Dermatologic Manifestations of Systemic Diseases

Steven Nwe, DO
IL ACP Chapter Meeting
Friday, October 25, 2019
Conflict of interest

I HAVE NO CONFLICT OF INTERESTS TO REPORT
Learning objectives

The healthcare provider will be able to

1. Recognize commonly encountered dermatologic conditions and employ clues to distinguish them from other differentials
2. Predict dermatologic conditions that may be associated with a systemic disease
3. Employ knowledge of interrelated conditions to create a wholistic approach to patient care
"I HAVE THIS RASH"

- A majority of rashes are diagnosed and treated by Primary Care Physicians
- 30-40% of patients who presented to their PCP have at least one skin concern
- FEAR
Breakdown

• Discuss the most commonly encounter rashes and differentials
• Dermatologic conditions that have systemic implications
• Dermatologic signs of systemic disease
• Potpourri
Atopic dermatitis
Atopic dermatitis
Dyshidrotic Eczema (PomphyloX)

- Very common presentation in adulthood
- Notable for “tapioca-like” firm and deep seated pruritic vesicles
- Often chronic and relapsing
SCABIES

- Burrows
- Scabetic nodules
- Incredibly pruritic
- Intertriginous involvement
Cutaneous Larva Migrans

- “Creeping eruption”
- Caused by larvae of hookworms (ancylostomatidae)
- Serpentine, linear streaks mostly on the feet
- Pruritic
- Move about 2 cm a day
- Exposure to animal feces on soil/sand
Allergic Contact dermatitis
Allergic contact dermatitis

- Patterns
- Exposures
- Occupation
Eyelid dermatitis
Dermatomyositis

- Heliotrope Rash
- More edema than epidermal changes
- Arises as a result of inflammation of underlying orbicularis oculi muscle
Dermatomyositis

- Clinical and laboratory signs of proximal extensor inflammatory myopathy
- Distinctive, photo-distributed, pink–violet poikiloderma favoring the scalp, periocular region, and extensor surfaces, in addition to nail fold telangiectasias
Gottrons papules
Nail changes

- Cuticular hypertrophy
- Splinter hemorrhages
- Periungual telangiectasia
Okay but back to Eczema
Asteatotic Dermatitis
(Eczema Craquele)

- Typically > 60 YO
- Favors lower legs
- Resembles cracked porcelain

Stasis Dermatitis

- Very common mimic of cellulitis
- Bilateral
- Edema, hemosiderin deposits
- Skin changes often begin on medial ankle
- Leg elevation, compression stockings
Treatment

• Emollients
• Dry skin care
• Avoiding triggers
• Topical steroid use for itching and erythema
<table>
<thead>
<tr>
<th>Class</th>
<th>Generic Name</th>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1, Very High Potency</td>
<td>Betamethasone dipropionate</td>
<td>0.05% O O (dipropionate)</td>
</tr>
<tr>
<td></td>
<td>Clobetasol</td>
<td>0.05% F O L O</td>
</tr>
<tr>
<td></td>
<td>Difluridine disubrate</td>
<td>0.05% O</td>
</tr>
<tr>
<td></td>
<td>Halobetasol propionate</td>
<td>0.05% O C</td>
</tr>
<tr>
<td>Class 2, High Potency</td>
<td>Amcinonide</td>
<td>0.1% O</td>
</tr>
<tr>
<td></td>
<td>Betamethasone dipropionate</td>
<td>0.05% O C (dipropionate)</td>
</tr>
<tr>
<td></td>
<td>Decortinamide</td>
<td>0.05% O C 0.25% C O</td>
</tr>
<tr>
<td></td>
<td>Flucinonide</td>
<td>0.05% O C 0 S</td>
</tr>
<tr>
<td></td>
<td>Halcinonide</td>
<td>0.1% C</td>
</tr>
<tr>
<td></td>
<td>Mometasone furoate</td>
<td>0.1% O</td>
</tr>
<tr>
<td>Class 3, High Potency</td>
<td>Amcinonide</td>
<td>0.1% C L</td>
</tr>
<tr>
<td></td>
<td>Betamethasone dipropionate</td>
<td>0.05% C (non-dipropionate)</td>
</tr>
<tr>
<td></td>
<td>Betamethasone valerate</td>
<td>0.1% O</td>
</tr>
<tr>
<td></td>
<td>Decortinamide</td>
<td>0.05% C</td>
</tr>
<tr>
<td></td>
<td>Difluridine disubrate</td>
<td>0.05% C</td>
</tr>
<tr>
<td></td>
<td>Flucinonide</td>
<td>0.05% C 0 S</td>
</tr>
<tr>
<td></td>
<td>Halcinonide</td>
<td>0.1% O 0 S</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone</td>
<td>0.1% O</td>
</tr>
<tr>
<td>Class 4, Mid Potency</td>
<td>Betamethasone valerate</td>
<td>0.12% F</td>
</tr>
<tr>
<td></td>
<td>Fucinonide acetate</td>
<td>0.25% O</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide</td>
<td>0.05% O</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone valerate</td>
<td>0.2% O</td>
</tr>
<tr>
<td></td>
<td>Mometasone furoate</td>
<td>0.1% C</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone</td>
<td>0.1% C</td>
</tr>
<tr>
<td>Class 5, Mid Potency</td>
<td>Betamethasone dipropionate</td>
<td>0.05% L</td>
</tr>
<tr>
<td></td>
<td>Betamethasone valerate</td>
<td>0.1% C</td>
</tr>
<tr>
<td></td>
<td>Fucinonide acetate</td>
<td>0.25% C</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide</td>
<td>0.05% C</td>
</tr>
<tr>
<td></td>
<td>Flucinonide</td>
<td>0.05% C</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone butrate</td>
<td>0.1% C</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone valerate</td>
<td>0.2% C</td>
</tr>
<tr>
<td>Class 6, Low Potency</td>
<td>Alcortisol dipropionate</td>
<td>0.05% C O</td>
</tr>
<tr>
<td></td>
<td>Betamethasone valerate</td>
<td>0.1% L</td>
</tr>
<tr>
<td></td>
<td>Decortinamide</td>
<td>0.05% C L O</td>
</tr>
<tr>
<td></td>
<td>Fucinonide acetate</td>
<td>0.01% C S</td>
</tr>
<tr>
<td>Class 7, Low Potency</td>
<td>Hydrocortisone acetate</td>
<td>0.5% C L O 0.1% C O 0 F</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone hydrochloride</td>
<td>0.25% C L 0.5% C L O 0 1% C L O 0 2% L 2.5% C L O 0 S</td>
</tr>
</tbody>
</table>

C = Cream, F = Foam, O = Oint, L = Lotion, G = Gel, S = Solution | Source: Dermatol Nurs © 2006 Jannett Publications, Inc.
Easy general rules

- Ointments are stronger than creams
- Creams are more user friendly, but can burn more on open sores
- Foams and solutions work well for scalp
- Low Potency for Face, intertriginous areas, genital skin
- Hands, feet and scalp may need stronger potency steroids
<table>
<thead>
<tr>
<th>Class</th>
<th>Generic Name</th>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1, Very High Potency</td>
<td>Betamethasone dipropionate</td>
<td>0.05% O-D (diprostone)</td>
</tr>
<tr>
<td></td>
<td>Clobetasol</td>
<td>0.05% F-O-L-G/0.025% C</td>
</tr>
<tr>
<td></td>
<td>Difluradex</td>
<td>0.05% O</td>
</tr>
<tr>
<td></td>
<td>Halobetasol/proprionate</td>
<td>0.05% O-D</td>
</tr>
<tr>
<td>Class 2, High Potency</td>
<td>Aminosteroid</td>
<td>0.1% O</td>
</tr>
<tr>
<td></td>
<td>Betamethasone dipropionate</td>
<td>0.05% C-D (diprostone)</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone</td>
<td>0.05% O, 0.25% C-O</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide</td>
<td>0.05% C-O-S</td>
</tr>
<tr>
<td></td>
<td>Fluricosone</td>
<td>0.1% C</td>
</tr>
<tr>
<td></td>
<td>Mometasone furoate</td>
<td>0.1% O</td>
</tr>
<tr>
<td>Class 3, High Potency</td>
<td>Aminosteroid</td>
<td>0.1% C-L</td>
</tr>
<tr>
<td></td>
<td>Betamethasone dipropionate</td>
<td>0.05% C (non-diprostone)</td>
</tr>
<tr>
<td></td>
<td>Betamethasone valerate</td>
<td>0.1% O</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone</td>
<td>0.05% C</td>
</tr>
<tr>
<td></td>
<td>Difluradex</td>
<td>0.05% C</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide</td>
<td>0.05% C-O-S</td>
</tr>
<tr>
<td></td>
<td>Fluricosone</td>
<td>0.05% C-O-S</td>
</tr>
<tr>
<td></td>
<td>Mometasone furoate</td>
<td>0.1% C-O-S</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone</td>
<td>0.1% O</td>
</tr>
<tr>
<td>Class 4, Mid Potency</td>
<td>Betamethasone valerate</td>
<td>0.12% F</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide</td>
<td>0.05% C</td>
</tr>
<tr>
<td></td>
<td>Fluricosone</td>
<td>0.05% C</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone valerate</td>
<td>0.2% C</td>
</tr>
<tr>
<td></td>
<td>Mometasone furoate</td>
<td>0.1% C</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone</td>
<td>0.1% C</td>
</tr>
<tr>
<td>Class 5, Mid Potency</td>
<td>Betamethasone dipropionate</td>
<td>0.05% L</td>
</tr>
<tr>
<td></td>
<td>Betamethasone valerate</td>
<td>0.1% C</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide</td>
<td>0.05% C</td>
</tr>
<tr>
<td></td>
<td>Fluricosone</td>
<td>0.05% C</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone butrate</td>
<td>0.2% C</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone</td>
<td>0.1% C</td>
</tr>
<tr>
<td>Class 6, Low Potency</td>
<td>Betamethasone dipropionate</td>
<td>0.05% C-O</td>
</tr>
<tr>
<td></td>
<td>Betamethasone valerate</td>
<td>0.1% L</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone</td>
<td>0.05% C-O-L-D</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide</td>
<td>0.01% C-S</td>
</tr>
<tr>
<td>Class 7, Low Potency</td>
<td>Hydrocortisone acetate</td>
<td>0.5% C-O-L, 0.1% C-O-F</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone hydrochloride</td>
<td>0.25% C-L, 0.5% C-O-L-B, 1% C-L-B, 2% L, 2.5% C-O-L-B</td>
</tr>
</tbody>
</table>

C = Cream, F = Foam, O = Ointment, S = Solution

Seborrheic Dermatitis
Seborrheic Dermatitis

- HIV
- Parkinsonism
- CVA
Psoriasis

• Affects 2% of the population
• Extensor surfaces
• Occipital and post auricular scalp
• Superior, intergluteal fold
Psoriasis as a systemic disease

Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with awareness and attention to comorbidities

Table I. Clinical questions

What are the available screening and/or therapeutic interventions in managing the following comorbidities in adults:

i. Psoriatic arthritis
ii. Cardiovascular disease
iii. Metabolic syndrome
iv. Mental health
v. Lifestyle choices
vi. Inflammatory bowel disease
vii. Malignancy
viii. Renal disease
ix. Sleep apnea
x. Chronic obstructive pulmonary disease
xi. Uveitis
xii. Hepatic disease
Discoid Lupus

• Begin with red macules or plaques
• Atrophy, Scarring, central hypopigmentation and peripheral hyperpigmentation
• ANA + in 5-25%
• 5-25% progress to SLE
  - 5% for just head involvement
  - 20% for diffuse involvement
Discoid Lupus
Sarcoidosis

- Multisystem granulomatous disease
- 35% of sarcoidosis with skin lesions
- Red brown, or erythematous papules and plaques with apple jelly color with diascopy
Sarcoidosis
Erythema Nodosum

- Most common panniculitis
- Women in 2\textsuperscript{nd} to 4\textsuperscript{th} decades
- Idiopathic, Streptococcal infection, GI infection (Yersinia, Salmonella, Campylobacter), Viral URI, Coccidiomycosis, TB, histoplasmosis
- Drugs: OCPs, sulfa, NSAIDS
- Sarcoidosis (Lofgrens)
- IBD (Crohns > UC)
Gouty Panniculitis

- While gouty tophi are relatively common, gouty panniculitis is rare
- May precede or follow the onset of arthritic changes
- Since Neimi et al. first described gouty panniculitis in 1977, there have only been a few case reports
Diabetes related skin changes
Acanthosis Nigricans

- Dark velvety patches
- Armpits, groin and neck
- Insulin resistance
- Hypothyroidism
- Malignancy associated AN tends to be more inflammatory than asymptomatic
Confluent and Reticulated Papillomatosis

- Starts at puberty
- F > M
- More common in black > whites
- Unknown etiology
- Responds well to minocycline x 6 weeks
Diabetic Dermopathy

- Most common skin condition in patients with DM
- Small, round, atrophic skin lesions on the shins

http://www.pcds.org.uk/clinical-guidance/diabetic-dermopathy
Granuloma Annulare

- Benign self limiting
- Asymptomatic annular/arciform plaques composed of multiple small non scaly papules
- Dorsal hands most common, but can be generalized
  - Dyslipidemia 45%
  - DM in 21% (10% in localized version)
Necrobiosis lipoidica Diabeticorum

- Firm reddish papules that lead to atrophic plaques on both shins.
  - Erythematous borders and central yellow brown discoloration
- Only 0.03% of patients with DM will have NLD, but 22% of patients with NLD will develop DM
- Those with both NLD and DM have an increased risk of retinopathy, neuropathy and joint immobility
Acquired perforating disorders
Eruptive Xanthomas
Xanthelasma

- Sharply demarcated yellow deposits around the eye
- Dyslipidemia, hypothyroidism, DM

https://www.dermnetnz.org/topics/xanthoma
Skin manifestations of GI disease
Dermatitis Herpetiformis

- Extremely pruritic herpetiform vesicles on urticarial plaques
- Vesicles rupture easily
- Extensor extremities, buttocks, back/neck
- Hemorrhagic palmoplantar lesions
- Only 20% of patients with DH have symptomatic GI disease, but over 90% have some degree of gluten-sensitive enteropathy on GI biopsy (Celiacs)
Dermatitis herpetiformis

• Strongly associated with other autoimmune diseases:
  • Hashimotos thyroiditis
  • insulin dependent DM
  • pernicious anemia
  • alopecia areata
  • myasthenia gravis
  • vitiligo
  • SLE
Cutaneous Crohn's

• Can be either contiguous or distant “metastatic”
• Dusky red papules, plaques that lead to ulcerations with undermined edges, fistulas, sinuses and scarring
• Most common sites
  - Lower extremities 38%
  - Abdomen/trunk 24%
  - Upper extremities 15%
  - Face 11%
  - Flexures 8%
Sweet’s Syndrome

- Neutrophilic dermatosis
- F > M (for classic Sweets)
  - M = F for cancer associated
- Tender, burning, well demarcated, juicy plaques with rapid onset
- Favors head and neck
- Infections (strep and yersinia), AML, IBD
- Drugs: G-CSF, minocycline, OCPs
Pyoderma Gangrenosum

- Starts as inflammatory bullae leading to painful undermining ulcer with overhanging, violaceous border on a vegetative base
- Heals with cribriform scaring
- PATHERGY
- IBD, AML, CML
Pyoderma Gangrenosum

- Diagnosis of exclusion
Pyoderma gangrenosum

Major Criteria

• rapid progression of a painful, necrotic cutaneous ulcer with an irregular, violaceous, undermined border and 1 to 2 cm per day or 50 percent increase in size within one month

• exclusion of other causes of ulceration such as infection, systemic vasculitides, autoimmune diseases, and vascular insufficiency
Pyoderma Gangrenosum

Minor Criteria

- a history suggestive of pathergy
- diagnosis of a systemic disease associated with PG
- compatible histopathologic findings
- rapid treatment response to systemic glucocorticoid therapy
Hepatitis C
Dermatologic associations in HCV: Cryoglobulinemia

- Essential mixed cryoglobulinemia (Type II)
- Deposition of circulating immune complexes in to small and medium sized blood vessels
- More than 90% of patients with essential mixed cryoglobulinemia are infected with HCV
## Dermatologic associations in HCV: Cryoglobulinemia

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Molecular Composition</th>
<th>Associations</th>
<th>Pathophysiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Monoclonal IgM or IgG</td>
<td>Plasma cell dyscrasias, lymphoproliferative disorders</td>
<td>Cryogelling → Vascular Occlusion</td>
</tr>
<tr>
<td>II</td>
<td>Monoclonal IgM with polyclonal IgG</td>
<td>HCV, HIV, autoimmune connective tissue diseases, lymphoproliferative disorders</td>
<td>Immune complex mediated vasculitis</td>
</tr>
<tr>
<td>III</td>
<td>Polyclonal IgM, IgG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caliber of affected vessel</td>
<td>Classification</td>
<td>subclassification</td>
<td></td>
</tr>
<tr>
<td>----------------------------</td>
<td>----------------------------------------</td>
<td>-------------------</td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>Leukocytoclastic vasculitis (LCV, CSVV)</td>
<td>HSP</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acute hemorrhagic edema of infancy</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urticarial vasculitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Erythema elevatum diutinum</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Secondary (drugs, infxn, cancer)</td>
<td></td>
</tr>
<tr>
<td>Small and medium (mixed)</td>
<td>Cryoglobulinemia</td>
<td>Types II and III</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ANCA-associated</td>
<td>Microscopic polyangiitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wegener’s granulomatosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Churg-Strauss syndrome</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Secondary</td>
<td>Infxn, inflammatory disorders</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>Polyarteritis nodosa (PAN)</td>
<td>Classic (systemic) PAN</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cutaneous PAN</td>
<td></td>
</tr>
<tr>
<td>Large</td>
<td>Temporal arteritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Takayasu’s arteritis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Dermatologic associations in HCV: Cryoglobulinemia
Dermatologic associations in HCV: Porphyria cutanea tarda

- Reduced activity of the enzyme uroporphyrinogen decarboxylase → increased uroporphyrinogen in blood and urine
Dermatologic associations with HCV: Porphyria cutanea tarda

- Risk Factors
  - Alcohol
  - Hereditary hemochromatosis
  - Estrogen therapy
  - Family history
  - Exposure to polyhalogenated compounds
  - Hemodialysis
  - HIV
  - Myeloproliferative diseases
Dermatologic associations with HCV: Porphyria cutanea tarda

Prevalence of hepatitis C virus infection in porphyria cutanea tarda: systematic review and meta-analysis

Javier P. Gisbert*, Luisa García-Buey, José María Pajares, Ricardo Moreno-Otero

• A systematic review of 50 studies with 2167 patients with PCT found an overall HCV prevalence of 50%
Dermatologic associations with HCV: Porphyria cutanea tarda

- Unclear mechanism
- Screen for HIV, Hepatitis and iron overload
- Role of HCV treatment
Dermatologic associations with HCV: Lichen planus

- Associations have varied anywhere from 10-40% of patient with LP
- Reports of LP worsening with interferon therapy
Dermatologic associations with HCV: Lichen planus

- Pruritic, purple, polygonal, flat topped papules
- Wickhams striae
- Koebnerization is common
- Most common sites: oral mucosa, ventral wrists/forearms
- Drugs: HCTZ, B-blockers, ACE-I, antimalarials, gold, TNF-a, NSAID
Lichen planus and hepatitis C virus: a multicentre study of patients with oral lesions and a systematic review

G. LODI, M. GIULIANI, A. MAJORANA, † A. SARDELLA, C. BEZ, F. DEMAROSI AND A. CARRASSI

• Both cross sectional and meta analysis
• 309 biopsy proven LP cases and matched controls were tested for HCV antibody
• 19.1% in the LP group vs. 3.2% in controls
Summary of response of HCV associated dermatologic conditions to IFN based therapy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Response to IFN</th>
<th>Level of evidence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC</td>
<td>Improvement in symptoms. Antiviral therapy is treatment of choice. Dermatologic symptoms of MC may be an early, sensitive marker for virologic response.</td>
<td>Level 1a for IFN monotherapy Level 2a for combination therapy</td>
</tr>
<tr>
<td>PCT</td>
<td>Insufficient data, variable responses reported.</td>
<td>Level 4</td>
</tr>
<tr>
<td>LP</td>
<td>Insufficient data, variable responses reported.</td>
<td>Level 4</td>
</tr>
</tbody>
</table>
Dermatologic Associations with HCV: Nectoltic Acral erythema

- The only dermatologic disorder diagnostic for HCV infection
- Tender, well demarcated, erythematous, dusky plaque on lower extremities
Dermatologic associations with HCV: other dermatologic associations

- Psoriasis
- Psoriatic arthritis
- Sarcoidosis
- Polyarteritis Nodosum
- Pruritus
Amyloidosis

- Primary cutaneous Amyloidosis
- A-Kerartin
Amyloidosis

- Cutaneous signs of systemic amyloidosis
Thank You
Questions?