

A Case of Rectal Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma Treated Twice with Antibiotic Therapy for *Helicobacter pylori*

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Abstract

Background: The effectiveness of treatment with antibiotic for mucosa-associated lymphoid tissue (MALT) lymphoma in the stomach has been widely recognized in the last few decades. On the other hand, MALT lymphoma of the rectum is rare, and some literature has reported the usefulness of eradication of *Helicobacter pylori*, but the standard method of treatment has not been established.

Case presentation: A 72 year old woman was referred to our department with submucosal tumor of the rectum. Colonoscopy revealed three flat elevation lesions on the right wall of the lower rectum and positron emission tomography-computed tomography (PET-CT) showed accumulation of fluorodeoxyglucose (FDG) in the same area. Pathological examination was compatible with MALT lymphoma. She was diagnosed with rectal MALT lymphoma. *H. pylori* infection was evaluated by gastrointestinal fiber and anti *H. pylori* IgG antibody serology, and her stomach was infected with *H. pylori*. Under her consent, we selected *H. pylori* eradication therapy as the first-line treatment. After first-line treatment, eradication of *H. pylori* was unsuccessful and the tumor had reduced in size but had not disappeared. We prescribed second-line treatment drugs and her tumor had disappeared completely and she had become negative for *H. pylori*. Now, she has no recurrence five years after the treatment.

Conclusion: We treated a case of rectal MALT lymphoma with antibiotic therapy twice. Eradication of *H. pylori* was as useful for the rectum MALT lymphoma as it is for gastric MALT lymphoma. There are some reports that describe methods of treatment: surgical removal, medication, radiation, chemotherapy, and some cases had received more invasive therapy like surgical removal, radiation, and chemotherapy. In those cases, there were some instances in which medication was unsuccessful so the treatment was changed to more invasive therapy. There are controversial points about appropriate amount of time needed to determine additional treatment and the criteria for determination. Due to this lack of clarity, we reviewed the literature and speculate about them. We want to emphasize the point that administering antibiotic therapy twice or more might be useful to cases that did not respond to first line treatment and therefore had to receive more invasive therapy. Antibiotic treatment has fewer side effects than other types of therapy, so if it is useful, patients receive great benefits.

Keywords: MALT lymphoma; Rectum; *Helicobacter pylori*; Eradication

Introduction

Mucosa-associated Lymphoid Tissue (MALT) lymphoma, also called extra nodal marginal zone lymphoma, starts in tissues or organs outside of the lymph nodes and originates from B-cells in the marginal zone. They account for a small percentage of all cases of non-Hodgkin lymphoma, and can be commonly seen in the stomach, but also occur in other parts of the gastrointestinal tract. Isaacson and Wright firstly reported MALT lymphoma in 1983 [1], and treatment for cases in the stomach is well developed. Gastric MALT lymphoma has shown to be closely related to *H. pylori* infection [2-6], and antibiotic treatment to eradicate *H. pylori* is currently well recognized as the first line therapy for stage 1 or 2-1 (Lugano staging system) gastric MALT lymphoma. On the other hand, primary rectum MALT lymphoma is rare [7,8], and a standard therapy has not yet been established. There are some reports about rectum MALT lymphoma which provides us various treatment options, such as surgical removal, medication, radiation and

chemotherapy [9], including some which claim that antibiotic treatment for *H. pylori* is as effective for rectum MALT lymphoma as it is for gastric MALT lymphoma [10].

Recently, patients with early stage of rectum MALT lymphoma tend to receive antibiotic therapy as the first line treatment because it has fewer side effects than other types of treatment. Although eradication therapy often works well for rectum MALT lymphoma, if it results in failure, more invasive treatment is selected. In this case, we treated a case of rectal MALT lymphoma with antibiotic therapy twice. There are a few cases in which eradication therapy is administered for rectum MALT lymphoma twice or more, and tumors have regressed completely. There is a possibility that even if first-line medication is unsuccessful, the disease may respond to second-line medication and patients can avoid receiving more invasive treatment.

Case Presentation

A 72 year old woman was referred to our hospital with submucosal tumor of the rectum. Colonoscopy revealed three flat elevation lesions

on the right wall of the lower rectum (Figure 1). Endoscopic ultrasonography, performed with 12 MHz, showed hypoechoic tumors of second mucosal layer. Biopsy specimens showed infiltration of centrocyte-like cells within the lamina propria and lymphoepithelial lesions (Figure 2). Immunohistochemistry revealed that the specimens were positive for CD20, CD79a and Bcl-2 (Figure 3), but negative for CD5 and CD10. Positron emission tomography-computed tomography (PET-CT) showed accumulation of fluorodeoxyglucose (FDG) in the same area (Figure 4). Computed tomography was also performed, and no metastatic lesion was detected.



Figure 1: Colonoscopy revealed three flat elevation lesions on the right wall of the lower rectum.

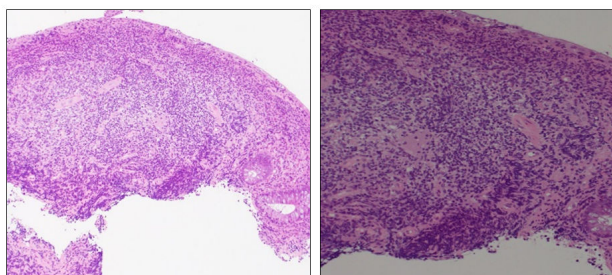


Figure 2: Biopsy specimens showed infiltration of centrocyte-like cells within the lamina propria and lymphoepithelial lesions.

Three months later, we performed colonoscopy and checked for infection. Although tumor of rectum was reduced in size, it did not disappear and she was still infected with *H. pylori*. To treat the tumor completely and to eradicate *H. pylori*, we performed second-line treatment with oral lansoprazole at 60 mg/day, oral amoxicillin (AMPC) at 1500 mg/day, and oral metronidazole at 500 mg/day. Three months after the second-line treatment, we performed colonoscopy, and tumor of rectum was flattened (Figure 5). Biopsy specimens showed no MALT lymphoma. In addition, *H. pylori* infection disappeared after the patient received eradication therapy twice. Now, she has no recurrence five years after the second-line medication. Rectum MALT lymphoma of clinical stage I (Lugano staging system)

was diagnosed. Biopsy specimens from the gastric mucosa revealed *H. pylori* infection and anti *H. pylori* IgG antibody was high. Under the patient's consent, she received *H. pylori* eradication therapy as first-line treatment. We used triple therapy of oral lansoprazole at 60 mg/day, oral amoxicillin (AMPC) at 1500 mg/day, and oral clarithromycin (CAM) at 400 mg/day.

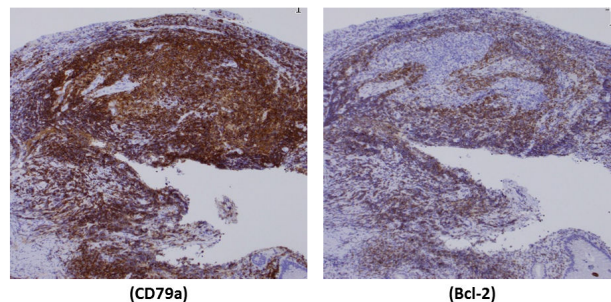


Figure 3: Immunohistochemistry revealed that the specimens were positive for CD20, CD79a, and Bcl-2, but negative for CD5 and CD10 (not shown).

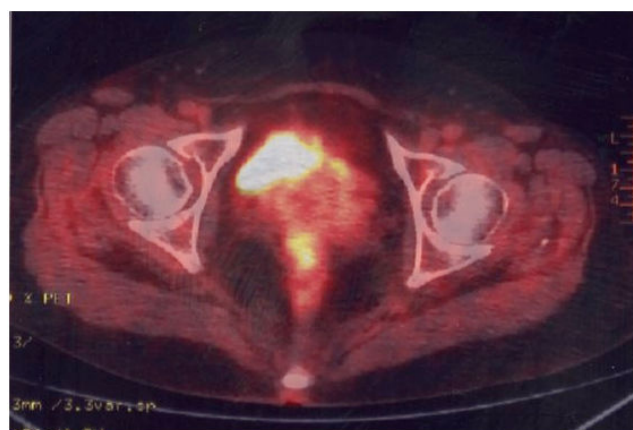


Figure 4: PET-CT showed accumulation of fluorodeoxyglucose (FDG).

Discussion

The association of gastric MALT lymphoma with *H. pylori* has been widely recognized and antibiotic therapy, which is now first-line treatment, has been established for the early-stage of gastric disease. Furthermore, after Matsumoto et al. first reported the effectiveness of *H. pylori* eradication therapy for rectum MALT lymphoma in 1997 [11], some cases have reported the possibility that antibiotic therapy for *H. pylori* is as effective for rectum MALT lymphoma as it is for gastric MALT lymphoma. Interestingly, some of these cases have reported that rectum MALT lymphoma has responded to antibiotic therapy regardless of whether patients are infected with *H. pylori* or not [12-16]. This fact indicates an unspecified pathogen other than *H. pylori* but its detail is not well proved. Now, although the standard treatment for rectum MALT lymphoma has not been established, it has been recognized that antibiotic therapy for rectum MALT lymphoma

has a certain effect and patients with early-stage rectum disease frequently receive antibiotic therapy because it has fewer side effects than other treatment such as surgical removal, radiation and chemotherapy.

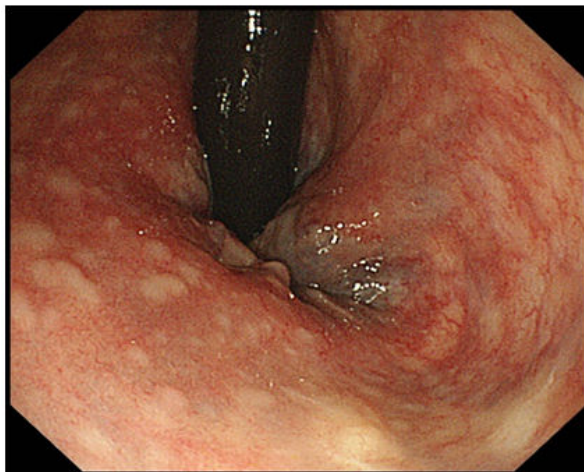


Figure 5: Colonoscopy performed 3 months after the second-line treatment showing flattened tumor.

In this case, we used eradication therapy for primary rectum MALT lymphoma. Tumor had reduced in size three months after first antibiotic therapy, and we determined to perform additional antibiotic therapy. Firstly, the appropriate amount of time to consider whether other treatment should be performed or not, instead of first-line treatment, has not been decided. Neubauer et al. reported that the median time of gastric MALT lymphoma to reach a complete remission from the start of therapy was 5.5 months [17]. Also, Takashi et al. reported the period of ten cases in which rectum MALT lymphoma had been treated with antibiotic therapy and the mean period was 116.5 days (10 days to 365 days) [18]. These reports indicate that even if patients were judged to receive other more invasive treatment because eradication therapy was unsuccessful, these diseases might achieve a complete remission without additional invasive therapy. In these cases, to perform antibiotic therapy twice or more might be useful. Secondly, are there any criteria to distinguish between responder and non-responder to eradication therapy? Liu et al. proposed the t(11;18)(q21;q21), which results in a chimeric transcript between the AP12 and MLT genes [19]. In their report, the AP12-MLT transcript was detected in nine (75%) of 12 patients non-responsive to antibiotic therapy but not in responsive patients. Other researchers also reported the usefulness of the t(11;18)(q21;q21) [20,21]. There is a high possibility that we can predict disease resistance to antibiotic therapy by checking the t(11;18)(q21;q21). When antibiotic therapy ends in a failure, these facts may help us to determine whether to change antibiotic therapy to other treatment or not.

Conclusion

Eradication of *H. pylori* was as useful for the rectum MALT lymphoma as it is for gastric MALT lymphoma. We want to emphasize the point that administering antibiotic therapy twice or more might be useful to cases that did not respond to first line treatment and therefore

had to receive more invasive therapy. Antibiotic treatment has fewer side effects than other types of therapy, so if it is useful, patients receive great benefits.

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