Primary Duodenal MALT Lymphoma

Muneatsu Toshima, Keiko Aikawa, Kenji Soga, Koichi Shibasaki, Keisuke Yoshida* and Iwao Emura**

Primary duodenal MALT lymphoma (MALToma) is a very rare neoplasm arising from the mucosa-associated lymphoid tissue of the duodenum. We report a 55-year-old woman with MALToma located in the descending duodenum and accompanying Helicobacter pylori infection of the stomach. We performed operative resection due to involvement of the papilla of Vater and submucosal tumor infiltration. Despite wide mucosal spreading, postoperative examination revealed only a small amount of MALToma cells infiltrating into the submucosa. No invasion into the adjacent structure or metastasis to regional lymph nodes was confirmed, suggesting the disease could have been controlled by eradication of Helicobacter pylori.

Introduction

MALT lymphoma (MALToma) is a neoplasm with low grade malignancy, arising from mucosa-associated lymphoid tissue of various organs (1–3). The tumor represents B-cell surface markers and characteristic histopathology such as the proliferation of centrocyte-like cells, infiltration of tumor cells into mucosal epithelium (lymphoepithelial lesion), formation of lymphoid follicles in the tumor and plasma cell infiltration. MALToma occurs more often in the gastrointestinal tract than in salivary glands, lungs, thyroid glands, thymus, mammary glands or lacrimal glands. Among these sites, MALToma arising from the gastric mucosa is most frequently reported and it has been considered to be correlated with Helicobacter pylori (H. pylori) infection, because of the high incidence of coexistence of patients with H. pylori (4–6) and the tumor regression or remission after eradication of the bacteria (7–10).

On the contrary, duodenal MALToma is a very rare neoplasm, and its clinical and pathological characteristics remain obscure. We describe a case of duodenal MALToma to clarify the features of this disease.

Case Report

A 55-year-old woman was referred to our hospital for examination of the upper gastrointestinal tract without any symptoms or signs. She had normal hematological findings, and no significant biochemical abnormality except for a slight elevation of alkaline phosphatase (313 IU/l) and total bilirubin (1.5 mg/dl). The serum level of each immunoglobulin was within the normal range. The ratio of pepsinogen I/II was 3.3 (normal range 3.0<), whereas pepsinogen I and II were 70.6 ng/ml (70.0 ng/ml<) and 21.7 ng/ml, respectively. Gastroduodenoscopy revealed whitish irregular granular change of the duodenal mucosa extending from the bulb to the superior angle of the duodenum (Fig. 1). In the stomach, only mucosal atrophy was observed but no tumor or ulcer was detected. The culture of gastric mucosa propagated the microaerophilic bacteria, H. pylori. Histopathological examination proved that the biopsied duodenal specimen was composed of lymphoid tumor cells, positive for B-cell surface marker L26 (CD20/cy) and negative for UCHL-1 (CD45RO) of T-cell marker, as well as infiltrating mucosal epithelium which formed lymphoepithelial lesions (Fig. 2). They also represented a negative immunohistochemical reaction for CD5 and cyclin D1 (data not shown).

The patient was admitted for further examination and treatment of the disease on November 18, 1997. Barium contrast study revealed extension of a granular and partly nodular lesion toward the anal side of the ampulla of Vater but no depressed lesion or ulcer was pointed out (Fig. 3). Submucosal infiltration of tumor cells was suggested by endoscopic ultrasonography on the upper part of the descending portion. Computed tomography (CT) and magnetic resonance imaging (MRI) detected significant thickening of the mucosal wall of the descending part, but no metastasis was observed by CT, MRI or 67Ga-citrate scintigraphy. No significant abnormality in the

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small intestine, colon or rectum was detected by barium contrast study or total colonoscopy. Southern blot analysis of the immunoglobulin (Ig) genes of tumor cells revealed rearrangement in each gene of Ig-light chain C\textsubscript{\text{\textgamma}} and Ig-heavy chain J\textsubscript{\text{\textgamma}}.

Due to the wide extension involving the ampulla of Vater and submucosal infiltration of MALToma cells, pylorus-preserved pancreato-duodenectomy was carried out and followed by histopathological examination. The lesion was 7 cm long longitudinally and was composed of granular or nodular elevation, 2–10 mm in diameter (Fig. 4A). Monotonous infiltration of tumor cells into the submucosa of the duodenum was seen (Fig. 4B and 4C) but no tumor involvement of the pancreas, choledochus, peritoneum or regional lymph nodes was recognized. Intraoperatively we could not detect hepatic metastasis and the surgical margin was completely free of tumor cells, so the operation was considered to be a curative resection. The patient was discharged and was followed up uneventfully without recurrence for about 1 year after the operation.
Duodenal MALToma

Figure 2. Histopathology and immunohistochemistry of the biopsied specimen. Small lymphoid cells (centrocyte-like cells) proliferate in propria mucosae and infiltrate in mucosal epithelium (lymphoepithelial lesion; arrowhead) (HE stain, \( \times 100 \)) (A). Immunohistochemistry using L26 antibody (CD20/cy) exhibits a positive reaction of tumor cells (\( \times 100 \)) (B), whereas UCHL1 (CD45RO) does not react with them (\( \times 100 \)) (C).

Discussion

MALToma arises from the mucosa-associated lymphoid tissue of gastrointestinal tracts, salivary glands, lungs, and thyroid glands. MALToma is a lymphoid tumor with low-grade malignancy, representing characteristic histopathological features, such as centrocyte-like cells with positive B-cell surface markers, lymphoepithelial lesions, lymphol follicular proliferation and infiltration of plasma cells (1-3). In the gastrointestinal tract, the tumors most frequently arise from the stomach, small intestine, cecum, and rectum in that order, but duodenal MALToma is extremely rare. The first case of duodenal MALToma was reported by Isaacson and Wright in 1983 (1), in which a 23-year-male had exhibited lesions of both the proximal duodenum and terminal ileum and was treated by chemotherapy. To our knowledge, five studies (six cases) on duodenal MALTomas have been reported (1, 11-14). Three of these cases were reported in the Japanese proceedings of a gastroenterological congress (13, 14). The patients, aged 23, 41, 54, 58, 63 and 67 years, consisted of four men and two women. There was neither symptoms nor signs in three cases, but diarrhea and epigastric pain in one patient and a fainting episode and melena in one patient. Ilial fossa pain, probably due to a tumor of the terminal ileum, and anemia was noticed in another patient. The lesions of two cases involved only the duodenal bulb. Two involved the descending part and the other two involved both. No case concurrently exhibited gastric MALToma. Endoscopically, whitish elevated lesions were observed in three patients, one of which indicated giant rugae, while erosions or ulcers were found in three cases.

Interestingly, obstructive jaundice was observed in two cases of primary non-Hodgkin’s lymphoma and follicle center lymphoma of the ampulla of Vater, reported by Pawade et al (15) and Misdraji et al (16), respectively. In these cases, the tumors were curatively resected using Whipple’s procedure even though the tumor infiltration of the sphincter of Oddi and the head of the pancreas was recognized. In our case, whitish granular or partly nodular lesions extended around the ampulla, but the infiltration was restricted to the submucosa so that the sphincter of Oddi remained intact. The findings suggested that duodenal MALToma differs in the nature of infiltration from
Figure 3. Barium contrast study of the duodenum. Fine granular and partly nodular lesions are extended from the superior duodenal angle (left) to the lower third of the descending portion (right).

Figure 4. Pathological findings of the resected specimen. Whitish granular and partly nodular lesions infiltrate the upper two thirds of the duodenum circumferentially, while the ampulla of Vater and choledochus remain free of tumor (A). Lymphfollicular proliferation (HE stain, x10) (B) and submucosal infiltration (HE stain, x40) (C) are also noticed.
other lymphomas.

Recently, gastric MALToma was shown to be closely related to gastromucosal infection of \textit{H. pylori}, for which eradication with antibiotics and proton pump inhibitors have been successfully employed (7–10). According to Nagashima et al, primary duodenal MALToma regressed after eradication of \textit{H. pylori} of the stomach, showing that the therapy may also be effective for MALToma of the duodenal mucosa free from \textit{H. pylori} infection (12). The mechanism of this anti-tumor effect of eradication has not been elucidated, but MALToma cells might respond to the antigen of \textit{H. pylori} via sensitized T-cells and proliferate extensively. When the mechanism and the clinical effect of eradication therapy are clarified, drug therapy will take the place of surgical resection. As only one study concerning the efficacy of eradication for duodenal MALToma has been reported to date, a large number of cases must be analyzed to evaluate the principles of this therapy.

References