Dermatology Grand Rounds 2019

*skin signs of internal disease*

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“Normal” abnormal skin findings in internal disease
- Thyroid
- Renal insufficiency
- Diabetes

“Abnormal” skin findings as clue to internal disease
- Markers of infectious disease
- Markers of internal malignancy risk

“Consultation Cases”
- Very large dermatology finding
- A very tiny dermatology finding
The "Red and Scaly" patient

“Big and Small” red rashes not to miss
29 Year old man with two year pruritic eruption
PMHx:
- seasonal allergies
- childhood eczema
- no medications
Erythroderma
Erythroderma

• Also called "exfoliative dermatitis"
• Not stevens-Johnson / toxic epidermal necrosis
  (More sudden onset, associated with target lesions, mucosal)
• Generalized erythema and scale >80-90% of body surface
• May be associated with telogen effluvium

It is not a diagnosis per se
Erythroderma
Erythroderma

Work up
1) Exam for pertinent positives and negatives:
   • lymphadenopathy
   • primary skin lesions (i.e. nail pits of psoriasis)
   • mucosal involvement
   • Hepatosplenomagaly

2) laboratory
   • Chem 7, LFT, CBC
   • HIV
   • Multiple biopsies over time

3) review of medications
4) age-appropriate malignancy screening
5) evaluate hemodynamic stability
Erythroderma

Management
1) remove possible offending medications
   • Medication can be recent or long-standing

2) monitor fluids and hemodynamic stability

3) treat with topicals
   • mid-potency (triamcinolone)0.1% ointment
   • Open-wet dressings

4) treat underlying disease
Erythroderma

Management: open wet dressings
1) bedsheet in warm water; all water wrung out
2) ointment (1 lb jar) applied to total body
3) damp (not wet!) bedsheet placed over body
4) Evaporation / convection of water vapor rapidly repairs skin barrier
5) Repeat q3h

72 hours of therapy:
Which of the following treatments should take priority in any patient with erythroderma?

A. Systemic steroids

B. Oral antibiotics

C. Discontinuation of all unnecessary medications and topical products

D. Topical corticosteroids
Erythroderma

**Categories:**

1) Exacerbation of a skin disorder
   - Atopic dermatitis
   - psoriasis
   - seborrheic dermatitis
   - pityriasis rubra pilaris
   - contact allergic dermatitis

2) Medications

3) Secondary to malignancy
   - CTCL (cutaneous T-cell lymphoma) = Sézary syndrome
   - HTLV-1 disease (adult T-cell leukemia/lymphoma)
   - Paraneoplastic manifestation of internal malignancy
• 35 Year old construction supervisor
• Admitted to local hospital for hypotension
• $70,000 4 day inpatient work-up
• Patient left AMA
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• History by Dermatologist:
  • “I have some psoriasis”
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• Diagnosis = **erythroderma** secondary to psoriasis
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• Diagnosis = **erythroderma** secondary to psoriasis
• **Rx= oral methotrexate**
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Medications Implicated in Erythroderma

- The most commonly implicated drugs include:
  - Anti-epileptics
  - Allopurinol
  - Amiodarone
  - ACE inhibitors
  - Antibiotics
    - Penicillin
    - Sulfonamides
    - Vancomycin
  - NSAIDs
  - Calcium channel blockers
  - Cimetidine
  - Dapsone
  - Gold
  - Isoniazid
  - Lithium
  - Thiazides
  - Quinidine
  - St. John’s wort
• 55 Year old woman
• Hx: DM type 2
• 5 month year history of generalized pruritus and rash
• Exam: + LAD in neck, groin
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• Diagnosis = erythroderma secondary to HTLV-1 disease
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• No history of psoriasis
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  • childhood eczema
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• Diagnosis = biopsy consistent with psoriasis
• No history of psoriasis
Marker of HIV infection:
• New Psoriasis
• or dramatically worse psoriasis or other papulo-squamous disorder
“Abnormal” skin findings as clue to internal disease

• Markers of infectious disease
• Markers of internal malignancy risk
Flexor Wrist

Buccal Mucosa
LICHEN PLANUS

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LICHEN PLANUS

• Purple, pruritic, polygonal papules
• Wickham’s striae - are fine white lines on top of papules
• Koebner phenomenon -
  • in linear groups due to trauma of scratching
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  • in linear groups due to trauma of scratching
• Usually self limiting 2-3 years.
• Rx:
  • Topicals> IM triamcinolone
• Two complications
  • Variable association of 0.1% to 35% with Hepatitis C
  • Evolution to mucosal SCC
SUMMARY OF CUTANEOUS MANIFESTATIONS OF HEPATITIS C VIRUS

• Lichen Planus
• Porphyria Cutanea Tarda
• Polyarteritis Nodosa
• Necrolytic Acral Erythema
• Cryoglobulinemia
• Pruritus
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• not “eczema” not fungus”
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NECROLYTIC ACRAL ERYTHEMA

- Psoriasiform eruption on acral surfaces
- HCV+
- Manifestation of Zinc deficiency
- Treat with zinc supplementation
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PORPHYRIA CUTANEA TARDA

- Vesicles on sun-exposed areas, scarring, milia HCV+
- Hypertrichosis
- Fragile skin with sclerodermoid changes
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- DDx: pseudoporphyrria due to NSAIDS, OCP, etc.
Not true porphyria

- Normal blood urine testing
- Associated with renal disease
- Associated with medications
  - NSAIDS
  - Dapsone - Furosemide - Nalidixic Acid - Tetracycline - Pyridoxine
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• Polyarteritis Nodosa
  • Small vessel vasculitis (LCV = palpable purpura) and
  • Medium vessel vasculitis (nodules on lower extremities)
  • Multi system disease due to ischemic injury
  • Associated with HCV or HBV
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  • Medium vessel vasculitis (nodules on lower extremities) = livedo
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PALPABLE PURPURA IS SMALL VESSEL VASCULITIS

THIS IS MEDIUM VESSEL INJURY
HEPATITIS B OR C

- About 30% may have Urticaria or present a serum sickness like picture (because of circulating immune complexes)
- HBV Associated with 30% of PAN
- Variants are
  - Classical PAN
  - Cutaneous PAN
  - Single organ PAN
  - Childhood PAN (associated with strep infections)
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VASCULAR DISEASES

• 62 year old woman
VASCULAR DISEASES

• 62 year old woman
  • Arthralgias,
  • Elevated LFT
  • Glomerulonephritis
VASCULAR DISEASES

Cryoglobulenemia

- Small vessel vasculitis (LCV = palpable purpura)
- Clotting in vessels: livedo reticularis
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- Clotting in vessels: livedo reticularis

- Systemic symptoms:
  - Arthralgias,
  - Elevated LFT
  - Glomerulonephritis

- Due to:
  - IgG reversibly precipitate in cold
  - Mixed (type 3) polyclonal IgG/IgM

- Associated with
  - HCV
  - Multiple myeloma
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Pruritus

- lesions where can reach
- often in linear arraignment
- multiple phases of healing
- hemmoragic crust: largely unique to trauma (and Herpes infections)
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- Skin findings:
  - linear erosions
  - lichenification
  - Prurigo nodules
PRURITUS

Causes:

- Iron deficiency
- Liver disease
- Malignancy (e.g. Hodgkin’s lymphoma)
- Neurological disorders
- Polycythemia
- Renal failure
- Thyroid dysfunction

Work-up:

CBC, LFT, BUN/Cr, TSH
Chest x-ray
HBV, HCV, HIV
NOT PRURITUS
Dermatitis herpetiformis:

- Symmetric, grouped vesicles on extensors
- Very pruritic
- Associated with Hashiomoito’s thyroiditis, lymphoma, DM
- Due to IgA antibodies against epidermal transglutaminase-3
- GI gluten sensitivity demonstrated in 20%
Bullous Pemphigoid

- Symmetric, grouped vesicles on flexors
- Over age 60
- not oral
- Associated with drug reactions
- May find no bullae
- pink background (urticaria) is key
- Eosinophil-mediated
- Rx: Tetracycline ± nicotinamide
- Corticosteroids with steroid-sparing agents
“Normal” skin findings in chronic disease
• Thyroid
• Renal
• Diabetes
HYPERTHYROIDISM AND THE SKIN

Thyroid dermopathy (pretibial myxedema)

- Coalescing, waxy papule and vesicles
- Increased hyaluronic acid
Scleromyxedema

- Coalescing, waxy papule and vesicles
- Increased hyaluronic acid
- Increased fibroblasts
HYPERTHYROIDISM AND THE SKIN

Generalized Myxedema

- diffuse deposition of hyaluronic acid, chondroitin
- non-pitting
- Characteristic facies: swollen lips, broad nose, macroglossia, and puffy eyelids, hands, feet
- Nerve entrapment: carpal tunnel, facial palsy
HYPERTHYROIDISM AND THE SKIN

Auto-immune diseases

- Vitiligo, alopecia
- Pernicious anemia
- Connective tissue diseases
HYPOTHYROIDISM AND THE SKIN

Nonspecific changes

- Xerosis
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- palmoplantar keratoderma
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Nonspecific changes

- Xerosis
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- Madarosis: loss of lateral 1/3 of brows
- Caroteimia, poor wound healing, clotting
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CUTANEOUS MANIFESTATIONS OF DIABETES

• 30% of patients with DM develop skin lesions
  • Type I patients get more autoimmune-type lesions
  • Type II patients get more cutaneous infections
• May be the first presenting sign
• Approach:
  • Skin diseases associated with DM
  • Cutaneous infections
  • Cutaneous manifestations of diabetic complications
  • Skin reactions to diabetic treatment
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CUTANEOUS MANIFESTATIONS OF DIABETES

Diabetic Dermopathy “shin spots”

- Most common skin finding in diabetes
- Lesions are predominantly situated on the shins, forearms, thighs and over bony prominences
- The color is due to hemosiderin in histiocytes near the vessels
- Trauma and microvascular disease may play a role
Diabetic Bullae

- Painless bullae on non-inflamed base
- Contain clear, sterile fluid
- Trauma and microvascular disease may play a role
CUTANEOUS MANIFESTATIONS OF DIABETES

Acanthosis nigricans
CUTANEOUS MANIFESTATIONS OF DIABETES

Acanthosis nigricans

- **Mechanism:** *Insulin binds to Insulin-like growth factor* —> *growth of keratinocytes, fibroblasts*
- Incidental finding in obesity
- Associated with gastric CA
- Secondary to medications (nicotinic acid, estrogen, or corticosteroids)
- Pineal tumors
- Other endocrine syndromes (PCOS, acromegaly, Cushing’s disease, hypothyroidism)
Scleredema diabeticorum

- Painless, symmetric, woody “peau d’orange” induration
- Upper back and neck
CUTANEOUS MANIFESTATIONS OF DIABETES

NLD: Necrobiosis lipoidica diabeticorum

- atrophic, telangiectatic plaques
- yellow-brown
- 20% of NLD patients have diabetes
CUTANEOUS MANIFESTATIONS OF DIABETES

Eruptive Xanthomas

- Sudden crops on firm, non-tender yellow papules with a red rim on extensors
- Slowly resolve when the diabetes is properly managed
- Hypertriglyceridemia >2000mg/dl
- Secondary to EtOH, estrogens
CUTANEOUS MANIFESTATIONS OF DIABETES

Candidiasis in DM

- Intertrigenous areas
  - “satellite” lesions
- Angular cheilitis:
  - White, curdlike material adherent to erythematous, fissured
  - oral commisure;
- Median rhomboid glossitis
  - middle of tongue
- Chronic paronychia
  - fingernails
- Erosio interdigitale blastomycetia
  - fissures in finger web spaces
CUTANEOUS MANIFESTATIONS OF DIABETES

Erytrasma

- *Corynebacterium minutissimum*

- Well demarcated red or brown patches
- Topical clindamycin
CUTANEOUS MANIFESTATIONS OF DIABETES

Rhinocerebral mucormycosis

- Uncontrolled diabetics with ketosis
- Involves the terbinates, septum, palate, maxillary and ethmoid sinuses
- Headache, fever, lethargy, nasal congestion and facial ocular pain
- Treatment:
  - Correction of ketosis
  - Debridement
  - IV antifungal agents

- Mortality ranges from 15-34%
CUTANEOUS REACTIONS TO INSULIN

Lipoatrophy and lipodystrophy

• Lipoatrophy
  • Circumscribed depressed areas of skin at the insulin injection site 6-24 months after starting insulin

• Lipodystrophy
  • Soft dermal nodules that resemble lipomas at sites of frequent injection
  • May be a response to the lipogenic action of insulin
  • Treat and prevent by rotating sites of injection
SKIN FINDINGS OF RENAL FAILURE

Findings

- General
  - Xerosis, Pruritus
  - Pigmentary alteration
  - Nail Changes, Hair Changes
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“Uremic Frost”

• Very Rare
  • blood urea nitrogen level of more than 250-300 mg/dl
  • frequent in the pre-dialysis era
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• Acquired perforating disorder
• Bullous disease of dialysis
• Calcinosis cutis (metastatic)
• Calciphylaxis
• Nephrogenic systemic fibrosis
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Perforating dermatosis

- Primary diseases: rare (Kyrlies, Elastosis Perforans serpiginosa)
- Secondary to:
  - Renal Failure (worse in diabetics)
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• **Calciphylaxis**
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Metastatic dermal calcification

- Arteriopathy —> gangrene
- Findings:
  - Angular ulcerations
  - Very painful
  - Elevated PTH
  - High mortality
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- **Nephrogenic systemic fibrosis**
Scleroderma + Contractures

- Peau d’orange
- Very firm skin
  - advancing arcuate edges develop on limbs and trunk
  - relative sparing of head neck
- Specific to radiography contrast

NEPHROGENIC FIBROSINGDERMOPATHY (NFD)
Local consultation cases
• **HPI:** 51 yo male
• HTN and diverticulitis
• worsening myalgias and arthralgias x 3 weeks
• severe lethargy and fevers x1 week.
• admitted for hyponatremia
• Dermatology consulted for a *pigmented* lesion on the abdomen
- **VSS:** T 98.3, P 88, RR 20, BP 140/73, O₂ 98
- **PE:** Gen: NAD, AAOx3
  - Skin: Fitzpatrick II, multiple tender 1-2mm erythematous purpuric papules on the palmar side of the fingers and dorsal aspect of toes.
  - Ø cervical lymphadenopathy, Ø conjunctival, mucosal or other cutaneous lesions
- **Labs**
  - **CBC:** WBC 19.1, HB 12.3, HCT 35.2, PLT 330, EOS 0.6%,
  - **CMP:** Na 119, K 3.1, Cl 86, CO₂ 30, BUN 16, Cr 0.7, CRP 16.8
  - Viral panel (-), HIV (-), pending blood cultures
Tender erythematous, purpuric papules on third digit of L hand
Tender erythematous purpuric papule at the on the R foot.
Tender erythematous purpuric papule at the L foot
Differential

• Osler nodes or Janeway lesions
  – Secondary to:
    • **Most likely:** Subacute/acute endocarditis
    • **Other:**
      – Systemic lupus erythematosus
      – Gonococcemia
      – Hemolytic anemia
Dense dermal inflammatory pattern
Thrombi within vessel wall

Endothelial cell obliteration

Thrombi within vessel wall
Dermal Abscess
Radiologic and Microbiologic Workup

• Blood cultures (+) S. aureus x 4 → (-) x 3.
• MRI back: epidural abscess of L5-S1.
• TEE: (12/23/15)
  • small vegetation of the aortic valve,
  • large vegetation of the mitral valve with a large perforation. EF: 65%.
Classic Cutaneous Findings in Endocarditis

• >50% of patients have a finding”
  – Petechiae:
  – Subungual (splinter) hemorrhages: Dark-red, linear lesions in the nail beds
  – Osler nodes: Tender subcutaneous nodules usually found on the distal pads of the digits
  – Janeway lesions: Non-tender maculae on the palms and soles
  – Roth spots: Retinal hemorrhages with small, clear centers; rare
- Splinter hemorrhages: 10%
- Petechial rash: 40-50%
- Subconjunctival hemorrhage: 2-5%
- Roth spots: < 5%
- Osler nodes: 5%
- Janeway lesions
- Mucosal petechiae: 20-30%
- Clubbing: 10%, long standing only
- Pallor
- Loss of pulses
- Splinter hemorrhages: 10%
Osler Nodes and Janeway Lesions
Overview

- **Cutaneous manifestations of bacterial endocarditis.**
  - Also rarely described in systemic lupus erythematosus, gonococcemia, hemolytic anemia and typhoid fever.

- **Osler nodes:** red-purple, slightly raised tender nodules often with a pale center. Average diameter 1 to 1.5mm.
  - Can occur at any time during the course of endocarditis (usually late in subacute)

- **Janeway lesions:** non-tender, hemorrhagic
  - palms and soles
  - More commonly seen in acute endocarditis
Pathogenesis

• **Two disparate theories**
  – *Circulating immune complex* mediated vasculitis – Gutman et al.
  – Microembolization
“Purple Toe”
cholesterol emboli

not red

Osler Node
Infectious emboli from endocarditis

red
• 45 year old woman
• Works in construction
• History of systemic lupus erythematosus
The "Red and Scaly" patient: Medium-size

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- Biopsy of arm = squamous cell carcinoma
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  - radiation therapy to the rest
Re-biopsy= SCLE lupus
The "Red and Scaly" patient: Medium-size

- 45 year old woman
- Works in construction
- History of systemic lupus erythematosus
- Biopsy of arm = squamous cell carcinoma
- Plan:
  - Photoprotection
  - Emollients
Re-biopsy = SCLE lupus
40 yo Caucasian otherwise healthy male
Chronic “rash” x 9 months in groin
    not responsive to antifungals, antibiotics, corticosteroids
    admitted for altered mental status
40 yo Caucasian otherwise healthy male
Chronic “rash” x 9 months in groin
not responsive to antifungals, antibiotics, corticosteroids
admitted for altered mental status
Ddx:

- Atopic dermatitis
- Necrolytic Migratory erythema (glucagonoma syndrome, pseudoglucagonoma syndrome)
- Acrodermatitis enteropathica (zinc deficiency)
- Pellagra (niacin deficiency)
- Cutaneous T-Cell Lymphoma (“Mycosis fungicides”)
- Tinea
Laboratory studies & Data

**Labs:** CBC – microcytic anemia, CMP – hypoglycemia, elevated LFTs (alkp 340, AST 97, ALT 146), TSH 38

**Specialty labs:**
Zinc level wnl, Vitamin C wnl
Insulin- **41.2** (2.0-19.6), c-peptide- **4.48** ng/ml (0.8-3.85)
Chromogranin A- **682** (1.9-15)
**AFP 55.22**, Ca 19-9 **89**
5HIAA wnl

**Radiologic studies:**
Portable abd x-ray: hepatomegaly with no obstruction
CT abd w/contrast: massively enlarged liver with numerous hepatic masses.
Confluent parakeratosis

Buckshot dyskeratosis
Diagnosis

- Atopic dermatitis
- **Necrolytic Migratory erythema** (glucagonoma syndrome, pseudoglucagonoma syndrome)
- Acrodermatitis enteropathica (zinc deficiency)
- Pellagra (niacin deficiency)
- Cutaneous T-Cell Lymphoma (“Mycosis fungicides”)  
- Tinea
Needle core biopsy - liver
Needle core biopsy - liver

insulin-secreting tumor
Needle core biopsy - liver

Insulin-secreting tumor

High insulin $\Rightarrow$ High Glucagon

Needle core biopsy - liver
Medical Student & Resident Teaching

- U. Miami: MD/MPH Dual Degree Curriculum
- FAU: MD program and Internal medicine residents

- Dermatology Rotation for students or residents
- Comprehensive self-instruction online
- Rotations in a variety of dermatology settings
- Publications:
  - with student or resident as primary author
  - collaborations with BRRH faculty
  - collaboration with FAU college of science
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### Journal Articles


Medical Student & Resident Teaching

Dermatology Medical Missions, Inc

local & overseas medical mission program

International Medical Missions: 2008
AlbinoCare
Africa

International Medical Missions: 2012
CommunityCare
Grenada

Comprehensive Dermatology & Cancer Care 2005
Caridad Center

Healthy Skin Head to Toe 2016
Education Project for Community Health Workers

TeleDermatology Service for Free Clinics 2019

Dermatology Medical Missions, Inc

a not-for-profit 501 (c)(3) Medical Service, Education, and Research Organization

www.DermatologyMissions.org
Thank you

Child with albinism in Africa