Dermatology Grand Rounds 2019 skin signs of internal disease

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Dermatologist and Internal Medicine

"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



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Dermatologist and Internal Medicine

The "Red and Scaly" patient

"Big and Small" red rashes not to miss



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The "Red and Scaly" patient



- 29 Year old man with two year pruritic eruption
- PMHx:
 - seasonal allergies
 - childhood eczema
 - no medications



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- 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





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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





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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





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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
- Evaporation / convection of water vapor rapidly repairs skin barrier
- 5) Repeat q3h

72 hours of therapy:





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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





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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



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- 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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Diagnosis = **erythroderma** secondary to

psoriasis



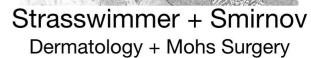
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• Rx= oral methotrexate



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Medications Implicated in Erythroderma

- The most commonly implicated drugs include:
 - Anti-epileptics
- Cina atidia a

Calcium channel blockers

Allopurinol

- Cimetidine
- Amiodarone
- Dapsone
- ACE inhibitors
- Gold

Antibiotics

- Isoniazid
- Penicillin
- Lithium
- Sulfonamides
- Thiazides
- Vancomycin
- Quinidine

NSAIDs

St. John's wort





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- 55 Year old woman
- Hx: DM type 2
- 5 month year history of generalized pruritus and rash

Dermatology + Mohs Surgery

• Exam: + LAD in neck, groin







DIAGNOSIS:

Right Upper Arm

SUPERFICIAL AND DEEP LYMPHOHISTIOCYTIC INFILTRATE WITH FEW SCATTERED EQSINOPHILS AND FOCAL PAUTRIER-LIKE MICROABSCESSES AND EPIDERMOTROPISM.

Note: The histologic changes are suspicious for an atypical lymphoproliferative disorder associated with HTLV-1 conditions such as adult T-cell leukemia (ATLL). The differential includes mycosis fungoides and pseudolymphoma or cutaneous lymphoid hyperplasia mimicking leukemia/lymphoma. Multiple original and deeper sections were examined.

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- No history of psoriasis



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The NEW ENGLAND JOURNAL of MEDICINE

IMAGES IN CLINICAL MEDICINE

Chana A. Sacks, M.D., Editor

Erythrodermic Psoriasis and HIV Infection





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pruritic, erythematous, and scaly rash that had first appeared 2 years earlier. He had sought no medical treatment until this presentation. His medical history included eczema during childhood and seasonal allergies. He was taking no medications. A physical examination showed erythematous, violaceous plaques (Panel A) that involved more than 90% of the patient's body-surface area, with some areas (for example, on the back) that were spared and reflect the baseline appearance of the patient's skin (arrow, Panel B). The differential diagnosis for generalized erythema and plaque formation includes erythrodermic psoriasis, seborrheic dermatitis, and pityriasis rubra pilaris. A punch biopsy specimen obtained from two areas on the back confirmed the diagnosis of erythrodermic psoriasis. An erythrodermic papulosquamous eruption can be associated with an underlying systemic disease. In this case, testing for human immunodeficiency virus (HIV) infection was positive. The patient received highly active antiretroviral therapy as well as topical triamcinolone. At a follow-up visit 3 months later, the patient had complete clearance of the skin eruption with some residual hyperpigmentation.

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Our first publication of 2019

Marker of HIV infection:

- New Psoriasis
- or dramatically worse psoriasis or other papulo-squamous disorder





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"Abnormal" skin findings as clue to internal disease

- Markers of infectious disease
- Markers of internal malignancy risk







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Flexor Wrist



Buccal Mucosa



Flexor Wrist



Buccal Mucosa



- 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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- Wickham's striae are fine white lines on top of papules
- Koebner phenomenon -
 - 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





- Lichen Planus
- Porphyria Cutanea Tarda
- Polyarteritis Nodosa
- Necrolytic Acral Erythema
- Cryoglobulinemia
- Pruritus



• not "eczema" not fungus"

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NECROLYTIC ACRAL ERYTHEMA

- Psoriasiform eruption on acral surfaces
- HCV+
- Manifestation of Zinc defeciency
- Treat with zinc supplementation











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PORPHYRIA CUTANEA TARDA

- Vesicles on sunexposed areas, scarring, milia HCV+
- Hypertrichosis
- Fragile skin with sclerodermoid changes



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PORPHYRIA CUTANEA TARDA

- Vesicles on sunexposed areas, scarring, milia HCV+
- Hypertrichosis
- Fragile skin with sclerodermoid changes
- DDx: pseudoporphyria due to NSAIDS, OCP, etc.



PSEUDOPORPHYRIA

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



Polyarteritis Nodosa

- Small vessel vasculitis (LCV = palpable purpura) and
- <u>Medium</u> vessel vasculitis (nodules on lower extremities) = **livedo**
- Multi system disease due to ischemic injury
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THIS IS MEDIUM VESSEL INJURY

PALPABLE PURPURA IS SMALL VESSEL VASCULITIS





HEPAIIIS 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 (assiciated with strep infections)





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• 62 year old woman



- 62 year old woman
 - Arthralgias,
 - Elevated LFT
 - Glomerulonephritis



Cryoglobulenemia

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



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- Systemic symptoms:
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- Small vessel vasculitis (LCV = palpable purpura)
- 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





- Lichen Planus
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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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Pruritus

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



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



NOT PRURITUS

Dermatitis herpetiformis:

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



NOT PRURITUS

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
- Eosiniphil-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



HYPERTHYROIDISM AND THE SKIN

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



Auto-imunne diseases

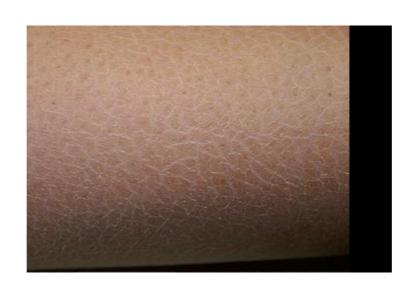
- Vitiligo, alopecia
- pernicious anemia
- connective tissue diseases





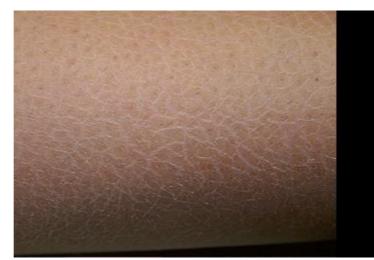
Nonspecific changes

Xerosis



Nonspecific changes

- Xerosis
- palmoplantar keratoderma







Nonspecific changes

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







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- Madarosis: loss of lateral 1/3 of brows
- Caroteimia, poor wound healing, clotting







- 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 manifestions of diabetic complications
 - Skin reactions to diabetic treatment

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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



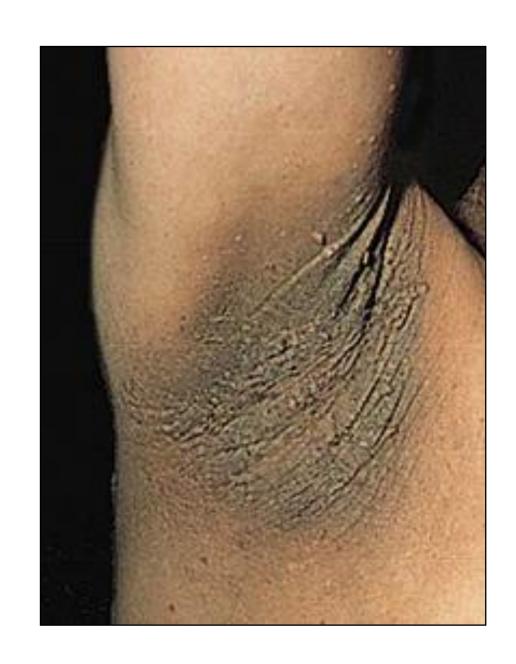
Acanthosis nigricans





Acanthosis nigricans

- Mechanism: Insulin binds to Insulin-like growth factor —> growth of keratinocytres, 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



NLD: Necrobiosis lipoidica diabeticorum

- atrophic, telangiectatic plaques
- yellow-brown
- 20% of NLD patients have diabetes



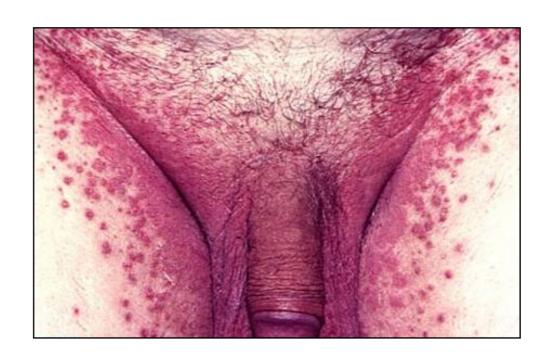
Eruptive Xanthomas

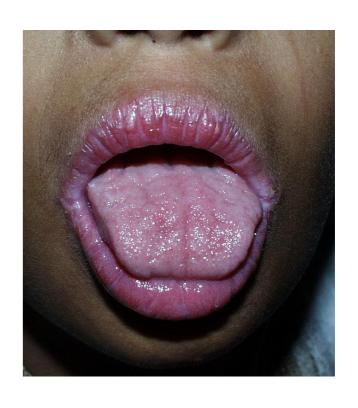
- Sudden crops on firm, non-tender yellow papules with a red rim on extensors
- Slowly resolve when the diabetes is properly managed
- Hypertriglyceridemia >2000mg/dl
- Secondary to to EtOH, estrogens



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





Erytrasma

- Corynebacterium minutissimum
- Well demarcated red or brown patches
- Topical clindamyin



Rhinocerebral mucormycosis

- Uncontrolled diabetics with ketosis
- Involves the terbinates, septum, palate, maxiillary 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





- General
 - Xerosis , Pruritus
 - Pigmentary alteration
 - Nail Changes, Hair Changes

Findings

- General
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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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- 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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Hands of a transfusion-dependent patient on long-term hemodialysis. Several uremiarelated cutaneous disorders are visible. The pigmentary alteration results from retained urochromes and hemosiderin deposition. The large bullae are consistent with either porphyria cutanea tarda or the bullous disease of dialysis. All nails show the distal brownred and proximal white coloring of half-and-half nails.

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CALICIPHYLAXIS

Metastatic dermal calcification

- Arteriopathy —> gangrene
- Findings:
 - Angular ulcerations
 - Very painful
 - Elevated PTH
 - High mortality



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NEPHROGENIC FIBROSING DERMOPATHY (NFD)

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



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





Strasswimmer + Smirnov Dermatology + Mohs Surgery

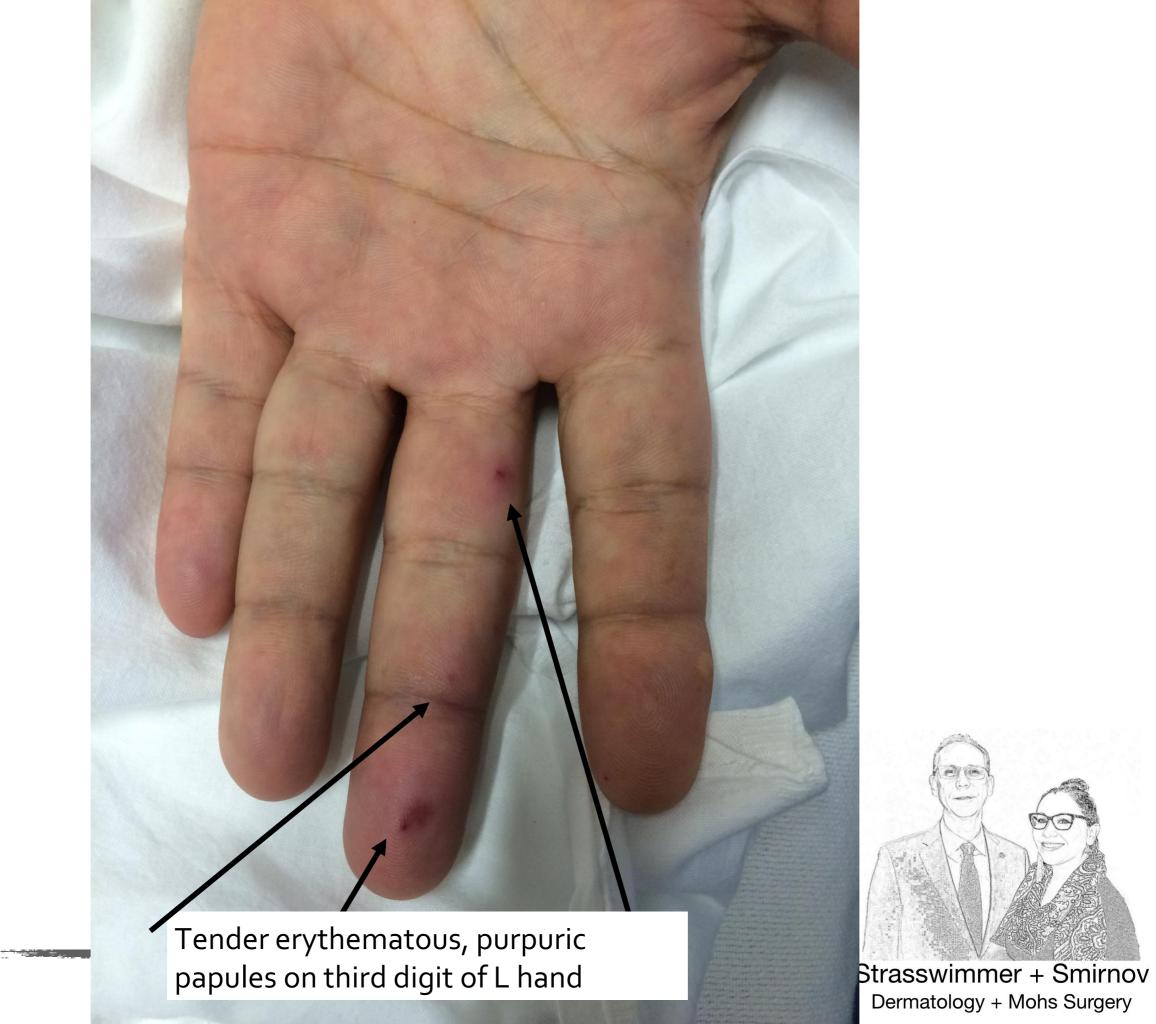
- VSS: T 98.3, P 88, RR 20, BP 140/73, O₂ 98
- PE: Gen: NAD, AAOx3
 - Skin: Fitzpatrick II, multiple tender 1-2mm erythematous purpuric papules on the palmar side of the fingers and dorsal aspect of toes.
 - Ø cervical lymphadenopathy, Ø conjunctival, mucosal or other cutaneous lesions

Labs

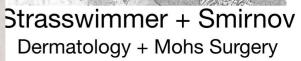
- CBC: WBC 19.1, HB 12.3, HCT 35.2, PLT 330, EOS 0.6%,
- CMP: Na 119, K 3.1, Cl 86, CO₂ 30, BUN 16, Cr 0.7, CRP 16.8
- Viral panel (-), HIV (-), pending blood cultures



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Tender erythematous purpuric papule at the on the L foot



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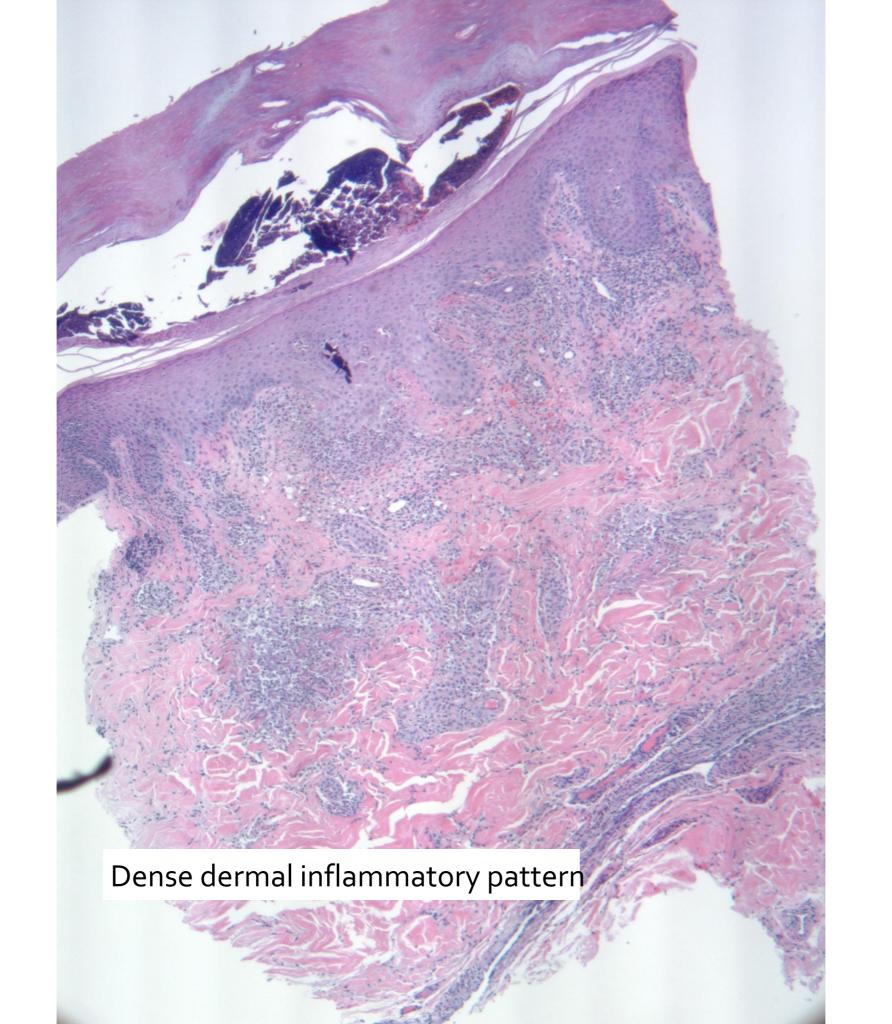
Differential

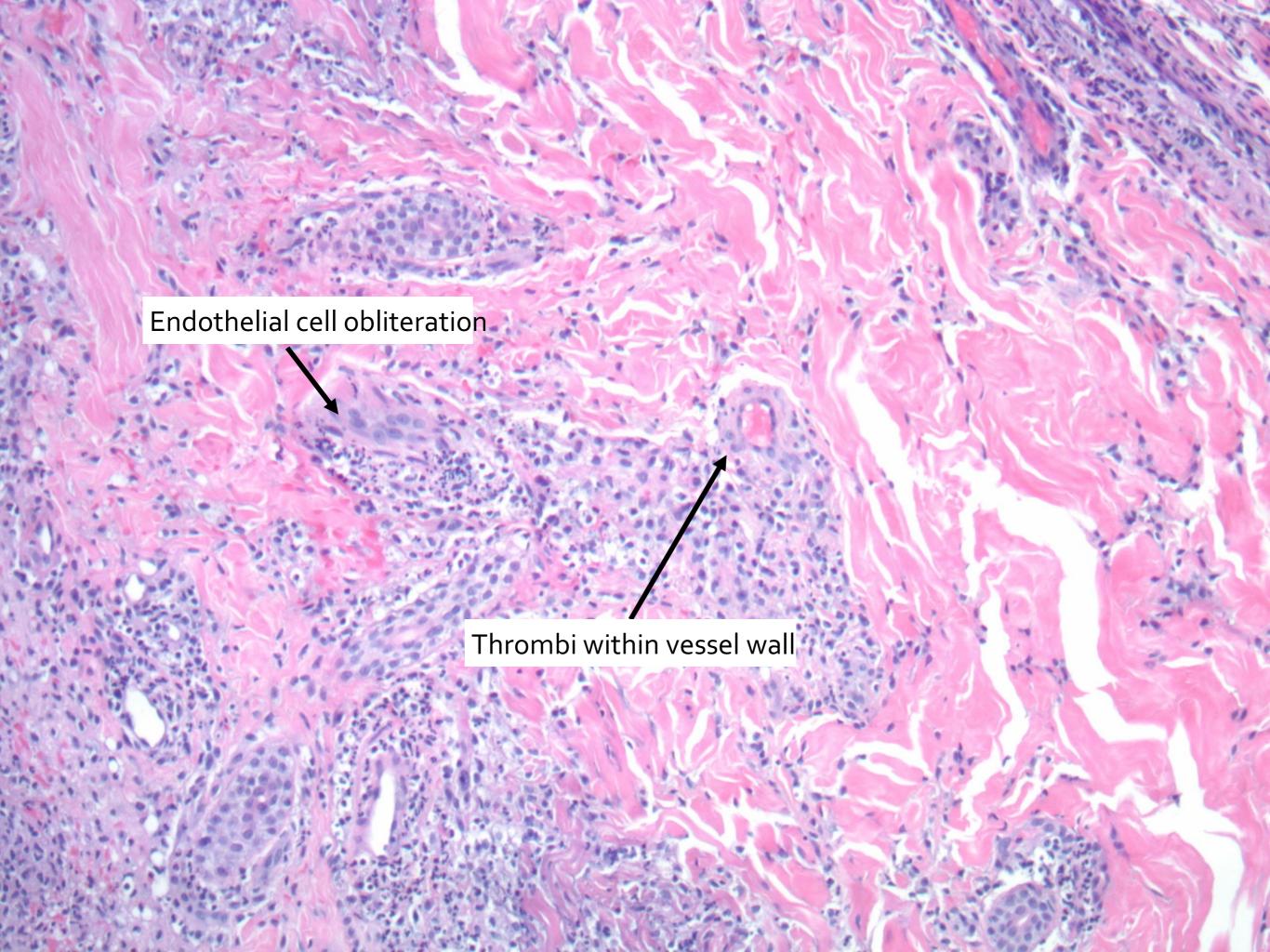
- Osler nodes or Janeway lesions
 - Secondary to:
 - Most likely: Subacute/acute endocarditis
 - Other:
 - Systemic lupus erythematosus
 - Gonococcemia
 - Hemolytic anemia

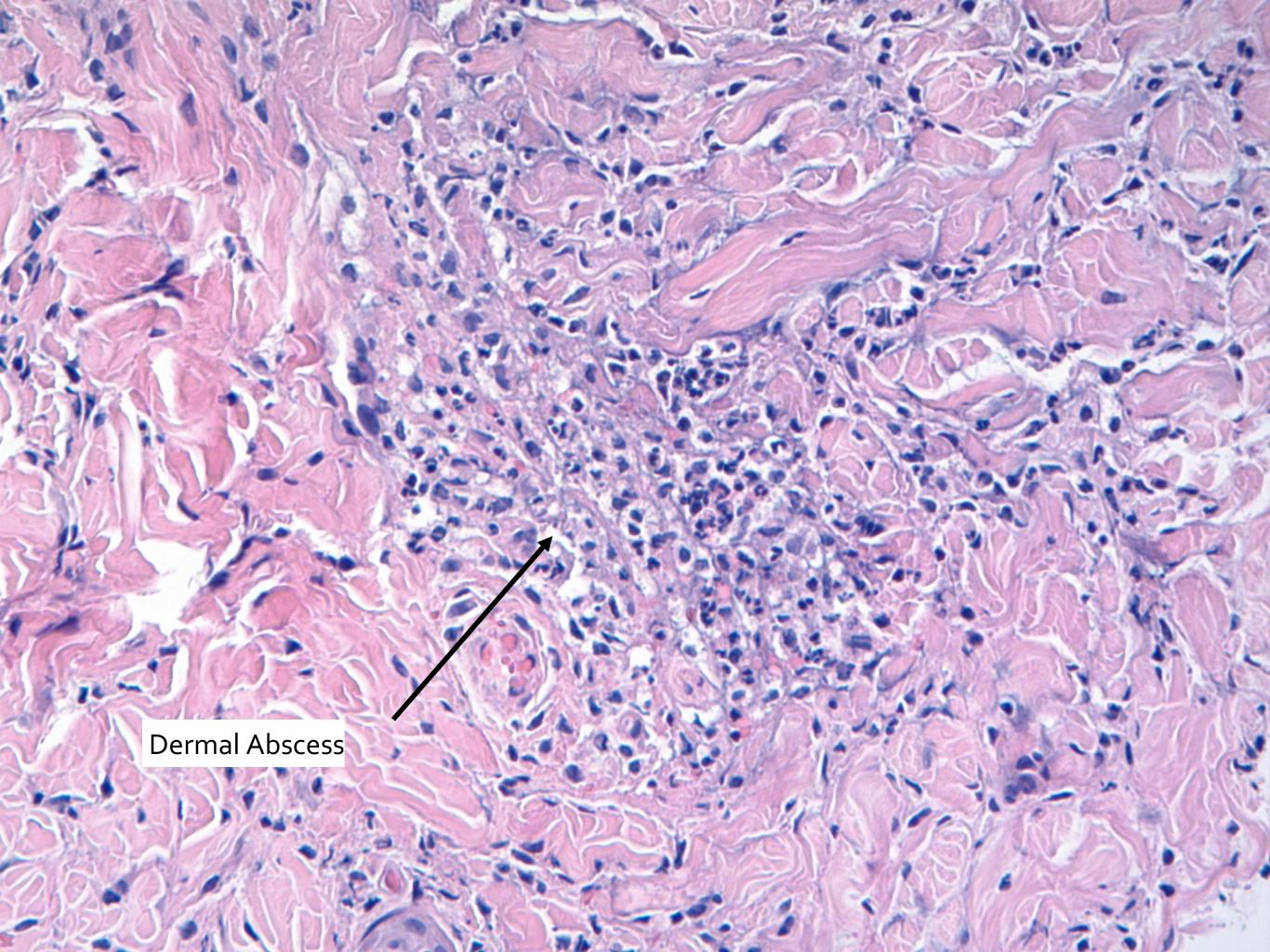


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Radiologic and Microbiologic Workup

- Blood cultures (+) S. aureus $x 4 \rightarrow$ (-) 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%.



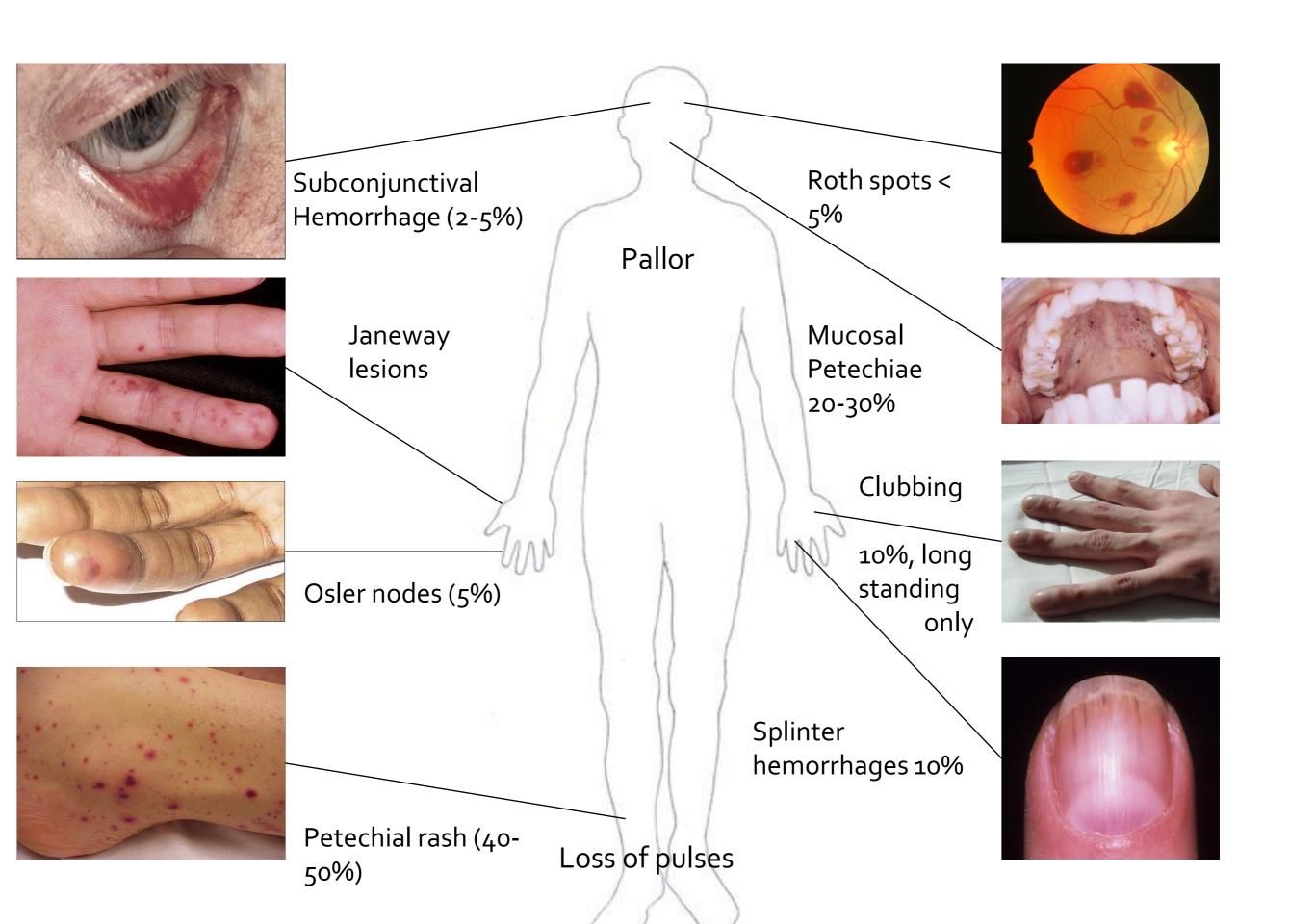
Classic Cutaneous Findings in Endocarditis

- >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





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Osler Nodes and Janeway Lesions Overview

- Cutaneous manifestations of bacterial endocarditis.
 - Also <u>rarely</u> 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 see in <u>acute</u> endocarditis



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Pathogenesis

- Two disparate theories
 - Circulating immune complex mediated vasculitis Gutman et al.
 - Microembolization



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- 45 year old woman
- Works in construction
- History of systemic lupus erythematous





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The "Red and Scaly" patient: Medium-size



- 45 year old woman
- Works in construction
- History of systemic lupus erythematous
- Biopsy of arm = squamous cell carcinoma





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The "Red and Scaly" patient: Medium- size



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- Plan:
 - wide excision by plastic surgeon and
 - radiation therapy to the rest





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Re-biopsy= SCLE lupus





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- Biopsy of arm = squamous cell carcinoma
- Plan:
 - Photoprotection
 - Emollients

Re-biopsy= SCLE lupus





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40 yo Caucasian otherwise healthy male
Chronic "rash" x 9 months in groin not responsive to antifungals, antibiotics, corticosteroids admitted for altered mental status



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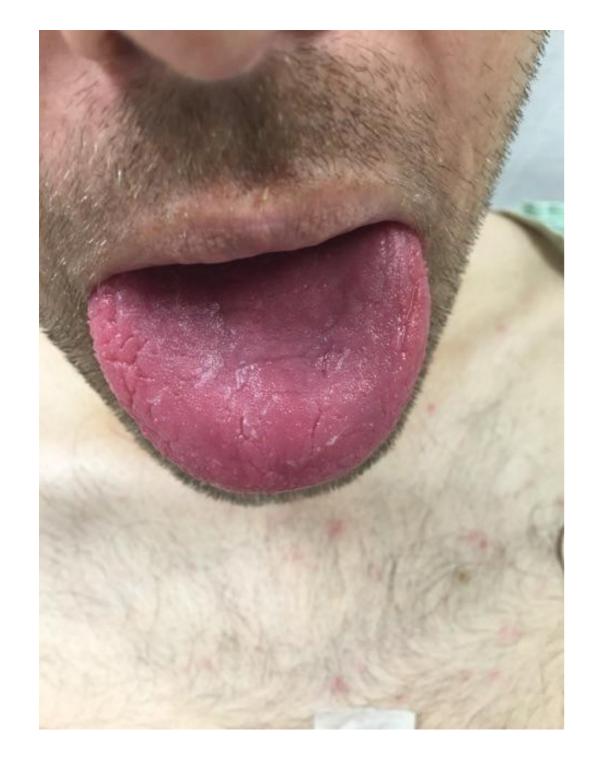
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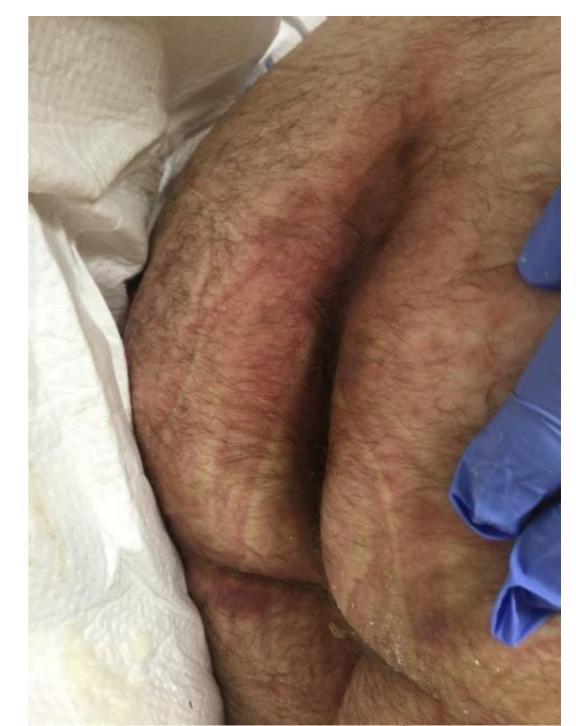




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Ctro continuo or a Continuo vi

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Dermatology + Mohs Surgery





Ddx:

- Atopic dermatitis
- Necrolytic Migratory erythema (glucagonoma syndrome, pseudoglucagonoma syndrome)
- Acrodermatitis enteropathica (zinc deficiency)
- Pellagra (niacin deficiency)
- Cutanous T- Cell Lymphoma ("Mycosis fungicides")
- Tinea



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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.



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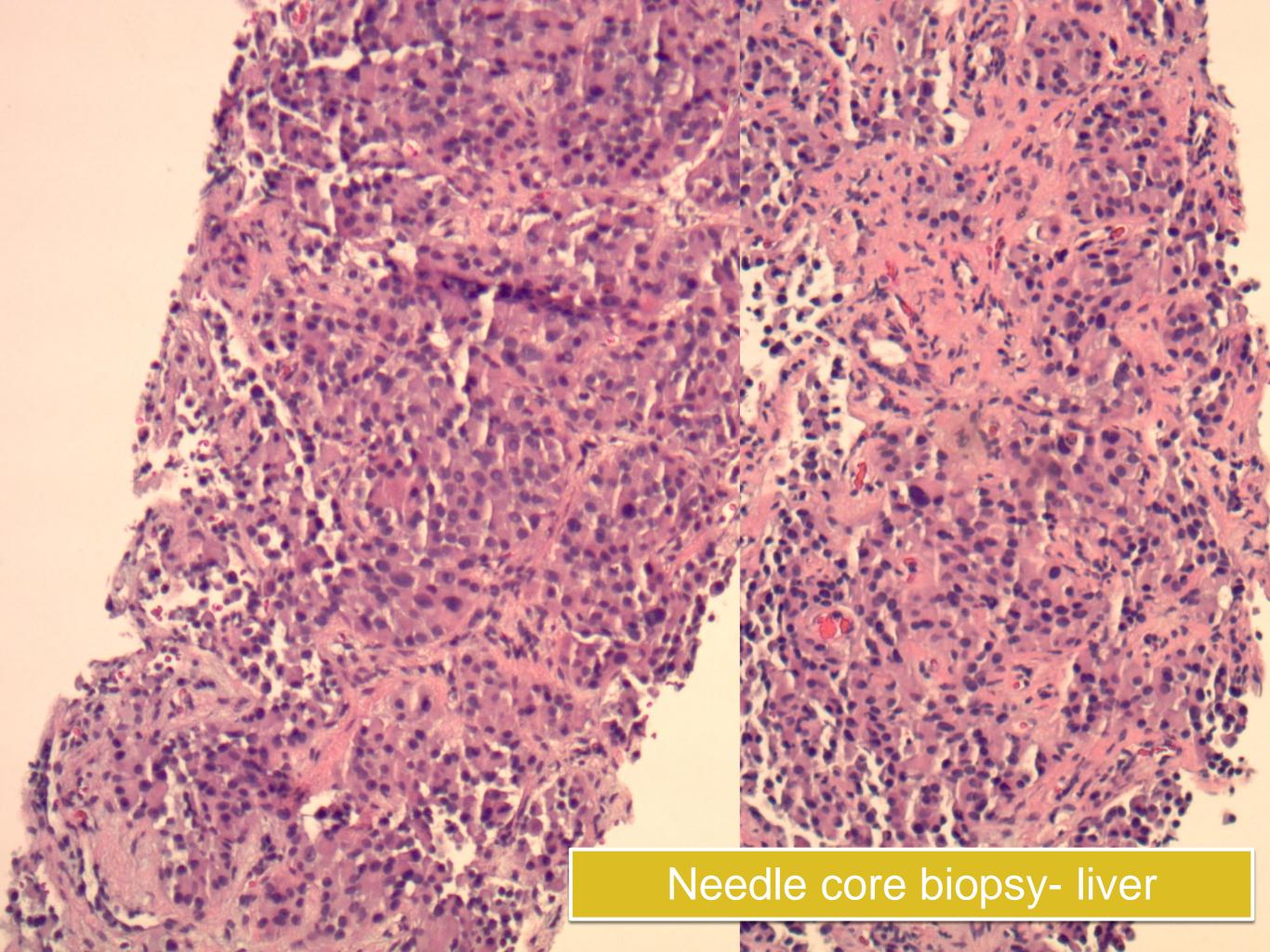


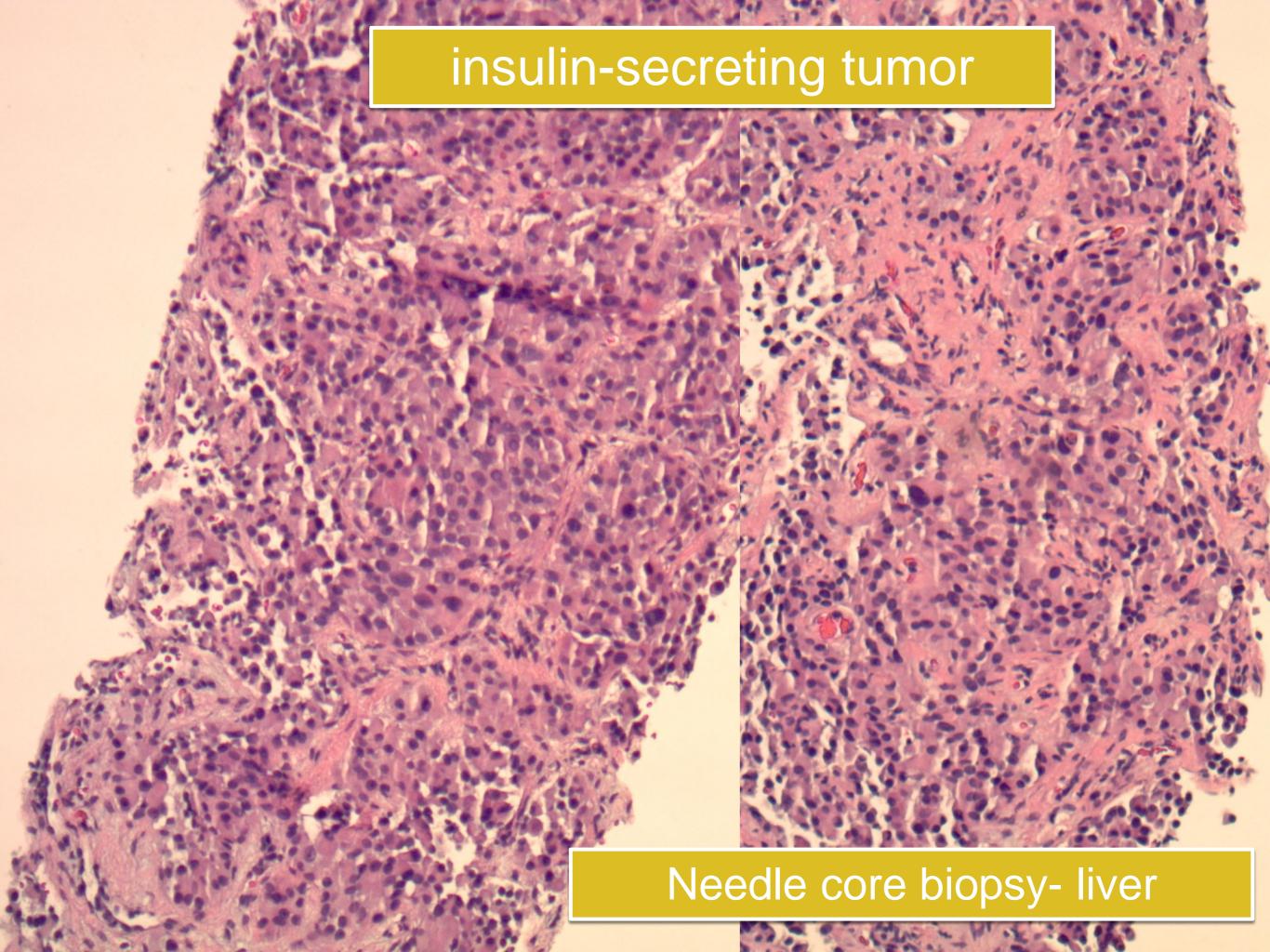
Diagnosis

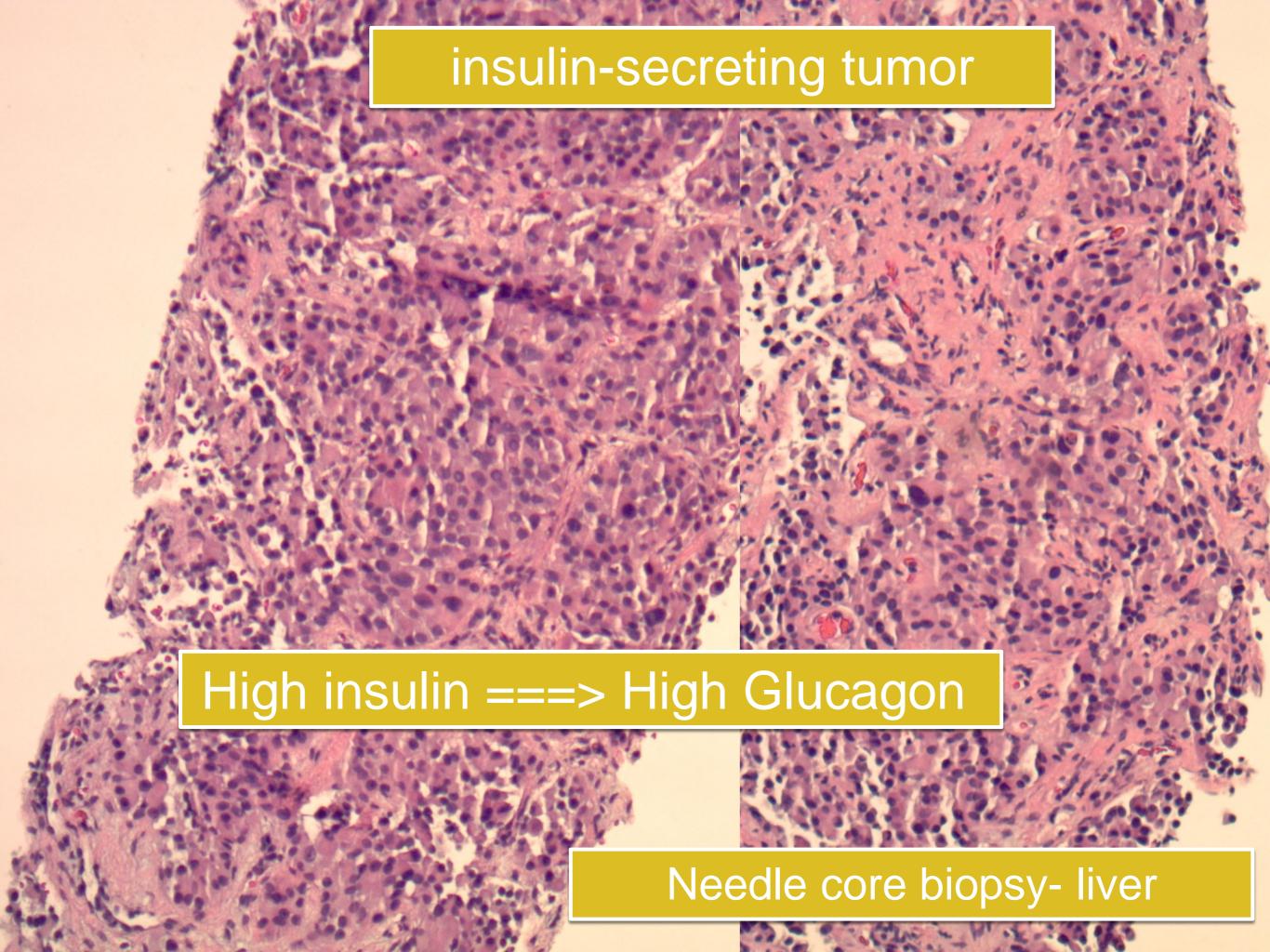
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Medical Student & Resident Teaching

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
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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

Thank you



Child with albinism in Africa



Strasswimmer + Smirnov Dermatology + Mohs Surgery