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CASE REPORT | SMALL BOWEL

Distal Ileitis Caused by Diffuse Large B-Cell Lymphoma in an Elderly Patient From Honduras

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ABSTRACT

Primary gastrointestinal non-Hodgkin lymphoma, while rare, most often presents as diffuse large B-cell lymphoma located in the stomach or ileocecal region. Presenting symptoms include abdominal pain, gastrointestinal bleeding, weight loss, or obstructive symptoms. Imaging can reveal ileitis or obstruction. We report a case of a man from Honduras with latent tuberculosis and chronic hepatitis B who presented with features of Crohn's disease through clinical, radiologic, and endoscopic findings but was ultimately diagnosed with diffuse large B-cell lymphoma by histology. We emphasize the importance of maintaining a broad differential for ileitis and the importance of histologic sampling when evaluating ileitis.

KEYWORDS: Gastrointestinal Lymphoma; Diffuse Large B-Cell Lymphoma; Colonoscopy; Stricture; Crohn's Disease

INTRODUCTION

Gastrointestinal non-Hodgkin lymphoma is rare and may present as a diagnostic dilemma. Primary extranodal non-Hodgkin lymphoma of the gastrointestinal (GI) tract represents approximately 10%–15% of all cases of non-Hodgkin lymphoma (NHL).[1] Primary GI NHL (PGINHL) accounts for 30%–40% of all primary extranodal NHLs.[1] Among PGINHLs, 50%–66% are diffuse large B-cell lymphoma (DLBCL), more commonly found in the stomach and ileocecal regions where lymphoid tissue is abundant.[2] The differential diagnosis for distal ileitis includes Crohn's disease (CD), bacterial infections such as *Yersinia*, intestinal tuberculosis (ITB), ischemia, medications, and malignancy.[3]

CASE REPORT

A 74-year-old Spanish-speaking man visiting the United States from Honduras with previous appendectomy and recently treated Helminth infection presented with postprandial abdominal pain, nausea, night sweats, early satiety, and weight loss for the past 2 months. A week earlier, abdominal/pelvic computed tomography (CT) showed distal ileitis; he was given antibiotics without improvement. Upon representation, he reported difficulty tolerating oral intake and overall worsening symptoms. Repeat abdominal/pelvic CT revealed persistent ileitis.

The patient was admitted due to concern for a new presentation of CD given his presentation of abdominal pain and weight loss; however, he denied hematochezia and diarrhea. External examination showed no evidence of perianal disease. Erythrocyte sedimentation rate and C-reactive protein were elevated. Fecal calprotectin was slightly elevated. Stool studies were negative for enteric infections. Ileocolonoscopy demonstrated a normal terminal ileum; however, distal ileitis, a nontraversable distal ileal stricture; cecal ulcers; and patchy loss of vascularity throughout the colon were visualized (Figure 1). Segmental biopsies of the bowel were obtained for histologic examination. QuantiFERON-TB Gold and hepatitis B virus (HBV) serologies revealed latent TB and chronic hepatitis B. Isoniazid was prescribed for latent TB (Table 1).

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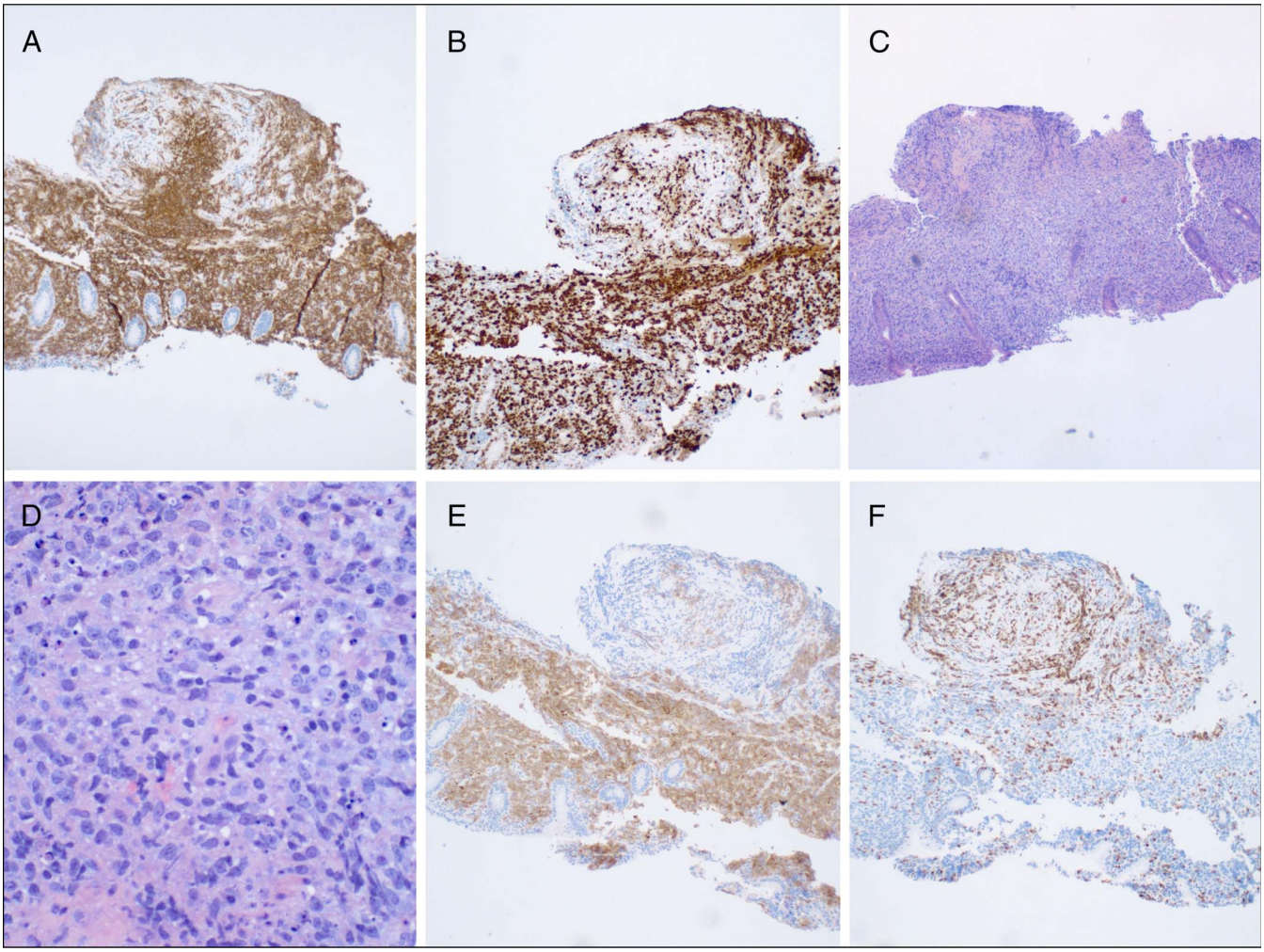

Figure 1. Ileocolonoscopy demonstrating distal ileitis, a nontraversable distal ileal stricture; cecal ulcers; and patchy loss of vascularity throughout the colon. Magnification in A, B, C, E, F is 10×; magnification in D is 40×.

The patient's course was complicated by small bowel obstruction requiring total parenteral nutrition and ultimately an ileocecectomy. Hematopathology review of ileal and cecal biopsies returned positive for DLBCL, germinal center B-cell subtype with a high proliferative rate (90%–95%) (Figure 2). acid fast bacilli (AFB) and Fite staining were negative. positron emission tomography (PET) scan revealed Lugano Stage IV disease with hypermetabolic activity in the distal ileum, cecum, esophagus, and bone marrow. He was ultimately discharged home with oncology follow-up for outpatient chemotherapy initiation.

DISCUSSION

A 74-year-old man from Honduras presented with many classic signs of CD including abdominal pain, weight loss, ileitis on CT, and elevated serum inflammatory markers. Given these findings, CD was initially considered; however, ITB was also considered.

TB has a higher incidence in Honduras of 30 cases per 100,000 people in 2020 compared with 2.4 in the United States.[4,5] ITB may appear on CT as enteritis or present as small bowel obstruction from strictures as late complications.[3,6,7] While

Table 1. Relevant bloodwork

Test	Result
Fecal calprotectin	94 mcg/mg
erythrocyte sedimentation rate (ESR)	42 mm/hr
c-reactive protein (CRP)	35 mg/L
HBsAG	Negative
HBV core IgM	Negative
HBV core total Ab	Reactive
HBV DNA quantitative	Negative
HBeAg	Reactive
HIV Ab	Negative
QuantiFERON (QFT)-TB gold plus	Positive

Ab, antibody; CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IgM, immunoglobulin M; QFT-TB, QuantiFERON tuberculosis.

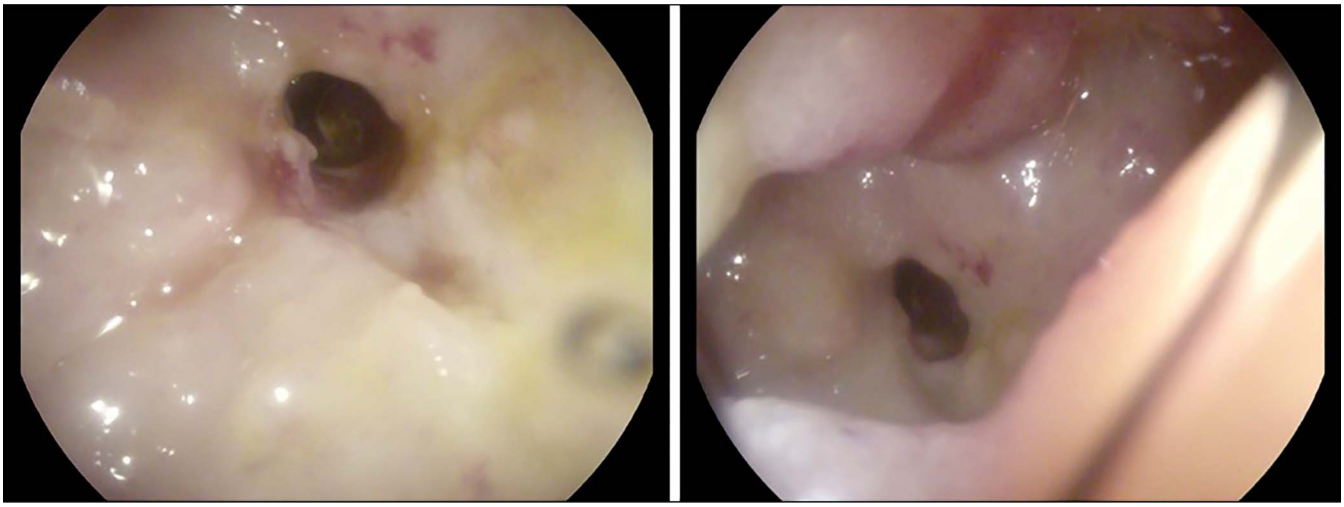

Figure 2. Distal ileum biopsies under low and high-power magnification. (A) CD20 immunohistochemistry (IHC) stain highlights the diffuse, infiltrative, large, atypical cells that are also positive for CD10 (E). 10× magnification. (B) Ki-67 IHC stain with high positivity, indicative of a very high proliferative fraction (90%–95%). 10× magnification. (C) Low-power hematoxylin and eosin (H&E) staining shows diffuse infiltration of large, atypical cells. 10× magnification. (D) High-power H&E staining shows diffuse infiltration of large, atypical cells with irregular nuclear contours, dispersed chromatin, and variable nucleoli. 40× magnification. (E) CD10 IHC stain with high positivity. 10× magnification. (F) CD3 IHC stain highlights rare scattered reactive T cells. 10× magnification.

endoscopic biopsy is less reliable for diagnosing ITB, clinical suspicion for ITB was low, given negative AFB and Fite stains of tissue.[3] Ultimately, the diagnosis of NHL, specifically DLBCL, was confirmed by histologic evaluation.

PGINHL is rare, representing 3%–6% of all NHLs.[1] Small bowel lymphoma most commonly presents with abdominal pain; however, palpable abdominal mass, bleeding, obstruction, change in bowel habits, weight loss, and perforation are possible.[13] Stricture, while rare, is seen more with B-cell over T-cell types due to formation of polypoid lymphoid aggregates.[8] Traditionally, the diagnosis of PGINHL depends on (i) lymph node involvement confined to the drainage area of the primary site; (ii) no hepatic, splenic involvement or palpable superficial lymph nodes; (iii) normal chest radiograph; and (iv) normal peripheral white blood cell count. More than half of PGINHLs are DLBCL, most often found in the lymphoid abundant stomach and ileocecal regions.[2] Generally, PGINHL of the ileocecal region has improved event-free survival compared with other small intestine regions or multiple GI site lymphomas.[14] In this case, the primary site was the distal ileum with distant metastasis to the cervical chain. PGINHL in the distal ileum is a rare subset of NHL.

Diagnosis of DLBCL is dependent on morphology and immunophenotyping of biopsy samples showing large atypical lymphoid cells with expression of B-cell markers such as CD20, as seen in this patient.[15] BCL-6 gene abnormalities are common and lead to unchecked cell proliferation. Gene expression profiling is most useful for prognostication and classifies 2 subgroups of DLBCLs, germinal center B-cell-like and activated B-cell-like. Our patient exhibited germinal center B-cell-type, which carries a more favorable prognosis.[16] cyclophosphamide, doxorubicin, vincristine, prednisolone (CHOP) regimen is the standard therapy and confers 40%–50% long-term survival.[18] Additional treatment with rituximab provides a 10%–15% increase in survival without increased risk of adverse events.[17]

While the etiology of DLBCL is not well defined, risk factors in our patient include age older than 55 years, male sex, and hepatitis B.[14,15] Recent research has demonstrated a 2–3 fold higher risk of NHL development in HBV-positive patients.[10] Further research is needed to determine the etiopathogenic mechanisms of lymphomagenesis. A prospective study showed that pretherapy HBV DNA was detected in 21% of patients with NHL, which were primarily DLBCL, and 42% of patients with DLBCL had HBV DNA in their plasma, supporting an association with hepatitis B virus (HBV) and DLBCL ($P < 0.0001$).[11] Furthermore, a meta-analysis including 40,000 patients demonstrated that HBV-infected individuals have an odds ratio of 2.24 of developing NHL.[12] We hypothesize that our patient's chronic HBV infection was a risk factor of NHL development. Treatment of HBV seropositivity should be started before chemotherapy and continued for 6–12 months after its cessation, due to the risk of HBV reactivation, especially when coadministered with immunomodulating therapies such as rituximab.[12]

Our patient began isoniazid treatment for latent pulmonary TB with plans to initiate entecavir and R-CHOP chemotherapy 1 month after ileocecectomy. Overall, his prognosis was poor with an National Comprehensive Cancer Network International Prognostic Index (NCCN-IPI) of 4 (indicating high risk), a high proliferative rate, and the aggressive nature of metastatic NHL.

In summary, intestinal lymphoma is rare and may be mistaken for acute infectious processes, inflammatory bowel disease, or

ITB. Endoscopic biopsy with immunophenotypic evaluation should be considered to provide a timely and accurate diagnosis given that presenting symptoms and signs can be nonspecific. Although presenting symptoms overlap with conditions such as inflammatory bowel disease and ITB, this case emphasizes the importance of maintaining lymphoma as a differential diagnosis in such patients, especially in those with positive HBV serologies.

DISCLOSURES

Author contributions:

J. Newman, A. Hong, J. Zhang, A. Dabash, J. Gehring, L. Lynn, M. Borum, S. Bhattacharya were responsible for drafting of the text, sourcing and editing of clinical images, investigation results, and critical revision for important intellectual content. M. Borum and S. Bhattacharya provided the final review and approval for submission. J. Newman is the article guarantor.

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Informed consent was obtained for this case report.

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