SCLERODERMA

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Background

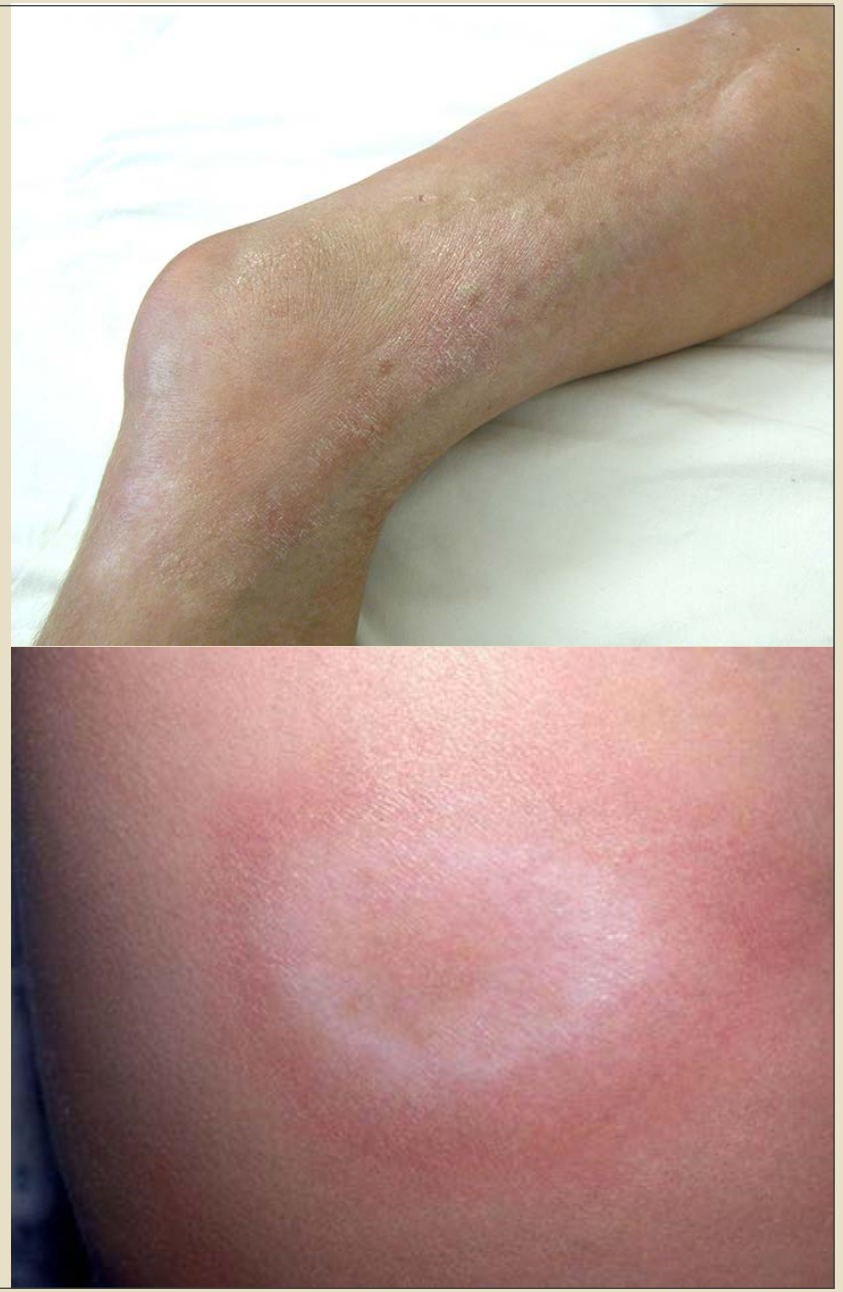
- Scleroderma: autoimmune disease that cause inflammation in skin→skin becomes unusually thick and hard
  - Overproduction of collagen-->fibrosis and scarring
- 2 main types: localized and systemic
  - Localized only affects skin in some areas of body, not internal organs
  - Systemic: generalized thickened skin all parts of body, scar tissue in internal organs
    - Children: Reynaud's present early, fatigue, joint pain, abdominal pain, dysphagia, diarrhea, SOB
    - Juvenile systemic sclerosis
- Affects 5,000-7,000 children in US
  - 2% develop before age 10, 7% between 10-19
- Predominant childhood form: localized (also called morphea)
  - 10x more common than systemic sclerosis in children
  - Skin, muscle, fascia, bones

Pathogenesis

- Skin lesions: initial marked inflammatory response→matrix deposition (collagen)→fibrosis→atrophy
- Abnormal fibroblasts leading to overproduction collagen
- Autoimmune component
- Environmental triggers

Localized scleroderma in childhood (LSc)

- Cutaneous involvement (underlying musculature/bony structures) but no internal organ involvement
- Distinguished by types of skin lesions:
- 1. Linear: most common type in children. Fibrotic lesion linear pattern
  - Transverse on trunk, longitudinal limbs
  - May develop contractures
- 2. Circumscribed (plaque) morphea: most benign form
  - oval or round circumscribed areas of induration with a central waxy, ivory color surrounded by a violaceous halo
  - Discrete, few, 2 or less anatomic areas
- 3. Generalized morphea: ≥4 plaques that affect two or more anatomic sites and become confluent
- 4. Pansclerotic: least common but most disabling form
  - Primary site: panniculus or subcutaneous tissue
- 5. Mixed morphea: combination of above 2 or more subtypes



LSc: Clinical Features

- 20% extracutaneous manifestations
  - Most common with linear scleroderma
- Arthritis
- Neurologic
  - Headaches, behavioral changes, learning disability
- Other autoimmune conditions
  - Reynaud's
- Small percentage also have ocular, vascular, GI, pulmonary, cardiac involvement

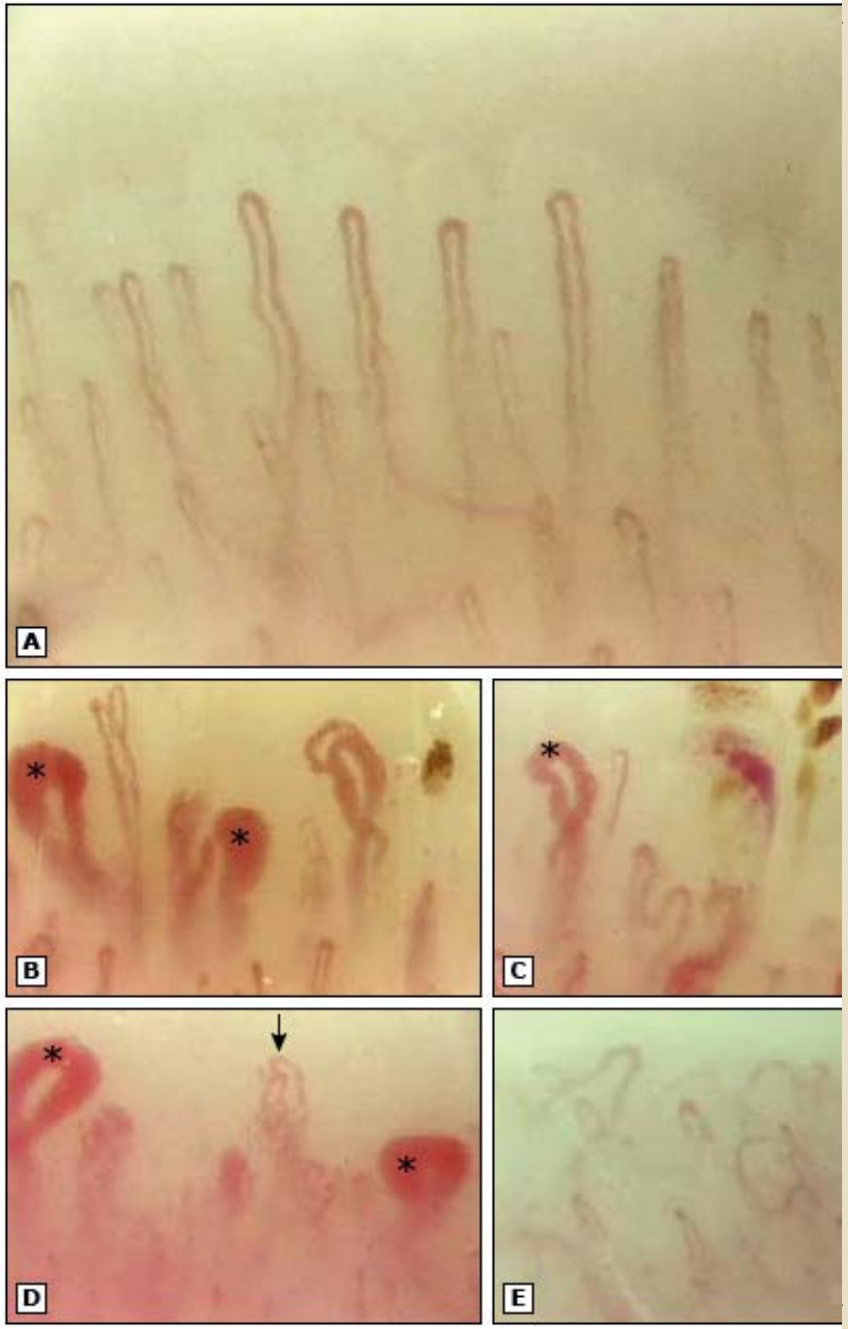
LSc: Diagnosis & Management

- Labs: routine labs normal
  - Antibodies to ssDNA
  - Elevated ESR and CRP, +ANA more common in Lsc with extracutaneous involvement
- Clinical diagnosis
  - Biopsy
- Tx: Physical therapy, emollients, low potency corticosteroids
  - Moderate-severe LSc: methotrexate
- Prognosis: main morbidity skin, muscle, bone atrophy
  - Growth defects
  - Deformities of varying severity depending on subtype

Management of LSc

Management of localized scleroderma in children

	Circumscribed (plaque) morphea	Generalized morphea	Linear morphea	En coup de sabre
Clinical features	One or a few circumscribed sclerotic plaques with hypo- or hyperpigmentation and an inflamed violaceous border.	Individual plaques (four or more and larger than 3 cm) that become confluent and involve at least two anatomic sites.	Linear induration involving dermis, subcutaneous tissue, and sometimes muscle and underlying bone, and affecting the limbs and/or the trunk.	Linear morphea affecting the face or scalp, involving underlying subcutaneous tissues, muscles, and bone. Underlying cerebral abnormalities have been reported.
Treatment	Often unnecessary. Topical corticosteroids for active lesions.	Suppress inflammation with oral or IV glucocorticoids for three months in addition to methotrexate (15 mg/m^2/week) for 24 months. Mycophenolate mofetil can be used in methotrexate-refractory cases.	Suppress inflammation with oral or IV glucocorticoids for three months in addition to methotrexate (15 mg/m^2/week) for 24 months. Mycophenolate mofetil can be used in methotrexate-refractory cases.	Suppress inflammation with oral or IV glucocorticoids for three months in addition to methotrexate (15 mg/m^2/week) for 24 months. Mycophenolate mofetil can be used in methotrexate-refractory cases.
Prognosis	Good prognosis lesions less active within three years, but pigmentary changes often persist.	Generally improves within five years of onset, although textural and pigmentary changes can	Long-term effects of childhood onset form minimized by effective suppression of inflammatory process. Ultimately the disease tends to resolve, but it can remain active for	Scarring, growth defects, and alopecia persist, but inflammatory component usually resolves.



Juvenile systemic sclerosis (JSSc)

- Rare in pediatrics but more serious, life-threatening complications
- Fibrous thickening of skin and internal organs
- Classified based on skin thickening and/or induration of fingers
  - Reynaud's, telangiectasia, fingertip lesions, abnormal nailfold capillaries
- Epidemiology: 0.27 to 2.9 cases per million children per year
  - Children only 3% of systemic sclerosis per year
- Mean age onset 8-11 years
- Females and males = young children, >8 yrs females 3x males

JSSc Subsets

- Diffuse cutaneous systemic sclerosis- skin induration affecting proximal and distal limbs, chest, abdomen
  - Digital ulcers and gangrene common
  - Internal organ involvement
- Overlap syndrome: some features of SSc with other connective tissue disorders
  - Dermatomyositis, SLE, Sjogren, juvenile arthritis
- Limited cutaneous systemic sclerosis: skin induration involving fingers, sometimes extending to hand/arm
  - Digital ulceration, Reynaud's, calcinosis, telangiectasia, esophageal dysfunction
- Systemic sclerosis-sine scleroderma: only internal organ, no skin involvement
  - rare in childhood

JSSc Clinical Features

- Majority present with skin changes of hands or face, + Reynaud's
  - Proximal skin induration
  - MSK sx (arthralgia, muscle weakness, arthritis)
  - Weight loss
  - Dyspnea
  - Dysphagia
- Rarely present with organ involvement but can progress to affect GI, pulmonary, cardiac, and renal involvement
  - Cardiac leading cause of death, though rare
  - Pulm: pulmonary fibrosis rare compared to adults

Diagnosis

- Labs: usually no elevation of CRP/ESR
  - No one lab confirmatory but autoantibodies support dx
    - High ANA
    - Anti-topoisomerase (Scl-70) and anti-centromere abs less frequent in children than adults
- Clinical dx: skin findings not localized to one area + visceral involvement

Provisional classification criteria for juvenile systemic sclerosis by the Pediatric Rheumatology European Society, the American College of Rheumatology, and the European League against Rheumatism

Major criterion	Proximal sclerosis/induration of the skin	
Minor criteria	Skin	Sclerodactyly
	Vascular	Raynaud phenomenon
		Nailfold capillary abnormalities
		Digital tip ulcers
	Gastrointestinal	Dysphagia
		Gastroesophageal reflux
	Renal	Renal crisis
		New-onset arterial hypertension
	Cardiac	Arrhythmias
		Heart failure
	Respiratory	Pulmonary fibrosis (seen on HRCT or radiograph of the chest)
		DLCO
		Pulmonary hypertension
	Musculoskeletal	Tendon friction rubs
		Arthritis
		Myositis
	Neurologic	Neuropathy
		Carpal tunnel syndrome
	Serology	Antinuclear antibodies
		SSc selective autoantibodies (anticentromere, antitopoisomerase I, antifibrillarin, anti-PM/Scl, antifibrillin, or anti-RNA polymerase I or III)

In a patient less than 16 years of age, juvenile systemic sclerosis is diagnosed if the major criterion and at least 2 of 20 minor criteria are present.

HRCT: high-resolution computed tomography; DLCO: diffusing capacity of the lung for carbon monoxide; SSc: systemic sclerosis; anti-PM/Scl: anti-polymyositis/scleroderma antinuclear antibodies, also called anti-exosome antibodies.

JSSc: Monitoring & Management

- Organ systems monitored every 3-4 mos
- Tx: focus on controlling sx and minimizing progression
- Nonpharmacologic: General skin care
  - Avoid cold, trauma, sun and heat exposure
  - Encourage physical activity / PT
- Pharmacologic: immune modulators (mycophenolate, steroids, cyclophosphamide)
- Organ targeted treatment: vascular: vasodilators
  - Interstitial lung disease & cardiac complications: immunomodulators
  - Skin & MSK: low dose steroids + DMARD (methotrexate)
  - GI: PPI
- Biologics under experiment for adults

JSSc Prognosis

- Prognosis better than adults
- Majority have slow disease course with lower mortality
  - Most active in 3-5 years following onset
  - After 5 yrs: constitutional sx stop, skin improves, but visceral involvement progress
- 5% children have rapid development internal organ involvement→disability & death
- Most common causes of death: cardiac, pulmonary, renal
  - cardiomyopathy

References

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