare; only several cases have been reported to date.[7–12] Herein reported is a case of ileal MALT lymphoma occurring in a young (35 years) woman.

2. CASE REPORT

A 35-year-old woman was injured in the head by traffic accident, and was admitted to our hospital ER immediately. The head CT and MRI showed minimal changes without immediate treatment. During the admission, she hoped systemic medical examinations. The upper and lower gastrointestinal endoscopy, abdominal sonography, blood and urine tests, and systemic CT were performed. The blood test showed nonspecific changes including mildly increased gamma-GTP, LAP, and CRP. The urine test and other examinations showed no significant changes. However, the lower endoscopic examination revealed an ulcerated tumor measuring 4 cm $\times$ 4 cm in the terminal ileum (see Figure 1).

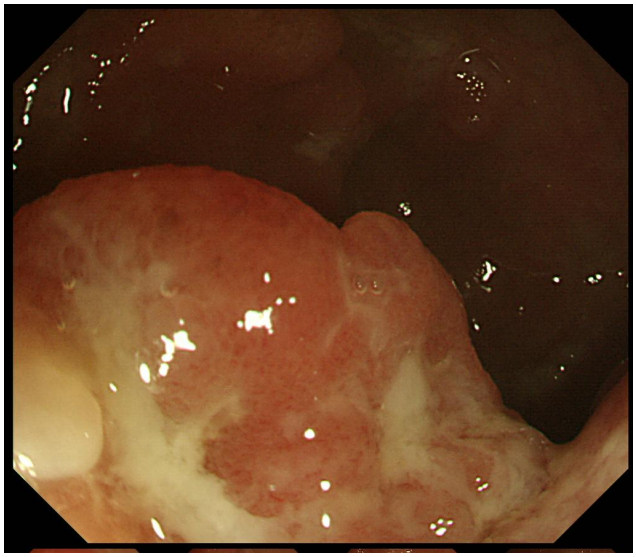

Figure 1. Endoscopic findings of the terminal ileum. An ulcerated tumor is seen in the ileum.

Biopsies were taken, and they showed proliferation of atypical lymphocytes (see Figure 2A). The atypical lymphocytes were small or medium-sized, and resembled centrocytes (see Figures 2B and 2C). Centroblastic or immunoblastic cells with nucleoli and monocytoid cells were also seen (see Figures 2A-2D). Plasma cell differentiation (see Figures 2A-2D), lymphoepithelial lesions (LELs) (see Figure 2D) and germinal center-like nodular areas were seen.

An immunohistochemical study was performed by the use of Dako Envision method (Dako Corp, Glostrup, Denmark) as described previously.[13–15] Immunohistochemically, the atypical lymphocytes show high proliferative activity; Ki-67 labeling was 82% (see Figure 3A). The Ki-67-positivities were seen largely in the atypical lymphocytes in particular in those forming nodular areas, but it was also seen in cryptal epithelial cells and stromal cells. In this study, Ki-67 labeling index was determined as the ratio of positive atypical lymphocytes to total atypical lymphocytes. The atypical lymphocytes were positive for p53 protein (see Figure 3B). The aypical lymphocytes were positive for vimentin (see Figure 3C), CD45 (see Figure 3D), CD20 (see Figure 3E), CD79α (see Figure 3F), CD30, λ-chain, κ-chain, CD10, and bcl-2, but negative for cytokeratin (CK) AE1/3, CK CAM5.2, CD45RO, CD3, CD23, CD68, CD56, TdT, CD4, CD5, CD8, CD43, cyclin D1. Plasma cell differentiation was positive for CD38, CD79α, and CD138. Light chain restriction was present (κ-chain> λ-chain, seeming 10:1, significantly). The germinal center-like nodules were not labeled by bcl-2.

Since only B-cell markers were positive and histological features suggested low grade B-cell neoplasms, the tumor was of low grade B-cell neoplasms including MALT lymphoma, mantle cell lymphoma, lymphoplasmacytic lymphoma, follicular lymphoma, small lymphocytic lymphoma/CLL. The discrimination was performed, and the overall appearances were determined to be those of MALT lymphoma. The pathological diagnosis was ileal MALT lymphoma.

She underwent whole body CT, MRI, PET and sonography; they revealed no tumors and lymphoadenopathy other than the ileal tumor. The upper gastrointestinal endoscopy showed no significant changes. The patient is now treated by chemotherapy and radiation. The prognosis seems good.

3. DISCUSSION

The present case was histologically malignant lymphoma. Immunohistochmeically, the ileal tumor was positive for CD45. The Ki-67 labeling index (82%) was high, and p53 was positive. Therefore, the present ileal tumor is concluded as malignant lymphoma. The high Ki-67 labeling was seen largely in the atypical lymphocytes, indicating the atypical lymphocytes shows high proliferative activity. P53 was positive, suggesting p53 mutations. These Ki-67 and p53 alterations may suggest transformation of the MALT lymphoma into diffuse large B-cell lymphoma (DLBCL), but the HE histological features are yet within indolent B-cell lymphoma with no apparent foci of DLBCL within the ileal tumor.

The histology of the present tumor consisted of relatively small mature-like atypical lymphocytes, and immunohsitochemically the infiltrates were composed of only B-cells with B-cell markers (CD20, CD10, CD79α, light chains, and

bcl-2). Light chain restriction was present, being predominant kappa chains over lamda chain. Therefore, the present B-cell tumor was monoclonal in immunohistology though no gene rearrangement studies of IgH and IgL were not carried out. In any way, the present tumor was low-grade B-cell neoplasm, which include small lymphocytic lymphoma/CLL, lymphoplasmacytic lymphoma, follicular lymphoma, MALT lymphoma, and mantle cell lymphoma.[1–6]

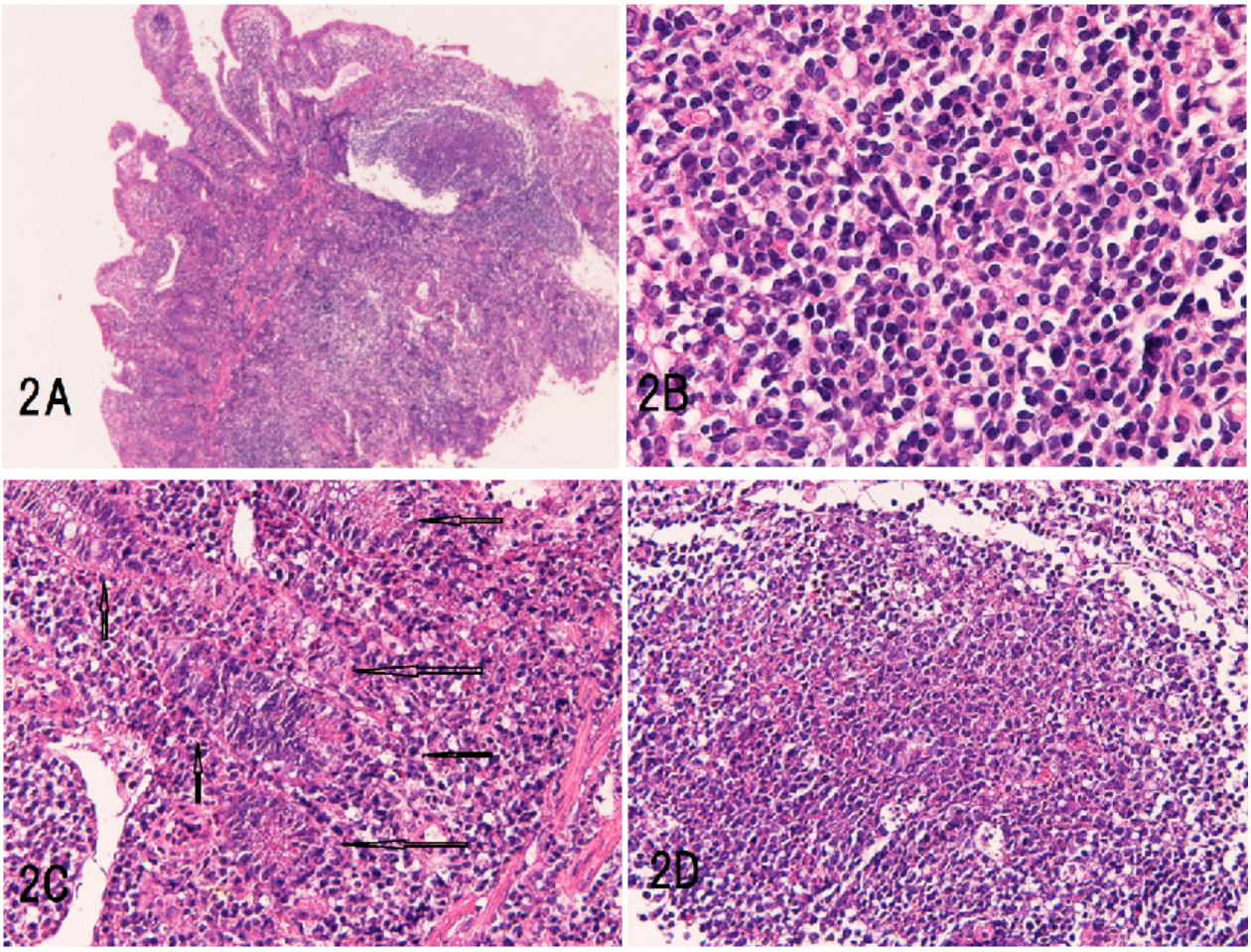

Figure 2. Biopsy findings of the lesion of the terminal ileum

A: The biopsy shows severe proliferation of atypical small lymphocytes. HE: ×40; B: The atypical lymphocytes show centrocyte-like cells, monocytoid lymphoacytes, and plasma cells. HE: ×200; C: The atypical lymphocytes show lymphoepithelial lesions (arrows). HE: ×200; D: The atypical lymphocytes form nodular or follicular structures. HE: ×200.

The present case is different from mantle cell lymphoma, which has characteristic nuclei with nuclear grove and immunohistochemical findings of positive cyclinD1.[1–6] The current B-cell tumor showed no such characteristic nuclei and showed no cyclinD1. Thus, the present case is not mantle cell lymphoma. The present tumor is different from follicular lymphoma, in which the nodular formation is characteristically positive for bcl-2.[1–6] Thus, the absence of bcl-2 in the nodular areas and different histology in the present tumor imply that the present tumor is not follicular lymphoma. The present case is different from small lymphocytic lymphoma/CLL, which shows monotonous proliferation of small lymphocytes with mild atypia.[1–6] In the present tumor, the morphology is not so monotonous; the nodular formation, LELs, monocytoid cells, plasma cells, centrocytes-like cells, lymphoblastic cells were seen in the present tumor. Therefore, the present tumor is not small lymphocytic lymphoma/CLL. The most difficult differential diagnosis of the present tumor is from lymphoplasmacytic lymphoma, which consisted of small atypical lymphocytes and plasma cells.[1–6] In the present study, certainly plasma cells and small atypical lymphocyte were seen. However, the present tumor showed much more heterogenous histologies such as monocytoid cells, lymphoblastic cells (CD30 positive), LELs, centrocytes-like cells, and germinal center formations, which are not seen in lymphoplasmacytic lymphoma.

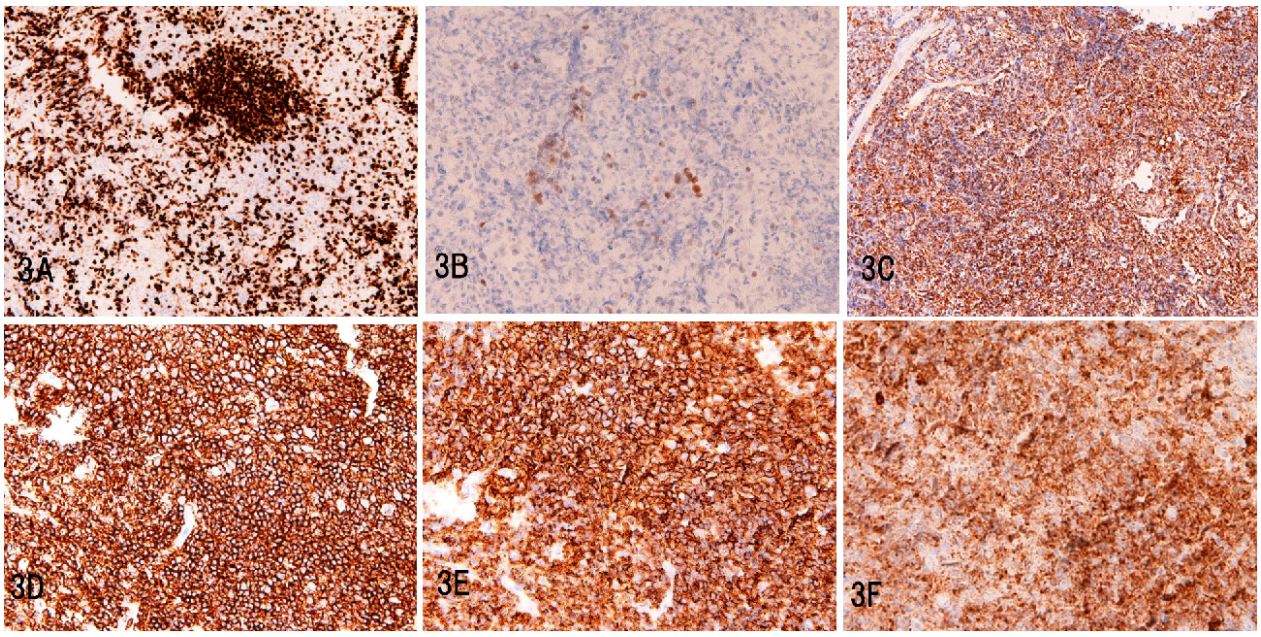

Figure 3. Immunohistochemical features

A: The Ki-67 labeling is high (82%); B: The atypical lymphocytes were positive for p53 protein; C: The aypical lymphocytes are positive for vimentin; D: The atypical lymphocytes are positive for CD45; E: The atypical lymphocytes are positive for CD20; F: The atypical lymphocytes are positive for CD79α. A-F: Immunostaining: ×200.

A panel of antibodies has been proposed for differential diagnosis of these low-grade B-cell lymphomas.[1–6] The antigens include CD5, CD10, CD23, CD43, and cyclinD1.[1–6] In small lymphocytic lymphoma, the expression pattern is CD5-, CD10-, CD23+, CD43+, and cyclinD1-. In follicular lymphoma, the expression pattern is CD5-, CD10+, CD23-, CD43-, and cyclinD1-. In MALT lymphoma, the expression pattern is CD5-, CD10-, CD23-, CD43+/-, and cyclinD1-. In mantle cell lymphoma, the expression pattern is CD5+, CD10+/-, CD23-, CD43+/-, and cyclinD1+.[1–6] In the present tumor, the expression pattern was CD5-, CD10-, CD23-, CD43-, cyclin D1-. Thus, the expression pattern in the current ileal tumor is compatible with MALT lymphoma.

4. Conclusion

An extremely rare case of ileal MALT lymphoma occurring a young woman (35 years) was reported. Immunohistochemical findings and differential diagnoses were discussed.

Conflicts of Interest Disclosure

The authors declare no conflicts of interest.

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