Successful treatment of protein-losing enteropathy due to AA amyloidosis with somatostatin analogue and high dose steroid in ankylosing spondylitis


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ABSTRACT

Secondary amyloidosis is an occasional complication of ankylosing spondylitis (AS) and in most cases renal amyloidosis presents with proteinuria, nephrotic syndrome and decreased renal function. We describe a 32-year-old male patient with AS manifested by frequent diarrhea, intermittent abdominal pain and low serum albumin levels. He has suffered from severe inflammatory back pain for 14 years with multiple peripheral joint involvement. Protein-losing enteropathy due to gastrointestinal amyloidosis was diagnosed with 99mTc-human albumin scintigraphy, fecal α-1 antitrypsin clearance and colonoscopic biopsy with Congo red staining. Somatostatin analogue octreotide and prednisolone were introduced with successful result.

Introduction

Most articles about the association of ankylosing spondylitis (AS) and secondary amyloidosis focus on renal involvement (1-3). However, some case reports on colonic perforation due to amyloidosis in patients with AS have been published (4, 5). We describe our experience in the management of severe diarrhea with the somatostatin analogue octreotide in a patient with longstanding AS with protein-losing enteropathy (diagnosed by 99mTc-human albumin scintigraphy) due to amyloidosis.

Case report

A 32-year-old male with a 14-year history of AS presented with diarrhea and abdominal pain lasting for a month. He had been treated with nonsteroidal anti-inflammatory drugs for the inflammatory back pain, and sulfasalazine and methotrexate for peripheral arthritis. He had a persistently elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) with history of multiple recurrences of uveitis.

When admitted to hospital on March 31, 1999, the frequency of diarrhea was 4 to 5 times a day. Mentally he was alert but was in acute distress. Body temperature and blood pressure were normal. Body weight was 45 kg. On physical examination, the skin was dry with decreased skin turgor. There were slightly pale conjunctivae. No macroglossia was found. The lung sound was clear and there was no heart murmur. The liver and spleen were not enlarged. The neurologic examination was normal. Musculoskeletal examination revealed limitation of motion in neck and chest wall expansion, and severe restriction of motion of the lumbosacral spine. The joints of the shoulders, elbows and knees were warm and swollen.

The laboratory findings included hemoglobin 8.1 g/dl, WBC 5,100/mm³, platelets 666,000/mm³, reticulocytes 0.1%, iron 12 µg/dl, TIBC 140 µg/dl, ferritin 123 ng/ml, ESR (Wintrobe method) 45 mm/hr, sodium 135 mEq/l, potassium 4.9 mEq/l, chloride 107 mEq/l, creatinine 1.1 mg/dl, blood urea nitrogen 10 mg/dl and normal transaminases. Levels of total protein and albumin decreased to 4.3 g/dl and 1.8 g/dl, respectively. HLA-B27 antigen was present. Urine analysis was within normal limit without any kind of cast. Stool examination revealed WBC 0-1/HPF, positive occult blood, no cysts and ova, and no growth of salmonella and shigella.

Radiographs of the pelvis showed bony ankylosis of the bilateral sacroiliac joints and joint space narrowing with multiple subchondral cysts bilaterally in the hip joints. Colonoscopically there were discrete erosive lesions with friability of the mucosa through the whole colon. In the colonoscopic biopsy amyloid fibril deposits were detected under polarized light in Congo red-stained specimens (Fig. 1a). Immunohistochemical staining showed that these deposits were AA-type amyloid (Fig. 1b). The 99mTc-human albumin scintigraphy findings revealed leakage of 99mTc-albumin into the small bowel loops (Fig. 2). The calculated value of fecal α-1 antitrypsin clearance was 213.9 ml/day (normal < 12).

Moderate doses of prednisolone (20 mg/d) and colchicine were added to the patient’s regimen and subcutaneous methotrexate was prescribed. There was gradual resolution of the diarrhea and abdominal pain. After discharge, he did well for about 7 months without worsening of the abdominal symptoms until his readmission on December 1, 1999 with cachexia due to severe epigastric and dif-
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Fig. 1. (a) Extensive deposition of Congo red positive amyloid materials is present in the interstitial tissue of the lamina propria of the sigmoid (x200); (b) immunohistochemical staining for AA protein shows positive staining in the lamina propria and arterial wall in the submucosa (x100).

Fig. 2. (a) Leakage of $^{99m}$Tc-human albumin into the small bowel loops reveals radioactivity at 10 minutes, and (b) the radioactivity shows distal passage through the colon at 22 hours.

Fig. 3. Course of diarrhea in a 32-year-old patient with protein-losing enteropathy due to AA amyloidosis secondary to ankylosing spondylitis. The diarrhea frequency decreased dramatically after the somatostatin analogue octreotide and high dose steroids were administered.
fuse abdominal pain with intractable diarrhea. The gastrofiberscopy and colonfiberscopy revealed severe discrete erosive and ulcerative lesions throughout the stomach, duodenum and colon without any evidence of normal mucosa. There were no *H. pylori* on the gastric mucosa. The histologic biopsy was consistent with AA type amyloidosis. Anti-ulcer therapy with omeprazole, antacid, and H2-blocker produced no beneficial effects and the periumbilical pain waned and waned. Abdominal ultrasonography failed to reveal any signs of organomegaly, abnormal masses or ascites, but suggested edema of the bowel wall. Abdominal computed tomography with enhancement, done to rule out vascular abnormalities, only showed diffuse edema of the bowel wall in the jejunum.

Treatment with loperamide hydrochloride, dioctahedral smectite, low dose steroid, and another preparation with kaolin and bismuth did not reduce the diarrhea. On December 8, 1999 the somatostatin analogue octreotide acetate, 100 μg 3 times per day, and high dose steroid (50 mg of prednisolone equivalent) was initiated. After the start of therapy, the diarrhea dramatically decreased without complete cessation. During octreotide treatment, the frequency and amount of the diarrhea was dose-dependent. By February 20, 2000, the diarrhea and abdominal pain had improved to a frequency of 1 to 2 times a day, and the amount of oral intake and serum albumin level increased (Fig. 3). After his discharge, octreotide therapy was discontinued and the diarrhea completely ceased with one normally formed stool daily.

**Discussion**

The association of amyloidosis and collagen vascular diseases, such as rheumatoid arthritis, juvenile rheumatoid arthritis, systemic lupus erythematosus, and scleroderma has been documented in detail (3). Secondary amyloidosis has been described in AS, but studies focusing on its prevalence in AS are scarce. According to a recent survey using abdominal fat aspiration, the prevalence of secondary amyloidosis in AS was 7% in patients with a disease duration of more than 5 years (2). However, the clinical importance of silent amyloid fibril deposits in abdominal fat is not known. Therefore, the frequency of clinically recognizable amyloidosis in live AS patients would be lower than 7%.

Secondary amyloidosis in AS is often related to renal involvement with proteinuria and renal insufficiency. However, as mentioned above, intestinal involvement with colonic perforation due to amyloidosis has been documented in 2 patients with AS.

To our knowledge, ours is the first case report precisely documenting the occurrence of amyloidosis in AS with the eventual development of protein-losing enteropathy, and the successful use of octreotide in the treatment of severe diarrhea.

Diarrhea due to secondary amyloidosis is thought to be due to an autonomic neuropathy or to amyloid infiltration of the blood vessels and submucosa of the gastrointestinal tract (6, 7). Its treatment is not firmly established and often not successful. Corticosteroid therapy is supported by its ability to suppress the generation of serum amyloid A and intestinal exudation by reducing systemic and intestinal inflammation, but it is important to use these drugs with caution due to the possibility of infectious complications (8). The efficacy of colchicines in the treatment of secondary amyloidosis presenting with proteinuria due to AS is supported by only one case report (1).

After reports of its effectiveness in treating the secretary diarrhea that occurs in Werner-Morrison syndrome and carcinoid syndrome, a long-acting somatostatin analogue, octreotide, has been used anecdotally in the treatment of severe diarrhea in primary and secondary amyloidosis due to multiple myeloma (9, 10). We conclude through our experience that combination therapy with octreotide and high dose steroid may be effective in treating intractable diarrhea linked to AA type amyloidosis in ankylosing spondylitis that is not responsive to conventional therapy.

**References**