Clinical Case Report

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Protein-losing enteropathy secondary to nonocclusive mesenteric ischemia

A case report

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Abstract

Rationale: Nonocclusive mesenteric ischemia (NOMI) is a life-threatening disorder; prompt diagnosis is vital. Surgical treatment is often required, but some cases can be treated conservatively. We herein report an extremely rare case wherein protein-losing enteropathy (PLE) developed after conservative treatment of NOMI.

Patient concerns: The patient was a 66-year-old man. He underwent laparoscopic super low anterior resection and temporary ileostomy for sigmoid colon cancer and rectum cancer. During the postoperative course, he developed ileus. Subsequently, he developed shock. On examination, the possibility of NOMI could not be denied, but intestinal necrosis was absent. Conservative treatment was initiated. His general condition improved, but the ileus persisted. Therefore, we performed a stoma closure. Ten days after stoma closure, he developed continuous unexplained diarrhea. The serum albumin and total protein levels were low. The symptoms improved after administration of an antidiarrheal drug, but the root cause was yet untreated.

Diagnosis: The patient's alpha-1 antitrypsin clearance was increased. A CT scan revealed an enhanced hypertrophied wall of the short segment of the small intestine, and 99m Tc-labeled human serum albumin scintigraphy revealed protein leakage into the thickened wall of the small intestine. We arrived at a definitive diagnosis of PLE secondary to NOMI.

Interventions: Partial resection of the affected small intestine was performed.

Outcomes: The patient recovered uneventfully and was discharged on the 30th postoperative day.

Lessons: NOMI has a high mortality rate, often requiring intestinal resection immediately after onset. To our knowledge, there is no report of PLE developing after conservative treatment, as in our case. Further study of cases is necessary to determine the reversibility of the condition, which will influence the therapeutic plan. We herein present an extremely rare case of PLE after conservative treatment for NOMI. The possibility of PLE also needs to be considered when hypoalbuminemia occurs after conservative treatment of NOMI.

Abbreviations: NOMI = nonocclusive mesenteric ischemia, PLE = protein-losing enteropathy, TPN = total parenteral nutrition.

Keywords: conservative therapy, nonocclusive mesenteric ischemia, protein-losing enteropathy

1. Introduction

Nonocclusive mesenteric ischemia (NOMI) is a life-threatening disorder. It has a mortality rate of up to 70%; a prompt diagnosis and, very often, surgical treatment, are essential.[1,2] However, conservative treatment is possible. Although there are reports of intestinal stenosis occurring after conservative management,[3,4] there are no reports of protein-losing enteropathy (PLE). We herein report an extremely rare case of PLE developing after conservative treatment of NOMI.

2. Case presentation

The patient was a 66-year-old man. He had undergone laparoscopic super low anterior resection and temporary ileostomy for sigmoid colon cancer (pT3, pN2 (#251(4/10), #252(0/5), #253(0/8)), M0, H0, P0, PUL0, pStage IIIb, D3, pPM0, pDM0, RM0, R0, CurA, tubular adenocarcinoma, moderately differentiated type, intermediate, INFb, ly0, v0, PN0), and rectal cancer (pT1b, pN0 (#241(0/1), #242(0/1), #253 (0/8)), M0, H0, P0, PUL0, pStage I, D3, pPM0, pDM0, RM0, R0, CurA, tubular adenocarcinoma, well-differentiated type, intermediate, INFb, ly0, v1, PN0) in September 2016. From the 5th day after surgery, he developed subileus. His symptoms improved after conservative treatment: transileostomy decompression tube. However, 16 days after surgery, he complained of abdominal fullness and pain. No signs of peritoneal irritation were detected. Nasogastric tube decompression was performed,

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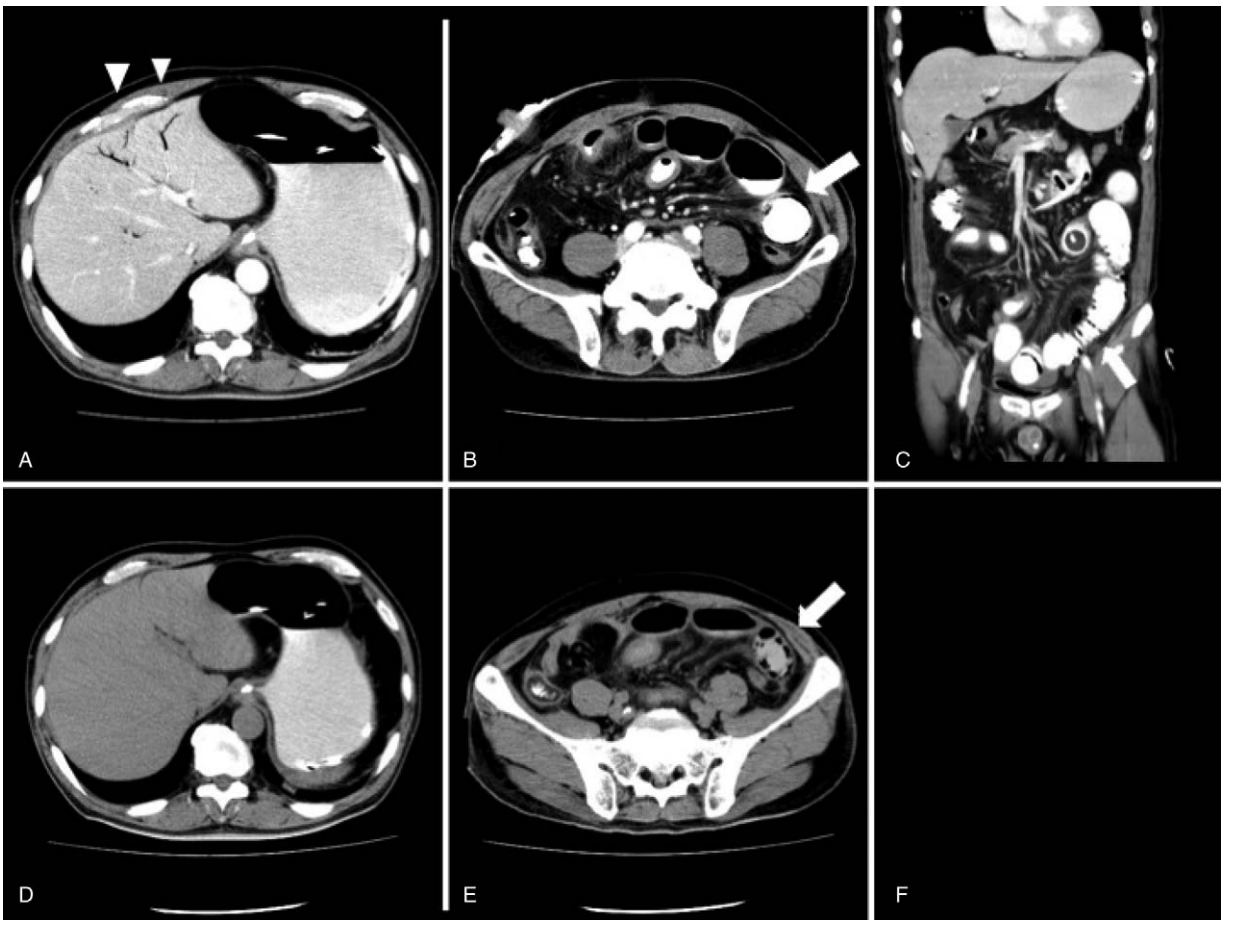

Figure 1. CT scan findings. (A–C) CT scan revealed portal vain gas (triangles) and pneumatosis cystoides intestinalis (arrow) but did not accompany intestinal blood flow disturbance. (D, E) CT scan after 9 h revealed portal vein gas had disappeared, however, pneumatosis cystoides intestinalis remained (arrow).

but the symptoms did not improve. The color of the drainage from the nasogastric tube was brown. The vital signs were normal, except for the blood pressure, which was low (70/46 mm Hg). Blood tests revealed severe dehydration and metabolic acidosis (pH, 7.224; HCO_3, 6.8 mmol/L; base excess, −19.7 mmol/L). Dehydration was considered on the basis of the elevated level of blood urea nitrogen and serum creatine. The patient's lactate dehydrogenase and creatine kinase levels were normal. We considered and investigated the possibility of a blood flow disorder such as NOMI. A contrast-enhanced abdominal CT scan revealed portal vein gas, pneumatosis cystoides intestinalis, and intestinal emphysema but no signs of intestinal blood flow disturbance (Fig. 1A–C). We suspected that portal vein gas had occurred due to internal pressure change caused by ileus rather than by intestinal necrosis. Conservative treatment resulted in improvement in the general condition and the portal vein gas disappeared; however, pneumatosis cystoides intestinalis persisted on a repeat CT scan performed 9 h later (Fig. 1D and E). Since intestinal necrosis was not suspected, conservative treatment was continued. Although his general condition improved, the volume of drainage from the nasogastric tube remained high. We thought that the cause of ileus was adhesion of intestinal tract around the temporary ileostomy. We also considered the possibility of intestinal necrosis. We planned a stoma closure and decided to perform intestinal resection if necrosis was detected in the intestinal tract. Laparotomy was performed 20 days after the original surgery. Serous ascites was found in the peritoneal cavity. The small intestine on the oral side of the stoma was enlarged, and a portion was seen to have a poor color. We thought that the diagnosis was transient NOMI; it was considered to be reversible because clear-cut intestinal necrosis was not seen. Therefore, only stoma closure was performed. Approximately 10 days after the stoma closure, the patient developed unexplained diarrhea, which persisted. The serum albumin and total protein levels were low (2.0 and 4.7 g/dL). The symptoms improved after administration of antidiarrheal drugs. Therefore, the patient was discharged on the 65th postoperative day after stoma closure and was instructed to follow-up on an outpatient basis. However, the diarrhea continued even after discharge, and the patient visited our department on postoperative day 79. The serum albumin value at the visit was very low (1.1 g/dL). Because of this, he was emergently hospitalized, and total parenteral nutrition (TPN) was started. The symptoms did not improve, and the serum albumin level also remained around 1.5 to 1.8 g/dL. We therefore suspected the possibility of PLE. The patient's alpha-1 antitrypsin clearance was 44.2 mL/day, the normal value being less than 13 mL/day. CT scan revealed an enhanced hypertrophied wall of the short segment of the small intestine (Fig. 2A and B), and 99m Tc-labeled human serum albumin scintigraphy revealed protein leakage into the thickened wall of the small intestine (Fig. 2C and D). An X-ray study of the small intestine revealed an abnormal mucosal pattern suggesting intestinal narrowing at the left flank and right lower abdomen (Fig. 3A and B). We arrived at a definitive diagnosis of PLE

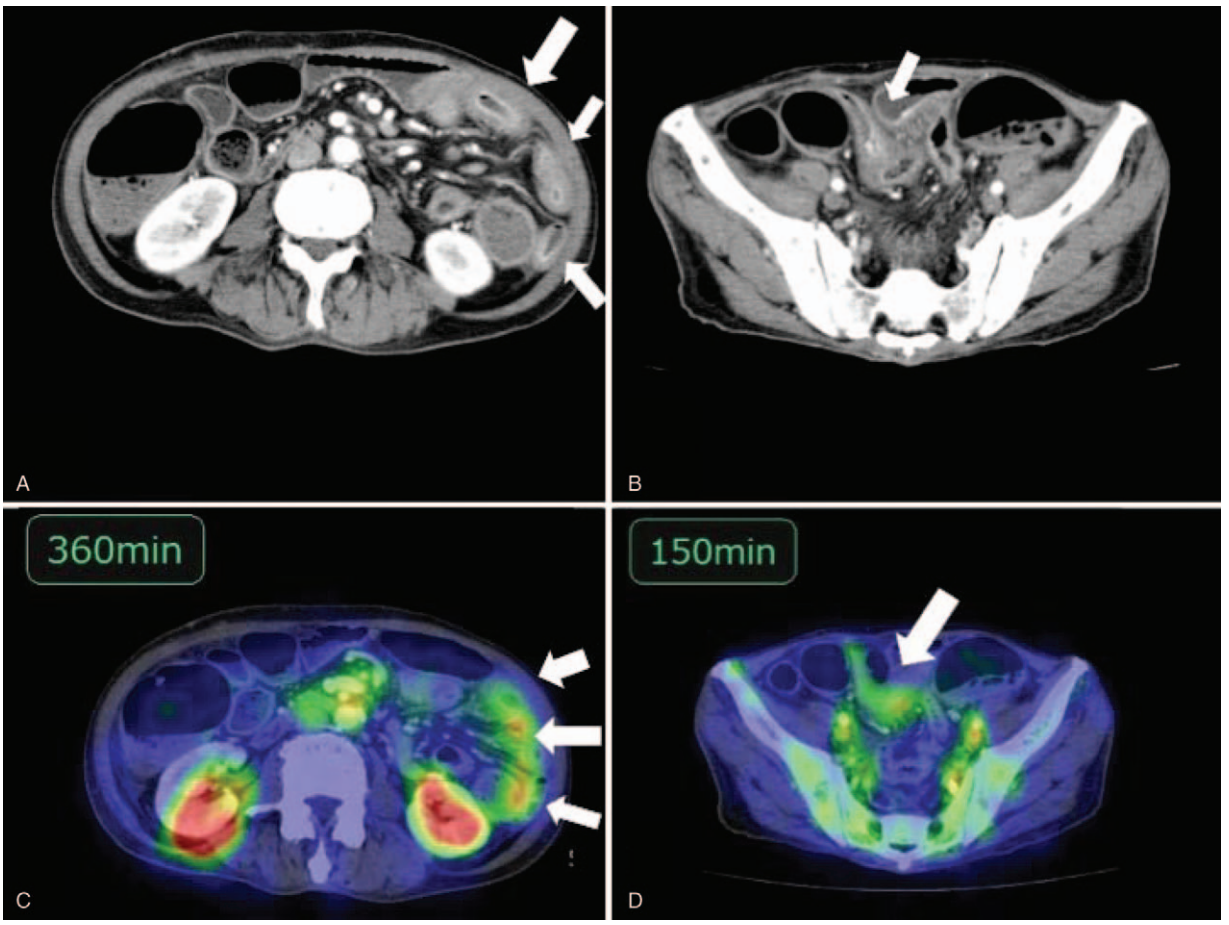

Figure 2. CT scan and 99m Tc-labeled human serum albumin scintigraphy findings. (A, B) CT scan revealed an enhanced hypertrophied wall of the short segment of small intestine (arrows). (C, D) 99m Tc-labeled human serum albumin scintigraphy revealed protein leakage into the wall thickened small intestine (arrows).

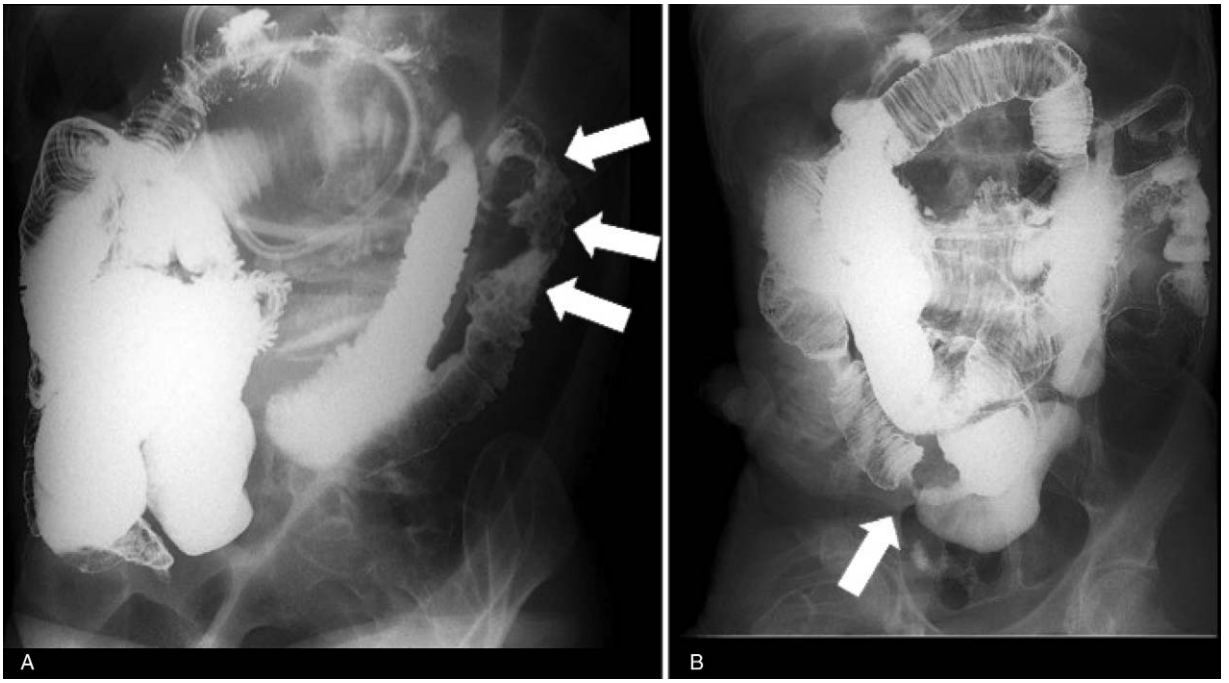

Figure 3. X-ray study of the small intestine findings. (A, B) The X-ray study of the small intestine revealed that an abnormal mucosal pattern suggesting narrowing of the internal organs is observed at left flank and right lower abdomen (arrows).

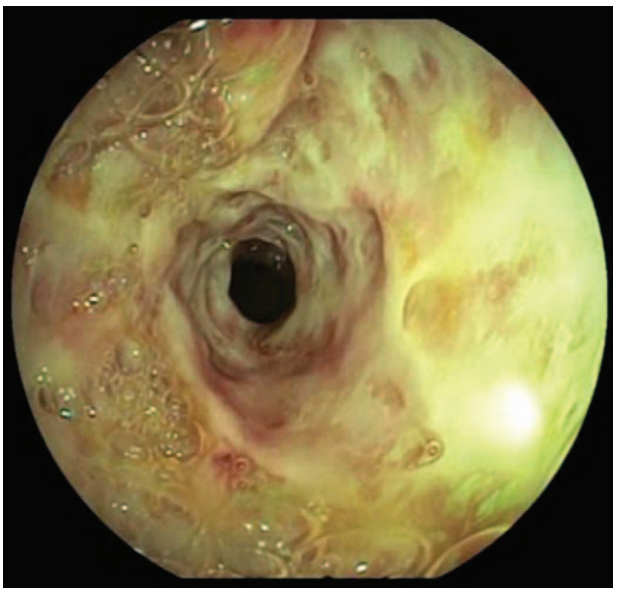

Figure 4. Intraoperative small intestine endoscopy findings. An intraoperative small intestine endoscopy revealed white coat adhere continuously and multiple ulcerative lesions.

secondary to NOMI. Shortly after starting TPN, a gradual improvement in the lower extremity edema and a transient increase in the serum albumin level were observed. Therefore, conservative treatment was continued; however, it did not lead to the patient being cured. As a result, at about 1 month after the diagnosis of PLE was finalized, conservative treatment was thought to be difficult and partial resection of the affected small intestine was performed. During surgery, the intestinal wall was seen to be thicker at 100 cm and at 170 cm from the Treitz ligament on the anal side, and poor intestinal peristalsis was recognized at the same site. A small incision was made near the portion of the small intestine to be resected, and an intraoperative small intestine endoscopy was performed using sterilized colon fiber. Intraoperative small intestine endoscopy revealed a white coat adherent continuously from the center to the anal side of the small intestine, and multiple ulcerative lesions (Fig. 4). Partial resection of the affected small intestine was performed. An operative specimen revealed defluxion of the normal mucosa as well as white coat adhesions over a wide area of the mucosal surface; multiple ulcers were also observed (Fig. 5). Histopathological examination showed increase in the small blood vessels and invasion of advanced inflammatory cells was observed in the mucosal layer, along with moderate inflammatory cell infiltration from the submucosal layer to the muscle layer (Fig. 6). After surgery, the diarrhea decreased and the serum albumin value increased. He had an uneventful recovery and was discharged on the 30th postoperative day. Currently, he is following up for the sigmoid colon cancer and rectal cancer on an outpatient basis.

3. Discussion

NOMI is reported to occur in approximately 20% of cases of acute mesenteric ischemia,[5] similar to its incidence in our study population. The increase in the occurrence of NOMI is likely a

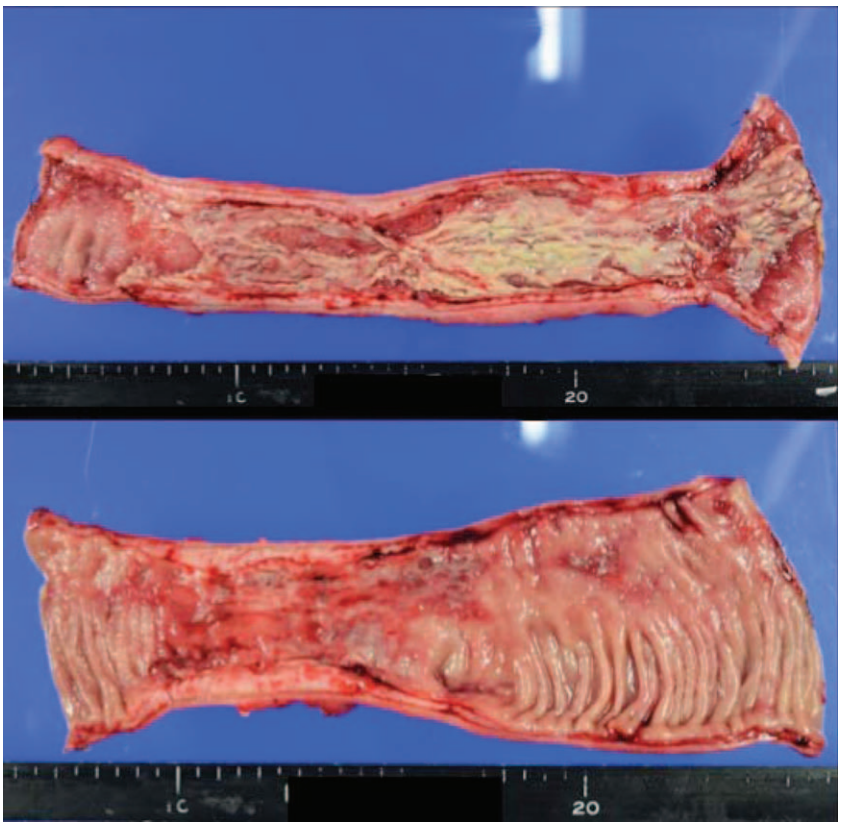

Figure 5. Operative specimen findings. Operative specimen revealed defluxion of the normal mucosa as well as white coat adhesions over a wide area of the mucosa surface; multiple ulcers were also observed.

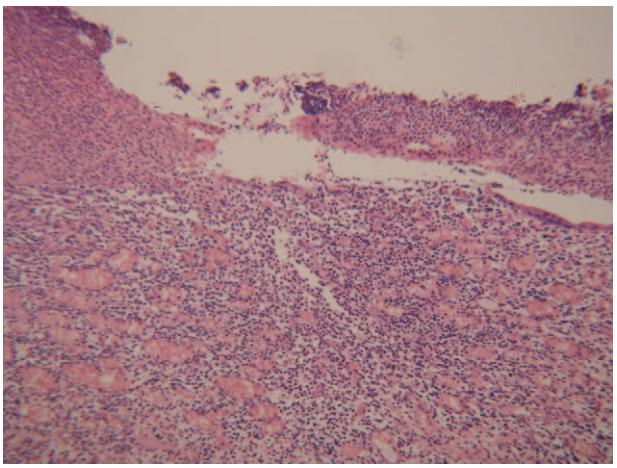

Figure 6. Histopathological findings. Histopathological examination revealed increase in the small blood vessels and invasion of advanced inflammatory cells were observed in the mucosal layer. Moderate inflammatory cell infiltration was observed from the submucosal layer to the muscle layer.

consequence of ageing of society and a rise in the dialysis rate.[6,7] When circulation is compromised, blood flow to the important bodily organs such as the heart is maintained, with a correlated decrease in blood flow to the intestinal tract. Intestinal ischemia due to spasm of the peripheral vessels of the mesenteric artery is thought to occur if a compromised state of the circulation persists beyond a certain period.[8] If necrosis of intestinal tract is caused by NOMI, extensive resection of the intestinal tract is required in several cases. Since the report by Boley et al[9] in 1977, the efficacy of selective intravenous therapy for dilatation of the mesenteric artery has been widely recognized as a treatment for NOMI. This treatment stops the progression of intestinal ischemia and allows time to perform resection of the necrosed segment.[10] However, there are reports of small intestinal narrowing after conservative treatment for NOMI.[3,4] Even if conservative treatment is possible, it may cause sequelae. In our case, NOMI was transient and did not progress to intestinal ischemia, due to which conservative treatment was possible. However, the PLE that developed subsequently necessitated partial resection of the small intestine. To the best of our knowledge, no report has mentioned the occurrence of PLE after conservative treatment for NOMI, as it was considered extremely rare. PLE is a relatively rare condition characterized by loss of protein in the intestines, causing hypoalbuminemia, hypoproteinemia, edema, and occasionally, diarrhea.[11] PLE is mainly a diagnosis by exclusion. The diagnosis of PLE should be considered in patients with hypoproteinemia after other causes, such as malnutrition, proteinuria, and impaired protein synthesis due to cirrhosis, have been excluded. The most efficient examination is fecal alpha-1 anti-trypsin clearance and a scintigraphy using 99mTc-human serum albumin. In our case, the fecal alpha-1 anti-trypsin clearance was high. The accumulation of 99mTc-human serum albumin was also recognized in the thickened wall of the small intestine, which led to the diagnosis of PLE.

The mechanism of protein loss in the gut, in general, includes an increase in microvascular permeability to protein, mucosal inflammation or ulceration, abnormal enterocytes, and stagnation of lymphatic flow.[12] In our case, the presence of abnormal enterocytes and stagnation of lymphatic flow were not found. Mucosal inflammation or ulcers might lead to massive protein leakage into the intestinal lumen. The reasons for incomplete repair in our patient are unclear but are possibly related to the severity of the original ischemic insult and inadequate revascularization. Of note, the decline in the serum albumin and protein level occurred over a long time, as the patient's intake of protein and calories was inadequate. This triggered the albumin outflow from the gastrointestinal tract. As mentioned above, no reports exist of PLE secondary to NOMI, which made it difficult to determine the final diagnosis. Determining the exact timing of surgery was also difficult in our case. The length of the intestinal tract requiring resection should be carefully determined. In our case, the extent of resection required could not be determined through observation of the serosal surface. Only after an endoscope was used to observe the mucosal surface, we could reliably determine the length of the small intestine to be resected.

NOMI has a high mortality rate, often requiring intestinal resection immediately after onset. There is no report on the development of PLE after conservative treatment for NOMI, as in our case. Further accumulation of cases is desirable in order to determine the correct timing and method of treatment.

In summary, we have reported a rare case of PLE that occurred after conservative for NOMI. Clinicians should also consider the possibility of PLE when hypoalbuminemia occurs after conservative treatment of NOMI.

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Author contributions

All authors contributed the daily medical treatment of the patient.
All the authors have read and approved the final manuscript.
Conceptualization: Takafumi Shima.
Data curation: Takafumi Shima.
Writing – original draft: Takafumi Shima.
Writing – review & editing: Maiko Ozeki, Takashi Kinoshita, Kotaro Honda, Hitoshi Inoue, Shinsho Morita.

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