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Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma of the Colon: A Case Report and a Literature Review

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, 56
Final Diagnosis: Colonic MALT lymphoma
Symptoms: Epigastric pain
Medication: —
Clinical Procedure: Colonoscopy and biopsy
Specialty: Gastroenterology and Hepatology

Objective: Rare disease

Background: Non-Hodgkin lymphoma (NHL) is a well-known hematologic malignancy. The gastrointestinal (GI) tract is the most commonly involved extra nodal site. MALT lymphomas are uncommon, accounting for 5% of all NHL. Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is the prototype seen in association with *Helicobacter pylori*. Colonic MALT lymphoma is rare and comprises only 2.5% of the MALT lymphomas. Its etiology and treatment is not well established.

Case Report: A 56-year-old Hispanic woman presented to the clinic with symptoms of chronic epigastric pain for the past three years and a 13-pound weight loss over the past two months. The patient did not have any prior medical conditions. Her systemic examination was unremarkable, while her routine labs revealed mild anemia. An upper endoscopy and colonoscopy for colorectal cancer screening were performed revealing erosive gastropathy with duodenal ulcers and a 5 cm broad based polypoid mass in the hepatic flexure respectively. Computed tomography (CT) of the abdomen revealed a round, well demarcated mass at the hepatic flexure of the colon. The histopathology and immunophenotyping were consistent with extra nodal marginal zone of MALT lymphoma. Stool testing for *H. pylori* was positive. The patient received two weeks of *H. pylori* eradication therapy and four cycles of rituximab. Repeat colonoscopy after completion of chemotherapy showed complete resolution of the MALT lymphoma.

Conclusions: Unlike gastric MALT lymphoma, treatment of colonic MALT lymphoma is not standardized. Chemotherapy and surgical resection have been utilized to successfully treat it. Only a handful of cases have reported successful treatment of colonic MALT lymphoma with rituximab monotherapy.

MeSH Keywords: Colonic Neoplasms • Gastrointestinal Neoplasms • *Helicobacter pylori* • Lymphoma, B-Cell, Marginal Zone

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/902843>

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Background

Non-Hodgkin Lymphoma (NHL) has an extra nodal presentation in about one third of cases. The gastrointestinal (GI) tract is the most commonly involved extra nodal site, particularly the stomach [1–4]. Lymphoma of the mucosa-associated lymphoid tissue (MALT) and diffuse large B cell lymphoma (DLBCL) are the two most common varieties of the lymphomas involving the GI tract [5]. MALT lymphomas are uncommon, accounting for 5% of all NHL [6,7] and gastric MALT lymphoma is the prototype of this group [8], seen in the setting of chronic inflammation and is associated with *Helicobacter pylori* infection [9,10]. Colonic MALT lymphoma is a rare entity, and comprises only 2.5% of MALT lymphomas [7,11]. The etiology and treatment is not well established. We report here on a case of MALT lymphoma of the colon successfully treated with chemotherapy.

Case Report

A 56-year-old Hispanic woman presented to the gastroenterology clinic of our hospital to schedule her screening colonoscopy. During the visit, she also reported chronic epigastric pain for the past three years. The patient had been generally well without any prior medical conditions until three years ago when these symptoms began. She described the pain as localized to the epigastric region, crampy, intermittent without any precipitating factors. There was no association with intake of food or bowel movement but symptoms were relieved sometimes with histamine receptor-2 blockers or proton pump inhibitors.

There was no nausea, vomiting, diarrhea, constipation, fever, early satiety, or appetite changes. However, she reported a 13 pound weight loss over two months. There was no history of smoking, alcohol use or illicit drug use. The patient did not have a personal history of hepatitis C, autoimmune diseases, or colon carcinoma. Her uncle and grandfather had a history of cancer. Premedication included calcium and vitamin D supplements, and ranitidine.

On examination, her temperature was 36.6 °C, her blood pressure was 117/70 mm Hg, her pulse rate was 72 beats per minute, and her respiratory rate was 14 breaths per minute. Her abdomen was non distended, soft, with mild tenderness in the epigastrium, and her bowel sounds were normal. The rest of the systemic examination was unremarkable. Results of laboratory parameters are given in Table 1.

Computed tomography (CT) of abdomen and pelvis was performed after intravenous administration of contrast material and it revealed a round, well demarcated soft tissue focus associated with the hepatic flexure of the colon (3.9×2.7×3.2 cm) (Figures 1, 2). An upper endoscopy and colonoscopy were performed. The upper endoscopy revealed few nonbleeding gastric antrum erosions and multiple clean based duodenal ulcers. The colonoscopy revealed a 4 cm broad based polypoid mass in the hepatic flexure (Figure 3), and two diminutive rectal polyps. Histopathologic examination of the gastric antrum erosions biopsy revealed chronic gastritis and inflammation (CLO test negative). The rectal polyps were hyperplastic in nature, and the biopsy specimen from the hepatic flexure mass revealed colonic mucosa with dense lamina propria infiltrates of small

Table 1. Initial laboratory work-up.

Parameter	Initial laboratory results	Reference range	Parameter	Initial laboratory results	Reference range
Hemoglobin(g/dl)	12.1	12–16	Blood urea nitrogen (mg/dL)	20	6–20
Hematocrit (%)	34.9	42–51	Creatinine (mg/dL)	0.7	0.5–1.5
Platelet count (k/ul)	259	150–400	Total protein (g/dL)	8.3	6–8.5
White blood cell count (per mm ³)	6.8	4.8–10.8	Albumin (g/dL)	4.7	3.2–4.8
Sodium (mEq/L)	137	135–145	Alanine transaminase (U/L)	22	5–40
Potassium (mEq/L)	4.1	3.5–5.0	Aspartate transaminase (U/L)	28	9–48
Bicarbonate (mEq/L)	29	24–30	Alkaline phosphatase (U/L)	190	53–141
Chloride (mEq/L)	99	98–108	Bilirubin Total (mg/dL)	0.3	0.2–1.2
Calcium (mEq/L)	9.4	8.5–10.5	Bilirubin Direct (mg/dL)	0.1	0.2–1.2
Glucose (mg/dL)	91	70–120	Lipase (U/L)	42	<61

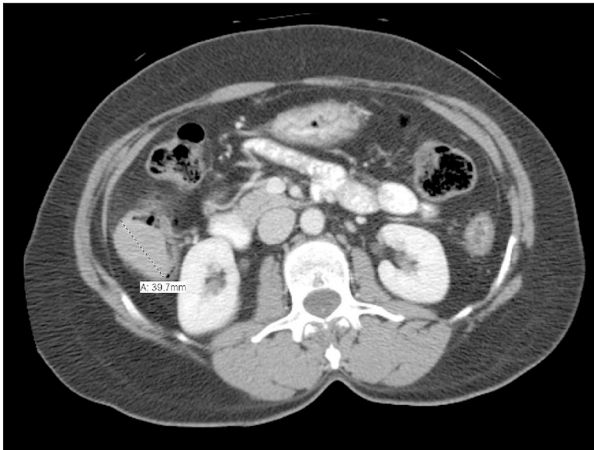


Figure 1. Computed tomography (CT) of abdomen (horizontal view) showing a colonic mass at the hepatic flexure (size appreciated with the help of a ruler).

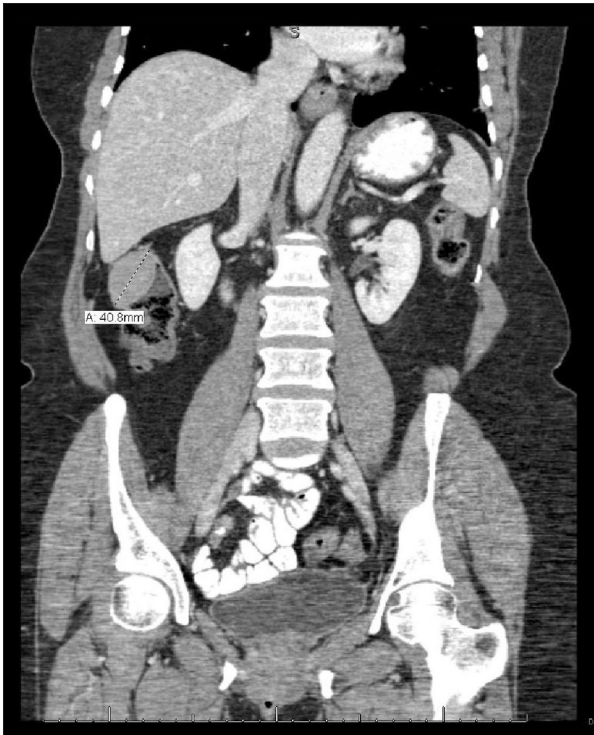


Figure 2. Computed tomography (CT) of abdomen (coronal view) showing a colonic mass at the hepatic flexure (size appreciated with the help of a ruler).

to medium sized lymphocytes extending into the submucosa, focal lymphoepithelial lesions, and plasma cells (Figure 4). Immunohistochemical stains of the biopsy specimen showed extensive infiltrates of B cells positive for CD20 (Figure 5), CD79a, and CD19. The immunophenotyping and the morphological findings were consistent with extra nodal marginal zone of MALT lymphoma. Biopsies obtained during the upper endoscopy did not reveal *H. pylori*; however, stool testing was



Figure 3. Colonoscopic image of hepatic flexure MALT lymphoma.

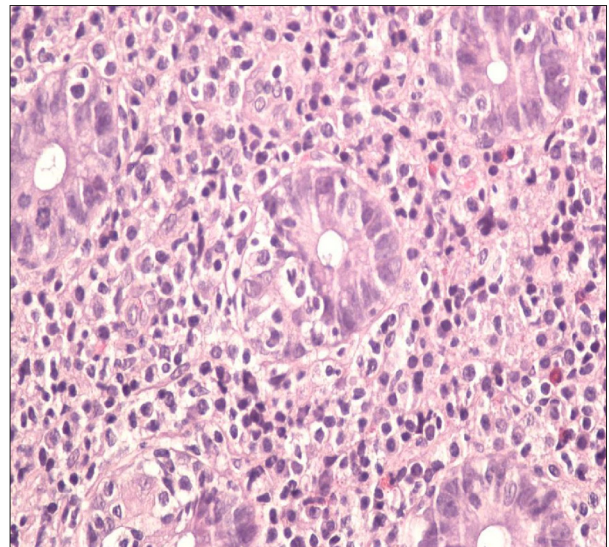


Figure 4. MALT lymphoma involving colon. There is a diffuse infiltrate comprised of small to medium sized lymphocytes with monocytoid features and plasmacytoid cells.

positive, which was checked later during the course of treatment. Bone marrow biopsy was performed for further staging and was found to be negative for any neoplastic process. The patient received two weeks of antibiotic therapy comprising of amoxicillin, clarithromycin with a proton pump inhibitor for *H. pylori*, and four cycles of rituximab. Repeat stool testing for *H. pylori* four weeks after completion of the course of antibiotics, confirmed eradication. Repeat colonoscopy after the completion of chemotherapy cycles showed complete resolution of the MALT lymphoma (Figures 6–8).

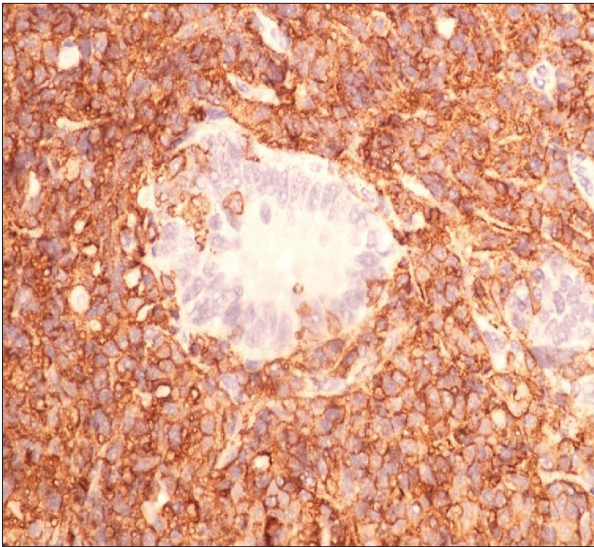


Figure 5. Immunostain CD20 show strong positivity in lymphoma cells.

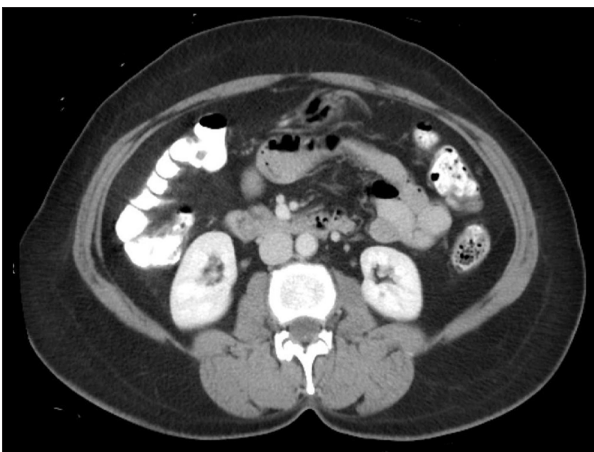


Figure 6. Computed tomography (CT) of abdomen (horizontal view) showing resolution of colonic mass at the hepatic flexure that was seen on previous imaging after completion of treatment with rituximab monotherapy.

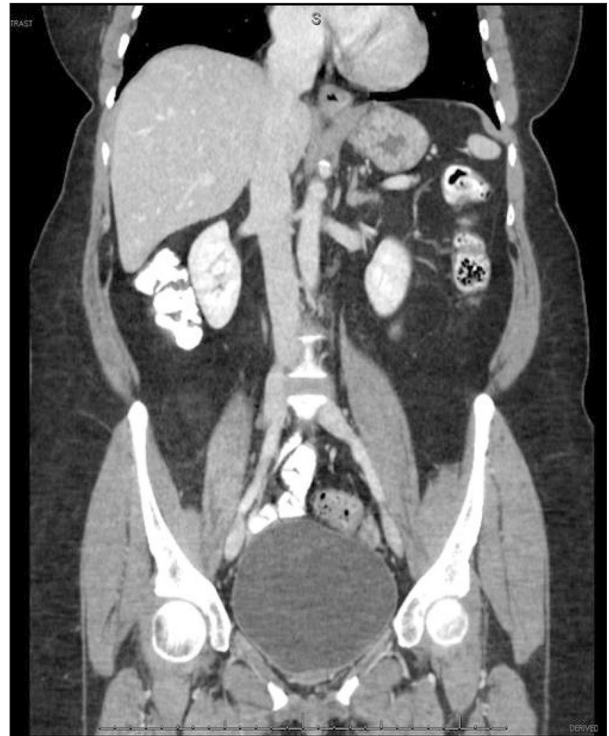


Figure 7. Computed tomography (CT) of abdomen (coronal view) showing resolution of colonic mass at the hepatic flexure that was seen on previous imaging after completion of treatment with rituximab monotherapy.

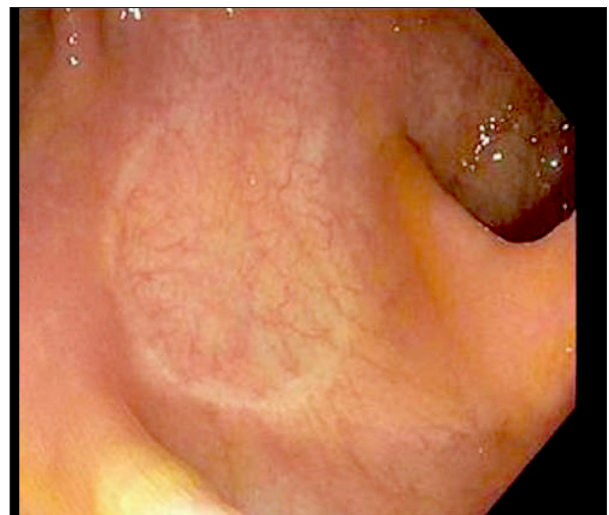


Figure 8. Endoscopic appearance of hepatic flexure after rituximab therapy completion.

Discussion

Disease incidence and prevalence

NHL is a common hematologic malignancy in the USA and worldwide. NHL has an extra nodal presentation in 25% to 33% of patients with GI tract being the most common site. Stomach is the most commonly involved part of the GI tract in about 50% of these cases [1–4], whereas small intestine is the most common site in Middle Eastern nations. Lymphomas of the GI tract include a variety of histologic subtypes: MALT lymphoma, DLBCL, Burkitt lymphoma, enteropathy-associated T-cell lymphoma, mantle cell lymphoma, and follicular lymphoma [5].

MALT or extra nodal marginal zone lymphoma comprises 5% of NHL [7]. MALT lymphoma was first described by Isaacson and Wright in 1983 [8] as a low grade B cell lymphoma involving extra nodal organs [7]. The most common site of occurrence of MALT lymphoma is the stomach in 60% to 75% of cases, followed by small intestine, ileum, cecum, colon, and rectum [12,13].

Involvement of the esophagus has also been reported [14], as well as the extra-intestinal sites including lungs, ocular adnexa, lung breast, and skin [6,8,15]. The colon is involved in only 2.5% of cases making it a rare entity, and to date only a handful of cases have been reported in the medical literature [7,11].

Demographics and etiology

MALT lymphomas are predominantly seen in the sixth decade of life. The mean age of presentation is 60 years. Although female predominance is seen in a 2: 1 ratio compared to males in some studies, there is no difference among the genders according to one review [11,16–18].

MALT lymphoma has two types, one that originates from normally present lymphoid tissue like Peyer patches in the gut and the second that arises from acquired lymphoid tissue that develops in response to inflammation in the setting of *H. pylori* infection or autoimmune disease [6]. Pathogenesis of gastric MALT lymphoma includes chronic antigenic stimulation by *H. pylori* and subsequent chronic inflammation that leads to proliferation of B cell in lymphoid tissue to MALT lymphoma. Association between extra-gastric MALT lymphoma of the small intestine and campylobacter jejuni infection has been reported [8,10]. Infectious etiology has not yet been established for colonic MALT lymphoma [6].

Clinical presentation

Primary colonic MALT lymphomas most commonly present with GI bleeding [11,16,17]. Abdominal pain, rare perforation [6,19], and intussusception have also been reported [20]. Isolated primary MALT lymphoma of the colon is seen less often. It is usually present with simultaneous occurrence at other sites in the GI tract [21]; therefore, at the time of diagnosis, synchronous lesions should also be ruled out. Staging for MALT lymphomas should include gastroscopy, colonoscopy, bone marrow biopsy, and CT of thorax and abdomen [6,15,22,23].

Endoscopic appearance

Endoscopic features of the MALT lymphoma of the colon are not well defined. Most often a single polypoid lesion is seen [7,24,25], but multiple polypoid lesions have also been reported [20]. Colonic MALT lymphoma may also present as an ulcer or a nodule [6,21,26].

Treatment

The association between gastric MALT lymphoma and chronic *H. pylori* infection is well established [5,9,10]. The mainstay of treatment for localized gastric MALT lymphoma is antibiotic therapy directed against *H. pylori* infection [27–29], with complete remission reported in 70% to 80% of cases [5,30–33].

If inadequate response or relapse occurs, irradiation of the stomach is indicated either alone or in combination with chemotherapy and surgery [5,34–37]. Advanced stage lymphoma requires treatment with radiotherapy or chemotherapy. If the tumor involves distant lymph nodes or extra nodal sites then the treatment comprises chemotherapy only.

Extra-gastric MALT lymphoma of the small intestine is associated with campylobacter jejuni infection [8,10], but no recommendations for testing or antibiotic treatment have been made as yet and further studies are needed [38]. Response to *H. pylori* eradication in these cases is variable [39,40]. In localized lymphomas of the small intestine, resection is the preferred treatment. In a few cases, localized disease has been successfully treated with radiotherapy [5,41–43]. In cases where surgical resection is not possible due to location or spread, chemotherapy with chlorambucil or rituximab with cyclophosphamide, vincristine, and prednisone is indicated.

For colonic MALT lymphoma there is no standardized therapy and the best treatment modality has long been debated. While most cases use surgery or chemotherapy as the first-line treatment, and rarely complete resolution with *H. pylori* therapy has been reported [17,40,44,45]. The chemotherapy regimen comprised of mitoxantrone, chlorambucil, and prednisone has been used to successfully treat colonic MALT lymphoma [46,47]. Other regimens are chlorambucil or rituximab with cyclophosphamide, vincristine, and prednisone [5,41–43]. More recently rituximab alone as a single agent has also been used in successful treatment of colonic MALT lymphoma [48–50]. Single agent or combination chemotherapy has shown a 50% response rate [10,51–53]. Besides surgical resection and chemotherapy; radiation and endoscopic resection have also been employed [17,54]. Curative endoscopic resection of a large polypoid MALT lymphoma after downsizing with radiotherapy has also been reported [10].

Conclusions

Colonic MALT lymphoma is a rare type of extra nodal NHL. Unlike the prototype gastric mucosa associated lymphoid tissue lymphoma, treatment for colonic variety is not standardized. Chemotherapy, as well as surgical resection, has been used to successfully achieve cure. Recently, rituximab was been reported as a promising treatment modality as monotherapy in a few case reports. Our case not only reports a rare disease presenting as a large mass as an unusual presentation, but also reports on the successful use of novel treatments, such as rituximab, in treating colonic MALT lymphoma without recurrence.

Disclosures

None.

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