Guy's and St Thomas' NHS
NHS Foundation Trust

Interactive slide seminar: potpourri
Hot Topics in Dermatopathology
Rome, April 4-5/2025

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St John's Institute of Dermatology

Guy's and St Thomas´s Hospital NHS Foundation Trust

London, United Kingdom

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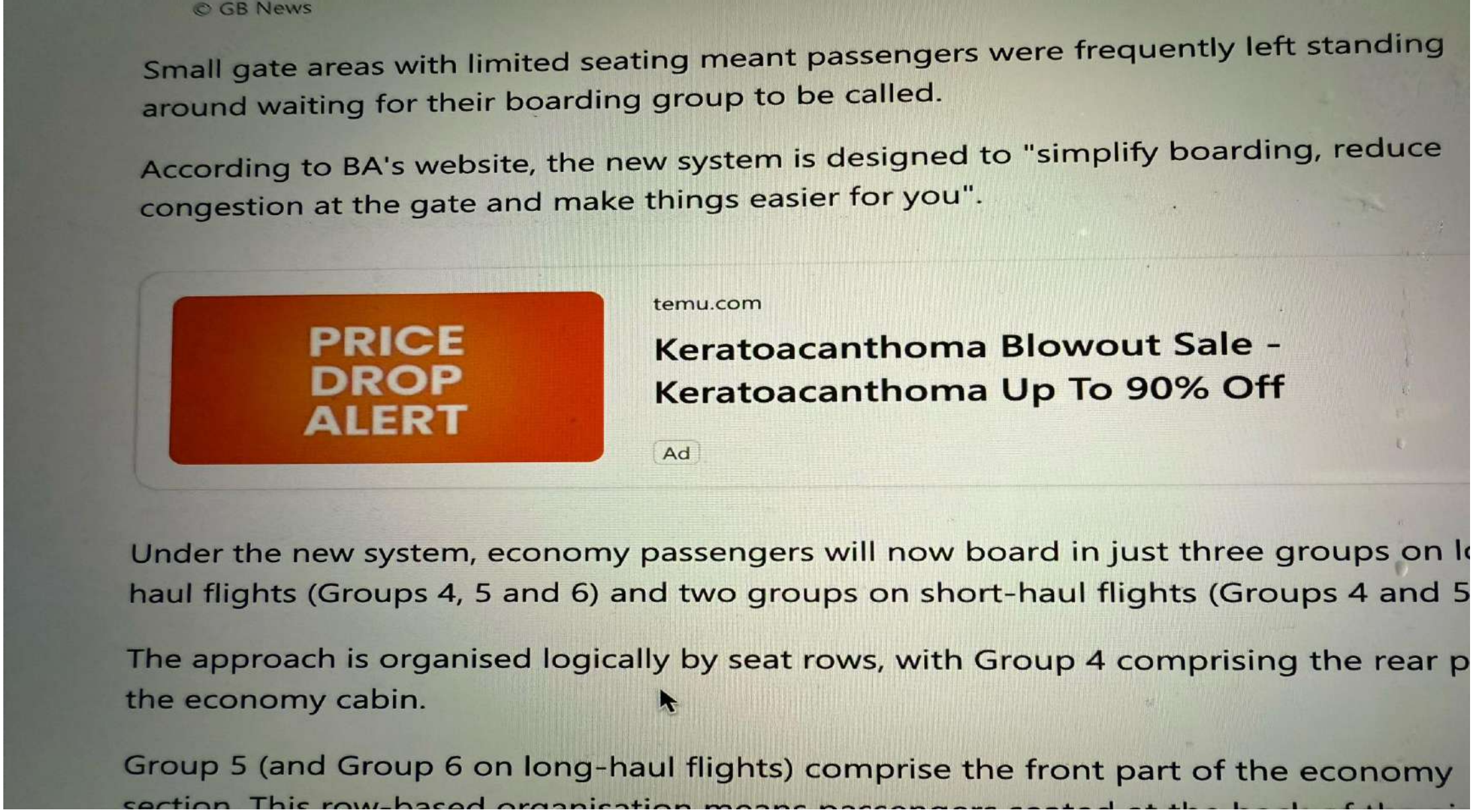
Small gate areas with limited seating meant passengers were frequently left standing around waiting for their boarding group to be called.

According to BA's website, the new system is designed to "simplify boarding, reduce congestion at the gate and make things easier for you".

Under the new system, economy passengers will now board in just three groups on l haul flights (Groups 4, 5 and 6) and two groups on short-haul flights (Groups 4 and 5

The approach is organised logically by seat rows, with Group 4 comprising the rear p the economy cabin.

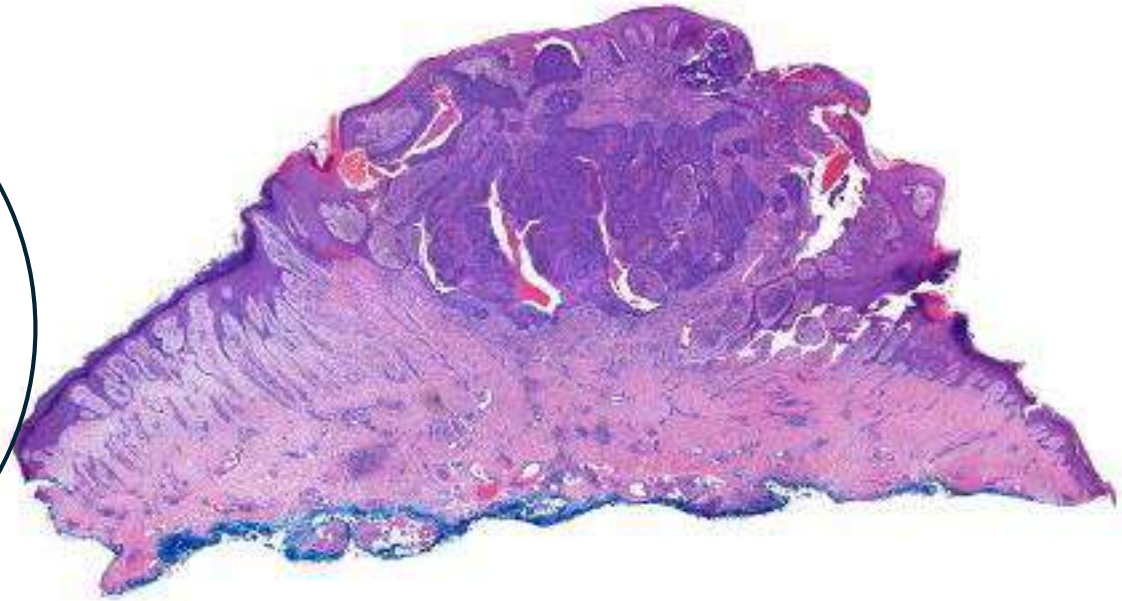
Group 5 (and Group 6 on long-haul flights) comprise the front part of the economy section. This row-based organisation means passengers seated at the back of the

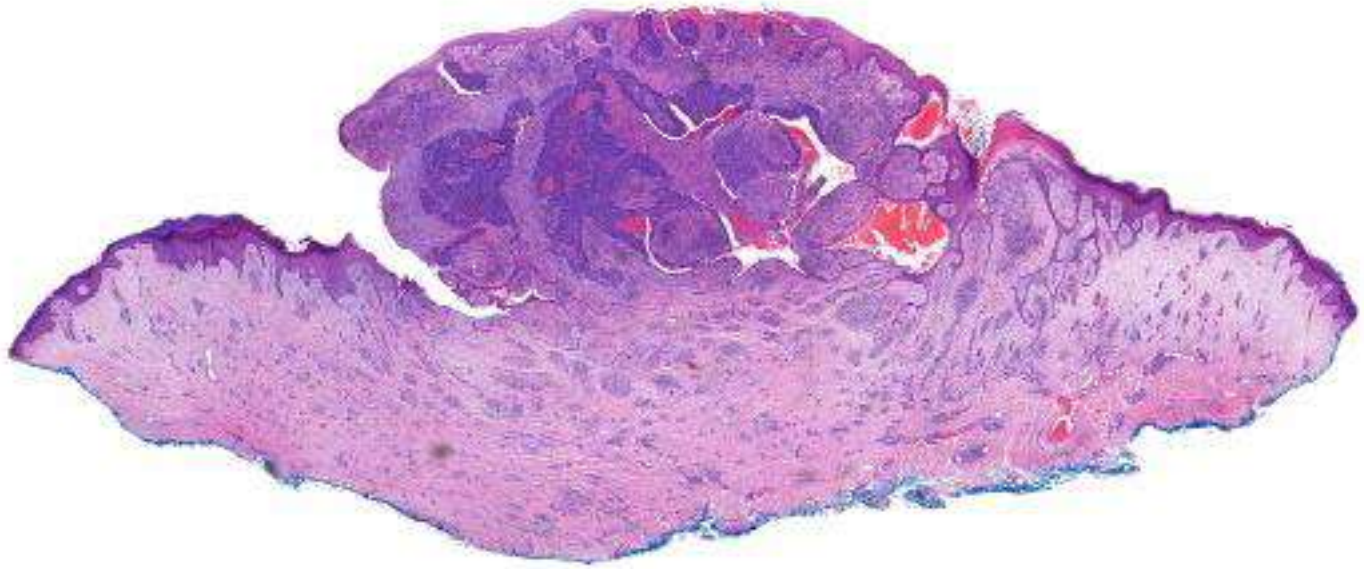


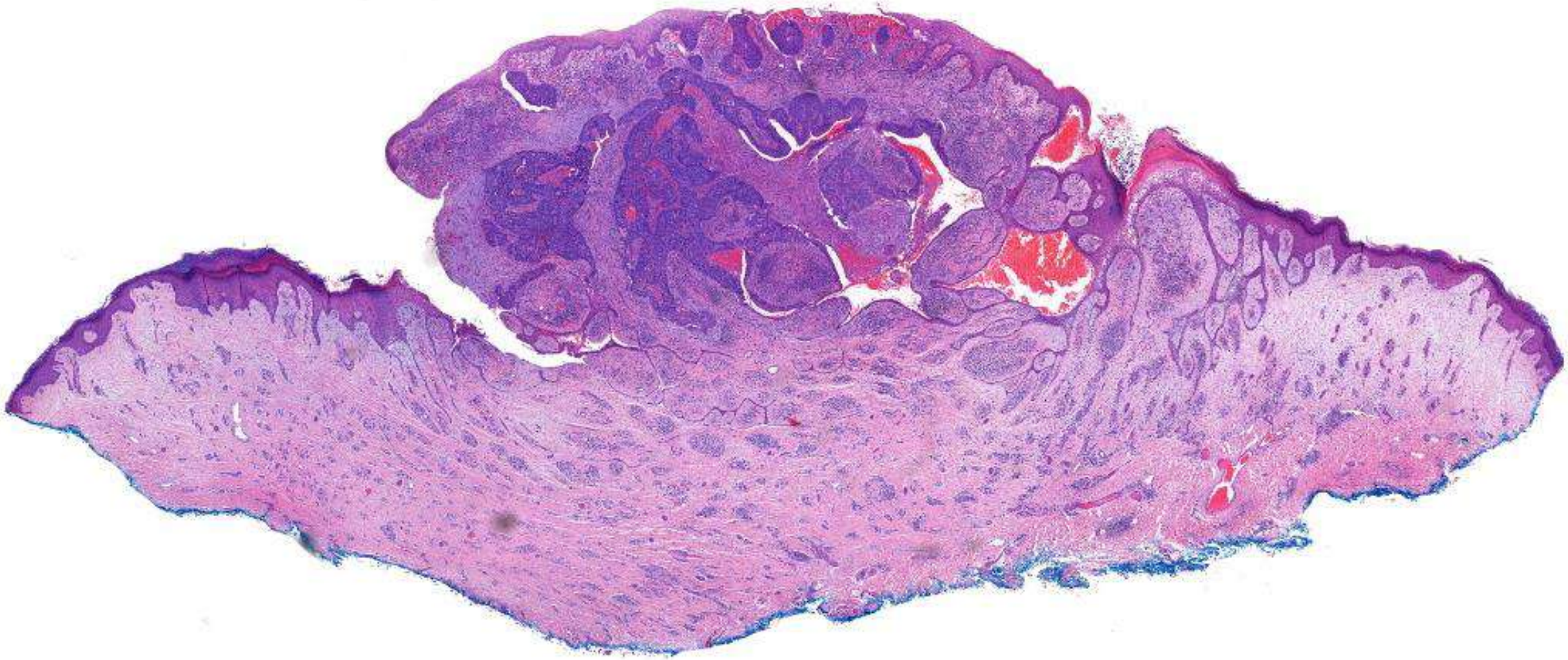
Better but quickly before Richard Carr buys them all!!!!

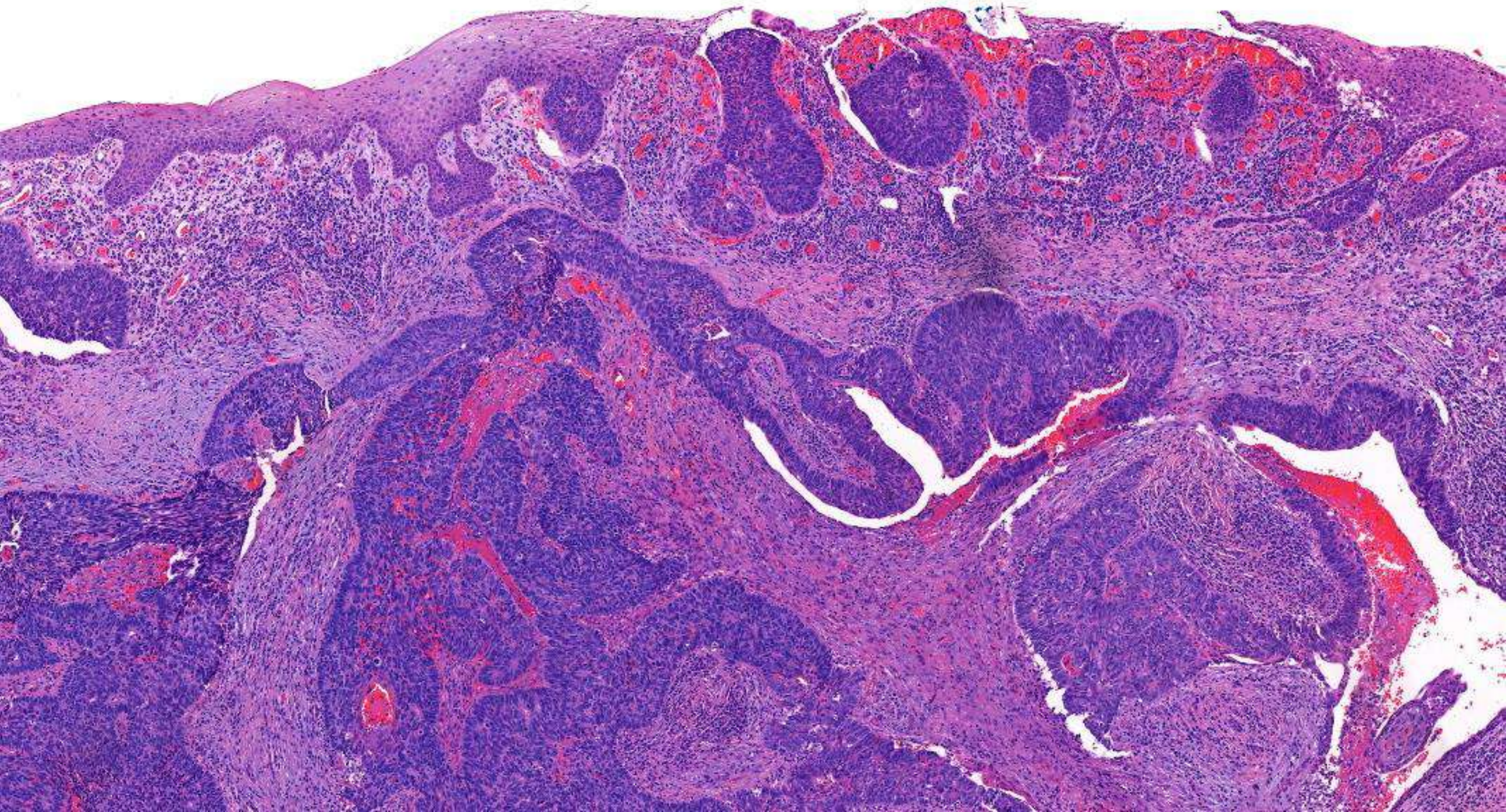
Case 1/a.

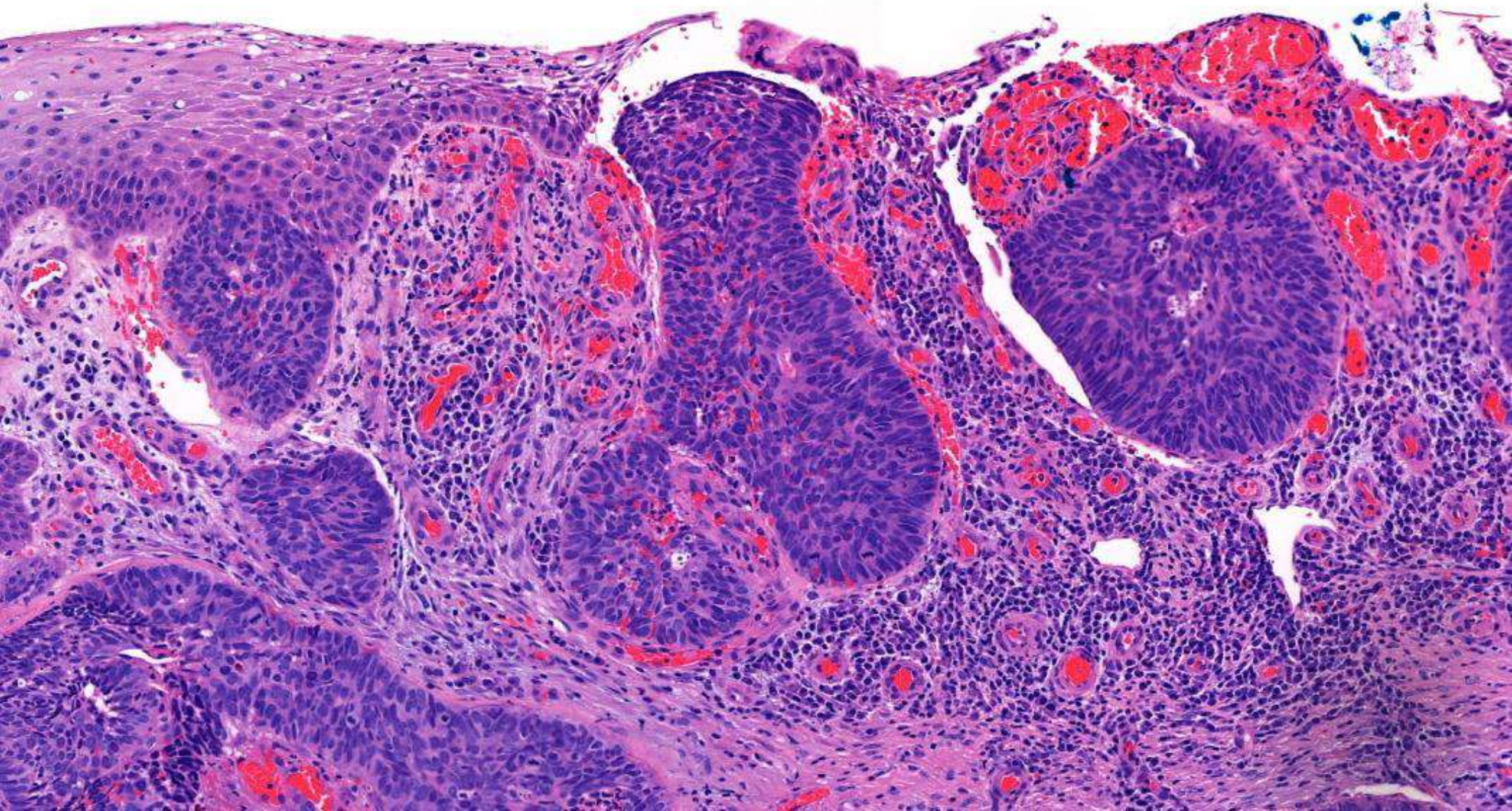
89-year-old male
Eroded, ulcerated lesion on the left heel
Present for many months
Exuberant granulation tissue? (SCC)?

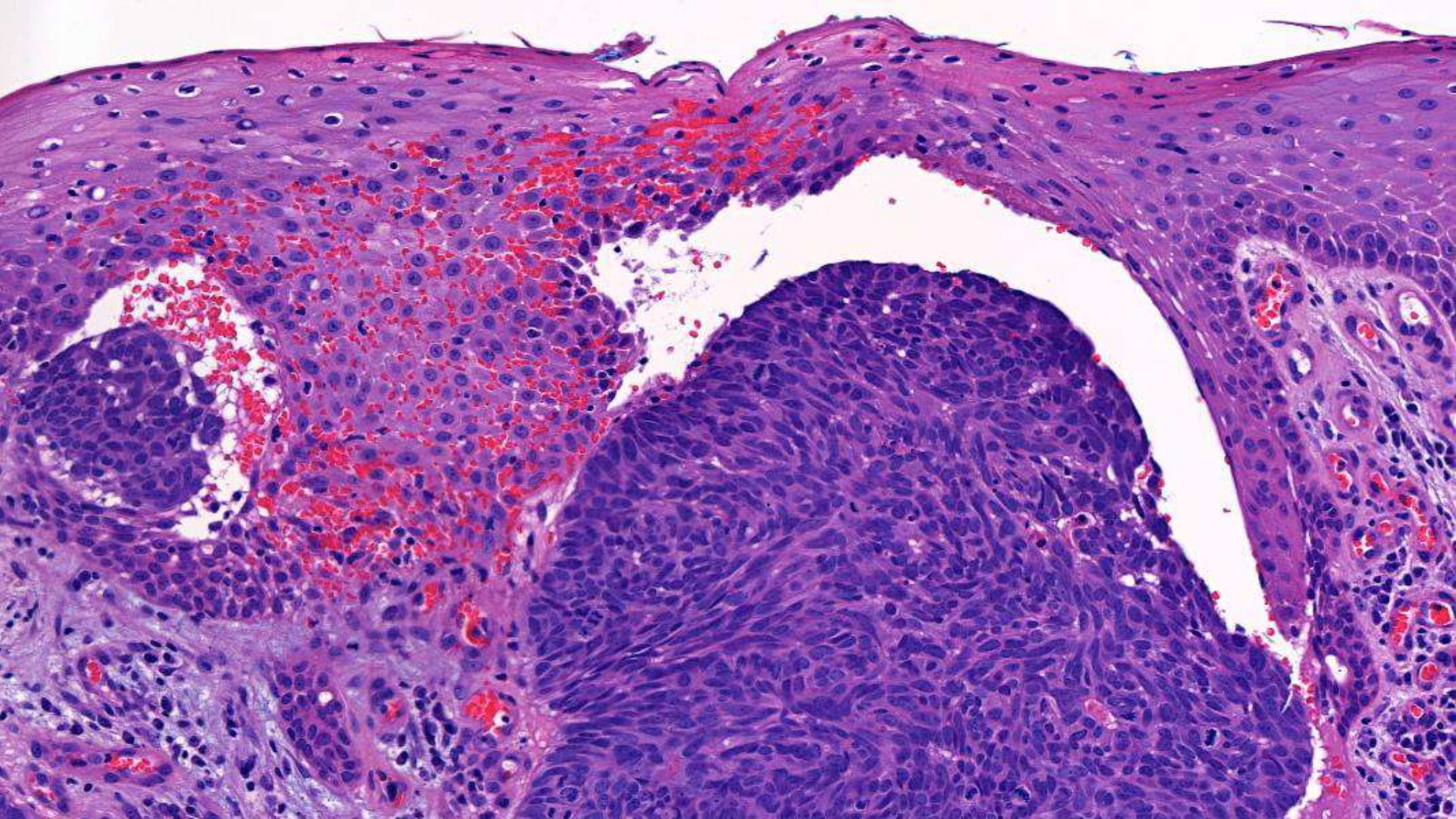


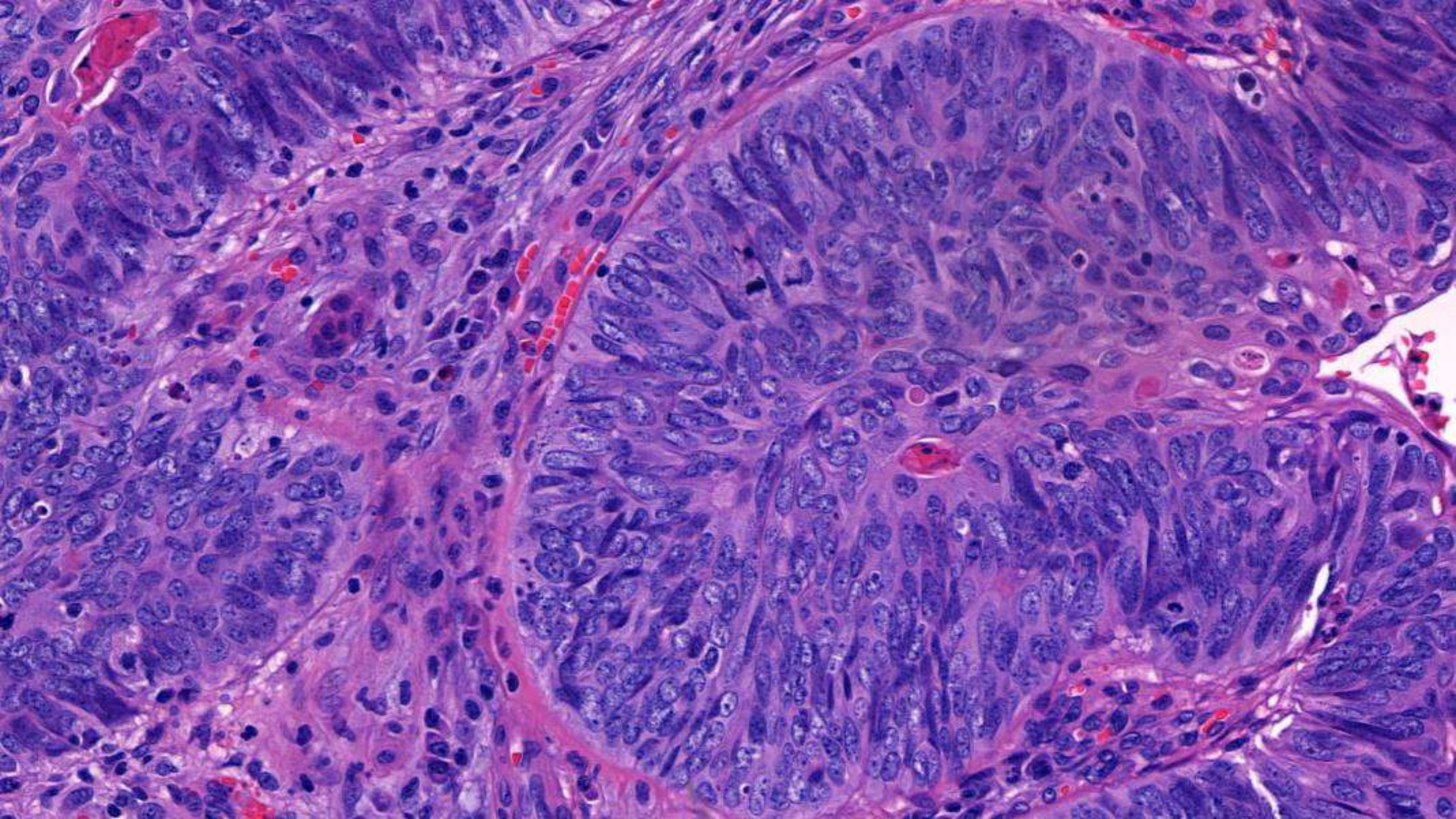


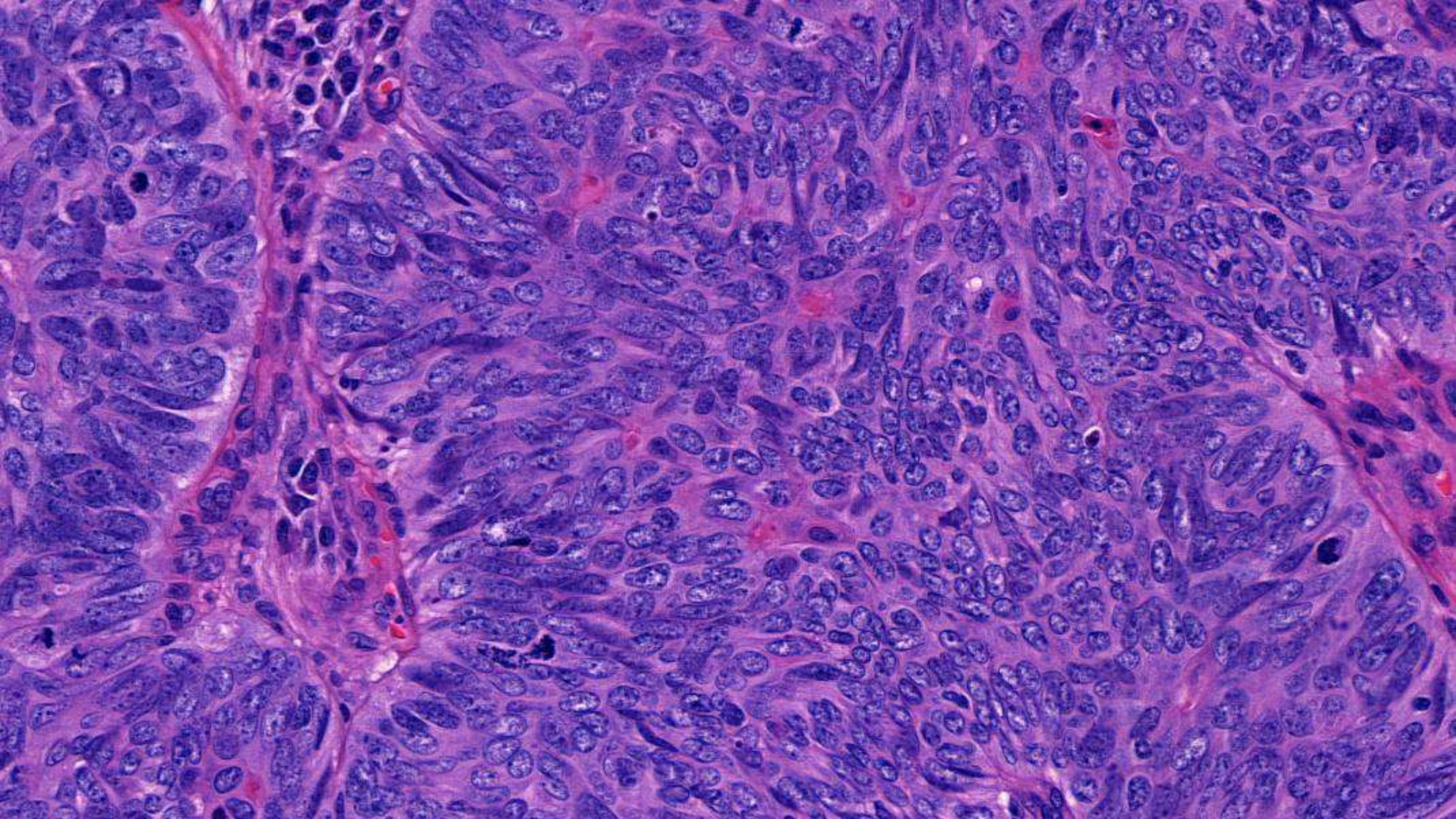


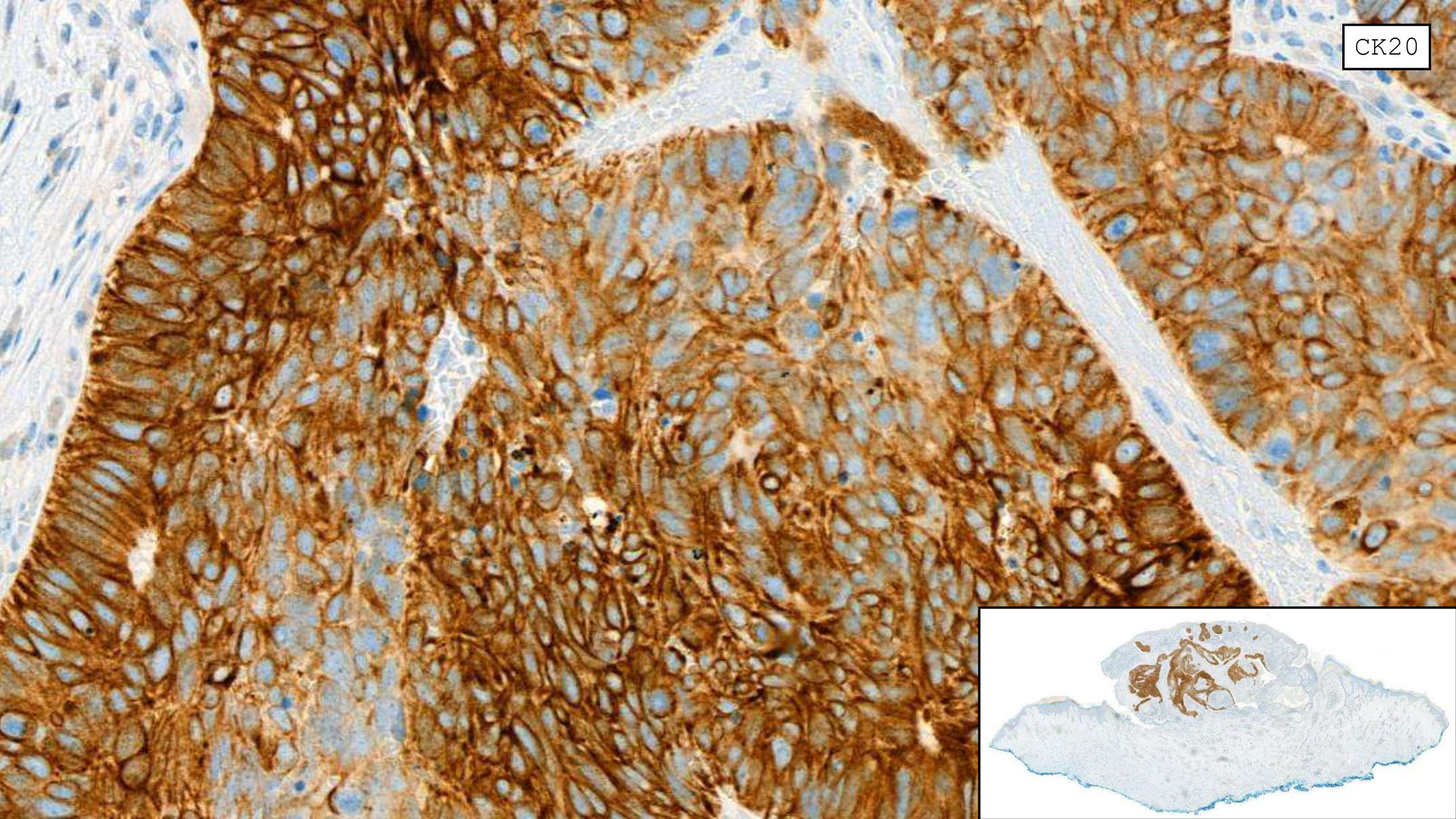








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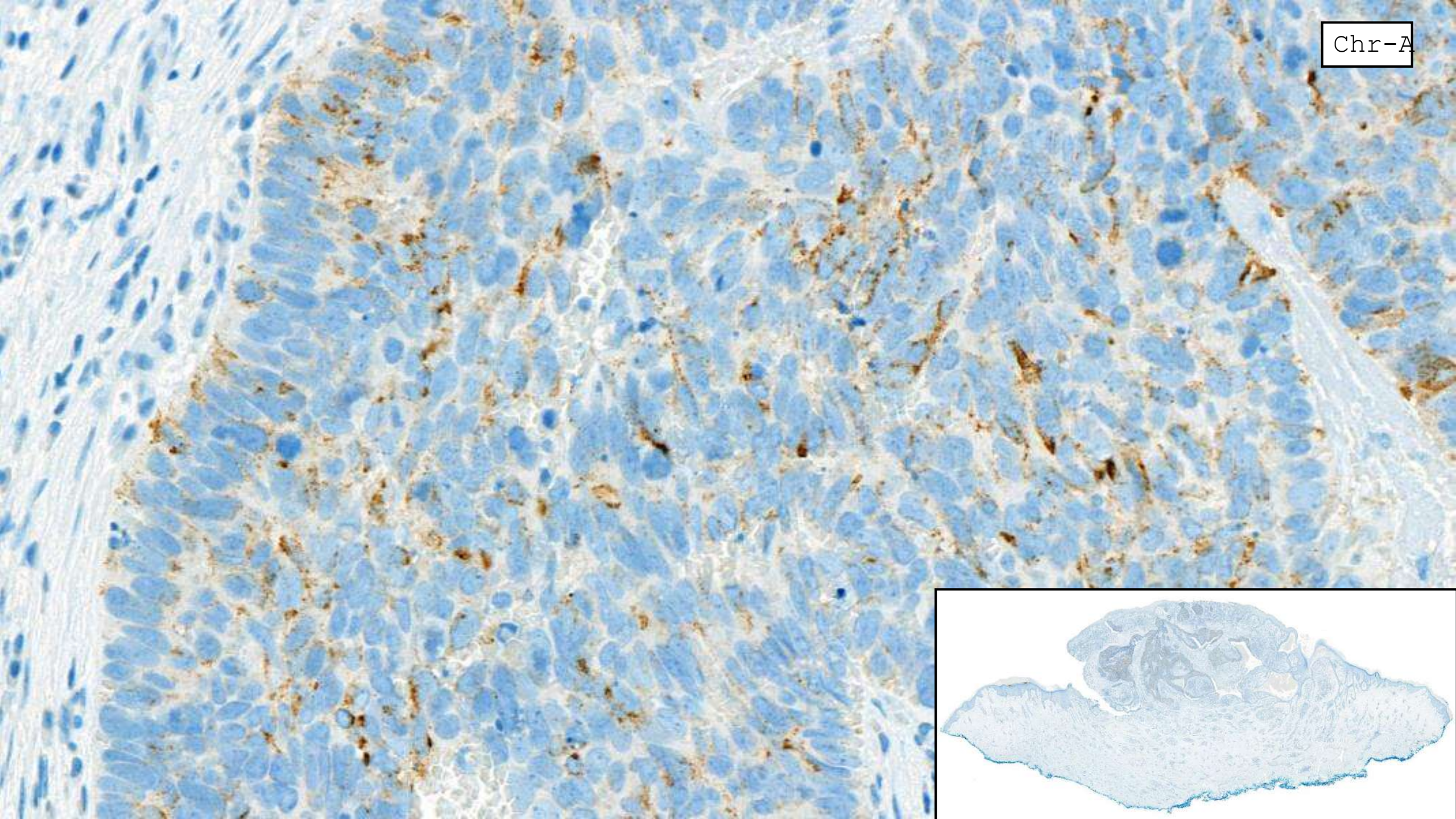
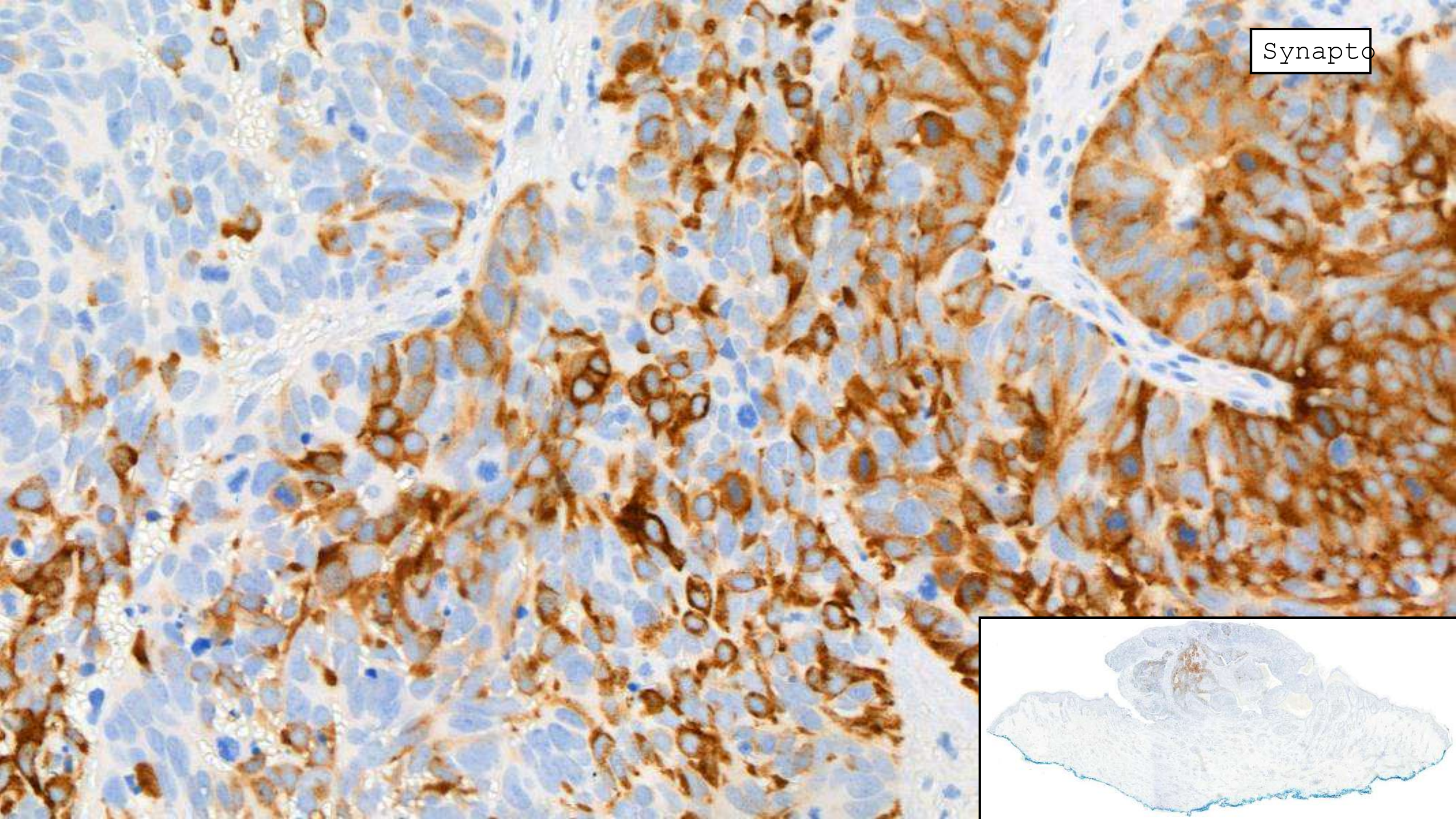

Chr-A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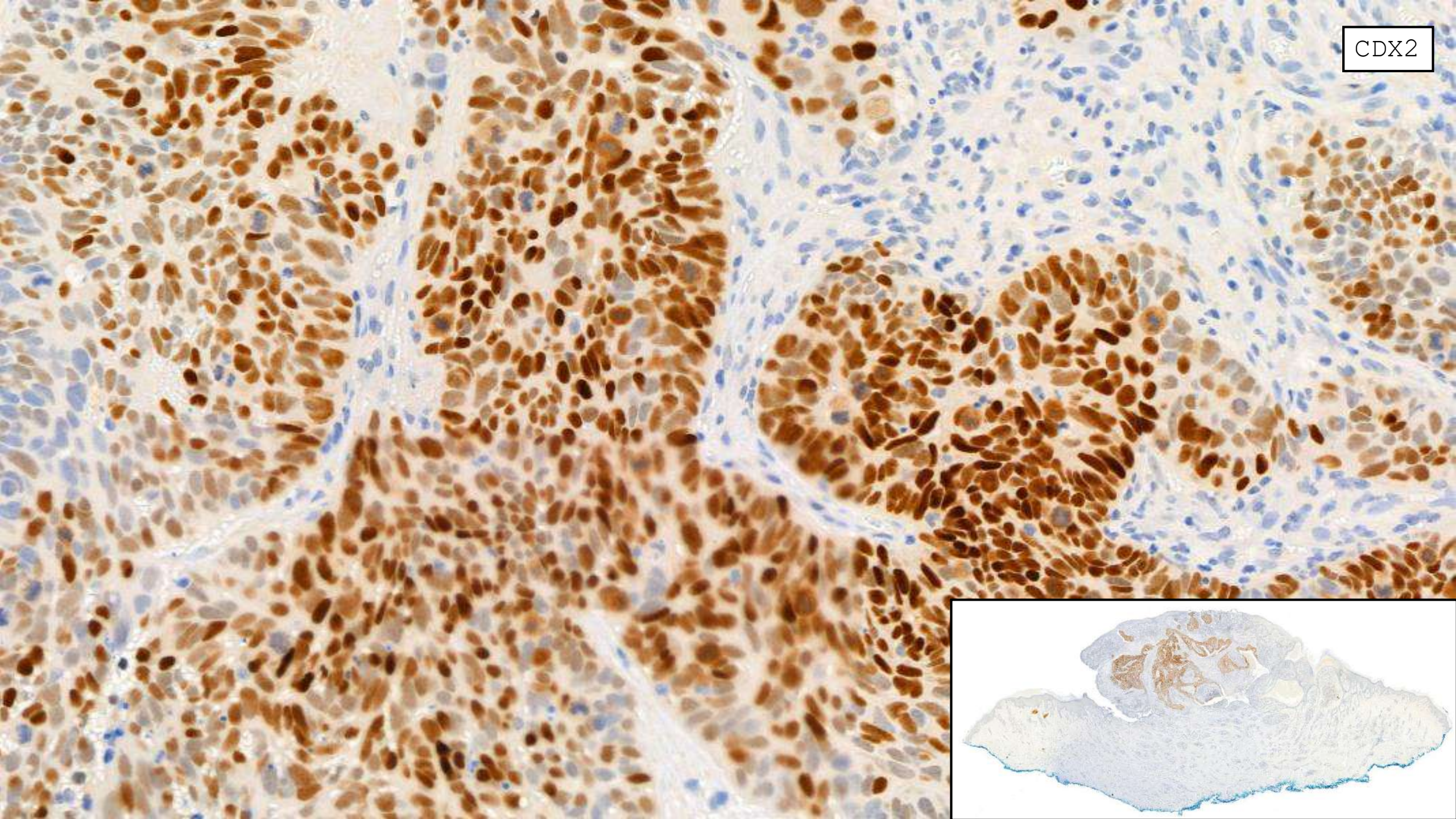
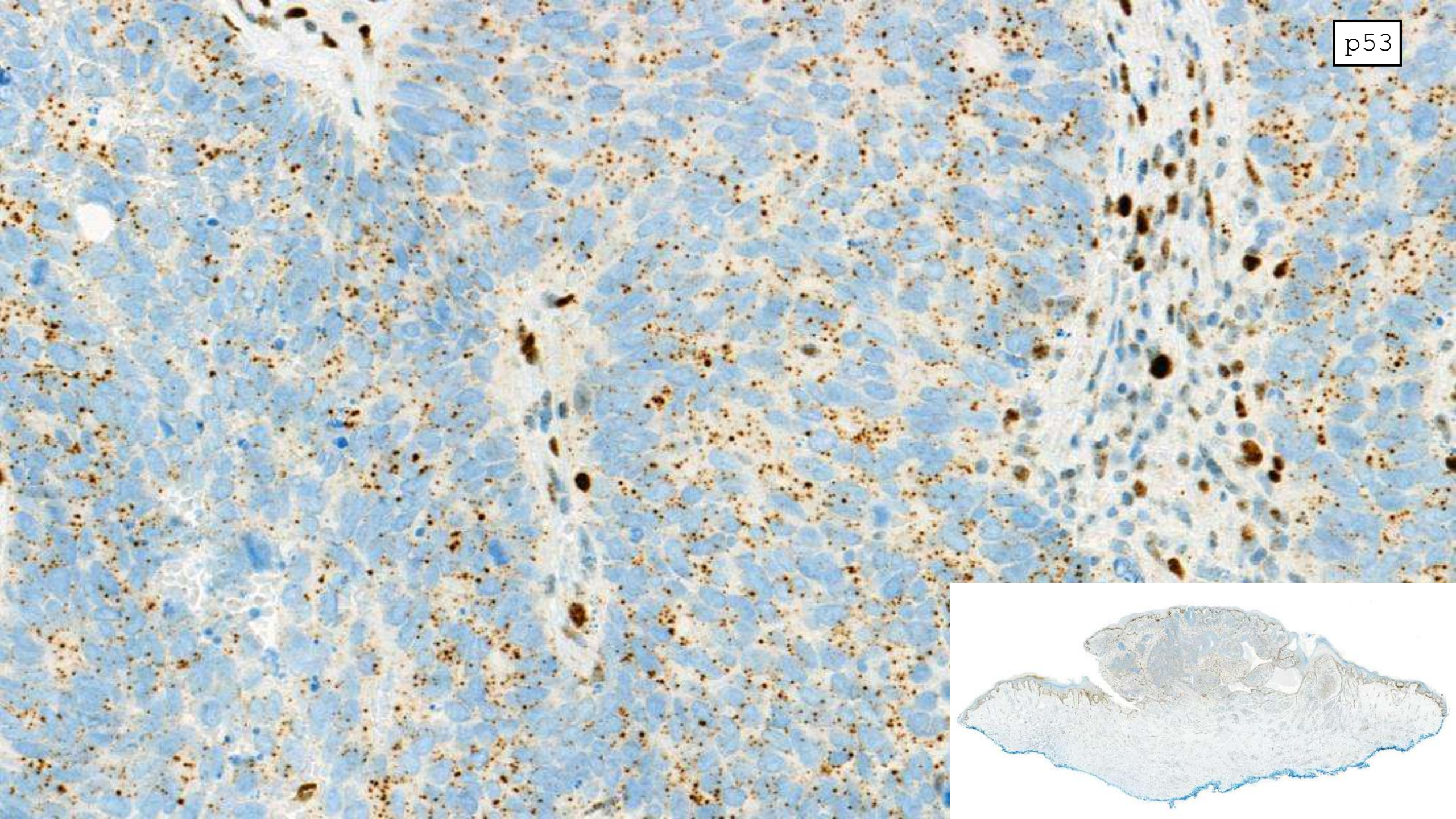

CDX2

RB-1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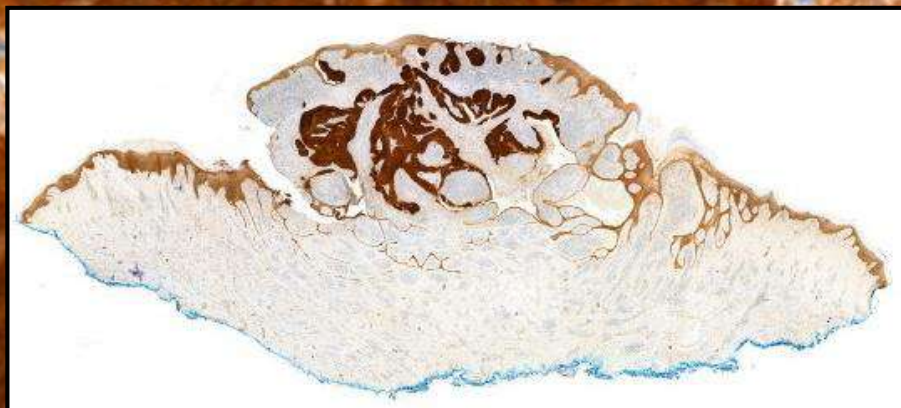
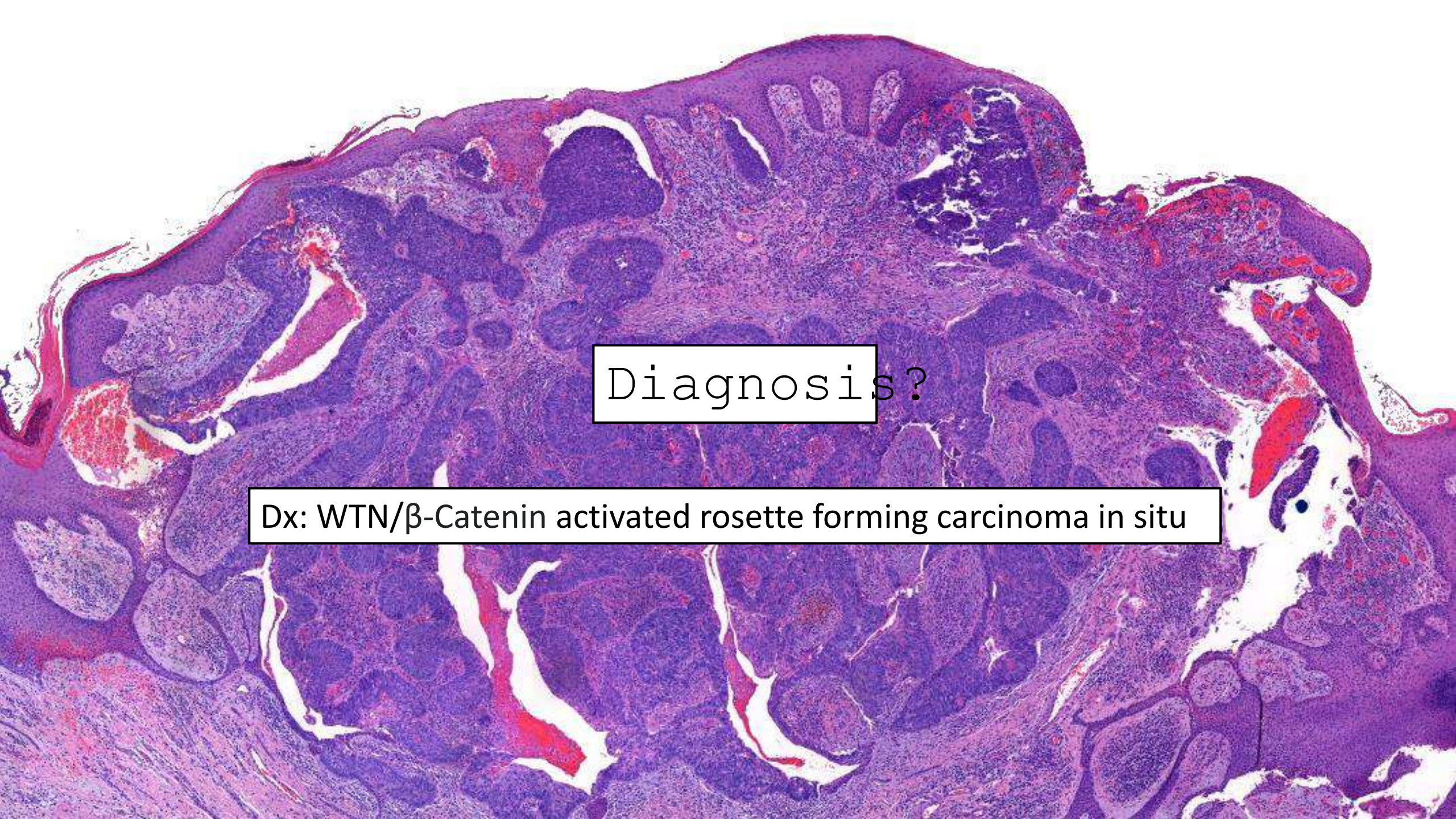
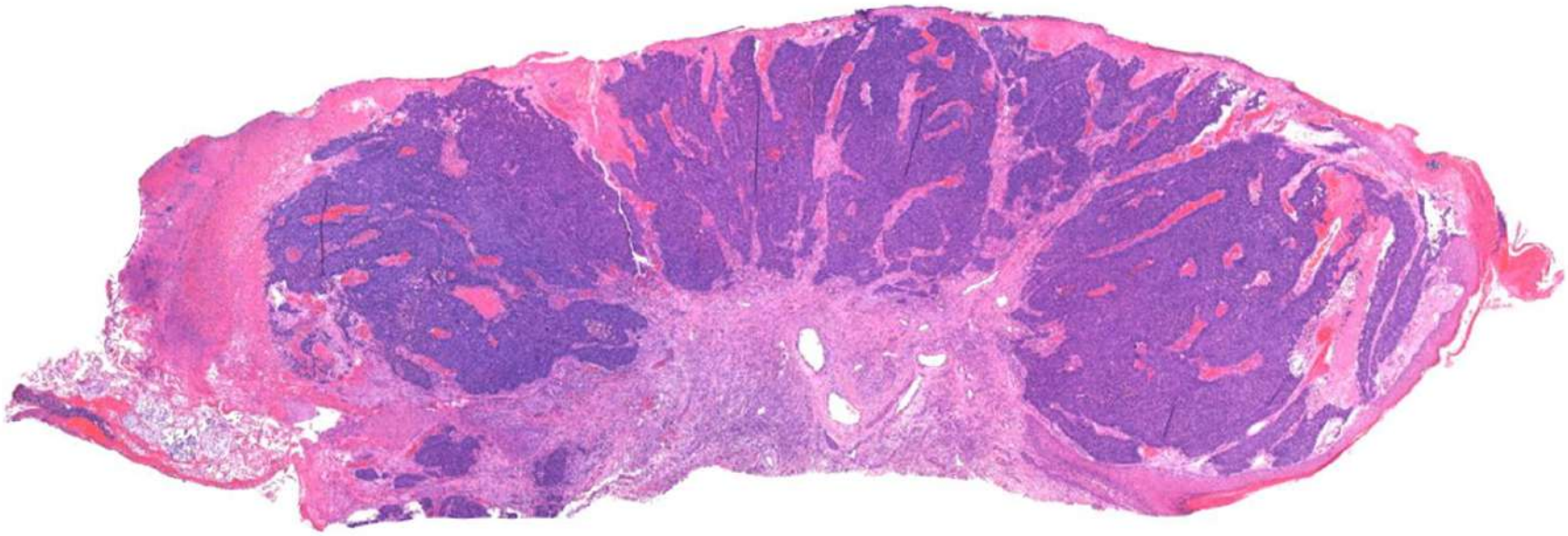
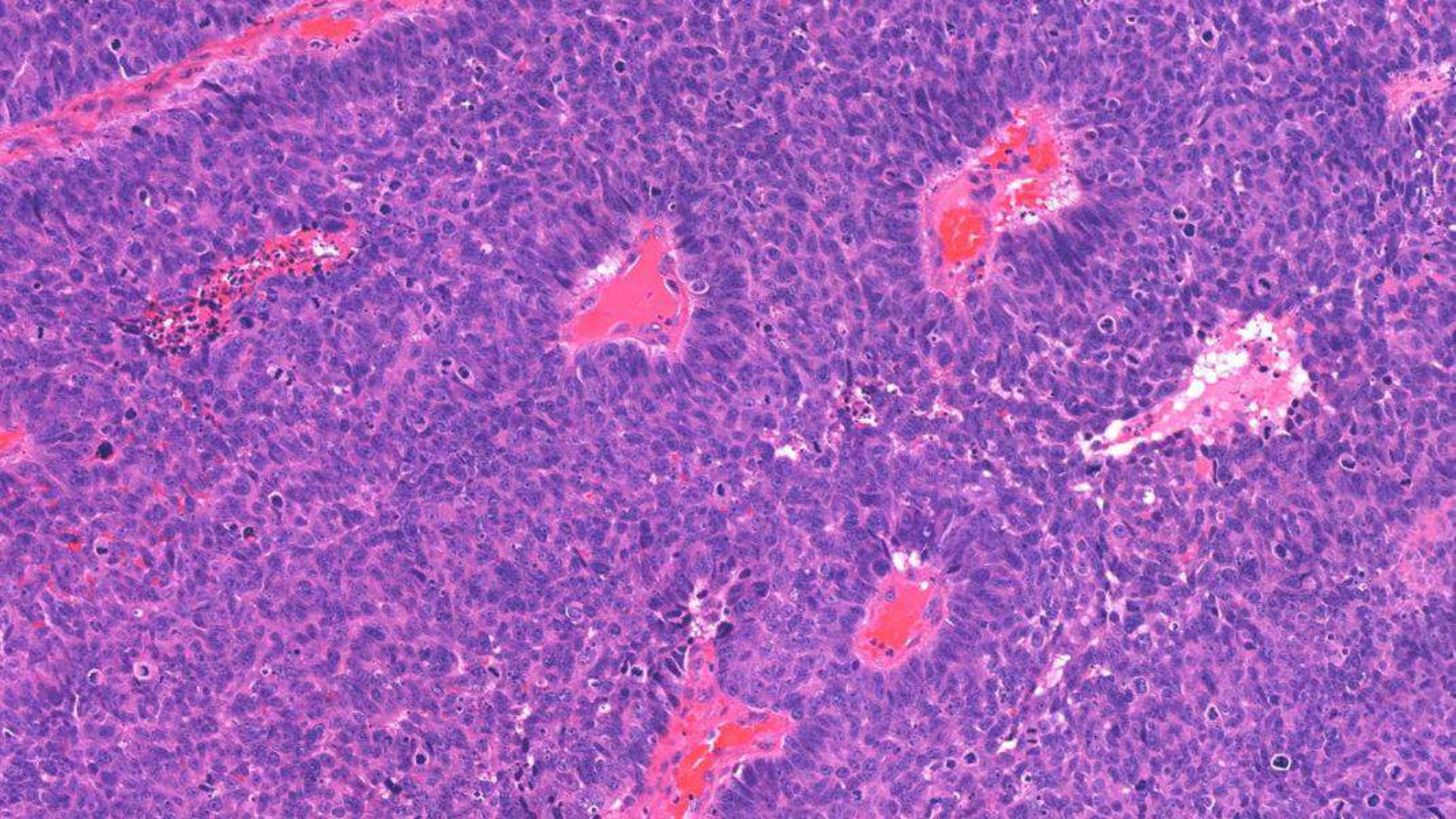
β-Catenin

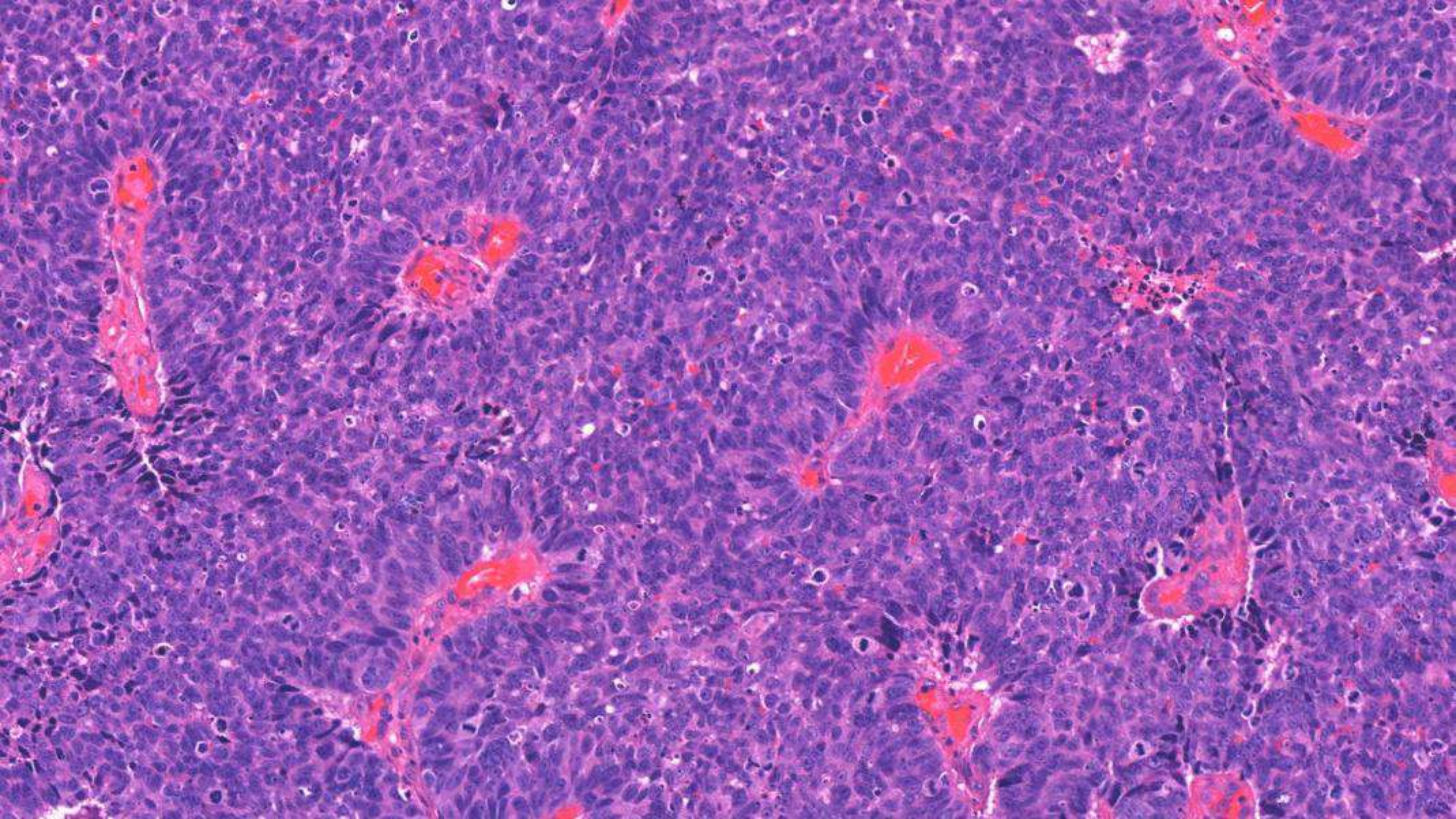


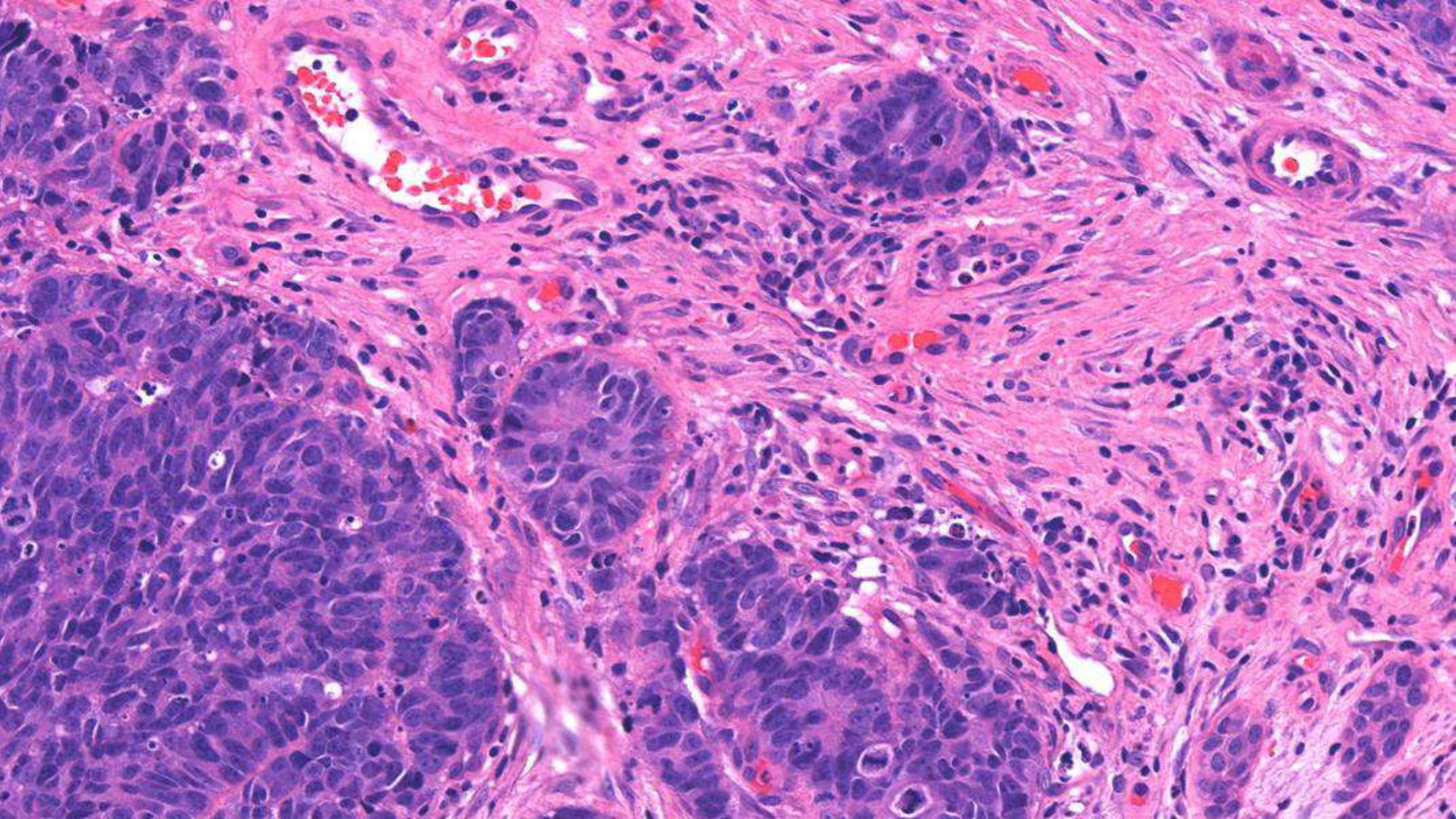

Diagnosis?
Dx: WTN/β-Catenin activated rosette forming carcinoma in situ

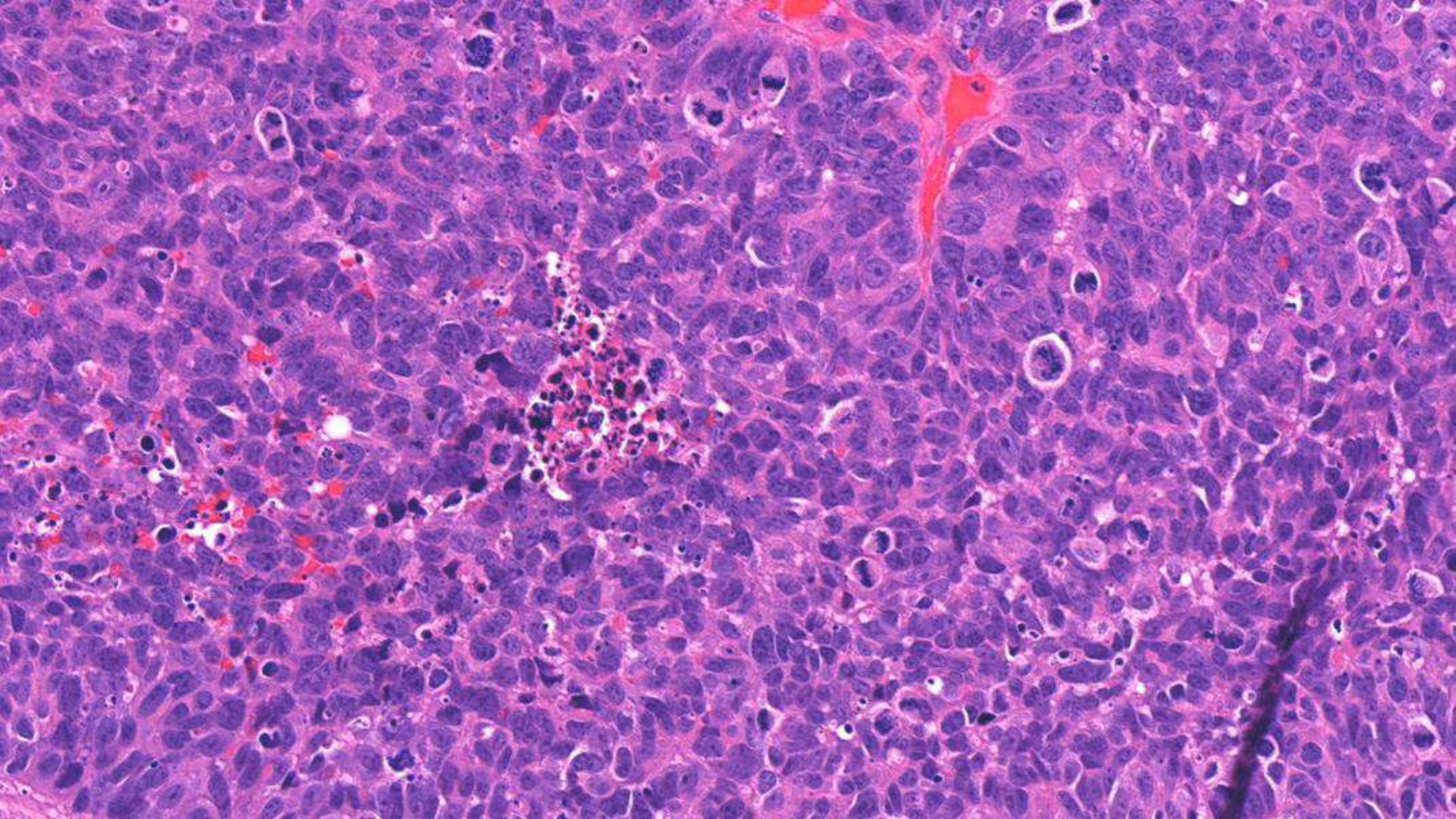
Case
1/b.

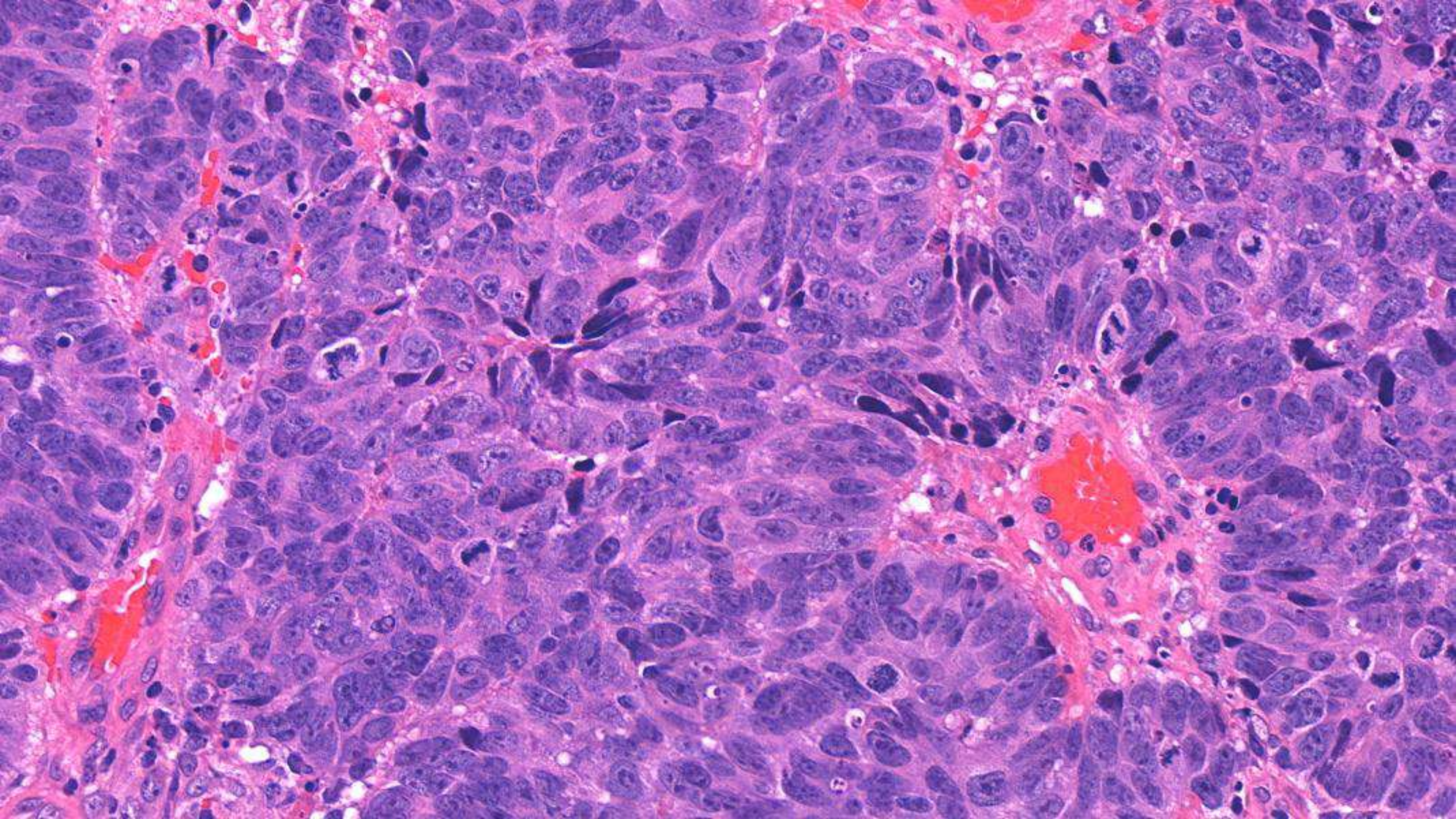


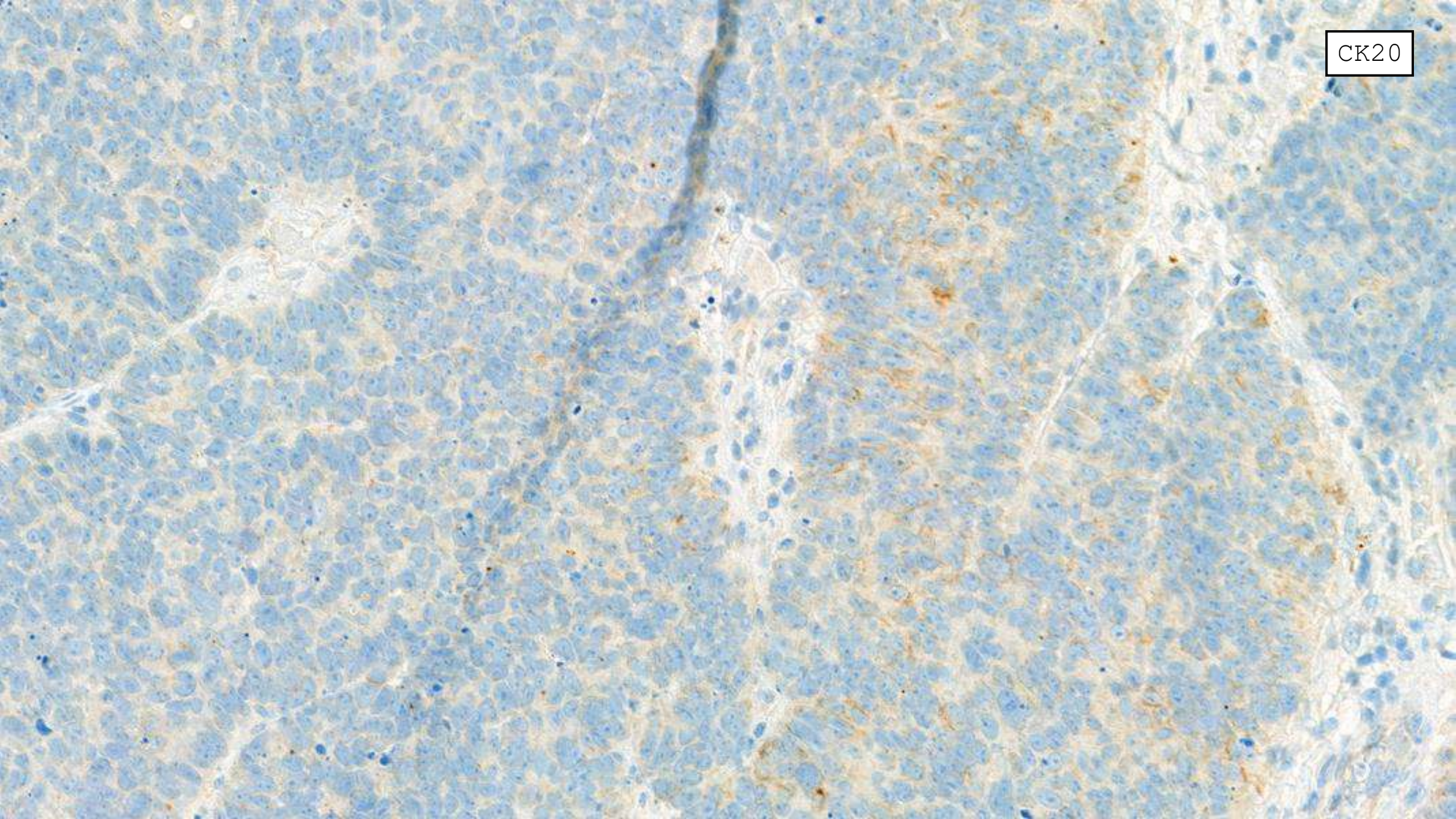








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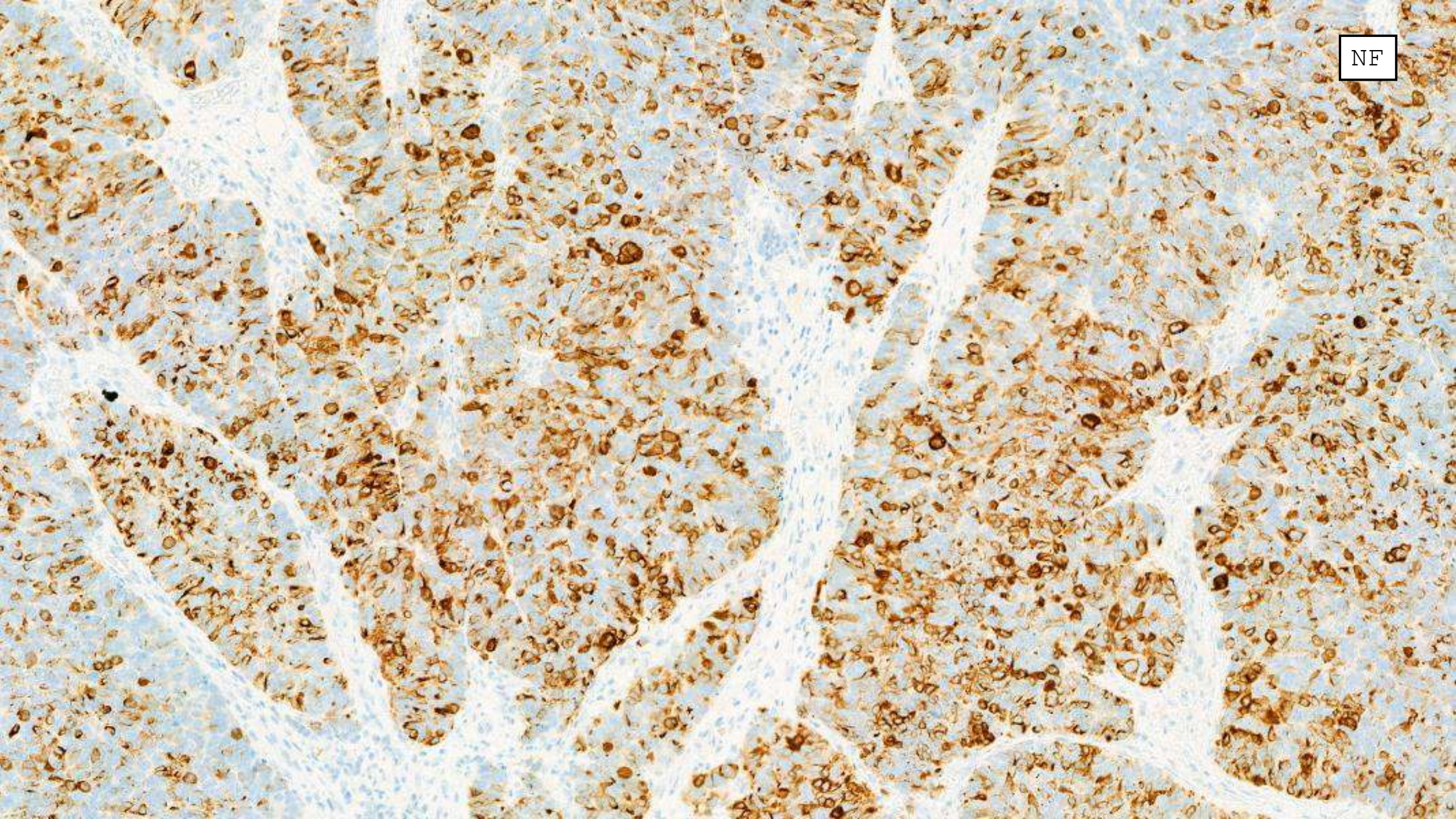
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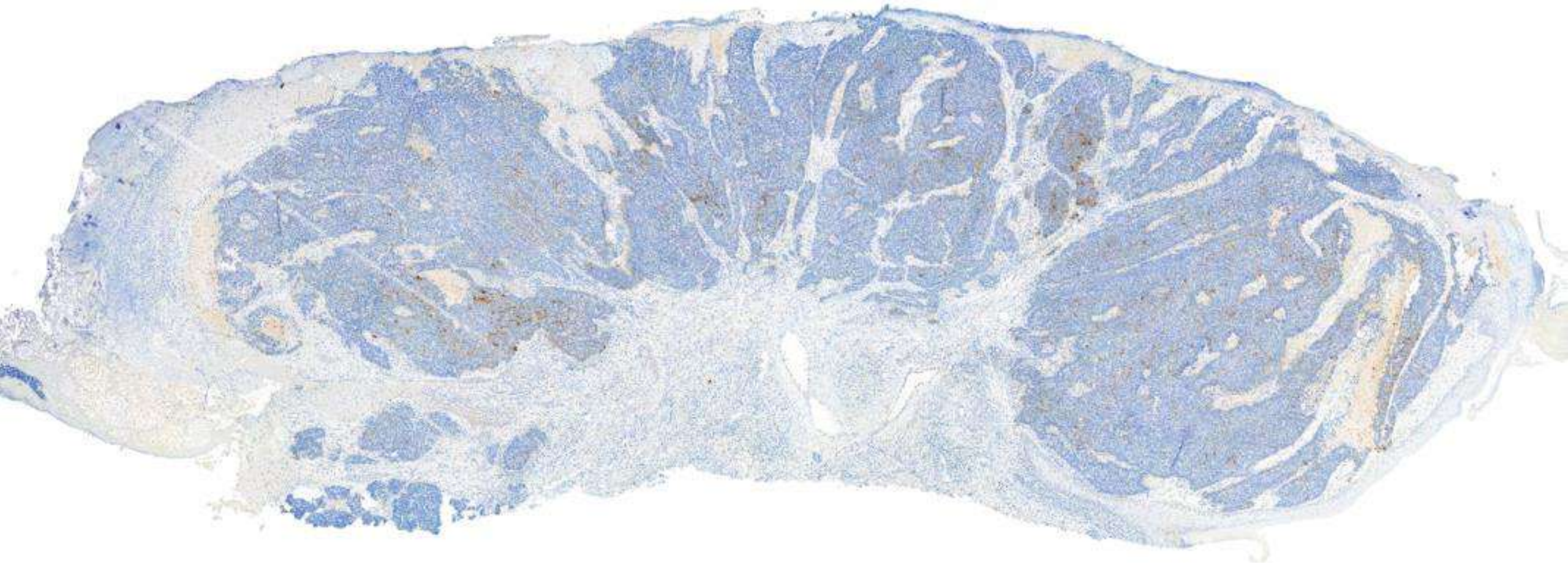

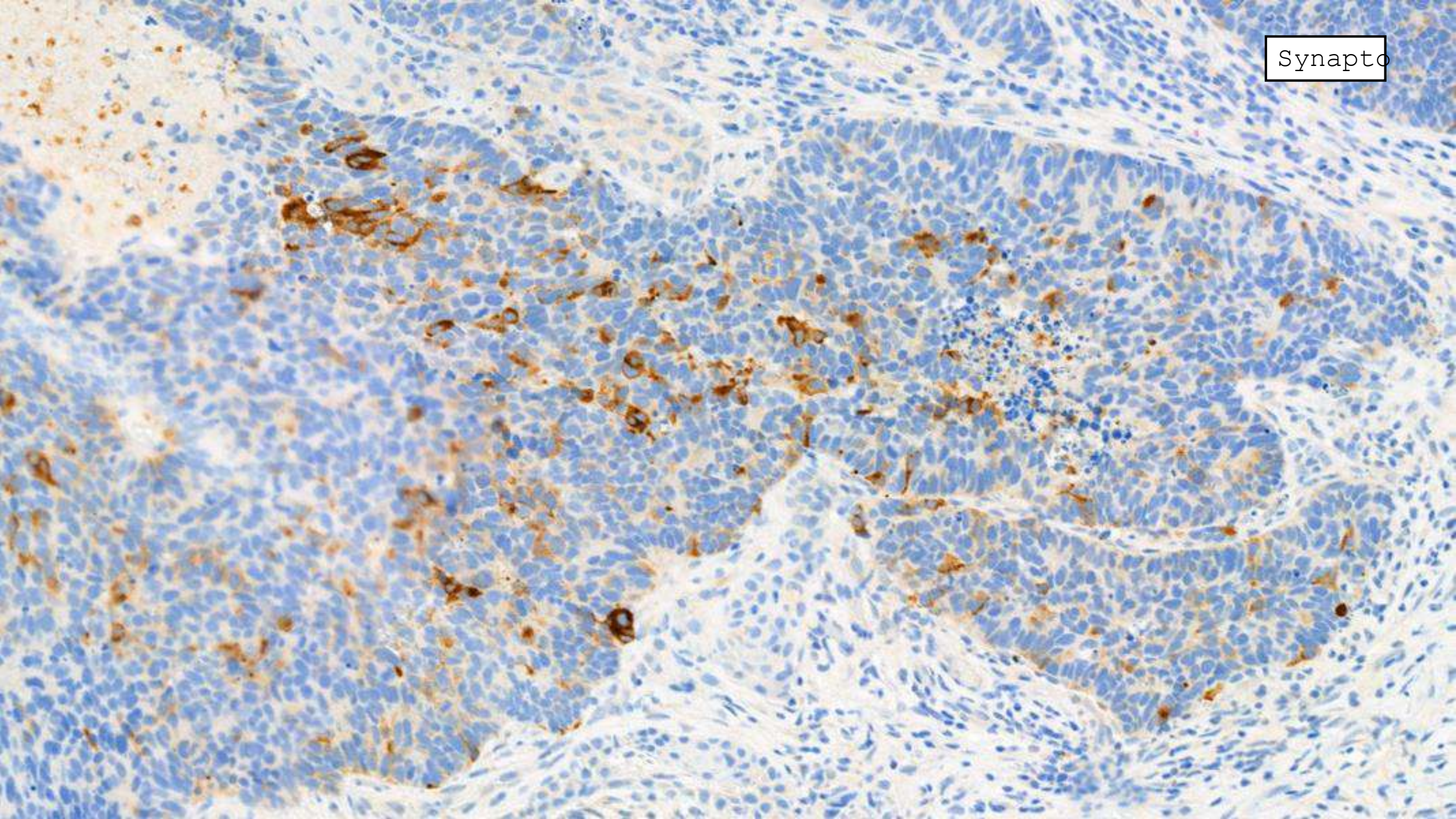
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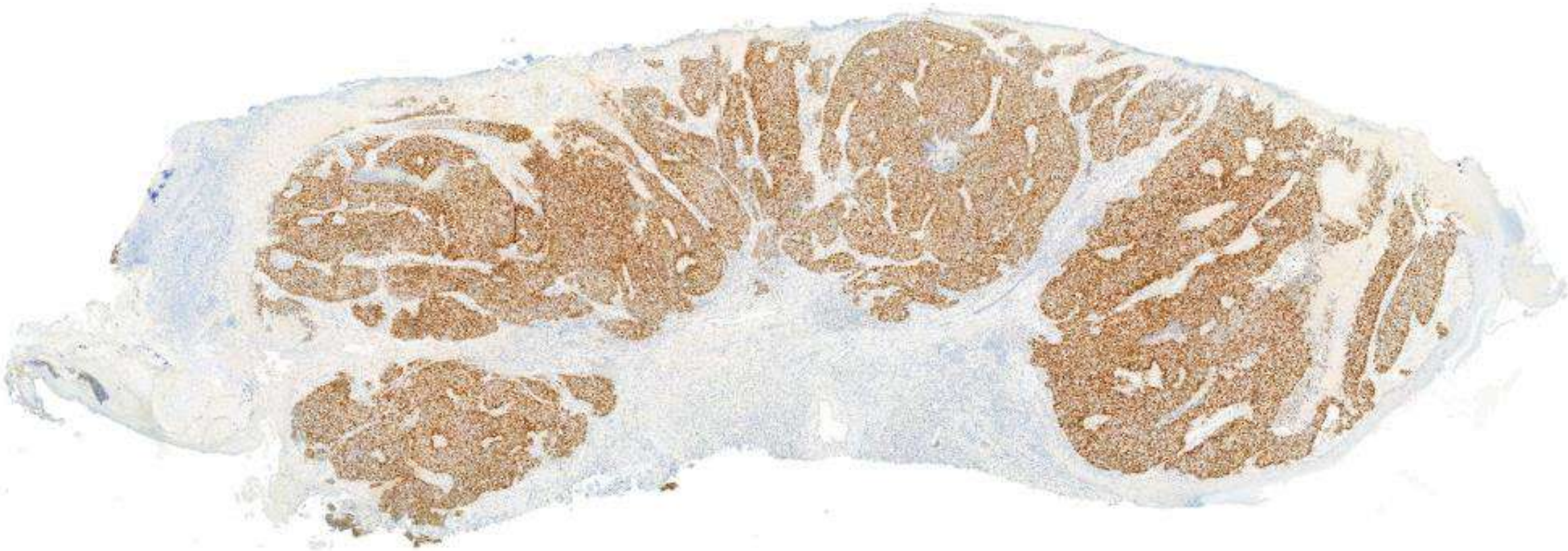
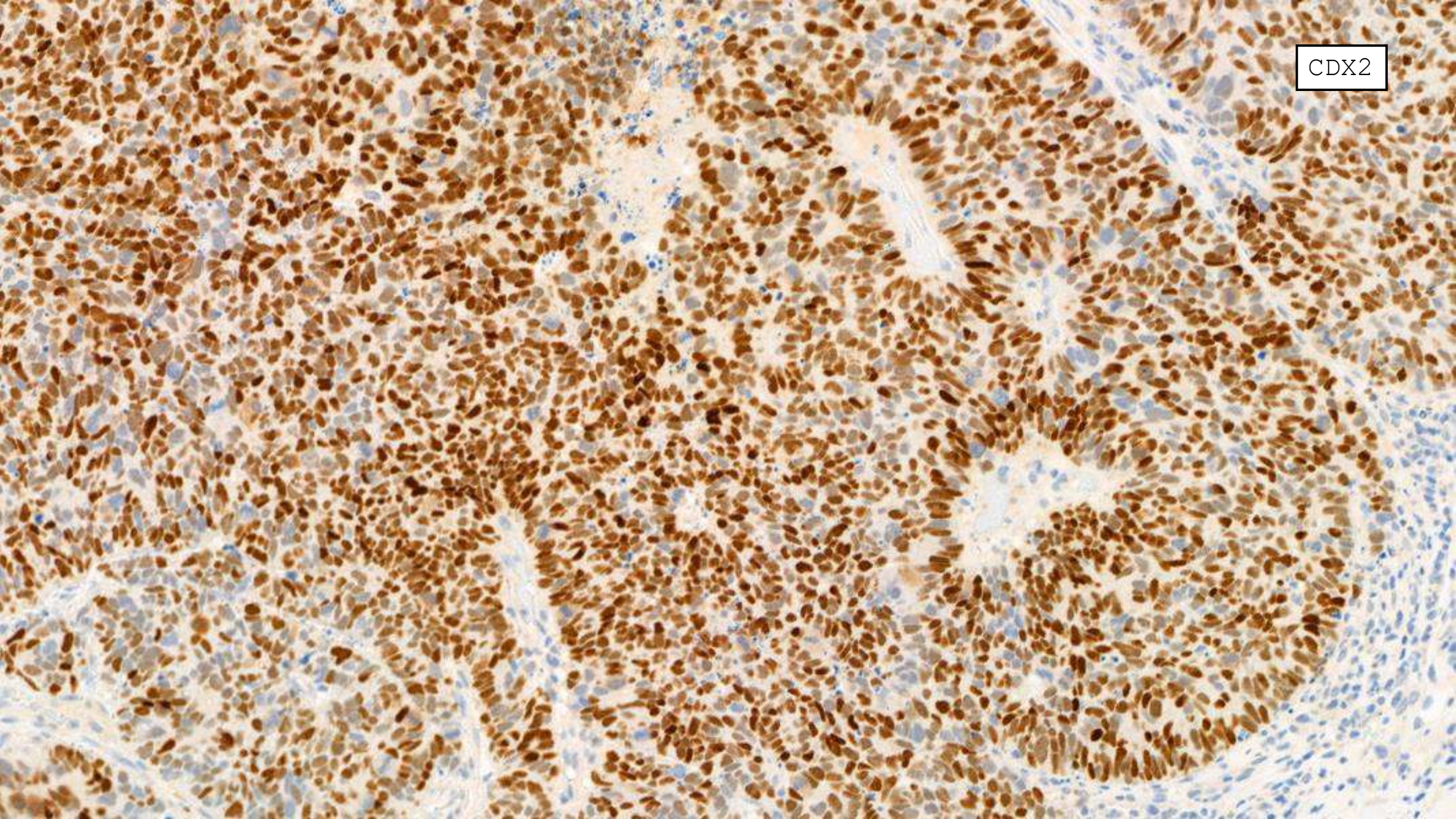
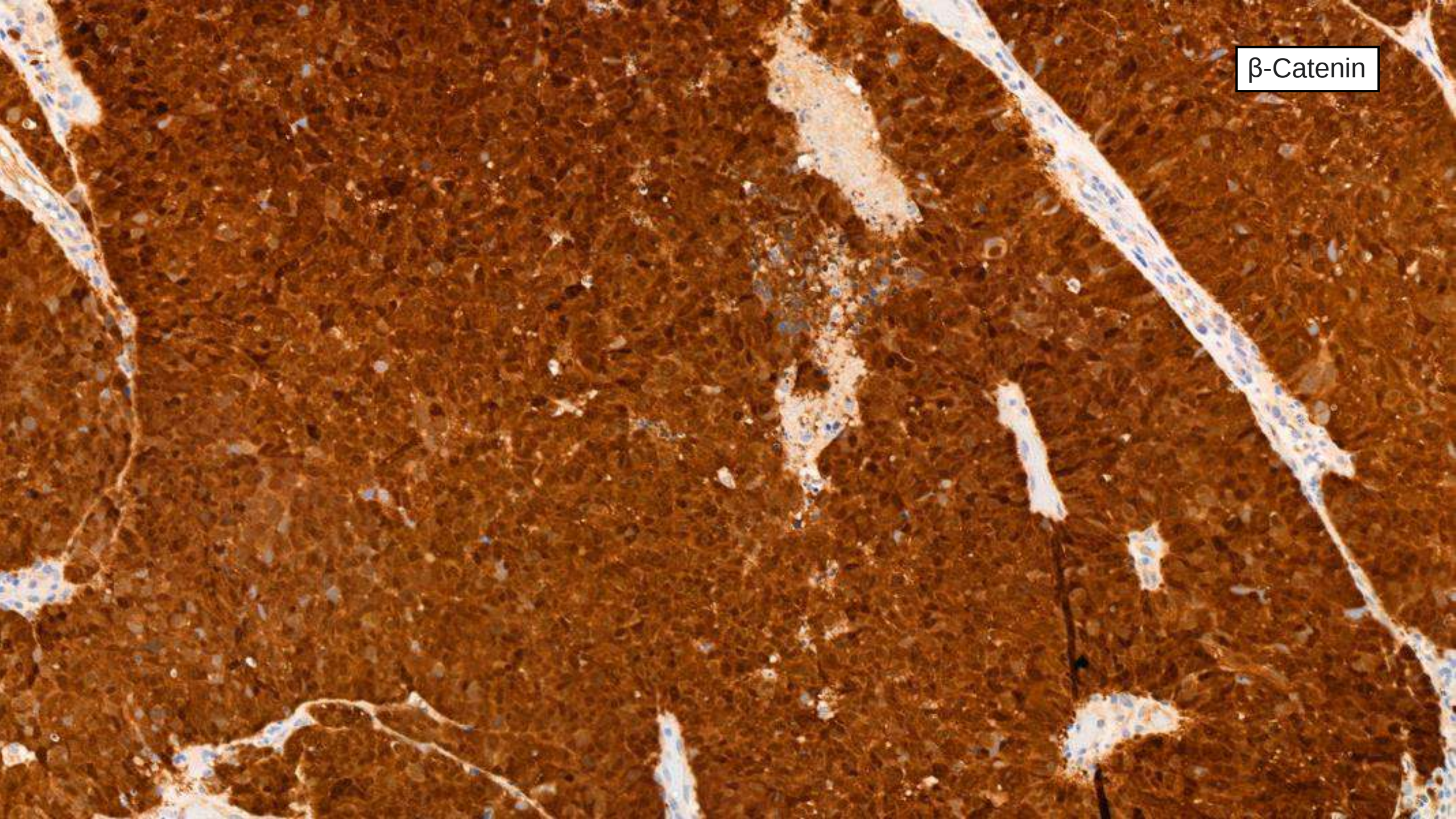
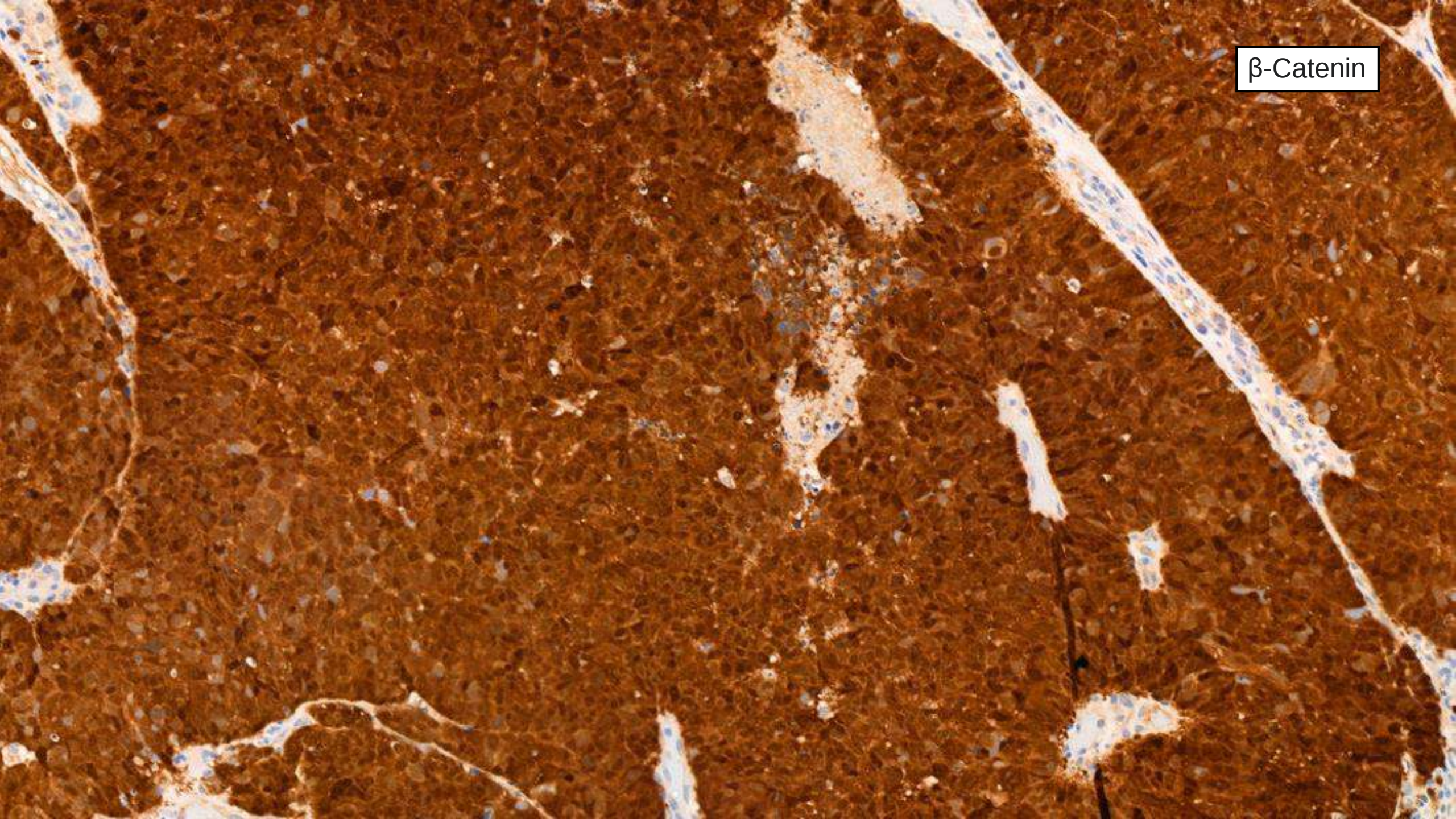
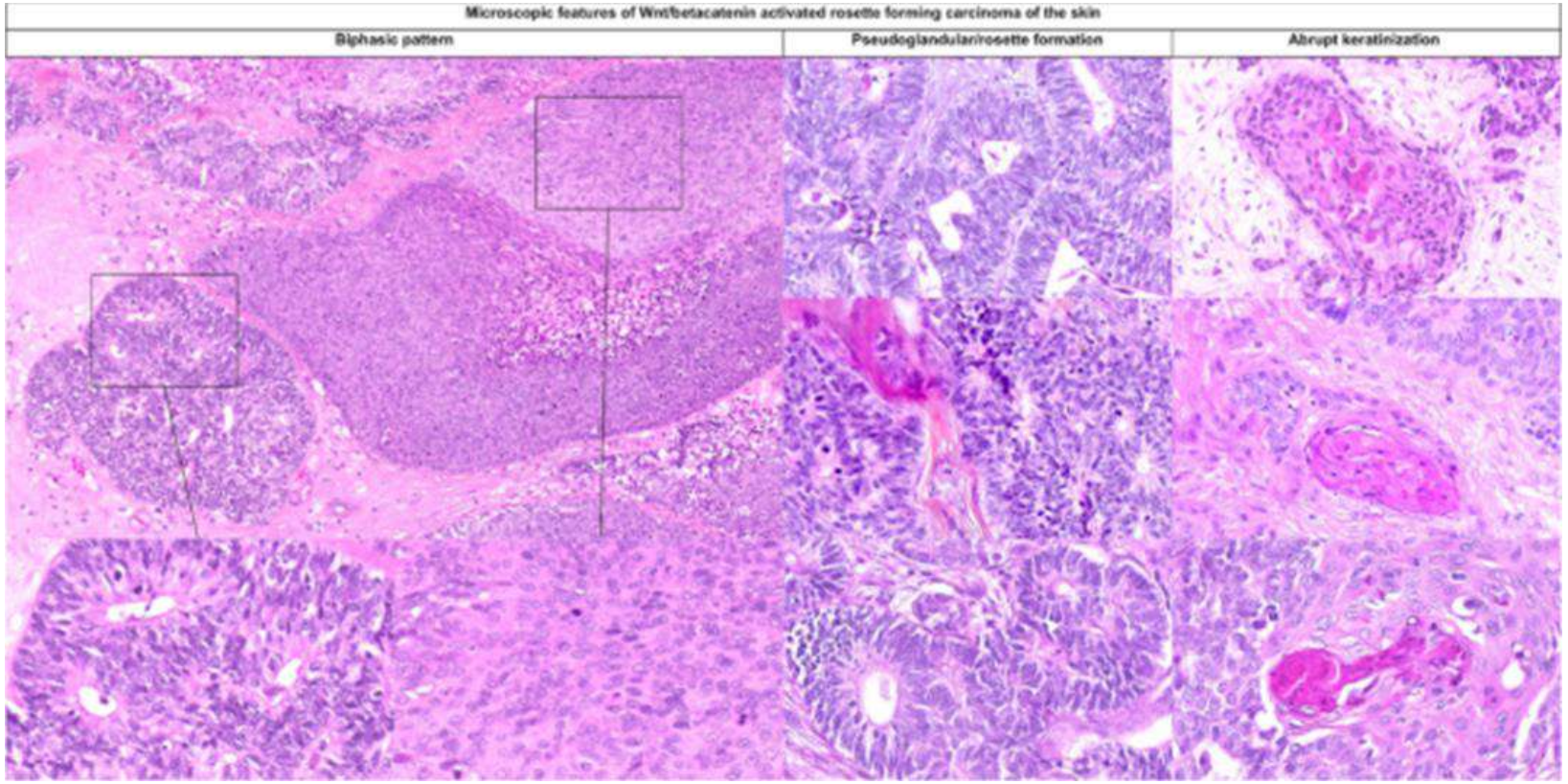

CDX2


CDX2


β-Catenin


β-Catenin

WTN/β-Catenin activated rosette forming carcinoma



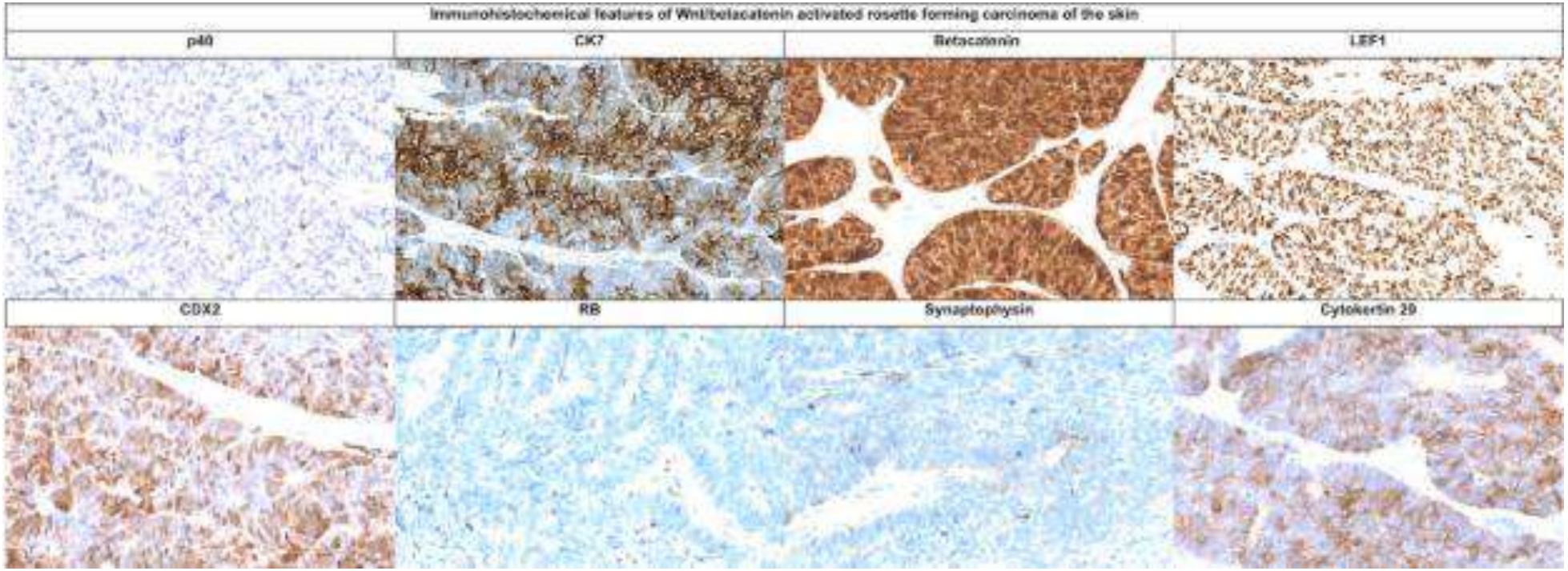
16 primary cutaneous carcinomas harboring mutations activating the Wnt/b-catenin pathway without evidence of matrical differentiation

4 combined tumors in which a similar Wnt/b-catenine activated carcinoma component was associated with Merkel cell carcinoma (MCC) or pilomatrical carcinoma

- Microscopically all cases were poorly differentiated neoplasms infiltrating the dermis and/or subcutaneous tissue

- Solid "squamoid" areas were associated with a basophilic component characterized by rosette/pseudoglandular formation resulting in a biphasic appearance

Kervarrec T et al. Wnt/β-Catenin-Activated Nonpilomatrical Carcinoma of the Skin: A Case Series. Mod Pathol. 2024 Nov;37(11):100586. doi: 10.1016/j.modpat.2024



EMA +++(100%)
BerEP4 +++(100%),
Cytokeratin 7 +++(94%)
Chromogranin A +(44%),
Synaptophysin +++(82%)
Cytokeratin 20 + (69%)
Complete loss of Rb expression
Nuclear β-catenin and CDX2 expression was detected in all cases

Recurrent pathogenic somatic mutations were observed in APC, CTNNB1 and RB-1

In addition, we identified **4 combined neoplasms** in which there was a component showing a similar poorly differentiated rosette-forming carcinoma demonstrating Rb loss and b-catenin activation associated **with either**
MCC or pilomatrical carcinoma

- Wnt/b-catenine activated non-pilomatrical carcinoma with biphasic appearance and rosette formation called **"Wnt/b-catenineactivated rosette-forming carcinoma" (WARFC)** distinct from the other skin tumor entities

- RB-1 expression loss, a constant feature of WARFC
- Pilomatrical carcinomas and observed a preserved RB-1 expression in all except 1 case
- Pilomatrical carcinoma loss of or reduced cytokeratin 5/6 expression and preserved p40 expression in all cases also contribute to the distinction between WARFC and pilomatrical carcinomas

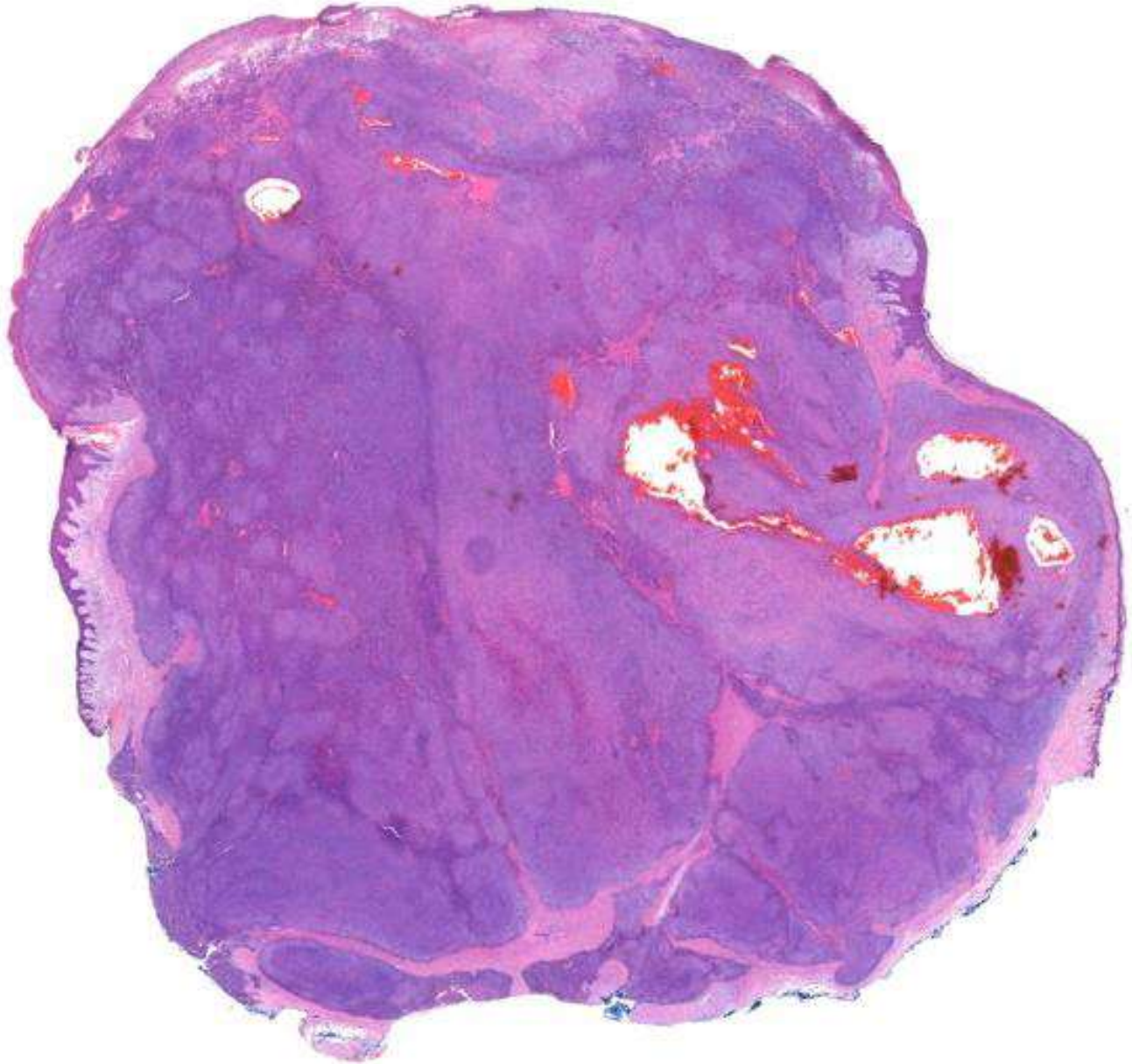
- MCC predominant membranous b-catenin expression was detected with only focal positive nuclear expression
- Focal LEF1 expression was observed in 6 cases without nuclear b-catenin accumulation
- No CDX2 expression was observed
- β-catenin activation is not a common feature of MCC in contrast to WARFC.

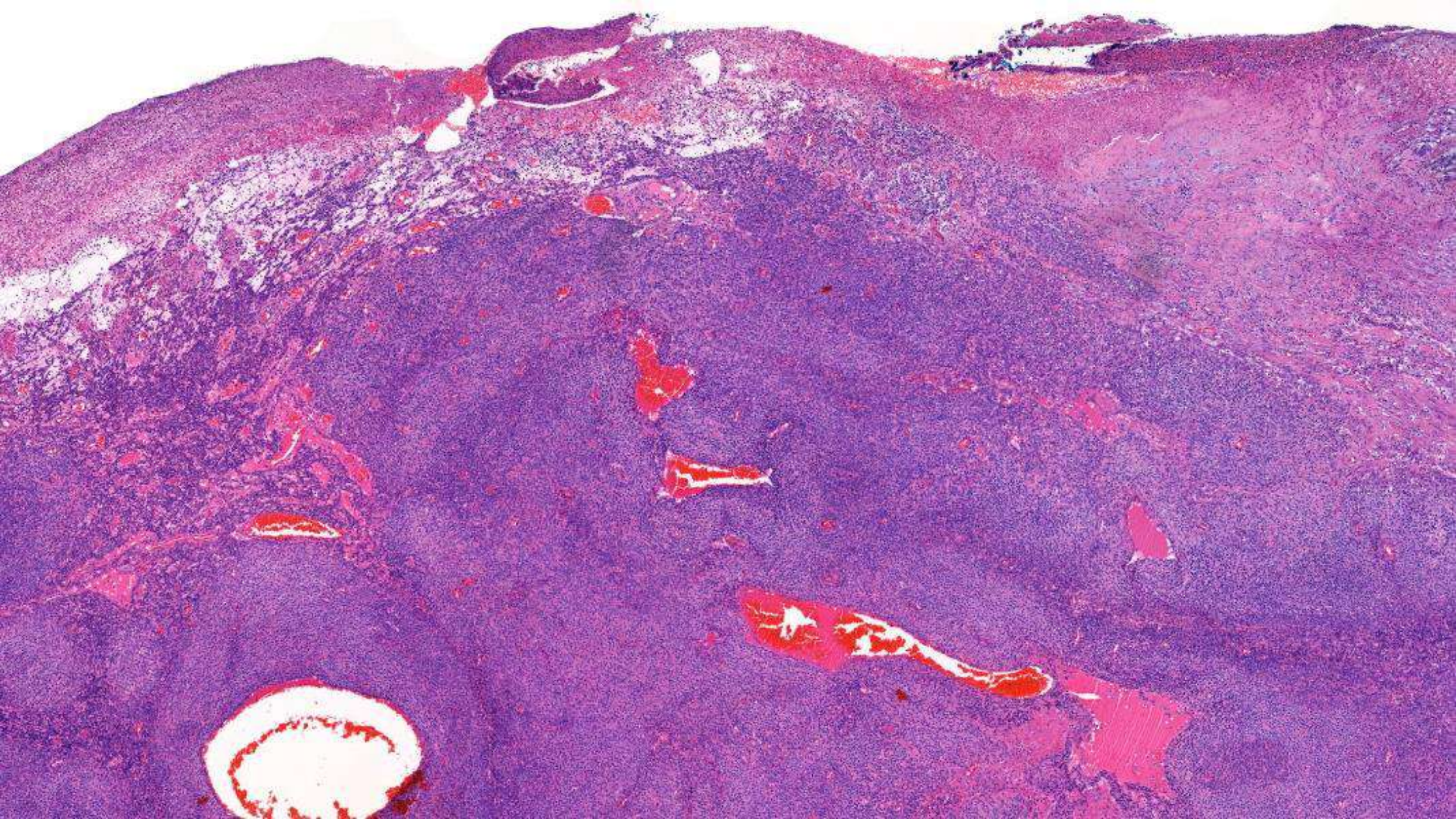
	WARFC	Pilomatrical carcinoma	MCC
β-Catenin	+++	+++	Focal+/- (membranous)
LEF-1	+++	+++	Focal+/-
Rb-1	Loss	Loss /Preserved	Loss
CK-20	-	+++	+++
p40	-	+++	
CDX-2	+++		-
CK5/6	+++	-	+++

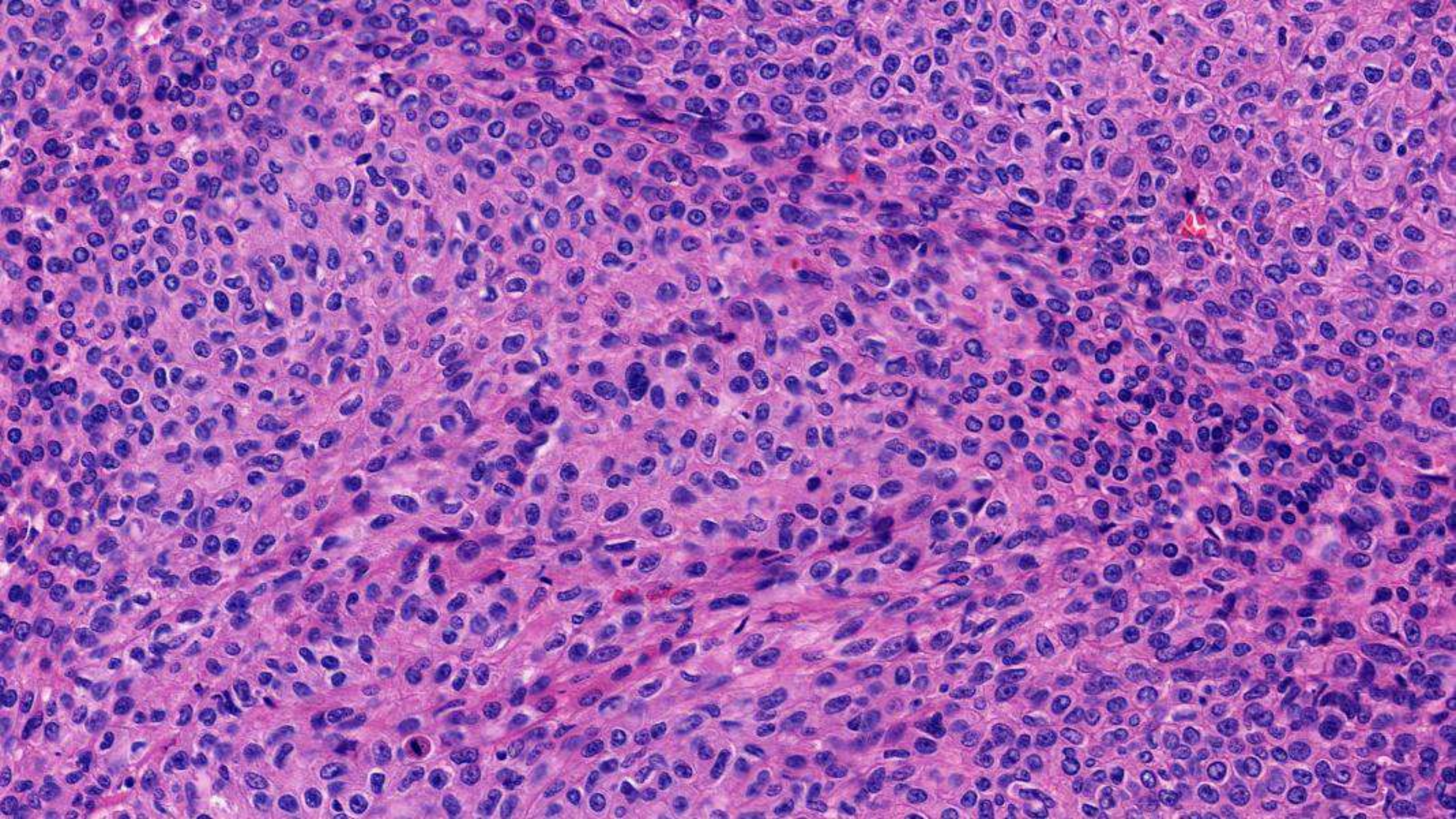
Kervarrec T et al. Wnt/β-Catenin-Activated Nonpilomatrical Carcinoma of the Skin: A Case Series. Mod Pathol. 2024 Nov;37(11):100586. doi: 10.1016/j.modpat.2024

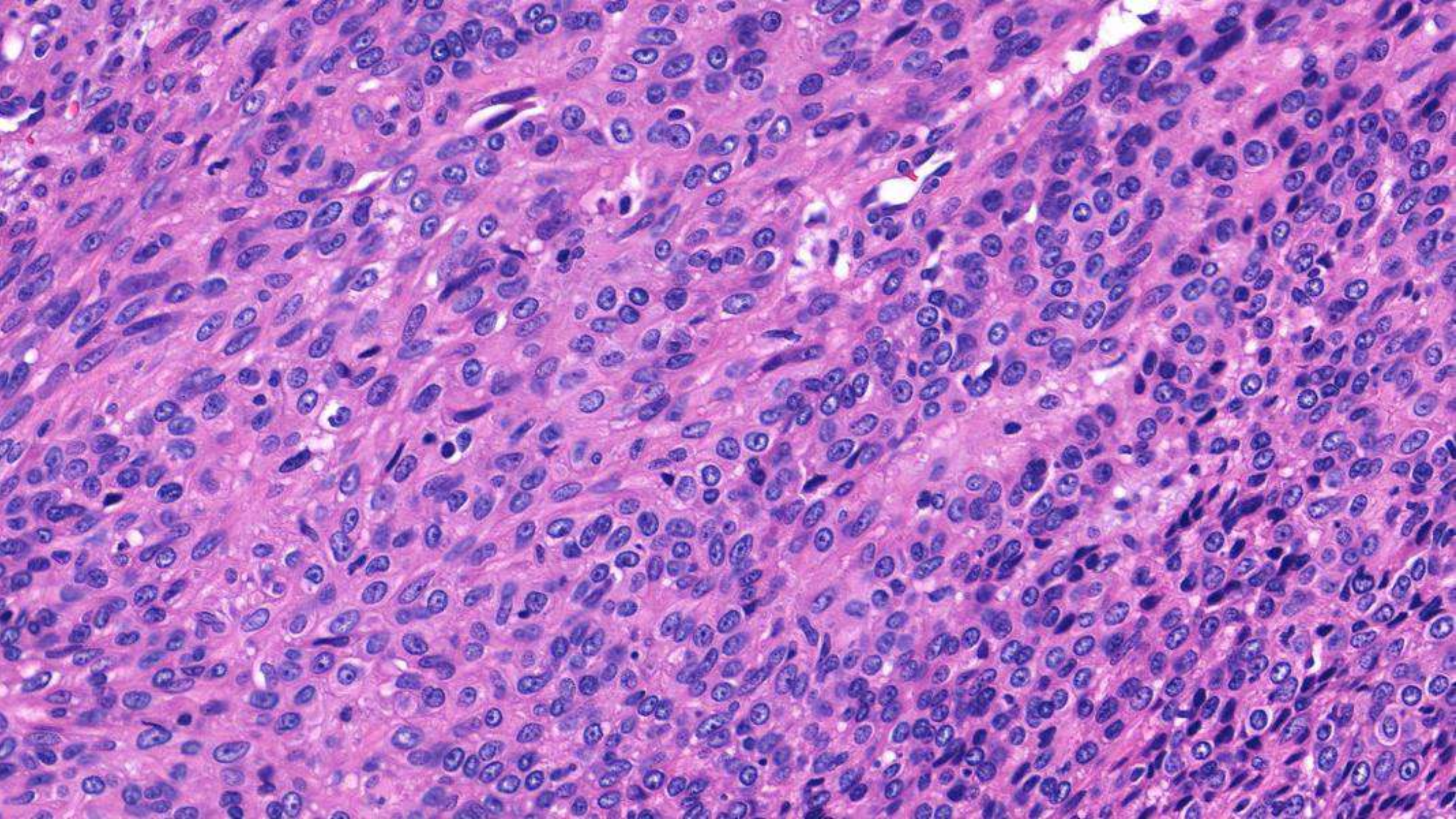
Case 2

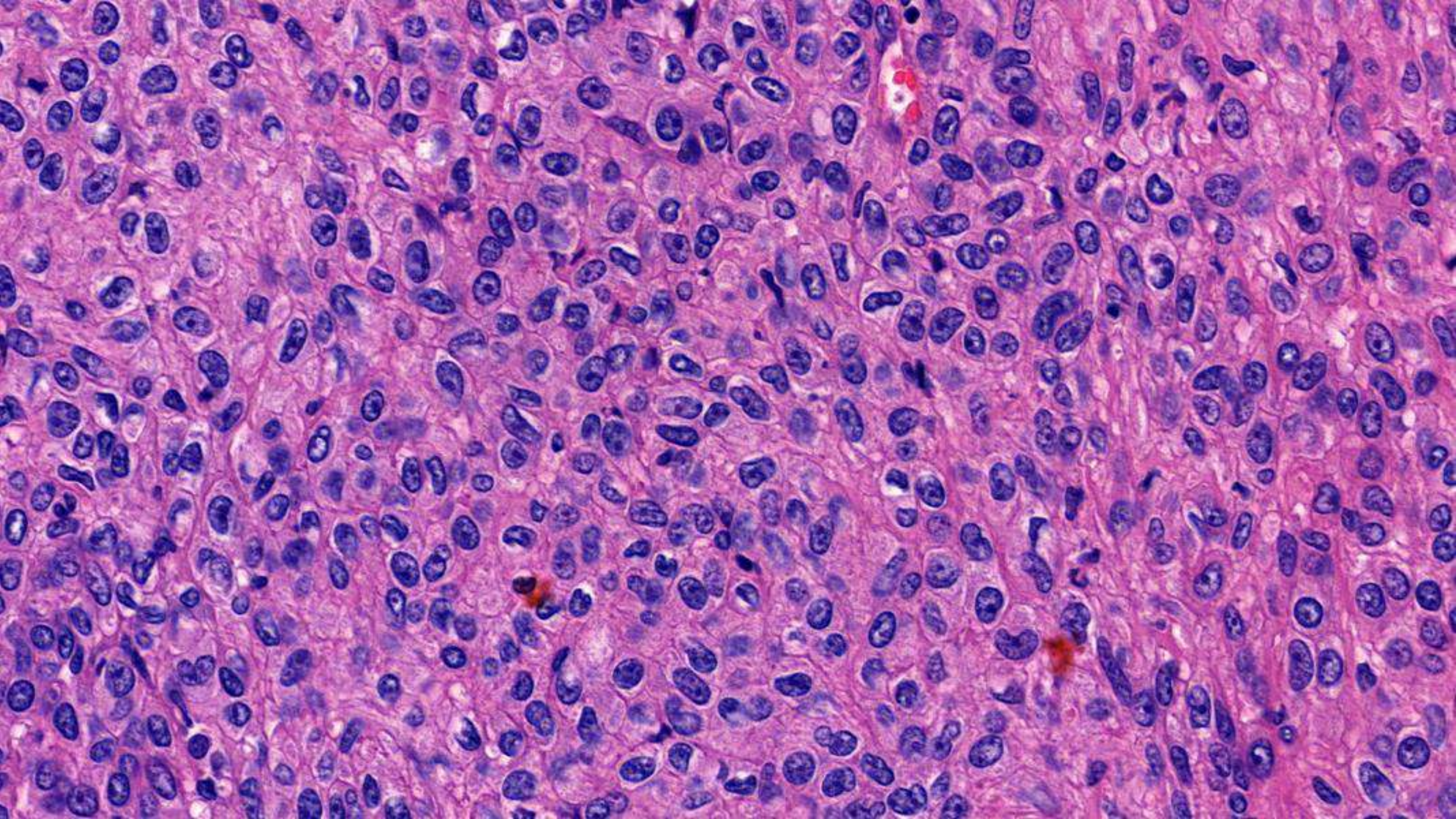
13-year-old male
Growing lesion on the left elbow
Present for 9 months
Vascular?

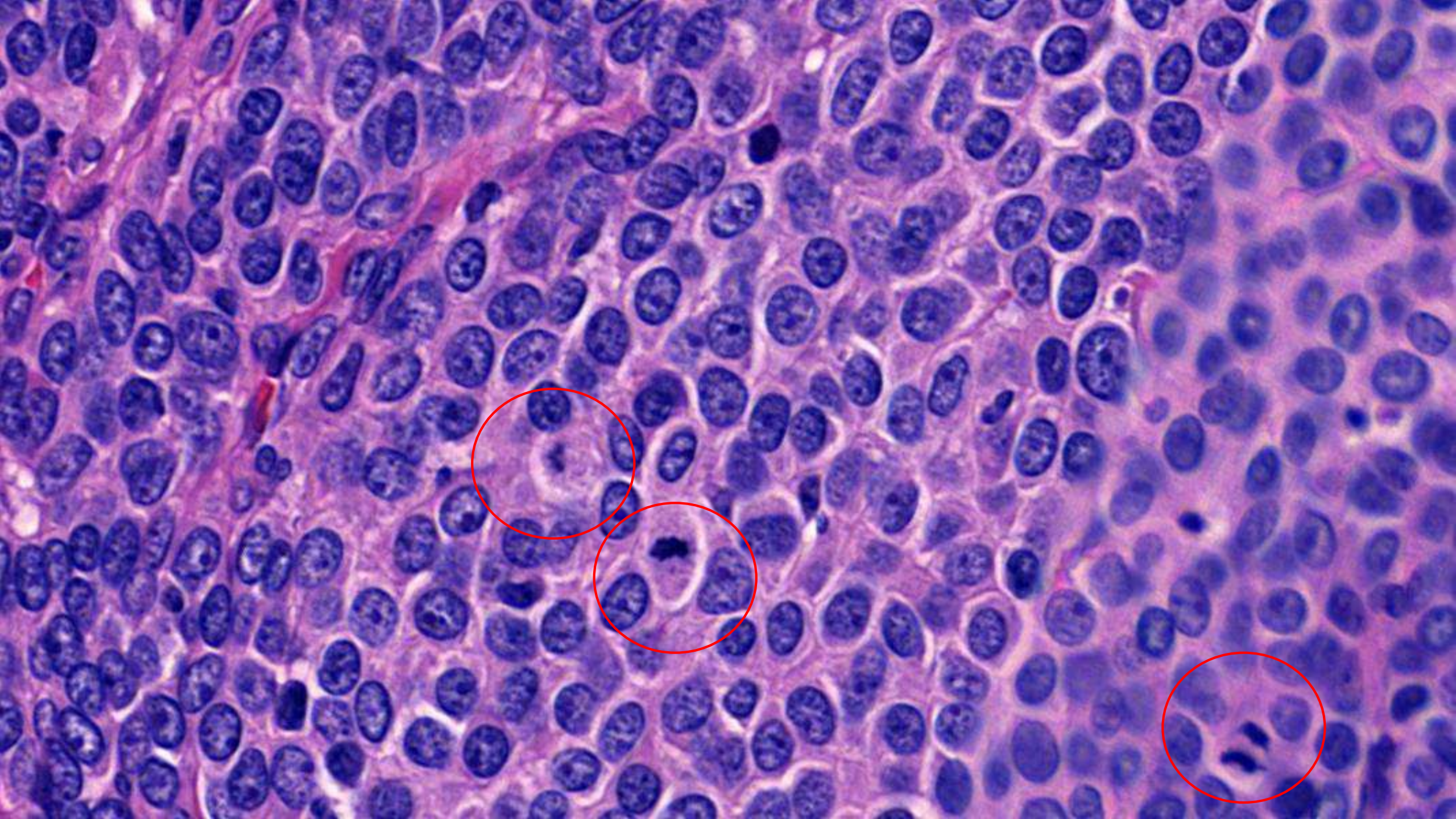




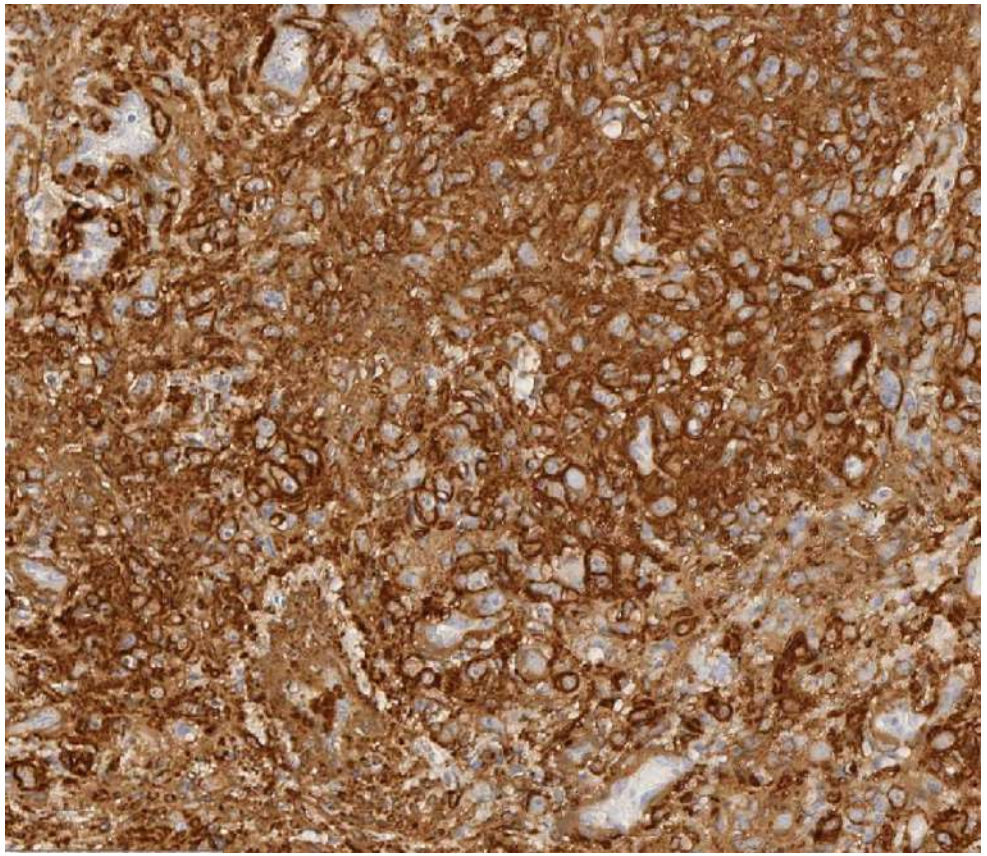


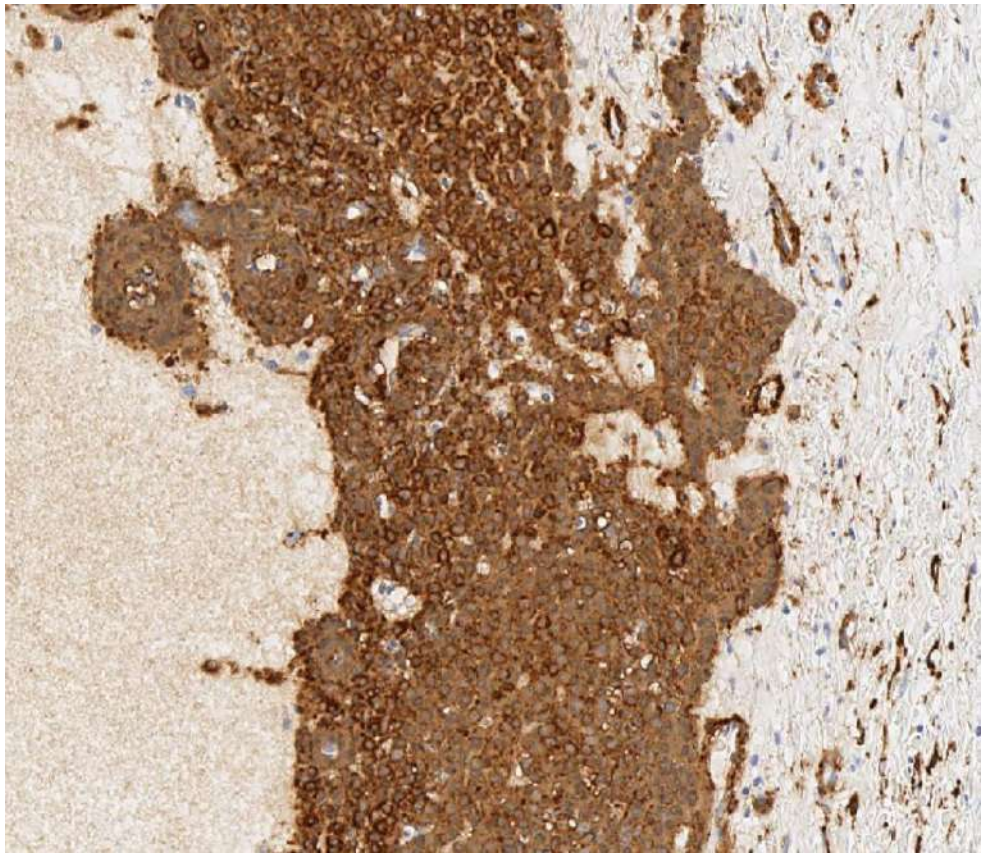




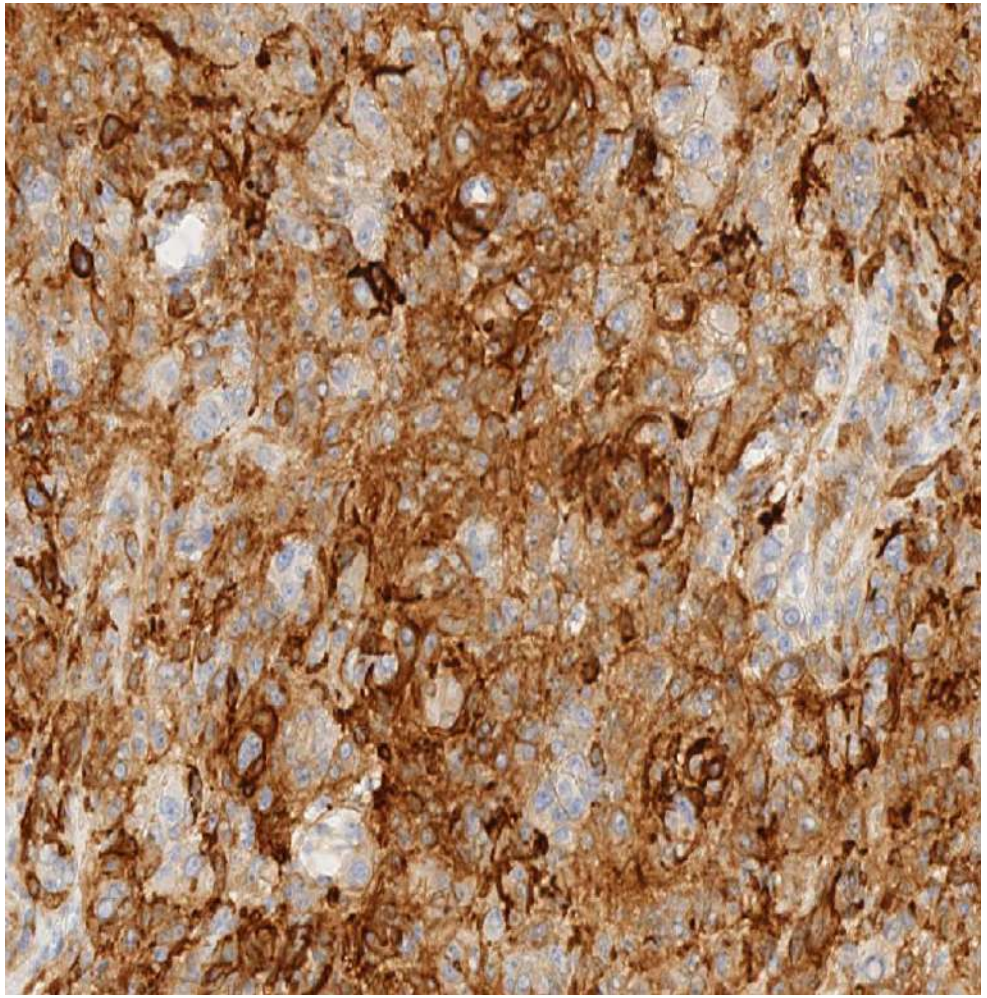


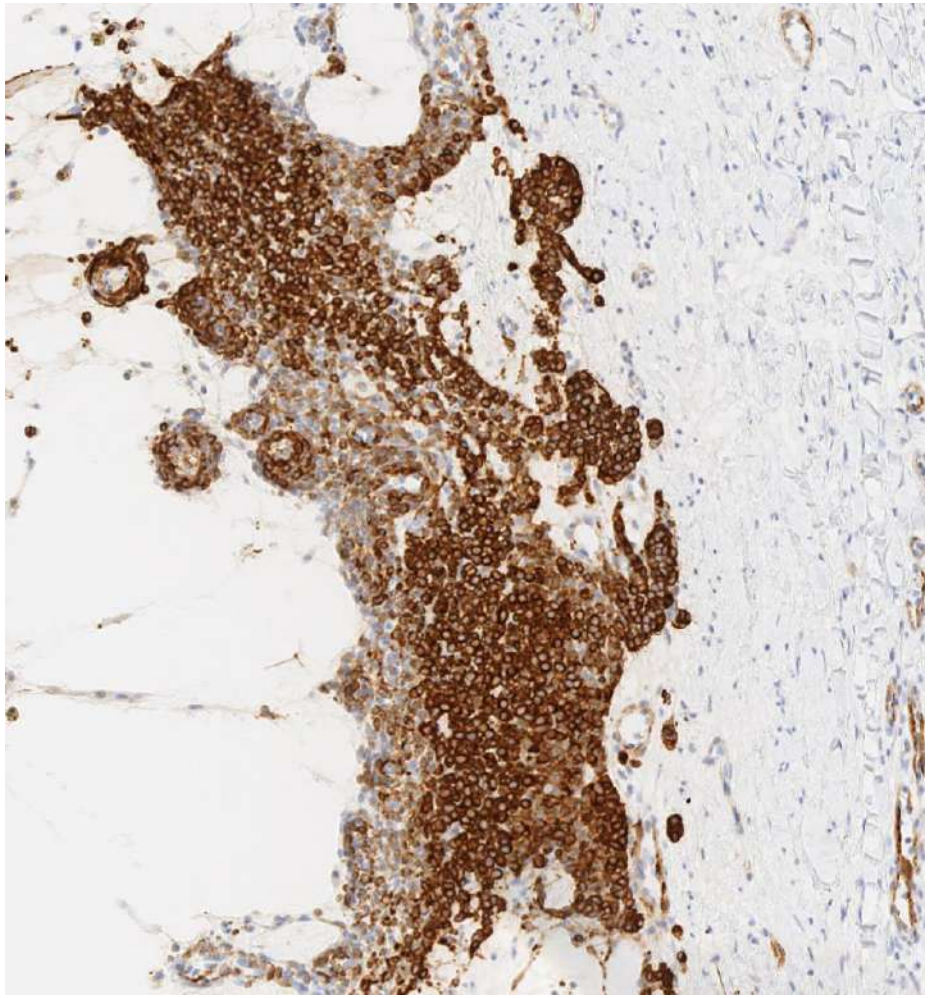
SMA

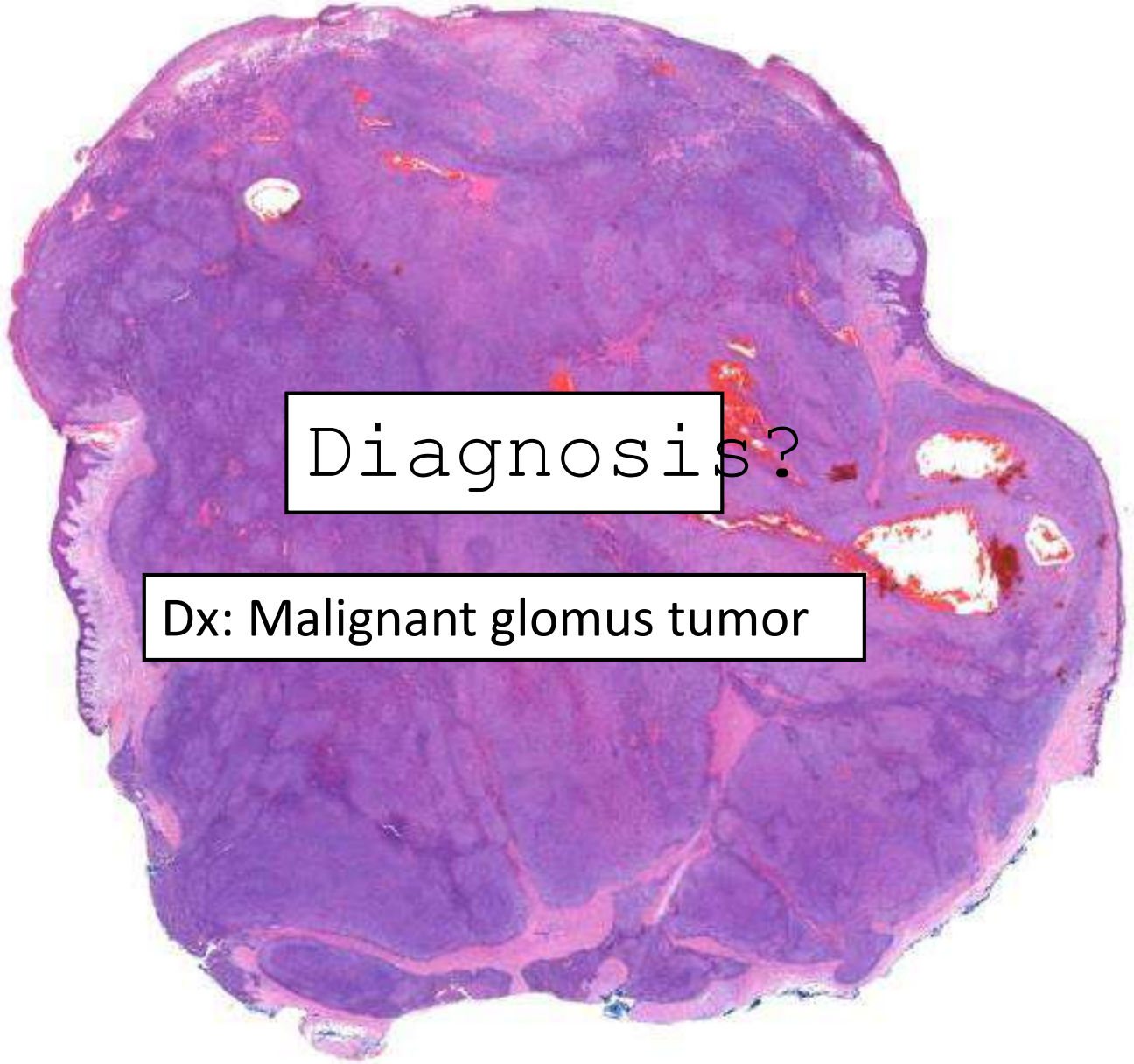




H-Caldesmon






Diagnosis?
Dx: Malignant glomus tumor

WHO classified the glomus tumor (GT)

- Location
- Size
- Nuclear atypia
- Atypical mitosis
- Mitotic activity

1. Malignant GT
2. GT of uncertain malignant potential
3. Symplastic GT
4. Glomangiomyoma
5. Glomangiomatosis

Classification of skin tumors (WHO, 2018)

Malignant GT should be made when:

- (1) marked nuclear atypia and <u>any level of mitotic activity;</u> or
- (2) atypical mitoses

- Cutaneous malignant GTs are very rare
- Male to female ratio 1:1
- Lower extremities, upper extremities and trunk occurrence on the face was much less common
- Most frequent presenting symptom was an enlarging nodule or, less often, an ill-defined mass, which was on occasion painful
- Cutaneous malignant GTs were generally smaller than their deep soft tissue and visceral counterparts

- Grow in the dermis and subcutis, with a nodular or infiltrative growth pattern
- Composed of an admixture of cells with epithelioid and spindle cell morphology and moderate or severe degrees of cytological atypia
- Mitotic activity was invariably present with a mean number of 9 mitoses per 10 HPFs
- Vascular invasion and tumoral necrosis were present infrequently
- Around half of these tumors have a benign GT at their periphery
- Local recurrence occurs in about 20% of cases, usually due to incomplete excision
- Metastases were rare in this study
- Tumor size, mitotic activity, and nuclear atypia did not correlate with outcomes, although tumor necrosis was associated with poor prognosis

Luzar B, Martin B, Fisher C, Calonje E. Cutaneous malignant glomus tumours: applicability of currently established malignancy criteria for tumours occurring in the skin. Pathology. 2018 Dec;50(7):711-717

Table 2 Summary of clinicopathological data of current series of 11 cutaneous malignant glomus tumours

No	Age	Sex	Site	Size	Depth	Pre-existent glomus tumour	Nuclear grade	Mitoses/ 10 HPF	Infiltrative pattern	Vascular invasion	Areas with spindle cells	Necrosis	Follow-up	Outcome
1	36	M	Leg	10	D	Yes	Moderate	12	No	No	Yes	No	94	Alive, NED
2	54	F	Arm	6	D	No	Mild	3	No	No	No	No	77	Alive, NED
3	46	M	Leg	7	D-SC	Yes	Mild	35	No	No	Yes	No	81	Alive, NED
4	73	M	Nose	8	D-SC	No	Severe	20	Yes	No	Yes	No	87	Alive, NED
5	40	F	Leg	14	D	Yes	Moderate	14	No	No	Yes	No	41	Alive, NED
6	64	F	Arm	6	D	No	Moderate	5	No	No	No	No	62	Alive, NED
7	21	M	Leg		D	Yes	Moderate	4		No	No	No	59	Alive, NED
8	66	F	Arm	12	D-SC	Yes	Moderate	5	No	No	Yes	No	132	Alive, NED
9	55	M	Arm	8	D-SC	Yes	Moderate	7	No	Yes	Yes	No	36	Recurrence
10	75	F	Leg	5	D-SC	No	Mild	8	Yes	No	No	No	NA	NA
11	13	F	Leg	6	D	No	Mild	19	Yes	No	No	No	NA	NA

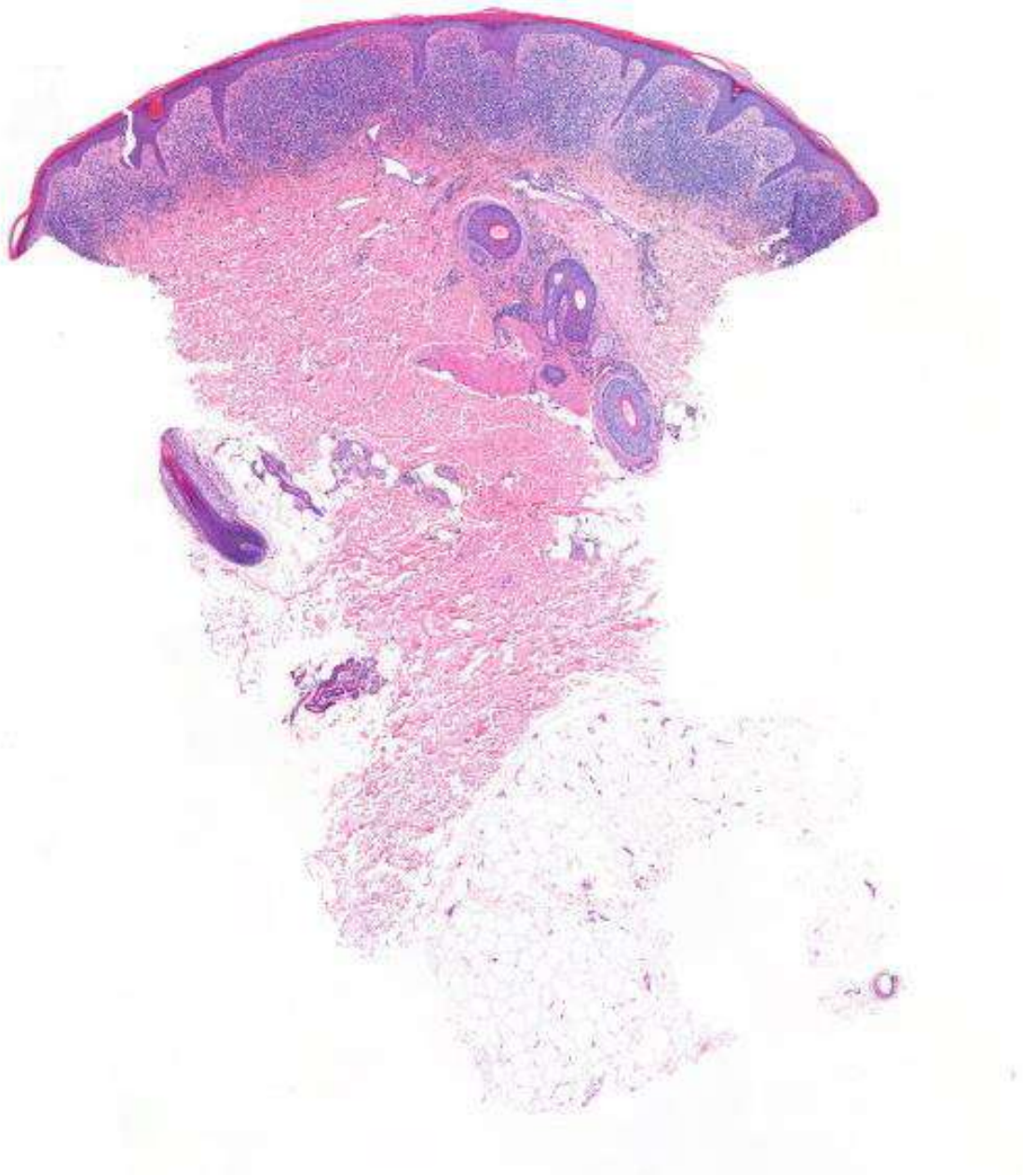
D, dermis; D-SC, dermis and subcutis; HPF, high power fields; NA, not available; NED, no evidence of disease; S, subcutis.

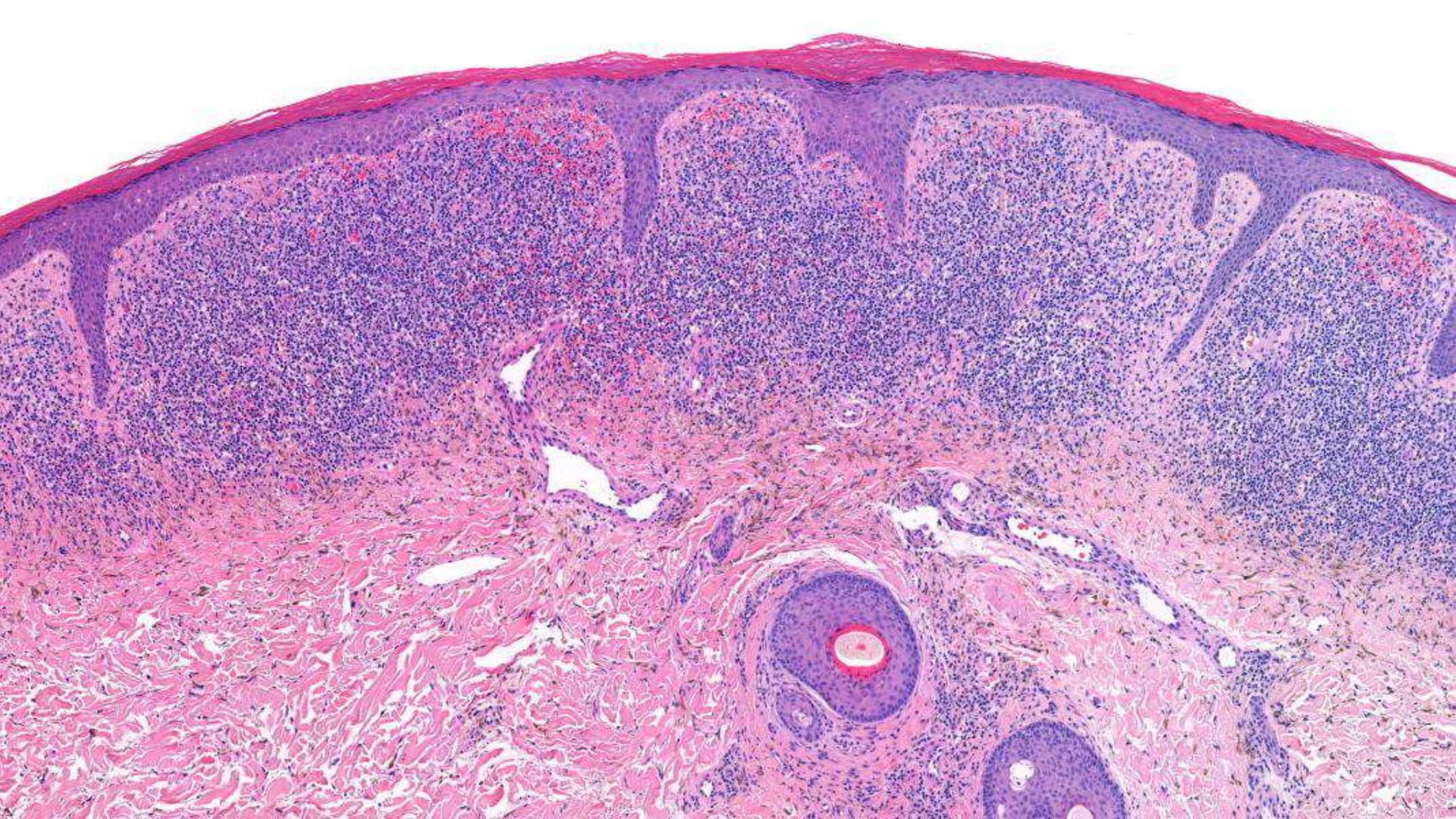
- Superficial GTs are detected earlier, leading to better outcomes
- Treatment focuses on complete excision and long-term follow-up
- Current malignancy criteria may not fully capture the biological potential of these tumor, especially in superficial cases

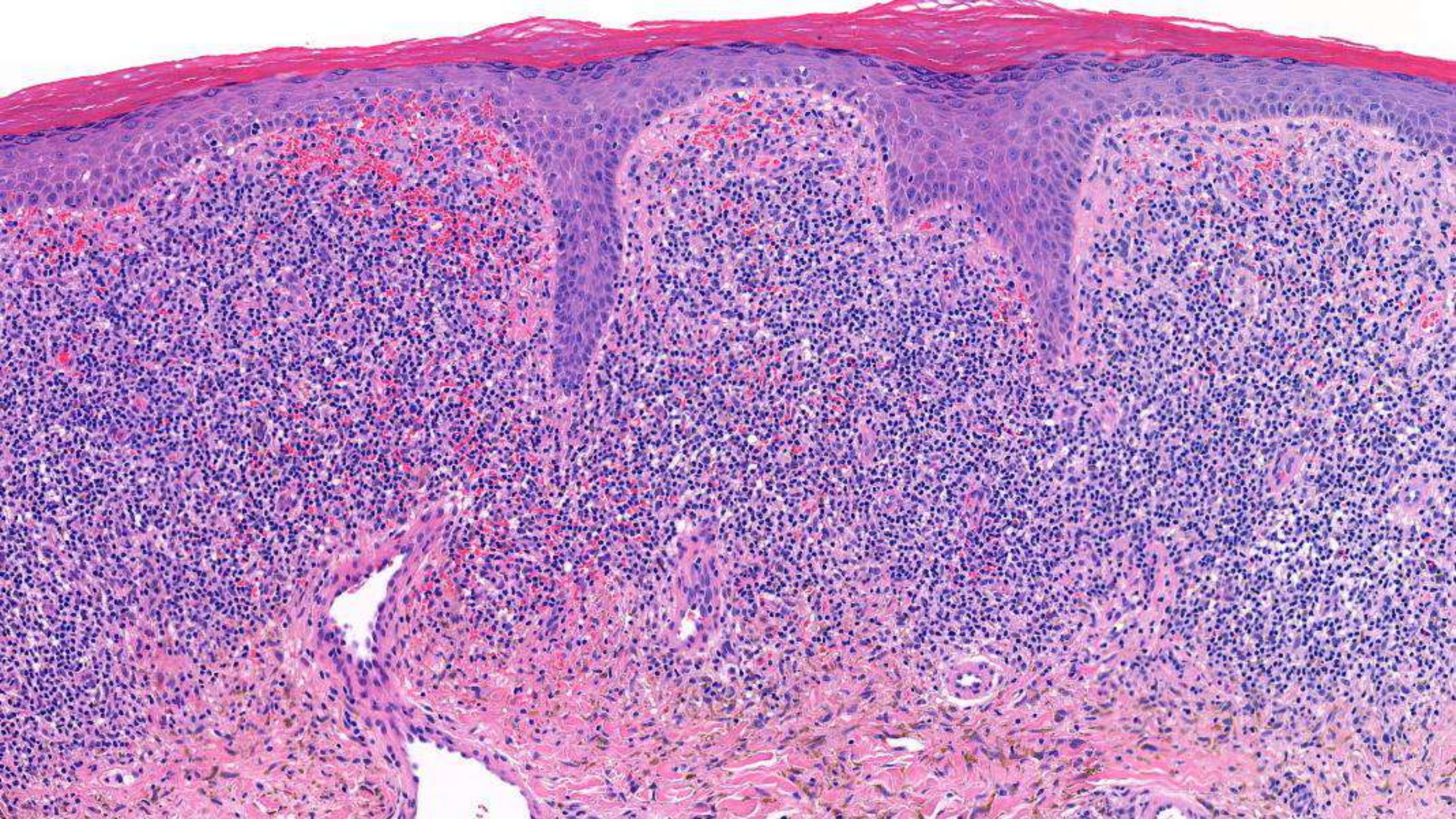
Luzar B, Martin B, Fisher C, Calonje E. Cutaneous malignant glomus tumours: applicability of currently established malignancy criteria for tumours occurring in the skin. Pathology. 2018 Dec;50(7):711-717

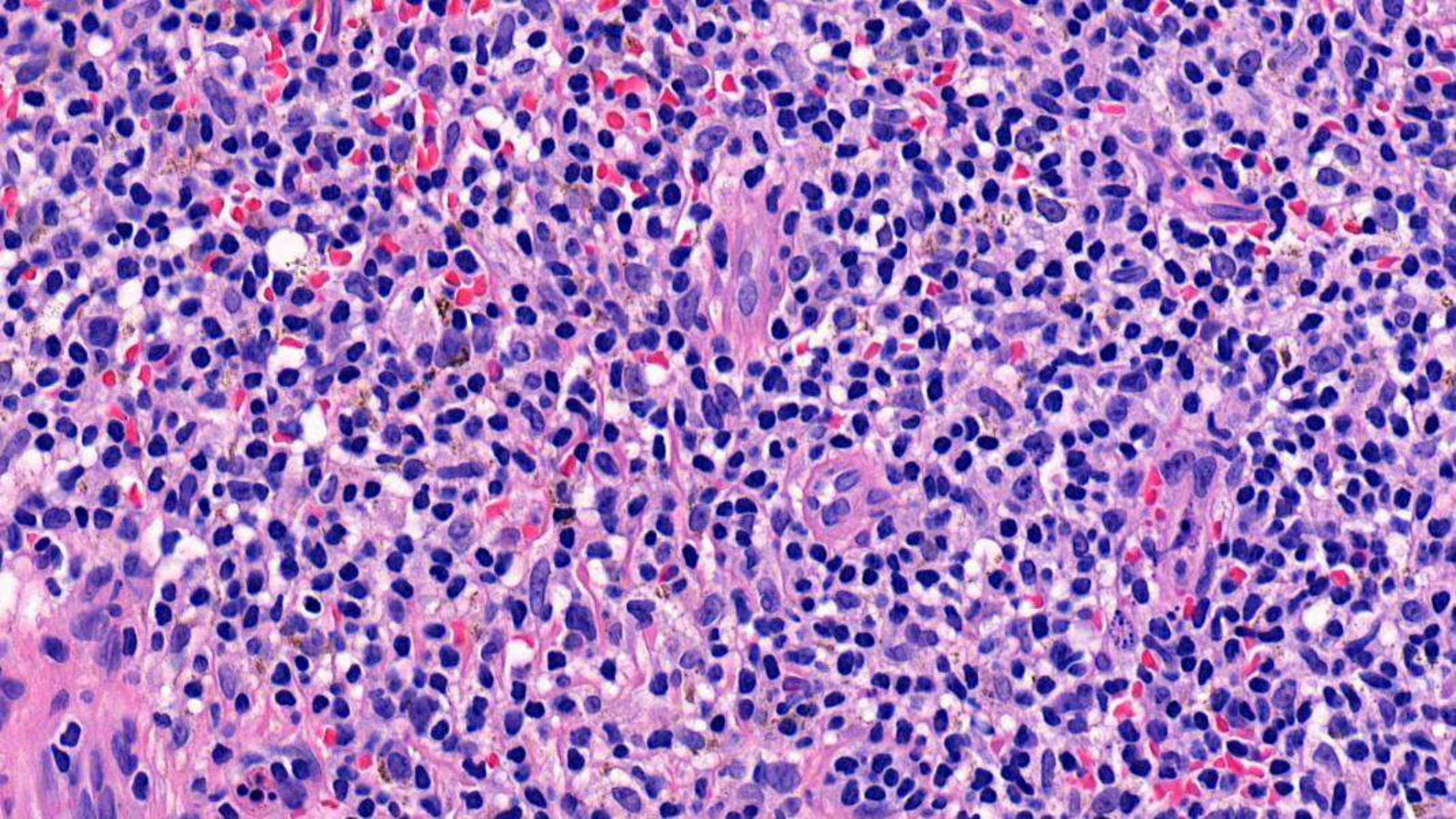
Case 3.

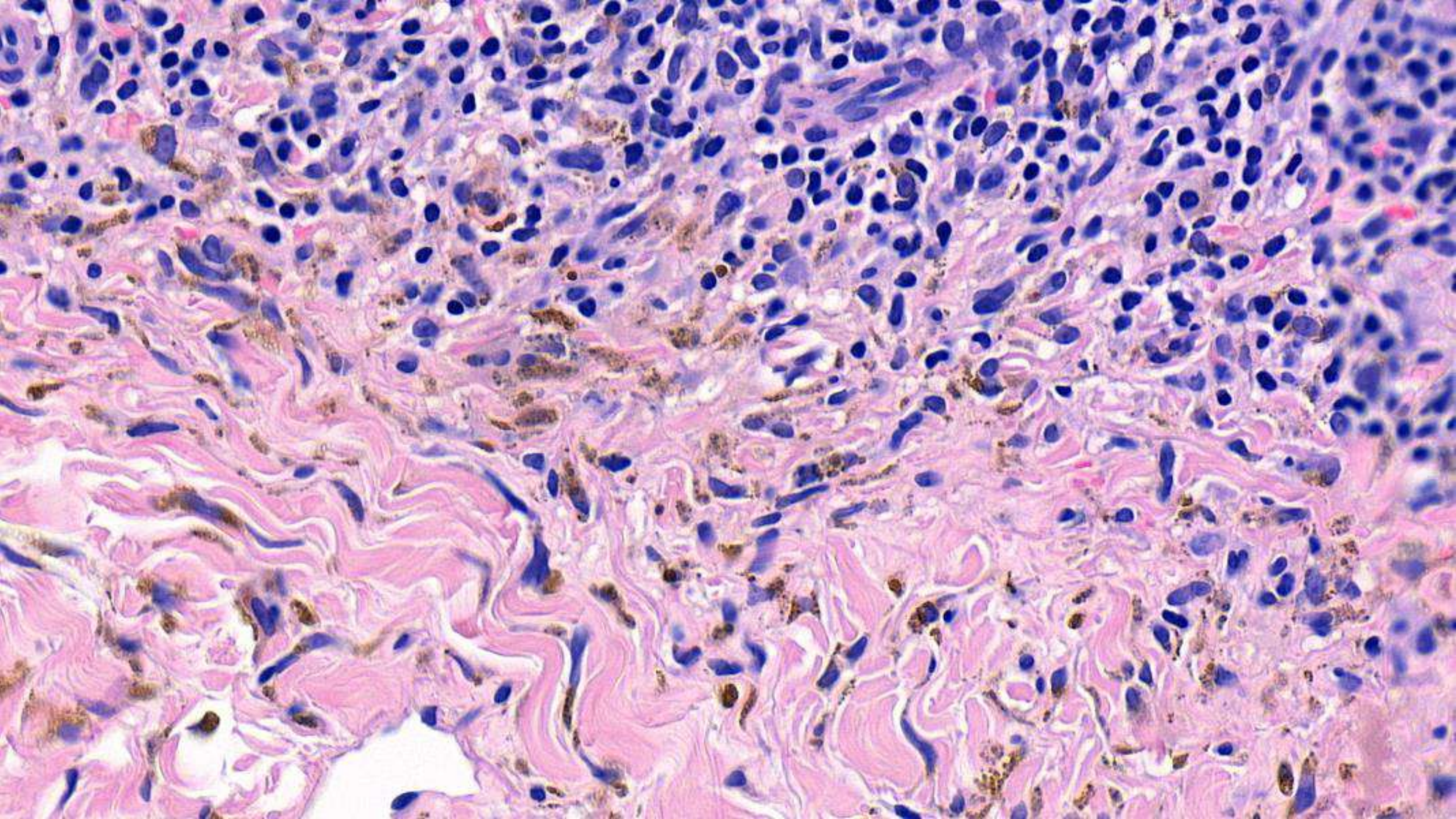
27-year-old
male
Lesion on the
right lower leg
Persistent

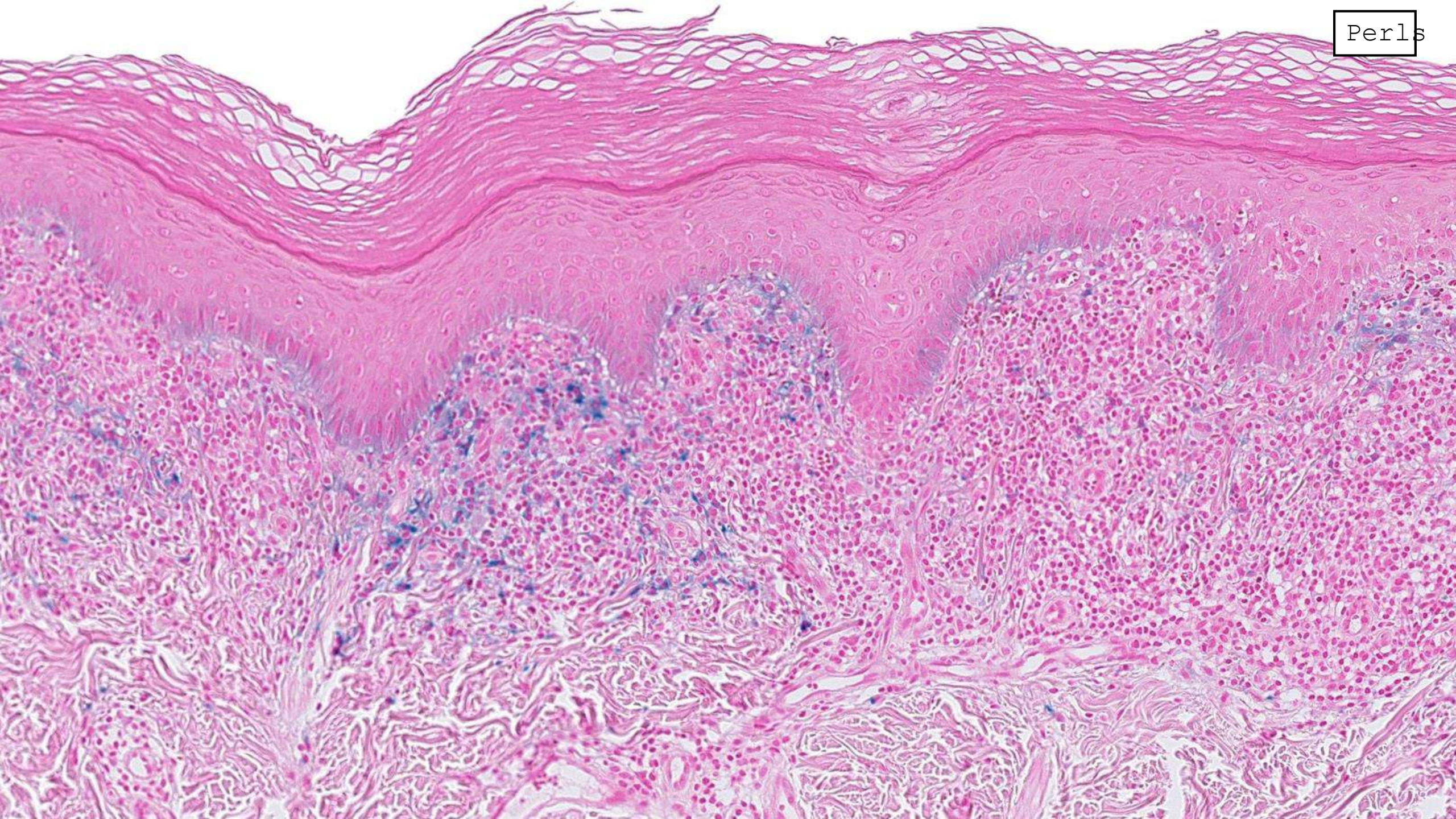








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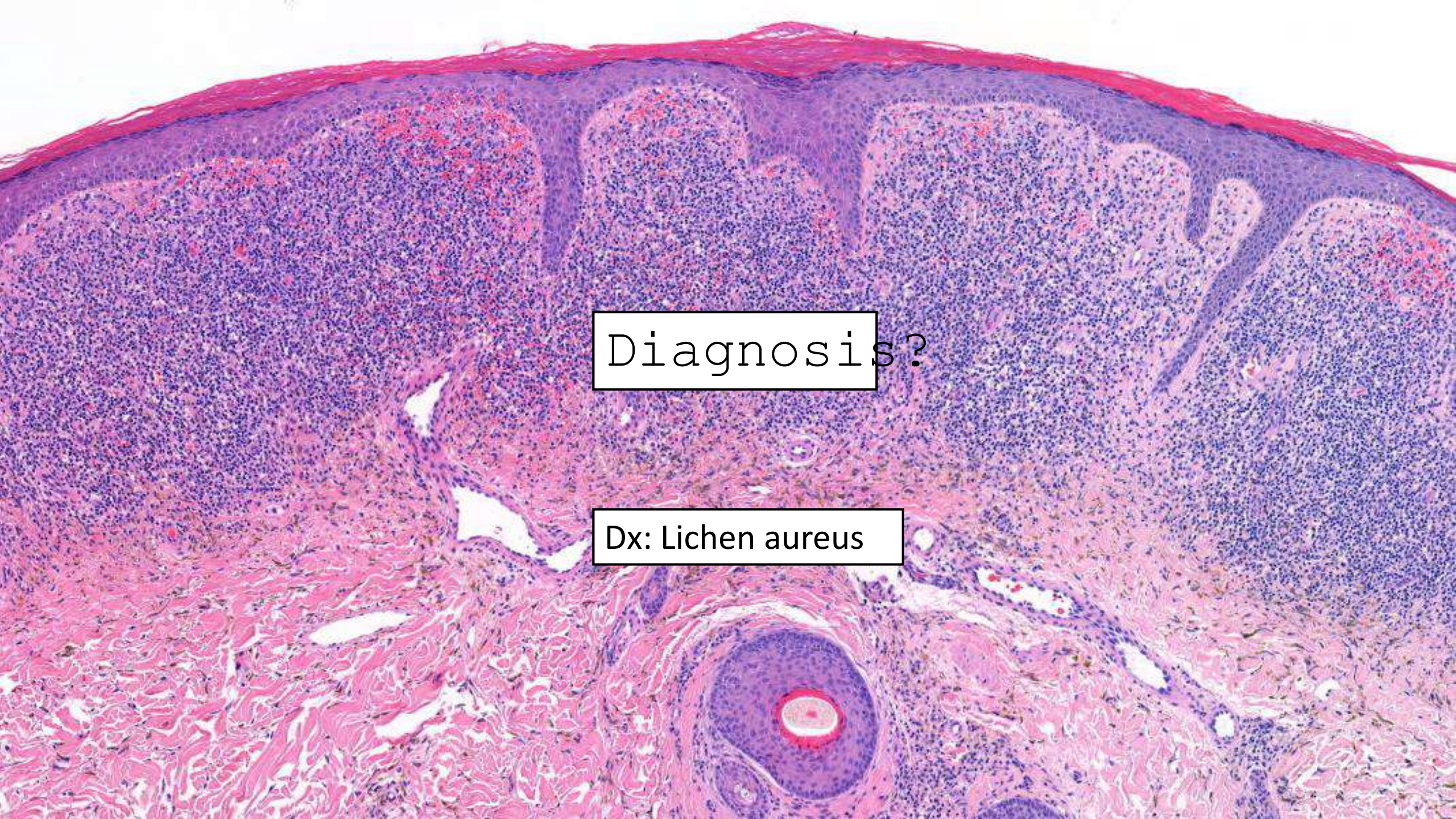
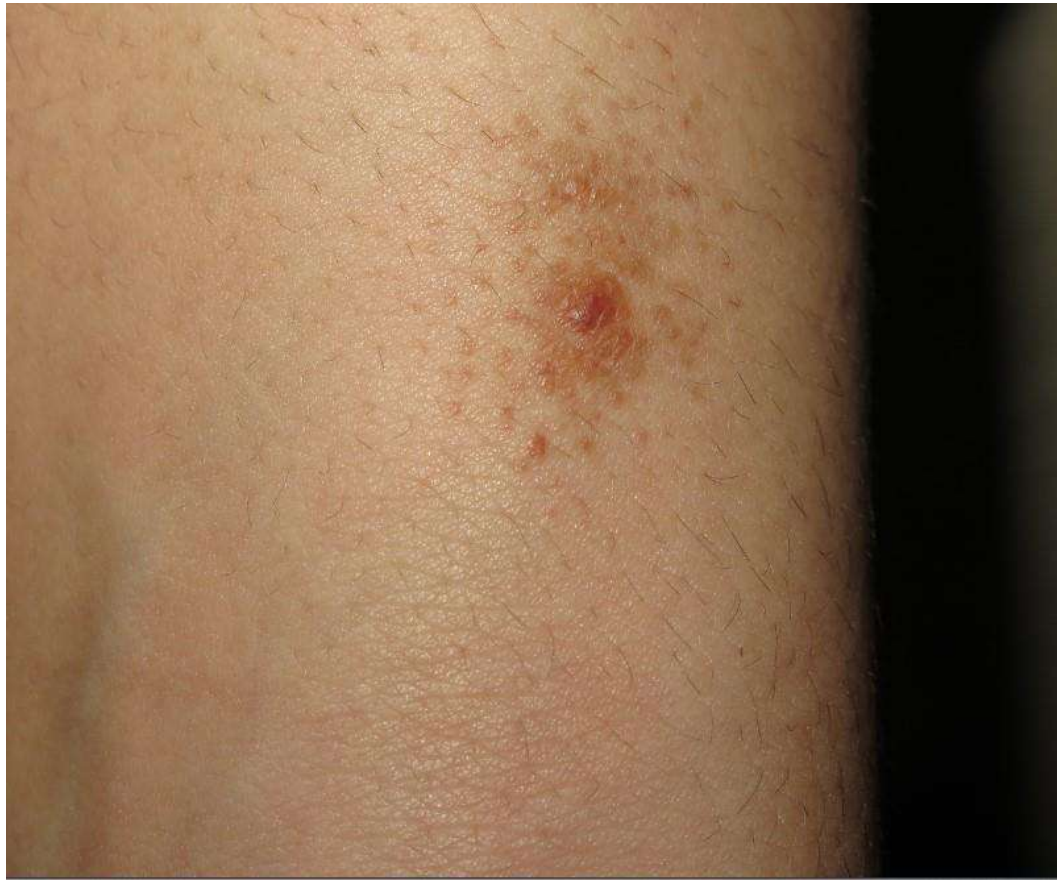

Diagnosis?
Dx: Lichen aureus

PPD (Pigmented purpuric dermatosis) is a rare, chronic skin condition with unknown causes, characterized by perivascular lymphocytic infiltrates, extravasated erythrocytes, and hemosiderin deposits

1. Schamberg disease
2. Purpura annularis telangiectodes of Majocchi
3. Pigmented purpuric lichenoid dermatitis of Gougerot and Blum
4. Eczematoid-like purpura of Doucas and Kapetanakis
5. Lichen aureus (LA)
6. Linear pigmented purpura
7. Granulomatous pigmented purpura



LA typically appearing :

- Solitary reddish-brown macular lesion
- Intense infiltrates and more papillary dermal fibrosis compared to other PPD types

Kolm I, Buset C, Flury U, Nosek D, Kazakov DV, Kempf W. Lichen aureus with pseudolymphomatous infiltrate. J Cutan Pathol. 2021 May;48(5):669-673.

- LA must be differentiated from MF and lymphomatoid drug eruption and Borreliosis

- A granulomatous pattern in PPD may be linked to dyslipidemia and autoimmune diseases

- In some reported cases, the histopathological findings were unusual, with dense infiltrates extending to deeper dermal and subcutaneous layers, raising concerns about cutaneous lymphoma

- However, the absence of nuclear atypia and other features ruled out MF

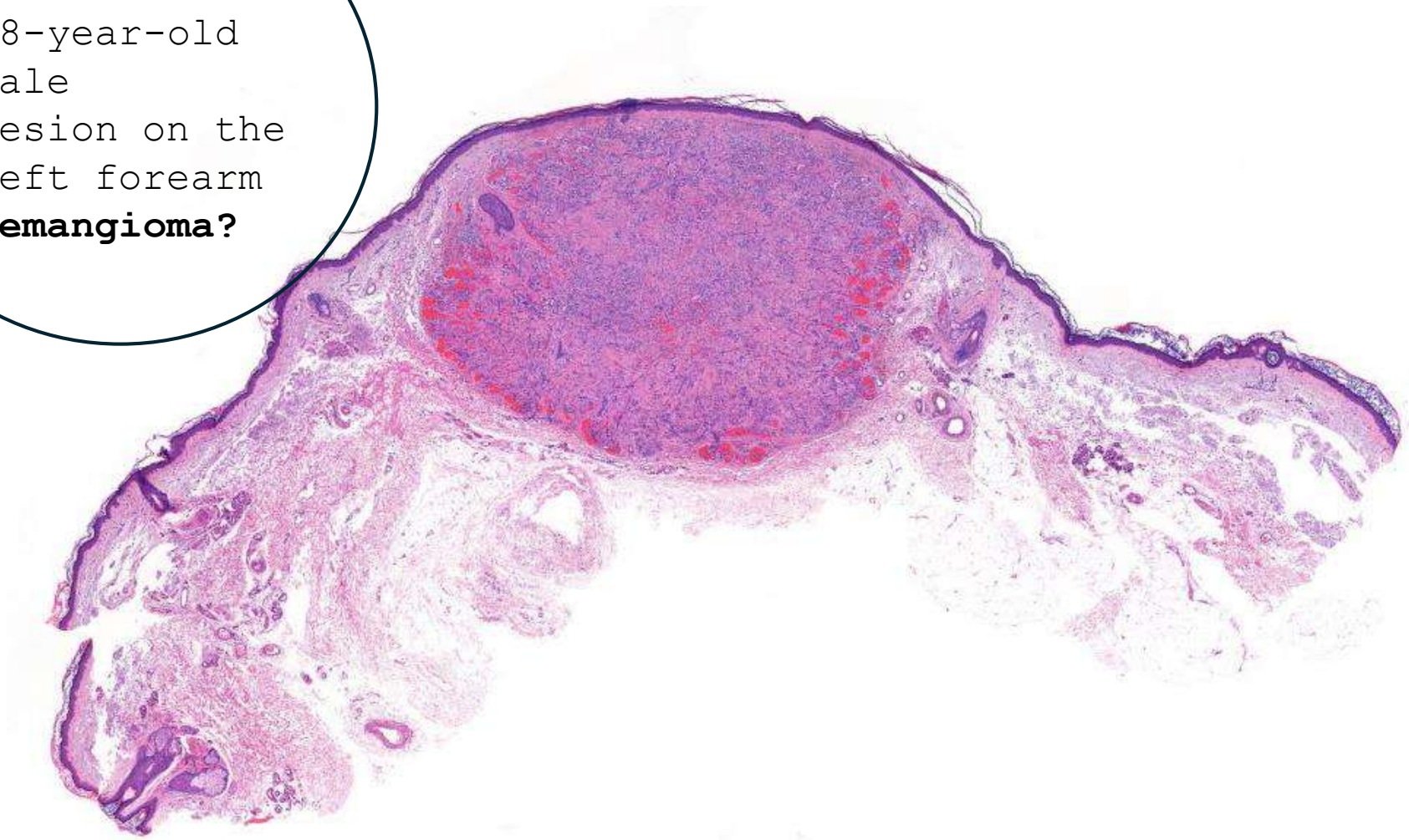
- Monoclonal T-cell rearrangements, seen in up to 50% of PPD cases, complicate the distinction between PPD and MF

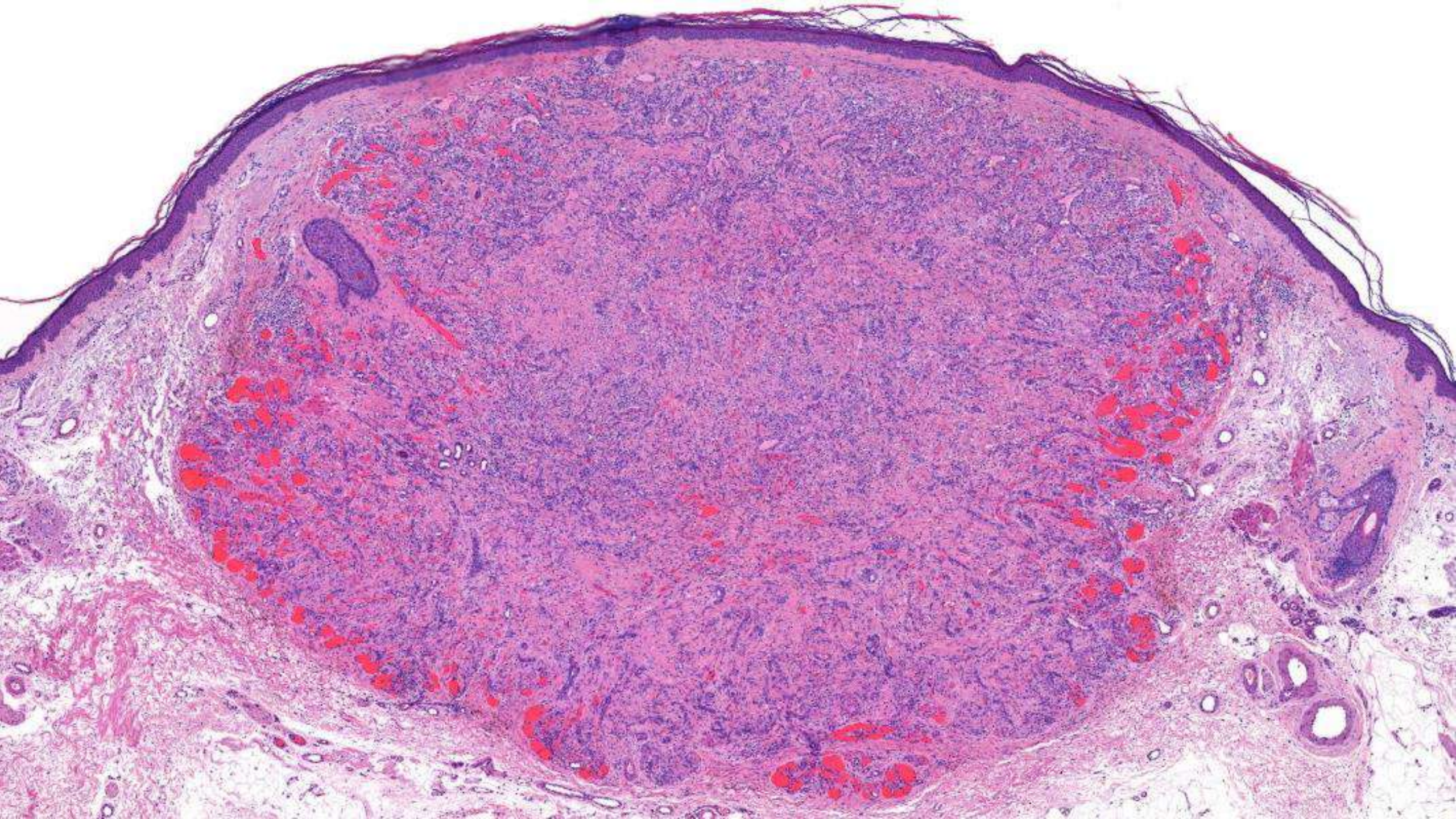
- Although LA and MF share some features, long-term follow-up and serial biopsies are recommended for persistent cases

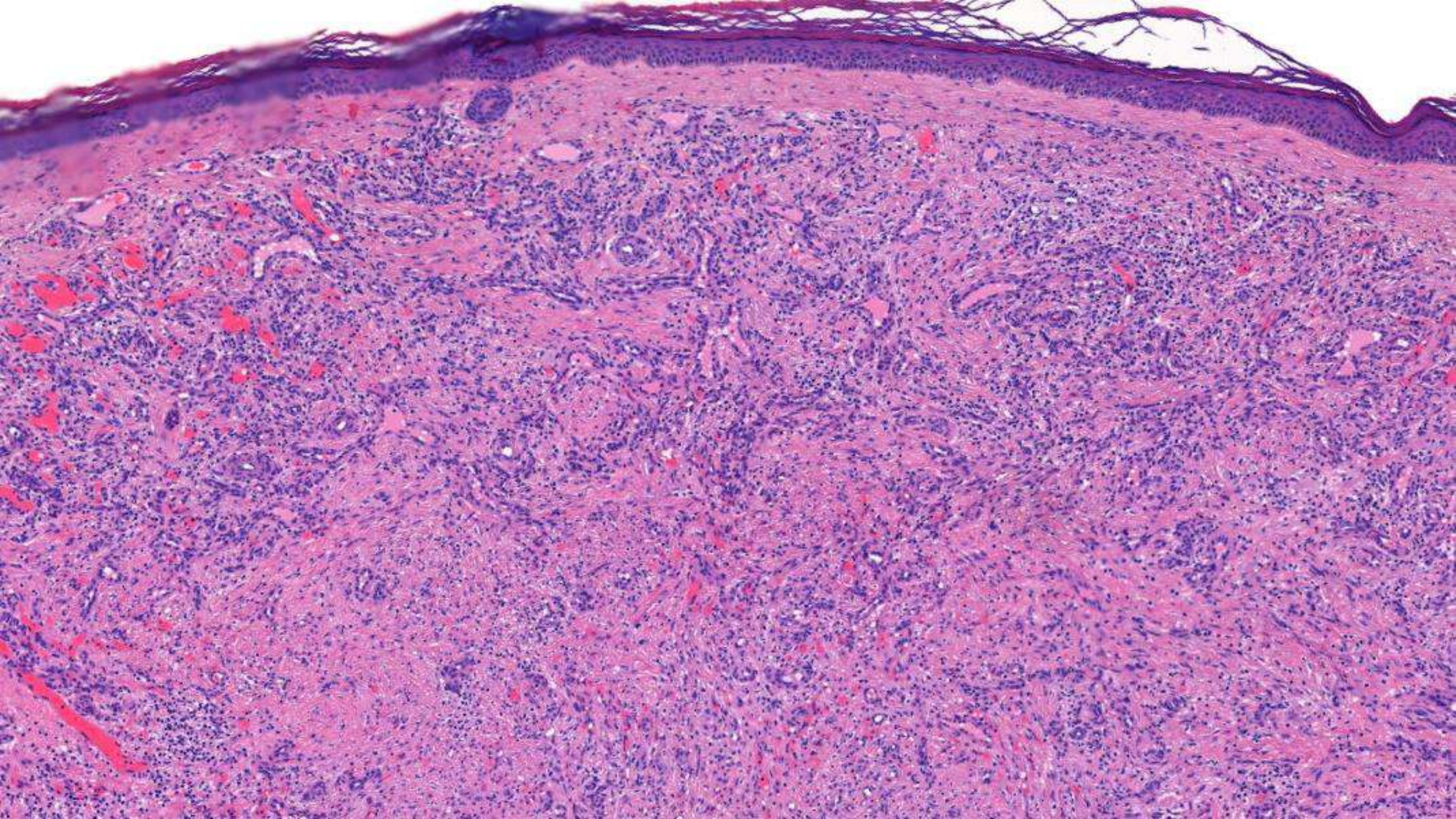
Kolm I, Buset C, Flury U, Nosek D, Kazakov DV, Kempf W. Lichen aureus with pseudolymphomatous infiltrate. J Cutan Pathol. 2021 May;48(5):669-673.

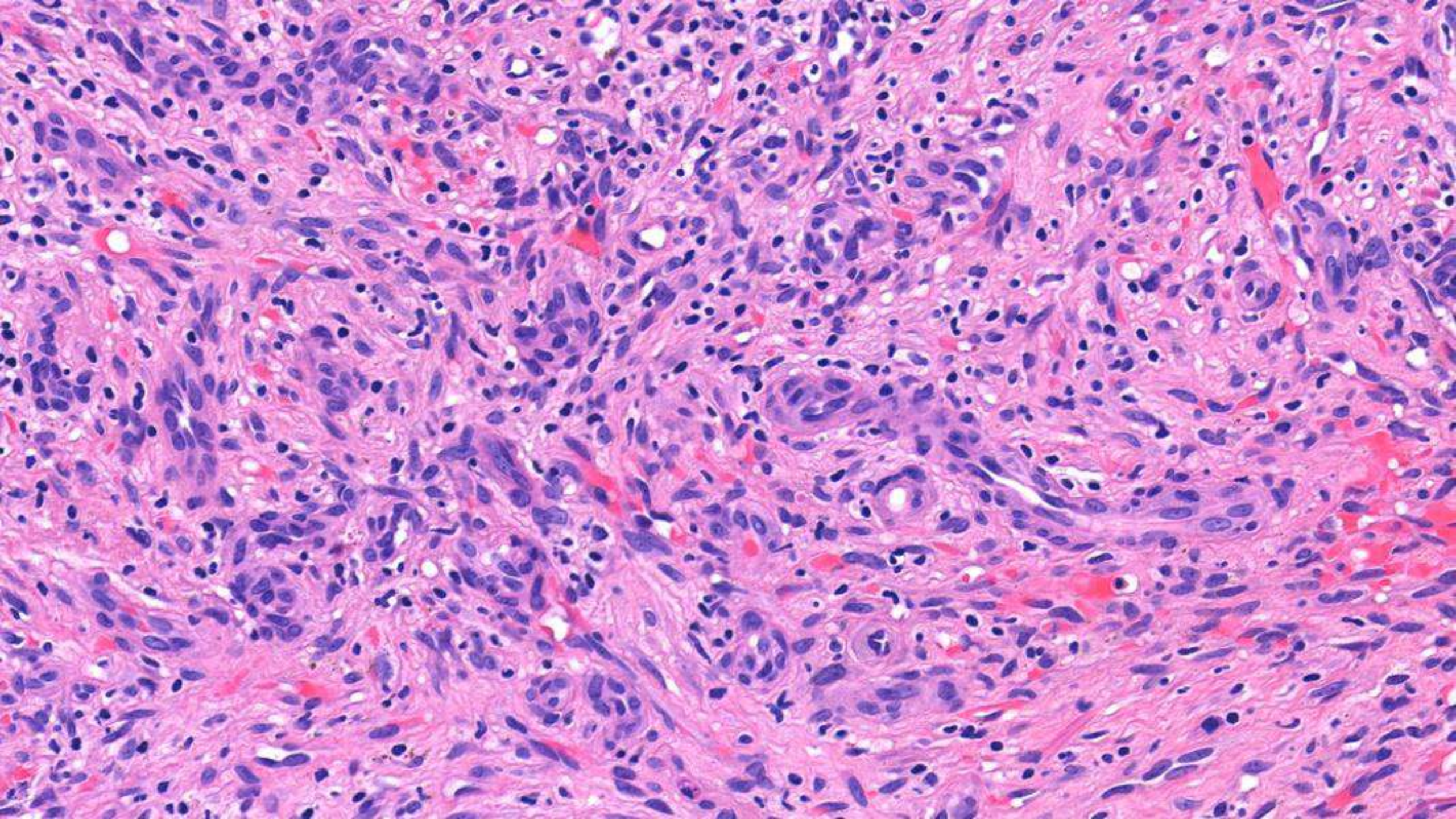
Case 4.

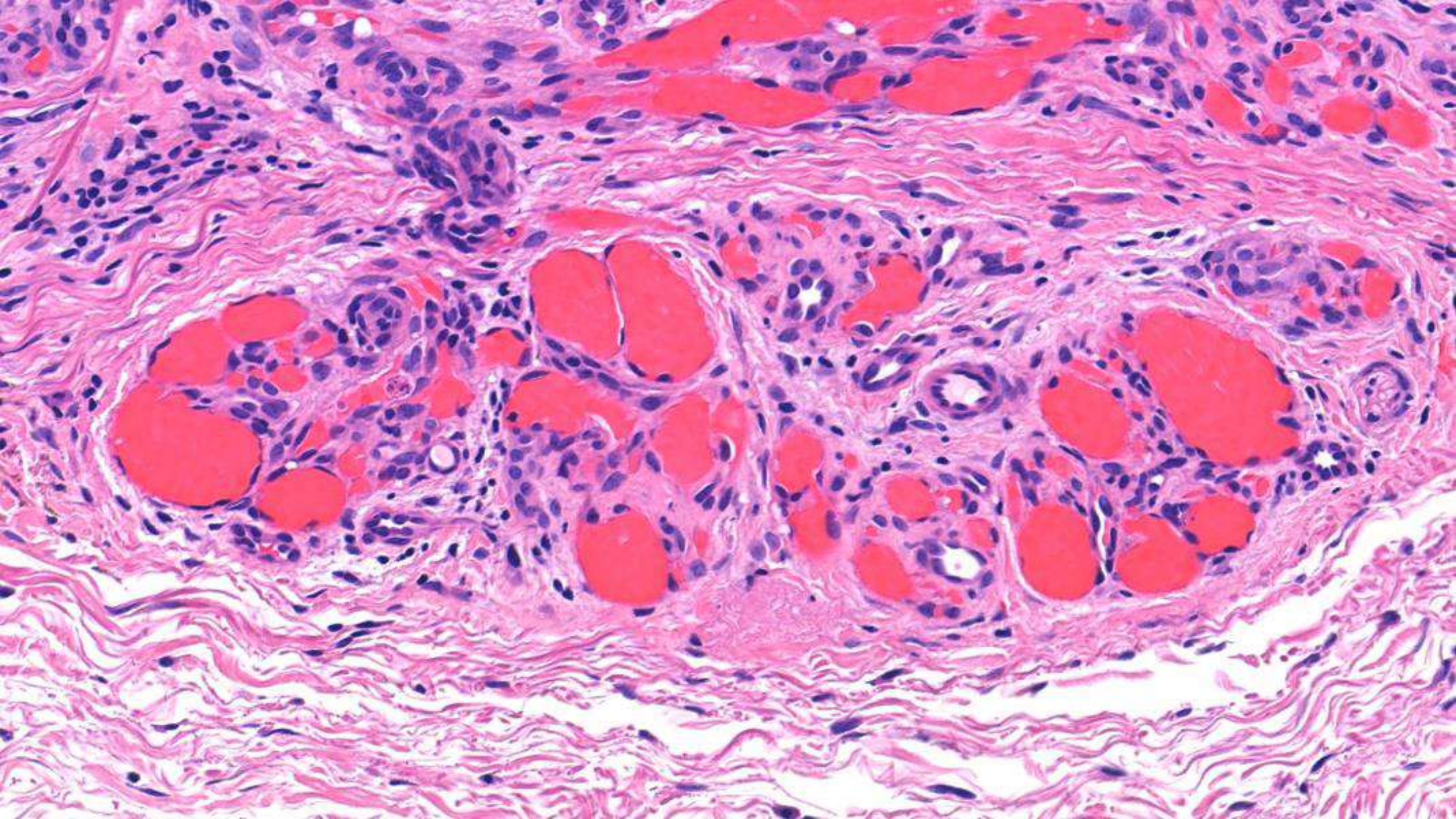
88-year-old male
Lesion on the left forearm
Hemangioma?

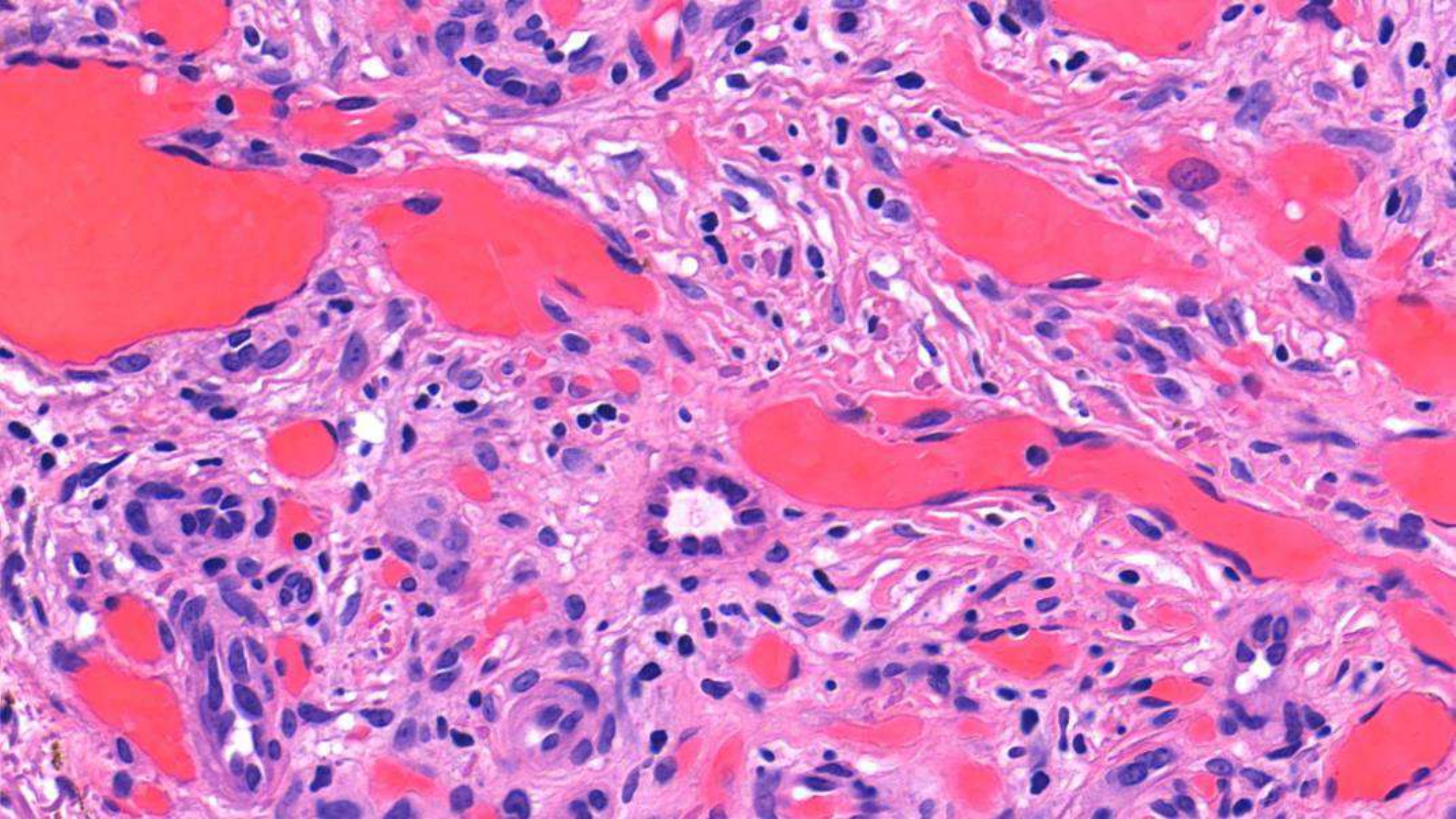


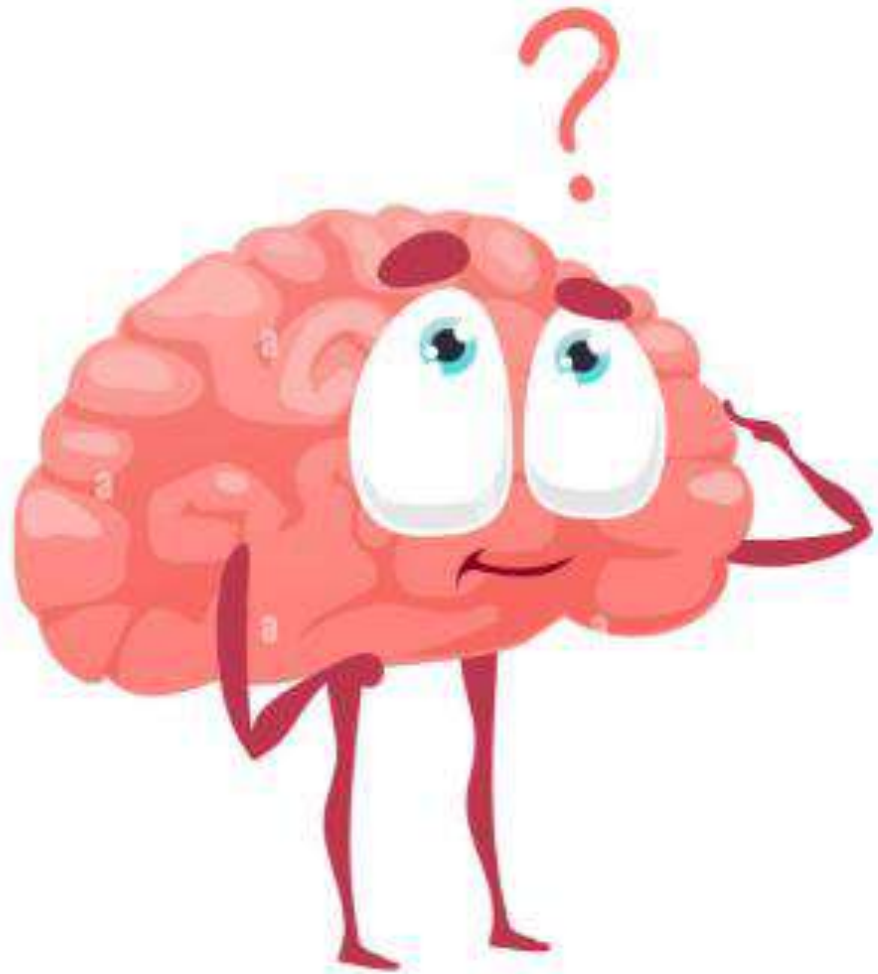


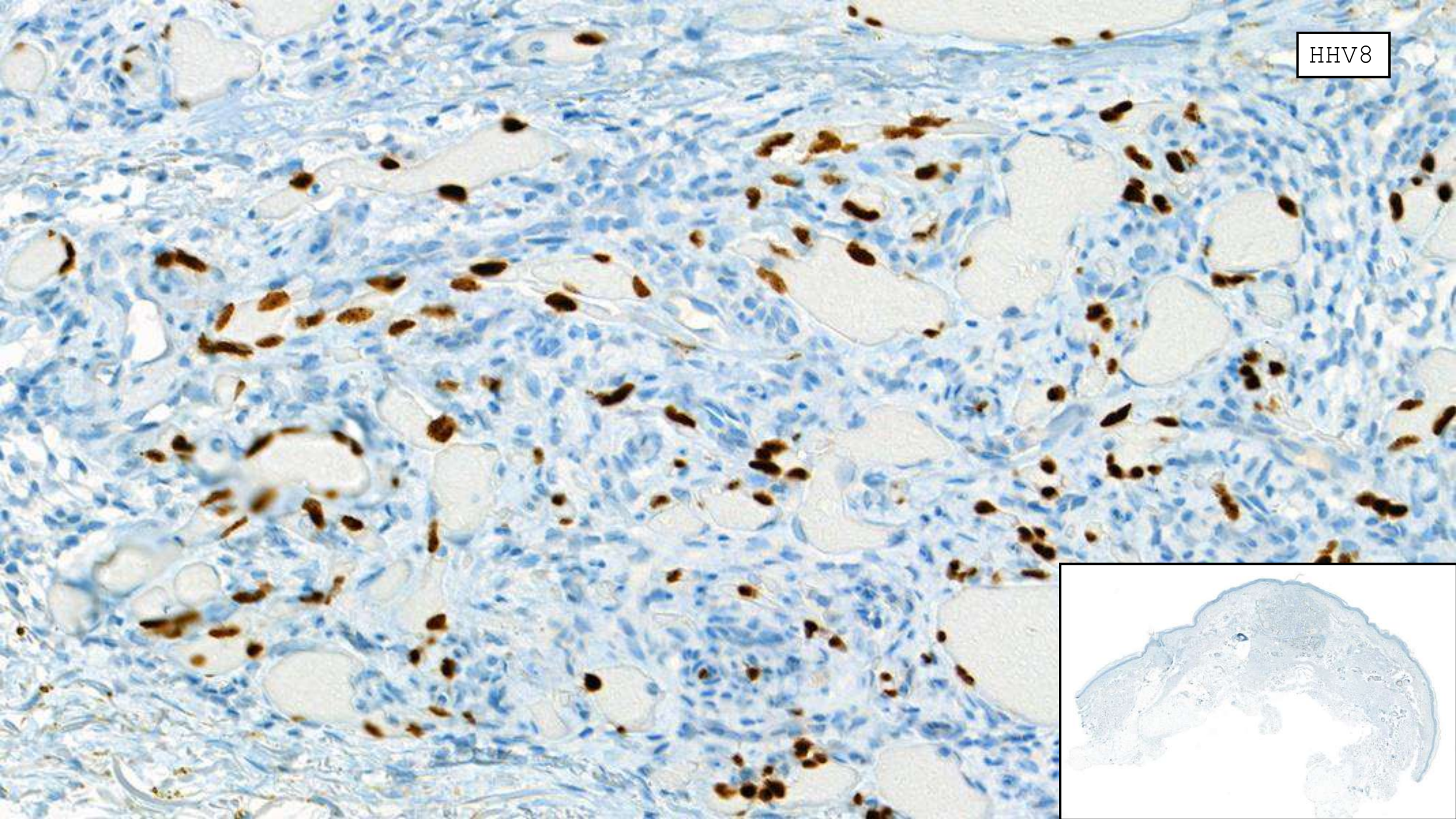








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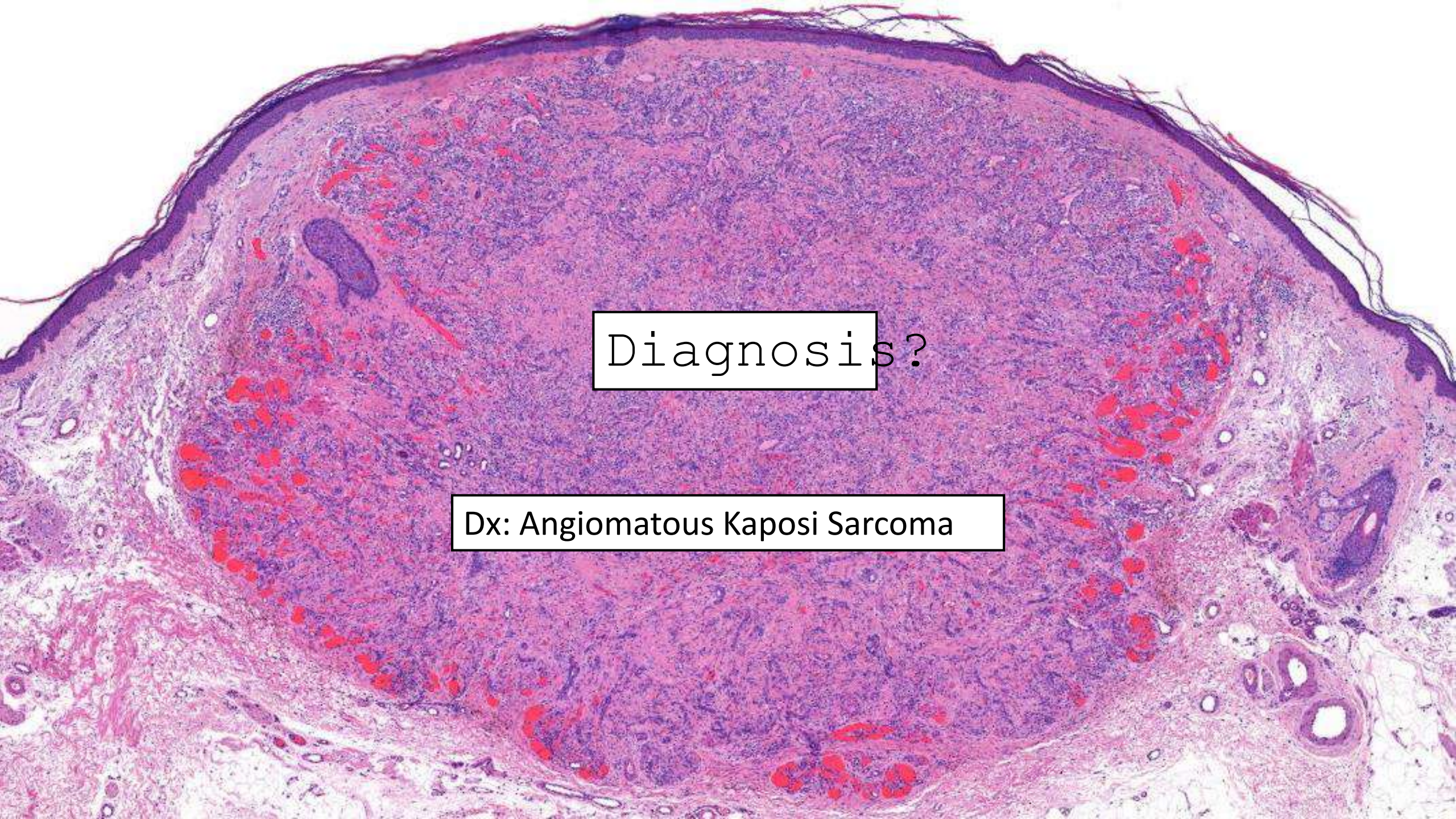
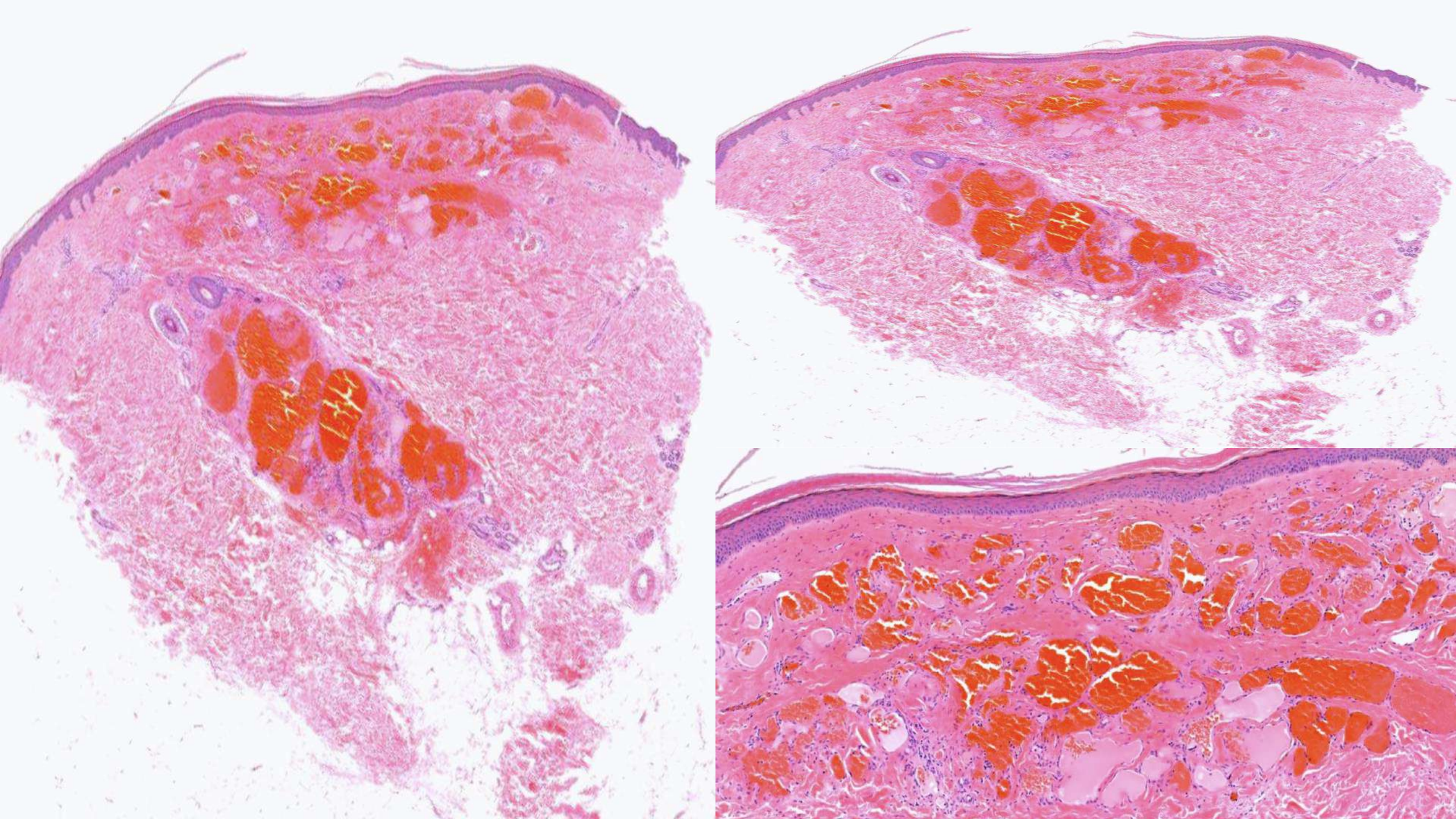
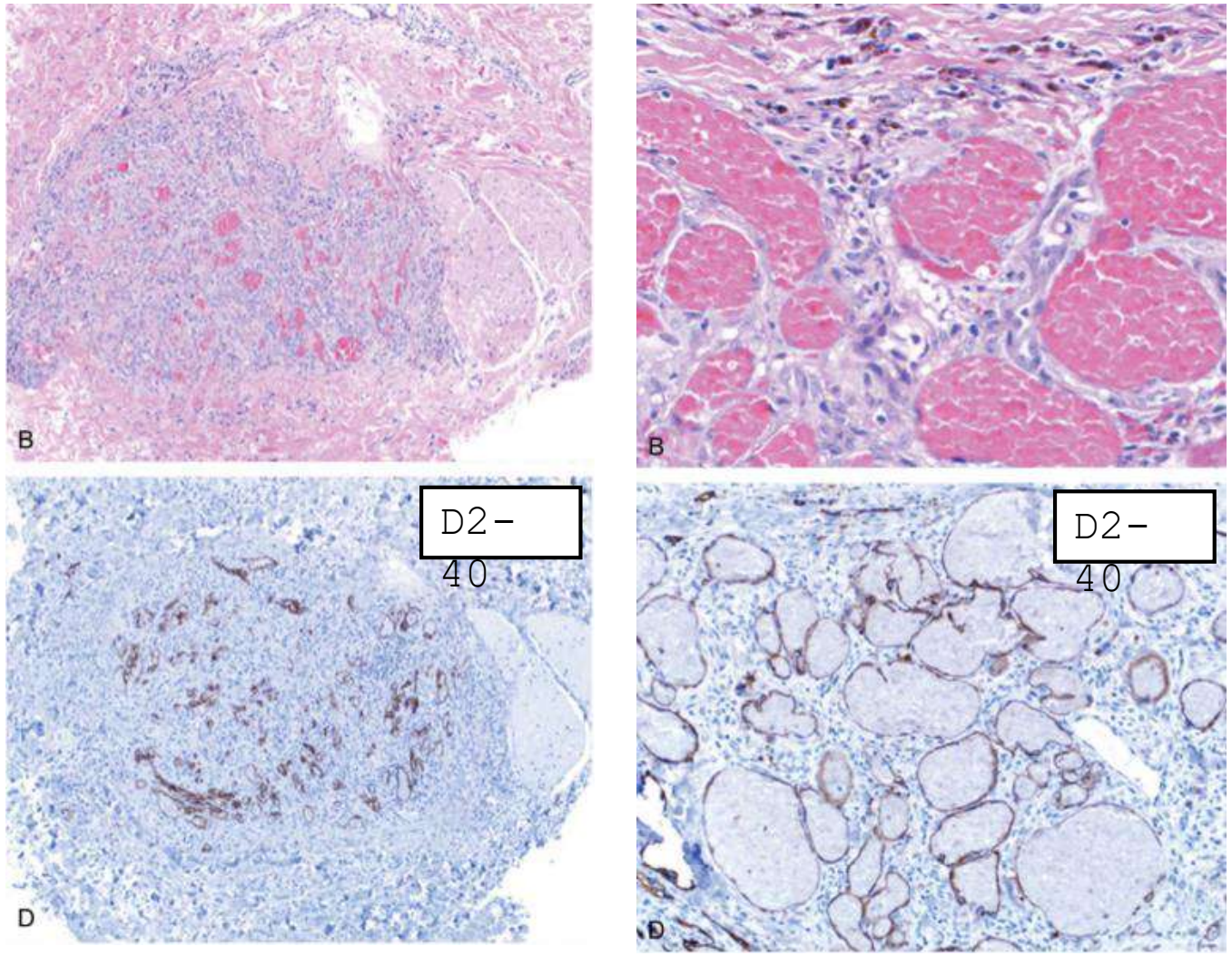

Diagnosis?
Dx: Angiomatous Kaposi Sarcoma



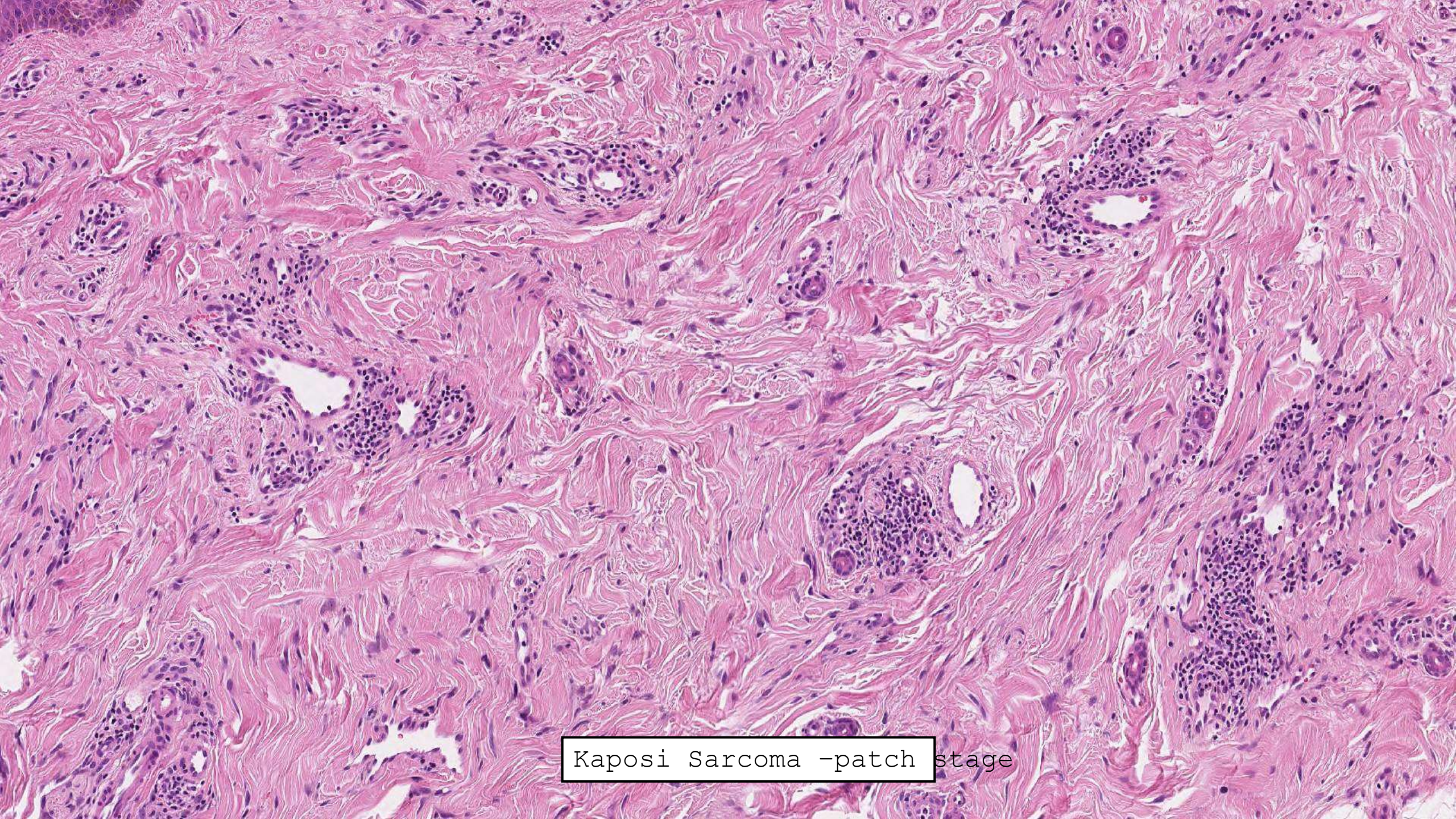


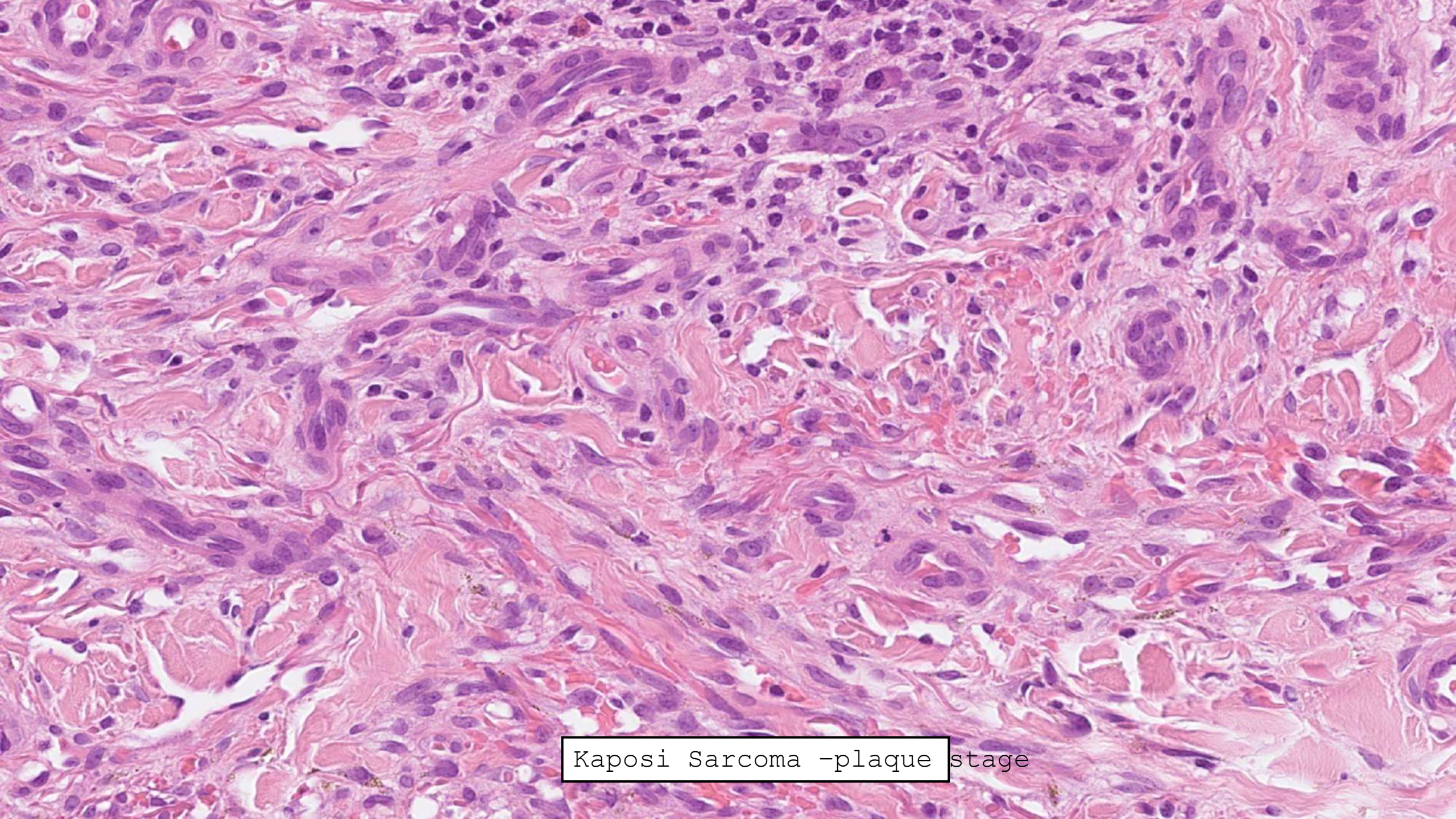
- First identified by Gottlieb and Ackerman in 1988
- Immunohistochemical analysis revealed prominent podoplanin (D2-40) staining in the neoplastic vasculature of angiomatous KS, suggesting lymphatic differentiation, although the vessels contained erythrocytes
- Angiomatous KS can resemble benign vascular proliferations like hemangiomas due to its thin, dilated vessels

- Hemangiomas have larger vessels with occluded lumens

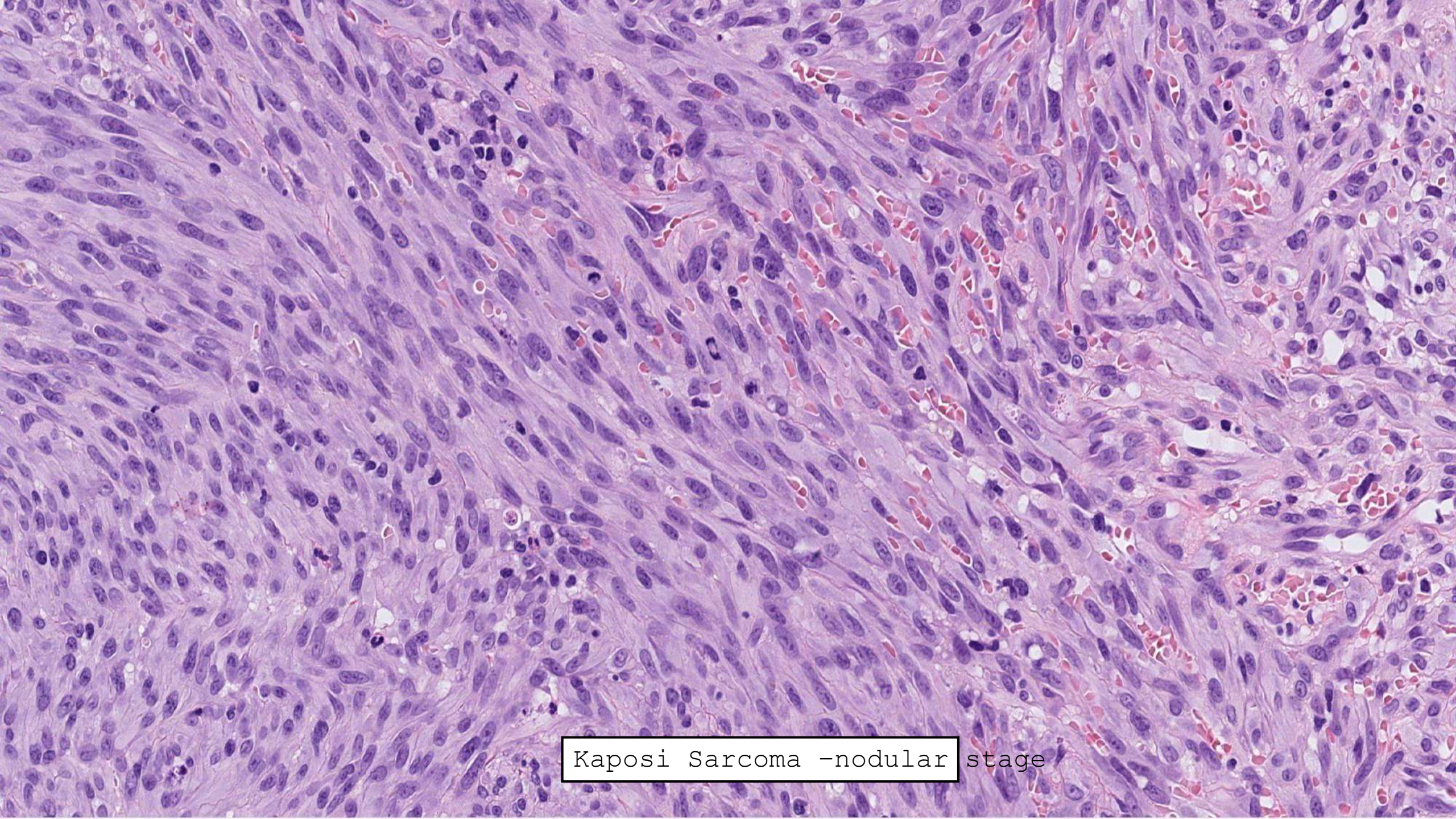
- It is harder to distinguish angiomatous KS from sinusoidal hemangiomas, but KS can be identified by its "sinusoidal" vessel appearance and spindle cells

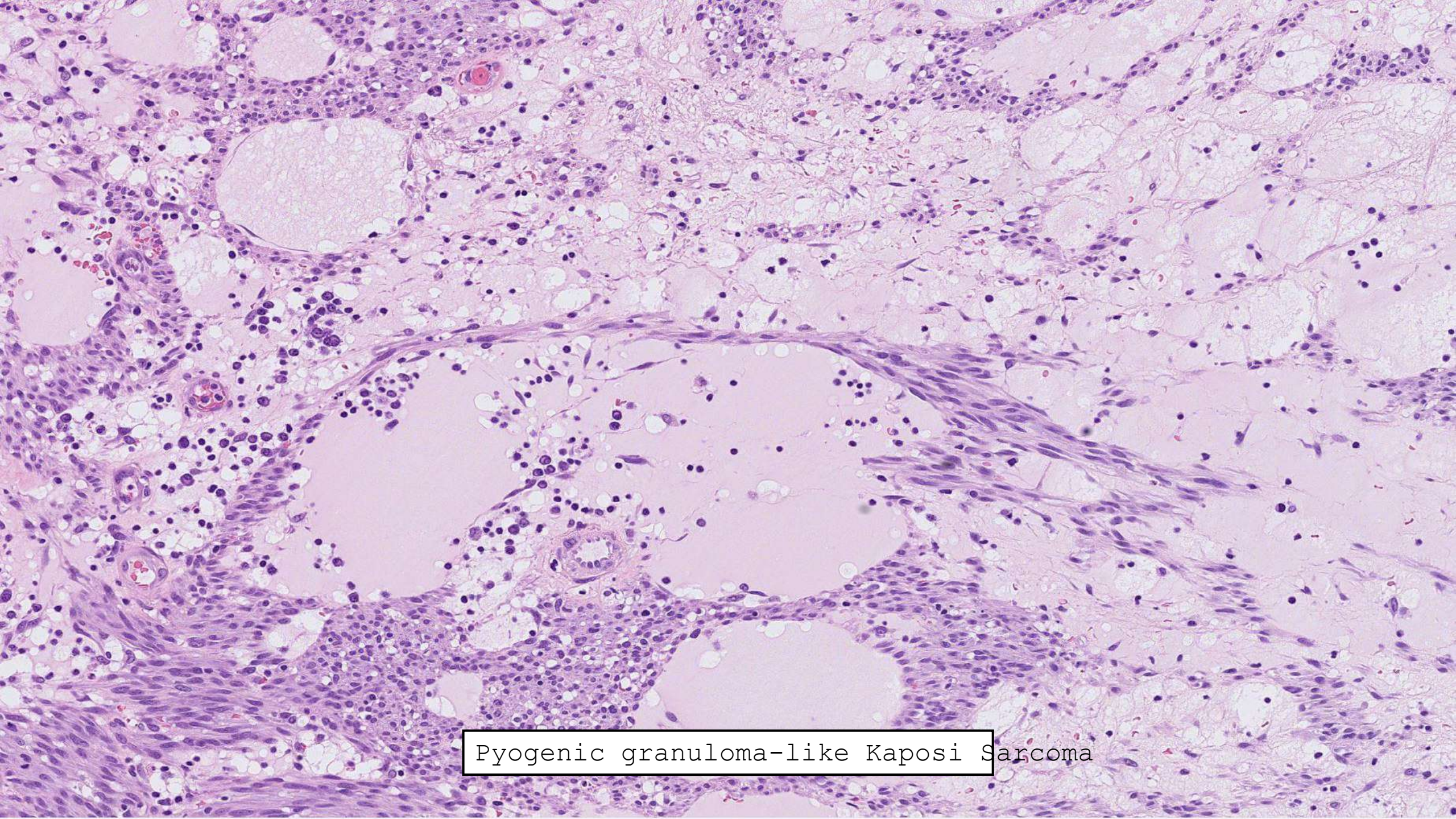
Yang SH, LeBoit PE. Angiomatous kaposi sarcoma: a variant that mimics hemangiomas. Am J Dermatopathol. 2014 Mar;36(3):229-37.

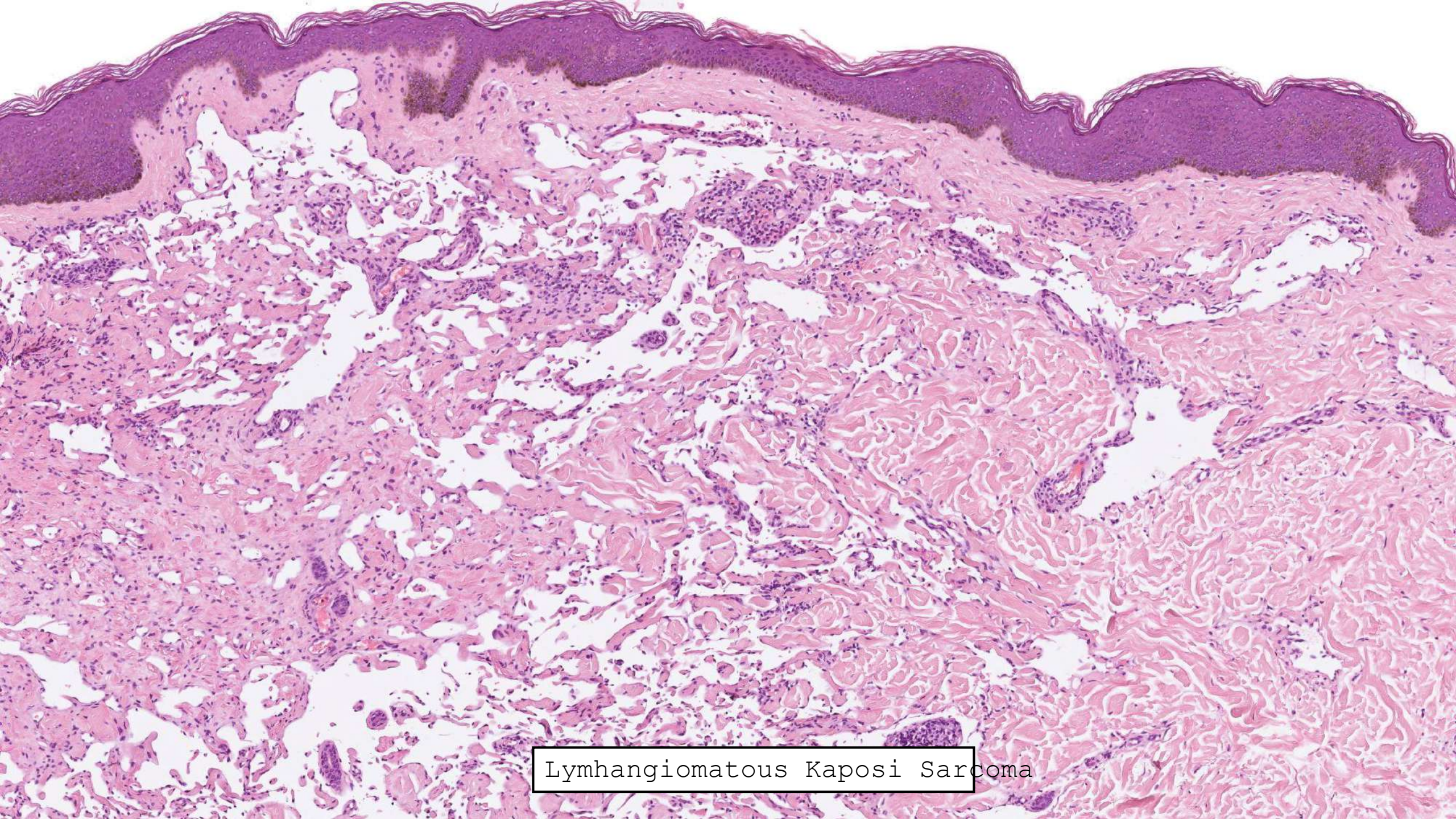

Kaposi Sarcoma –patch stage

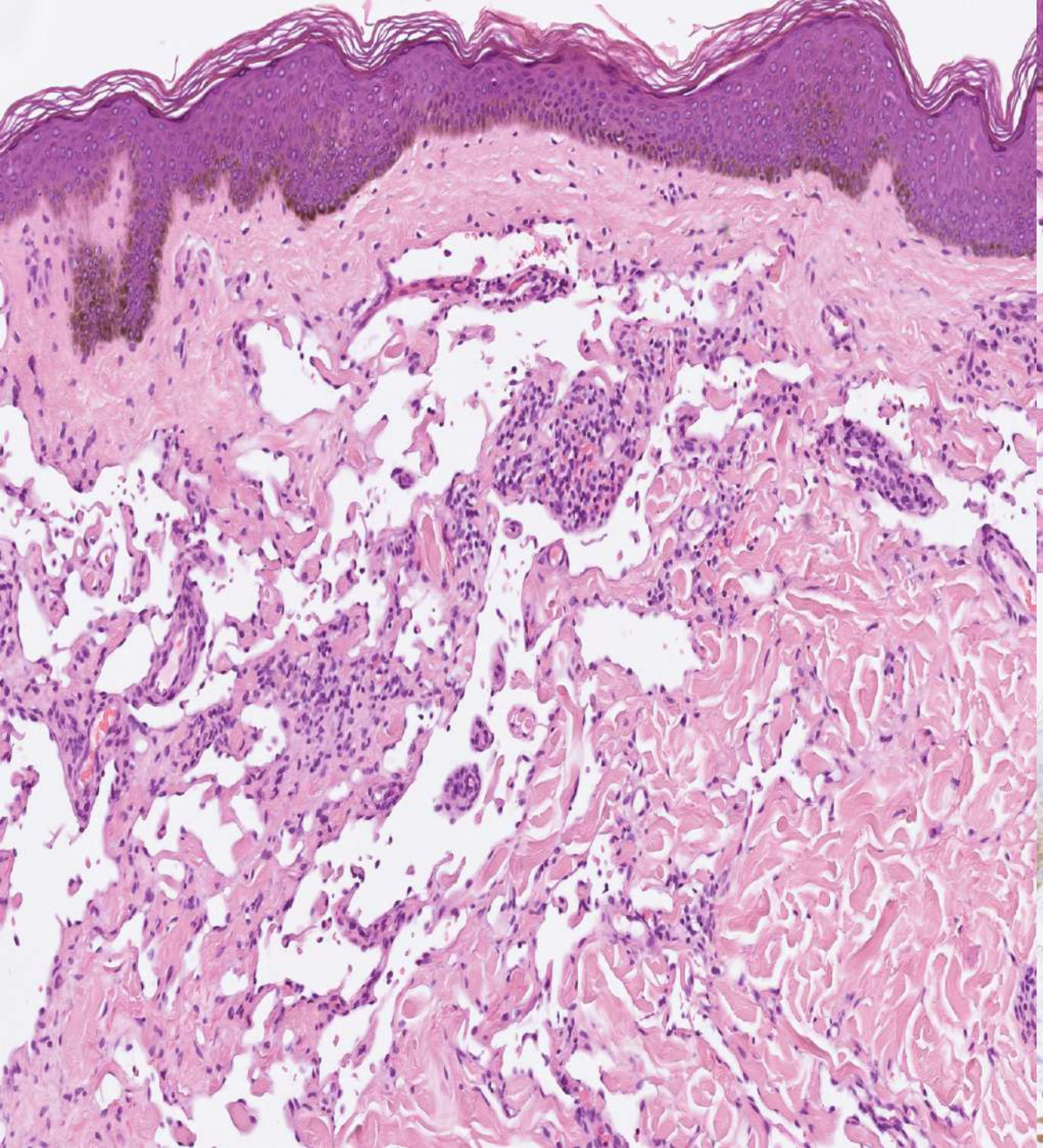


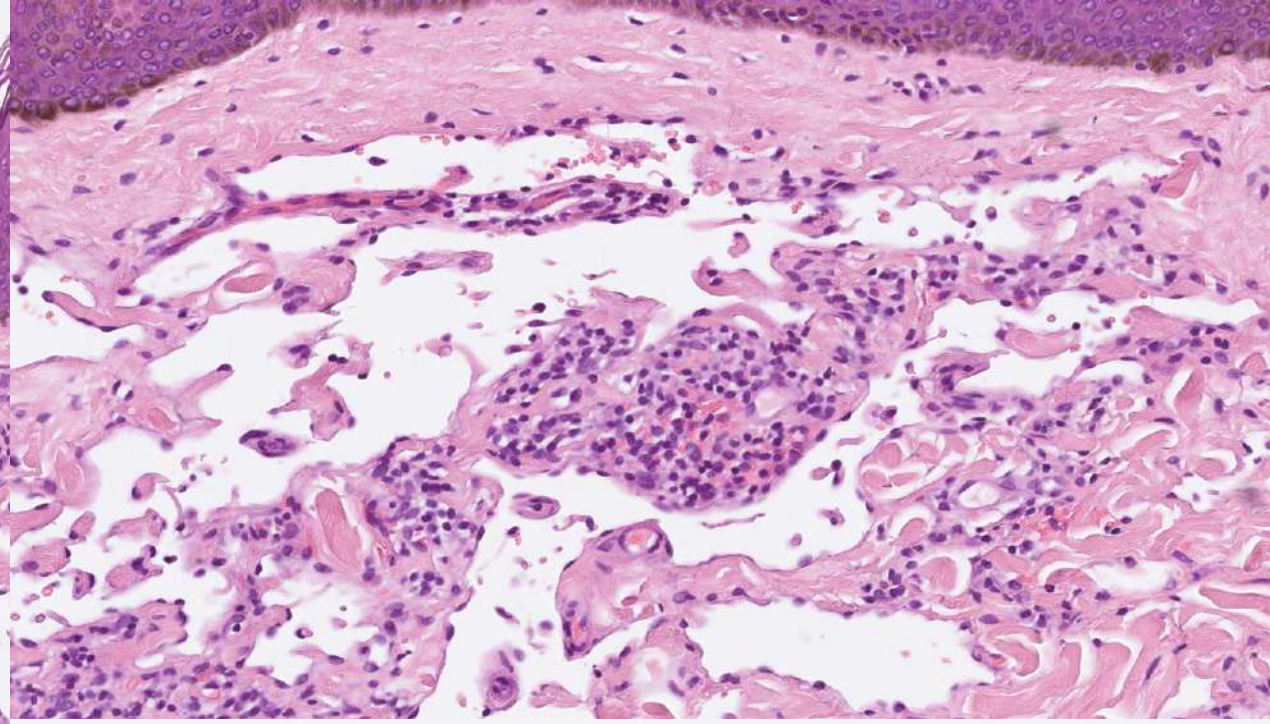
Kaposi Sarcoma –plaque stage

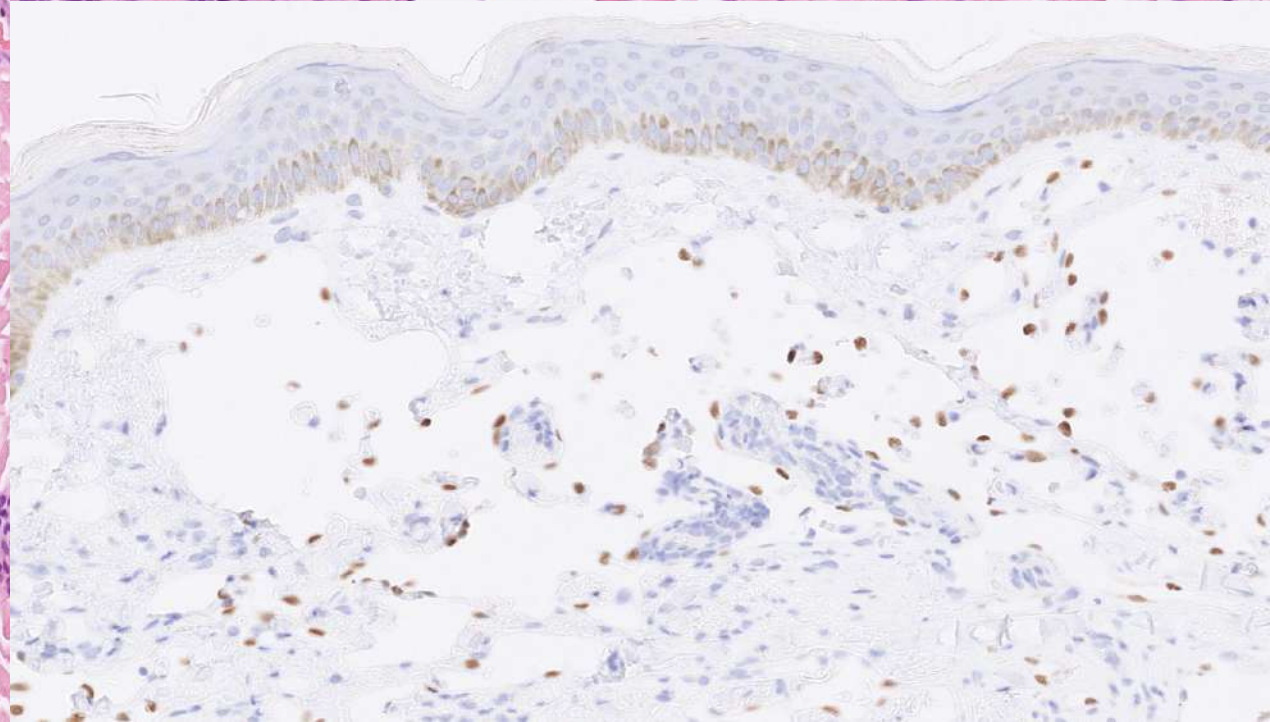

Kaposi Sarcoma –nodular stage

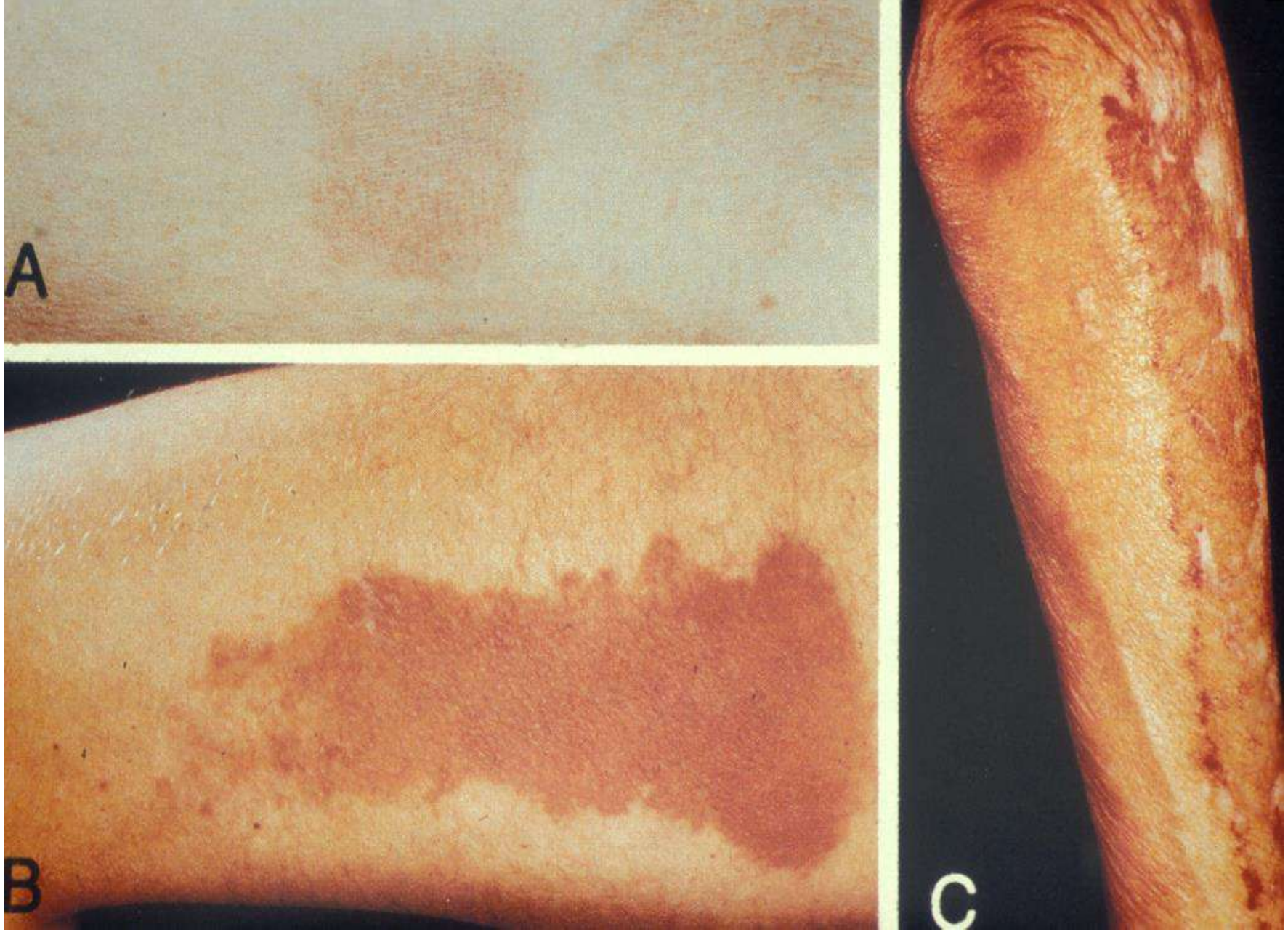

Pyogenic granuloma-like Kaposi Sarcoma


Lymhangiomatous Kaposi Sarcoma

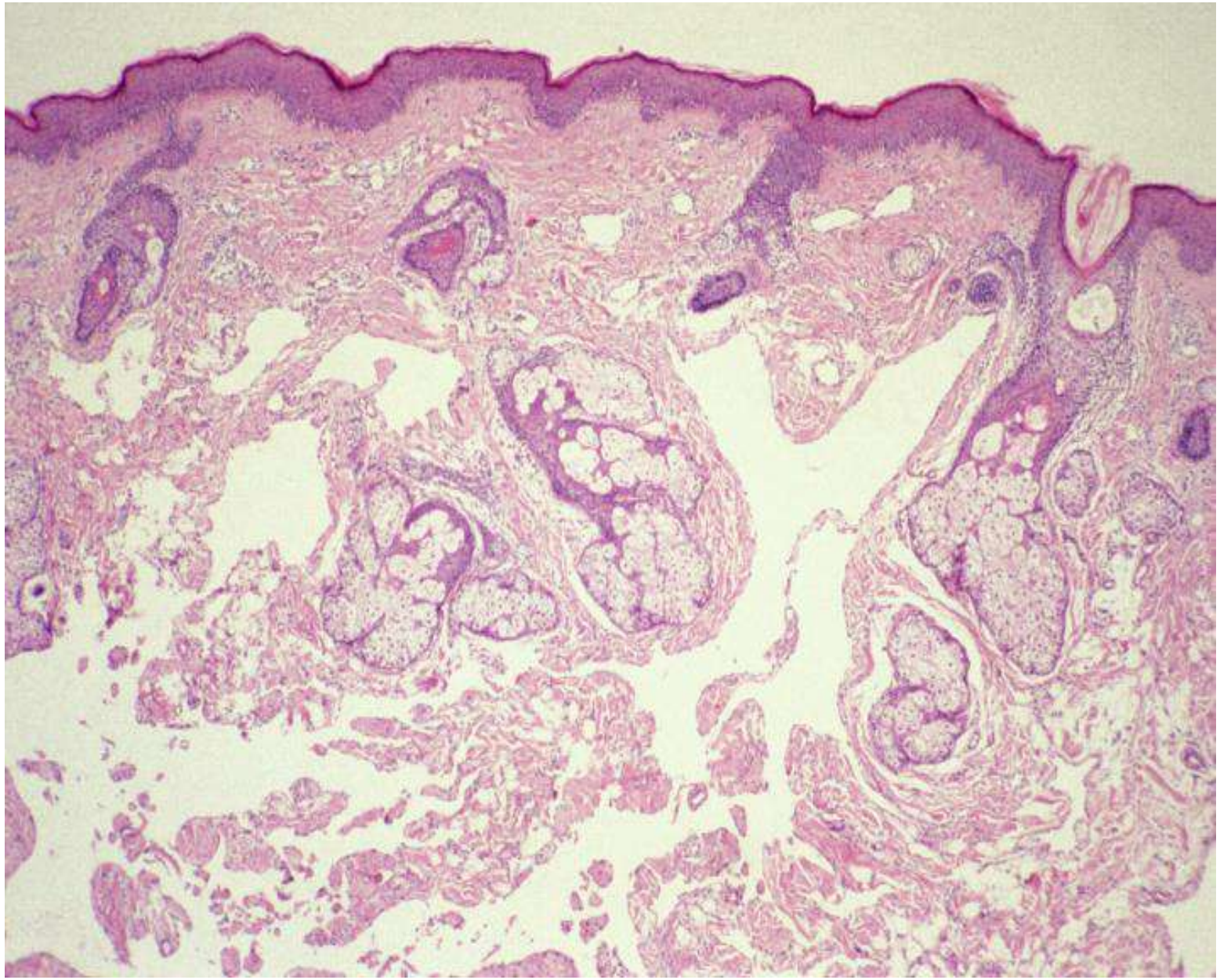








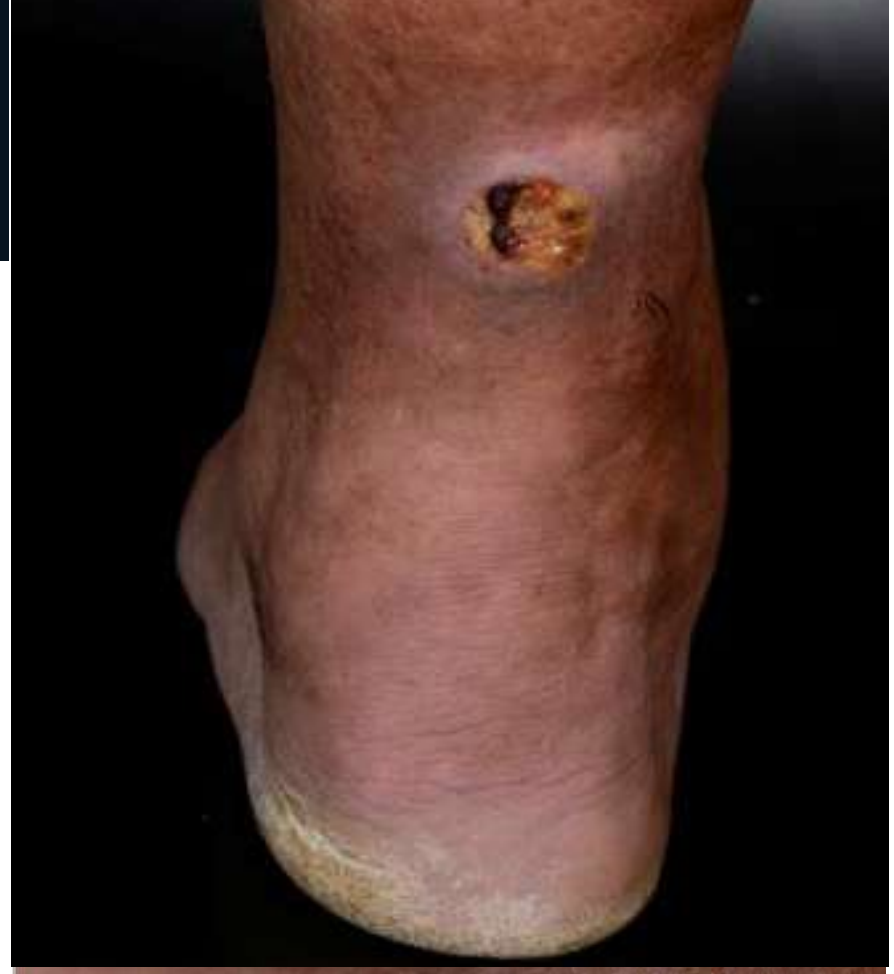
BENIGN LYMPHANGIOENDOTHELIOMA (ACQUIRED PROGRESSIVE LYMPHANGIOMA)

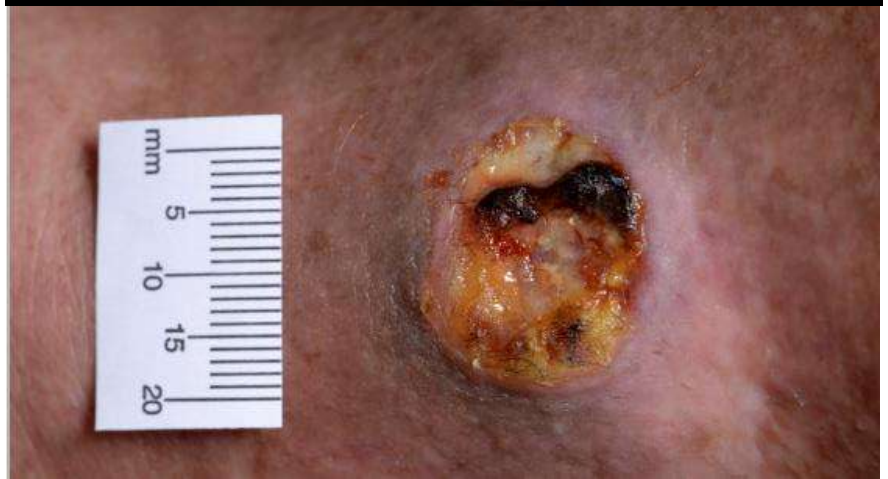


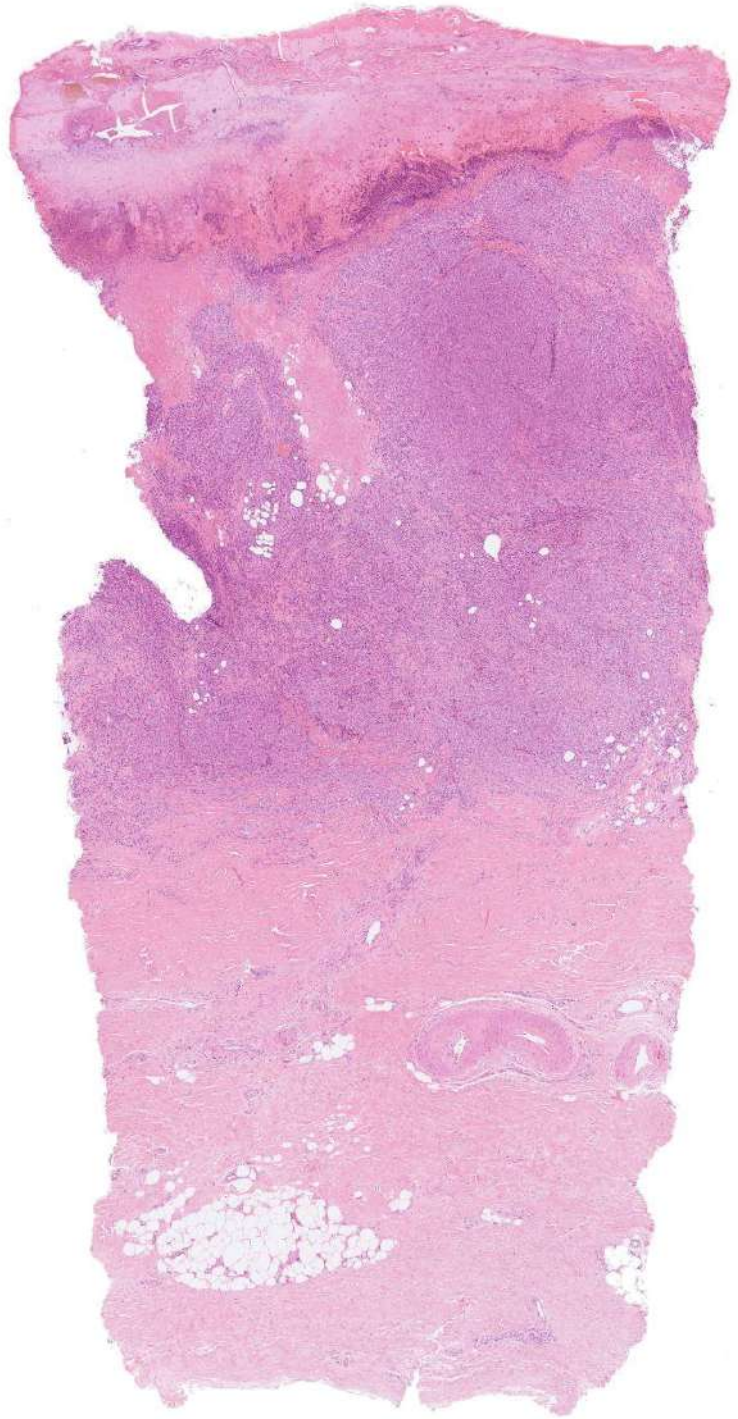
Benign lymphangioendothelioma

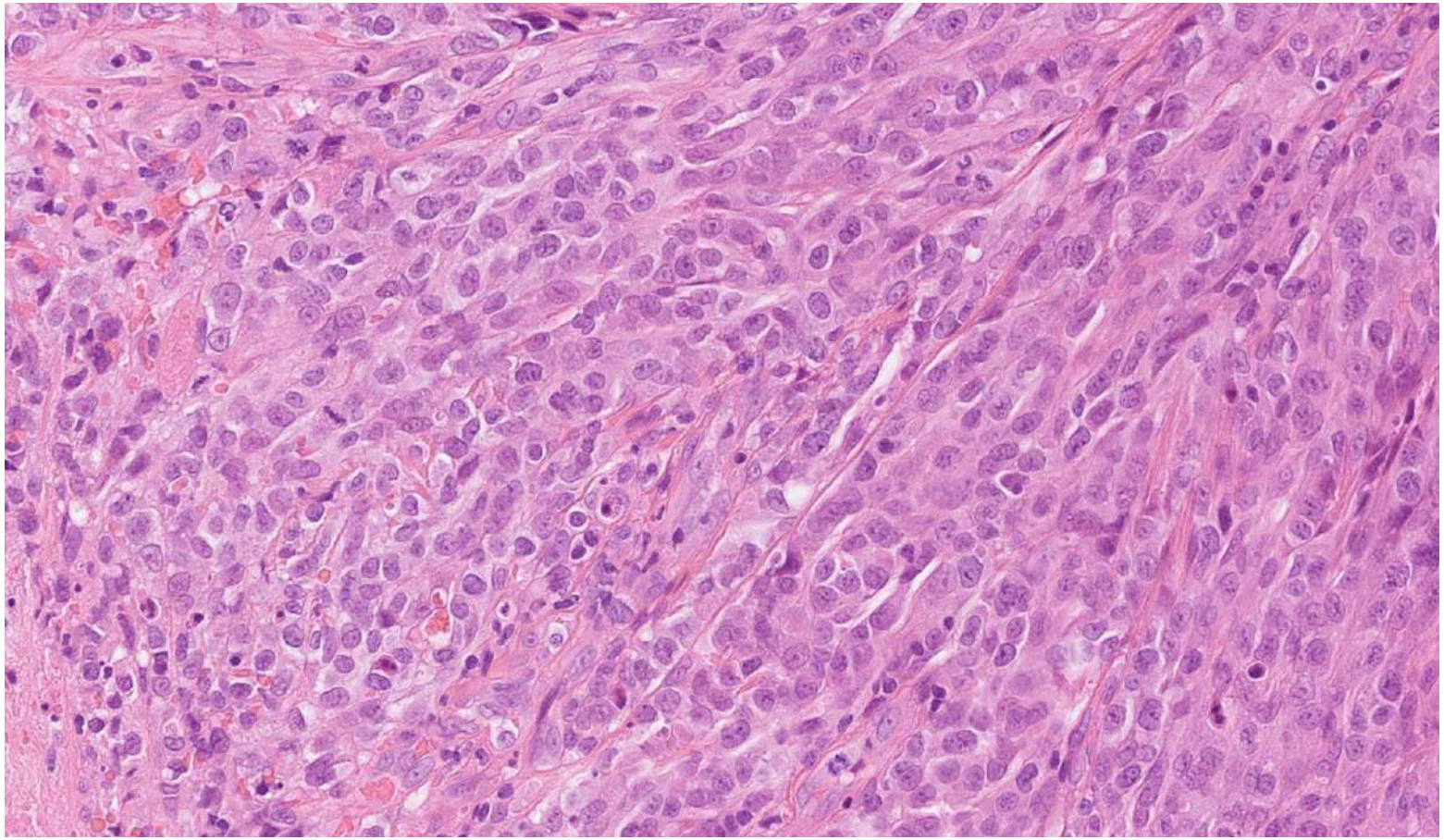
Anaplastic KS

- High Aggressive
- Deep invasion
- Metastasis

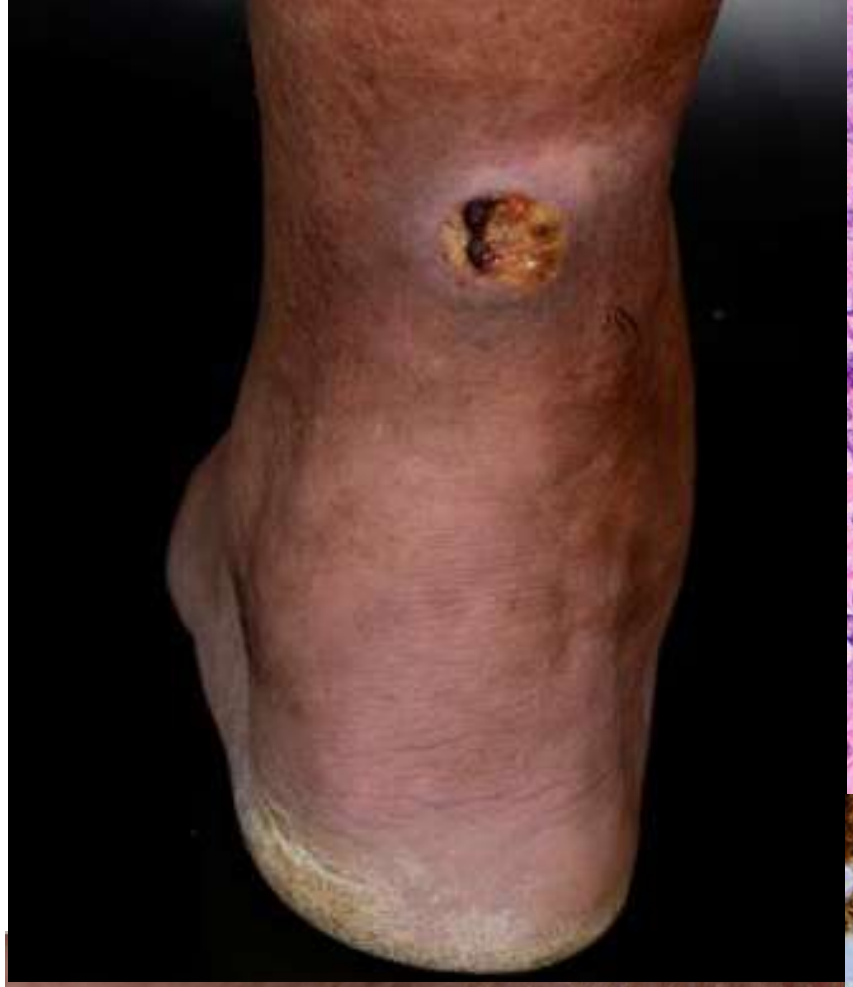


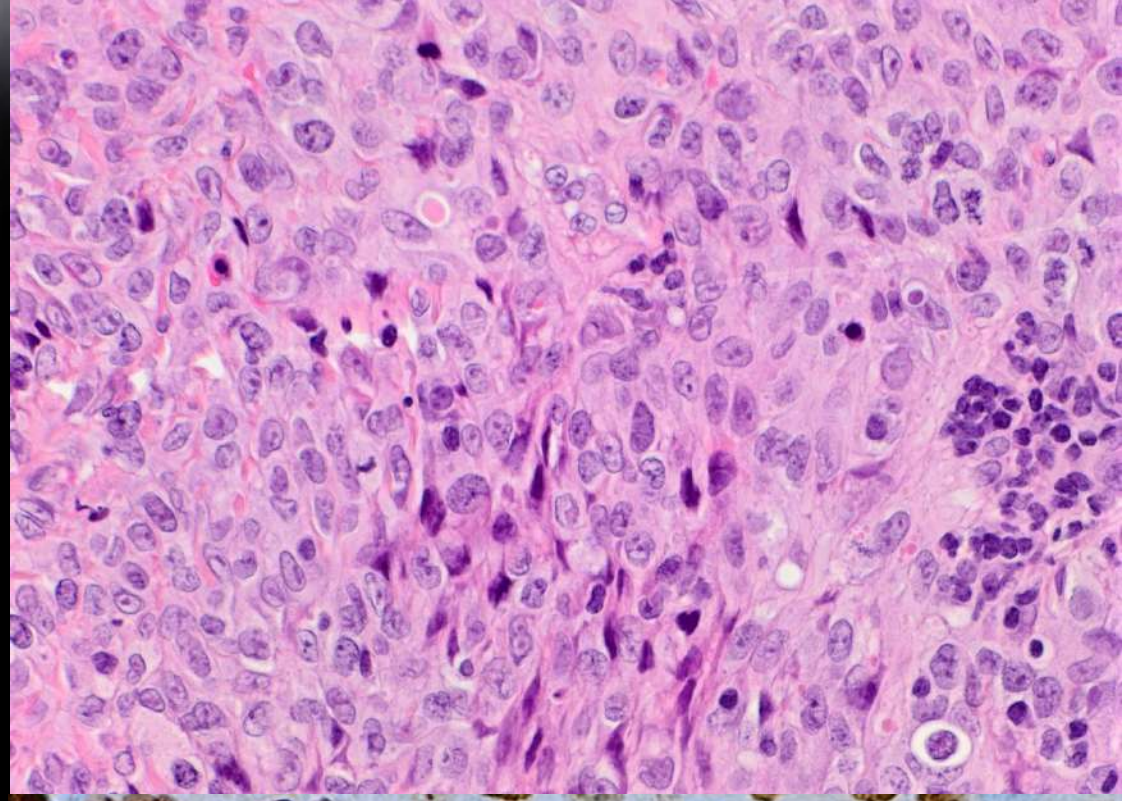


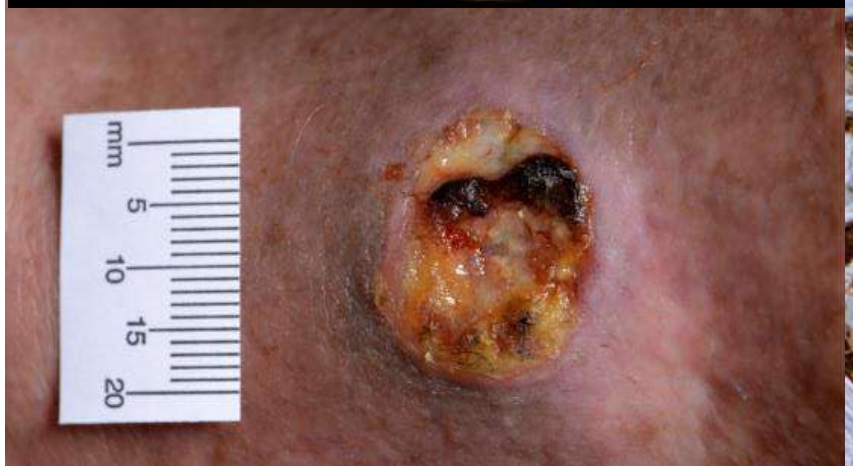




Anaplastic Kaposi Sarcoma



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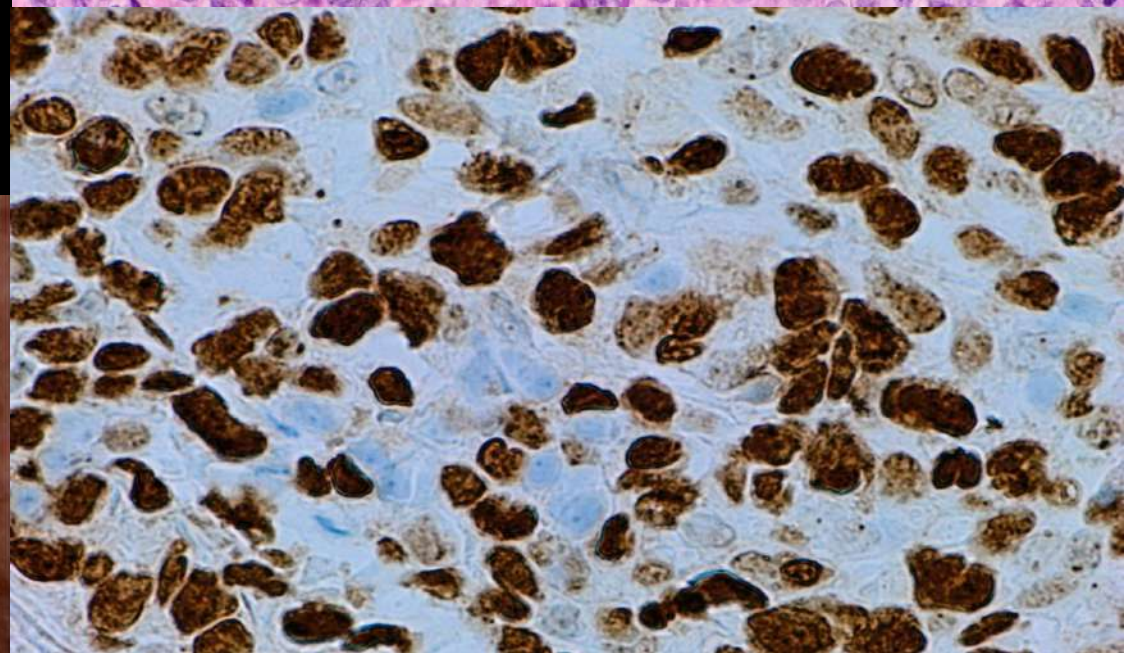
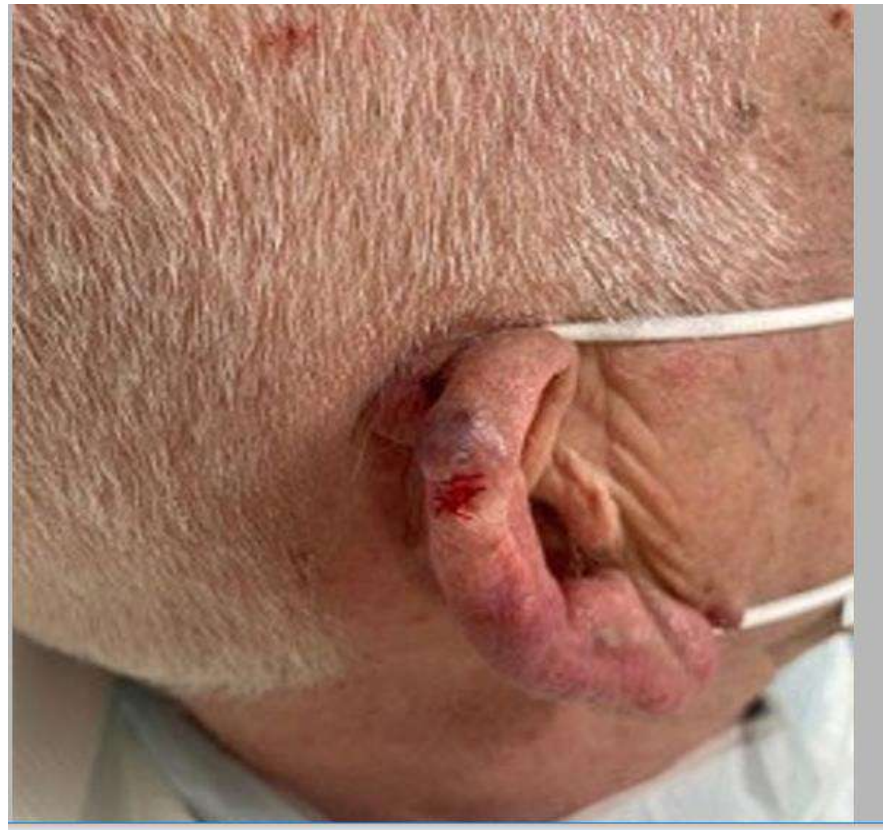
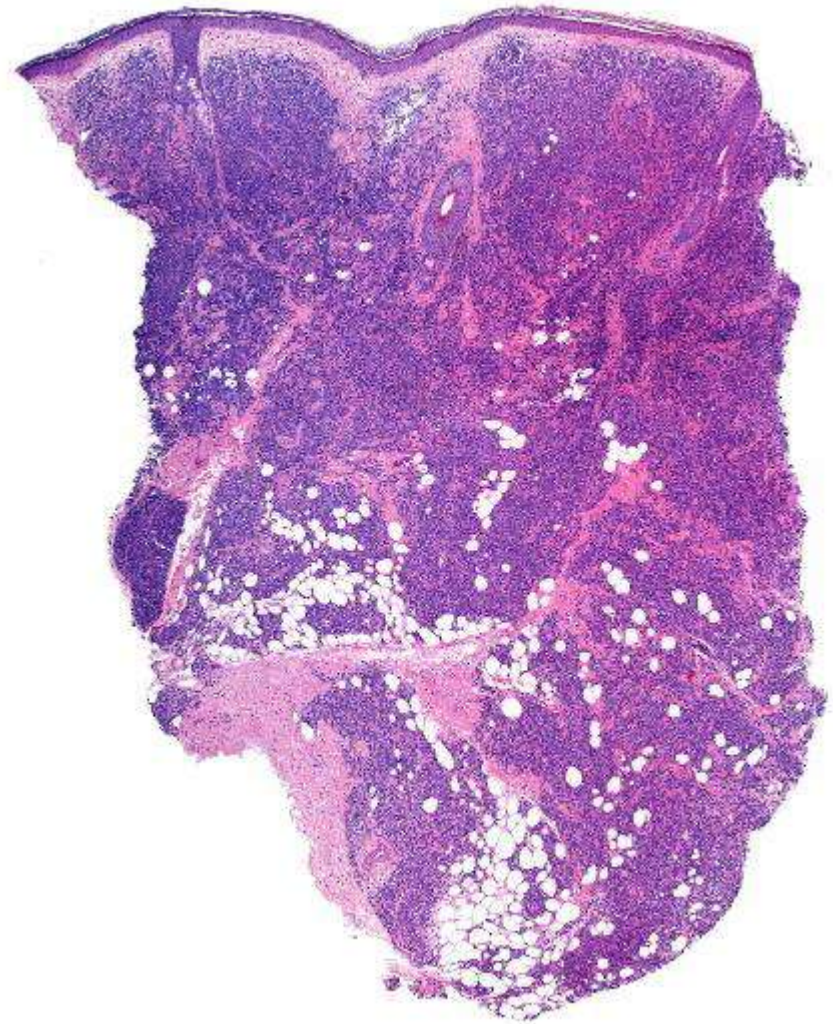
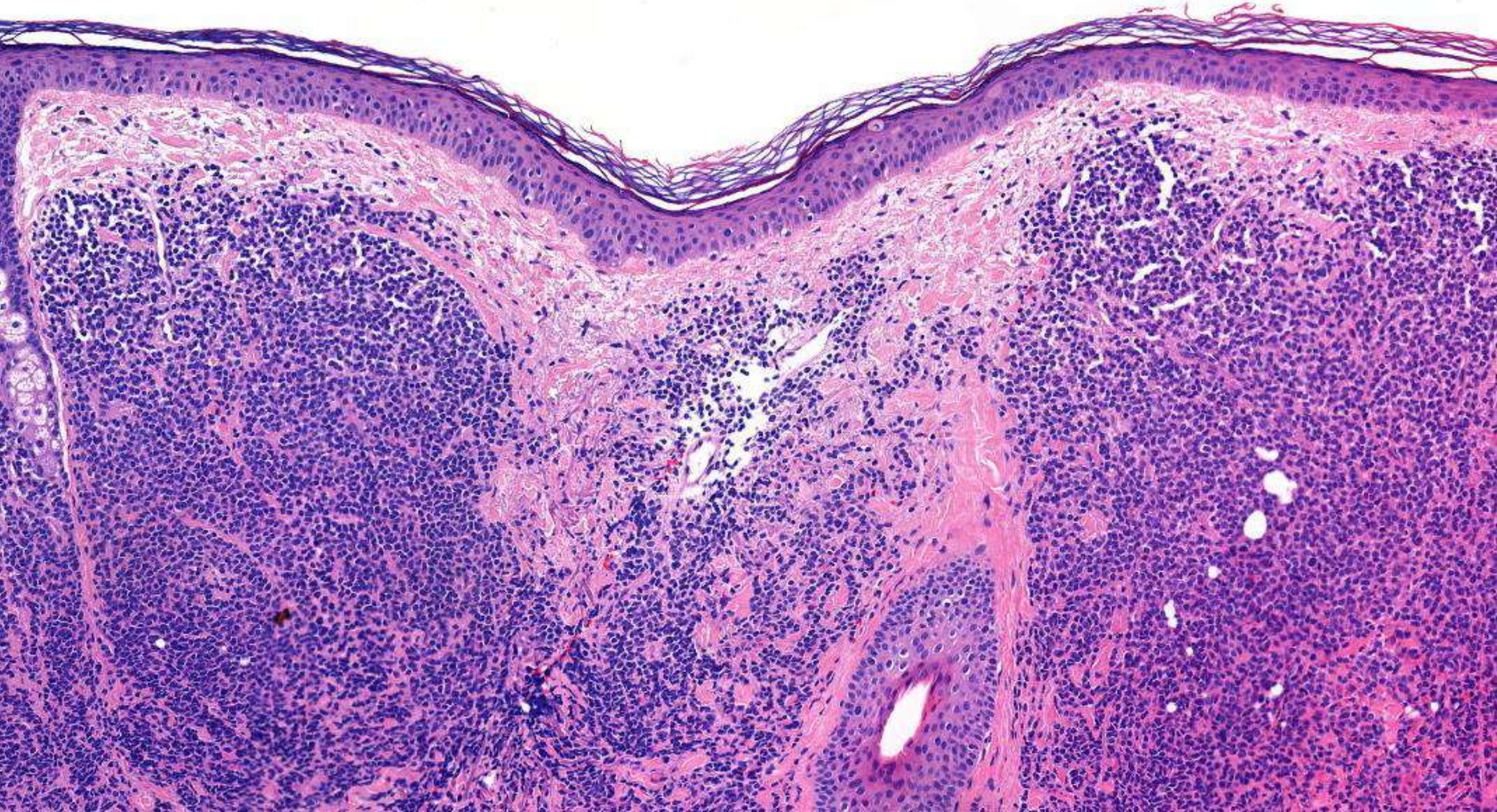


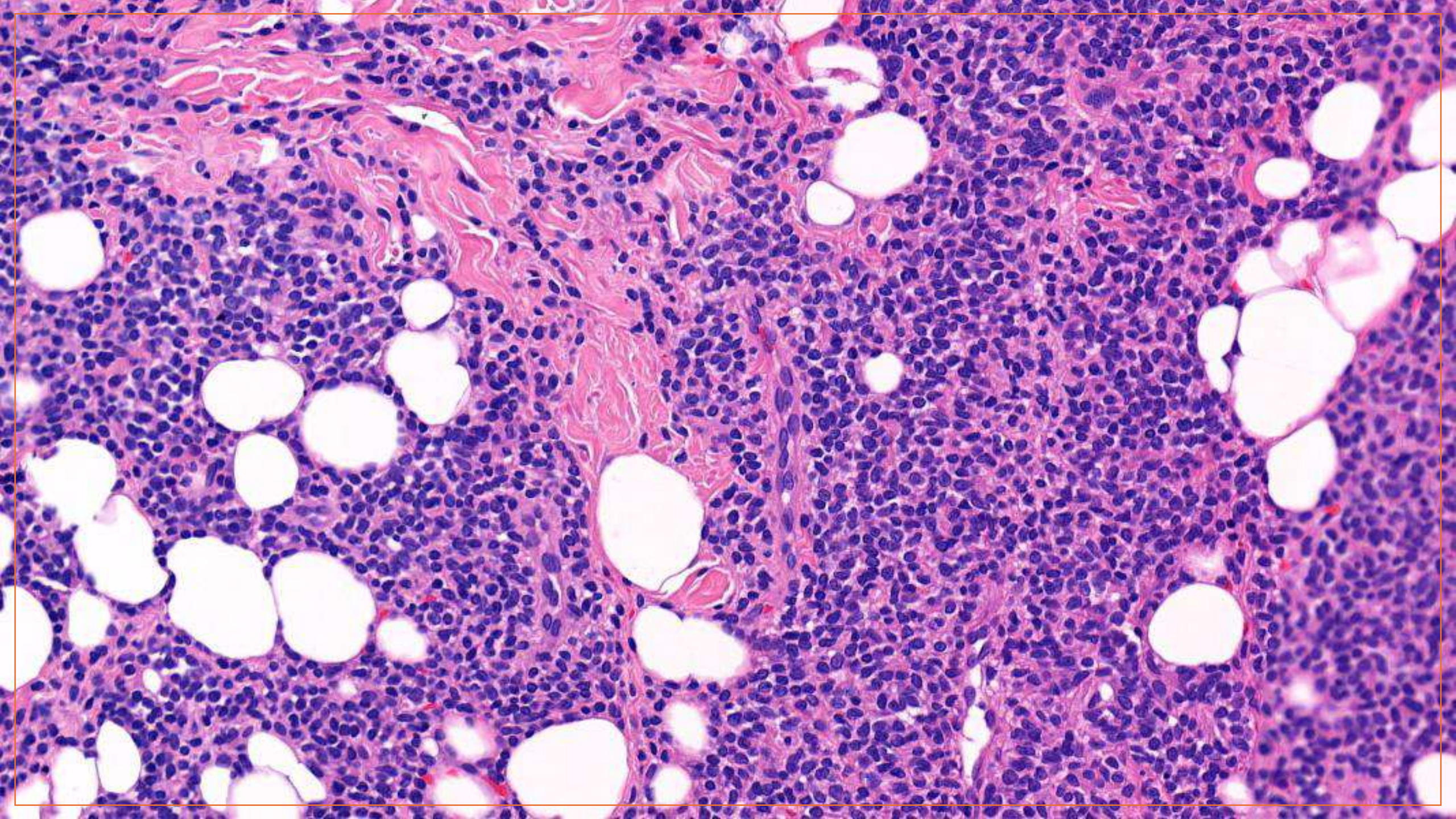
Case 5

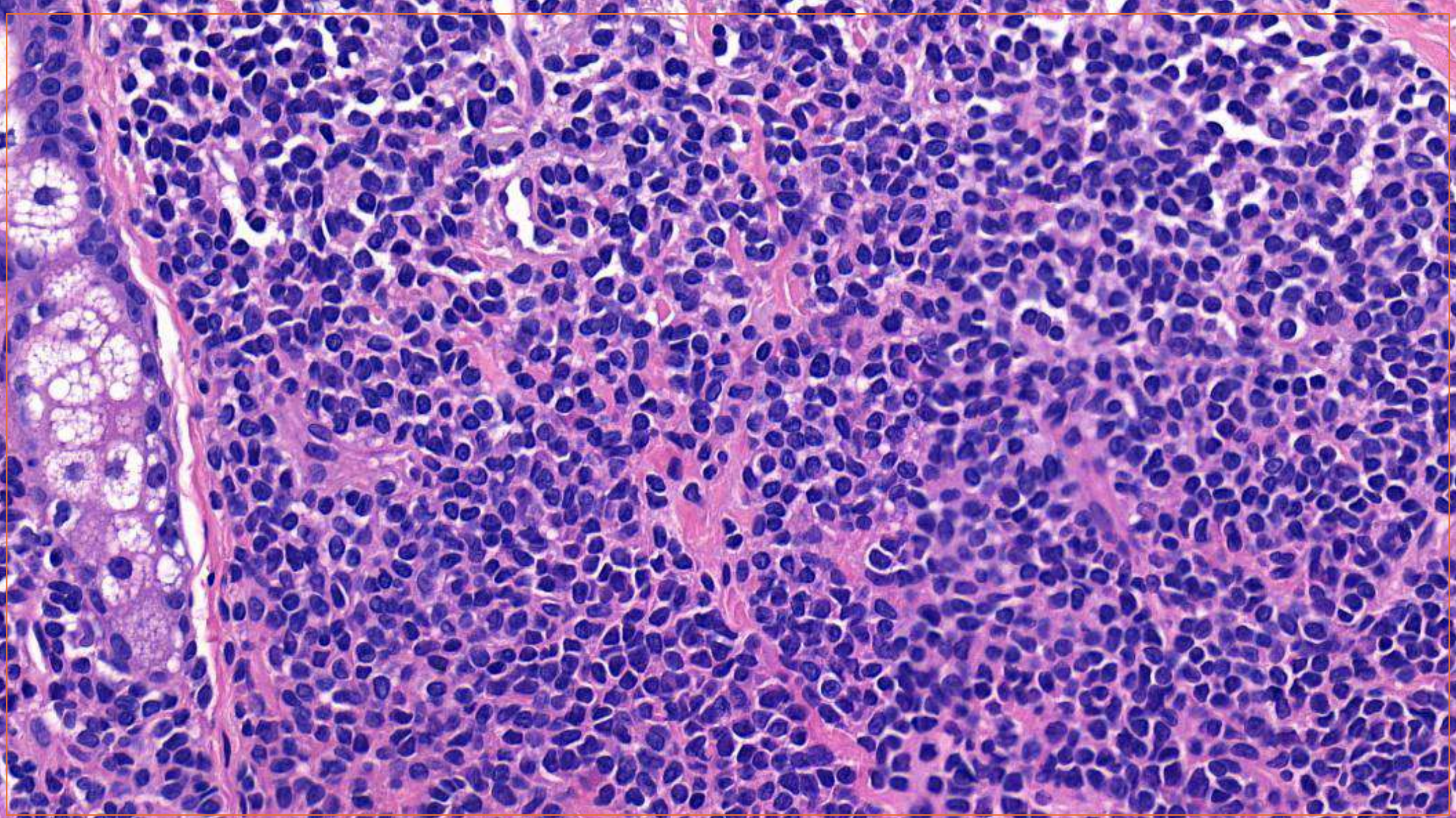
72-year-old male
Previous lesion on the right ear in 2019
New lesion on the right ear

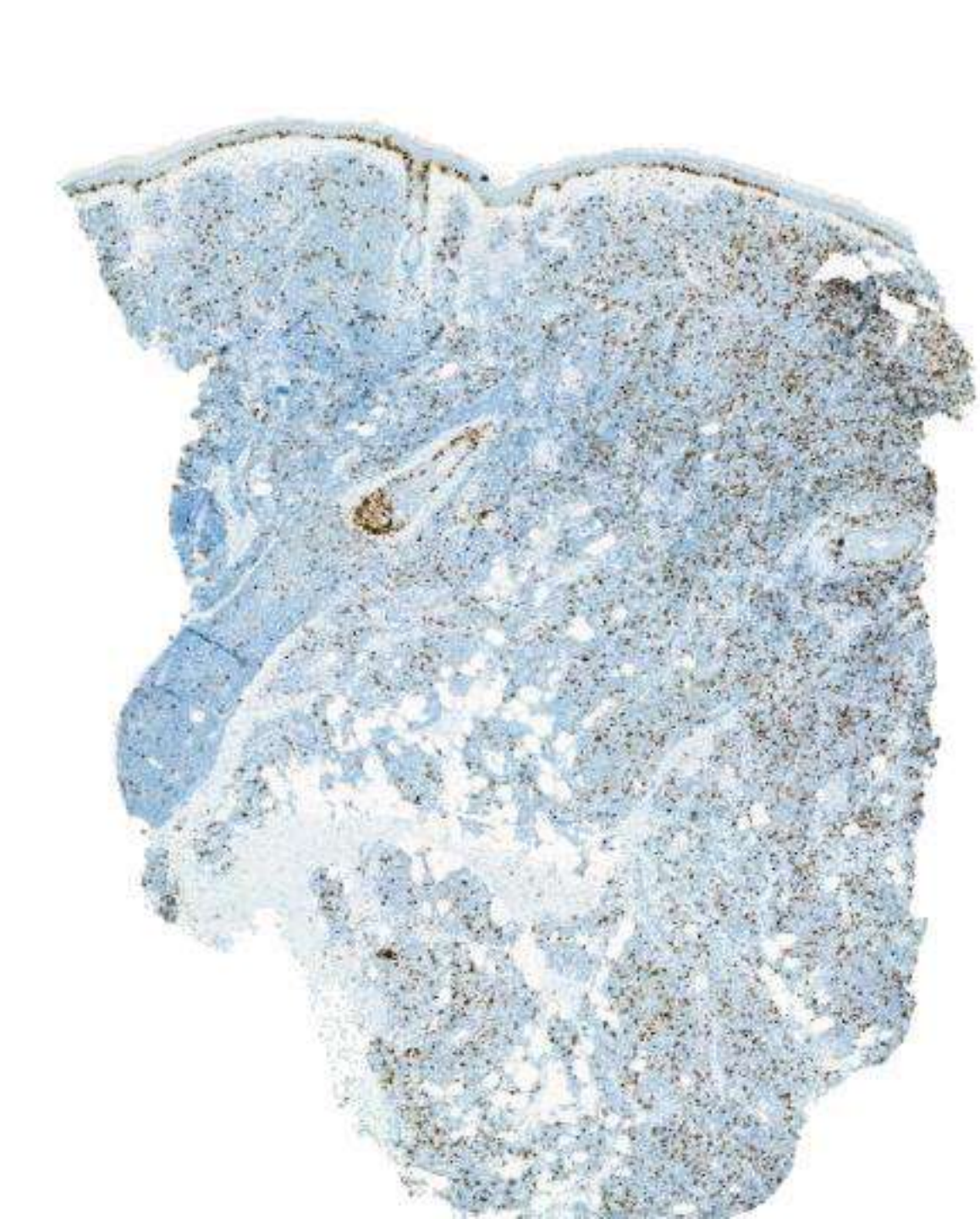


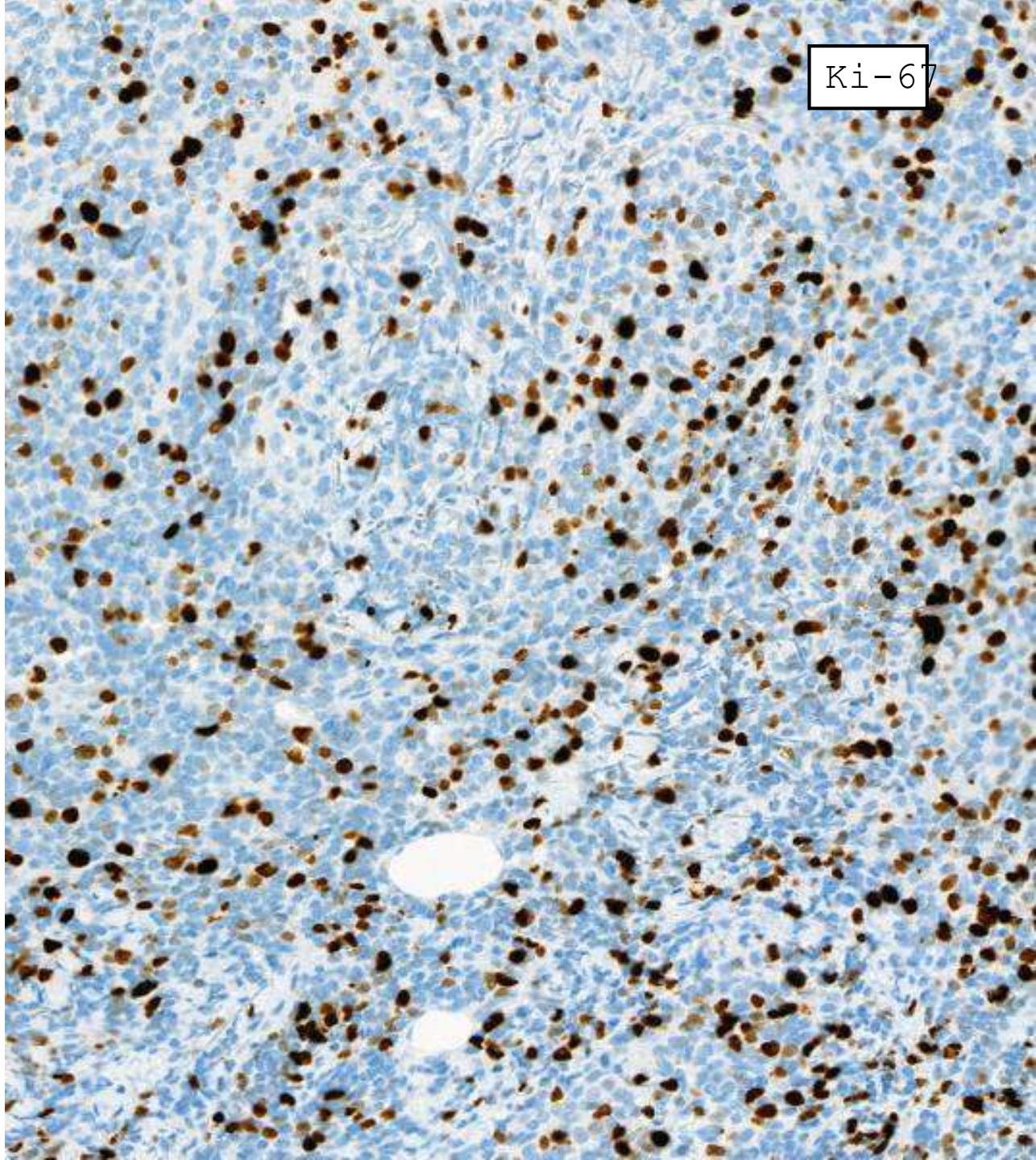


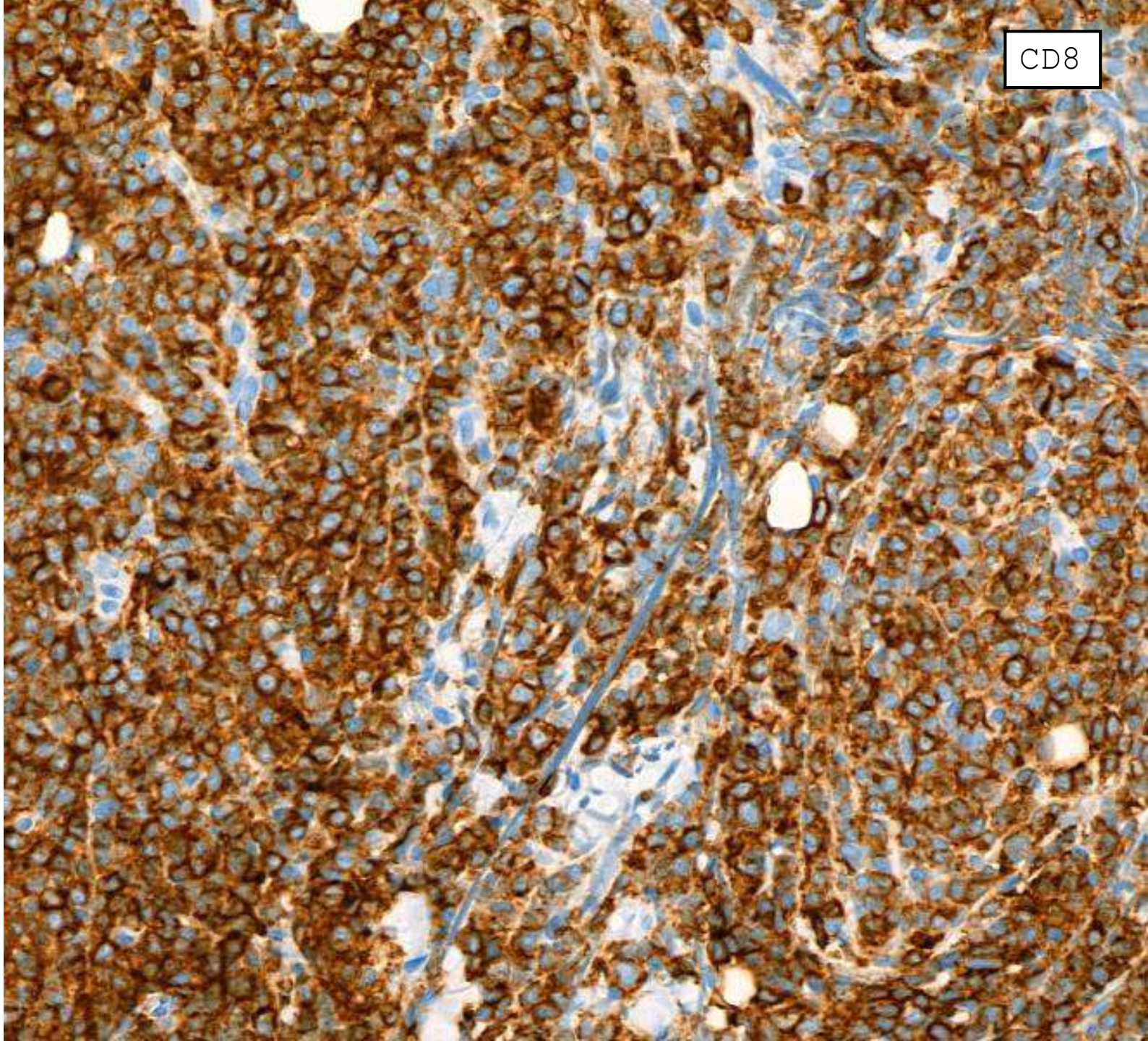


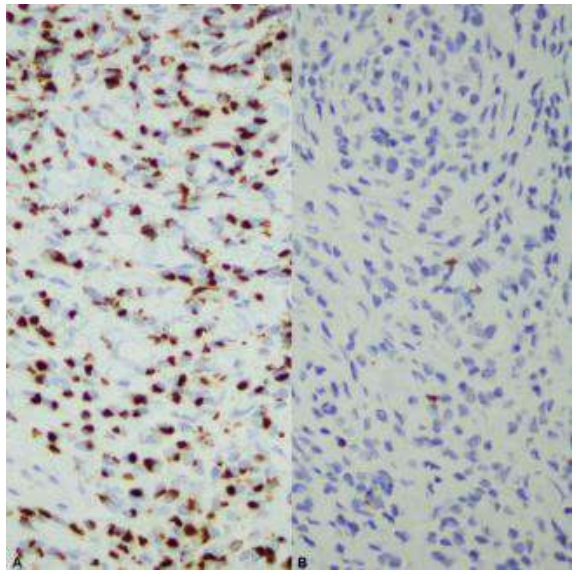




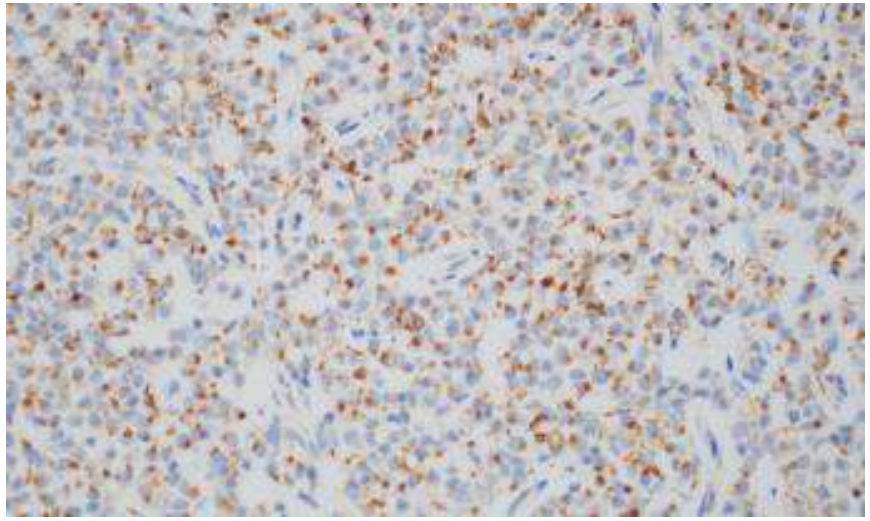



Ki-67

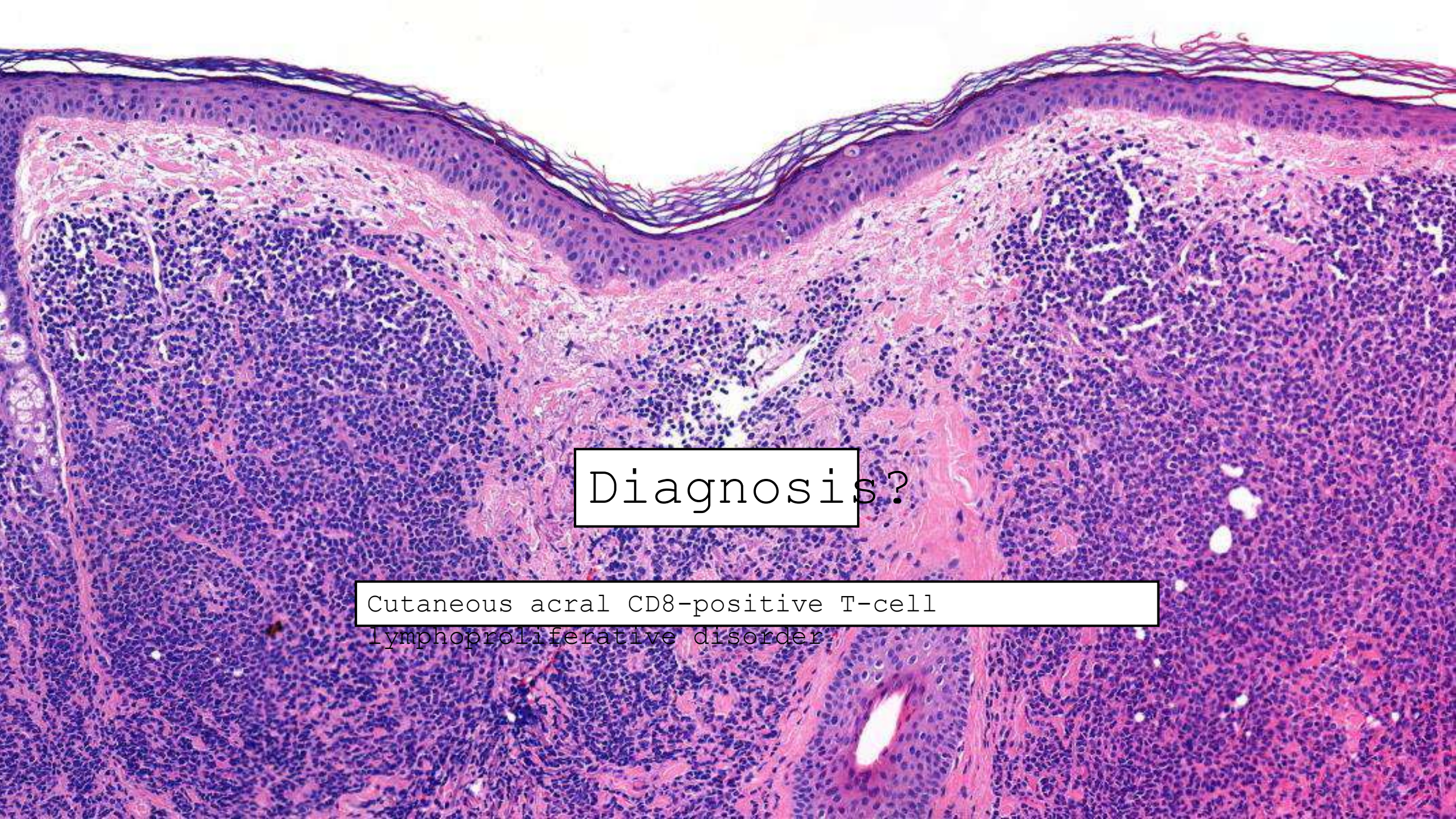

CD8



The atypical lymphocytes expressed TIA-1 an
pression of granzyme

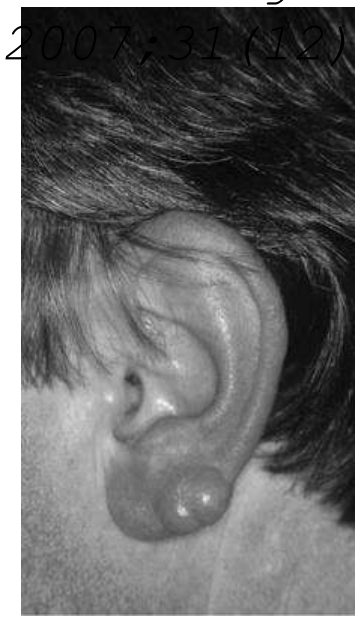


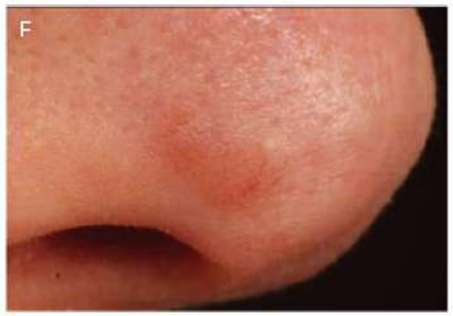
Characteristic dot-like
pattern of CD68

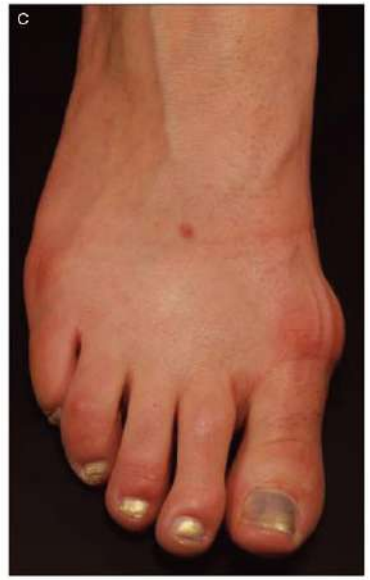

Diagnosis?
Cutaneous acral CD8-positive T-cell lymphoproliferative disorder

Petrella T et al. Indolent CD8-positive lymphoid proliferation of the ear: a distinct primary cutaneous T-cell lymphoma?

Am J Surg Pathol 2007;31(12):1887-92







J Cutan Pathol 2013: 40: 248–258
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Journal of
Cutaneous Pathology

Indolent CD8^{+} lymphoid proliferation of acral sites: a clinicopathologic study of six patients with some atypical features

CD3+, CD8+, CD56-, BF1+, TIA-1+, GrB

Table 2. Histopathologic parameters of all currently published cases of indolent CD8+ lymphoid proliferation

References	Grenz zone	Epidermotropism	CD8	CD4	CD2/CD5/CD7	TIA	Perforin	Granzym	CD56	PD-1	EBV	T-cel clone	Ki67 (%)
Khamaysi[6]	+	–	+	–	ND/ND/+	+	ND	ND	–	ND	ND	+	<10
Eich[7]	+	–	+	–	ND	+	ND	–	–	ND	–	+	ND
Fika[8]	+	–	+	–	ND/ND/ND	+	ND	ND	–	ND	–	+	ND
Petrella[5]	+	–	+	–	–/+/–	+	ND	–	–	ND	–	+	<10
	+	–	+	–	+/–/–	+	ND	–	–	ND	–	+	<10
	+	–	+	–	+/+/–	+	ND	–	–	ND	–	+	<10
	+	–	+	–	+/+/–	+	ND	–	–	ND	–	ND	<10
Li[9]	+	–	+	–	+/+/–	+	ND	–	–	ND	–	+	5
Ryan[10]	+	–	+	–	–/+/–	–	ND	–	–	ND	–	+	10
Beltraminelli[11]	+	–	+	–	ND/+/ND	+	–	ND	–	ND	–	+	<20
	+	–	+	–	ND/+/ND	+	ND	ND	–	ND	–	+	<20
	+	–	+	–	ND/+/ND	ND	ND	ND	–	ND	–	+	<20
Suchak[12]	+	–	+	–	ND/–/–	+	ND	+	–	ND	–	+	<10
	+	–	+	–	+/+/–	+	ND	ND	–	ND	–	+	ND
Geruad[13]	+	–	+	–	ND/+/ND	+	–	ND	ND	ND	ND	ND	ND
Swick[14]	+	–	+	–	ND/ND/ND	+	ND	ND	–	ND	–	+	10
	+	–	+	–	ND/ND/ND	+	ND	ND	–	ND	–	+	ND
Zeng[15]	+	–	+	–	ND/ND/–	+	+	–	–	ND	–	+	25
Valois[16]	+	–	+	–	ND/+/ND	+	ND	ND	–	ND	–	+	20
Milley[17]	+	–	+	–	ND/+/ND	+	–	–	–	ND	ND	+	10
Greenblatt[18]	+	–	+	–	+/+/+	+	ND	–	–	–	–	+	40
	+	–	+	–	–/+/–	+	ND	–	–	–	–	+	10
	+	–	+	–	+/–/+	+	ND	ND	–	ND	–	+	10
	+	+ (focally)	+	–	–/+/–	+	ND	20%	–	<5%	–	+	30
	+	–	+	–	+/+/+	+	ND	–	–	ND	–	ND	10
	+	+ (focally)	+	–	+/+/+	+	ND	10%	–	-	–	–	40
Butsch[19]	UNK	+ (focally)	+	–	ND/ND/ND	ND	ND	ND	–	ND	–	+	10
Kempf[20]	+	–	+	–	+/+/+	–	ND	60%	–	ND	–	–	10
	+	–	+	–	–/+/+	–	ND	60%	–	ND	–	+	10
	+	–	+	–	+/+/+	–	ND	–	–	ND	–	+	10

- This retrospective study identified 11 cases of primary cutaneous acral CD8-positive T-cell lymphoproliferative disorder

- Predominantly affects males with a mean age of 56
- Notably, only 55% of cases occurred at acral sites, with 36% at non-acral sites and 9% exhibiting both

- For patients with solitary or confined disease, complete excision or radiation was curative

- Granzyme expression varied across cases, with some showing significant positivity

- The authors suggest updating the nomenclature to "primary cutaneous CD8-positive T-cell lymphoproliferative disorder, acral type" to

Stephan C, Grossman ME, Magro CM. Primary cutaneous acral CD8-positive T-cell lymphoproliferative disorder: A clinical and histologic retrospective cohort study. Clin Dermatol. 2023 Nov-Dec;41(6):666-679.

The dermal CD8+ lymphoproliferations

Cutaneous acral CD8+ T-cell lymphoproliferative disorder

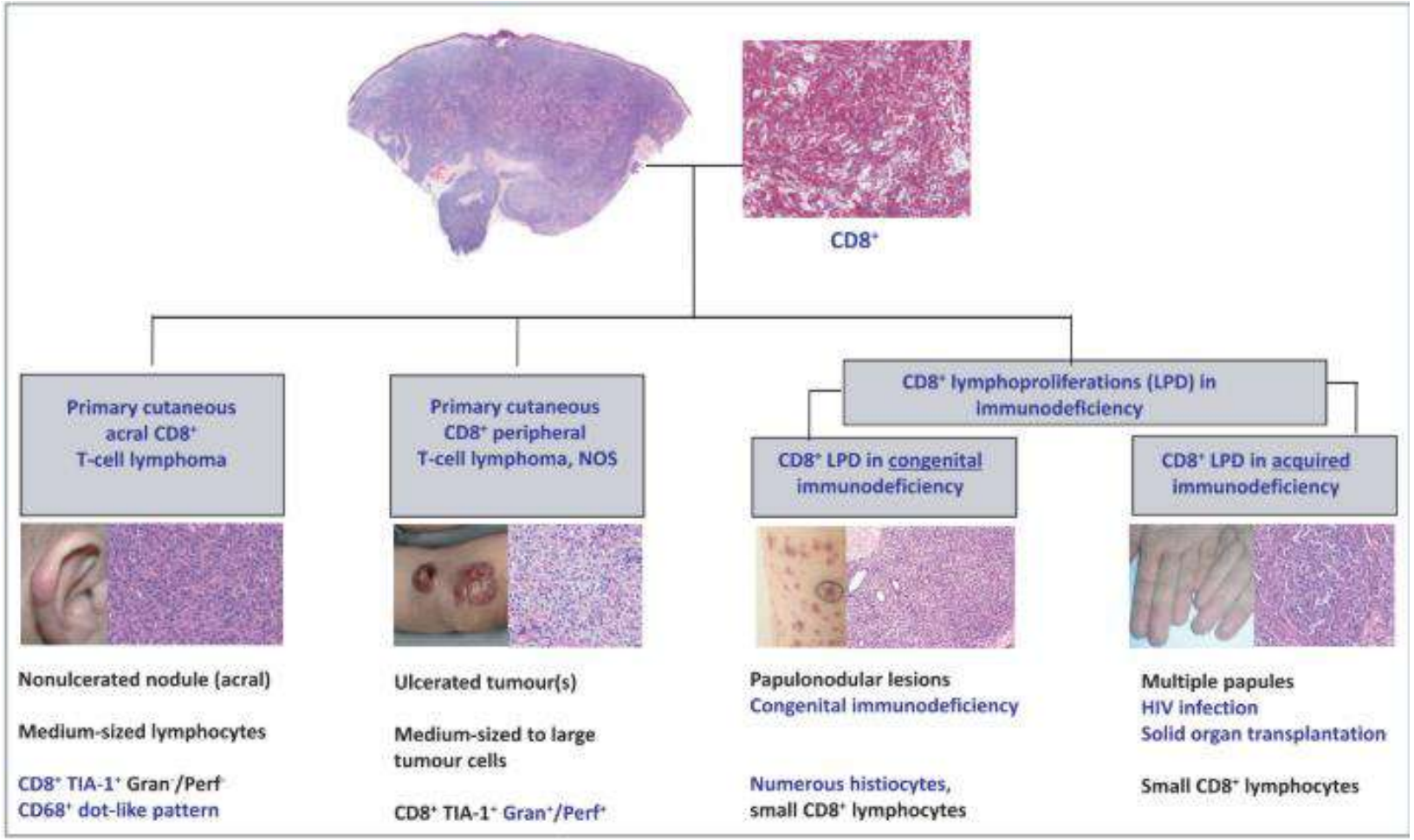
- Solitary nodule arising at acral sites
- Monotonous dermal infil-trate of small-to-medium-sized CD8+ lymphocytes
- Characteristic dot-like pattern of CD68
- Low proliferation rate
- Excellent prognosis

Primary cutaneous CD8+ peripheral T-cell lymphoma unspecified/NOS

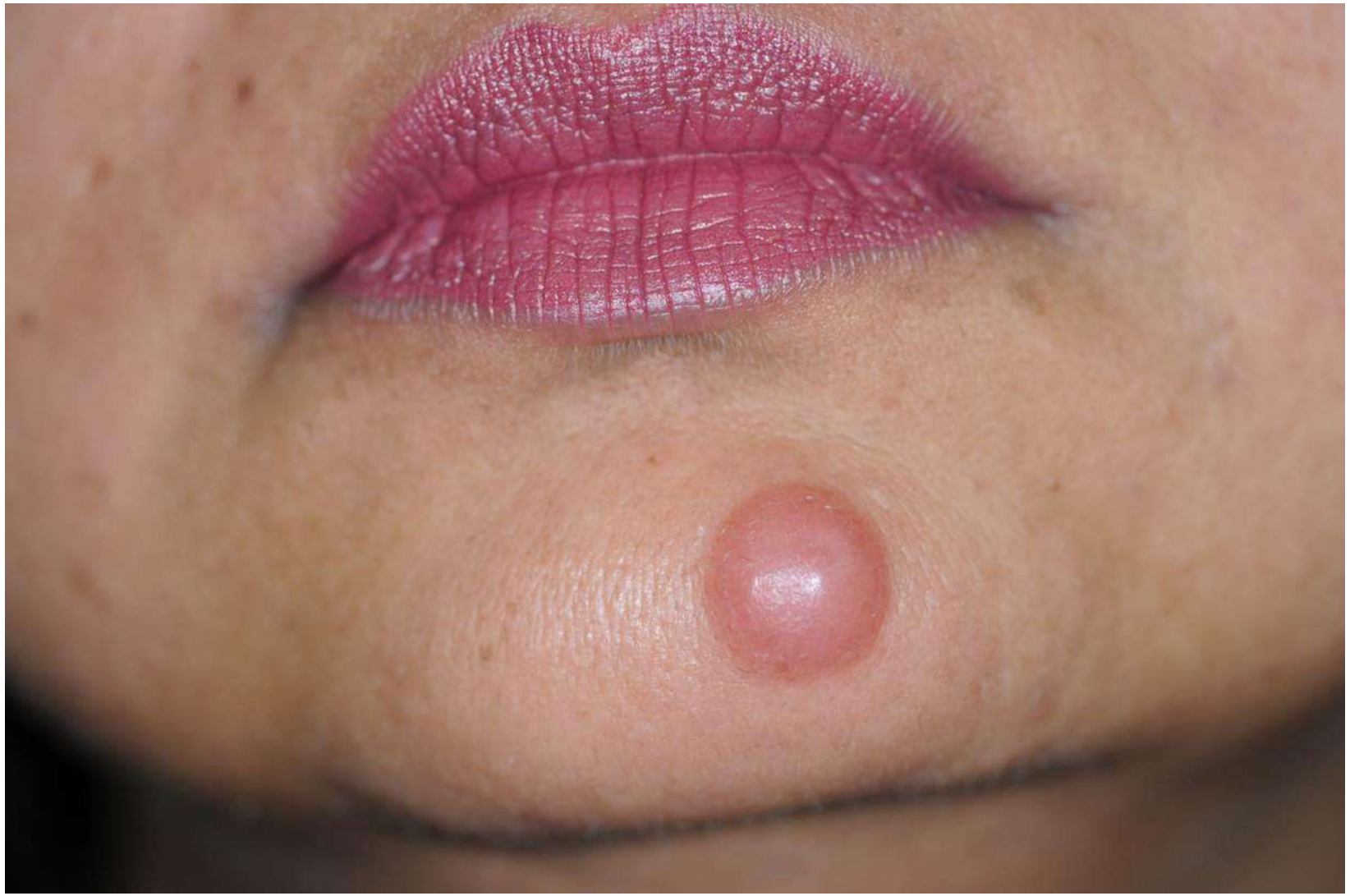
- One or multiple rapidly evolving tumors
- Mostly medium-sized
- Pleomorphic CD8+ tumor cells with expression of several cytotoxic markers
- High proliferative activity

Cutaneous CD8+ lymphoproliferations associated with congenital immunodeficiency syndromes

- Persisting localized or disseminated violaceous to brownish plaques on the
- extremities
- Histiocyte-rich infiltrate of mostly small CD8+ lymphocytes with
- subtle atypia
- Papular CD8+

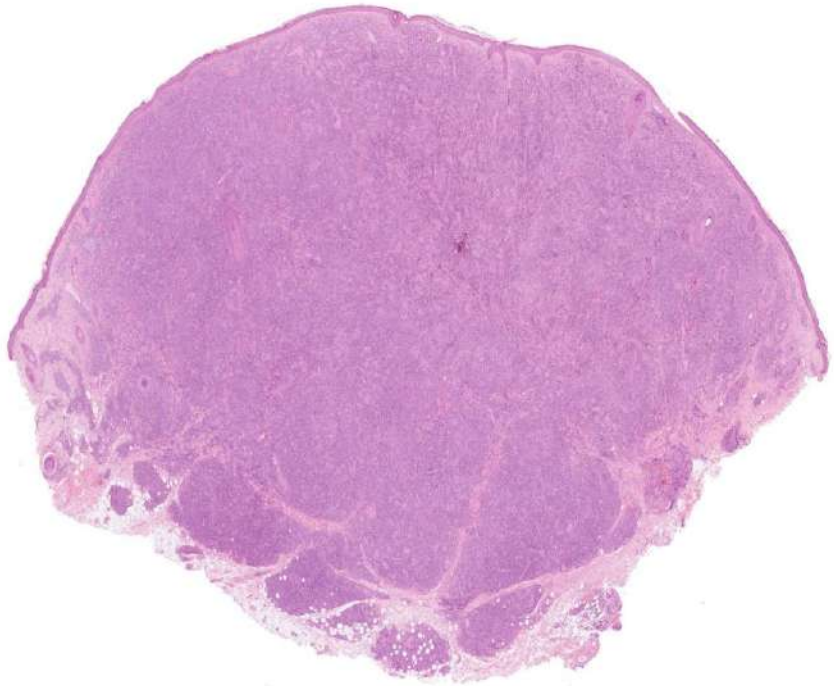


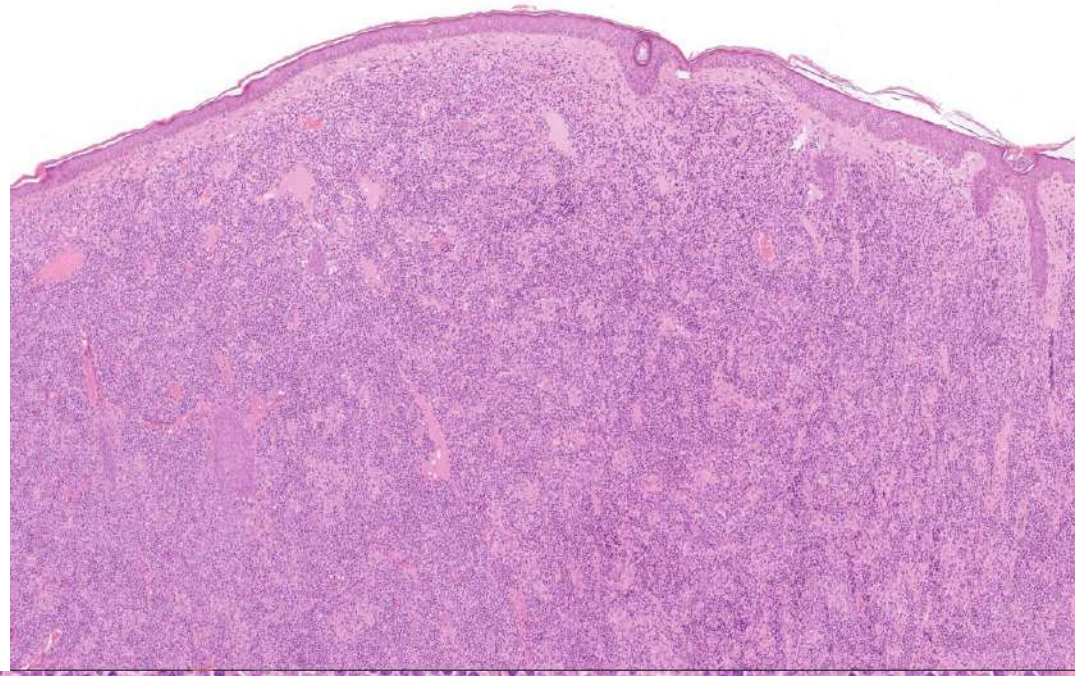
Kempf W et al. Clinical, histopathological and prognostic features of primary cutaneous acral CD8+ T-cell lymphoma and other dermal CD8+ cutaneous lymphoproliferations: results of an EORTC Cutaneous Lymphoma Group workshop. Br J Dermatol. 2022 May;186(5):887-897.

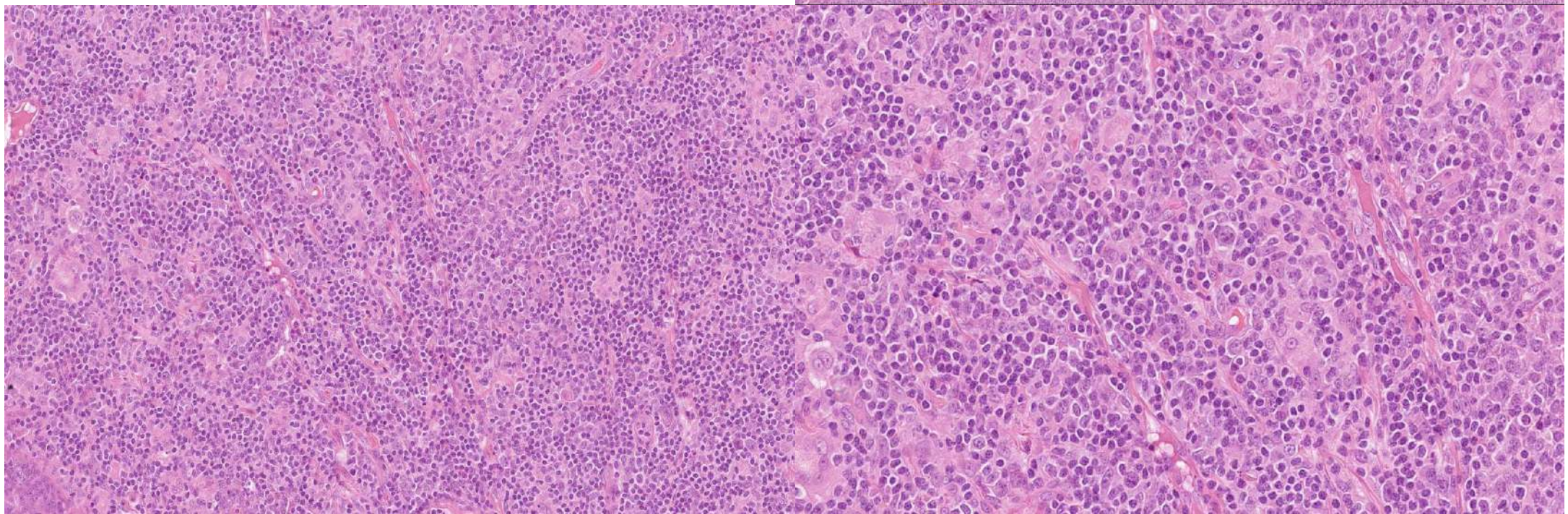


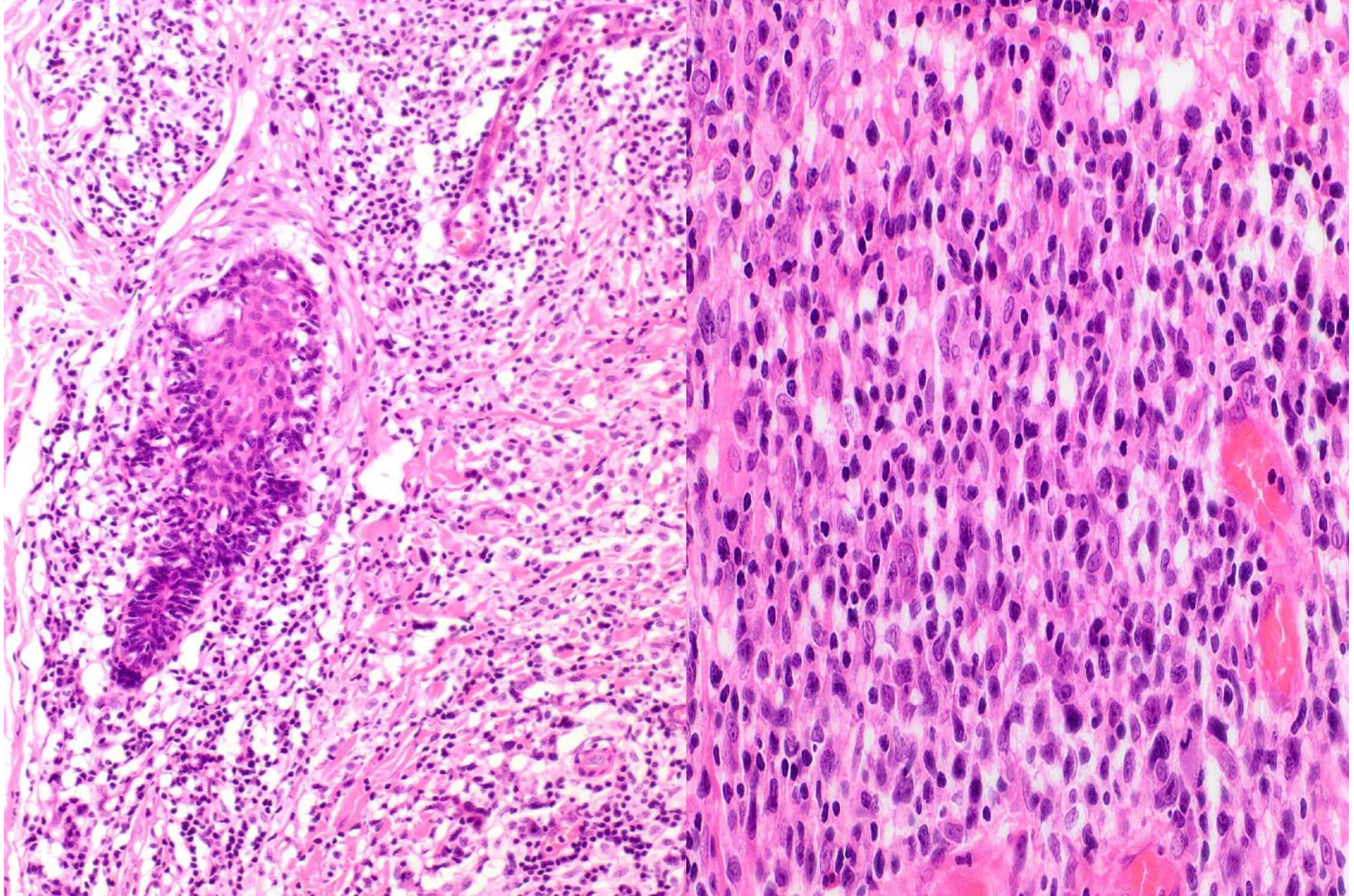
Primary Cutaneous CD4+ Small/medium T-cell Lymphoma (PCSM-TCL) Histological Features

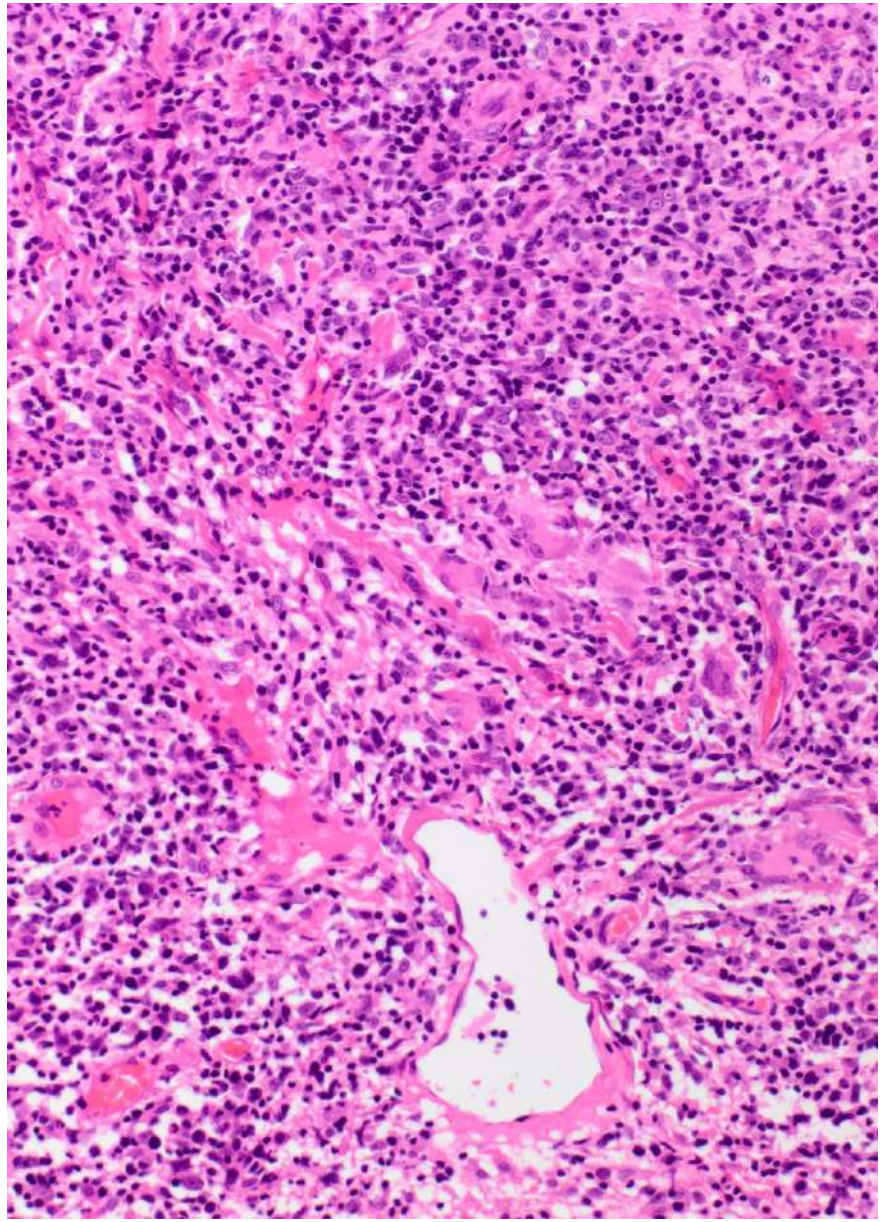
- Two patterns: dermal diffuse or superficial plaque-like.
- Epidermotropism and or folliculotropism may be present
- Small to medium-sized cells (twice the size of a normal lymphocyte)
- Scattered large cells (less than 30%)
- Pan-T helper phenotype (may be loss of CD5 and/or CD7)
- Expression of at least two markers of follicular T-helper cells (PD1: 25%, ICOS: 25%, BCL6: 10%, CXCL13: 5%)
- B-lymphocytes 20% of less
- No formation of germinal centres
- Low proliferation rate
- T-cell clone

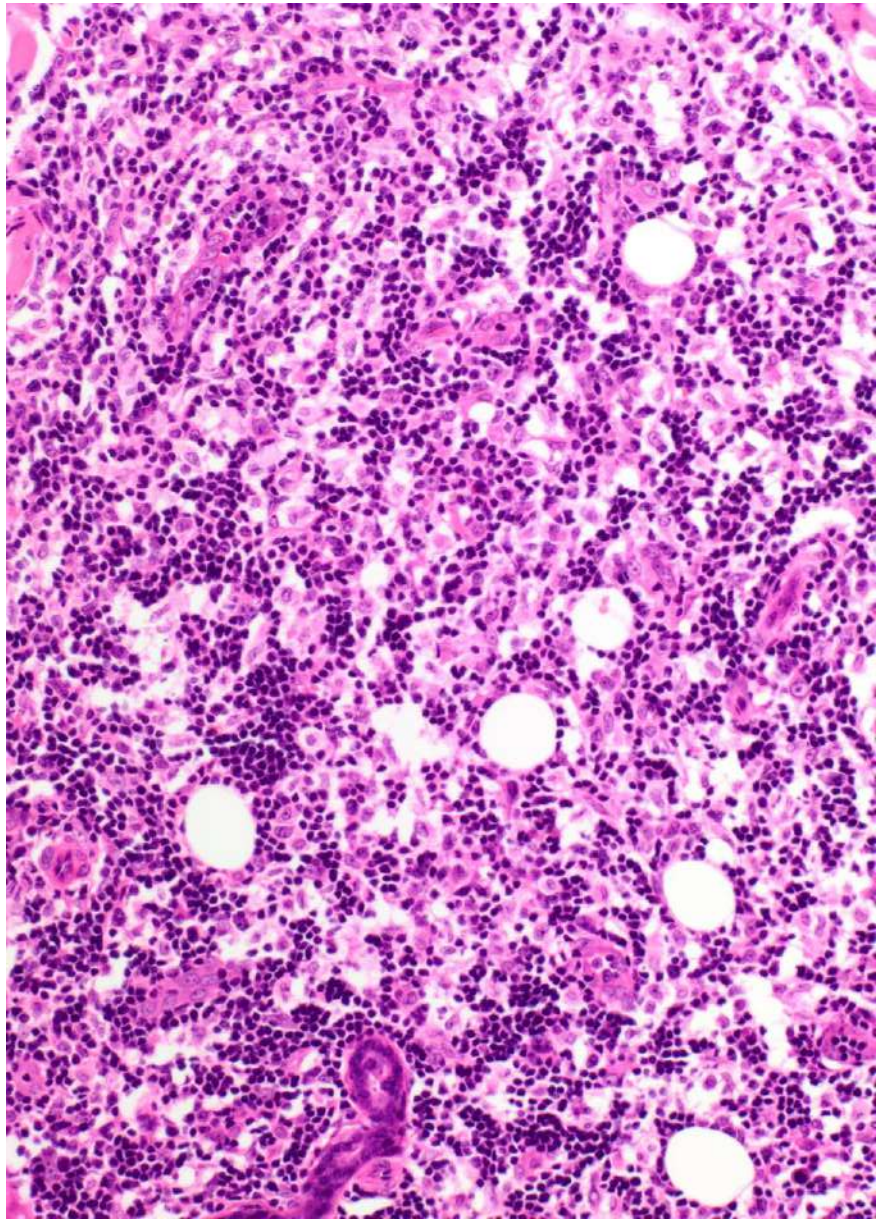


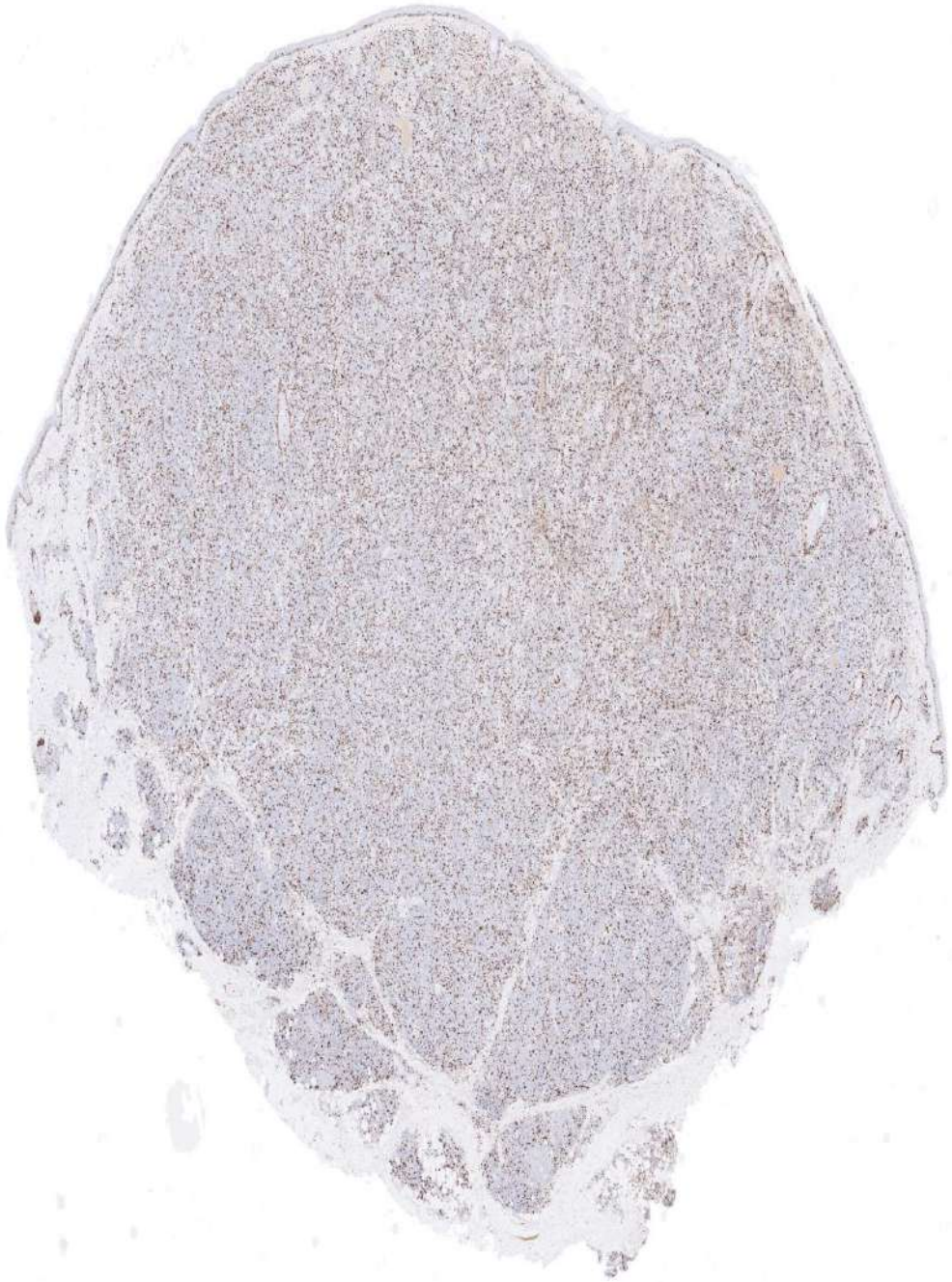


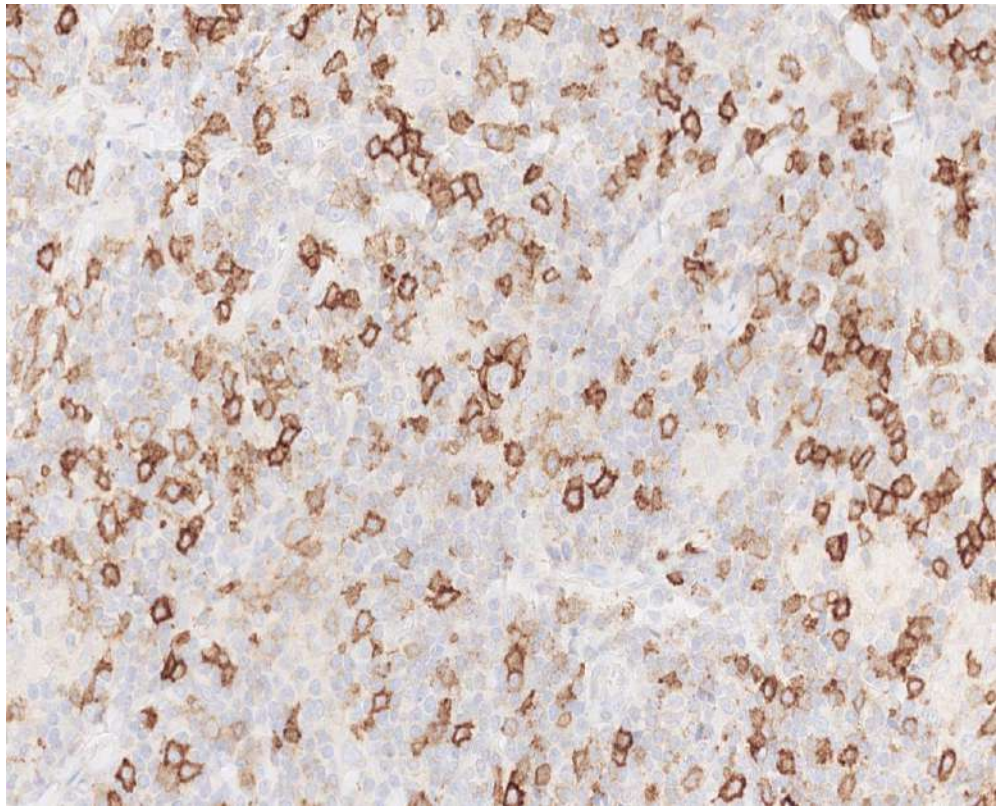




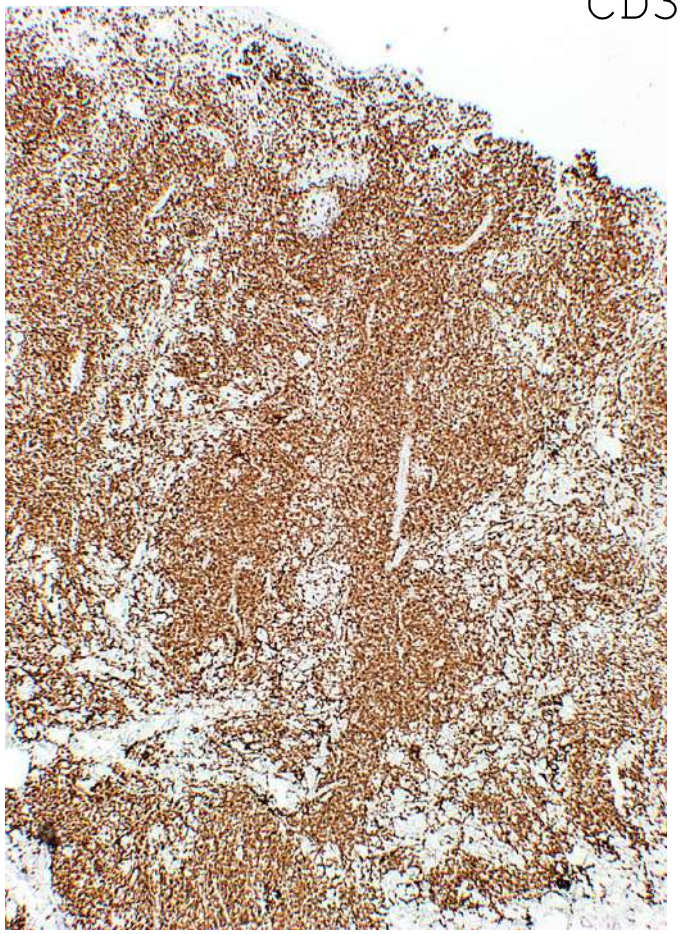








CD3



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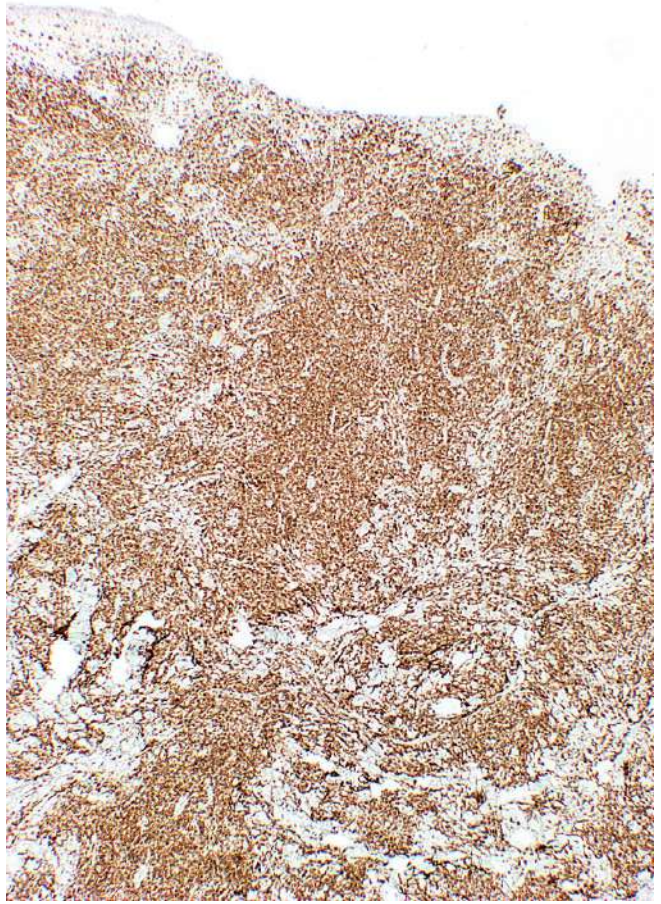

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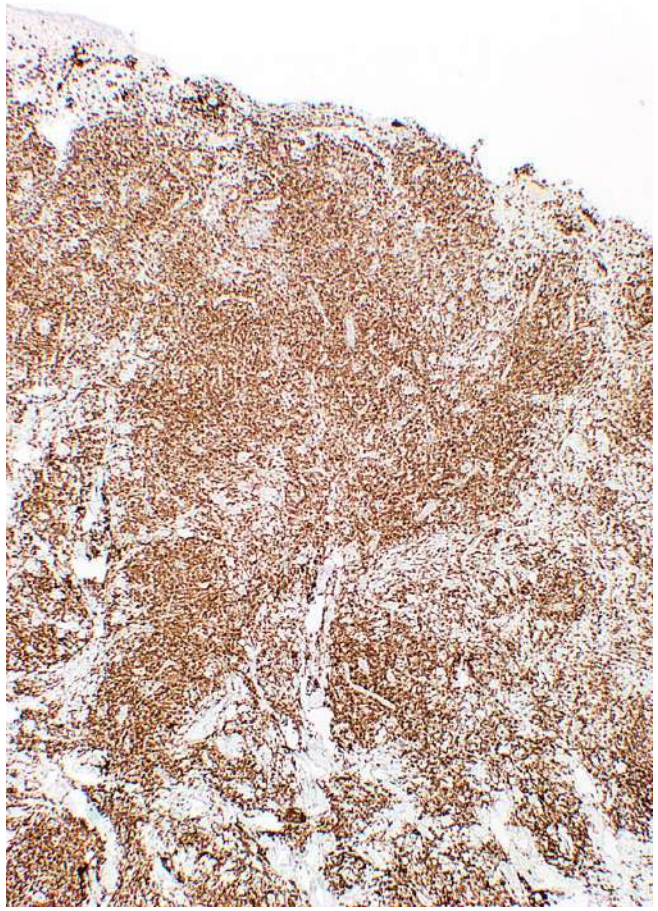

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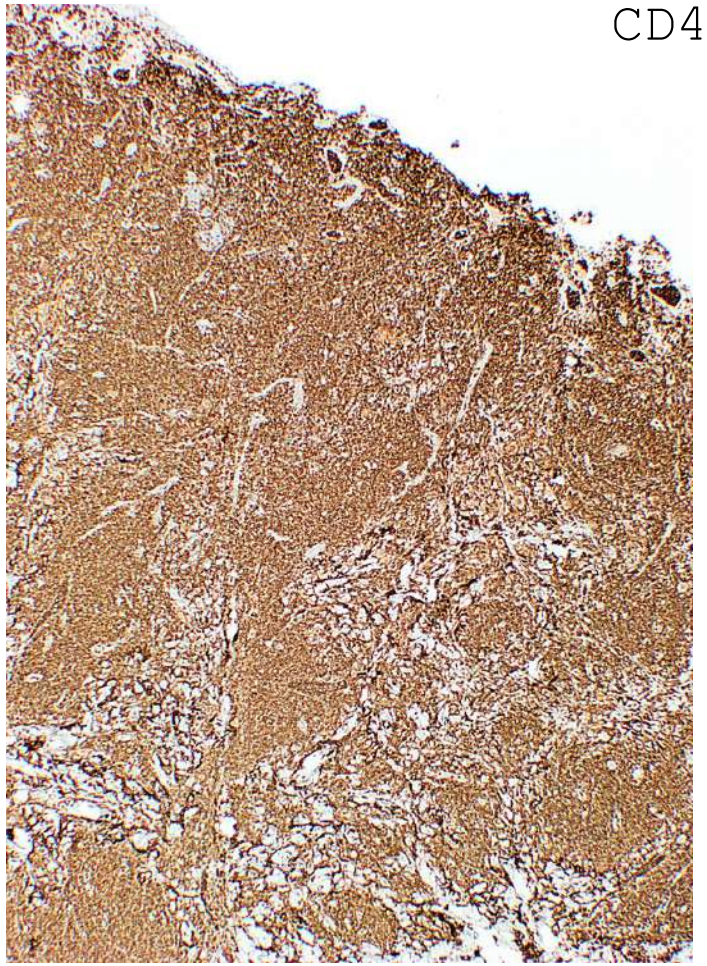

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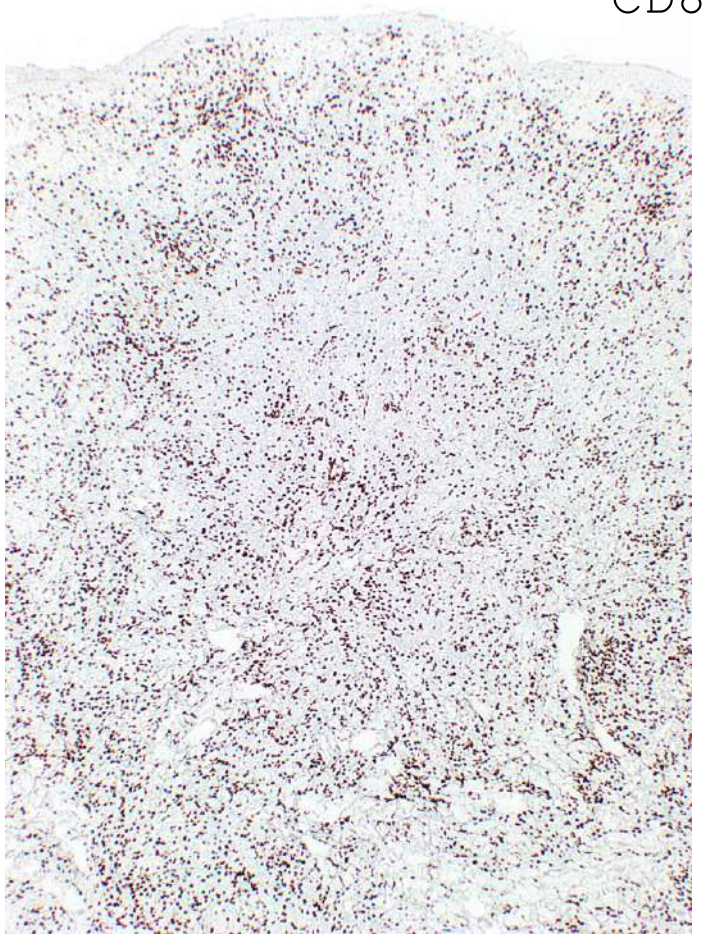

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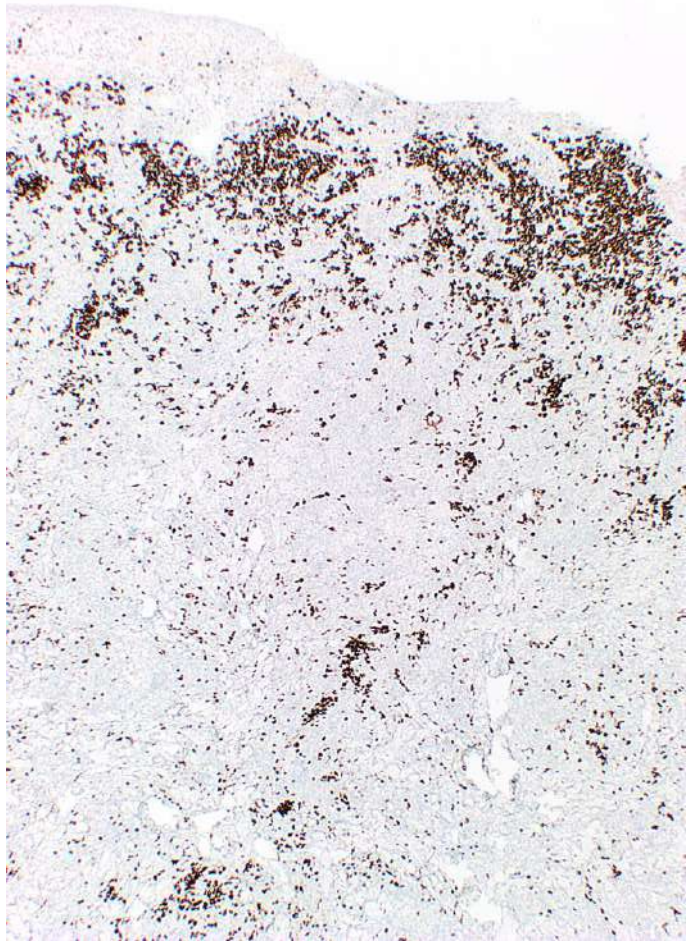

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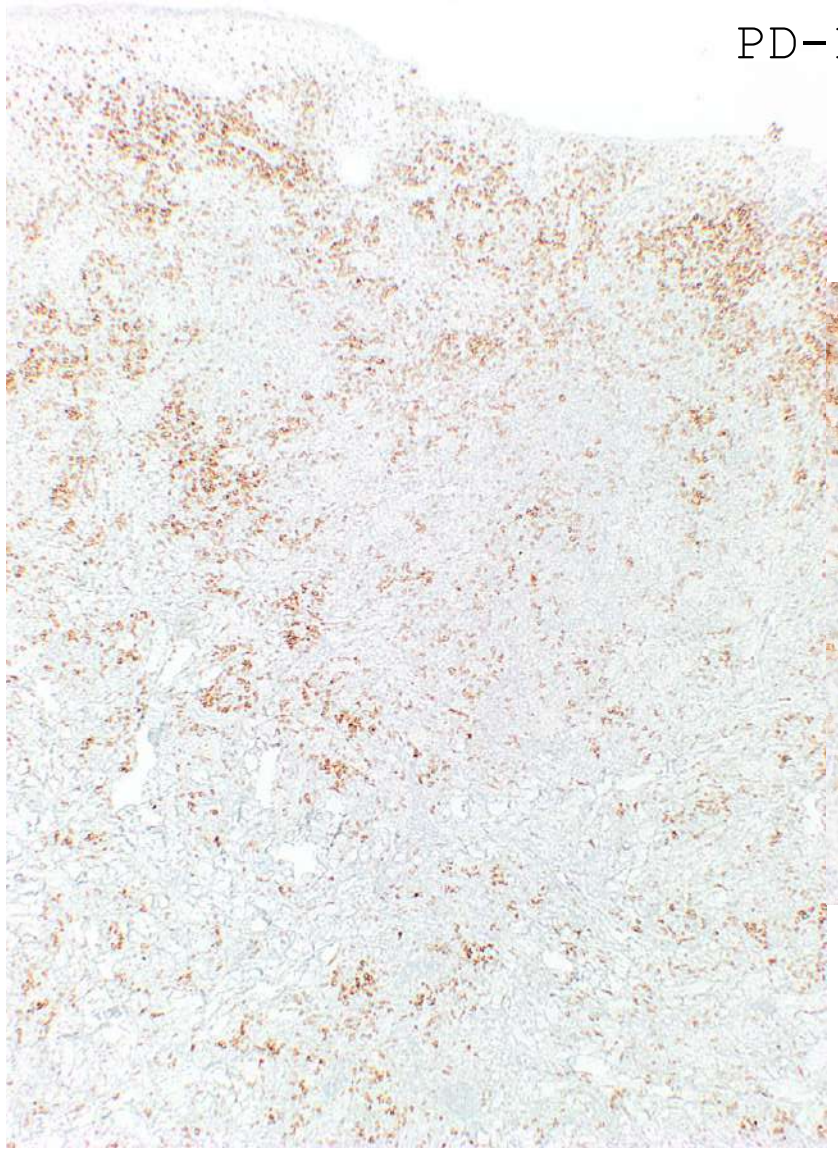

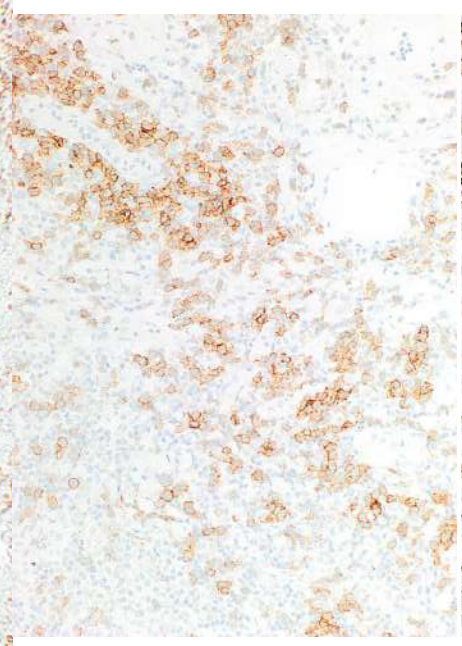

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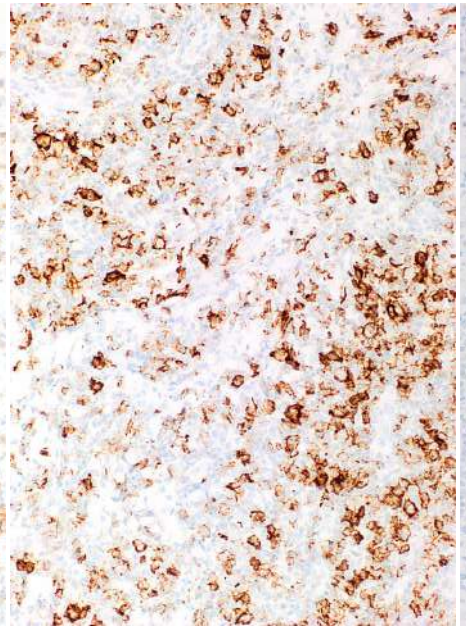
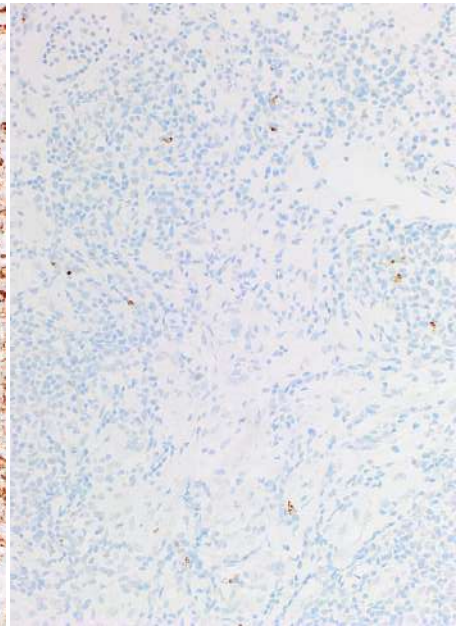
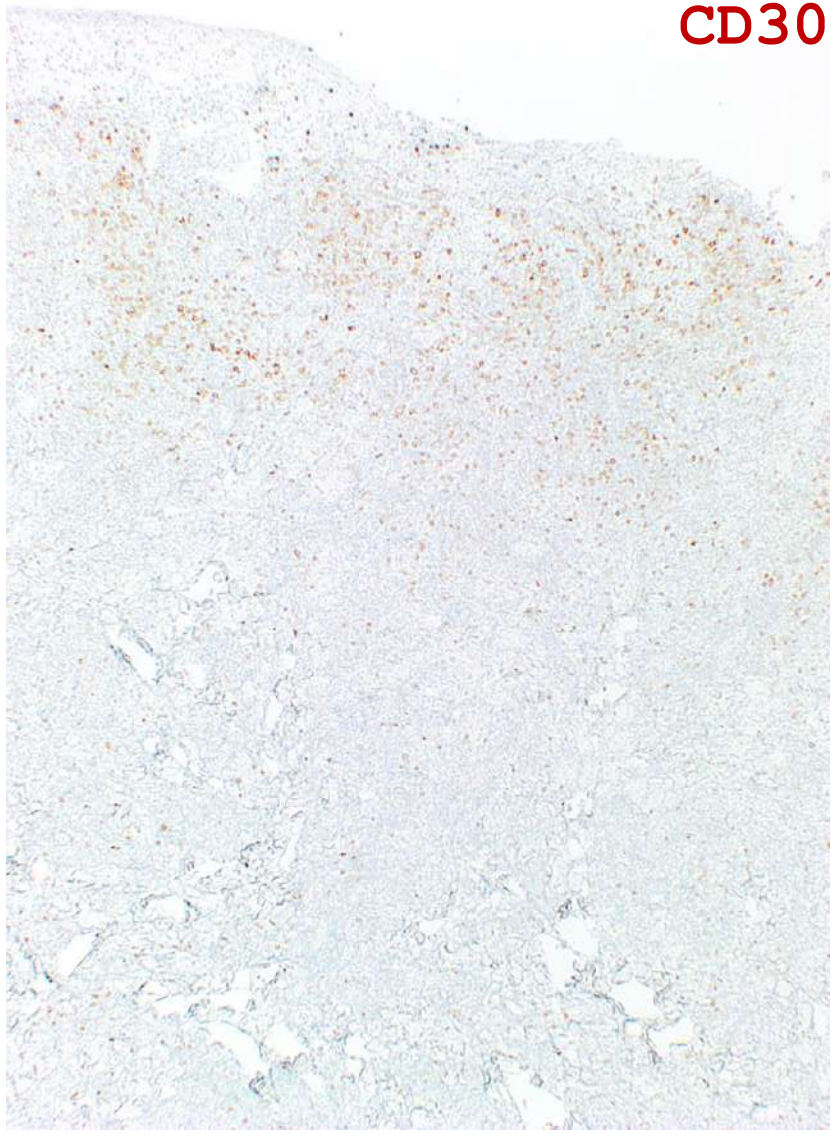


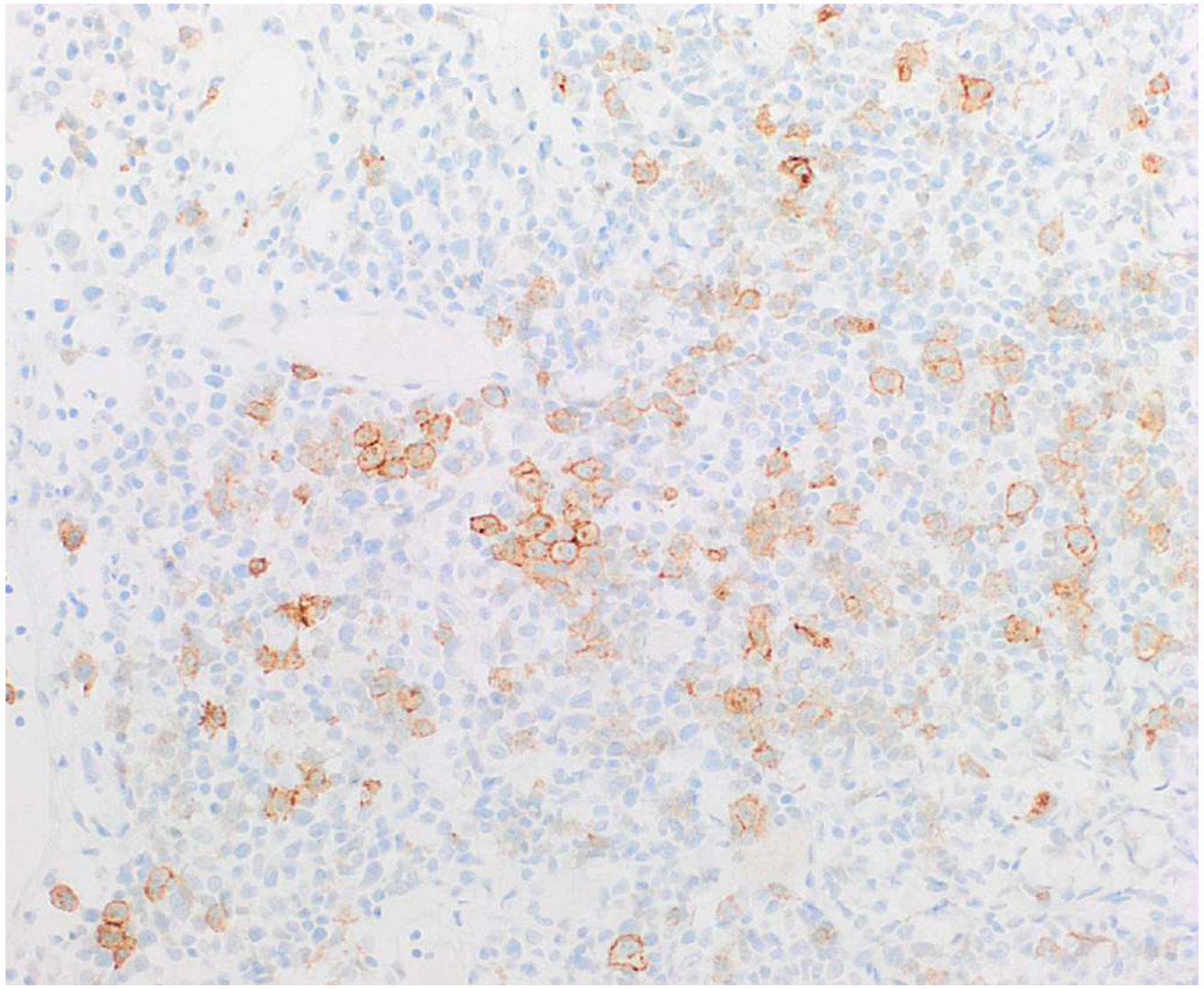
ICOS

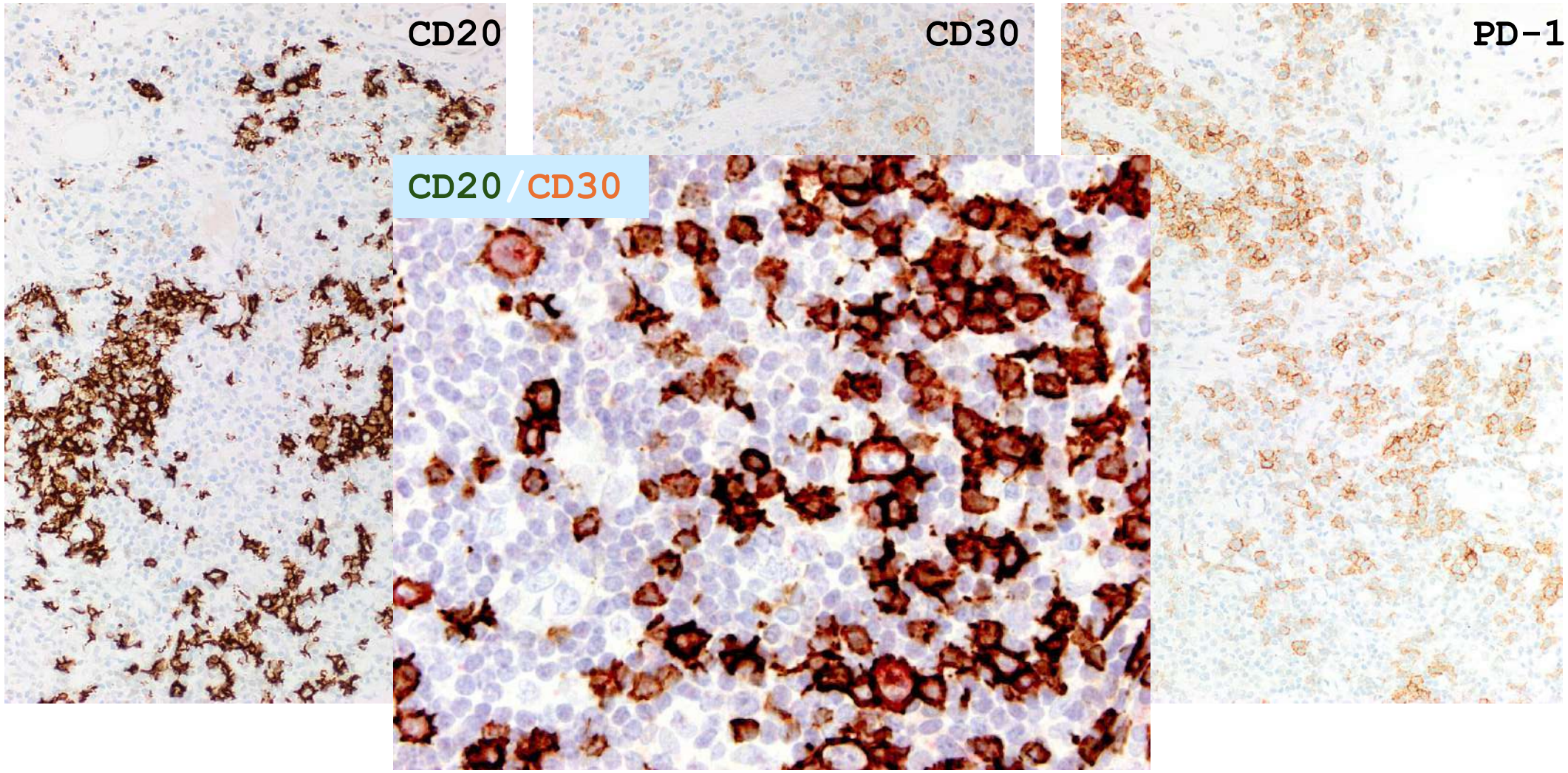


CXCL13

CD30

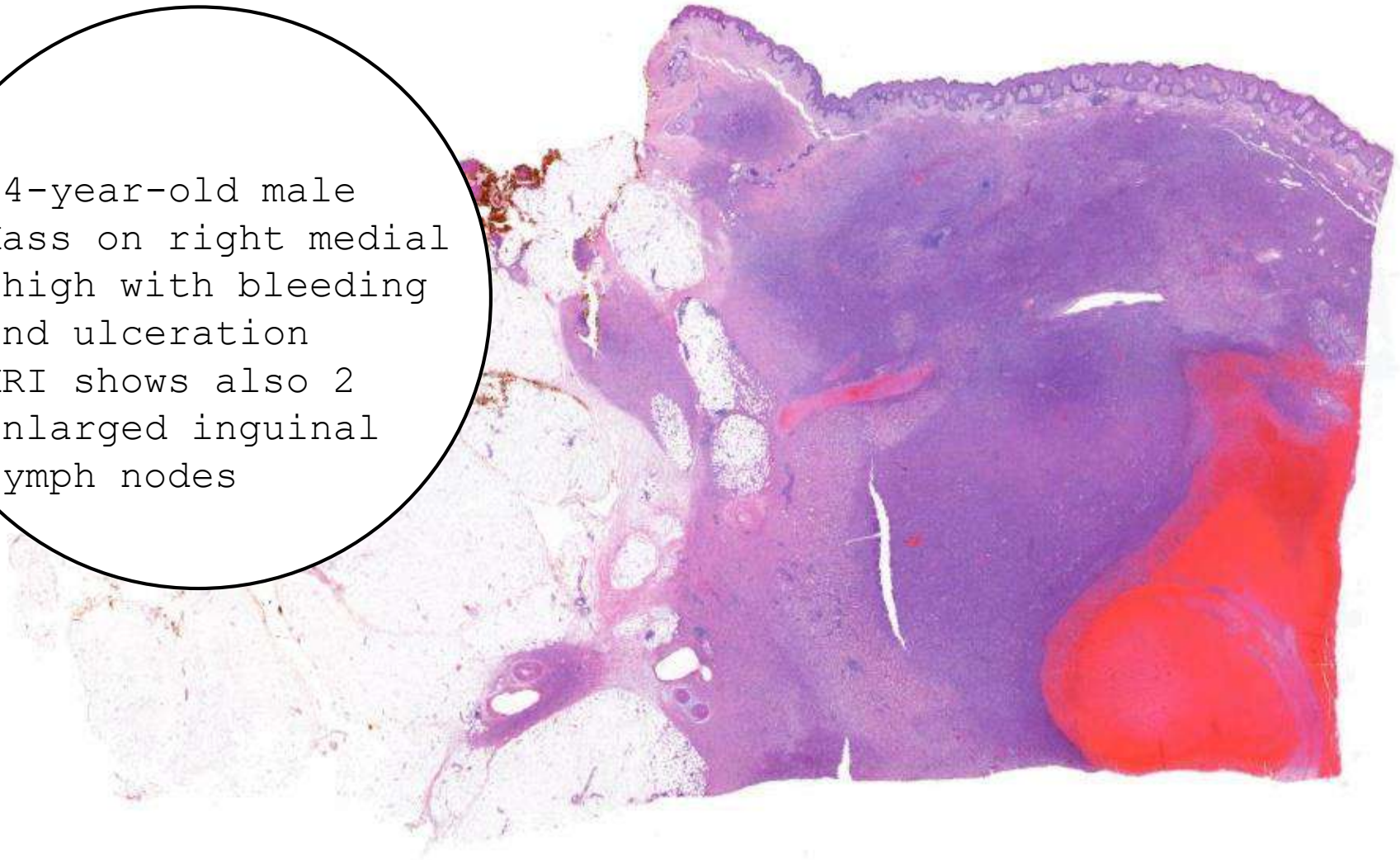


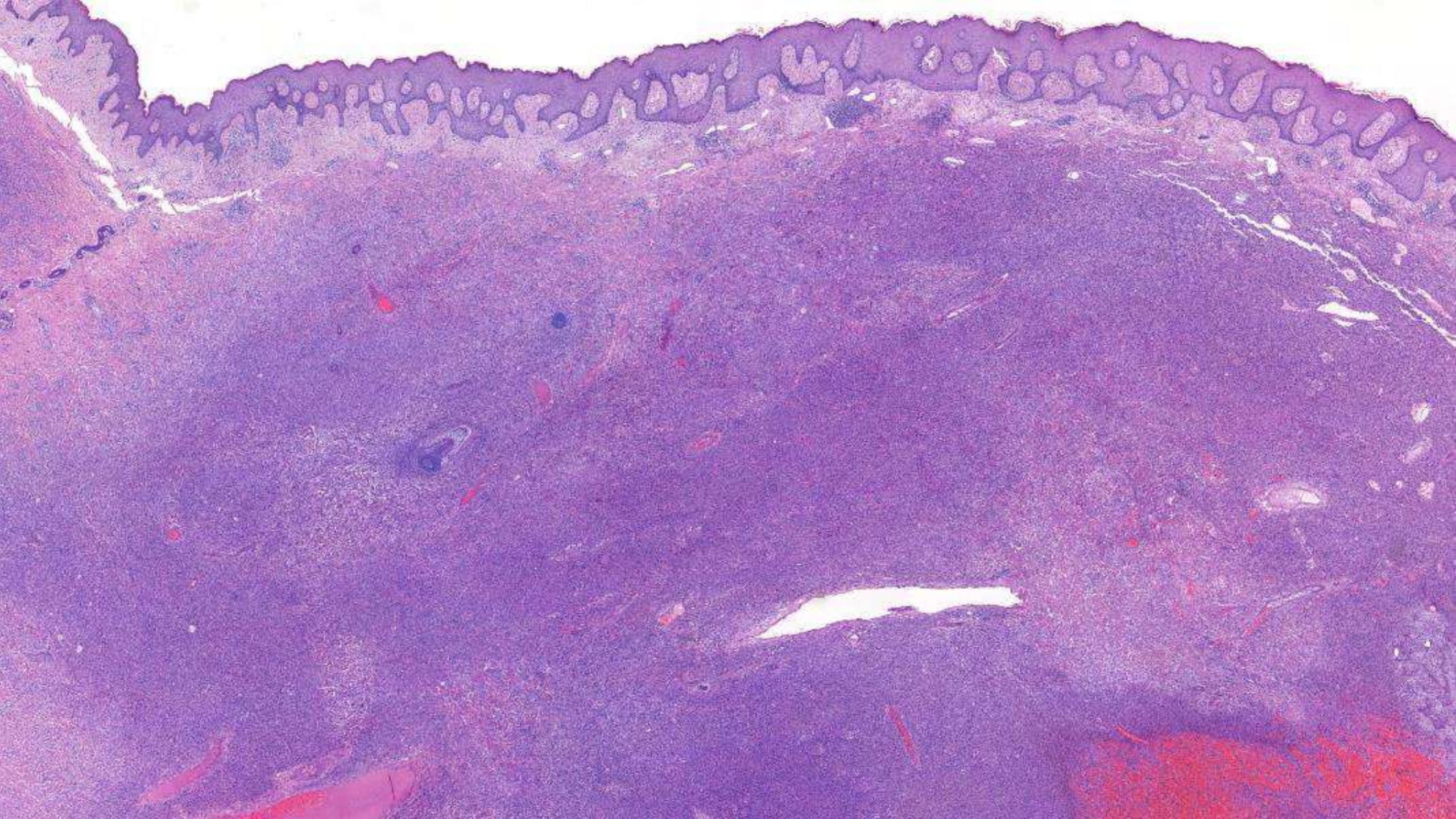


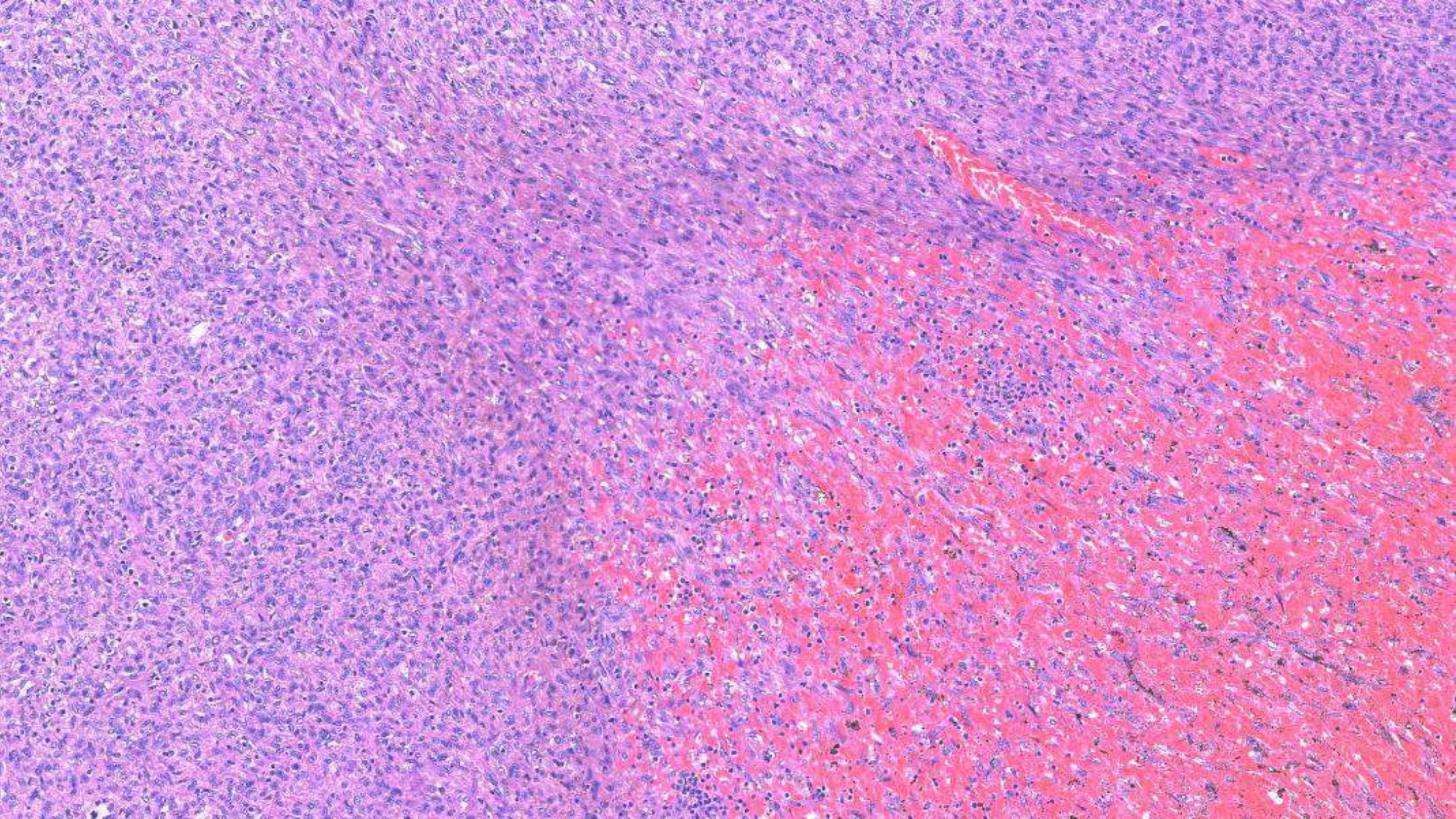

CD20
CD30
PD-1
CD20/CD30

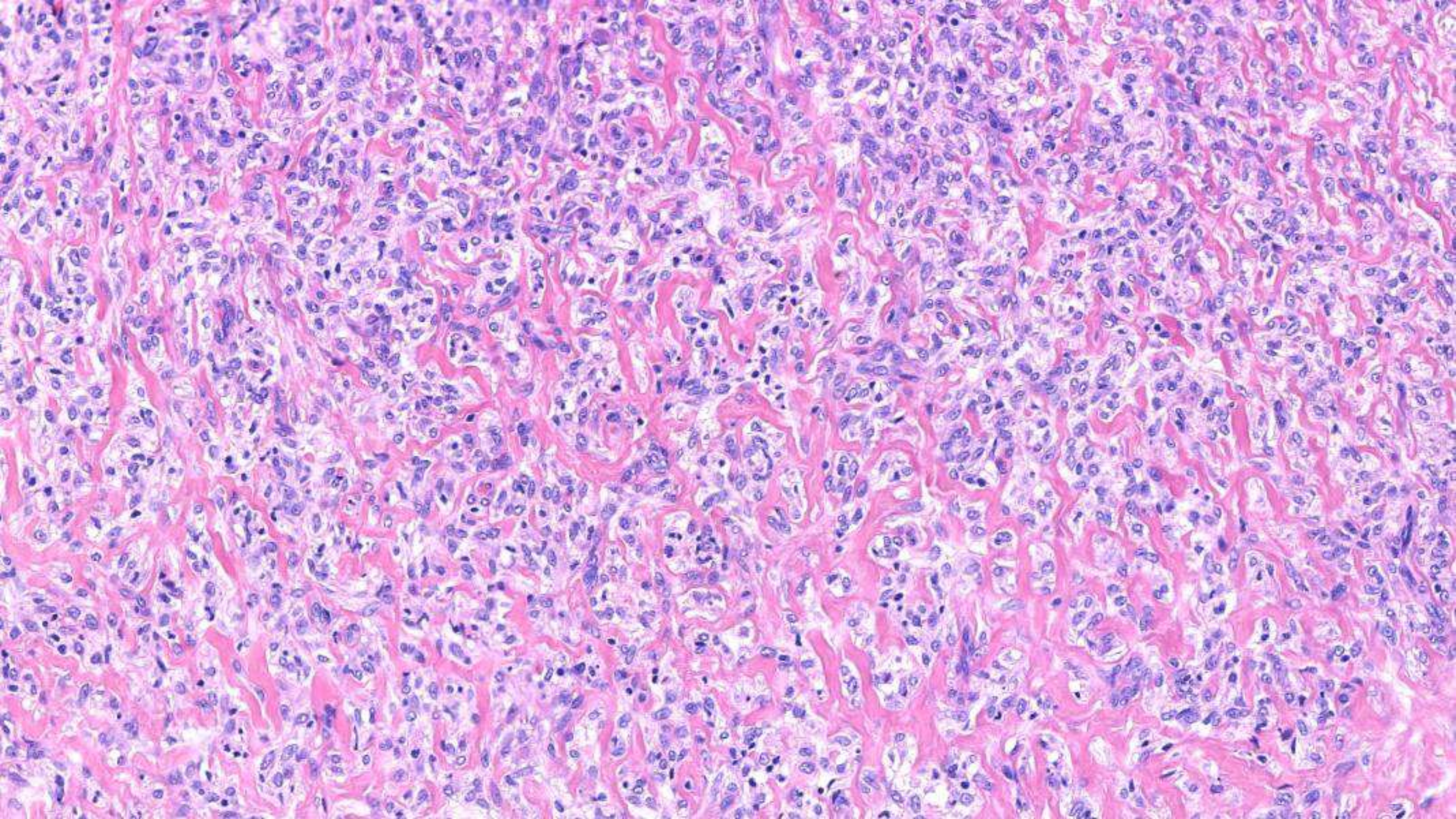
Case 6

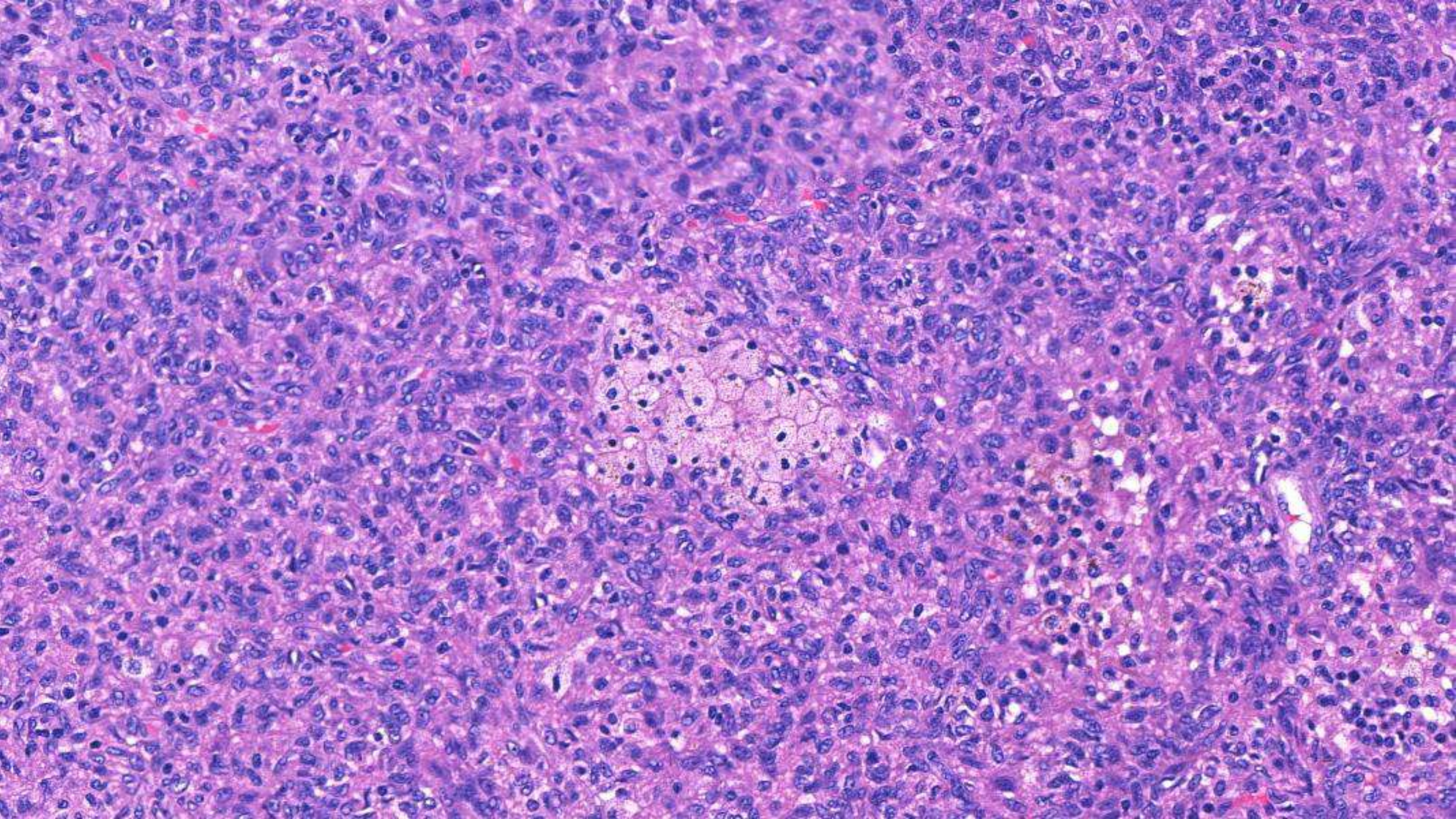
54-year-old male
Mass on right medial thigh with bleeding and ulceration
MRI shows also 2 enlarged inguinal lymph nodes

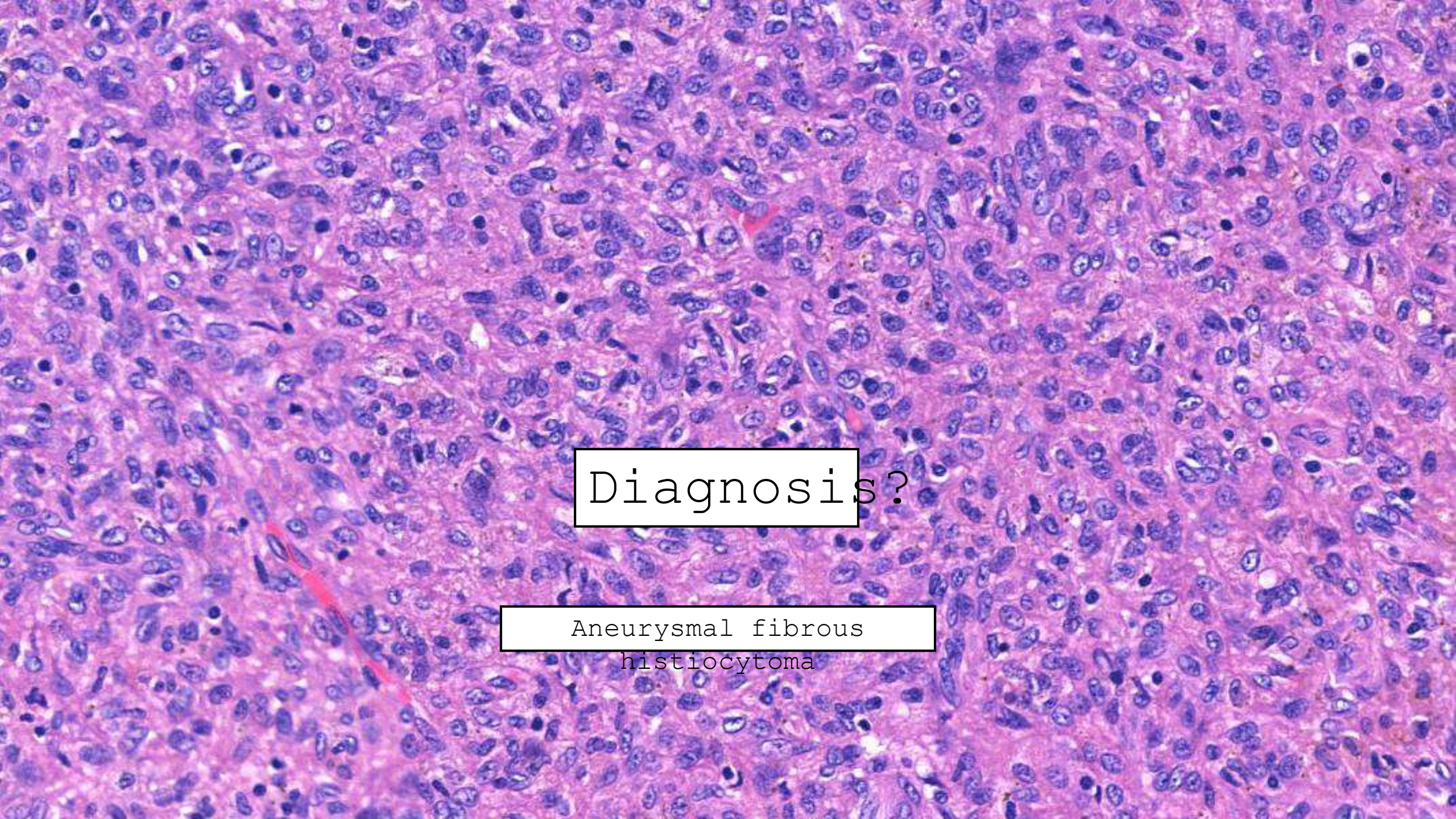




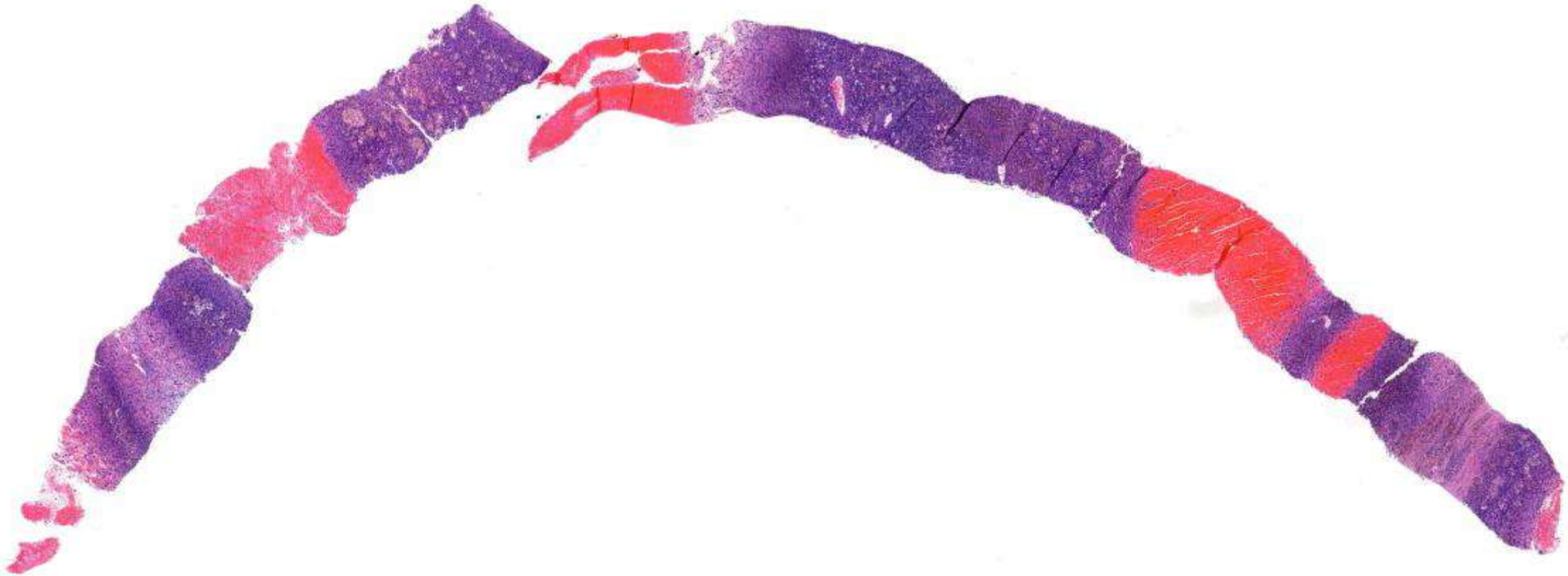


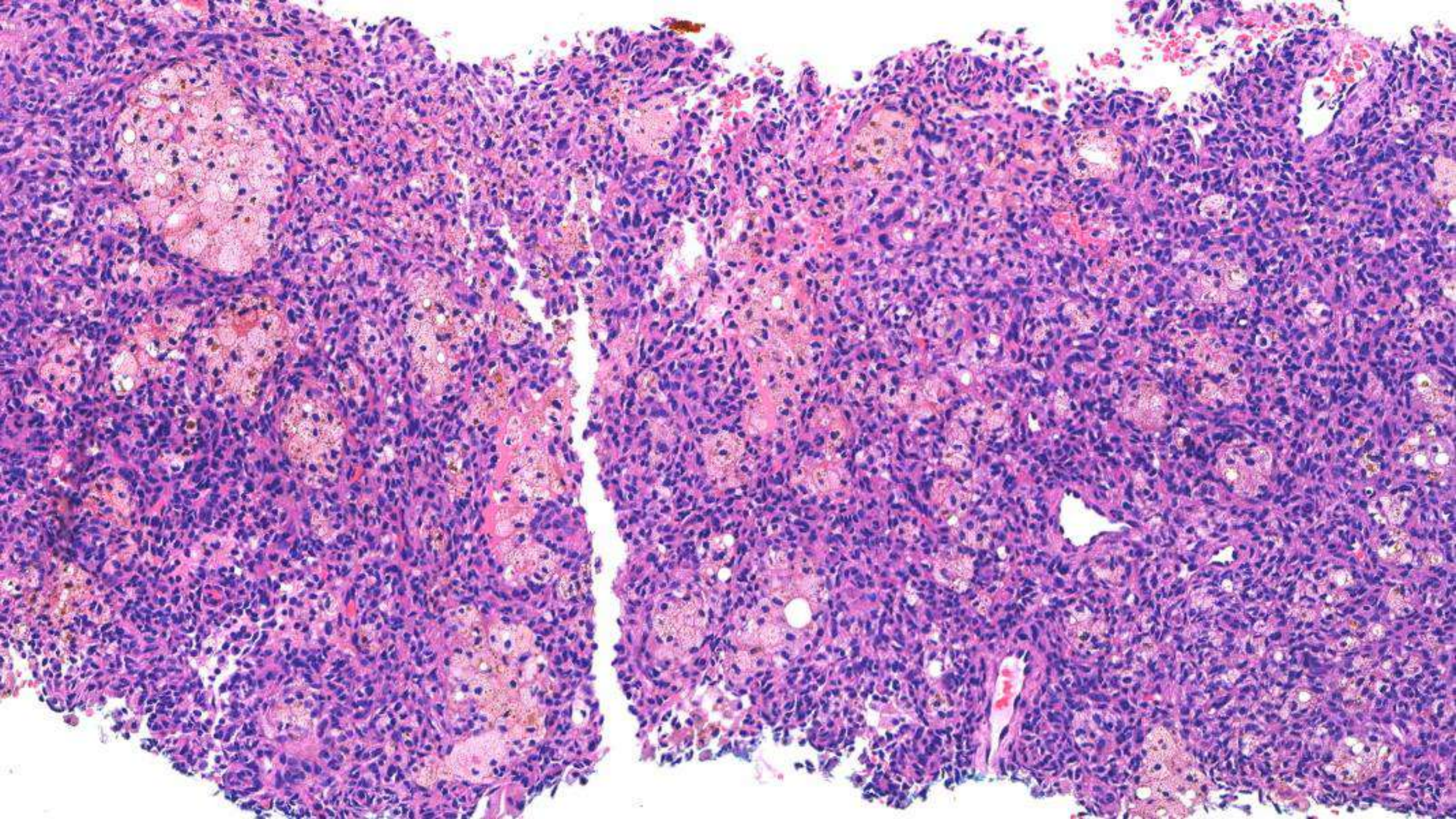


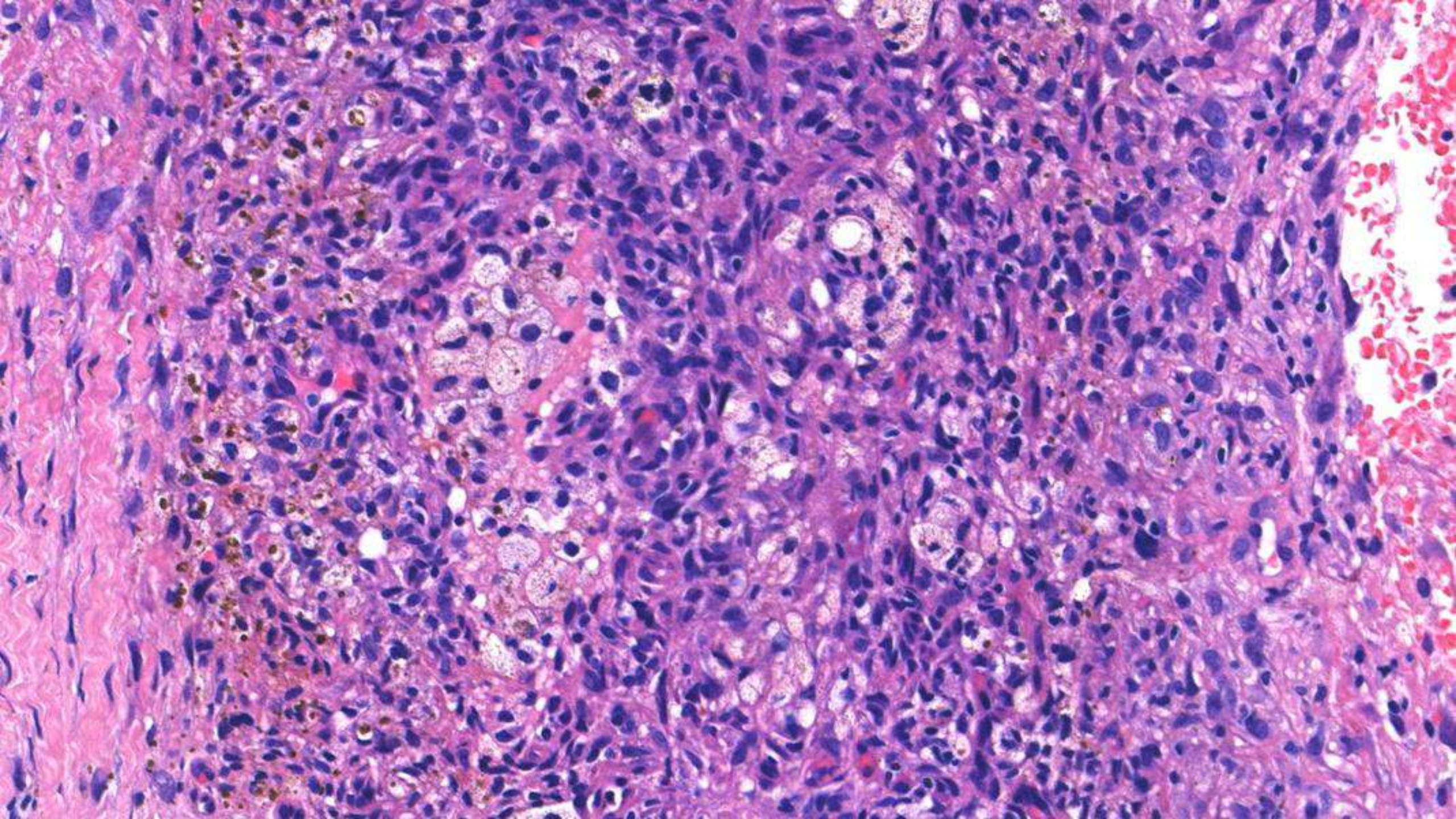


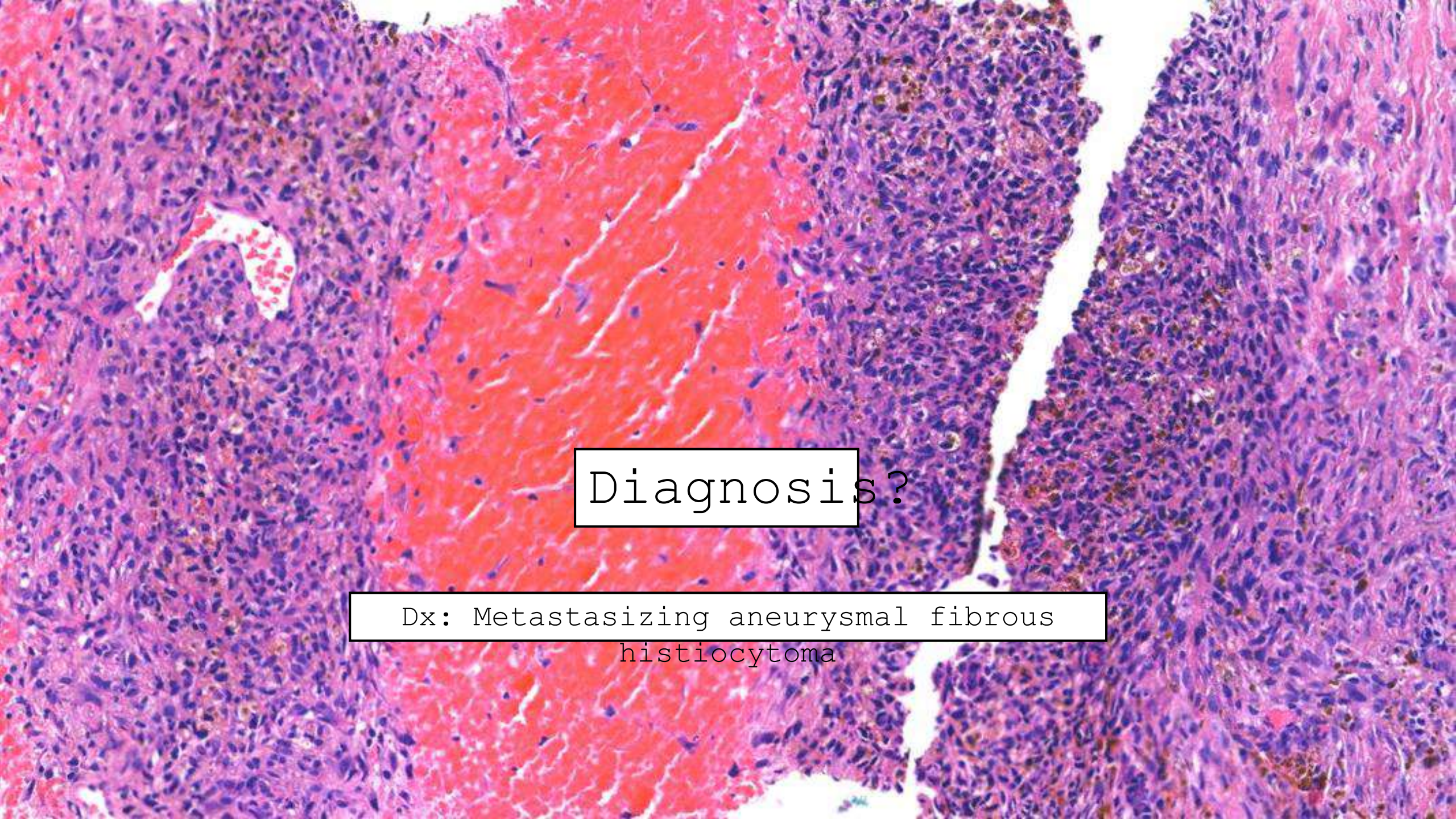

Diagnosis?
Aneurysmal fibrous histiocytoma

Core biopsy from inguinal lymph





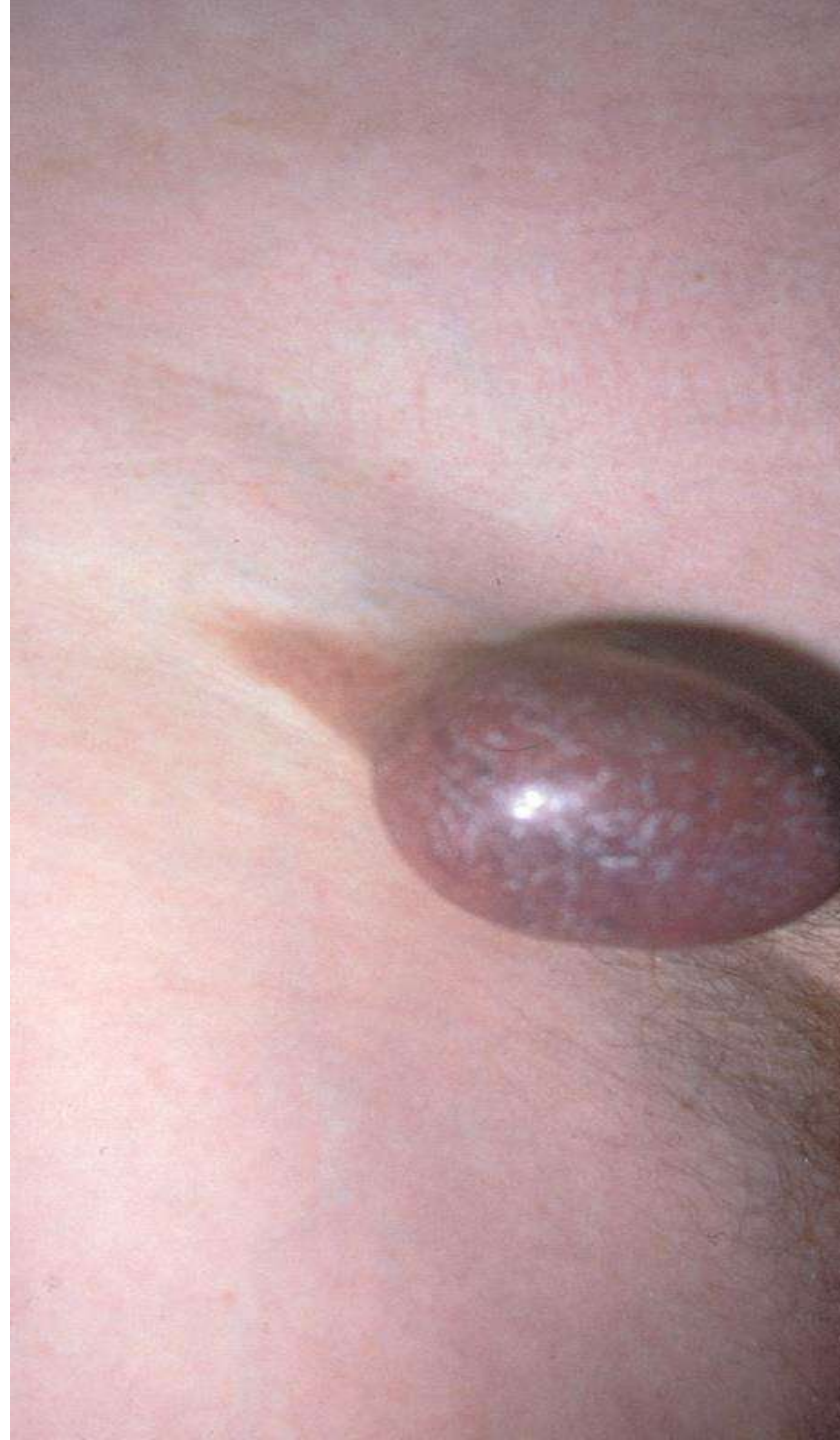



Diagnosis?
Dx: Metastasizing aneurysmal fibrous histiocytoma

ANEURYSMAL FIBROUS HISTIOCYTOMA (FH)

CLINICAL FEATURES

- Middle age adults
- F > M
- Up to 4 cm (occasionally larger)
- Rapid growth
- Often confused with vascular tumour
- 19% recurrence rate



ANEURYSMAL FH

HISTOLOGICAL FEATURES

- Often polypoid
- Numerous blood-filled cystic spaces
- Resemblance to cavernous vascular channels
- No endothelial lining
- Abundant haemosiderin
- Moderate mitotic rate
- Background as that of common FH
- Different variants of FH can overlap

Subcutaneous Mx
AFH

- 16 cases of cutaneous fibrous histiocytoma (FH) that were morphologically benign but had locoregional or distant metastasis
- The patients, with a mean age of 42, had primary tumors located on various body parts, such as the leg, trunk, and shoulder
- Histologically, the tumors displayed a mix of spindle and histiocytoid cells, with varying features like cellular, aneurysmal, or atypical types
- Tumor sizes ranged from 1 to 5 cm, and most involved the dermis, with some extending into the subcutis
- 10 patients experienced local recurrence, with 4 having multiple recurrences, and metastasis occurred primarily in the lungs, lymph nodes, and soft tissues
- 6 patients died from the disease, while others are alive with metastatic disease or disease-free. The study highlights that while metastasis in benign FH is rare, aggressive behavior may occur, especially with early or frequent local recurrences, which warrants closer clinical monitoring

Doyle LA, Fletcher CD. Metastasizing "benign" cutaneous fibrous histiocytoma: a clinicopathologic analysis of 16 cases. Am J Surg Pathol. 2013 Apr;37(4):484-95.

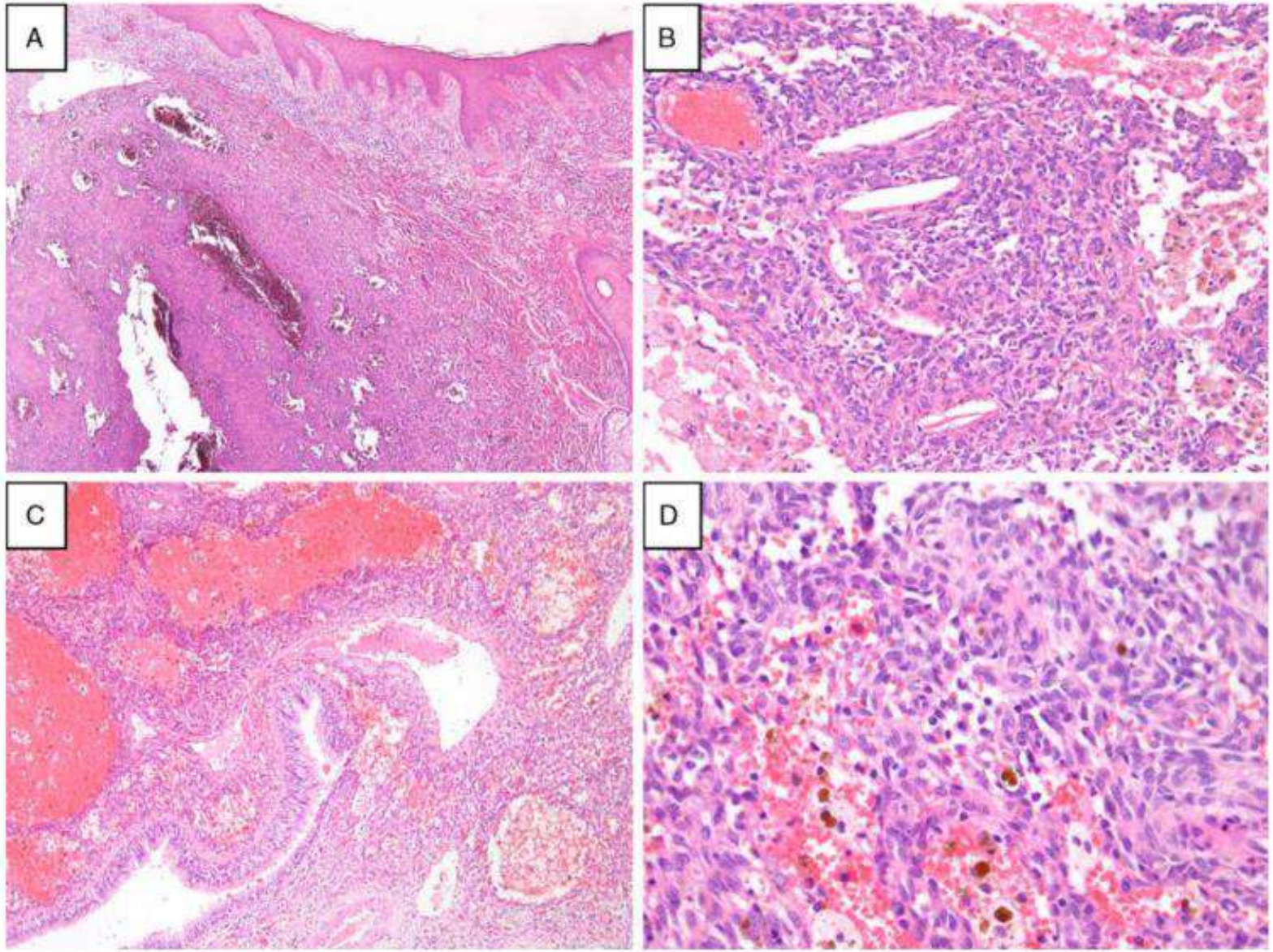


FIGURE 2. Aneurysmal cutaneous FH (shoulder, patient 5) with dilated blood-filled spaces (A). Biopsy of an axillary lymph node with bland histiocytoid tumor cells associated with prominent stromal hemorrhage, hemosiderin deposition, and cholesterol clefts (B). Lung metastases in this patient were solid and cystic (C), and the tumor was morphologically similar to the primary aneurysmal FH (D).

VARIANTS WITH CLINICOPATHOLOGICAL RELEVANCE

- Cellular FH (local recurrence 25%)
- Aneurysmal FH (local recurrence 18%)
- Atypical FH (local recurrence 19%)

Anecdotal metastasis in the three variants plus ordinary and epithelioid

(latter not a variant of DF/FH)

TABLE 2. Summary of Previously Reported Cases of Metastasizing Cutaneous FHs

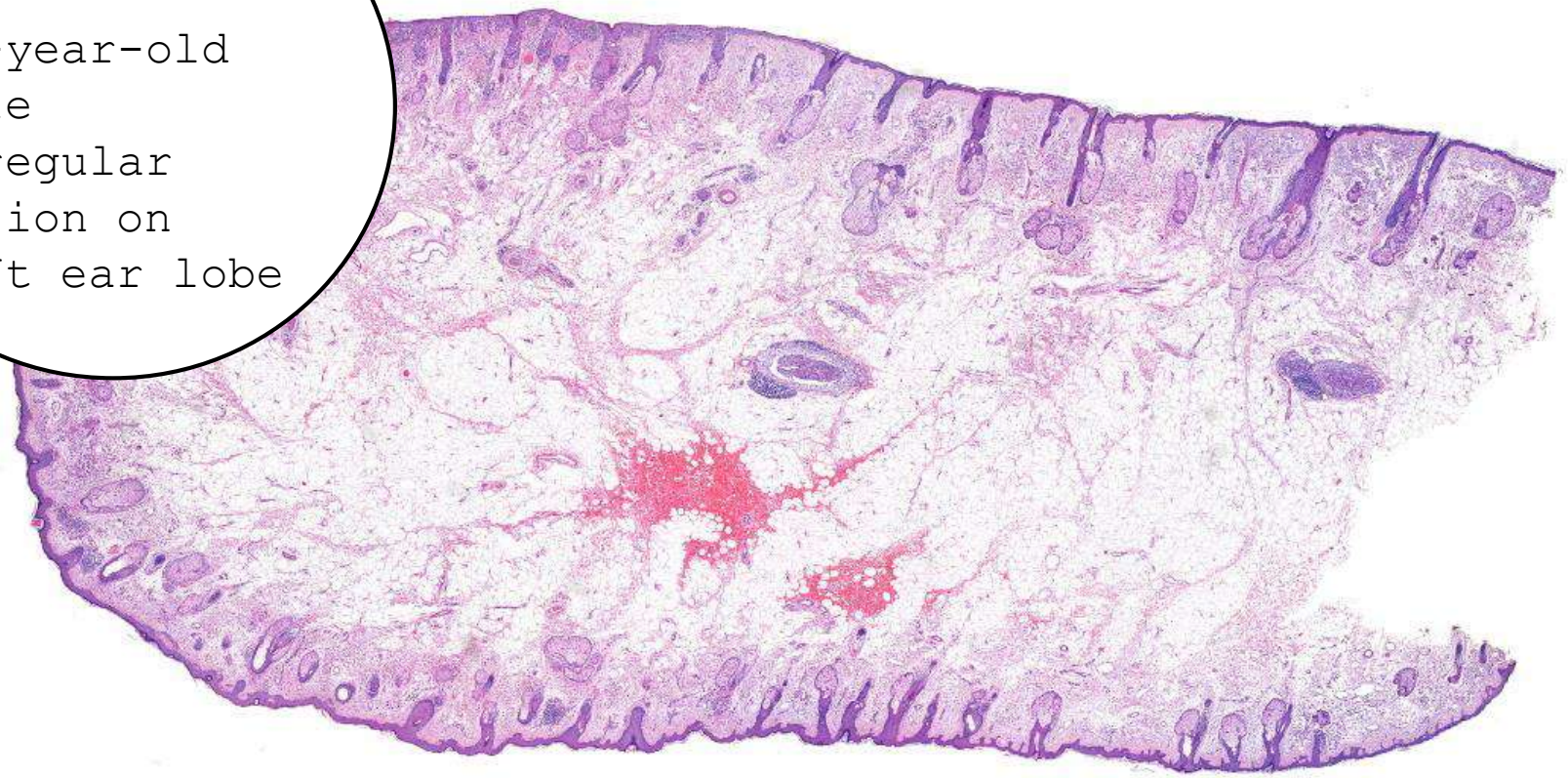
References	No. Cases	Histologic Type(s)	Local Recurrence	Metastatic Site(s)	Outcome
Joseph et al[24]	1/?2	Ordinary	Yes	Lung	AWD, 22 y
		NK	NK	Lung	AWD, 2 y
Calonje and Fletcher[5]*	1	Aneurysmal	Yes, multiple	Lymph node	Case 1 of present study
Colome-Grimmer and Evans[25]	2	Cellular	Yes, multiple	Lung, lymph nodes	NED, 9 y
		Cellular	Yes	Lung, lymph nodes	AWD, 15 y
Guillou et al[26]	3	Aneurysmal/ atypical	No	Lymph node	Mets, 19 y
		Cellular	No	Lymph node	Mets, 4 mo; NED, 14 y
		Cellular	Yes, multiple	Lymph node	Mets, 20 mo; NED, 36 mo
De Hertogh et al[13]*	1	Cellular	No	Lung	Case 3 of present study
Kaddu et al[7]*	2	Atypical/cellular	No	Lung	Case 3 of present study
		Atypical	Yes	Lymph nodes, soft tissues	Case 15 of present study
Osborn et al[27]	2	Cellular	Yes, multiple	Lung	AWD, 4 y
		Cellular	NK	Lung	NK
Bisceglia et al[28]	2	Ordinary	Yes, multiple	Lymph nodes	NED, 5 y (11 mo after mets)
		Cellular	Yes	Lymph nodes	NED, 12 y (12 mo after mets)
Gu et al[29]	1	Cellular	No	Lung	NK
Szumera-Ciecklewicz and Ptaszynski[30]	1	Ordinary	No	Lymph nodes	NED, 3 y (1 y after mets)

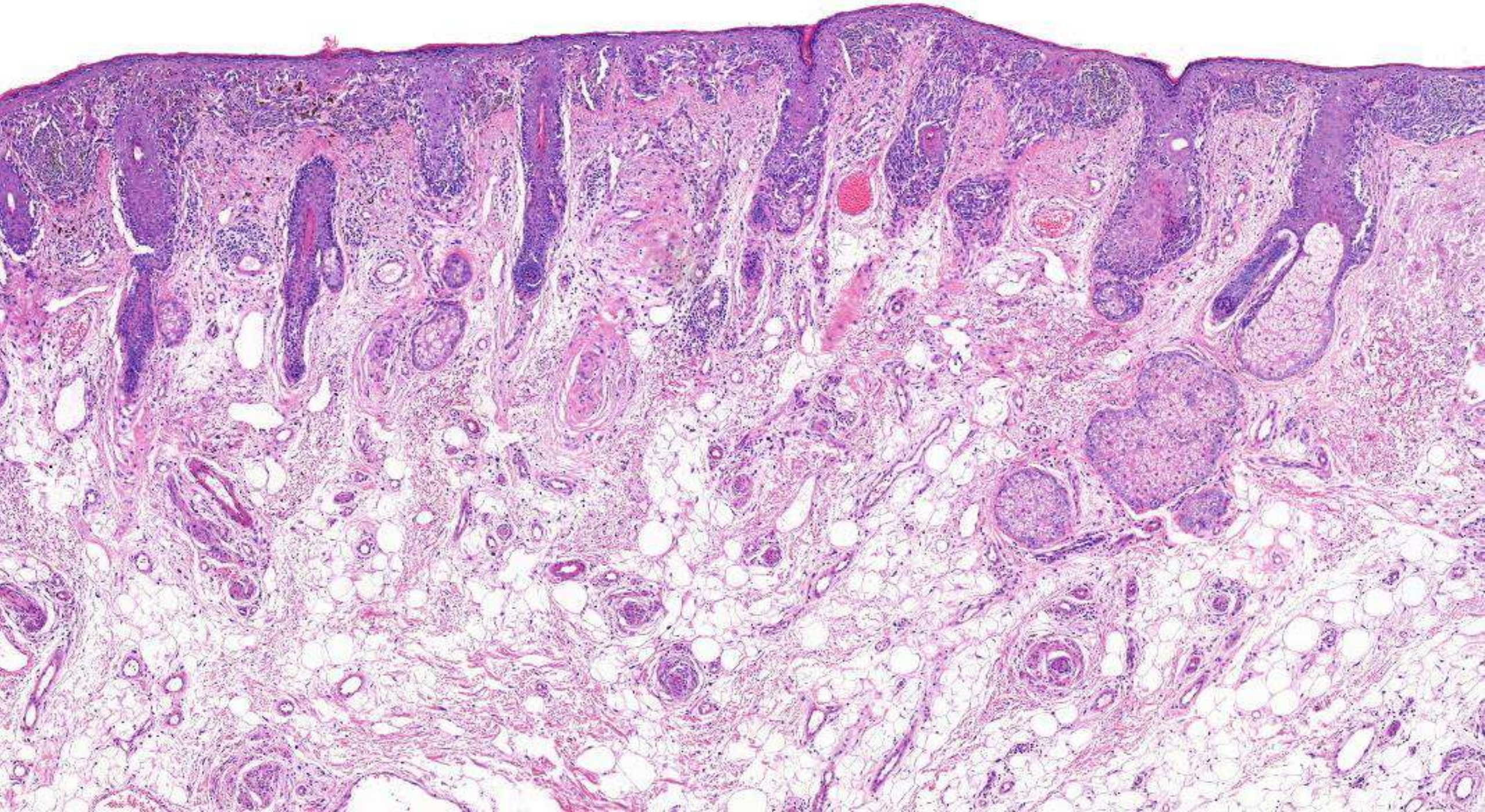
*Cases (3) included in the current study.
AWD indicates alive with disease; DOD, died of disease; NA, not applicable/not available; NED, no evidence of disease; NK, not known.

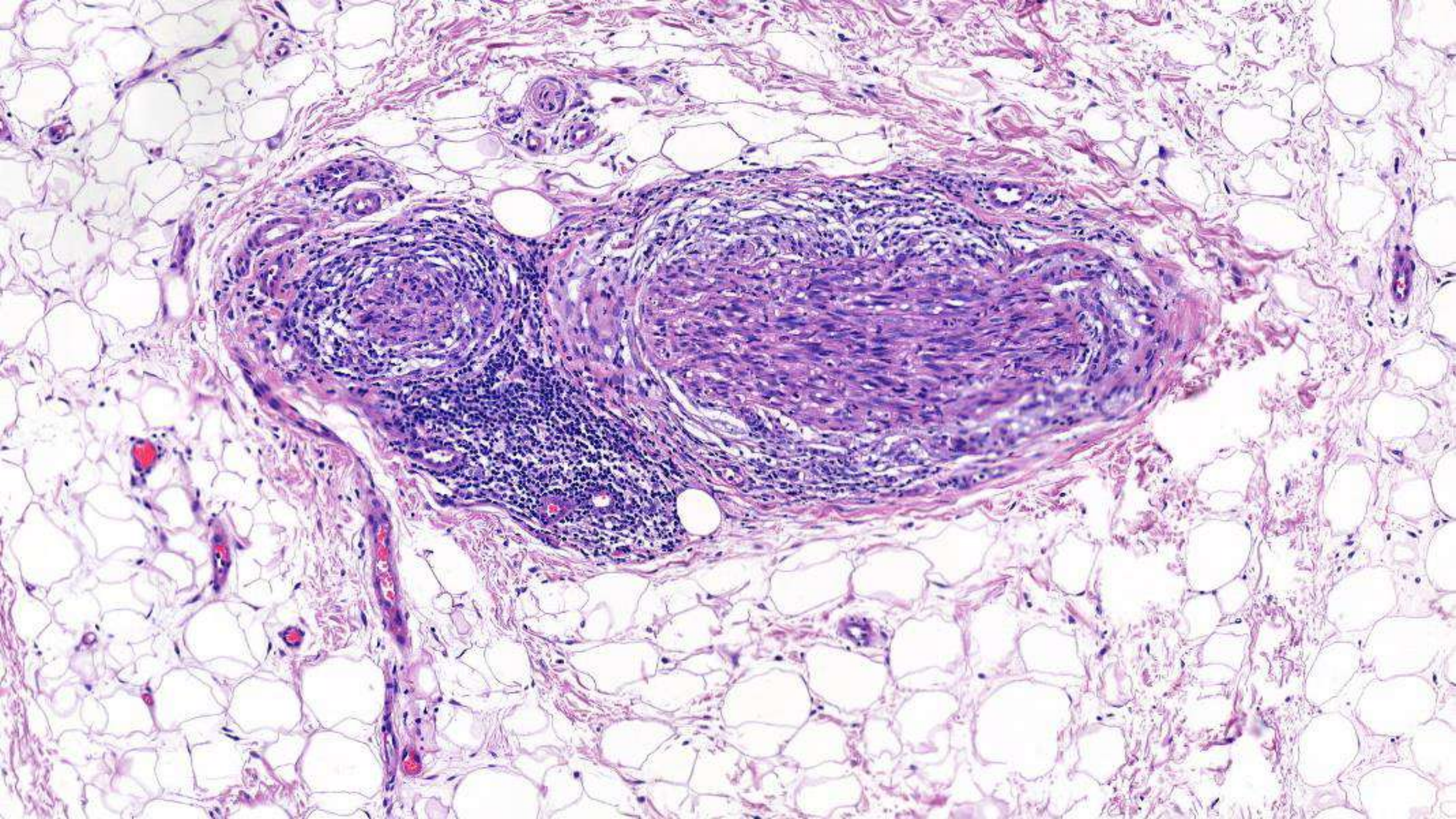
Doyle LA, Fletcher CD. Metastasizing "benign" cutaneous fibrous histiocytoma: a clinicopathologic analysis of 16 cases. Am J Surg Pathol. 2013 Apr;37(4):484-95.

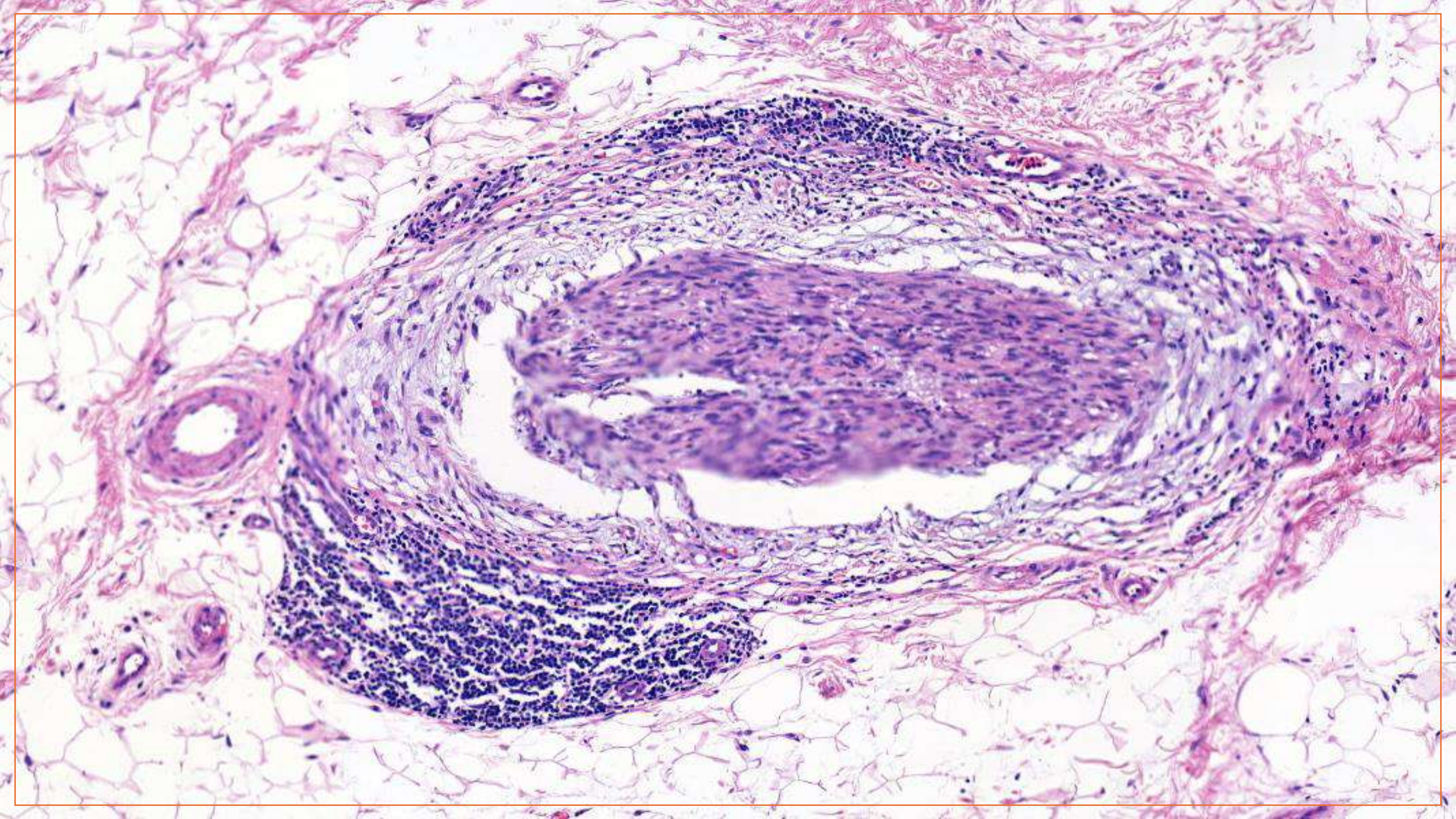
Case 7

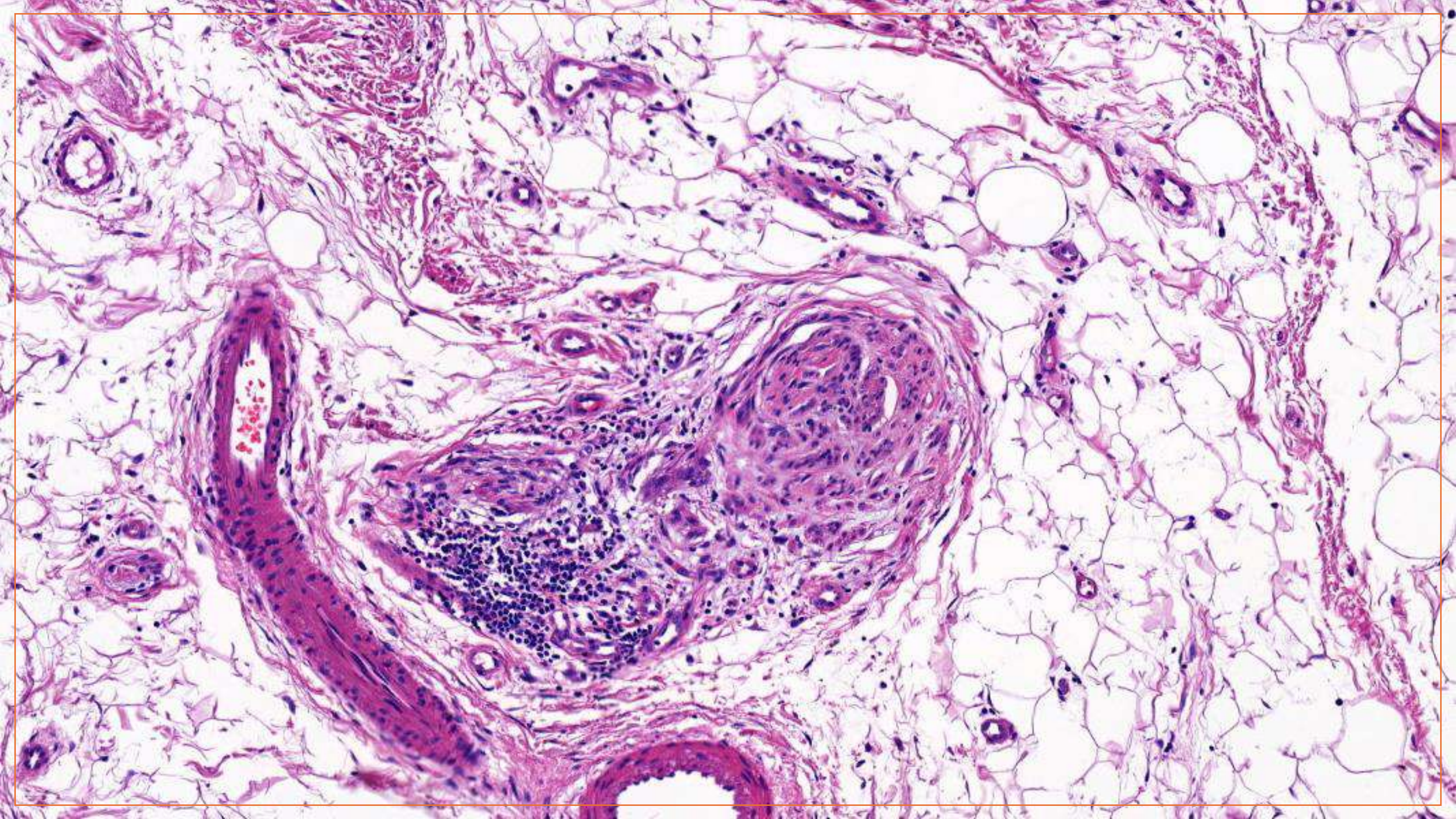
82-year-old male
Irregular lesion on left ear lobe

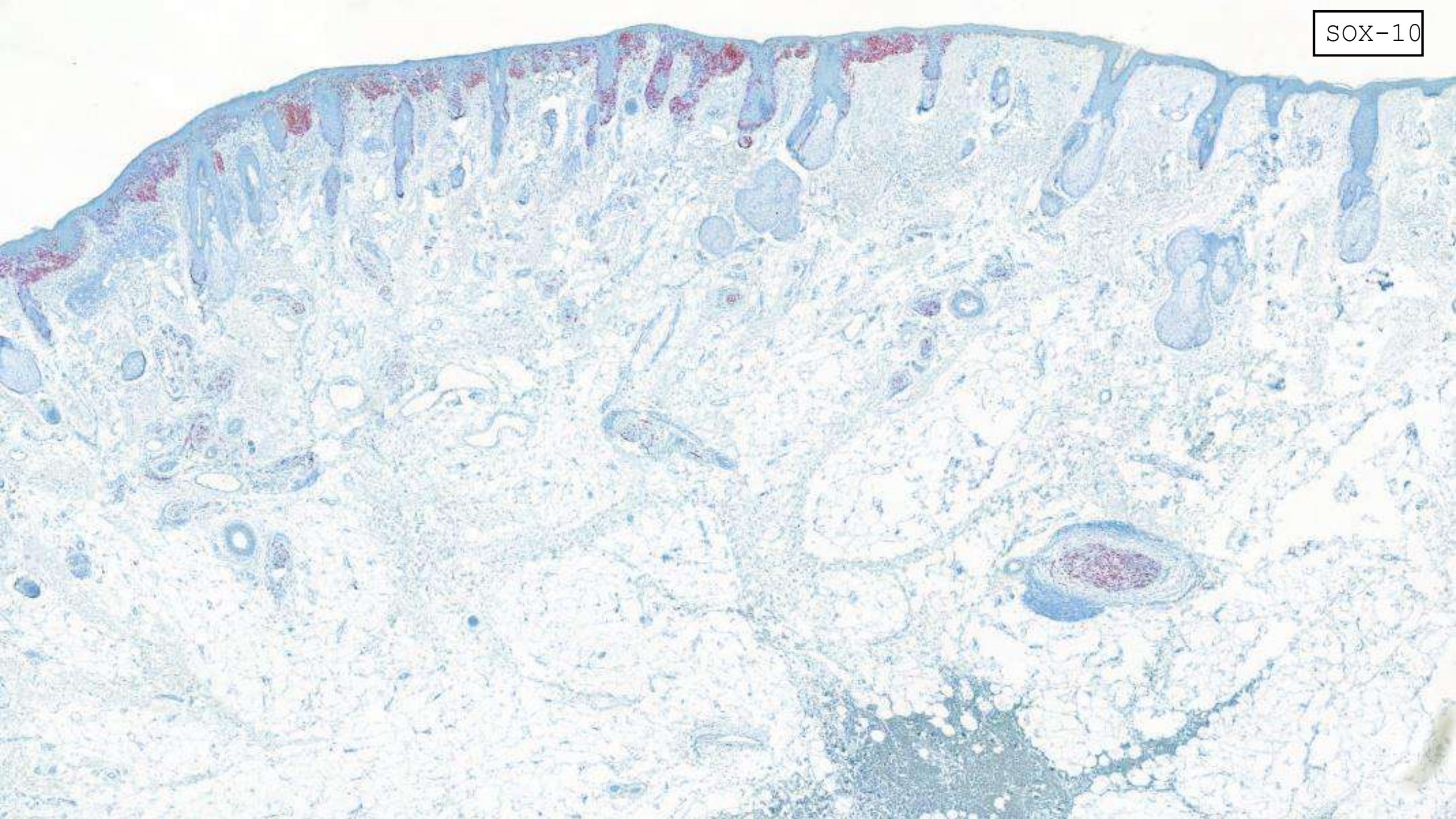


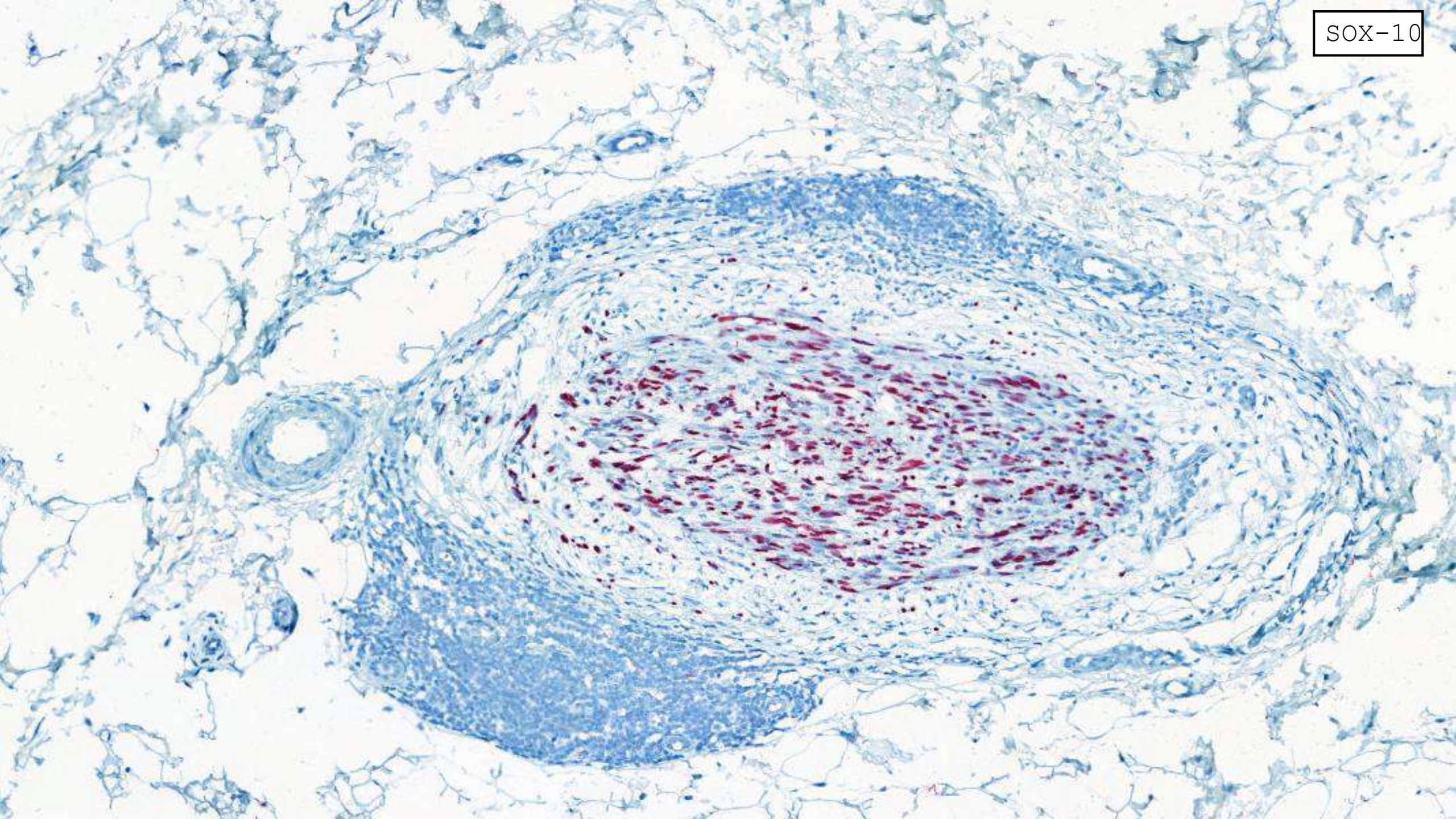


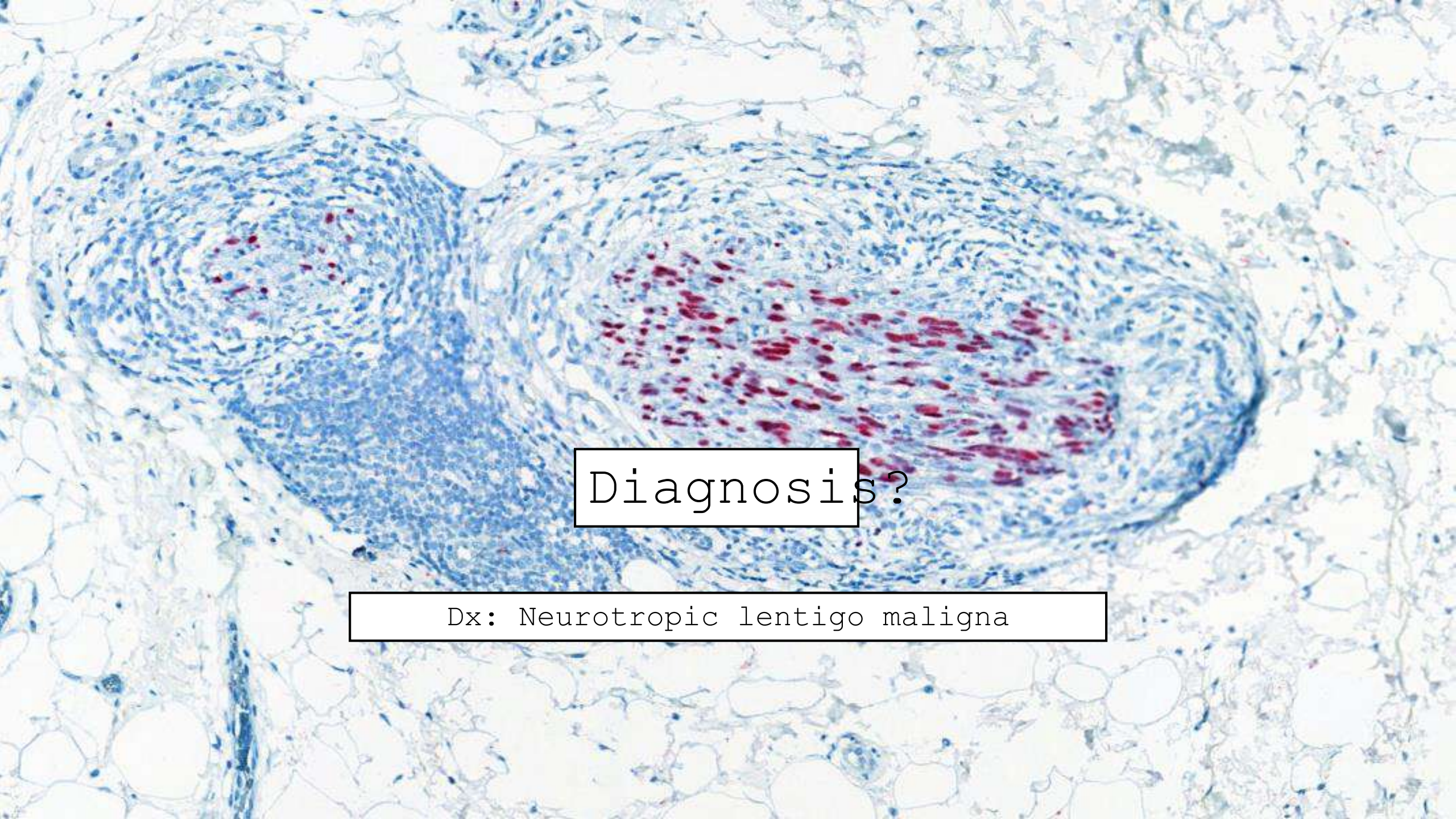







SOX-10


SOX-10


Diagnosis?
Dx: Neurotropic lentigo maligna

- Neurotropic cutaneous melanoma is a rare form of melanoma where tumor cells invade nerves, either through perineural invasion (around the nerve) or intraneural invasion (within the nerve)

- Occasionally, melanoma cells may form nerve-like structures, known as neural transformation, though this is not widely accepted

- Neurotropism is most commonly seen in desmoplastic melanoma, but it can also occur in non-desmoplastic melanomas

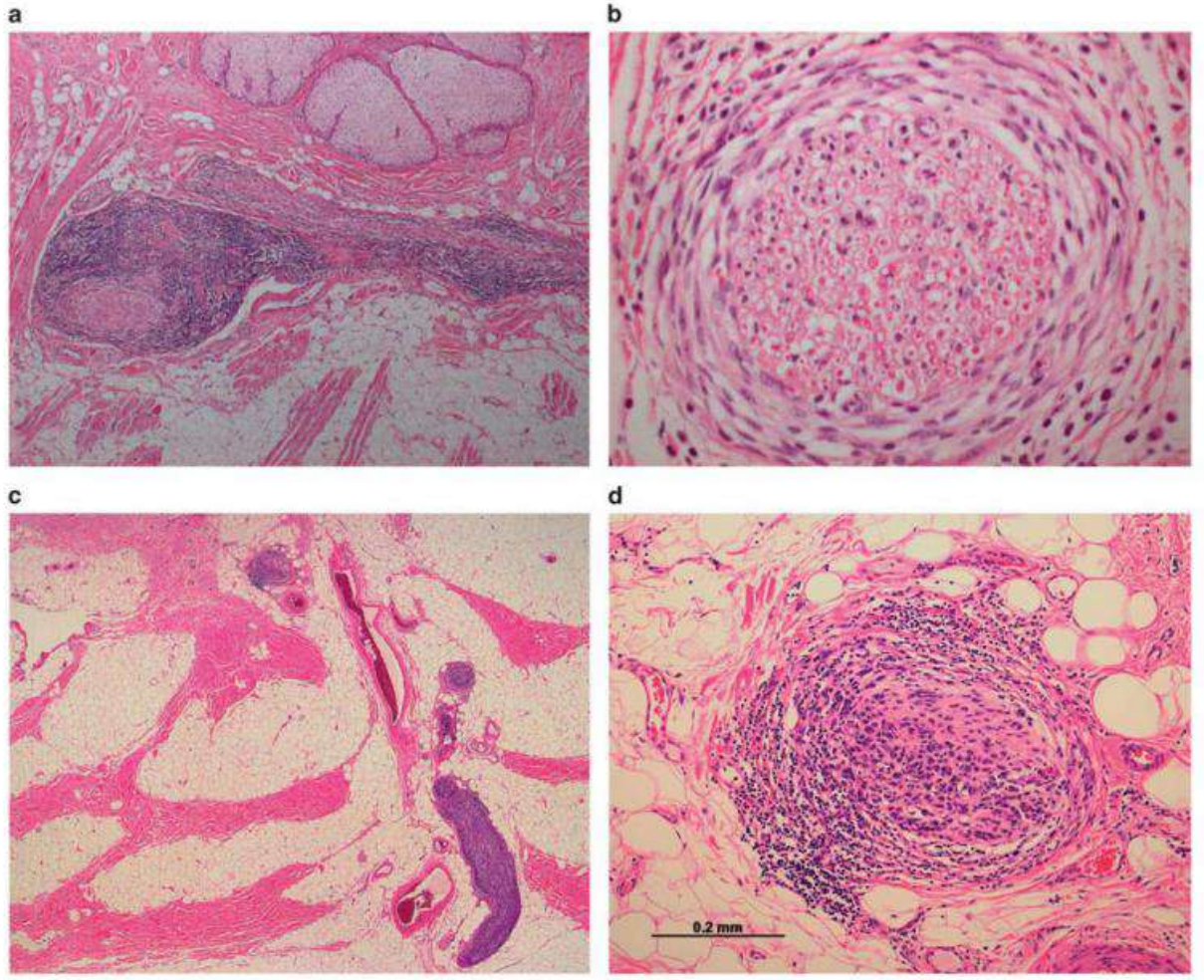


Figure 1 (**a** and **b**) Melanoma involving the nose of 73-year-old male with prominent neurotropism including perineural invasion. (**c** and **d**) Melanoma on the back of a 58-year-old male showing intraneural invasion by epithelioid melanoma cells.

Varey AHR et al. Neurotropic melanoma: an analysis of the clinicopathological features, management strategies and survival outcomes for 671 patients treated at a tertiary referral center. Mod Pathol. 2017 Nov;30(11):1538-1550.

- Neurotropism in melanoma, whether in desmoplastic or non-desmoplastic forms, does not affect survival or recurrence risk compared to other clinicopathological predictors

- Neurotropic melanomas were nearly three times more likely to have a borderline excision margin, increasing the risk of local recurrence fourfold and regional or distant recurrence twofold

- Nonetheless, neurotropic melanomas with borderline margins respond well to adjuvant radiotherapy, which can reduce the risk of local recurrence by half

Varey AHR et al. Neurotropic melanoma: an analysis of the clinicopathological features, management strategies and survival outcomes for 671 patients treated at a tertiary referral center. Mod Pathol. 2017 Nov;30(11):1538-1550.

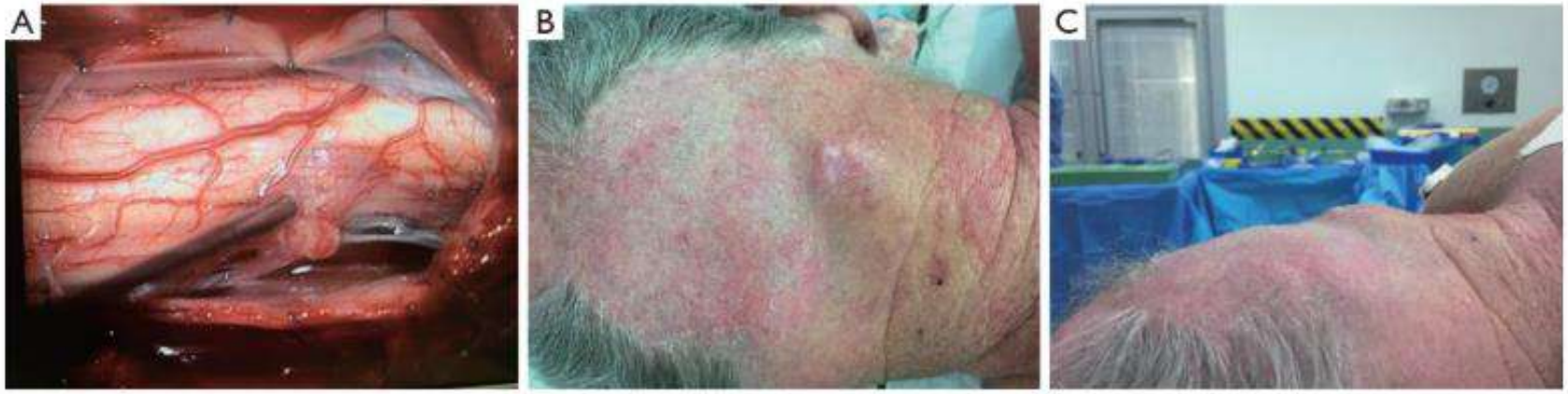


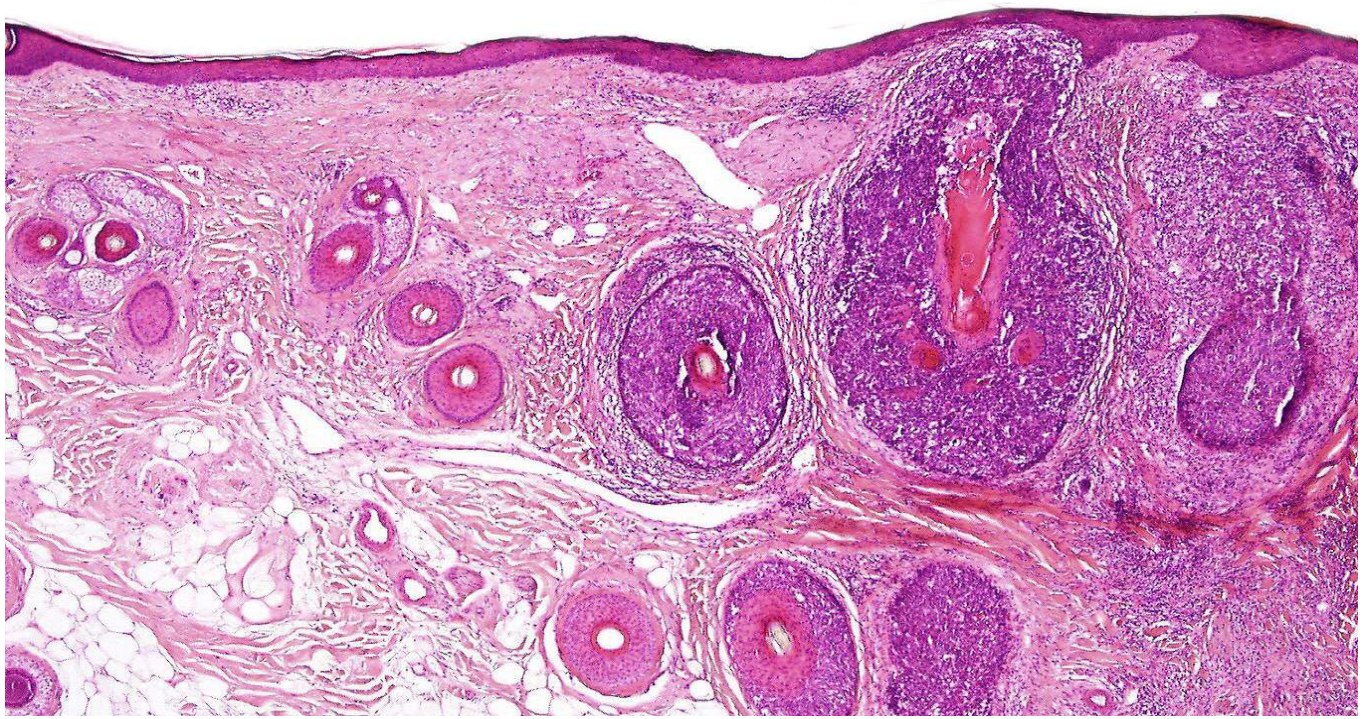
Figure 3 Morphological features of neurotropic melanoma. (A) intra-operative finding of intramedullary extension of the neurotropic melanoma; (B) suboccipital posterior neck region showing amelanotic nodular cutaneous lesion; (C) discoid nodule shaped cutaneous lesion (characteristic morphological appearance of desmoplastic neurotropic melanomas).

- 73-year-old male who experienced rapid deterioration due to neurotropic melanoma spread to the spinal cord, causing myelopathy, loss of sphincter function, and cranial nerve involvement
- He underwent cervical decompression and resection of the intramedullary spinal cord lesion, leading to significant recovery
- Treatment typically involves wide local excision (WLE) with adjuvant radiotherapy, with chemotherapy reserved for disseminated cases

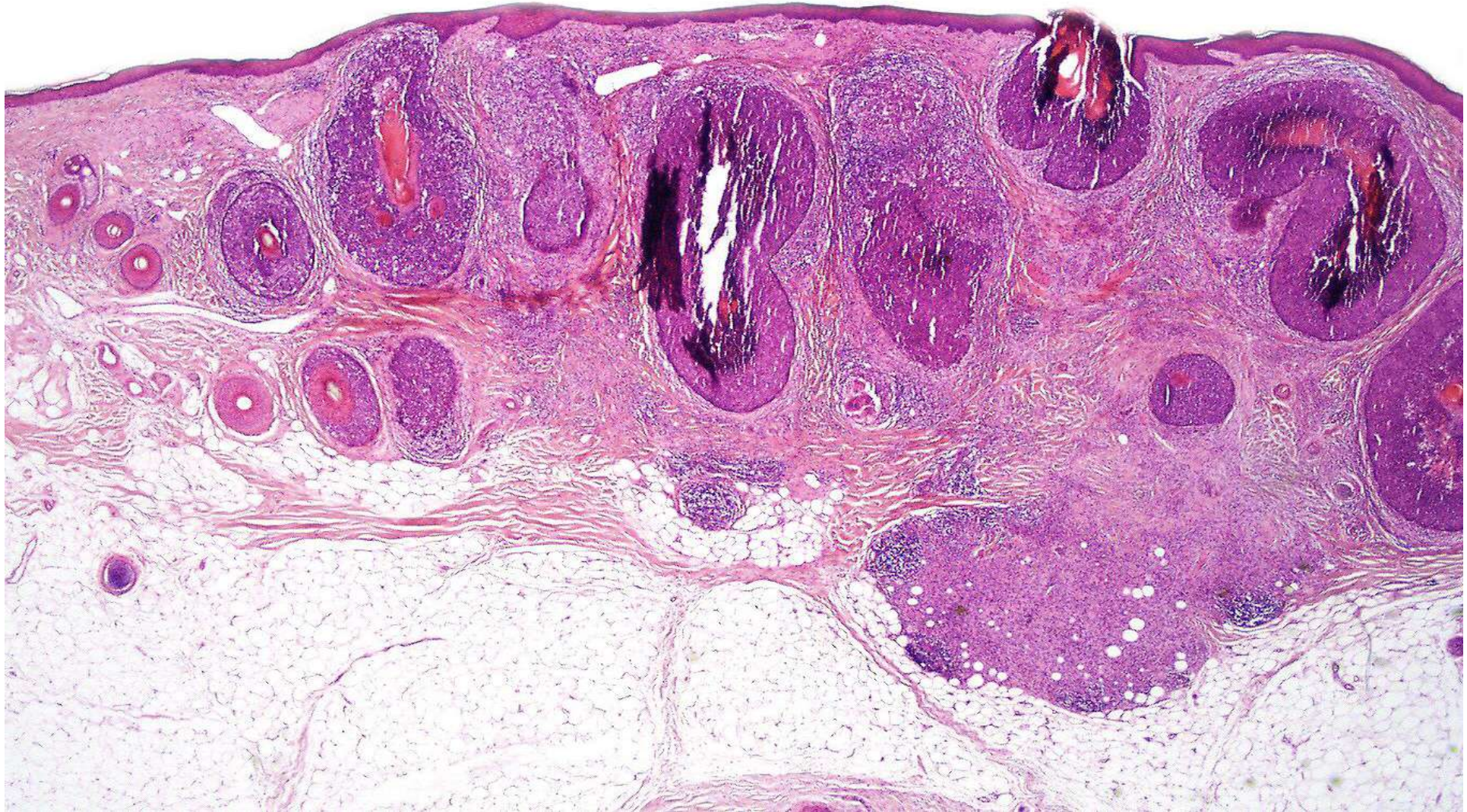
Asad S, Sher I, Peters-Willke J, Jessup P. Neurotropic cutaneous malignant melanoma with contiguous spread to spinal cord, an extremely rare presentation. J Spine Surg. 2016 Mar;2(1):76-81.

Case 8

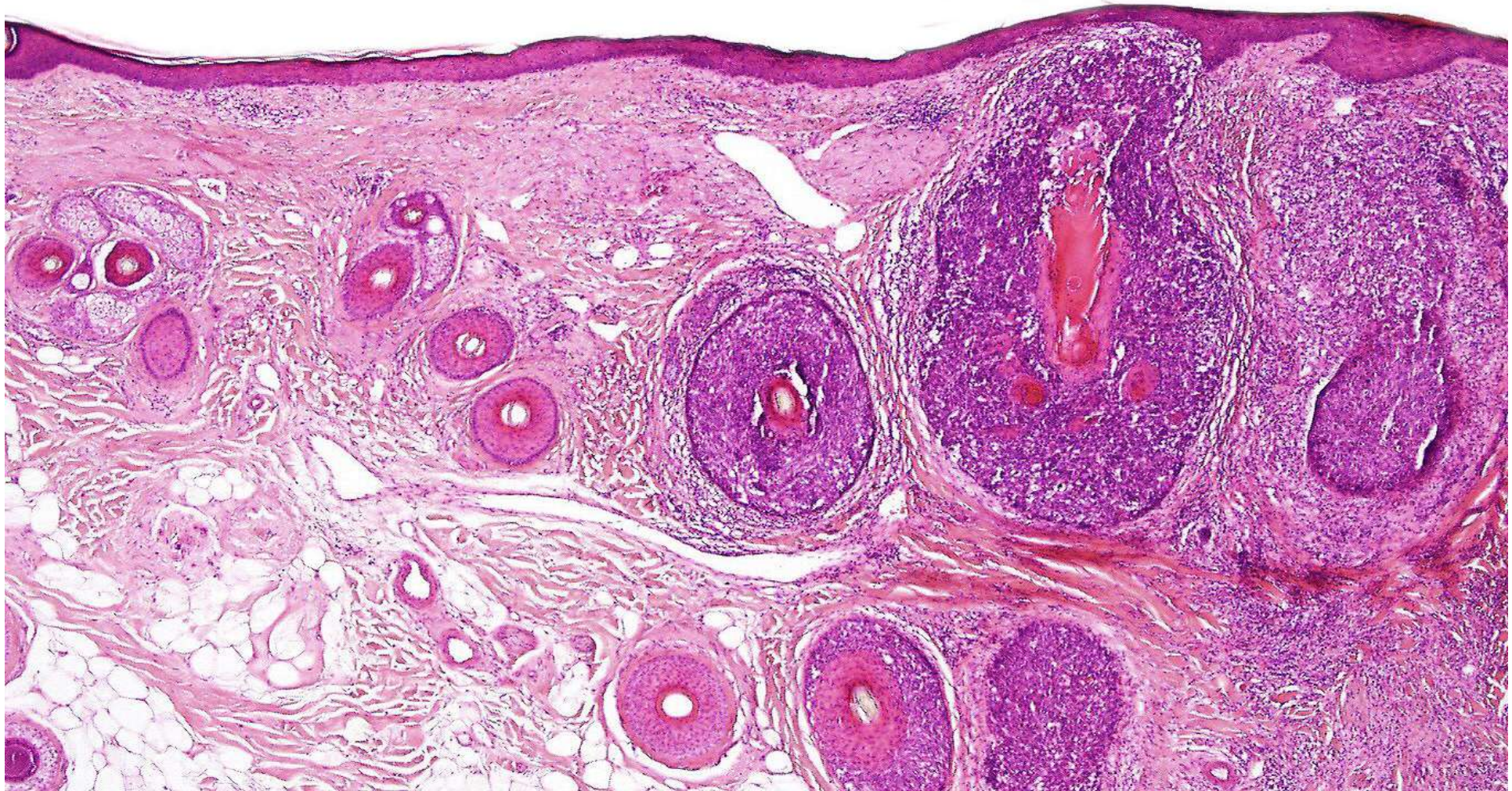
82, female, rapidly growing lesion on scalp
Clinical diagnosis:
?BCC
??Other



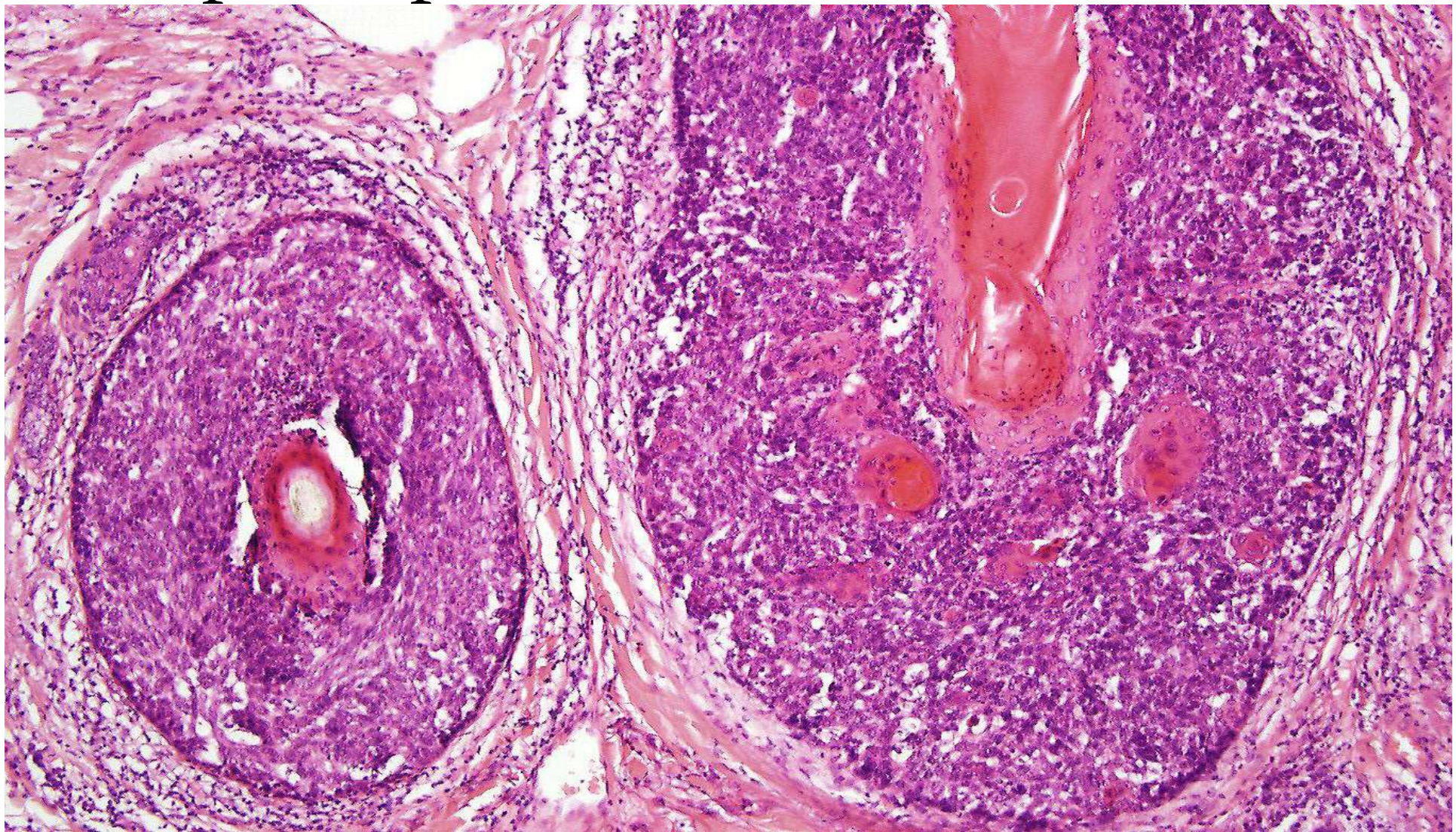
Skin with a relatively normal epidermis and poorly circumscribed dermal tumour extending into subcutaneous tissue



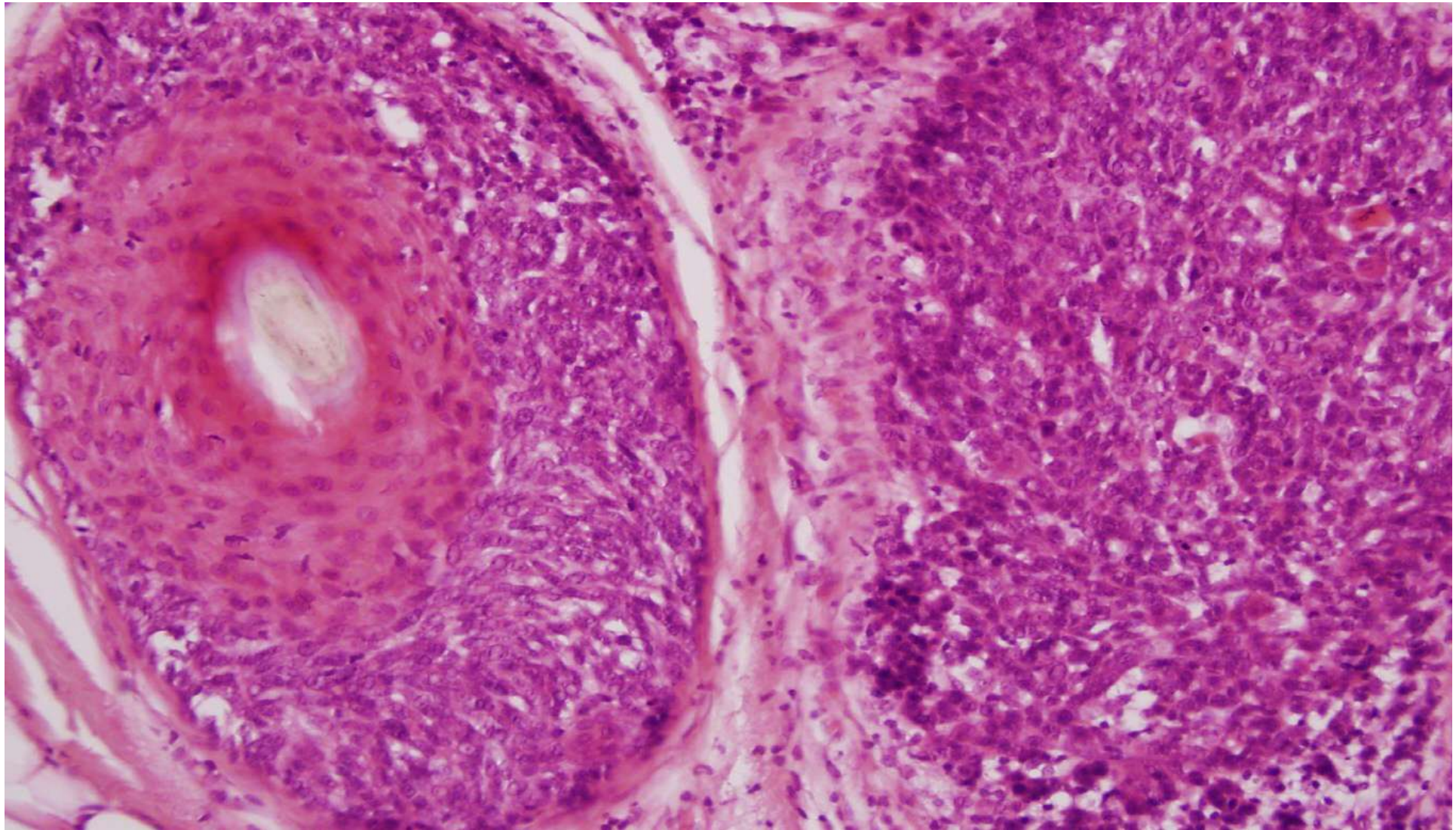
Enlarged and distorted hair follicles with abrupt keratinization resembling a follicular tumour



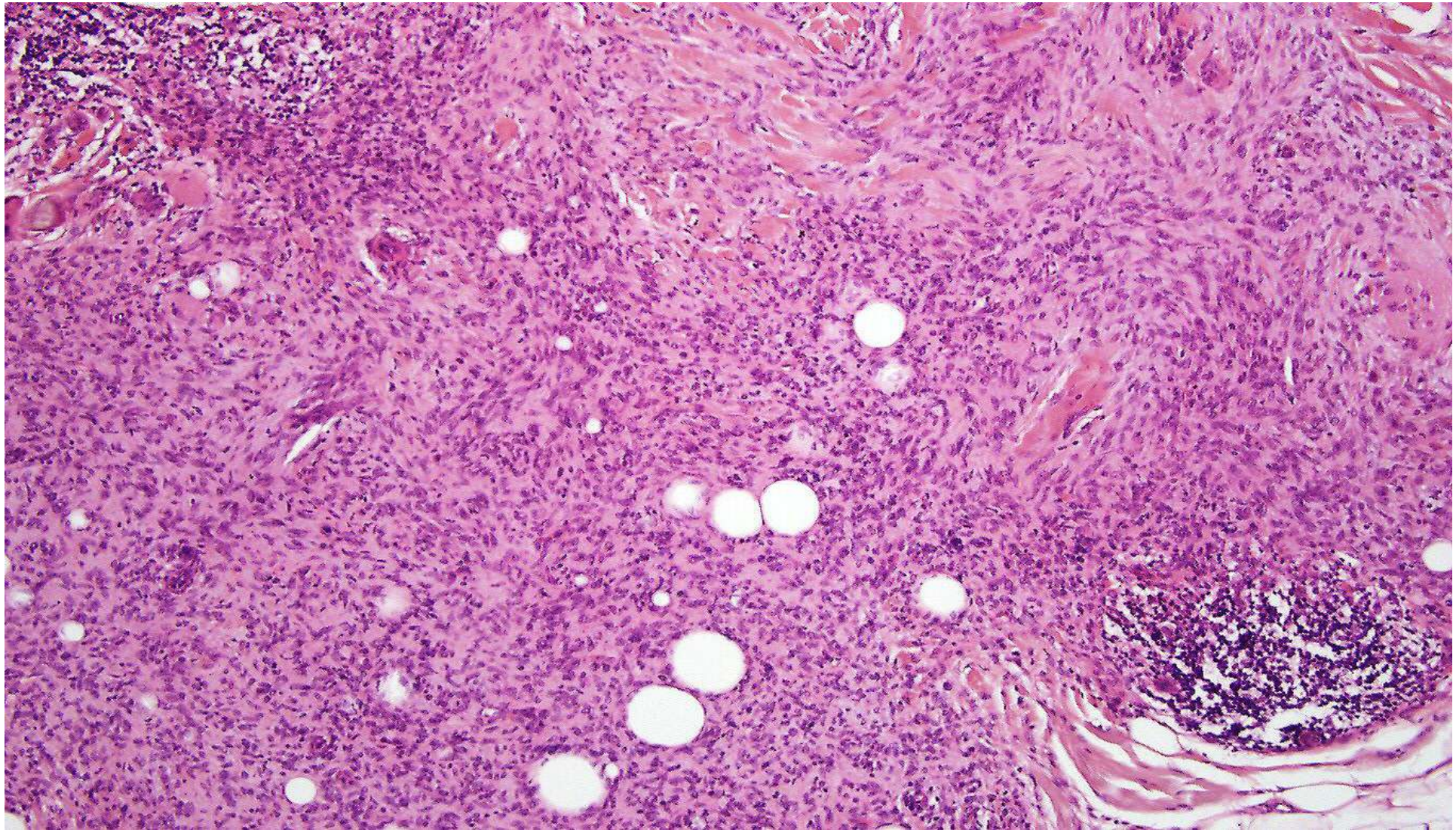
Hair follicles are entirely replaced by pleomorphic epithelioid cells

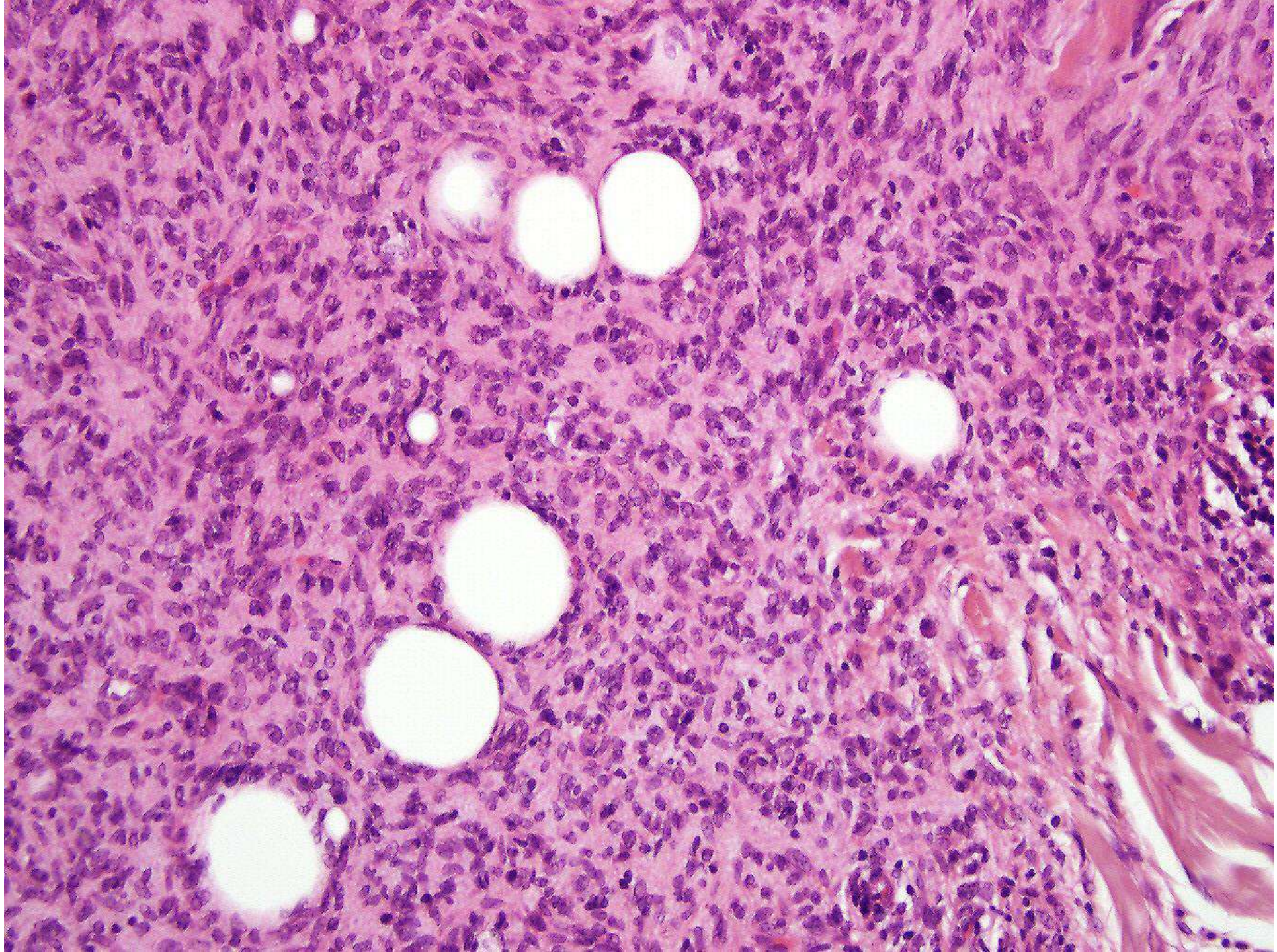


Intrafollicular component

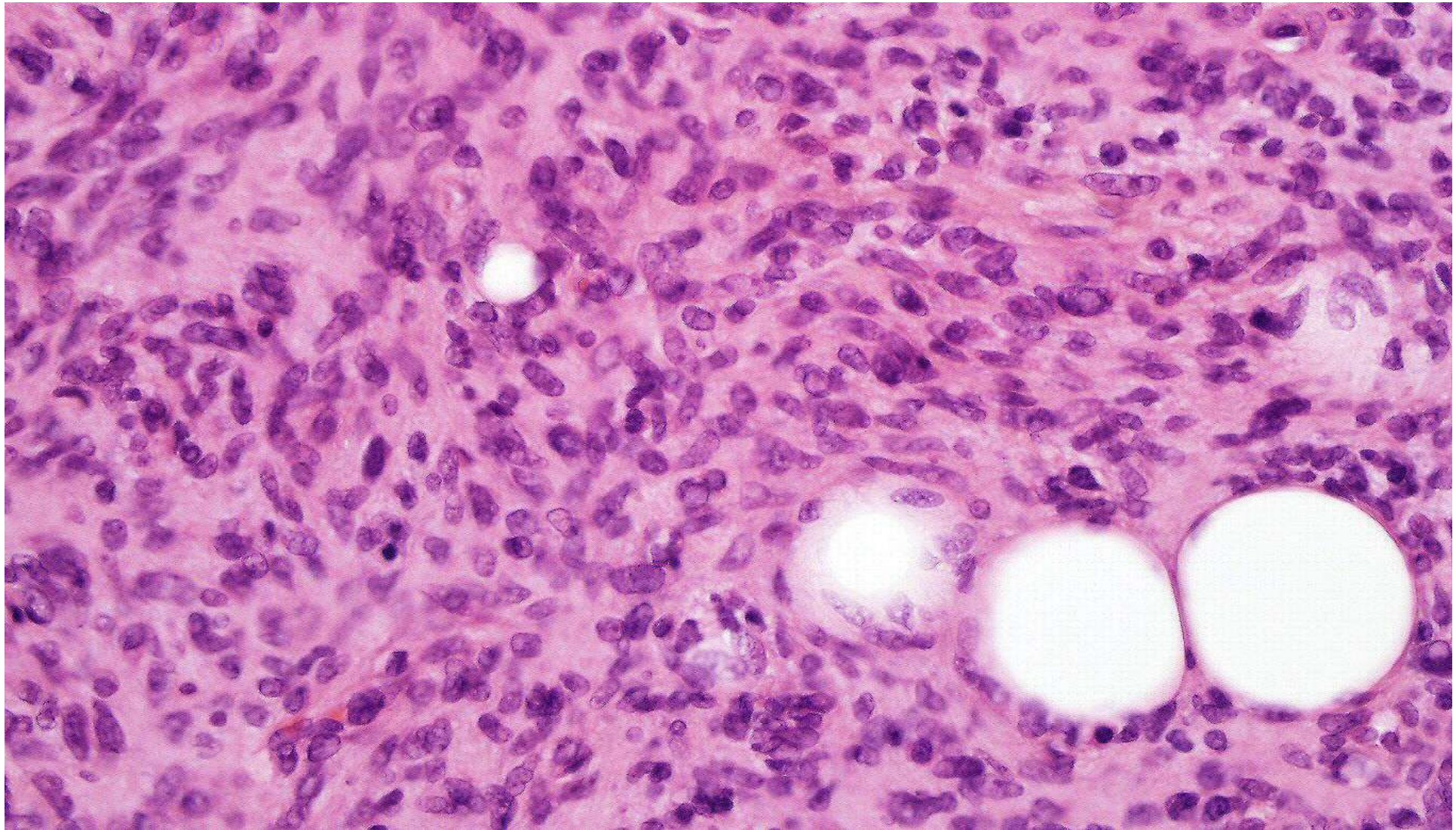


Invasive dermal and subcutaneous component





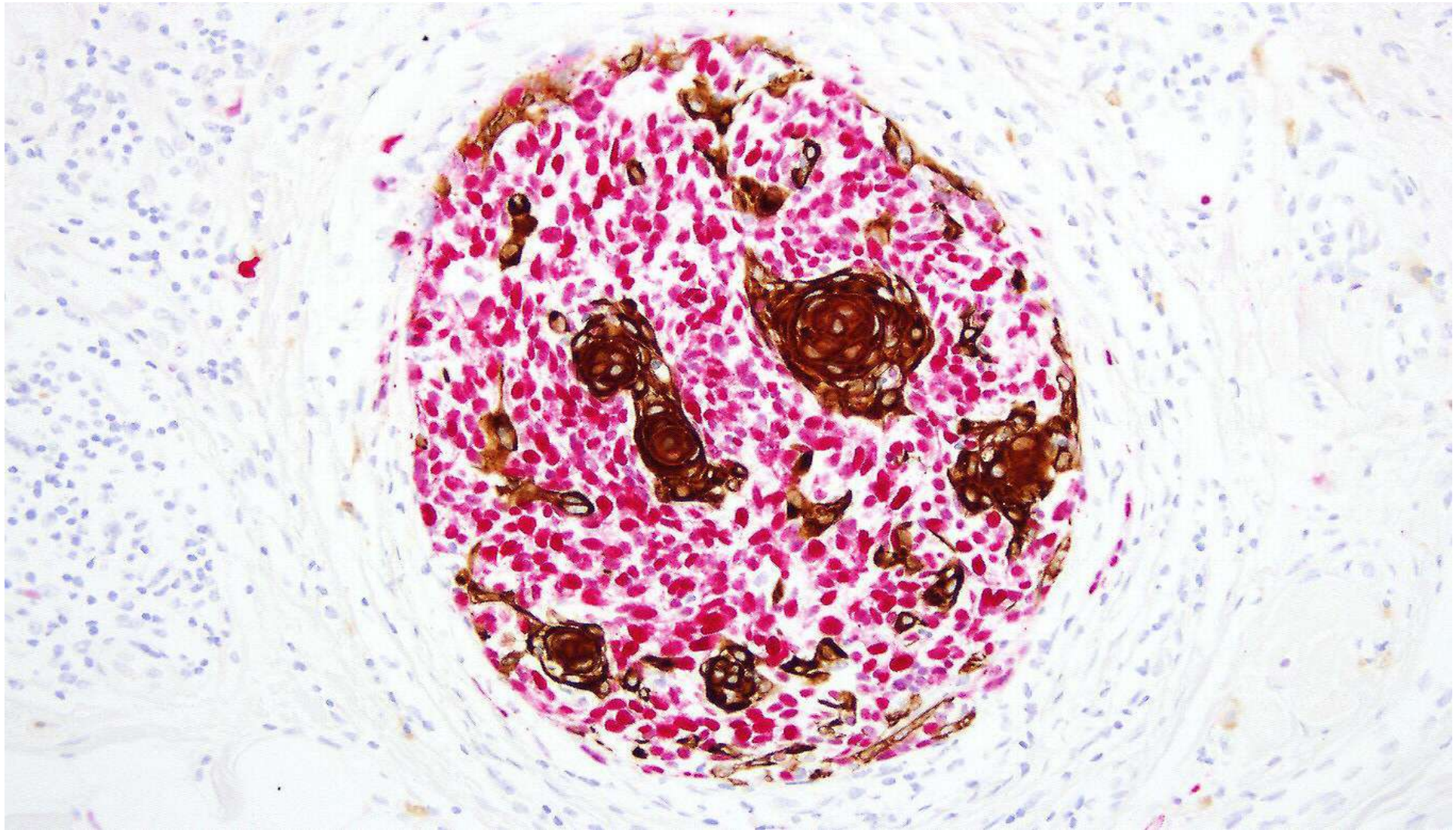
Cells with moderate cytological atypia and low mitotic activity



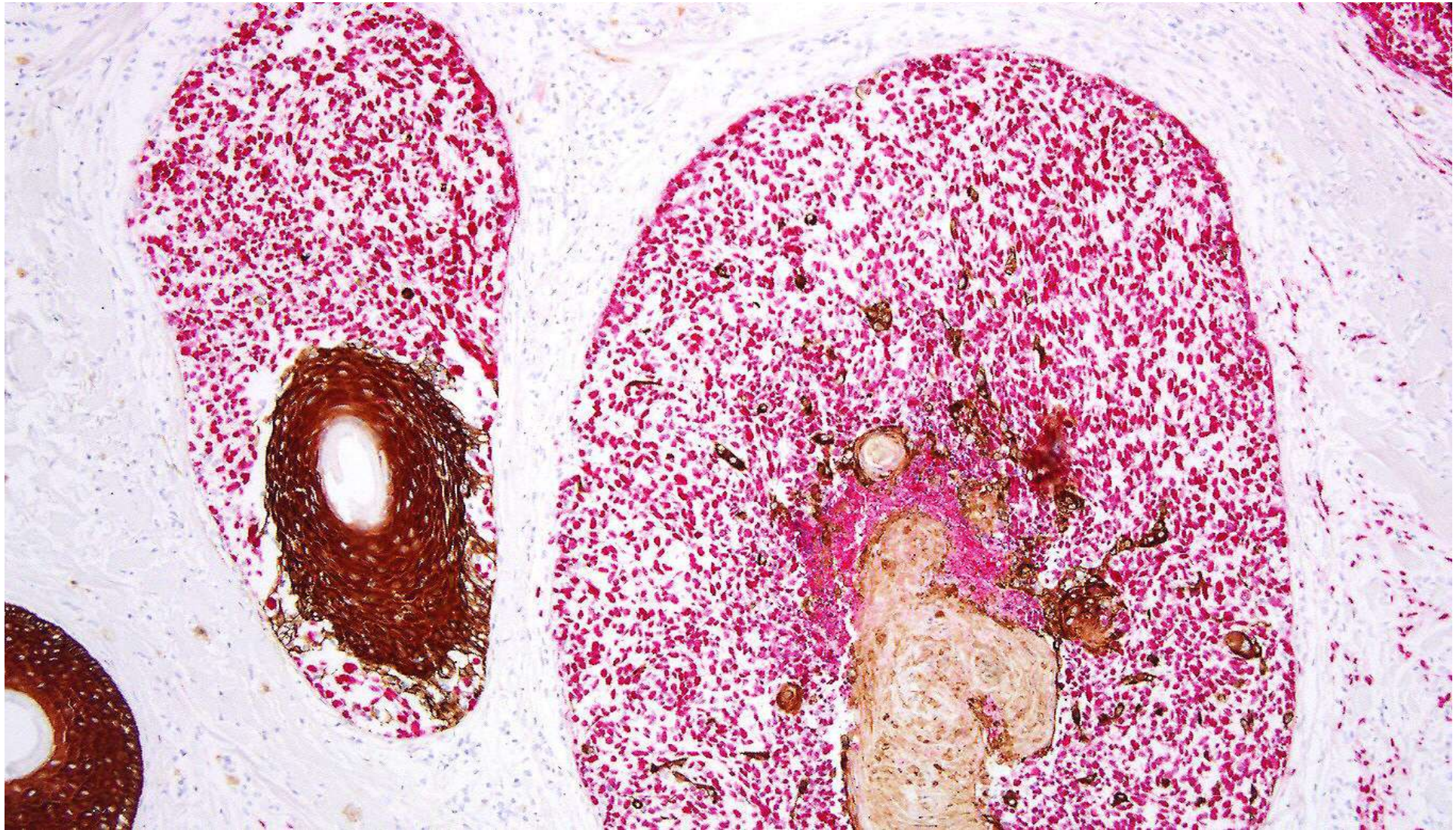
Additionally

- Skin shows prominent solar elastosis
- No junctional component
- Perineural invasion was seen
- No vascular invasion
- Mitotic count 1per mm^2

Immunoperoxidase double staining for MNF116 and Melan A



Hair follicles almost completely destroyed by the tumour cells



Immunohistochemistry

The intrafollicular component is diffusely positive for S100 and Melan A and focally for HMB45

The dermal and subcutaneous component is positive for S100 and negative for Melan A and HMB45

MNF116 highlights the remaining follicular epithelium

DIAGNOSIS

FOLLICULAR MELANOMA WITH AN INVASIVE SPINDLE CELL

FOLLICULAR MELANOMA

Definition: It is a rare variant of lentigo maligna

6 cases described to the date: a case report and a series of 5 cases

‘Multiple Primary Melanomas of the Hair Follicles: a Special Form of Malignant Melanoma of the Skin’
Sigg C., Pelloni F., Hardmeier T,
Hautarzt 1988; Jul, 39 (7):447-52

- **First description of 79 year-old male patient**
- **Multiple tumours originating from hair follicles of the scalp**

‘Follicular malignant melanoma. A variant of Melanoma to be distinguished from Lentigo Maligna Melanoma’

Hantschke M., Mentzel T.,Kutzner H.: American Journal of Dermatopathology; Vol 26(5) Oct 2004

- **5 cases**
- **Patients between 61 and 82years old**
- **3 male and 2 female patients**
- **Head and neck: 3 lesions on nose, 1 cheek, 1 on the back of the neck**
- **All cases in the background of pronounced actinic keratosis**
- **Clinical diagnosis: pigmented cyst, comedone**
- **Follow up from 4 months to 2 years: no recurrence or metastasis in any case**

Histological features

All tumours were originating from pilosebaceous units with or without secondary involvement of the epidermis (in 2 cases small areas of epidermal involvement were seen in the form of Lentigo Maligna)

Polygonal and epithelioid heavily pigmented melanocytes similar to that of LM and LMM.

All 5 tumours showed invasion of the adjacent dermis in the form

Depth of invasion ranged form 1.8 to 2.7mm

Tumour thickness ranged from 0.25 to 0.47mm

With immunostains all cases were positive with S100, Melan A and HMB-45

Definitions:

Follicular Malignant Melanoma as a melanoma originating from pilosebaceous units with or without secondary involvement of the epidermis

The length of epidermal involvement to each side should not exceed the depth of follicular structure (as opposite to ordinary LM with secondary involvement of adnexal structures)

With no sign of regression of a possible previous epidermal LM in any part of the lesion

Measurements

Tumour thickness was measured from the outer root sheath epithelium of the follicular structures to the deepest point of invasion of the adventitial or reticular dermis.

As an opposite to

Depth of invasion measured from the granular layer of epidermis

Conclusion

Follicular malignant melanoma is a special variant of melanoma which should be distinguished from classic lentigo maligna

Is Breslow thickness adequate ?

References:

- **Multiple Primary Melanomas of the Hair Follicles-a Special Form of Malignant Melanoma of the Skin**

  Sigg C., Pelloni F., Hardmeier T.: Hautarzt. 1988 Jul;39(7):447-51

- **Follicular Malignant Melanoma. A Variant of Melanoma to be Distinguished from Lentigo Maligna Melanoma**

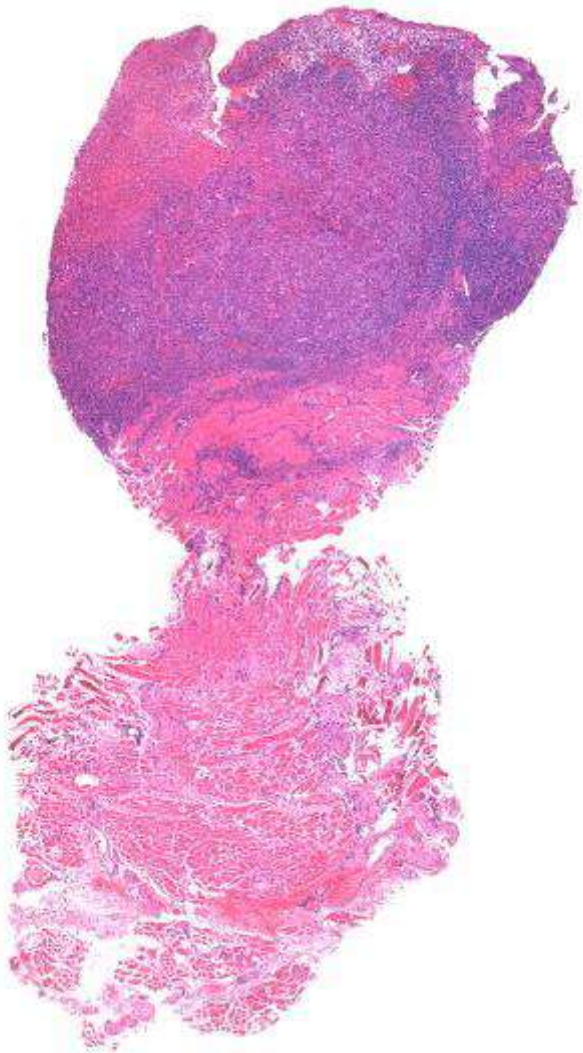
  Hantschke M., Mentzel T.,Kutzner H.: American Journal of Dermatopathology; 2004; 26(5):359-363

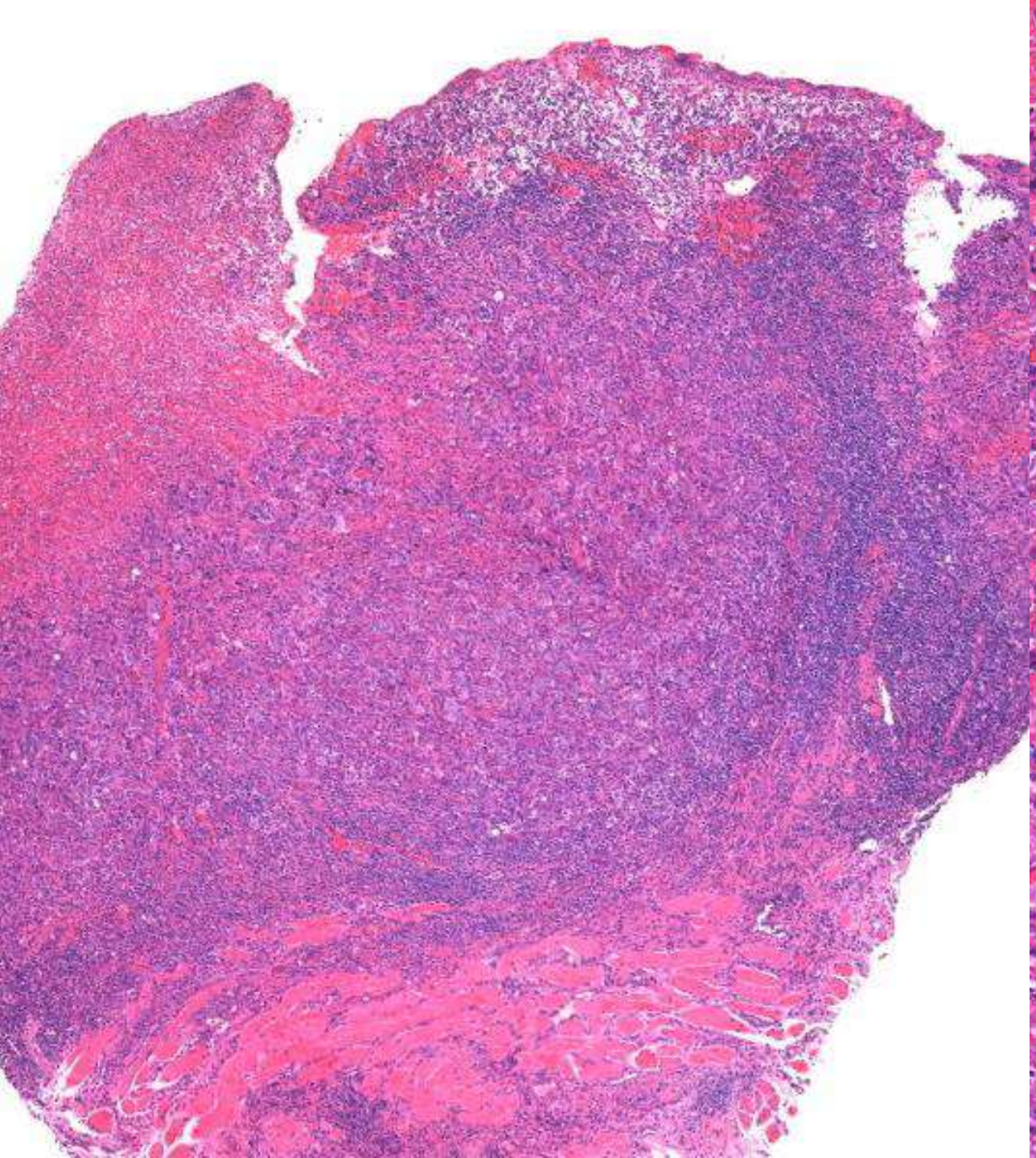
- **The Hair Follicle Barrier to Involvement by Malignant Melanoma**

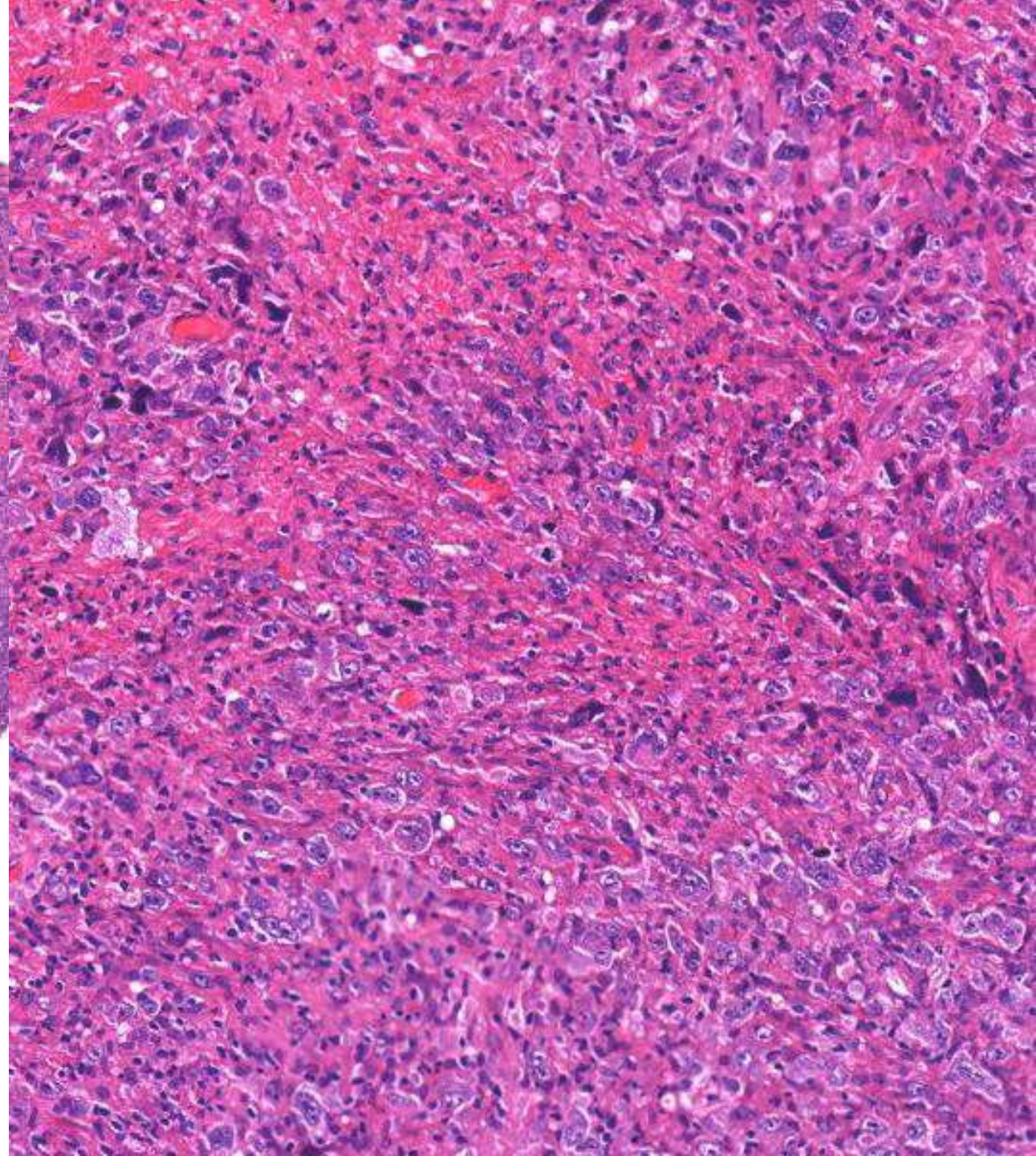
  Pozdnyakova O., Grossman J.,Barbagallo B., Lyle S.: Cancer; 2009; 115: 1267-1275

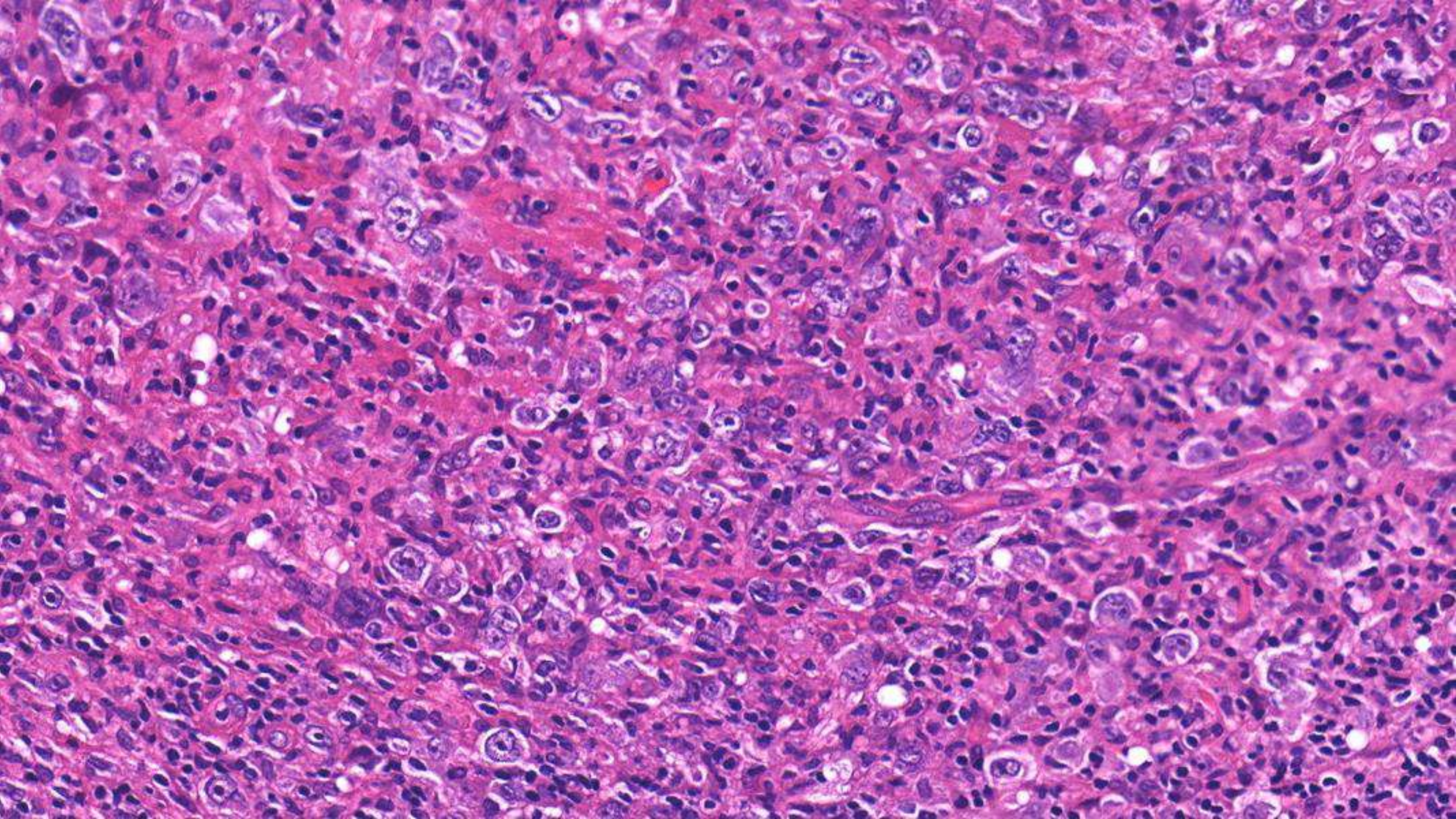
Case 8

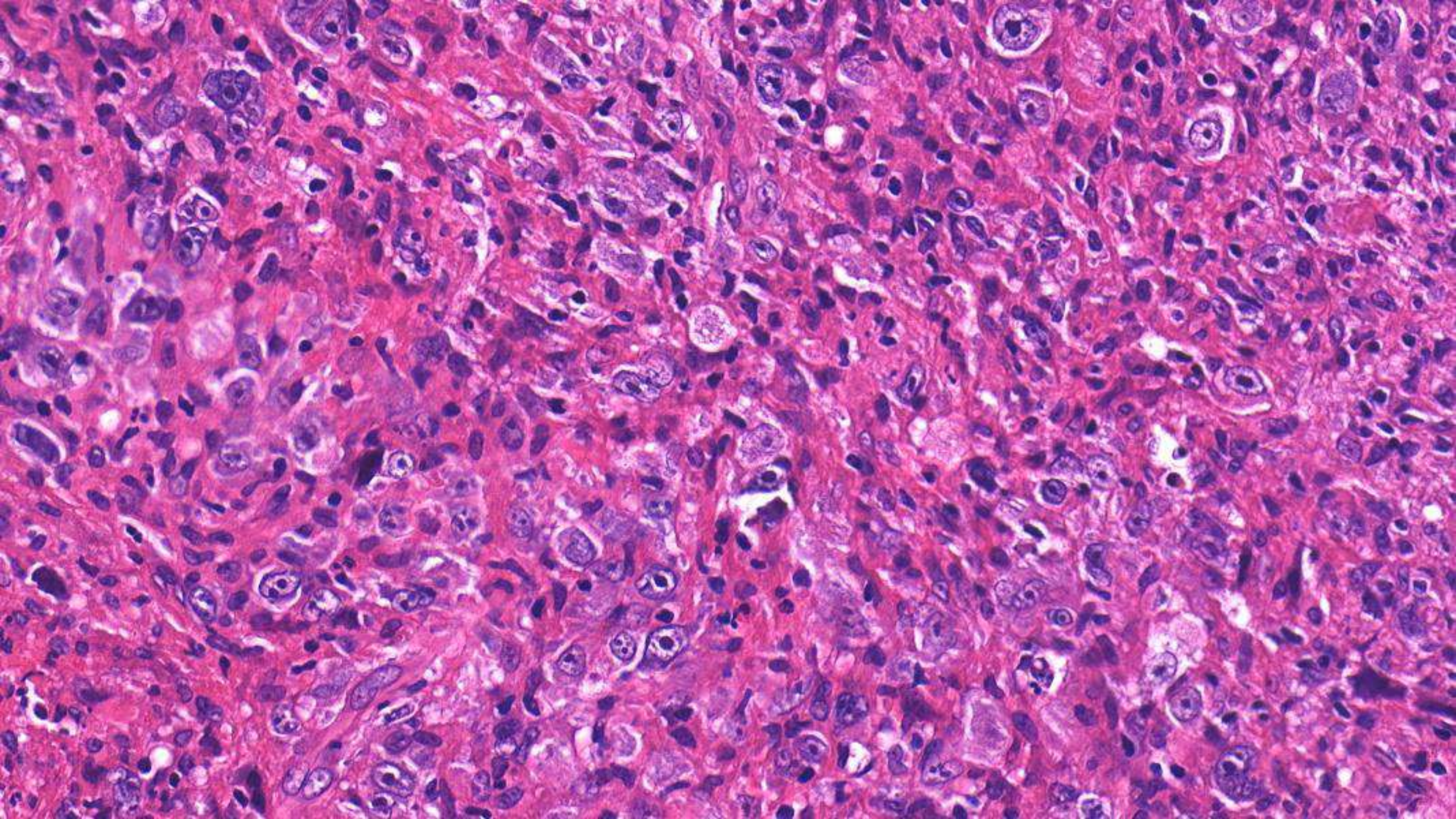
76-year-old male
Ulcerated non-healing lesion on the left side of the mouth
On Methotrexate for rheumatoid arthritis

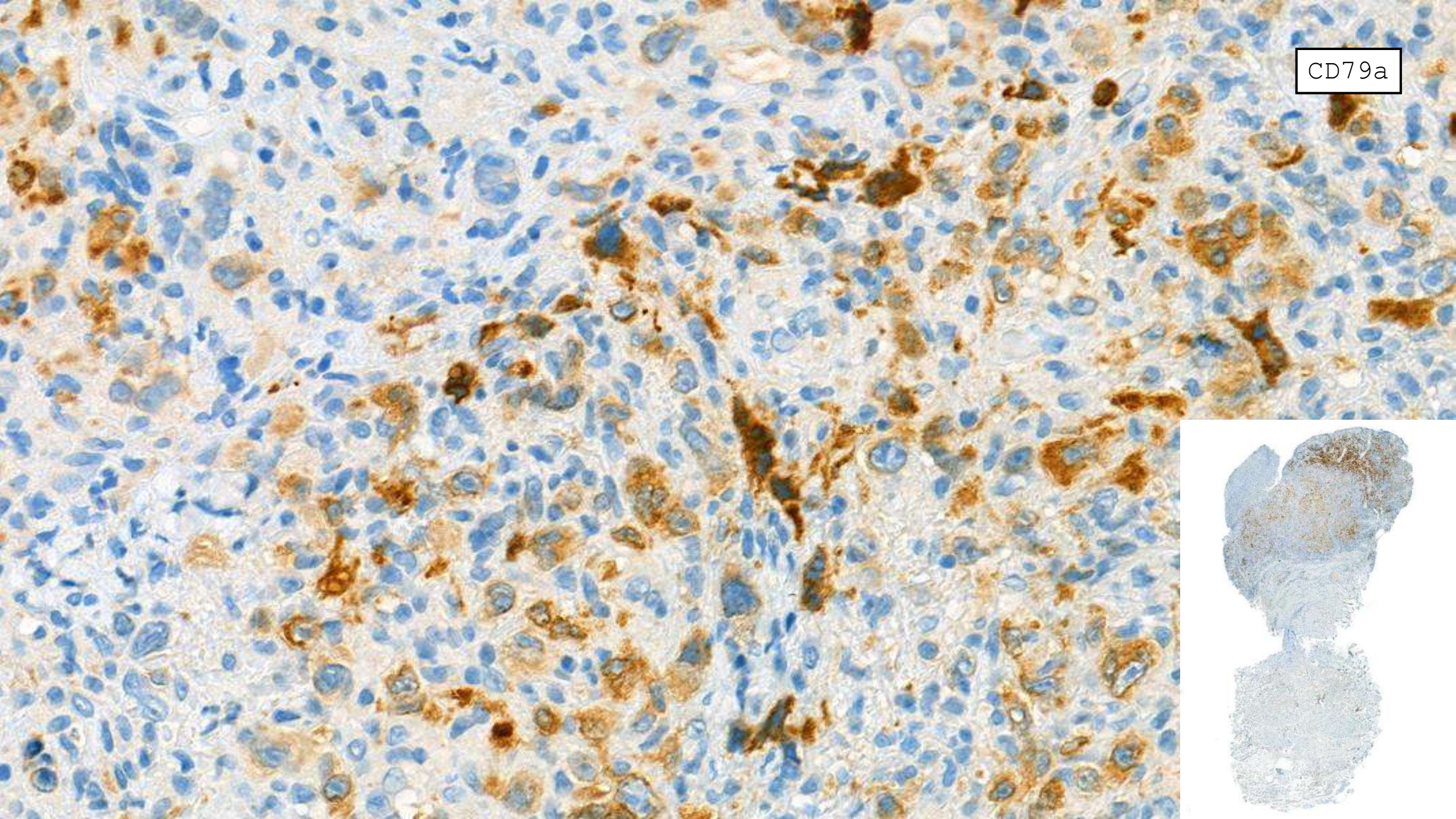








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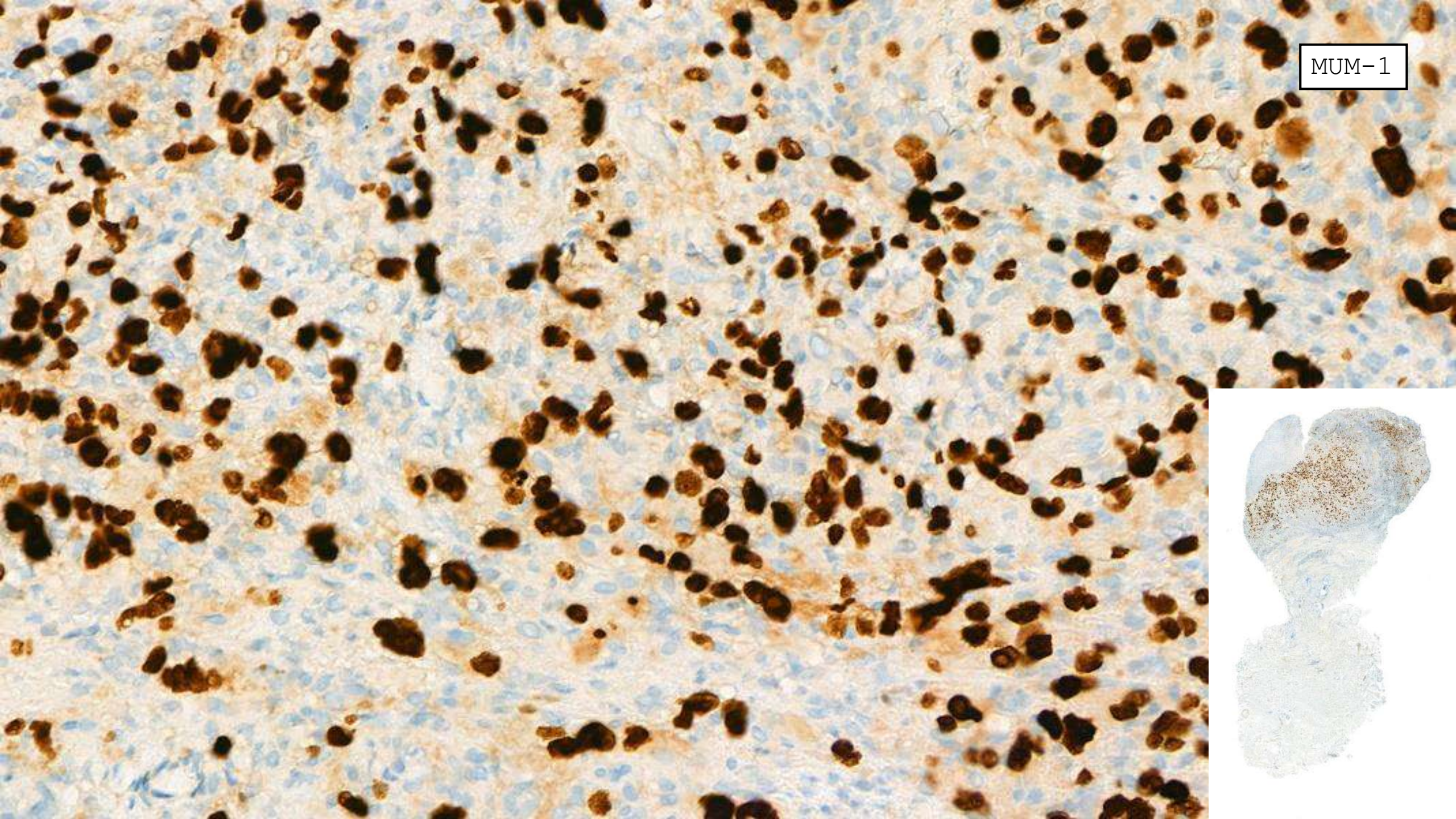
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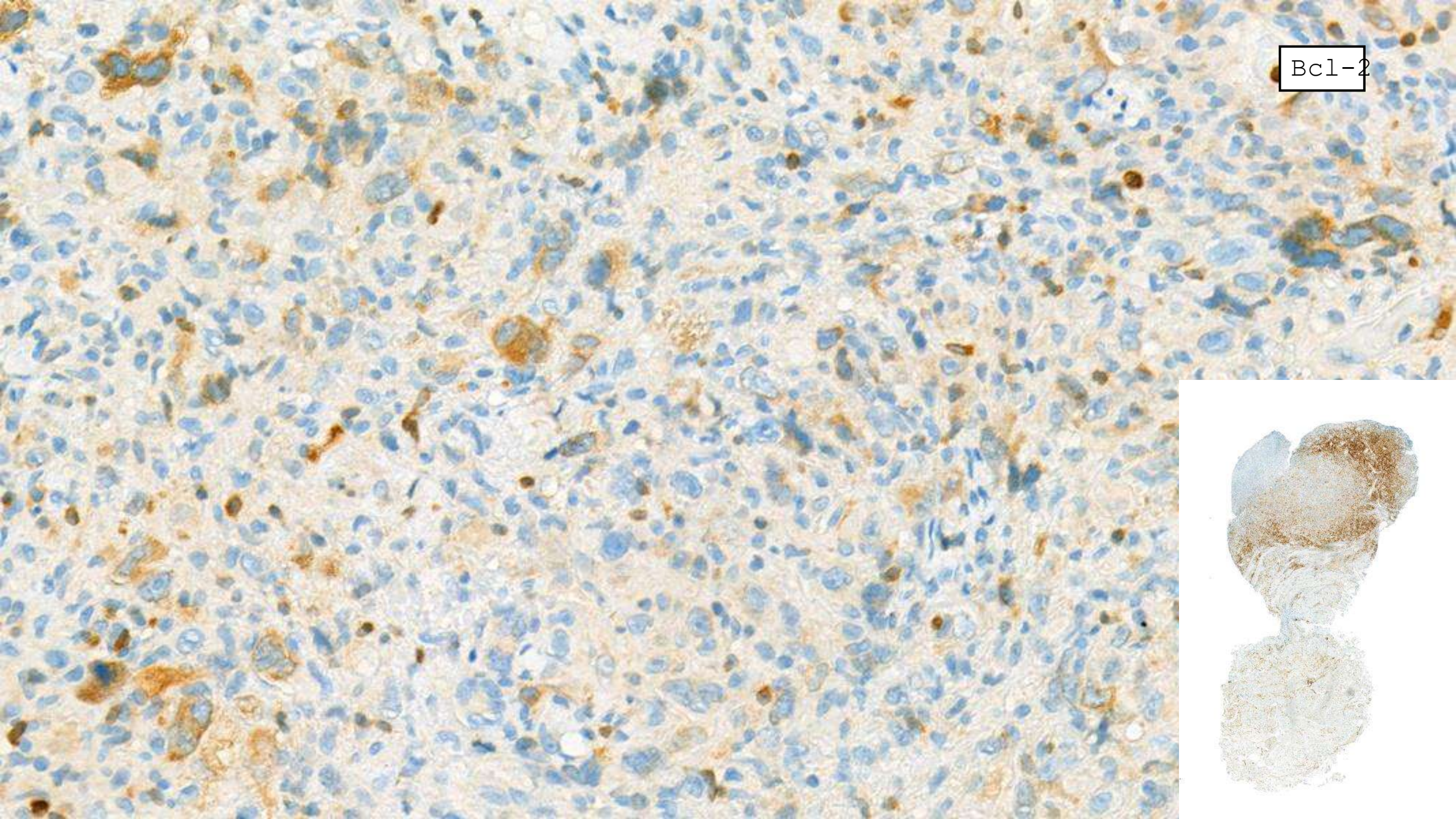
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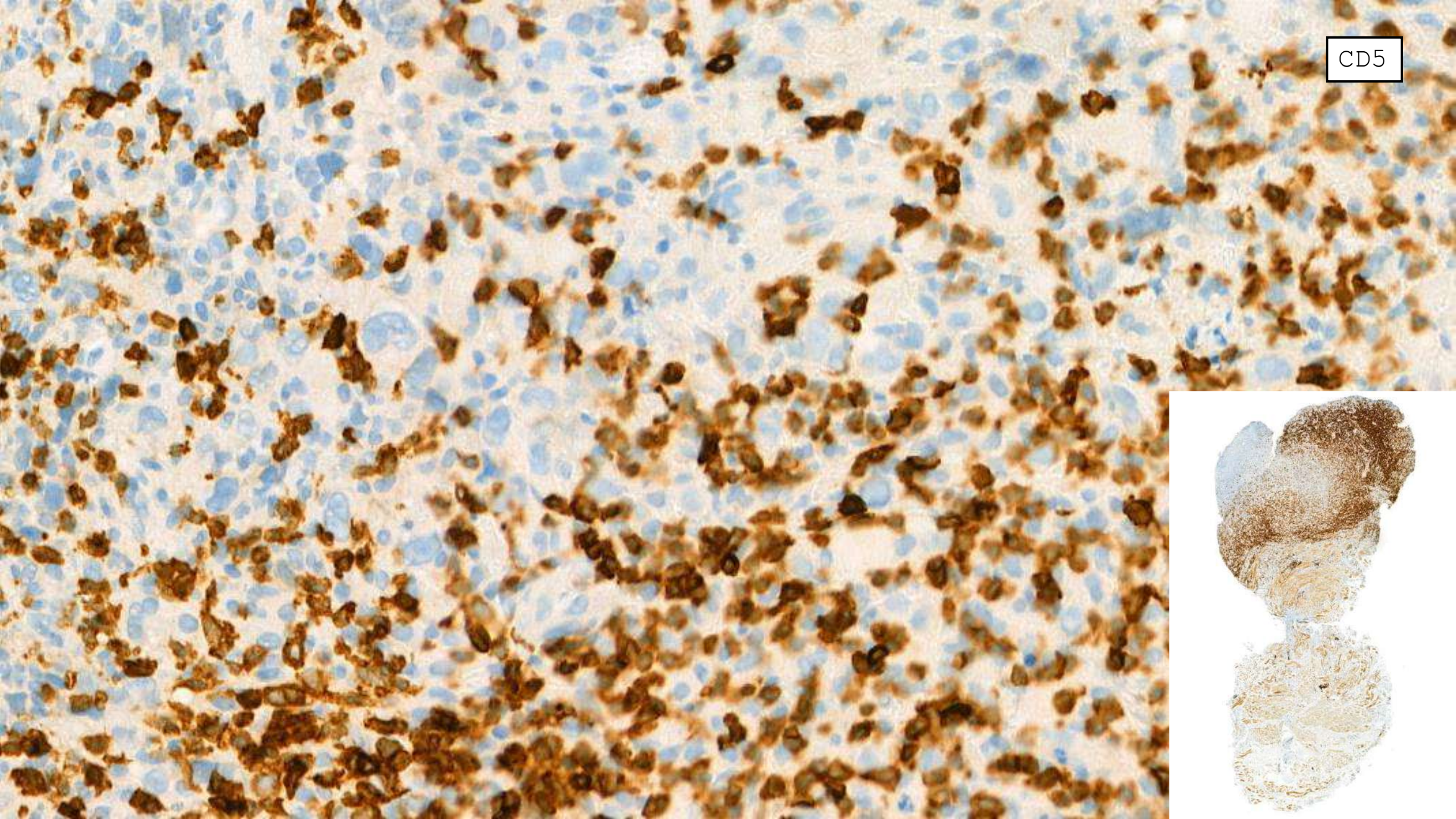
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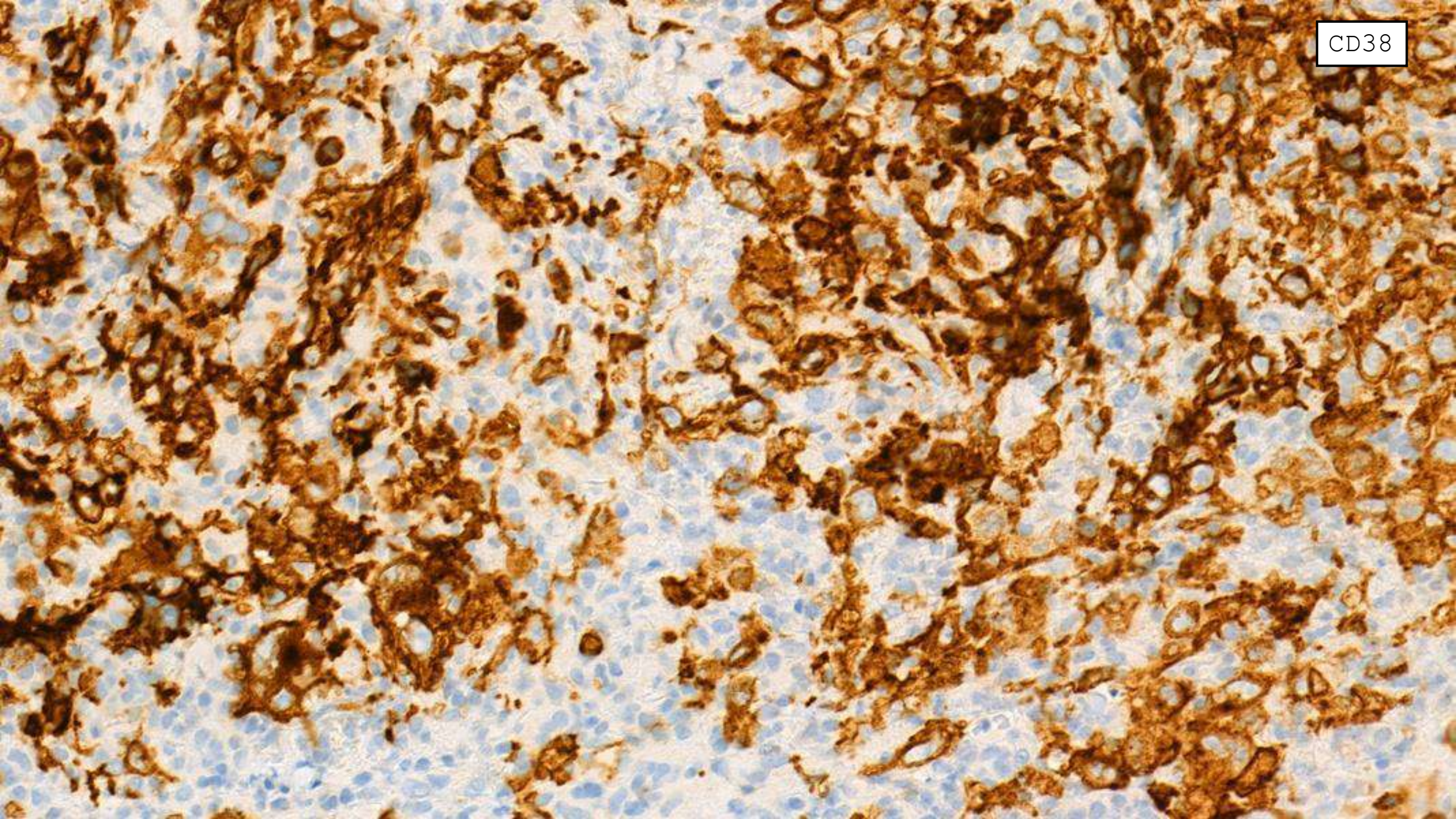
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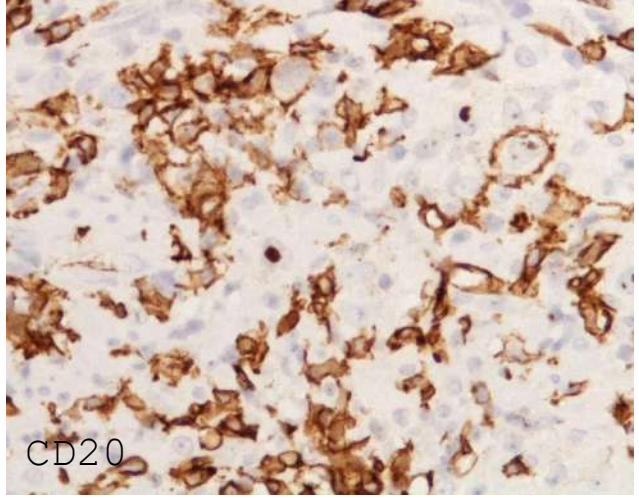
EBER-ISH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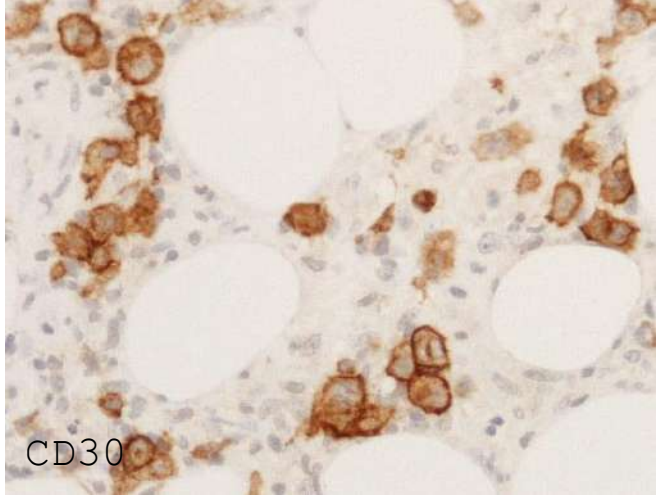
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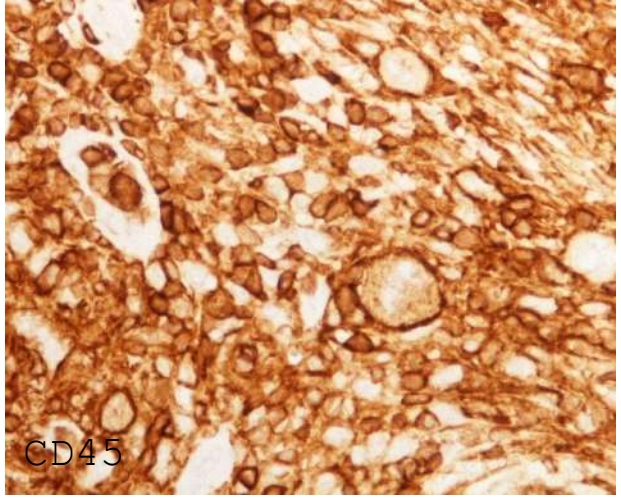
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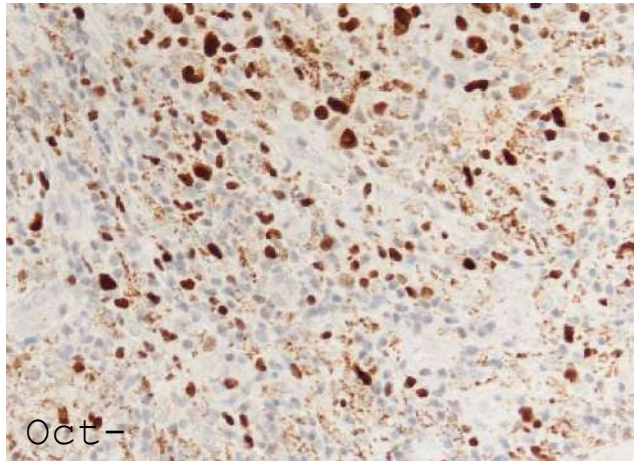
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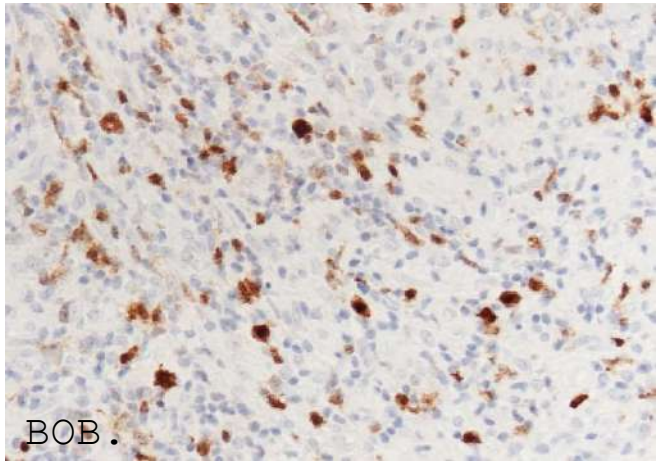
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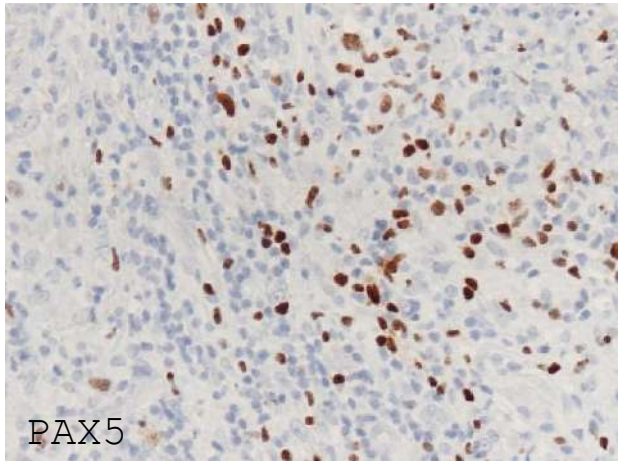
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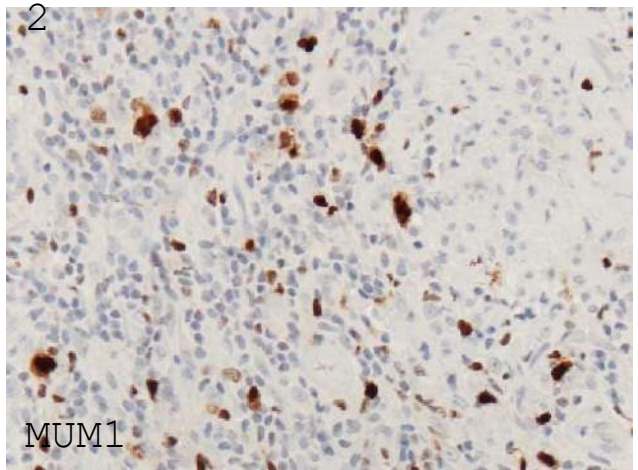
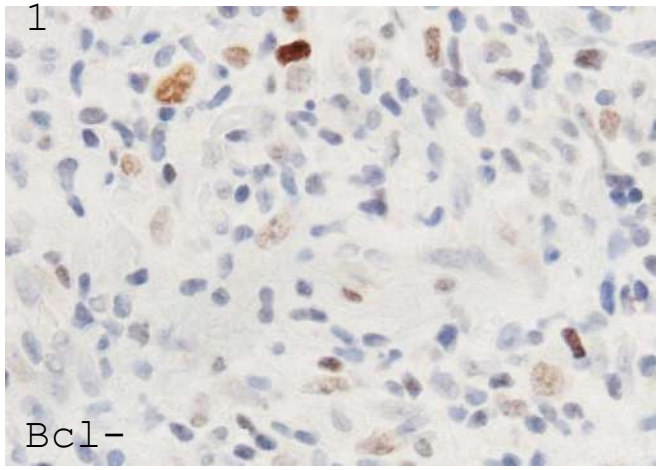

MUM1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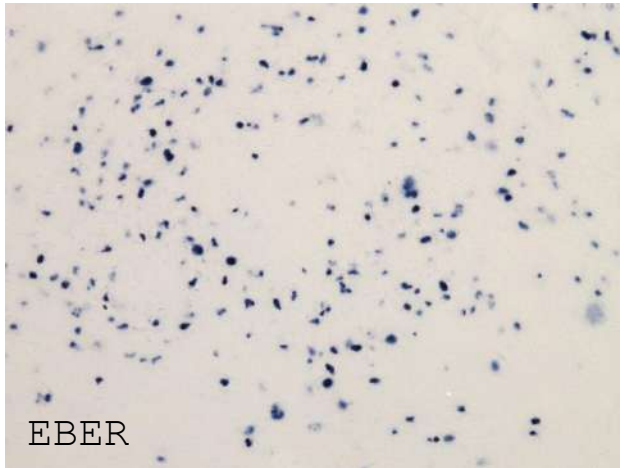
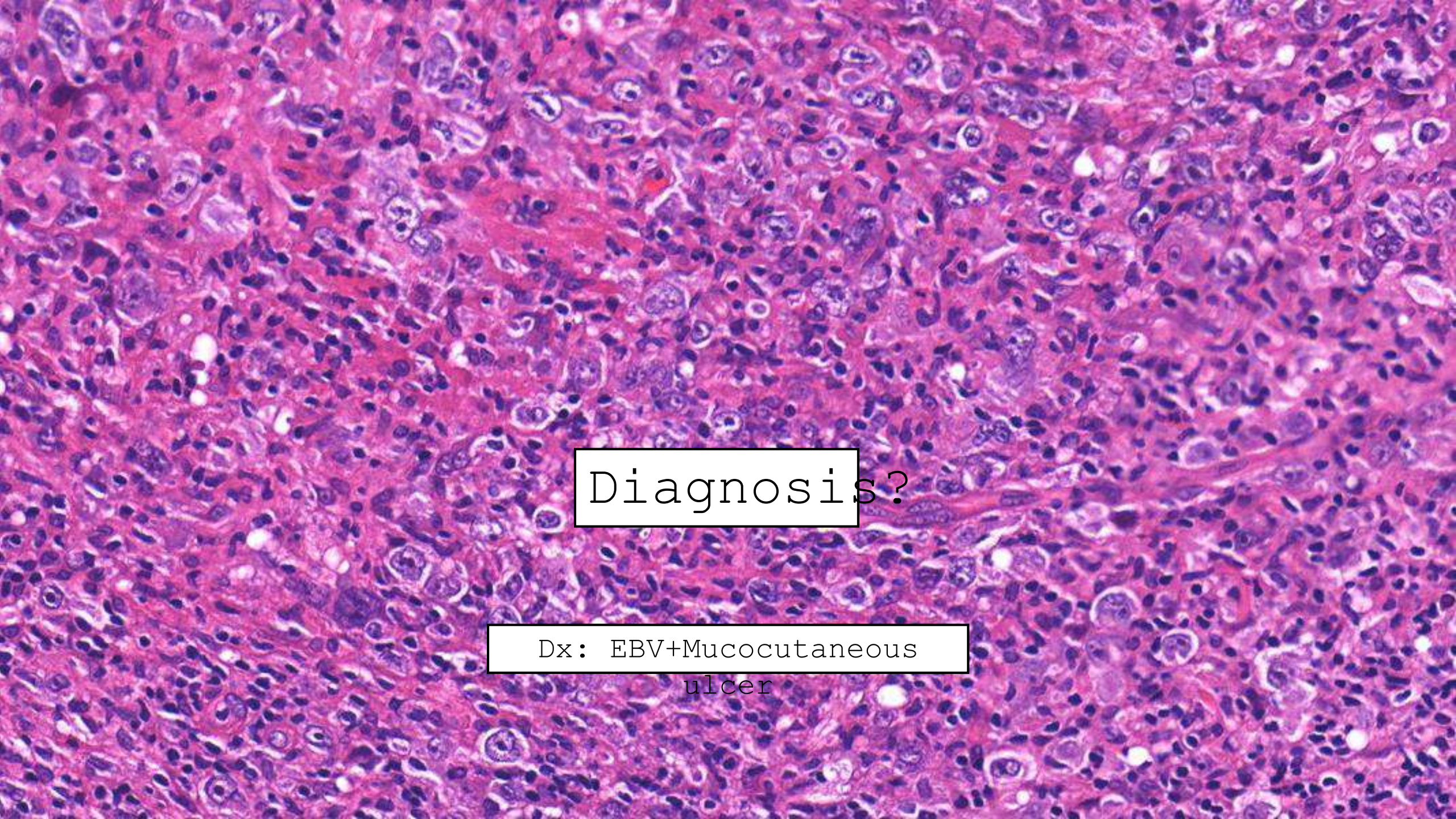

EBER


Diagnosis?
Dx: EBV+Mucocutaneous ulcer

Category	Phenotype	Pattern of positivity
EBV association in the majority of or in all cases		
Classic Hodgkin lymphoma	B	Only large neoplastic cells
EBV+ mucocutaneous ulcer	B	Several cells (small, mid-sized, and large lymphocytes)
Extranodal NK/T-cell lymphoma, nasal-type	NK/T	Virtually all cells
Lymphomatoid granulomatosis	B	Angiocentric lymphocytes
EBV+ diffuse large B-cell lymphoma of the elderly	B	Different cut-offs used in different publications
Hydroa vacciniforme-like lymphoma	T	Majority of neoplastic cells
Hydroa vacciniforme	T	Majority of cells
Intravascular > large NK/T-cell lymphoma	NK/T	Virtually all cells
Primary effusion lymphoma	B	Virtually all cells
Plasmablastic lymphoma	B	Virtually all cells
Post-transplant lymphoproliferative disorders and lymphoproliferative disorders associated with other immune deficiencies	B	Variable number of cells depending on type (polymorphic: few cells; monomorphic: majority of cells)
Aggressive NK-cell leukemia	NK	Virtually all cells
Angioimmunoblastic T-cell lymphoma*	B (reactive)	Scattered cells
EBV association in a distinct proportion of cases		
Burkitt lymphoma†	B	Virtually all cells
EBV association in sporadic or anecdotal cases		
Subcutaneous panniculitis-like T-cell lymphoma	T	Majority of neoplastic cells
Cutaneous γ/δ T-cell lymphoma	T	Majority of neoplastic cells
Peripheral T-cell lymphoma, NOS	T	Majority of neoplastic cells
Cutaneous $CD4^+$ small-medium T-cell lymphoma	T	Some neoplastic cells

*EBV present in non-neoplastic B lymphocytes.

†In nearly 100% of cases of endemic Burkitt lymphoma and in 15–35% of sporadic cases.

EBV Positive Mucocutaneous Ulcer—A Study of 26 Cases Associated With Various Sources of Immunosuppression

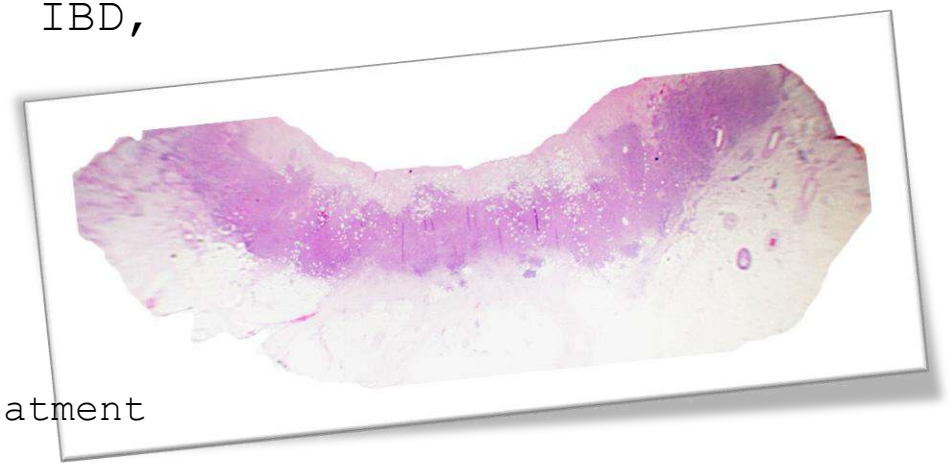
Stefan D. Dojcinov, MD, FRCPath, Girish Venkataraman, MD,†*
Mark Raffeld, MD,† Stefania Pittaluga, MD, PhD,† and Elaine S. Jaffe, MD†

(*Am J Surg Pathol* 2010;34:405–417)

Iatrogenic systemic IS

(SLE, Sarcoidosis, RA, IBD, Transplant)

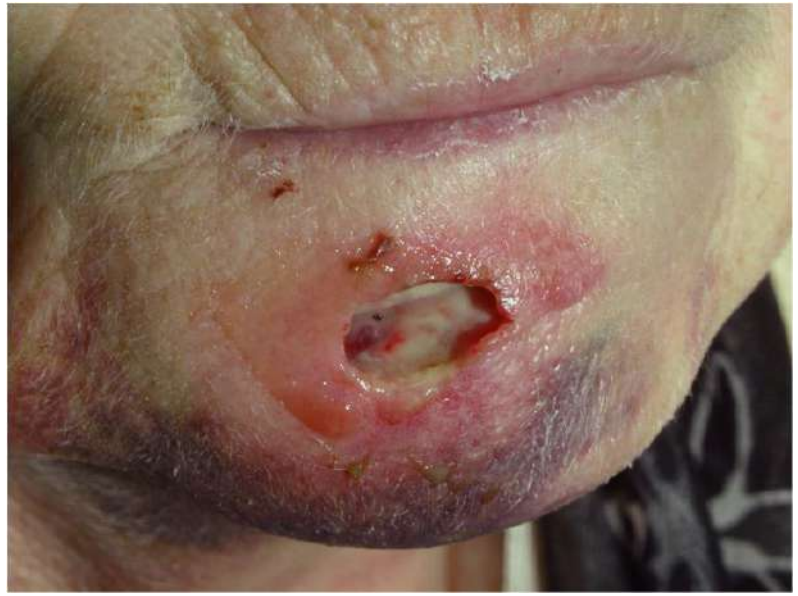
- Methotrexate
- Cyclosporin A
- Azathioprine
- MMF
- Anti TNF
- Topical steroid treatment

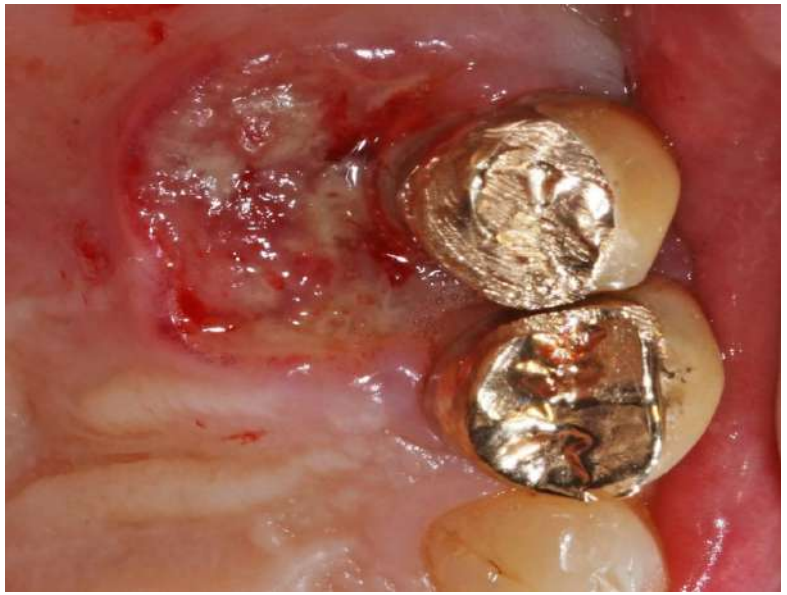


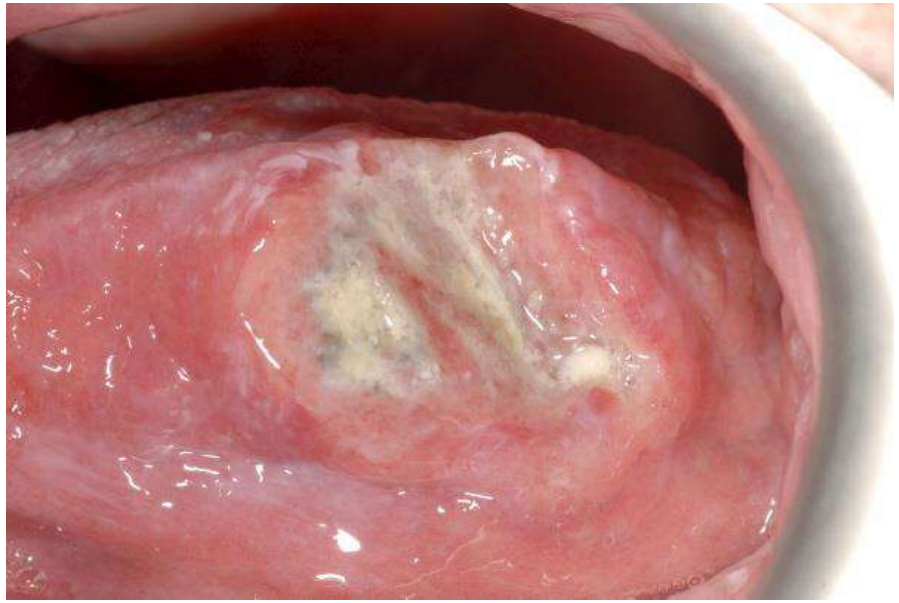
No immunosuppressson – Immunosenescence

HIV

Courtesy of Stefan D Dojcinov, Swansea, UK





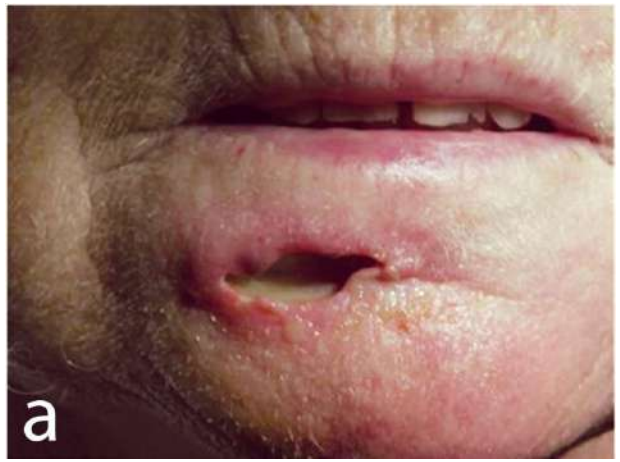


Skin
Buccal/pharyngeal mucosa
Oesophagus
Stomach
Bronchus
Small bowel
Colon
Anus
Vagina

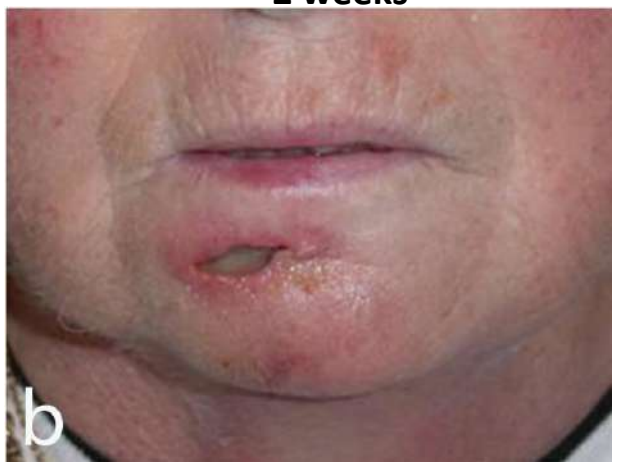
- Rare condition first recognized in 2010, with only 51 reported cases
- It is characterized by ulcers with polymorphous infiltrates of lymphocytes and immunoblasts, occasionally showing Hodgkin-like features
- The condition usually presents as a solitary lesion, often in the oropharynx, but can also affect the skin and GI tract
- EBVMCU is more common in patients with iatrogenic immunosuppression, primary immunodeficiencies, and older adults, where it is linked to diminished immune surveillance
- It can present as indolent and self-limited, with many patients responding to a reduction in immunosuppression However, some cases require more aggressive treatments like rituximab, radiation
- Most cases are indolent, with 68% of immunosuppression-associated cases showing remission with reduced immunosuppression
- Some cases may need additional treatments like rituximab or R-CHOP chemotherapy
- Treatment strategies are similar to those for post-transplant lymphoproliferative disorders (PTLD), involving a combination of immune modulation and surgery
- The disease can have a varied course, from self-limiting to aggressive, and requires careful management tailored to the patient's condition

Roberts, T.K., Chen, X. & Liao, J.J. Diagnostic and therapeutic challenges of EBV-positive mucocutaneous ulcer: a case report and systematic review of the literature. *Exp Hematol Oncol* **5**, 13 (2015).

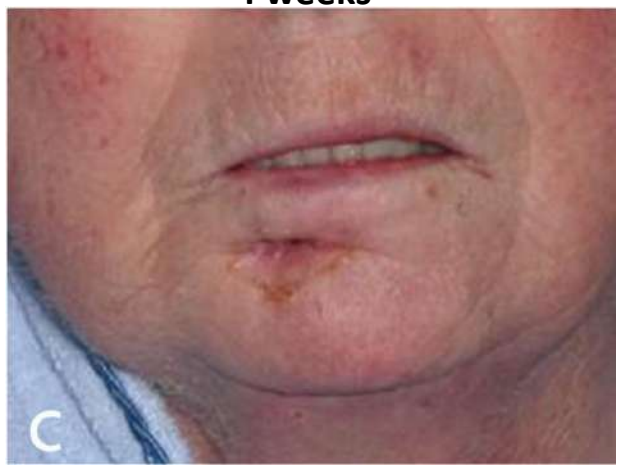
All iatrogenic IS cases – full remission upon IS withdrawal



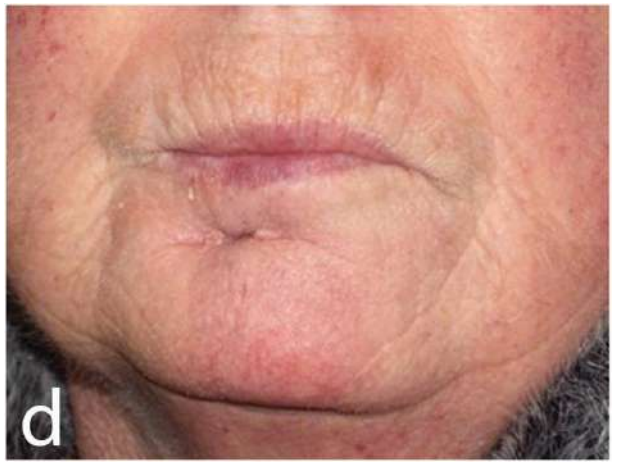
2 weeks



4 weeks



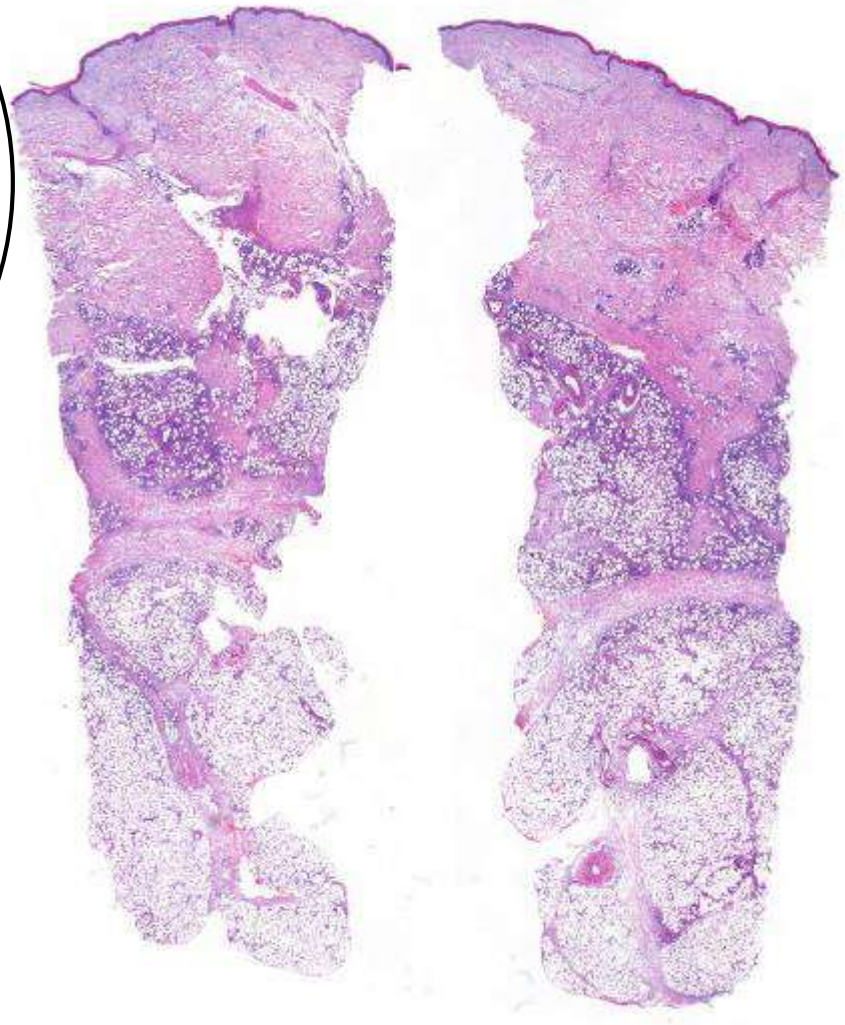
8 weeks

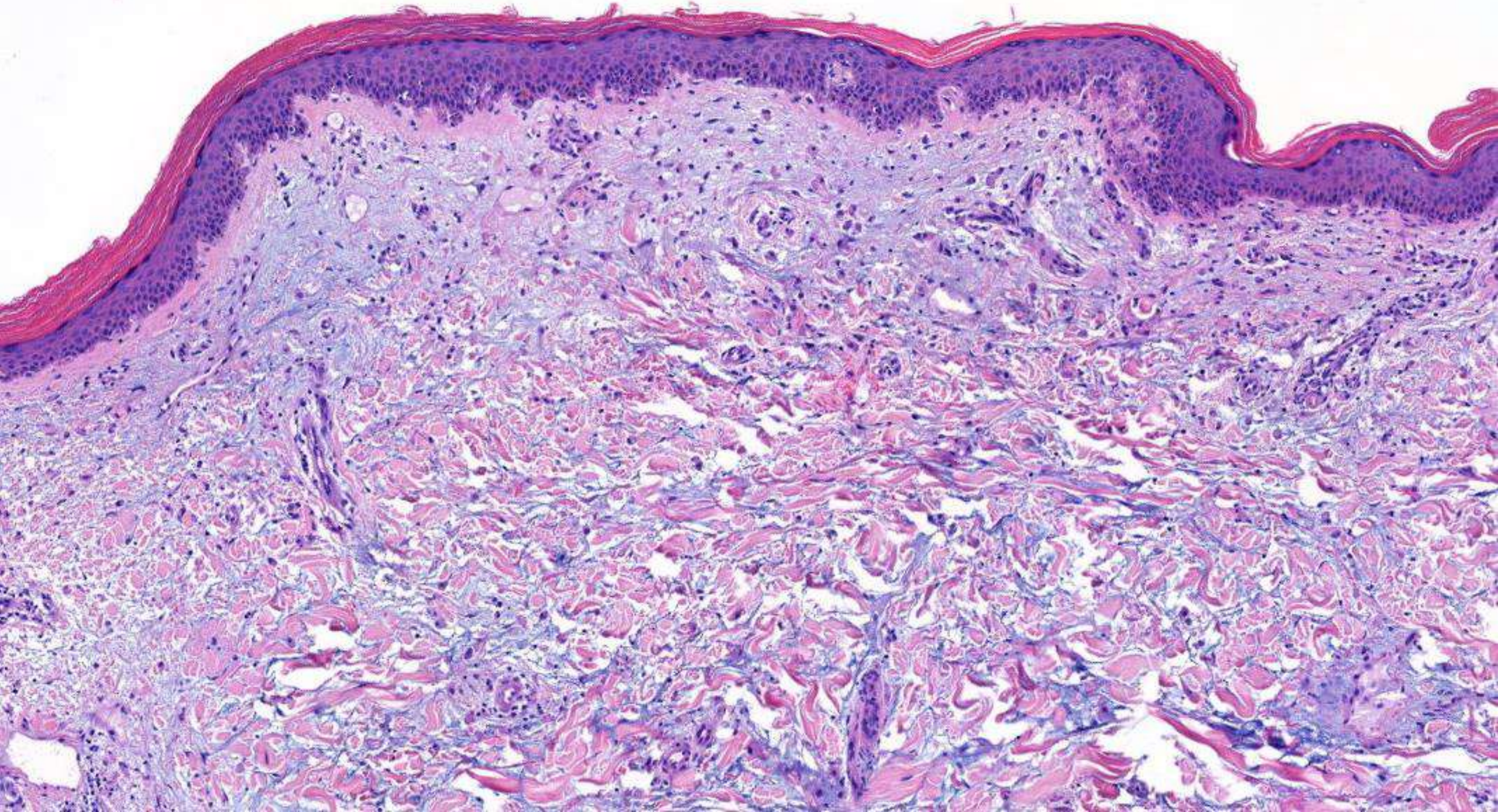


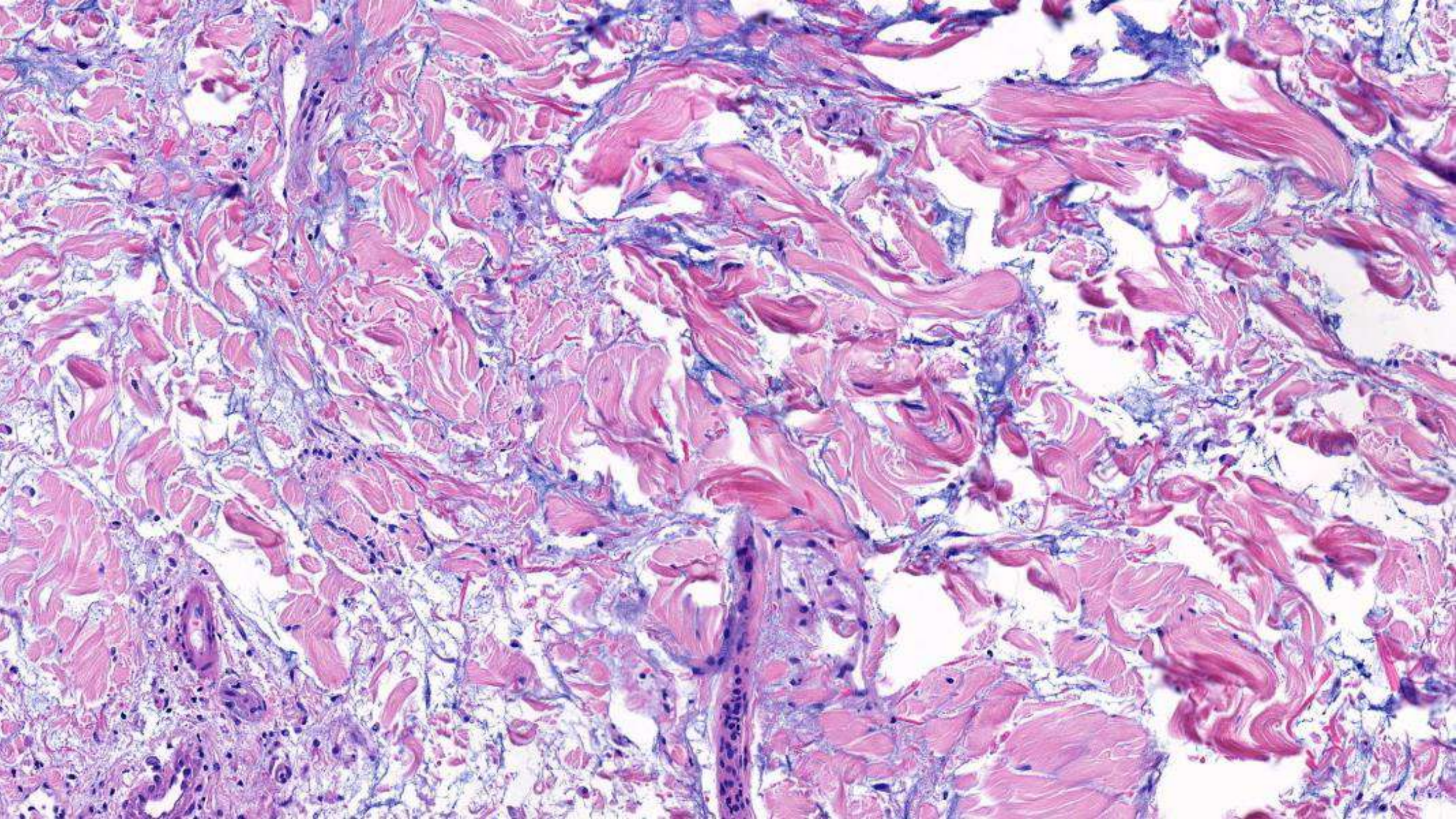
Dojcinov et al. Am J Surg Pathol 2010; 34: 405-417

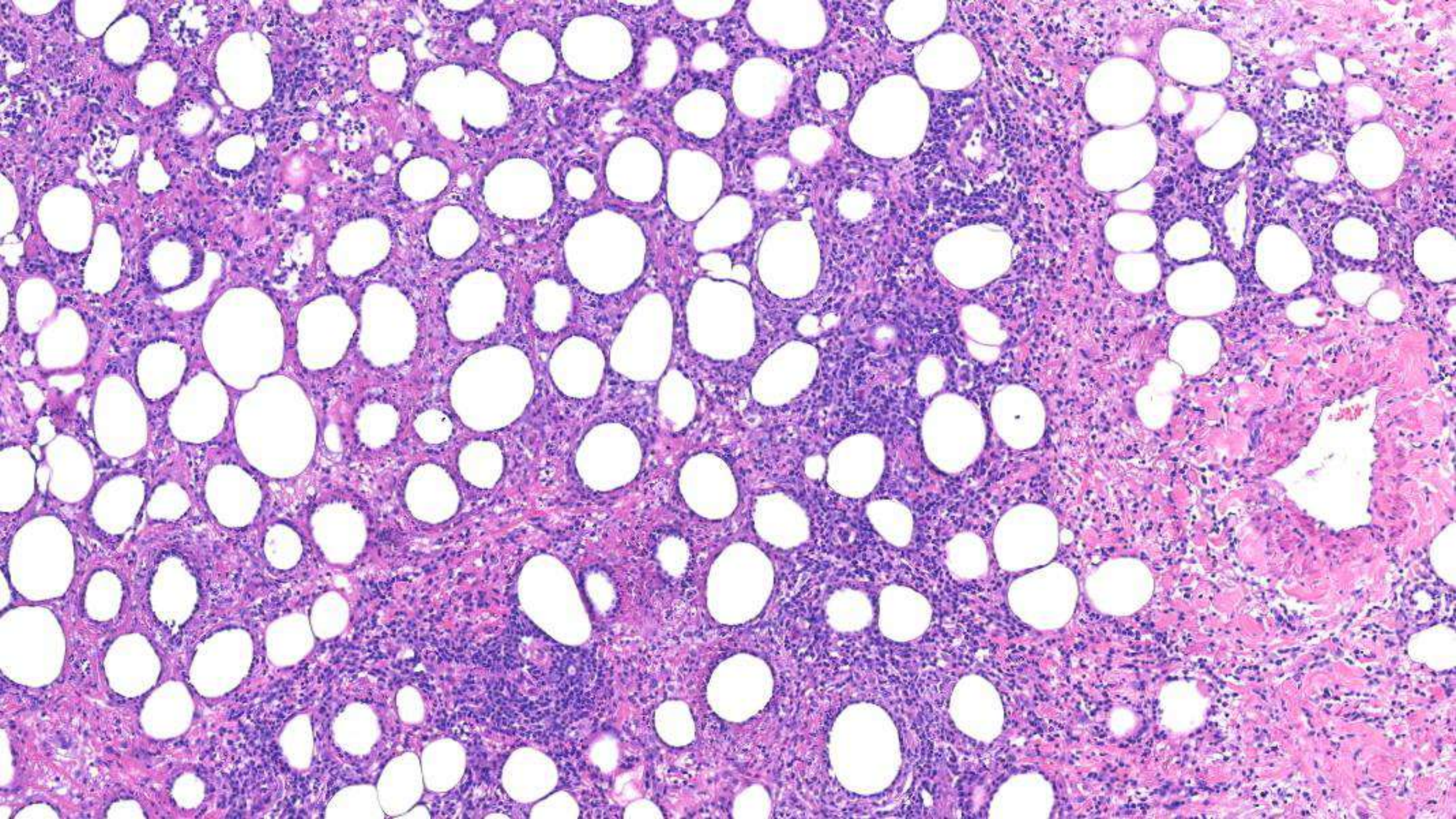
Case 9 and10

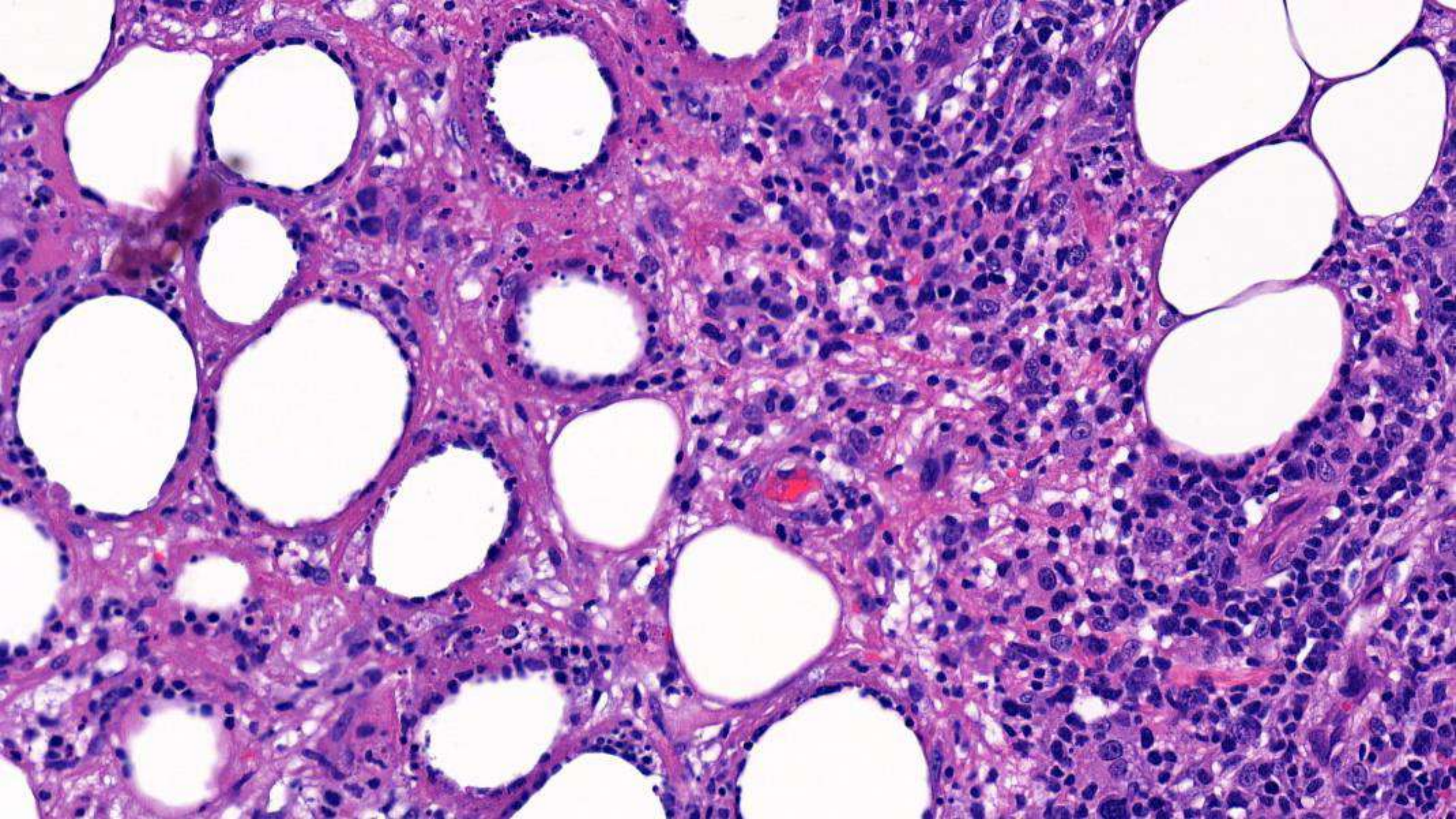
72-year-old female
4 month unwell, weight loss.
Painfull nodules on lower extremities
Erythema nodosum?

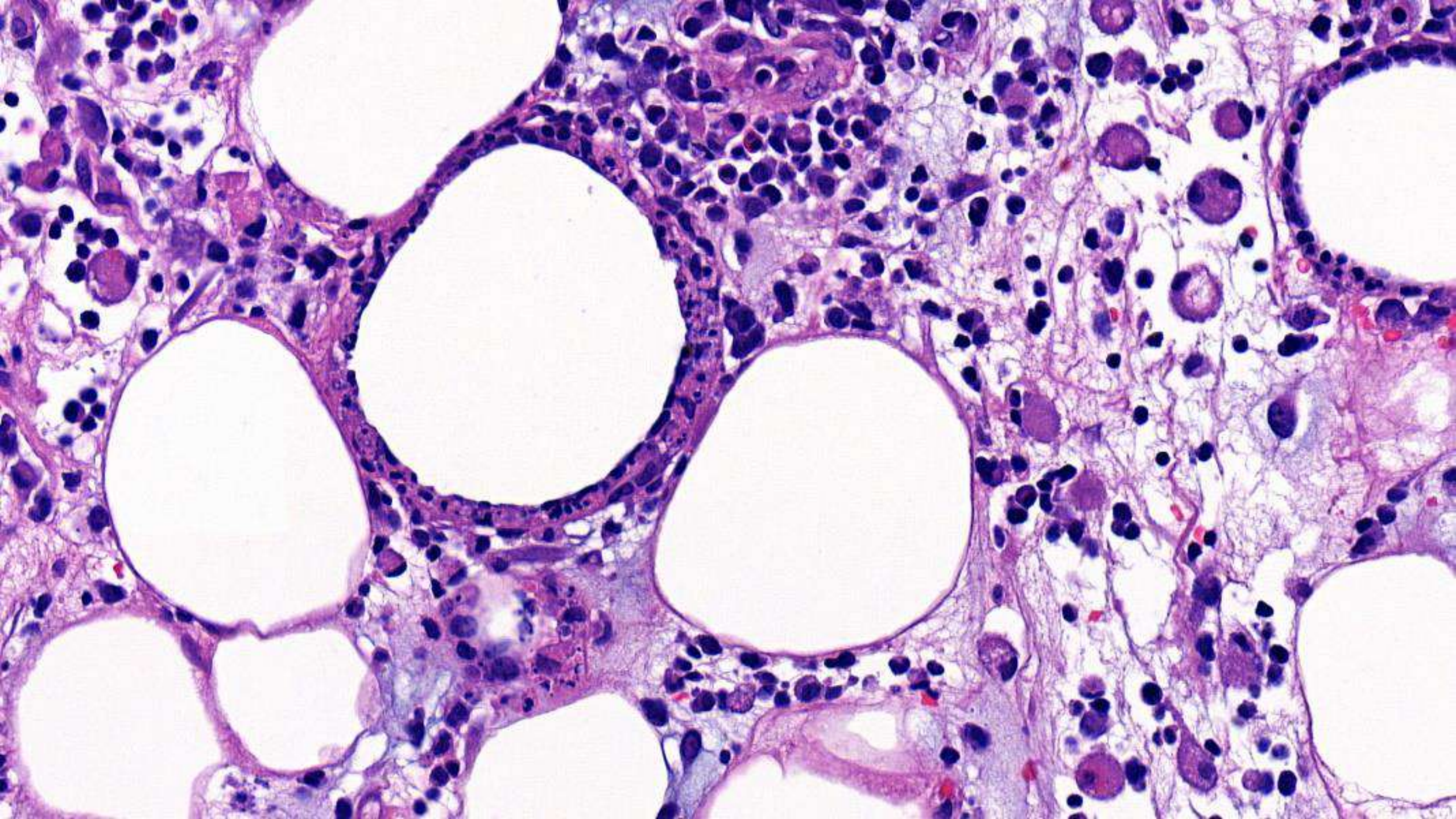


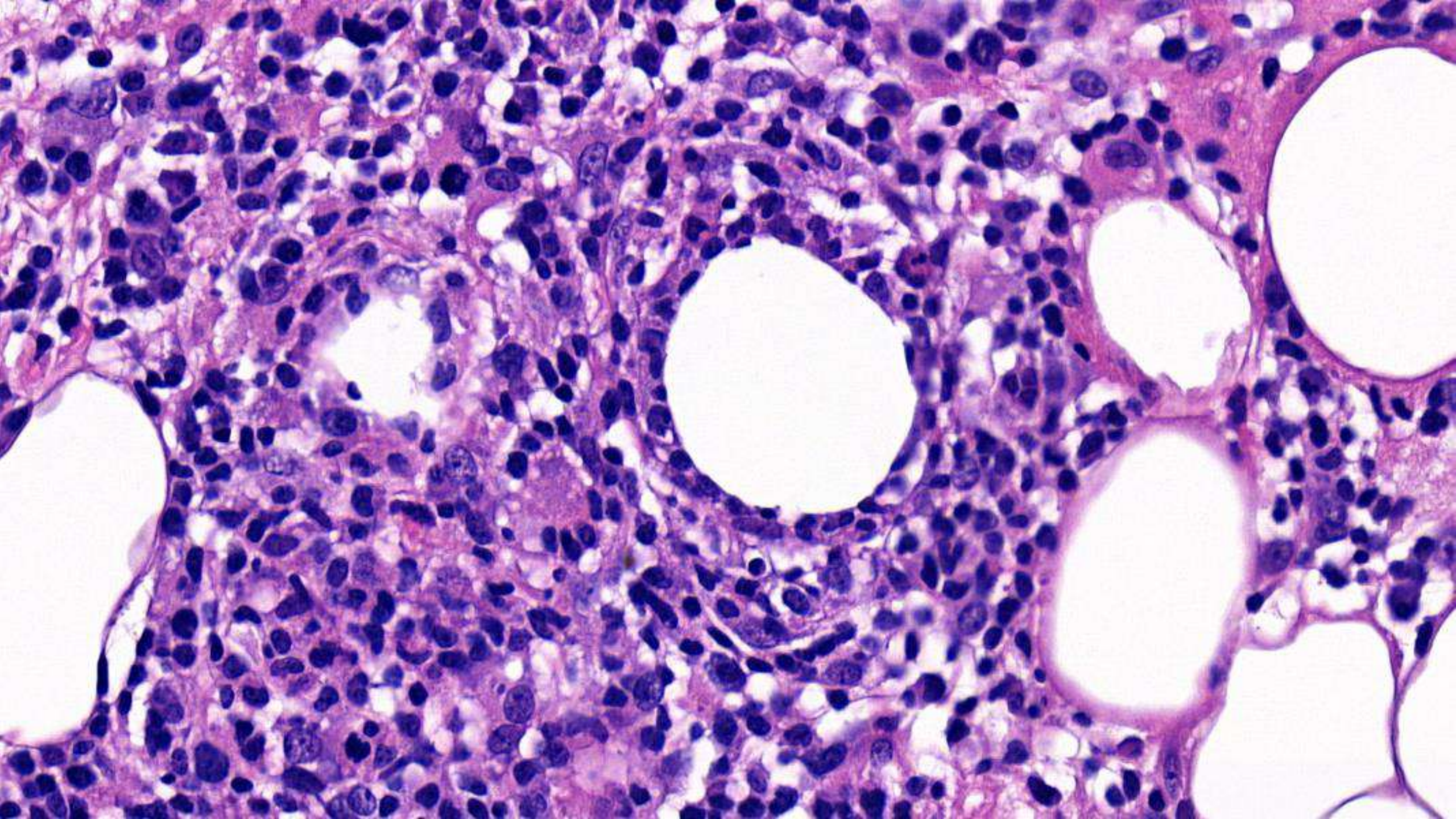


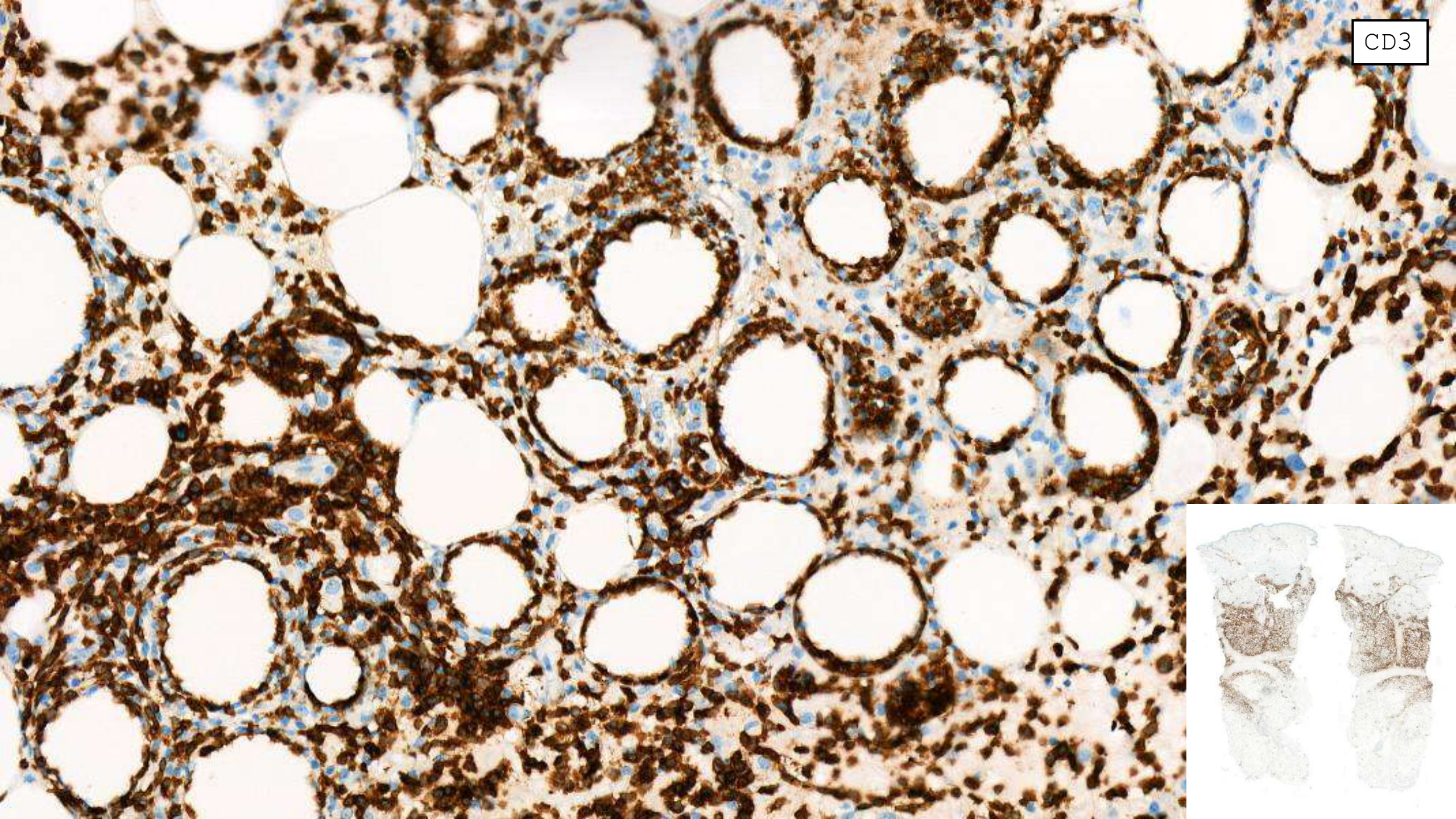








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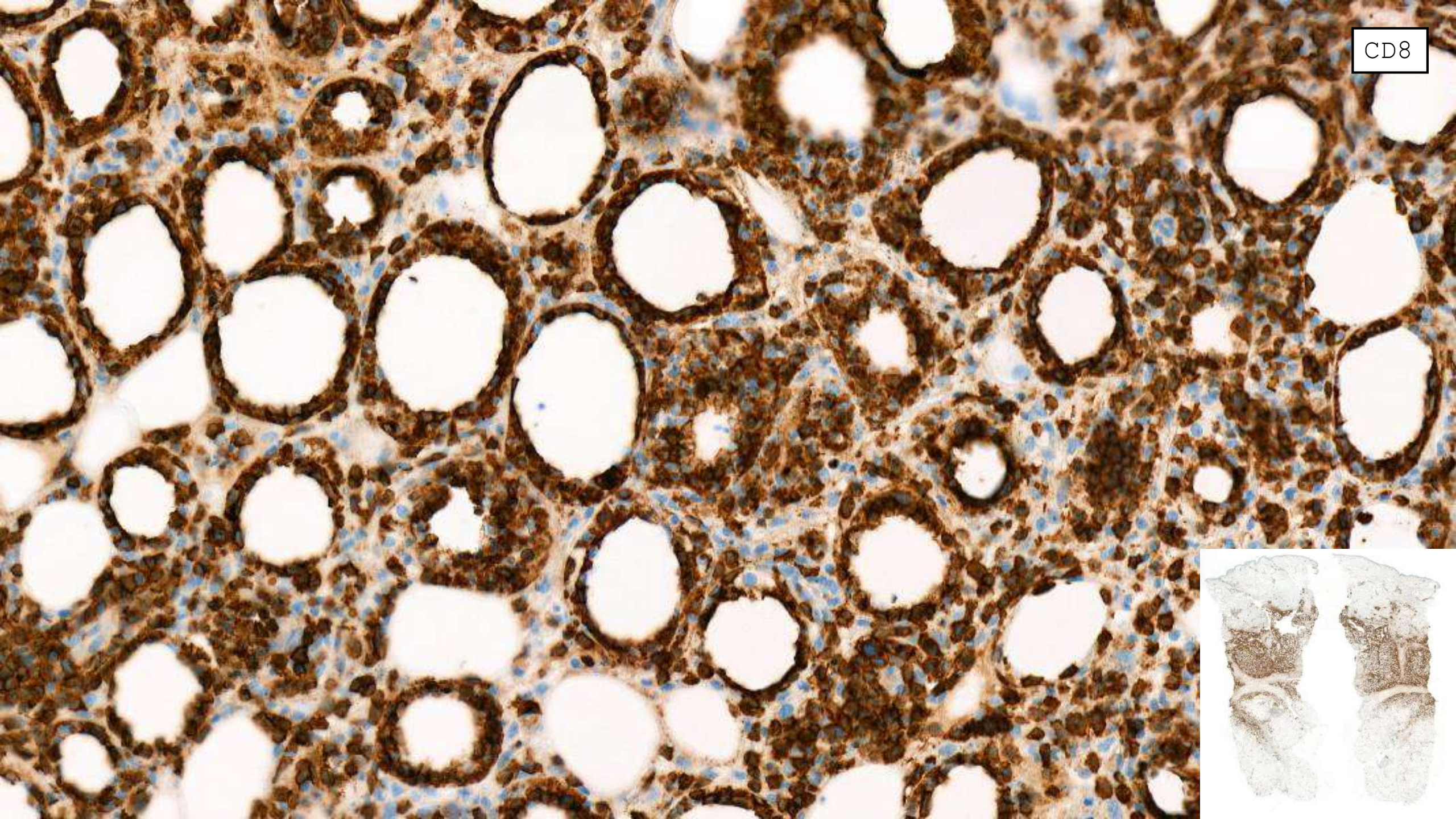
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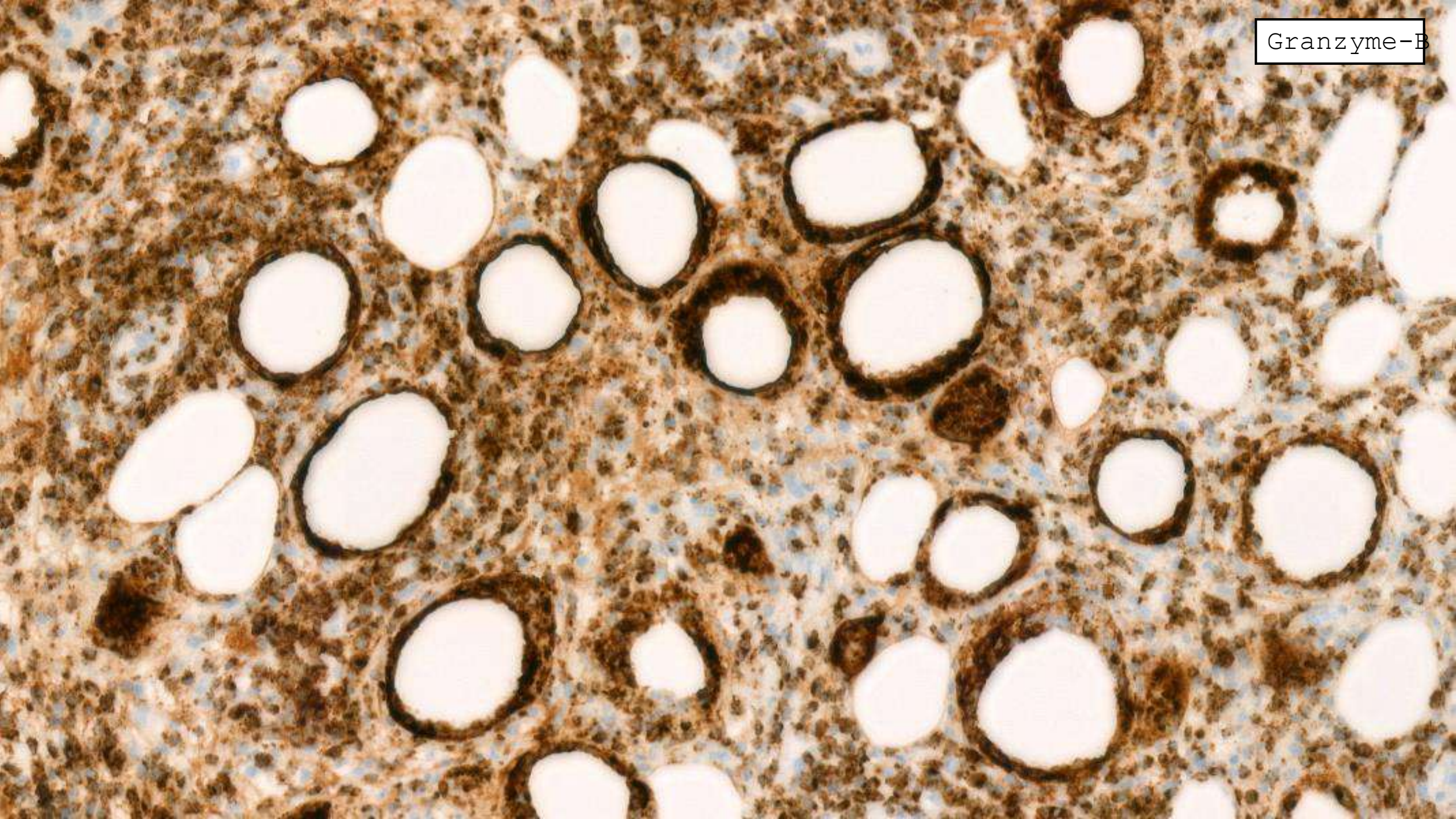
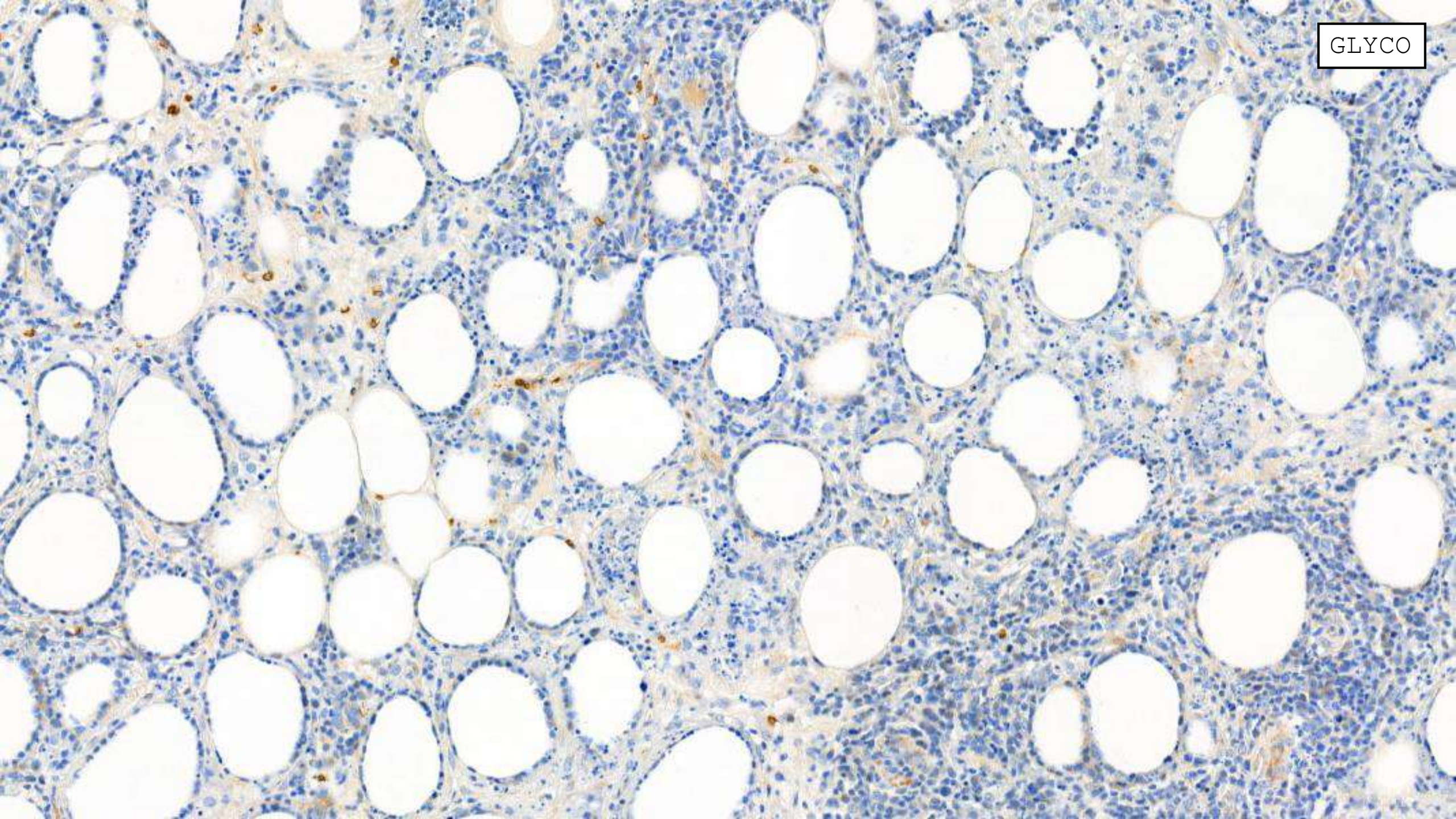
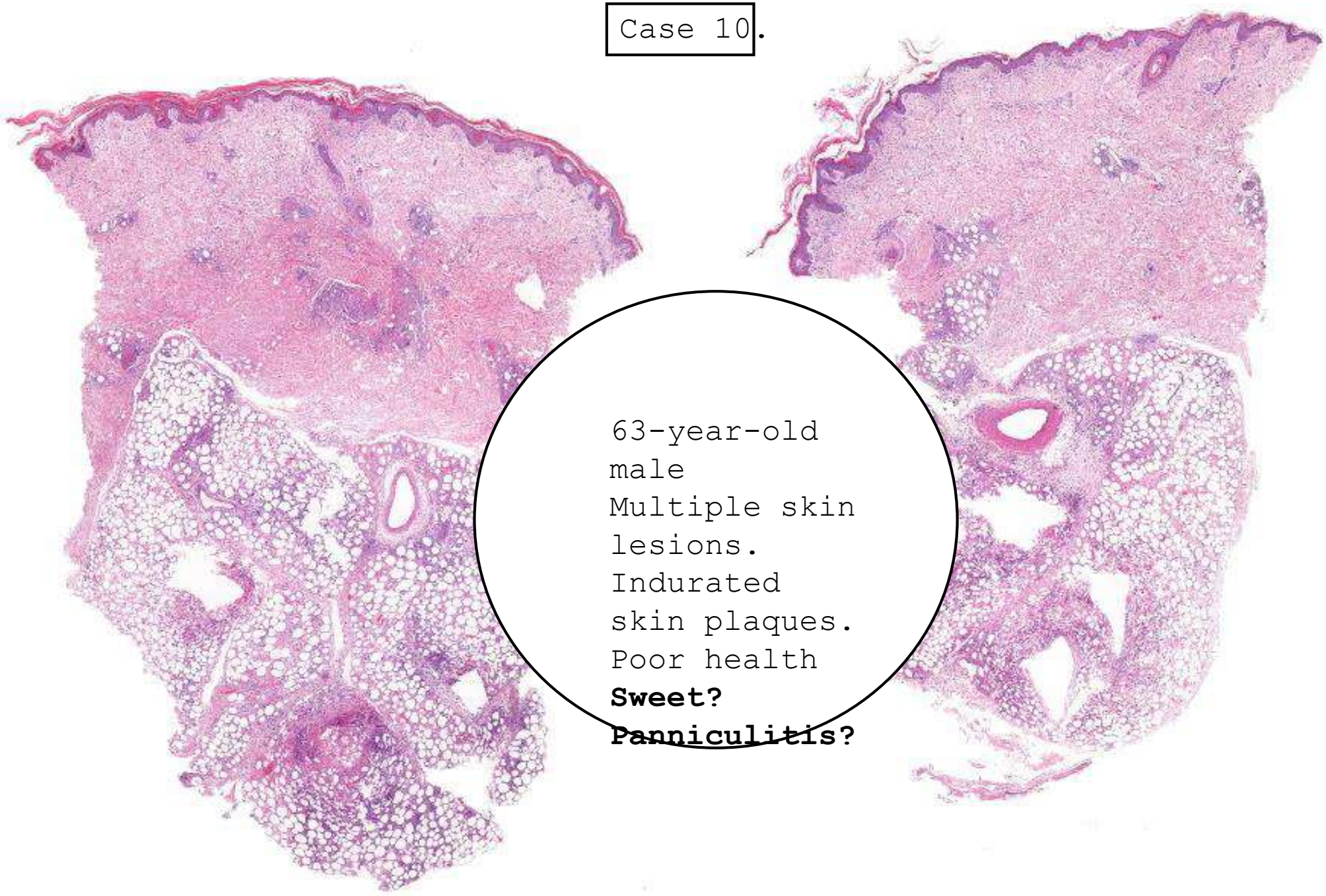
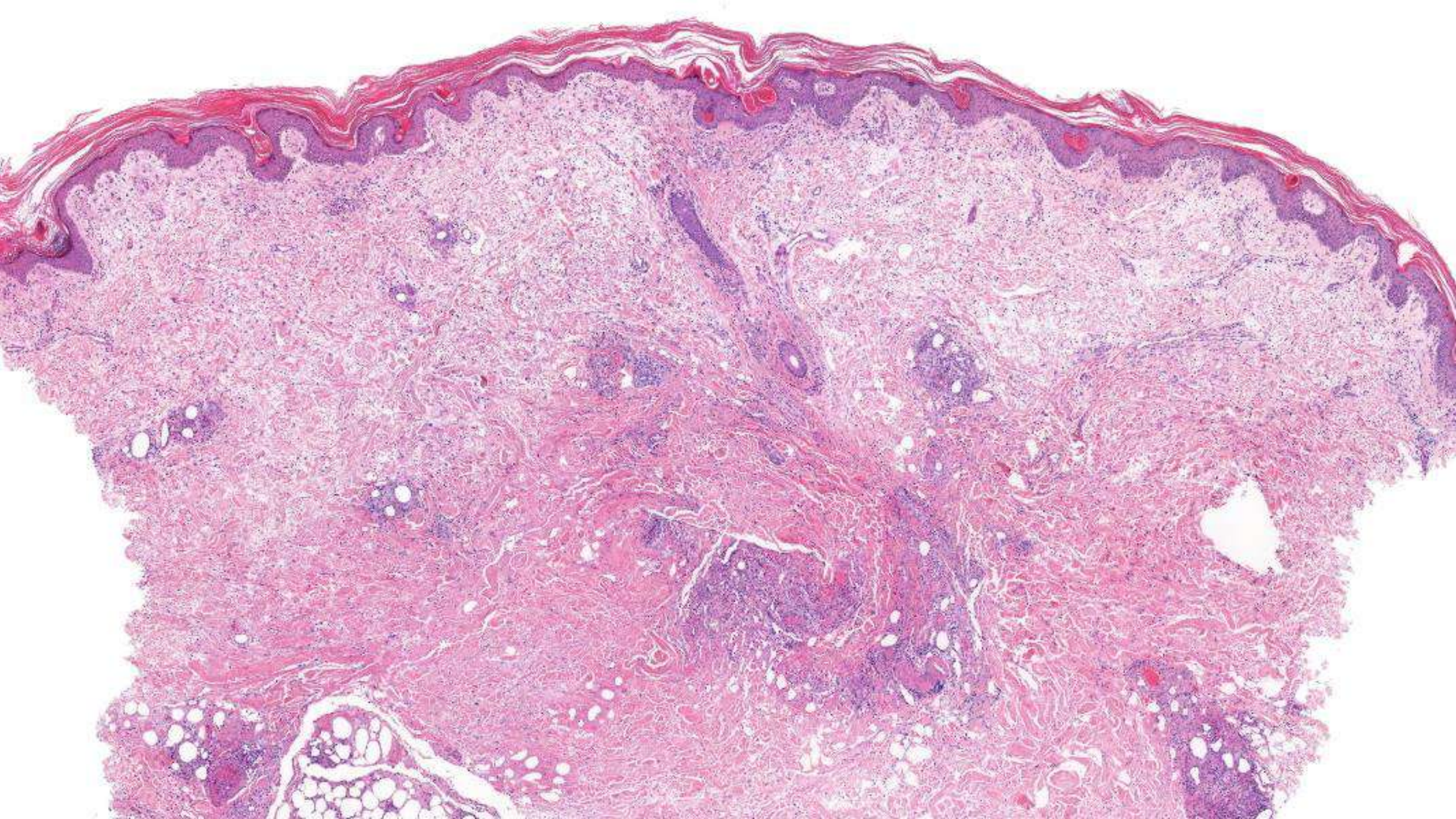

Granzyme-B

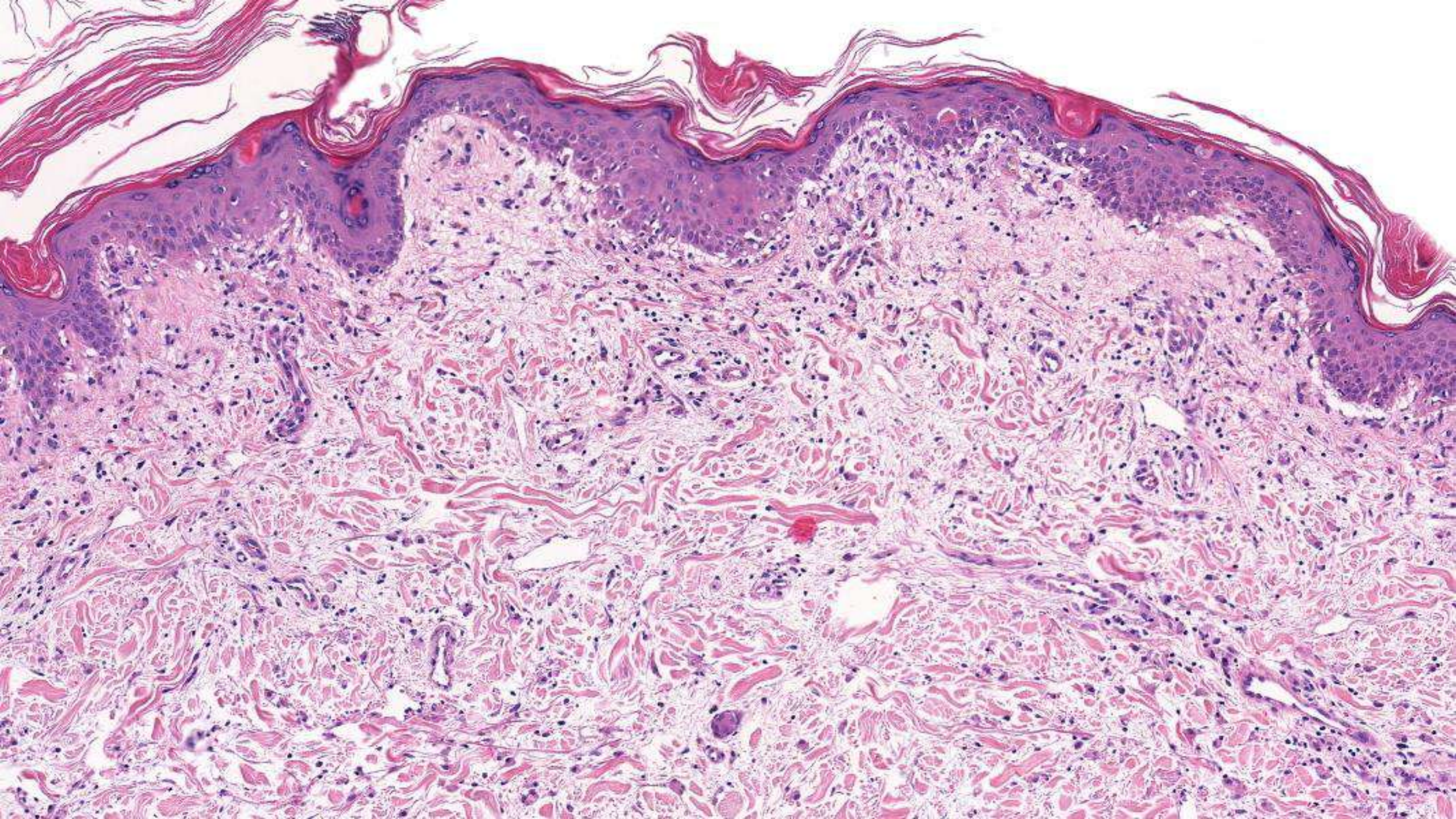

GLYCO

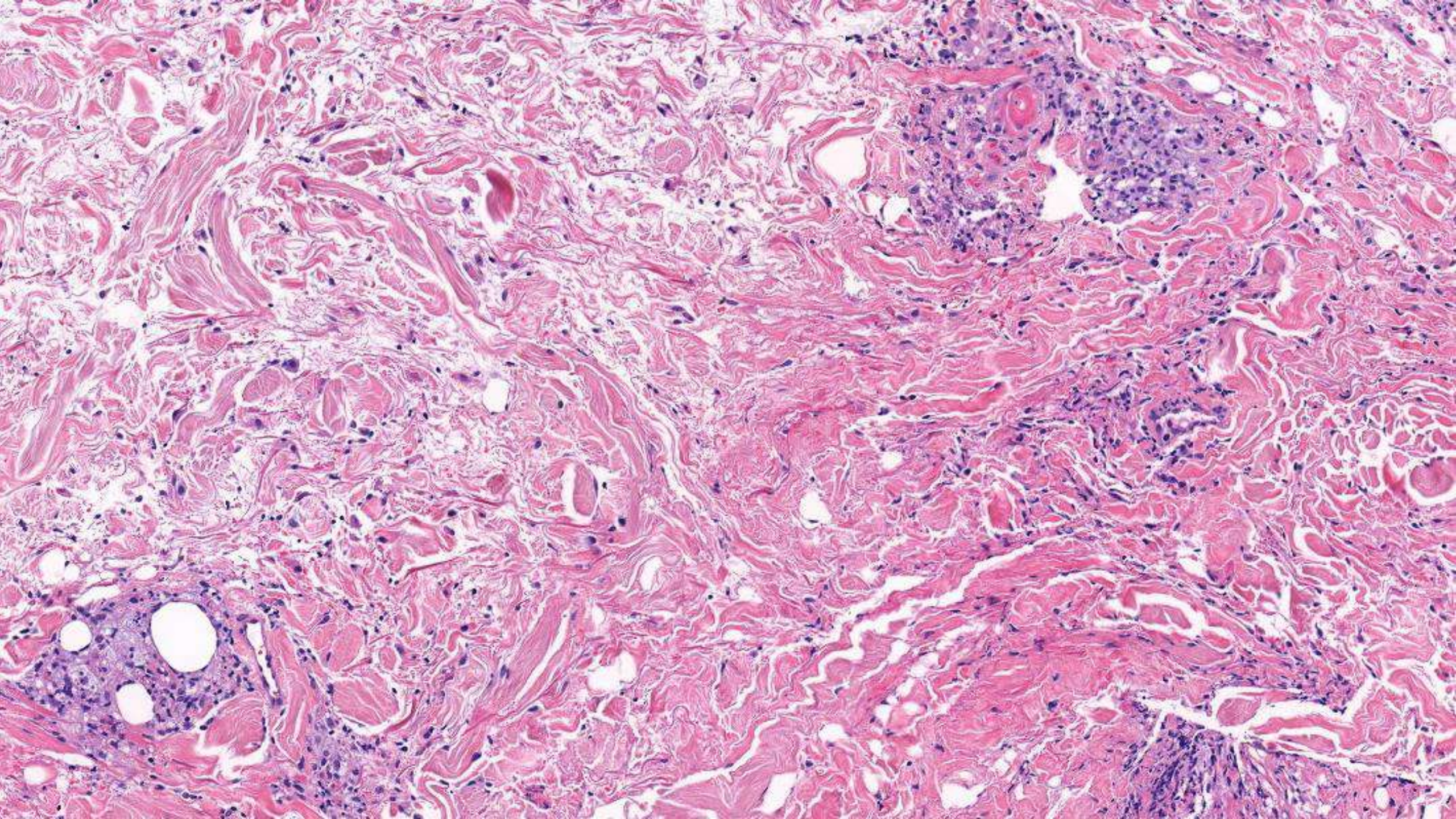
Case 10.

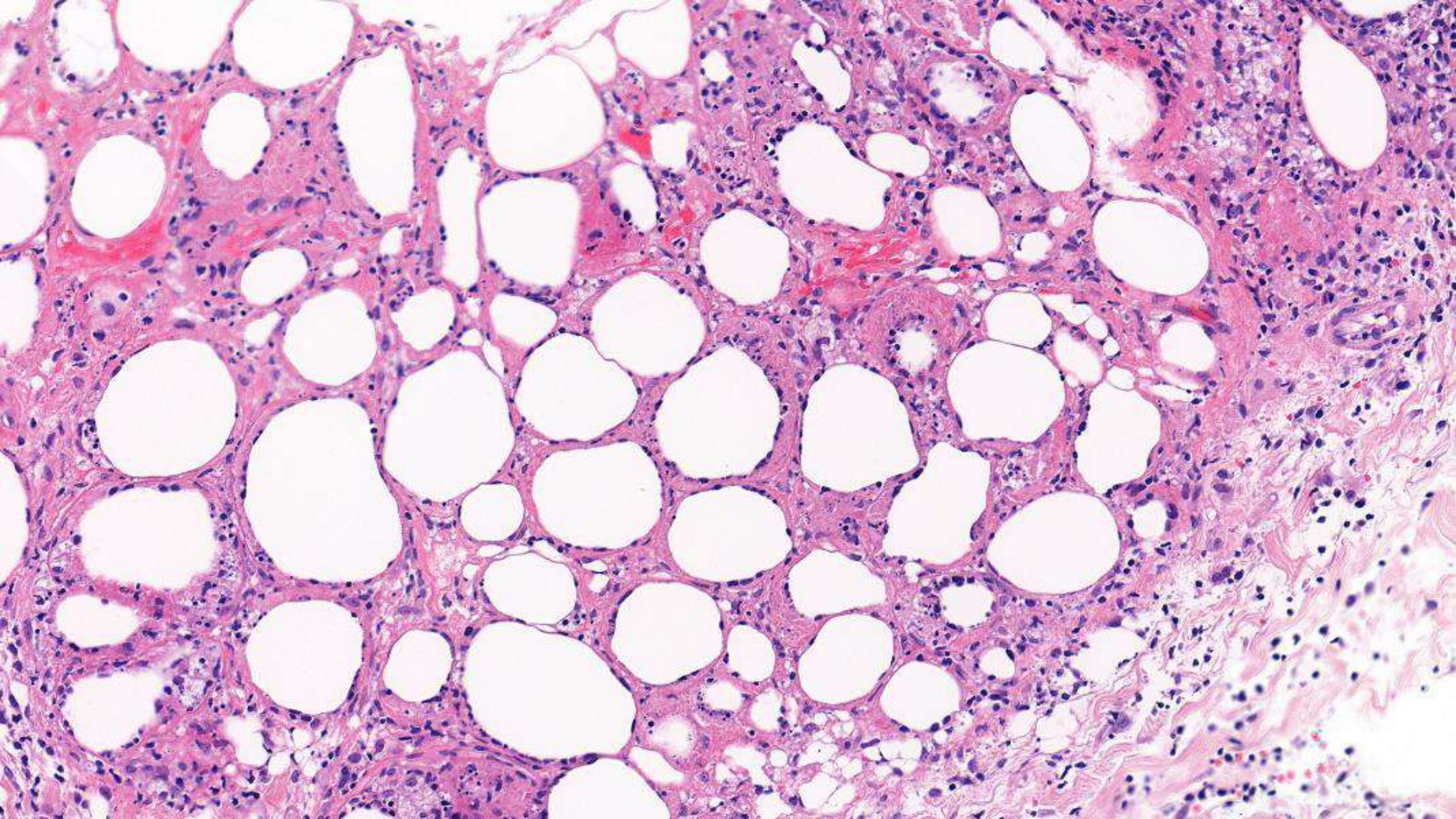


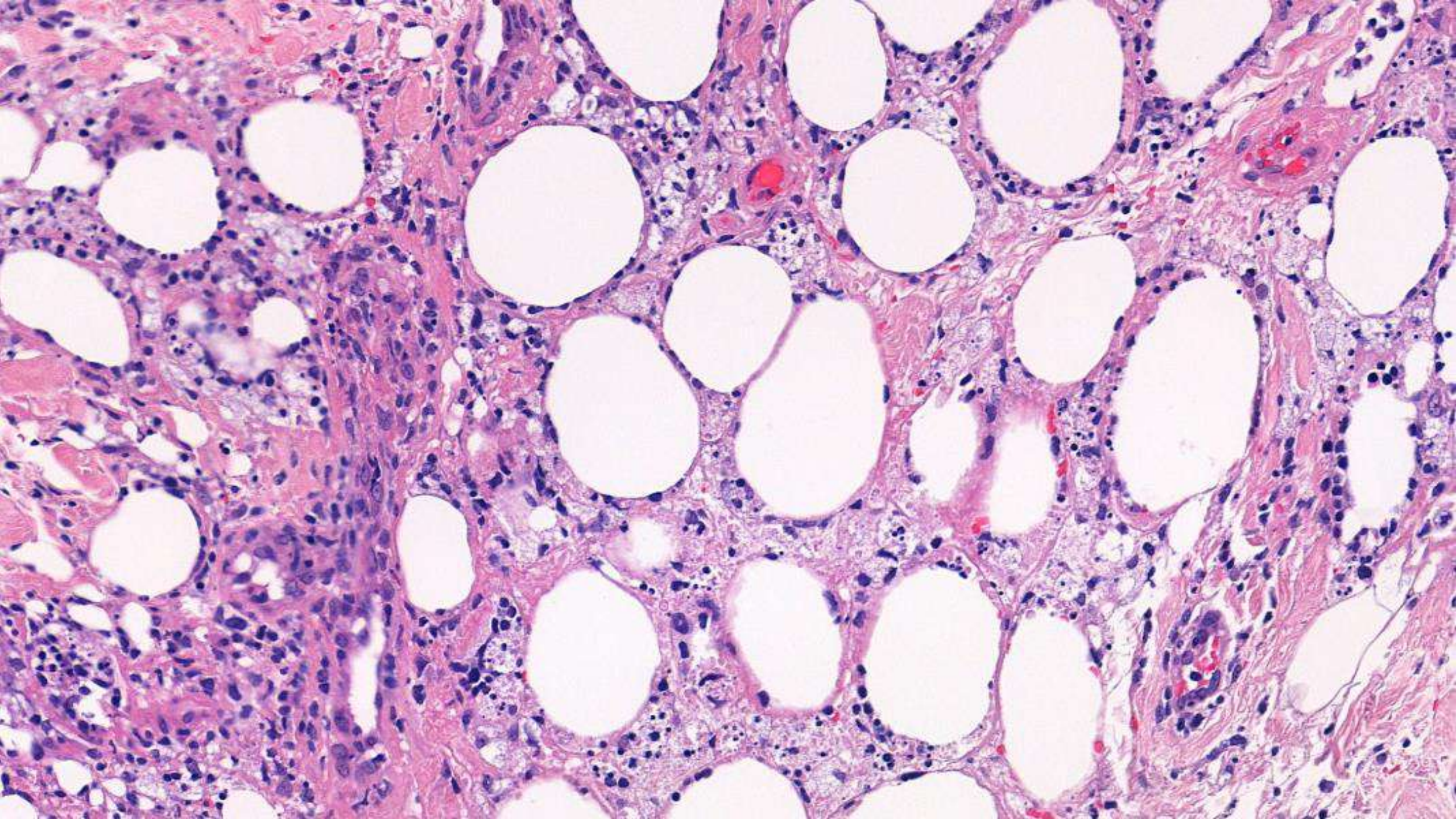
63-year-old male
Multiple skin lesions.
Indurated skin plaques.
Poor health
Sweet?
Panniculitis?

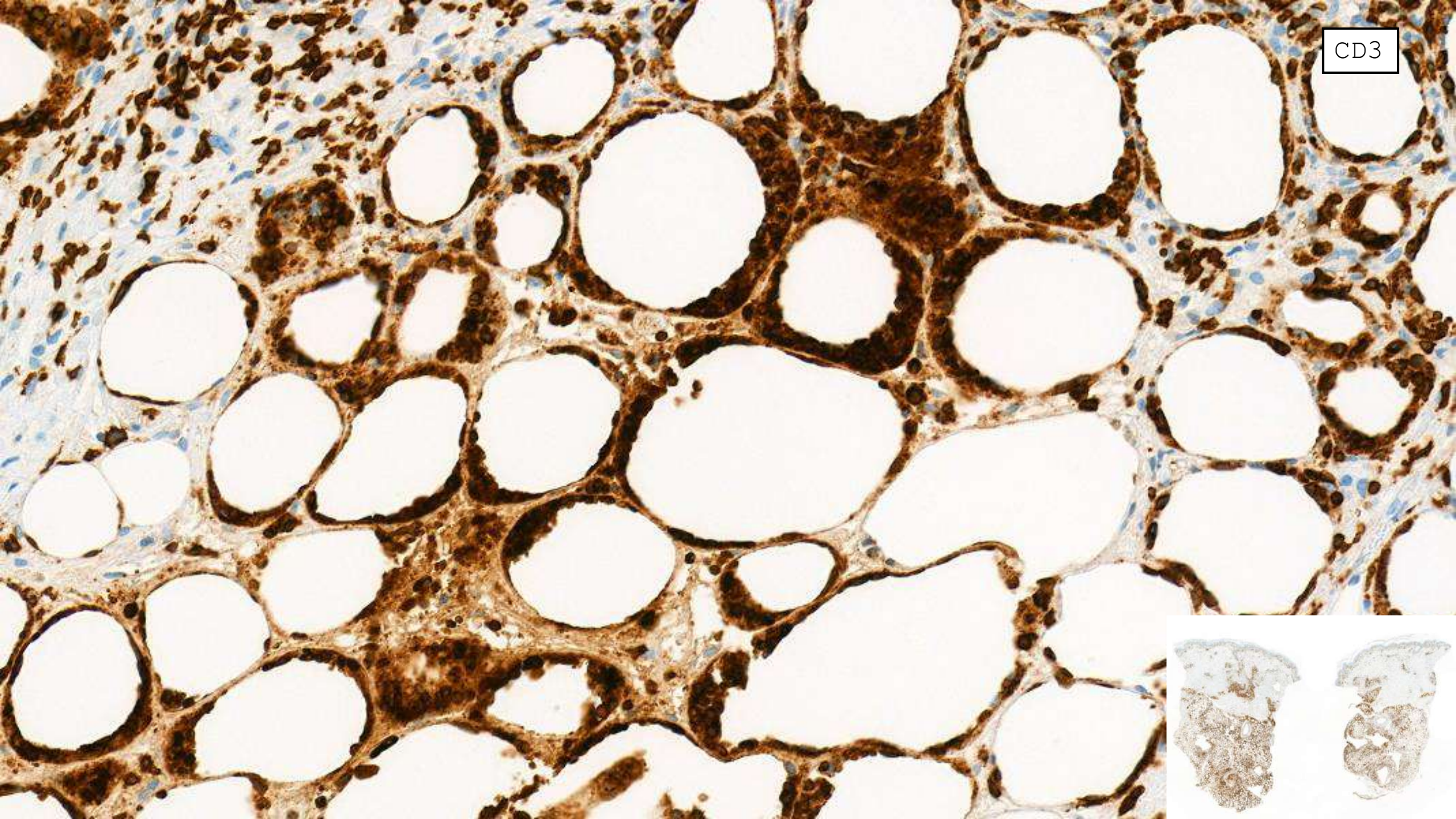








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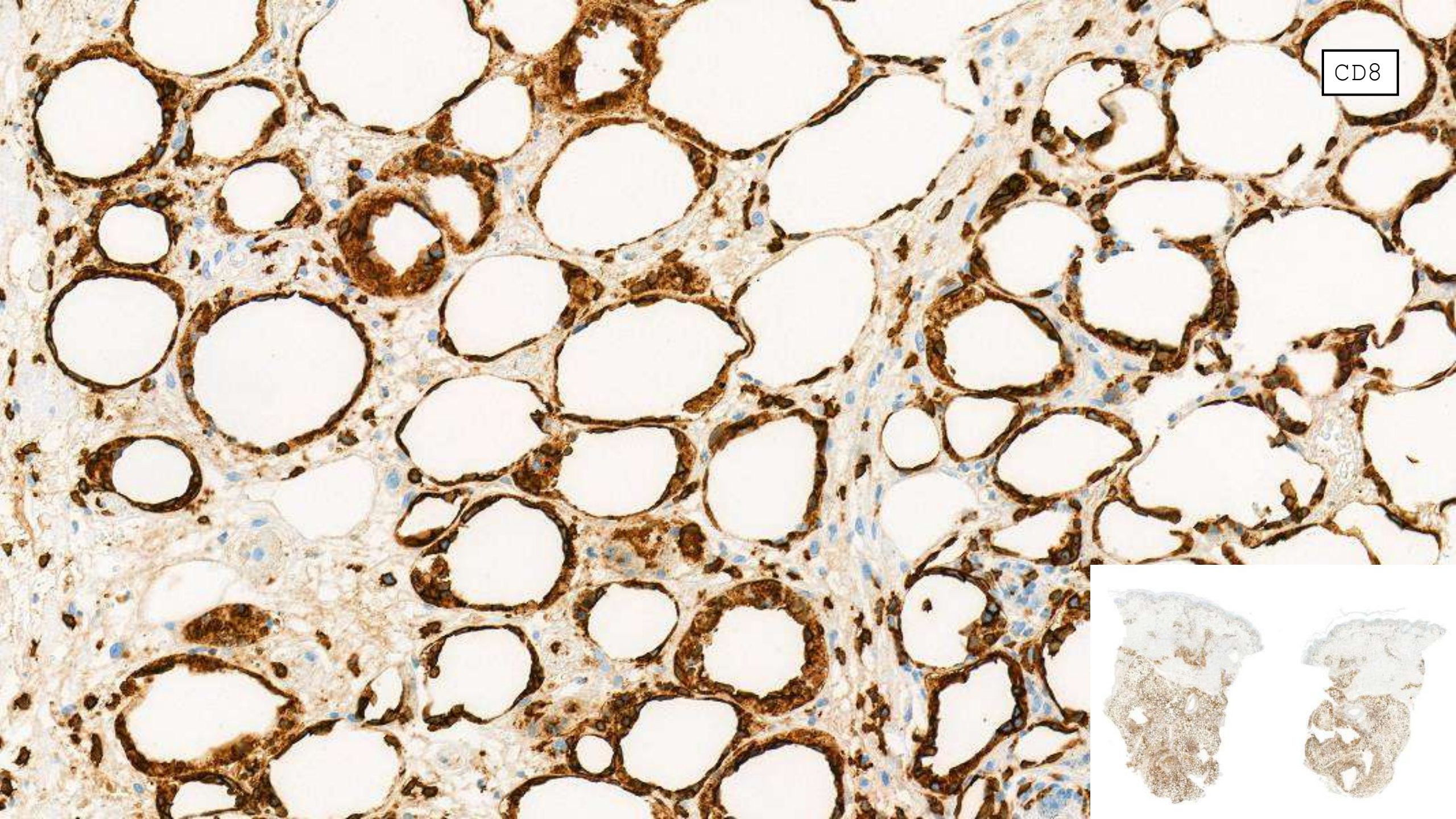
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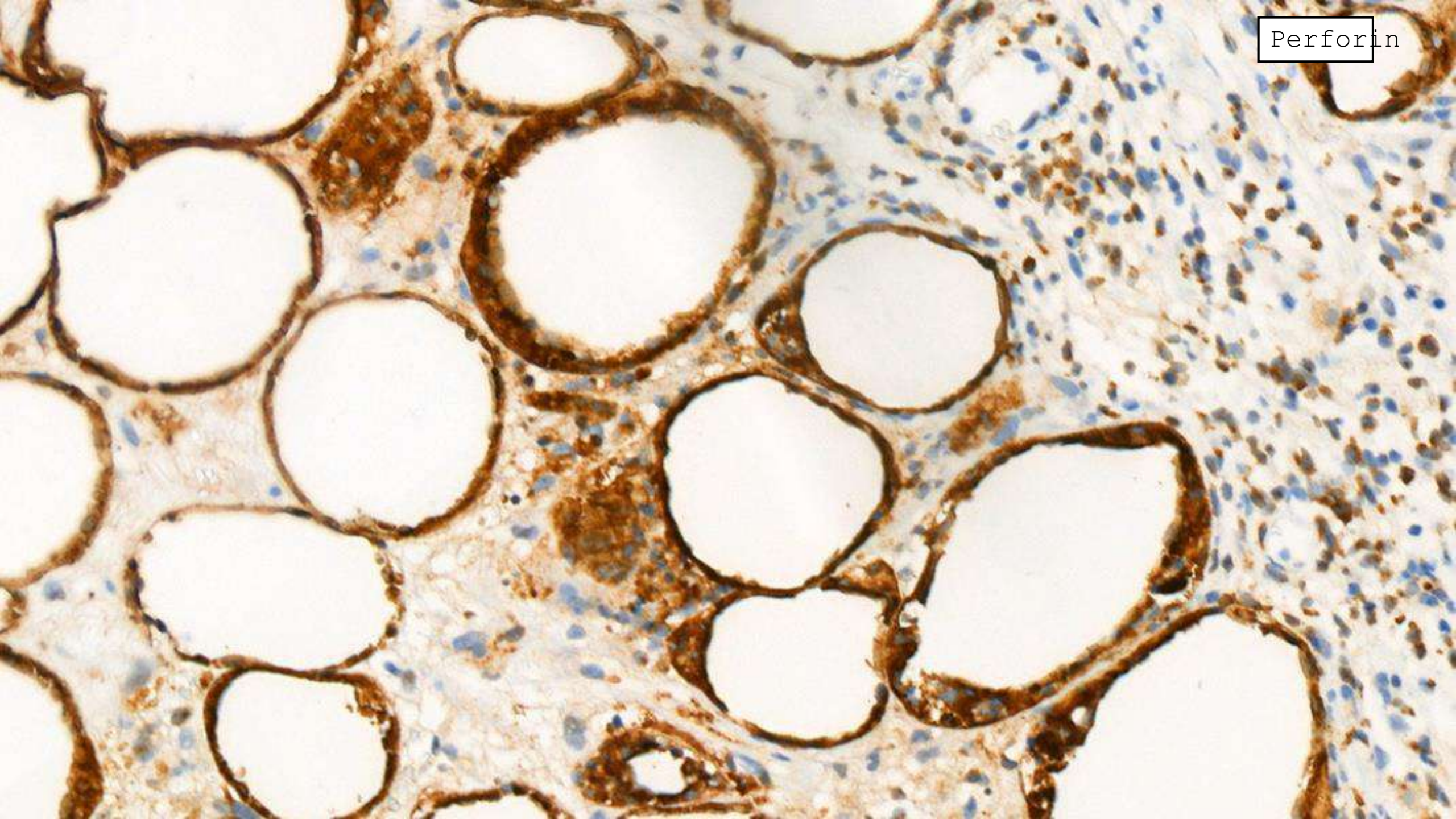
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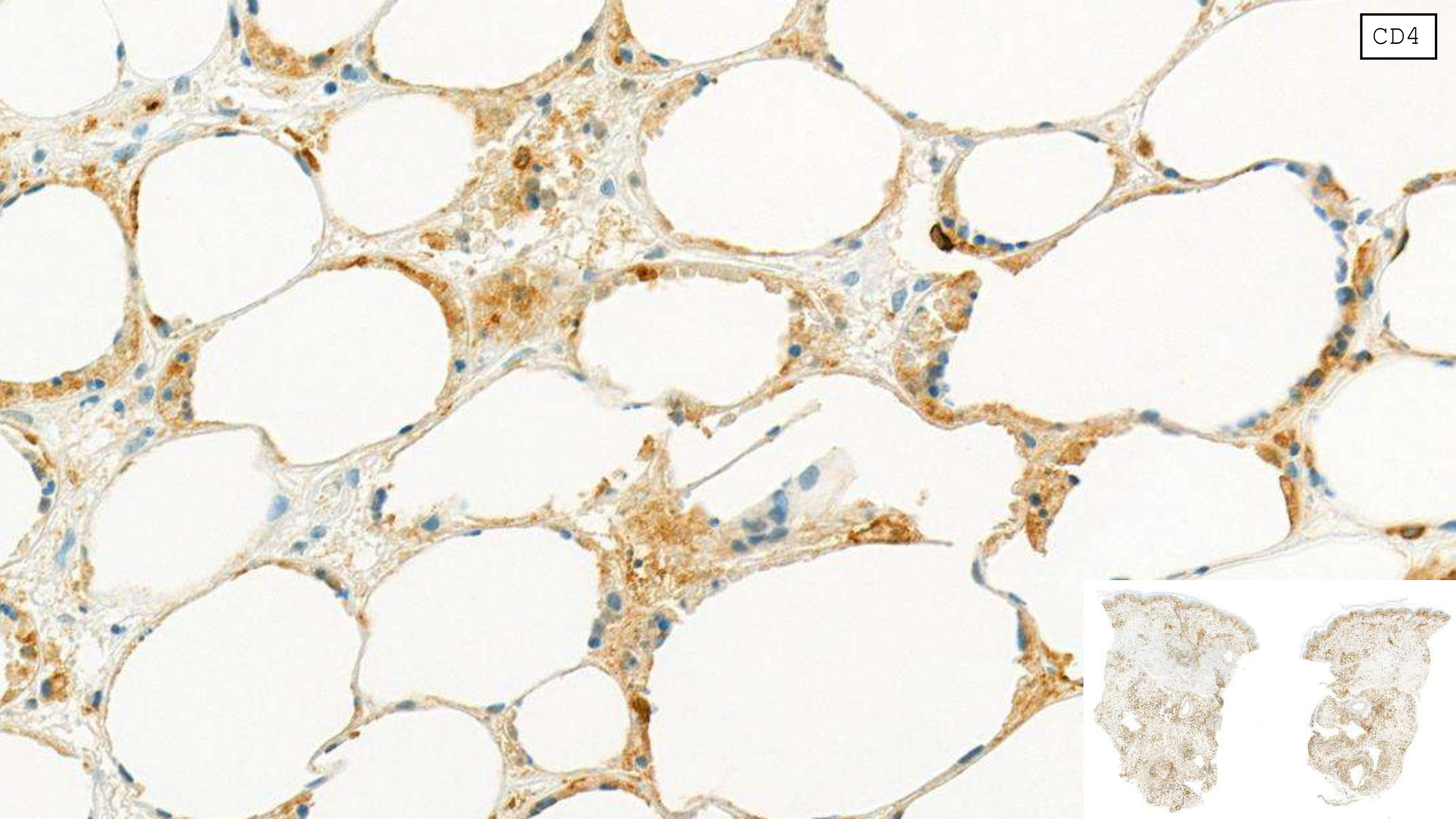
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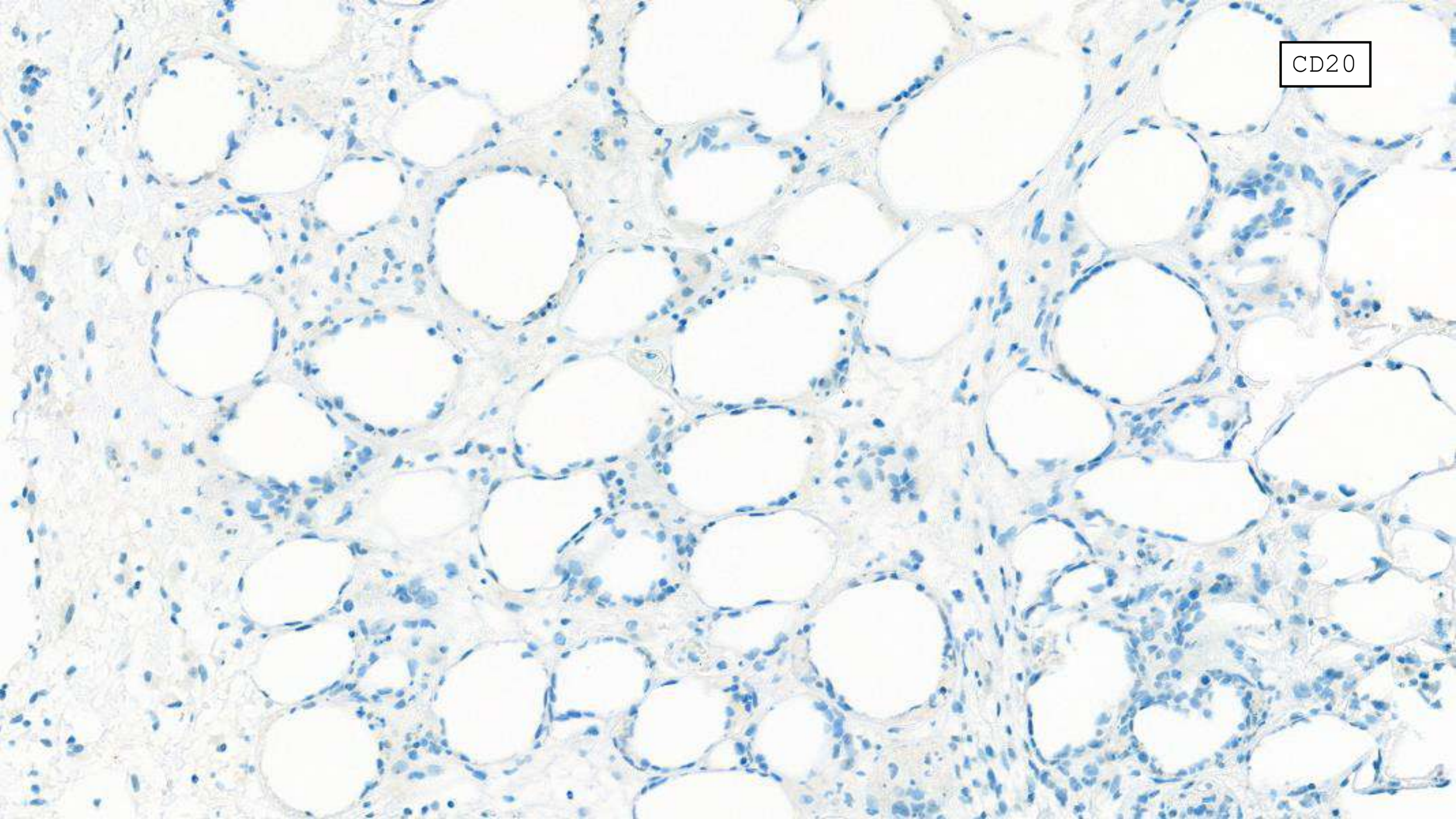
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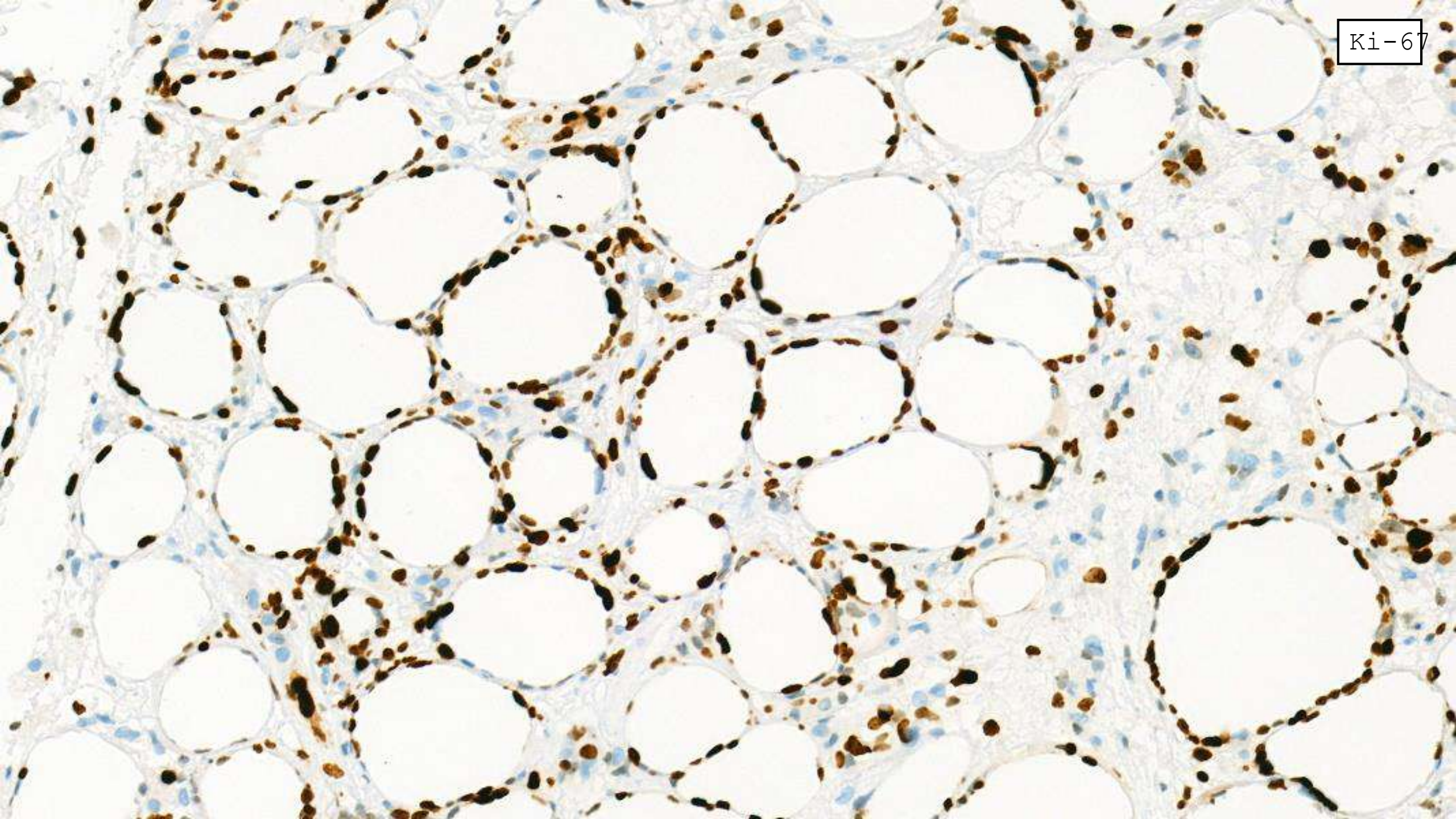
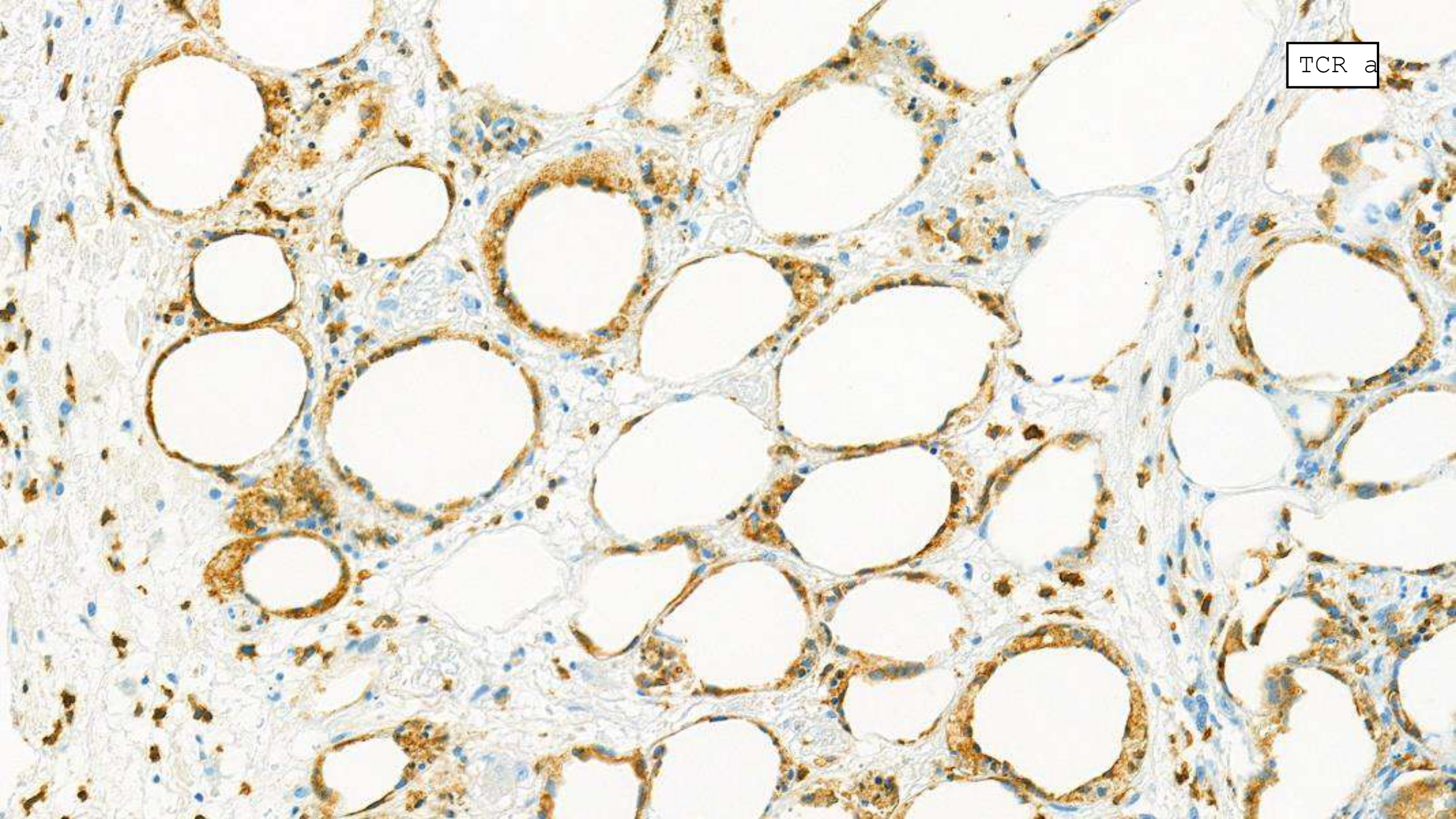
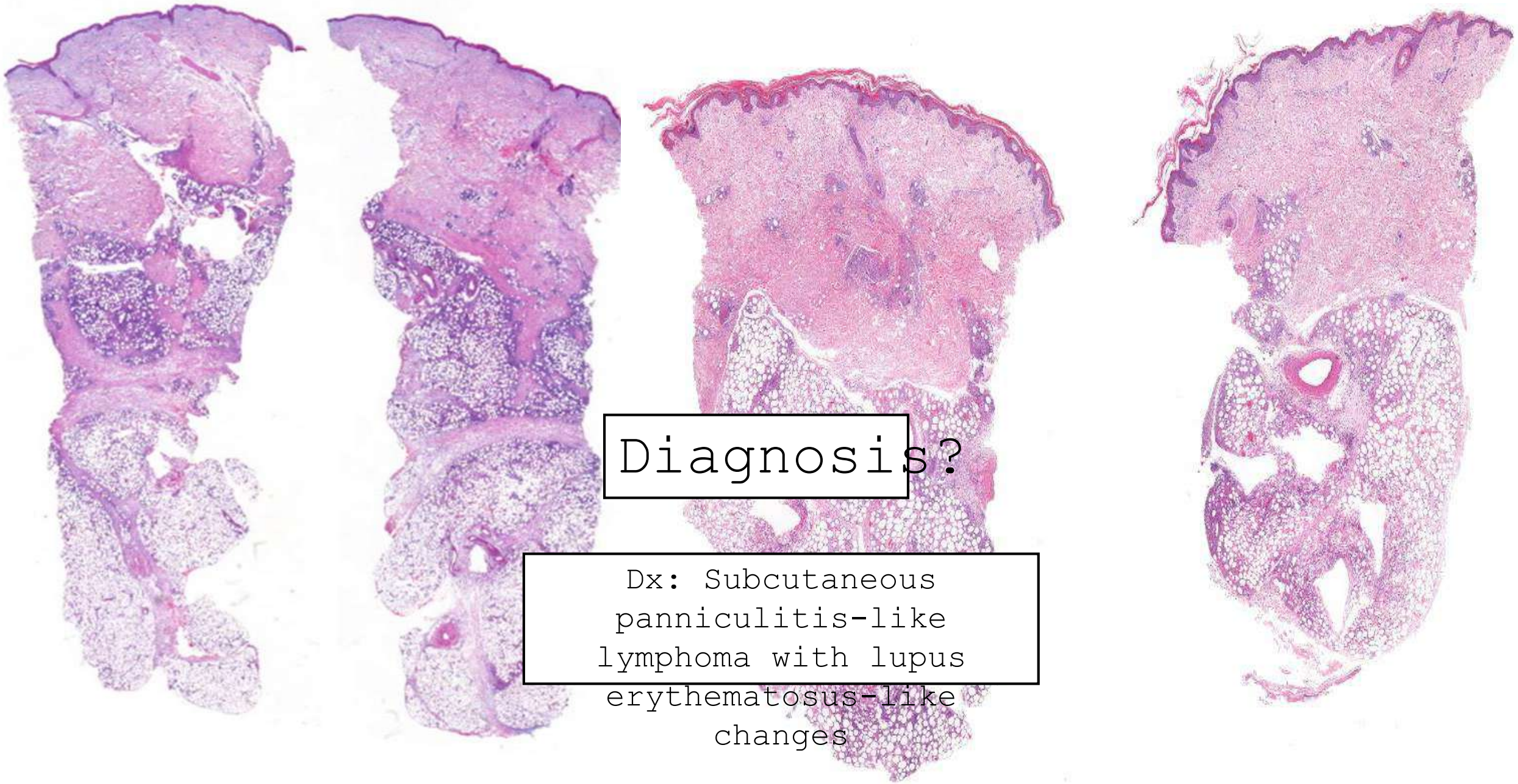

Ki-67


TCR a



Diagnosis?

Dx: Subcutaneous panniculitis-like lymphoma with lupus erythematosus-like changes

- Clinical and histopathologic overlap between subcutaneous panniculitis-like T-cell lymphoma (SPTCL) and lupus erythematosus panniculitis (LEP) suggesting that they may represent opposite ends of a disease spectrum
- SPTCL is associated with higher morbidity, including the risk of hemophagocytic lymphohistiocytosis (HLH), making accurate diagnosis critical
- SPTCL is typically associated with a good prognosis, but the development of hemophagocytic lymphohistiocytosis (HLH) dramatically reduces the 5-year overall survival rate
- Lymphocyte atypia combined with adipocyte rimming of CD8+ T cells within Ki-67 hotspots was also highly specific for the diagnosis of SPTCL
- T-cell clonality analysis showed polyclonal infiltrates in LEP, whereas SPTCL may exhibit monoclonality,

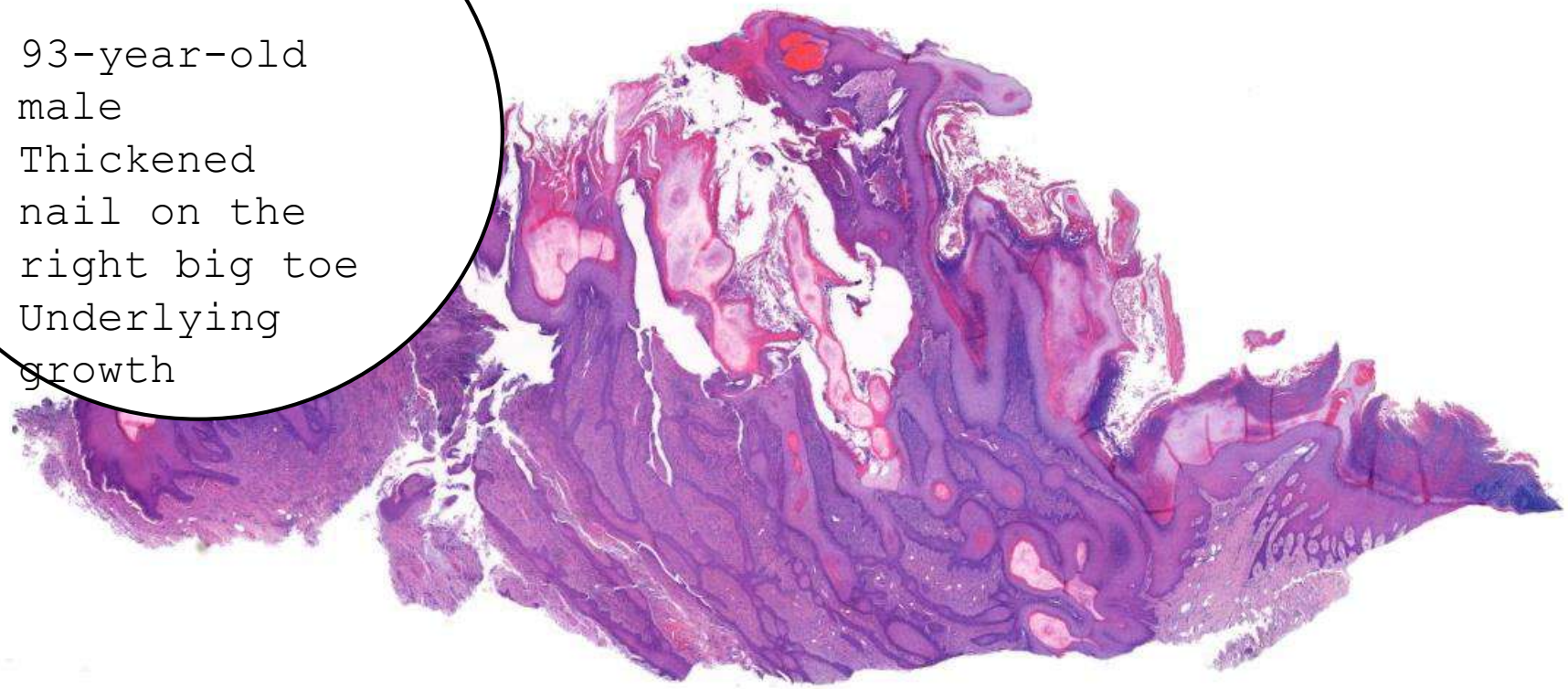
TABLE 2. Histomorphologic Comparisons Between LEP and SPTCL Biopsies

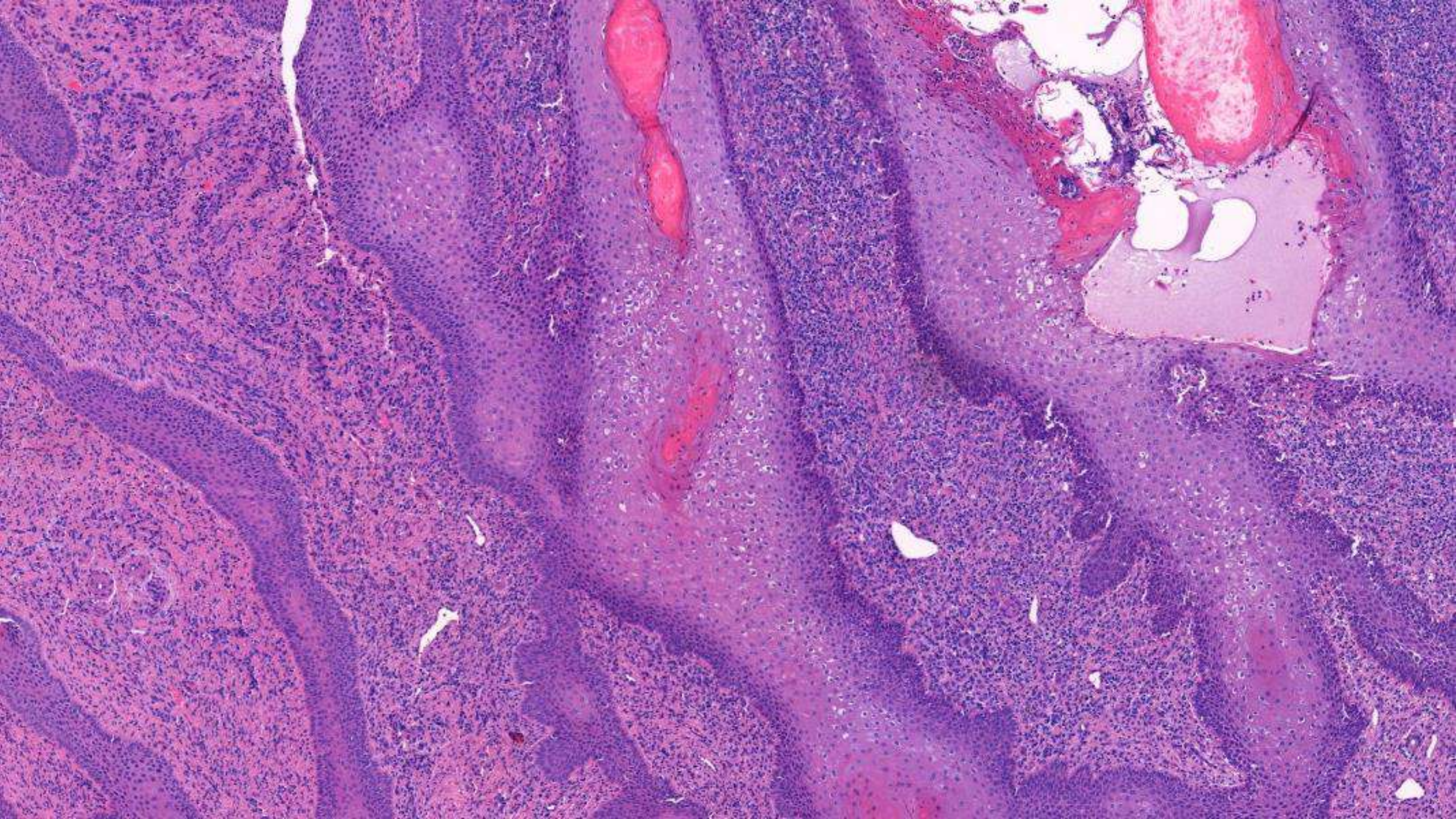
	LEP (n = 15)	SPTCL (n = 22)
Vacuolar interface change		
Present	4	2
Absent	9	17
Perieccrine inflammation		
Present	10	9
Absent	3	10
Dermal interstitial mucin deposition		
Present	9	5
Absent	5	15
Hyaline lipomembranous change		
Present	14	4
Absent	1	17
Karyorrhectic debris and macrophages		
Present	14	20
Absent	1	1
Lymphocytic vasculitis		
Present	11	5
Absent	4	17
Well-formed granulomas		
Present	3	4
Absent	12	18
Lymphocyte atypia and adipocyte rimming		
Present	0	18
Absent	15	4

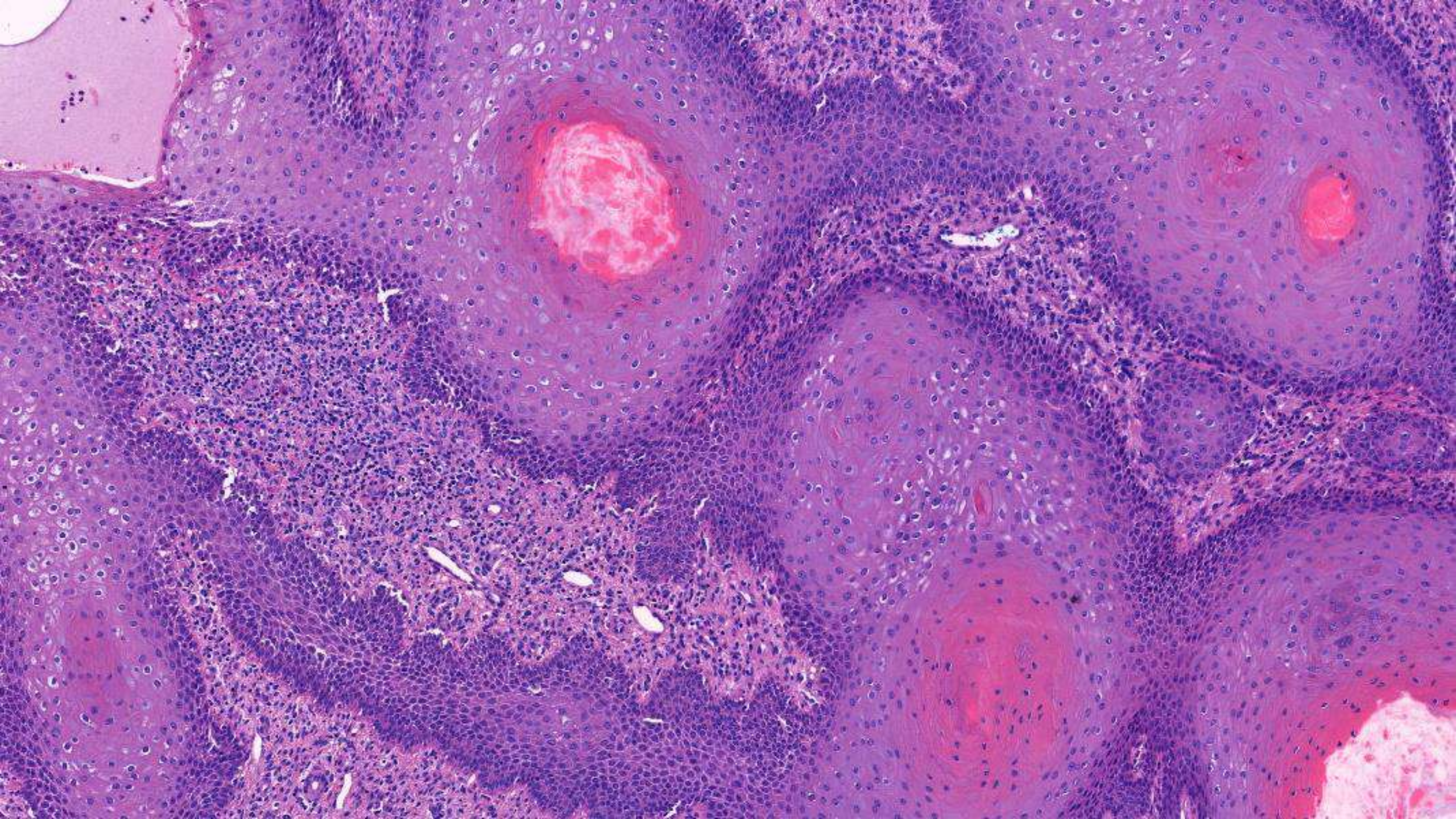
LeBlanc RE, Tavallaee M, Kim YH, Kim J. Useful Parameters for Distinguishing Subcutaneous Panniculitis-like T-Cell Lymphoma From Lupus Erythematosus Panniculitis. Am J Surg Pathol. 2016 Jun;40(6):745-54.

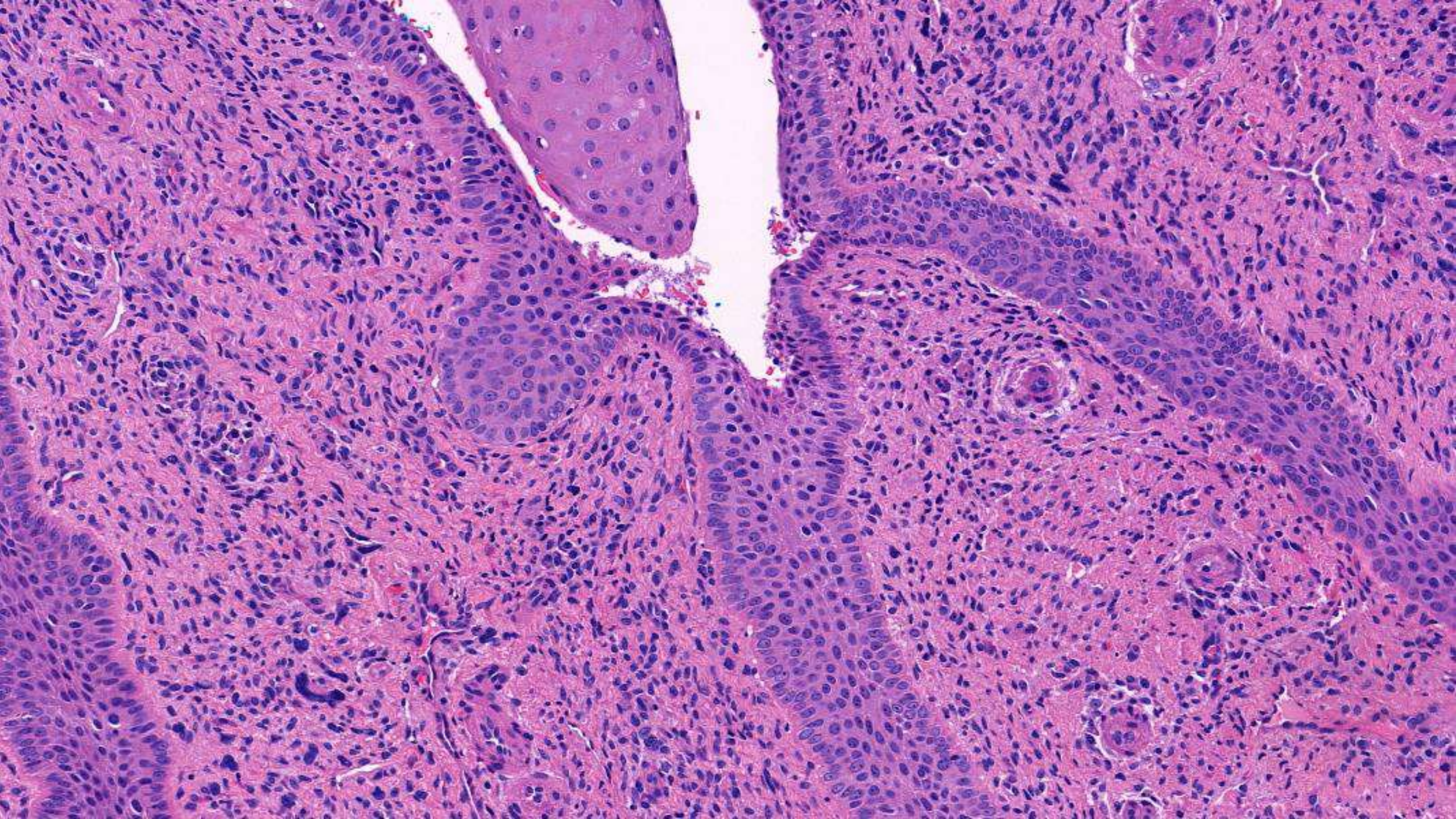
Case 11

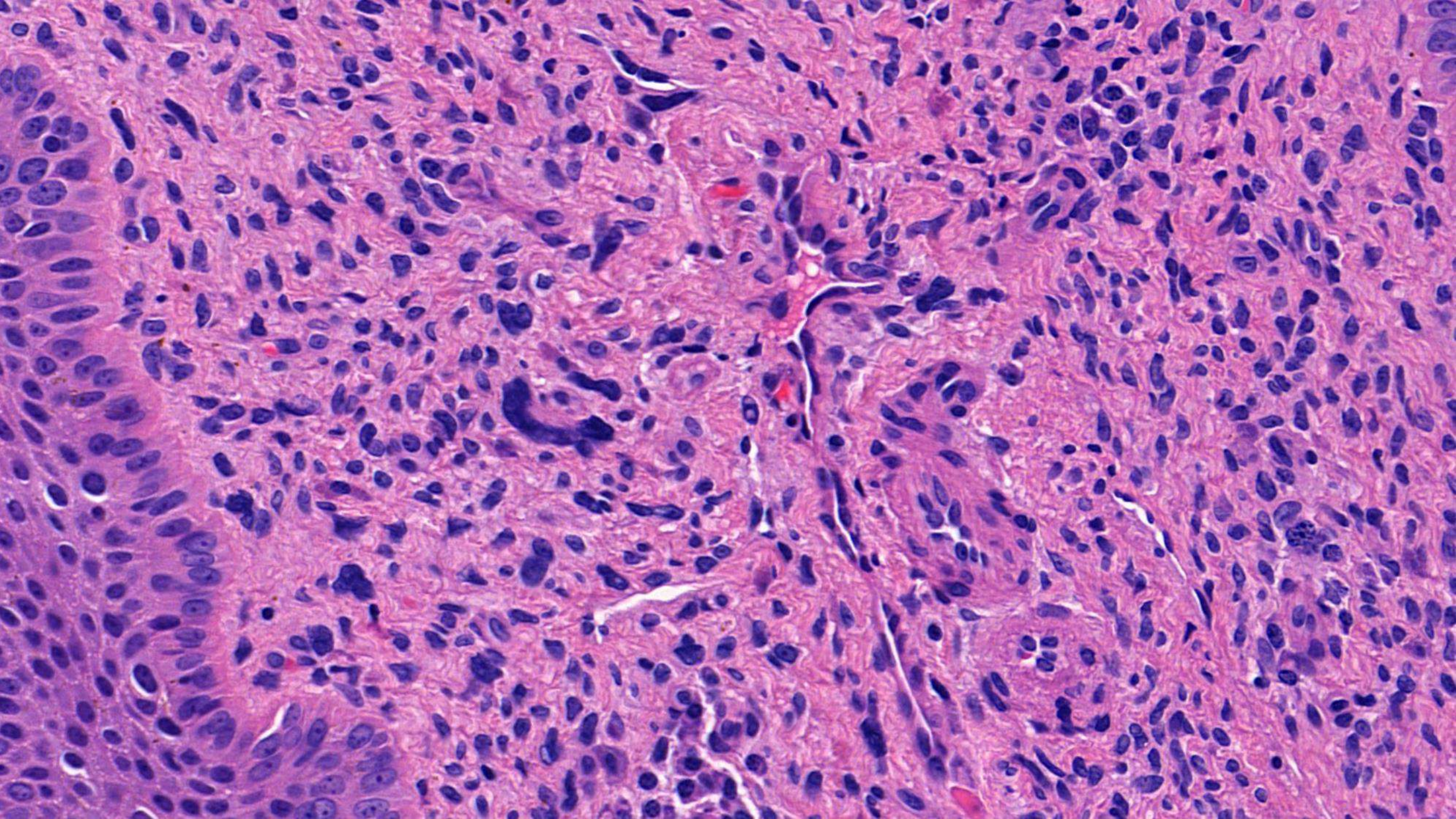
93-year-old male
Thickened nail on the right big toe
Underlying growth

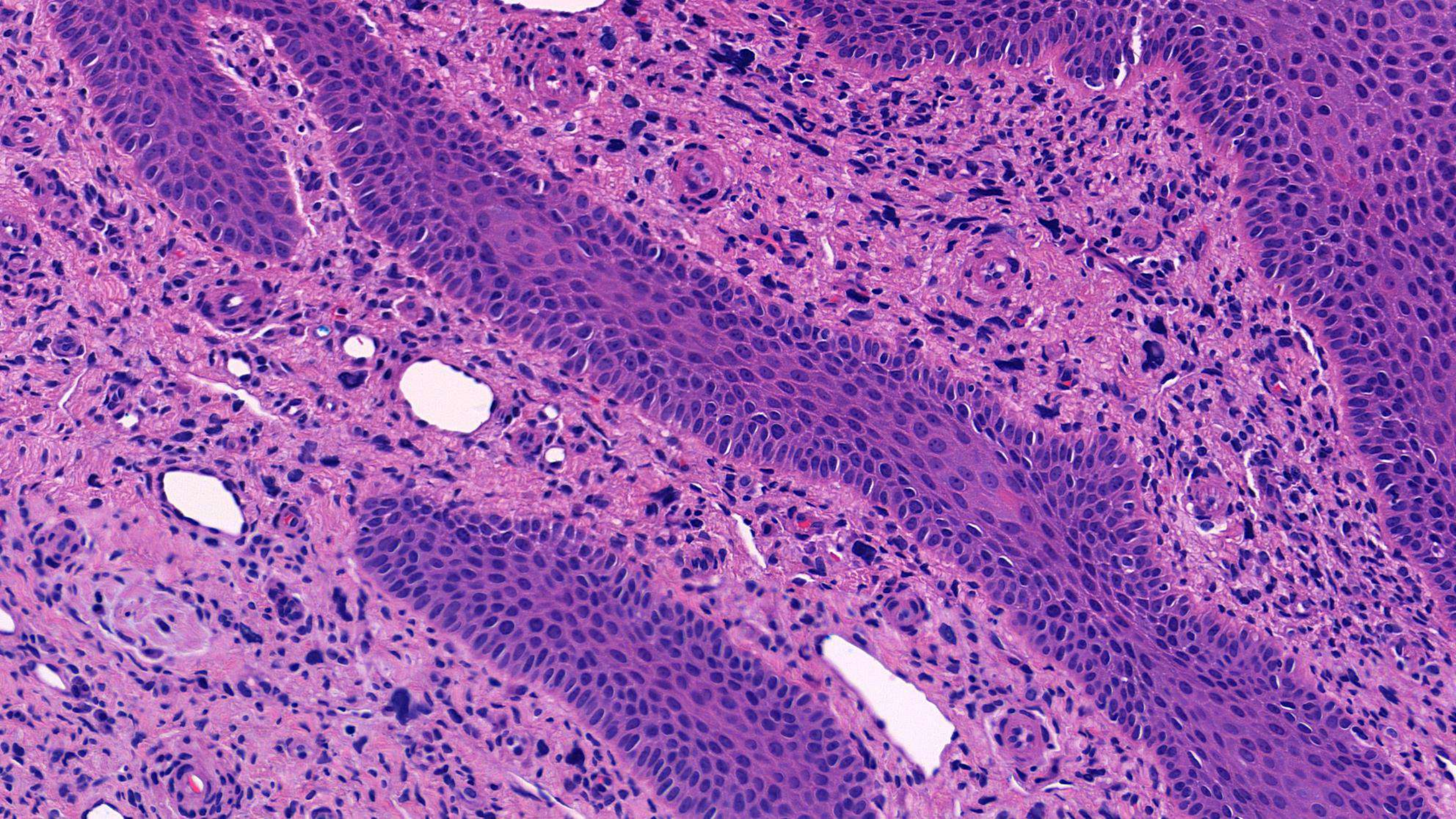


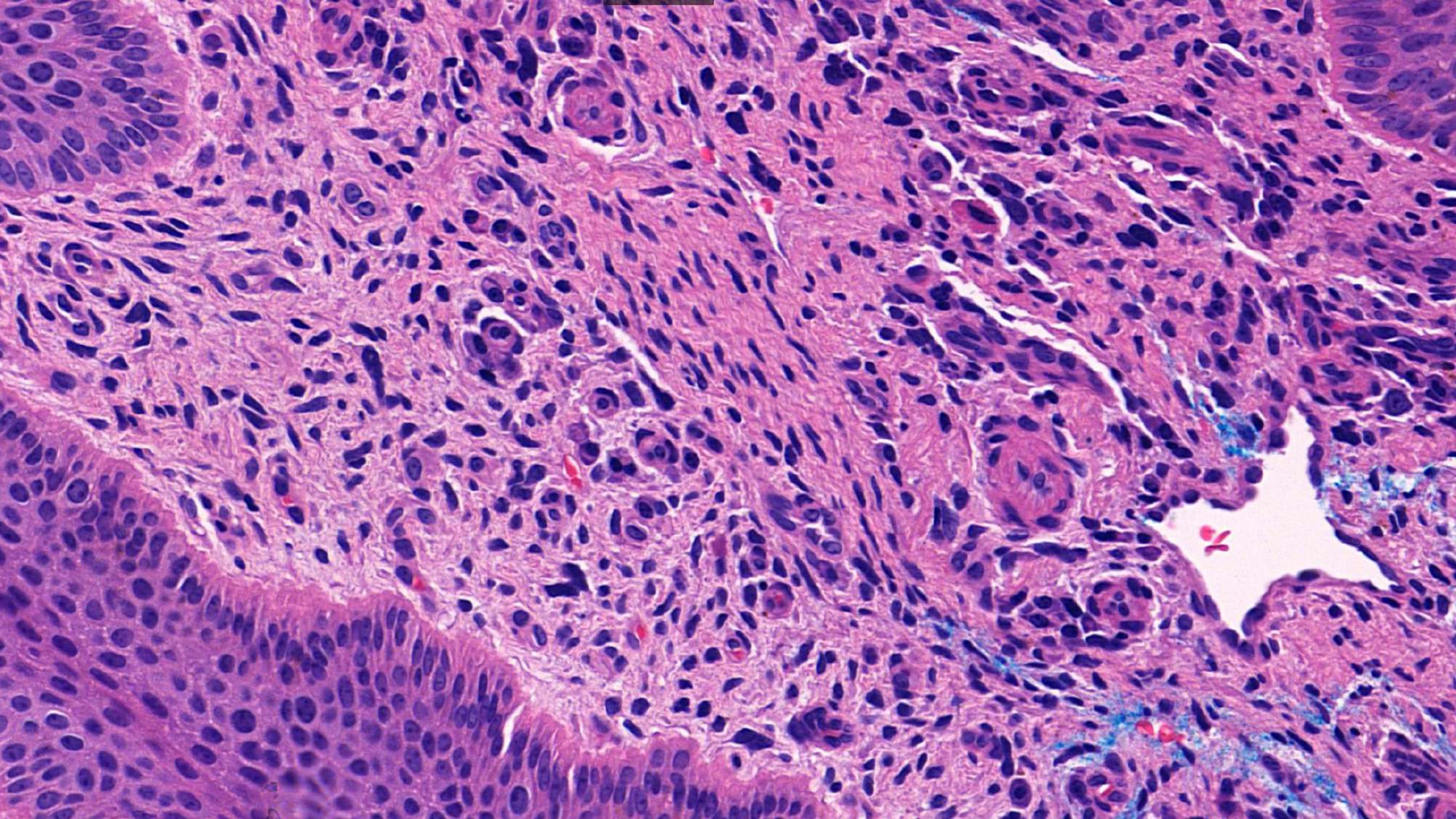












Diagnosis?

Dx: Onychomatricoma-pleomorphic variant

- Pleomorphic onychomatricoma is a rare tumour mimicking malignancy

This study proposes diagnostic criteria for pleomorphic onychomatricoma that clinically include free edge thickening and pitting pattern of the nail plate with an additional feature of projecting line pattern

Histologically, this benign condition is characterized by

- Small size, low cellularity,
- Degenerative nuclear atypia
- Superficial location in the stroma of the atypical cells
- Ki67 proliferation rate inferior to 5%
- Absence of mitotic figure or necrosis
- Distinctive immunophenotypical profile restricted to the diffuse expression of CD34 with focal or negative CD10 expression

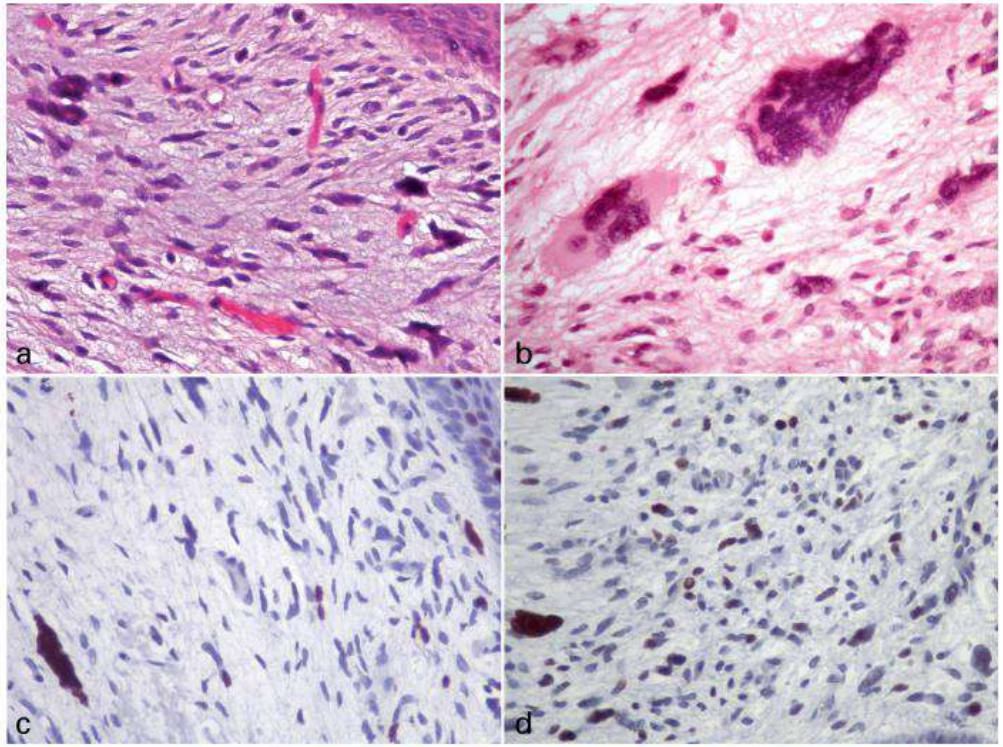


Fig. 4. High-power histological view (H&E, **orignal mgnification×400) showing multinucleate cells with a floret-like arrangement of** (a) nuclei and (b) an epithelioid feature. (c) Ki67 proliferative index in spindle cells is inferior to 5% overall, but approximately 20% in the large atypical cells. (d) Focal p53 overexpression on atypical cells.

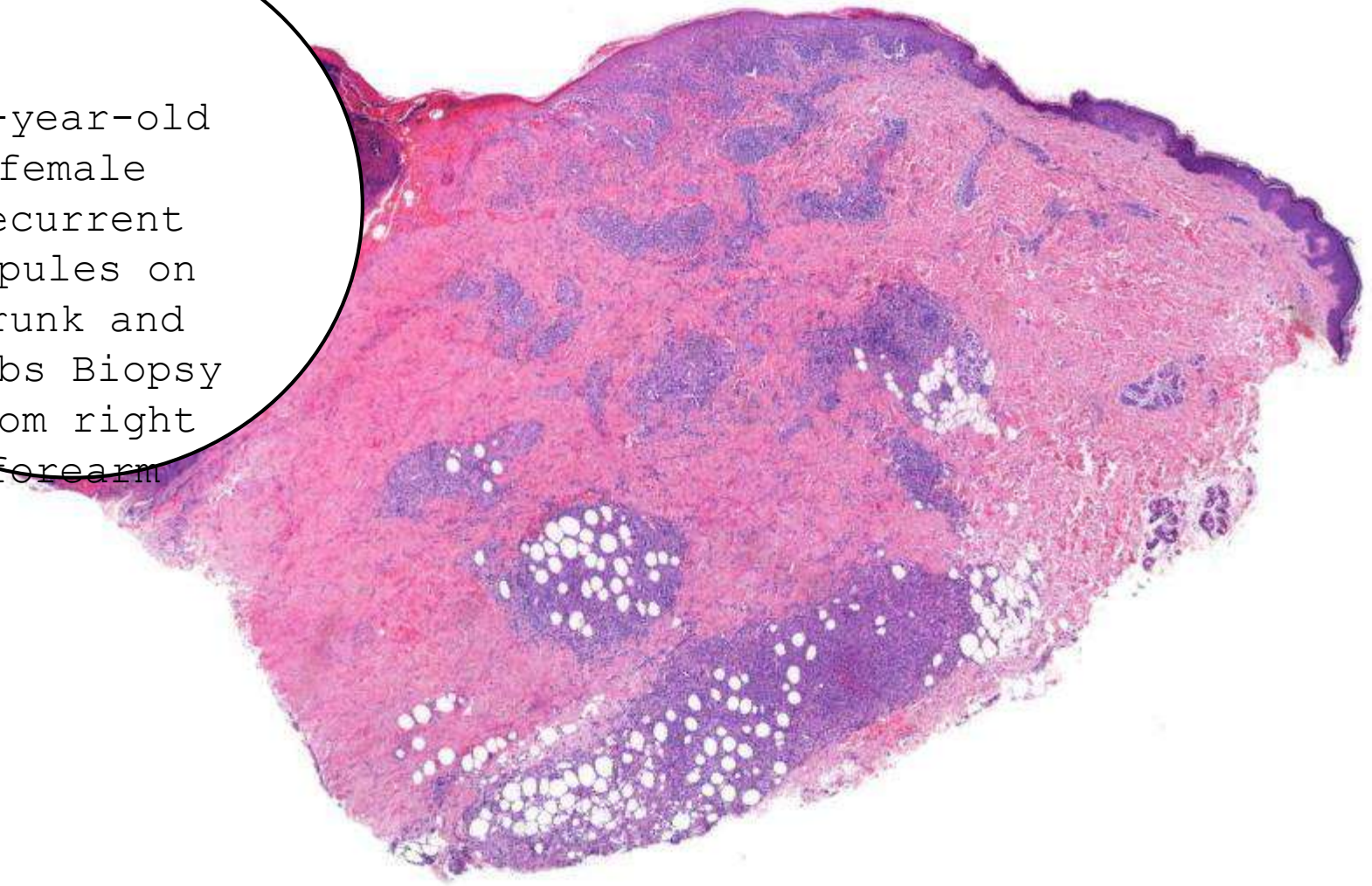
Perrin C, Ambrosetti D. Pleomorphic Onychomatricoma: A Mimicker of Malignancy. Acta Derm Venereol. 2022 Jan 5;102:adv00628.

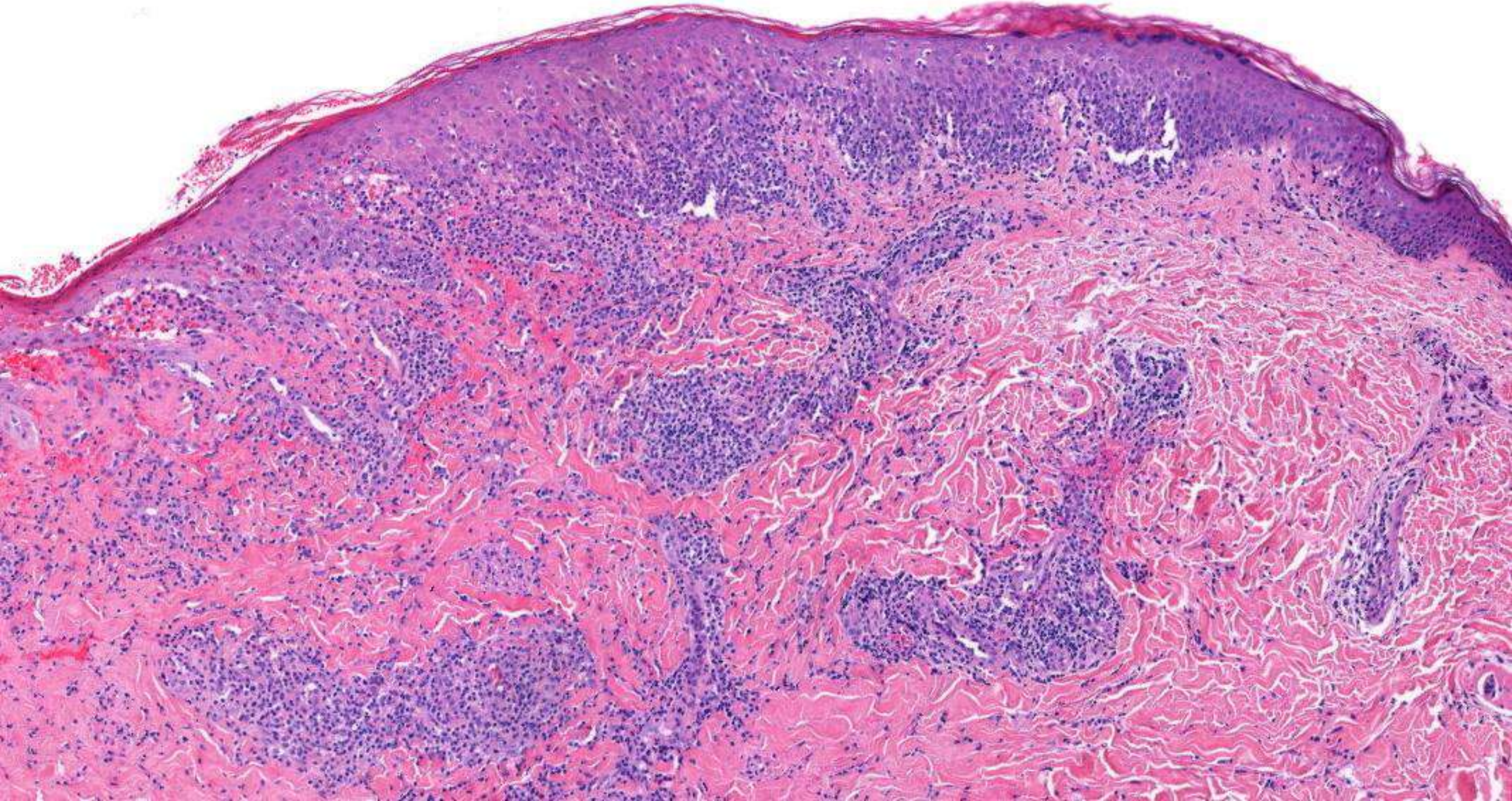
Differentialdiagnosis

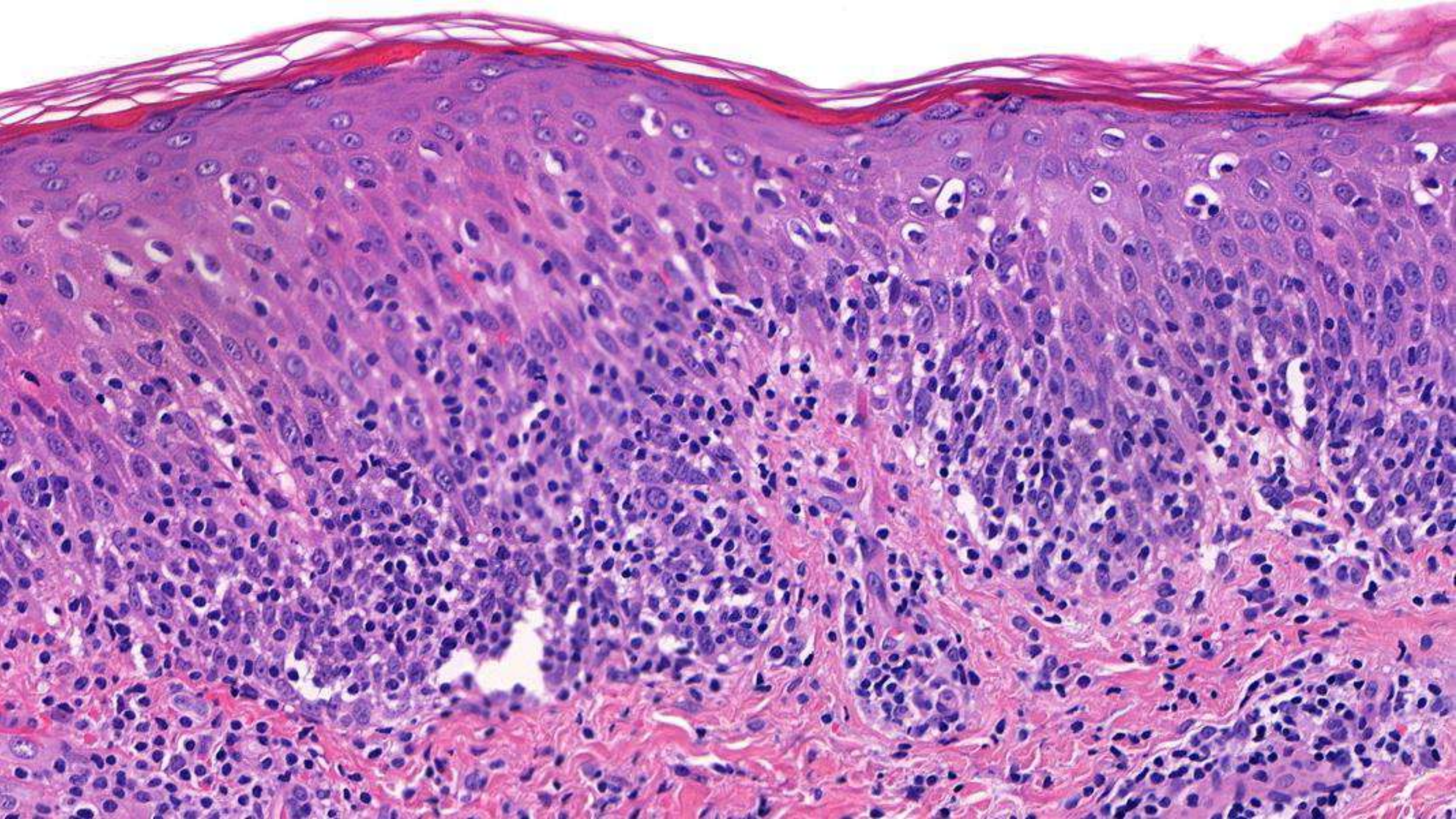
Differential Diagnosis	Key Features	Diagnostic Markers
Pleomorphic SAF	Subungual location, epithelial component with papillary digitations, bizarre-appearing cells, low mitotic activity	CD99 (positive), focal EMA reactivity (positive)
Pleomorphic Perineuromia	Expresses EMA and Glut-1	EMA (positive), Glut-1 (positive), POM is negative for both markers
Cellular Angiofibroma	Hyalinized vessels, absence of biphasic stroma, focal bcl2 staining	bcl2 (positive)
Superficial ALK-Rearranged Myxoid Spindle Cell Neoplasm	Diffuse ALK1 expression, frequent expression of S100 protein	ALK1 (positive), S100 protein (positive)
CD34-Positive Fibrosing Sarcomatous Family (e.g., SCFT)	Multibranched fibrokeratoma-like architecture, nuclear atypia, lack of mitotic activity, low Ki67 index, keratin immunoreactivity	Keratin (positive in SCFT, absent in POM), CD34 (positive in SCFT)
Myxoinflammatory Fibroblastic Sarcoma	Bizarre-appearing cells in a myxoid stroma, low mitotic activity, acral location, prominent nucleoli, inflammatory infiltrate, perivascular hyalinization	No specific markers mentioned
Dedifferentiated Solitary Tumor	p53 and p16 overexpression in anaplastic component, STAT6 positivity, fibromyxoid sarcoma with Muc4 expression	p53 (positive), p16 (positive), STAT6 (positive), Muc4 (positive in low-grade fibromyxoid sarcoma)
Pleomorphic Dermatofibrosarcoma	Infiltrative spindle cell neoplasm, increased proliferative index, diffuse bcl2 expression, higher p53 expression, decreased CD34 positivity	bcl2 (positive), p53 (positive), CD34 (decreased positivity)

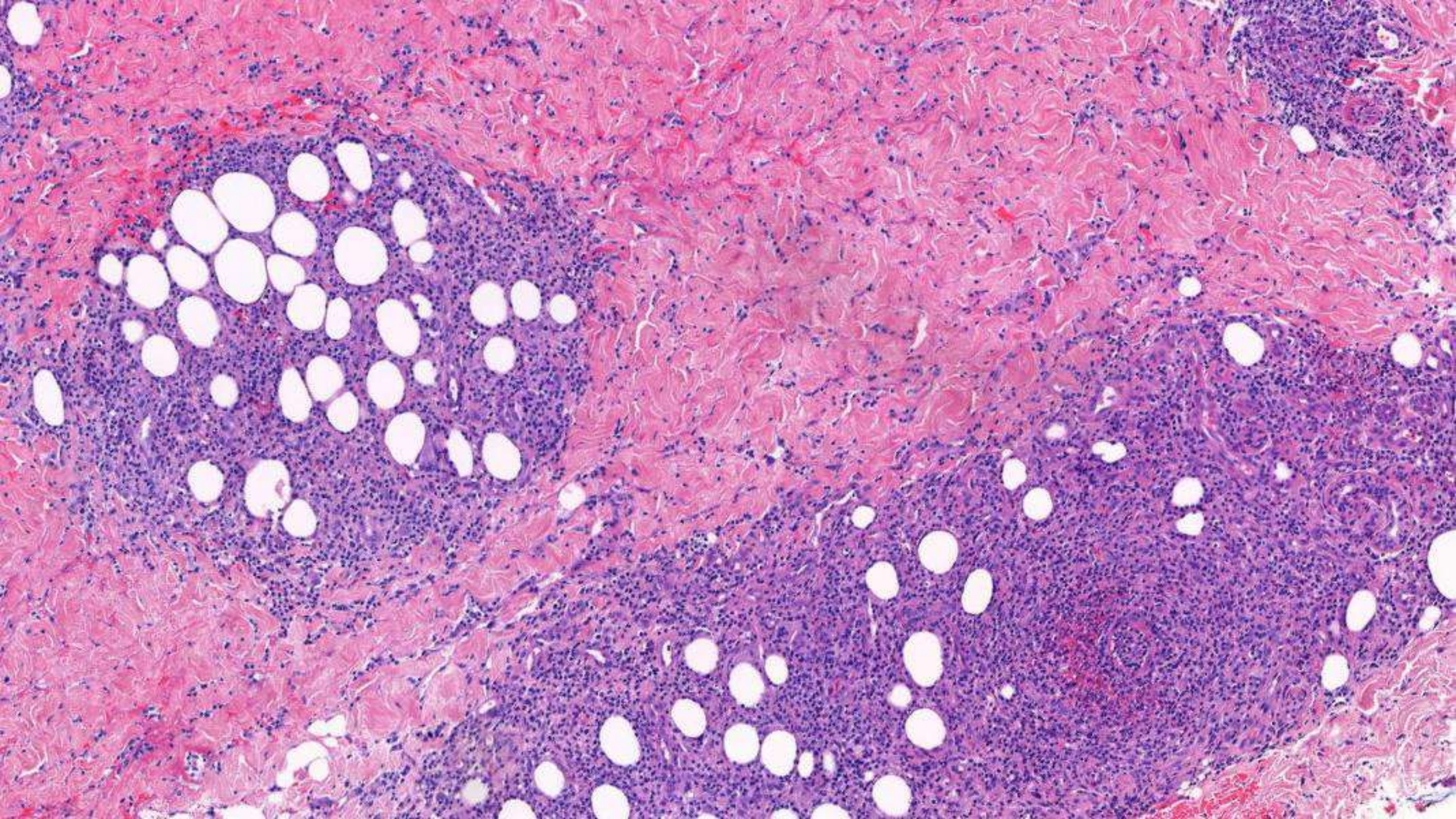
Case 12

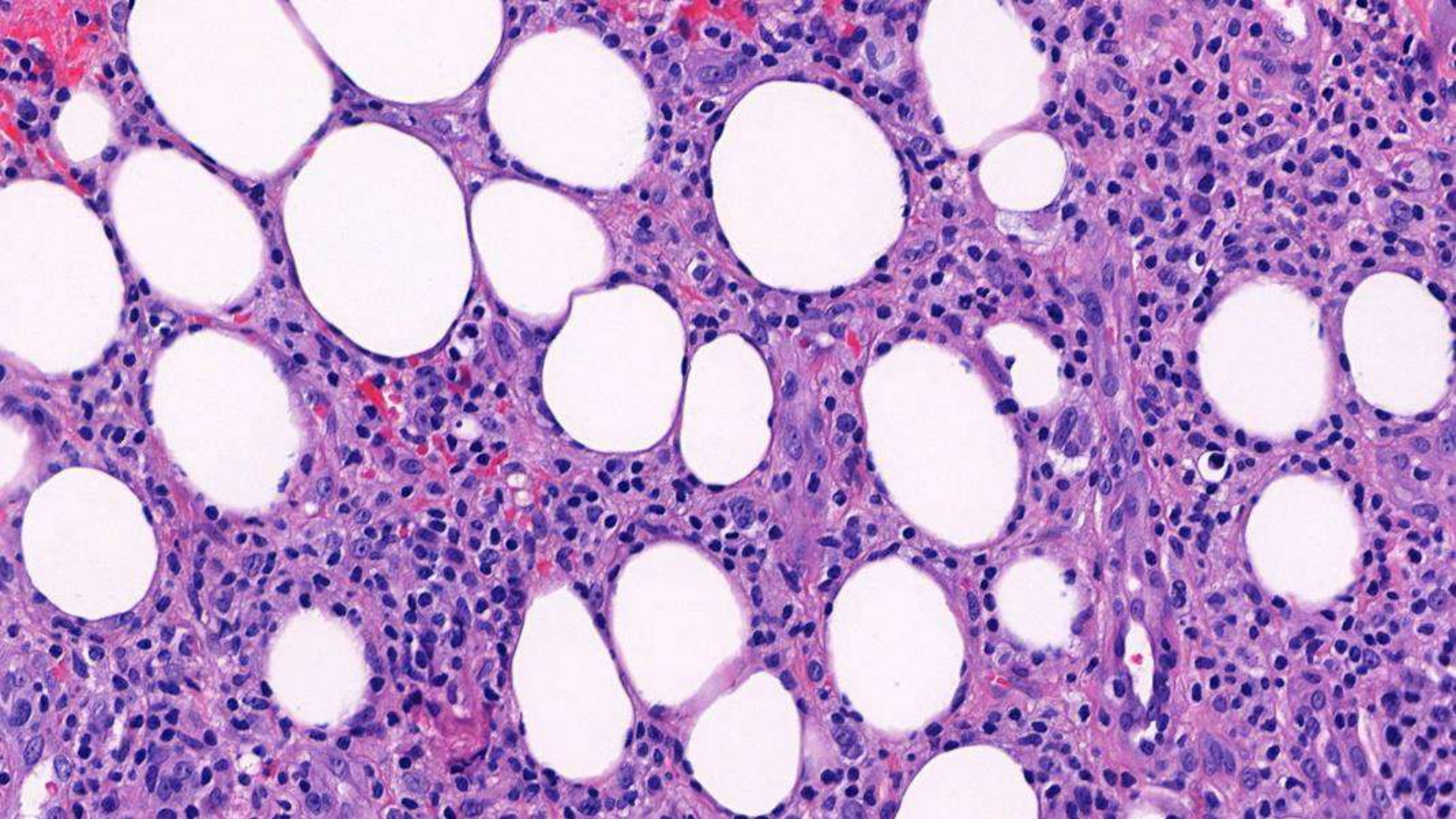
17-year-old female Recurrent papules on trunk and limbs Biopsy from right forearm

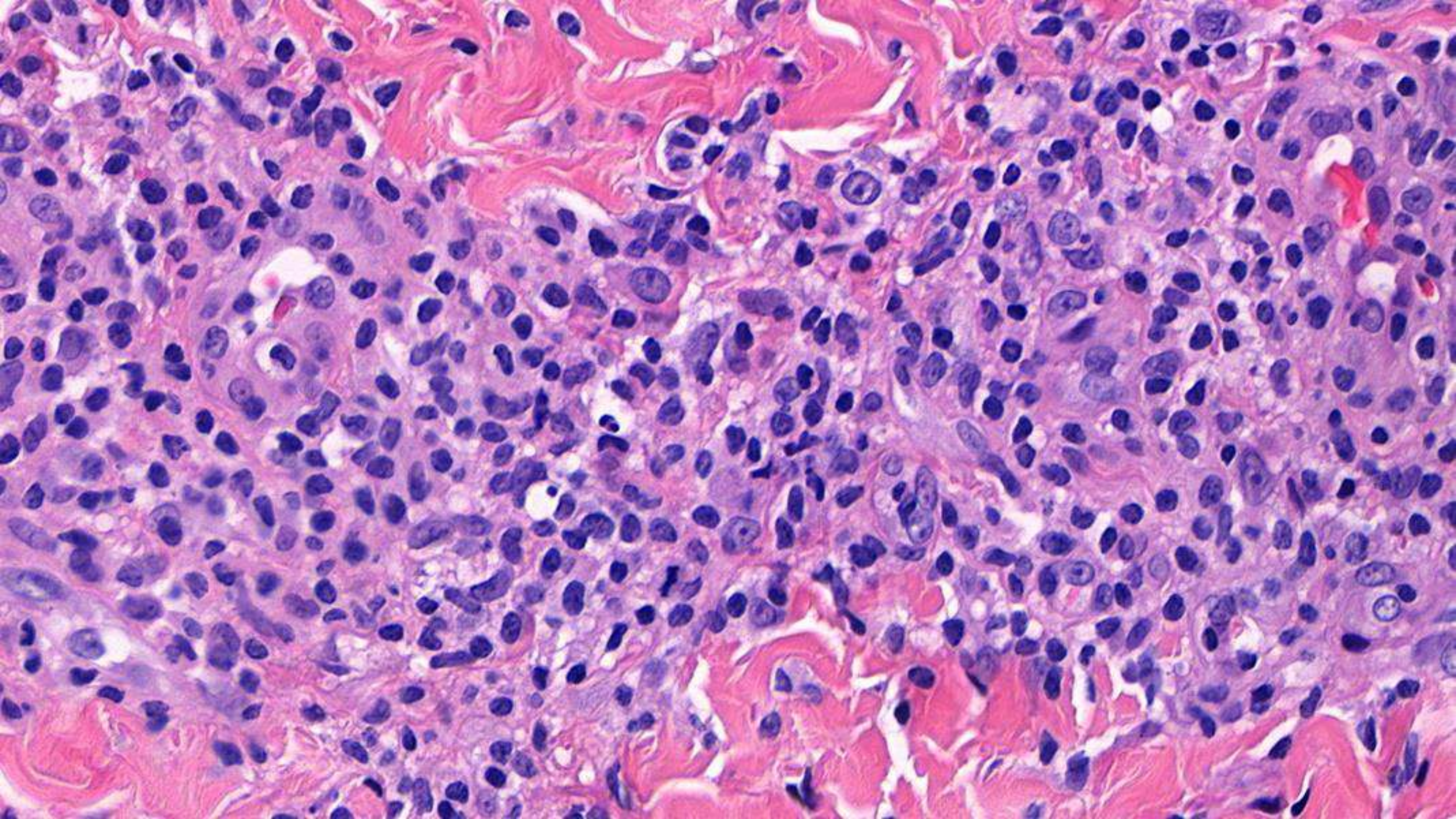


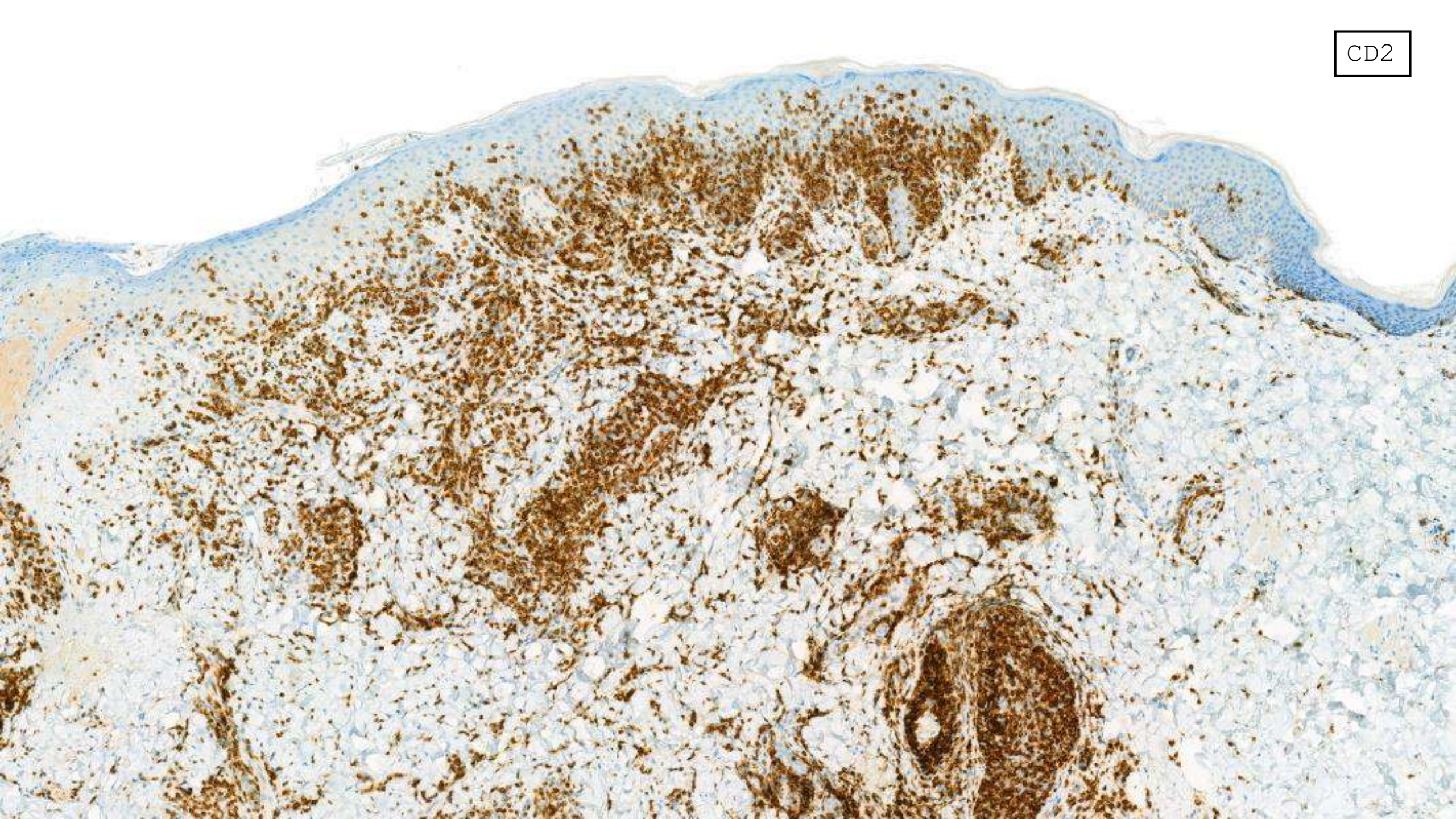


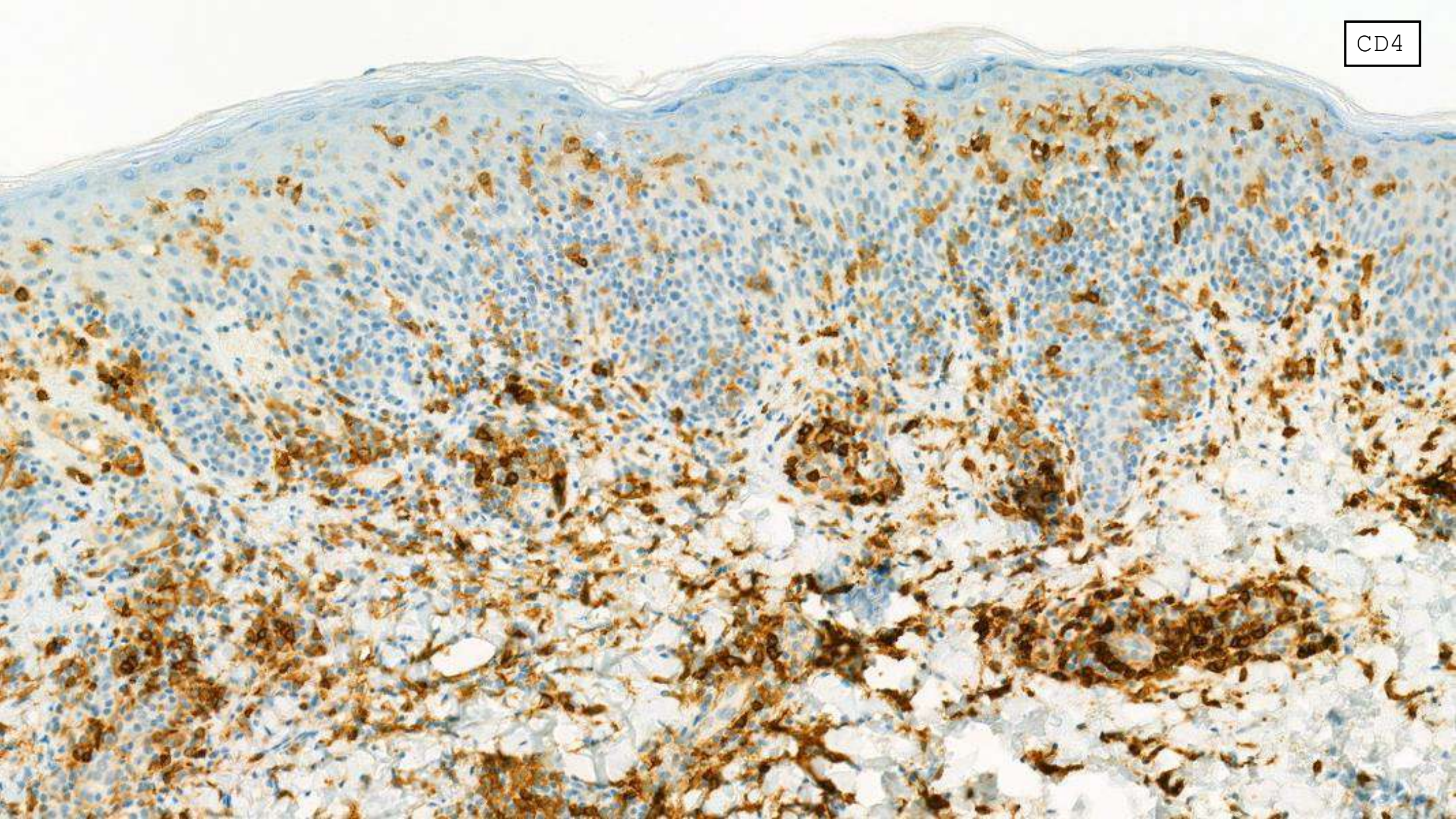









CD2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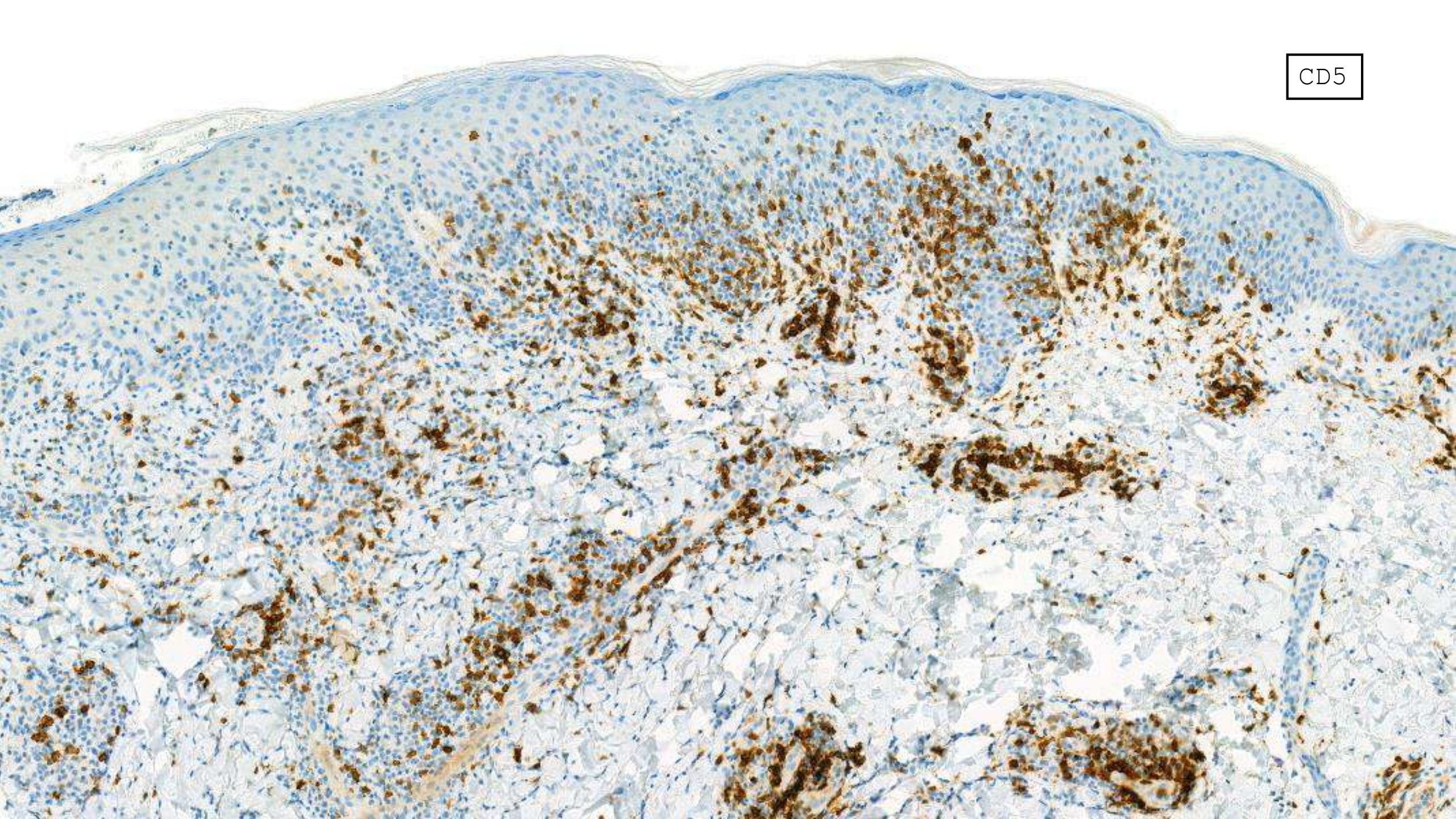
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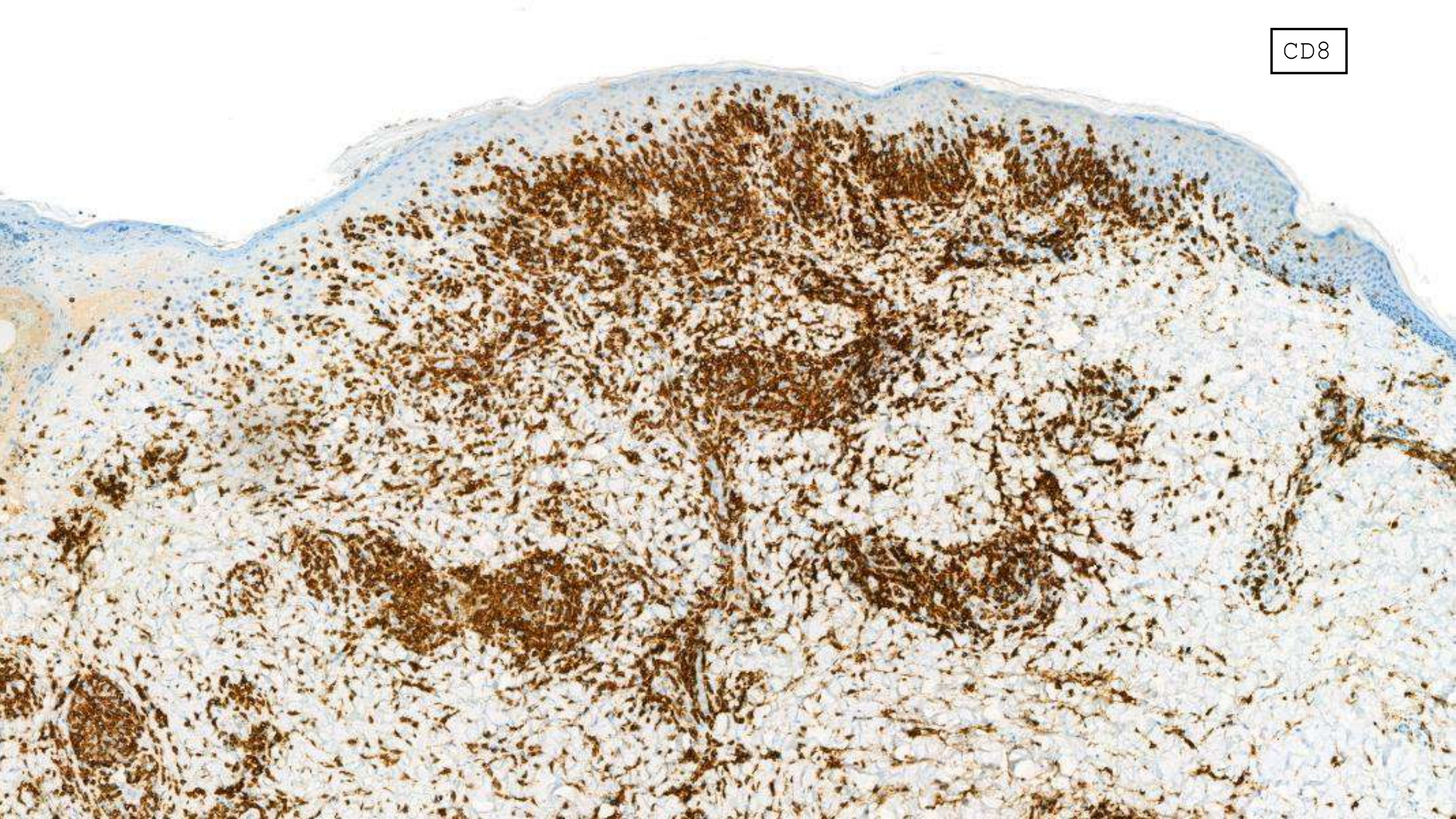
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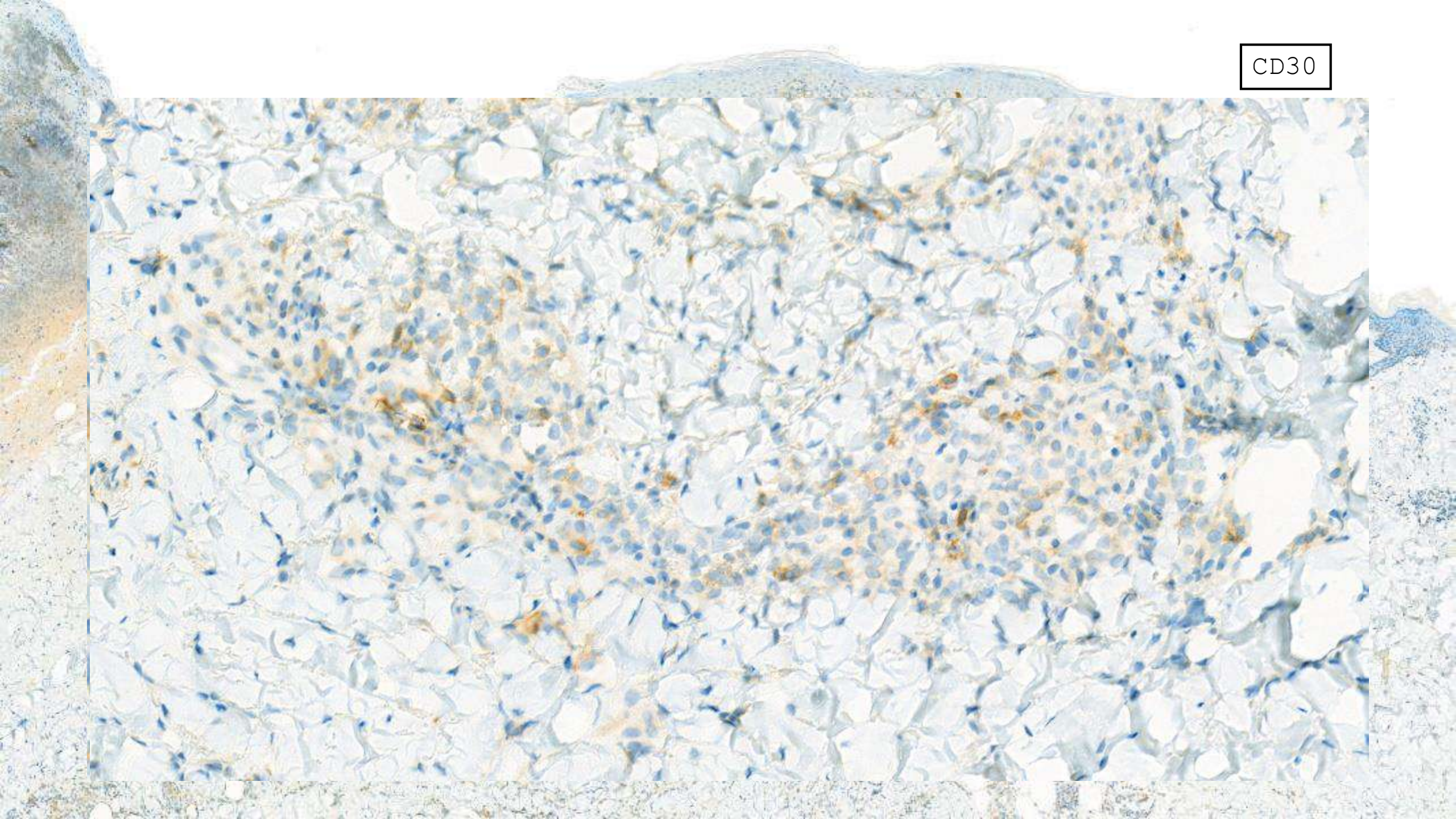
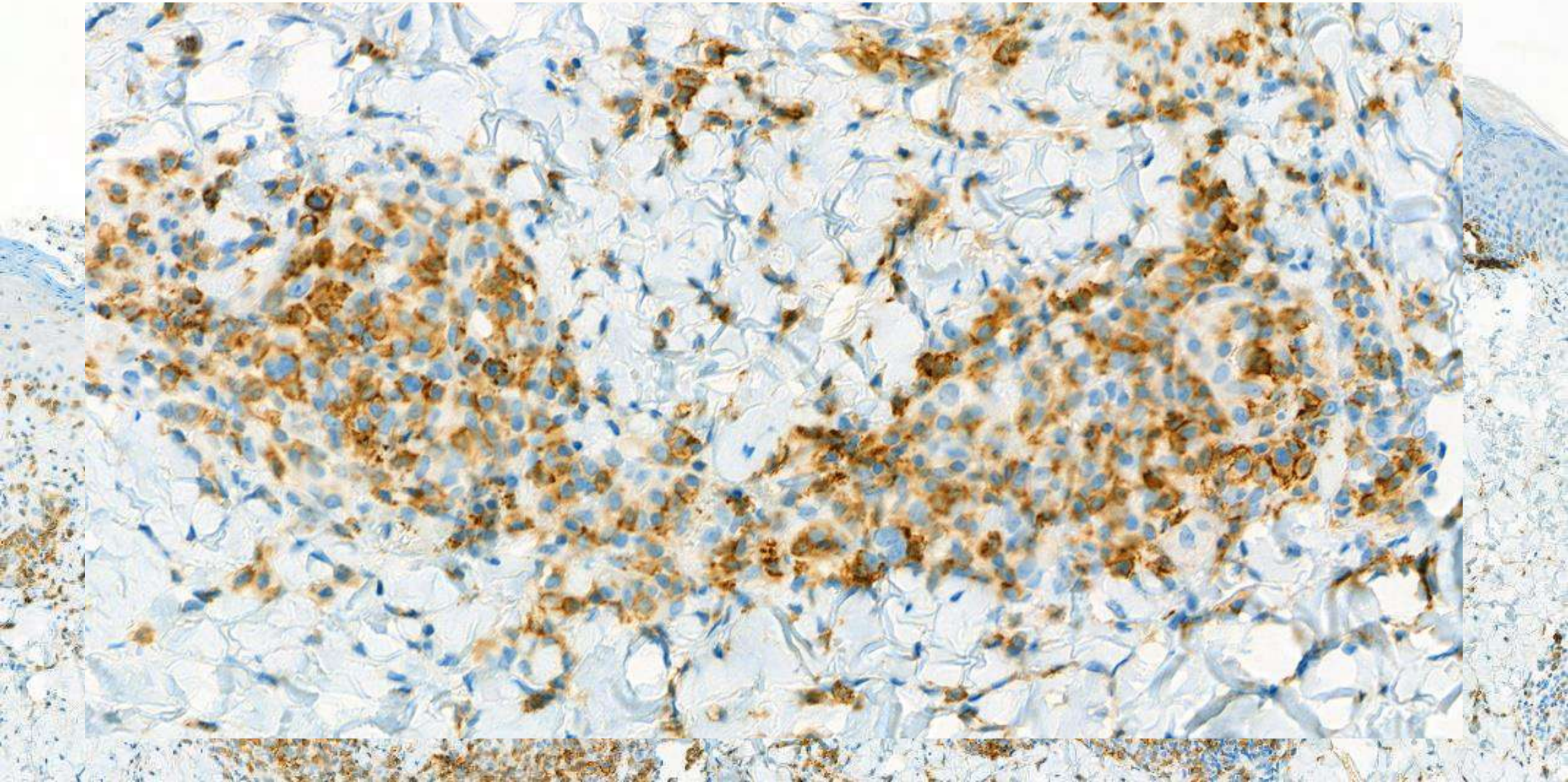
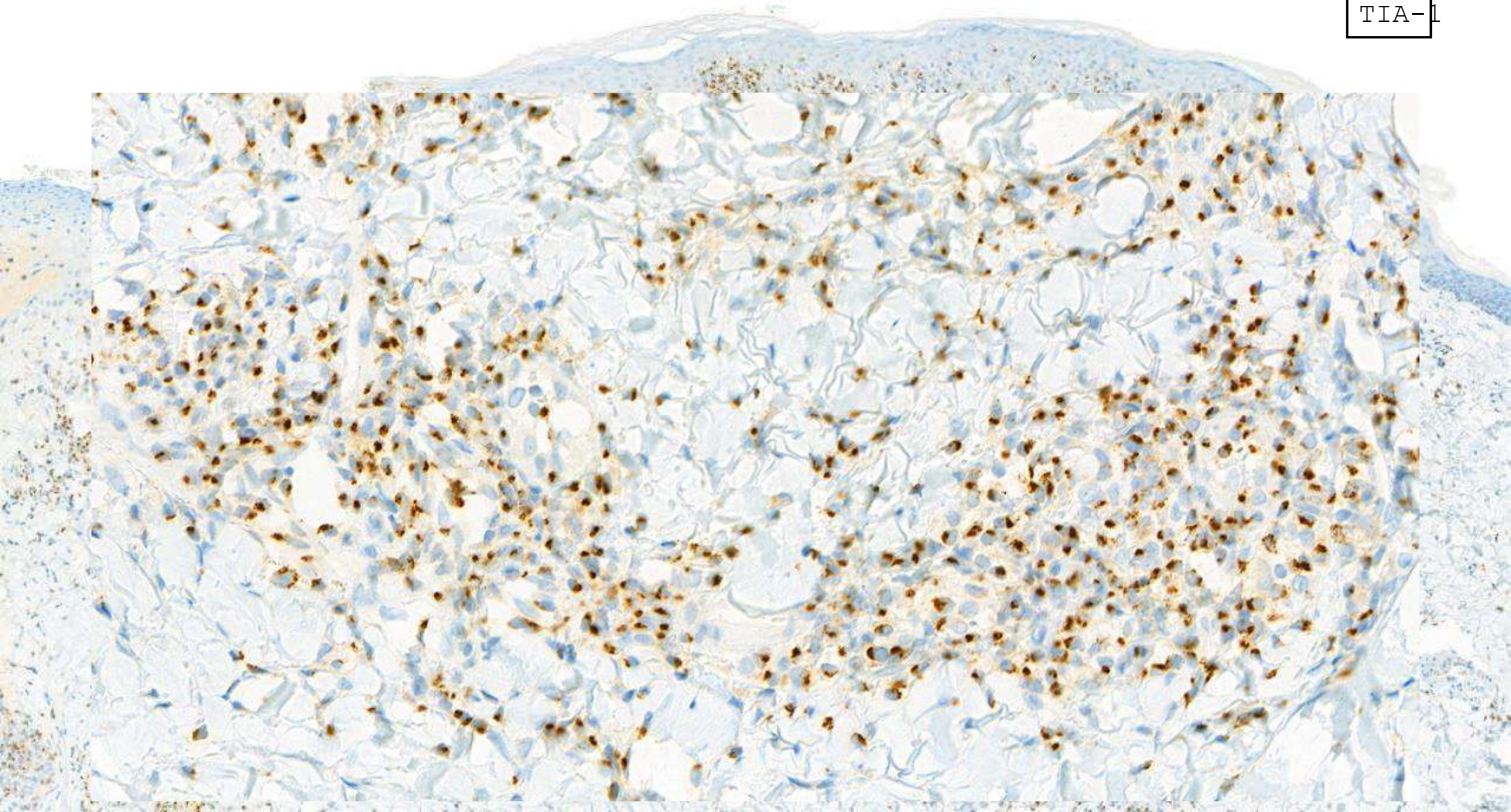

CD30

CD56

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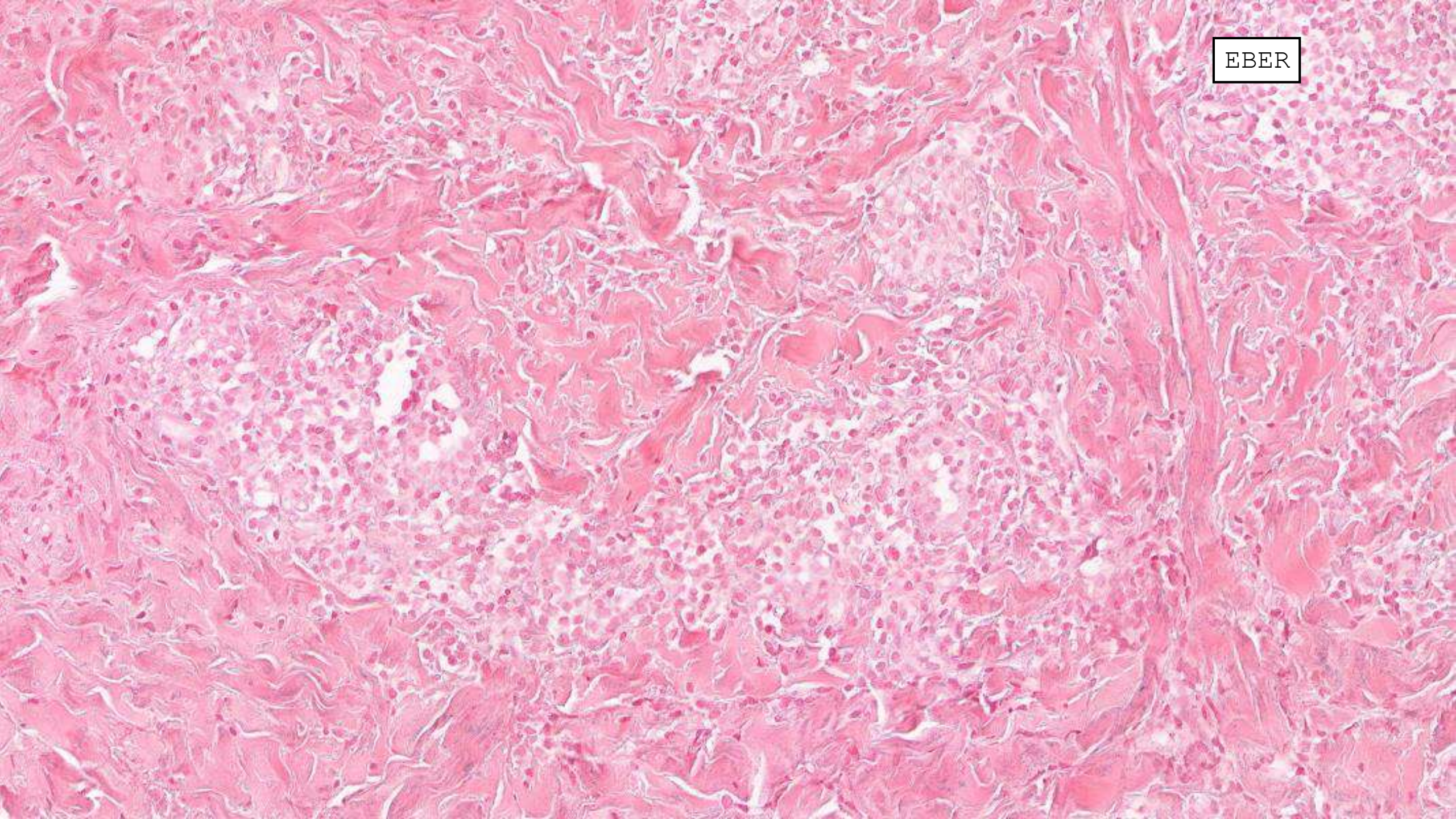
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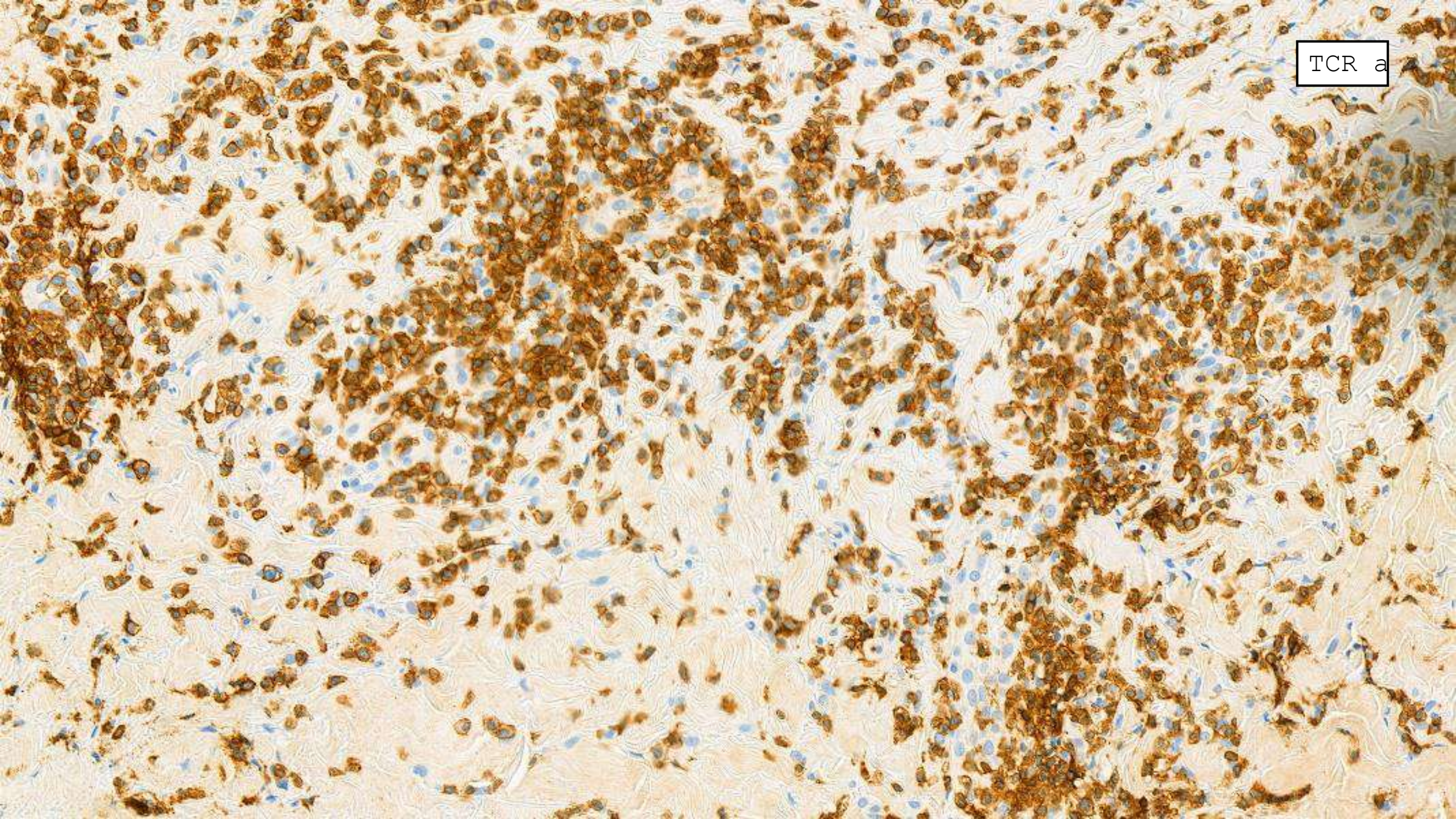
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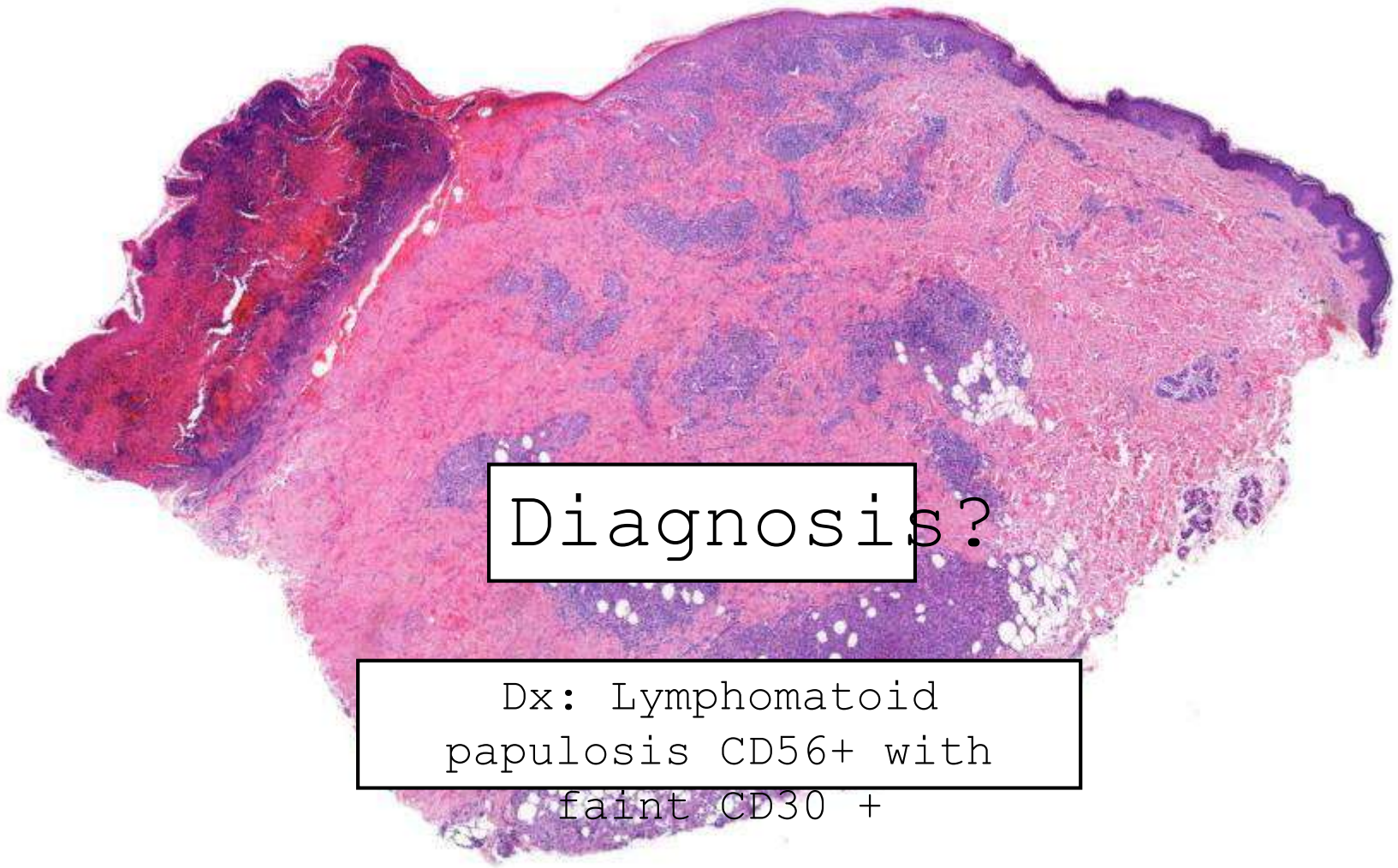
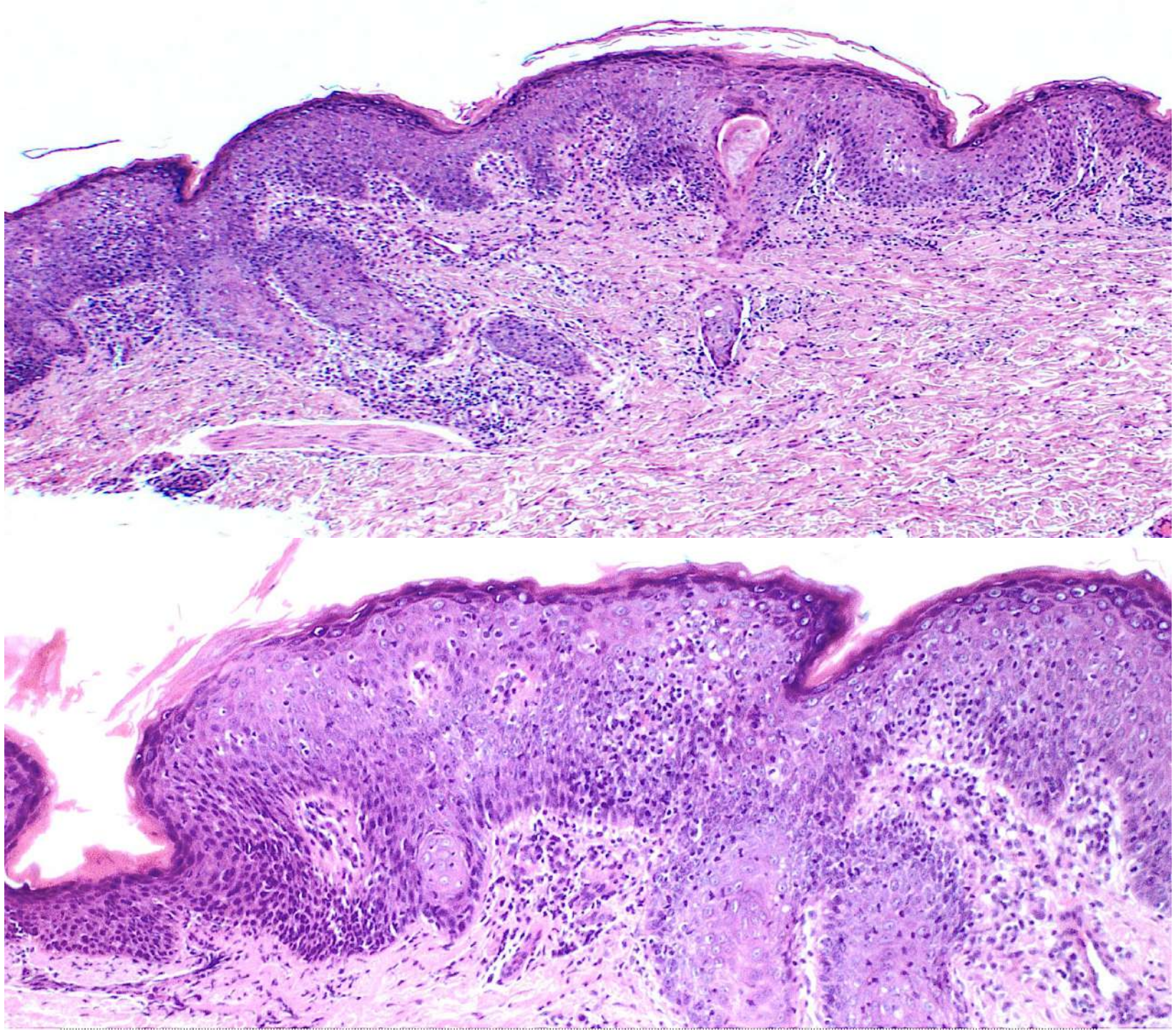
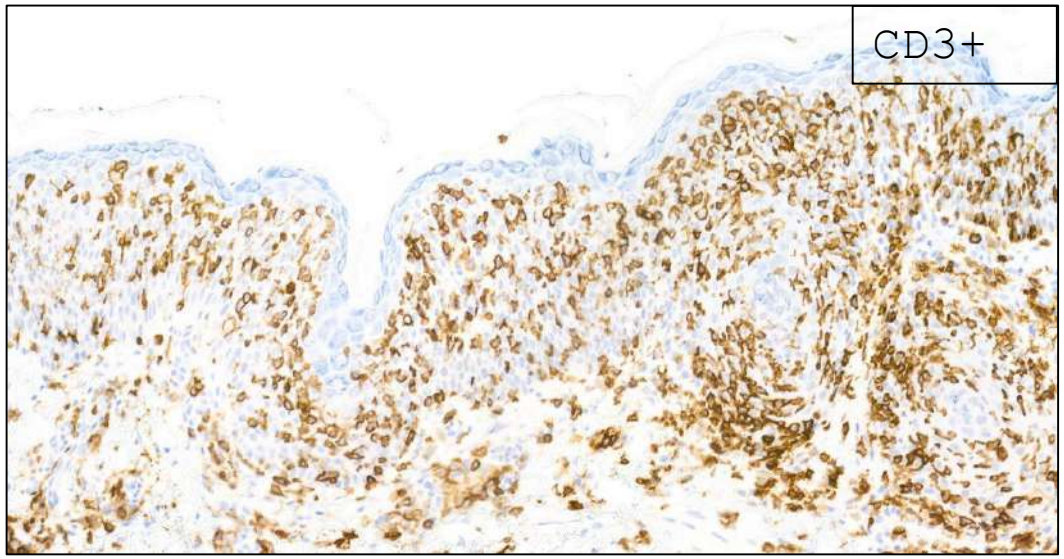
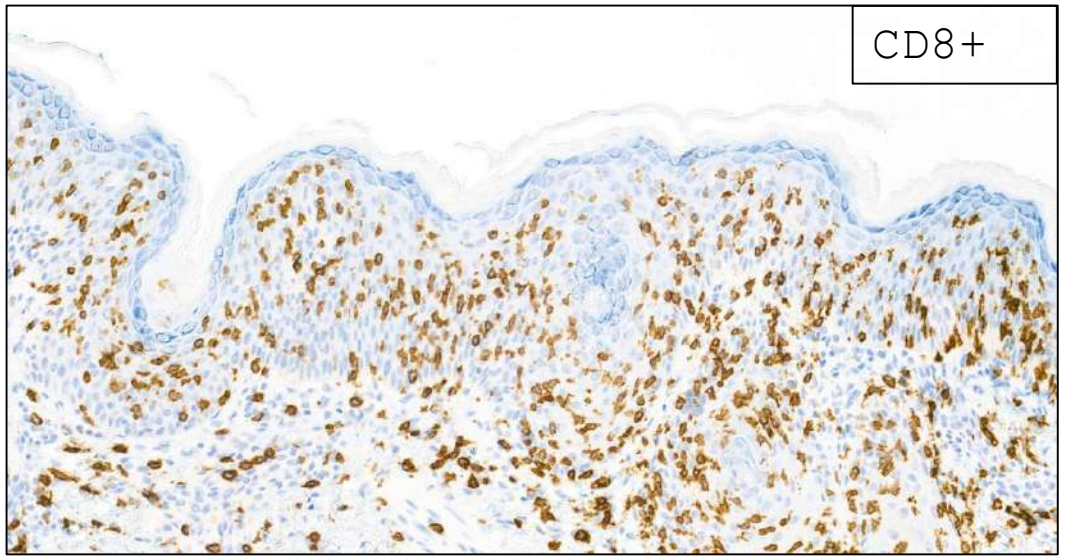


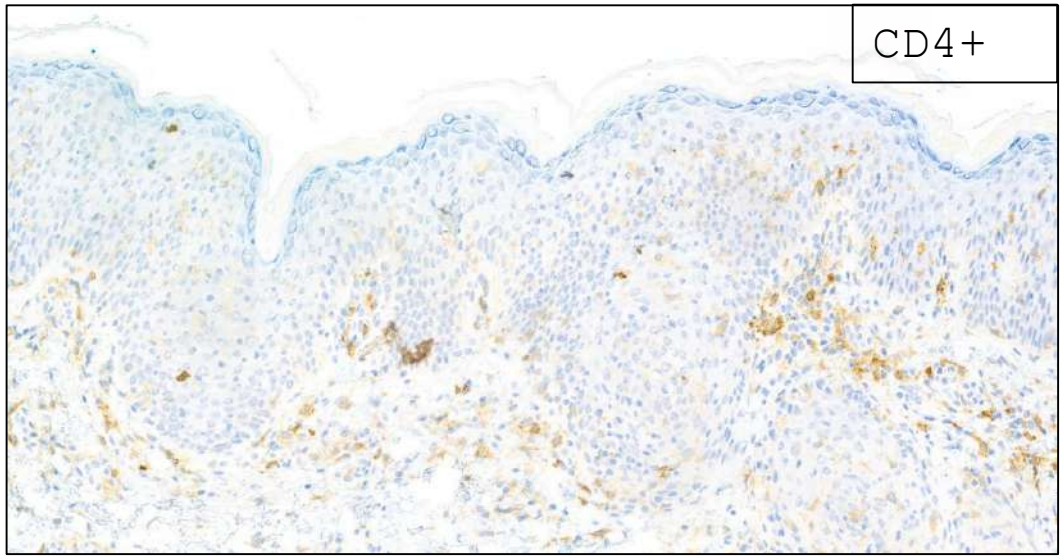
Diagnosis?

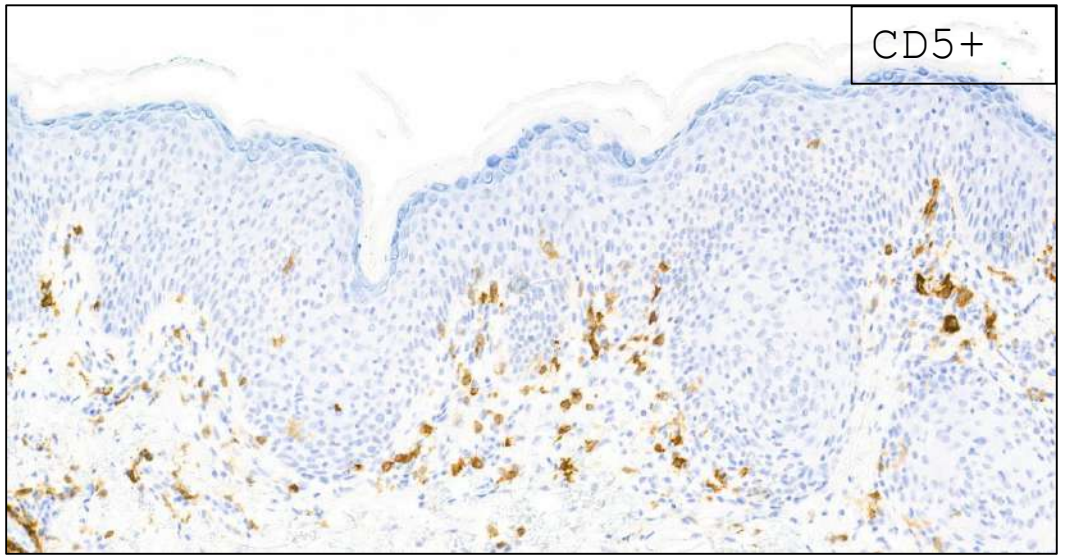
Dx: Lymphomatoid papulosis CD56+ with faint CD30 +





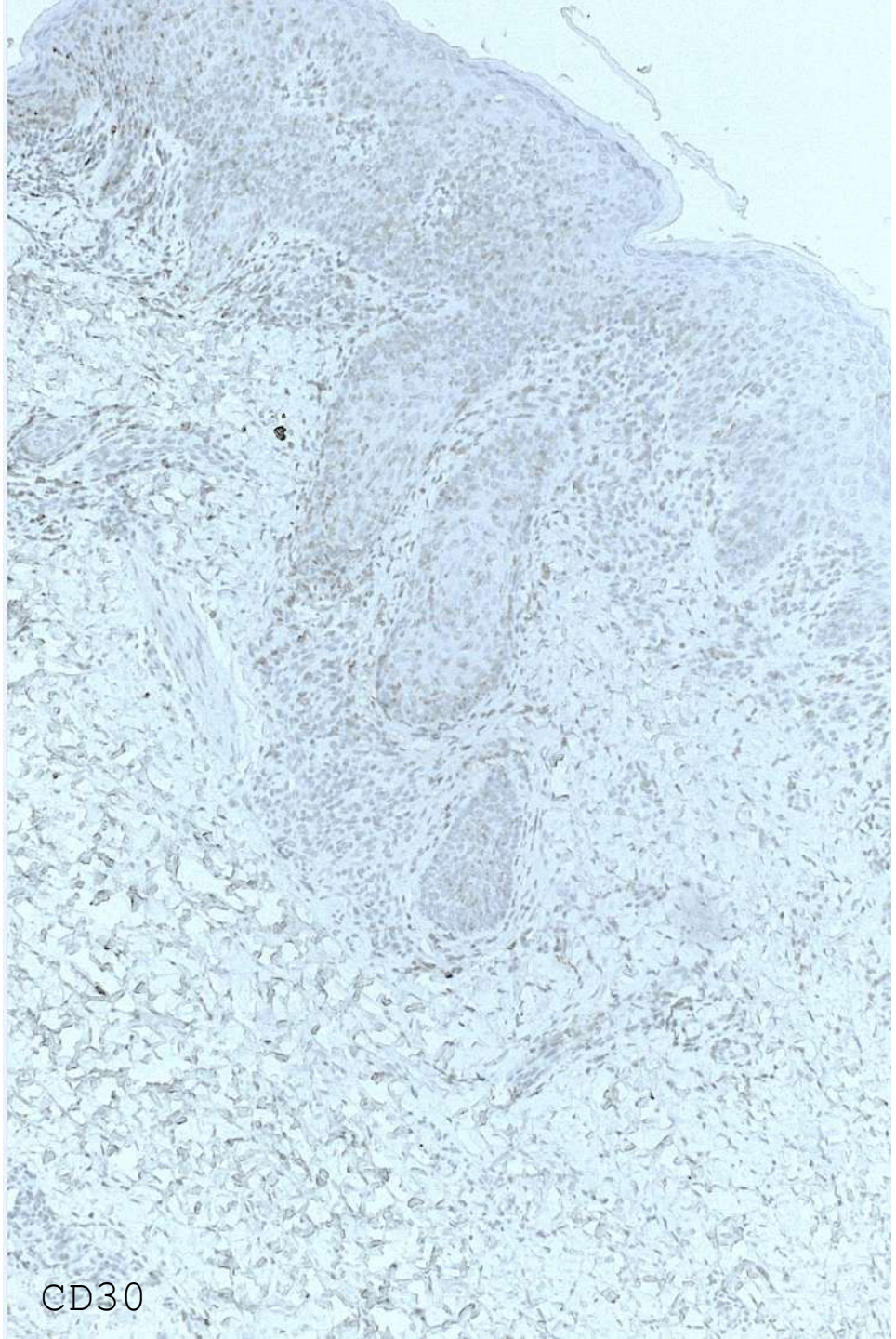


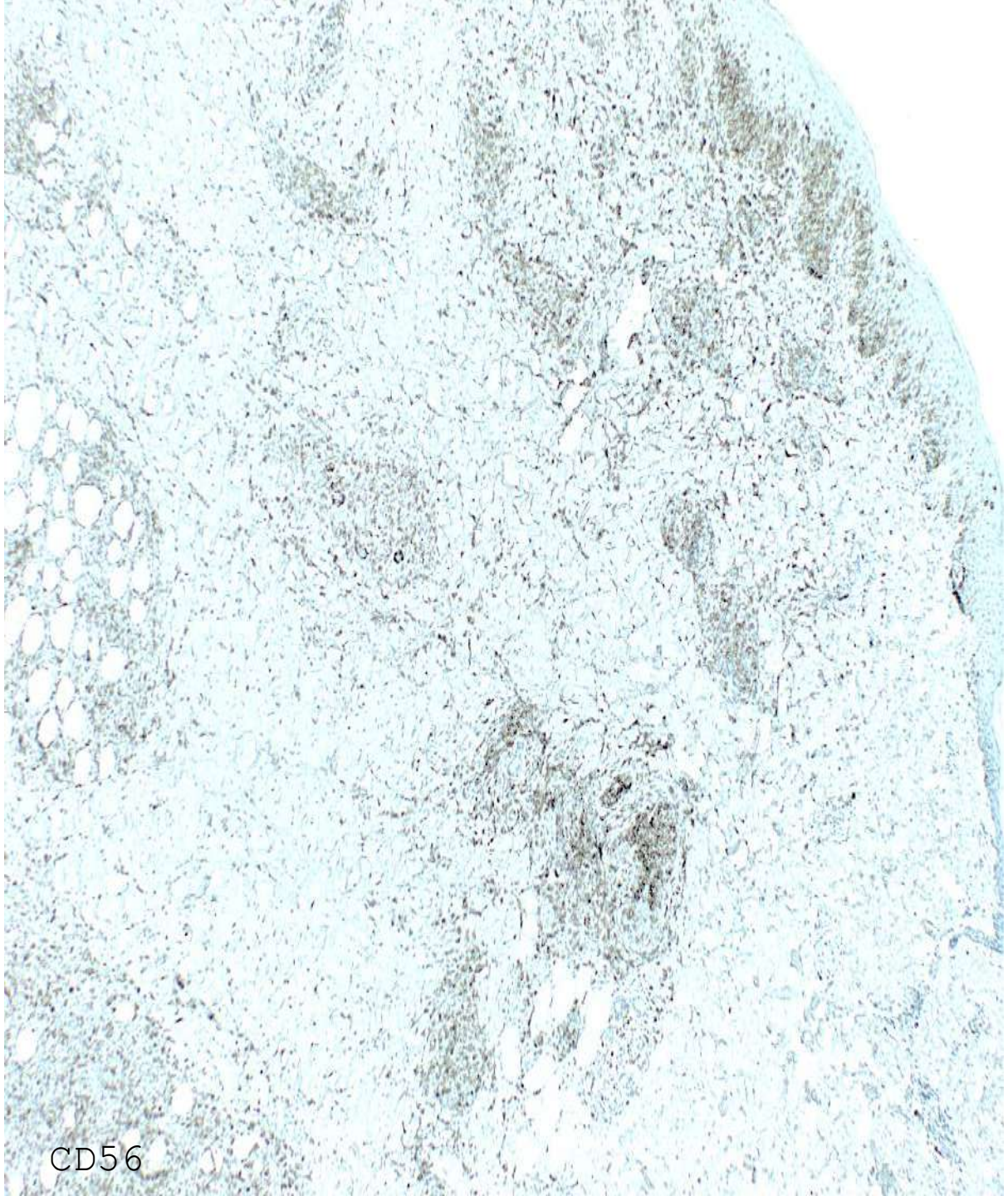




In-situ hybridisation negative for Epstein Barr Virus

PCR and Molecular Genetics: T-cell clonality demonstrated clonal TRG and TRB


CD30


CD56

Diagnostic dilemma

- Histological diagnosis very challenging because:

Atypical cells small

Mainly epidermotropic and focally angiocentric (in the second specimen)

CD30 should be positive in all LyP cases. In this case it was initially reported as negative but it was actually faintly positive

CD56 which is usually negative in LyP was positive

Conclusion: unusual variant of LyP with faint C30 positivity and diffuse positivity for CD56

- Some cases of LyP can be CD56 positive
- CD30 negativity (?) or faint focal positivity has also been reported
- Clinicopathological correlation is crucial

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Case Report

Three cases of lymphomatoid papulosis with aCD56+ immunophenotype

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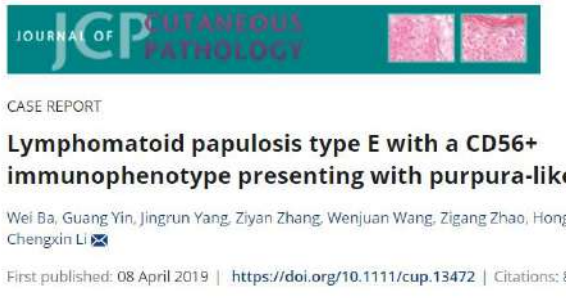

JOURNAL OF CUTANEOUS PATHOLOGY

CASE REPORT

Lymphomatoid papulosis type E with a CD56+ immunophenotype presenting with purpura-like lesions

Wei Ba, Guang Yin, Jingrun Yang, Ziyan Zhang, Wenjuan Wang, Zigang Zhao, Hongxiao Chen, Chengxin Li

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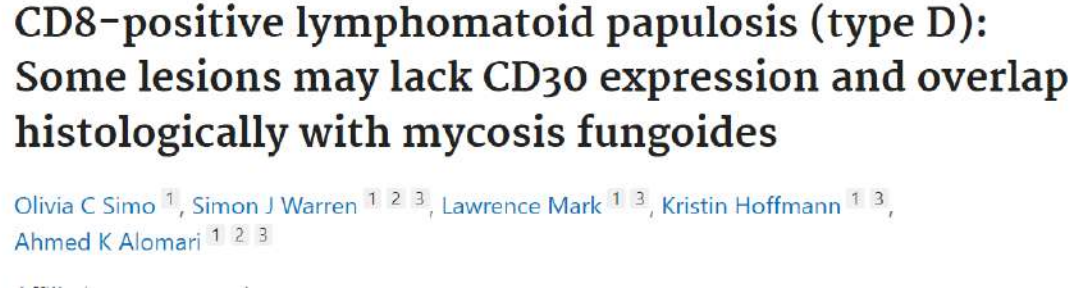


CD8-positive lymphomatoid papulosis (type D): Some lesions may lack CD30 expression and overlap histologically with mycosis fungoides

Olivia C Simo [1], Simon J Warren [1 2 3], Lawrence Mark [1 3], Kristin Hoffmann [1 3], Ahmed K Alomari [1 2 3]

LETTERS TO THE EDITOR

CD30-Negative Lymphomatoid Papulosis Type D in an Elderly Man

Cho-Vega, Jeong Hee MD, PhD*; Vega, Francisco MD, PhD†

Author Information

The American Journal of Dermatopathology 36(2):p 190-192, February 2014. | DOI: 10.1097/DAD.0b013e3182a64388

Metrics

Type	Histopathological features	Main phenotype	Main histopathological differential diagnosis	Comment
A	Wedge-shaped infiltrate with several large, atypical cells admixed with small lymphocytes, eosinophils, and neutrophils.	$CD4^+$	Arthropod bite reactions	This is the most common histopathological subtype of lymphomatoid papulosis
B	Band-like or wedge-shaped infiltrate of small/medium-sized atypical cells with epidermotropism	$CD4^+$	Mycosis fungoides	$CD30^-$ cases are reported in the literature but should be evaluated critically; in my experience type B lymphomatoid papulosis is always $CD30^+$
C	Large nodules or sheets of large, atypical cells	$CD4^+$	Anaplastic large cell lymphoma	Differentiation from anaplastic large cell lymphoma possible only upon clinical correlation
D	Band-like or wedge-shaped infiltrate with prominent (pagetoid reticulosis-like) epidermotropism of cytotoxic atypical cells	$CD8^+$	Aggressive epidermotropic $CD8^+$ cytotoxic T-cell lymphoma	Differentiation from aggressive epidermotropic $CD8^+$ cytotoxic T-cell lymphoma possible only upon clinical correlation
E	Presence of angiotropism/angiodestruction with perivascular and intraluminal infiltrates of atypical cells	$CD4^+$ or $CD8^+$	Aggressive "angiotropic" lymphomas (e.g., extranodal NK/T-cell lymphoma, nasal type)	This subtype is sometimes present in lesions of other histopathological variants
F	Infiltrate centered around a hair follicle with pilotropism (with or without mucin deposition within the follicle)	$CD4^+$	Follicular mycosis fungoides	In some cases it may represent a chance finding (i.e., lymphomatoid papulosis arising in the vicinity of a hair follicle)
G	Gamma/delta cytotoxic phenotype	$CD8^+$	Cutaneous gamma/delta T-cell lymphoma and other T-cell lymphomas with gamma/delta phenotype	Differentiation from cutaneous gamma/delta T-cell lymphoma or other T-cell lymphomas with gamma/delta phenotype possible only upon clinical correlation
H	Presence of Hodgkin and Reed–Sternberg-like cells	$CD4^+$	Hodgkin lymphoma	Similar cells may be encountered also in cutaneous anaplastic large cell lymphoma
I	Presence of intralymphatic complexes of atypical cells	$CD4^+$	Intravascular lymphoma, benign intralymphatic proliferation of blasts	Staining for podoplanin crucial for a precise classification
K	Presence of "keratoacanthoma-like" pseudoepitheliomatous epidermal hyperplasia	$CD4^+$	Keratoacanthoma	In some cases association with genuine keratoacanthomas has been documented
R	Regional lymphomatoid papulosis: lesions are localized to one area of the body; recurrences occur at the same site	$CD4^+$ or $CD8^+$	Arthropod bite reactions, anaplastic large cell lymphoma	Clinically should be differentiated from cutaneous anaplastic large cell lymphoma with satellites
6	Presence of a chromosomal rearrangement of the *DUSP22–IRF4* locus on 6p25.3	$CD4^-CD8^+$ or $CD4^-CD8^-$	Anaplastic large cell lymphoma, transformed mycosis fungoides	Often "biphasic" pattern with epidermotropism of small lymphocytes and larger cells in the dermis

Feature	Lyp Subtype B Findings
Epidermotropism Frequency	High in one study (potential overlap with Lyp Subtype D)
CD8+ Expression in Lyp B	High number of cases (suggested overlap with Lyp Subtype D)
CD30 Negative in Lyp B	14% of cases (consistent with existing definition)
Folliculotropism & Syringotropism	High rates observed, but only in two studies (26,52)
Investigation of Adnexotropic Patterns	Not studied in 9/11 studies
Occurrence of Adnexotropic Patterns in Other Subtypes	Seen in subtypes C–E and 6p25.3 rearranged Lyp but rarely investigated

Feature	Lyp Subtype D Findings
Total Publications Reviewed	19
Total Cases Analyzed	74
CD8+ Phenotype	94% (64/68 cases)
Double-Positive (CD4+/CD8+)	4% (3/68 cases)
Double-Negative (CD4-/CD8-)	2% (1/68 cases)
Pagetoid Epidermotropism	67% (43/64 cases)
Basal Layer Epidermotropism	85% (57/67 cases)
Case without Epidermotropism	1 case diagnosed as subtype D
Cytotoxic Markers (TIA-1, granzyme, perforin)	80% (37/46 cases)
CD56 Positivity	28% (13/47 cases)
γ/δ-Phenotype	50% (2/4 evaluated cases)
α/β-Phenotype	83% (10/12 cases)

Fricke T, Kempf W, Schön MP, Mitteldorf C. Histologic and Immunohistochemical Patterns in Lymphomatoid Papulosis: A Systematic Review of Published Cases. Dermatopathology (Basel). 2025 Feb 12;12(1):6.

- A retrospective study assessed the clinical and histopathological characteristics of EBV-positive cases with papulo-nodular morphologies and CD30-positivity
- 12 patients (7 M, 5 F mean age 69) presented with papular lesions, without prior patch/plaque disease
- Biopsies showed mixed lymphoid infiltrates of atypical CD30-positive T cells (5 cases) or B cells (7 cases), with variable EBV-encoded small RNA (EBER) expression
- These cases suggest that EBV-positive lymphoproliferative disorders with lymphomatoid papulosis-like clinical presentations could be an early sign of immunodeficiency
- LyP-like cutaneous papulonodular eruption presenting in immunosuppressed or elderly patients should be evaluated histologically for EBV expression, followed by testing for active EBV viremia when EBER is positive
- Accurate clinicopathological correlation and

dissimilar to LyP, since LyP is commonly treated

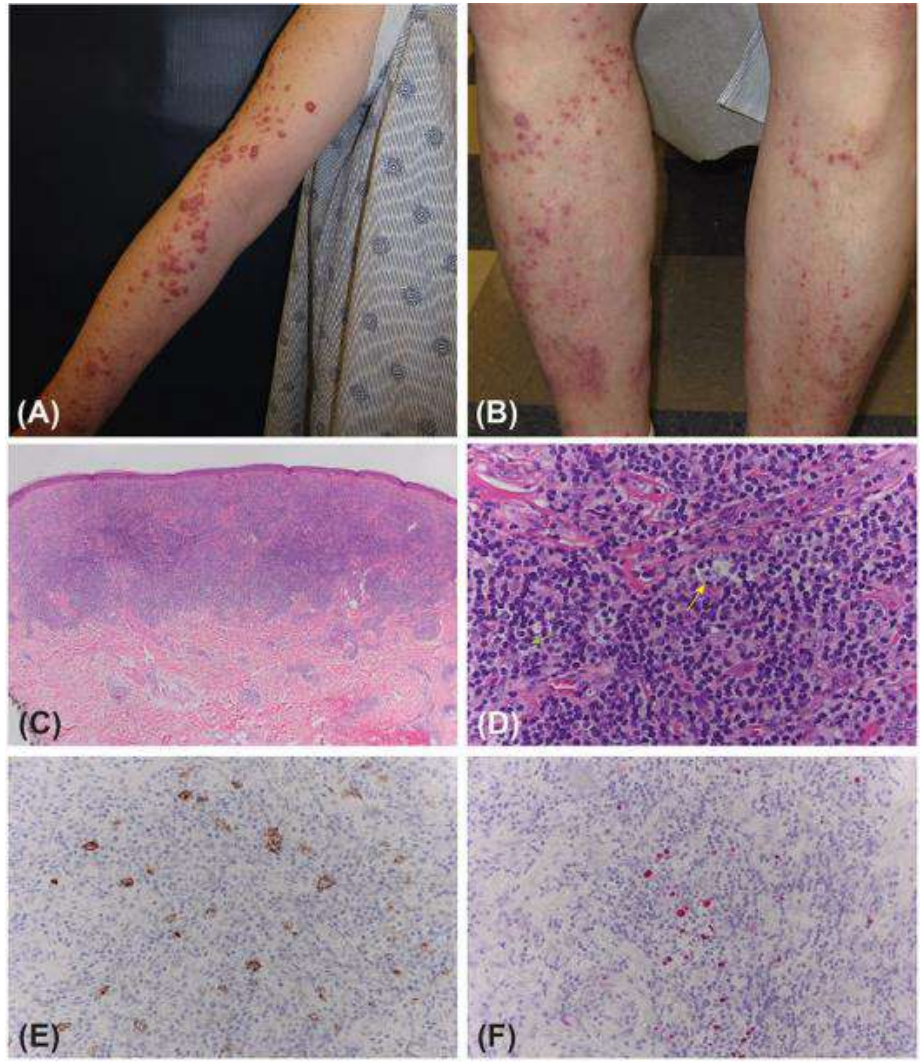
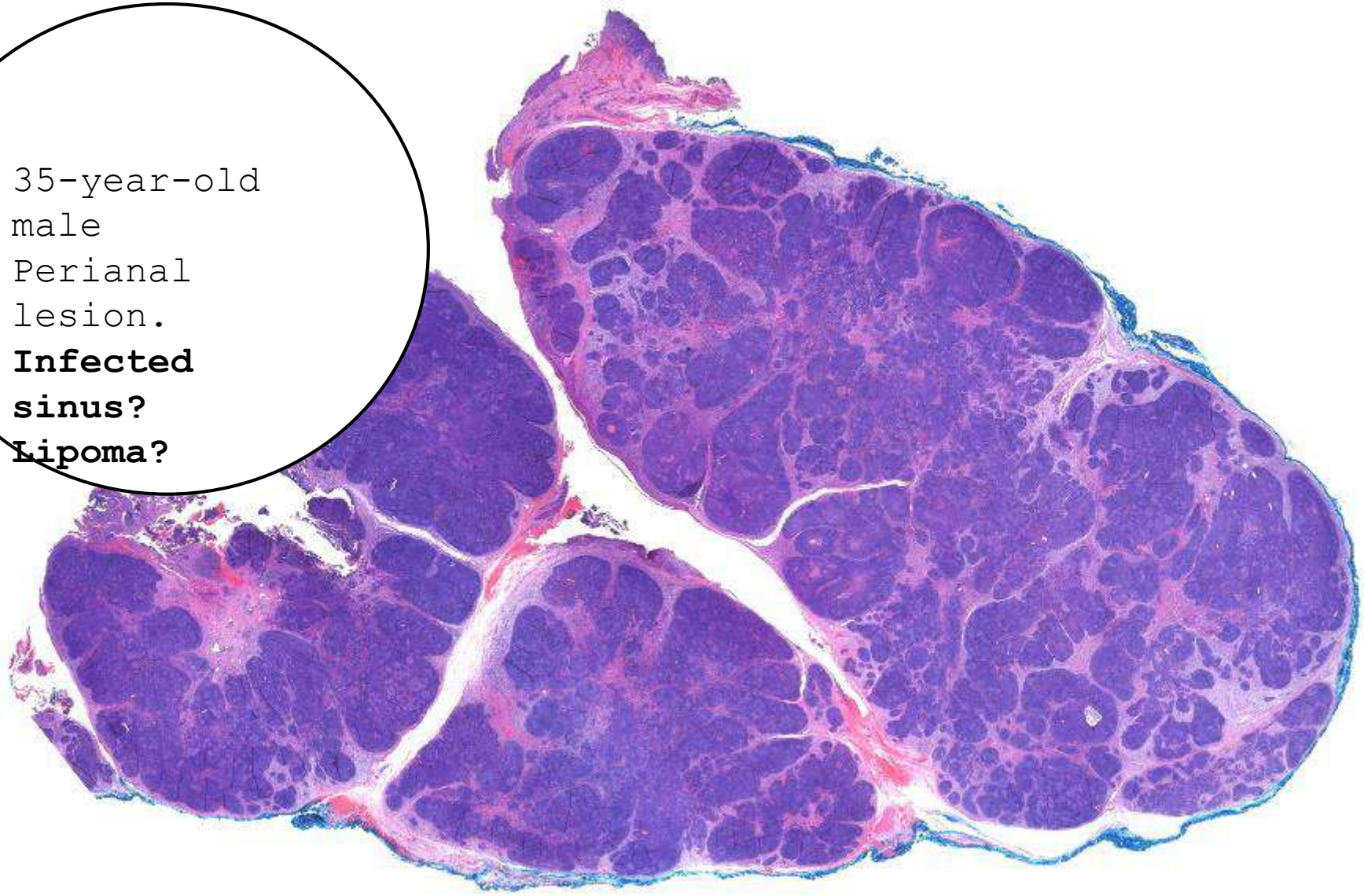


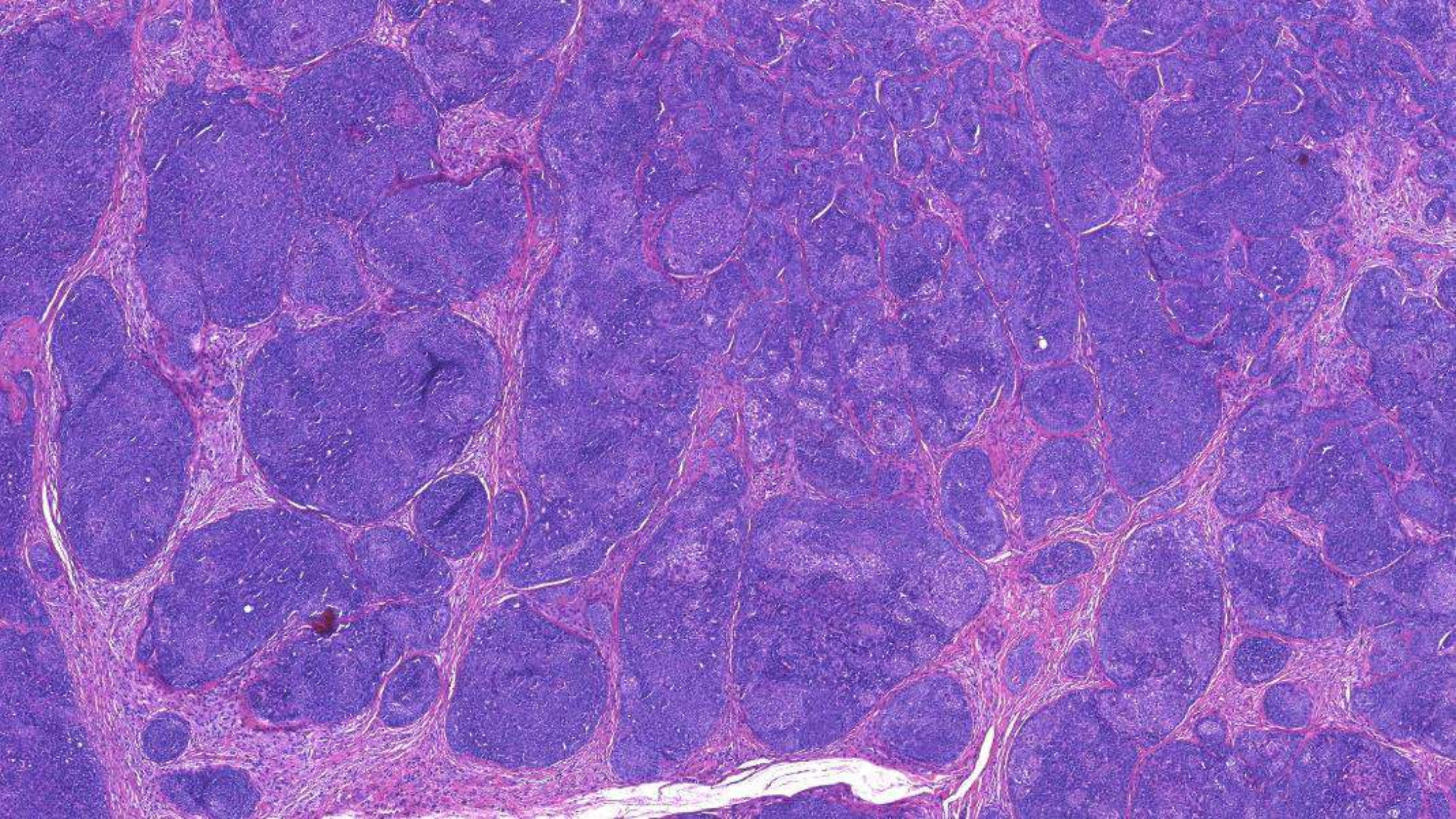
Figure 2.
Clinical and histopathological images from Case 10. (A) Exophytic and polypoid, smooth, red papules of the right arm. (B) Clusters of pink-purple macules and papules on bilateral legs. (C) Atypical dermal lymphocytic infiltrate (H&E, x10) with eosinophils, plasma cells, mitotic bodies (green arrow), and lamellar nucleoli (yellow arrow) visible at higher power (D: H&E, x60). (E) Large cells demonstrate CD30 expression (CD30, x40). (F) In situ hybridization revealed positive Epstein-Barr Virus-encoded RNA (EBER) large cells (EBER, x40).

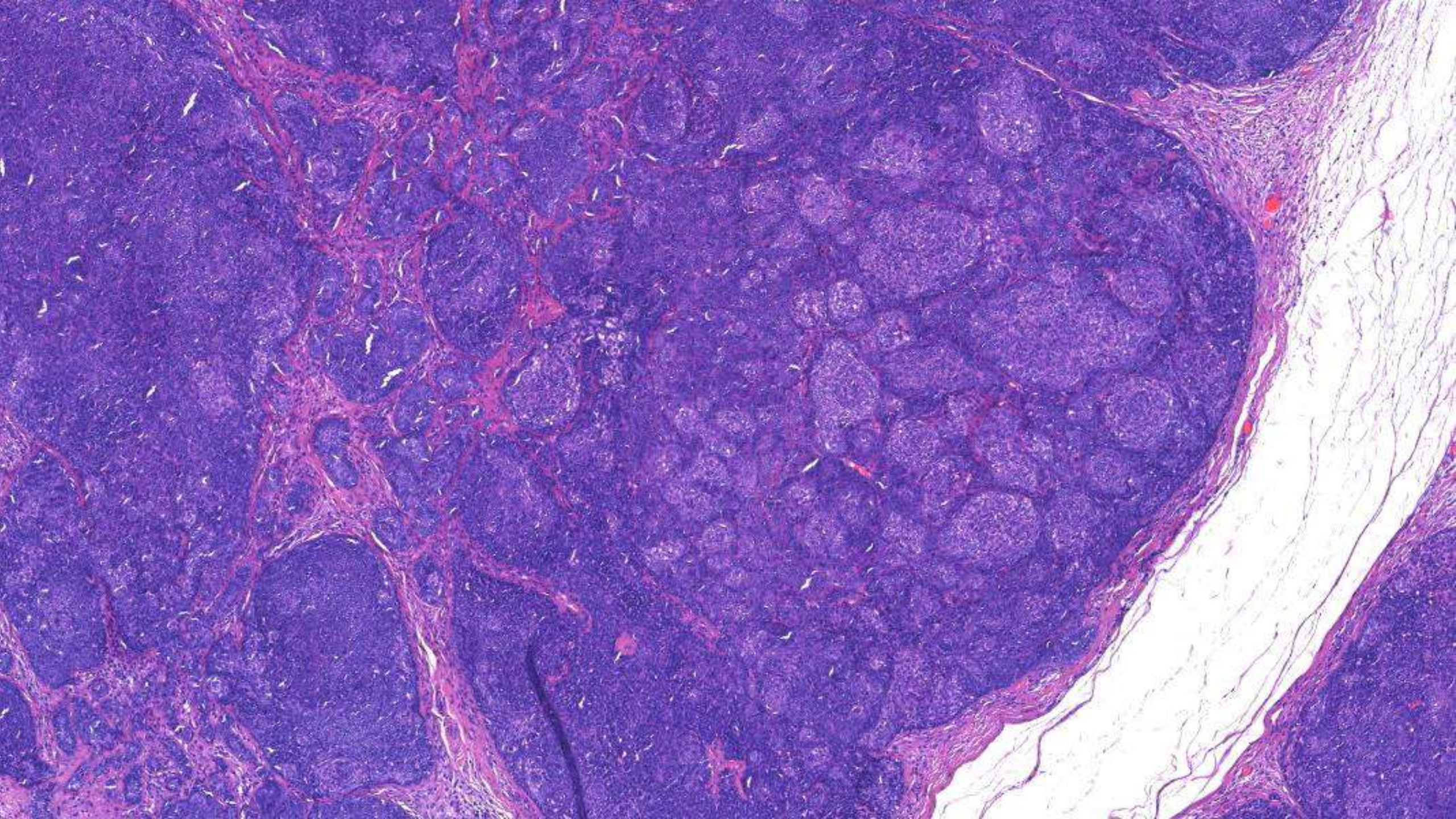
Hooper Mjet et al. Epstein-Barr Virus-Associated Lymphomatoid Papules: A Sign of Immunosuppression Resembling Lymphomatoid Papulosis. Am J Dermatopathol. 2023 Dec 1;45(12):789-800.

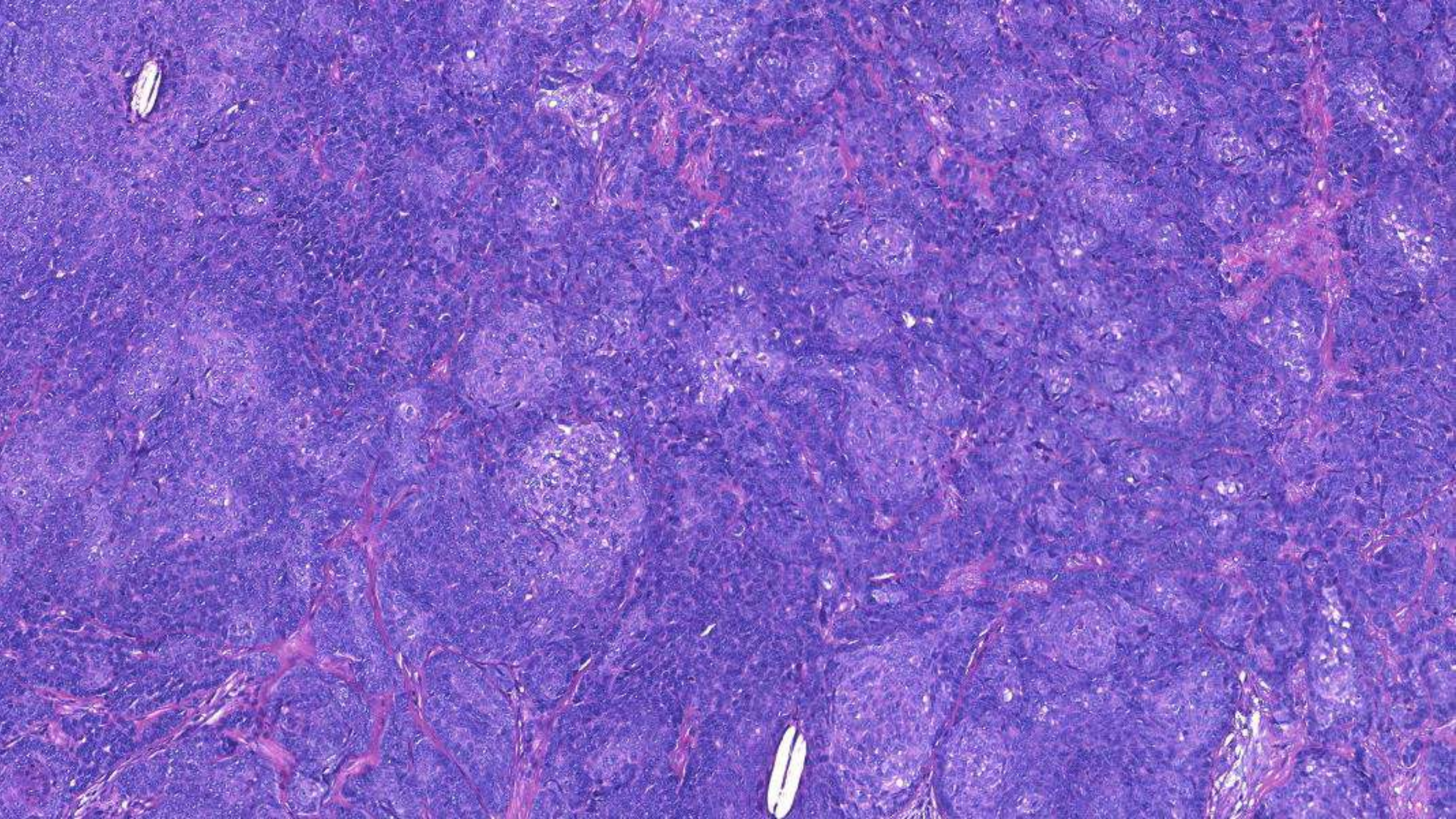
Case 13

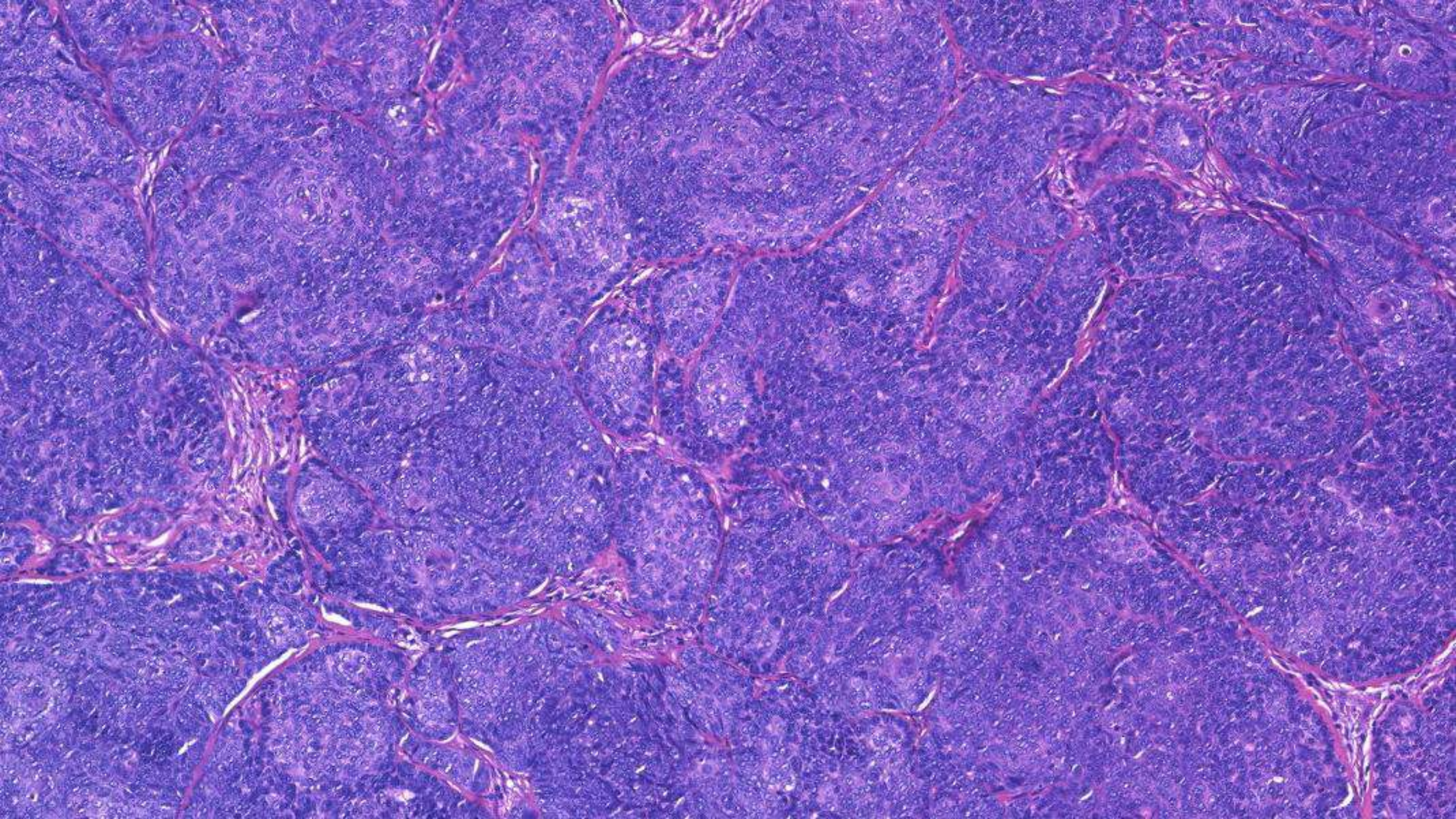
35-year-old male
Perianal lesion.
Infected sinus?
Lipoma?











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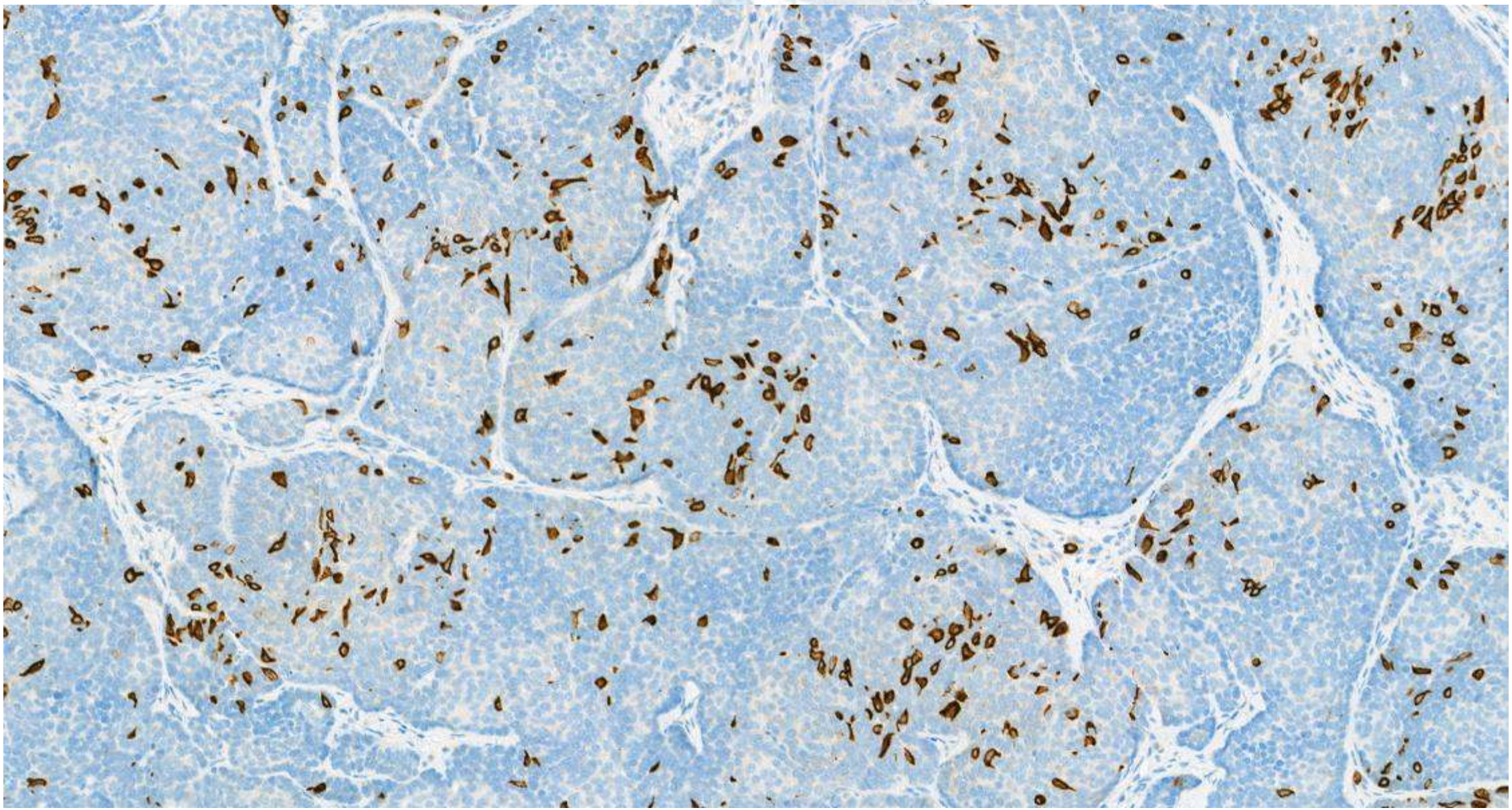
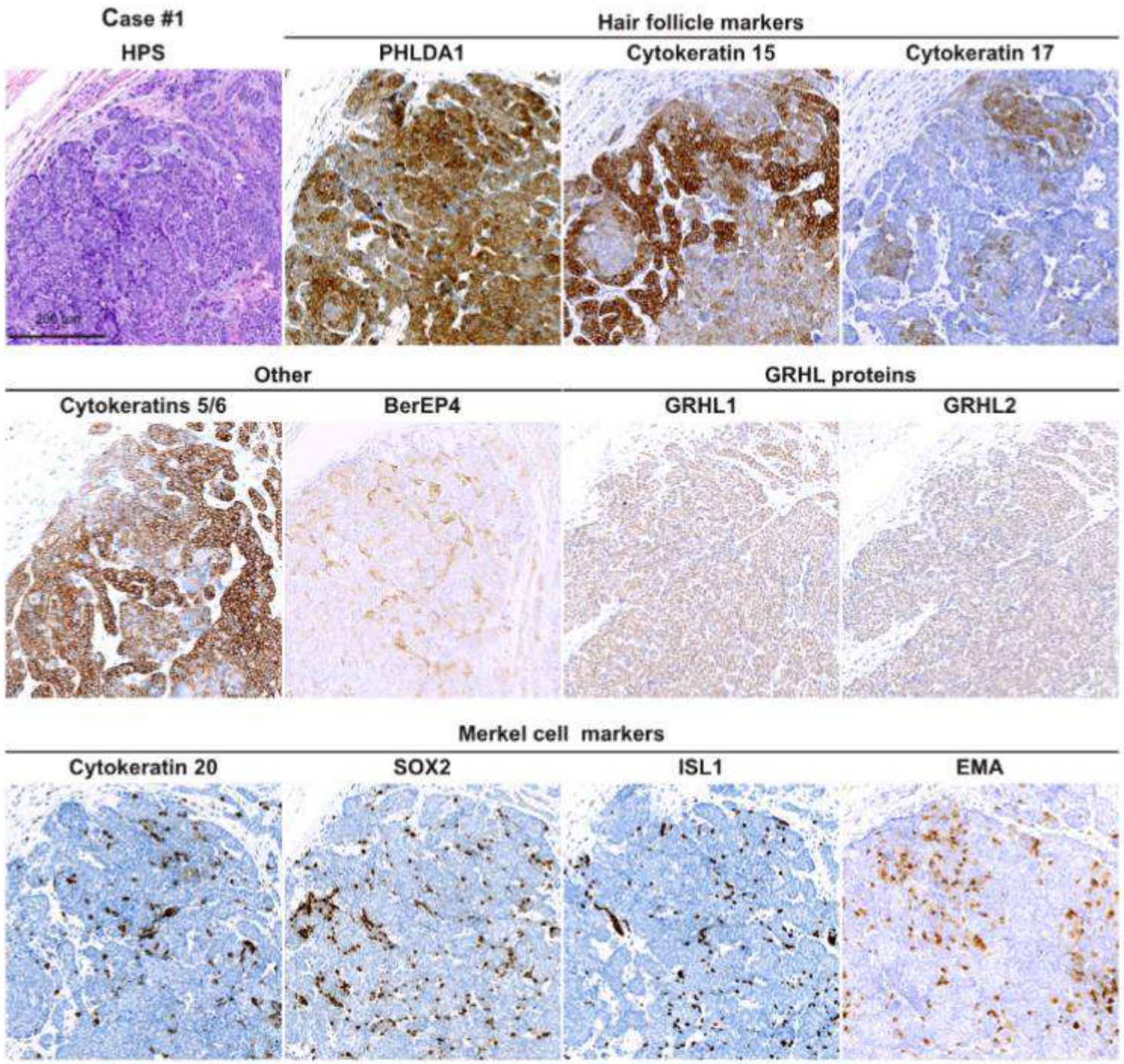
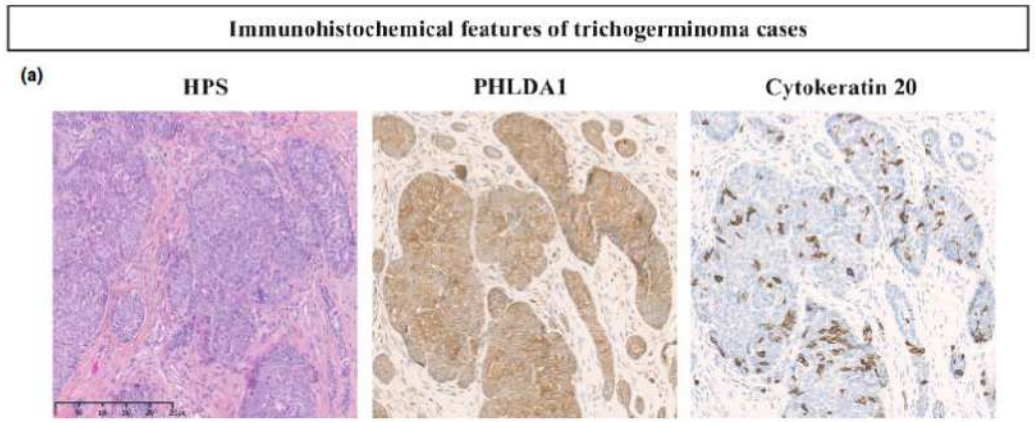



Diagnosis?
Dx: Trichogerminoma

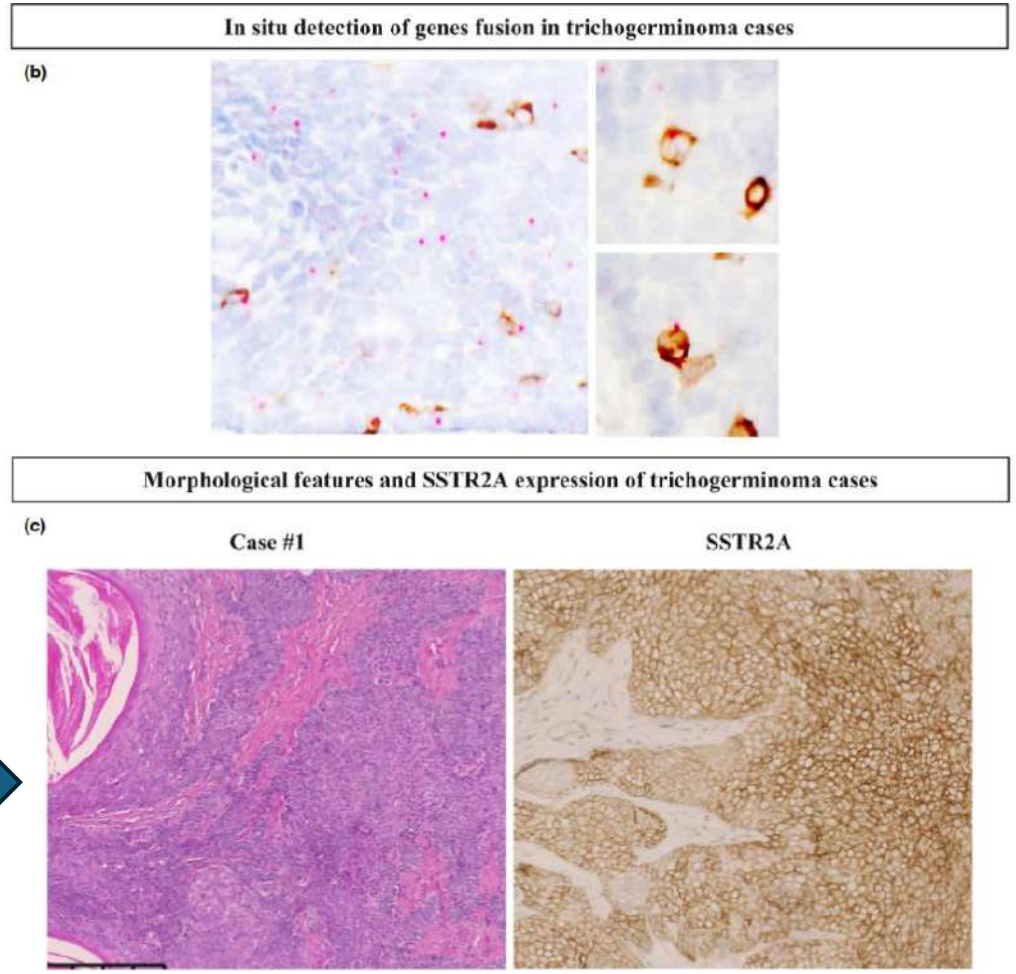


Identified recurrent genefusions of FOXK1::GRHL1/2 and GPS2::GRHL1/3 in a series of 22 trichogerminomas, a subset of folliculartumours characterized by immature features and numerous Merkel cells

Kervarrec T et al: Recurrent FOXK1::GRHL and GPS2::GRHL fusions in trichogerminoma. J Pathol. 2022 May;257(1):96-108.



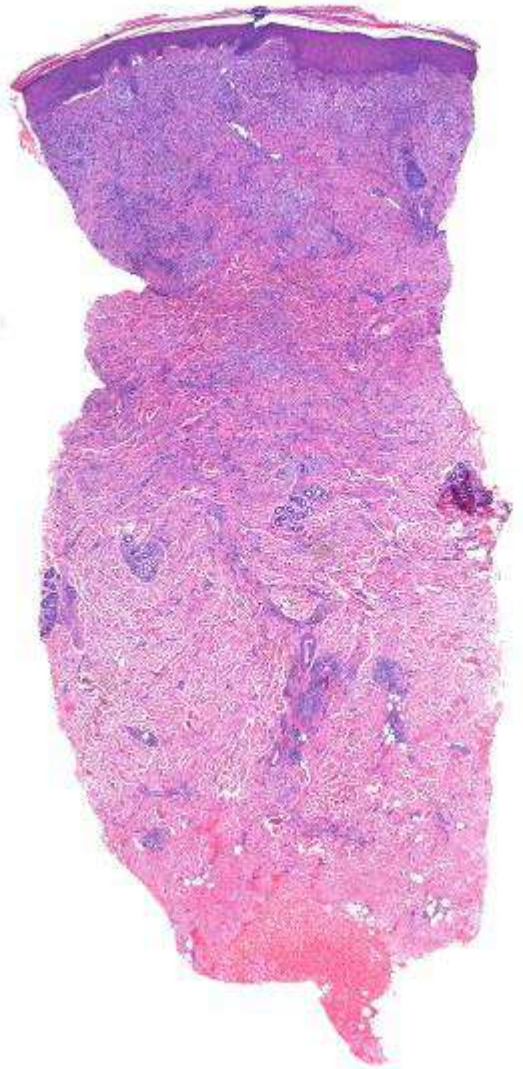
Strong and widespread expression of SSTR2A in more than 50% of tumor cells in TG, suggesting its potential as a valuable immunohistochemical marker for diagnosing

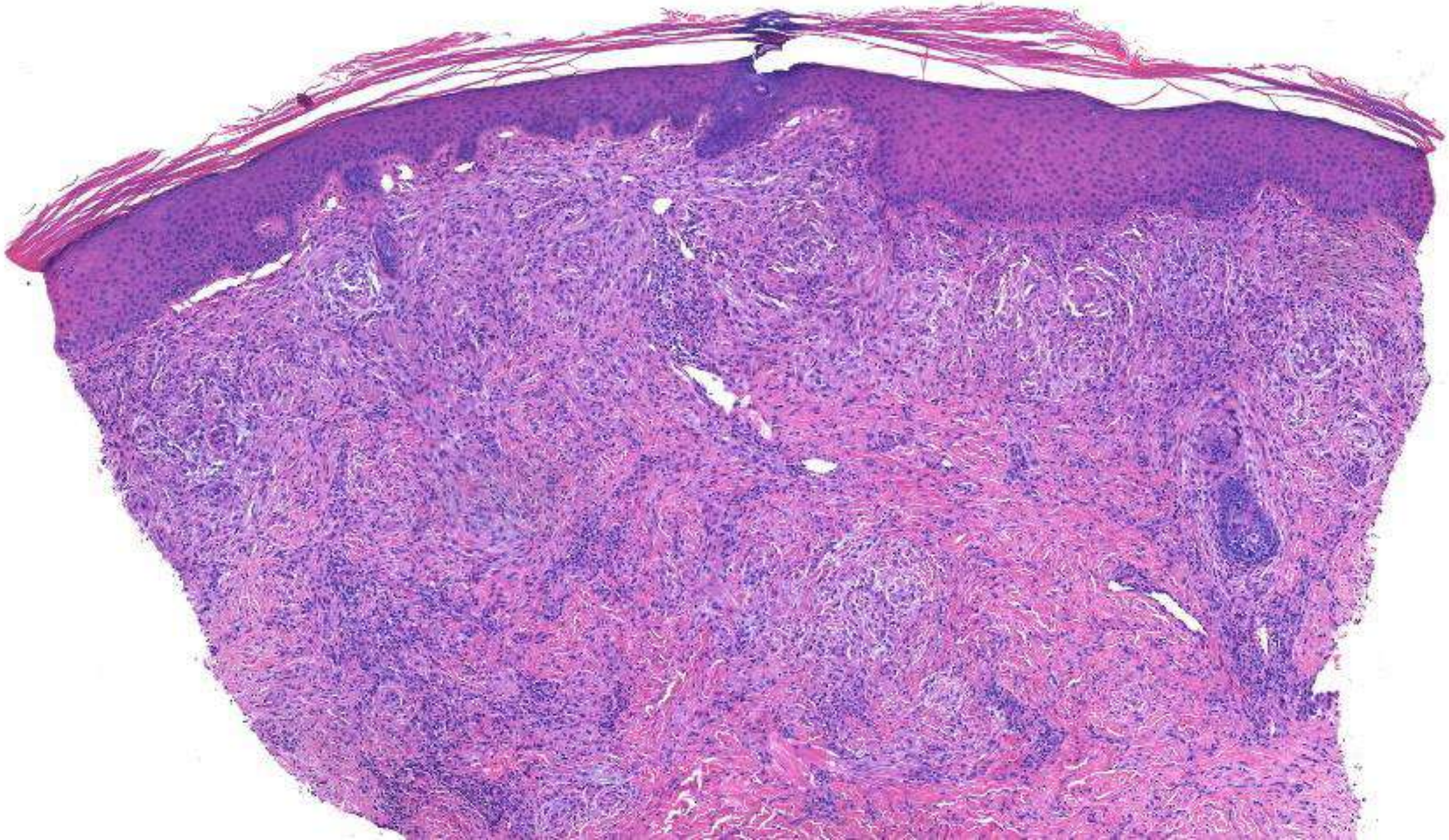


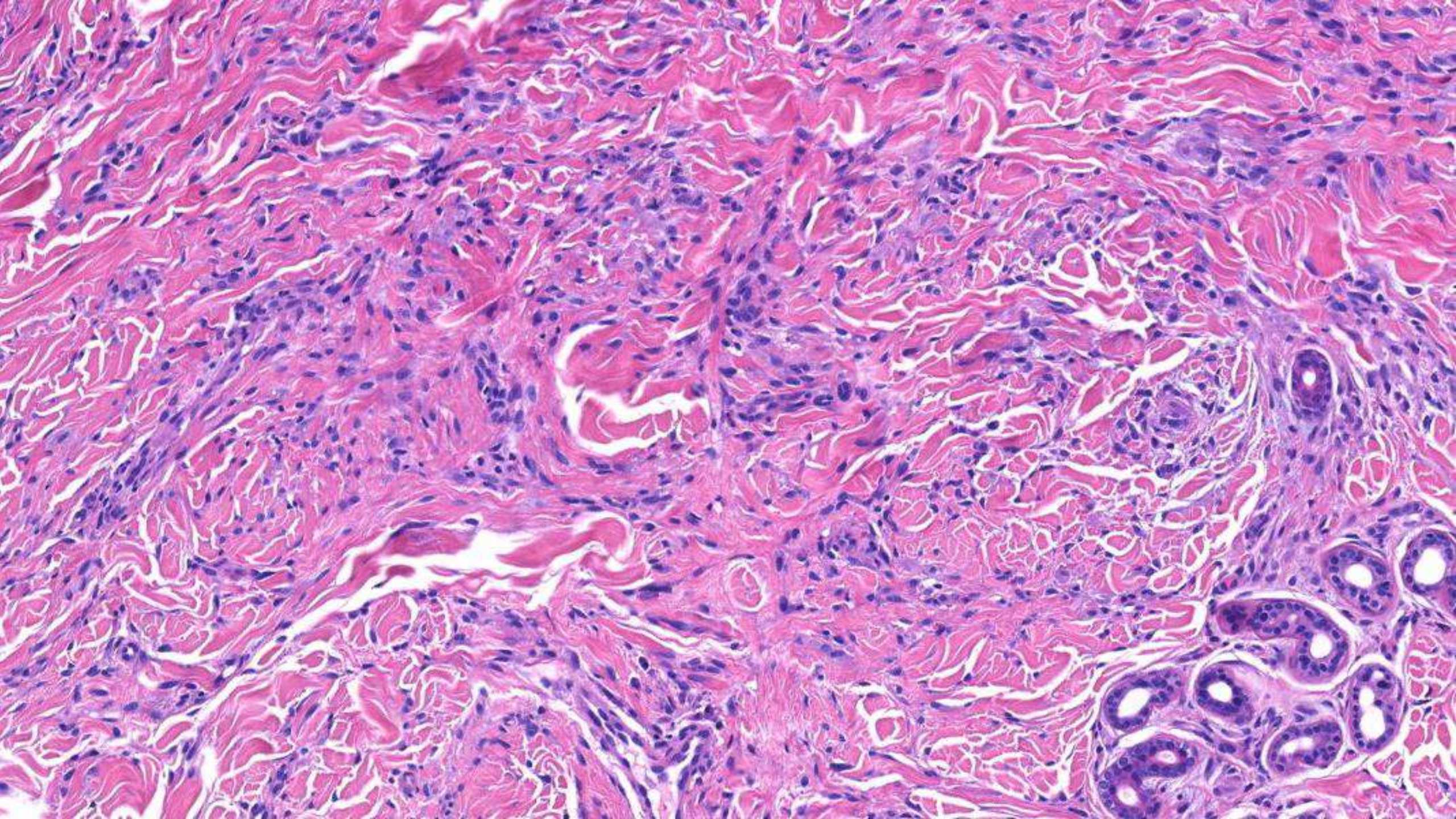
Legrand, M et al. (2023), SSTR2A is a diagnostic marker of trichogerminoma. J Eur Acad Dermatol Venereol, 37: e1344-e1347.

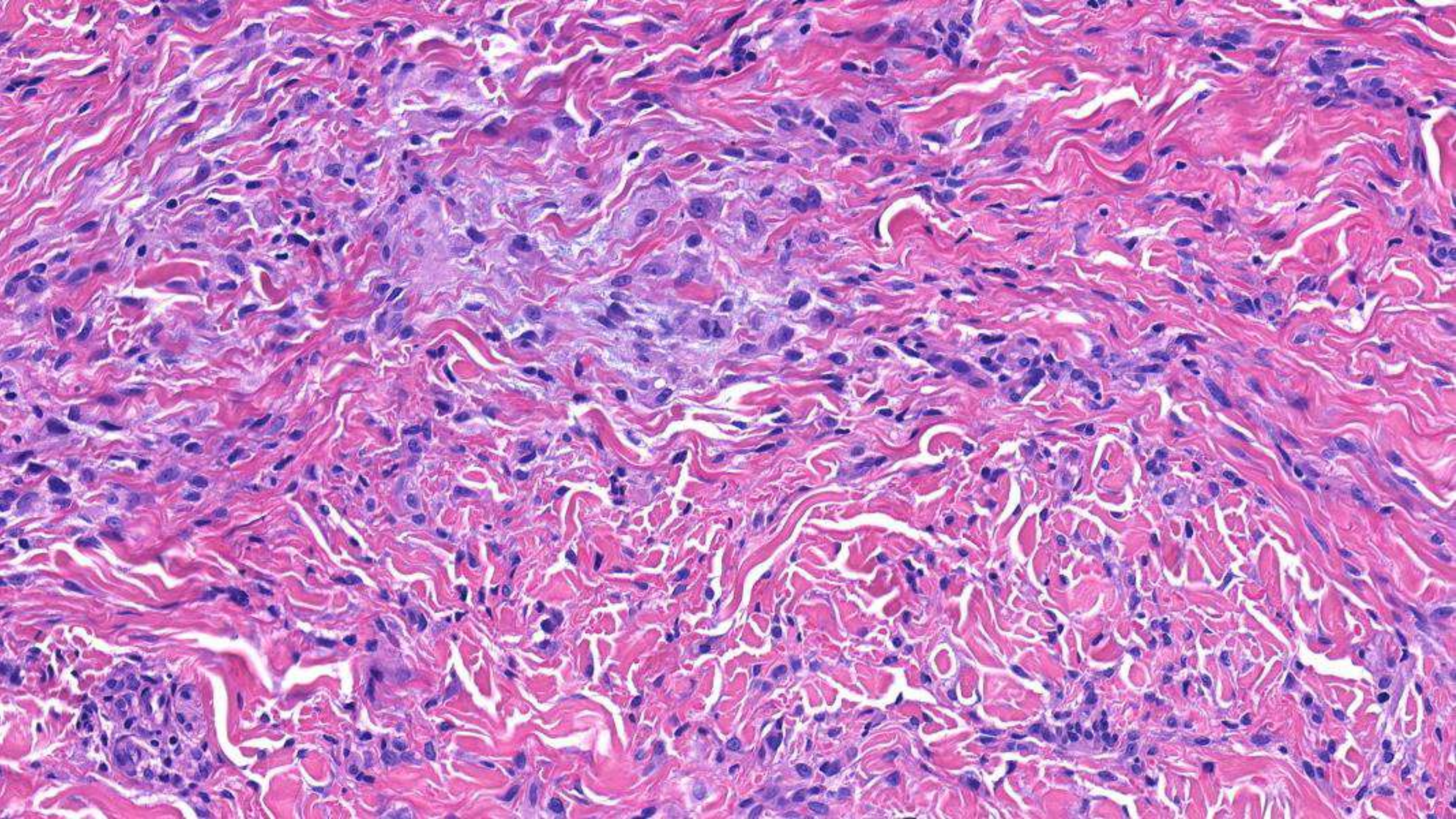
Case 14

56-year-old male
For four years, multiple popular lesions on the face, trunk and limbs









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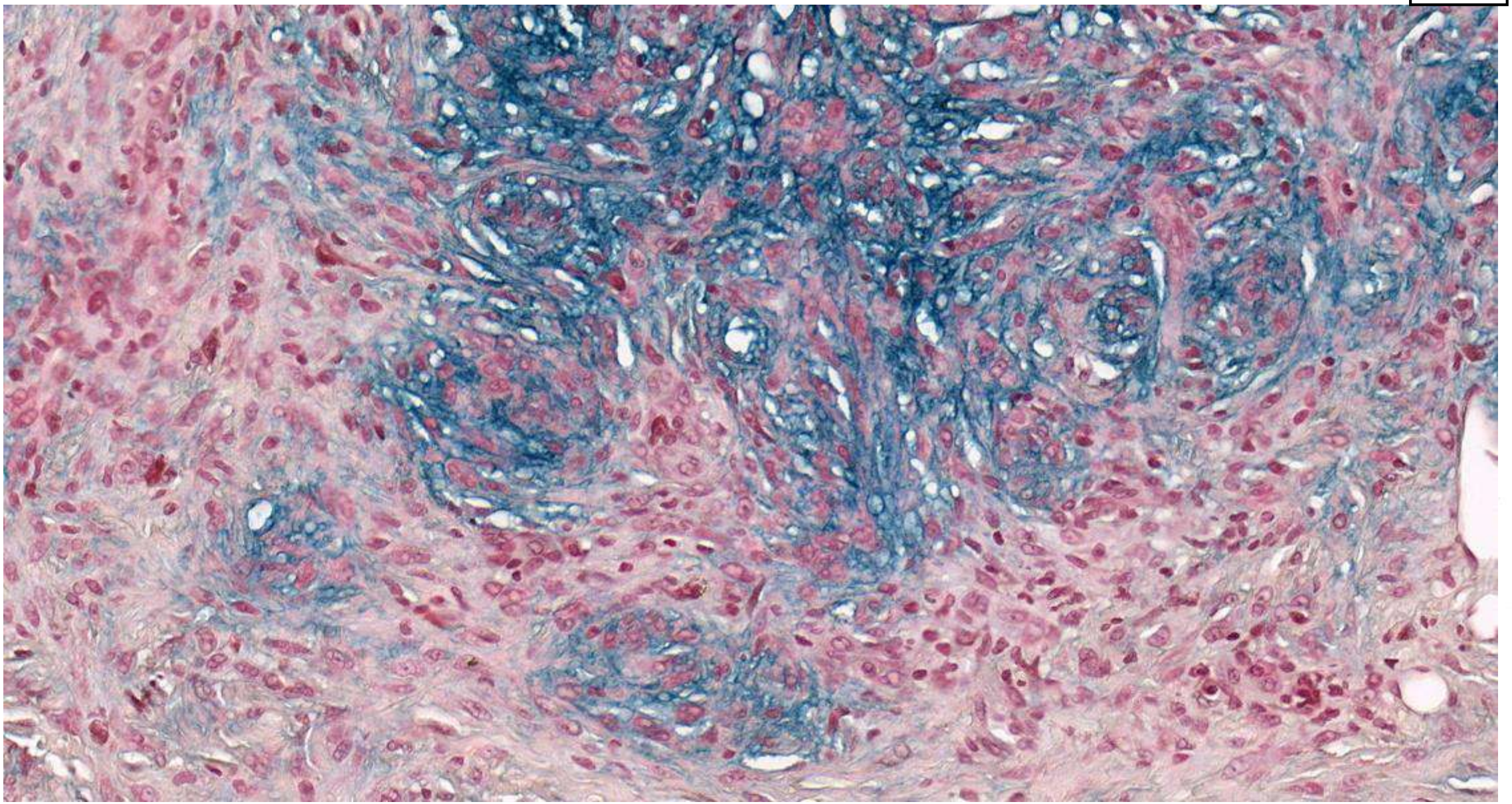
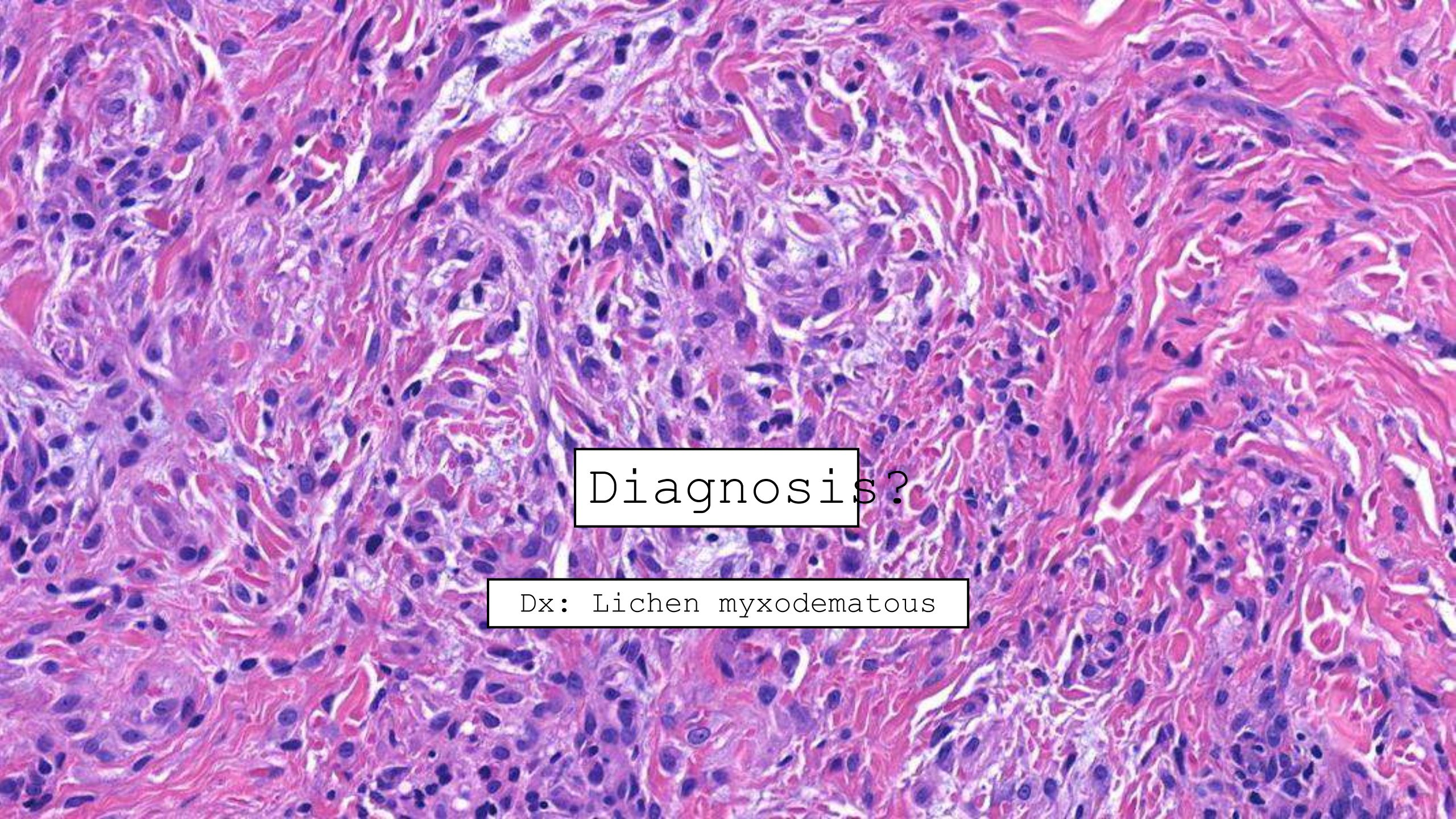



Diagnosis?
Dx: Lichen myxodematous

Investigations – Bloods (17/12/24)

- Holotranscobalamin: >128 (normal)
- Allergens (house dust mite, grass & tree pollen): normal
- MTX polyglutamate levels: low (? Compliance v absorption)
- Immunology
  - IgA/total IgG/IgM/CTD/anti dsDNA antibodies, IgG: normal range
  - Kappa: lambda ratio: 0.90
  - Serum kappa light chains: 34.98
  - Serum lambda light chains: 38.95
  - Serum protein electrophoresis: IgG lambda monoclonal band without immunoparesis

Classification of lichen myxoedematosus (LM)

Generalised form:

- Scleromyxoedema

Localised forms:

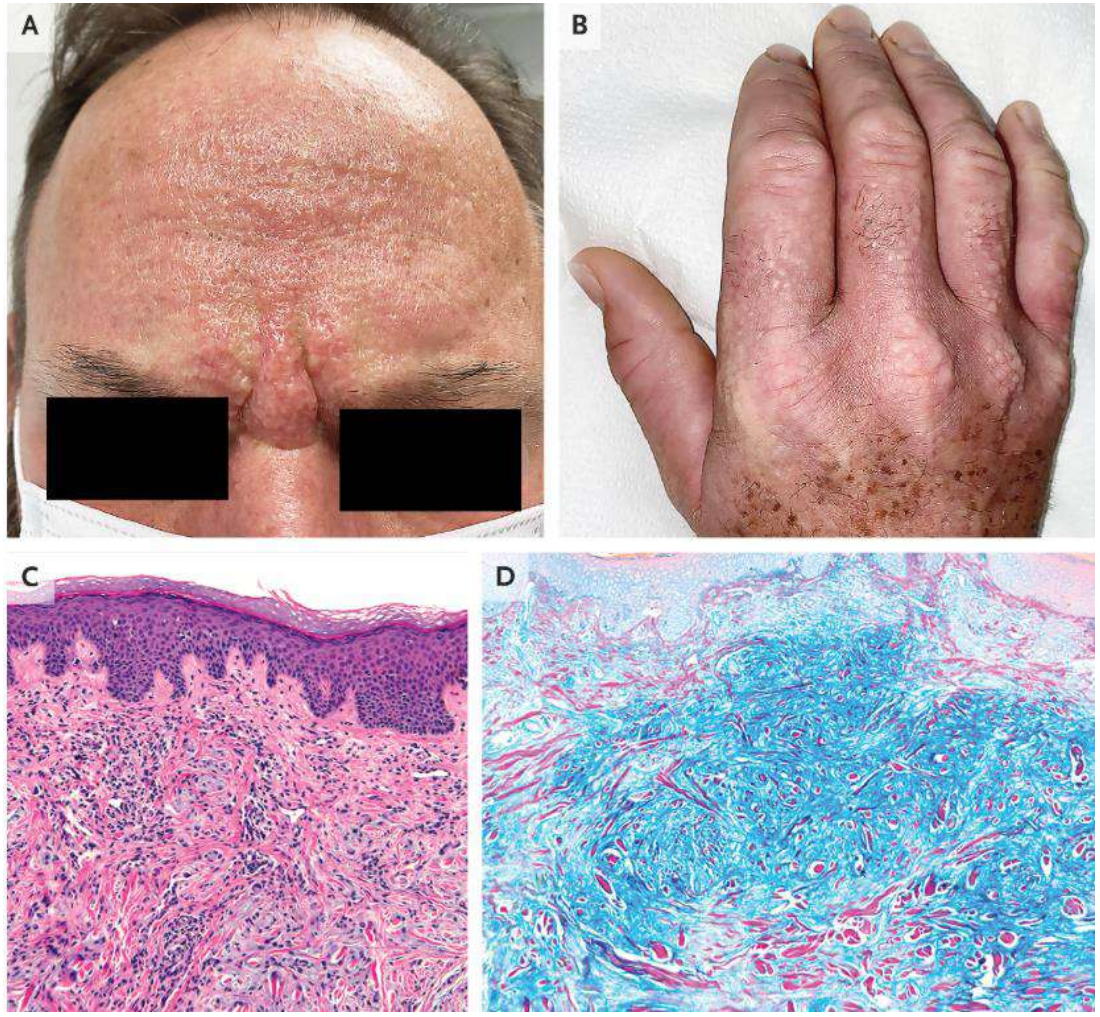
- Discrete papular LM
- Acral persistent papular mucinosis
- Juvenile and adult variants of self-healing papular mucinosis
- Papular mucinosis of infancy
- Nodular LM.

Atypical forms:

- Scleromyxoedema without monoclonal gammopathy
- Localised LM with monoclonal gammopathy
- Localised LM with mixed features of different subtypes
- Not otherwise specified.

Always associated with monoclonal gammopathy Association with cancers of the bone marrow such as myeloma, lymphoma and leukaemia

Few cases of localised form have been linked with HIV infection, Hepatitis C virus, exposure to toxic oil and contaminated L-tryptophan



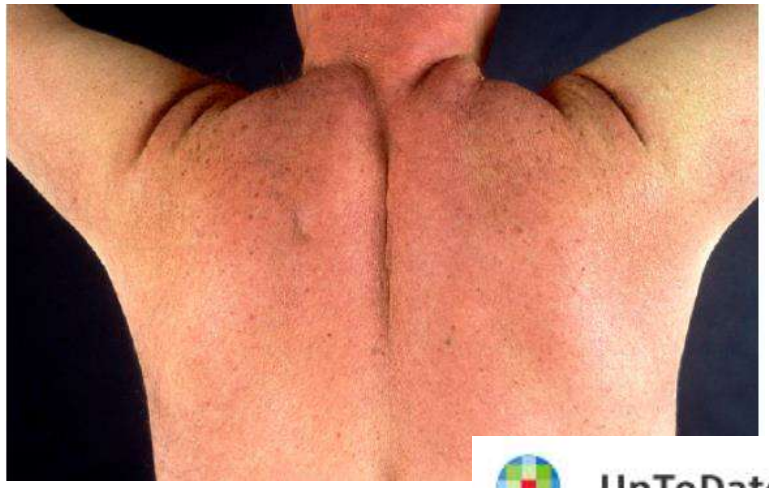
Oesophagus	Swallowing becomes difficult
Skeletal muscle	Inflamed weak muscles
Lungs	Reduced oxygen intake
Joints	Arthritis
Blood vessels	Raynaud phenomenon
Kidneys	Renal failure
Bone marrow	Reduced blood count
Nervous system	Brain and peripheral nerve damage

Chatterjee S, Fernandez AP. Scleromyxedema. N Engl J Med. 2023 Nov 23;389(21):1992. doi: 10.1056/NEJMicm2302207.

Differential diagnosis

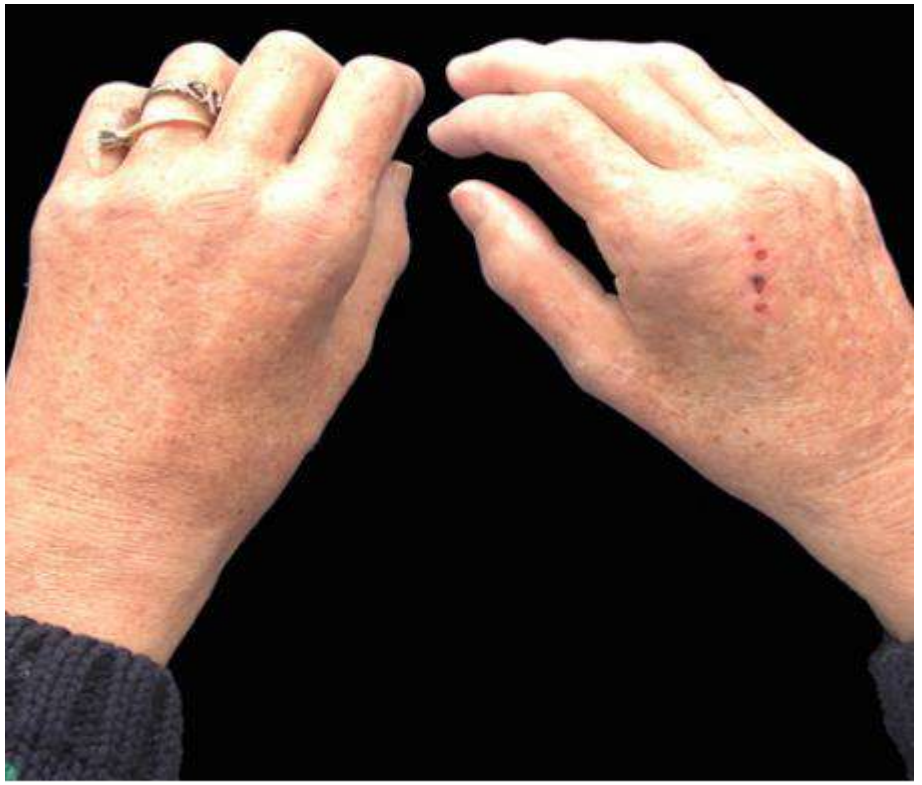
Feature	Scleromyxedema	Scleroderma
Sclerodactyly	Present	Present
Raynaud Phenomenon	Rare	Common
Esophageal Dysmotility	Present	Present
Skin Papules	Diffuse, waxy papules in linear arrays	Absent
Glabella & Posterior Auricular Involvement	Present	Absent
Middle Back Involvement	Present	Always spared
IgG Monoclonal Gammopathy	Present	Absent

Condition	Scleredema (Scleredema adultorum of Buschke)
Characteristics	Symmetrical, nonpitting induration of the skin
Initial Affected Area	Neck
Spread	Shoulders and upper trunk
Additional Symptoms	Occasional erythema
Associated Conditions	Upper respiratory infection, diabetes mellitus, blood dyscrasia
Histologic Findings	Lacks fibroblast proliferation (unlike scleromyxedema)



Differential diagnosis

Condition	Nephrogenic Systemic Fibrosis (NSF)
Affected Individuals	Those with renal dysfunction and gadolinium exposure
Histologic Features	Mucin and fibroblastic proliferation (similar to scleromyxedema)
Common Cutaneous Findings	Bilateral, symmetric, fibrotic, indurated papules, plaques, or subcutaneous nodules
Initial Affected Areas	Distal extremities
Progression	Spreads proximally



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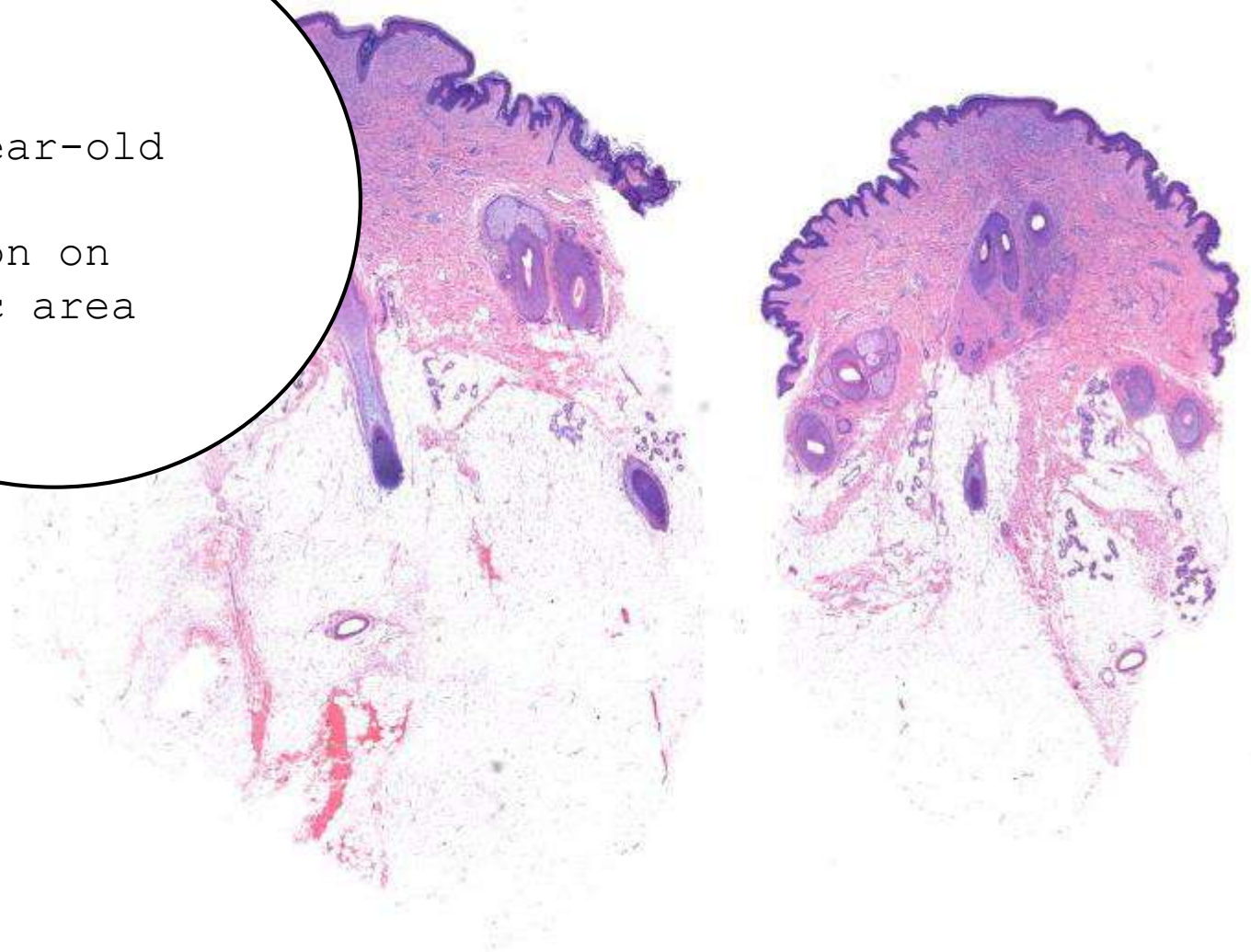
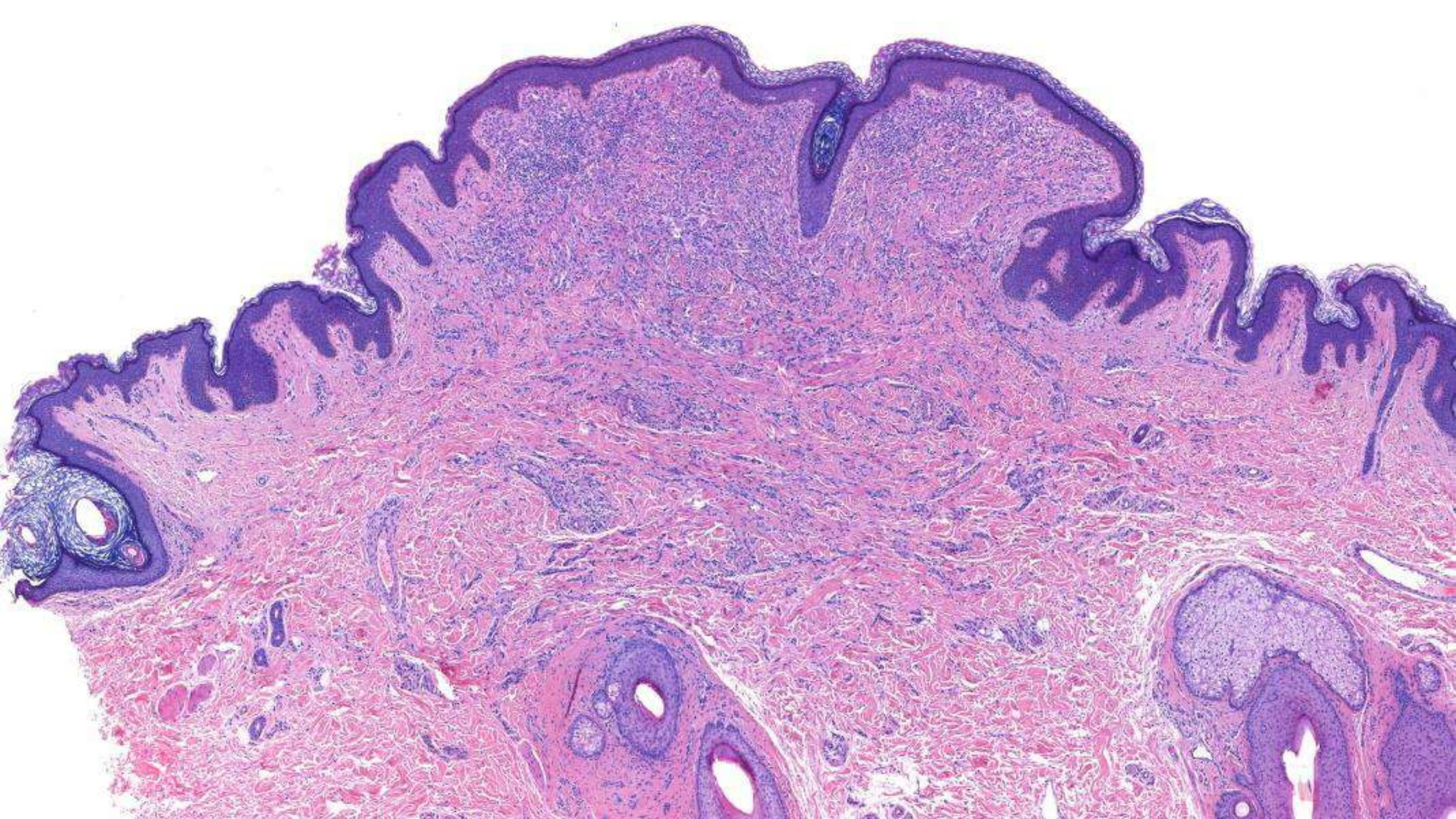
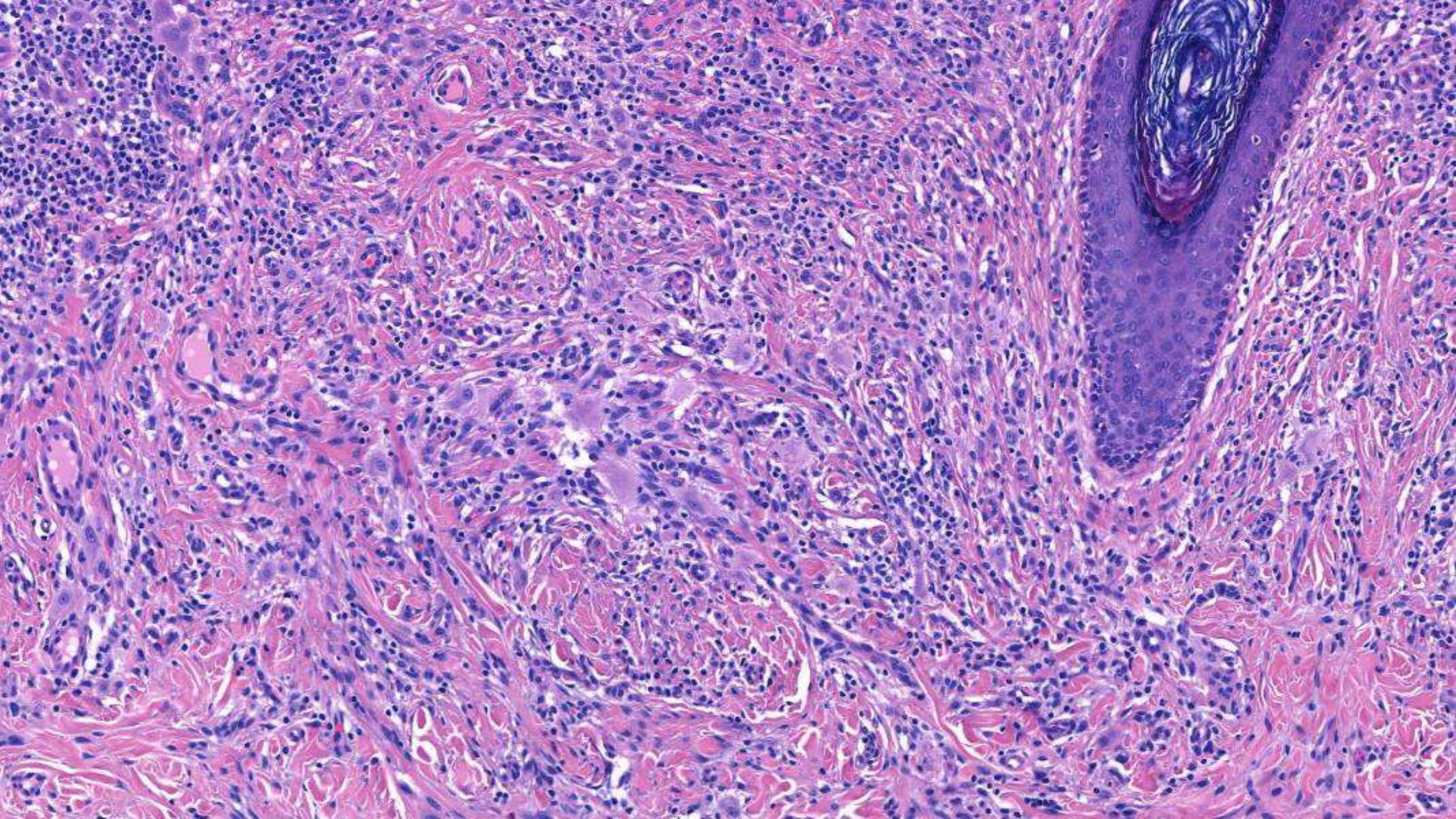
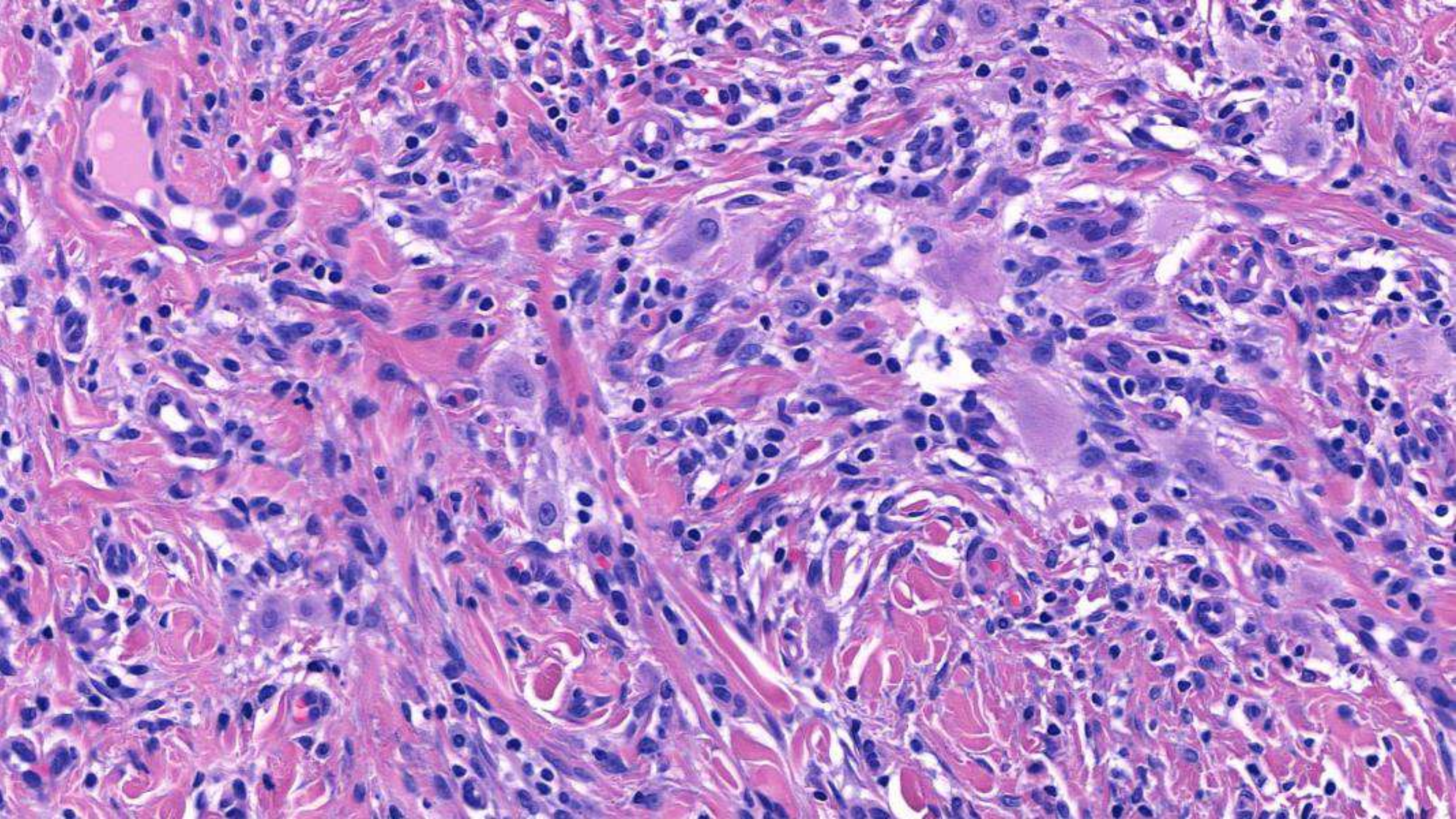
Case 15

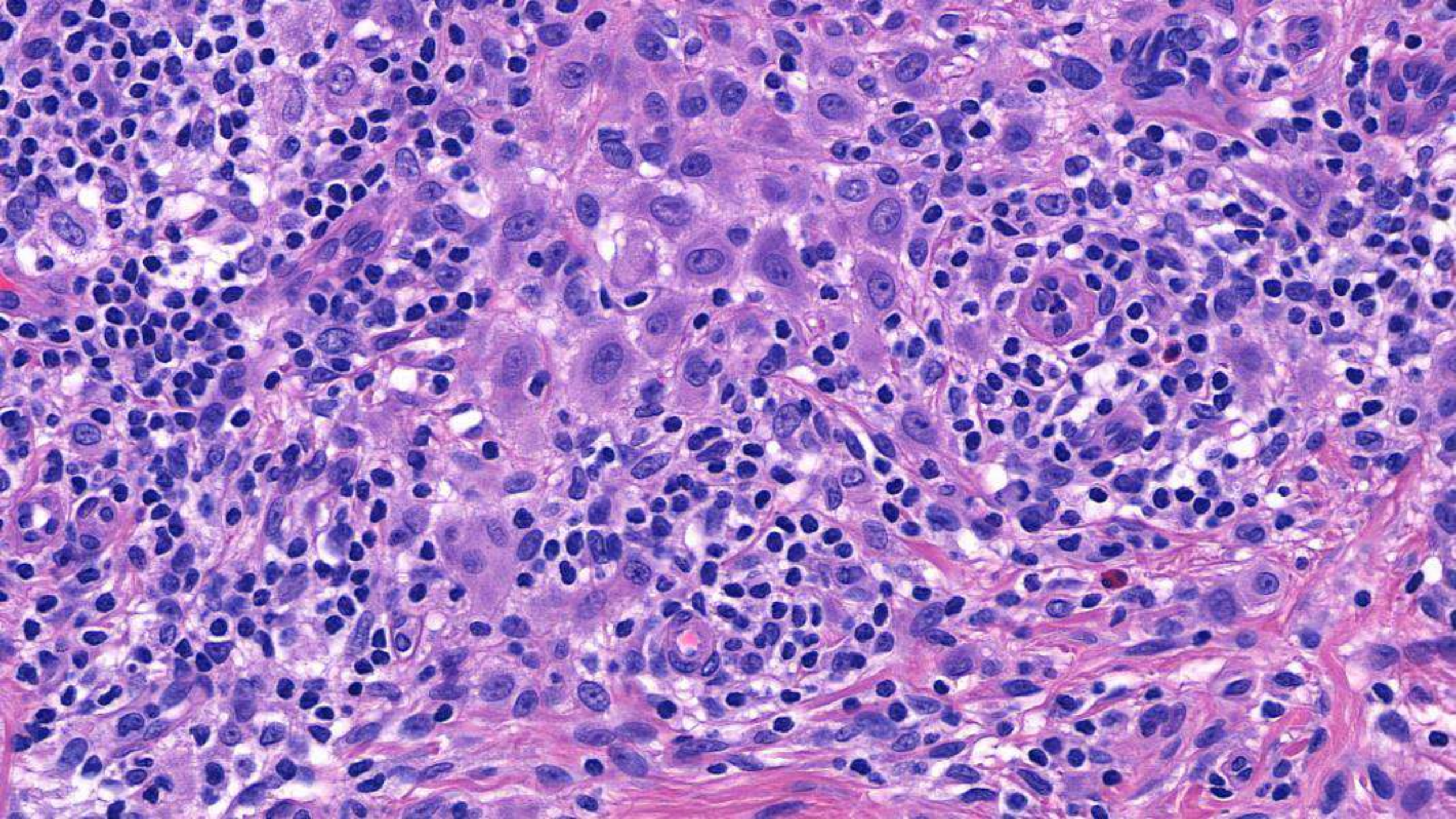
38-year-old male
Lesion on pubic area

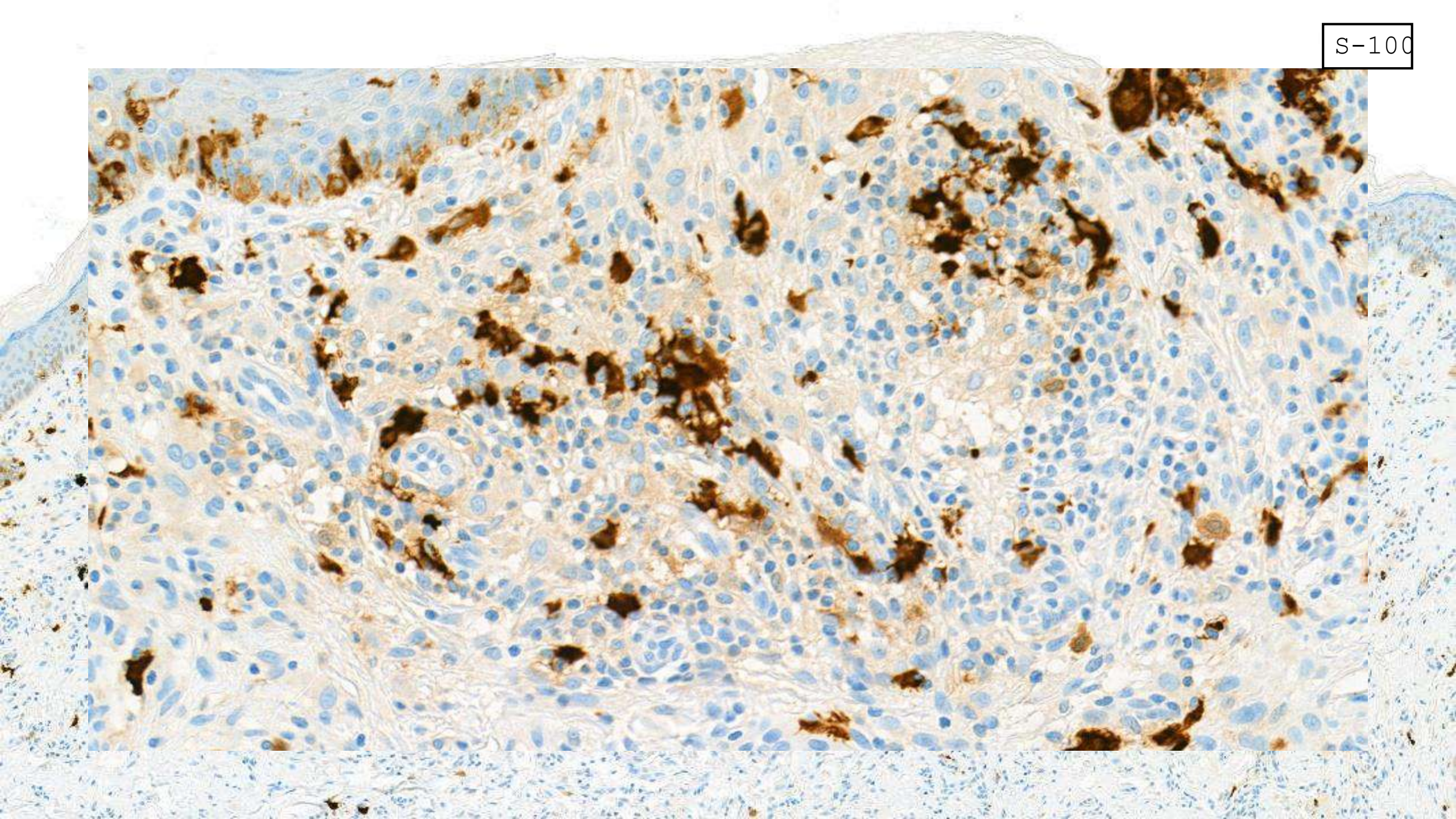








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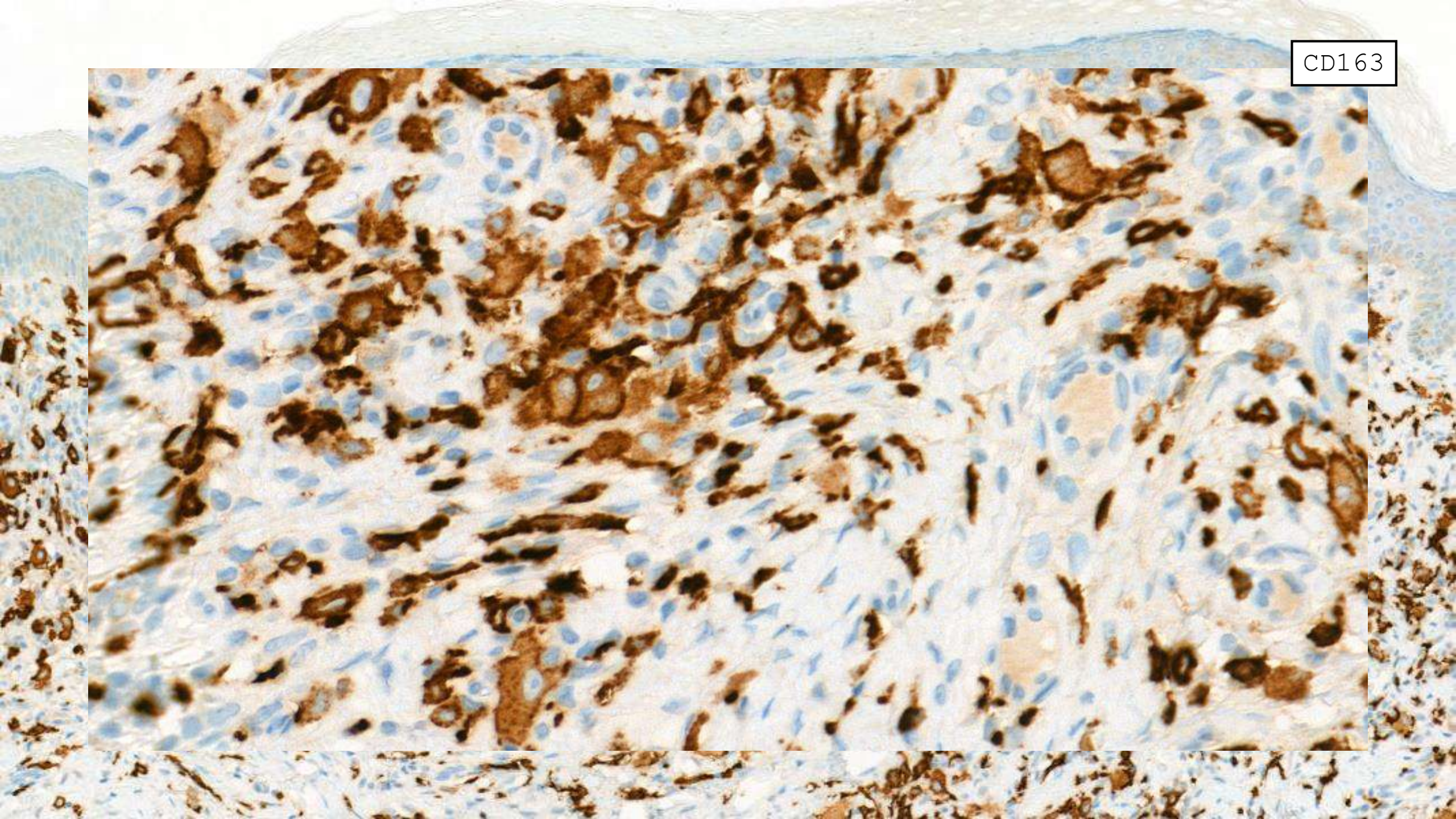
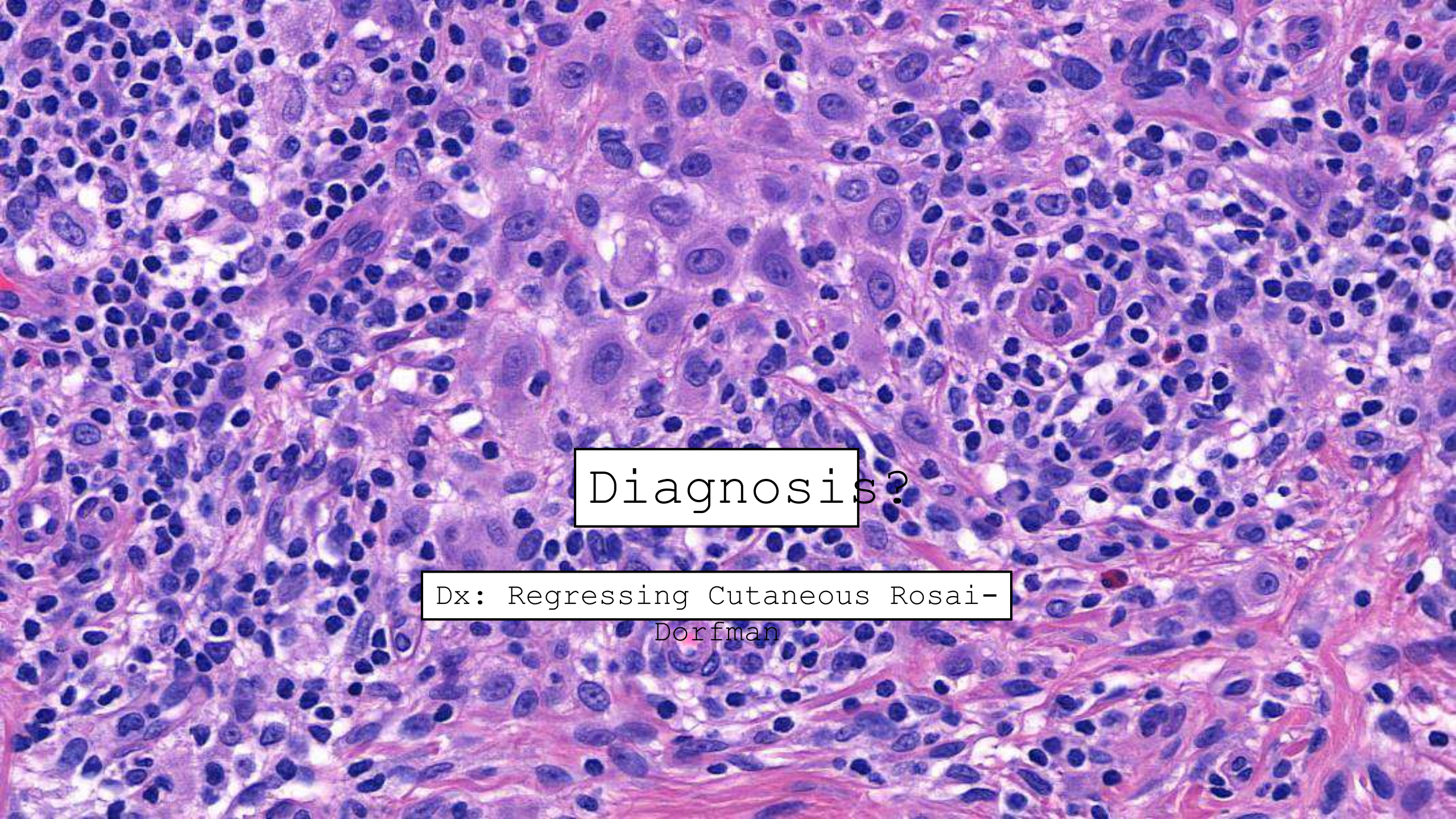

CD163


Diagnosis?
Dx: Regressing Cutaneous Rosai-Dorfman

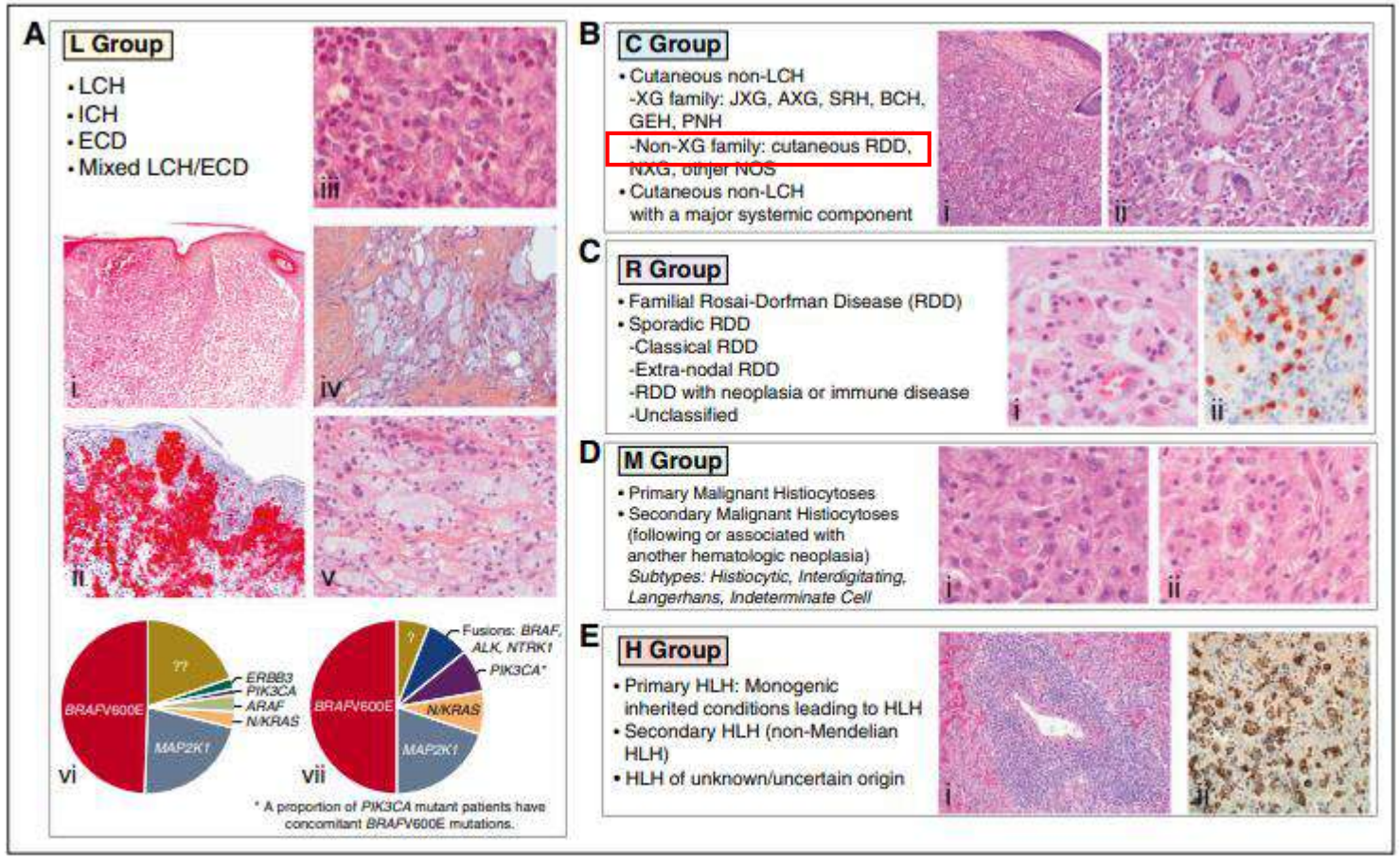


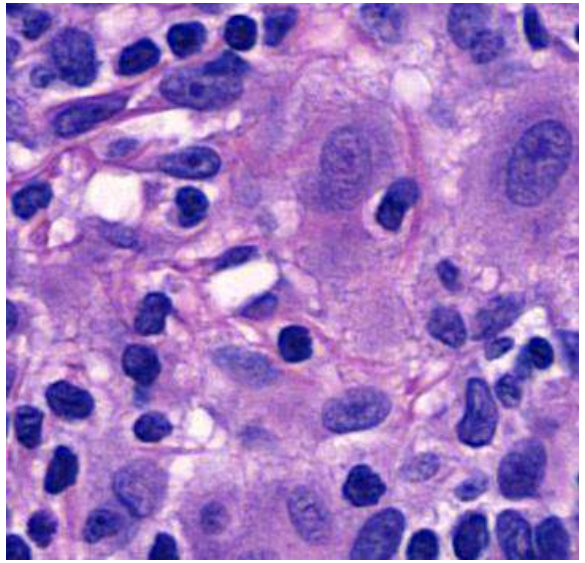
Figure 1. Histology and somatic mutations of histiocytoses of group L, C, R, M, and H. (A) L group: Histology of LCH (skin [i-ii] and bone [iii]) and of ECD (perirenal [iv-v]). Pie chart of relative frequencies of activating kinase mutations in LCH (vi) and ECD (vii). (B) C group: Histology of JXG (i-ii). (C) R group: Histology of RDD (meningeal with high IgG4$^+$ plasma cell infiltration [i-ii]). (D) M group: Histology of MH (i-ii). (E) H group: Histology of inherited HLH (liver [i-ii]). Staining with CD1a (Lii in red), IgG4 (Rii in brown), CD163 (Hii in brown), or hematoxylin and eosin (all others). NOS, not otherwise specified.

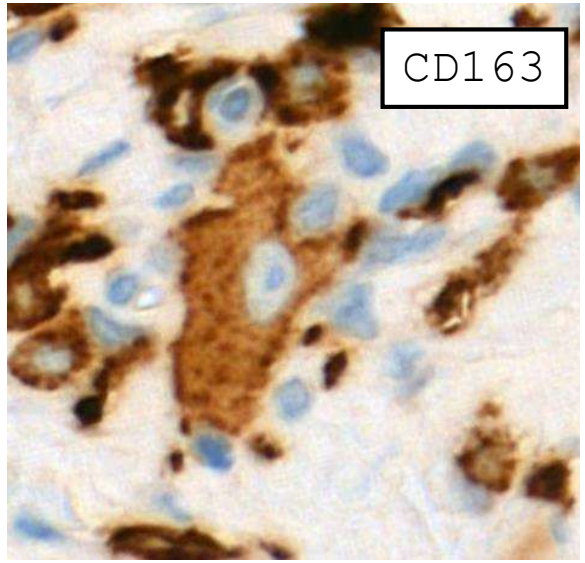
Emile JF et al: Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood. 2016 Jun 2;127(22):2672-81. doi: 10.1182/blood-2016-01-690636. Epub 2016 Mar 10.

- Cutaneous and superficial subcutaneous RDD presents as papules and nodules
- often discolored and multifocal
- No specific site preference
- The study involved 22 patients, ages 15 to 68, with follow-up showing lesion resolution in 6 cases, while 7 patients had persistence or recurrence
- Histologically, lesions exhibit S100-positive histiocytes with emperipolesis, mixed inflammation, and variable growth patterns (storiform and lobulated)
- The cutaneous form is more common in Asians and whites

Clues to the diagnosis of cutaneous RDD

- Presence of the typical large polygonal histiocytes with abundant palely eosinophilic cytoplasm
- Their positivity for S100 protein by immunohistochemistry
- Identification of emperipolesis





Brenn T, Calonje E, Granter SR, Leonard N, Grayson W, Fletcher CD, McKee PH. Cutaneous rosai-dorfman disease is a distinct clinical entity. Am J Dermatopathol. 2002 Oct;24(5):385-91.

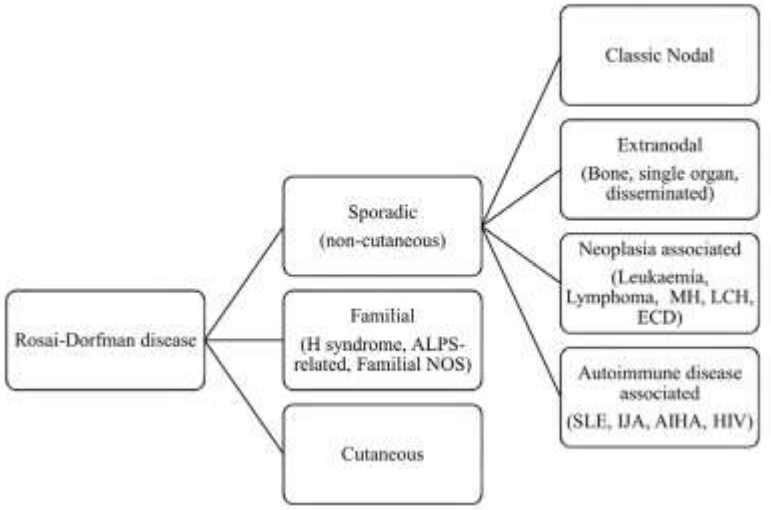
- Various viral agents, such as **human herpesvirus 6, parvovirus B19** and **Epstein-Barr virus**, have been investigated as potential inciting agents, but studies have failed to establish a causative
- Kinase mutations in nodal and extranodal Rosai-Dorfman Disease (RDD), but not in cutaneous RDD

- Mutations in genes like ARAF, MAP2K1, NRAS, and KRAS have been observed

- One study found that up to 33% of RDD cases had KRAS or MAP2K1 mutations, suggesting a subset of cases may be clonal

- Presence of KRAS and/or MAP2K1 mutations was associated with a younger age, head and neck site and multifocal disease

- BRAF V600E mutations, which are present in other histiocytic neoplasms like Langerhans Cell Histiocytosis (LCH) and Erdheim-Chester
- Few recent cases have reported BRAF mutations



Bruce-Brand C, Schneider JW, Schubert P. Rosai-Dorfman disease: an overview. J Clin Pathol. 2020 Nov;73(11):697-705.

Immunohistochemistry

TABLE 3. Characteristic Phenotype of Histiocytic Diseases

IHC Marker	RDD	ECD	LCH
CD68	+	+	+
CD163	+*	+	−†
Cyclin D1	+	+	+
S100	+	−/+‡	+
OCT2	+	−	−†
Factor 13a	−/+§	+	−
CD1a/langerin	−	−	+
ZBTB46	−	−	+

*CD163 is negative in a minority of RDD cases (~10%).
†OCT2 and CD163 are expressed in a minority of LCH cases (5% to 10%).
‡S100 is expressed in ~20% to 30% of ECD cases.
§Factor 13a expression is increased (2 to 3+) in 30% of RDD cases.

Ravindran A et al: Rosai-Dorfman Disease Displays a Unique Monocyte-Macrophage Phenotype Characterized by Expression of OCT2. Am J Surg Pathol. 2021 Jan;45(1):35-44.

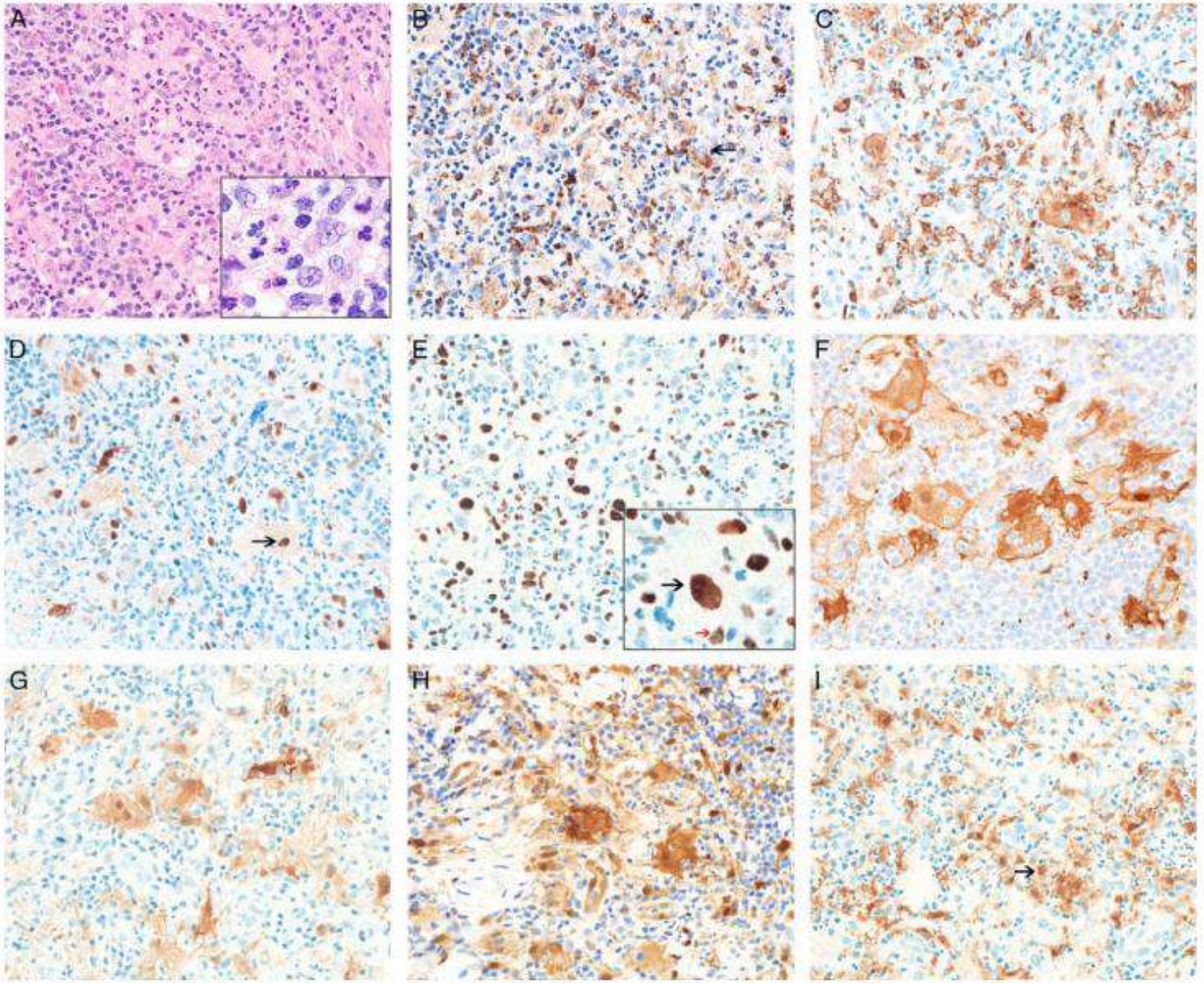


FIGURE 1. Immunophenotype of RDD: Skin biopsy (patient #13, Table 2) demonstrating the lesional macrophages with emperipolesis on light microscopy (A: hematoxylin and eosin), with 2+ positive staining for CD68 (B, black arrow points to RDD macrophage), 2+ positive staining for CD163 (C), 3+ positive staining for cyclin D1 (D, black arrow points to RDD macrophage), 3+ positive staining for OCT2 (E, black arrow points to RDD macrophage, red arrow marks OCT2-positive B cell), 3+ positive staining for S100 (F), 2+ positive staining for p16 (G), 3+ positive staining for pERK (H), and 1+ positive staining for factor 13a (I, black arrow points to RDD macrophage). The insets (A, E) highlight the individual RDD lesional cells.

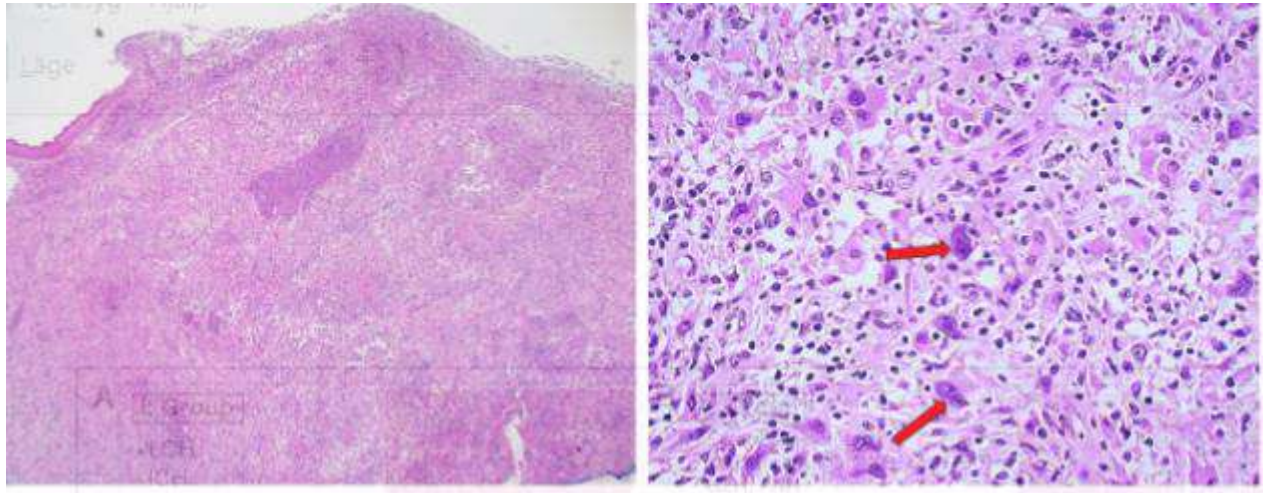
JOURNAL OF CUTANEOUS PATHOLOGY

CASE REPORT

KRAS 117N positive Rosai-Dorfman disease with atypical features

Zainab A. Jafri, Shivani P. Reddy MD, David S. Cassarino MD, PhD

First published: 25 September 2020 | https://doi.org/10.1111/cup.13883 | Citations: 4

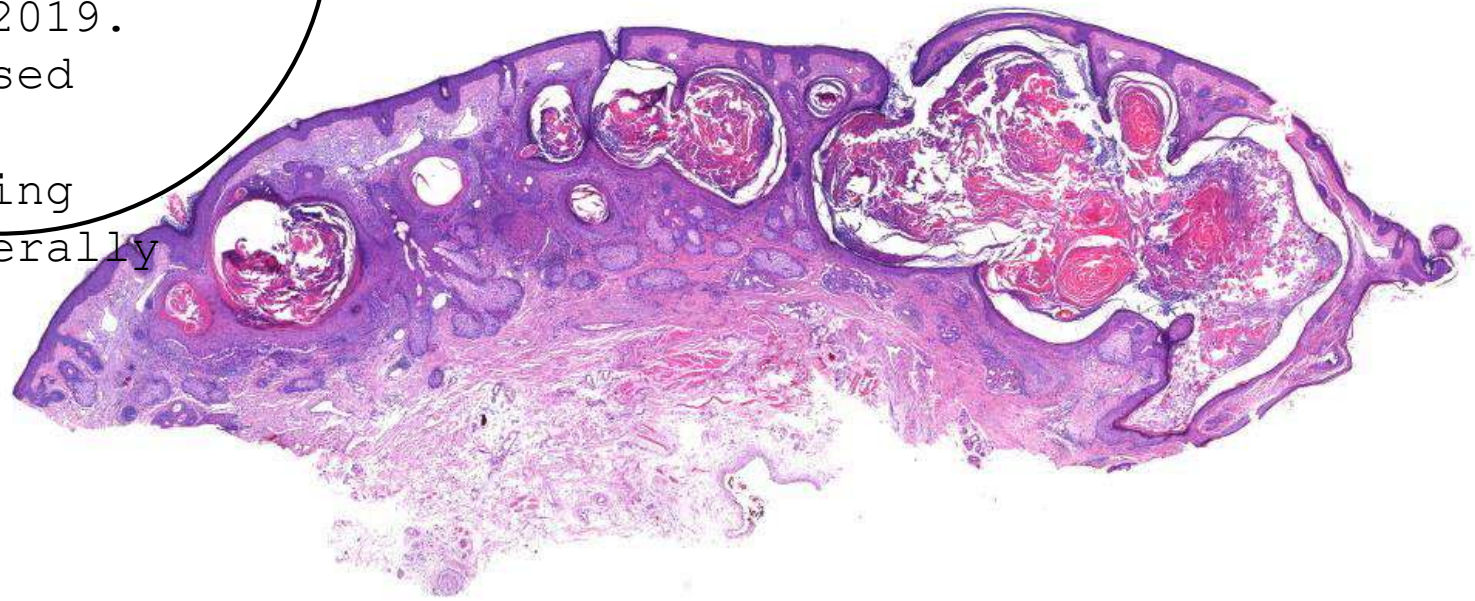


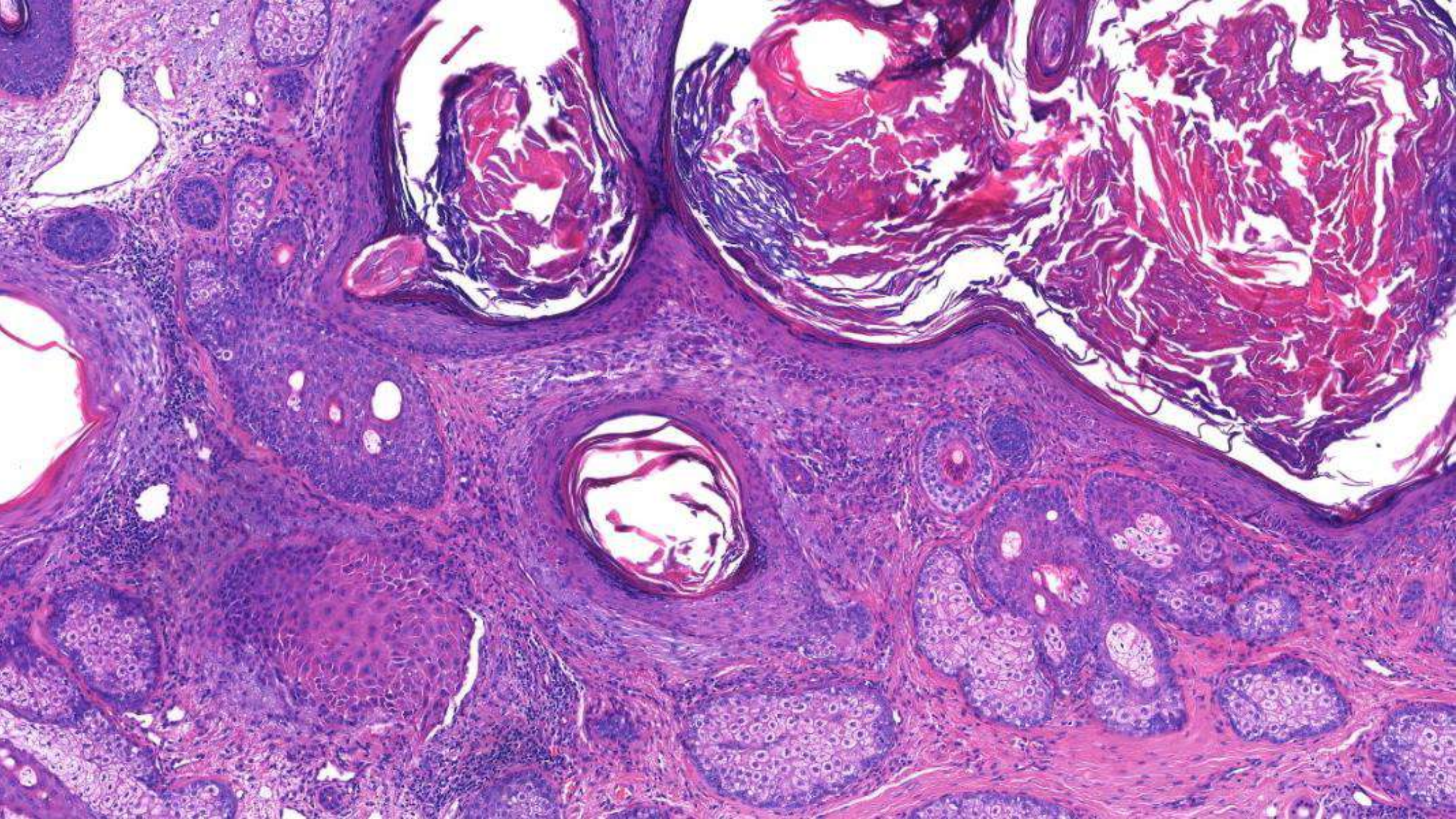
RDD with atypical histopathological features, and no other primary malignant diagnosis, may be tested for MAP2K1 pathway mutations, particularly in widespread cases where nonsurgical treatments like MEK inhibitors are

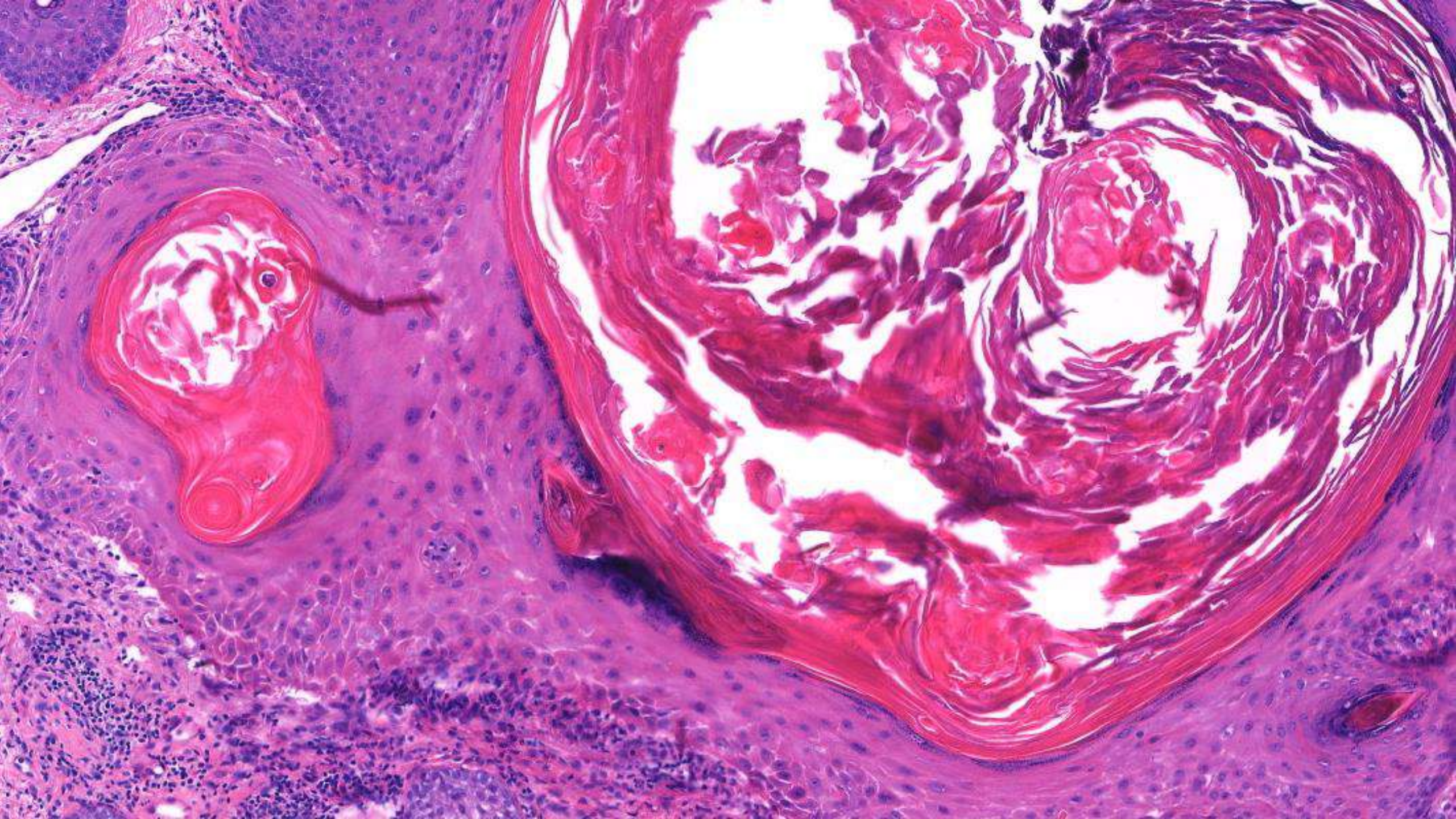
Jafri ZA, Reddy SP, Cassarino DS. KRAS 117N positive Rosai-Dorfman disease with atypical features. J Cutan Pathol. 2021 Jan;48(1):147-150.

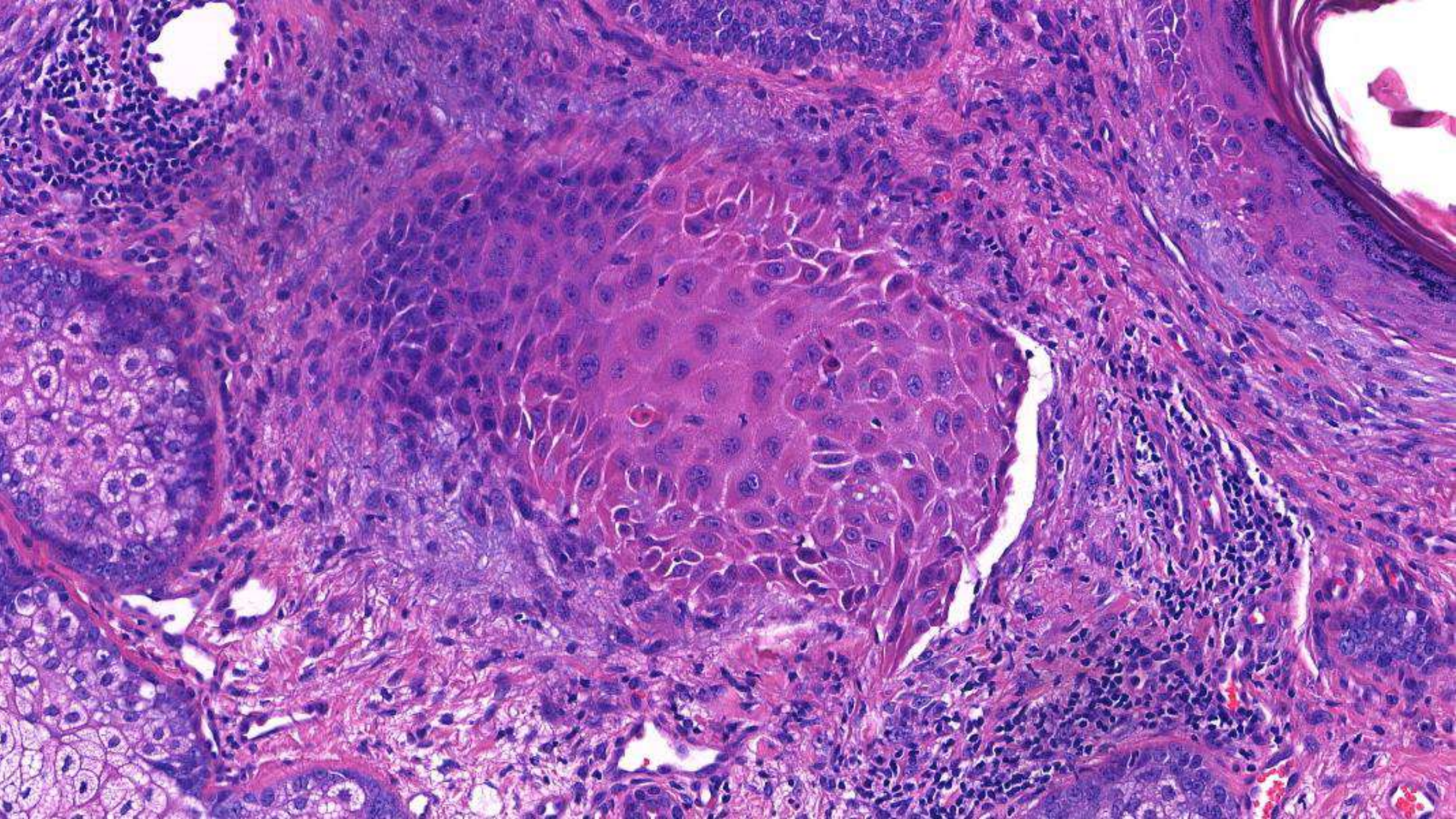
Case 16

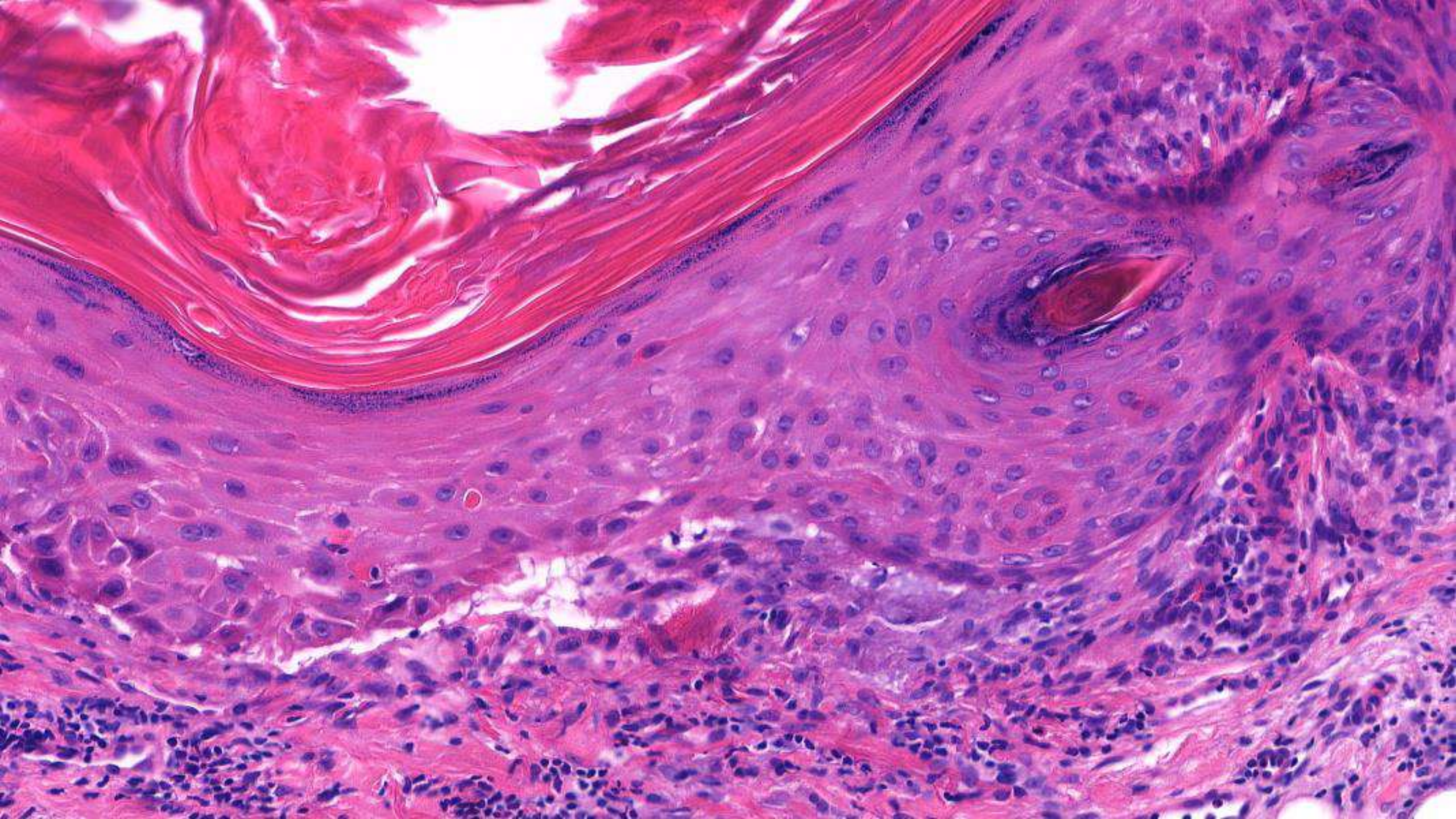
60-year-old female
Enlarging scally plaque since 2019.
Depressed centre
Enlarging peripherally

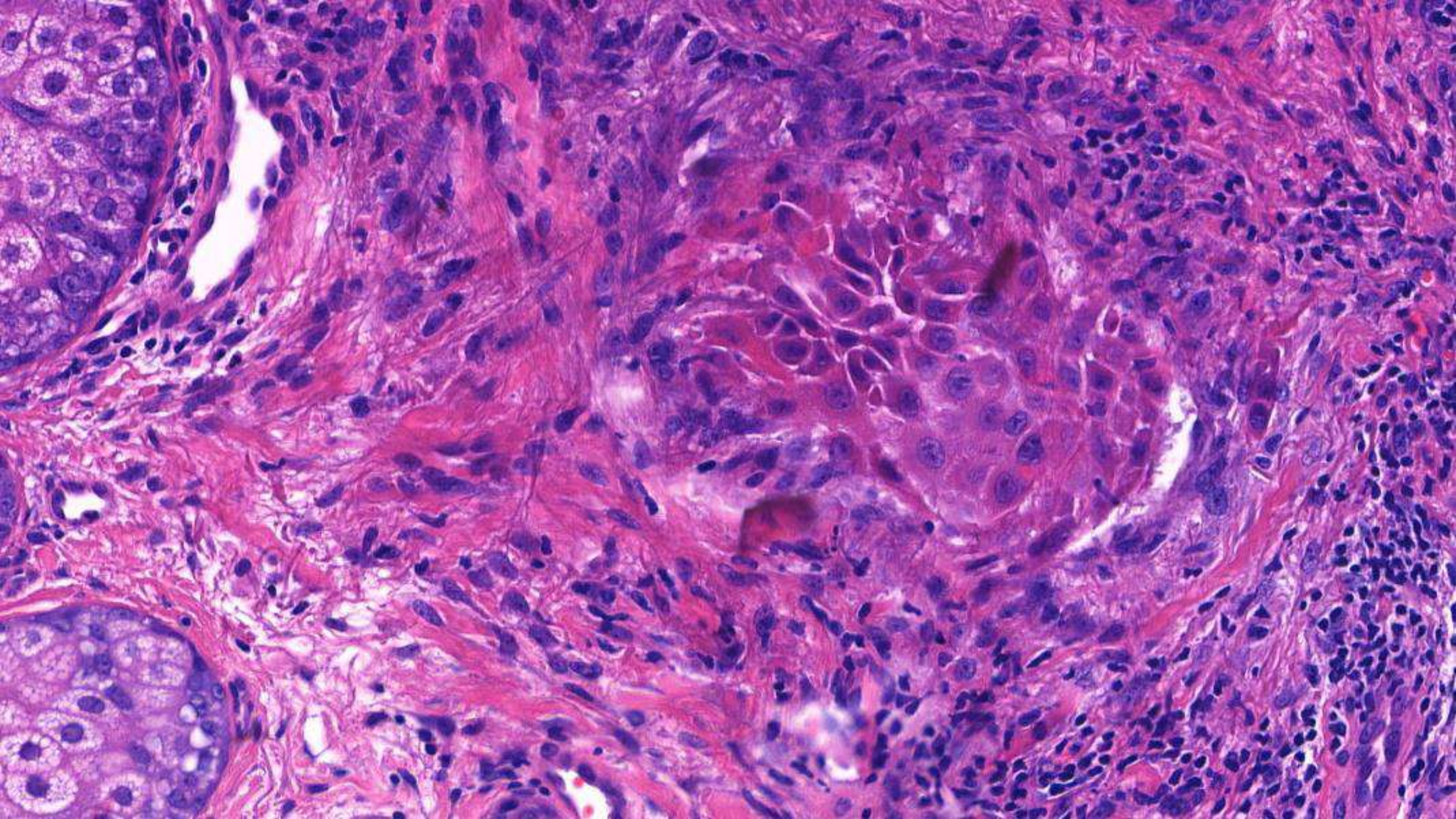


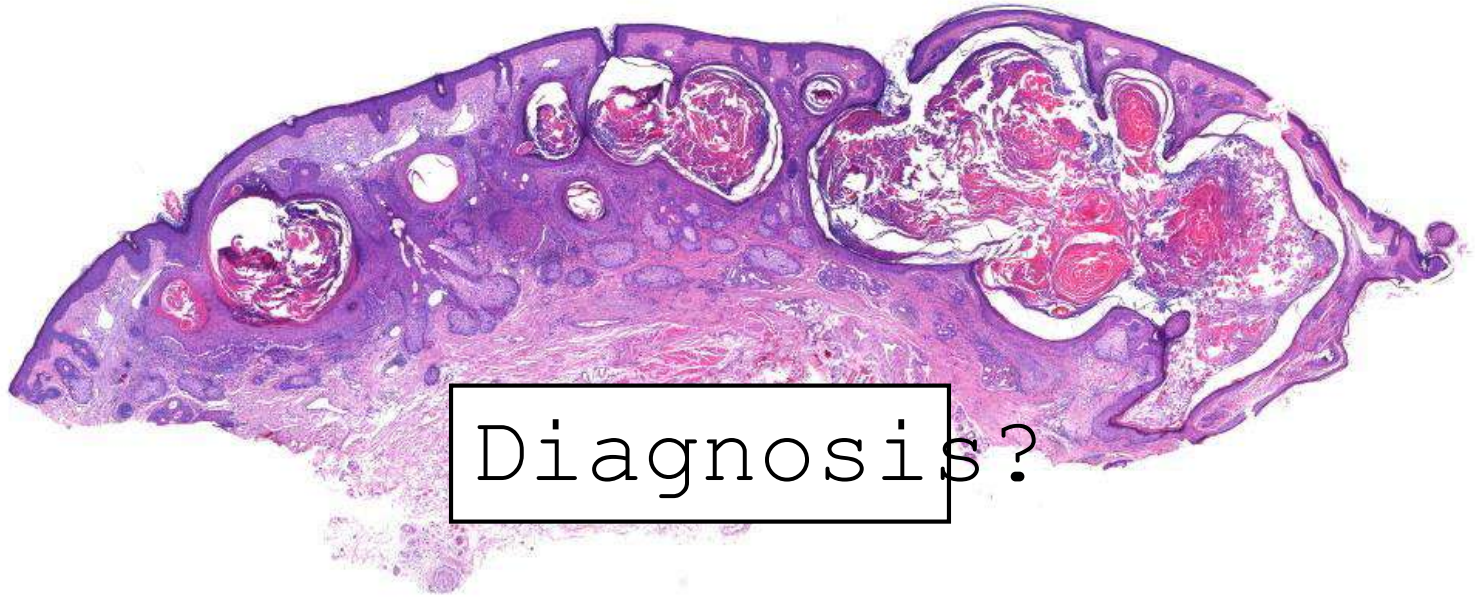












Diagnosis?

Dx: Keratoachantoma centrifugum marginatum (KCM)

- KCM was first reported in 1962 and described as a distinct entity by Belisario in 1965
- Risk factors include UV exposure, smoking, and trauma
- KCM is challenging to diagnose and requires a high level of clinical suspicion
- Though mostly an adult condition, rare pediatric cases have been documented.

- Multiple KCMs may be associated with certain KA-related syndromes, such as **Muir-Torre syndrome**, **Grzybowski-type** KAs, and **Ferguson-Smith type** KAs, each presenting with specific patterns of lesion appearance and involution

- Treatment for KCM generally involves surgical excision, but when surgery is not feasible due to lesion size, medical therapies like oral retinoids, intralesional methotrexate, and bleomycin have shown variable success

- Given the lack of standardized treatment protocols, a patient-centered approach with close monitoring is essential

- KCM is a locally destructive neoplasm that requires careful diagnosis and tailored management

Xiao H, Hooper PB, Umphress BA, Wolverton JE. Keratoacanthoma centrifugum marginatum. Dermatol Online J. 2021 Mar 15;27(3):13030/qt5vp5f7bq.

- Keratoacanthoma centrifugum marginatum (KCM) is a very rare variant of keratoacanthoma
- Progressive centrifugal growth, central healing,and atrophy
- No tendency for spontaneous resolution
- More frequent on chronic sun-exposed areas
- Usually in white-skinned adult patients in the fifth or sixth decade of life, mostly in men.
- Locally destructive, it is generally accepted that KCM is a benign entity
- Pseudoepitheliomatous hyperplasia with a few central irregular craters filled with keratin
- The keratinocytes of pseudoepitheliomatous hyperplasia had enlarged nuclei with glassy eosinophilic cytoplasm and minimal atypia in the dermal component

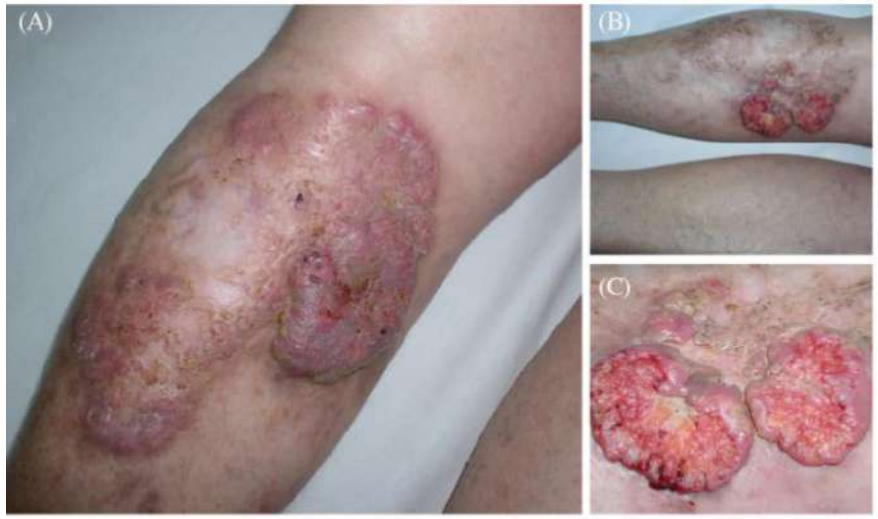


FIGURE 1 A, A large plaque with an elevated polycyclic margin and verrucoid surface with tiny ulcerations, on the patient's right shin. B and C, Ulcerated plaques with verrucoid progressive border and central clearing

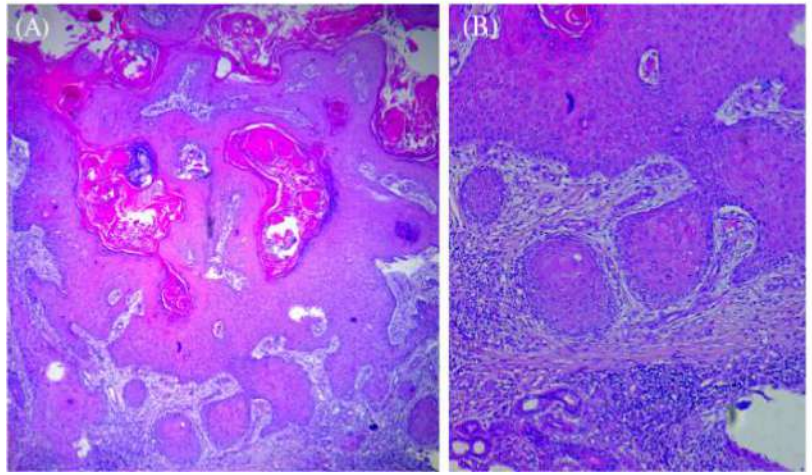
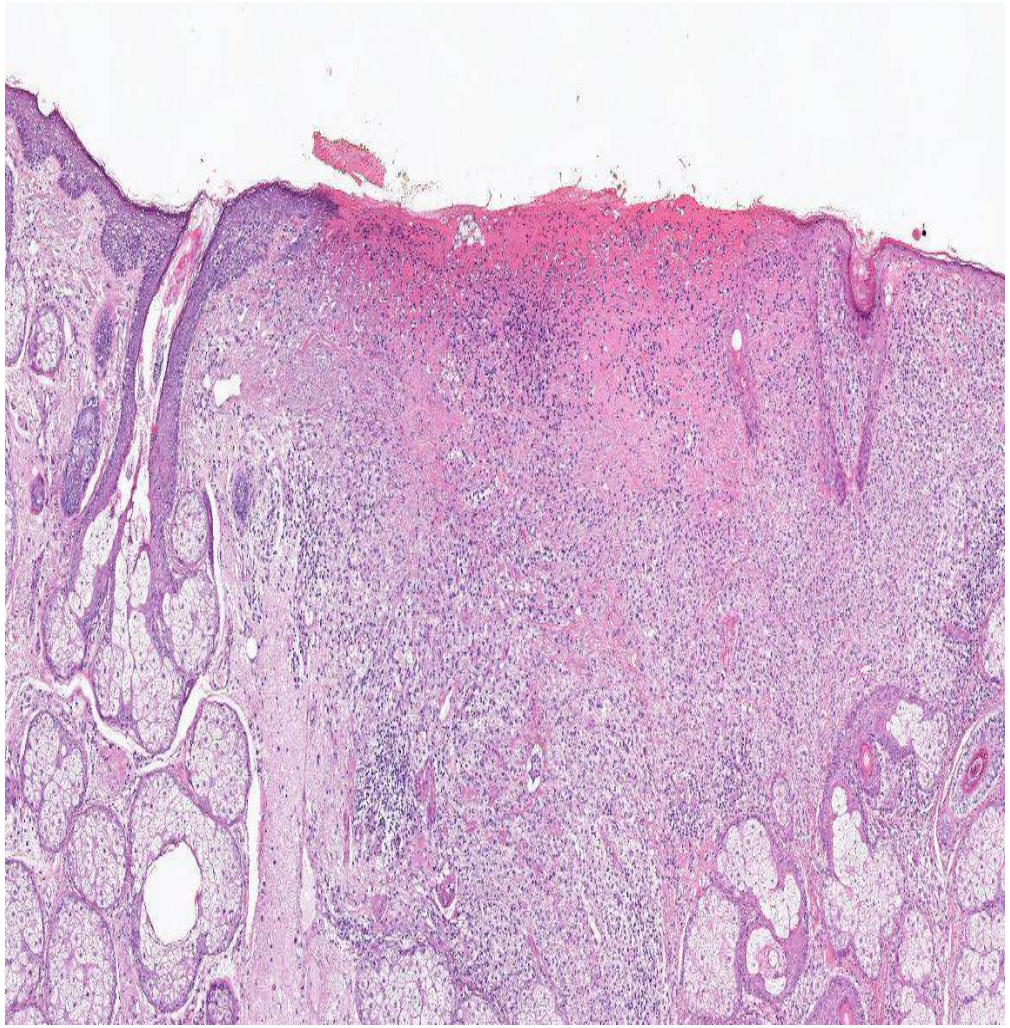


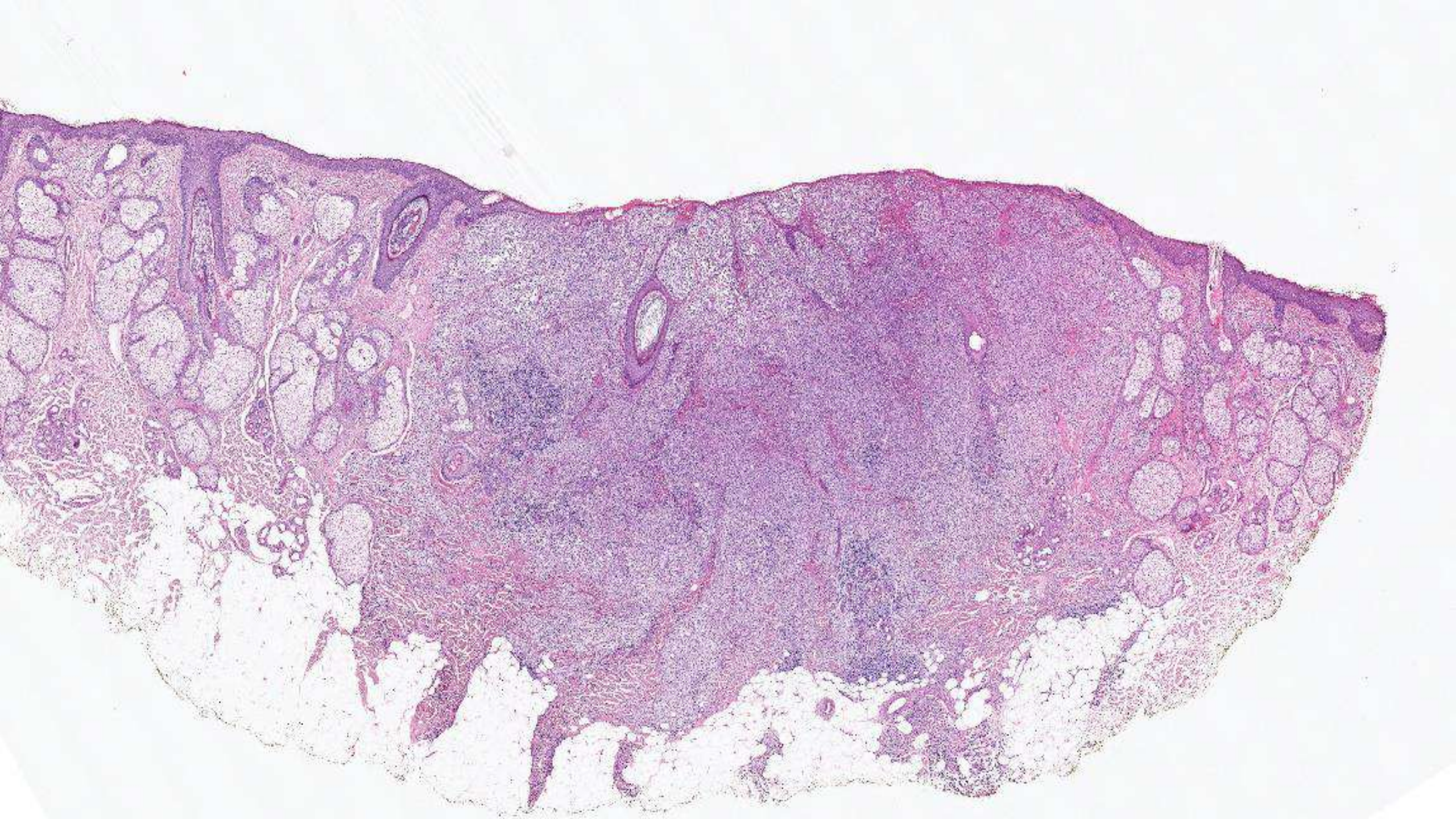
FIGURE 2 A, Epidermal invagination with lip-like shoulder and central keratin plug with pseudoepitheliomatous hyperplasia and a dense a mixed chronic inflammatory cell infiltrate in the dermis (H&E ×40). B, Pseudoepitheliomatous hyperplasia with underlying islands of glassy, eosinophilic keratinocytes with squamous pearls and minimal atypia in the dermal component (H&E ×100)

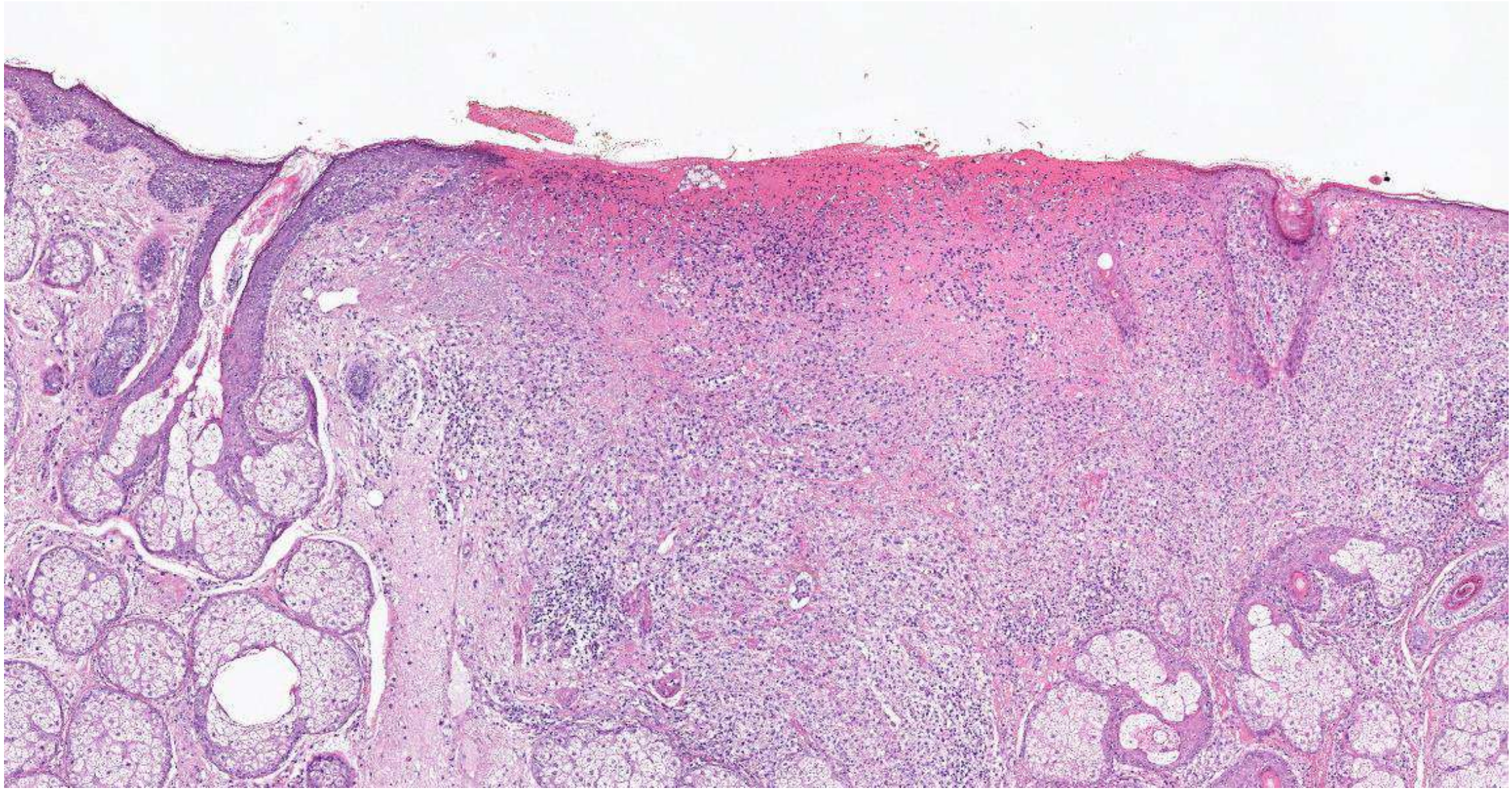
Gavric G et al. Keratoacanthoma centrifugum marginatum associated with mechanical trauma: Response to acitretin-A case report and review of the literature. Dermatol Ther. 2020 May;33(3):e13397.

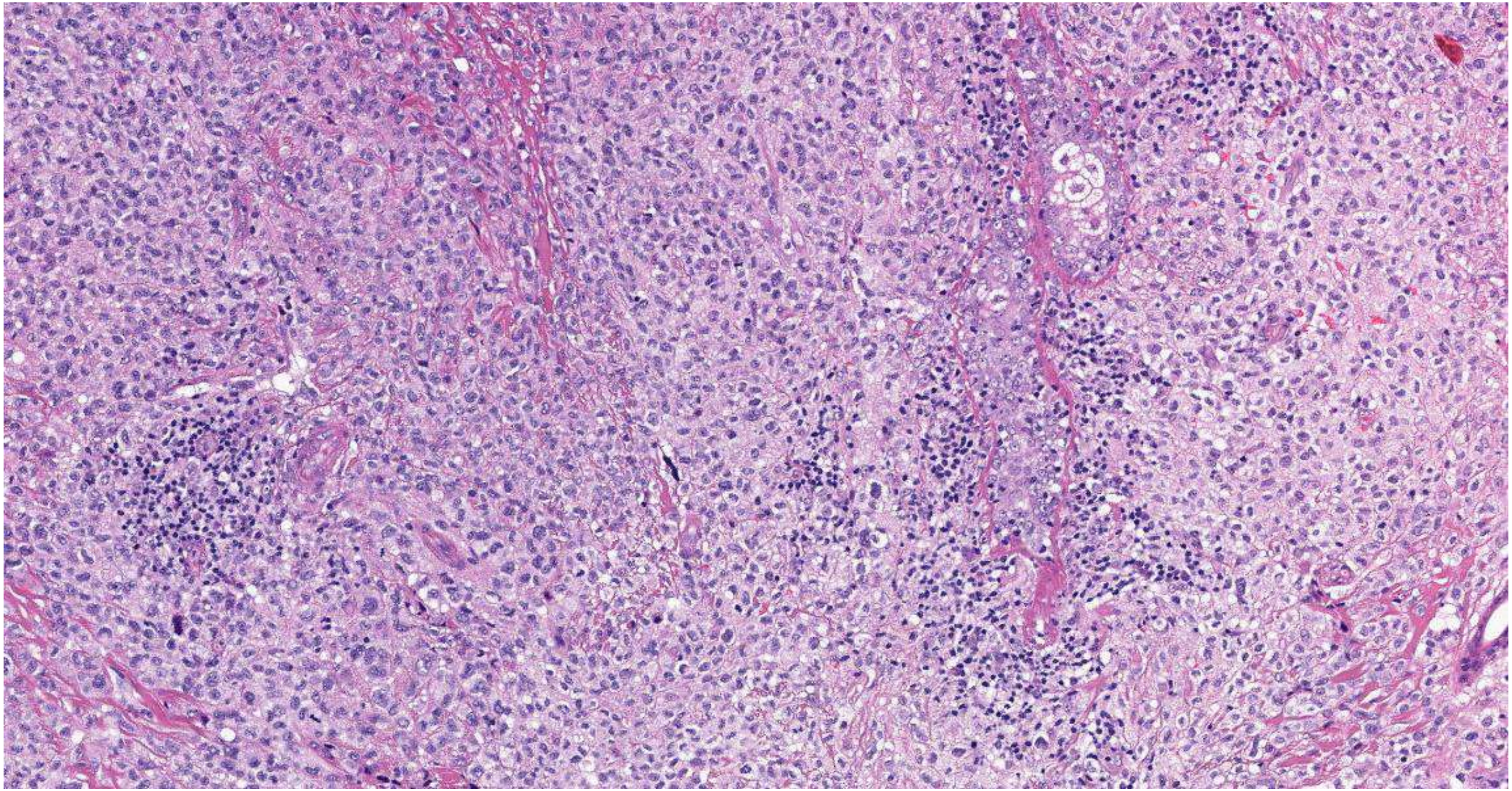
Case 16

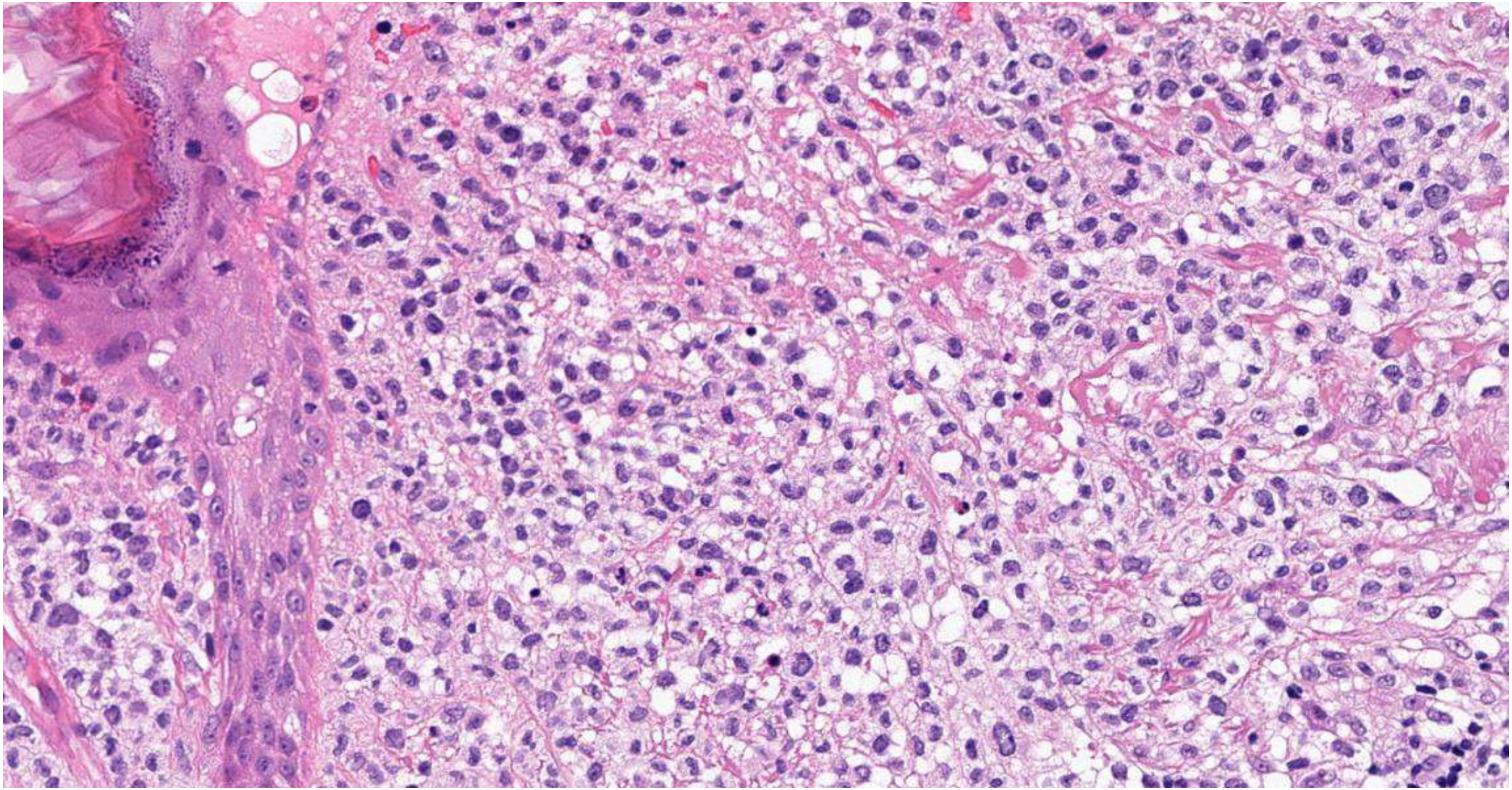
Male, 74 years old
8mm lesion with poorly defined margins, with cream and beige appearance located
Forehead

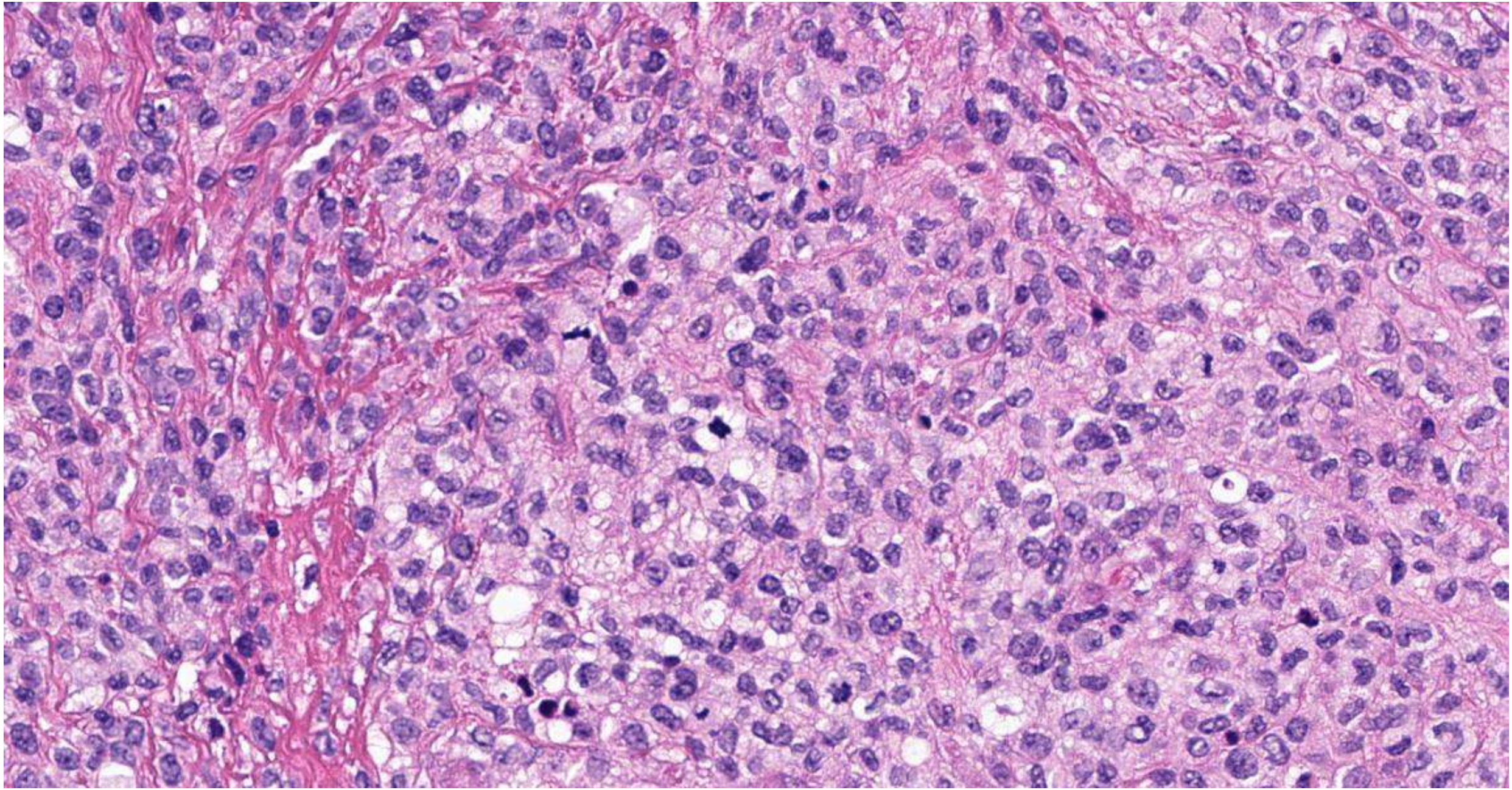












Negative:

HMB-45

Melan-A

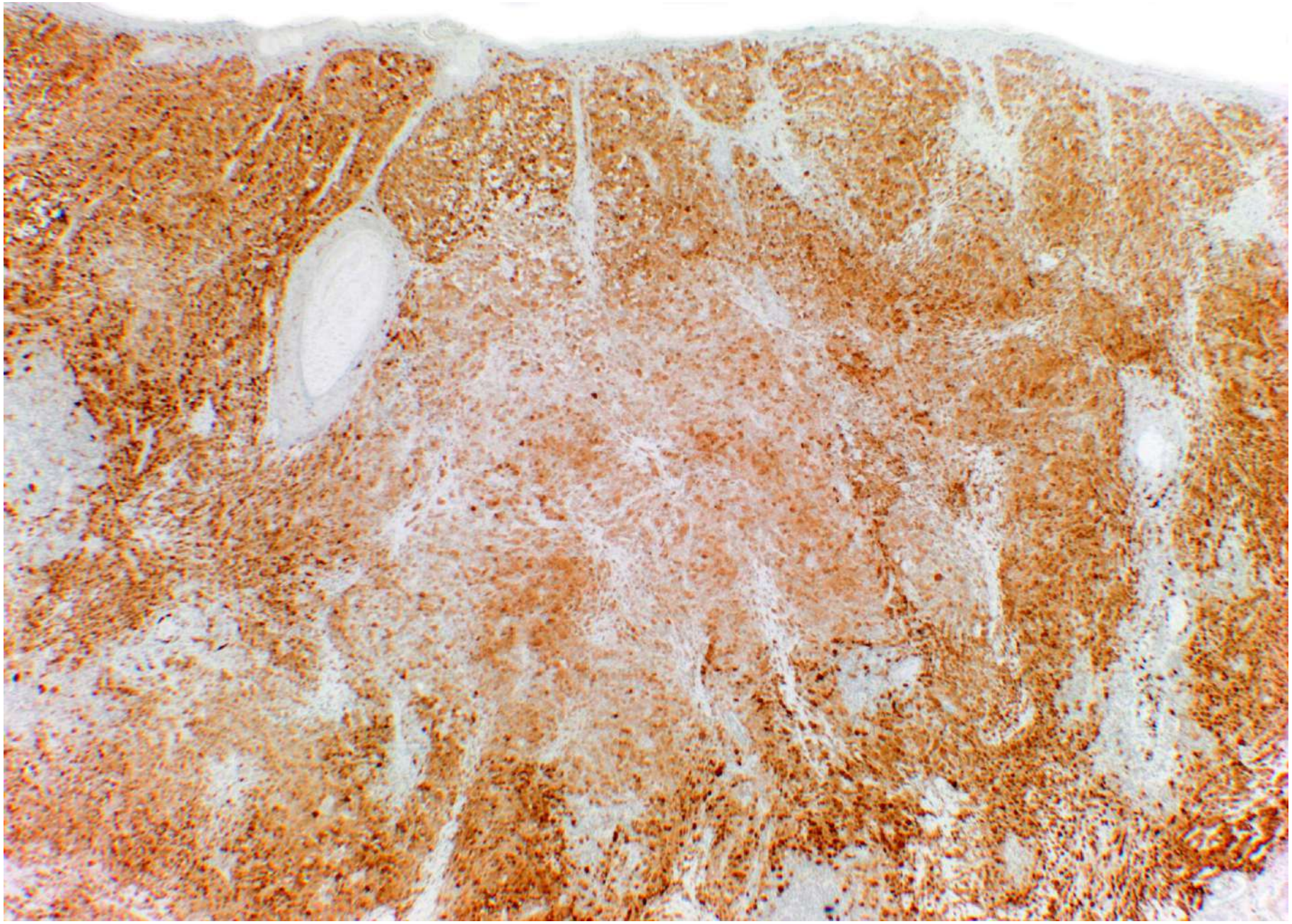
AE1/AE3

CD45

CD30

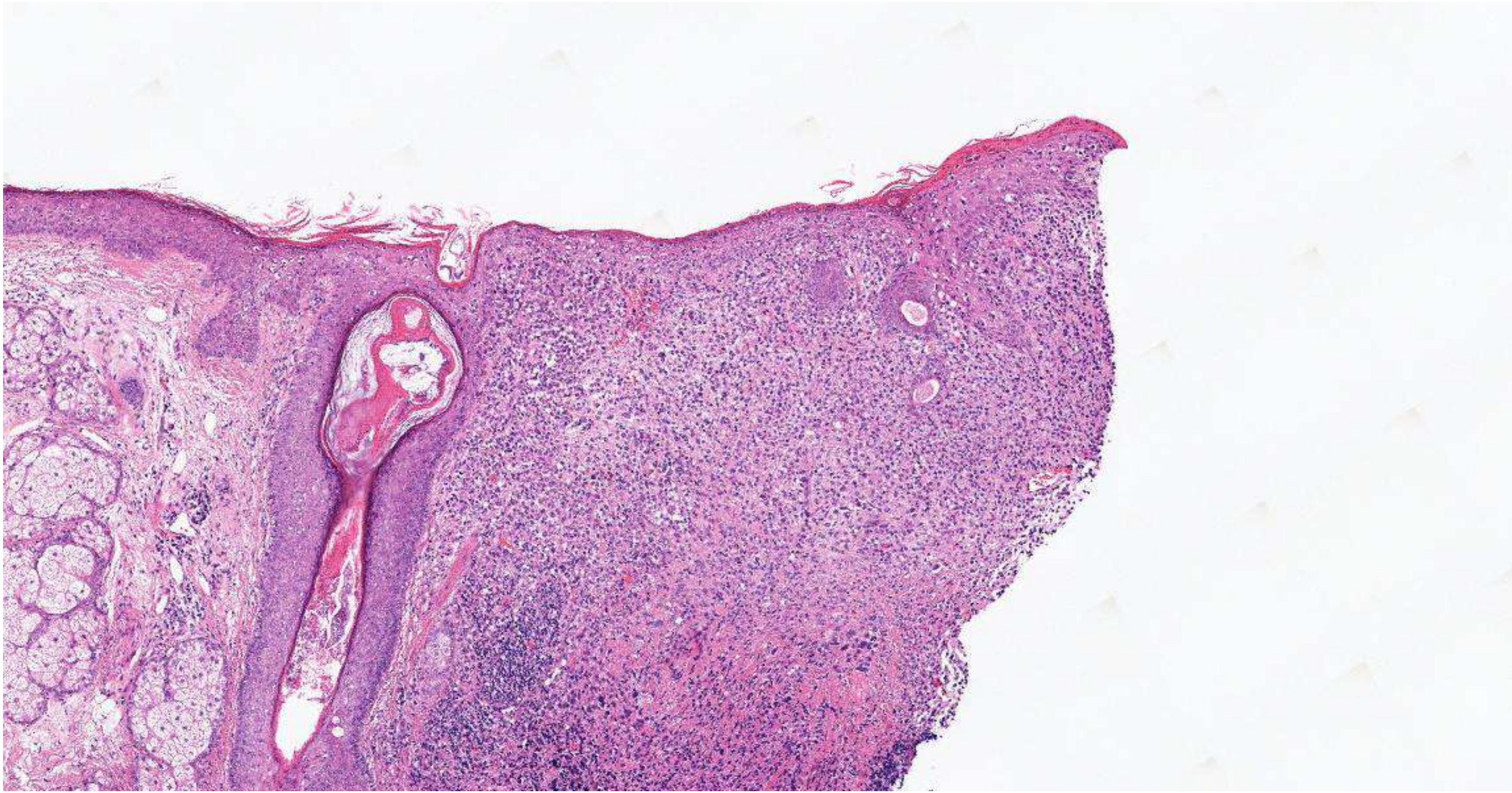
SOX-10 not performed

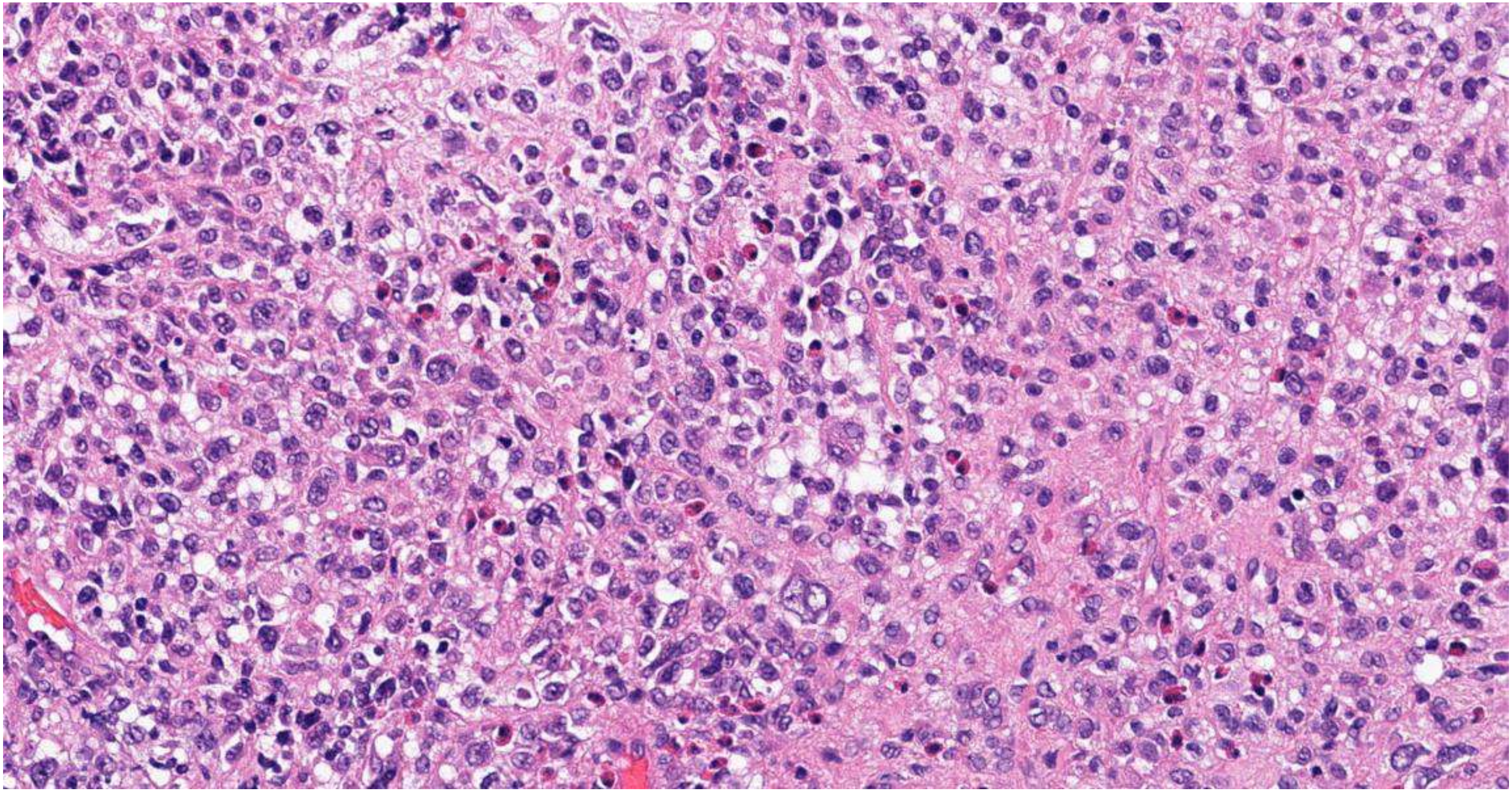
S100

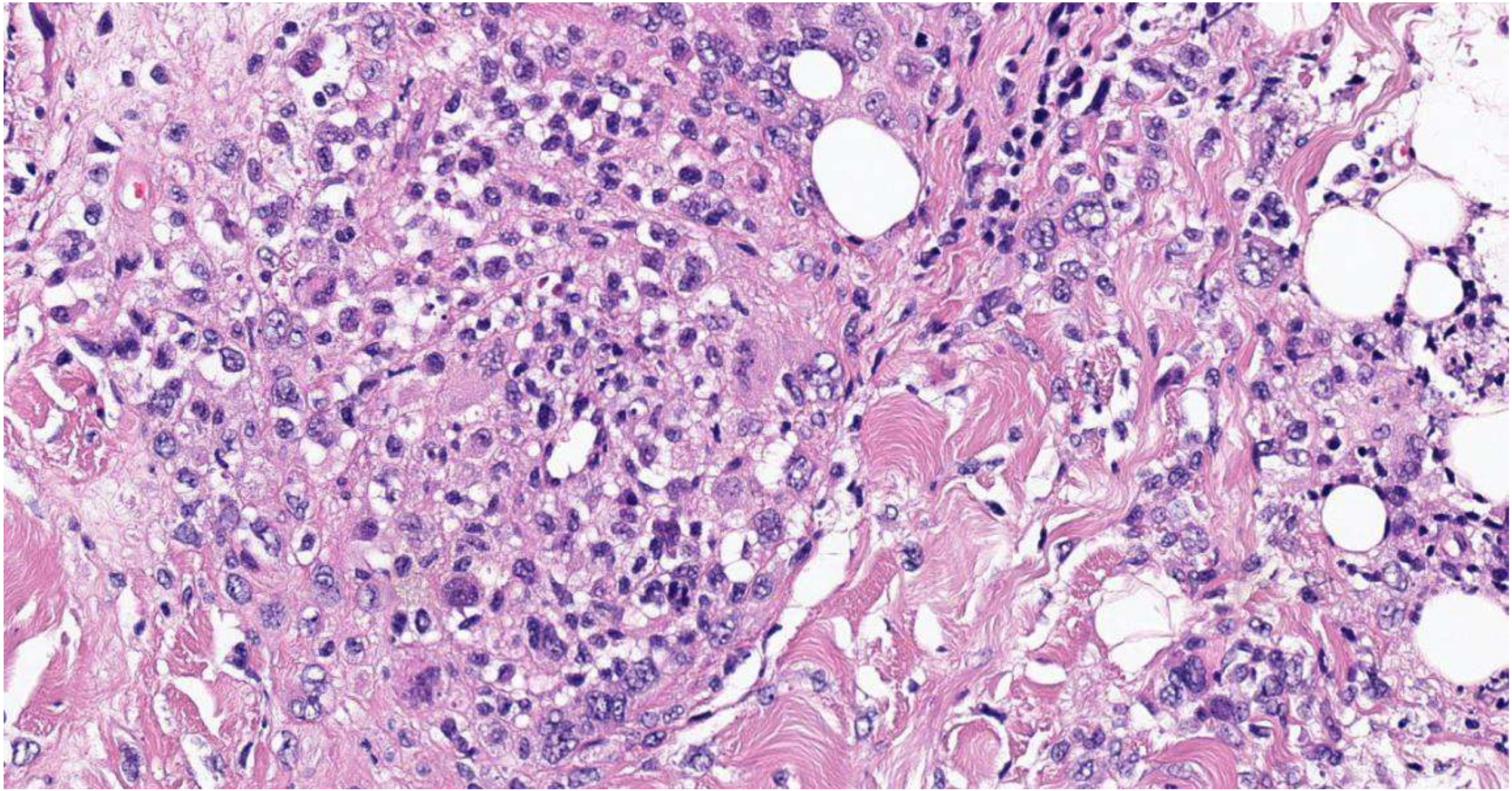


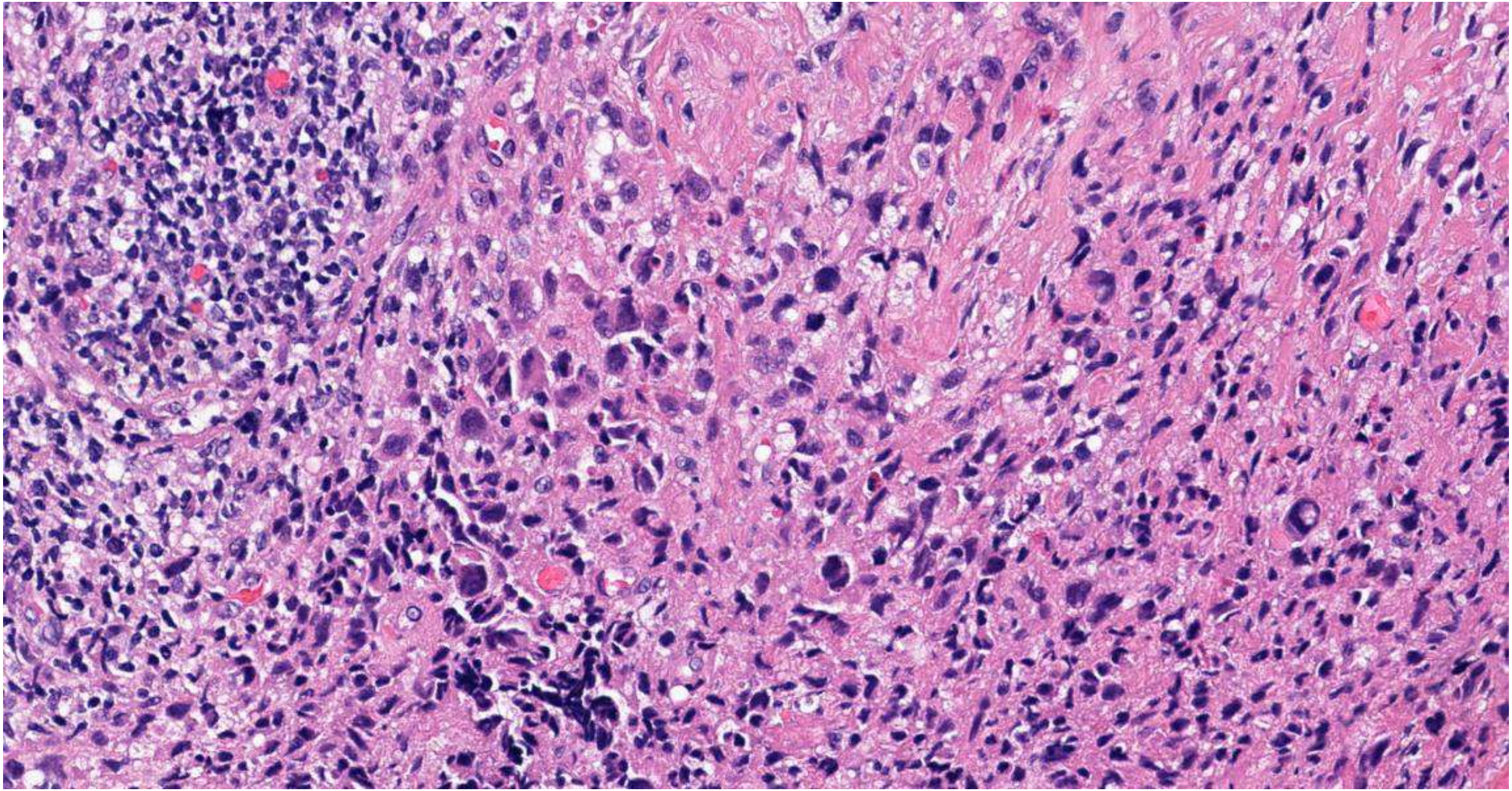
Primary diagnosis

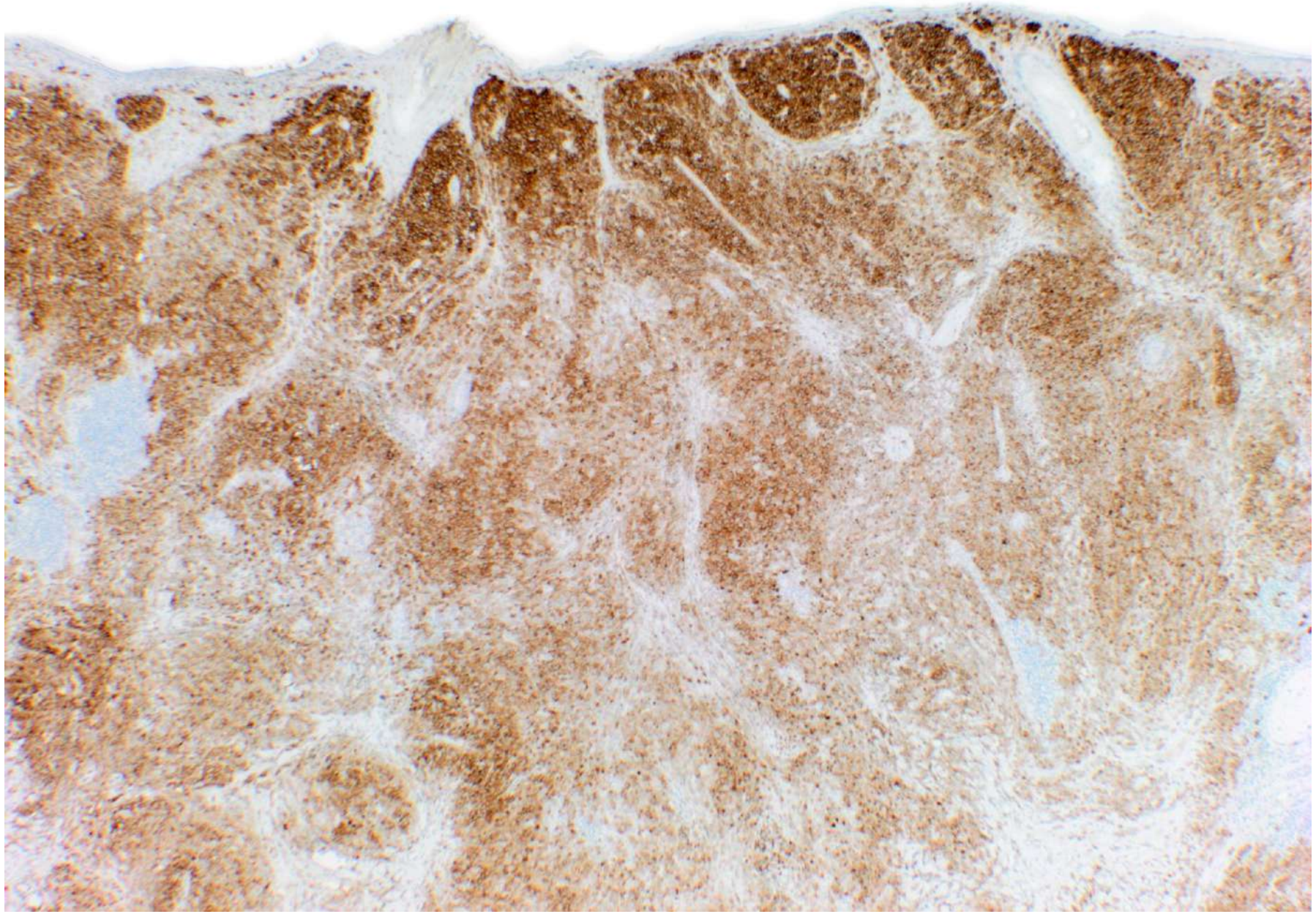
- **Cutaneous malignant melanoma**
  - **Breslow 3.1 mm**
  - **Clark level: V**
  - **Ulcerated**
  - **Mitotic index 9 per mm^2**
- **No mutation detected in *BRAF* nor *NRAS***
- One year after presents with a light brown depressed lesion at a scar of previous excision
- Punch biopsy was performed



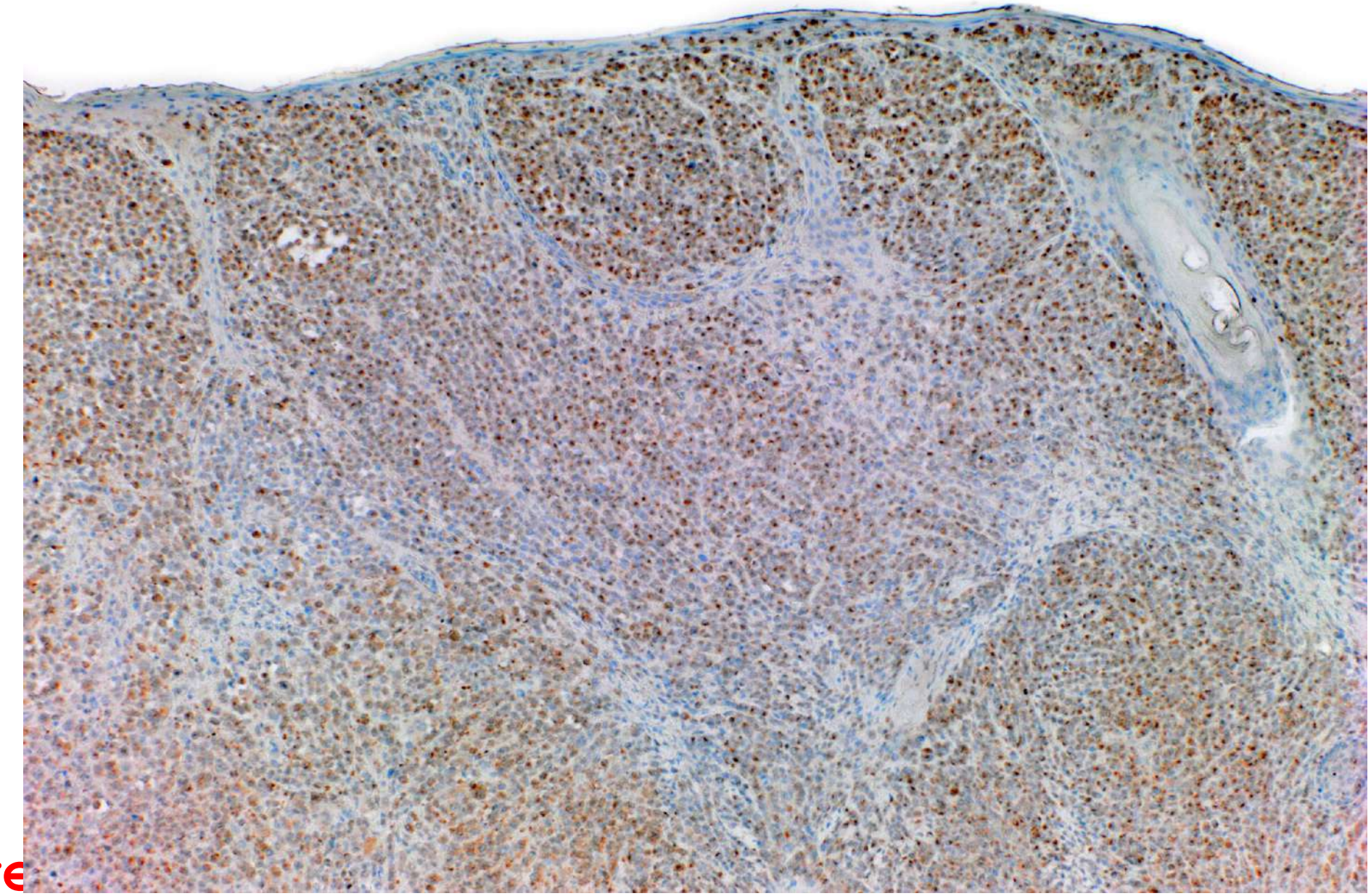




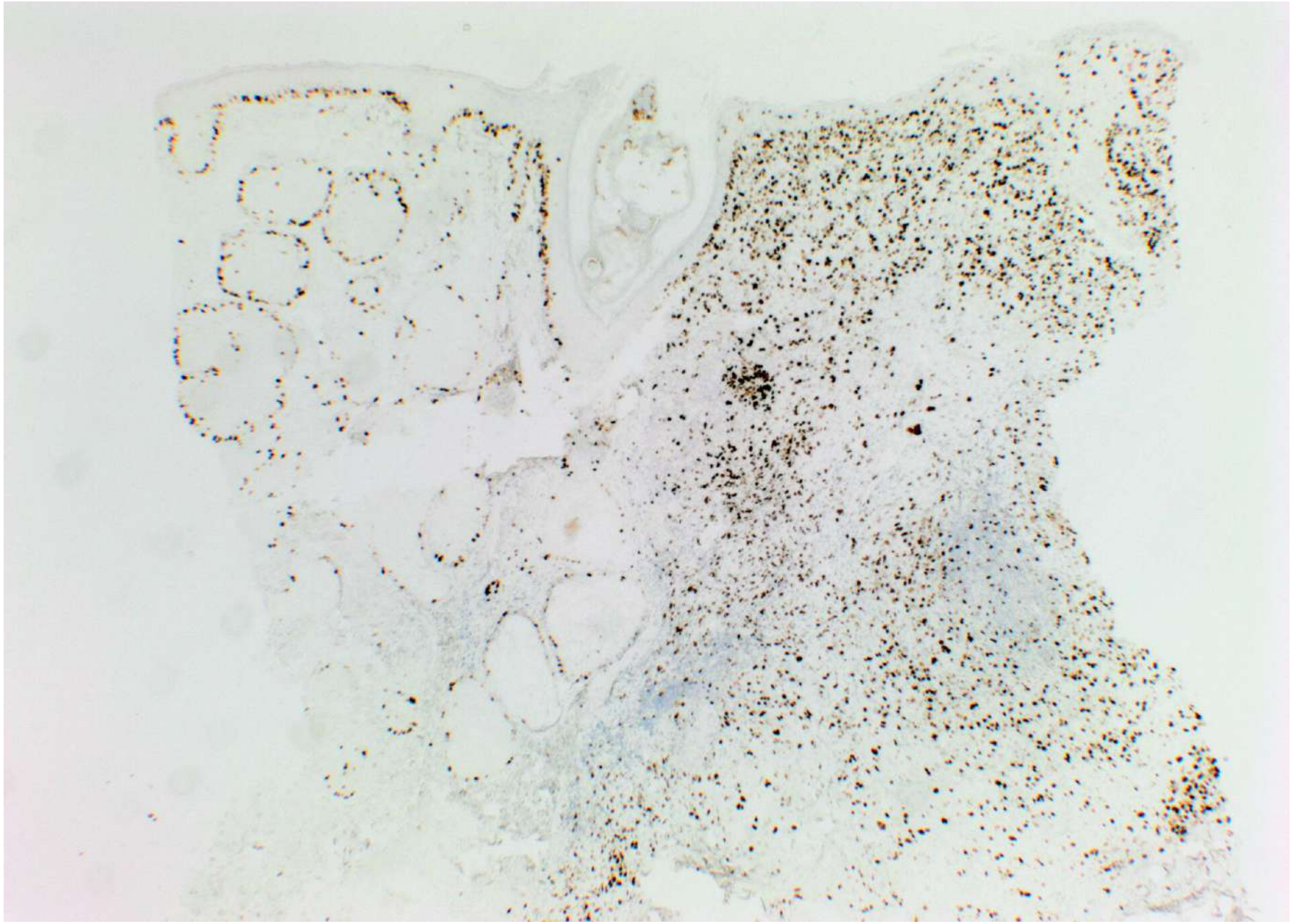




CD1a



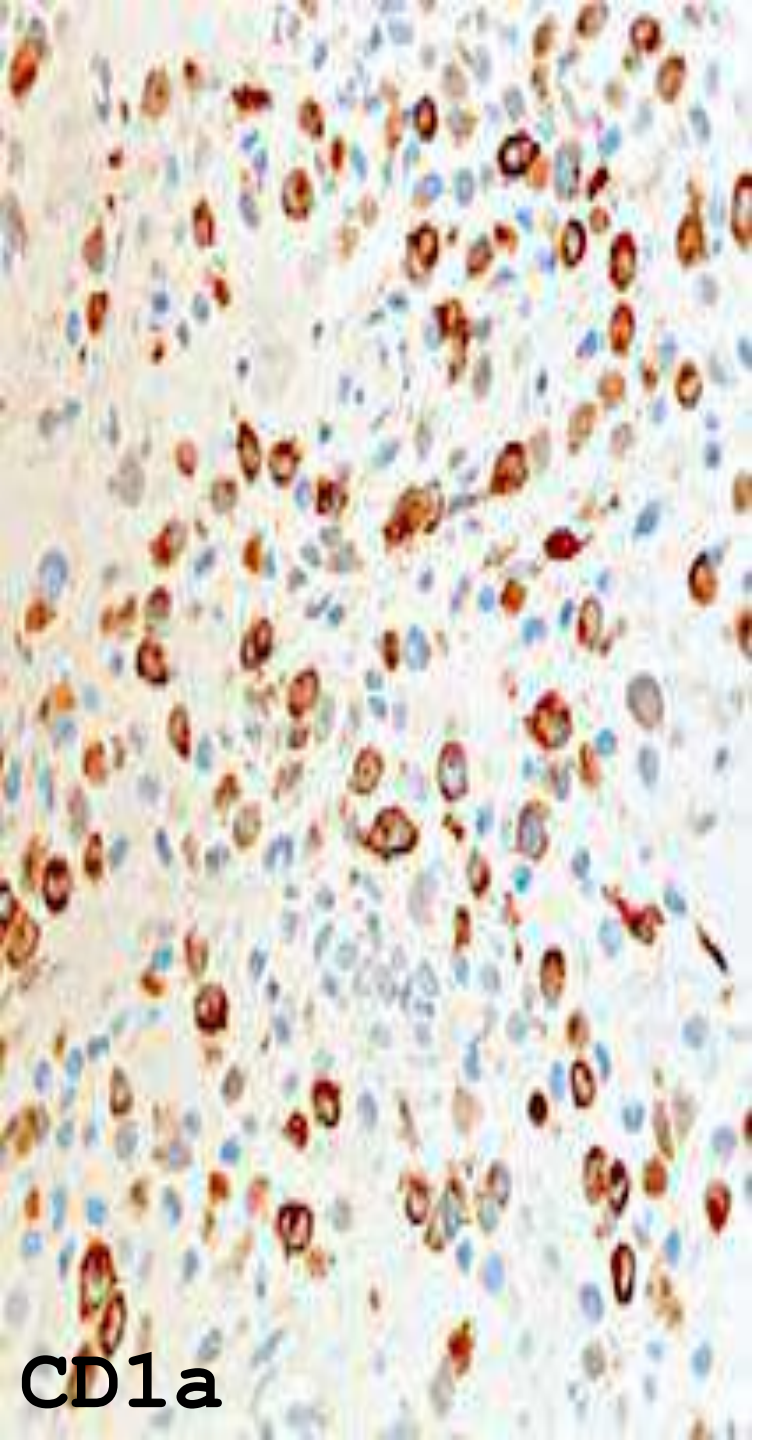
CD207/lange
in

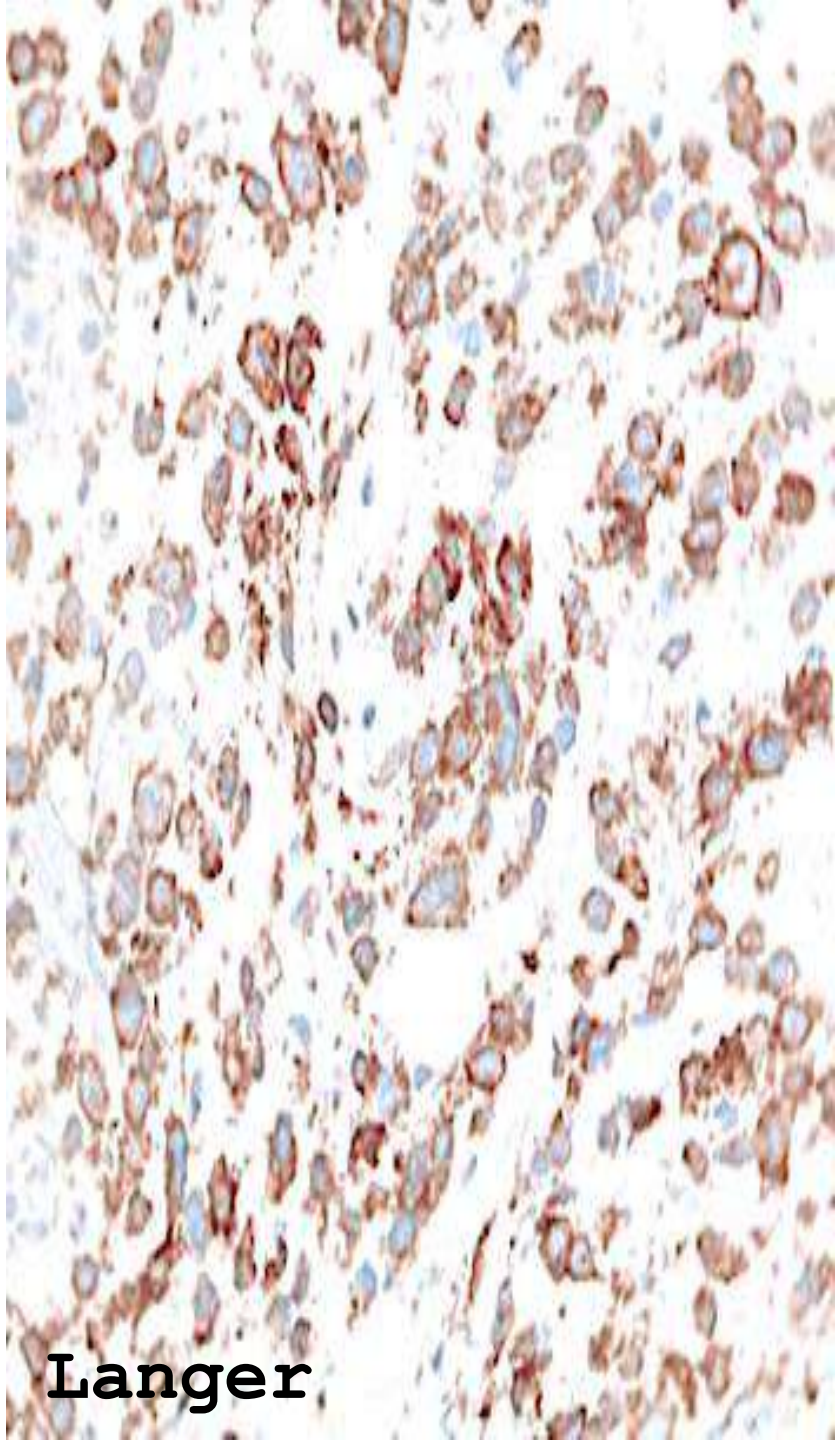


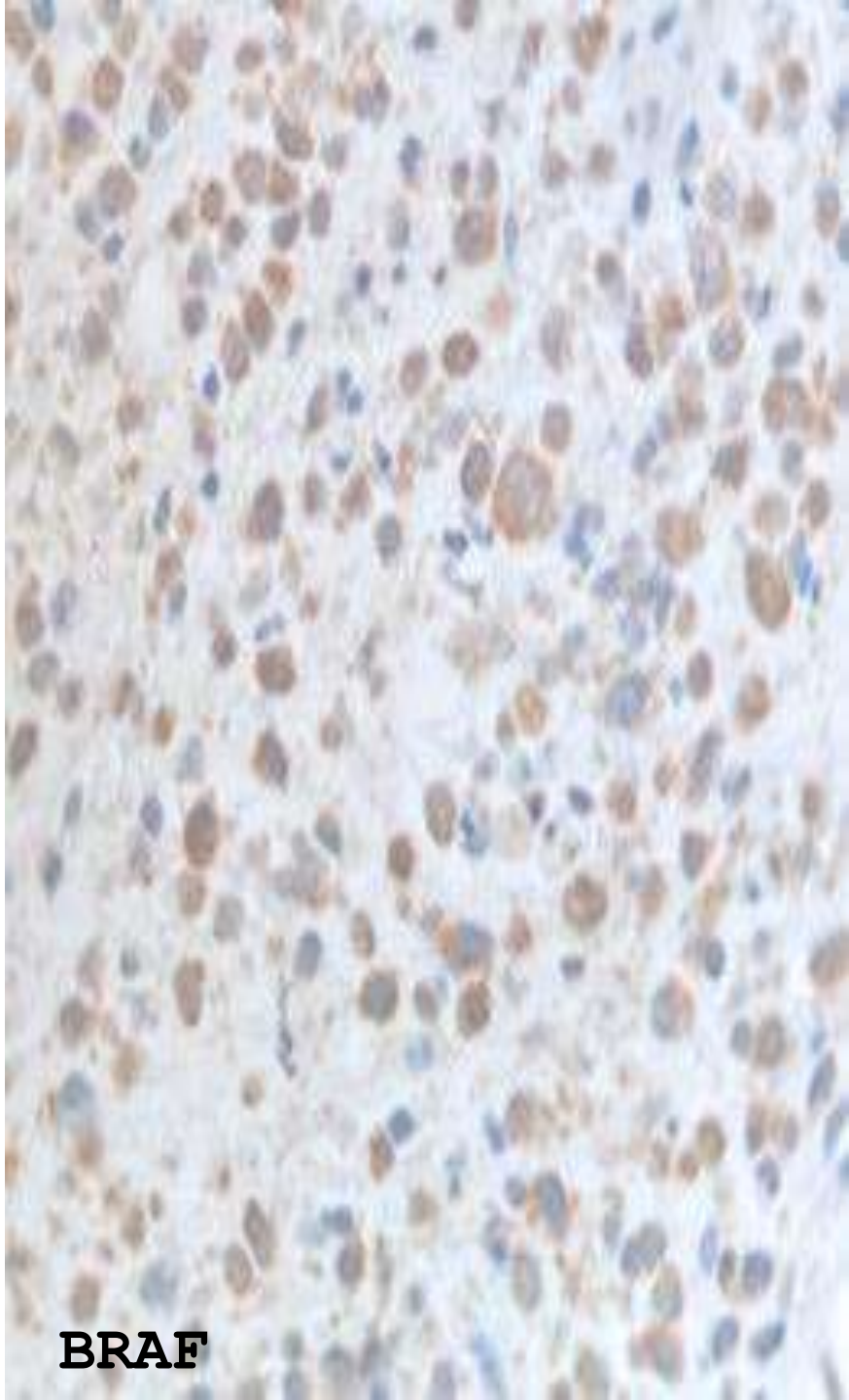
KI-67

Diagnosis

Langerhans cell sarcoma

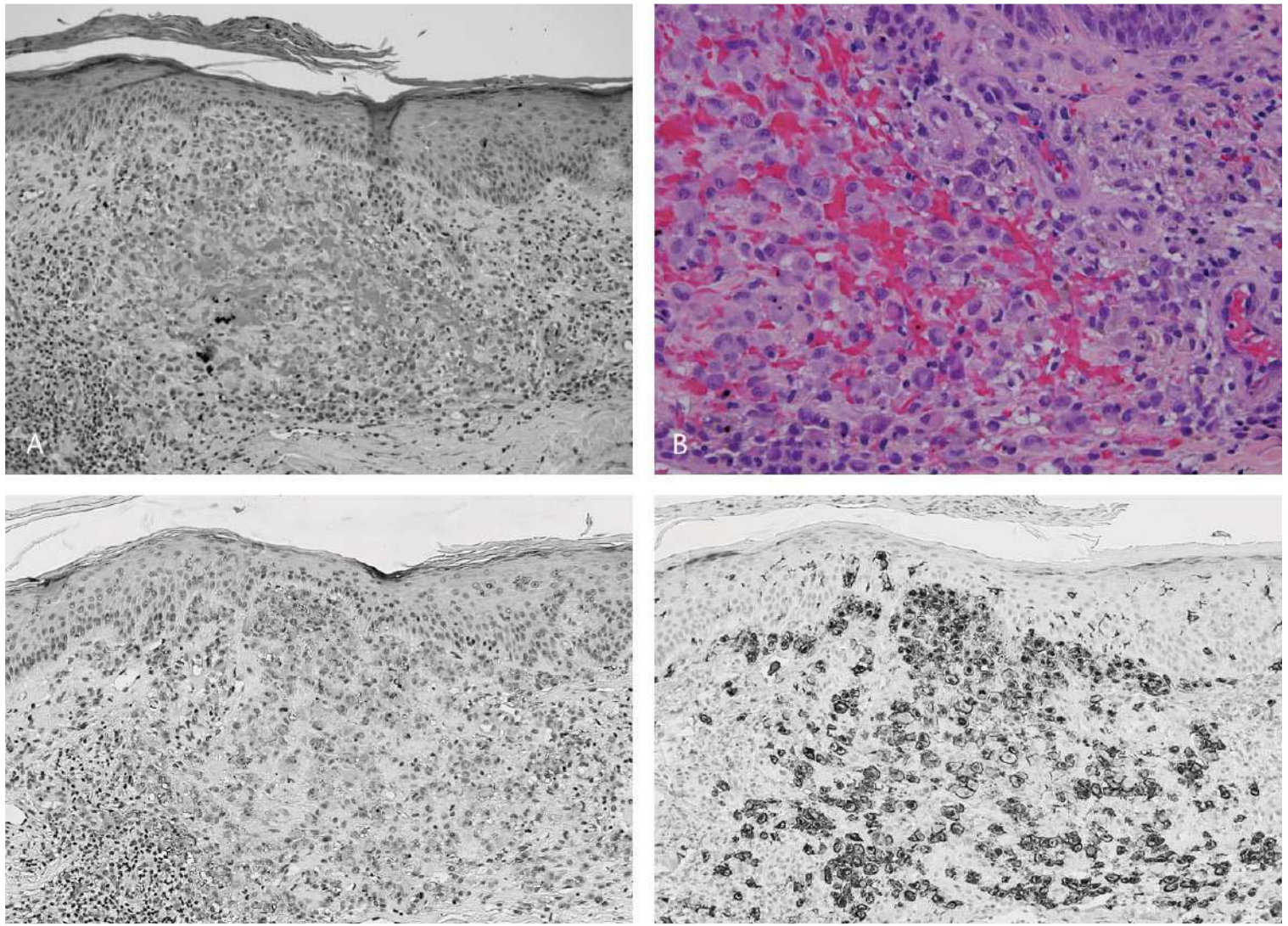

CD1a


Langer


BRAF

Langerhans Cell Histiocytosis Mimicking Malignant Melanoma: A Diagnostic Pitfall

Tomomi L. Billings, MD, Ronald Barr, MD,‡ and Senait Dyson, MD*†*



Am J Dermatopathol. 2008 Oct;30(5):497-9.

Langerhans Cell histiocytosis with malignant features

- Langerhans cell sarcoma
- Primary or secondary to LCH
- Rare disease (incidence of 0.02 per 1 million)
- Mean age at presentation is 50 years
- Male: female ratio (1.3:1)
- Multi-organ disease (45%)
- Skin is the commonest primary site (42.4%) Cancer Treat Rev. 2015 Apr;41(4):320
- Also lung, bone and soft tissue
- Isolated lymph node involvement 20%

Pathogenesis

CDKN2A deletion (50%).

Deletion and mutation *MAP2K1* and *NRAS* associated with aggressive behaviour Am J Surg Pathol. 2018 Feb;42(2):150-159.

TP53 (40%)

DNA damage by UV Pathol Int. 2020 Nov;70(11):881-887

***KRAS* (40%).**

***BRAF V600E* (10%).**

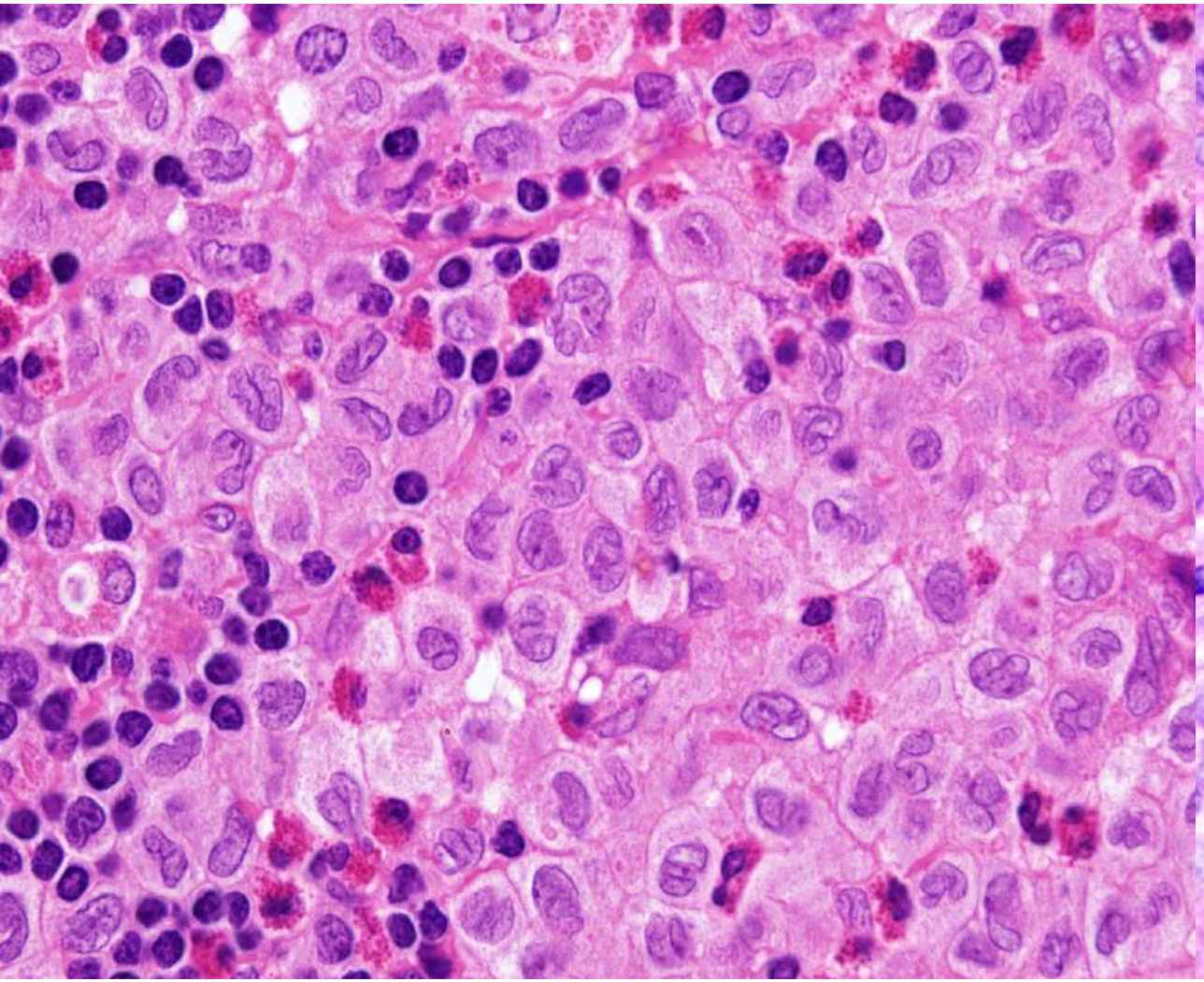
PTEN (30%).

LCH

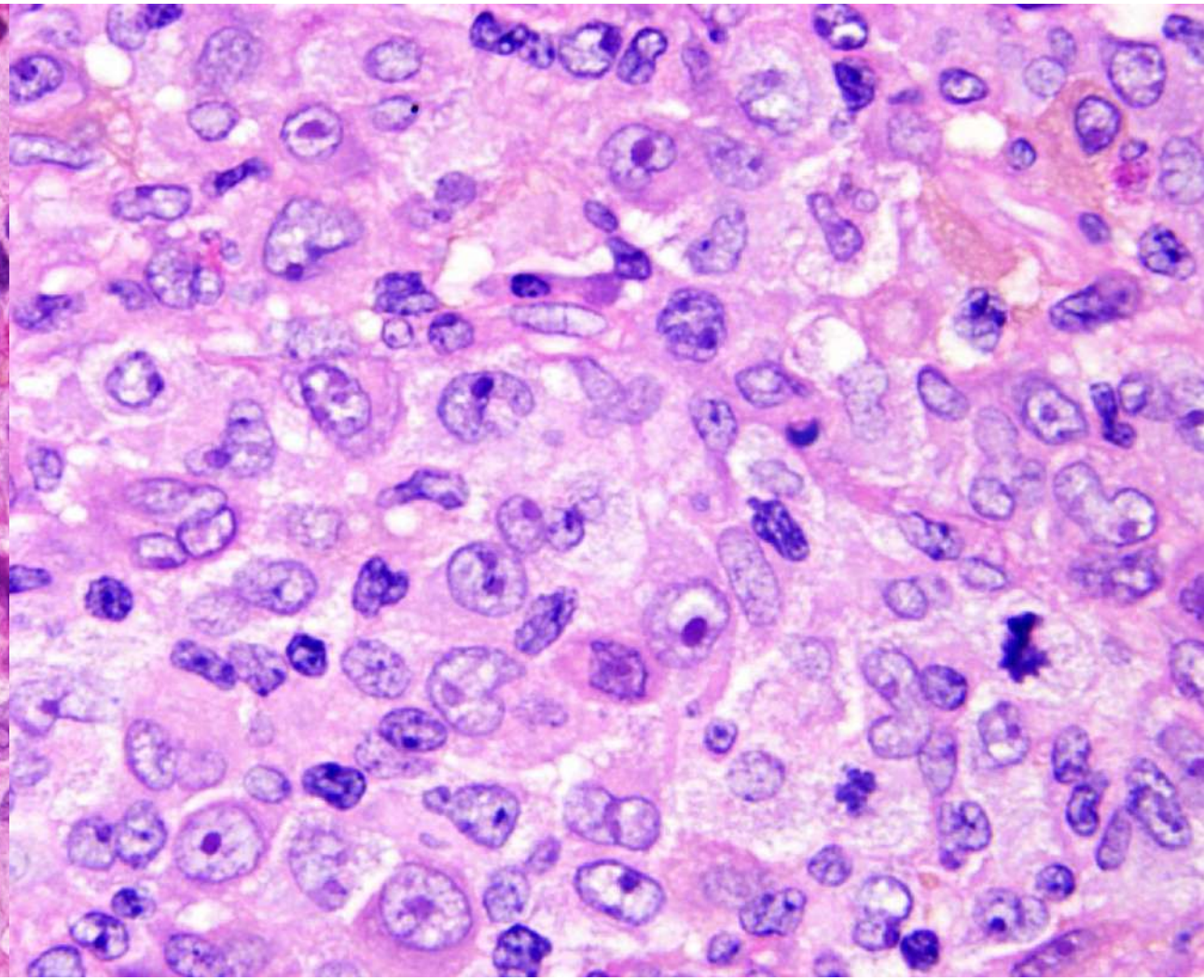
MAPK pathway mutated in 95%

- *BRAF p.V600E* (39-70%).
- *MAP2K1* (46% *BRAF* negative) Hum Pathol. 2016 Jun;52:61-7.

Oncologist. 2021 Jul;26(7):e1263-e1272.



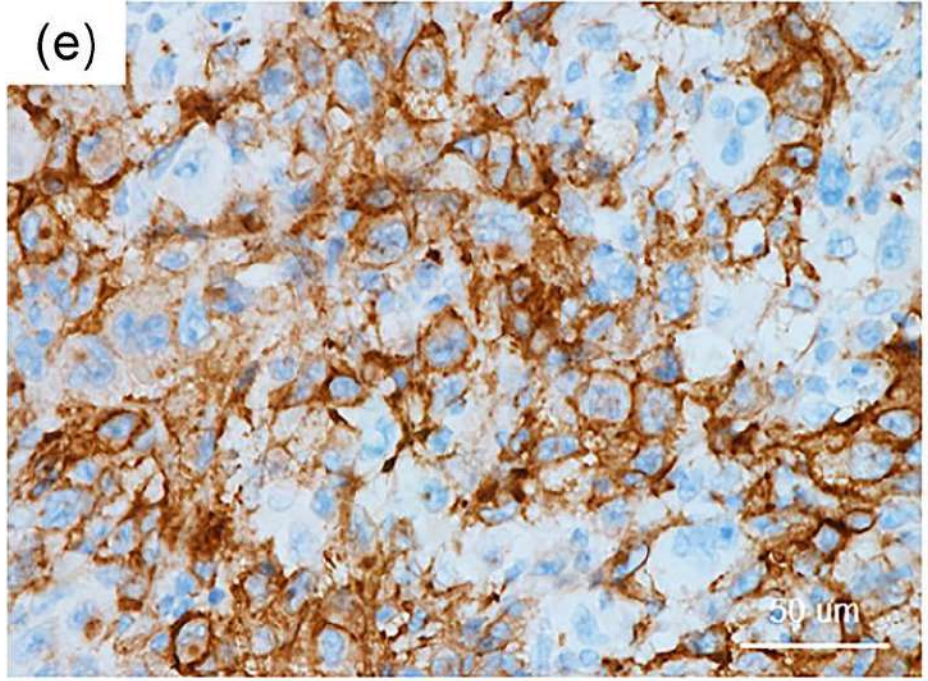
Langerhans cell histiocytosis

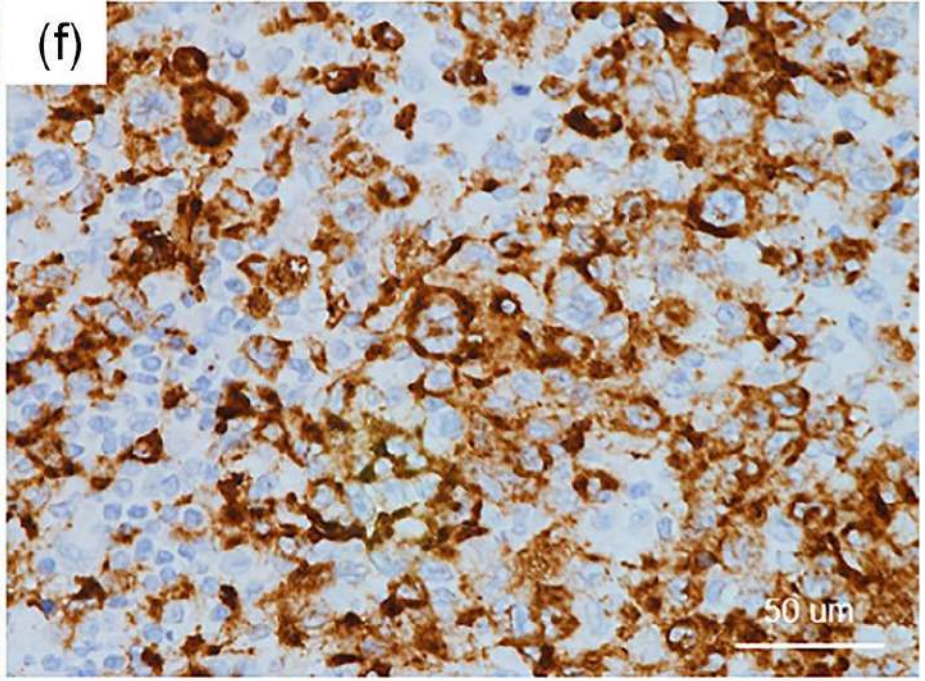


Langerhans cell sarcoma

IARC

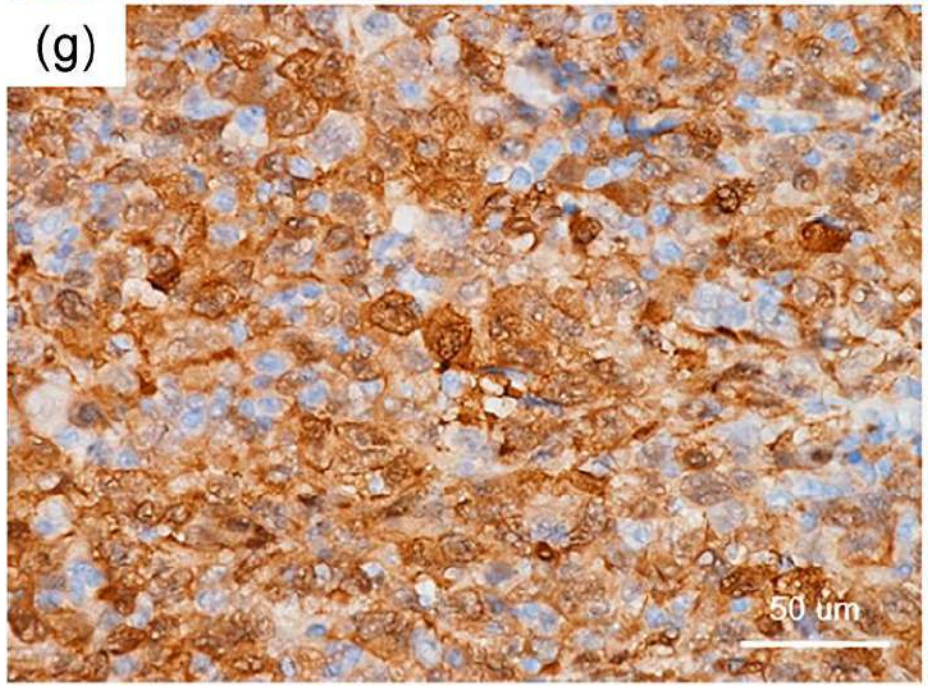
CD1a

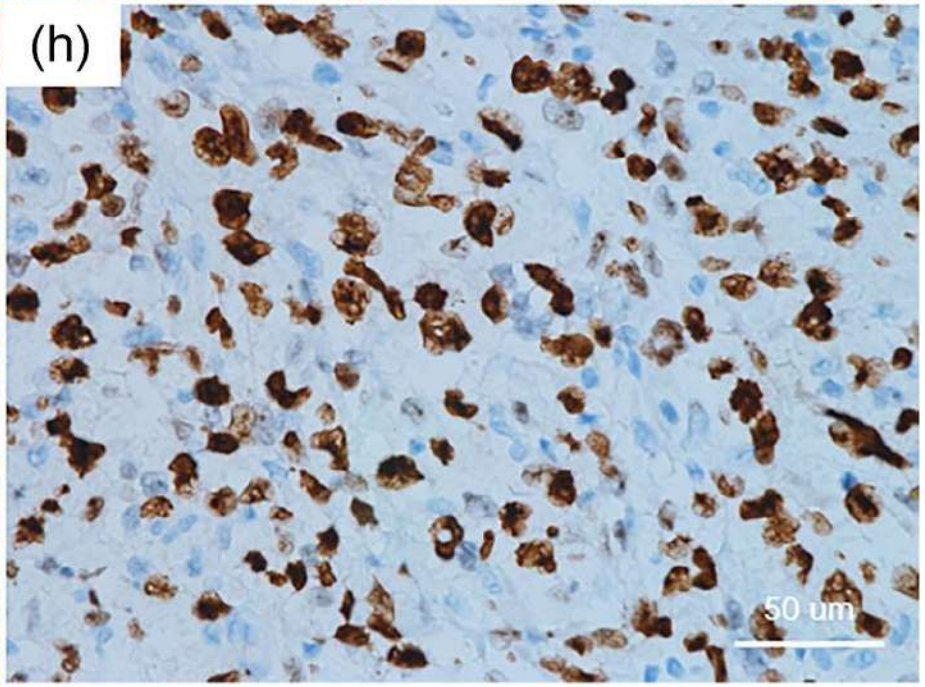




CD207/ langerin

S100





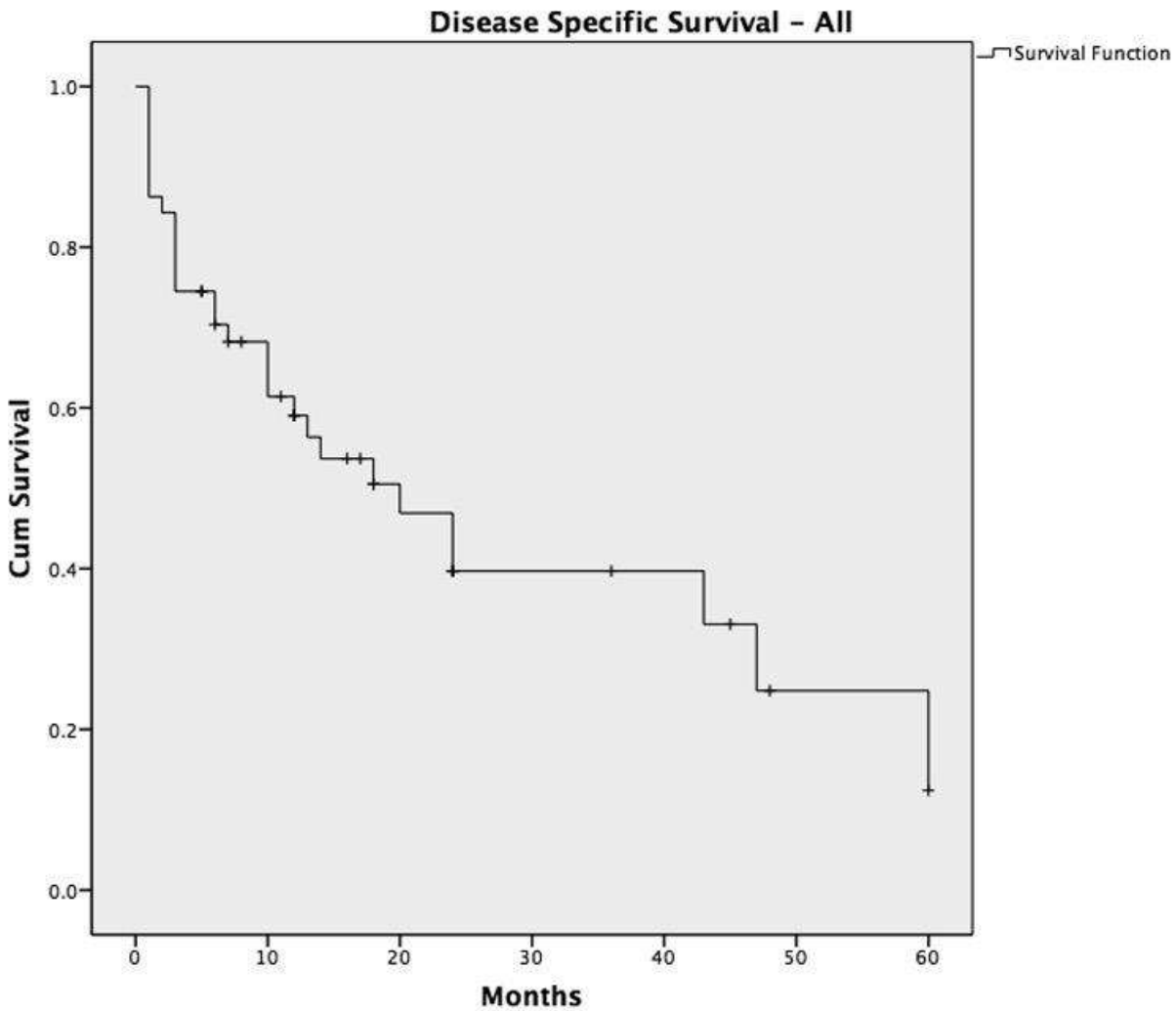
KI-67 >10%

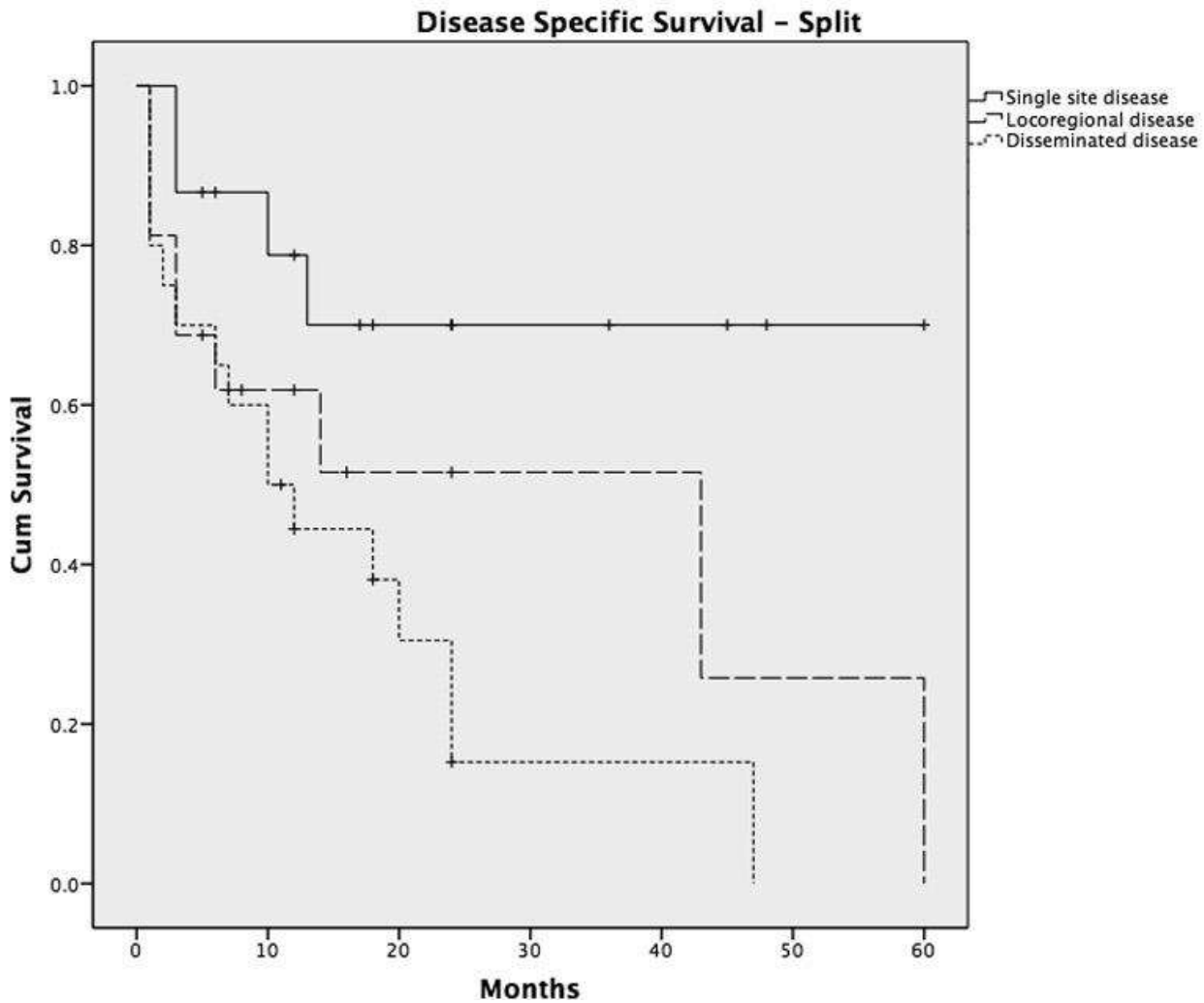
Pathol Int. 2020 Nov;70(11):881-887.

Tumour Review

Langerhans cell sarcoma: A systematic review

James E.F. Howard [a,*,1], Raghav C. Dwivedi [a,1], Liam Masterson [a,b,1], Piyush Jani [a]

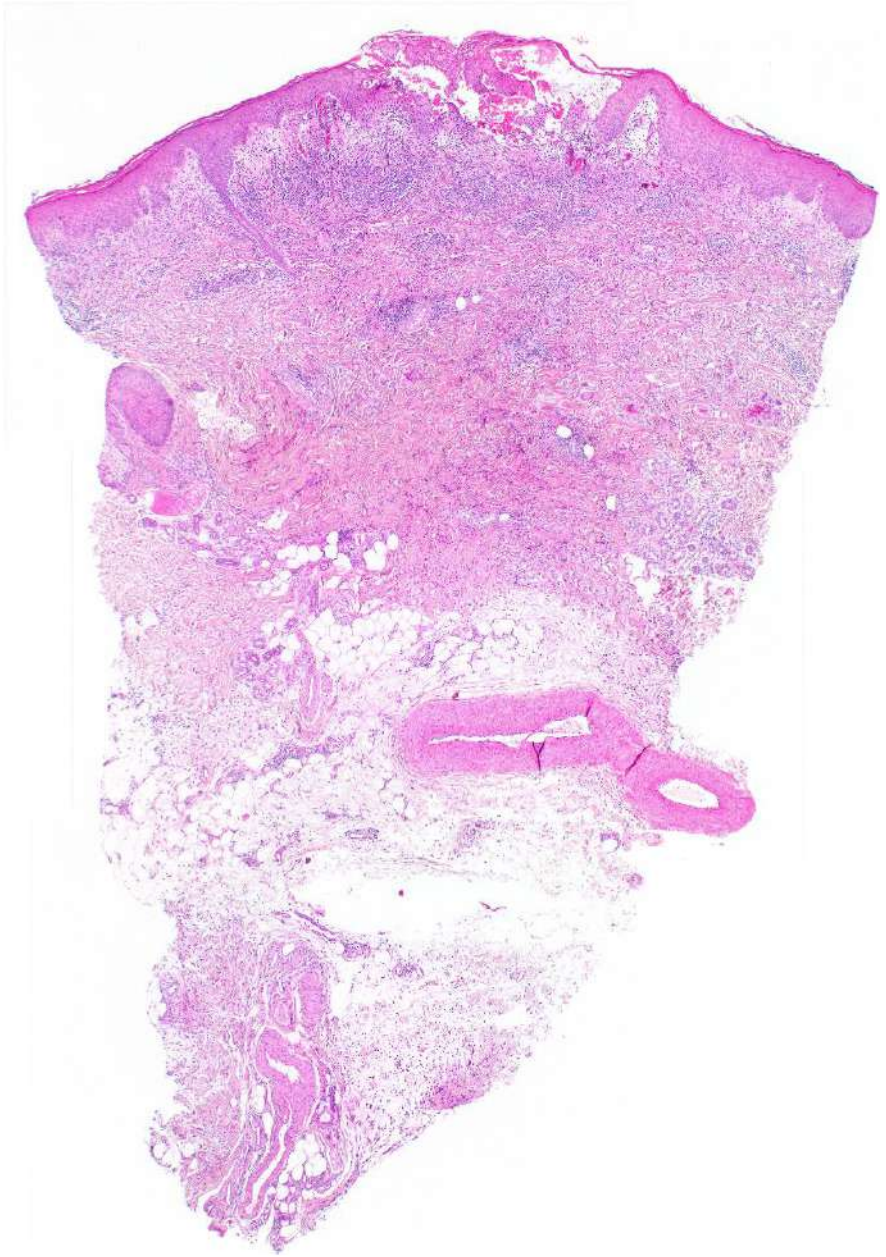


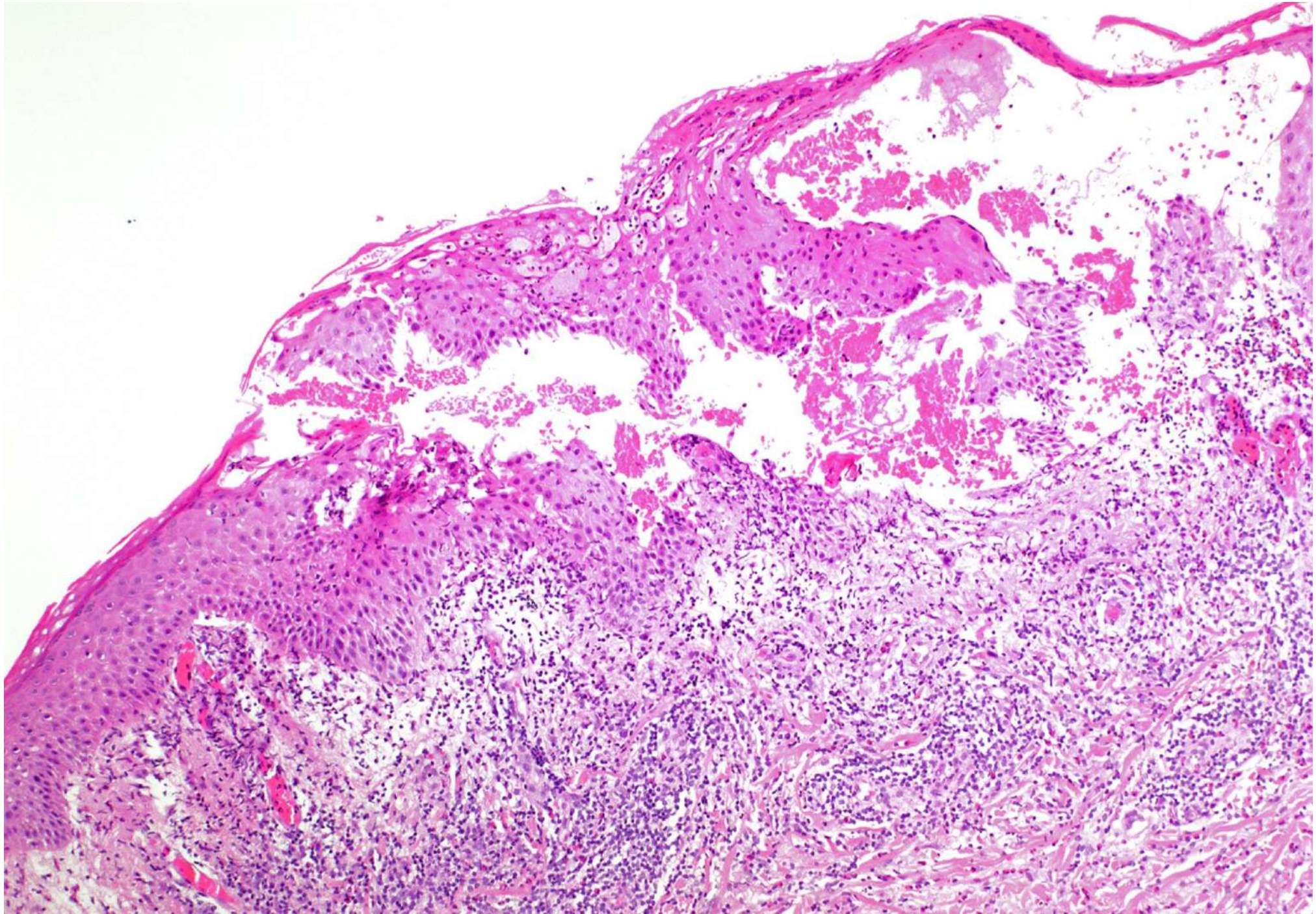


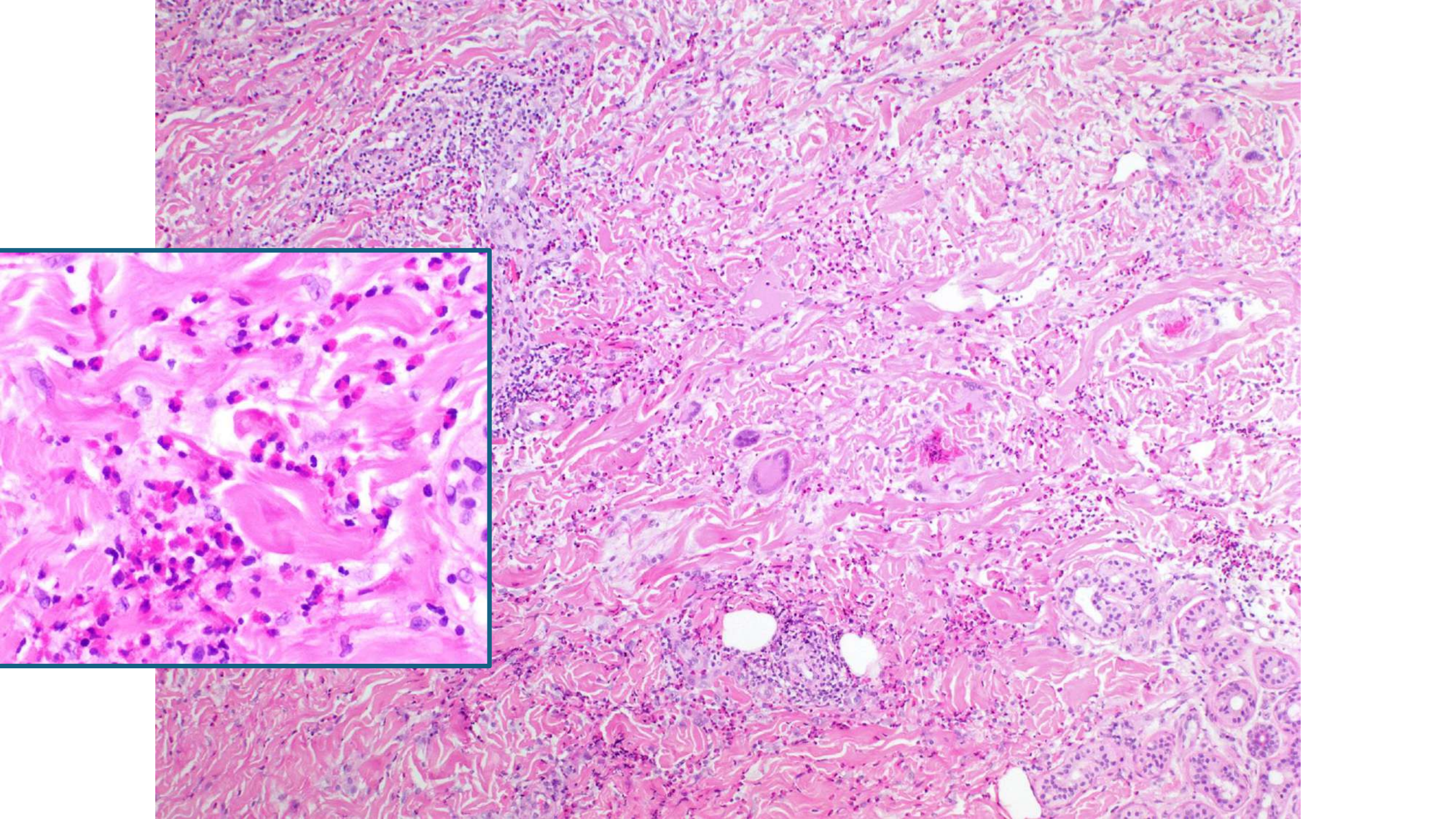
Cancer Treat Rev. 2015 Apr;41(4):320-31.

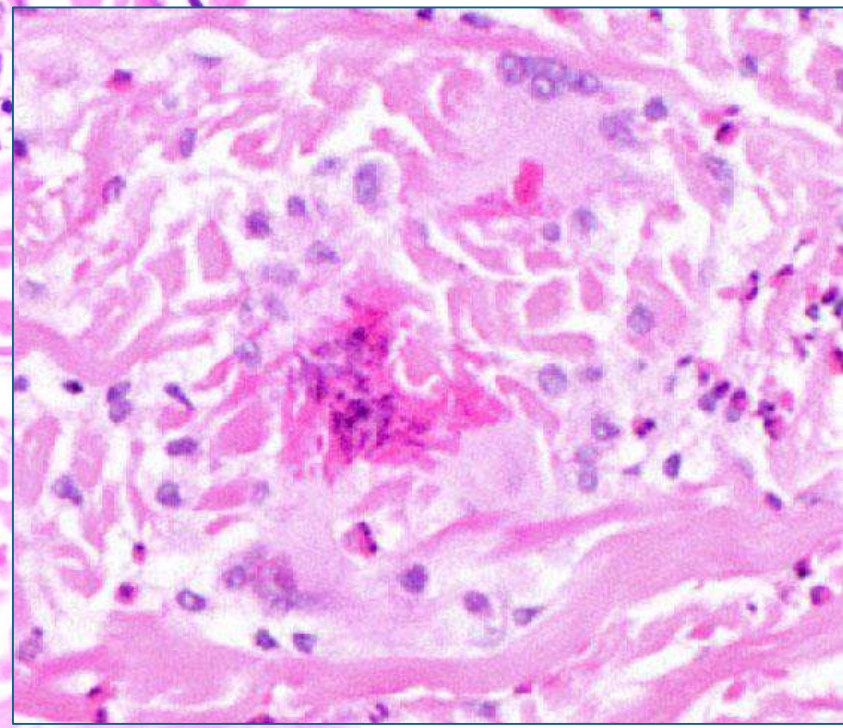
Case 17

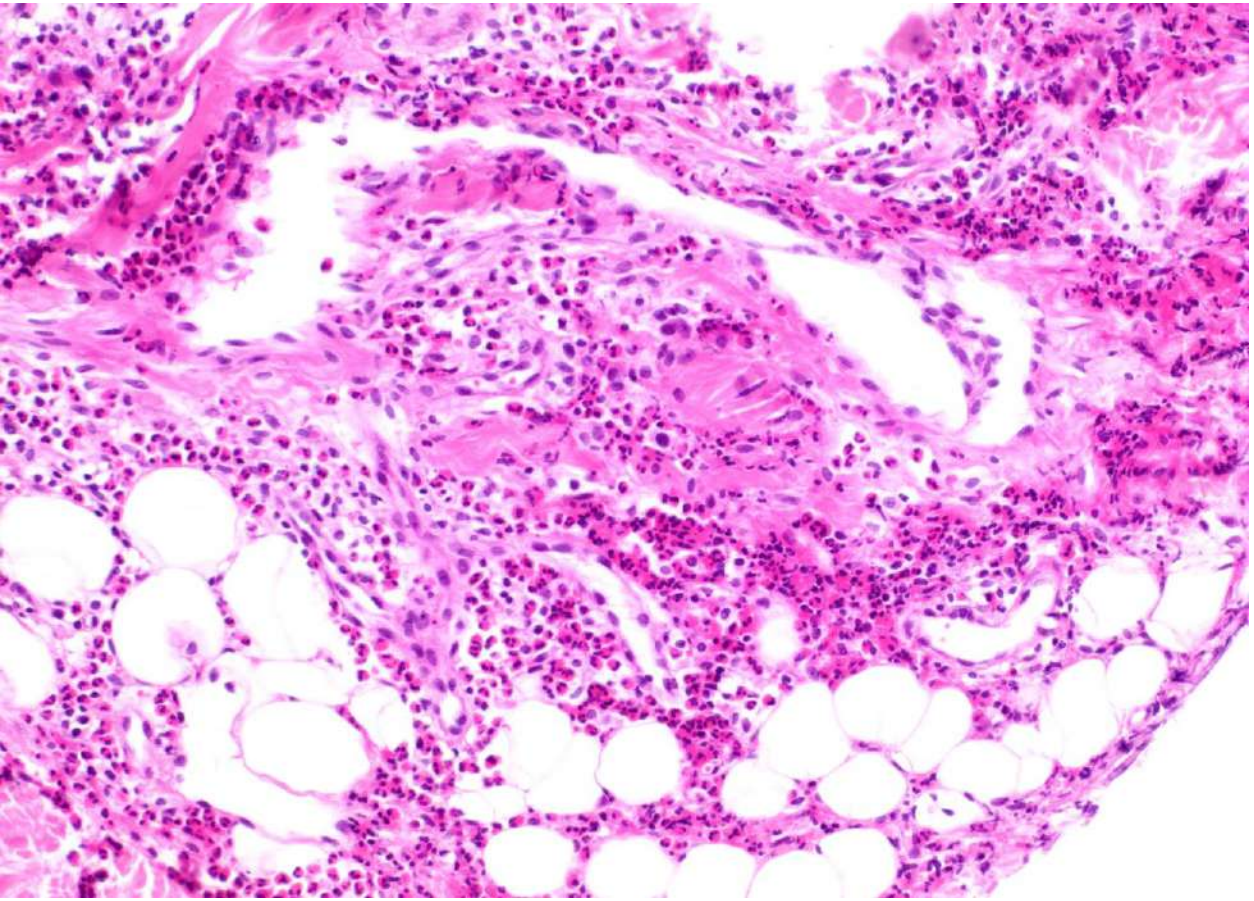
55-year-old male Itchy erythematous vesicular rash on the dorsal aspect of both hands with development of infiltrated lesions with a green ~~hue~~

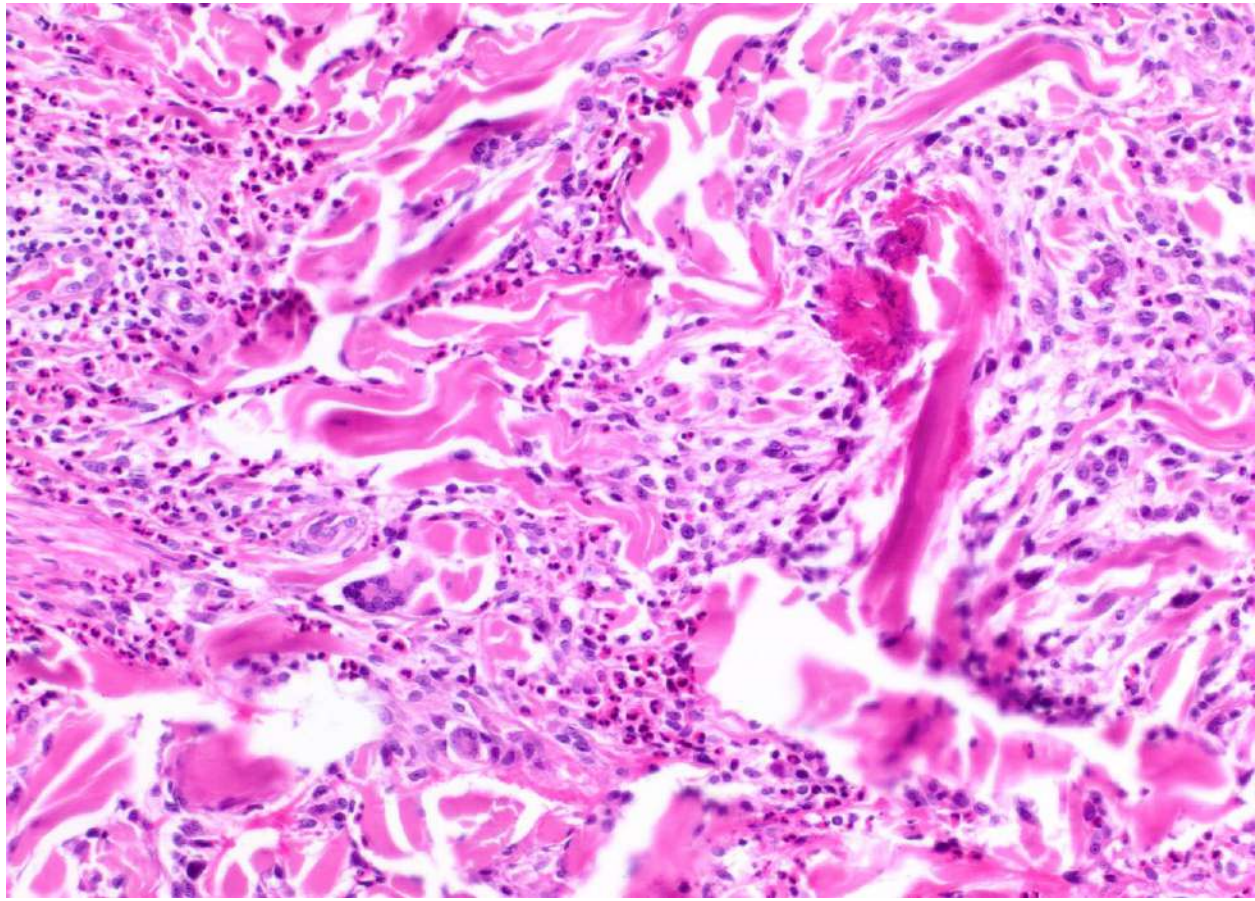


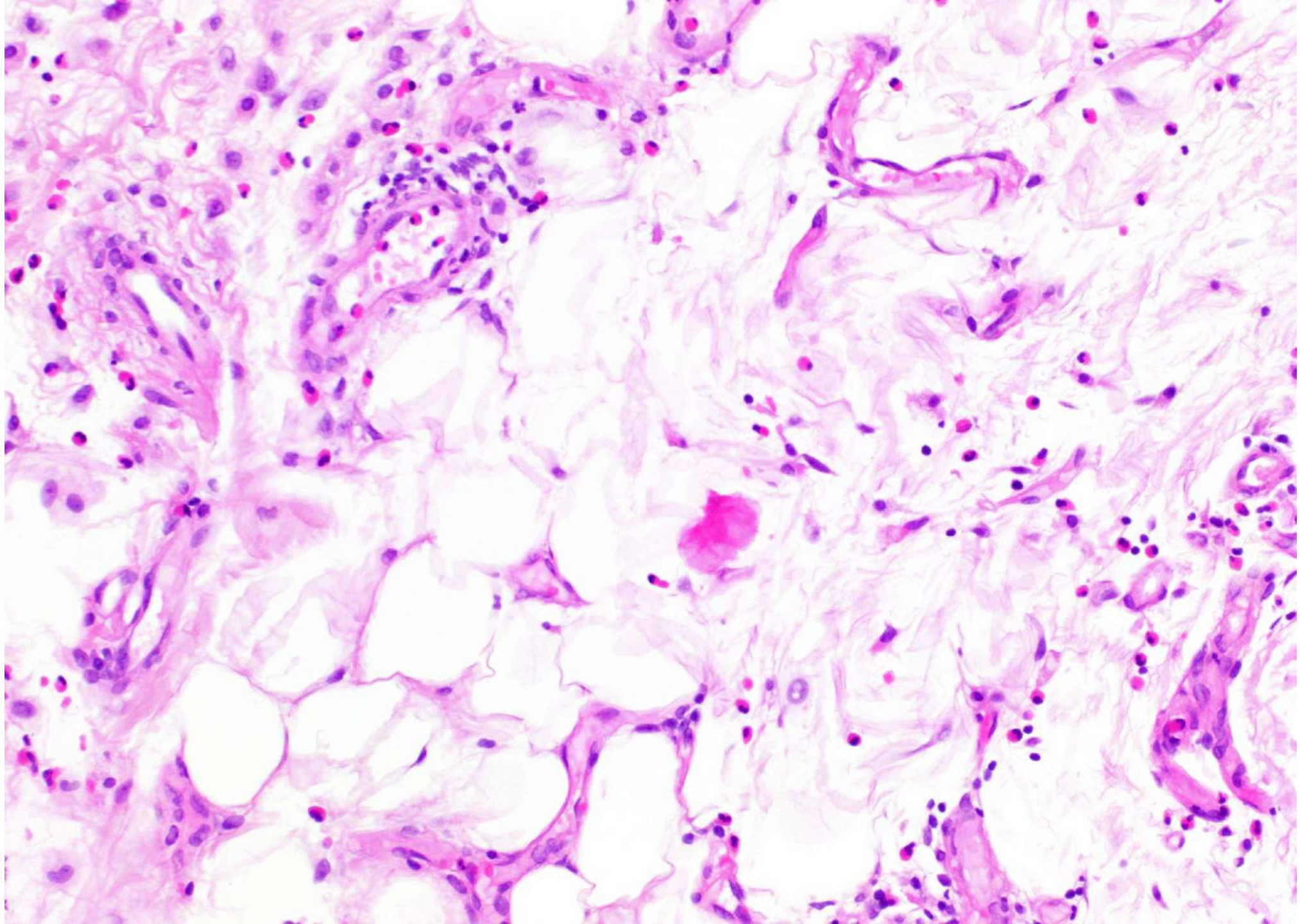




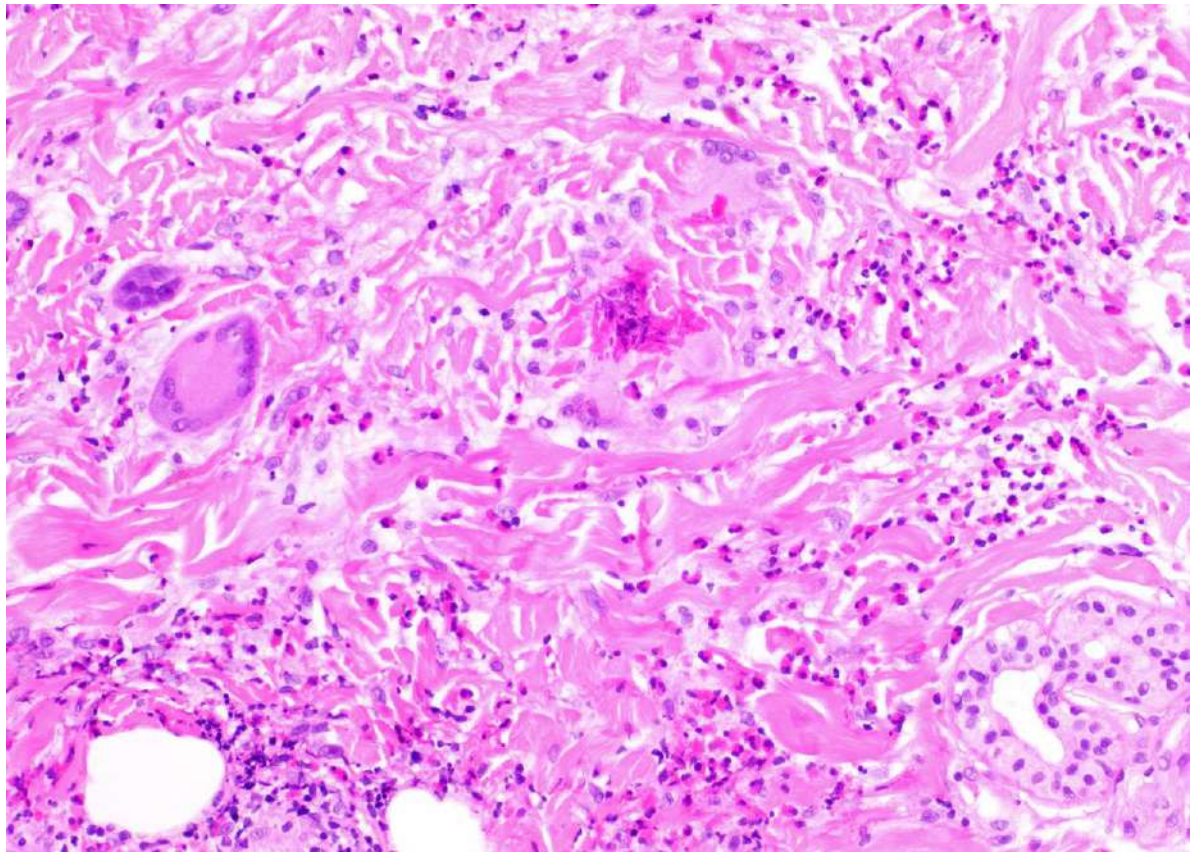








Diagnosis

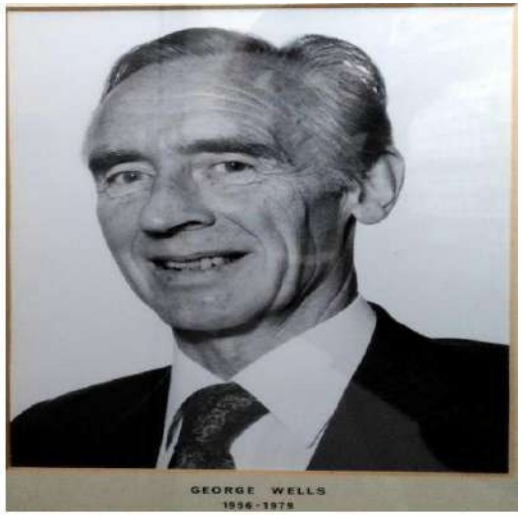


Wells syndrome

Recurrent granulomatous dermatitis with eosinophilia

Wells GC *Trans St Johns Hosp Dermatol Soc 1971;57:46-56*

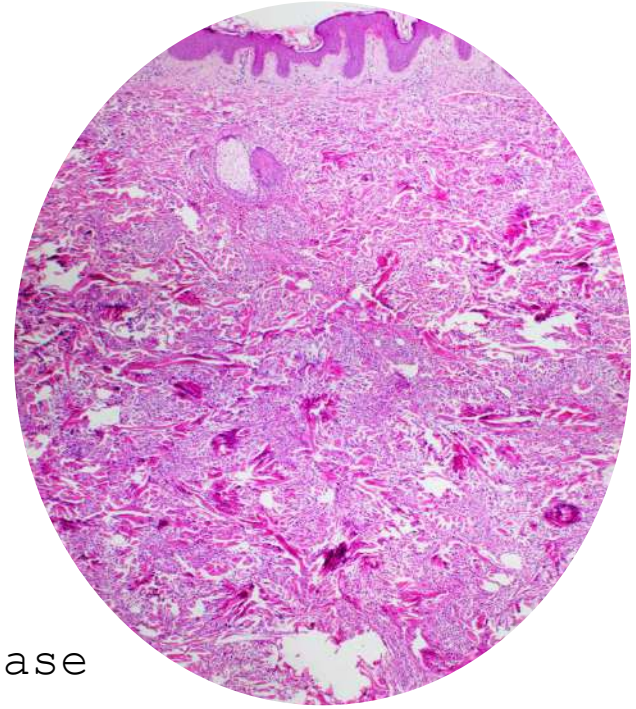
- George Wells first described this syndrome as a recurrent granulomatous dermatitis with eosinophilia
- 4 cases
  - unsual dermatosis
  - distinctive clinical picture and histopathology



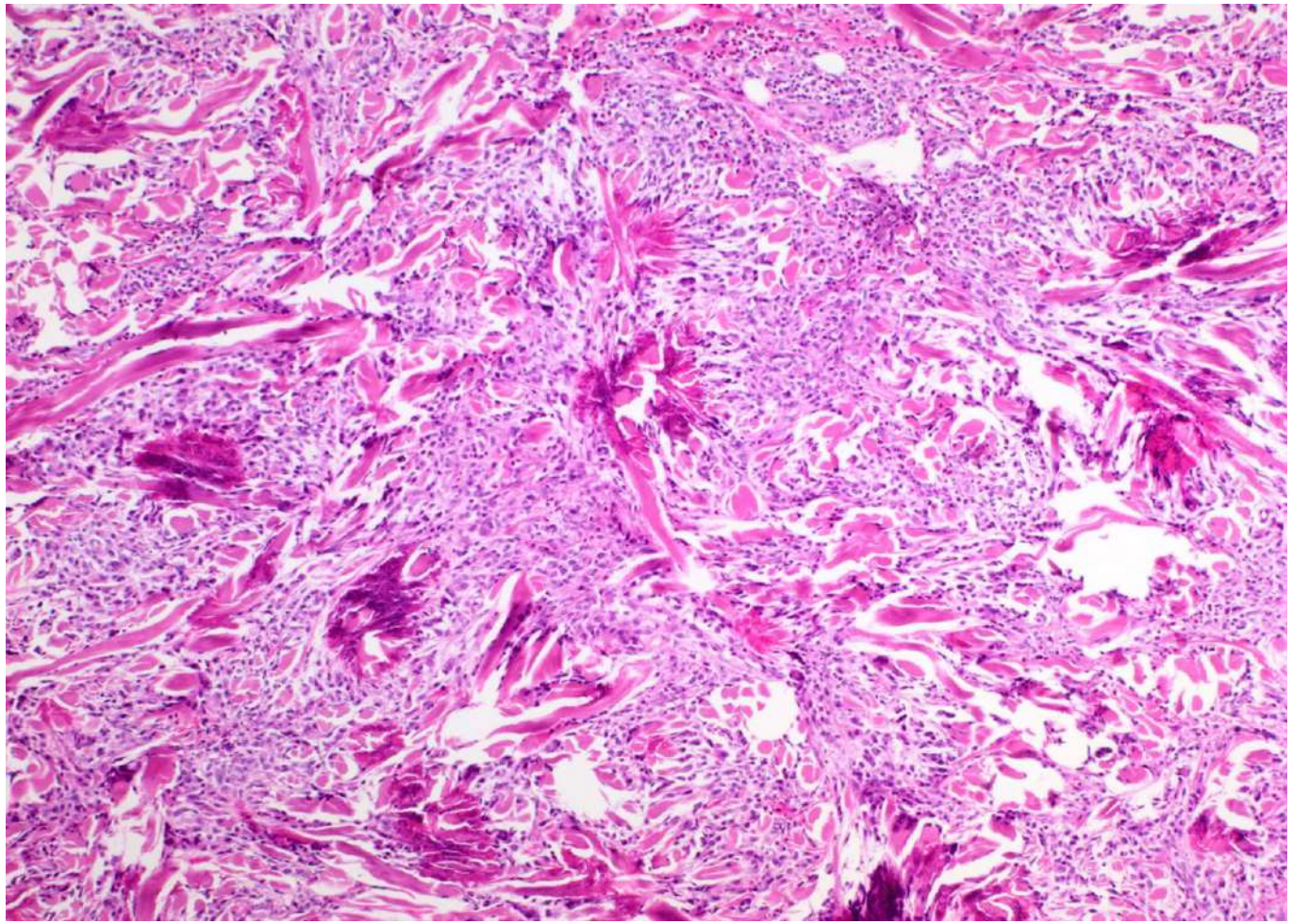
George Wells

It lays the foundation for what would later be known as Wells Syndrome.

Wells GC. *Recurrent granulomatous dermatitis with eosinophilia. Trans St Johns Hosp Dermatol Soc 1971;57:46-56*



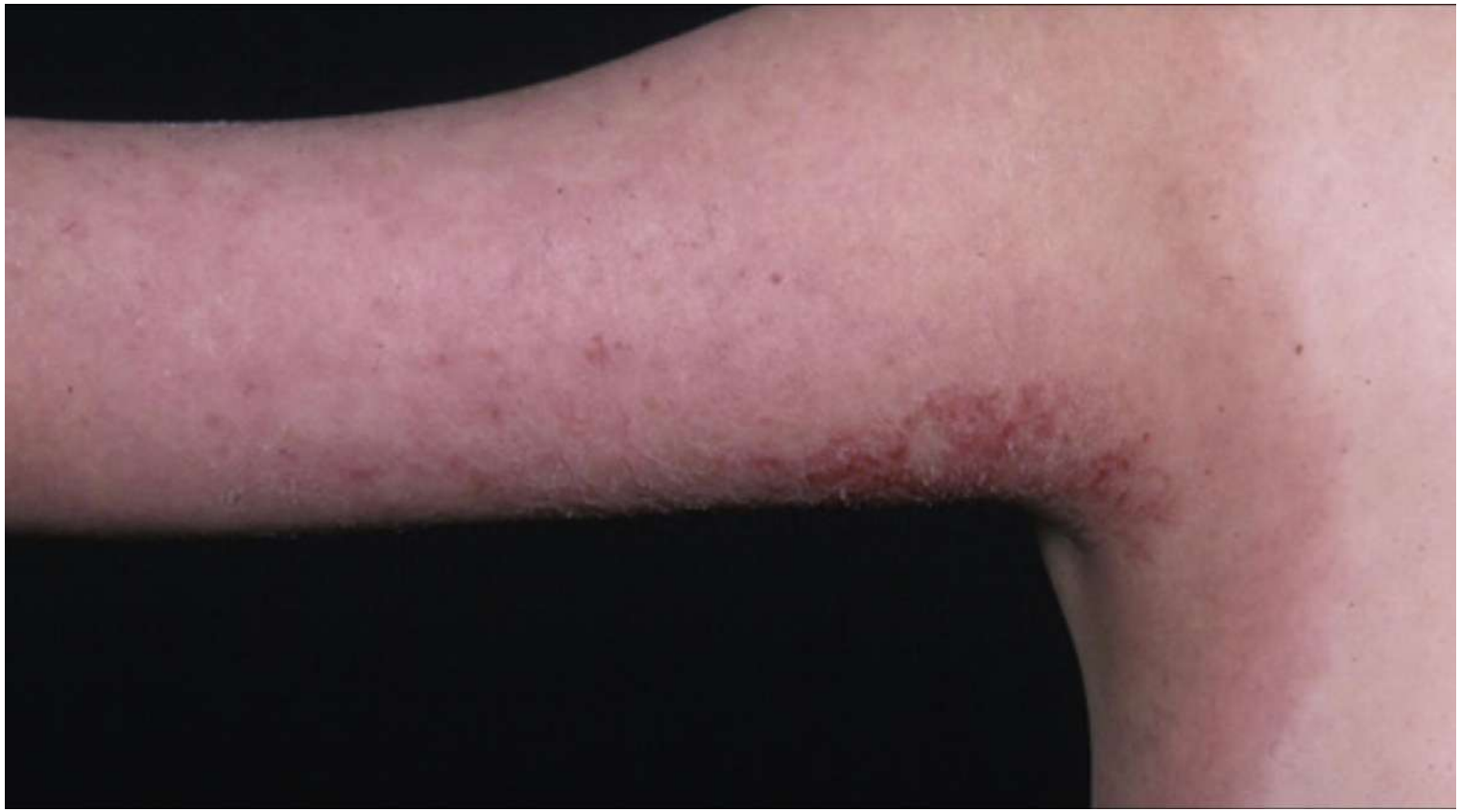
"Case 7" 60-2104



Eosinophilic cellulitis

= Wells syndrome

- Clinically:
  - Recurrent erythematous lesions
  - Mean age: 37 years old
  - Particularly affects extremities and trunk
  - Presents
    - Well defined (cellulite-like) annular erythematous plaques
      - Edematous
      - Firm
  - May ocasionally be mistaken for an infective process



Eosinophilic cellulitis—persistent cutaneous swelling with phagocytosis of eosinophilic debris

G.C. WELLS AND N. SMITH

St John's Hospital for Diseases of the Skin, London WC2

Wells et Smith (1978)

- Renamed as eosinophilic cellulitis
- Precised
  - Early lesions
    - Densal infiltration with eosinophils
    - Dermal oedema
  - Few weeks later
    - Infiltrate — dominate histiocytes
    - Dermis — "Flame figures" — Central flame-like mass
      - Part of collagen bundle coated with eosinophilic debris surrounded by a palisade of large histiocytes and foreign body giant cells.
      - Appears to be a phagocytic response to the products of disintegrating eoinophils

Wells syndrome (histopathology)

- acute stage: dermal oedema and an eosinophilic infiltrate are seen in the upper and deep dermis
- subacute stage: flame figures consisting of eosinophils and histiocytes around amorphous depositions of collagen
- resolving stage: gradual disappearance of eosinophils with the persistence of histiocytes and appearance of giant cells around collagen deposits, forming microgranulomas

Arch Dermatol. 2006;142(9):115

Wells syndrome (eosinophilic cellulitis)

- Uncommon inflammatory dermatosis of unknown aetiology
- Characterized by a pruritic rash
- Usually follows a relapsing and remitting course
- Rarely associated with systemic involvement, but peripheral blood eosinophilia is common
- Pruritus can be intractable and unresponsive to anti-histamines

Wells syndrome (clinical variants)

- plaque type (children)
- annular granuloma-like (adults)
- urticaria-like
- papulovesicular
- bullous
- papulonodular
- and fixed drug eruption-like

Arch Dermatol. 2006;142(9):115

However…

Am J Dermatopathol. 1986 Jun;8(3):186-93.

Eosinophilic infiltration with flame figures. A distinctive tissue reaction seen in Wells' syndrome and other diseases.

Wood C, Miller AC, Jacobs A, Hart R, Nickoloff BJ.

Abstract

We report five cases, all male, of diverse clinical findings of scattered erythematous, violaceous, or centrally blue plaques. Eight biopsies from the five patients showed nodular or diffuse dermal and subcutaneous infiltration, predominantly of eosinophils and histiocytes, with "flame figures" composed of granules of eosinophils that surround collagen bundles, whose staining quality is thereby altered. Two patients were children, the younger only 18 months old. Three patients initially presented clinical evidence of insect bites, and in one of these the biopsy showed cutaneous pseudolymphoma underlying dermal changes of eosinophilic cellulitis. Eosinophilic infiltration with flame figures is a distinctive reaction to various stimuli. It may be seen in a wide variety of clinical conditions and is not confined solely to patients with Wells' syndrome, which may be an acceptable term for clinically typical cases. Eosinophilic infiltration with flame figures is preferred descriptively to identify the microscopic changes in Wells' syndrome and in other cases like that of our patient with pseudolymphoma, in which the cutaneous reaction may be secondary to some other disease.

EDITORIAL

Reflections on Eosinophils and Flame Figures

Where There's Smoke There's Not Necessarily Wells Syndrome

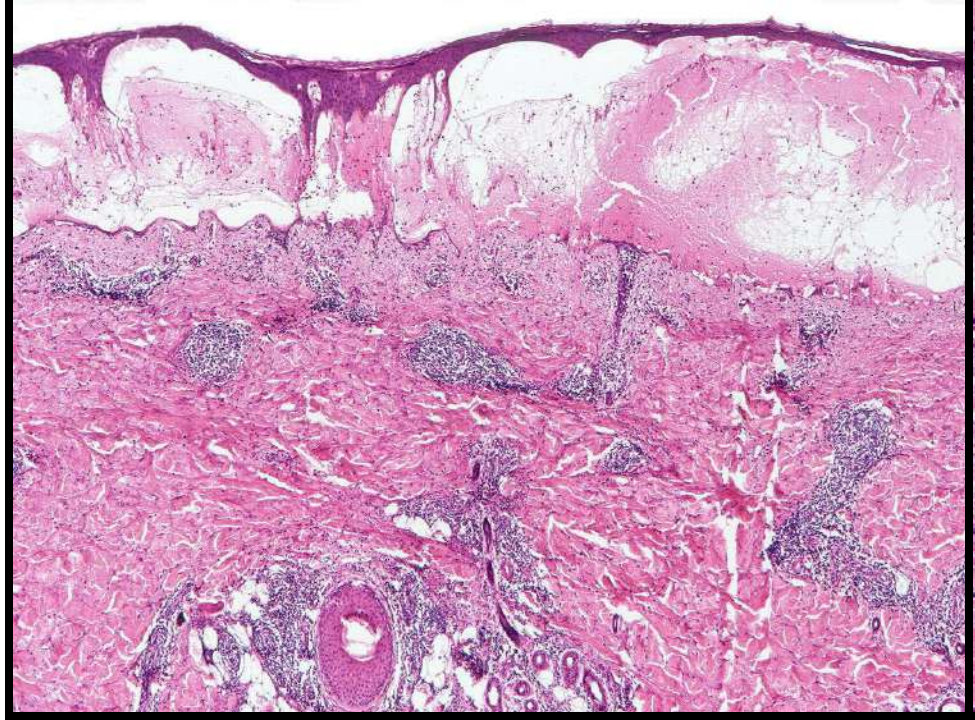
Arch Dermatol. 2006;142(9):1215-121

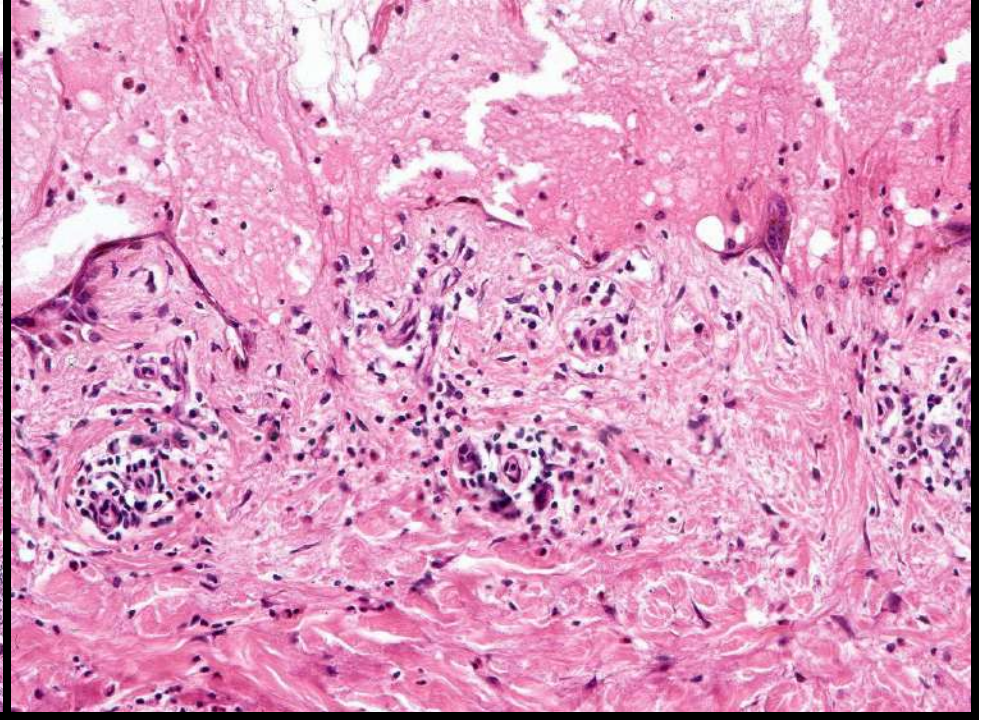
bullous pemphigoid
prurigo
herpes gestationis
drug eruption
scabies
eczema
even molluscum contagiosum !!! *(Am J Dermatopathol. 2004; 26 (5): 441-442)*

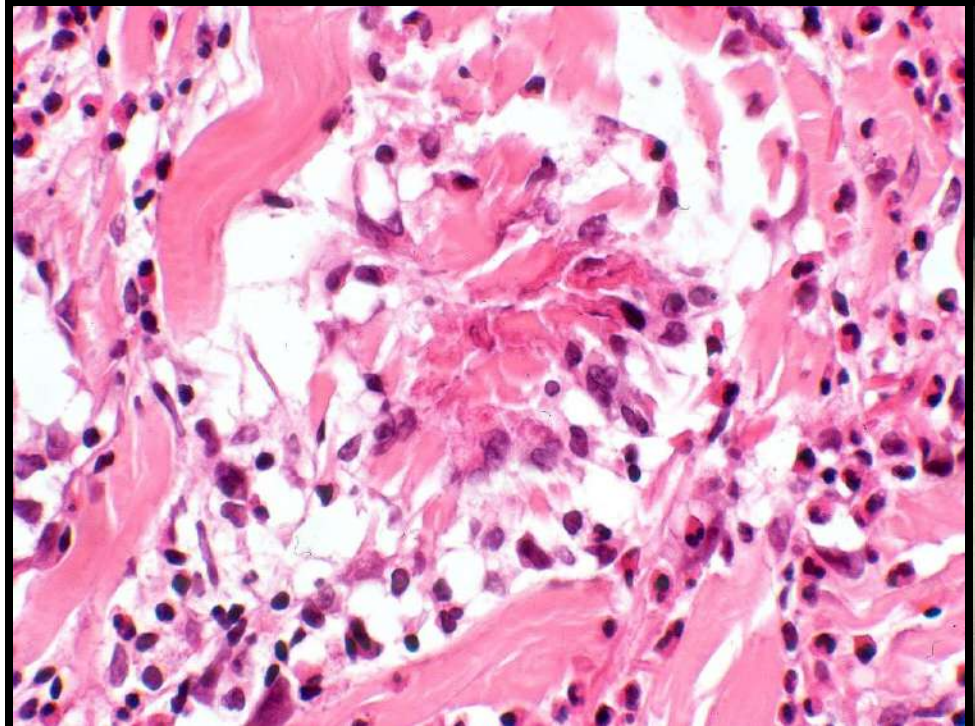
Differential diagnosis

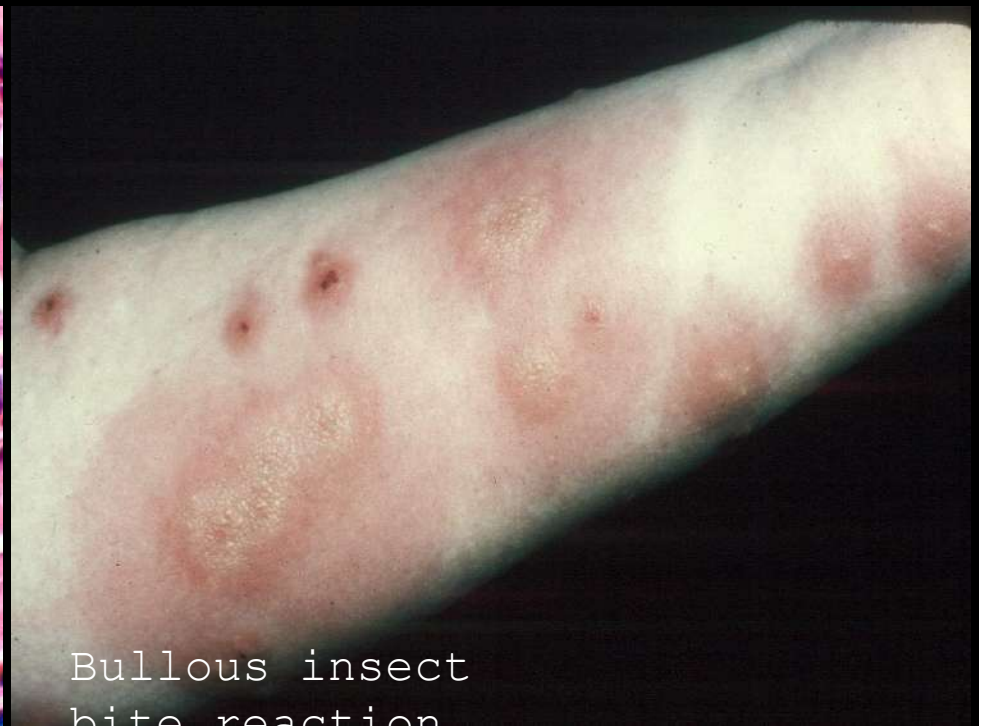
- Cellulitis*
- Granuloma Annulare*
- Erysipelas*
- Urticaria
- Allergic Granulomatosis (Churg-Strauss Syndrome)
- Hypereosinophilic Syndrome
- Bullous Disorders
- Drug Eruptions
- Toxocara canis and other parasitic disorders
- Insect Bites
- Lyme Disease

Not everything is what it seems








Bullous insect
bite reaction

Case report

Eosinophilic cellulitis (Wells' syndrome) caused by a temporary henna tattoo

Postep Derm Alergol 2014; XXXI, 5: 322–324

Is Wells syndrome a true disease or a histologic reaction
Pattern to many diverse stimuli??

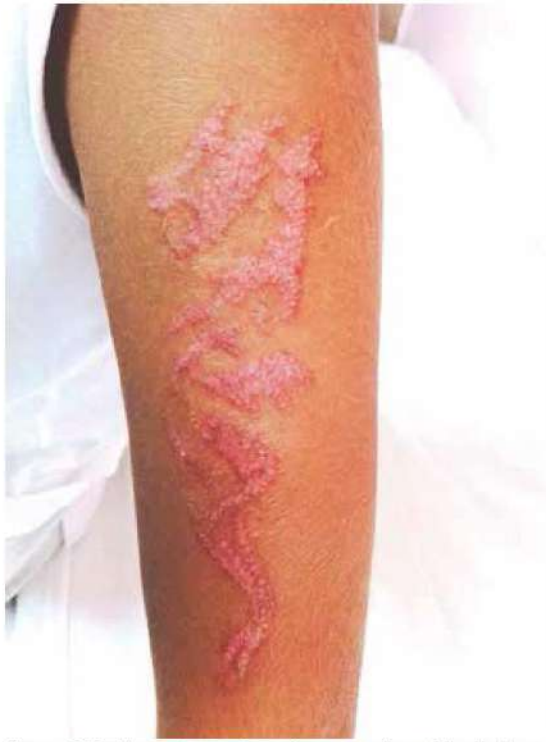


Figure 1. Erythematous, edematous, papulonodular lesions on the tattoo area

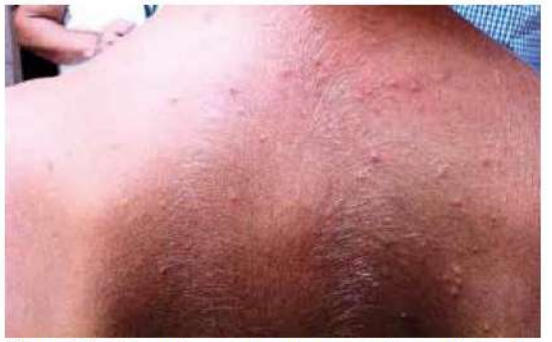


Figure 2. Erythematous, edematous papules on the back

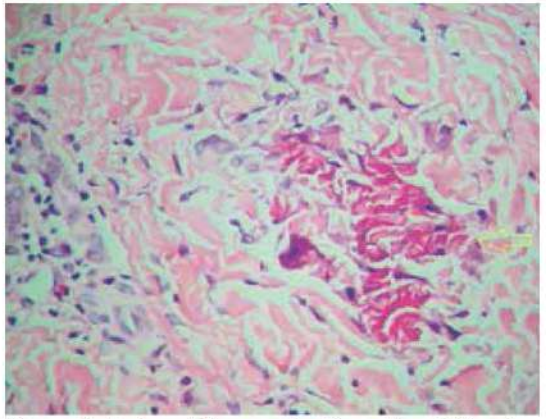


Figure 3. Eosinophilic granular formation defined as a flame figure in dermis (H + E 400×)

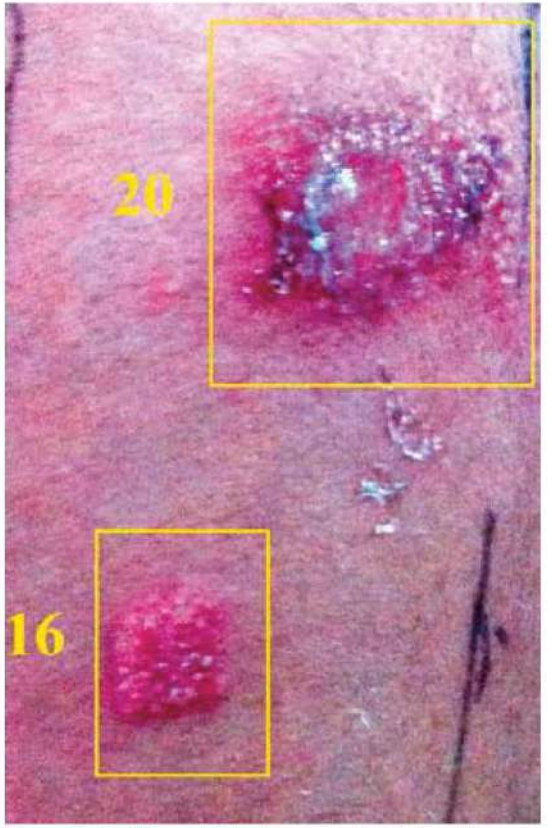
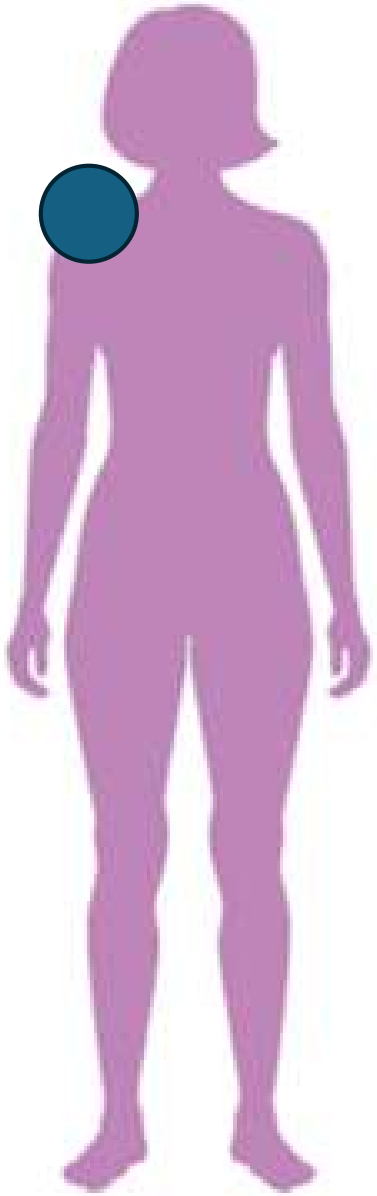
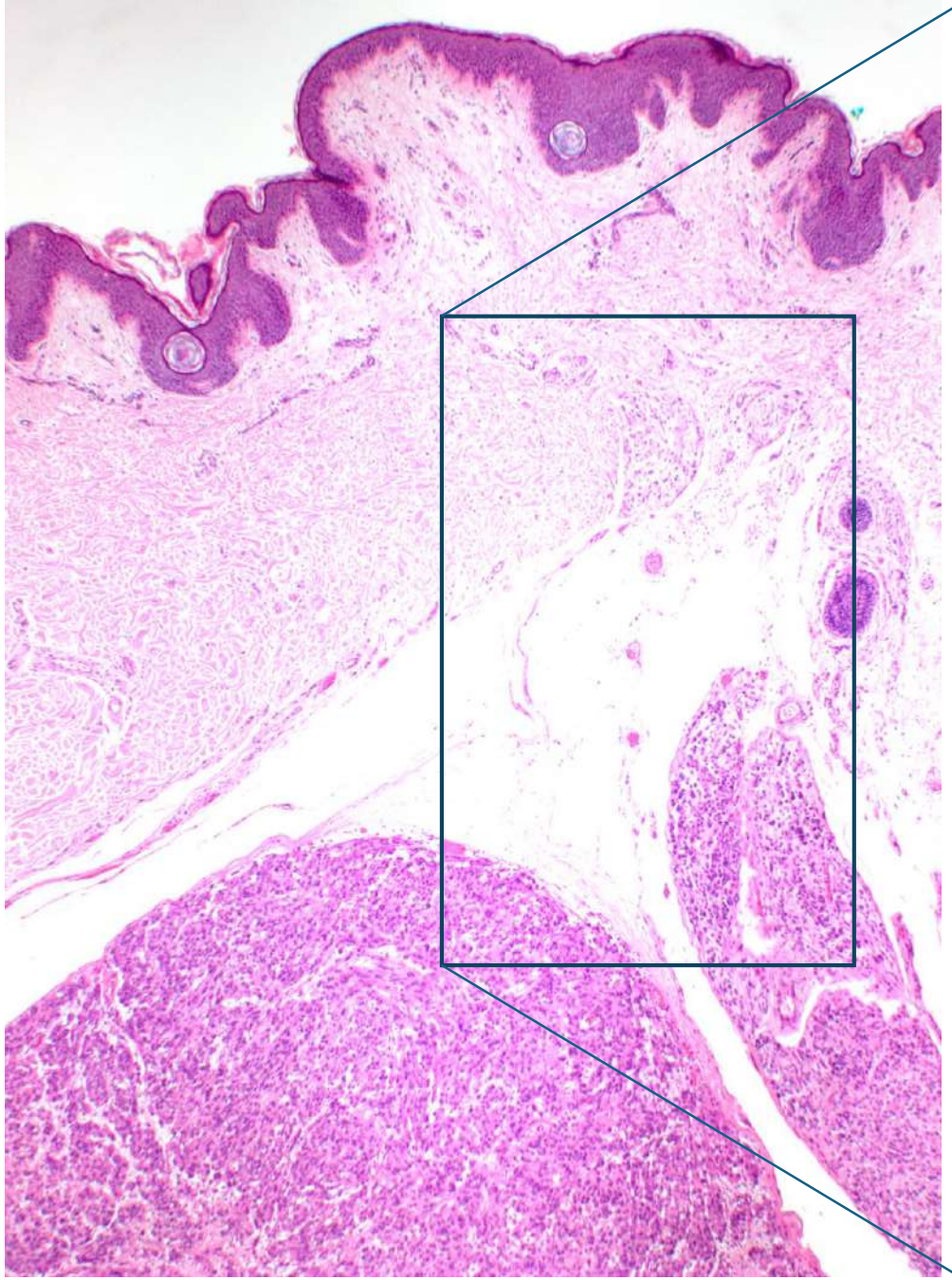


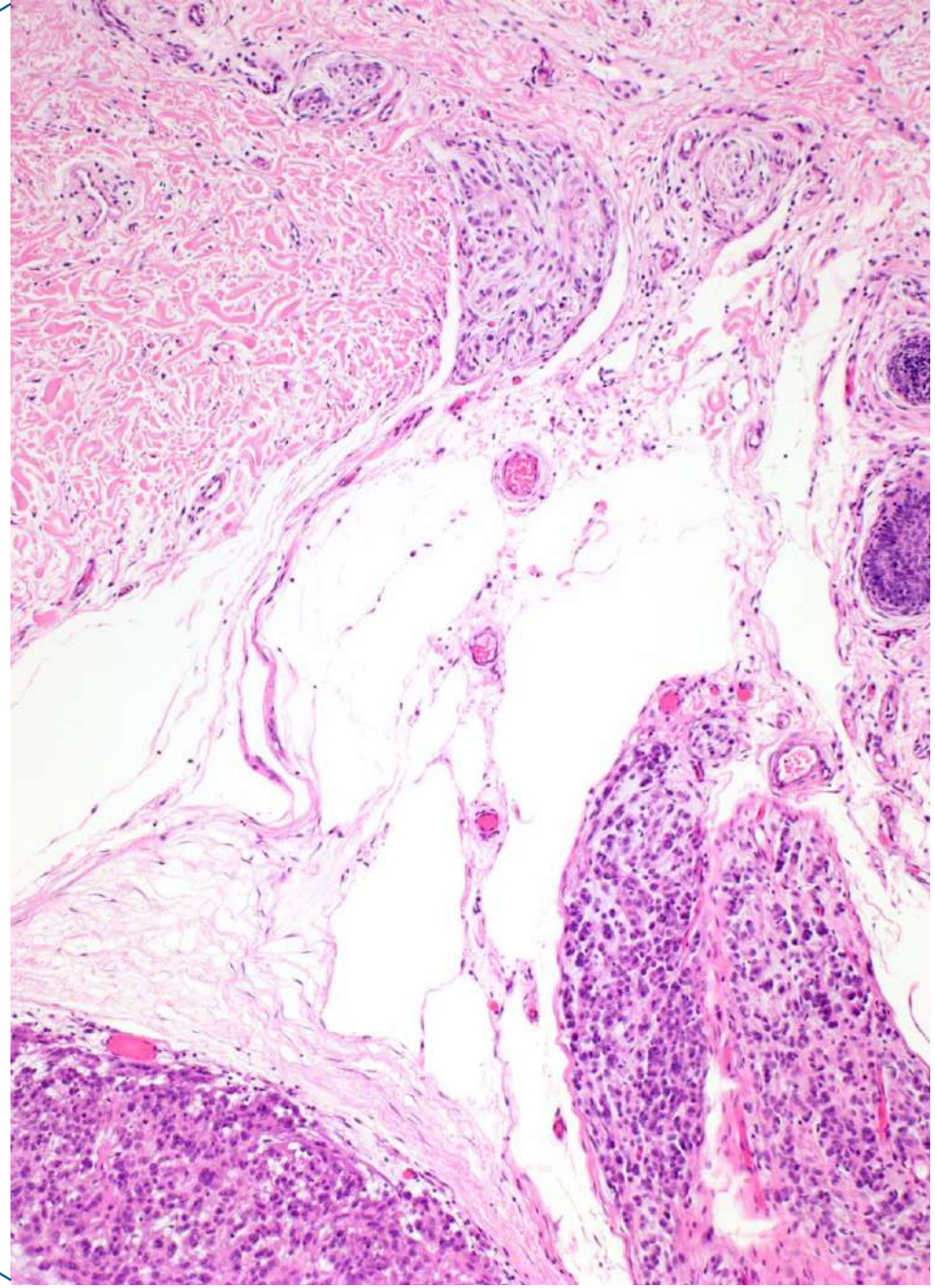
Figure 4. Positive patch test reaction to black rubber mix (16) and paraphenylenediamine (20) in 48 h

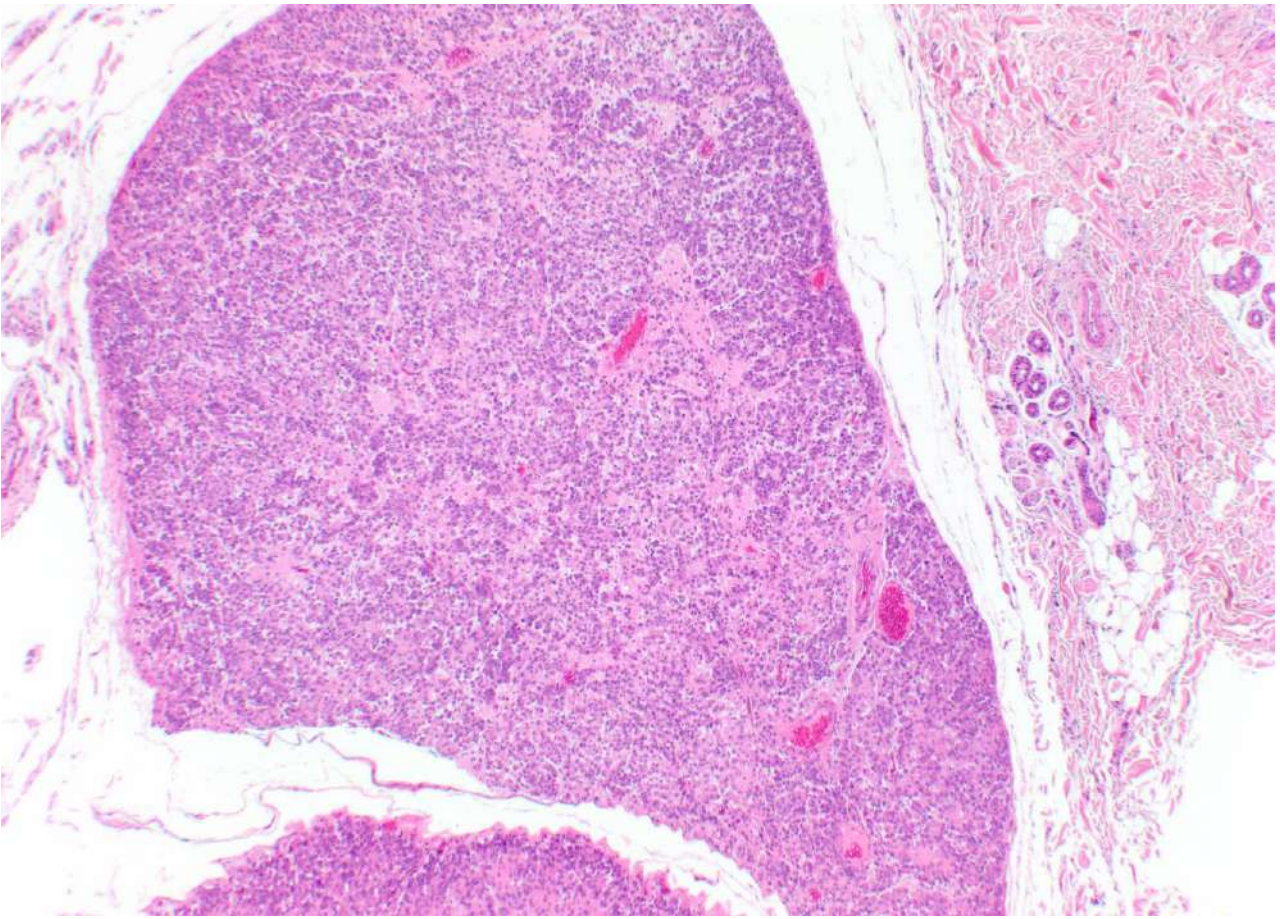
Case 17

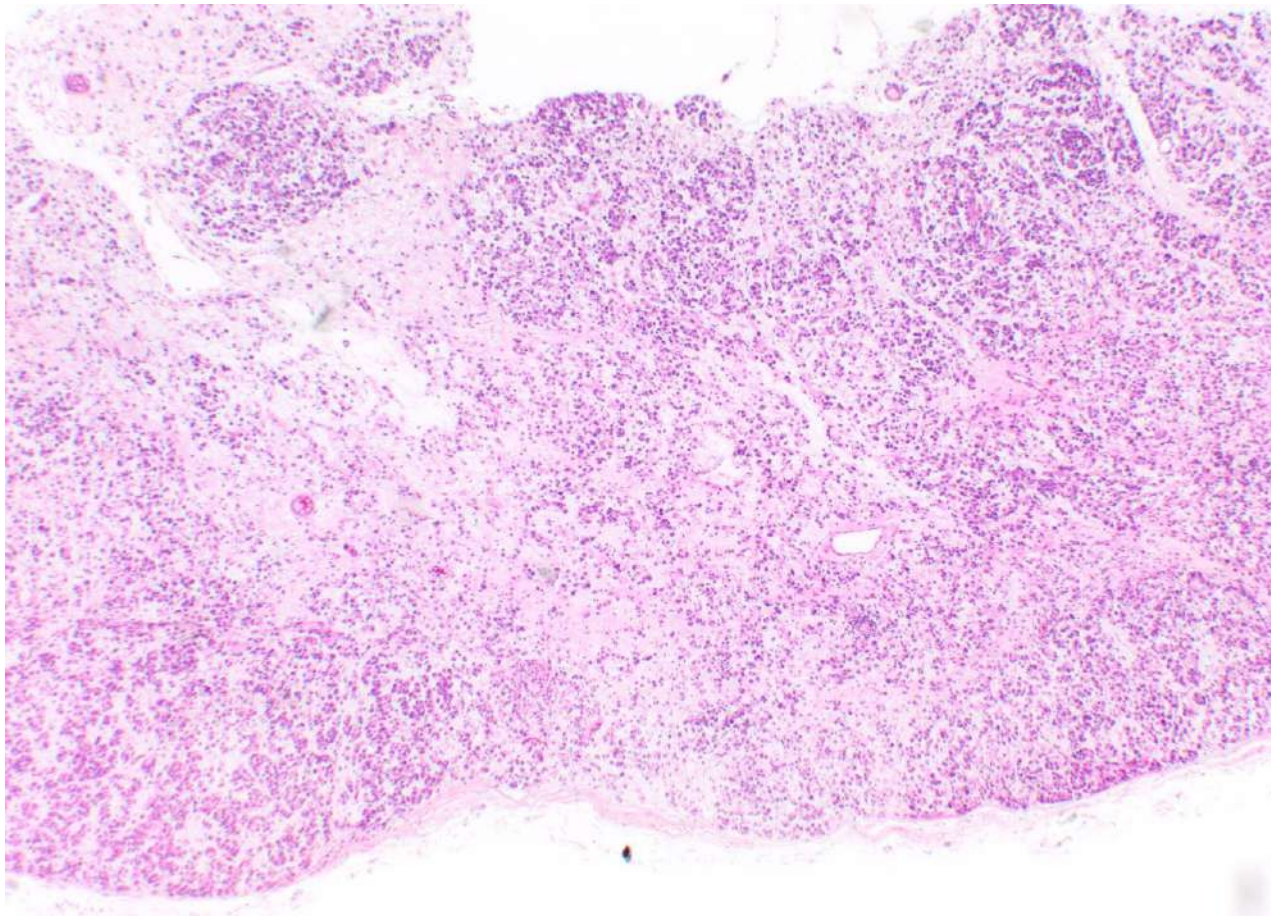
23 year old female
1 year history of slightly tender lump at right side trapezoid area

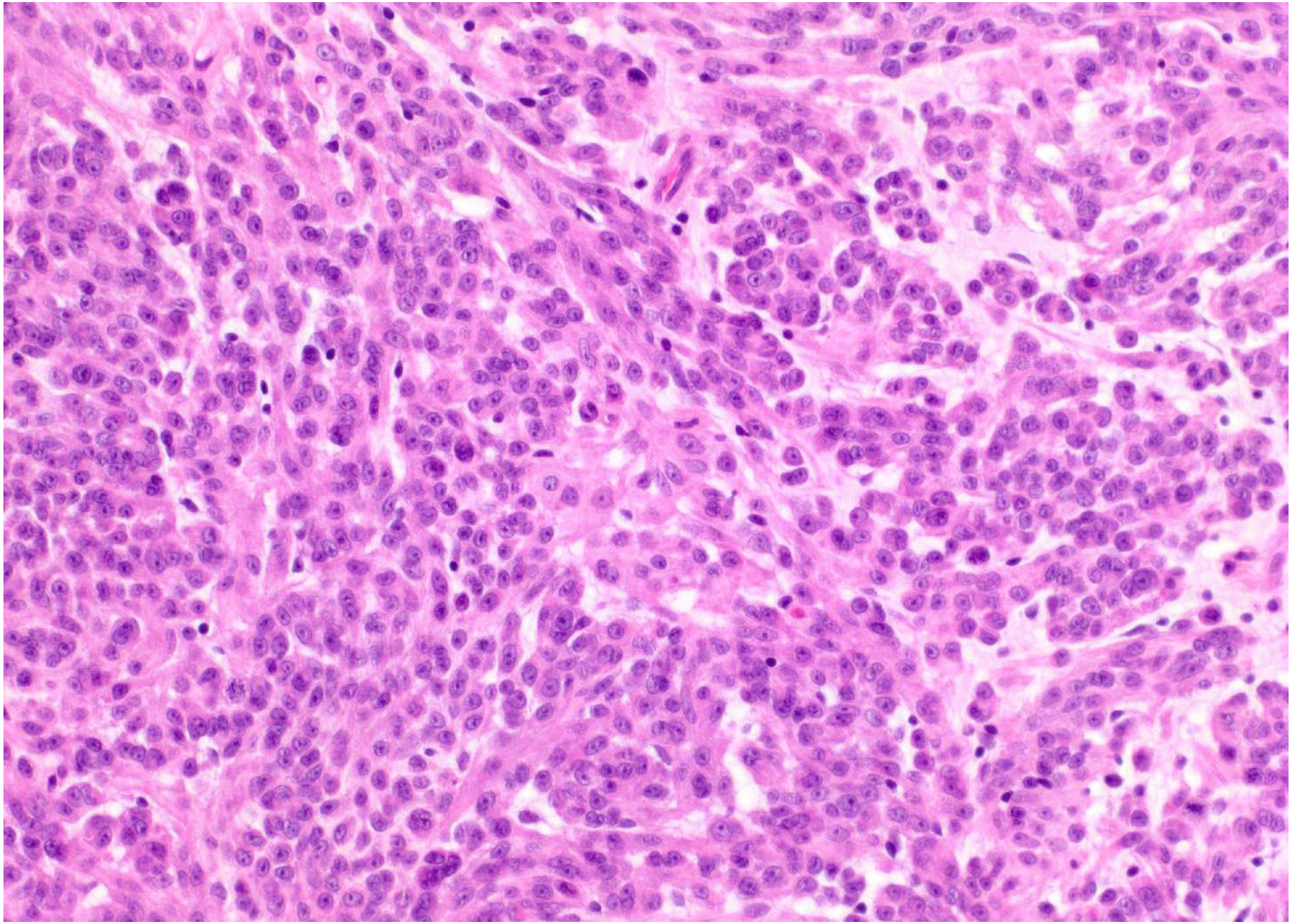


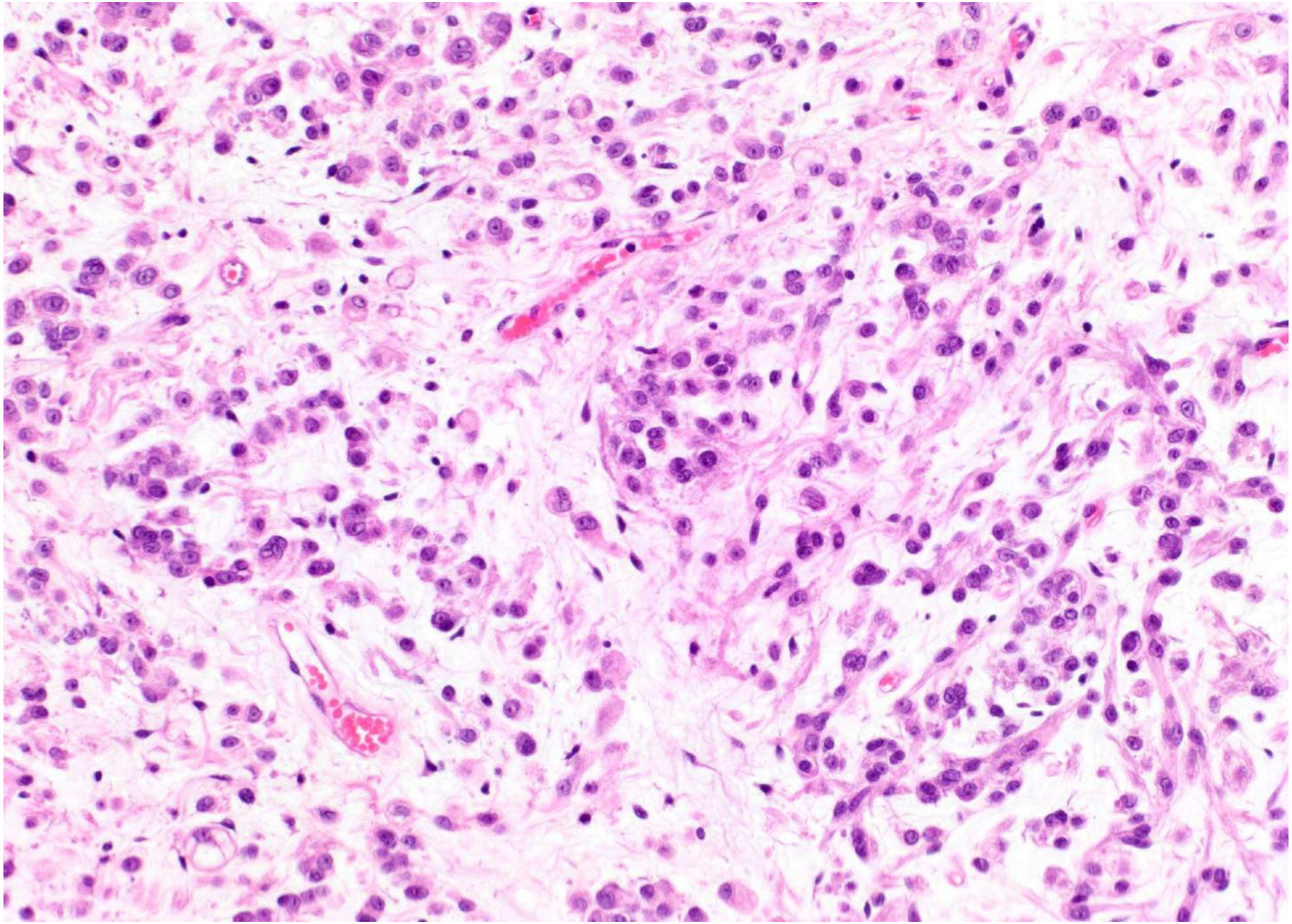


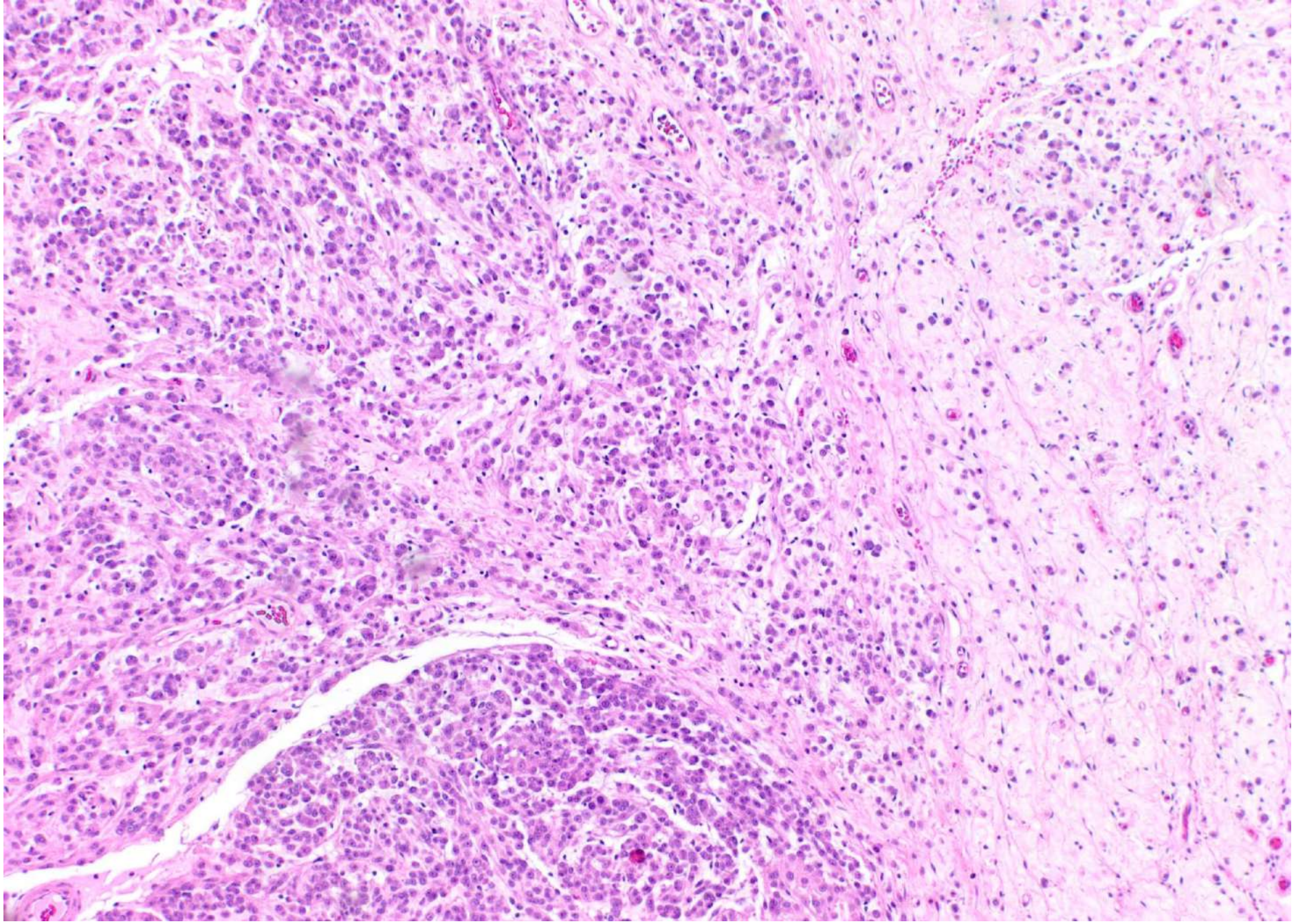


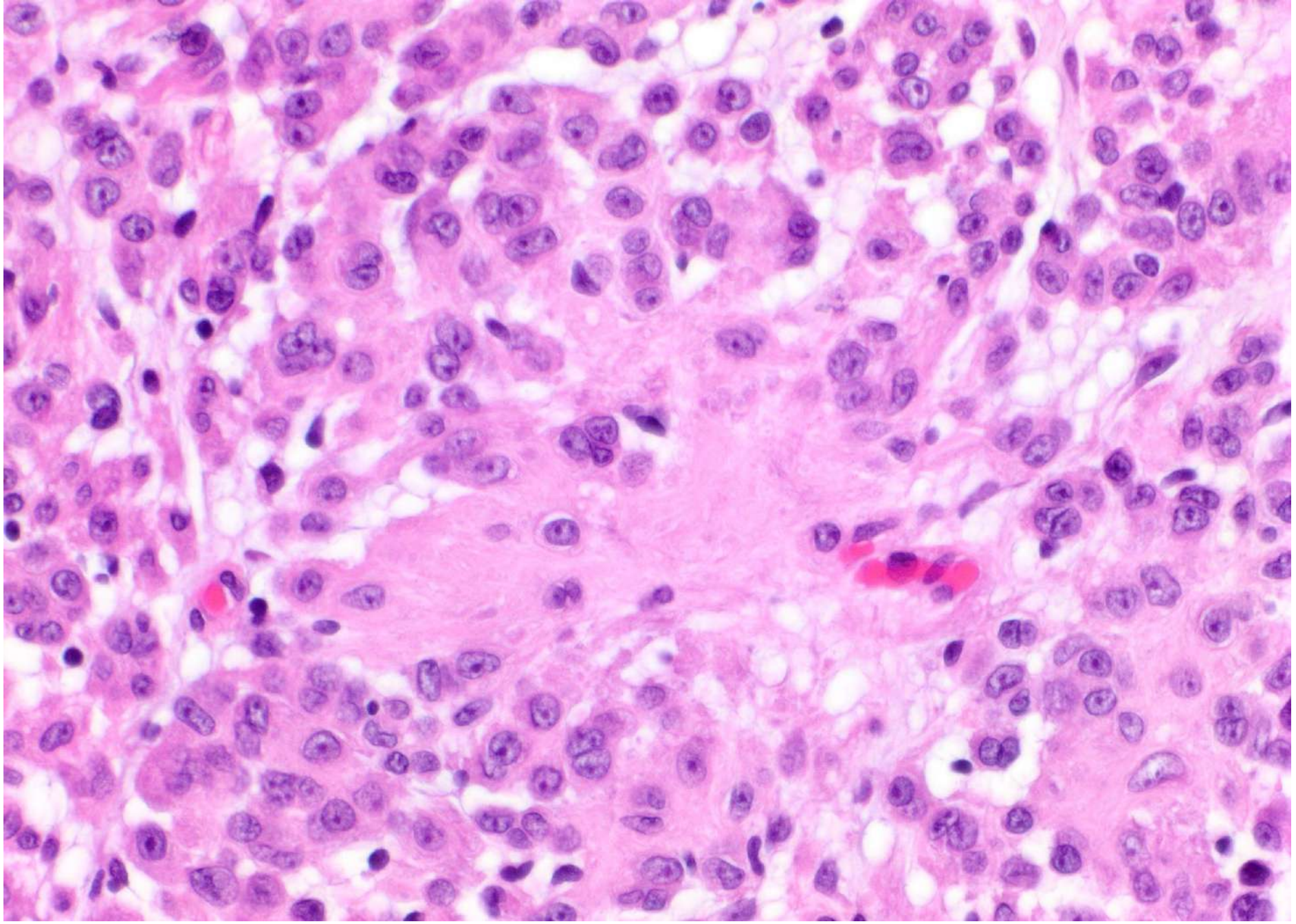


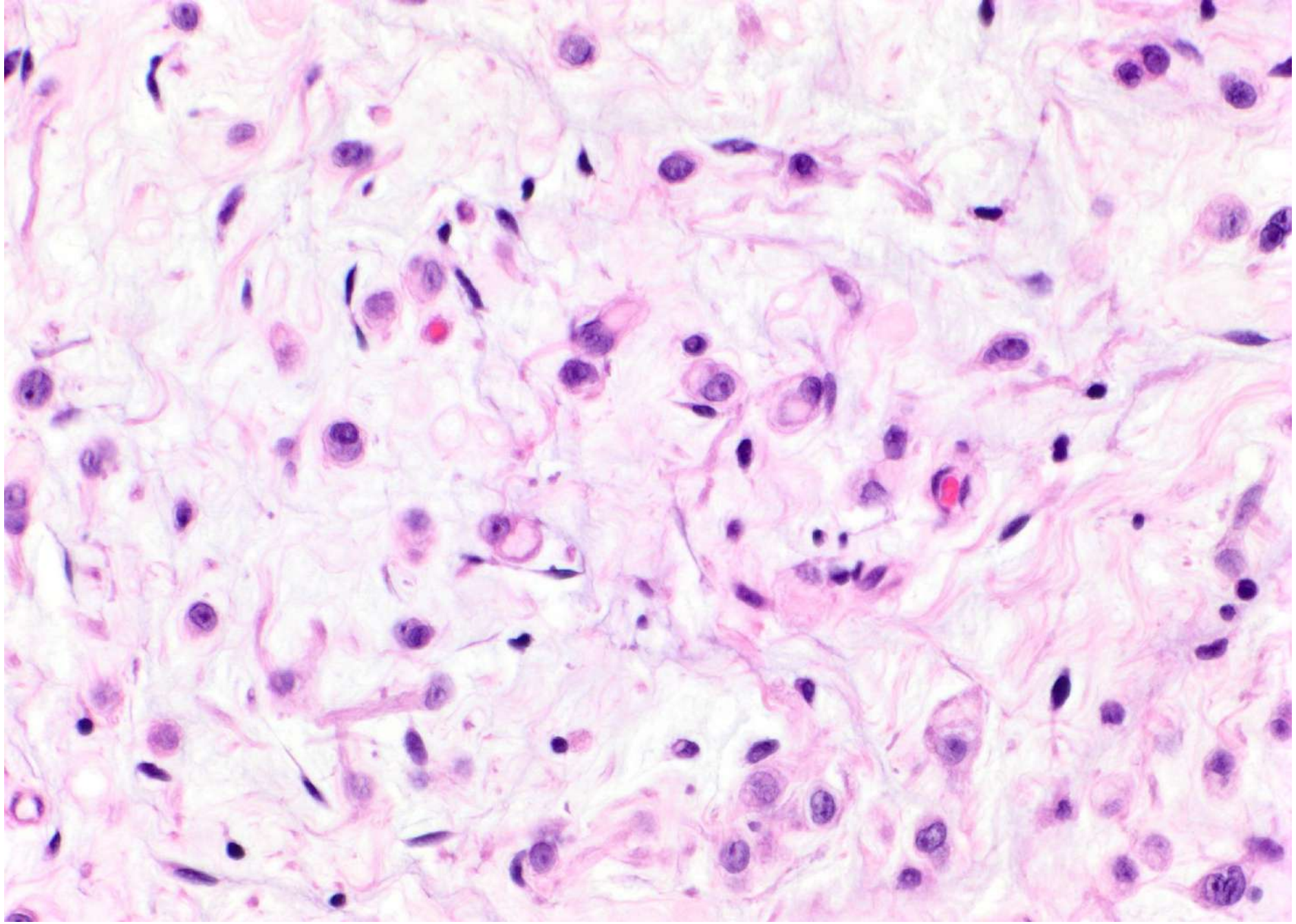


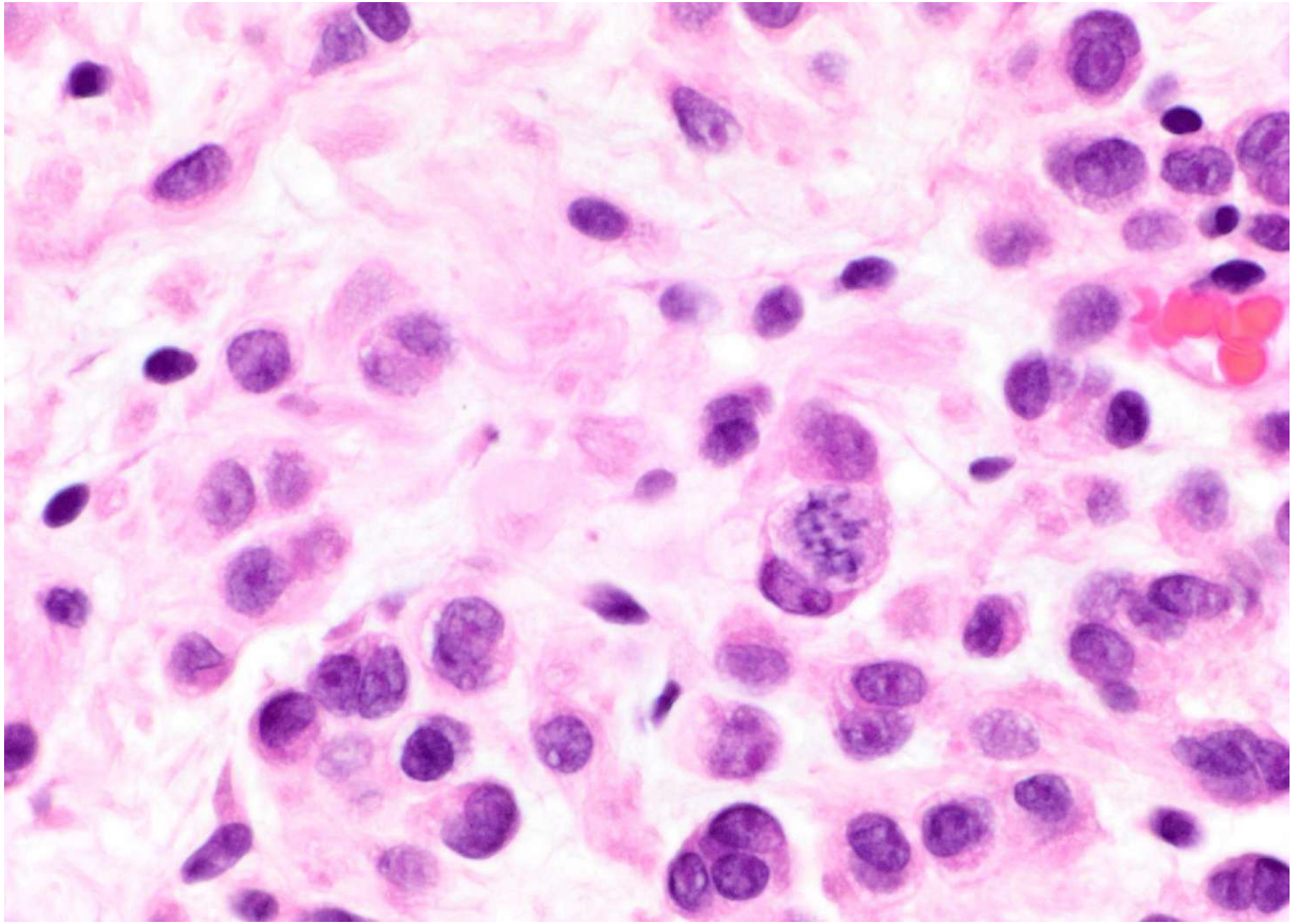






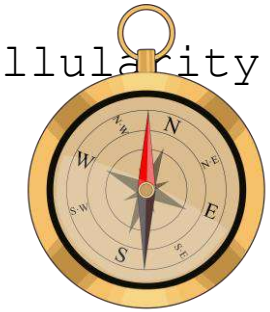






Differential diagnosis

- Dermal and subcutaneous tumour
- Epithelioid cellularity
- Myxoid areas
- Mild atypia
- Scarce mitosis



Non-mesenchymal neoplasms

- Metastasis (melanoma, carcinoma, mesothelioma)
- Melanocytic tumour
- Hematologic neoplasm

Mesenchymal neoplasms

- Epithelioid Fibrous Histiocytoma
- Cutaneous myopepithelioma
- Epithelioid hemangioma
- Epithelioid hemangioendothelioma
- Epithelioid angiosarcoma
- Cellular neurothekeoma
- Epithelioid schwannoma
- Epithelioid malignant peripheral nerve sheath tumor
- Epithelioid sarcoma
- Sclerosing epithelioid fibrosarcoma

Hornick JL. Practical Soft Tissue Pathology: A Diagnostic Approach. A Volume in the Pattern Recognition Series. 2nd Edition - November 14, 2017

IHC

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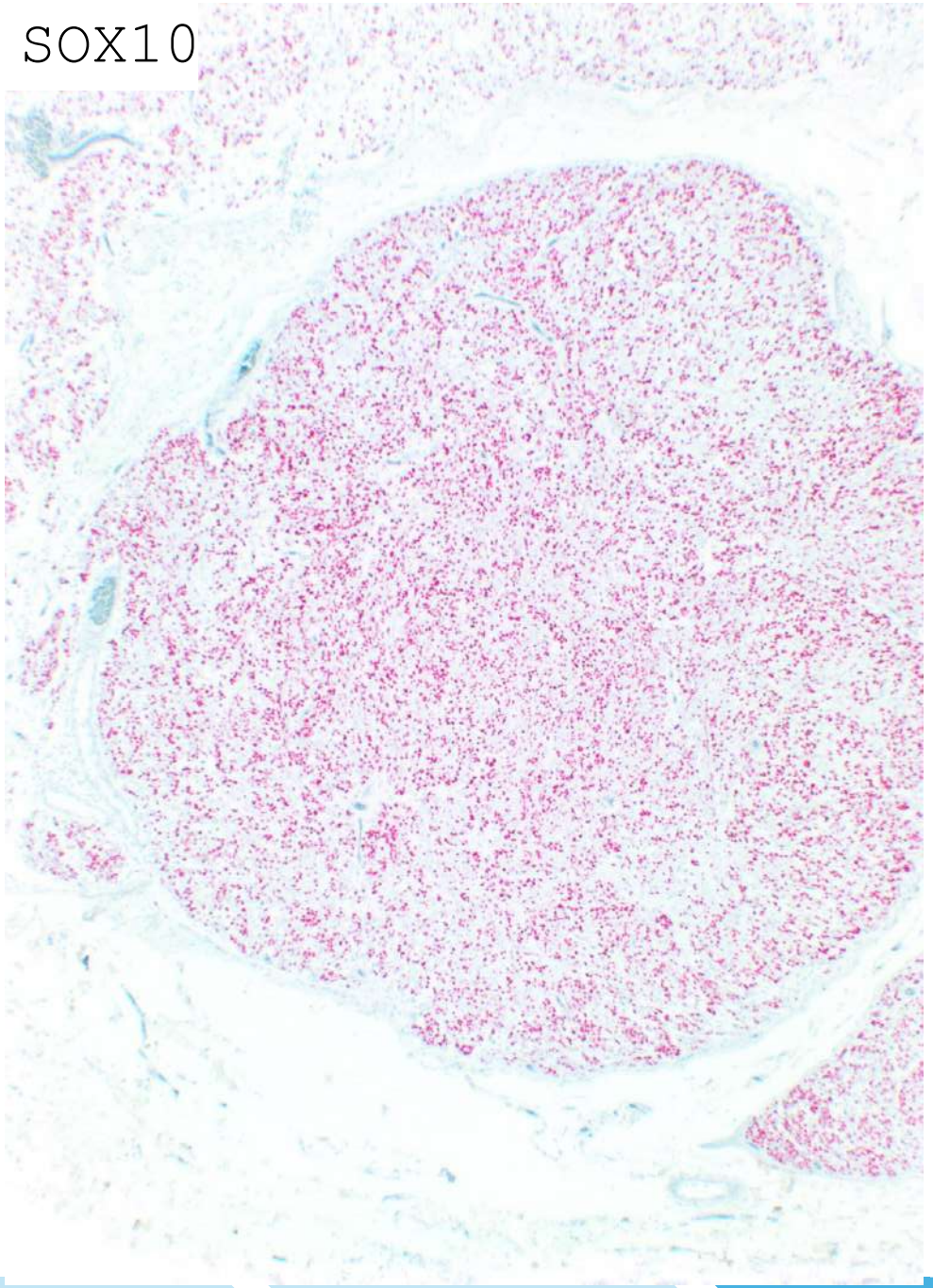

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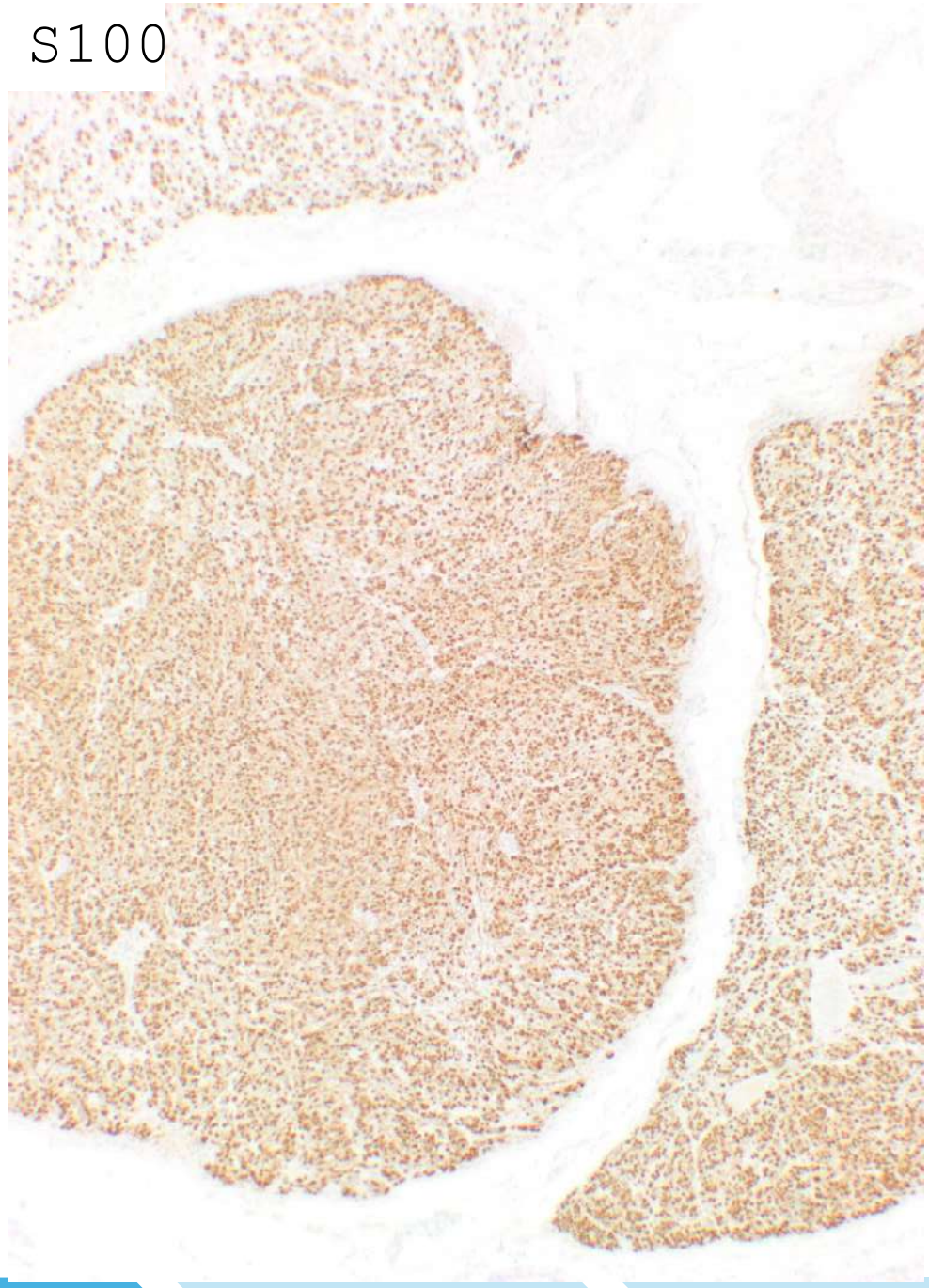

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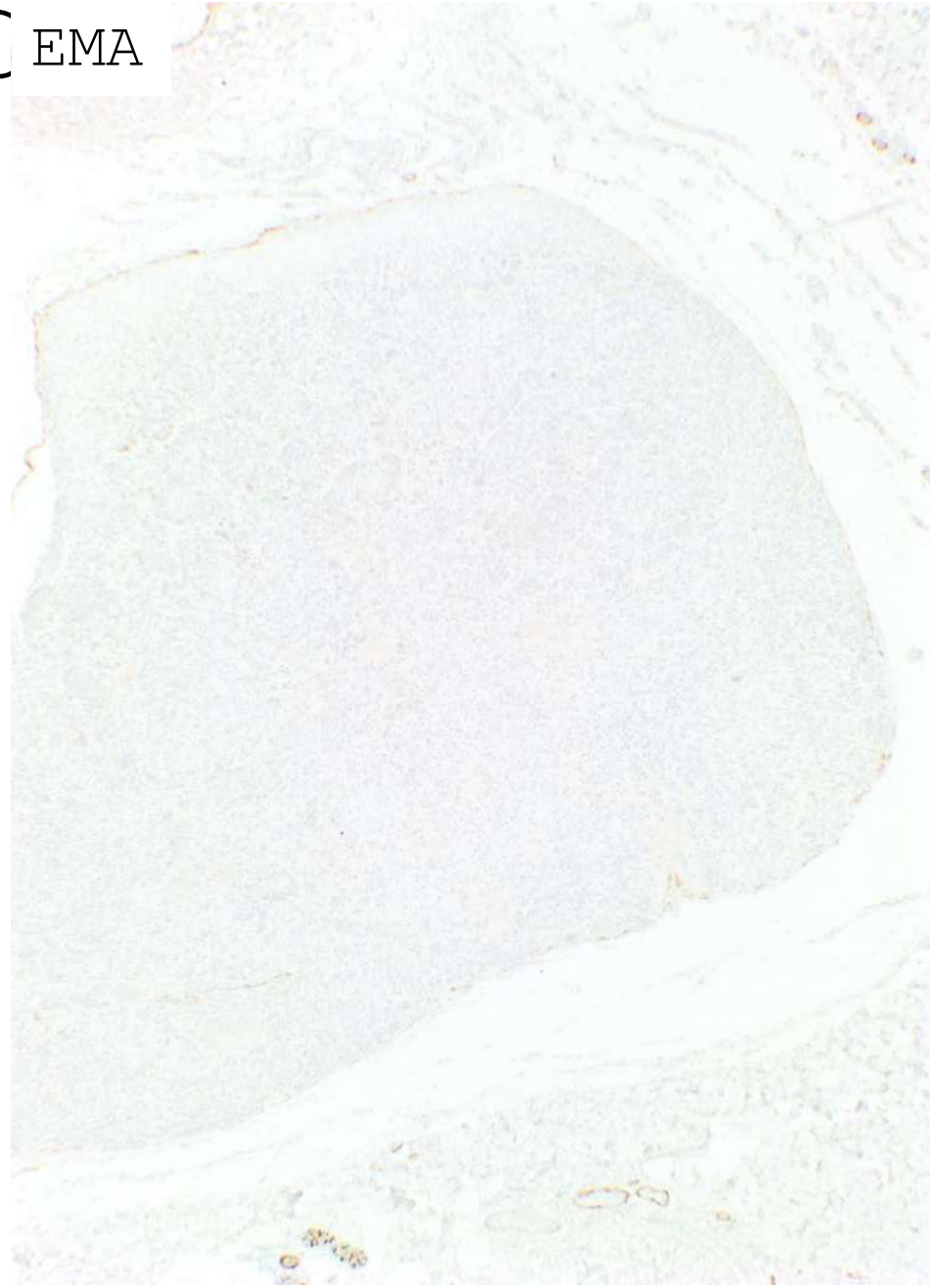
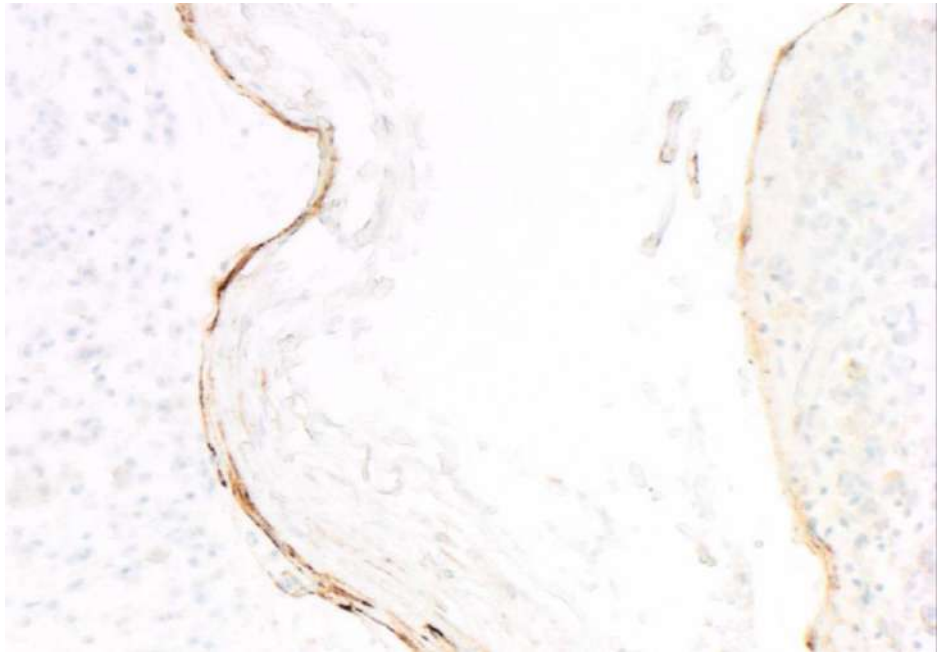
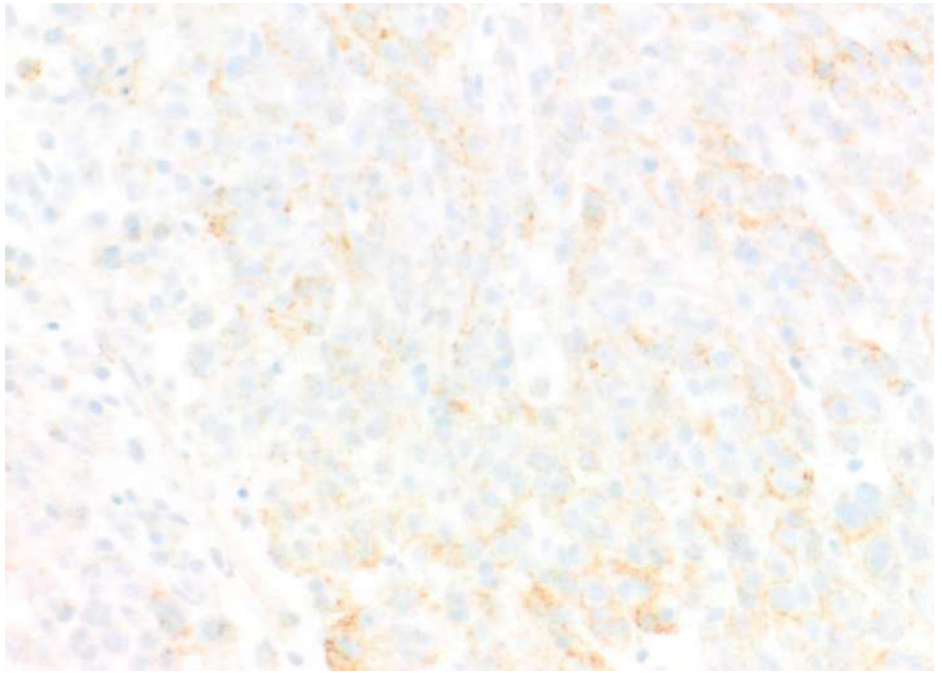
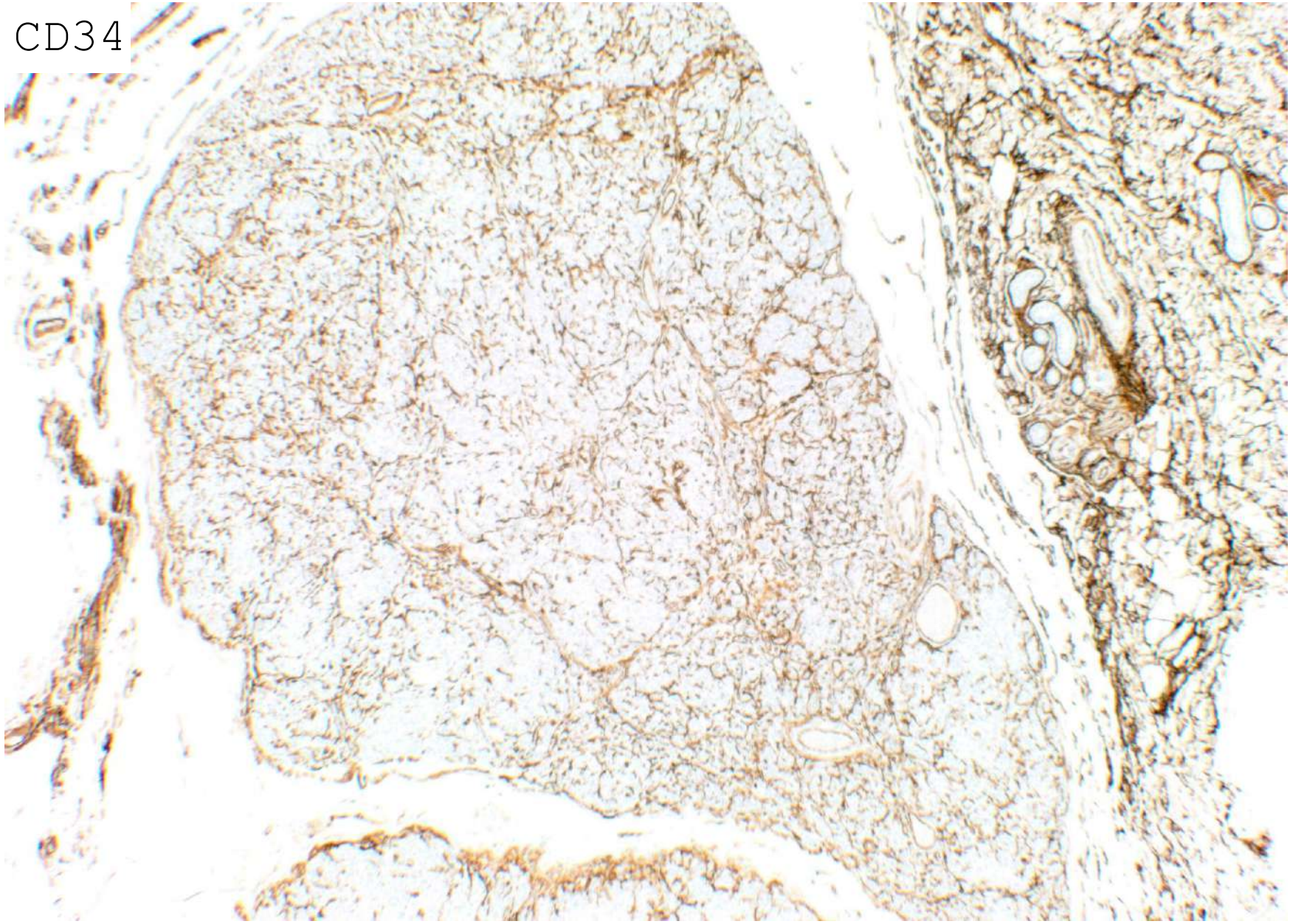






IHC

CD34

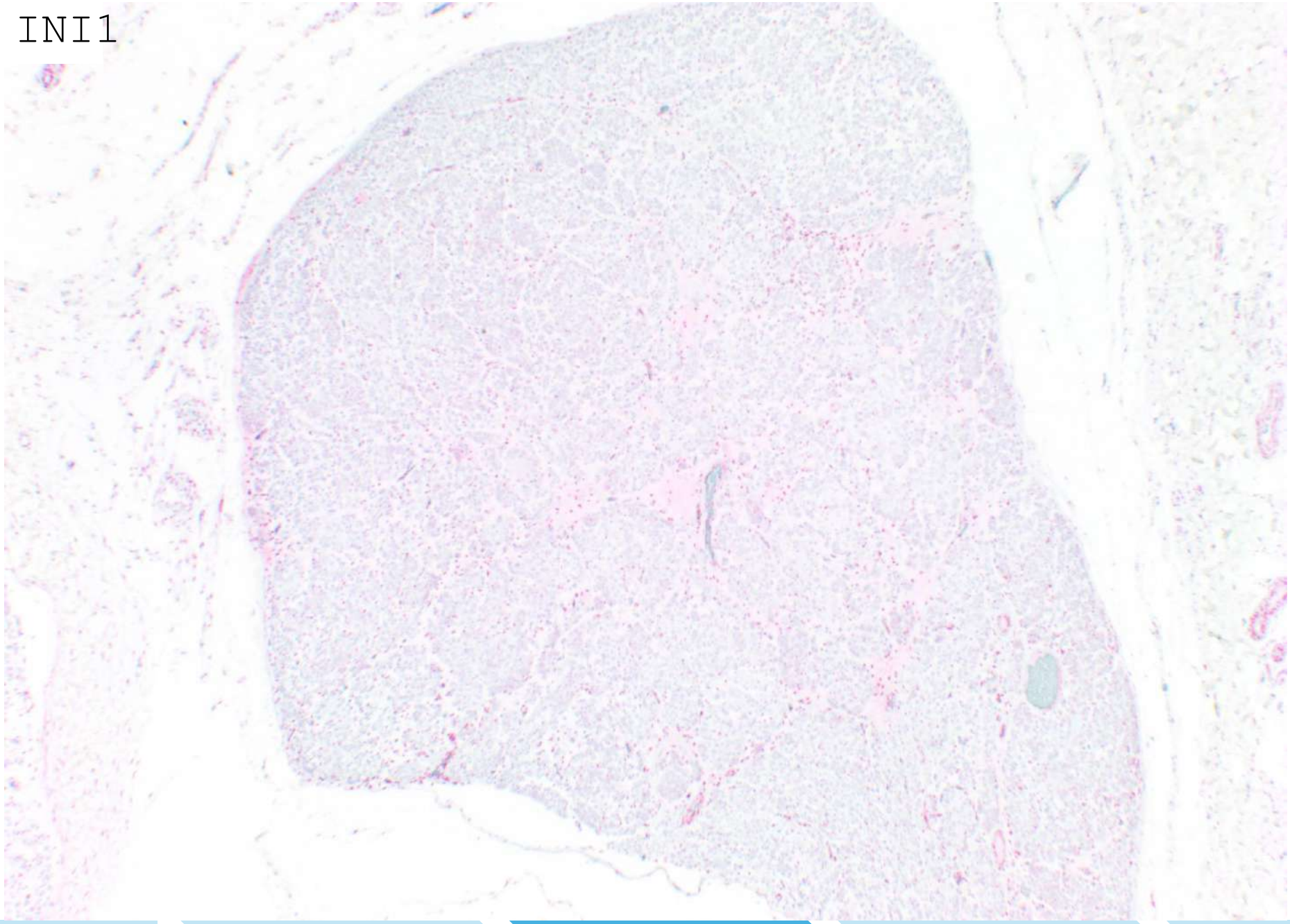


Negative for

- Melan-A
- AE1/AE3
- HMB45
- CK7
- CD31
- GFAP
- CK14
- CK5
- CK8 and 18
- P63
- CD34
- Actin

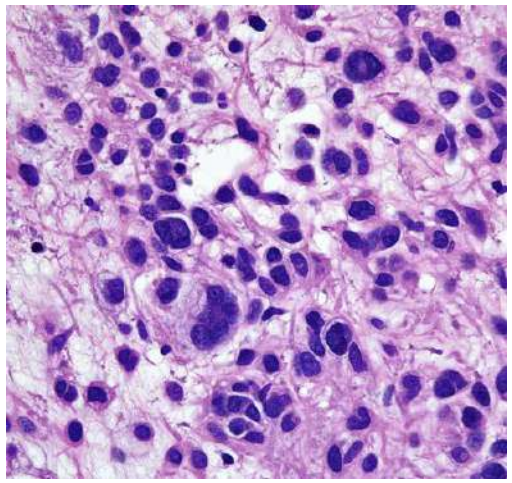
IHC

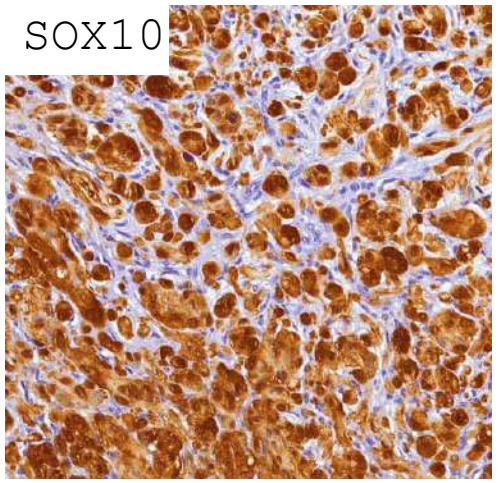
INI1



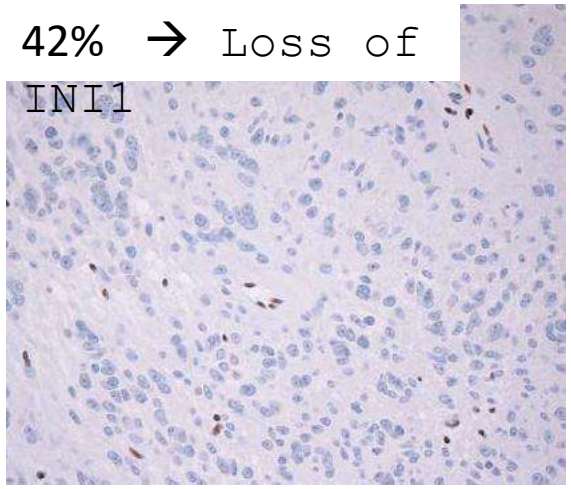
Differential diagnosis

Epithelioid Schwannoma





42% → Loss of INI1

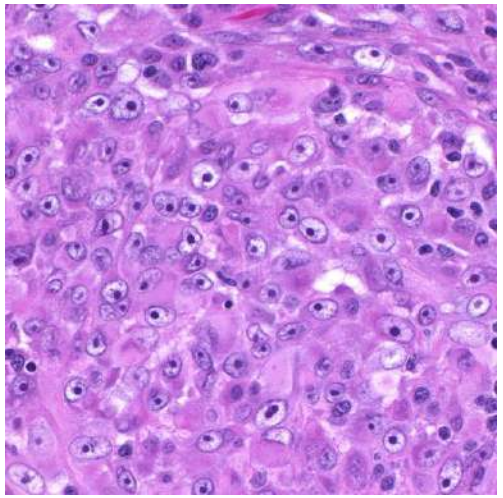


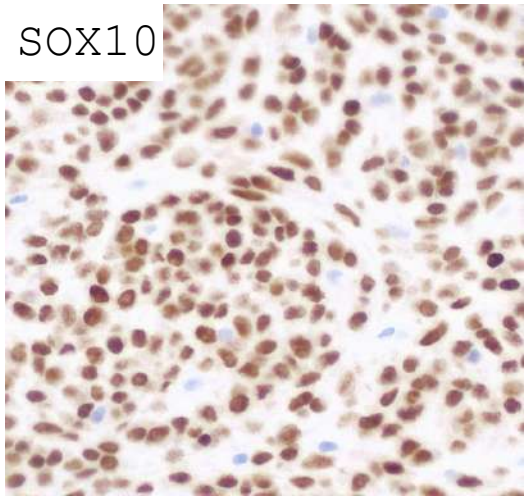
Hart J et al. Am J Surg Pathol. 2016

Jo VY, Fletcher CDM. Am J Surg Pathol. 2017

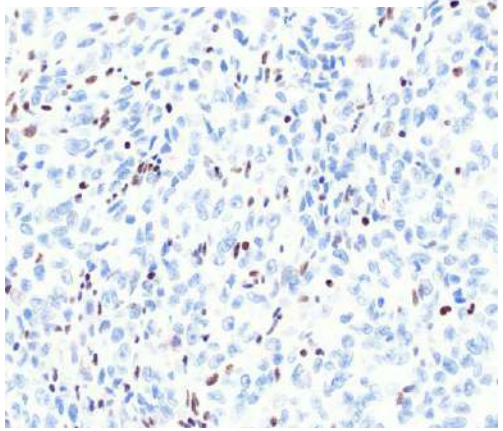
VS

Epitheloid MPNST





67% → Loss of INI1



WHO Classification of Tumours online. Skin Tumours (5th ed.)

Jo VY, Fletcher CD. Am J Surg Pathol. 2015

Differential diagnosis

Epithelioid Schwannoma

- Generally benign clinical course
- Recurrence and malignant transformation are infrequent

VS

Epitheloid MPNST

- Aggressive
- Distant metastases (50% of patients)
- Superficial tumours more favourable prognosis than deep tumours (metastatic rate of 12% vs 30%)

Hart J et al. Am J Surg Pathol. 2016

Jo VY, Fletcher CDM. Am J Surg Pathol. 2017

Differential diagnosis (ihc)

Epithelioid Schwannoma

- Well circumscribed
- Encapsulated
- Dermal and/or subcutaneous
- Lack significant citological atypia

Epitheloid MPNST

- Multilobular
- Usually arises in deep soft tissue
- Usually lacks an EMA-positive capsule
- Diffuse nuclear atypia with large nucleoli
- Mitosis
- Necrosis

- Can have degenerative nuclear atypia
- Atypical variants*

BUT

- Can have mild citological atypia

*
- Nuclear atypia
  - Nuclear enlargement with either nuclear hyperchromasia or prominent nucleoli
  - AND
  - >=3 nuclear size variation among cells
- AND
- Elevated mitotic activity (>3 mitoses/10HPFs)

Jo VY, Fletcher CD. Am J Surg Pathol. 2015

Final diagnosis → **Epithelioid Shwannoma**

Epithelioid Shwannoma

- Adults (median age 45 yo)
- No gender predilection
- Extremities > trunk > viscer
- Dermis and subcutis
- Single lesion

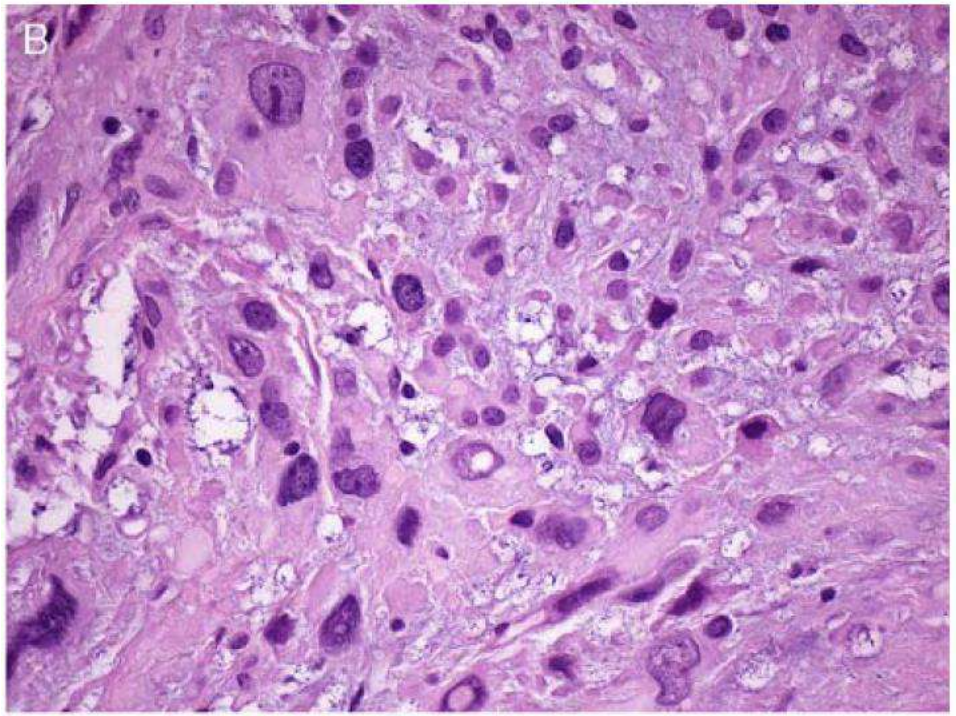
TABLE 2. Clinicopathologic Features of Epithelioid Schwannomas (N = 65)

Features	n/N (%)
Age (median [range]) (y)	45 (13-75)
Sex	
Male	32/65 (49)
Female	33/65 (51)
Anatomic site	
Lower extremity	15/65 (23)
Upper extremity	20/65 (31)
Trunk	13/65 (20)
Shoulder/axilla	2/65 (3)
Buttock	2/65 (3)
Groin	1/65 (1.5)
Scalp	1/65 (1.5)
Gastrointestinal	8/65 (12)
Spinal cord	2/65 (3)
Uterus	1 (1.5)
Anatomic depth	
Somatic tumors	54/65 (83)
Dermal/subcutaneous	53/54 (98)
Deep (subfascial)	1/54 (2)
Visceral	8/65 (17)
Tumor size (median [range]) (cm)	1.2 (0.4-22.7)

Modified from Jo VY, Fletcher CDM. Am J Surg Pathol. 2017

Epithelioid Shwannoma

- Median mitotic count: 1/10 H
- Degenerative atypia: 35%
- Cytologic atypia: 11%



Focally striking cytologic atypia

Association with a peripheral nerve	11/65 (17)
Presence of a capsule (among somatic tumors)	53/54 (98)
Stromal features	
Myxoid	49/65 (75)
Hyalinization	30/65 (46)
Features of conventional schwannoma	
Areas with spindle morphology	29/65 (45)
Antoni B or Verocay bodies	8/65 (12)
Hyalinized thick-walled vessels	16/65 (25)
Mitotic count (median count [range]) (per 10 HPFs)	1 (0-9)
Degenerative nuclear atypia	23/65 (35)
Cytologic atypia	7/65 (11)
Transformation to epithelioid MPNST	3/65 (5)
Follow-up (median [range]) (mo)	37 (1-108)
Alive, NED*	30/31 (97)
Recurrence	1/30 (3)
Metastasis	0/31

*Including 3 cases with cytologic atypia, 1 of which with transformation to epithelioid MPNST.
NED indicates no evidence of disease.

Modified from Jo VY, Fletcher CDM. Am J Surg Pathol. 2017

Epithelioid Shwannoma

Atypical variants suggest a morphologic continuum with low-grade epithelioid malignant peripheral nerve sheath tumor

TABLE 3. Clinicopathologic Features of 7 Epithelioid Schwannomas With Significant Atypia

Feature	n/N (%)
Age (median [range]) (y)	39 (20-64)
Sex	
Male	3/7 (43)
Female	4/7 (57)
Anatomic site	
Lower extremity	2/7 (29)
Upper extremity	3/7 (43)
Trunk	1/7 (14)
Buttock	1/7 (14)
Anatomic depth	
Dermal/subcutaneous	6/7 (86)
Deep (subfascial)	1/7 (14)
Tumor size (median [range]) (cm)	1.7 (1-5.5)
Association with a peripheral nerve	2/7 (29)
Presence of a capsule (among somatic tumors)	7/7 (100)
Stromal features	
Myxoid	6/7 (86)
Hyalinization	2/7 (29)
Features of conventional schwannoma	
Areas with spindle morphology	4/7 (57)
Antoni B or Verocay bodies	1/7 (14)
Hyalinized thick-walled vessels	3/7 (43)
Mitotic count (median count [range]) (per 10 HPFs)	3 (1-9)
Transformation to epithelioid MPNST	3/7 (43)
Follow-up (mo) (n = 3)	3, 7, and 46
Recurrence	0/3
Metastasis	0/3

Jo VY, Fletcher CDM. Am J Surg Pathol. 2017

TABLE 1. Characteristics of Epithelioid Schwannomas With Atypical Features

Case No.	Age (y)/ Sex	Location (Tissue)	Size (cm)	Follow-up (mo)
9	20/M	Arm (sq)	U	ANED (170)
12	26/M	Lip (sq)	1.7	Lost
15	25/M	Forearm (sq)	U	ANED (95)
16	46/M	Leg (sq)	U	Lost
19	31/F	Knee (sq)	2.5	ANED (83)
27	31/M	Forearm (sq)	2.3	Lost
29	24/M	Ankle (d)	1	Lost
30	27/M	Hand (sq)	2	ANED (101)
35	23/M	Scalp (sq)	3.2	ANED (78)
47	75/M	Back (u)	U	ANED (18)
48	43/M	Hip (sq)	3.4	ANED (28)
49	54/M	Foot (sq)	1	ANED (38)
51	23/M	Forearm (sq)	U	ANED (25)

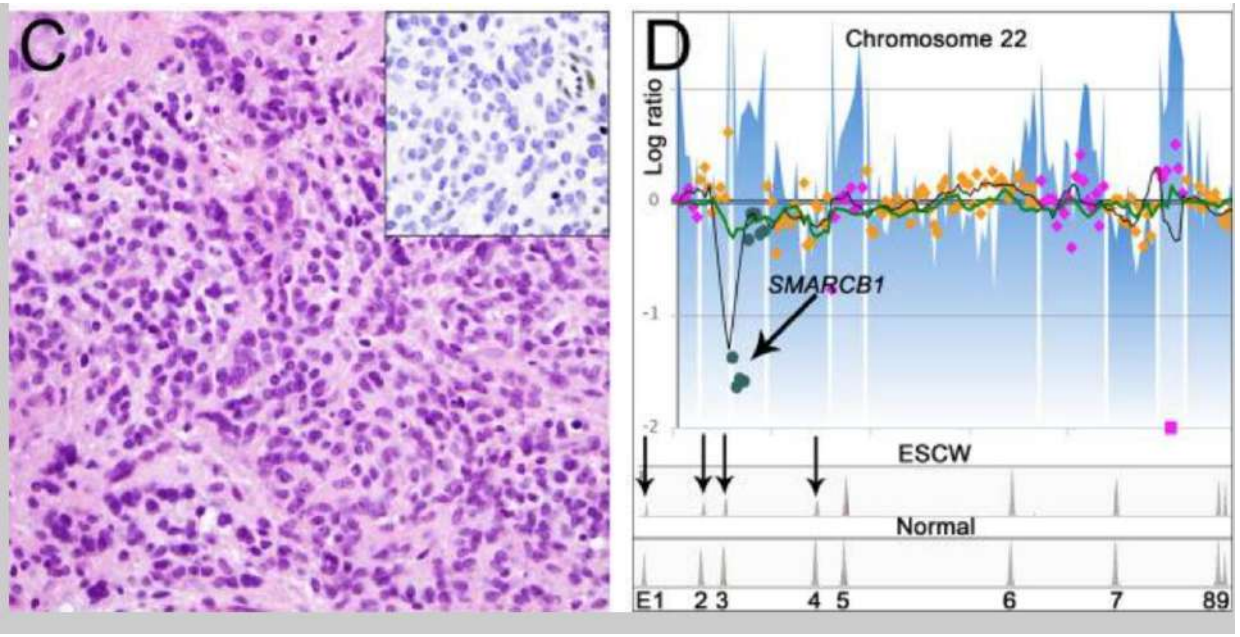
ANED indicates alive with no evidence of disease; d, dermis; F, female; Lost, lost to follow-up; M, male; mo, length of follow-up in months; sq, subcutaneous; u, undetermined tissue site; U, unknown tumor size.

Hart J et al. Am J Surg Pathol. 2016

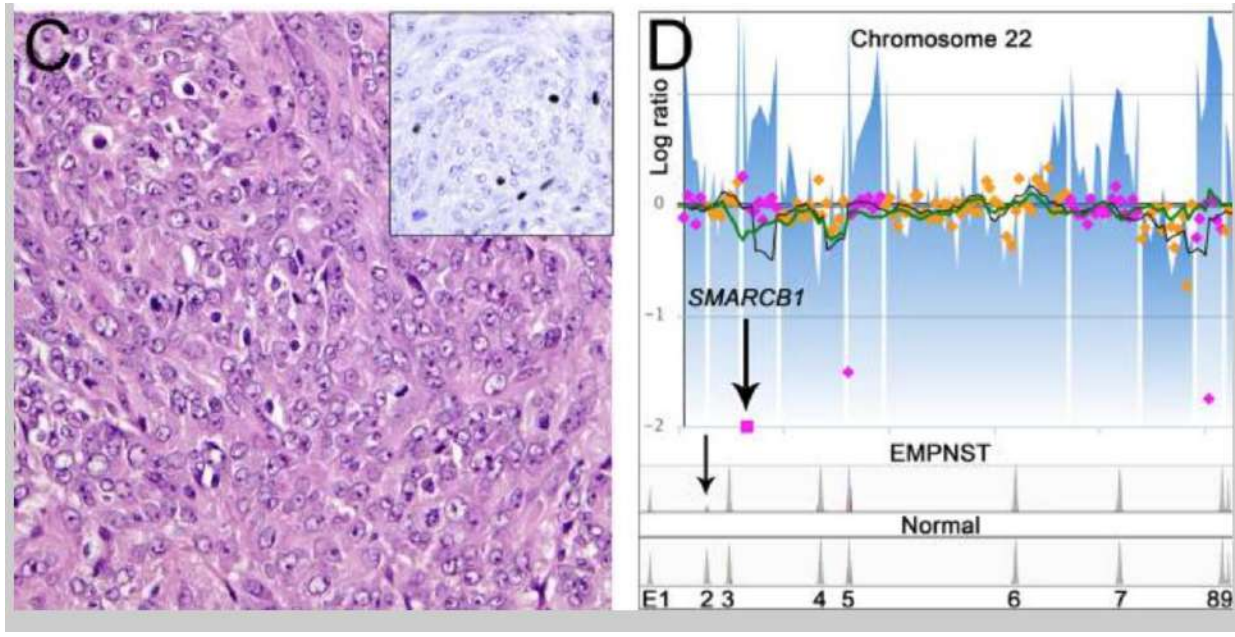
Epithelioid Shwannoma

- SMARCB1 genomic inactivation in both entities → **homozygous** deletion, nonsense, frameshift or splice site mutations

ES



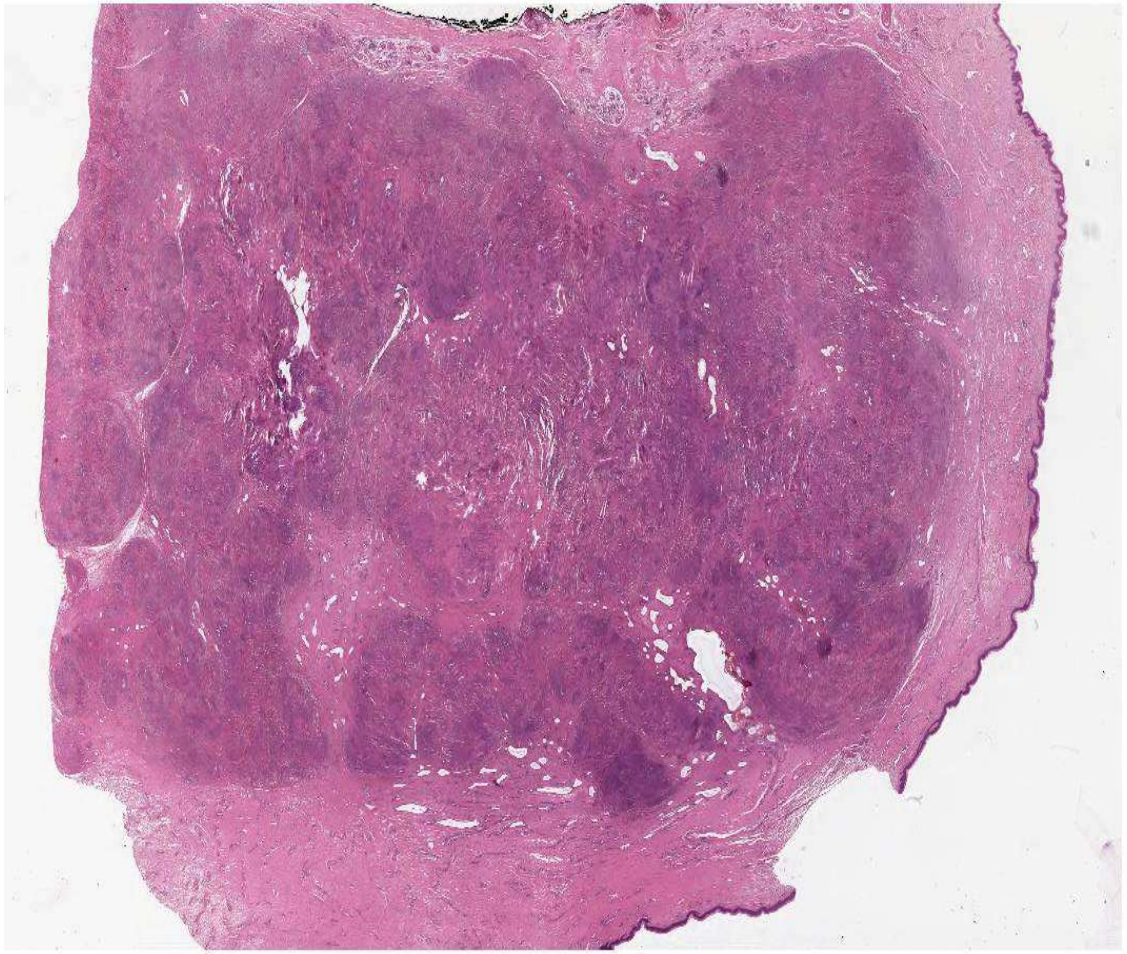
EMPNST

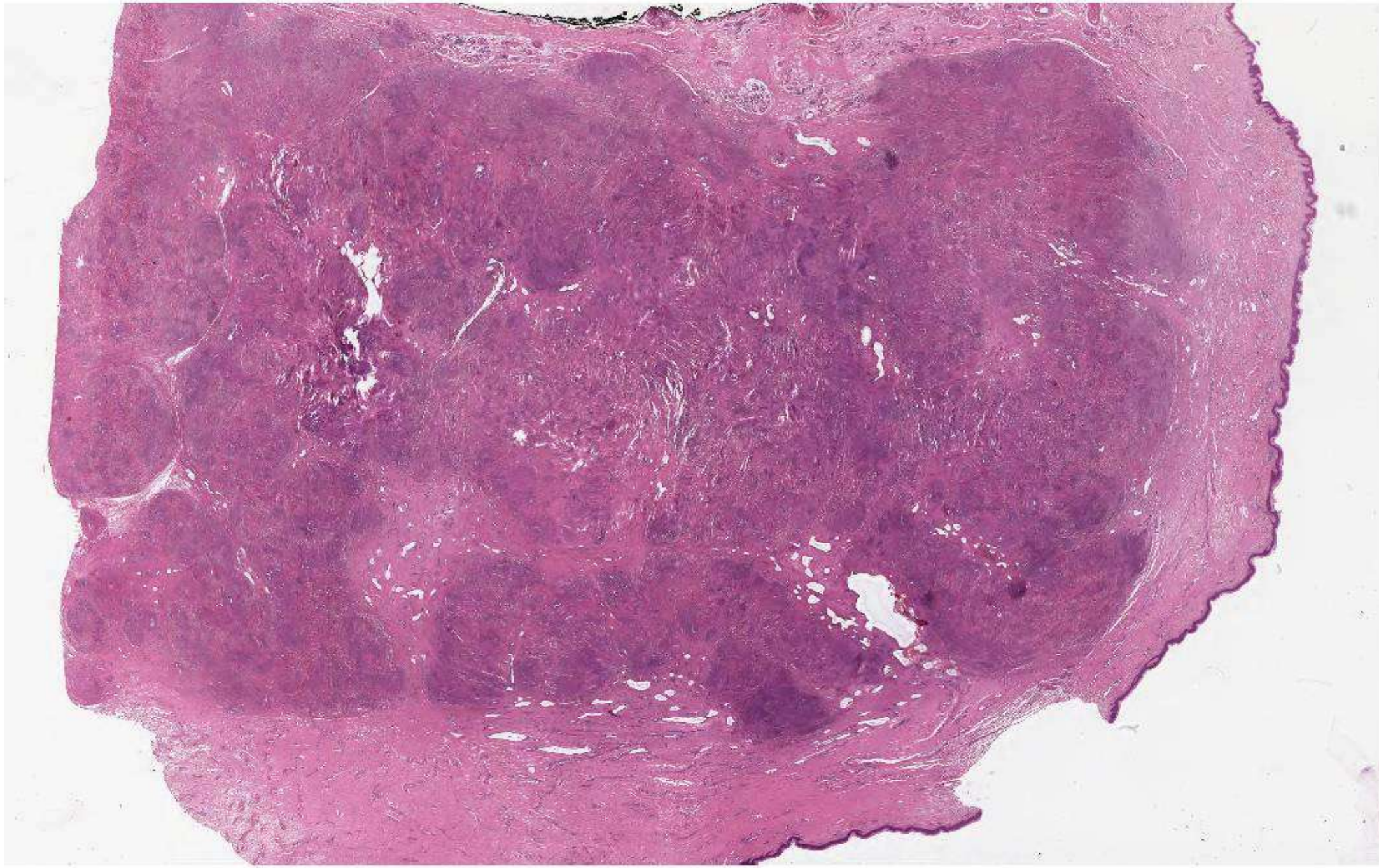


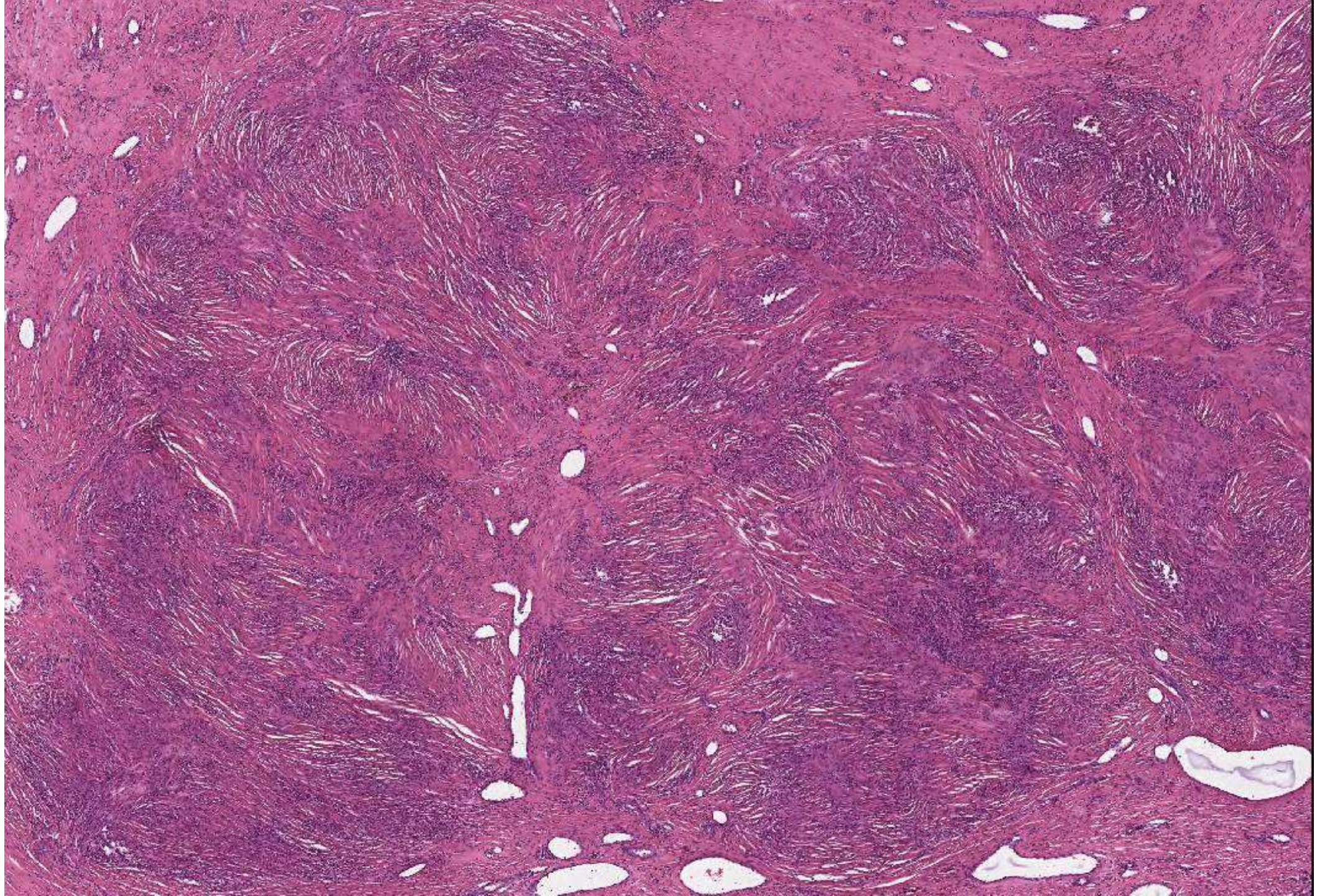
Schaefer IM, Dong F, Garcia EP, Fletcher CDM, Jo VY. Am J Surg Pathol. 2019

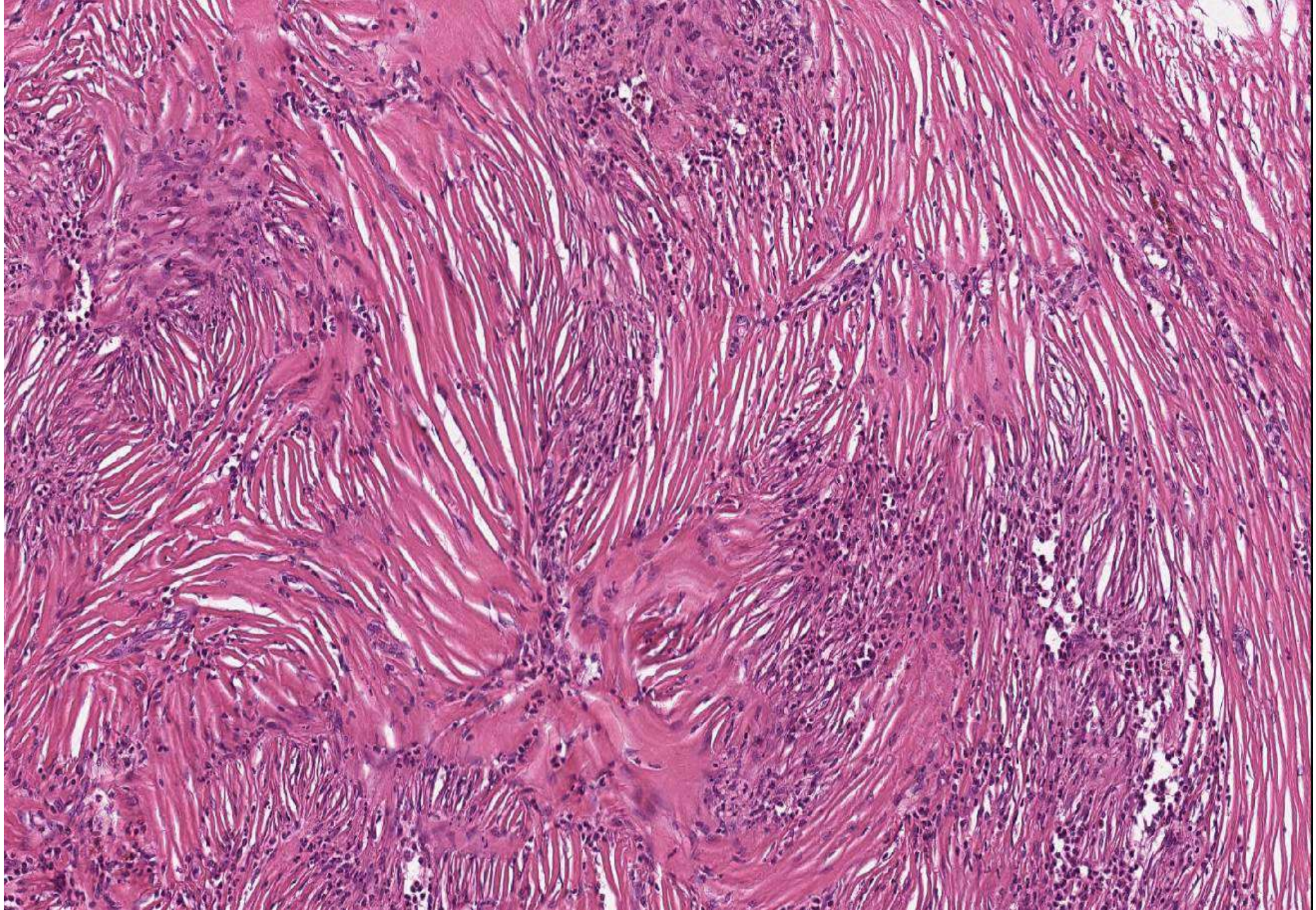
Case 18

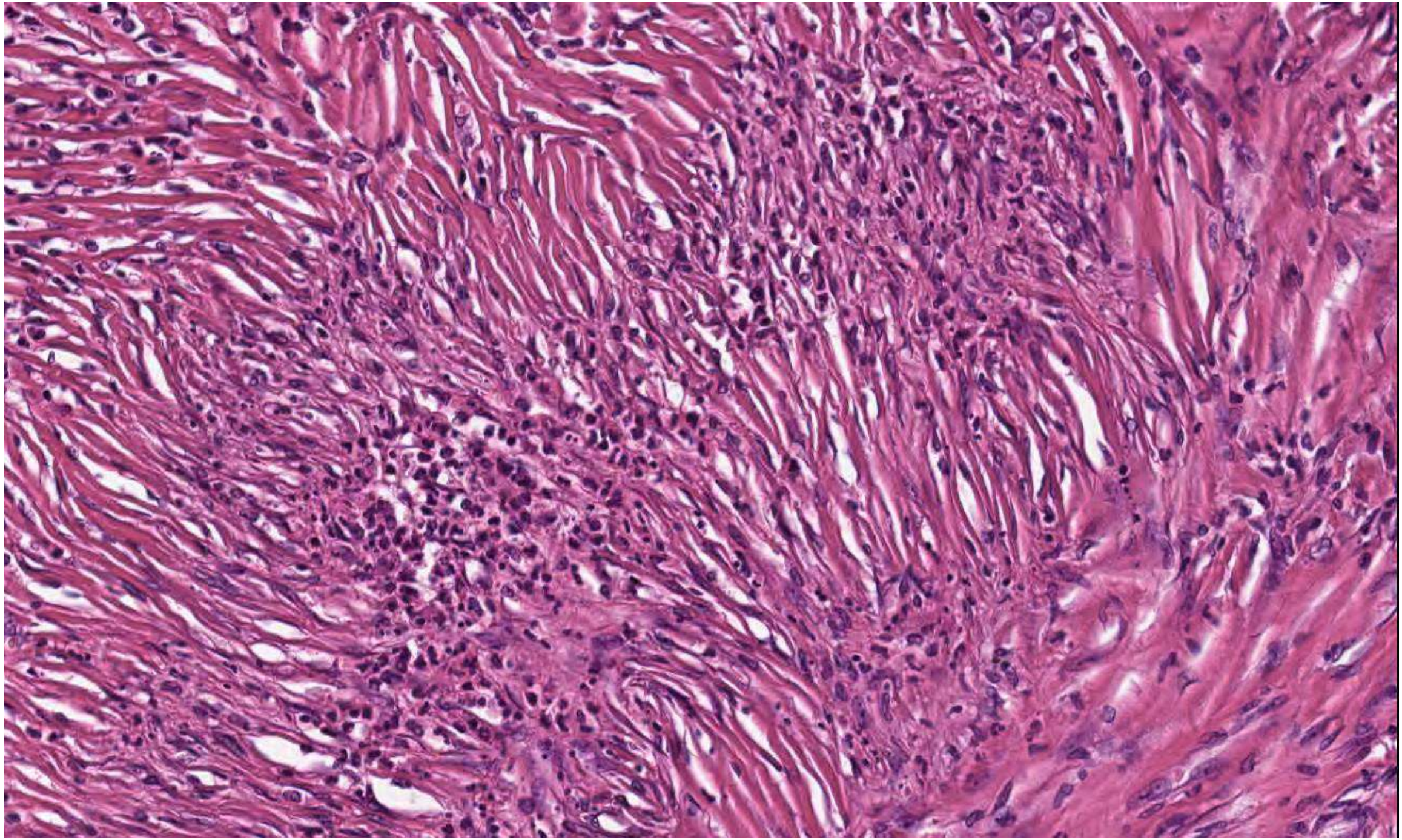
78-yr old male - DM type 2, Parkinson disease, and chronic renal failure. For two years, nodular lesions on elbows and ankles

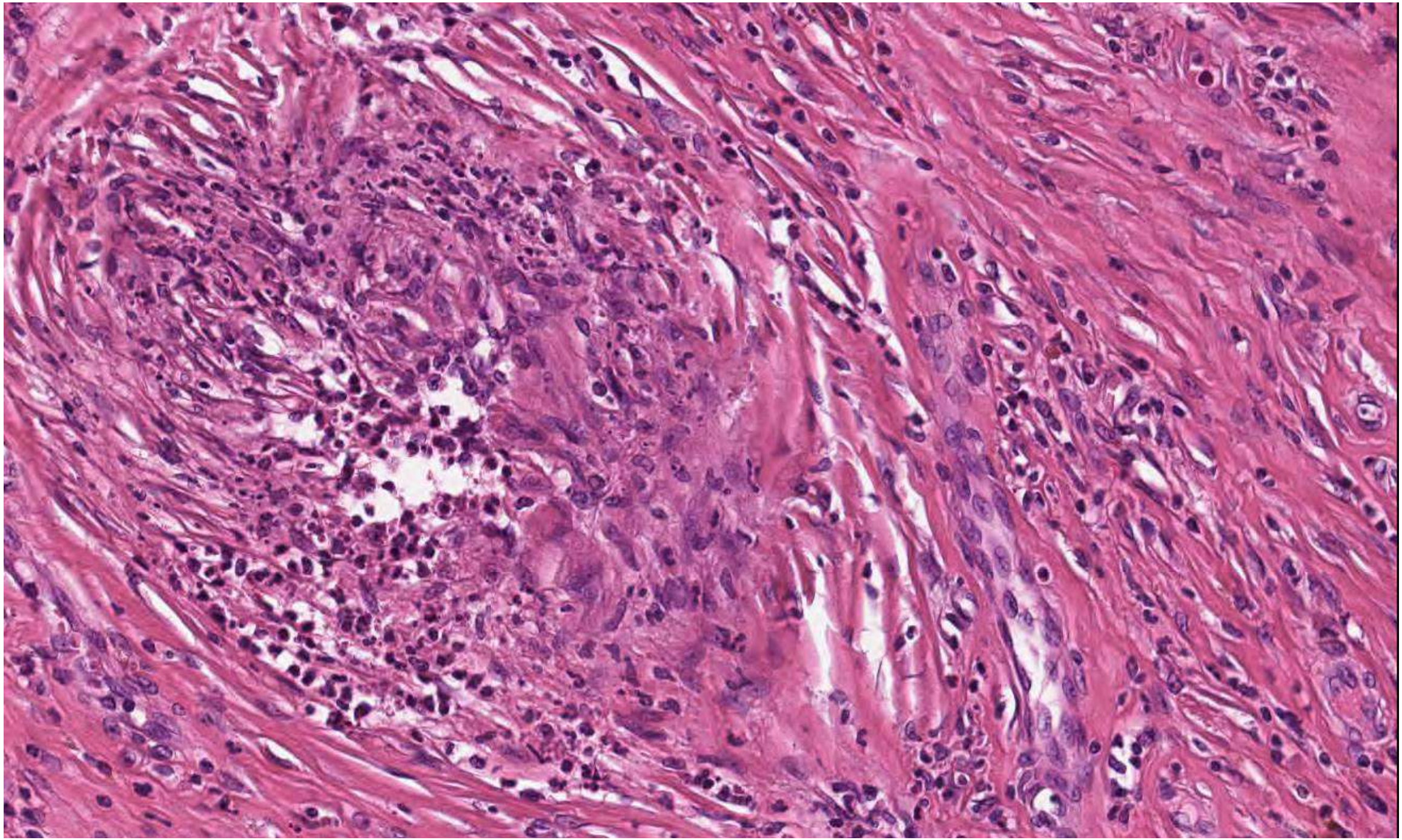












Dx: Erythema elevatum diutinum, late stage

Am J Dermatopathol. 2017 Dec 28. doi: 10.1097/DAD.0000000000001088. [Epub ahead of print]

Late-Stage Erythema Elevatum Diutinum Mimicking a Fibroblastic Tumor: A Potential Pitfall.

Llamas-Velasco M[1], Stengel B[2], Pérez-González YC[3], Mentzel T[4].

Author information

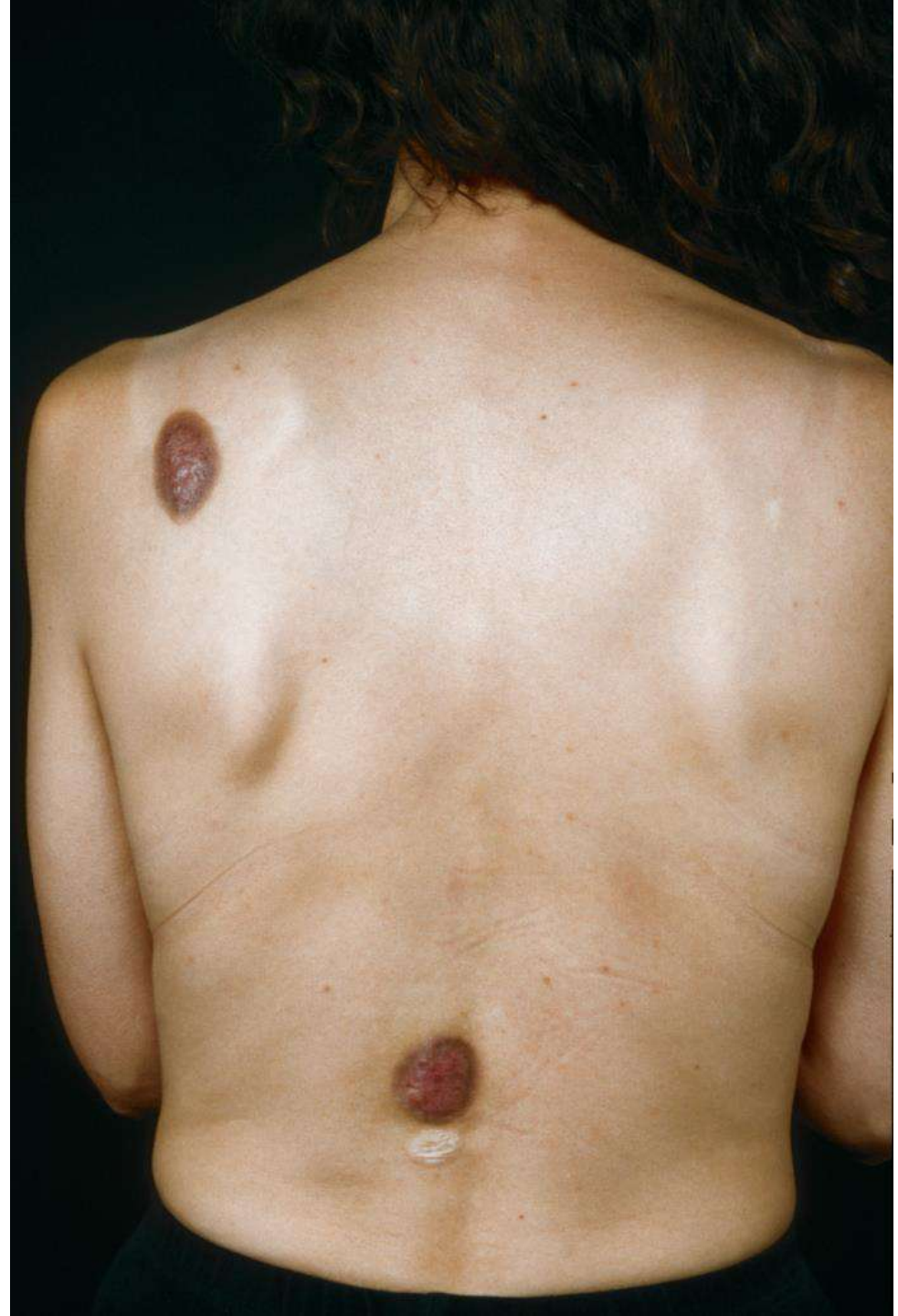
Abstract

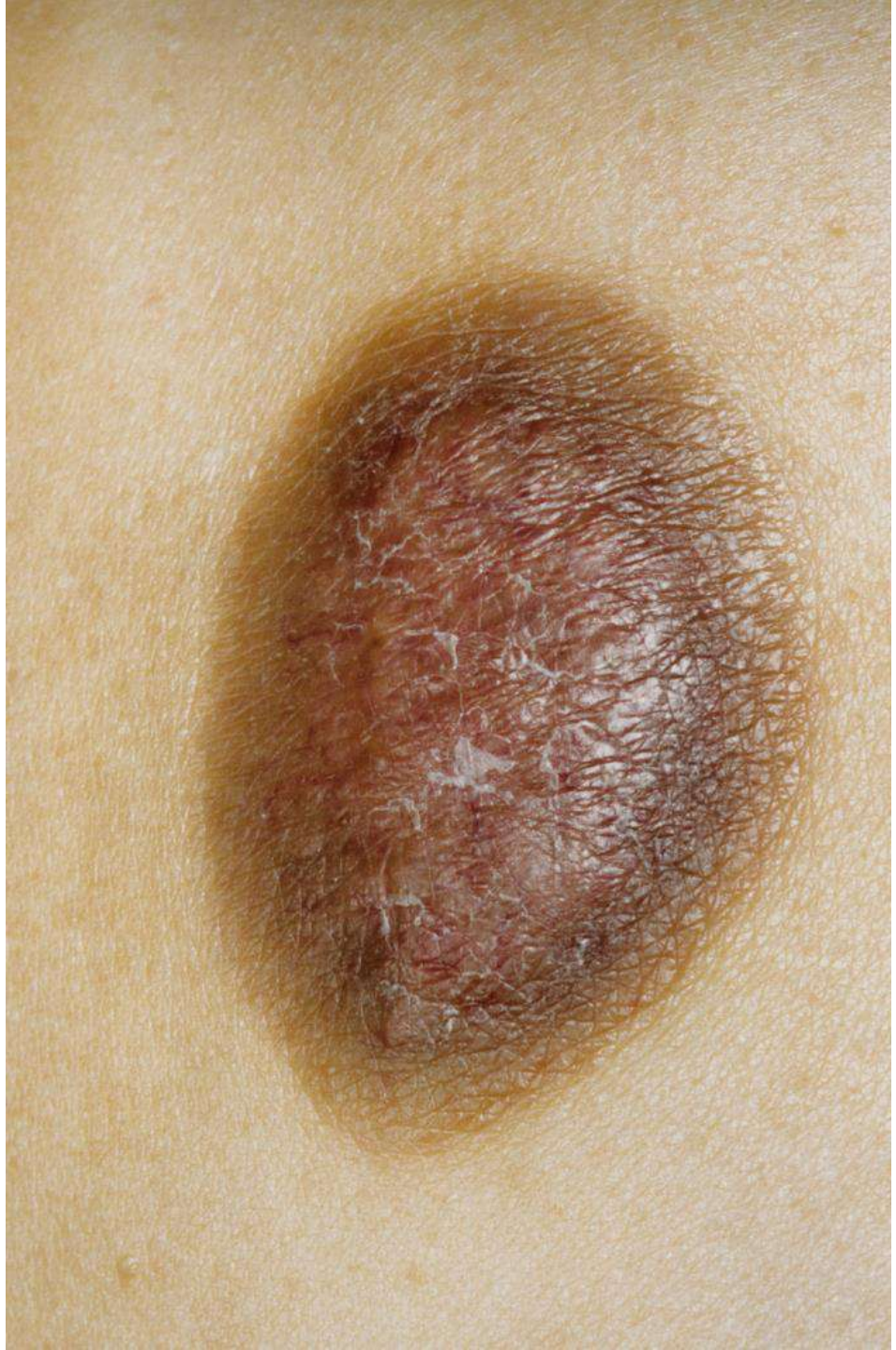
Erythema elevatum diutinum (EED) is a rare dermatosis with evolving histopathological features that vary according to the age of the lesions, with a variable fibrosis and a fascicled proliferation of spindle cells in late phases. The authors present an otherwise healthy 57-year-old woman with multiple indurated nodules on the inner aspect of both feet. Skin biopsy showed storiform interlacing bundles of spindled cells with plump nuclei and some areas with neutrophils and leukocytoclasia. CD34 and S100 were negative. This case is noteworthy clinically due to its location and its histopathological presentation that comprises a wide differential diagnosis, including inflammatory pseudotumor, dermatofibrosarcoma protuberans, superficial nodular fasciitis, hyalinized leiomyoma, sclerosing spindle cell perineuroma, and sclerotic fibroma. The authors have reviewed the main histopathological and immunohistochemical features that help in the differential diagnosis of this rare variant of EED. A careful search for leukocytoclasia and neutrophilic vasculitis is mandatory to establish the right diagnosis of nodular or late-stage EED and avoid the pitfall of considering this a neoplastic process.

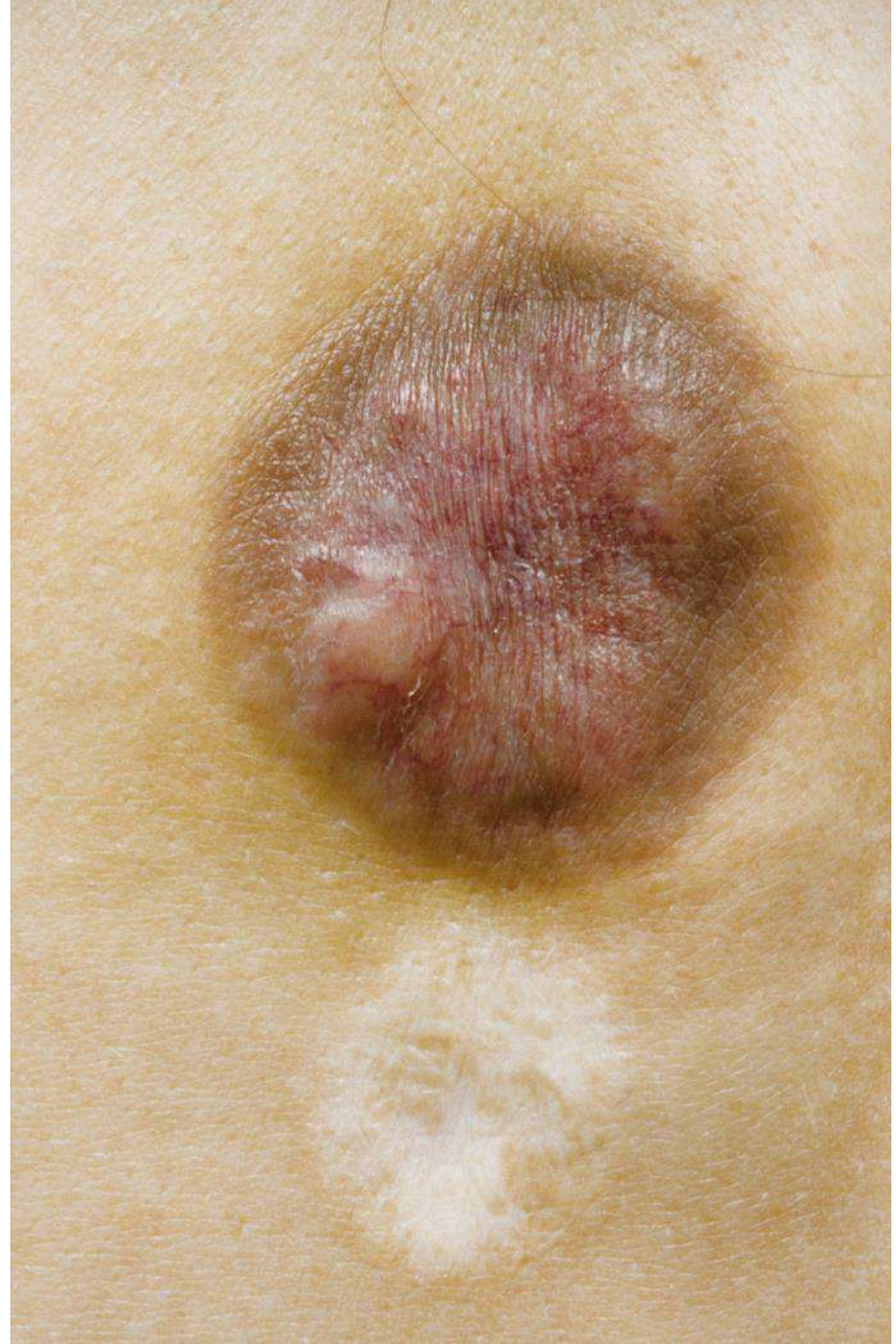
Chronic localised vasculitis syndromes

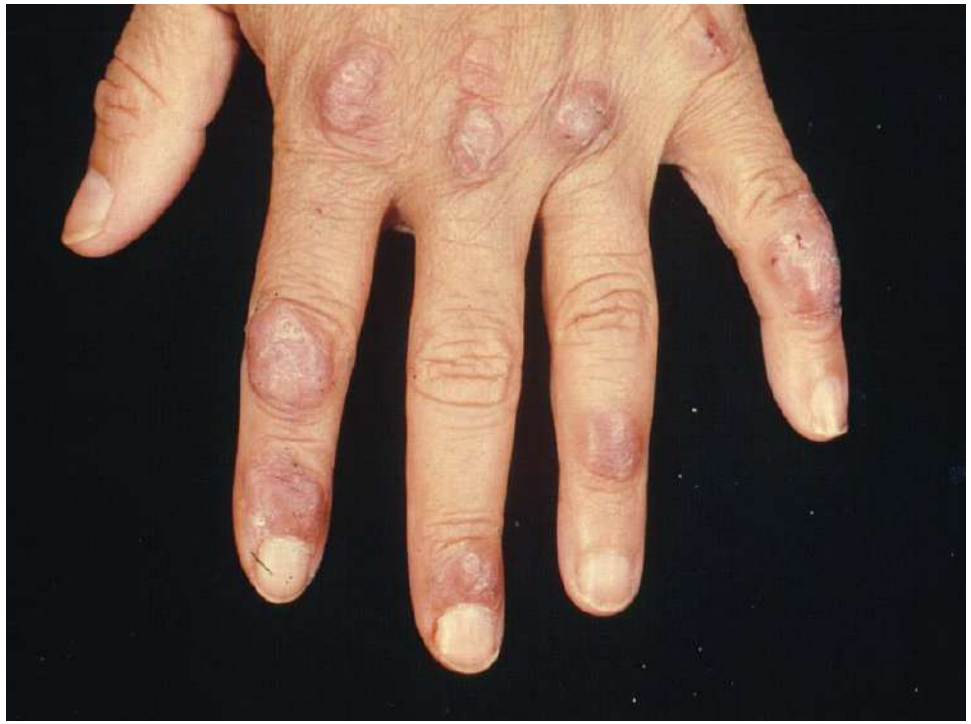
Erythema elevatum diutinum

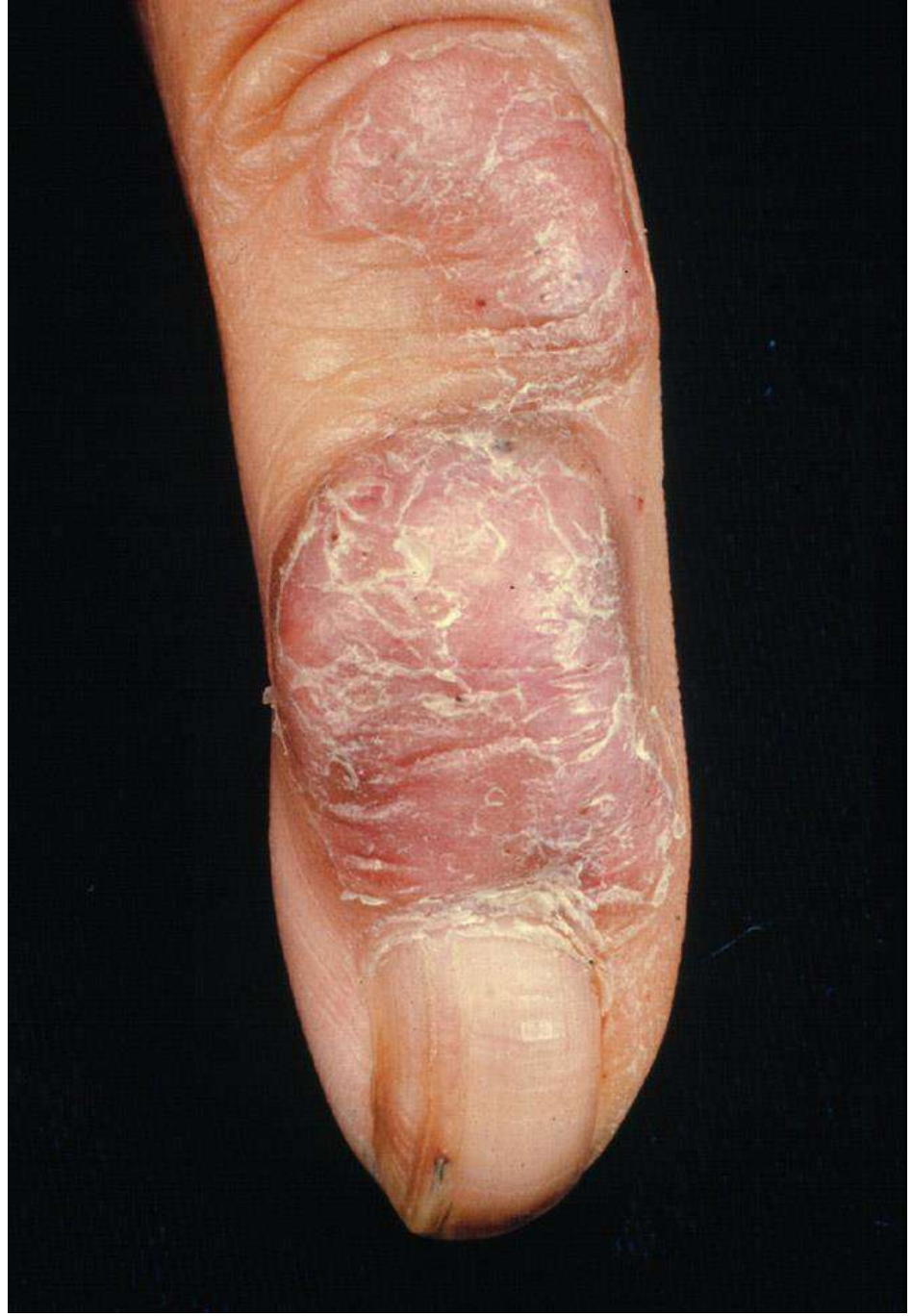
- Extensor surfaces, symmetrical
- Paraproteinaemia, IgA, IgA ANCA
- Polycythaemia rubra vera, hairy cell leukaemia
- Rheumatoid, SLE, Wegener, Crohn
- HIV

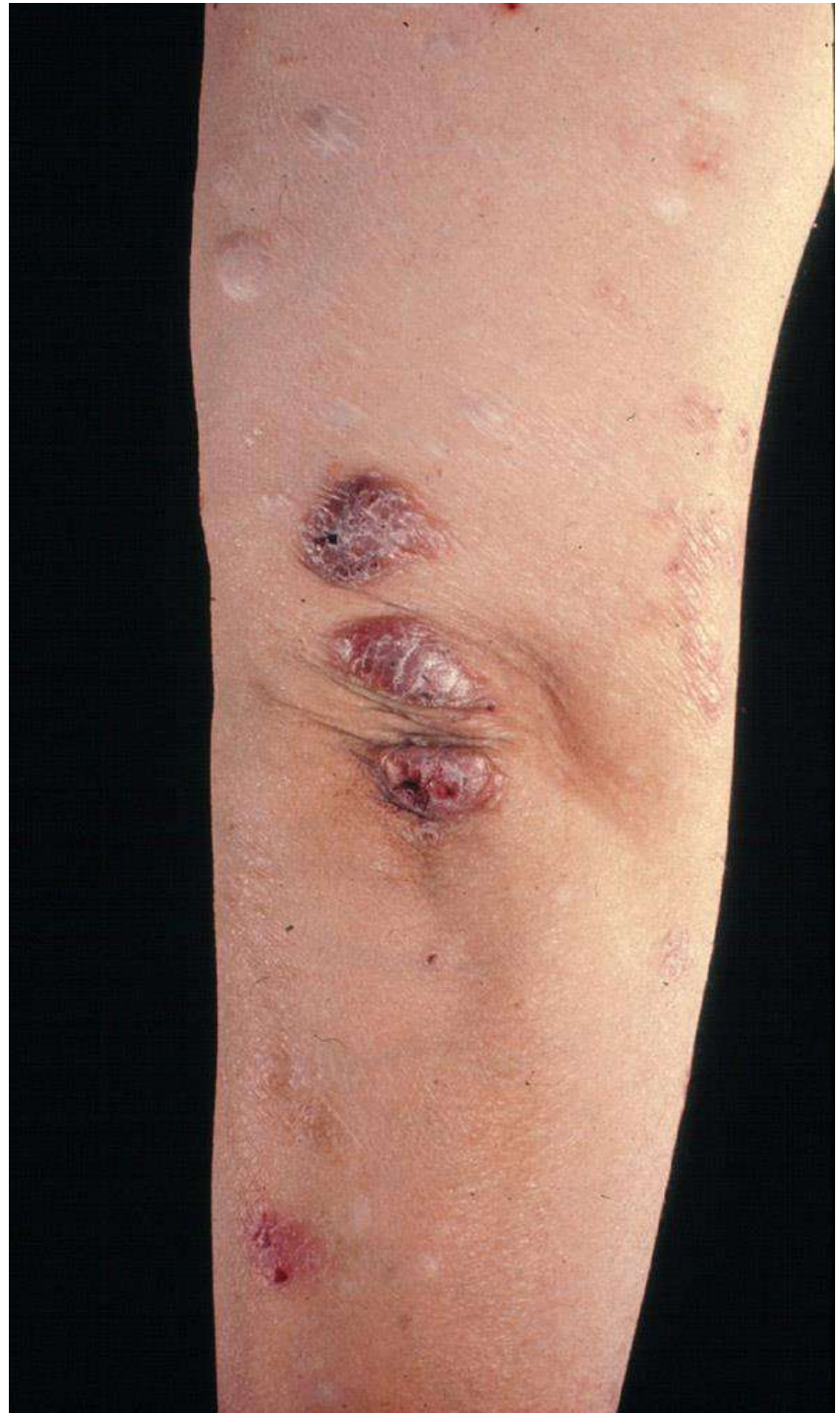


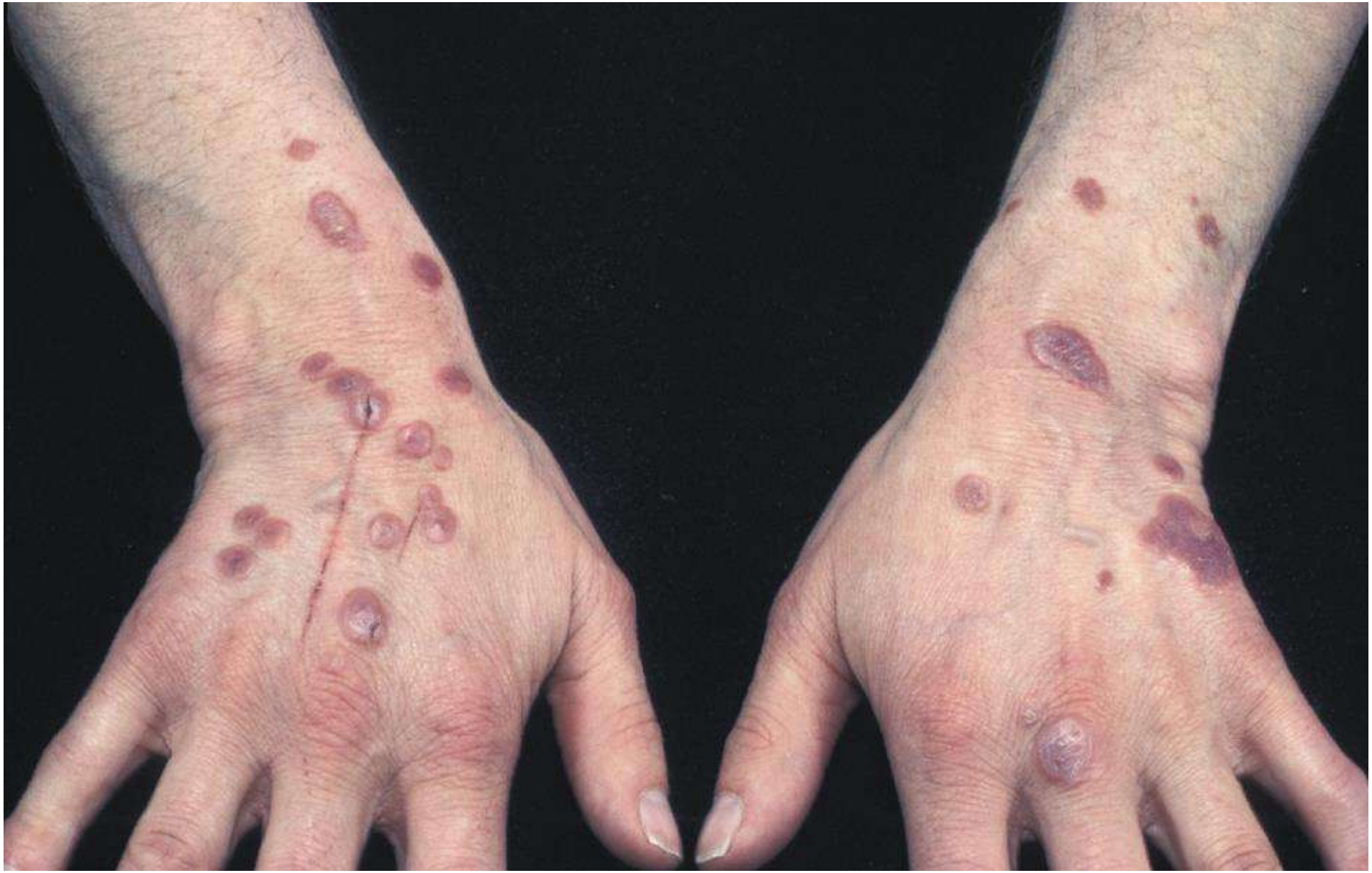


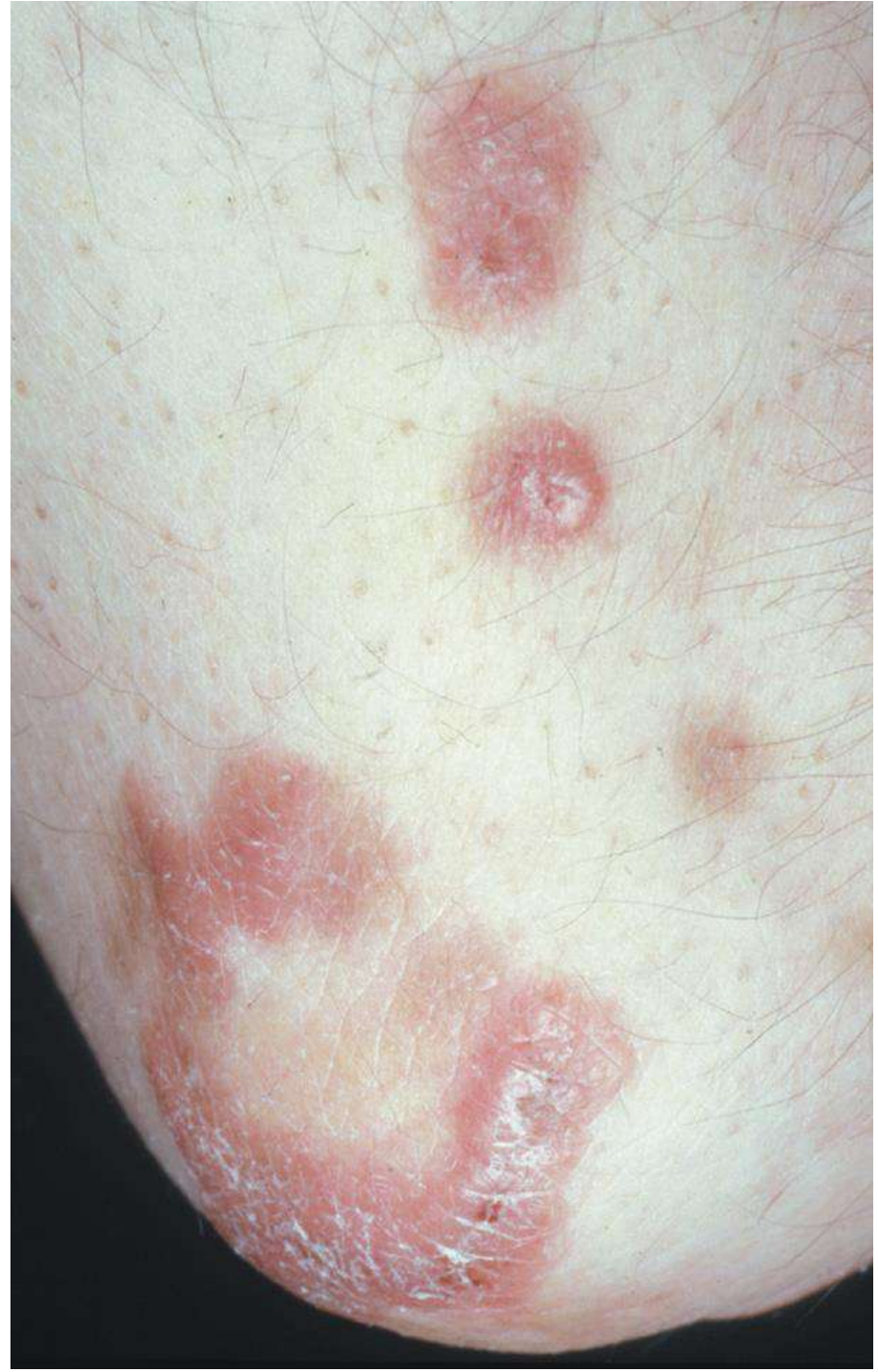


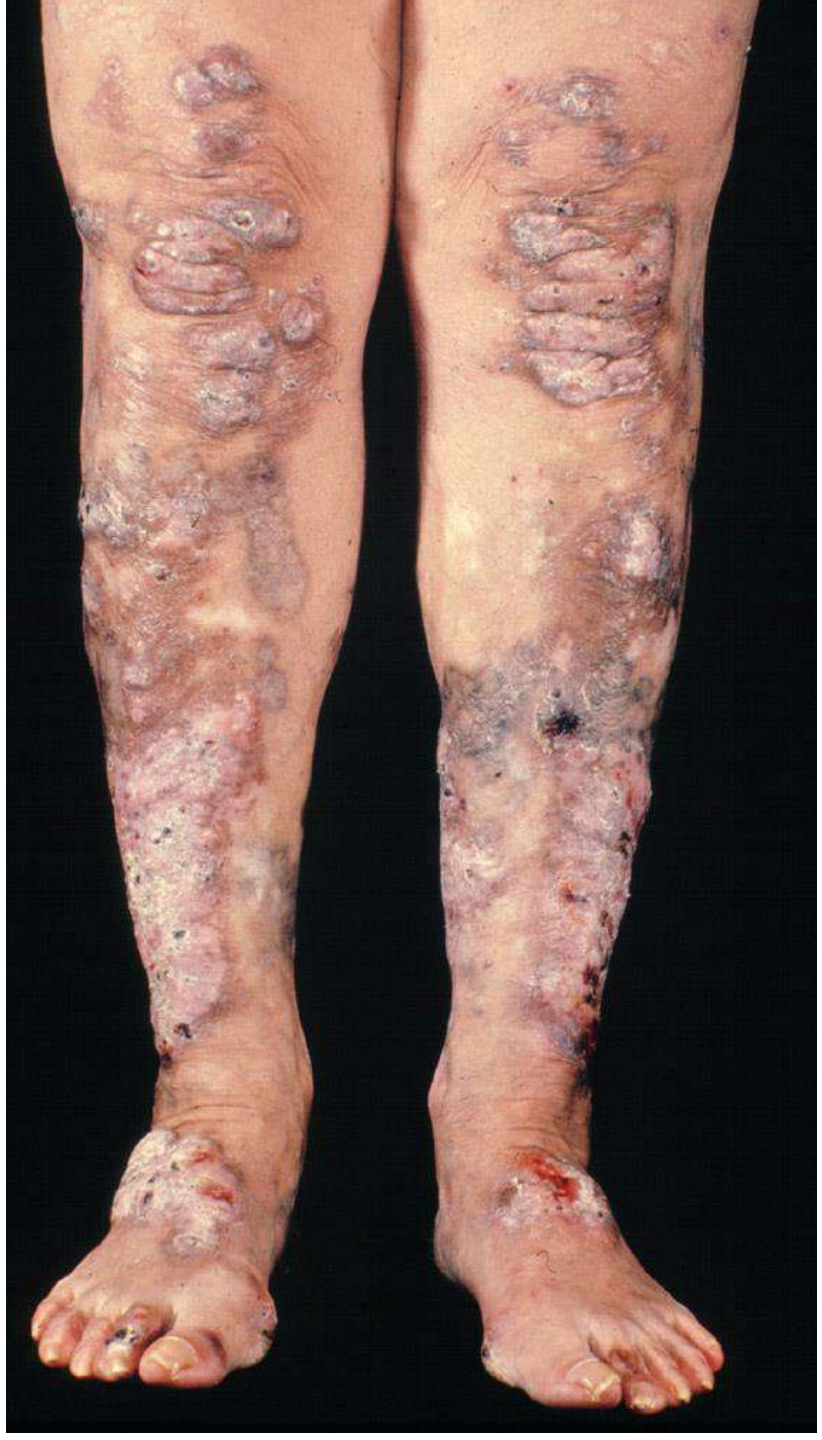


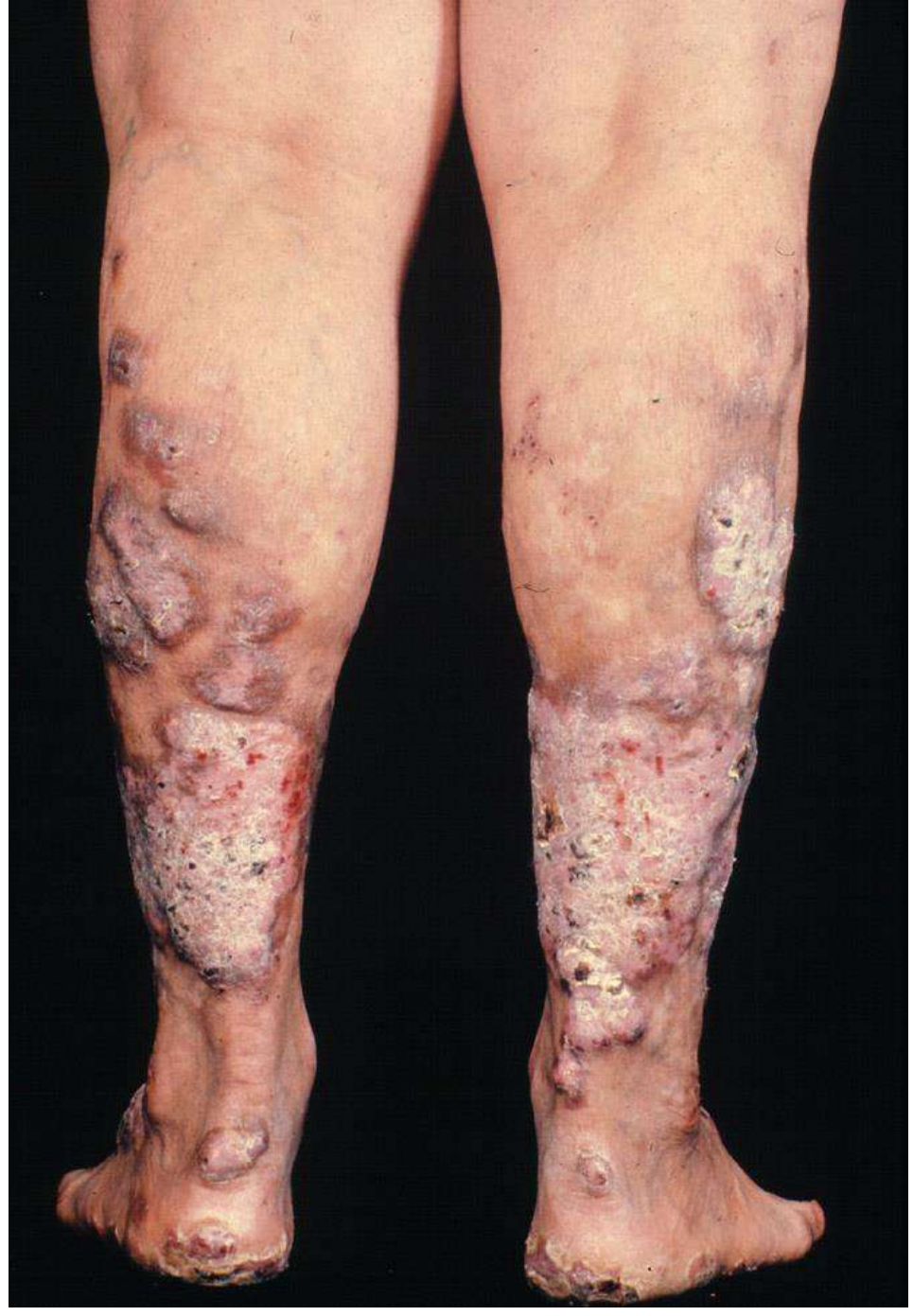


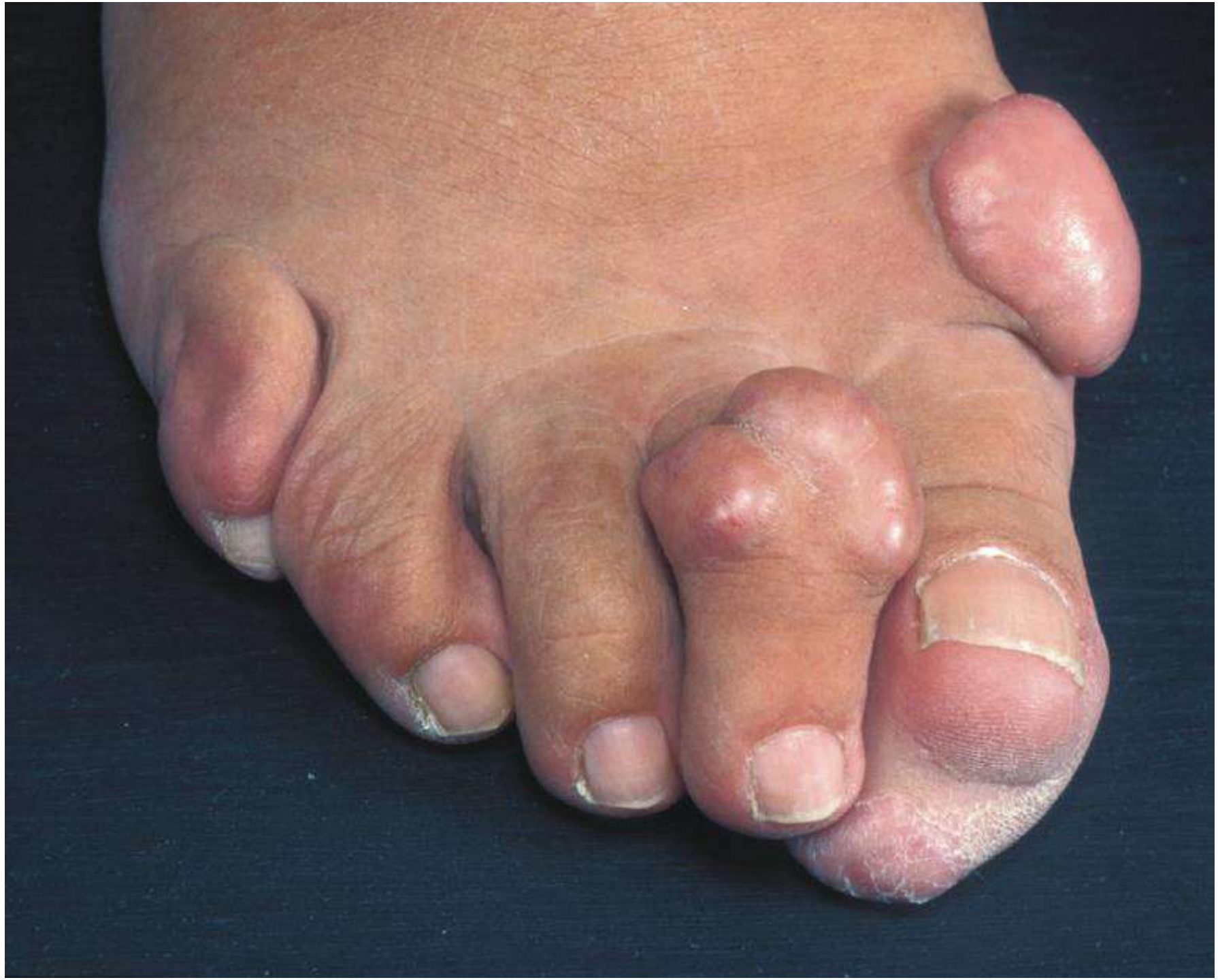


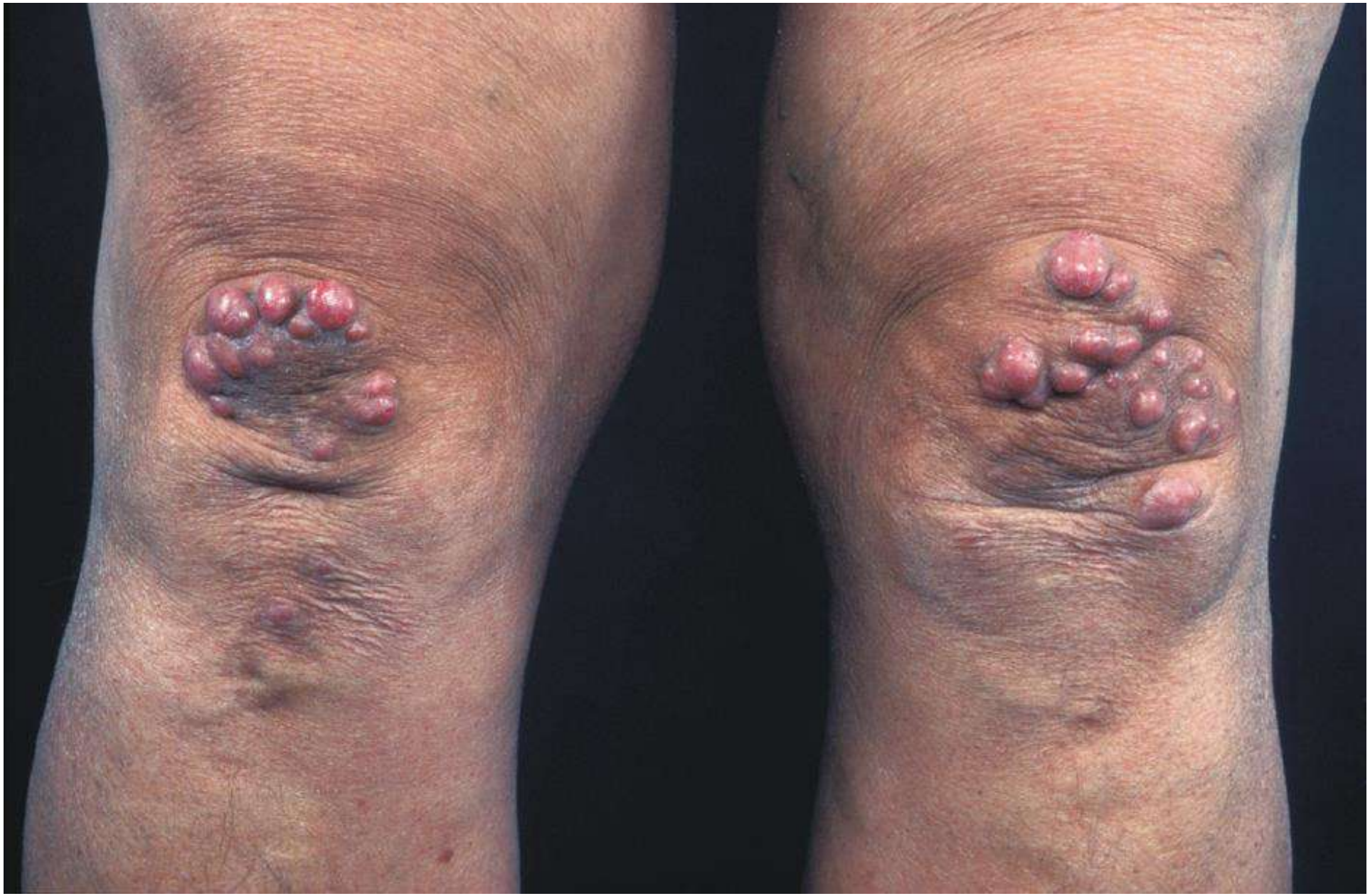






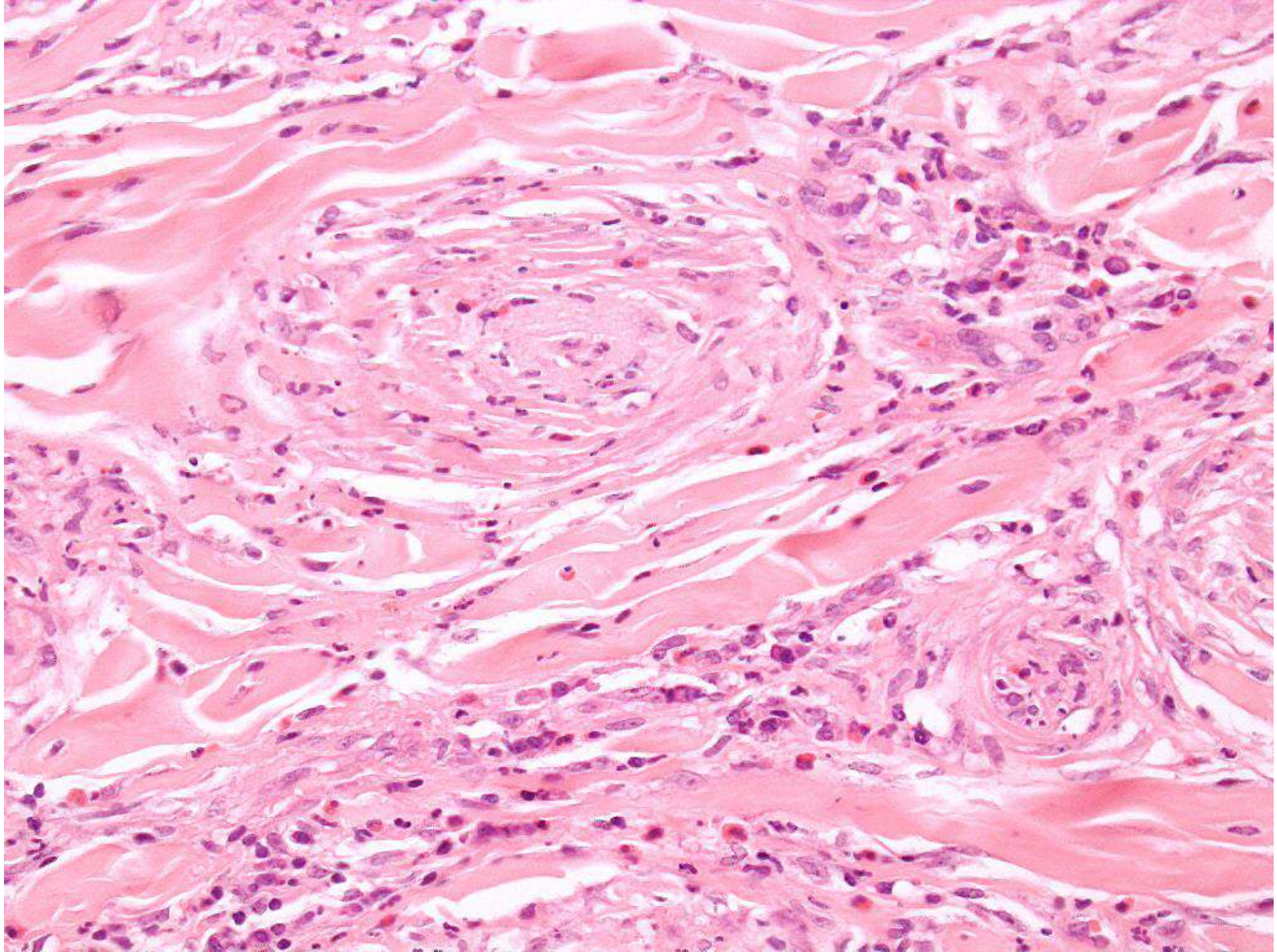


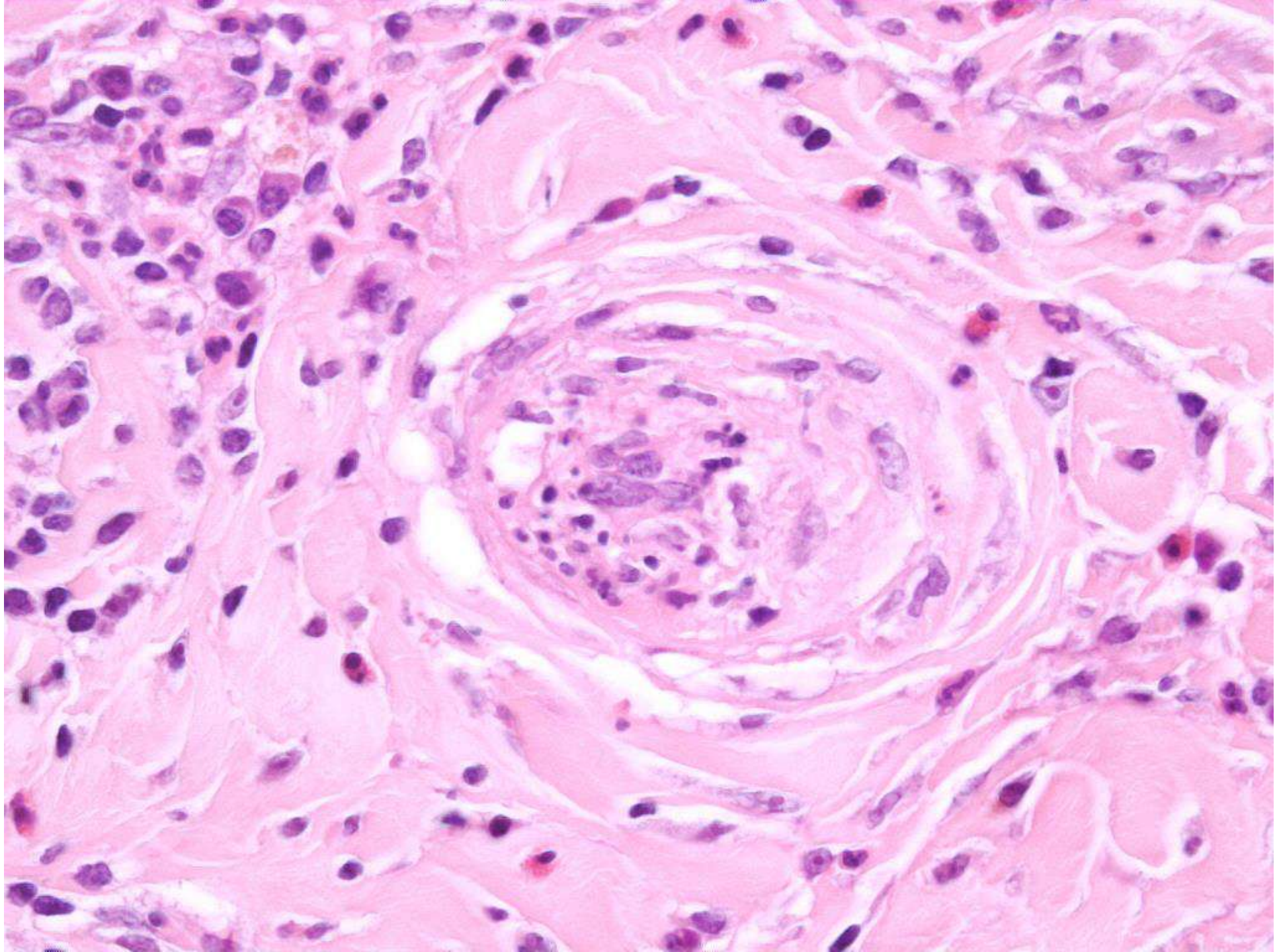


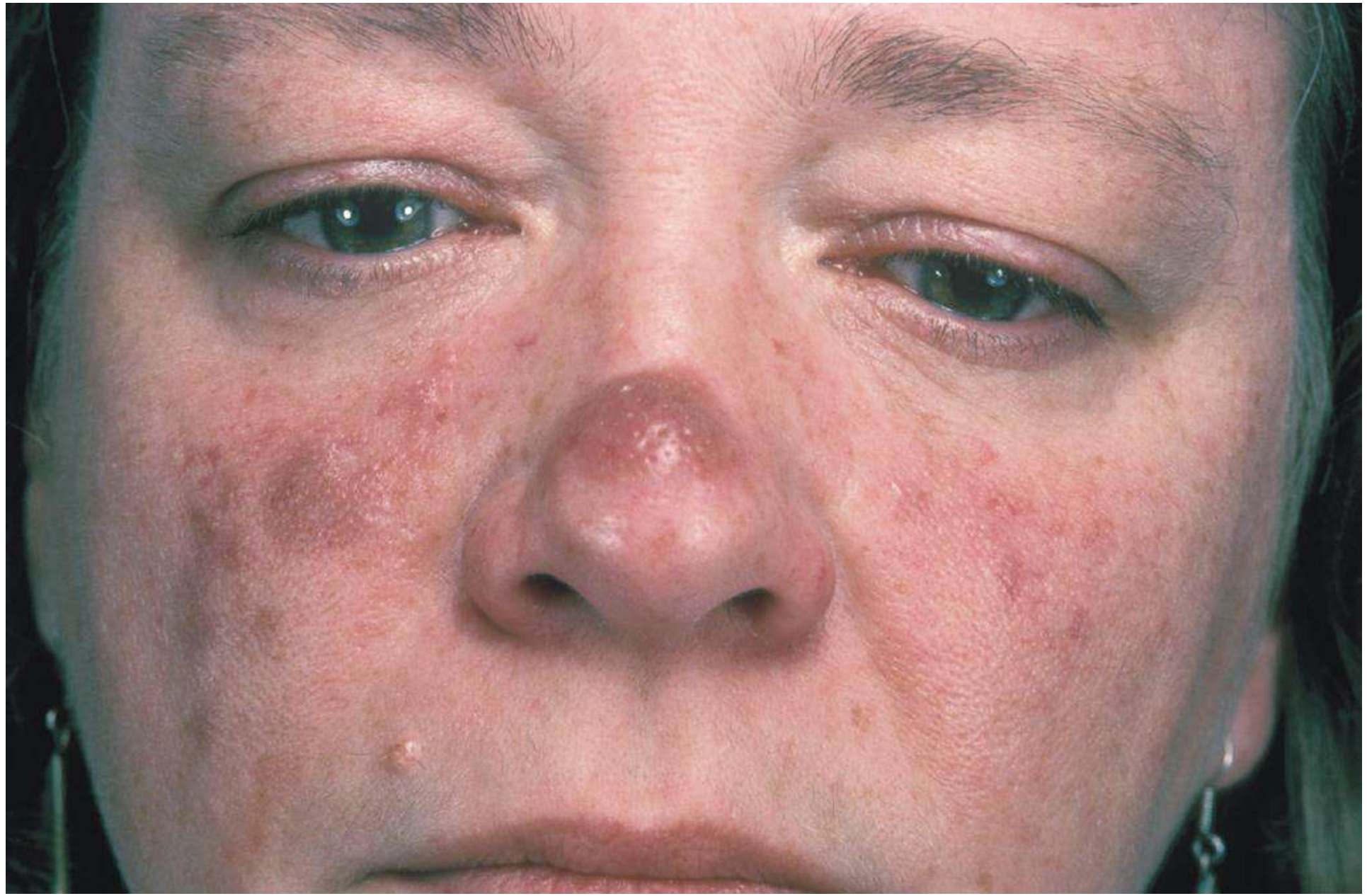


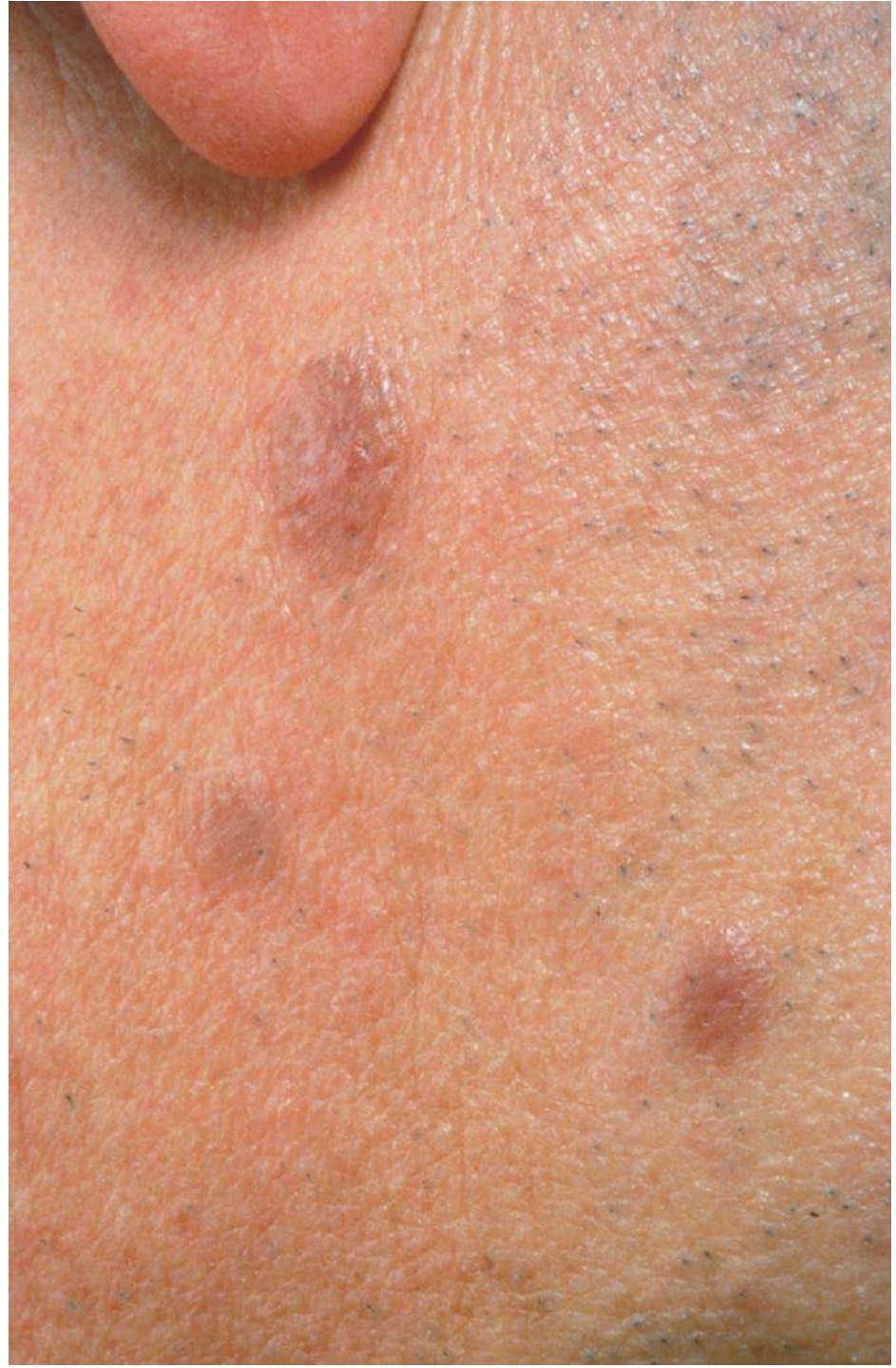
Erythema elevatum diutinum

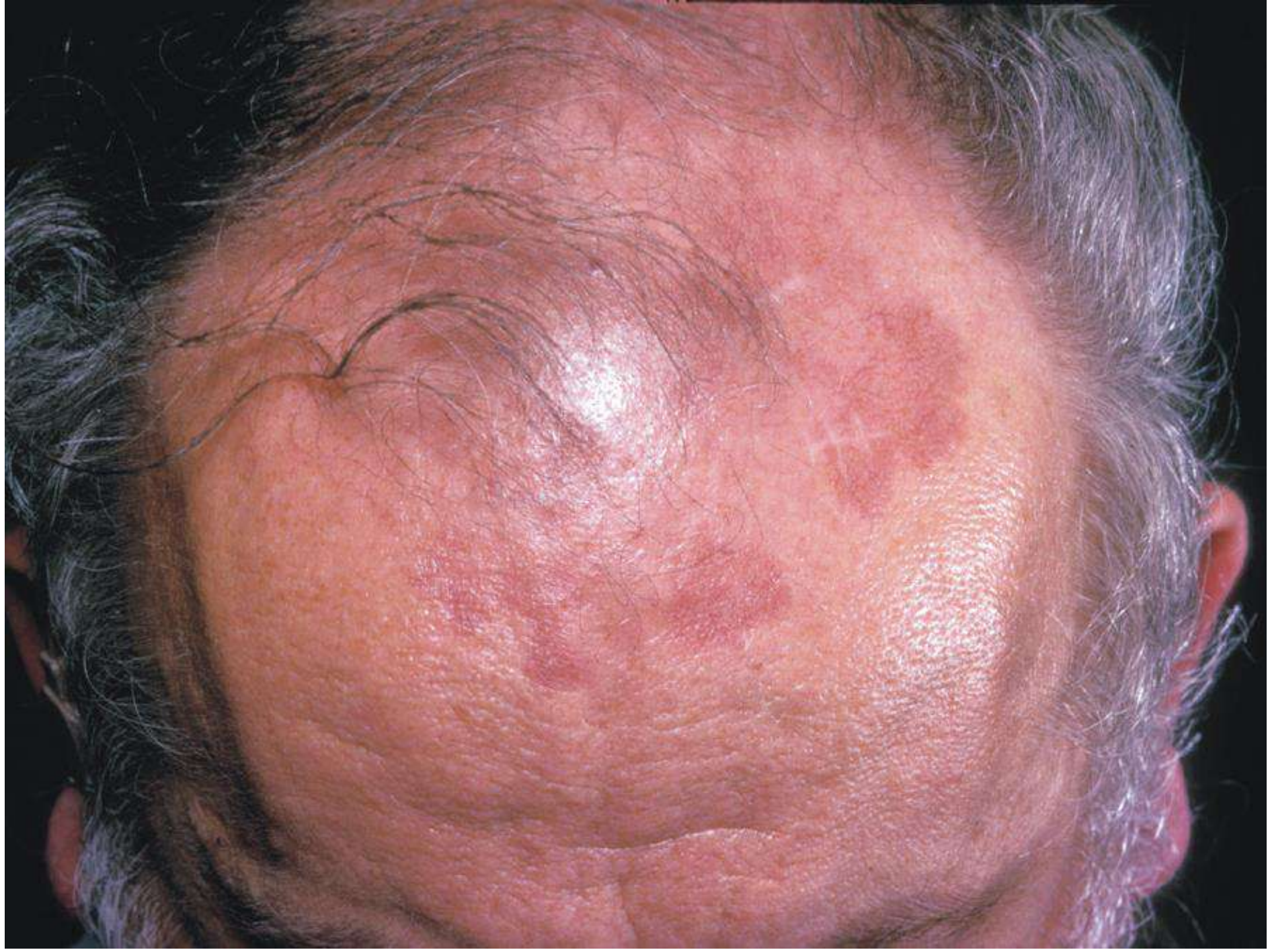
- LCV focal in early stages
- Neutrophils predominate, DH-like areas
  - No grenz zone
- Fibrosis – concentric, scar-like or fibrous histiocytoma-like

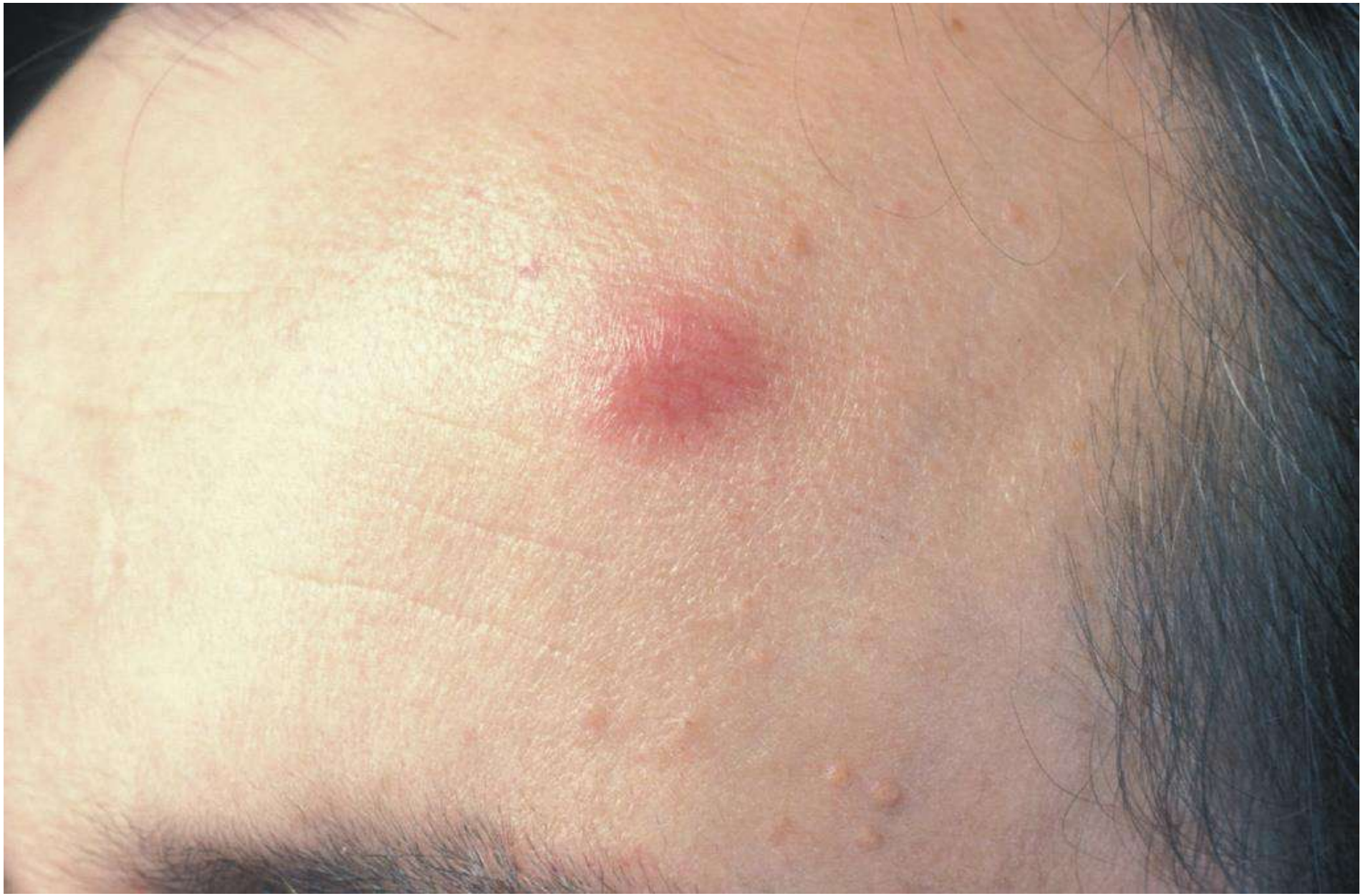


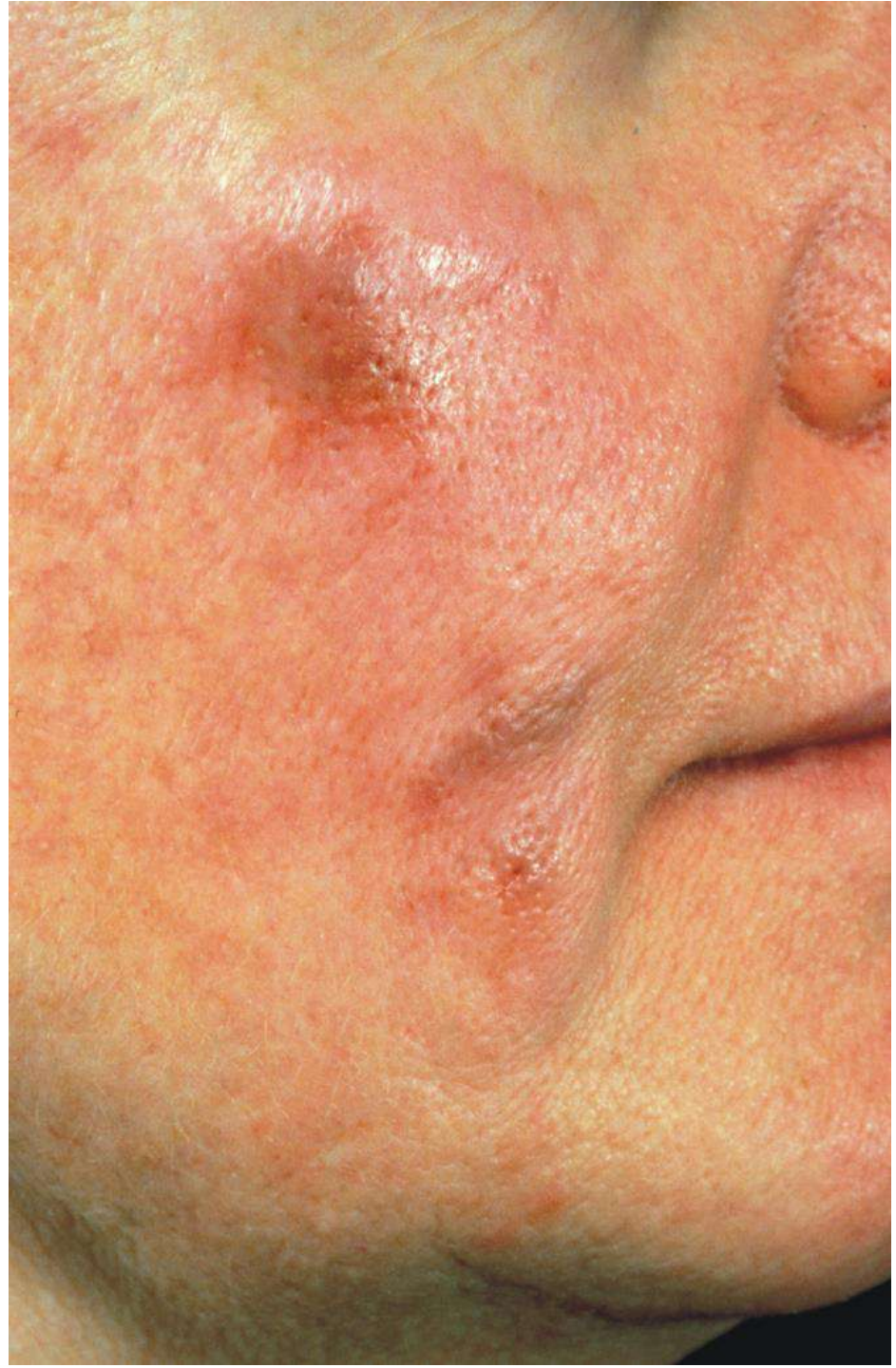


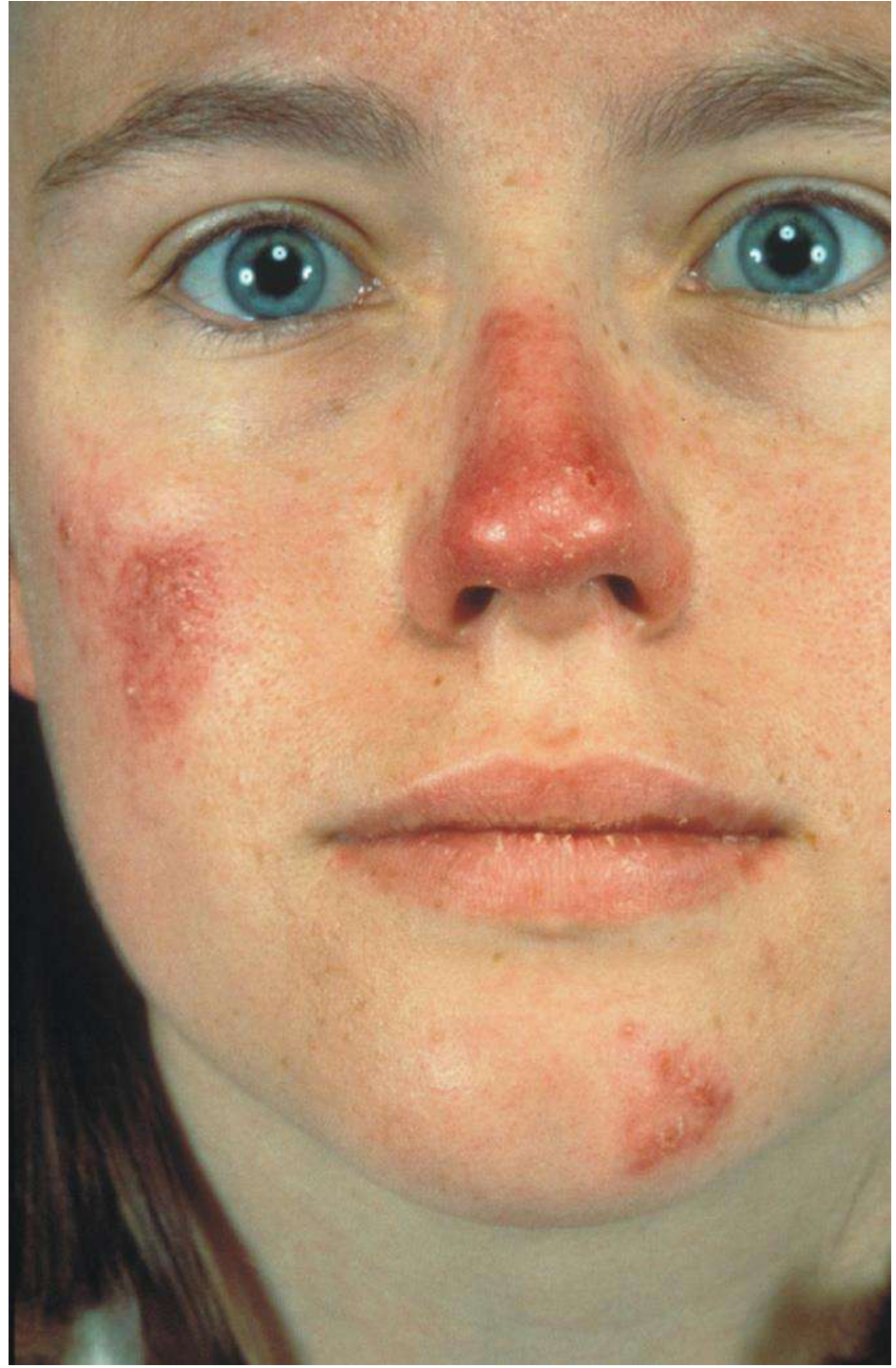






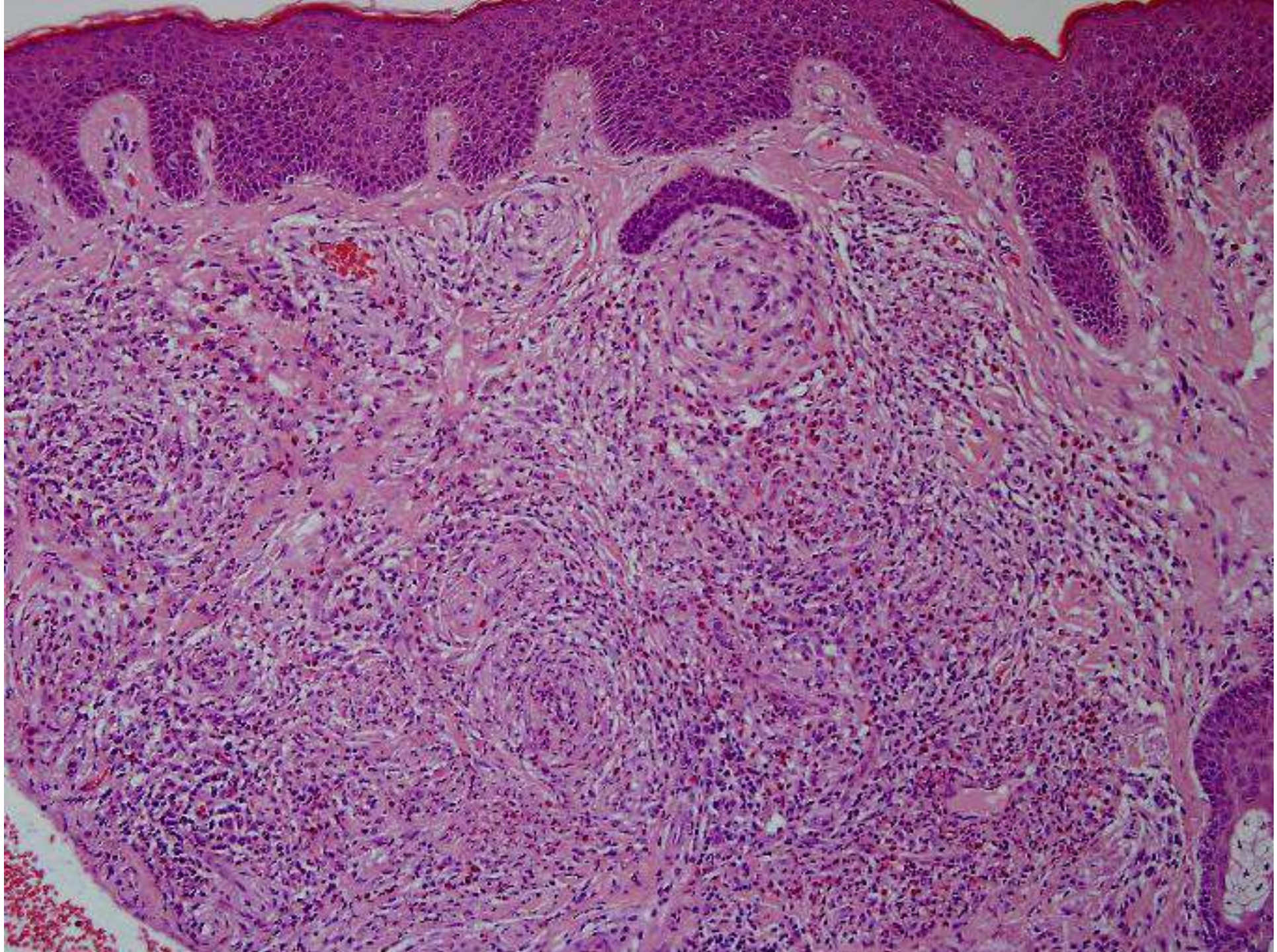


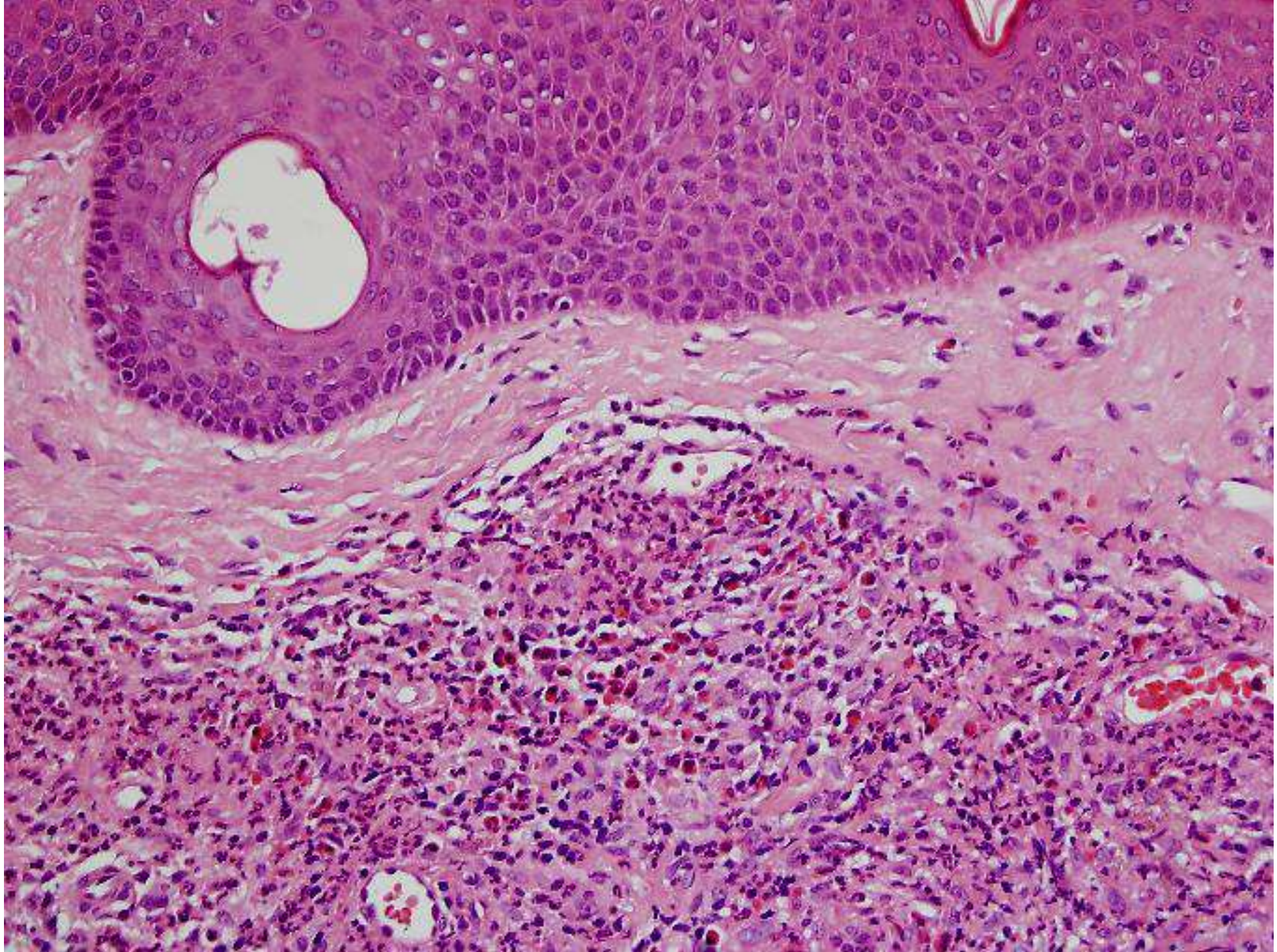


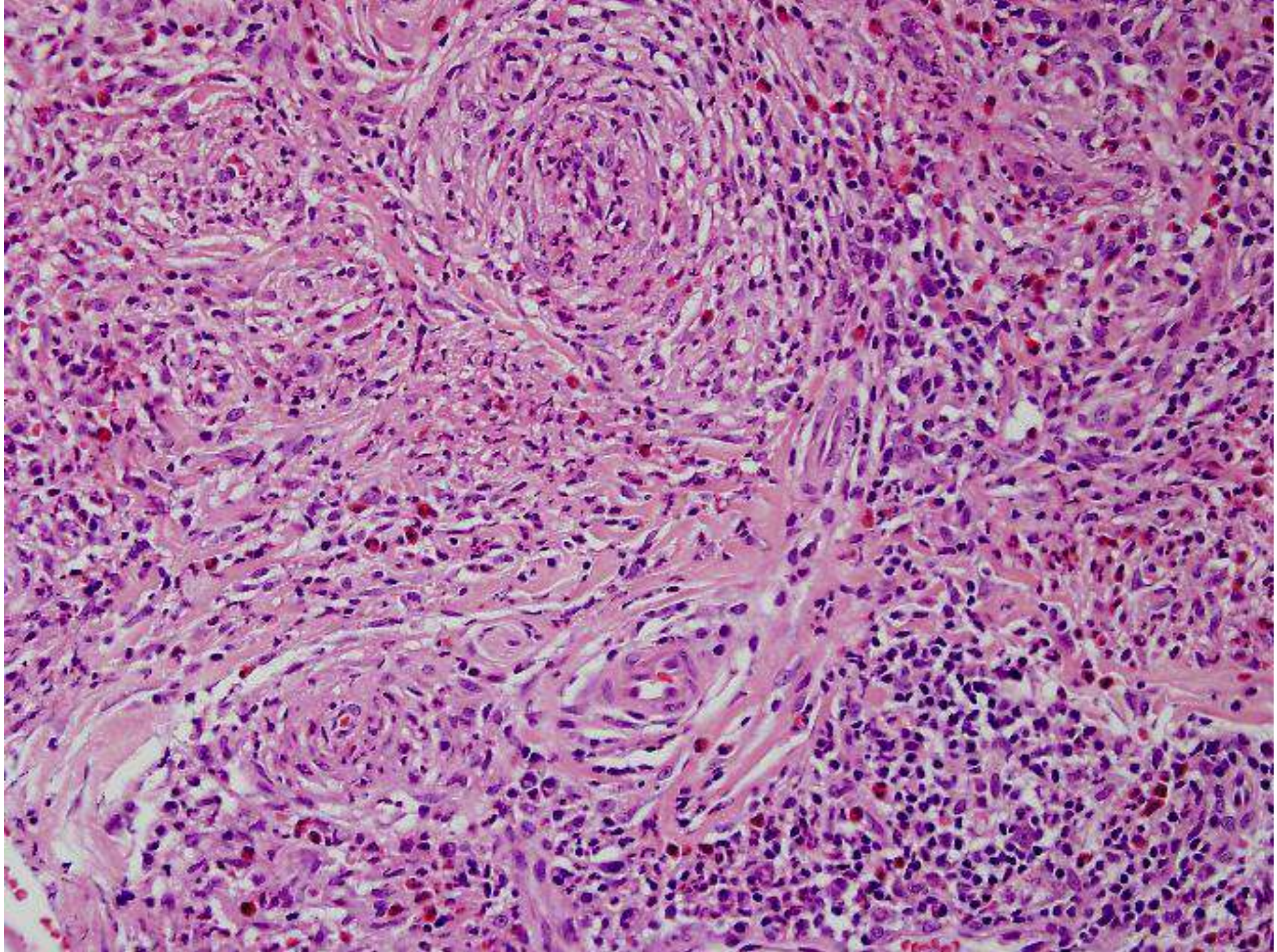


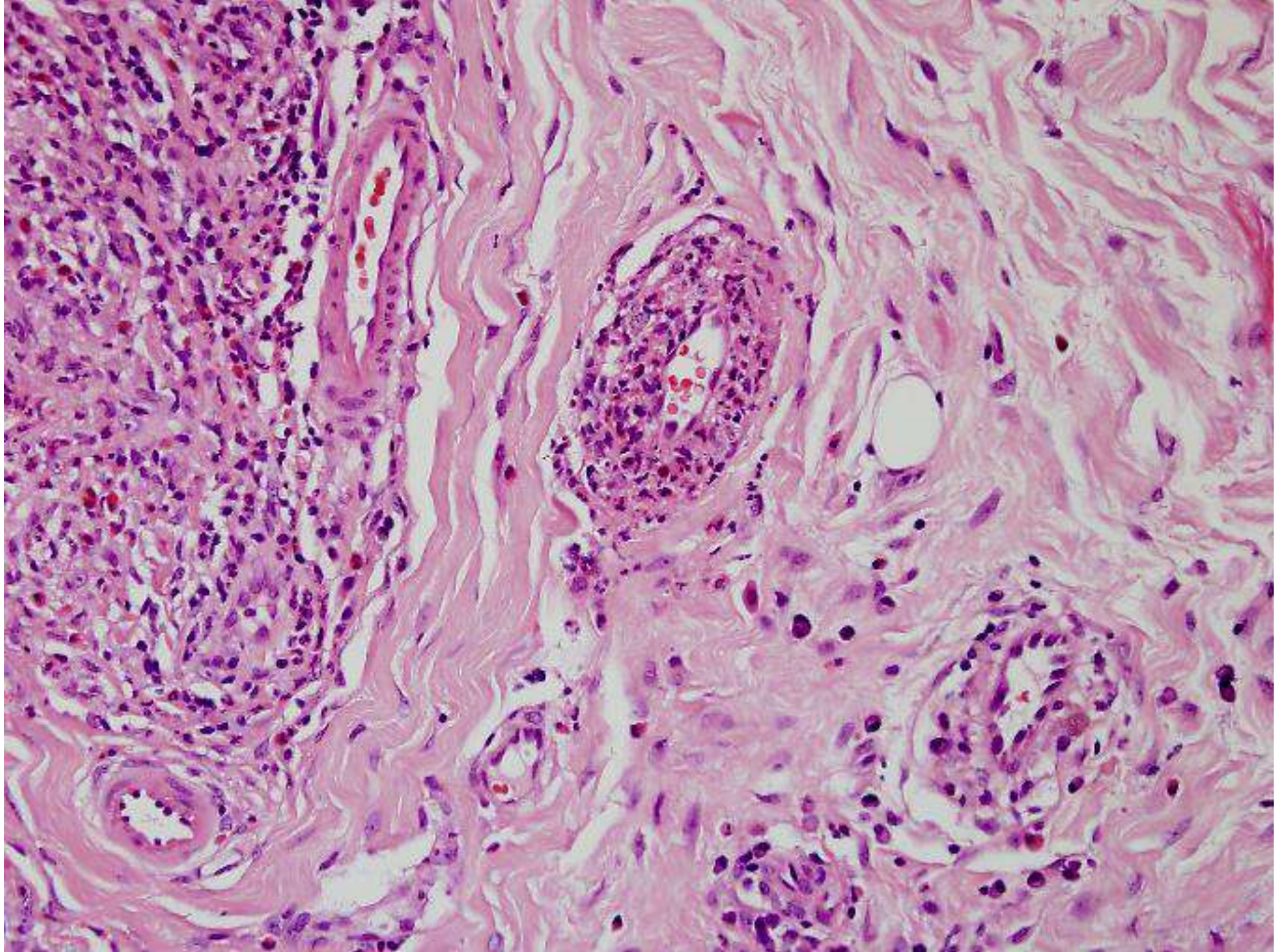
Granuloma faciale

- **Mixed inflammation**
  - **Upper and mid-dermis**
  - **Grenz zone present**
  - **Eosinophils predominate**
  - **Neutrophisl vary but always present**
  - **Plasma cells also seen**
  - **Vasculitis usually minimal**
  - **Perivascular concentric fibrosis in late lesions**
  - **Association with angiocentric eosinophilic fibrosis in the upper respiratory tract**









Thank You for Your Attentio

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DR AGNES PEKAR