

# Diffuse Large B-Cell Lymphoma Mimicking an Ulcerative Colitis Flare

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## ABSTRACT

We present a case of non-Hodgkin lymphoma of the rectum in a 41-year-old African American male with a 1 year history of ulcerative colitis and no previous immunomodulatory therapy. The patient presented with a 10-day history of hematochezia, for which endoscopy was performed with gross findings indicative of ulcerative colitis flare. Tissue biopsy, however, demonstrated significant lymphoid infiltrating regions with histologic findings suggestive of a diffuse large B-cell lymphoma. Non-Hodgkin's lymphoma accounts for less than 1% of all cases of colorectal cancer. Associated risk factors have been previously reported but, were absent in the patient's history. This suggests the possibility of distinct genetic abnormalities inherent to the tumor and/or an underlying germline mutation inherent to the patient that may have contributed to the premature development of diffuse large B-cell lymphoma.

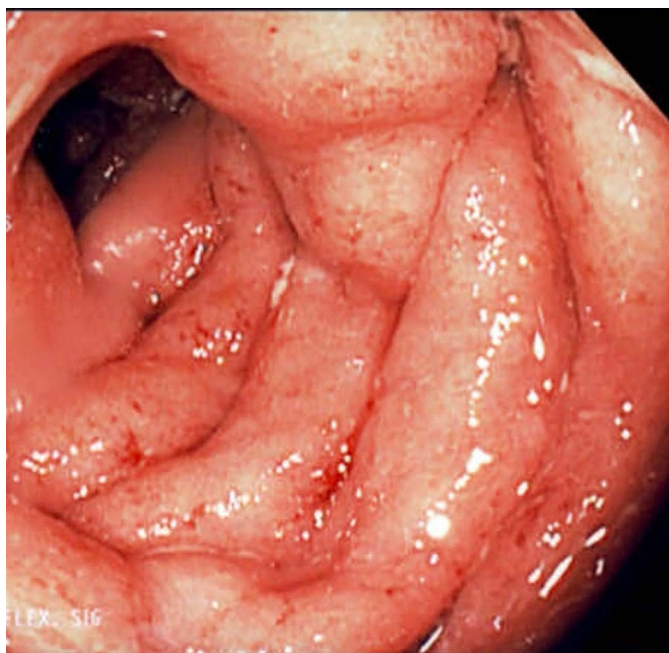
## INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is a rare malignancy of the gastrointestinal (GI) system, and an especially rare form of colorectal carcinoma. The association between ulcerative colitis (UC) and non-Hodgkin's lymphoma (NHL) has been well documented. The common associations between these links typically include chronicity of underlying inflammatory bowel disease (IBD), a history of immunosuppressive therapy, and Epstein-Barr virus (EBV) positive lymphocytes.<sup>1,2</sup> We present a case where these commonly associated risk factors were absent. This suggests currently elusive pathophysiologic mechanisms underlying the causal association between UC and NHL. Furthermore, it highlights the important clinical considerations that must be accounted for when managing what may appear to be a typical UC flare.

## CASE REPORT

A 41-year-old African American male presented to the hospital in October of 2016 with a chief complaint of 10 days of diarrhea. The patient reported 4 to 5 bowel movements (BMs) per day, which were initially watery, then became bloody. Associated symptoms included cramping/spasming abdominal pain, nausea, and a 6 to 7 lbs weight loss. The patient had a colonoscopy approximately 10 years before for hematochezia, which was normal per the patient, although unconfirmed in the absence of records. Other medical history only included intermittent tobacco abuse and a hospitalization 1 year before for acute alcoholic pancreatitis. He had no surgical history and no family history of bowel cancers or inflammatory bowel disease.

On admission, a computed tomography of the abdomen showed colitis from the rectum to transverse colon in continuity. C-reactive protein (CRP) was elevated at 48.5 mg/L. Stool studies revealed numerous leukocytes, but were negative for infectious etiology including *Clostridium difficile* (*C. diff*). A lower GI endoscopy was performed on the second day of admission. This showed continuous colitis from the rectum to the transverse colon with edema, erythema, friability, and small ulcerations consistent with a Mayo endoscopic subscore of 3 (severe disease) (Figure 1).<sup>3</sup> Multiple biopsies were performed that revealed areas of cryptitis, abscess formation, and chronic surface inflammation without dysplasia. The patient was started on intravenous methylprednisolone with symptom improvement and down-trending CRP. He was transitioned to oral prednisone and prescribed mesalamine enemas and discharged home.



**Figure 1.** Initial sigmoidoscopy showing diffuse inflammatory changes suggestive of ulcerative colitis.

At a follow-up outpatient visit 10 days later, the patient was experiencing 4 to 5 nonbloody BMs per day while on oral prednisone. Daily mesalamine was initiated along with a tapered steroid wean by 5 mg per week.

Three months later, he was seen at a tertiary center's inflammatory bowel disease clinic reporting 8–10 bloody BMs daily with mild abdominal pain. He had tapered off prednisone completely 1 month prior, and was reporting poor adherence with oral mesalamine. He was restarted on a prednisone taper, and continued on oral mesalamine.

The patient was lost to follow-up for a 4-month period and then in May of 2017, he returned to the local clinic with complaints of 8–10 intermittent bloody BMs per day. He reported compliance with oral mesalamine, and stated he had been doing well since tapering off steroids 4 months prior. Laboratory and stool studies were obtained with findings as follows: complete blood count within normal limits aside from an elevated red blood cell distribution width of 17.3%; CRP normal at 4.8 mg/L; albumin normal at 3.8 g/dL; *C. diff* toxin was negative and fecal calprotectin was normal at 36.8 mcg/g.

A colonoscopy was performed and revealed mild-to-moderate left-sided colitis of the splenic flexure, consistent with a Mayo endoscopic subscore of 1 (mild disease) (Figure 2).<sup>3</sup> This was improved from his previous lower GI endoscopy in October of 2016. Significant colonic pseudopolyps throughout the entire colon were noted. Biopsies from the right and left colon revealed mild reactive epithelial change and areas of mild focal chronic active inflammation without any dysplasia. However, biopsies from the rectum were significant for prominent lymphoid



**Figure 2.** Colonoscopy showing loss of vascular markings, erythema, and friability in the rectum.

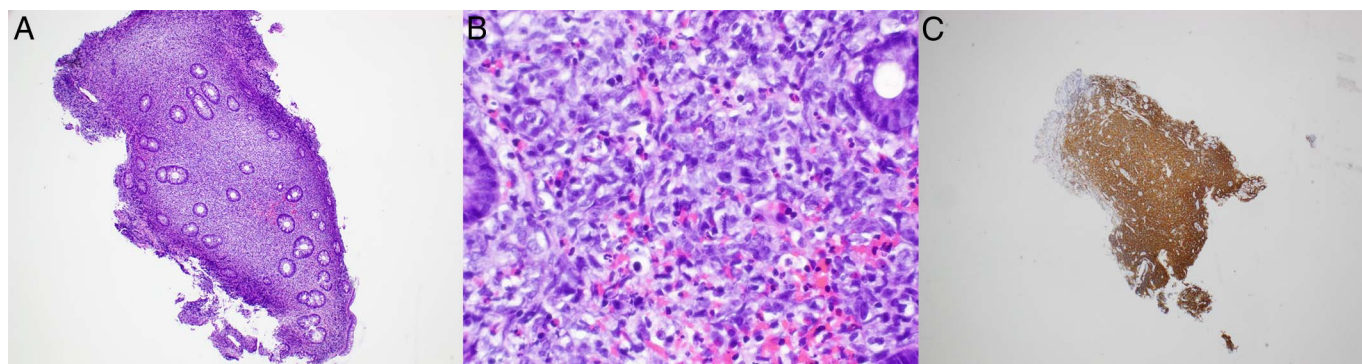
tissue. A consultation from the Mayo Clinic was obtained that revealed a final diagnosis of DLBCL. Immunohistochemistry was positive for myelocytomatosis and negative for BCL2. Fluorescence *in situ* hybridization analysis was negative for myelocytomatosis gene rearrangement, making this unlikely to be high-grade B-cell lymphoma (Figure 3). He underwent 6 rounds of R-CHOP (rituximab, cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin), vincristine sulfate (Oncovin), and prednisone) chemotherapy, and surveillance bone marrow biopsy and positron emission tomography scan were negative for lymphoma.

## DISCUSSION

Lymphoma accounts for approximately 1%–5% of all GI malignancies and only 0.16% of all colon cancers.<sup>4,5</sup> Up to 40% of extranodal NHL occurs in the GI system. The large intestine is a less common site accounting for 10%–20% of GI lymphomas.<sup>6</sup> Those that do occur in the large intestine most commonly take place in the cecum.<sup>5</sup> Diffuse large B cell is the most common subtype of colorectal NHL.<sup>5</sup> Colorectal NHL is an overall aggressive cancer, with studies suggesting a 5-year survival rate in the range of 27%–33%.<sup>5,7</sup>

Manifesting symptoms of colorectal NHL include abdominal pain, bloody stool, and weight loss. Patients can also present with a palpable mass or signs and symptoms that mimic a bowel obstruction.<sup>4</sup> Endoscopic findings commonly include an obstructing mass, whereas mucosal ulcerations are less frequently seen.<sup>5</sup> Immunohistochemistry of biopsy specimens is often required to differentiate UC from lymphoma.<sup>8</sup>

When primary colorectal lymphoma is diagnosed in UC, it typically occurs many years later. One study suggests a mean average of 12 years between the diagnosis of UC and NHL. Men are more commonly affected than women. Interestingly, a retrospective report found patients with UC who subsequently develop



**Figure 3.** Rectal biopsy showing (A) lymphocytes effacing the lamina propria and displacing crypts, (B) large number of irregular lymphocytes, and (C) CD20-positive staining indicating the presence of B cells.

a diagnosis of colorectal NHL were diagnosed with UC at a much later age than those without a diagnosis of NHL (46 vs 19 years old).<sup>2</sup> Other common associated findings included EBV-positive lymphoma cells, and the use of immunomodulatory therapy.<sup>9</sup>

A similar case of primary rectal DLBCL was documented in a patient with approximately a 3-year history of UC. Although overall similarities were apparent between the 2 cases with respect to the clinical spectrum of the diseases, notable differences included the presence of both EBV-positive lymphocytes and previous exposure to immunomodulatory agents in the reported case.<sup>10</sup> This suggests that perhaps there are other underlying mechanisms that predispose the UC patient to NHL. One theory is that chronic colorectal inflammation leads to overstimulation of the immune system and proliferation of immune cells.<sup>11</sup> Previous literature has suggested a correlation between NHL and underlying infectious etiology as well as associated EBV-positive lymphocytes.<sup>1,2</sup> Our case suggests that, perhaps even in the absence of infection or EBV positivity, the presence of an underlying chronic inflammatory process may trigger an immunoproliferative process and ultimately NHL.

Although GI NHL is not uncommon there are several unique features to this case. The large intestine in particular is an uncommon site, with the rectum being especially rare. If NHL does present in the large intestine, it more commonly does so as an obstructive mass rather than an ulcerative lesion. When NHL presents in a patient with UC, there is typically a prolonged period between the diagnoses. In our patient, however, that time period was less than 1 year. Our patient did not have EBV-positive lymphocytes, and he had no history of anti-metabolite, anti-tumor necrosis factor, or immunomodulatory therapy. This suggests the possibility of distinct genetic abnormalities inherent to the tumor and/or an underlying germline mutation inherent to the patient that may have acted as predisposing factors contributing to the premature development of DLBCL in this particular setting. It is important to keep a wide differential diagnosis for patients presenting with IBD symptoms, even those with a history of IBD.

## DISCLOSURES

**Author contributions:** All authors wrote the manuscript. J. Miller is the article guarantor.

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**Informed consent** was obtained for this case report.

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