Amyloidosis is characterized by the accumulation of an insoluble amyloid protein in the extracellular space of many different tissues. It is a multisystem disorder and clinical involvement of a single organ is rare. Diagnosis is established by histologic demonstration of amyloid protein in affected tissues. The gastrointestinal tract is frequently involved in amyloidosis. Common presenting symptoms include abdominal pain, weight loss, anorexia, nausea, vomiting, diarrhea, and rarely obstruction. Although the gastrointestinal complications may result in significant morbidity, they are usually not the cause of death, which is most often due to renal failure, restrictive cardiomyopathy, or ischemic heart disease. We report a case of gastrointestinal amyloidosis in an elderly gentleman who presented with diarrhea and weight loss.

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A CASE TO REMEMBER

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The incidence of amyloidosis is about twelve cases per million population per year (1). Although renal disease in the form of nephrotic syndrome and congestive heart failure with restrictive cardiomyopathy are the most common presentations, 30 to 60 percent of patients with amyloid experience gastrointestinal symptoms (2). Amyloid associated dysmotility may be presented as intestinal pseudo-obstruction or diarrhea. We report an interesting case of an elderly male who presented with diarrhea and weight loss as a manifestation of gastrointestinal amyloidosis.

**CASE REPORT**

A 78 year old male presented with a six month history of fatigue, anorexia, and diarrhea. The patient described the diarrhea as approximately eight loose bowel movements per day. Previous medical history included hypertension and monoclonal gammopathy of undetermined significance (MGUS). On review of systems, it was noted that the patient also had a 15 pound weight loss, exertional dyspnea, and frequent syncopal episodes. He denied any sick contacts or recent travel. Surgical history included drainage of a subdural hematoma secondary to a fall three months prior. Family history was noncontributory. He was an ex-smoker and drank one beer a day.

On presentation, the patient was noted to have orthostatic hypotension. Physical examination revealed a cachetic elderly gentleman with a large tongue, three plus edema in the lower extremities, and diffuse hyporeflexia.

The patient was mildly anemic and EKG showed low voltages on all anterior limb leads. Twenty-four hour urine collection revealed proteinuria within the nephrotic range (4g/24hr). Colonoscopy was unremarkable and an upper endoscopy was done with examination to mid-jejunum (130cm). Areas of flattened mucosa was noted (Fig. 1). Biopsy tissue revealed increased submucosal deposits, congo red stain confirmed amyloidosis (Fig. 2).

The patient experienced numerous syncopal episodes during the admission. Pulmonary status also deteriorated, requiring mechanical ventilation. He expired due to multi-system organ failure shortly after the diagnosis of amyloidosis.

**DISCUSSION**

The biochemical description of each type of amyloid is represented by two letters: “A” for amyloid, followed by a second letter specifying the type of amyloid. The amyloid derived from immunoglobulin light chains is called AL. Although more than ten different types of amyloid are described in the literature, AL (primary), AA (secondary or reactive), AF (familial), and AH (hemodialysis-related) amyloid account for 90% of all cases of amyloidosis producing GI symptoms (3). The most common causes of reactive amyloidosis are rheumatoid arthritis, inflammatory bowel disease, and familial Mediterranean fever. Gastrointestinal disease is present in as many as 60% of patients with reactive amyloidosis (4). On the other hand, GI involvement appears to be less common in AL amyloidosis.

**Clinical Syndromes of GI Amyloidosis**

Gastrointestinal complaints are common in patients with amyloidosis, even if the chief complaint is not always GI related. Typical presenting symptoms include abdominal pain, weight loss, fatigue, and anorexia. Amyloid-associated dysmotility may be manifested as intestinal pseudo-obstruction, diarrhea, or achalasia. In our case presentation, the patient presented with diar-

**Figure 1. Area of flattened mucosa in the mid-jejunum.**
rhea. Diarrhea in patients with amyloidosis is often severe. It is thought to be due to a combination of autonomic neuropathy, amyloid infiltration of the submucosa resulting in malabsorption, and bacterial overgrowth (4). Recent reports of the efficacy of somatostatin analogue in cases of refractory diarrhea suggest that a secretory mechanism may be involved (5).

Systemic amyloidosis affects every part of the gastrointestinal tract from the mouth to the anus. Macroglossia occurs in 20% to 50% of primary amyloid patients and causes difficulties with speech, mastication, and deglutition (2). Patients with esophageal involvement usually present with dysphagia and symptoms of esophageal reflux. In their study of 30 patients with systemic amyloidosis, Rubinow, et al described abnormal esophageal manometric findings involving the lower esophageal sphincter, the body of the esophagus, or both in 63% of patients (6). Patients with gastric involvement can present with gastroparesis, epigastric pain, gastric outlet obstruction, peptic ulceration, hematemesis, and melena. Korelitz and Spindell reported in primary amyloidosis that at initial assessment, 5% of patients had a gastric ulcer, 7% hematemesis, 9% tumor, and 20% nausea and vomiting related to amyloid deposition (7). Liver involvement varies considerably in amyloidosis. Detectable hepatomegaly occurs in 33% to 50%, but marked abnormalities of liver serology are rare (2).

Interestingly, some patients who ultimately show clinical evidence of primary amyloidosis present with monoclonal gamopathy of undetermined significance (MGUS). It has been reported that three to four percent of patients with MGUS eventually develop symptoms related to amyloidosis (8).

**Endoscopic Features**

Characteristic endoscopic findings in GI amyloidosis include erosions, ulcerations, polypoid protrusions, and fine granular appearance. In their review of endoscopic findings in amyloid, Tada, et al found that fine granular appearance and polypoid protrusions to be the most common endoscopic features of GI amyloidosis (9). However, biopsy should be done in every case because grossly normal mucosa does not preclude histologic evidence of amyloid.

**Diagnosis**

Barium radiography is of limited diagnostic utility, since the changes that may be seen, such as dilatation of the small bowel or colon, are not specific for amyloidosis. The definitive diagnosis of gastrointestinal
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Amyloidosis requires histological confirmation. Tada, et al found small bowel biopsy to have the highest sensitivity for amyloid (100%), followed by biopsy of colon, stomach, and esophagus (9). Overall, endoscopic biopsies of the upper GI tract are more sensitive than those from the lower GI tract—86% versus 80% (9). By comparison, rectal biopsy and abdominal fat aspiration have a reported sensitivity of 75% to 85% (10). The amyloid fibrils can be identified by their characteristic appearance on the electron microscopy and by their ability to bind Congo red, leading to apple-green birefringence under polarized light.

Treatments

Chemotherapy has been useful in the treatment of AL amyloidosis. Two major trials, which used slightly different regimens of intermittent oral melphalan and prednisone, have confirmed the efficacy of this therapy over no therapy or therapy with colchicine alone. The response rate is low, however, with an increase in survival of approximately 6 months in those receiving chemotherapy (11). Patients must also live long enough to receive several cycles of melphalan before a survival benefit occurs.

Although the gastrointestinal complications may result in significant morbidity, they are not usually the cause of death. Therapy is directed at symptomatic control of the gastrointestinal manifestations and at the underlying disease. Those who are malnourished or unable to tolerate feeding due to dysmotility may benefit from total parenteral nutrition. Patients with gastroparesis can be treated with reglan. Octreotide acetate has been shown to be very effective in treating patients with diarrhea due to GI amyloidosis. This may indicate that a secretory mechanism is involved. Other treatment options being tested now are thalidomide and TNF receptor antagonists (Emrel) (1).

There has been a recent vast increase in the understanding and treatment of patients with amyloidosis. Early diagnosis is essential for the optimal effect of treatment on patient survival and quality of life. In the future, it is hoped that clinicians will diagnose early, treat promptly, and halt the progress of an almost uniformly fatal disease.

References


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