Dermatology for the Rheumatologist:
A Novel of Classic Clues and Important Mimickers

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No relevant conflicts of interest to disclose

Objective

- Review of classic cutaneous clinical presentations of autoimmune disorders
- Review of mimickers of systemic vasculitis, cutaneous lupus, dermatomyositis, and sclerosing disorders via clinical cases
- Improve the rheumatologic differential diagnosis to include non-autoimmune processes

Rheumatic diseases with notable dermatologic mimickers

1. Vasculitis
2. Lupus
3. Dermatomyositis
4. Sclerosing Disorders

Chapter I
Vasculitis

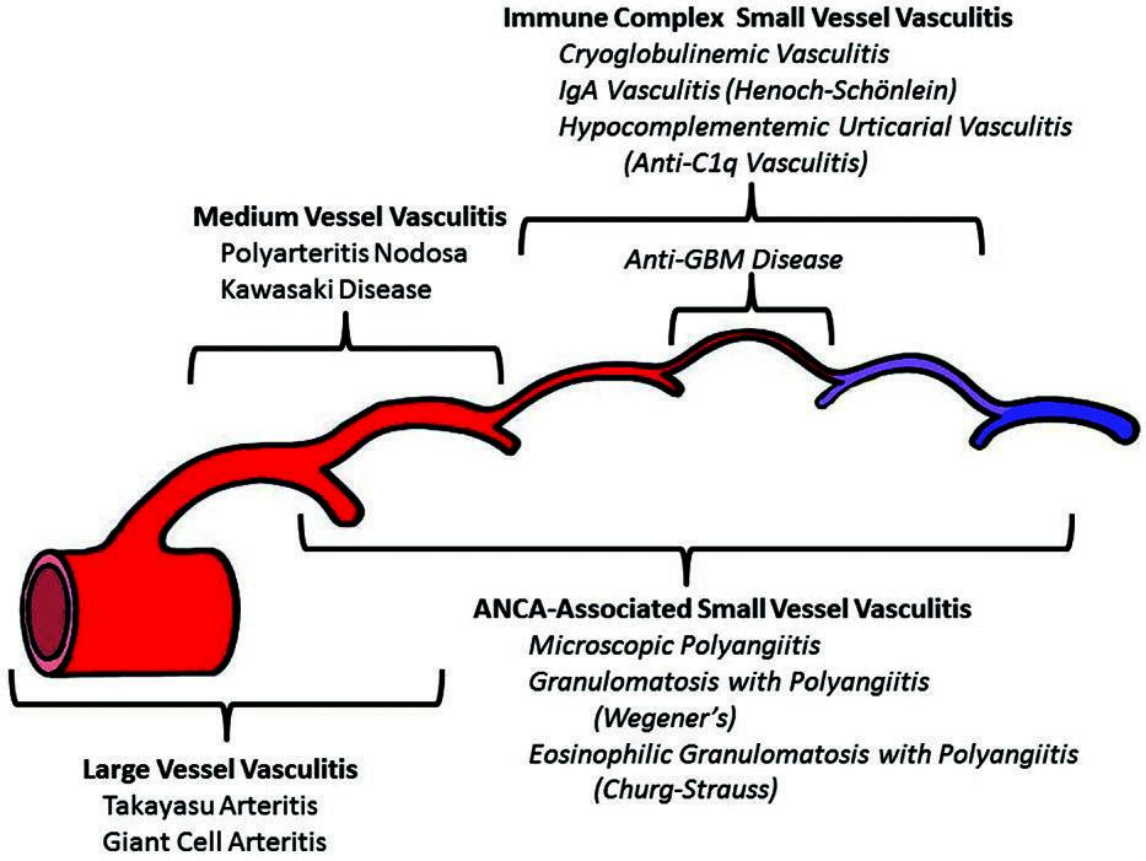
Vasculitis

- Vasculitis or “inflammation” of the blood vessel is defined by the presence of inflammatory leukocytes (neutrophils) in vessel walls which cause damage to the mural surface

- Currently vasculitis is defined by the affected blood vessel size

- Vasculitis can be 1) systemic and affecting multiple organ systems or 2) cutaneous only

Distribution of vasculitis by size of vessel involvement



Jennette JC et al. 2012 Revised International Chapel Hill Consensus Conference Nomenclature Of Vasculitides.
Arthritis & Rheumatism, vol. 65, No.1, 2013, 1-11.

Small vessels:

- Capillaries
- Arterioles
- Venules
- Small arteries

Medium vessels:

- Medium-sized arteries

Skin involvement status by vasculitis category and disease

CHCC2012 vasculitis category, name	Skin involvement status	
	Cutaneous component of systemic vasculitis	Skin-limited or skin-dominant variant
Large vessel vasculitis		
Takayasu arteritis	No	No
Giant cell arteritis	Rare	No
Medium vessel vasculitis		
Polyarteritis nodosa	Yes	Yes
Kawasaki disease	No	No
Small vessel vasculitis		
Microscopic polyangiitis	Yes	Yes
Granulomatosis with polyangiitis	Yes	Yes
Eosinophilic granulomatosis with polyangiitis	Yes	Yes
Anti–glomerular basement membrane disease	No	No
Cryoglobulinemic vasculitis	Yes	Yes
IgA vasculitis (Henoch-Schönlein)	Yes	Yes
Hypocomplementemic urticarial vasculitis (anti-C1q vasculitis)	Yes	Yes
Variable vessel vasculitis		
Behçet's disease	Yes	Yes
Cogan's syndrome	Rare	No
Vasculitis associated with systemic disease		
SLE, rheumatoid arthritis, sarcoidosis, etc.	Yes	Yes
Vasculitis associated with probable etiology		
Drugs, infections, sepsis, autoimmune diseases, etc.	Yes	Yes
Cutaneous SOV (not included in CHCC2012)		
IgM/IgG vasculitis	No (not observed yet)	Yes (as SOV)
Nodular vasculitis (erythema induratum of Bazin)	No	Yes (as SOV)
Erythema elevatum et diutinum	No	Yes (as SOV)
Hypergammaglobulinemic macular vasculitis	No	Yes (as SOV)
Normocomplementemic urticarial vasculitis	No	Yes (as SOV)

* CHCC2012 = 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides; SLE = systemic lupus erythematosus; SOV = single-organ vasculitis.

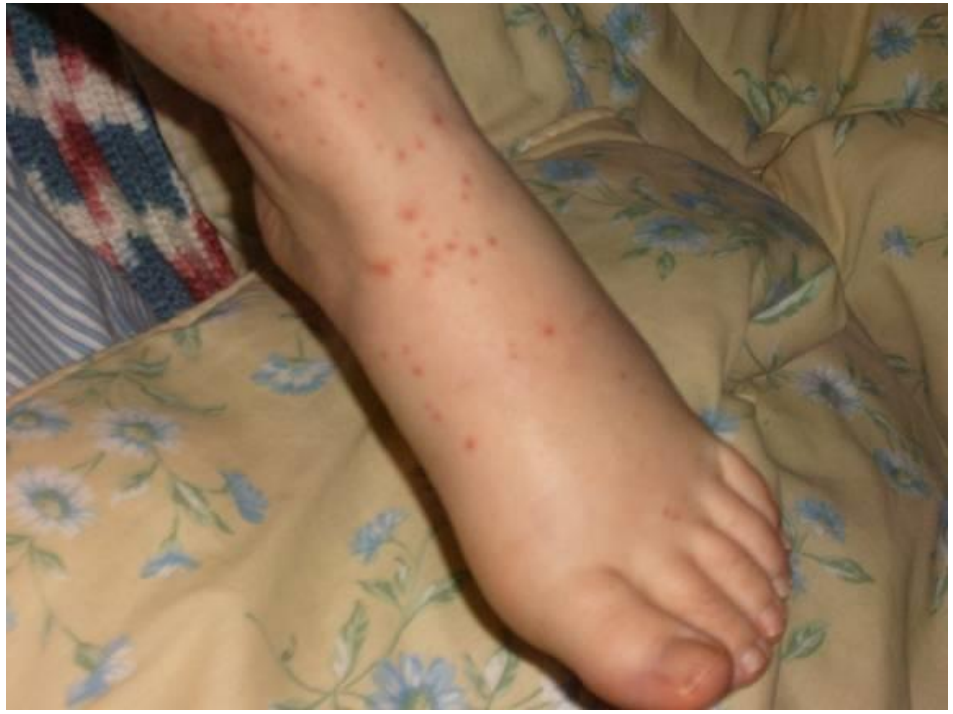
Sunderkotter CH et al. Nomenclature of Cutaneous Vasculitis: Dermatologic Addendum to the 2012 Revised International Chapel Hill Consensus Nomenclature of Vasculitides Conference. Arthritis & Rheumatology, vol. 70, No.2, 2018, 171-184

Cutaneous presentation of vasculitis

- Vasculitis can present in a variety of manner on the skin, which leads to a large differential diagnosis
- The hallmark cutaneous symptom of vasculitis is **purpura**
  - Skin morphology caused the extravasation of RBCs into the skin or mucous membranes due to disorders of blood vessels or the hematopoietic system.
  - Can present at petechiae, ecchymosis, palpable or retiform lesions
  - May be associated with serious underlying systemic disease
    - Systemic vasculitis when affecting the skin will cause either palpable or retiform purpura

Palpable purpura

- Hallmark sign of small vessel involvement in vasculitis
- Immune complex vasculitis causes palpable purpura, but also infections and drugs can trigger this category of vasculitis

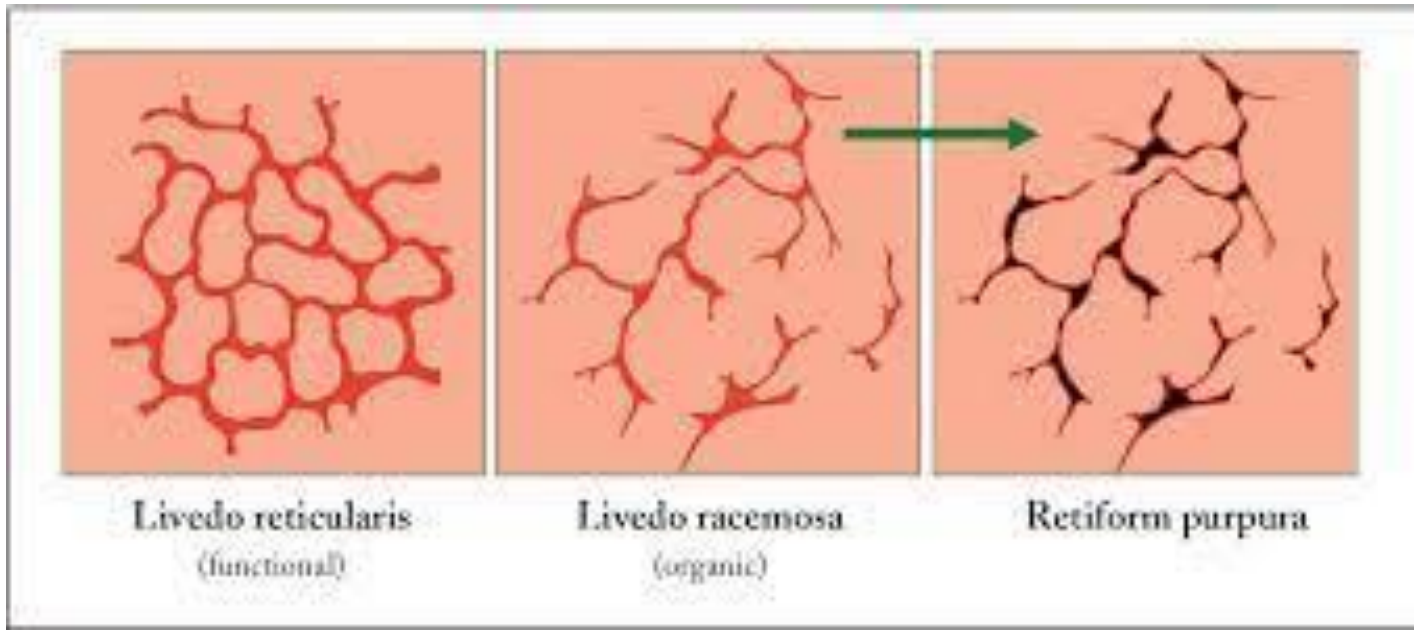


Immune complex vasculitis

IgA vasculitis (IgAV)(Henoch-Schönlein purpura) - systemic IgAV - skin-limited IgAV - provisional: IgA nephropathy (IgAN) (if considered as kidney-limited IgAV)	Vasculitis, with immune deposits of hypogalactosidated IgA (Gd-IgA1), affecting small vessels (predominantly post-capillary venules)
IgM/IgG vasculitis (provisional, skin-limited)	Vasculitis, with IgM and/or IgG dominant immune deposits, not containing IgA, and independent of Gd-IgA1, affecting small vessels (predominantly post-capillary venules) in the skin
Cryoglobulinemic vasculitis (CV) - systemic CV - skin-limited CV	Vasculitis with cryoglobulin immune deposits, mostly IC, affecting small vessels and associated with serum cryoglobulins, usually type II or III
Vasculitis associated with systemic, usually collagenous vascular, disease: e.g., - rheumatoid vasculitis (RV) - LE vasculitis - systemic skin-limited forms of vasculitis	Vasculitis that is associated with and maybe secondary to (caused by) a systemic disease (e.g., rheumatoid vasculitis, LE, sarcoid vasculitis, etc.). The name (diagnosis) should have a prefix term specifying the systemic disease (e.g., rheumatoid vasculitis, lupus vasculitis, etc.)
Hypo-complementemic urticarial vasculitis (HUV) (anti-C1q vasculitis)	Vasculitis accompanied by urticarial lesions and hypo-complementemia affecting small vessels and associated with anti-C1q antibodies. Glomerulonephritis, arthritis, obstructive pulmonary disease, and ocular inflammation are common.
Hypo- or normocomplementemic urticarial vasculitis (non-anti-C1q) (provisional) (skin-limited)	Cutaneous, leukocytoclastic vasculitis, clinically appearing as urticarial lesions or wheals with hemorrhagic macules, affecting small vessels and not associated with anti-C1q antibodies (it is a provisional term); several previously published cases of so-called urticarial vasculitis may today be diagnosed as neutrophilic urticarial dermatosis (NUD) and not as vasculitis
Recurrent macular vasculitis in hypergammaglobulinemia (formerly benign hypergammaglobulinemic purpura of Waldenström) or recurrent macular vasculitis mediated by exertion (Golfer's vasculitis, cocktail party vasculitis, heat-induced vasculitis)	Relapsing, short-lasting cutaneous small vessel vasculitis with recurring macules and purpura associated with vascular immunoglobulin deposits and hypergammaglobulinemia or possibly vasodilation induced by exertion, alcohol, long standing, or heat

Sunderkötter C, et al. Pathophysiology and clinical manifestations of immune complex vasculitides. *Front Med (Lausanne).* 2023

The livedo spectrum

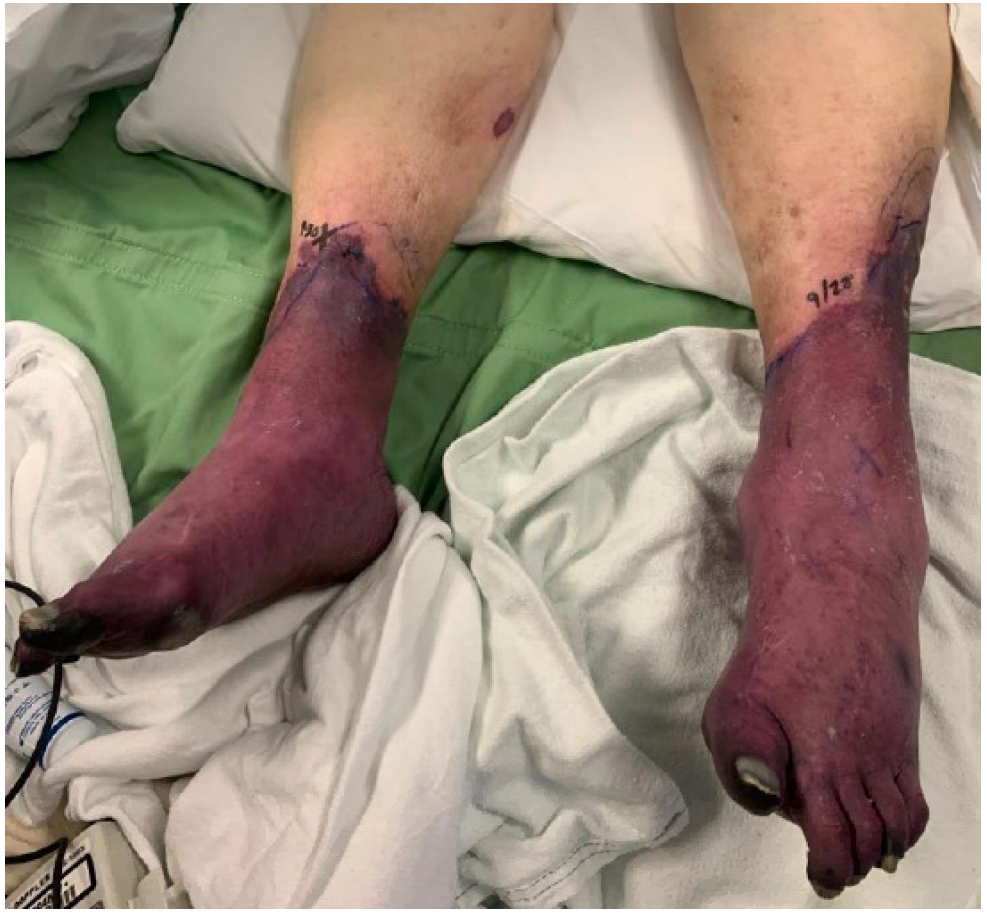


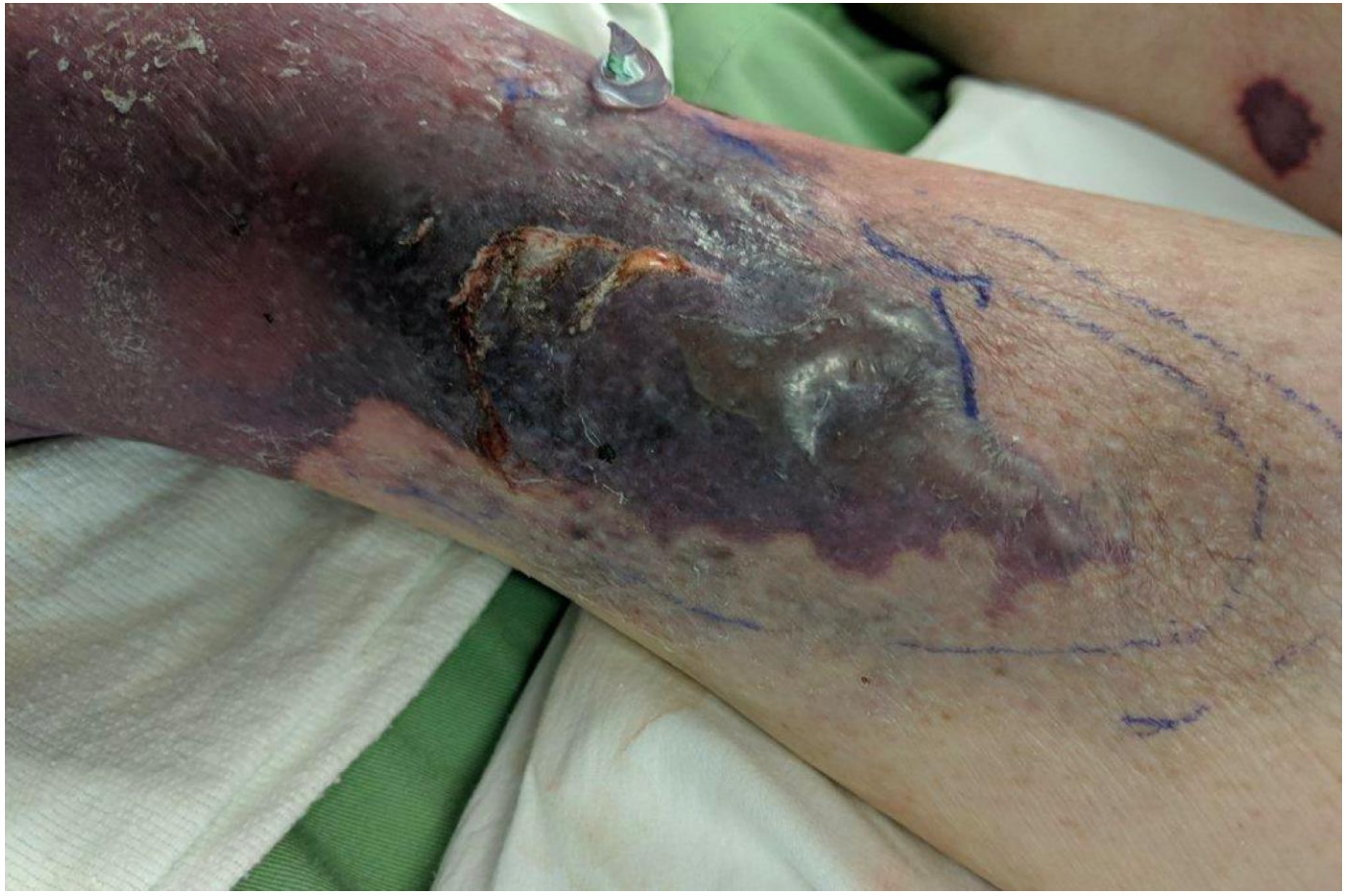
- Livedo reticularis: contiguous, blanchable, violaceous rings that form a netlike pattern. Due to reduction or interruption of blood flow from dermal arteries or arterioles. Mostly benign, but when fixed, necessitates vasculitic/thrombotic workup.
- Livedo racemosa: fixed “livedo” in discontiguous rings. More vessel damage. Usually only partially blanchable lesions, almost always due to a vasculitic/thrombotic etiology and may be more generalized.
- Retiform purpura: “end stage” vessel damage and necrosis.

Retiform purpura

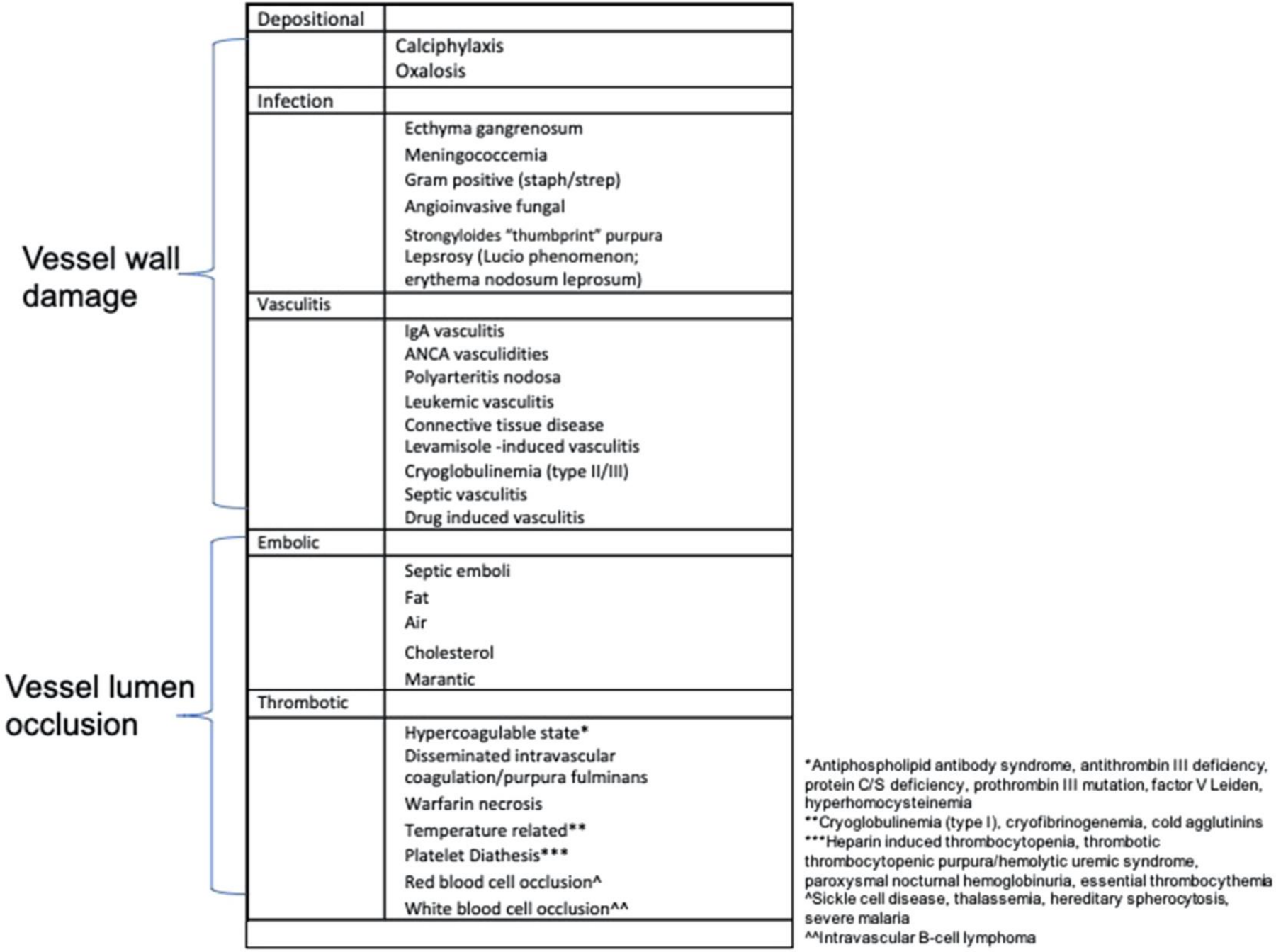
- Retiform purpura is a specific morphologic pattern that occurs when blood vessels serving the skin are compromised, resulting in **cutaneous ischemia, purpura and necrosis**.
  - Blood vessels affected should be at least medium sized arteries
- The shape of the purpura is described as being stellate or geometric
- Occurs by 1 of 2 mechanisms: **vessel wall damage** or **vessel lumen occlusion**
- Often a marker of severe underlying disease
- Has a broad differential diagnosis

PDL-1 inhibitor induced thrombotic vasculopathy

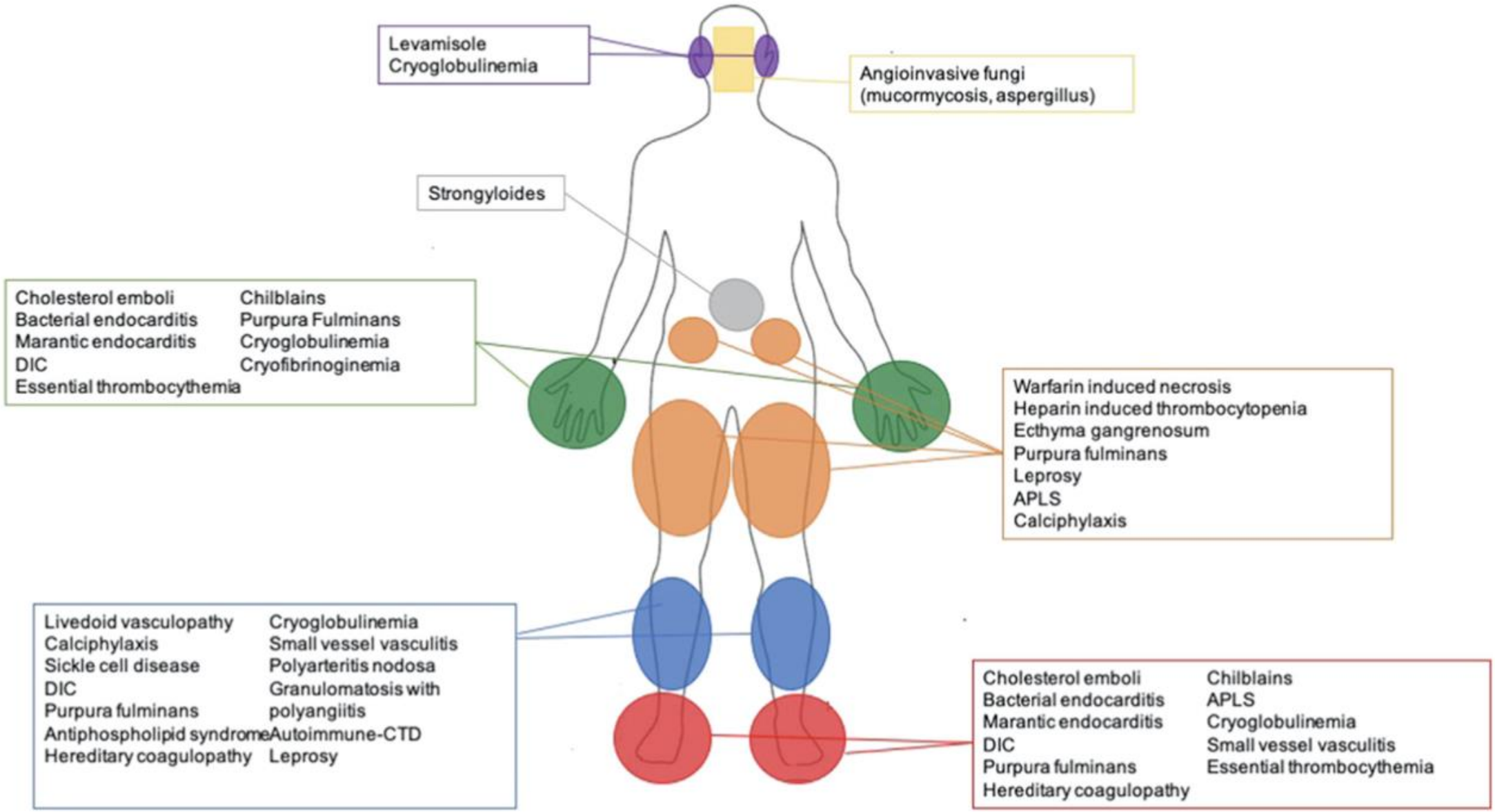




Kang BY et al. Rapidly progressing dyspnea and retiform purpura. *JAAD Case Rep*. 2022.



Georgesen C, et a. *JAAD*. 2020.

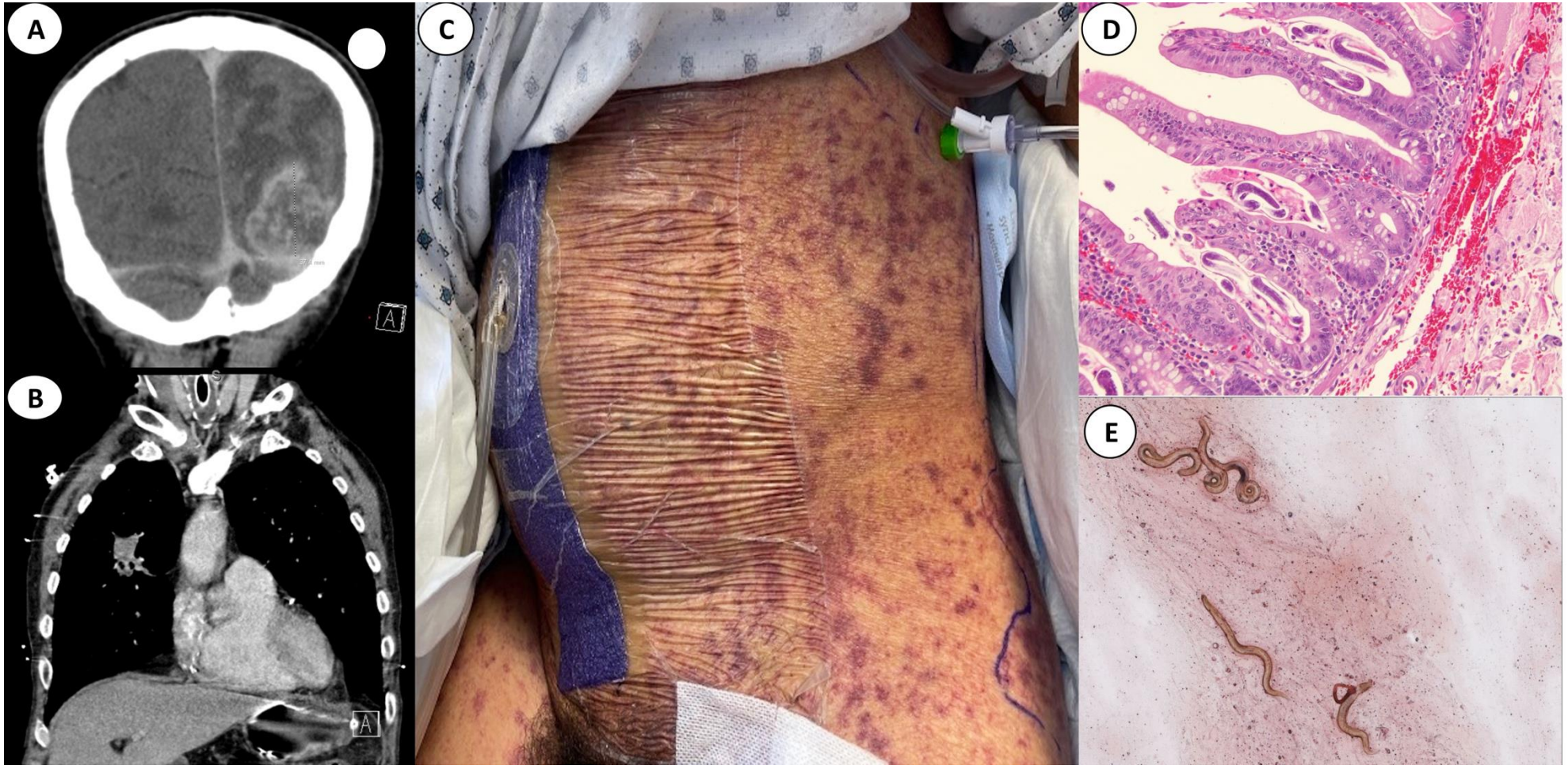


Georgesen C, et a. *JAAD*. 2020.

Notable mimickers of vasculitis

Palpable Purpura	Livedo patterns	Retiform Purpura	Subcutaneous nodules
• Petechiae (from thrombocytopenia or platelet dysfunction) • Capillaritis	• Physiologic livedo reticularis due to cold temperature • Consider hypercoagulable states (thrombotic/embolic phenomenon)	• Consider depositional disorders (ie, calciphylaxis) • Severe infections • Thrombotic/embolic phenomenon	• Consider erythema nodosum

Disseminated strongyloidiasis

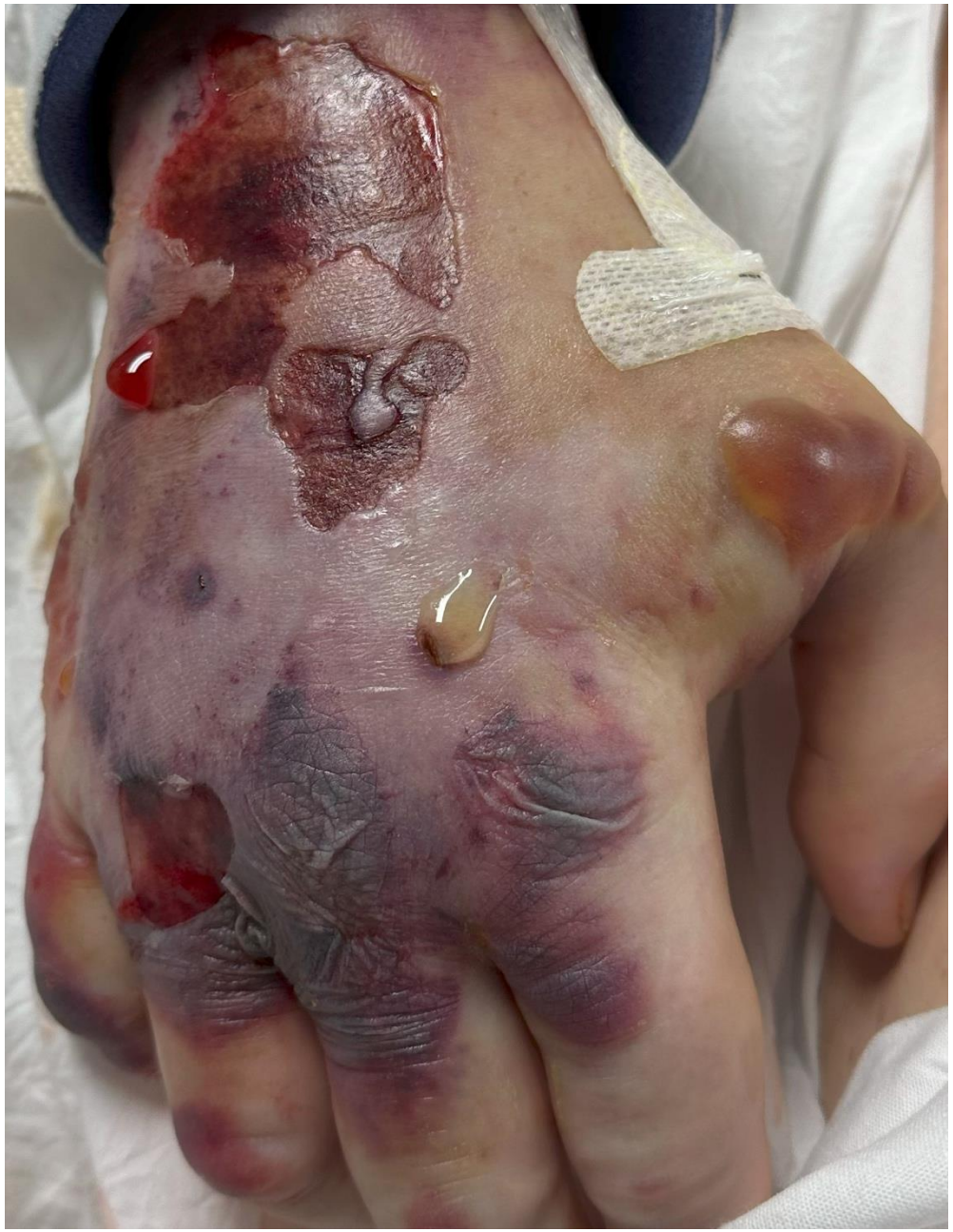


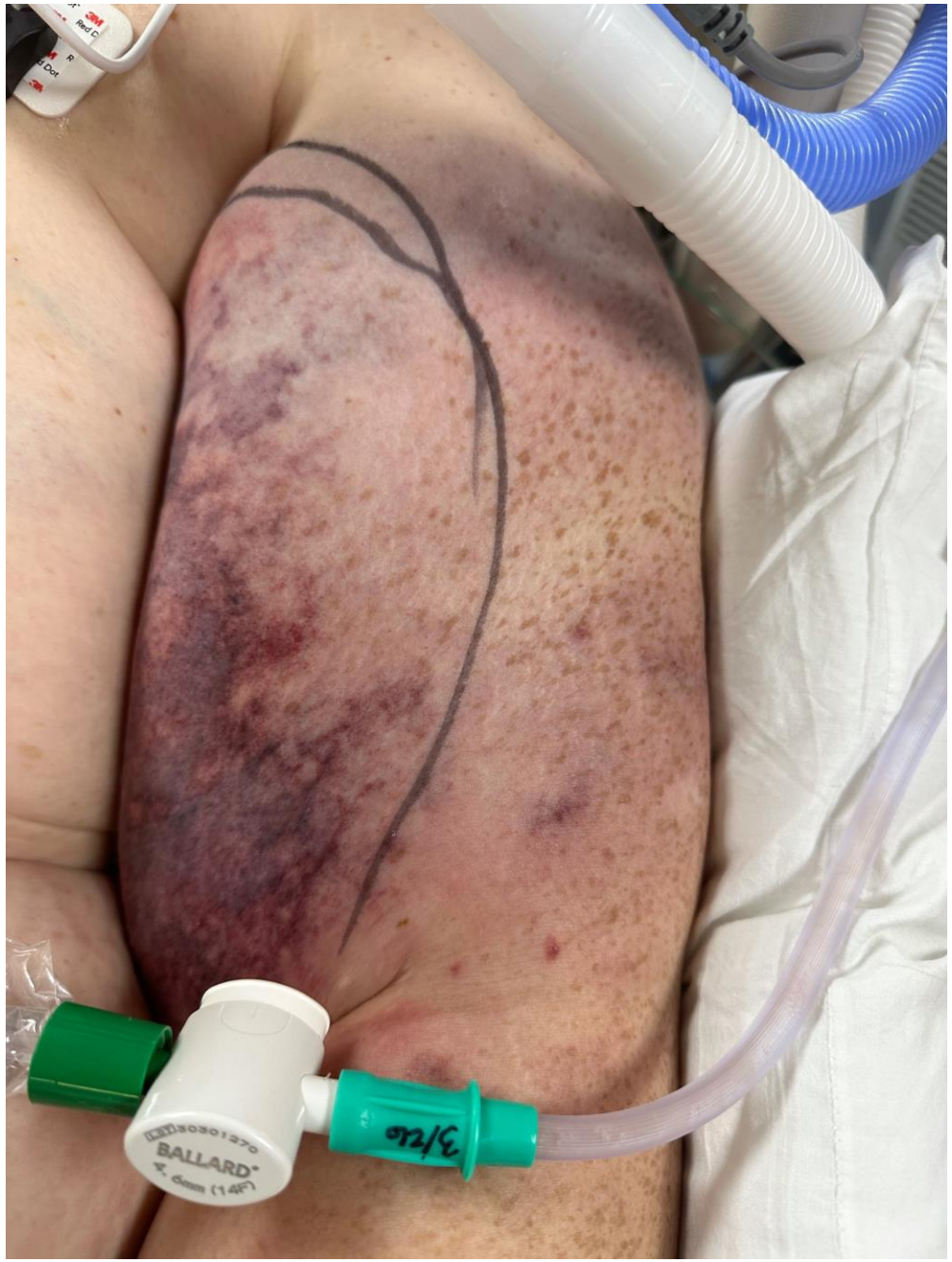
Cortez JL, et al. Thumbprint abdominal retiform purpura. *AIMCC.* 2024.

A Case to Contrast Vasculitis

History

- 40-year-old male with a history of ESRD on hemodialysis, +p-ANCA, and HTN treated with hydralazine, presents to hospital after being found down.
- Pertinent events:
  - Computed tomography angiography of head at outside hospital demonstrated subarachnoid hemorrhage.
  - Referral to UNM neurointensive care unit with continued neuromonitoring and neurosurgical evaluations.
  - 2 days following admission, patient developed rapidly progressive purple lesions. Dermatology was consulted.

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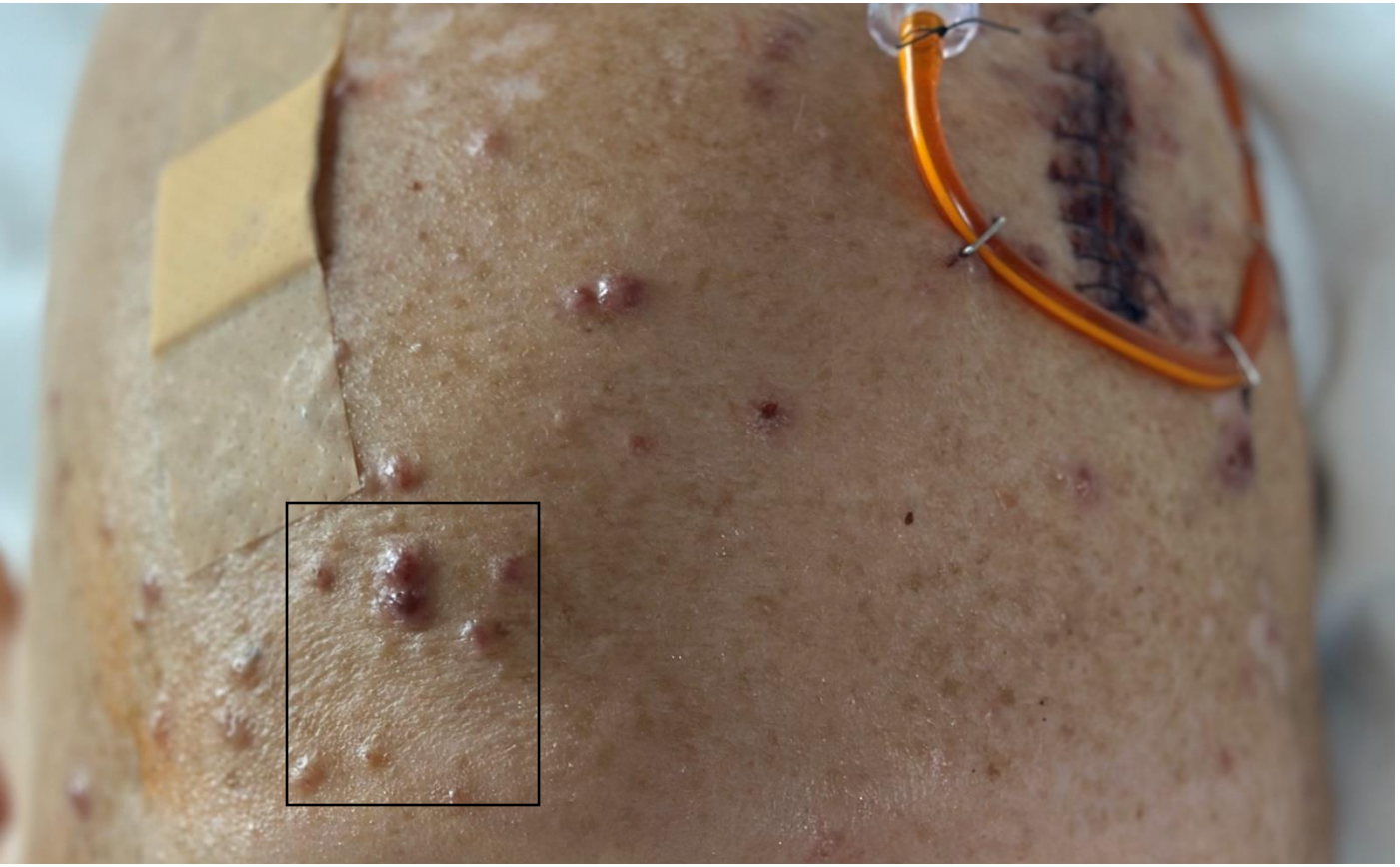
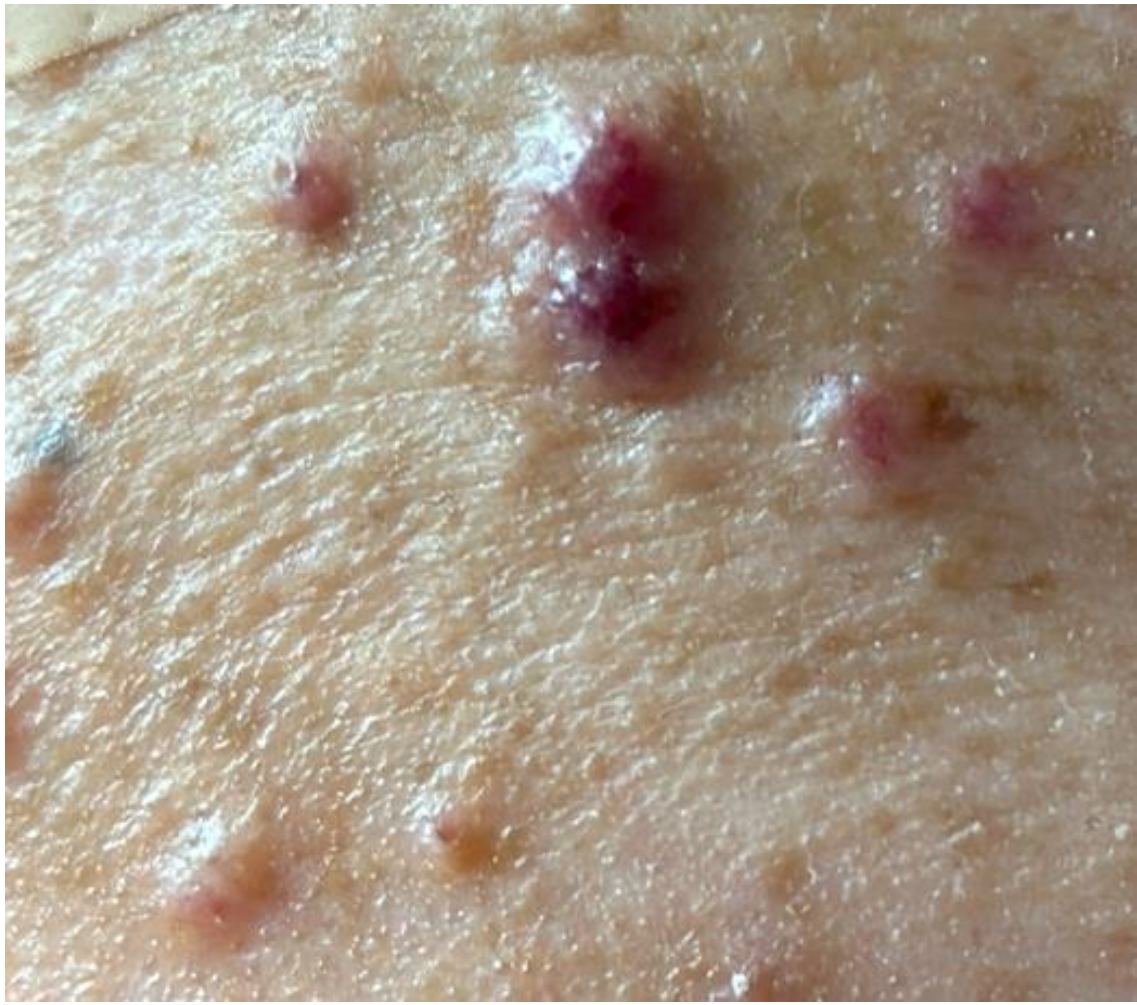
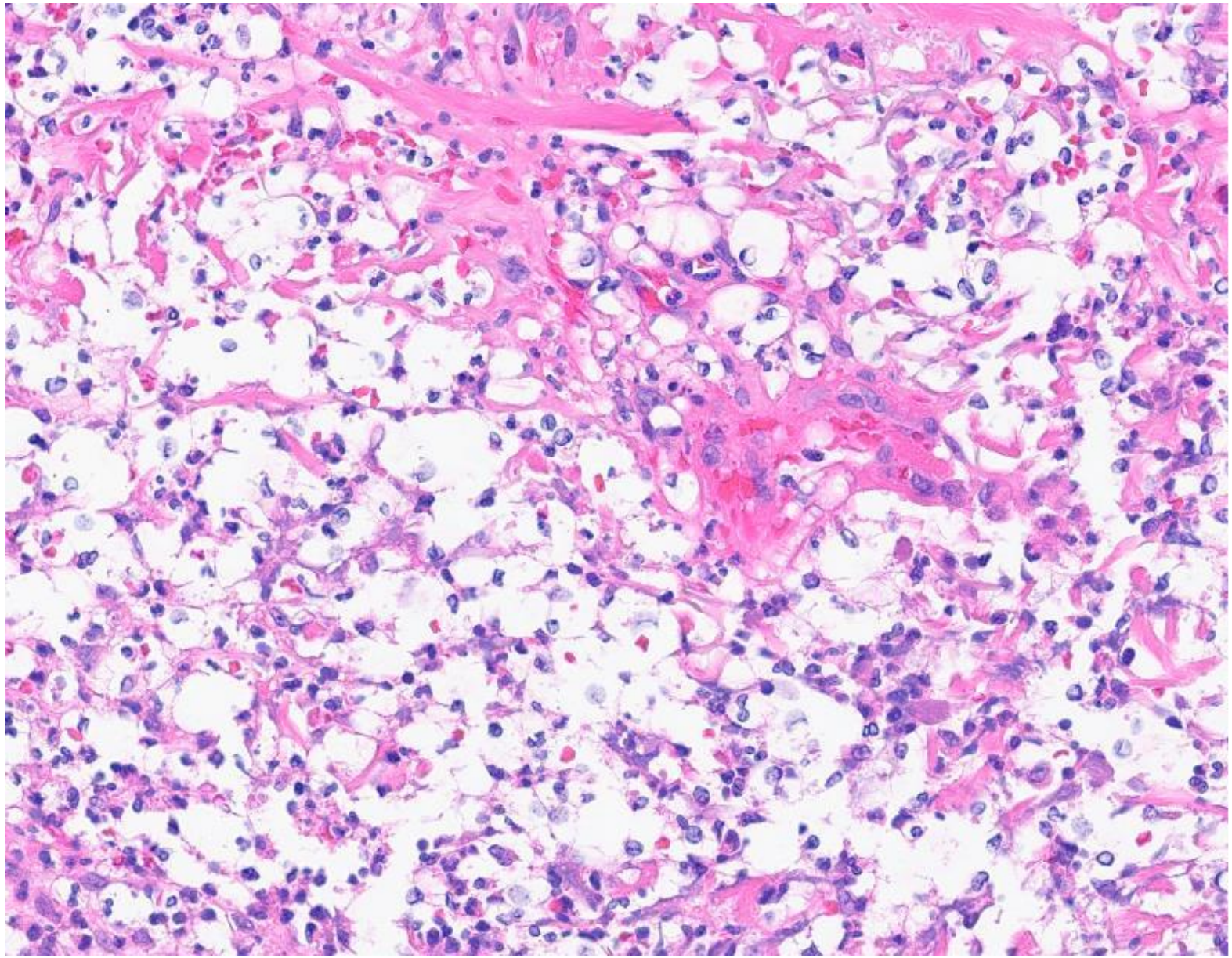




Cryptococcoid-like histiocytic inflammation seen predominantly down a hair follicle

- **(+) : CD163, CD68, CD15, and myeloperoxidase**



Diagnostic studies

- **Infectious work up: negative**
  - Blood and tissue (bacterial, AFB, and fungal) cultures
  - Hepatitis B and C serologies
  - Human Immunodeficiency Virus (HIV)
  - QuantiFERON gold
  - Coccidiomycosis serologies
  - Histoplasmosis antigen

CBC and peripheral blood smear: normal

Urine drug screen: normal

Immunologic assays: normal

- Antinuclear antibody
- Myeloperoxidase/proteinase 3 (MPO/PR3) antibodies
- Cryoglobulins
- Complement levels (C3/C4)
- Antiphospholipid antibody panel

+p-ANCA

CT scan: 3.0 x 1.8 centimeter (cm) nodule in the left lung, upper lobe

Serum iodine level: > 100,000 (units)

Iododerma

- Rare, rapidly progressive halogenoderma that occurs after pathologic accumulation of iodine within the skin
- Increased exposure to iodine and iododerma has been reported with:
  - Oral intake (potassium iodide)
  - Topical use (povidone iodine)
  - **IV exposure to iodine containing contrast**
- Risk factors:
  - Inability to renally clear iodinated compounds: ie, CKD, ESRD
- Morphology:
  - Various cutaneous morphologies including acneiform, papular, vesiculopustular, vegetative plaques
  - Purpuric morphology also also been described

Iododerma additional pearls

1. Cryoptococcoid-like histiocytes in the setting of hemorrhagic/purpuric lesions may be seen in iododerma or Sweets syndrome
2. In patients with impaired renal function, iodinated contrast media and concurrent use of hydralazine may confer an increased risk of iodine toxicity
3. Systemic manifestations, including pulmonary infiltrates, may develop

Runge M et al. Iodine toxicity after iodinated contrast: New observations in iododerma. *JAAD Case Rep.* 2020.

Patient history continued

- After the diagnosis of iododerma was made, the patient was started on 125 mg IV methylprednisolone, tapered by 20 mg every 5 days
  - Rapid resolution of papules of face and scalp
  - Slower resolution of purpuric plaques
  - Lung nodular reduction

- Iodinated contrast was added as an allergy

Chapter II
Lupus

Lupus

- Skin disease is the second most common clinical manifestation of SLE after arthralgias
  - Occurs in 70-80% of patients
  - First manifestation of disease in 23-28% of patients

- Cutaneous lupus erythematosus (CLE) can present with varying clinical morphologies and mimickers, making biopsy an important aspect in diagnosis

- CLE can occur as a part of SLE or be independent of SLE

Werth V, et al. Chapter 41: Skin. *Systemic Lupus Erythematosus.* 5th Ed. 2011.

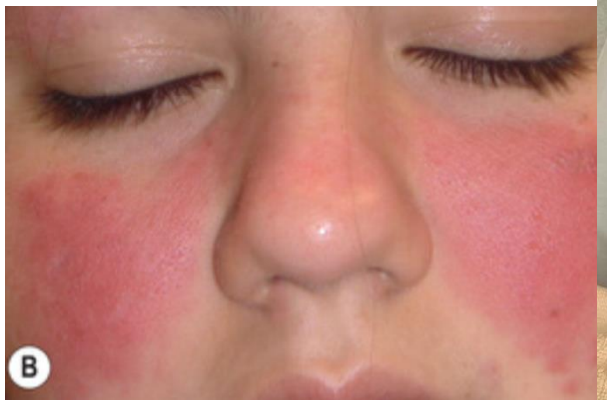
Table 1 Modified Gilliam nomenclature and classification system of CLE

Lupus-specific cutaneous manifestations	Lupus-non-specific cutaneous manifestations
Acute cutaneous lupus erythematosus and bullous forms of lupus A. Limited acute cutaneous lupus B. Generalized acute cutaneous lupus C. Toxic epidermal necrolysis-like acute cutaneous lupus D. Bullous systemic lupus erythematosus E. Rowell syndrome	Vascular disease A. Vasculitis - Small vessel vasculitis - Medium vessel (polyarteritis nodosa-like) vasculitis - Large vessel vasculitis - Lymphocytic vasculitis - Urticarial vasculitis B. Vasculopathy - Antiphospholipid syndrome, including catastrophic variant - Atrophie blanche and Degos-like lesions - Calciphylaxis - Cryoglobulinemia - Erythromelalgia - Livedo reticularis - Periungual telangiectasia - Raynaud phenomenon - Thrombophlebitis
Subacute cutaneous lupus erythematosus A. Annular and psoriasiform subacute cutaneous lupus B. Neonatal lupus erythematosus	Non-scarring alopecia A. Alopecia areata B. Telogen effluvium
Chronic cutaneous lupus erythematosus A. Discoid lupus erythematosus B. Lupus tumidus *C. lupus* panniculitis D. Chilblain lupus E. Lichenoid cutaneous lupus erythematosus/lichen planus overlap F. Mucosal lupus erythematosus G. Non-scarring alopecia with lupus-specific histologic findings	Other A. Photosensitivity B. Sclerodactyly C. Rheumatoid nodules D. Calcinosis cutis E. Urticaria F. Papulonodular mucinosis G. Cutis laxa/anetoderma/mid-dermal elastolysis H. Acanthosis nigricans I. Leg ulcers

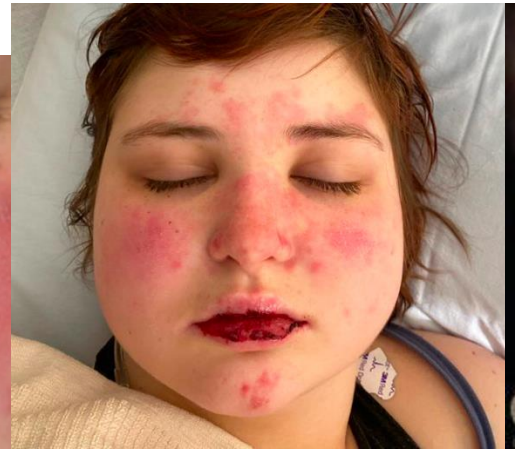
What is the risk of SLE with a lupus specific rash?

- Acute cutaneous lupus = nearly all patients meet SLE classification criteria
- Subacute cutaneous lupus: ~50% meet SLE classification (10-15% have severe manifestations)
  - Neonatal lupus erythematosus; risk for SLE may be more from genetic predisposition, but overall risk is lower
  - 1/3 of SCLE cases are drug-induced
- Chronic cutaneous lupus
  - Discoid lupus: between 5-28% have SLE (less with localized disease, more with generalized)
  - Chilblain lupus: ~25% meet classification criteria for SLE
  - Lupus profundus/panniculitis: ~10% meet criteria for SLE
  - Tumid lupus: low risk of SLE

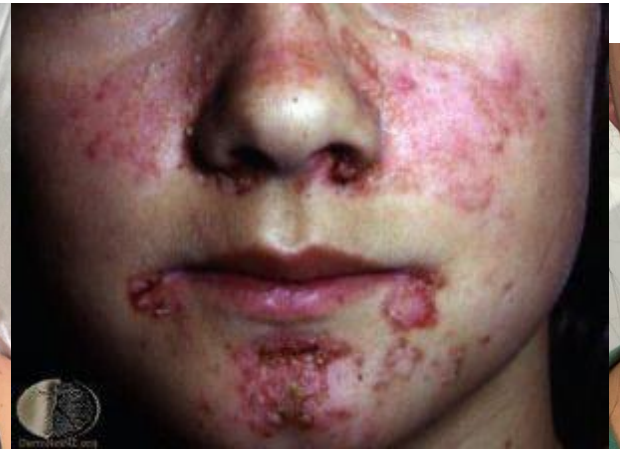
Clinical heterogeneity of malar rash of lupus



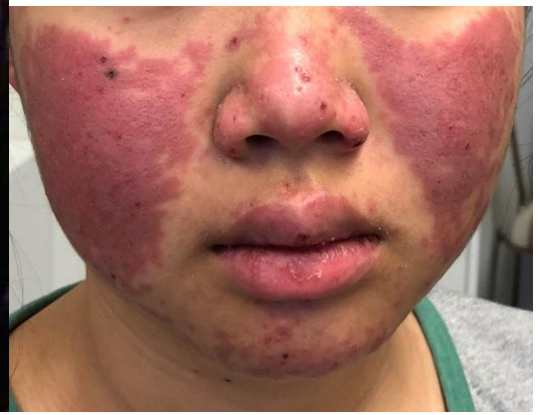
Bilateral malar cheek erythema with relative sparing of the nasal bridge; sparing of the nasolabial fold



Bilateral malar cheek erythema with papular lesions, some involvement of nasolabial fold and crusting of lip

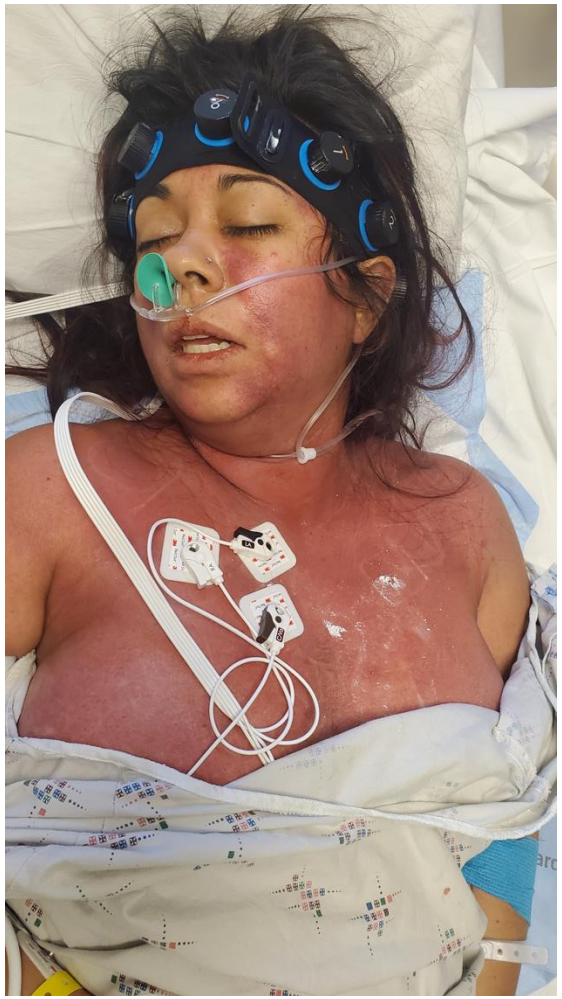


Bilateral malar cheek plaques with fine scale and papulo-pustular lesions on chin

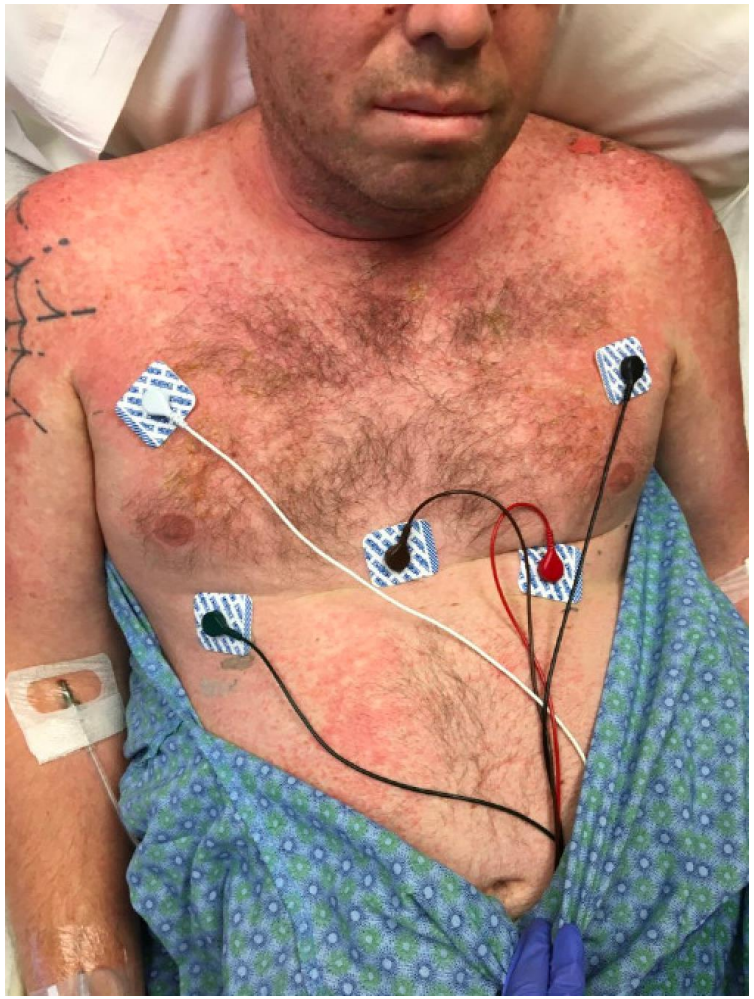


Sharply demarcated pink edematous plaques of the malar cheeks sparing nasolabial folds

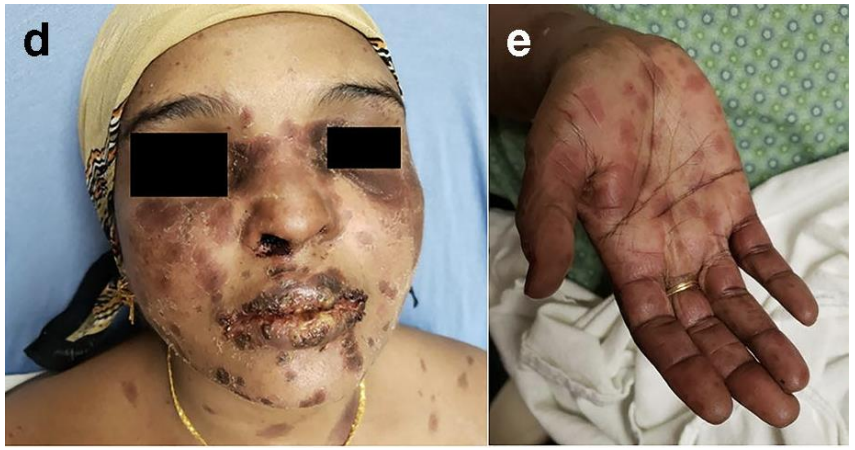
Rare forms of acute cutaneous lupus



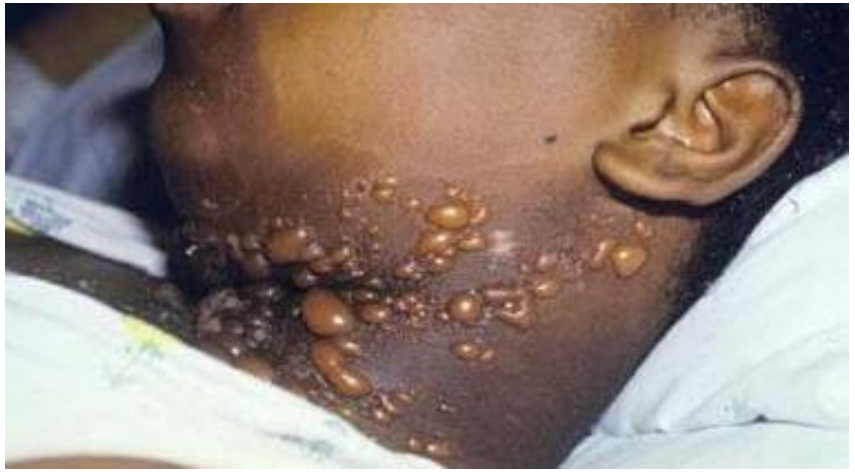
Generalized ACLE



TEN-like ACLE

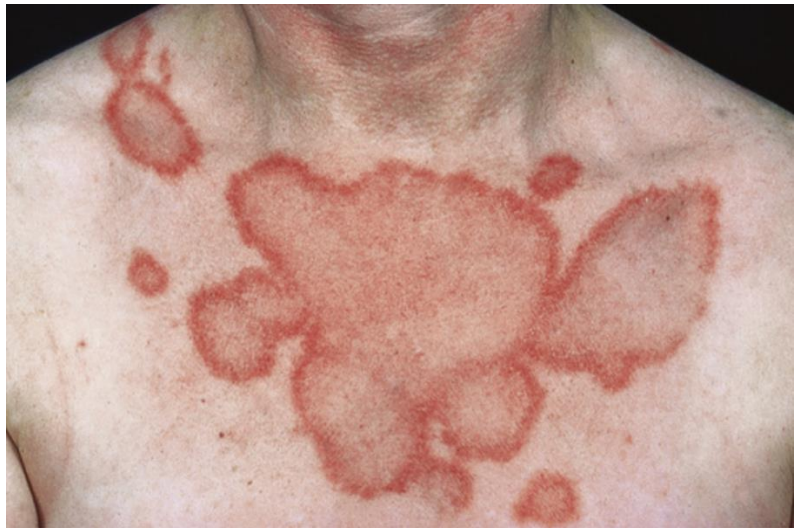


Rowell's Syndrome

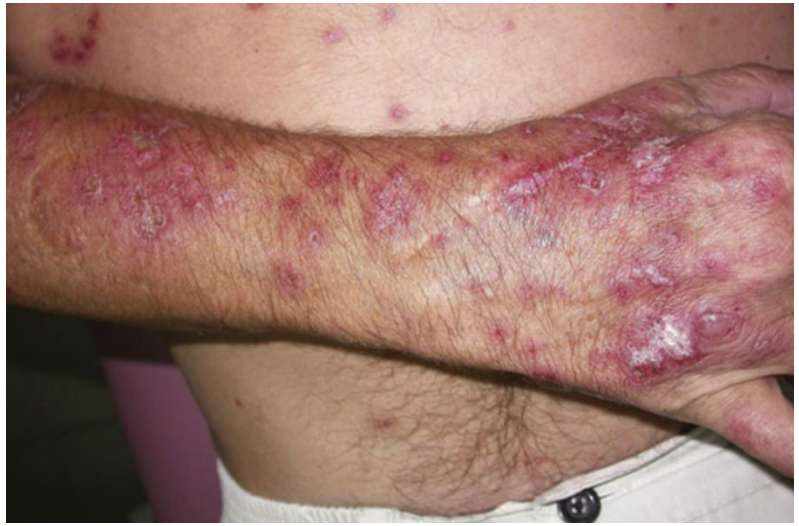


Bullous lupus

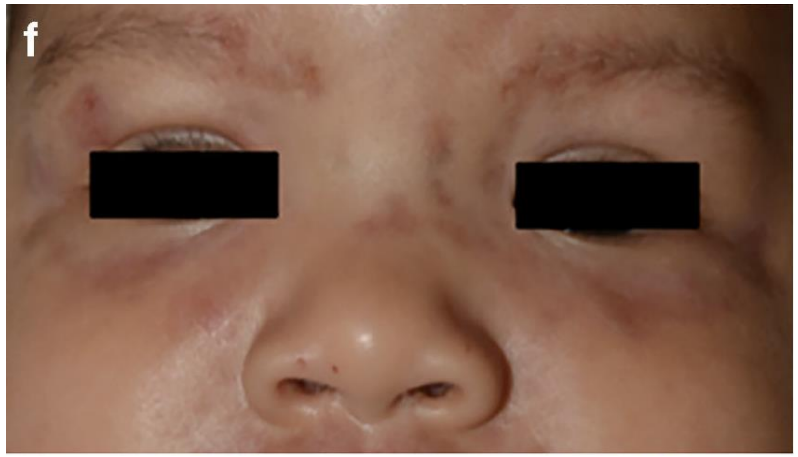
Subacute cutaneous lupus (SCLE)



Annular/polycyclic morphology



Psoriasiform morphology



Neonatal lupus

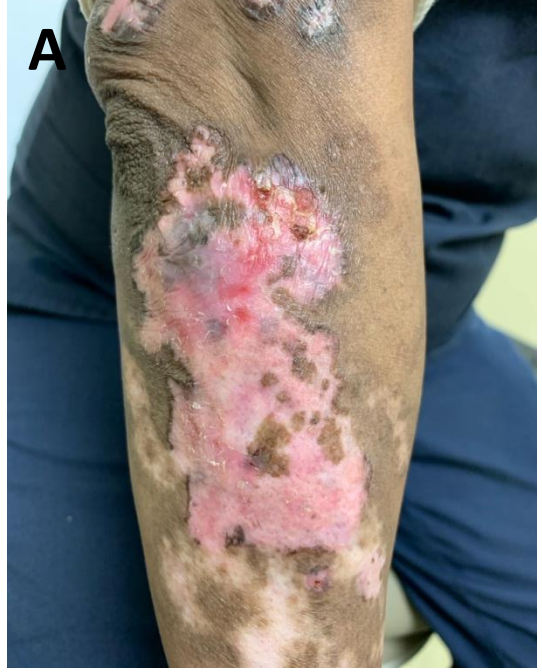
Chronic cutaneous lupus

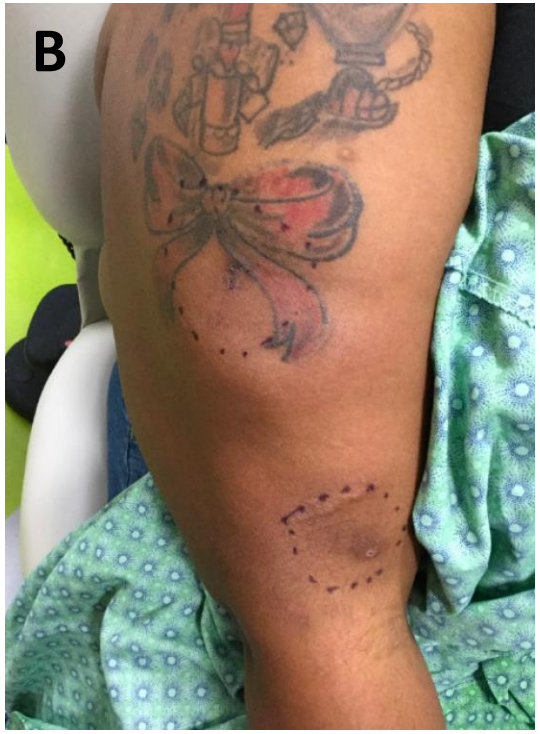
A- Discoid lupus

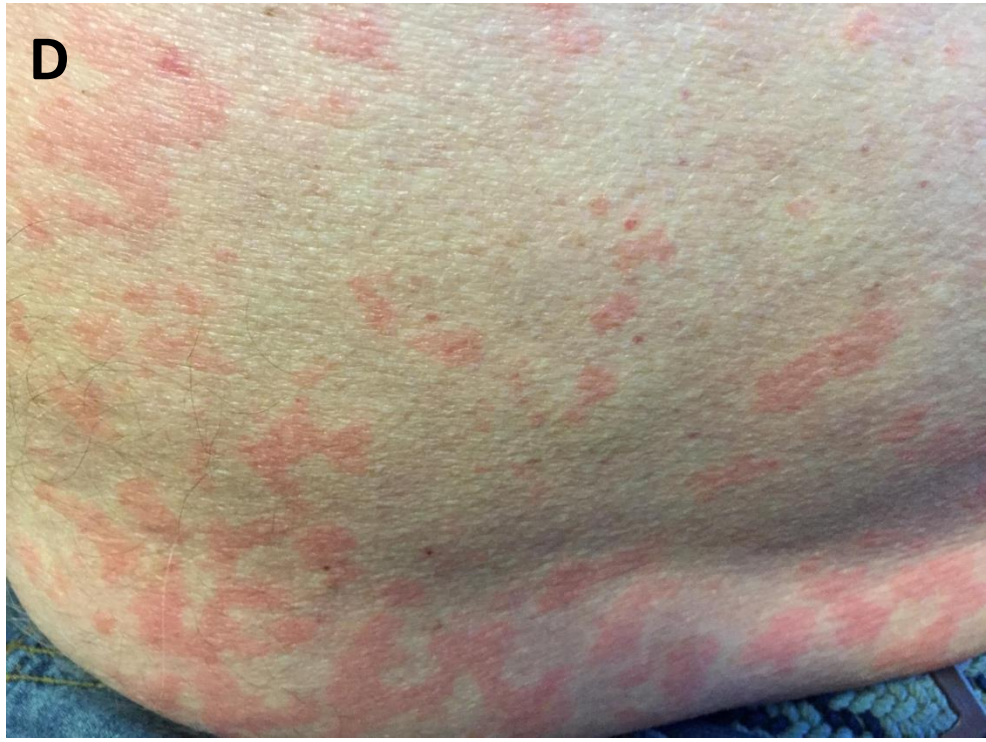
B- Lupus panniculitis

C- Chilblains lupus

D- Tumid lupus



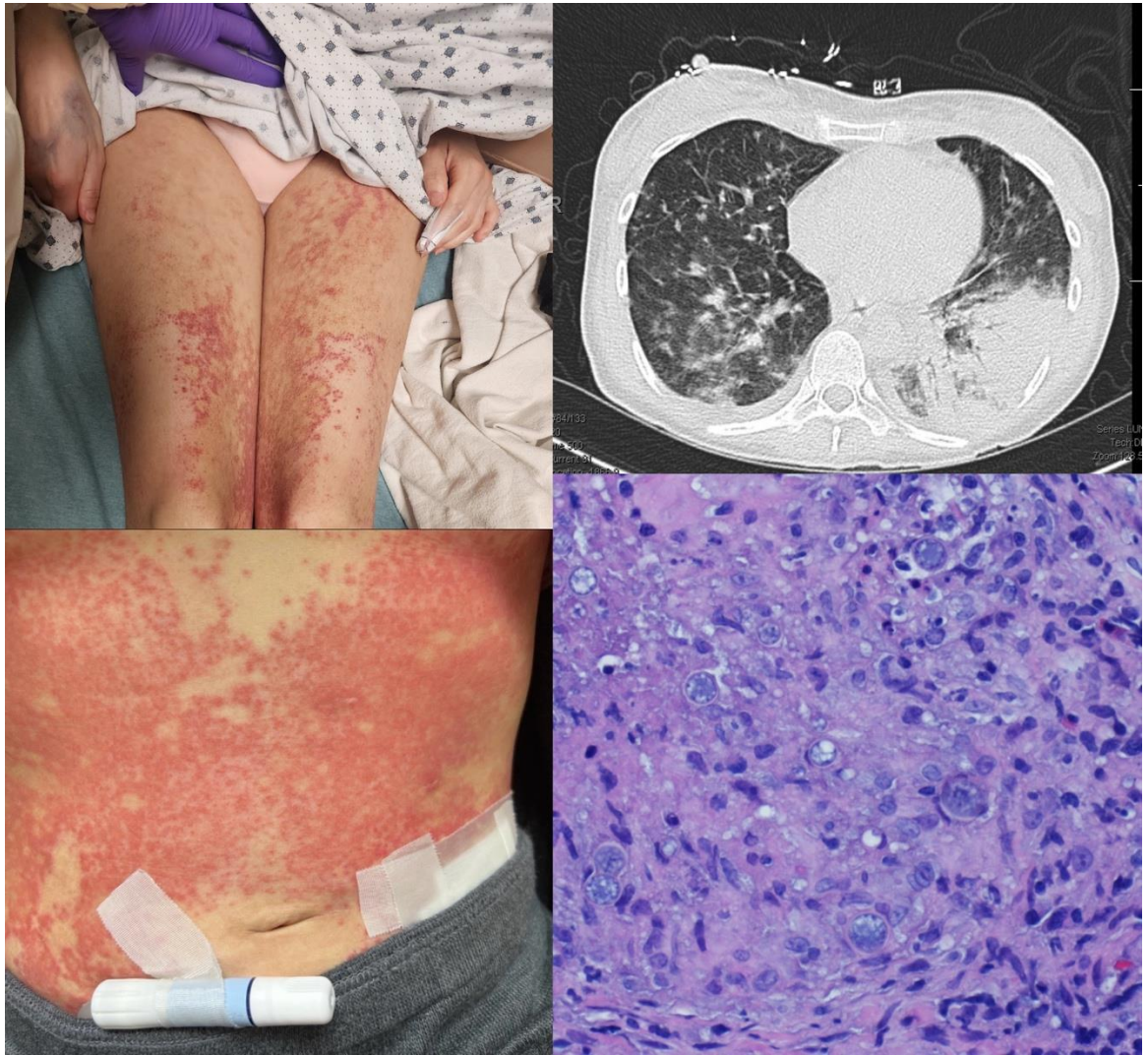




Notable mimickers of cutaneous lupus

Acute Cutaneous Lupus	Subacute Cutaneous Lupus	Chronic Cutaneous Lupus	Lupus non-specific manifestations	Serologic mimickers
Malar rash: -Rosacea -Seborrheic dermatitis -Dermatomyositis -Lupus pernio -Lupus vulgaris -Contact/eczematous reactions -Dermatomyositis **Generalized acute cutaneous lupus:** -Drug/viral exanthems -Toxic shock syndromes **Bullous forms:** -Erythema multiforme -Toxic epidermal necrolysis -Autoimmune blistering disorders -GVHD	**SCLE** -Psoriasis -Dermatophyte infections -Secondary syphilis -Gyrate erythema **NLE** -Secondary syphilis	**DLE** -Lichenoid reactions -Cutaneous tuberculosis -Atypical mycobacterial infections -Scarring alopecias **Lupus panniculitis** -SPTCL -Erythema nodosum -Infectious panniculitis **Chilblains lupus** -Raynauds phenomenon -Pernio not related to lupus	**Alopecia** -Alopecia areata -Scarring alopecias -Telogen effluvium **Vascular manifesatations** -Other causes of vasculitis -Calciphylaxis -Primary antiphospholipid syndrome **Angioedema** -Food/environemental triggers	DFS pattern Drug-induced dsDNA (ie, TNF-inhibitors) Autoimmune hepatitis

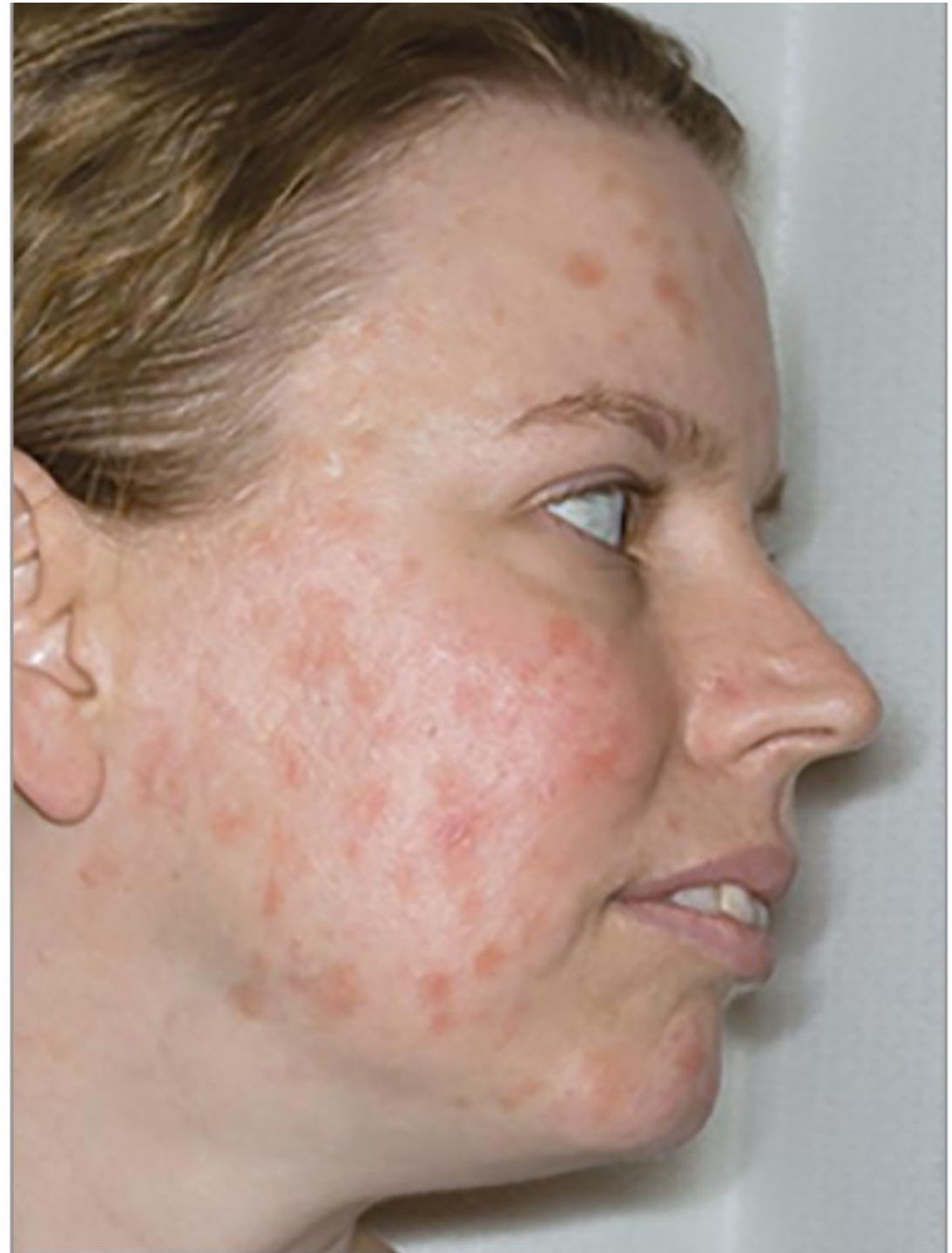
Exanthem of acute pulmonary coccidioidomycosis

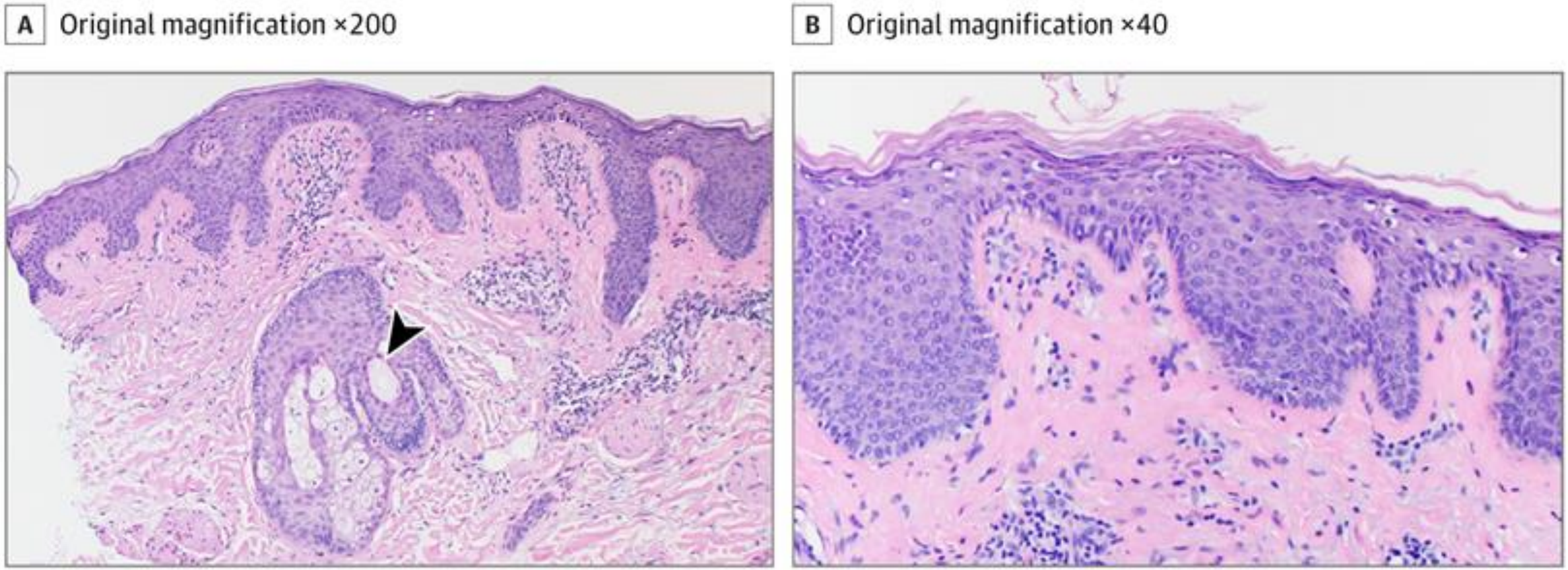


Discoid papules and plaques on the face

History

- 40-year-old woman presents with a 10-year history of a facial rash that involves her forehead, cheeks, jawline and neck.
- Prior skin biopsy mentioned a “perivascular lymphocytic infiltrate” and given clinical concern, favored to be discoid lupus.
- Patient has trialed various topical medications, as well as hydroxychloroquine with minimal to no improvement.
- A new punch biopsy was performed





A, Mild psoriasiform epidermal hyperplasia with subtle follicular hyperkeratosis (arrowhead) and superficial perivascular lymphocytic infiltrate (hematoxylin-eosin [H&E]). B, Psoriasiform hyperplasia with small mounds of parakeratosis alternating with compact orthokeratosis. A mild superficial perivascular lymphocytic infiltrate is also present (H&E).

Facial discoid dermatosis

- Variant of pityriasis rubra pilaris (PRP) that exclusively affects the face
- Pityriasis rubra pilaris is a rare, inflammatory papulosquamous disorder that is characterized typically by follicular, hyperkeratotic papules, or waxy, yellow palmoplantar keratoderma; or erythroderma with islands of sparing
- May occur in both children and adults and there are 6 different clinical phenotypes
- Clinical features of FDD has overlapping features with psoriasis, discoid lupus, seborrheic dermatitis and PRP
- Pathogenesis of PRP/FDD not fully understood but the IL23/Th17 axis plays an important role
    - This patient cleared on ustekinumab treatment

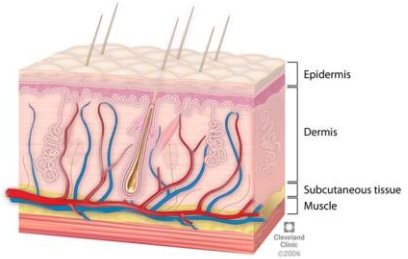
Rypka KJ, et al. Improvement of Facial Discoid Dermatosis with Ustekinumab Treatment. *JAMA Dermatol.* 2022.

Chapter III

Dermatomyositis

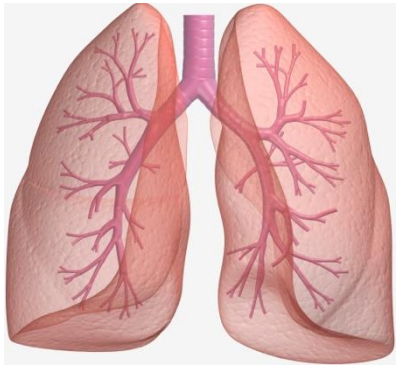
Dermatomyositis

Autoimmune disorder and a subgroup of the idiopathic inflammatory myopathies characterized by:

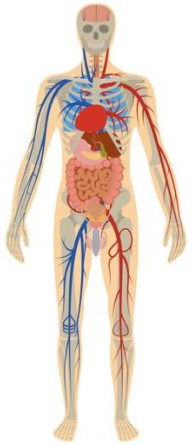


Skin rashes

Muscle inflammation + weakness



Interstitial lung disease



Other systemic manifestations

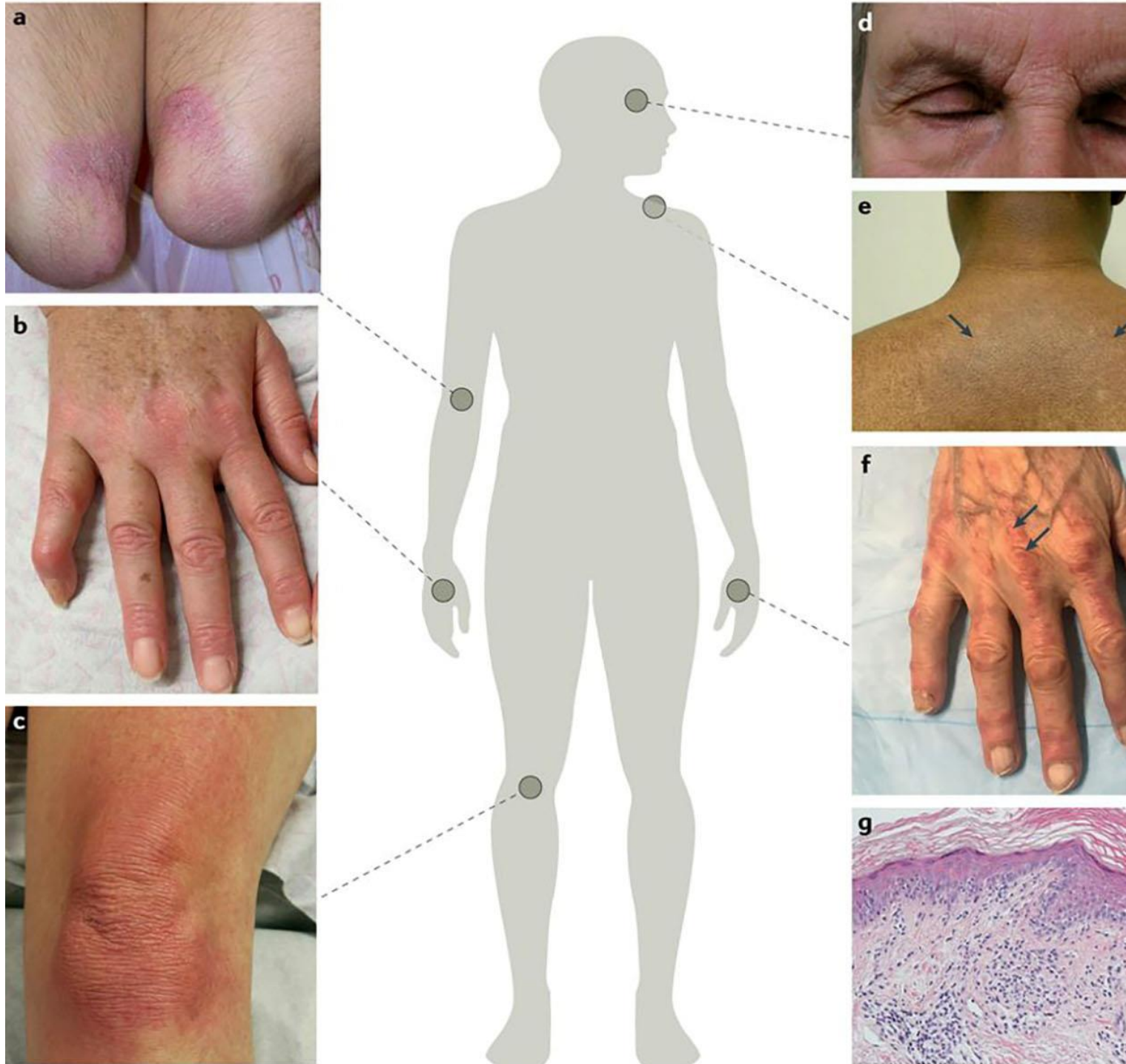
It is a **multisystem disease,** not only skin and muscle

And sometimes associated with malignancy

Cutaneous features of dermatomyositis

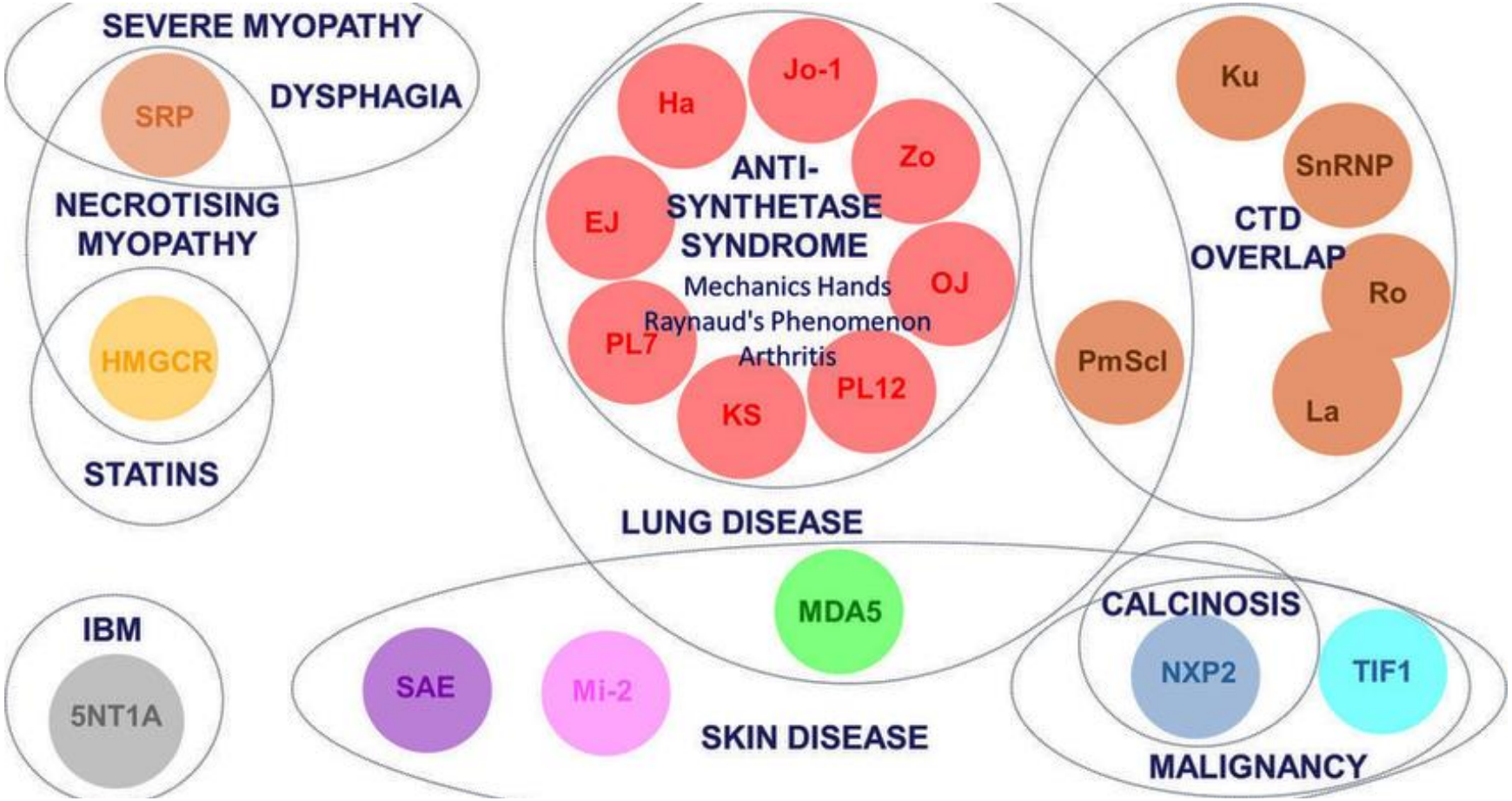
Work in progress

Shown are the classic cutaneous features of DM



Lundberg IE, et al. Classification of myositis. *Nat rev.* 2018.

Dermatomyositis specific rashes based on autoantibody profile



McHugh NJ, Targoff IN. Role of ANA and Myositis Autoantibodies in Diagnosis. *Managing Myositis.* 201

Anti-SAE positive dermatomyositis

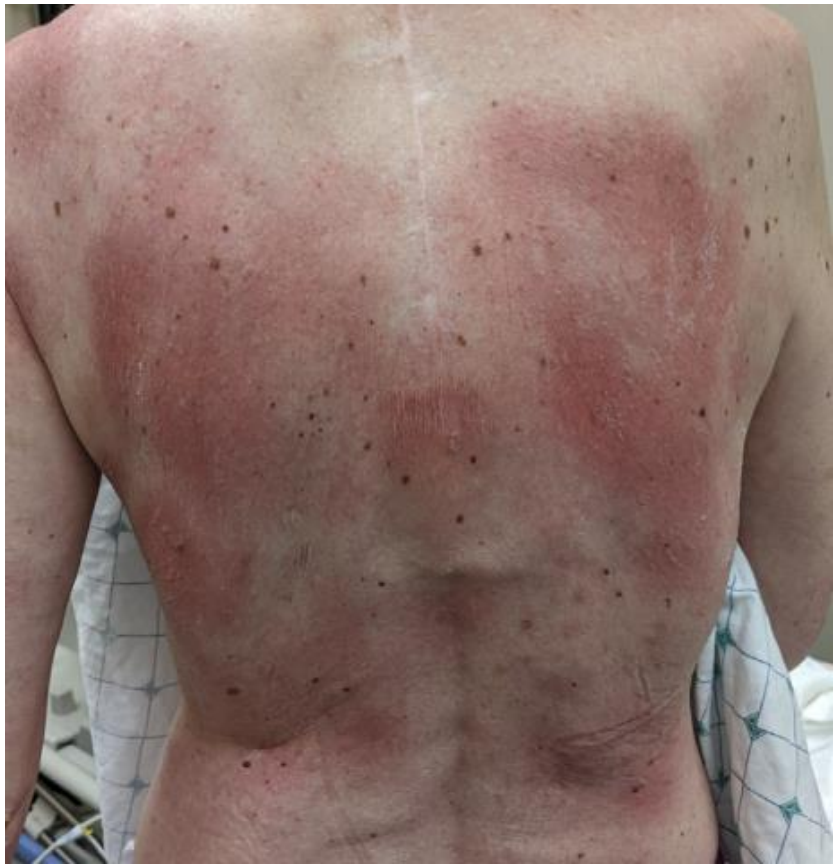
The reversible attachment of small-ubiquitin-like modifier (SUMO) proteins to lysine side chains of specific proteins is necessary for genome stability and transcription. The process is controlled by the SUMO- activating enzyme (SAE), which is the target of the anti-SAE Abs.

Cutaneous involvement is usually severe and precedes muscular involvement at disease onset

Severe dysphagia

Higher risk of **Plaquenil-exacerbated rash** and **angel-wings rash** (more seen in Japanese patients)

ILD seems to be rare / cancer reported in only one case series



Anti-TIF 1 - positive dermatomyositis

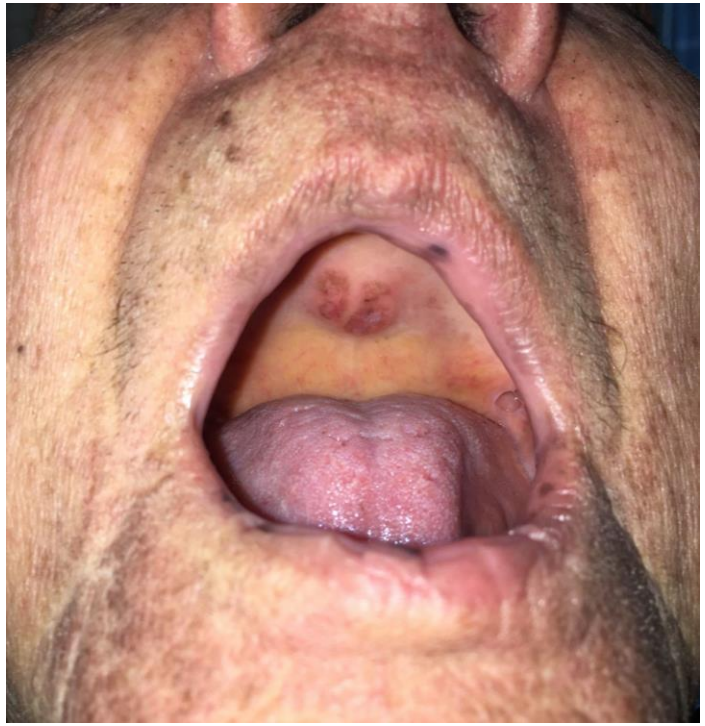
Transcription intermediary factors-1 (TIF-1) family belongs to tripartite motif-containing proteins (TRIM) superfamily important for cycle regulation, mitosis, innate immunity

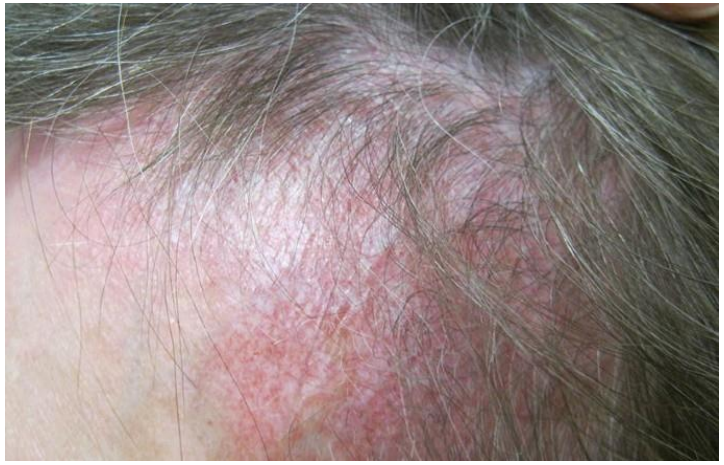
Two Abs are directed against 155 kDa (TIF1γ) and 140 kDa (TIF1α) and are found in 2 age groups:

1. Younger than 40-year-olds with a classical DM at presentation:

Gottron's papules, **"red-on-white lesions",** atrophic hypopigmented patches with telangiectasia's, **ovoid palatal patch**, psoriatic-like dermatitis. "Nutcracker esophagus". Mild muscle disease.

2. Older than 40-year-olds with cancer-associated myositis (ovary, lung, breast) The risk of **malignancy** is higher in pts with both anti-TIF1γ/α than in those with anti-TIF1γ alone.



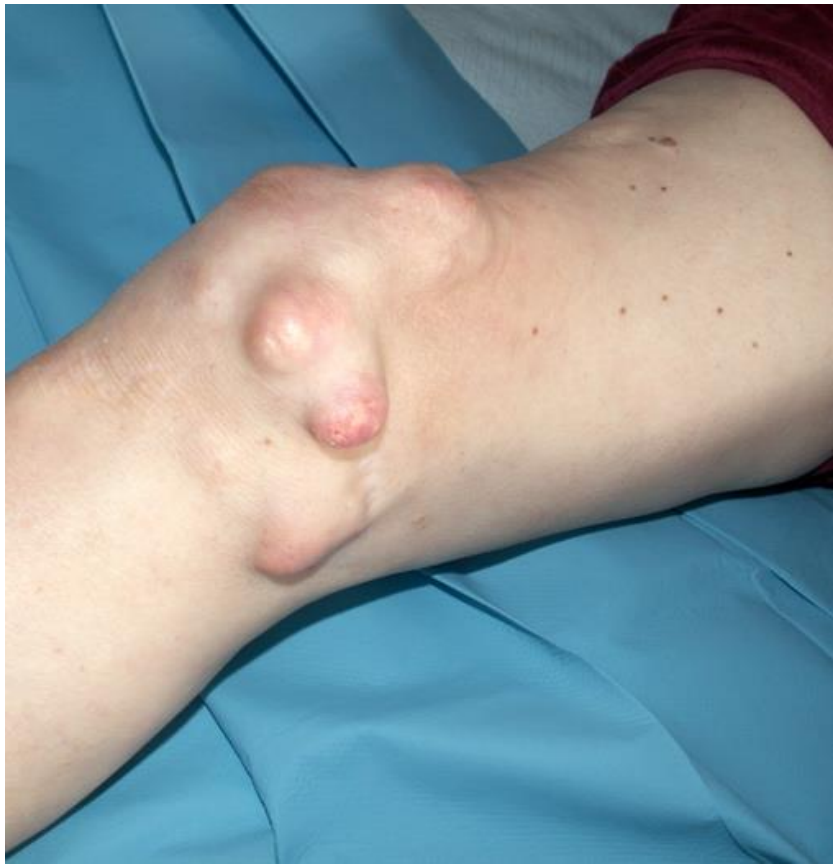


Anti-NXP2 - positive dermatomyositis

Nuclear matrix protein 2 (NXP2) is a 140 kDa protein involved in epigenetic regulation, RNA metabolism, and preservation of chromatin architecture.

Antibodies seen in severe **juvenile DM** complicated by **calcinosis**, polyarthritis, **intestinal vasculitis**, marked muscle weakness, persistent disease activity after 2 years

Cancer in the elderly (males!) with lower prevalence when compared to anti-TIF1.



Anti-MDA5-positive dermatomyositis

Melanoma Differentiation-Associated gene 5 (MDA5) is a 140 kDa innate cytosolic sensor, able to initiate signaling events leading to type I interferons production (also called clinically amyopathic DM; anti-CADM140)

Typical DM rash combined with mechanic's hands

Absent / low grade muscle inflammation

Papules with ivory-colored center

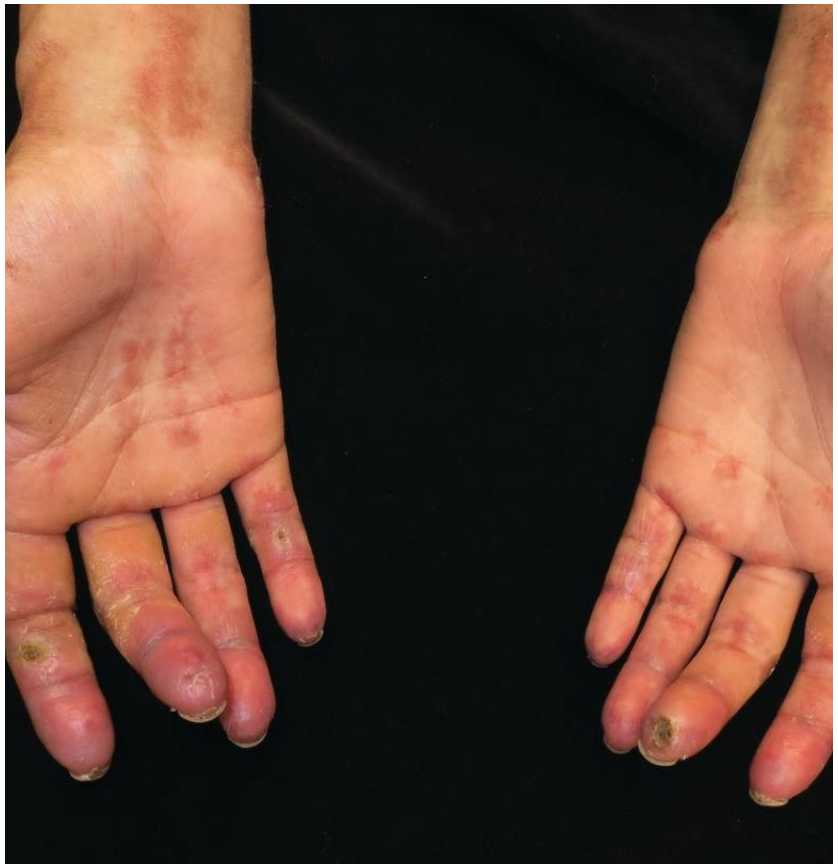
and **ulcers** on palms, called

"inverse Gottron's papules"

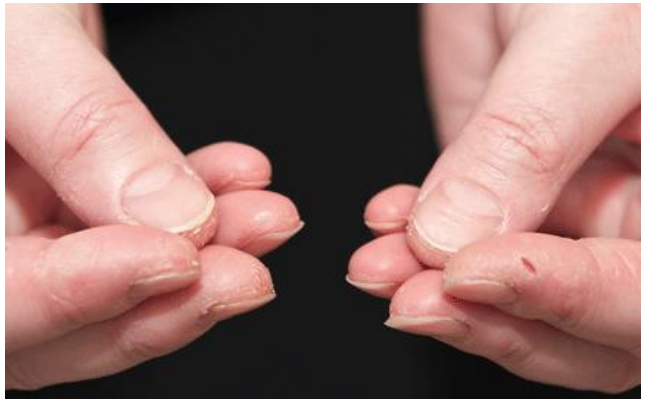
Rapidly progressive ILD

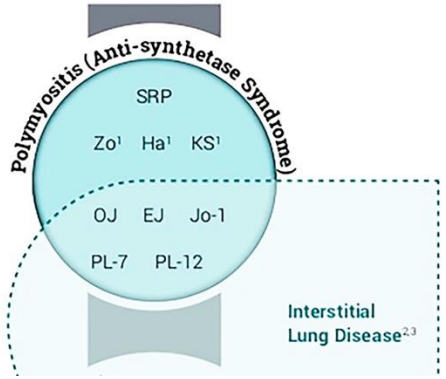
Most frequent target Ag in patients of **Asian ancestry** (10-48%)

No cancer association

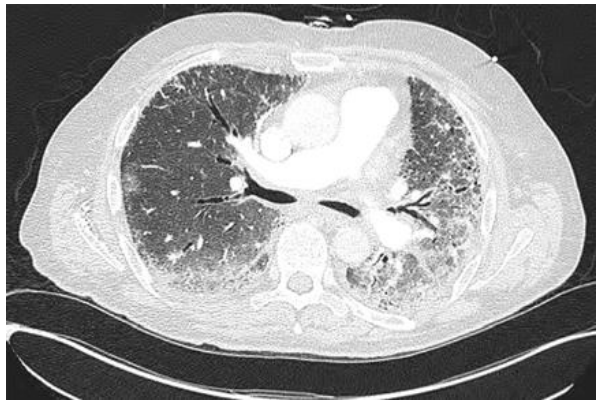


Anti-aminoacyl-tRNA synthetase antibodies





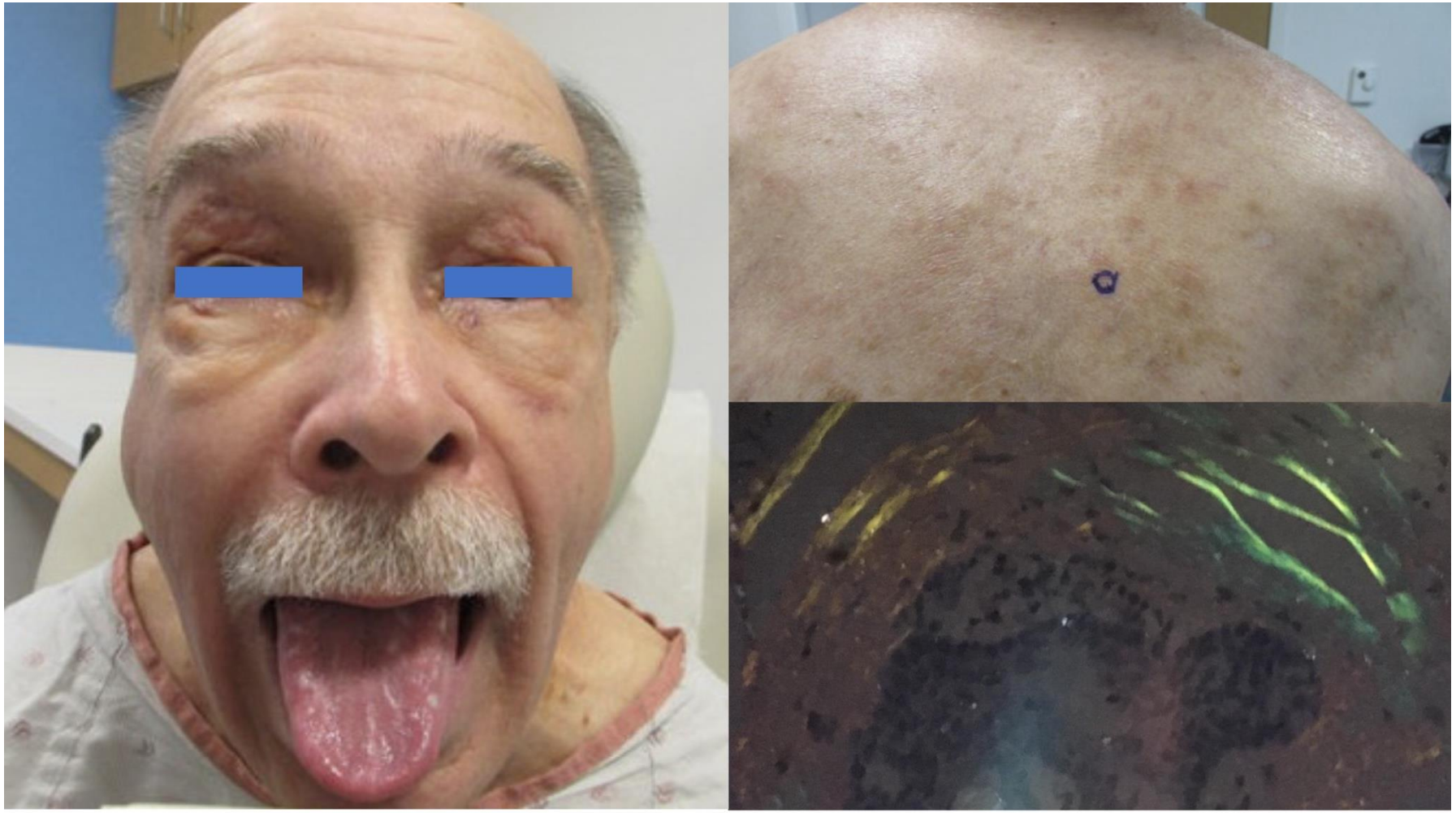
* tRNA synthetase autoantibody
* myositis
* ILD
* arthralgias
* Raynaud's phenomenon
* mechanic's hand
* perifascicular necrosis on biopsy



Notable mimickers of dermatomyositis

Gottrons papules	Dermatomyositis lilac erythema	Nailfold capillary changes	Scalp dermatomyositis	Other findings
Flat warts Lichen planus Dyshidrotic eczema	Depends on body site location. In general eczema/eczema-like disorders and/or lupus is usually considered	Seen with systemic sclerosis and lupus	Seborrheic dermatitis Contact dermatitis Psoriasis	*Calcinosis*: Rheumatoid nodules, tophaceous gout *Ulcerated and inverse Gottron's papules*: other causes of vasculopathy

Primary systemic amyloidosis

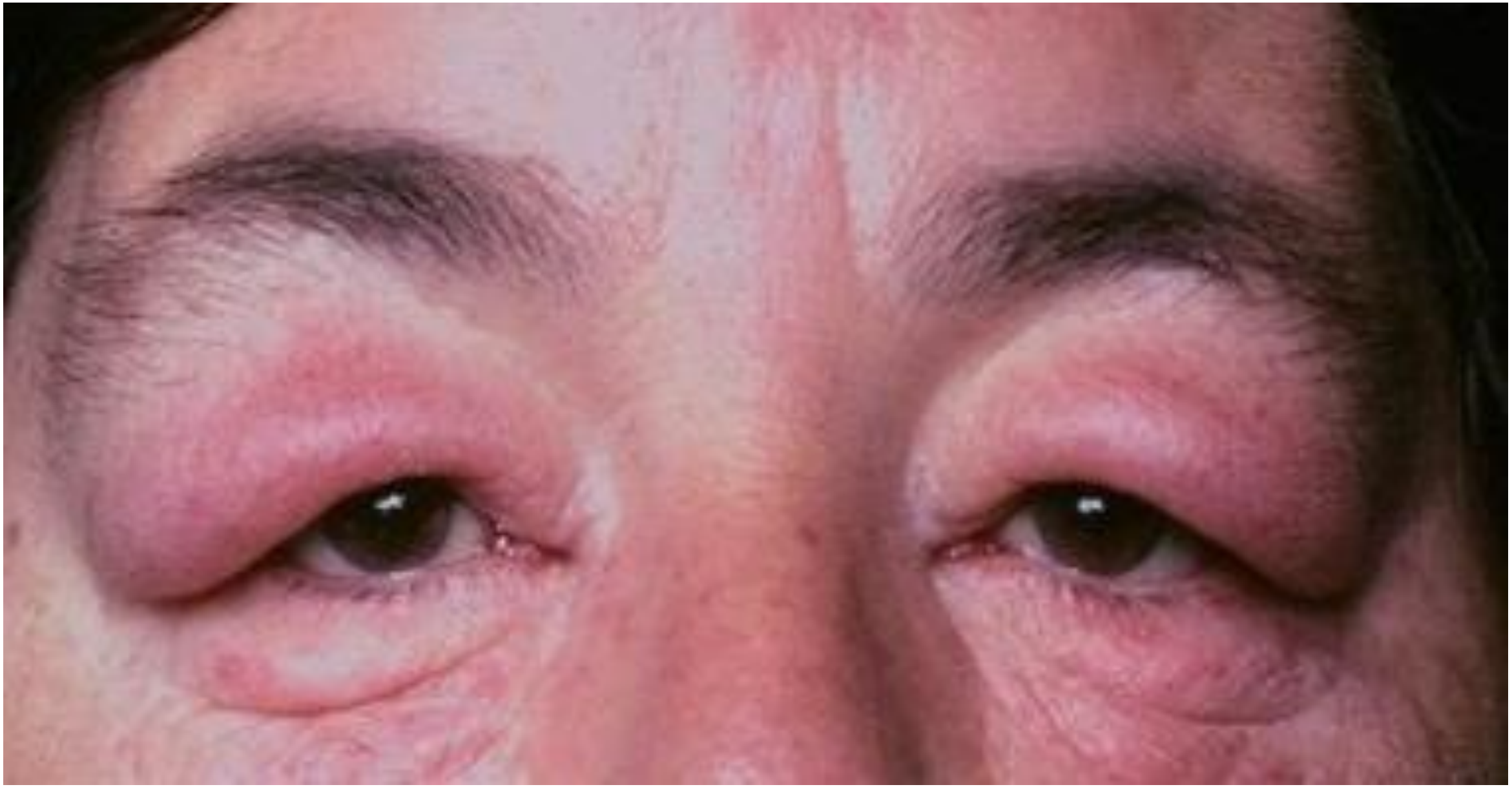


Unmasking an unusual diagnosis

History

- 35 yo female with history of ulcerative colitis on chronic prednisone and adalimumab who had progressive periorbital swelling, induration and erythema.
  - Initially admitted with preseptal cellulitis and group A Streptococcal bacteremia, completed 14 days of antibiotics
  - Presented again with Clostridium difficile infection and worsening swelling/induration preseptal/periorbital area
  - S/p I+D abscesses showing GPC but no growth in culture
- Initial CT maxillofacial w/ contrast revealed:
  - Bilateral facial and periorbital soft tissue edema extending superiorly to scalp, which may represent cellulitis or inflammatory/allergic angioedema. No drainage fluid collection.
- MRI neck and face w/ and w/o contrast reveals large bilateral periorbital soft tissue swelling compatible with cellulitis
- On treatment with broad spectrum antibiotic

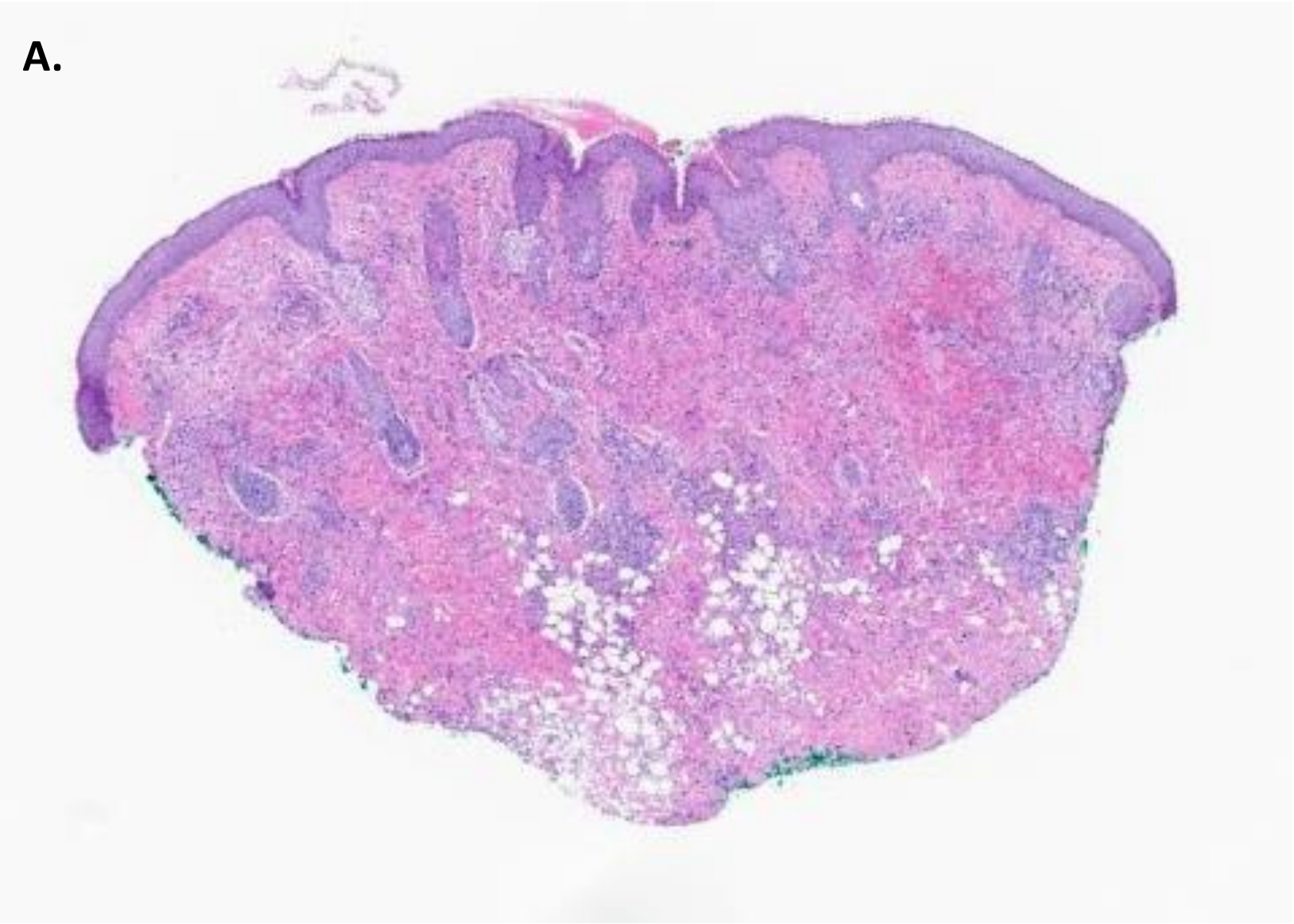
Representative photo (not my patient)

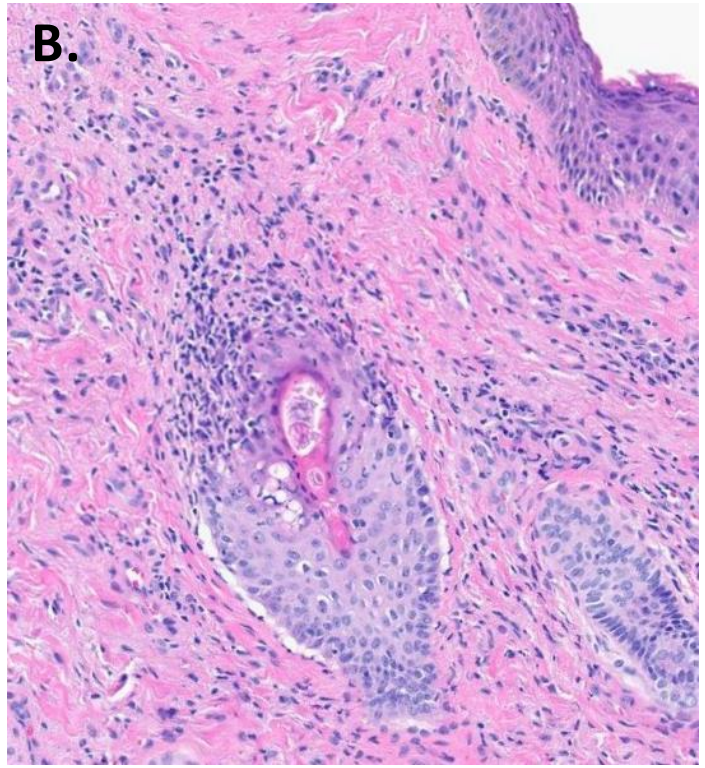


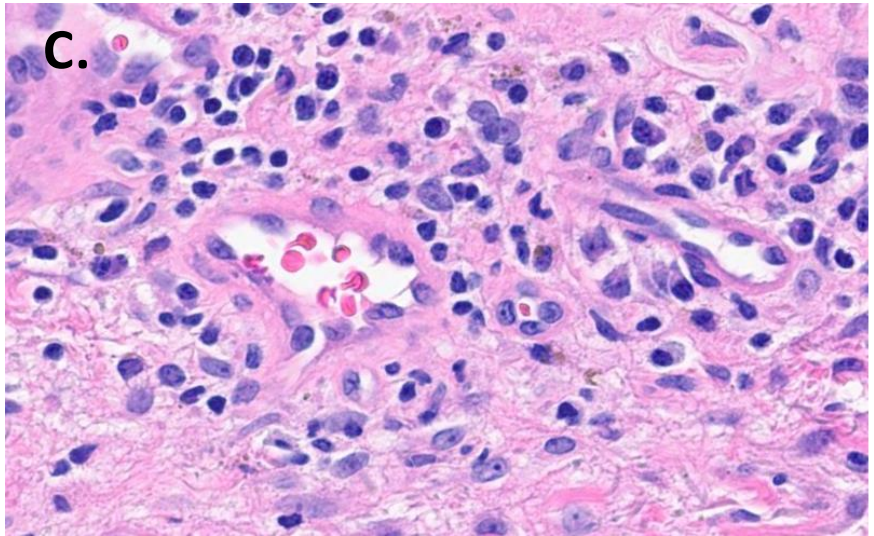
From Journal of Clinical and Medical Research

Diagnostic studies

- CBC
  - Notable for microcytic anemia, no leukocytosis
- CMP: unremarkable
- Urinalysis: unremarkable
- Infectious workup:
  - Tissue cultures negative for bacteria, AFB, fungal
  - Cocci serologies: negative
  - T pallidum antibody: negative
  - Aspergillus Ab: negative
  - Quantiferon gold: negative
  - Chronic hepatitis panel: unremarkable
- CK and aldolase WNL
- IgA, IgM, IgE, IgG subserologies: unremarkable
- ACE: normal
- **Soluble IL—receptor: 1522** (ULN 858)
- **IL-10: 5** (ULN 2.8); rest of interleukin levels WNL
- Autoimmune serologies:
  - ANA by IIF: negative
  - dsDNA and ENA panel: negative
  - Normal C3/C4
  - C1 esterase inhibitor and functional assay: normal
  - **Positive c-ANCA; 1:20 titer**
  - Negative anti-MPO and anti-PR3
  - Myositis specific antibody panel negative







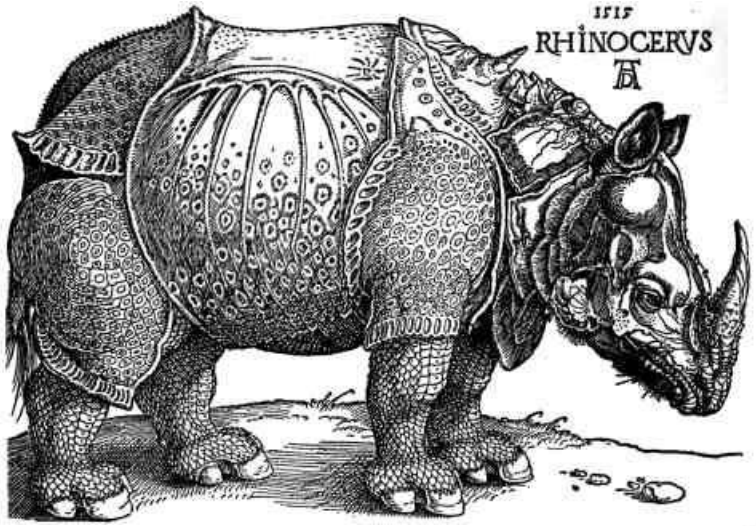
A. Low power view showing dermal based process; B. Demodex mite in hair follicle; C. Telangiectasias with lymphocytes and a few plasma cells

Morbihan's disease

- AKA solid facial lymphedema or rosacea lymphedema
- Rare disorder but would most often develop as a complication of rosacea
- Clinical presentation:
  - Persistent erythema and firm non pitting swelling involving the central and upper parts of the face
  - Typically symmetric though asymmetric presentations also reported
  - Skin often feels firm and indurated
- Pathogenesis not fully elucidated but impaired lymphatic drainage can result from lymphatic obstruction and/or damage to blood and lymphatic vessels
- Treatment options:
  - Tetracycline antibiotics
  - Isotretinoin
  - Surgical debulking
  - Manual lymphatic drainage

van der Linder MM, et al. Diagnosis and Treatment of Morbihan's Disease: A Practical Approach based on Review of the Literature. *J Clin Aesthet Dermatol.* 2023.

Chapter IV
Sclerosing Disorders



Sclerosing disorders of the skin

- Heterogenous spectrum of entities that share in common cutaneous sclerosis with excessive local accumulation of collagen and/or other extracellular matric components in the dermis, subcutaneous tissues, and/or underlying soft tissues.

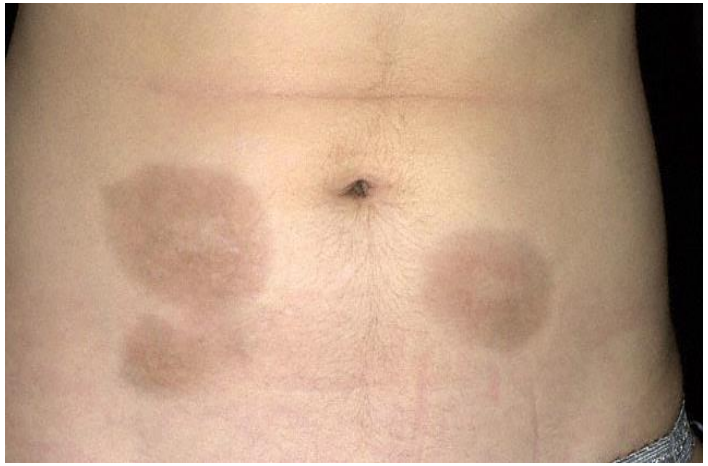
- Clinical course may vary from benign disease with localized skin involvement to systemic life-threatening disorders

Sclerosing Disorders 1.

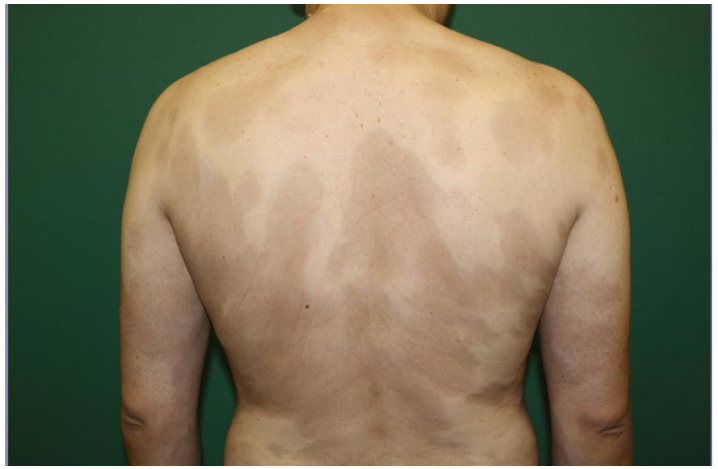
Localized idiopathic cutaneous sclerosing disorders

Disorder	Features
Morphea	Circumscribed sclerotic plaques
Linear scleroderma	Circumscribed linear sclerotic plaques
Scleredema	Neck, shoulders, upper back; not the extremities;
Lipodermatosclerosis	Painful, brownish tightening of lower legs, chronic venous insufficiency

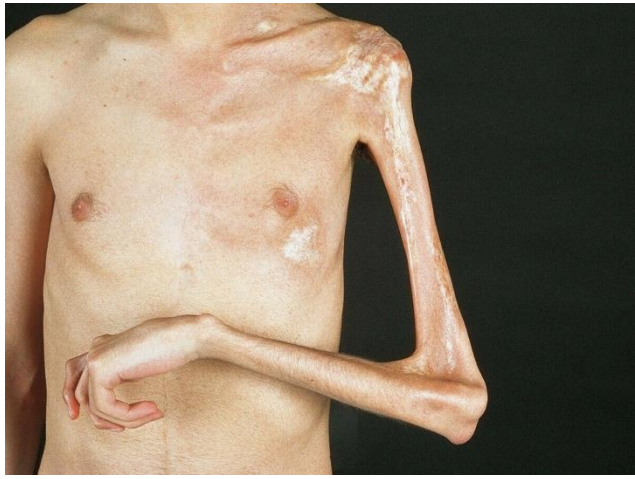
Morphea clinical spectrum



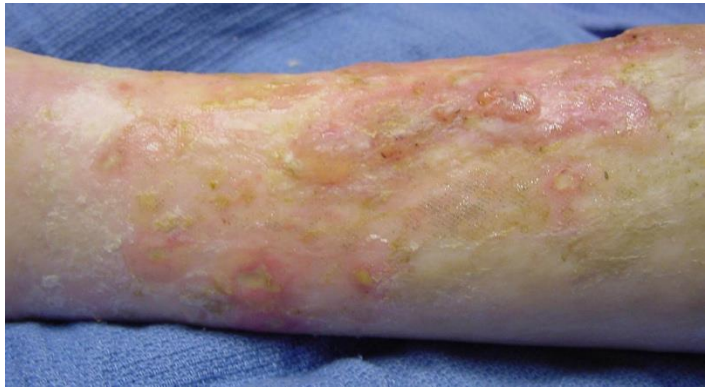
Patch/Plaque



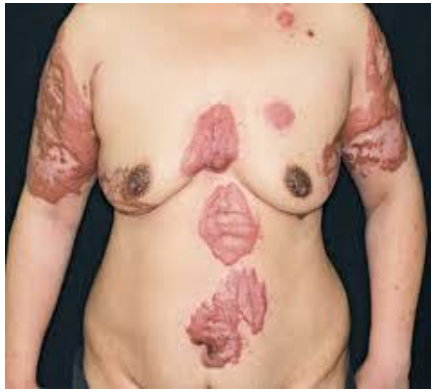
Generalized morphea



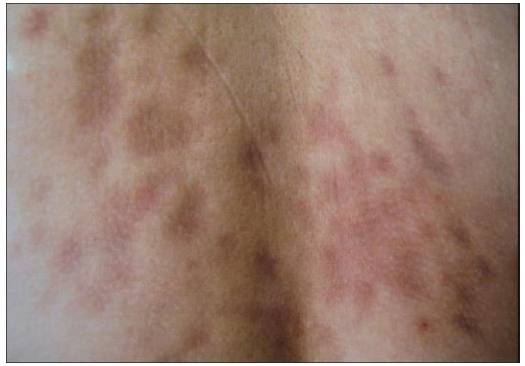
Pansclerotic morphea



Bullous morphea

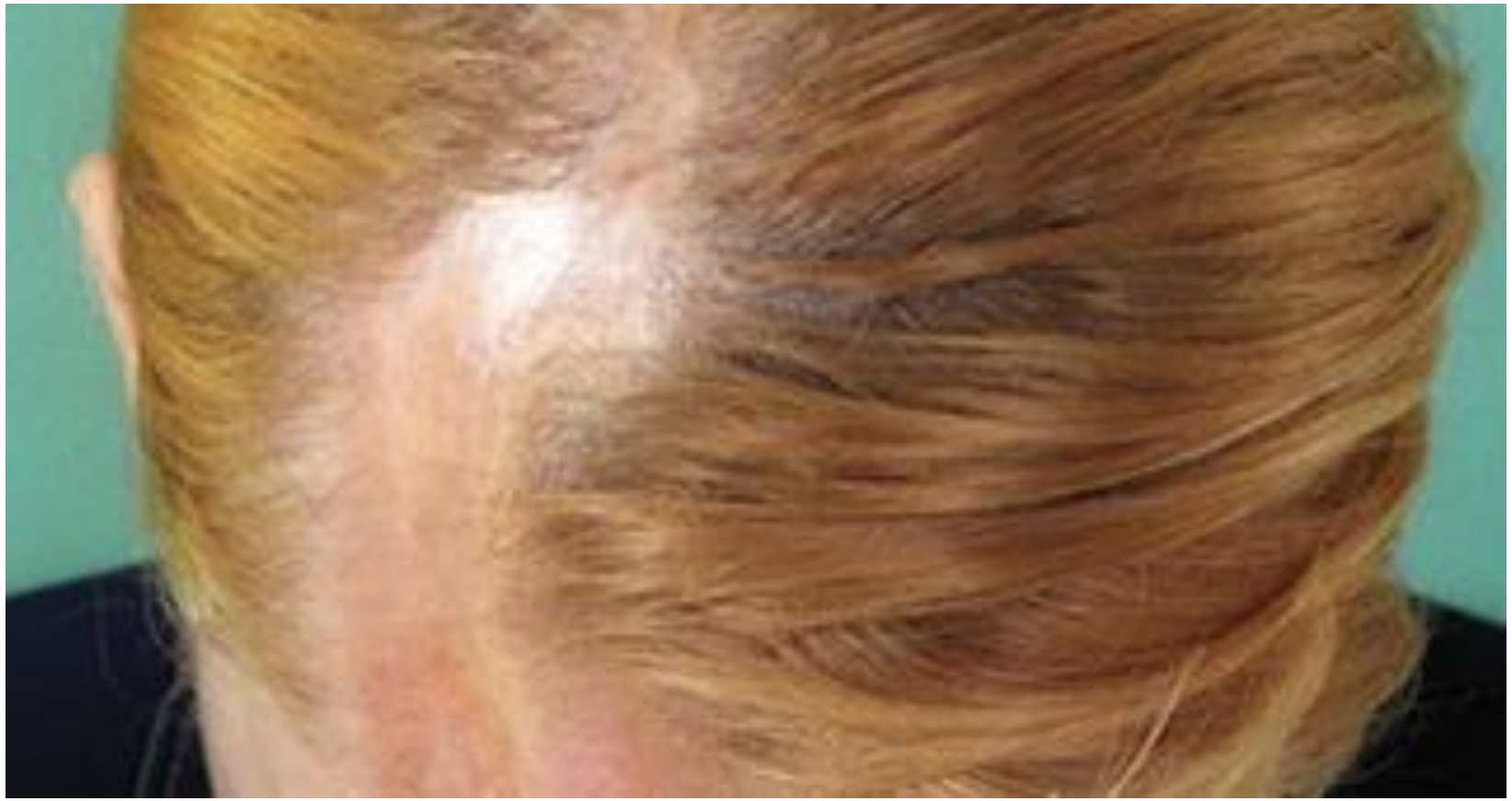


Keloidal morphea



Atrophoderma of P&P

En coup de sabre

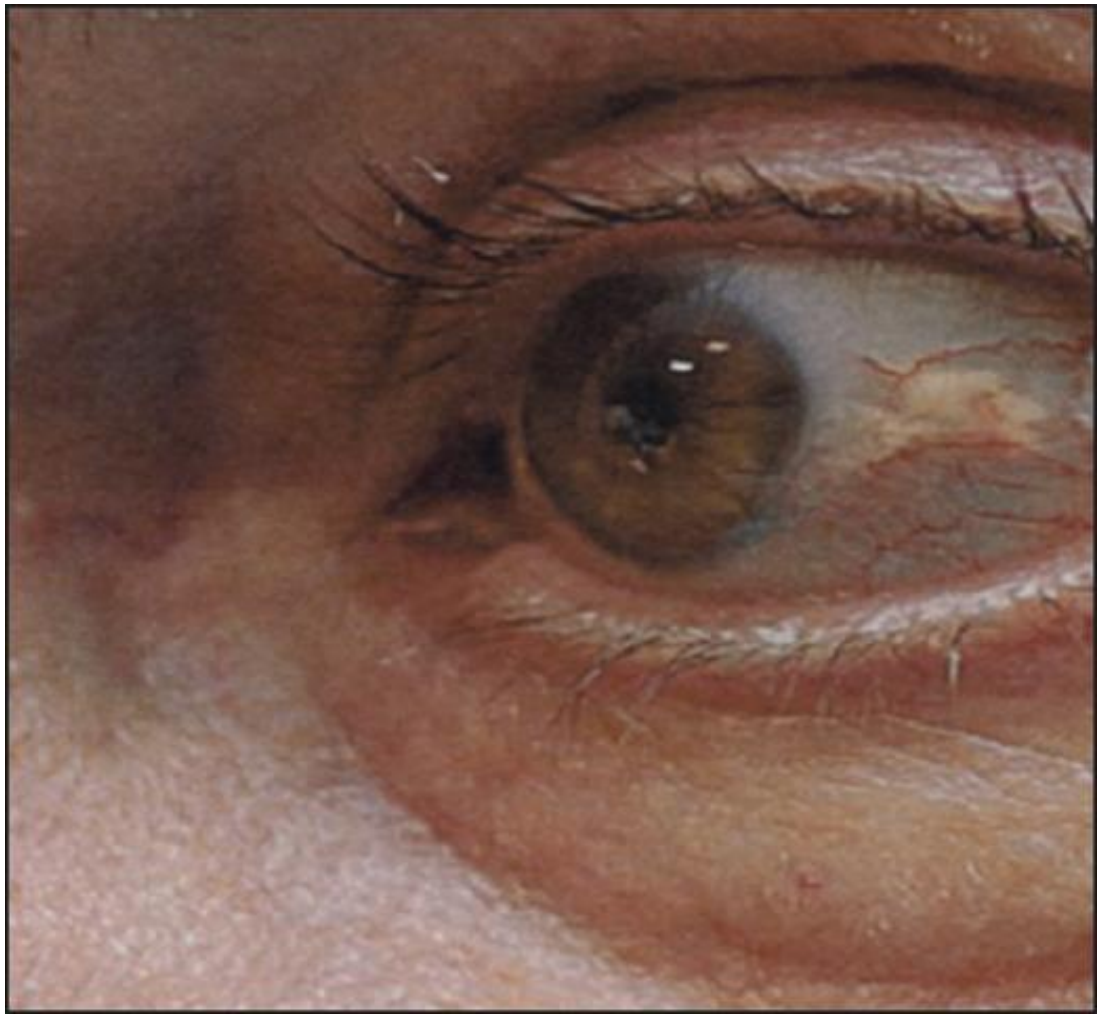


Sclerosing Disorders 2.

Sclerosing disorders with identified cause

Disorder	Features
Spanish toxic oil s-me	Olive oil adulterated with rapeseed oil
Eosinophilia-myalgia s-me	Contamination of L-tryptophan with 1,1 ethilidenebis (L-tryptophan)
Graft-versus-host disease	Previous bone marrow transplantation
Nephrogenic systemic fibrosis	Gadolinium-containing contrast in the setting of chronic kidney disease

Scleral plaque in nephrogenic systemic fibrosis



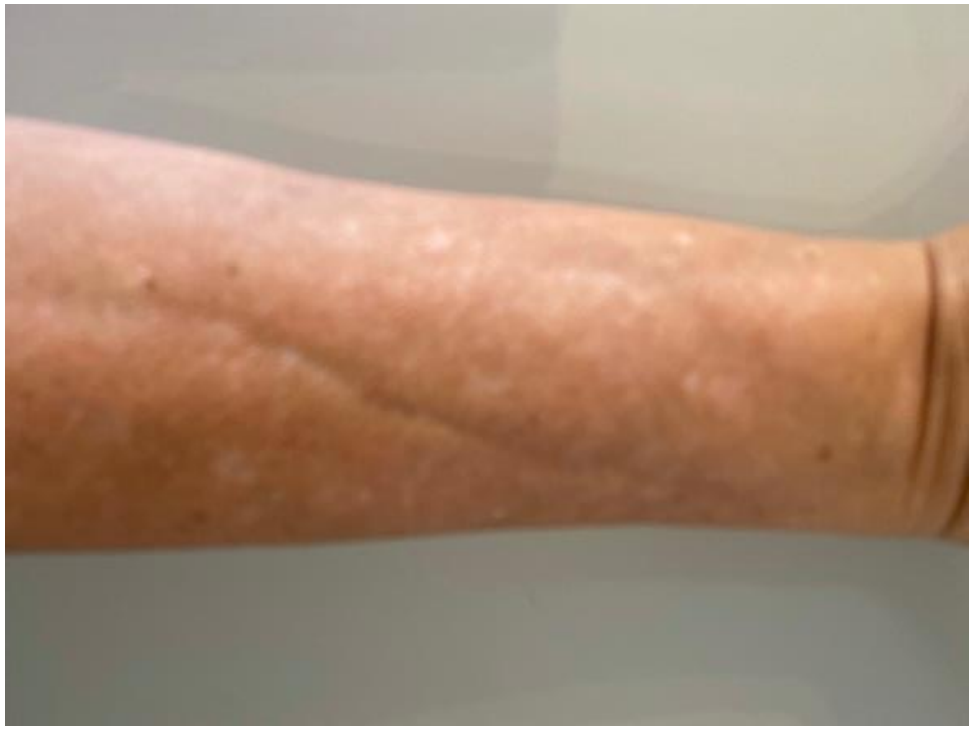
Barker-Griffith A, et al. Ocular Pathologic Features and Gadolinium Deposition in Nephrogenic Systemic Fibrosis. *Arch Ophthalmol.* 2011.

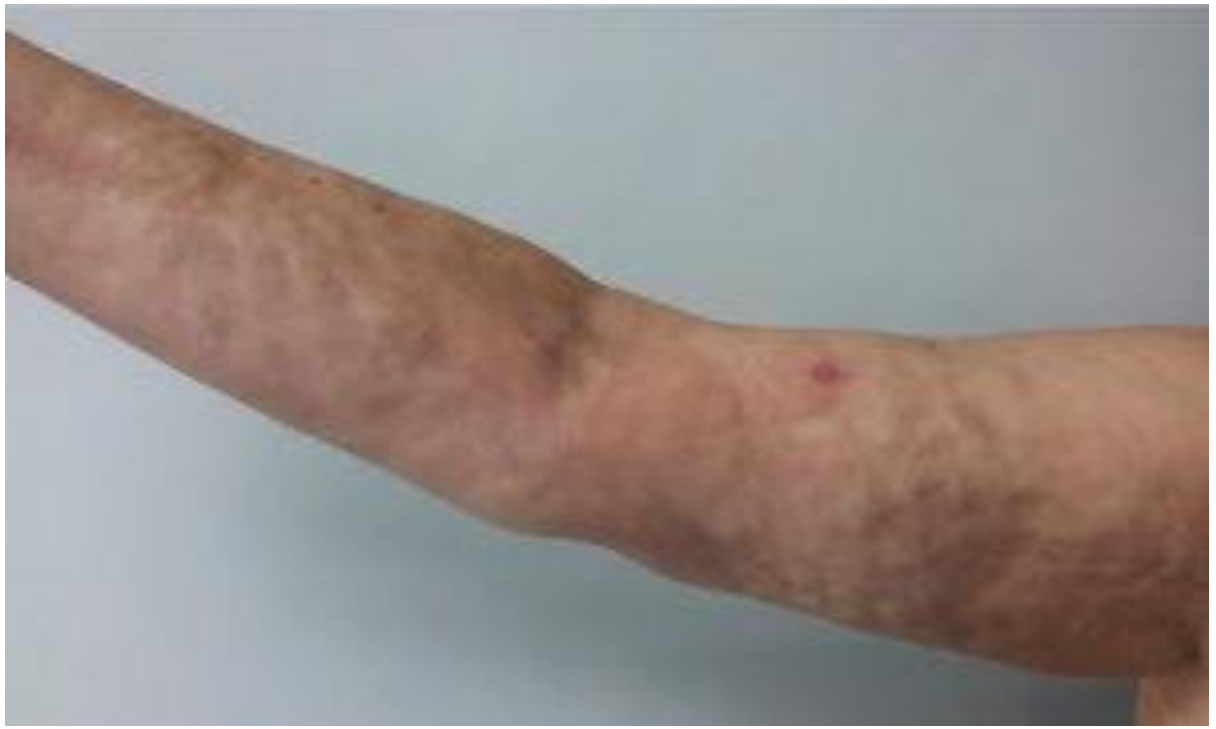
Sclerosing Disorders 3.

Systemic idiopathic sclerosing disorders

Disorder	Features
Systemic sclerosis	Raynaud's; dysphagia, GERD, facial involvement, ANA
Scleromyxedema	Facial involvement, circulating monoclonal paraprotein (usually IgG lambda)
Eosinophilic fasciitis	Joint stiffness, eosinophilia (intermittent), spares digits and toes

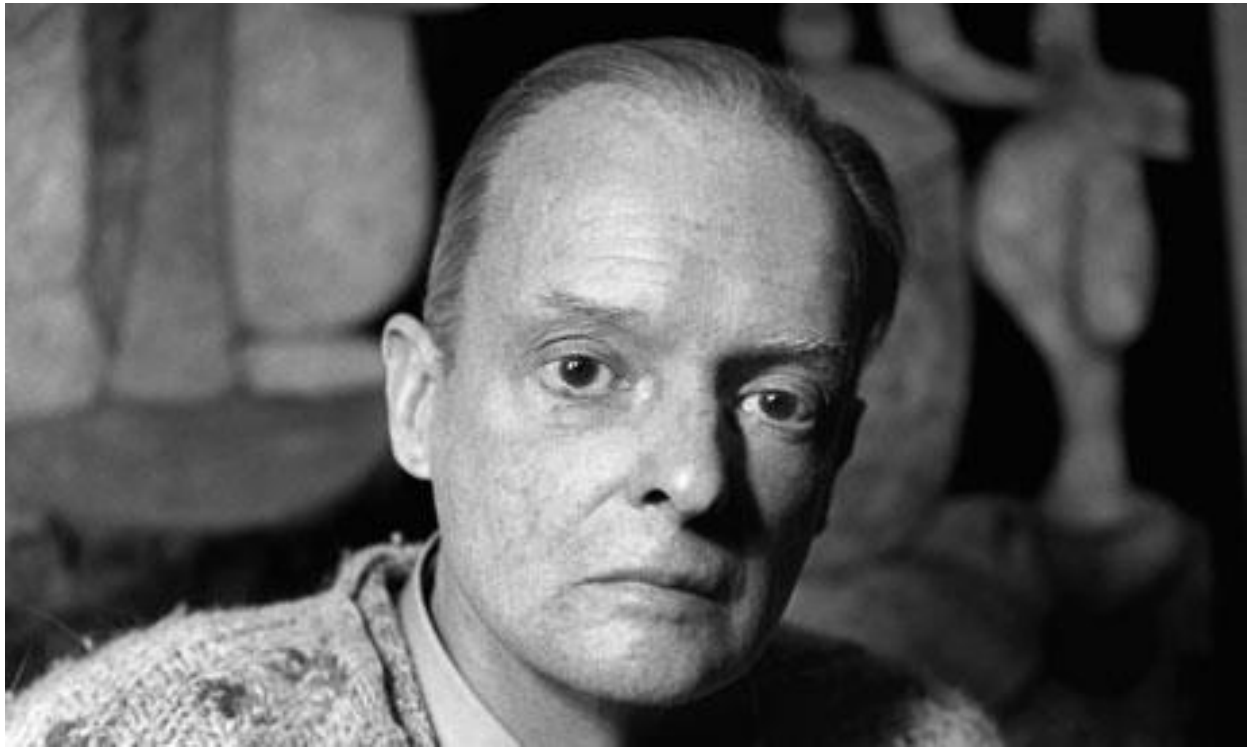
”Groove-sign” in eosinophilic fasciitis





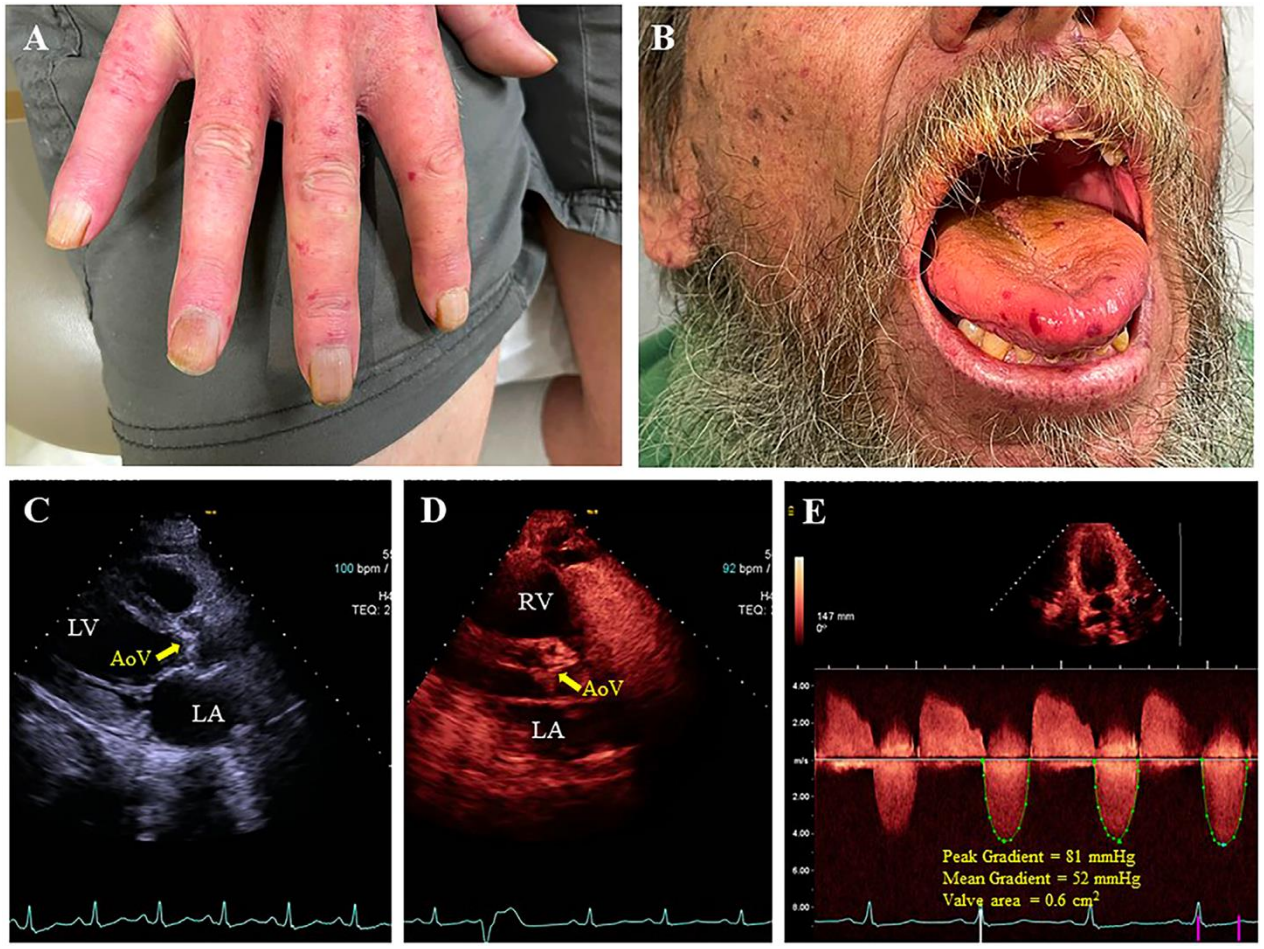
Systemic sclerosis—evolution of a disease

Paul Klee as a young man



Paul Klee with advanced systemic sclerosis

Systemic sclerosis

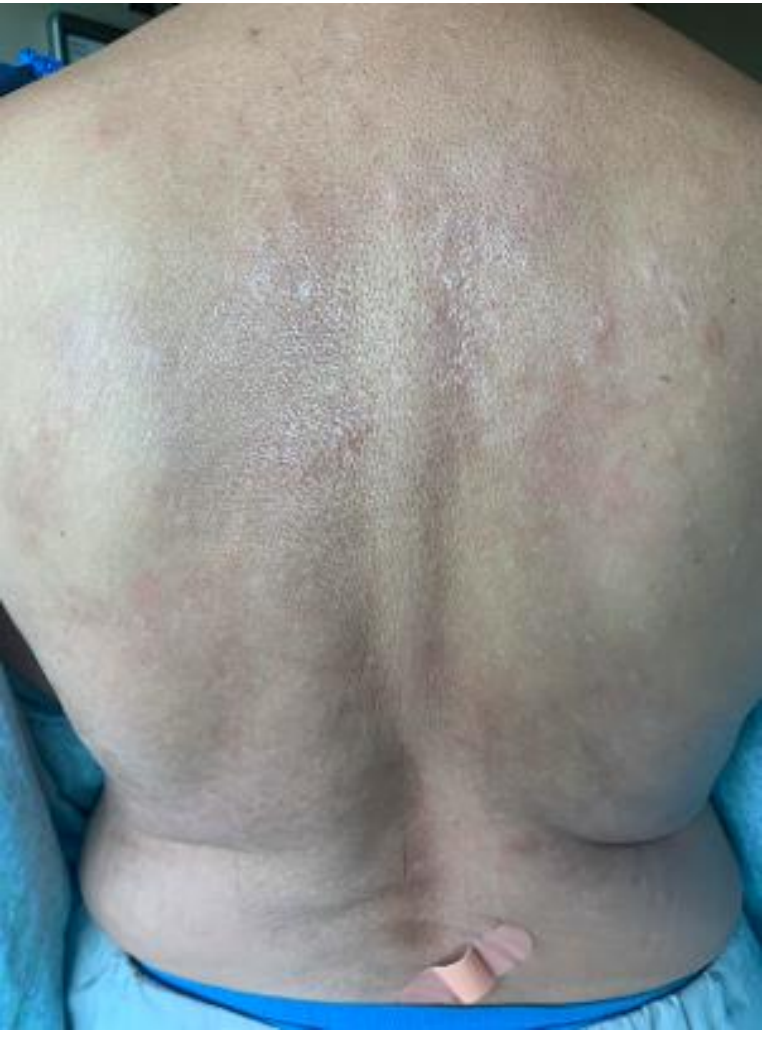


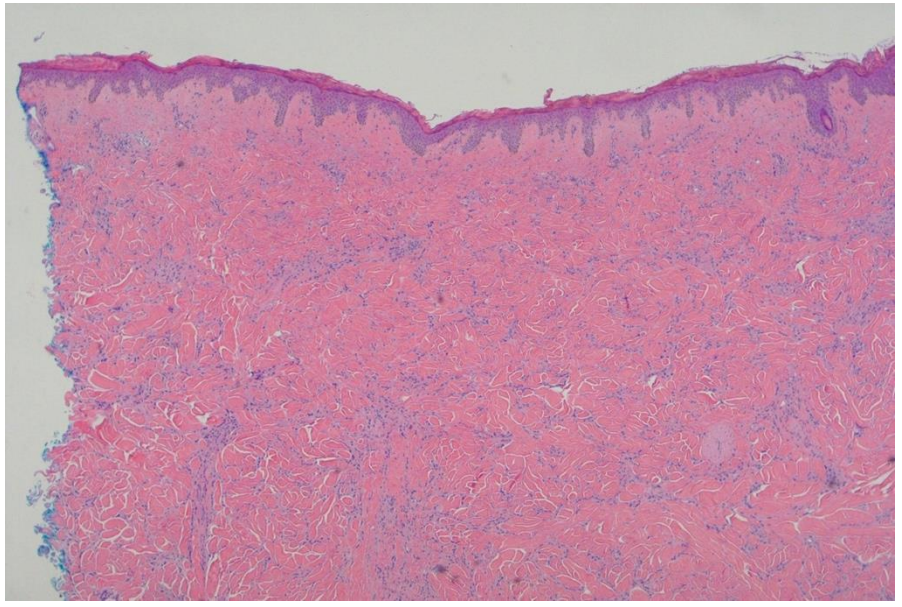
Konstantinov KN, et al. Sclerodactyly, Tongue Telangiectasias, Premature Severe Aortic Stenosis, and RNA Polymerase III Autoantibodies in a Patient with Syncope. *Am J Med.* 2024.

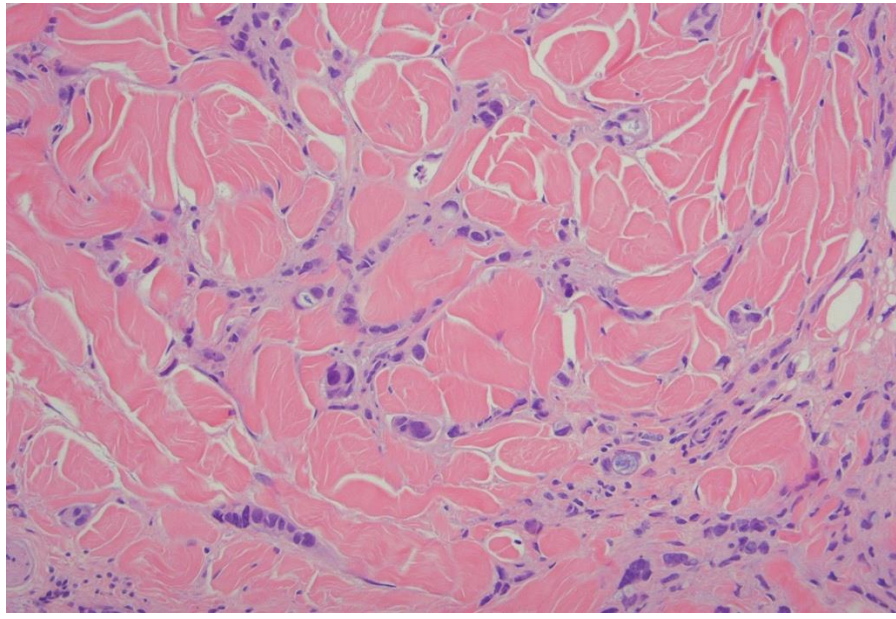
Notable Mimickers of Sclerosing Disorders

Morphea	Systemic sclerosis
• Conditions listed in prior slides • Extra-genital lichen sclerosus • Panniculitis various causes	• Conditions listed in prior slides • POEMS syndrome • Remitting, seronegative, symmetric synovitis with pitting edema (RS3PE) • Diabetic cheiroarthropathy • Myxedema • Porphyria cutanea tarda

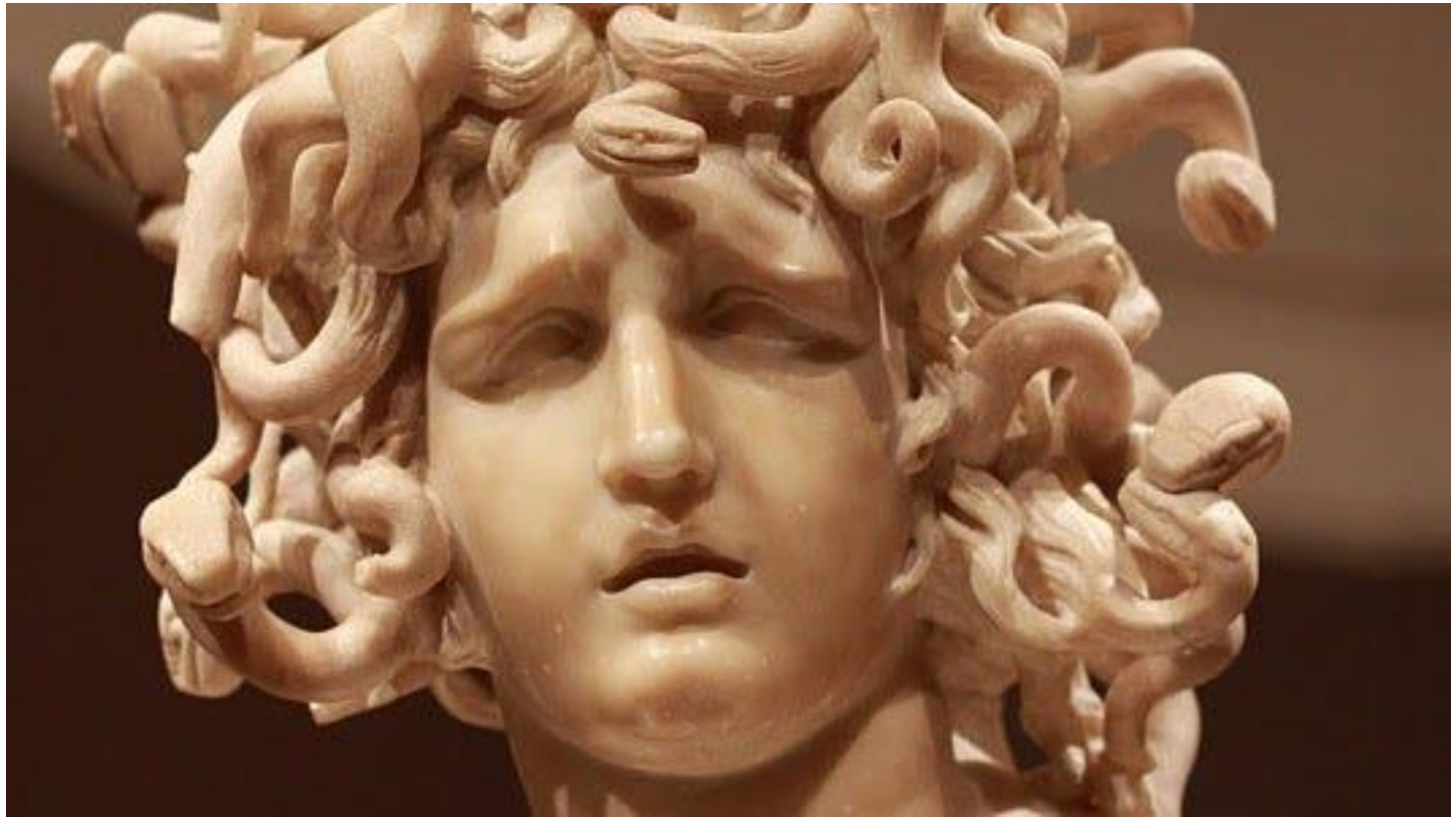
Carcinoma en cuirasse







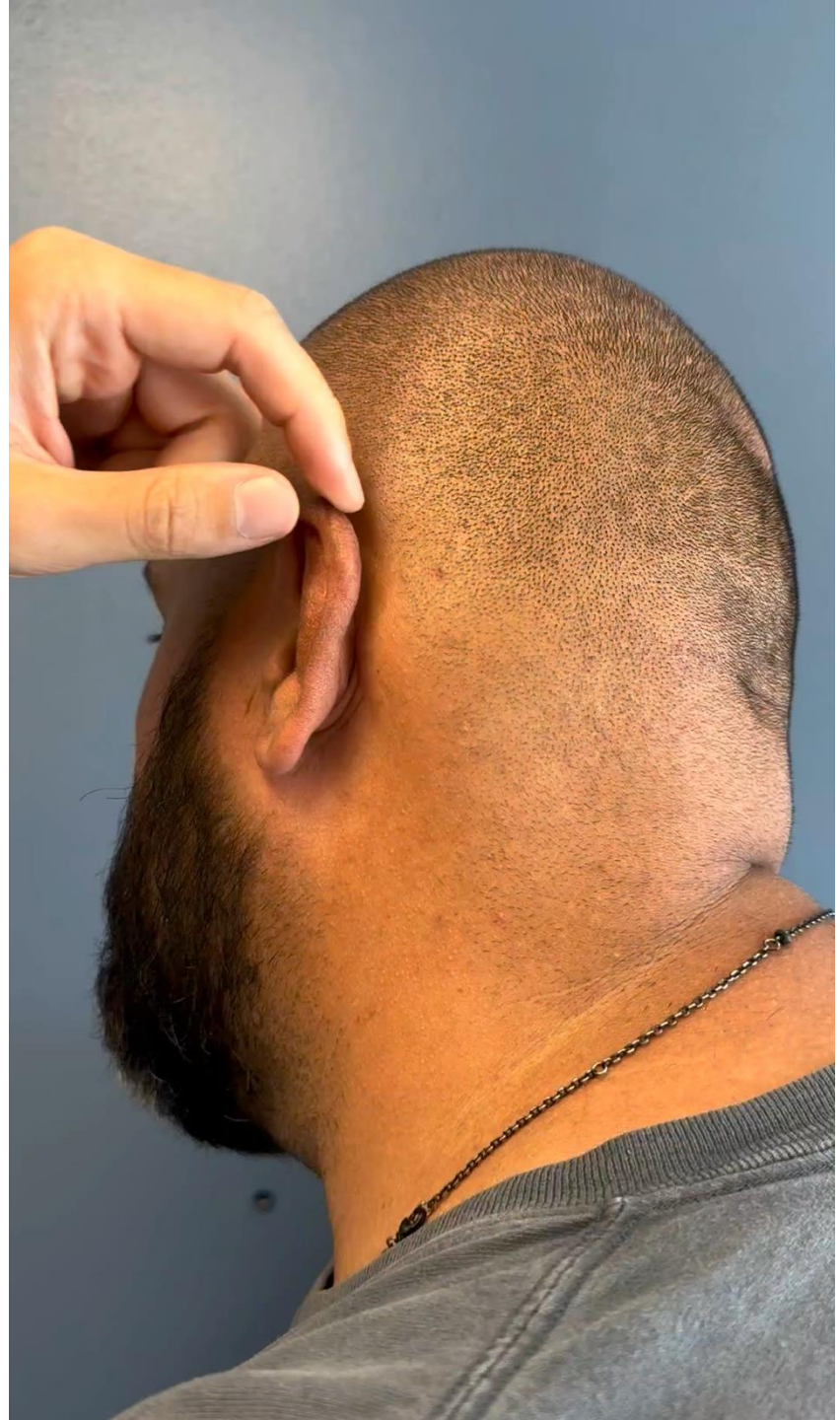
Ears as Hard as Stone



History

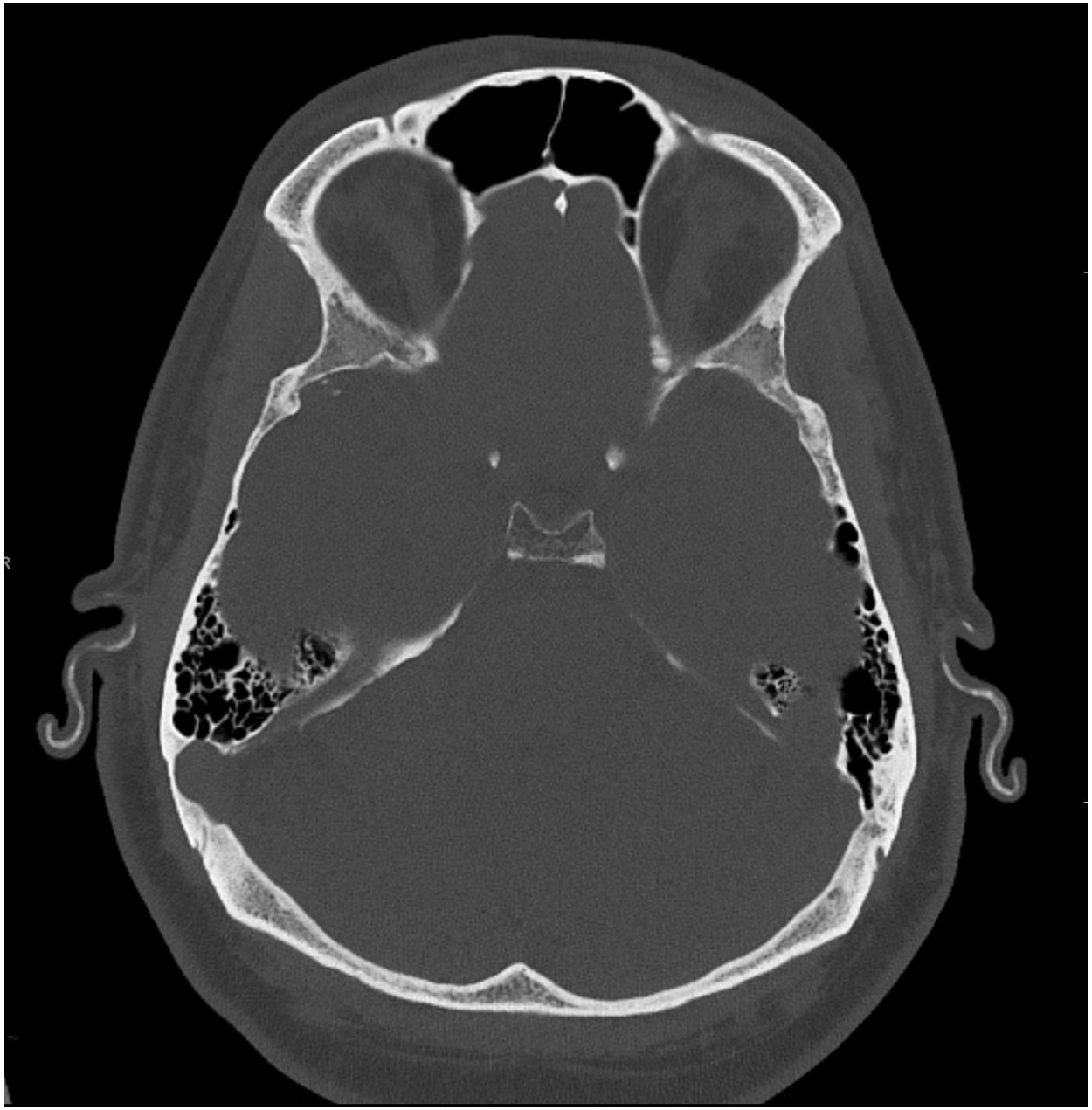
- A 48-year-old male with a history of Hashimoto's thyroiditis, Addison's disease, and IgA vasculitis presented to clinic for progressive stiffening of his ears.

- He noted a ten-year history of a non-painful stiffening of both ears, without acute hearing loss or tinnitus



CT non-contrast head:

Diffuse, smooth ossification of the auricles bilaterally



Petrified Ears

- Clinical entity that describes auricular cartilage hardening due to ectopic calcification of ossification
- Rare condition, but most commonly associated with endocrinopathies, particularly with adrenal insufficiency
- May also see as part of autoimmune polyendocrine syndrome type 2 (characterized by at least 2 of the 3 following endocrinopathies:
  - Type 1 diabetes mellitus
  - Autoimmune thyroiditis
  - Addison's disease
- Condition may precede endocrinopathy
- Therapy can involve surgical resection, but generally asymptomatic and not needed

Valea A, et al. Endocrine Petrified Ear: Associated Endocrine Conditions in Auricular Calcification/Ossification. *Diagnostics.* 2024.

Epilogue

- Familiarity with cutaneous manifestations of autoimmune disease should also involve consideration of important mimickers
- Skin biopsies are usually helpful, but changes in autoimmune disorders are often subtle or may be nonspecific, and familiarity with clinical morphology may be more helpful in diagnosis
- Multidisciplinary approach is often essential in the accurate diagnosis, management and follow-up of patients with autoimmune disease

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