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Case Report

Perforation of the Sigmoid Colon and Massive Ischemia of the Small Intestine Caused by Amyloidosis Associated With Multiple Myeloma: A Case Report

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Amyloidosis is a metabolic disease that results in organ dysfunction because of the deposition of amyloid proteins in body tissues and organs. Amyloid accumulation in the gastrointestinal tract can lead to severe complications with poor outcomes. We report a case showing simultaneous perforation of the sigmoid colon and massive segmental intestinal ischemia caused by amyloidosis associated with multiple myeloma. A 75-year-old woman presented to the emergency department in our hospital with a chief complaint of abdominal pain. Results of several examinations indicated sigmoid colon perforation and acute generalized peritonitis. She underwent an emergency exploratory laparotomy. Operative finding was a perforation of the sigmoid colon and many segmental discoloration sites appeared intraoperatively in the small intestine. A loop colostomy was performed by employing a double-barrel ileostomy with a massive resection of the segmentally discolored small bowel. Pathological findings suggested that the causative factor was amyloidosis with multiple myeloma. The patient was successfully treated with adequate surgery and with melphalan and prednisone after the operation. Meticulous and appropriate treatment for severe complications involving amyloidosis associated with multiple myeloma can prevent a fatal outcome.

Key words: Intestinal amyloidosis – Multiple myeloma – Perforation of sigmoid colon – Intestinal ischemia

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Ischemic intestinal disease is caused by various disease states such as thrombi, emboli, arteriosclerosis, vasculitis, incarcerated hernia, adhesive bands, and systemic illness.[1,2] Acute massive gastrointestinal (GI) ischemia often induces severe sepsis and subsequent life-threatening conditions such as GI perforation, which can be caused by local disease such as ulcer and neoplasm, as well as by systemic illness.[3–5] Emergency surgery is frequently required for both perforations and ischemic intestinal diseases.

Amyloidosis, a systemic disease, involves multiple organ dysfunction as a result of amyloid protein accumulation. However, GI complications are relatively rare in patients with amyloidosis, and only a few GI complications including bleeding and perforation have been reported.[6,7] Herein, we report the successful treatment of a notable case involving a simultaneous perforation of the sigmoid colon and massive segmental intestinal ischemia caused by amyloidosis associated with multiple myeloma (MM). Pathological findings suggested that accumulation of amyloid protein in the vascular wall of the sigmoid colon and small intestine by amyloidosis with MM led to ischemia of those and perforation of sigmoid colon.

This case is rare in terms of beginning with a sigmoid perforation and intestinal ischemia rapidly progressing during operation. According to a MEDLINE search with a combination of keywords relating to intestinal amyloidosis with MM such as AL-type amyloidosis, intestinal amyloidosis, perforation, and ischemia, there are no reported cases beginning with a perforation and intestinal ischemia progressing during operation.

Case Report

A 75-year-old woman presented to the emergency department in our hospital with a chief complaint of abdominal pain for 3 days. The patient, who had no significant medical history, had abdominal wall tenderness with peritoneal signs. Her blood pressure and pulse were 150/72 mm Hg and 120 beats/minute, respectively, and her respiratory rate was 28 breaths/minute. Her body temperature had risen to 39.5°C. A biochemical blood examination showed a normal white blood cell count of 4000/μL with a left sift (88.4% neutrophils, 8.4% lymphocytes, 3.0% monocytes, and 0.2% eosinophils) and a slightly elevated C-reactive protein level of 1.45 mg/dL (normal: 0–0.2 mg/dL). An upright abdominal radiograph revealed an abnormal air presence and

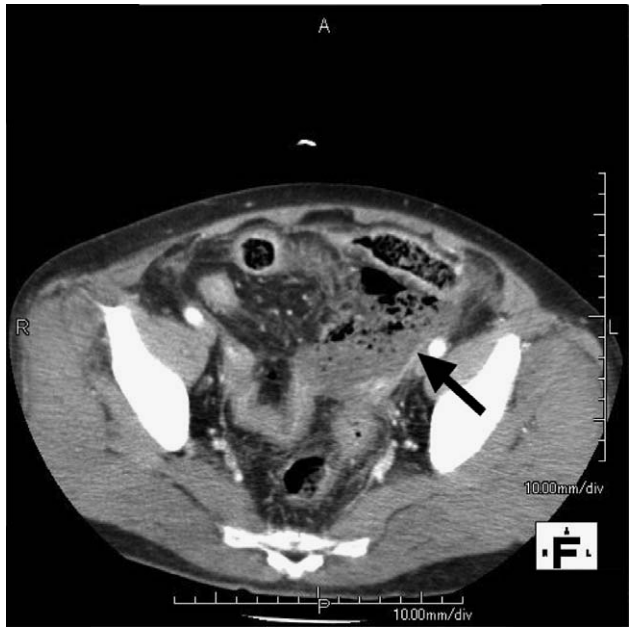

Fig. 1 An abdominal computed tomography revealed free intraperitoneal air and stool around the sigmoid colon because of a sigmoid colon perforation (arrow).

elevated levels of bowel gas, indicating ileus. Further examination using abdominal computed tomography revealed extraluminal free air and stool around the sigmoid colon. Therefore, she underwent an emergency exploratory laparotomy on the basis of the preoperative diagnoses of sigmoid colon perforation and acute generalized peritonitis (Fig. 1).

Massive bloody ascites with stool were found intraperitoneally during the laparotomy. Further examination revealed a 4-cm-diameter perforation at the mesenteric site of the sigmoid colon, accompanied by a surrounding hematoma and necrotic tissue. No possible organic etiology such as diverticula or ulcers was found. Many segmental discoloration sites appeared intraoperatively in the small intestine and mesentery. Pulsations were preserved in the superior mesenteric artery, but not in the marginal artery of the mesentery (Figs. 2, 3a). A loop colostomy was performed at the perforated site along with a double-barrel ileostomy and massive resection of the small intestine (Fig. 3b).

Macroscopic observations of the resected specimen revealed scattered wine-red, submucosal, hematoma-like lesions and some circumferential, segmental discoloration in the small intestine. Histological examination revealed vascular wall thickening and vascular lumen stenosis, predominantly in the submucosa, as well as ischemic

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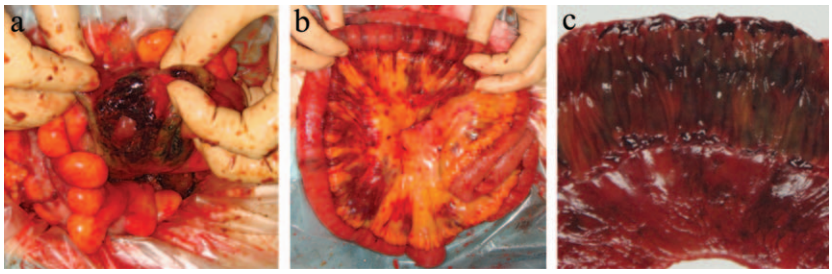

Fig. 2 (a) A 4-cm-diameter perforation site was noted in the sigmoid colon. The bowel wall around the perforation site formed a hematoma and was necrotic. (b) A dark-red segmental discoloration of the small intestine and mesentery was seen 30 minutes after the start of the operation. (c) Macroscopic findings of the resected intestine showed multiple blackish-brown protrusions such as submucosal masses on the small intestine mucosa; full circumferential and segmental blackish-brown changes were observed in some sections of the intestine.

changes in the small intestine. The thickened vascular wall stained positive with a Congo red stain, and the staining remained after a potassium permanganate treatment (Fig. 4). The vascular wall stained positive for an amyloid P component, but negative for amyloid A (AA) protein. These results suggested that the causative factor was an AL-type amyloidosis. A postoperative urinalysis yielded positive results for Bence Jones protein and immunoglobulin-G (λ) type. The Bence Jones protein was also identified by serum protein immunoelectrophoresis. A bone marrow examination revealed that atypical clonal plasma cells accounted for more than 10% of the plasma cells (Fig. 5). On the basis of the thorough examination results, the patient was diagnosed with multiple myeloma (MM) caused by amyloidosis. The patient went into septic shock during surgery; however, she was successfully treated with antibiotics and transfusions. One month after surgery, the double-barrel ileostomy was closed, and chemotherapy involving melphalan and prednisone was started for the MM-associated amyloidosis.

Discussion

Amyloidosis is a metabolic disease resulting in the deposition of amyloid proteins in body tissues and organs. It is classified as "systemic" or "localized" depending on whether one or more body organs or systems are affected.[8] In addition, amyloidosis is subclassified according to the type of deposited amyloid proteins. Amyloidosis associated with MM involves light-chain (AL) immunoglobulin deposits of amyloid proteins in organs. A concurrent diagnosis of AL amyloidosis, especially with λ-type Bence Jones protein, is made upon presentation or sometime during the myeloma disease course in 10–15% of patients.[9–12]

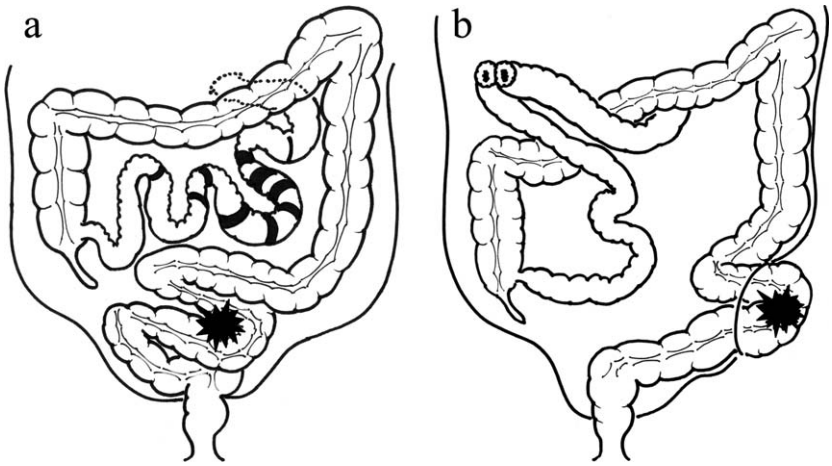

Fig. 3 (a) A schema about an abdominal state intraoperation. A 4-cm-diameter perforation of the sigmoid colon (star shape) and many segmental discoloration sites appeared intraoperatively in the small intestine and mesentery (stripe). (b) A schema about an operation procedure carried out. A loop colostomy was performed at the perforated site and a double-barrel ileostomy and massive resection of the small intestine.

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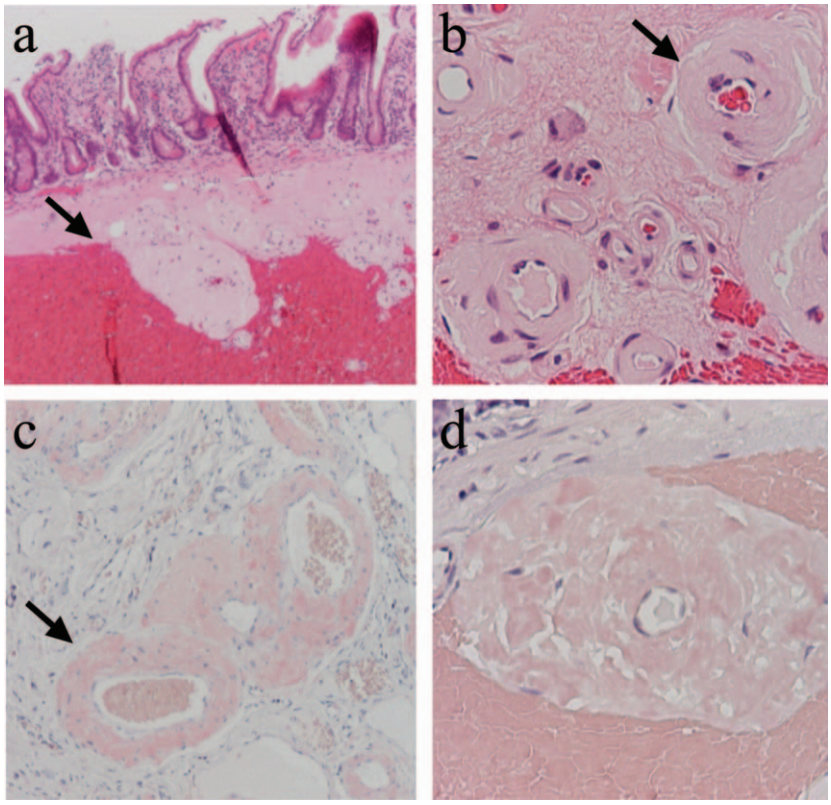

Fig. 4 (a, b) Hematoxylin and eosin staining of the specimen showed a hematoma (arrow) and submucosal vascular wall thickening (arrow) at the submucosal mass lesions and lesions with circumferential ischemia. (c) The thickened vascular wall stained positive with Congo red stain (arrow). (d) Congo red staining remained after a potassium permanganate treatment.

Gastrointestinal amyloidosis is present in as many as 60% of patients with AA amyloidosis and occurs secondary to or in response to rheumatoid arthritis and inflammatory bowel disease. In contrast, GI involvement is present in only 20% of patients with AL amyloidosis and is thus less common than in AA amyloidosis.[13] However, little is known about the reason for this difference. Symptoms of GI amyloidosis include anorexia (found in 80% of patients), intractable diarrhea (80%), abdominal distention (68%), and abdominal pain (68%).[6–7,14] Perforation is an uncommon complication of GI amyloidosis; an even more remarkable fact in this case was that the first sign of disease was perforation of the sigmoid colon.

Amyloid deposition in AL amyloidosis is found mainly in accumulations within vascular walls and in all layers of the intestinal walls, especially the muscularis mucosae, submucosa, and muscularis propria.[15] In this case, massive amyloid deposits seemed to cause vascular wall thickening and vascular lumen stenoses and result in intestinal ischemic changes.

There is no established treatment for GI amyloidosis because an accumulation of amyloid protein in the organs is generally believed to be an irreversible phenomenon. However, some reports have suggested that accumulation is reversible at an early stage, so it is important to attempt early detection and rapid cure. It should be noted that current therapeutic strategies for amyloidosis are aimed at inhibiting production of amyloid protein by using chemotherapy with melphalan and prednisone.

Surgical treatment for perforation and ischemia of the intestine because of amyloidosis can also vary depending on patient situations. In this case, the patient was experiencing a life-threatening condition including sepsis upon arrival that lapsed into septic shock and progression of ischemia or disseminated intravascular coagulation during the operation. We believe a surgical technique involving a loop colostomy directly at the perforation site along with a double-barrel ileostomy including both the distal and proximal ends after resection of the small intestine was especially safe because no anastomosis, intestinal suture line, or lesion in the abdominal cavity occurred. It was reported that an end ileostomy has the lowest complication rate.[16] Additionally, it can decrease the duration of operation because an anastomosis is not required. It was reported that a loop colostomy could have many complications such as prolapse; however, it did not

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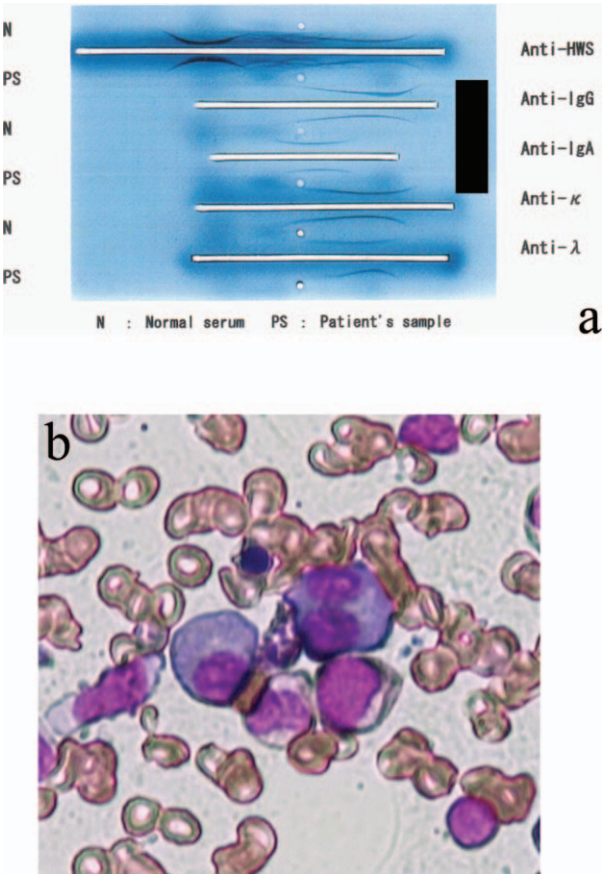

Fig. 5 (a) Immunoglobulin G (λ)-type M-protein was identified in the serum by immunoelectrophoresis. (b) A bone marrow examination demonstrated a blue-stained cytoplasm, eccentric nuclei, and binuclear and perinuclear pale zones.

have as many potentially severe complications during the acute postoperative stage such as retraction. In addition, less time was necessary to perform this type of surgery because in this case, a loop colostomy was directly performed at the perforation site. Therefore, this surgery was suitable for a severe operative situation such as in this life-threatening case. We suggest performing this technique in situations that require rescue surgical treatment such as our case.

Vela-Ojeda et al.[17] indicated the prognosis of 201 MM patients, with a median overall survival for MM patients with amyloidosis of 13 months, which was significantly lower than the 64-month survival period for those without amyloidosis. Amyloidosis is a significant prognostic factor in MM, as well as congestive heart and renal failure.

The postoperative mortality of patients with GI amyloidosis with perforation is high, regardless of multiple myeloma (50–69%). The reasons for this high mortality rate are preoperative organ damage by amyloid deposits in the heart, kidney, and liver and also the frequent preoperative complication of disseminated intravascular coagulation. It has been noted that surgical treatment and postoperative management should be considered in an emergency setting only to identify vital organ damage by amyloid deposits.[18–20]

In our case, no relapse of symptomatic intestinal amyloidosis occurred after postoperative chemotherapy, although the patient died 2 years after surgery because of heart failure related to amyloidosis. Life-threatening intestinal perforation, ischemic disease, or both should be recognized as one of the amyloidosis-related GI complications, and an early diagnosis and rapid surgical treatment is the key to curing this lethal disease. Furthermore, in case of two severe lesions such as a bowel perforation and intestinal ischemia, a safer surgical treatment should be selected.

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