Gastrointestinal amyloidosis: Clinical manifestations, diagnosis, and management

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INTRODUCTION

Amyloidosis is a generic term that refers to the extracellular tissue deposition of fibrils composed of low molecular weight subunits (5 to 25 kD) of a variety of serum proteins, many of which circulate as constituents of plasma [1]. The subunit proteins forming amyloid deposits are derived from soluble precursors which have undergone conformational changes that lead to the adoption of a predominantly antiparallel beta-pleated sheet configuration. These fibrils can be identified on biopsy specimens both by their characteristic appearance on electron microscopy and by their ability to bind Congo red (leading to green birefringence under polarized light) and thioflavine T (producing an intense yellow-green fluorescence). These deposits may result in a wide range of clinical manifestations depending upon their type, location, and the amount of deposition.

This topic will review the clinical manifestations, diagnosis, and management of gastrointestinal amyloidosis. A general overview of the genetics, pathogenesis, clinical manifestations, diagnosis, and treatment of the different amyloid disorders is discussed in detail, separately. (See "Genetic factors in the amyloid diseases" and "Overview of amyloidosis" and "Renal amyloidosis" and "Treatment of amyloid cardiomyopathy" and "Clinical presentation, laboratory manifestations, and diagnosis of immunoglobulin light

chain (AL) amyloidosis" and "Dialysis-related amyloidosis" and "Musculoskeletal manifestations of amyloidosis" and "Cardiac amyloidosis: Clinical manifestations and diagnosis".)

TYPES OF AMYLOID

There are several major forms of amyloidosis. Amyloidosis is classified based on the fibril precursor protein. Nomenclature for amyloid subunit proteins includes the letter "A," followed by the abbreviation of the name of the precursor protein [2]. (See "Overview of amyloidosis", section on 'Types of amyloidosis'.)

The most common causes of systemic amyloid deposition are as follows:

- AL amyloid, caused by a plasma cell dyscrasia, is due to deposition of protein derived from immunoglobulin light chain fragments. AL amyloidosis is the most prevalent type of amyloidosis [3]. The prognosis of patients with AL amyloidosis and gastrointestinal (GI) involvement appears to be worse than in patients without GI involvement; in addition, those with GI involvement may have more other organs involved and more advanced disease than those without organ involvement [4].

- AA amyloidosis is a potential complication of chronic diseases in which there is ongoing or recurring inflammation that results in the production of serum amyloid A protein, a normal acute phase reactant protein sometimes referred to as SAA, which can form amyloid deposits (eg, chronic degenerative arthropathies, particularly rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis, inflammatory bowel disease).

- Other major forms of amyloid seen clinically include dialysis-related amyloidosis (in which the non-glycosylated protein, beta 2-microglobulin, is deposited in organs), age-related (also called senile amyloidosis) systemic amyloidosis, and organ-specific amyloid.

- A rare form of hereditary amyloidosis is hereditary transthyretin amyloidosis that results from a single amino acid substitution in TTR gene 21, was previously called transthyretin familial amyloid polyneuropathy (TTR-FAP) or familial amyloid cardiomyopathy (TTR-FAC). Although, there are 120 amyloidogenic TTR mutations identified. The most common mutations in the United States are Val122Ile, Thr60Ala,

and Val30Met [5]. The phenotype is variable (as in other types of amyloidosis), although polyneuropathy or cardiomyopathy may be more likely with certain TTR mutations.

EPIDEMIOLOGY

Amyloidosis of the gastrointestinal tract may be limited to the gut or part of systemic involvement. In a retrospective review of 2334 patients with amyloidosis, 76 patients (3 percent) had biopsy-proven amyloid involvement of the gastrointestinal tract of which approximately 80 percent had systemic amyloidosis and 20 percent had amyloidosis of the gastrointestinal tract without evidence of an associated plasma cell dyscrasia or other organ involvement [6].

The distribution of clinically apparent gastrointestinal involvement varies with the type of amyloidosis [7]. Gastrointestinal disease is present in as many as 60 percent of patients with AA amyloidosis [8]. In contrast, gastrointestinal tract involvement appears to be less common in AL amyloidosis, with biopsy diagnosed disease and clinically apparent disease occurring in 8 and 1 percent of patients, respectively [9]. In autopsy series, 56 to 95 percent of patients with amyloidosis have hepatic involvement [10,11]. Hepatic amyloid has been reported in up to 90 percent of patients with AL amyloid and 60 percent of patients with AA amyloid.

The prevalence of dialysis-related amyloidosis has not been well studied but clinically apparent disease does not appear to be common [12]. Senile amyloidosis is found in 10 to 36 percent of patients over 80 years old and mainly involves the heart, but can also be seen throughout the gastrointestinal tract. Amyloid has been reported in subserosal veins of 41 to 44 percent of older adult patients, mainly in the large and small bowel [13].

PATHOGENESIS

Gastrointestinal disease in amyloidosis results from either mucosal infiltration or neuromuscular infiltration. In addition, an extrinsic autonomic neuropathy may also affect gut function.

- **Mucosal infiltration** – The most common sites of mucosal infiltration are the second part of the duodenum (100 percent), the stomach and colorectum (>90 percent), and the esophagus (approximately 70 percent) (picture 1A-C) [14].
    - In AL amyloidosis, amyloid deposition in the muscularis mucosae, submucosa, and muscularis propria leads to polypoid protrusions and thickening of the valvulae conniventes. As a result, AL amyloidosis usually presents with constipation, mechanical obstruction, or chronic intestinal pseudo-obstruction.
    - In AA amyloidosis, granular amyloid deposition occurs mainly in the mucosa, resulting in the fine granular appearance, mucosal friability, and erosions. As a result, AA amyloidosis presents with diarrhea and malabsorption [15].
    - In patients with dialysis-related amyloid, the development of gastrointestinal amyloidosis is associated with the length of time on dialysis [12]. Vascular deposition can range from subtle hyalinization of the vascular intima and media within submucosal vessels to significant thickening of the vessel wall with resultant mucosal ischemia. Interstitial deposits are usually localized to the mucosa, submucosa, and muscularis propria but can range from immunoreactive $beta_{2}$-microglobulin amyloid without mural expansion to macroscopic nodular deposits (amyloid tumors) within the muscularis propria.
- **Neuromuscular infiltration** – Neuromuscular infiltration has been reported in patients with AL, AA, and dialysis-related amyloid and usually induces stasis syndromes. Neuromuscular infiltration initially affects the intrinsic nervous system and results in a neuropathic process that is characterized by normal amplitude but uncoordinated contractions [16,17]. Tissue wall infiltration results in a myopathic process with low amplitude contractions that are typically associated with significantly prolonged transit (waveform 1) [18]. The preferential site of amyloid infiltration varies by the type of amyloidosis [19,20]. In one study that evaluated 16 patients with amyloidosis and intestinal pseudo-obstruction (13 with AA, 2 with AL, and 1 with dialysis-related amyloidosis), extensive infiltration and replacement of the muscularis propria by amyloid deposits throughout the gastrointestinal tract, especially the small intestine, were found in AL and dialysis-related amyloidosis cases. In contrast, in patients with AA amyloidosis, there was amyloid infiltration in the myenteric plexus without appreciable muscle infiltration.

CLINICAL MANIFESTATIONS

Clinical presentation

Gastrointestinal tract amyloidosis — Patients with symptomatic gastrointestinal amyloidosis usually present with one of four syndromes [9,21-26]:

- **Gastrointestinal bleeding** – Bleeding is the presenting symptom in 25 to 45 percent of patients with gastrointestinal tract amyloidosis [27,28]. Bleeding may be due to ischemia or infarction, vascular friability, or mucosal lesions (ulcers, nodularity or polypoid lesions, erosions, submucosal hematomas, and small mucosal hemorrhages) [6,29,30]. Occult bleeding is the most commonly reported gastrointestinal (GI) presentation of B2M-amyloidosis [31]. (See 'Types of amyloid' above.)

- **Malabsorption** – Patients with amyloidosis may develop malabsorption due to mucosal infiltration, pancreatic insufficiency or bacterial overgrowth and present with weight loss (median 13.6 kg in one series), diarrhea, or steatorrhea [32,33]. Less common features included anorexia, dizziness, hypotension, or orthostatic changes in blood pressure. (See "Approach to the adult patient with suspected malabsorption", section on 'Clinical manifestations'.)

- **Protein-losing gastroenteropathy** – Patients with protein-losing gastroenteropathy usually present with diarrhea, edema, ascites, pleural or pericardial effusion and have laboratory evidence of hypoalbuminemia [34]. (See "Protein-losing gastroenteropathy", section on 'Clinical features'.)

- **Chronic gastrointestinal dysmotility** – Less often, patients may present with constipation, or nausea, vomiting, abdominal pain, bloating, or chronic intestinal pseudo-obstruction [16,19]. Dysmotility can also result in rapid intestinal transit and cause diarrhea [35]. In hereditary transthyretin amyloidosis R amyloidosis, 24-hour, small, intestinal motility studies show more daytime phase III migrating motor complexes than patient controls (which may be a feature of vagal denervation) and a lower amplitude of small intestinal contractions; together these features would be consistent with a combined neuromyopathic disorder [36]. (See 'Types of amyloid' above.)

- Other rare symptoms of amyloidosis include:

- Cholangitis due amyloid deposition at the ampulla of Vater [37].
- Bowel obstruction due to encapsulating peritonitis or extraluminal amyloidoma [38,39].
- Bowel perforation in light chain amyloidosis, which may occur after the initiation of anti-AL therapy (eg, bortezomib, lenalidomide or thalidomide-based therapy) [40].
- Esophageal involvement due to amyloid deposition in nerves and resulting in dysphagia, heartburn, dysmotility (up to asperistalsis that may mimic achalasia), dilatation, and low lower esophageal sphincter (LES) pressure.
- Pneumatosis intestinalis [41].

While patients with AA amyloidosis usually present with diarrhea and malabsorption, patients with AL amyloidosis usually present with constipation, mechanical obstruction, or chronic intestinal pseudo-obstruction [15].

When there is involvement of the GI tract in senile systemic amyloidosis, it is usually discovered incidentally on histological examination within subserosal veins of the large and small bowel. It is present in about 40 percent of those >80 years of age [42].

Amyloidosis secondary to inflammatory bowel disease — AA amyloidosis is a rare complication of inflammatory bowel disease (~1 in 200 cases), and is 10 to 15 times more likely in Crohn disease than ulcerative colitis, presumably because of the greater systemic inflammation. Typically, AA amyloidosis occurs in association with male sex, fistulizing behavior, extraintestinal manifestations, perianal disease, and ileocolic anatomical location. Renal disease is the most common organ involved in AA amyloidosis associated with inflammatory bowel disease [42].

Hepatic amyloidosis — Clinical manifestations of hepatic amyloid deposition are usually mild with hepatomegaly and elevated alkaline phosphatase being the most frequent findings [43]. Patients with hepatic amyloidosis often have concurrent symptoms of fatigue, weight loss, and anorexia due to systemic amyloidosis.

Hepatomegaly is present in 57 to 83 percent of patients with hepatic amyloidosis and does not correlate with the amount of amyloid deposition [10,44]. While patients may have associated ascites, this is more likely due to concurrent heart failure or hypoalbuminemia. Chronic liver disease and portal hypertension are rare. The most frequently abnormal test of hepatic function is an elevated serum alkaline phosphatase level. In one study that included 98 patients with hepatic amyloidosis, an elevated alkaline phosphatase was noted in 86

percent of patients, of which 61 percent had values of 500 int. units/L or more [45]. The serum aspartate aminotransferase (AST) was more than twice the upper limit of normal in 37 percent of patients.

Hepatic involvement can be seen in up to 90 percent of patients with AL amyloid and 60 percent of patients with AA amyloidosis [10,11,46]. Clinical features of hepatic involvement in AA amyloidosis are similar to those seen in AL amyloidosis. Although histologic differences between AL and AA amyloidosis have been described, there is considerable overlap making the significance of these observations unclear [46-48].

Although some case reports have suggested that patients with hepatic amyloidosis have an increased risk of bleeding and/or hepatic rupture following the biopsy, this has not been consistently demonstrated [21]. (See "Approach to liver biopsy".) Rarely, ascites may result from peritoneal amyloidosis [49].

Imaging findings — Radiologic and endoscopic findings of gastrointestinal amyloidosis are nonspecific [50] and the diagnosis typically requires biopsy and special stains to identify the amyloid infiltration and the specific nature of the amyloid protein infiltration [51].

- **Gastrointestinal tract amyloidosis** – On small bowel follow-through and cross sectional imaging with computed tomographic (CT) scan or magnetic resonance imaging (MRI) in patients with AA amyloid, the mucosa may have a coarse mucosal pattern with innumerable fine granular elevations due to expansion of the lamina propria by amyloid deposits [52]. In patients with AL amyloid, findings include polypoid protrusions, thickening of the folds, luminal narrowing, loss of haustrations, thickened mucosal folds, mucosal nodularity, and ulceration. Dilatation of the small bowel or colon may be seen in patients with neuromuscular amyloid infiltration (image 1). Rarely mesenteric thickening or adenopathy may be seen on CT scan [52]. The appearance of primary amyloidosis in the intestine may mimic Crohn disease [53].

- **Hepatic amyloidosis** – Ultrasonographic findings of hepatic amyloidosis include heterogeneous echogenicity [50]. On CT scan, diffuse or focal regions of decreased parenchymal attenuation with or without extensive calcification may be seen. MRI demonstrates significantly increased signal intensity on T1-weighted images of the liver without significantly altered signal intensity on T2-weighted images; the reason for high signal intensity on T1 is unclear.

DIAGNOSIS

Gastrointestinal amyloidosis should be suspected in patients with diarrhea, weight loss, or gastrointestinal bleeding and disorders known to be associated with amyloidosis (eg, plasma cell dyscrasia, chronic inflammatory disease, and chronic renal failure on maintenance dialysis). Amyloidosis should also be suspected when there is involvement of other organs characteristic of systemic amyloid deposition (eg, proteinuria, hepatomegaly and elevated alkaline phosphatase, restrictive cardiomyopathy, neuropathy, unexplained edema, carpal tunnel syndrome, unexplained facial or neck purpura, or macroglossia). The diagnosis of gastrointestinal amyloid requires a tissue biopsy with positive staining of amyloid by Congo red or the presence of amyloid fibrils on electron microscopy. (See "Overview of amyloidosis", section on 'Clinical manifestations'.)

- **Tissue biopsy** – Based on the gastrointestinal symptoms, we perform a colonoscopy and/or an upper endoscopy to obtain rectal or duodenal mucosal biopsies in patients with suspected amyloidosis and to exclude other etiologies. In patients with unexplained hepatomegaly and elevated alkaline phosphatase, a liver biopsy serves to establish the diagnosis of hepatic amyloid and rule out other infiltrative liver diseases. (See 'Differential diagnosis' below.)

    - **Endoscopy** – The endoscopic appearance of amyloidosis is not specific. The gastrointestinal tract mucosa may have a fine granular appearance, polypoid protrusions, erosions, ulcerations, friability, and thickening of the wall [14,54]. Rarely, patients have tumor-forming deposits of amyloid, called amyloidomas [55-57].

    - **Histology** – On hematoxylin and eosin stained biopsy sections, amyloid appears as a pink, amorphous, waxy substance with a characteristic 'cracking' artifact (picture 1A-C). In the gastrointestinal tract, amyloid deposits may be seen in the mucosa and submucosa and are best identified in the wall of blood vessels. In patients with hepatic amyloid, deposits are usually seen periportally in the space of Disse but the deposits are occasionally centrilobular. Atrophy of hepatocytes may be seen due to compression by amyloid fibrils [58].

      The presence of amyloid fibrils can be confirmed by their characteristic appearance on electron microscopy and by their ability to bind Congo red (leading

to green birefringence under polarized light) or thioflavine-T (producing an intense yellow-green fluorescence) [2]. It is important to note that biopsy sections that are very thin (ie, 6 microns or less) may not stain appropriately with Congo red despite the presence of amyloid fibrils on electron microscopy. AL, Aβ2M, and ATTR amyloids are likely to deposit submucosally, while AA amyloid is easily deposited in the superficial layer of the mucous membrane [59]. Among 521 patients with biopsies from the gastrointestinal tract, the type of amyloid deposition was ALλ amyloid in 286 (52.8 percent), ATTR in 88 (16.2 percent), ALκ in 74 (13.7 percent), AA in 58 (10.7 percent), and apolipoprotein A- amyloid in four (0.7 percent) patients [7].

- **Determining the type of amyloid and underlying etiology** – Once the histologic diagnosis of amyloidosis is made, it is important to determine the type of amyloid and the underlying cause [60]. This evaluation is discussed in detail, separately. (See "Clinical presentation, laboratory manifestations, and diagnosis of immunoglobulin light chain (AL) amyloidosis", section on 'Determining the type of amyloid' and "Overview of amyloidosis", section on 'Histopathology and protein analysis'.)

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of gastrointestinal amyloidosis varies based on the clinical presentation. Other causes of diarrhea with mucosal erosions include inflammatory bowel disease (ulcerative colitis and Crohn disease), radiation colitis, gastrointestinal malignancies, and medication-induced enteropathy. Gastrointestinal tract amyloidosis can be differentiated from these by a history which may be suggestive of the underlying cause and by histology. The differential diagnosis for chronic diarrhea and the evaluation of diarrhea are discussed in detail, separately. (See "Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults", section on 'Differential diagnosis' and "Approach to the adult with chronic diarrhea in resource-rich settings".)

The differential diagnosis of hepatomegaly and elevated alkaline phosphatase includes other infiltrative disorders of the liver including sarcoidosis, tuberculosis, malignancy, and glycogen storage diseases. These can be distinguished from hepatic amyloidosis by liver

biopsy. (See "Approach to the patient with abnormal liver biochemical and function tests", section on 'Elevated alkaline phosphatase'.)

MANAGEMENT

Therapy is directed at the gastrointestinal manifestations and at the underlying cause of amyloidosis.

Symptomatic treatment — In patients with nausea and vomiting or abdominal pain, which is often due to amyloid-related dysmotility, management consists of dietary modification, hydration, and pharmacologic therapy with prokinetics (eg, metoclopramide, and, where approved, domperidone) and anti-emetics (eg, promethazine, dimenhydrinate, ondansetron). Small meals consisting of liquid or homogenized foods are better tolerated than solids. Hypercaloric liquid formulations should be used in patients with low caloric intake. Parenteral nutrition may be necessary for patients with severe dysmotility who have failed enteral nutrition together with prokinetics and antiemetic therapy [19]. (See "Treatment of gastroparesis", section on 'Prokinetics' and "Chronic intestinal pseudo-obstruction", section on 'Prokinetic agents'.)

In patients with diarrhea and bloating and demonstrated small intestinal bacterial overgrowth, we suggest empiric treatment with antibiotics for small intestinal bacterial overgrowth (eg, quinolones, doxycycline, metronidazole). In case reports, patients with severe diarrhea and hypoalbuminemia due to a protein-losing enteropathy have responded to glucocorticoids and octreotide [61,62]. (See "Small intestinal bacterial overgrowth: Management", section on 'Antibiotic therapy' and "Protein-losing gastroenteropathy", section on 'Management'.)

The initial management of patients with gastrointestinal bleeding includes triage to the appropriate setting for management (outpatient, inpatient, intensive care unit), general supportive measures (eg, oxygen, establishment of adequate intravenous access), appropriate fluid and blood product resuscitation, and management of coagulopathies, anticoagulants, and antiplatelet agents. In many cases, the bleeding can be controlled with therapies applied at the time of endoscopy or angiography. The management of gastrointestinal bleeding is discussed in detail, separately. (See "Approach to acute lower gastrointestinal bleeding in adults" and "Approach to acute upper gastrointestinal bleeding in adults".)

Treatment of the underlying disorder — Treatment of the underlying disease has been associated with regression of gastrointestinal amyloid (table 1) [63-67]. As examples, therapy is aimed at the underlying infectious or inflammatory disorder in secondary AA amyloidosis (eg, anti-TNF therapy in Crohn disease), at the underlying plasma cell dyscrasia in AL amyloidosis, and at either altering the mode of dialysis or considering renal transplantation in patients with dialysis-related amyloidosis. The management of underlying cause of amyloidosis is discussed in detail, separately [68-75]. (See "Overview of amyloidosis", section on 'Treatment' and "Treatment of AA (secondary) amyloidosis" and "Treatment and prognosis of immunoglobulin light chain (AL) amyloidosis and light and heavy chain deposition diseases".)

PROGNOSIS

Although the gastrointestinal complications can result in significant morbidity, they are not usually the cause of death, which is most often due to renal failure, restrictive cardiomyopathy, or ischemic heart disease. However, the presence of hepatic manifestations has a poor prognosis as it likely reflects relatively severe systemic disease [43,76]. In one series of 98 patients with hepatic amyloidosis, the median survival in patients with hepatic amyloidosis was nine months [45]. Independent predictors of shortened survival included heart failure, a total bilirubin >2 mg/dL, and a platelet count >500,000/microL.

SUMMARY AND RECOMMENDATIONS

- Amyloidosis is a generic term that refers to the extracellular tissue deposition of a variety of serum proteins, many of which circulate as constituents of plasma. The most common causes of systemic amyloid deposition are AL amyloid caused by a plasma cell dyscrasia and AA amyloidosis due to ongoing or recurring inflammation from chronic disease. Other major forms of amyloid seen clinically include dialysis-related amyloidosis, heritable amyloidosis, age-related systemic amyloidosis, and organ-specific amyloidosis. (See 'Introduction' above and 'Types of amyloid' above.)

- Gastrointestinal disease in amyloidosis results from either mucosal or neuromuscular infiltration. In addition, an extrinsic autonomic neuropathy may also affect gut function. (See 'Pathogenesis' above.)

- Patients with symptomatic gastrointestinal amyloidosis usually present with one of four syndromes: gastrointestinal bleeding, malabsorption, protein-losing gastroenteropathy, and, less often, gastrointestinal dysmotility. While patients with AA amyloidosis usually present with diarrhea and weight loss, patients with AL amyloidosis usually present with constipation, mechanical obstruction, or chronic intestinal pseudo-obstruction.

  Clinical manifestations of hepatic amyloid deposition are usually mild with hepatomegaly and elevated alkaline phosphatase being the most frequent findings. However, patients usually have weight loss, fatigue, and anorexia due to systemic involvement. (See 'Clinical presentation' above.)

- Gastrointestinal amyloidosis should be suspected in patients with diarrhea, weight loss, or gastrointestinal bleeding and disorders known to be associated with amyloidosis (eg, plasma cell dyscrasia, chronic inflammatory disease, and chronic renal failure on maintenance dialysis). Amyloidosis should also be suspected when there is involvement of other organs characteristic of systemic amyloid deposition (eg, proteinuria, hepatomegaly and elevated alkaline phosphatase, restrictive cardiomyopathy, neuropathy, unexplained edema, carpal tunnel syndrome, unexplained facial or neck purpura, or macroglossia). The diagnosis of gastrointestinal amyloid requires a tissue biopsy with positive staining of amyloid by Congo red or the presence of amyloid fibrils on electron microscopy. (See 'Diagnosis' above.)

- Although the gastrointestinal complications can result in significant morbidity, they are not usually the cause of death, which is most often due to renal failure, restrictive cardiomyopathy, or ischemic heart disease. However, the presence of hepatic manifestations has a poor prognosis as it likely reflects relatively severe systemic disease. Therapy is directed at the gastrointestinal manifestations and at the underlying cause of amyloidosis. (See 'Management' above and 'Prognosis' above.)

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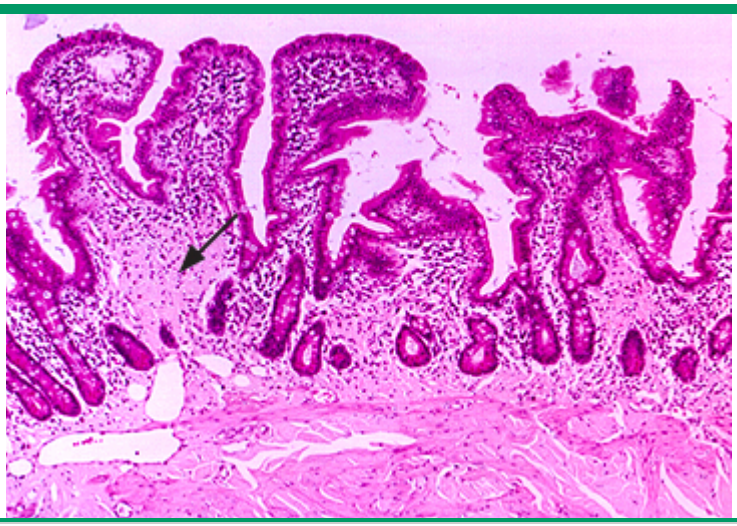
Topic 2642 Version 14.0

GRAPHICS

Amyloidosis

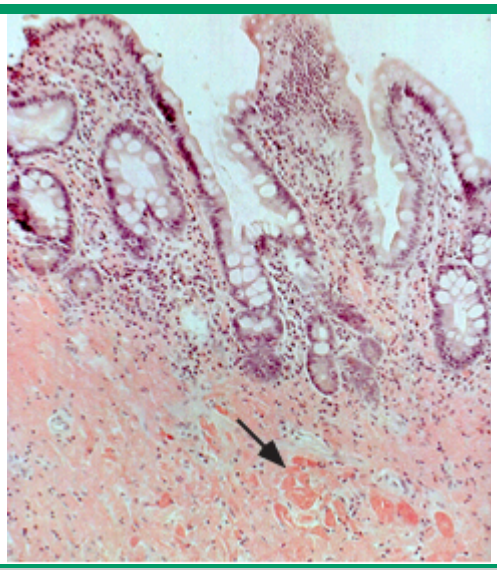


Endoscopic biopsy of nodular duodenal epithelium stained with hematoxylin and eosin. Note the pink amorphous deposit in the lamina propria (arrow).

Courtesy of Michael Camilleri, MD.

Graphic 81395 Version 1.0

Amyloidosis

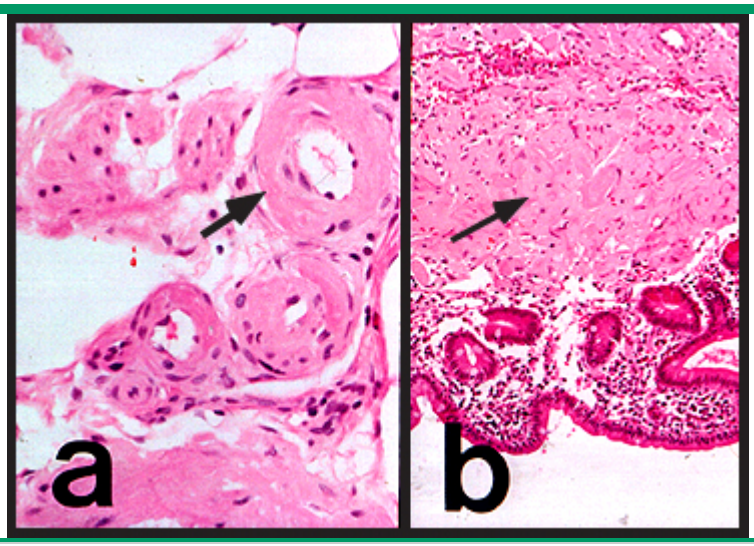


Endoscopic biopsy of nodular appearing duodenal mucosa stained with Congo red. Note the positive staining of the lamina propria and blood vessels (arrow).

Courtesy of Michael Camilleri, MD.

Graphic 73928 Version 1.0

Amyloidosis



High power magnification of blood vessels (a) and lamina propria (b) using hematoxylin and eosin stain from a patient with gastrointestinal amyloidosis. There is prominent infiltration by eosinophilic amyloid deposits (arrows).

Courtesy of Michael Camilleri, MD.

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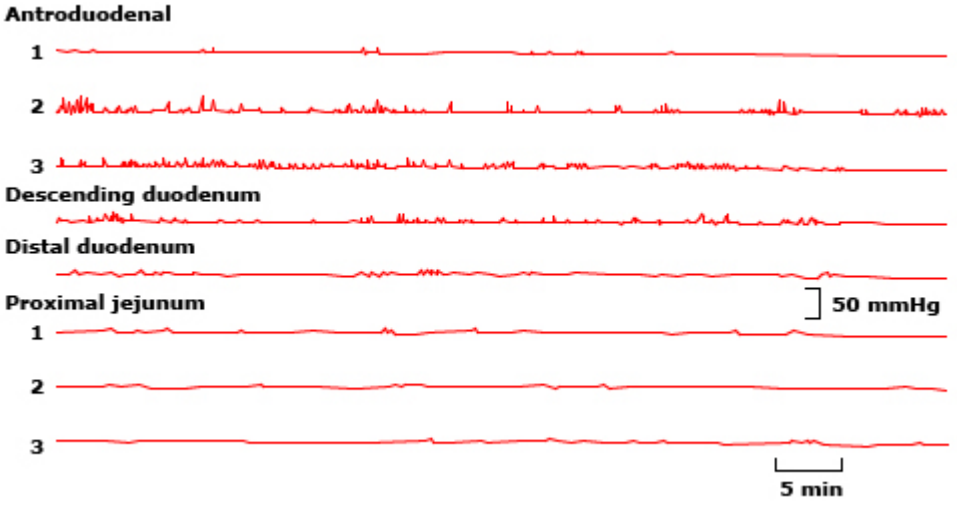
Gastrointestinal manometry in amyloidosis



Gastrointestinal manometric tracing during fasting in a 60-year-old patient with primary amyloidosis. There are low amplitude contractions at all levels.

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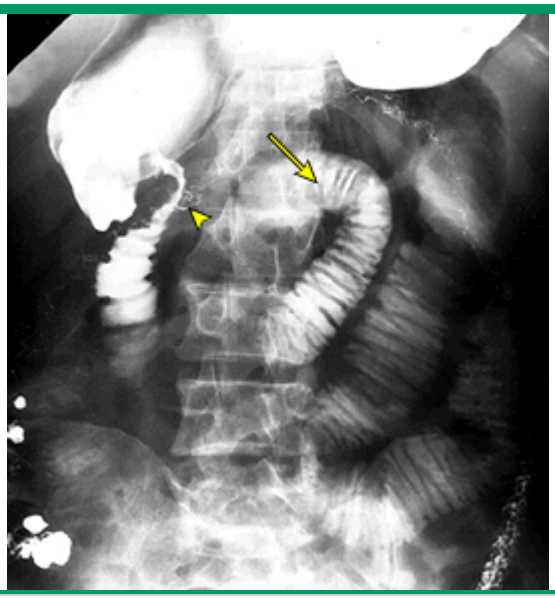
Graphic 62577 Version 4.0

Amyloidosis



Upper gastrointestinal series showing nonspecific dilatation of small bowel loops (arrow) with a stricture in the duodenal loop (arrowhead) in a patient with secondary amyloidosis.

Graphic 77965 Version 3.0

Reducing the supply of fibril precursors in systemic amyloidosis

Disease	Aim of treatment	Example of treatment
AA amyloidosis	Suppress the acute phase response and thereby reduce the production of serum amyloid A protein	Anti-inflammatory and immunosuppressive therapy in patients with rheumatoid arthritis and Crohn disease (eg, anti-TNF antibodies, humanized anti-IL6 receptor antibody) Colchicine for patients with familial Mediterranean fever Surgery for patients with osteomyelitis and rare cytokine-producing tumors
AL amyloidosis	Suppress production of monoclonal immunoglobulin light chains	Chemotherapy directed at plasma cell dyscrasia
Hereditary amyloidosis	Eliminate source of genetically variant protein	Orthotopic liver transplantation for patients with familial amyloid polyneuropathy secondary to variant transthyretin or renal amyloidosis secondary to variant fibrinogen A α-chain
β_2-microglobulin amyloidosis	Reduce plasma concentration of β_2-microglobulin	Renal transplantation

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Contributor Disclosures

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Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy