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Unusual Occlusive Vasculopathies: Clinicopathological Insights

Sunday 10th Nov 2024
Session: Insights in Dermatology

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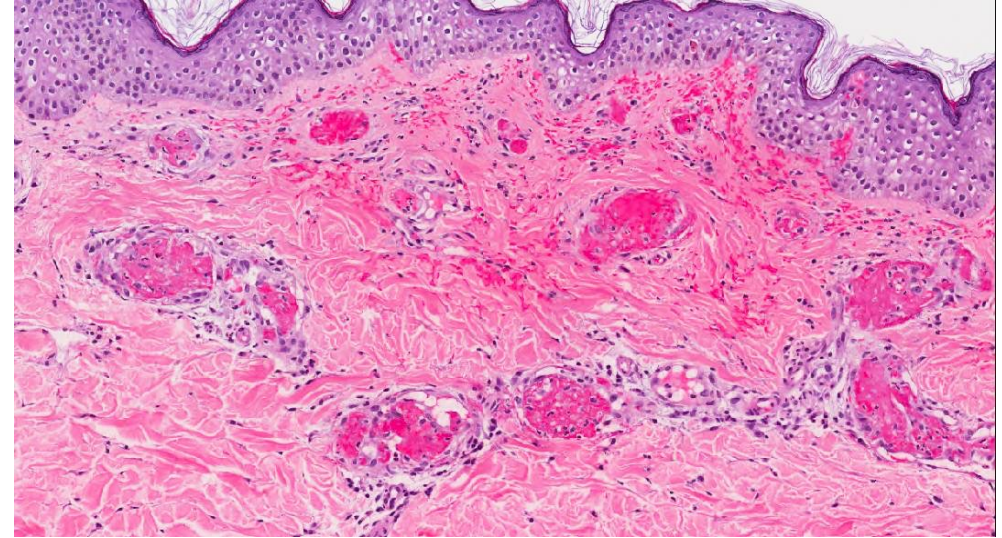
**27th WORLD CONGRESS
OF DERMATOLOGY 2031**
DUBAI - CANDIDATE CITY

Conflict of Interest

- I have no conflicts of interest to declare

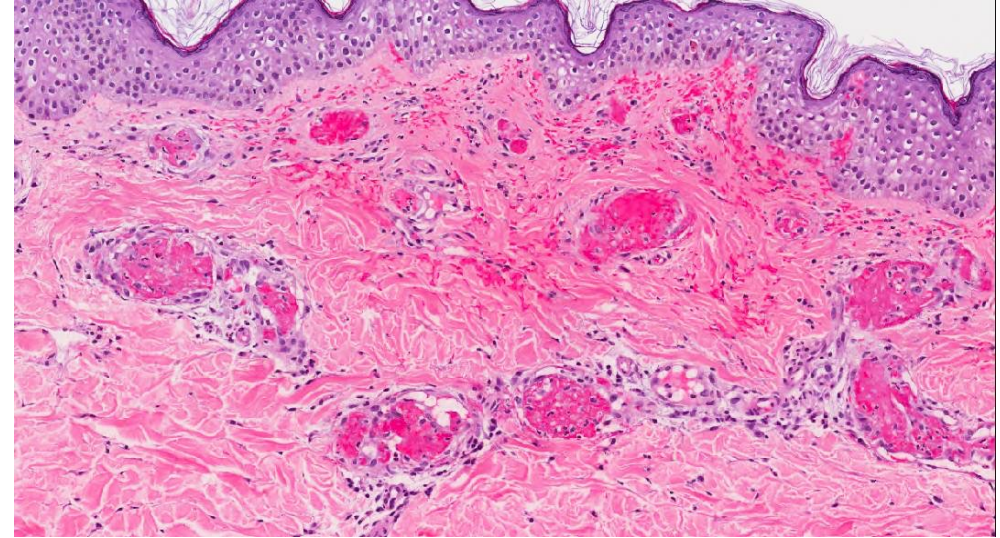
Occlusive vasculopathies

- Non-vasculitic occlusions of blood vessels
- Clinically characterized
 - Retiform purpura
 - Ulcers
 - Infarcts
 - Purple toe syndrome



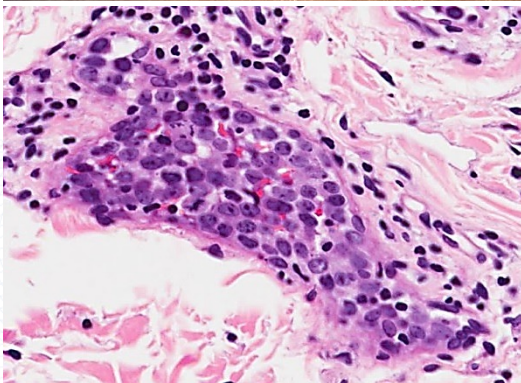
Types of occlusive vasculopathies

- Embolization
- Platelet plugging
- Cold-related gelling or agglutination
- Vessel-invasive micro-organisms
- Coagulopathies
- Etc.

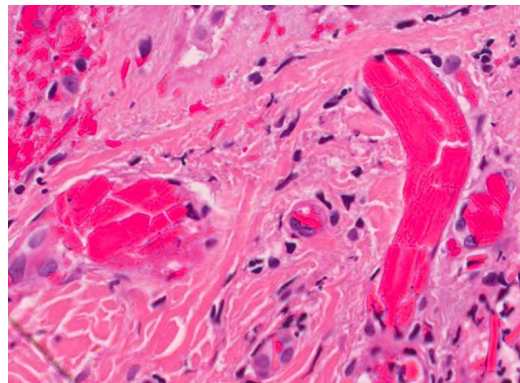


Unusual Occlusive Vasculopathies: Clinicopathological Insights

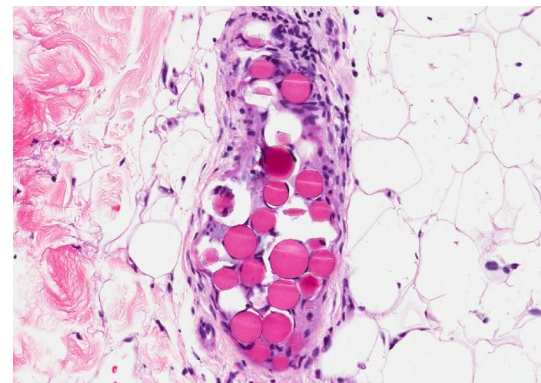
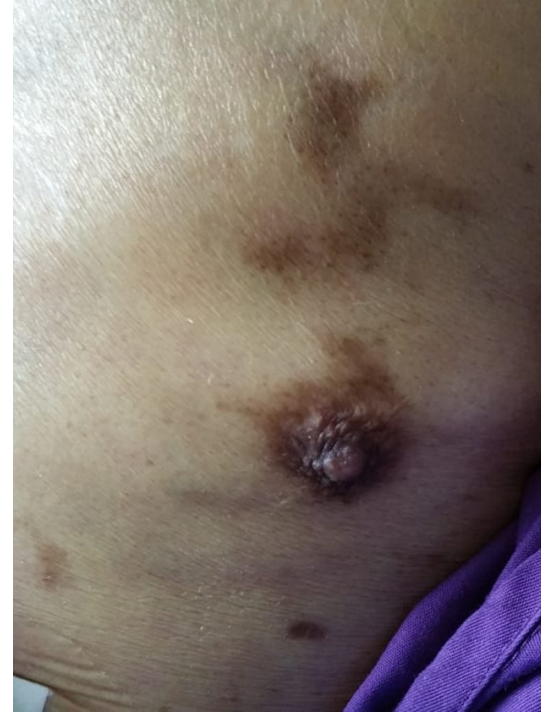
Case 1



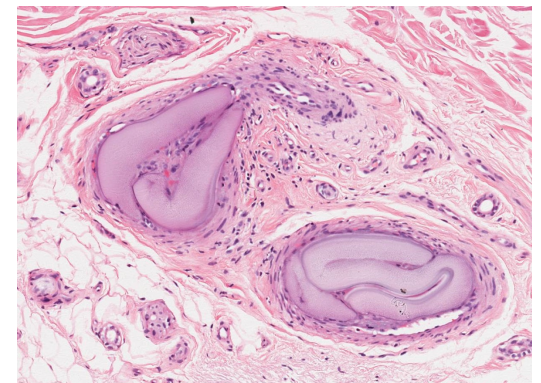
Case 2



Case 3



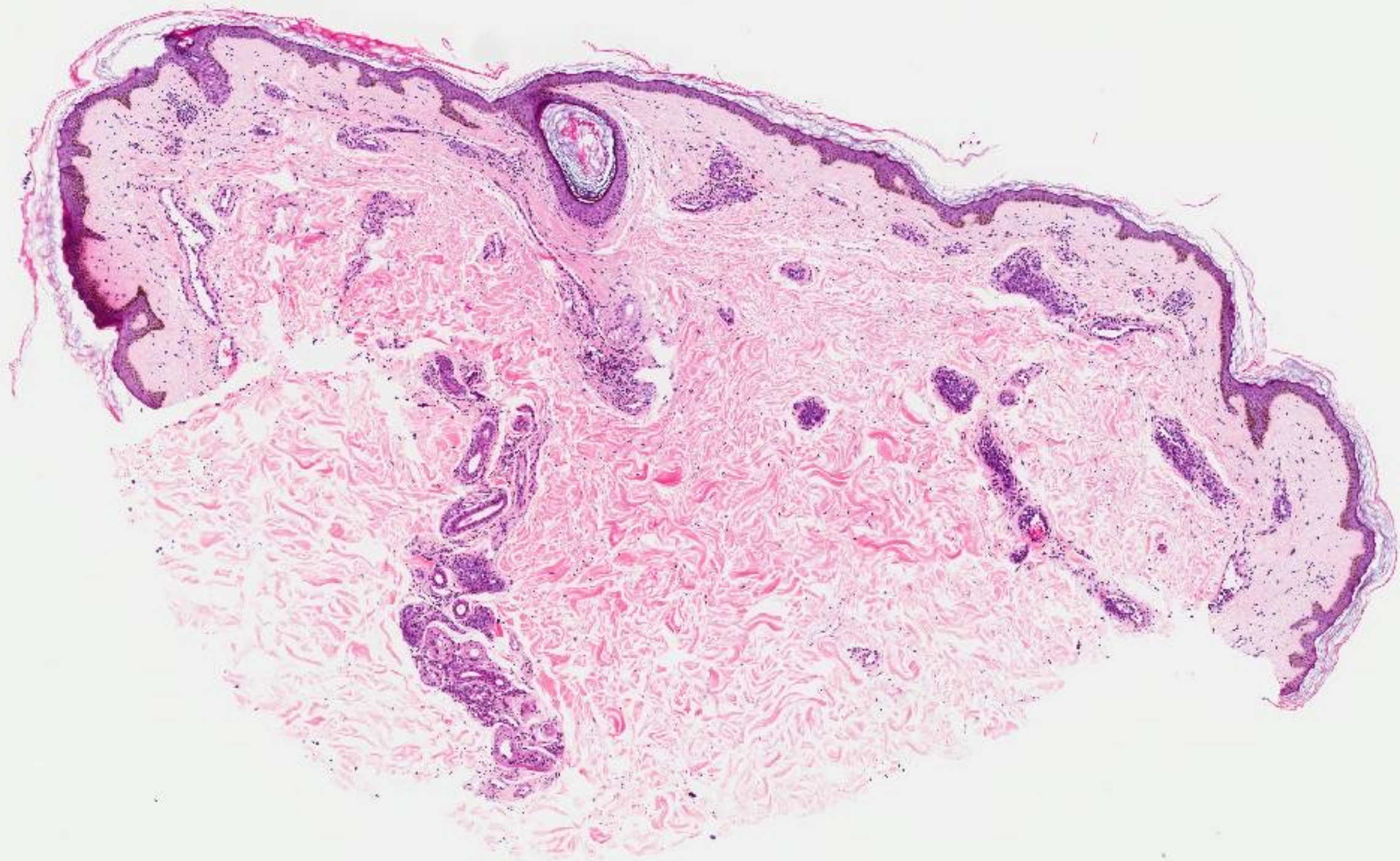
Case 4

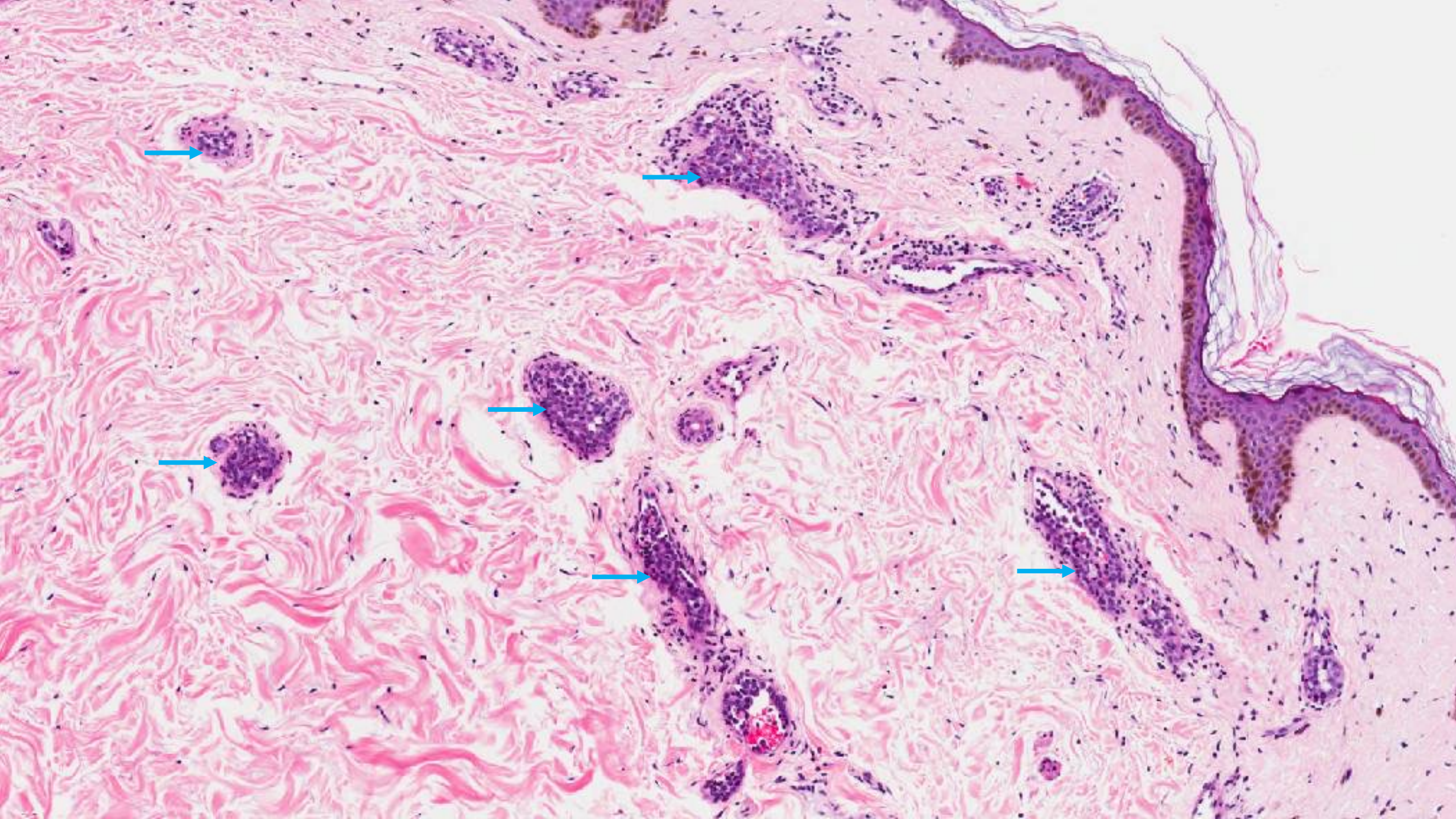


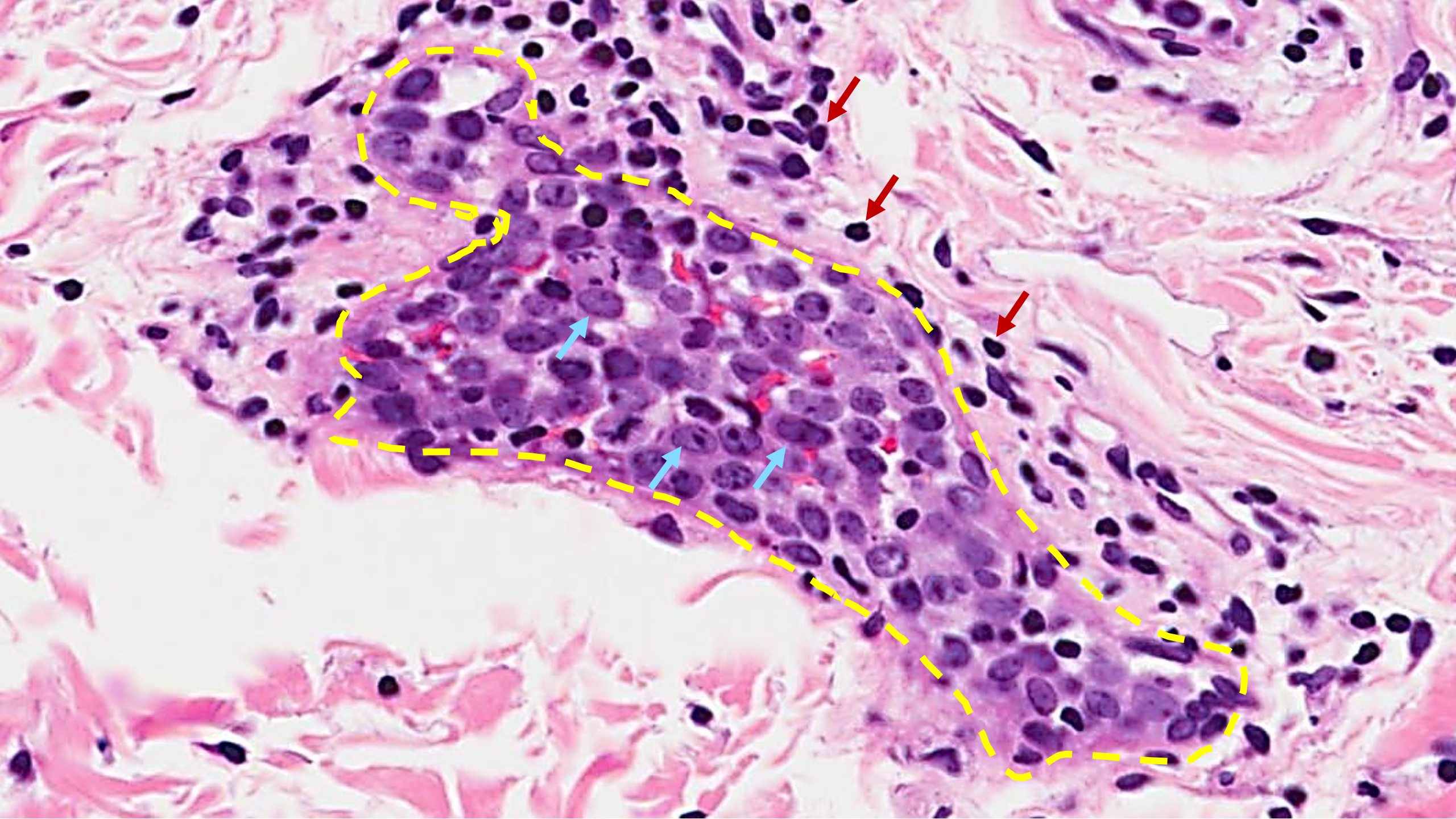
Case 1

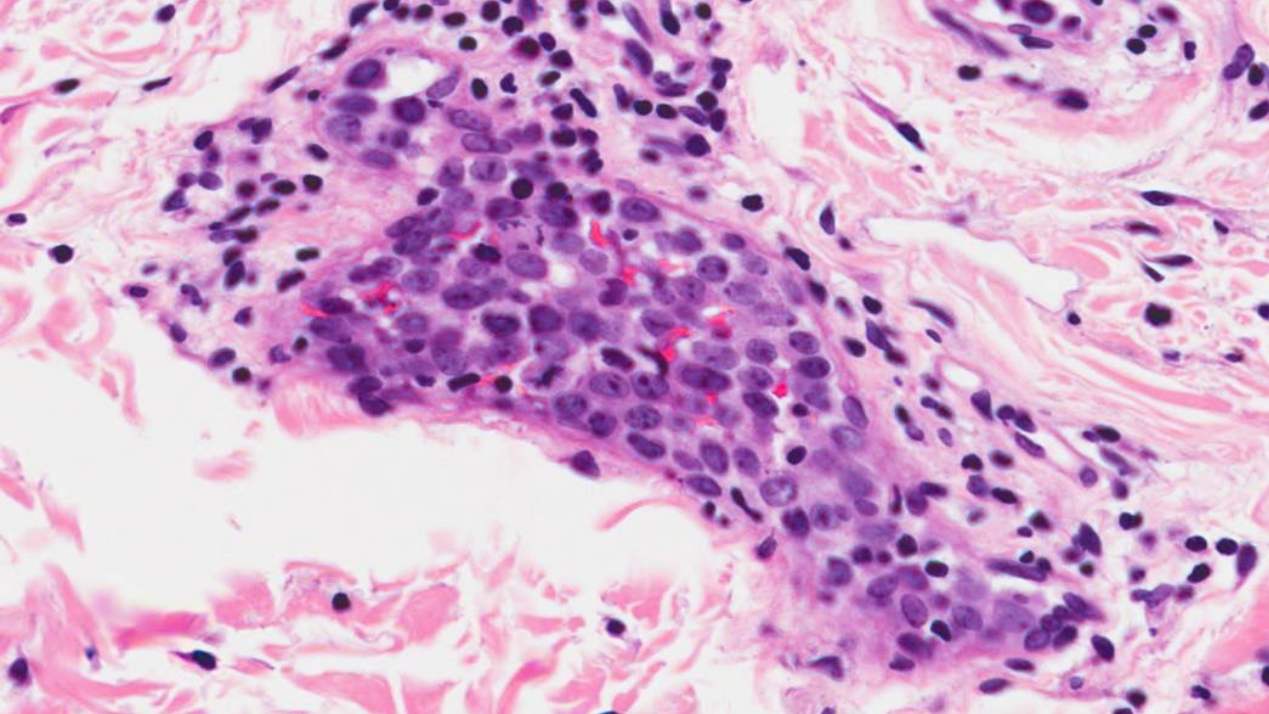
- 65-year-old male
- Intermittent fever and chills
- Telangiectatic and erythematous macules over the chest for 2 months
- 20-kg weight loss over 6 months
- Pancytopenia (TW: $3.3 \times 10^9/L$, Hb: 7.7 g/dl, plt: 103K)
- Raised lactate dehydrogenase (>2500 U/L)



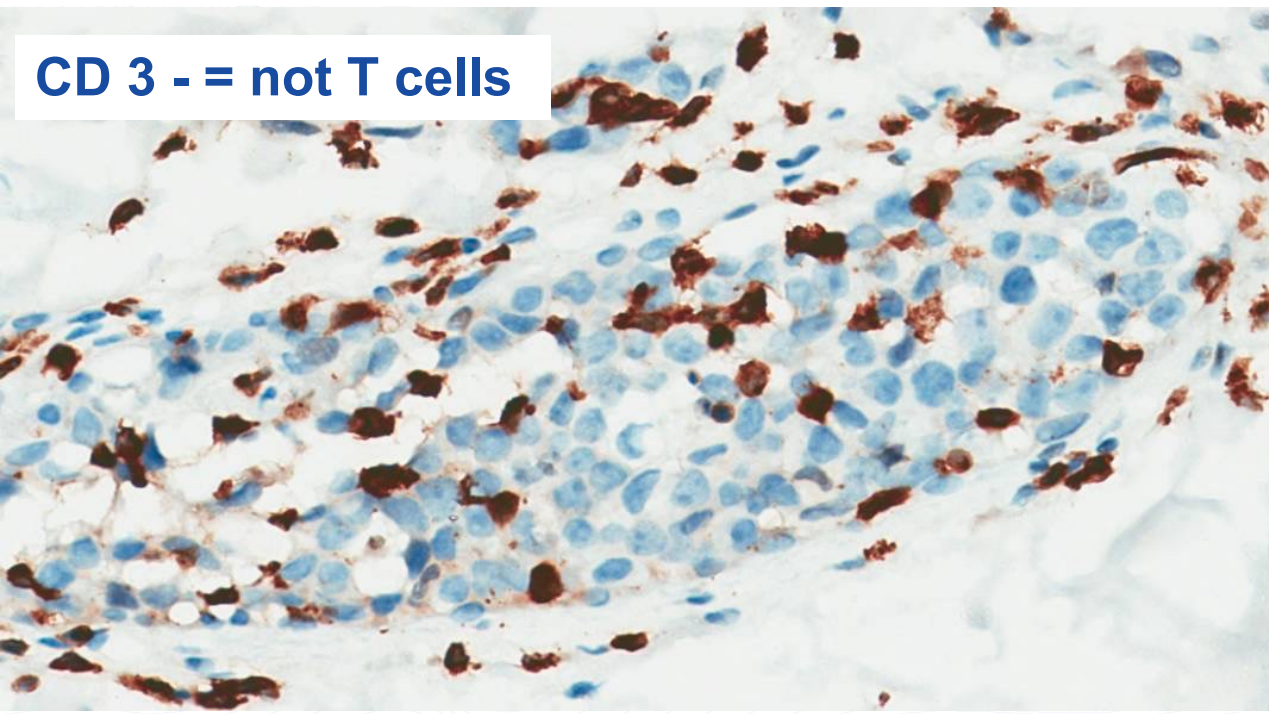
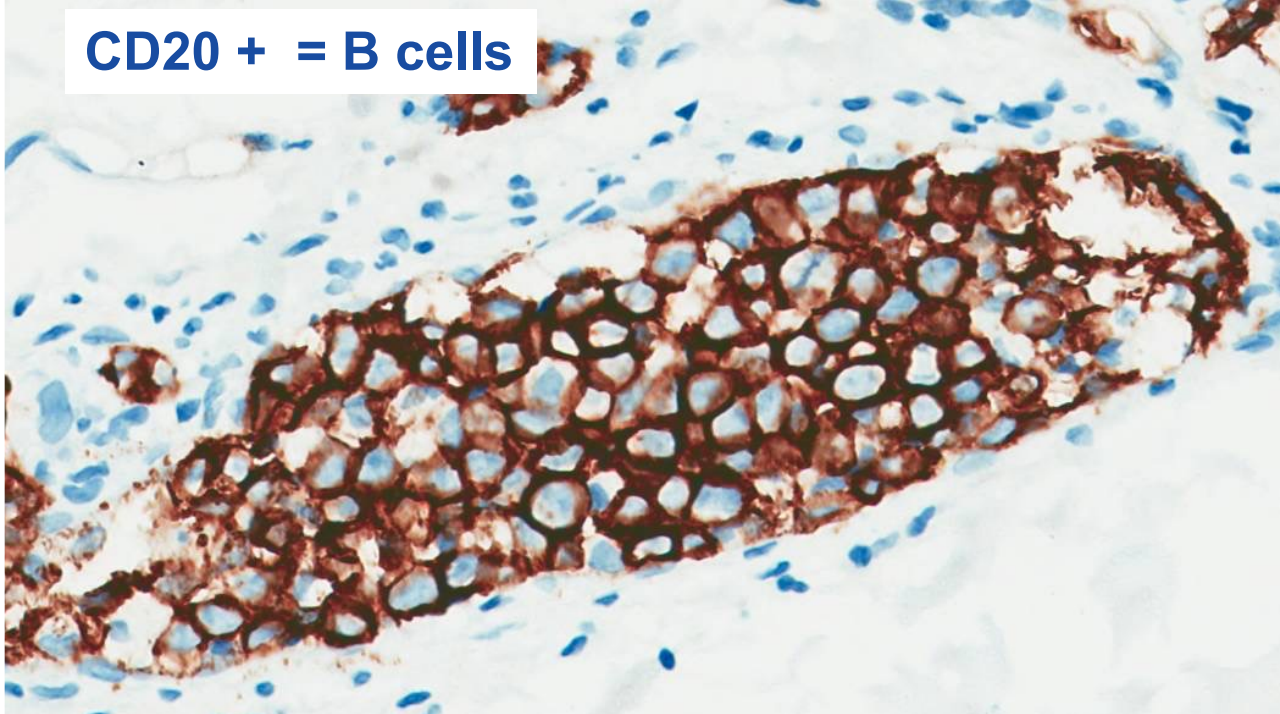




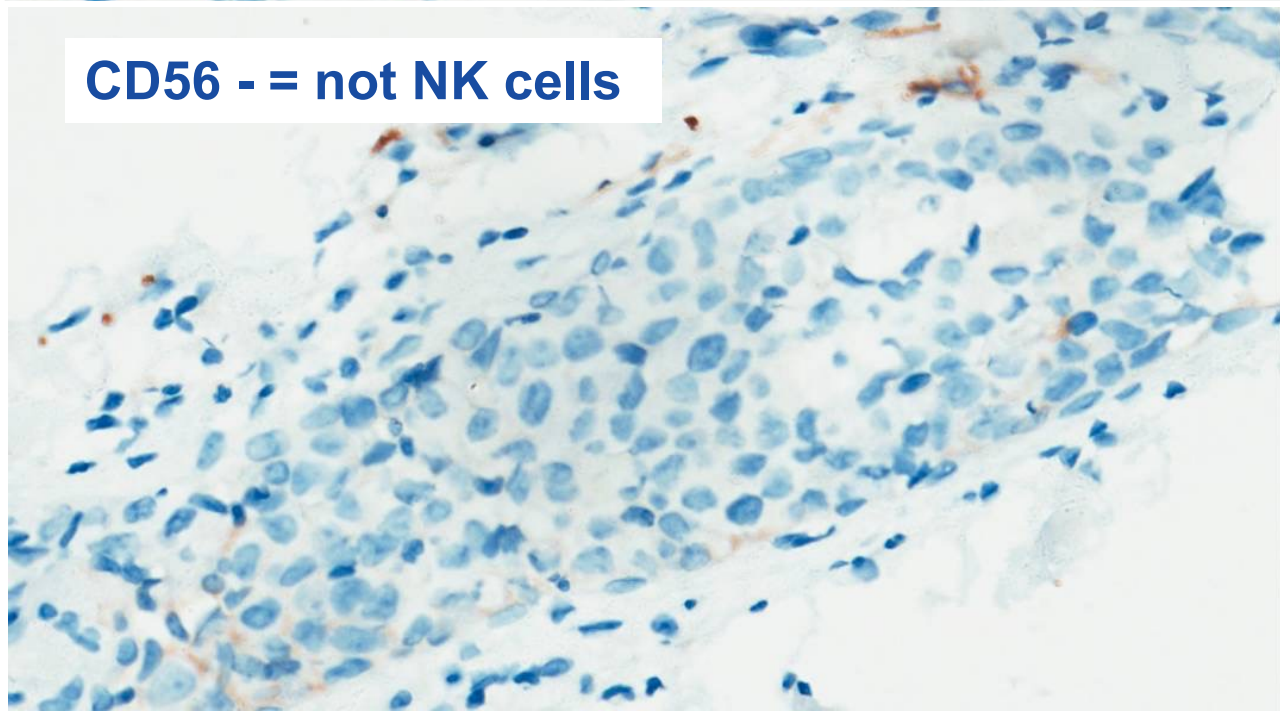




CD20 + = B cells



CD 3 - = not T cells

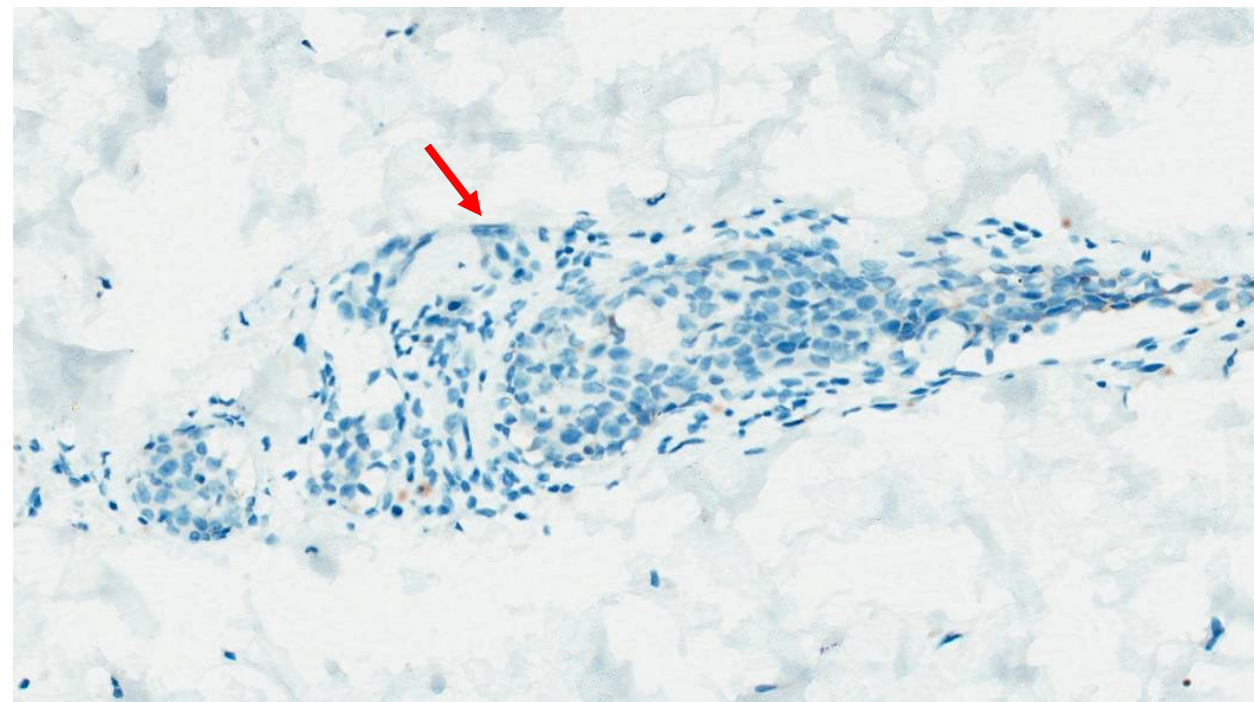
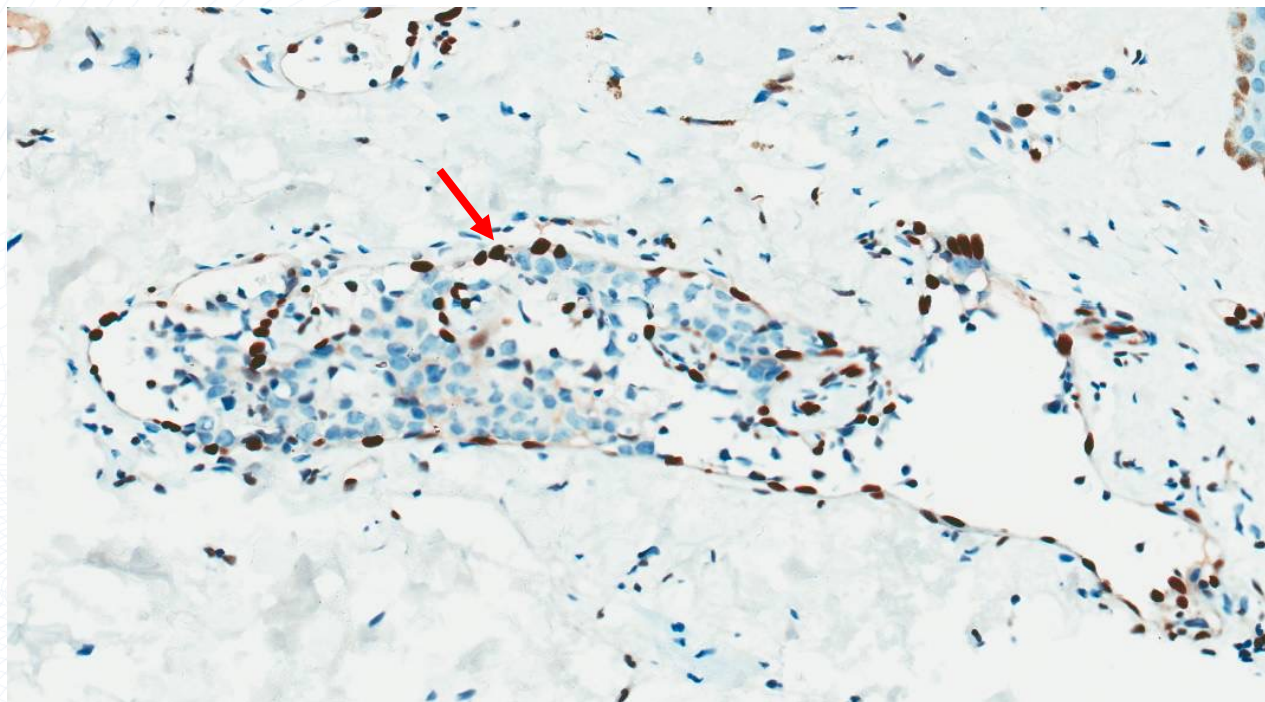


CD56 - = not NK cells

The atypical cells were within blood vessels, not lymphatics

ERG +

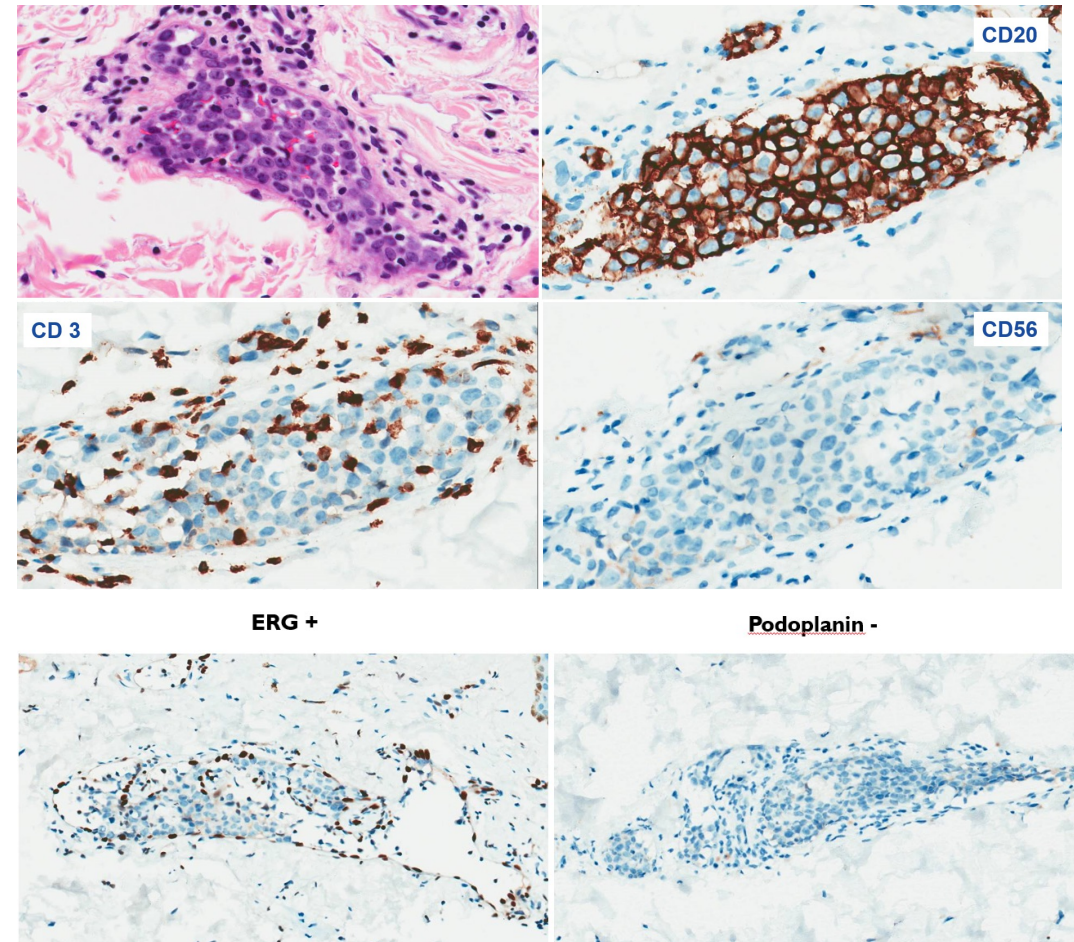
Podoplanin -



Atypical large B cells within lumina of blood vessels

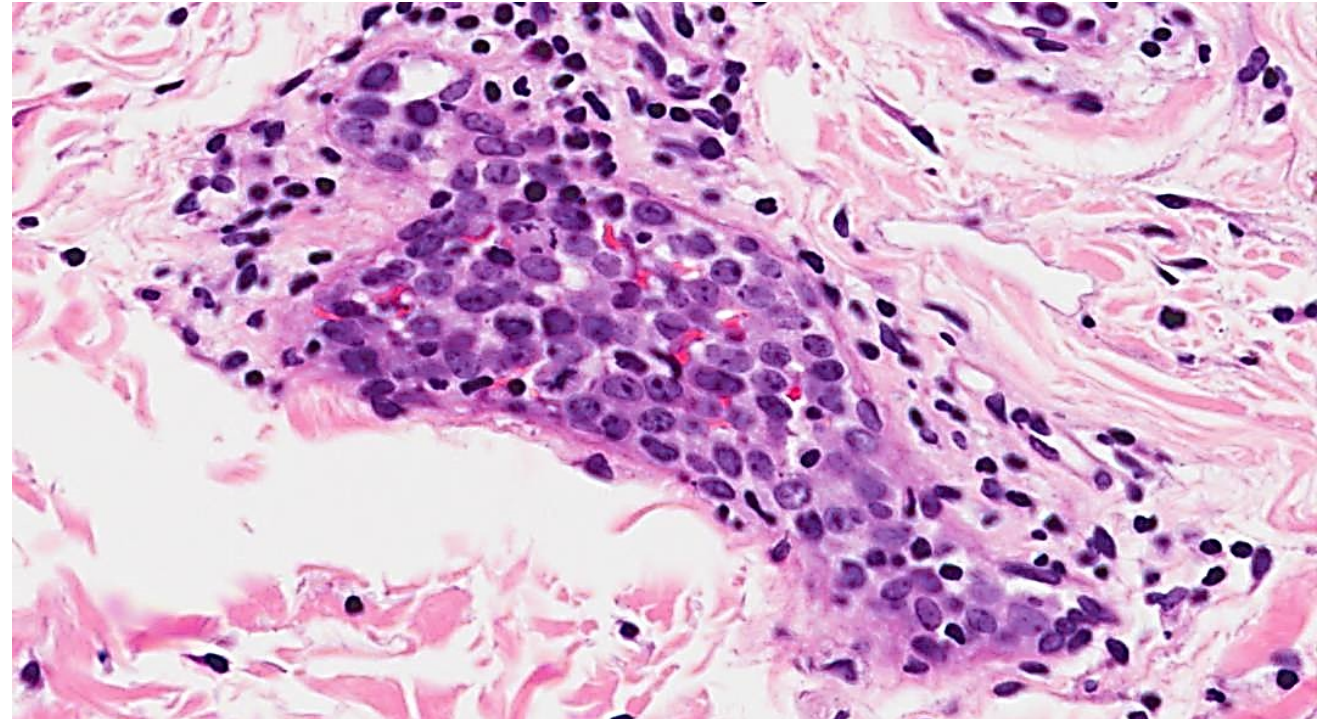
Diagnosis:

**Intravascular Large
B cell Lymphoma
(IVLBCL)**



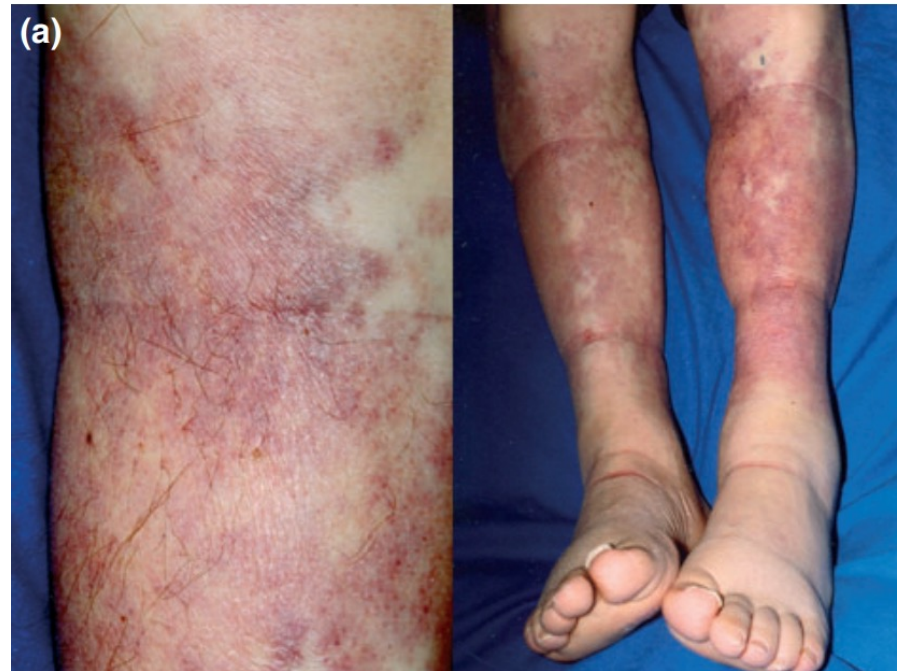
Intravascular Large B cell Lymphoma (IVLBCL)

- Rare extranodal lymphoma
- Selective growth of large atypical B cells within the lumina of blood vessels
- Fever and B symptoms
- Skin involved in 40%
- Hemophagocytic syndrome and multi-organ failure
- Aggressive course with high mortality
- Prognosis may be better in skin-limited disease

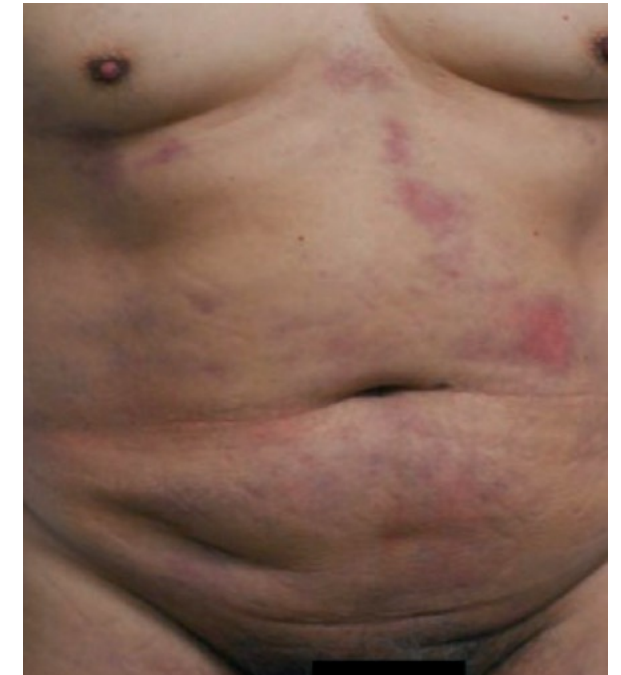


Intravascular Large B cell Lymphoma (IVLBCL) Cutaneous Manifestations

- Heterogeneous presentation
- Macules, plaques, nodules
- Reticulated
- Confluent patches



Wahie S, et al. *Clin Exp Dermatol.* 2011;36:288-91

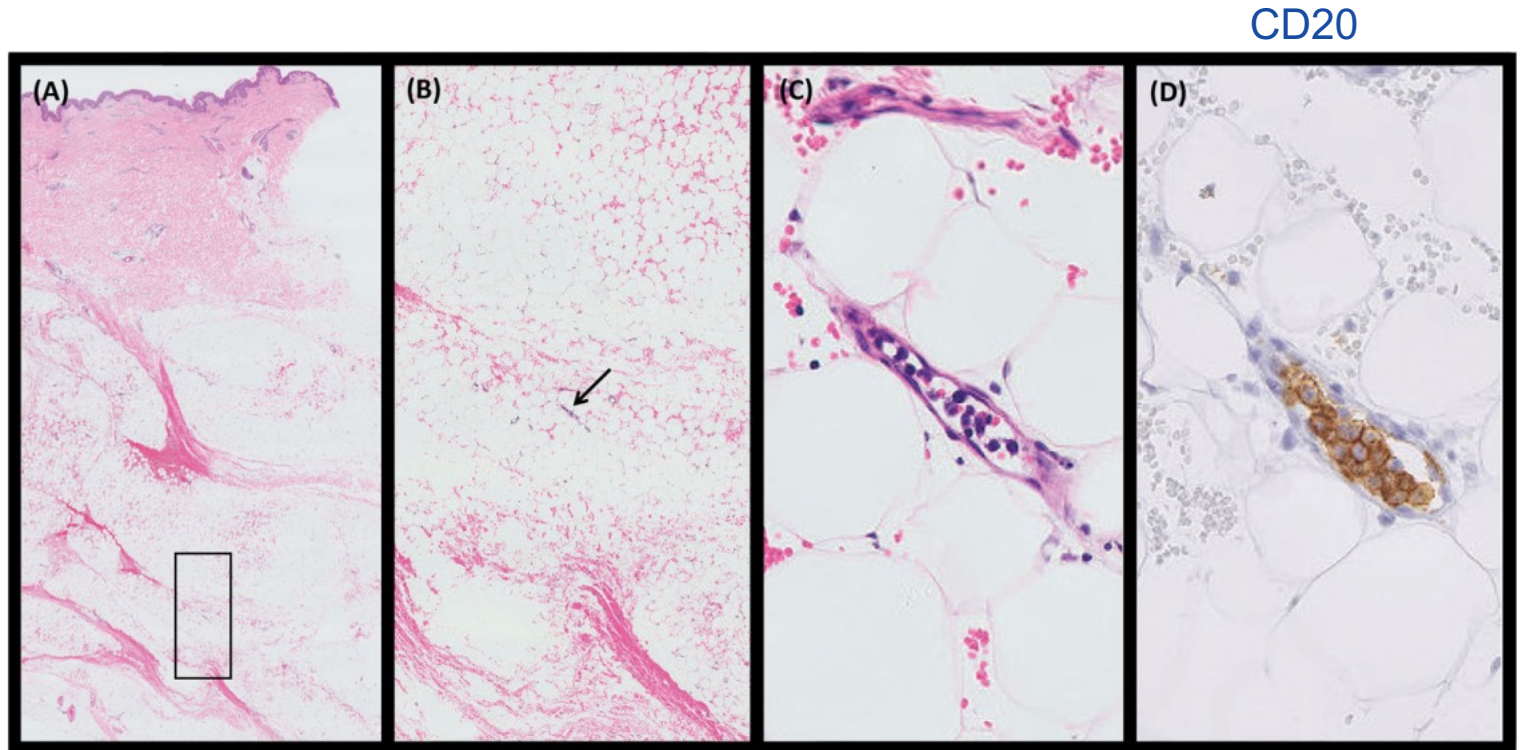


Park JH et al. *Journal of Dermatology* 2011; 38: 160–163

Intravascular Large B cell Lymphoma (IVLBCL)

Skin biopsies

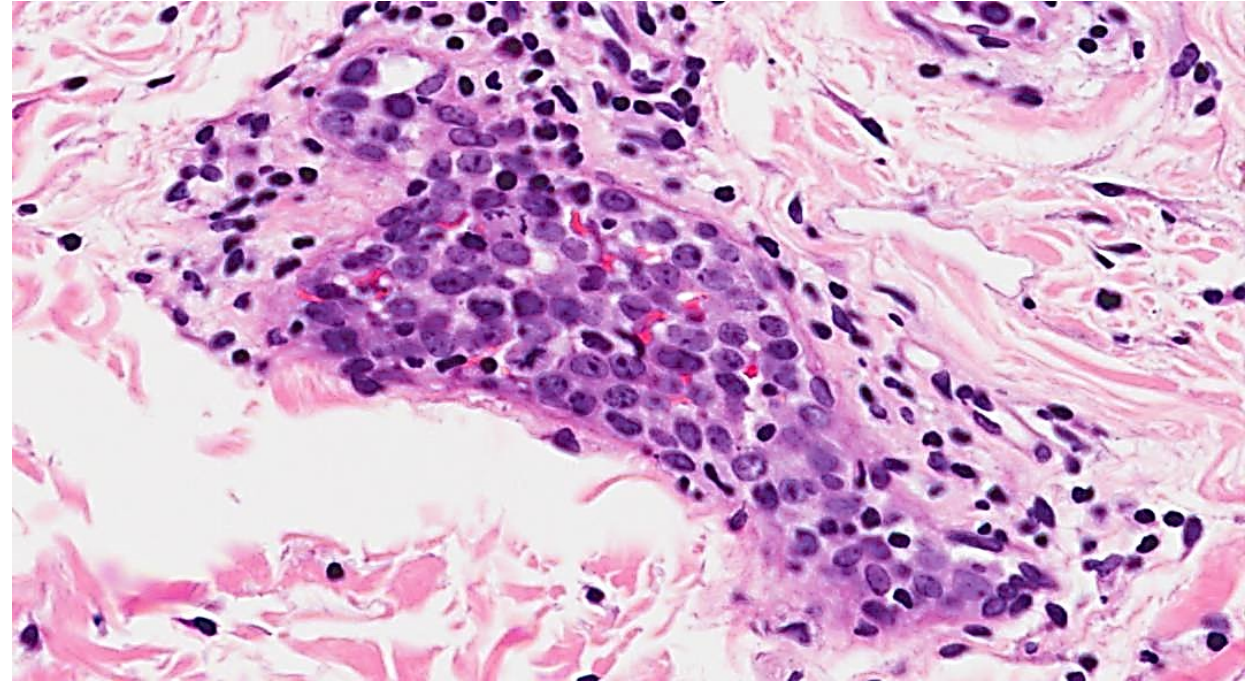
- Skin biopsies are very helpful to diagnose IVLBCL
- Even in normal-looking skin, random skin biopsies can be useful
- Helpful tips
 - Include subcutis
 - Thighs and lower abdomen
 - Senile hemangiomas



Enzan N, et al, J Cutan Pathol. 2021;48(4):589-591.

Take home message for case 1

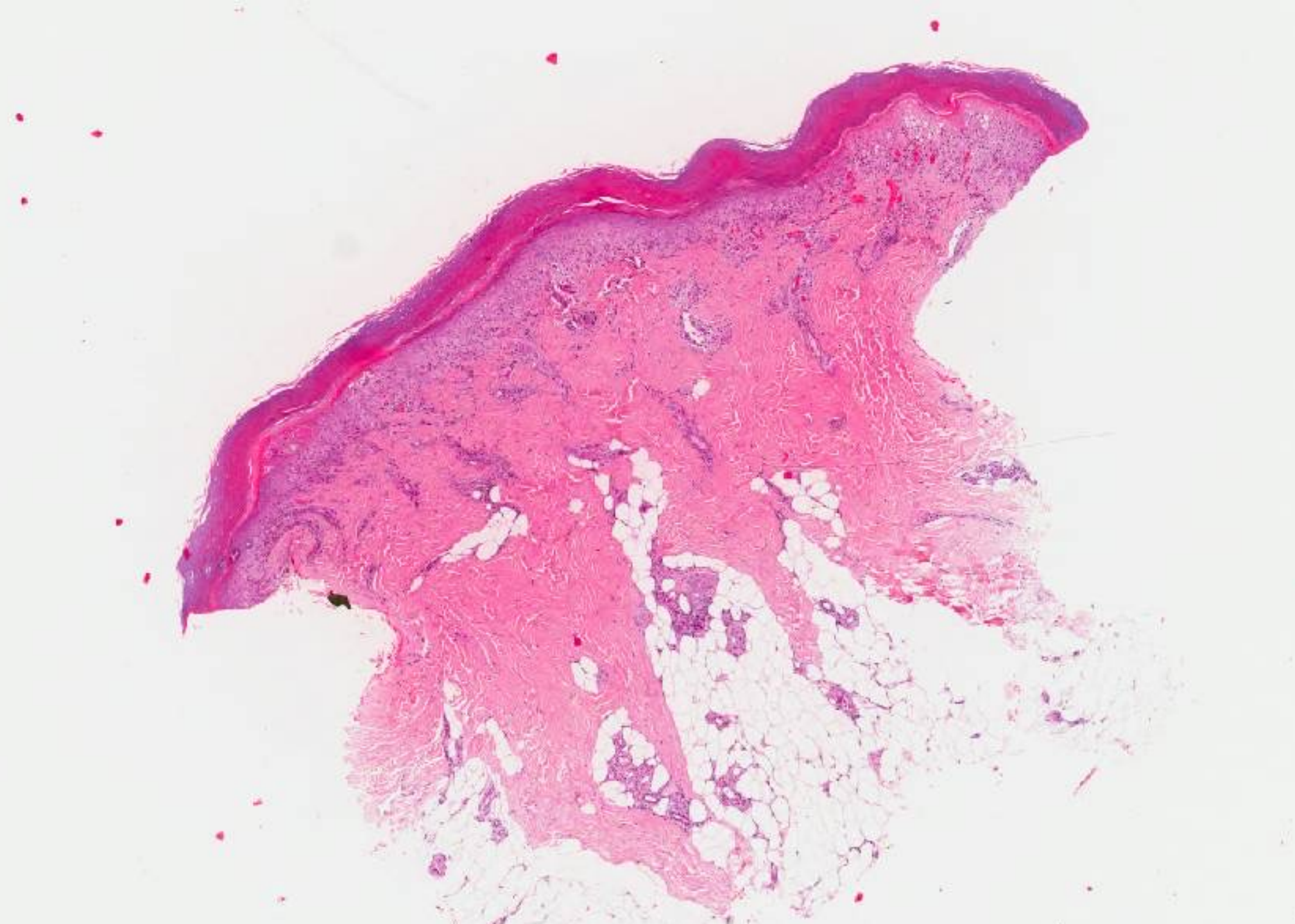
- IVLBCL can present with non-specific cutaneous findings
- Random skin biopsies even on normal-looking skin may be helpful
- Capillaries within subcutis, hemangiomas
- Important to recognize and diagnose this entity early to avoid delay in treatment of this aggressive disease

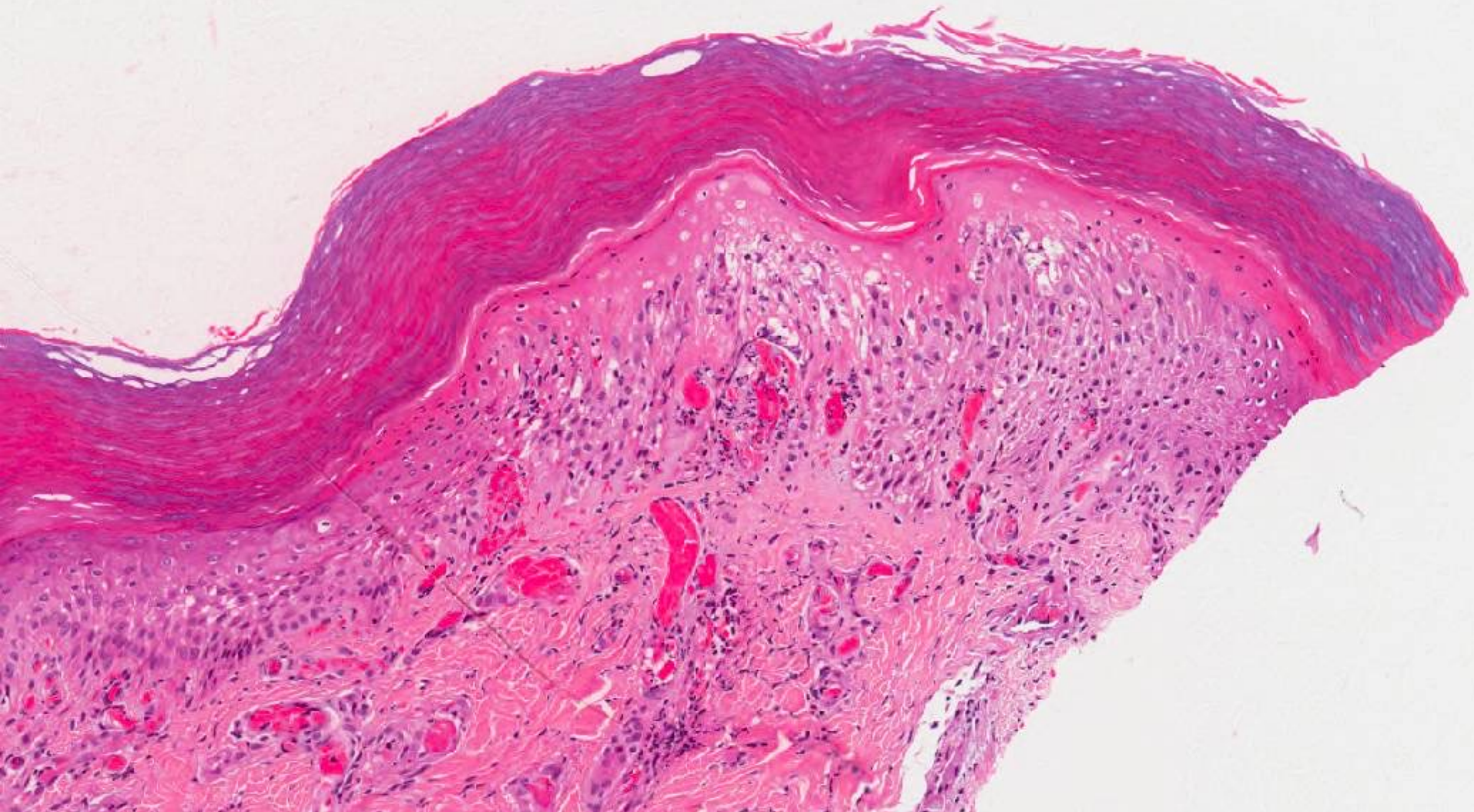


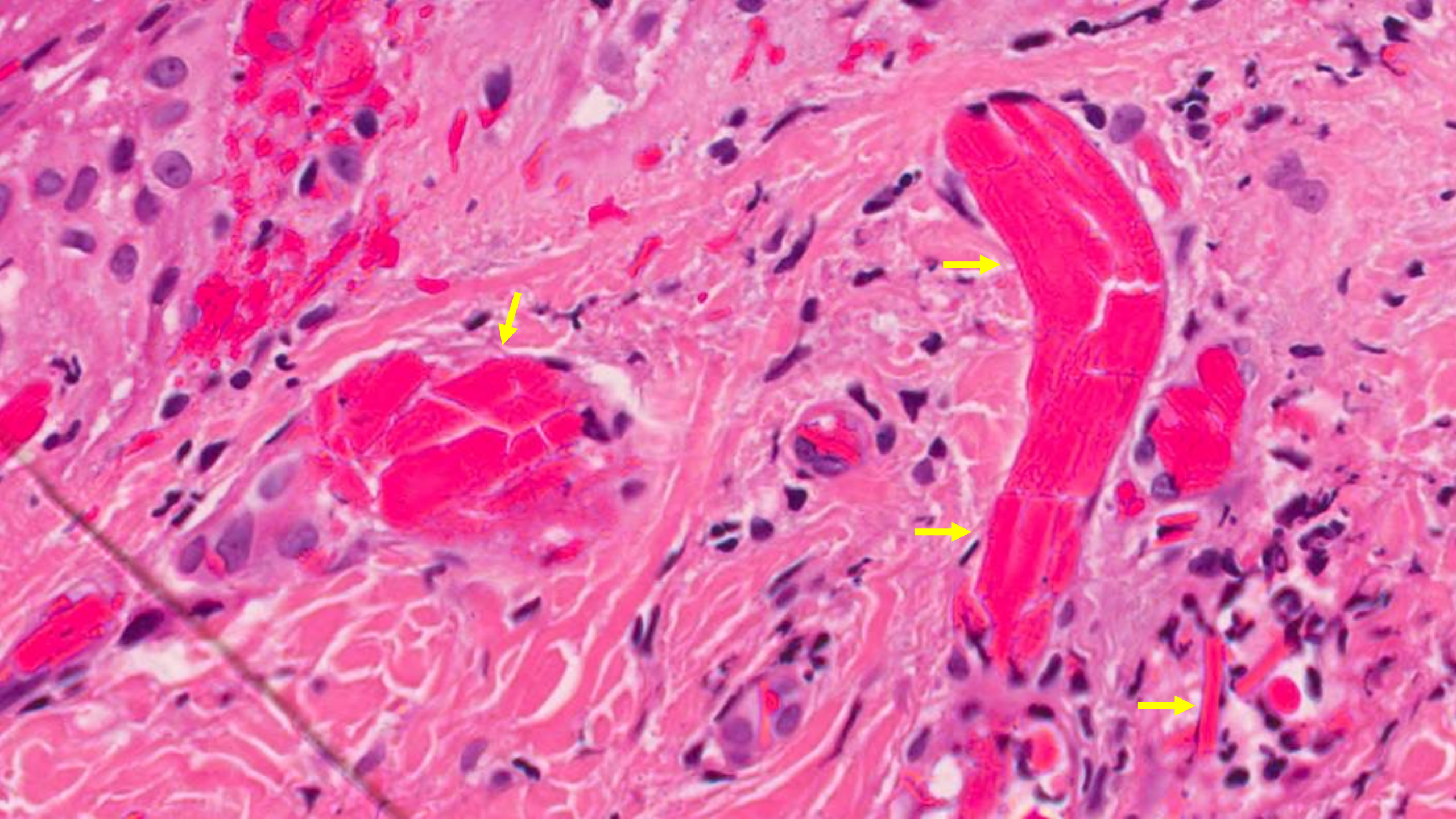
Case 2

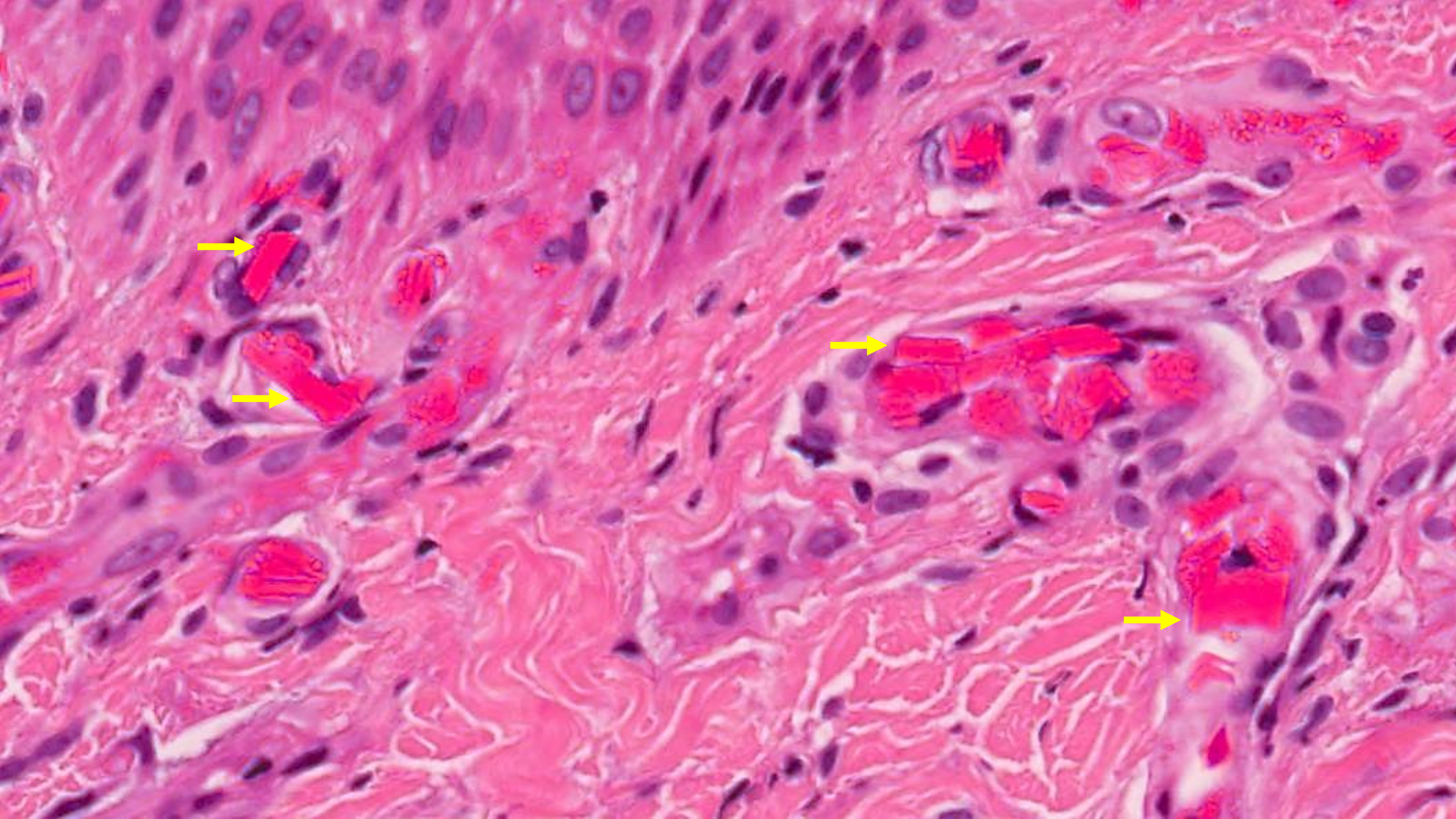
- 65-year-old male
- Tender eruption over both feet for 2 months
- Reticulate erythema, purpura and ulcers
- Pain over the finger joints
- Intermittent fevers
- Weight loss of 7kg over 5 months
- Punch biopsy from the heel was performed



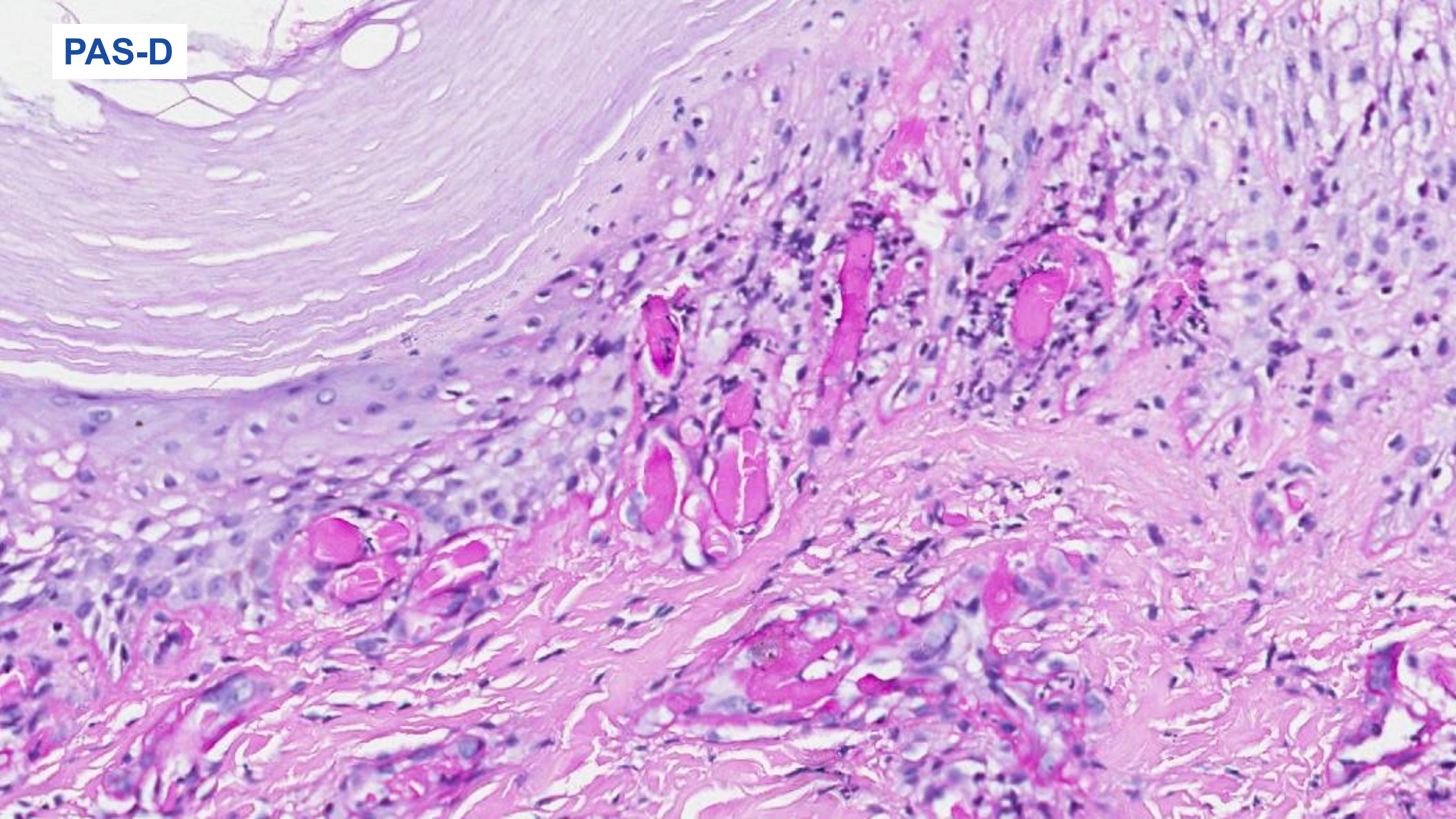








PAS-D



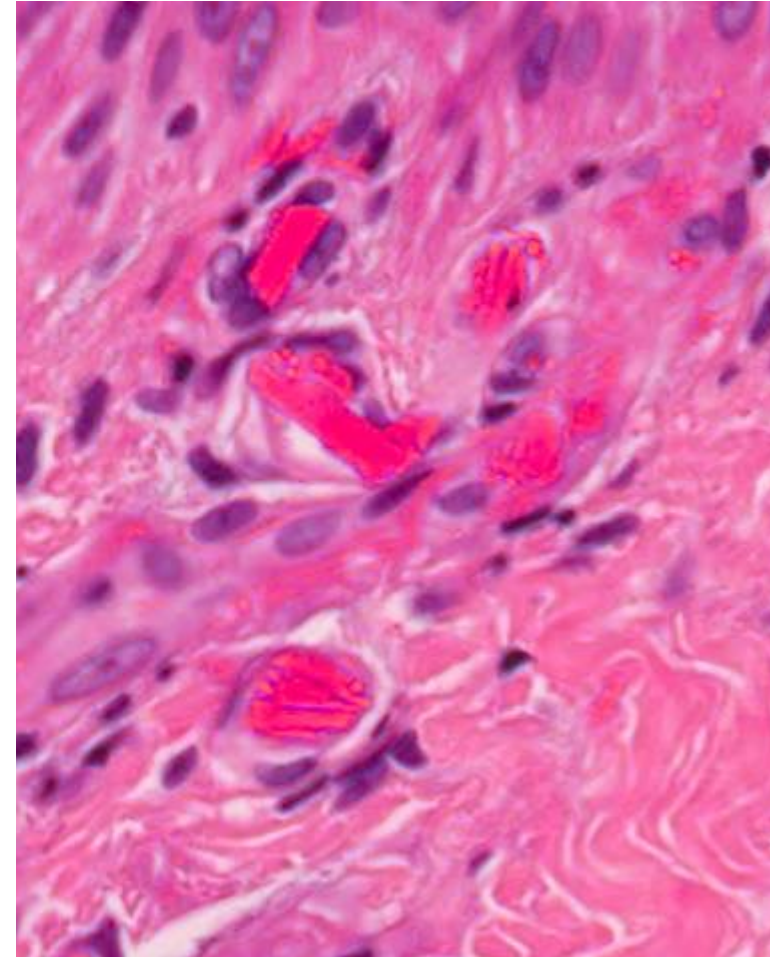
Subsequent investigations

- Raised serum cryoglobulins
- Serum protein electrophoresis
 - Monoclonal IgGκ paraprotein of 26.0g/L (reference range 8.5–18.0g/L)
 - Free kappa light chain of 95.9mg/L (reference range 3.3–19.4mg/L),
- Diagnosis of multiple myeloma

Crystalglobulinaemia

Crystalglobulinaemia

- Intravascular crystallisation of monoclonal immunoglobulins (IgG)
- Underlying monoclonal gammopathy
- If the crystals are cryoprecipitating, the disease is termed cryocrystalglobulinemia (CCG)



Crystalglobulinaemia

Clinical manifestations

- Purpuric, retiform eruption
- Necrosis, ulceration, infarcts
- Pain
- Extremities, areas of stasis and cooling

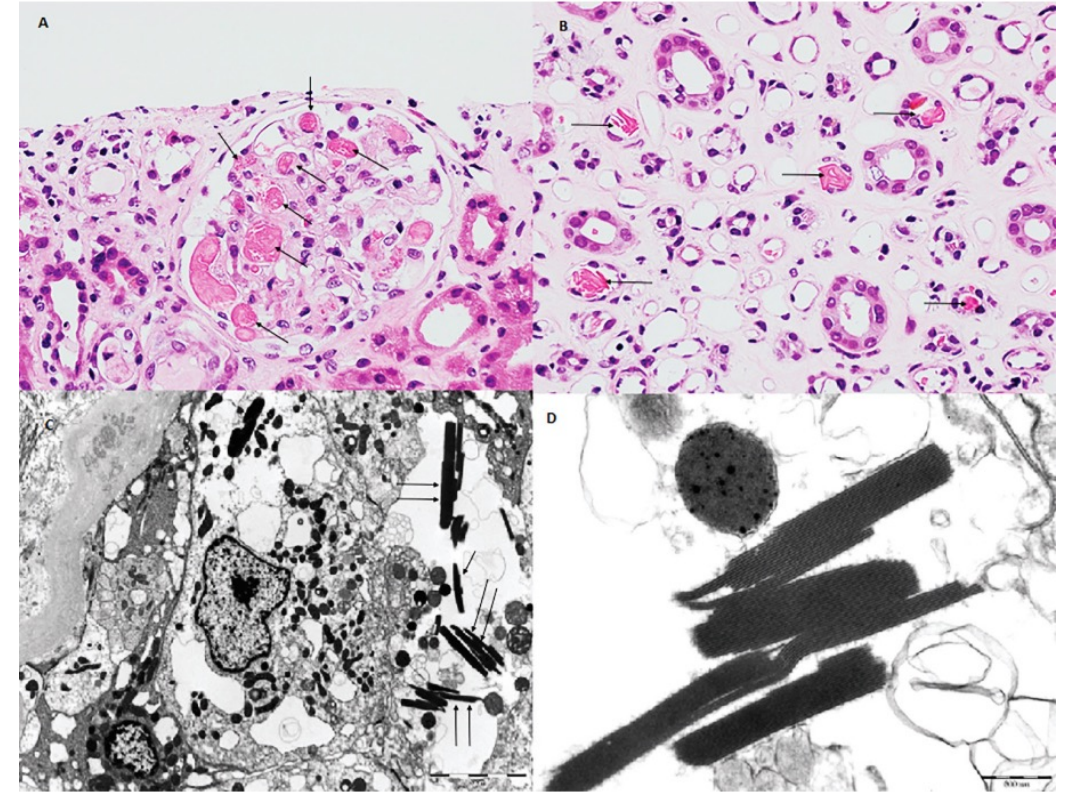


Abe N, et al. Medicine (Baltimore). 2017;96(16):e6643.

Crystalglobulinaemia

Clinical manifestations

- Kidney
 - Crystals deposit in the arteries and glomerular capillary lumina
 - Acute kidney injury often with a fatal outcome
- Joints, nerves, gut and eye can be affected

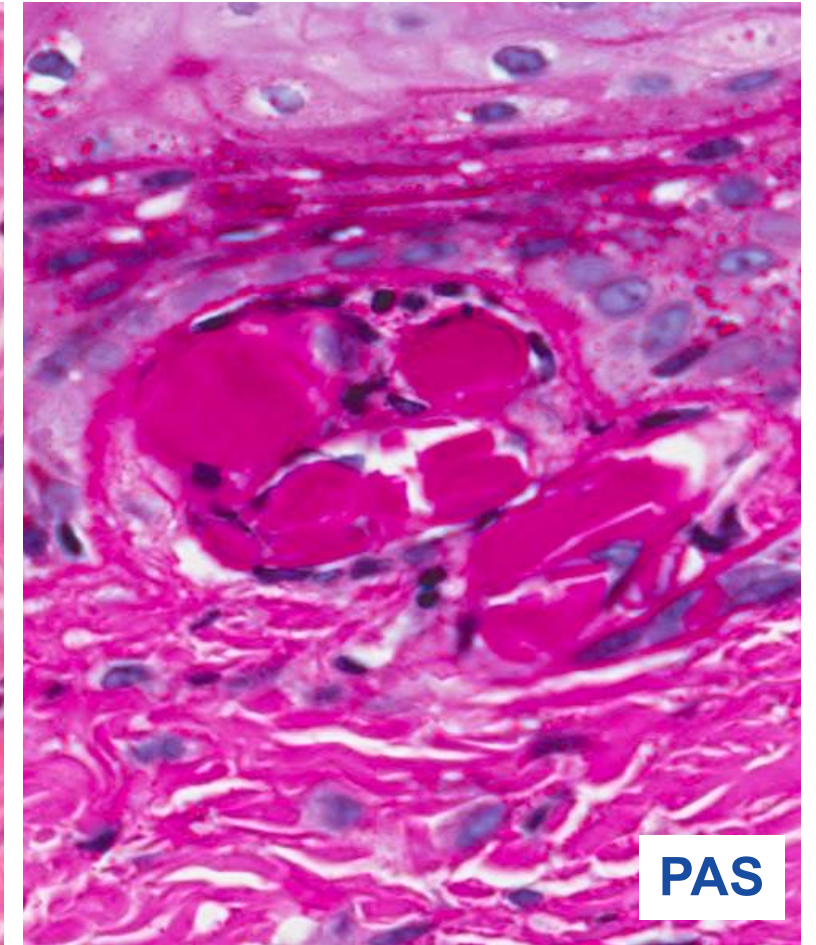
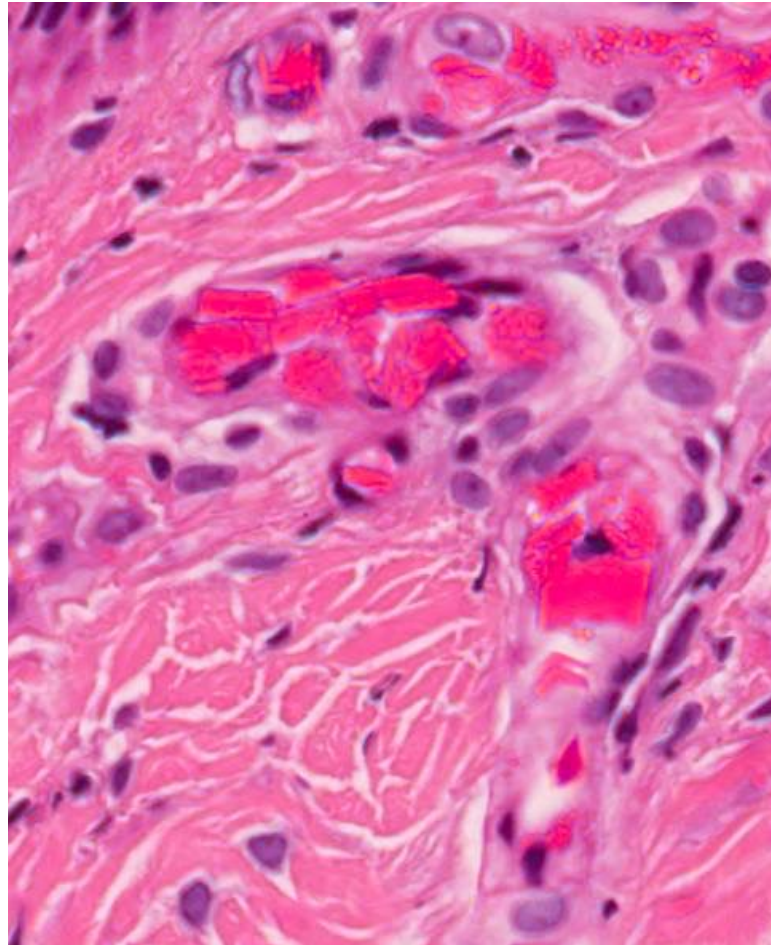


Chou A, Long C, Vonthehoff L, et al. Can J Kidney Health Dis. 2020 May 18;7:2054358120922629.

Crystalglobulinaemia

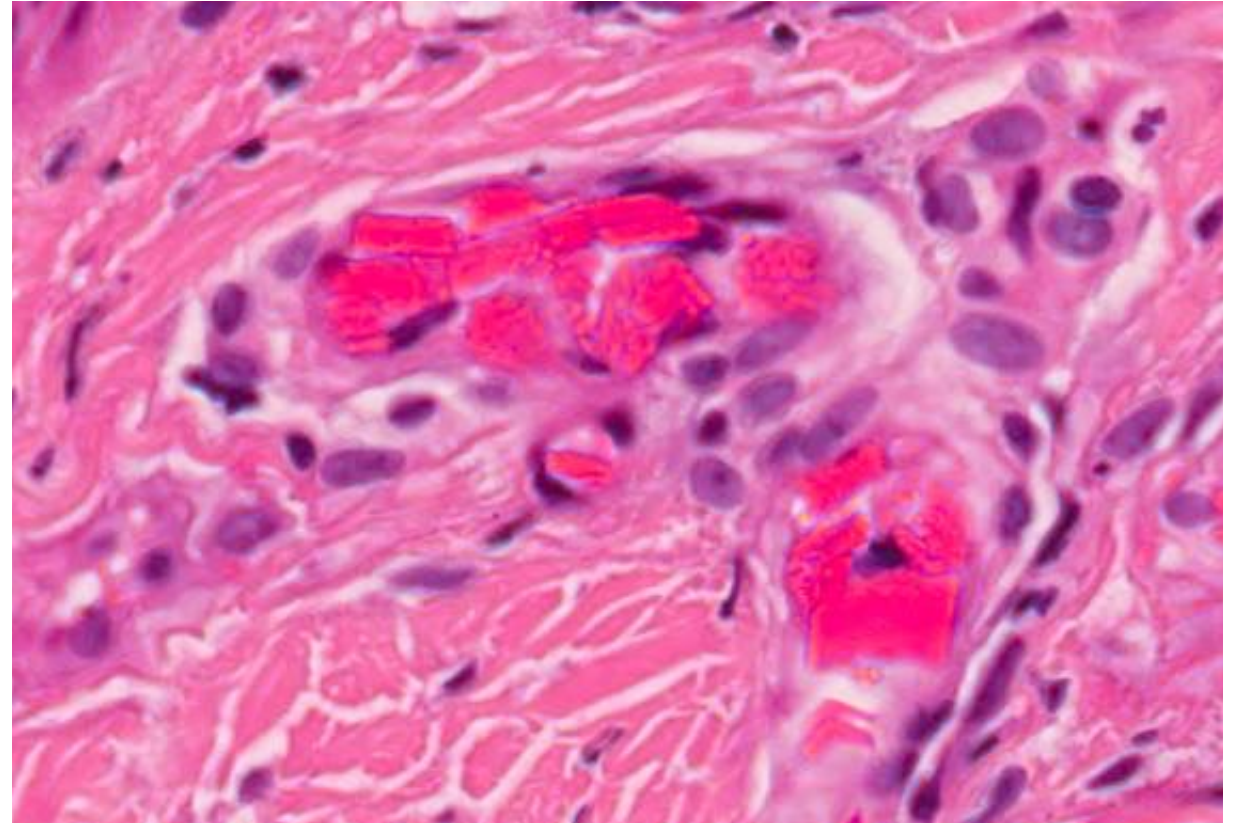
Histopathological Findings

- Crystalline oblong structures within lumina of blood vessels
- PAS-positive
- Absence of vasculitis



Take home message for case 2

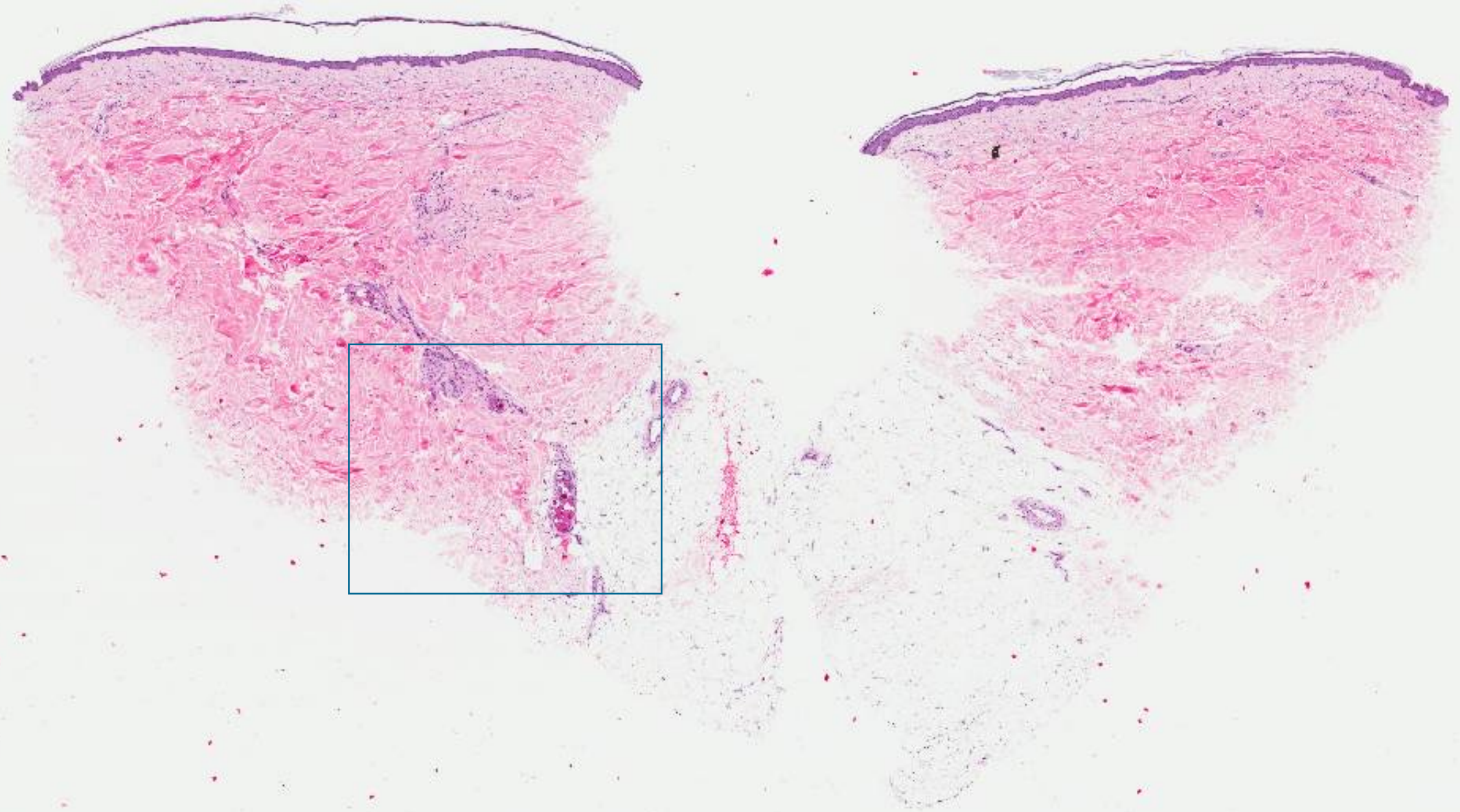
- Crystalglobulinemia is a very rare cause of occlusive vasculopathy
- High morbidity and mortality, mainly from acute renal failure
- Skin manifestations may be the earliest presentation of CG
- Recognition of this entity with early diagnosis and therapeutic intervention can improve the prognosis

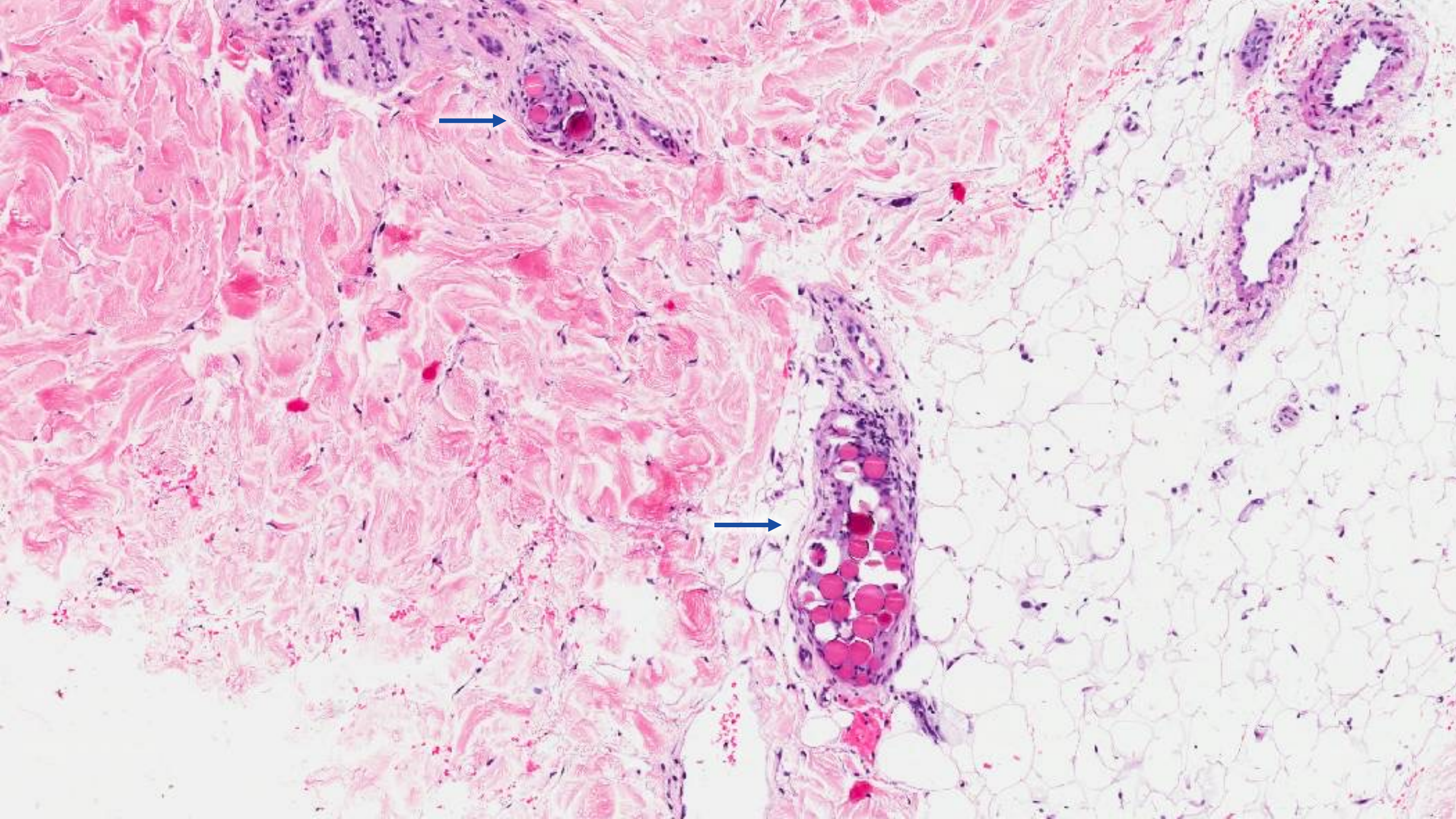


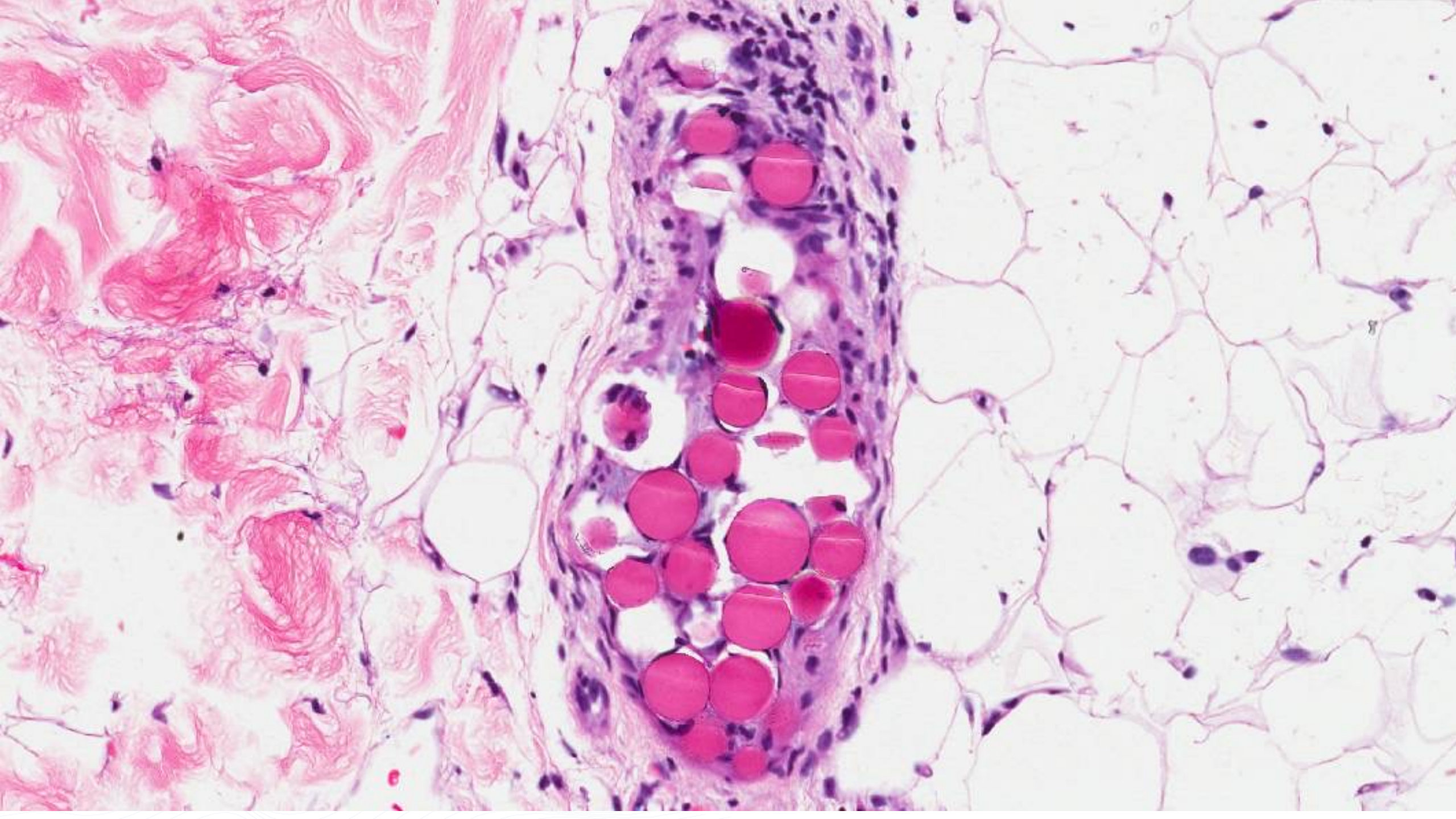
Case 3

- 77-year-old male
- Hepatocellular carcinoma
- Reticulated macular pigmentation over the chest and upper abdomen
- Clinical impression:
 - Paraneoplastic thrombotic phenomenon? Vasculitis?





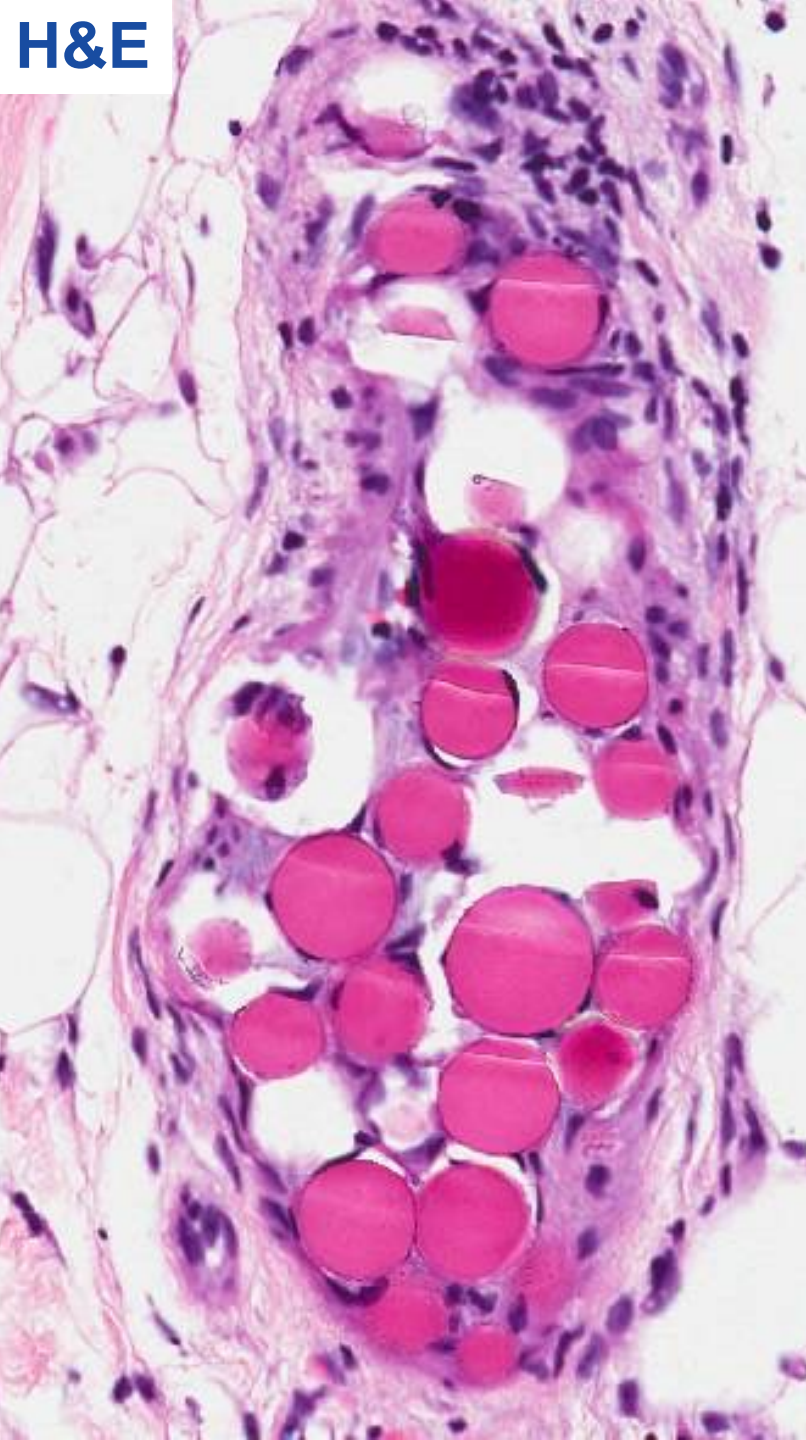




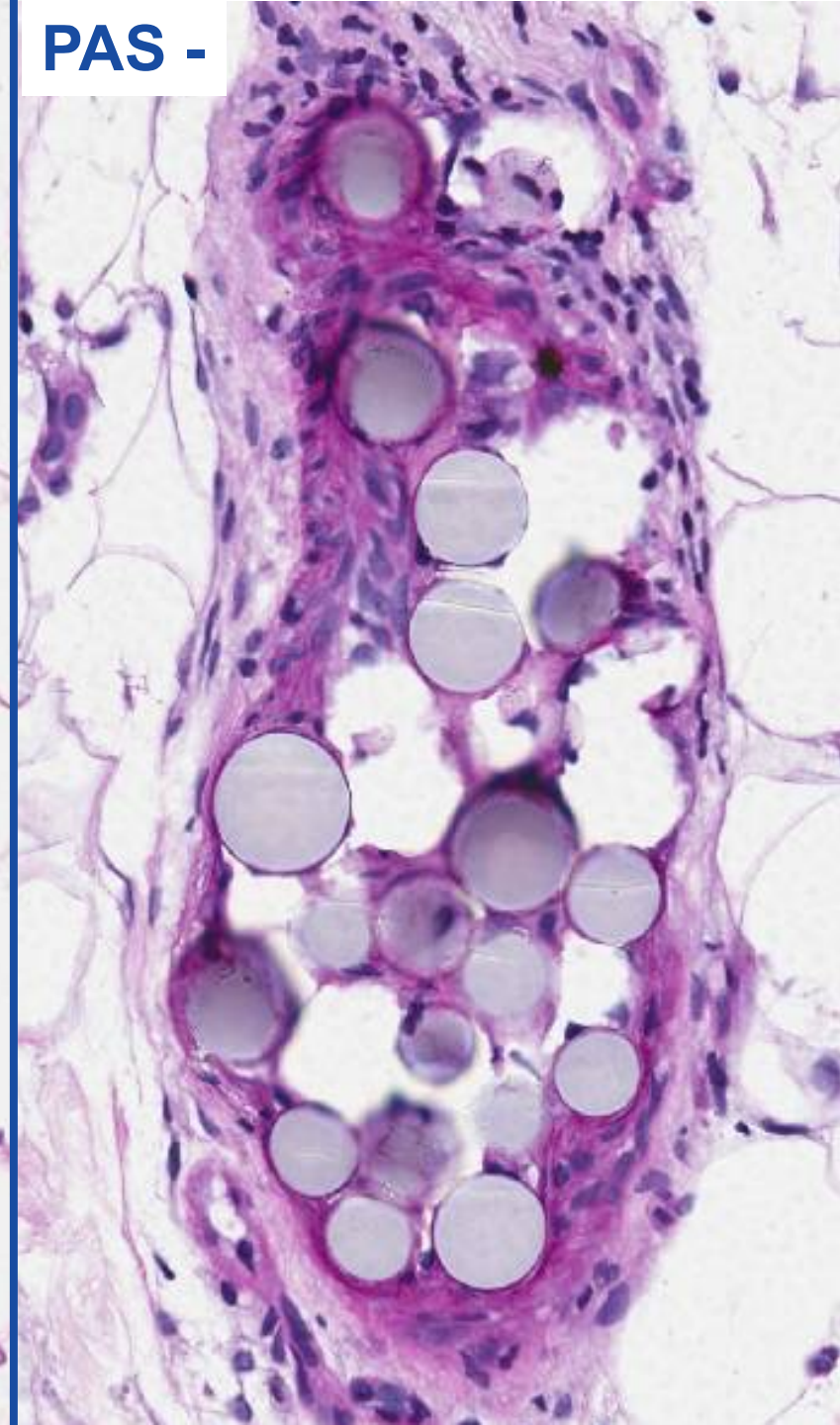


40.68 um

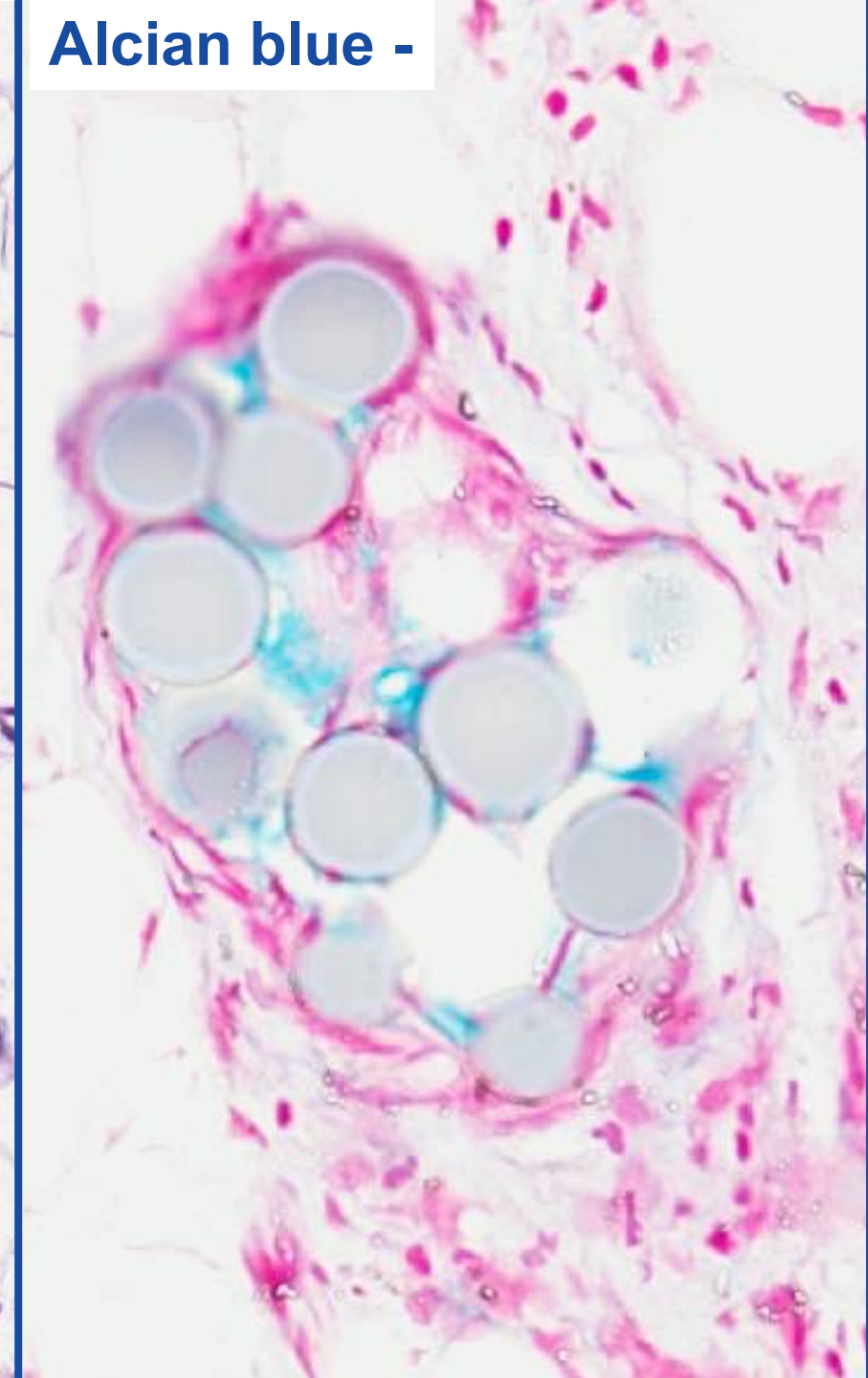
H&E

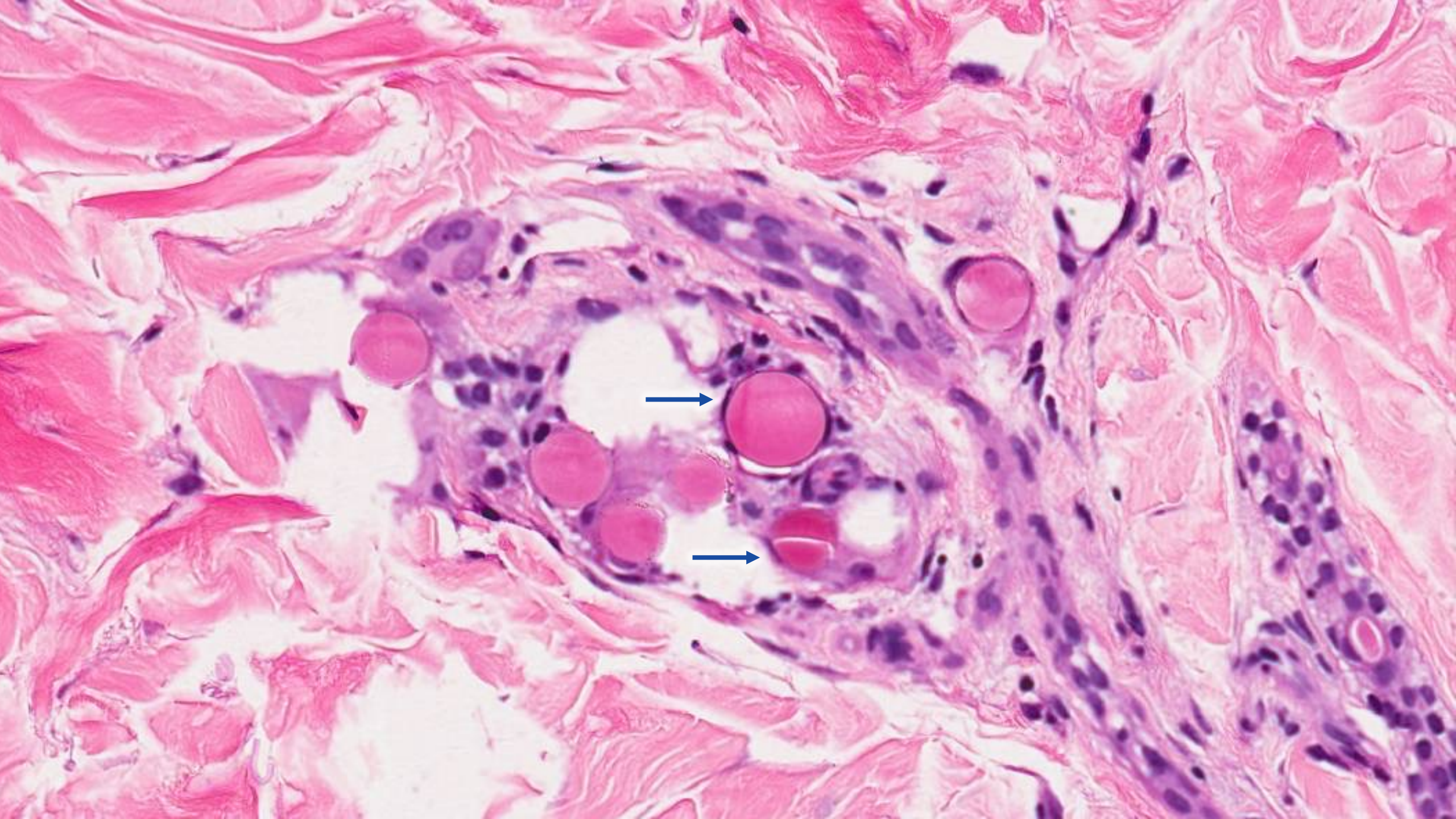


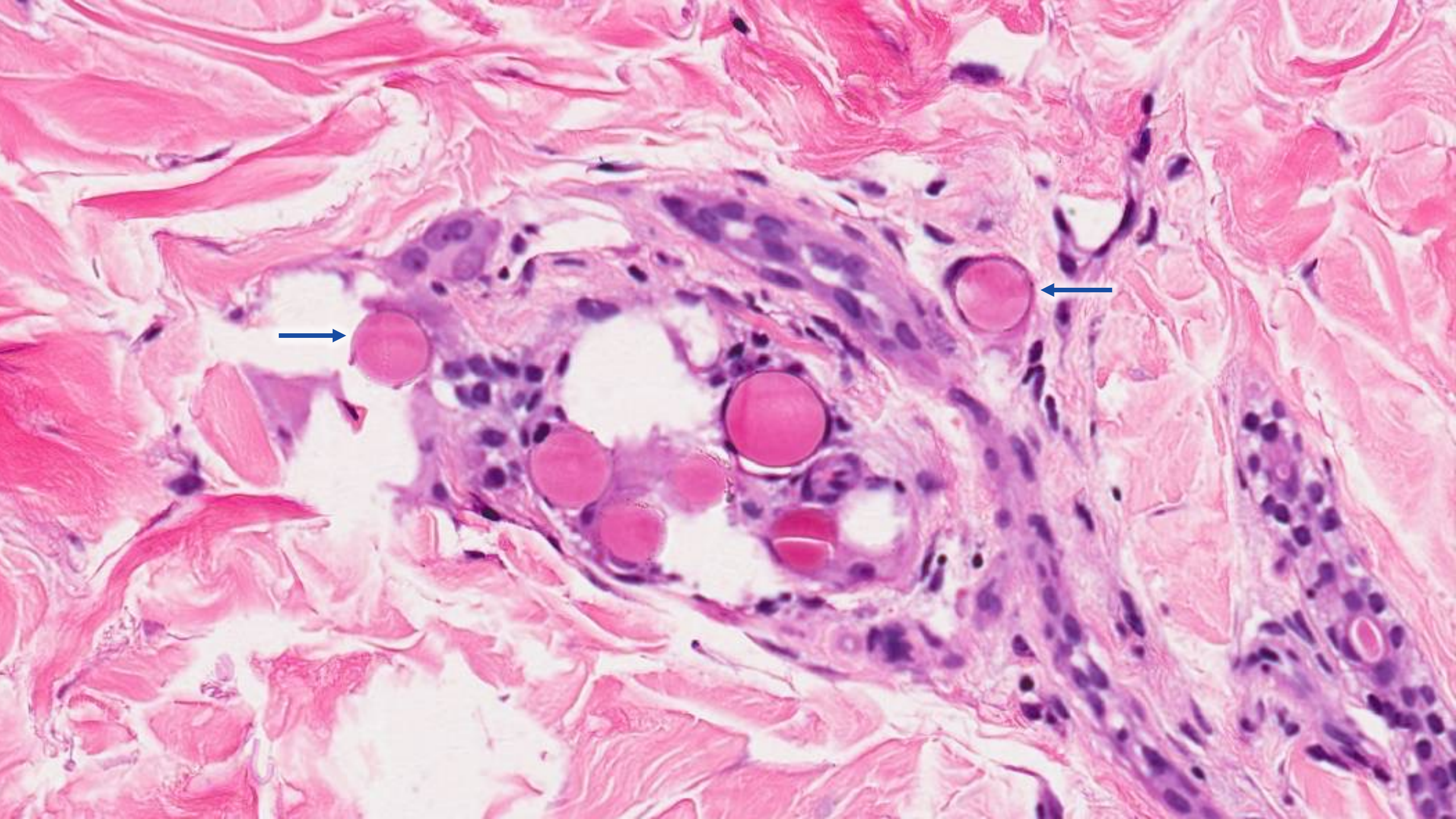
PAS -



Alcian blue -









What is an important question that we need to ask the clinician?



**Any recent intervention for
Hepatocellular carcinoma?**



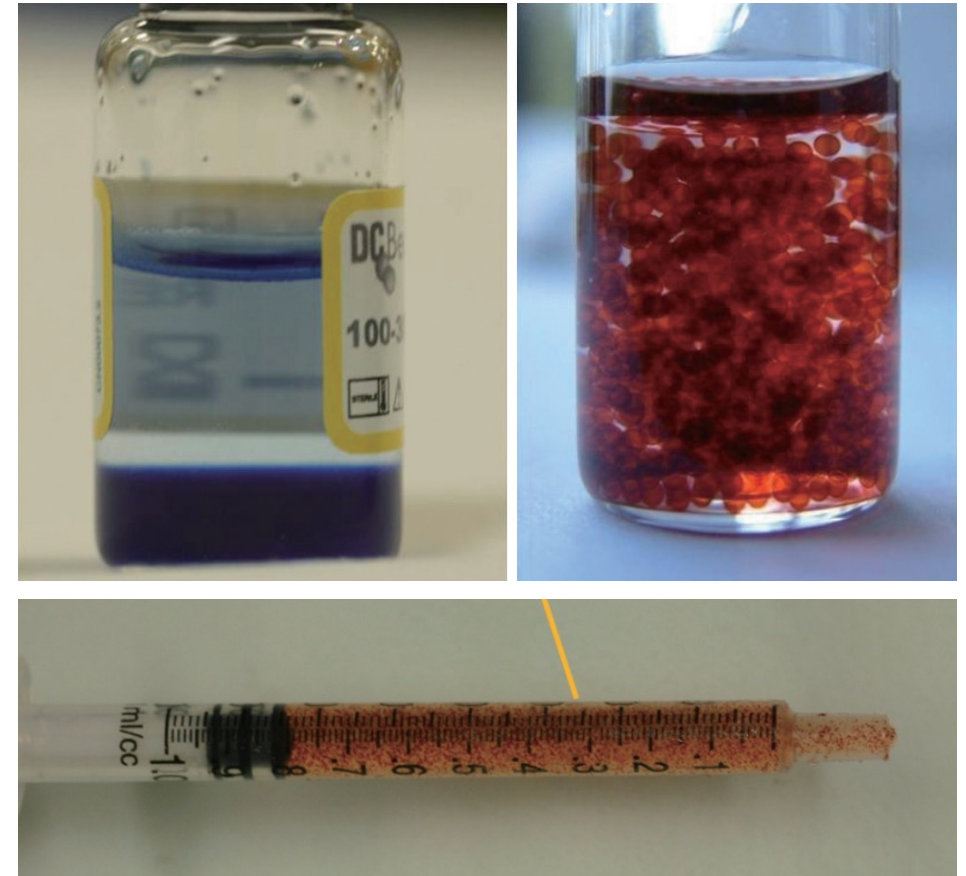
Further history...

- Had recently received transarterial chemoembolization with drug eluting beads (DEB-TACE) for advanced hepatocellular carcinoma

**Cutaneous microsphere embolism
DEB-TACE therapy**

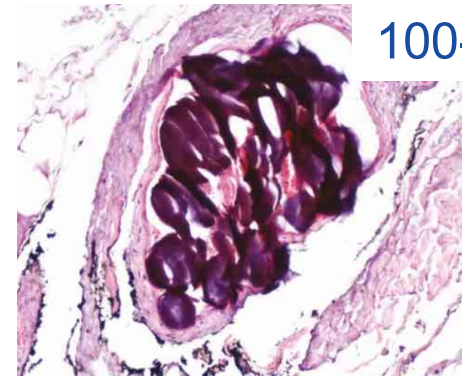
Drug-eluting bead transarterial chemoembolization (DEB-TACE)

- Treatment used in advanced hepatocellular carcinoma
- Drug-eluting beads/microspheres (DEBs) are loaded with chemotherapeutic agents
- Injected into the hepatic artery via radiologic guidance
- Sustained release of chemotherapy
- Embolization of tumour vasculature
- Made of biocompatible polymers eg. polyvinyl alcohol (PVA) hydrogel
- DC Bead[®], HepaSphere[™]

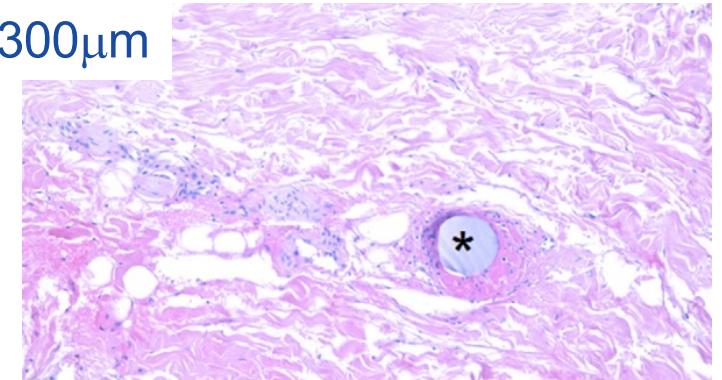


Drug-eluting bead transarterial chemoembolization (DEB-TACE)

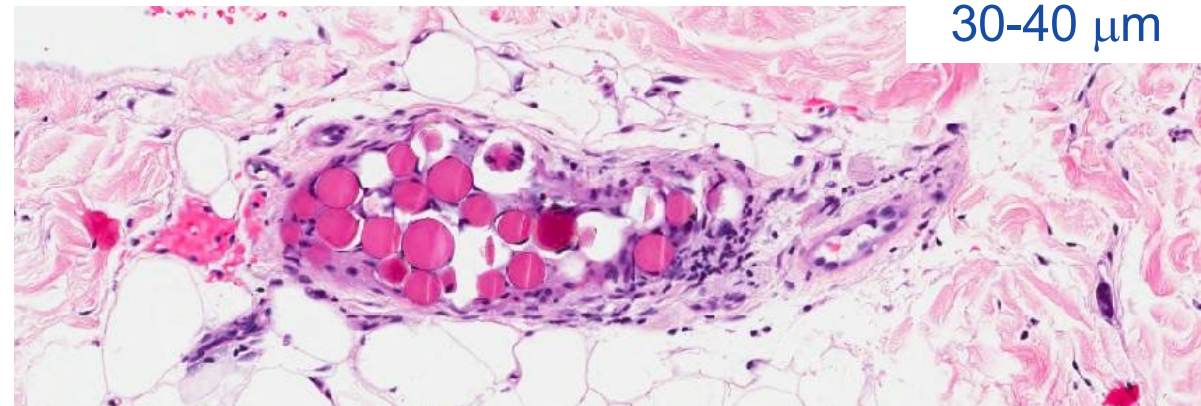
- Size: 30 - 800 μm
- Smaller DEBs (<100 μm)
 - Greater distal penetration, more effective embolization
 - Higher the chance of cutaneous microembolism via collateral vasculature



Grieshaber E, et al.
JAMA Dermatol.
2014;150:1118-20.



Stalder G, et al. Diagn Interv
Imaging. 2018;99:179-180.





Cutaneous embolism from DEB-TACE

- Extremely rare side effect
- Cutaneous signs occur within a few days after the TACE procedure
- Upper abdominal / supra-umbilical area

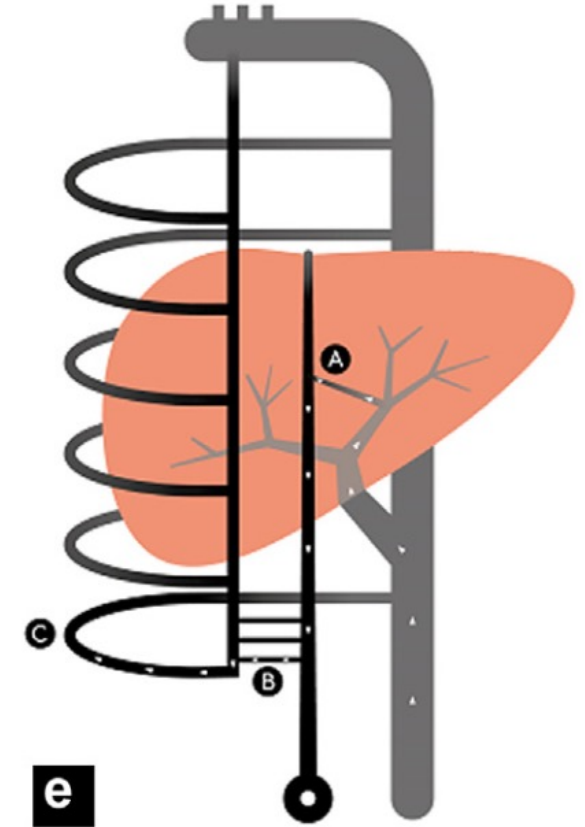
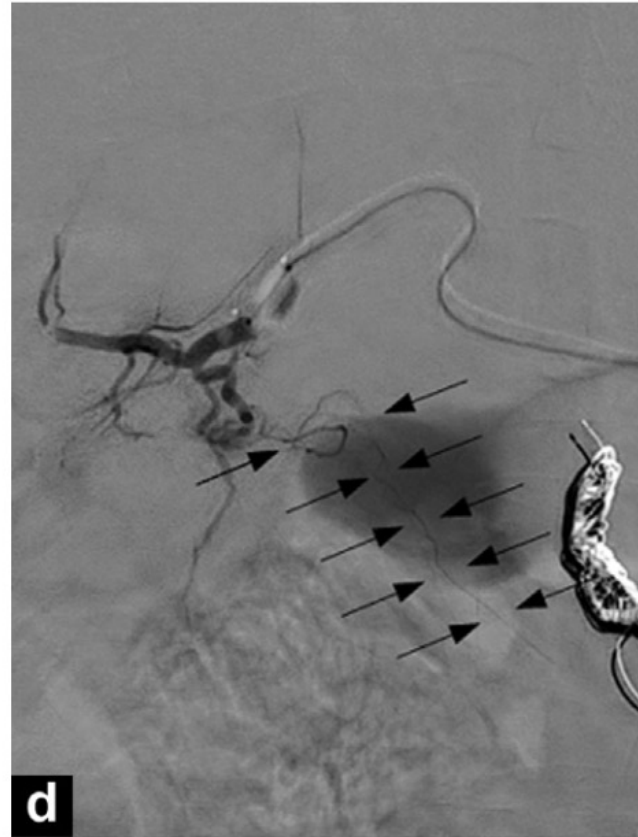


Stalder G, et al. Diagn Interv Imaging. 2018;99(3):179-180.



Cutaneous embolism from DEB-TACE

- Patent hepatic falciform artery (anatomical variant)
- Anastomoses with cutaneous arteries which feed the supra-umbilical anterior abdominal wall



Stalder G, et al. *Diagn Interv Imaging*. 2018;99(3):179-180.



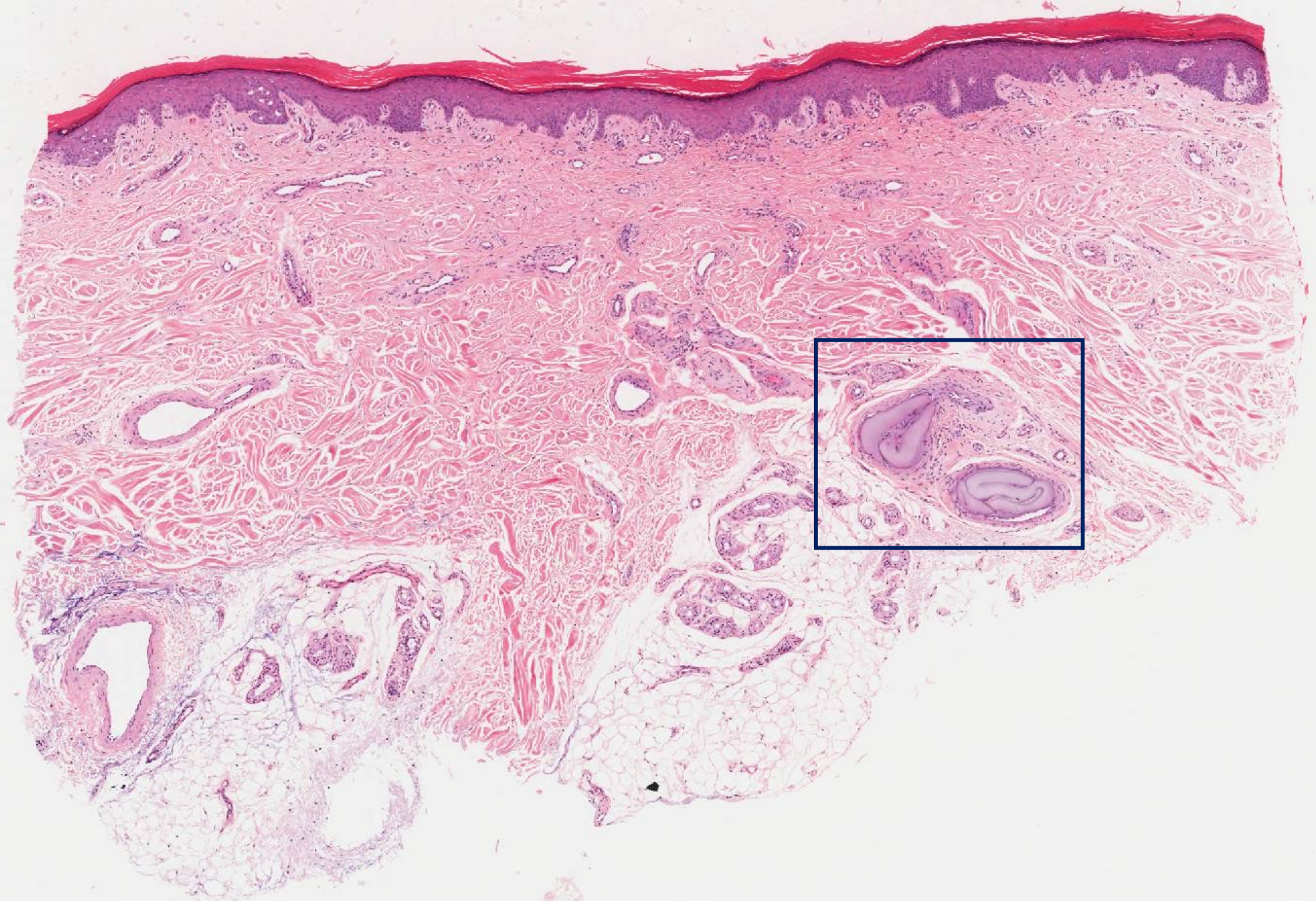
Take home message for case 3

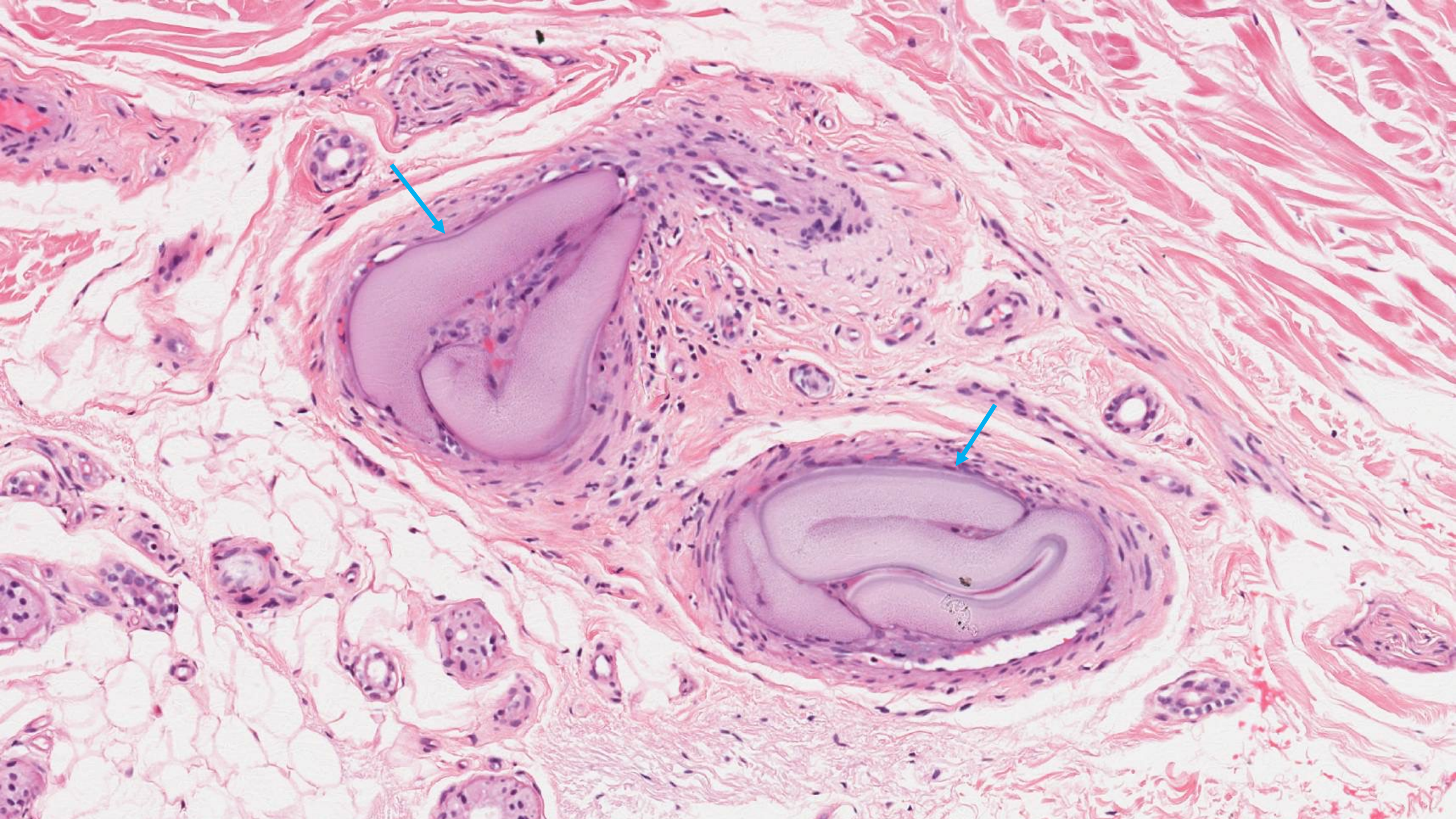
- Cutaneous microsphere embolism is a very rare complication from DEB-TACE for treatment of hepatocellular carcinoma
- Important to recognize this condition in the light of more widespread adoption of DEB-TACE and the use of smaller microspheres

Case 4

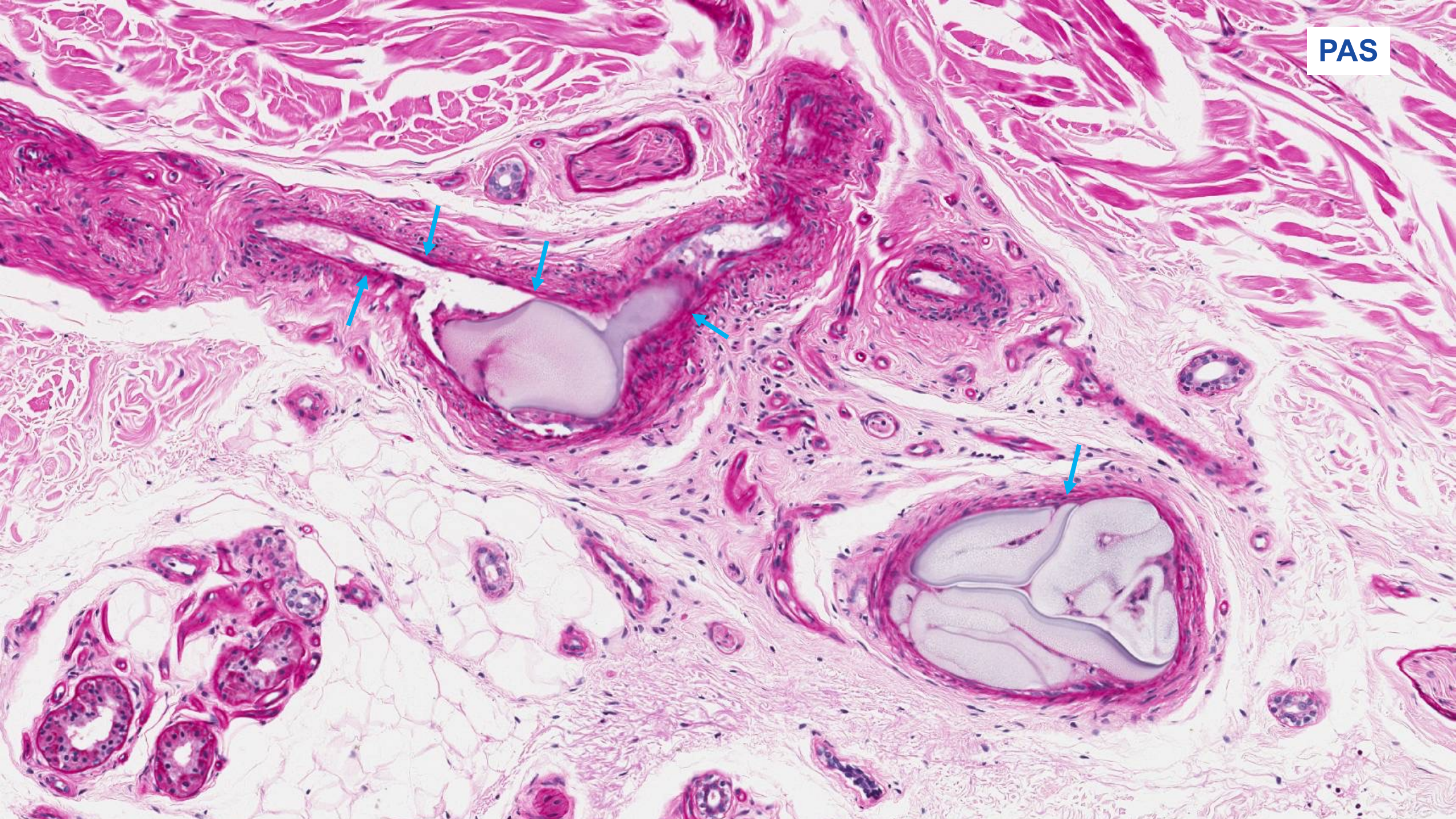
- 68-year-old man
- Bilateral calcaneal livedo racemosa and reticulate purpura



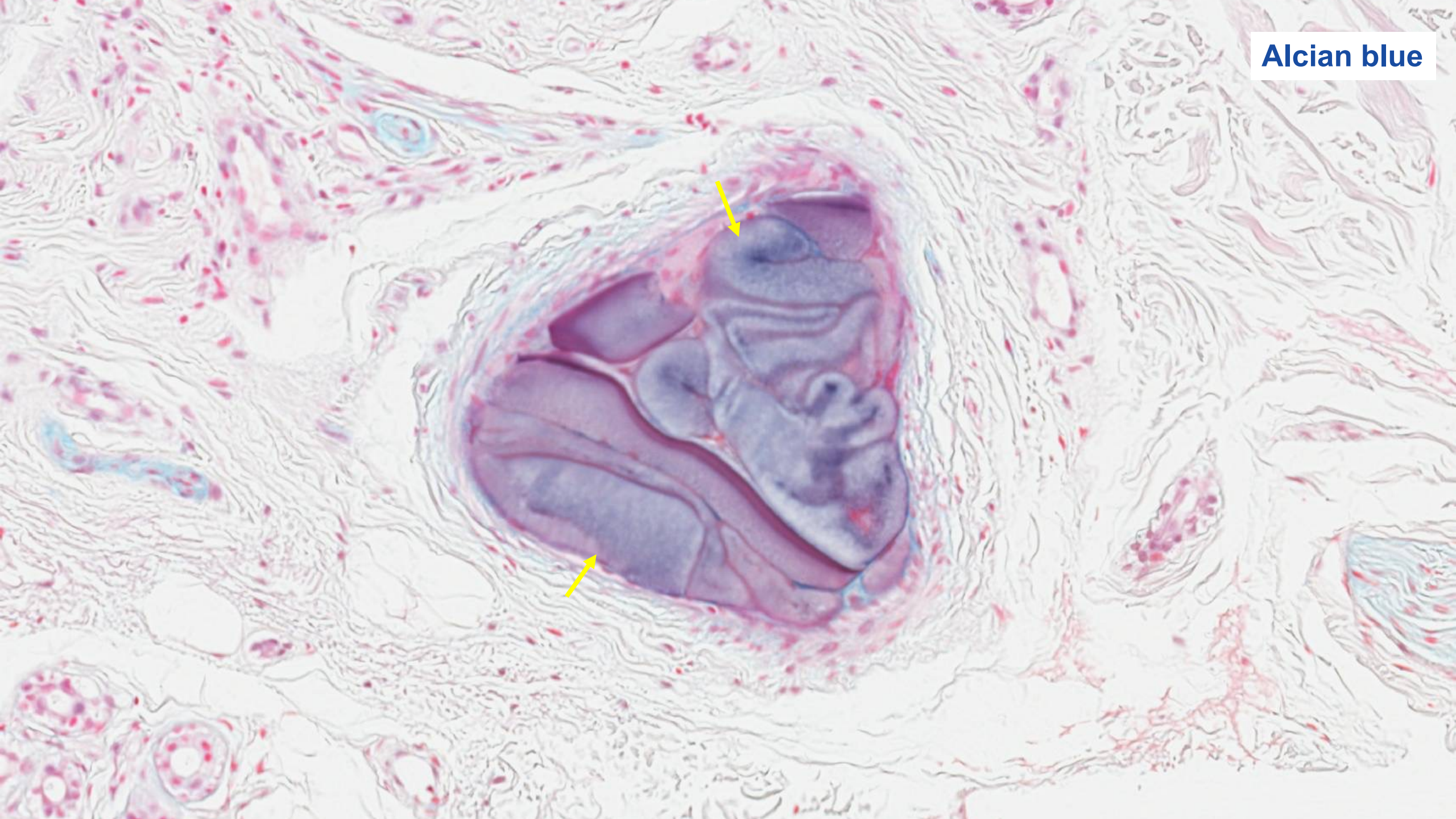




PAS



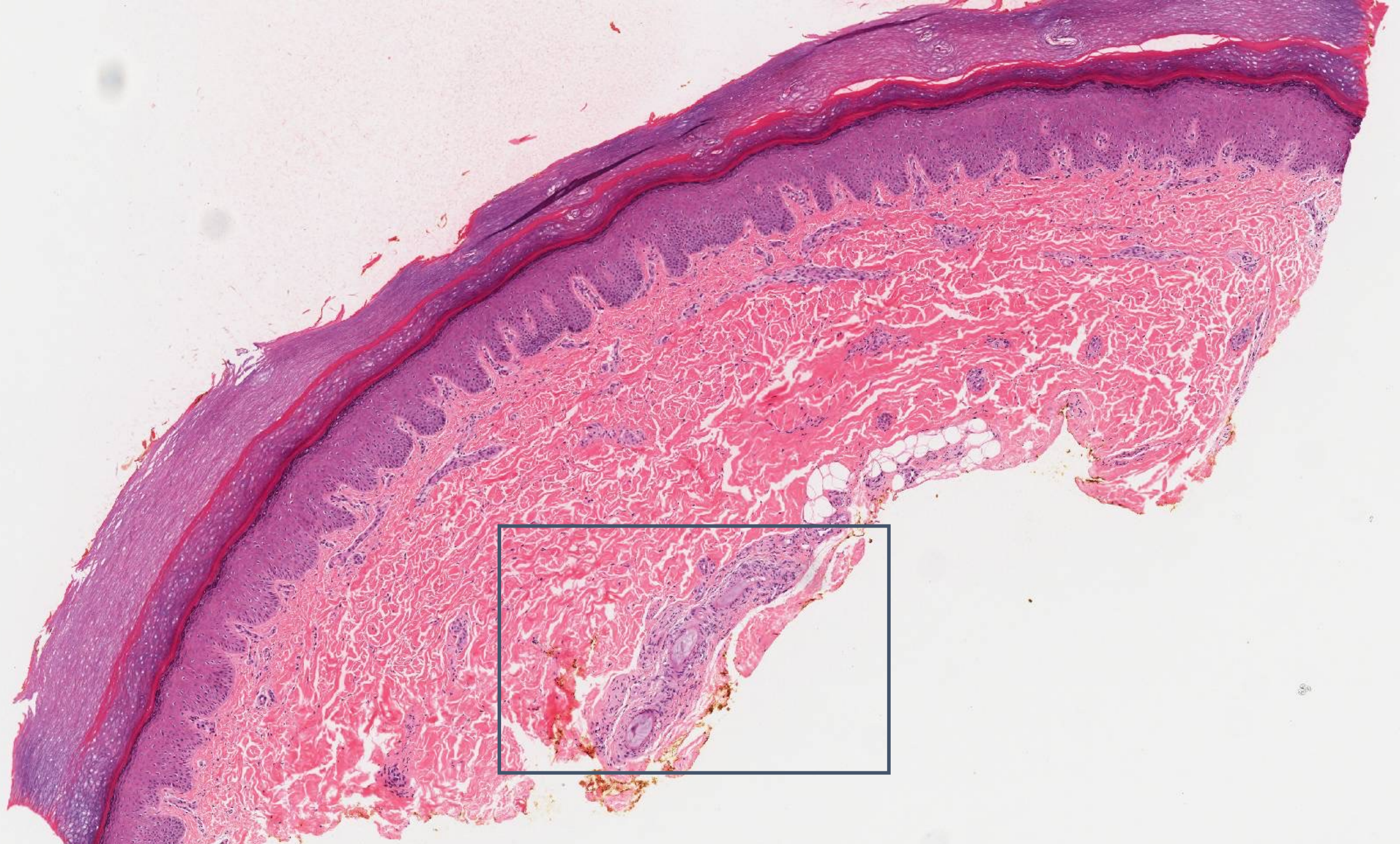
Alcian blue

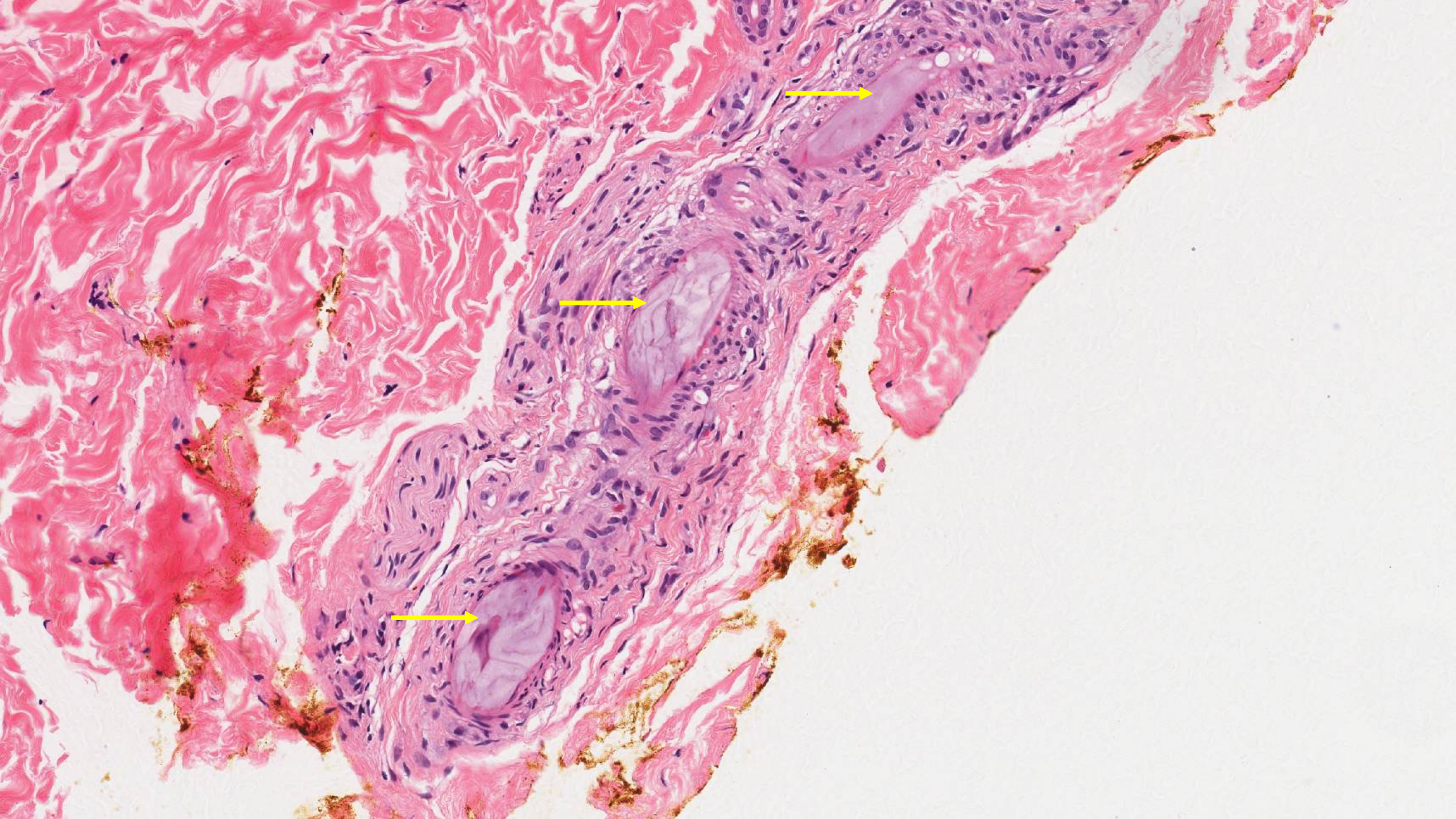


Another similar case...

- 29-year-old man
- Bilateral livedo racemosa and reticulate purpura over both heels









What do both patients have in common?



History of instrumentation where guidewires coated with hydrophilic polymers were used

Lesions developed 1 week after left lower limb angioplasty through a trans-femoral route

Lesions developed 1 month after thoracic and abdominal endovascular repair of an aortic aneurysm (EVAR)

Hydrophilic polymer embolism

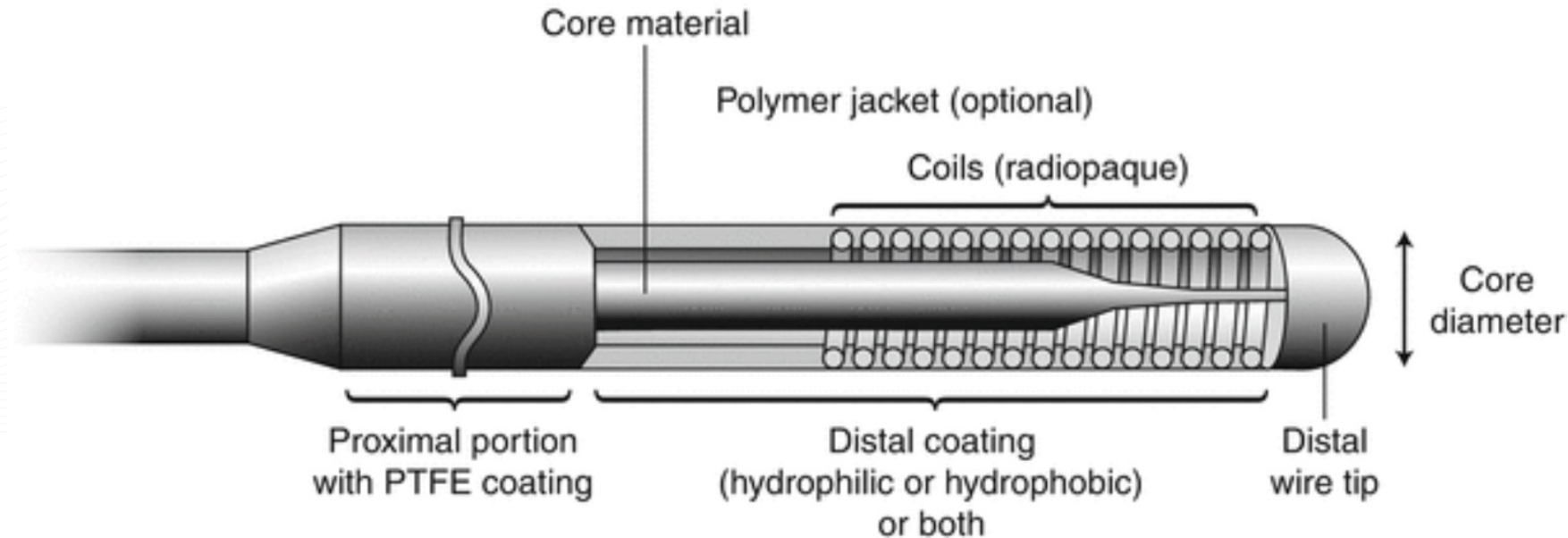


History of instrumentation where guidewires coated with hydrophilic polymers were used

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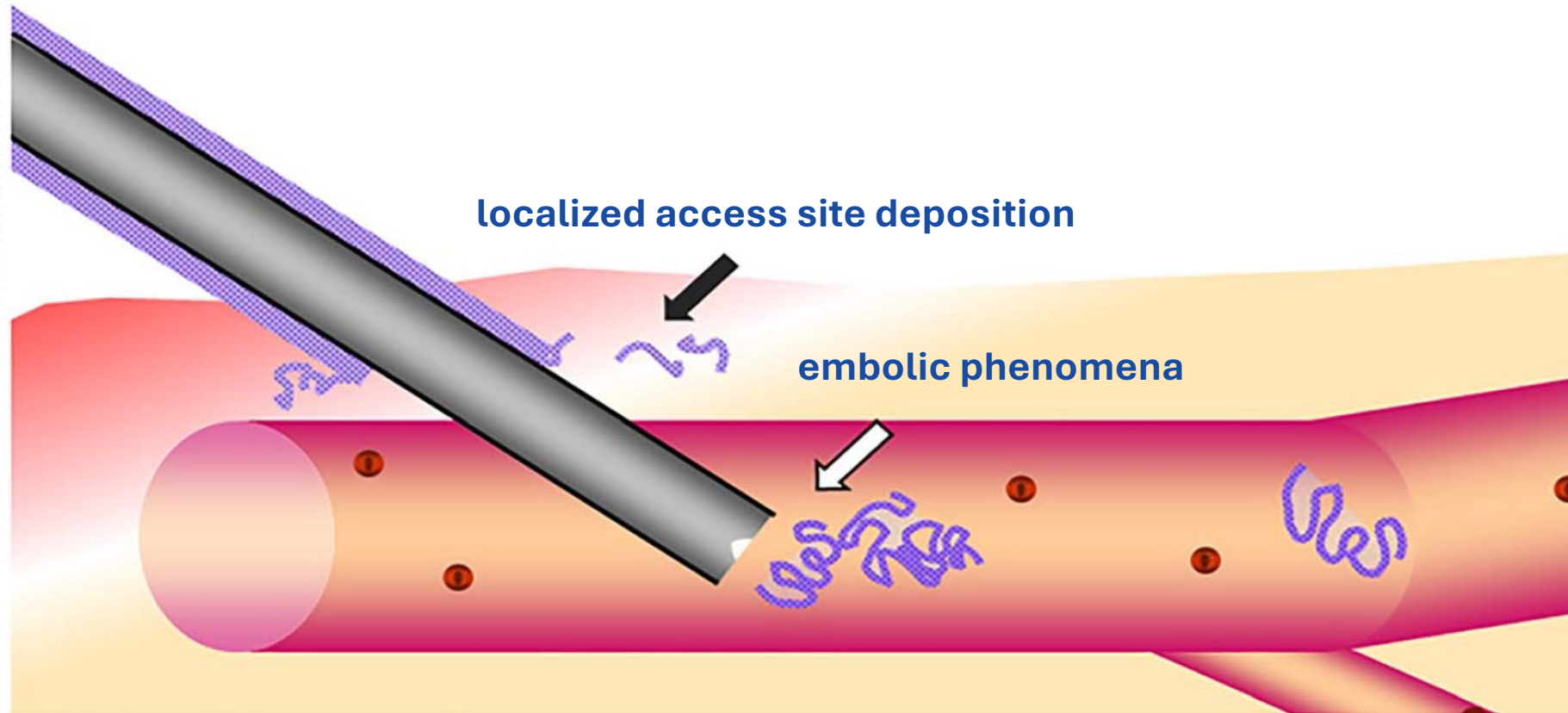
Lesions developed 1 month after thoracic and abdominal endovascular repair of an aortic aneurysm (EVAR)

Hydrophilic polymers



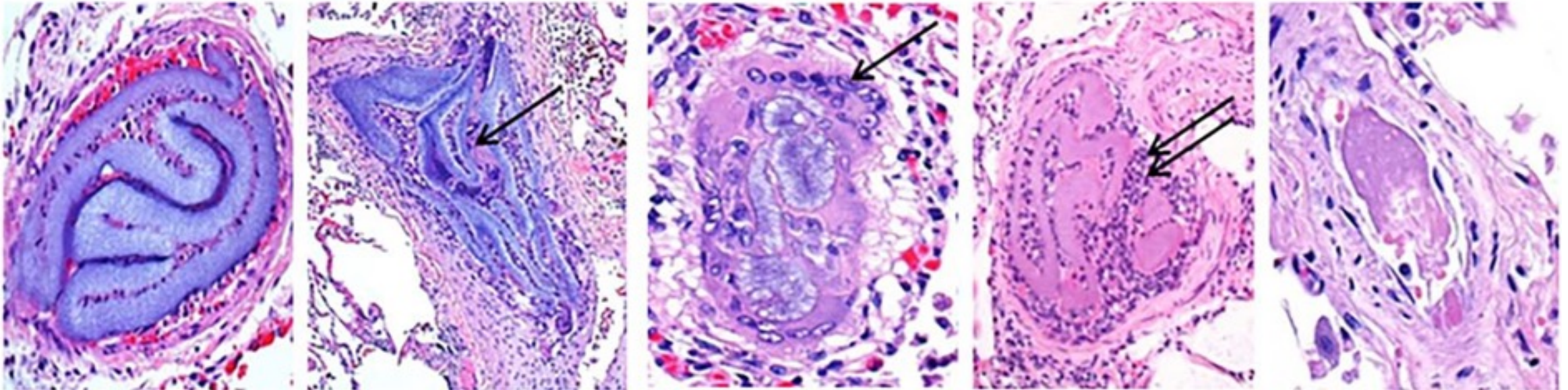
- Widely used as surface coatings on vascular medical devices
 - E.g. guidewires, introducer and delivery sheaths, implantable stents and coils, and various cardiac catheters
- Enhance biocompatibility and maneuverability of endovascular instruments, while decreasing friction and reducing trauma to vessel walls

Hydrophilic polymer delamination from a vascular medical device surface



Mehta RI, Mehta RI. *Hydrophilic Polymer Embolism: Implications for Manufacturing, Regulation, and Postmarket Surveillance of Coated Intravascular Medical Devices.* *J Patient Saf.* 2021 Dec 1;17(8):e1069-e1079.

Hydrophilic polymer embolism histopathological features



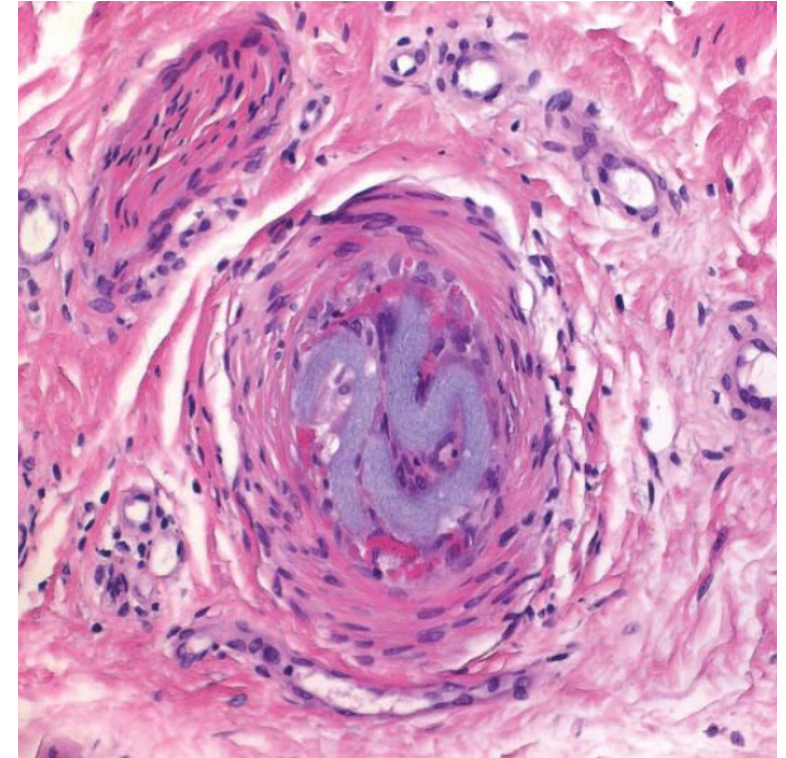
Non-refractile, nonpolarizable, basophilic, granular lamellated foreign bodies

Varying degrees of inflammation (nil, acute with neutrophils, chronic with giant cells)

Mehta RI, Mehta RI. Hydrophilic Polymer Embolism: Implications for Manufacturing, Regulation, and Postmarket Surveillance of Coated Intravascular Medical Devices. J Patient Saf. 2021 Dec 1;17(8):e1069-e1079.

Hydrophilic polymer embolism

- Reported to involve multiple organs
- Brain and lungs - most common
- Cutaneous involvement unusual, with less than 30 cases reported in the literature
- Self-limiting, or lead to parenchymal necrosis, even death



Berríos-Hernández M, et al. Cutaneous Polymer-Coating Embolism After Endovascular Procedures: Report of Two Cases and a Literature Review. Am J Dermatopathol. 2021;43:662-666.

Most common cutaneous manifestations are retiform purpura, followed by ulcers



Thompson AK, Peters MS, El-Azhary RA, et al. Cutaneous microemboli from hydrophilic polymer after endovascular procedures. J Am Acad Dermatol. 2015;73:666-71

Cutaneous Polymer-Coating Embolism After Endovascular Procedures: Report of Two Cases and a Literature Review

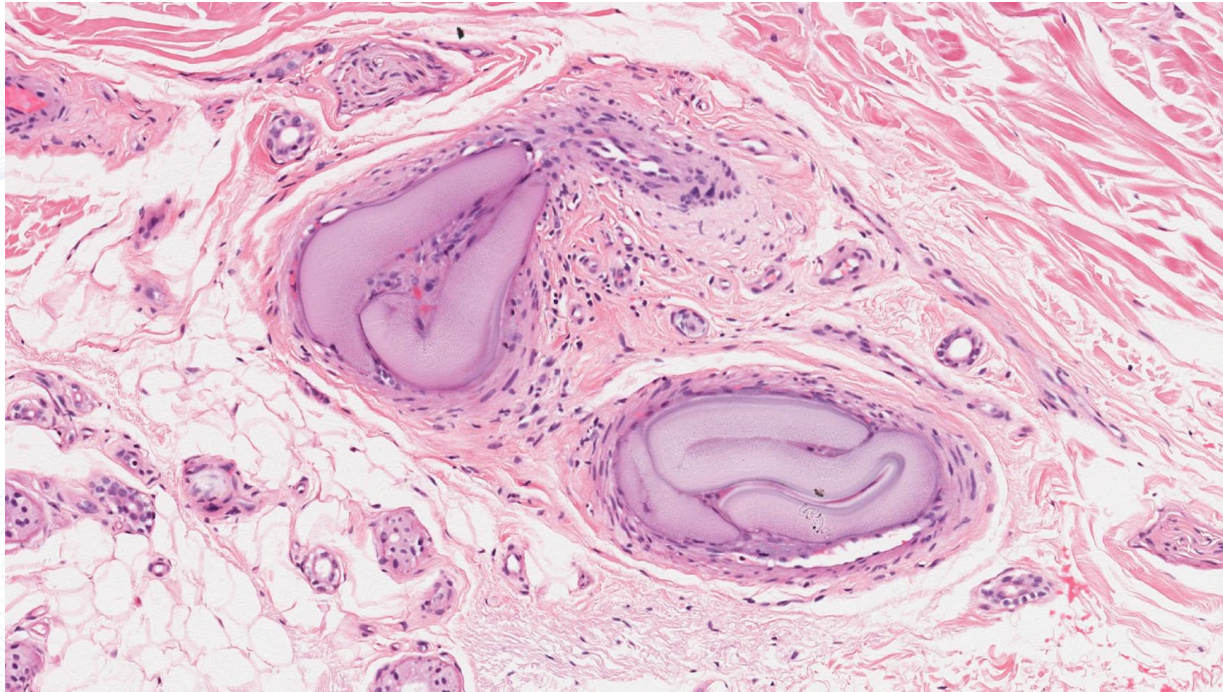
Mario Berríos-Hernández, MD, Charigan Abou-Jokh Casas, MD,† Laura Sainz-Gaspar, MD,‡
Javier Ginarte-Val, MD, PhD,‡ Virginia Fernández Redondo, MD, PhD,‡§ Diego López-Otero, MD,†
Carlos Aliste, MD,* and Jose M. Suárez-Peñaranda, MD, PhD*¶*

Am J Dermatopathol. 2021;43:662-666.

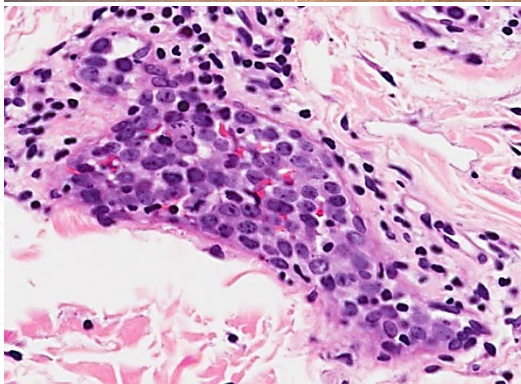
- Usually within the first week post op but may manifest even at 6 months after surgery.
- Aortic aneurysm reparation and transcatheter aortic valve replacement (TAVR) are the most common procedures associated with HPE
- May explain the exclusive location on lower limbs

Take Home Message

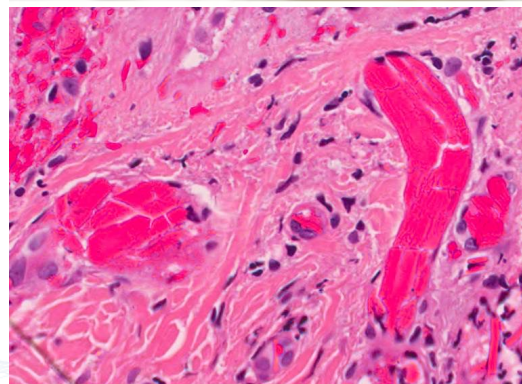
- In a patient who presents with retiform purpura or ulcers especially over the lower limbs after intravascular or intra-cardiac procedures, apart from cholesterol embolism, think of hydrophilic polymer embolism



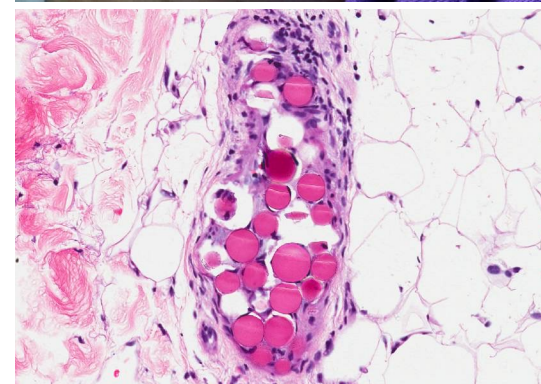
Intravascular large B cell lymphoma



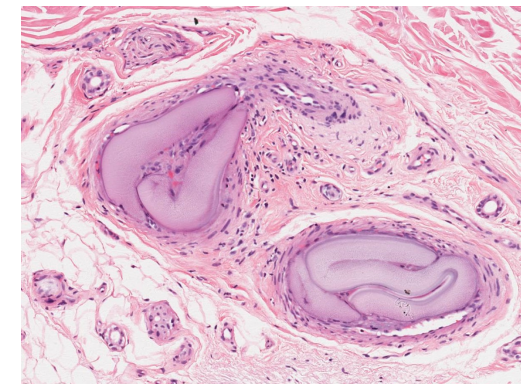
Crystalglobulinaemia from multiple myeloma



Cutaneous embolism of microspheres from DEB-TACE



Hydrophilic polymer embolism



Thank you!

joycelee@nsc.com.sg



NATIONAL
SKIN
CENTRE

A member of National Healthcare Group
Adding years of healthy life