DERMATOLOGIC MANIFESTATIONS OF SYSTEMIC DISEASE

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ALLEN-TAINTOR DERMATOLOGY

DISCLOSURES

- Speaker for Castle Biosciences

ALLEN-TAINTOR DERMATOLOGY

OBJECTIVES

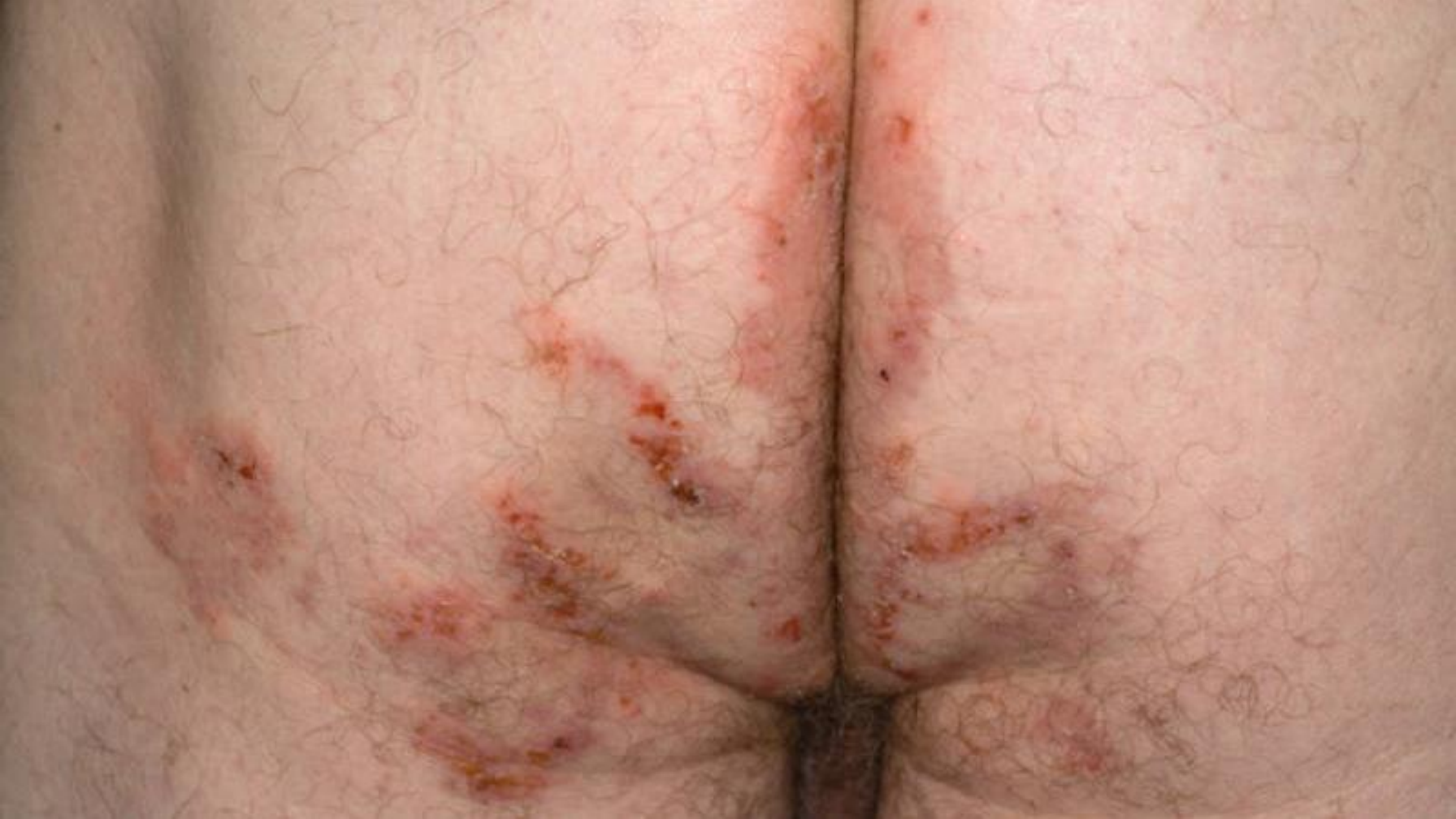
- Share dermatologic pearls that can assist in the diagnosis of systemic disease
  - Clues on the outside to what is going on on the inside
- Improve patient care
  - Help to know when further workup and treatment options are needed

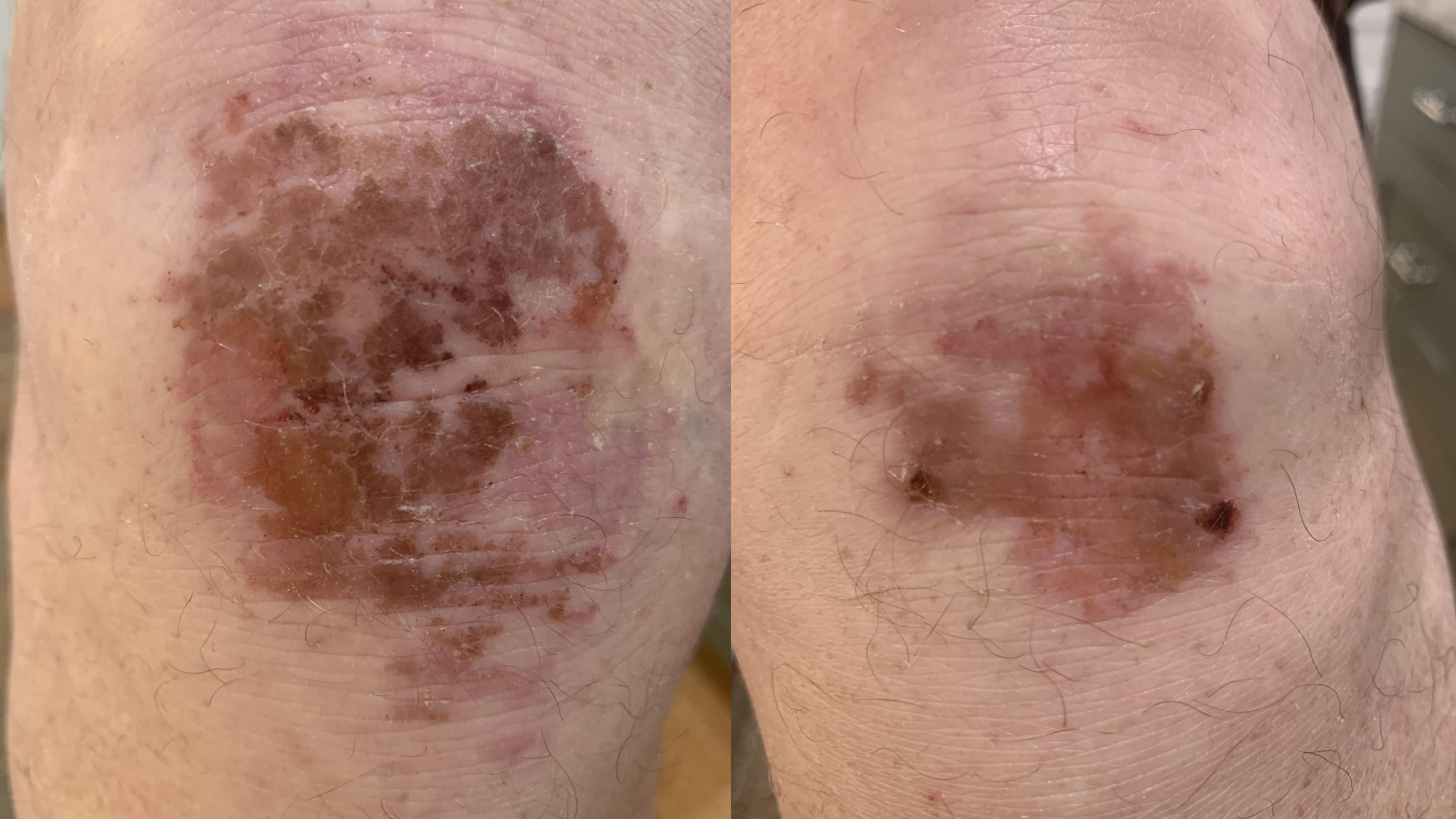
CASE 1

ALLEN-TAINTOR
DERMATOLOGY

CASE 1

- 71 yo Caucausian male with 4-week history of rash on the buttocks, elbows and knees
- Otherwise healthy





DERMATITIS HERPETIFORMIS

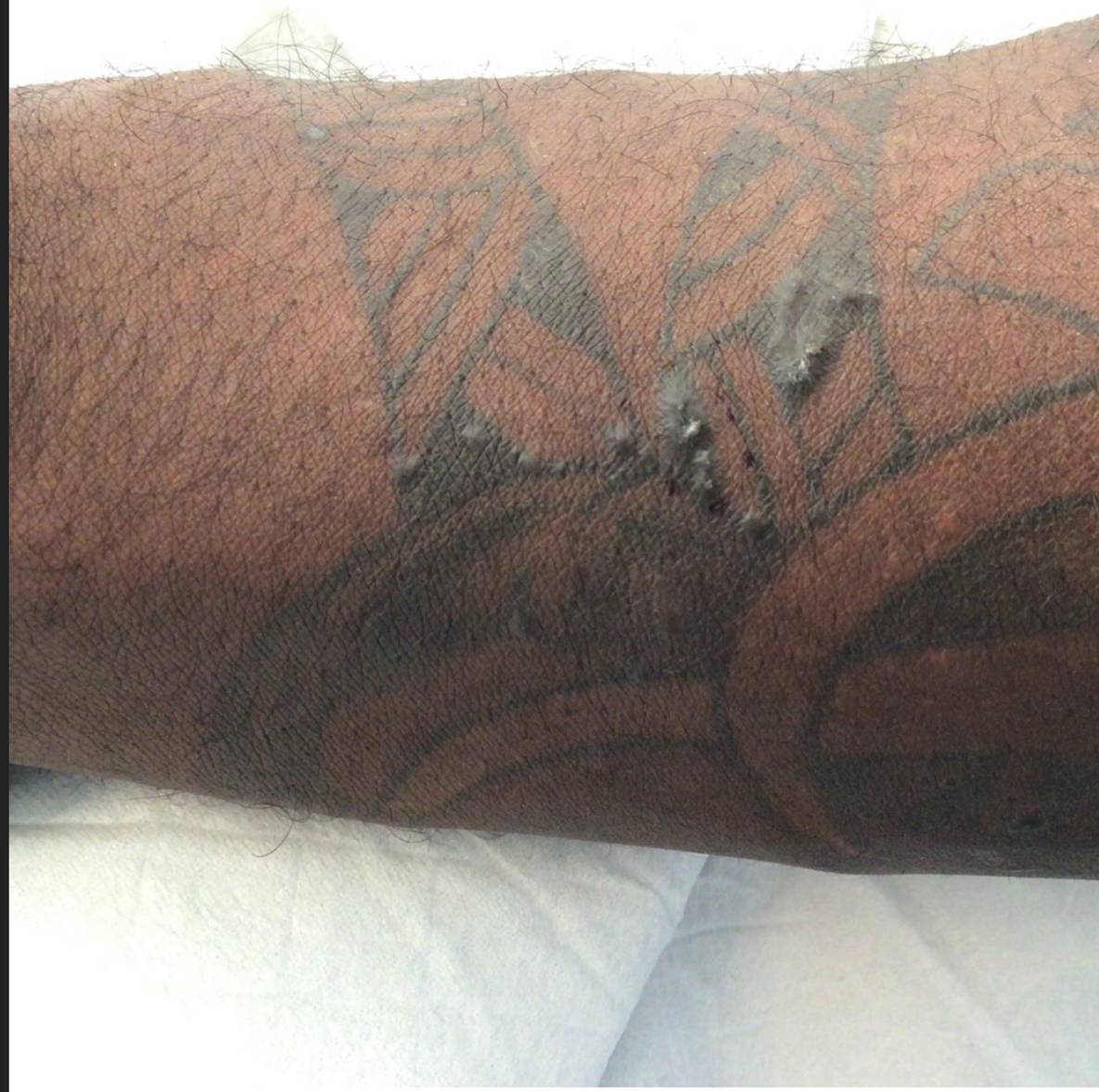
- Biopsy and DIF consistent with dermatitis herpetiformis
- No complaints of abdominal pain or family history of celiac disease
  - Indirect immunofluorescence consistent with celiac disease
- Patient's rash quickly clears with dapsone
- Patient decided to discontinue dapsone and attempt to treat with gluten-free diet

CASE 2

ALLEN-TAINTOR
DERMATOLOGY

CASE 2

- 42 yo African American male with 6-month history of spreading tender bumps without a tattoo
- Tattoo performed 4 years ago
- PMH: DM1
- No complaints of SOB



ALLEN-TAINTOR DERMATOLOGY

MODE

CUTANEOUS SARCOIDOSIS

- Biopsy consistent with sarcoid
- Labs significant for hypercalcemia
- Referred to pulmonology and ophthalmology for evaluation

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Increased risk of systemic and cardiac sarcoidosis in Black patients with cutaneous sarcoidosis

Bina Kassamali, BA • Camila Villa-Ruiz, MPH • Kylee J.B. Kus, BS • ... Ruth Ann Vleugels, MD, MPH, MBA • Avery H. LaChance, MD, MPH • Sotonye Imadojemu, MD, MBE • Show all authors

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CASE 3

ALLEN-TAINTOR
DERMATOLOGY

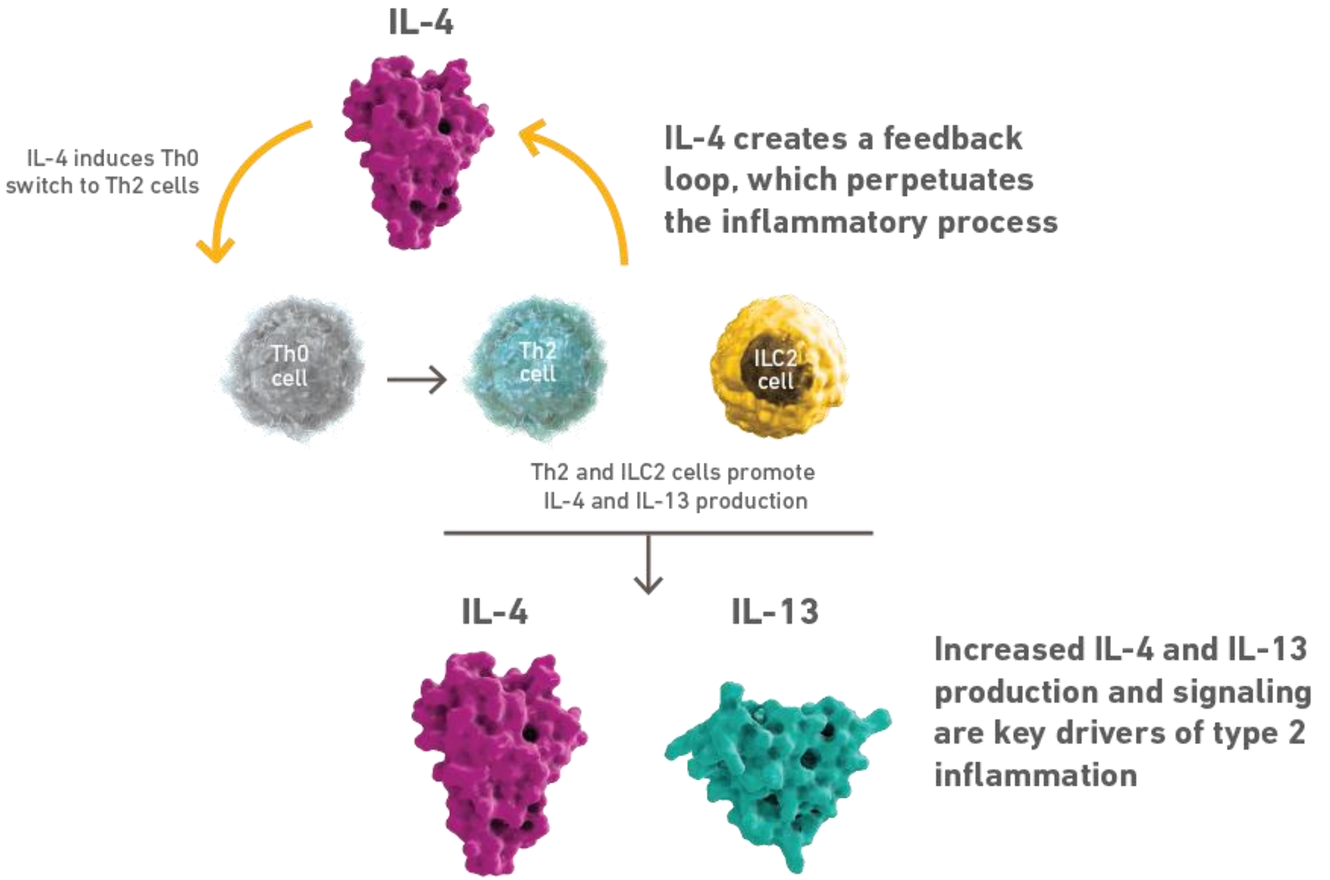
CASE 3

- 48 yo Asian American male with lifelong history of atopic dermatitis
- PMH: hospitalization for eczema herpeticum in 2018, gout, followed by hematology for polycythemia and thrombocythemia
- FH: CAD, MI

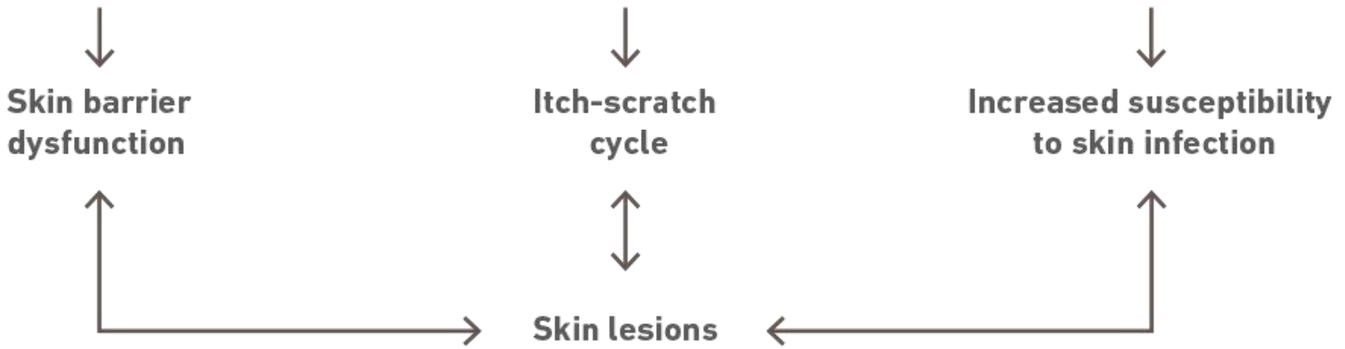
- Atopic dermatitis well controlled for 3 years on dupilumab (Dupixent)

- Dupilumab well controlled with the exception of moderate – severe conjunctivitis

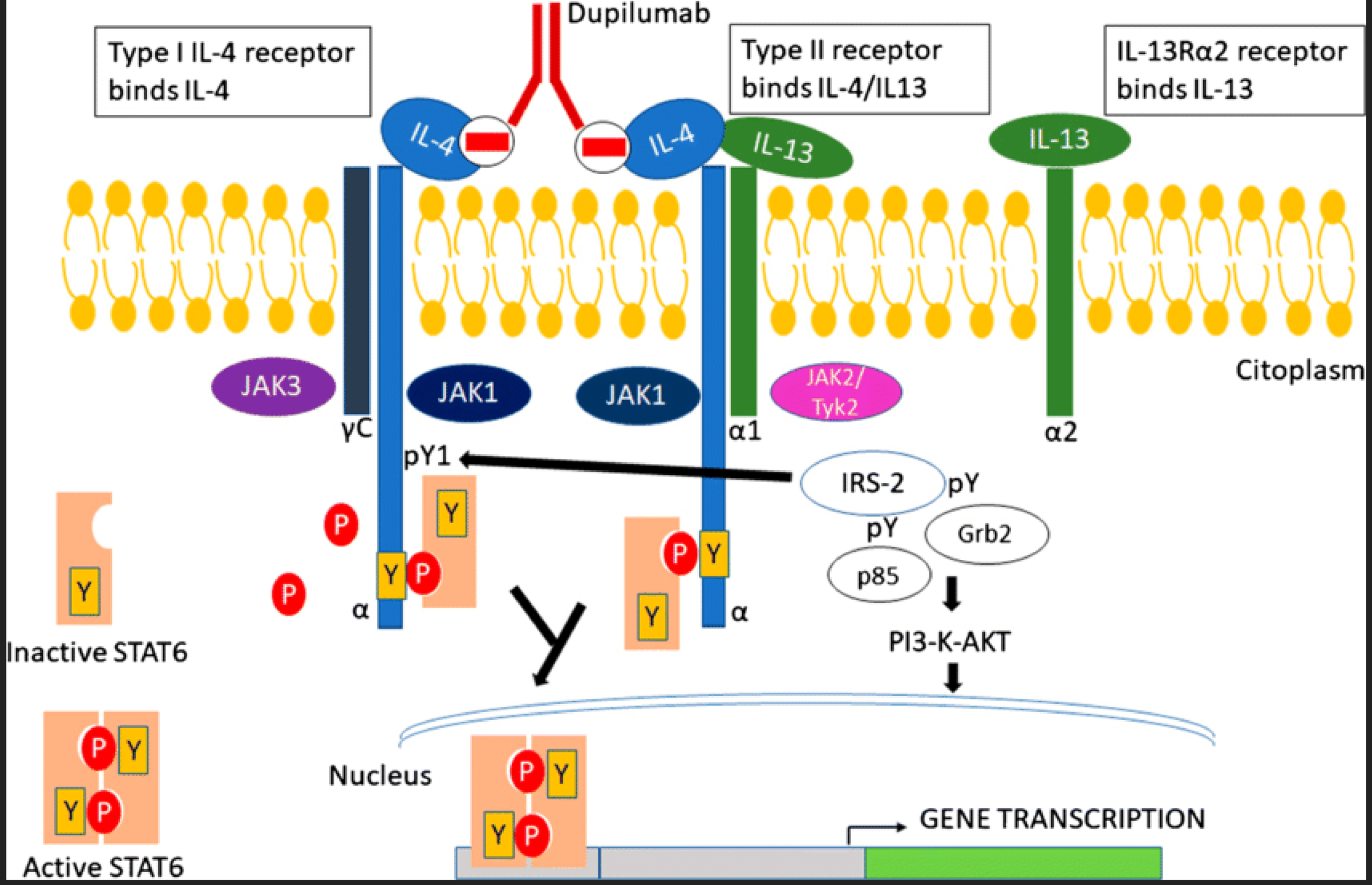
ALLEN-TAINTOR DERMATOLOGY



Increased IL-4 and IL-13 signaling contributes to[4-6]:



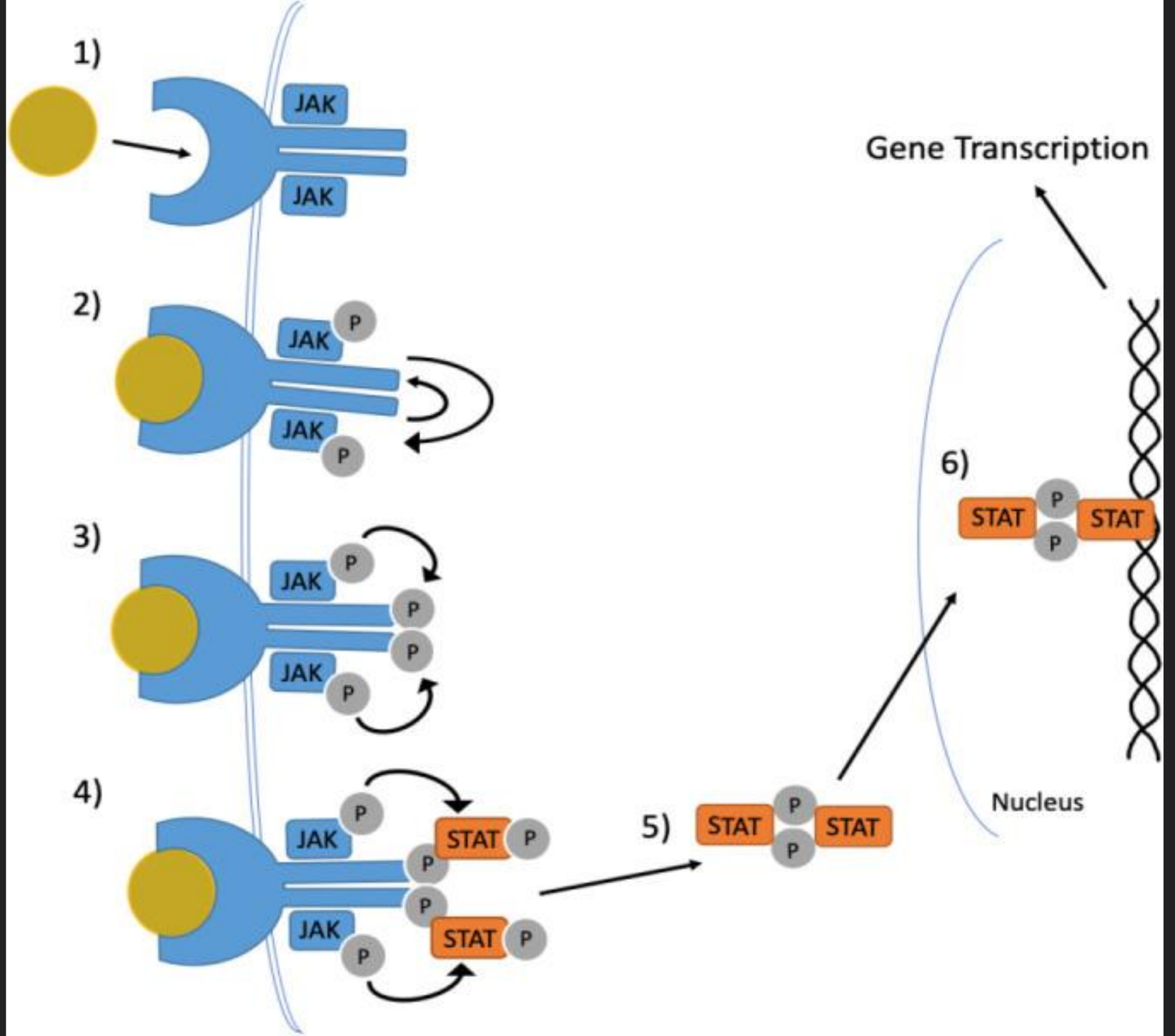
https://www.dupixenthcp.com/atopicdermatitis/about/mechanism-of-action


Type I IL-4 receptor binds IL-4
Dupilumab
Type II receptor binds IL-4/IL13
IL-13Rα2 receptor binds IL-13
IL-4
IL-4
IL-13
IL-13
JAK3
JAK1
JAK1
JAK2/ Tyk2
Citoplasm
γC
α1
α2
pY1
IRS-2
pY
pY
Grb2
p85
PI3-K-AKT
P
Y
α
α
Inactive STAT6
Active STAT6
Nucleus
GENE TRANSCRIPTION

ATOPIC DERMATITIS

- Patient mentions addition of hydroxyurea for treatment of thrombocytosis and polycythemia

- Recently had genetic testing
  - mutation in JAK2 (V614F mutation)
  - Upregulation of JAK2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Nucleus

JAK2 UPREGULATION MUTATION

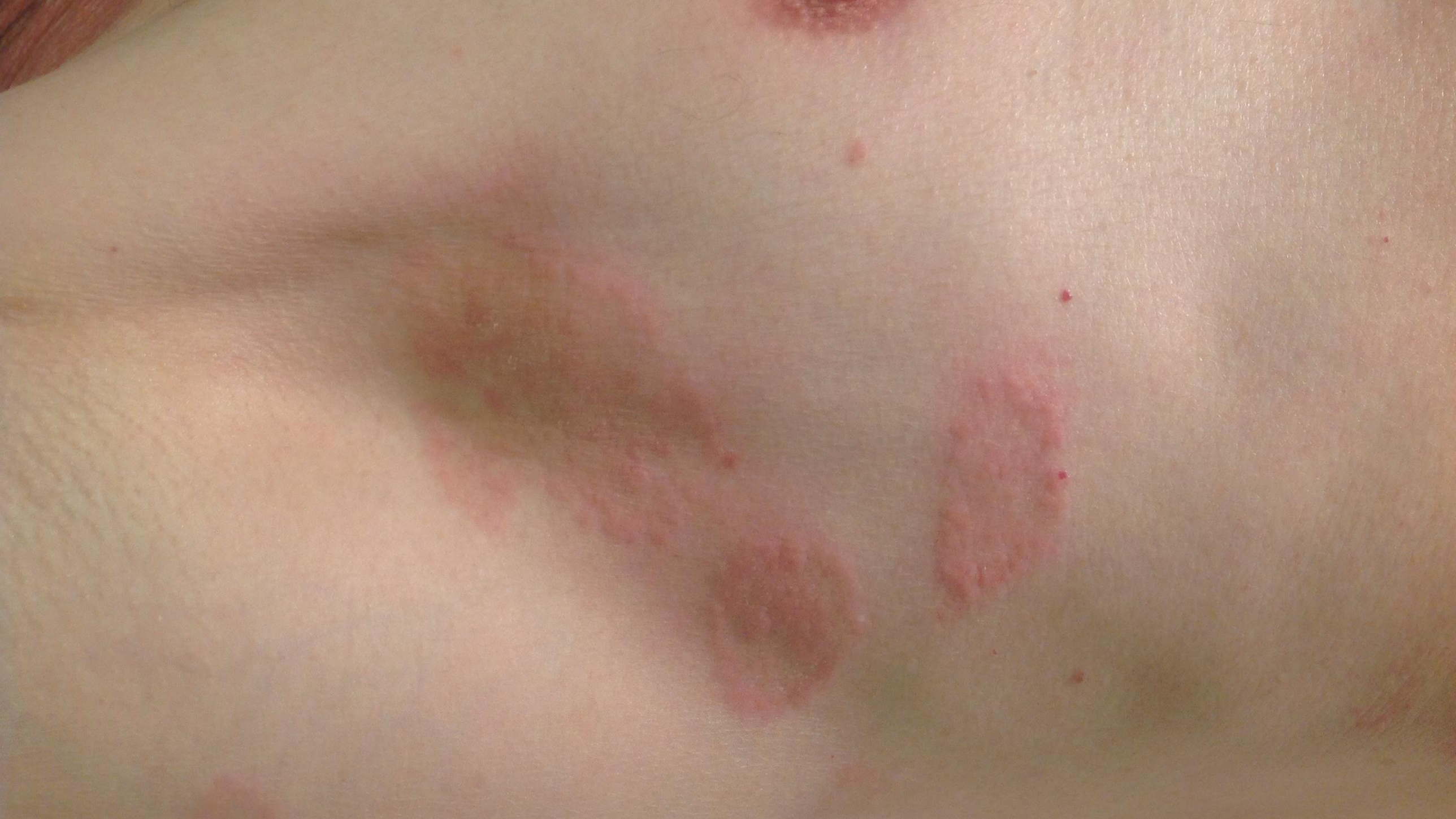
- Worked with hematology to switch patient from dupilumab to ruxolitinib (Jakafi®)
  - Blocks JAK1 and JAK2 signaling
  - Risk of malignancy, herpes infection and MACE events

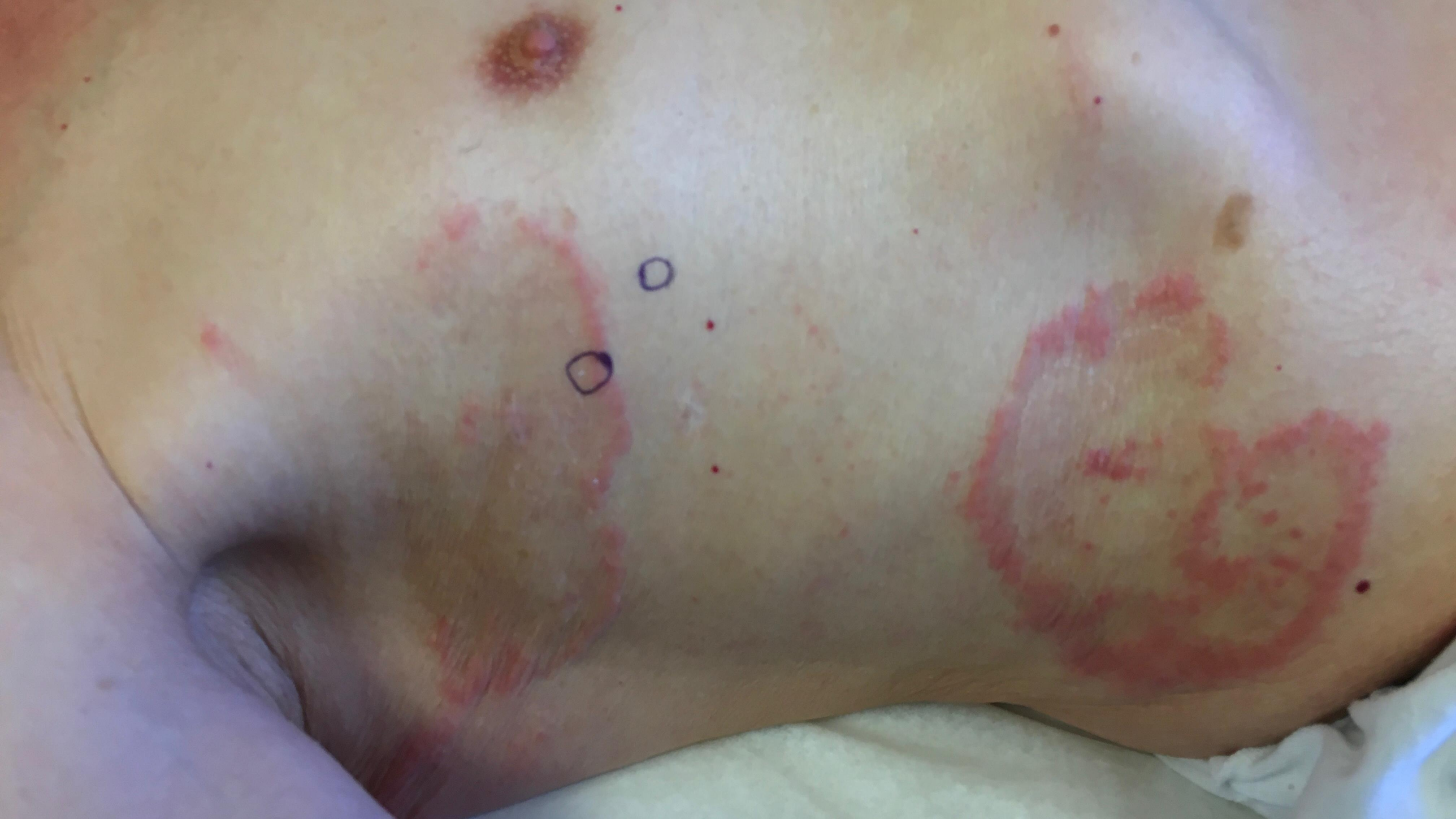
- Now, 6 months later, atopic dermatitis is well controlled with no conjunctivitis
- TCP and polycythemia recalcitrant to high dose ruxolitinib 25 mg BID

- Restarting hydroxyurea. May switch back to dupilumab

CASE 4

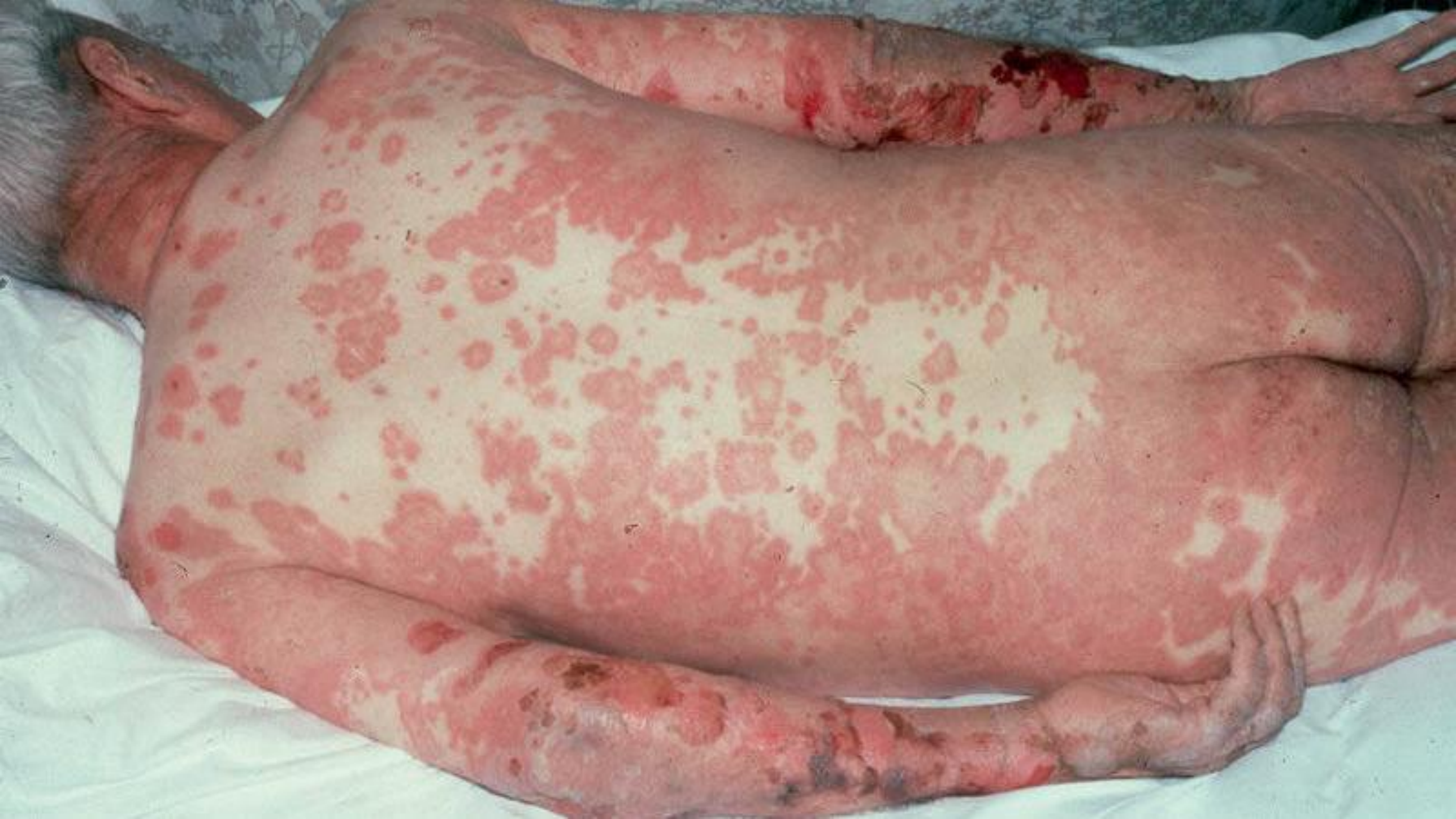
ALLEN-TAINTOR
DERMATOLOGY

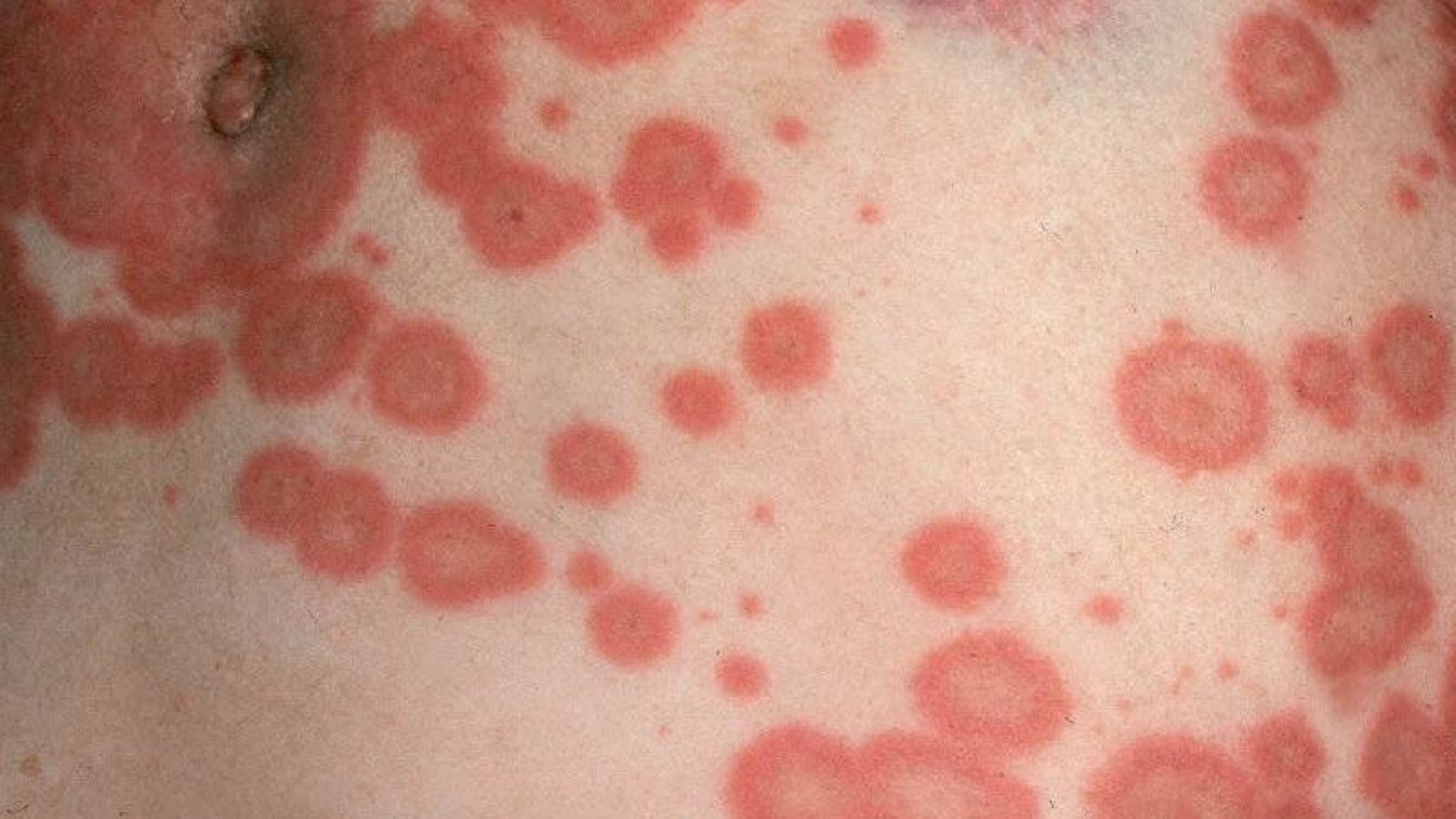


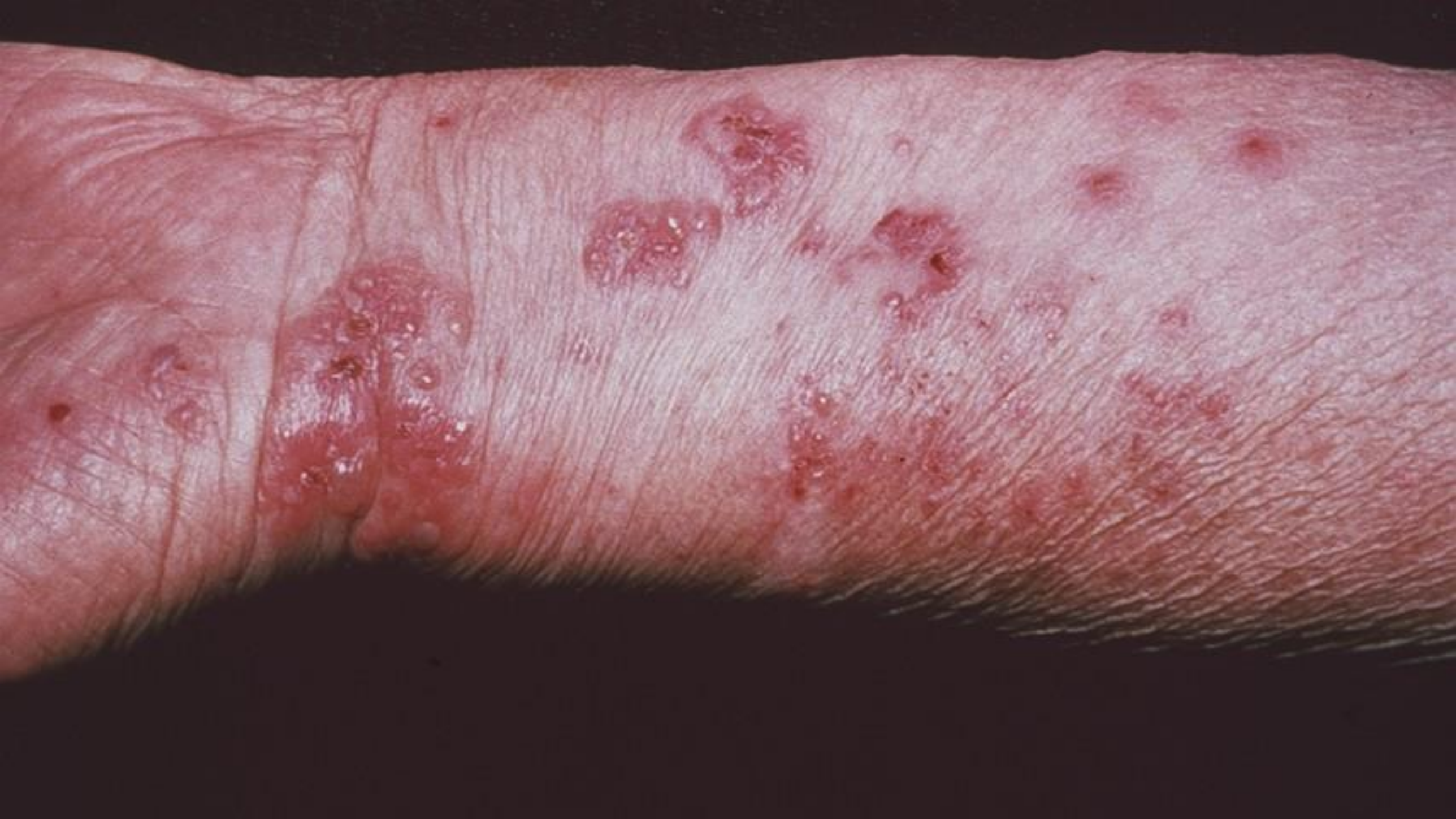


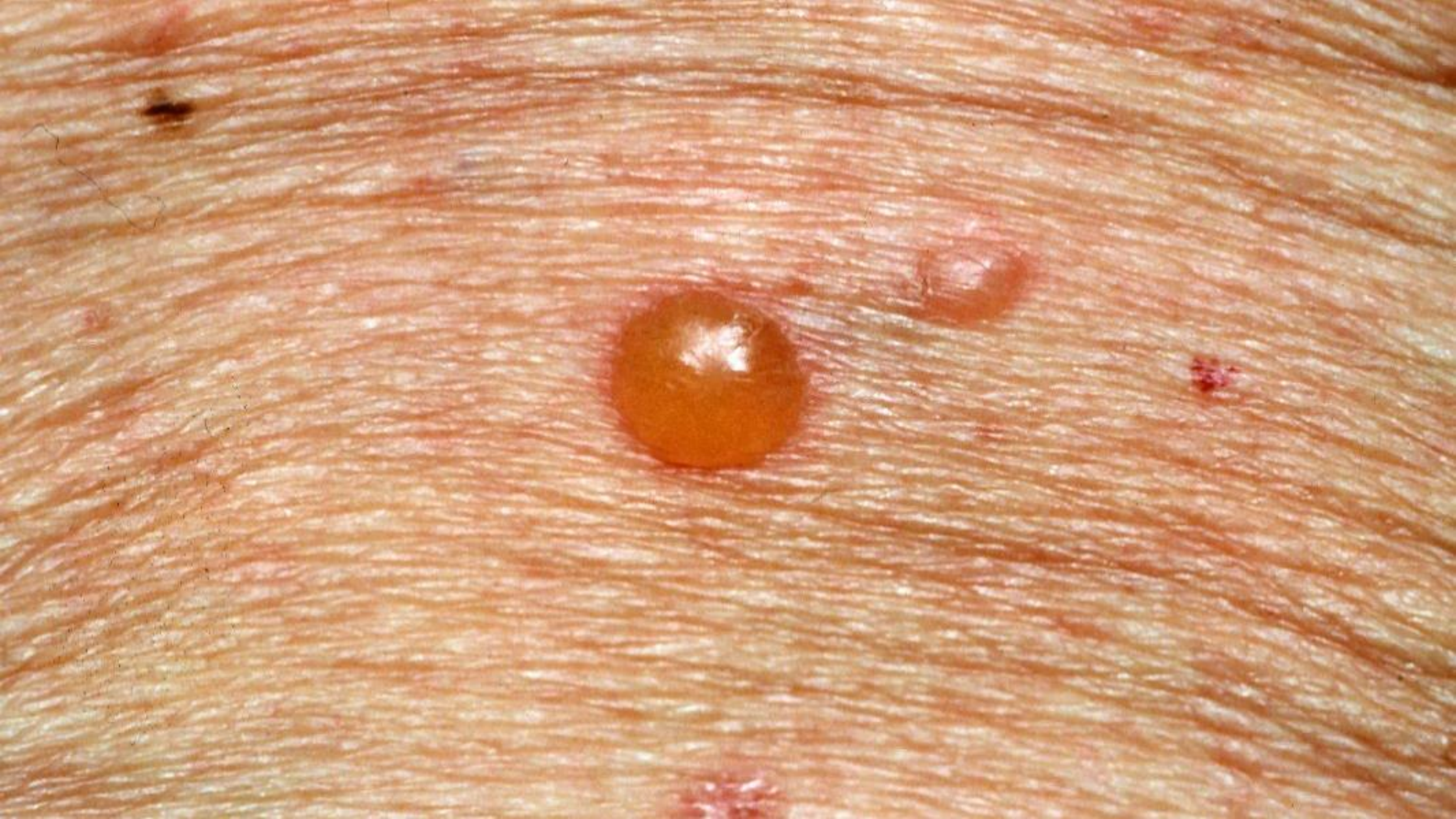
BULLOUS PEMPHIGOID

- 80 yo Caucasian male with biopsy consistent with bullous pemphigoid
- Had been treated effectively with doxycycline, niacinamide and topical steroids but recently non-responsive to treatment









BULLOUS PEMPHIGOID

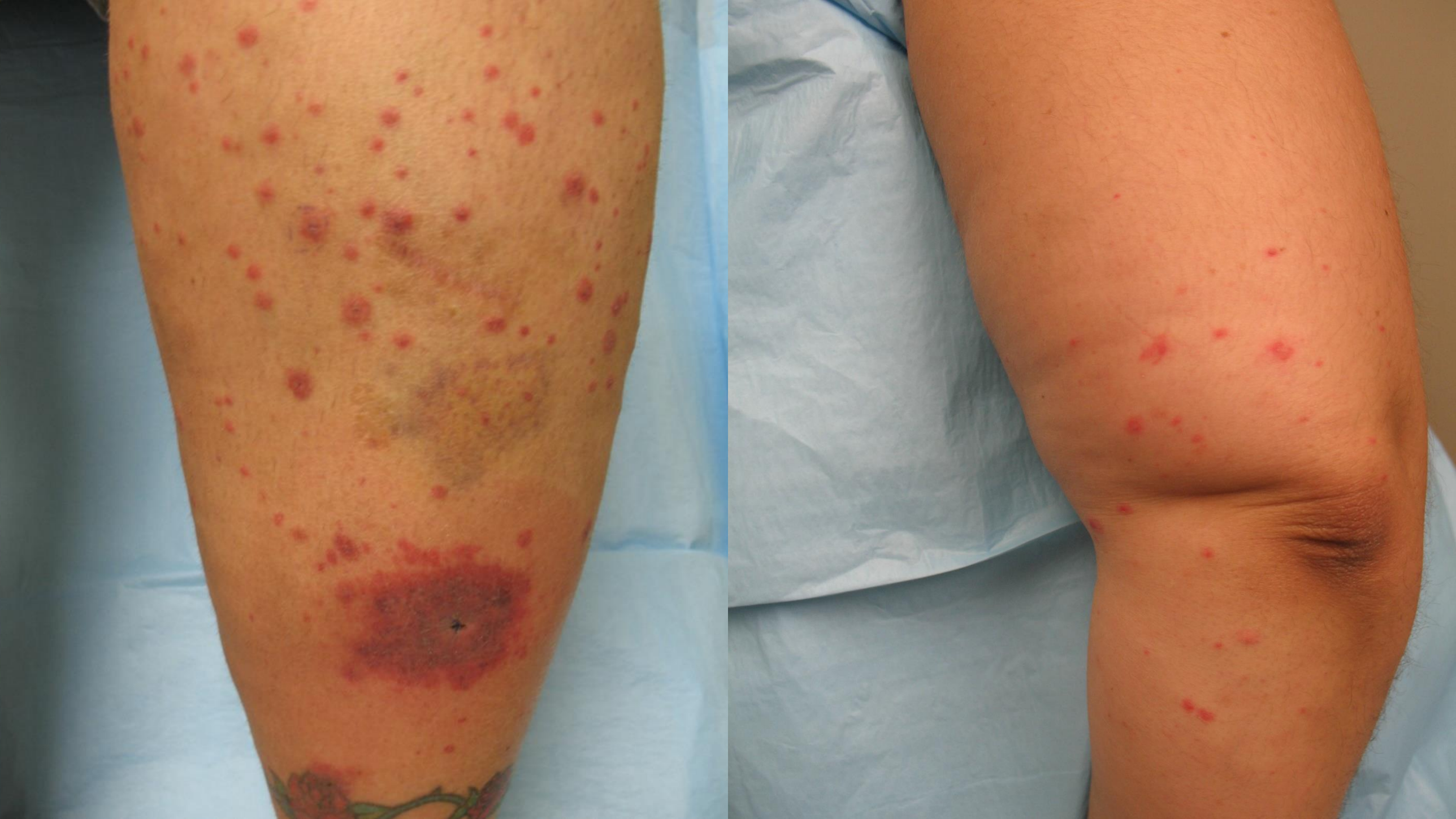
- Drug-induced secondary to analgesics, penicillins, captopril, furosemide, spironolactone, sulfasalazine, PD-1 inhibitors, antidiabetic drugs (-gliptins)
- Recalcitrant cases usually respond to dupilumab
  - IL-4 blocker ⇒↓ TH2 response
  - Patient started on samples of dupilumab with good response

CASE 5

ALLEN-TAINTOR
DERMATOLOGY

CASE 5

- 39 yo female with 10 day history of pruritic rash on legs, 24 hr history of crampy abdominal pain and nonbloody diarrhea
- Abdominal pain improved after pain meds in ED but rash progressed while inpatient



LABS

- Afebrile
- ESR 38
- WBC 11.3 (admission 18.6)
- Platelets normal
- INR 4.2
- LFTs normal
- BUN and creatinine normal

HENOCH-SCHONLEIN PURPURA

- Biopsy for H&E and DIF consistent with Henoch Schonlein purpura
- Discharged home
- Clinic visit 7 days after initial presentation
  - Increased lesions, more on UE, painful and pruritic.
  - BUN/Creatinine normal
- Recommended prednisone, pt refused
- Started on Triamcinolone 0.1% ointment

ALLEN-TAINTOR DERMATOLOGY

HENOCH-SCHONLEIN PURPURA

- 10 days after initial presentation,pt called to report several large bloody bowel movements overnight and abdominal pain
- Readmitted, found to have jejunal intussusception on CT
  - Self resolved
- Started on prednisone 60mg/day.
- Abdominal pain improved, no further hematochezia, d/c'd home on 3 wk taper
- BUN and creatinine remained normal x 6 months

ALLEN-TAINTOR DERMATOLOGY

HENOCH-SCHONLEIN PURPURA

- IgA vasculitis
- Cutaneous, renal, arthralgias, GI involvement

- Renal disease risk greater in adults and those with cutaneous disease above the waist
  - Monitor renal function for at least 6 months

- Often triggered by viral or strep infection

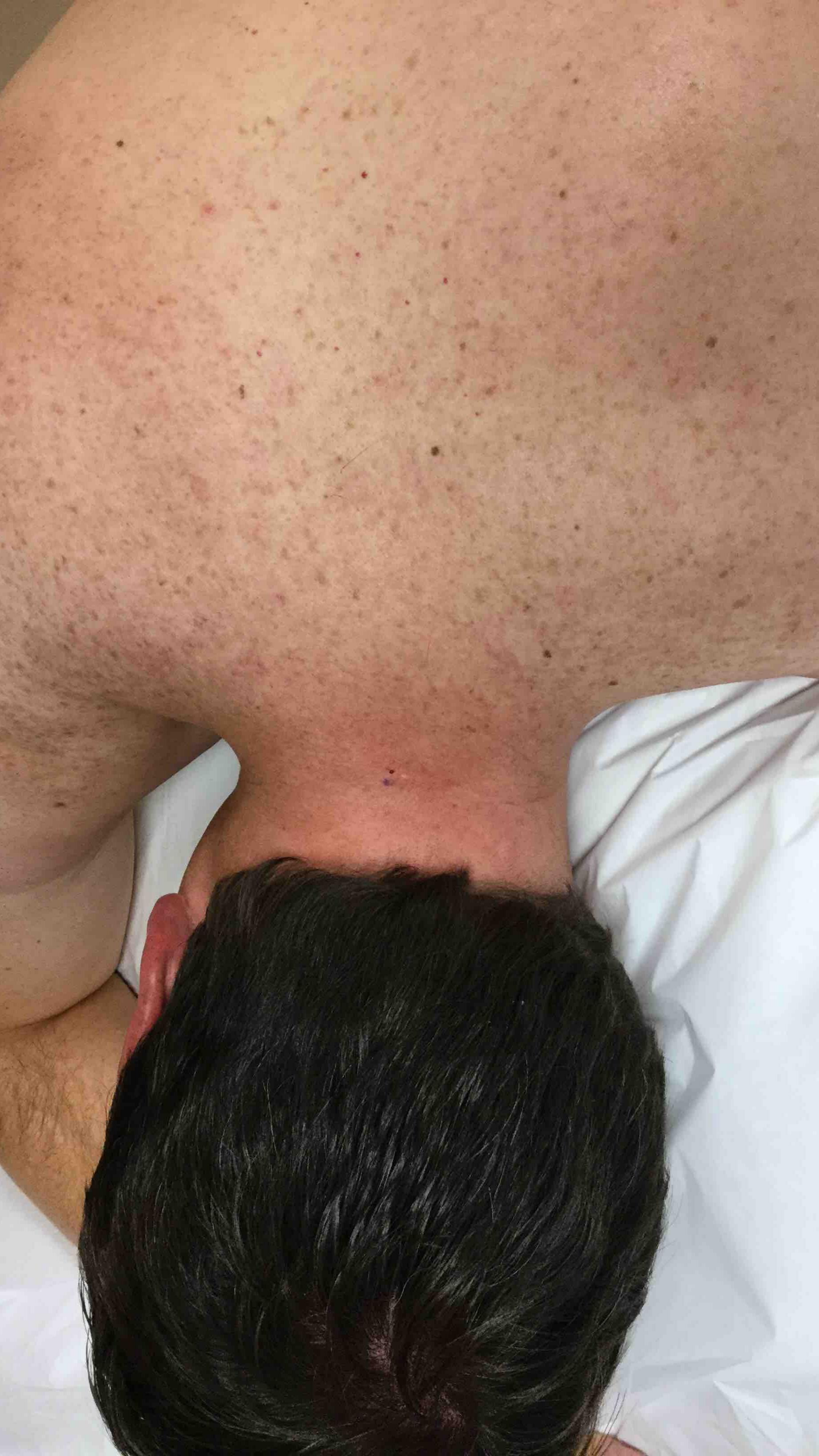
- Treatment
  - Self-resolving, 6-16 wks
  - Prednisone can alleviate GI symptoms, probably no affect on renal disease

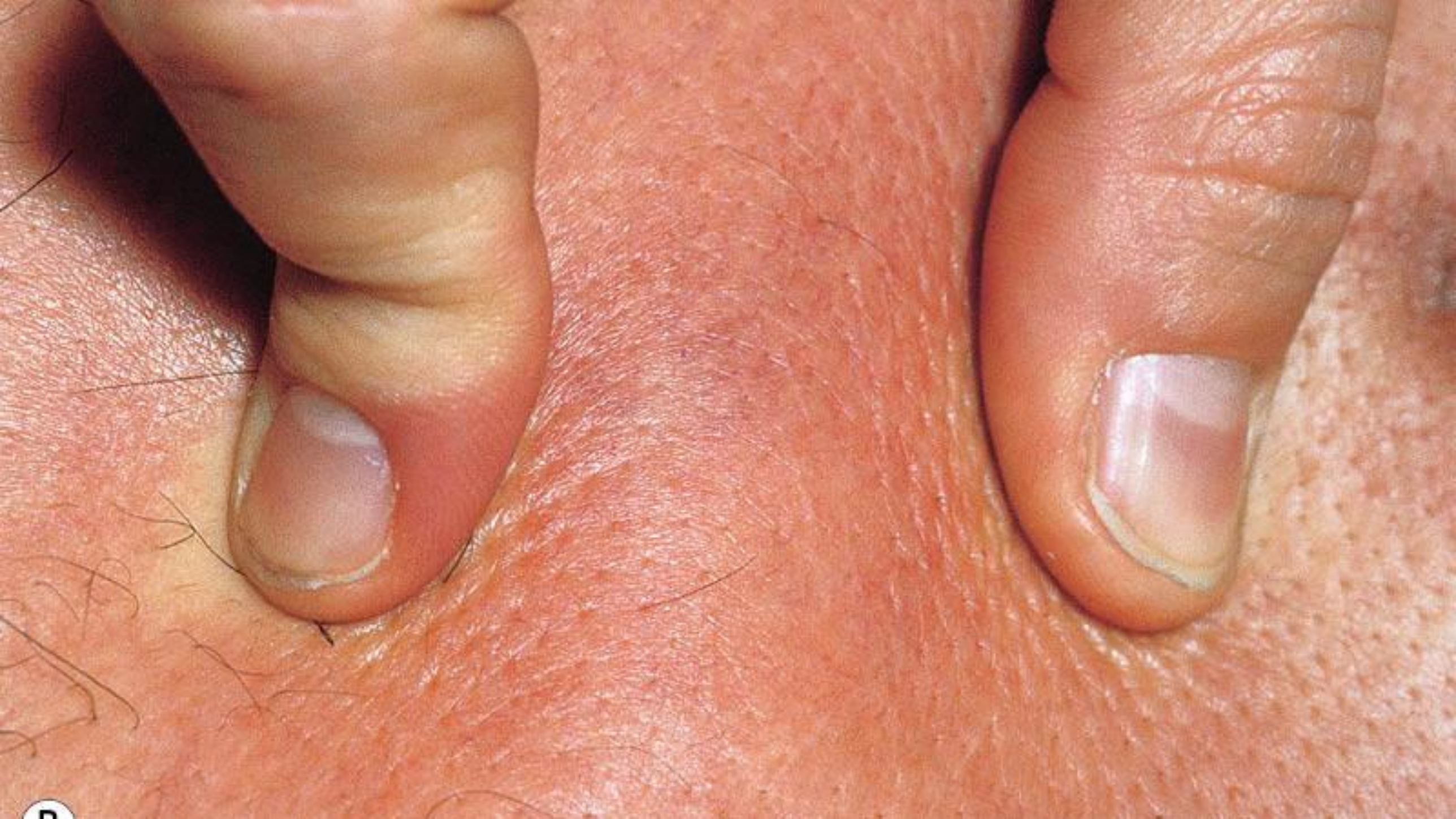
CASE 6

ALLEN-TAINTOR
DERMATOLOGY

CASE 6

- 55 yo Caucasian male referred for possible amyloidosis
- Stiff shoulders and skin tightness of the arms, shoulders, face and neck
- Difficulty raising his arms above the shoulders x 5 years
- History of GERD and esophageal dilatation





LABS

- Negative ENA, DNDNA, Sm ab, Scl70, SSA, SSB, anticentromere and antichromatin ab
- Positive RNP of 1.2
- Monoclonal IgA kappa
- XR bone survey: lytic lesions in the occipital bone

SCLEREDEMA

- Divided into three types:
  - First type:
    - Seen in middle aged women and children
    - Preceded by fever, malaise, and infection (strep)
    - Usually resolves within a few months
  - Second type:
    - Same clinical features, but a more subtle onset
      - No preceding illness
    - Persists for years
    - Associated with a monoclonal gammopathy
  - Third type:
    - Seen in obese middle aged men with DM
    - Subtle onset and persistent

TREATMENT

- PUVA
- Cyclophosphamide
- Cyclosporine

- Treatment unnecessary if associated with strep

- If associated with multiple myeloma, may resolve with treatment of myeloma.

- Control of hyperglycemia has no influence on the skin

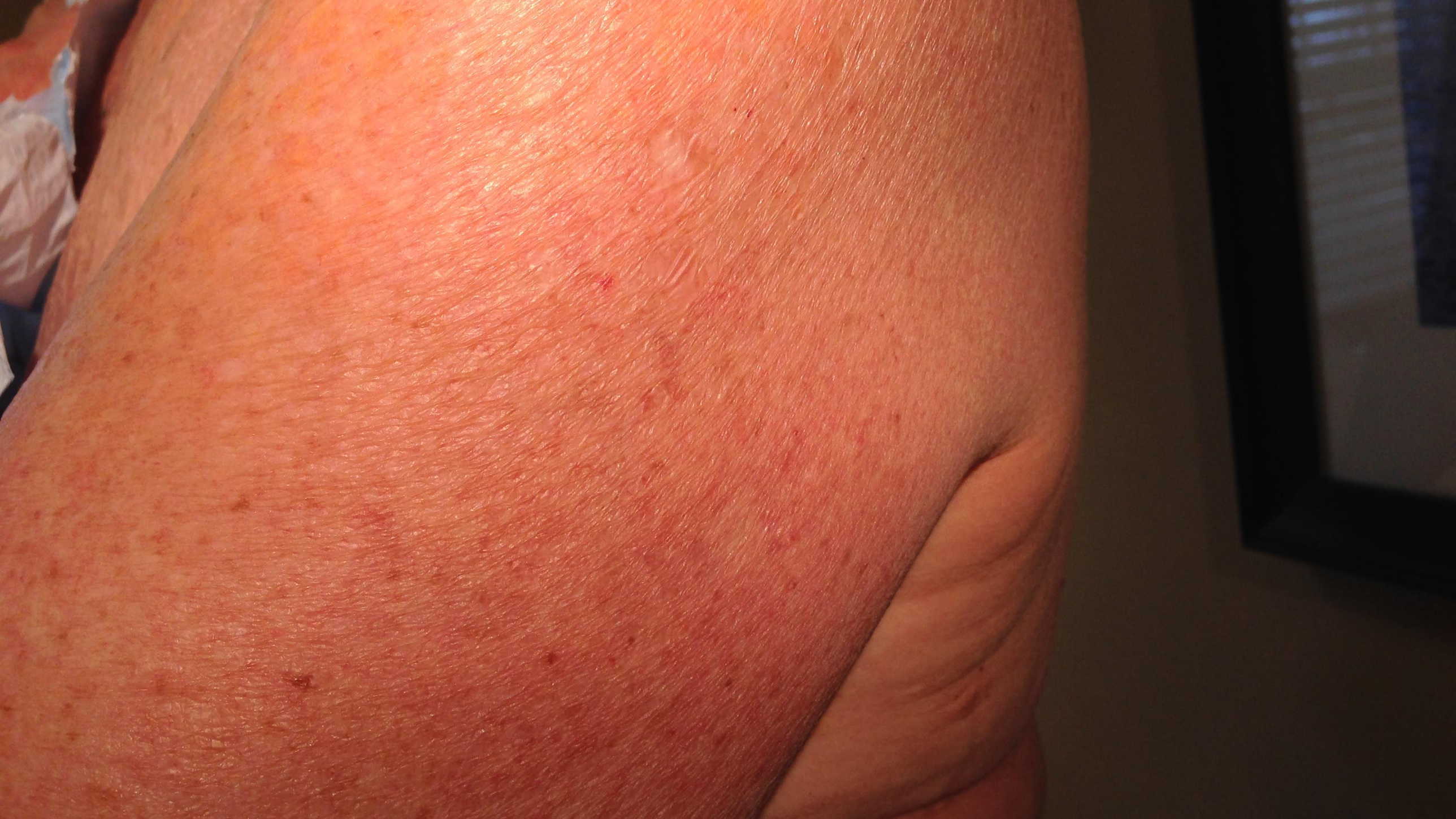
ALMOST ALWAYS ASSOCIATED WITH MONOCLONAL GAMMOPATHY

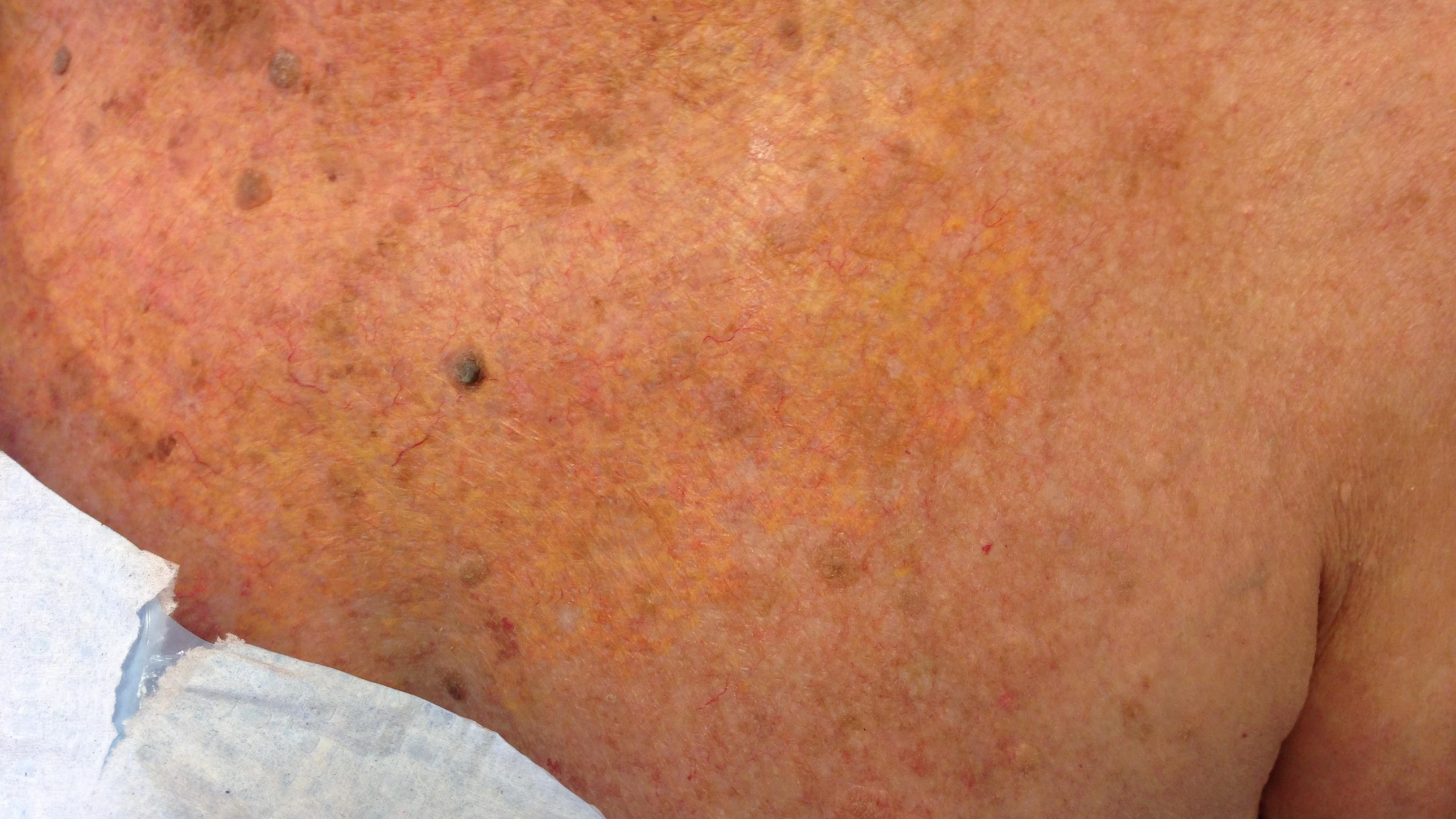
- Scleromyxedema
- POEMS syndromes
- AESOP syndrome - adenopathy and extensive skin patch overlying a plasmacytoma; may coexist with POEMS syndromes
- Schnitzler syndrome
- Necrobiotic xanthogranuloma

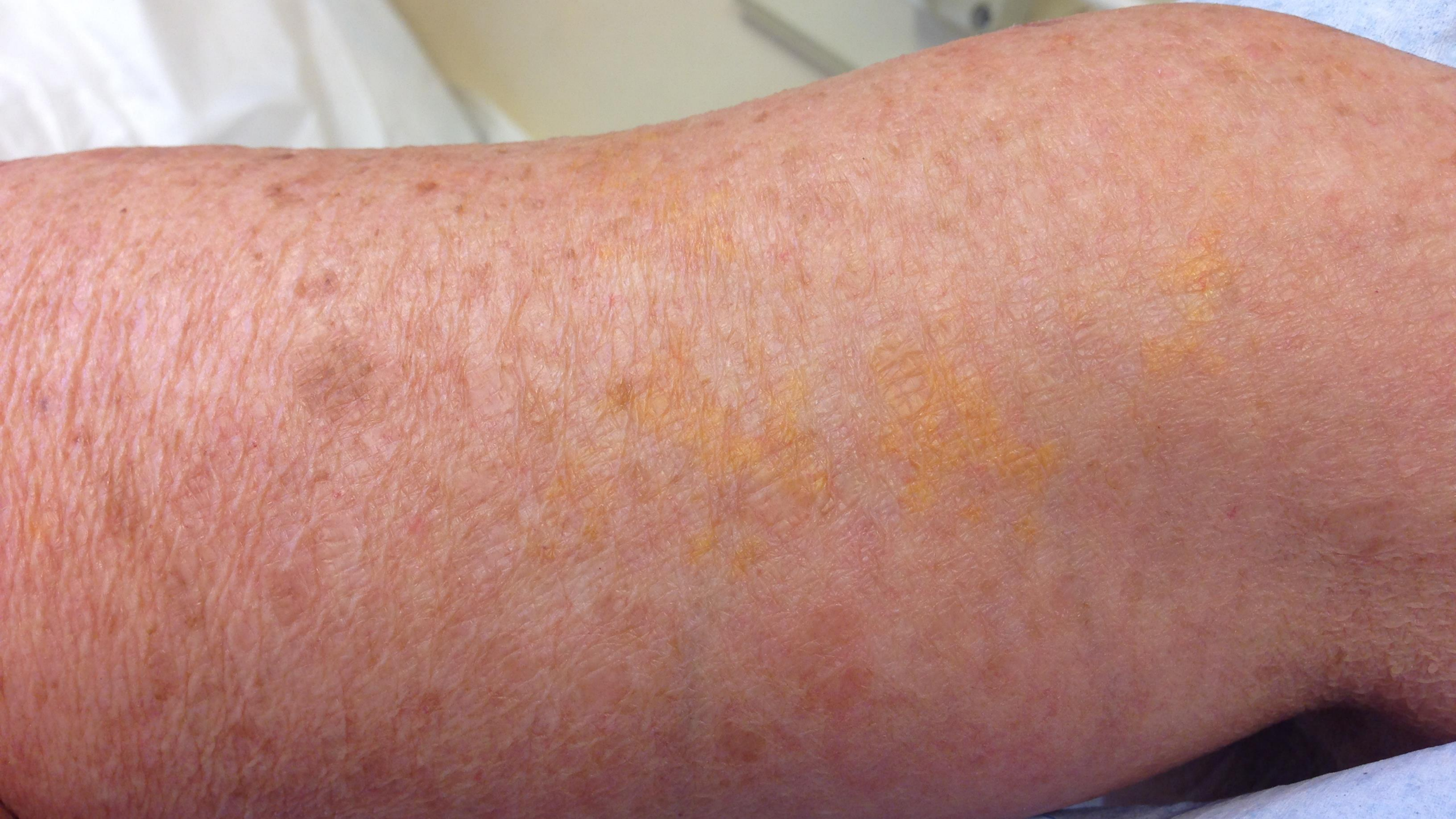
FREQUENTLY ASSOCIATED WITH MONOCLONAL GAMMOPATHY

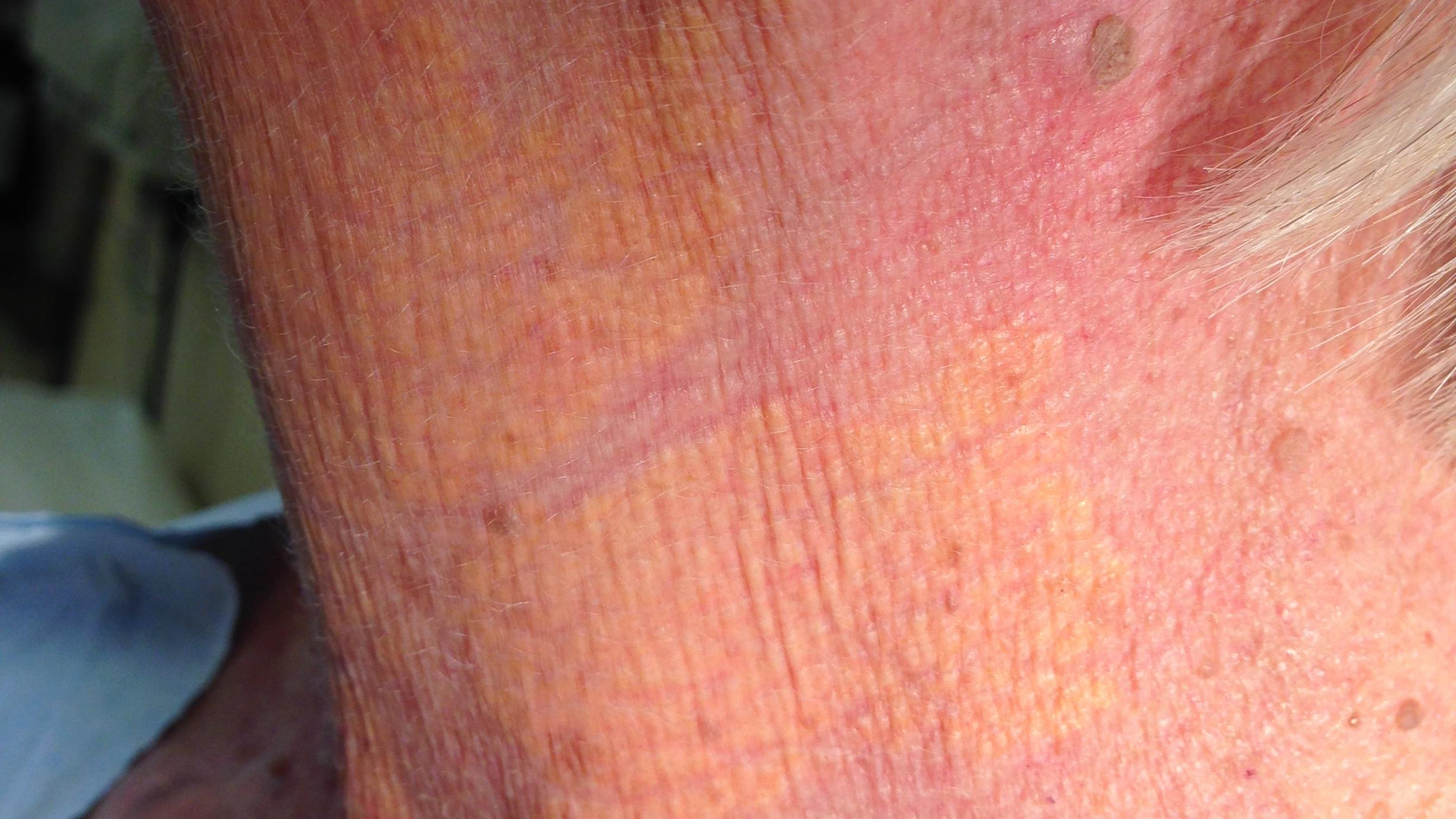
- Normolipemic plane xanthoma
- Scleredema (type 2)
- Angioedema secondary to acquired C1 esterase inhibitor deficiency
- Clarkson syndrome (idiopathic systemic capillary leak syndrome)

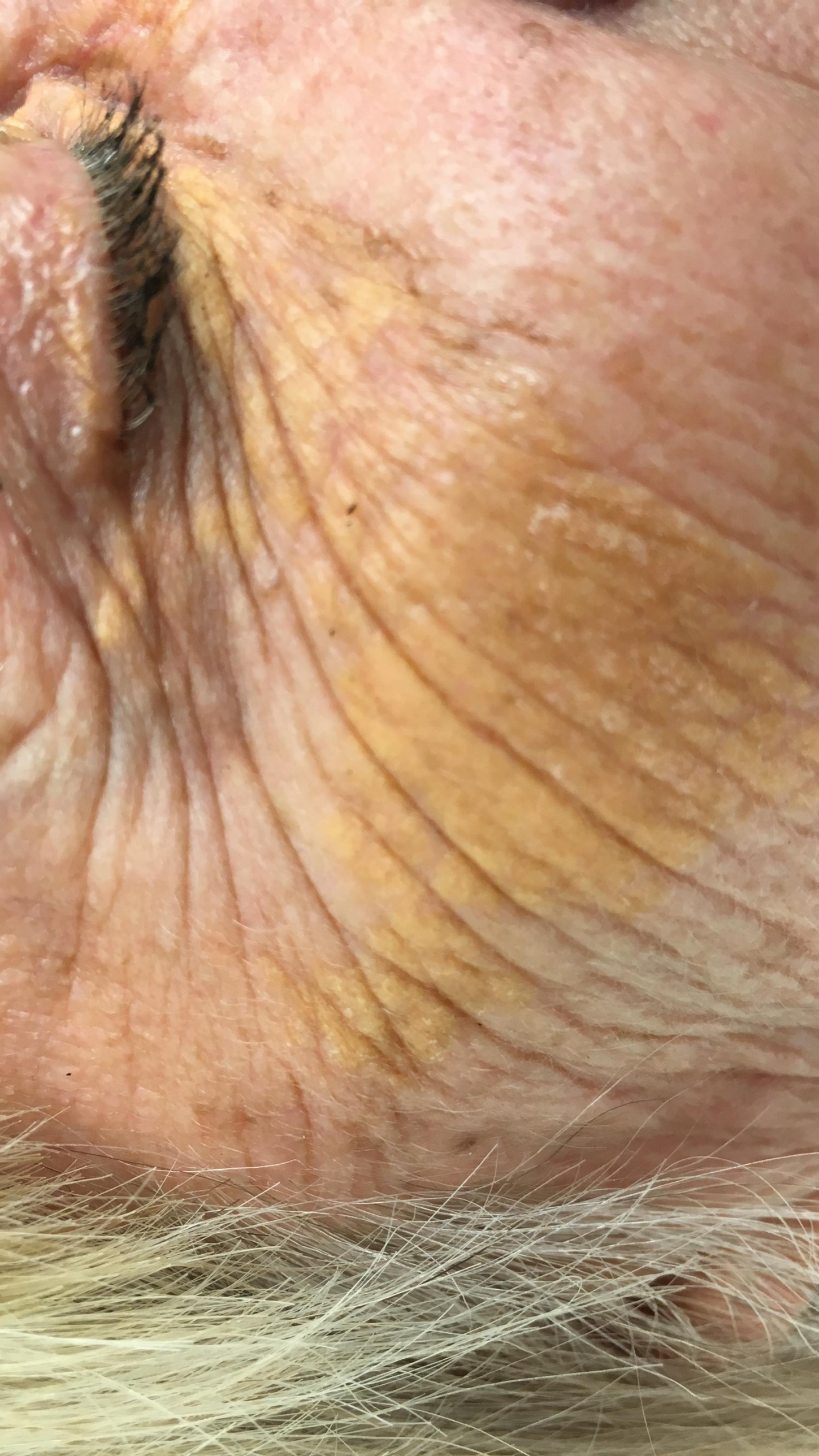
PLANE XANTHOMA





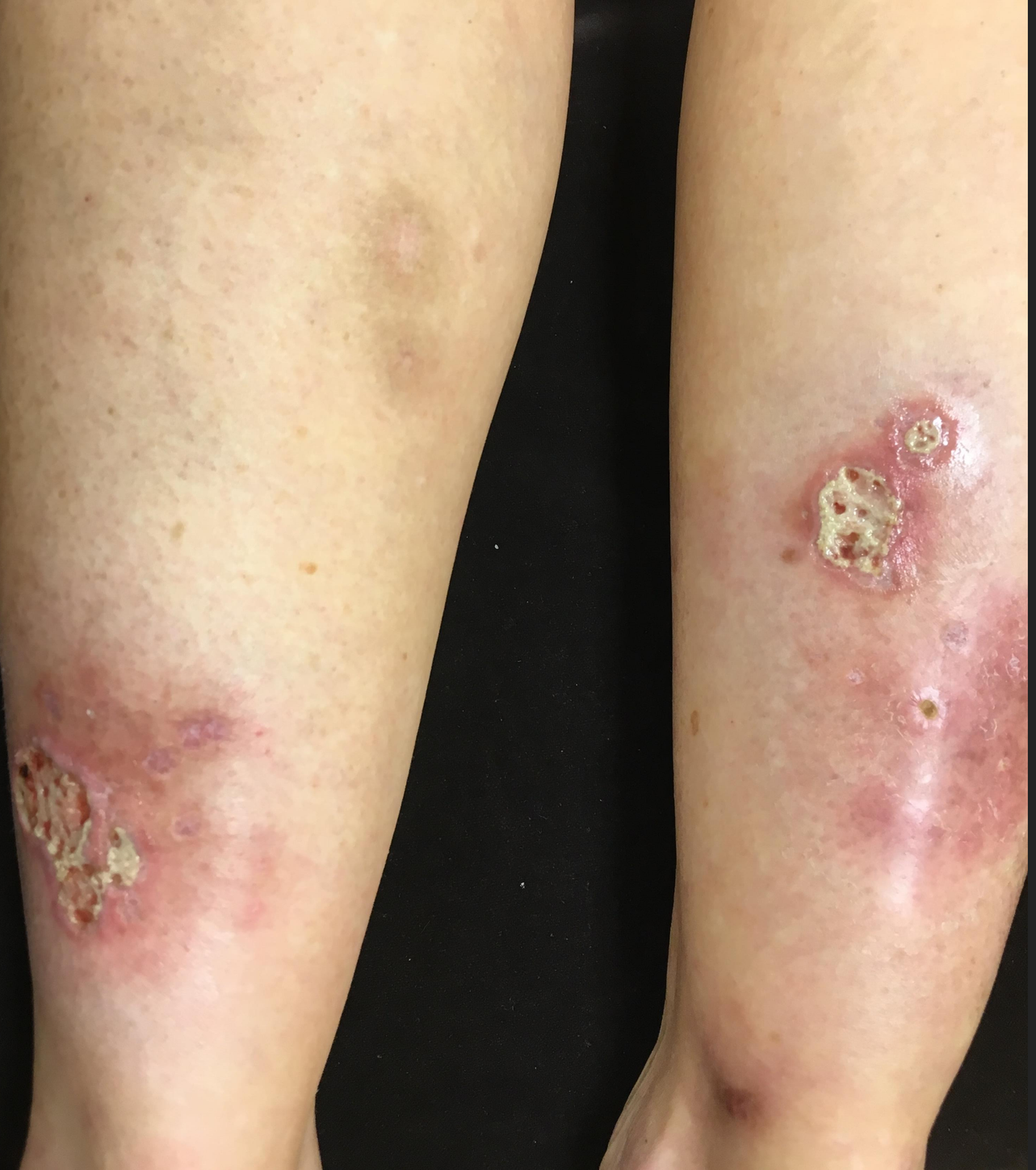


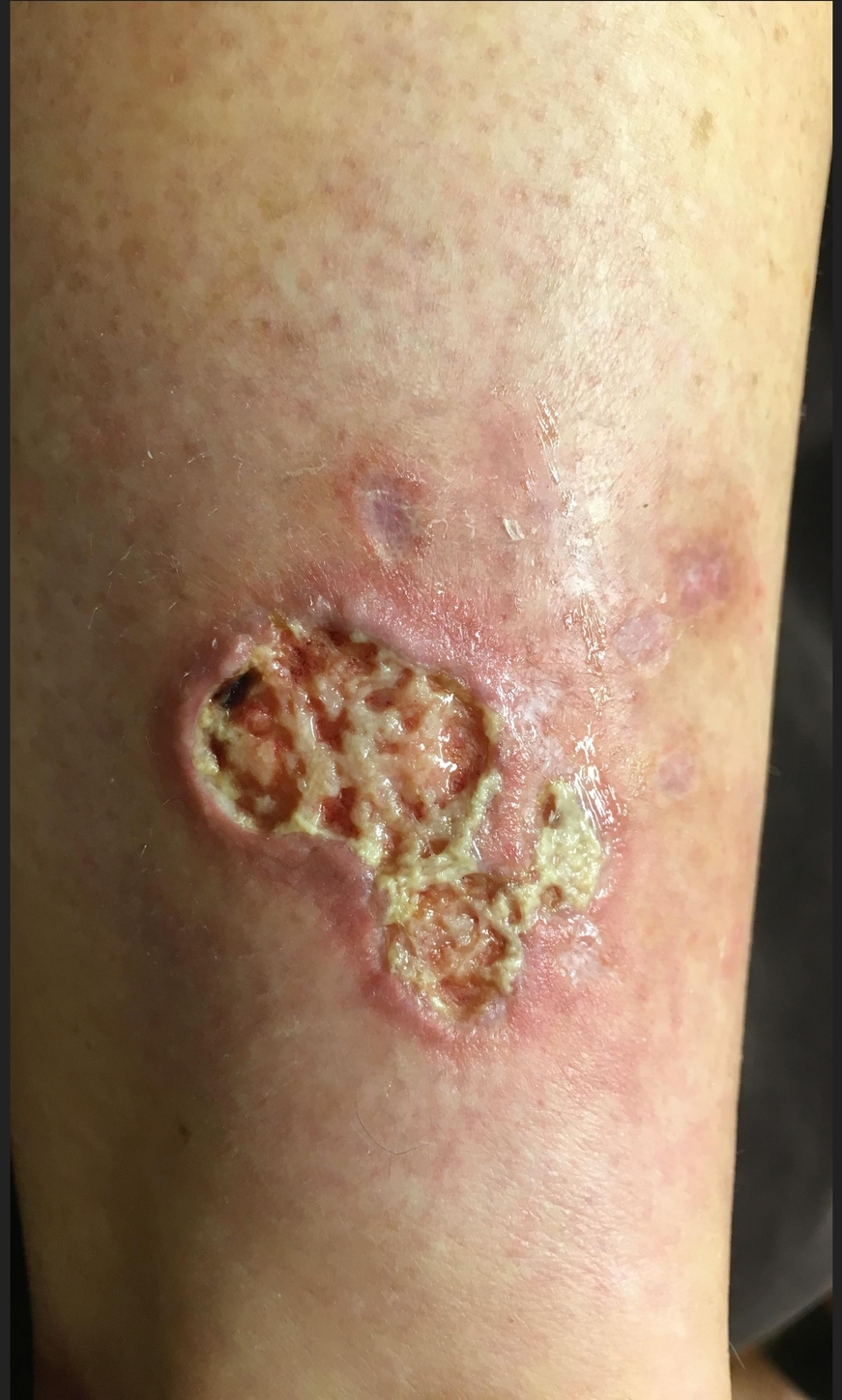


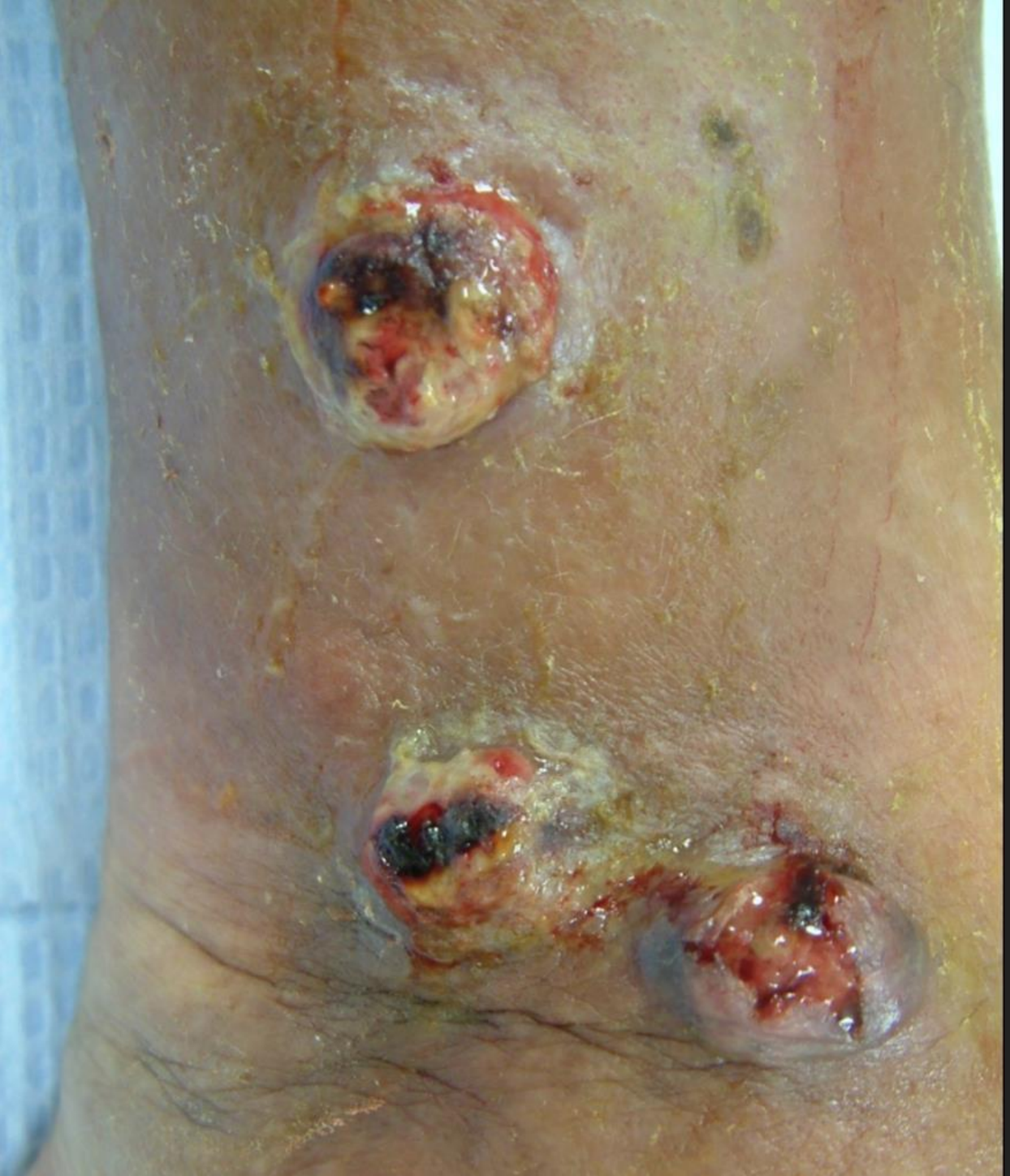
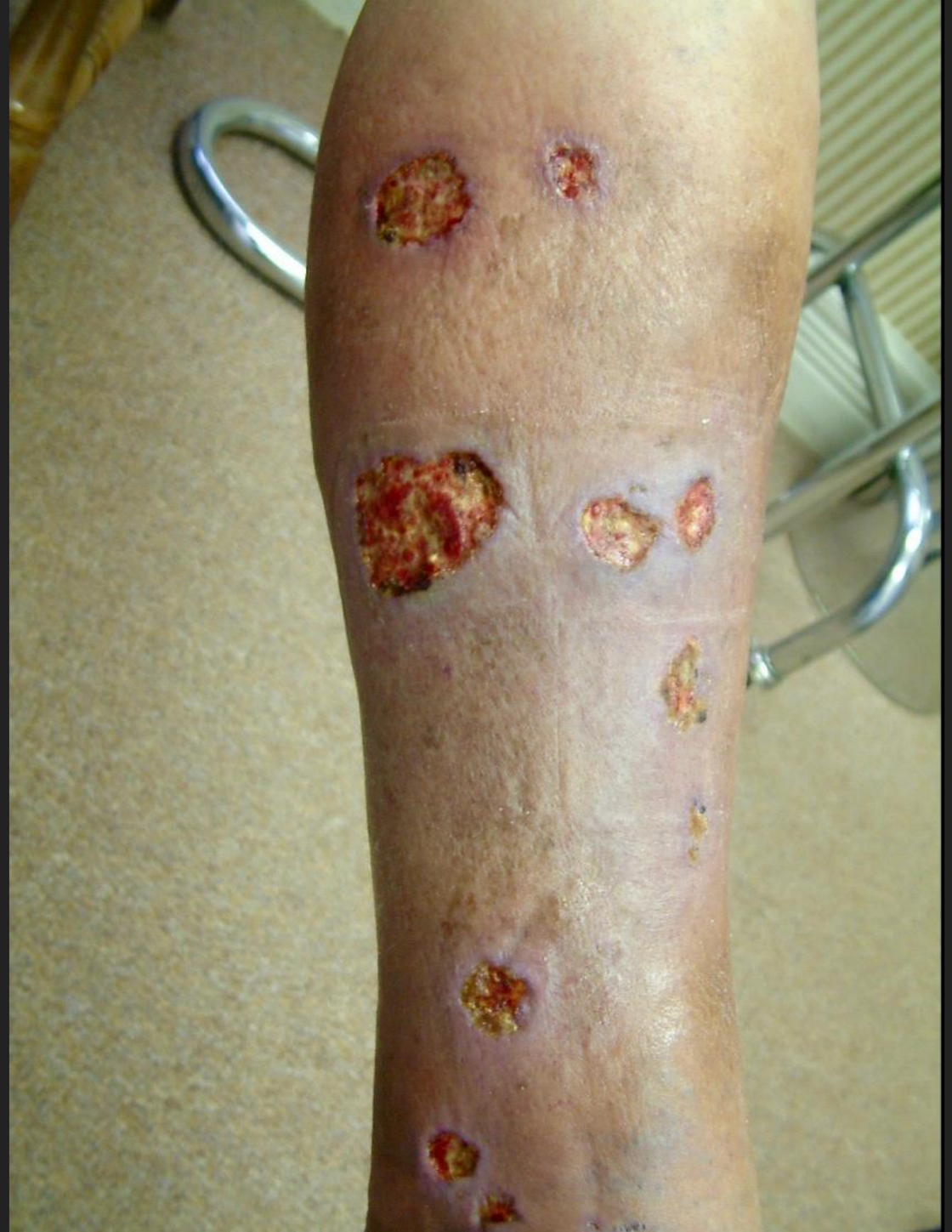


SIGNIFICANT ASSOCIATION WITH MONOCLONAL GAMMOPATHY, PRIMARILY IGA

- Erythema elevatum diutinum
- Subcorneal pustular dermatosis (SPD) and SPD-type IgA pemphigus
- Pyoderma gangrenosum





PYODERMA GANGRENOSUM

- Neutrophilic disorder, with ulceration
- Pathergy
- Associated with
  - inflammatory bowel disease primarily (UC>Crohn's)
  - Myelogenous leukemias
  - Rheumatoid arthritis
- Treatment
  - Do not debride
  - Ultrapotent topical/intralesional steroids
  - Immunosuppresants
  - TNF-α inhibitors

OCCASIONALLY ASSOCIATED WITH MONOCLONAL GAMMOPATHY

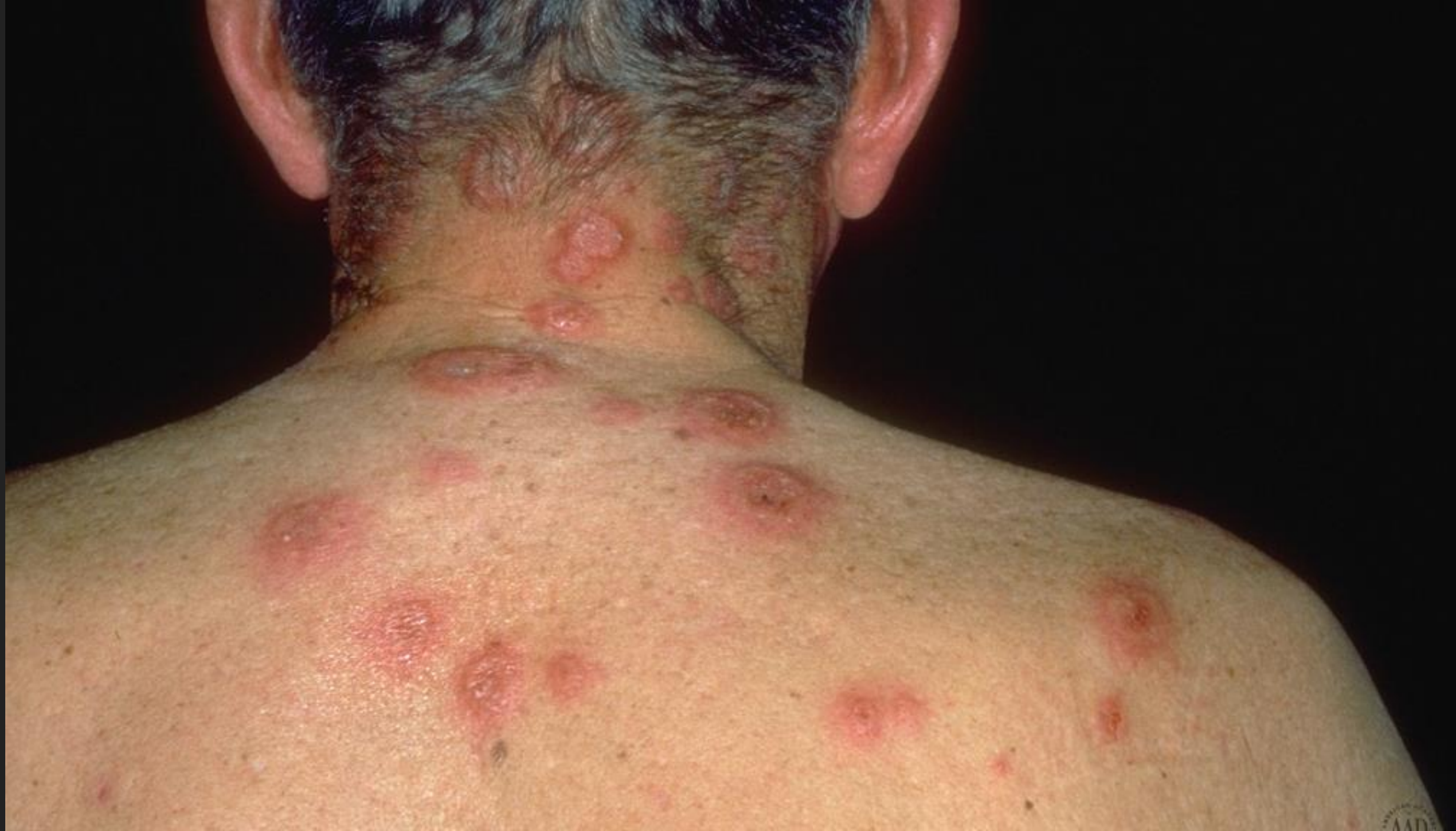
- Sweet syndrome
- Cutaneous small vessel vasculitis
- Xanthoma disseminatum
- Epidermolysis bullosa acquisita
- Paraneoplastic pemphigus
- Atypical scleroderma

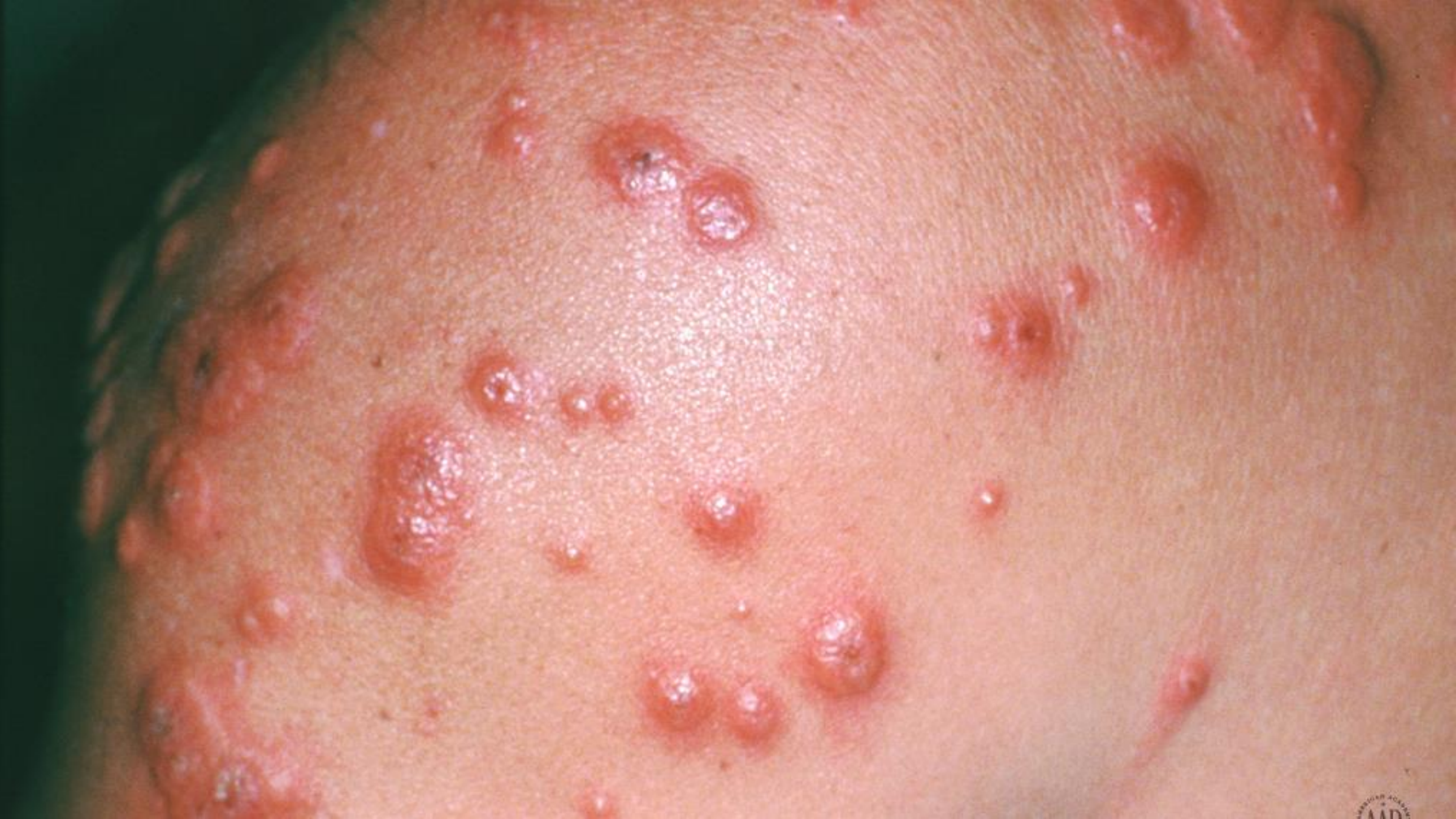
CASE 7

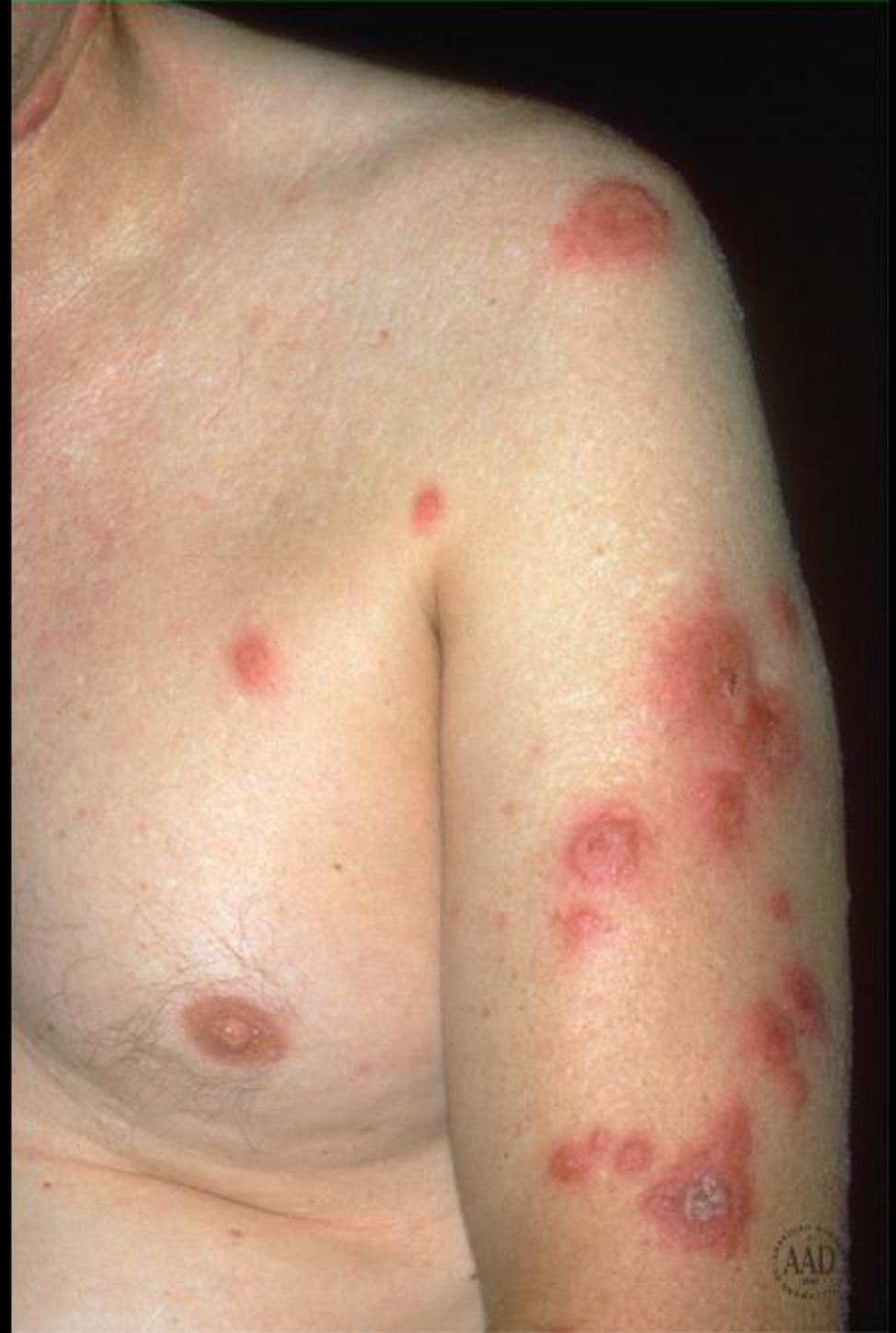
ALLEN-TAINTOR
DERMATOLOGY

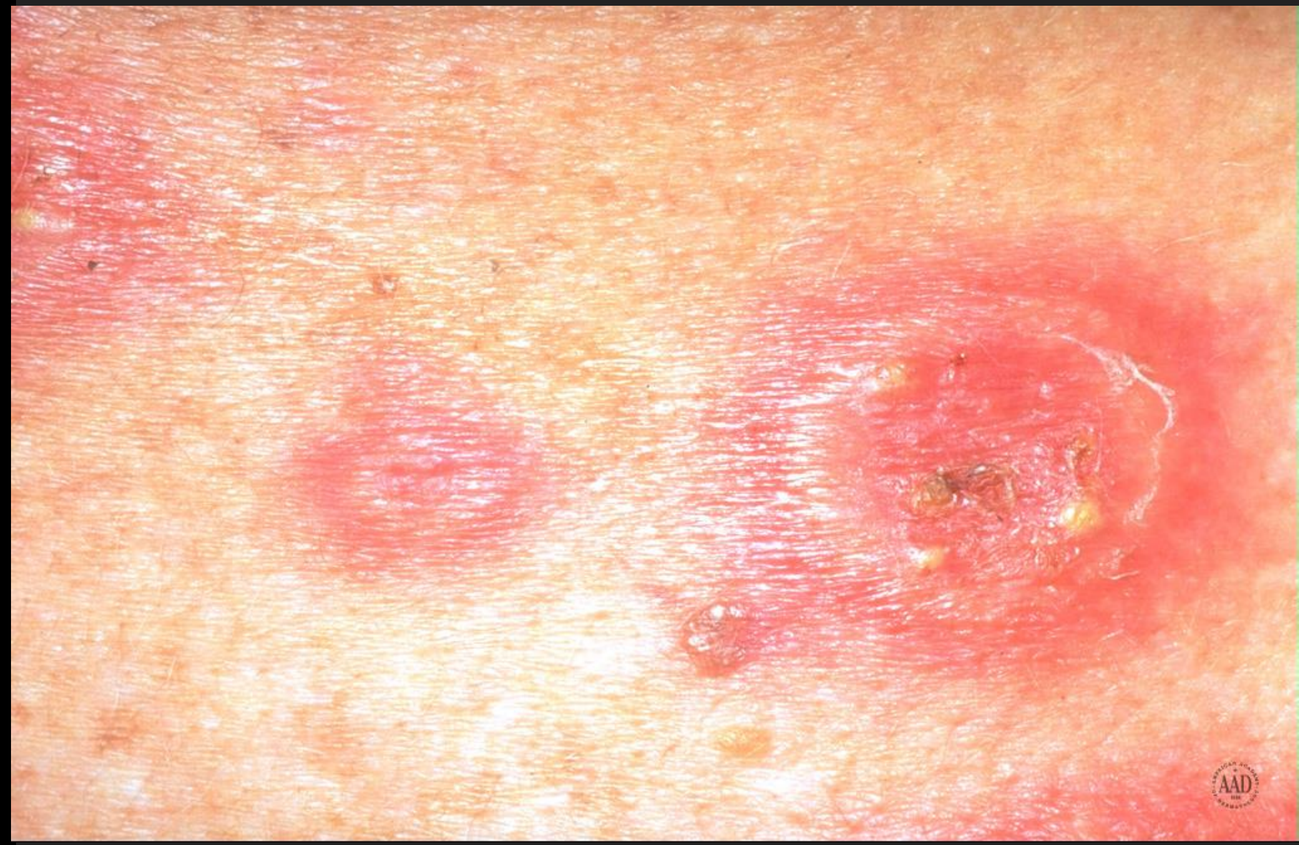
CASE 7

- 68 year-old male
- Presents to ED with skin lesions and fever
- Initial CBC suggests new dx of AML



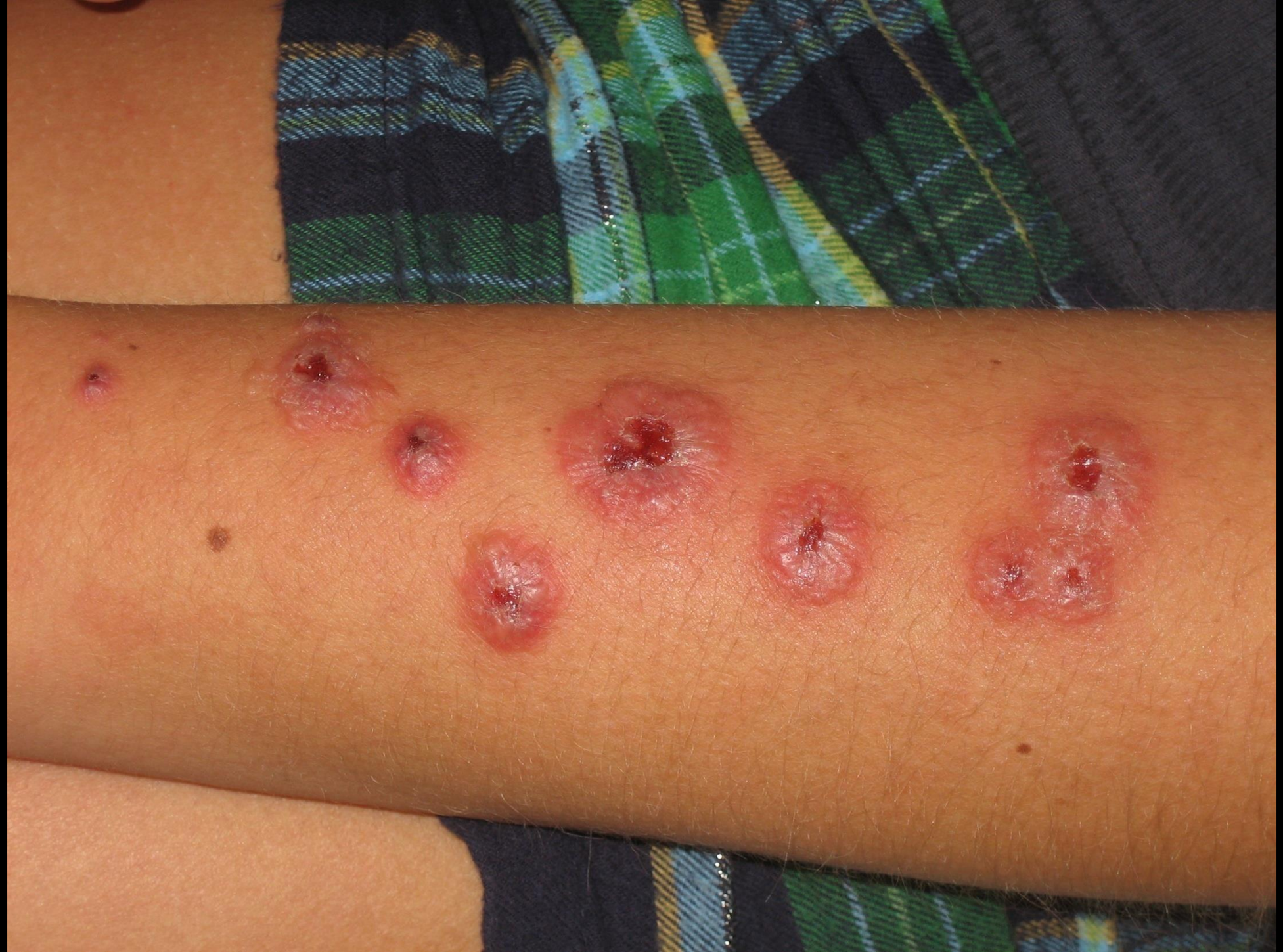


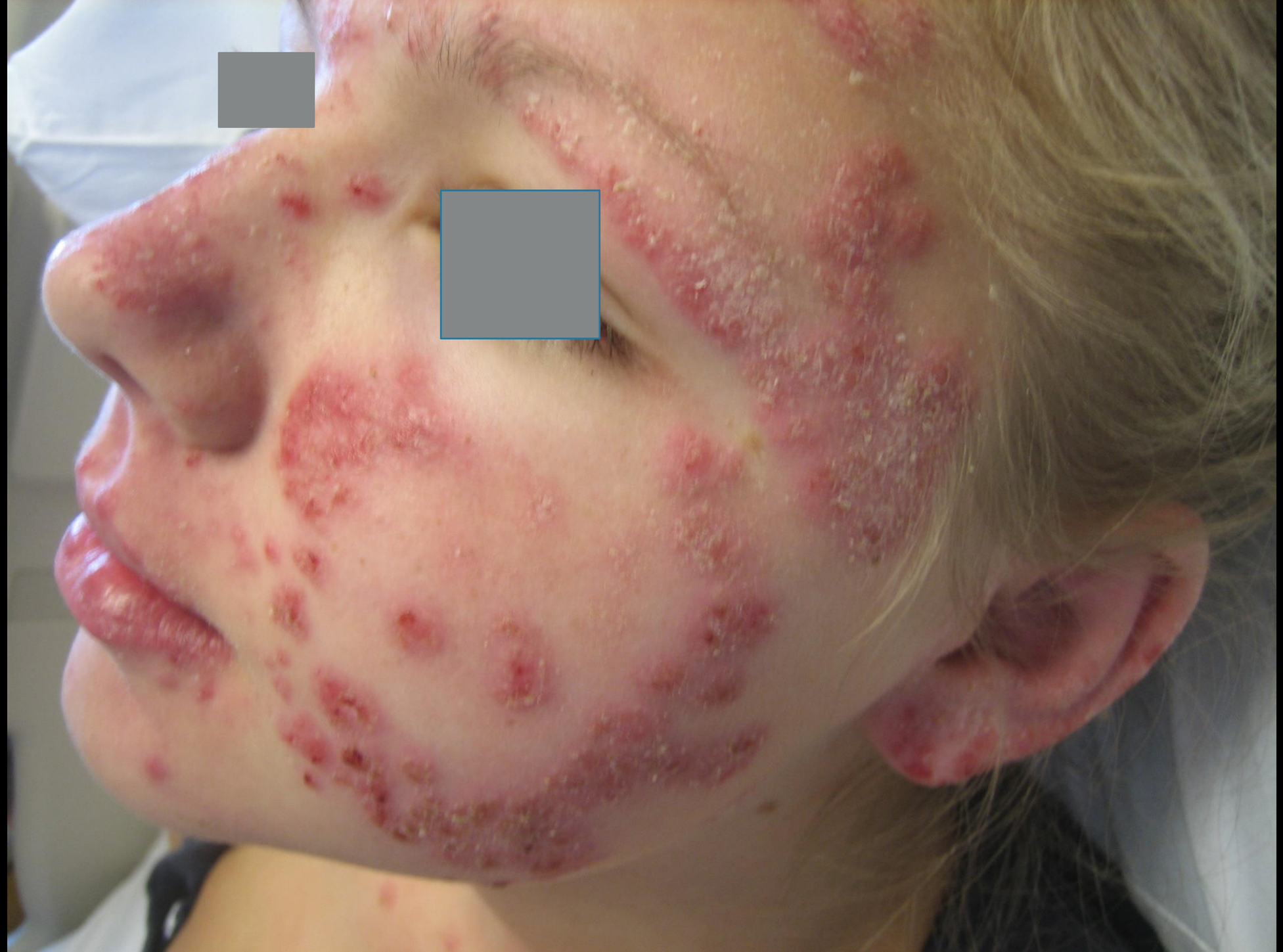


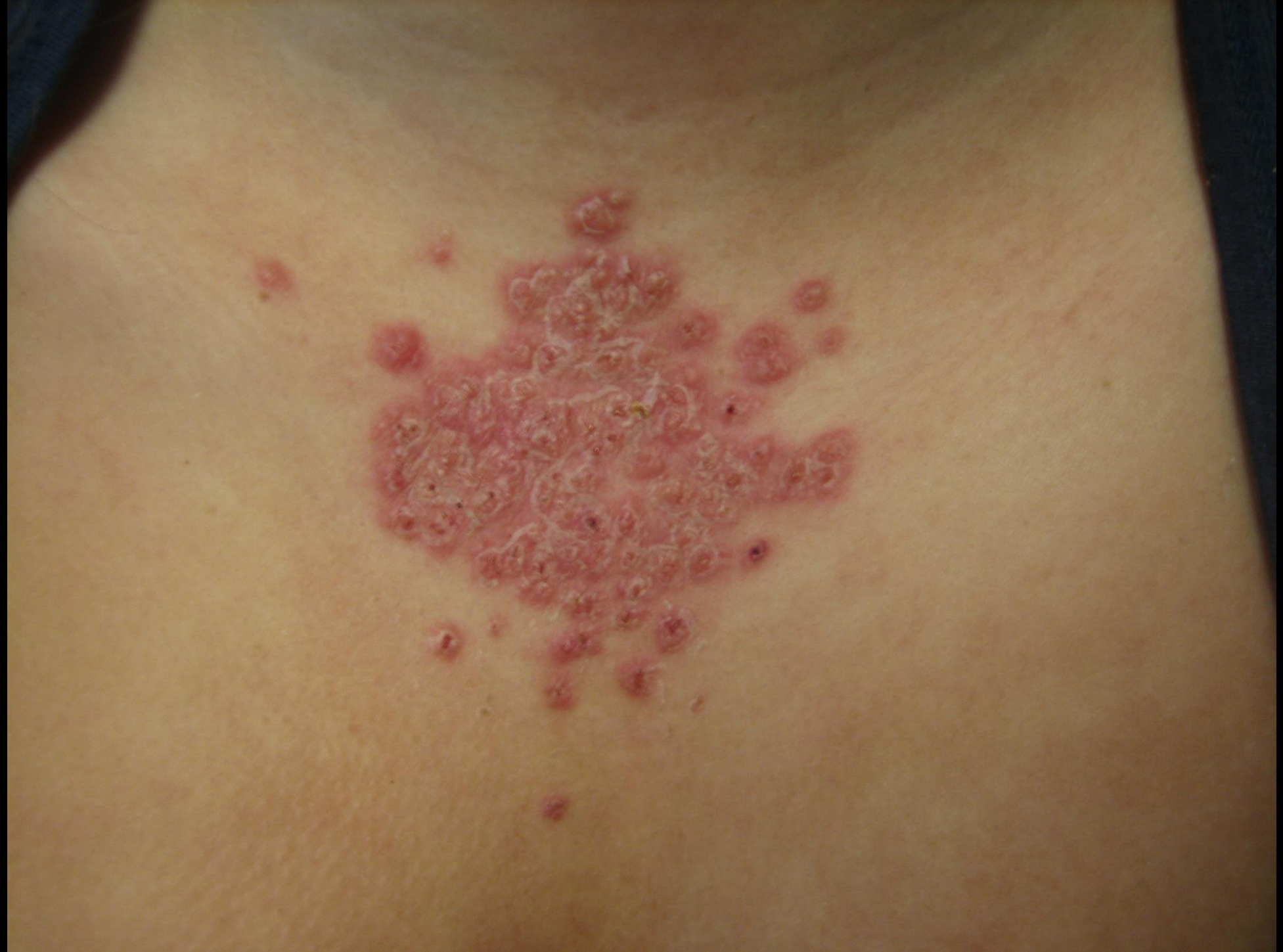


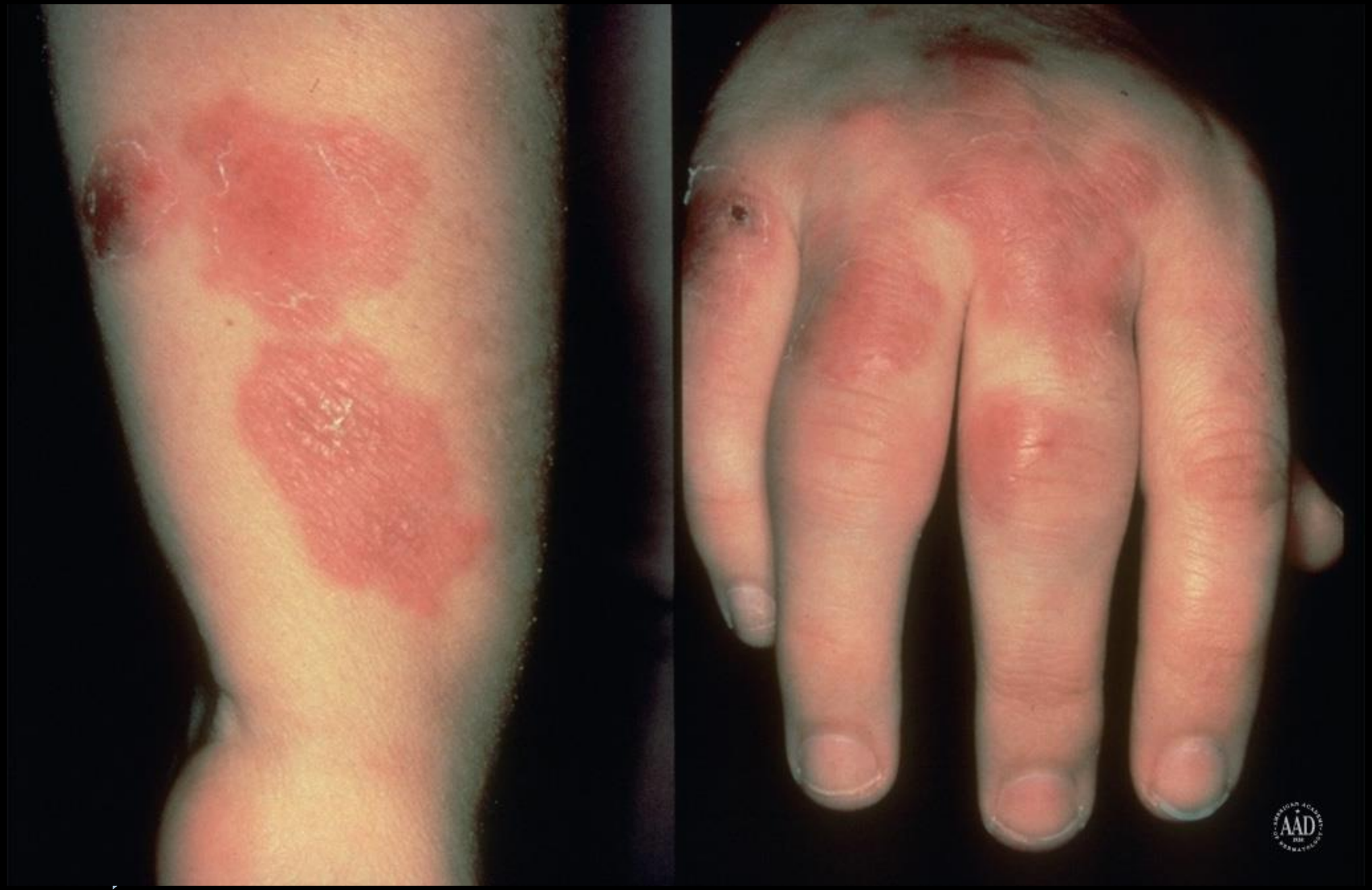
SWEET'S SYNDROME

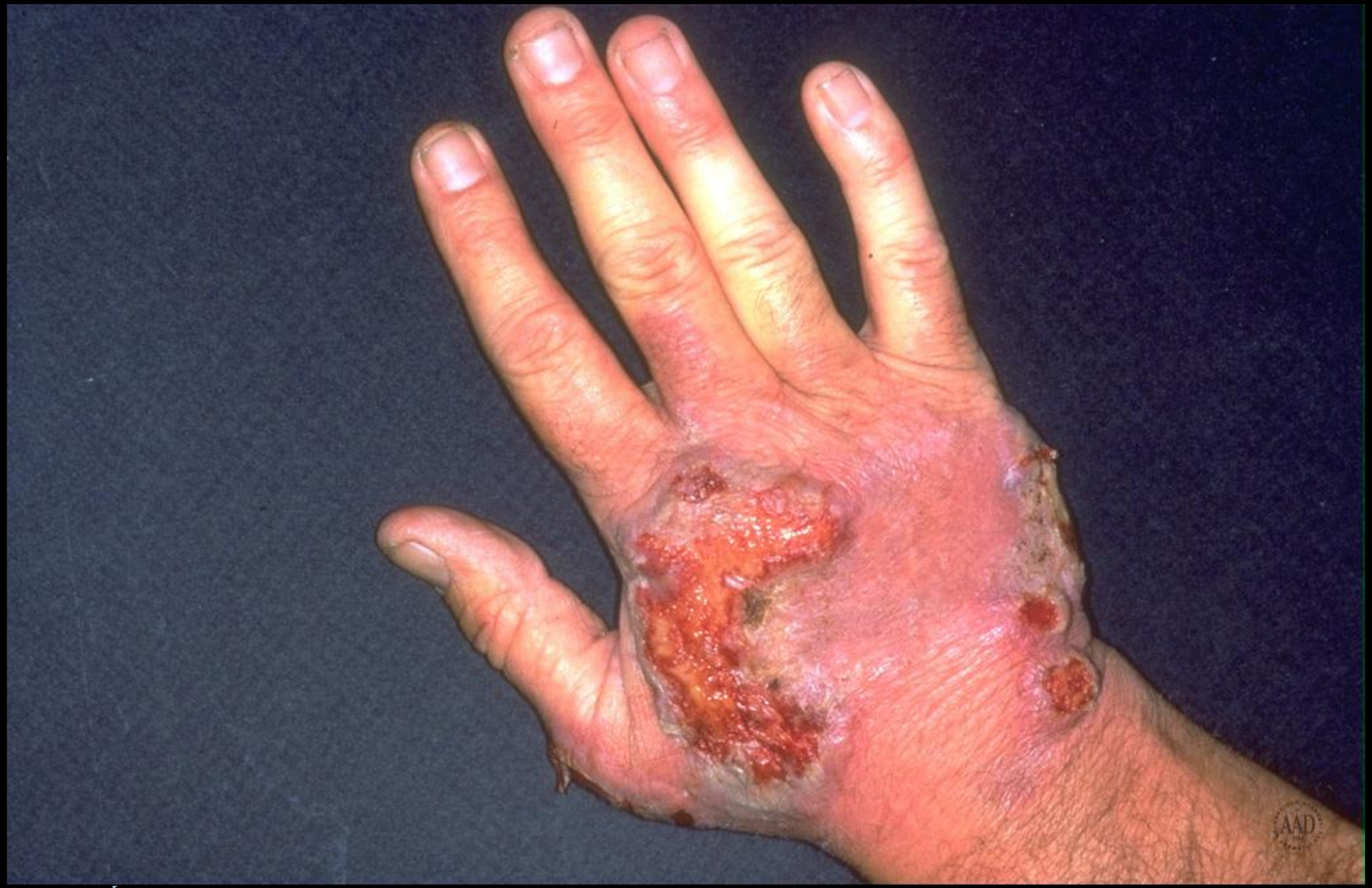
- Acute Febrile Neutrophilic Dermatosis
- Usually face, neck, upper trunk, extremities
- Reactive
  - Post-infectious
    - URI, GI bacterial infections, toxoplasmosis, histoplasmosis
  - Neoplasia: AML > other heme > solid tumors
    - Can occur in neutrophilic patients
  - Bowel disease
  - Drug-induced (G-CSF, OCPs, TMP-SMX)
- Very steroid responsive











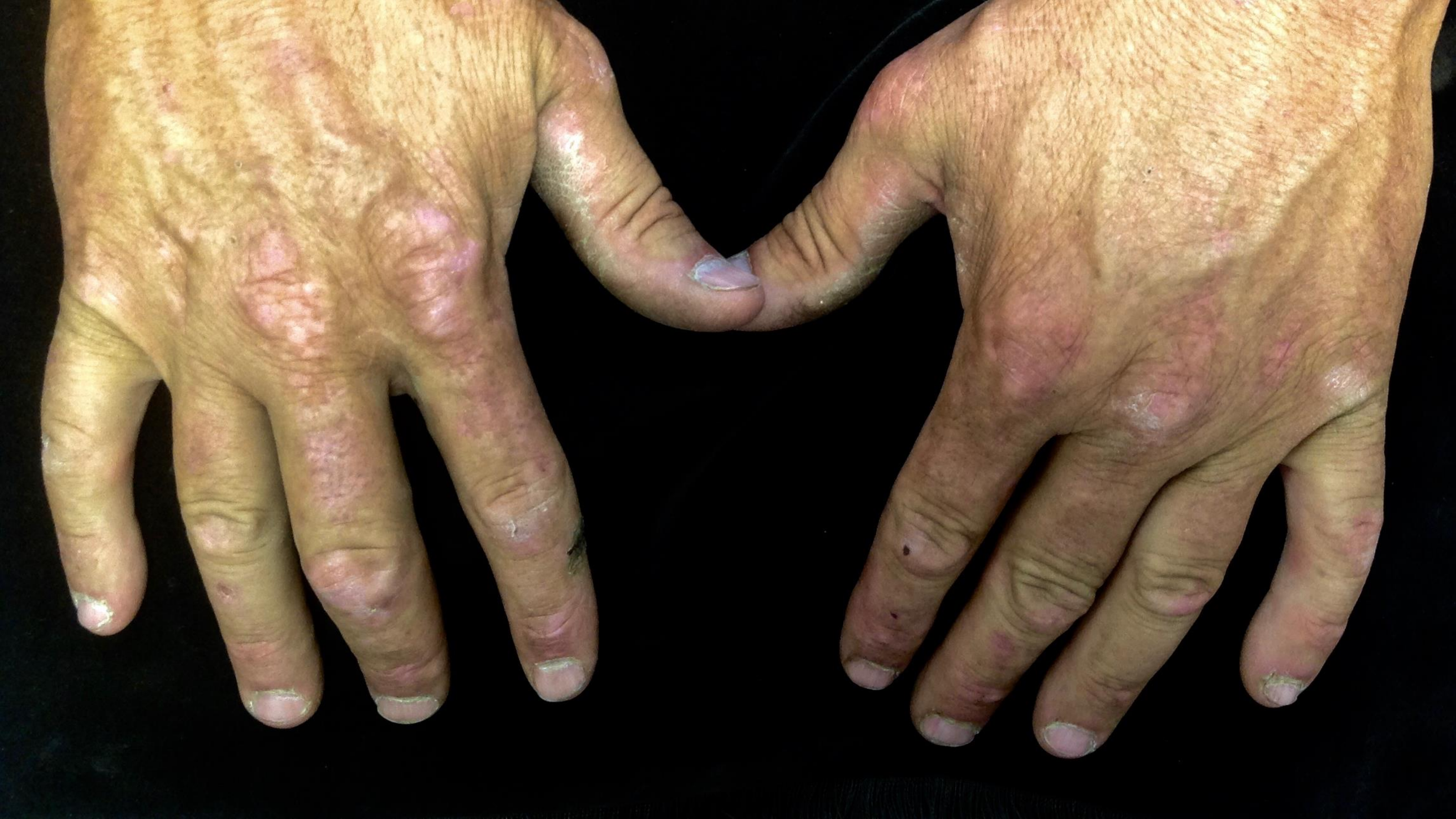
CASE 8

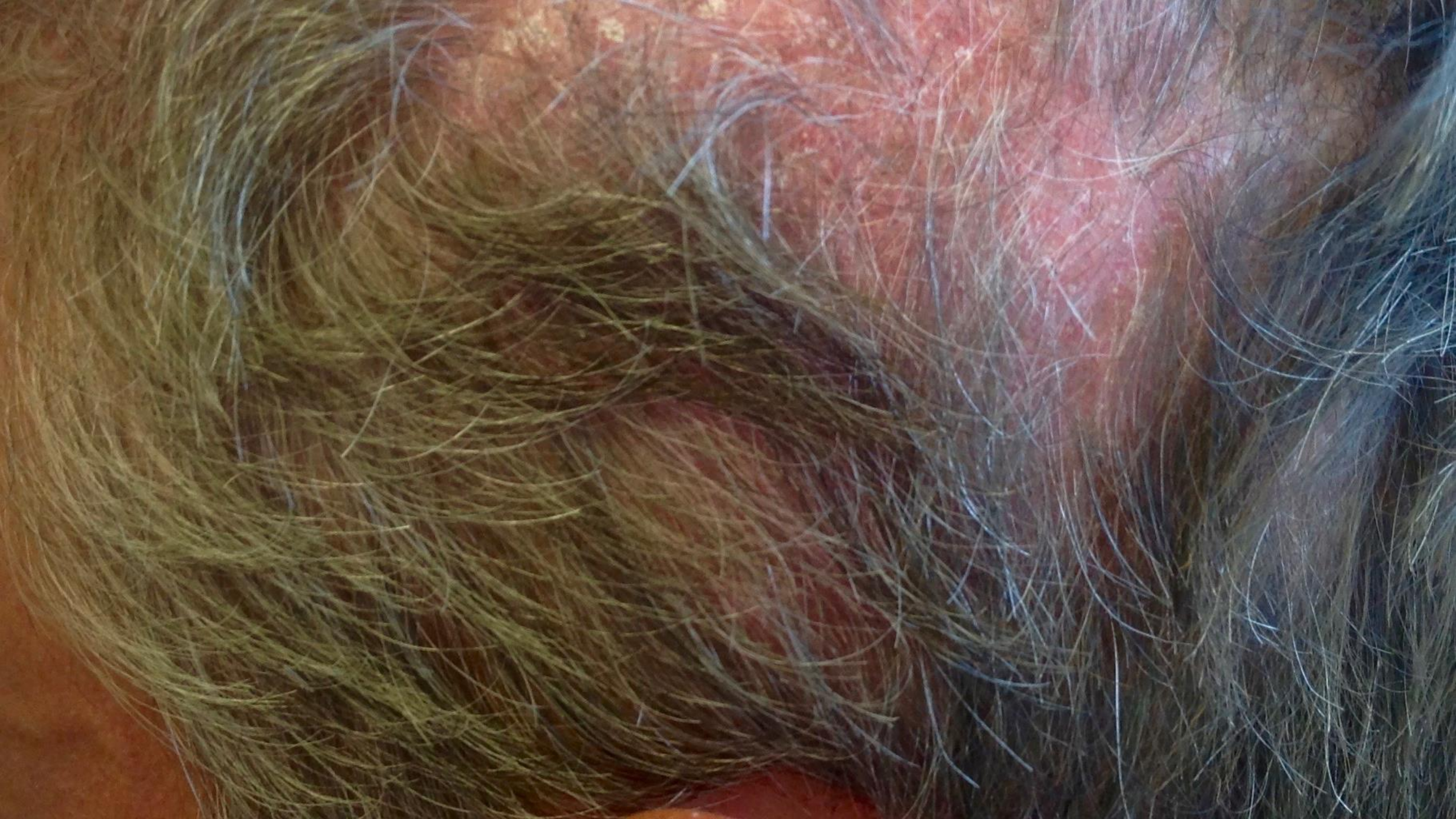
ALLEN-TAINTOR
DERMATOLOGY

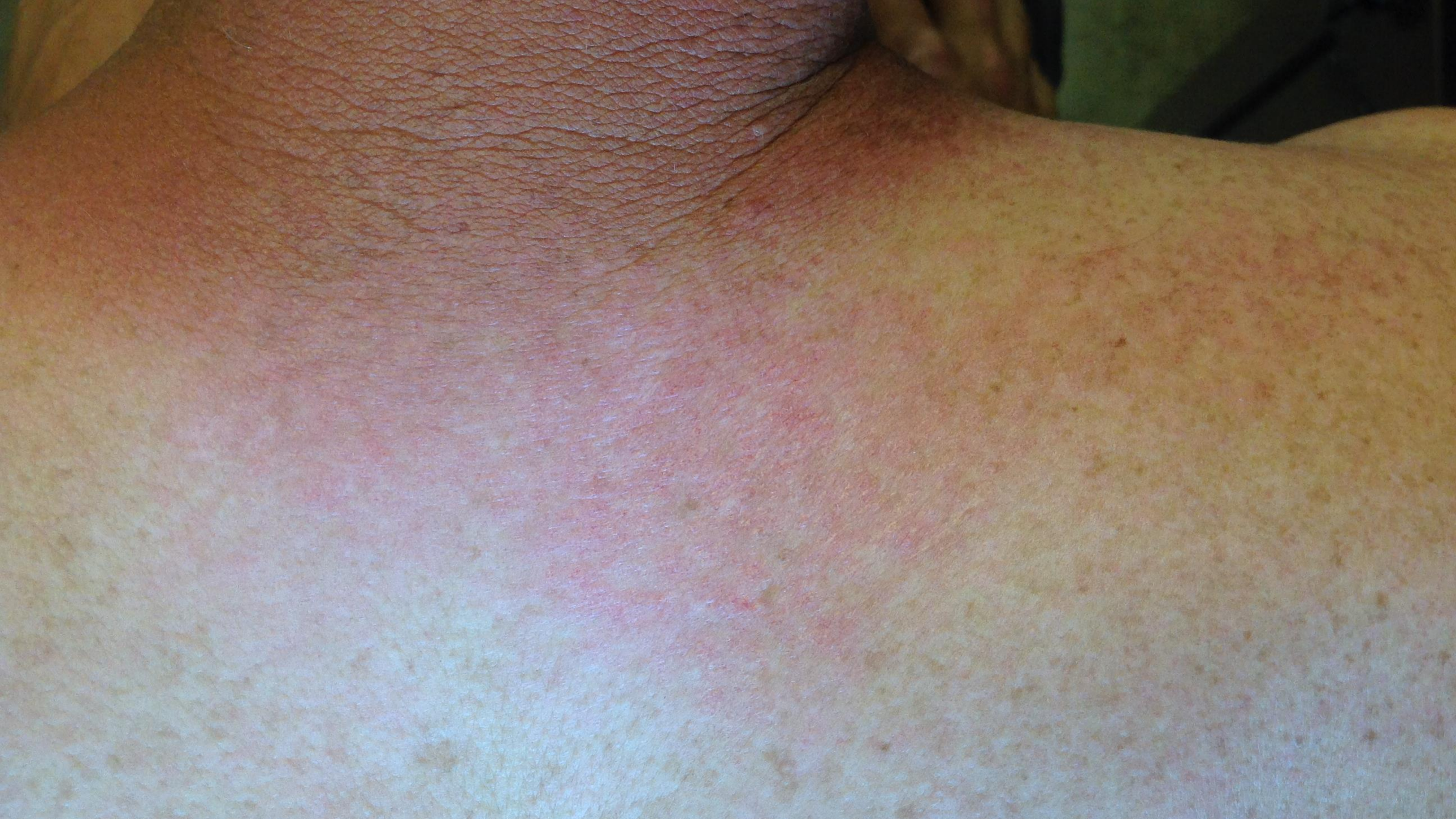
CASE 8

- 80 yo Caucasian male with muscle weakness and rash that worsens with rash that worsens in the sun.

- Recent diagnosis of adenocarcinoma of the lungs





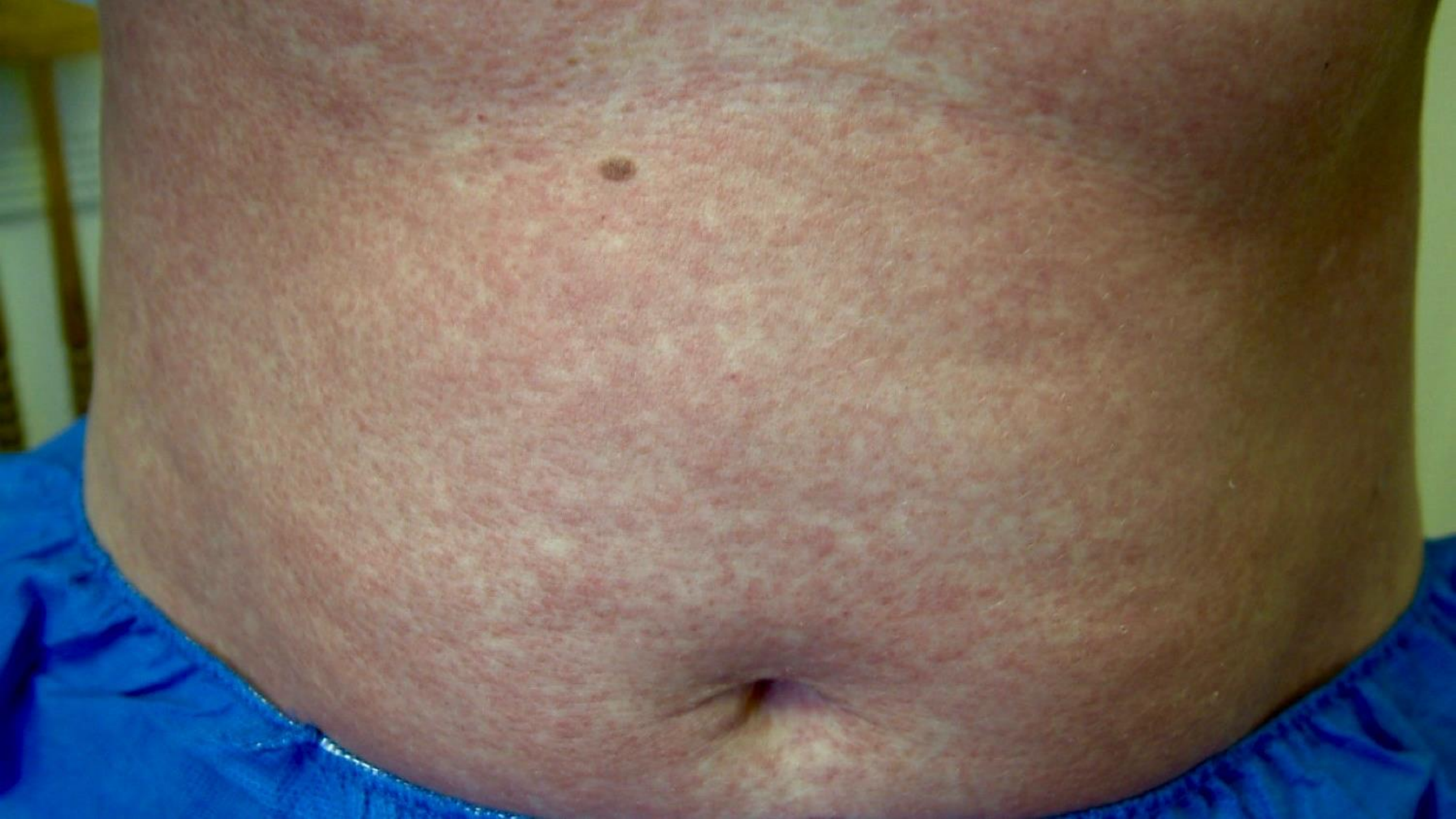


DERMATOMYOSITIS

- Associated neoplasia in adults 10-50%
  - GU, **ovarian**, colon most common
  - Breast, lung, pancreatic and lymphoma
- May overlap with other CTDs
- Interstitial lung disease may be fatal – highly associated with anti-Jo-1 antibodies

CASE 9

ALLEN-TAINTOR
DERMATOLOGY



CASE 9

- 32 year old woman mother of 2

- Eos slightly elevated at 8%.
- AST was 9880; ALT 10,230; T. Bill 3.5;
- Fevers 104.5F
- Severe pan lymphadenopathy. Significant facial edema

CASE 9

- DRESS secondary to Bactrim
- IVIG rapidly reversed course.

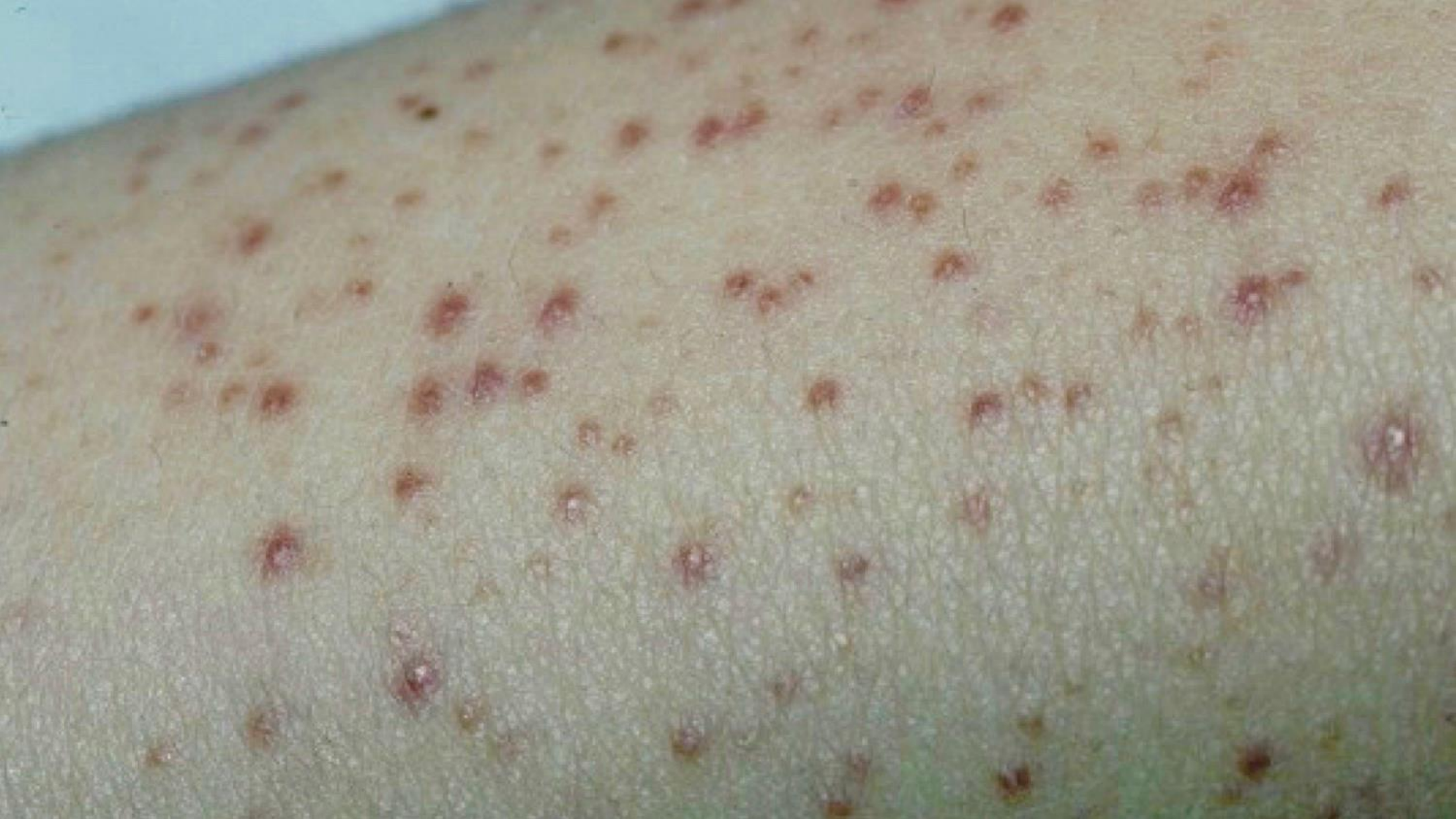
CASE 10

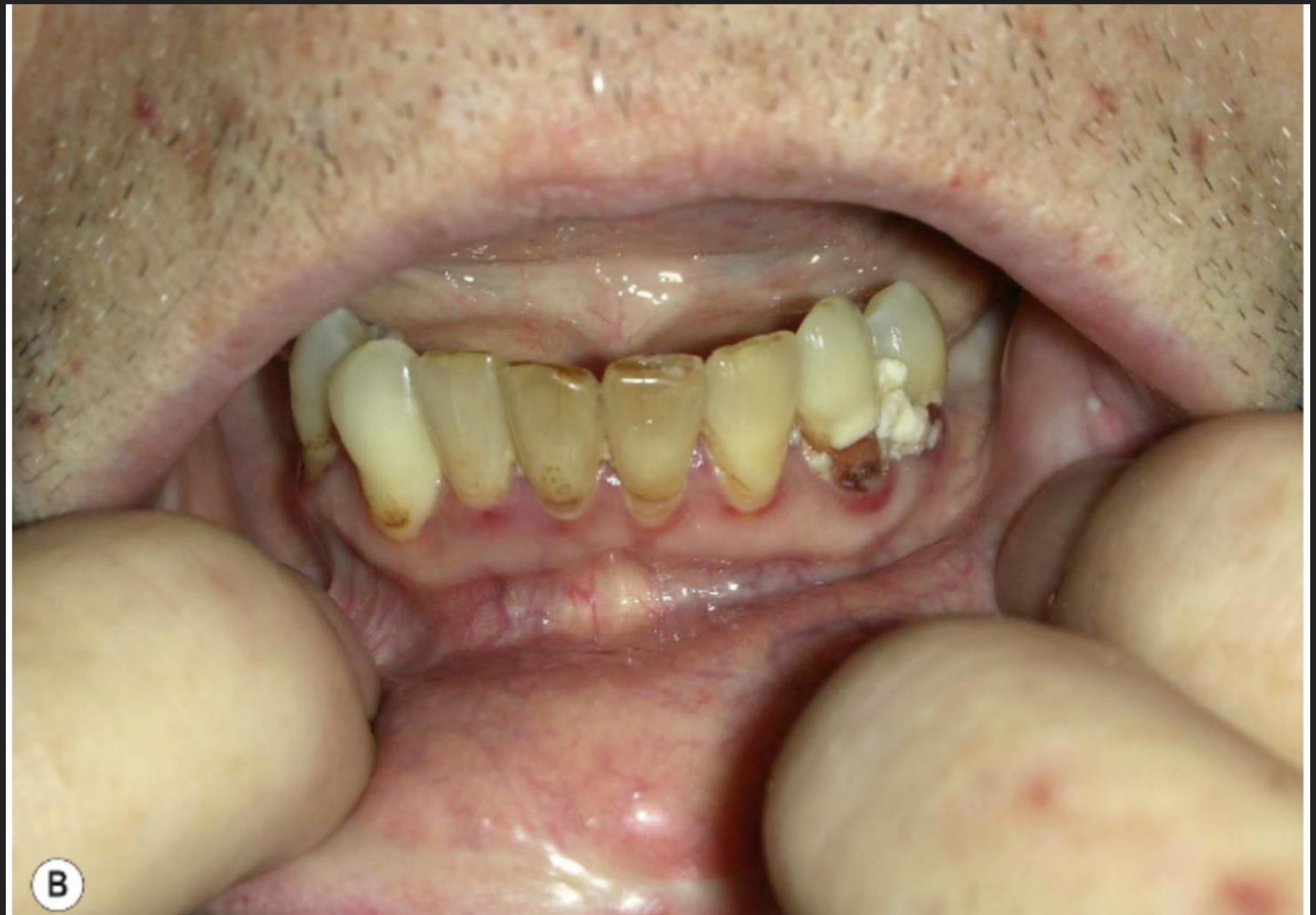
ALLEN-TAINTOR
DERMATOLOGY

CASE 10

- Patient with complaints of pain all over
- Purple macules seen at base of follicles on legs, tenderness to palpation over several joints and long bones

- History of a partial small bowel resection

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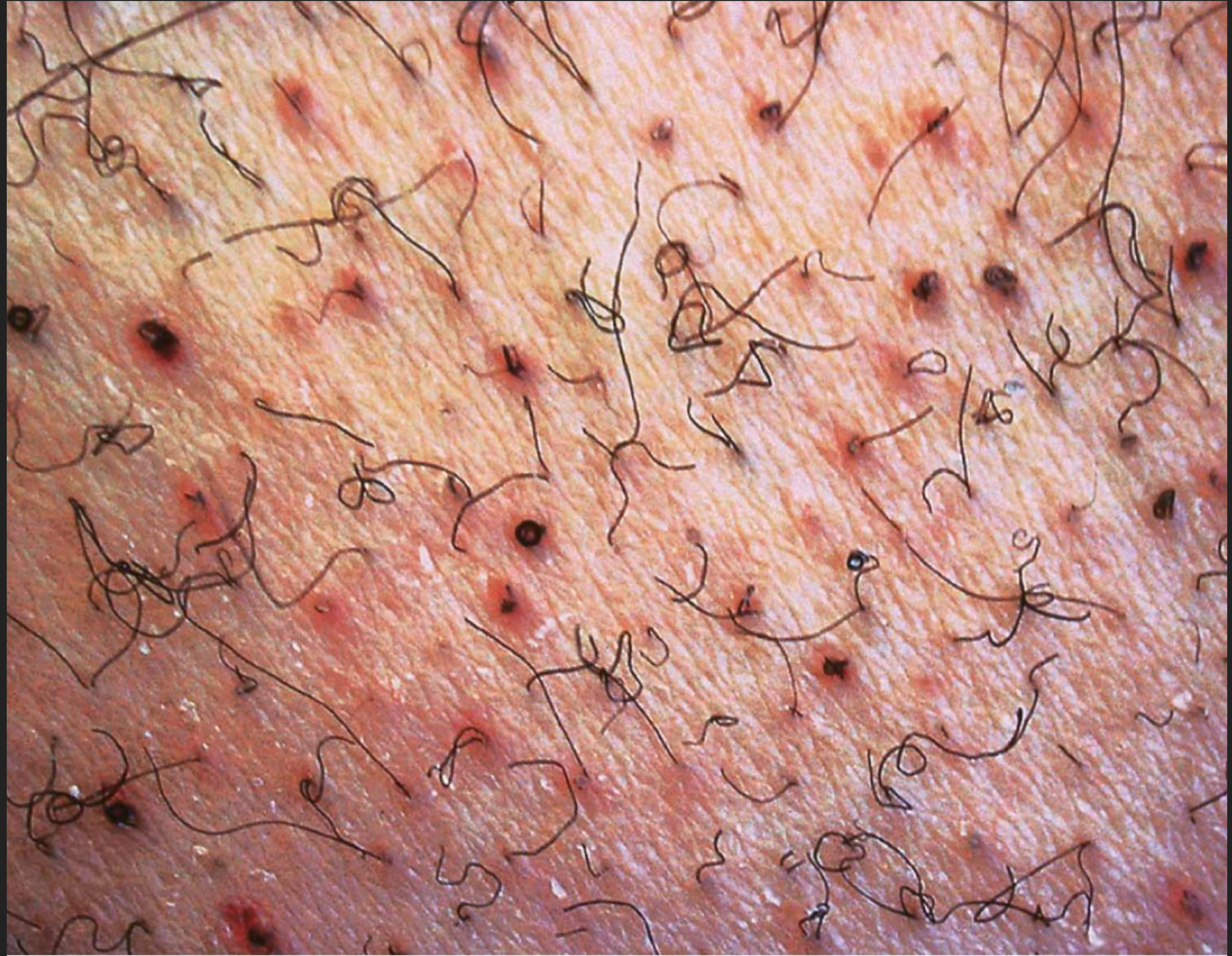


VITAMIN C DEFICIENCY

- Scurvy
- Alcoholics, psychiatric disease: limited diets
- Hemorhage:
  - Gingival, subperiosteal, intramuscular, subungual, intra-articular, cutaneous
- Perifollicular hemorhage and hyperkeratosis, corkscrew hairs
- Hematologic abnormalities

CASE 11

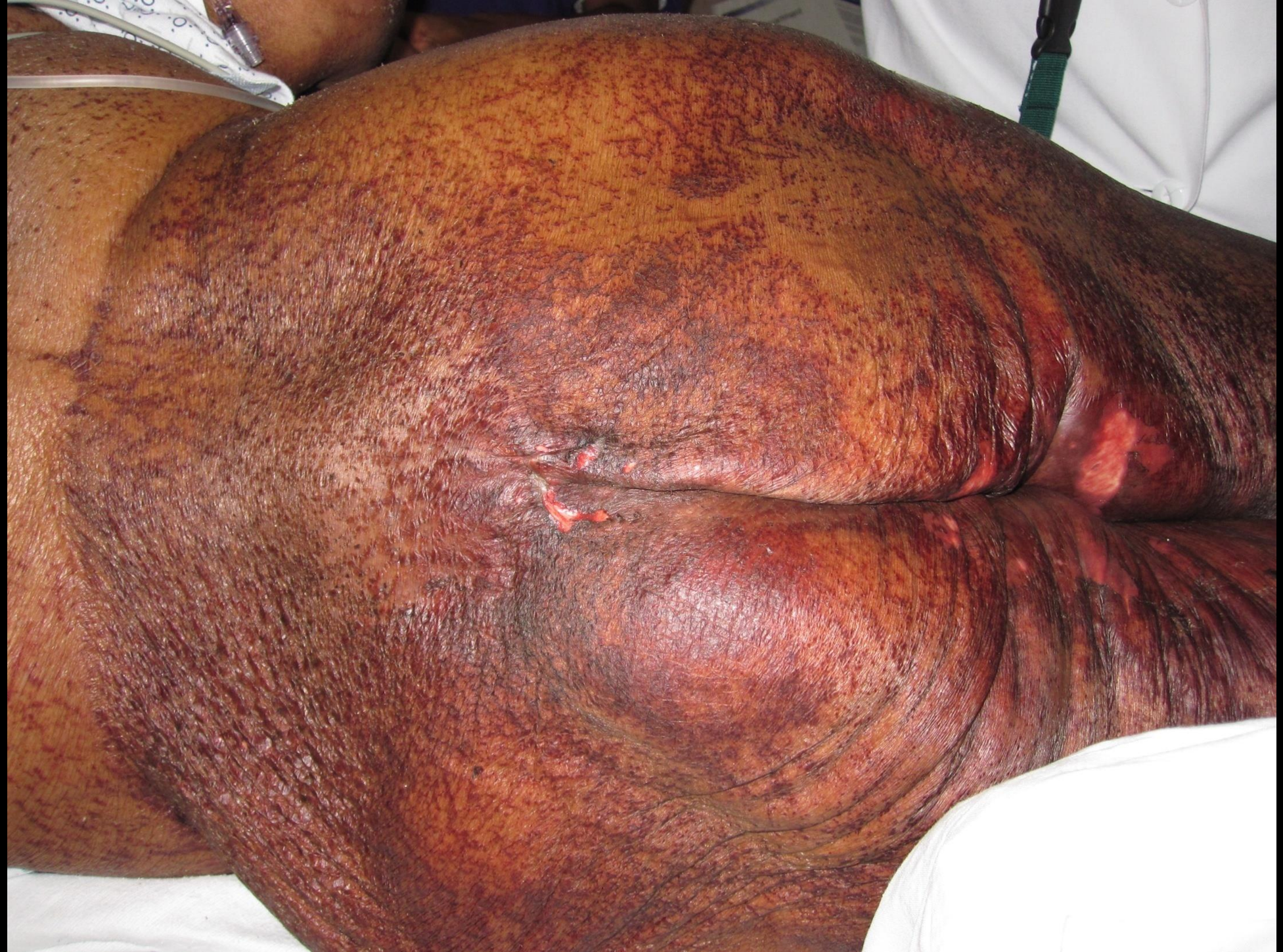
ALLEN-TAINTOR
DERMATOLOGY

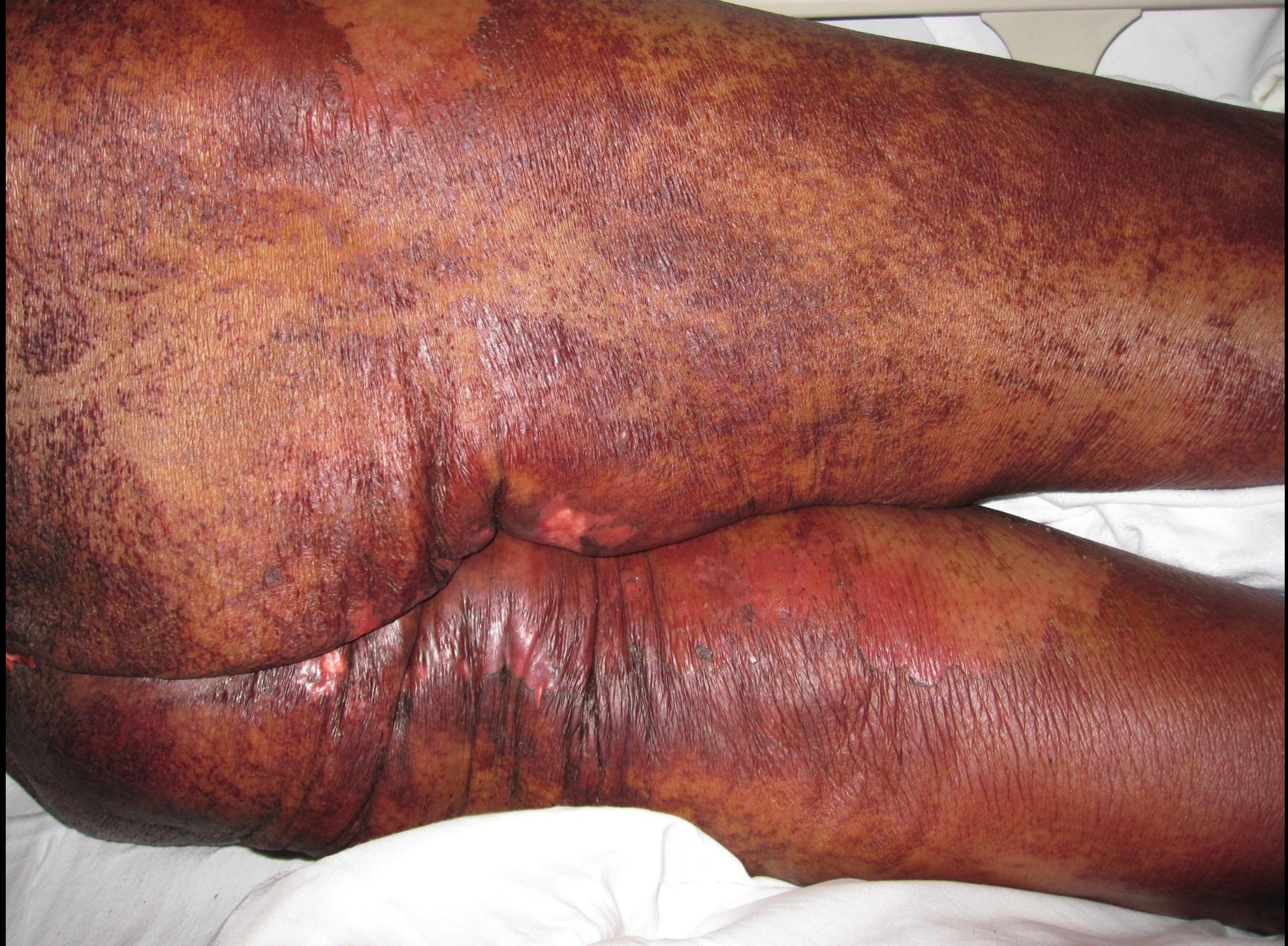
CASE 11

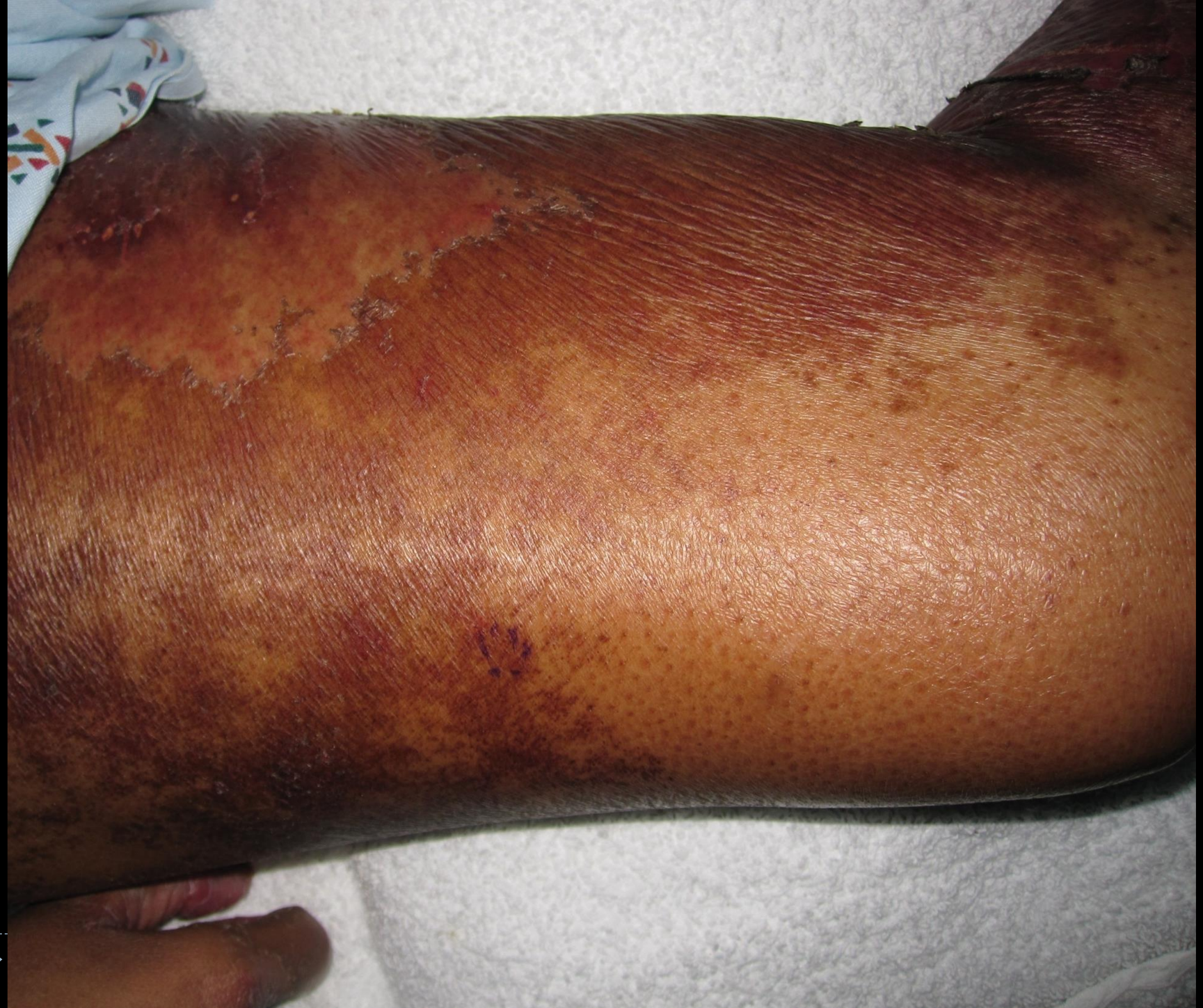
- 36 yo African American female with history of gastric bypass (357lbs → 120lbs)
- Complaints of:
  - 8-10d desquamating, painful skin eruption around the mouth, abdomen, groin and buttocks with perineal pain with defecation/urination
  - Peeling of the hands and feet
  - Fatigue, weakness
  - Poor PO intake due to mouth pain
  - Worsening diarrhea

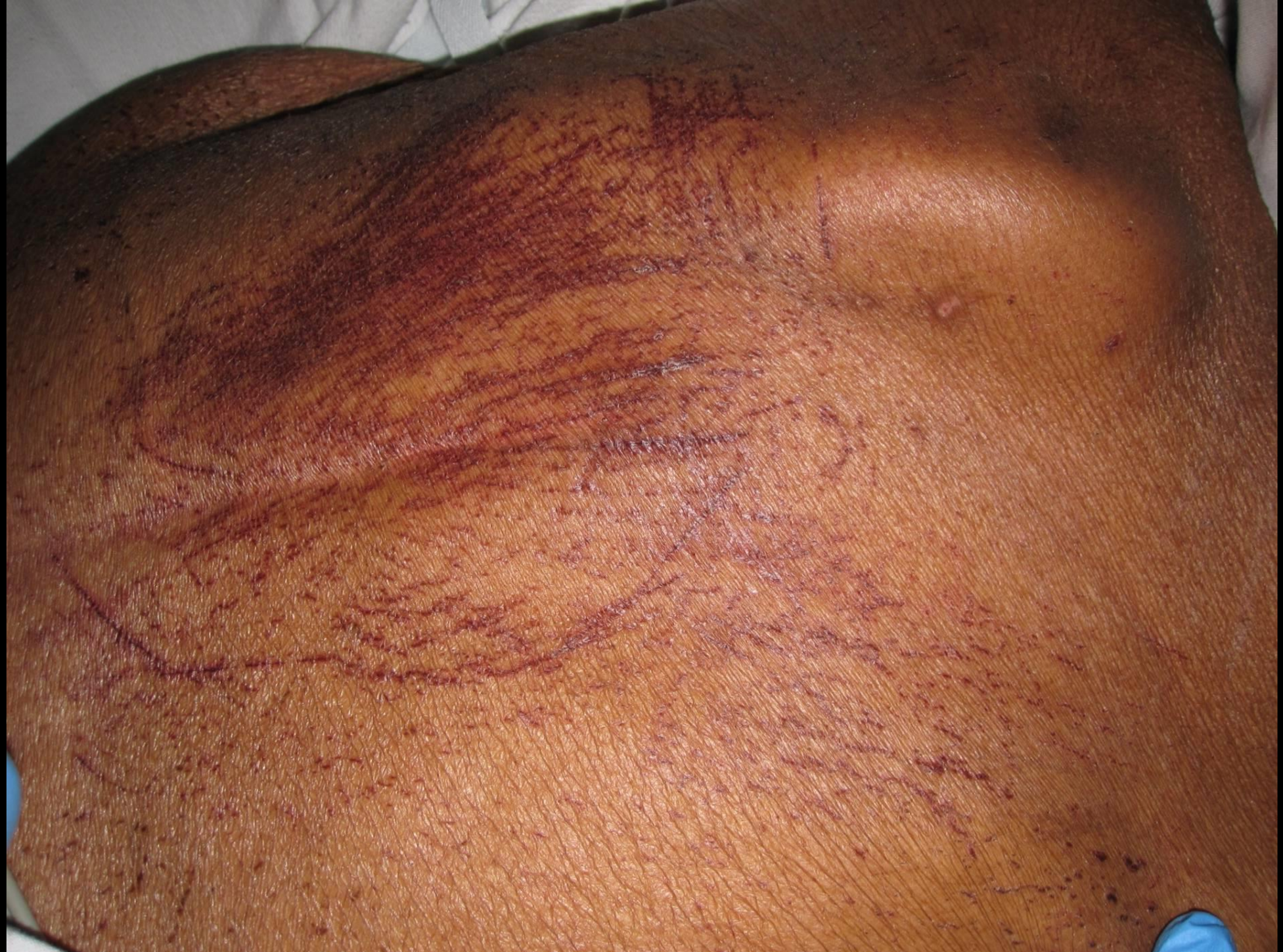
PMH

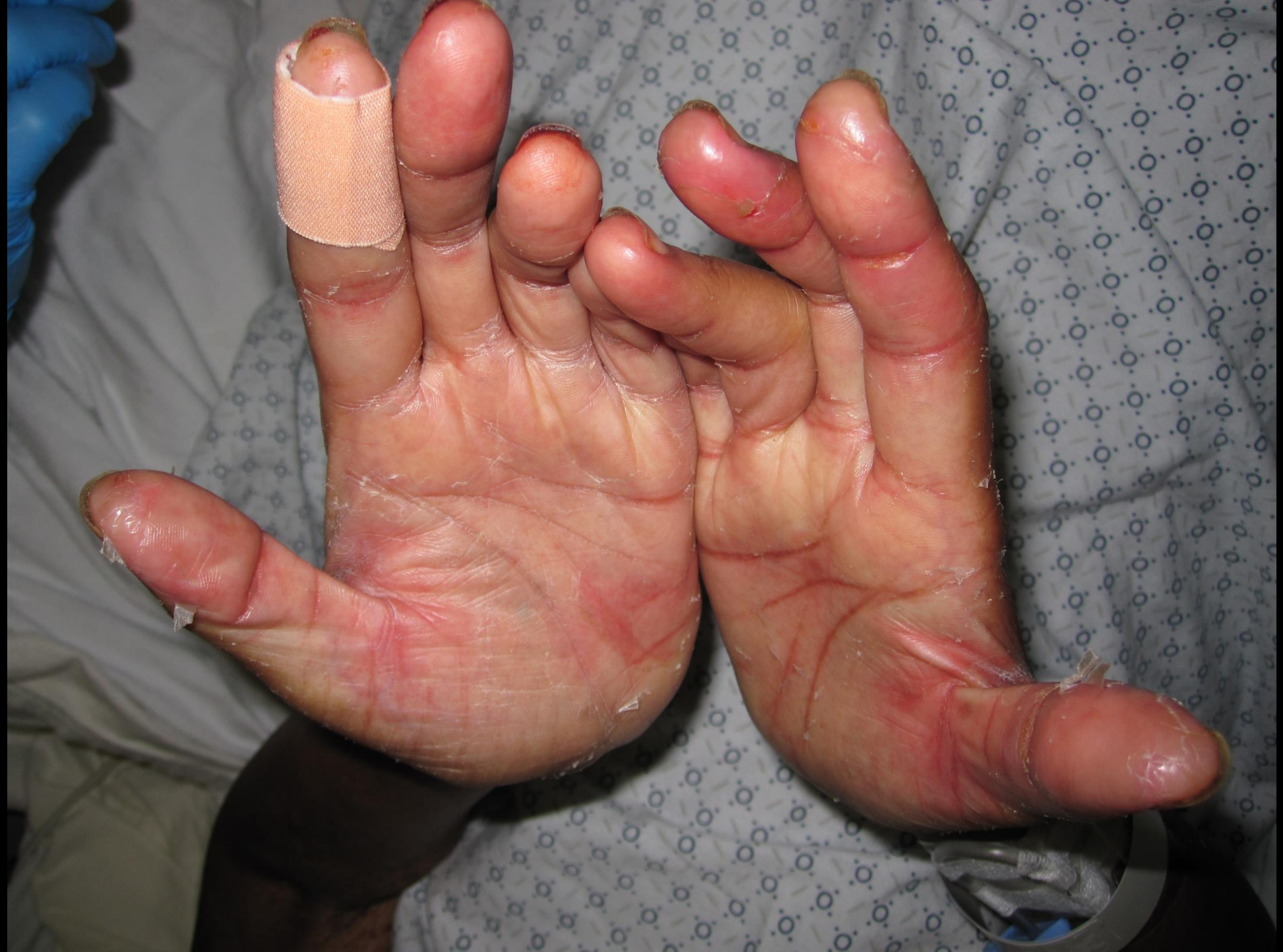
- Bypass complicated by:
  - Recent depression
  - Hypoalbuminemia
  - Anemia
  - Continued weight loss/diarrhea
  - Abdominal pain.
- 4 month history of progressively worsening diarrhea
  - Thought possibly to be due to C. Difficile infection but negative cultures and not responding to antibiotics

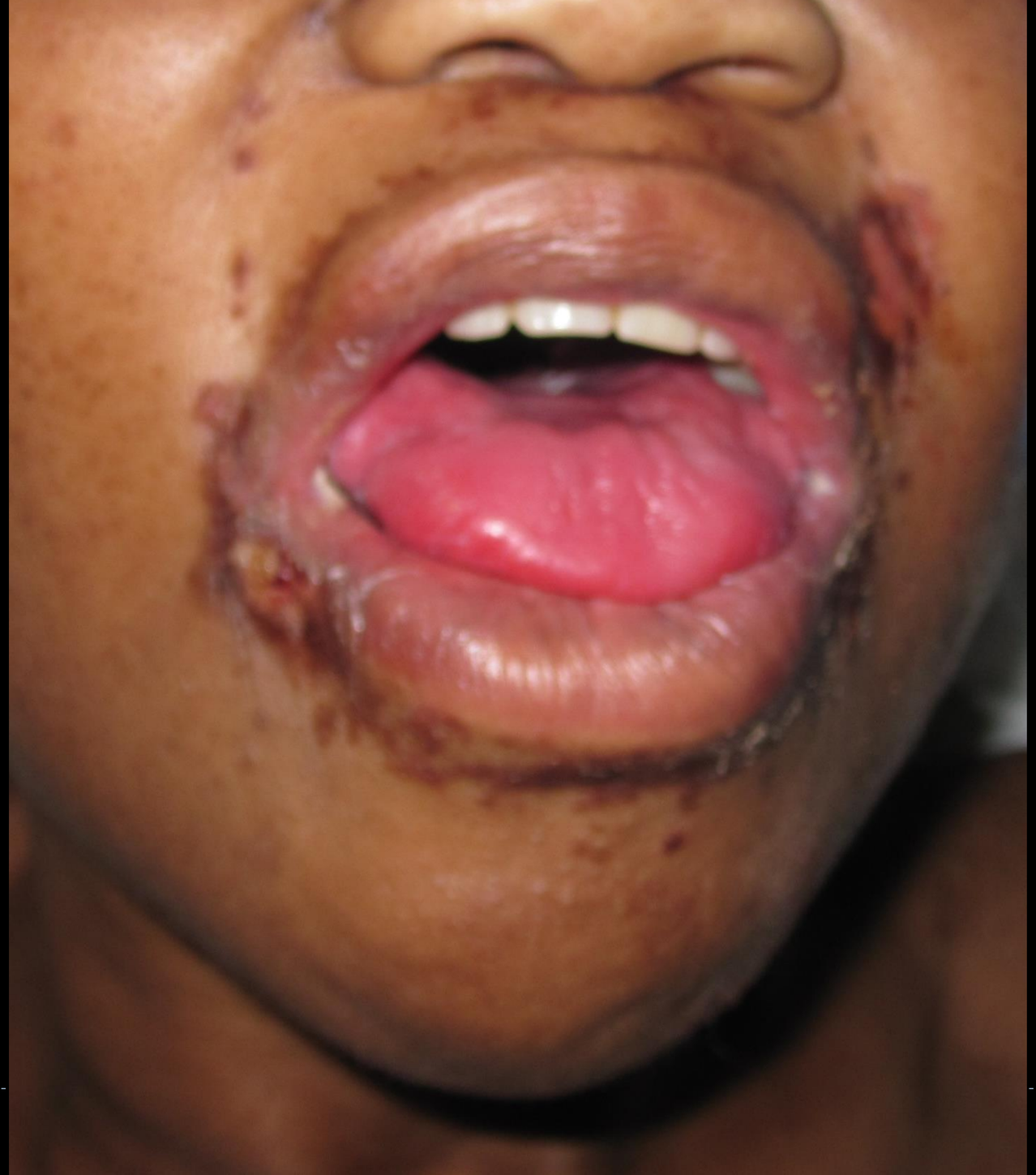


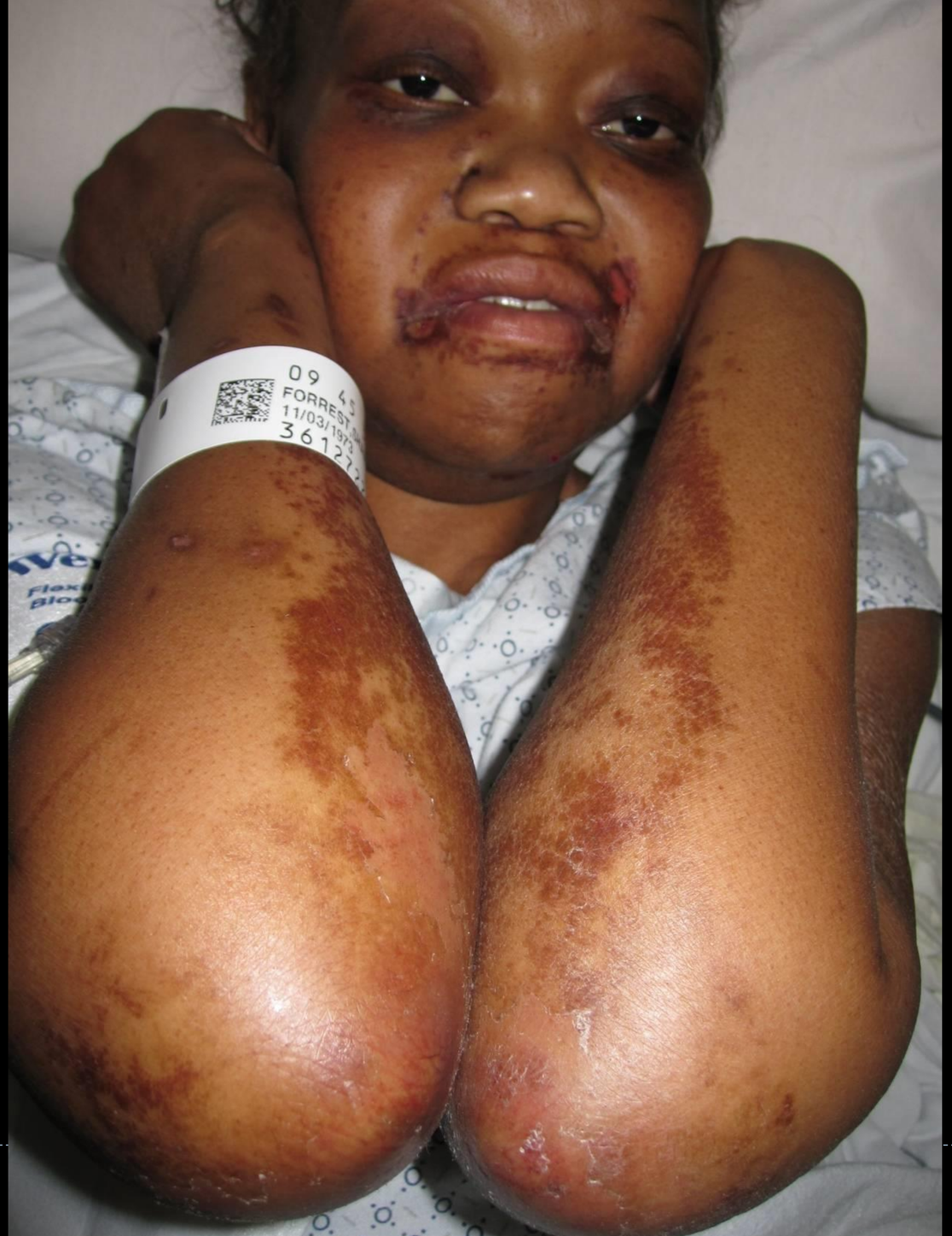








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FORREST
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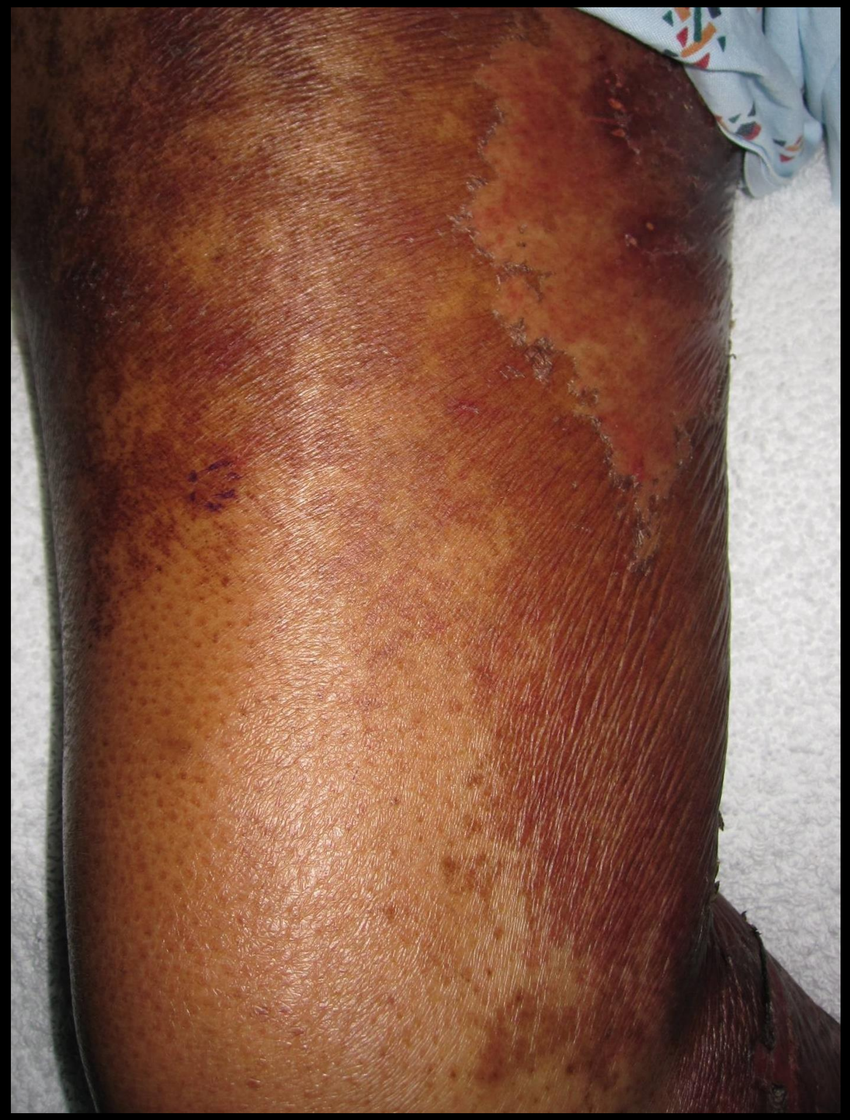
361272

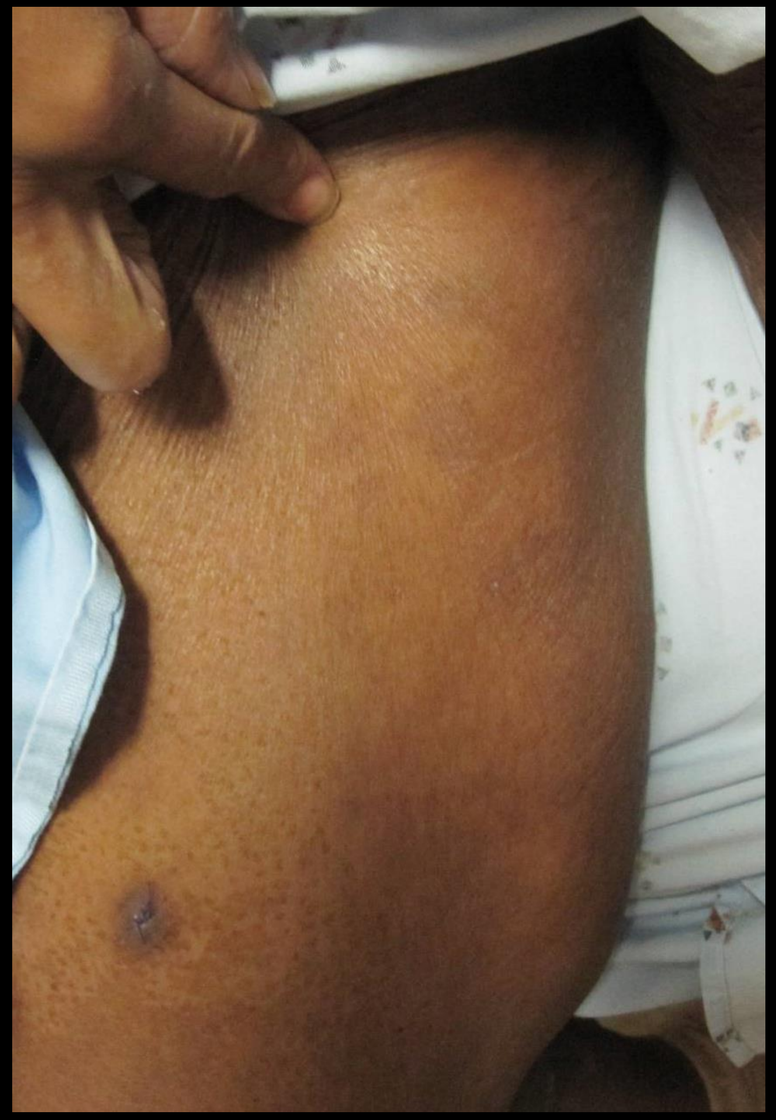
ZINC DEFICIENCY

- Congenital
  - Acrodermatitis enteropathica (genetic form, AR defect in zinc absorption from gut)
- Acquired
  - GI Fistulas, surgeries, high fiber diet
  - TPN w/o zinc supplementation
  - HIV infection

October 8



October 28



CASE 12

ALLEN-TAINTOR
DERMATOLOGY

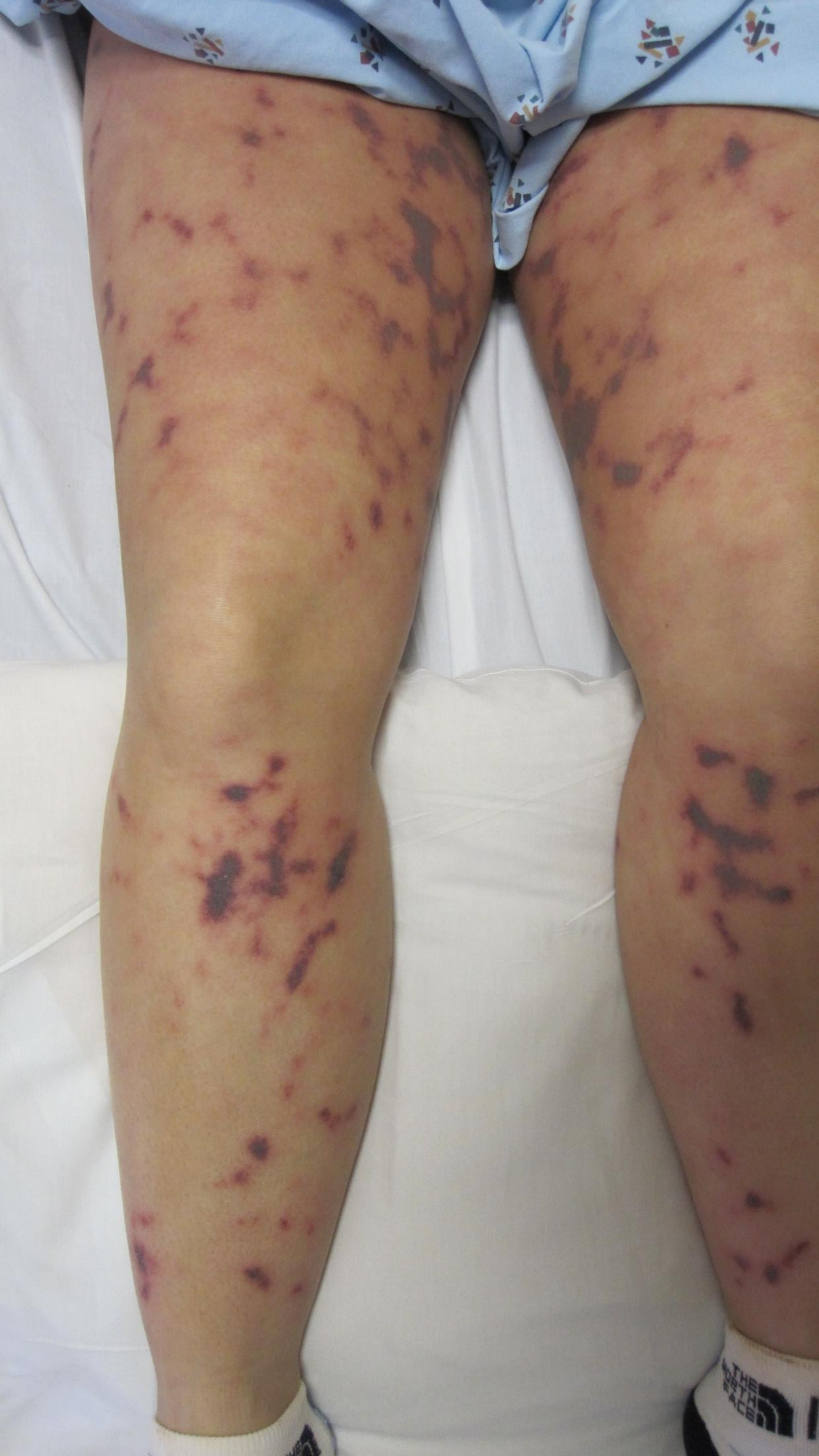
CASE

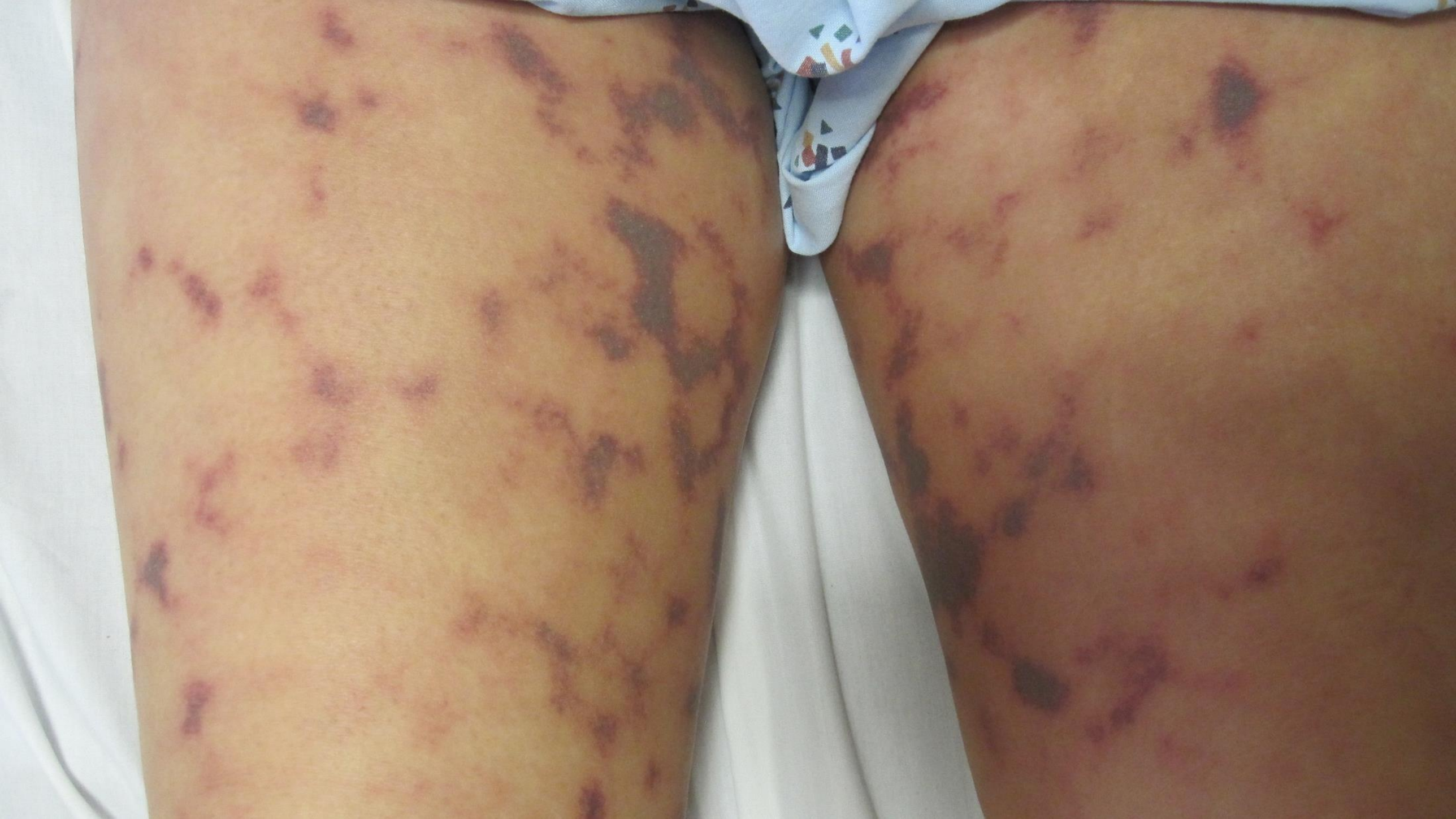
- 44yo previously healthy Caucasian female
- 3-day history of “bruise-like,” extremely painful rash on the lower legs and buttocks
- No history of similar eruption

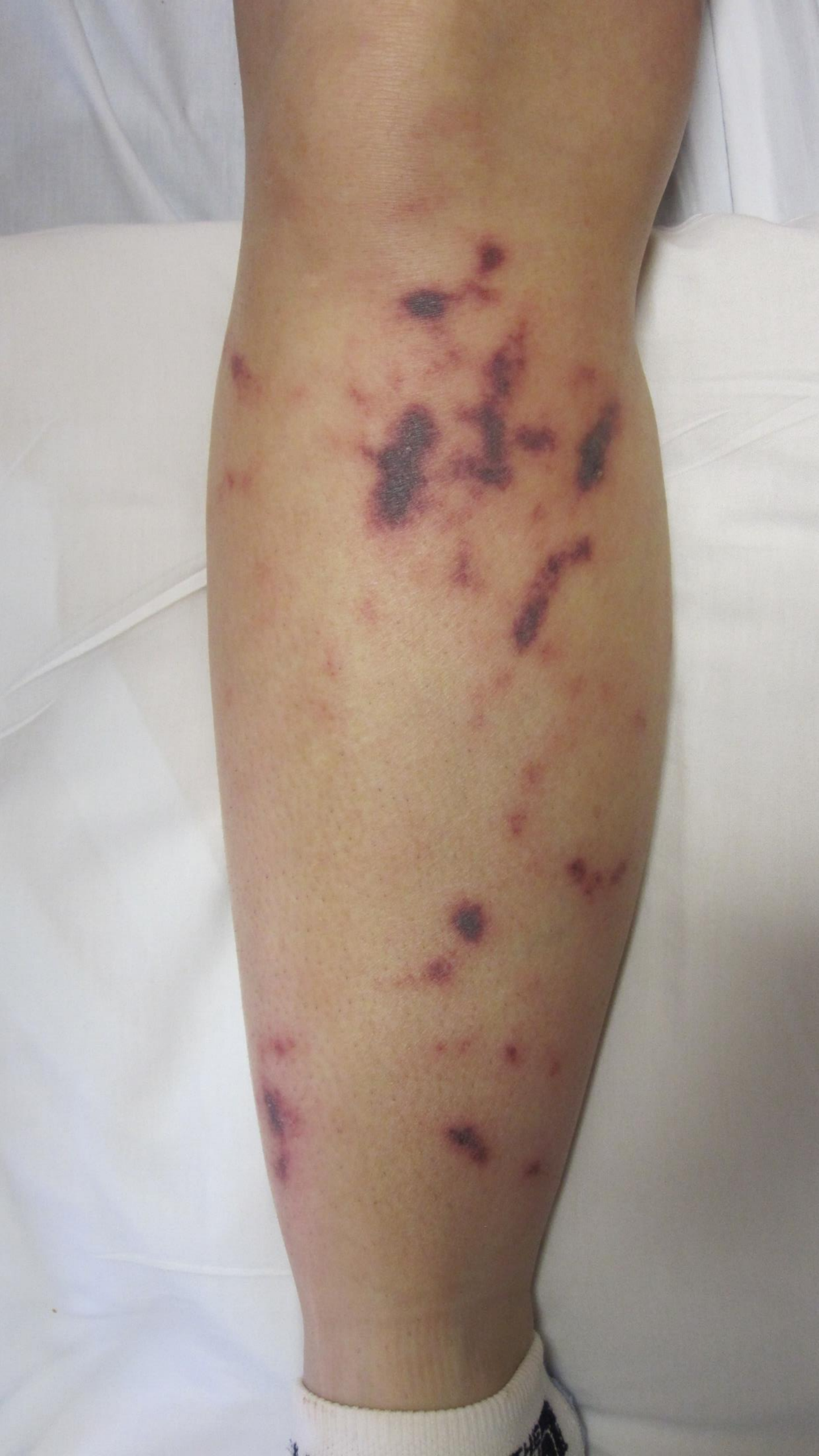
CASE

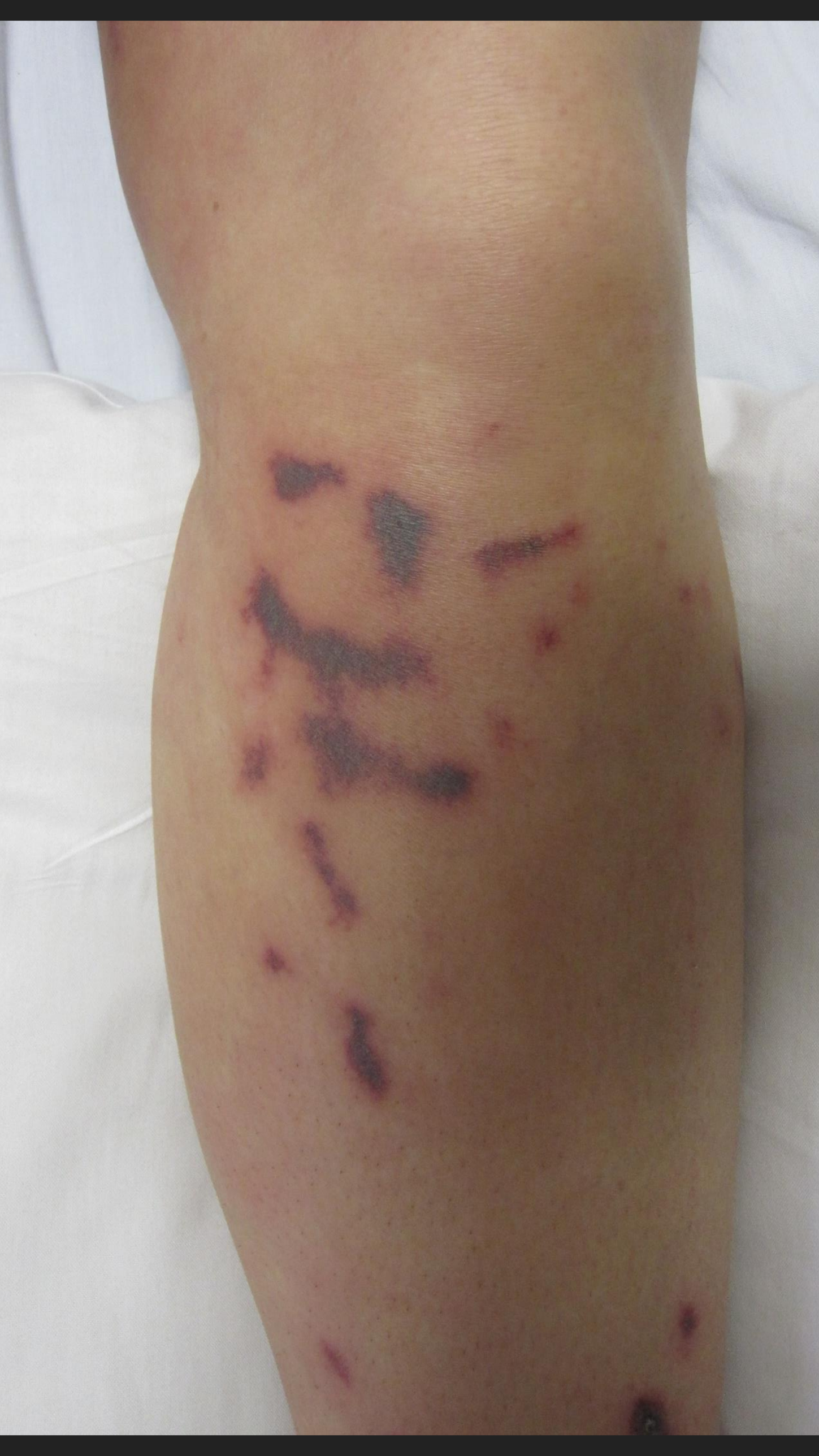
- Pt currently on probation for cocaine abuse
  - “Clean” for 2.5 years
  - Recent use 4 days ago (1 day prior to onset of rash)

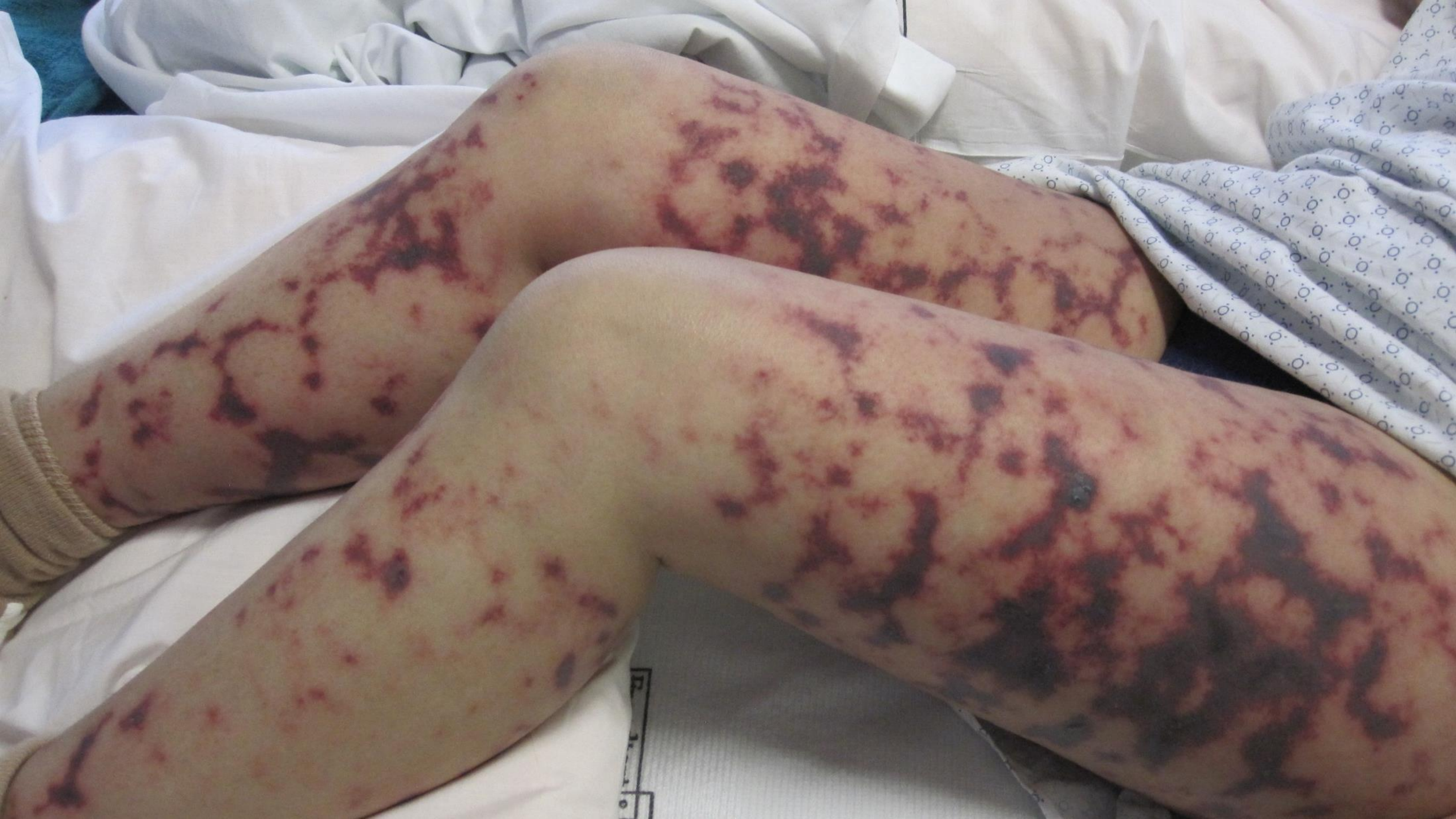
- No FHx autoimmune disease

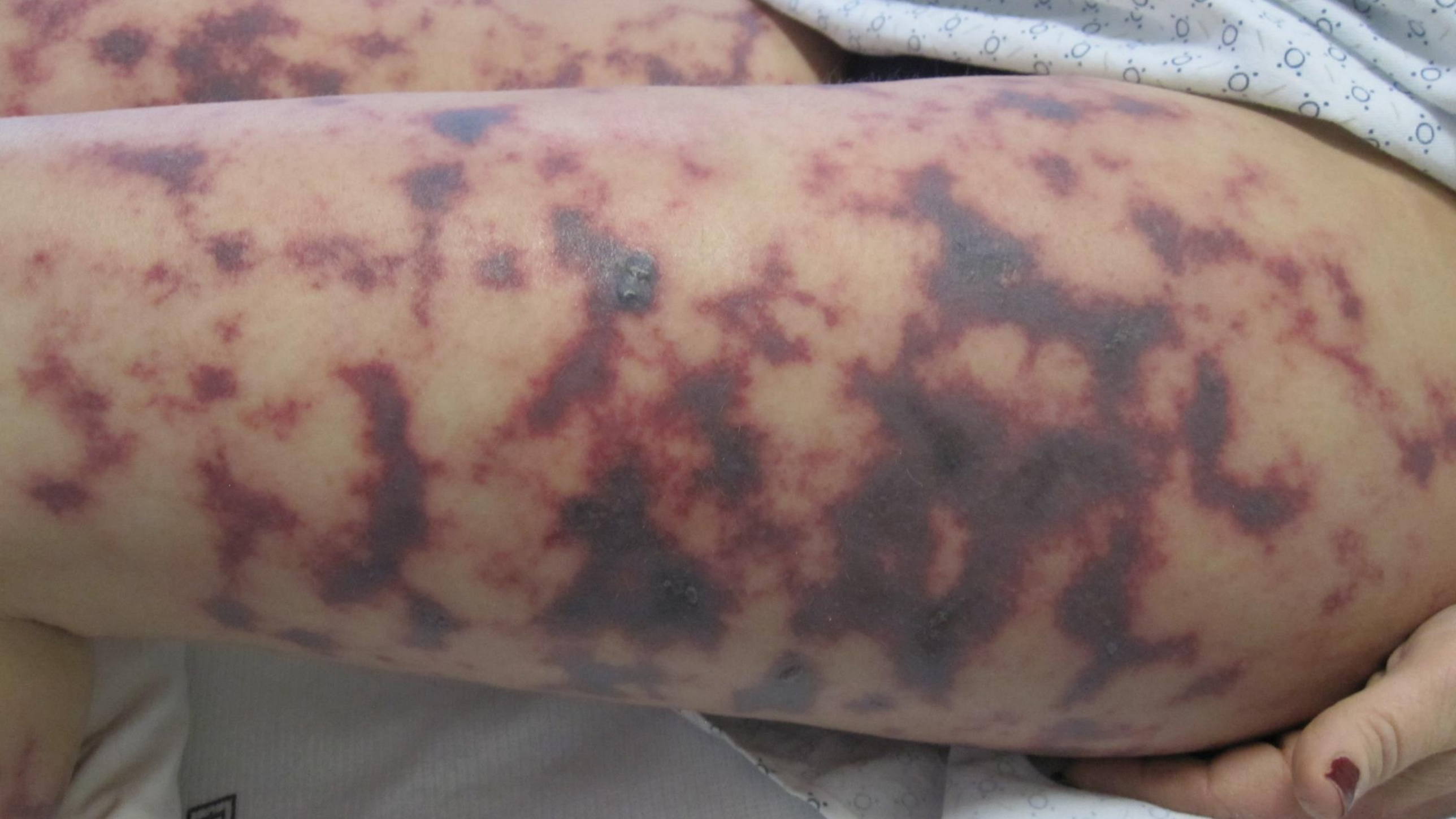

THE NORTH FACE











LABS

- H/H: 8.5/28
- WBC: 3.8
- Platelets: 99

- Hep B+C negative
- HIV: negative

- ANA +8.0
- Anti-dsDNA: 1 (0-4)
- ENA panel: negative

- ESR +28
- CRP +1.8

- Lupus anticoagulant: positive
- Anticardiolipin IgG 22 (0-14)
- Anticardiolipin IgM 73 (0-12)
- Beta-2 glycoprotein IgG/IgM: negative

- Complement C3/C4 low
- D Dimer: 6.5 (0-0.6)
- Fibrinogen: 135 (180-350)
- pANCA: 1:640 (<1:20)
- cANCA: negative

ALLEN-TAINTOR DERMATOLOGY

LABS

- Utox: + Cocaine

LEVAMISOLE VASCULOPATHY

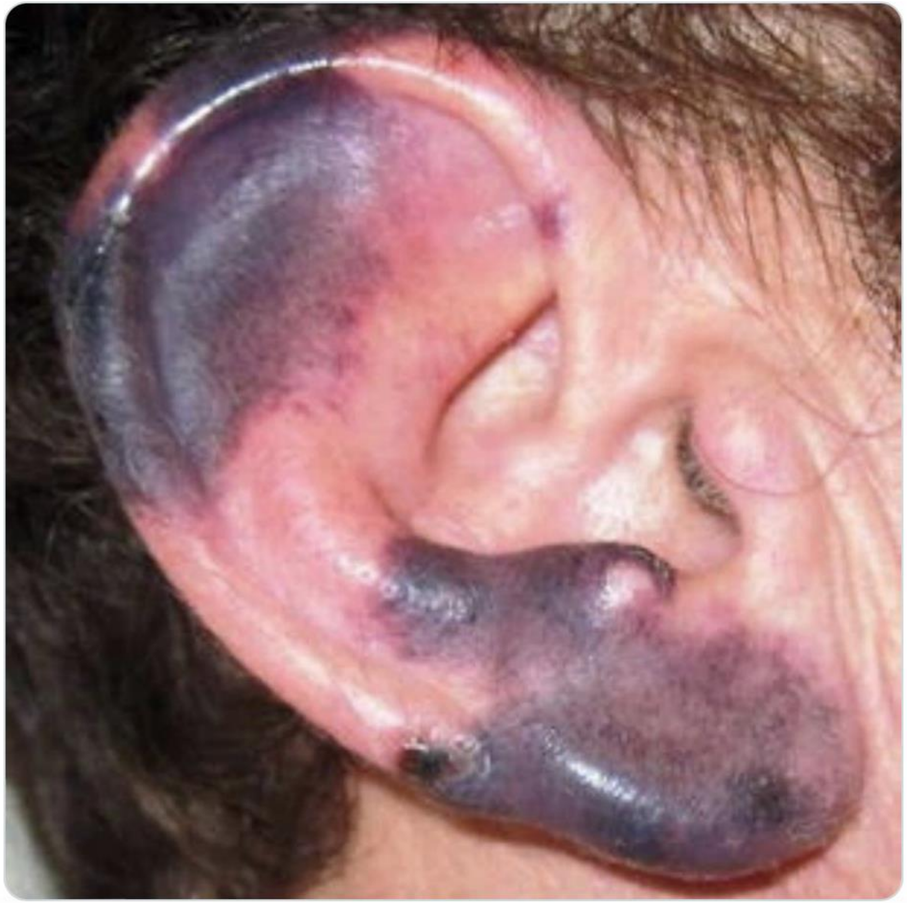
- Transient:
  - pANCA +
  - antiphospholipid panel +
  - Agranulocytosis
  - ANA +
  - Combination vasculitis/thrombo-occlusive
  - Common locations - ears

Josh Trebach, MD
@jtrebach

A 31-year-old man presents to the emergency department with ear pain. The patient tells you he uses cocaine. Physical exam shows this rash.

☠️☠️

What do you think is going on?



10:15 AM · Jan 29, 2022

Search Amazon

Description

Expel-P (Levamisole HCl), is an anthelmintic (anti-worm) and immunostimulant agent and is effective against many internal parasites, especially nematodes when used as directed. It is effective against Nematodes, Roundworms, Nodular Worms, and Hookworms. Can be used as a coral dip to treat flatworms and pest nudibranchs. DIRECTIONS: Use 1 packet Expel-P per 10 gallons of water. Perform a 25% water change taking to remove excreted worms/parasites after 24 hours. Repeat the cycle one additional time one week later to prevent reinfection. Repeat weekly treatments as necessary.

CASE 13

ALLEN-TAINTOR
DERMATOLOGY

CASE

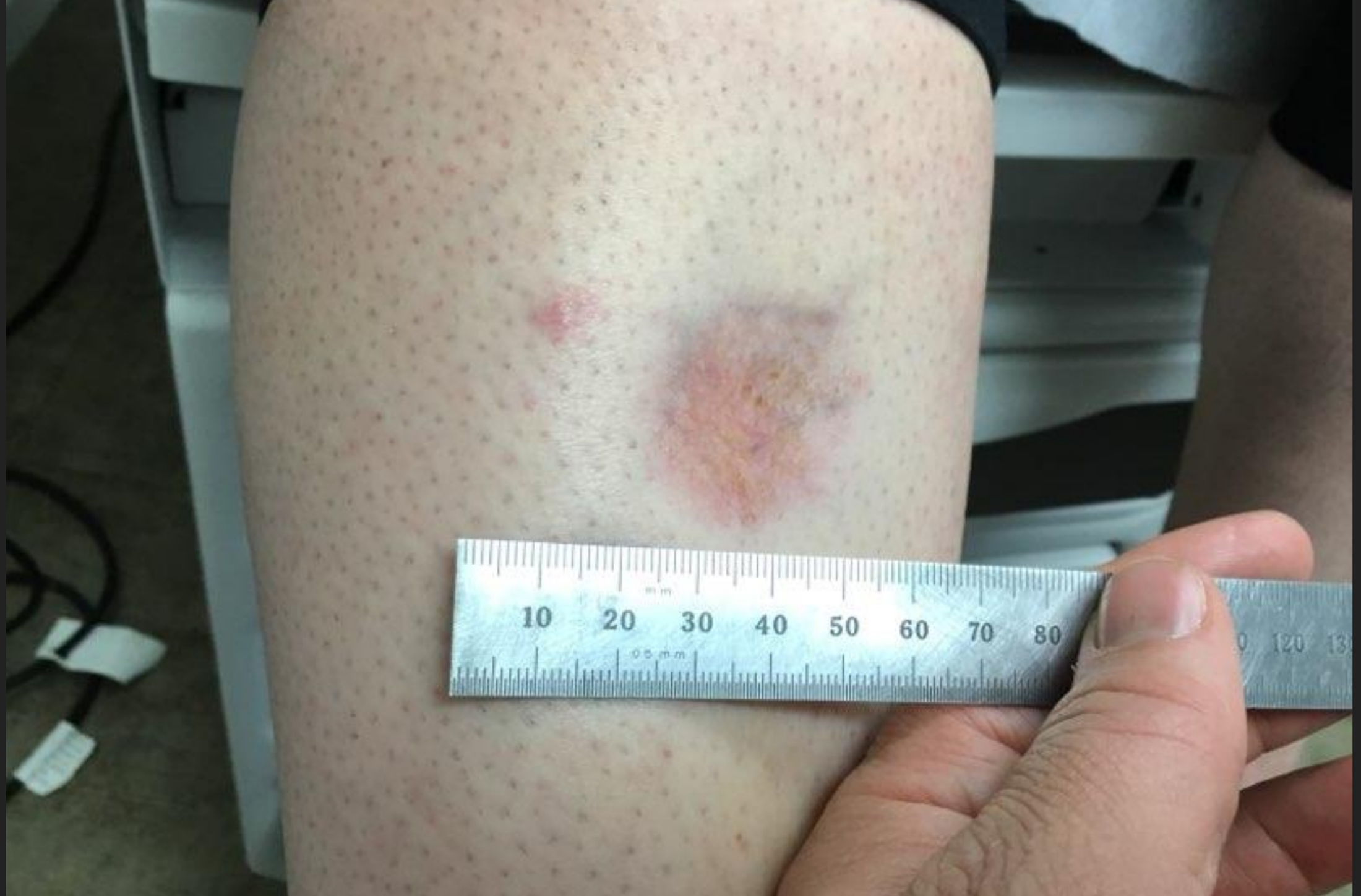
- 20 yo Caucasian female
- Red rash on the legs x 1 year

- History of Type 1 Diabetes

NECROBIOSIS LIPOIDICA DIABETICORUM

- Plaques with violaceous to red-brown palpable rim, atrophic yellow center
- Pathogenesis unknown
  - Possibly immune mediated vascular damage

- 0.03% of pts with DM will develop NLD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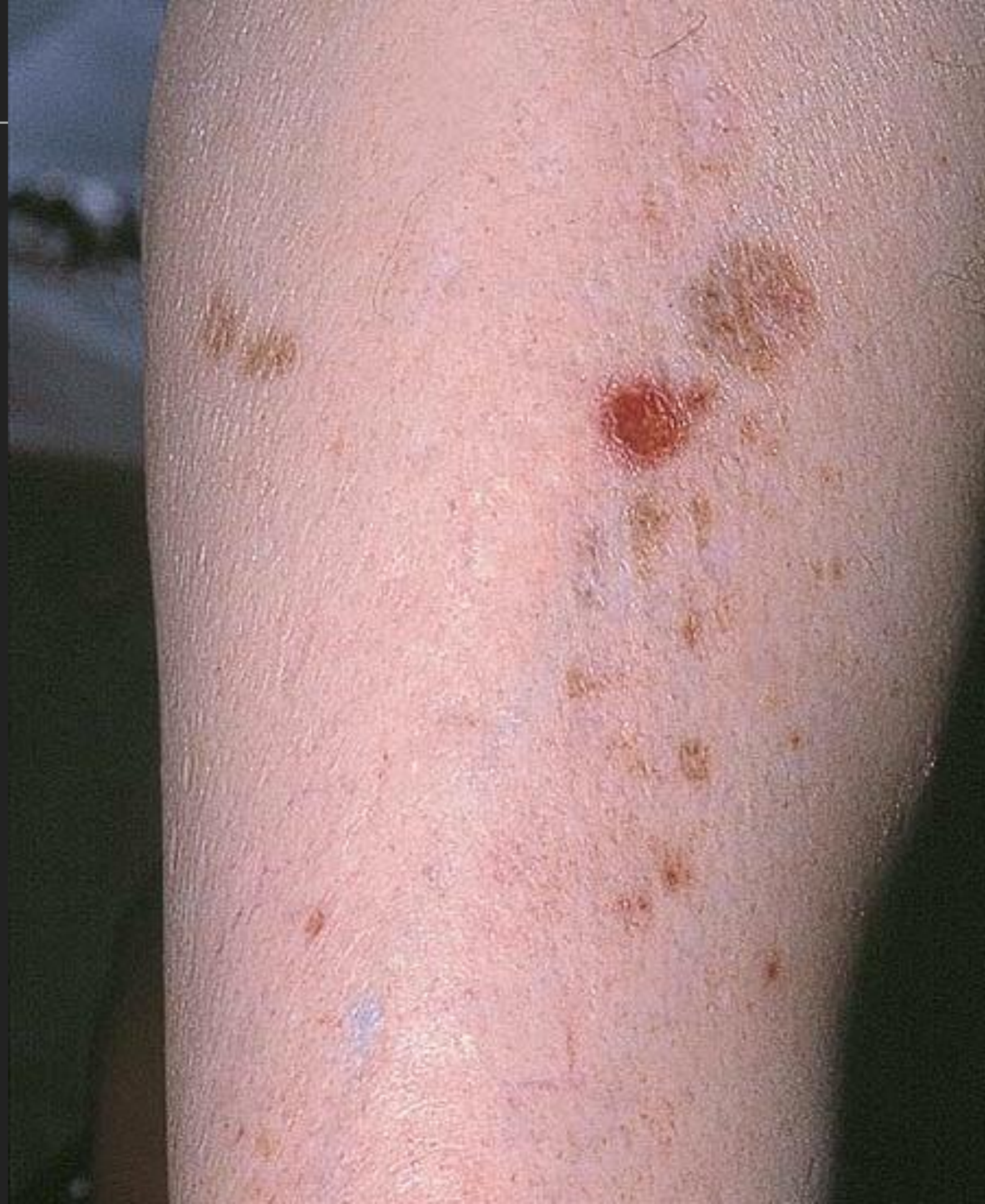
DIABETIC DERMOPATHY

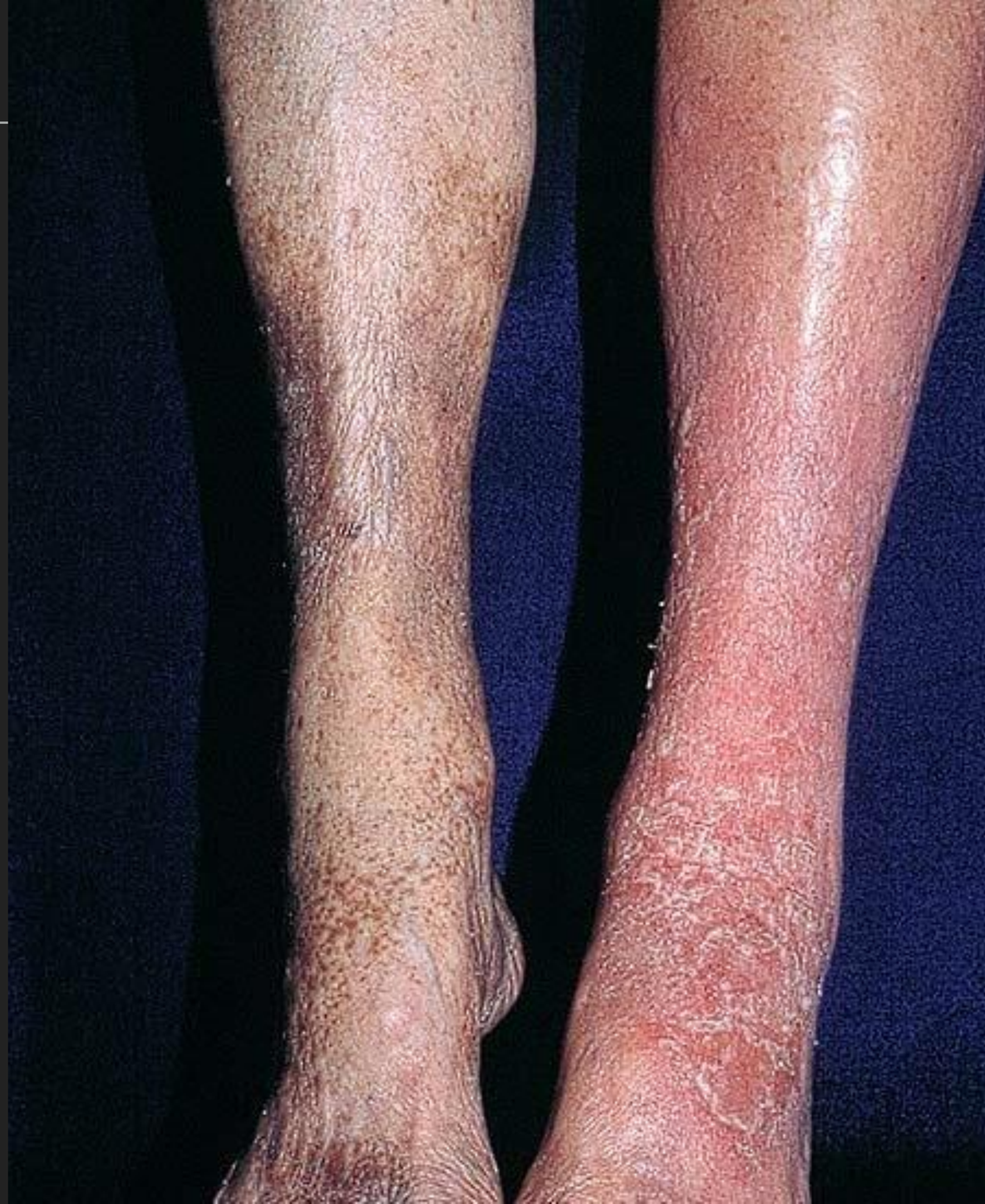
- AKA shin spots
- May be a sign of microvascular damage elsewhere
- Occur at sites of trauma



ALLEN-TAINTOR DERMATOLOGY

STASIS DERMATITIS

- Can mimic cellulitis
- “Bilateral cellulitis” is usually stasis
- Use mid potency corticosteroids like triamcinolone 0.1% ointment
- Compression



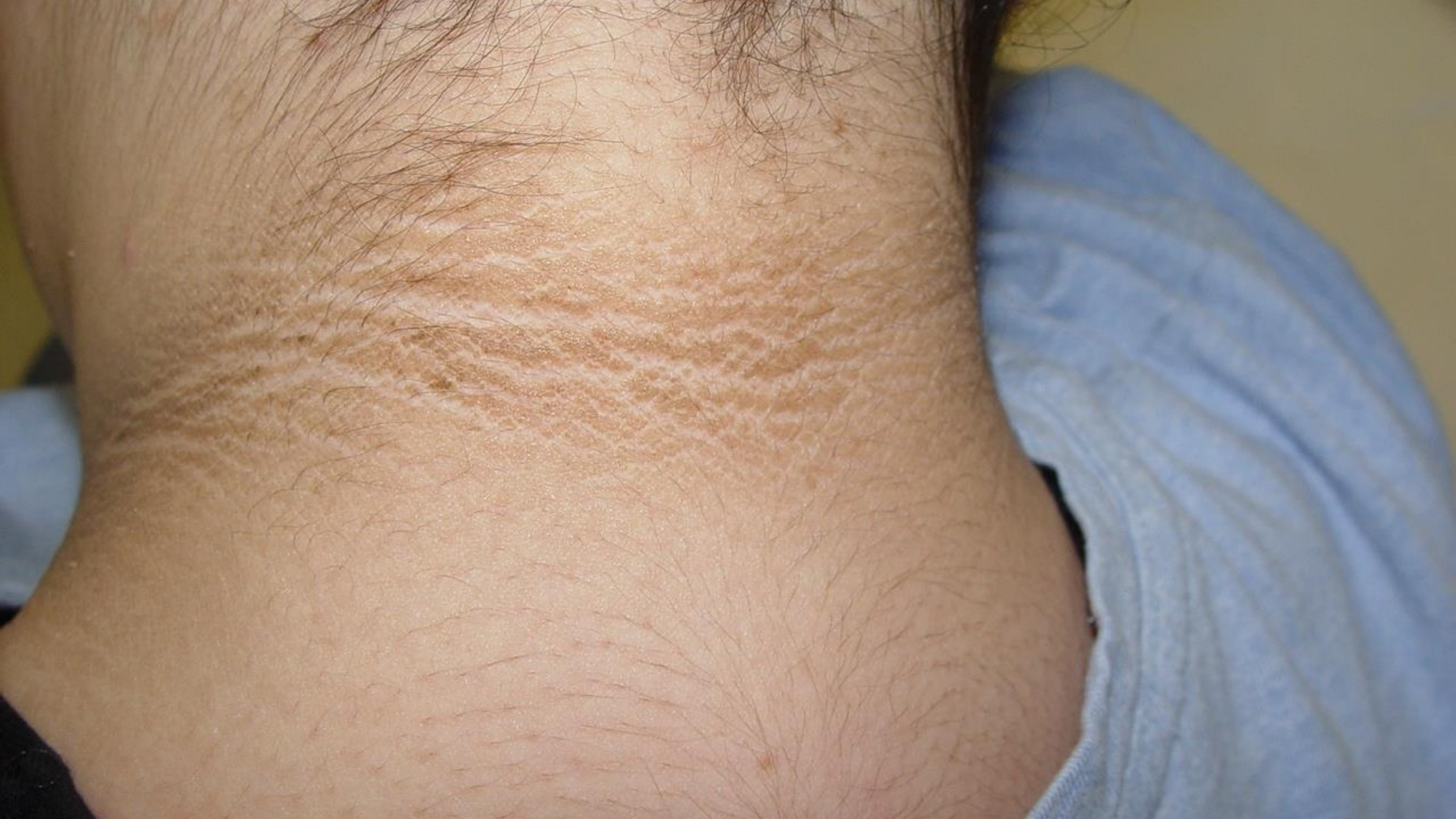
ALLEN-TAINTOR DERMATOLOGY

CASE 14

ALLEN-TAINTOR
DERMATOLOGY

CASE 14

- Obese young adult
- Bothered by rash on neck and other folds
- Hemoglobin A1C is fine, fasting blood sugar within normal limits, but borderline



ACANTHOSIS NIGRICANS

- Obesity and multiple endocrine disorders
  - Acromegaly, PCOS, Cushing syndrome, diabetes mellitus, hypothyroidism, Addison's disease, hyperandrogenic states, hypogonadal syndromes, insulin-receptor defect
- Malignancy: Adeno CA of stomach, lung, breast, others
- Familial: childhood presentation, AD
- Medication induced
  - Nicotinic acid, niacinamide, testosterone, OCP, glucocorticoisds

QUESTIONS?

ALLEN-TAINTOR
DERMATOLOGY