EMIRATES DERMATOLOGY SOCIETY
2024
ANNUAL CONFERENCE

8th YEAR

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InterContinental Dubai - Festival City
United Arab Emirates

EMIRATES DERMATOLOGY SOCIETY

Medical Dermatopathology – Challenging Cases and Recent Entities

Friday 8th Nov 2024
Session: Clinical cases

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Head, Dermatopathology Division

National Skin Centre, Singapore

NATIONAL SKIN CENTRE
National Healthcare Group

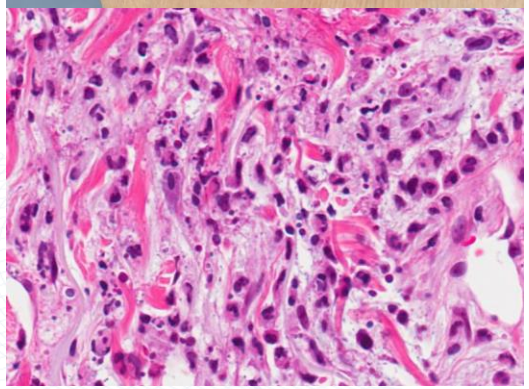
27TH WORLD CONGRESS OF DERMATOLOGY 2031
DUBAI - CANDIDATE CITY

Conflict of Interest

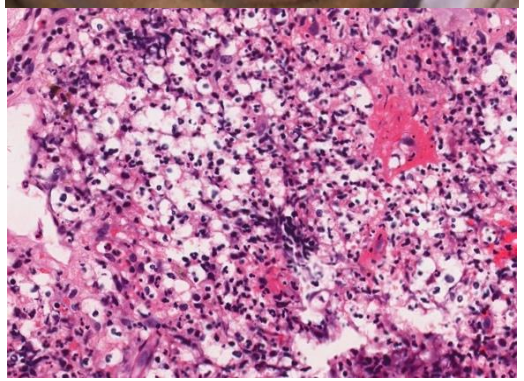
I have no conflicts of interest to declare

Medical Dermatopathology – Challenging Cases and Recent Entities

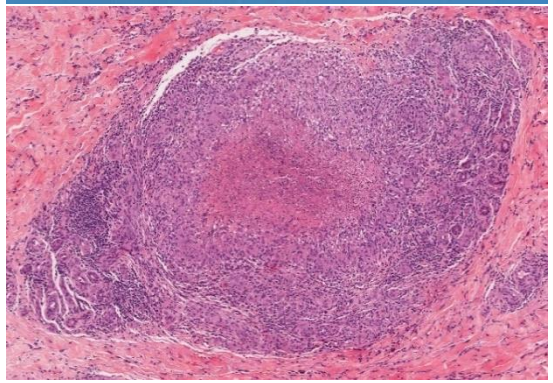
Case 1



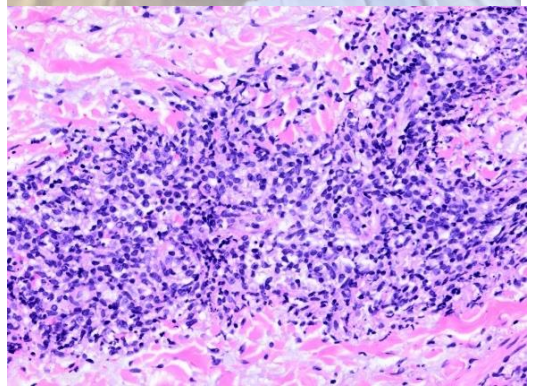
Case 2



Case 3

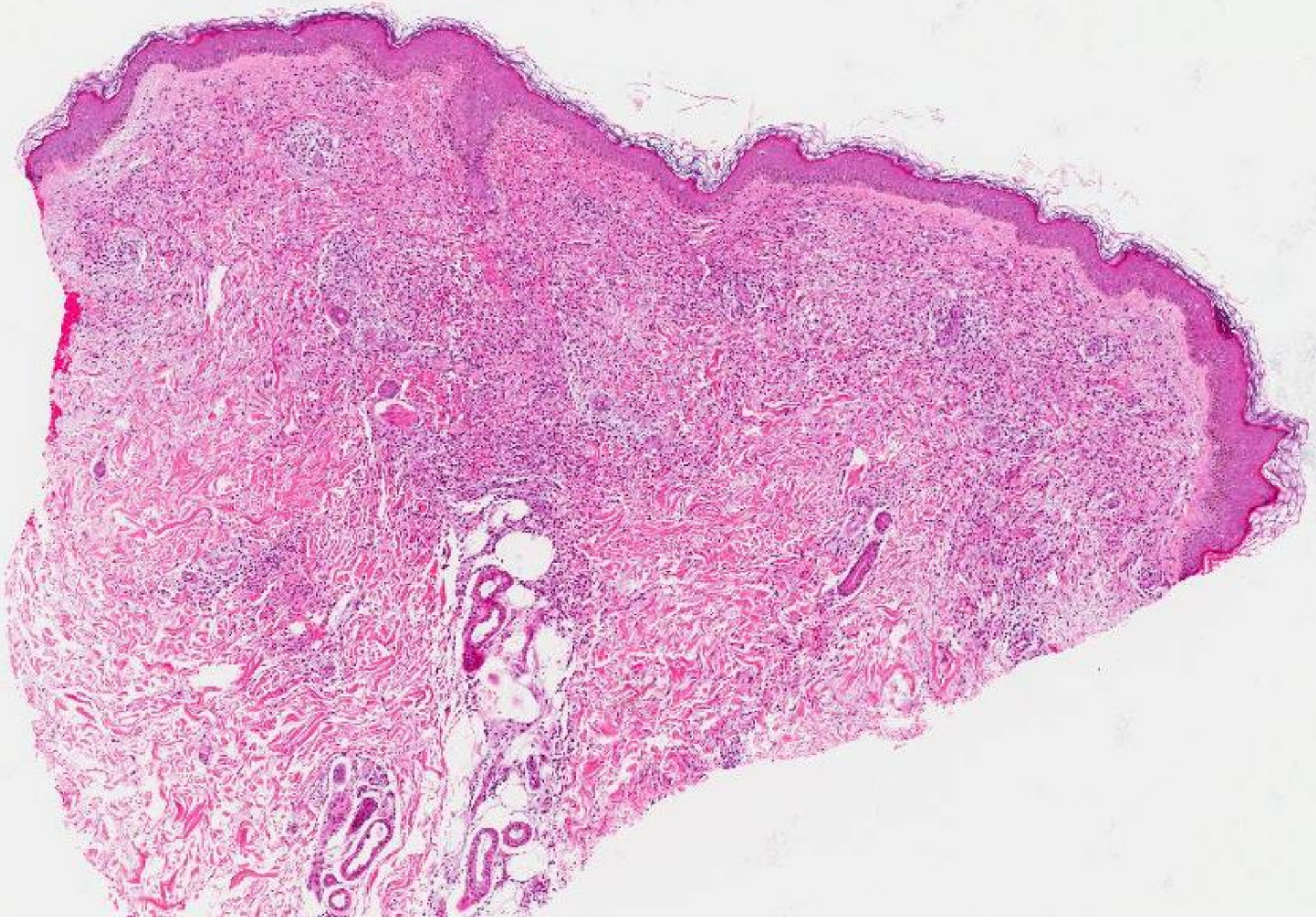


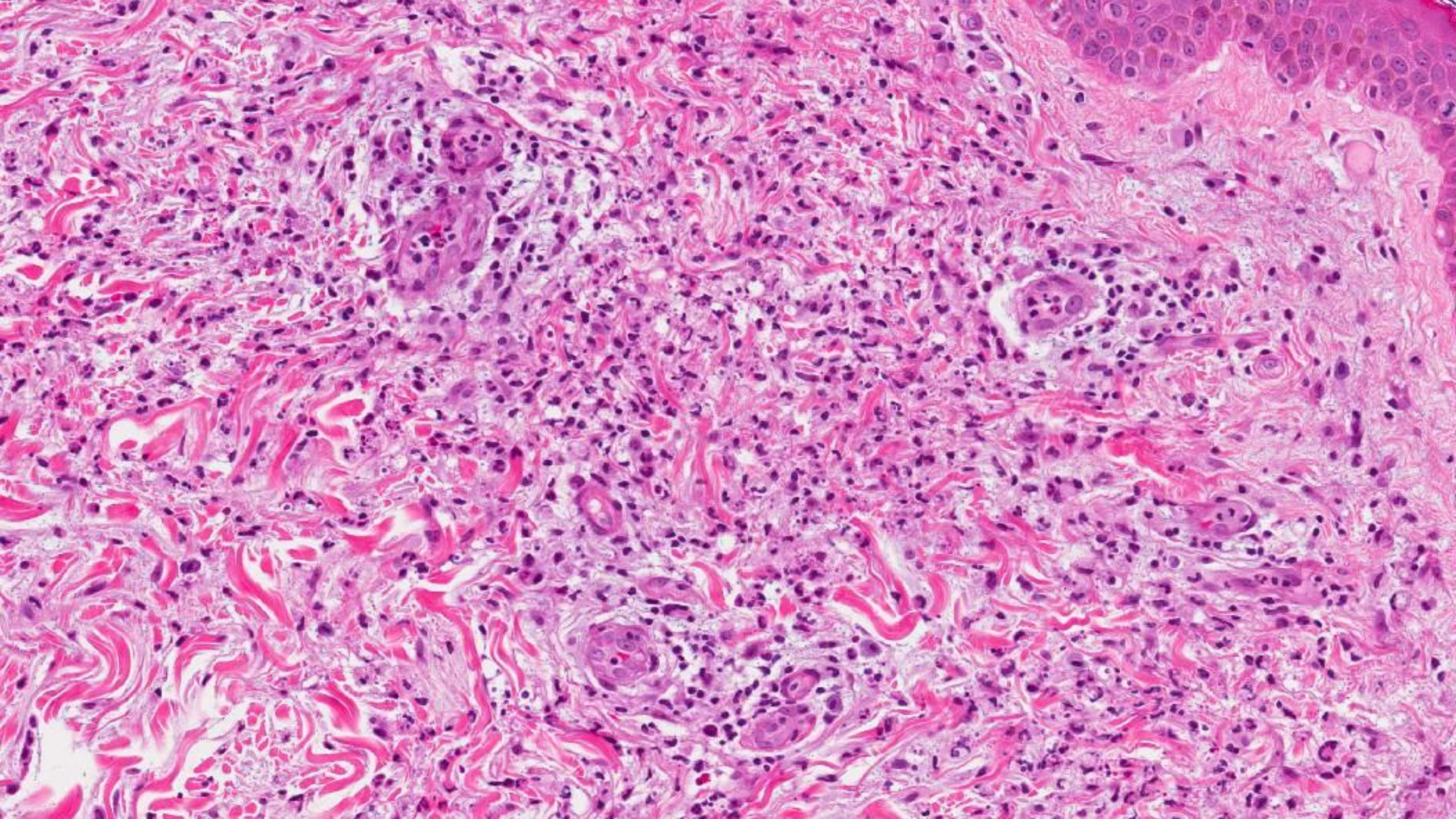
Case 4

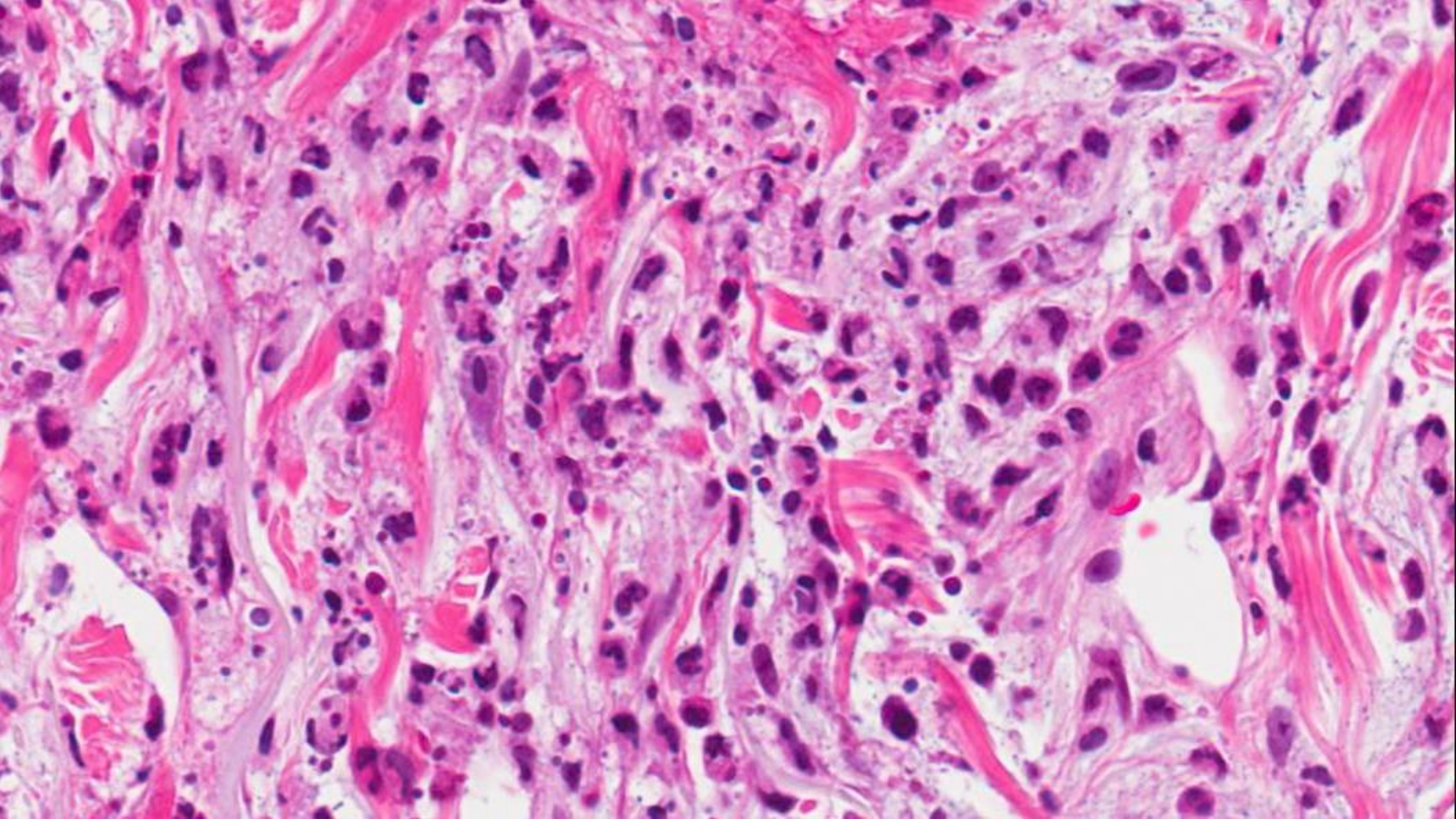


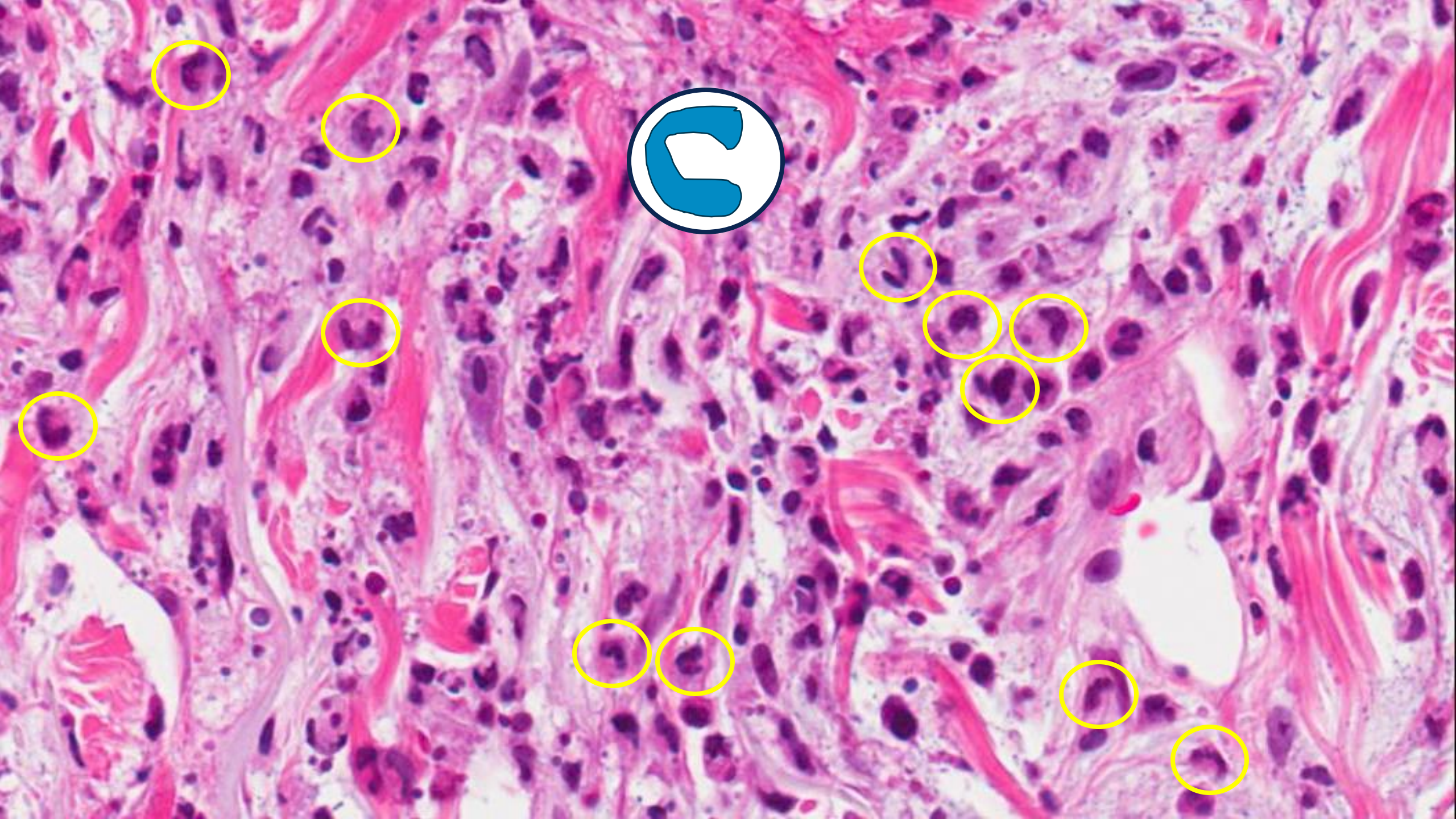
Case 1

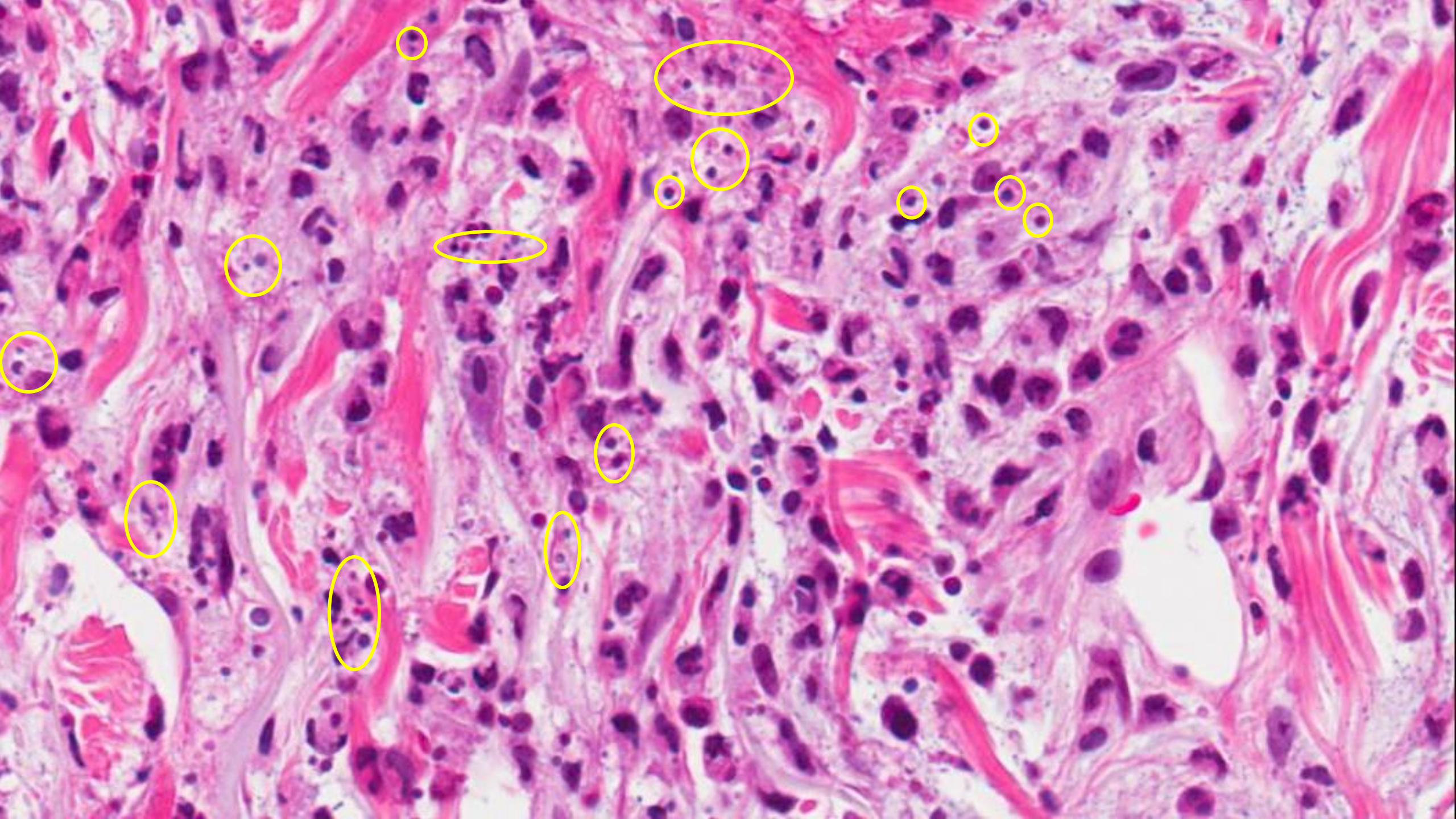
- 68-year-old male
- Recurrent fever
- Urticated papules over the chest and limbs

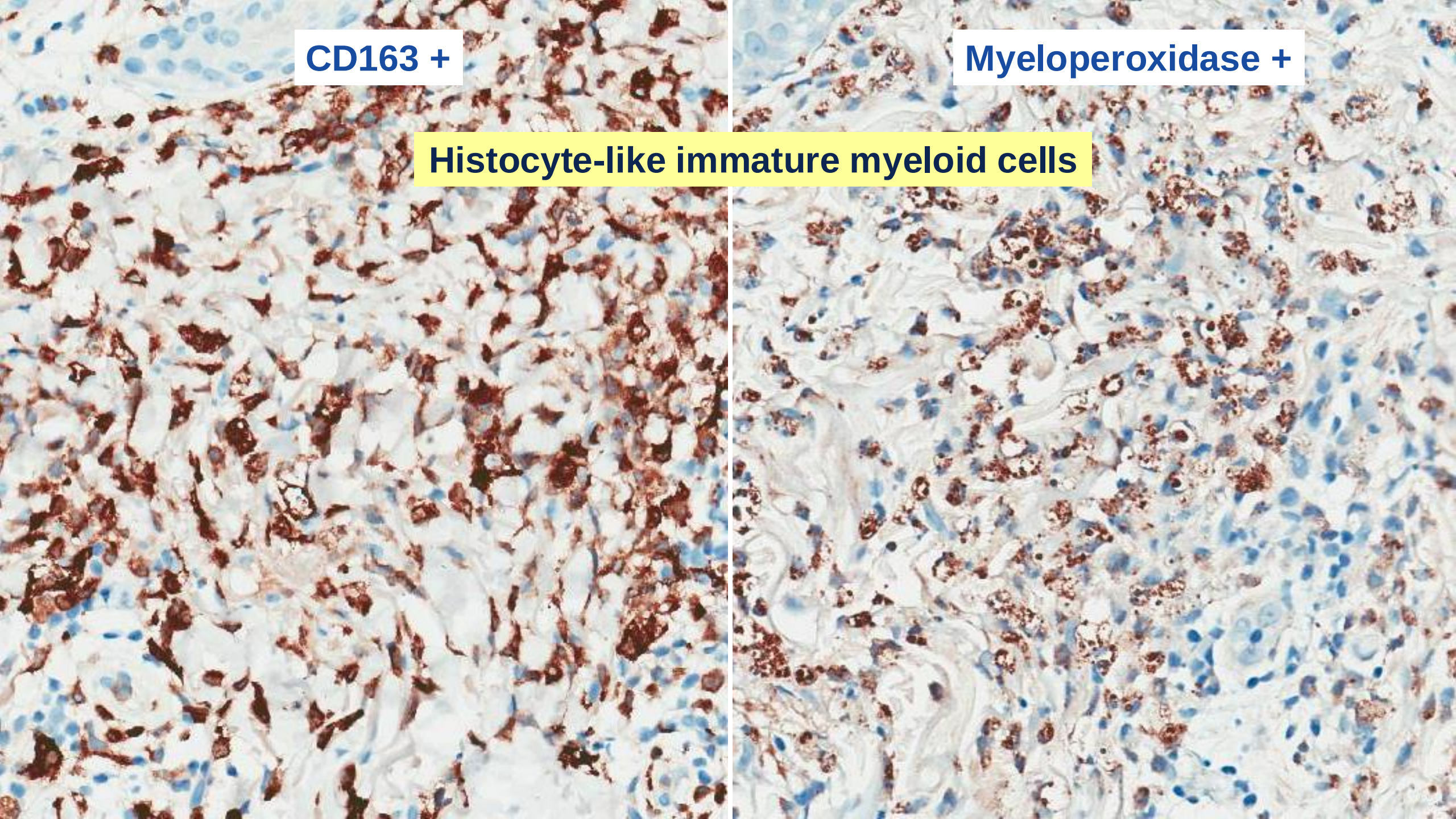











CD163 +
Myeloperoxidase +
Histocyte-like immature myeloid cells

CD163+, MPO+ histiocyte-like immature myeloid cells

- Histiocytoid Sweet syndrome

Systemic involvement

- Cervical lymphadenopathy
- Migratory arthralgia
- Relapsing polychondritis
- Anterior scleritis
- Right femoral vein DVT and Pulmonary embolism
- Anaemia with macrocytosis

Investigations

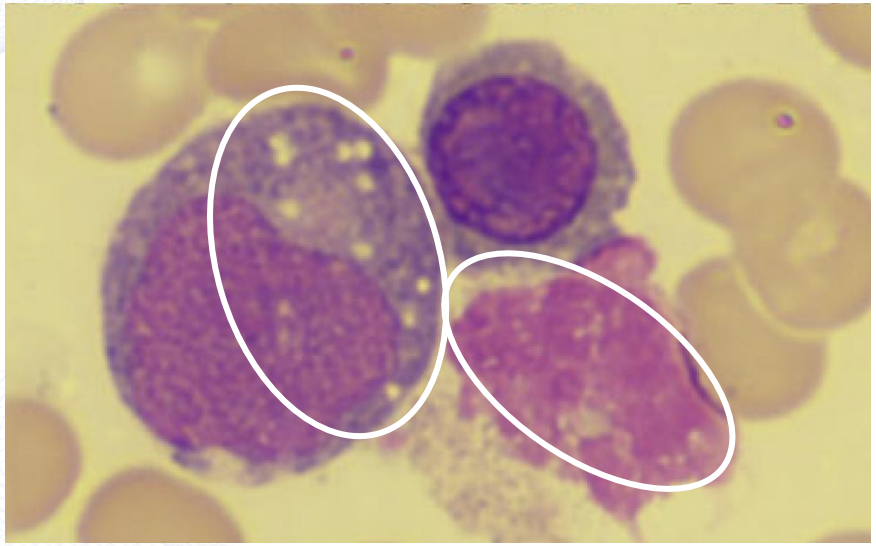
Bone marrow aspirate:

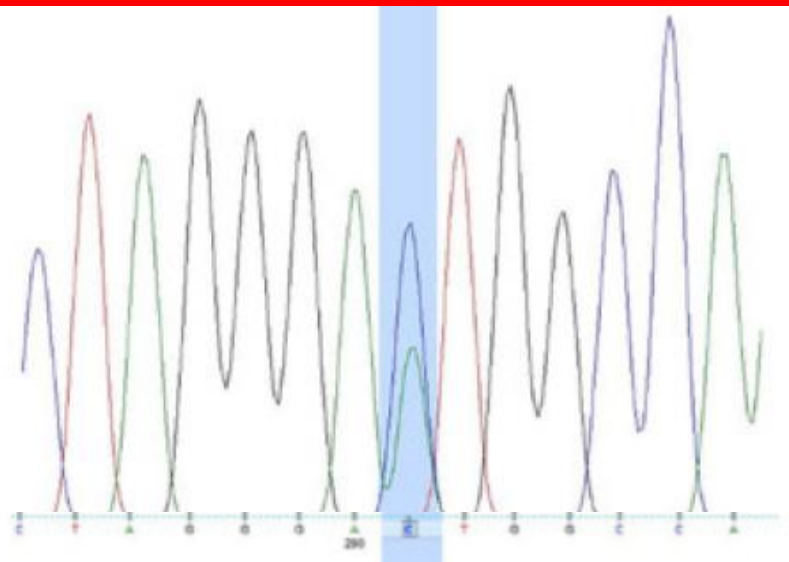
Vacuoles in the cytoplasm of myeloid and erythroid precursors

Sanger sequencing:

Somatic missense mutation UBA1 c. 121A>C, p.(Met41Leu)

VEXAS syndrome with histiocytoid Sweet syndrome





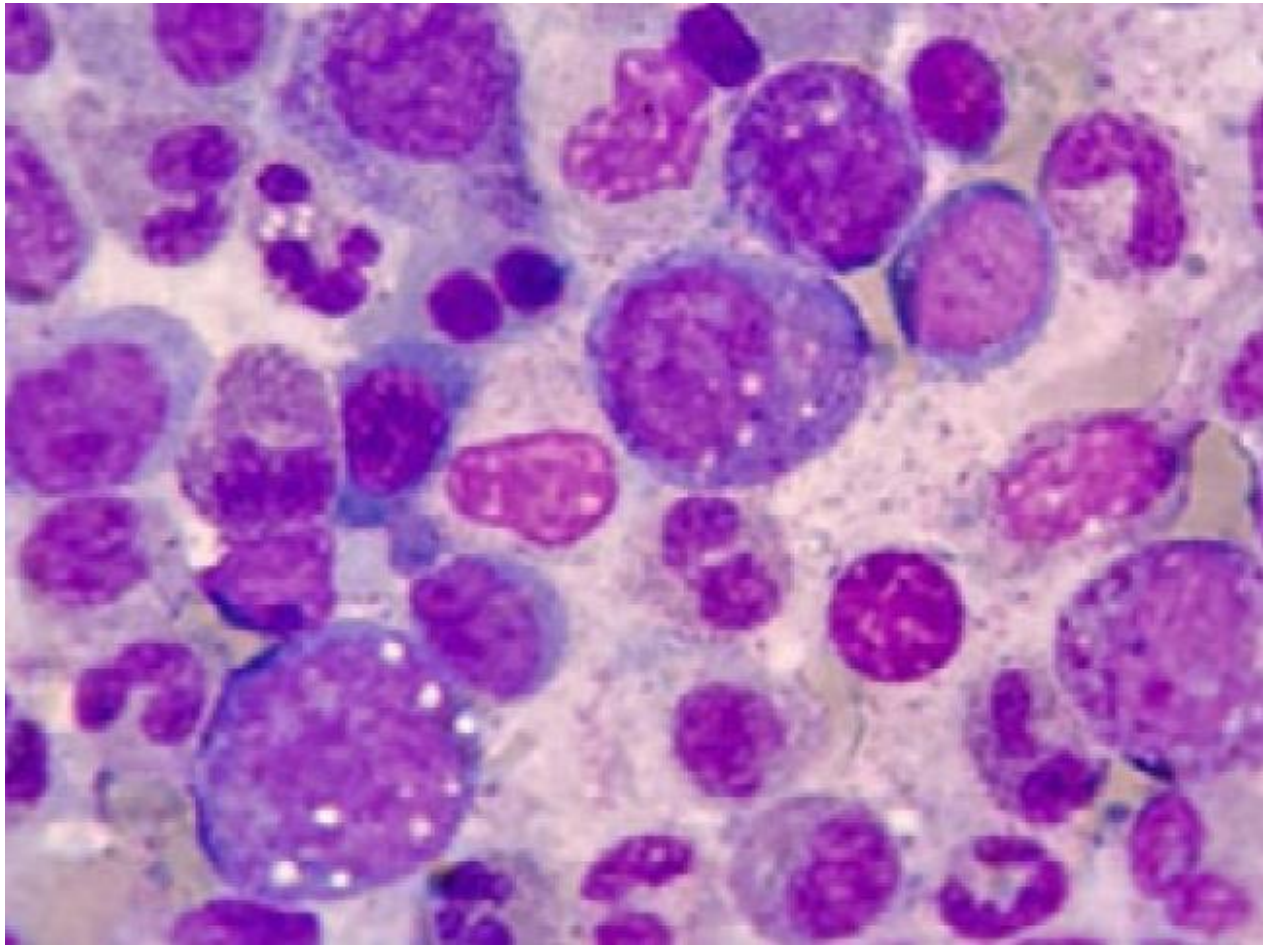
VEXAS syndrome

- **VEXAS** = **V**acuoles, **E**1 enzyme, **X**-linked, **A**utoinflammatory, **S**omatic
- First described in 2020
- Typically occurs in men in their 60s-70s
- Multiorgan autoinflammatory condition
- Somatic mutations in the UBA1 gene located on the X chromosome
- UBA1 encodes for the ubiquitin-activating enzyme E1 (catalyzes the first step in the ubiquitination reaction)

VEXAS syndrome

- Characteristic vacuoles in bone marrow myeloid and erythroid precursor cells

- Sensitive for the diagnosis of VEXAS



Loeza-Uribe MP, et al. VEXAS syndrome: Clinical manifestations, diagnosis, and treatment. Reumatol Clin (Engl Ed). 2024 Jan;20(1):47-56.

Research

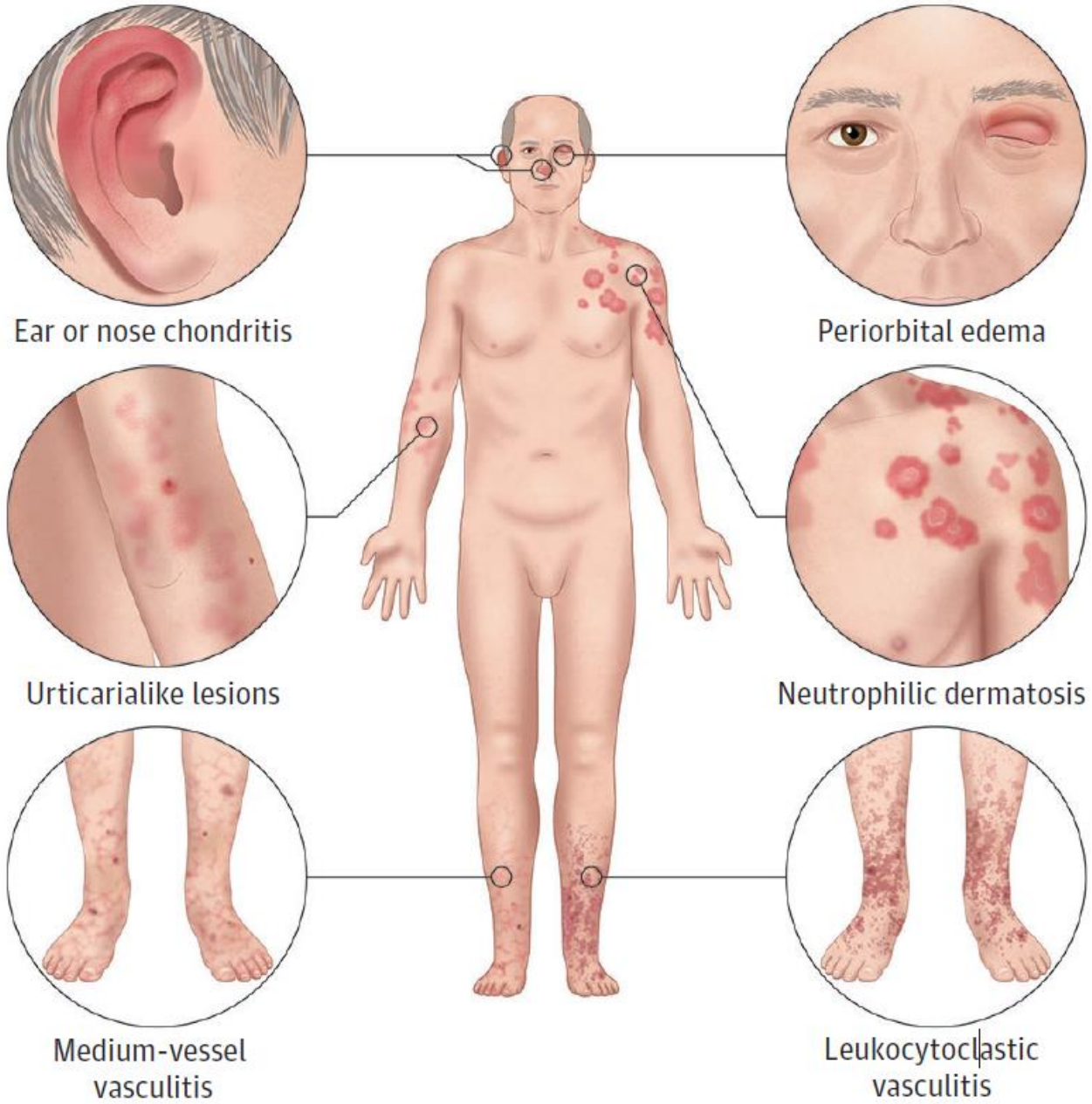
JAMA Dermatology | Original Investigation

Skin Manifestations of VEXAS Syndrome and Associated Genotypes

Isabella J. Tan, BS; Marcela A. Ferrada, MD; Serene Ahmad, MD; Alice Fike, MSN; Kaitlin A. Quinn, MD, MHS; Emma M. Groarke, MD; David B. Beck, MD, PhD; Jill Allbritton, MD; Leslie Castelo-Soccio, MD, PhD; Neal S. Young, MD; Bhavisha A. Patel, MD; Peter C. Grayson, MD, MSc; Edward W. Cowen, MD, MHSc

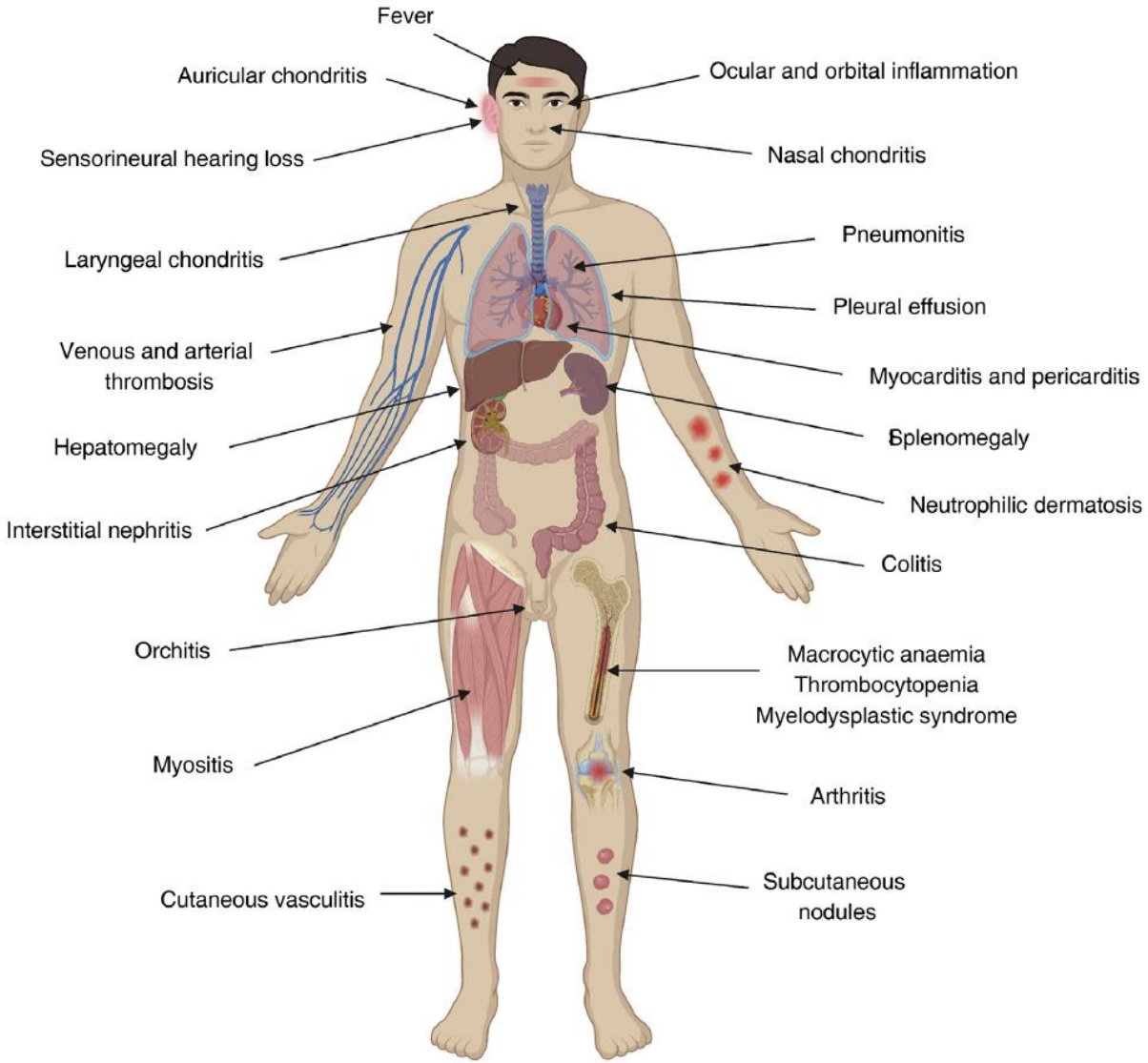
Tan IJ, Ferrada MA, Ahmad S, et al. JAMA Dermatol. 2024 Aug 1;160(8):822-829

- Study of 112 patients with genetically confirmed UBA1 mutation, **skin involvement was present in 83% patients** and was the **presenting feature in 61%**



Tan IJ, et al. Skin Manifestations of VEXAS Syndrome and Associated Genotypes. JAMA Dermatol. 2024;160(8):822-829

Multiorgan, autoinflammatory



More common Associations	Frequency (%)
Constitutional symptoms (eg. fever, weight loss)	88%
Skin involvement	83%
Pulmonary disease	81%
Arthritis	57%
Eye disease	54%
Ear or nose chondritis	48%
Thromboembolic disease (eg. DVT)	38%
Hematologic disorder (eg. myeloma, MDS etc)	21%
Audio-vestibular disease	21%

Tan IJ, et al. Skin Manifestations of VEXAS Syndrome and Associated Genotypes. JAMA Dermatol. 2024;160(8):822-829

Multiorgan, autoinflammatory

Laboratory abnormalities, No./total No. (%)	
Elevated ESR	86/86 (100)
Elevated C-reactive protein	89/89 (100)
Macrocytic anemia	95 (85)
Thrombocytopenia	69 (62)
Leukopenia	69 (62)

Older male patient

Neutrophilic dermatosis

(esp. histiocytoid Sweet's)

VEXAS

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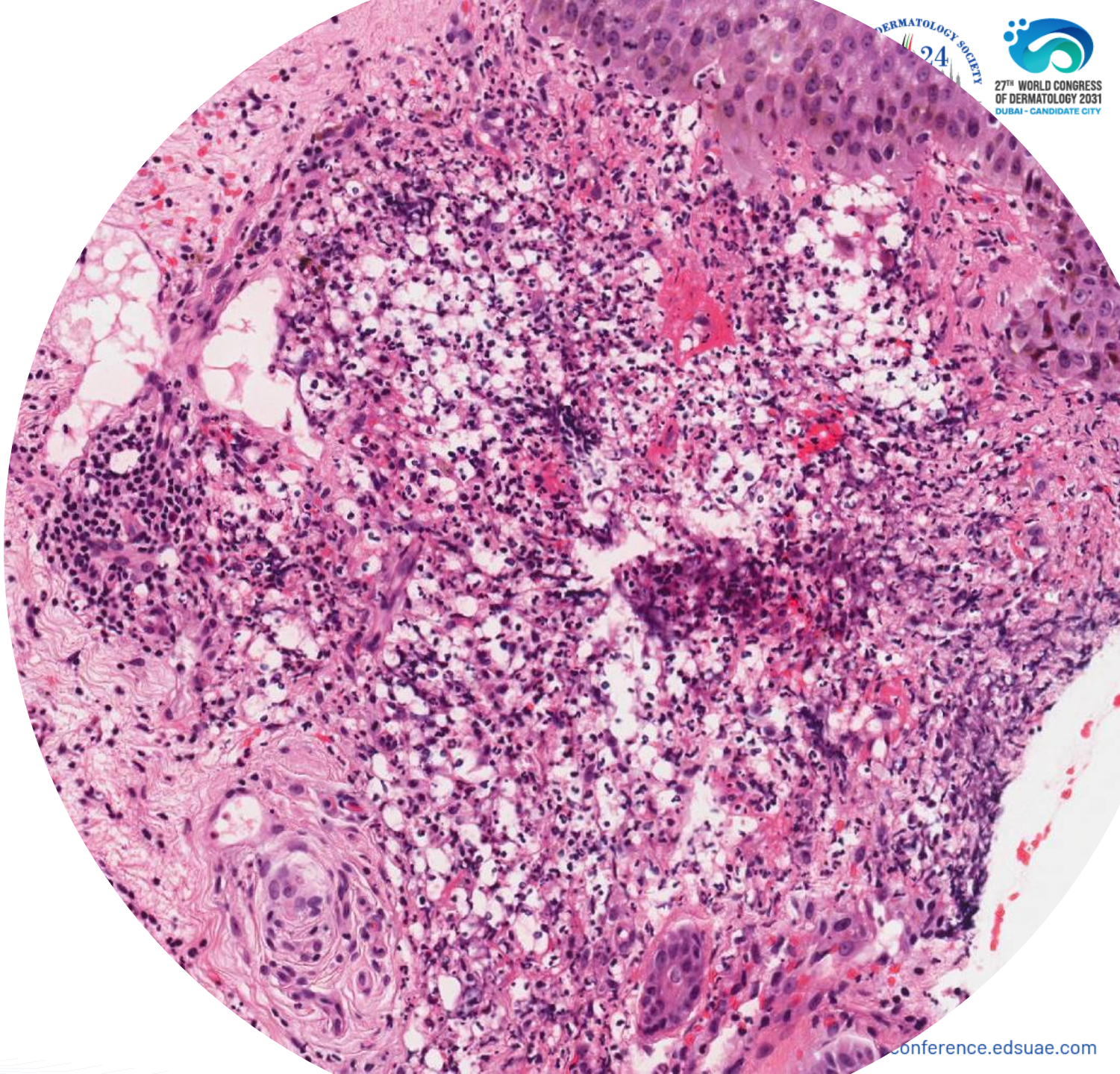
Tan IJ, et al. Skin Manifestations of VEXAS Syndrome and Associated Genotypes. JAMA Dermatol. 2024;160(8):822-829

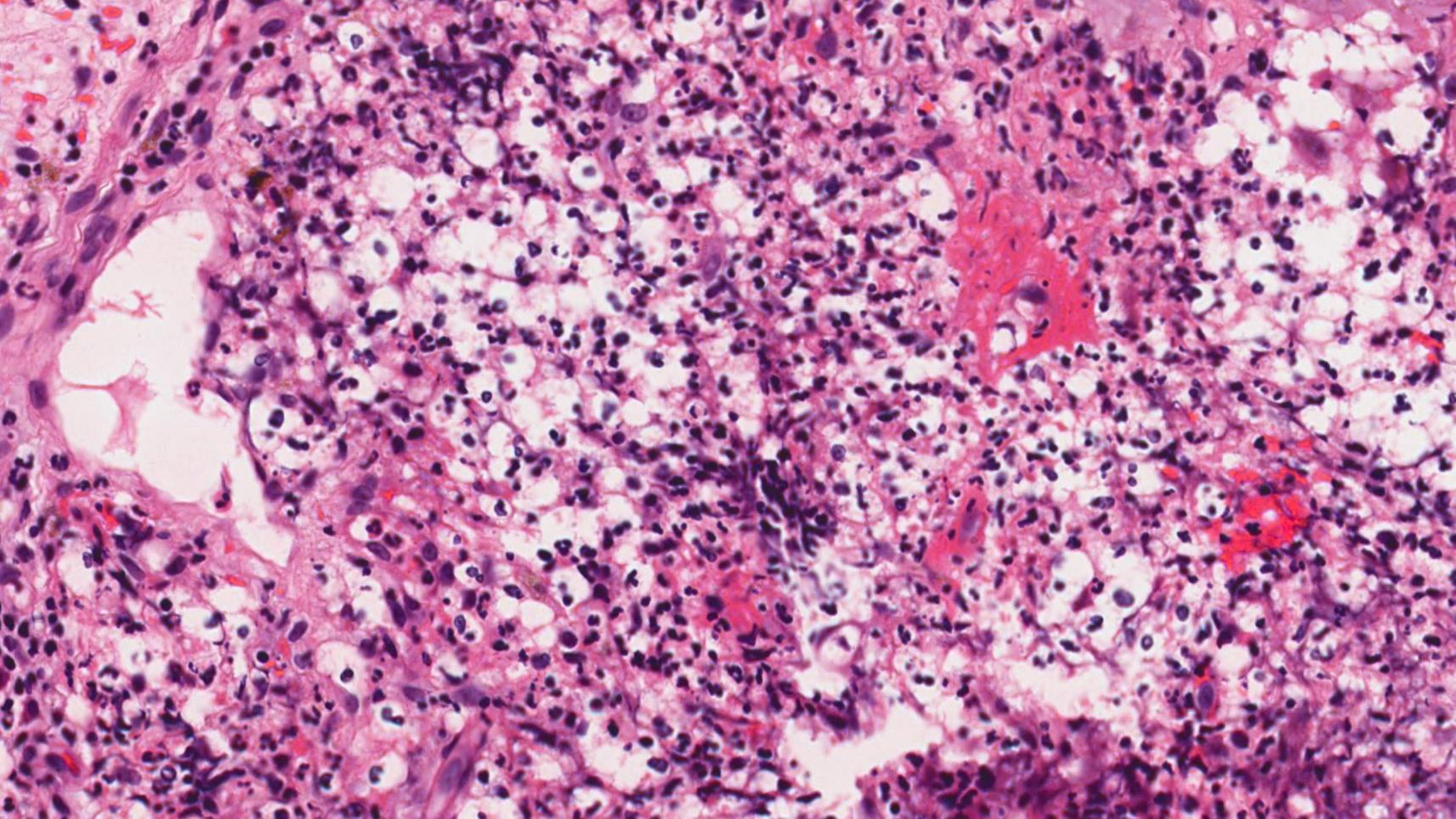
Case 2

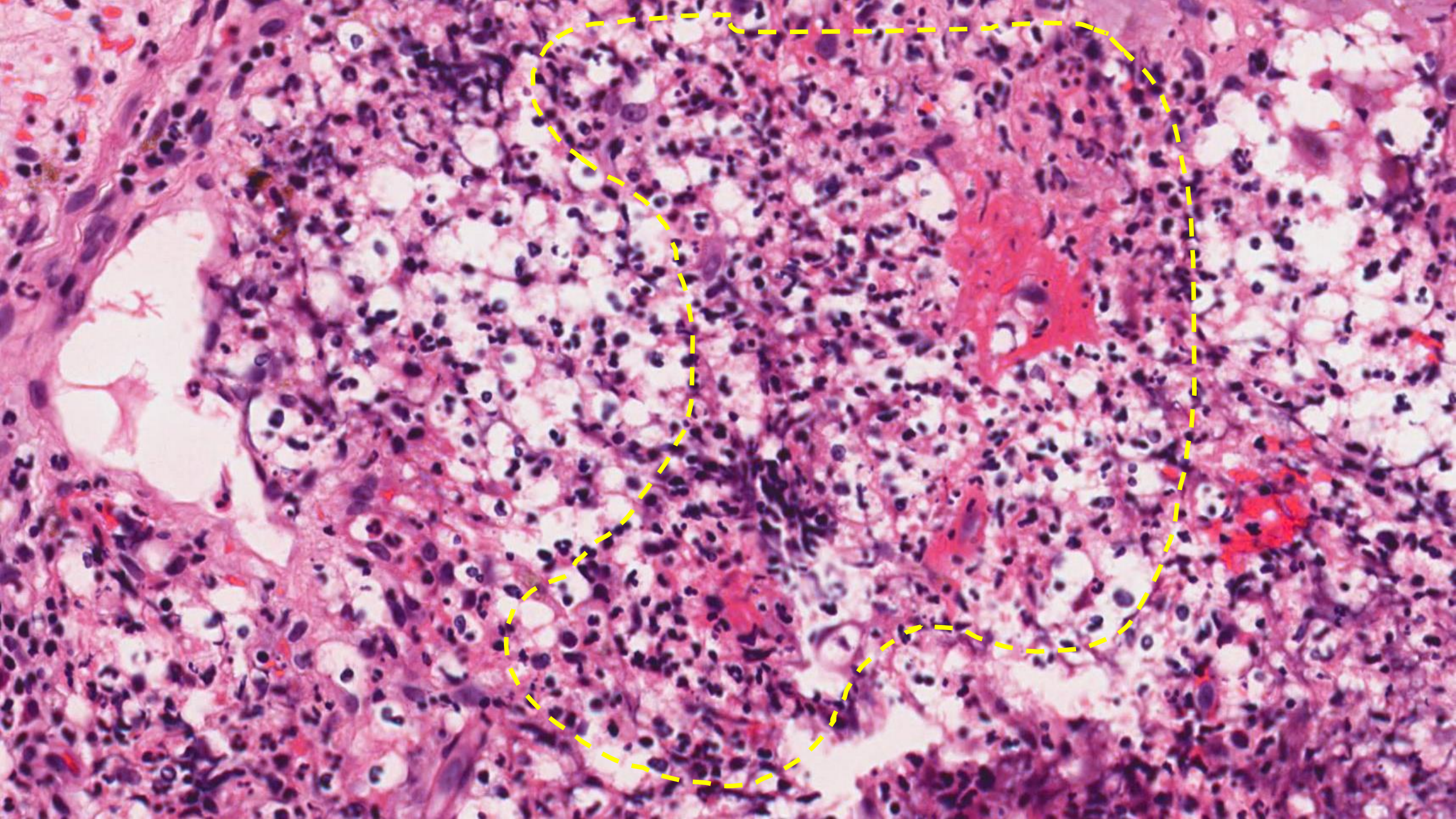
- 68-year-old woman with a history of end-stage renal failure (ESRF)
- Admitted for pyrexia of unknown origin

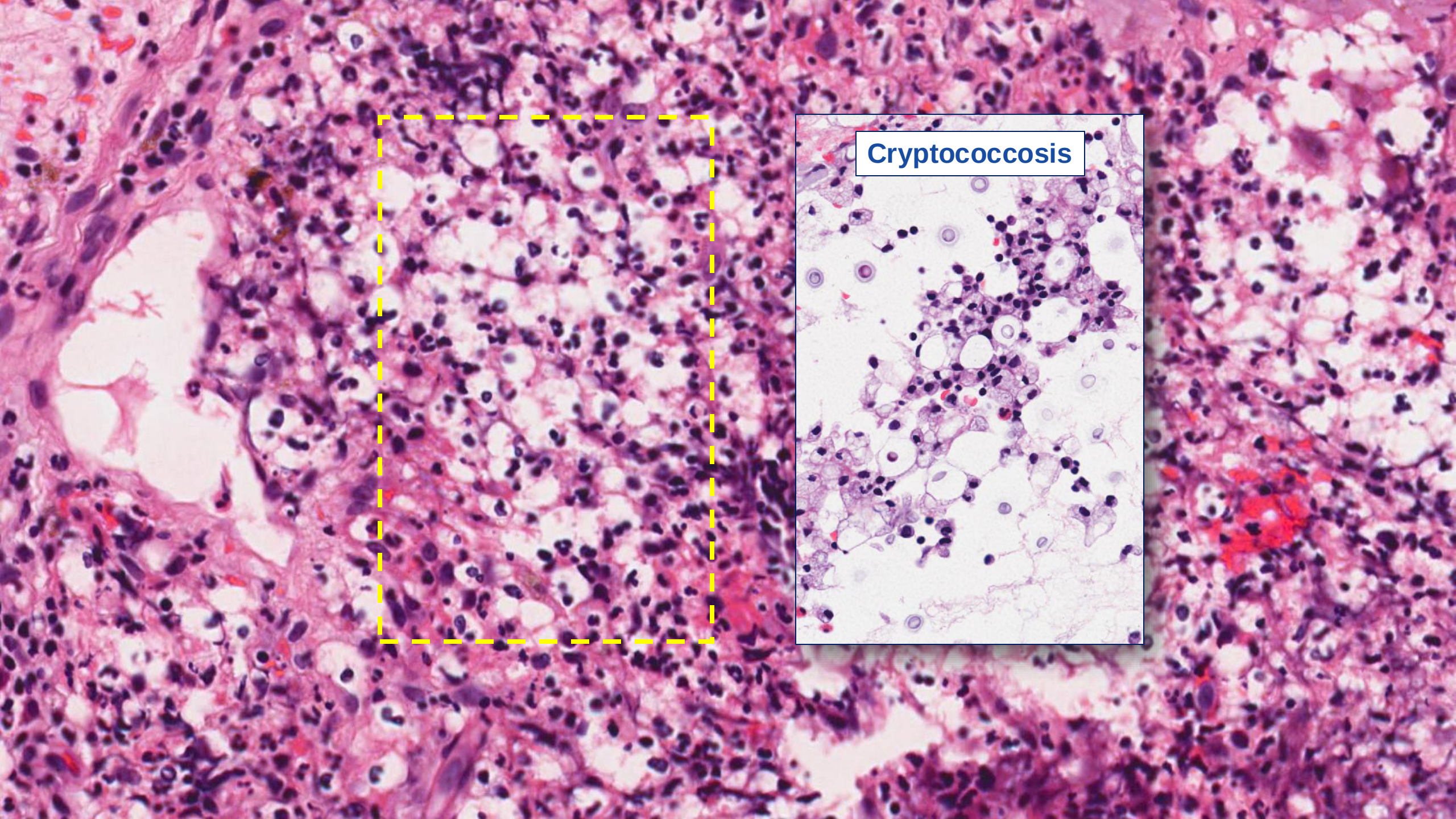
6 days into admission …

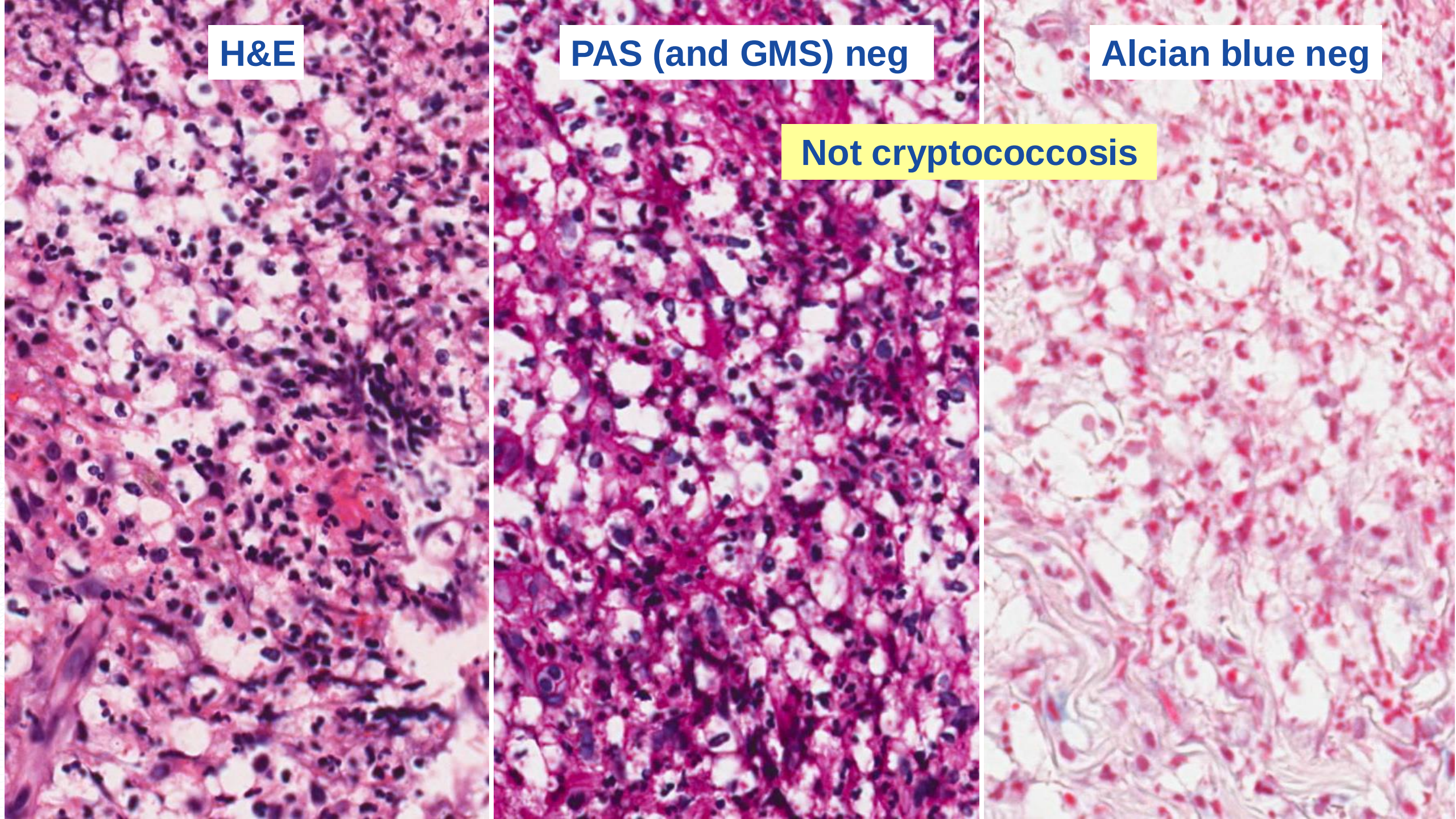
Courtesy of Dr Joel Lim





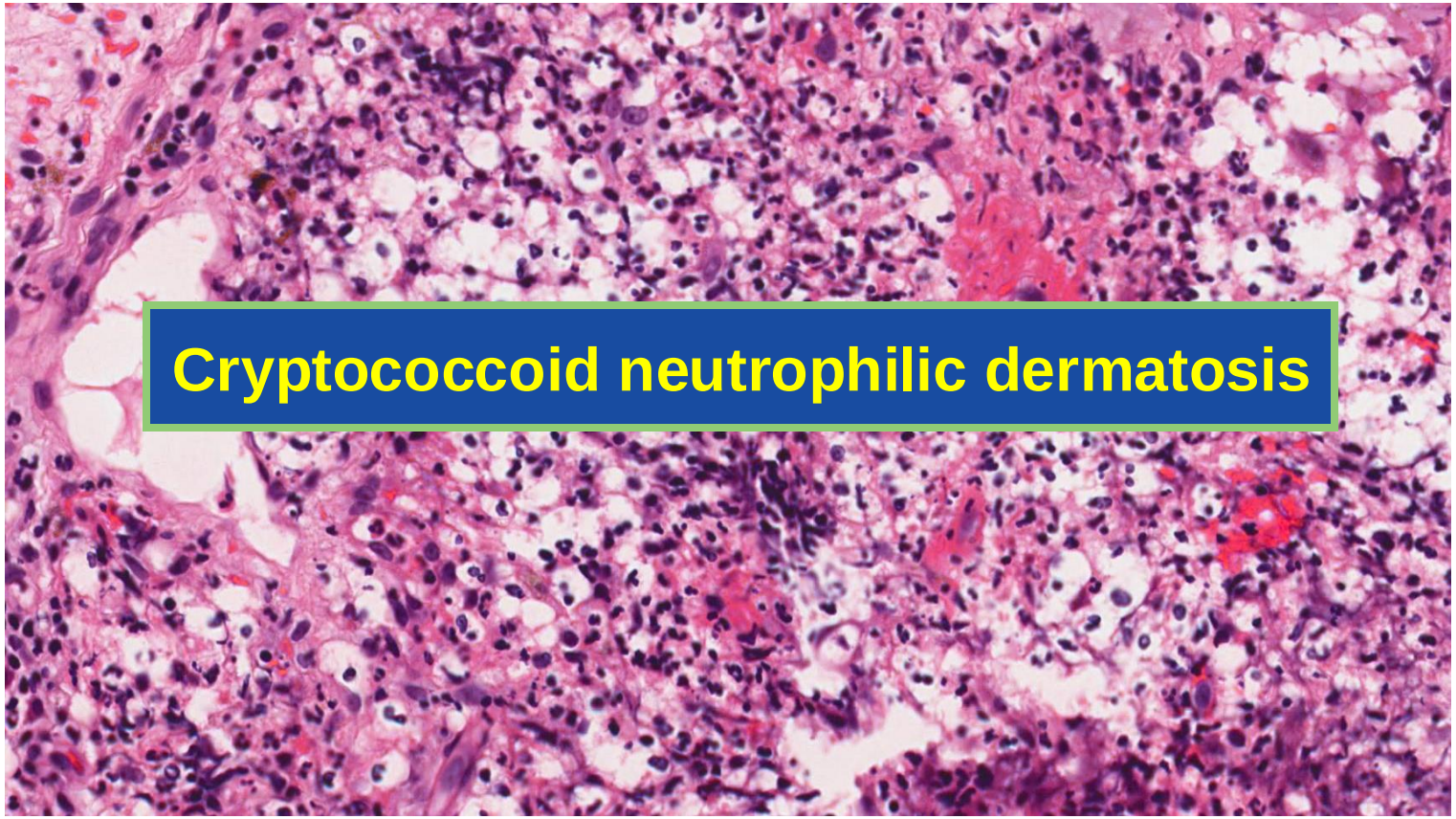



Cryptococcosis


H&E
PAS (and GMS) neg
Alcian blue neg
Not cryptococcosis

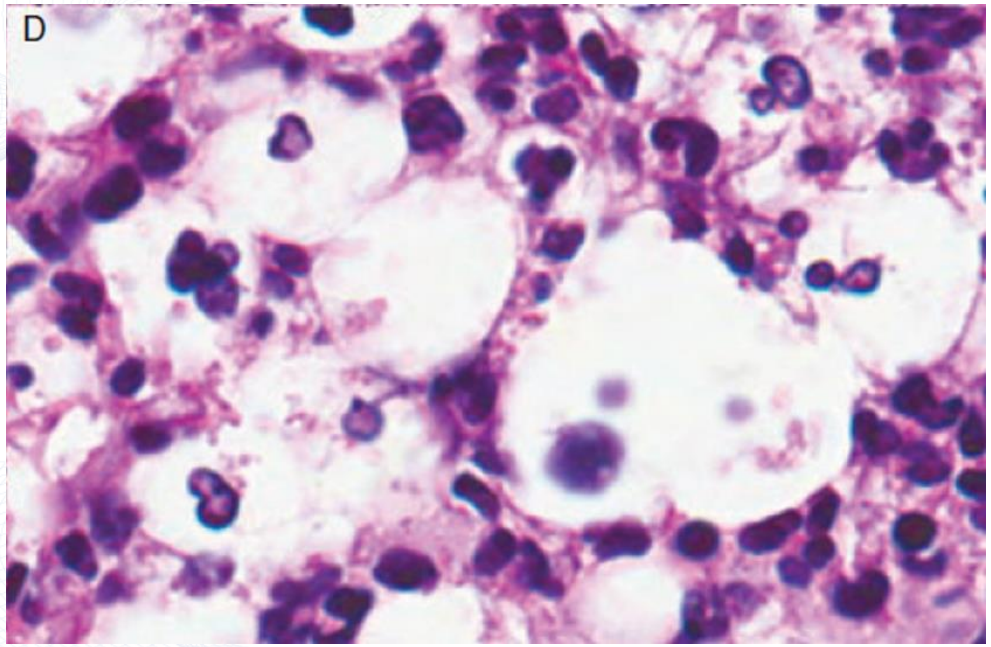
Investigations

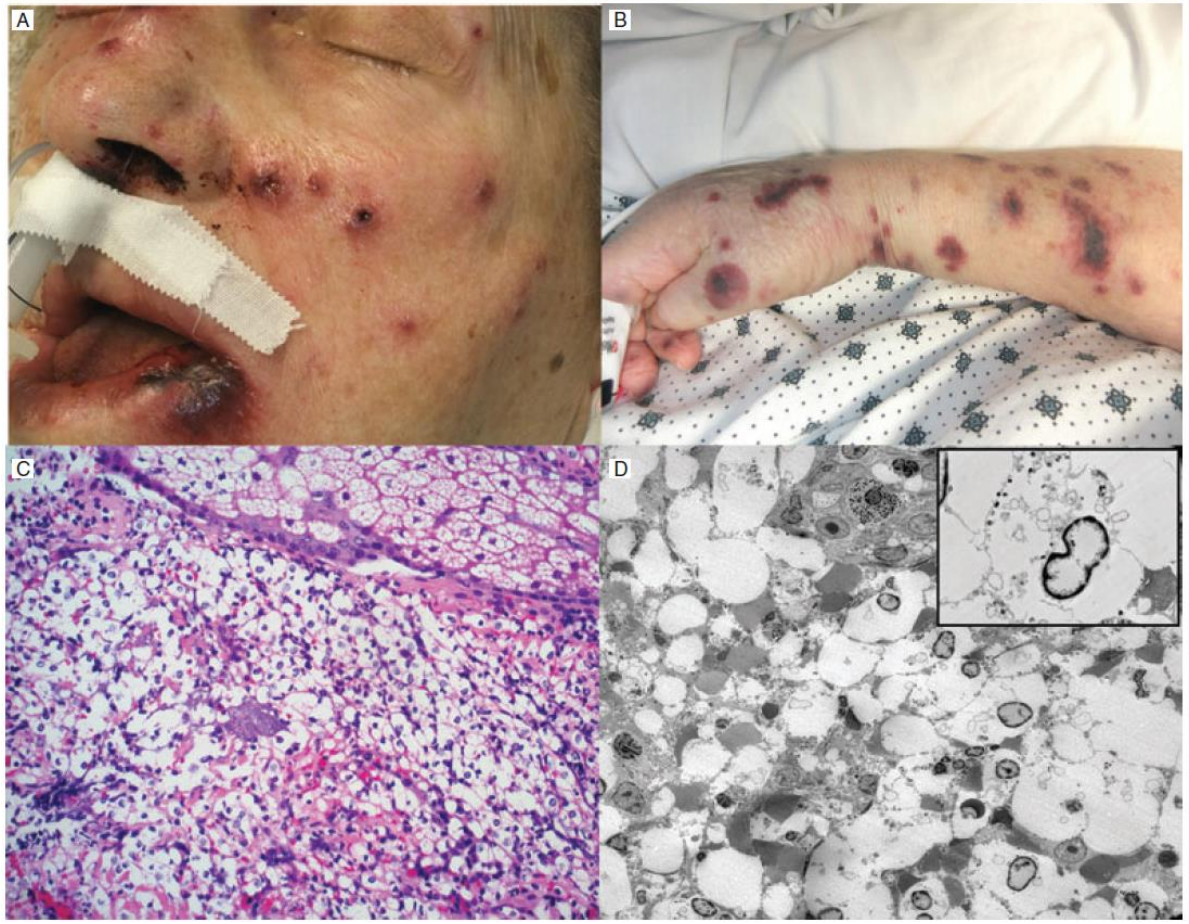
- Fungal culture and serum cryptococcal antigen were negative



Cryptococcoid neutrophilic dermatosis

Morphologic mimickers of *Cryptococcus* occurring within inflammatory infiltrates in the setting of neutrophilic dermatitis: a series of three cases highlighting clinical dilemmas associated with a novel histopathologic pitfall





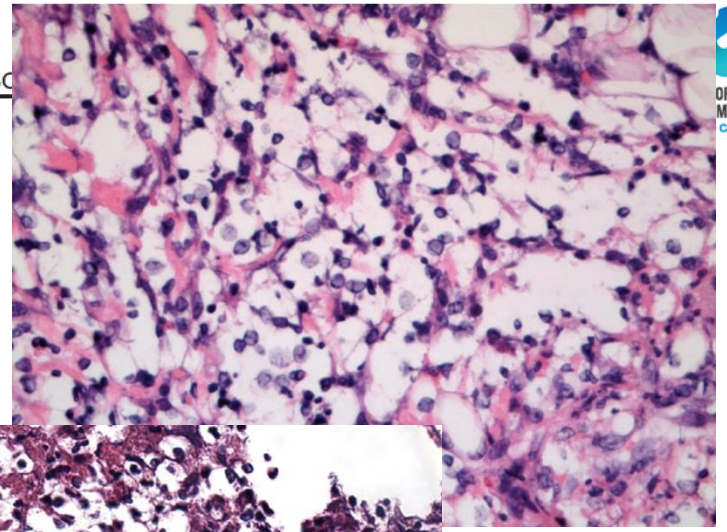
TEM: Vacuolated spherical structures

= Apoptotic degenerate neutrophils

Ko JS, Fernandez AP, Anderson KA, et al. J Cutan Pathol. 2013;40(1):38-45.

Cryptococcoid Sweet's syndrome: Two reports of Sweet's syndrome mimicking cutaneous cryptococcosis

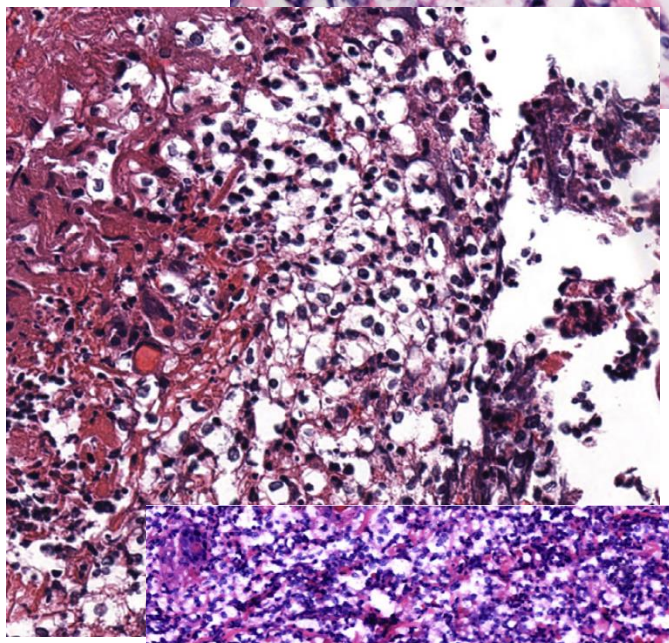
Janice Wilson MD[1] | Kristyna Gleghorn BS[2] | Brent Kelly MD[1]



CASE REPORT

A hydralazine-induced triumvirate: Lupus, cutaneous vasculitis, and cryptococcoid Sweet syndrome

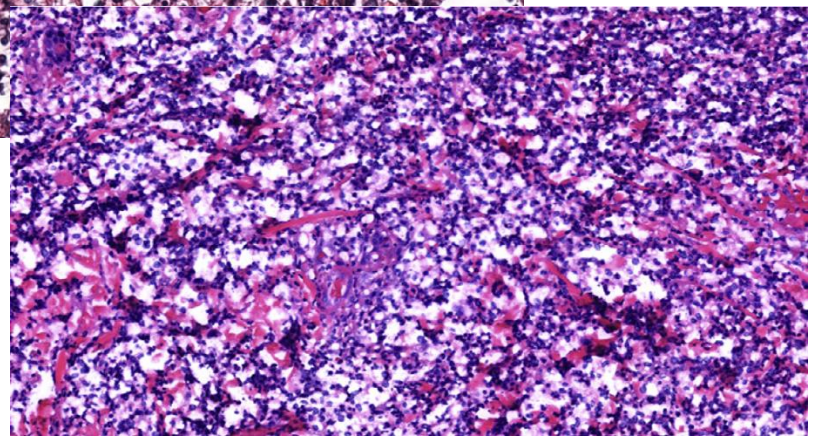
Meliha Skaljic, BA,[a] Ashwin Agarwal, MD,[b] Robert J. Smith, MD,[b] Cuong V. Nguyen, MD,[b]

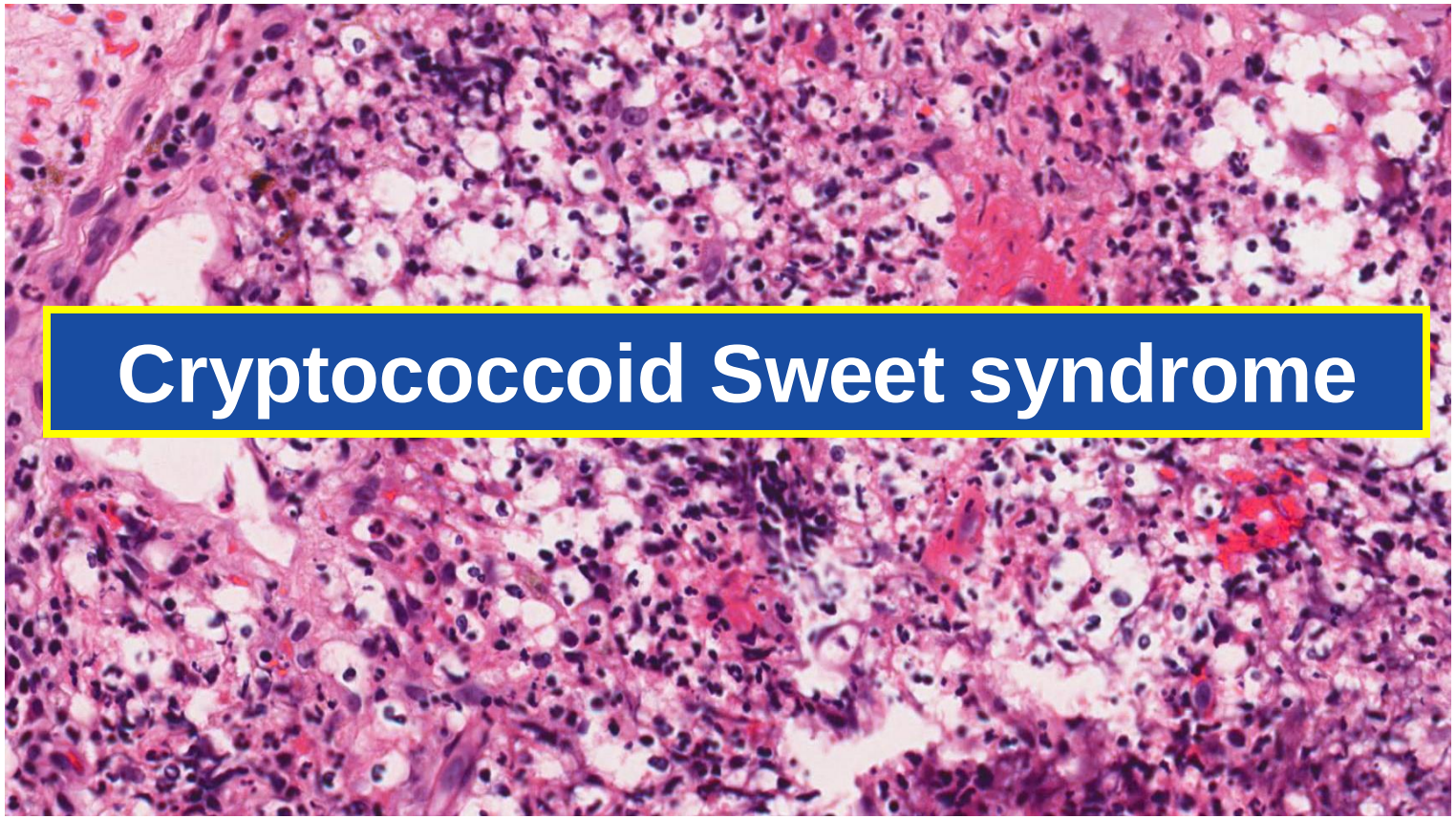


CASE SERIES

Bullous hemorrhagic Sweet syndrome with cryptococcoid neutrophils in patients positive for antineutrophil cytoplasmic antibody without primary vasculitis

Alex Sherban, BM,[a] Collin Fuller, MD,[b] Mansha Sethi, MD,[b] Eleni McGeehin, MD,[b]
Dawn Hirokawa, MD, MPH,[c] Courtney Guerrieri, MD,[c] Jason Lee, MD,[b] and Sherry Yang, MD[b]
Philadelphia, Pennsylvania and Newark, Delaware



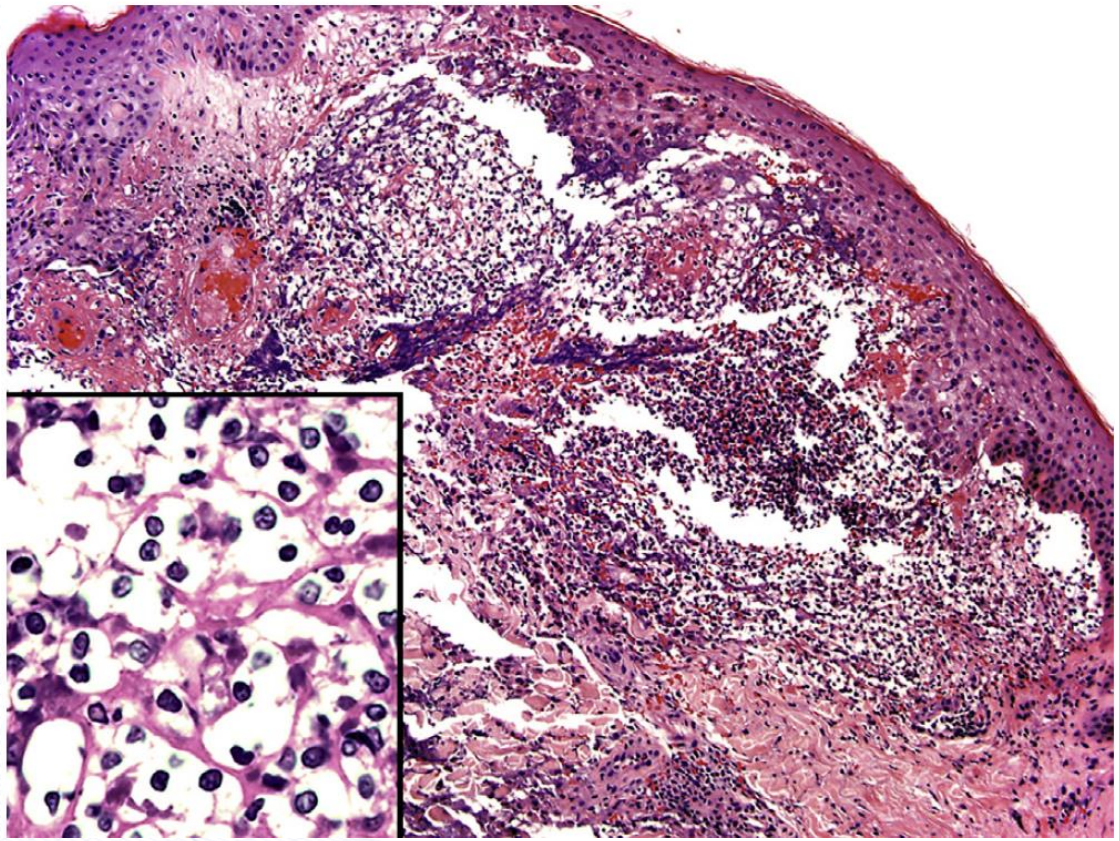


… or is it?

Acute iododerma presenting as cryptococcoid neutrophilic dermatosis

Iodine toxicity after iodinated contrast: New observations in iododerma

Mason Runge, BA,[a] Kiyanna Williams, MD,[b] Thomas Scharnitz, MD,[b] Mio Nakamura, MD,[b] Milad Eshaq, MD,[b] Jennifer Mancuso, MD,[b] Yolanda Helfrich, MD,[b] Scott C. Bresler, MD, PhD,[b,c] Aleodor Andea, MD,[b,c] May P. Chan, MD,[b,c] and Lori Lowe, MD[b,c]
Ann Arbor, Michigan



- 3 patients with **cryptococcoid neutrophilic dermatoses** on histology:
- All had **ESRF**
- All had received **iodinated contrast media** for CT scans a few days prior to skin eruption:
- **24-hour urine iodine levels** taken within 3 days after skin eruption were all in the toxic range:
  - **1st pt: 185,174 g/L**
  - **2nd pt**: greater than **488,960 g/24 hours**
  - **3rd pt**: greater than **17,920 g/24 hours**
  - (normal <851 g/24 hours).

JAAD Case Rep. 2020 Mar 25;6(4):319-322.

Investigations and further history for our patient…

- Received intravenous iohexol (iodinated contrast medium) for a CT scan 3 days prior to the onset of skin lesions

- **Iodine levels** taken 6 days into her eruption
  - Serum : **12 000 IU/L** (<50 IU/L)
  - Urine: **>15 000 IU/L** (<150 IU/L)

Iodine toxicity → Acute iododerma

JAAD Case Rep. 2020:25;6:319-322

Br J Dermatol. 2014;170:1377-9

Our case

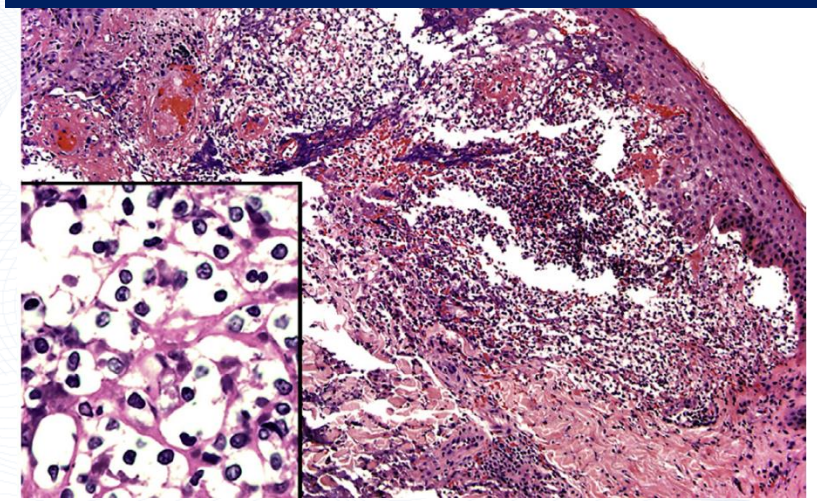
J Cutan Pathol. 2023;50:29-34

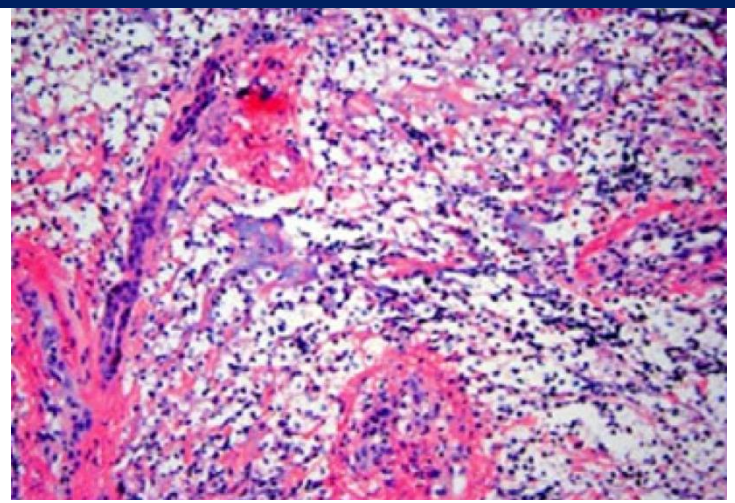
Acute iododerma

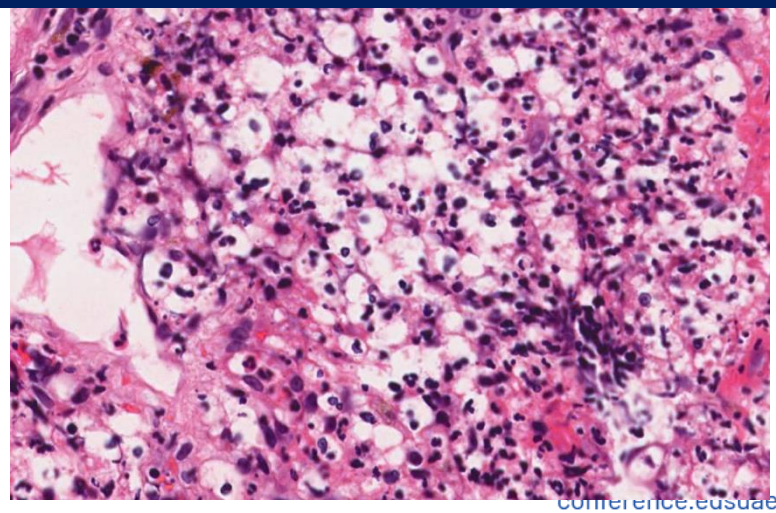
All had urine iodine levels many times the normal levels

All had renal insufficiency, had received iodinated contrast media for CT scan a few days prior

Cryptococcoid Neutrophilic Dermatosis on skin biopsy







JAAD Case Rep. 2020:25;6:319-322

Br J Dermatol. 2014;170:1377-9

Our case

J Cutan Pathol. 2023;50:29-34

Acute iododerma

Predilection for the face (toxic effects on sebaceous glands)

Acneiform, pustular and haemorrhagic bullous or nodular vegetative eruption

JAAD Case Rep. 2020:25;6:319-322

Br J Dermatol. 2014;170:1377-9

Our case

J Cutan Pathol. 2023;50:29-34

Acute iododerma

Predilection for the face (toxic effects on sebaceous glands)

Acneiform, pustular and haemorrhagic bullous or nodular vegetative eruption

Received: 11 April 2022 | Revised: 31 July 2022 | Accepted: 3 August 2022

DOI: 10.1111/cup.14310

CASE STUDY

JOURNAL OF CUTANEOUS PATHOLOGY WILEY

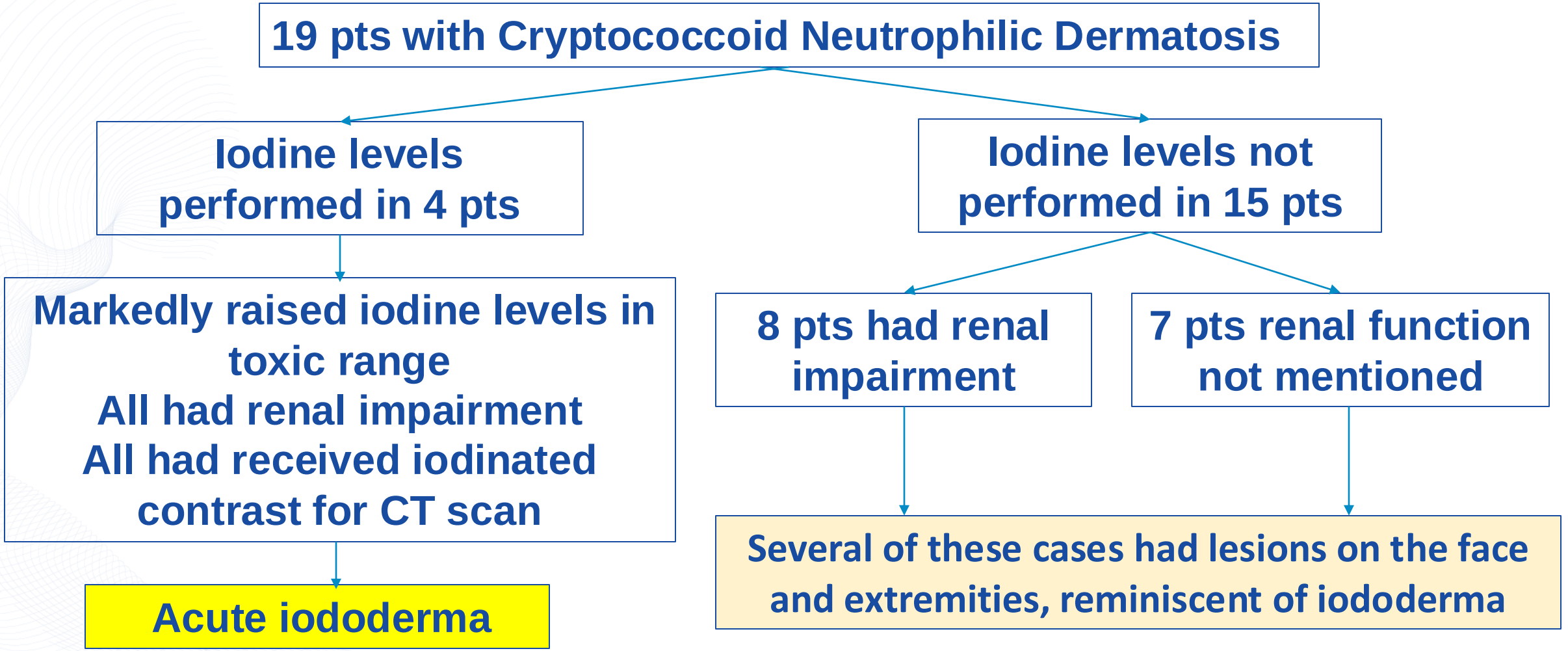
Acute iododerma presenting as cryptococcoid neutrophilic dermatosis: A clinicopathological pitfall and interesting findings gleaned from a review of the literature

Joel Hua-Liang Lim MBBS, MRCP (UK), M.Med (S'pore) |

Joyce Siong-See Lee Joyce MBBS, MRCP (UK), M.Med (Int. Med), FAMS (Dermatology), Dip. Dermatopathology (ICDP-UEMS)

J Cutan Pathol. 2023;50:29-34

Lim JH, Lee JS. Acute iododerma presenting as cryptococcoid neutrophilic dermatosis: A clinicopathological pitfall and interesting findings gleaned from a review of the literature. J Cutan Pathol. 2023;50:29-34



Cases of Cryptococcoid Sweet syndrome in the literature where exposure to iodinated compounds was not explored

?Possible cases of acute iododerma

Chronic renal impairment

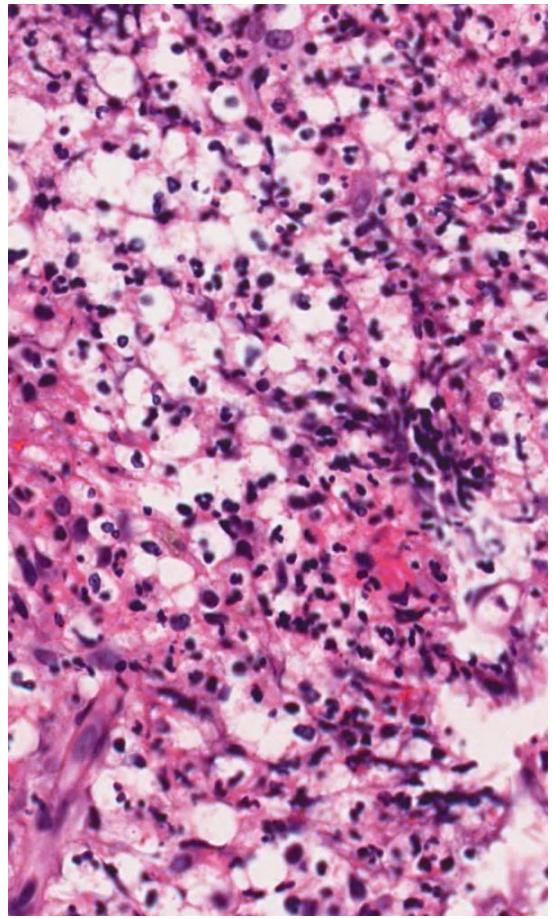
Skaljic M, Agarwal A, Smith RJ, et al. A hydralazine-induced triumvirate: Lupus, cutaneous vasculitis, and cryptococcoid Sweet syndrome. JAAD Case Rep. 2019 Oct 31;5:1006-1009

ESRF
Had CT scan
Face involvement

Sherban A, Fuller C, Sethi M, et al. Bullous hemorrhagic Sweet syndrome with cryptococcoid neutrophils in patients positive for antineutrophil cytoplasmic antibody without primary vasculitis. JAAD Case Rep. 2020 Oct 15;6(12):1196-1200

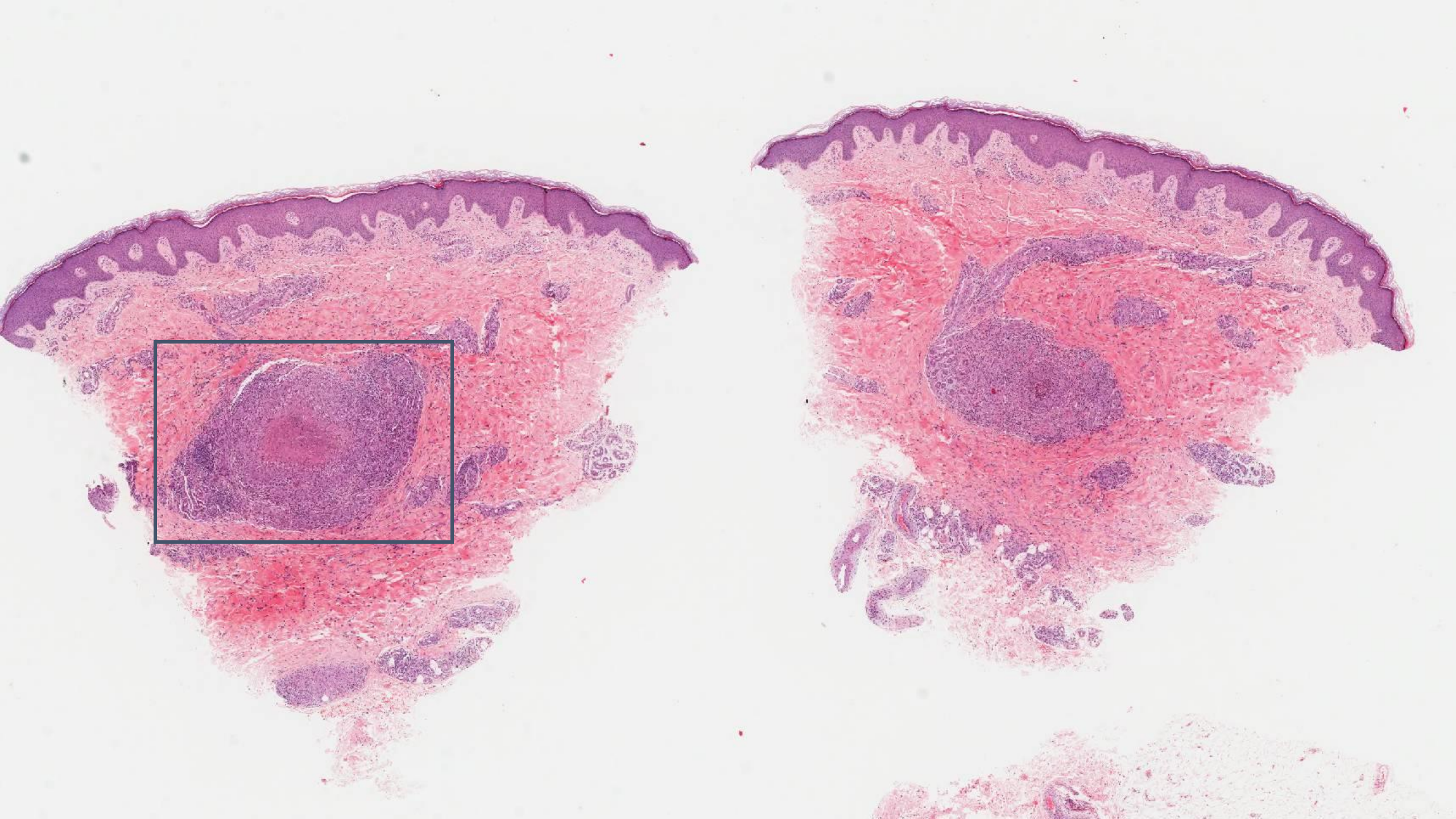
Take home message for case 2

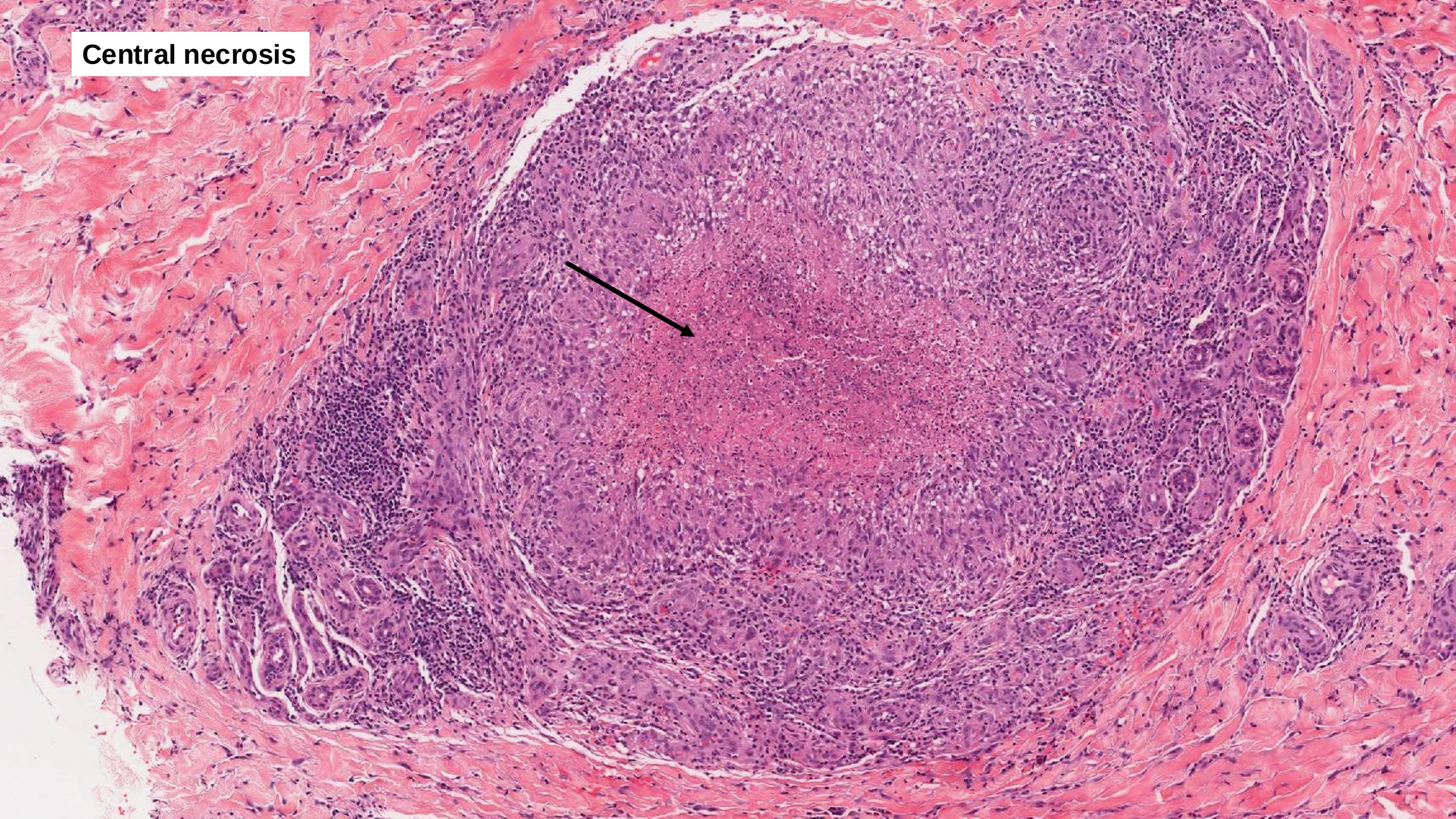
- Skin biopsy: Cryptococcoid neutrophilic dermatosis
- Enquire about recent exposure to iodinated compounds (esp. contrast used in CT scans) and renal function
- Think of **acute iododerma**
- Consider performing urine and serum iodine levels

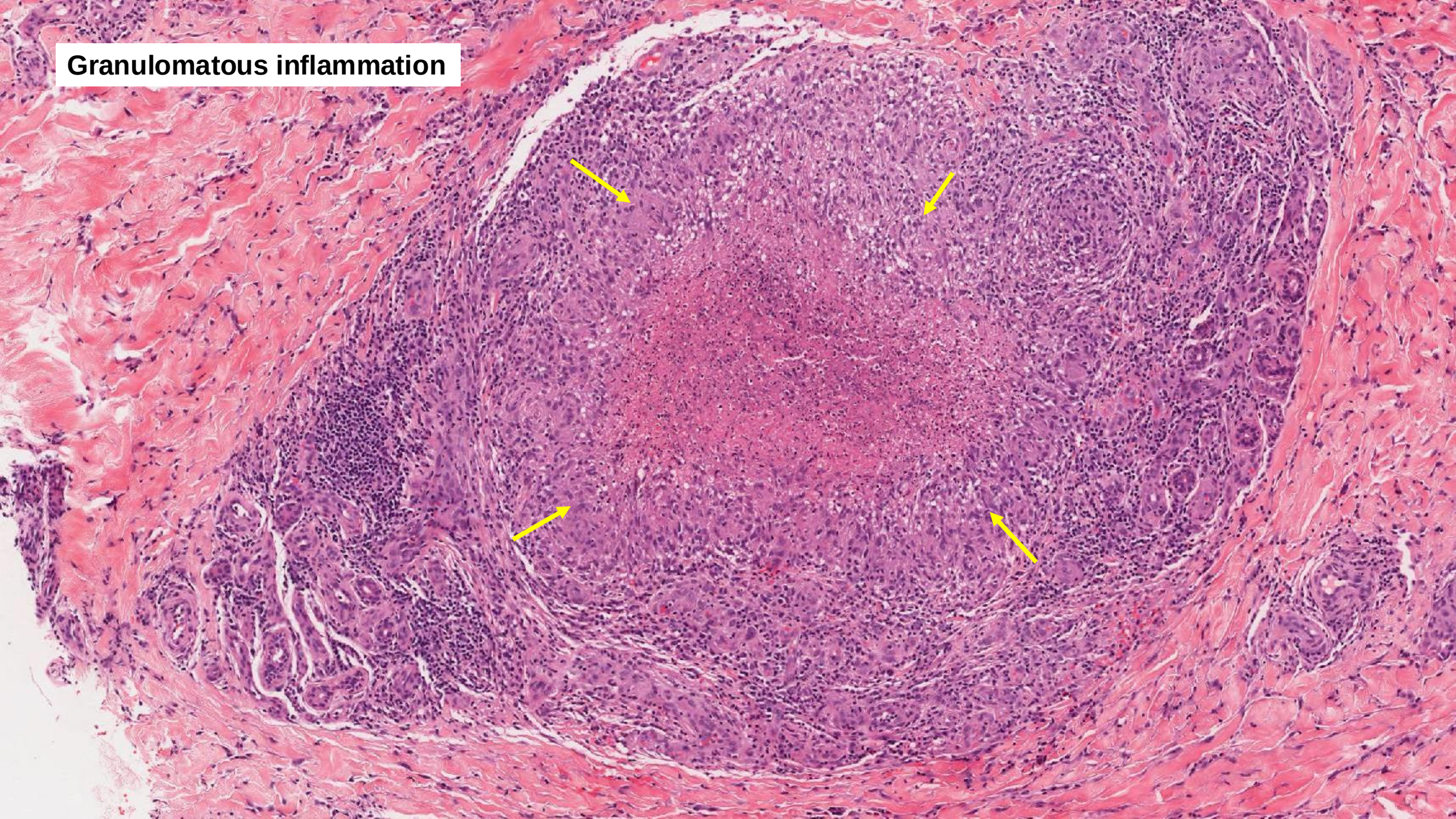


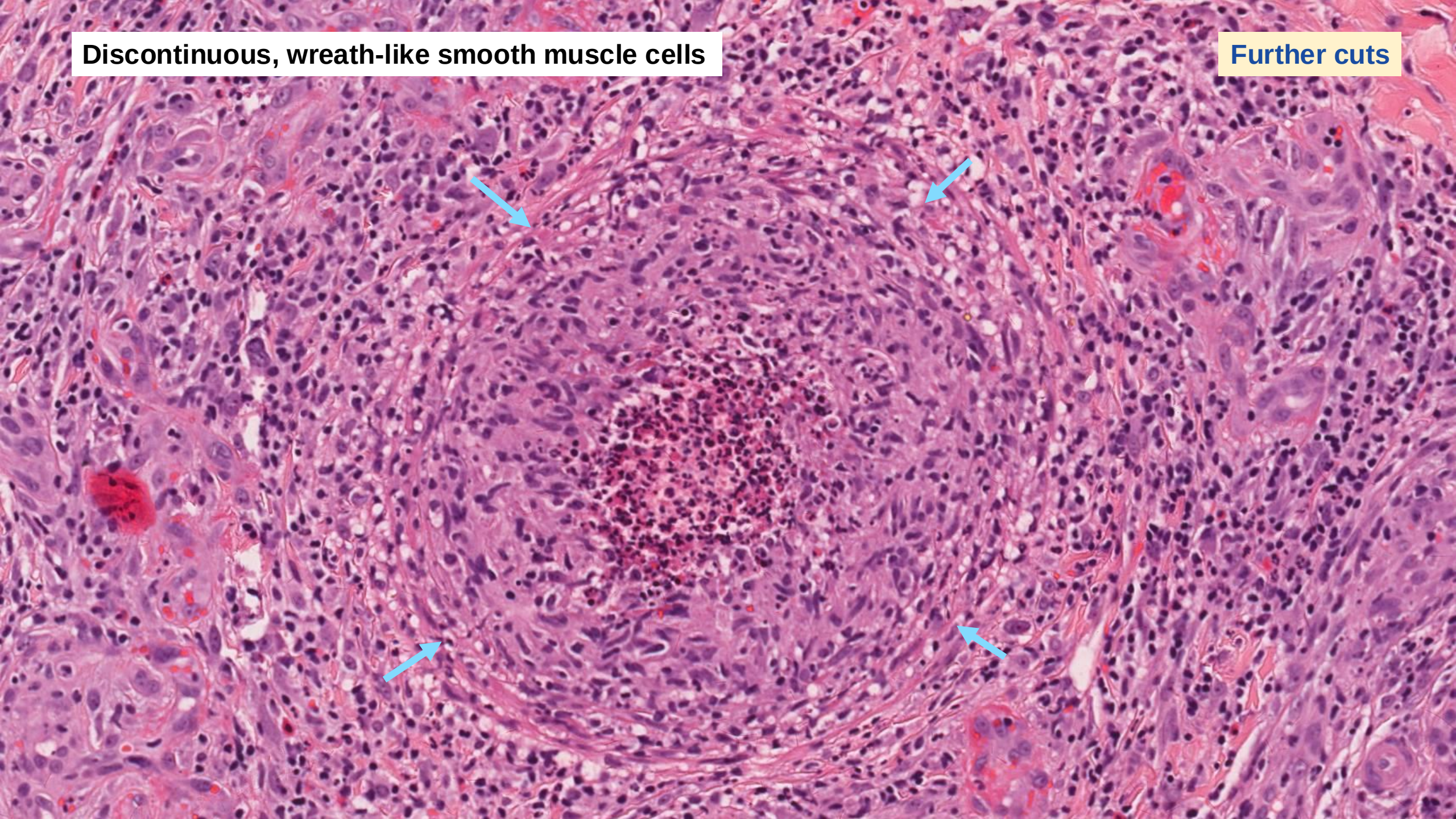
Case 3

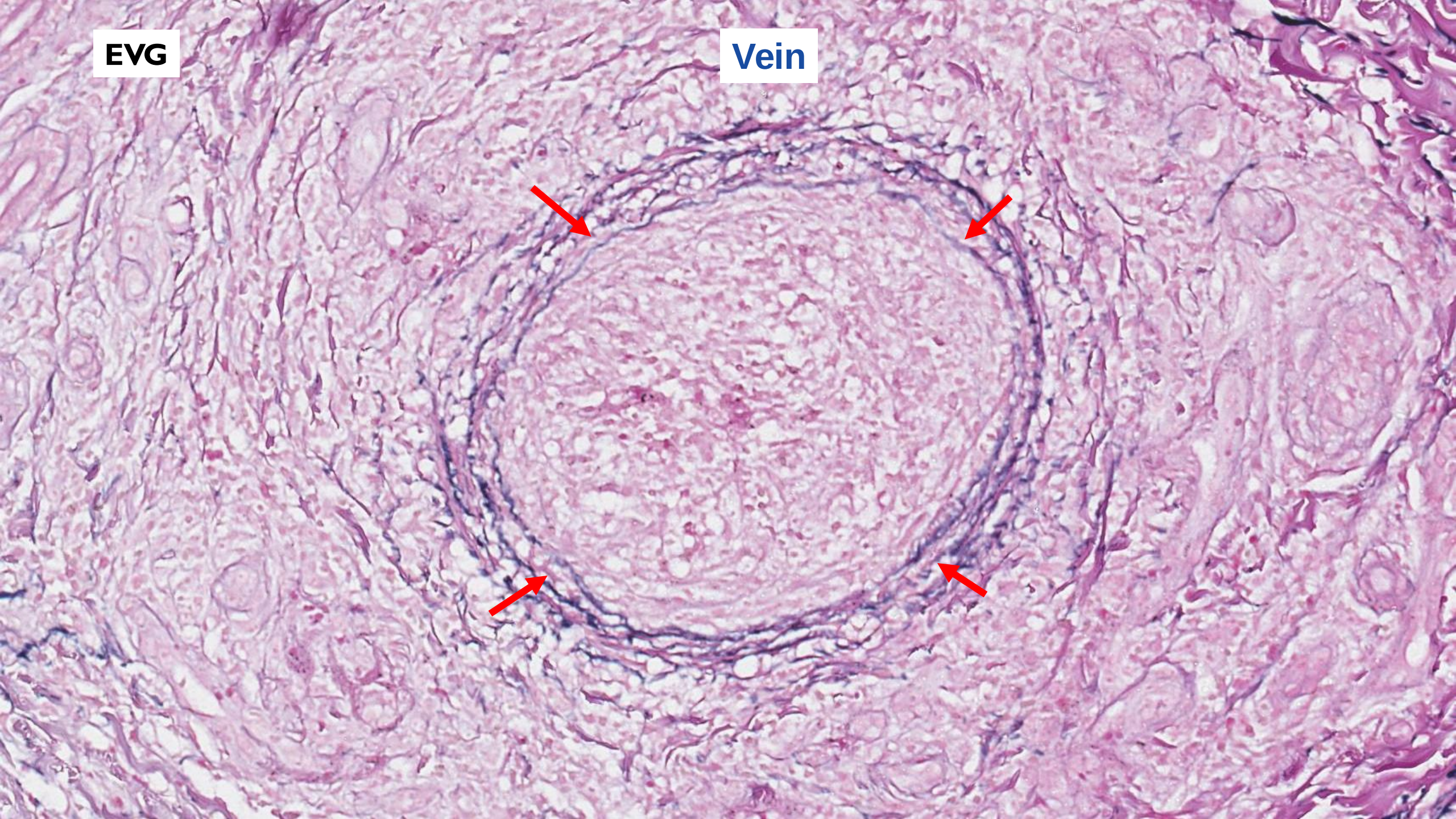
- 17-year-old girl
- Recurrent bilateral tender nodules on her feet and shins for 1 year



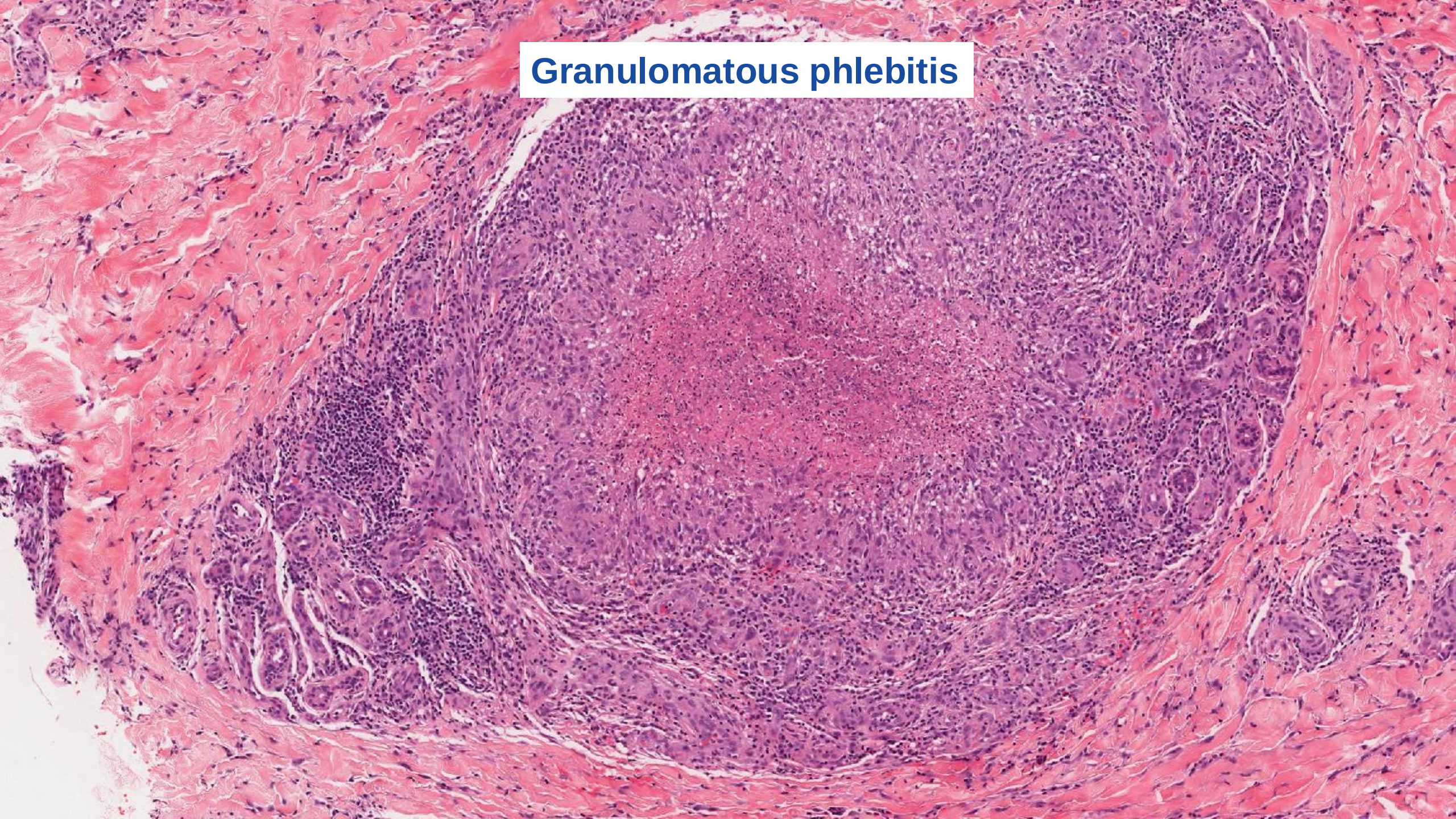

Central necrosis


Granulomatous inflammation


Discontinuous, wreath-like smooth muscle cells
Further cuts


EVG
Vein

Granulomatous phlebitis



Investigations and clinical course

- Histochemical stains:
  - Ziehl-Neelsen, Wade-Fite, PAS and GMS stains were negative
- Tissue cultures: negative
- ANCA negative
- T-SPOT tuberculosis test was reactive
- CXR showed a 1.2-cm pulmonary nodule in the right mid-zone
- Sputum cultures grew *Mycobacterium tuberculosis*

- Started on anti-TB therapy, and both the lung nodule and leg lesions resolved after 2 months

Pulmonary tuberculosis with nodular granulomatous phlebitis (a tuberculid)

Nodular granulomatous phlebitis of the skin: a fourth type of tuberculid

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HARA K., TSUZUKI T., TAKAGI N. & SHIMOKATA K.

(1997) *Histopathology* **30**, 129–134

Nodular granulomatous phlebitis
Clinical Presentation

Subcutaneous nodules along the superficial veins of the lower limbs

Hara K, et al. Histopathology. 1997;30:129-34

McHugh A, et al. Australas J Dermatol. 2008;49:220-2

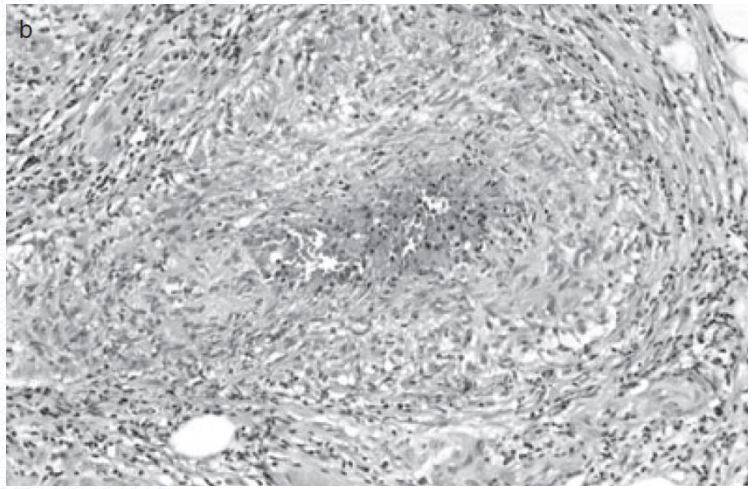
Motswaledi HM, et al. Int J Dermatol. 2006;45:1337-40

Our case

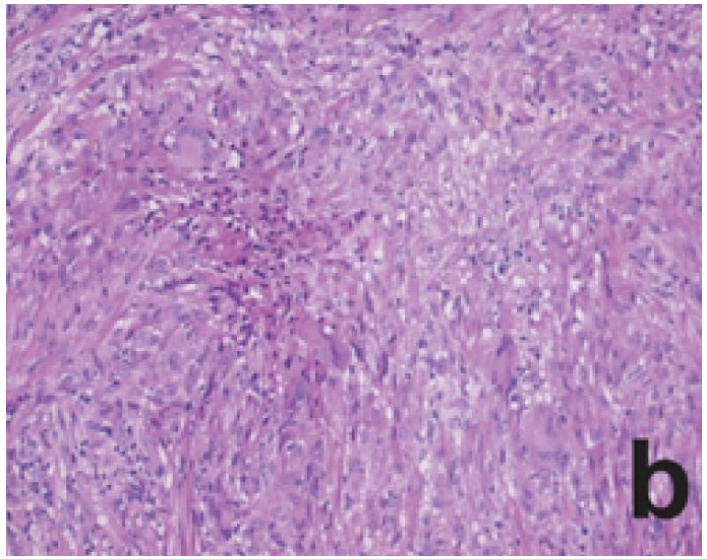
Nodular granulomatous phlebitis
Histopathological features

Granulomas within the walls of cutaneous veins

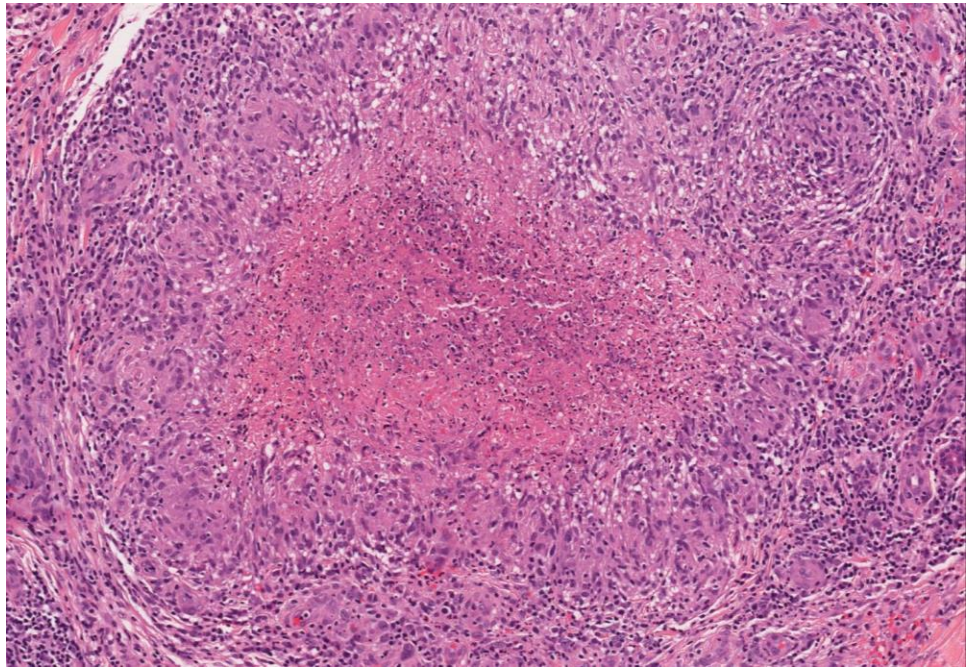
Variable central necrosis



McHugh A, et al. Australas J Dermatol. 2008;49:220-2



Motswaledi HM, et al. Int J Dermatol. 2006;45:1337-40



Our case

Nodular granulomatous phlebitis – the 4th tuberculid

- Types of tuberculids
  1. Lichen scrofulosorum
  2. Erythema induratum of Bazin
  3. Papulonecrotic tuberculid

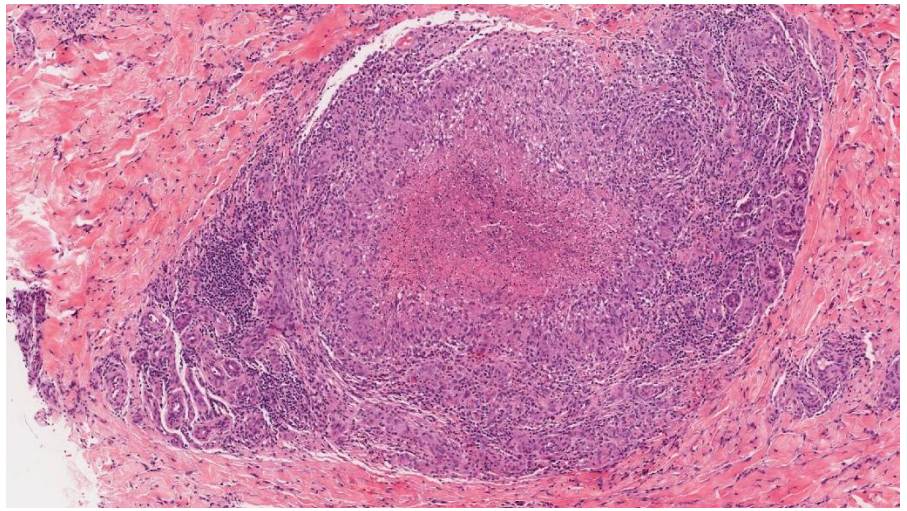
- NGP - represents a form of delayed type hypersensitivity to MTB antigen within the vessel wall

- Tissue cultures and Ziehl-Neelsen stains are generally negative, but TB PCR may be positive

Take home message for case 3

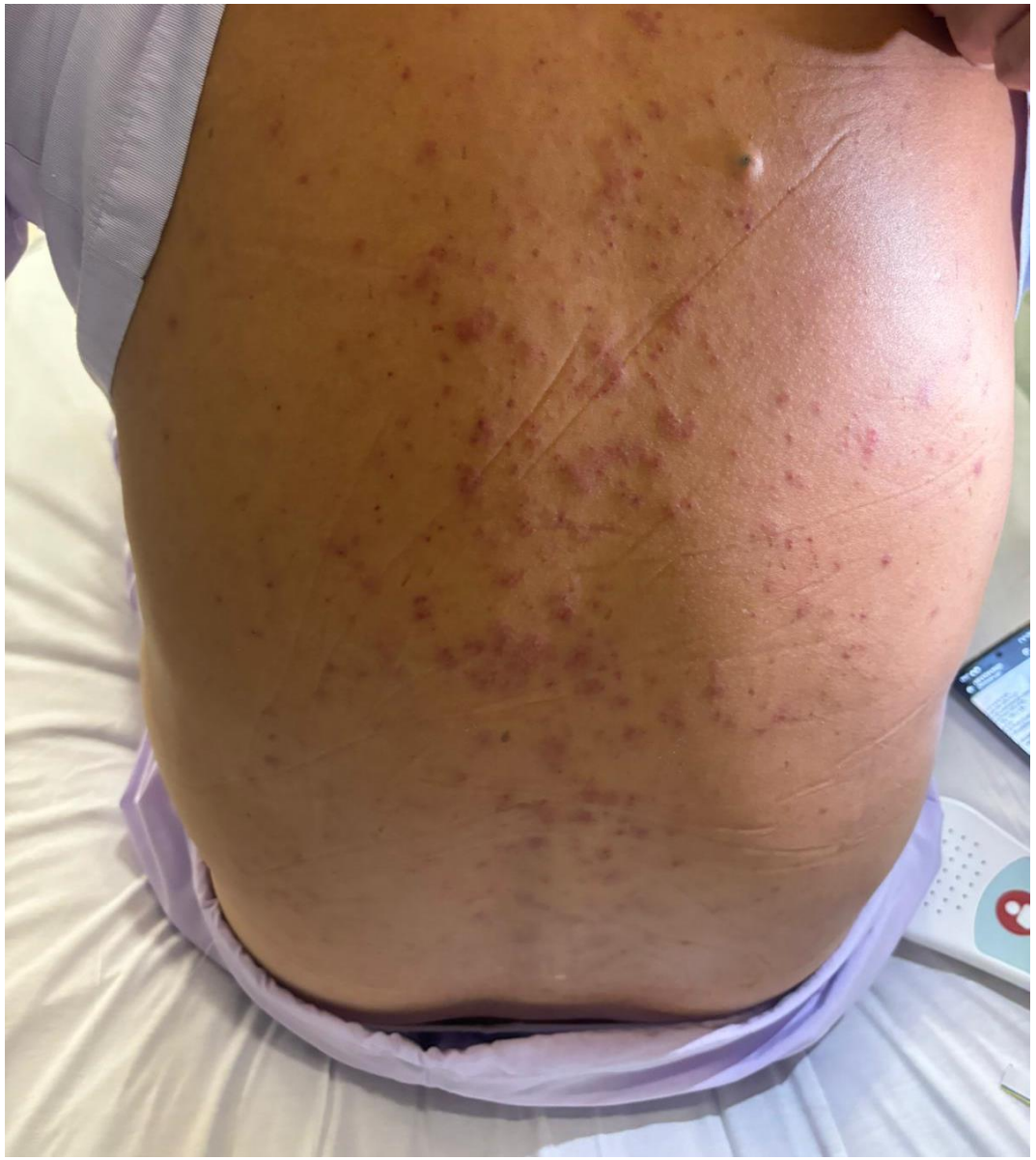
- Recognize nodular granulomatous phlebitis as a rare form of tuberculid usually affecting superficial veins of the lower limbs

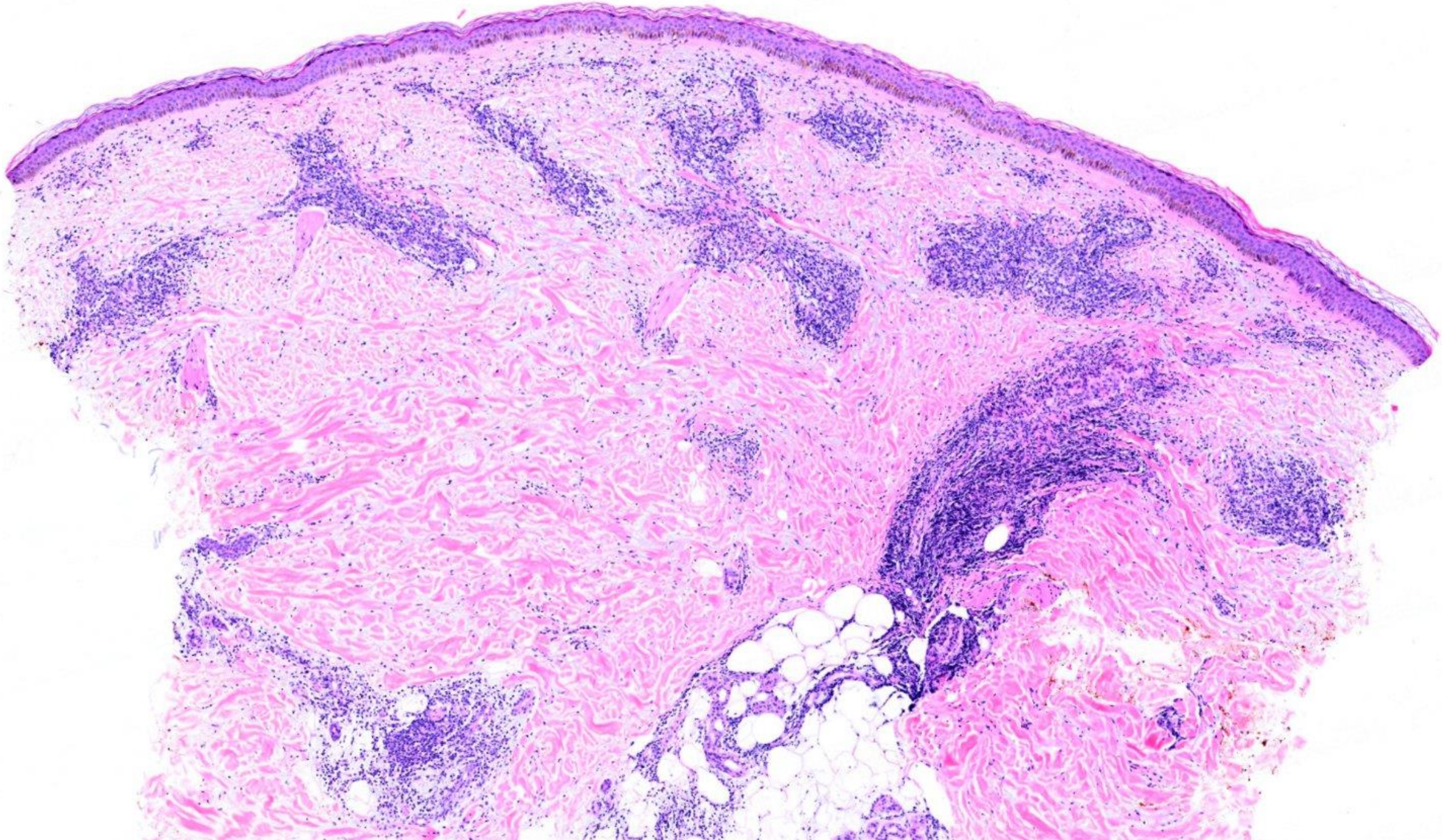
- Responds to anti-TB treatment

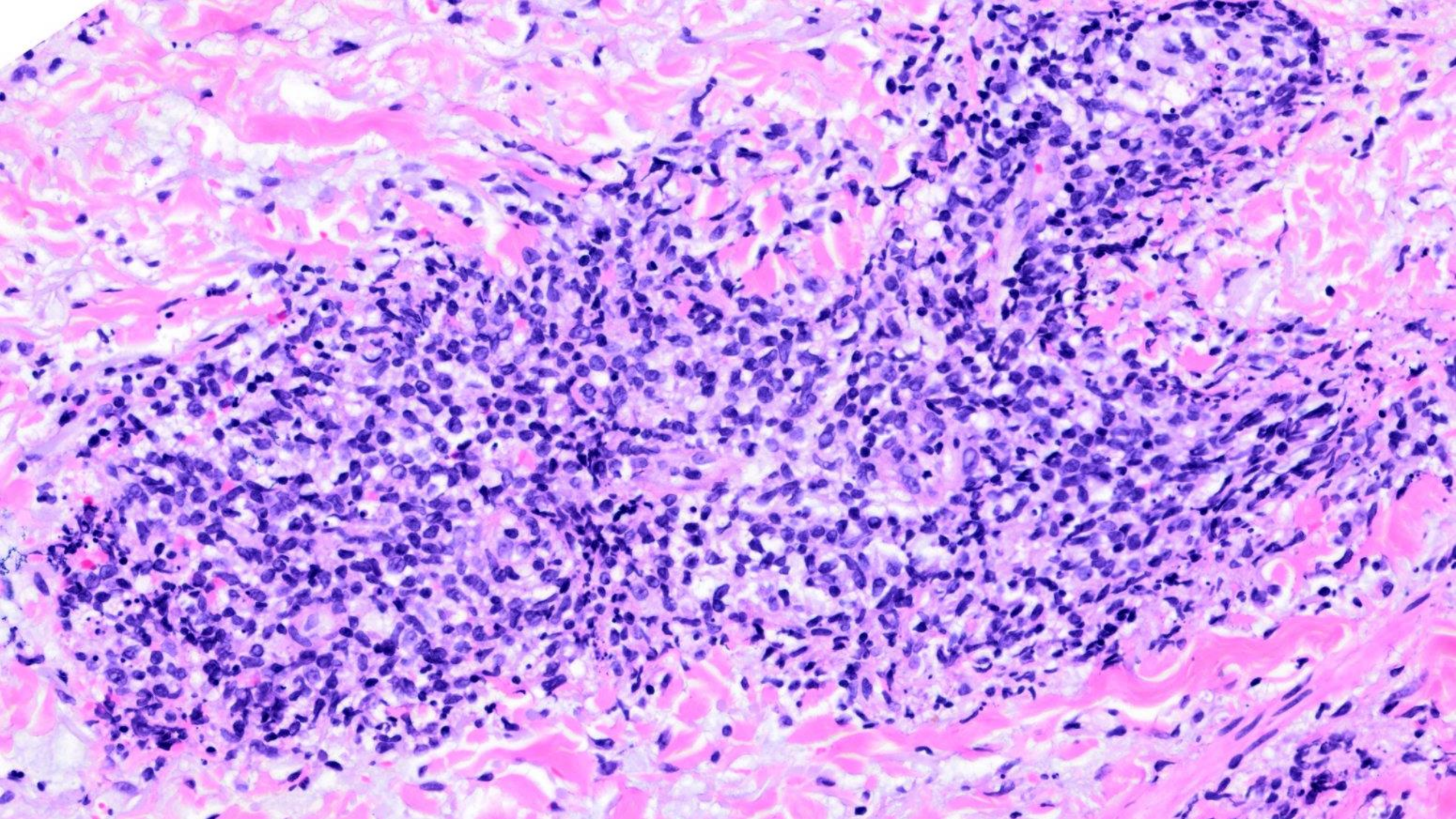


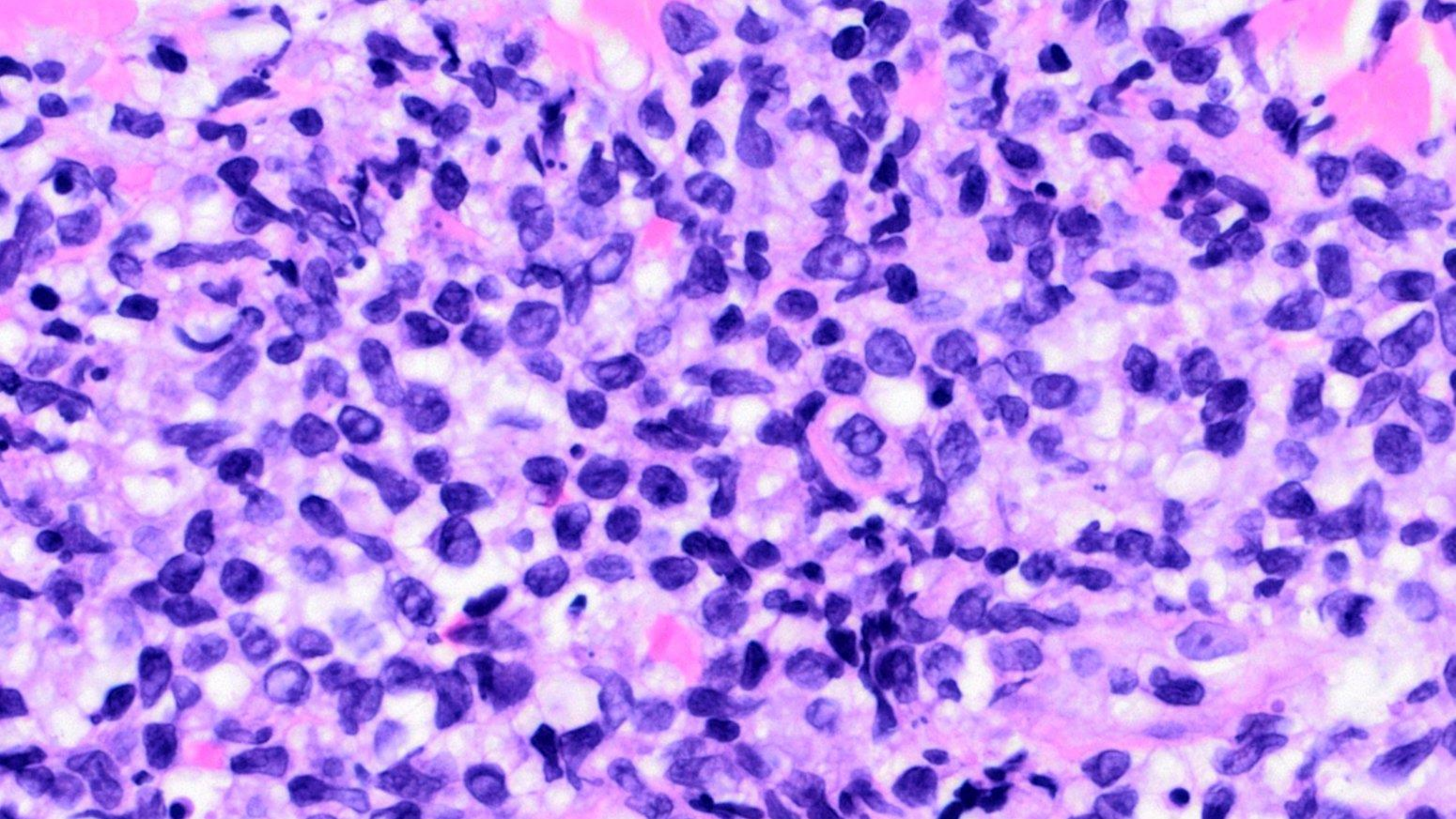
Case 4

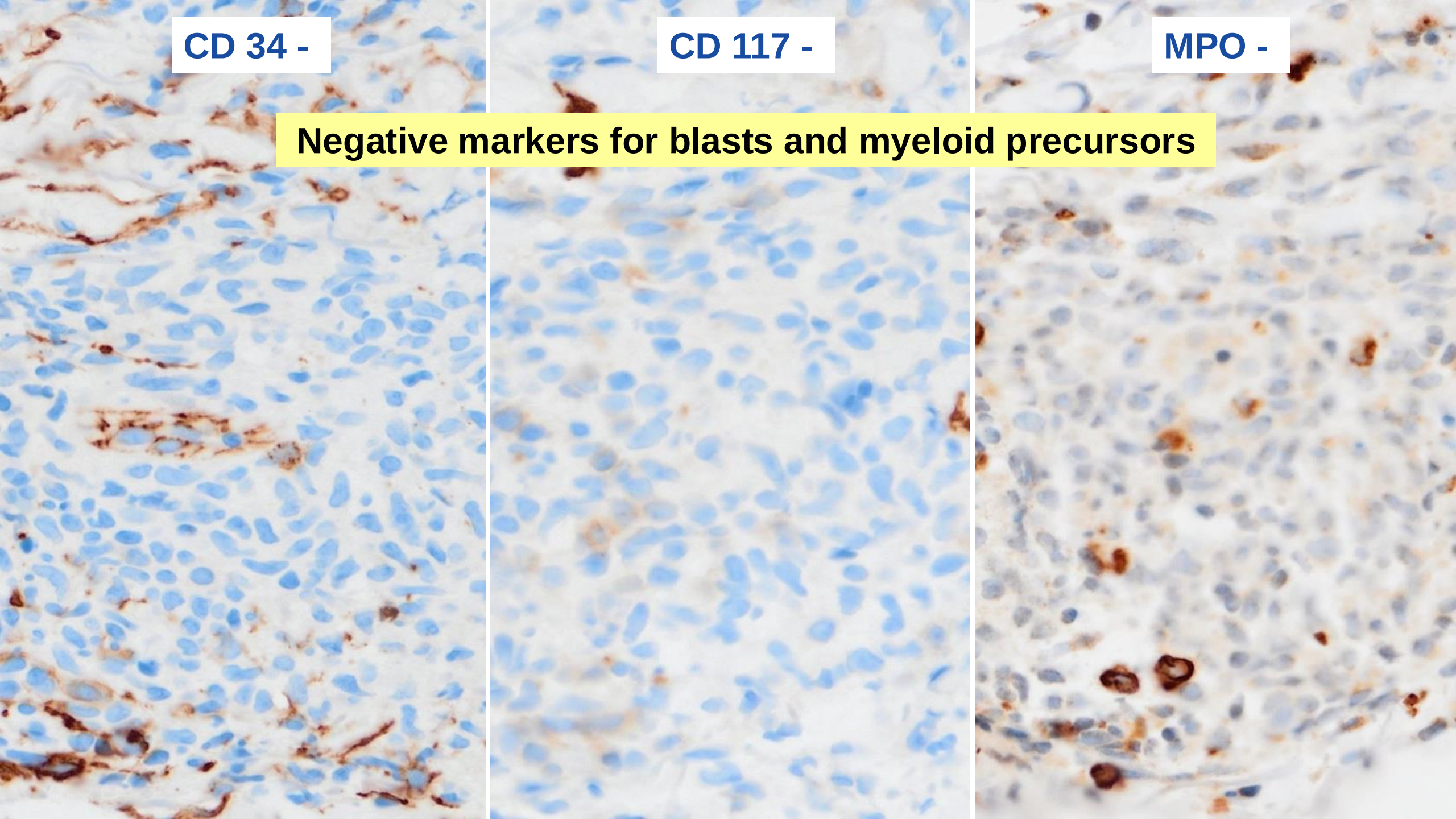
- 70-year-old male
- Recent onset of erythematous to dusky plaques and petechiae over his body and limbs
- Newly diagnosed with acute myeloid leukaemia

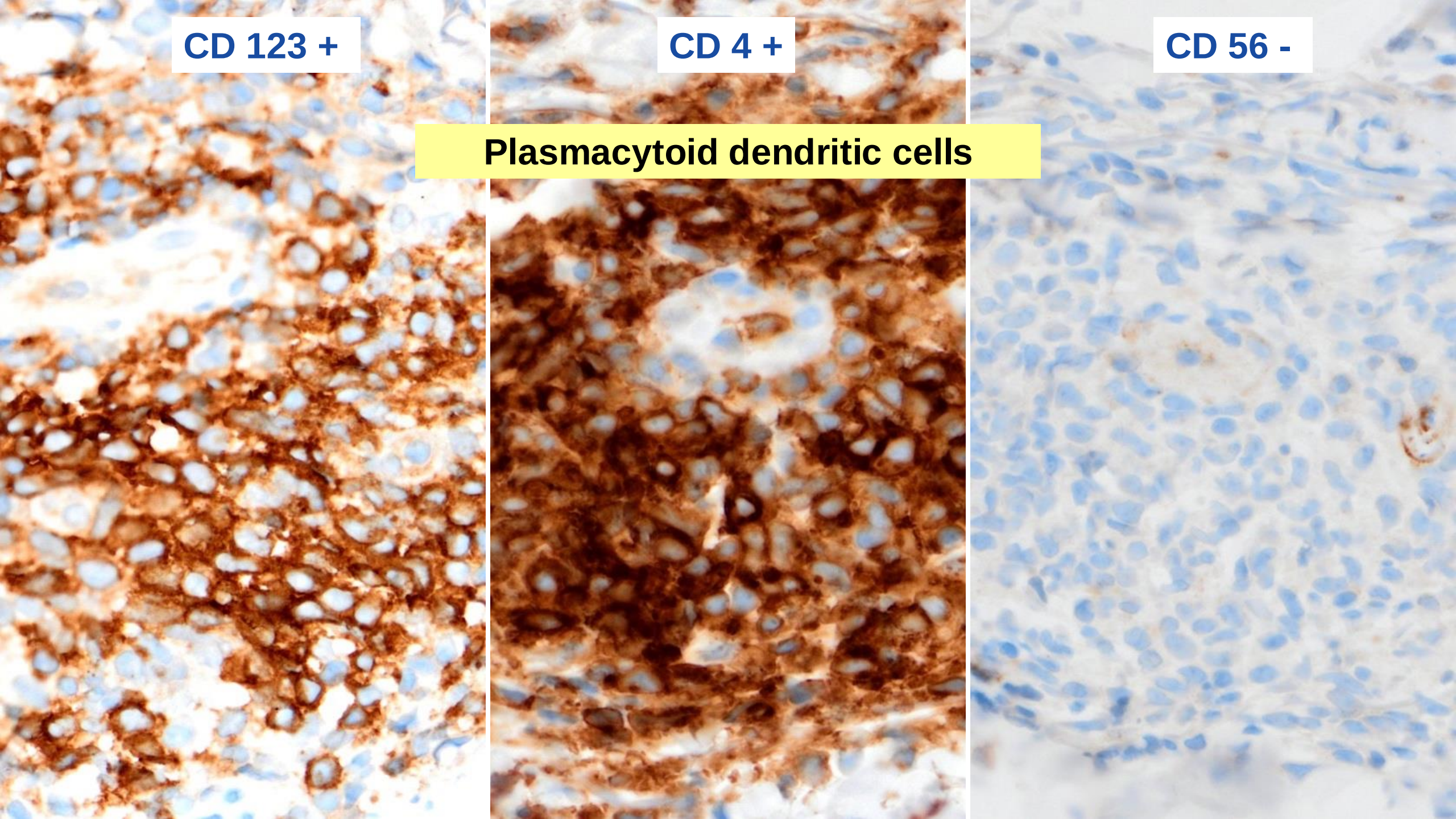


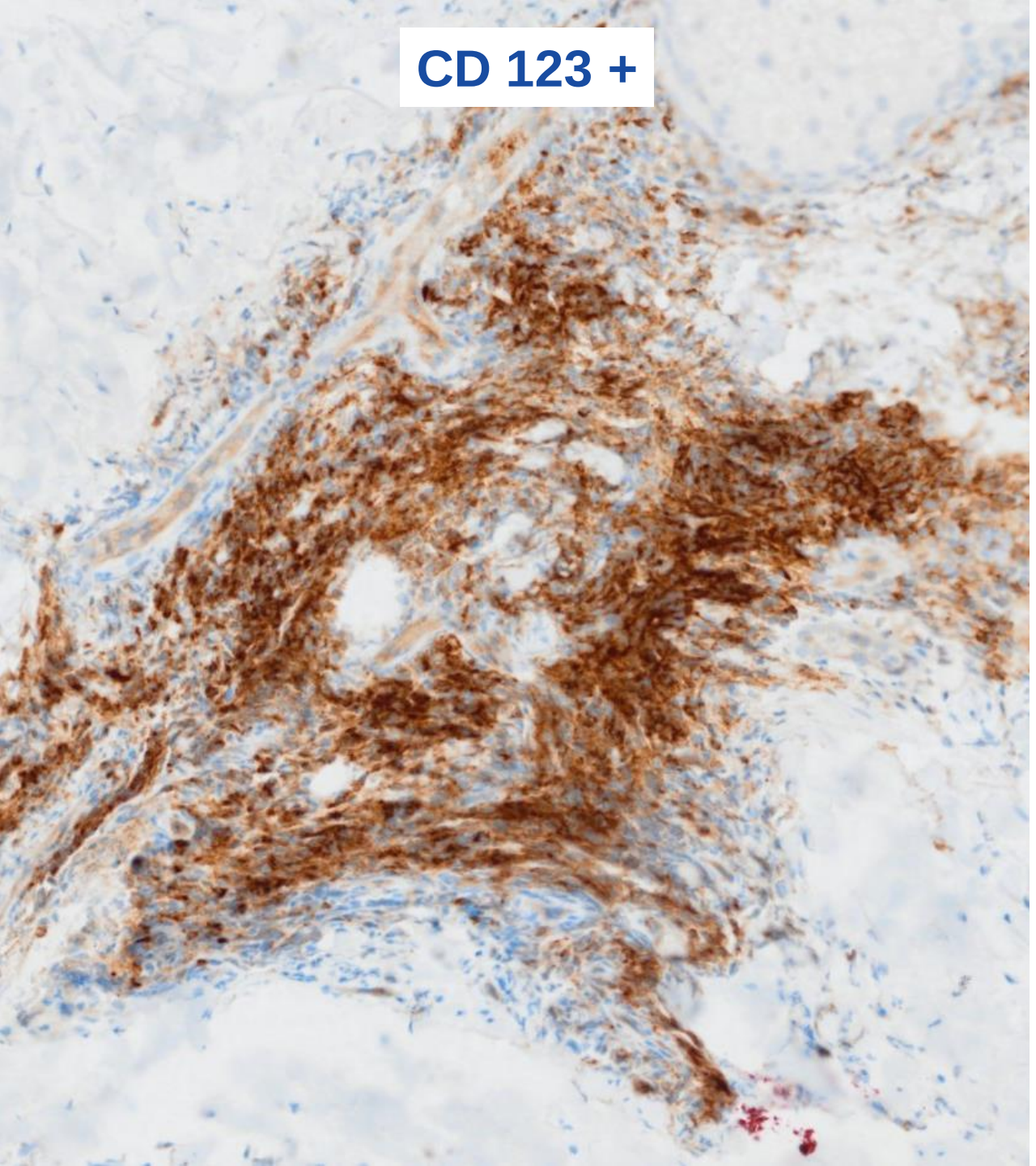


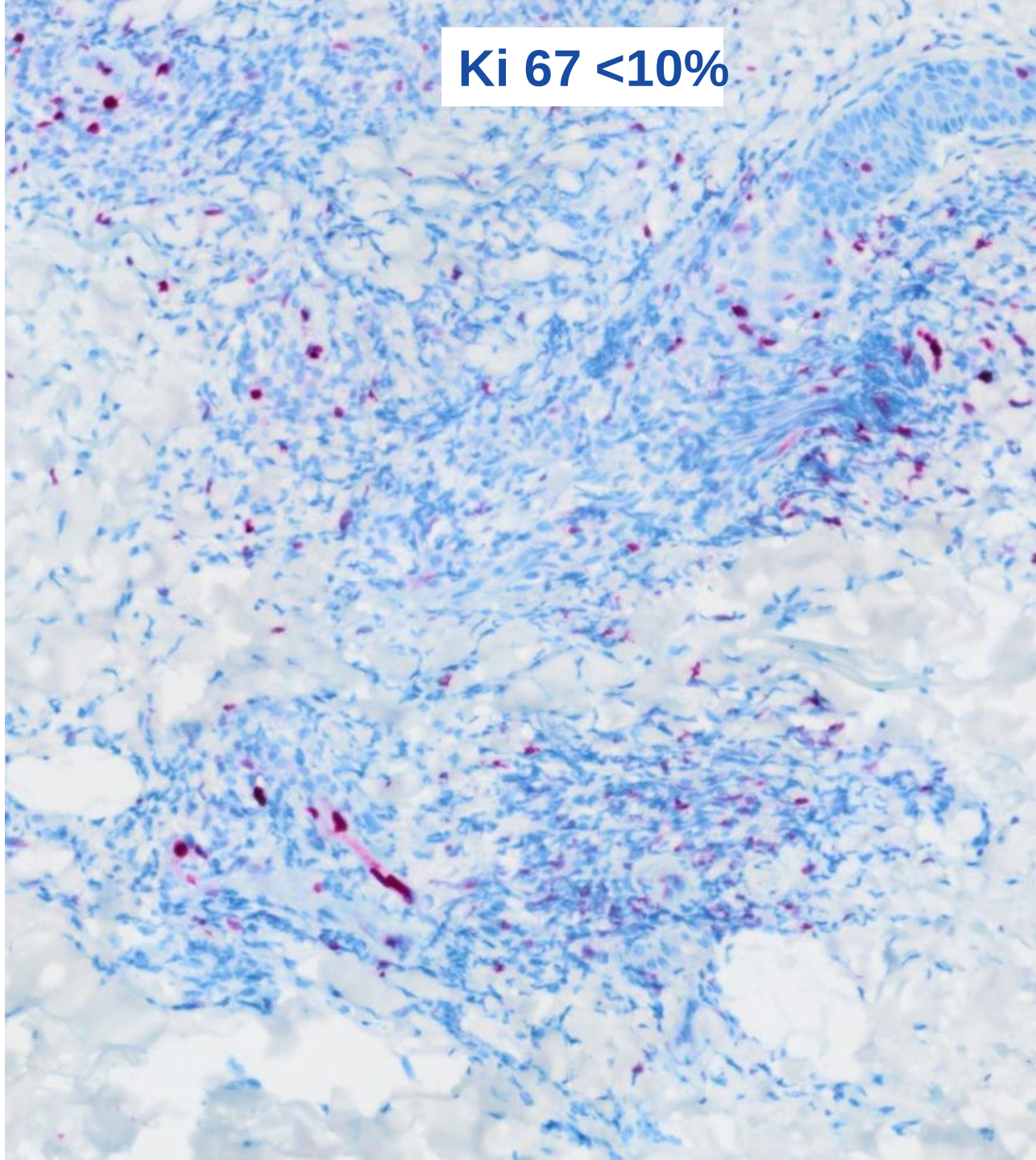





CD 34 -
CD 117 -
MPO -
Negative markers for blasts and myeloid precursors


CD 123 +
CD 4 +
CD 56 -
Plasmacytoid dendritic cells


CD 123 +


Ki 67 <10%

Diagnostic considerations

- Low grade cytomorphology of cells
- Positive markers for plasmacytoid dendritic cells
- Negative markers for blasts and myeloid precursors
- Low proliferative index
- In the setting of a patient with myeloid neoplasm (AML)

Mature plasmacytoid dendritic cell proliferation associated with myeloid neoplasm (MPDCP)

Mature plasmacytoid dendritic cell proliferation associated with myeloid neoplasm

Definition

Mature plasmacytoid dendritic cell proliferation (MPDCP) associated with myeloid neoplasm is a clonal proliferation of plasmacytoid dendritic cells (pDCs) with low grade morphology identified in the context of a defined myeloid neoplasm.

ICD-O coding

Code as underlying neoplasm

ICD-11 coding

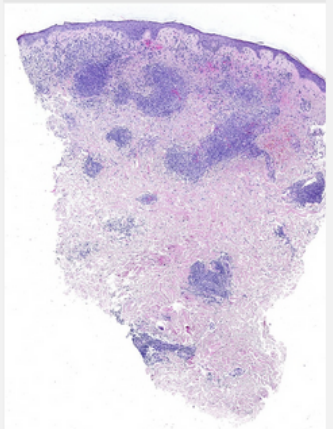
Code as underlying neoplasm

Related terminology

Acceptable: mature plasmacytoid dendritic cell proliferation

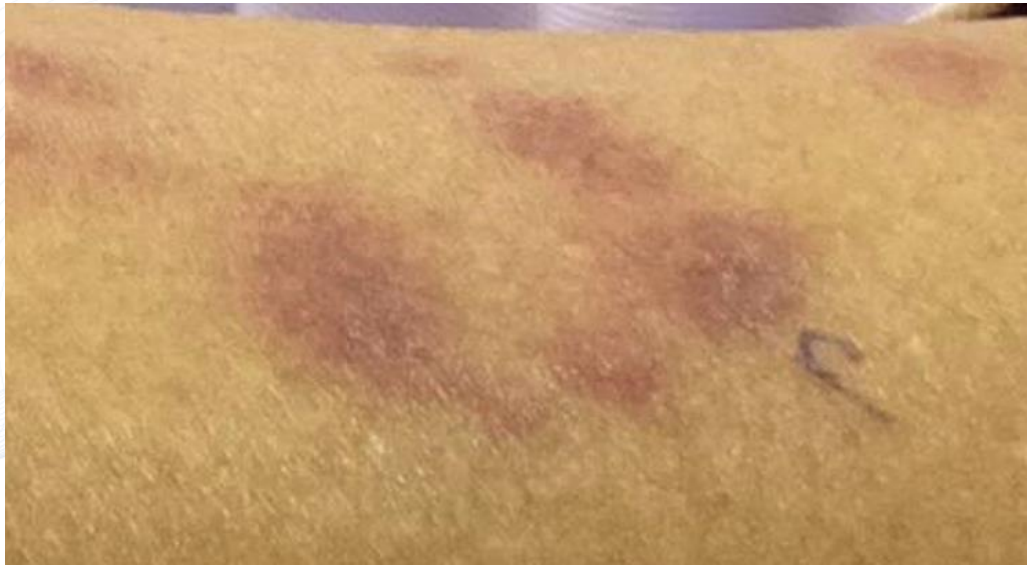
Subtype(s)

None



#35211
Mature plasmacytoid dendritic cell proliferation associate with myeloid neoplasm

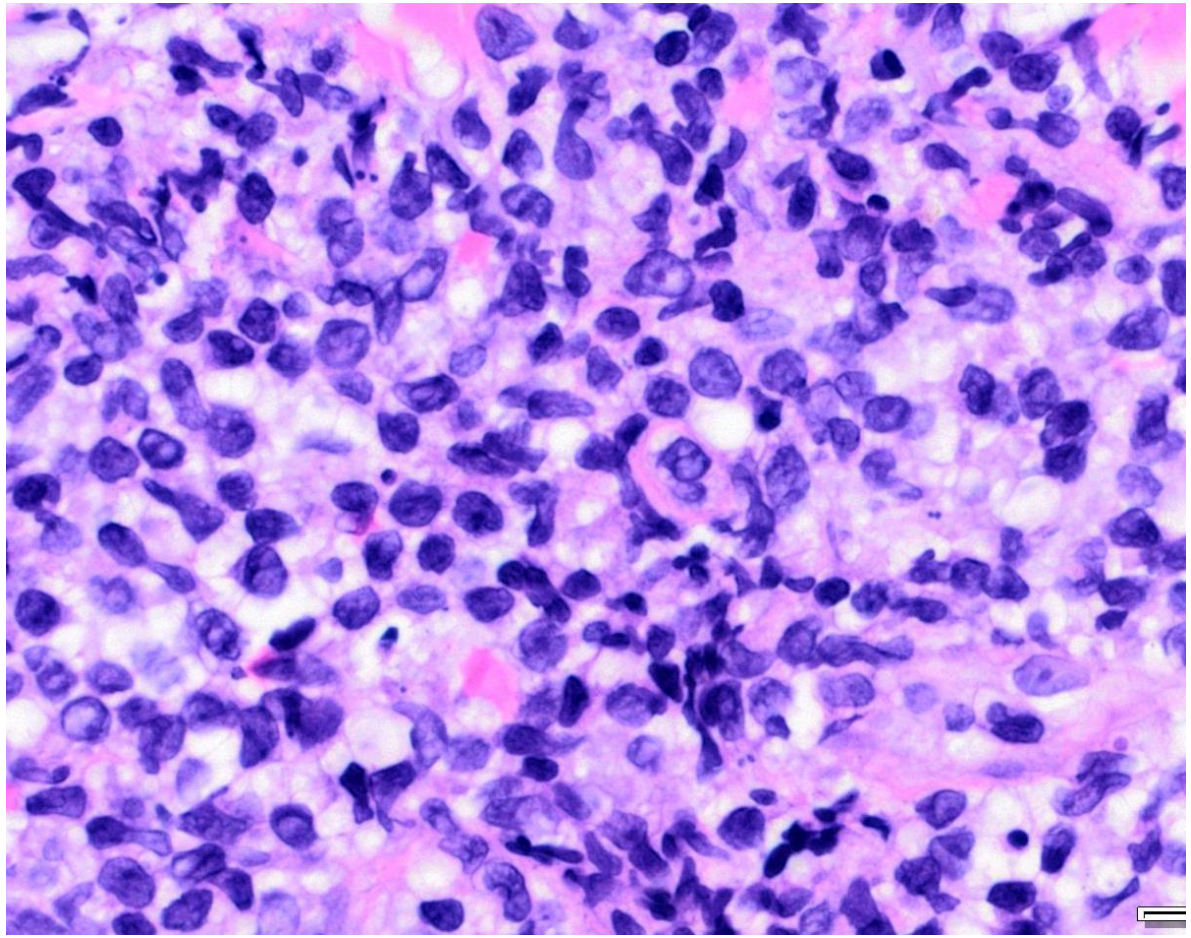
Mature plasmacytoid dendritic cell proliferation associated with myeloid neoplasm (MPDCP)



- A clonal proliferation of plasmacytoid dendritic cells (pDCs) with low grade morphology identified in the context of a defined myeloid neoplasm
- Predominantly in elderly males
- Shares clonality with the accompanying myeloid neoplasm

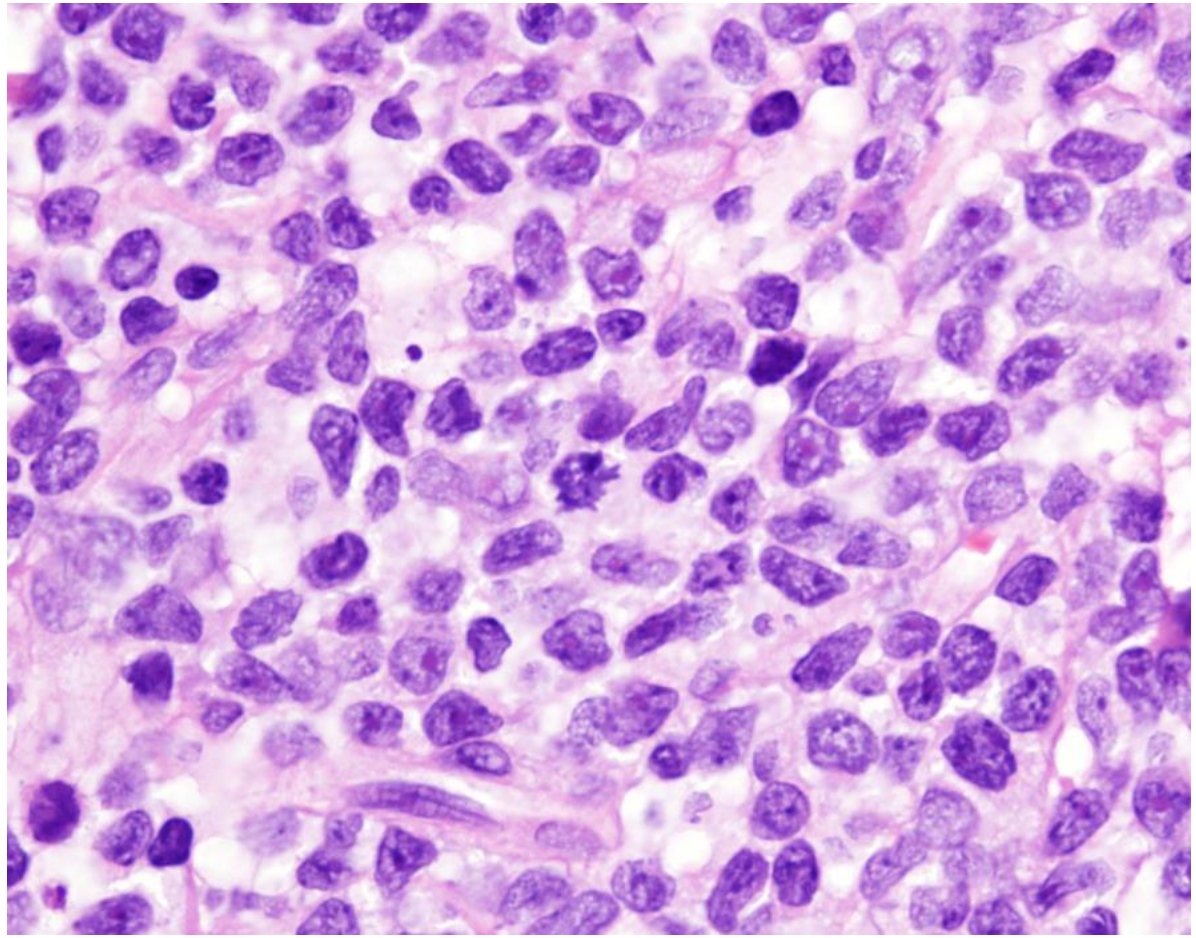
Mature pDC proliferation (MPDCP)

Medium-sized mature to low-grade pDCs with low to absent mitoses

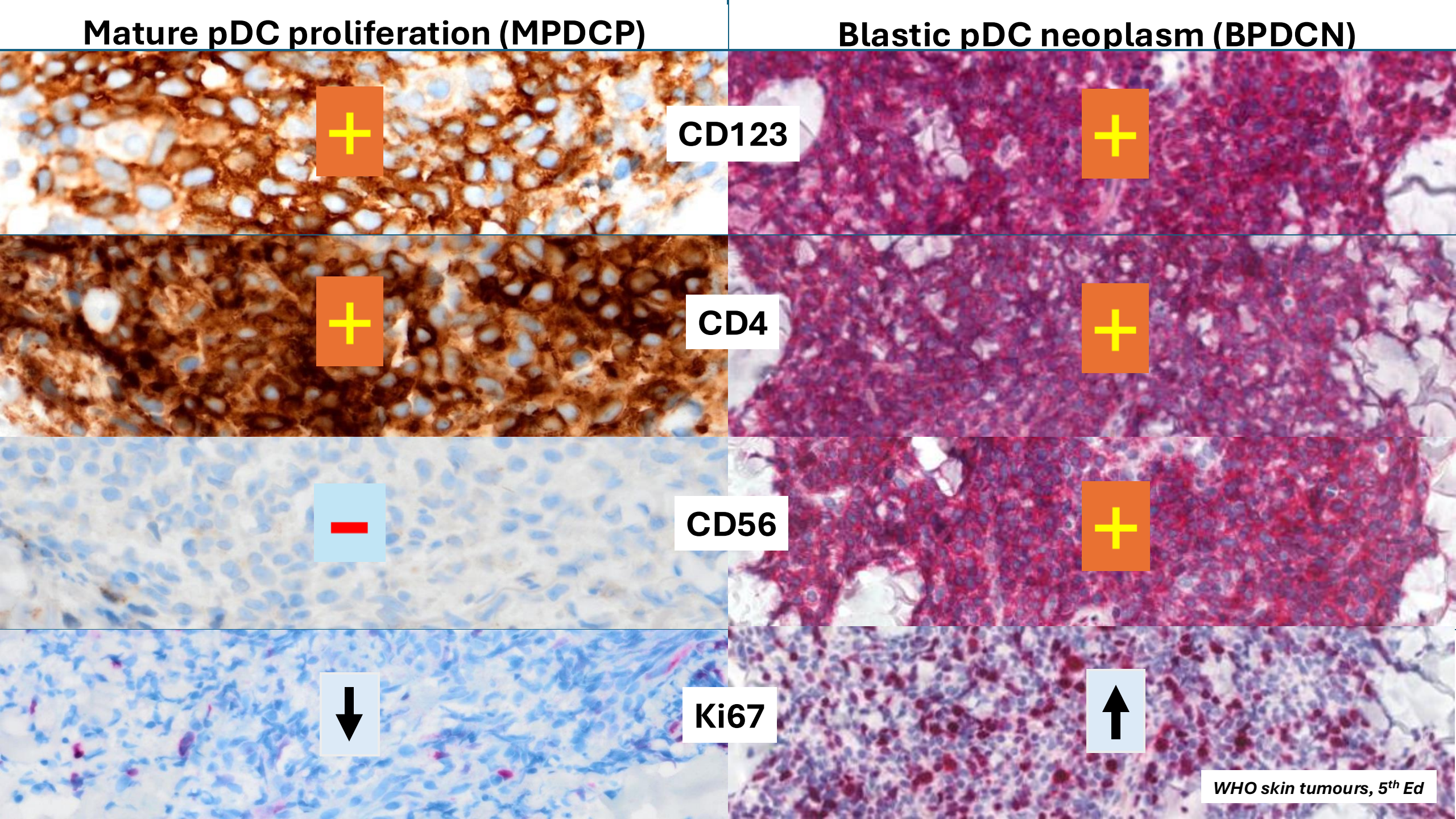


Blastic pDC neoplasm (BPDCN)

Medium-sized immature blastic cells with increased mitoses



WHO skin tumours, 5th Ed


Mature pDC proliferation (MPDCP)
Blastic pDC neoplasm (BPDCN)
CD123
CD4
CD56
Ki67
WHO skin tumours, 5th Ed

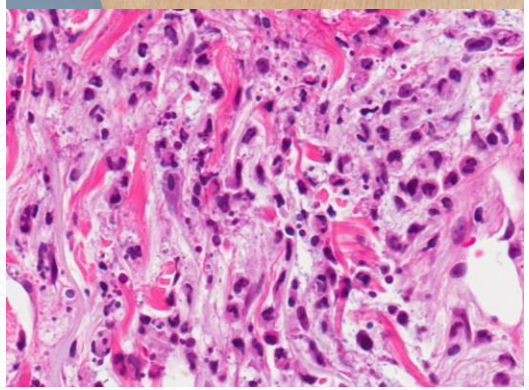
Treatment and prognosis of MPDCP

- Dependent on the treatment of the underlying myeloid neoplasm
- Associated with poorer outcomes
- Higher risk of acute leukemia transformation

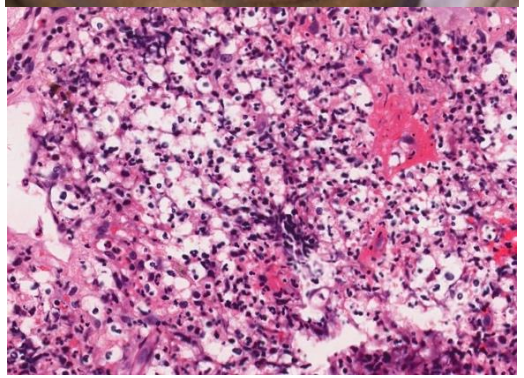
Take home message for case 4

- Mature plasmacytoid dendritic cell proliferation associated with myeloid neoplasm (MPDCP) is a recently described entity which needs to be considered in the setting of a patient with myeloid malignancy and cutaneous lesions

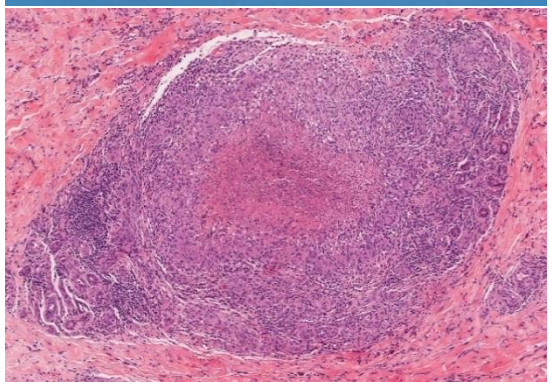
VEXAS syndrome



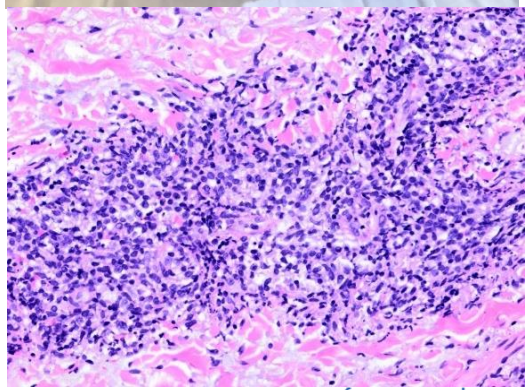
Acute iododerma with cryptococcoid neutrophilic dermatosis



Nodular granulomatous phlebitis in TB



MPDCP in AML



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