Systemic sclerosis and GI involvement

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Objectives

• Describe systemic sclerosis
• Outline general features
• Discuss specific GI aspects
• To increase knowledge of systemic sclerosis
Scleroderma (Systemic Sclerosis) is ...

“sclero” (Greek meaning **hard**) + “derma” (Greek meaning **skin**)

= **scleroderma** (hard skin)

- Hippocrates
- 1945 association with systemic disease
Overall scheme illustrating a current understanding of SSc pathogenesis. Hypothetical sequence of events involved in tissue fibrosis and fibroproliferative vasculopathy in SSc. An unknown causative agent induces activation of immune and inflammatory cells in genetically predisposed hosts resulting in chronic inflammation. Activated inflammatory and immune cells secrete cytokines, chemokines, and growth factors which cause fibroblast activation, differentiation of endothelial and epithelial cells into myofibroblasts, and recruitment of fibrocytes from the bone marrow and the peripheral blood circulation. The activated myofibroblasts produce exaggerated amounts of ECM resulting in tissue fibrosis. Medscape rheumatology
Terminology

Scleroderma

Localised
- Morphea
- Linear (en coup de Sabre)

Systemic
- Limited (distal to elbows or knees)
- Diffuse

Images from ACR Image bank
Many aspects of scleroderma

- **Vascular system**
  - Raynauds
  - Healed pitting ulcers in fingertips
  - Cutaneous and mucosal telangiectasia

- **Gastrointestinal system**
  - GERD, GAVE
  - Dysmotility
  - Constipation /diarrhea

- **Respiratory system**
  - ILD
  - Pulmonary hypertension

- **Musculoskeletal system**
  - Arthritis/myositis
  - Flexion contractures
  - Carpal tunnel syndrome
  - Muscle weakness

- **Constitutional:** Fatigue/weight loss

- **Skin**
  - Sclerodactyly
  - Edema
  - Digital ulcers
  - Calcinois
  - Hyper or hypo-pigmentation

- **Cardiovascular system**
  - Pulmonary hypertension
  - Arrhythmias

- **Genitourinary system**
  - Erectile dysfunction
  - Dyspareunia

- **Ears, nose, and throat**
  - Sicca syndrome
  - Poor dentition
  - Hoarseness due to acid reflux with vocal cord inflammation or fibrosis

- **Endocrine system**
  - Hypothyroidism

- **Renal system**
  - Hypertension
  - Renal crisis
  - Chronic renal insufficiency
Pearl 1: clinical aspects

- Usually presents with Raynauds, and puffy hands
- Particularly affects lungs, heart, kidneys and skin
- Can affect almost any organ
- May overlap with other autoimmune diseases
# Red flag symptoms or signs in Raynauds

<table>
<thead>
<tr>
<th>Red flag Symptoms</th>
<th>Red flag Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden and late onset</td>
<td>Dry eyes/mouth</td>
</tr>
<tr>
<td>Constitutional features</td>
<td>Apthous ulcers</td>
</tr>
<tr>
<td>Thickened skin</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Digital ulcers</td>
<td>Dyspnea</td>
</tr>
<tr>
<td>Rashes</td>
<td>Muscle weakness</td>
</tr>
<tr>
<td>Calcium deposits</td>
<td>Swallowing difficulties</td>
</tr>
<tr>
<td>Arthritis</td>
<td>GI disturbances</td>
</tr>
</tbody>
</table>
Pearl 2: Raynauds Red flags

Bottom Lines:

• Older age
• Male
• Digital ulcers
• Other features of autoimmune diseases
New criteria aid early diagnosis

- Puffy fingers
- Raynauds phenomenon
- Dilated nail fold capillaries
- (ANA)

Koenig et al A&R 2008

ACR Image bank
### 2013 ACR/EULAR SSc guidelines

<table>
<thead>
<tr>
<th>Item</th>
<th>Sub-item</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin thickening of fingers of both hands extending proximal to MCP joints (sufficient criterion)</td>
<td></td>
<td>9</td>
</tr>
<tr>
<td>Skin thickening of fingers (<em>only count higher score</em>)</td>
<td>Puffy fingers</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Sclerodactyly of fingers (distal to MCP joints but proximal to PIP joints)</td>
<td>3</td>
</tr>
<tr>
<td>Fingertip lesions (<em>only count higher score</em>)</td>
<td>Digital tip ulcers</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Fingertip pitting scars</td>
<td>3</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>

Van den Hoogen 2013
## 2013 ACR/EULAR SSc guidelines

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<th>Item</th>
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<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal nailfold capillaries</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary arterial hypertension and/or interstitial lung disease (maximum score is 2)</td>
<td>Pulmonary arterial hypertension Interstitial Lung Disease</td>
<td>2</td>
</tr>
<tr>
<td>Raynaud’s phenomenon</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>SSc-related autoantibodies (anticentromere, anti-RNA polymerase III, anti-topomerase I [anti-SCl-70] (Maximum score is 3)</td>
<td>Anti-centromere Anti-topomerase I Anti-RNA polymerase</td>
<td>3</td>
</tr>
</tbody>
</table>

Total score = Sum of maximum score in each category  
Total Score ≥ 9 Classified as Definite SSc; Maximum Score is 19
Early diagnosis allows improved monitoring and treatment of complications

- Diffuse disease – more likely to get ILD, PAH, renal disease
- Intensive monitoring necessary – ECHO, PFTs, renal function, BP
- Improved treatments available
Pearl 3: early diagnosis

• New criteria make it easier to diagnose SSc early
• Consider in patients with Raynaud’s, puffy hands and dilated nailfold capillaries
Pearl 4: Outcome – 75% 10 yr survival

Bottom Lines:

• Important causes of premature death
  • pulmonary fibrosis,
  • pulmonary hypertension,
  • renal failure

• Significant morbidity associated
Pearl 5: risk factors for poor outcome

- Diffuse skin involvement
- Proteinuria
- PAH
- Pulmonary fibrosis
- NYHA class 2
- Late onset Raynauds
Part 1: Take Home Messages

• Consider SSc in:
  – new onset Raynauds
  – Raynauds in older patient
  – Puffy fingers
  – Digital ulcers

• Monitor for:
  – pulm fibrosis with annual PFTs (6 monthly if less than 5 yrs)
  – PAH with annual ECHO refer for RHCath if pressures ≥40 and dyspnoeic
  – BP and creatinine carefully esp in diffuse disease

• Beware of steroid dose in SSc – ≥15mg may precipitate Scleroderma Renal Crisis (SRC)

• Multisystem disease: Talk to colleagues...
Gastrointestinal disease

- Multidisciplinary approach – GI, nutritionist, speech therapist
- GERD may trigger or worsen ILD
- Screen for malnutrition
- Manage constipation

Fibrosis is likely to be the key pathological process in GI involvement in SSc
Gastrointestinal imaging

Plain abdominal radiograph shows a gas-filled, dilated stomach (black arrow) and duodenum (red arrow). Barium-meal study in the same patient shows a dilated duodenum. Note also several diverticulae in the small bowel.

Left, Barium-meal study shows a dilated duodenum. Right, High-resolution CT (HRCT) scan of the thorax in the same patient shows lung fibrosis.

From: Medscape rheumatology Gastrointestinal scleroderma imaging
GI tests

• *Endoscopies +/- biopsy*

• Esophageal manometry assessment, and pH monitoring

• Gastric emptying

• *Breath Test*: fast for 12 hours, breathe into a small balloon, ingest a precise amount of sugar, and repeat breath samples every 15 minutes for 3 or more hours. Abnormal breath tests can also signify pancreatic insufficiency and celiac disease.
## Treatment of GI manifestations

<table>
<thead>
<tr>
<th>Feature</th>
<th>Treatment</th>
</tr>
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<tbody>
<tr>
<td><strong>Oral cavity</strong> – dry mouth, dental caries</td>
<td>Artificial saliva, sugar-free gum, secretagogues - pilocarpine</td>
</tr>
<tr>
<td><strong>GERD</strong></td>
<td>Conservative measures PPI – high doses</td>
</tr>
<tr>
<td><strong>GAVE (Watermelon stomach)</strong></td>
<td>Laser photocoagulation Transfusions</td>
</tr>
</tbody>
</table>
| **Gastroparesis, Dysmotility Pseudoobstruction** | Domperidone 20mg tid  
Prucalopride 2mg od  
Octreotide 25-50mcg bid  
1G liquid Erythromycin q3 days  
Pyrido- or Neostigmine 1g slow ivi |
| **Bacterial overgrowth**                     | Cyclical antibiotics  
Rifamixin 200mg tid for 3 days                                            |
| **Constipation**                             | Prucalopride 2mg od  
Laxatives                                                                |
| **Diarrhoea**                                | Codeine or loperamide                                                     |
| **Incontinence**                             | Low dose loperamide  
Sacral nerve stimulator                                                  |
Small bowel bacterial overgrowth (SIBO)

- Common – 30-40%
- Change in flora cause
  - Competition for essential nutrients (B12)
  - Deconjugation of bile acids leading to fat malabsorption
  - Reduced oral intake
  - Diarrhoea
- Symptoms of bloating, gas, diarrhoea

- Diagnosed by
  - Jejunal culture
  - Breath tests (hydrogen best using glucose or lactulose)
  - Schilling test
- Treatment often empiric
- Antibiotics 14 days repeating
  - Tetracycline 250mg qid
  - Doxycycline 100mg bid
  - Minocycline 100mg bid
  - Amox + clav 875mg bid
  - Cephalexin (250mg qid) +Metronidazole (250mg tid)
  - Ciprofloxacin 500mg bid
  - Chloramphenicol 250mg qid
- Probiotics (Frech et al 2011)
Pearl 6: GI treatments

- High dose PPI for dyspepsia
- Domperidone 10mg tid for dysphagia
- Prucalopride 2mg od
- Rifamixin (newer non absorbed antibiotic) or cyclical antibiotics for SIBO
Summary

• Described many clinical features of SSc
• Discussed investigations and management of
  – Raynauds
  – GI involvement
• Outlined new diagnostic guidelines
• Discussed importance of early diagnosis
  
• Management of pulm hypertension, pulm fibrosis and renal disease will be covered in next talks
Thanks

• St Joseph`s Foundation
• Multidisciplinary colleagues at Hamilton Scleroderma Group – Ellen McDonald – the patient’s quarterback!
• Scleroderma Society of Ontario

• Questions: mlarche@mcmaster.ca