

## CASE NOTE

# Lymphoma following ileal pouch anal anastomosis

Jossie Swett Cosentino, MD\*  
Richard J. Davies, MA, MChir\*†  
Robin S. McLeod, MD\*†‡  
Zane Cohen, MD\*†

From the \*Division of General Surgery, Mount Sinai Hospital, and the Departments of †Surgery and ‡Health Policy, Management and Evaluation, University of Toronto, Toronto, Ont.

**Correspondence to:**

Dr. Z. Cohen  
Mount Sinai Hospital  
600 University Ave., Ste. 451  
Toronto ON M5G 1X5  
fax 416 586-8644  
zcohen@mtsina.on.ca

Ileal pouch anal anastomosis (IPAA) has become the standard operation for most patients with ulcerative colitis<sup>1</sup> and familial adenomatous polyposis (FAP)<sup>2</sup> requiring surgery. This procedure allows patients to have bowel movements without needing a permanent ileostomy.

Patients with ulcerative colitis are at increased risk for colorectal cancer (CRC). The main risk factors include the duration and extent of colitis, family history and the presence of primary sclerosing cholangitis.<sup>3-5</sup>

Lymphoma is one of the most infrequently reported types of cancers associated with pouch surgery. Non-Hodgkin lymphoma encompasses a wide variety of lymphoid-derived tumours and may originate from B cells, T cells or histiocytes. They are likely to spread in a noncontiguous fashion, and one-third of all cases originate outside the lymph nodes in organs that normally have nests of lymphoid tissue (mucosal surfaces, bone marrow and skin). The most common extranodal affected site is the gastrointestinal tract.<sup>6</sup>

The presenting symptoms of a patient with ileal lymphoma are fever, fatigue, malaise, weight loss and vague abdominal pain. Only 25% of patients with intestinal lymphoma present with fever, occult blood loss, anemia, a palpable mass or an acute abdomen,<sup>7</sup> making its diagnosis more challenging. Additionally, the diagnosis of any kind of cancer in the pouch following IPAA remains difficult but is a growing concern.

We describe the case of a 64-year-old man with a 30-year history of ulcerative colitis who presented with low-grade fever and symptoms of prostatism and urinary retention 10 years after undergoing an IPAA procedure.

## CASE REPORT

A 64-year-old family doctor received a diagnosis of ulcerative colitis in 1976. In 1986, at the age of 44, he underwent a subtotal colectomy with side-to-end ileorectal anastomosis. The indication for surgery was dysplasia. The patient refused other surgical options at that time. The postoperative pathology report showed changes of chronic, active ulcerative colitis with several foci of moderate dysplasia. He was followed-up annually with endoscopy and biopsies that consistently showed only mild inflammation of the rectum without evidence of dysplasia.

However, in 1996, a biopsy showed mildly active ulcerative colitis and high-grade dysplasia within the rectal stump. The patient underwent proctectomy, mucosectomy and hand-sewn IPAA with loop ileostomy. The latter was closed within 4 months. Pathology of mucosal strippings showed mild dysplasia with no evidence of invasive cancer. The patient continued with annual follow-up. In 2001, he presented with his first episode of pouchitis, which was treated successfully with a standard course of antibiotics. Thereafter, he continued to have episodes of endoscopically and pathologically proven pouchitis and experienced weight loss. In 2006, a computed tomography (CT) scan showed a focal region of mural thickening

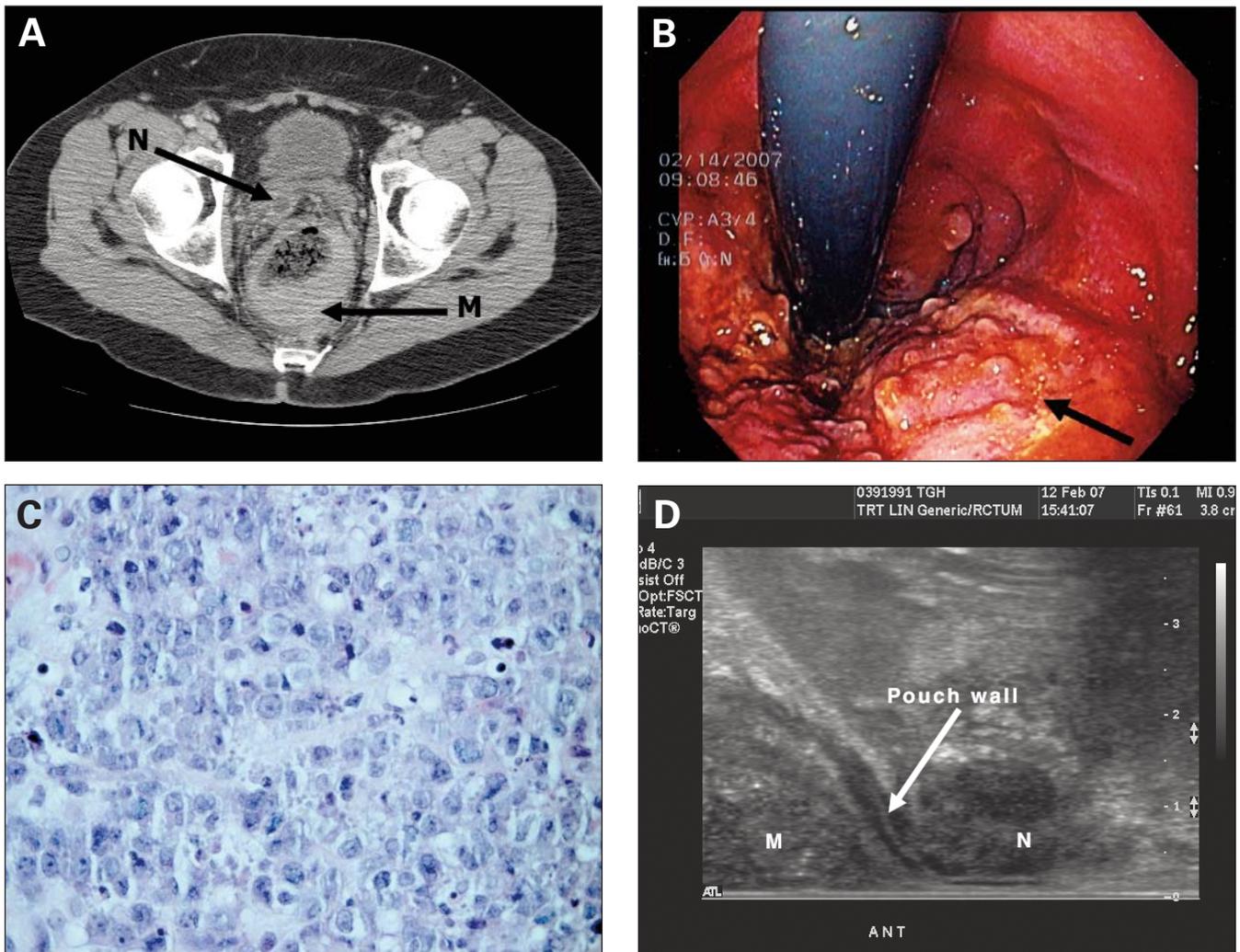
along the posterolateral aspect of the pouch wall that looked like it might represent postsurgical change and a solitary enlarged lymph node measuring  $2.6 \times 1.5$  cm. Over the subsequent year, the patient underwent multiple endoscopies and biopsies of the pouch, the pathology of which revealed no dysplasia or malignancy.

In January 2007, he presented with low-grade fever and symptoms of prostatism with urinary retention. On this occasion, the CT scan showed an increased thickening of the posterolateral wall of the ileal pouch and multiple enlarged lymph nodes in the pelvis and retroperitoneum, some suggesting central areas of necrosis (Fig. 1A).

On retroflexion of the scope, a repeat endoscopy revealed a nodular tumour at the base of the pouch (Fig. 1B). Biopsies were consistent with a diagnosis of B-cell lymphoma (Fig. 1C). Microscopy showed tissue replaced by large discohesive malignant cells with prominent nucleoli.

Immunohistochemistry revealed that the cells were positive for CD45, CD20 and CD10. A subsequent pelvic and transrectal ultrasound showed what appeared to be an extensive tumour: at least a T3 pouch cancer with nodules extending to the periprostatic region, the largest measuring 3.5 cm (Fig. 1D). A bone marrow biopsy was negative for lymphoma. We treated the patient immediately with cyclophosphamide, adriamycin, vincristine and prednisone (CHOP).

Two months later, a CT scan showed only residual thickening of the pouch, which appeared smaller than on previous scans. Also, there was substantial reduction in the size of the pelvic lymph nodes, with the largest remaining node measuring 0.9 cm, and no residual retroperitoneal or pelvic lymphadenopathy (Fig. 2A). A pouch endoscopy performed in June 2007 revealed an area of ulceration at the base of the pouch (Fig. 2B) where the previous tumour mass had been.



**Fig. 1.** (A) A computed tomography scan of the pelvis of a 64-year-old man obtained in January 2007 showing a mass on the posterolateral wall of the ileal pouch and a lymph node with central areas of necrosis. (B) Retroflexion of the scope during a pelvic pouch endoscopy showing a nodular tumour at the base of the pouch. (C) The biopsy report shows large discohesive malignant cells with prominent nucleoli, consistent with B-cell lymphoma (hematoxylin and eosin stain). (D) Transrectal ultrasound showing a T3 pouch mass and a 3.5-cm lymph node.

## DISCUSSION

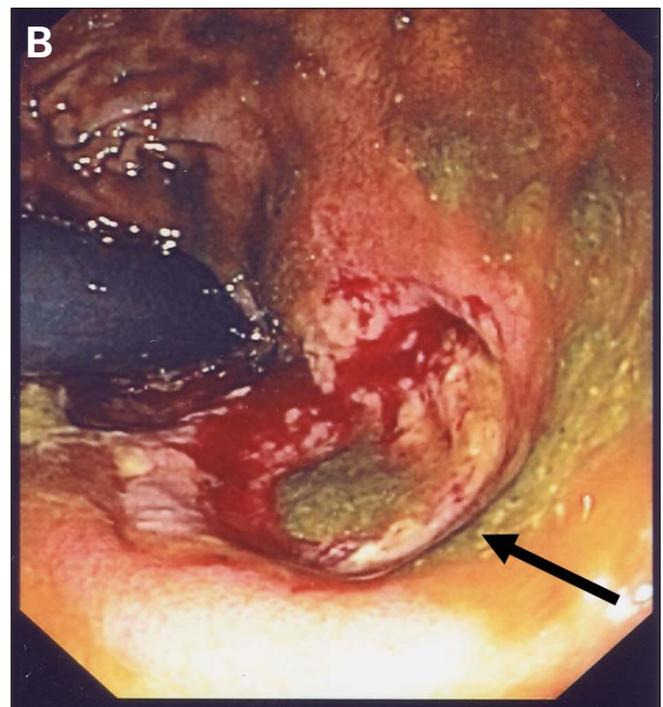
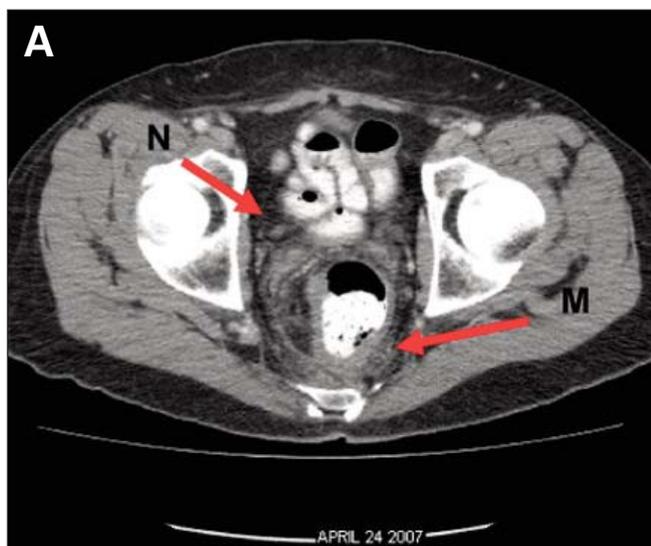
To our knowledge, ours is the fourth case of B-cell lymphoma occurring in a pouch following IPAA reported in the literature. In 1997, Nyam and colleagues<sup>8</sup> reported the first case of primary B-cell lymphoma in the pouch 10 years after an IPAA procedure. The diagnosis was made when the patient decided to have elective surgery to remove the pouch after living nearly 10 years with poor pouch function (chronic and refractory pouchitis at times requiring blood transfusions). The second case, reported by Frizzi and colleagues<sup>9</sup> in 2000, described the first case of lymphoma arising in an intact ileal pouch 8 years after the IPAA procedure. In this case, the diagnosis was made within months of the patient presenting with hematochezia, tenesmus and a mass on digital rectal examination. After multiple tests and biopsies, the pathology revealed B-cell lymphoma. The patient was treated with chemotherapy and external beam radiation that resulted in a complete clinicopathologic response, preserving the pouch viability and function. The third case, reported in 2007 by Jones and colleagues,<sup>10</sup> was the first case of pouch lymphoma in an HIV-positive patient. Presentation was 5 years after the IPAA procedure, and the diagnosis of lymphoma was made several months after repeated multiple biopsies were obtained. While undergoing chemotherapy, the patient experienced severe complications, resulting in excision of the pouch. Pathology of the resected pouch showed no residual lymphoma but revealed the presence of cytomegalovirus, which led to the diagnosis of HIV (Table 1).

As described, there is a wide range in the time from presenting symptoms to diagnosis. In the cases described, just

1 patient presented with hematochezia, tenesmus and a mass on digital rectal examination; the other 3 patients presented with symptoms related to pouchitis, making the diagnosis or suspicion of lymphoma difficult. When IPAA patients present with longstanding symptoms, clinicians should consider the possibility of a lymphoma. A CT scan or magnetic resonance image of the pelvis after pouch endoscopy should be the first imaging test used to look for this type of abnormality when there is a clinical suspicion. A thickened bowel, adjacent organ extension or nodal enlargement should heighten suspicion.<sup>7</sup>

The risk of cancer developing in the pouch or in the anal canal after an IPAA is a growing concern, despite the fact that the number of cases reported remains small. It is difficult to estimate the total number of IPAAAs performed worldwide. However, to our knowledge there have been 24 published reports to date of cancer occurring in patients with ulcerative colitis, including patients with lymphoma and adenocarcinoma.<sup>11-13</sup>

Specific risk factors for cancer related to ulcerative colitis after the IPAA procedure include chronic active pouchitis, dysplasia or cancer in the resected bowel and at-risk retained or residual mucosa.<sup>14</sup> Specifically, for non-Hodgkin lymphoma, the risk factors also include prior chemotherapy or radiotherapy; immunosuppressive therapy; HIV infection; HTLV-1 infection; *Helicobacter pylori* gastritis; Hashimoto thyroiditis; Sjogrens syndrome; and congenital disorders such as ataxia-telangiectasia,



**Fig. 2.** (A) A computed tomography scan of the pelvis of a 64-year-old man obtained in April 2007, postchemotherapy, showing residual thickening of the pouch where the original mass was present and a 0.9-cm node. (B) Retroflexion of the scope during pelvic pouch endoscopy, postchemotherapy, showing an area of ulceration at the base of the pouch where the previous tumour was present.

**Table 1. Ileal pouch anal anastomosis and pouch lymphoma in patients with ulcerative colitis**

Study	Ileal pouch anal anastomosis					Pouch cancer presentation				
	Age/sex	Pre-/postoperative diagnosis	Year of pouch	Type of procedure	Year of cancer	Time from symptoms to diagnosis	Pathology, stage	Location	Outcome	Presenting symptoms
Nyam et al <sup>8</sup>	54/male	Refractory ulcerative colitis / NA	1984	Mucosectomy + handsewn anastomosis	1994	10 yr of poor pouch function	Large cell lymphoma, T1N1M1	Pouch	Bone marrow dissemination	Multiple episodes of pouchitis
Frizzi et al <sup>9</sup>	42/male	16-yr history of ulcerative colitis + cancer / adenocarcinoma of transverse colon / T1N0M0	1989	S pouch	1997	Within months	Low-grade B-cell lymphoma, T1N0M0	Pouch	Alive	Hematochezia, tenesmus, mass on digital rectal examination
Jones et al <sup>10</sup>	40/male	Ulcerative colitis / severe pancolitis	NA	J pouch	5 yr after previous surgery	7 d	High-grade B-cell lymphoma	Pouch	Alive	Pouchitis, cytomegalovirus and HIV
Swett Cosentino	54/male	30 yr of ulcerative colitis + dysplasia of rectal stump / mild dysplasia no cancer	1996	Mucosectomy + J pouch handsewn anastomosis	2007	1.2 yr	Diffuse large B-cell lymphoma, uT3uN1	Pouch	Alive	Pouchitis

NA = not available.

Wiskott–Aldrich syndrome and celiac disease.<sup>5</sup> There are a wide variety of risk factors to be considered, suggesting that a very detailed history may be helpful in diagnosing lymphoma.

Of the 4 ulcerative colitis patients in whom lymphoma developed after IPAA, 2 had cancer or dysplasia in their resected specimen, 1 reported longstanding chronic ulcerative colitis and in 1 the information was not available. None of the lymphoma patients presented with primary sclerosing cholangitis, and only 1 patient had HIV (Table 1).

As previously mentioned, the presenting symptoms for 3 of the 4 lymphoma patients were not specific to the type of cancer that developed. The difficulty in the diagnosis is due to the similarity of presenting symptoms with other typical complications of the IPAA. Three of the 4 lymphoma patients presented with symptoms of pouchitis (e.g., anal and abdominal pain, increased frequency of bowel movements, rectal bleeding) and strictures, previously reported as common complications of an IPAA procedure.

Diagnosing lymphoma can be difficult for other reasons. It is very difficult for pathologists to make this diagnosis given the small tissue samples taken at the time of biopsy, which are often superficial and may not include enough tissue.

In summary, lymphoma of the pouch is and likely will remain fairly rare. However, we should be aware of this possibility, particularly in IPAA patients with longstanding poor function and pouchitis. An accurate history, sufficient biopsy material for assessment, a detailed review of imaging studies and a high index of suspicion will allow for more rapid diagnosis and treatment.

**Competing interests:** None declared.

**References**

1. Pemberton JH, Kelly KA, Beart RW, et al. Ileal pouch-anastomosis for chronic UC: long term results. *Ann Surg* 1987;206:504-13.
2. Ambroze WL Jr, Dozois RR, Pemberton JH, et al. Familial adenomatous polyposis: results following ileal pouch anal anastomosis and ileorectostomy. *Dis Colon Rectum* 1992;35:12-5.
3. Nuako KW, Ahlquist DA, Sandborn WJ, et al. Primary sclerosing cholangitis and colorectal carcinoma in patients with chronic ulcerative colitis: a case control study. *Cancer* 1998;82:822-6.
4. Broome U, Lofberg R, Veress B, et al. Primary sclerosing cholangitis and ulcerative colitis: evidence for increased neoplastic potential. *Hepatology* 1995;22:1404-8.
5. Brentnall TA, Haggitt RC, Ravinovitch PS, et al. Risk and natural history of colonic neoplasia in patients with primary sclerosing cholangitis and ulcerative colitis. *Gastroenterology* 1996;110:331-8.
6. Way LW, Doherty GM. *Current surgical diagnosis and treatment*. 11th ed. New York (NY): McGraw-Hill Medical; 2003.
7. Feig BW, Berger DH, Fuhrman GM, editors. *The MD Anderson surgical oncology handbook*. Philadelphia (PA): Lippincott Williams & Wilkins; 2006.
8. Nyam DC, Pemberton JH, Sandborn WJ, et al. Lymphoma of the pouch after ileal pouch anal anastomosis: report of a case. *Dis Colon Rectum* 1997;40:971-2.
9. Frizzi JD, Rivera DE, Harris JA, et al. Lymphoma arising in an S-pouch after total proctocolectomy for ulcerative colitis: report of a case. *Dis Colon Rectum* 2000;43:540-3.
10. Jones OM, Mc Cutcheon J, Heriaka E, et al. High grade lymphoma of the ileoanal pouch in an HIV-positive patient. *Colorectal Dis* 2007;9:184-5.
11. Chambers WM, McC Mortensen NJ. Should ileal pouch-anal anastomosis include mucosectomy? *Colorectal Dis* 2007;9:384-92.
12. Lee SW, Sonada T, Milson JW. Three cases of adenocarcinoma following restorative proctocolectomy with hand sewn anastomosis for ulcerative colitis: a review of reported cases in the literature. *Colorectal Dis* 2005;7:591-7.
13. Knupper N, Straub E, Terpe HJ, et al. Adenocarcinoma of the ileoanal pouch for ulcerative colitis. A complication of severe chronic atrophic pouchitis? *Int J Colorectal Dis* 2006;21:478-82.
14. Das P, Johnson MW, Tekkis PP, et al. Risk of dysplasia and adenocarcinoma following restorative proctocolectomy for ulcerative colitis. *Colorectal Dis* 2007;9:15-27.