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CASE REPORT | COLON

Primary Diffuse Large B-Cell Lymphoma of the Rectosigmoid Colon in a Patient With Ulcerative Colitis Who Never Received Immunosuppression

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ABSTRACT

Primary rectal lymphoma is extremely rare, accounting for approximately 0.05% of all primary rectal neoplasms. We present a patient with long-standing ulcerative colitis, who was never treated with immunomodulators or biologic agents, diagnosed with primary diffuse large B-cell lymphoma of the rectosigmoid colon, and achieved remission after chemotherapy. As per current data, incidence of primary colorectal lymphoma has been associated with medications used for inflammatory bowel disease treatment, such as thiopurine, methotrexate, or tumor necrosis factor-α antagonist, and not with the inflammation itself. Given the rarity of this phenomenon, more data should be gathered before determining that no such association exists.

INTRODUCTION

Colorectal cancer is the second leading cause of cancer death in the United States for both men and women, and the third most commonly diagnosed cancer, with a global burden that is expected to increase by 60% by 2030.[1,2] Lymphomas are classified as Hodgkin and non-Hodgkin lymphoma (NHL), which are further divided into nodal and extranodal NHL. Primary lymphomas of the gastrointestinal (GI) tract, involving only regional lymph nodes without systemic disease, are extremely rare, accounting for 1%–4% of GI neoplasms.[3] The stomach is the predominant site of GI lymphoma, involved in 60%–75% of the cases, whereas rectal lymphoma was only seen in 2% of reported cases.[4,5] We report a case of a patient with a history of long-standing ulcerative colitis (UC), diagnosed with primary diffuse large B-cell lymphoma of the rectosigmoid colon. The patient was never treated with immunomodulators or biologic agents.

CASE REPORT

A 74-year-old man with a medical history of UC, as well as mechanical aortic and mitral valves was admitted for a surveillance colonoscopy with preprocedural anticoagulation bridging. At the time of presentation, the patient had UC for 16 years and no family history of cancer. His UC was controlled with oral mesalamine and rectal enemas. He maintained adequate follow-up with his primary gastroenterologist and was never treated with immunomodulators or biologics. Before his admission, the patient had 6 surveillance colonoscopies, annual or biennial, revealing only mildly active inflammation without dysplasia on pathology. His inpatient surveillance colonoscopy revealed mild inflammation in the distal transverse, descending, and sigmoid colon, unchanged from previous examinations. Also, a single circumferential serpentine ulcer about 10 cm in length was found in the proximal rectum and rectosigmoid colon, extending from 8 to 20 cm from the anal verge (Figure 1).

Biopsies taken from the edge and center of the ulcer revealed colonic mucosa with ulceration and sheets of large atypical B cells, most compatible with diffuse large B-cell lymphoma (germinal center B-cell subtype). The neoplastic cells were positive for CD20 and BCL6 and were negative for CD3, CD5, CD10, BCL1, BCL2, MUM1, CD30, c-MYC, CD138, and LMP1 (EBV-encoded latent membrane protein 1), with a proliferation index (Ki-67) of about 70%–80%, reflecting a highly proliferative and aggressive tumor

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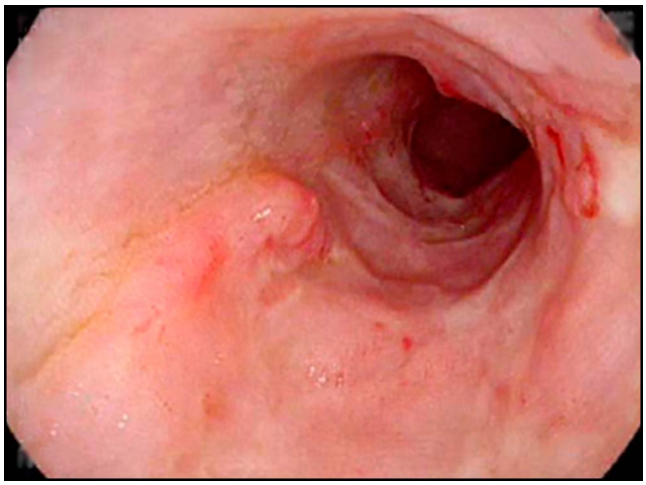

Figure 1. Endoscopic image showing a circumferential serpentine ulcer about 10 cm in length in the rectosigmoid colon extending from 8 to 20 cm from the anal verge.

(Figure 2). Staging thoracic, abdominal, and pelvic computed tomography (CT) scan revealed thickening of the rectum and sigmoid colon, small retroperitoneal lymph nodes, and a 1.0 × 0.8-cm mesenteric lymph node. Otherwise, no significant lymphadenopathy or organomegaly suspicious for involvement by lymphoma was seen.

A positron emission tomography–CT scan showed increased fluorodeoxyglucose (FDG) avidity involving the sigmoid colon up to the anal region with corresponding thickening on low-dose CT. Results were compatible with the patient's newly diagnosed lymphoma in the background of colitis. A mildly avid left external iliac node, suspicious for disease involvement, was also noted. No other areas of FDG uptake were found. Bone marrow biopsy was significant for variable cellular marrow (30%–60%) with trilineage hematopoiesis and no morphologic or immunophenotypic evidence of involvement by lymphoma. Given the above findings, the patient was diagnosed with primary colorectal, early-stage, diffuse large B-cell lymphoma. He was treated with 6 cycles of systemic chemotherapy with rituximab, cyclophosphamide, vincristine, and prednisone. Posttreatment positron emission tomography–CT showed significant interval decrease in FDG uptake and wall thickness of the rectosigmoid colon. It also demonstrated interval decrease in the size and activity of the previously noted left external iliac node (Figure 3).

One year after the index colonoscopy, posttreatment colonoscopy was performed, revealing mild circumferential inflammation from the rectum to sigmoid. Notably, severe stenosis was seen in the rectum measuring 3 cm in length, extending from 10 to 13 cm from the anal verge, with ulceration and nodules within the stenosis. Hematopathology was compatible with benign lymphoid aggregate with no definite large atypical B cells identified.

DISCUSSION

Primary rectal lymphoma is very rare, accounting for only 0.05% of all primary rectal malignancies.[6] It typically involves only regional lymph nodes.[7] Aggressive diffuse large B-cell lymphoma accounts for 44.5% of GI NHL and is associated with a less favorable prognosis than patients with mucosa-associated lymphoid tissue.[8] The treatment for primary GI lymphoma is usually chemotherapy followed by radiation when feasible, with surgery reserved for patients with life-

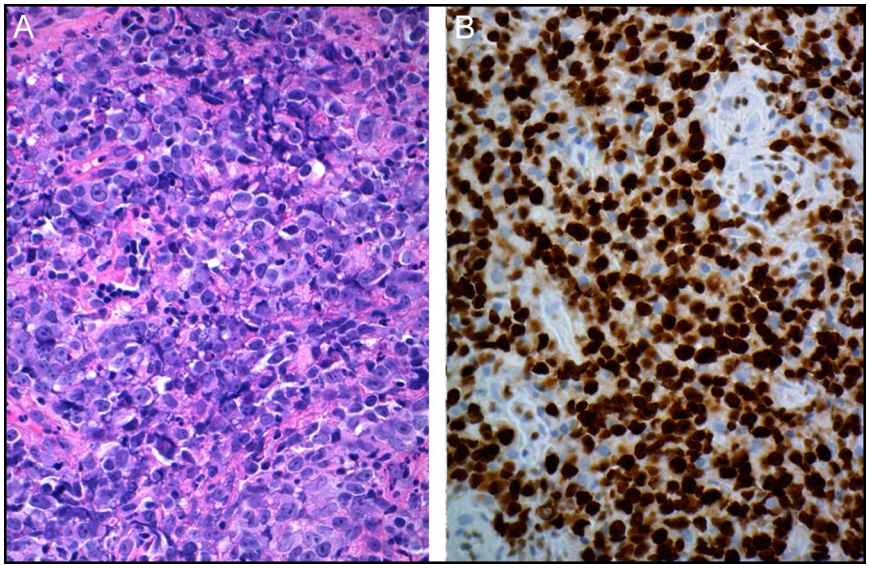

Figure 2. Histopathological findings of the resected rectosigmoid ulcer revealing (A) large atypical B cells, most compatible with diffuse large B-cell lymphoma, germinal center B-cell subtype, and (B) stain positive for BCL6 and negative for CD3, CD5, CD10, BCL1, BCL2, MUM1, CD30, c-MYC, CD138, and LMP1 (hematoxylin and eosin stain, 40× magnification).

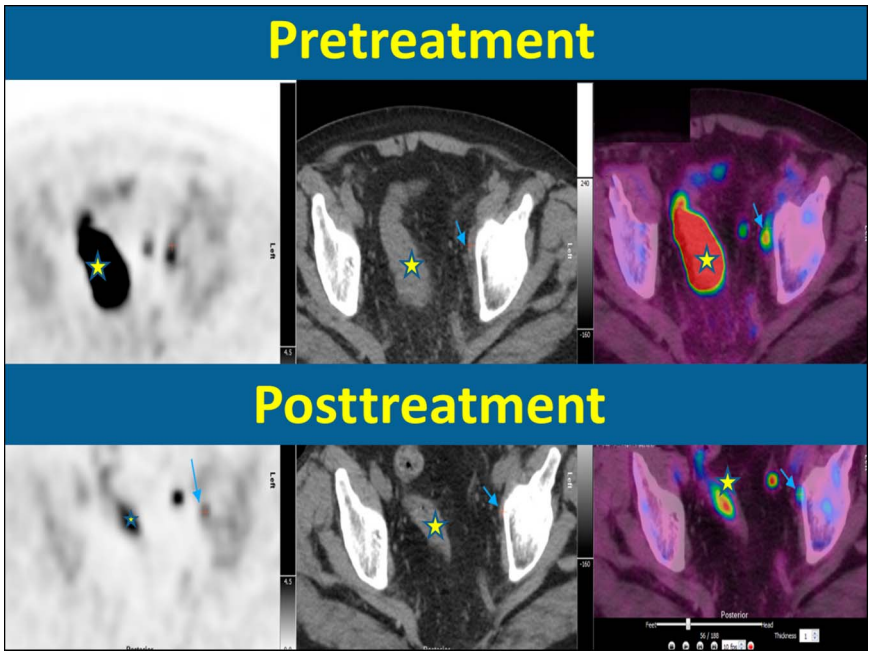

Figure 3. Positron emission tomography–computed tomography: Pretreatment (top 3 images) showing increased fluorodeoxyglucose activity involving the sigmoid colon (star) up to the anal region with corresponding thickening on low-dose computed tomography compatible with the patient's newly diagnosed lymphoma in the background of colitis. Also seen, a mildly avid left external iliac lymph node suspicious for disease involvement (blue arrow). Posttreatment (bottom 3 images) showing significant interval improvement in activity and wall thickness of the rectosigmoid colon, as well as interval improvement in the size and activity of the left external iliac node.

threatening bleeding, bowel obstruction, or perforation. Complete response has been achieved in 67.5% of patients either by surgery or by chemotherapy.[9]

Primary GI lymphomas have been associated with *Helicobacter Pylori* infection, celiac disease, and autoimmune diseases such as rheumatoid arthritis and Sjögren syndrome.[10,11] Although inflammatory bowel disease (IBD) confers a 1.5 to 2 times greater risk of colorectal cancer than the general population, the association with GI lymphomas is still unclear.[12] Published in 2012, a prospective study revealed an increased incidence of primary intestinal lymphoma with IBD, especially middle-aged male Crohn's patients after 8 years of disease, in the setting of chronic inflammation and Epstein-Barr virus infection.[13] Unlike this evidence supporting an association with primary intestinal lymphoma, studies show conflicting data regarding the association between IBD and primary colorectal lymphoma. Some studies associated IBD itself and primary colorectal lymphoma.[14,15] Other studies suggest that sustained treatment with thiopurines, methotrexate, or tumor necrosis factor-α antagonists are the possible causes for primary GI lymphoma seen in patients with IBD.[16–20]

The association between IBD and primary colorectal lymphoma is yet to be established. Given the rarity of this phenomenon, more data should be gathered before declaring that no such association exists. One should recognize that primary colorectal lymphoma can present in long-standing UC, despite no use of immunomodulators or biologic therapies.

DISCLOSURES

Author contributions: BB Mulat, K. Boroda, and H. Guddati wrote the manuscript. N. Kiyici revised the manuscript for intellectual content. BB Mulat is the article guarantor.

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