

CASE REPORT

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# A case of primary gastrointestinal lymphoma presenting as colonic perforation

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## ABSTRACT

**Introduction:** Non-Hodgkin lymphoma represents 0.3% of colonic malignancies. It presents in older males with comorbid infection, autoimmune disease or immunosuppression. Presenting symptoms are often non-specific including abdominal pain, decreased appetite, weight loss and anemia. Colonic perforation or obstruction from primary colonic lymphoma is commonly reported after treatment with chemotherapeutic agents. We present a rare case of primary gastrointestinal lymphoma presenting with perforation of the descending colon causing retroperitoneal abscess formation. **Case Report:** A 65-year-old, hepatitis C virus positive, white male presented to primary care with chronic abdominal pain and forty pound weight loss. Computed tomography of the abdomen showed a locally invasive mass arising from the descending colon and extending into both the perirenal space and abdominal wall with evidence of contained colonic rupture. One week later, the patient presented to the hospital with

sepsis. Emergent exploratory laparotomy was performed with removal of the affected colonic section and debridement of the retroperitoneal abscess to control the sepsis source. Surgical specimen pathologic analysis revealed primary diffuse large B cell lymphoma of the colon. The patient was discharged home in stable condition with scheduled outpatient oncologic treatment. **Conclusion:** Lymphoma should be considered in older men with a history of immunosuppression and viral infections such as HCV presenting with signs and symptoms of colon cancer. We emphasize that colonic perforation is a rare, yet important, initial presentation of primary colonic non-Hodgkin lymphoma. Surgical intervention is the primary treatment in this scenario to control bacteremia and sepsis, as seen in our patient.

**Keywords:** Colonic perforation, Diffuse large B cell lymphoma, Gastrointestinal lymphoma

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## INTRODUCTION

Non-Hodgkin lymphoma represents 0.3% of all colonic malignancies. Diffuse large B-cell lymphoma is the most common histologic subtype. This

neoplasm usually presents in older males, and is often associated with infection, autoimmune disease and immunosuppression [1–3]. Presenting symptoms include non-specific findings such as abdominal pain, decreased appetite, weight loss and anemia [3]. Several cases have reported colonic perforation or obstruction from primary colonic lymphoma, but these events typically occur after treatment with chemotherapeutic agents [4–8]. To our knowledge, gastrointestinal diffuse large B cell lymphoma presenting with colonic perforation has not been previously reported. We present a rare case of primary gastrointestinal lymphoma presenting as a perforation of the descending colon with subsequent retroperitoneal abscess formation.

## CASE REPORT

A 65-year-old Caucasian male with a history of hepatitis C virus (HCV) infection, chronic kidney disease, hypertension, on anticoagulation presented to his primary care physician with chronic abdominal pain. The patient also reported a decreased appetite and a forty-pound weight loss over four months. No family history of gastrointestinal or hematological malignancy was noted. The patient had not been previously screened for colorectal cancer.

Initial evaluation included abdominal radiographs and laboratory studies. Radiographs demonstrated a mass in the descending colon. Laboratory results were significant for leukocytosis of 14.3 k/uL with normal differential, decreased hemoglobin and hematocrit of 9.9 g/dL and 32.0%, and an abnormal iron study with iron of 16 ug/dL, transferrin of 172 mg/dL, total iron binding capacity of 240.8 ug/dL, and percent iron saturation of 6.6%. The patient's most recent hepatitis C viral load was greater than seven million. Serum carcinoembryonic antigen and carbohydrate antigen 19-9 values were not measured during his initial workup. The patient was referred for gastroenterology and surgical consultations along with computed tomography (CT) and colonoscopic evaluation of the mass.

Computed tomography scan of the abdomen with contrast showed an infiltrating locally invasive mass measuring 7.2x6.5 cm arising from the mid descending colon with extension into the perirenal space and abdominal wall musculature. The scan also showed colonic rupture, fistulization to the posterior abdominal wall, and invasion into the left perirenal space (Figure 1A–B). Colonoscopy showed a circumferential, friable obstructive mass in the descending colon fifty centimeters from the anal verge. A biopsy of the mass was obtained and sent for pathology. Pathology results showed mucosal ulceration with extensive necrosis and an atypical lymphoid infiltrate. The biopsy did not depict invasive carcinoma, demonstrated by negative pankeratin immunohistochemistry. Although there was evidence of acute inflammation in the biopsy, the biopsy results

were concerning for lymphoma. The majority of the inflammatory cells were lymphoid, predominantly B cells positive for CD20 and demonstrating a high proliferative rate as measured by Ki-67 staining. There was equivocal positivity for BCL-2 and BCL-6. The lymphoid infiltrate was negative for CD5, CD10, and Cyclin D1.

Chronic colonic perforation was strongly suspected from the imaging and pathology results. However, the results did not differentiate an infectious versus neoplastic etiology of the perforation. Further evaluation for suspected malignancy was conducted because the clinical picture suggested colon cancer with left kidney and abdominal wall invasion. The patient was referred to hematology/oncology department and a PET scan was ordered for further staging workup. The PET scan showed a large circumferential invasive left colon mass extending approximately fifteen centimeters in length with intense FDG activity concerning for a primary malignancy. The mass appeared to invade the left kidney cortex, left psoas muscle, and left posterior abdominal wall muscles. The cecum and right colon showed intense circumferential FDG activity with no definitive mass, likely secondary to an inflammatory/infectious process. Plans were made for a laparoscopic left hemicolectomy with a possible left nephrectomy and abdominal wall resection.

One week prior to the scheduled surgery, the patient presented with acute on chronic left flank pain unresponsive to hydrocodone. He was afebrile, but had a leukocytosis (24,000) and was unable to ambulate independently. Physical examination revealed exquisite tenderness in the left flank without signs of peritoneal irritation. He was admitted for intravenous antibiotic treatment (piperacillin/tazobactam) and close clinical monitoring. Blood cultures were positive for gram negative rods, thought to be secondary to colonic perforation.

Emergent surgery was planned for retroperitoneal sepsis. The patient was sent to the operating room for an exploratory laparotomy. The entirety of the descending colon spanning from the splenic flexure to the sigmoid was removed and sent for pathologic analysis. During surgery, the descending colon was noted to be firmly stuck to the retroperitoneum and the lateral sidewall. A portion of the abscess cavity was excised and the cavity was debrided. Notably, the cavity had a thick rind with septations and contained gastrointestinal contents. Upon completion of debridement and confirmation of hemostasis, an omental flap was created and used to fill the cavity. A 10 French Jackson-Pratt drain was placed into the cavity. Due to the degree of contamination noted intraoperatively, decision was made to proceed with a Hartmann's procedure rather than a primary anastomosis. The patient was stable throughout the procedure and was transferred to the surgical intensive care unit for recovery.

Intraoperative frozen section results from the colon specimen showed atypical leukocytes, suspicious for lymphoma. The colonic mucosa was noted to be ulcerated with an atypical small blue cell infiltrate, also suspicious for lymphoma. Definitive features of carcinoma were



not identified. The official pathology report showed a final diagnosis of diffuse large B cell lymphoma (DLBCL, CD10 positive germinal center type) (Figures 2 and 3). The lymphomatous process was noted to extend through the muscularis propria of the colon into the subserosal adipose tissue, causing subsequent colonic perforation and a left flank abscess (Figure 4). Immunohistochemical stains were positive for BCL-6, CD10 (diffuse, weak), CD79a, and BCL-2 (focal, weak) (Figure 5). The sample was negative for CD30 and Cyclin D1. CD3 and CD5 were positive in the surrounding background T lymphocytes. Ki-67 was markedly increased at 95–99%. Later oncology workup revealed that the patient had a Stage IE DLBCL.

Postoperatively, the patient progressed appropriately and was discharged on postoperative day-8. He was monitored closely for signs of sepsis, but remained afebrile with a steadily declining white blood cell count. On discharge, the patient has normal ostomy function, was tolerating PO intake and had his pain well controlled on oral pain medications. The patient followed-up with hematology/oncology department as an outpatient for further medical treatment of his lymphoma.

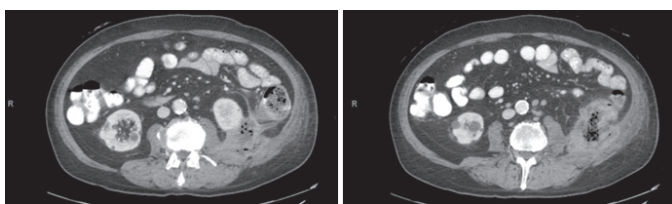


Figure 1: (A, B) Representative slices from computed tomography imaging showing an infiltrating, locally invasive mass measuring 7.2x6.5 cm arising from the mid descending colon. It extends posteriorly through the perirenal space to invade the left posterior abdominal wall musculature with colonic rupture, fistulation to the posterior abdominal wall, and invasion into the left perirenal space.

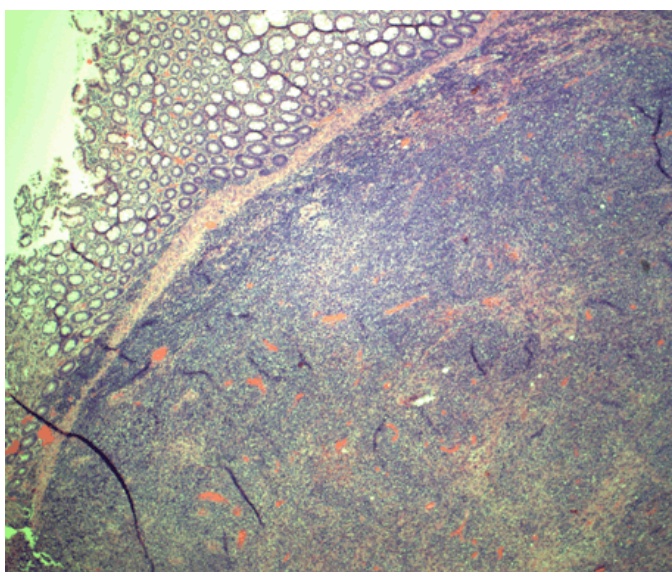


Figure 2: Low power image of effaced atypical lymphoid proliferation consistent with lymphoma.

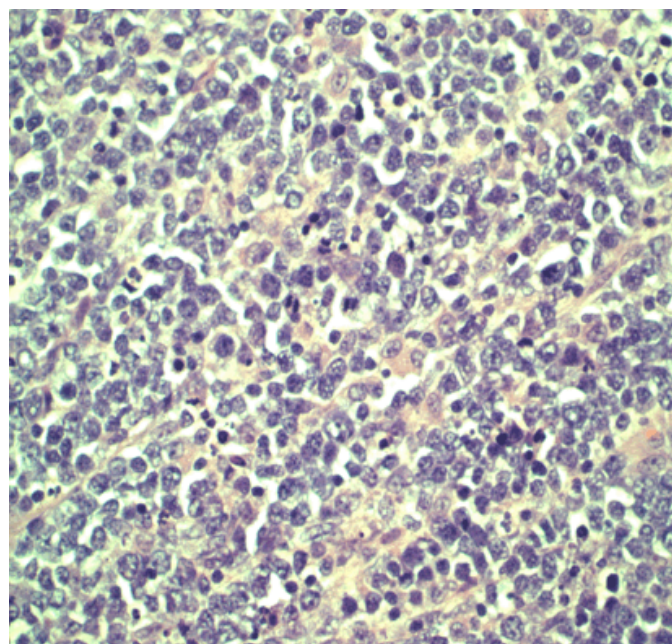


Figure 3: High power image of effaced malignant large B cells consistent with lymphoma.

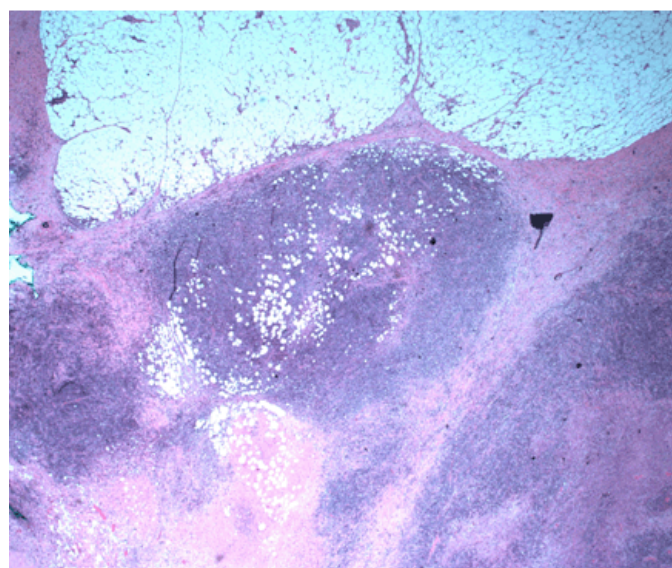


Figure 4: Low power image depicting lymphoma at area of colonic perforation.

## DISCUSSION

The gastrointestinal tract is the most common site of primary extra-nodal non-Hodgkin lymphoma. The most commonly affected site is the stomach, followed by the small bowel, colon, and esophagus [9]. The DLBCL is the most common histological subtype of NHL overall and the most common form of extra-nodal non-Hodgkin lymphoma seen in the gastrointestinal tract [10]. However, its low incidence and commonly non-specific symptoms often lead to delays in diagnosis, having a direct effect on morbidity and mortality [1, 11].



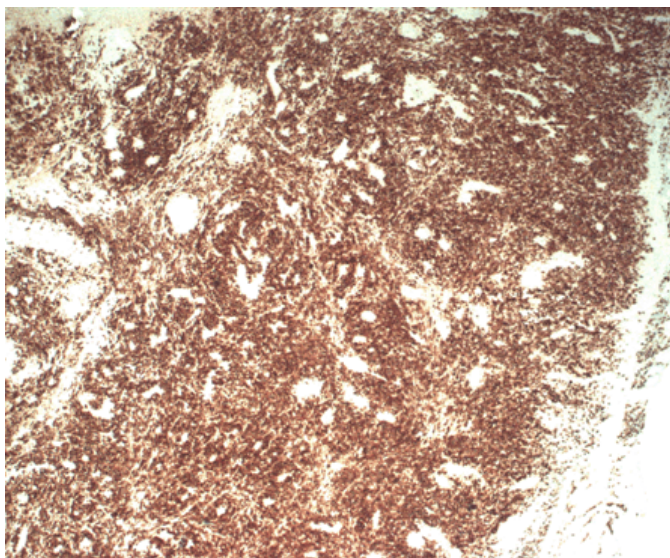


Figure 5: CD79a B cell immunohistochemistry demonstrating diffuse staining.

Uncommon presentations including colonic perforation increase the difficulty of diagnosis and delay treatment.

Family history, infections, environmental exposures, autoimmune disease, immunosuppression and immunodeficiency are important risk factors for the development of non-Hodgkin lymphoma. Specifically, HCV infection has been strongly associated with non-Hodgkin lymphoma. Four to twenty-two percent of patients diagnosed with non-Hodgkin lymphoma have a history of hepatitis C with B cell lymphomas being the most commonly associated subtype [12–15]. Up to 60% of patients with DLBCL reported comorbid HCV infection with an average of 15 years between diagnoses [12]. This patient's longstanding history of untreated HCV placed him at significantly increased risk for the development of non-Hodgkin lymphoma.

The evaluation of any patient with abdominal pain begins with a focused history and physical exam. However, the diagnostic accuracy of clinical findings alone is known to be poor [16]. In the setting of abdominal pain and a history of significant weight loss in an older male with HCV, evaluation is guided by a high suspicion for colorectal cancer. Laboratory tests including complete blood count with differential, complete metabolic panel, amylase, lipase, liver function tests, serum iron, total iron binding capacity and ferritin should be ordered. However, no diagnostic laboratory tests for colorectal cancer currently exist. Serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) are commonly measured, but these tests are no longer recommended for colorectal cancer screening or diagnosis [17, 18].

Computed tomography scan and colonoscopy are the next diagnostic steps. Computed tomography scan with contrast allows evaluation of the entire bowel and identification of sites of perforation. Colonoscopy allows follow-up localization, biopsy and possibly removal of

suspected lesions. Unfortunately, endoscopic findings do not correlate to histologic subtypes of non-Hodgkin lymphoma and tissue biopsies are often non-diagnostic for non-Hodgkin lymphoma [19]. Diagnosis is often only made after surgical exploration with resection of affected bowel. Bone marrow biopsy is not recommended for extra nodal DLBCL.

Traditional therapy includes a combination of surgery, radiation, CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) chemotherapy, and rituximab-based chemotherapy [20, 21]. Concomitant HCV infection necessitates the implementation of additional treatment strategies. Hepatitis C doubles the five year mortality in patients with DLBCL. Interferon-based antiretroviral therapy has been associated with an increase in mean survival from diagnosis, regression of indolent DLBCL without the use of chemotherapy, and greater success of first-line chemotherapy protocols [22]. This indicates the importance of screening for HCV infection in non-Hodgkin lymphoma patients and need for aggressive management once an infection is identified.

Surgical resection for gastrointestinal DLBCL is only performed in the setting perforation, obstruction, bleeding, or resistant disease [20, 23]. Bowel perforation is a poor prognostic sign. A 30% mortality rate with a mean survival of less than one year is directly associated with perforation, particularly in patients suffering bowel perforation after chemotherapy [8]. However, no studies evaluated the prognosis of patients presenting with bowel perforation compared to non-perforated patients. The literature also does not delineate the outcomes of patients with colonic perforations before versus after radiation treatment. Further research is needed to clarify the treatment outcomes and prognosis of patients presenting with colonic perforation secondary to DLBCL.

## CONCLUSION

Lymphoma represents a minority of primary gastrointestinal cancers and usually presents with an insidious onset of non-specific symptoms, such as weight loss, fatigue, anemia, and abdominal pain. Colonic lymphoma most commonly presents in older men, the same demographic as colonic adenocarcinoma. However, when an older man presents with signs and symptoms of colon cancer, lymphoma should be considered, particularly in patients with a history of immunosuppression and viral infections such as hepatitis C virus (HCV). We also emphasize that colonic perforation is a rare, yet important, initial presentation of primary colonic non-Hodgkin lymphoma. This is a dangerous scenario that can lead to rapid development of bacteremia and sepsis, as seen in our patient. Timely surgical intervention is of utmost importance in these cases.

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## Author Contributions

Jeffrey P. Fleming - Substantial contributions to conception and design, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Katie Smith – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Robert Bennett – Substantial contributions to conception and design, Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Gino F. Piparo – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Andrew Taitano – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

## Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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