Amyloidosis & the GI Tract

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Topics to cover

1) Patterns of GI amyloid involvement
2) Symptoms associated with amyloidosis
3) Diagnostic tests at our disposal
4) Treatment options
5) Epidemiology & data regarding variants
Patterns of GI amyloid

• Amyloid can deposit anywhere in the GI tract or nerves that regulate it
• Luminal GI Patterns:
  – Mucosal infiltration
  – Muscle infiltration
  – Neuropathy
  – Vascular
Patterns of GI amyloid

- Mucosal involvement
  - Role: site of absorption
  - Symptoms
    - Diarrhea
    - Malabsorption
  - Diagnosis
    - Endoscopic biopsy
Patterns of GI amyloid

• Muscular infiltration
  – Role: site of contraction & motility
  – Symptoms
    • Decreased motility/stasis
      – Small intestinal bacterial overgrowth
        » Diarrhea
        » Malabsorption
    – Constipation
    – Pseudo-obstruction
    – Nausea/vomiting/abdominal pain

– Diagnosis
  • Imaging studies
  • Transit studies
  • Manometry
Patterns of GI amyloid

• Neuropathy
  – Role: coordination of GI motility & neuroendocrine secretion
  – Symptoms
    • Dysmotility
      – Nausea/vomiting/pain
      – Diarrhea
      – Constipation
    • Increased sensation
  – Diagnosis
    • Manometry
Patterns of GI amyloid

• Vascular
  – Role: delivery of blood flow to gut
  – Symptoms
    • GI Bleeding
    • Ischemia (pain/diarrhea)
  – Diagnosis
    • Endoscopy
Non-luminal GI patterns

- Liver involvement
  - Liver enlargement
  - Elevated liver tests (alkaline phosphatase)
  - Clinical manifestations usually mild but a marker of widespread systemic deposition

- Cholangitis
- Pancreas
- Peritonitis
Symptoms

- Symptoms are linked to area of involvement & are often non-specific
  - Esophagus:
    - Reflux
    - Dysphagia
    - Food impaction
  - Stomach:
    - Abdominal pain
    - Nausea
    - Vomiting
    - Distention
  - Small intestine:
    - Diarrhea
    - Malabsorption
    - Weight loss
    - Pseudo-obstruction
  - Colon:
    - Diarrhea
    - Constipation
    - Fecal incontinence
Symptoms Caveat

- When evaluating symptoms in amyloid, it is important to remember that most symptoms are nonspecific and can also be seen outside of amyloid
  - Reflux: 20% adults
  - Dysphagia: 4% adults
  - Functional dyspepsia: 20-30% adults
  - IBS: 13% adults
  - Constipation: 15% adults
  - Fecal incontinence: 6% adults
- Just because someone has amyloid, doesn’t mean they can’t have other GI conditions
  - Inflammatory bowel disease
  - Celiac disease
  - Eosinophilic esophagitis
  - Cancers
- Symptoms can also relate to medication adverse effects
  - GI symptoms most common adverse effects listed for most medications
  - > 80% of people who take 5 of more medications will have at least one adverse effect
Diagnostic tests

- Endoscopy & colonoscopy are usually the first tests performed
  - Allows option to take biopsies for diagnosis
  - Can also allow treatment
    - Bleeding control
    - Dilation
  - Findings can be nonspecific
  - Will only pick up mucosal GI involvement
  - Rectum commonly chosen as yield high (> 75%) and easy to get to
  - Highest yield in GI tract is in duodenum
Diagnostic tests

- Other tests to consider
  - Imaging studies
    - CT
    - MRI
    - Barium
  - Motility studies
    - Scintigraphy
    - Manometry
    - Wireless motility capsule
    - Sitz marker study
  - Breath tests
Treatment options

- Treatment should be tailored to symptoms & GI involvement
Treatment options

• Esophagus
  – Reflux treatment options
    • Dietary modification
    • Antacids
    • Histamine receptor blockers
    • Proton pump inhibitors
    • Endoscopic/surgical options in carefully selected patients
  – Dysphagia treatment options
    • Dietary modification
    • Dilatation
    • Botox
Treatment options

• Stomach
  – Dietary modification
  – Prokinetics
    • Metoclopramide (Reglan)
    • Erythromycin/azithromycin
    • Domperidone (not FDA-approved)
    • Prucalopride (not FDA-approved)
    • Bethanechol
    • Pyridostigmine
  – Agents to help stomach expansion
    • Herbal therapies (peppermint/caraway)
    • Buspirone
  – Neuromodulators
    • Tricyclics (amitriptyline)
    • Mirtazapine (Remeron)
    • Gabapentin/pregabalin (Lyrica)
  – Anti-emetics
  – Endoscopic options: Botox
Treatment options

• Small bowel
  – Dietary modifications
  – Prokinetics
  – Antibiotics (focused on small intestinal bacterial overgrowth)
  – Octreotide
  – Steroids
  – Anti-diarrheals
    • Imodium
    • Lomotil
    • Tincture of opium
  – Parenteral nutrition (rare cases)
Treatment options

• Colon
  – Dietary modifications
  – Laxatives
    • Over the counter
      – Miralax
      – Senna
    • Prescription
      – Lubiprostone (Amitiza)
      – Linaclotide (Linzess)
      – Plecanatide (Trulance)
  – Prokinetics
Epidemiology

- GI involvement in amyloid as a whole is (to me at least) reported to be surprisingly low:
  - 2013: In retrospective study of 2334 patients with amyloidosis, only 76 (3%) had amyloid on GI biopsies
  - 2015: In Korean study, only 24 of 155 symptomatic; all with amyloid on biopsy (15%)
  - 2017: In retrospective study of 583 amyloid patients, only 96 reported GI symptoms; 82 underwent endoscopy with biopsies; only 45% had amyloid on biopsies (16% symptomatic; 6% amyloid on biopsies)

Cowan AJ. Haematologica 2013
Young Lim A. Korean J Intern Med 2015
Yen T. Neurogastroenterol Motil 2017
Data regarding variants

• Extremely limited
  – I could find not data on GI manifestations of TTR variants
  – All GI series published on amyloid are > 80% AL/AA
  – Weight loss reported to be in 30% range, but multifactorial
  – Frequent diarrhea/constipation mentioned in TTR articles in other fields (cardiac mostly)

• My subjective impression
  – Perhaps more neuropathy than AL/AA
  – All distribution patterns seen

• Needs a good study
Thank you

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