CASE REPORT

Ileal Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma with a Large-Cell Component That Regressed Spontaneously

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Reported herein is a case of mucosa-associated lymphoid tissue (MALT) lymphoma of the terminal ileum with a large-cell component, which regressed spontaneously. To the best of our knowledge, only five cases of spontaneously regressing MALT lymphoma have been reported in the English-language literature, and all of these cases were low-grade lymphomas. Spontaneous regression of a MALT lymphoma with a high-grade component is very rare. The present case suggests that MALT lymphoma cells have a reversible nature, even in the presence of a high-grade component. (*Gut Liver* 2010;4:117-121)

Key Words: Mucosa-associated lymphoid tissue lymphoma; Large cell component; Regression; Ileum, Low grade

INTRODUCTION

Since Isaacson and Wright first proposed the concept of mucosa-associated lymphoid tissue (MALT) lymphoma in 1983,¹ MALT has become established as a distinct clinical pathologic entity that is characterized histologically by diffuse infiltration of small lymphoid cells (centrocyte-like or monocytoid cells), invasion of lymphoma cells around the epithelium (lymphoepithelial lesions), and proliferation of plasma cells in the lamina propria of the mucosa.

The clinical behavior of MALT lymphomas has been reported as favorable.² However, several studies on gastric lymphomas have shown that the presence of high grade component, either with or without a low grade MALT

lymphoma component, is usually associated with more advanced disease and a worse outcome than typical MALT lymphomas.³⁻⁶ High grade component is consisted of a proliferation of lymphoid blasts with large, vesicular nuclei with one or more nucleoli, which resembles diffuse large B cell lymphoma (DLBCL) cells. In this paper, we describe a very rare case of MALT lymphoma with a large-cell component that showed spontaneous complete regression.

CASE REPORT

In January 2007, a 38-year-old male visited the Keio University Hospital with the chief complaint of epigastralgia after meals. Physical examination revealed no abnormalities. The laboratory data were as follows: white blood cell count (WBC) 7,300/ μ L; serum C-reactive protein (CRP) 3.0 mg/dL; hemoglobin 16.0 g/dL; serum level of soluble IL-2 receptor 285 U/mL, serum test for antibody against *Helicobacter pylori* (*H. pylori*) negative, serum test for antibody against *Yersinia enterocolitica* negative. There was no significant growth found from the stool culture. Serum levels of IgG, IgM and IgA were within normal limit.

A small bowel series revealed a radiolucent area with an irregular border measuring 7 to 10 mm in diameter in the terminal ileum. Computed tomography (CT) revealed slightly enlarged ileocecal lymph nodes (Fig. 1A). Colonoscopic examination disclosed multiple protruding lesions in the terminal ileum with erosive tops covered by edem-

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Fig. 1. Radiological and endoscopic findings of an ileal lesion in one patient. (A) February 3, 2007: computed tomography (CT) finding of slightly enlarged ileocecal lymph nodes (arrow). (B) February 16, 2007: colonoscopic examination disclosed multiple protruding lesions with erosive tops and covered by edematous mucosa in the terminal ileum. (C) March 23, 2007: CT findings of no detectable ileocecal lymph nodes. (D) April 5, 2007: no lesions could be found in the terminal ileum on colonoscopic examination.

atous mucosa (Fig. 1B). The lesion was about 10 mm in diameter. Hematoxylin-eosin staining of biopsy specimens from these lesions revealed dense homogenous plasmacytoid cell infiltration to the epithelium, which is different from the normal lymphatic tissue (Fig. 2A). The histological sections also showed lymphoepithelial lesions characterized by infiltration of lymphoma cells to the epithelium (Fig. 2B). Immunohistochemical staining revealed that the majority of the cells were positive for CD20. In addition to these typical MALT lymphoma cells, we also found a small area of different cell aggregates with solid or sheet-like proliferations of transformed cells. These cells had swollen, light-colored nuclei and a high nuclear-cytoplasmic ratio, resembling the cells of diffuse large B-cell lymphoma (DLBCL) (Fig. 2C). Most cells were positive for MIB-1 staining, implying a high proliferative activity, and negative for CD10 (Fig. 2D) and for Bcl-2 (Fig. 2E). Extensive examination (chest abdominal and pelvic CT, head magnetic resonance imaging, positron emission tomography, upper gastrointestinal endoscopy, and bone marrow aspiration) revealed no other pathological lesions other than the one at the terminal ileum. A rapid urease test and microscopic examination of the gastric biopsy specimens confirmed the absence of *H. pylori* infection. No MALT lymphoma lesions were detected in orbita, thyroid and salivary glands. Based on the findings, we diagnosed the lesion as primary MALT lymphoma of the terminal ileum with high grade transformation.

Due to the presence of the DLBCL-like component, the MALT lymphoma was considered to be a more advanced disease. We planned surgical therapy and adjuvant chemotherapy. In March 2007, the patient was admitted to our hospital for the surgery. To our utter surprise, we could detect neither the enlarged ileocecal lymph nodes by CT (Fig. 1C), nor the lesion in the terminal ileum during the preoperative colonoscopic examination (Fig. 1D). Biopsy specimens obtained from the same region revealed only mild inflammation with lymphoid cell infiltration, no lesions compatible to MALT lymphoma. A small bowel series also failed to reveal any pathological regions. Surgery was given up, and the patient was determined to be on close follow-up by endoscopy.

DISCUSSION

As mentioned above, MALT lymphomas with high grade component have known to be an advanced disease with worse prognosis than typical MALT lymphomas. de Jong *et al.*⁵ revealed only if 1-10% of all tumor cells showed high grade character with or without non-confluent clusters of blasts, the tumor would have worse outcome than pure low grade MALT lymphomas. In our case, the cells had composed an apparent cluster similar to DLBCL. It was a small area, but from biopsy specimens. We could assume larger area in the lesion was occupied by high grade components. Then, we had concluded the lesion had been a high grade MALT lympho-

Fig. 2. Pathological findings of ileal lesions. (A) Dense, homogeneous, diffuse mononuclear cell infiltration was demonstrated in biopsy specimens of the terminal ileal mucosa (H&E stain, original magnification, $\times 100$). (B) Lymphoepithelial lesions were clearly detected by immunohistochemistry against cytokeratin AE1/AE3 (DAKO; original magnification, $\times 400$). (C) Diffuse large-B-cell lymphoma-like cells with swollen, light-colored nuclei and a high nuclear-cytoplasmic ratio in a biopsy specimen of the terminal ileum. (D) Immunohistochemistry against CD10 (original magnification, $\times 400$). (E) Immunohistochemistry against BCL2 (original magnification, $\times 400$).

ma, however, the tumor had disappeared only in 2 months.

It is known that some gastrointestinal lymphomas show spontaneous regression. But these reports were almost limited to gastric lymphomas, and not defined as MALT lymphomas.⁷⁻¹³ To the best of our knowledge, there are only 5 well-documented cases of MALT lymphoma that showed spontaneous regression; these cases are summarized in the Table 1.¹⁴⁻¹⁸ None of these patients showed a

large-cell component in the pathological specimen. Only one of these cases relapsed with the appearance of DLBCL cells. Our case report presented herein would be the very rare case of MALT lymphoma with a high grade, large-cell component, in which the tumor showed spontaneous regression.

How could high grade MALT lymphoma can completely disappear in such a short interval? We could not have found out any good answer to this question. We had

Table 1. Summary of Spontaneous Regression Cases of the MALT Lymphoma Reported in the English-Language Literature

First author (ref. no.)	Country	Age (years)/ Sex	Site of the tumor	<i>H. pylori</i>	Ann Arbor stage	High-grade component	Follow-up (months)	Relapse
Takenaka R (14)	Japan	76/M	Rectum	—	I	Negative	19	No
Sakuma H (15)	Japan	70/F	Hard palatine	NR	I	Negative	38	No
Okamura S (16)	Japan	54/M	Rectum	—	I	Negative	NR	NR
Uohashi A (17)	Japan	68/F	Thyroid	NR	I	Negative	2	Occurred
Ohno Y (18)	Japan	14/M	Stomach	+	II	Negative	120	No
Present case	Japan	38/M	Terminal ileum	—	I or II	Positive	15	No

NR, not reported.

speculated that the MALT lymphoma in our case developed on a background of some infection, and it could happen that the lymphoma regressed with resolution of the infection, just like some gastric MALT lymphomas are known to regress after the eradication of *H. pylori*. There was some evidence of inflammation in this case, such as increase of the WBC count, elevation of the serum CRP, or the macroscopic appearance of an inflamed terminal ileum on colonoscopy. The association between gastric *H. pylori* infection and gastric MALT lymphoma is the most firmly established,¹⁹⁻²² but a number of infections other than *H. pylori* have been implicated in the development of MALT lymphoma. However, in our present case, we had failed in finding any evidence of *H. pylori* and other infections which include *Campylobacter jejuni* through serum antibody test and stool culture. On the other hand, it is believed that eradication therapy would only succeed in cases with low grade MALT lymphomas, based on the contention that only low grade lymphomas exhibit reversible reactivity to infection. The present case shows, however, high grade lymphomas may also show reversible reactivity.

We need to consider the possibility of immunoproliferative small intestinal disease (IPSID) which is endemic in Middle-Eastern and Mediterranean countries. Representative patients of IPSID usually present with malabsorption syndrome, weight loss, and abdominal pain of months' to years' duration and often reveal peripheral edema, clubbing, or an abdominal mass. In addition, the number of circulating lymphocytes is often reduced and levels of serum IgG and IgM would be abnormal. Proximal portion of small intestine is often shifted to abnormal change.²³ However, in the present case with lesion at terminal ileum, since no abnormalities in physical examination and in WBC counts or serum Ig were shown, it was very difficult to diagnose the present case as a representative IPSID.

Among the 5 cases cited in Table 1, one case showed relapse of the lymphoma, with high grade transformation.

Therefore, we believe that in the present case, close-follow-up by colonoscopy is necessary. Until now, 24 months after the lesion was first detected, there has been no evidence of relapse of the lesion through colonoscopic study of this patient.

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