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Case Report

Three Cases of Primary Gastrointestinal Malignant Lymphoma

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Introduction

Extranodal lymphoid tissus of the permeable mucosa sites, such as the gastrointestinal tract and bornchi are different in structure and function from peripheral lymph nodes, and it is named as mucosa-associated lymphoid tissue (MALT). Therefore, the clinicopathological features of extranodal lymphomas arising from these mucosal sites have been considered to be different from those of nodal lymphomas.

In 1983 and 1984, Isaacson and his colleagues[1,2] have reported a certain low-grade B-cell lymphoma of the gastrointestinal tract called as MALT lymphomas. The concept of MALT lymphomas extended later to include extranodal lymphomas of the lung, salivary gland, thyroid, thymus[3], breast[4] and gallbladder[5].

Recently, a definite nodal B-cell lymphoma called mantle cell lymphoma, were also reported[6,7]. The histological and clinical features of mantle cell lymphomas are somewhat different from MALT lymphomas.

In this paper, we reported three cases with primary gastrointestinal lymphomas of low grade malignancy and discuss the differential diagnosis of MALT and mantle cell lymphomas.

Case report

Case 1: A 58-years-old female visited Ohara General Hospital because of epigastric discomfort in 1984. An endoscopical examination showed chronic gastritis. She received drug therapy, but the symptom was not improved. A diagnosis of malignant lymphoma was made from biopsied specimen and she subsequently underwent total gastrectomy in 1985. The surgically resected stomach revealed multiple shallow ulcers in antrum and the histological features were consistent with MALT lymphoma.

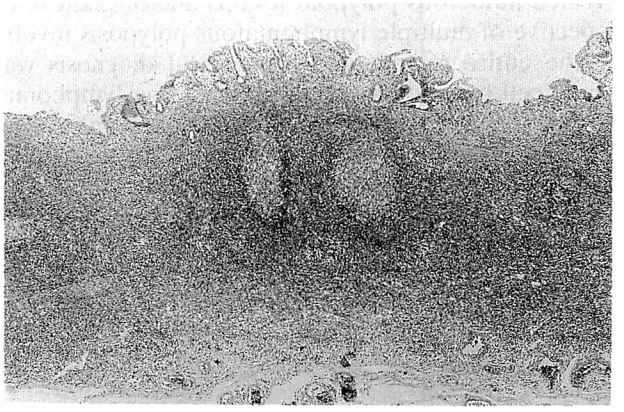

Fig. 1. Case 1. HE×10. Lymphoma cells infiltrate diffusely in mucosa propria and submucosal layer. Germinal centers surrounded by thin mantle zones were found.

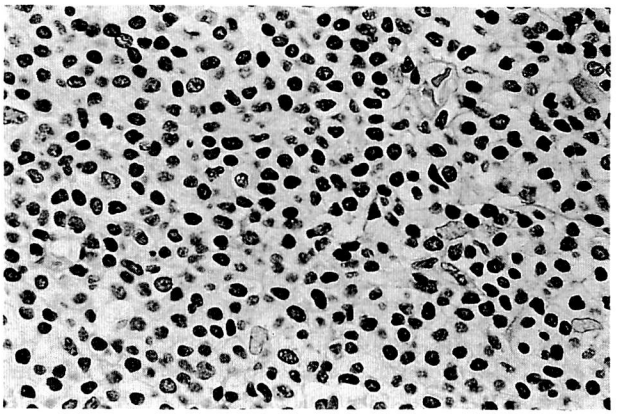

Fig. 2. Case 1. HE×200. Lymphoma cells have round or slight indented nuclei and abundant pale cytoplasms, resembled to monocytoid B cells.

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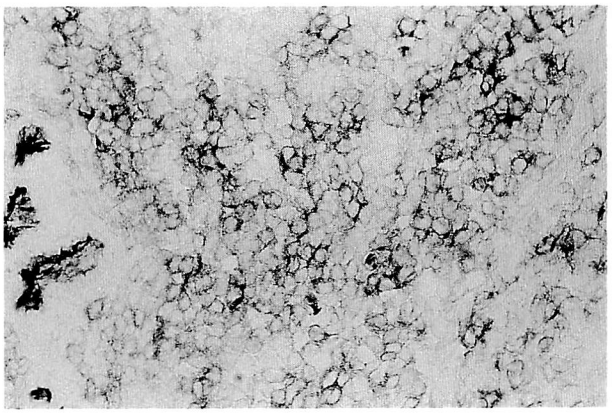

Fig. 3. Case 1. ALP×160. Lymphoma cell are positive for alkaline phosphatase.

Case 2: A 62-years-old female visited Hanawa Hospital because of itching in the anal region and constipation in July, 1988. Rectal carcinoma was suspected from digital examination and she underwent the resection of the rectum in August, 1988. The surgically resected rectum revealed numerous polypoid lesions and/or giant folds suspective of multiple lymphomatous polyposis involving the entire rectum and histological diagnosis was mantle cell lymphoma and/or mantle zone lymphoma. She was treated with one cycle of combination chemotherapy, but no response was noted and she died 2 years after the onset of her illness.

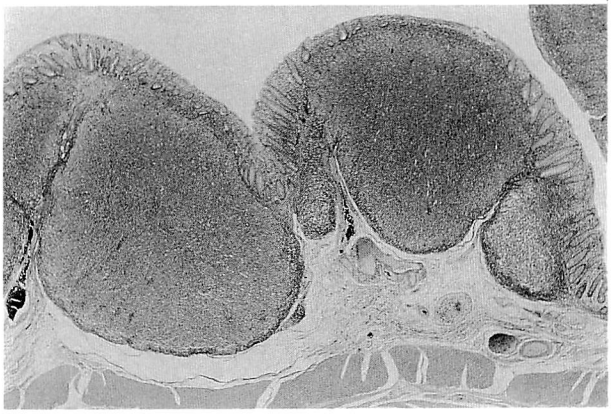

Fig. 4. Case 2. HE×5. Lymphoma cells infiltrate massively in mucosa propria of the rectum, resulting in marked thickening of the wall.

Case 3: A 81-years-old male with a complaint of three years history of gastric ulcer was admitted to Ohara General Hospital in 1989. An endoscopic examination revealed multiple shallow ulcers in gastric antrum, and malignant lymphoma was detected by a biopsied specimen and he subsequently underwent gastrectomy in 1990. The surgically resected stomach revealed multiple shallow ulcers in antrum and the histological diagnosis was made as MALT lymphoma.

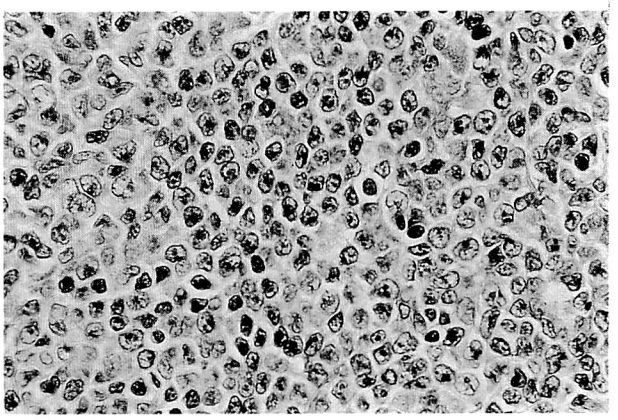

Fig. 5. Case 2. HE×200. Lymphoma cells are medium in size and have scant cytoplasm with round or polygonal nuclei.

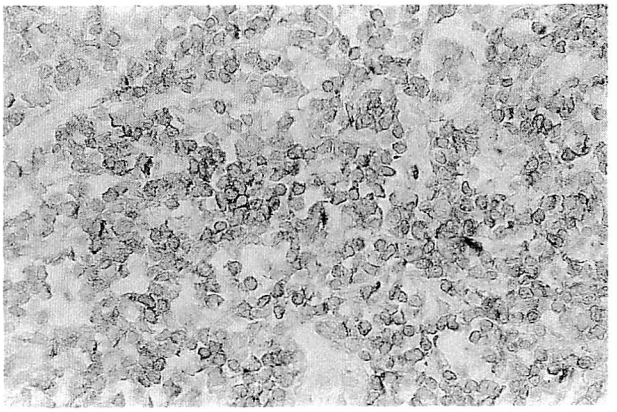

Fig. 6. Case 2. CD5×160. Lymphoma cells are weakly positive for CD5.

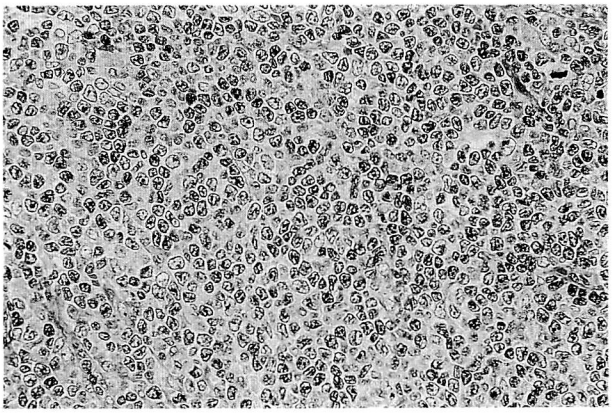

Fig. 7. Case 3. HE×100. Medium-sized lymphoma cells infiltrate diffusely intermingled with large lymphoma cells. Neumerous lymphoma cells have round or polygonal nuclei and less abundant cytoplasms than those of Case 1.

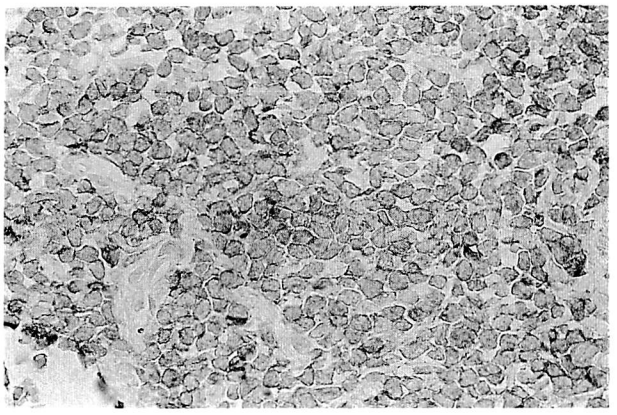

Fig. 8. Case 3. CD5×160. Lymphoma cells are weakly positive for CD5.

Table 1, Results of histochemistry

	Case 1	Case 2	Case 3
CD19	+	+	+
CD20	+	+	+
CD3	−	−	−
CD5	−	+	+
CD10	−	−	−
CD25	−	−	−
CD30	−	−	−
IgM	+	+	+
IgD	−	−	−
ALP	+	−	+

Results

1. *Clinical features:*

The ages of these patients ranged from 58 to 81 years (mean; 67 years). Two patients were female and one was male. Endoscopically, Case 1 and 3 showed shallow ulcerated or erosive lesions existed in gastric antrum. Case 2 showed numerous polypoid lesions or giant folds through the entire gastrointestinal tract, which is usually called multiple lymphomatous polyposis. The patient died of malignant lymphoma 2 years after onset, but the prognosis of Case 1 and 3 was unknown.

2. *Histological findings and histopathological diagnosis:*

Case 1 and 3 showed a diffuse lymphoma cell proliferation in mucosa propria and submucosal layer of the stomach. Lymphoma cells were medium in size and had pale abundant cytoplasm (Case 1, Case 3), containing round to slightly indented nuclei. A few mitotic figures were present and lymphoepithelial lesions were often found. Atrophic germinal centers surrounded by thin mantle zones were observed. The pathologic diagnosis was malignant lymphoma, MALT type, according to the Kiel classification. Case 2 showed a massive proliferation of lymphoma cells mainly in mucosa propria of the rectum, and a few infiltration to submucosal layer resulting in the thickening of mucosa. Morphologic contours of lymphoma cells were very similar to those of Case 3. Lymphoepithelial lesions were not found. Naked germinal centers were found in Case 2, and pathologic diagnosis was made as mantle zone lymphoma.

Lymph follicles with atrophic or hypertrophic germinal centers were found in all 3 cases. In Case 1 & 3, germinal centers were surrounded by thin mantle zone, and in Case 2 germinal centers were naked without mantle zone.

3. *Immunohistochemical findings:*

Both snap frozen sections and formalin-fixed paraffin embedded tissuse were used for an immunohistochemical and enzymehistochemical analysis.

All 3 cases showed B cell phenotype, showing IgM^+, IgD^-, $CD19^+$, $CD20^+$, $CD10^-$ and $CD3^-$. CD5 was expressed in Case 2 and 3, and negative in Case 1. Alkaline phosphatase (ALP) staining was positive for Case 1 and 3, but was negative for Case 2. All 3 cases were negative for CD25 and CD30.

4. *Genetical analysis:*

Southern blotting analysis was performed in Case 2 and 3. Both cases showed the rearrangement of JH, and germline of bcl-1, bcl-2 and TCRβ.

Discussion

Diagnostic criteria of MALT lymphoma proposed by Isaacson and his coworkers[2,8] are as follows : 1) neoplastic proliferation of centrocyte-like or small cleaved cell-like cells, 2) neoplastic plasma cell infiltration in the subepithelial layer, 3) remaining of atrophic or hypertrophic lymph follicles, 4) lymphoepithelial lesions, 5) CD5 negative, 6) localized lymphoma lesion for long period, and 7) good prognosis. MALT lymphoma is usually included in low-grade malignancy, but there are some reports of high grade malignancy.

We studied three cases of primary gastrointestinal lymphomas by the use of histologic, immunohistochemical and genetic methods. Case 1 and 3 showed localized lesions in the stomach and satisfied above diagnostic criteria from 1) to 4). Case 1 was thought as a typical or classical MALT lymphoma, because lymphoma cells had abundant pale cytoplasm similar to monocytoid B cells[9] and were positive for CD19, CD20, IgM, and ALP, but negative for IgD, CD5 and CD10, indicating that the origin seemed to be marginal zone B lymphocytes. Histologic appearance of Case 3 was consistent with MALT lymphoma, but the foci contained large blastoid lymphoma cells. Therefore, Case 3 was diagnosed MALT lymphoma with blastic transformation namely follicular colonization[10]. In addition, the immunohistochemical data of Case 3

demonstrated some difference from MALT lymphoma, because of the positivity for ALP and CD5. Although MALT lymphomas usually lack of CD5, Case 3 was compatible with MALT lymphoma except CD5-positivity, therefore, Case 3 appeared to be an exceptional case among MALT lymphomas. Morphological features of Case 2 were similar to those of Case 1 and 3 with exception of scanty cytoplasm. In Case 2, the most striking features different from Case 1 and 3 were the presence of naked germinal centers and the absence of lymphoepithelial lesions. Immunohistochemical data of Case 2 were different from those of Case 1 and 3: lymphoma cells showed IgM^+, IgD^-, $CD19^+$, $CD20^+$, $CD5^+$, $CD10^-$ and ALP^-. These results suggest that Case 1 and 3 were MALT lymphoma, and Case 2 was mantle cell lymphoma[11], corresponding with multiple lymphomatous polyposis described by Cornes[12], because the usual phenotype of MALT lymphoma is $SIgM^+$, IgD^-, $CIgM^{+/-}$, $CD5^-$ and ALP^+, whereas the unusual phenotype of mantle cell lymphoma is $SIgM^+$, IgD^+, $CD5^+$ and $ALP^{+/-}$. Therefore, IgD, CD5 and ALP are useful markers to distinguish MALT lymphoma from mantle cell lymphoma.

In conclusion, we have reported two cases with MALT lymphoma and one case with mantle cell lymphoma arising from the gastrointestinal tract. Immunohistochemical and enzymehistochemical methods are able to differentiate MALT lymphoma from mantle cell lymphoma: MALT lymphoma showed the expression of ALP and lack of CD5 and IgD, whereas mantle cell lymphoma showed the expression of CD5 and IgD and lack of ALP.

key words: Malignant lymphoma, gastrintestinal tract, MALT lymphoma, mantle cell lymphoma

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