Unusual Treatment of Gastric Mucosa Associated Lymphoid Tissue Lymphoma Unresponsive to *Helicobacter pylori* Eradication

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The connection between *Helicobacter pylori* and mucosa-associated lymphoid tissue (MALT) lymphoma is well established. *H. pylori* eradication is the initial treatment for MALT lymphoma. However, in *H. pylori* negative cases or unresponsive patients after successful eradication, radiation, systemic therapies, and surgical resection should be considered. Also local treatment modalities such as endoscopic mucosal resection (EMR) may be a therapeutic option in cases of low grade, localized MALT lymphoma component, the proximal location of the tumor, and the exophytic nature of the tumor, we decided to perform EMR for complete resection. After EMR, the patient remained in complete remission throughout the 15-month follow up. In our case, endoscopic resection could lead to a more rapid complete remission. Therefore, we suggest that endoscopic resection may be a useful option for low-grade exophytic-type gastric MALT lymphoma treatment with no response to *H. pylori* eradication. (Korean J Helicobacter Up Gastrointest Res 2013;13:109-113)

**Key Words:** Lymphoma, B-cell, Marginal zone; Endoscopy

**INTRODUCTION**

Primary gastric lymphoma is an uncommon disease, accounting for 1∼4% of malignancies arising in the stomach.1,2 Gastric mucosa-associated lymphoid tissue (MALT) lymphoma accounts for at least 40∼50% of primary gastric lymphomas.1,2 Several studies have shown the importance of *Helicobacter pylori* infection in the development of MALT lymphoma3-5 and *H. pylori* eradication is the primary treatment strategy in early stages.6,7 Radiation, systemic therapies, and surgical resection should be considered in *H. pylori*-negative cases or patients unresponsive after successful eradication. Additionally, endoscopic mucosal resection (EMR) can be used as a curative method in some patients.5,8 We report a case of low-grade gastric MALT lymphoma treated with EMR that had no response for 5 months after *H. pylori* eradication.

**CASE REPORT**

A 53-year-old man visited our hospital due to a protruding mass in his stomach identified during health screening endoscopy. The patient had no previous medical history. He had frequent dyspepsia and epigastric pain. A physical examination was unremarkable. An endoscopic examination showed a 1.7 cm-sized ovoid, polypoid mass with central dimpling on the greater curvature of the upper body of the stomach. It had a granular surface and a smooth border (Fig. 1A). Abdominal pelvic computed tomography showed no regional lymph node enlargement (Fig. 1B). Laboratory findings including complete blood count and peripheral blood smear were unremarkable. A gastric biopsy was performed, and the patient was diagnosed with low-grade marginal zone B-cell lymphoma of the MALT type (Ann Arbor stage IE1) that was *H. pylori* positive (Fig. 2). Anti-*Helicobacter* antibiotics were administered for 2 weeks. *H. pylori* eradication was confirmed by a urea breath test after 4 weeks. However, after 5 months, follow-up endoscopic examination revealed no change in the polypoid mass (Fig. 3A, B). In histologic examination, The Wotherspoon...
Fig. 1. Initial upper gastrointestinal endoscopic and abdominal computed tomography images. (A) The endoscopic view of polypoid mass on the greater curvature of the upper body in stomach. (B) The abdominal pelvic computed tomography showed a 1.7 cm sized polypoid mass on greater curvature of upper body in stomach and no regional lymph node enlargement.

Fig. 2. Histologic finding. (A) Lymphoid follicle and atypical lymphocytes were infiltrated in mucosa layer (H&E, ×40). (B) Neoplastic lymphocytes invaded the epithelial lining with forming characteristic lymphoepithelial lesion (H&E, ×200). (C) Immunostain for cytokeratin to highlight lymphoepithelial lesions was positive (×200). (D) Atypical lymphoid cells diffusely positive for CD20 (×40).
histological score was 5 suggesting non-response. We recommended waiting and watching or radiotherapy, but the patient refused them. And also, he had bad feeling for chemotherapy or surgery. Because of no early response to *H. pylori* eradication, the possibility of the presence of a high-grade lymphoma component, the proximal location of the tumor, and the exophytic type, we cannot but think it might have poor response to *H. pylori* eradication therapy. So we decided to perform EMR for complete resection. EMR was performed successfully (Fig. 3C). The resected specimen revealed that a lymphoid follicle and atypical lymphocytes was infiltrated in mucosa layer and neoplastic lymphocytes invaded the epithelial lining with forming characteristic lymphoepithelial lesion. No visible tumor cells on marginal area were seen. It is consistant with low-grade MALT lymphoma. After EMR, follow-up endoscopic examination showed no mass in the stomach (Fig. 4). And follow-up biopsy showed Wotherspoon histological score 1 chronic gastritis without no residual tumor cells suggesting complete remission. The patient has been doing well for the last 15 months.

**DISCUSSION**

The stomach is the most common site of MALT lymphoma. The incidence of primary gastric lymphoma has increased in recent years, but it is a rare disease. There are three patterns of appearance on endoscopy: a tumor-like appearance with a polypoid mass (exophytic type); ulceration or multiple small erosions (ulcerative type); and large, nodular, sometimes giant folds (hypertrrophic type). However, these patterns are not specific for MALT lymphoma, and they can also be found in gastritis and gastric adenocarcinoma. Suekane et al. suggested the usefulness of EMR in cases of an obscure diagnosis through conventional forceps biopsy and Taal et al. reported histologic discrepancies between forceps biopsy and EMR in the diagnosis of MALT lymphoma (25% in low-grade cases and 21% in high-grade cases). Therefore, EMR has been used for a more accurate diagnosis of gastric lymphoma.

The importance of *H. pylori* in the development of MALT lymphoma is already well known. The prevalence
of *H. pylori* infection in gastric MALT lymphoma is almost 90%, and *H. pylori* eradication is effective in treating approximately 80% of patients with low-grade MALT lymphoma.\(^9,12\) The time between *H. pylori* eradication and complete remission of gastric MALT lymphoma can vary. Complete remission of gastric MALT lymphoma after *H. pylori* eradication can take even longer than 12 months.\(^12\) Therefore, most protocols recommend to wait at least for 12 months after successful eradication therapy before a non-responder is defined and second-line therapy is applied. But, in most patients, the response after *H. pylori* eradication is rapid and can be observed even in the first month.\(^9,13\)

Generally, a surgery, chemotherapy, and radiotherapy and so on have been performed as a second-line therapy.\(^3,12\) However, for gastric MALT lymphoma that does not respond to *H. pylori* eradication, the treatment modality is not yet established.\(^3,12\) Radiotherapy has been known most suitable treatment with 97% remission rate, but the optimal dose, patient characteristics and relative role of it are not well defined. Radical gastrectomy has significant morbidity and is not optimal in many patients. Chemotherapy has been reported to have 85% remission rate that is lower than radiotherapy or surgery.\(^14,15\) Thus, treatment should be individualized based on lymphoma type, stage, *H. pylori* status and quality of life.\(^6\)

Histological responses were graded using the Wotherspoon histological score, considering scores 0~2 to be a complete regression, score 3 to be a partial remission and scores 4~5 to be no response. A persistence score of 5, mainly characterized by the presence of lymphoepithelial lesions after antibiotics treatment was the criterion for tumor resistance to therapy.\(^7\)

Various predictive factors for resistance to *H. pylori* eradication in gastric MALT lymphoma have been reported, such as absence of *H. pylori* infection, advanced stage, high-grade lymphoma, endoscopic exophytic type, involvement of the submucosa or perigastric lymph nodes, a proximal tumor location in the stomach, the presence of t (11;18) (q21;q21), and tumors with greater than 50% CD19-and CD20-positive cells.\(^3,16-20\)

In our case, the patient had an exophytic-type MALT lymphoma mass in the proximal portion of his stomach. Despite *H. pylori* eradication, there were no changes in the endoscopic mass or histologic tumor cells after 5 months. No early response to *H. pylori* eradication, the possibility of the presence of a high-grade lymphoma component, the proximal location of the tumor, and the exophytic type suggest un-response to *H. pylori* eradication therapy. We recommended waiting and watching or radiotherapy, but the patient refused them. And also, he had bad feeling for chemotherapy or surgery. Recently, EMR has been known to be a supplementary treatment modality for local control of the gastric MALT lymphoma.\(^16\) After sufficient discussion with the patient, we decided to perform EMR for complete resection. We thought that if complete resection would not be achieved, reduction of the tumor burden could be got. And we get the complete remission by EMR. After 15 months, there was no mass on endoscopy and no tumor cells on histology. The patient has been doing well for the past 15 months.

The role of EMR has not yet established in treatment of gastric MALT lymphoma. However, like in our case, EMR might be another treatment option of gastric MALT lymphoma. Of course, it is required a large-scale and a prospective study for EMR.

Therefore, we suggest that endoscopic resection might be of use to supplementary treatment for obscure diagnosis and persistent endoscopic masses after *H. pylori* eradication.

### REFERENCES

5. Wotherspoon AC, Ortiz-Hidalgo C, Falzon MR, Isaacson PG.