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CASE REPORT

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# Primary intestinal T-cell lymphoma resembling lymphomatous polyposis: report of a case

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**Abstract** We report an interesting case of primary intestinal T-cell lymphoma (ITL) resembling lymphomatous polyposis (LP) in a 24-year-old man. The neoplasm macroscopically showed numerous small polyps throughout the colon and microscopically showed diffuse proliferation of small-sized tumor cells with occasionally cleaved or irregularly shaped nuclei. The tumor cells were immunohistochemically positive for CD3, CD8, TIA-1, and CD56, and a polymerase chain reaction study showed a single band, indicating monoclonal rearrangement of the T-cell receptor β gene. The phenotypic features in the current case are consistent with those of ITL derived from cytotoxic CD56+CD8+ intraepithelial lymphocytes. This is the second documented case of primary ITL with a morphologic pattern of LP.

**Keywords** Lymphomatous polyposis · T-cell lymphoma · Intestinal lymphoma

## Introduction

Lymphomatous polyposis (LP) is a distinct clinicopathologic condition, described as an unusual form of lymphoma manifested by numerous polyps affecting long segments of the gastrointestinal (GI) tract [3]. In 1984, Isaacson et al. [8] definitively distinguished LP from other primary gastrointestinal lymphomas because of its poor prognosis and suggested that LP was the intestinal counterpart of nodal mantle zone lymphoma. In 1994, Lavergne et al. [9] confirmed that LP consisted of a mantle-cell B-cell phenotype of nodular and monotonous growth of small cleaved cells. Recently, Hirakawa et al. [7] reported a case of primary GI T-cell lymphoma resembling LP.

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### Clinical history

A 24-year-old man who had been clinically diagnosed as having ulcerative colitis was transferred to our hospital because of ineffective long-term treatments with corticosteroids and sulphasalazine. First endoscopy of the colon and histological examination showed chronic inflammatory bowel disease without typical signs of ulcerative colitis including crypt abscesses. He intermittently complained of abdominal pain and diarrhea with bleeding, followed by body weight loss and the development of a perianal ulcer. However, there was no evidence of hypochromic anemia, vitamin-K deficiency, or night blindness, which would have been suggestive of celiac disease.

During physical examination, the patient complained of lower abdominal pain and described 8–12 occurrences of bloody stools per day. Neither superficial lymphoadenopathy nor hepatosplenomegaly was detected. Laboratory examinations showed mild inflammatory activity, increased total white blood cells but no differential abnormality, and normal immunoglobulin (Ig) values. A serological test for HTLV-1 was negative. Repeated stool cultures were negative. A chest X-ray, abdominal ultrasonography and computed tomography showed no evidence of lymphoadenopathy and hepatosplenomegaly. A colonoscopy showed numerous small polyps with their central depression throughout the entire colon (Fig. 1). An upper GI examination showed no abnormal findings. The patient underwent the construction of an artificial stoma with partial resection of the sigmoid colon to relieve the intractable perianal ulcer.

The patient began to deteriorate after the operation. Lymphoma cells appeared in the peripheral blood at the terminal stage of the disease. No chemotherapy was giv-

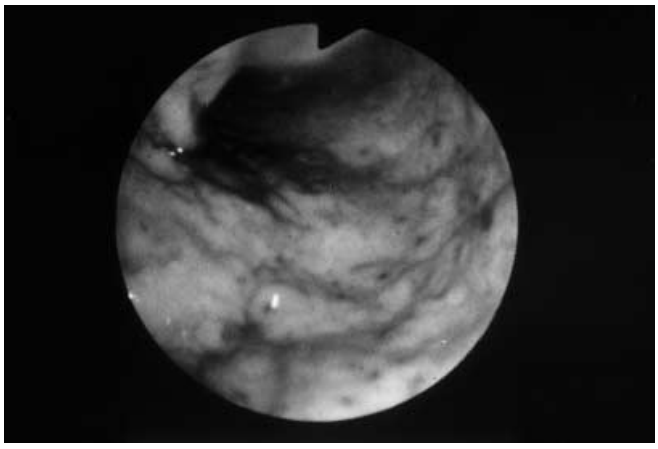

**Fig. 1** Colonoscopy shows numerous small polypoid lesions with a central depression

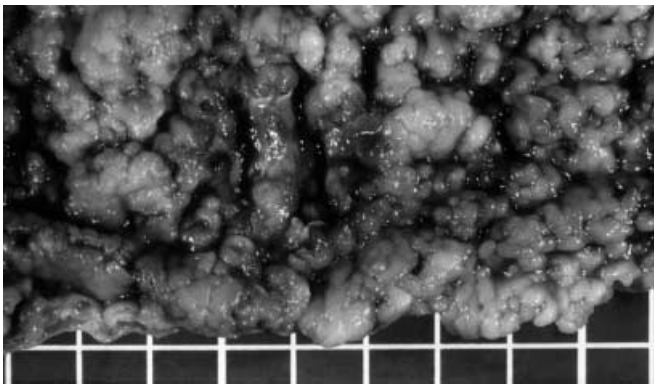

**Fig. 2** Gross appearance of the resected colon. Note numerous polypoid lesions and excavating ulcers

en because his general condition was poor. He died of respiratory distress 2 months after the operation. An autopsy was not performed.

## Materials and methods

The resected tissues were fixed in 10% formalin, routinely processed, and paraffin embedded. Sections were stained with hematoxylin and eosin and examined.

Formalin-fixed, paraffin-embedded tissue sections were evaluated immunohistochemically using the streptavidin–biotin–peroxidase complex method with a HISTOFINE kit (Nichirei, Tokyo, Japan). The primary antibodies used were: rabbit polyclonal antibodies against each heavy and light chain of Ig molecules (Dako, Glostrup, Denmark; 1:50) and granzyme B (Santa Cruz, Calif.; 1:100), and mouse monoclonal antibodies to CD3 (Dako; 1:50), CD4 (Novocastra, Newcastle, UK; 1:10), CD8 (Dako; 1:30), CD20 (Dako; 1:200), CD43 (Bioscience products, Emmenbrüke, Switzerland; 1:200), CD45R (Bioscience products; 1:200), CD45RO (UCHL1, Dako; 1:100), CD45RO (OPD4, Dako; 1:100), CD56 (Sanbio, Uden, Netherlands; 1:100), TIA-1 (Immunotech, Marseille, France; 1:800), and Ki-67 (Immunotech; 1:50). Appropriate positive and negative controls were also performed.

Electron microscopic examination was performed. The microsectioned tissue was fixed with 3% glutaraldehyde and embedded in Epon 812. Ultrathin sections were double-stained with uranyl acetate and lead citrate.

Polymerase chain reactions (PCR) were also performed. DNA was prepared from formalin-fixed, paraffin-embedded tissues for determining clonal rearrangement of B-cell and/or T-cell genes and for detection of Epstein-Barr virus (EBV) DNA. The template DNA was denatured for 5 min at 94°C, and the reaction mixture was subjected to 35 cycles of amplification of the Ig heavy chain (IgH) gene [1], the T-cell receptor β-chain gene [10], and EBV DNA [4]. The amplification products were analyzed on 8% polyacrylamide gels stained with ethidium bromide and visualized under ultraviolet light.

## Pathologic findings

A 25-cm segment of sigmoid colon was resected; the segment contained numerous polyps, varying from 5 mm to 10 mm in size, and some excavating ulcers (Fig. 2). There were no mesenteric lymph node enlargements.

Microscopically, the specimen showed dense and uniform lymphoid infiltration mainly in the mucosa and submucosa, and focally in the proper muscle and serosal layers of the colon (Fig. 3A). An increased number of intraepithelial lymphocytes was found. The lymphoid cells were small and had cleaved or irregularly shaped nuclei with scanty cytoplasm (Fig. 3B). The surface mucosa showed regeneration with enlarged, hyperchromatic nuclei, but no crypt abscesses. No lymphoepithelial lesions were noted. Mesenteric lymph nodes showed normal architecture. A biopsy of the bone marrow showed no involvement of lymphoma cells.

Immunohistochemically, the tumor cells were diffusely positive for LCA, CD3, CD8 (Fig. 3D), CD43, TIA-1, CD45RO, and CD56, and negative for CD4 (Fig. 3C), CD20, CD45R, granzyme B, IgH, and Ig light chains. The MIB-1 (Ki-67) labeling index, determined as the percentage of positive nuclei, was 21.5%.

Ultrastructurally, the tumor cells had small nuclei with thick nuclear membranes and a small amount of cytoplasm. The total number of cell organelles was small (Fig. 4).

The PCR products for the T-cell receptor β-chain gene showed single bands when two different sets of primers were used, indicating monoclonal T-cell proliferation in the tumor cells. Products for IgH appeared as smears, indicating a polyclonal B-cell population. Products for EBV DNA were negative.

## Discussion

A very rare case of primary T-cell GI lymphoma resembling LP is presented. The case was diagnosed as intestinal T-cell lymphoma without enteropathy according to the REAL classification [6] because the lymphoma was limited to the colon at the initial phase, the tumor cells were positive for several T-lineage markers, and clonal TCR gene rearrangement was noted.

T-cell lymphoma in the GI tract occurs commonly in the jejunum with multiple ulcers. However, Nakamine et al. [11] reported a case of UCHL-1-positive GI lympho-

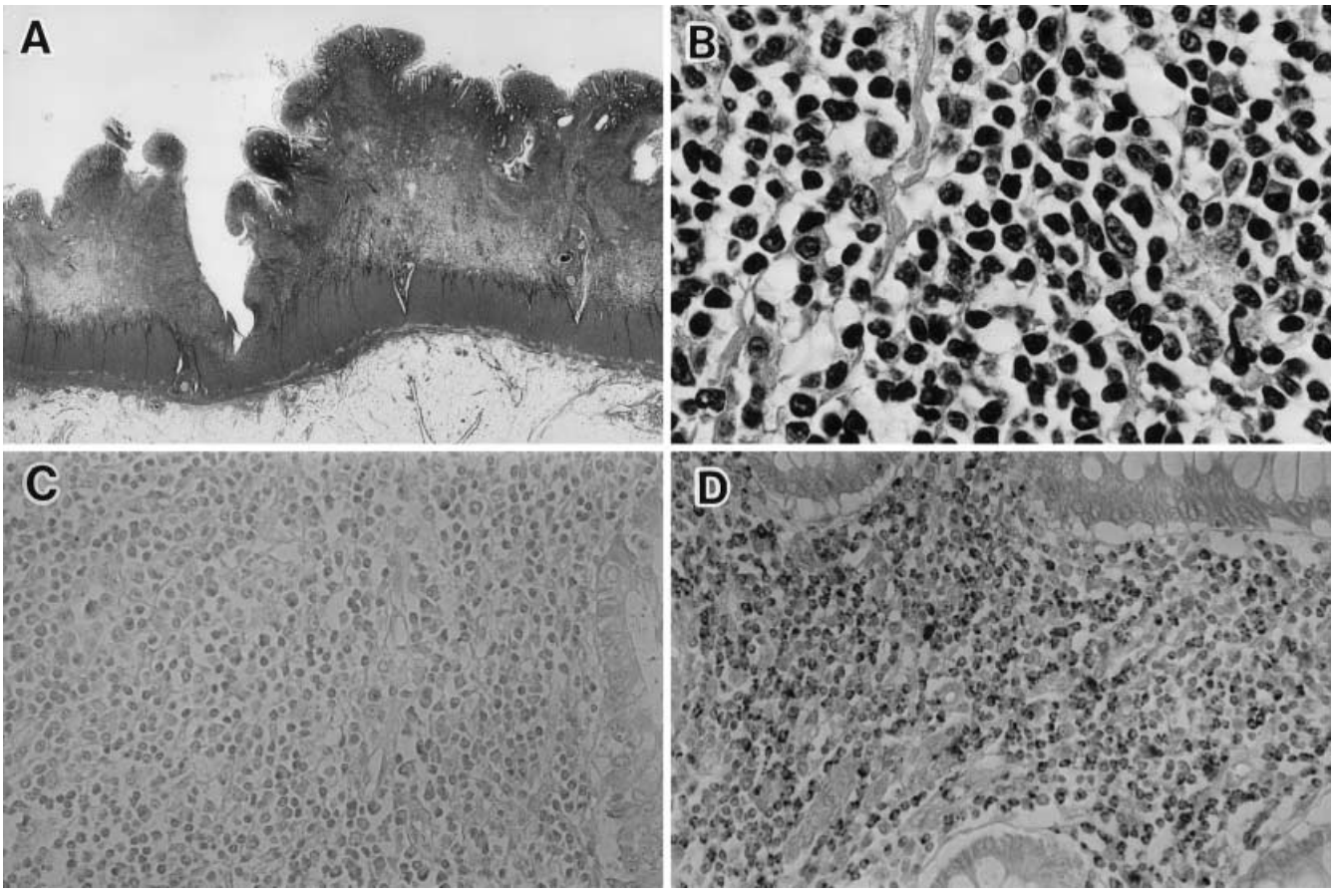


**Fig. 3** **A** Low-power appearance in sections of the polypoid lesions. Note diffuse proliferation of lymphoid cells in the whole wall of the colon (hematoxylin-eosin stain, original magnification ×2.5). **B** At high magnification, these cells are characterized by small nuclei with occasionally cleaved or irregular shapes (hematoxylin-eosin stain, original magnification ×400). **C** Immunohistochemically, most tumor cells are negative for CD4 (original magnification ×200). **D** Most tumor cells are immunoreactive for CD8 (original magnification ×200)

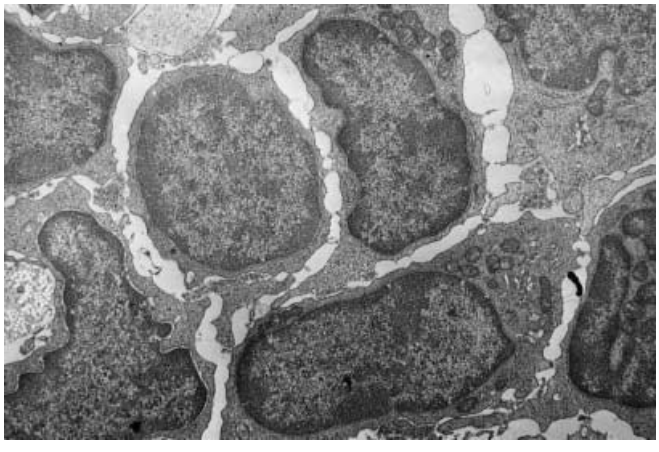

**Fig. 4** Electron microscopy shows large N/C ratio and few cell organelles (original magnification ×5000)

ma resembling LP. The case was histologically a monomorphic medium-sized cell lymphoma involving the alimentary tract from the esophagus to the rectum, abdominal lymph nodes, spleen, liver, and bone marrow. Although Nakamine et al. did not have confirmation of a T-cell origin using PCR analysis or immunohistochemical examination, the case provided important information with regard to the relationship between phenotypes and morphologic patters of proliferation. Subsequently, Hirakawa et al. [7] reported a case of primary GI T-cell lymphoma resembling LP. Because the tumor cells expressed human mucosal lymphocyte-1 antigen (HML-1), Hirakawa et al. proposed that the tumor cells had arisen from intraepithelial T lymphocytes. In the present case, immunohistochemical examination of HML-1 could not be done because there was no fresh or frozen material available. However, a homing of tumor cells was deduced from the numerous polyps affecting long segments of the colorectum. Drillenburg et al. [5] reported that expression of integrin $\alpha_4\beta_7$ was strongly related to the primary localization in mucosal T-cell lymphomas. They suggested that the presence of this receptor might play an important role in determining a characteristic mucosal dissemination pattern.

Chott et al. [2] reviewed 70 intestinal T-cell lymphomas (ITLs). Fifteen of the 70 cases (21%) were positive for CD56; the majority of the CD56+ lymphomas was of monomorphic small- to medium-sized histology and

shared the common phenotype CD3+CD8+CD4-CD5-CD57-TIA-1+. They proposed that the majority of CD56+ intestinal lymphomas were morphologically and phenotypically distinct T-cell lymphomas most likely derived from activated cytotoxic CD56+CD8+ intraepithelial lymphocytes (IELs). In the current case, the phenotypic features are consistent with those of ITLs derived from cytotoxic IELs. The clinicopathologic features, however, were unusual. Our case was a young patient whose tumor showed multiple small polyps involving the entire colon, although the entity of ITL is characterized by features such as median age around 60 years and jejunal perforation or obstruction.

To the authors' knowledge, the present case is the second documented case of primary T-cell GI lymphoma resembling LP. The first case, reported by Hirakawa et al. [7] was a low-grade T-cell lymphoma, and had no progress for 12 months after chemotherapy. However, the patient in the present case had no chance to be treated with chemotherapy. When he was diagnosed with intestinal lymphoma, the disease was in its terminal stage.

In conclusion, we demonstrated an interesting case of primary intestinal T-cell lymphoma resembling LP. We believe this case expands the spectrum of intestinal lymphoma macroscopically showing multiple polyps.

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