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Case Report

Monomorphic Epitheliotropic Intestinal T-Cell Lymphoma in the Ileum with Successful Preoperative Endoscopic Evaluation

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Keywords

Monomorphic epitheliotropic intestinal T-cell lymphoma · Monomorphic epitheliotropic intestinal T-cell lymphoma · Single-balloon enteroscopy · Small intestine

Abstract

A 80-year-old man with the history of operations for gastric cancer and adhesive ileus developed abdominal pain. Positron emission computed tomography (CT) showed prominent wall thickening in the ileum with a maximal standardized uptake value of 12.1. Prior CT to diagnose adhesive ileus just taken only 4 months before did not show any masses in the abdomen. Single-balloon enteroscopy via colon showed a protruding mass at approximately 40–50 cm proximal point from the ileum end. Pathological examination of the biopsied specimen showed diffuse infiltration of medium- to large-sized atypical lymphocytes. Immunohistochemistry analysis showed that the atypical cells were positive for CD3 and CD56 and negative for CD8 and CD20. MIB-1 labeling index was extremely high as 80%. Under the diagnosis of intestinal T-cell lymphoma, the patient underwent tumorectomy, leading to the diagnosis of monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) after the negativity confirmation of Epstein-Barr virus-encoded mRNAs. The patient recovered with manageable complication and is going to receive chemotherapy. This is the first case of MEITL with extremely rapid progression in the distal ileum to be observed and diagnosed with single-balloon enteroscopy.

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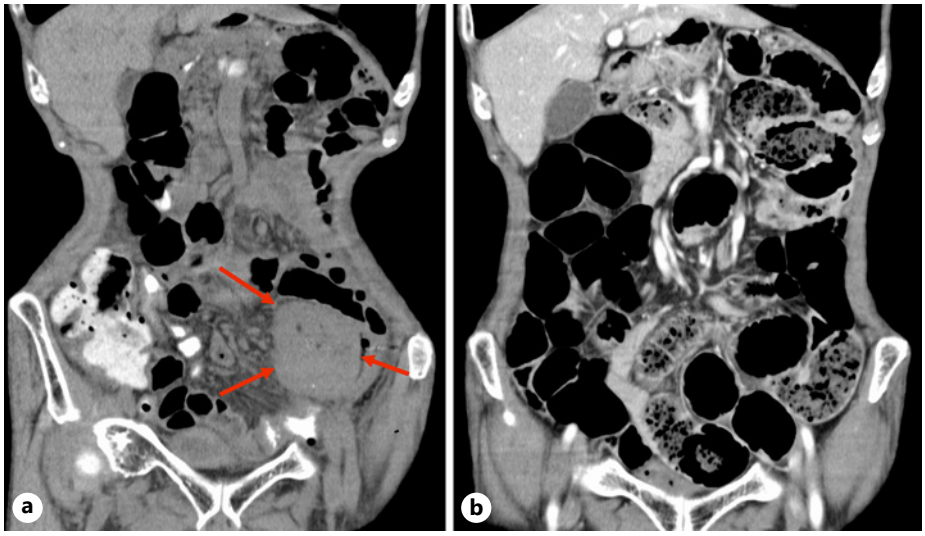

Fig. 1. CT of the abdomen. **A** An oval mass (arrows) was observed in the left lower abdomen on CT. **B** No evident mass was observed on CT just only 4 months before. CT, computed tomography.

Introduction

Except for indolent subtype, chemotherapy ± targeting therapy plays an essential role for the treatment of malignant lymphoma. In addition to lymph nodes, malignant lymphoma can occur in various organs. When occurred in the gastrointestinal tract, especially in the small intestine, special considerations should be payed for the diagnosis and treatment of malignant lymphoma.

Among gastrointestinal malignant lymphoma, gastric, the most common, malignant lymphoma can be easily diagnosed with upper gastrointestinal endoscopy. Thanks to the development of single-/double-balloon technique, not only distal duodenum but also almost all the jejunum can be observed with enteroscopy using pushing techniques in some cases. On the other hand, most of the ileum has also come to be observable with balloon enteroscopy via the large intestine [1]. We herein report an extremely rare case of monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) in the distal ileum with successful preoperative endoscopic evaluation.

Case Report

A 80-year-old man had undergone total gastrectomy with splenectomy and partial resection of the invaded pancreas for his gastric cancer. Seventy-seven months later, the patient had developed adhesive ileus, treated with surgery, that is, release of strangulation, without any problems. The patient further developed abdominal pain with low-grade fever only in 4 months after the surgery for adhesive ileus. Contrast-enhanced computed tomography (CT) showed prominent wall thickening in the small intestine (Fig. 1A). This lesion had not been detected by abdominal CT for the diagnosis of adhesive ileus (Fig. 1B). Ultrasonography also showed marked wall dilatation of the presumed ileum. Laboratory examinations demonstrated a white blood count of 14,100 (normal range, 3,300~8,600) and C-reactive protein (CRP) of 25.5 mg/dL (normal range, 0~0.14). Under the tentative diagnosis of recurrent ileus, the patient was initially treated with fluid and antibiotics therapy after the admission to our

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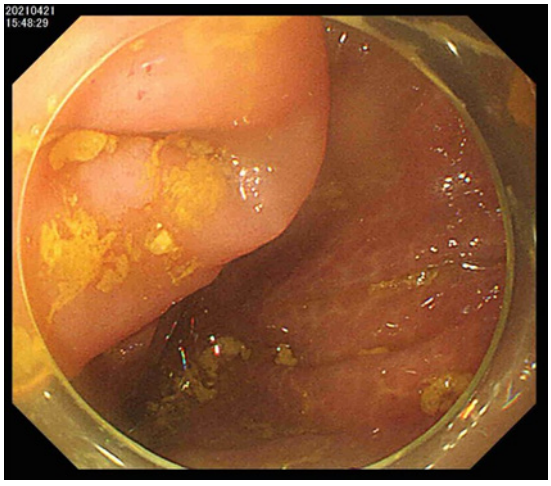

Fig. 2. Single-balloon enteroscopic findings. Single-balloon enteroscopy via colon showed a protruding mass. Due to the mechanical stenosis of the ileum, we could only observe the anal sidewall of the mass.

hospital, promptly leading to symptom relief with improvement of inflammatory response on laboratory test. To further examine the wall thickening of the ileum, serum soluble interleukin-2 receptor level was checked as high as 838 U/mL (normal range, 122~496) and enteroscopy was done to the patient. After full examination from rectum to cecum, distal ileum was examined with single-balloon enteroscopy. At approximately 40–50 cm proximal point from the ileum end, a protruding and circumferential mass was observed and made the further examination of the more proximal ileum impossible (Fig. 2). Pathological examination of the biopsied specimen showed diffuse infiltration of medium- to large-sized atypical lymphocytes (Fig. 3A, B). Immunohistochemistry analysis showed that the atypical cells were positive for CD3, CD7, CD45RO, CD56, and BCL2, and negative for CD4, CD5, CD8, CD10, CD15, CD20, CD30, CD79a, BCL6, cyclin D1, ALK, MUM1, and LMP (Fig. 3C–E). MIB-1 labeling index was extremely high as 80%. Based upon the immunohistochemistry analysis, the tumor was diagnosed as an intestinal T-cell lymphoma. Positron emission tomography/CT showed marked fluorodeoxyglucose-avidity, that is, a maximal standardized uptake value of 12.1, in the tumor. Under the preoperative diagnosis of stage 1 intestinal T-cell lymphoma, the patient underwent laparoscopic tumor resection with sufficient safety margins. Postoperative pathological study of the tumor showed a Borrmann type 2 tumor, 10 cm × 6 cm in size, extending throughout the ileal wall with no invasion to the neighboring colon. In addition to the similar immuno-phenotypes to those of biopsy specimen, intraepithelial lymphocytosis and the negativity of Epstein-Barr virus-encoded small RNAs lead us to the final diagnosis of MEITL. The patient recovered with manageable surgical site infection and was discharged on the 28th day after the operation. The patient is going to receive chemotherapy after achieving a full recovery, including complete healing of the surgical site infection, from the operation.

Discussion

MEITL was once classified as type II enteropathy-associated T-cell lymphoma (EATL). Type I EATL is well known to be closely correlated with the celiac disease, prevalent in northern European countries [2], and shows polymorphic morphology and T-cell receptor expression of predominantly alpha-beta. Due to the marked differences in etiology, morphology, and immunophenotype of the 2 subtypes, WHO changed the terms type I EATL and type II EATL to EATL and MEITL, respectively [3].

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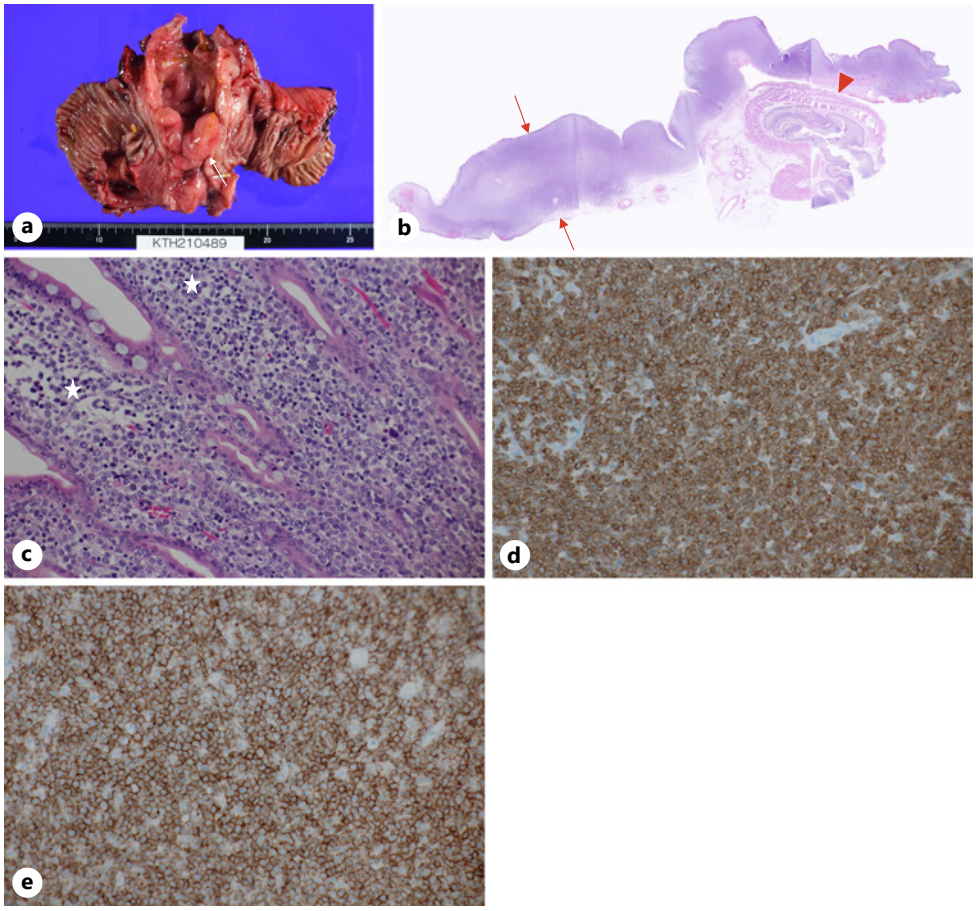

Fig. 3. Pathological findings. **A** Excised specimen showed a Borrmann type II tumor (arrow) in the ileum. **B** Low magnified view showed the tumor extending throughout the ileal wall and no invasion to the neighboring colon (arrow head). **C** High magnified view of the tumor showed widened villi (stars) and diffused infiltration of medium- to large-sized atypical lymphocytes. Immunostaining showed the tumor was highly positive for CD3 (**D**) and CD56 (**E**).

MEITL tends to form protruding masses, leading to clinical features such as sudden abdominal pain and ileus based on intestinal obstruction when occurring in the small intestine [4]. MEITL, therefore, cannot generally be detected until the stenosis of the small intestine progresses to a certain extent and causes some kind of symptoms. On the other hand, EATL forms rather ulcerating nodules, plaques, and strictures than large exophytic masses to the gastrointestinal lumen, leading to the gradual onset of abdominal pain and diarrhea due to the underlying condition of celiac disease [5]. Symptoms observed in this case were the sudden onset of abdominal pain, well matching the MEITL symptoms.

The prognoses of both the MEITL and EATL are extremely poor, showing identical median survival time of 7 months [3, 6]. These facts imply that when once clinically detected either tumor grows very aggressively. On the diagnosis of prior ileus only 4 months before, abdomen of this patient was assessed with CT and had no masses. It is well known that malignant cells grow in a Gompertz model [7], suggesting both high proliferative capacity of clinical tumor and long-term low proliferative nature of subclinical malignant cell agglomeration. In addition to the extremely high Ki-67 labeling index, clinical outcomes of this case should well explain the dismal prognosis of MEITL.

Diffuse large B-cell lymphoma, most common malignant lymphoma, at various sites extremely well responds to combination chemotherapy plus anti-CD20 antibody [8], often leading to a cure of the diffuse large B-cell lymphoma. On the other hand, majority of MEITL have long failed to respond to conventional chemotherapies. Tan et al. [9] reported that one-fourths of MEITL cases had aberrant CD20 positivity. Efficacy of adding rituximab to conventional chemotherapy should be explored in CD20-positive MEITL cases. In addition, PD-L1 positivity should be examined for the application of immune checkpoint inhibitor(s) to the treatment of both MEITL and other malignant lymphomas with dismal prognosis including EATL [10].

We needed urgent operation to the present T-cell malignant lymphoma in the small intestine whether the target foci should be EATL, MEITL, or extranodal NK/T-cell lymphoma. To our knowledge, this is the first case of intestinal T-cell lymphoma in the small intestine successfully observed and histologically diagnosed with single-balloon enteroscopy. Attending physicians should try to preoperatively diagnose the target foci even in the small intestine. In conclusion, a very rare case of MEITL in the distal ileum with extremely rapid progression was observed and diagnosed with single-balloon enteroscopy.

Statement of Ethics

The aricle is exempt from Ethical Committee approval due to the nature of reporting based on daily clinical practice. Informed written consent was obtained from the patient for the publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Y. Kitano contributed to the design of the report. S. Oura drafted the manuscript. Y. Mushiake treated the patient. S. Makimoto revised the manuscript. All the authors have read and approved the final version of the manuscript.

Data Availability Statement

All data generated during this study are included in this article. Further enquiries can be directed to the corresponding author.

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