Magnifying Endoscopic Observation of Duodenal Involvement of Follicular Lymphoma before and after Chemotherapy

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Abstract

A 60-year-old Japanese man was diagnosed with systemic follicular lymphoma with duodenal, jejunal, and ileal involvement. The duodenal lesion showed typical endoscopic features with multiple whitish granules. Chemotherapy with bendamustine and rituximab was administered, and complete remission was confirmed by CT scanning and positron emission tomography scanning. Although the duodenal granular lesions did not completely disappear, magnifying observation for the remaining lesions showed no evidence of residual lymphoma. Complete remission was pathologically confirmed by biopsy examinations. This case suggests the usefulness of magnifying observation in evaluating the effects of treatment for duodenal follicular lymphoma lesions.

Key words: follicular lymphoma, duodenal neoplasms, magnifying endoscopy, rituximab, gastrointestinal lymphoma

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Introduction

Follicular lymphoma is one of the common subtypes of non-Hodgkin lymphomas. Though most follicular lymphomas arise in the lymph nodes, this disease sometimes affects the gastrointestinal tract as a primary site or due to secondary extranodal involvement from a nodal origin. Of the gastrointestinal tract, the small intestines (i.e., the duodenum, jejunum, and ileum) are most frequently involved (1-4). Small, whitish granular lesions are typical endoscopic images of intestinal follicular lymphoma observed by esophagogastroduodenoscopy or enteroscopy examinations. Moreover, the current abilities of endoscopy devices allow for high-magnification observation of intestinal follicular lymphoma lesions. Enlarged villi, opaque whitish spots, and coiled vascular pattern within the villi have been reported as more detailed endoscopic features of intestinal follicular lymphoma (5-12).

We herein describe the case of a patient with systemic follicular lymphoma involving the duodenum, jejunum, and ileum presenting with small whitish granular lesions. Esophagogastroduodenoscopy performed after chemotherapy with bendamustine and rituximab revealed that the size of the duodenal granular lesions decreased, but they did not entirely disappear. In our magnifying observations, the residual lesions lacked enlarged villi and opaque whitish spots, suggesting no lymphoma cell infiltration into the duodenal mucosa. The pathological evaluation of biopsy specimens confirmed complete remission. This case underscores the potential utility of magnifying endoscopic observation for evaluations of the effects of treatment for intestinal follicular lymphoma lesions.
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ogastrointestinal mucosa, forming lymphoid
onspective features of intestinal follicular lymphomas (Fig. 1, 2).
Figure 1. Esophagogastroduodenoscopy images. Multiple granular lesions were observed in the
duodenal bulb (A) and second portion (B). Lesions in the duodenal second portion presented typical
morphology of intestinal follicular lymphoma, showing “multiple whitish granules.” Magnifying ob-
ervation of the lesions visualized enlarged, whitish duodenal villi and small white deposits (C). The
size of the deposits varied and the margin was unclear. These were compatible with known features
of intestinal follicular lymphoma.

Figure 2. Pathological images of the duodenal lesions. In the biopsy specimen from the duodenal
lesion, small to medium-sized lymphoid cells had infiltrated the duodenal mucosa, forming lymphoid
 follicles (A; Hematoxylin and Eosin staining). The lymphoid cells were negative for CD3 (B) and
positive for CD20 (C), CD10 (D), and BCL2 (E).

Case Report

A 60-year-old Japanese man underwent esophagogastro-
duodenoscopy as part of a routine medical checkup screen-
ing. Multiple granular lesions were detected by the endo-
scopy examination, but the histological diagnosis of the bi-
opsied samples was reactive lymphoid hyperplasia. A
colonoscopy revealed no specific abnormalities in the termi-
nal ileum, cecum, colon, or rectum. Three months later, an-
other esophagogastro-duodenoscopy was performed, and a di-
agnosis of duodenal follicular lymphoma was made by a bi-
opsy examination with immunostaining results that included
positivity for CD20, CD10, and BCL2 (13). The pathological
grade was classified according to the WHO classification
as grade 1 (1). The patient was referred to our hospital for
further investigation and treatment.

The patient had been taking medication for hyperlipide-
mia but had no history of gastrointestinal or lymphoprolif-
erative diseases. A physical examination revealed no abnor-
malities, and there was no evidence of hepatosplenomegaly
or peripheral lymphadenopathy. Laboratory findings revealed
an elevated level of soluble interleukin-2 receptor (sIL-2R)
to 568 U/mL (normal range: 122–496 U/mL), but the levels
of lactate dehydrogenase (LDH) and β2 microglobulin and
the blood cell counts were within the normal ranges.

Esophagogastroduodenoscopy showed multiple whitish
granular lesions in the duodenum, which are typical macro-
scopical features of intestinal follicular lymphomas (Fig. 1, 2).
Magnifying observation of the lesions visualized enlarged,
whitish duodenal villi and small white deposits. The size of the deposits varied, and the margin was unclear (2). Capsule endoscopy revealed multiple white nodules in the jejunum and ileum, in addition to the involvement of the duodenum (Fig. 3).

Enlarged lymph nodes were detected by CT scanning in the mesenteric, retroperitoneal, external iliac, and supraclavicular areas. Positron emission tomography (PET) showed tracer uptake in the duodenum and pleura, as well as in the multiple enlarged lymph nodes. The bone marrow aspirate and biopsy were positive for lymphoma infiltration. Consequently, the patient’s clinical stage was classified as IV.

The patient had no symptoms, and thus he was followed with a “watch and wait” strategy. However, a new lesion appeared close to the cervical vertebra and enlargement of the intra-abdominal lymph nodes was exacerbated 10 months later. Combination therapy with bendamustine plus rituximab was administered to treat the progression of the follicular lymphoma. Two courses of combination therapy were administered, and because angioptathy appeared and was suspected to be a side effect of bendamustine, four doses of rituximab monotherapy (375 mg/m² intravenous infusion 1×/week for 4 weeks) were administered. The chemotherapy resulted in the disappearance of the enlarged lymph nodes in CT scanning and disappearance of the abnormal tracer uptake in PET scanning.

In the second, post-chemotherapy esophagogastroduodenoscopy, the size of the duodenal granular lesions had significantly decreased but they were not completely gone (Fig. 4A, B). There were tiny nodules of approximately 1–2 mm in diameter. These nodules in the duodenal second portion were emphasized after indigo carmine spraying (Fig. 4C). However, magnifying observation revealed that there were no longer any whitish enlarged villi or small white deposits (Fig. 4D, E). Despite the presence of residual tiny nodules, the magnified endoscopic features obtained were suggestive of the extinction of lymphoma cell infiltration.

The histological evaluation showed only fibrous tissue, and there was no evidence of lymphoma cell infiltration in the duodenal mucosa (Fig. 5A, B). Immunostaining for CD3 (Fig. 5C) and CD20 (Fig. 5D) revealed that CD20-positive lymphoma cells no longer existed. Consequently, complete remission was confirmed by imaging studies and histopathological studies.

![Figure 3. Capsule endoscopy images. Multiple white nodules were detected in the jejunum (A) and ileum (B) by video capsule endoscopy.](image)

**Discussion**

The use of magnifying imaging systems is well established in the field of gastrointestinal endoscopy and such systems are now widely used as a valuable examination tool for presence diagnoses and qualitative diagnoses of various neoplastic lesions in the gastrointestinal tract. For example, in intestinal follicular lymphoma lesions, magnifying imaging technologies provide detailed pictures such as enlarged villi, opaque whitish spots, and coiled vascular pattern within the villi (5-12). In our latest study, we retrospectively investigated magnified endoscopic features of duodenal follicular lymphoma (n=9) and other diseases showing whitish lesions in the duodenum, including lymphangiectasia (n=7), adenoma (n=10), duodenitis (n=4), erosion (n=1), lymphan-gioma (n=1), and hyperplastic polyp (n=1) (12). Our findings revealed that: (i) enlarged villi and elongated microvessels can be observed in lymphangiectasias and lymphangiomas as well as follicular lymphomas and (ii) the white spots that we observed in the follicular lymphomas and lymphangiomas were of various sizes with clear margins, whereas the white spots of the lymphangiectasias were of homogenous sizes with clear margins. Therefore, we concluded that magnified endoscopic features, in combination with macroscopic features, are useful for differentiating follicular lymphomas from other duodenal diseases presenting whitish lesions (12).

In the present patient, esophagogastroduodenoscopy with magnifying observation at the initial diagnosis showed enlarged, whitish duodenal villi and small white deposits with various sizes and unclear margins. These are compatible with the typical magnified endoscopic features of intestinal
Figure 4. Esophagogastroduodenoscopy images after chemotherapy. The size of duodenal granular lesions significantly decreased in the duodenal bulb (A) and second portion (B). However, tiny nodules (approximately 1-2 mm in diameter) existed in the duodenal second portion. These nodules were more clearly visualized after indigo carmine spraying (C). Magnifying observation (D) and that with narrow band imaging (E) revealed that whitish enlarged villi or small white deposits no longer existed, suggesting the extinction of lymphoma cell infiltration.

Figure 5. Pathological images of the duodenal lesions after chemotherapy. Histological evaluation showed only fibrous tissue and there was no evidence of lymphoma cell infiltration in the duodenal mucosa (A, B; Hematoxylin and Eosin staining). Immunostaining for CD3 (C) and CD20 (D) revealed that CD20-positive lymphoma cells no longer existed. Particularly, there were no CD3-positive cells or CD20-positive cells in the fibrous area.
fOLLICULAR LYMPHOMA lesions that we reported previously (12). We speculate that enlarged whitish villi may result from the deposition of lymphoid cells in the villi, and white depositions appear to be formed by lymphoid follicles formed within the mucosa or submucosa (9, 10). These microscopic features can be found in the biopsy samples of present patient as well (Fig. 2).

Conversely, after chemotherapy with bendamustine plus rituximab was administered in our patient, the magnifying observation showed the disappearance of the whitish enlarged villi and small white deposits, although tiny granular lesions remained (Fig. 4D, E). The histological analysis revealed that the patient’s chemotherapy resulted in the extinction of lymphoid follicles and the emergence of fibrous tissues within the duodenal mucosa instead of lymphoid follicles. We suspect that the tiny residual granular lesions were probably formed by fibrous tissues. Therefore, magnifying observation provides us with practical information in order to evaluate the effects of treatment for intestinal follicular lymphoma lesions because magnified endoscopic features likely reflect the underlying pathological structures. Taking these findings together, we speculate that white substances which are endoscopically seen as whitish villi or white depositions are infiltrated lymphoma cells. The disappearance of such a white substance may thus be an indicator of pathological remission, as seen in the present patient.

It was noteworthy in the present case that tiny granular lesions remained in the duodenum after complete remission of the systemic follicular lymphoma was obtained. To the best of our knowledge, this is the first report presenting such endoscopic images. Generally once complete remission is obtained, duodenal lesions disappear and restoration to intact mucosa is achieved. Endoscopic pictures showing such a recovery of duodenal mucosa after CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine, and prednisone) (14), CHOP plus rituximab (3), or radiotherapy (15, 16) have been presented in previous reports. Moreover, a spontaneous disappearance of duodenal lesions in two cases has been described (10). However, there have been no previous reports describing the presence of fibrous tissues that emerged after the disappearance of lymphoid follicles. Future examinations should determine whether the formation of fibrous tissues is related to the drug action of bendamustine and/or rituximab and whether the fibrous tissue will be absorbed and reduced as time passes.

In summary, we experienced a case of systemic follicular lymphoma involving the duodenum. The potential value of endoscopic magnifying observation for the evaluation of the effects of treatment on intestinal follicular lymphoma lesions was described. We therefore believe that, although a biopsy examination is essential, a better understanding of the characteristic magnifying endoscopic features of this disease will enable prompt judgments of the effects of treatment for duodenal follicular lymphomas.

The authors state that they have no Conflict of Interest (COI).

References