Sigmoid Colon Perforation in a Case with Dialysis-Related Amyloidosis

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Abstract

A 56-year-old male had a 20-year-history of hemodialysis (HD) for chronic renal failure of an unidentified cause. He had a surgical history for destructive spondyloarthropathy (DSA) (53 years old) and bilateral carpal tunnel syndrome (CTS) (55 years old). With chief complaints of abdominal pain and fever at 38−39°C, he was admitted to the hospital in May 2004. On admission, body temperature was 36.1°C and blood pressure was 101/61 mmHg. Physical examination revealed tenderness at the left lower abdomen. WBC was elevated to 14,000/μl and CRP was 15.6 mg/dl. Abdominal CT demonstrated free air, and perforative peritonitis was diagnosed. On the same day, emergency partial sigmoidectomy with colostomy was performed. Macroscopically, there was a perforation in the resected sigmoid colon. Pathologically, amyloid deposits were observed in the vascular walls of the submucosal layer. On admission, β₂-microglobulin was as high as 36.3 mg/l, and dialysis-related amyloidosis seemed to be involved in the ischemia-associated intestinal perforation. Taken together, in patients undergoing long-term HD, dialysis-related amyloidosis should be considered as a risk factor for intestinal perforation.

Key words

Dialysis-related amyloidosis, Hemodialysis, Intestinal perforation

Introduction

Dialysis-related amyloidosis (DRA) is characterized by systemic deposition of amyloid, β₂-microglobulin (β₂MG), occurring in patients undergoing long-term hemodialysis (HD), is a precursor protein of amyloid. DRA causes functional disorder by the deposition of amyloid into joints and organs. In this report, a case of sigmoid colon perforation associated with DRA in a patient undergoing long-term HD is described.

Case

Patient: A 56-year-old male.
Chief complaint: Fever and left lower abdominal pain.

Past history: Destructive spondyloarthropathy (DSA) (53 years old) and bilateral carpal tunnel syndrome (CTS) (55 years old).

Family history: Nothing remarkable.

Present history: He had undergone HD three times a week since 1984 for chronic renal failure of an unidentified cause. With chief complaints of abdominal pain and fever at 38−39°C, he visited our outpatient clinic in May 2004. Physical examination revealed tenderness at the left lower abdomen. WBC and CRP were elevated to 14,000/μl and 15.6 mg/dl, respectively, which indicated severe inflammation, and abdominal computed tomography (CT) demonstrated free air. On suspicion of perfo-
rative peritonitis, he was urgently admitted to the hospital on the same day.

**Physical examination on admission:** Height, 170.0 cm; body weight, 72.3 kg; body temperature, 36.1°C; blood pressure, 101/61 mmHg; pulse, 66 beats/min (regular); and consciousness, clear. Spontaneous pain and tenderness were present at the left lower abdomen. There was no rebound tenderness or muscular defense. A fist-size mass was palpable at the left lower abdomen.

**Laboratory data on admission:** WBC and CRP were elevated to 14,000/μl and 15.6 mg/dl, respectively, which indicated severe inflammation. Anemia was found with Hgb at 6.9 g/dl and Hct at 22.8%. Renal dysfunction was observed with Cr at 10.08 mg/dl and UN at 69.8 mg/dl. β2MG was as high as 36.3 mg/l.

**Results by imaging examinations (Fig. 1):** Abdominal X-ray showed no remarkable change, but abdominal CT demonstrated free air at the sigmoid-descending (SD) junction of the colon.

**Clinical course after admission:** Clinical findings and examination led to the diagnosis of sigmoid colon perforation, intraperitoneal abscess, and localized peritonitis. An emergency operation was performed later on the day of admission. Intraoperative findings revealed a 9×3 cm abscess formation in the mesenterium at the SD junction (Fig. 2). The sigmoid colon was partially resected as long as 16 cm, and a stoma was created at the descending colon (Fig. 3). Histopathological findings revealed amyloid deposition in the walls of small vessels and veins in the submucosal layer and subserosal area with vessel occlusion. Amyloid deposition was observed in the proper muscle layer and the layer became partially thinner (Fig. 4). After the operation, fever was temporarily observed with increased inflammatory reaction, but the symptom subsided with administration of antibiotics. Hemofiltration (HF), instead of HD, was performed because the circulatory system was unstable for a while after admission. Later, HD was performed briefly, but eventually hemodiafiltration (HDF) using high-performance membrane (HPM) was performed. After discharge from the hospital in June, he has undergone HD at the nearby clinic uneventfully.

**Discussion**

In 1975, Warren and Otieno reported that the CTS was frequently complicated in patients undergoing HD for a long time. In 1980, Assenat et al. mentioned that the CTS was caused by deposition
of amyloid fibrils around the median nerve and synovial membranes of joints. In 1985, Gejyo et al. biochemically identified β2MG as the precursor protein of dialysis related amyloid fibrils. Later, however, it turned out that DRA had no correlation with plasma β2MG concentrations. Currently β2MG is thought to deposit in a variety of organs after modification with advanced glycation end-products (AGE).

Risk factors for DRA are thought to be the initiation of HD at an older age (40 years or older), long periods of HD (10 years or longer), and low biocompatibility of dialysis membranes. In the present case, the age of HD initiation was as early as 26 years old, but the HD history was as long as 20 years with a history of DSA and CTS, and the case was thought to be advanced DRA.

In DRA, amyloid deposition generally starts at the bones and joint tissues. In advanced stages, the deposition extends to organs in the whole body such as the urinary system, subcutaneous tissue, gastrointestinal tract, tongue, heart, and liver. It is known that the disease develops symptoms in the whole body such as giant tongue, habitual constipation and diarrhea, ischemic colitis, and heart failure other than CTS, DSA, cystic bone lesions, and subcutaneous amyloid nodules. Intestinal perforation rarely occurs in DRA, and to the best of our knowledge, only 11 cases have so far been reported (Table). The colon was the most frequent perforation site and it has been reported in seven other cases. In a case, esophageal perforation led to a harsh clinical course.

Amyloid deposition is found mainly in the vascular walls in the submucosal layer of the gastrointestinal tract. Ischemia and amyloid deposition to the muscle layer were presumed to render the gastrointestinal tract fragile, resulting in intestinal perforation with the additional burden of increased inner pressure of the bowel due to constipation. It is thought that amyloidosis of the gastrointestinal tract delays healing from injury because of insufficient blood flow in the submucosal layer. Therefore, there is a high risk for rupturing of sutures, and some have proposed that colostomy should be selected instead of direct gastrointestinal anastomosis.

A variety of countermeasures have been taken for DRA, and clinical improvement has been

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Fig. 4. Histopathological findings revealed vascular occlusion due to amyloid deposition in the walls of small vessels and veins in the submucosal layer and subserosal area. The proper muscle layer became partly thinner with amyloid deposition and inflammatory cell infiltration was observed in the fat tissue and muscle layer (Congo-Red staining ×40).
shown to some degrees. Long-term use of HPM with high capacities to eliminate $\beta_2$MG and excellent bioavailability have been shown to be useful in a number of clinical studies.\cite{1,10} Clean-up of dialysate buffer is also important and the use of dialysate buffer containing almost no endotoxin and HPMs significantly decreased serum $\beta_2$MG.\cite{3} In addition, to eliminate $\beta_2$MG accumulating in blood, dialysis has been modified. HDF, which harbored combined advantages of dialysis and filtration, increased the elimination of $\beta_2$MG without reducing elimination efficiency of blood urea nitrogen or creatinine. Furthermore, direct hemoperfusion (Lixelle\textsuperscript{R}) has widely been used for reduction of $\beta_2$MG.

In the present case, on-line HDF had been performed at the previous clinic. However, advancement of DRA could not be stopped. For drug treatment, nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids can be options. Nevertheless, it remains unclear as of today whether these drugs can prevent DRA. Recently, an intriguing report showed an association between activity of DRA lesions and matrix metalloproteinase-3 (MMP-3) in blood, and administration of etidronate disodium inhibited advancement of bone cystic lesions and reduced MMP-3 concentrations in blood. Further studies along this line are anticipated.

In summary, we experienced a case of sigmoid colon perforation due to amyloid deposition in the intestinal walls in a patient undergoing HD for as long as 20 years. When acute abdomen such as peritonitis occurs in patients undergoing long-term HD, gastrointestinal amyloidosis needs to be considered.

The gist of the paper was reported at the 523\textsuperscript{rd} meeting of the Japanese Society of Internal Medicine, Kanto Region (December 2004).

References


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S状結腸穿孔をきたした透析アミロイド症の1例

抄録

症例は56歳、男性。原疾患不詳の慢性腎不全にて20年間の透析歴あり。既往には破壊性脊椎関節症（53歳）、両側手根管症候群（55歳）の手術歴を有している。今回2004年5月発熱、発熱（38℃台）を主訴に当院入院。体温36.1℃、血圧101/61mmHg、左下腹部に圧痛を認め、WBC14,000/μl、CRP15.6mg/dl、腹部CTではfree airを認め穿孔性腹膜炎と診断。同日緊急でS状結腸部分切除術＋人工肛門造設術が施行された。切除されたS状結腸の肉眼所見ではS状結腸の穿孔が疑われ、病理所見は粘膜下層の血管壁にアミロイドの沈着を認めた。また、入院時β2MG36.3mg/lと高値を示し、透析アミロイド症が腸管虚血性穿孔に関与したものと考えられた。長期透析患者では消化管穿孔の危険因子として透析アミロイド症を考慮する必要がある。

索引用語
透析アミロイド症、血液透析、消化管穿孔

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