Amyloidosis

Bible-Class 11.03.2020

Definition

Definition

- 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

Types of amyloid

Types of amyloid

Amyloid Protein	Precursor of Fibril Protein	Clinical Syndrome
AA	Serum amyloid A protein (SAA)	Reactive (secondary) amyloidosis associated with chronic inflammatory diseases
AL	Immunoglobulin light chains	Amyloidosis associated with occult immunocyte dyscrasia ("primary"), multiple myeloma, macroglobulinemia, or monoclonal gammopathy
AH	Heavy chain of Immunoglobulin G-1	Same as AL
Aβ2M	Plasma β_2-microglobulin	Hemodialysis-associated amyloidosis
ATTR	Normal plasma transthyretin or genetic variants (multiple)	Senile systemic amyloidosis, autosomal dominant familial amyloid polyneuropathy
ACys	Genetic variant Leu68Gln of cystatin C	Hereditary cerebral hemorrhage with amyloidosis, Icelandic type
AGel	Genetic variant Asp187Asn or Asp187Tyr of gelsolin	Familial amyloid polyneuropathy (Finland)
AApoAI	Genetic variant of apolipoprotein A-I	Non-neuropathic systemic amyloidosis (Ostertag type)
AApoAII	Genetic variants stop78Gly or stop78Ser of apolipoprotein A-II	Non-neuropathic systemic amyloidosis (Ostertag type)
ALys	Genetic variants Ile56Thr, Trp64Arg or Asp67His of lysozyme	Non-neuropathic systemic amyloidosis (Ostertag type)
AFib	Genetic variants of fibrinogen	Non-neuropathic systemic amyloidosis (Ostertag type)

Epidemiology

Gastrointestinal disease is present in:

A. 30%
B. 50%
C. 60%
D. 80%
E. 95% of patients with AA amyloidosis

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Pathogenesis

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Mucosal infiltration

Neuromuscular infiltration

Pathogenesis

Mucosal infiltration

Most common sites of mucosal infiltration

1. 2nd part of the duodenum (100 %)
2. stomach and colorectum (>90 %)
3. esophagus (70 %)

AL: amyloid deposition in the muscularis mucosae, submucosa, and muscularis propria leads to polypoid protrusions and thickening of the valvulae conniventes

=> constipation, mechanical obstruction, or chronic intestinal pseudo-obstruction

AA: amyloid deposition occurs mainly in the mucosa, resulting in the fine granular appearance, mucosal friability, and erosions

=> diarrhea and malabsorption

Neuromuscular infiltration

AL, AA and dialysis-related amyloid

⇒ stasis syndromes

Affection of the intrinsic nervous system

⇒ neuropathic process: normal amplitude , uncoordinated contractions

Tissue wall infiltration

⇒ myopathic process : low amplitude contractions, prolonged transit

Clinical manifestations

Clinical presentation

- Gastrointestinal bleeding
- Malabsorption
- Protein-losing gastroenteropathy
- Chronic gastrointestinal dysmotility
- Cholangitis due amyloid deposition at the ampulla of Vater
- Bowel obstruction due to encapsulating peritonitis or extraluminal amyloidoma
- Bowel perforation in light chain amyloidosis, which may occur after the initiation of anti-AL therapy
- Pneumatosis intestinalis

Clinical manifestations

Amyloidosis secondary to IBD

Clinical manifestations

Amyloidosis secondary to IBD

- AA amyloidosis is a rare IBD complication
- 10 to 15 times more likely in CD than UC
- male sex, fistulizing behavior, extraintestinal manifestations, perianal disease, ileocolic anatomical location
- Renal disease

Clinical manifestations

Hepatic amyloidosis

Clinical manifestations

Hepatic amyloidosis

Hepatomegaly

elevated alkaline phosphatase

fatigue, weight loss, anorexia (due to systemic amyloidosis)

ascites (due to concurrent heart failure or hypoalbuminemia)

Hepatic involvement in: 90% of patients with AL and 60% of patients with AA

Imaging findings

Gastrointestinal tract amyloidosis

AA amyloid:

coarse mucosal pattern with innumerable fine granular elevations due to expansion of the lamina propria by amyloid deposits

AL amyloid:

polypoid protrusions, thickening of the folds, luminal narrowing, loss of haustrations, thickened mucosal folds, mucosal nodularity, ulceration

may mimic Crohn Disease

Hepatic amyloidosis

US

heterogeneous echogenicity

CT scan

diffuse or focal regions of decreased parenchymal attenuation with or without extensive calcification

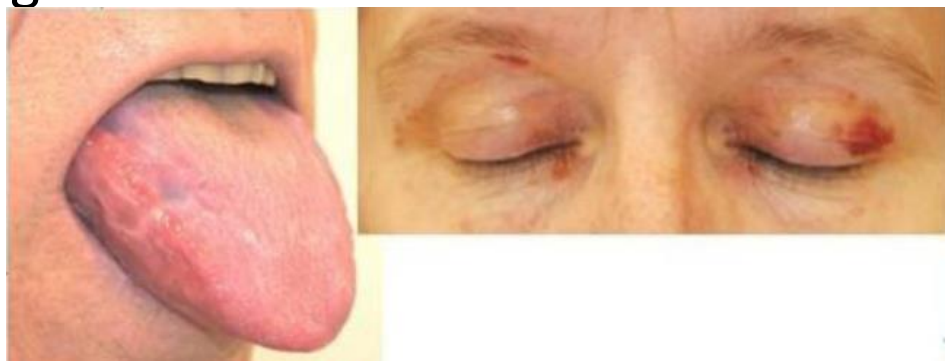
MRI

significantly increased signal intensity on T1-weighted images

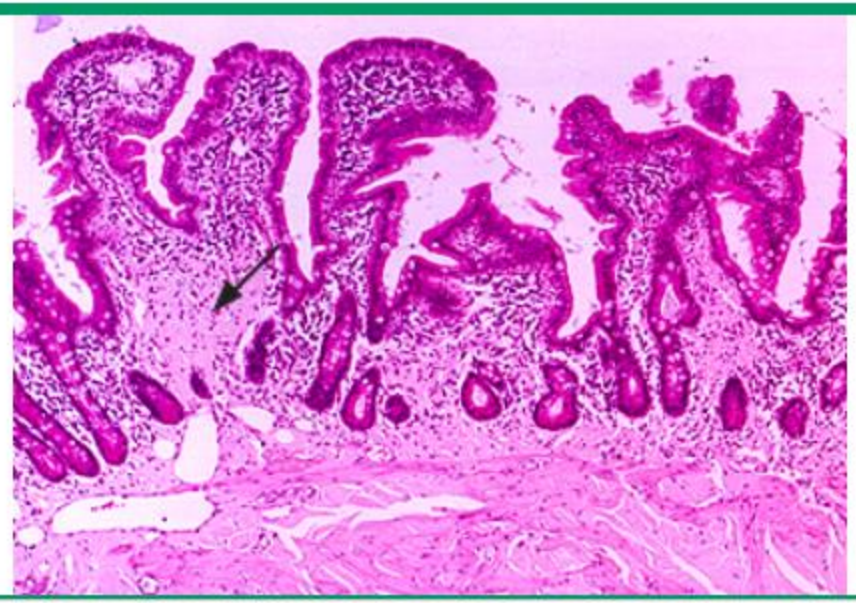
Diagnosis

- 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)

- restrictive cardiomyopathy, neuropathy, unexplained edema, carpal tunnel syndrome, unexplained facial or neck purpura, macroglossia

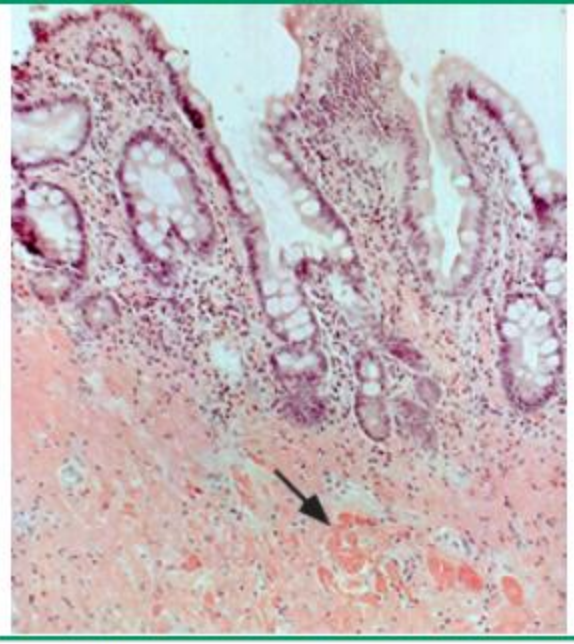


- Gold standard: BIOPSY rectal or duodenal

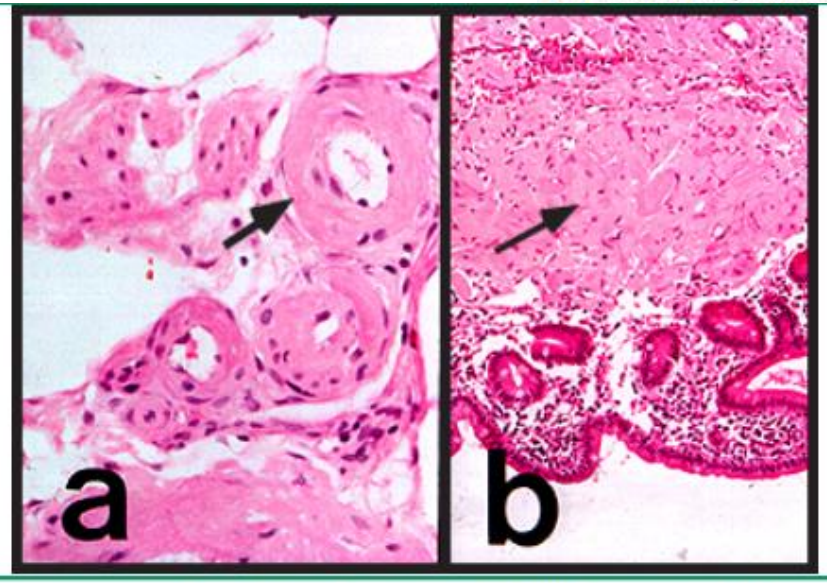


Endoscopic biopsy of nodular duodenal epithelium stained with hematoxylin and eosin. Note the pink amorphous deposit in the lamina propria (arrow).

Courtesy of Michael Camilleri, MD.



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



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).

Next step?

Determine the type of amyloid

- Immunohistochemistry (reliable for AA, TTR)
- Amino acid sequencing
- Mass spectroscopy

Search for monoclonal immunoglobulin

treatment

therapy is aimed at :

- the underlying infectious or inflammatory disorder in secondary (AA) amyloidosis
- the underlying plasma cell dyscrasia in primary (AL) amyloidosis
- either altering the mode of dialysis or considering renal transplantation in patients with dialysis-related amyloidosis

- Hereditary amyloidosis (mutant amyloid precursor protein is produced by the liver (eg, transthyretin)) => consider OLT