Follicular Lymphoma of the GI Tract

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Introduction

Forty percent of follicular lymphomas in the United States are non-Hodgkin lymphomas.[1] The presentation is usually nodal; extra-nodal involvement is rare. The most common extra-nodal involvement is the gastrointestinal (GI) tract. We present a patient who presented with recurrent episodes of partial small bowel obstruction secondary to a primary follicular lymphoma of the GI tract.

Case Report

A 57-year-old female with a history of fibromyalgia presented with recurrent episodes of partial small bowel obstruction recurring every 2 to 8 weeks, and lasting for up to 3 days. Her episodes started two years prior after she underwent surgery for release of an internal hernia secondary to adhesions as well as an incidental appendectomy. One year later, her symptoms recurred. They usually started with abdominal pain, progressing to nausea and vomiting, and ultimately resolving spontaneously. She denied weight change, change in bowel habits, melena, hematochezia, fevers, chills, or night sweats.

An exploratory laparotomy was performed to reveal any pathology that would explain the symptoms. As it was non-revealing, an esophagogastroduodenoscopy was performed, but it also was benign. A colonoscopy showed the presence of collagenous colitis, but it required no treatment. Finally, a capsule endoscopy revealed an ulcerated area and stricture in the distal ileum, followed by double balloon enteroscopy with findings suggestive of grade A esophagitis and an ulcerated strictured mucosa in the proximal to mid ileum which was biopsied and tattooed (Figure 1). Pathology was non-diagnostic.

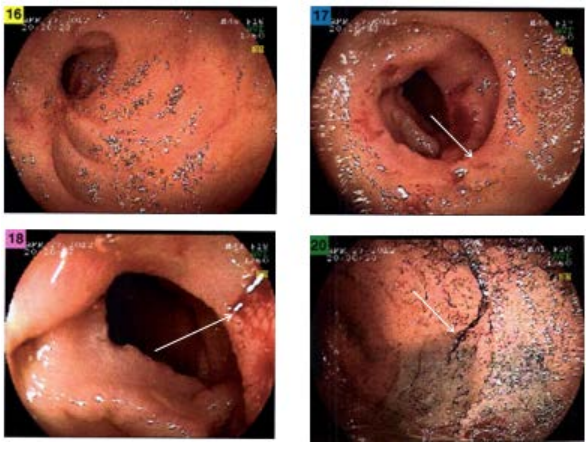

Figure 1. Images taken during double balloon enteroscopy revealing ulcerated strictured mucosa in the proximal to mid ileum.

In view of the patient's continuous problems, she underwent small bowel resection of the tattooed section. Immunophenotypes were positive for CD 20 (Figure 2), BCL-2 (Figure 3), and BCL-6 (Figure 4) with a Ki-67 of 20% and negative for cyclin B1, CD 3 and CD 5.

Immunohistochemical stains on the regional lymph nodes were reactive and not involved in the lymphoma, thus the diagnosis was consistent with stage 1E primary follicular lymphoma.

The patient had a follow-up PET scan that was negative for any suspicious hypermetabolic mass or adenopathy. Her management was mainly observation with follow-up PET scans. She improved with no evidence of recurrence.

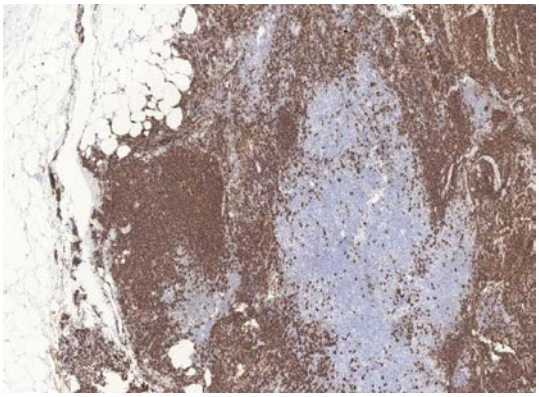

Figure 2. Immunophenotypic staining of the surgical specimen (CD 20).

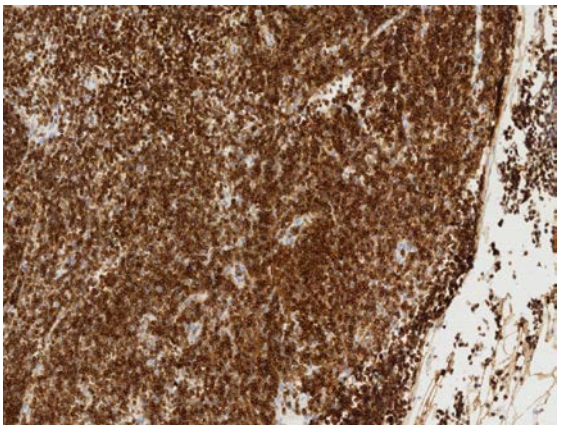

Figure 3. Immunophenotypic staining of the surgical specimen (BCL-2).

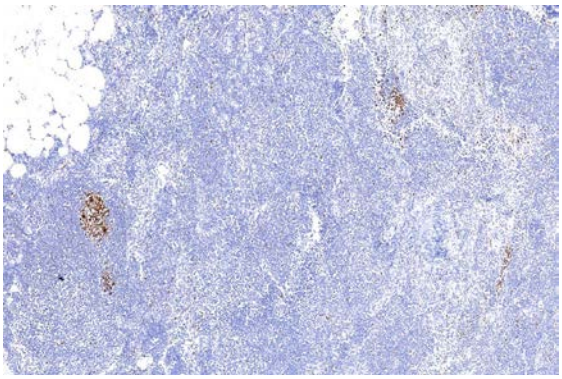

Figure 4. Immunophenotypic staining of the surgical specimen (BCL-6).

Discussion

The most common primary gastrointestinal lymphoma is marginal zone lymphoma.[2] Risk factors for the development of GI lymphomas include H. pylori infections, immunosuppression, inflammatory gastrointestinal diseases, and HIV. Primary follicular lymphoma was first described in 1997.[3] It is rare and constitutes 1% to 3.6% of all GI lymphomas.[2] Primary follicular lymphoma is more prevalent amongst females and the average age at diagnosis is 56 years. Until 2010, 249 cases were reported in the literature; half were in Japan.

Mucosa-associated lymphoid tissue (MALT) lymphoma differs from nodal marginal zone lymphoma as it usually arises in organs that lack lymphoid tissues but accumulates B-cells in response to chronic inflammation. It may arise in the stomach, lung, ocular adnexa, or salivary gland and is associated with gastroduodenitis caused by Helicobacter Pylori.[4] Patients are usually asymptomatic; 10% of cases present with vague gastrointestinal symptoms.[2] The most common GI symptoms include abdominal pain, nausea and vomiting, and GI bleed. The absence of palpable lymphadenopathy in the chest and abdomen based on imaging and sole involvement of the GI tract with a normal white cell count and differential are needed for diagnosis. Immunophenotype of

the tumor cells are B cells, and it tests negative for CD43, CD5, D1 and cyclin.

Gastrointestinal lymphoma is usually unifocal, but with the increase in use of capsule endoscopy, there have been more reports with regards to multifocal disease.[2] The second portion of the duodenum is involved most commonly, followed by the terminal ileum, stomach, and rarely the colon and rectum. LeBrun et al.[5] hypothesized that those neoplasms had a predilection to the terminal ileum because of the relatively abundant lymphoid tissue, Peyer's patches, that are prevalent in the small intestine.

Similar to other gastrointestinal malignancies, the gross appearance of GI lymphoma relates to the site of involvement. It appears as ulcers in the stomach, an obstructing mass in the small intestine, or polyps in the colon.[1,5] Surgical removal is almost impossible because of the large involvement of the viscus. Spread to regional and distant lymph nodes, liver, spleen, and bone marrow may occur at later stages.[5] Differential diagnosis of primary follicular lymphoma based on histology includes follicular lymphoid hyperplasia, GI involvement from follicular lymphomas originating from nearby lymph nodes, primary marginal zone lymphomas, and lymphomatous polyposis.[2]

Examination of the small bowel is challenging. Current modalities include enteroclysis, push enteroscopy, and capsule endoscopy.[6] Capsule endoscopy, first introduced in 2000, is a procedure to visualize the entire small bowel. Capsule endoscopy identifies lymphomas more than what was hypothesized previously and serves as a good modality for assessing success of treatment. Double balloon enteroscopy was shown to be an invaluable tool for diagnosis of diminutive small bowel lesions, but was a recommended procedure for the extensive staging of primary follicular lymphomas.[7] Video capsule endoscopy should be used initially as a screening procedure and follow-up, whereas double balloon enteroscopy should be added to the examination prior to the initiation of the treatment.[8]

There have been no prospective randomized clinical trials that elucidate optimal treatment modalities for non-Hodgkin lymphoma. Management ranges from surgery, if the patient has obstructive symptoms, to radiation and chemotherapy.[1] The CHOP regimen with rituximab has been shown to be effective in complete regression of the neoplasm during an early stage.[8] Survival in those patients ranges from 10 to 16 years and treatment is individualized.[2] Patients usually have an indolent course and a favorable outcome.[1,9,10]

Our case alerts physicians, particularly gastroenterologists, to consider the diagnosis of follicular lymphoma as one with a favorable outcome despite it being rare. This case highlighted the need of both capsule endoscopy and double balloon enteroscopy in reaching the diagnosis, however, in rare cases, the need for surgical resection is warranted to establish the diagnosis.

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*Keywords***:** follicular lymphoma, capsule endoscopy, double-balloon enteroscopy