Clinical Pearls in Autoimmune Connective Tissue Diseases

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Case 1

A 49-year-old female presents with an itchy rash on face, chest and hands which began last summer. It is unresponsive to topical steroids.

PMH: asthma, migraines
ROS: shortness of breath and headaches
PE: skin findings, audible wheezing, normal muscle strength
Labs: + ANA, normal: CBC, renal function, LFTs, CK, aldolase
Biopsy: interface dermatitis, c/w lupus

What test(s) are the most important to obtain?

A. CXR, mammogram*
B. Patch testing
C. Lupus serologies
D. Tissue transglutaminase
E. Photosensitivity testing

Dermatomyositis

- Amyopathic Dermatomyositis
  (Dermatomyositis sine myositis)
- Association: internal malignancy (lung, breast, ovary
Interface dermatitis... a potential “pathologic pitfall”

- **DDX:**
  - Lupus
  - Dermatomyositis
  - Graft versus host disease
  - CTCL
  - Drug reaction
  - Lichen sclerosus
  - Etc.
- Cutaneous lupus and dermatomyositis can look identical under the microscope!
- Dermatopathologists usually include a differential diagnosis and suggest that “clinical pathologic correlation” is necessary... but not always.

**Skin Signs of Dermatomyositis**

- *Heliotrope rash*
- *Gottron’s papules*
- *Photosensitivity/photo-distribution*
- *Confluent macular violaceous erythema*
- *Poikiloderma*
- *Gottron’s sign*
- *Periorbital edema*
- *Scalp erythema, pruritus, hair loss*
- *Periungual erythema, telangiectasia, cuticle overgrowth, cuticle hemorrhage- infarct*
- *Mechanic’s hands*
- *Oral ulcers, lichenoid changes, pain*
- *Shawl sign*
- *V-sign*
- *Holster sign*
- *Calcinosis cutis*
- *Ulcers and bullae*
- *Panniculitis*
- *Ovoid Palatal Patch*
- *Red-on-white patches*
- *Palmar papules (inverse Gottron’s papules)*
- *Flagellate erythema*
- *Etc.*

**Important Symptom**

- Pruritus!

**Clinical Pearls: Dermatomyositis**

- Pathologic Pitfall: interface dermatitis is seen in both lupus and dermatomyositis
- Dermatomyositis is often misdiagnosed as cutaneous lupus erythematosus
- Dermatomyositis has LOTS of skin signs and a symptom (ITCH!) that help to differentiate it from cutaneous lupus
- Important to diagnose and differentiate! Dermatomyositis is a skin sign of internal malignancy
Case 2

A 69-year-old female develops a new rash on chest, arms, hands and hairline this summer. It is unresponsive to topical steroids.

PMH: HTN, hyperlipidemia, GERD

Meds: dexamethasone, amlodipine, naproxen, atorvastatin

Biopsy: interface dermatitis

DIF: particulate staining with IgG

Labs: + ANA, SSA, SSB

What medication do you think induced her Subacute Cutaneous Lupus Erythematosus?

A. Dexamethasone*
B. Amlodipine
C. Atorvastatin
D. Naproxen
E. None of the above

Subacute Cutaneous Lupus Erythematosus: Mayo Clinic Experience, 1996-2011 90 patients

- Photodistributed: upper back, chest, arms, neck. Central face spared!
- Non-scarring
- Papulosquamous (58%) or Annular
- 20% met criteria for SLE, only 1 patient had serious systemic disease
- Anti-Ro (SS-A): 99%
- 74% respond to antimalarial therapy
- 12% Drug-induced SCLE

Drug-induced SCLE: New drug categories!

2009

- Antihypertensives 34.2%
- Antifungals 25.6%
- Chemotherapeutics 8.5%
- Antihistamines 7.7%

2017
Proton pump inhibitors 35.8%
- Chemotherapeutics 21.1%
- Biologics 12.8%
- Antihypertensives 5.3%

**Drug-Induced SCLE**
- Proton pump inhibitors
- TNF-α inhibitors
- Hydrochlorothiazide (including combo drugs)
- Calcium channel blockers
- ACE-inhibitors
- Beta blockers
- Terbinafine
- Griseofulvin
- Select NSAIDs
- Anti-seizure drugs
- Docetaxel, paclitaxel, tamoxifen etc.
- Statins
- Interferon a and b
- Antibiotics
- Etc.

**Clinical Pearls: Subacute Cutaneous Lupus Erythematosus**
- SCLE is not always annular, the psoriasiform variant is common!
- Review medications in any case of lupus
- Drug-induced SCLE is caused by some pretty common drugs. . .
- Proton pump inhibitors are a potential culprit

**Case 3**

*57-year-old female presents in May with new mouth findings, her dentist sends her for treatment of lichen planus*

PMH: dx with discoid lupus one year ago. At that time, a biopsy and DIF were consistent with lupus. She was treated with steroids and hydroxychloroquine and it resolved. She has stopped treatment.

PE: chest, scalp plaques and mouth

Mucosal Biopsy: atypical squamous proliferation, favor reactive, DIF: c/w lichenoid tissue reaction

**What do you think is the diagnosis of the new oral changes?**

A. Oral erosive lichen planus

B. Discoid lupus and oral lichen planus
C. Discoid lupus*

D. Drug reaction

E. None of the above

**Discoid Lupus Erythematous**

- Most common form of cutaneous lupus
- Head and neck (80%), especially scalp and conchal bowl
- Red, scaly plaques
- Spreads peripherally leaving atrophic central scarring with alopecia, telangiectasia and dyspigmentation
- Adherent “carpet tack” scale: follicular involvement

**Oral Discoid Lupus Erythematous**

- 24% of discoid lupus patients have mucosal involvement
- Chronic “lichen planus-like’’ plaques
- Central atrophic red area with white dots and irradiating white lines
- Honey comb appearance
- Buccal mucosa, palate, alveolar process at site of missing teeth
- Underestimated: asymptomatic

**Clinical Pearls: Oral findings in Discoid Lupus**

- Oral findings are common in patients with cutaneous lupus. . .look for them!
- Malignant transformation of oral lupus has been described.

**Case 4**

*57-year-old male presents with 2 months of swelling of arms and leg. Now he has rapid onset of tightness and constriction of the extremities.*

PMH: prostate ca, asthma  ROS: No Raynaud’s

PE: Symmetric arm & leg erythema & induration, decreased range of motion at ankle and wrist, no sclerodactyly, no nail fold capillary changes

Labs: CBC with eosinophilia 1.4, CRP 30.1

Negative: ANA, Scl70, anti-centromere, SPEP

MRI: thickening, edema and enhancement of superficial and deep fascia

Biopsy: c/w eosinophilic fasciitis

**What do you think is the best initial treatment?**

A. Topical clobetasol

B. Narrow band UVB
C. Methotrexate or mycophenolate mofetil
D. Systemic corticosteroids +/- methotrexate*
E. TNF-α inhibitor

**Eosinophilic Fasciitis (Shulman’s Disease)**
- Abrupt onset of edema, erythema, then induration
- Extremities, generally sparing digits, trunk
- +/- Inflammatory arthritis
- Peripheral eosinophilia
- Negative autoantibodies
- Fascial thickening on MRI and/or deep incisional biopsy
- Controversy: morphea variant, up to 50% have concurrent morphea
- Association: Hematologic disorders such as aplastic anemia, lymphoma and leukemia

**DDX:**
- Systemic sclerosis
- Scleromyxedema
- Scleredema
- Nephrogenic systemic fibrosis
- Deep or pansclerotic morphea
- Eosinophilic disorders

**Skin Signs**
- Groove Sign or Dry Riverbed Sign (elevate!)
- Dimpling or Pseudo-cellulite sign

**Eosinophilic Fasciitis: Mayo Clinic Experience, 1997-2016, 83 patients**

**Clinical features:**
- Groove sign 29%
- Dimpling 25%

Exercise as a possible trigger in 25%

9.5 months to diagnosis (range 1-45)

**Treatment:**
- Complete response 57%
- Diagnostic delay inversely associated with treatment response
- Most common treatment: systemic steroids +/- methotrexate
- Recurrence rate 47%

**Therapy: Eosinophilic Fasciitis**
- Multisite, retrospective review
- 63 cases
- 11 months to diagnosis (79% of patients were initially misdiagnosed)
- Complete response most likely with combination of systemic corticosteroids and methotrexate 21/33 (64%)

**Clinical Pearls: Eosinophilic Fasciitis**

- Abrupt onset of edema and progressive induration of the extremities, skin signs, peripheral eosinophilia, fascial thickening on MRI and/or biopsy
- Incisional biopsy including fascia is gold standard
- Early, aggressive treatment for an aggressive disease: systemic corticosteroids +/- methotrexate

**References**


