

**DERMATOLOGIC CLINICOPATHOLOGIC
CORRELATION:**

**PINK & BLUE
OR SHADES OF GRAY?**

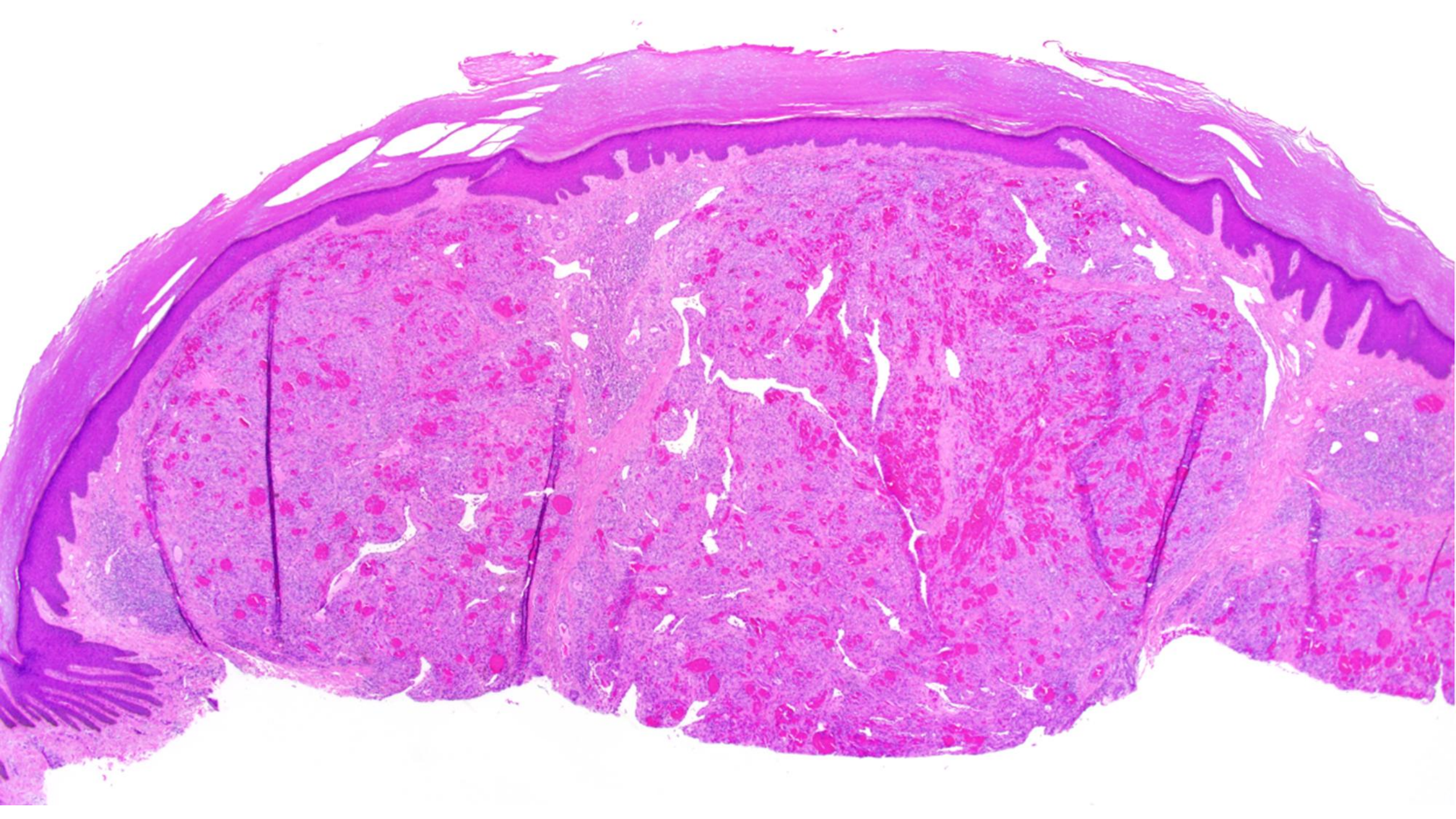
Cathy M. Massoud, MD, FAAD
Dermatology/Dermatopathology
Central Virginia VA Healthcare System
October 19, 2025

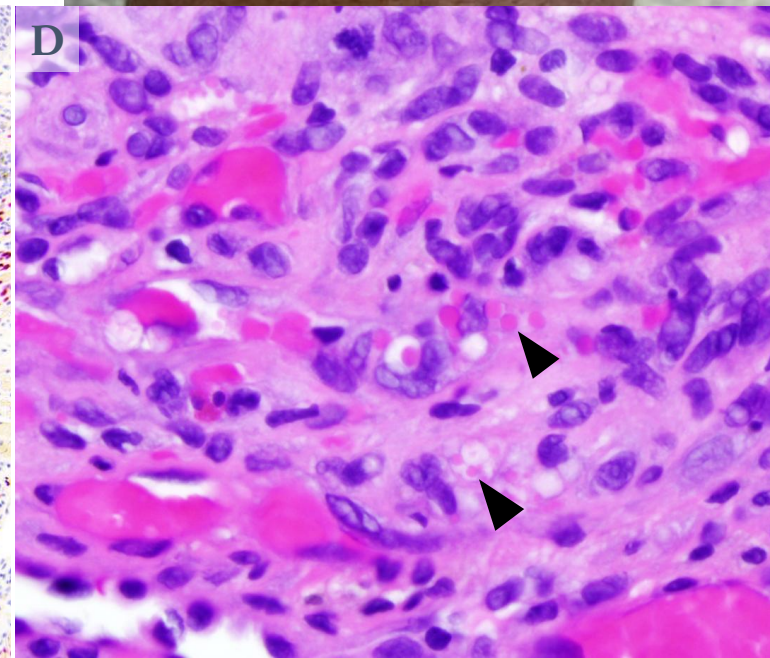
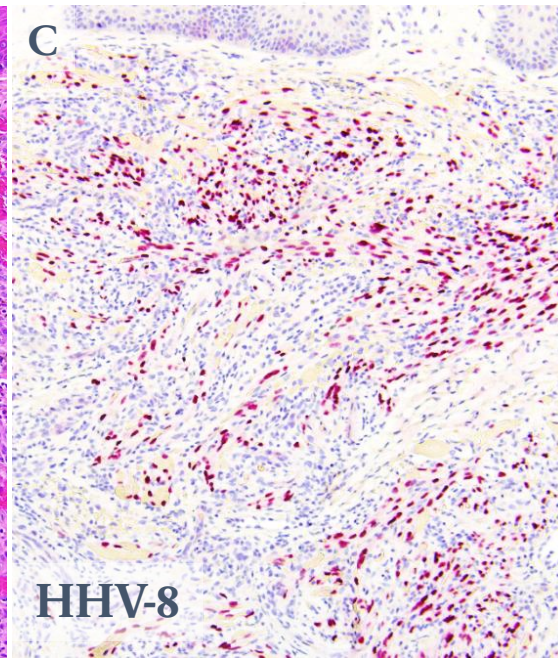
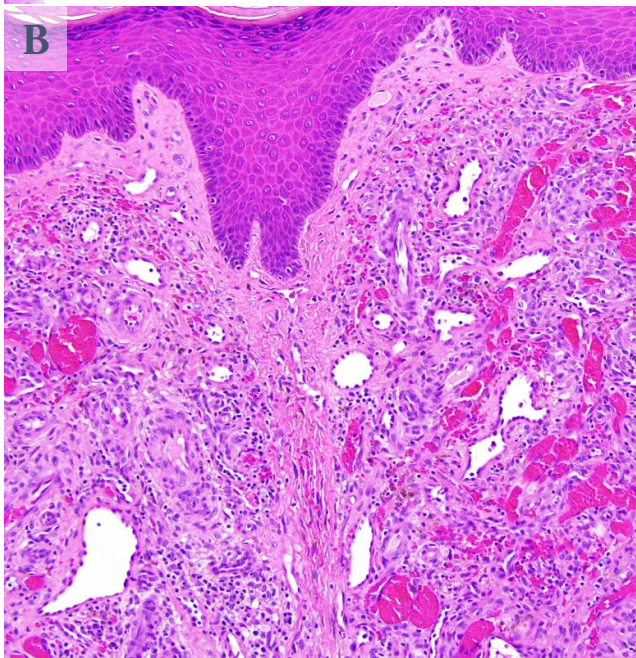
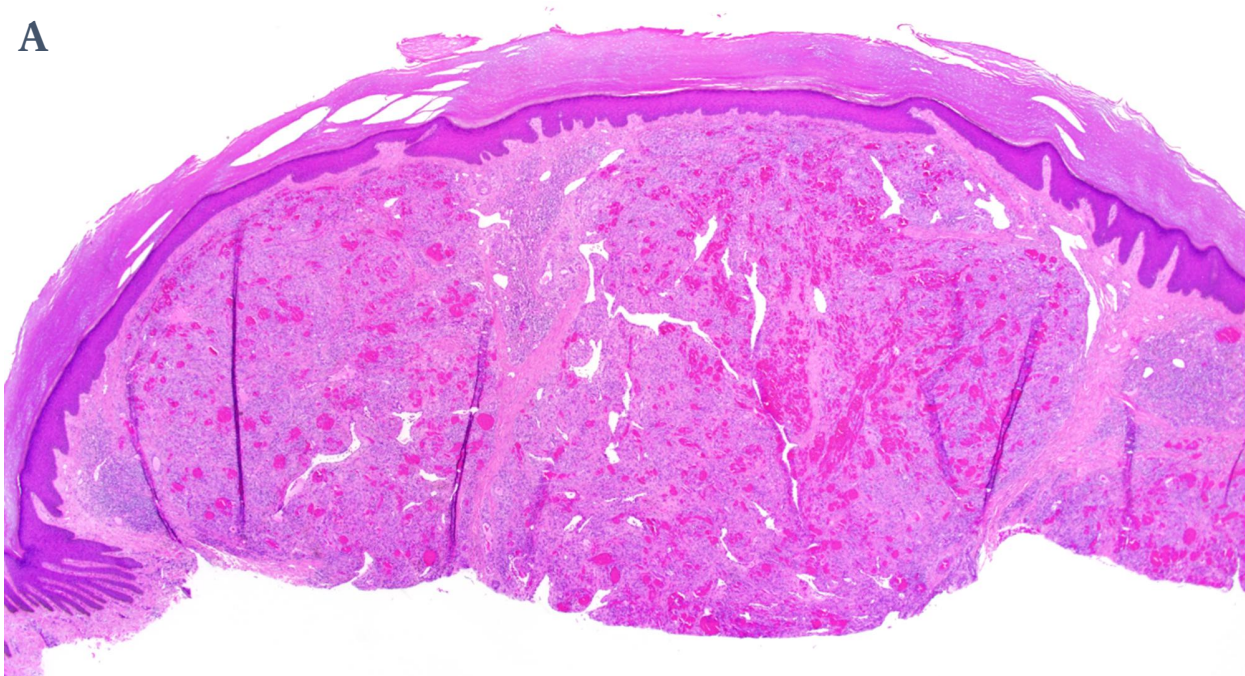
- 
- I have no relevant conflicts of interest to disclose.
 - The content provided will reference off-label uses of drugs.
 - The views expressed in this presentation are my own and do not necessarily represent the views of the Veterans Health Administration or the United States Government.



OBJECTIVES

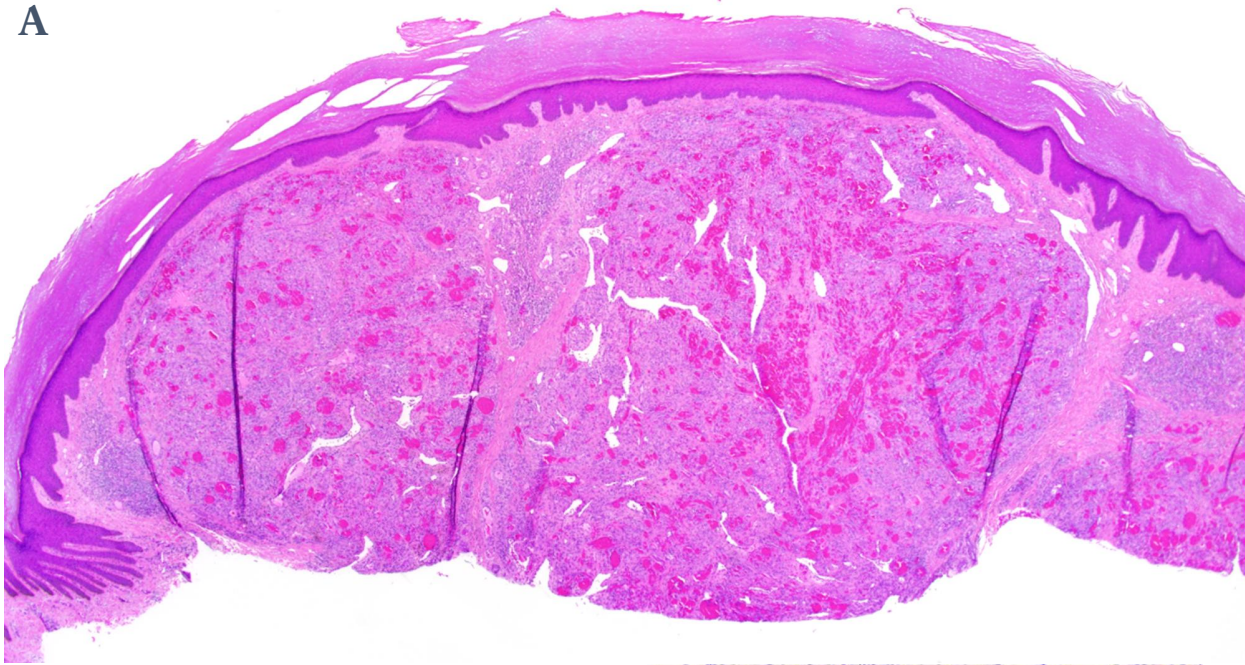
- Describe typical and atypical presentations of dermatologic disorders.
- Discuss the limits of histopathologic evaluation.
- Recognize the importance of clinicopathologic correlation.





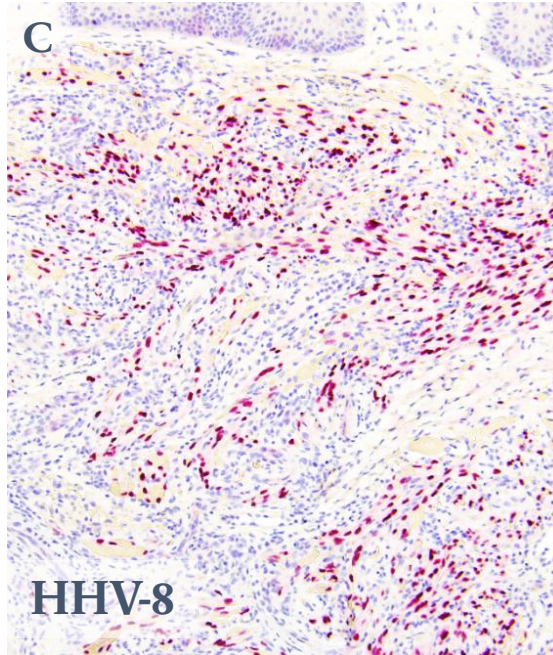
*Original
magnification
A) x20, B) x100,
C) x200 D) x400*

A

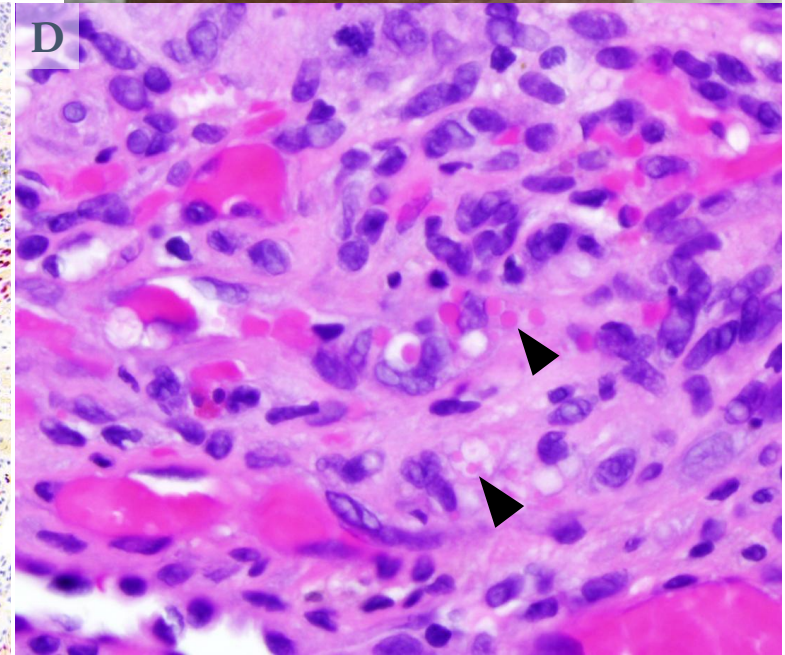


NODULAR KAPOSI SARCOMA

C

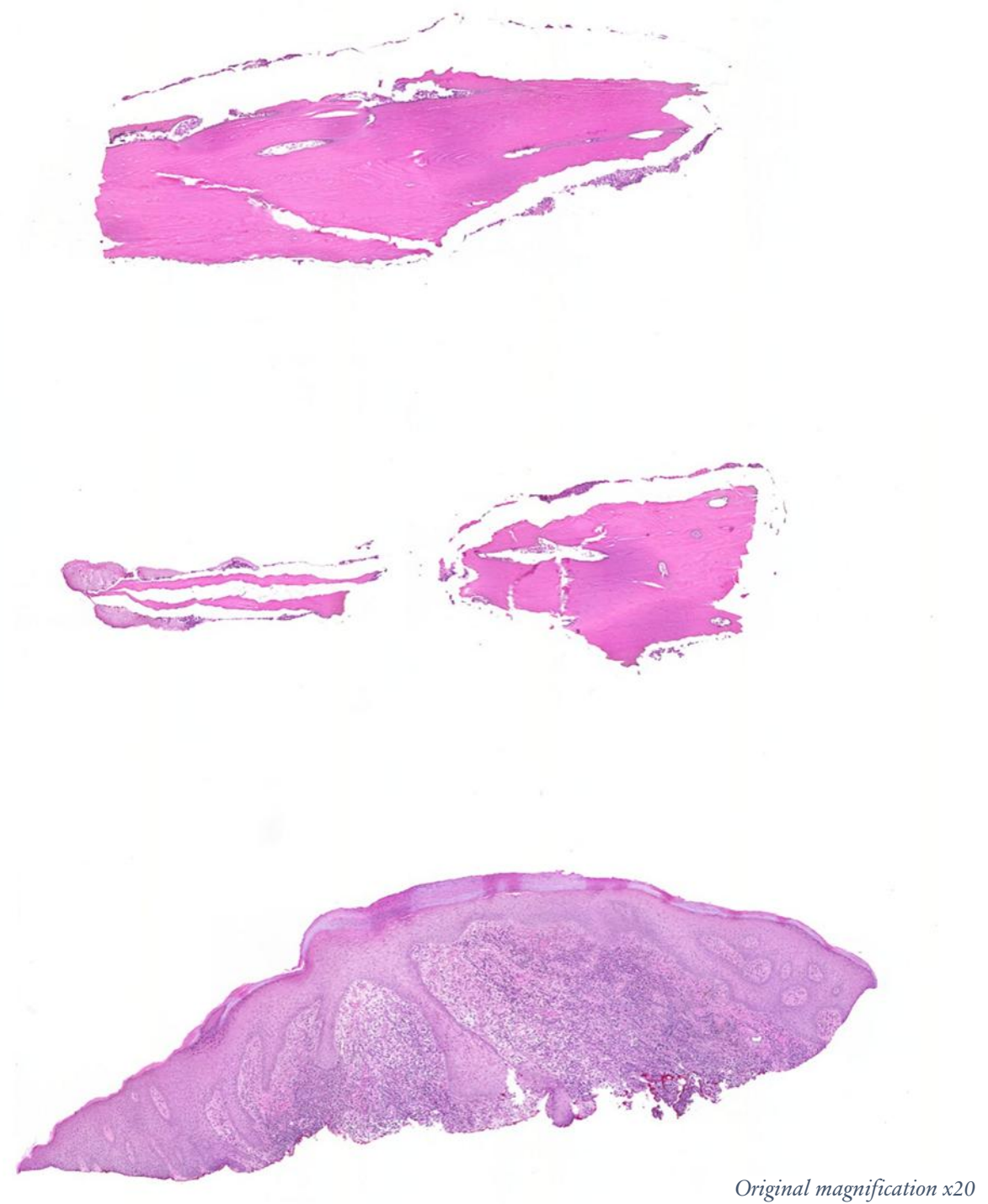


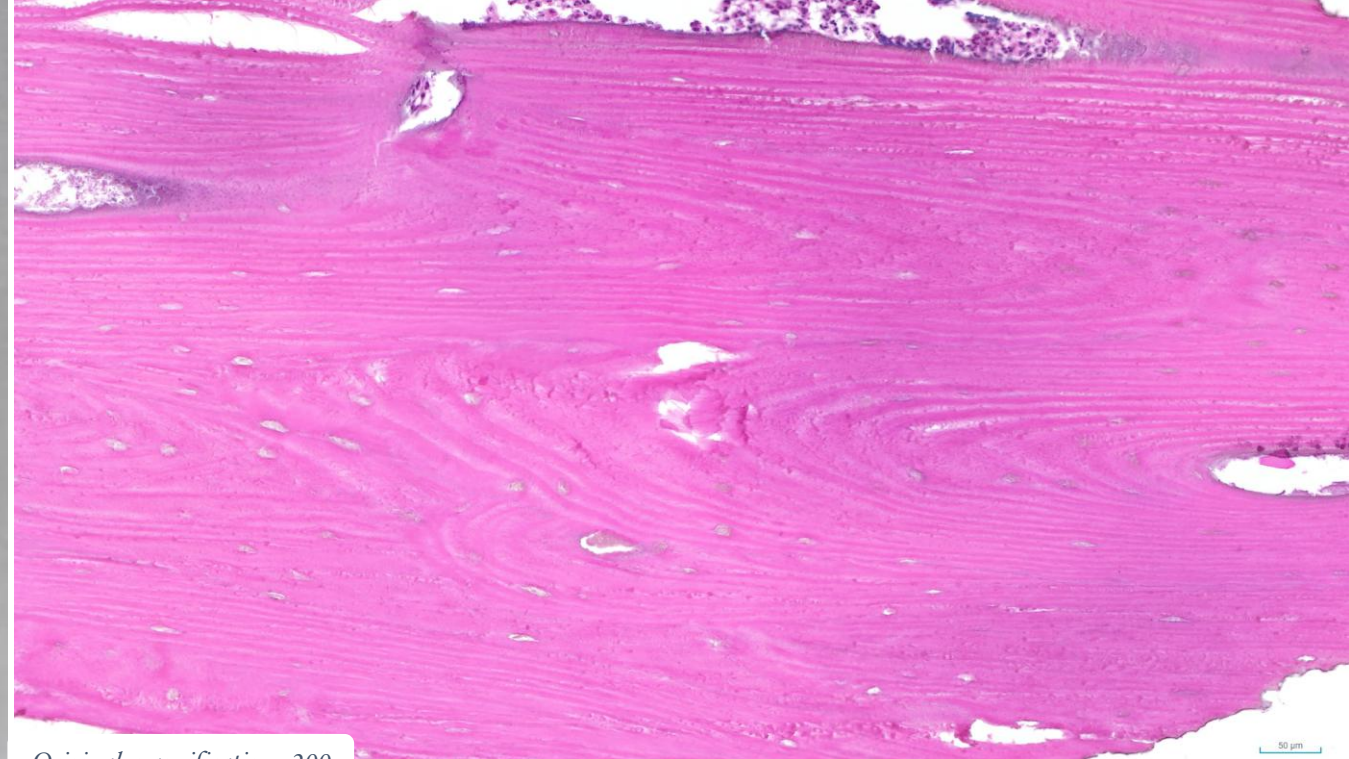
D



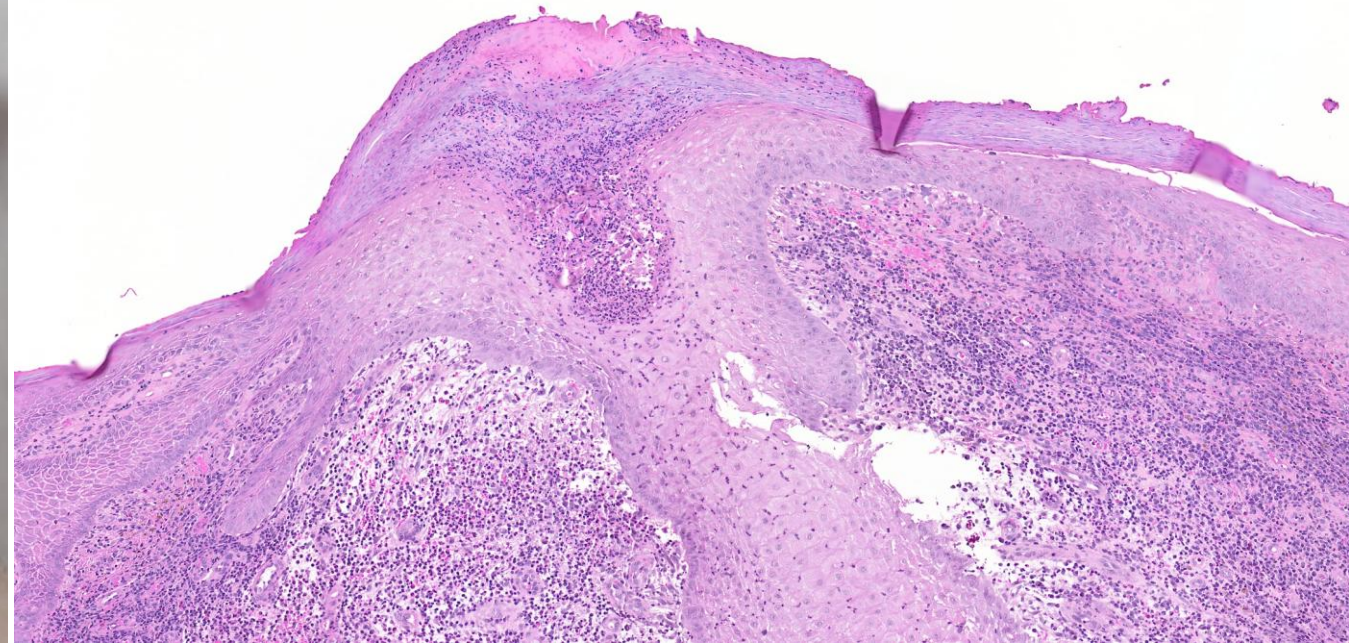
*Original
magnification
A) x20, B) x100,
C) x200 D) x400*







Original magnification x200

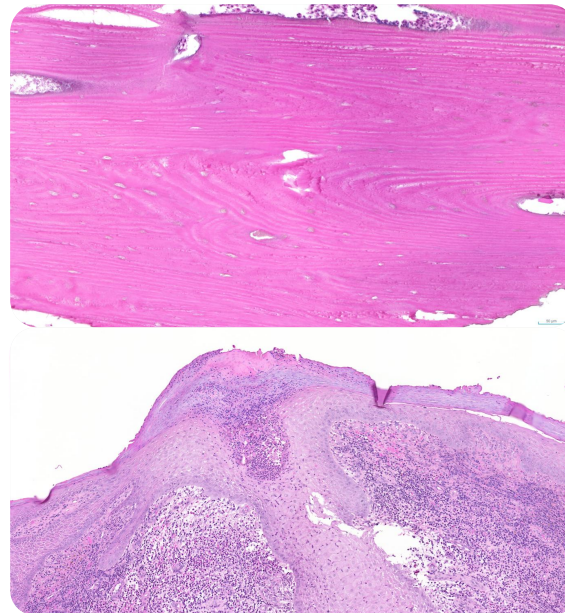


OSTEOMA CUTIS

15% *Primary*
genetic
isolated
disseminated
miliary
plate-like

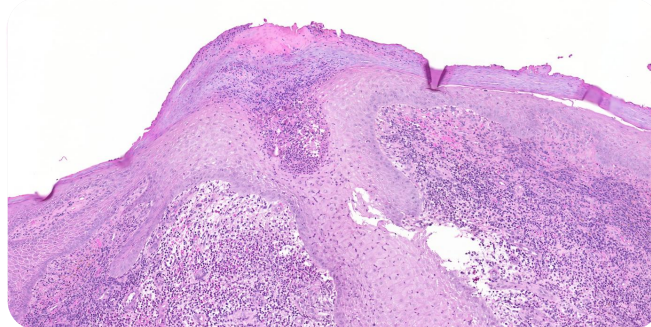
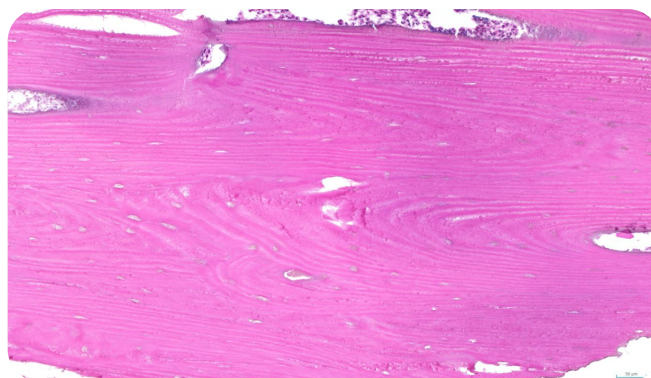
85% *Secondary*
venous stasis
acne
CTD
NSF
neoplasms
trauma*

- **10** cases of solitary perforating** osteoma cutis
 - 1° or 2°
 - forehead, lower leg, elbow, breast
 - *cryotherapy, chronic irritation, tattoo, stasis
 - **underreporting likely
- Lesion duration: <1m to 20y
- Tangential biopsy or excision without recurrence





arm grafts
multiple operations



Heterotopic ossification first described during the American Civil War status-post amputations

High energy penetrating extremity wounds

Pro-inflammatory cytokines and chemokines upregulated (*IL-6, -10, BMP, MIP-1 α , IP10*)

Osteopotent cells
(*muscle, endothelial cells, dermal fibroblasts, primitive dermal mesenchymal cells*)

Osteoblasts

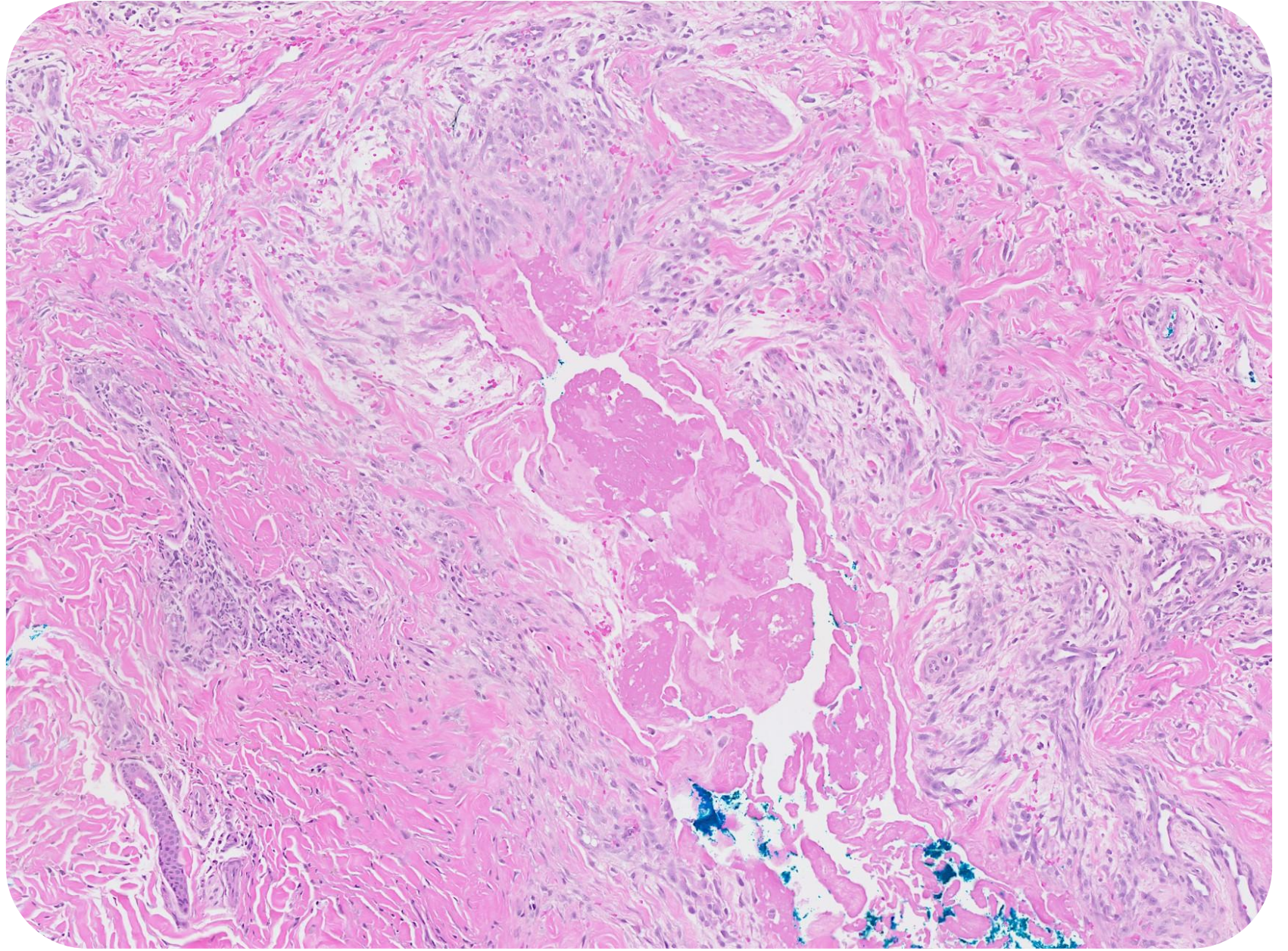
Heterotopic ossification



2 weeks
doxycycline PO
triamcinolone 0.1%
ointment

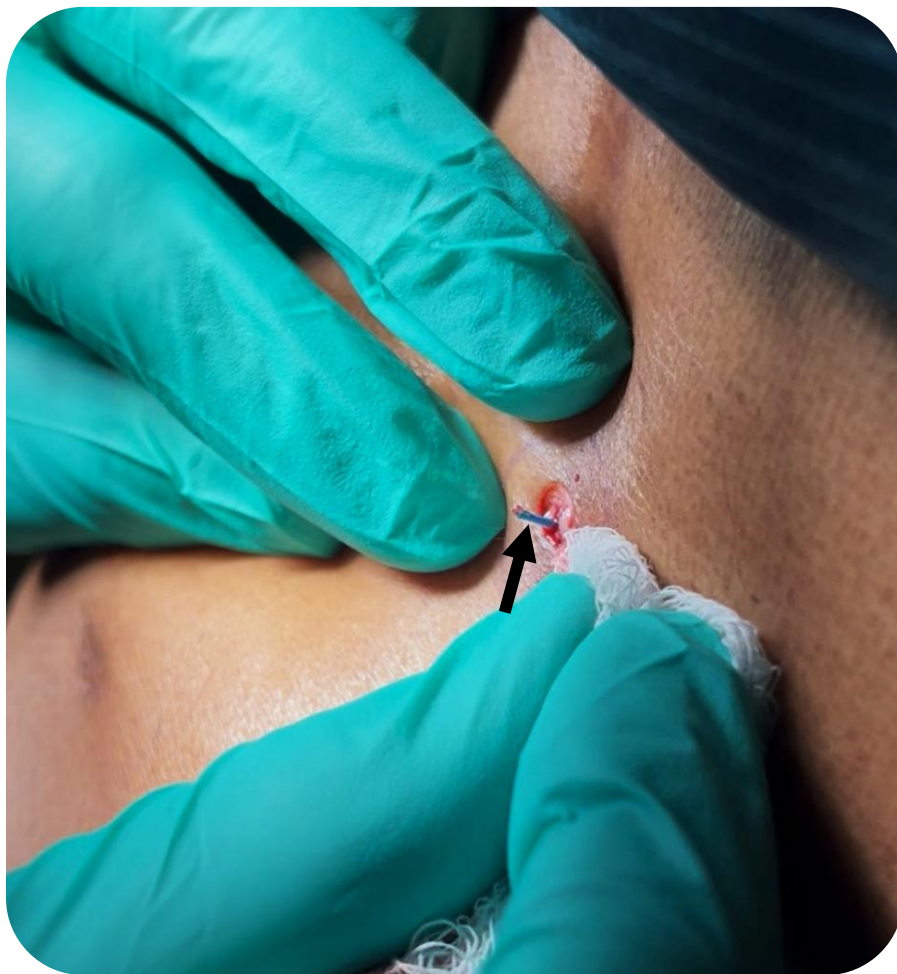








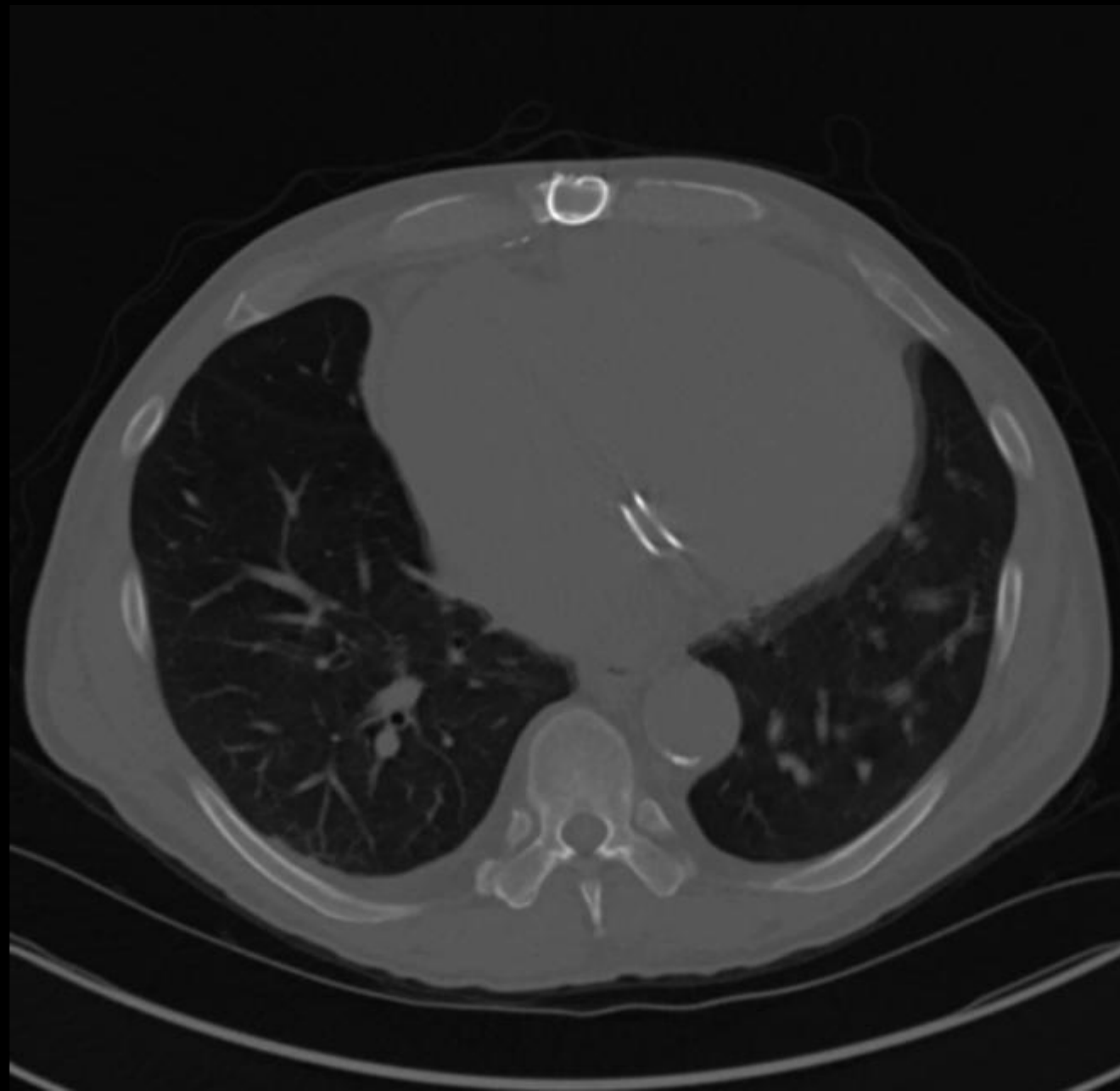




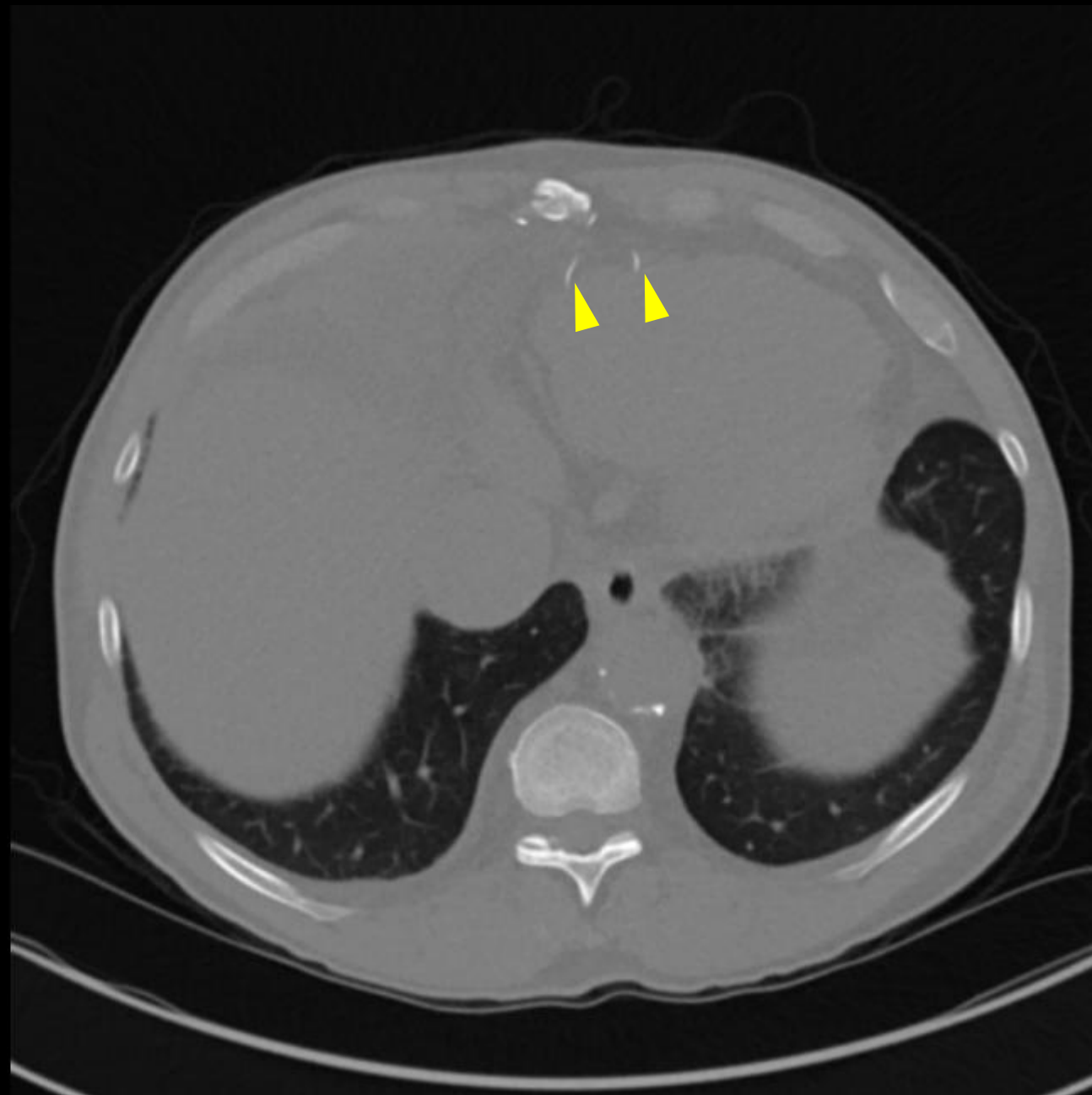
4 days status-post pacemaker placement for tachycardia-bradycardia syndrome

17 years status-post mitral valve replacement

R



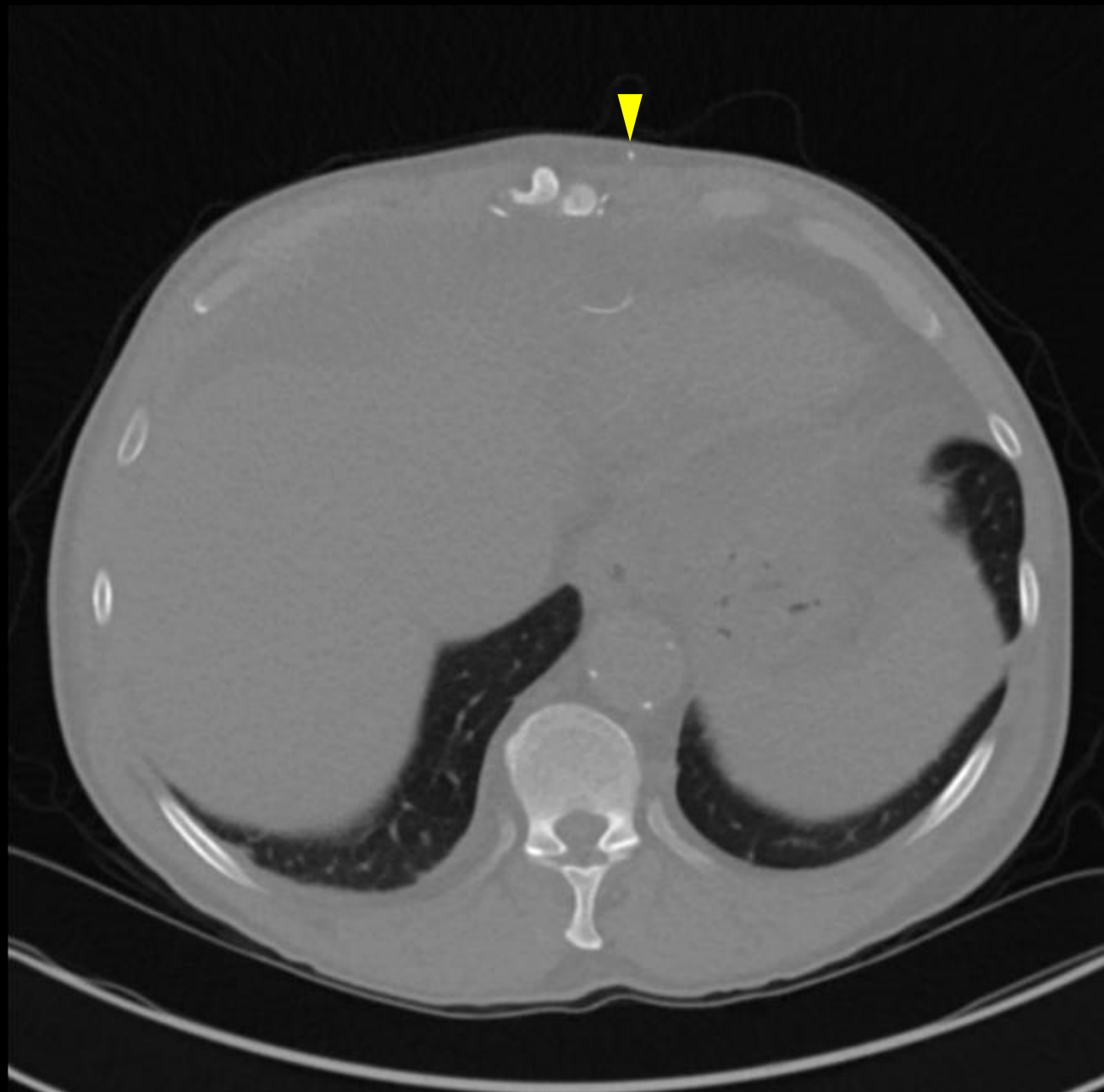
R



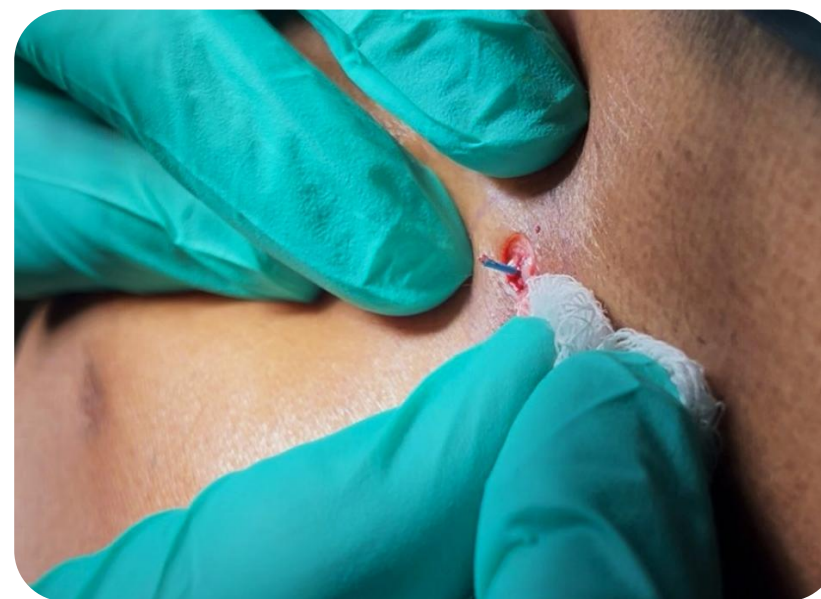
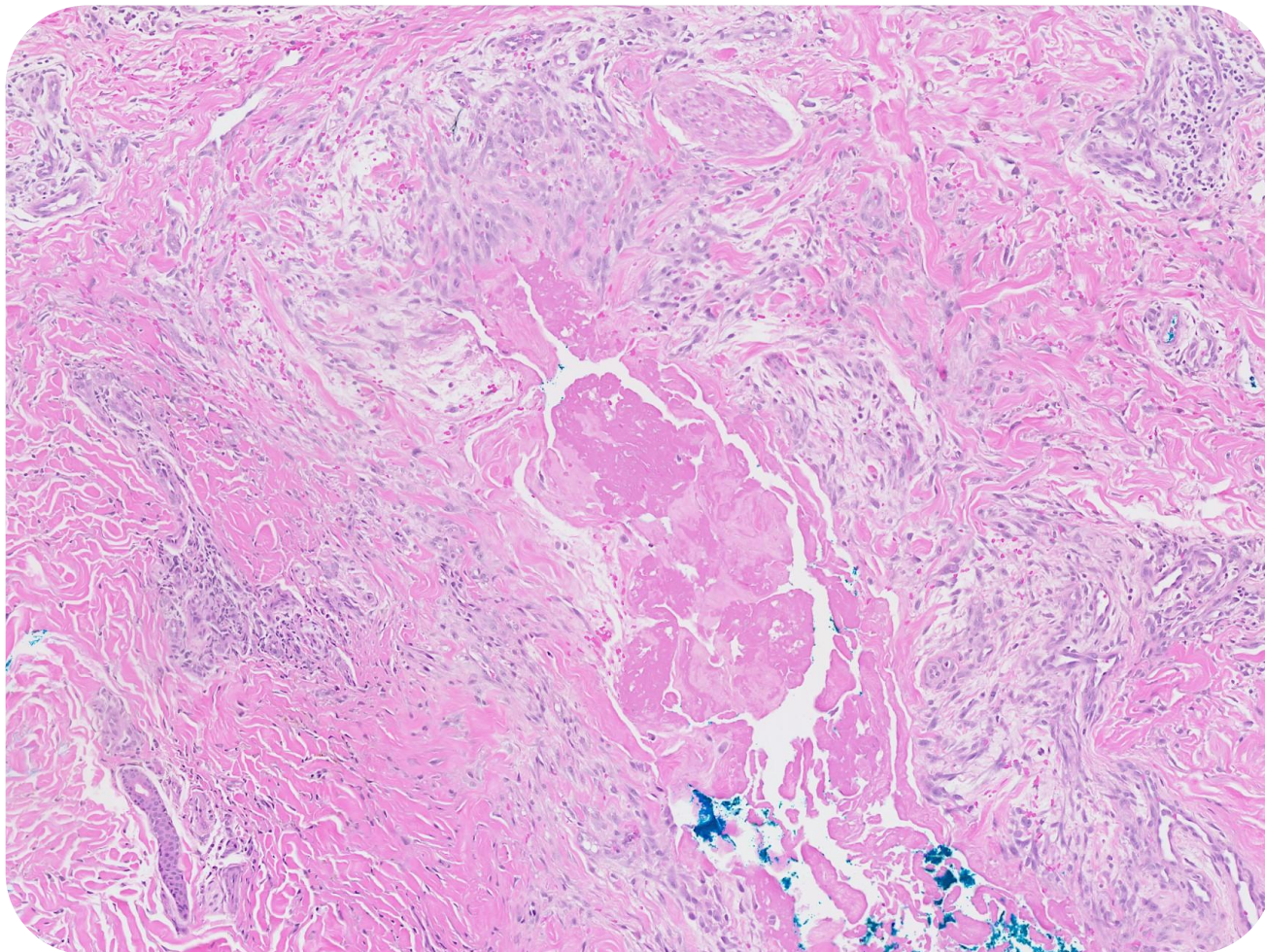
R



R



FOREIGN BODY GRANULOMATOUS PSEUDOCYST TO RETAINED EPICARDIAL PACING WIRE



TEMPORARY EPICARDIAL PACING WIRES

- Placement for various cardiac surgeries
- Typically removed within 5 days post-op
- If difficulty removing, common practice is to leave in place
 - Decreases risk of atrial/ventricular injury, dysrhythmias, cardiac tamponade, infection



TEMPORARY EPICARDIAL PACING WIRES

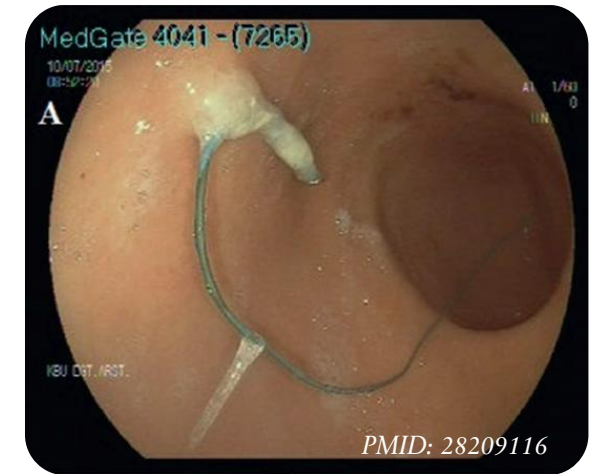
- Delayed complications (1 month – 24 years)

Mediastinal

- retroaortic abscess
- infectious endocarditis
- **sterno-bronchocutaneous fistula**
- pericardial hematoma
- endobronchial obstruction
- ventricular fibrillation

Extra-mediastinal

- dyspepsia (gastric)
- **breast abscess**
- **submental fistula**
- **abdominal dermal nodule**
- abdominal aortic aneurysm
- perforated colon



TEMPORARY EPICARDIAL PACING WIRES

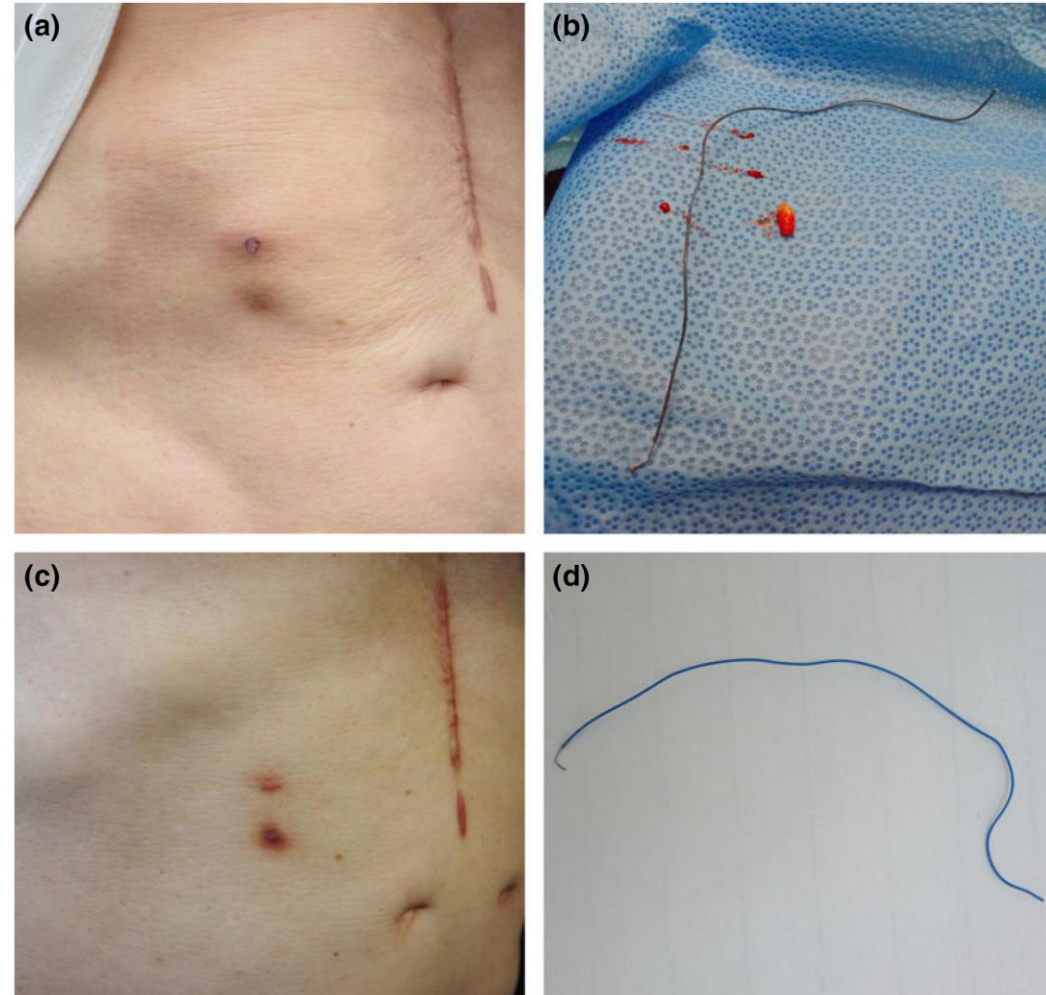
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Lee JW, Chung KY, Kim JY. Subsequent transepidermal migration of two temporary cardiac pacing wires. *J Dermatol.* 2018;45(2):237-238.

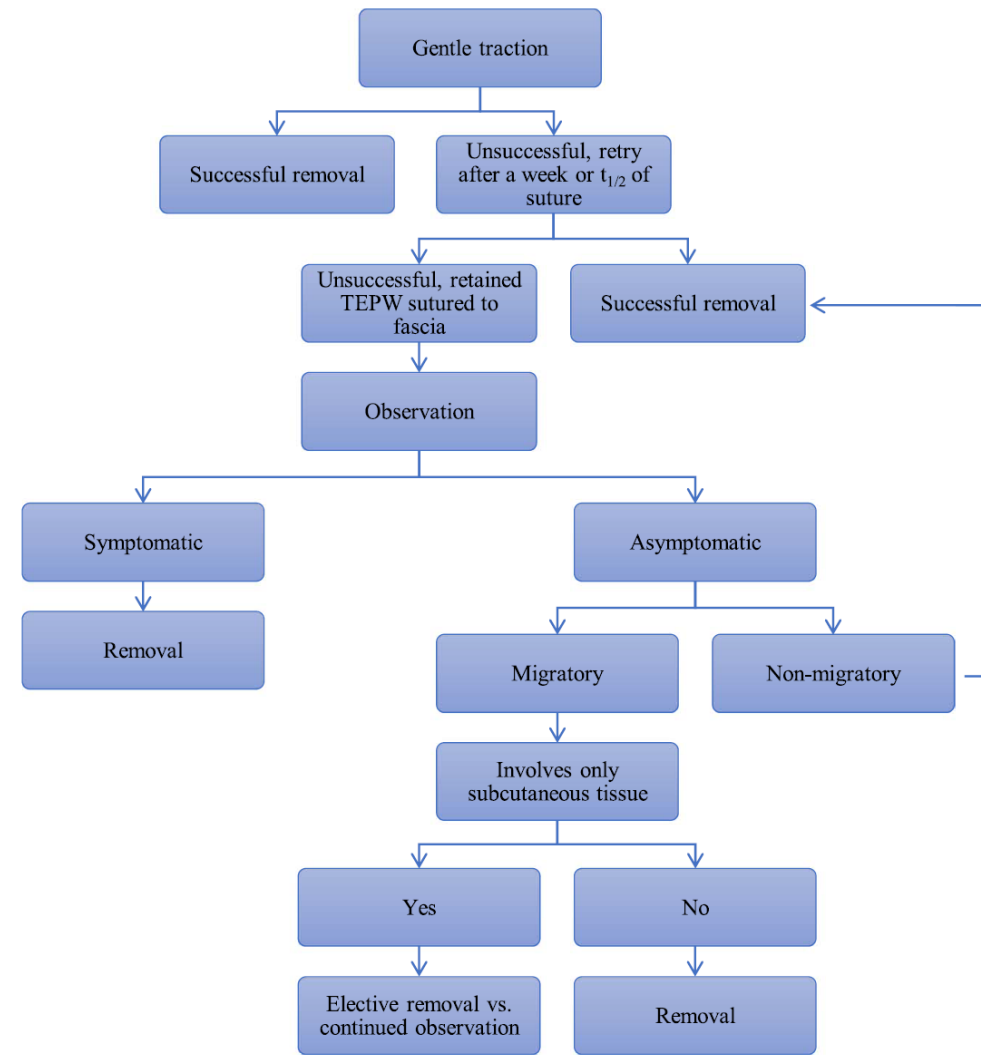
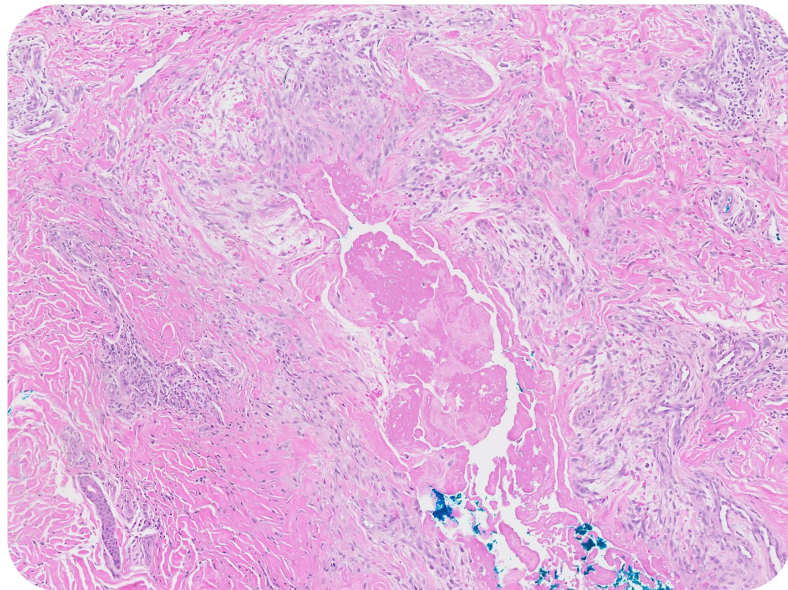
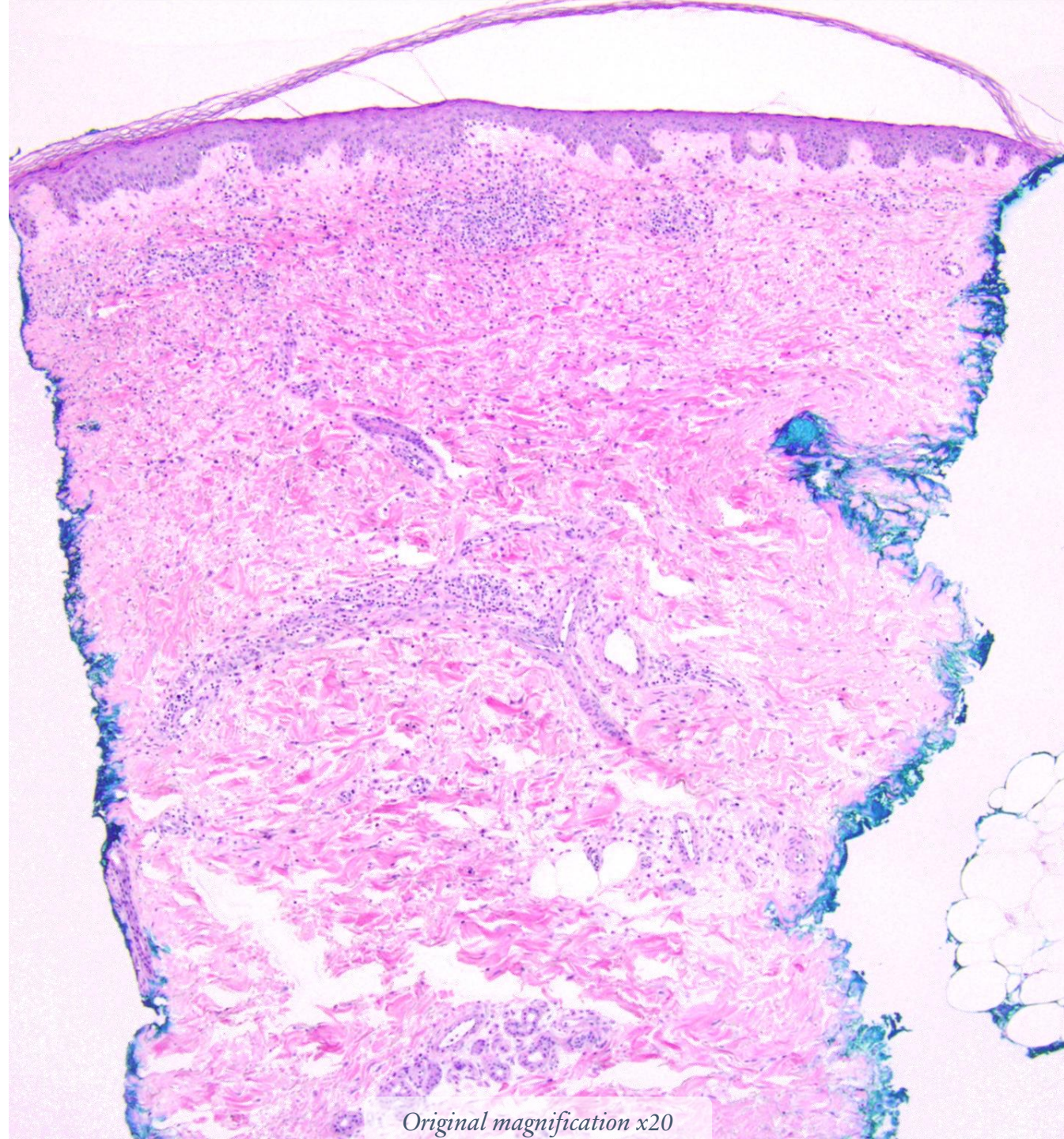


FIGURE 2. TEPW removal algorithm. full color online

A 75-year-old man with Crohn's disease on methotrexate presents with lower extremity ulcerations.

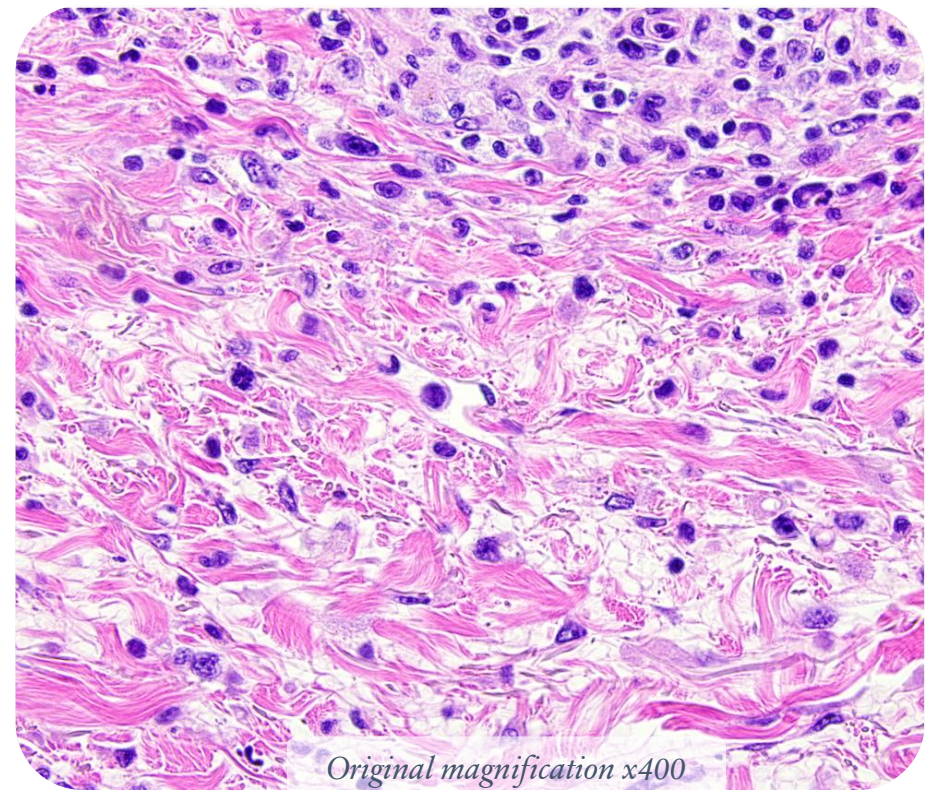
- PMH
 - Crohn's disease s/p ileocelectomy
 - macrocytic anemia
 - past osteomyelitis
 - past toe amputation
 - *atrial fibrillation, gout*
- Medications
 - **methotrexate** 25mg PO qweek
 - folic acid 1 mg PO daily
 - allopurinol, amlodipine, apixaban, dronedarone, furosemide, tamsulosin
 - **prednisone** 80 mg PO daily



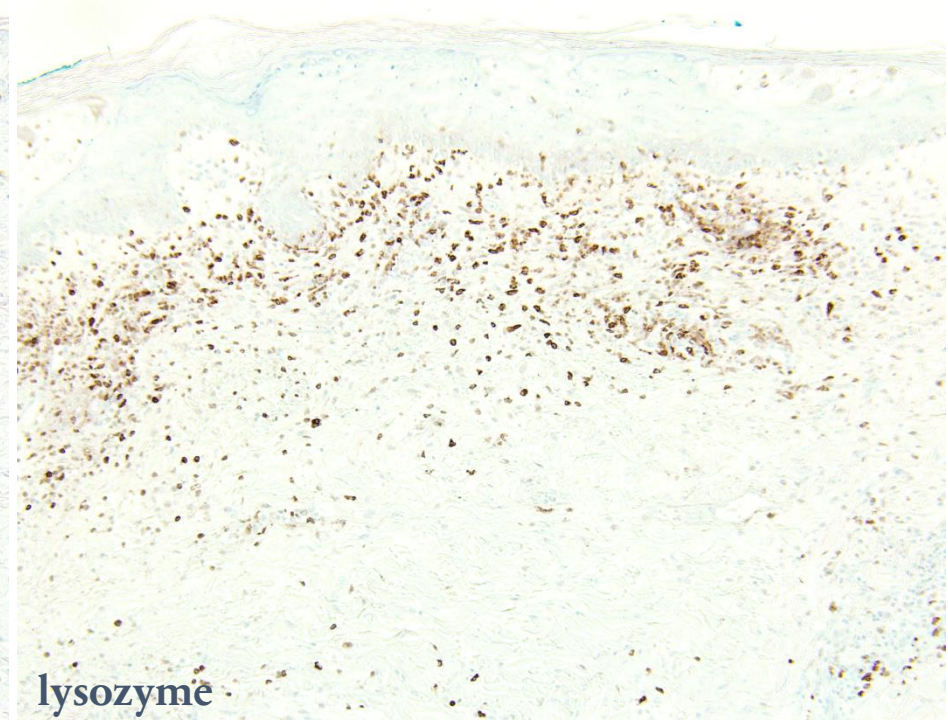
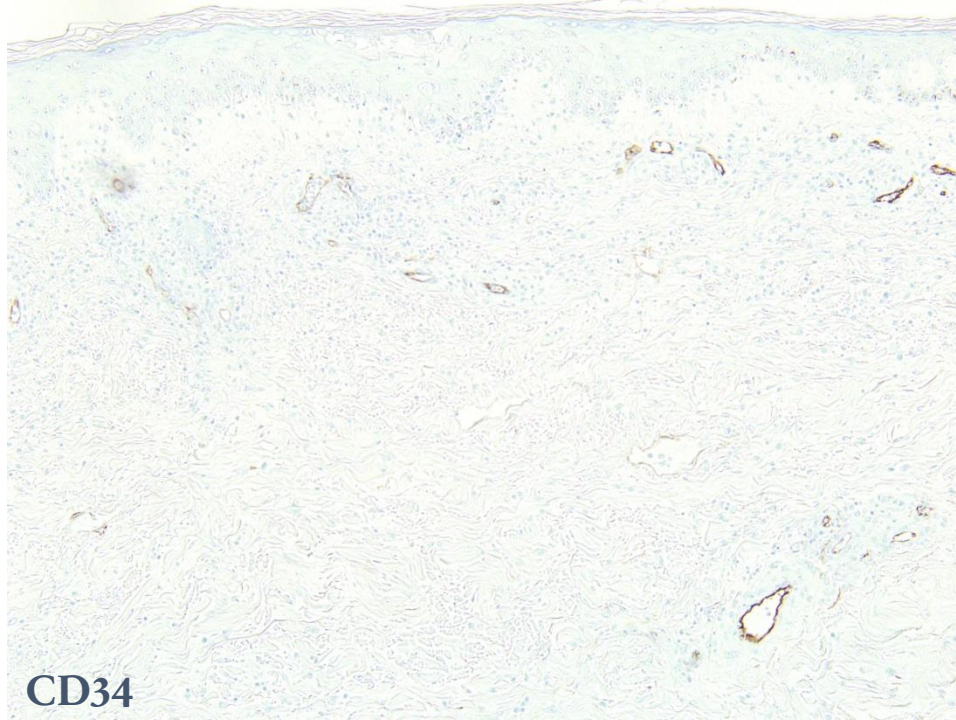
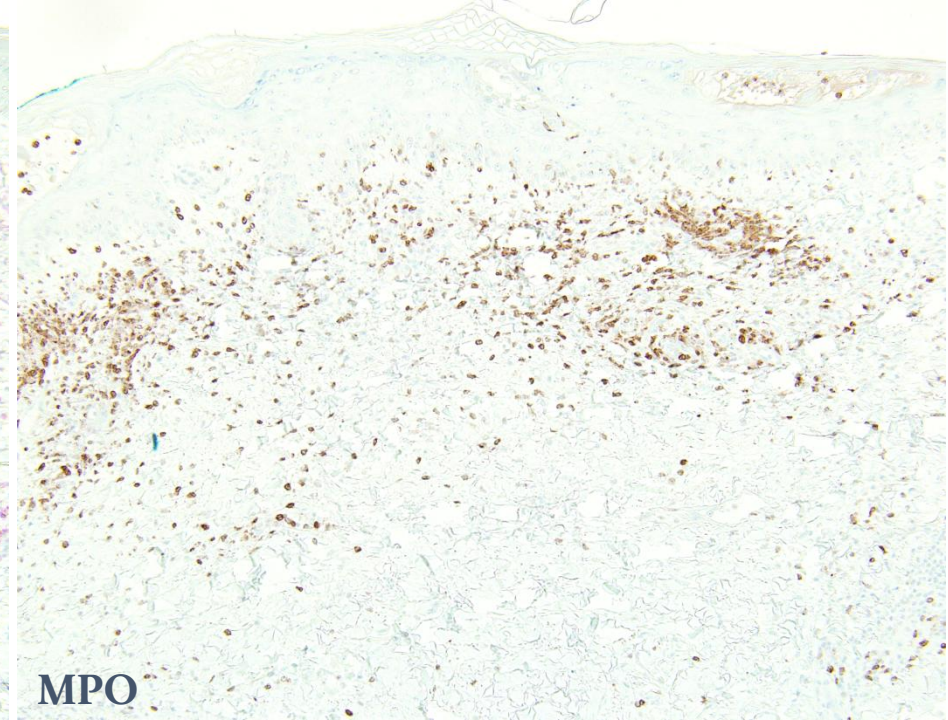
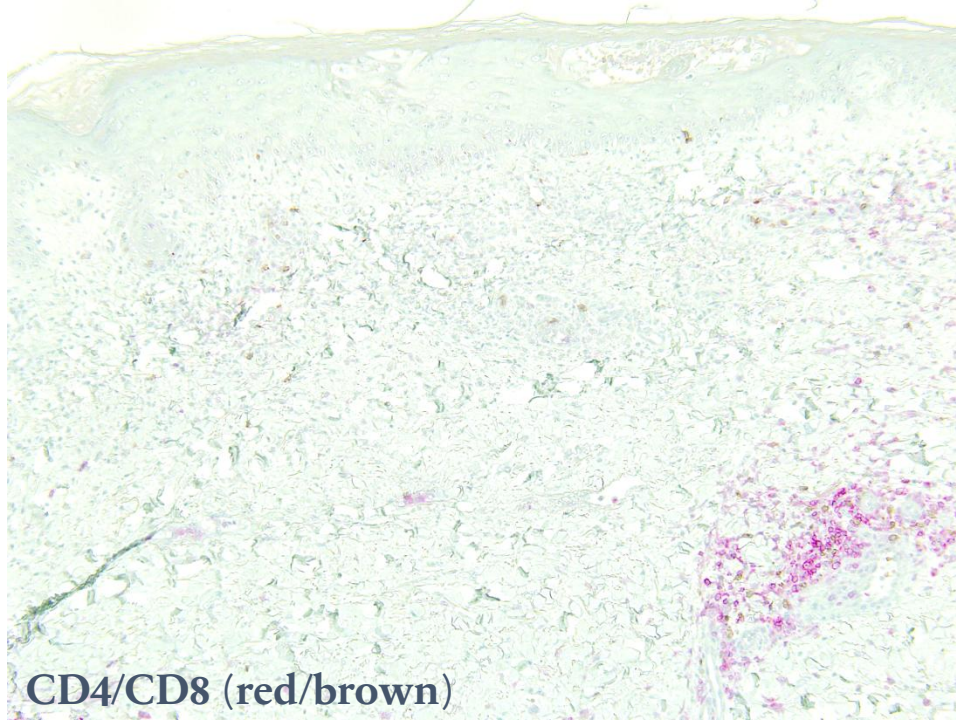
Original magnification x20



Original magnification x200

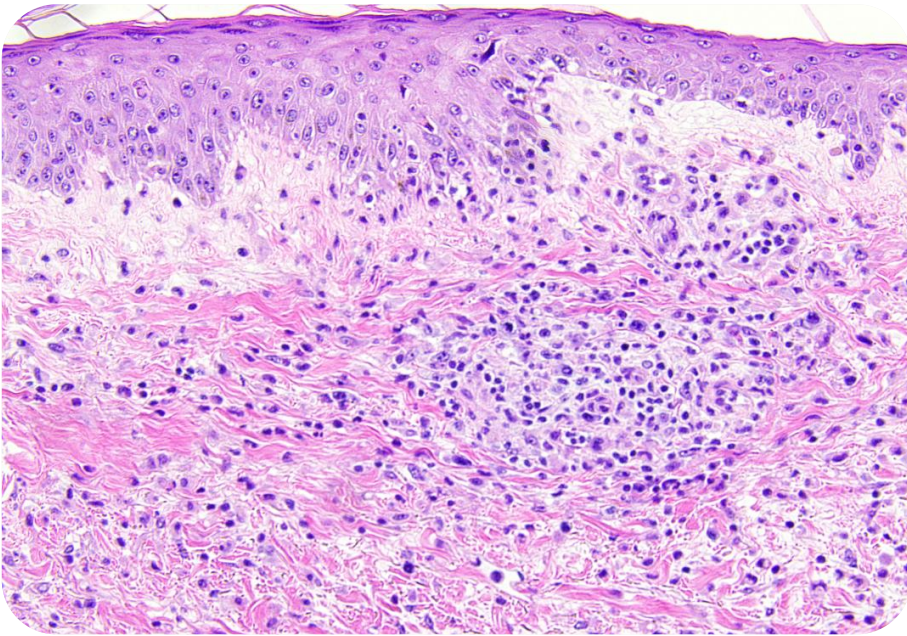


Original magnification x400



Negative:
CD20, CD30

A 75-year-old man with Crohn's disease on methotrexate presents with lower extremity ulcerations.

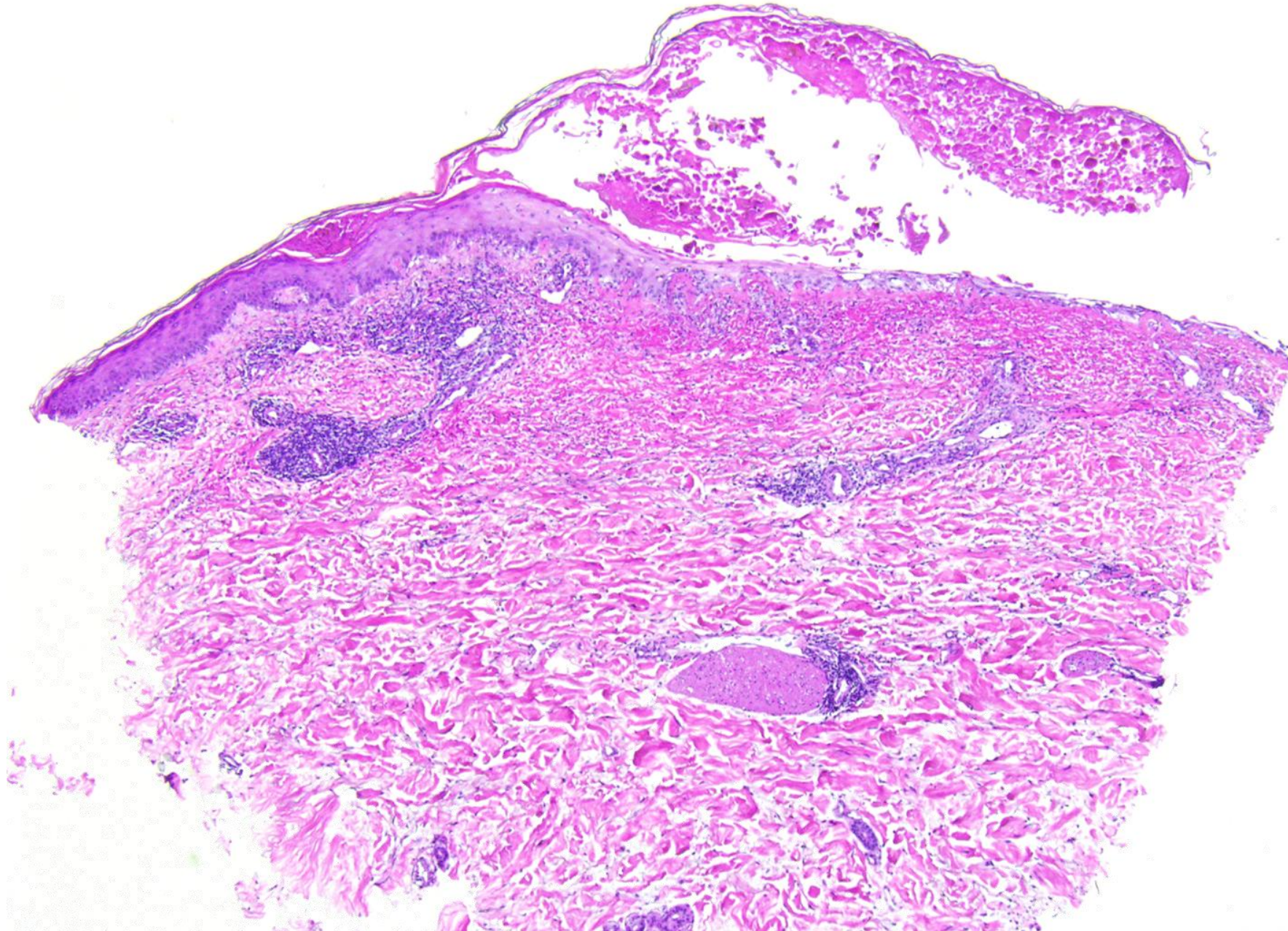


Atypical myeloid infiltrate

- **Clinical:**
 - dual immunosuppression
 - LLE ulcerations
 - macrocytic anemia
- **Skin biopsy:** atypical myeloid infiltrate
- **Assessment/Plan:**
 - rule out leukemia cutis
 - peripheral blood flow cytometry **No evidence of blasts**
 - bone marrow biopsy **Normal**

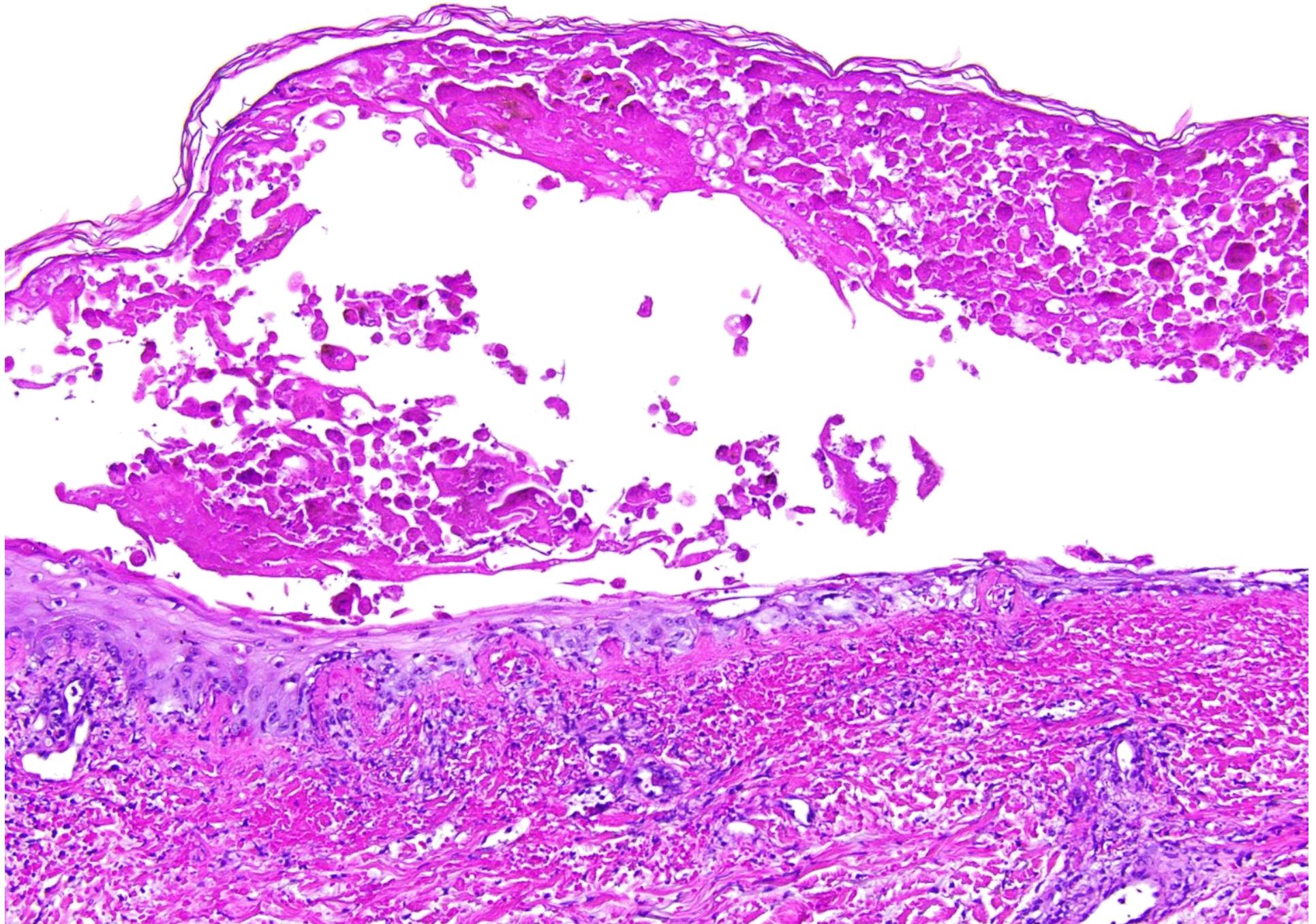


Punch biopsy #2



Original magnification x40

Punch biopsy #2

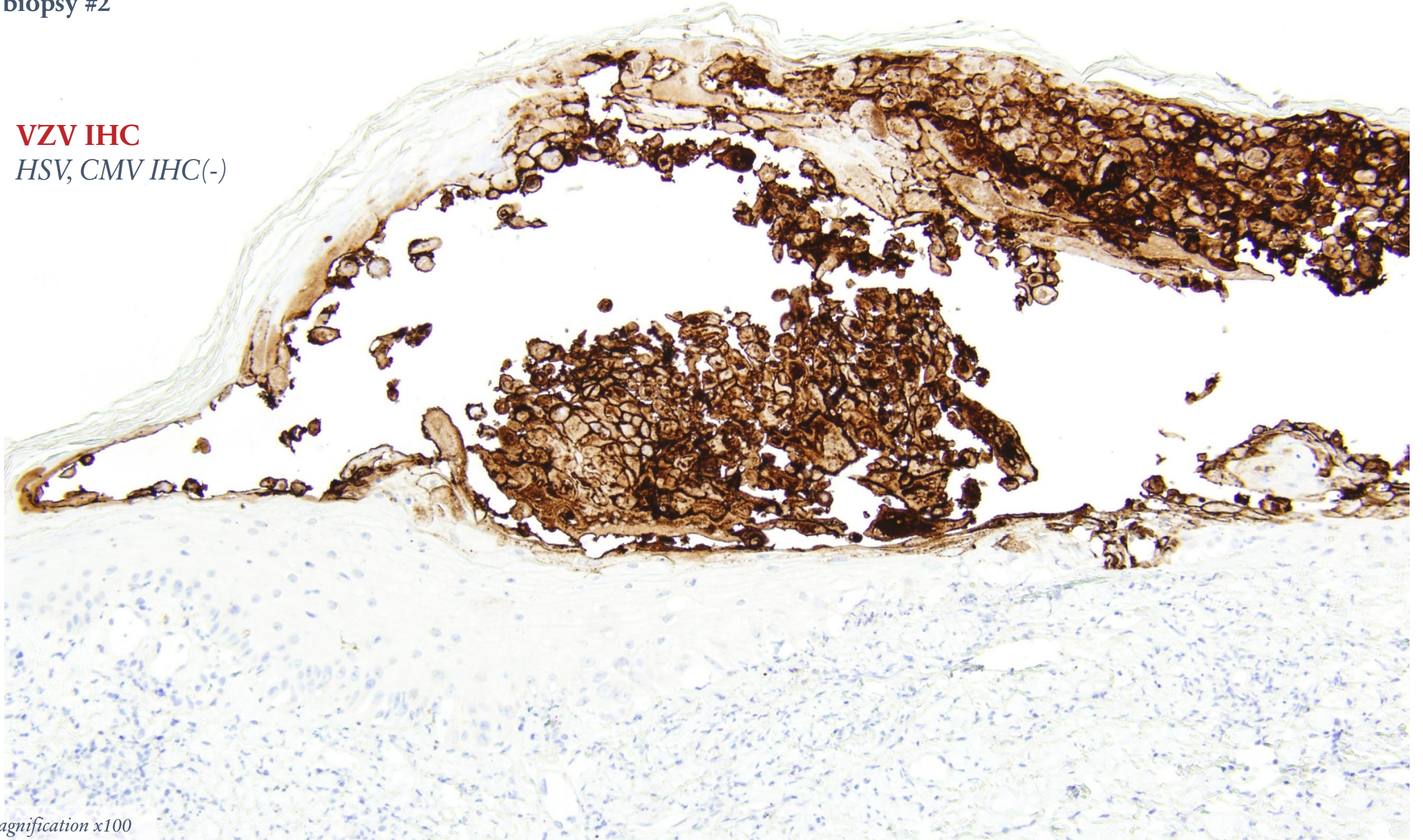


Original magnification x100

Punch biopsy #2

VZV IHC

HSV, CMV IHC(-)



Original magnification x100

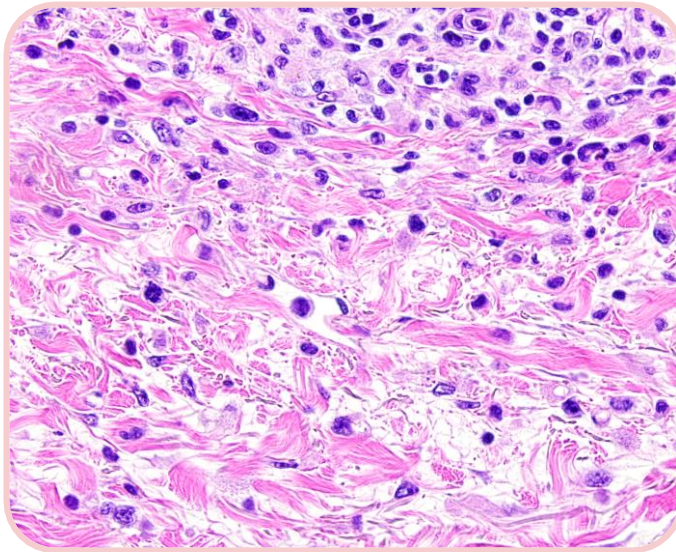


1 month
valacyclovir PO



In the setting of **dual immunosuppression** with methotrexate and other systemic agents **disseminated herpes zoster** may present as **lower extremity ulcers**.

Myeloproliferative disorders may arise in the setting of therapy for autoimmune disorders (including methotrexate for Crohn's disease).



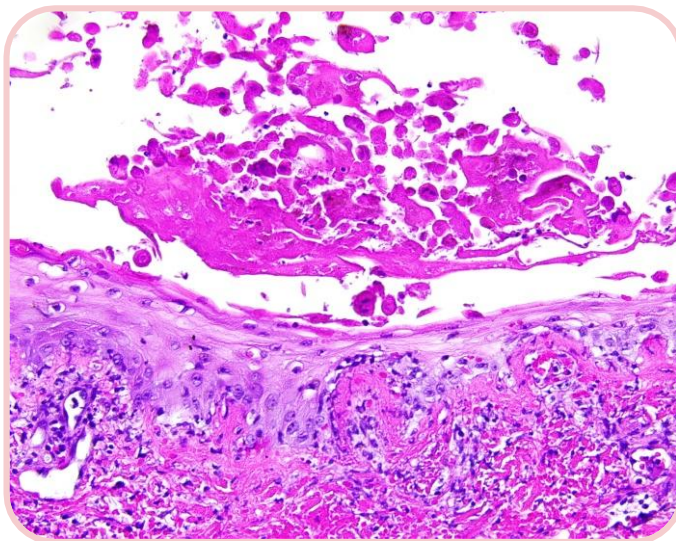
Herpesviridae histopathologic mimics

Inflammatory disorders

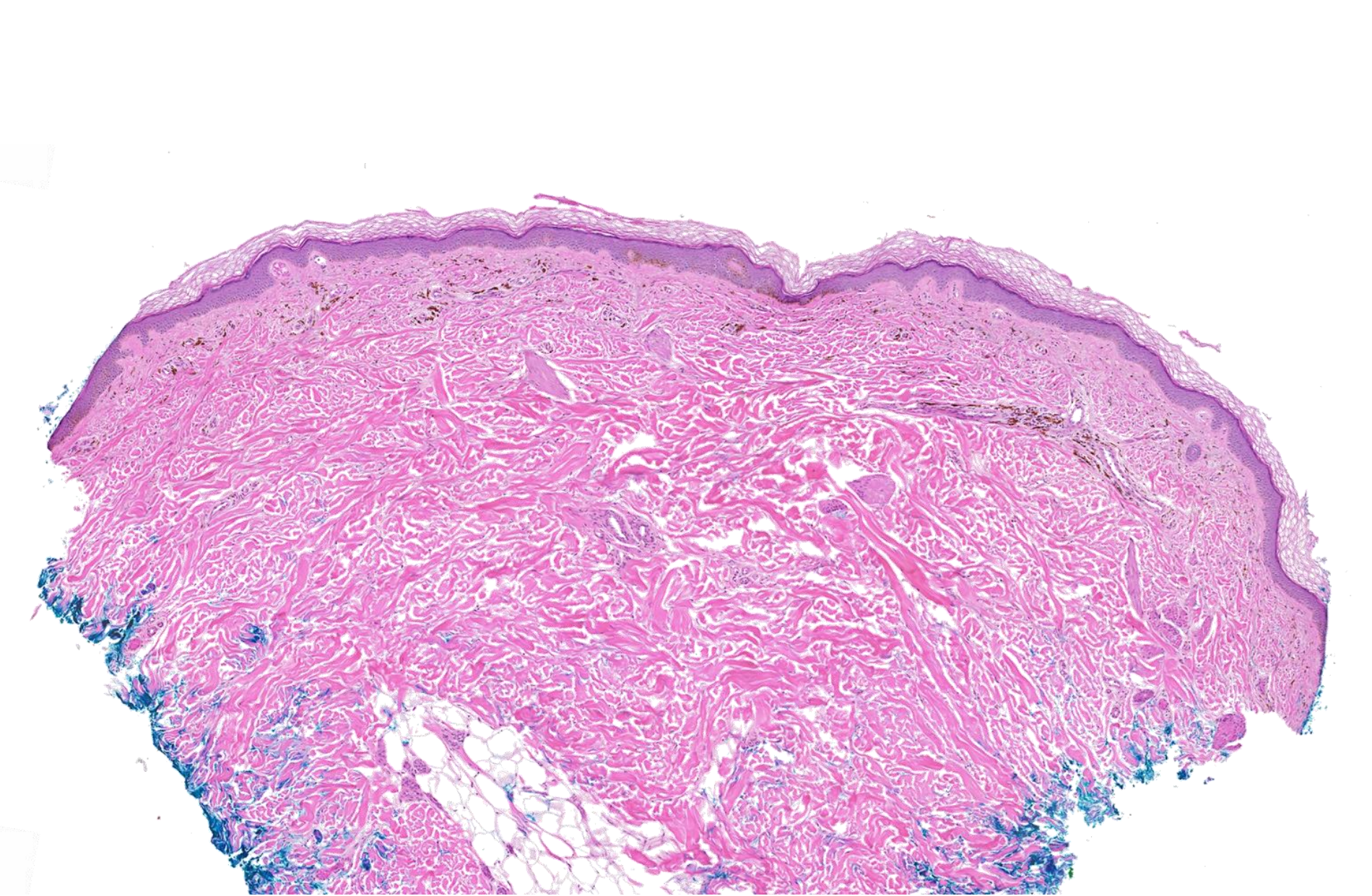
- Lupus erythematosus (HSV)
- Rosacea (HSV)
- Linear IgA bullous dermatosis (VZV)

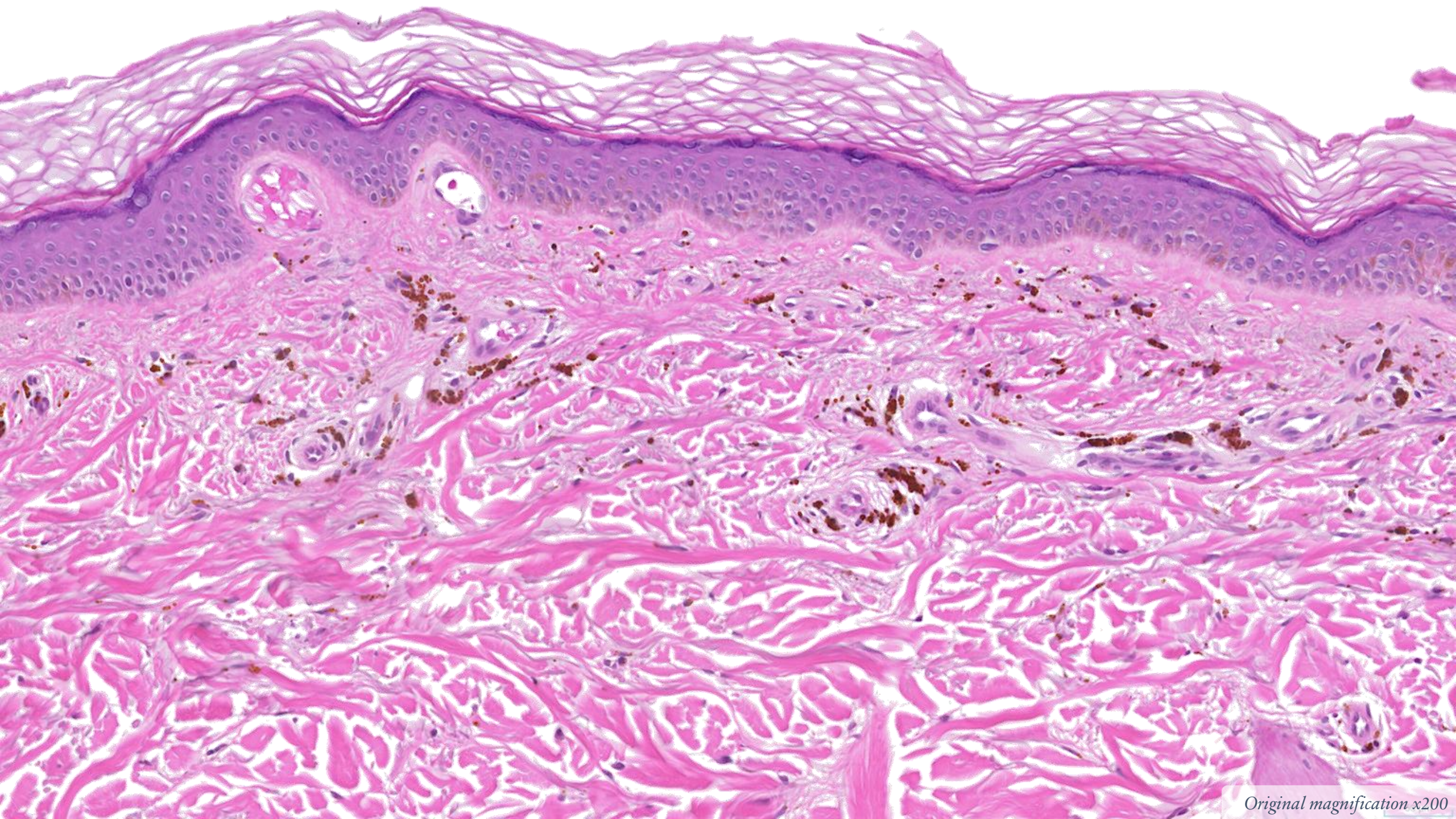
Lymphoproliferative disorders & hematologic malignancy

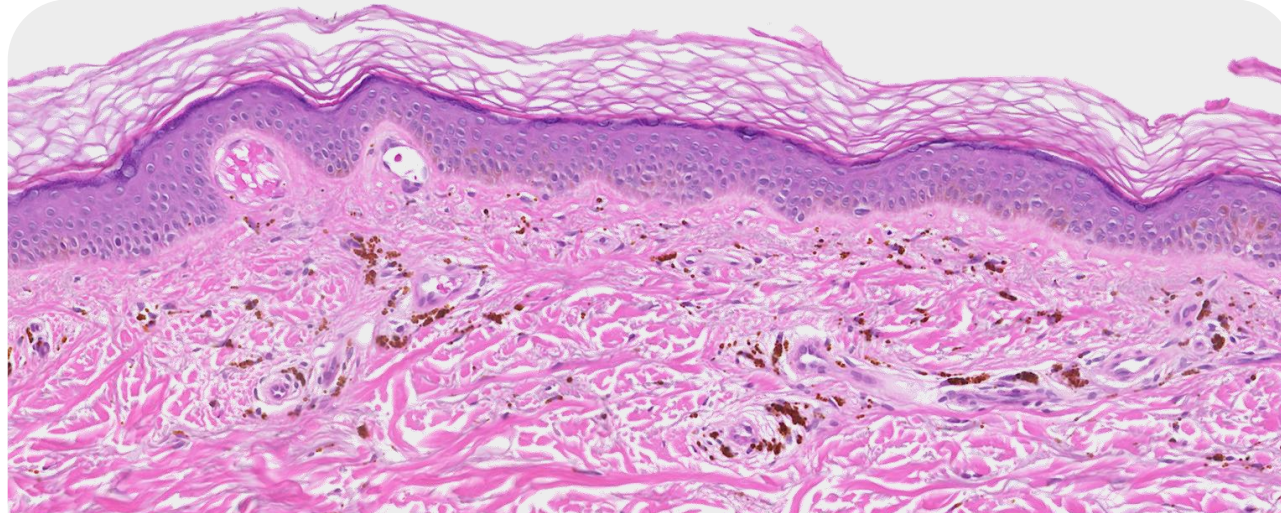
- Lymphomatoid papulosis (VZV)
- B-cell lymphoma (HSV)
- NK-T-cell lymphoma (HSV)
- Plasmacytoma (HSV)
- Lymphocytic leukemia cutis (HSV)
- *Myeloid leukemia cutis (VZV)**











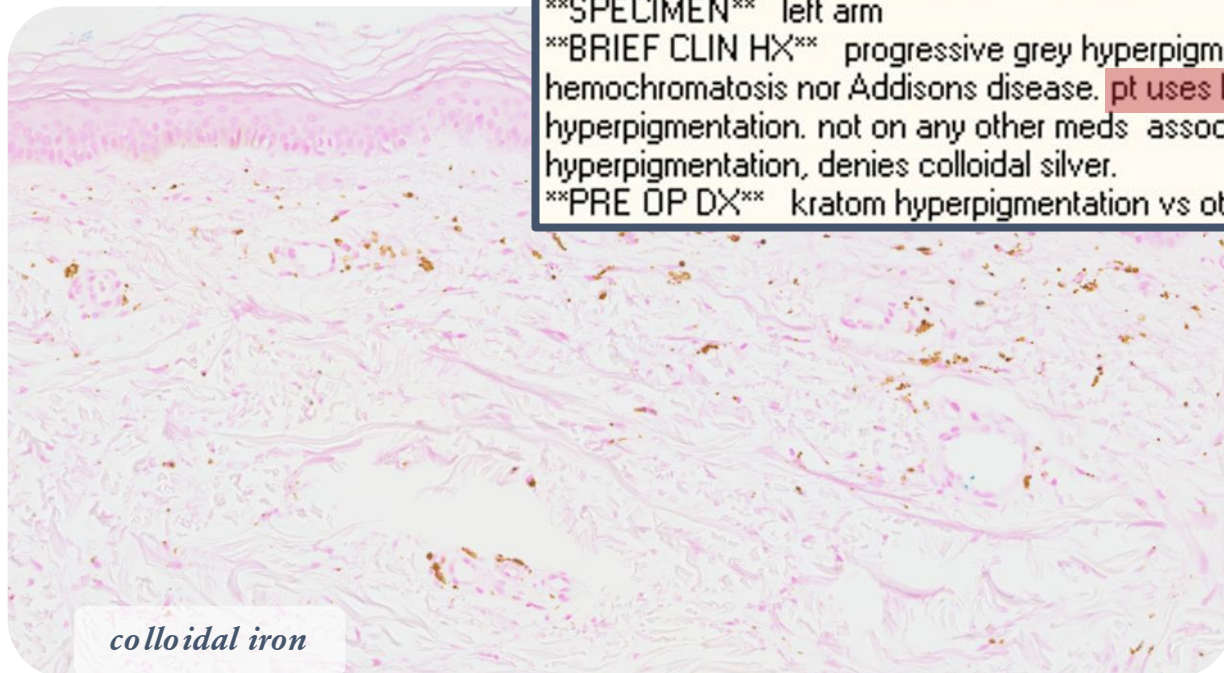
>> TISSUE EXAM (SF-515) - DERMATOLOGY
 PRINT THIS ORDER AND SEND WITH SPECIMEN

SUBMITTED BY Laurel Cummings, MD

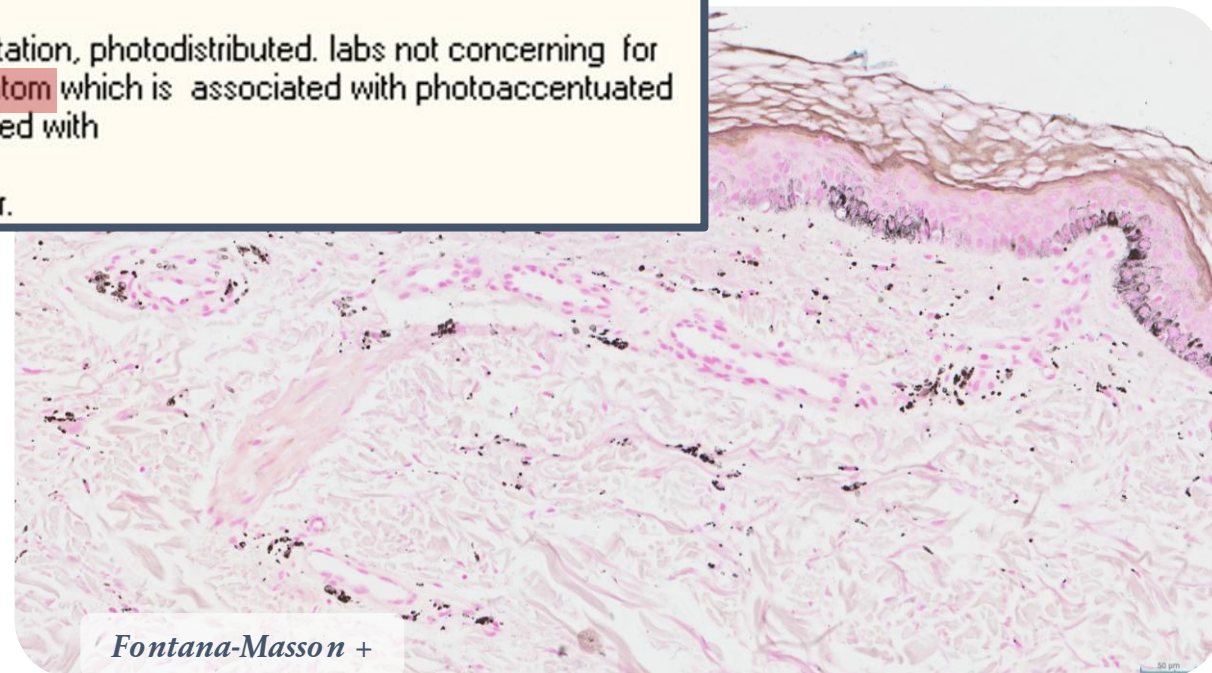
SPECIMEN left arm

BRIEF CLIN HX progressive grey hyperpigmentation, photodistributed. labs not concerning for hemochromatosis nor Addisons disease. **pt uses kratom** which is associated with photoaccentuated hyperpigmentation. not on any other meds associated with hyperpigmentation, denies colloidal silver.

PRE OP DX kratom hyperpigmentation vs other.



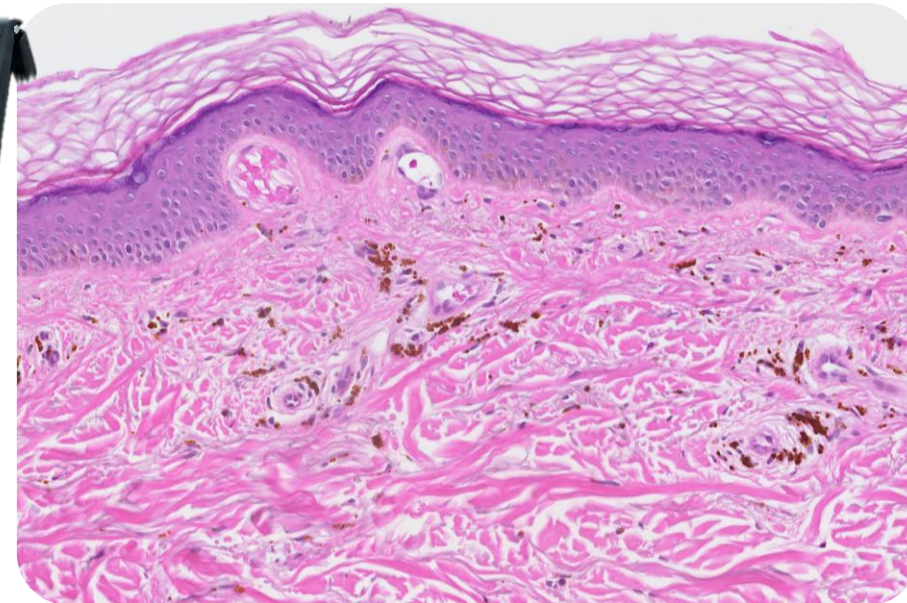
colloidal iron



Fontana-Masson +

KRATOM HYPERPIGMENTATION

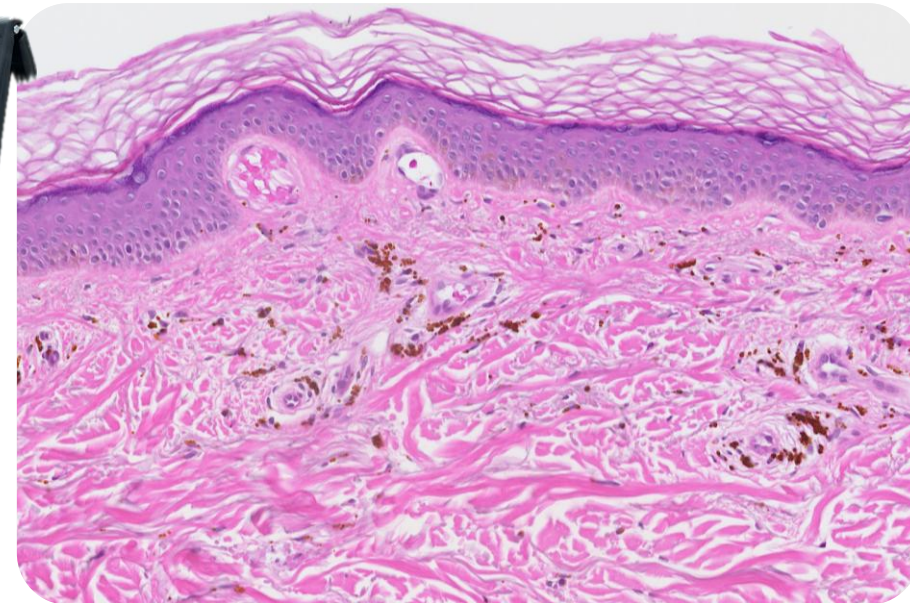
- Tropical evergreen (*Mitragyna speciosa*), Rubiaceae family
- **FDA:** kratom is not lawfully marketed in the U.S. as a drug product, a dietary supplement, or a food additive in conventional food.
- Opioid-like (high dose) & stimulant-like (low dose)
 - alkaloids: mitragynine, 7-OH-hydroxymitragynine



KRATOM HYPERPIGMENTATION

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Hyperpigmentation: alkaloids may stimulate melanocyte activity via mu-opioid receptor agonism; mitragynine antagonism of pituitary dopamine D2 receptors → increased alpha-melanocyte stimulating hormone

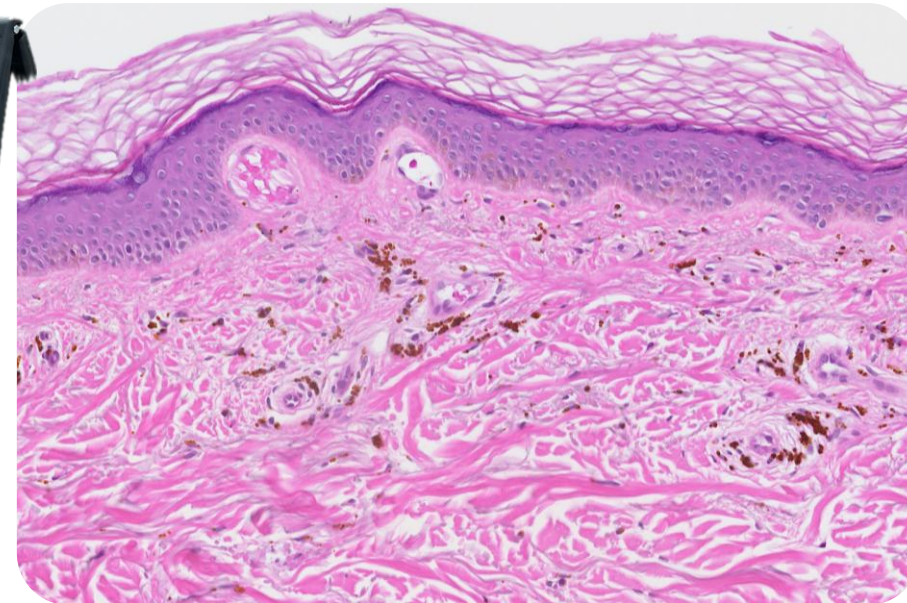


KRATOM HYPERPIGMENTATION

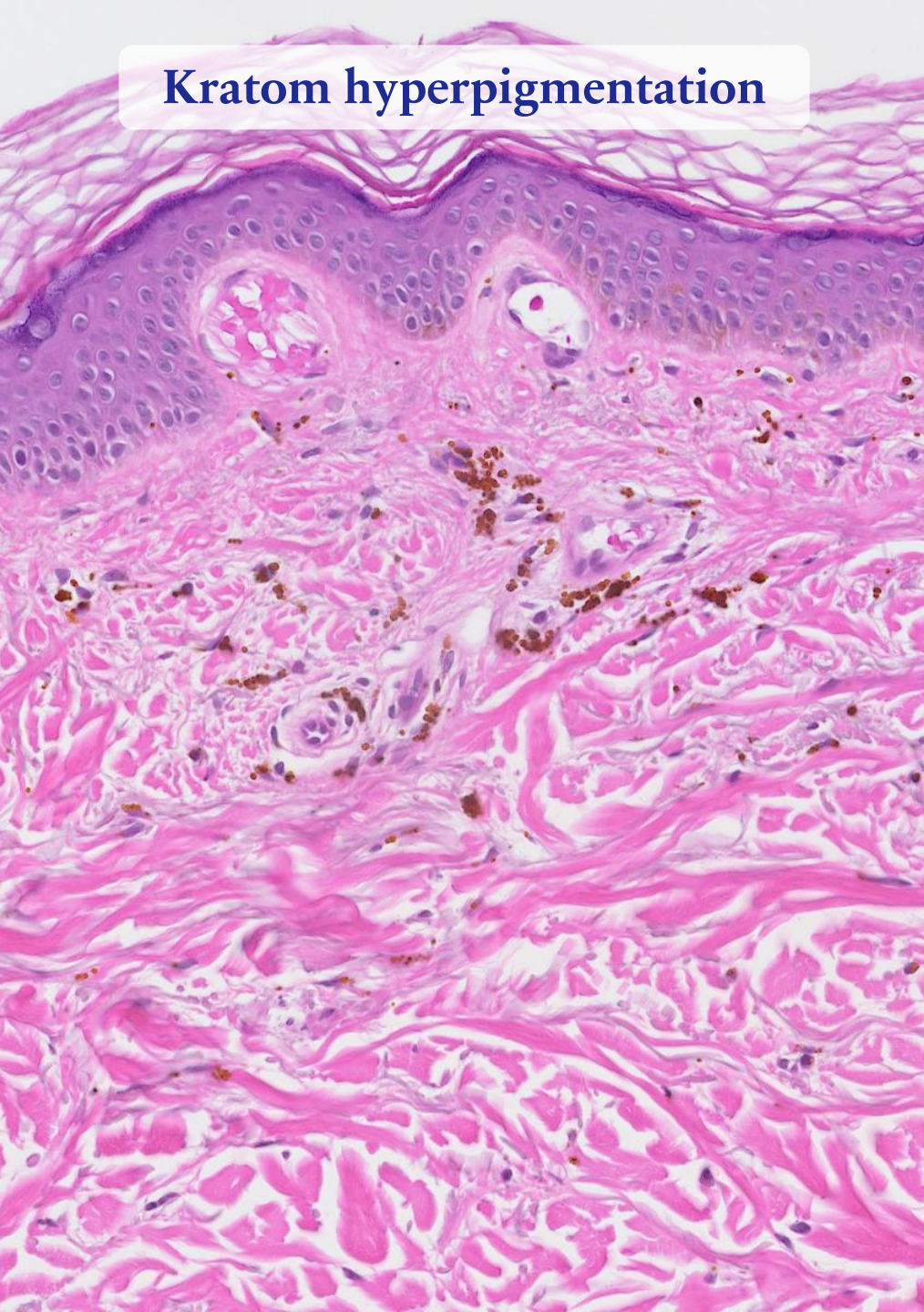
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- **FDA:** *kratom is not lawfully marketed in the U.S. as a drug product, a dietary supplement, or a food additive in conventional food.*
- Opioid-like (high dose) & stimulant-like (low dose)

Other adverse effects: kratom use disorder, tachycardia, nausea/vomiting, lethargy, confusion, psychosis, HTN, dyspnea, hepatic injury, rhabdomyolysis, renal failure, anorexia, insomnia, hair loss, tremor, constipation, temporary erectile dysfunction, hypothyroidism, seizures, **death**

Misbranding, adulteration, heavy metal contamination, bacterial contamination (*Salmonella*)

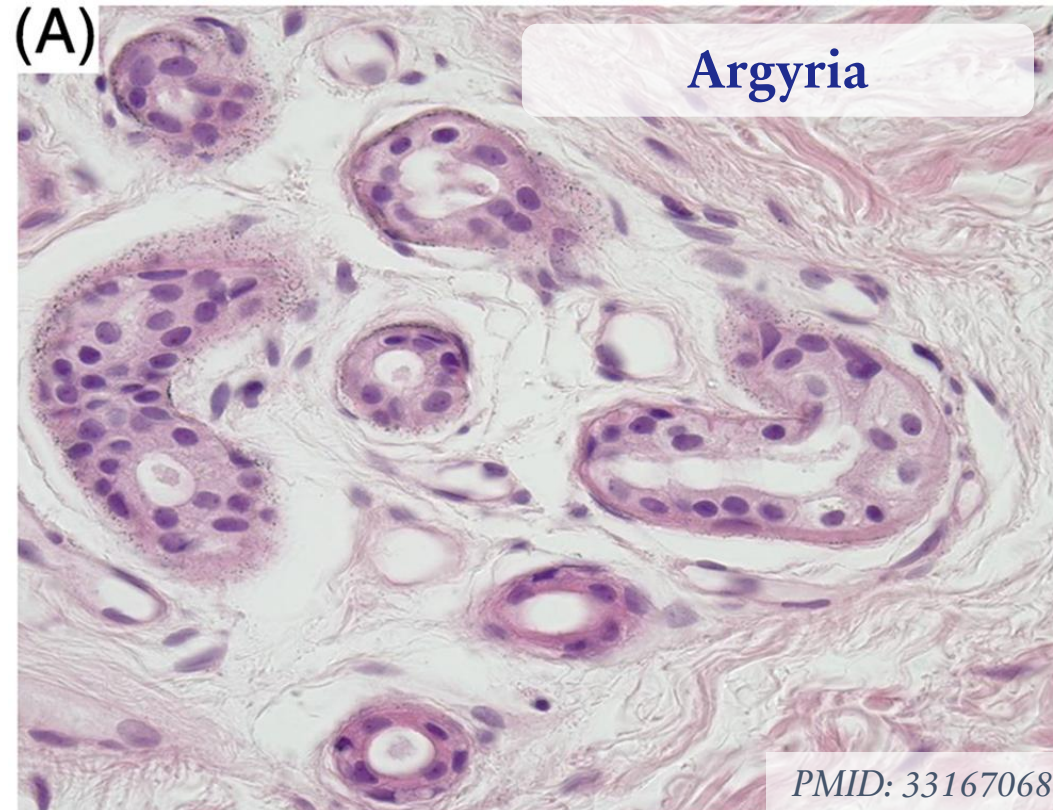


Kratom hyperpigmentation



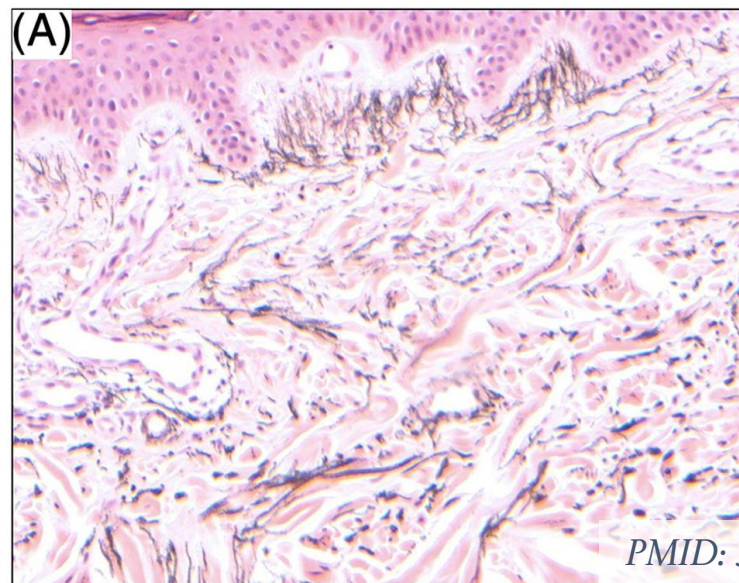
(A)

Argyria

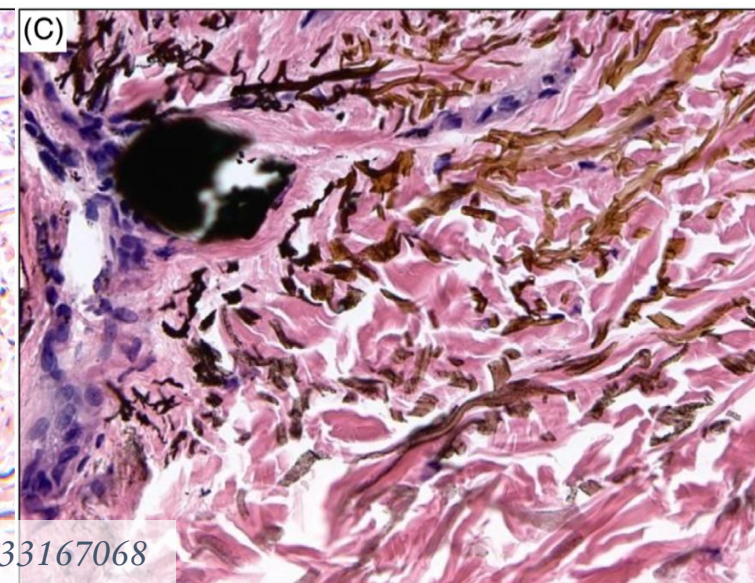


PMID: 33167068

(A)

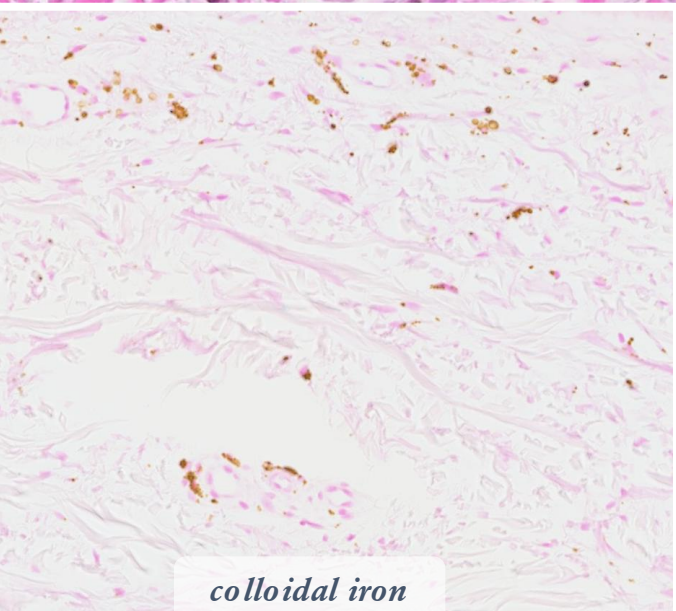


(C)



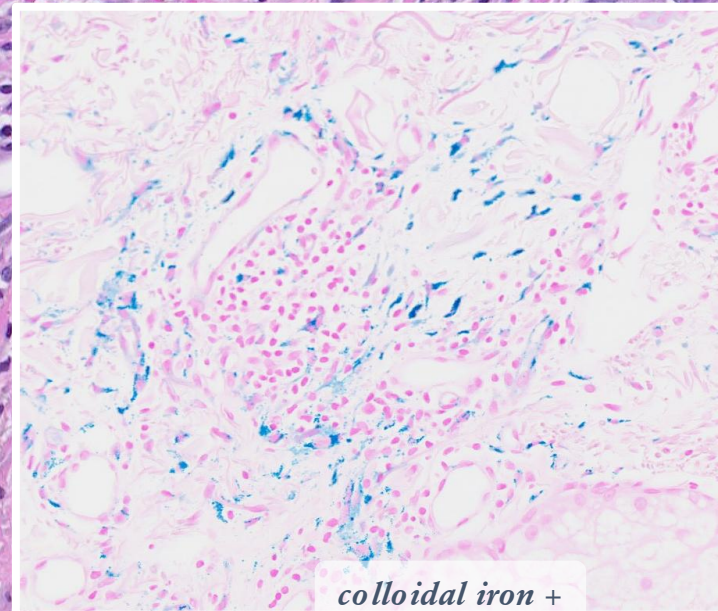
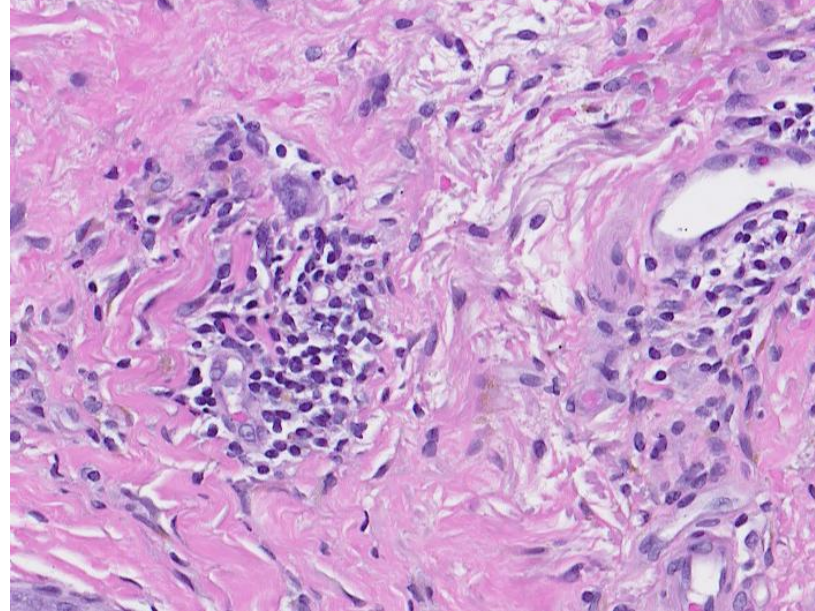
PMID: 33167068

Kratom hyperpigmentation



colloidal iron

Minocycline hyperpigmentation

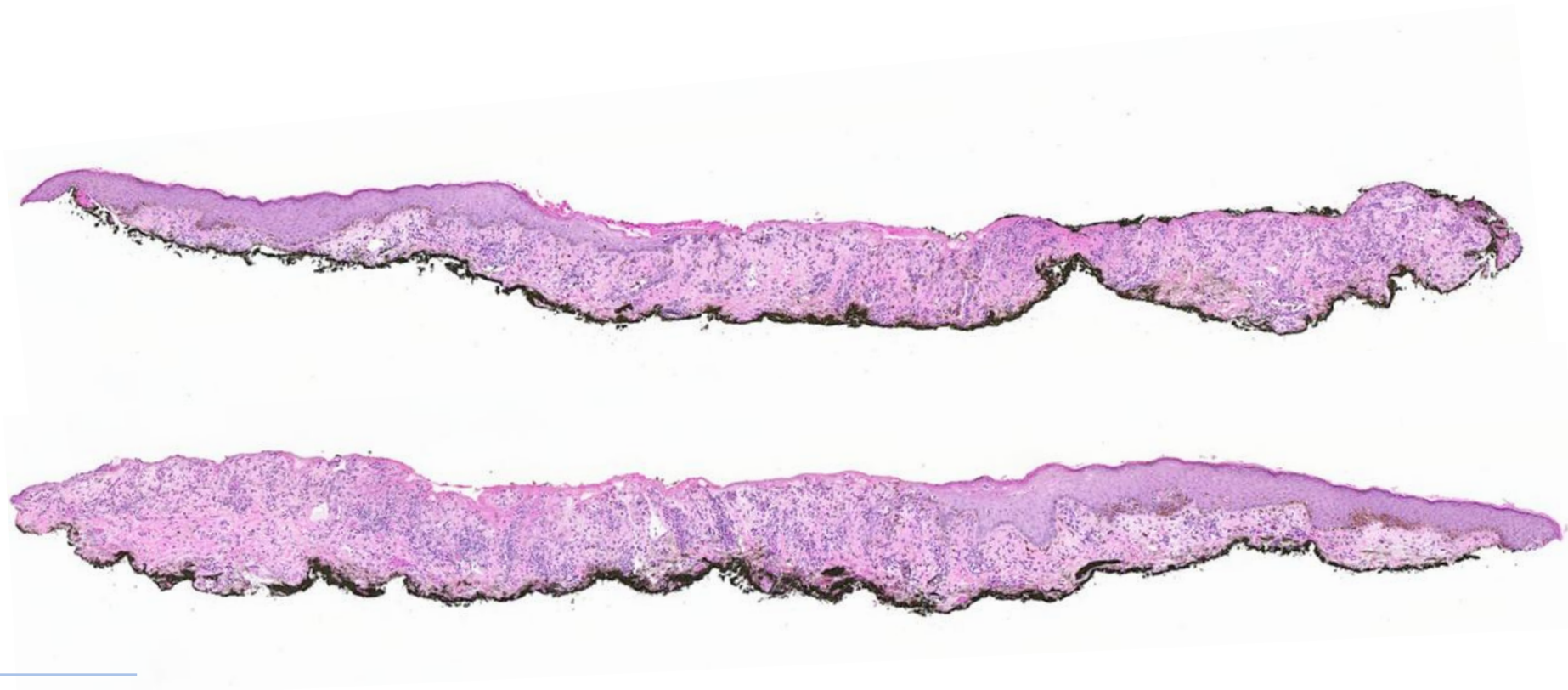


colloidal iron +

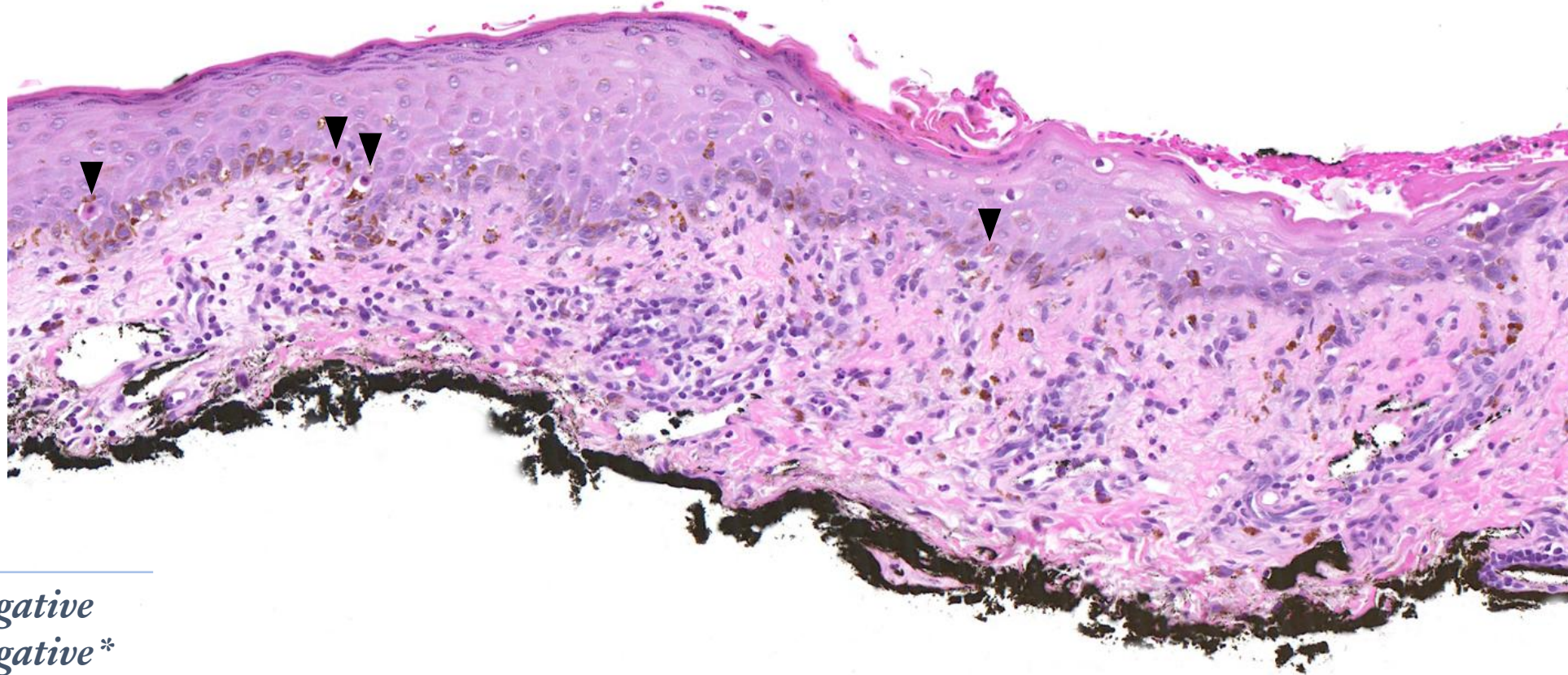
80-year-old man with diabetes, ETOH associated pancreatic insufficiency, and recent UTI presented with malaise, fever, non-productive cough, and ulcerative mucositis.



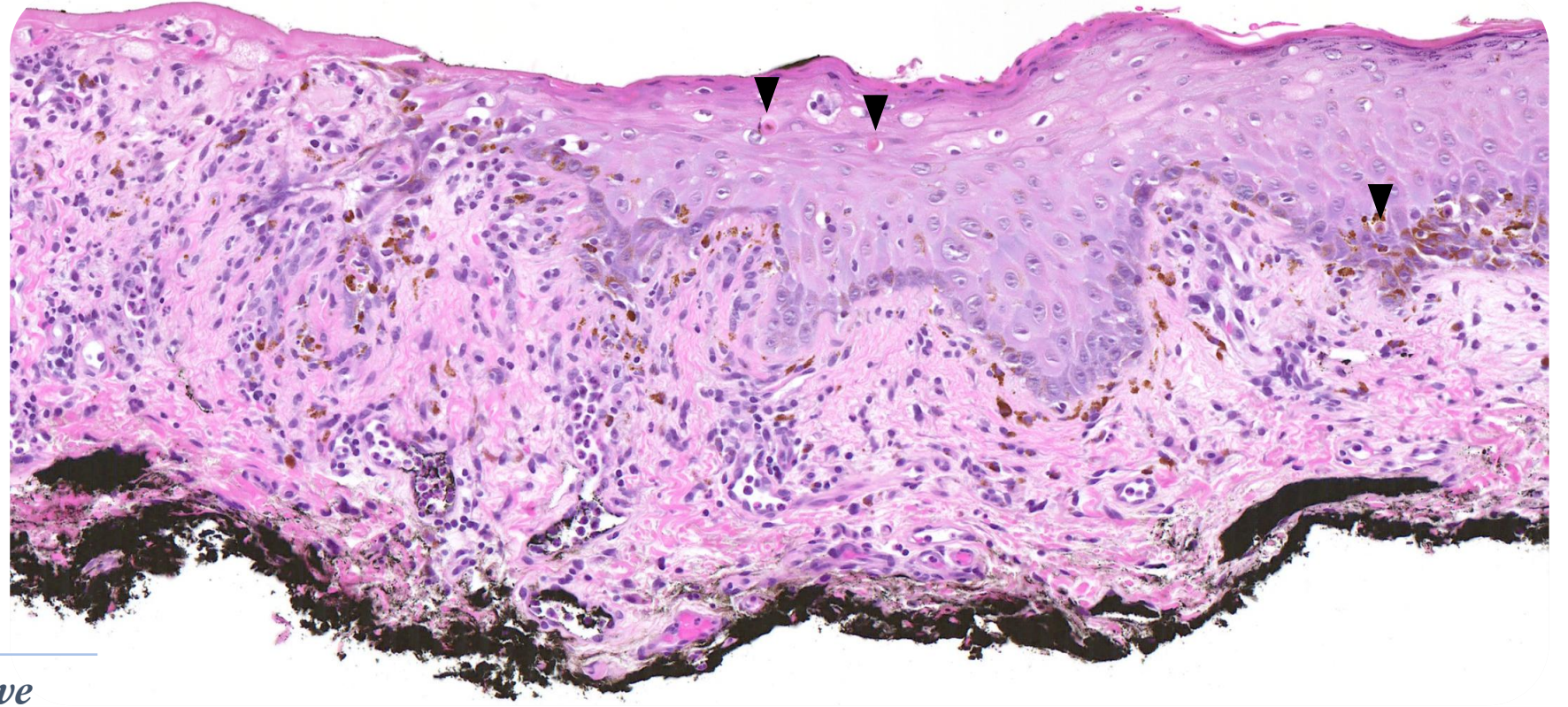
- 2 days prior to admission, completed 7-day course of trimethoprim/sulfamethoxazole (TMP/SMX) PO
- Oral mucositis noted on last day of PO ABX
- CT chest on admit demonstrated bibasilar peribronchial wall thickening, pulmonary atelectasis, and consolidations
- IV ceftriaxone/azithromycin initiated for community acquired PNA vs. aspiration PNA



Bacterial swab cx	<i>negative</i>
Fungal swab cx	<i>negative*</i>
VZV, HSV PCR swab	<i>negative</i>
Respiratory panel	<i>negative</i>
Blood cx	<i>negative</i>



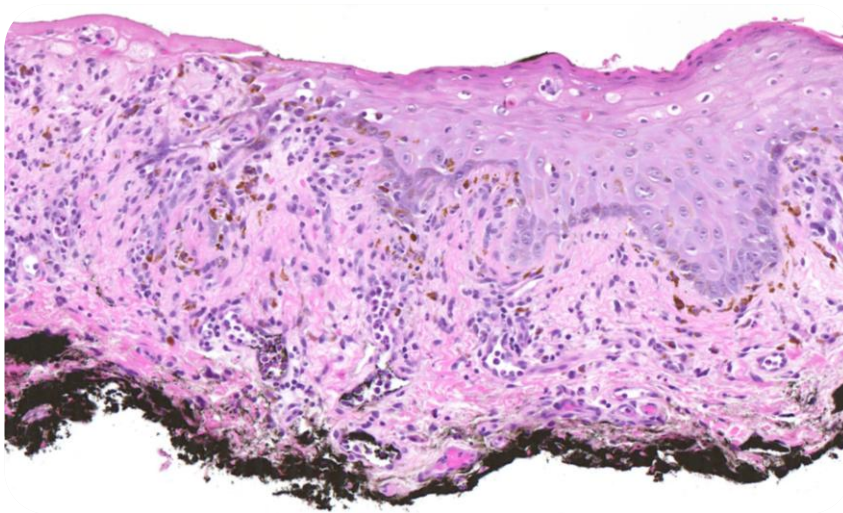
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<i>Bacterial swab cx</i>	<i>negative</i>
<i>Fungal swab cx</i>	<i>negative*</i>
<i>VZV, HSV PCR swab</i>	<i>negative</i>
<i>Respiratory panel</i>	<i>negative</i>
<i>Blood cx</i>	<i>negative</i>

Ulcerative lichenoid mucositis

FDE | OLDE | EM | RIME | PNP

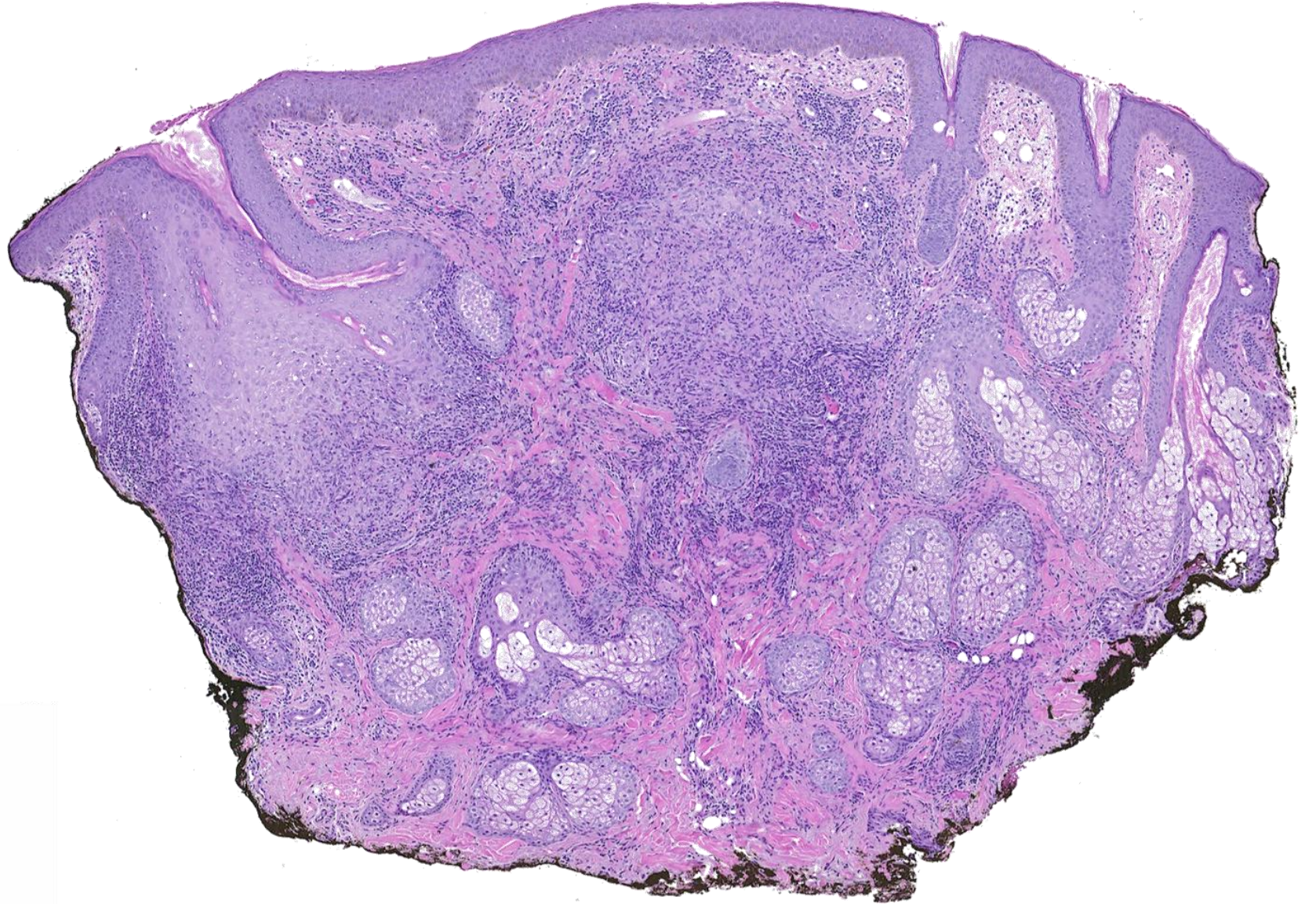


1 week

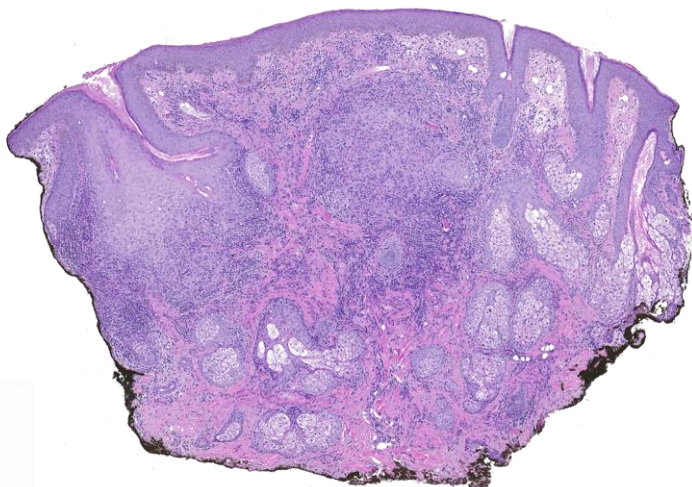


tacrolimus 0.1% ointment
mupirocin 2% ointment
clotrimazole troche
chlorhexidine gluconate 0.12% oral rinse

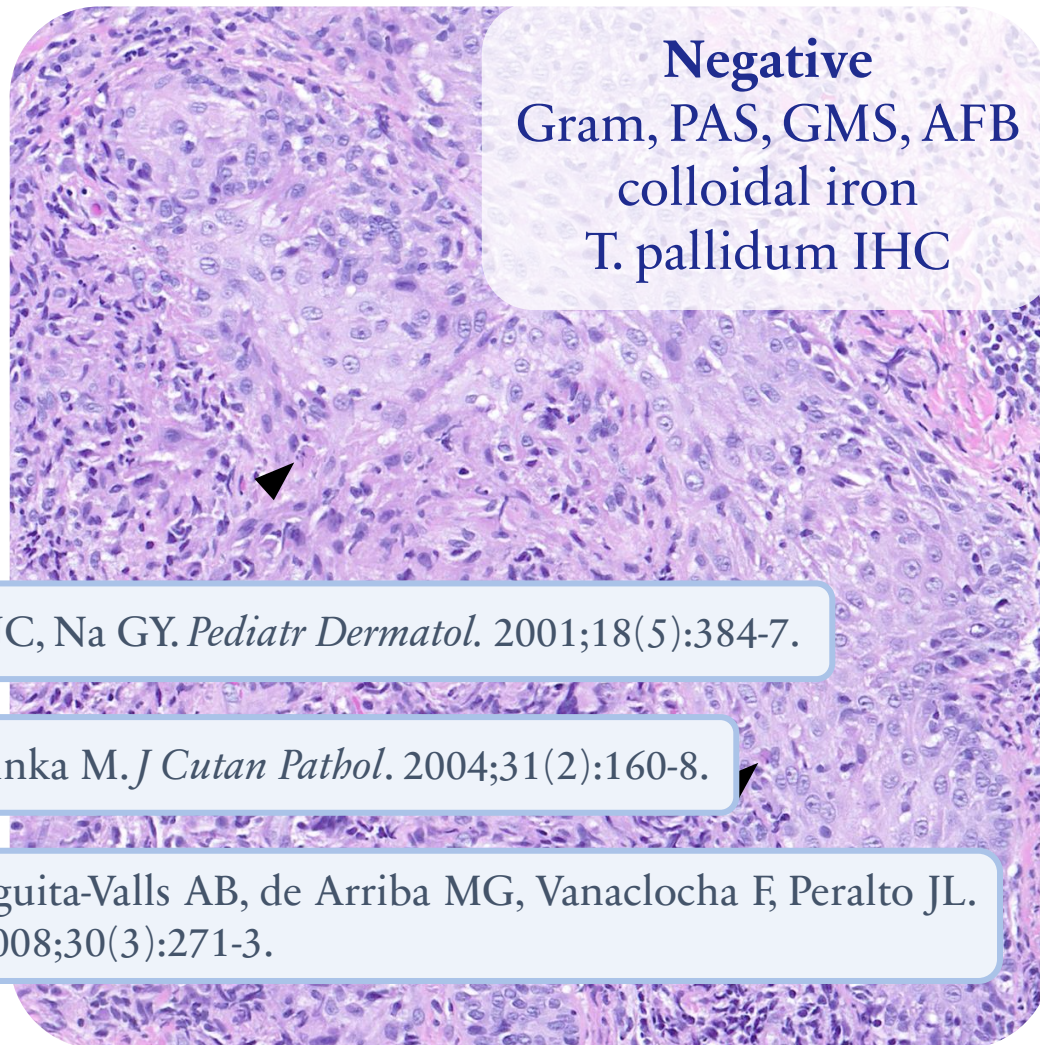




LICHENOID SARCOIDOSIS*



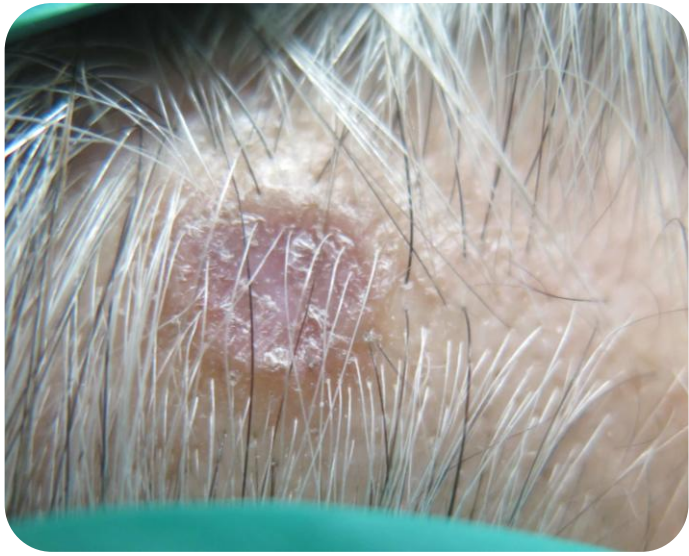
Negative
Gram, PAS, GMS, AFB
colloidal iron
T. pallidum IHC



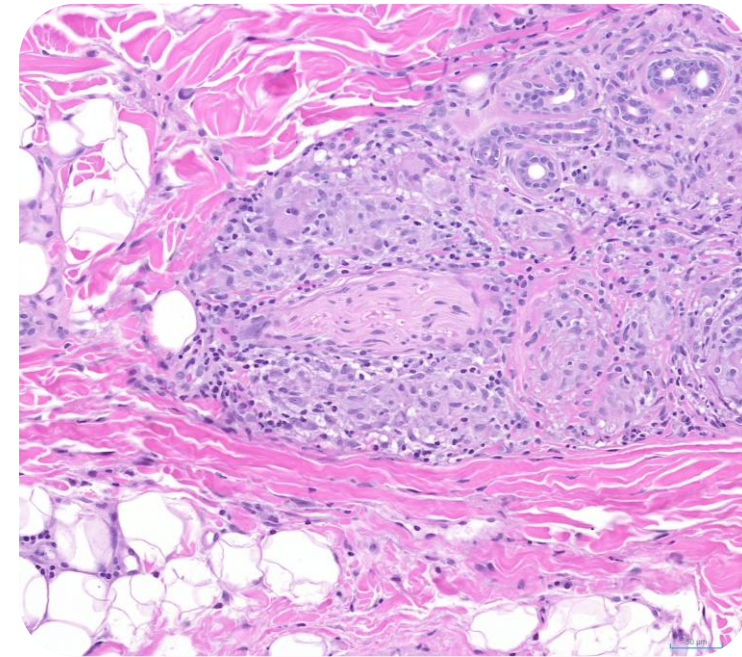
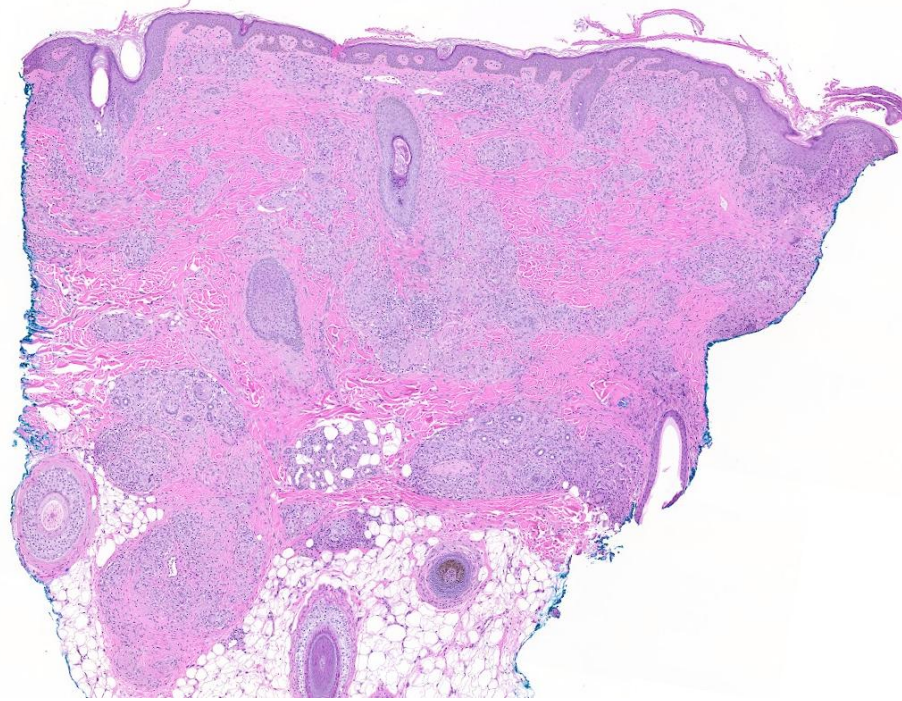
Seo SK, Yeum JS, Suh JC, Na GY. *Pediatr Dermatol.* 2001;18(5):384-7.

Ball NJ, Kho GT, Martinka M. *J Cutan Pathol.* 2004;31(2):160-8.

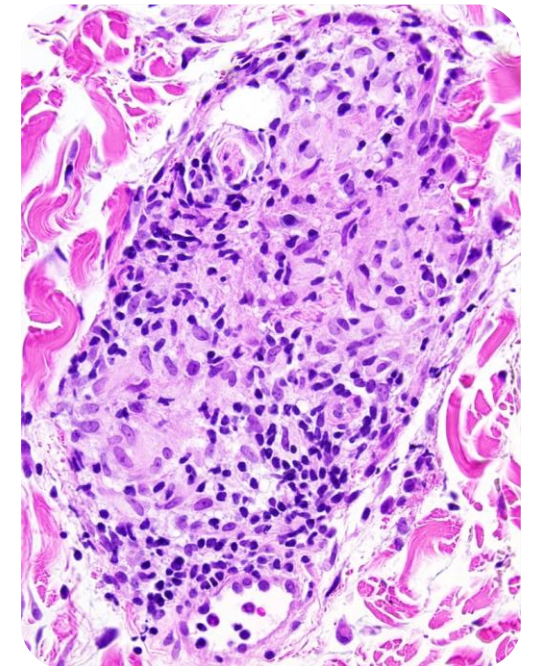
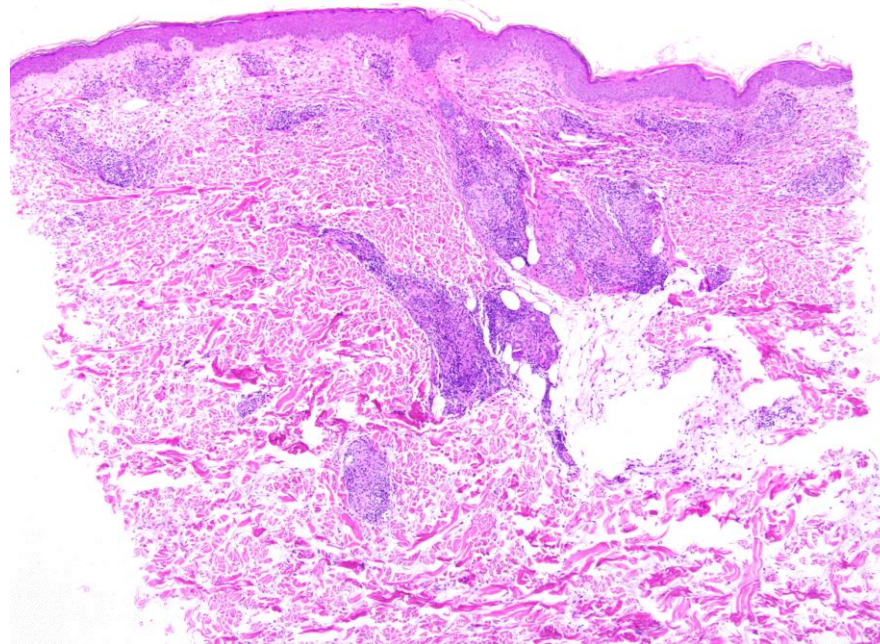
Garrido-Ruiz MC, Enguita-Valls AB, de Arriba MG, Vanaclocha F, Peralto JL. *Am J Dermatopathol.* 2008;30(3):271-3.



PCR negative for *Mycobacterium leprae*



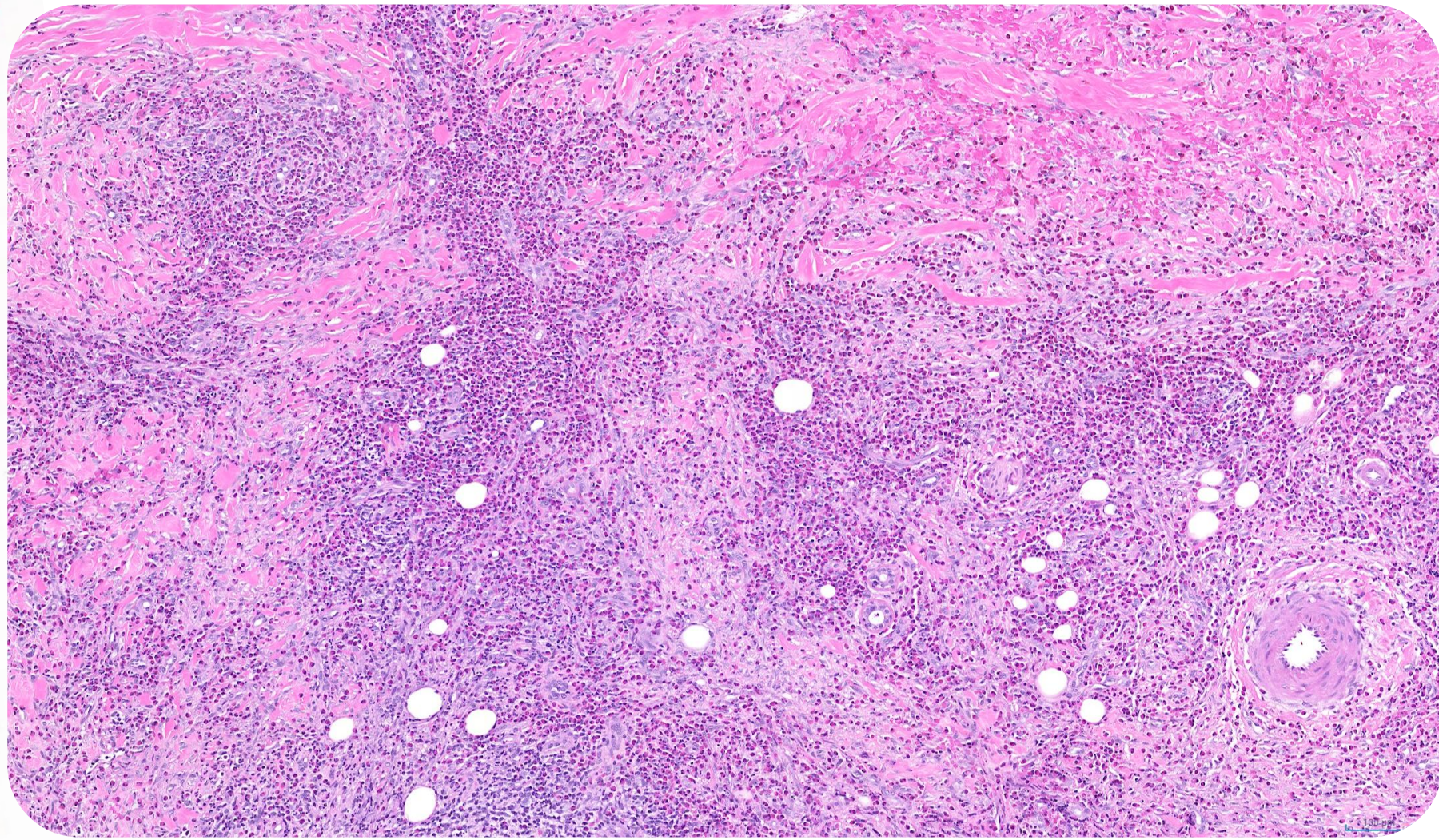
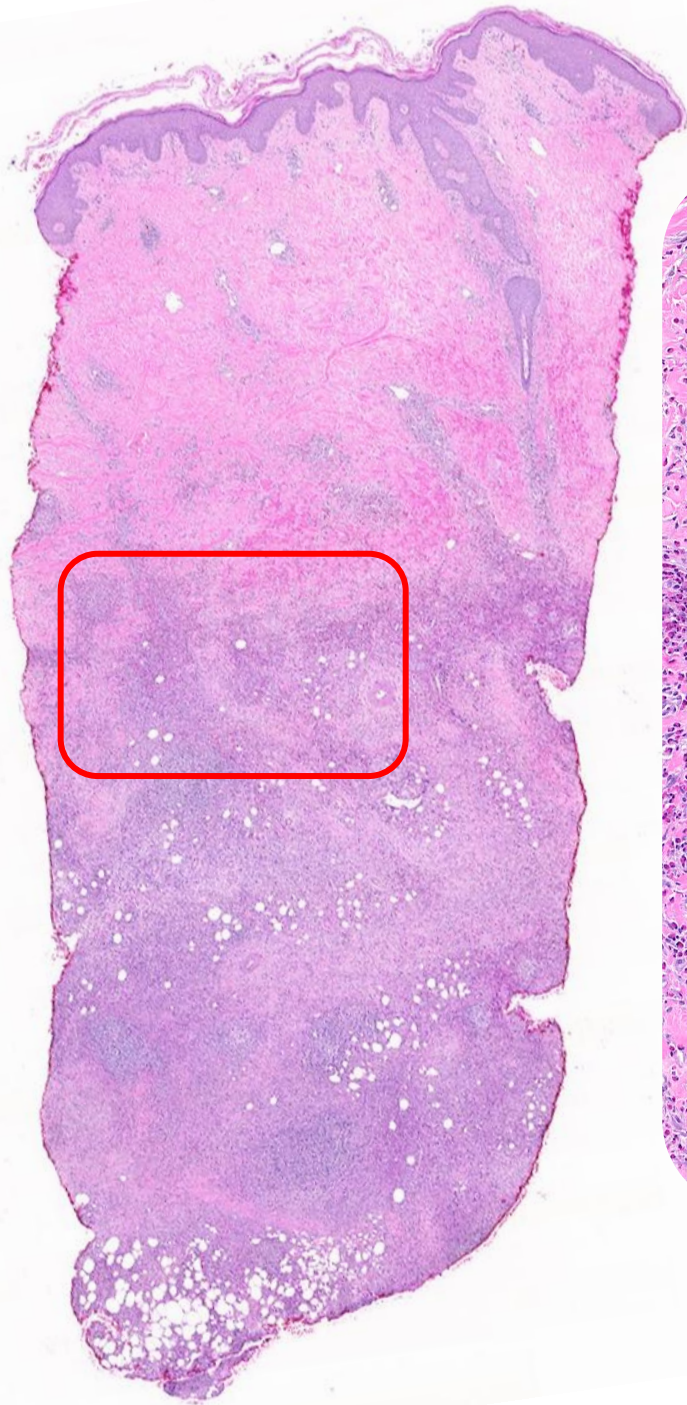
PCR **positive** for *Mycobacterium leprae*



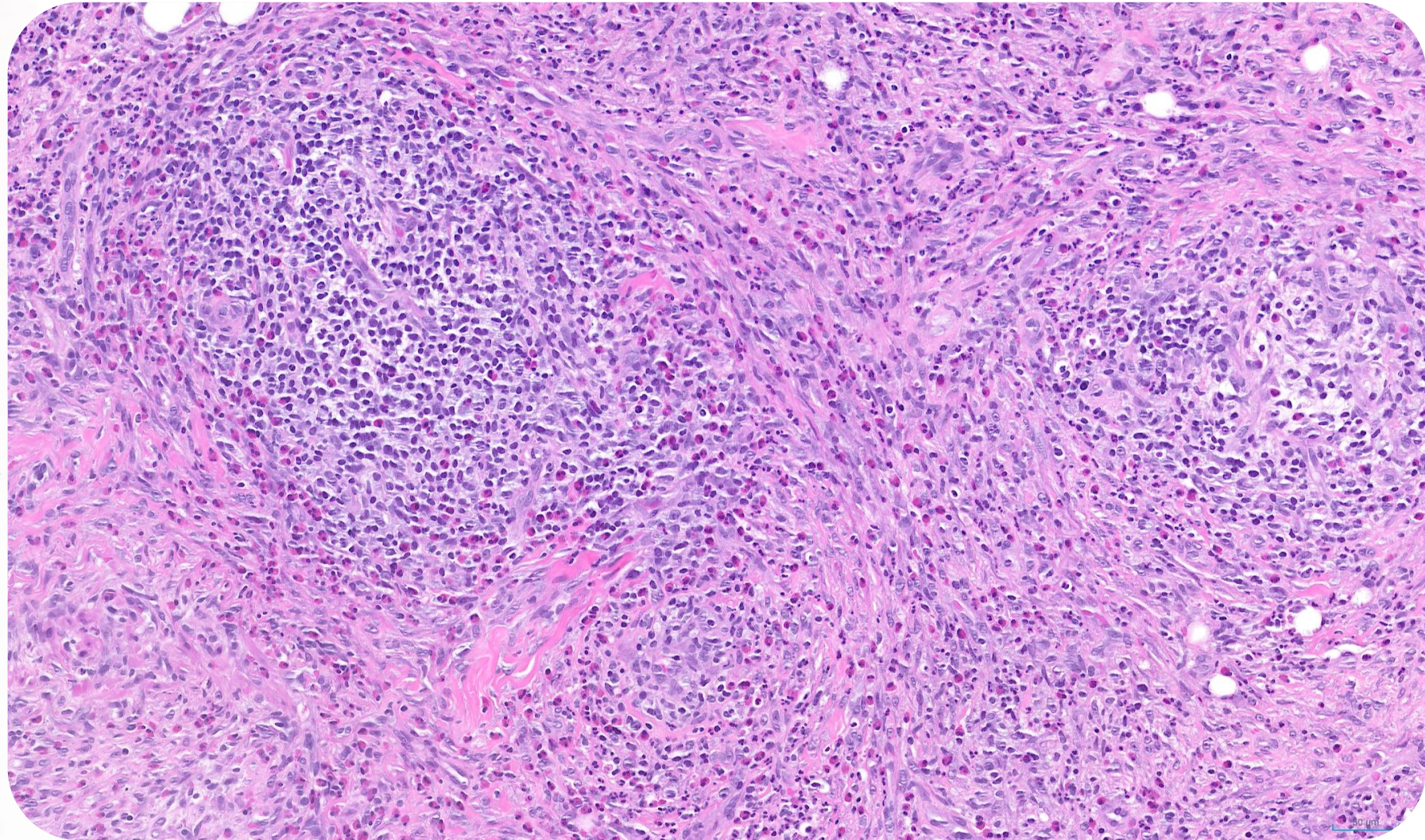
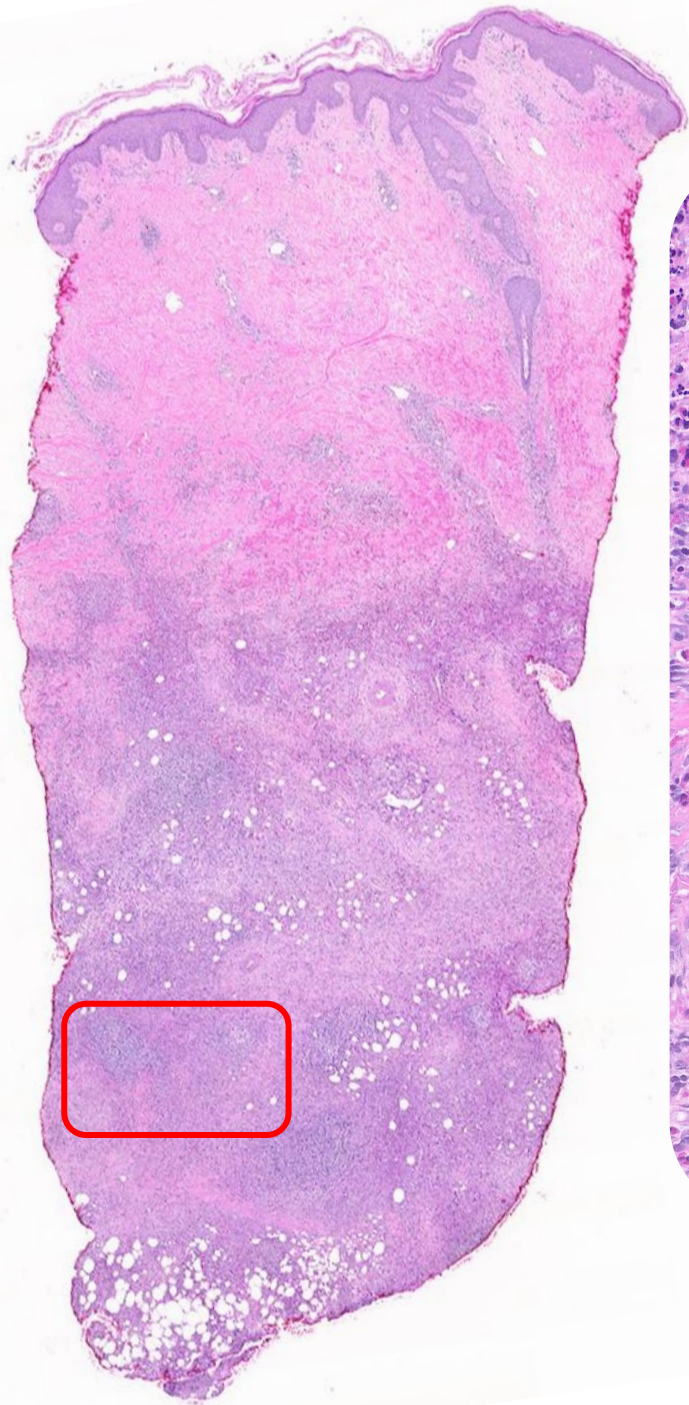
71-year-old man with recent diagnosis of mycosis fungoides with large cell transformation on brentuximab vedotin presented with painless left axillary nodules.



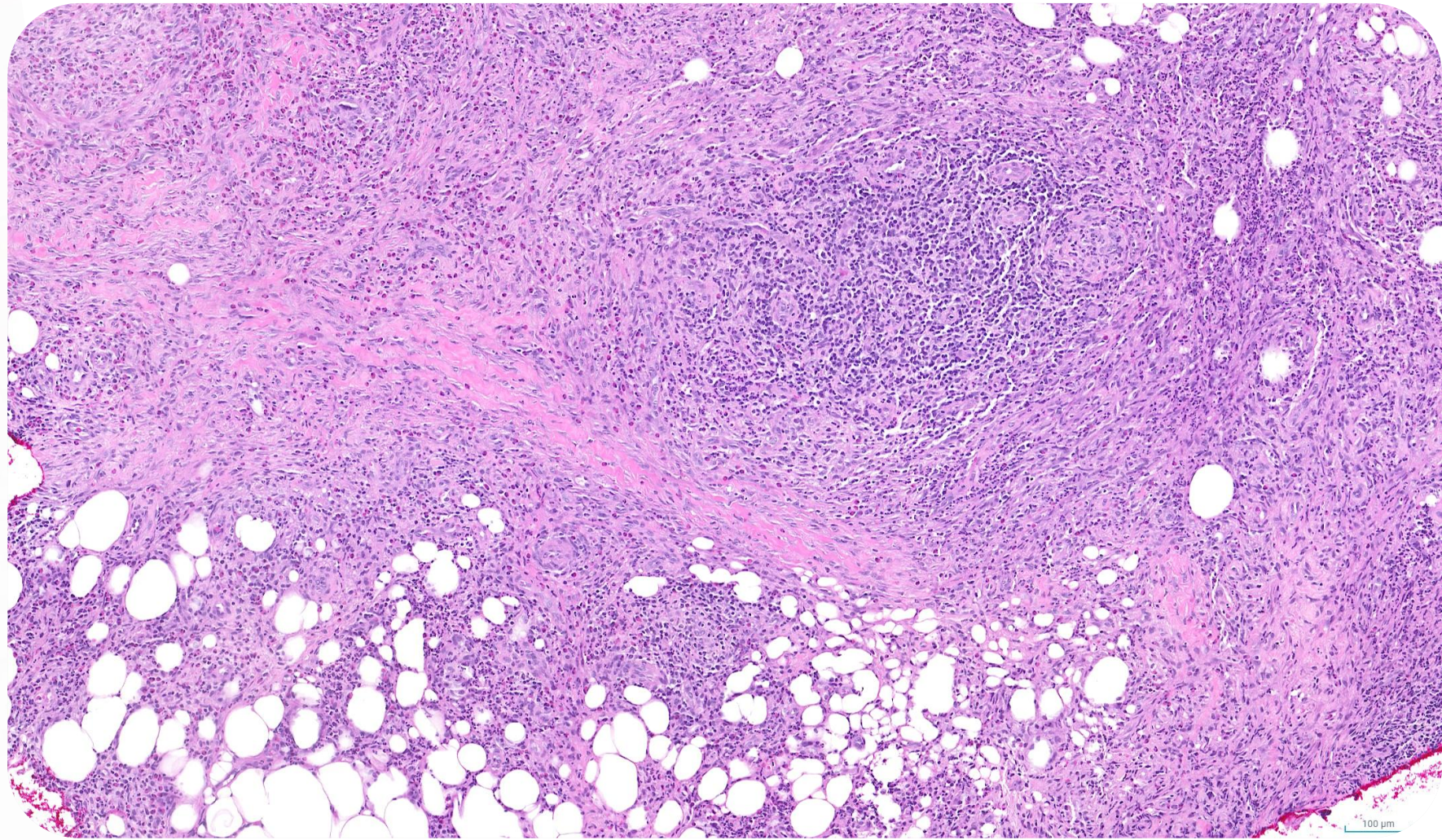




Original magnification x50



Original magnification x100



Original magnification x100

IHC

CD4:CD8 ratio retained; no epidermotropism or folliculotropism

BCL2 highlighted B-cells within lymphoid hyperplasia, T-helper cells

BCL6 failed to demonstrate germinal centers

PD1 highlighted helper T-cells, without rosette formation

CD34 highlighted increased vascularity

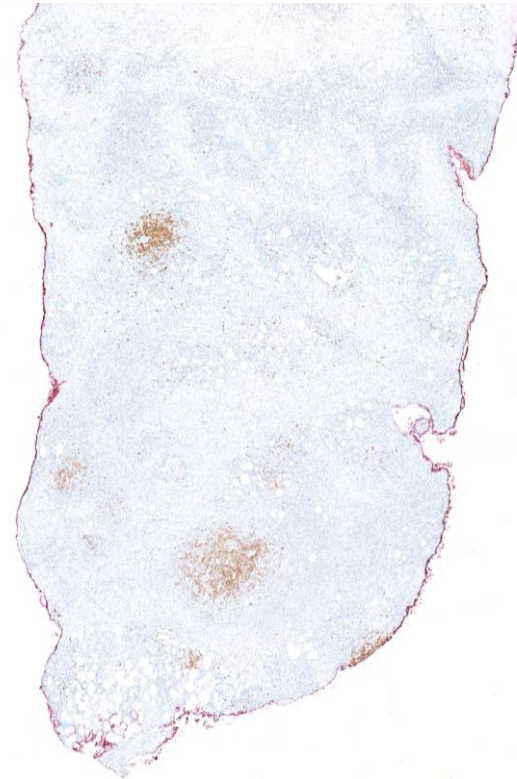
EBV ISH negative



CD3



CD20



CD30



KIMURA DISEASE*

Clin: unilateral head/neck; + LAD
trunk, breast, buttocks, groin, axillary, UE; **painless MC**
*epidermal changes uncommon: *lichenification, pustules*

Path: cellular / fibrocollagenous / vascular

Lab: peripheral eosinophilia, elevated IgE

Co-morbidities: eczema, **Hodgkin lymphoma**, **mycosis fungoides** | nephrotic syndrome

Tx: surgery, radiation, regional/systemic steroids; self resolution

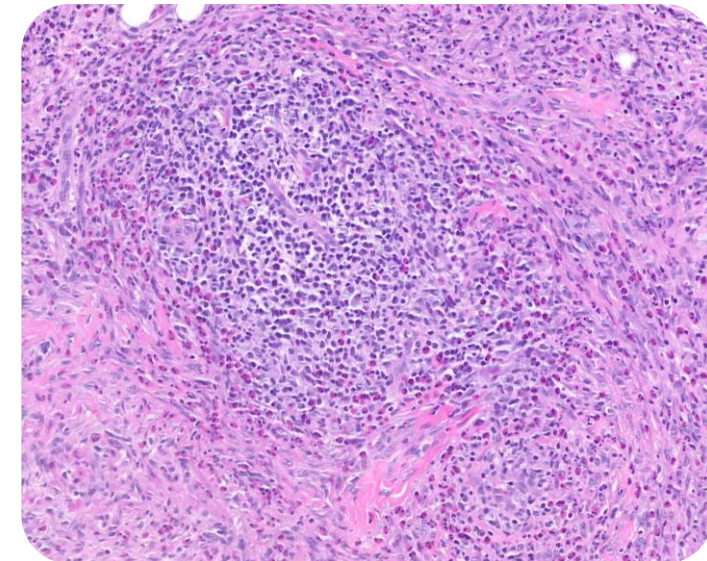
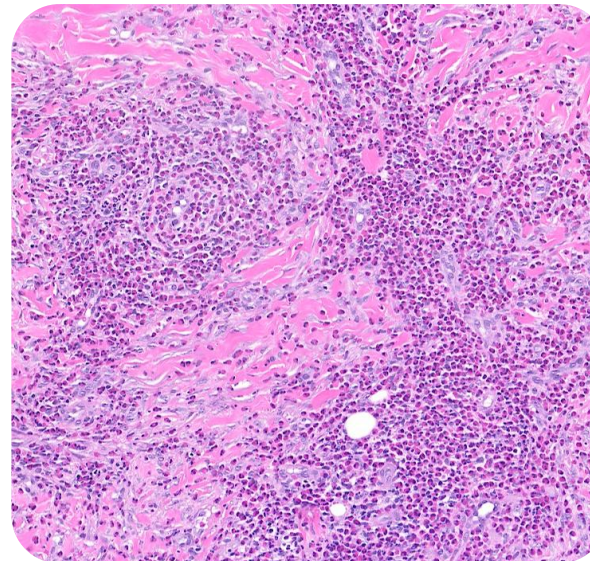
PRESENT CASE

Unilateral axillary/trunk; +LAD
painless*; epidermal change noted

lymphoid hyperplasia, eosinophil microabscesses,
fibrosis, vascular proliferation | no germinal centers

peripheral eosinophilia 750/ μ L; IgE 13388 kU/L

self-resolution during treatment of underlying
mycosis fungoides with large cell transformation



■Table 3■

Comparison of Clinical and Pathologic Features of ALHE, KD, and IgG4-RD^a

	ALHE	KD	IgG4-RD
Clinical			
PB eosinophilia, % ^b	10-20 ^c	80-90 ^d	~30 ^e
Serum IgE, %	10 ^c	90 ^d	30-60 ^e
Serum IgG4	Insufficient data	Insufficient data	60 ^e
Papulonodular skin lesions	Common	Rare	Occasional
Lymphadenopathy	Rare	Common	Common
Usual location	Head/neck	Head/neck	Any
Pathologic			
Plasma cells	Yes	Yes	Yes
Eosinophilic microabscesses	Rare	Yes	Rare
Vascular proliferation	Yes (plump ECs)	Yes (flat ECs)	No
Fibrosis	Yes	Yes	Yes

ALHE, angiolymphoid hyperplasia with eosinophilia; EC, endothelial cell; IgG4-RD, IgG4-related disease; KD, Kimura disease; PB, peripheral blood.

^aPB eosinophilia is present in the indicated percentages of patients at presentation. Elevated IgE levels and elevated serum IgG4 levels are present as indicated in IgG4-RD, but insufficient data have been collected on patients with ALHE and KD.

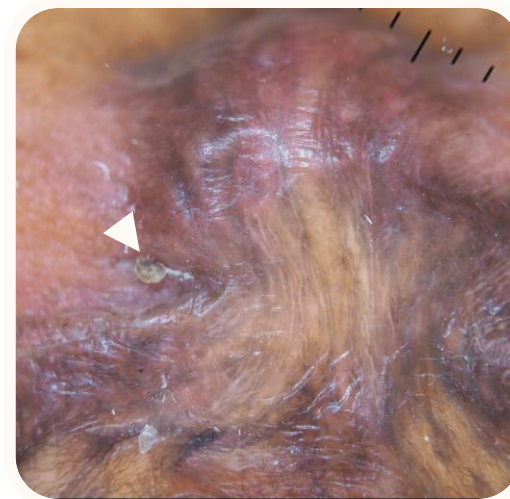
^bVariable definitions for eosinophilia are used in this area. In general, this represents data defined as values above a normal reference range.

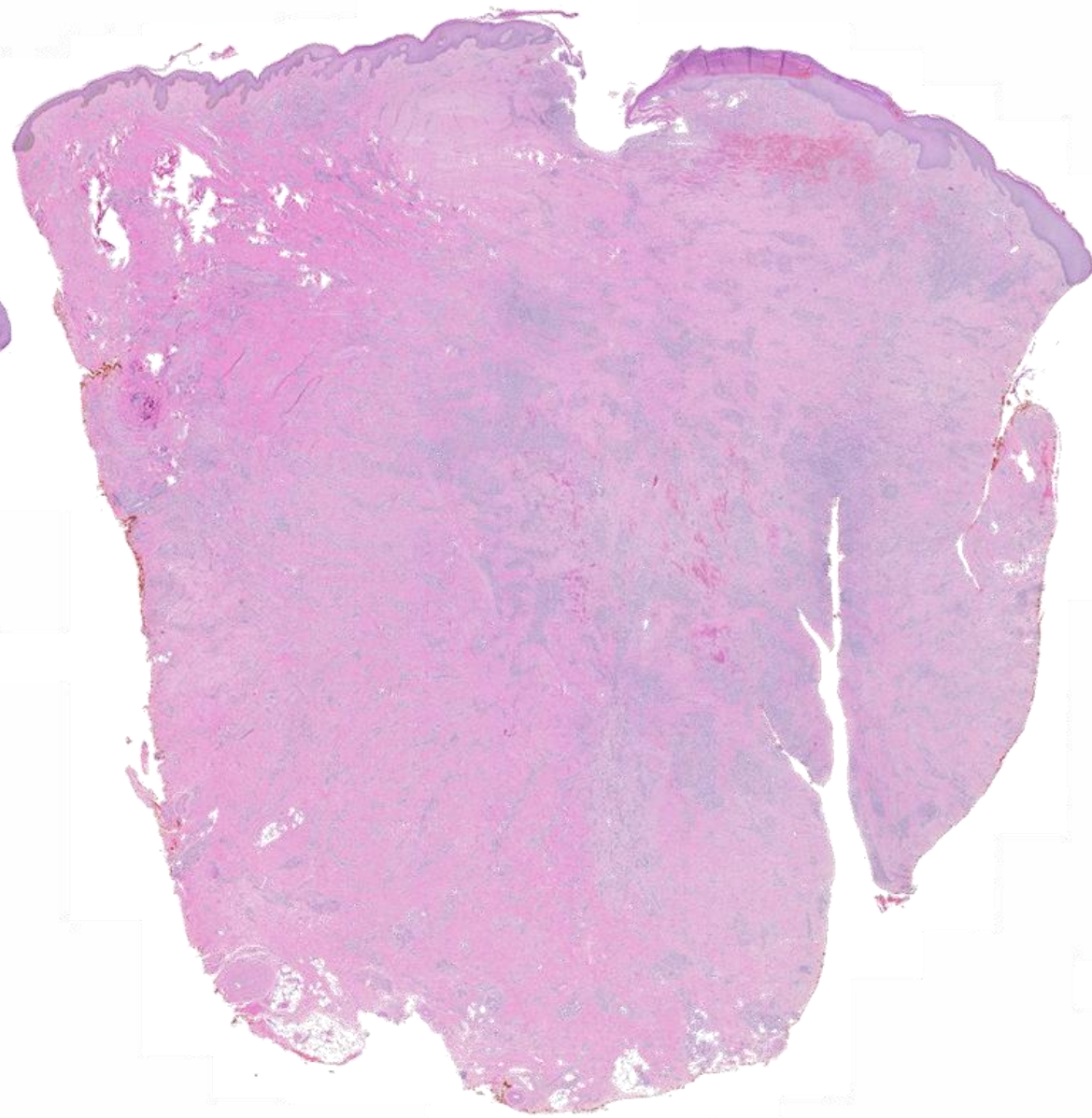
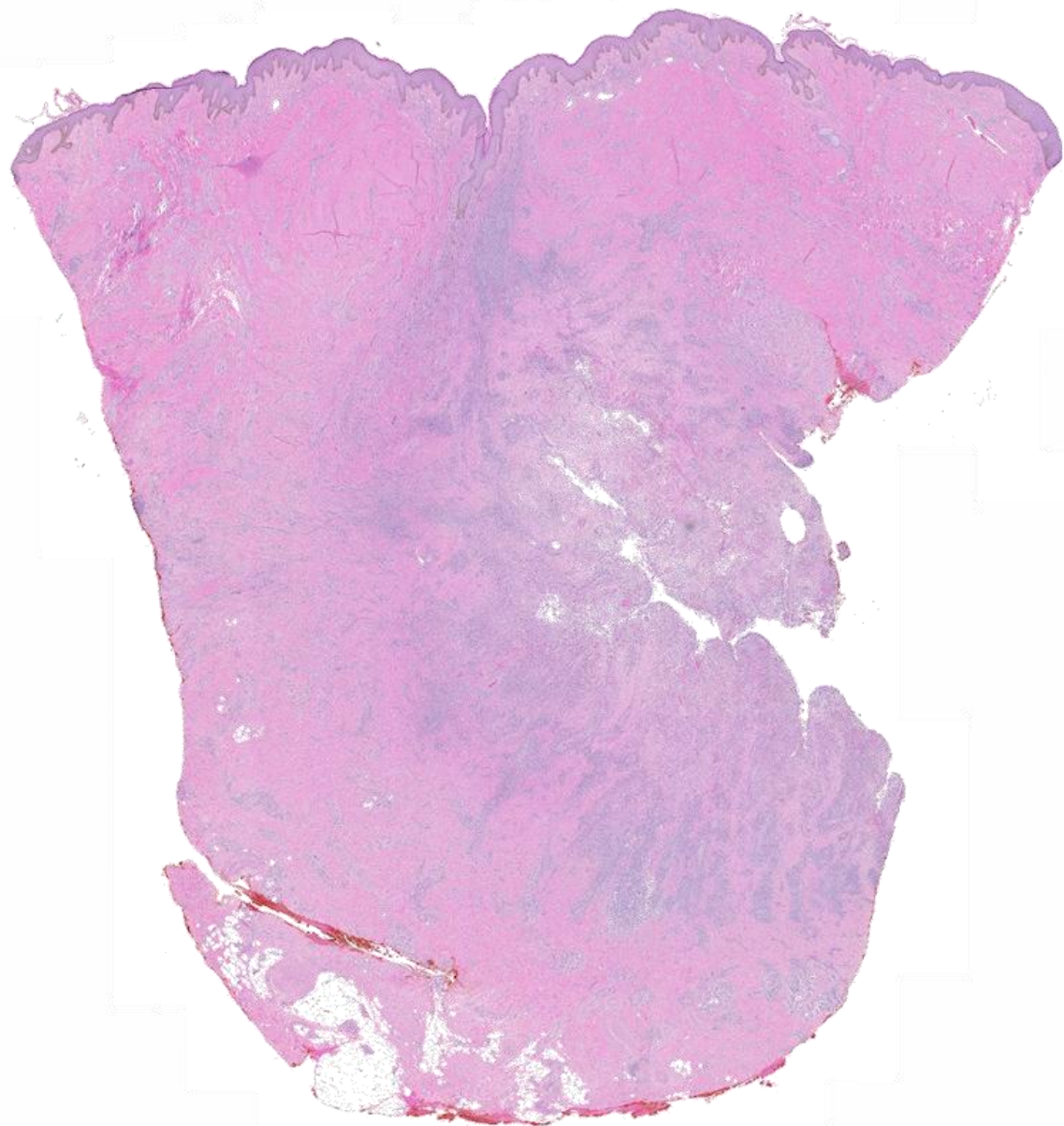
^cGuo et al²⁰ and Bahloul et al.⁵

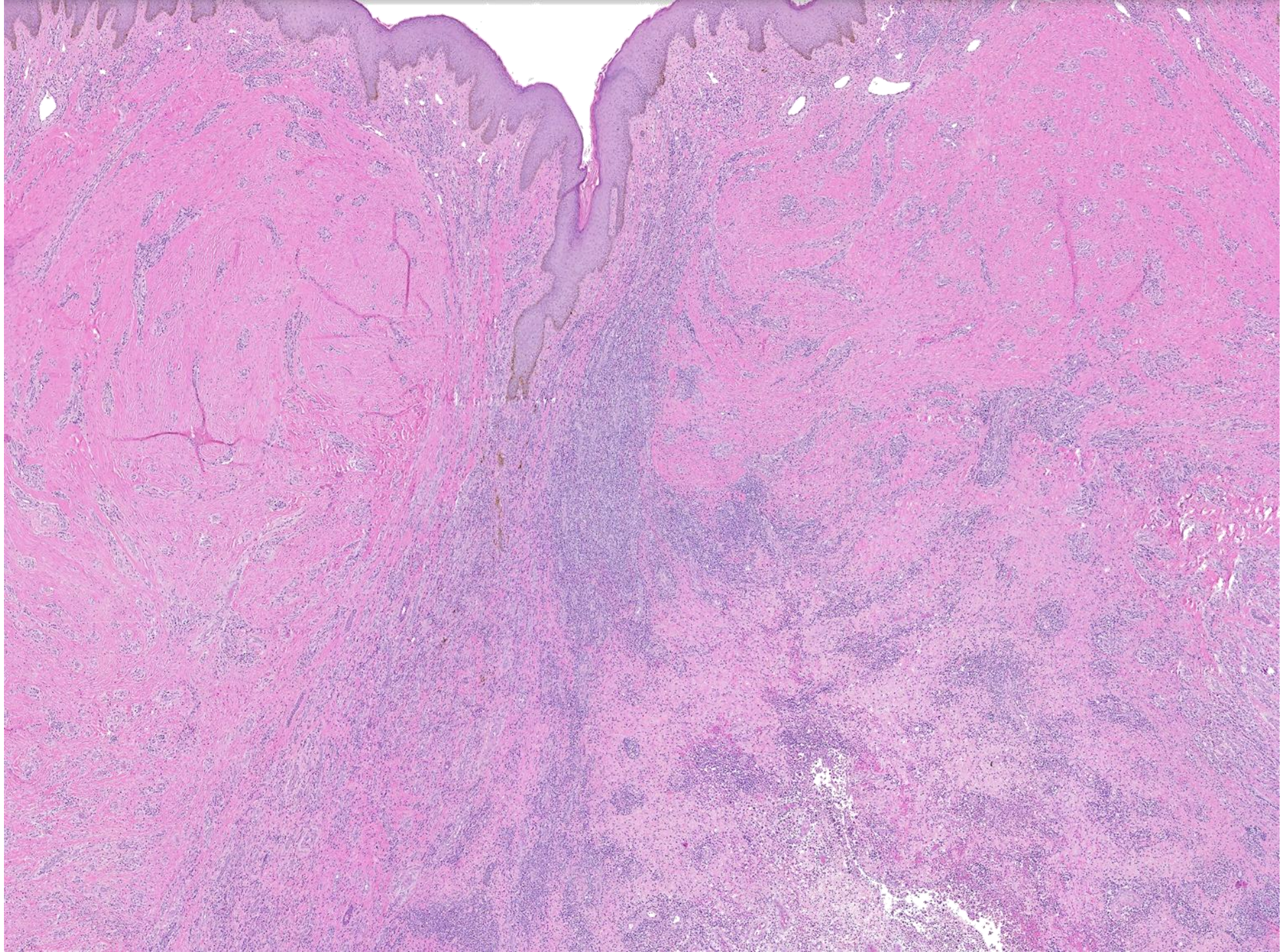
^dKottler et al.⁴

^eDella-Torre et al.¹⁸

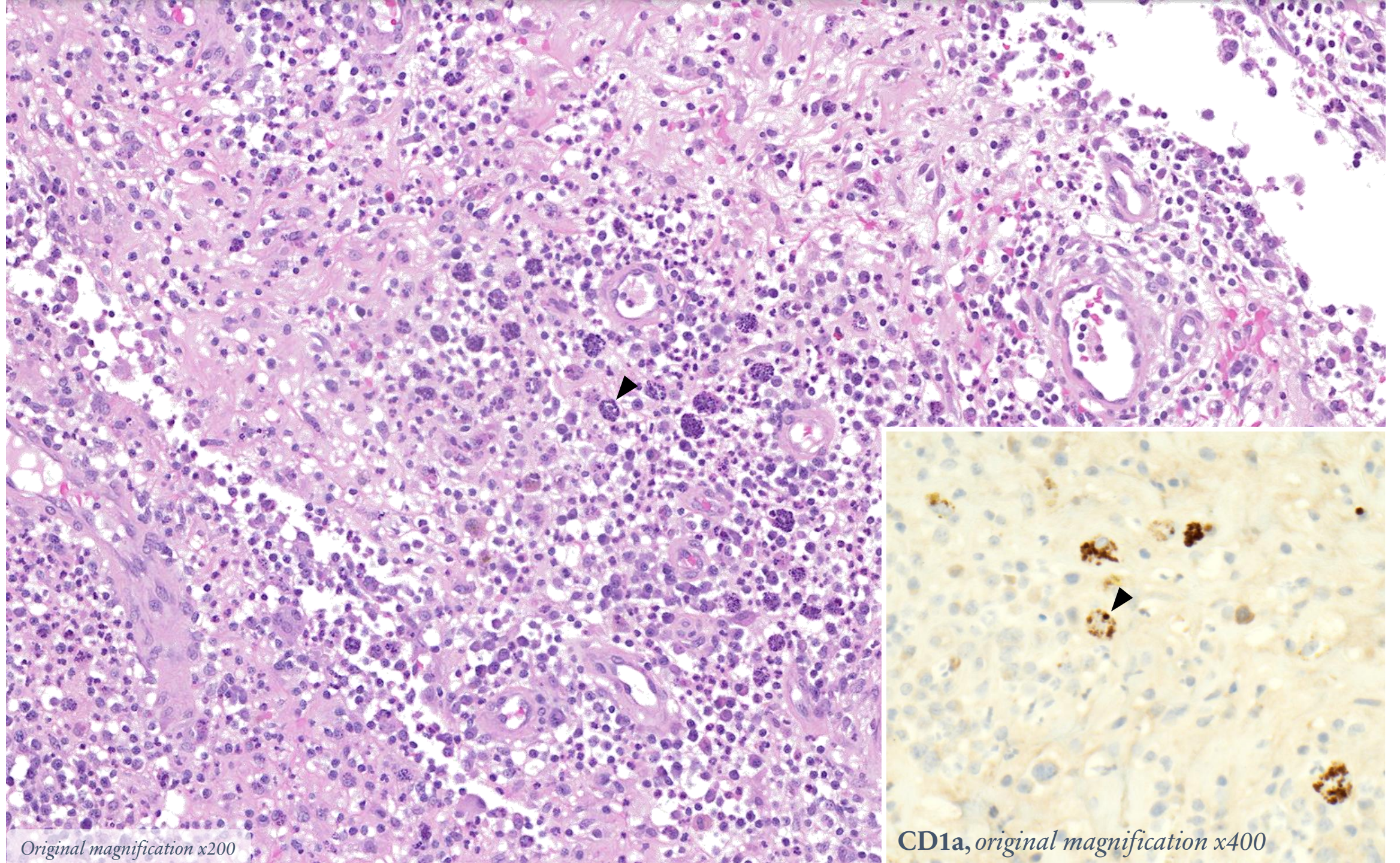
41-year-old man with no significant past medical history presents for excision of a mid-chest symptomatic keloid.



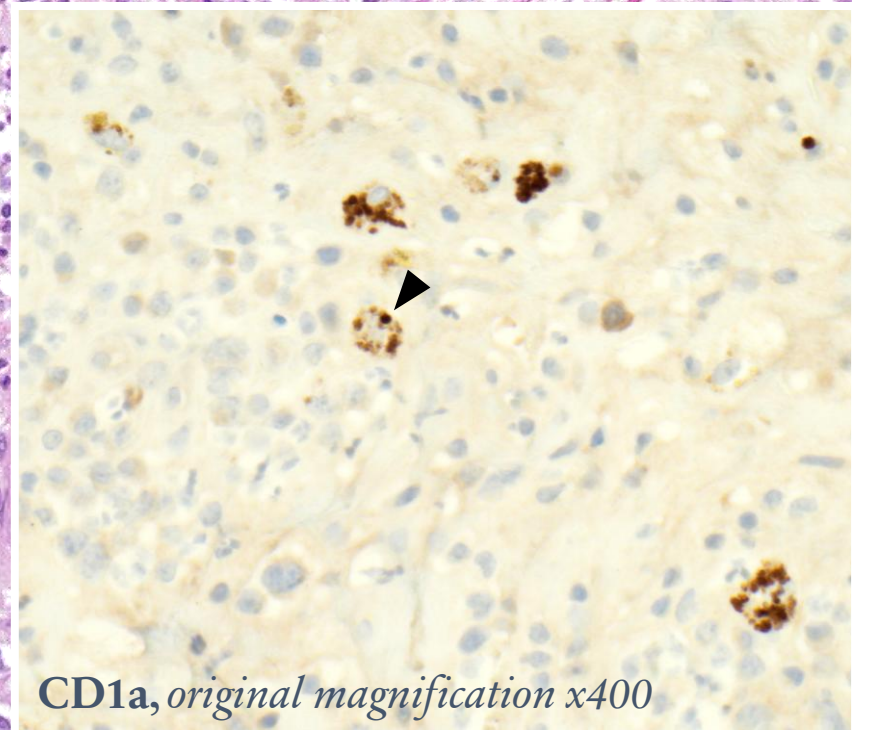




Original magnification
x20

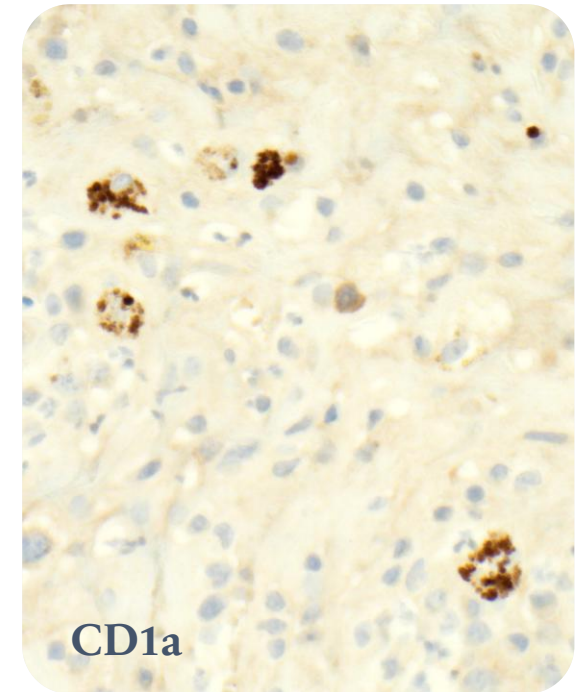
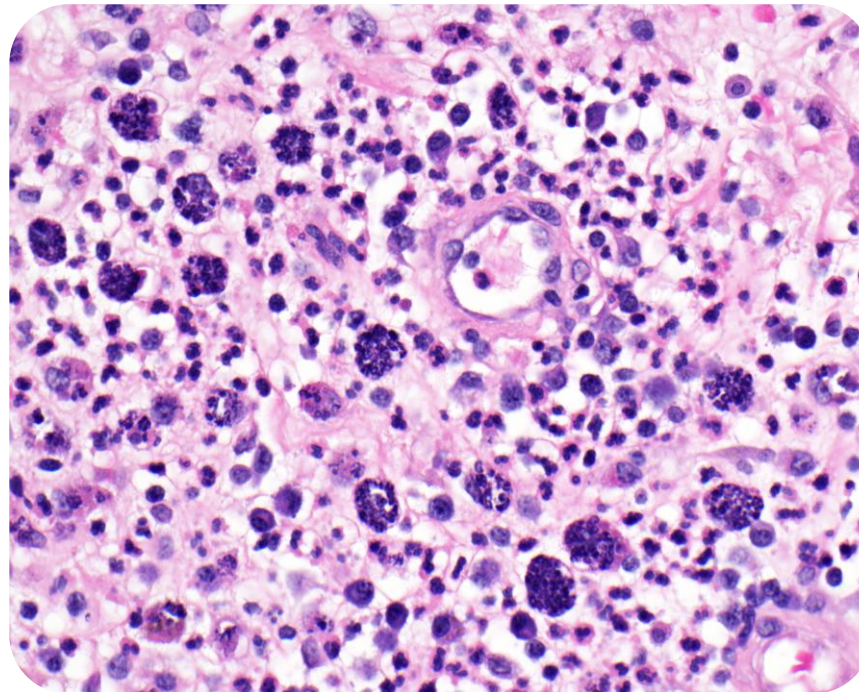


Original magnification x200



CD1a, original magnification x400

41-year-old man with cutaneous leishmaniasis presenting as a mid-chest symptomatic keloid.



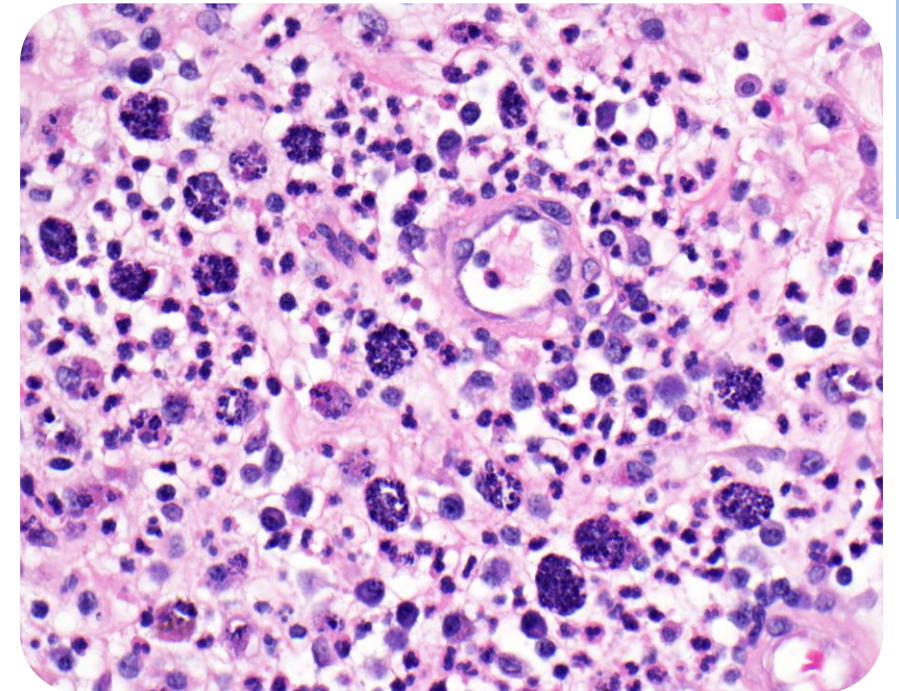
Molecular pathology, punch biopsy (8mm), fresh tissue, PCR analysis by CDC demonstrated *Leishmania tropica*.

41-year-old man with cutaneous leishmaniasis presenting as a mid-chest symptomatic keloid.



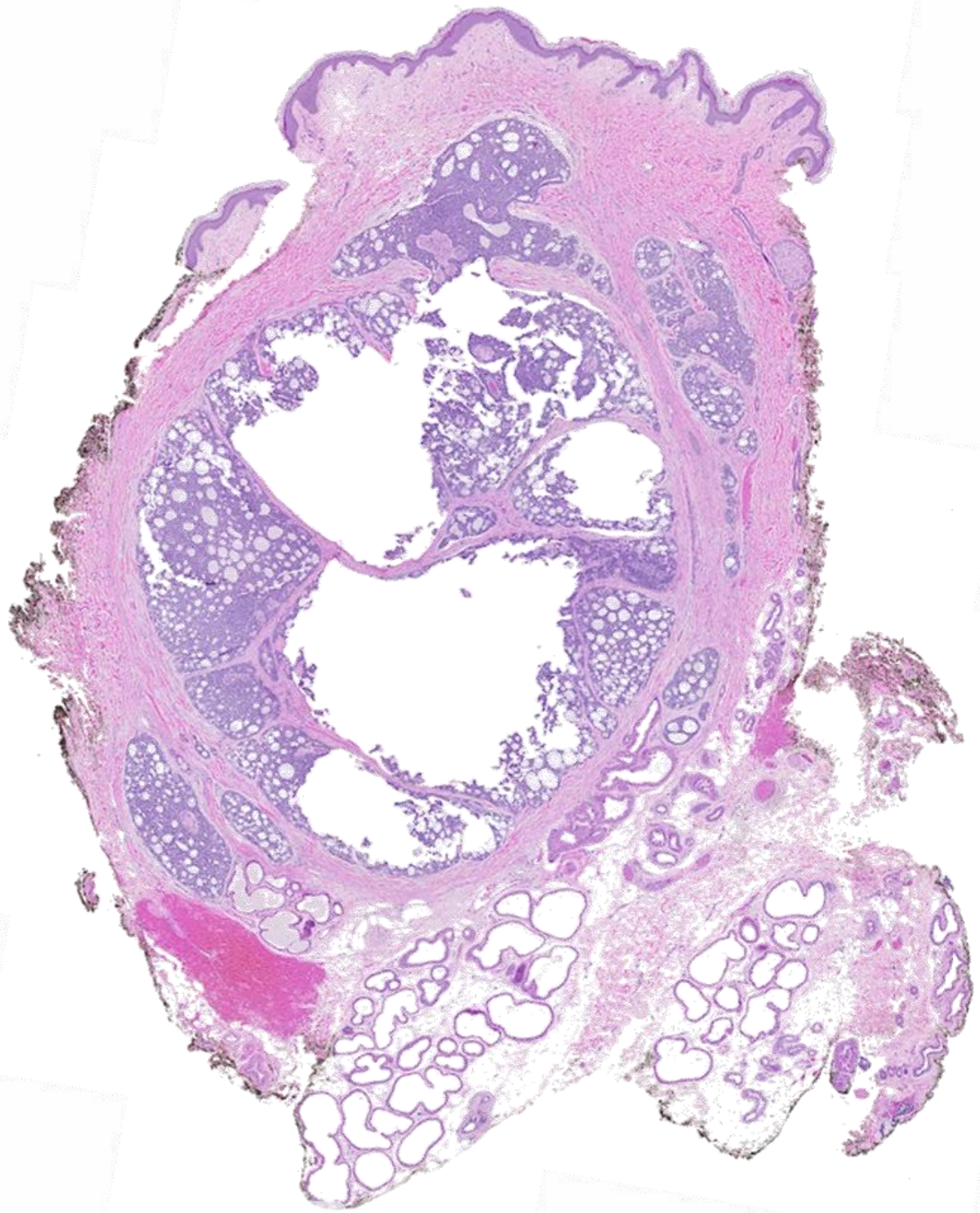
Cutaneous leishmaniasis elicits a Th1 cell-mediated immune response.

Keloids demonstrate increased Th2 cytokine expression → potential nidus for prolonged leishmaniasis infection.

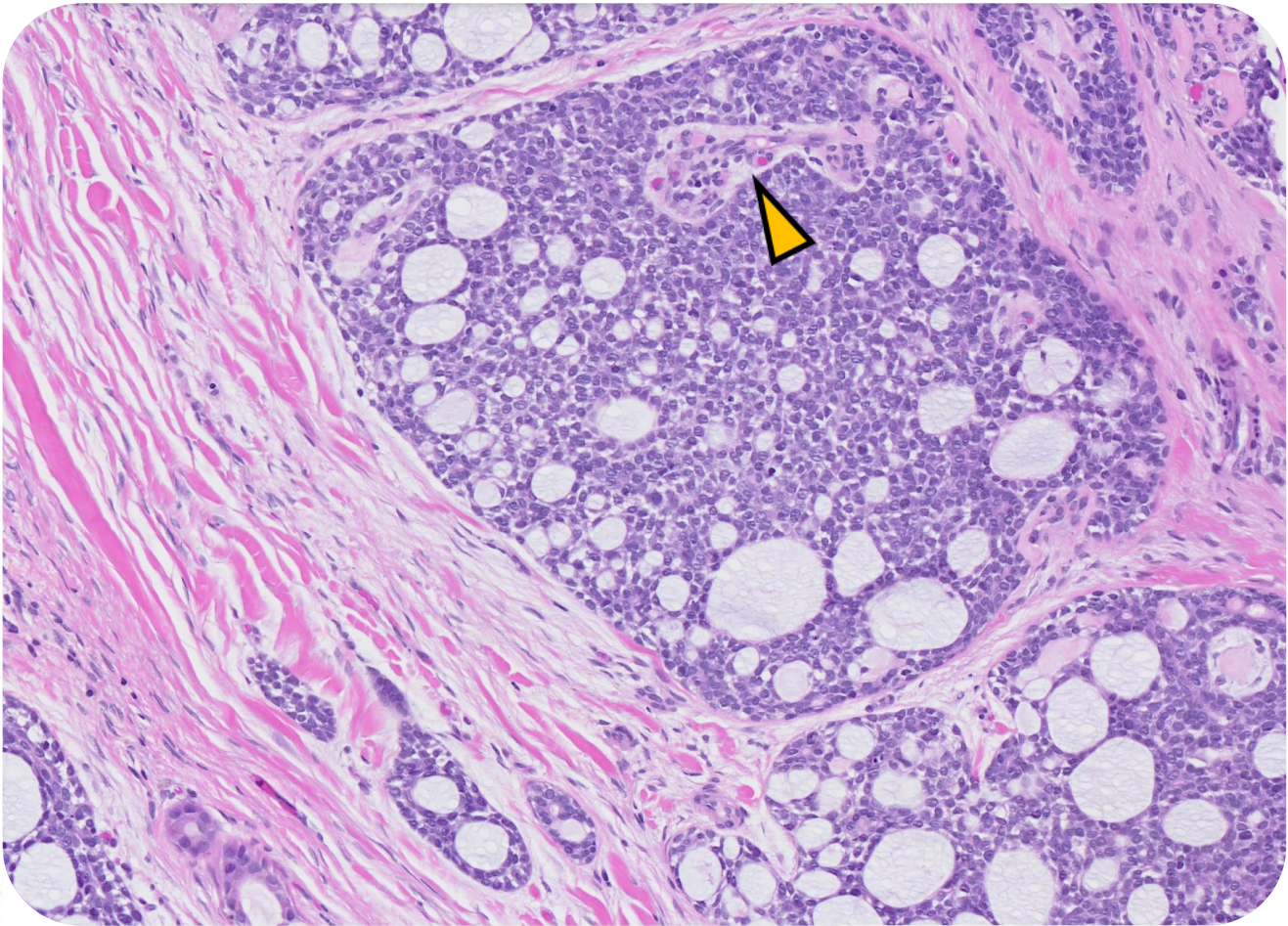


67yo man presented with right axillary nodule present for ~1 year, newly tender.

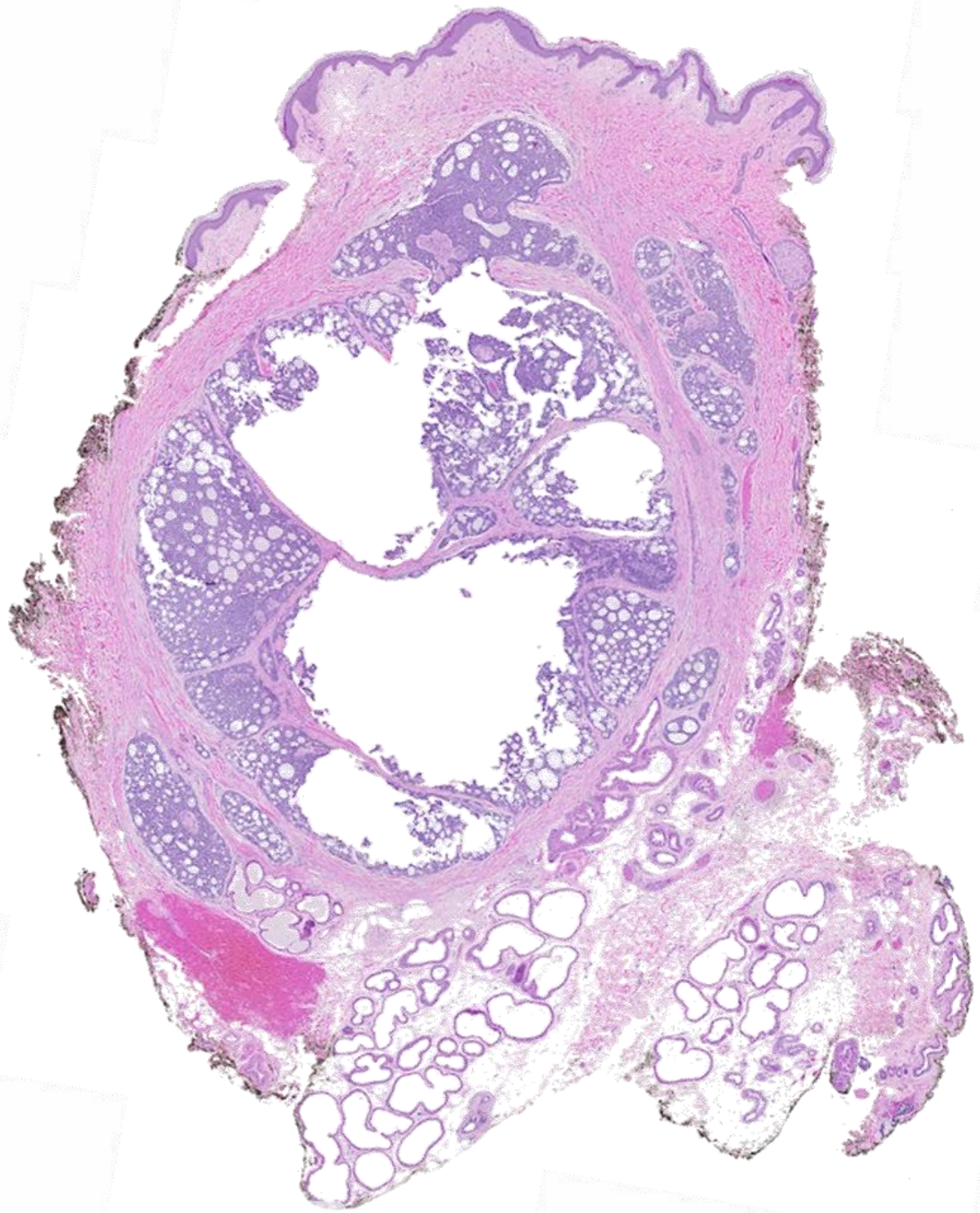




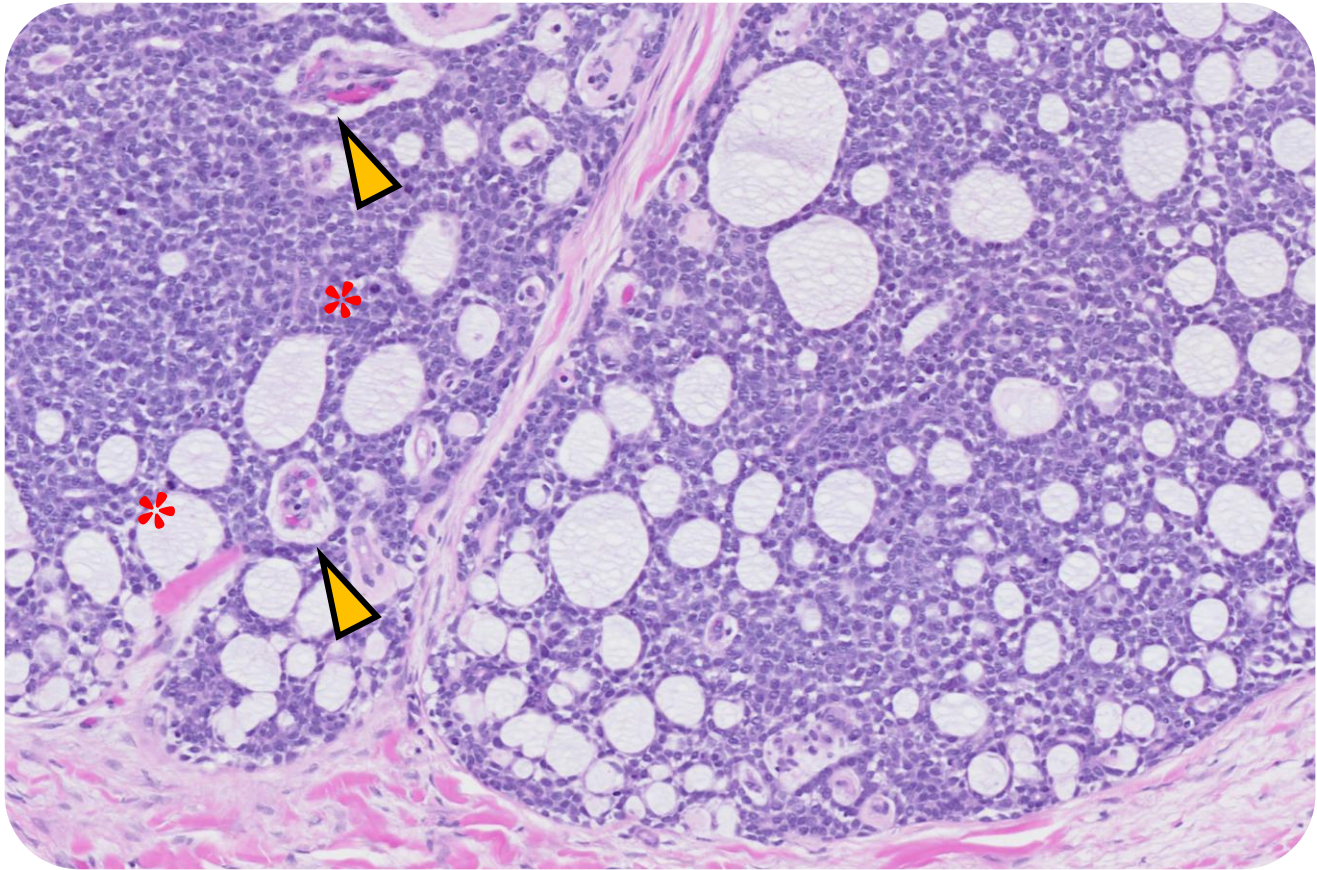
Original magnification x10



Original magnification x200



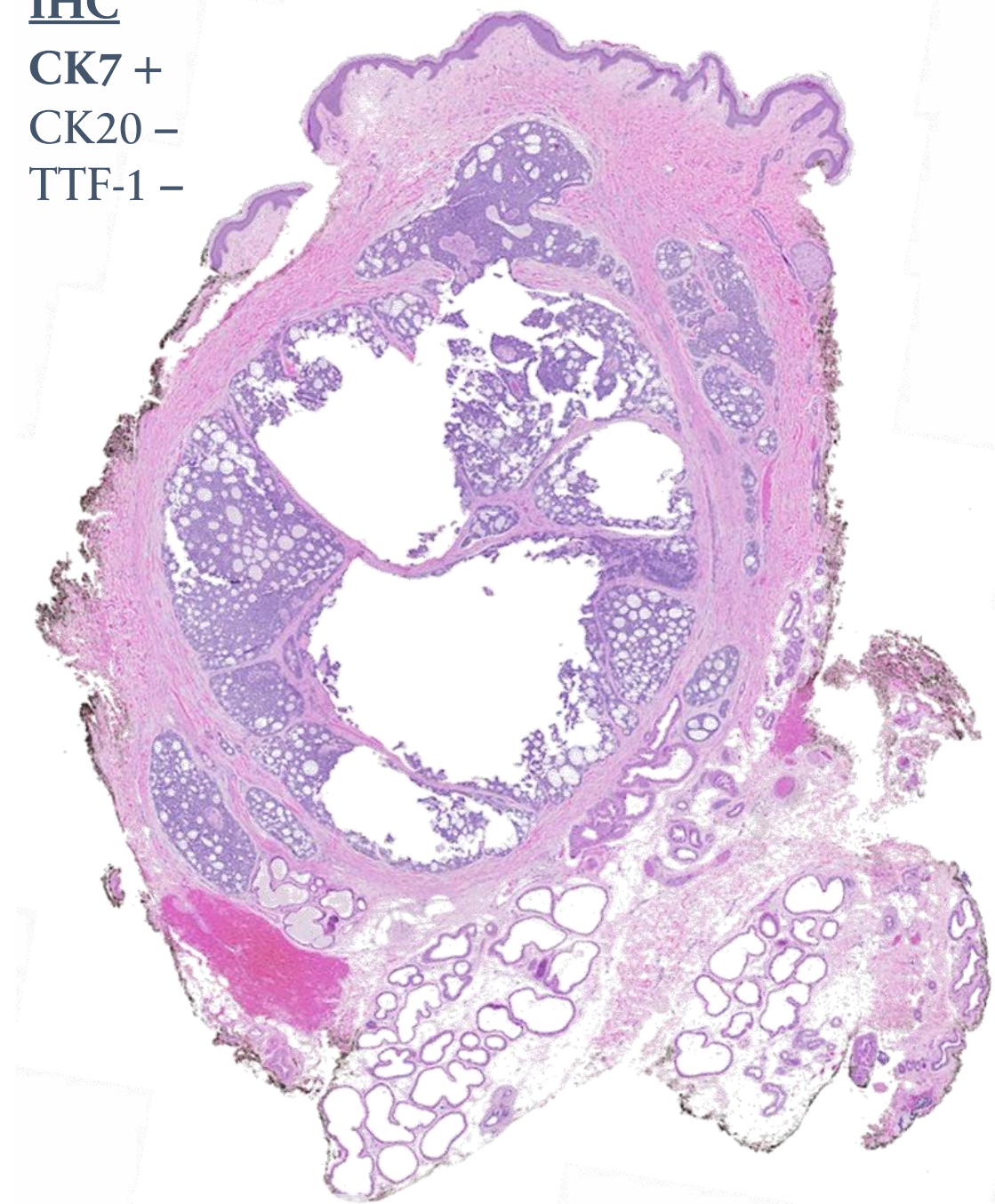
Original magnification x10



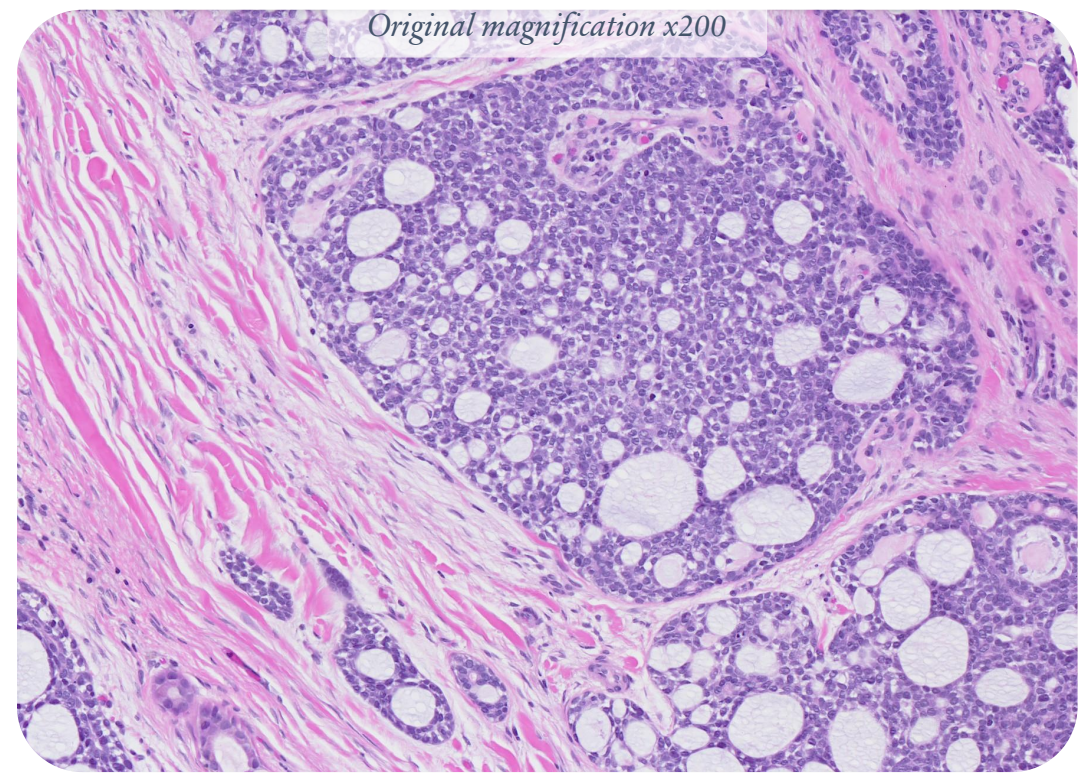
Original magnification x200

IHC

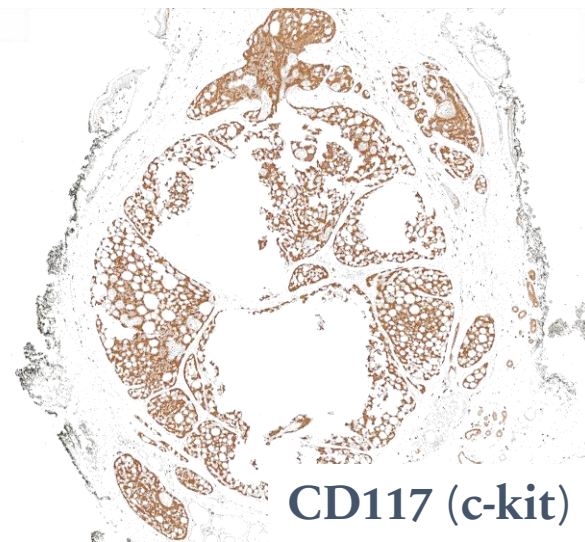
CK7 +
CK20 -
TTF-1 -



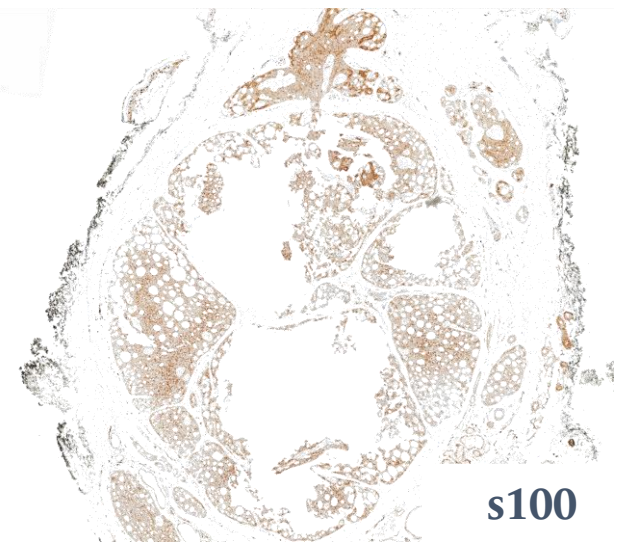
Original magnification x10



Original magnification x200



CD117 (c-kit)



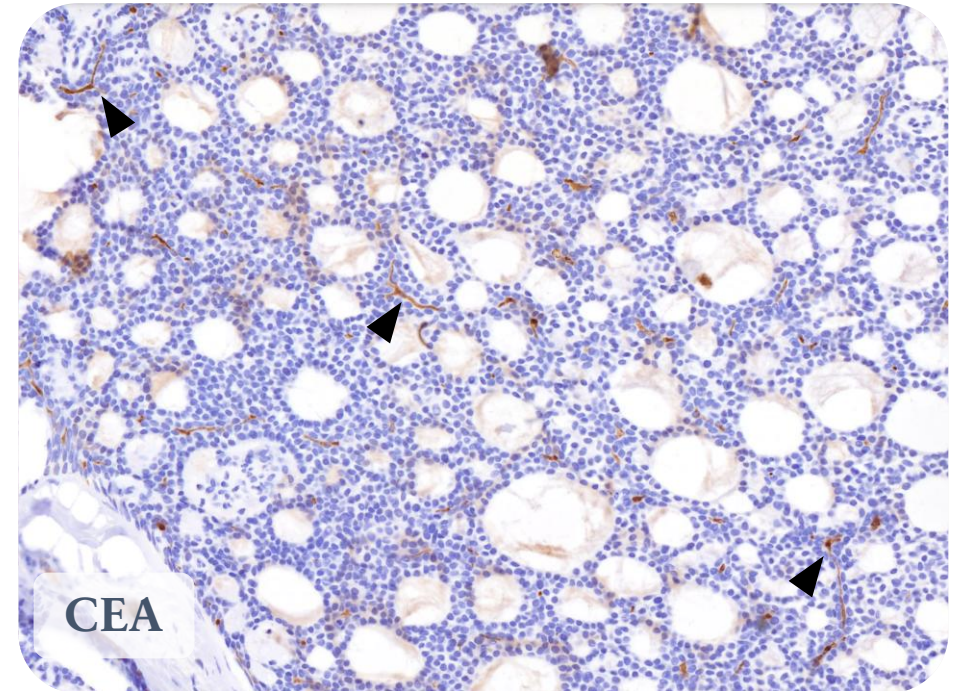
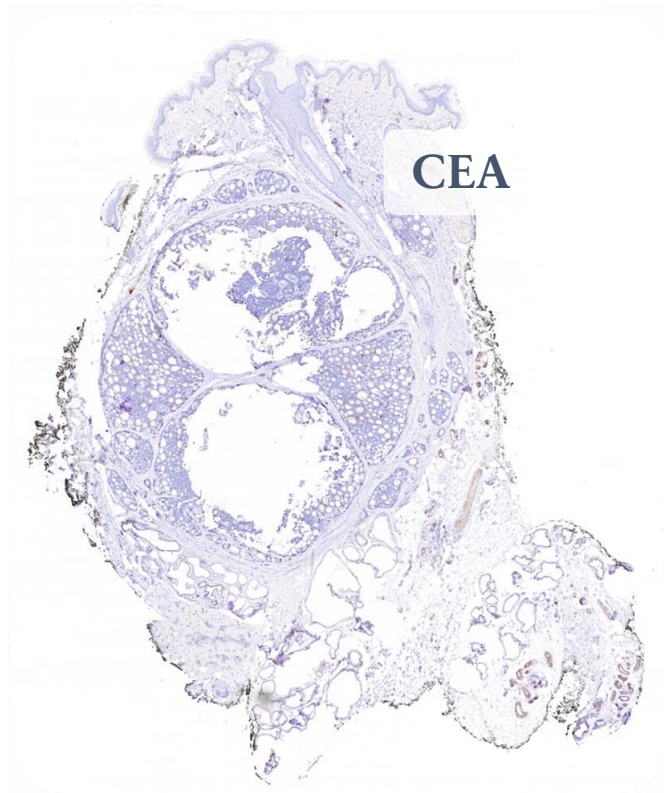
s100

Original magnification x20

Adenoid cystic carcinoma-like spiradenocarcinoma*

*IHC **not** helpful in distinguishing spiradenoma with ACC-like features from PCACC
~60-70% of PCACCs demonstrate MYB gene activations

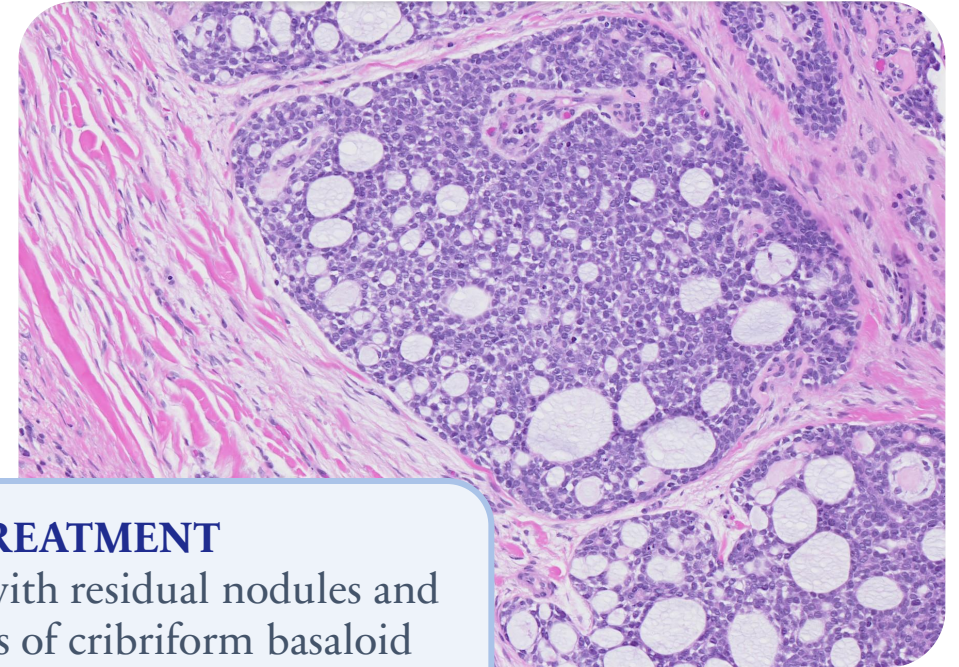
PRESENT CASE
MYB translocation **negative** (FISH)
robust, diffuse s100+
lack of perineural invasion



Adenoid cystic carcinoma-like spiradenocarcinoma*

*IHC **not** helpful in distinguishing spiradenoma with ACC-like features from PCACC
~60-70% of PCACCs demonstrate MYB gene activations

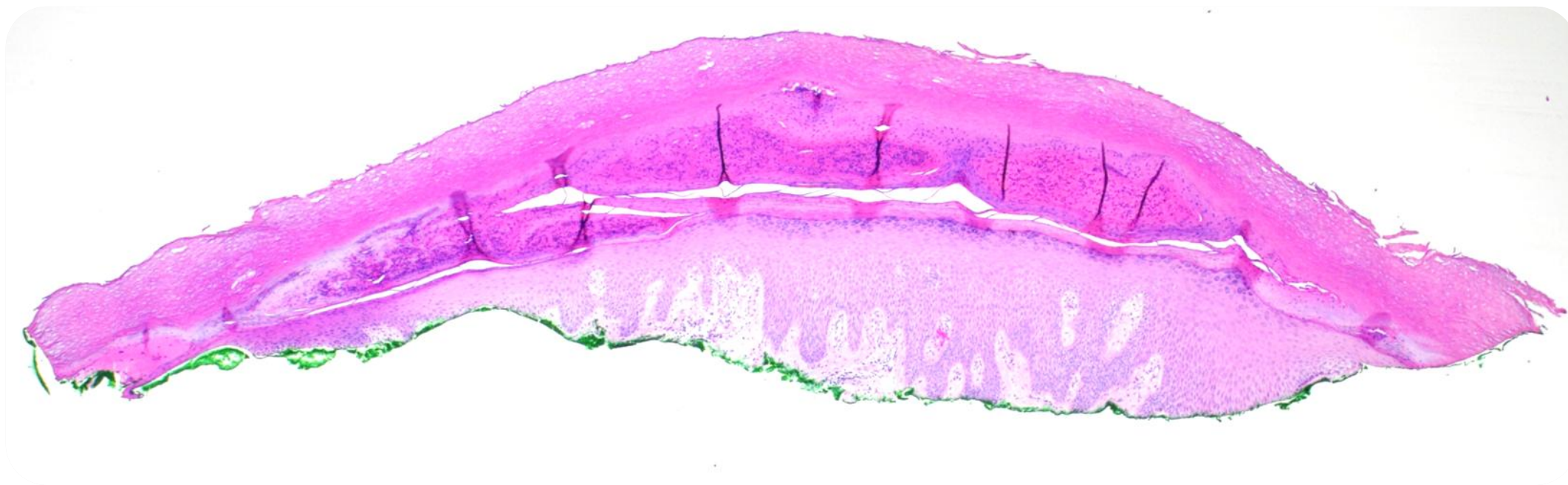
PRESENT CASE
MYB translocation **negative** (FISH)
robust, diffuse s100+
lack of perineural invasion



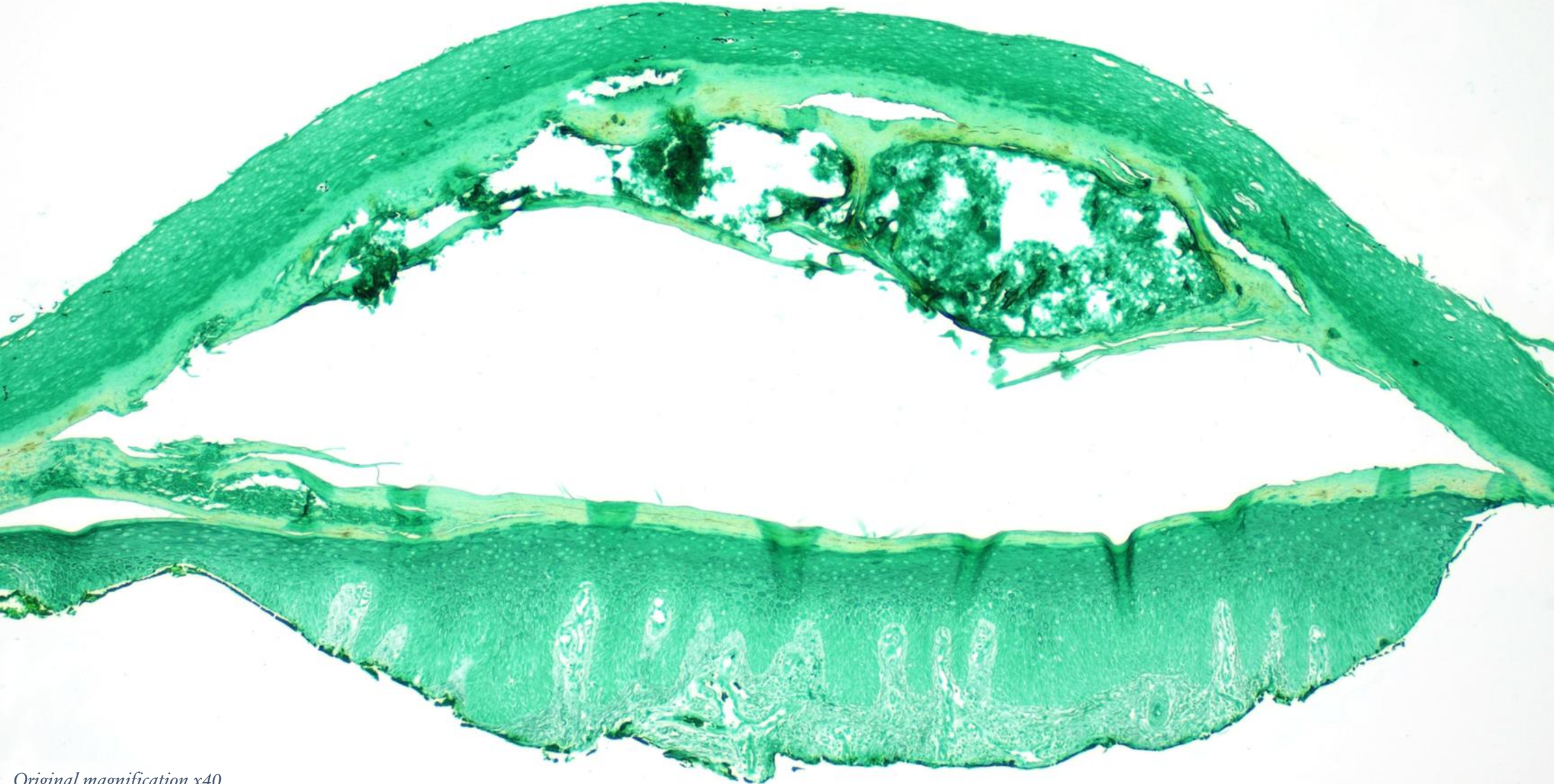
IMAGING
PET-CT **negative** for metastatic disease

TREATMENT
WLE to fascia with residual nodules and infiltrative cords of cribriform basaloid tumor, surgical margins narrowly free



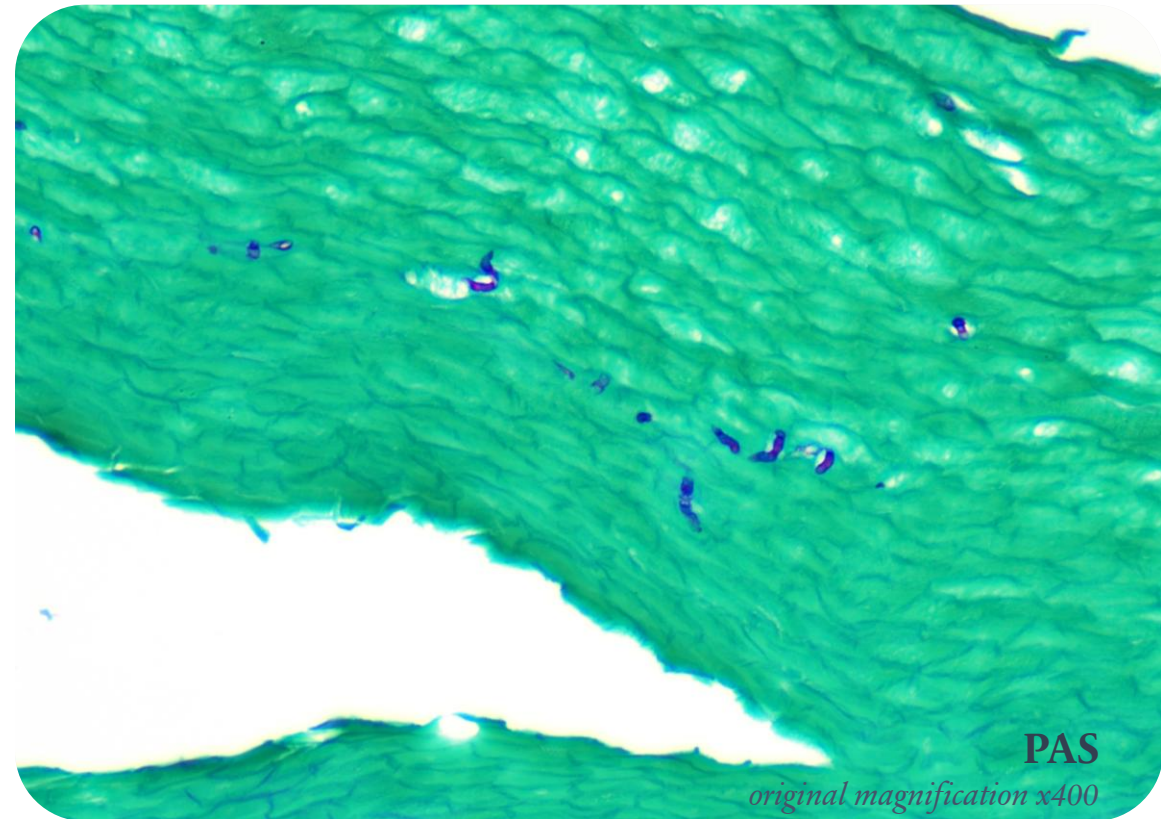


GMS



Original magnification x40

Bullous tinea mimicking perniosis



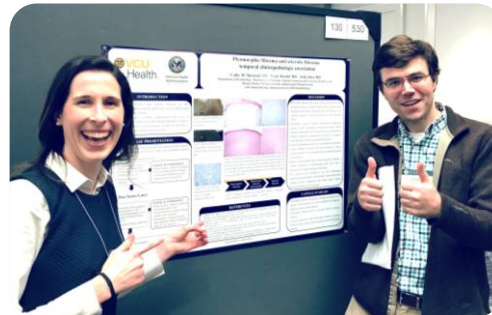


CAPSULE SUMMARY

- Clinicopathologic correlation is key!
- Keep an open mind.



**THANK
YOU**



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**DERMATOLOGIC CLINICOPATHOLOGIC
CORRELATION:**

**PINK & BLUE
OR SHADES OF GRAY?**

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