Peripheral T-cell lymphoma of the colon associated with hemophagocytic lymphohistiocytosis

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Received April 10, 2011; accepted September 23, 2011

Abstract

Peripheral T-cell lymphoma (PTCL) of the colon is classified as a subtype of intestinal T-cell lymphoma, which usually has multiple ulcerations. Herein, we report a case of multiple ulcers in the large intestine of a 55-year-old male, who presented to us with symptoms of abdominal pain and watery diarrhea for a month. In addition, results of his endoscopic biopsy revealed crypt abscess with dense inflammatory cells infiltrated in the lamina propria of the colon. One week later, he presented with pancytopenia and jaundice, and results of a biopsy of the bone marrow showed the appearance of hemophagocytosis. Unfortunately, colon perforation occurred during the 10th day of hospitalization, and a histopathological analysis of the colonic resection revealed PTCL. Finally, the patient died of sepsis on the 29th day of hospitalization. The endoscopic character of ulcerative colon T-cell lymphoma is easily confused with Crohn’s disease, tuberculosis colitis, and viral colitis. In addition, it is also difficult to distinguish between lymphoma cells and dense inflammatory cells while performing endoscopic biopsy of the mucosa in colon lymphoma. Once a typical geographic and punched out ulcers of the colon are found accompanying the presentation of hemophagocytic lymphohistiocytosis, the diagnosis of PTCL involving the colon should be highly suspected, even if the initial endoscopic biopsy has failed to confirm it.

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Keywords: colon lymphoma; hemophagocytic lymphohistiocytosis; peripheral T-cell lymphoma

1. Introduction

There is an increase in the incidence rate of peripheral T-cell lymphoma (PTCL) in Asia than in Western countries, and it is more aggressive than B-cell lymphoma and has poor prognosis.1 Hemophagocytic lymphohistiocytosis (HLH) is well-known to be associated with PTCL, and most of the patients die shortly after its presentation.2 Endoscopic pictures of PTCL present as a diffuse or focal segment of extensive mucosal ulceration, mimicking Crohn’s disease or tuberculosis.3 PTCL involving the colon is very rare, and only limited cases can be diagnosed correctly after performing initial colonoscopic biopsy. A final diagnosis could be delayed anywhere between 8 months and 2 years.3 Therefore, understanding the endoscopic appearance and familiarity with the clinical presentation are essential to avoid delayed diagnosis. We herein report the case of a patient with PTCL of the colon associated with HLH.

2. Case report

A 55-year-old man was admitted to our institute with symptoms of abdominal pain and watery diarrhea for a month. His body weight had decreased from 70 to 62 kg in 1 month, and he complained of low-grade fever in the afternoon and...
night. There was no superficial lymphadenopathy, including the bilateral areas of neck, axilla, and inguinal regions. Microscopic examination results of the stool were positive for occult blood and pus cells. A routine complete blood count and liver profile test results were normal initially. Colonoscopic analysis revealed multiple, deep, and geographic ulcers coated with inflammatory exudate throughout the entire colon. Ulcers with skip sign in the background of edematous mucosa could be confused with Crohn’s disease (Fig. 1A and B). The histological picture revealed dense inflammatory cells in the lamina propria (Fig. 2). The results of polymerase chain reaction (PCR)-detected tuberculosis and cytomegalovirus inclusions were negative. One week later, the patient’s condition deteriorated, and he presented with jaundice and pancytopenia. During this time, laboratory data showed the following: white blood cell count, 900 leukocytes/mm$^3$ (normal: 4000–11,000 leukocytes/mm$^3$); hemoglobin, 6.6 g/dL (normal: 12.3–18.3 g/dL); platelet count, 36,000/mm$^3$ (normal: 150,000–40,000/cumm); total bilirubin, 5.1 mg/dL (normal: 0.1–1.2 mg/dL); alkaline phosphatase, 1067 U/L (normal: 50–190 U/L); lactate dehydrogenase, 817 U/L (normal: 160–240 U/L); aspartate aminotransferase, 77 U/L (normal: 8–38 U/L); alanine transaminase, 18 U/L (normal 4–44 U/L). A computed tomography scan revealed hepatosplenomegaly without evidence of lymphadenopathy. Results of a biopsy of the bone marrow revealed the appearance of hemophagocytosis (Fig. 3). Unfortunately, colon perforation near the splenic flexure with peritonitis occurred during the 10th day of hospitalization. He underwent laparotomy and Hartmann’s procedure. A histological analysis of the specimen obtained by colonic resection revealed diffuse infiltration of medium to large atypical lymphocytes (Fig. 4). Immunohistochemical stains were positive for CD3, CD56, CD30 (focally), and negative for CD20. Although in situ hybridization of Epstein-Barr virus (EBV) was negative, the EBNA-1 and LMP-1 genes analyzed by nested PCR were positive. The T-cell receptor (TCR) gene rearrangement revealed polyclonal TCR-$\beta$ and TCR-$\gamma$. A diagnosis of the PTCL involving the colon was carried out. The patient died of sepsis on the 29th day of hospitalization.

3. Discussion

The most common gastrointestinal lymphomas are of B-cell type origin, while those of the T-cell type are the least common, and are usually seen in the small intestine and often associated with an enteropathy, the condition that is termed as enteropathy-associated T-cell lymphoma. Colonic T-cell lymphoma is extremely rare and is much less seen in the Western world. According to the Revised European-American Lymphoma classification, PTCL that involves the colon might be classified into a subtype of intestinal T-cell lymphoma having multiple ulcerations, often with perforations.

The endoscopic characteristics of ulcerative colon T-cell lymphoma usually present with multiple, skipped, confluent, and geographic ulcers in the background of edematous mucosa, which are easily confused with Crohn’s disease, tuberculous colitis, or nonspecific colitis. When analyzed microscopically, these specimens showed heavy infiltration of inflammatory cells, and the lymphoma cells are difficult to

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Fig. 1. Endoscopic characteristics of ulcerative colon T-cell lymphoma. (A) Geographic ulcer; (B) punched out ulcer in the background of edematous mucosa with mosaic pattern.

Fig. 2. Histological picture of the colonic specimens obtained by endoscopic biopsy (200×; hematoxylin and eosin stain). Crypt abscess with dense inflammatory cells infiltrated in the lamina propria. Intraepithelial infiltration of atypical lymphocytes was also noted.
conditions were also reported in Korea by Son et al in 1997, and in Taiwan by Hsiao et al in 2002. They concluded that any dense lymphocyte infiltrates seen in the biopsy specimens obtained from lesions simulating ulcerative colitis or Crohn’s disease should be assessed to exclude intestinal lymphoma.  

Because there is a great limitation in the diagnosis of PTCL involving the colon by colonoscopy, awareness of its clinical presentation is important. Unfortunately, almost all the clinical presentations including abdominal pain, diarrhea, bloating, and perforation are nonspecific.  

Hemophagocytic syndrome, characterized by persistent fever, pancytopenia, and hepatosplenomegaly, is a life-threatening complication of CD8\(^+\) PTCL. The mechanism of PTCL-associated hemophagocytic syndrome has not been fully clarified yet. An et al reported that interferon-γ and tumor necrosis factor-α, produced by phytohemagglutinin-stimulated interleukin-2-dependent CD8\(^+\) PTCL lymphoma cell (T8ML-1), caused human monocytes with surface expression of the TCR molecule to exhibit erythrophagocytosis and thrombophagocytosis in vitro. They concluded that exogenous activation of TCR signaling in PTCL cells might play an important role in the formation of PTCL-associated hemophagocytic syndrome.  

In conclusion, a prompt diagnosis of PTCL the involving colon is important yet challenging. It relies on a high index of clinical suspicion once a typical geographic and punched out ulcers of the colon mimicking Crohn’s disease are found and accompanied by the presentation of HLH. This presentation offers an important diagnostic clue beyond colonoscopy and indicates poor prognosis.

**References**


