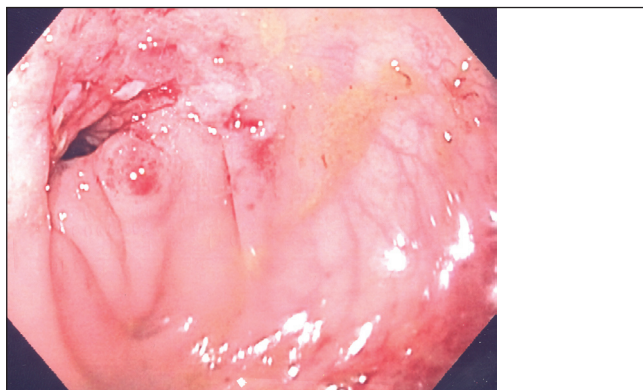


# Anaplastic large cell lymphoma of the colon in a patient with colonic Crohn disease treated with infliximab and methotrexate

Tushar Shukla MD, Jennifer Jin MD, Esmeralda Celia Marginean MD FRCPC, Nav Saloojee MD FRCPC

## CASE PRESENTATION

A 57-year-old woman, with colonic Crohn disease (CD) diagnosed four years previously, presented to the emergency department with a six-week history of severe abdominal pain. She did not have diarrhea. She had inactive perianal fistulas. Laboratory tests at presentation showed an elevated C-reactive protein level of 103 mg/L, and low albumin of 24 g/L. Other bloodwork was unremarkable. Stool testing was negative for *Clostridium difficile*, and culture and sensitivity. Her medical history was significant for rheumatoid arthritis (RA). She had been receiving infliximab and methotrexate for RA and CD. A computed tomography scan revealed wall thickening in the ascending, transverse and descending colon. No lymphadenopathy was present. Pericolonic inflammatory changes were apparent. No obstruction was present. Colonoscopy at the time of admission, to confirm what appeared to be a CD flare, revealed a benign-appearing ulcerated stricture at 40 cm from the anal verge (Figure 1). The colonoscope could not pass the stricture. There was no active CD in the colon distal to the stricture. The stricture was biopsied. The patient was treated with intravenous solumedrol and, subsequently, prednisone for a presumed CD flare. Steroids led to resolution of her pain. Biopsies of the stricture unexpectedly revealed an anaplastic large cell lymphoma (ALCL) (Figure 2). Infliximab and methotrexate were discontinued. A bone marrow biopsy was negative for lymphoma and computed tomography enterography showed a normal small bowel. The patient successfully completed six cycles of CHOP (cyclophosphamide, hydroxy doxorubicin, vincristine, prednisone) chemotherapy. Repeat biopsies of the stricture postchemotherapy showed no lymphoma, but atypical cells were present (Figure 3). A tattoo was used to mark the location of the stricture. The stricture was balloon-dilated to allow visualization of the proximal colon. There was only a single, discrete patch of ulceration in the ascending colon. Biopsies here were consistent with CD. It was believed that her risk of lymphoma recurrence was high. She was referred for surgical intervention and underwent a left hemicolectomy.



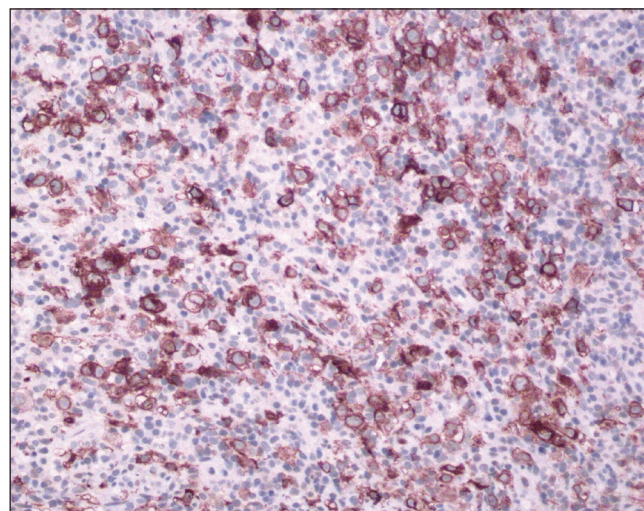
**Figure 1)** Endoscopic image. Stricture at 40 cm from the anal verge apparent on colonoscopy before chemotherapy

Total proctocolectomy and ileostomy were considered. Total proctocolectomy would have reduced the risk of recurrent CD, which would be difficult to manage given uncertainties about reinitiating immunomodulators or biologics in a patient with treated lymphoma. The patient believed she would not be able to manage a stoma due to debility from RA. Subtotal colectomy and ileorectal anastomosis was considered, but the concern was that this might worsen her perianal disease due to looser bowel movements. Pathology of the resected colon showed the ulcerated stricture, but no lymphoma or malignancy. Thirty-one lymph nodes were negative for malignancy. The patient is well, and not taking biologics and immunomodulators eight months postoperatively. Colonoscopy eight months postoperatively revealed a patch of mild ulceration at 50 cm from the anal verge. Biopsies were consistent with CD. There is no evidence of lymphoma recurrence.

## DISCUSSION

The relationship between inflammatory bowel disease (IBD) and lymphoma is unclear. Previous population-based studies have suggested that male patients with CD may have an increased risk of developing lymphoma (1). Other research does not support this finding, showing only a marginal increase in risk for the development of lymphoma in CD, and no evidence for an increase in risk for ulcerative colitis (2).

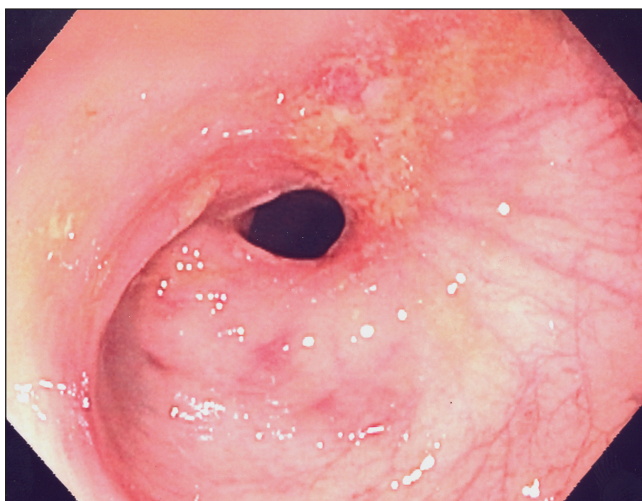
Medical management of IBD with immunomodulators (azathioprine or 6-mercaptopurine) is associated with an increased risk of developing lymphoma (3). Hepatosplenic T cell lymphoma is recognized to occur in a small number of patients taking tumour necrosis



**Figure 2)** Biopsy of colonic stricture. The large malignant cells express CD30 (CD30 immunohistochemistry, original magnification  $\times 200$ ). The cells were also immunoreactive for MUM1, BCL-2, BCL 6, p53, CD4, Ki67 (70%) and weakly for ALK1 (not shown)

The Ottawa Hospital, University of Ottawa Faculty of Medicine, Ottawa, Ontario  
Correspondence: Dr Tushar Shukla, University of Ottawa, Faculty of Medicine, 451 Smyth Road, Ottawa, Ontario K1H 8L6.

Telephone 613-737-8899, fax 613-737-8599, e-mail tshuk078@uottawa.ca  
Received for publication October 5, 2013. Accepted October 10, 2013



**Figure 3)** Endoscopic image. Stricture at 40 cm from the anal verge seen on colonoscopy after chemotherapy

factor (TNF)-alpha inhibitors, especially if concomitant immunomodulators are used (4). To our knowledge, the present case is the third report of ALCL of the colon. It is also the first reported case of ALCL occurring in a CD patient treated with a TNF-alpha inhibitor (infliximab) and concurrent immunomodulator (methotrexate). There have been two previously reported cases of colonic ALCL. One involved a patient with ulcerative colitis on no medications (5). The other was a patient with ileocolonic anastomosis for colonic adenocarcinoma (6). It is unclear whether our patient developed ALCL due to CD, medications or both.

Our patient presented with laboratory and radiological findings suggestive of a typical CD flare. Had she been managed without

endoscopy, her lymphoma would have been missed. This highlights the importance of considering endoscopy to confirm the clinical impression of active CD. A dilemma is the future management of her CD and RA should they become active. Our patient's infliximab and methotrexate were discontinued due to concern they were involved in the genesis of her lymphoma. Fortunately, her CD and RA have been quiescent. Should her CD or RA reactivate, it will be difficult to decide whether to restart TNF-alpha inhibitors or immunomodulators, given that these medications may increase the risk of lymphoma recurrence. Overall, it is unclear whether the development of ALCL in our patient was related to her medications, her CD or both. It is important to consider the risk of lymphoma when managing patients with IBD.

#### REFERENCES

1. Bernstein CN, Blanchard JF, Kliever E, Wajda A. Cancer risk in patients with inflammatory bowel disease. *Cancer* 2001;91:854-62.
2. Askling J, Brandt L, Lapidus A, et al. Risk of haematopoietic cancer in patients with inflammatory bowel disease. *Gut* 2005;54:617-22.
3. Kandiel A, Fraser AG, Korelitz BI, Brensinger C, Lewis JD. Increased risk of lymphoma among inflammatory bowel disease patients treated with azathioprine and 6-mercaptopurine. *Gut* 2005;54:1121-5.
4. Parakkal D, Sifuentes H, Semer R, Ehrenpreis ED. Hepatosplenic T-cell lymphoma in patients receiving TNF- $\alpha$  inhibitor therapy: Expanding the groups at risk. *Eur J Gastroenterol Hepatol* 2011;12:1150-6.
5. Tsutsumi Y, Nakamura M, Machimura T. CD30-positive T cell lymphoma of the intestine, complicating ulcerative colitis. *Pathol Int* 1996;46:384-8.
6. Cooperberg MR, Fiedler PN. Ki-1 anaplastic large-cell lymphoma occurring at the site of ileocolonic anastomosis in a patient treated surgically for colonic adenocarcinoma: Case report and review of the literature. *Ann Diagn Pathol* 2001;5:162-7.






**Hindawi**

Submit your manuscripts at  
<http://www.hindawi.com>

