A Case of Intestinal Marginal Zone B-cell Lymphoma of Mucosa-associated Lymphoid Tissue (MALT Lymphoma) with Signet-ring Cell Morphology

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Abstract

We report a case of intestinal mucosa-associated lymphoid tissue (MALT) lymphoma with signet-ring cell morphology in a 59-year-old man. The tumor was located at the terminal ileum and the root of the vermiform appendage. The tumor showed lymphoproliferative lesions involving the mucosa and submucosa of the intestine. The lesion consisted of small lymphocytes and large immunoblastic cells in the center and plasmacytic cells with Russell bodies in the periphery. A diagnosis of intestinal MALT lymphoma was made by characteristic features of plasmacytic differentiation with monoclonality, lymphoepithelial lesion, centrocyte-like or monocytoid lymphocyte infiltration, and destruction of normal lymphoid structure. The majority of neoplastic plasma cells had single or multiple Russell bodies and took a signet-ring cell morphology. Although lymphoma with prominent Russell bodies or signet-ring cell lymphoma (SRCL) is rare, this case is a representative case of MALT lymphoma with abundant Russell bodies in the small intestine or intestinal SRCL, MALT lymphoma type. Although a differential diagnosis with reactive lesions and other neoplasms showing signet-ring cell morphology is necessary, immunohistochemical study should prove useful in making the final diagnosis.

Key words

MALT lymphoma, Signet-ring cell lymphoma, Russell bodies, Intestine

Introduction

Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is a representative B-cell neoplasm frequently seen in extranodal sites, especially in gastrointestinal tract. Intestinal MALT lymphoma is occasionally encountered, but is less frequent than that in gastric MALT lymphoma. The histology of MALT lymphoma is characterized by centrocyte-like or monocytoid lymphocyte infiltration with marginal zone distribution, and destruction of gastrointestinal mucosa designated as lymphoepithelial lesion (LEL). Plasmacytic differentiation of neoplastic B-lymphocytes is also characteristic in MALT lymphoma. This case is an intestinal MALT lymphoma with prominent plasmacytic differentiation. Neoplastic plasma cells in the peripheral area of the lesion have prominent Russell bodies, and many of these cells take signet-ring cell morphology. No case of intestinal MALT lymphoma with prominent Russell bodies has been
reported to date. Herein we report the characteristic histological, immunohistochemical, and electron microscopical findings observed in this case.

Case

Clinical history: A 59-year-old male was admitted to the hospital, because of abdominal distention and progressive abdominal pain. The patient had been well until two days earlier, when he had vomited and noted lower abdominal pain after returning home from travel. No superficial lymph nodes were enlarged. Laboratory data revealed elevated AST, ALT, and LDH, but no other abnormal findings including elevated total protein and gamma globulin were detected. Abdominal plain X-ray film disclosed an ectatic small intestine filled with gas. Abdominal computed tomography scan showed an ileocecal mass and ascites in the abdominal cavity.

Figure 1. (a) Abdominal plain X-ray film disclosing an ectatic small intestine filled with gas. (b) Abdominal CT scan showing an ileocecal mass and ascites in the abdominal cavity.

Pathological findings: The resected specimen showed yellowish white, slightly elevated, and ill-defined submucosal lesions at the terminal ileum and at the root of the vermiform appendix. Multiple small nodules were seen around the lesion (Fig. 2).

Microscopically, multiple and patchy lymphoproliferative lesions were seen mainly in the mucosal and submucosal areas with destruction of the lamina muscularis mucosae (Fig. 3a). These lesions were composed of small lymphoid cells and large immunoblastic cells in the central area (Figs. 3a and 3b) and of large cells with rich eosinophilic cytoplasm in the peripheral area (Figs. 3a and 3c). These large cells contained single to multiple eosinophilic round granules in the cytoplasm (Fig. 3d). Nuclei of these large cells varied in size and shape. The large cells showed signet-ring like morphology in many foci of the lesions in the peripheral area (Fig. 3e). The lymphoproliferative lesion spread through the entire intestinal wall at the root of vermiform appendage. Immunohistochemical study was carried out with Envision kit (DAKO) under the instruction of the manufacturer. Conditions and results of immunohistochemistry are shown in the

Figure 2. Gross appearance of the terminal ileum and cecum. The tumor is mainly located in the terminal ileum. (Arrows).
Small and large blastic lymphoid cells were positive for CD20 and CD79alpha. There were a few areas where the surface mucosa was destructed by lymphoid cells yielding lymphoepithelial lesions (LEL) (Fig. 4). In the peripheral area, these large cells with abundant eosinophilic globules were positive for kappa light chain (Fig. 5a), IgG, CD38, and CD138 (Fig. 5b), but negative for lambda, IgM, IgD, and IgA. Mesenteric lymph nodes revealed widened interfollicular spaces and sinuses with prominent infiltration of large cells containing eosinophilic globules (Figs. 6a and 6b). Lymphoid follicles were atrophic. Results of immunohistochemistry of these large cells with globules were also positive for kappa light chain, IgG, CD38, and CD138, which were identical to those in the intestinal lesion. To clarify the ultrastructure of neoplastic cells, electron microscopic examination was carried out using formalin-fixed tissue samples. The examination revealed large cells with multiple round dense bodies in distended granular endoplasmic reticula (Figs. 7a and 7b).

**Discussion**

Lymphoproliferative lesions in the present case were composed of two characteristic areas; central and peripheral areas. The central area was composed of small lymphocytes and immunoblastic cells of CD20+ and CD79 alpha+ B-cell phenotype. No normal structure of lymphoid follicles was detected in the lesions. There was a prominent infiltration of abnormal large cells with single or multiple round and eosinophilic globules located mainly in the peripheral area. These cells reacted to anti-CD38, anti-CD138, anti-kappa, and anti-IgG, but no reaction was present against anti-lambda, anti-IgM, anti-IgD or anti-IgA. These findings suggested that these cells were monoclonal plasma cells containing Russell bodies. Some of these plasma cells had large and bizarre nuclei. The characteristic features of this case were a mucosa without normal lymphoid structure, LEL, destruction of muscularis mucosa, and extensive monoclonal plasmacytic infiltration with Russell bodies. These features led to the diagnosis of intestinal marginal zone B-cell lymphoma of MALT type with abundant Russell bodies. Differential diagnosis should include lymphoplasmacytic lymphoma, plasmacytoma, and lymphoma with reactive infiltration of plasma cells. This lymphoproliferative lesion was composed of various kinds of lymphoid cells with plasmacytic differentiation and disclosed IgG and kappa light chain restriction in the neoplastic plasma cells making it possible to exclude the diagnosis of lymphoplasmacytic lymphoma, plasmacytoma, and reactive lesions. Immunoproliferative small intestinal disease (IPSID) is a subtype of MALT lymphoma, which may express alpha heavy chain but do not express any light chain\(^1\)\(^3\). MALT lymphoma involving small intestine is frequently seen in the patients with IPSID. However, because of immunohistochemical results of reactivity for IgG and kappa light chain, this case is not based on IPSID.

It is of interest that this case was characterized by prominent Russell bodies in the neoplastic cells. Plasmacytic differentiation is one of the characteris-

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**Table 1. Results of Immunohistochemistry**

<table>
<thead>
<tr>
<th>Antibodies</th>
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<td>Large cells** in</td>
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* : Lympohocytes include small lymphocytes and large immunoblastic cells
** : Large cells with multiple eosinophilic globules in cytoplasm or cells with signet-ring cell morphology
Figure 3. (a) Lymphoproliferative lesion involving the wall of terminal ileum with destruction of the lamina muscularis mucosae. (b) Small lymphoid cells and large immunoblastic cells in the central area (*). (c) Large cells with multiple eosinophilic small globules in the peripheral area (**). (d) Large cells with multiple eosinophilic globules. (e) Large cells with signet-ring cell morphology.

Figure 4. Immunohistochemistry for cytokeratin (AE1AE3) showing a destructive epithelium (Lymphoepithelial lesion).

Figure 5. Immunohistochemistry of large cells with eosinophilic globules.
(a) Kappa light chain  (b) CD138.

Figure 6. (a) A lymph node showing atrophic lymphoid follicles with widening of interfollicular spaces and sinuses. (b) Interfollicular spaces and sinuses exhibit prominent infiltration of large cells containing eosinophilic globules.
tics of MALT lymphoma\textsuperscript{1}, and abundant Russell bodies in cytoplasm are rarely encountered in clinical aspect. Gastric lymphoma with abundant Russell bodies was reported as Mott cell tumor by Y. Fujiyoshi \textit{et al.}\textsuperscript{4} in which the term "Mott cells" are an alternative name of plasma cells with abundant Russell bodies. However, intestinal MALT lymphoma associated with massive Russell bodies has not been documented to date. Most of the reported cases of lymphoma with prominent Russell bodies have been discussed as signet-ring cell lymphomas. Similarly the tumor cells containing Russell bodies in this case presented signet-ring cell morphology. A case of signet-ring cell lymphoma (SRCL) of lymph node was first introduced by Kim \textit{et al.} in 1978\textsuperscript{5}. SRCL has been reported to be associated with various kinds of lymphoma including MALT lymphoma\textsuperscript{6}, follicular lymphoma\textsuperscript{7, 8}, diffuse large B-cell lymphoma\textsuperscript{9}, and myeloma\textsuperscript{10, 11}. T-cell lymphoma\textsuperscript{12-14} and null cell type anaplastic large cell lymphoma\textsuperscript{15} can also take this form. SRCL can develop in any organ, especially extranodal sites. Since an intestinal SRCL case has not been reported to date, this case may be one of the representative intestinal SRCLs, MALT lymphoma type.

Though it was difficult to diagnose whether this lesion was neoplastic or not, the evidence of blastic cells infiltration, a few LEL, and destructive lymphoid aggregation led to the diagnosis of MALT lymphoma. Clinically, it may also be difficult to differentiate SRCL and other neoplasms with signet-ring cell morphology representing signet-ring cell adenocarcinoma of colon, but because the main lesion showed atypical lymphoproliferation, it was not a problem in this case. Correct diagnosis for signet-ring cell neoplasms is important from a therapeutic point. Immunohistochemical analyses for lymphoid markers are useful to make a differential diagnosis among reactive lesions, lymphoma, and other neoplasms with signet-ring cell morphology\textsuperscript{16}.

Electron microscopic examination revealed intracisternal electron-dense globular structures, Russell bodies, in the cytoplasm of the plasma cells. Electron microscopical findings of cells with signet-ring appearance differed among cases. Three types of signet-ring cells have been reported. These types include Russell body type\textsuperscript{17}, vacuolar type\textsuperscript{18}, and granular/fibrillar material type\textsuperscript{19}. Since the neoplastic plasma cells in this case had homogenous electron-dense materials in distended granular endoplasmic reticula, this case should be classified as Russell body type. Many of the Russell body type SRCLs have intracytoplasmic IgM, whereas a few cases of Russell body type have IgG\textsuperscript{5, 18, 19, 20}. In the electron microscopic studies reported, most of IgG SRCLs disclosed electron-lucent vacuoles, and IgM SRCLs exhibited granular or electron-dense materials\textsuperscript{11}. These findings suggest that electron microscopic dense bodies represent eosinophilic Russell bodies on HE stain, but do not represent the type of immunoglobulin.

In conclusion, the present case is a representative case of intestinal MALT lymphoma with prominent Russell bodies or intestinal SRCL, MALT lymphoma type. Although the incidence is

\begin{figure}[h]
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\caption{Electron microscopical appearance. (a) Intracisternal electron dense globules. (b) Multiple electron dense globules with oppressed nucleus.}
\end{figure}
rare, it may be important to keep in mind that there exists a case of lymphoma with prominent Russell bodies and with signet-ring cell morphology. Immunohistochemical analyses concerning lymphoid markers are important for the differential diagnosis among reactive lesion, other types of lymphoma, and other neoplasms with signet-ring cell morphology.

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Reference


印環細胞形態を示した腸管粘腫辺縁帯

B 細胞リンパ腫の一例

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抄 録

腸管における粘膜関連リンパ組織より発生した粘腫辺縁帯 B 細胞性リンパ腫 (MALT リンパ腫) で腫瘍細胞が印環細胞形態を示した一例を経験したので報告する。症例は 59 歳男性。嘔吐および下腹部痛にて発症。入院時の腹部 X 線写真にてイレウスを認め、腹部 CT にて回盲部腫瘤と腹水が指摘された。イレウスの改善および腫瘍精査目的にて回盲部切開をおこなった。

切除材料の肉眼所見は、回腸末端部に境界不明瞭な粘膜下病変をみとめ、その周囲に小結節が散在していた。虫垂根部にも同様の病変をみとめた。組織学的にはリンパ増殖性病変が粘膜および粘膜下主体に広がっていた。病変の中心部は小リンパ球浸潤が主体で、芽球様細胞が散在性にみられた。病変の辺縁部はラッセル小体をもつ形質細胞が多数浸潤していた。病変は小リンパ球主体で形質細胞への分化がみられること、粘膜破壊 (Lymphoepithelial lesion) がみられること、さらに免疫組織学的に免疫グロブリン IgG および経鎖のκ鎖にモノクロナリティーがみられたことから腸管粘腫辺縁帯 B 細胞リンパ腫と診断した。多くの形質細胞はラッセル小体をもち、印環細胞の形態を示す細胞がみられたことから印環細胞リンパ腫の一例と考えられた。鑑別診断として反応性病変、他の垂のリンパ腫および印環細胞形態を呈する他の異圧腫瘍が挙げられるが、鑑別には免疫組織化学が有用であると考えられた。