CUTANEOUS SIGNS OF SYSTEMIC DISEASE

AARON MANGOLD M.D.
ASSOCIATE PROFESSOR OF DERMATOLOGY
MEDICAL DIRECTOR, CLINICAL TRIALS OFFICE
MAYO CLINIC, SCOTTSDALE AZ
OVERVIEW

• Diagnose common skin findings associated with metabolic diseases
• Recognize rare skin findings associated with common metabolic diseases
• Identify common skin findings associated with underlying infection
• Evaluate itch as a sign of internal disease
WHAT IS THIS PATIENT AT HIGHEST RISK FOR?

a) Hypertension
b) Hypothyroidism
c) Gastric Cancer
d) Diabetes

PMID: 23226673
ACANTHOSIS NIGRICANS

- Velvety hyperpigmentation in flexural and intertriginous areas
- Associated with insulin resistance
- More common in obese patients (up to 74%)
- Abrupt onset, atypical locations, and associated glossitis may be associated with underlying GI or GU malignancy

PMID: 25285297 & 25165638
TRIPE PALMS

PMID: 31334069
OVARIAN CANCER ASSOCIATED ACANTHOSIS NIGRICANS

PMID: 23741672
ASSOCIATED GLOSSITIS WITH ACANThOSIS NIGRICANS

PMID: 24596525
DIABETIC BULLAE AND DIABETIC DERMOPATHY

- Strongly associated with diabetes
- Diabetic dermopathy
  - Common in diabetics (approx. 40%)
  - Light brown patches on shins
- Diabetic bullae
  - Affects less than 1% of diabetics

PMID: 26649029 & 25653473
NECROBIOsis LIPOIDICA

- Necrobiosis lipoidica (NL) is an idiopathic, chronic granulomatous disease.

- NL is often oligo-lesional with large, 5 cm annular erythematous-yellow plaques on the shin which are often atrophic, indurated, telangiectatic.

- NL has strong association with diabetes mellitus (DM)
  - 0.3% of DM patients have a history of NL
NL DEMOGRAPHIC & COMORBIDITY

- Middle-aged Caucasian women
- Poorly controlled DM with mean HbA1c above 8
- Obese (BMI-32)
- Smoking history (59%)
- Common location on shin and lower extremity
NECROBIOsis LIPOIDICA

- Ulceration is seen in 30% of cases
- Pain was seen in 48%
WHICH OF THESE IS MOST LIKELY IN THIS PATIENT?

a) Diabetes Mellitus  
b) Hypertriglyceridemia  
c) Lung Cancer  
d) Myeloma
GRANULOMA ANNULARE

- Granulomatous skin eruption
- 0.1% and 0.4% of new visits to the dermatologist visits
- Most commonly seen on the distal extremities of young adults
- Localized GA tends to resolve within 2 years
- 25% of generalized cases can last longer than 5 years

PMID: 2822595
GA-ASSOCIATIONS

- Diabetes mellitus
  - Controversial but may be more common in generalized disease

- Dyslipidemia
  - 79% of cases
  - I screen for this

- Infections
- Thyroid disease
- Medications
- Malignancy
MALIGNANCY ASSOCIATED GA

- Extremely rare
- Refractory to treatment
- Often have other signs or symptoms which lead to screening tests or labs
- Routine malignancy screening often detects cancers in solid organ cases
WHAT IS MOST LIKELY TO BE ABNORMAL IN THIS PATIENT?

a) Blood pressure
b) Triglycerides
c) Blood glucose
d) Liver function
ERNITIVE XANTHOMAS

- 1-5mm yellow papules
- Concentrated on extensor surfaces, buttocks, and hands
- Lesions may be red, tender, and pruritic
- Always occur in setting of elevated triglycerides
PATIENT FROM PHOENIX PRESENTS WITH A 8 WEEK HISTORY OF A DRY COUGH AND THIS RASH. WHAT IS MOST LIKELY?

a) Tuberculosis
b) Cutaneous dermatophyte infection
c) Cutaneous T-cell lymphoma
d) Pulmonary Coccidioidomycosis
COCCIDIOIDOMYCOSIS

- *Coccidioides* species are soil dwelling fungi endemic to the Southwest
  - Valley Fever
- Coccidioidomycosis is acquired through the inhalation
- Most cases are asymptomatic or have mild, self-limited pulmonary symptoms 1-3 weeks after the initial infection

Courtesy of David J DiCauo M.D.
CUTANEOUS FINDINGS OF VALLEY FEVER

• Organism-specific findings
  • Results from dissemination or less commonly direct inoculations
  • Often present with verrucal plaques, abscess, or sinus tract

PMID: 17110216
REACTIVE MANIFESTATIONS

• Can be polymorphous
• Must maintain a high index of suspicious
• The rashes can occur in the acute, subacute, and chronic setting
• We have reported cases with skin eruptions and pulmonary cocci spanning decades
ACUTE EXANTHEM

- Often occurs within the first 48 hours of symptoms
- Lesions can be macular, papular, urticarial, morbilliform, or target-like

PMID: 17110216
ERYTHEMA NODOSUM

• Most common reactive cutaneous manifestation of coccidioidomycosis.

• 1 to 3 weeks after the onset

• Characterized by painful subcutaneous red nodules on the lower extremities.
COCCI LAB TESTS

• EIA – Enzyme-linked immunoassay (most sensitive)
• Immunodiffusion (most specific)
• Complement fixation

• Tests may take weeks to months to turn positive so repeat if there is a high clinical suspicion.
CHRONIC PRURITUS:

• Lasting more than 6 weeks
• May be caused by primary skin disease or related to underlying systemic disease
• History is extremely important
Chronic pruritus

Primary skin lesions with or without chronically scratched lesions present

Dermatologic cause
- Atopic eczema
- Psoriasis
- Xerosis
- Scabies
- Contact dermatitis
- Insect bite
- Lichen planus

No primary skin lesions; chronically scratched lesions present or absent

Nondermatologic cause

Systemic cause
- Chronic kidney disease
- Cholestasis
- Hodgkin's lymphoma
- Polycythemia vera
- HIV infection
- Hyperthyroidism

Neuropathic cause
- Brachioradial pruritus
- Notalgia paresthetica
- Postsurgical itch

Psychogenic cause
- Obsessive–compulsive disorder
- Delusions of parasitosis
- Substance abuse

Complete blood count and differential count
- Creatinine level
- Liver-function test
- Thyroid-function test
- Erythrocyte sedimentation rate
- HIV serologic analysis
- Chest radiography
- Drug history

PMID: 23614588
HISTORY

• How itchy?
  • Are you able to fall asleep?
  • Does it wake you up from sleep?

• Location
  • Localized or generalized

• Modifying factors
  • Bathing

• What drugs are they on?

• Does anyone else in the home itch?
A BIT MORE HISTORY

• Physical examination
  • Evaluate for primary skin conditions
  • KOH or scabies preparation
CLINICAL PEARLS

• KEY diseases that can present initially with isolated pruritus:
  • Hodgkin’s lymphoma
  • Primary biliary cirrhosis

• Primary lesions which may be subtle:
  • Dermatitis herpetiformis
  • Scabies
  • Bullous pemphigoid
SCABIES

PMID: 29492350
BULLOUS PEMPHIGOID

(a)

PMID: 28520234

PMID: 30773528
DERMATITIS HERPETIFORMIS

PMID: 31244841

PMID: 24068131
DRUGS- MOST SUSPECT

• Drugs started within 6 weeks of eruption should be most suspect
• Calcium Channel Blockers are 2-4 fold more likely to taken by individuals in elderly individuals with chronic itch
  • Verapamil is most suspect
  • Drug withdrawal improves the rash in 68-83% of cases
• Hydrochlorothiazide (HCTZ) to be twice as likely in pruritic elderly patients
SCREENING LABS FOR ITCH WITHOUT RASH

- CBC with differential
- BUN, Cr
- Alkaline Phosphatase, Liver enzymes
- Bilirubin
- Iron, Ferritin
- TSH
- HIV
- Chest X-ray
- Drug history
MY APPROACH

• Close examination for signs of primary dermatologic disease or scabies infestation
• Basic laboratory workup (per above)
• Aggressive moisturization with or without corticosteroids
• Discontinuation of suspect drugs
• If sleep is disrupted
  • Gabapentin
  • Mirtazapine
Questions?