CASE STUDY
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Diffuse Involvement of Primary Colorectal Lymphoma Simulating Ulcerative Colitis

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Diffuse involvement of colorectal lymphoma masquerading as colitis is a very rare presentation of primary colorectal lymphoma. Detecting occult lymphoma is difficult in the setting of diffuse colonic involvement with no definite mass and inflammatory mucosal changes. We encountered a case of diffuse-type primary colorectal lymphoma simulating ulcerative colitis in a previously healthy 31-year-old woman. Despite multiple mucosal biopsies, the biopsy diagnosis was not made due to unawareness of atypical lymphocytes admixed with dense lymphoplasmacytic infiltration. The present case emphasizes the importance of being aware of this rare presentation of primary colorectal lymphoma in order to avoid misdiagnosis.

Key Words: Colorectal lymphoma; Primary; Diffuse type; Colitis

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The incidence of primary colorectal lymphoma is very rare, accounting for 0.2%–0.6% of colorectal malignancies.[1] Primary colorectal lymphomas manifest in a variety of ways, ranging from solitary fungating masses to multiple polyps. In 1968, Friedman et al.[2] reported four cases of "lymphomatous colitis," a rare form of primary colorectal lymphoma mimicking ulcerative colitis (UC). Since then, a small number of patients with diffuse-type colorectal lymphoma have been reported, in whom a clinical and/or histological diagnosis of colitis, including inflammatory bowel disease (IBD), was made initially but were subsequently discovered to have diffuse lymphoma involvement of the colon within a short period of time.[3-17] IBD and immunosuppression have been reported as risk factors for primary colorectal lymphoma.[18] Most IBD-related lymphomas develop late in the course of an extensive longstanding disease. In that respect, these cases differ from most reports of primary colorectal lymphoma as a complication of longstanding IBD. We experienced a case of UC-like primary colorectal lymphoma in a 31-year-old woman who presented with profuse hematochezia, was misdiagnosed with UC, and died of a diffuse lymphoma involving the entire colon 12 months after hematochezia first developed.

CASE REPORT

A 31-year-old woman with no prior history of IBD presented with intermittent abdominal pain and mucoid diarrhea. Five months later, she developed hematochezia and was diagnosed with UC on the basis of endoscopic biopsy. She was treated with oral Pentasa and Pentasa enema. However, she continued to be symptomatic with marked weight loss (20 kg in 4 months). Follow-up colonoscopy revealed continuous mucosal changes from the rectum to the cecum, such as diffuse hyperemia, edematous changes, friability, loss of normal vascularity, and multiple variable-sized ulcers, consistent with UC (Fig. 1A). No mass-forming lesion was present throughout. Abdominal and pelvic computed tomography revealed diffuse edematous wall thickening in the whole colon and multiple enlargements of mesenteric lymph nodes. No hepatosplenomegaly was observed. Multiple biopsies were taken from the terminal ileum, cecum, transverse colon, sigmoid colon, and rectum. All biopsy specimens revealed diffuse infiltration of large, atypical lymphoid cells with a high nucleus-to-cytoplasmic ratio, occasional prominent nucleoli, and mitotic figures (Fig. 1B, C). They expanded the lamina propria, pushed the crypts apart, and invaded the submucosa. By immunochem-

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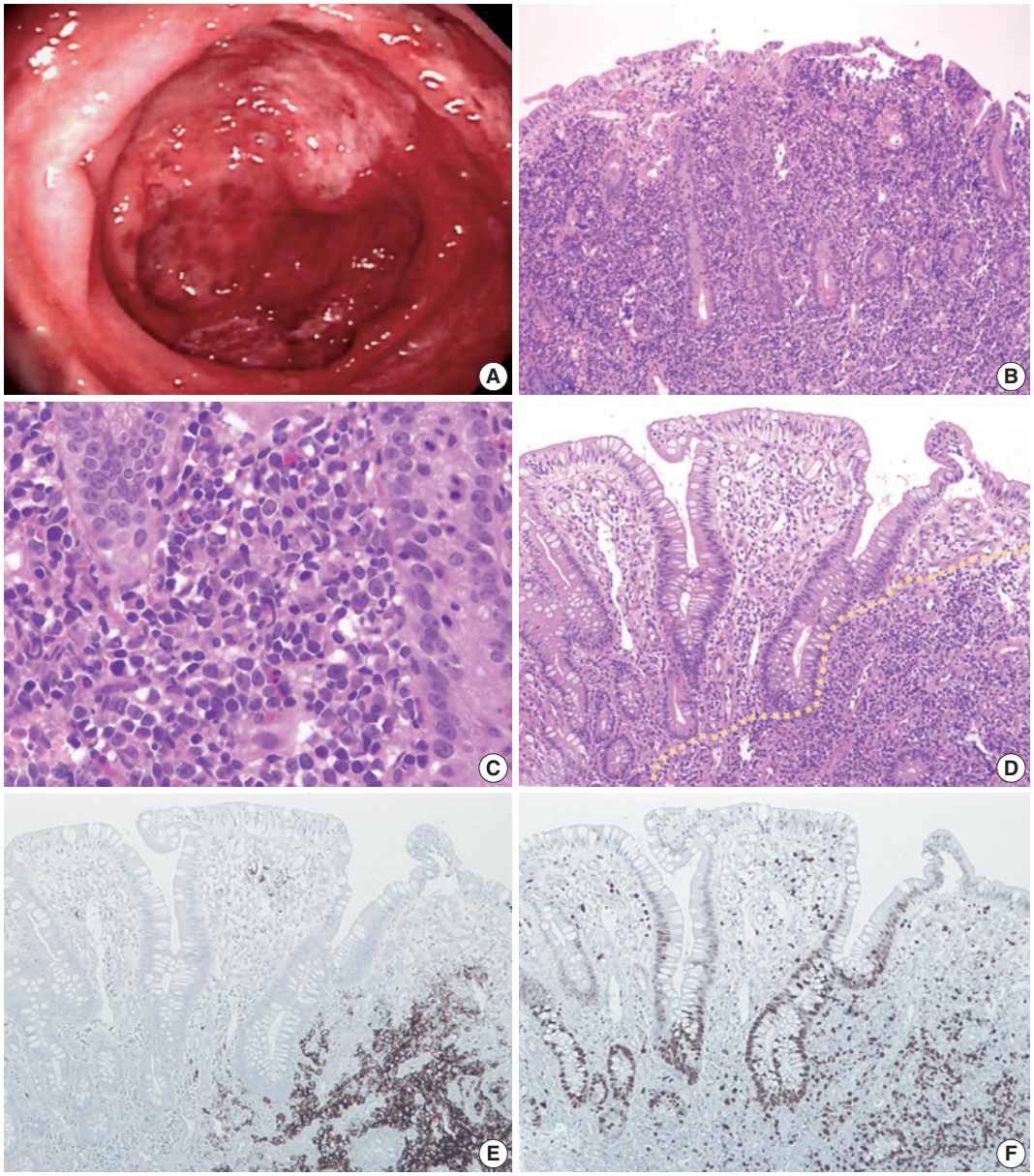

Fig. 1. (A) Colonoscopy reveals diffuse hyperemic inflamed mucosa with total loss of normal vascularity and surface ulceration from the rectum to the cecum. (B, C) Representative microphotographs of diffuse lymphoma involvement on the biopsy specimens. (B) The mucosa and submucosa are diffusely involved by densely packed lymphocytes with the background remnants of colonic crypts. Monotonous large-sized lymphocytes have vesicular chromatin and often membrane-bound nucleoli, resembling centroblasts (C). (D–F) Retrospective examination of initial colonoscopic biopsy. (D) The biopsied colonic mucosa displays crypt architectural distortion and dense inflammatory cell infiltration, resembling chronic colitis. Atypical lymphoid cells are aggregated in the bottom right corner (below the yellow dotted line), which show not only strong expression on CD20 immunostaining (E) but also high Ki-67 labeling index (F).

istry, the tumor cells were diffusely positive for CD20, bcl2, and p53, and negative for CD3, CD5, CD10, and cyclin D1. The Ki-67 labeling index was about 60%. The overall histology and immunophenotype supported a diagnosis of diffuse large B-cell lymphoma. There was no detectable evidence of extra-abdominal lymphadenopathy or lymphomatous involvement elsewhere. Bone marrow evaluation was also negative for lymphoma. As no extraintestinal disease was found, we considered it as a primary colorectal lymphoma. The patient died while receiving the second cycle of R-CHOP chemotherapy.

We retrospectively reviewed the colonoscopic biopsy specimens that were initially diagnosed with UC. At low magnification view, the background mucosa displayed crypt architectural distortion and dense inflammatory cell infiltration, resembling chronic

Table 1. Clinical and pathological findings of previously published cases of "colitis-like" diffuse-type colorectal lymphomas in the English literature

Year	Author	Sex/ Age (yr)	Pathologic diagnosis	Endoscopic findings	Revision of initial diagnosis	Superficial LAP at presentation	Extracolonic involvement
1968	Friedman et al.[2]	M/37	Reticulum cell sarcoma	UC	No	No	Liver
1968	Friedman et al.[2]	F/54	Malignant lymphoma	UC	Yes (colectomy)	No	No
1968	Friedman et al.[2]	M/73	Lymphosarcoma	UC	Yes (Bx)	No	No
1980	Weir et al.[3]	F/67	Lymphocytic lymphoma	CD	Yes (Bx)	Yes, generalized	BM
1992	McCullough et al.[4]	M/44	Mantle cell lymphoma	UC	Yes (Bx)	Yes, cervical axillary	Pancreas
1995	Lenzen et al.[5]	F/53	MALT lymphoma	UC	No	No	Upper GI tract, BM
1996	Robert et al.[6]	F/71	Mantle cell lymphoma	UC	Yes (colectomy)	No	No
1996	Hirakawa et al.[7]	M/47	T-cell lymphoma	UC	No	No	Upper GI tract
1997	Son et al.[8]	F/40	Peripheral T-cell lymphoma	CD	Yes (Bx)	No	No
2003	Isomoto et al.[9]	M/47	Adult T-cell leukemia/lymphoma	UC	No	Yes, generalized	Stomach, skin
2004	Payne et al.[10]	F/76	High-grade T-cell lymphoma	Colitis	No	Yes, generalized	No
2004	Tamura et al.[11]	M/61	Mantle cell lymphoma	Colitis	No	No	Tonsil, upper GI tract
2008	Berkelhammer et al.[12]	F/82	MALT lymphoma	CD	Yes (Bx)	No	No
2014	Koksal et al.[13]	M/73	Mantle cell lymphoma	UC	No	No	Stomach
2015	Zaheen et al.[14]	M/74	EBV-negative NK cell lymphoma	Colitis	No	No	BM, pleural effusion
2015	Wu et al.[15]	M/56	T-cell lymphoma	Ulcers	Yes (Bx)	Yes, generalized	No
2016	Cheung et al.[16]	NA/12	EBV-positive T-cell lymphoma	Colitis	No	No	Hepatosplenomegaly
2016	Cheung et al.[16]	NA/6	EBV-positive T-cell lymphoma	CD	No	No	No
2017	Zenda et al.[17]	M/59	Follicular lymphoma	UC	No	Yes, cervical inguinal	Spleen, BM
	Present case	F/32	Diffuse large B-cell lymphoma	UC	Yes (Bx)	No	No

LAP, lymphadenopathy; M, male; UC, ulcerative colitis; F, female; Bx, biopsy; CD, Crohn's disease; BM, bone marrow; MALT, mucosa-associated lymphoid tissue; GI, gastrointestinal; EBV, Epstein-Barr virus; NA, not available.

colitis. However, we found some lymphoma cells, which were admixed with other inflammatory cells or showed focal aggregation in the basal portion of the mucosa (Fig. 1D). Those lymphoma cells were more distinguishable on immunostaining for CD20 and Ki-67 (Fig. 1E, F).

Ethics statment

This study was approved by the Institutional Review Board of Inje University Ilsan Paik Hospital with a waiver of informed consent (IRB No. ISPAIK 2019-05-005) and performed in accordance with the principles of the Declaration of Helsinki.

DISCUSSION

Twenty cases (including the present one) of "colitis-like" diffuse-type colorectal lymphoma were reported in the English literature.[2-17] We excluded cases of colorectal lymphoma developed in patients with a longstanding IBD or prior established diagnosis of extracolonic lymphoma. The clinical and pathological findings of these patients are summarized in Table 1. There were 10 men, 8 women, and two children. Their mean age at presentation was 53.2 years (range, 6 to 82 years). The main symptoms were diarrhea/hematochezia (90%), loss of weight (50%), abdominal pain (25%), and fever (10%). Endoscopic findings were consistent with UC (55%), Crohn disease (20%), diffuse colitis (20%), and multiple ulcers (5%): no localized mass-like lesion was present. All cases were non-Hodgkin's lymphoma: eight were B-cell type (four mantle cell lymphomas, two mucosa-associated lymphoid tissue lymphomas, one diffuse large B-cell lymphoma, and one follicular lymphoma), seven were T-cell type, one was natural killer cell lymphoma, and four other unclassified lymphoreticular malignancies (one malignant lymphoma, one reticulum cell sarcoma, one lymphosarcoma, and one lymphocytic lymphoma). Of note, there were nine patients in whom colitis was histologically confirmed with multiple biopsy or colectomy but were subsequently found to have lymphoma involvement in a retrospective review of previous slides. Taken together, diffuse type primary colorectal lymphoma is a very rare disease and is easily misdiagnosed, particularly in reliance on endoscopic biopsy examination alone. The possibility of a hidden lymphomatous involvement would have to be considered in patients with medically refractory and rapidly progressive colitis.

Lymphoma involvement of the gastrointestinal (GI) tract may occur either as an isolated primary neoplasm or as a manifestation of systemic generalized lymphoma. To distinguish between primary and secondary GI lymphoma, Dawson's criteria is generally

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applied: (1) no palpable superficial lymphadenopathy at initial presentation, (2) a normal chest X-ray with no mediastinal lymphadenopathy, (3) no evidence of leukemia, (4) a predominant mass in the bowel with only local lymphadenopathy, and (5) no hepatosplenomegaly.[19] When the diagnostic criteria of primary colonic lymphoma are strictly applied, only seven of 20 cases of "colitis-like" colorectal lymphoma are eligible for diffuse-type primary colorectal lymphoma: 13 cases were excluded due to synchronous other organ involvement at initial presentation, such as superficial or generalized lymphadenopathy (six cases), upper GI involvement (five cases), bone marrow involvement (four cases), or hepatosplenomegaly (three cases), etc. Consequently, it is a reflection that "colitis-like" diffuse involvement of colorectal lymphoma seems to be more often secondary. Accurate discrimination between primary and secondary colorectal lymphoma is important for proper staging and management. In conclusion, since primary colorectal lymphoma can rarely manifest as "colitis-like" diffuse colonic involvement, awareness of this rare presentation is important to ensure proper diagnosis and treatment.

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Conflicts of Interest

The authors declare that they have no potential conflicts of interest.

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