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Single Case

Multiple Small Intestine Ulcers with Desquamation of the Fingers

Azusa Kawasaki Kunihiro Tsuji Hisashi Doyama

Department of Gastroenterology, Ishikawa Prefectural Central Hospital, Kanazawa, Japan

Keywords

Small intestine · Ulcers · Desquamation of the fingers · *Yersinia pseudotuberculosis* · Infection · Kawasaki disease

Abstract

A 73-year-old female was admitted to our hospital with abdominal pain and diarrhea. Computed tomography detected distension of the small intestine. A palmar erythema, multiple oral ulcers, and desquamation of the fingers appeared after hospitalization. Small-bowel endoscopic images showed multiple ulcers. We attributed this case to infection with *Yersinia pseudotuberculosis* based on the changes in *Y. pseudotuberculosis* antibody titers throughout the course of the illness. This report is valuable, as it illustrates the endoscopic characteristics of a *Y. pseudotuberculosis* infection with skin lesion and ileus, which may enable us to deepen the pathologic understanding of this disease.

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Introduction

Advances in medical device development have enabled the evaluation of lesions in the small intestine that were previously difficult to assess. Small intestine ulcers are representative small-intestine lesions, and their etiology can be idiopathic, infectious, drug-induced (aspirin and other NSAIDs), or avasculitis-related [1]. The two main *Yersinia* species that are known to cause abdominal symptoms are *Yersinia enterocolitica* and *Yersinia pseudotuberculosis*. Reportedly, *Y. pseudotuberculosis* infection is associated with Kawasaki disease-like constitutional symptoms [2–5]. However, the underlying pathogenic mechanism is unclear. Additionally, it is said that there are no clear differences in endoscopic images of patients with an infection by either bacteria [6].

We report a case of multiple small intestine ulcers and desquamation of the fingers. After thorough investigations, the characteristics of our case did not meet the diagnostic criteria for Kawasaki disease. Additionally, we thought that the etiology in this case was very likely to be *Y. pseudotuberculosis* infection given its frequent occurrence in small intestine ulcers and the change in *Y. pseudotuberculosis* antibody titers in pair serum samples of the patient during the course of the illness. Both Kawasaki disease and *Y. pseudotuberculosis* infection are characterized by an intestinal tract lesion as the main constitutional symptom. However, to the best of our knowledge, no previous reports have included endoscopic images of intestinal lesions caused by *Y. pseudotuberculosis* infection. Thus, it is important to deepen the pathologic understanding of these lesions by reporting the endoscopic images associated with this disorder.

Case Report

A 73-year-old female was admitted to our hospital on May 2015. She presented abdominal pain and diarrhea during 5 days, for which she was examined and treated by a primary care physician. As her symptoms did not improve, she was admitted to our hospital. She had a history of cholecystectomy 20 years earlier. She had no history of smoking or alcohol abuse. She did not take any medication. Furthermore, she denied drinking well water.

On admission, her temperature was 37.7°C, her pulse was 90 beats/min, and her blood pressure was 143/66 mm Hg. Her abdomen was distended, but no other abnormality was observed upon physical examination. Laboratory testing on admission showed an increased C-reactive protein level (Table 1). Distension of the small intestine was also detected on computed tomography (CT).

The patient was initially managed conservatively. She received ceftriaxone 1 g/day by intravenous drip infusion. Her C-reactive protein levels improved transiently and then continued to increase. Several other tests were performed but all yielded negative results (Table 2), for example: bacterial cultures of blood and stool, antinuclear antibodies, cytoplasmic anti-neutrophil cytoplasmic antibody, myeloperoxidase ANCA, anti-double stranded DNA IgG antibody, enzyme-linked immunospot assay (T-SPOT®.TB), among others. A CT scan performed on hospitalization day 7 showed that the distension of the small intestine continued to worsen. Abdominal distension occurred as a consequence of intestinal tract distension, and she thus underwent ileus tube insertion. On hospitalization day 12, her symptoms

began to improve. Fluoroscopy via the tube showed that there was no obvious stenosis, but there was stagnation of the contrast medium. On hospitalization day 13, we performed a small-bowel endoscopy. We obtained endoscopic images of the affected area that showed a variety of lesions, including multiple ulcers running along the direction of the minor axis, map-like ulcers, and portions of disrupted mucous membrane involving the entire circumference of the ileum (Fig. 1). On hospitalization day 20, we performed an esophagogastroduodenoscopy. We obtained endoscopic images of the mucous membrane lesions presenting as redness, erosions, and an ulcer extending from the duodenal angulus to the second part of the duodenum (Fig. 2). However, no specific findings were obtained pathologically (Fig. 3). On hospitalization day 9, the patient presented a palmar erythema, with the subsequent appearance of multiple oral ulcers on hospitalization day 11. Desquamation of the fingers occurred on hospitalization day 13 (Fig. 4). We suspected adult-onset Kawasaki disease or *Y. pseudotuberculosis* infection as possible etiologies for the patient's condition based on the presence of finger desquamation. A coronary artery CT and an echocardiography were performed, but these examinations did not reveal any abnormalities. Additionally, there was no evidence of coronary aneurysm. Thus, based on the clinical findings, our case did not meet the diagnostic criteria for Kawasaki disease. Antibody titers of *Y. pseudotuberculosis* were measured in pair serum samples showing an 80-fold increase on hospitalization day 11; these titers decreased thereafter (Table 3). Conservative medical treatment was continued and the patient's symptoms gradually improved. She was discharged after 44 days of hospitalization.

Discussion

We reported a case of multiple small intestine ulcers associated with desquamation of the fingers. To the best of our knowledge, our report is the first to describe such a presentation of *Y. pseudotuberculosis* infection and provide endoscopic images of the intestinal lesions. Although we were unable to isolate the bacterium, it is extremely likely that this was a case of *Y. pseudotuberculosis* infection for the following reasons.

First, the patient presented desquamation of the fingers. Based on the differential diagnosis, we considered Kawasaki disease and *Y. pseudotuberculosis* infection as the possible underlying etiologies. Desquamation of the fingers is highly specific for Kawasaki disease and *Y. pseudotuberculosis* infection. This symptom is seen in 96% of Kawasaki disease cases and in 83% of *Y. pseudotuberculosis* infection cases [7, 8].

Second, it is difficult to isolate the bacteria in cases of *Y. pseudotuberculosis* infection. We performed bacterial cultures of stool, but the results were negative. The presence of ileus precluded us from performing bacterial cultures of biopsy samples early on. Although a low-temperature culture is ideal, even if the culture is maintained at a low temperature and preferential segregation culture medium is used, there is only about a 40% likelihood of isolating these bacteria [9]. Since we did not consider *Y. pseudotuberculosis* infection early during the disease course in the present case, we were unable to conduct a low-temperature culture.

Third, after measuring *Y. pseudotuberculosis* antibody titers in pair serum samples of the patient, we observed a rise in the initial levels with a subsequent drop. We were not able to examine initial antibody titers given the delay in establishing the primary diagnosis and the

titer change did not reach 160-fold increase. However, we strongly consider that *Y. pseudotuberculosis* was the causal agent based on the 4-fold antibody titer rise in only one type of the serum group. It seems unlikely that such change in antibody titers was attributable to the presence of bacteria other than *Y. pseudotuberculosis*.

We were able to document the intestinal lesions by endoscopy. The characteristic endoscopic images of enteritis by *Yersinia* species comprise terminal ileitis, scattered mucosal ulcers with white mossy appearance, ileocecal valve swelling, aphthous ulcers on the right large intestine, and punctate irregular redness [10]. It has been reported that there is no clear difference between the endoscopic characteristics and distribution of lesions by *Y. enterocolitica* and *Y. pseudotuberculosis* [6]. Notably, endoscopic images of cases similar to ours have not been reported previously. In a previous report, the main lesion of enteritis by *Yersinia* was terminal ileitis [11, 12]. Matsumoto et al. [12] reported that these lesions are changes of the solitary lymph nodes and Peyer's patch. In the present case, the lesions were extensive in the duodenum and widespread in the small intestine. Furthermore, the endoscopic images were also different from the representative lesions of *Y. pseudotuberculosis* infection reported so far.

Some patients with Kawasaki disease and *Y. pseudotuberculosis* infection may present with ileus, as in the present case [13–16]. Miyake et al. [15] reported that 7 of 310 patients with Kawasaki disease developed pseudo-obstruction. In this case, we observed multiple ulcers running along the direction of the minor axis, map-like ulcers, and mucous membrane disruption involving the entire circumference of the ileum. The mechanism of such changes has been proposed to be mesenteric artery vasculitis with bowel ischemia and associated dysfunction of the myenteric plexus [15, 17].

Pathological examination of the ischemic changes also shows nonspecific inflammatory cell infiltrates consisting of lymphocytes and plasma cells [18]. The present case shows pathologic findings of ischemia. The endoscopic image of the present case closely resembles ischemic enteritis (Fig. 5). Therefore, we consider that the endoscopic images of the intestinal lesions in the present case support the proposed mechanism of ischemia leading to ileus secondary to *Y. pseudotuberculosis* infection. The condition may worsen depending on which area is affected in relation with the mesentery. Furthermore, annular ulcers were mixed with map-like ulcers and villi atrophy.

Kawasaki disease is a systemic vasculitis and some cases of *Y. pseudotuberculosis* infection show clinical conditions similar to Kawasaki disease. However, the etiology of the Kawasaki disease remains largely unclear. Previous studies have reported an association between Kawasaki disease and *Y. pseudotuberculosis* infection [2–5]. In a previous report, *Y. pseudotuberculosis* infection was identified in 9.3% of patients with Kawasaki disease [5]. Further, in some reports, Kawasaki disease diagnostic criteria were met in 8.8–16.6% of cases with *Y. pseudotuberculosis* infections [3, 19]. Some cases of *Y. pseudotuberculosis* infection present with skin lesions, and ileitis are thought to develop secondary to vasculitis triggered by infection. We think that the endoscopic images obtained in our case are the first to have captured these changes.

In conclusion, we observed *Y. pseudotuberculosis* infection presenting with skin lesions and ileus on endoscopic images. These endoscopic images suggested the presence of ischemic changes. Thus, our findings seem to indicate that some cases of *Y. pseudotuberculosis* infection, particularly those presenting with skin lesions and ileus, may develop vasculitis trig-

gered by the infection. Further, it is important to consider not only the characteristics of *Y. pseudotuberculosis* infection, but also those of Kawasaki disease, in order to understand these conditions, which have overlapping presentations in some cases. Some cases of Kawasaki disease involve pseudo-obstruction, as in the present case. Additionally, it was difficult to further the understanding of this condition, as it was considered to be a childhood illness only. We consider that even in Kawasaki disease with pseudo-obstruction, there is a possibility that the endoscopic images are similar to those observed in this case. This report is valuable, as it illustrates the endoscopic characteristics of a *Y. pseudotuberculosis* infection with systemic manifestations, which may enable us to deepen the pathologic understanding of this disease.

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Statement of Ethics

Informed consent was obtained for this case report.

Disclosure Statement

The authors declare that they have no conflicts of interest.

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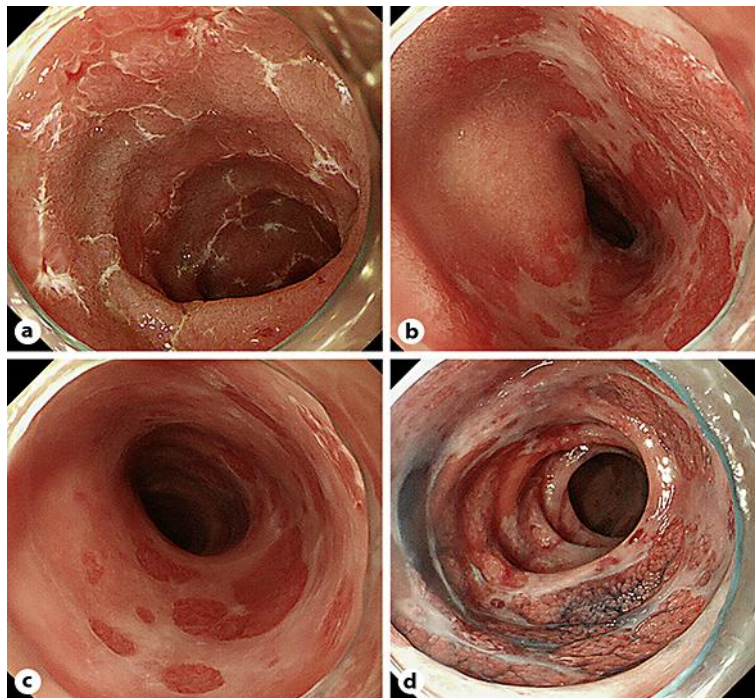


Fig. 1. **a** Small-bowel endoscopy shows multiple ulcers running along the direction of the minor axis of the ileum. **b** Small-bowel endoscopy shows map-like ulcers in the ileum. **c, d** Small-bowel endoscopy shows mucous membrane disruption involving the entire circumference of the ileum.

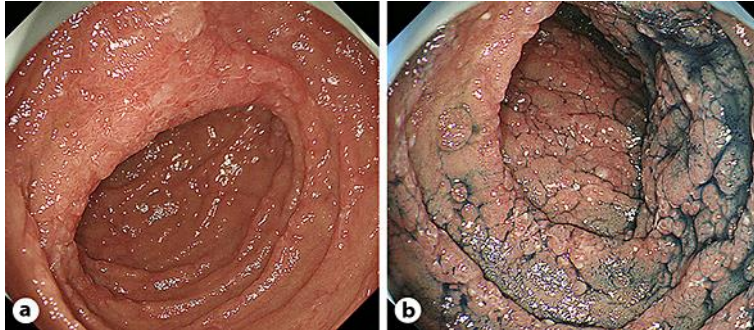


Fig. 2. a, b Esophagogastroduodenoscopy illustrates the mucous membrane disorder with redness, erosion, and ulcers in the duodenum.

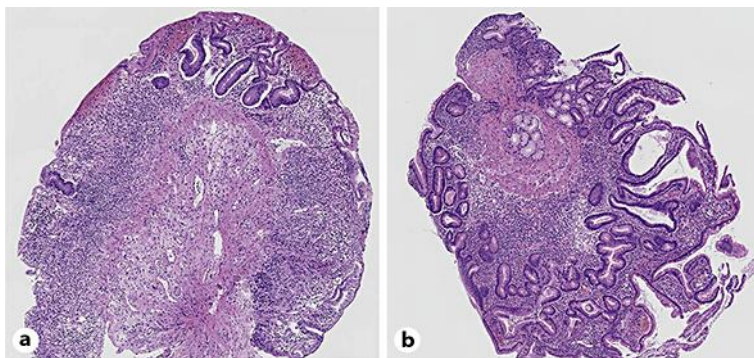


Fig. 3. a Pathological findings in the small intestine showing nonspecific inflammatory cell infiltrates consisting of lymphocytes and plasma cells. H&E, original magnification $\times 40$. **b** Pathological findings in the duodenum showing nonspecific inflammatory cell infiltrates consisting of lymphocytes and plasma cells. H&E, original magnification $\times 40$.



Fig. 4. Desquamation of the fingers occurred on hospitalization day 13.

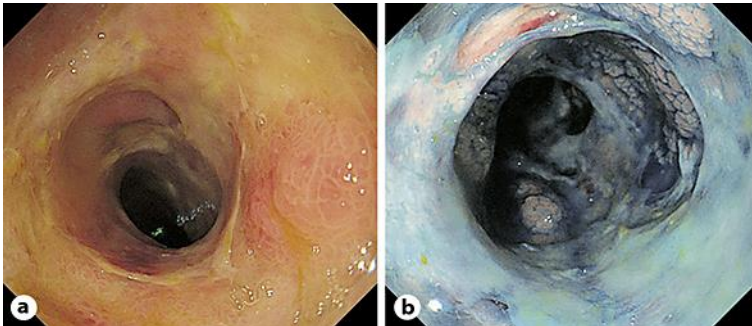


Fig. 5. a, b Endoscopic image showing ischemic enteritis (from Okado et al. [18]).

Table 1. Laboratory data on admission

<i>Complete blood count</i>	
White blood count (all), μL	4,610
Neutrophils, %	84.4
Lymphocytes, %	11.1
Monocytes, %	4.3
Eosinophils, %	0.0
Basophils, %	0.2
Red blood count, μL	554×10^4
Hemoglobin, g/dL	16.0
Hematocrit, %	48.0
Platelets, μL	26.9×10^4
<i>Blood biochemistry</i>	
Total protein, g/dL	6.2
Total bilirubin, mg/dL	0.50
Alkaline phosphatase, U/L	146
Aspartate aminotransferase, U/L	86
Alanine aminotransferase, U/L	38
Lactate dehydrogenase, U/L	584
γ -glutamyltranspeptidase, U/L	22
ZTT, KU	1.5
TTT, KU	0.4
Creatine kinase, U/L	996
AMY, U/L	93
Blood urea nitrogen, mg/dL	22.5
Creatinine, mg/dL	0.68
Na, mEq/L	131
K, mEq/L	4.4
Cl, mEq/L	96
C-reactive protein, mg/dL	15.5
PCT, ng/mL	0.5~2
C3, mg/dL	90.1
C4, mg/dL	23.7
IgA, mg/dL	132.8
IgG, mg/dL	503.4
IgM, mg/dL	28.8
CEA, ng/mL	1.5
CA19-9, U/mL	7.1

Table 2. Additional laboratory findings

Bacterial cultures	
Blood	negative
Stool	negative
ANA, ×	<40
C-ANCA, EU/L	<1.0
P-ANCA, EU/L	<1.0
ds-DNA-IgG, IU/mL	<1.2
ds-DNA-IgM, U/mL	<1.0
ELISA (T-SPOT)	negative

ANA, antinuclear antibodies; C-ANCA, cytoplasmic anti-neutrophil cytoplasmic antibody; P-ANCA, myeloperoxidase ANCA; ds-DNA-IgG, anti-double-stranded DNA IgG antibody; ds-DNA-IgM, anti-double-stranded DNA IgM antibody; ELISA, enzyme-linked immunospot assay.

Table 3. Change in *Y. pseudotuberculosis* antibody titer

Hospitalization day	Yp2a titer
11	1:80
21	1:40
25	<1:20

Yp, *Yersinia pseudotuberculosis*.