

A Rare Case of Colonic Leiomyosarcoma in Association with Ulcerative Colitis

Daisuke Akutsu¹, Yuji Mizokami², Hideo Suzuki², Masahiko Terasaki¹, Toshiaki Narasaka¹, Tsuyoshi Kaneko¹, Hirofumi Matsui¹, Tsuyoshi Enomoto³, Taiki Sato⁴ and Ichinosuke Hyodo¹

Abstract

Ulcerative colitis (UC) is known to be associated with an increased risk of colorectal cancer. However, the occurrence of non-epithelial malignancies is uncommon. An elevated lesion in the descending colon was found in a 51-year-old woman with a 30-year history of UC. Despite tumor progression, repeated biopsies showed no cancerous findings. Because the lesion was highly suspected to be a malignant tumor, a partial colectomy was performed. The pathological diagnosis was leiomyosarcoma. Leiomyosarcoma of the gastrointestinal tract is rare, and this is only the third known case reported in patients with UC.

Key words: colonic leiomyosarcoma, ulcerative colitis, colitic cancer

(Intern Med 55: 2799-2803, 2016)

(DOI: 10.2169/internalmedicine.55.6770)

Introduction

The number of patients with ulcerative colitis (UC) has been increasing in Japan, and recently, colitis-related cancer has attracted much attention (1-3). The risk of developing cancer is higher in patients with long-term morbidity due to UC. We experienced a rare colonic tumor that was difficult to differentiate from cancer in a patient with long-standing UC.

Case Report

A 51-year-old woman who had been experiencing frequent bloody mucosal diarrhea was diagnosed with UC involving the entire colon in 1978. Since the diagnosis, she maintained a state of remission for 30 years with while only being administered oral 5-aminosalicylic acid. Surveillance colonoscopy was regularly performed, and an elevated tumor measuring 15 mm in diameter with a small ulceration was noted in the descending colon in July 2011 (Fig. 1).

Examination with narrow band imaging and magnification

showed a type III L pit pattern. The inflammatory activity of the background mucosa was mild. We performed biopsies of the tumor, including a boring biopsy, but all biopsy findings demonstrated mildly inflamed colonic mucosa with regenerative changes. Neither any neoplasm nor dysplasia was detected. The laboratory blood test showed no abnormalities, including tumor marker levels, such as carcinoembryonic antigen and carbohydrate antigen 19-9, except for a slight elevation in the C-reactive protein level (1.4 mg/dL).

The tumor gradually progressed to resemble type-2 cancer after 14 months of observation (Fig. 2). Abdominal computed tomography images revealed a tumor measuring from 20-30 mm in diameter in the descending colon, but no enlarged lymph nodes or metastases were detected. Endoscopic ultrasonography revealed that the tumor was located mainly in the submucosal layer, and the muscle layer was compressed (Fig. 3A). We considered the possibility of colitis-related cancer and recommended surgical resection, but the patient rejected this. Thereafter, we continued to perform colonoscopy examinations and biopsies every few months. A pathological examination detected no cancer cells, despite the continued growth of the tumor after 18 months

¹Department of Gastroenterology and Hepatology, University of Tsukuba, Japan, ²Gastrointestinal Endoscopy Division, University of Tsukuba Hospital, Japan, ³Department of Surgery, University of Tsukuba, Japan and ⁴Department of Pathology, University of Tsukuba Hospital, Japan
Received for publication October 30, 2015; Accepted for publication January 13, 2016

Correspondence to Dr. Daisuke Akutsu, dakutsu11@yahoo.co.jp

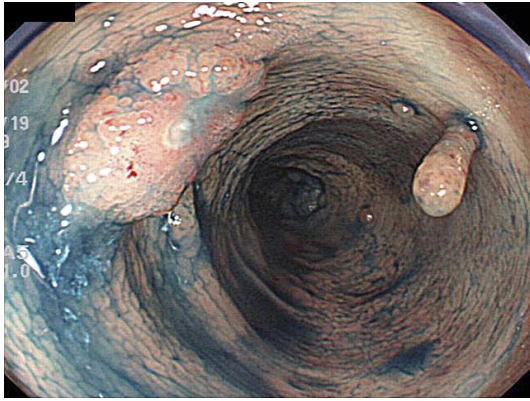


Figure 1. Colonoscopy shows an elevated tumor with an unclear boundary and small ulceration in the descending colon. A small polyp at the opposite site is an inflammatory polyp.

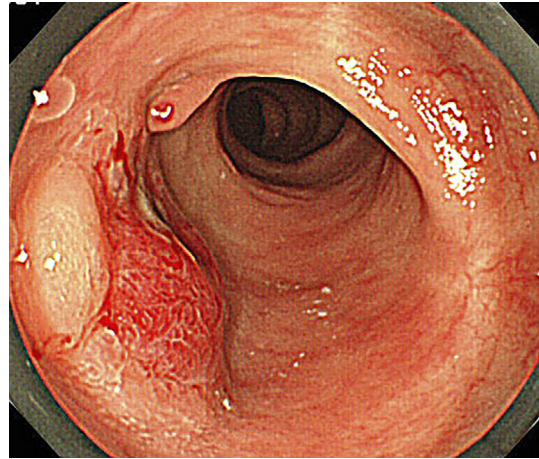


Figure 2. The tumor gradually progressed to resemble type-2 cancer after fourteen months.

(Fig. 3B). A contrast enema showed a smoothly elevated lesion with a central depression in the descending colon. Positron emission tomography computed tomography (PET-CT) was not performed.

In March 2013, the patient finally agreed to undergo surgery and received a laparoscopic partial resection of the descending colon. The gross appearance and low-power magnification of the specimen showed a protruded transmural tumor with ulceration (Fig. 4). The tumor was mainly composed of spindle cells having eosinophilic cytoplasm and cigar-shaped nuclei with a blunt end (Fig. 5). The tumor showed high mitotic activity (10/HPF). Tumor necrosis foci were scattered. Immunohistochemical staining was positive for the conventional smooth muscle markers of α -smooth muscle actin and desmin, and entirely negative for c-KIT, DOG-1, CD34, and S-100 (Fig. 6). These findings were compatible with leiomyosarcoma (LMS). The background colonic mucosa was edematous and accompanied with mild to moderate chronic inflammatory cell infiltration. No obvious cryptitis or crypt abscesses were observed. In addition, there was no dysplasia. After surgery, no recurrence or metastasis has been detected thus far (October 2015).

Discussion

Patients with UC are known to be at an increased risk of developing colorectal adenocarcinoma; however, non-epithelial malignancies are uncommon. Among non-epithelial tumors associated with inflammatory bowel disease, there have only been two reported cases of LMS in UC (Table) (4, 5) and five cases of sarcomas associated with Crohn's colitis as far as we searched PubMed with term "inflammatory bowel disease and leiomyosarcoma". The two reported cases of LMS in UC showed active colitis, uncontrolled bleeding, and polypoid tumors. Our case had minimal activity of UC with no symptoms and a tumor with a type-2 cancer-like appearance.

LMS of the gastrointestinal (GI) tract is extremely rare. The recent classification of mesenchymal tumor differenti-

ates LMS from gastrointestinal stromal tumors as a newly defined disease entity. Agaimy and Wunsch reported only three cases (1.1%) of LMS among 262 cases of GI mesenchymal lesions at their institution during a 12-year period (6). Yamamoto et al. clinicopathologically reviewed 55 reported cases of LMS in the GI tract, and found 25 small intestinal, 21 large intestinal, 5 gastric, and 4 esophageal tumors (7). The association of LMS with UC is not described in these papers, and its exact incidence is unclear. LMS might be easier to detect by surveillance endoscopy for colorectal cancer in UC. Nevertheless, there have been a few such reports so far. This suggests its rarity. We cannot deny the incidental concomitance of the diseases. However, chronic inflammation is suggested to be a risk factor for testicular LMS in some case reports (8-11), and further study may thus be needed to reveal the causal relationship between LMS and chronic bowel inflammation.

The differential diagnosis for LMS must include submucosal tumors such as lymphoma, gastrointestinal stromal tumor (GIST), and inflammatory fibroid polyp (12). Lymphoma usually occurs in the ileocecum and rectum. GIST appears most commonly in the rectum. The endoscopic findings of lymphoma and GIST are varied, but a pathological diagnosis may be possible with an appropriate biopsy. Inflammatory fibroid polyps form erosion and ulcers in the elevated mucosal surface and show an onion skin appearance on biopsy. Lipoma and lymphatic tumors can be ruled out by their color and hardness. Hemangiomas, carcinoid, and granular cell tumors have characteristic colors as well. Metastatic tumors of the colon that are most often found in gastric cancer and endometriosis that can occur in the rectum and sigmoid colon are rarely associated with an ulcer. An accurate diagnosis of submucosal tumors by biopsy is often difficult, and as a result, surgery is needed.

Pre-neoplastic lesions and invasive cancers associated with UC usually develop as multiple and superficially extended lesions called dysplasia-associated lesions or masses (DALM) (13), and patients with cancer or DALM are rec-

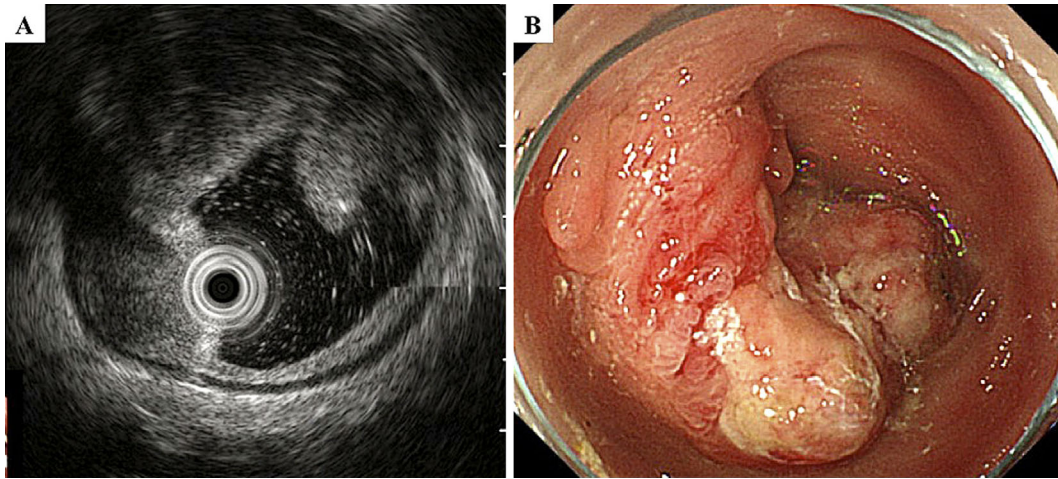


Figure 3. Endoscopic findings before the operation. Endoscopic ultrasonography shows a tumor of the submucosal layer, and the compressed muscle layer (A). The tumor demonstrates growth similar to type 2 cancer (B).

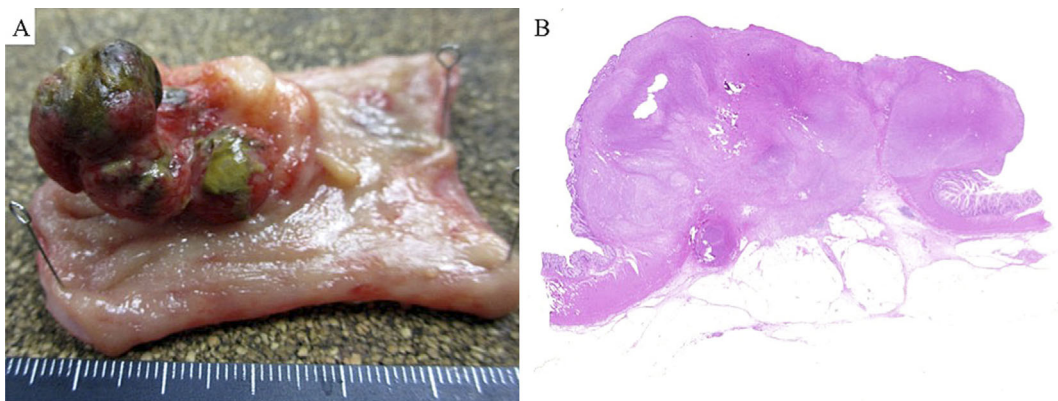


Figure 4. Resected specimen of the descending colon. The elevated tumor which resembles type-2 cancer measures 4.0x3.2 cm in size (A). Low-power magnification of the specimen stained with Hematoxylin and Eosin staining (H&E, x1) showing the transmurally growing tumor with an ulcerated superficial mucosa (B).

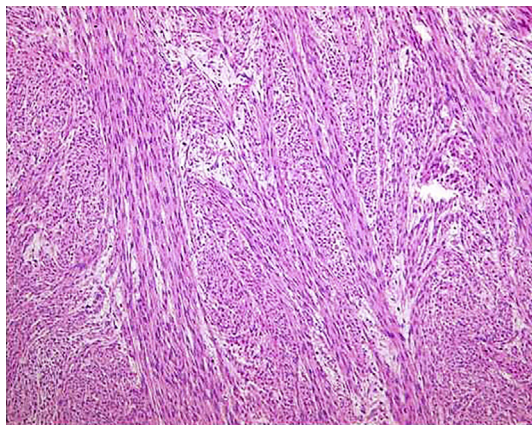


Figure 5. Pathological examinations of the tumor mainly composed of spindle cells having eosinophilic cytoplasm and cigar-shaped nuclei with a blunt end (Hematoxylin and Eosin staining, x200).

ommended to undergo prophylactic proctocolectomy with an ileoanal pouch (14). The endoscopic findings of UC-related neoplasias are so varied that morphological classification is difficult (15). A retrospective multi-institutional questionnaire survey (16) found reddish and elevated tumors with obscure boundaries in 70% of patients with UC-related neoplasias. In the present case, however, the boundary of the tumor was clear, and neither dysplasia nor cancer was observed in the biopsy specimens. Therefore, we performed a partial colectomy and could correctly diagnose the LMS by a detailed pathological examination. The reported clinical features of LMS in the GI tract are polypoid and intramural types that can arise from either the muscularis mucosae or propria (6, 17-19). Grossly, they resemble type-2 cancer, presenting with elevated and ulcerated tumors with transmural involvement (7), as was observed in this case. In most cases, the endoscopic and radiologic features are nonspecific; therefore, it is difficult to diagnose LMS preoperatively (20, 21).

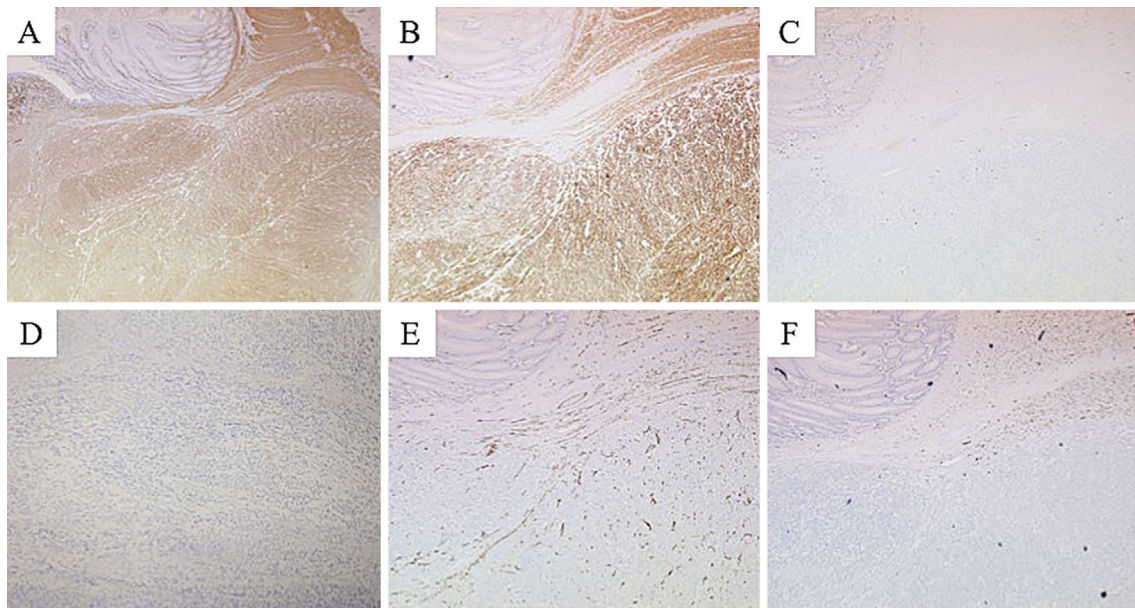


Figure 6. Immunohistochemistry showing that the tumor is positive for α -smooth muscle actin (A) and desmin (B), and negative for c-KIT (C), DOG-1 (D), CD34 (E), and S-100 (F) ($\times 40$).

Table. Reported Cases of Colonic Leiomyosarcoma in Ulcerative Colitis.

Reference	Age	Gender	Duration of UC	Treatment of UC	Activity of UC	Chief complaint	Location	Tumor form	Tumor size	Surgery
4	30	male	5 years	high dose of cortisone and azathioprin	active	bleeding	the left half colon	large polypous	40mm	Hartmann and an ileostoma
5	70	male	30 years	treated medically	active	bleeding	rectum	polypoid lesion	17mm	total proctocolectomy with end ileostomy
this case	51	female	30 years	5-ASA	remission	-	descending colon	type 2 cancer-like	30mm	descending colon resection

Lymphogenic spread is rare, and it is unnecessary to perform lymph node dissection for this tumor (6, 18). However, neighboring tissue invasion and liver metastases are common, and the prognosis of LMS is generally poor. Chemotherapy plays a limited role in the treatment of LMS (22, 23). A good prognosis can be expected only with complete surgical excision (21). Tumor larger than 5 cm in size significantly correlate with a shorter overall survival time (7). Our patient had a tumor measuring less than 5 cm in size and no metastasis, and she has survived with no recurrence for 2.5 years after surgery.

We herein reported a case of colonic LMS in an UC patient that was difficult to differentiate from a colitis-related cancer. Although its incidence in association with UC appears to be extremely rare, the possibility of LMS should be considered when a nonspecific tumor with repeatedly cancer-negative biopsy findings is found.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

We thank Dr. Takashi Nishigami and Dr. Seiichi Hirota for their excellent pathological assistance and advice.

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