Scleroderma and Myositis

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## Classification

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
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<tbody>
<tr>
<td>Sclero-hard Derma-skin</td>
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<tr>
<td>Scleroderma-like illnesses</td>
<td>caused by vinyl chloride, bleomycin, tainted rapeseed oil, L-tryptophan.</td>
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<tr>
<td>Localized Scleroderma</td>
<td>morphea and linear Scleroderma</td>
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<tr>
<td>Limited Scleroderma [systemic sclerosis (PSS or SSc)]</td>
<td>formerly known as CREST</td>
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<tr>
<td>Diffuse Scleroderma</td>
<td>(systemic sclerosis)</td>
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Epidemiology

Affects 19-75 /100,000 population

Peak occurrence- 35-65 years old

Females : males- 7-12 : 1

Choctaw Indians 469/100,000
Pathology

Inappropriate fibrosis of tissues and blood vessels.

Smooth-muscle cells proliferate within the intima of small vessels (small arteries, arterioles and capillaries) which narrows the lumen causing tissue ischemia.
Pathogenesis

Susceptible Host

Exogenous Events

Immune System Activation

Endothelial Cell Activation/Damage

IL-6, IL-4, TGF-β, PDGF, fibroblast growth factor, endothelin 1

Fibroblast Activation

End Stage Pathology
(Obliterative Vasculopathy and Fibrosis)
Clinical Features

Raynaud's Phenomenon

Caused by vasospasm
Tricolor change- white to blue to red
Digital pitting scars and loss of digital pads
Gangrene and autoamputation (acroosteolysis)

Occurs in 90 % of patients with scleroderma
Ulcers and scars occur on the tips of the digits in an individual with Raynaud's phenomenon.
Skin

Earliest Stage - Edema

Fibrotic stage - thick hard skin develops

Limited PSS - affects hands, distal forearm, face

Diffuse PSS - entire extremity, trunk, face

Hypo and hyperpigmentation

Subcutaneous calcinosis
2nd most common organ system involvement
GI bleeding from telangiectasias
Malabsorption

Face
Decreased oral aperture
Sicca

Esophagus
Esophageal dysmotility (decreased peristalsis) causing dysphagia
GERD- 2º to decreased lower esophageal sphincter pressure
Esophagitis (with the potential for Barrett's Esophagus)
Stricture formation
Gastrointestinal cont.

Small Intestine
Chronic pseudoobstruction 2° to decreased peristalsis
Diarrhea 2° to bacterial overgrowth

Large Intestine
Wide mouth diverticular

Liver
Primary biliary cirrhosis
The facial skin is taut with an immobile facies and limitation of the oral aperture.
Serositis
Alveolitis- inflammation in alveoli
Interstitial fibrosis- presumably 2° to alveolitis
Pulmonary Hypertension 30- 35% in diffuse PSS
up to 50% in limited PSS

Low DLCO
Low lung volumes on PFTs
Respiratory failure
Kidneys are affected in most patients with diffuse PSS.

**Scleroderma Renal Crisis**

Only occurs in diffuse disease and may be related to steroid use.

80% cases within first 5 years

Characterized by:
- Accelerated hypertension
- Active urine sediment
- Microangiopathic hemolysis
- Rapidly progressive renal failure
Cardiac

Primarily in diffuse PSS

Pericarditis and pericardial effusion- in 40% patients

Areas of contraction (band necrosis)- Fibrosis of conducting pathways causing palpitations and dysrhythmias
Musculoskeletal

Arthralgia
Arthritis
Atrophy and muscle weakness
Acroosteolysis
Tenosynovial involvement causing tendon friction rubs and contractures
Radiograph of the fingers revealing resorption of the phalangeal tufts and multiple areas of punctate subcutaneous calcinosis.
95% of patients with PSS have an ANA

anti-Scl-70 (anti-topoisomerase 1) antibody- directed against topoisomerase I, an enzyme that participates in the initial uncoiling of DNA prior to transcription.

20% to 40% of patients with diffuse PSS have anti-Scl-70. 60% -70% of patients with anti-Scl-70 have diffuse PSS
20% of limited scleroderma patients have anti-Scl-70.

Anti-centromere antibody occurs in 80% to 90% of patients with limited scleroderma.
10% to 15% of patients with diffuse PSS have anti-centromere.

The presence of anti-Scl-70 predicts a worse prognosis.
Diagnosis

**Major criterion**
Proximal scleroderma: Symmetric thickening, tightening and induration of the skin of the fingers and the skin proximal to the MCP or MTP joints. The changes may affect the entire extremity, face, neck, and trunk (thorax and abdomen).

**Minor criteria**
1. Sclerodactyly: Above skin changes limited to the fingers
2. Digital ulcers or finger pad substance loss: loss of finger tip or digital pad tissue as a result of ischemia.
3. Bibasilar pulmonary fibrosis: Bilateral linear or lineo-nodular pattern mostly in lung bases on CXR; may appear as diffuse mottling or “honeycomb lung” and should not be attributed to primary lung disease.

Patients should have the one major criteria or two or more minor criteria. Localized forms of scleroderma, eosinophilic fasciitis and the various forms of pseudo-scleroderma are excluded.
Outcome

Diffuse PSS has a 40-60% 10 year survival
Limited PSS has a > 70% 10 year survival (if no pulm HTN)

Cardiopulmonary disease is the leading cause of death.

Factors suggesting a poor prognosis include:
  - diffuse skin involvement
  - late age at disease onset
  - black or native americans
  - presence of tendon friction rubs
  - a diffusing capacity < 40% of predicted value
  - the presence of a large pericardial effusion
  - renal failure or proteinuria or hematuria
  - anemia
  - elevated ESR
  - abnormal ECG
## Treatment

### Raynaud's Phenomenon

**Local** - Avoid cold exposure  
Wear gloves  
Topical nitroglycerine

**Systemic** -  
**NSAID**  
Angiotensin receptor blockers (Cozaar)  
Angiotensin converting enzyme blockers  
Ca Channel blockers (Nifedipine, Diltiazem)  
Prostacyclin analogue (Iloprost)

### Renal

ACE inhibitors for hypertension and prevent renal failure
Treatment

Gastrointestinal

H₂ blockers,
Proton pump inhibitors
Dilation of esophageal strictures
Antibiotics for bacterial overgrowth
Metoclopramide and erythromycin for dysmotility

Pulmonary

Active lung inflammation- steroids and cyclophosphamide
Pulm HTN- bosentin (an endothelin receptor antagonist)
intravenous Prostacyclin,
O²
anticoagulation
Idiopathic Inflammatory Myopathy (IIM)

Polymyositis (PM)
Dermatomyositis (DM)
Juvenile (childhood) DM
Myositis associated with malignancy
Inclusion body myositis
Incidence

**PM/DM**
0.5 - 8.4 cases /million
Blacks : Whites = 2:1
Women : Men= 2:1
Peak ages:
10 and 15 y/o in children
At 45 and 60 yrs in adults

**Cancer Associated**
age > 50 yrs

**Inclusion Body Myositis**
age > 50 yrs
Men : Women= 2:1
Pathogenesis

HLA-DR3 seems associated

**Polymyositis**
Muscle fibers are invaded by CD8+ T cells and become necrotic.

**Dermatomyositis**
Perivascular infiltration by CD4+ T cells with immunoglobulin and complement deposition.
Clinical features of PM/DM

Begins insidiously (3-6 months)
Manifests as **proximal** muscle weakness
   (shoulder, pelvic girdle/thigh and neck)
Dysphagia 2° to esophageal dysmotility (due to upper third of esophageal involvement)
Raynaud's phenomenon
Pulmonary: diaphragmatic weakness, interstitial pneumonitis which causes fibrosis
Cardiac: supraventricular dysrhythmias, cardiomyopathy, CHF

Facial muscles and distal muscles are spared.
**Minimal muscle pain.**
Dermatomyositis has the above with rash, periorbital edema, heliotrope rash, gottron’s patches/papules scales and papules over joints and extensor surface of forearm and leg

Shawl sign- erythema of shoulders and neck
Anti-synthetase antibodies

Histidyl-tRNA synthetase (Jo-1)
Threonyl-tRNA synthetase (PL-7)
Alanyl-tRNA synthetase (PL-12)
Glycyl-tRNA synthetase (EJ)
Isoleucyl-tRNA synthetase (OJ)
Signal recognition particles (SRP)
Mi-2 protein complex (Mi-2)
Anti-synthetase antibody syndrome

1. Polymyositis/Dermatomyositis with relatively acute onset
   interstitial lung disease
   fever
   arthritis
   Raynaud’s phenomenon
   “Mechanic’s” hands (darkened or dirty-appearing cracking and fissuring of the lateral and palmar aspects of the fingers as seen on an auto-mechanic).
   AND

Elevated muscle enzymes: CPK, Aldolase, SGOT, SGPT, LDH

CPK usually in 1000’s

Unilateral EMG (in 85-90% patients) will show:
1. Increased insertional activity fibrillations
2. Sharp positive waves
3. High frequency discharges
4. Low amplitude, short duration polyphasic motor unit potentials

MRI shows muscle edema (inferring inflammation)
Muscle Biopsy

Inflammation - primarily lymphocytes and macrophages.
Muscle fiber necrosis and regeneration
Bohan and Peter Diagnostic Criteria for Polymyositis and Dermatomyositis

1. Symmetrical muscle weakness
2. Muscle biopsy evidence of an inflammatory myopathy
3. Elevation of serum muscle enzymes
4. Electromyographic evidence
5. Dermatologic features*

Definite polymyositis/dermatomyositis: Fulfill 4 criteria
Probable polymyositis/dermatomyositis: Fulfill 3 criteria
Possible polymyositis/dermatomyositis: Fulfill 2 criteria

*Cutaneous findings must be present for the diagnosis of DM
Inclusion Body Myositis

Older Males

Focal distal asymmetric weakness
Dysphagia
Atrophy
Diminished tendon reflexes

Neurogenic and myopathic changes on EMG

Intercellular vacuoles lined with basophilic granules on biopsy
Treatment

Prednisone 1 mg/kg/day

(IBM generally does not respond)

Methotrexate

Azathioprine

IV IgG

Plasmapheresis