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# Primary Diffuse large B-cell Lymphoma of the colon presenting as Idiopathic thrombocytopenia : A case report


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CASE REPORT

# Primary Diffuse Large B-cell Lymphoma of the Colon Presenting as Idiopathic Thrombocytopenia: A Case Report

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**Abstract**

*Introduction*: **Primary lymphoma of the colon and rectum is an uncommon form of cancer comprising less than 0.5% of all colorectal tumors combined. Typically, extra nodal lymphomas manifest in the gastrointestinal tract, with non − Hodgkin lymphoma being the most frequent subtype and the stomach being the most common location.**

*Case presentation*: **70 year old female with medical history of osteoarthritis and osteoporosis was evaluated for bilateral leg rash and thrombocytopenia. Eventual work up revealed cecal mass but inconclusive findings on colonoscopy. She underwent hemicolectomy due to persistent thrombocytopenia with histopathology positive for primary Diffuse Large B-cell Lymphoma (DLBCL). She underwent chemotherapy with complete resolution of her mass and lymphadenopathy.**

*Conclusion*: **We are presenting a rare case of Non - Hodgkin lymphoma in the colon. This disease can show up with unclear symptoms, so it's important to use different types of imaging and pathology tests to identify the specific type of lymphoma. The main treatment for this type of cancer involves using chemotherapy and radiation therapy.**

*Keywords:* Primary B cell lymphoma, DLBCL, Colonic lymphoma, Thrombocytopenia, Chemotherapy

## 1. Introduction

Non-Hodgkin's lymphoma consists of various cancers, most of which (85−90%) arise from B lymphocytes and the remaining cases originate from T lymphocytes or NK lymphocytes. NHL can occur in a variety of tissues, although they usually occur in the lymph nodes. Types of NHL range from unaggressive types like follicular lymphoma to more aggressive types like diffuse large B-cell lymphoma and Burkitt's lymphoma. The location and subtype of lymphoma, and the presence or absence of B symptoms determine the clinical presentation of NHL. Two-thirds of patients present with no symptoms of painless lymphadenopathy, which is more widespread compared to Hodgkin's lymphoma.[1] Colonic Lymphoma is a rare and understudied type of lymphoma that affects the colon, which is an uncommon site for non-Hodgkin's lymphoma. Colonic lymphoma is characterized by symptoms such as abdominal pain, change in bowel habits, and weight loss which usually persist for several months even before a diagnosis is made. During physical examination, a majority (50%) may have a detectable abdominal mass. Ileocecal area and cecum are the most frequently affected areas. The majority of cases involve aggressive lymphomas, except those of B-cell origin. In rare cases, patients may not experience any symptoms or present ambiguously as thrombocytopenia as in our patient.[2]

## 2. Case presentation

A 70-year-old female with a history of osteoarthritis presented to the Emergency room because of

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symptomatic thrombocytopenia. Four days prior to admission, she noticed purple spots on her legs. She had been experiencing night sweats and chills for the past six months and had lost about 3 kg during the same time. She had traveled to Peru a year prior to her current condition. She denied usage of any medications or supplements. Her previous blood test six months ago revealed a normal platelet count of 211 K/CMM. Her labs on admission revealed platelets 56 K/CMM, hemoglobin (Hg) 11.5 g/dL, Leucocytes 6K/mm3 with a differential of neutrophils 6k/mm3, lymphocytes 7K/mm3, Monocytes 200/mm3. A peripheral smear revealed to be normal and she underwent a thorough evaluation for thrombocytopenia, including flow cytometry, serum electrophoresis (SPEP), antinuclear antibody (ANA), hepatitis panel, human immunodeficiency virus (HIV), and Lyme's serology. All of these tests came back negative. Immunoglobulins (IgG) for Epstein–Barr virus (EBV) and Cytomegalovirus (CMV) were positive, but IgM levels were normal. An ultrasound (USG) of the abdomen showed no significant abnormalities with the liver or spleen. However, the patient's stool antigen test came back positive for *Helicobacter pylori*, leading to a discharge at day 5 on outpatient (OP) triple therapy with amoxicillin, proton pump inhibitor (PPI), and Clarithromycin. As there is reported literature on association between Immune Thrombocytopenia Purport (ITP) and H. Pylori, her initial presentation of thrombocytopenia was thought to be secondary to H. Pylori infection. Unfortunately, this treatment did not improve the patient's condition, and subsequent outpatient follow-up labs at 2 weeks revealed a further decrease in platelets to 29 K/CMM.

In order to delve into further etiology, we did a CT scan of chest, abdomen and Pelvis with and without contrast in Outpatient setting. It revealed focal colitis of the distal ileum and ascending colon that extended to the inferior edge of the liver. The appendix was dilated, measuring 2.1 cm in diameter. Due to a significant drop in platelets to 9K/CMM at the second outpatient follow-up in 4 weeks from initial discharge, the patient was admitted to the hospital due to the risk of spontaneous hemorrhage. While admitted, An EGD was done due to previous positive H. Pylori stool antigen and unknown cause of dropping platelets which did not reveal any abnormal findings. Gastric biopsies eventually tested positive for H. Pylori. She also underwent a colonoscopy which revealed a partially obstructing, ulcerated mass in the ascending colon (Fig. 1). The biopsy confirmed an abscess of the cecum with no evidence of high-grade dysplasia. Abscess cultures tested positive for polymicrobial infection with predominance of *Escherichia coli* (*E.coli*) & *Bacteroides fragilis*, both susceptible to Levofloxacin. During the hospital stay, the patient was treated with IV Levaquin 750 mg daily for five days, which improved the platelet count from 9 K/CMM to 82 K/CMM. The patient was discharged on Day 6 on triple therapy with Levaquin 750 mg to complete a course of 14 days.

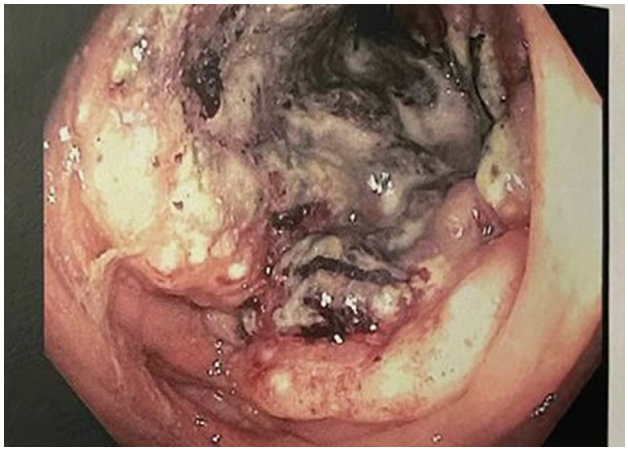


*Fig. 1. Colonoscopy of ascending colon revealing an irregular ulcerated mass.*

A month after discharge, the patient returned with worsening abdominal pain. A CT scan of the abdomen showed worsening cecal and ileal wall thickening with associated enlarging 6.5 × 5.5 cm soft tissue component suspicious for a colonic mass (Fig. 2). The scan also revealed increased inflammation in the surrounding fat tissue and several enlarged bowel loops and lymph nodes. The patient underwent a right hemicolectomy after consultation

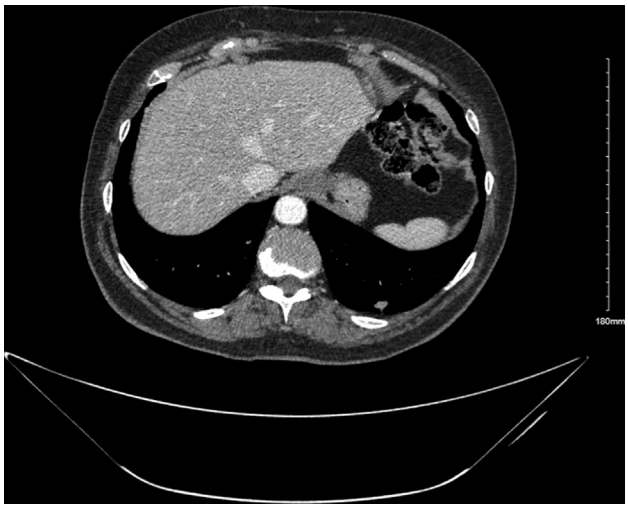


*Fig. 2. CT abdomen shows 6.5 × 5.5 cm colonic mass with cecal wall thickening.*

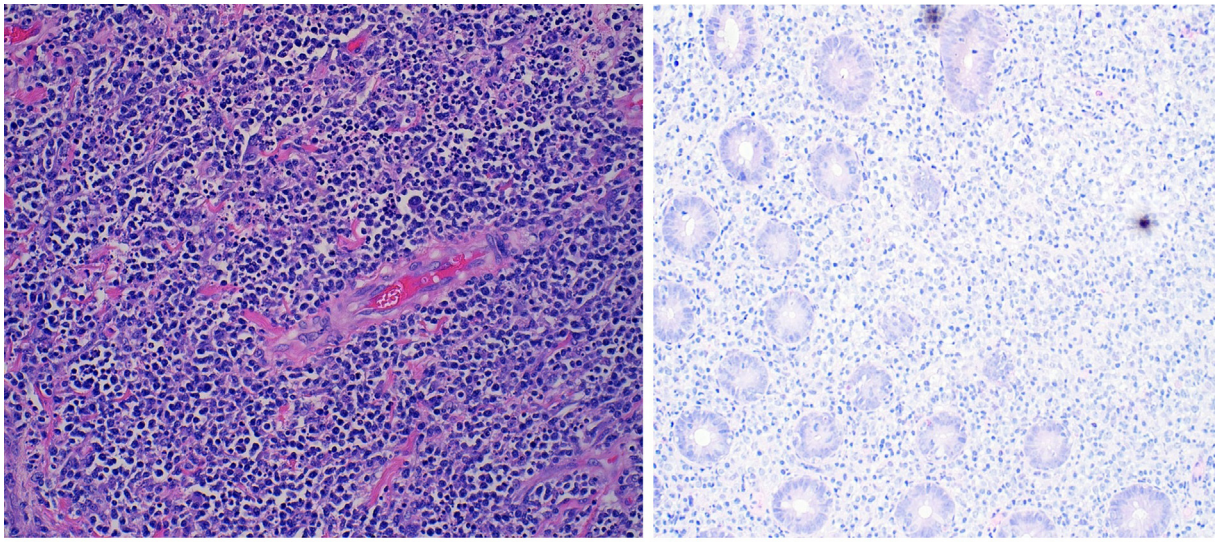
between gastroenterology and colorectal surgery. Pathology results confirmed diffuse large B- cell lymphoma-germinal center origin with CD20 (+), BCL2(+/−), CD10 (+), BCL6(+), MUM1 (−), CD21 (+), C-MYC(−) (Fig. 3). The patient is currently receiving R−CHOP regimen with cyclophosphamide, doxorubicin, prednisone, rituximab, and vincristine as an outpatient and has shown improvement in her platelet counts. PET scans revealed complete resolution in the abdomen and pelvis, and the patient continues to follow up with oncology and colorectal surgery.

## 3. Discussion

Non-Hodgkin lymphoma usually arises from natural killer cells, T - lymphocytes, B - lymphocytes and can be further categorized based on the subtype. Diffuse large B - cell Lymphoma (DLBCL) is the most common non-Hodgkin lymphoma subtype. Colonic non − Hodgkin's lymphoma is rare, constituting <1% of all colon neoplasms, and more common in males, with the median age being 55 years.[3,4]

Colonic lymphomas are associated with various risk factors, including inflammatory bowel disease, celiac disease, infections like *Campylobacter jejuni*, as well as viral infections like HIV, EBV, CMV, human T - cell leukemia virus - 1 (HTLV - 1), hepatitis C virus (HCV), Human herpesvirus − 8 (HHV - 8). The pathogenesis of colonic lymphomas involve the activation of proto-oncogenes and chromosomal mutations, including translocation t (14; 18), c-rel amplification, histone methyl-transferase mutations, and PTEN deletion. The most common translocation seen in colonic lymphomas is t (14; 18), leading to BCL2 overexpression and unchecked growth of B-cells in germinal centers.[5] While successful treatment of colonic lymphomas with *H.pylori* eradication has been observed, the relationship between colonic lymphomas and H. Pylori infection remains unclear. On the other hand, gastric mucosa-associated Lymphoid tissue (MALT) lymphomas are strongly associated with *H. Pylori*.[6]

The diagnosis of colonic lymphomas used to be established with five diagnostic criteria, which included the absence of abnormal white cell count, absence of enlarged mediastinal lymphadenopathy on chest X-ray, no palpable superficial lymphadenopathy, predominant bowel lesion with adjacent affected lymph nodes on laparotomy and absence of any liver/spleen tumors on laparotomy.[8] The commonly used staging systems for gastrointestinal lymphoma are the Lugano staging system and the Paris staging system, which correspond to the Tumor-Node-Metastasis (TNM) classification.[9] Clinicians should always keep in mind other differential diagnoses of gastrointestinal lymphomas such as Crohn's disease, adenocarcinoma, and other solid tumors, benign lymphoid hyperplasia, peptic ulcer disease, celiac disease, and bacterial and fungal infections of the gastrointestinal tract[9] Diagnosis requires imaging modalities such as contrast-enhanced CT of the abdomen, double-contrast



A. This high-power view shows the monotonous hyperchromatic lymphoma cells destroying the intestinal structure

B. Tumour cells invading lamina propria of ascending colon on biopsy

*Fig. 3. High power image on left shows B lymphocytes of germinal origin invading the colon mucosa; Right image shows infiltration of tumor cells in lamina propria of ascending colon.*

barium enema, colonoscopy, and biopsy for confirmation. Serological testing for Hepatitis B virus (HBV), HCV, HIV, and EBV is also necessary, as these viruses can be possible etiologies.[5]

Currently, the diagnosis is made by the presence of irregular round nuclei staining dark chromatin with distinct central nucleoli in large atypical mononuclear lymphoid cells. Additionally, there must be a strong positivity for the immunohistochemistry with CD20. The tumor immunohistochemistry staining showed CD 20 (+), BCL 2 (+/−), CD 10 (+), BCL 6 (+), MUM 1 (−), CD 21 (+), C MYC (−) with a confirmatory diagnosis of non-germinal center DLBCL in our patient (Figs. 2 and 3). B - cell differentiation is closely associated with the expression of CD10. Improved prognosis in patients with DLBCL is closely associated with the expression of CD-10. Hence CD-10 expression. Research has shown that when combined with clinical parameters, it could help determine the prognosis of DLBCL[3](8).

Treatment options for colonic lymphomas include multi-agent chemotherapy, surgical resection, and radiotherapy, alone or in combination, based on the staging of lymphoma, subtype, and co-morbidities. R−CHOP induction therapy is the gold standard regimen for colonic lymphomas, and the role of surgery is still debated. The gold standard treatment for DLBCL is anthracyclines, such as cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP). The addition of rituximab (CD20 monoclonal antibody) has effectively led to complete remission in most patients. The combined use of monoclonal antibodies with anthracyclines has been shown to improve outcomes and prolong the survival of these patients.[5]

Few authors suggest surgery as the primary treatment to increase the probability of cure and prevent complications. Conversely, others argue that only emergency situations warrant surgery. A study conducted by Cai and colleagues found that surgical intervention was common (61.3%) following the diagnosis of primary colonic lymphoma. The effectiveness of surgery appeared to be site-specific, with surgery demonstrating a benefit in outcomes of right-sided colonic lymphomas as opposed to those with left-sided or rectal lymphomas. There is a significant improvement in the survival of patients who underwent surgery.[3]

DLBCL presents with anemia, fatigue, abdominal pain, anorexia, weight loss, and bowel changes. However, due to the non-specific nature of these symptoms, diagnosis may be delayed, as was the case with this patient.[5] It is important for healthcare providers to consider the possibility of primary colorectal lymphoma in patients presenting with these symptoms and those with risk factors such as IBD, viral infections, and the use of immunosuppressant agents. When proctitis or colitis is observed during a colonoscopy, a broader differential diagnosis should always be considered.[7] Platelet count is a reliable indicator for predicting the survival outcome of patients undergoing immunochemotherapy in DLCBL. However, when it comes to assessing treatment response, platelet count proves to be a less effective predictor.[10]

The other differential for thrombocytopenia is ITP which is associated with various factors including infections like HIV, EBV, CMV, malignancies such as adenocarcinoma and lymphomas, autoimmune diseases like autoimmune hepatitis, thyroid disorders, Systemic Lupus Erythematosus (SLE). Certain drugs like digitoxin, carbamazepine, Aminosalicylic acid, Aspirin, Phenytoin, methyldopa, Rifampin, Sulfamethizole, allopurinol can also induce ITP. Diagnosis often involves ruling out other potential causes of thrombocytopenia. In our patient, almost all the above reasons were excluded through appropriate labs.[11] There is an established evidence that eradication of H. Pylori can lead to resolution of platelet auto-antibody response in cases of ITP. In such cases, complete eradication of *H.Pylori* and improvement of platelets are documented.[12]

## Conflict of interest

No conflict of interest.

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