Case Presentation

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PGY-4 Rheumatology Fellow

Clinical Presentation

33 y/o healthy AA female presents to the hospital with

- Dyspnea and chest pain on exertion
- Polyarthralgia, swelling in hands and feet, Raynaud's phenomenon
- Myalgia, muscle weakness
- GERD, dysphagia, increased freq of bowel movements
- Fatigue, unintentional weight loss (20 lbs in 2 months)

Duration ~2-3 months

Medical & Social History - Unremarkable

Family History - Mother (scleroderma)

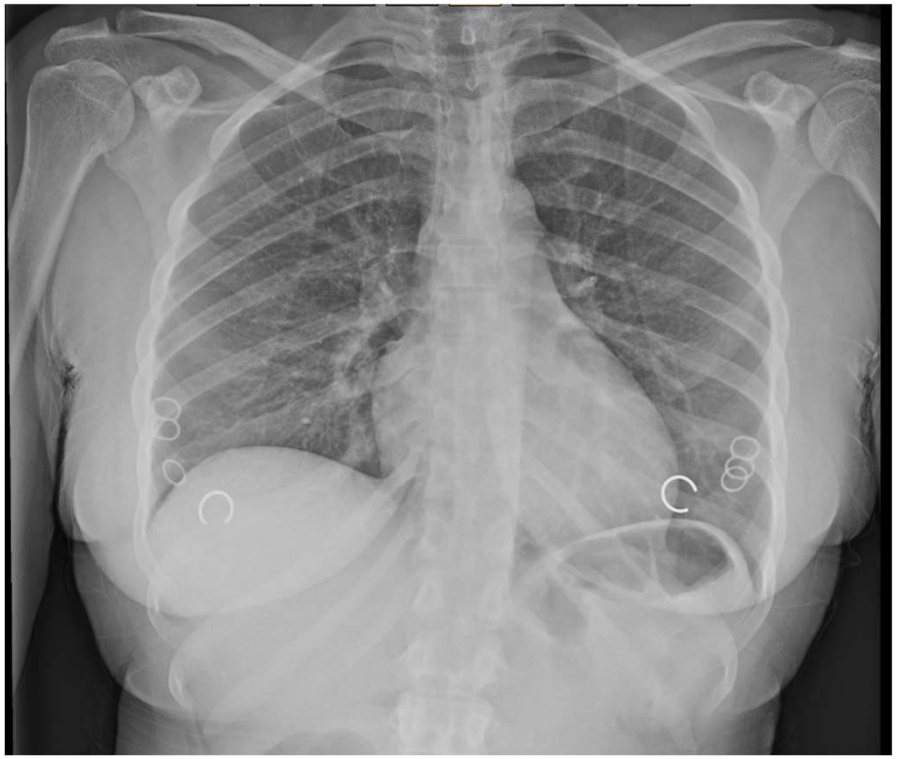
Exam

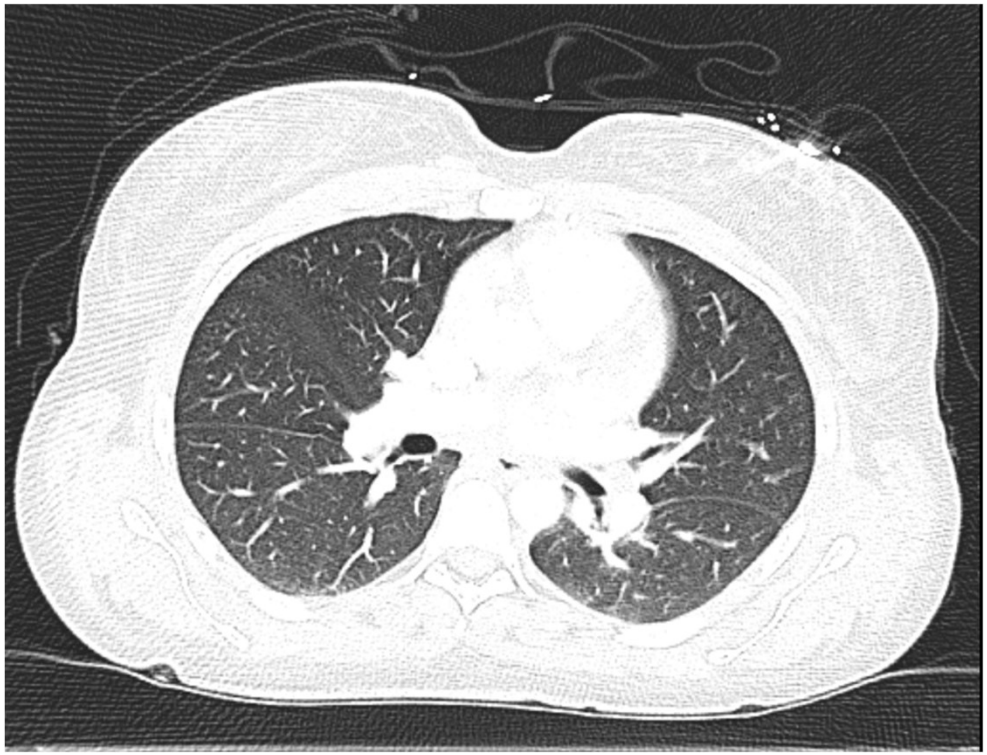
- BMI 36
- Reduced oral aperture
- Sclerodactyly
- Abnormal dilated nailfold capillaries
- Dyspigmentation of fingers, knuckles, & cheeks
- Tenderness on palpation of muscles in BUE
- Decreased muscle strength in all 4 extremities

Labs

- CBC with diff normal
- Cr and GFR normal
- **AST** 137 | **ALT** 44
- **ESR** 48 | **CRP** 0.9
- **CK** ~2000s | **Aldolase** 16.3
- **Troponin** ~250s
- UA normal | UPCR 0.09
- **RF** 17 | CCP neg
- ANA, dsDNA, Smith, SSA, SSB, centromere, scleroderma, RNP, RNA pol III neg

Chest Imaging





Cardiology Consult:

- TTE -- RV appeared mildly dilated; no concerns of PAH
- Cardiac MRI – nondiagnostic for myocarditis; small amount of pericardial fluid and pericardial enhancement suggesting mild pericarditis.
- LHC and RHC – normal; no PAH

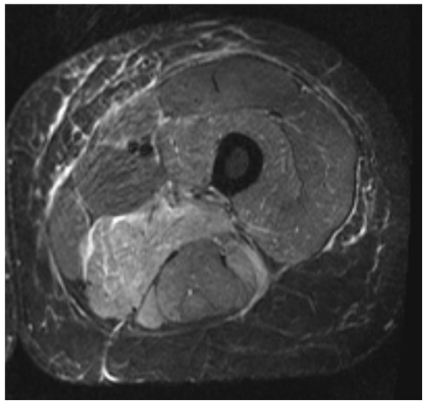
Rheumatology Consult:

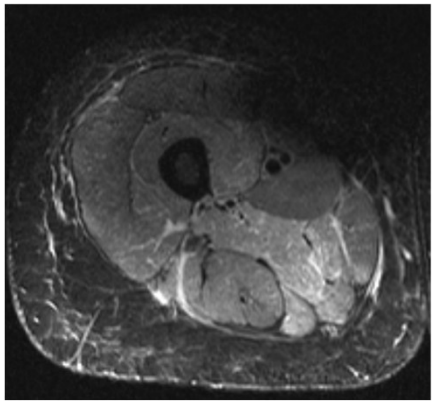
- Concern for SSc + myositis
- Ordered extended myositis panel
- MRI of BLE

MRI B/L Lower Extremities w/wo Contrast

Nonspecific multifocal myositis

Nonspecific mild to moderate subcutaneous and mild superficial fascial edema with minimal enhancement.





Muscle Biopsy (Site - Left Thigh)

Not diagnostic. Isolated focus of degeneration/necrosis and an isolated focus of lymphocytic inflammation. Correlate with autoimmune process.

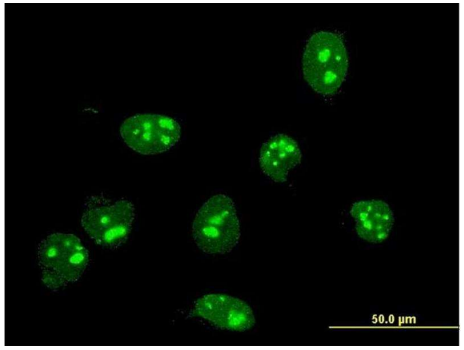
Rheum is still waiting for labs!

- Extended myositis panel – pending

10 days later ---

Fibrillarin antibody positive

Anti-Fibrillarin antibody / U3-RNP



- ANA (clumpy nucleolar pattern)
- Less common (4-10%) but specific

- Young, African Americans
- More digital ulcers, pericarditis, SSc related diarrhea (SIBO)

- PAH/ pulmonary fibrosis – no difference (ethnicity and Scl-70 – confounding factor)
- Contradictory evidence on myositis

Sharif R et al Anti-fibrillarin antibody in African American patients with systemic sclerosis: immunogenetics, clinical features, and survival analysis. J Rheumatol. 2011 Aug;38(8):1622-30
Benyamine A, Quantification of Antifibrillarin (anti-U3 RNP) Antibodies: A New Insight for Patients with Systemic Sclerosis. Diagnostics (Basel). 2021 Jun 9;11(6):1064

Closely following up in the clinic @ 2 weeks

3 months later -

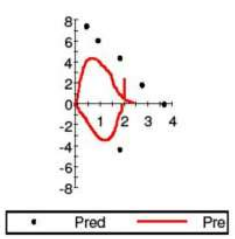
Admit in the hospital -- symptoms worsening (chest pain, dyspnea, dysphagia, BLE swelling (resistant to diuretics)

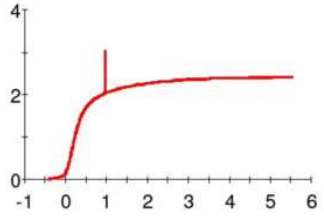
Pulm Consult:

- PFT – Restrictive pattern with reduced DLCO (?PAH)
- HRCT – No ILD

GI Consult:

- EGD – hiatal hernia





Rheum Consult:

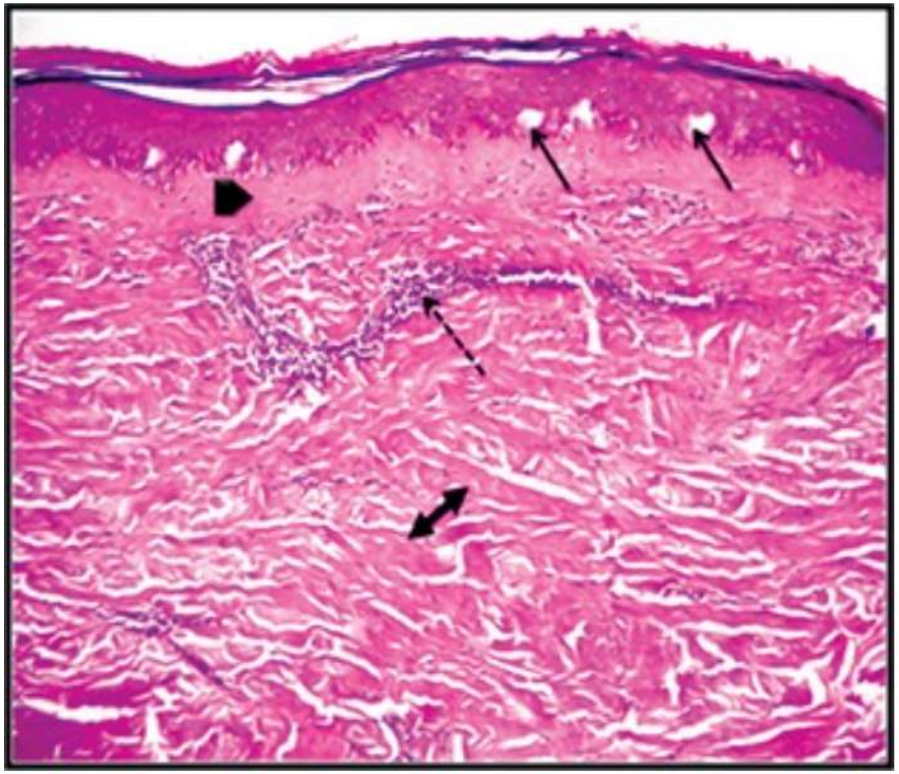
- Sclerodactyly better
- Skin tightening/ induration mainly on proximal areas of upper arms, chest, and lower extremities

Derm Consult:

- Skin biopsy from thigh

Skin Biopsy (Site - Right Thigh)

- Considerable histologic overlap with eosinophilic fasciitis. The deep fascia was not present in this biopsy.

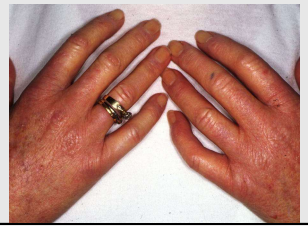


Skin specimen of systemic sclerosis patient showing epidermal thinning, loss of rete ridges, vacuolar interface dermatitis (thin arrows), dermal sclerosis (arrow head), perivascular mononuclear inflammatory infiltrate (dashed arrow) and thick sclerosed collagen bundles (double-headed thick arrow) (H&E × 200).

Farouk HM, Hamza SH, El Bakry SA, Youssef SS, Aly IM, Moustafa AA, Assaf NY, El Dakrony AH. Dysregulation of angiogenic homeostasis in systemic sclerosis. Int J Rheum Dis. 2013 Aug;16(4):448-54. doi: 10.1111/1756-185X.12130. Epub 2013 Jul 2. PMID: 23992267.

Scleroderma mimic conditions:

- **Morphea**
  - *Linear*
  - *Generalized*
  - *Pansclerotic*
- **Inflammatory/ Immune Mediated**
  - *Eosinophilic fasciitis*
  - *Graft versus host disease*
  - *Lichen sclerosus et atrophicus*
  - *POEMS syndrome*
- **Metabolic**
  - *Hypothyroidism (myxedema)*
  - *Phenylketonuria*
  - *Porphyria cutanea tarda*
  - *Diabetic cheiroarthropathy*
- **Deposition Disorders**
  - *Scleromyxedema*
  - *Systemic amyloidosis*
  - *Nephrogenic systemic fibrosis*
  - *Scleredema adultorum*
  - *Lipodermatosclerosis*
- **Occupational Exposure**
  - *Epoxy resins*
  - *Organic solvents*
  - *Polyvinyl chloride*
  - *Silica*
- **Toxin/ Chemical Induced**
  - *Bisoprolol*
  - *Bleomycin*
  - *Bromocriptine*
  - *Carbidopa*
  - *D-Penicillamine*

	SKIN	AREAS	HISTO/ LABS	ASSOCIATED CONDITIONS
SYSTEMIC SCLEROSIS 	Thick, tight, shiny, indurated	Hands & face; *Spares mid back*	- Thin epidermis, thickened acellular dermis with excess collagen & dense amorphous connective tiss. - Scleroderma specific Abs+	+ Anti-RNA Polymerase III associated with increased risk of malignancy

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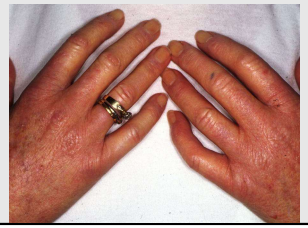
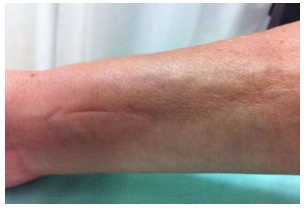
SYSTEMIC SCLEROSIS 	Thick, tight, shiny, indurated	Hands & face; *Spares mid back*	- Thin epidermis, thickened acellular dermis with excess collagen & dense amorphous connective tiss. - Scleroderma specific Abs+	+ Anti-RNA Polymerase III associated with increased risk of malignancy
EOSINOPHILIC FASCIITIS 	Woody induration extends beyond superficial dermis “Groove sign”	Trunk and extremities; *Spares face, hands & feet*	- Eosinophilic infiltrate (dermis & subcutaneous junction) - Thickened hypodermal & dermal fascia. - Eosinophilia, ↑ aldolase, hypergammaglobulinemia	- Myelodysplasia - Immune mediated cytopenias - Solid tumor & hematologic malignancies

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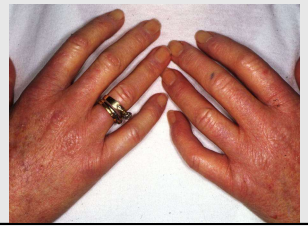
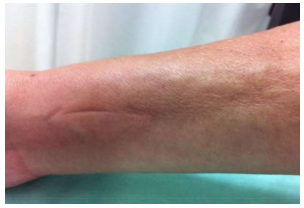
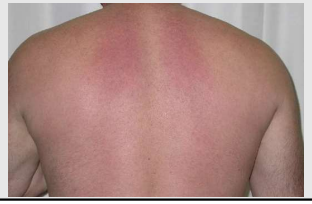
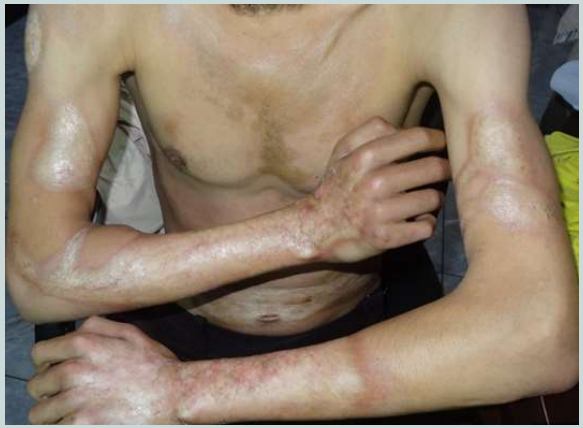
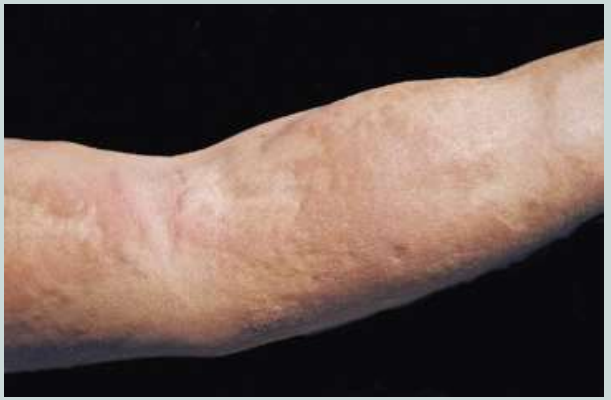
SYSTEMIC SCLEROSIS 	Thick, tight, shiny, indurated	Hands & face; *Spares mid back*	- Thin epidermis, thickened acellular dermis with excess collagen & dense amorphous connective tiss. - Scleroderma specific Abs+	+ Anti-RNA Polymerase III associated with increased risk of malignancy
EOSINOPHILIC FASCIITIS 	Woody induration extends beyond superficial dermis “Groove sign”	Trunk and extremities; *Spares face, hands & feet*	- Eosinophilic infiltrate (dermis & subcutaneous junction) - Thickened hypodermal & dermal fascia. - Eosinophilia, ↑ aldolase, hypergammaglobulinemia	- Myelodysplasia - Immune mediated cytopenias - Solid tumor & hematologic malignancies
SCLEREDEMA 	Doughy, indurated	Back, neck, face; *Spares hands & feet*	- Dermal accumulation of thick collagen bundles with mucin deposits - Inflammatory infiltrate absent - Hyperglycemia, monoclonal gammopathy (IgG kappa)	- Postinfectious - DM - Monoclonal gammopathy - Multiple myeloma

Scleromyxedema	Pansclerotic morphea	Nephrogenic Systemic Fibrosis
		

Characteristics that differentiate conditions that mimic scleroderma from SSc:

- Lack of Raynaud's
- Lack of nailfold capillary abnormalities
- Lack of positive ANA
- Lack of progression of cutaneous sclerosis in a centripetal ("center-seeking") fashion
- Lack of characteristic organ involvement associated with SSc

Learning points:

- Fibrillarin antibodies
- Question a diagnosis

References

- Morgan ND, Hummers LK. Scleroderma Mimickers. Curr Treatm Opt Rheumatol. 2016 Mar;2(1):69-84. doi: 10.1007/s40674-016-0038-7. Epub 2016 Feb 5. PMID: 28473954; PMCID: PMC5412724.
- Orteu CH, Ong VH, Denton CP. Scleroderma mimics - Clinical features and management. Best Pract Res Clin Rheumatol. 2020 Feb;34(1):101489. doi: 10.1016/j.berh.2020.101489. Epub 2020 Mar 5. PMID: 32147386.
- West, Sterling. Rheumatology Secrets. Available from: Elsevier eBooks+, (4th Edition). Elsevier - OHCE, 2019.
- Nashel J, Steen V. Scleroderma mimics. Curr Rheumatol Rep. 2012 Feb;14(1):39-46. doi: 10.1007/s11926-011-0220-8. PMID: 22131103.

Thank You!