Scleroderma & gastrointestinal disease

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Overview

• Introduction to scleroderma GI disease
• Function in the normal GI tract
• Dysmotility in scleroderma
• Approach to diagnosis
• Management
• Future directions
Introduction to scleroderma GI disease
Introduction to scleroderma GI disease

- Scleroderma GI disease affects up to 90% of scleroderma patients
- Both men and women are affected
- Involves a wide spectrum of severity

Scleroderma can affect any part of the gastrointestinal tract

Clinical complications of scleroderma GI dysmotility

- Dysphagia
- Acid reflux
- Nausea
- Early satiety
- Bloating and discomfort
- Diarrhea
- Constipation
- Fecal incontinence
Motility in the GI tract
Normal gastrointestinal motility

Smooth muscle layers
What do we know about the GI tract in scleroderma?

- Smooth muscle loss and some fibrosis may occur in any region of the GI tract, leading to weak contractions and ineffective transport of food.

- This may result in delayed food transit and the onset of symptoms.
All scleroderma GI disease is not the same

Significant clinical differences exist among patient subsets with GI dysmotility in scleroderma

<table>
<thead>
<tr>
<th>Patient</th>
<th>Pharynx</th>
<th>Esophagus</th>
<th>Stomach</th>
<th>Small intestine</th>
<th>Large intestine</th>
<th>IAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient A</td>
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<td>Patient B</td>
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<td>Patient C</td>
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<td>Patient D</td>
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<td>Patient E</td>
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<td>+++</td>
</tr>
</tbody>
</table>

1 year  The time frame on which these changes occur vary across patients  20+ years

Jaovishidha K, Csuka ME. Semin Arthritis Rheum 2005
What we have learned so far…

• Severity of GI disease in SSc is variable

• Different regions of the GI tract are affected in different patients

• The timing of symptoms of GI disease varies across the SSc population

Jaovishidha K, Csuka ME. Semin Arthritis Rheum 2005
Steen VD, Medsger TA. Arthritis Rheum 2000
What causes smooth muscle atrophy and slow GI motility in scleroderma?
Normal signaling between nerves and muscles

Stimulate the smooth muscle contraction

GI smooth muscle

Furness JB, Nature 2012
Do autoantibodies contribute?

Singh J et al. Gastroenterology 2012

Stimulate the smooth muscle contraction

Inhibit smooth muscle contraction

GI smooth muscle
Specific GI complications in SSc
Esophageal dysfunction in scleroderma

Lower esophageal sphincter

Esophagus

Large intestine

Small intestine

Stomach
Symptoms and mechanisms of esophageal dysmotility

• Symptoms
  – Dysphagia
  – Heartburn
  – Regurgitation
  – Chest pain

• Mechanisms of reflux
  – Decreased lower esophageal sphincter pressure
  – Peristaltic dysfunction
  – Delayed gastric emptying
  – Medications used to treat other aspects of SSc (e.g. CCB)

• Complications
  – scarring, bleeding, cancer, ?lung disease

Lifestyle Modification

• Dietary measures (avoidance)
  – Chocolate
  – Citrus fruits/fruit juices
  – Tomatoes
  – Peppermint
  – Onions/garlic
  – High-fat meals
  – Carbonation
  – Caffeine
• Small meal size
• Weight loss

• Smoking cessation
• Avoidance of alcohol
• Elevation of the head of the bed
• Sleeping in the left decubitus position
• No meals within 3 hours of sleeping


Slide is a courtesy of Dr. John Clarke
Lifestyle modification is not working…

- Try a medication
- Pursue objective testing
- Good response
Diagnostic testing

- Barium studies
- Endoscopy
  - Traditional or capsule
- Formal reflux testing
  - Wireless pH testing
  - 24-hour pH/impedance
- Esophageal manometry
Gastric dysfunction in scleroderma

Lower esophageal sphincter

Stomach

Esophagus

Large intestine

Small intestine
Symptoms of gastric dysmotility

- Symptoms
  - Reflux
  - Nausea
  - Vomiting
  - Bloating
  - Upper abdominal pain
  - Early satiety

- Complications
  - Weight loss
  - Poor quality of life
Diagnostic testing

Common forms of diagnostic testing:

- Endoscopy

- Gastric emptying scintigraphy
  - Solid +/- liquid

- Whole gut transit study or wireless motility capsule

Whole gut transit study

- Scintigraphy-based state-of-the-art test
- Evaluates motility from the esophagus through the colon
- Valuable in determining the exact location(s) of dysfunction in the GI tract
- Clinically useful for targeting therapy

Treatment of Gastric Dysfunction

• Lifestyle changes
  – Small volume, soft diet, low-fat meals
  – FODmap diet may help

• Prokinetics are often required
  – e.g. metaclopramide, erythromycin, domperidone, cisapride

• Alternative therapies
  – e.g. acupuncture, botulinum toxin injection

Small Intestinal Manifestations

• Symptoms of small intestinal dysmotility
  – Abdominal pain, distention, bloating, diarrhea
  – Pseudo-obstruction or malabsorption

• Mechanisms
  – Poor motility → stasis and dilation of the bowel
  – Small intestinal bacterial overgrowth

Diagnostic testing and treatment

- Imaging (barium studies or CT/MR enterography)
- Enteroscopy with jejunal aspirates
- Breath tests (glucose or lactulose)
- Whole-gut scintigraphy or wireless motility capsule

Treatment
- Lifestyle/dietary changes
- Trial of cyclic antibiotics
- Probiotics
- Prokinetics (e.g. octreotide, pyridostigmine)

Soudah HC, Hasler WL, Owyang C. NEJM 1991
Colonic manifestations: constipation and incontinence

- 1/3 or more of SSc patients complain of constipation, diarrhea and/or fecal incontinence

- Colon transit studies:
  - Radiopaque markers, whole-gut scintigraphy, wireless motility capsule

- Anorectal function studies:
  - Anorectal manometry or defecography

Management

- OTC Stool softeners or laxatives (lactulose, milk of magnesia, polyethylene glycol, etc)
- Minimize use of bulking agents
- Prescription medications
  - linaclotide, lubiprostone, pyridostigmine

### Summary of interventions in the management of GI disease in scleroderma

<table>
<thead>
<tr>
<th>Symptom Category</th>
<th>Symptoms</th>
<th>Management Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GERD</strong></td>
<td>Acid reflux, substernal burning, dysphagia</td>
<td>H2 blocker, PPI</td>
</tr>
<tr>
<td><strong>Delayed gastric emptying</strong></td>
<td>Early satiety, nausea, vomiting, bloating</td>
<td>Diet low in fiber and fat; Promotility agents (e.g. reglan)</td>
</tr>
<tr>
<td><strong>Small bowel dysmotility</strong></td>
<td>Diarrhea, bloating, malabsorption, pseudo-obstruction</td>
<td>Cyclic antibiotics; Promotility agents</td>
</tr>
<tr>
<td><strong>Large bowel dysmotility</strong></td>
<td>Constipation, bloating, pseudo-obstruction</td>
<td>OTC Stool softeners or laxatives; Minimize use of bulking agents; Prescription medications</td>
</tr>
<tr>
<td><strong>Anorectal dysfunction</strong></td>
<td>Fecal incontinence, constipation</td>
<td>Pelvic physical therapy; Medical or surgical intervention</td>
</tr>
</tbody>
</table>
Challenges we face

• Need markers of disease activity
  – To treat or not to treat
  – Risk benefit ratio of medications

• Need to know how to treat
  – Mechanisms of disease are not clear
  – Which are the best drugs to use?

• Defining a response to treatment
  – Knowing if the treatment is working
  – Knowing when to stop the treatment
We are making progress!

- Several studies evaluating the GI tract in scleroderma are ongoing in the Johns Hopkins Scleroderma Center

- Two other studies where we are actively recruiting:
  - GRASP
  - Identical twin study
Thank you!

Conference organizers
Johns Hopkins Scleroderma Center and lab
• Dr. Laura Hummers
• Dr. Fredrick Wigley
• Dr. Ami Shah
• Dr. Julie Paik
• Dr. Livia Casciola-Rosen
• Dr. Antony Rosen

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• Dr. Jay Pasricha
• Our patients and our staff