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A case of *Helicobacter pylori* negative low-grade gastric MALT lymphoma in an elderly female, successfully treated with rituximab

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 91
Final Diagnosis: Low-grade gastric MALT lymphoma
Symptoms: Recurrent epigastric and right upper quadrant discomfort
Medication: Rituximab
Clinical Procedure: esophagogastroduodenoscopy • gastric biopsy
Specialty: Gastroenterology

Objective: Unusual or unexpected effect of treatment





Background: Mucosa associated lymphoid tissue (MALT) lymphoma can occur in any extranodal organ or tissue, stomach being the common site. Most of the gastric MALT lymphomas are related to chronic *H. pylori* infection. *H. pylori* negative gastric MALT lymphoma is relatively uncommon and usually treated with a short course of chemotherapy, radiotherapy or surgery.

Case Report: Herein, we present a case of an elderly female with *H. pylori* negative, low-grade gastric MALT lymphoma that was successfully treated with a short course of rituximab.

Conclusions: This case report emphasizes that rituximab monotherapy can be an effective treatment for *H. pylori* negative low grade gastric MALT lymphoma especially in an elderly patient where surgery or radiotherapy may not be appropriate.

Key words: Mucosa Associated Lymphoid Tissue (MALT) • gastric lymphoma • chemotherapy • rituximab • surgery • radiation

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Background

The prevalence of *H. pylori* infection is approximately 90% in low-grade gastric MALT lymphoma [1]. In many cases, it is associated with other species of *Helicobacter* such as *H. felis* or *H. heilmannii* and hence true *H. pylori* negative gastric MALT lymphoma is a relatively uncommon diagnosis [2]. Among the available treatment options, such as radiotherapy, chemotherapy and surgery, our patient went into complete remission with a six-week course of rituximab therapy. However, it has been described in the literature that *H. pylori* eradication therapy can still be considered even in *H. pylori* negative MALT lymphoma [3].

Case Report

A 91-year-old Caucasian woman with past history of gastric ulcer thought to be secondary to aspirin usage 1 year prior to presentation and tubulovillous adenoma of the cecum presented to the emergency department complaining of recurrent epigastric and right upper quadrant discomfort. She also reported melena, fatigue and lightheadedness of several days duration. She denied nausea, vomiting, fever, chills, night sweats and weight loss. She was a lifetime non-smoker and denied any prior alcohol and recreational drug use. She denied any exposure to hazardous chemicals in the past. Family history was significant for a son diagnosed with colon cancer at the age of 45 years. Physical examination revealed normal vital signs. There was no evidence of lymphadenopathy, thyromegaly or mass. Abdominal examination revealed a soft, non-tender abdomen without hepatosplenomegaly. Digital rectal examination revealed hemoccult positive brown stool. Heart, lungs and neurological examinations were normal.

Laboratory findings revealed WBC count 7000/ μ L, platelets 247000/ μ L, Hemoglobin 11.2 gm/dL, sodium 137 meq/L, potassium 3.9 meq/L, bicarbonate 28 meq/L, Blood urea nitrogen (BUN) 7 meq/L, creatinine 0.75 mg/dL, blood sugar 98 mg/dL, bilirubin 0.6 mg/dL, AST 33 U/L, ALT 39 U/L and lipase 25 U/L. HIV 1 and 2 antibodies were negative. *H. pylori* IgG and IgM antibodies including cytotoxin-associated gene product A (Cag A) were negative. *H. pylori* stool antigen was also negative.

Esophagogastroduodenoscopy (EGD) revealed a 3 cm non-healed gastric ulcer with smooth base but elevated borders in the lesser curvature of the stomach in the same location as it was found the year prior. Abdominal CT scan showed gastric wall thickening without any evidence of metastatic disease elsewhere. Histopathological examination of the biopsy specimen revealed dense lymphoid infiltration consistent with low-grade gastric MALT lymphoma (Figures 1–3); however culture and rapid urea test for *Helicobacter pylori* were negative, as they had been at the time of the initial finding of the ulcer the year prior.

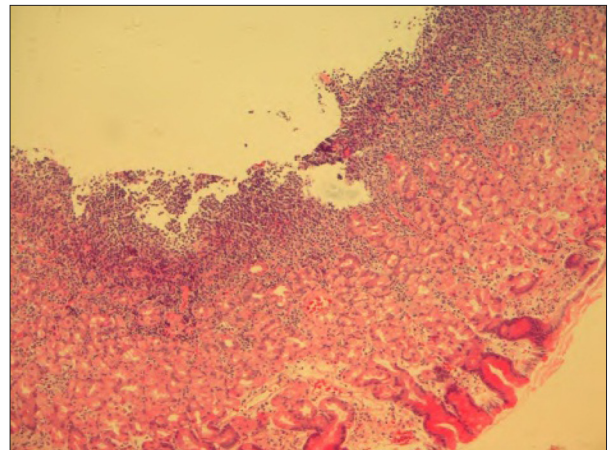


Figure 1. Gastric body mucosa at 10 \times H&E stain showing dense lymphoid infiltrate.

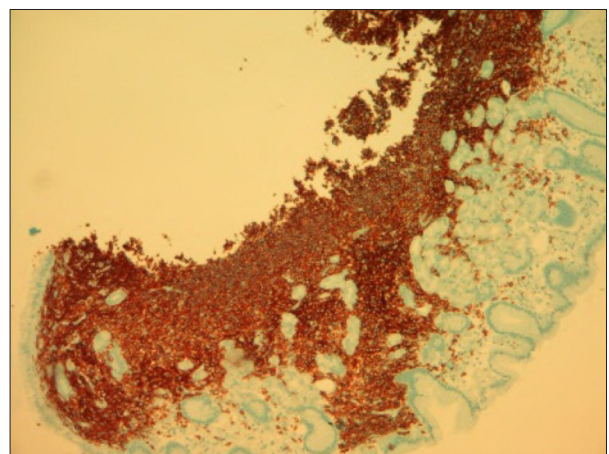


Figure 2. Gastric body mucosa at 10 \times immunohistochemistry for CD20 showing strongly positive staining in the B lymphocytes of MALT lymphoma.

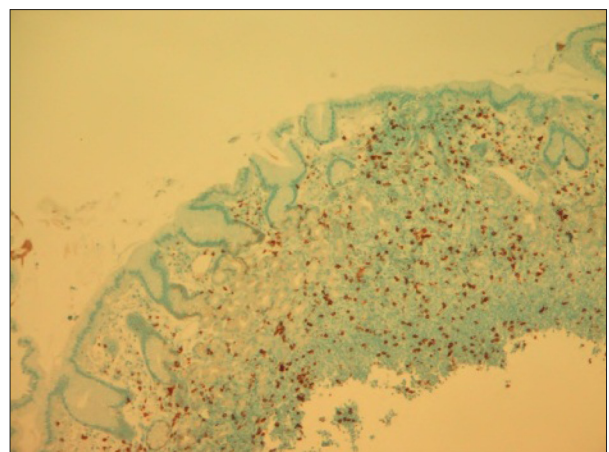


Figure 3. Gastric mucosa at 10 \times immunohistochemical stain for CD5 showing reactive T cells positively staining and negative staining in the B lymphocytes.

The patient was treated with pantoprazole 40 mg per oral twice daily, iron 364 mg once daily, and rituximab 375 mg/m² intravenous infusion once weekly for 6 weeks with gradual improvement in clinical symptoms. She did not have any side effects associated with rituximab. On follow up exam 3 months later, she was completely asymptomatic and her repeat EGD with biopsy was normal. Abdominal CT scan was negative for any mass and lymphadenopathy.

Discussion

MALT (Mucosa Associated Lymphoid Tissue) lymphoma was first described by Isaacson and Wright in 1983 [4]. MALT lymphoma can occur in any extranodal organ or tissue [5]. The incidence of Gastric MALT lymphoma is increasing and currently represents about 40% of all gastric lymphoma [6]. Most of the gastric MALT lymphoma are related to chronic *Helicobacter pylori* infection [7]. It has been incorporated into WHO lymphoma classification as marginal zone B-cell lymphoma of MALT-type [8]. Almost 5 to 10% of gastric MALT lymphomas are *H. pylori* negative and there is no clear explanation of its pathogenesis [9].

Though clinical presentation of low-grade gastric MALT lymphoma is vague and variable, most of the patients present with abdominal pain, dyspepsia, vomiting and gastric bleeding [10,11]. Our patient presented with epigastric discomfort, gastrointestinal bleeding as evidenced by hemoccult positive stool, fatigue and lightheadedness.

Every case of gastric MALT lymphoma must be tested for *H. pylori* infection by routine biopsies and/or rapid urease test, as approximately 90% of the cases are associated with it [7,8]. It has also been postulated that reduced number of *H. pylori* bacteria present in the infection may account for negative *H. pylori* and false negative results may be obtained if only one diagnostic test is utilized [12,13]. Diagnosis is confirmed by at least two negative tests for *H. pylori* as per the European guidelines [14]. If it turns out to be negative, serological analysis for *H. pylori* IgG antibodies and cytotoxin-associated gene product A (CagA) should be performed to identify truly negative gastric MALT lymphoma as there is a different therapeutic approach [8,15]. At the same time, other *Helicobacter* species such as *H. felis* or *H. heilmannii* should be excluded as treatment of these infections completely cure gastric MALT lymphoma [16,17]. EGD may reveal ulcerative, exophytic or

infiltrative lesions [8]. EGD combined with endoscopic ultrasound or CT scan is employed for the accurate determination of extent of gastric wall involvement or involvement of perigastric lymph nodes [8,18].

H. pylori eradication therapy is the first-line therapy for *H. pylori* positive gastric MALT lymphoma but its role in *H. pylori* negative gastric MALT lymphoma remains controversial. *H. pylori* eradication therapy has been described in limited studies as initial therapy even in *H. pylori* negative gastric MALT lymphoma especially with a single lesion [3,12]. There is still no clear explanation for the effectiveness of *H. pylori* eradication therapy in *H. pylori* negative gastric MALT lymphoma [19]. Treatment options include chemotherapy with a short course of rituximab, radiation therapy, or, rarely, surgery in *H. pylori* negative gastric MALT lymphoma [6,20]. Several studies have shown more than 90% five year survival rate with surgical resection alone in low grade gastric MALT lymphoma which is also useful to obtain accurate clinicopathological staging [21–23].

Although there are no specific guidelines available in the current literature, rituximab can be offered as a monotherapy for a low grade gastric MALT lymphoma, especially in an elderly patient who cannot tolerate radiotherapy, surgery or conventional combined chemotherapy.

Conclusions

True *H. pylori* negative gastric MALT lymphoma can be diagnosed by at least two negative tests for *H. pylori*. Based upon our case report, rituximab monotherapy can be one of the treatment options for the condition with low side effect profile. However further study is required to develop the definitive guidelines for the management.

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Competing interests

The authors have no competing interest and no financial disclosure to make.

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