

Mucosa-Associated Lymphoid Tissue Lymphoma of the Sigmoid Colon Discovered on Routine Screening Colonoscopy in Patient with Hepatitis C and *Helicobacter pylori* Infection

Rajiv Bhuta, MD¹, Michael Bromberg, MD, PhD², Ashish Bains, MD³, and Ron Schey, MD, FACP⁴

¹Department of Medicine, Temple University Hospital, Philadelphia, PA

²Department of Medicine, Section of Hematology/Oncology, Temple University Hospital, Philadelphia, PA

³Department of Pathology and Laboratory Medicine, Temple University Hospital, Philadelphia, PA

⁴Department of Medicine, Section of Gastroenterology, Temple University Hospital, Philadelphia, PA

ABSTRACT

Mucosa-associated lymphoid tissue (MALT) lymphoma is predominantly found in the stomach. Rarely, it is found in the proximal colon and even less so in the sigmoid colon. We present a rare case of primary sigmoid colon MALT lymphoma in a patient with concomitant *Helicobacter pylori* and hepatitis C infection. We also review current imaging, staging, and therapeutic modalities. To our knowledge, this is the first sigmoid colon MALT lymphoma reported in the United States.

INTRODUCTION

Mucosa-associated lymphoid tissue (MALT) lymphoma is a typically indolent subtype of non-Hodgkin lymphoma and is classified as an extranodal marginal zone B-cell lymphoma by the World Health Organization.¹ MALT lymphomas can occur in many locations, including the salivary glands, orbits, thyroid, lung, adnexa, and breast, but it is most often found in the stomach. Only rarely is it found in the colon, and then usually in the proximal colon or rectum.²⁻⁴ The sigmoid colon is rarely involved, and to our knowledge, this is the first reported case of sigmoid MALT lymphoma in the United States.^{5,6} Furthermore, gastric MALT lymphoma is classically seen in *Helicobacter pylori* infection while non-gastric MALT lymphomas have been associated with hepatitis C (HCV), *Borrelia burgdorferi*, *Chlamydia psittaci*, *Campylobacter jejuni*, and autoimmune disease.⁷

CASE REPORT

A 73-year-old man with past medical history significant for untreated HCV with liver cirrhosis and type 2 diabetes mellitus presented for routine screening colonoscopy. He was found to have a 2-mm pedunculated rectal polyp notable for tubular adenoma with low-grade dysplasia, and a 15-mm pedunculated sigmoid polyp, completely resected by hot snare (Figure 1). Pathology of the resected polyp demonstrated an expansile and vaguely nodular mucosal infiltration by small to intermediate-sized lymphocytes with pale cytoplasm, consistent with MALT lymphoma (Figure 2). Occasional lymphoepithelial lesions were identified. Immunohistochemical stains identified the neoplastic B-lymphocytes expressing CD20 and BCL2 with aberrant co-expression of CD43, while negative for CD10, CD5, and BCL1. Expanded follicular dendritic meshwork was marked by CD21 and light chain analysis by in-situ hybridization demonstrated a lambda skewed expression. Ki-67 showed a low proliferation rate <10%.

On follow-up examination, the patient's only complaint was decreased appetite, which had been present for years and was documented since at least 2011. He denied abdominal pain, nausea, vomiting, dysphagia, melena,

ACG Case Rep J 2016;3(4):e90. doi:10.14309/crj.2016.63. Published online: July 27, 2016.

Correspondence: Ron Schey, Section of Gastroenterology, Temple University Hospital, Philadelphia, PA 19122 (ron.schey@tuhs.temple.edu).



Copyright: © 2016 Bhuta et al. This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-nd/4.0>.



Figure 1. A single 15-mm pedunculated sigmoid colon polyp, resected with hot snare.

hematochezia, fevers, or night sweats. In 2011, he reported a 4.5-kg weight loss over the prior 3 years, but records indicate that he had since gained approximately 3 kg between 2011 and 2015 (BMI 21 kg/m²). Vital signs were normal and physical examination was unremarkable, with no peripheral lymphadenopathy, abdominal tenderness, or hepatosplenomegaly. Laboratory testing was notable for thrombocytopenia with platelets 122,000/uL and AST 51 U/L. Additionally, quantitative IgA and IgG were 602 mg/dL and 2,722 mg/dL, respectively, likely secondary to HCV cirrhosis. Uric acid was 8.3 mg/dL, LDH was normal, and tissue transglutaminase antibody was negative. HCV RNA viral load was 24,862 IU/mL. HIV was negative.

After post-colonoscopy follow-up, the patient underwent esophagogastroduodenoscopy (EGD), which revealed small (<5 mm) varices in the lower third of the esophagus and mild portal hypertensive gastropathy. Biopsies were positive for *H. pylori*, and the patient received eradication treatment with triple therapy. One month later, a positron emission tomography/computed tomography (PET/CT) demonstrated no sites of fluorodeoxyglucose hypermetabolic activity in the abdomen. CT with dilute barium did not show evidence for an anatomic lesion. Two mediastinal lymph nodes showed relatively low-grade fluorodeoxyglucose activity above mediastinal background, but they were not pathologically enlarged and likely represented inflammatory nodes. No other sites of fluorodeoxyglucose hypermetabolic activity raised concern for

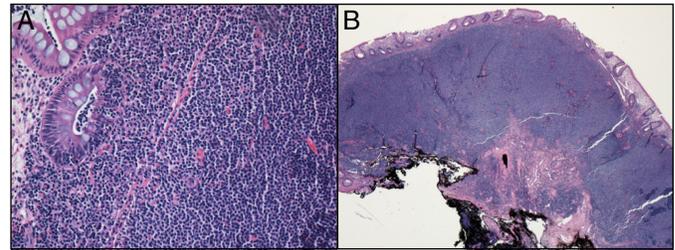


Figure 2. H & E section showing neoplastic lymphocytic infiltrate with pale cytoplasm. Glandular involvement/lymphoepithelial lesion is seen. (A) 40x magnification and (B) 2x magnification.

active nodal or extranodal disease. The patient is now asymptomatic and undergoing active surveillance with repeat colonoscopy in 4-6 months. He will undergo sofosbuvir and ribavirin treatment for HCV.

DISCUSSION

Primary colorectal lymphoma is a rare phenomenon, accounting for 10-20% of all gastrointestinal (GI) lymphomas, 2.5% of all lymphomas, and 0.2-0.6% of all colorectal malignancies.³ Rarer still is colorectal MALT lymphoma, which accounted for just 4% of all GI non-Hodgkin lymphoma over a 10-year period in one study.⁸ Sites of tumor growth have been reported to be the cecum (71.5%), rectum (16.9%), and ascending colon (6.2%); the sigmoid colon is only rarely affected.⁹

HCV has been linked to MALT lymphoma by epidemiological studies.¹⁰ Our patient's HCV infection may have contributed to the development of non-gastric MALT lymphoma via chronic antigenic stimulation, though again, not in the typical fashion. One study showed HCV infection in 35% patients with non-gastric MALT, with the skin, salivary gland, and orbit accounting for 75% of cases; bowel MALT lymphoma occurred in only 1%.¹⁰

Despite its rarity, the incidence of colonic GI non-Hodgkin lymphoma has increased nearly 5-fold since the 1990s, yet there is little consensus regarding its staging, treatment, and follow-up.^{8,11} The majority of recently published works regarding colorectal MALT lymphoma originate from Japan, Korea, and China; there is little known about the current state of the disease and its management in the United States.⁵

Clinical presentation of colonic MALT lymphoma can vary dramatically, ranging from patients who are asymptomatic to those with B symptoms, abdominal pain, and rectal bleeding, or even with frank bowel obstruction. Similarly, MALT lesions can have wide-ranging appearance on endoscopy. Reports include findings of pedunculated polyp, submucosal tumor, non-pedunculated polypoid mass, ulceration, nodule, or simple mucosal discoloration.^{2,3,12}

There is no current consensus on the optimal strategy for imaging, staging, or treatment of colonic MALT lymphoma. While some general recommendations exist, these are based on expert opinion and management is often highly individualized.¹³ Once an initial diagnosis is made, imaging can include chest/abdominal/pelvic CT, double-contrast barium enema, PET scan, capsule endoscopy, double balloon enteroscopy, and/or endoscopic ultrasound (EUS).¹³⁻¹⁵ Staging can also include bone marrow biopsy and/or flow cytometry.^{14,16} PET scans have generally not been recommended for evaluation of indolent lymphomas such as MALT lymphoma. However, a recent meta-analysis indicated that the pooled detection rate of MALT lymphoma by fluorine-18-fluorodeoxyglucose PET scan is 71%, though evaluation of the gut may be limited because of physiologically increased baseline uptake that may mask more indolent lesions.¹⁷

No studies have examined the efficacy of colonic MALT treatment modalities. However, for localized disease, polypectomy, eradication concomitant gastric *H. pylori* infection, or surgical resection tends to be first-line therapy, while chemotherapy is utilized for disseminated disease.^{2,13-15,18} MALT lymphoma is often treated with a rituximab-based regimen such as R-CHOP and radiotherapy to achieve complete remission without major complications.^{15,16}

Because our patient's MALT lymphoma was discovered on routine screening colonoscopy and the polyp was both small and easily resected, simple polypectomy was deemed to be sufficient initial therapy. He also has taken eradication treatment for *H. pylori* and will soon begin treatment for HCV, both of which should reduce his burden of antigenic stimulation. He will need continued close follow-up and surveillance for recurrence, which can range from 33 to 75%.¹³

DISCLOSURES

Author contributions: R. Bhuta performed the literature search and drafted the manuscript. M. Bromberg, A. Bains, and R. Schey critically revised the manuscript. R. Schey is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received February 10, 2016; Accepted February 18, 2016

REFERENCES

1. The International Agency for Research on Cancer. *WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues*. Vol 3. 4th ed. Lyon, France: IARC; 2008.
2. Lee YG, Lee S, Han SW, Lee JS. A case of multiple mucosa-associated lymphoid tissue (MALT) lymphoma of the colon identified as simple mucosal discoloration. *J Korean Med Sci*. 2005;20(2):325-8.
3. Kim MH, Jung JT, Kim EJ, et al. A case of mucosa-associated lymphoid tissue lymphoma of the sigmoid colon presenting as a semipedunculated polyp. *Clin Endosc*. 2014;47(2):192-6.
4. Seo SW, Lee SH, Lee DJ, et al. Colonic mucosa-associated lymphoid tissue lymphoma identified by chromoendoscopy. *World J Gastroenterol*. 2014;20(48):18487-94.
5. Kanneganti K, Balar B. Mucosa-associated lymphoid tissue lymphoma presenting as massive gastrointestinal bleeding: A case report. *Case Rep Gastroenterol*. 2008;2(3):296-300.
6. Ahlawat S, Kanber Y, Charabaty-Pishvaian A, et al. Primary mucosa-associated lymphoid tissue (MALT) lymphoma occurring in the rectum: A case report and review of the literature. *South Med J*. 2006;99(12):1378-84.
7. Zucca E, Conconi A, Pedrinis E, et al. Nongastric marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue. *Blood*. 2003;101(7):2489-95.
8. Howell JM, Auer-Grzesiak I, Zhang J, et al. Increasing incidence rates, distribution and histological characteristics of primary gastrointestinal non-Hodgkin lymphoma in a North American population. *Can J Gastroenterol*. 2012;26(7):452-6.
9. Chan JK. Gastrointestinal lymphomas: An overview with emphasis on new findings and diagnostic problems. *Semin Diagn Pathol*. 1996;13(4):260-96.
10. Arcaini L, Burcheri S, Rossi A, et al. Prevalence of HCV infection in nongastric marginal zone B-cell lymphoma of MALT. *Ann Oncol*. 2007;18(2):346-50.
11. Jiang C, Gu L, Luo M, et al. Primary rectal lymphoma: A case report and literature review. *Oncol Lett*. 2015;10(1):43-4.
12. Romaguera J, Hagemester FB. Lymphoma of the colon. *Curr Opin Gastroenterol*. 2005;21(1):80-4.
13. Quayle FJ, Lowney JK. Colorectal lymphoma. *Clin Colon Rectal Surg*. 2006;19(2):49-53.
14. Akasaka R, Chiba T, Dutta AK, et al. Colonic mucosa-associated lymphoid tissue lymphoma. *Case Rep Gastroenterol*. 2012;6(2):569-75.
15. Okamura T, Suga T, Iwaya Y, et al. *Helicobacter pylori*-negative primary rectal MALT lymphoma: complete remission after radiotherapy. *Case Rep Gastroenterol*. 2012;6(2):319-27.
16. Zucca E, Stathis A, Bertoni F. The management of nongastric MALT lymphomas. *Oncology (Williston Park)*. 2014;28(1):86-93.
17. Treglia G, Zucca E, Sadeghi R, et al. Detection rate of fluorine-18-fluorodeoxyglucose positron emission tomography in patients with marginal zone lymphoma of MALT type: A meta-analysis. *Hematol Oncol*. 2014;33(3):113-24.
18. Kikuchi Y, Matsui T, Hisabe T, et al. Deep infiltrative low-grade MALT (mucosal-associated lymphoid tissue) colonic lymphomas that regressed as a result of antibiotic administration: Endoscopic ultrasound evaluation. *J Gastroenterol*. 2005;40(8):843-7.