Cutaneous Manifestations of Systemic Diseases

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Disclosure

• I have no relevant conflicts of interest to disclose.
• I will be discussing off-label uses of medications.

Learning Objectives

• Identify classic cutaneous findings of rheumatologic disease
• Compare therapeutic options available for the treatment of cutaneous diseases

Case 1: 19yo F with rash and fatigue

• College Athlete
• Previously healthy
• C/o fatigue, arthralgias, rash on face, hands, and feet
Case 1: 19yo F with rash and fatigue

- Based on this photo, what are you worried about?
  - Psoriasis
  - Dermatomyositis
  - Contact Dermatitis
  - Cutaneous Lupus
  - Scleroderma

Case 1: Cutaneous Lupus

- Erythematous scaly plaques
- Slight violaceous hue
- Spares knuckles
- Periungual erythema
- Systemic symptoms
  - Fatigue
  - Arthralgias

Cutaneous Manifestations of Lupus

Lupus-Specific: Diagnostic Clues
- Acute (50% of SLE)**
- Subacute (10% of SLE)
- Chronic
  - Discoid**
  - Tumid
  - Chilblain

Lupus-associated (NOT specific)
- Markers of Disease Activity
  - Non-scarring alopecia (70% of SLE)
  - Photosensitivity **
  - Vasculitis, vasculopathy
  - Raynaud’s (33% of SLE)
  - Bullous dermatosis
  - Pyoderma Gangrenosum
  - Erythema multiforme
  - Livedo reticularis
  - Oral ulcers**
  - Leg ulcers
  - Periungual erythema
  - Purpura (15% of SLE)
  - Urticaria (10% of SLE)

**4/11 of the ACR Diagnostic Criteria for SLE are cutaneous
ACR Criteria for SLE

1. Malar Rash
2. Photosensitivity
3. Discoid Lesions
4. Oral Ulcers
5. Arthritis
6. Serositis
7. Renal Disorder
8. Neurologic Disorder
9. Hematologic Disorder
10. ANA
11. Immunologic Disorder

• 4/11 Criteria for diagnosis
• Must include 1 clinical and 1 lab
• OR biopsy-proven lupus nephritis and +ANA or +dsDNA
• Criteria do not need to be simultaneous

SLICC Criteria for SLE

CLINICAL CRITERIA
1. Acute cutaneous lupus
2. Chronic cutaneous lupus
3. Oral or nasal ulcers
4. Non-scarring alopecia
5. Arthritis
6. Serositis
7. Renal
8. Neurologic
9. Hemolytic anemia
10. Leukopenia
11. Thrombocytopenia

IMMUNOLOGIC CRITERIA
1. ANA
2. Anti-DNA
3. Anti-Smith
4. Antiphospholipid antibody
5. Low complement (C3, C4, CH50)
6. Direct Coombes’ test

At least 4 criteria (including 1 clinical and 1 laboratory) or biopsy-proven lupus nephritis with positive ANA or anti-DNA

Acute Lupus Mimics

- Lupus
- Rosacea
- Dermatomyositis

Acute Lupus Mimics

- Lupus
- Pellagra
Acute Cutaneous Lupus

- Photosensitive
- Spares NL folds and knuckles
- Non-scarring
- Highly associated with systemic lupus
- Need full systemic workup

Sun Protection

- High SPF (50+) physical blockers
  - Zinc oxide or Titanium dioxide
  - Apply 20-30min prior to sun exposure
  - Reapply Q1.5 hours
  - 1 oz per application
- Behavior
  - Clothing
  - Shade

Sun Protection

http://www.rheumaderm-society.org/protecting-your-skin-from-the-sun/

ACLE Treatment

- Sun Protection
- Topical Steroids
- Hydroxychloroquine
- Prednisone
- *Consider Vitamin D Status
- Eval and treat for SLE
Case 2: 78yoM with eruption x 2 wks

- Started after sun exposure
- Pruritic
- Progressive
- Unresponsive to OTC tx
- PMH: SLE, HTN, GERD, asthma, cardiomyopathy

Case 2: 78yoM with eruption x 2 wks

- What is your diagnosis?
  - Tinea corporis
  - Annular actinic granuloma
  - Subacute cutaneous lupus
  - Sarcoidosis
  - Annular psoriasis
**Subacute Cutaneous Lupus Erythematosus**

- 2 Morphologies
  - Annular
  - Psoriasiform Papulosquamous
- Neck, torso, UE
- Typically spares the face

**Subacute Cutaneous Lupus Erythematosus**

- 50% of SCLE have SLE, 10% of SLE have SCLE
- 85% of SCLE are photosensitive (2x more than SLE)
- >80% positive for anti-Ro/SSA Ab
- Idiopathic (2/3) indistinguishable from drug-induced SCLE (1/3)

**Implicated Drugs**

- ACE inhibitors
- Antiarrhythmics
- Anticonvulsants
- Antifungals (*terbinafine*)
- Antihistamines
- Antineoplastics
- Beta-blockers
- Calcium channel blockers
- Diuretics
- Immune modulators
- Lipid-lowering agents
- NSAIDs
- Proton-pump inhibitors
- Sulfonylurea
- TNF-alfa inhibitors
- Other (D-penicillamine, bupropion, ticlopidine, ranitidine)

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**Our Patient:**

- ANA: + 1:640
- SS-A Ab: 151
- SS-B Ab: 146

-- RECENTLY STARTED DILTIAZEM
**Drug-induced SCLE**

- PPI-induced SCLE
- Terbinafine-induced SCLE
- Diltiazem-induced SCLE

**Annular SCLE Mimics**

- Annular Psoriasis
- Tinea
- Sarcoid
- SCLE
- Granuloma Annulare

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**Subacute Cutaneous Lupus Erythematosus**

- Photo-distributed/upper torso and proximal extremities
- Non-scarring
- Annular or psoriasiform/papulosquamous
- Moderately associated with systemic lupus
- May be drug-induced
- Associated with SSA/anti-Ro Ab

**Treatment:**
- Topical steroids
- Sun protection
- Anti-malarials
- Systemic steroids
- D/c offending drug

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**Case 3: 60yoF with scarring rash**

- 6mo h/o eruption on back, arms, ears, face
Case 3: 60yoF with scarring rash

- What is your diagnosis?
  - Phototoxic Drug reaction
  - Psoriasis
  - Discoid Lupus
  - Lichen planopilaris
  - Subacute cutaneous lupus

Case 3: 60yoF with scarring rash

- What is your diagnosis?
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  - Psoriasis
  - Discoid Lupus
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  - Subacute cutaneous lupus

Discoid lupus

- Type of “chronic” cutaneous lupus
- Head and Neck, Conchal bowls, upper torso, UE
- Central scarring
- Peripheral erythema/hyperpigmentation
- Follicular plugging
- Scarring alopecia
- LOW assoc with SLE (5-20%)
- ANA positivity 35%
Discoid Lupus: Treatment

- Strict photoprotection
- Antimalarials
- Topical steroids
- Intrallesional steroids
- Steroid-sparing agents, thalidomide
- Treat aggressively to avoid permanent scarring, hair loss, and disfigurement
- Smoking cessation

Which topical steroid?

- Clobetasol
- Triamcinolone 0.1%
- Desoximetasone
- Fluticasone
- Desonide
- Hydrocortisone 2.5%

Apply BID, 2 weeks on, 1 week off, d/c when flat

Topical Steroids

- Amount:
  - Body >60g, Triamcinolone comes in 1lb jar (454g)
  - Face 30g

- Vehicle: cream or ointment?
  - Ointment is more hydrating and stronger
  - Consider location and patient preference
  - Solution for scalp if patient does not like greasiness on hair
  - Oils and foams are also available

Topical Steroids

- Counseling:
  - Avoid eyes
  - Stop when lesions are no longer palpable
  - Continuous use increases risk of:
    - Atrophy
    - Telangiectasia
    - Striae
Topical Calcineurin Inhibitors

- Good for thin-skinned areas, periocular and during breaks from topical steroids
- Tacrolimus 0.1% and 0.3% ointment
  - Generic in 2014
- Pimecrolimus cream
  - Less greasy, not as strong
- How to choose?
  - Patient preference
  - Insurance formulary
Case 4: 72yoF with rash and weakness

- No medical care in 37y
- What is your clinical Dx?
  - Systemic Lupus
  - Dermatomyositis
  - Scleroderma
  - Sarcoidosis
  - Paraneoplastic syndrome

Dermatomyositis

http://images.all-free-download.com/images/graphiclarge/vanilla_flower_heliotrope_solstice_228847.jpg

Courtesy of RA Vleugels MD MPH
Lupus vs Dermatomyositis

- Lupus spares NL folds
- DM “hugs” the NL folds

Lupus vs Dermatomyositis

- Lupus spares the knuckles
- DM favors the knuckles with Gottron’s papules

Dermatomyositis

- Clinically Amyopathic—no clinical muscle disease for >2y after appearance of classic skin findings
- Both classic and amyopathic forms in adults may be associated with cancer or lung disease
- Risk of cancer remains elevated for 3-5 years

Dermatomyositis

- Associated Malignancies
  - Lung
  - Breast
  - Ovary
  - Colorectal
  - Cervix
  - Bladder
  - Nasopharyngeal
  - Esophageal
  - Pancreatic
  - Kidney
  - Lymphoproliferative/Hematologic
Cancer-associated DM

- Best data suggest that **18-32%** of patients with dermatomyositis have or will develop a malignancy
- Risk highest in the first **3 years after diagnosis**; remains elevated for at least 5 years
- GU cancers are overrepresented

Case 4: 72yoF with rash and weakness

- What further workup is recommended?
  - CBC c diff, CMP, aldolase, CK, LDH
  - Myositis panel
    - Including P155/140 (tif1-γ) antibody
  - Age appropriate screening
  - Colonoscopy
  - Mammogram
  - Low-dose Chest CT
  - Pelvic ultrasound
    - Additional w/u based on age and symptoms

Dermatomyositis Work-up

- Myositis-specific antibodies (+ in 30%)
  - Anti-Mi-2: + in 25%, most specific for classic DM
  - Anti-Jo-1: pulmonary dz, poor prognosis
  - Anti-p155/140 (tif1-γ): assoc with malignancy
  - Anti-MDA-5: lung disease and skin ulcers

DM associated with Breast CA

- Positive anti-p155/140 (tif1-γ)
- Axillary LN 1.4cm
  - Bx: metastatic breast CA
- Breast MRI: 6mm focus
  - Invasive ductal carcinoma

- Treatment:
  - Prednisone for dermatomyositis
  - Letrosone: oral non-steroidal aromatase inhibitor
  - Surgery/radiation
  - Plaquenil
  - Gabapentin for pruritus
Dermatomyositis Antibodies

- Myositis-specific antibodies (+ in 30%)
  - Anti-Mi-2: + in 25%, most specific for classic DM
  - Anti-Jo-1: pulmonary dz, mechanic’s hands
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Courtesy of RA Vleugels

Dermatomyositis Antibodies

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Courtesy of RA Vleugels
Treatment

- Photoprotection
  - High SPF physical blockers
  - Sun avoidance
  - Consider vitamin D status
- Topicals
  - Corticosteroids
  - Calcineurin inhibitors
- Systemic
  - Antimalarials
  - Methotrexate, mycophenolate mofetil, azathioprine, IVIG, dapsone, thalidomide
  - Steroids are more effective for myositis
  - Vasodilation/anticoagulation in MDA-5
- Pruritus is often the #1 complaint—consider doxepin, gabapentin

Case 5: 55yo with darkening skin

Systemic Sclerosis

- Bound-down skin
Systemic Sclerosis

- Calcinosi cutis
- Raynaud’s
- Esophageal dysmotility
- Sclerodactyly
- Telangiectasias
- anti-centromere Ab
- More benign course than progressive systemic sclerosis

Limited Scleroderma

Calcinosis Cutis

Raynaud’s
Systemic Sclerosis

- Progressive **Systemic** Sclerosis
  - "Square" skin biopsy
  - Other organ system involvement
  - Pulmonary, GI, Renal, Cardiac
- CREST syndrome (Limited Scleroderma)
- Morphea—localized scleroderma WITHOUT systemic features
  - Usually lack sclerodactyly, acral/distal extremity involvement

Treatment

- Raynaud’s
  - Keep core warm, layered clothing
  - Avoid triggers
  - Avoid smoking, excess caffeine
  - Calcium channel blockers
  - PDE-5 inhibitors
  - Consider Botox, statin, SSRI
- Physical therapy
- Emollients
- Pulse-dye laser for telangiectasias
- Systemic therapy for scleroderma

Case 6: Persistent psoriasis?

- 35yo M
- 10yo Ps/PsA
- On adalimumab
- Joints well-controlled

- Skin clear except feet...why?
Case 6: Persistent psoriasis?

Psoriasis and red, scaly rashes

Case 6: Psoriasis and psoriatic arthritis

Psoriasis and red, scaly rashes

Case 6: Persistent psoriasis?

- Tinea incognito
- STOP topical steroids
- Treat with topical antifungal BID x 4 weeks
- May need oral antifungals
  - Terbinafine 250mg/d
  - 2 week course for skin
  - 6 weeks for fingernails
  - 12 weeks for toenails
What about treating psoriasis?

- Topical steroids
  - Consider body site in choosing:
    - Vehicle
    - Potency
  - 2 weeks/month
- Topical vitamin D analogs
  - Calcipotriene, Calcitriol
  - No atrophy risk
- Topical calcineurin inhibitors
- Topical retinoids
- Keratolytics for thick scale
  - Urea
  - Salicylic acid

Case 7: 55yo with RA and painful ulcer

- RA x decades
- Meds:
  - Prednisone 10mg/d
  - Adalimumab
- PMH:
  - Pulmonary fungal infection 5y ago

• What is the next step?
  - CBC
  - Increase steroids
  - Start antibiotics
  - Biopsy for H&E, bug stains and tissue cx
  - Wound debridement
55yo with RA and painful ulcer

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  - CBC
  - Increase steroids
  - Start antibiotics
  - Biopsy for H&E, bug stains and tissue cx
  - Wound debridement

55yo with RA and painful ulcer

- In the setting of immune suppression, you MUST rule out infection

  - Pyoderma Gangrenosum is a diagnosis of exclusion

Pyoderma Gangrenosum

- Autoinflammatory
- Ulcer(s) with rolled, dusky violaceous borders and cribiform scarring
- Associated with inflammatory bowel disease, inflammatory arthritis, and hematologic disorders

Pyoderma Gangrenosusm

- Hallmark is “Pathergy”
- Seemingly minor trauma induces new or expanding ulcers

  - Do not let fear of pathergy stop you from performing bx and cx!
What to do while awaiting bx/cx?

- Non-immunosuppressive option for initial tx

Minocycline

- Non-immunosuppressive option for initial tx while biopsy and culture are pending

PG Treatment

- Consider underlying disease(s)
- Control inflammation
- Control exacerbating factors
  - Smoking cessation
  - Adequate nutrition
  - Venous stasis
- Local Wound Care
- Prevent Pathergy
- Pain Management
- Augment Healing

PG Treatment

- Topical medications
  - High potency corticosteroids
  - Calcineurin inhibitors
  - Dapsone
    - 5% gel or crushed tablets
    - Cyclosporin drops
- Non-stick dressings
- Compression if tolerated
Pyoderma Gangrenosum

- >50% associated with systemic disease
- Hallmark is pathergy but only present in 1/3
- 80% on the lower extremity
- DDx includes infection
- Tx: anti-inflammatory/immunosuppressive meds, local wound care, attention to nutrition other risk fx

Case 8: 35yo M with facial lesions

- What is your diagnosis?
  - Lupus pernio
  - Sarcoidosis
  - Lupus vulgaris
  - Discoid lupus
  - Pernio

Case 8: 35yo M with facial lesions

- What other system are you most worried about?
  - Cardiac
  - Renal
  - Pulmonary
  - GI
  - Neuro
35yo M with facial lesions

- What other system are you most worried about?
  - Cardiac
  - Renal
  - Pulmonary
  - GI
  - Neuro

Sarcoidosis

- Non-caseating granulomas
- Often in scars/sites of trauma
- Elevated ACE levels
- May be systemic:
  - Pulmonary (90%)
  - Cardiac

Sarcoidosis

- Multi-system Disease with many possible cutaneous manifestations
- “Great mimicker”
- Lupus pernio is assoc with pulmonary disease

Case 9: 50yo F with ANA+ and ulcers

- PMH: HTN, anemia, fibroids, A-fib
- Painful LE ulcers
Calciphylaxis

- Rare and serious disorder
- Progressive systemic calcification of arterioles → ischemic necrosis
- Violaceous reticulated patches → necrotic ulcers
- Most commonly occurs in patients with end-stage renal disease
- Alterations in calcium, phosphate, vitamin D, and parathyroid hormone

Non-uremic calciphylaxis

- Reported predisposing factors:
  - Corticosteroid use
  - Warfarin use
  - Underlying diabetes mellitus
  - Albumin or blood transfusion
  - Protein C or S deficiency
  - Trauma
Caliphylaxis--Treatments

- Pain control
- Local wound care
  - High risk of infection/sepsis
  - Non-stick dressings
- Systemic treatment
  - Sodium thiosulfate
  - Cinacalcet
  - Bisphosphonates
- Eliminate exacerbating factors if possible
  - Coumadin
  - Systemic steroids
- Debridement is controversial

Thank you

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