

Gastrointestinal complications of Scleroderma and their treatment

Kenneth E. Fasanella, MD
 Assistant Professor of Medicine
 Associate Director, Gastroenterology Fellowship
 Division of Gastroenterology, Hepatology & Nutrition
 University of Pittsburgh Medical Center



Overview

- Affect over 80% of patients with scleroderma
- Pathologic abnormalities include both disorder of neuromuscular function and smooth muscle atrophy and fibrosis.
- Altered motility can lead to transit and absorption abnormalities
- Can affect sufferers from mouth to anus
- No correlation with skin involvement
- Main cause of death in 5-10% of patients, with 5 year mortality >50% in some circumstances



Organ involvement

- Oral aperture
- Salivary glands
- Esophagus
- Stomach
- Small intestine
- Colon
- Anal sphincter



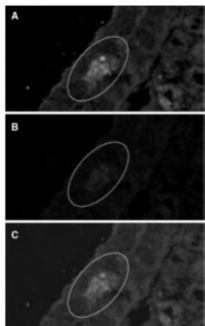
Pathophysiology (mechanism of disease)

- Unclear
- Proposed:
 - Neuropathic – altered function of gut neurons. Antibodies have been seen to both enteric neurons and neuromuscular junctions.
 - Fibrosis – excess collagen deposition within and atrophy of the muscle of the gut.
 - May be due to antibodies that increase production and inhibit degradation of collagen (scar tissue).



Neuropathic

Autoantibodies in serum of scleroderma patients against gut neurons.



Domsic, et al. *Dig Dis Sci*, 2008 (53):1163-74



Mouth

- Microstomia (decreased mouth opening size) is sometimes associated with compromised dental care but rarely affects ability to chew food or get adequate nutrition.



Mouth

- Dry mouth, part of a complex of “sicca” symptoms, is experienced by as many as 20% of scleroderma sufferers.
- Can affect swallowing due to decreased lubrication
- Can increase risk of tooth decay and gum disease
- Can contribute to acid reflux-related esophageal damage



Mouth

- Treatment
 - Generous use of fluids and/or oral lubricants
 - Meticulous oral hygiene
 - Preventative and restorative dental care



Esophagus

- Most commonly affected GI organ
- Symptoms include:
 - Heartburn
 - Regurgitation
 - Dysphagia (feeling of food getting stuck)
- Manifestations present in 20-95% of SSc patients depending on antibody profile.

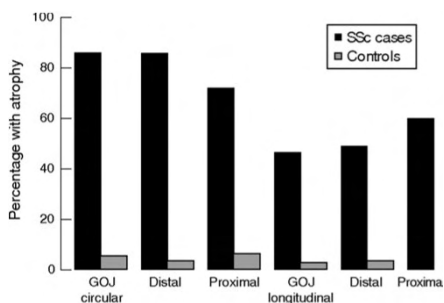


Esophagus

- Dysphagia can be due to one of two underlying processes:
 - Dysmotility
 - Stricture formation



Smooth-muscle atrophy is more common in (systemic sclerosis (SSc)) cases than in controls, and is most common in the circular layers of the distal esophagus and the gastro-esophageal junction (GEJ).



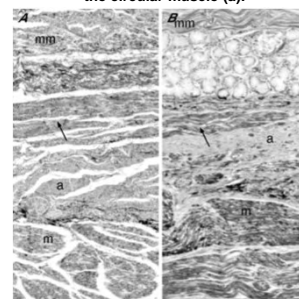
Roberts C G P et al. Gut 2006;55:1697-1703



GUT

©2006 by BMJ Publishing Group Ltd and British Society of Gastroenterology

Reproduction of two systemic sclerosis tissue specimens that have an aberrant strip of longitudinal smooth muscle (black arrow) on the luminal surface of the circular muscle that is not atrophic despite severe atrophy of the circular muscle (a).

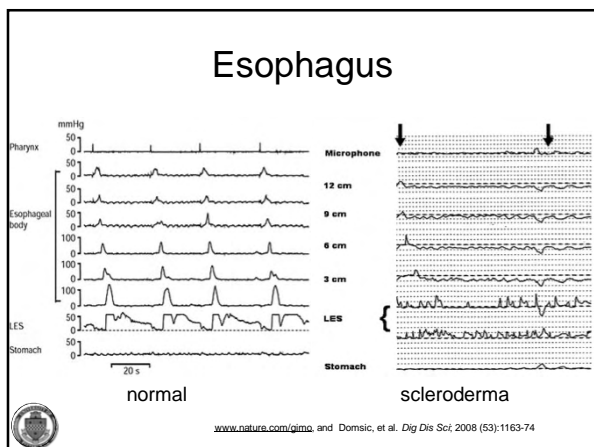
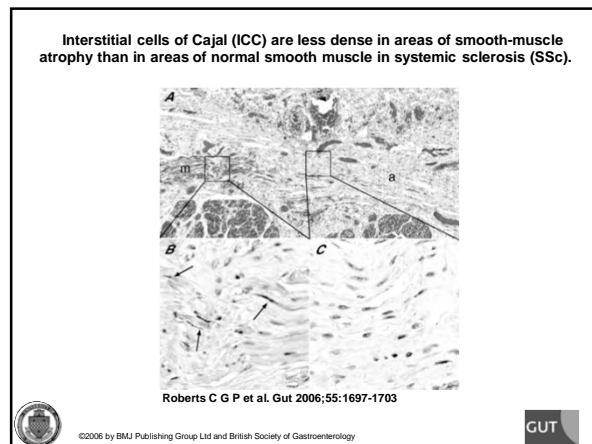
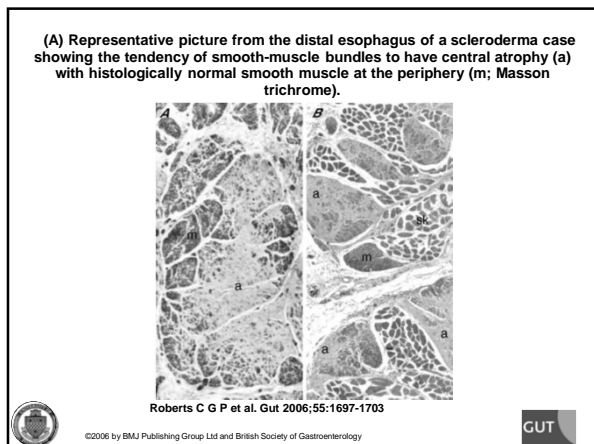


Roberts C G P et al. Gut 2006;55:1697-1703

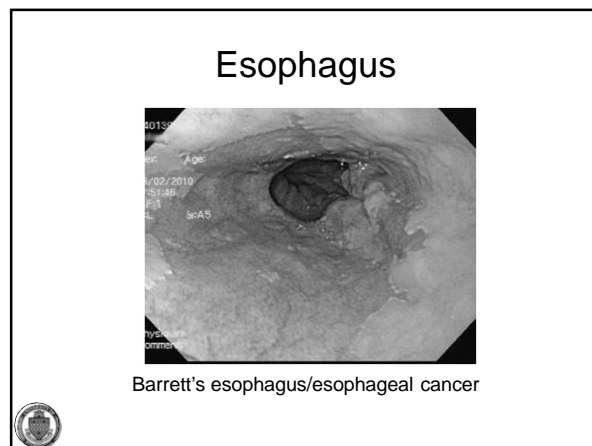
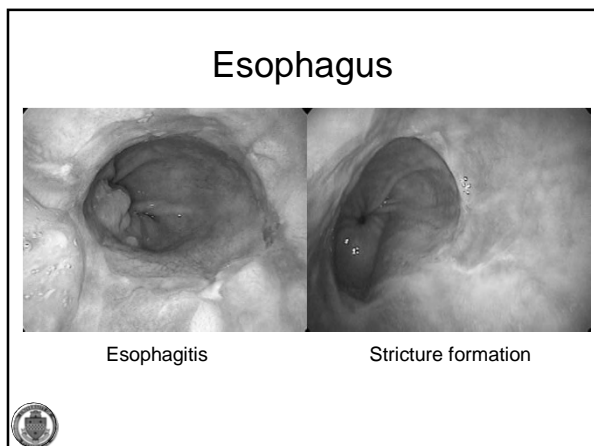


GUT

©2006 by BMJ Publishing Group Ltd and British Society of Gastroenterology



- ### Esophagus
- Altered motor function results in:
 - Delayed transit of esophageal contents to stomach
 - Increased reflux of gastric contents into esophagus
 - Delayed clearance of refluxate from esophagus
 - Risk of pill esophagitis
 - Risk of candida esophagitis (yeast infection)
 - ? Causal relationship to pulmonary manifestations of disease.



Esophagus

- Treatment
 - Proton pump inhibitors (PPI's – e.g. Prilosec, prevacid, aciphex, protonix, nexium, and dexilant)
 - Endoscopic screening with subsequent surveillance if Barrett's is found
 - Dilation if necessary
 - Antireflux surgery if absolutely necessary
 - Treat gastroparesis if found (described in stomach section)



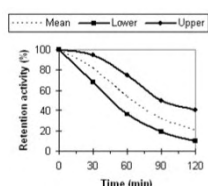
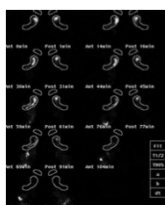
Stomach

- Delay in gastric emptying
 - Seen in up to 50% of patients
 - Symptoms include:
 - Early satiety
 - Bloating
 - Post-prandial fullness
 - Nausea +/- vomiting
 - Epigastric discomfort or pain



Stomach

- Diagnosis requires a gastric emptying test using nuclear imaging.



Stomach - gastroparesis

- Treatment
 - Dietary modification
 - Low fat, low residue, low volume with higher frequency of meals for milder symptoms
 - Liquid nutrition for severe symptoms



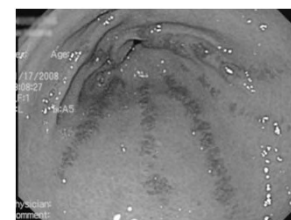
Stomach - gastroparesis

- Treatment (pharmacologic)
 - Metoclopramide (Reglan) – good initial benefit, unclear long-term.
 - ***Tardive dyskinesia risk with long-term use***
 - Domperidone – works using same mechanism but doesn't cross blood-brain barrier – less side effects/risk, limited availability in U.S.
 - Erythromycin
 - Cisapride – works well acutely but very limited availability in U.S.



Stomach

- Gastric Antral Vascular Ectasia (GAVE – a.k.a. “watermelon stomach”)
 - Can cause iron deficiency anemia or slow hemorrhage



Stomach - GAVE

- Treatment
 - Endoscopic ablation – typically argon plasma coagulation
 - May require repeated treatments



Small intestine

- Associated with altered motor function similar to esophagus, with decreased contractile activity, delayed transit, and fibrosis.
- Prevalence ranges from 8-50% depending on study.



Small intestine

- Symptoms:
 - Bloating
 - Fullness
 - Vomiting
 - Diarrhea
 - Flatulence
 - Weight loss
 - Nutritional intolerance (commonly lactose)
 - Nutritional deficiencies
 - Vitamin D/Ca – osteoporosis
 - Vitamin B12



Small intestine

- Radiograph demonstrates dilated small intestine which is associated with delayed transit
- This delay can lead to overgrowth of bacteria in small bowel.



Domsic, et al. *Dig Dis Sci*; 2008 (53):1163-74



Small intestine

- Bacterial overgrowth leads to malabsorption of intestinal contents
 - Bacteria break down pancreatic enzymes
 - Bacteria feed upon and inhibit absorption of vitamin B12
 - Fermentation in small bowel leads to gas formation and bloating



Small intestine – bacterial overgrowth

- Diagnosis
 - Enteroscopy with aspirate and quantitative cultures of jejunal aspirates.
 - Gold standard but invasive and logistically difficult
 - Hydrogen breath testing



Small intestine – bacterial overgrowth

- Treatment
 - Cycled antibiotics
 - Typically metronidazole (flagyl)
 - Augmentin
 - Tetracyclines
 - Ciprofloxacin
 - Try to have as long of an antibiotic free interval as possible between cycles



Small intestine

- SBBO associated with pseudoobstruction
 - Erythromycin
 - Octreotide – expensive, requires subcutaneous injection, and can impair absorption – last resort
 - Total Parenteral Nutrition – expensive, can be associated with risk of infection and liver disease - last resort



Small intestine

- Pneumatosis cystoides intestinalis and pneumoperitoneum
 - Presumed due to progressive distension of small bowel from gas formation due to SBBO.
 - Gas bubbles form in gut wall and can spontaneously rupture, putting gas but usually not intestinal contents into abdominal cavity
 - Symptoms include acute abdominal pain and distension



CT scan showing air in intestinal wall as well as some free air within abdominal cavity

Domsic, et al. *Dig Dis Sci*, 2008 (53):1163-74



Small intestine – pneumatosis cystoides/pneumoperitoneum

- Although this can present masquerading as a surgical emergency and often gets inappropriately treated as such, most patients respond to conservative management, including:
 - Bowel rest
 - Antibiotics
 - Long-term control of bacterial overgrowth



Colorectal manifestations

- About one-third of patients have constipation, diarrhea, and/or incontinence of stool.



Colorectal manifestations

- Constipation related to similar motor dysfunction affecting rest of bowel, leading to slow transit.
- Incontinence is typically due to impairment of function of the internal anal sphincter muscle, which can become atrophic and fibrotic, similar to other areas of the GI tract.



Colorectal manifestations

- Diagnostic studies for slow colon transit can include Sitz marker studies, but usually not necessary.
- Anorectal manometry can be diagnostic of internal anal sphincter dysfunction. However, decreased resting sphincter tone on digital rectal exam is characteristic.



Colorectal manifestations

- Treatment of constipation is usually accomplished with osmotic laxative agents, such as miralax, but can be complicated by incontinence and should be avoided in patients with pseudoobstruction.
- Scheduled defecation using loperamide interspersed with stimulant laxatives is another reasonable option.



Colorectal manifestations

- Pitfalls in treatment of constipation:
 - Bulk forming agents such as fiber can exacerbate gastroparesis, and be fermented by bacteria causing excess bloating
 - Non-absorbable sugars, such as lactulose, cause excessive bloating and cramps, also due to fermentation by gut bacteria.
 - Antidiarrheals can adversely affect upper GI tract, and thus should be avoided if possible.



Summary

- SSc affects the entire GI tract
- Common mechanism is altered motor function, smooth muscle atrophy, and fibrosis
- One of the potentially lethal complications of the disease
- Difficult cases should probably seek the opinion of a tertiary referral center with specialists trained in treatment of GI complications.



Thank you

