

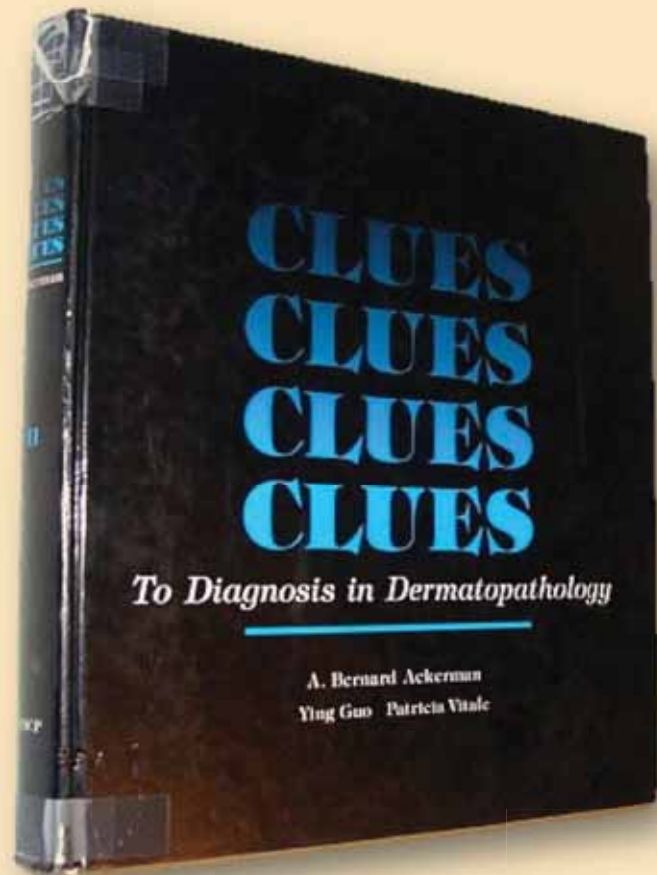
17th Summer Academy of Dermatopathology

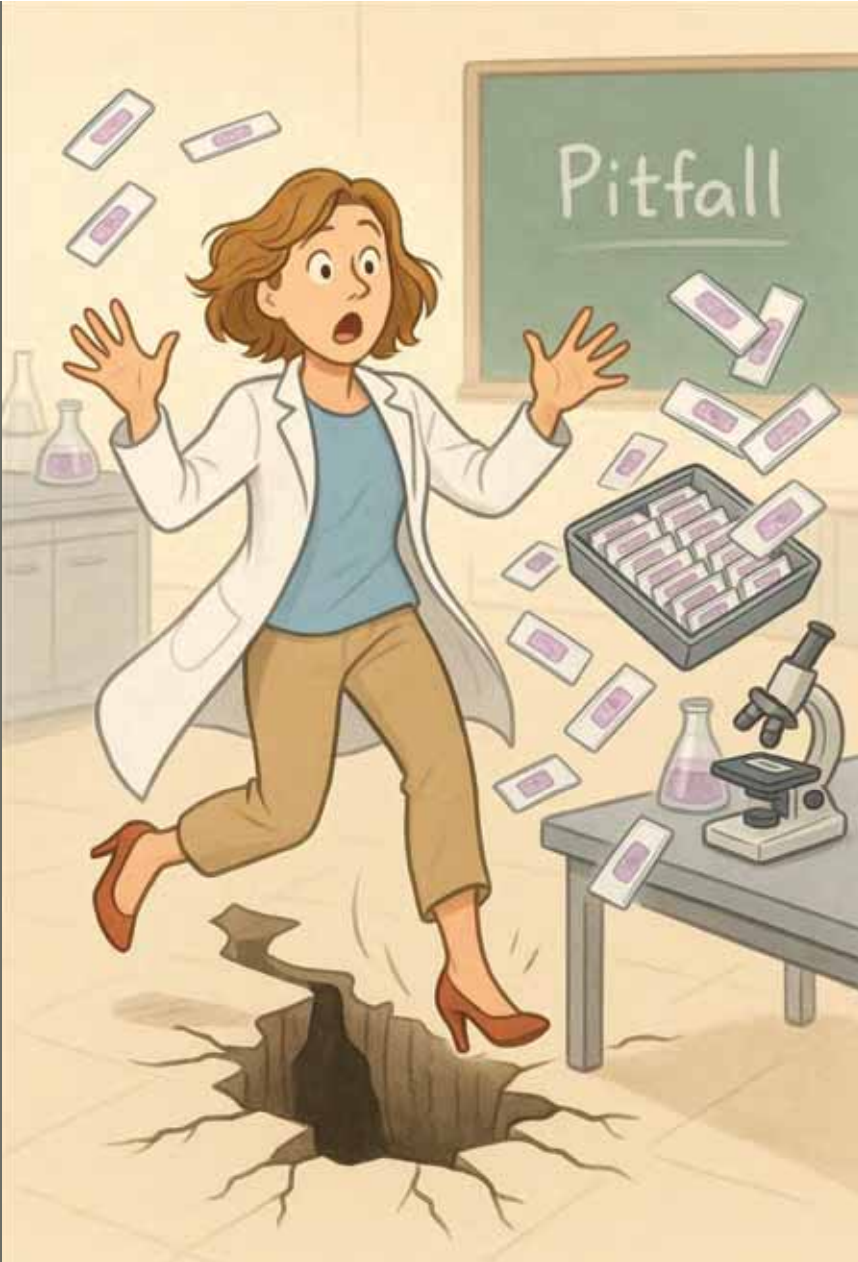


# Clues in Dermatopathology: the Barcelona experience

Maite Fernández Figueras

HU General de Catalunya. Grupo Quironsalud  
Universitat Internacional de Catalunya

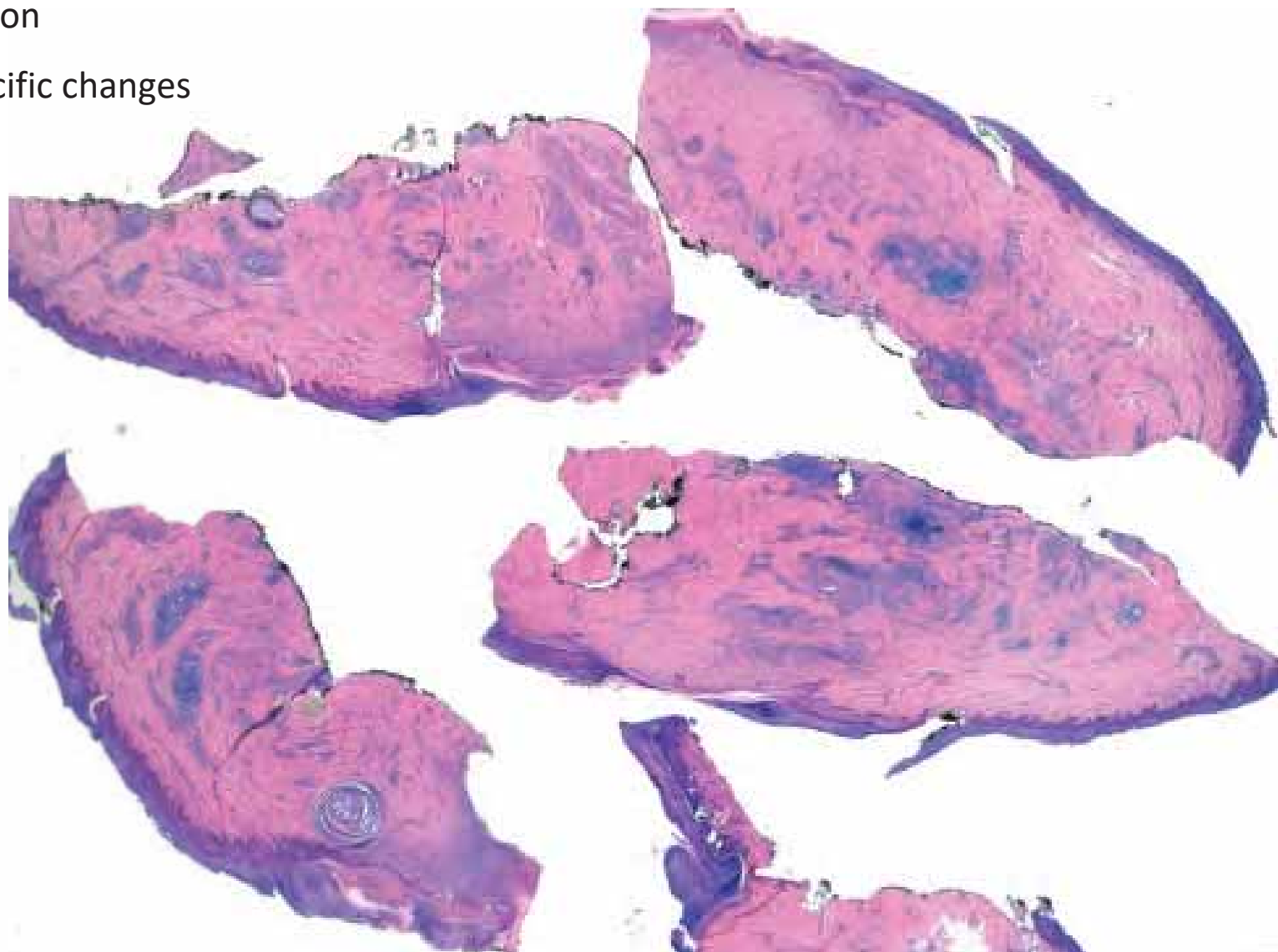




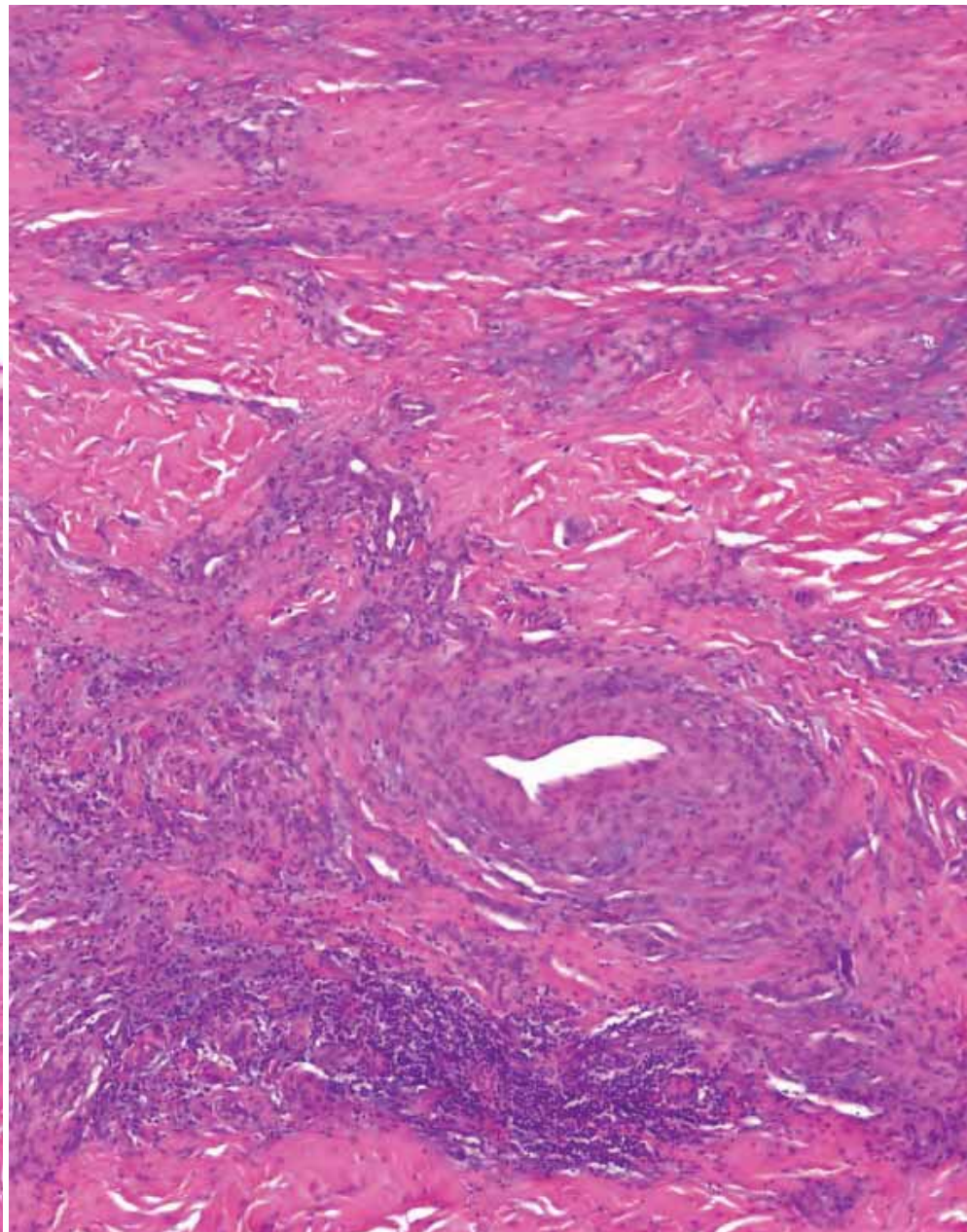
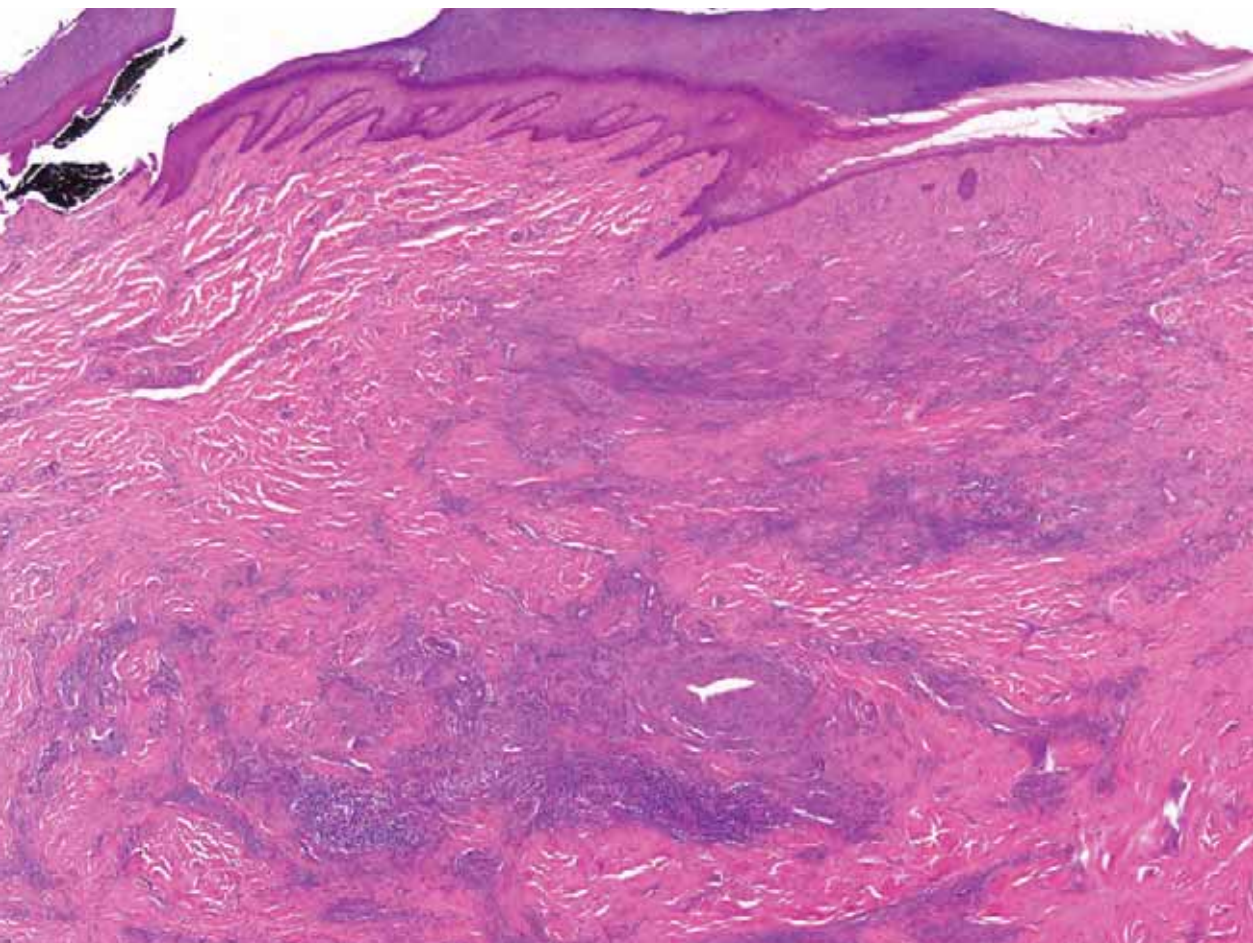
# Pitfalls

- ✓ Overlaps
- ✓ Look-alikes
- ✓ Red herrings
- ✓ Unusual locations
- ✓ Invisible dermatoses

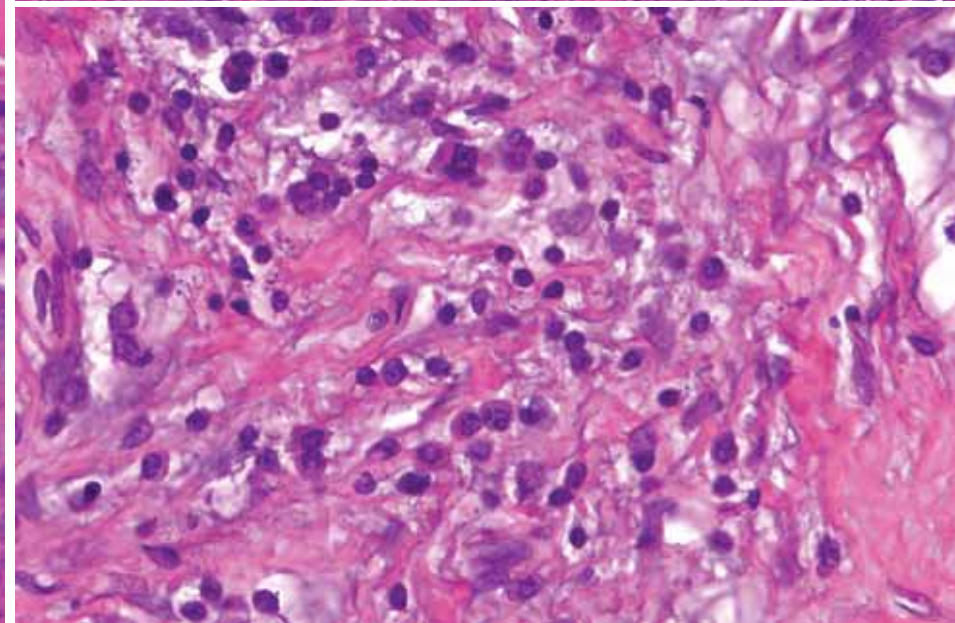
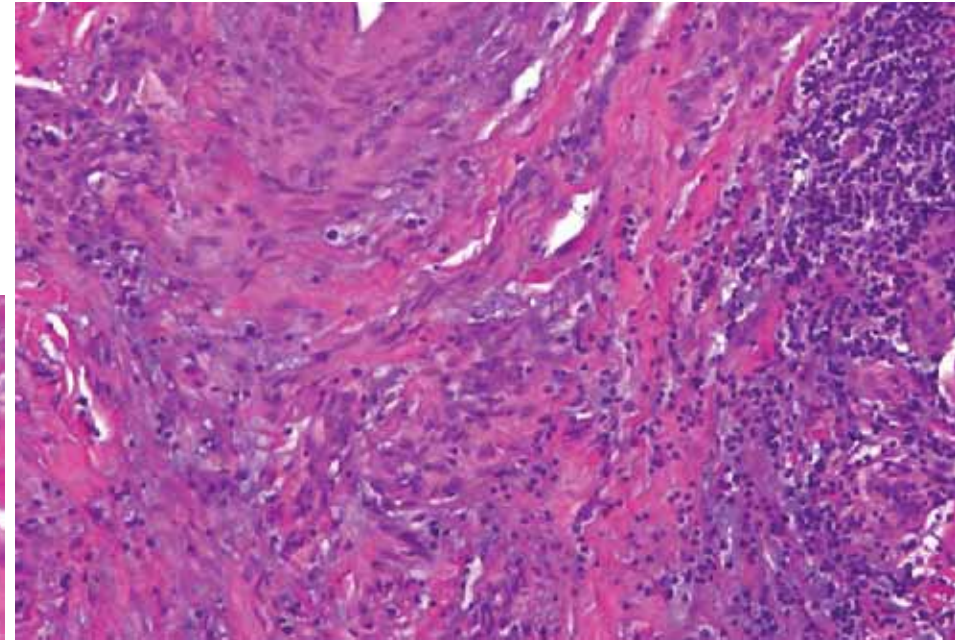
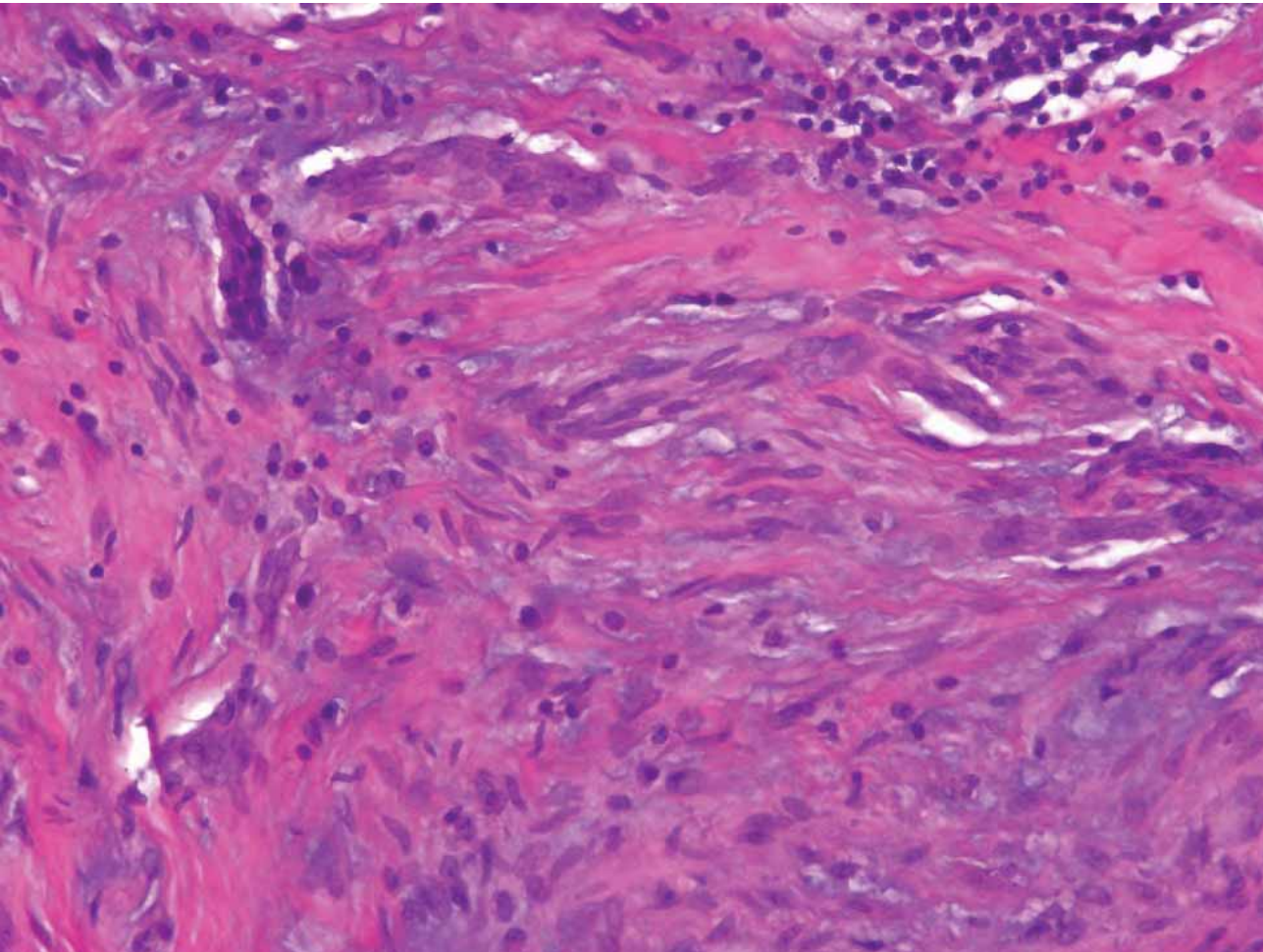
- 69-year-old man
- Extremely painful subungual lesion
- Two previous small Bx: Non-specific changes



- 69-year-old man
- Extremely painful subungual lesion
- Two previous small Bx: Non-specific changes



- 69-year-old man
- Extremely painful subungual lesion
- Two previous small Bx: Non-specific changes



# Painful skin tumors

## CALM HOG, FLED PEN AND GETS BACK

Chondrodermatitis nodularis helcis

Angioendotheliomatosis

Leiomyoma

Metastases

Hidradenoma

Osteoma cútis

Glomus tumor

Fibromyxoma

Leiomyosarcoma

Eccrine angiomatous hamartoma

Dercum's disease

Piezogenic pedal papule

Eccrine spiradenoma

Neurilemmoma

Angiolipoma

NEUROMA

Dermatofibroma

Granular cell tumor

Endometriosis

Thrombus

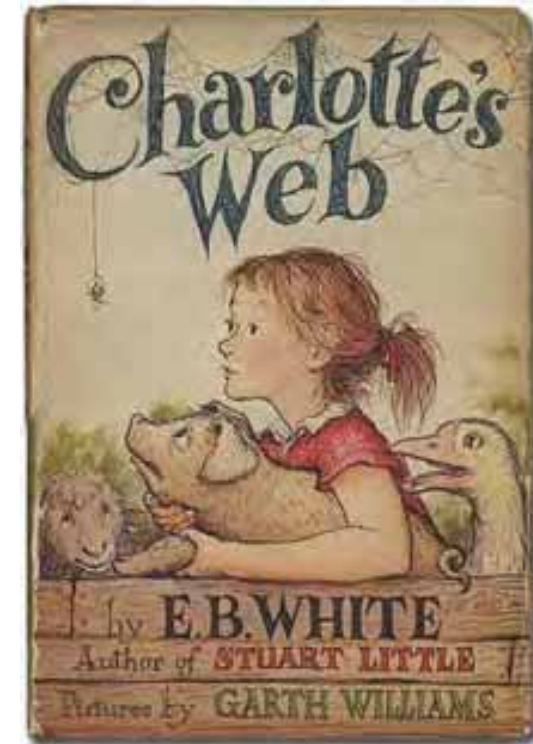
SCAR

Blue rubber bleb nevus

Angioma

Calcinosis cútis

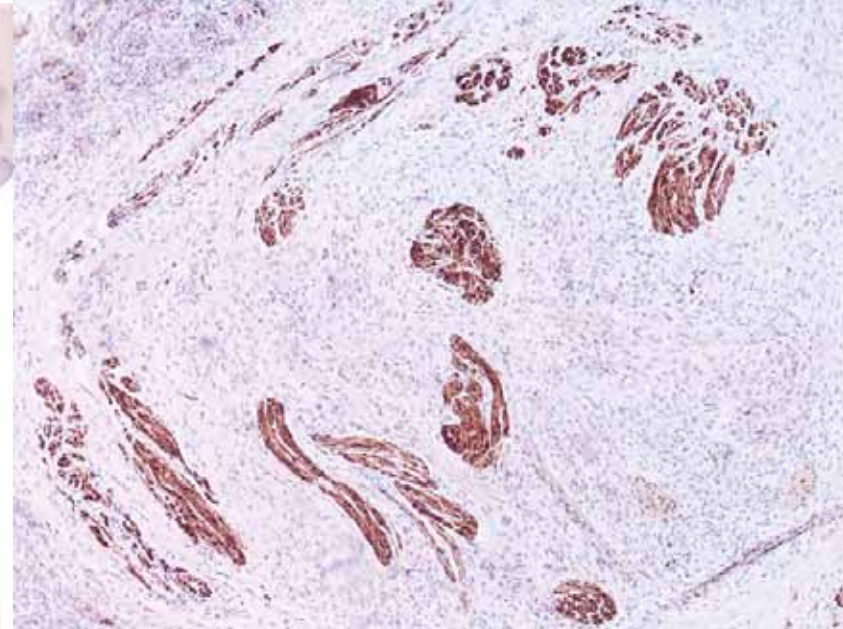
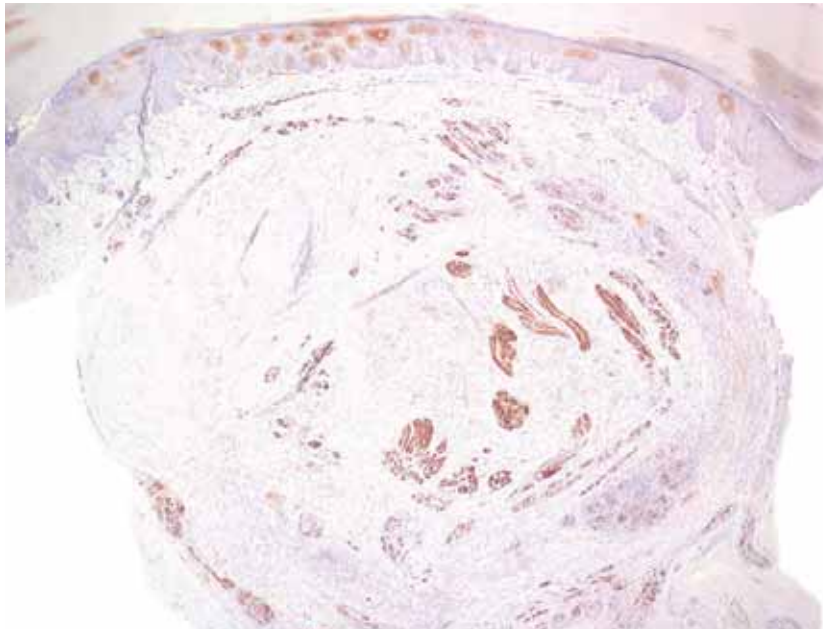
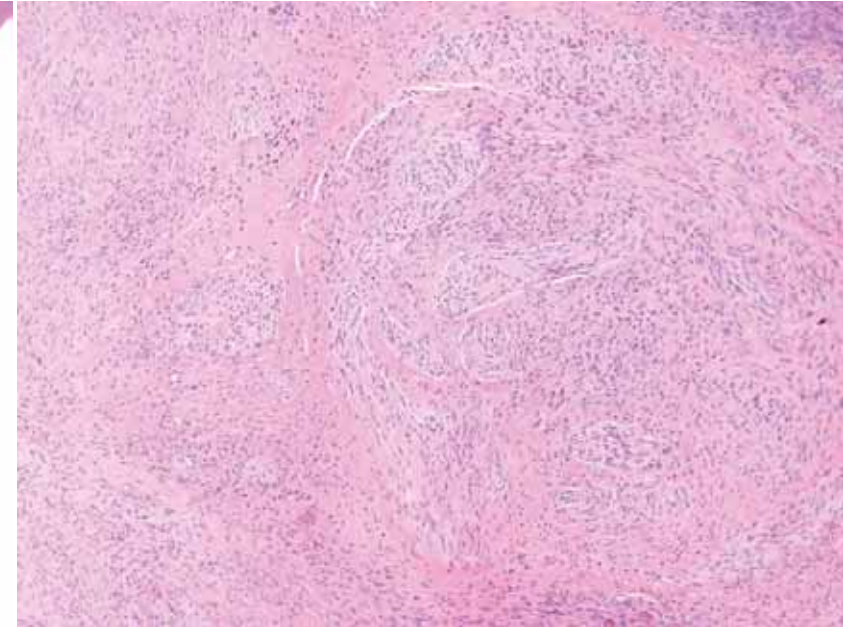
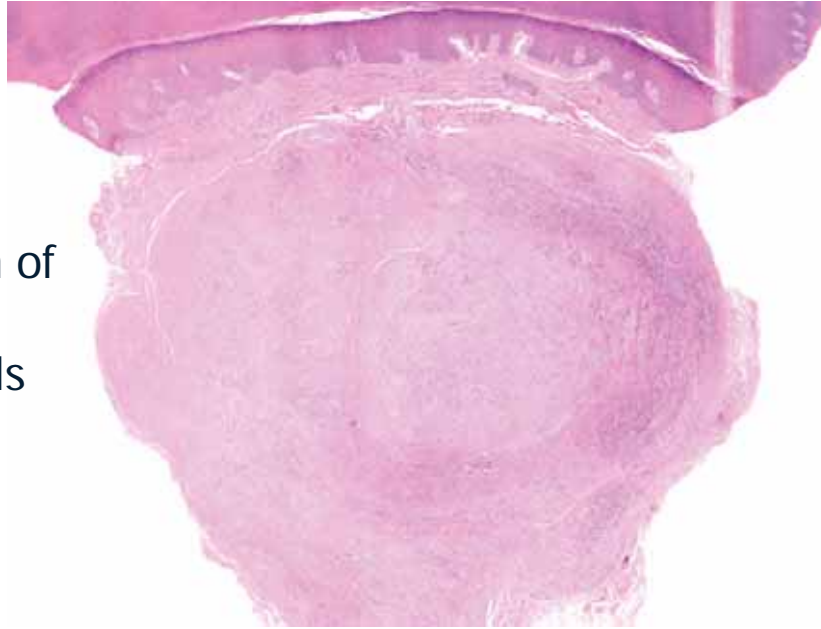
Keloid



*Clin Cosmet Investig Dermatol 2019;12 123–132*

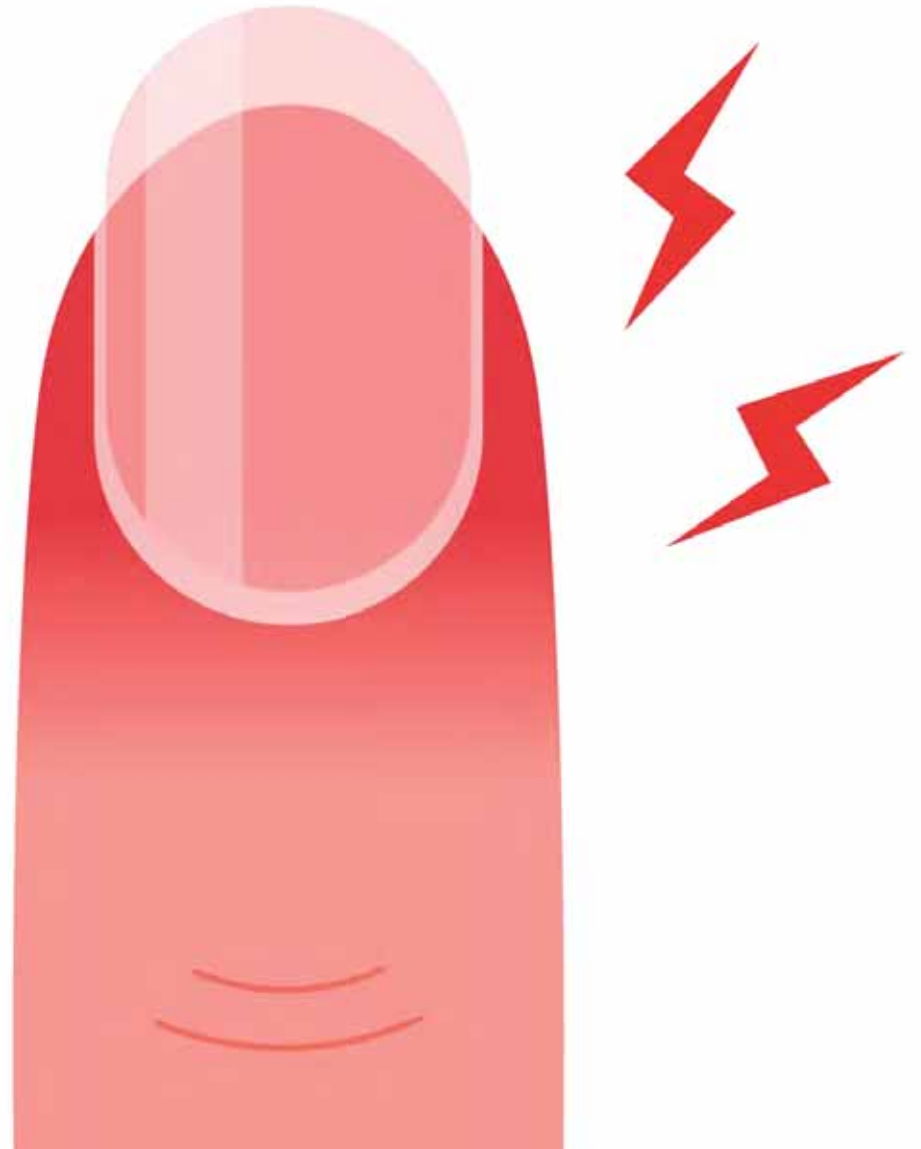
# Traumatic neuroma

- Disordered proliferation of nerve elements of with Schwann, perineural cells and neurofilaments
- Fibrous background
- Painful (under pressure)

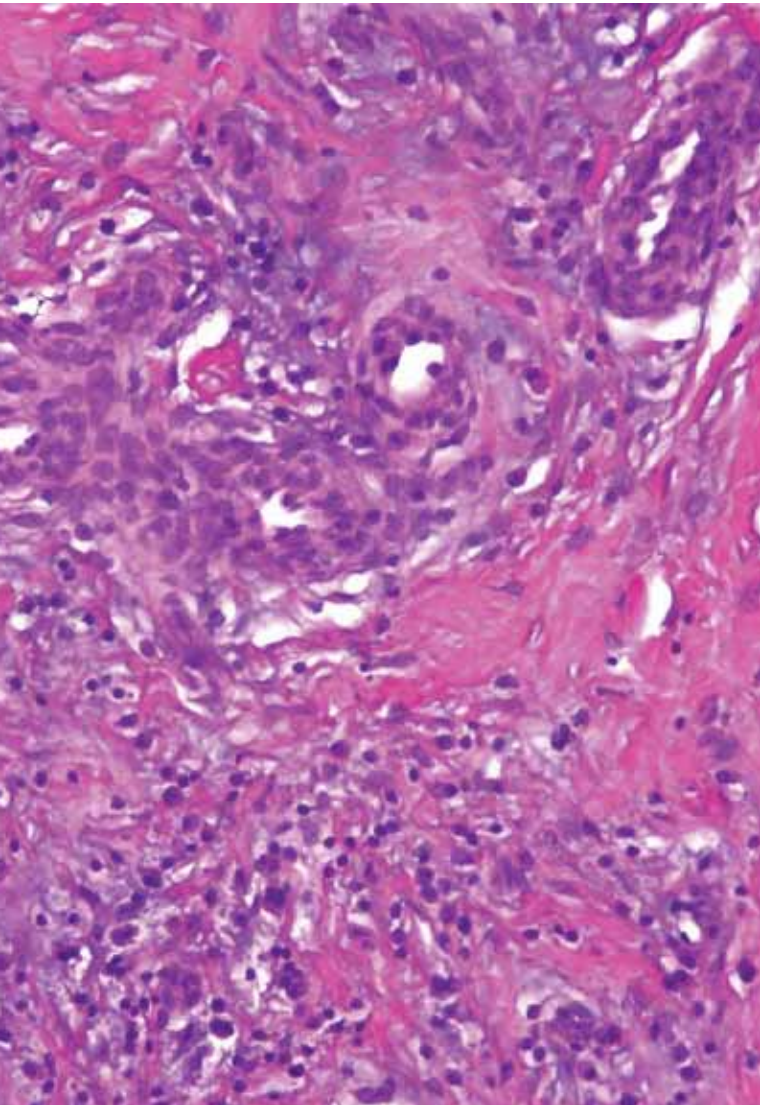


## Life lesson (LL) 1

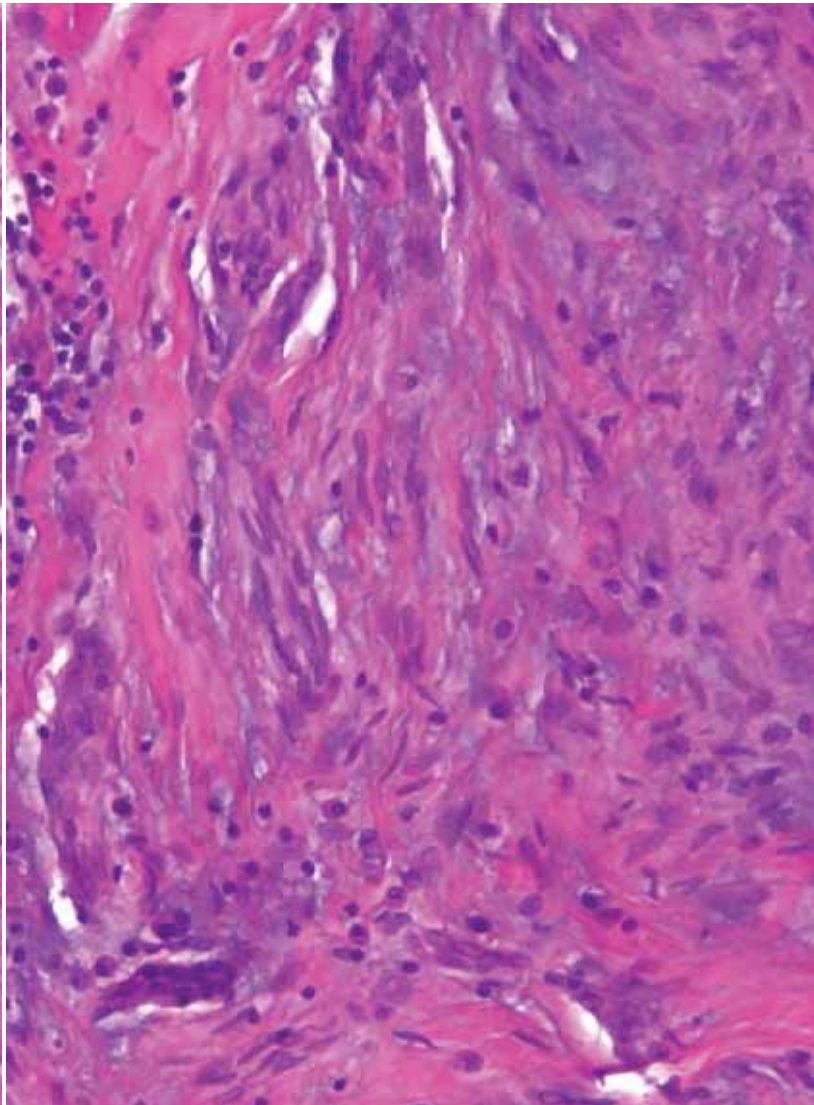
Any tumor can be painful, specially in the subungual region



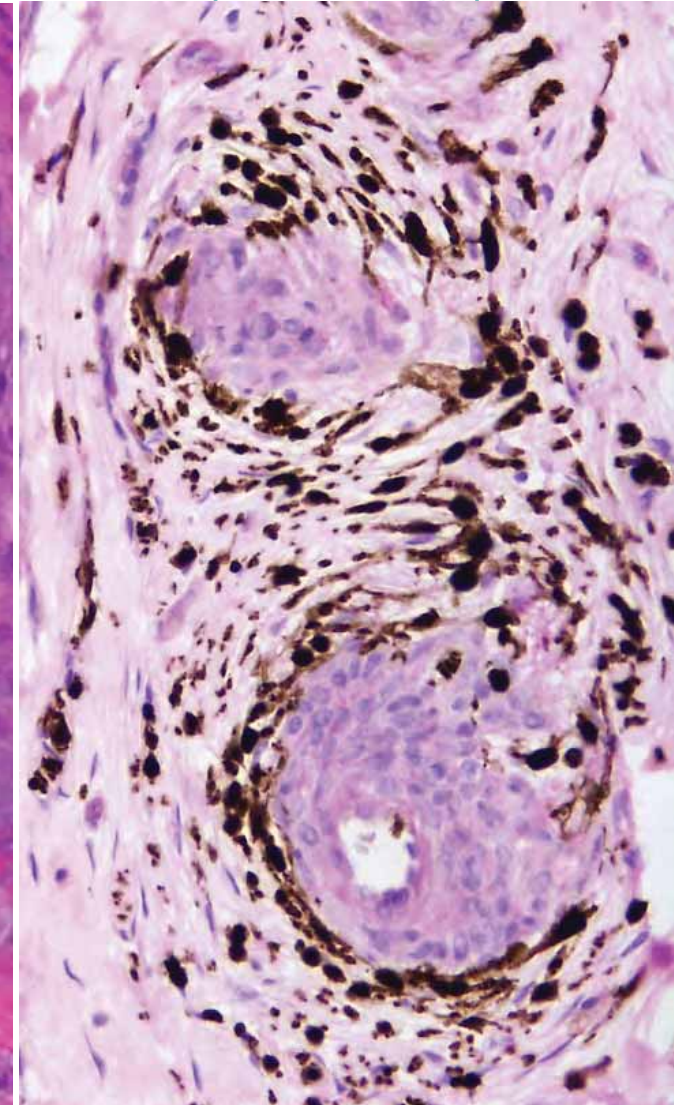
Normal glomus bodies and  
lymphoplasmacytic infiltrate



Scar tissue  
(SMA+ myofibroblasts)

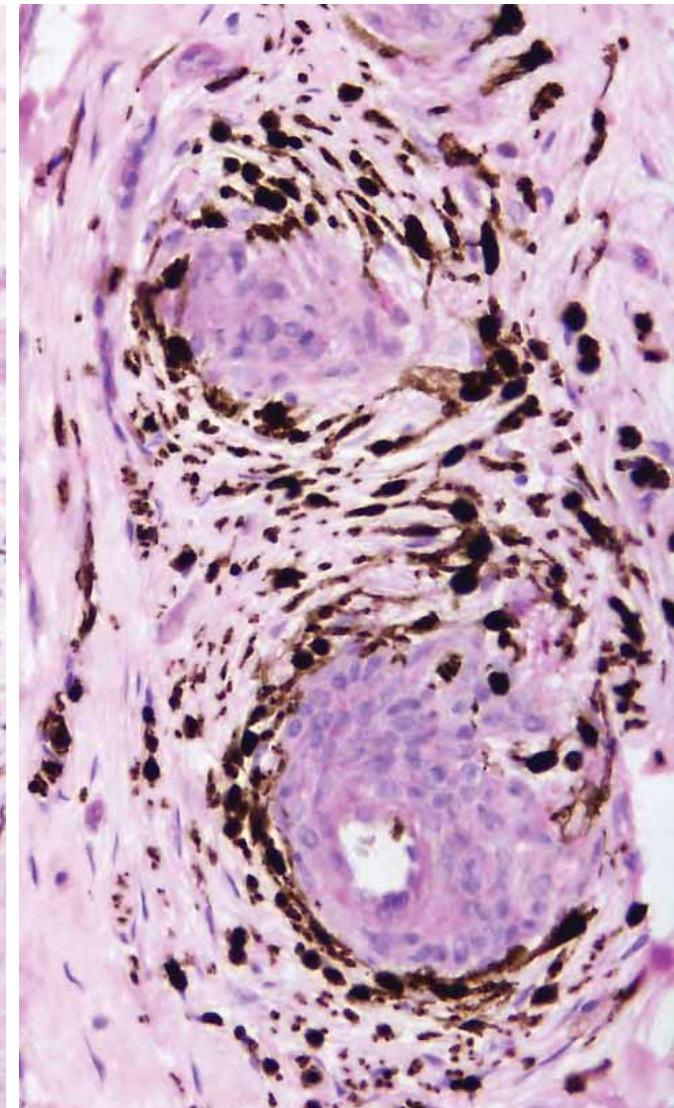
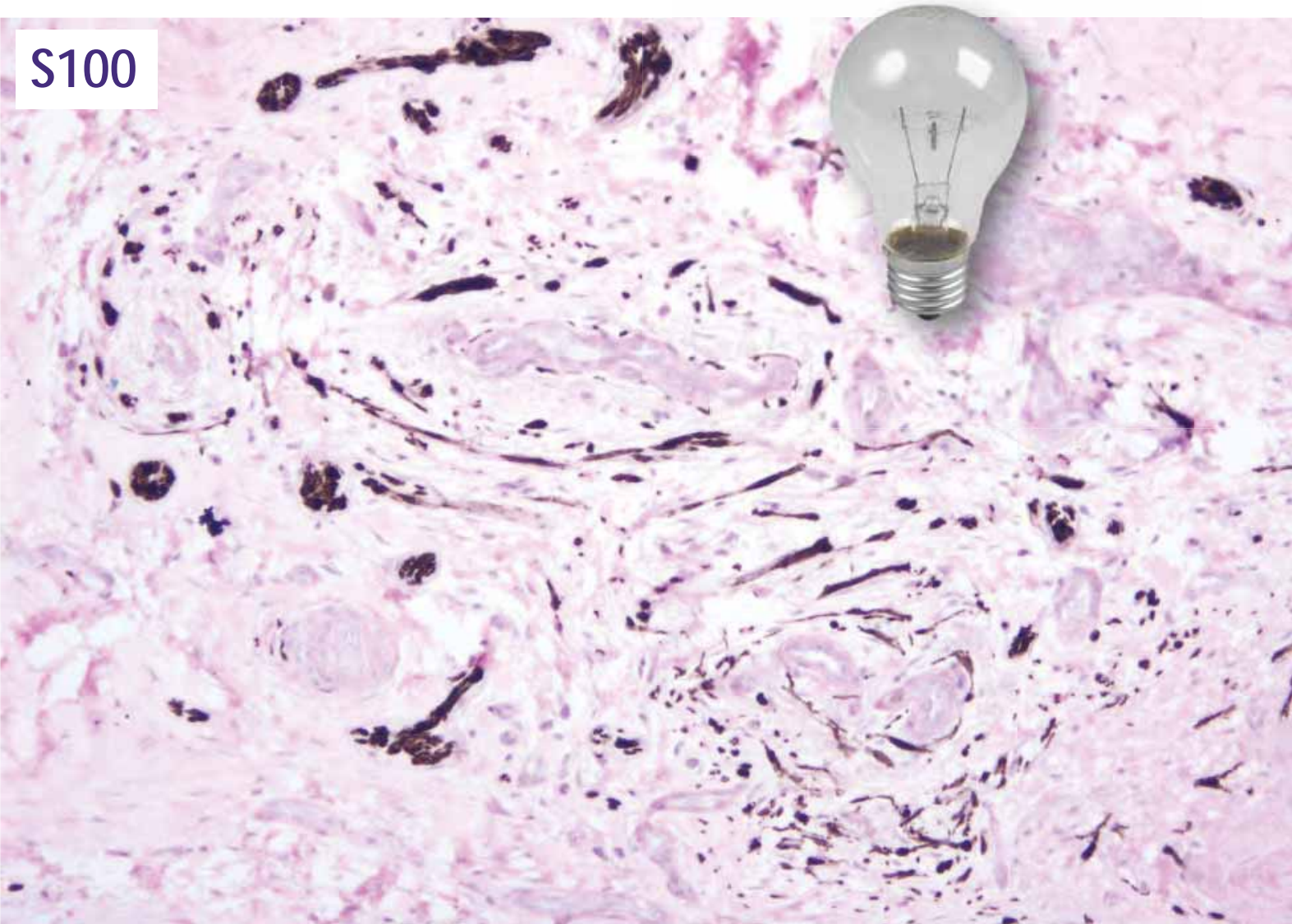


Reactive neural  
hyperplasia

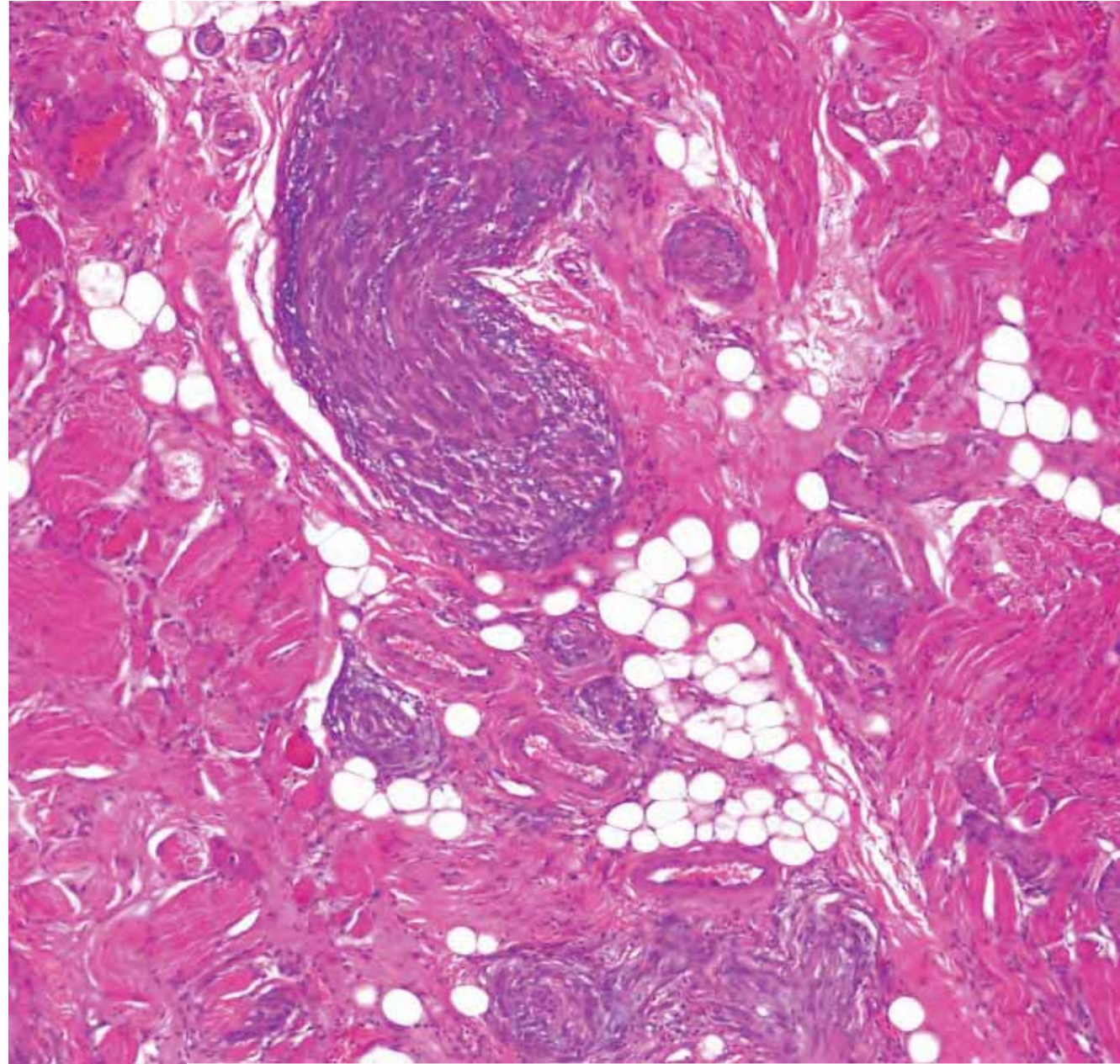
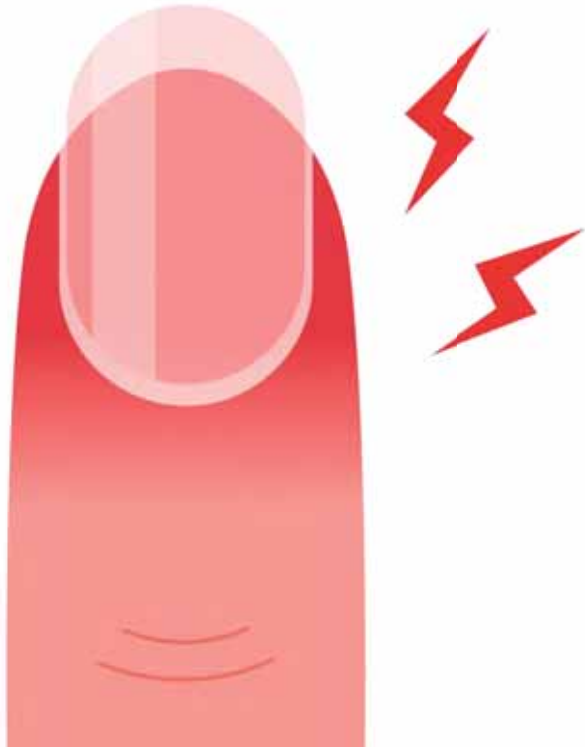


# ¿Desmoplastic melanoma?

S100



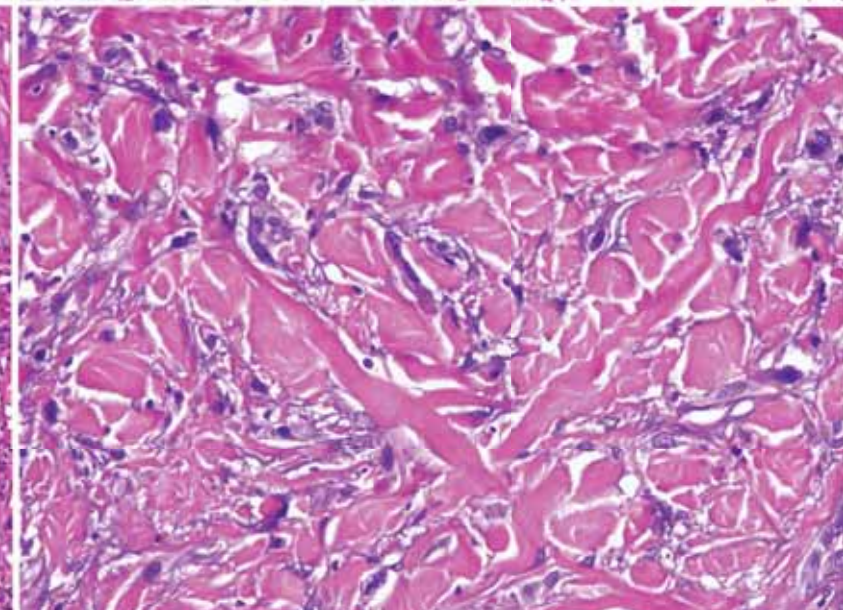
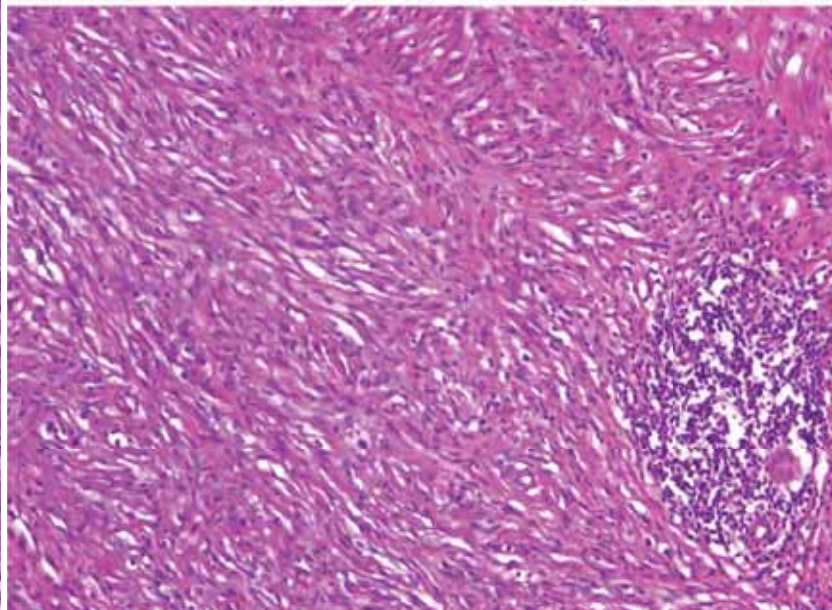
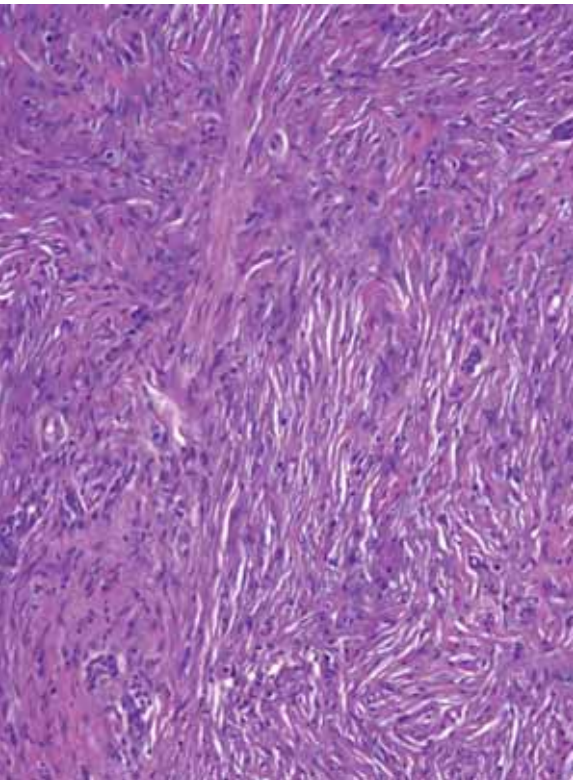
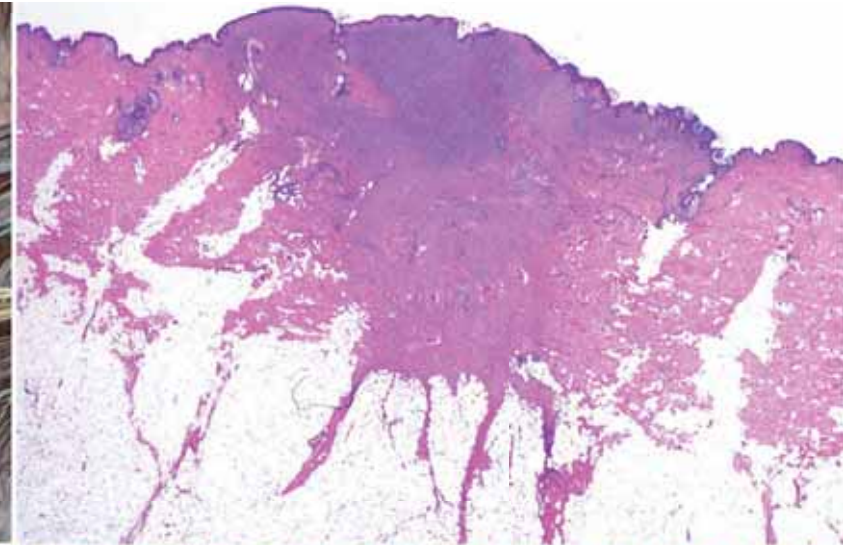
Wide resection:  
**Dx: Neurotropic  
desmoplastic melanoma**



# Desmoplastic melanoma in non-sun exposed areas

## Locations:

- Acral
- Subungueal
- Mucosal
  - ✓ Oral
  - ✓ Nasal
  - ✓ Genital



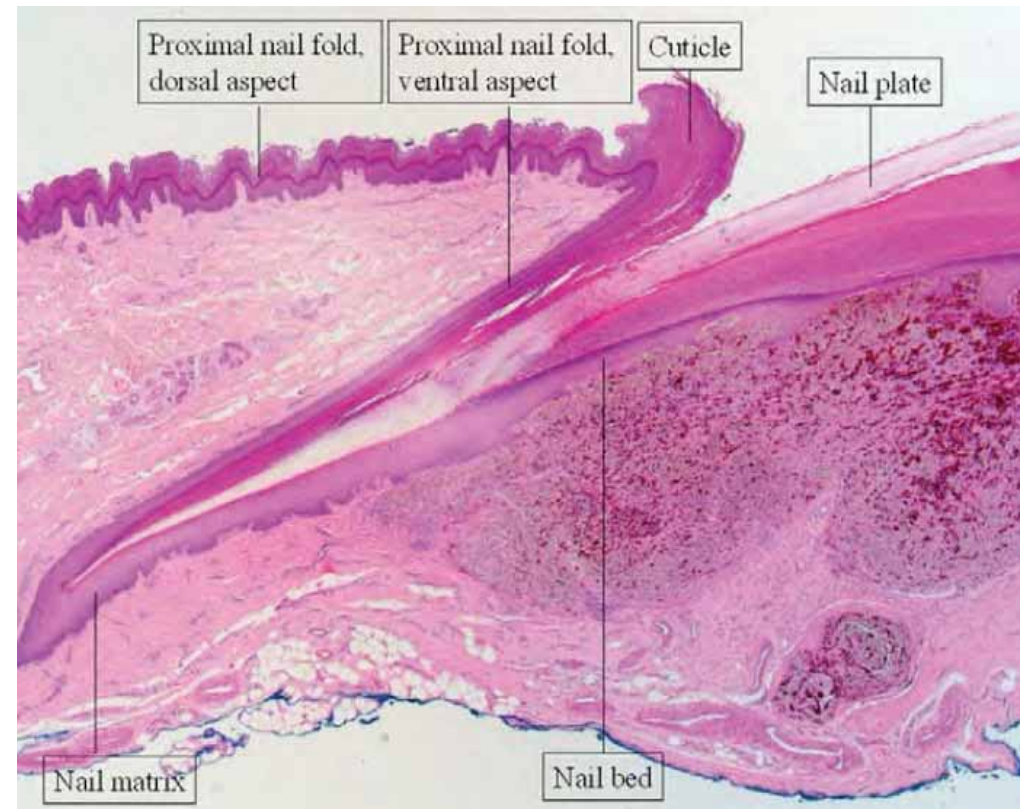
# Subungual Melanoma

## *A Study of 124 Cases Highlighting Features of Early Lesions, Potential Pitfalls in Diagnosis, and Guidelines for Histologic Reporting*

Kong-Bing Tan, MBBS, MRCPath, FRCPA,\*† Marc Moncrieff, MD, FRCS (Plast),‡  
John F. Thompson, MD, FRACS, FACS,‡§¶ Stanley W. McCarthy, MBBS, FRCPA,\*‡§  
Helen M. Shaw, PhD,‡§¶ Michael J. Quinn, MBBS, FRACS,‡§¶ Ling-Xi Lawrence Li, MBBS, PhD,‡§  
Kerry A. Crotty, MBBS, FRCPA, FACD,§\*# Jonathan R. Stretch, MBBS, FRACS, DPhil,‡§¶  
and Richard A. Scolyer, MD, FRCPA, FRCPath\*‡§\*#

*Am J Surg Pathol* 2007;31:1902–1912

- 7% of subungual melanomas are desmoplastic
- Risk for desmoplastic melanoma: subungual area x 7



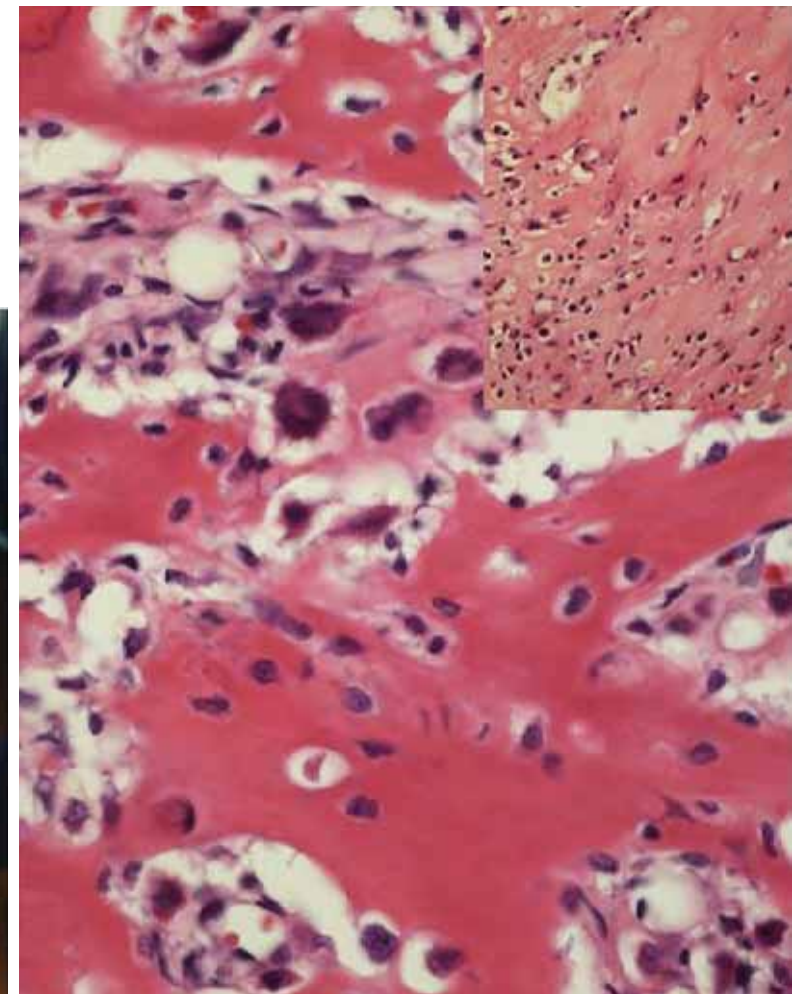
# Osteogenic melanoma: report of a case mimicking osteosarcoma and review of the literature

*Skeletal Radiol.* 2018 May;47(5):711-716.

Deepika Savant<sup>1</sup> • Shachar Kenan<sup>2</sup> • Samuel Kenan<sup>2</sup> • Leonard Kahn<sup>1</sup>

17 cases (all of them spindle cell/desmopl.)

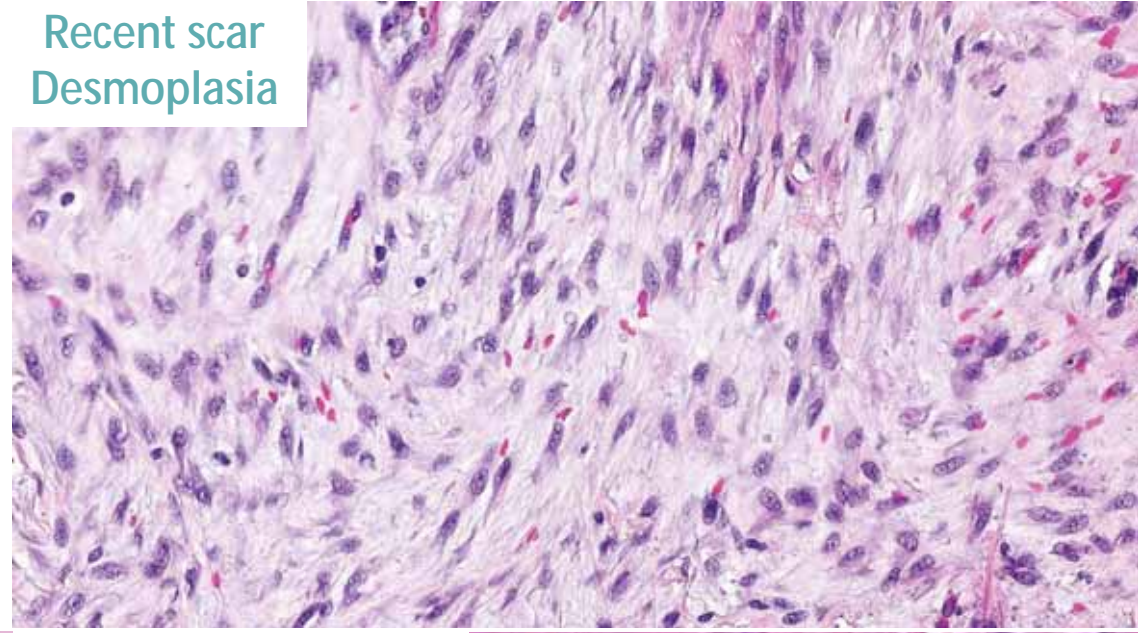
- 9 subungual, 3 of them desmoplastic
- 1 periungual
- 2 acral



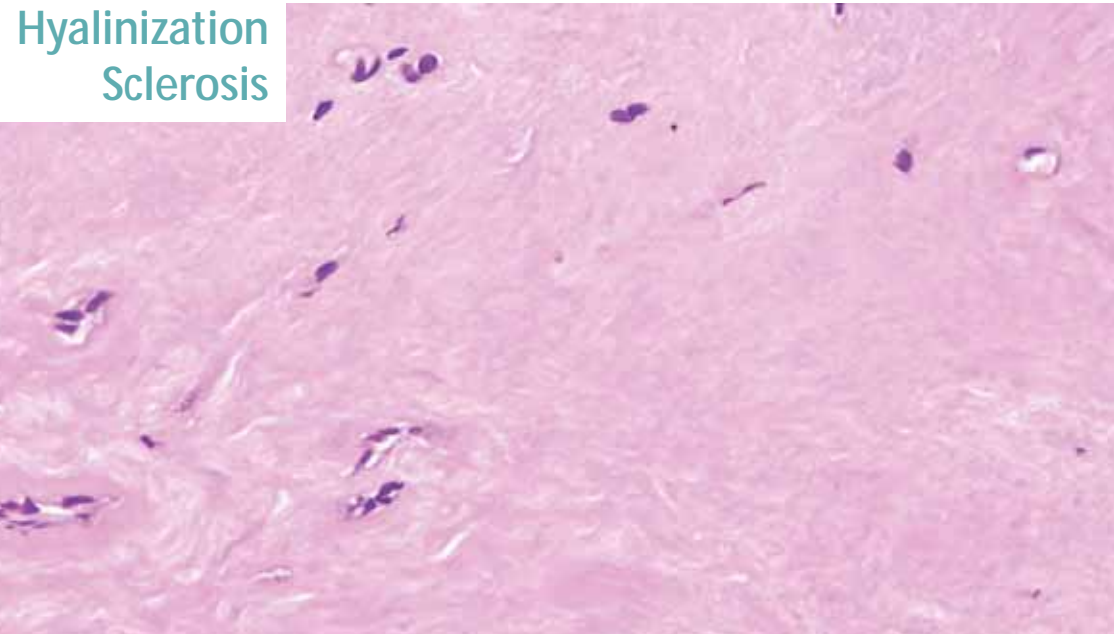
# LL 2

Pay attention to the stroma  
And learn how to interpret it!

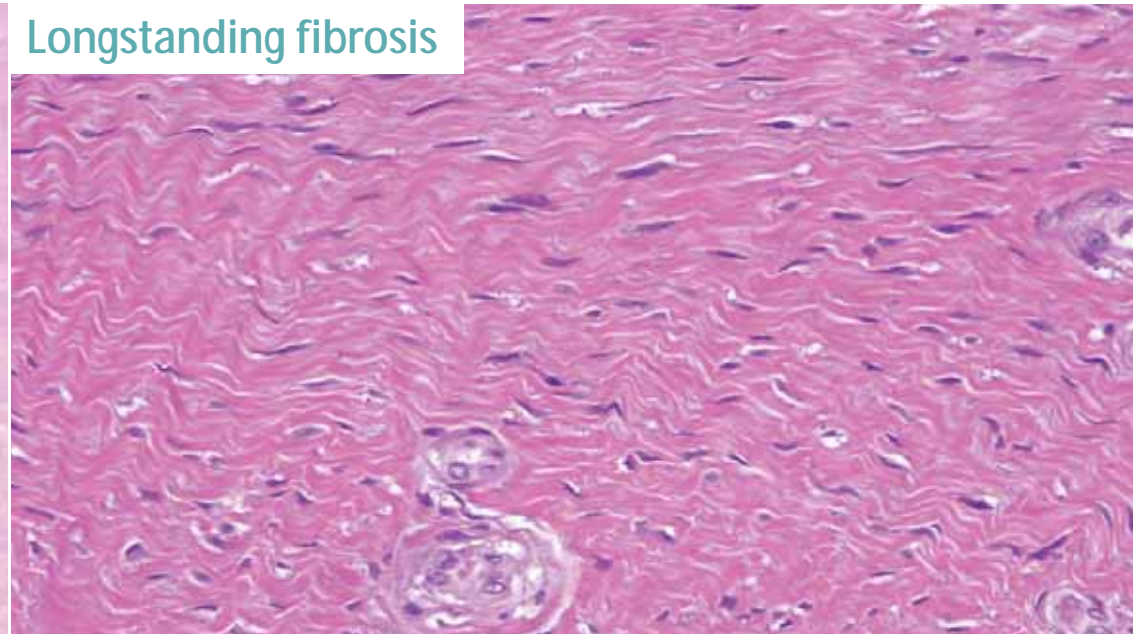
Recent scar  
Desmoplasia



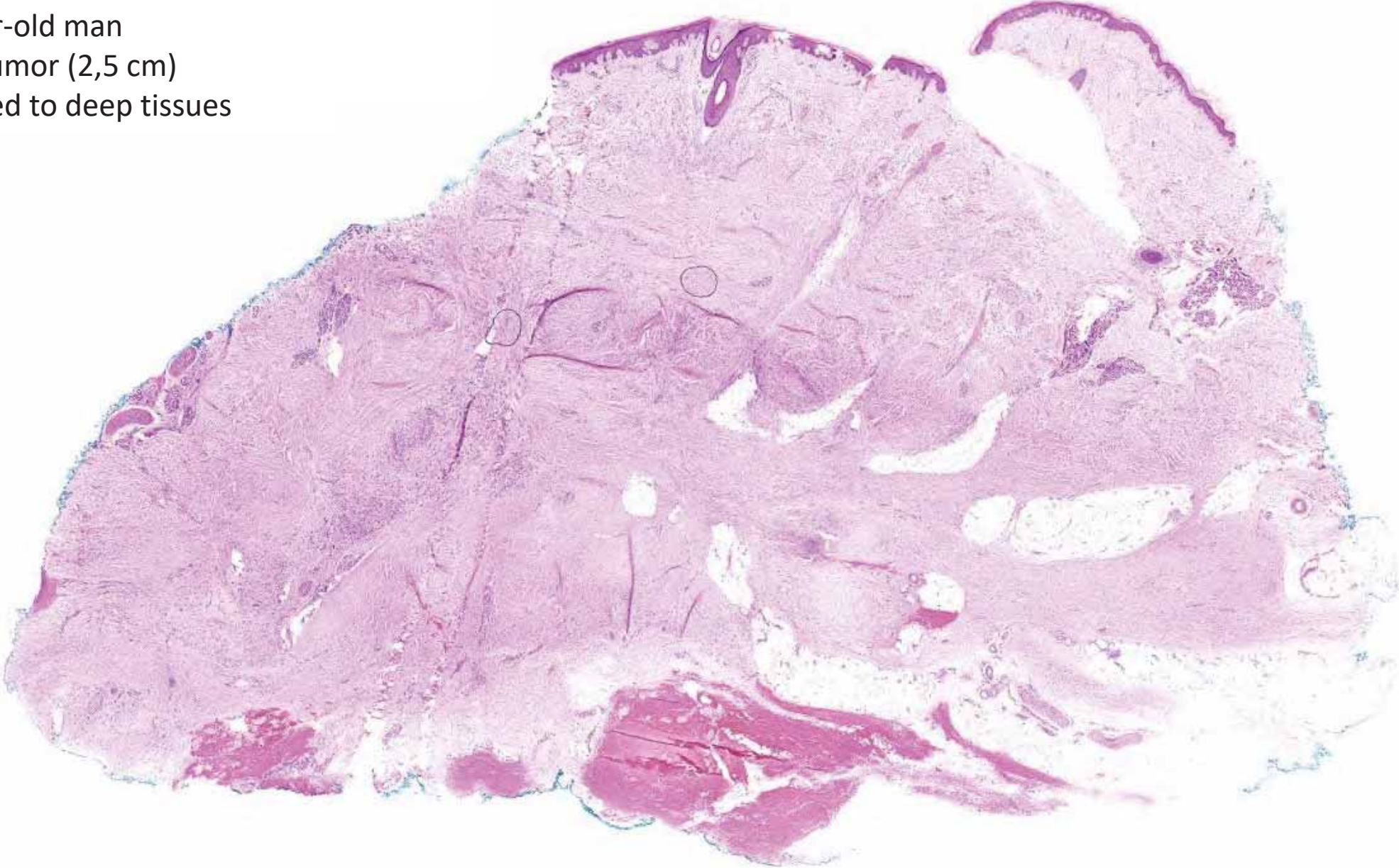
Hyalinization  
Sclerosis



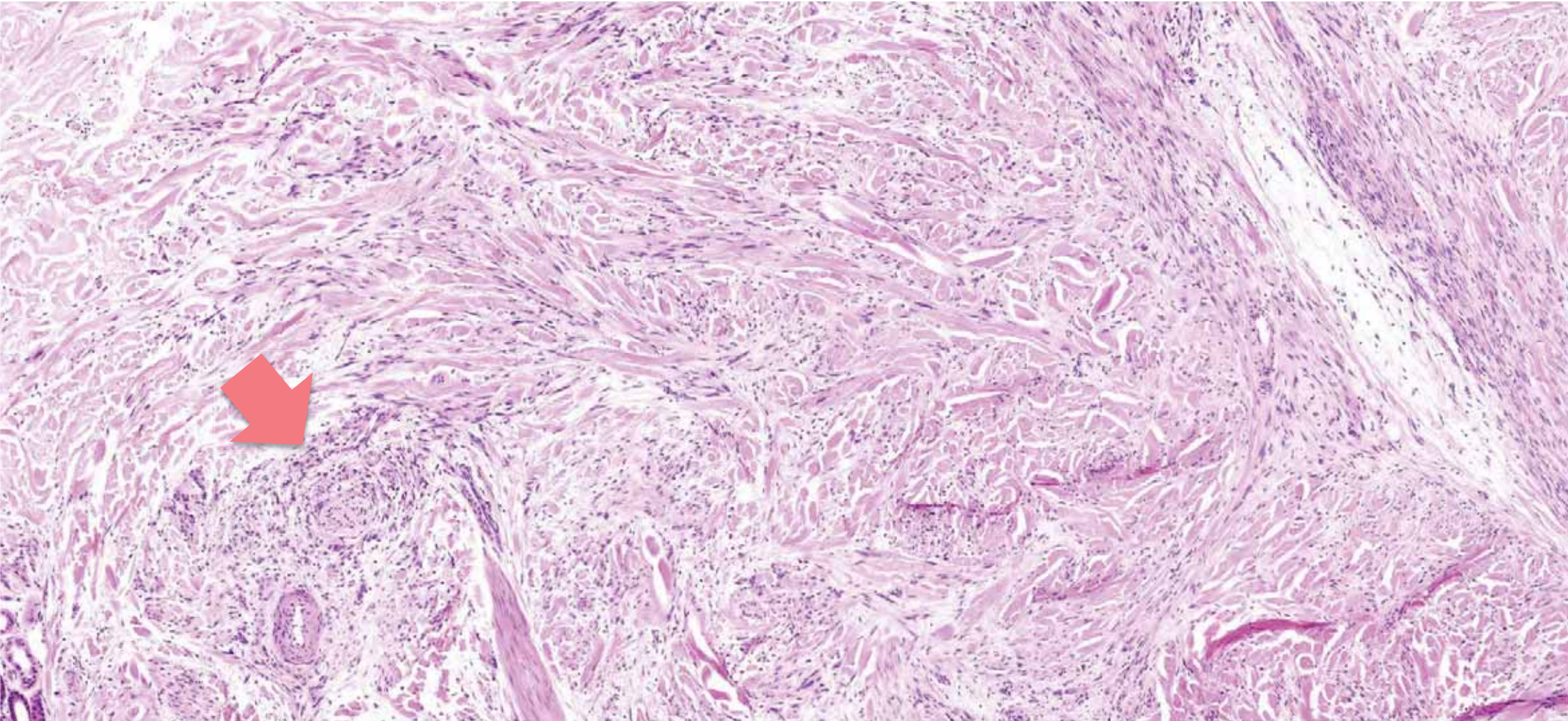
Longstanding fibrosis



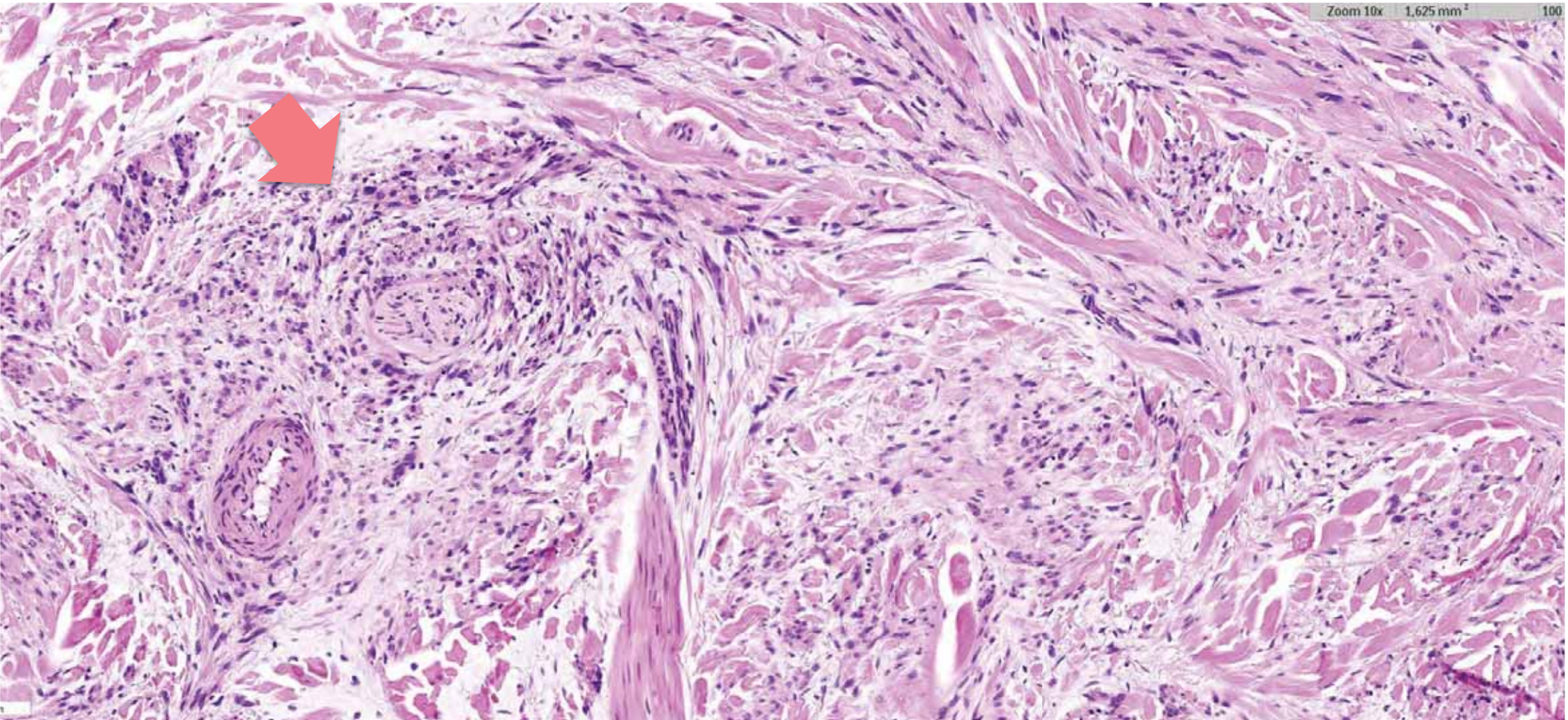
- 70-year-old man
- Knee tumor (2,5 cm)
- Attached to deep tissues



- 70-year-old man
- Knee tumor (2,5 cm)
- Attached to deep tissues



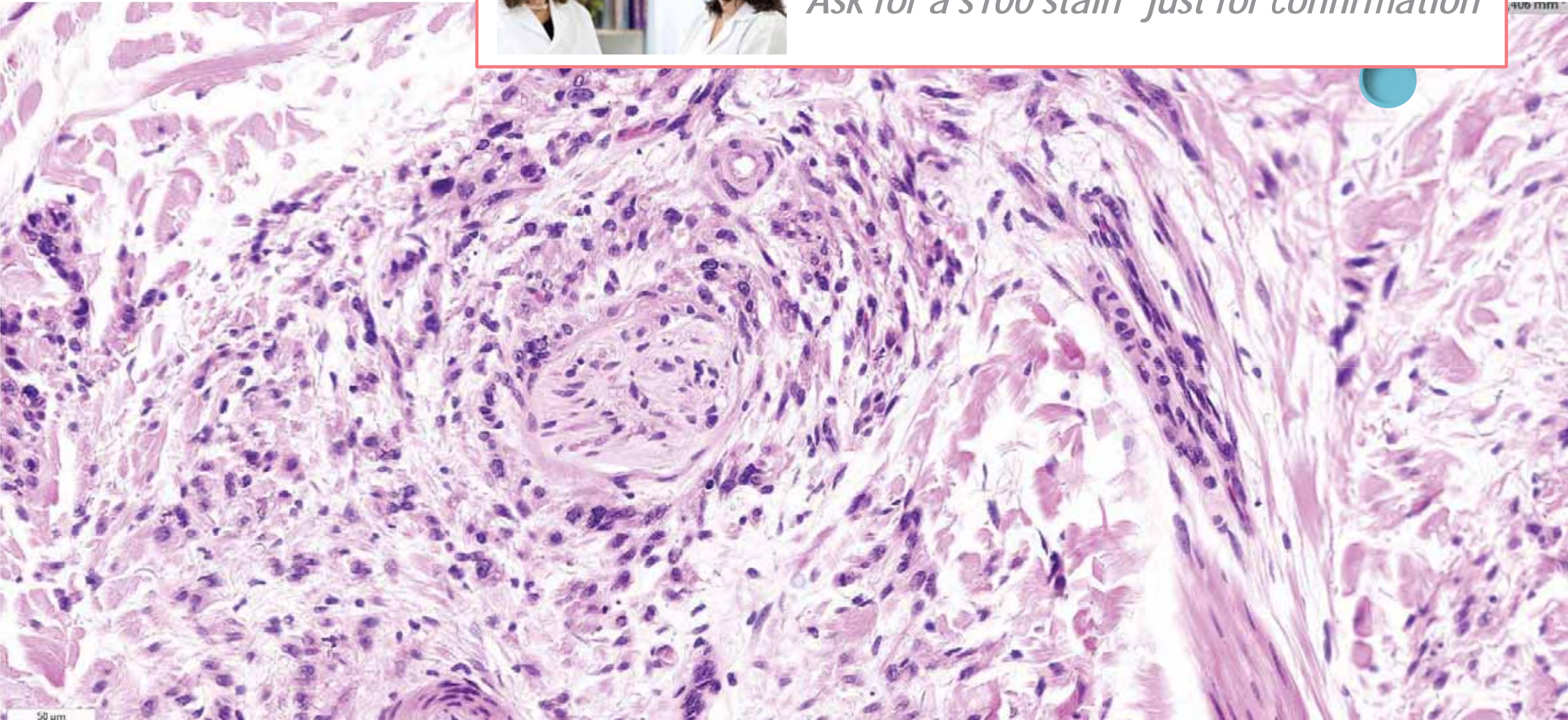
- 70-year-old man
- Knee tumor (2,5 cm)
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- 70-year-old man
- Knee tumor (2,5 cm)
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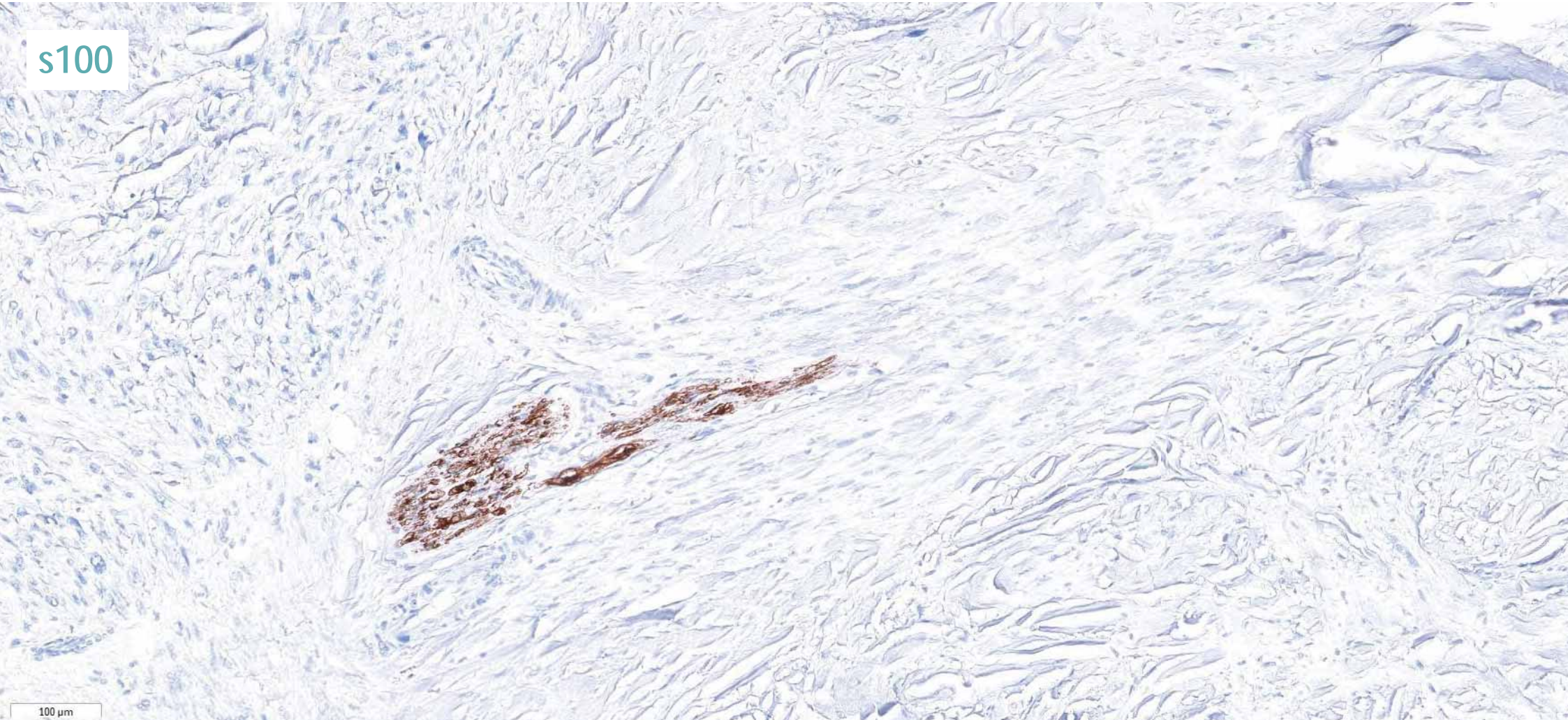


*It is a desmoplastic melanoma  
Ask for a s100 stain "just for confirmation"*



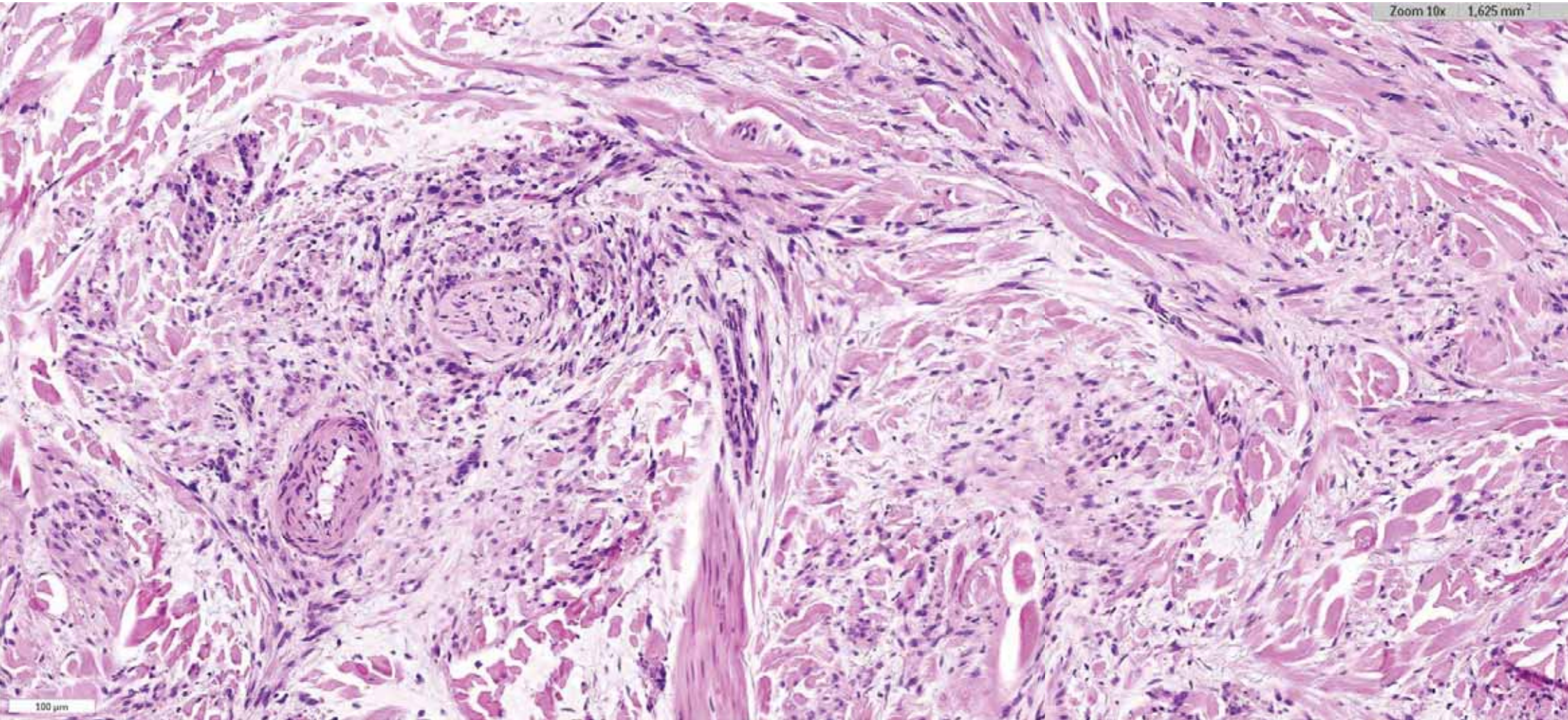
- 70-year-old man
- Knee tumor (2,5 cm)
- Attached to deep tissues

s100

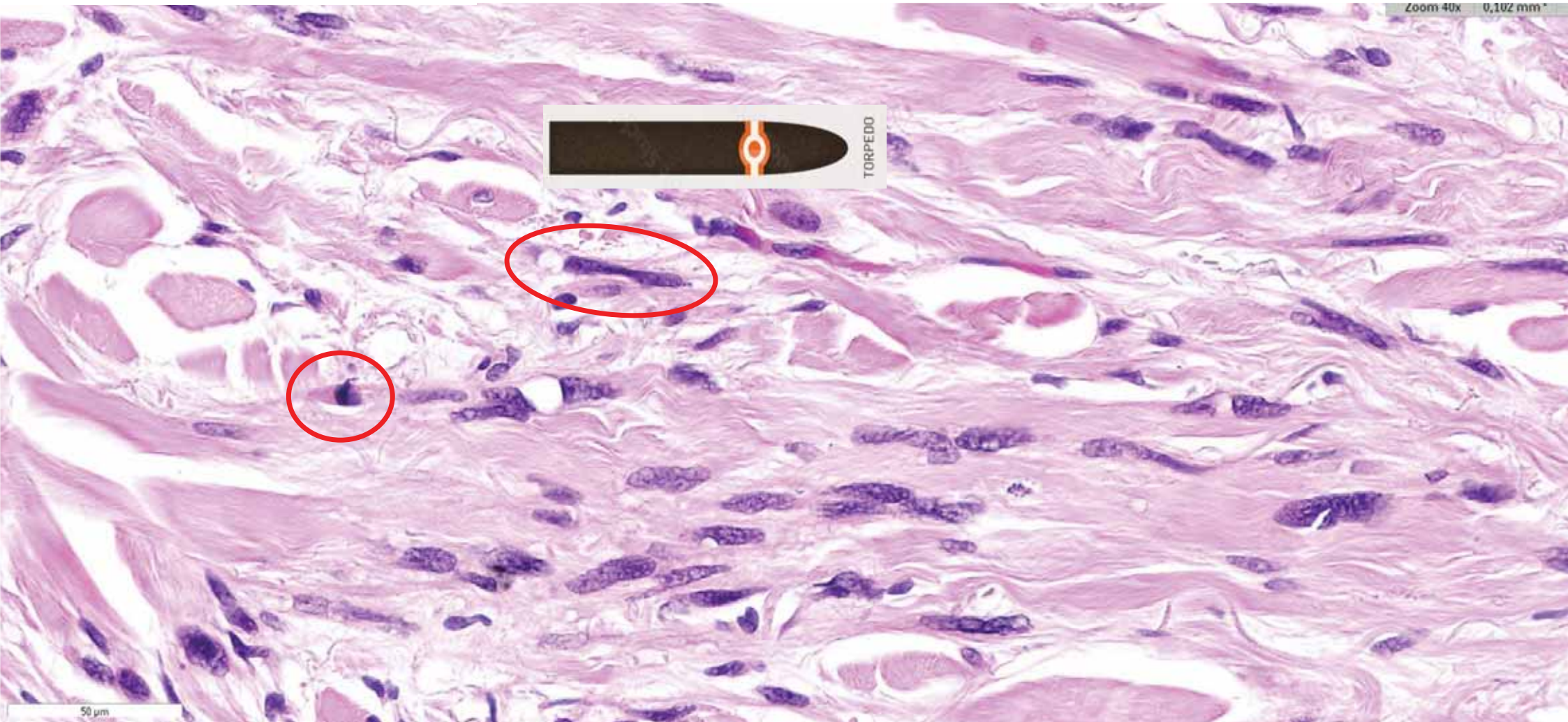


100 μm

- 70-year-old man
- Knee tumor (2,5 cm)
- Attached to deep tissues

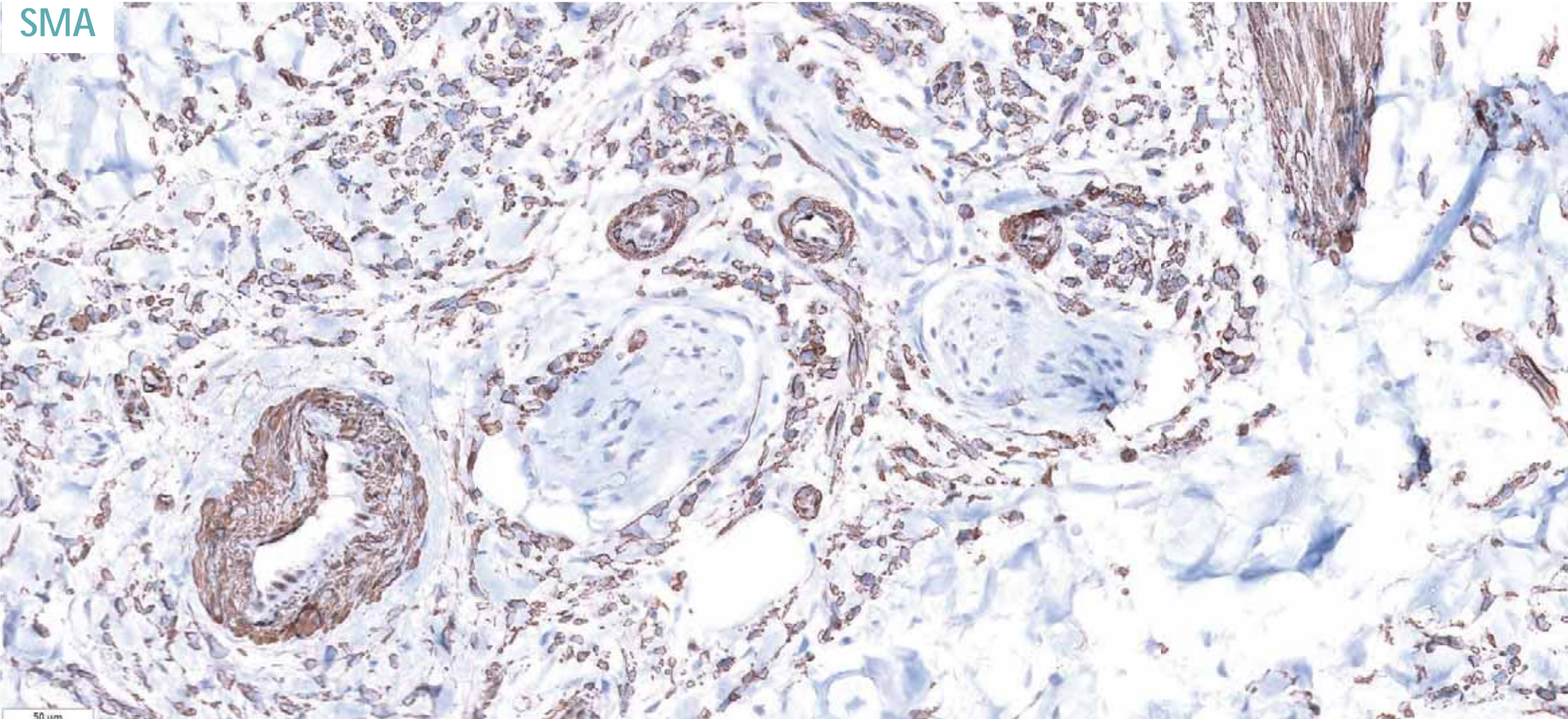


- 70-year-old man
- Knee tumor (2,5 cm)
- Attached to deep tissues



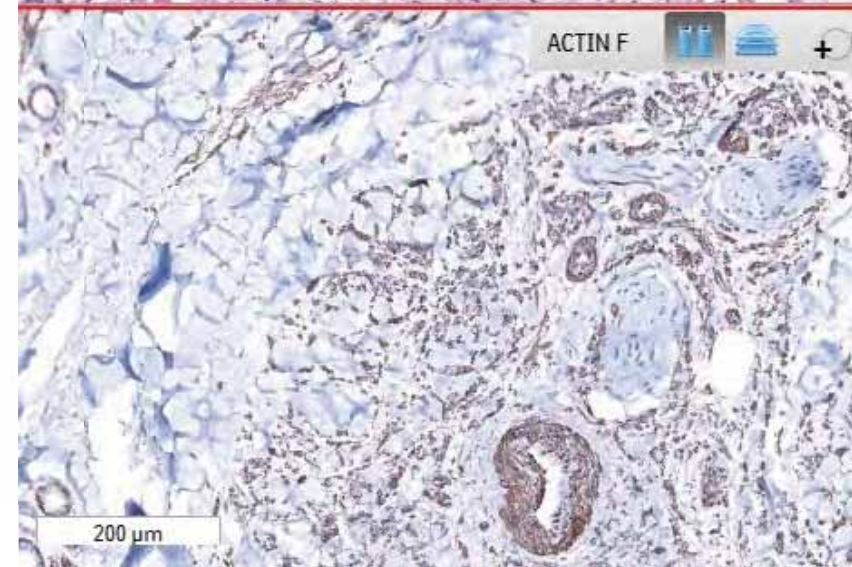
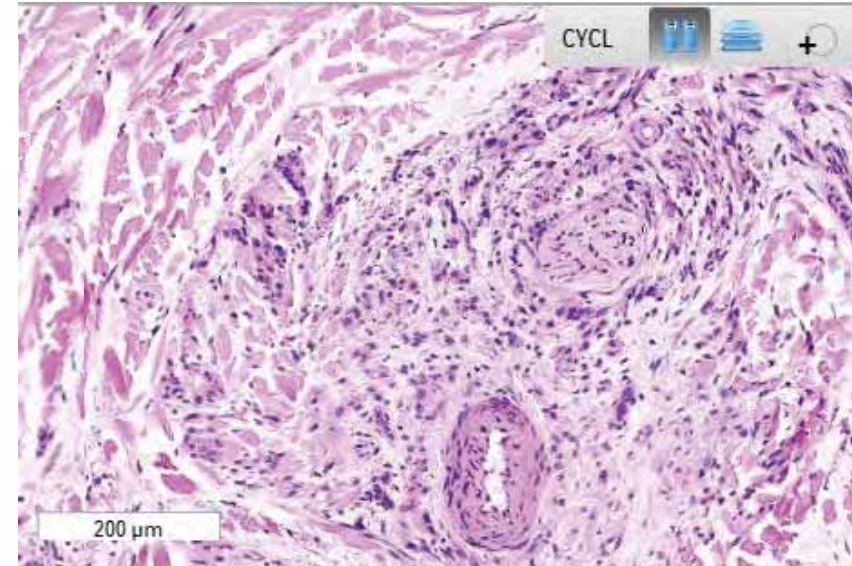
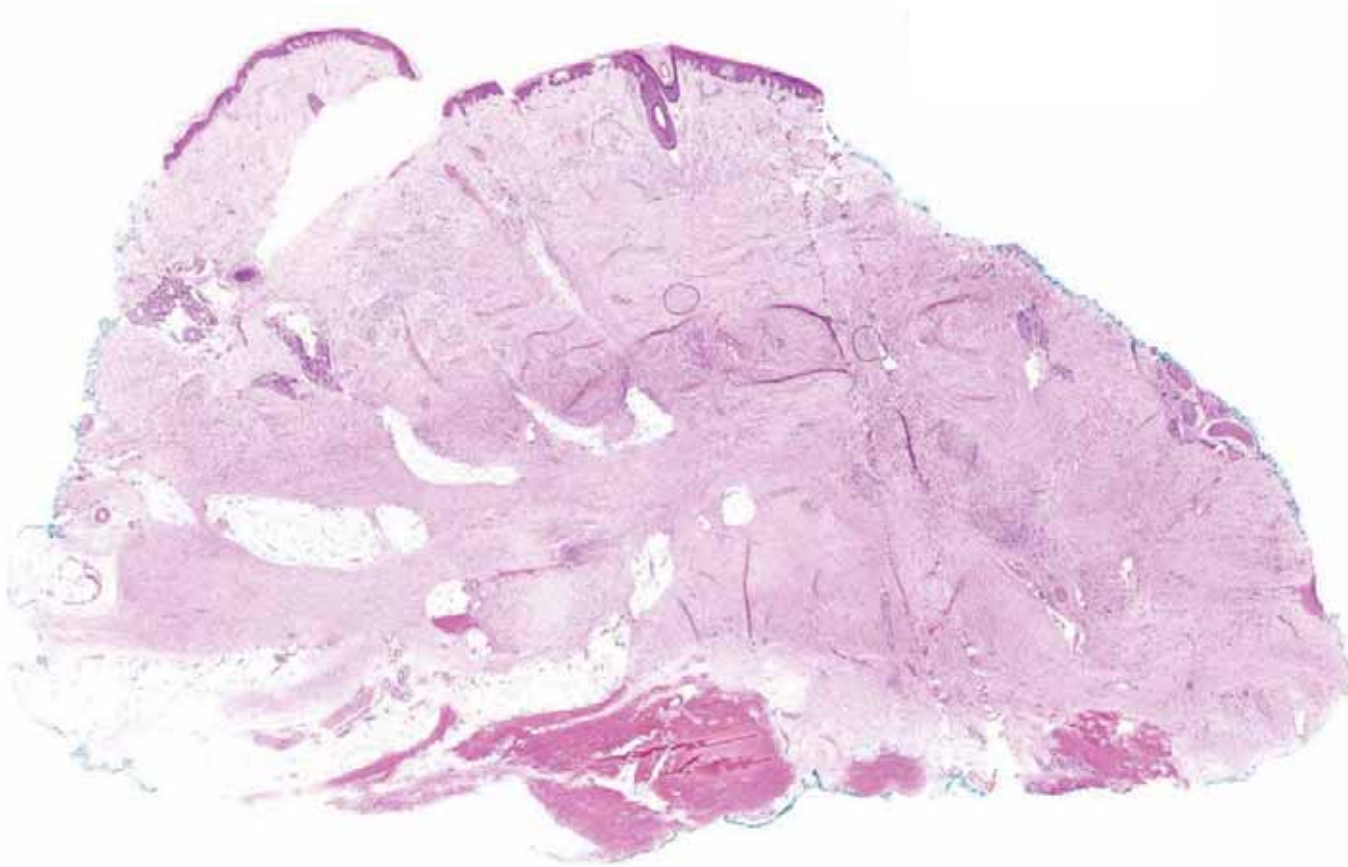
- 70-year-old man
- Knee tumor (2,5 cm)
- Attached to deep tissues

SMA



50 μm

# Dx: Desmoplastic leiomyosarcoma

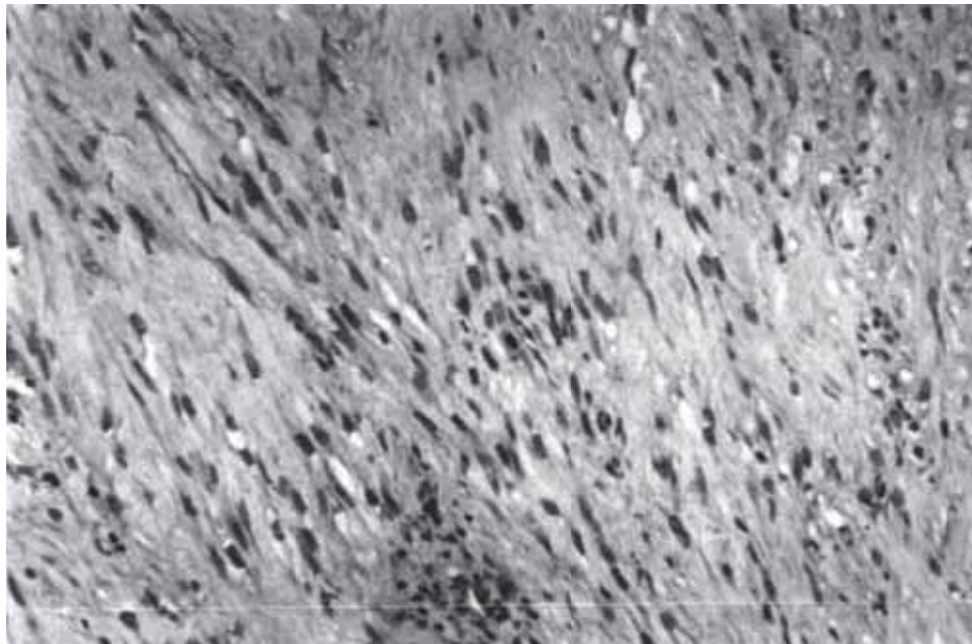


## Extraordinary Case Reports

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# Sclerotic Primary Cutaneous Leiomyosarcoma

John E. Karroum, M.D., Eugene G. Zappi, M.D., and  
Clay J. Cockerell, M.D.



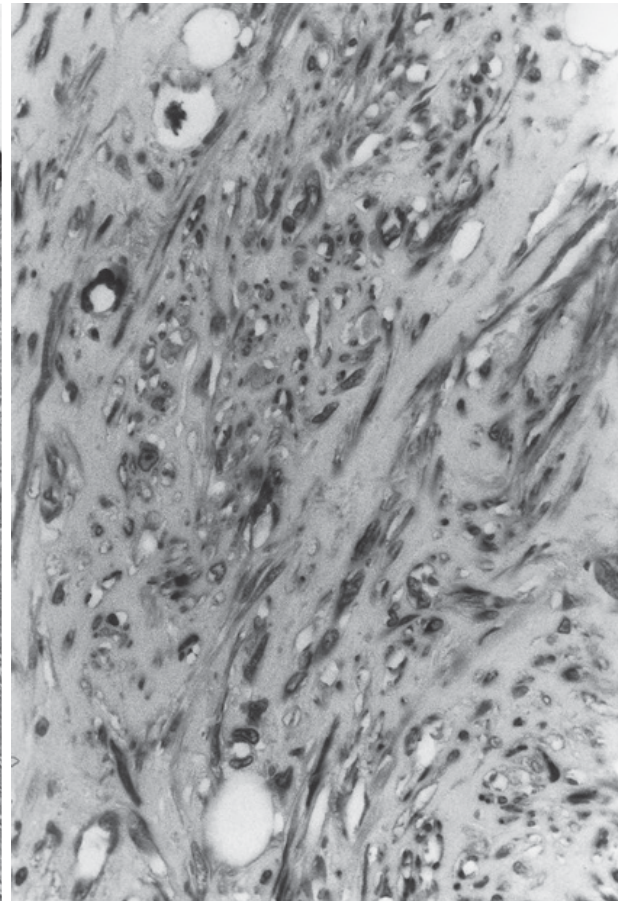
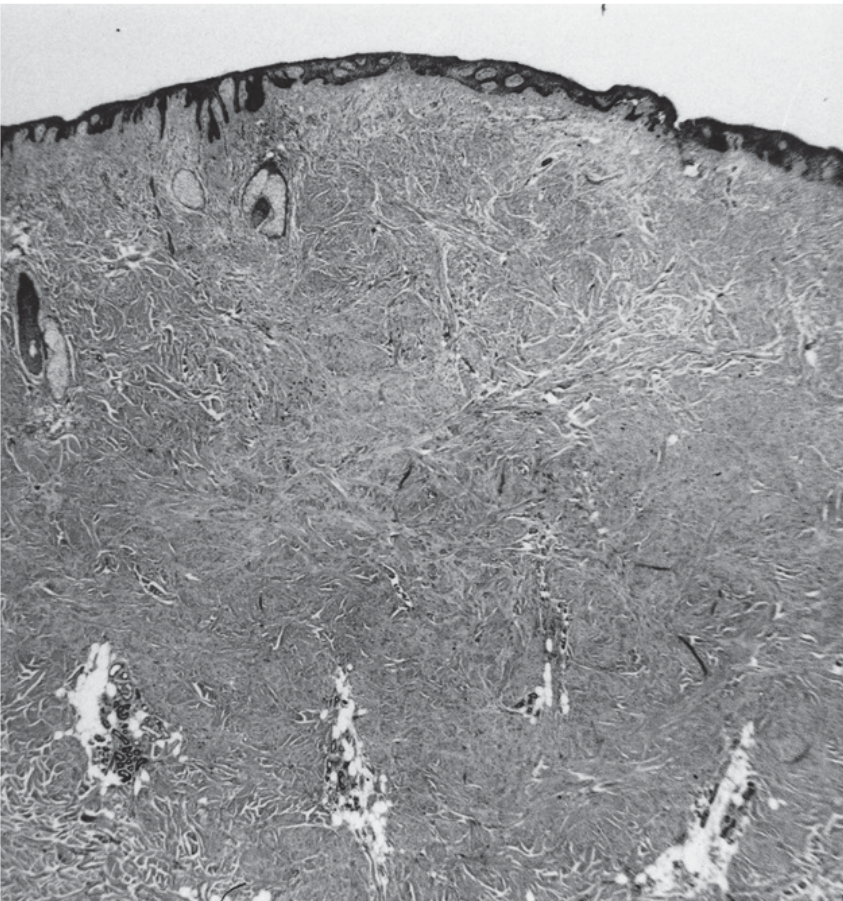
**FIG. 5.** Immunoperoxidase staining was positive with a smooth muscle actin-specific monoclonal antibody (HHF-35). Many of the cells contained small intracytoplasmic vacuoles. Note the perineural involvement.

# Desmoplastic Leiomyosarcoma of the Skin

Diaz-Cascajo, Carlos M.D; Borghi, Susanna M.D; Weyers, Wolfgang M.D

*The American Journal of Dermatopathology* 22(3):p 251-255, June 2000.

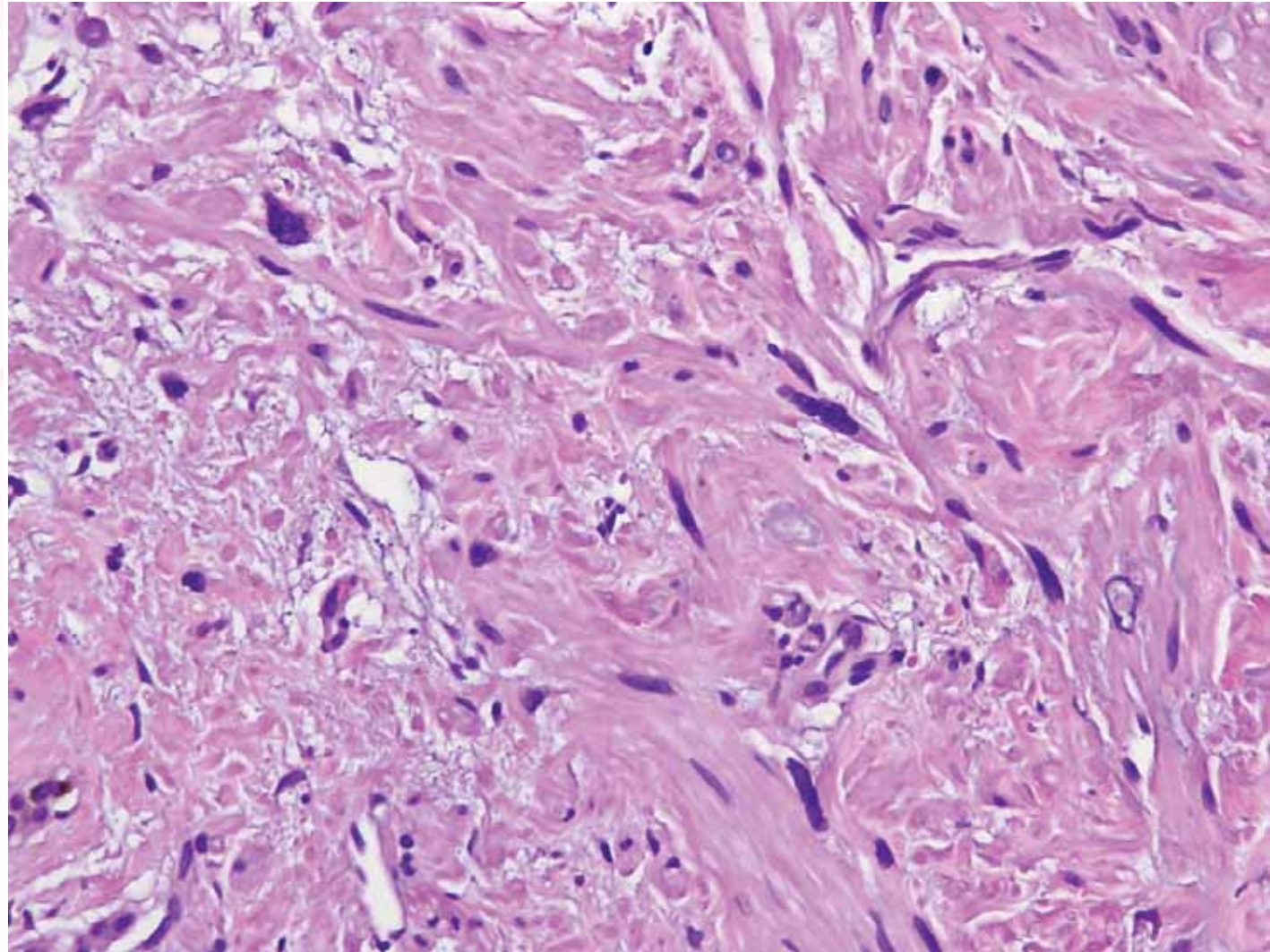
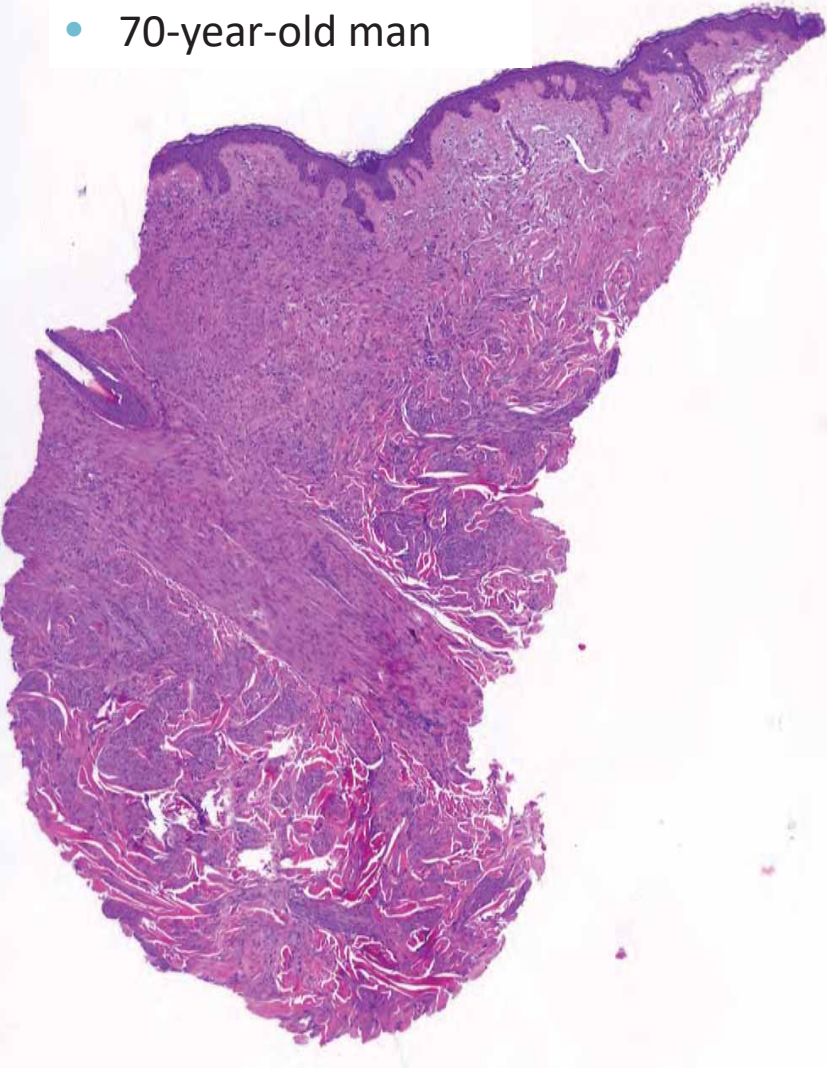
- 51-year-old woman thigh
- 78-year-old man upper part of the back
- One case desmin negative



# Symplastic leiomyoma

Bizarre nuclei, but small, superficial and minimal mitotic activity

- 70-year-old man





## LL 3

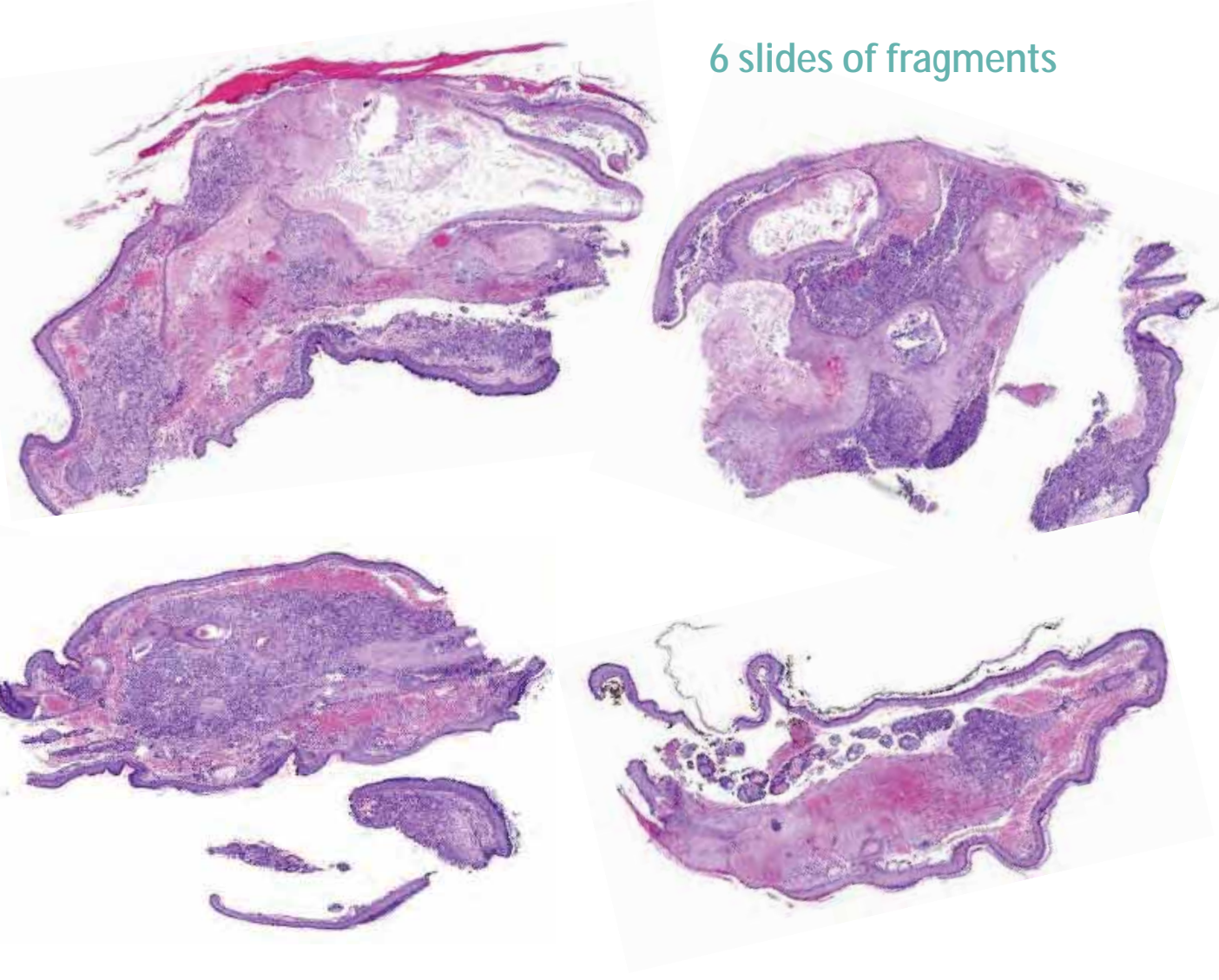
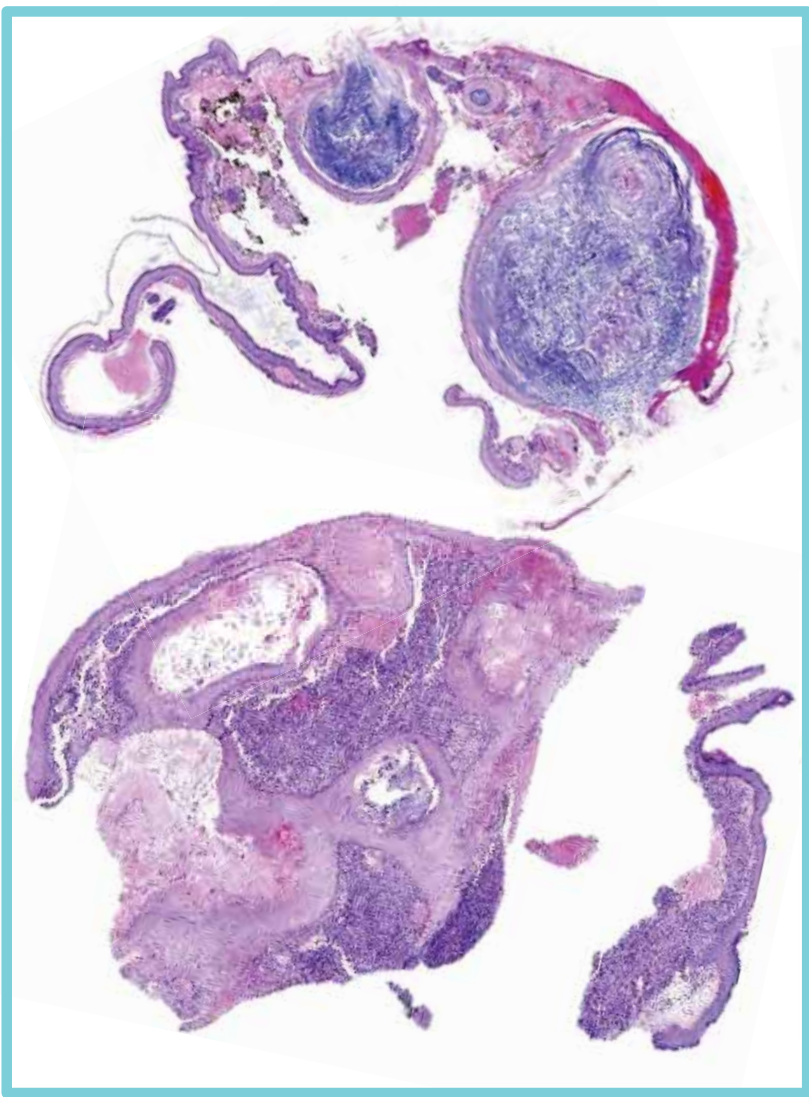
All things being equal,  
the simplest  
explanation is usually  
the most likely...

**but not always the  
correct one**

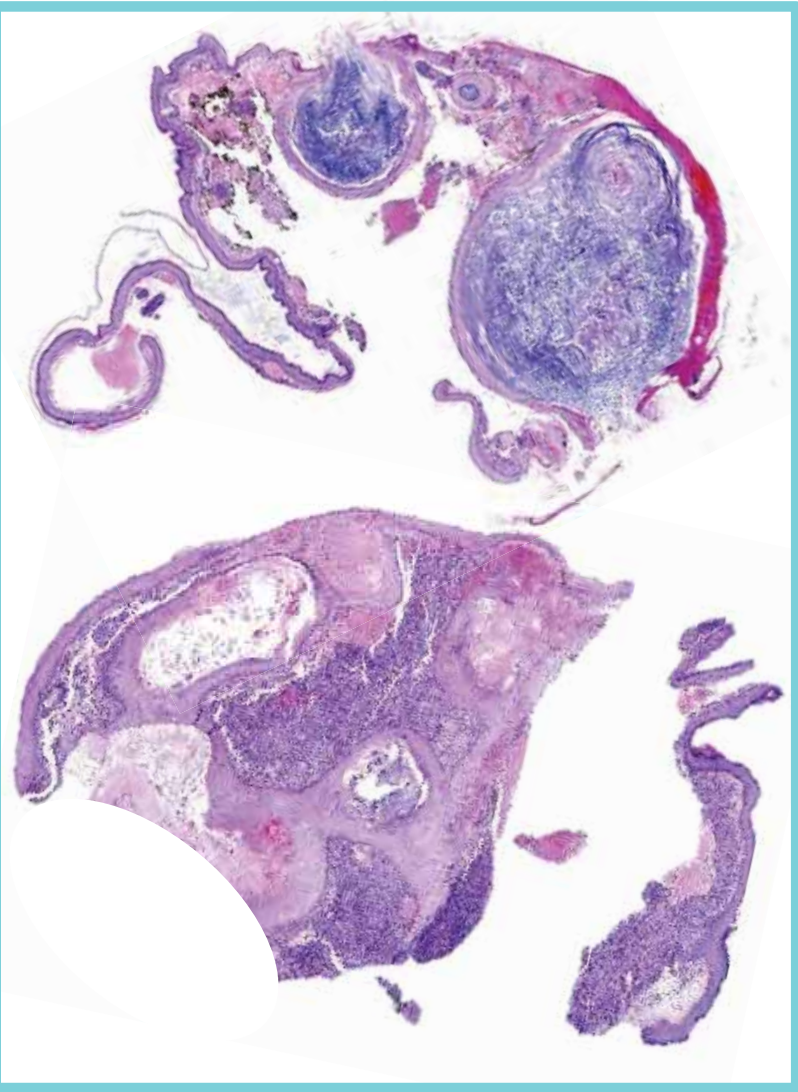
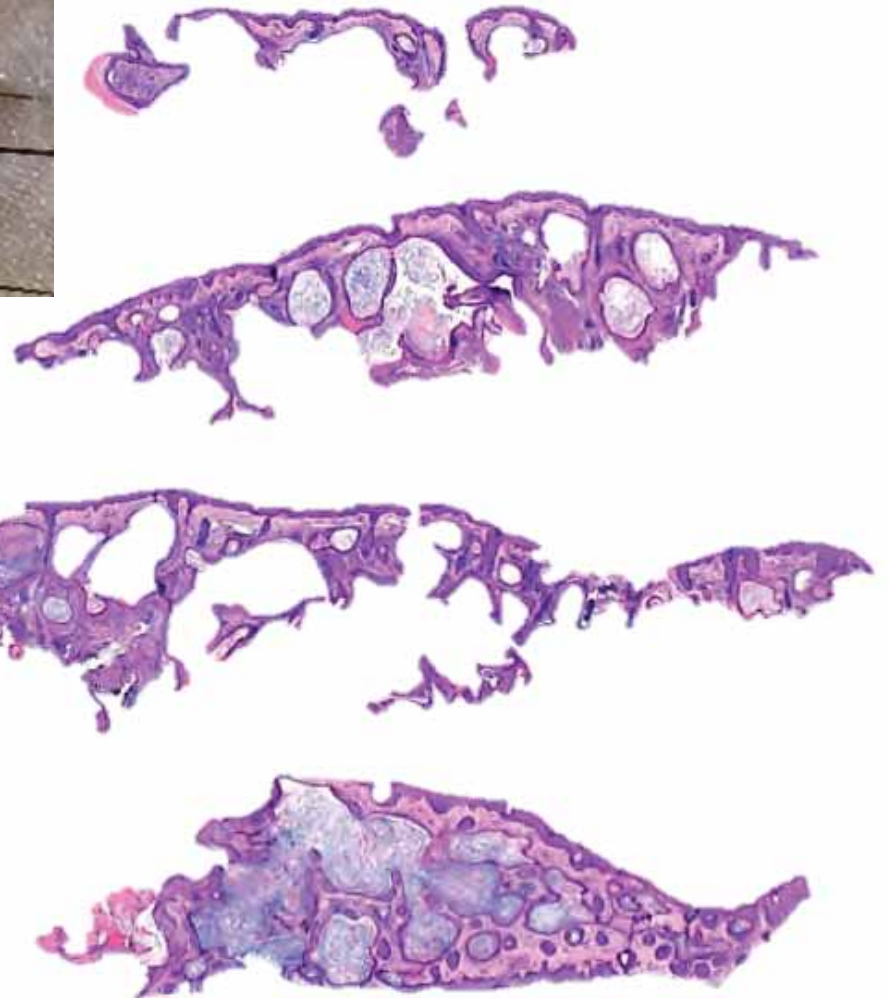
William of Ockham (1285-1347)

96-year-old woman. Inflamed comedones in the lower eyelid, 3 years after homolateral hemifacial herpes zoster

6 slides of fragments



## DDx: Milia en plaque?

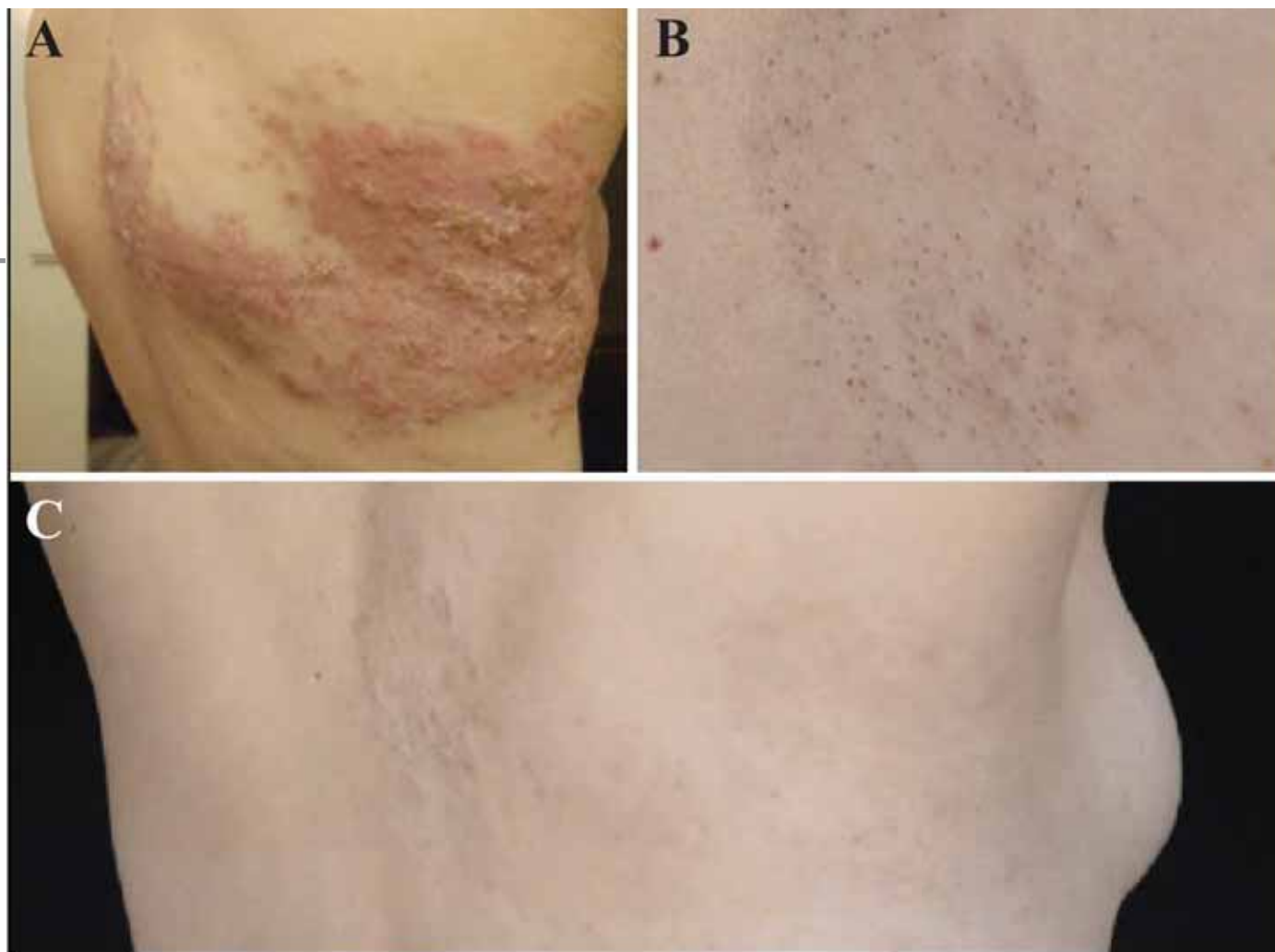


## Comedones appearing after herpes zoster infection: Koebner phenomenon or Wolf's isotopic response?

*EJD, vol. 29, n° 2, March-April 2019*

Jeffrey ZWEEGERS  
Satish F.K. LUBEEK

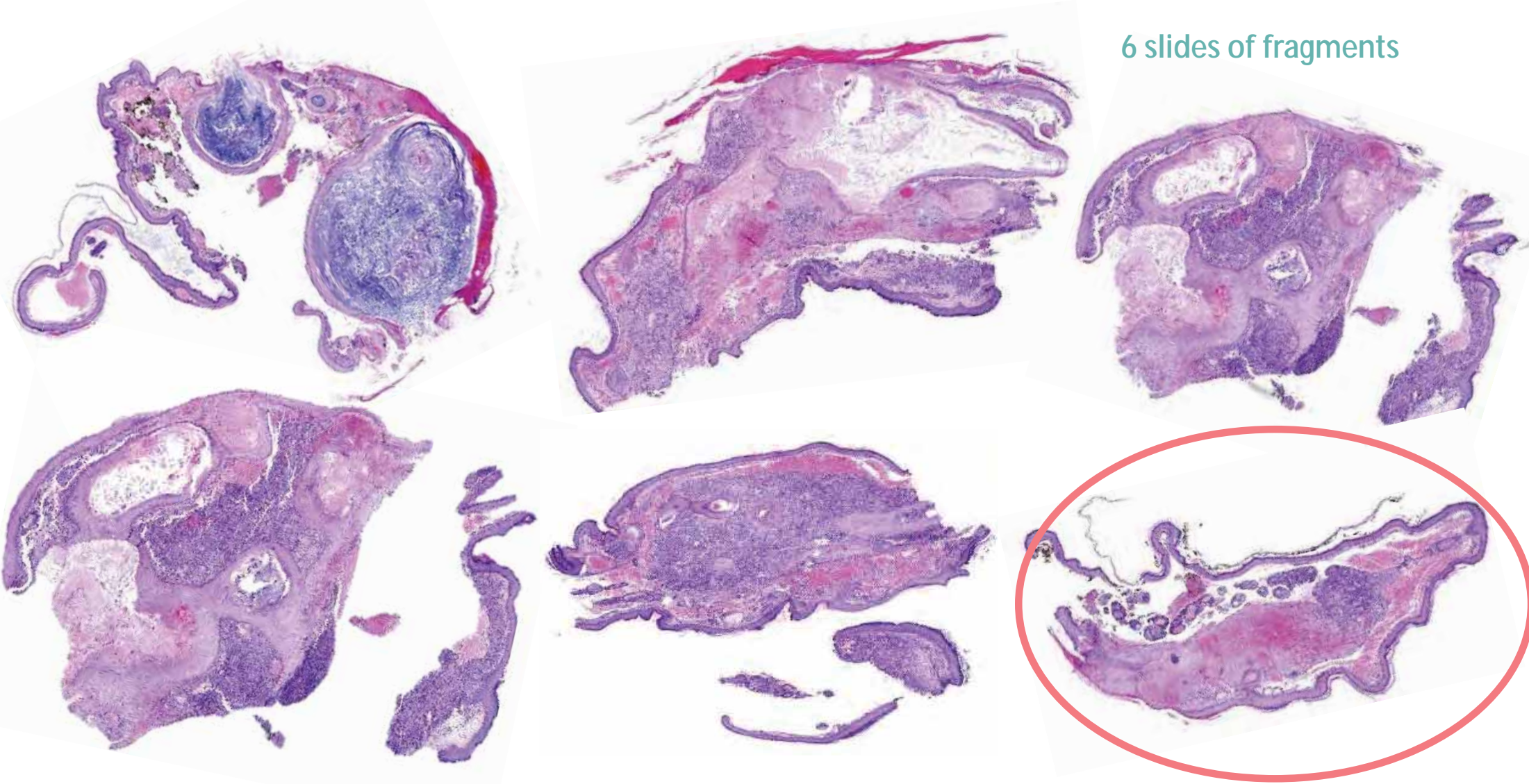
- 34-year-old immunocompetent female
- Comedones 5 months after herpes zoster healing
- **Koebner phenomenon** related to a "Locus minoris resistentiae"

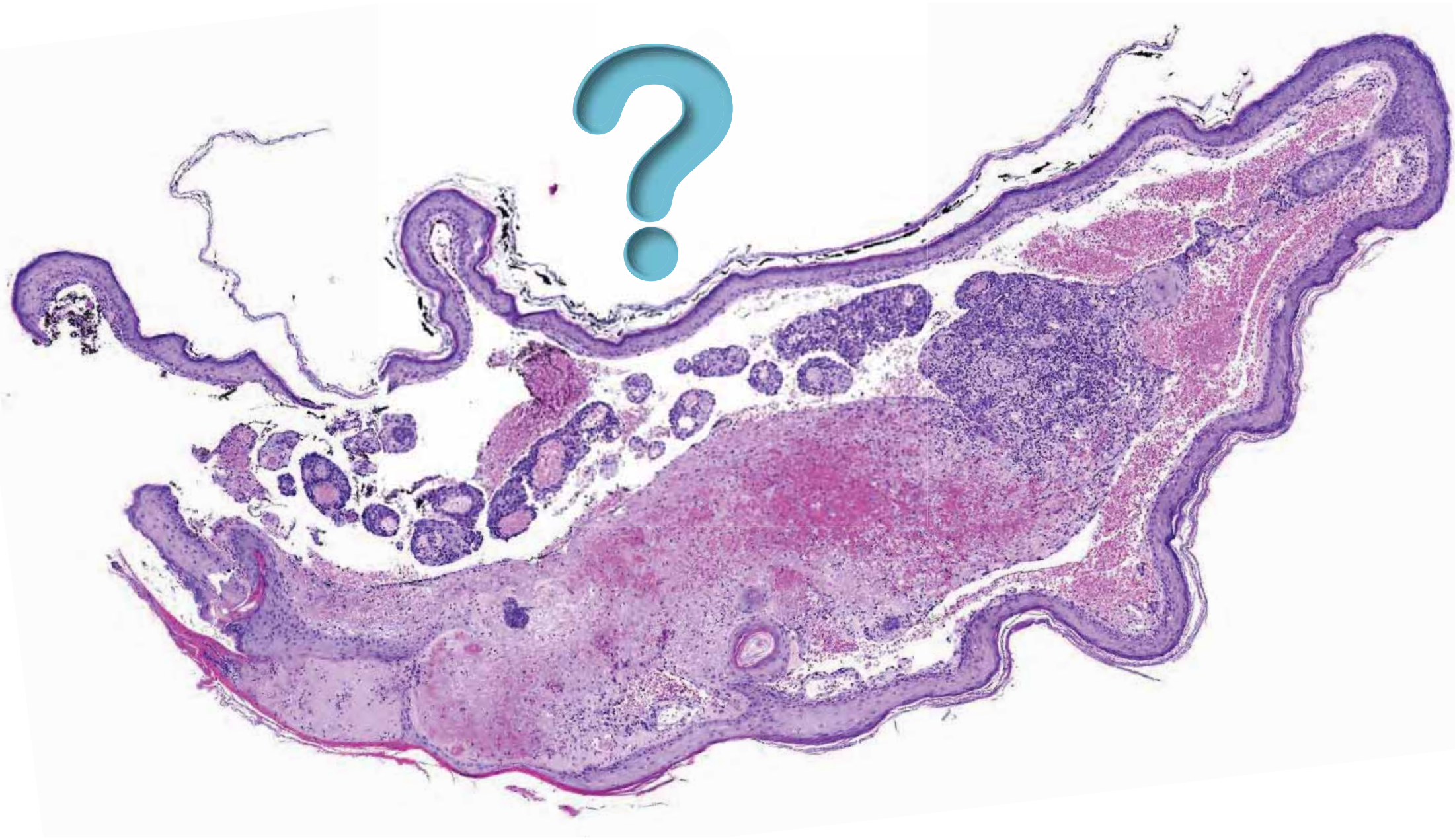


**Figure 1.** A) Distribution of the herpes zoster lesions. B) Close-up of the open comedones. C) Distribution of the open comedones.

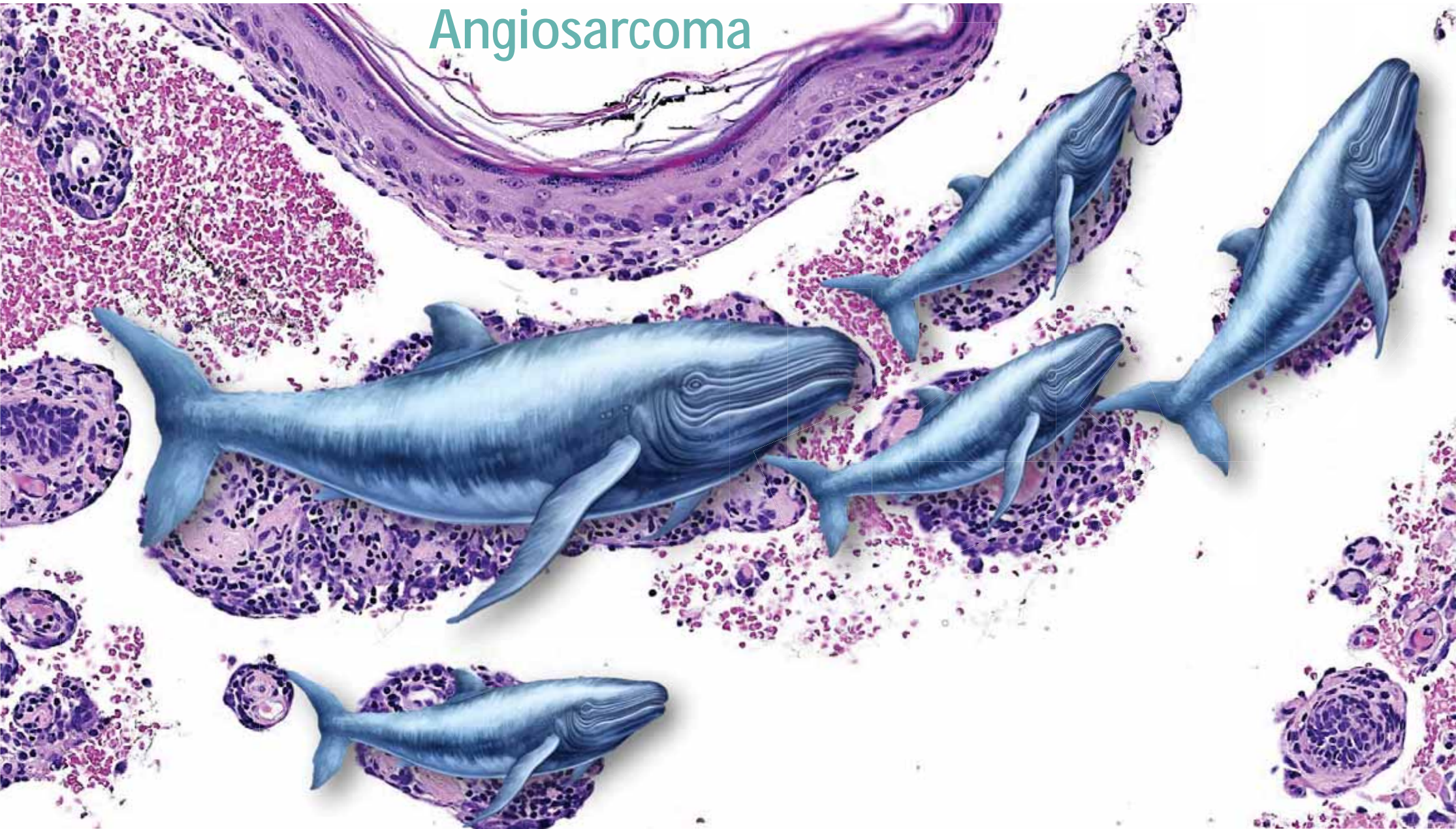
96-year-old woman. Inflamed comedones in the lower eyelid, 3 years after homolateral hemifacial herpes zoster

6 slides of fragments

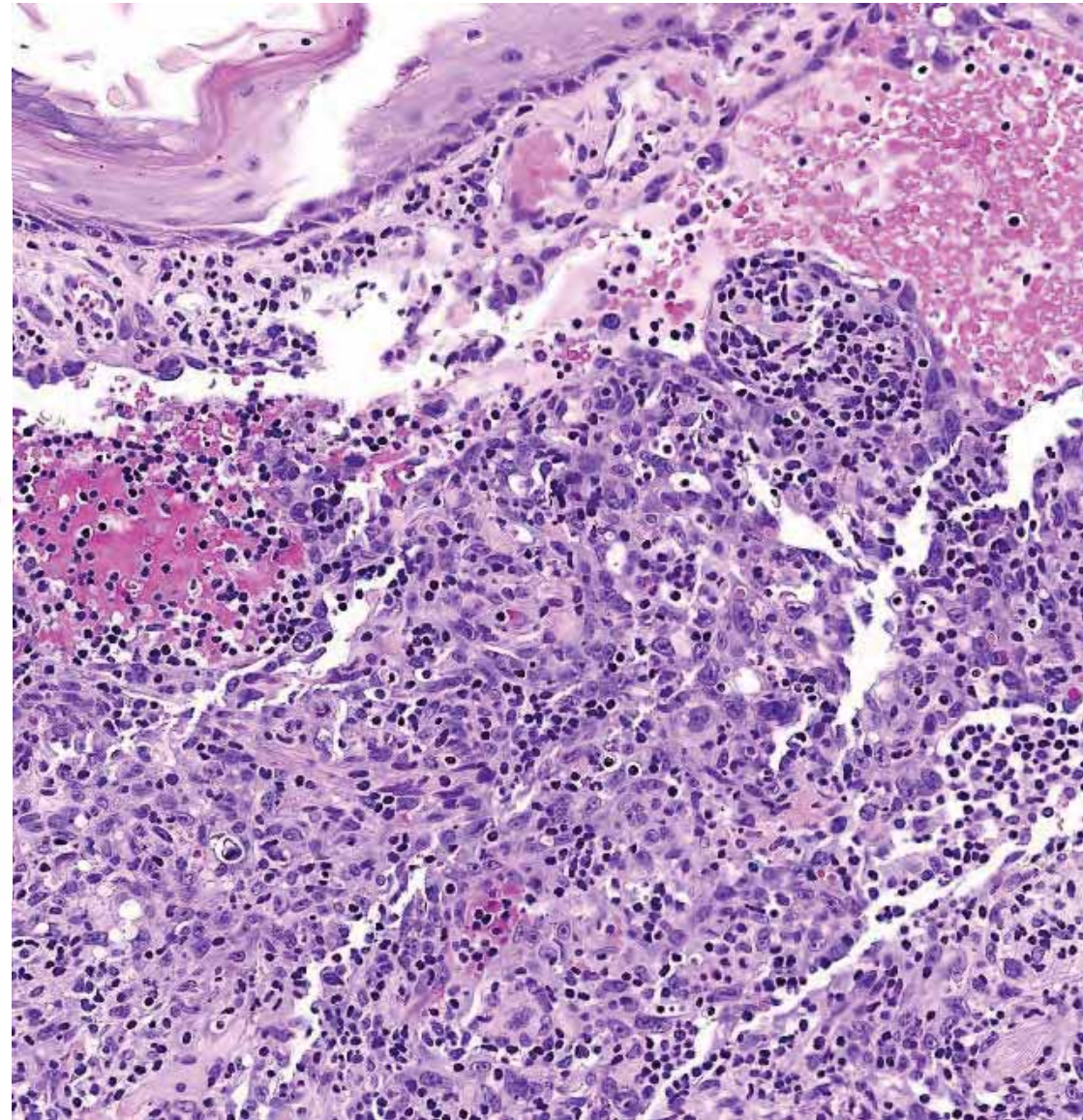




# Angiosarcoma



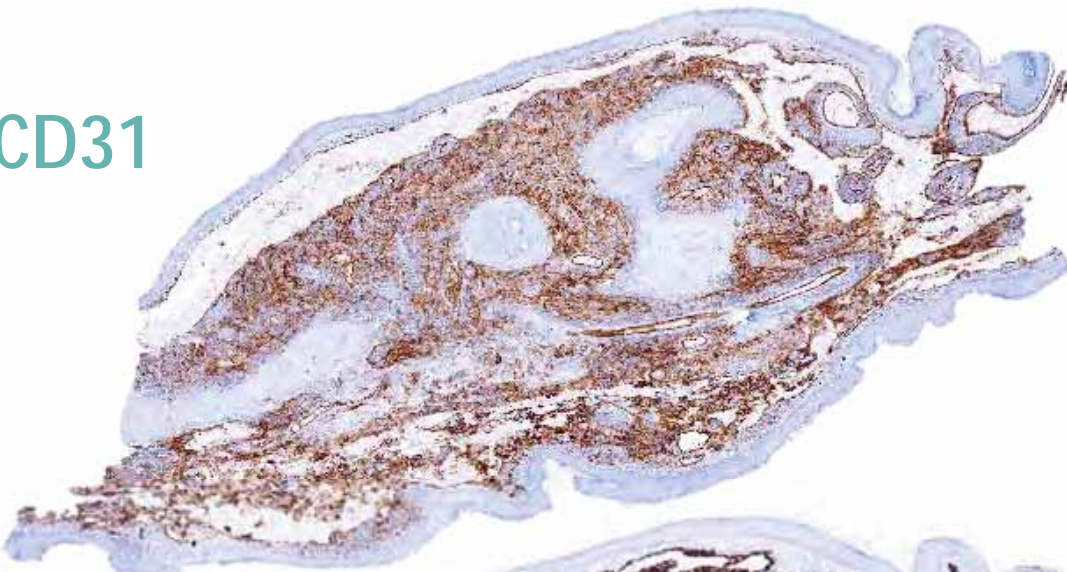
# Angiosarcoma



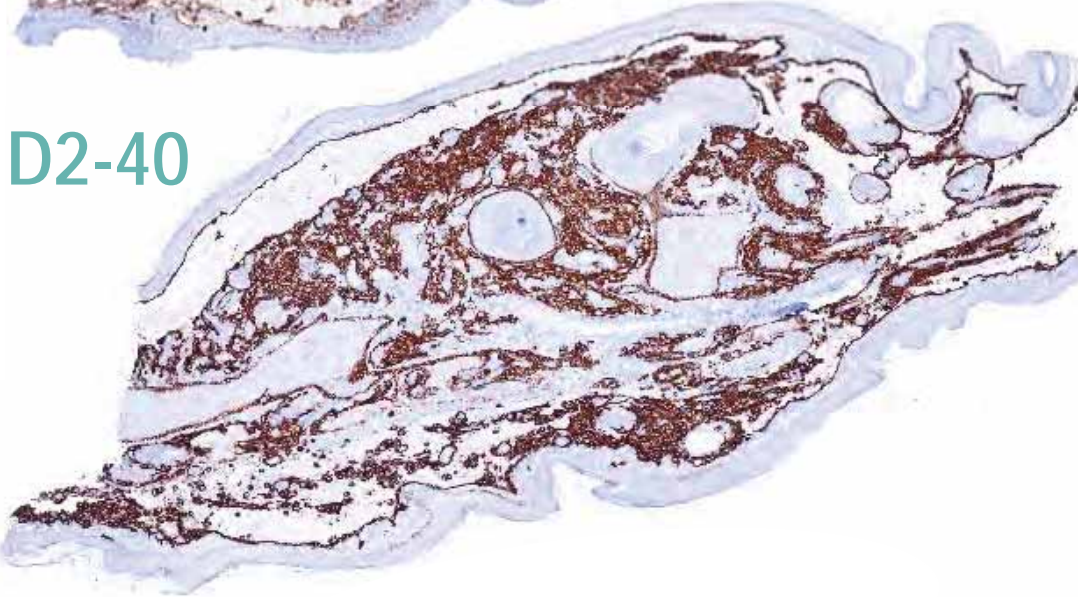
**Dx: Pseudolymphomatous angiosarcoma & comedones**



CD31

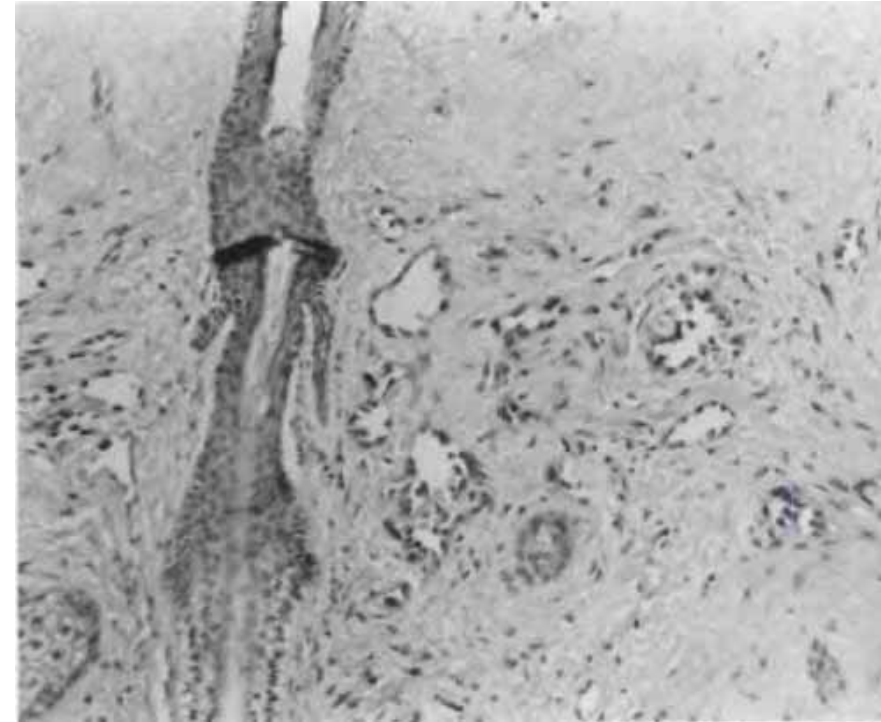
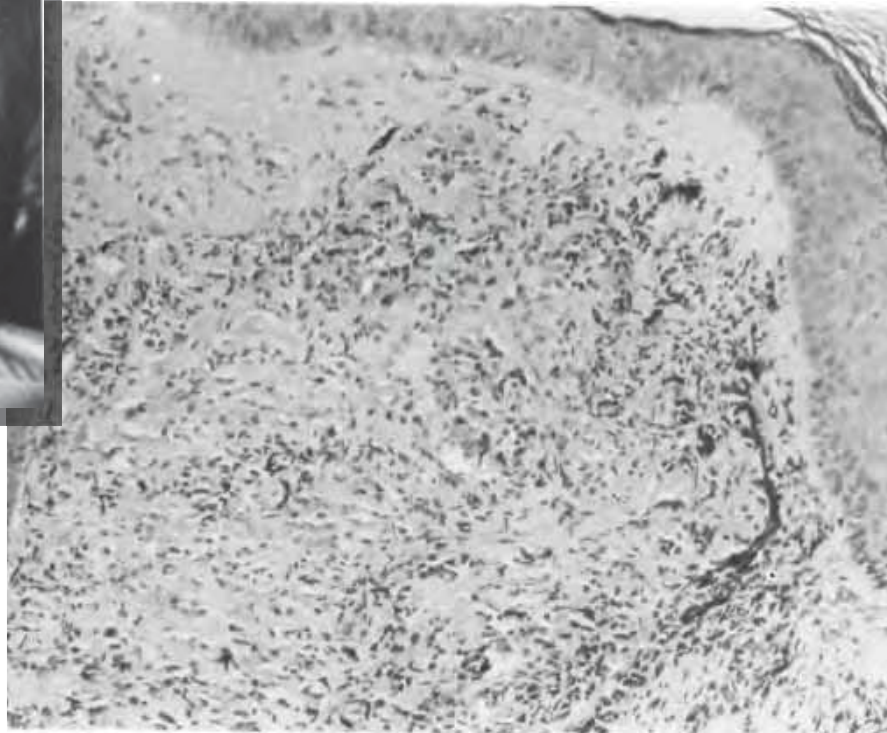


D2-40



# Cutaneous Angiosarcoma in a Site of Healed Herpes Zoster

CHARLES P. HUDSON, M.D., RUTH HANNO, M.D., AND JEFFREY P. CALLEN, M.D.



# Postherpetic Pseudolymphomatous Angiosarcoma Concealed Within Milia en Plaque: Expanding the Spectrum of Wolf Isotopic Response with a Literature Review

by Marina Corral-Forteza <sup>1</sup> ✉, Noelia Pérez-Muñoz <sup>2,3</sup> ✉ and Maria-Teresa Fernández-Figueras <sup>2,3,\*</sup> ✉

Term	First Described	Definition and * Interesting Facts
<b>Koebner isomorphic phenomenon</b> [4,5]	H. Koebner, 1872	Development of lesions from an existing cutaneous disease in previously healthy skin that has undergone non-specific injury, which can be mild. This disease may appear in locations where it typically does not occur.
<b>Wolf isotopic response</b> [2,3]	R. Wyburn-Mason, 1955; refined by R. Wolf, 1995	Appearance of new skin lesions at the site of a previously healed, unrelated skin disease.
<b>Locus minoris resistentiae</b> [34,35]	R.L. Zuehlke, 1982	Areas of the body that are more vulnerable than others to suffer some pathologic conditions. * Its origins trace back to ancient myths, such as Achilles' heel or Siegfried's shoulder.
<b>Isopathic phenomenon</b> [36]	F. Sagher, 1954	The injection of specific or non-specific proteins triggers the development of a disease already present in the patient.
<b>Pseudoisomorphic response (pseudo-Koebner)</b> [37,38,39]	Unknown. First examples in the literature from F. Lewandowsky, W. Lutz, 1922	Spread of a cutaneous infection along a line of previously damaged skin.
<b>Renboek/Renbök phenomenon (inverse or reverse Koebner phenomenon)</b> [40,41]	R. Happle, 1991	Disappearance of an existing skin condition following the onset of a new dermatosis at the same site. * The term "Renboek" or "Renbök" is not an eponym, but "Koebner" spelled backwards.
<b>Pathergy</b> [29]	Blobner, 1937	A minor trauma on healthy skin induces non-specific cutaneous lesions, often rich in neutrophils.

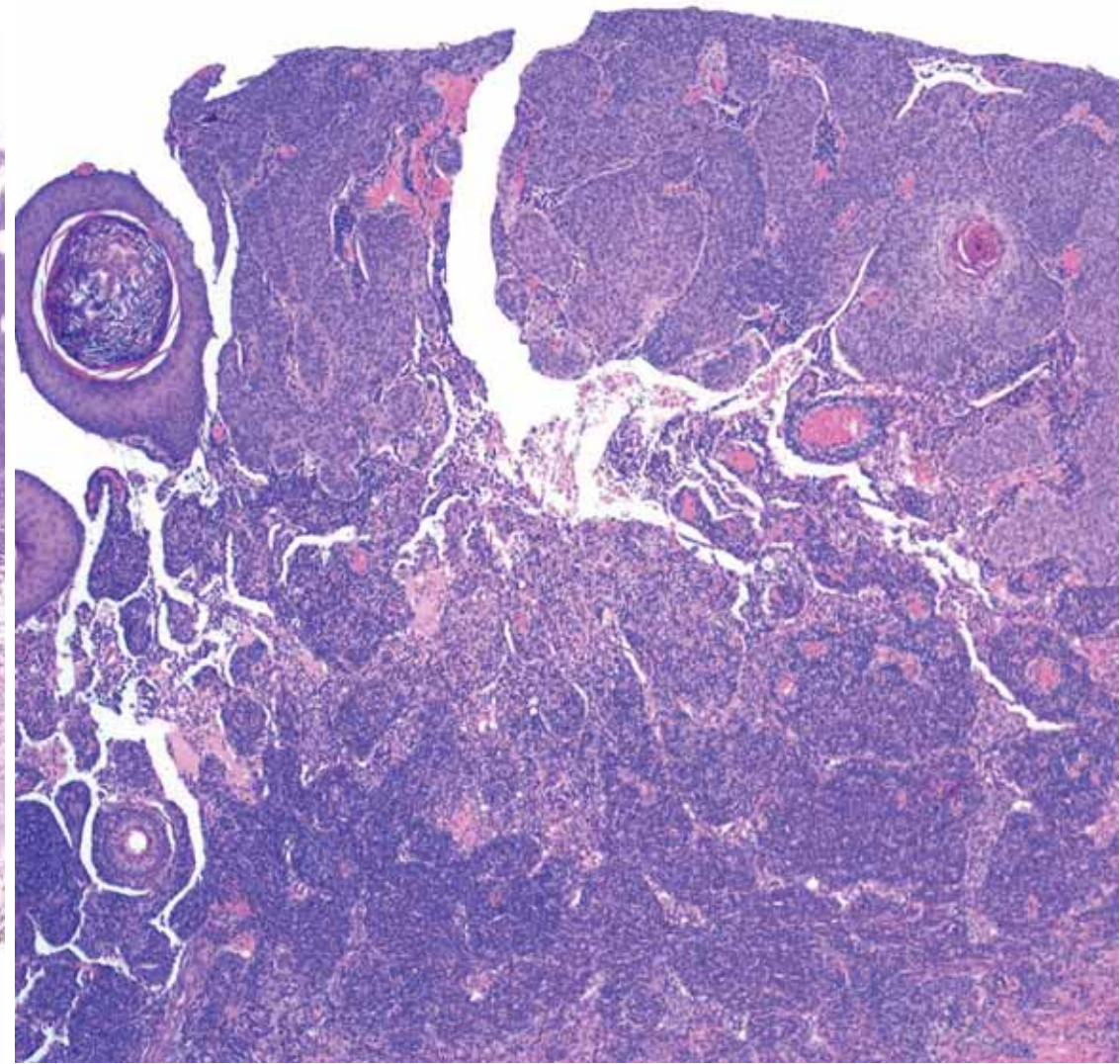
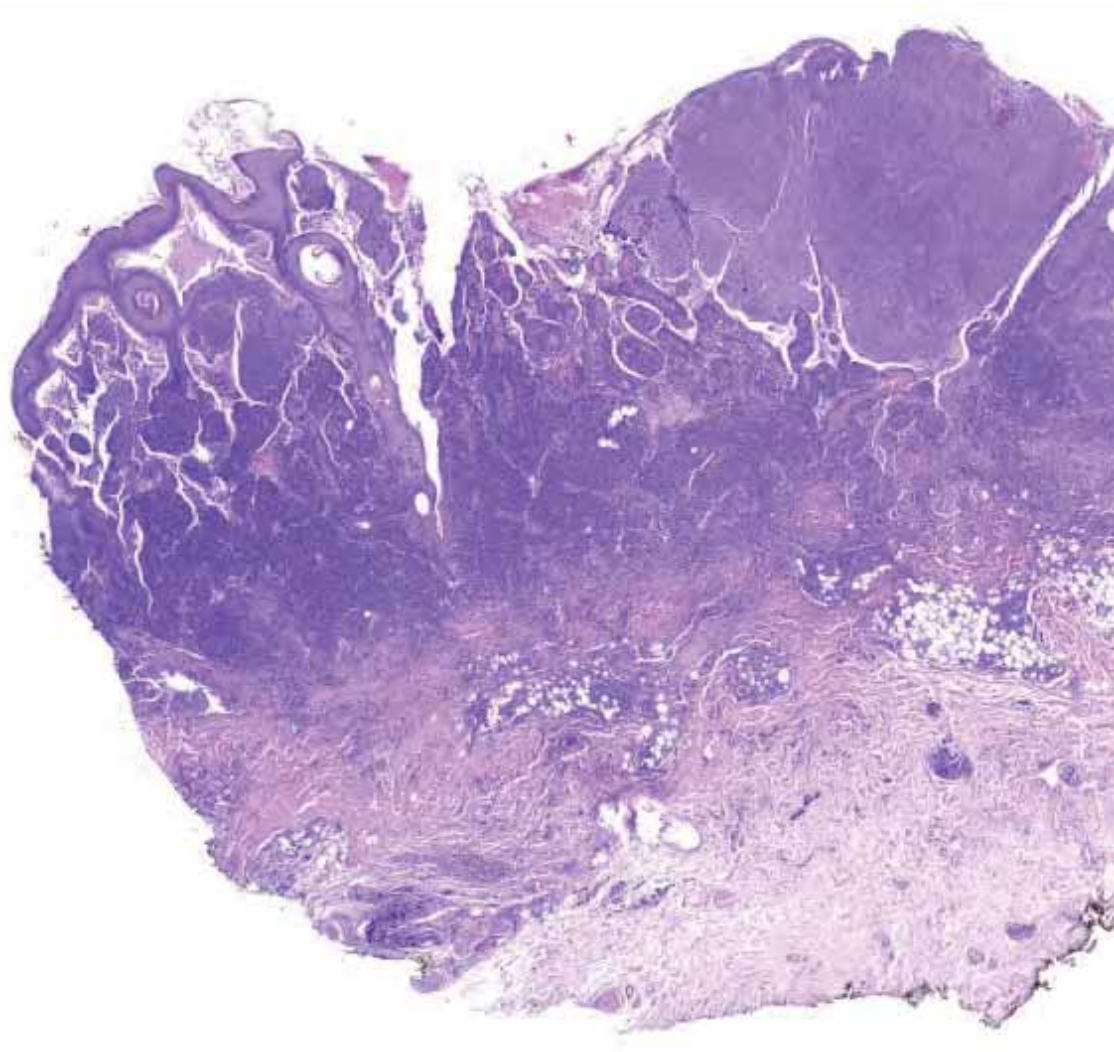
Inflammatory Diseases	Infections
Acne	Molluscum contagiosum
Acneiform lesions	Warts and papillomata
Actinic granuloma (O'Brien) [21]	Candidiasis
Bullous pemphigoid [18]	Dermatophytosis
Chronic cutaneous graft-versus-host disease	
Chronic small vessel vasculitis (Extracutaneous eosinophilic granuloma or Lever granuloma) [22]	
Chronic urticaria [23]	
Comedones	
Comedonic-microcystic reactions	
Contact dermatitis	
"Dysimmune" reactions	
Eosinophilic dermatosis	
Erythema annulare centrifugum	
Fibroelastolytic papulosis	
Folliculitis (granulomatous or eosinophilic) [24]	<b>Tumors and pseudotumors</b>
Follicular mucinosis [25]	Angiosarcoma
Furunculosis	Basal cell carcinoma
Granuloma annulare [26]	Besosquamous carcinoma
Granulomatous folliculitis	Benign lymphangi endothelioma [19]
Granulomatous reactions (necrotizing or non-necrotizing)	Bowen disease
Granulomatous vasculitis	Breast carcinoma
Grover disease (personal case)	Kaposi sarcoma
Infections	Leukemia
Keloid	Lymphangiogenesis (pseudotumors) [19]
Lichen planus	Lymphomas
Lichen sclerosus et atrophicus-morphea	Mastocytosis [27]
Lichen simplex	Metastases (from breast carcinoma and others)
Lichenoid dermatitis	Pseudo lymphoma
Linear IgA dermatosis	Rosai-Dorfman disease
Lupus erythematosus [28]	Squamous cell carcinoma
Milia	Syringoid eccrine carcinoma [18]
Mucinosis	Tufted Angioma [29]
Nodular solar degeneration	
Palpable purpura	
Pityriasis rosea (atypical) [30]	
Prurigo-like eruption	
Psoriasis	
Reactive perforating collagenosis	
Rosacea	
Sarcoidosis	
Unilateral nevoid telangiectasia [31]	
Vitiligo [32]	
Xanthoma [33]	

## LL 4

Never stop after the  
initial diagnosis!  
There may be additional  
hidden pathologies



- 79-year-old man. Erosive lesion on the scalp
- History of multiple squamous cell carcinomas



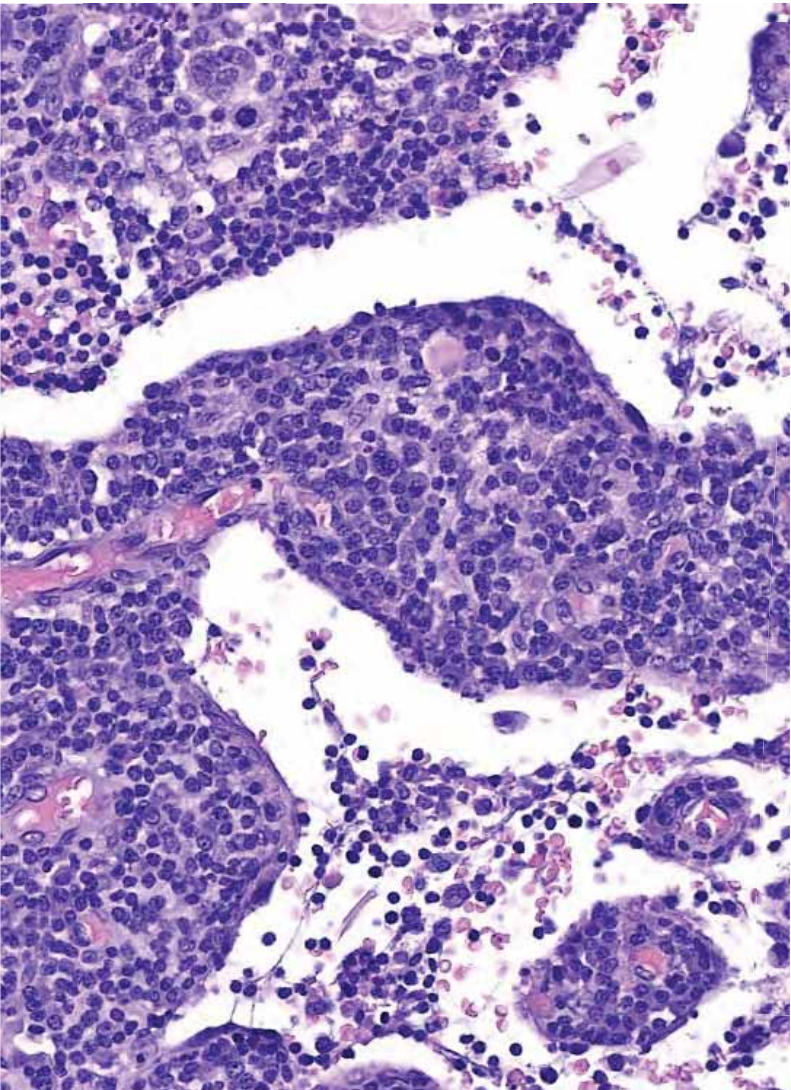


Squamous cell carcinoma

This histological slide shows a cross-section of tissue with two distinct pathological features. The upper portion of the image displays squamous cell carcinoma, characterized by nests and cords of atypical squamous epithelial cells with hyperchromatic nuclei and keratinization. The lower portion shows pseudolymphomatous angiosarcoma, which consists of irregular, anastomosing vascular channels lined by atypical endothelial cells, surrounded by a dense infiltrate of lymphocytes. The overall appearance is that of a mixed malignant tumor.

Pseudolymphomatous angiosarcoma

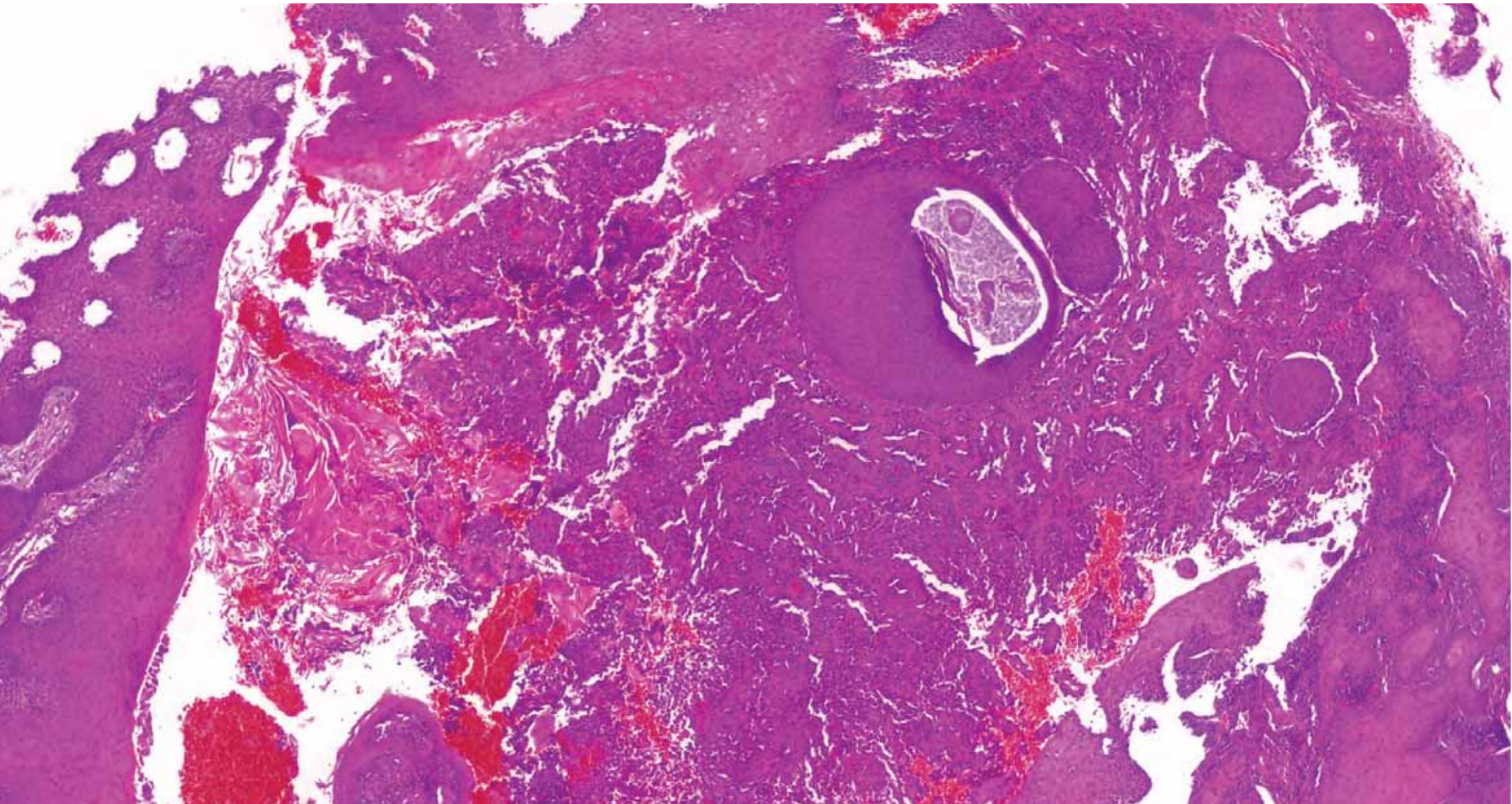
# Dx: Collision SCC & pseudolymphomatous angiosarcoma



D2-40

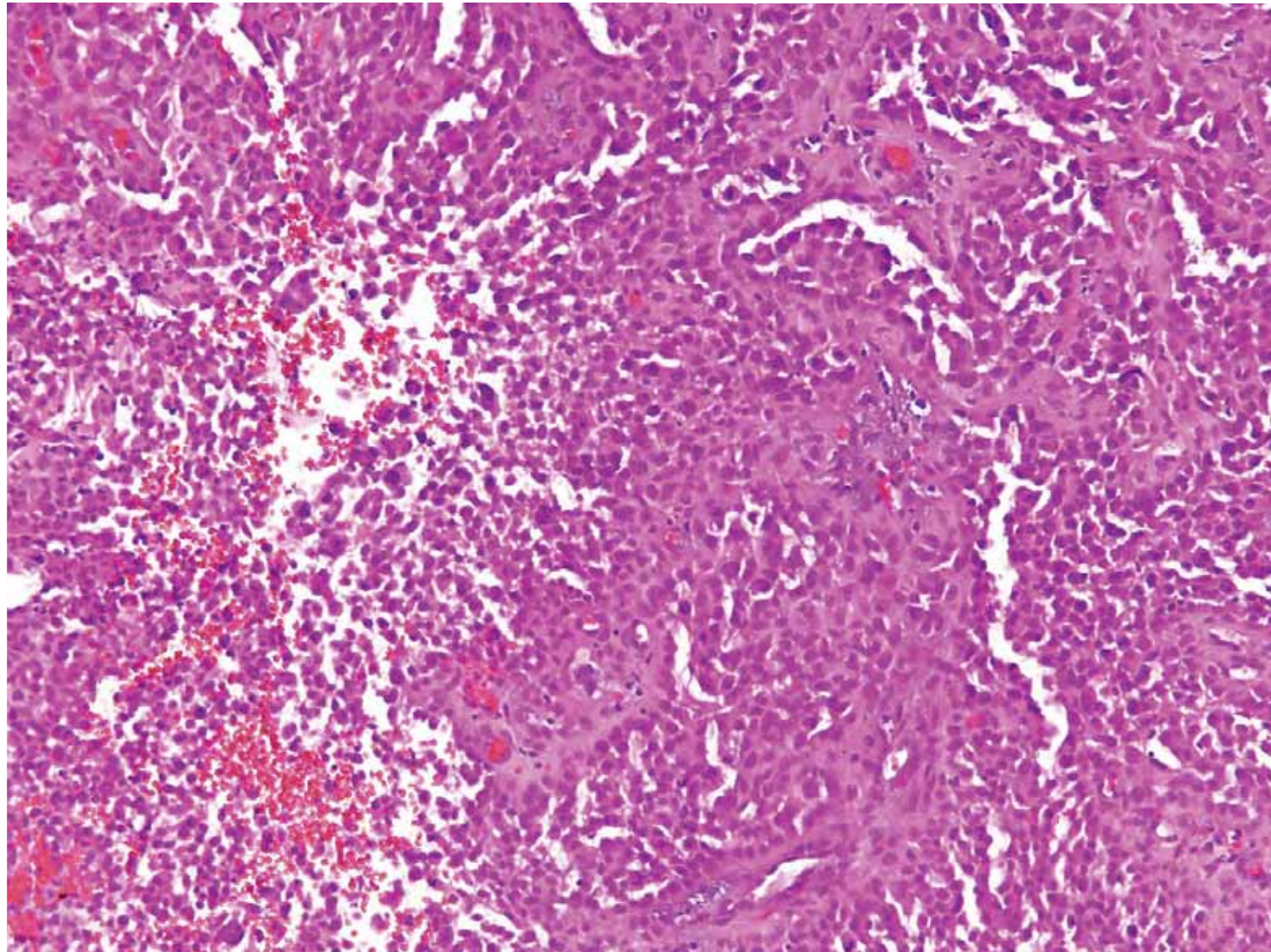
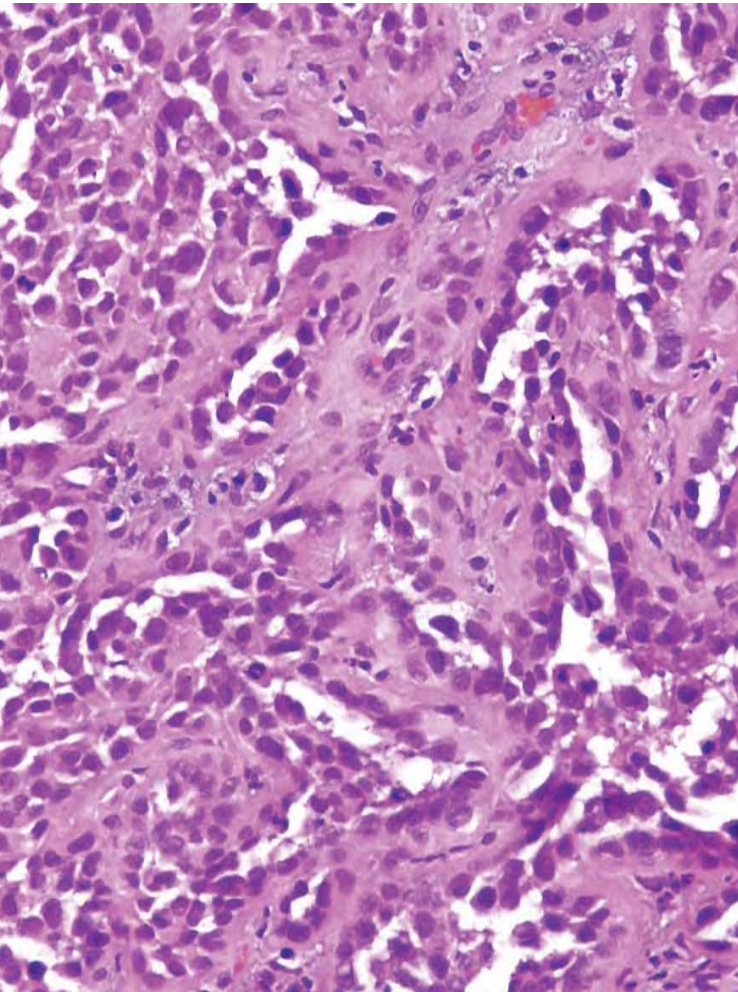


- Fast-growing tumor in the scalp of a 78-year old “VIP”



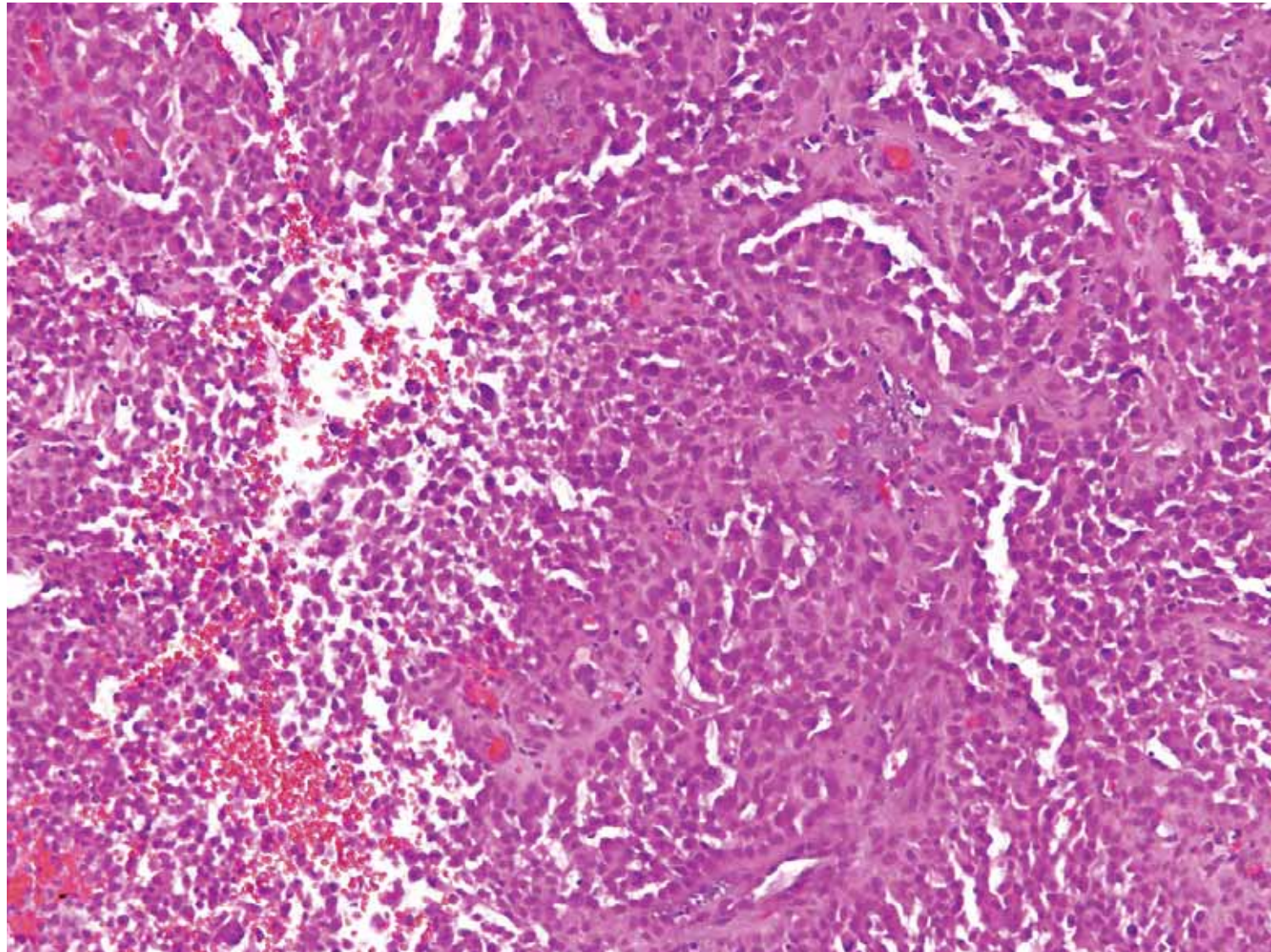
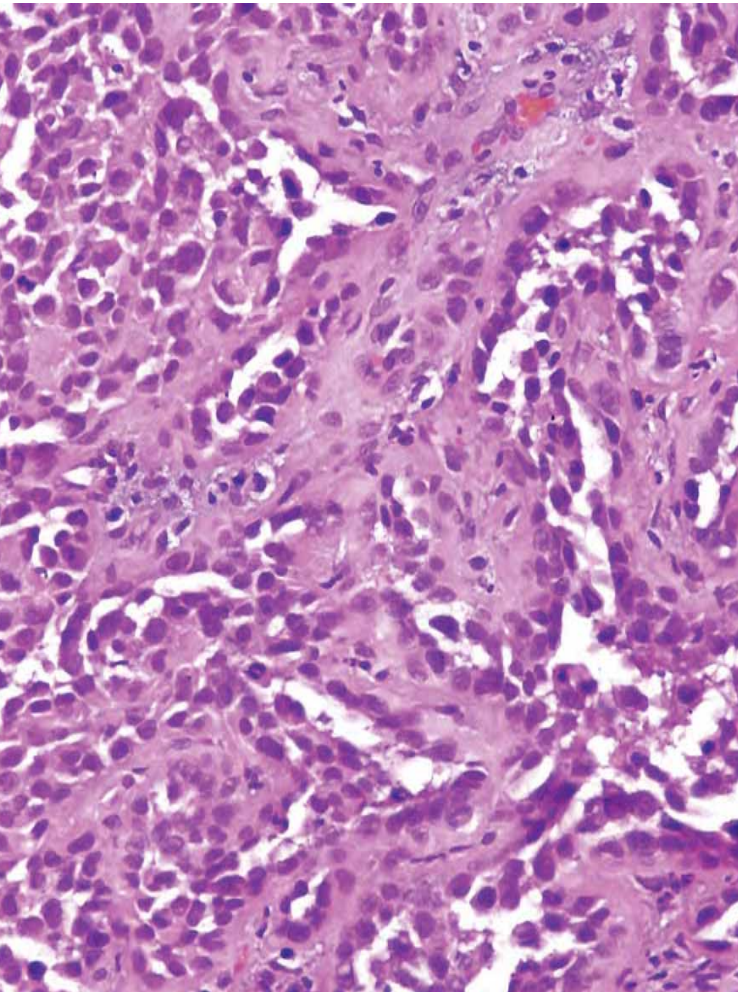
??????????

What's your diagnosis?



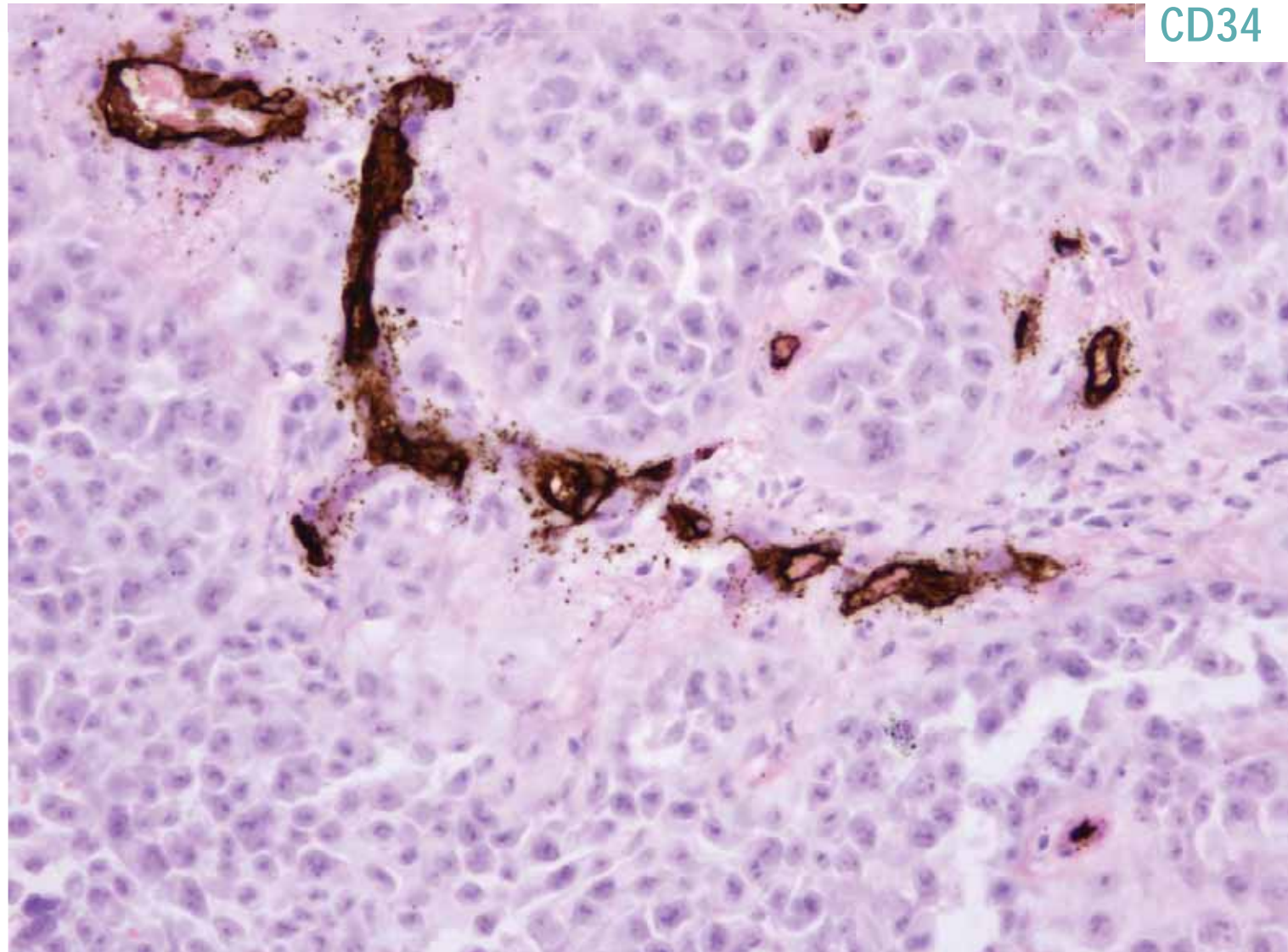
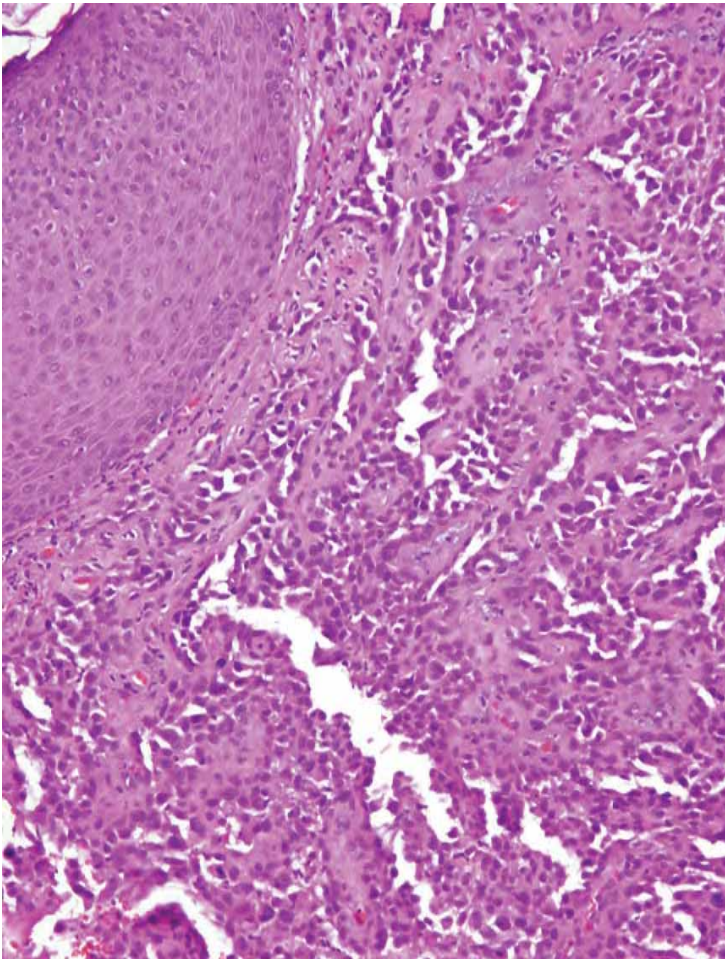
“Highly suggestive of **ANGIOSARCOMA**”

Pending immunohistochemical confirmation...



# Dx: Pseudoangiomatous squamous cell carcinoma

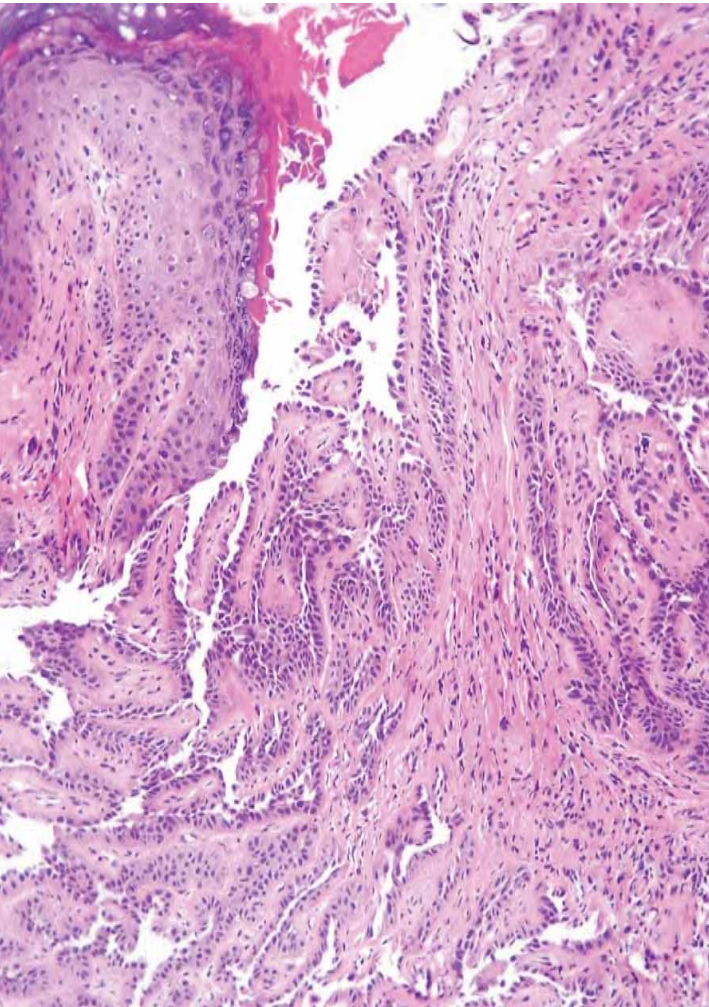
- Epithelial markers +
- Vascular markers -



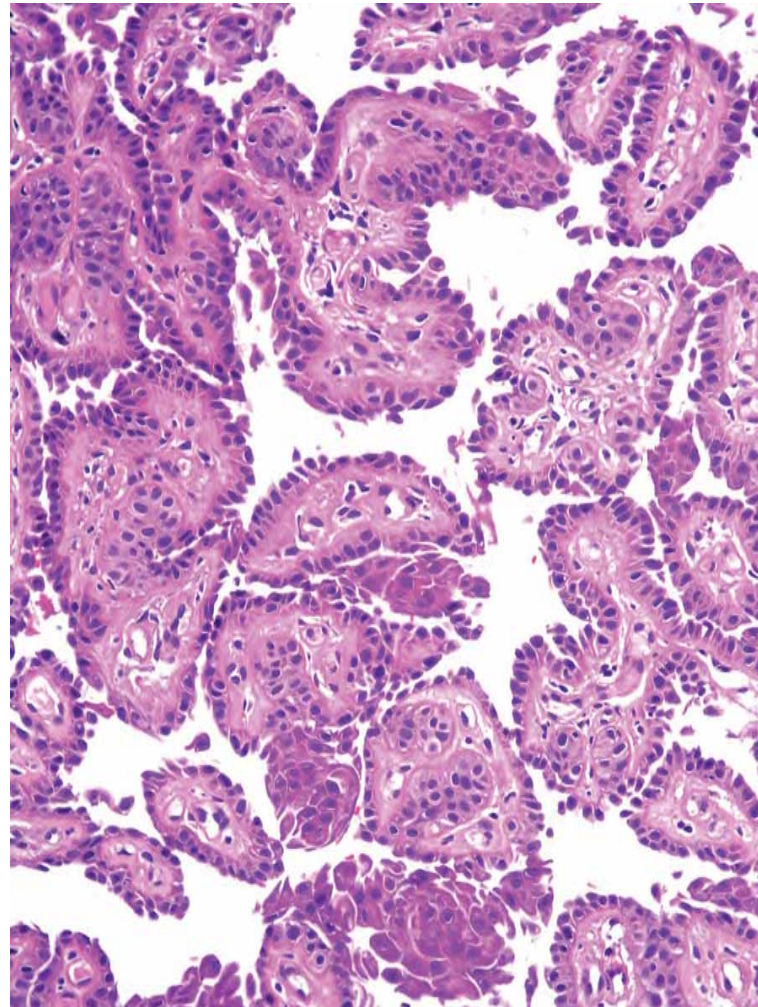
CD34

# Pseudoangiomatous squamous cell carcinoma

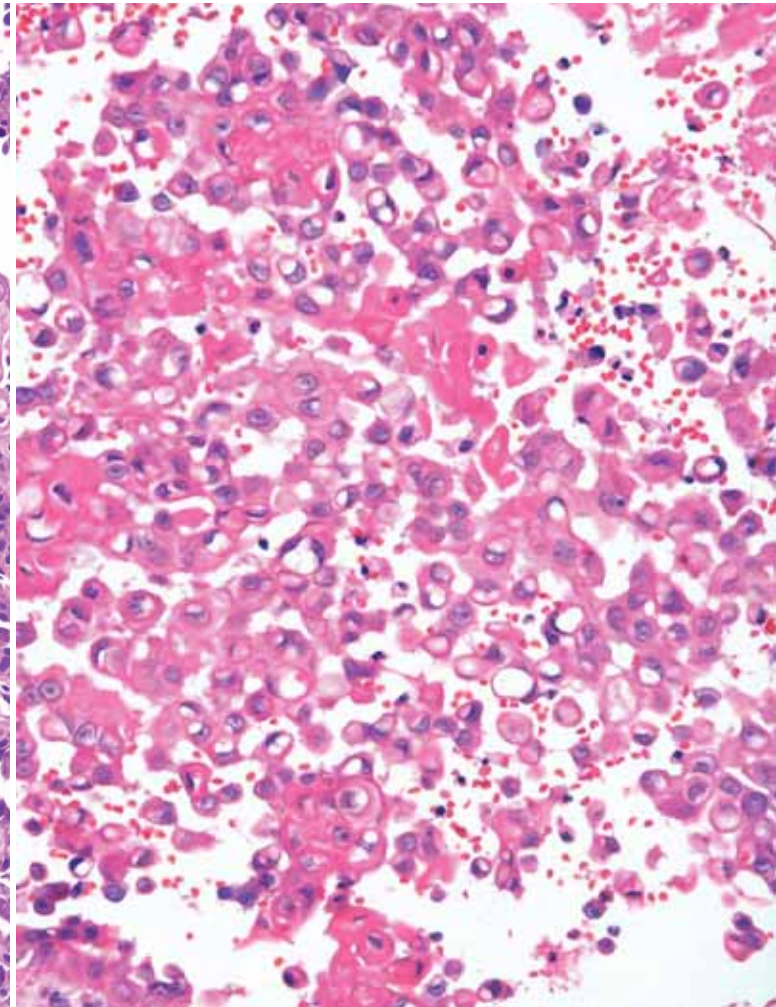
Interconnected channels



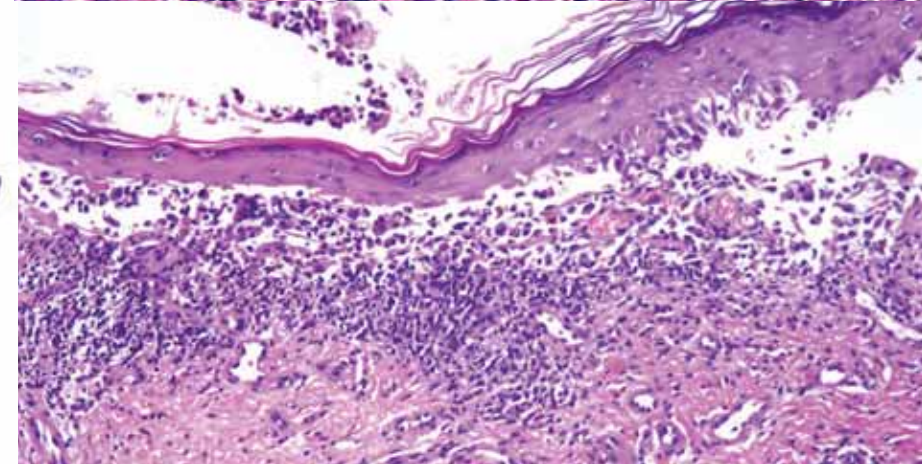
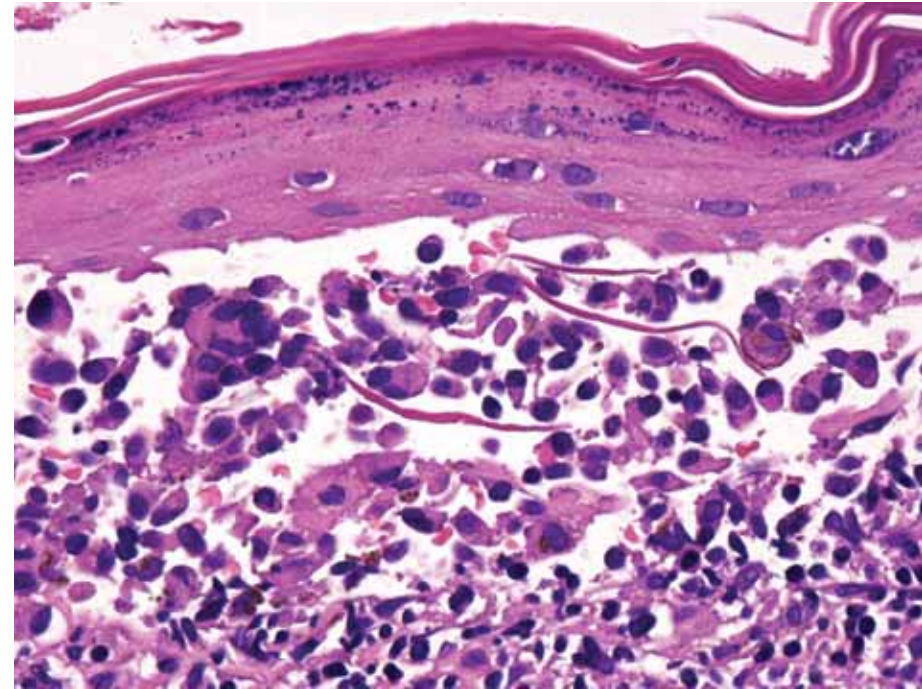
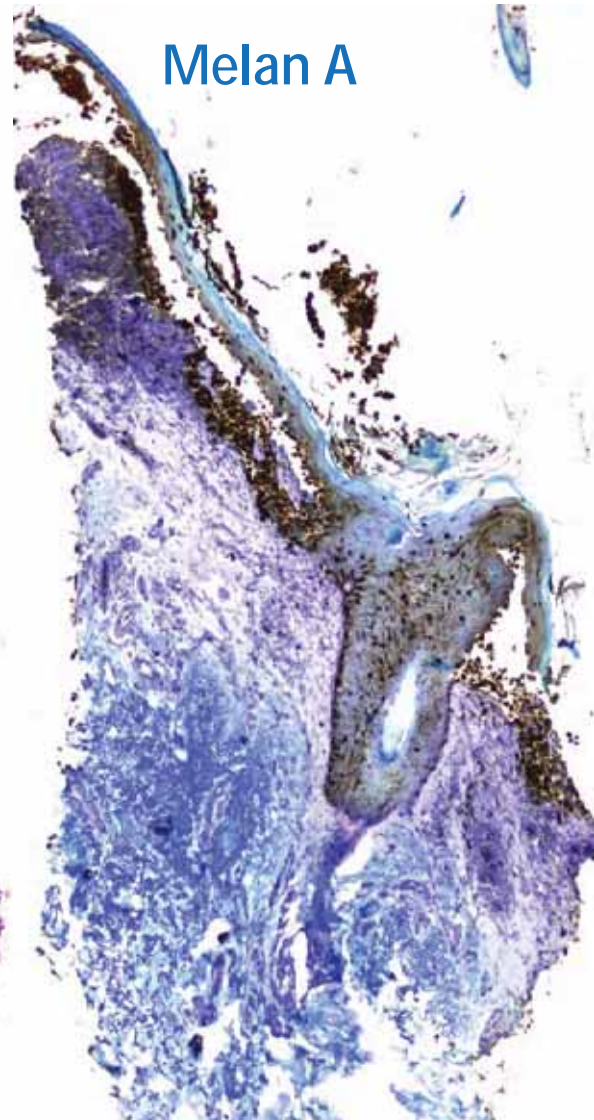
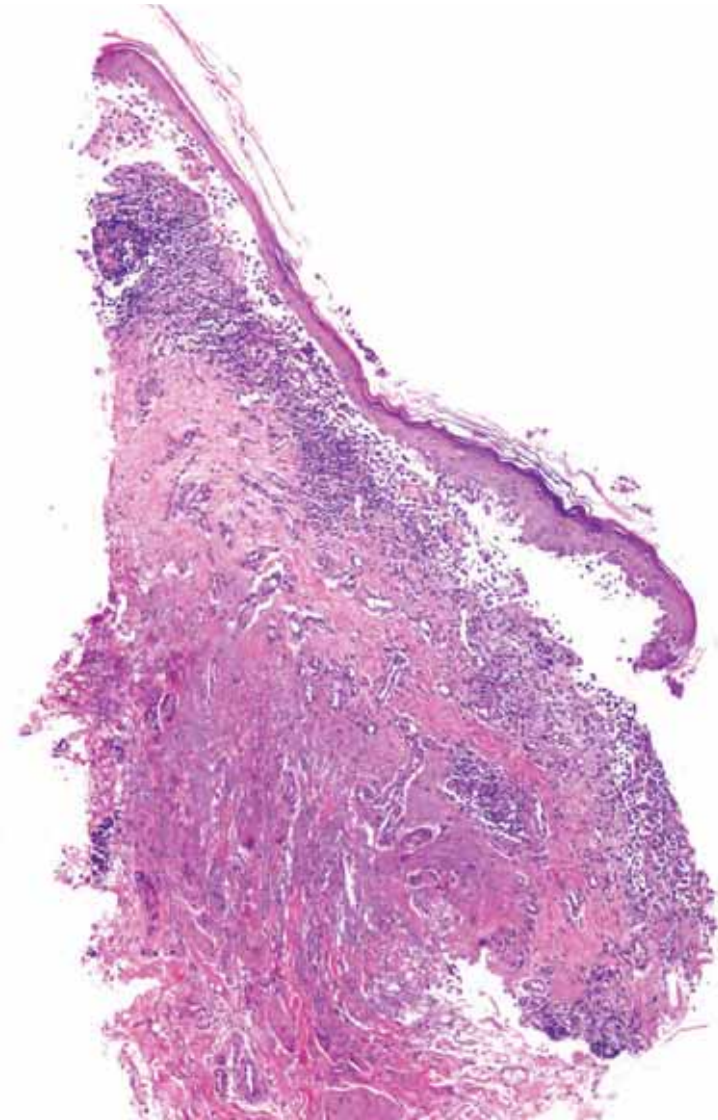
Pseudo-hobnail-endothelium



Intracytoplasmic lumens



# Pseudoacantholytic melanoma (simulating acantholytic AK)

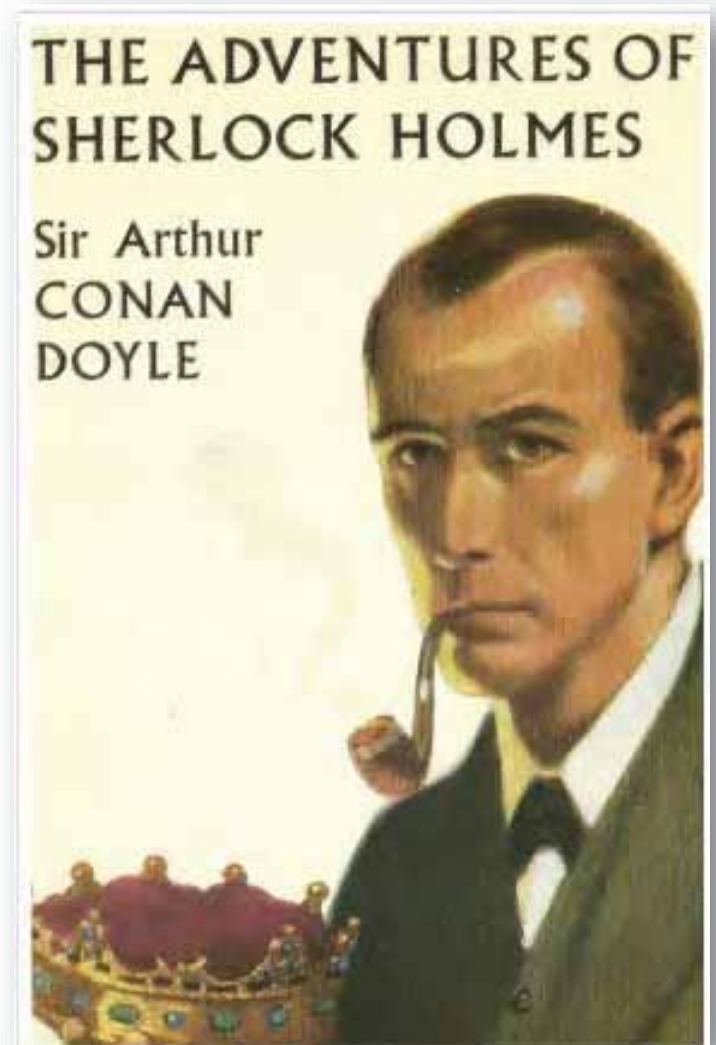


## LL 5

*“It is a capital mistake to theorize  
before you have all the evidence.*

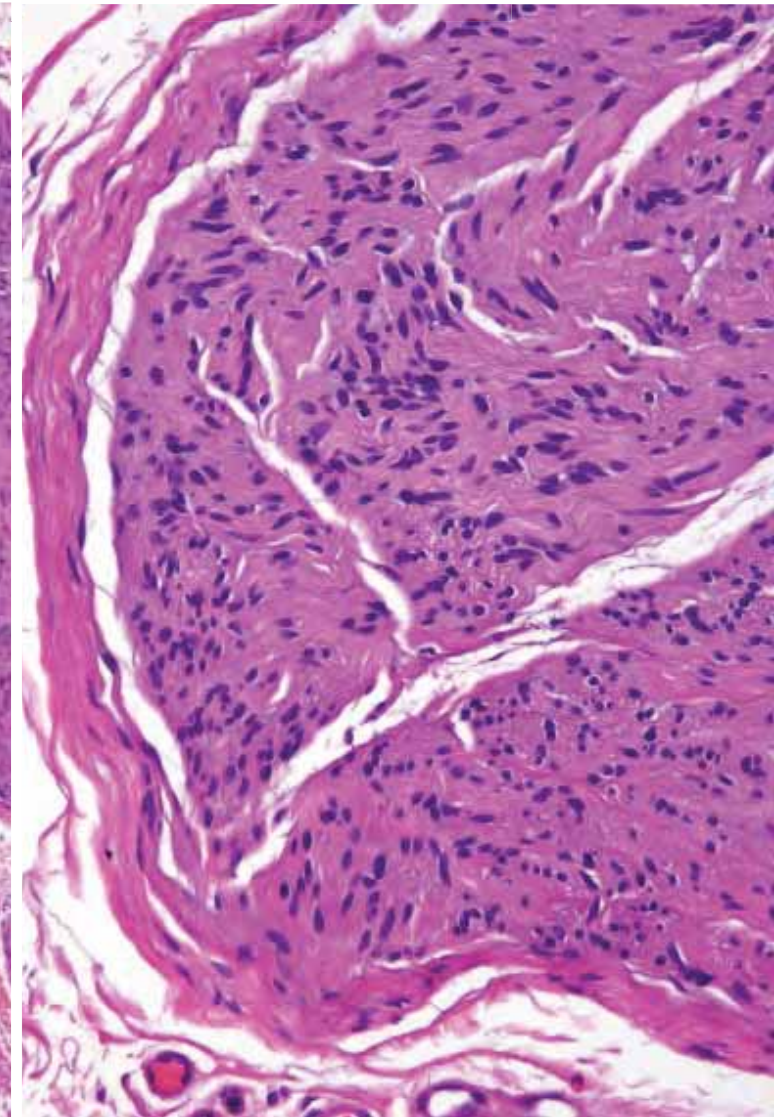
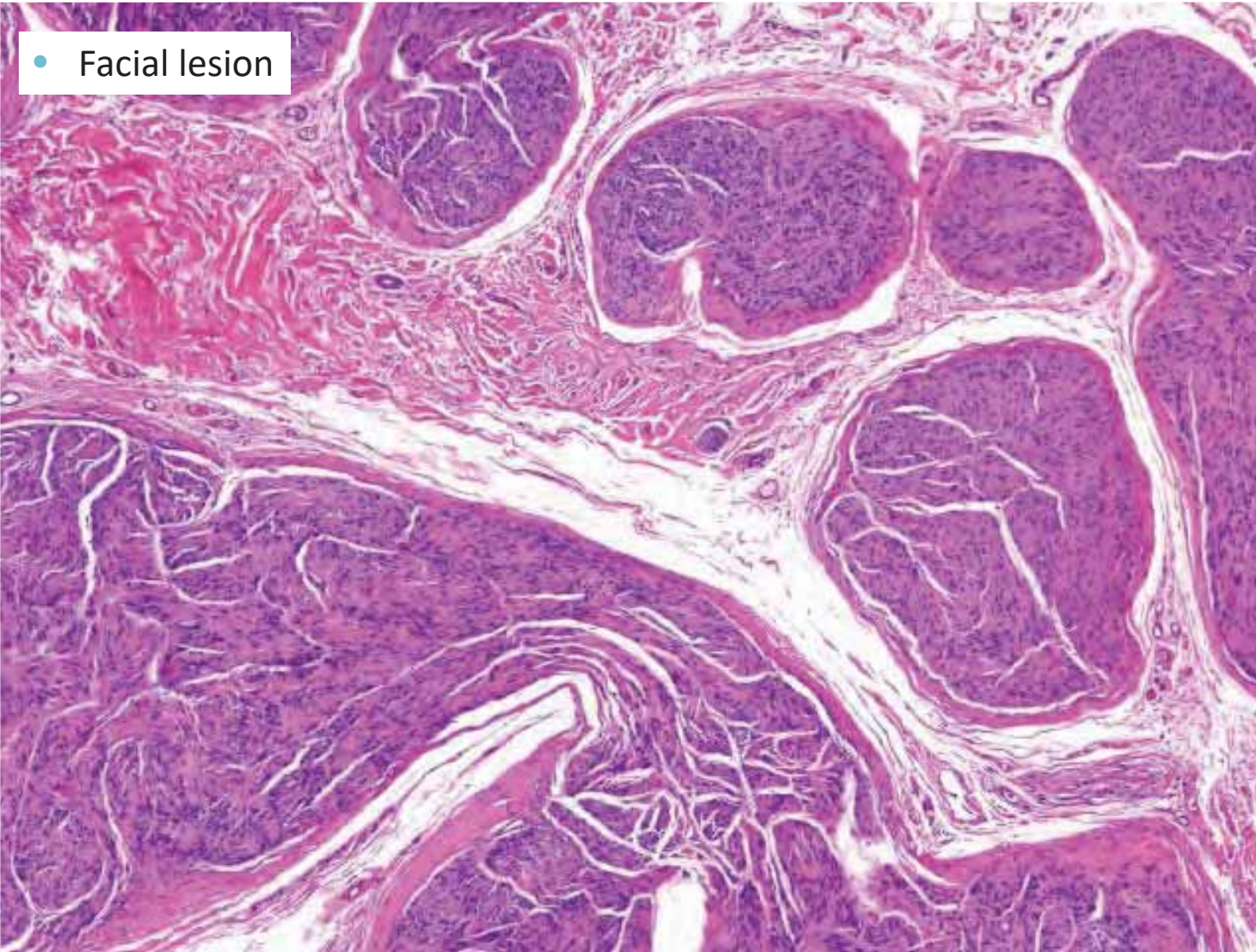
*It biases the judgment”*

*Part 1, chap. 3, p. 27*

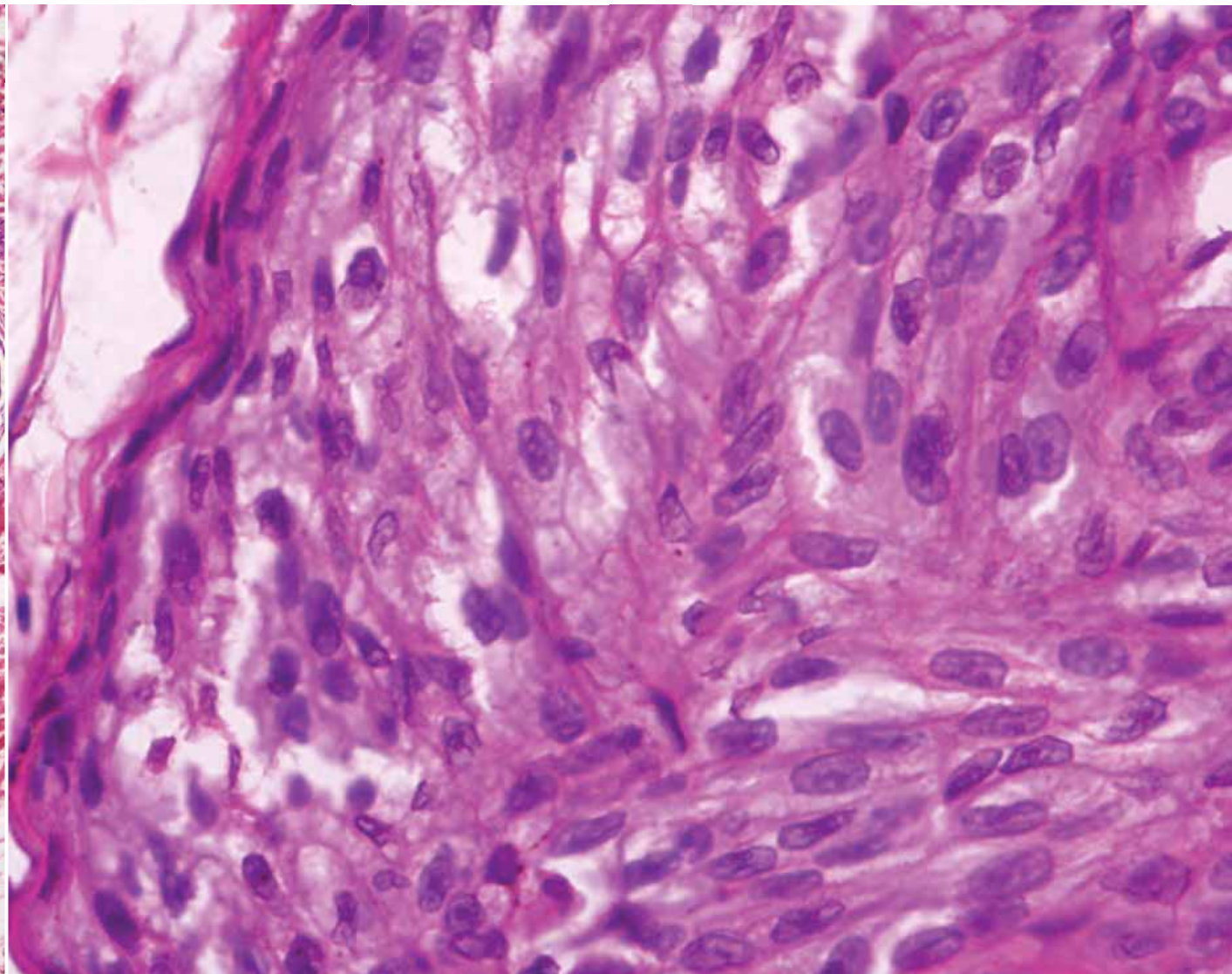
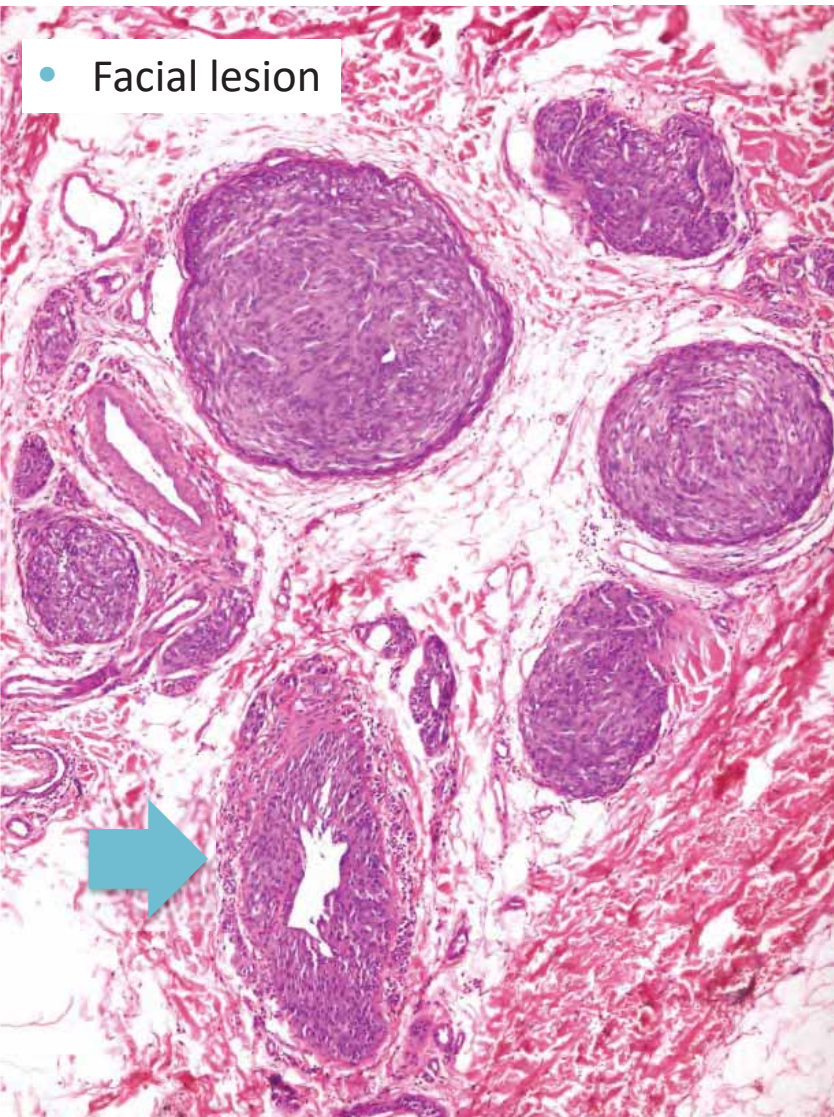


# Plexiform circumscribed “palisaded” neuroma

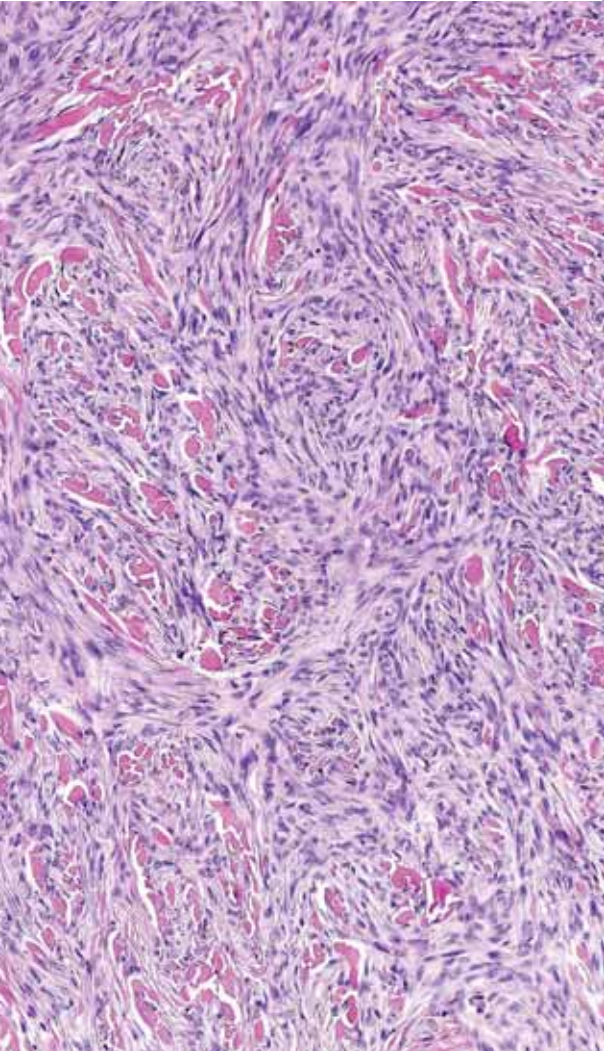
- Facial lesion



## Dx: Melanoma satellitosis

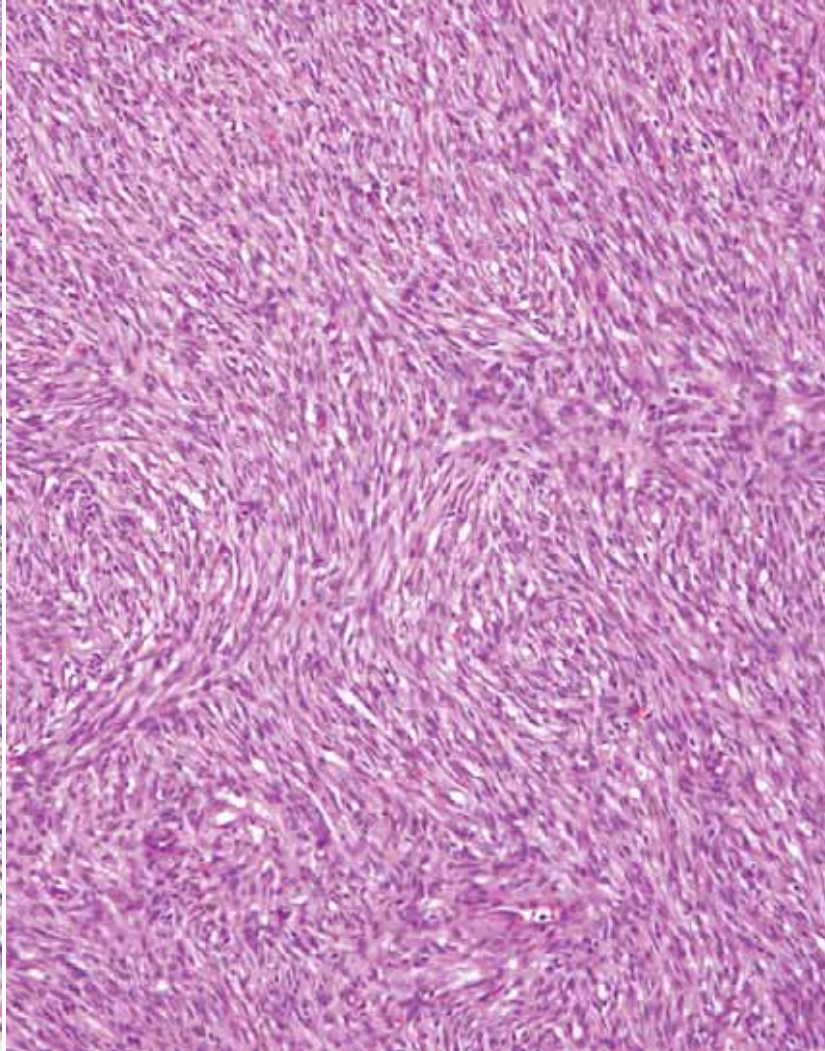


**Dermatofibroma**

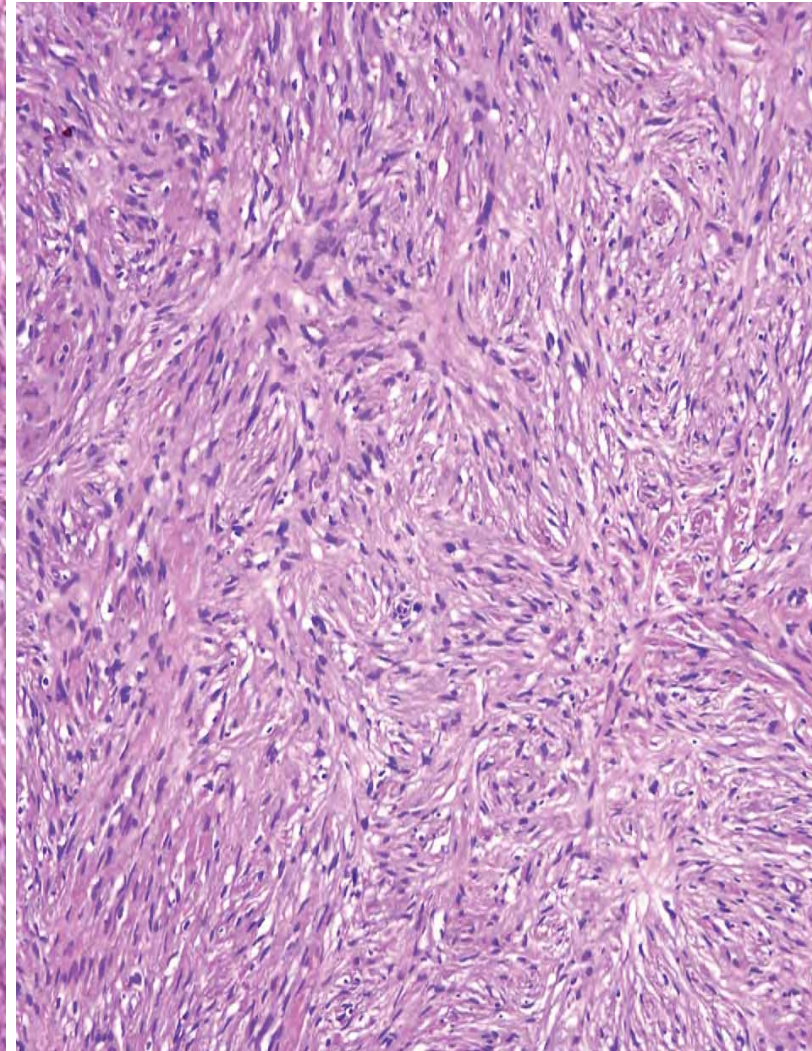


**Storiform pattern**

**DFSP**

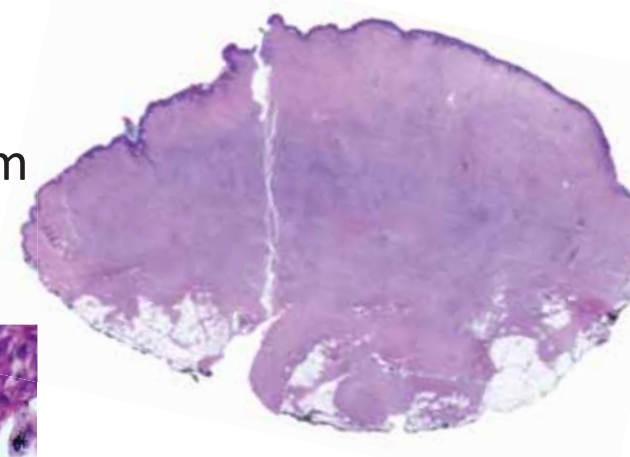
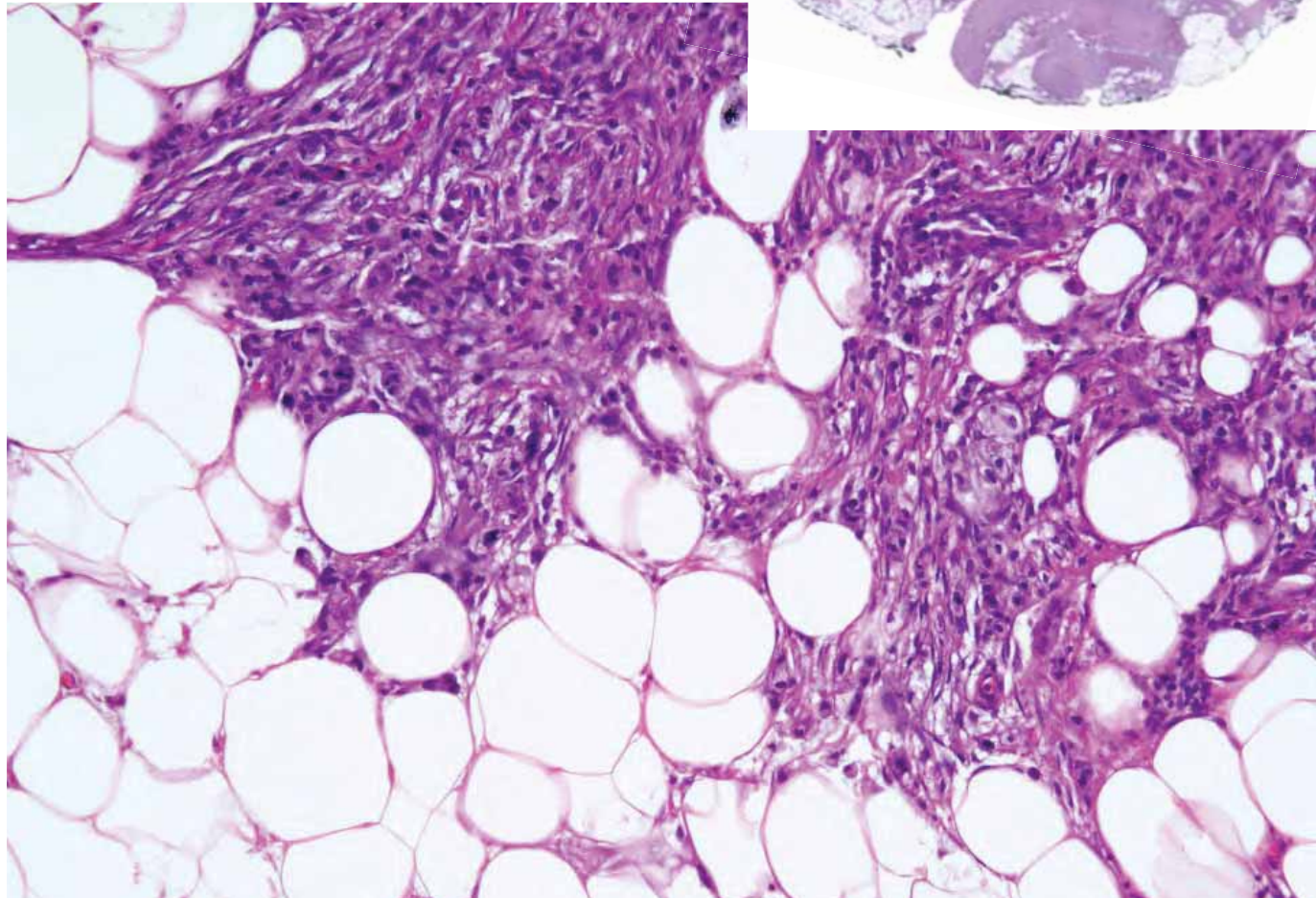
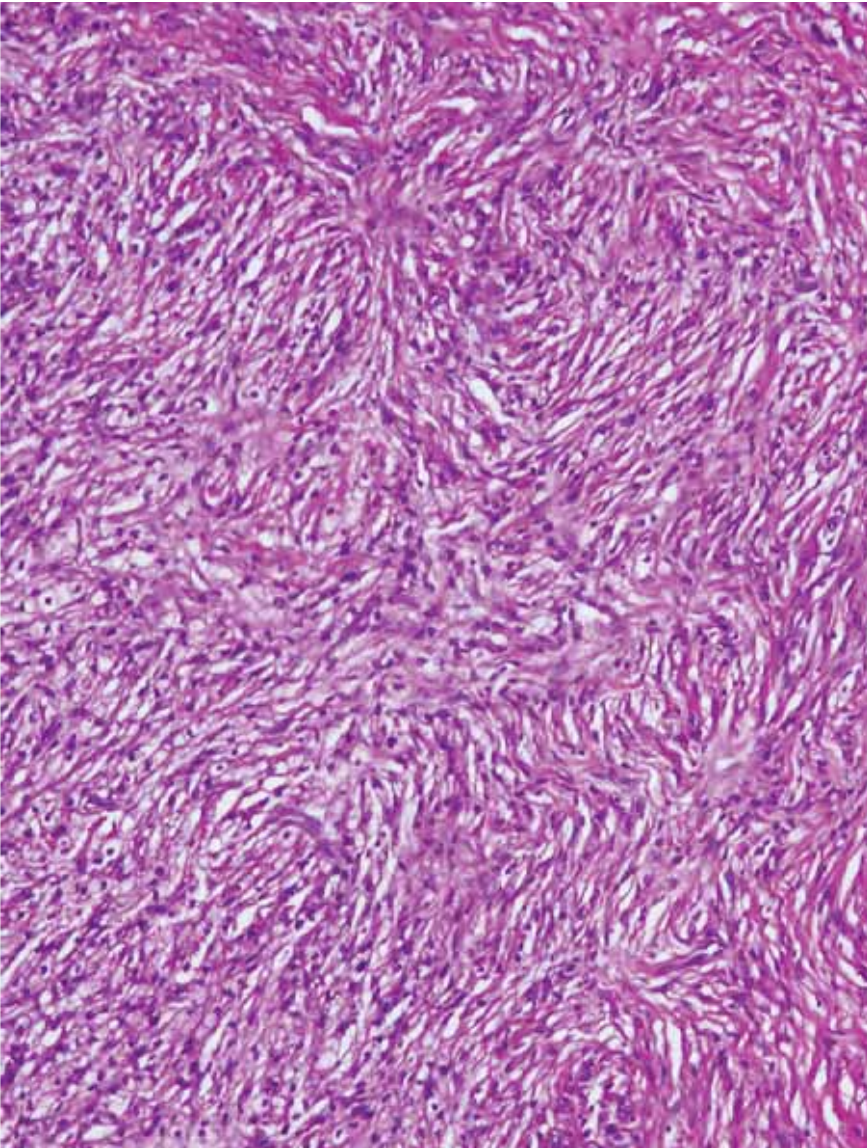


**Hybrid NF+perineurioma**



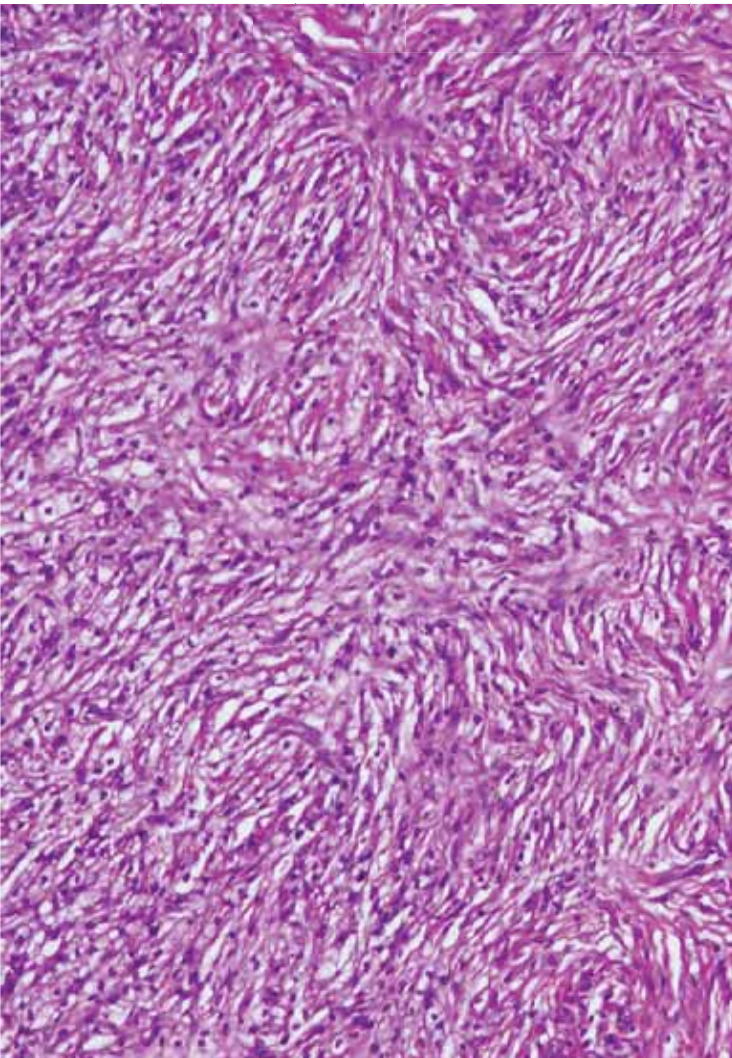
## Storiform pattern

- Hard nodule on the epigastrium
- Past history gastric cancer

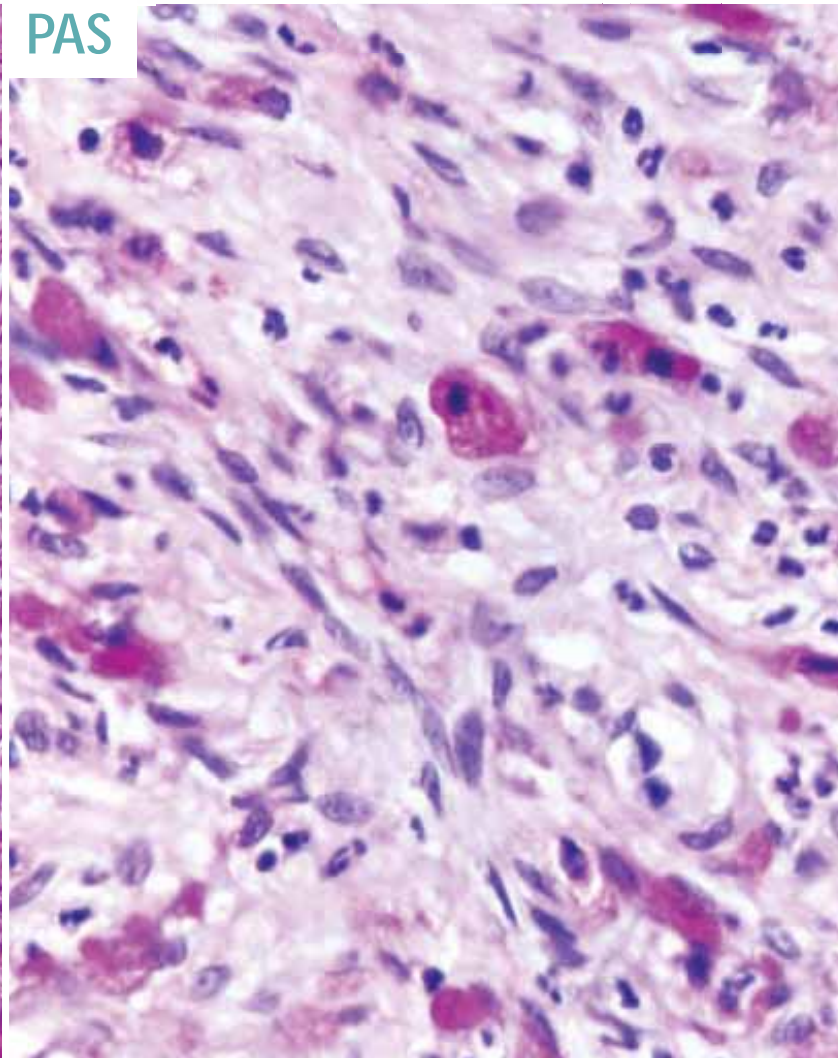


Storiform pattern

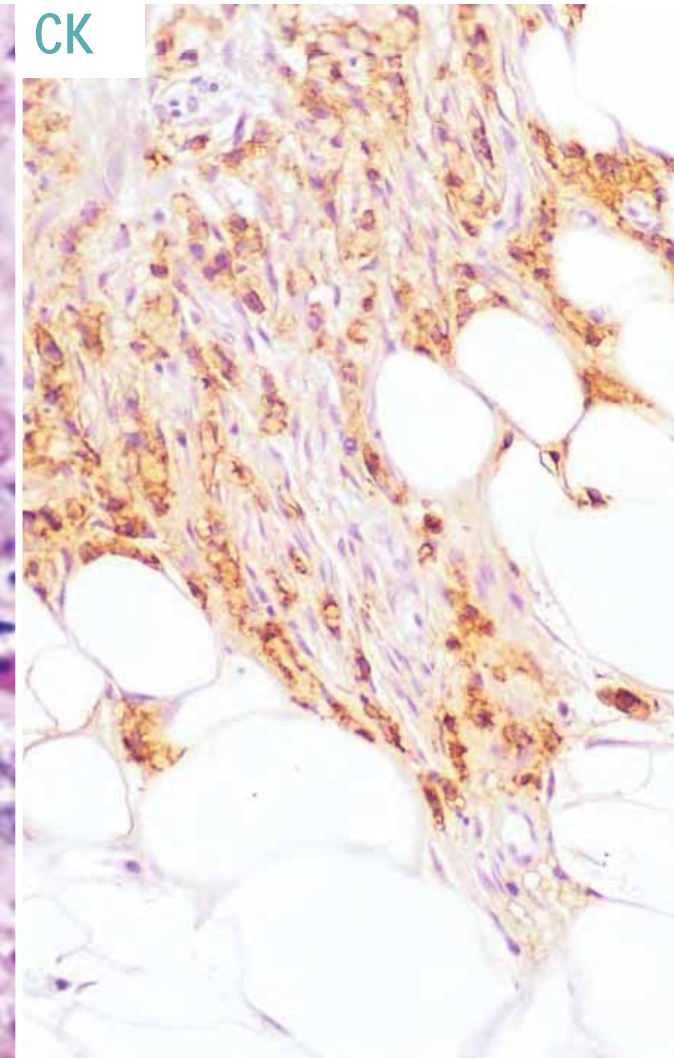
**Dx: Metastasis of a signet ring cell gastric carcinoma**



PAS



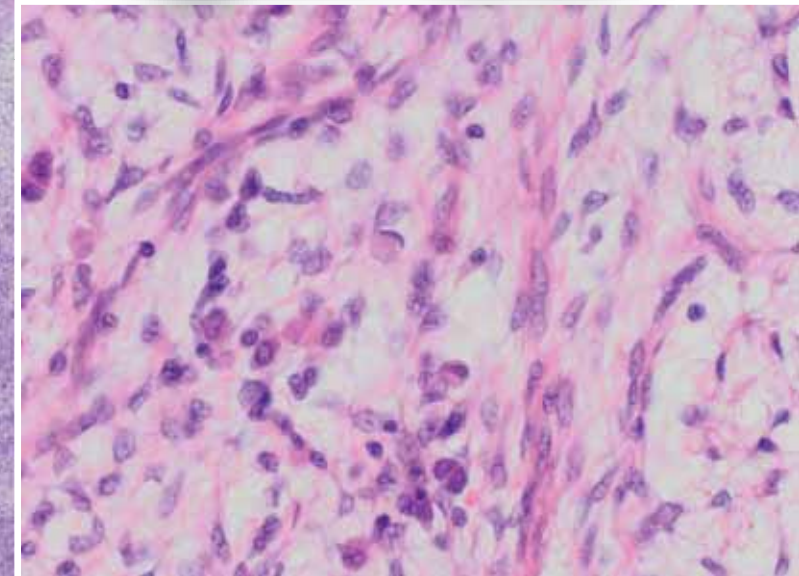
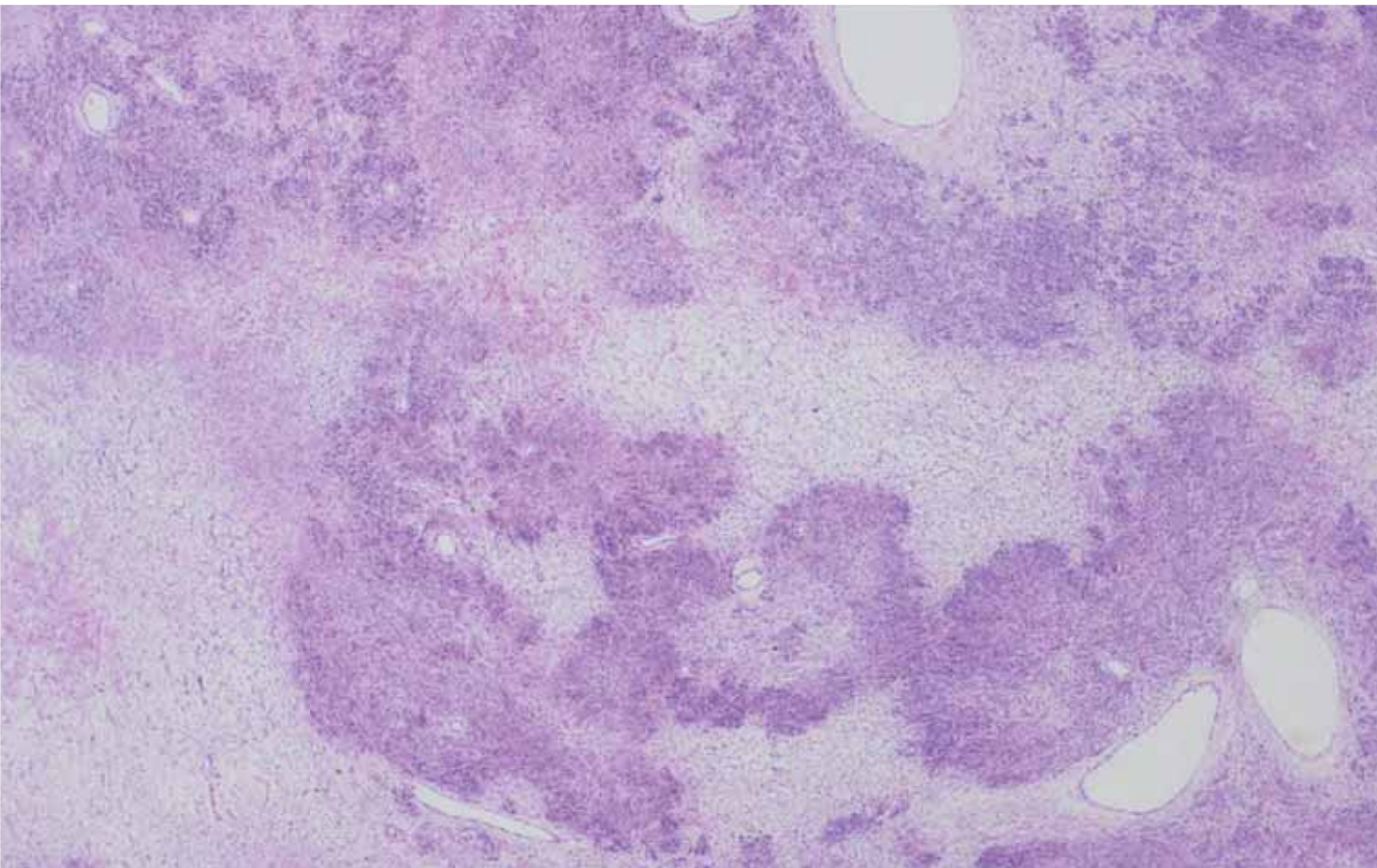
CK



# Florid mesenchymal/stromal proliferation in Krukenberg tumours; A case description illustrating this potential diagnostic pitfall

Human Pathology: Case Reports

Volume 23, March 2021, 200469



## Storiform collagenized pattern

### Sclerotic fibroma (storiform collagenoma)

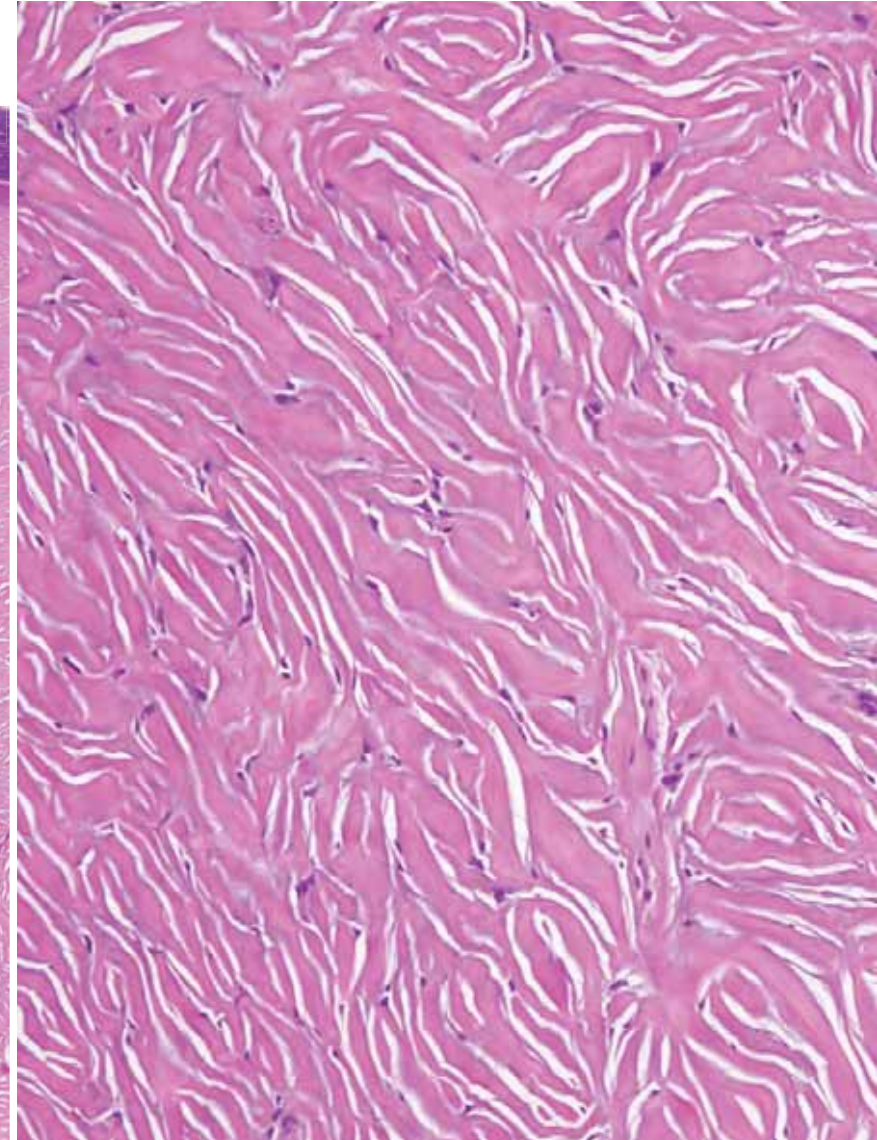
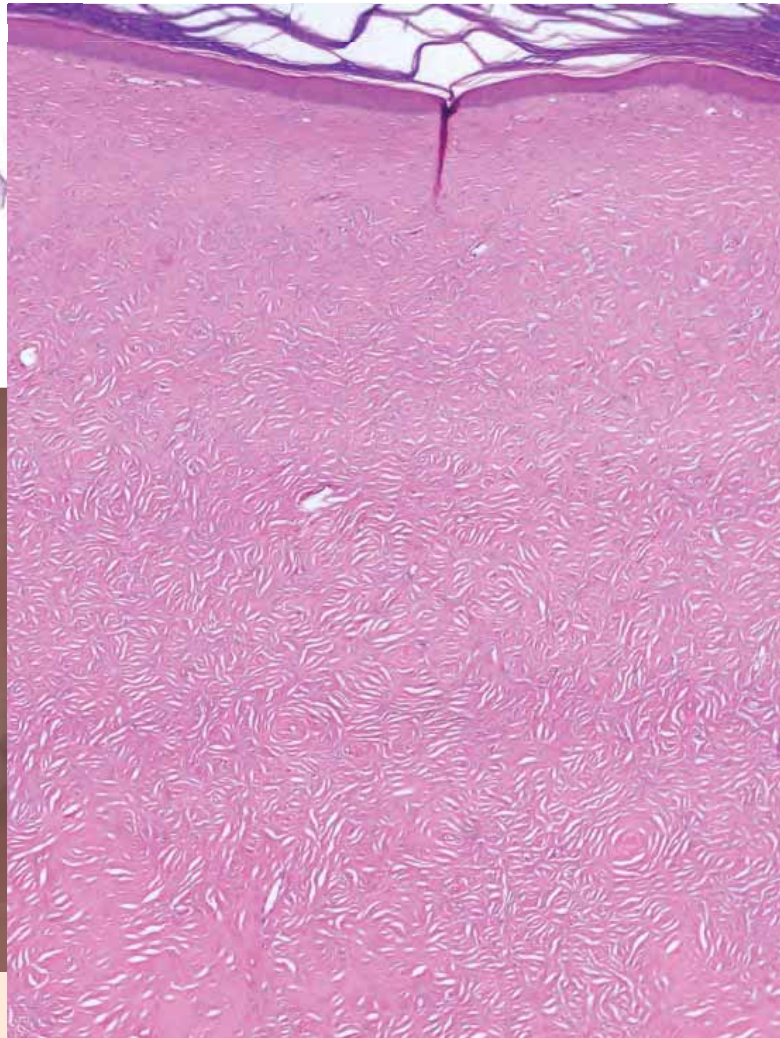
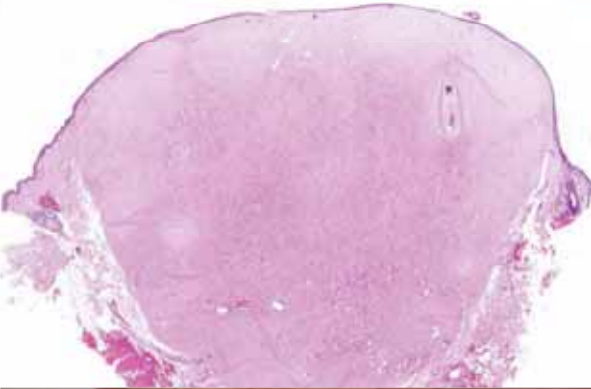
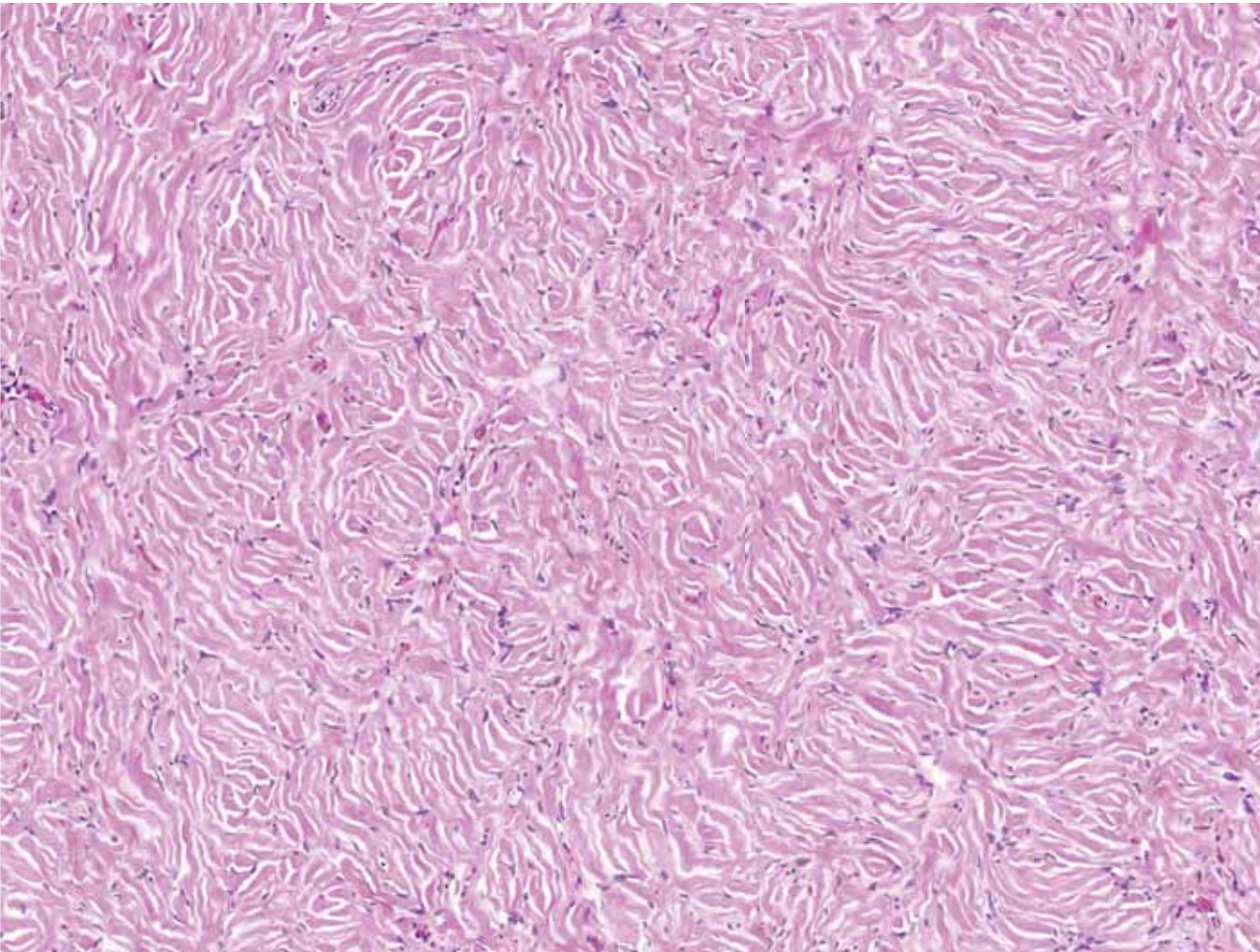


Image: Dr Gemma Melé

## Storiform collagenized pattern

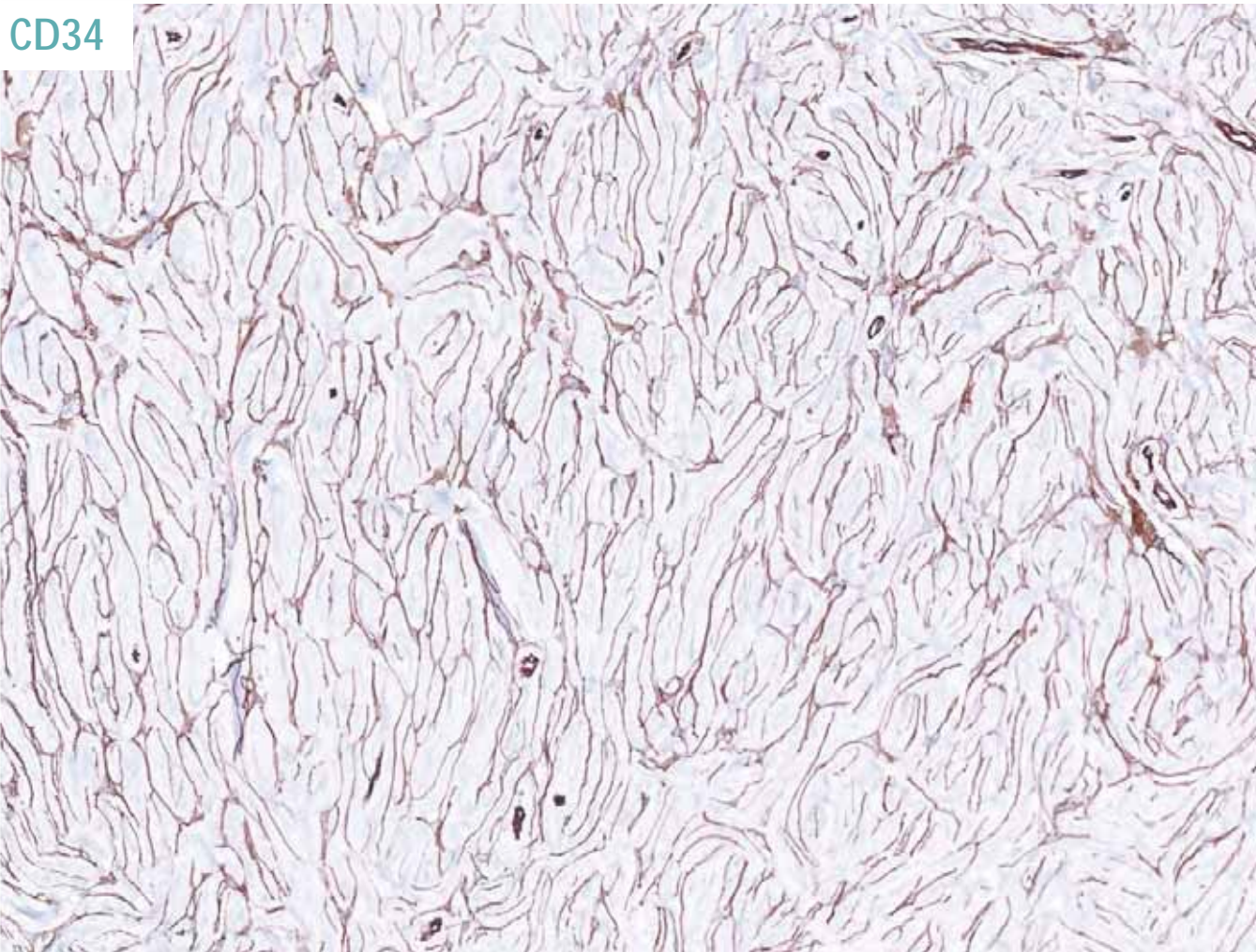
### Sclerotic fibroma (storiform collagenoma)



- AKA: Hypocellular fibroma, plywood fibroma
- Skin and mucous membranes of adults
- Solitary or Multiple (Cowden Sd)
- Storiform collagen bundles with slight interstitial mucin deposition
- Hypocellular **CD34+** **EMA+**

## Storiform collagenized pattern

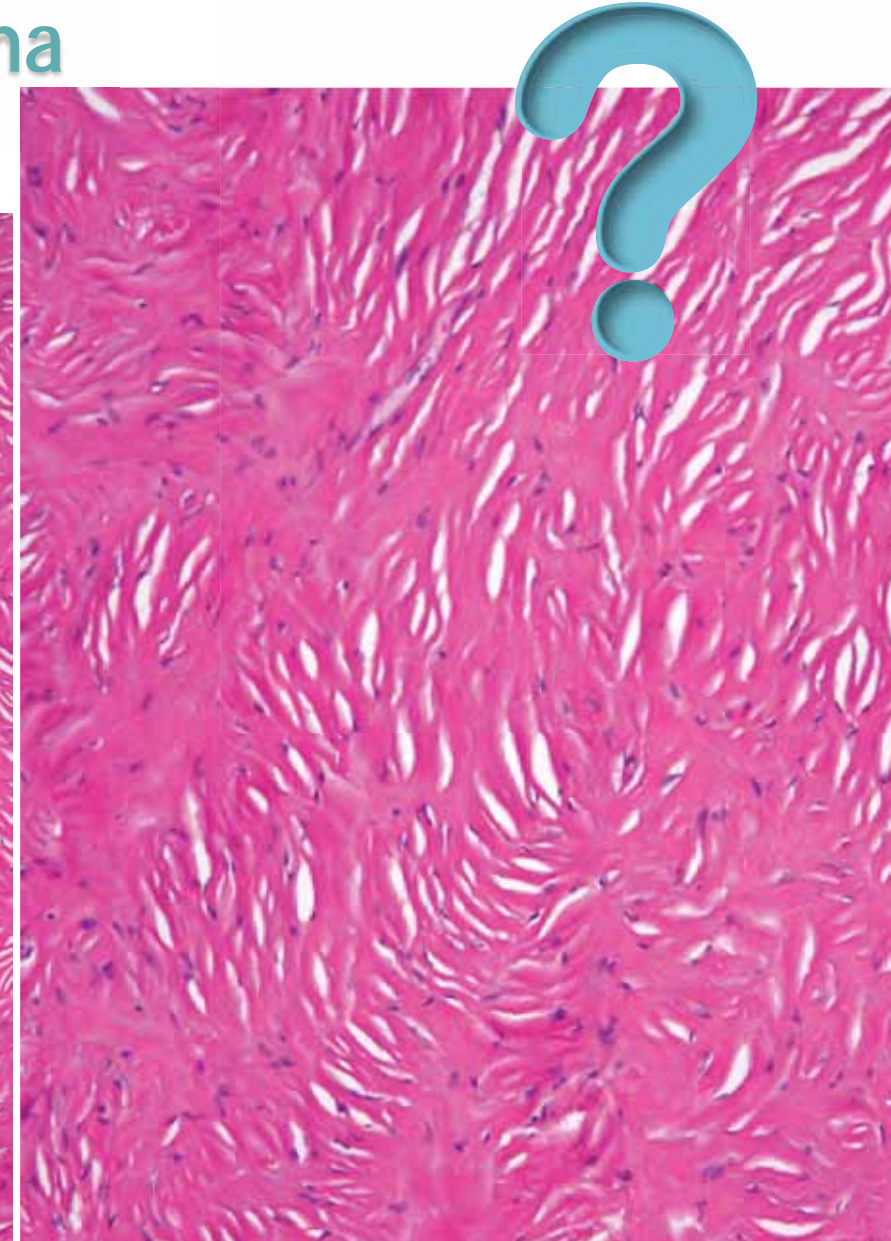
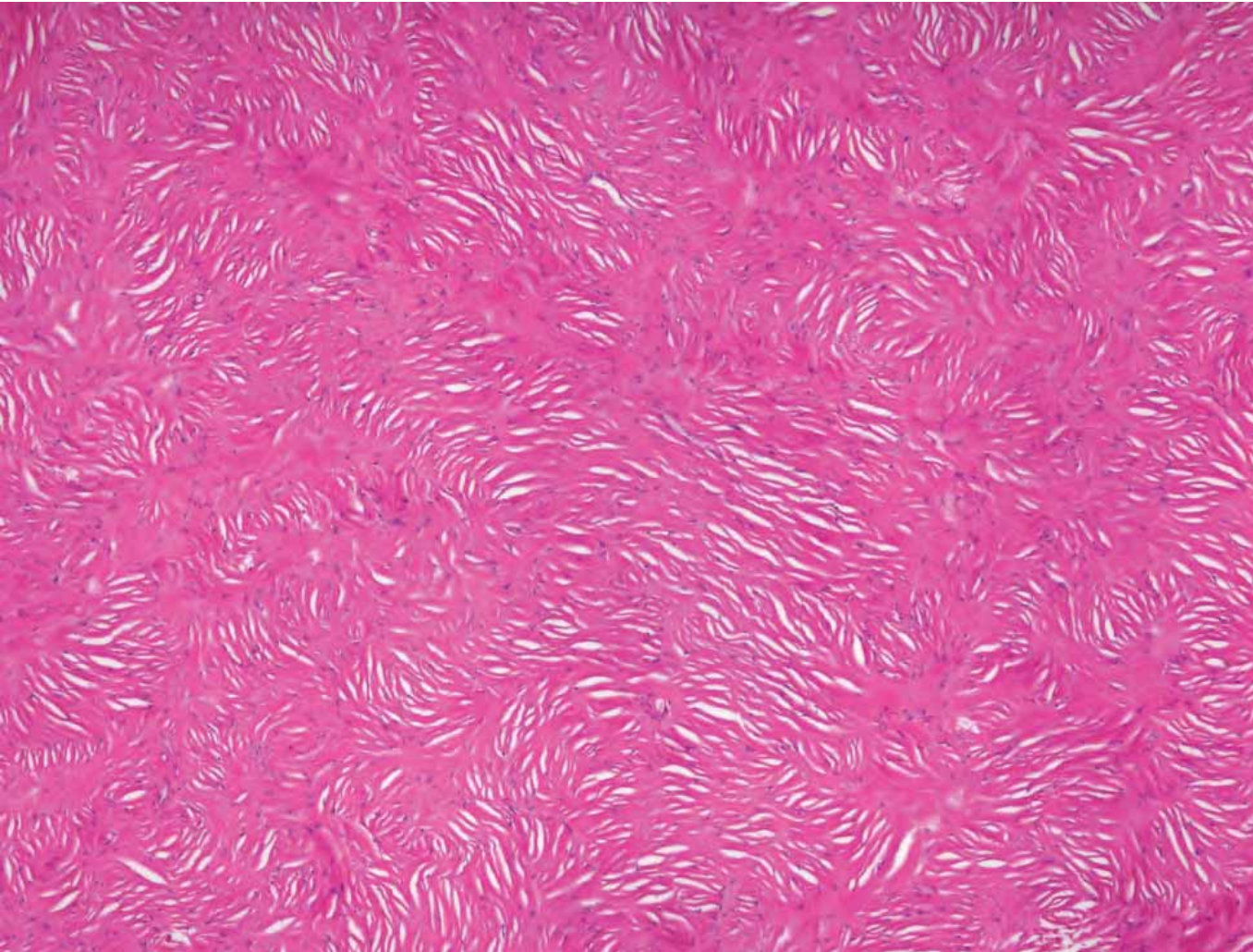
### Sclerotic fibroma (storiform collagenoma)



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- Storiform collagen bundles with slight interstitial mucin deposition
- Hypocellular **CD34+** **EMA+**

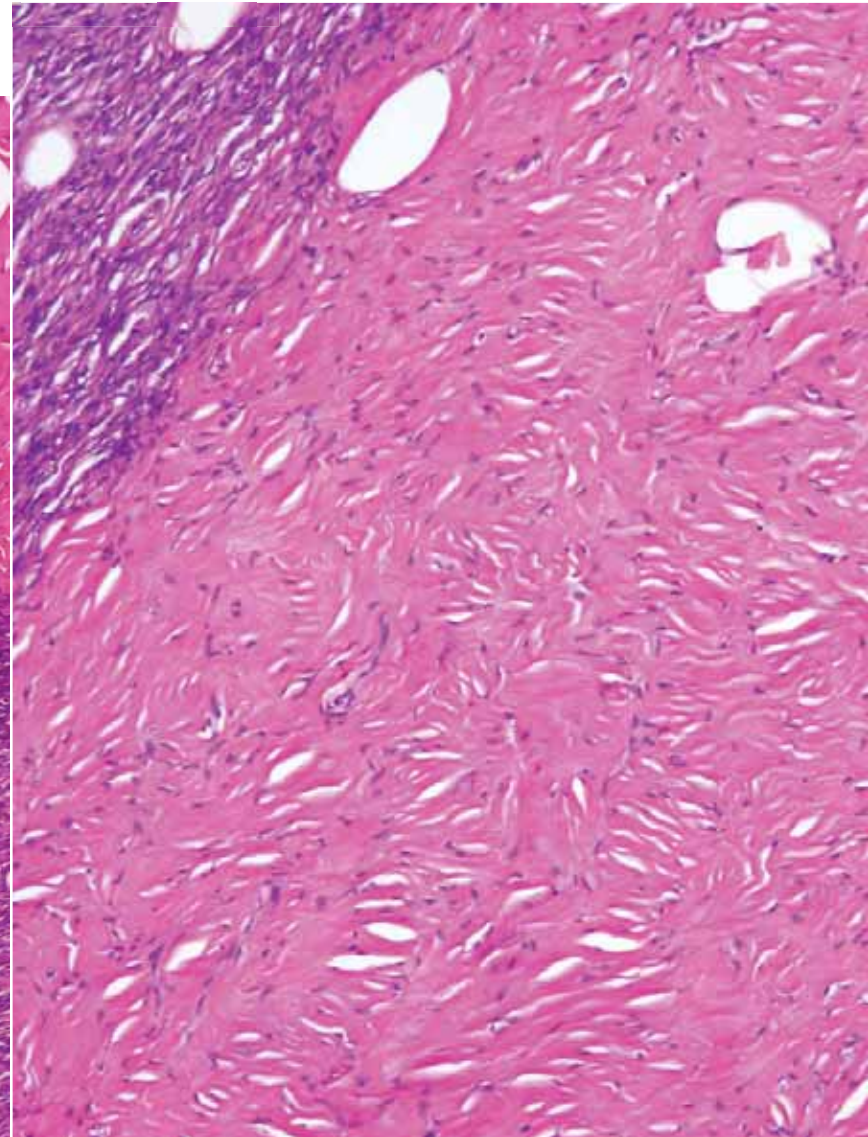
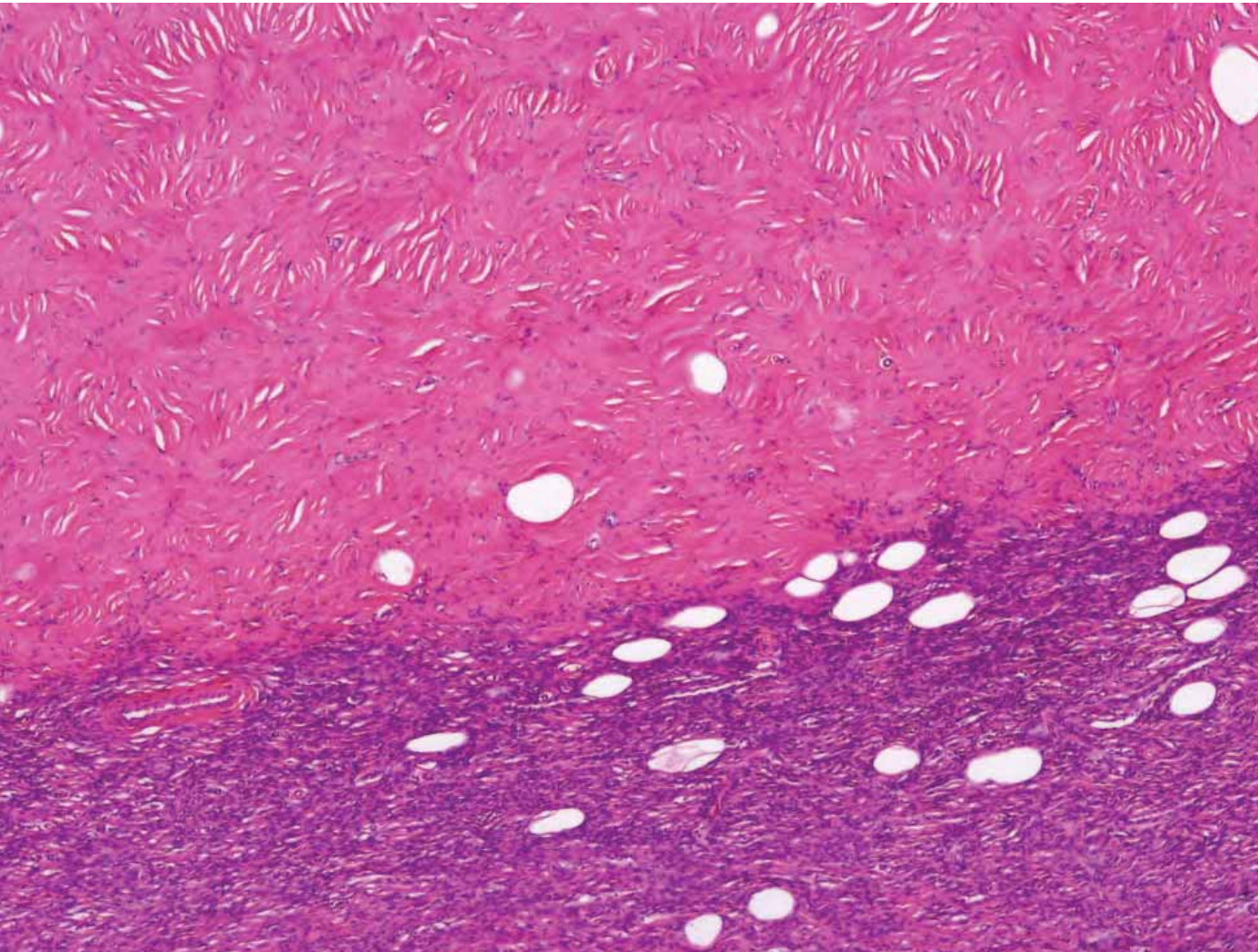
# Sclerotic fibroma

19-year-old boy. Curettage of a nodule on the arm



## DFSP (nodular sclerotic variant)

19-year-old boy. One year later!



# Non-polarizable collagen in dermatofibrosarcoma protuberans: a useful diagnostic aid

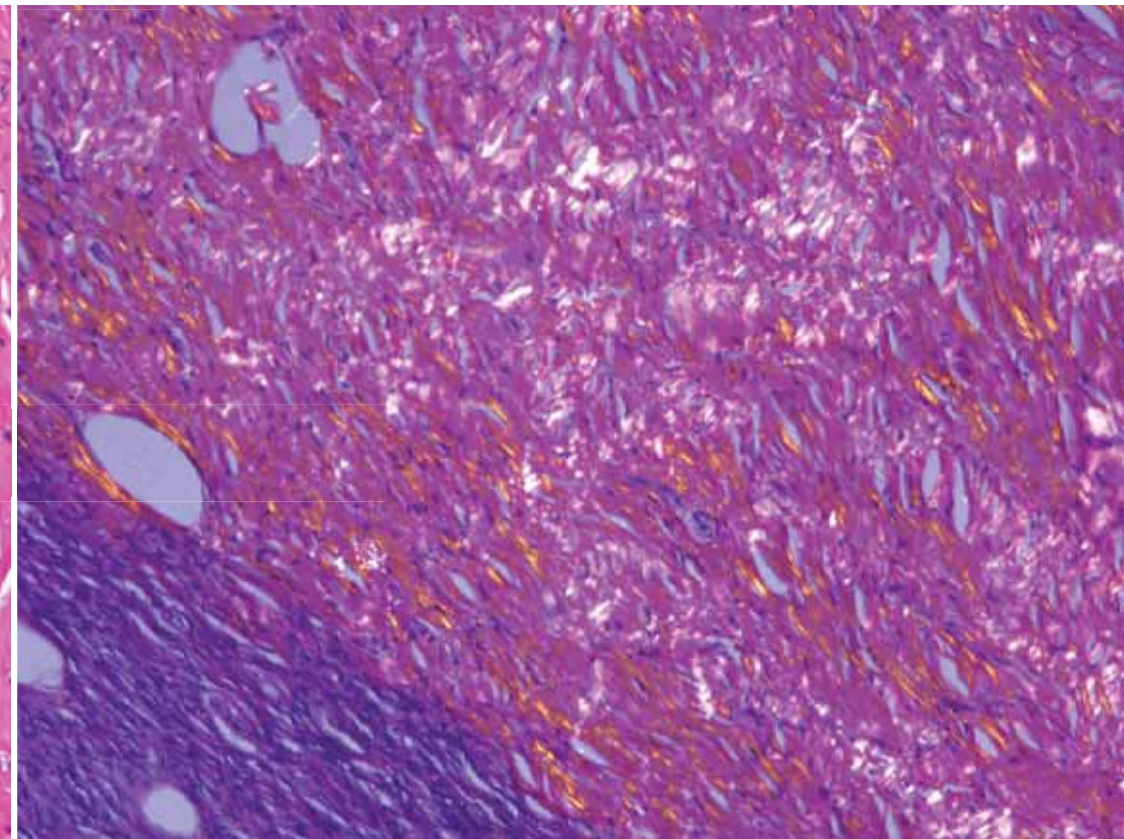
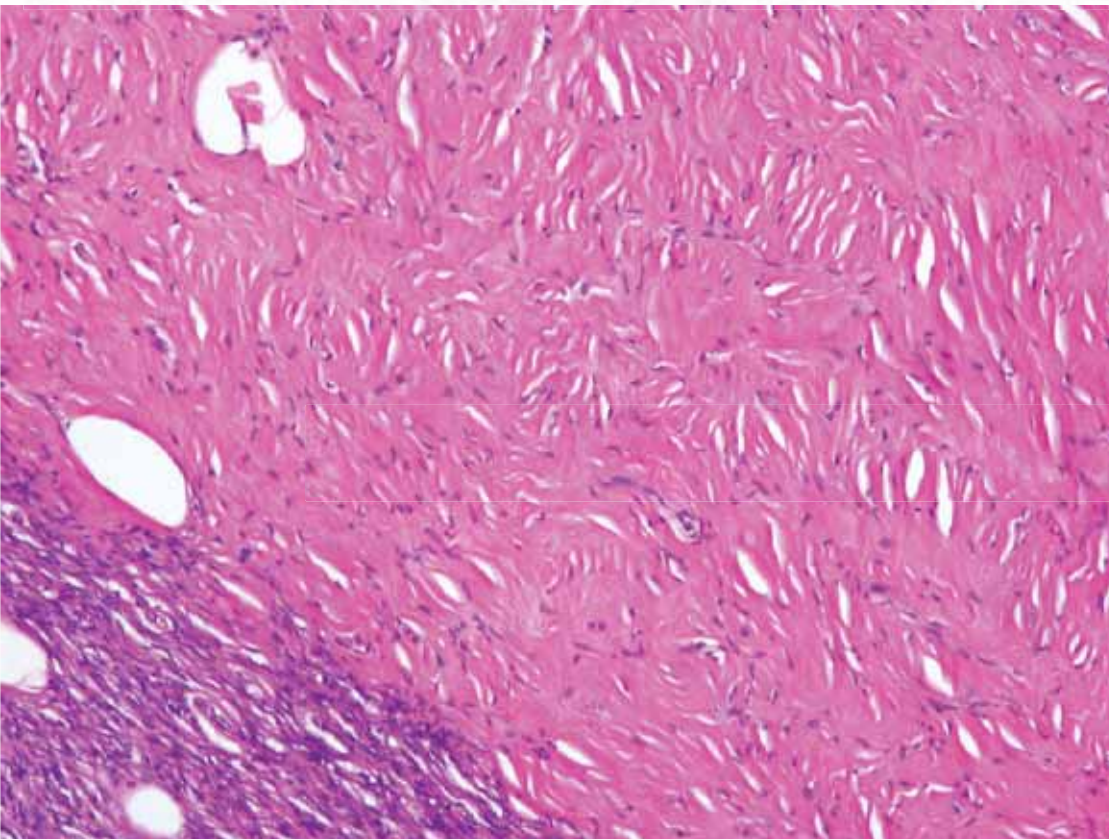
*Journal of Cutaneous Pathology* 1986; 13, 339-346

R. J. BARR, E. M. YOUNG, JR. and D. F. KING

the presence of nonpolarizable collagen appears to be an additional histological marker useful in differentiating DFSP from dermatofibroma and fibromatosis.



It did not work in our case



# A Study of Collagen Refractility in Dermatofibroma and Dermatofibrosarcoma Protuberans using Diffractive Microscopy

*J Cutan Pathol.* 2024 April ; 51(4): 306–310

Caroline Brailsford, MS<sup>1</sup>, Fatema Khamdan, MD<sup>2</sup>, McKenzie A. Dirr, MD<sup>1</sup>, Pelin Sagut, MD<sup>2</sup>, Paul J. Nietert, PhD<sup>3</sup>, Dirk Elston, MD<sup>2</sup>

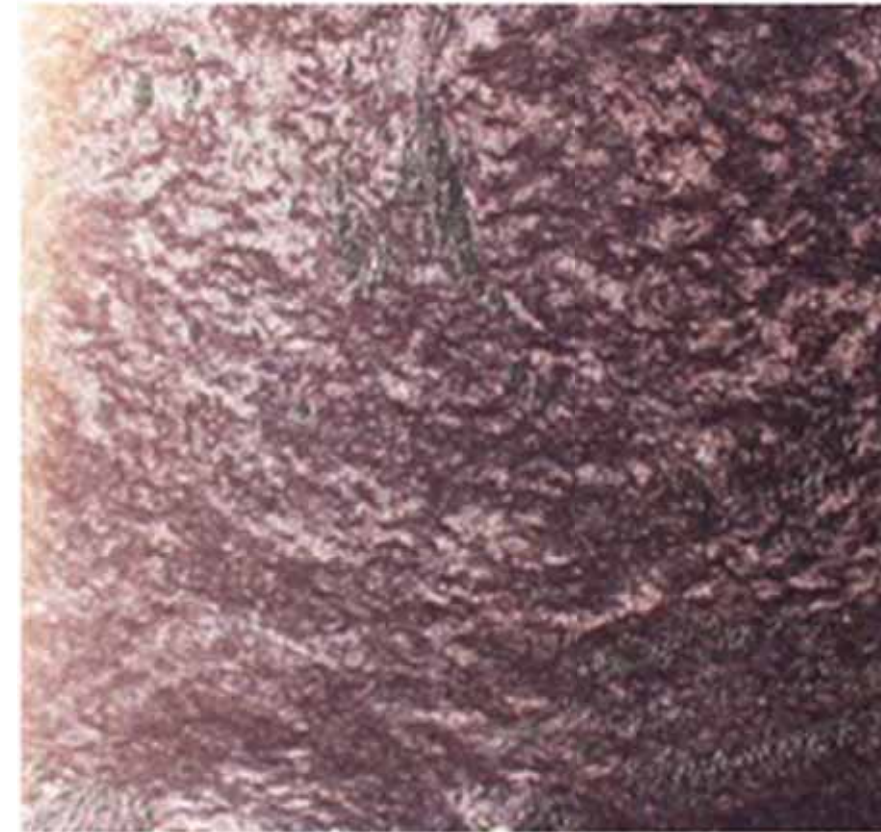
## Dermatofibrosarcoma protuberans

- Collagen
  - ✓ Weakly polarizable or non-refractile (82.9%)
  - ✓ Checkerboard pattern (typical)

## Dermatofibroma

- Collagen
  - ✓ Highly polarizable
  - ✓ Diffuse and homogeneous brightness

Low sensitivity and specificity



**Figure 3.** (A) DFSP exhibiting absence of bright diffraction (central) compared to bright diffraction of surrounding normal collagen (\*) at x20 magnification. (B) DFSP exhibiting characteristic diffuse checkerboard diffraction at x40 magnification.

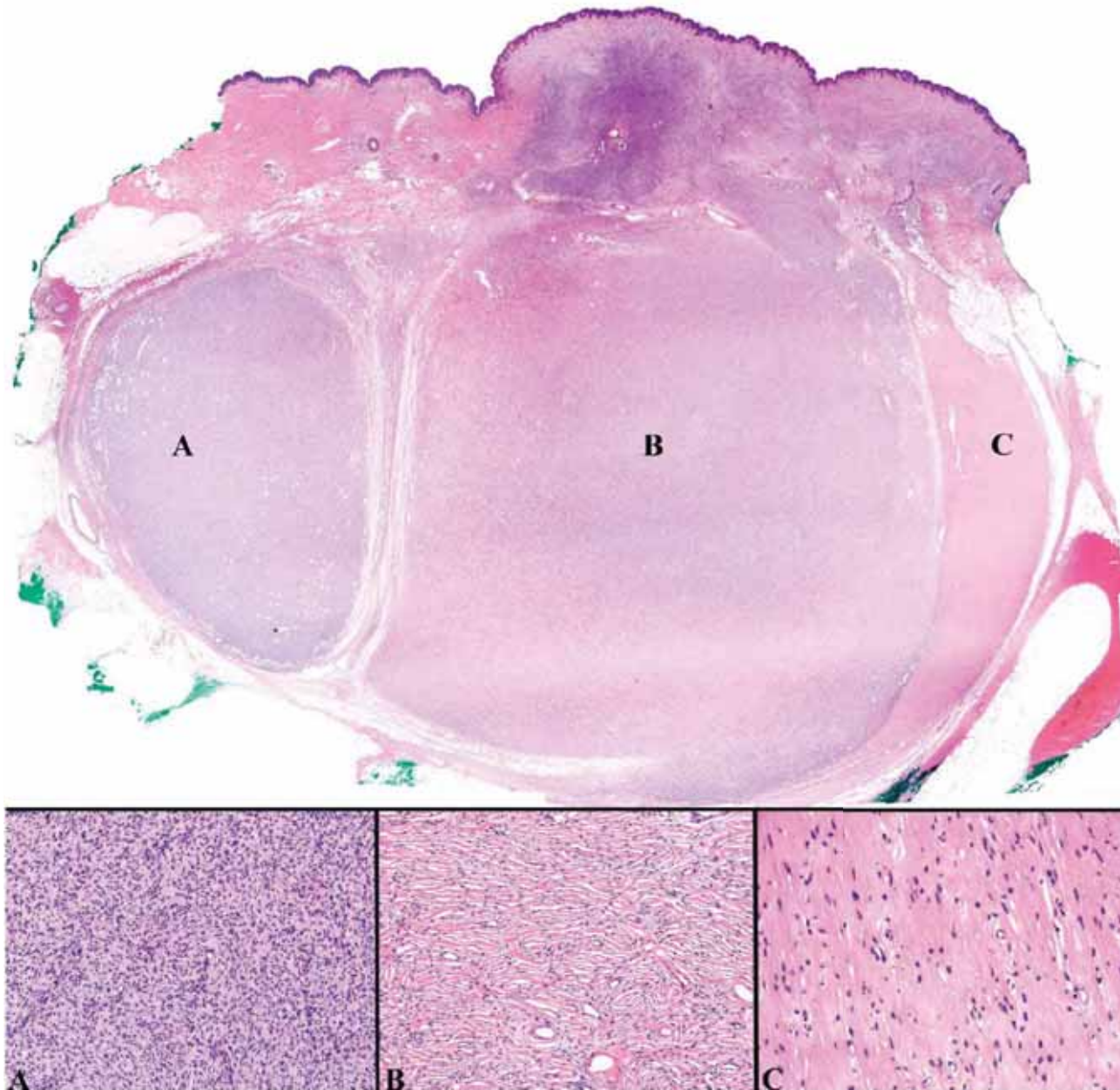
Sclerosing Dermatofibrosarcoma Protuberans Shows Significant Overlap With Sclerotic Fibroma in Both Routine and Immunohistochemical Analysis: A Potential Diagnostic Pitfall

Maram Yousef Odeh Abdaljaleel, MD\*† and Jeffrey P. North,

*Am J Dermatopathol* 2017;39:83–88

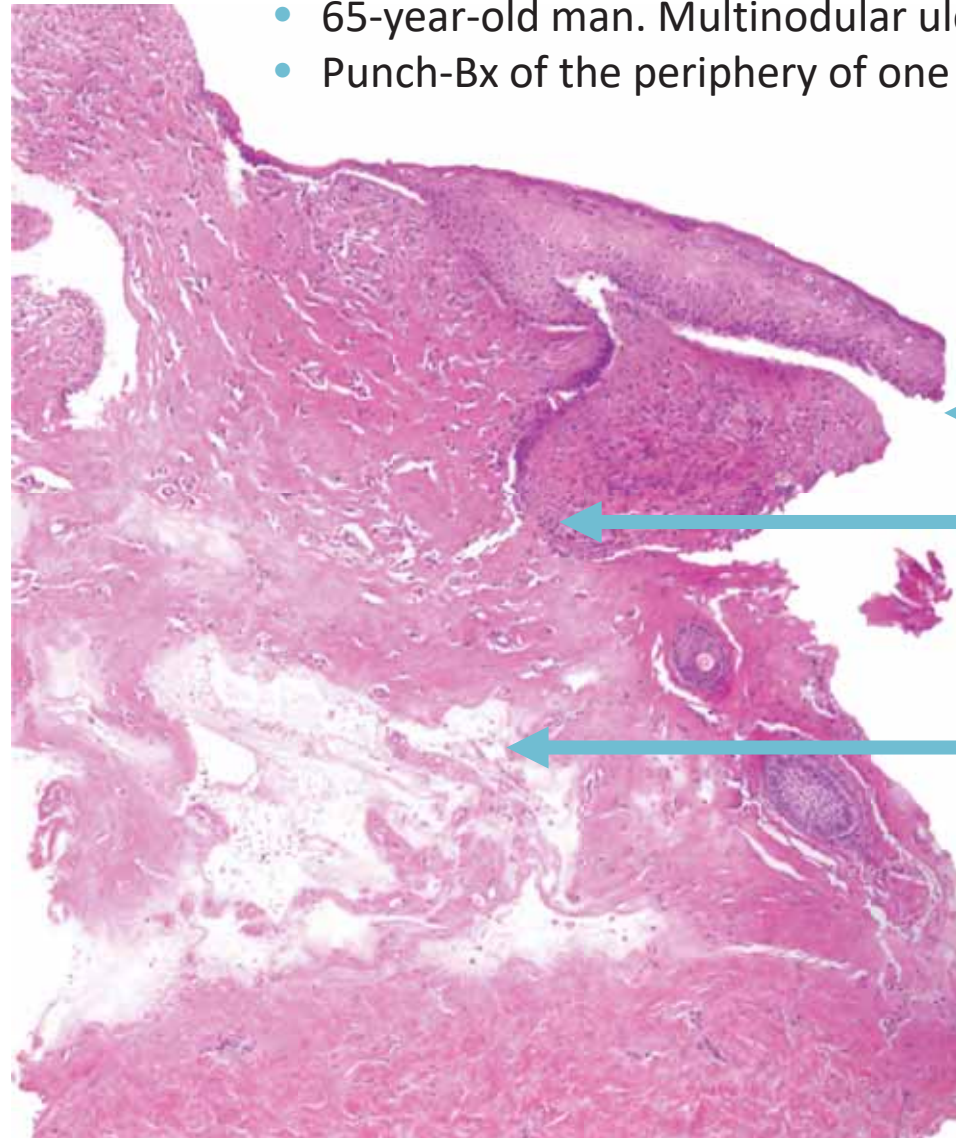
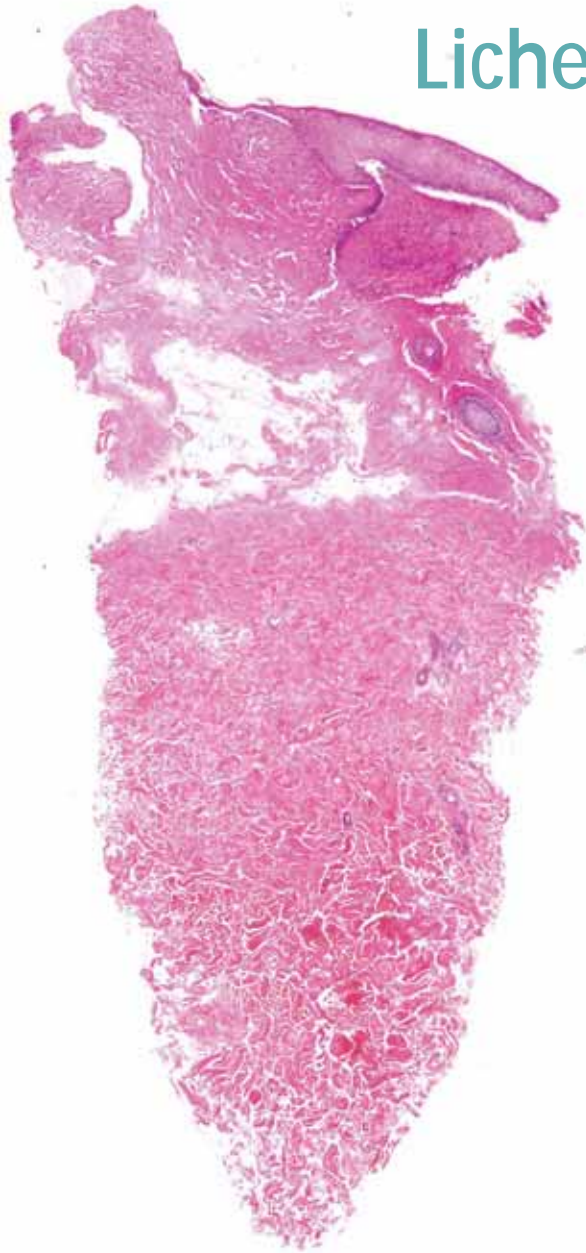
### Sclerotic DFSP

- Patterns
  - ✓ Morpheiform
  - ✓ Sclerotic fibroma-like
- DFSP & Sclerotic fibroma are CD34 + & EMA+



## Lichen sclerosis?

- 65-year-old man. Multinodular ulcerated mass on the chest
- Punch-Bx of the periphery of one of the nodules



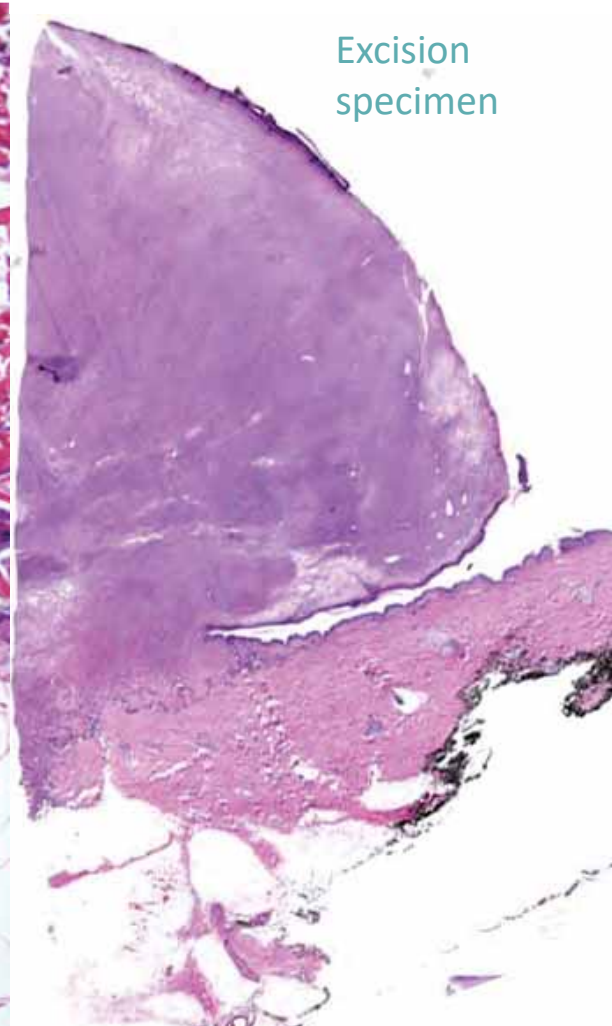
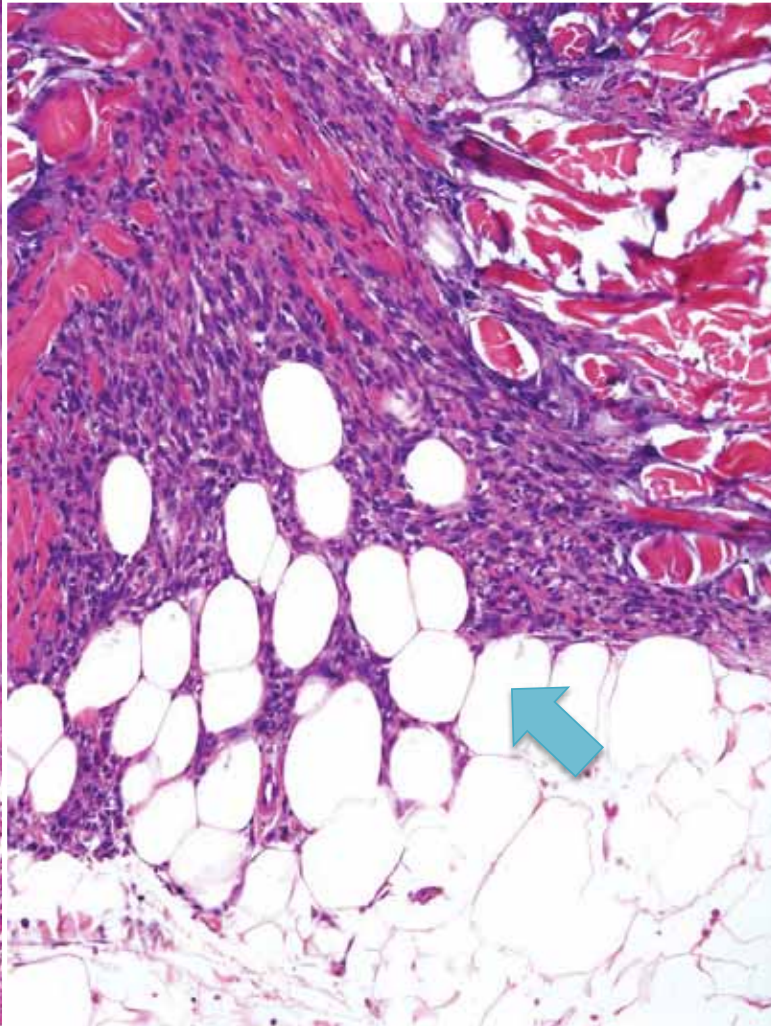
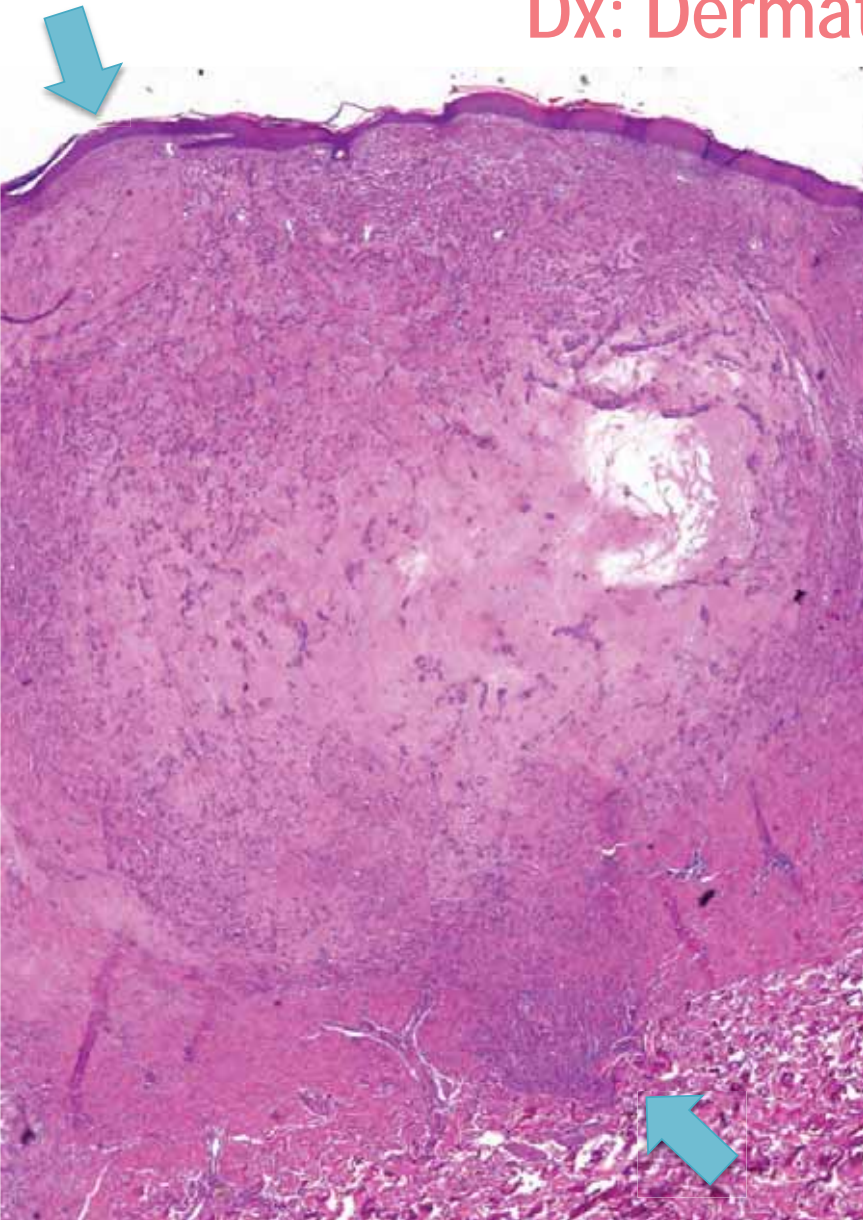
← Epidermal detachment

← Hyalinization

← Angiogenesis

## Dx: Dermatofibrosarcoma protuberans

- 65-year-old man. Multinodular ulcerated mass on the chest
- Punch-Bx of the periphery of one of the nodules



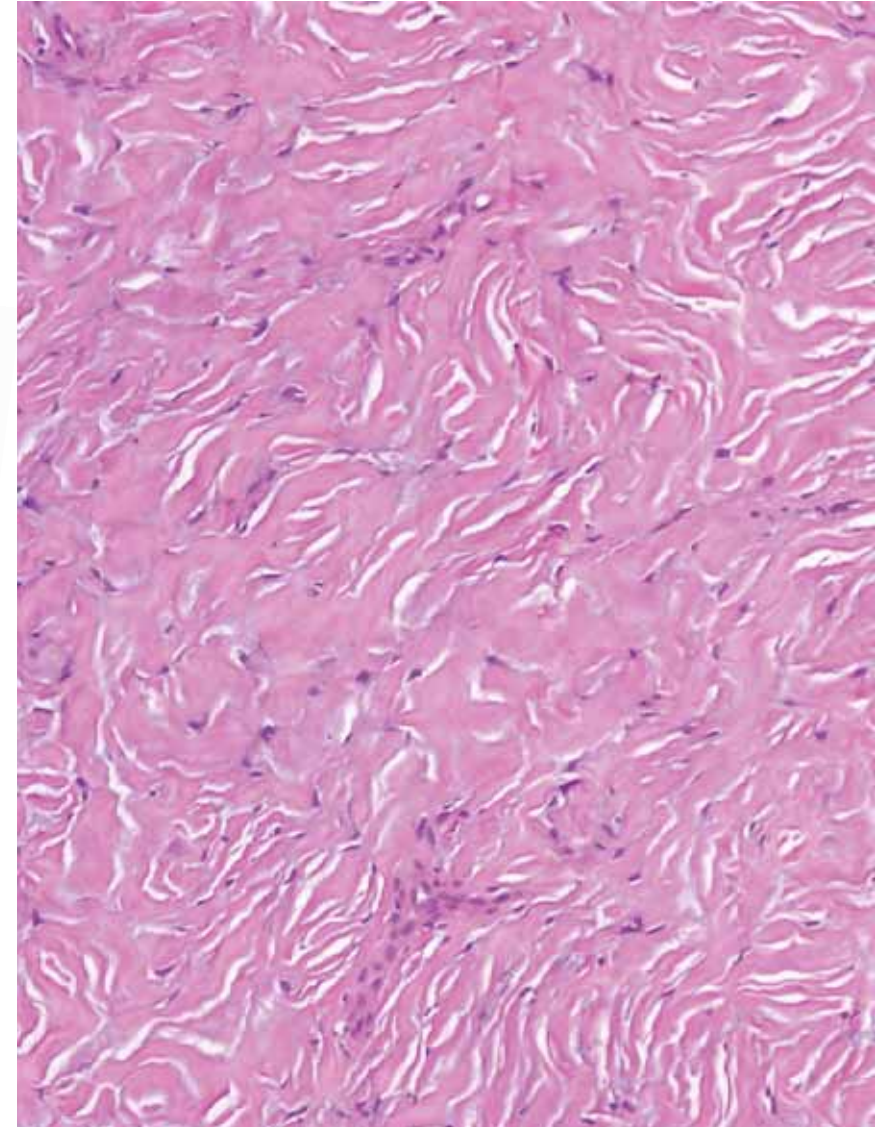
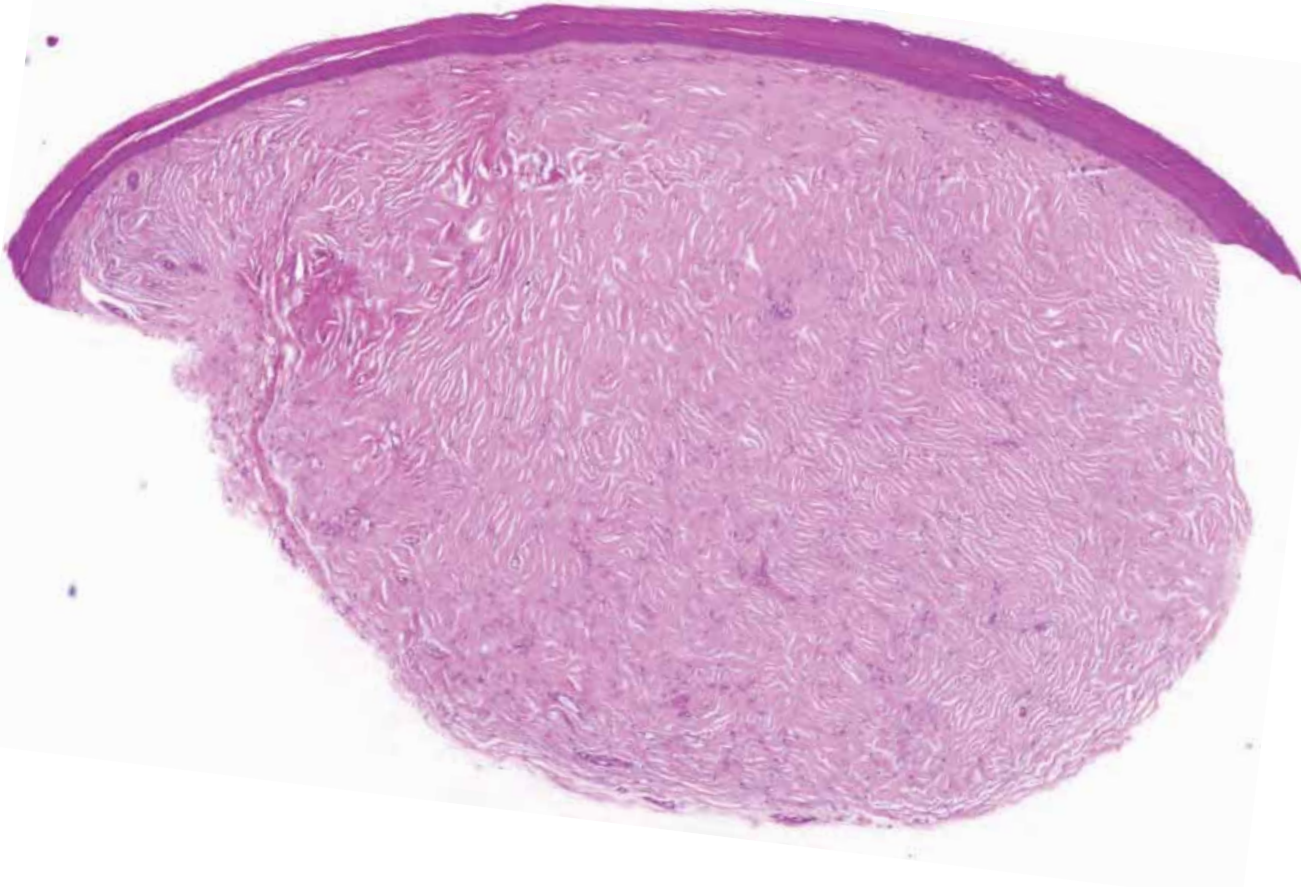
**Failure is not when you  
fall down but when  
you refuse to get back up**



## Storiform collagenized pattern

- 36-year-old woman
- Lesion on the leg

**Dx: Consistent with sclerotic fibroma** (DFSP cannot be ruled out)

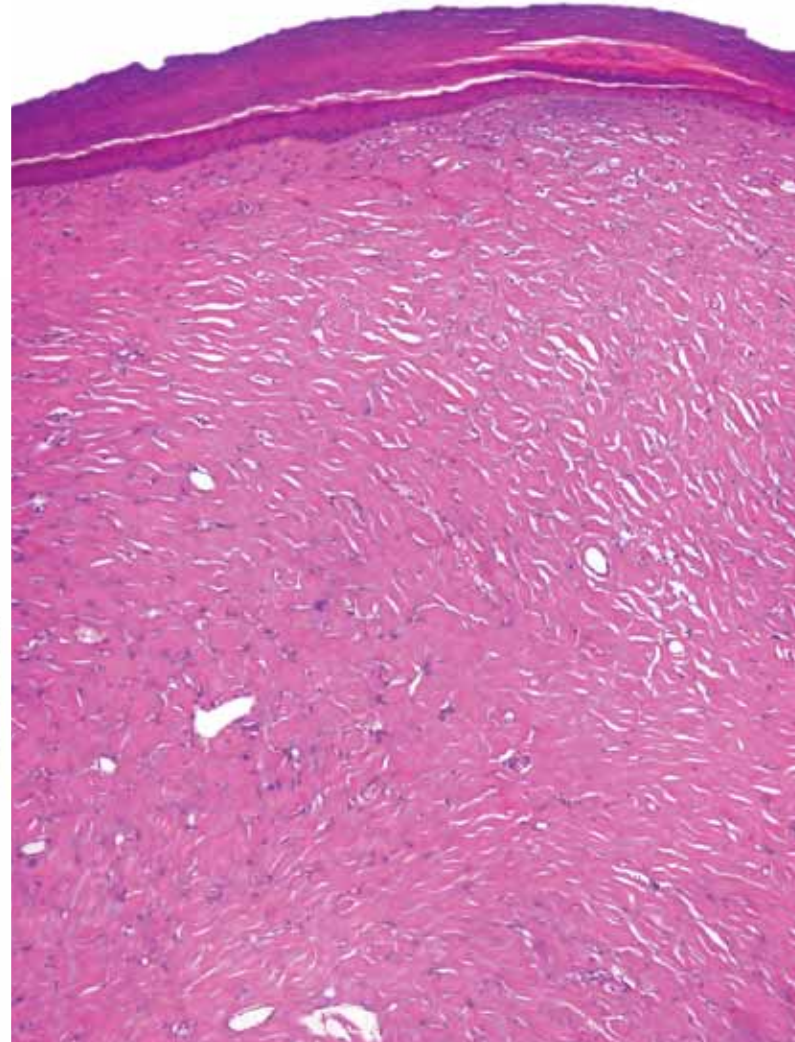


# Storiform collagenized pattern

- 36-year-old woman
- Lesion on the arm

**Dx: Sclerotic fibroma**

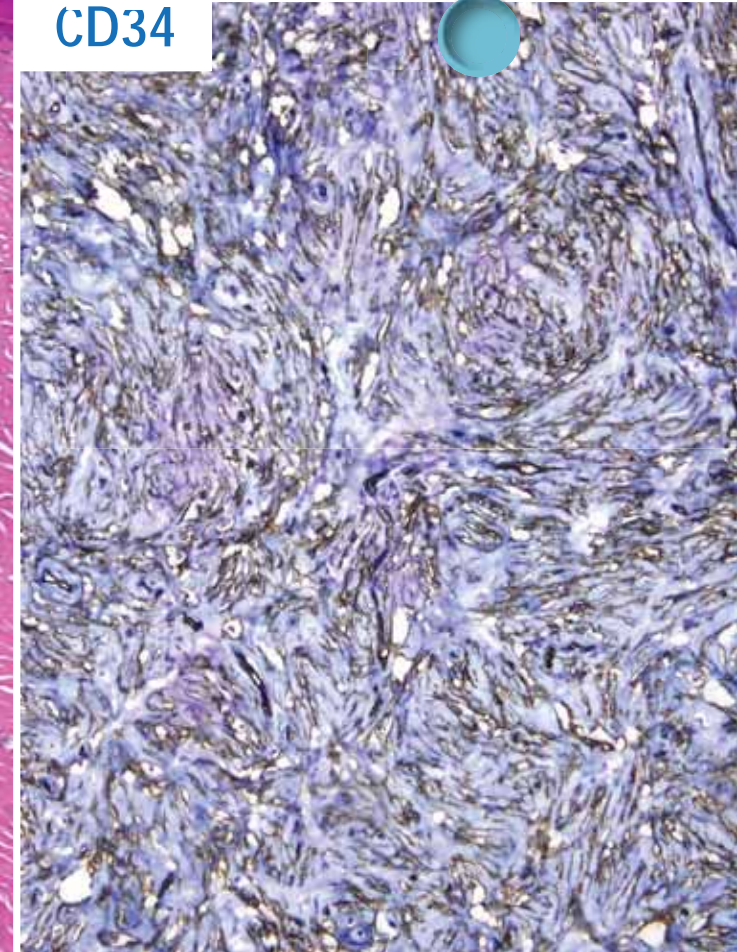
**Note:** It is advisable to rule out Cowden disease



**Multiple sclerotic fibromas of skin. A cutaneous marker of Cowden disease**

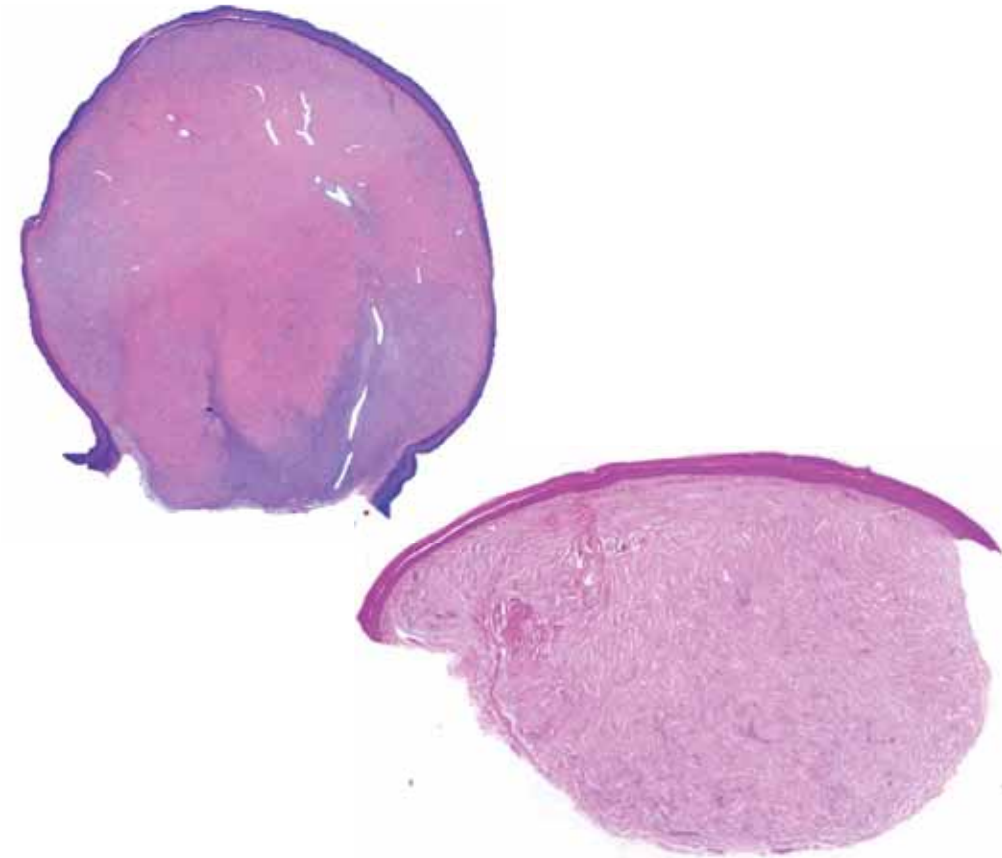
Requena L, Gutiérrez J, Sánchez Yus E.  
J Cutan Pathol. 1992; 19:46-51

**CD34**



## Dx: Nodular subepidermal fibrosis in chronic lymphedema

- 36-year-old woman
- Obesity with massive lymphedema
- Multiple nodules on her extremities



# Nodular subepidermal fibrosis in non-filarial endemic elephantiasis of the legs

Price EW. *Br J Dermatol.* 1973 Nov;89(5):451-6

Dermatology Online Journal  
14 (3):20



**Elephantiasis Nostras Verrucosa**

*Ann Dermatol.* 2009; 21: 326–329

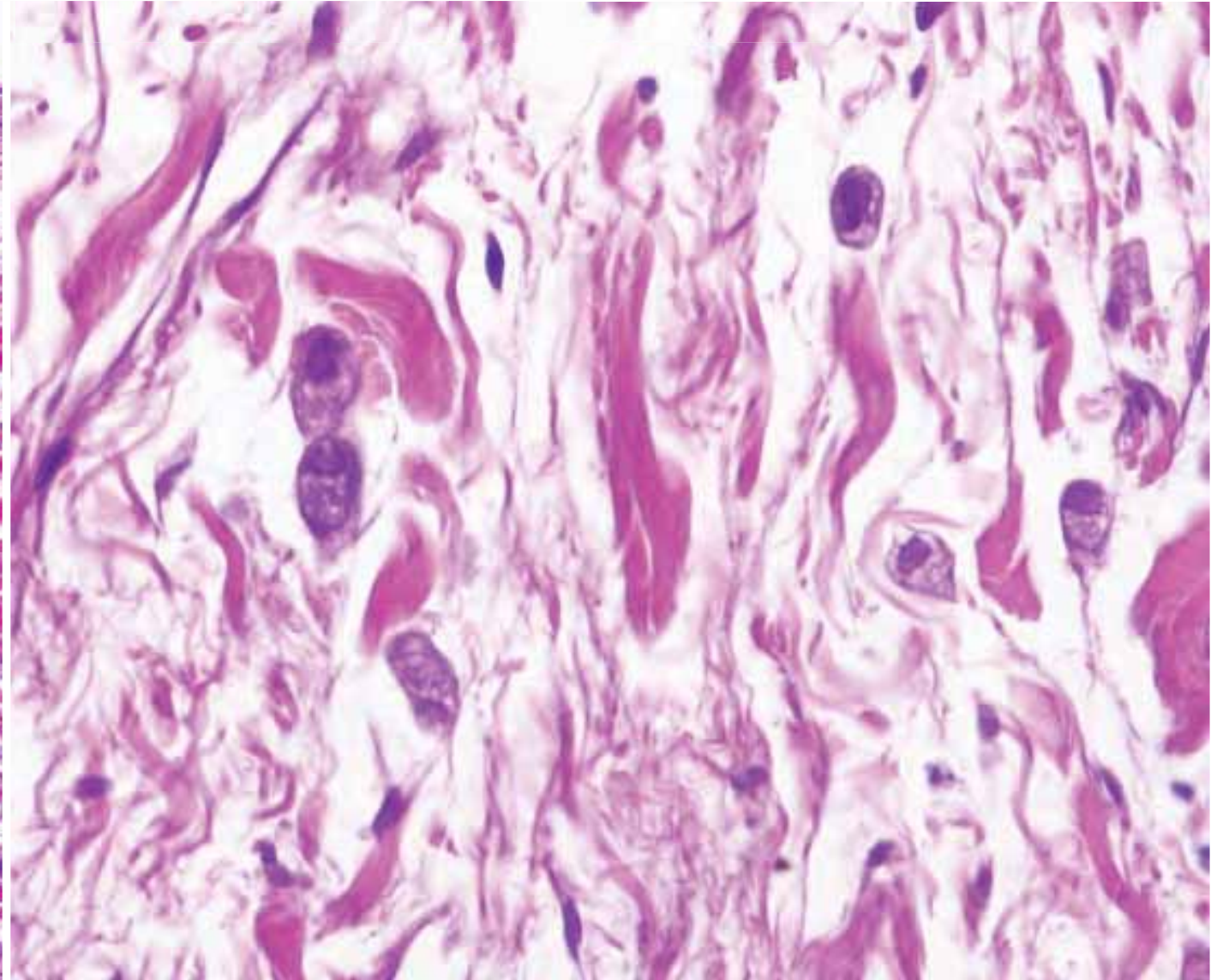
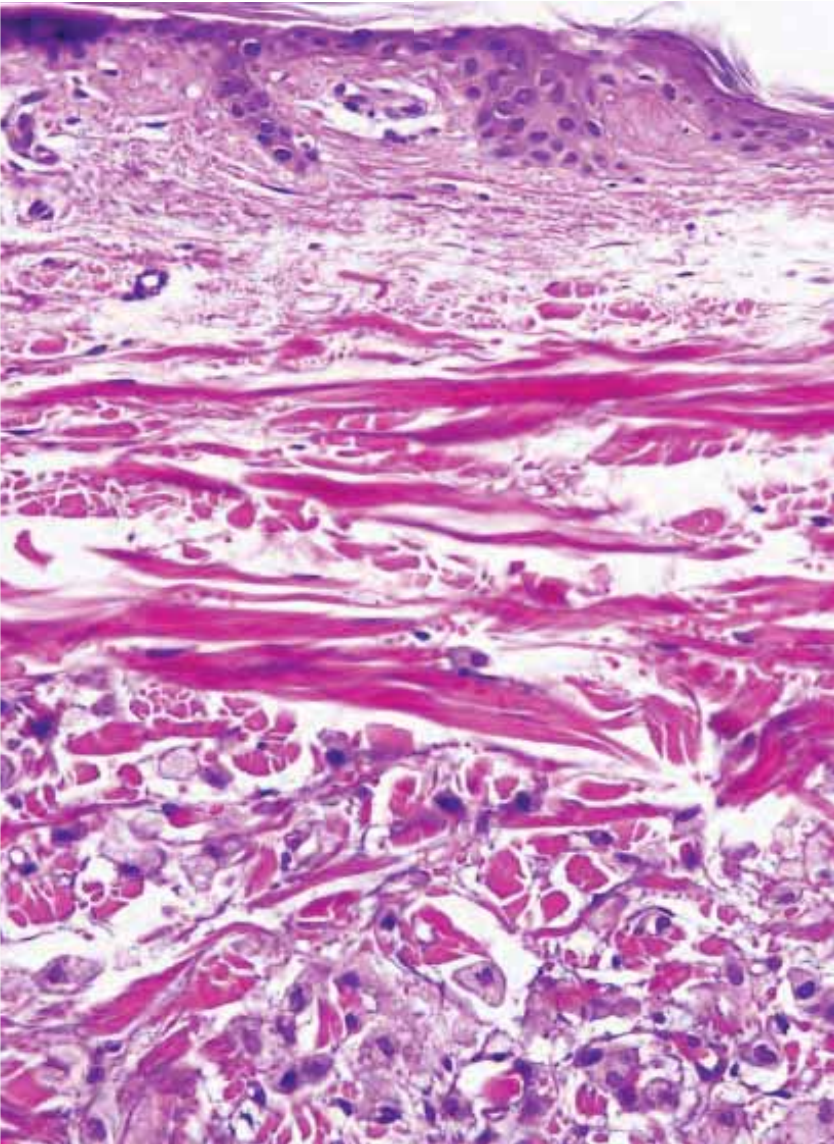


## LL 6

There are no specific patterns  
or cytological features  
Be aware of the look-alikes!



## Histiocytoid lobular breast carcinoma



LL 7



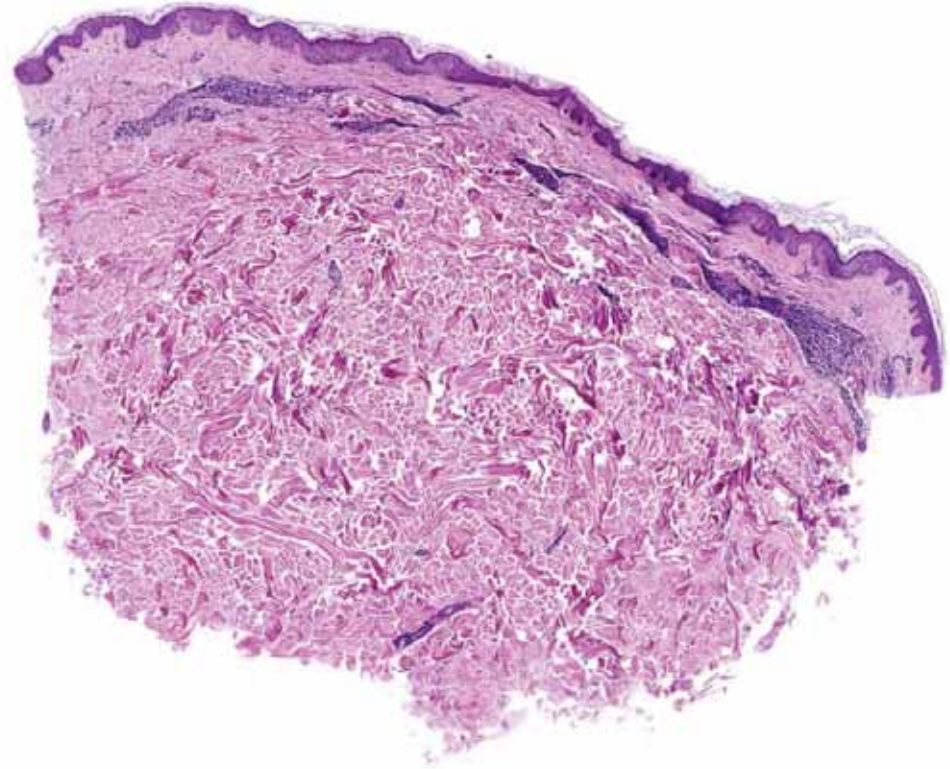
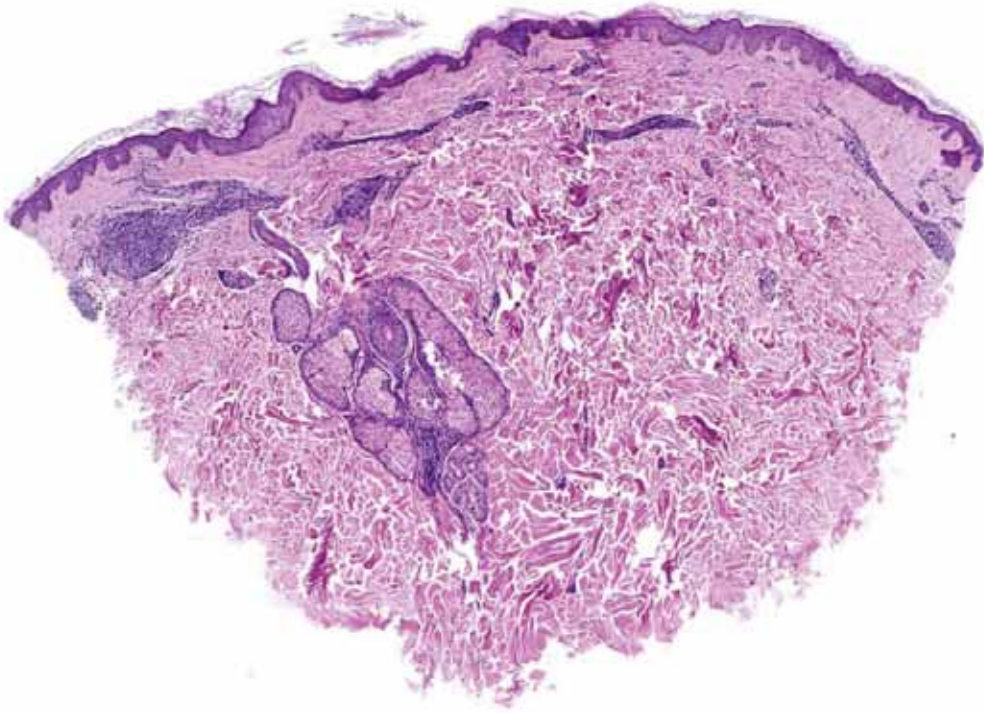
- 64-year-old man , otherwise, healthy
- Asymptomatic erythematous lesions on the left side of the trunk from 1 year
- Clinical Dx: MF, purpuric dermatosis, mastocytosis



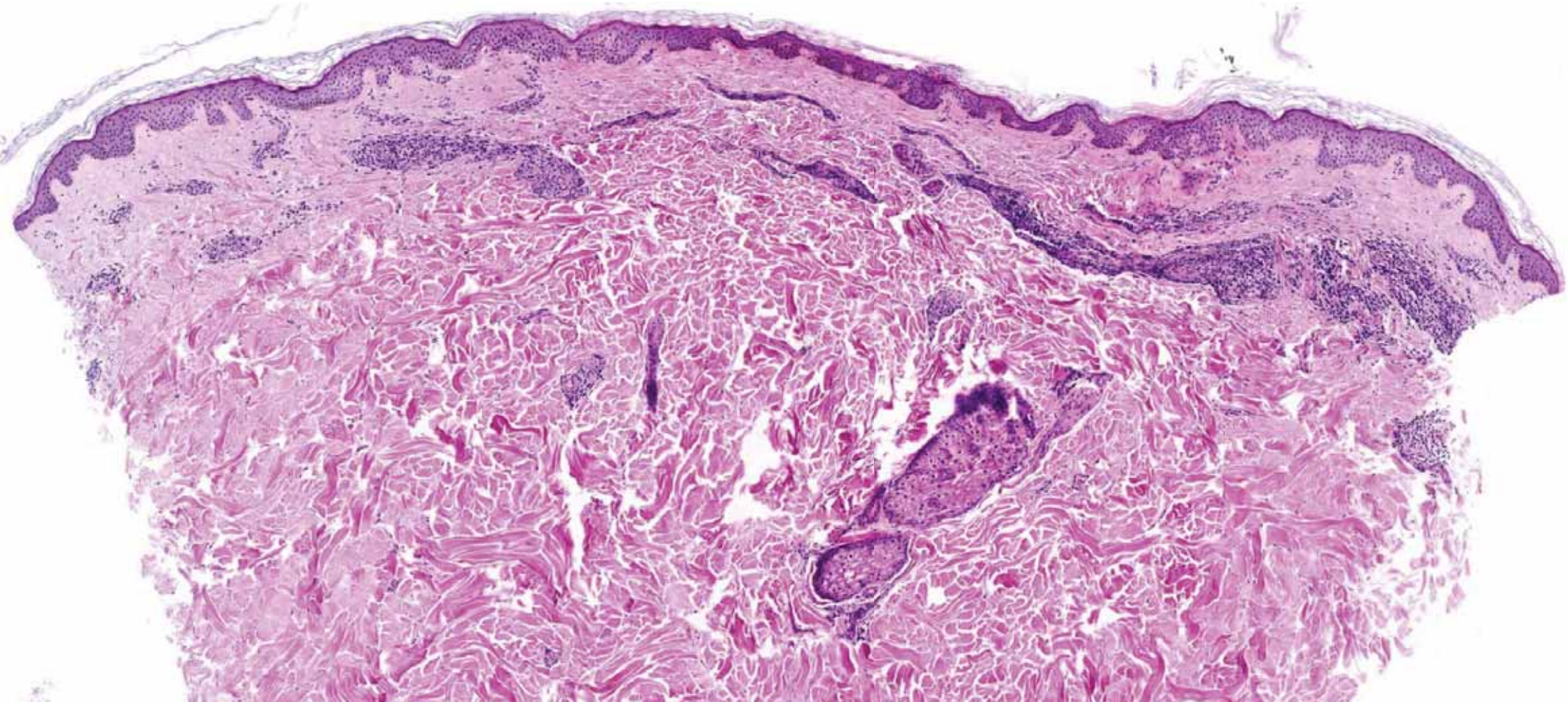
- 64-year-old man , otherwise, healthy
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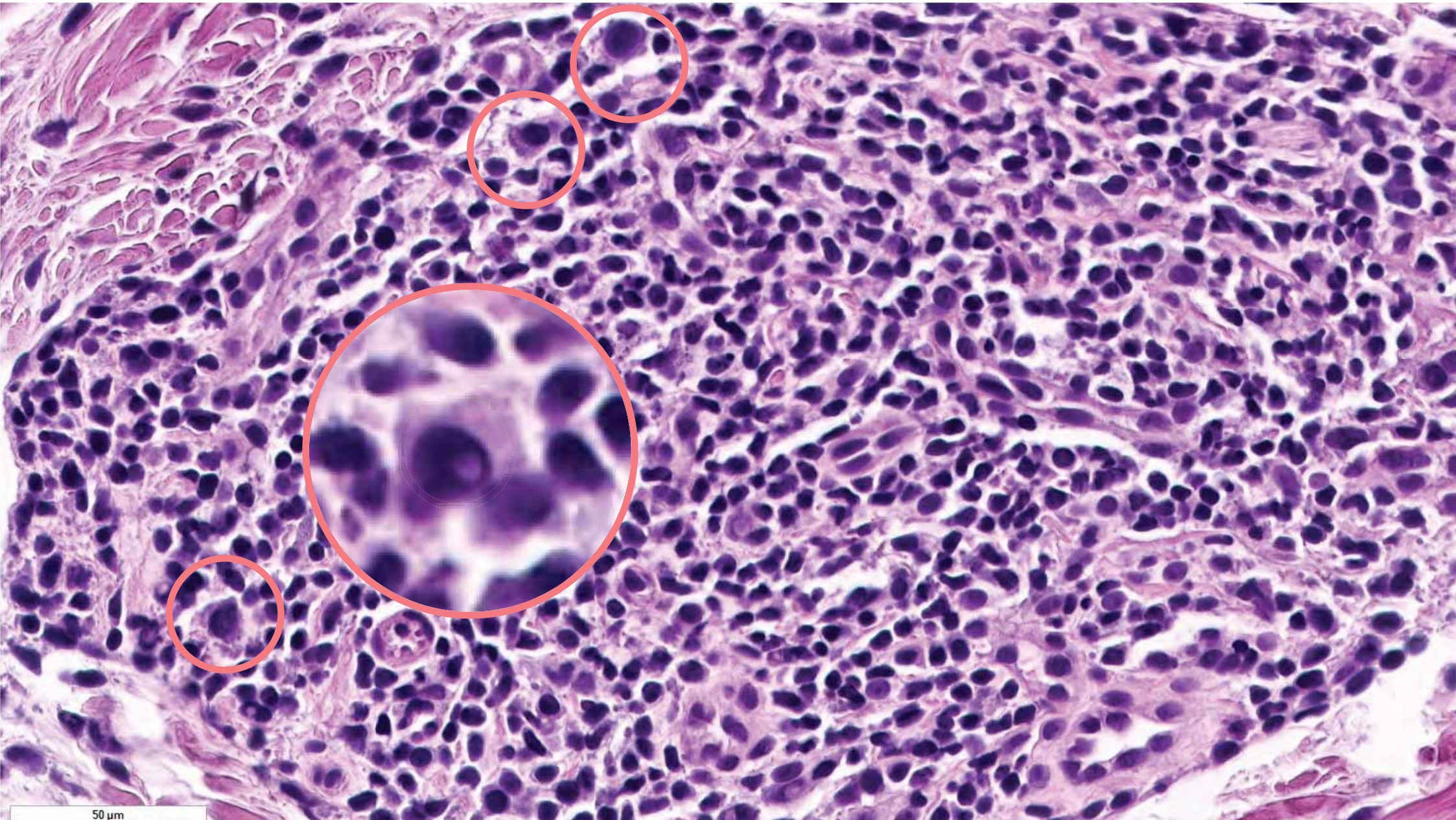


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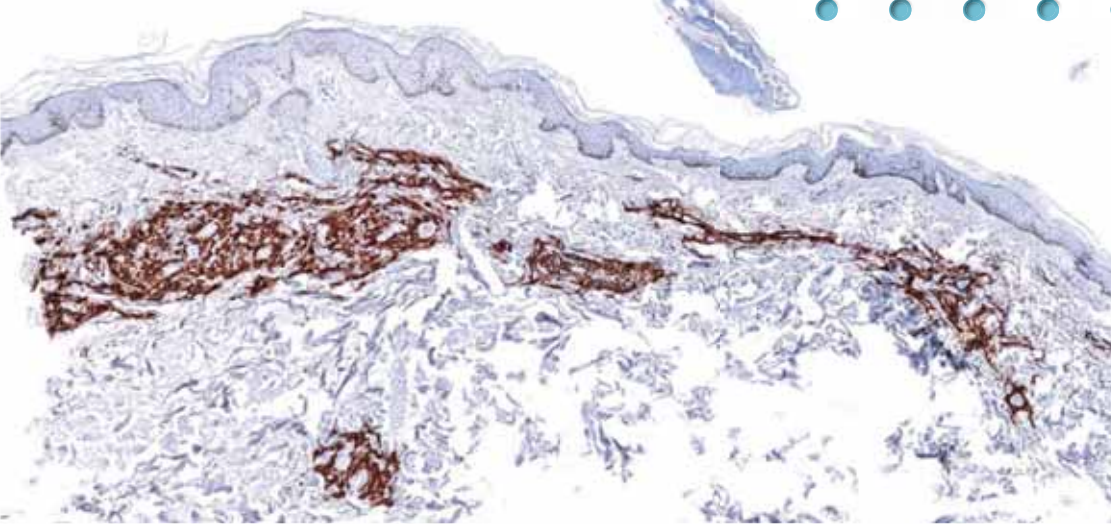


- 64-year-old man , otherwise, healthy
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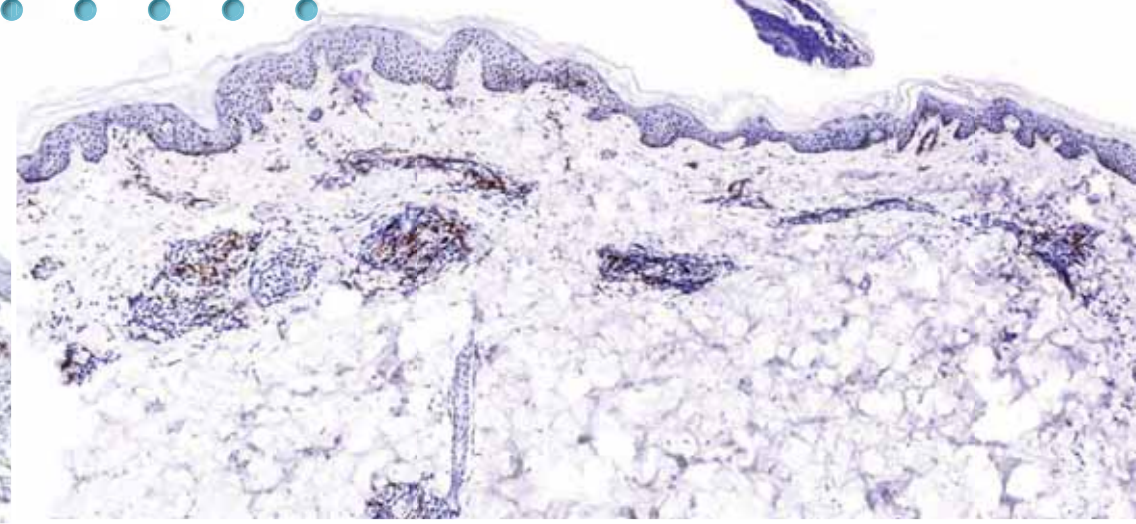


CD20

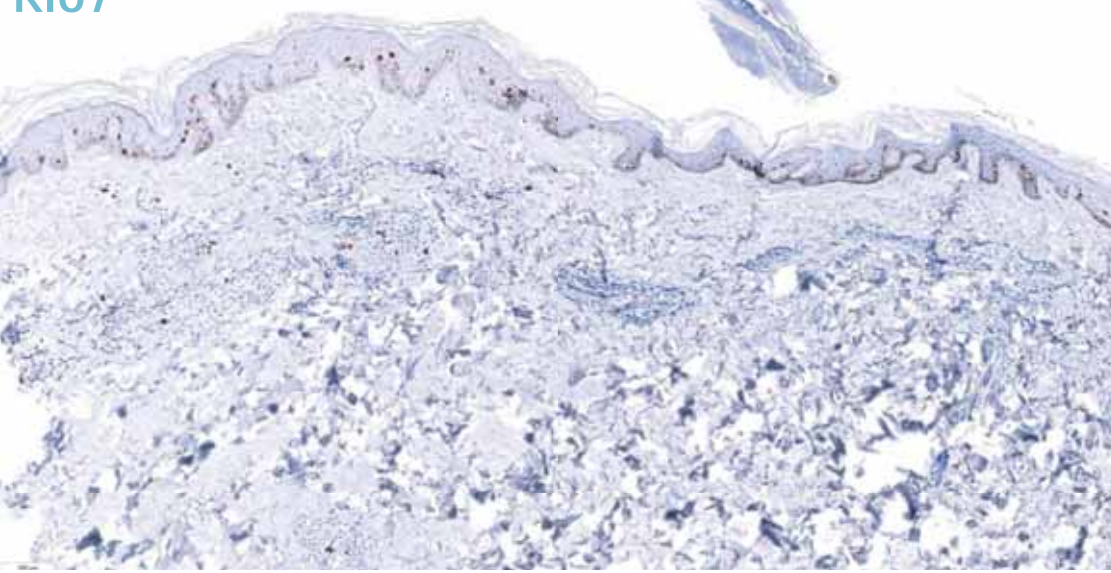


??????????

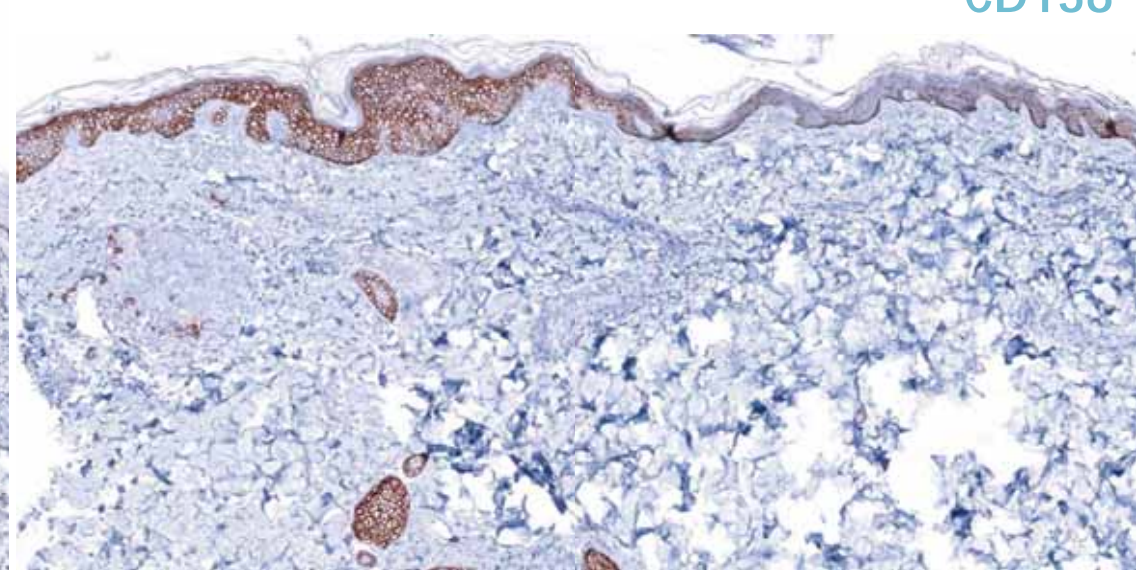
CD3



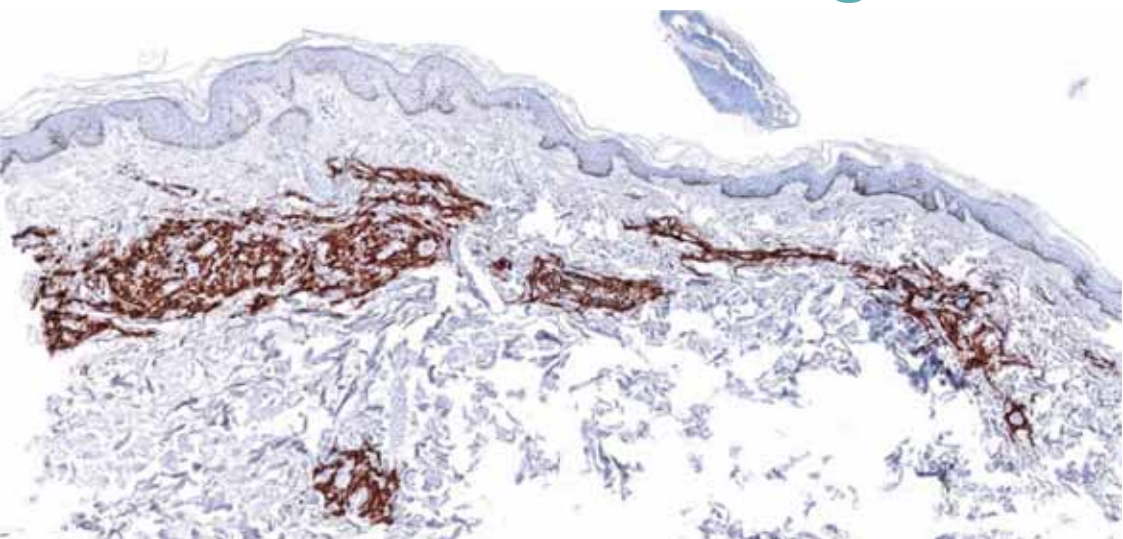
Ki67



CD138

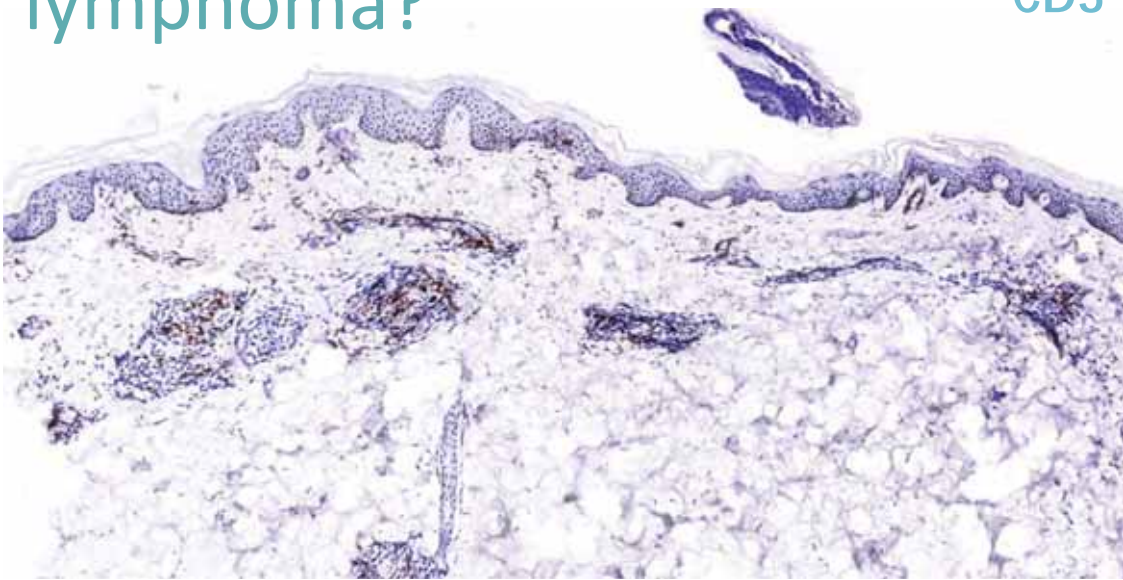


CD20

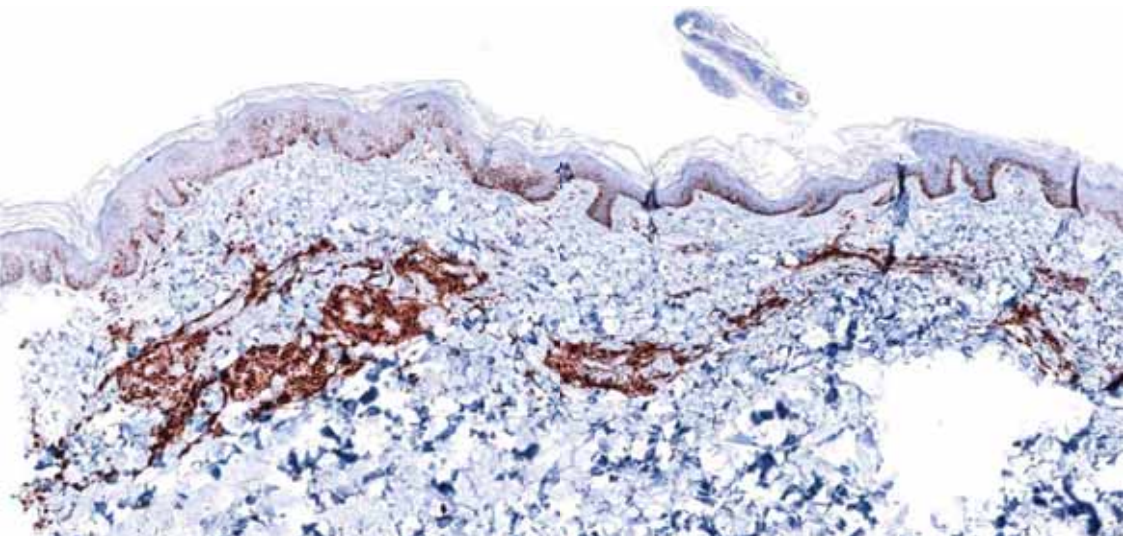


Marginal cell lymphoma?

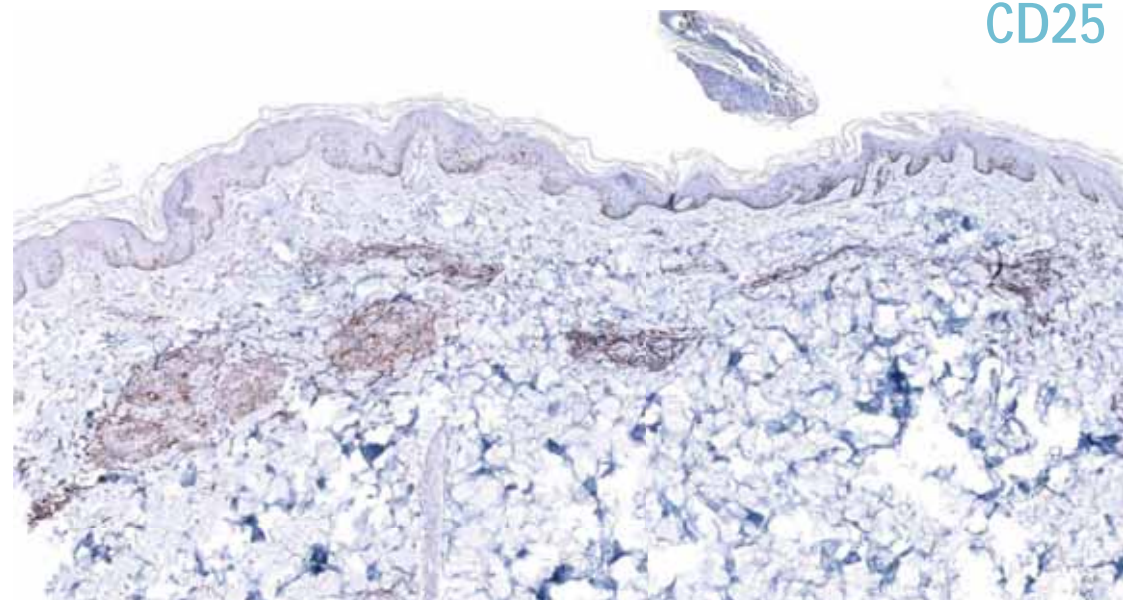
CD3



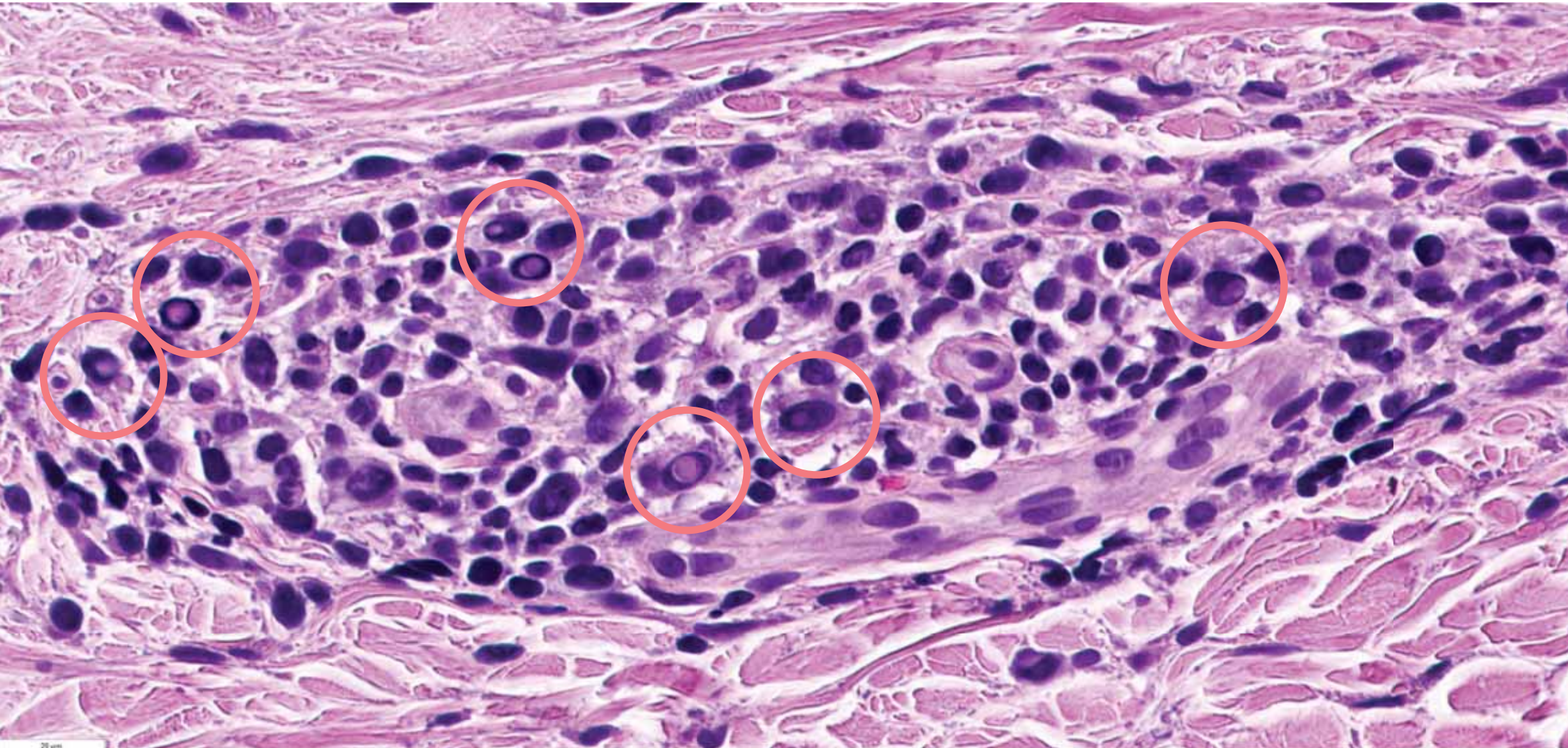
BCL2



CD25

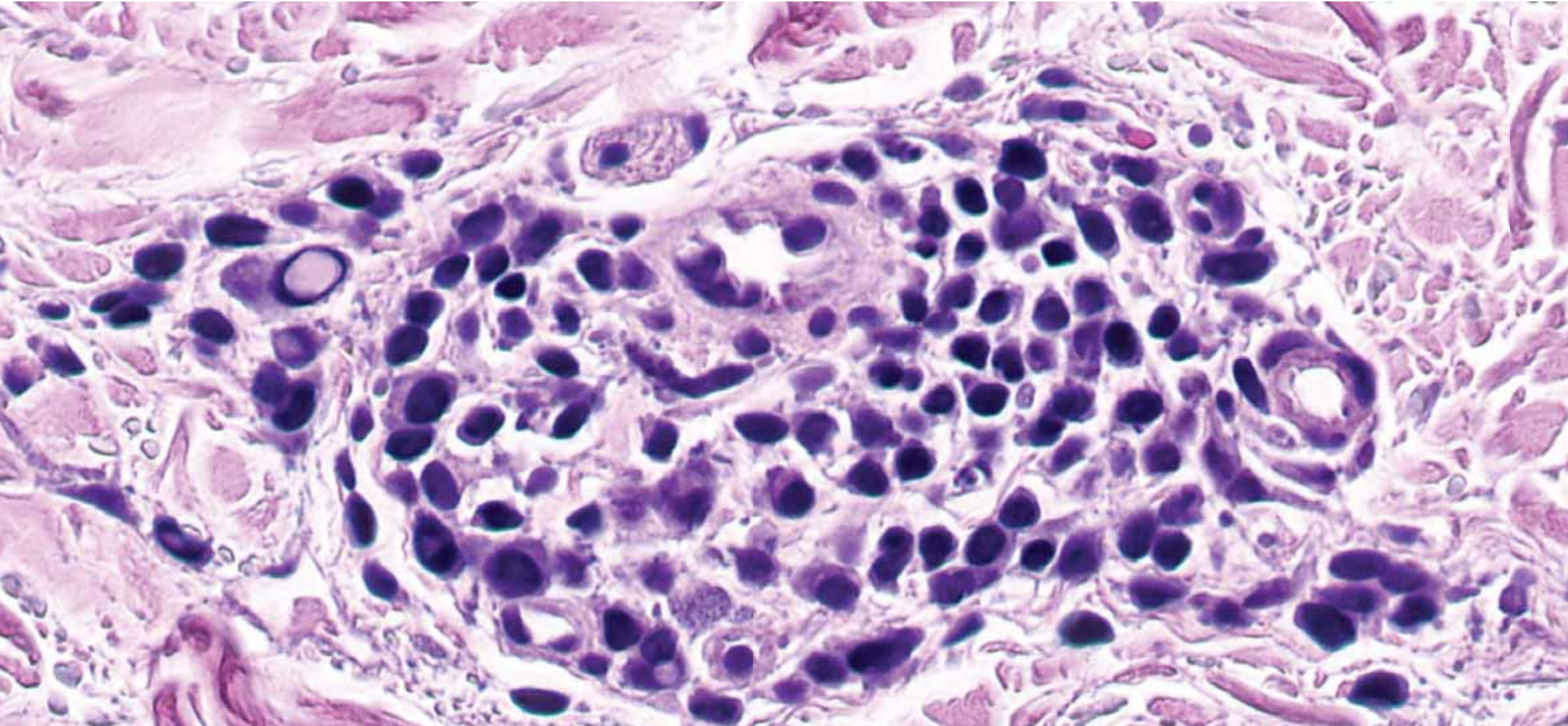


# Dutcher bodies



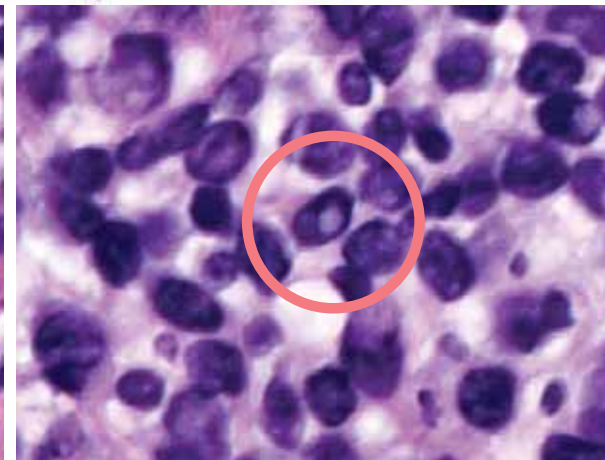
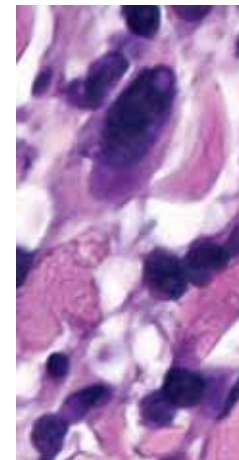
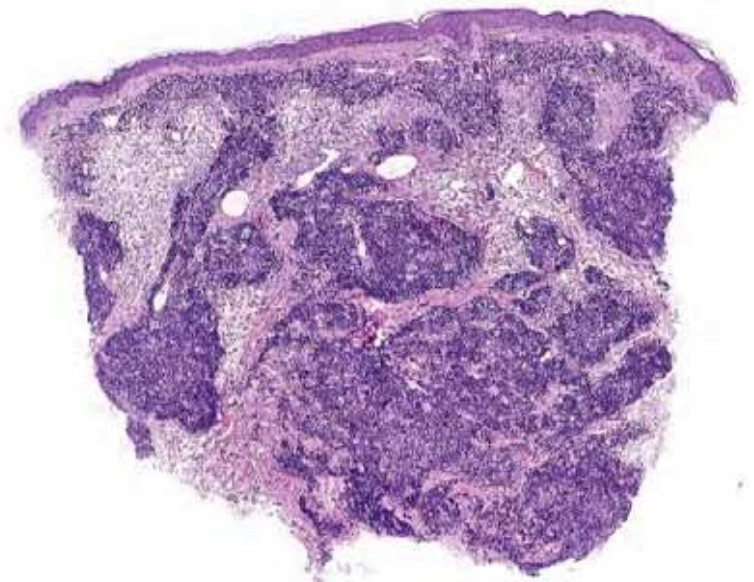
# Lymphoplasmacytic lymphoma (LPL) Waldenstrom macroglobulinemia

Bone marrow +



# Lymphoplasmacytic lymphoma (LPL) Waldenstrom macroglobulinemia

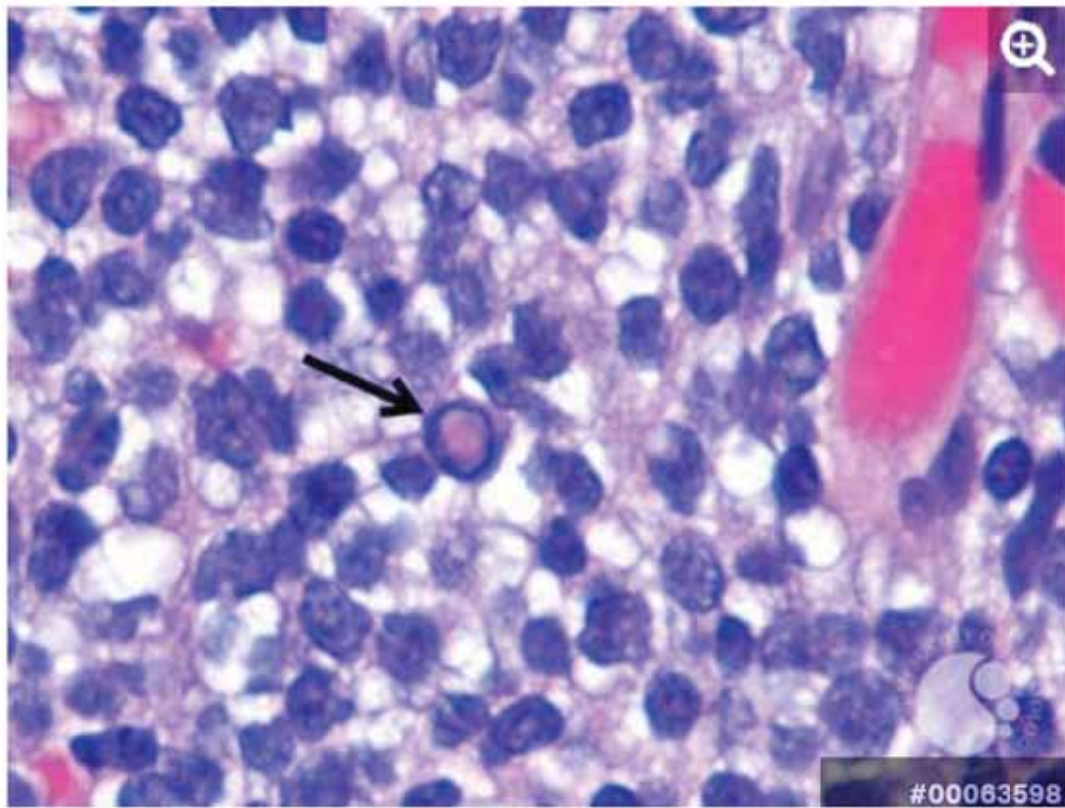
- Low-grade lymphoma
- B lymphocytes, plasmacytoid lymphocytes, and plasma cells
- Developmental arrest in the germinal center before terminal differentiation into plasma cells
- IgM monoclonal gammopathy
- **Symptoms:** related to bone marrow infiltration and IgM monoclonal gammopathy
- **DDx on the skin:** MZL ( *MYD88* p.L265P mutation in Waldenstrom)
- **Essential:** IgM+ (rarely IgG+ or IgA+), CD19+, CD20+, CD22+, CD25+, CD10-, CD23-, CD103-, CD138+/-.



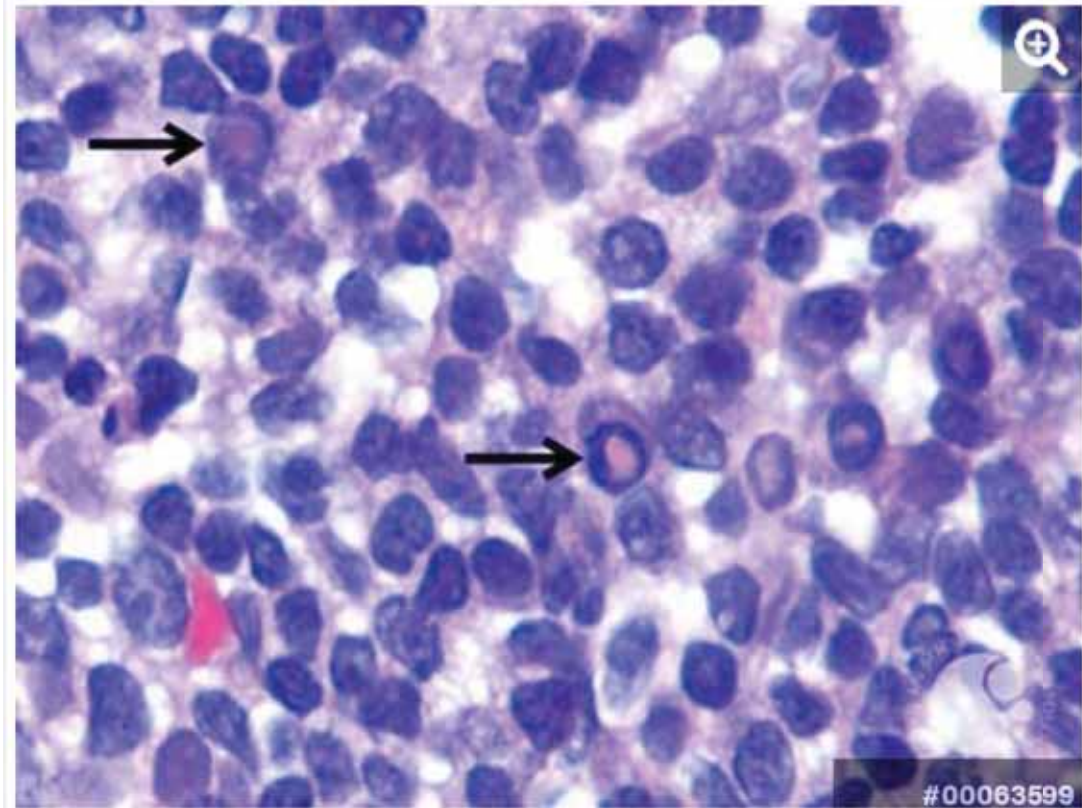


## ASH | Image Bank

Diagnosis of **Lymphoplasmacytic lymphoma, or Waldenstrom macroglobulinemia**, is challenging given its variable presentation and morphological similarity to other B cell lymphomas, particularly marginal cell lymphoma.



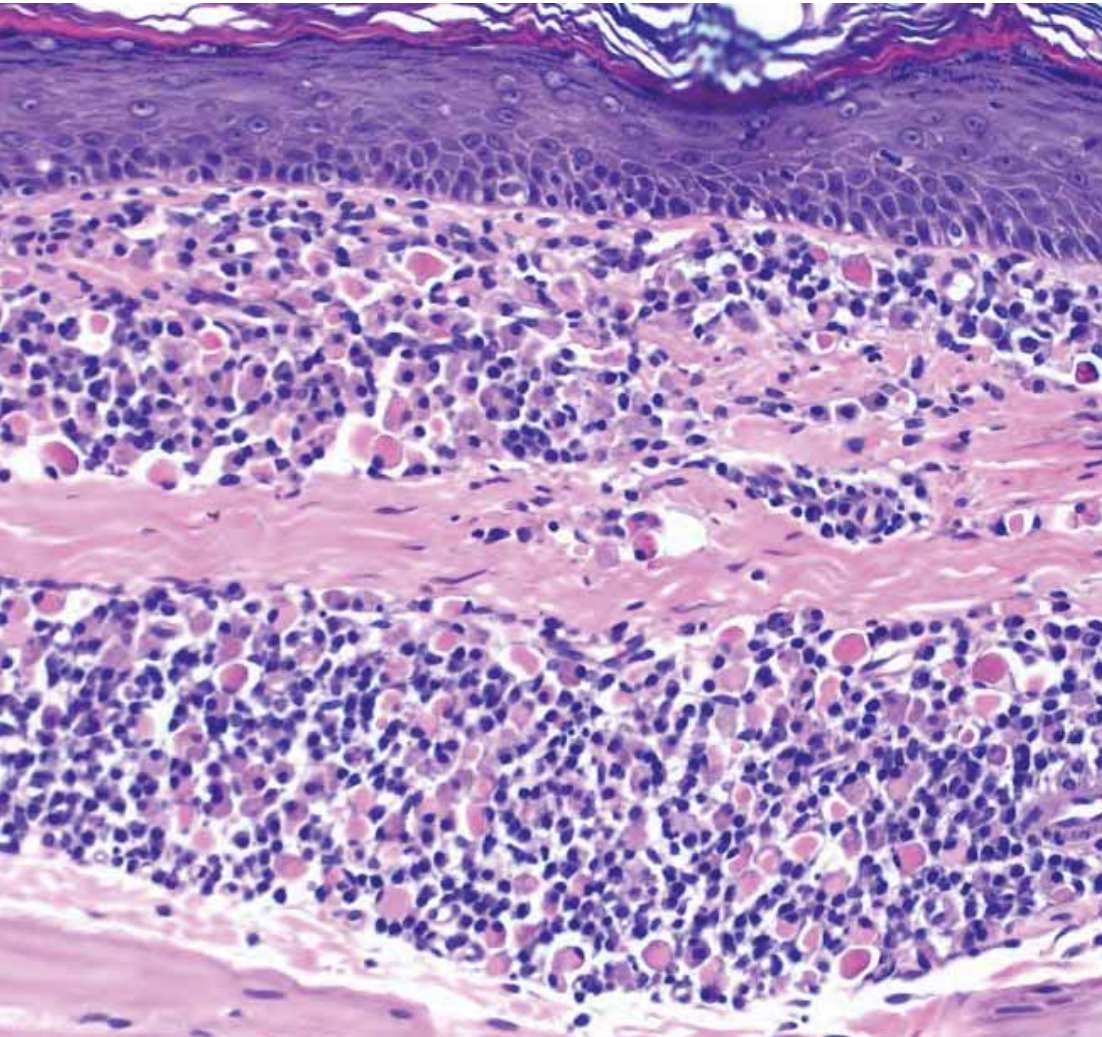
**Dutcher Bodies in Lymphoplasmacytic Lymphoma 2**



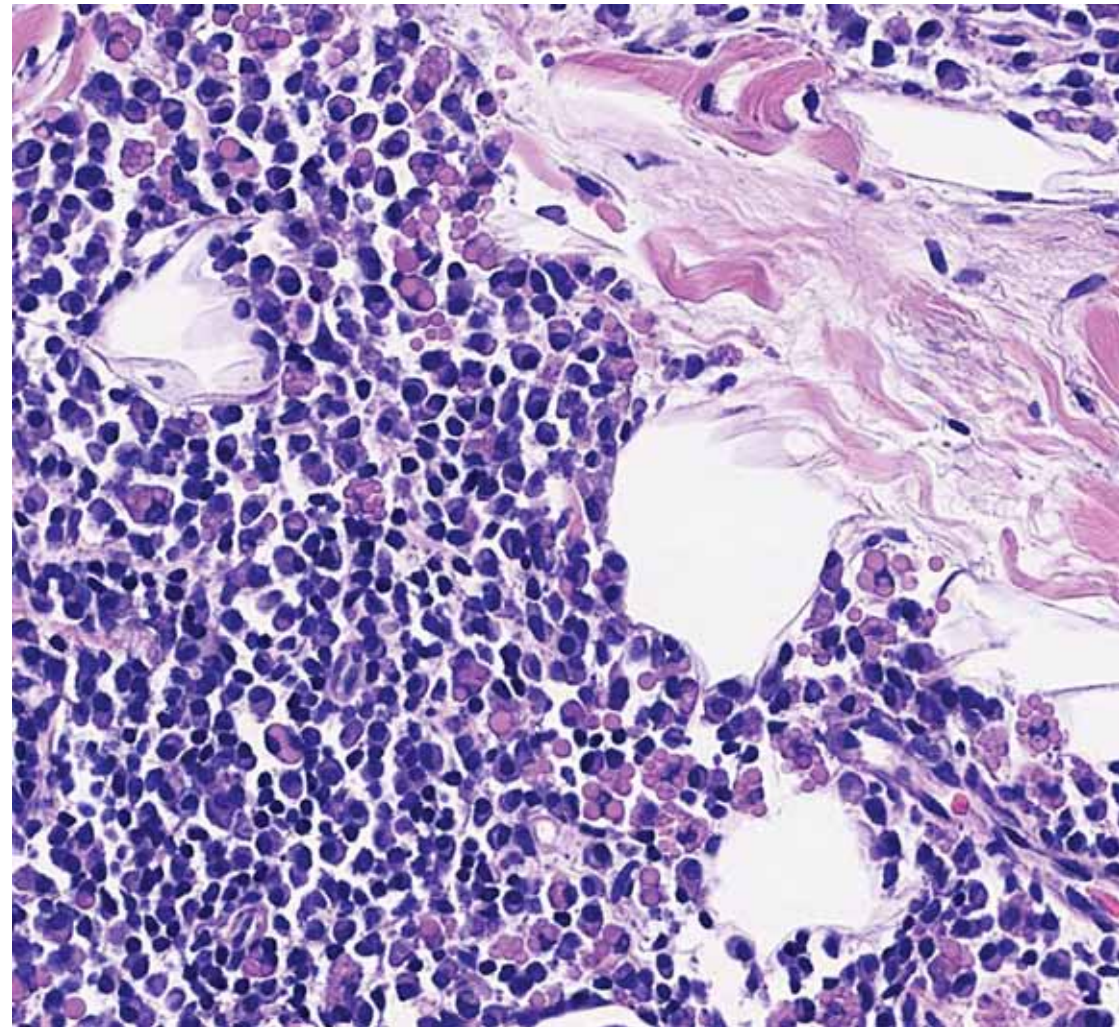
**Dutcher Bodies in Lymphoplasmacytic Lymphoma 3**

# Russell bodies

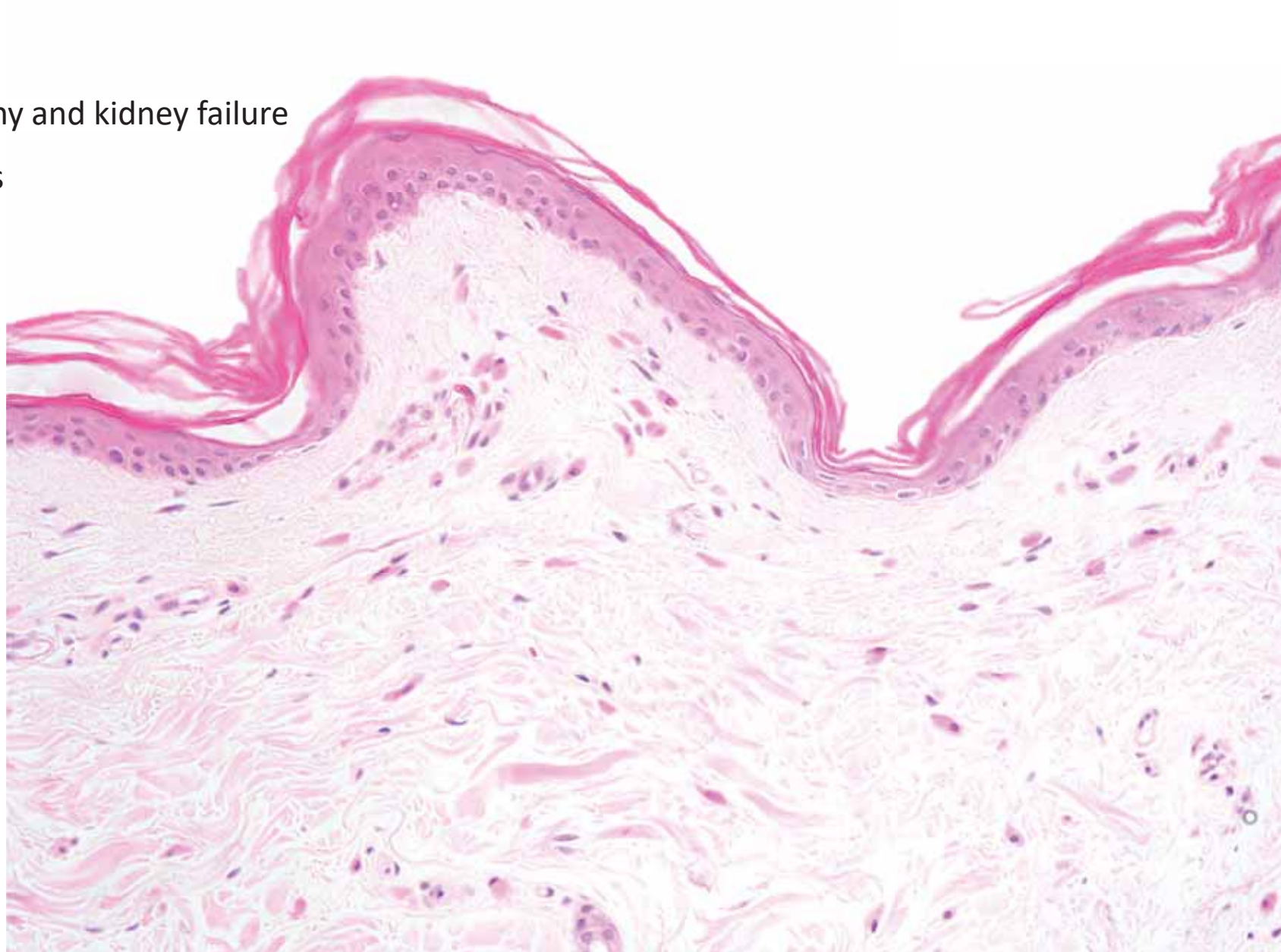
Folliculitis



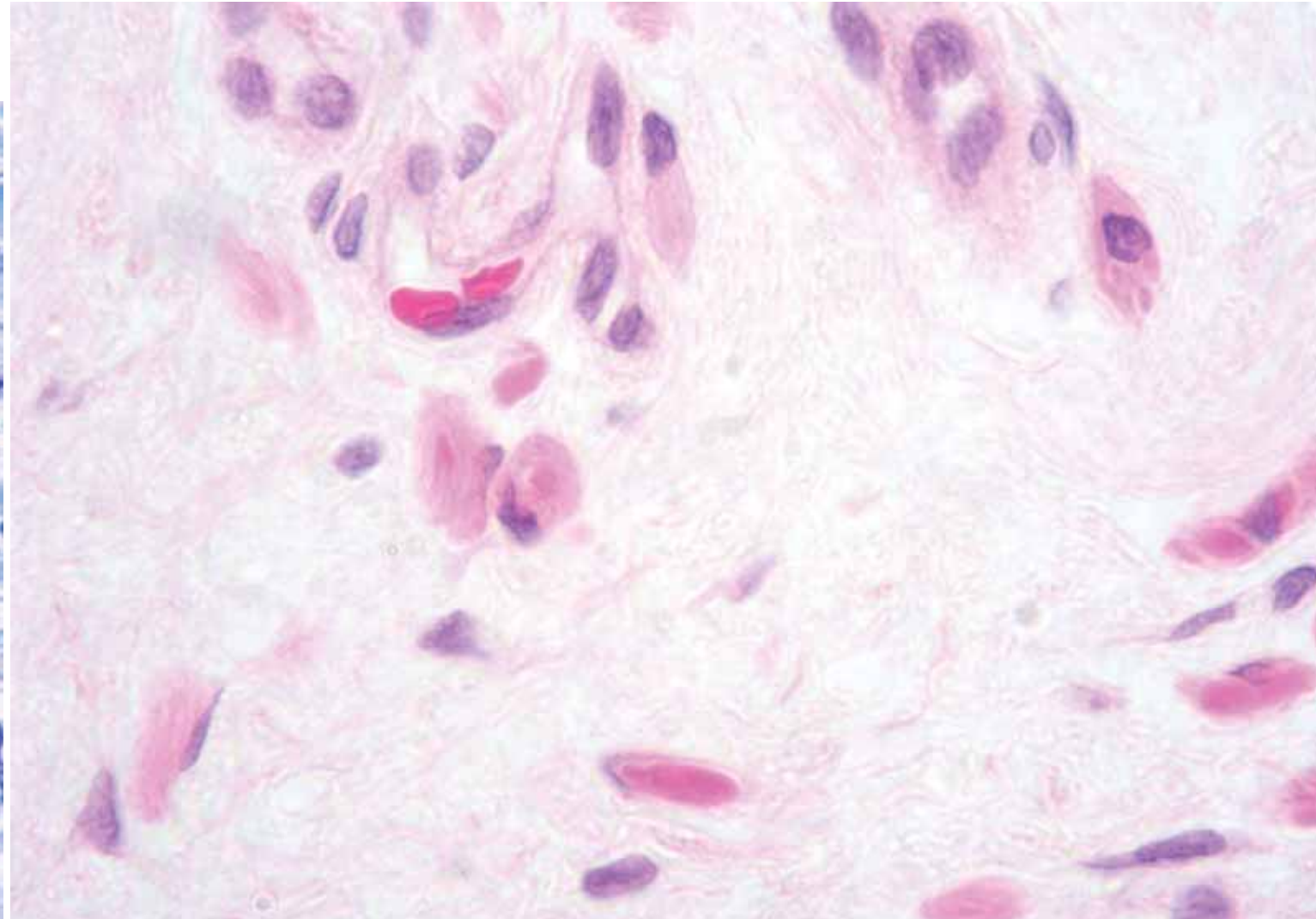
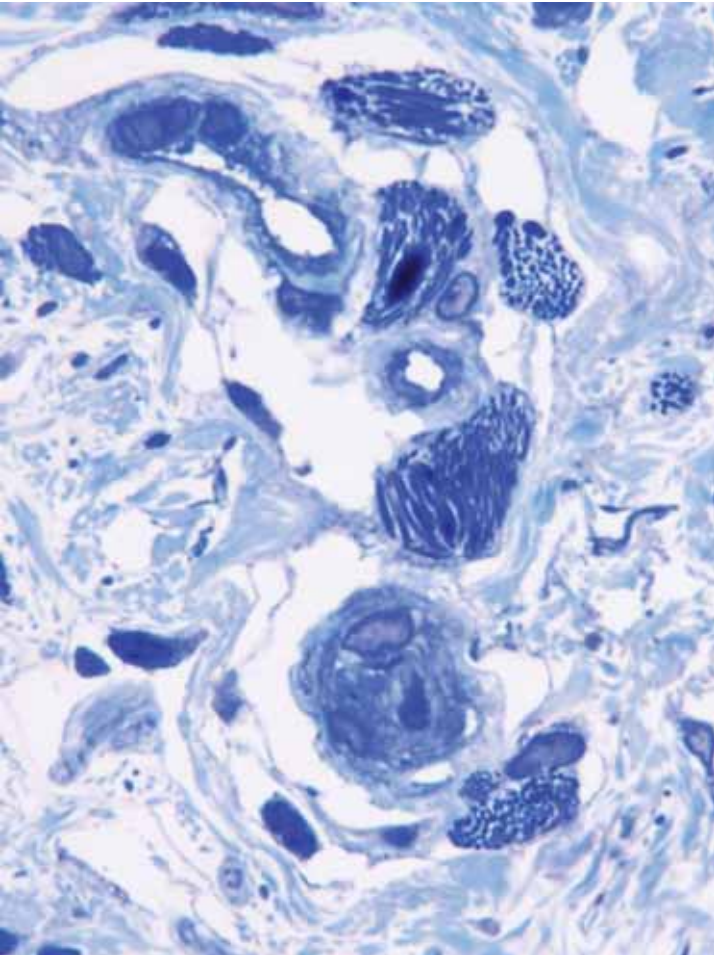
Marginal zone lymphoma



- 68-year-old female
- Monoclonal gammopathy and kidney failure
- Non-specific skin lesions

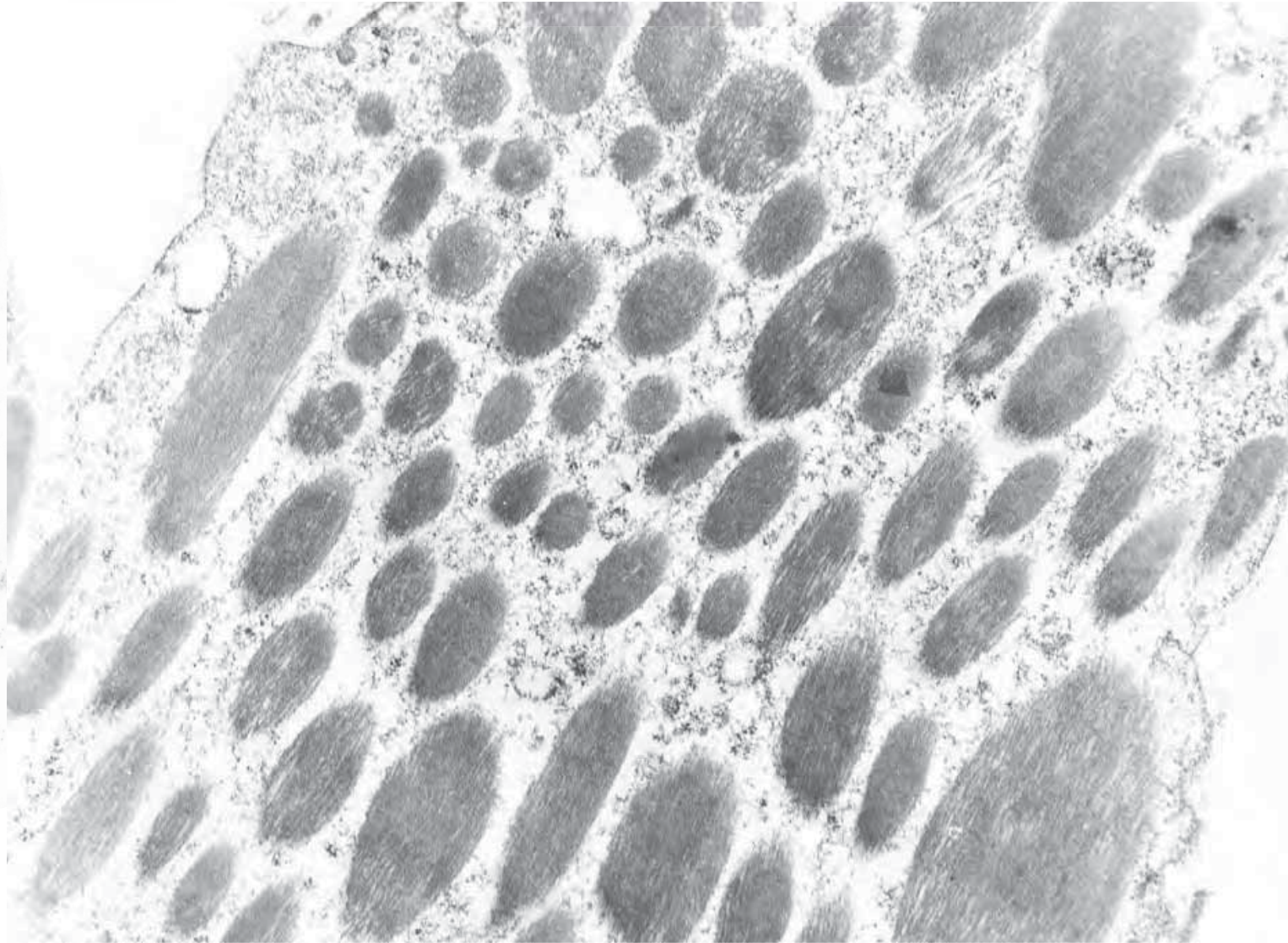
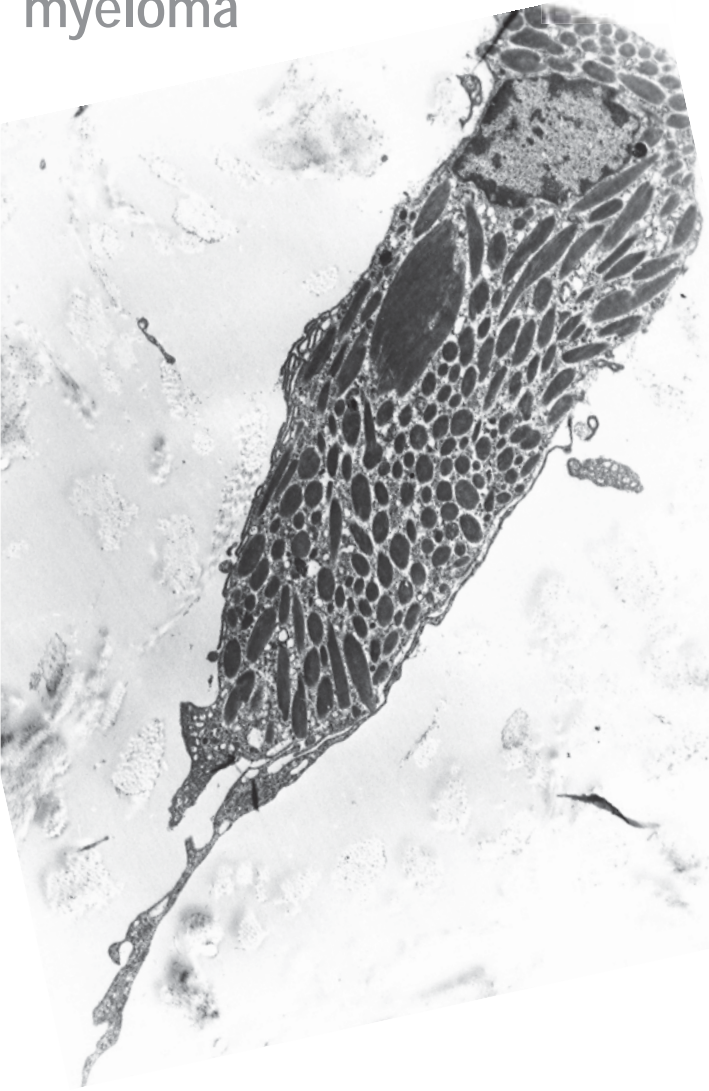


- 68-year-old female
- Monoclonal gammopathy and kidney failure
- Non-specific skin lesions



## Dx: Cristal storing histiocytosis

Bone marrow:  
myeloma

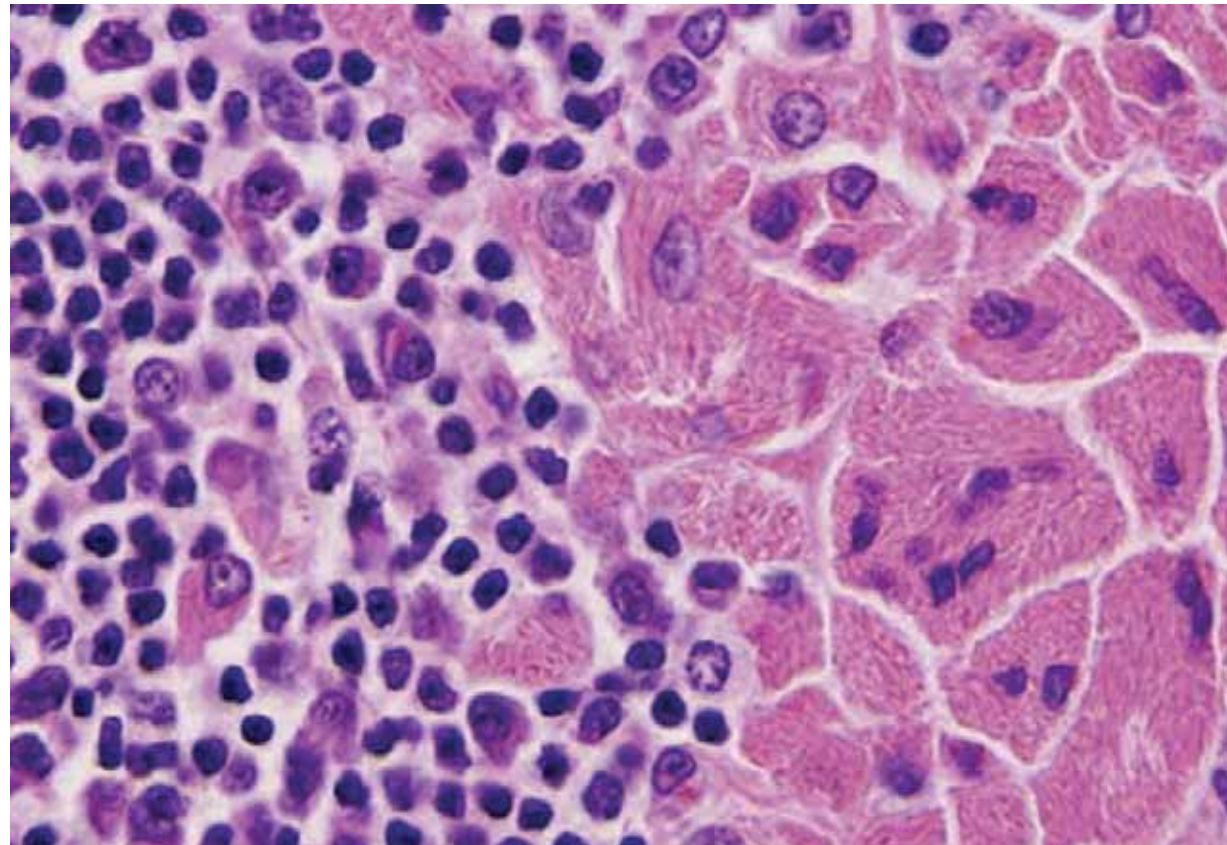


# Crystal-Storing Histiocytosis: A Clinicopathologic Study of 13 Cases

Rashmi Kanagal-Shamanna<sup>1,¶</sup>, Zijun Y. Xu-Monette<sup>1</sup>, Roberto N. Miranda<sup>1</sup>, Ahmet Dogan<sup>2</sup>, Dehui Zou<sup>3</sup>, Rajyalakshmi Luthra<sup>1</sup>, Donna Weber<sup>3</sup>, Dennis P. O'Malley<sup>4</sup>, Jeffrey L. Jorgensen<sup>1</sup>, Joseph D. Khoury<sup>1</sup>, Carlos E. Bueso-Ramos<sup>1</sup>, Robert Z. Orlowski<sup>3</sup>, L. Jeffrey Medeiros<sup>1</sup>, and Ken H. Young<sup>1,¶</sup>

*Histopathology*. 2016 March ; 68(4): 482–491

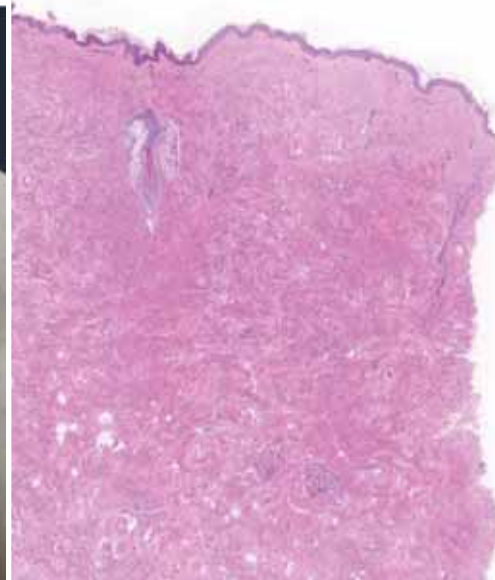
- Crystalline inclusions within the cytoplasm of histiocytes (pseudo-Gaucher cells)
- Typically composed of monoclonal kappa light chains; less commonly polyclonal immunoglobulins or drug-related material
- May involve multiple organs
- Strongly associated with an underlying plasma cell neoplasm or lymphoma with plasmacytic differentiation



# Cutaneous crystal storing histiocytosis: A case series with review of literature

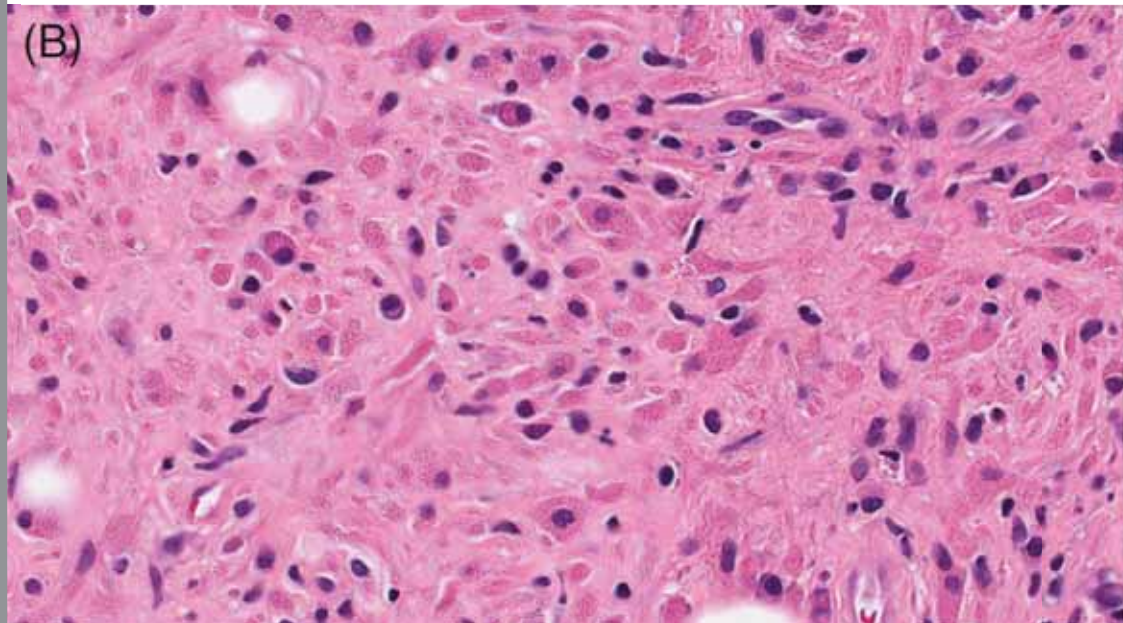
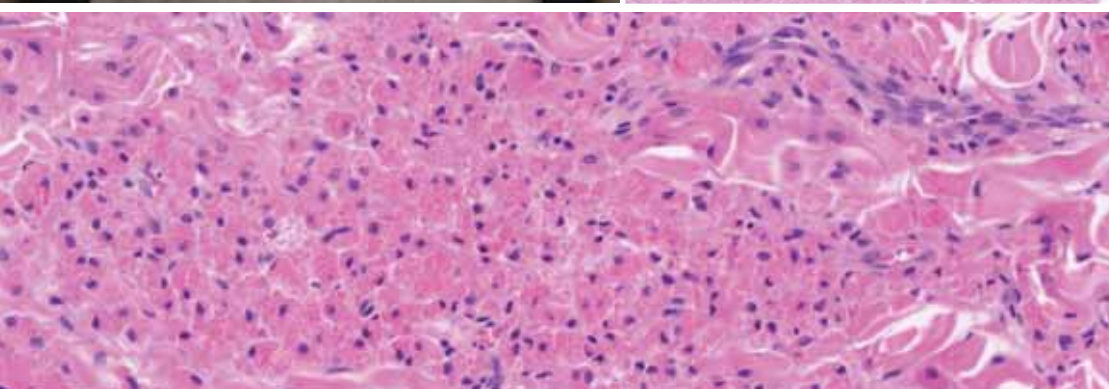
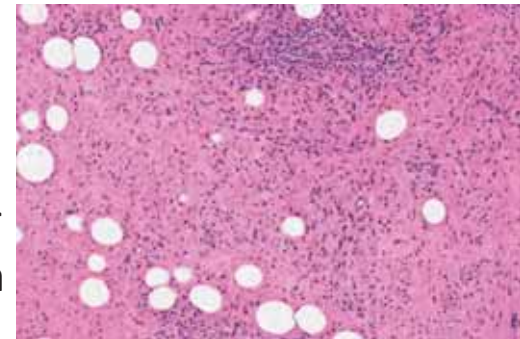
Haya A. Homsy MD, MPH | Calvin Knapp III MD | Shruti Agrawal MD  
Shweta Bhavsar MD | Jennifer S. Ko MD, PhD | Steven D. Billings MD  
Shira Ronen MD

*J Cutan Pathol.* 2024;51:506–512.



## Case 2

- 54-year-old female
- Soft palpable nodule on her left proximal dorsal forearm



# Cutaneous crystal storing histiocytosis: A case series with review of literature

Haya A. Homsy MD, MPH | Calvin Knapp III MD | Shruti Agrawal MD  
 Shweta Bhavsar MD | Jennifer S. Ko MD, PhD | Steven D. Billings MD  
 Shira Ronen MD

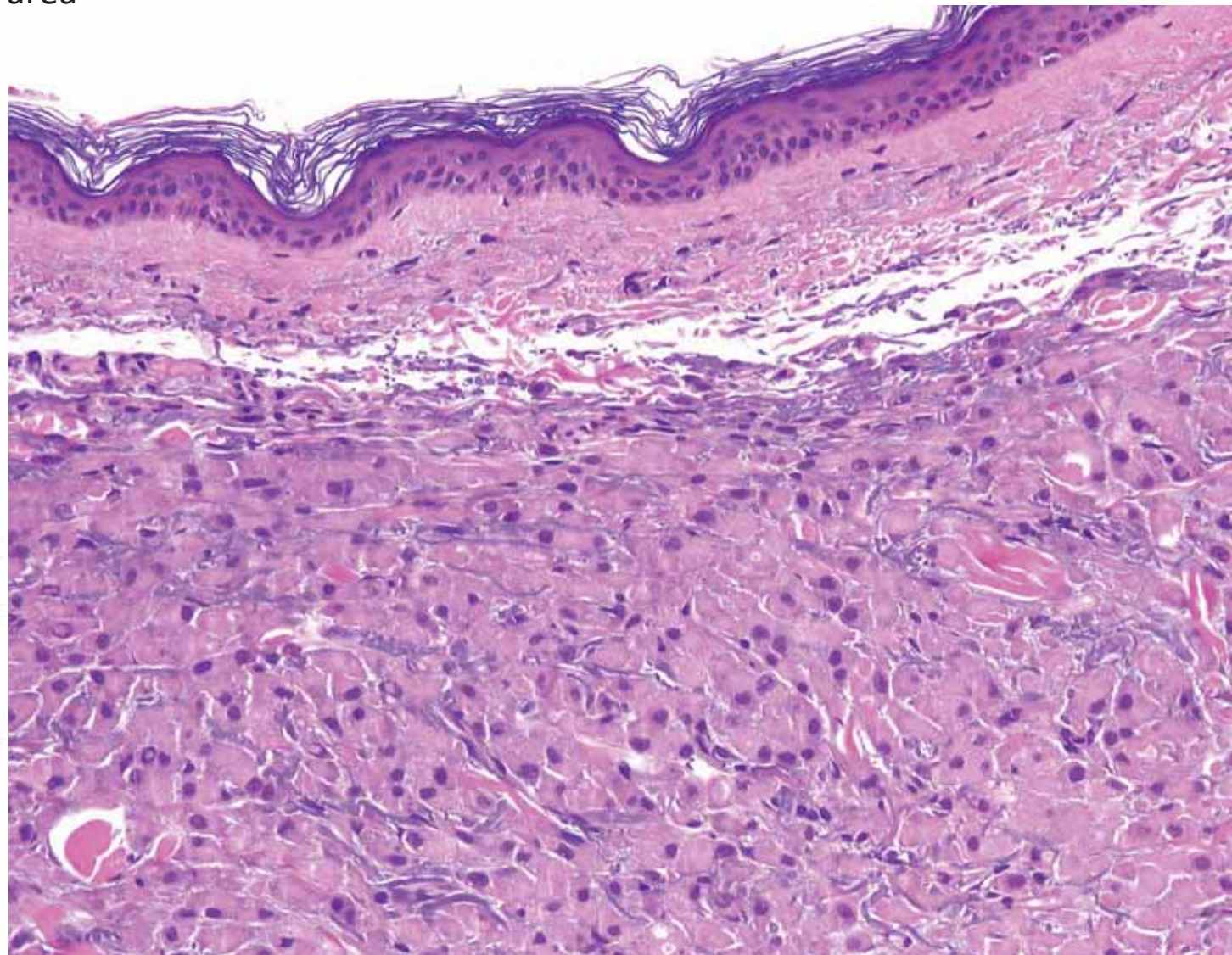
*J Cutan Pathol.* 2024;51:506–512.

- Only 13 cases of cutaneous involvement reported in the literature. 70% limited to skin
- Median age of 61 years (46– 84 years)
- 90% underlying **lymphoproliferative or plasma cell disorder** (multiple myeloma, MGUS or lymphoplasmacytic lymphoma)
- 10% **no underlying hematological disorder**
  - ✓ The hematological disease can appear months to years later
  - ✓ Can be related to:
    - Infections
    - Inflammatory benign diseases (Crohn disease or rheumatoid arthritis)
    - IgG4-related diseases

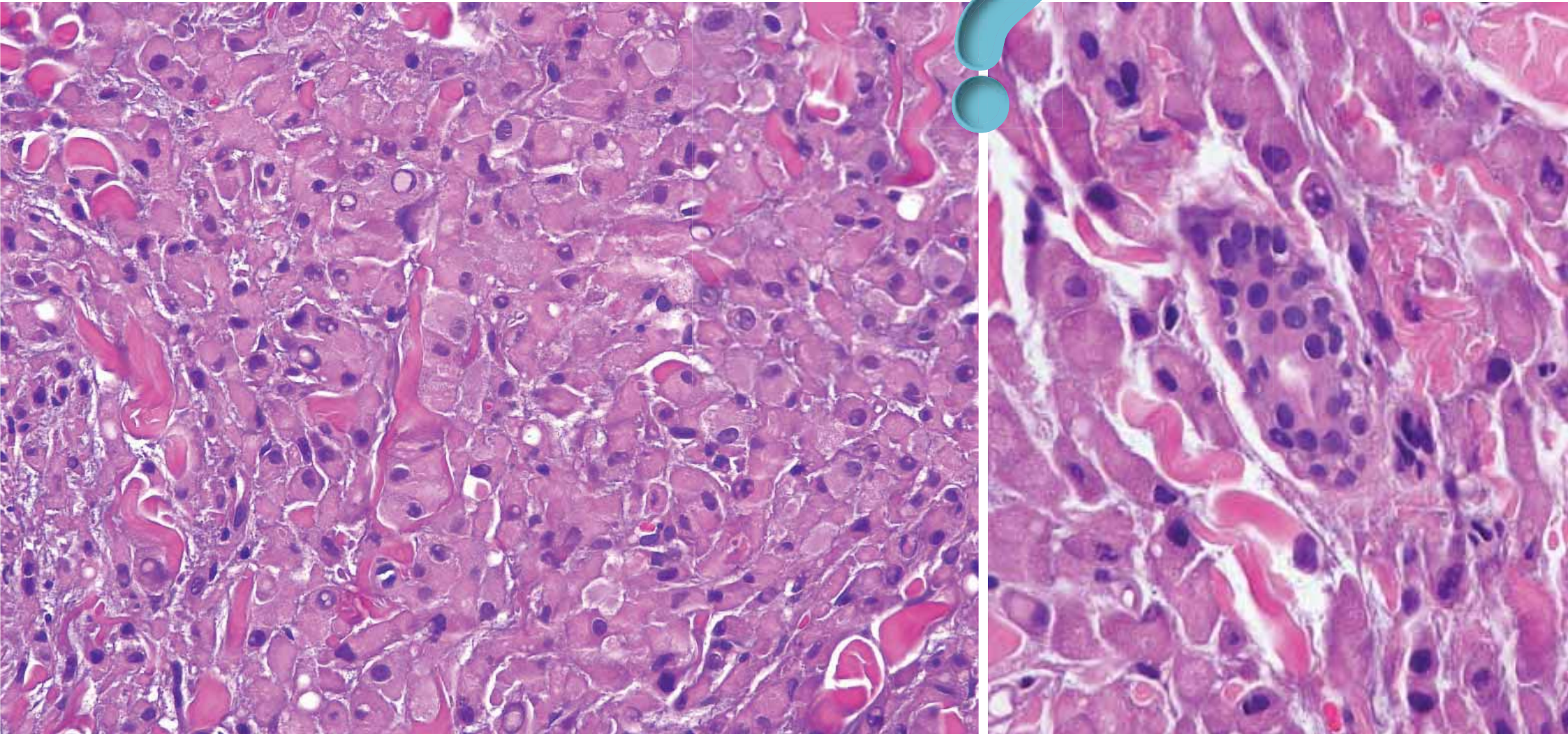
## DDx:

Diagnosis	Key histologic features	Key ancillary tests
<b>Infectious etiology</b>		
Mycobacteria	Inflammatory and necrotic background Uniform, thin organisms with haphazard arrangement	AFB Ziehl-Neelsen (+) AFB-Fite (+)
Fungal	Round/oval structures (yeasts) and/or long filaments (hyphae)	PAS/GMS (+)
<b>Histiocytic lesions</b>		
Langerhans cell histiocytosis	Cells with abundant lightly eosinophilic cytoplasm and large infolded or reniform vesicular nuclei with thin nuclear membranes and inconspicuous nucleoli Admixed eosinophils	S100, CD1a, langerin (+)
Rosai-Dorfman disease	Histiocytes with abundant pale eosinophilic cytoplasm with large centrally located vesicular nuclei with single distinct nucleolus Emperipolesis (the cytoplasm of histiocytes appears to contain red blood cells, lymphocytes, and/or granulocytes)	S100, CD68 (+)
Xanthogranuloma	Foamy histiocytes with scattered Touton giant cells Background of lymphocytes, plasma cells, eosinophils, and sometimes neutrophils	CD68 (+)
<b>Tumors</b>		
Granular cell tumor	Ill-defined tumor composed of sheets, nests, and trabeculae of large, monotonous epithelioid to polygonal cells with intensely eosinophilic, granular cytoplasm Often with overlying pseudoepithelial hyperplasia	PAS, S100, CD68 (+)
Rhabdomyoma	Large polygonal cells with abundant eosinophilic, granular, or vacuolated cytoplasm with focal cross-striation or crystalline inclusions. The cells exhibit small, round, centrally or peripherally located nuclei with vesicular chromatin and distinct nucleoli	Desmin, MYOD1, and myogenin (+)
<b>Inflammatory processes</b>		
Malakoplakia	Confluent sheets of histiocytes with eosinophilic granular cytoplasm and small, usually eccentric nuclei Cytoplasmic calcified inclusions	CD68 (+), Von Kossa stain (+ Michaelis-Gutmann inclusions)
<b>Miscellaneous</b>		
Gaucher disease	Crinkled paper cytoplasm	PAS (+)
Amyloidosis	Eosinophilic amorphous material	Congo red
Drugs: clofazimine	Dark brown pigment and bright red, birefringent crystals with polarized light	PAS (+)

- 80-year-old man
- Recent nodule on the right clavicular area

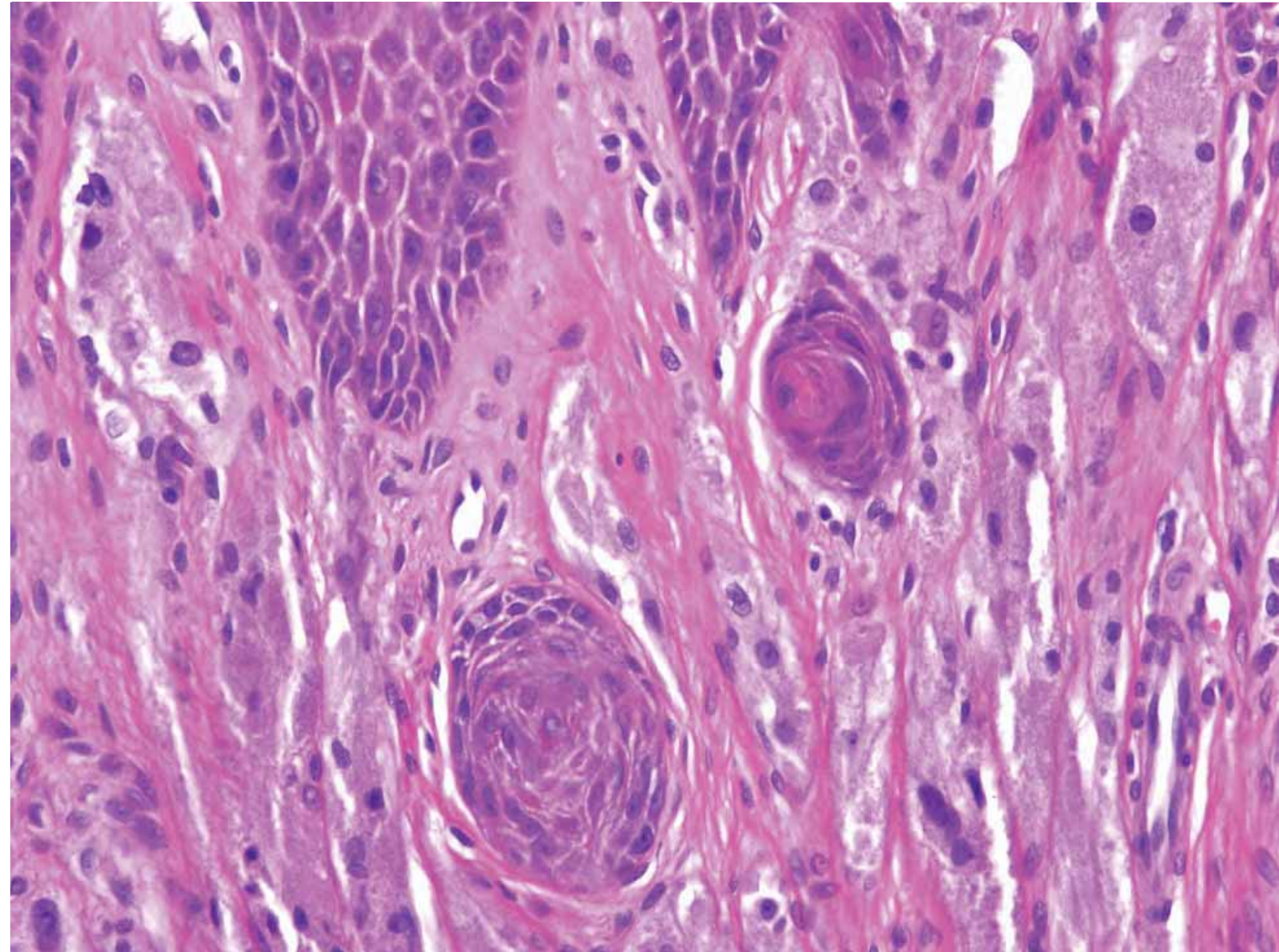
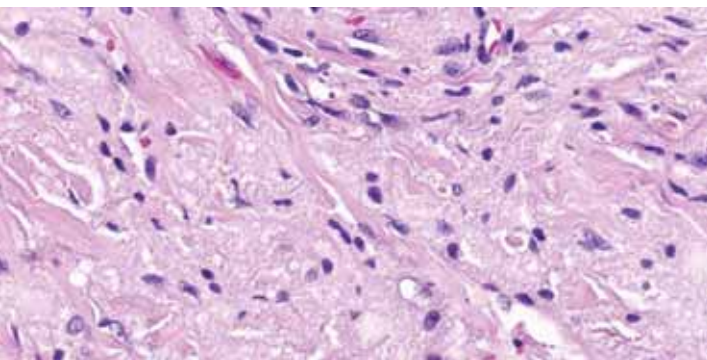
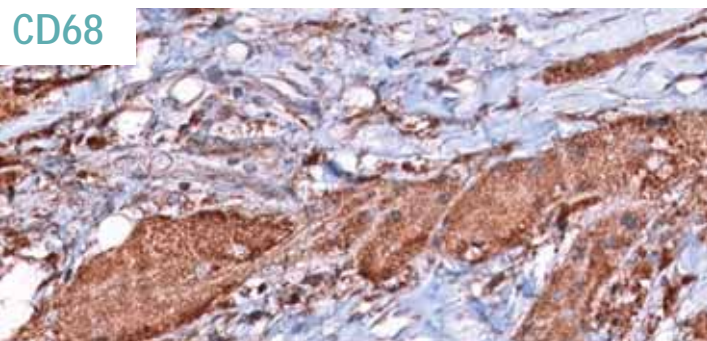
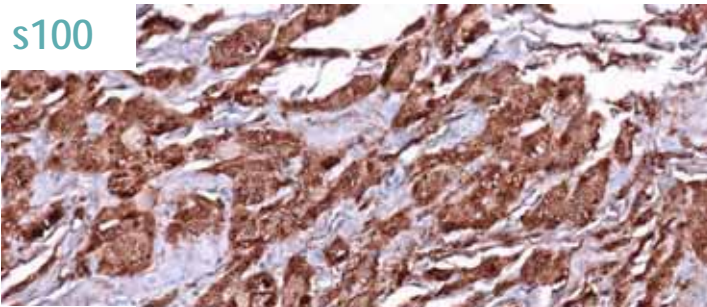


- 80-year-old man
- Recent nodule on the right clavicular area



# Granular cell tumor

- Amphophilic cytoplasm (lysosomal granules)

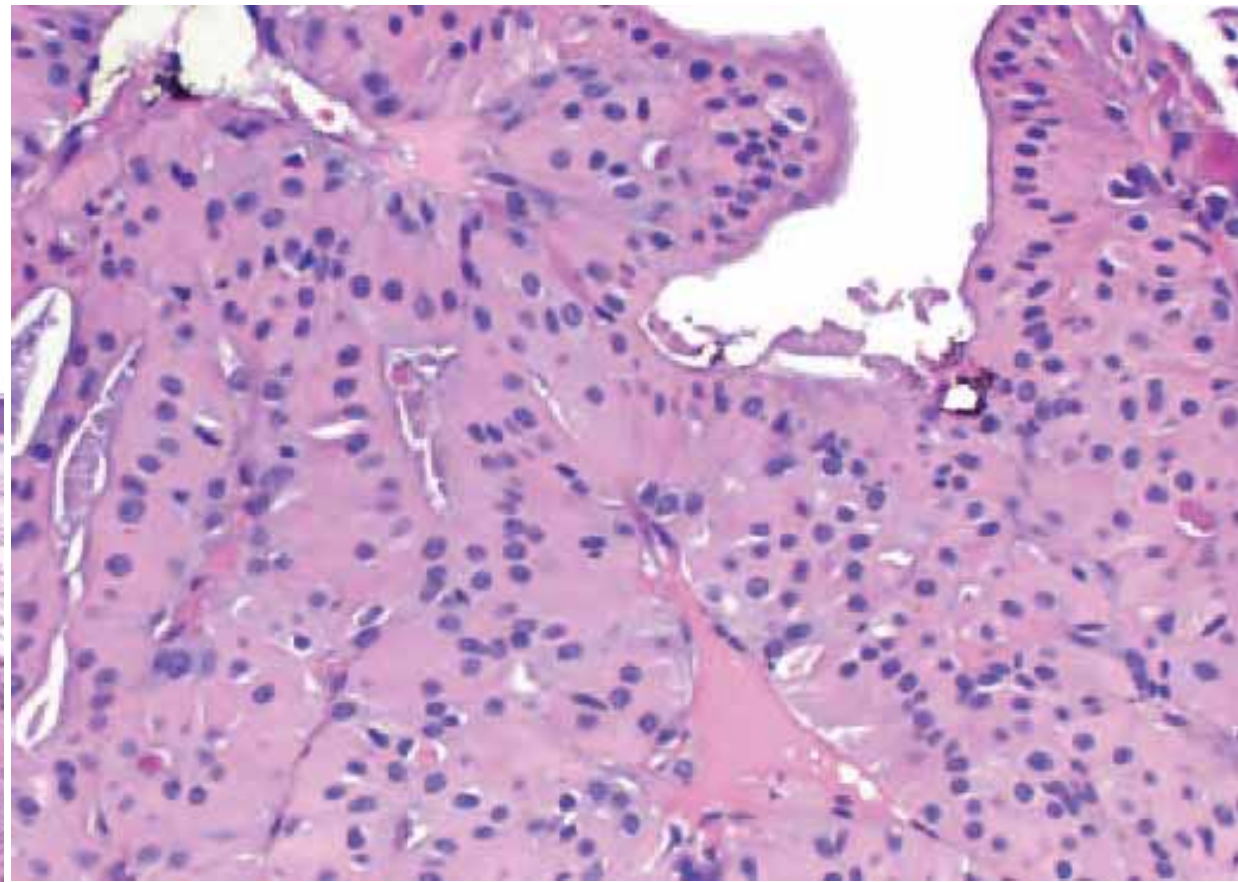
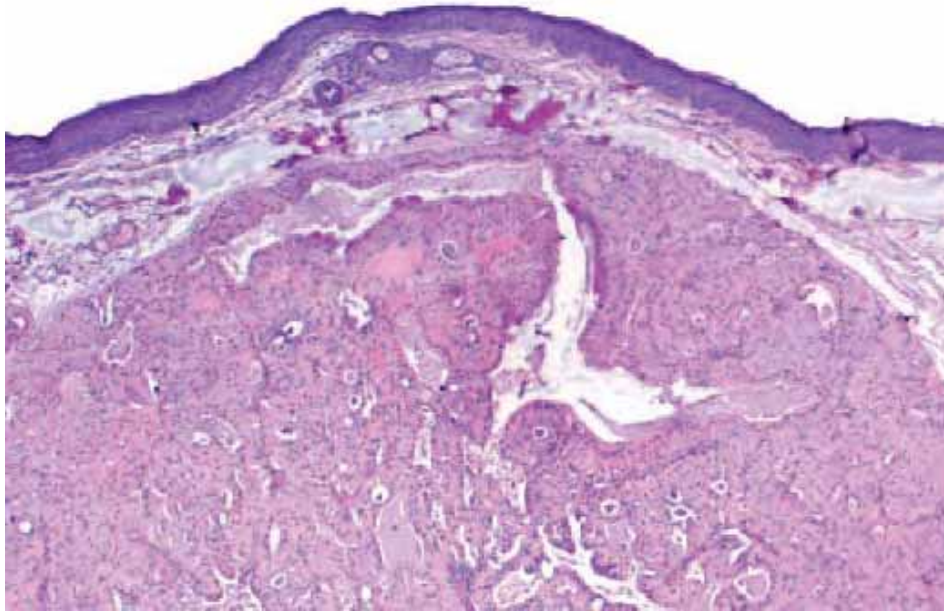


# Cutaneous oncocytoma – a report of three cases and review of the literature

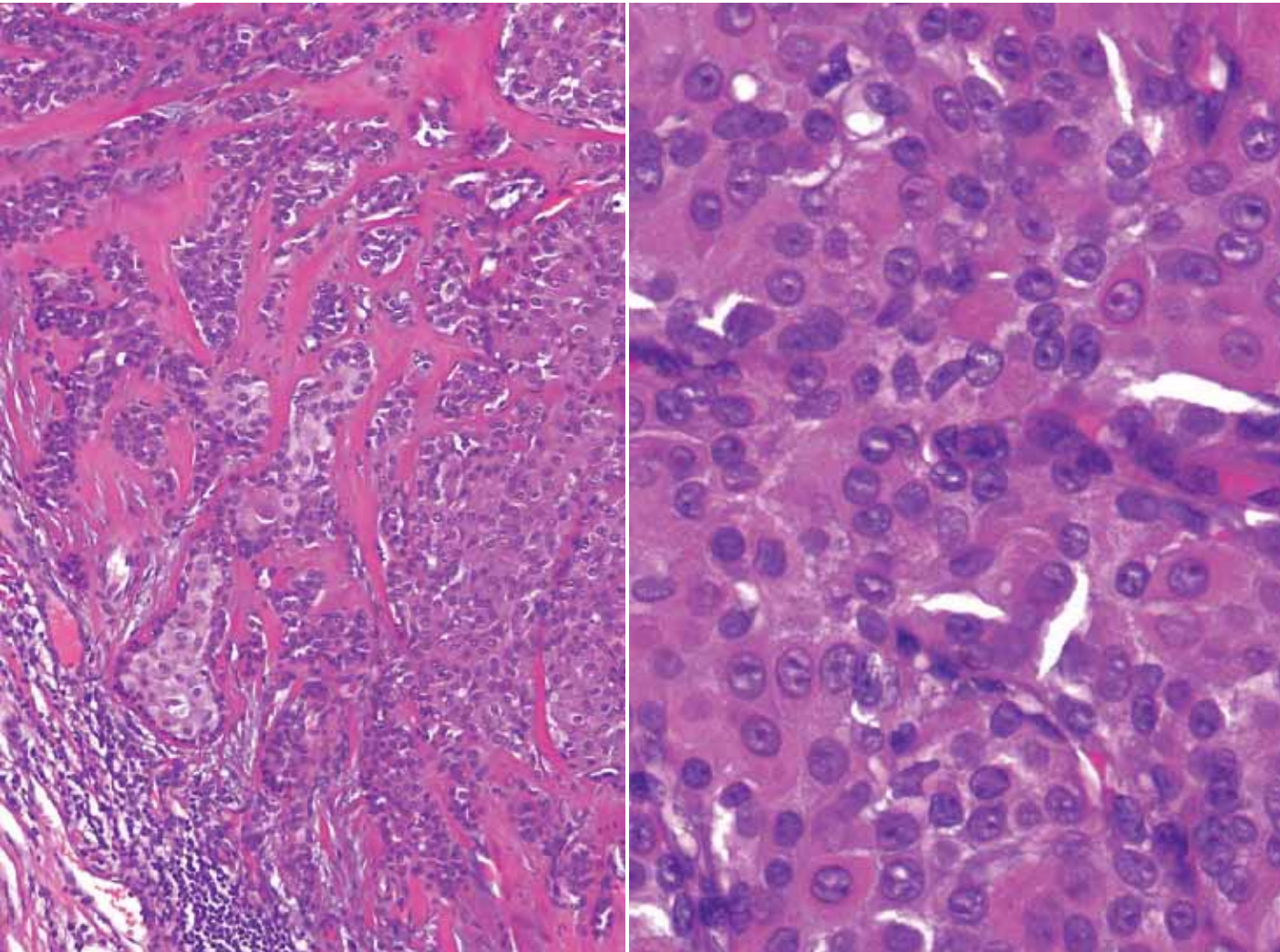
**Victoria Coburn<sup>1</sup>, Arash Radfar<sup>2</sup>,  
David Snook<sup>3</sup> and Meera  
Mahalingam<sup>1</sup>**

*J Cutan Pathol* 2007; 34: 355–359.

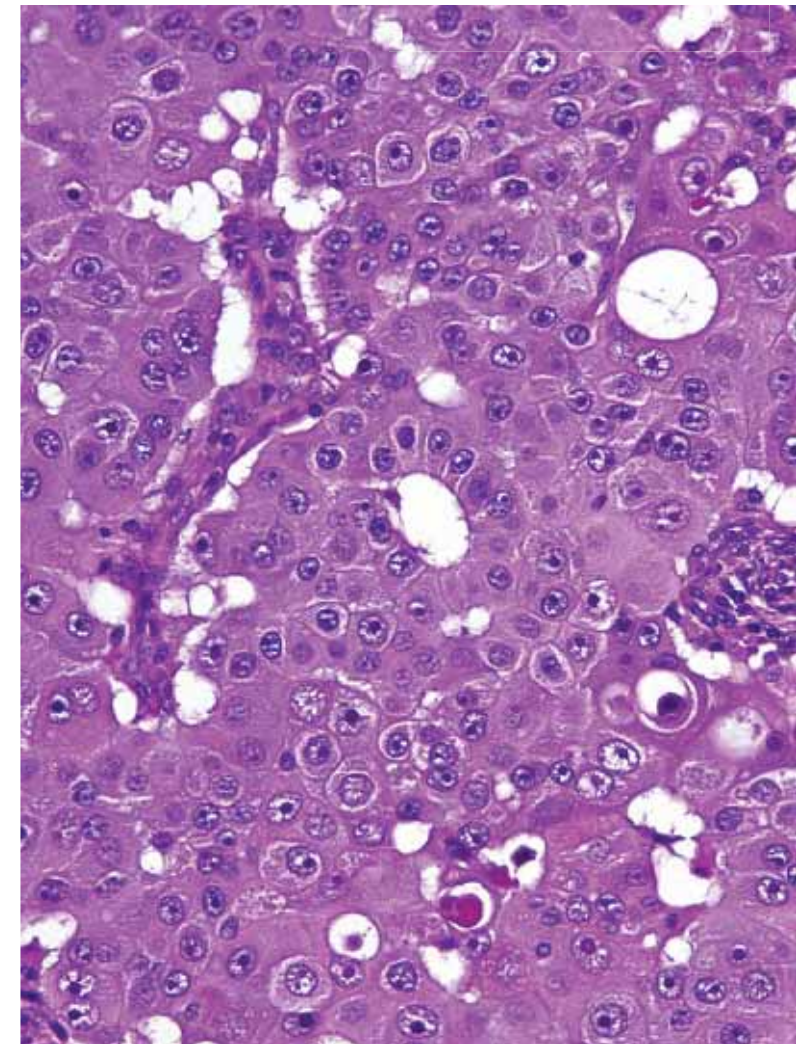
- Eosinophilic granular cells (mitochondria)
- Periocular (lacrimal)
- Lack of cytological atypia
- Benign behavior



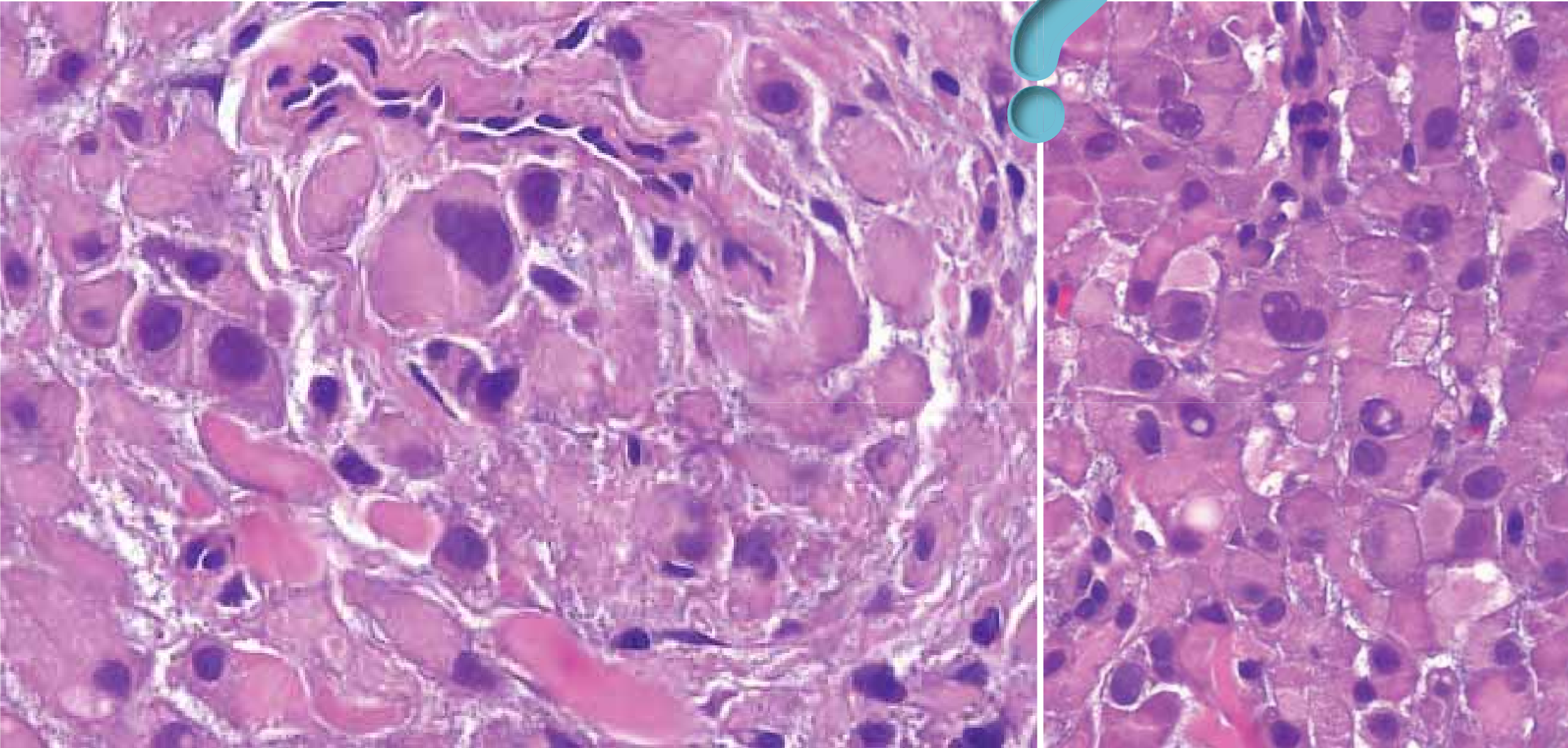
**Oncocytic apocrine hidradenoma**



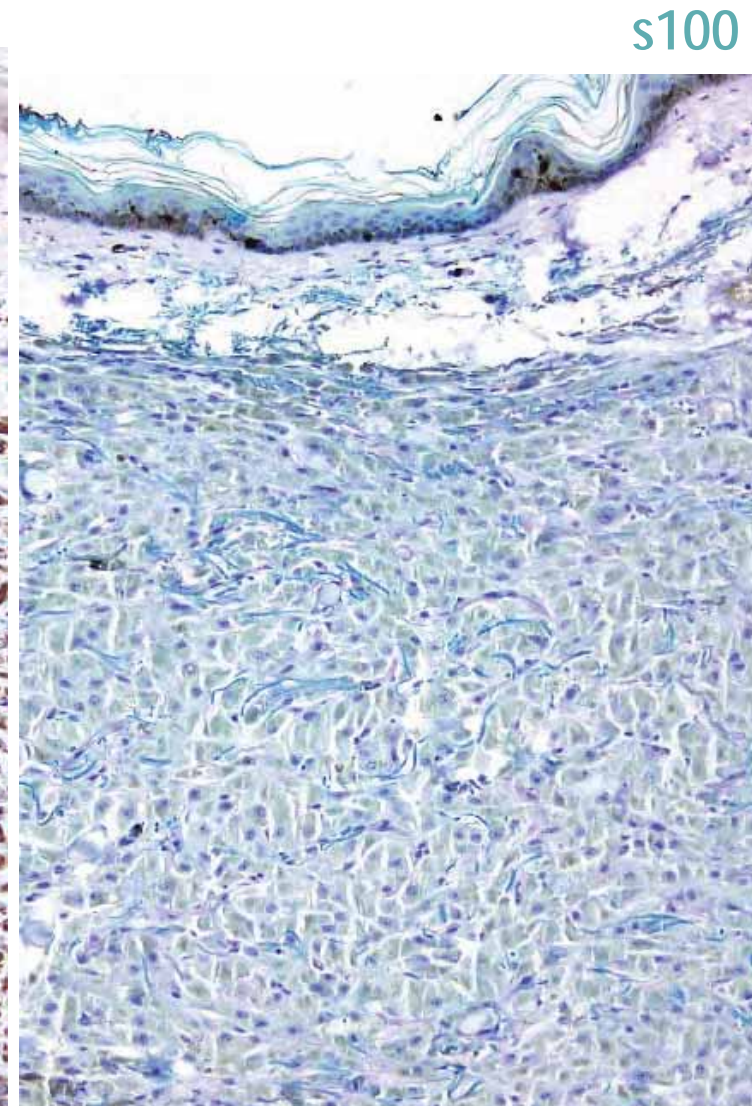
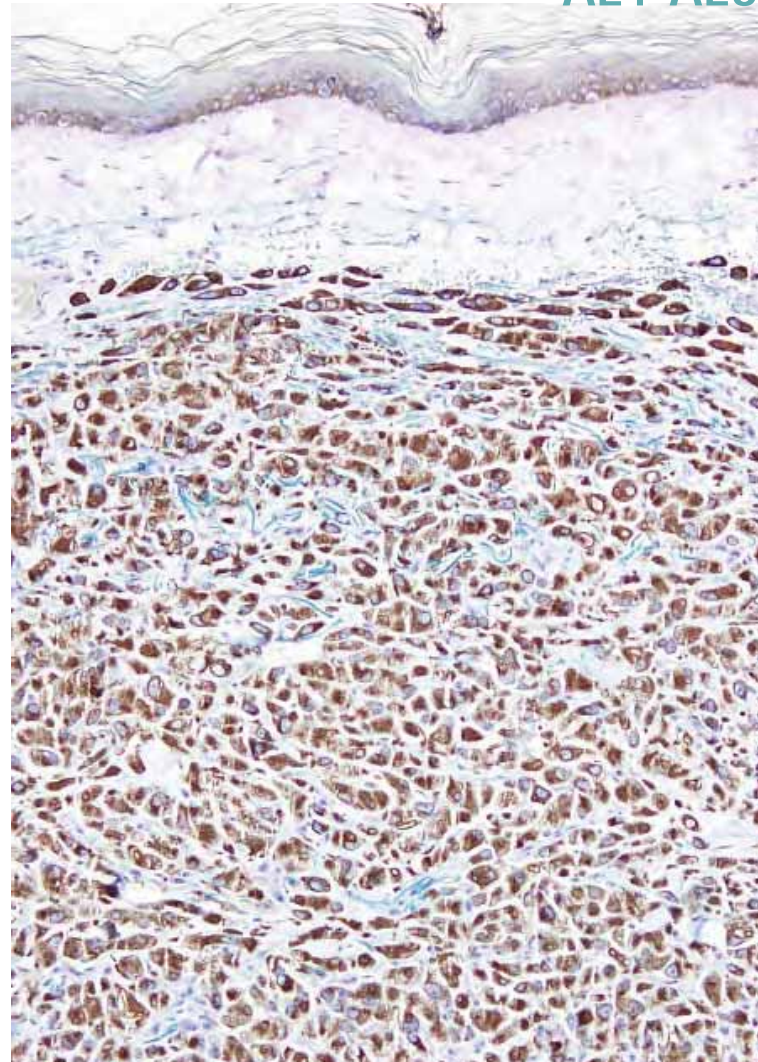
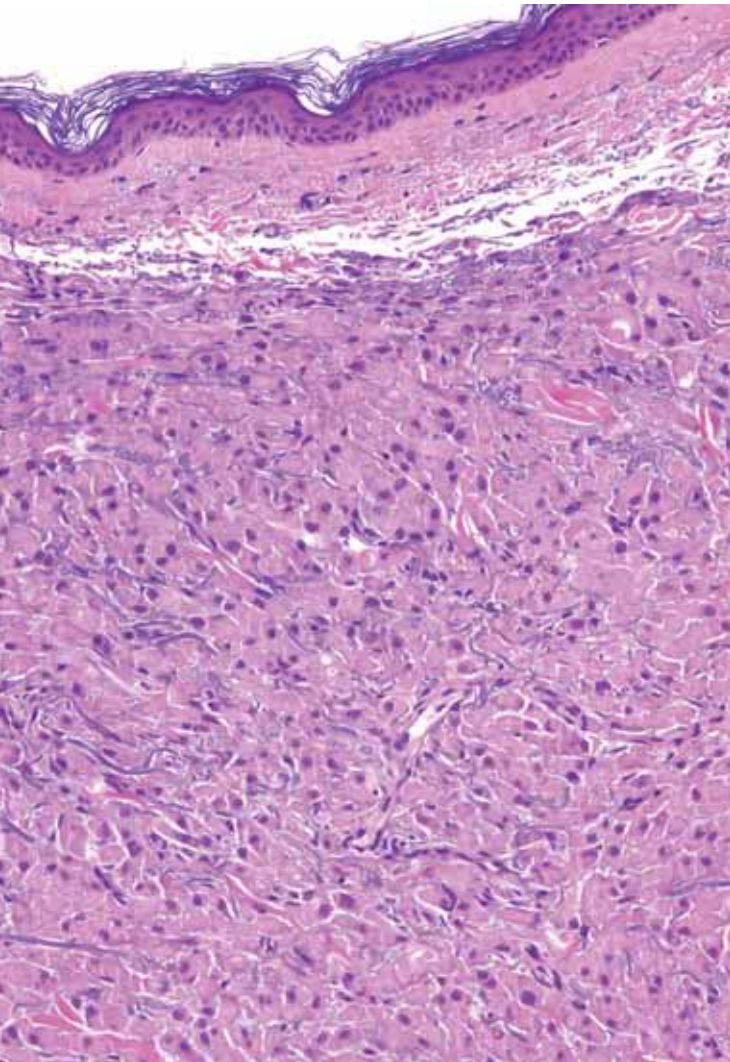
**Metastatic oncocytic breast carcinoma**



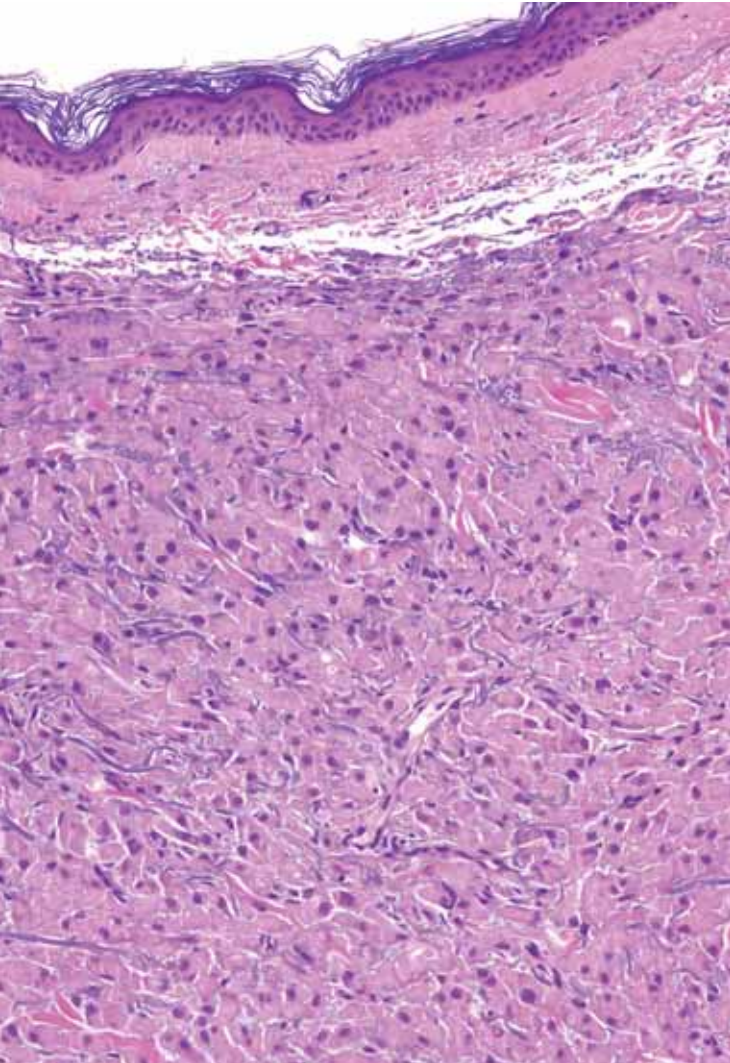
- 80 year-old man
- Recent nodule in the right clavicular area



- 80 year-old man
- Recent nodule in the right clavicular area



## Dx: Metastasis from an oncocytic salivary gland carcinoma

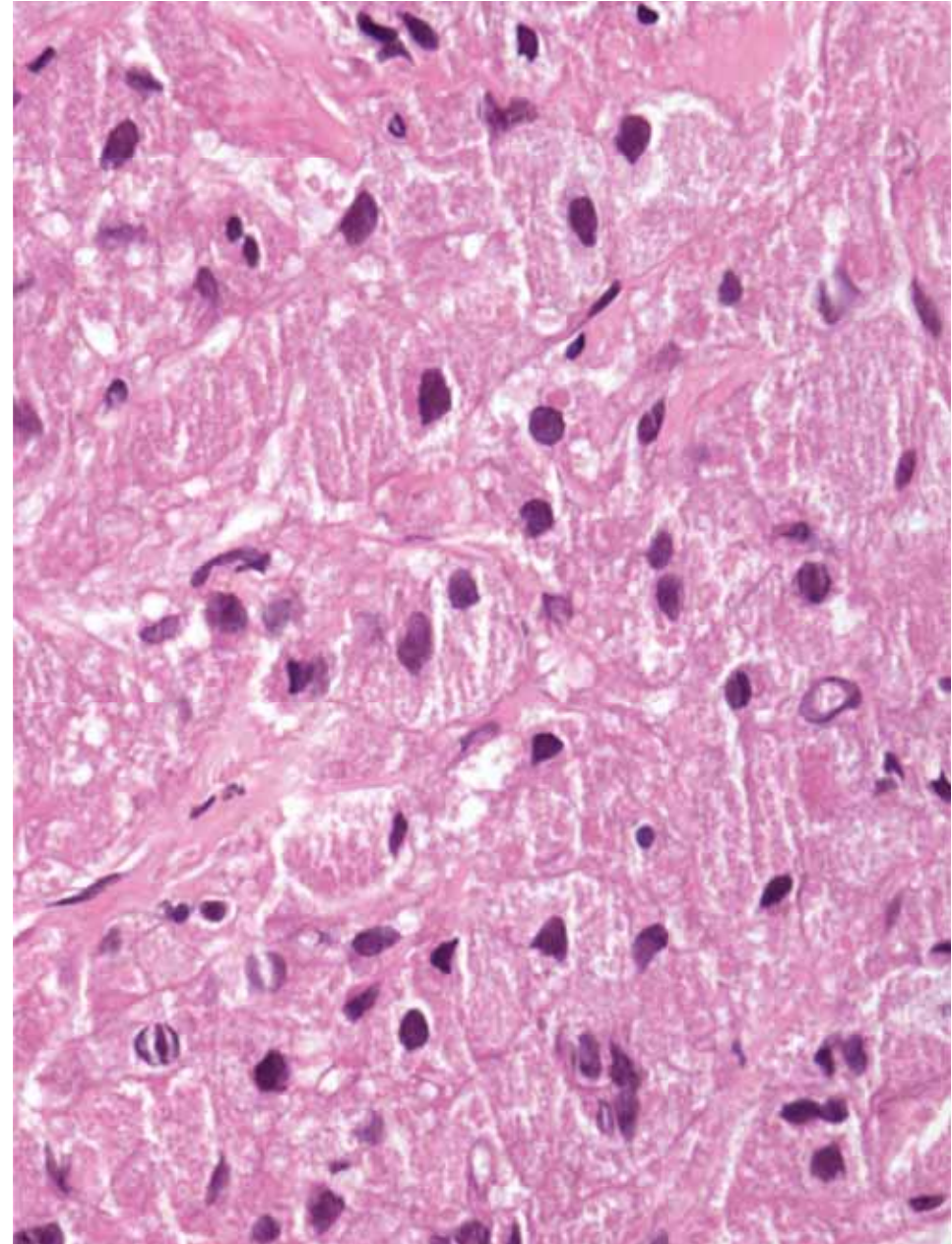


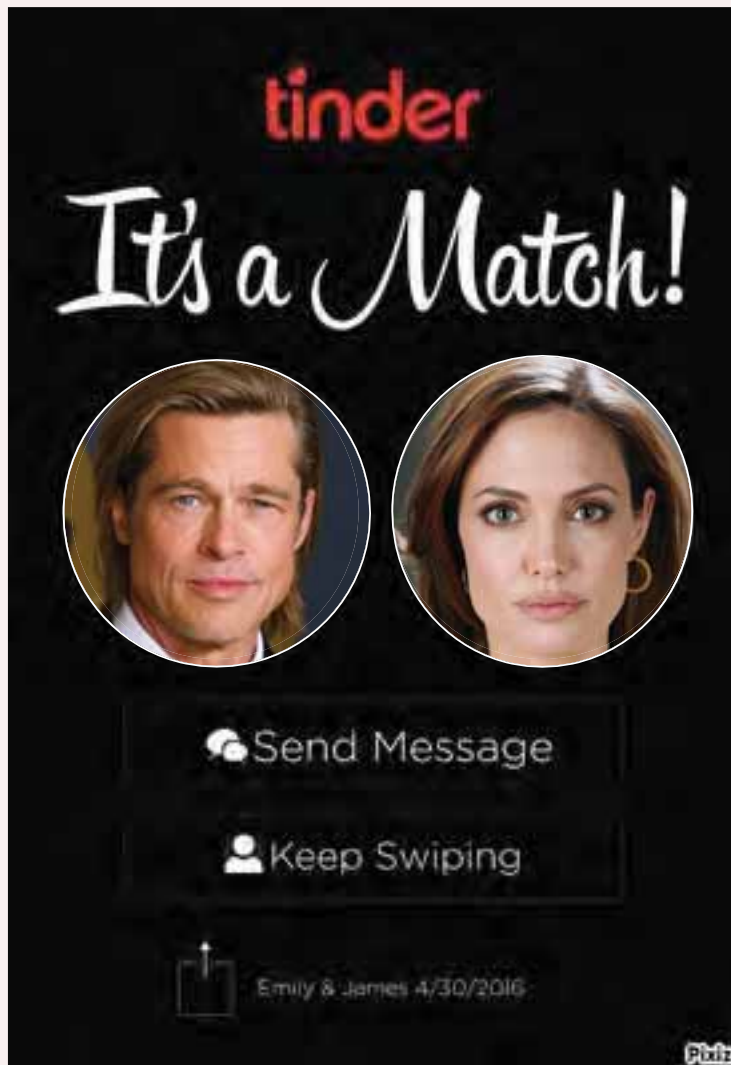
## Granular cell proliferations

- ✓ Granular cell tumors (including non-neural)
- ✓ Basal & Squamous cell carcinoma
- ✓ Dermatofibroma
- ✓ Dermatofibrosarcoma protuberans
- ✓ Nevus and melanoma
- ✓ Atypical fibroxanthoma
- ✓ Pleomorphic dermal sarcoma
- ✓ Leiomyoma & leiomyosarcoma
- ✓ Peripheral nerve tumors
- ✓ Angiosarcoma

## Oncocytic cells

- ✓ Cutaneous oncocytoma
- ✓ Adnexal tumors with oncocytic change
- ✓ Metastases (kidney, breast, etc.)





LL 8

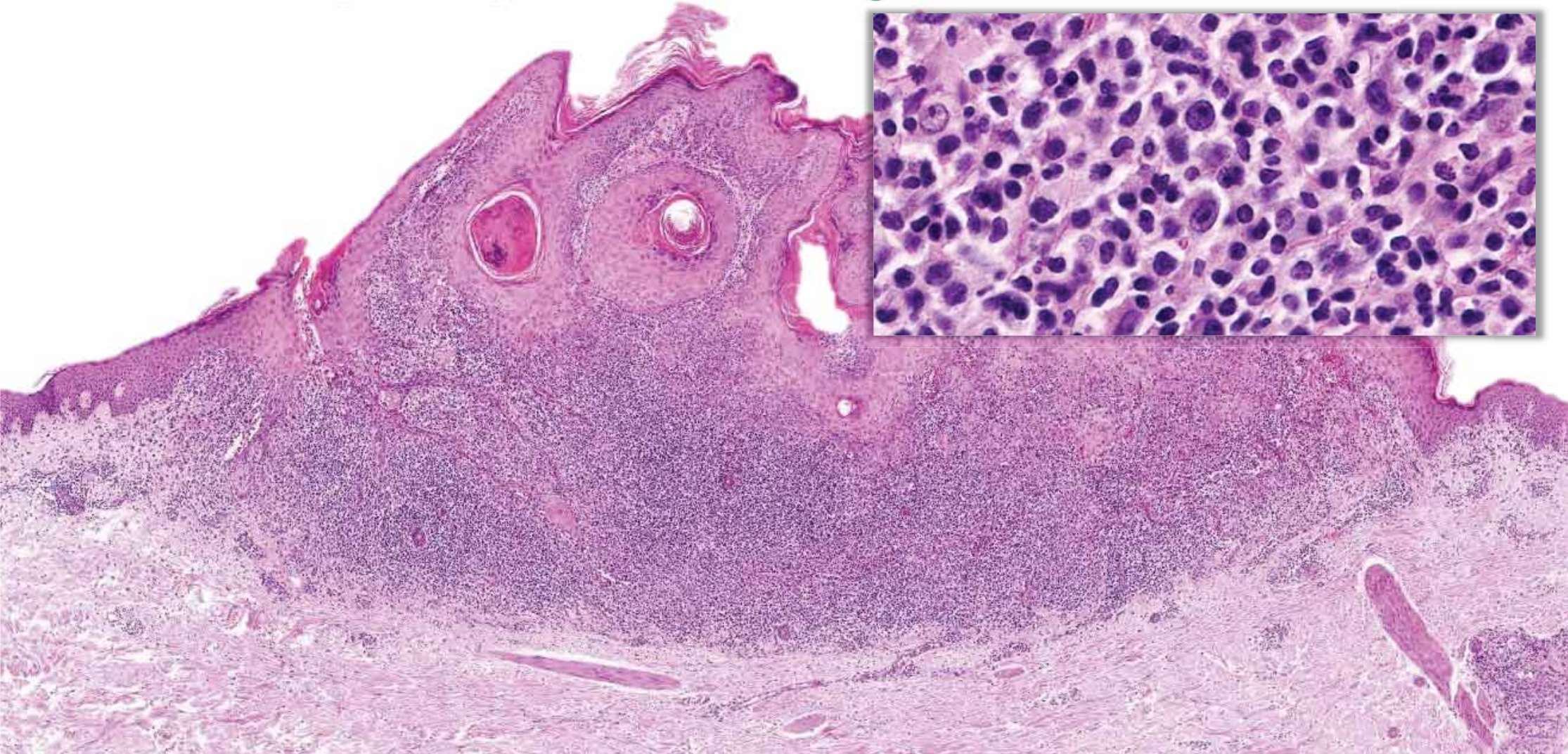
**Don't trust it,** even when it looks like a **"perfect clinicopathological match"**

A "perfect match" can be deceiving.

**Look twice!**

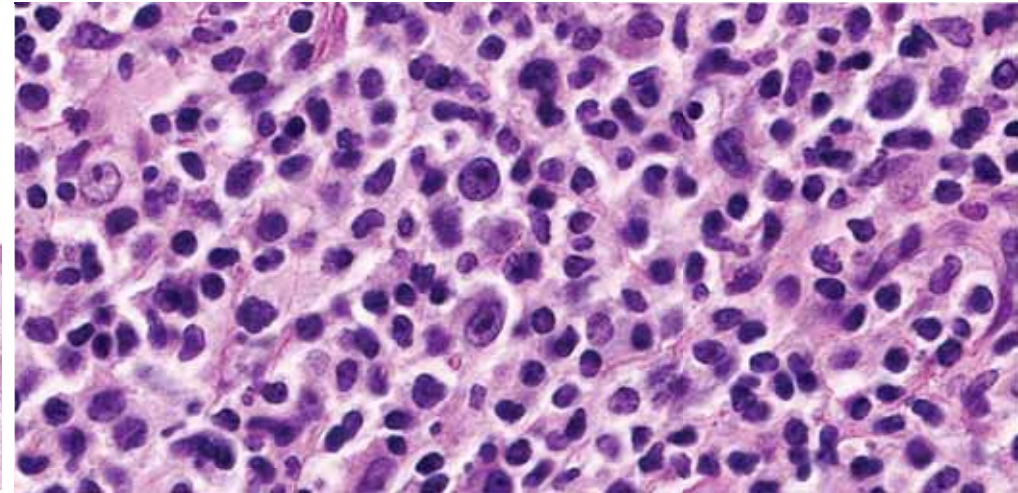
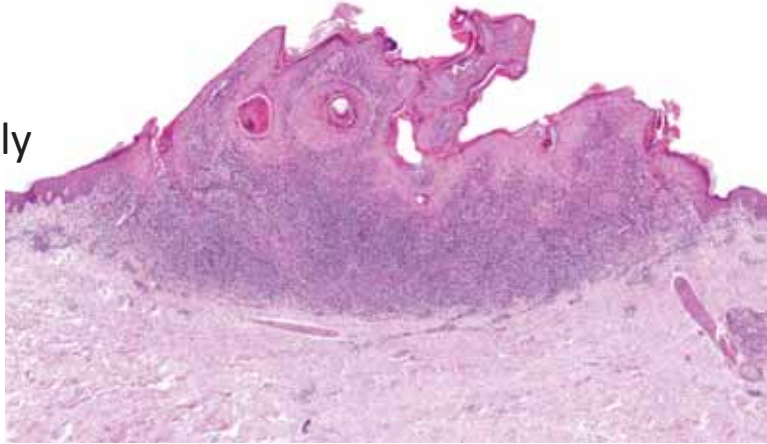
- Middle aged man with a keratotic lesion on the arm. Clinical Dx: Involuting keratoacanthoma

Histopathological Dx: **Involuting keratoacanthoma?**

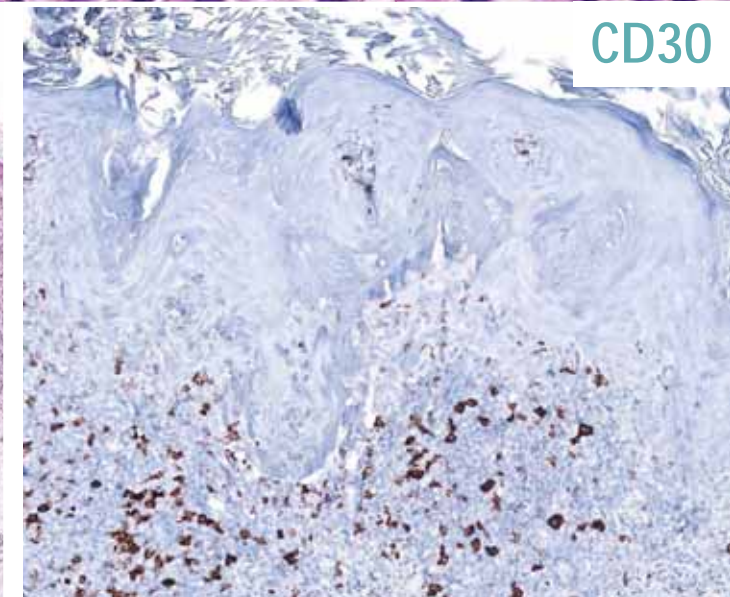
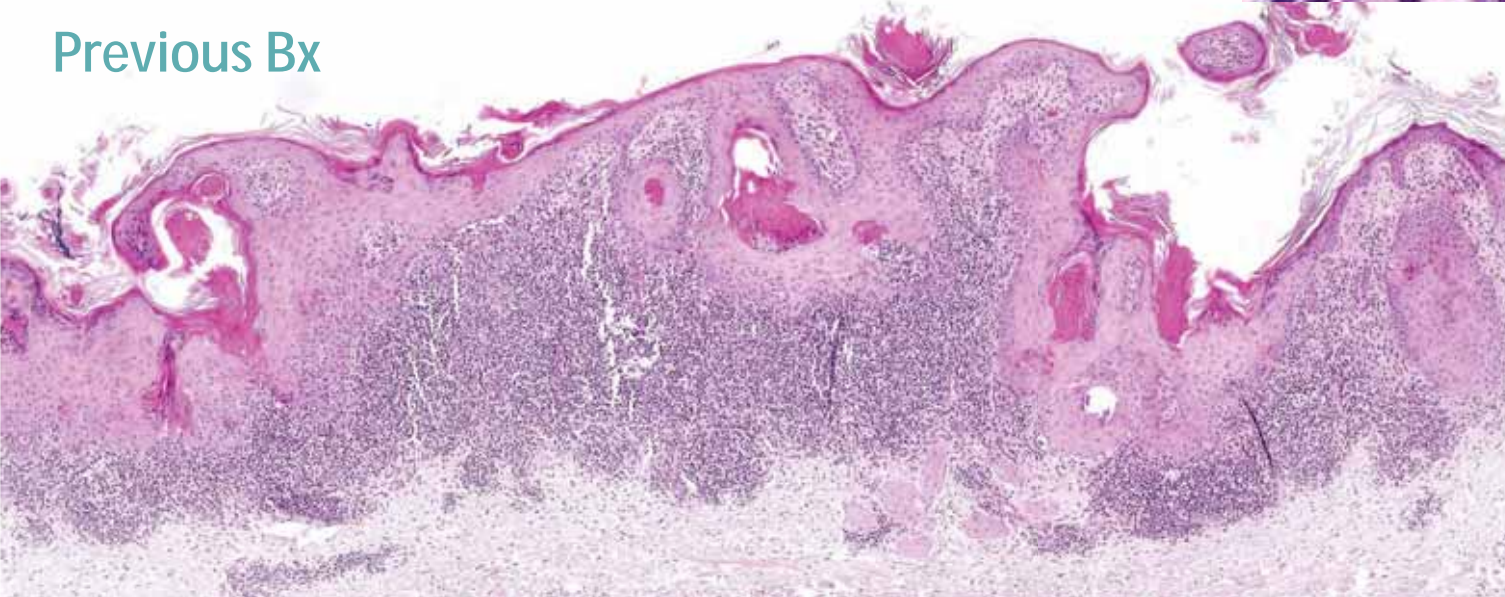


# Lymphomatoid papulosis + pseudocarcinomatous hyperplasia

Past history of lesions that disappeared spontaneously, wrongly diagnosed clinically and histologically as hypertrophic lichen planus



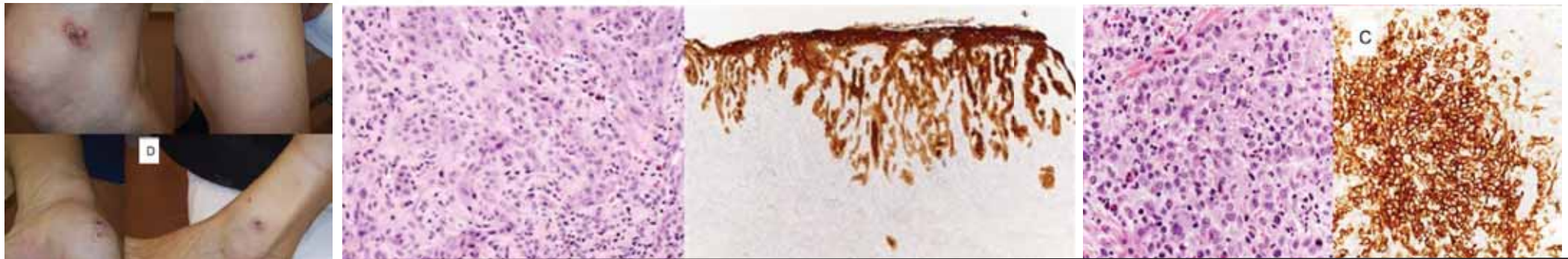
Previous Bx



CD30

# Pseudocarcinomatous Hyperplasia Hiding Lymphomatoid Papulosis: A “Low-Power View” Pitfall

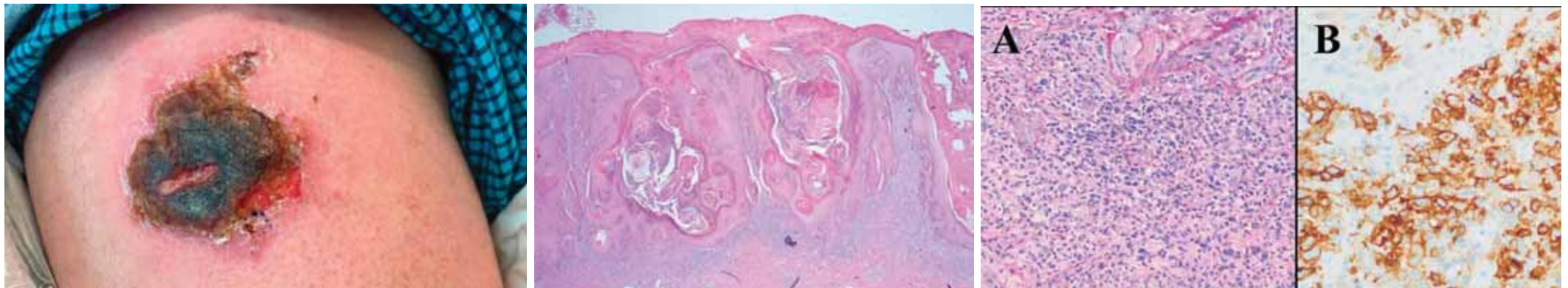
Salvatore Bellafiore, MD<sup>1</sup>, Laura Grenzi, MD<sup>1</sup>, Vito Simonetti, MD<sup>1</sup>, and Simonetta Piana, MD<sup>1</sup>



# Pseudocarcinomatous Hyperplasia Masquerading as a Well-Differentiated Squamous Cell Carcinoma Associated With Primary Cutaneous Anaplastic Large-Cell Lymphoma

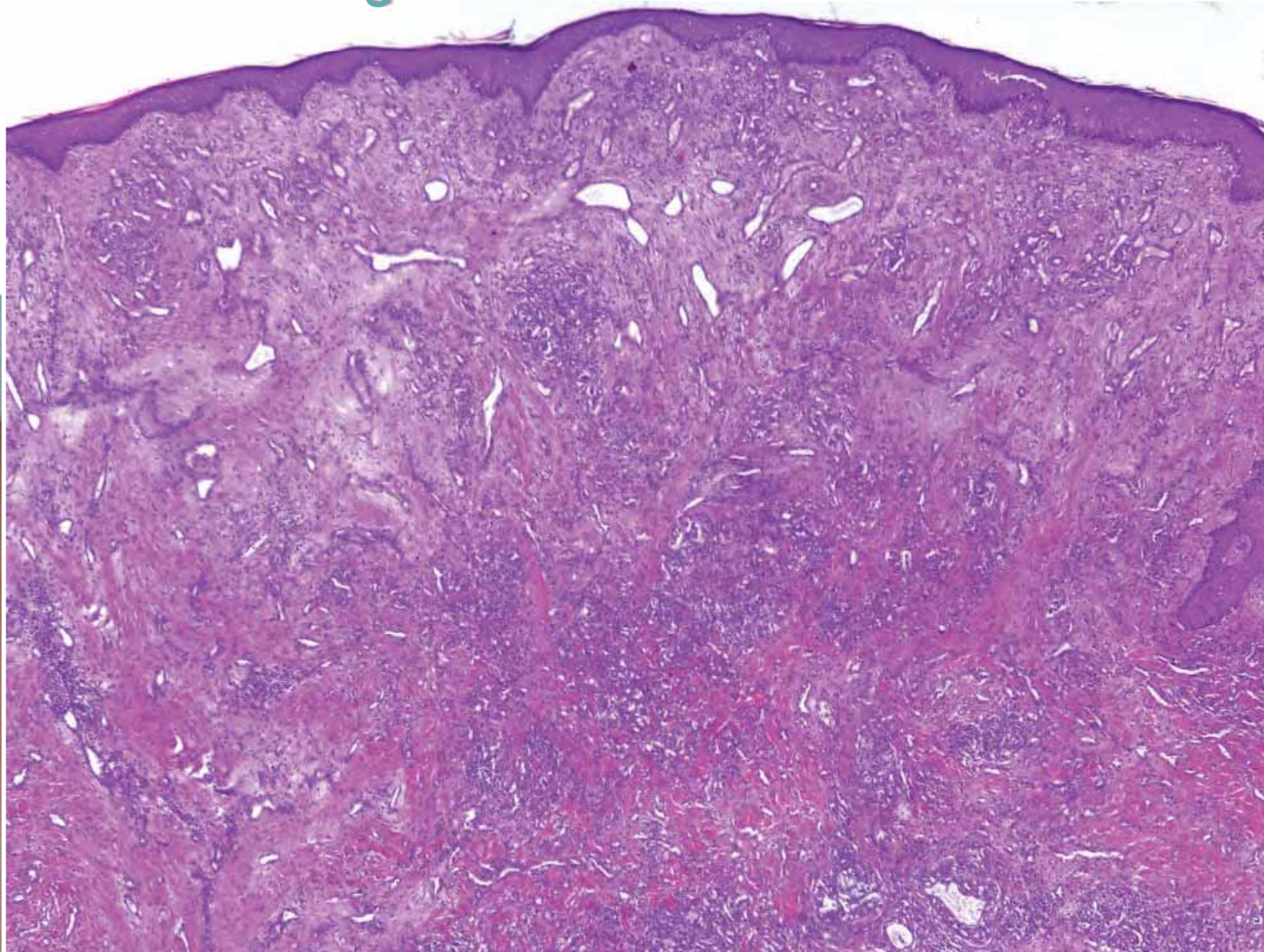
*Am J Dermatopathol* 2022;44:952–954

Donn LaTour, BS,\* Michael P. Lee, MD,† Jeffrey T. Gardner II, MD,† Harry Dao Jr, MD,† Justin Kerstetter, MD,‡ and Ashley Elsensohn, MD, MPH†‡



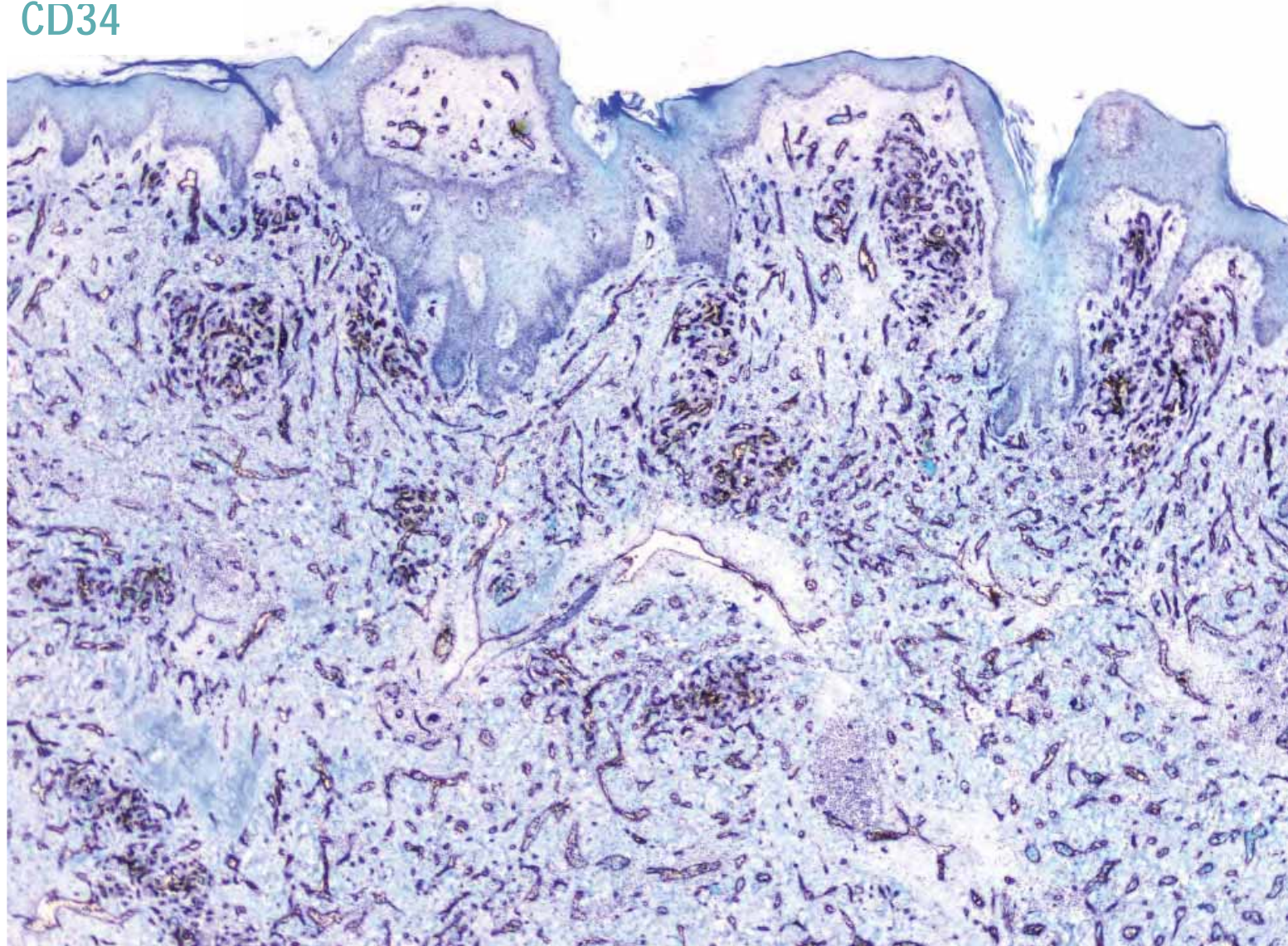
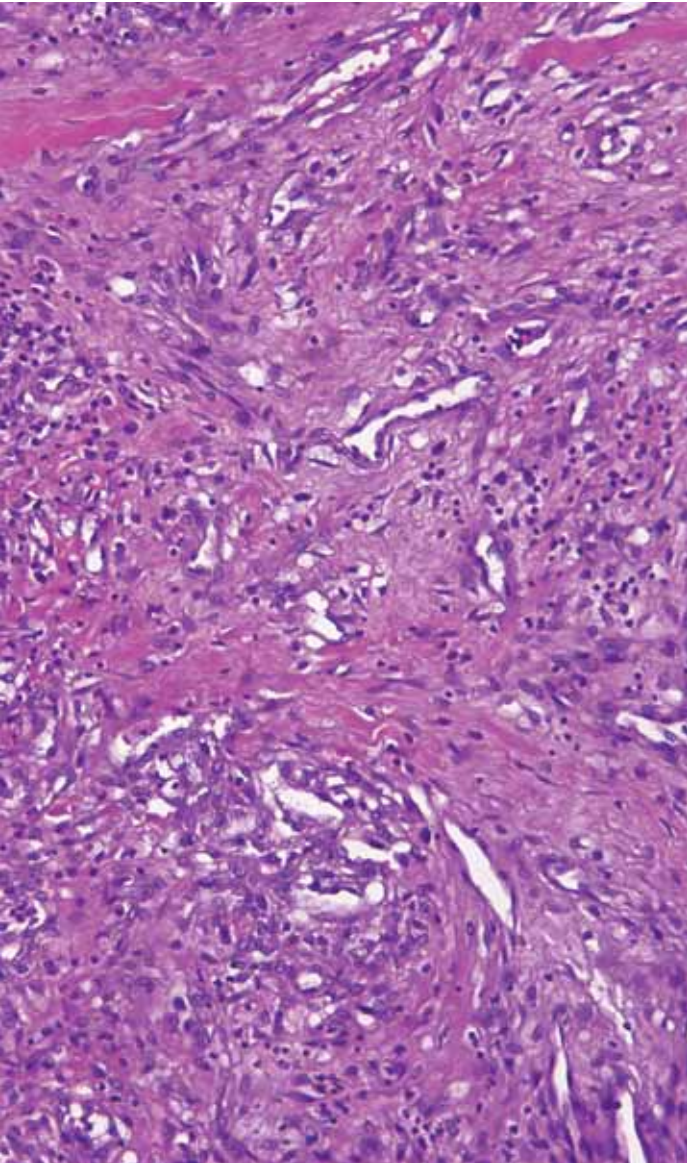
## Reactive angiomatosis

- Nodule and erythema on the hip 7 years after a melanoma on the back (pT4a)
- Two previous Bx (punch Bx and wedge Bx)
- Clinical Dx: Melanoma



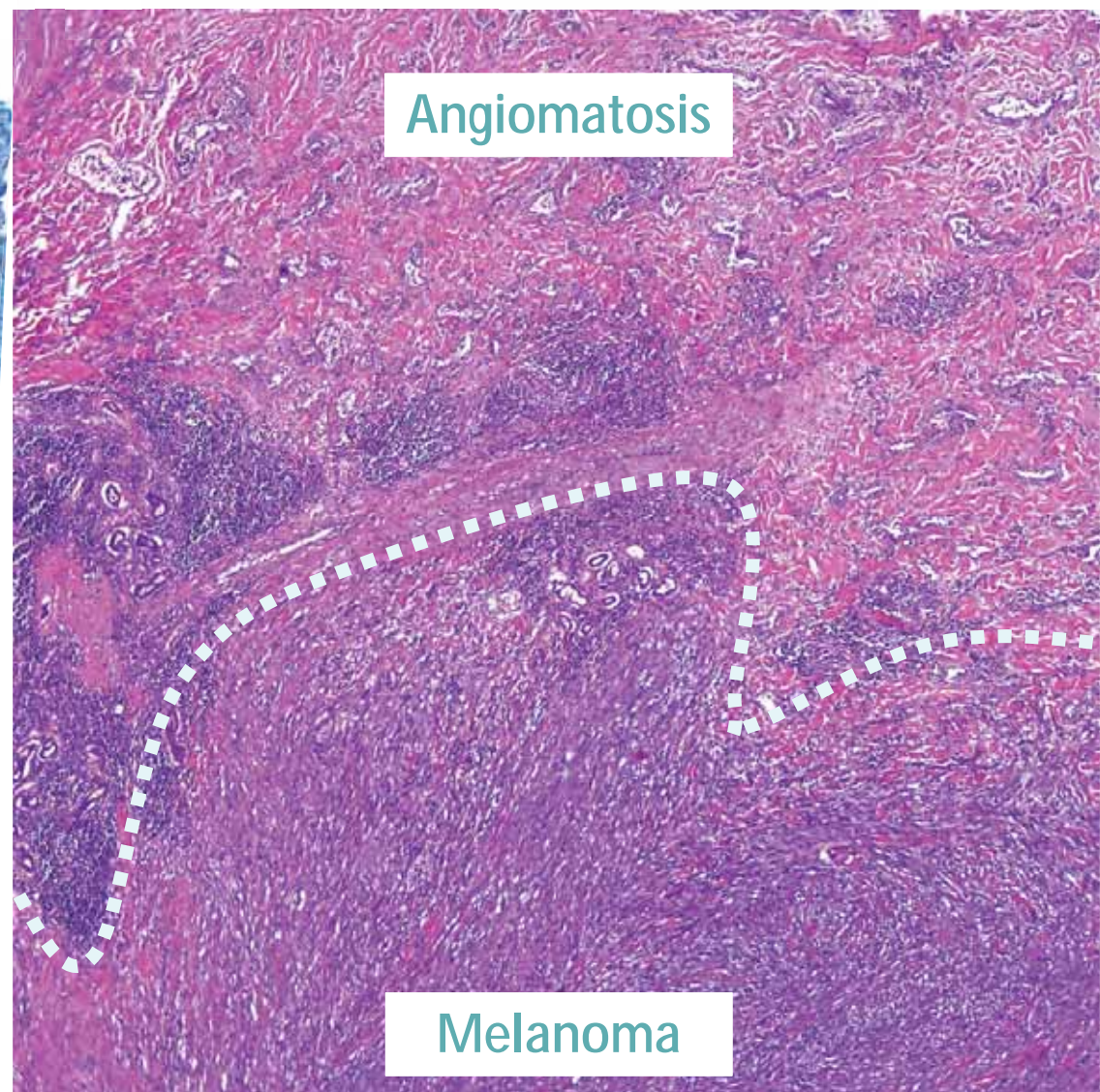
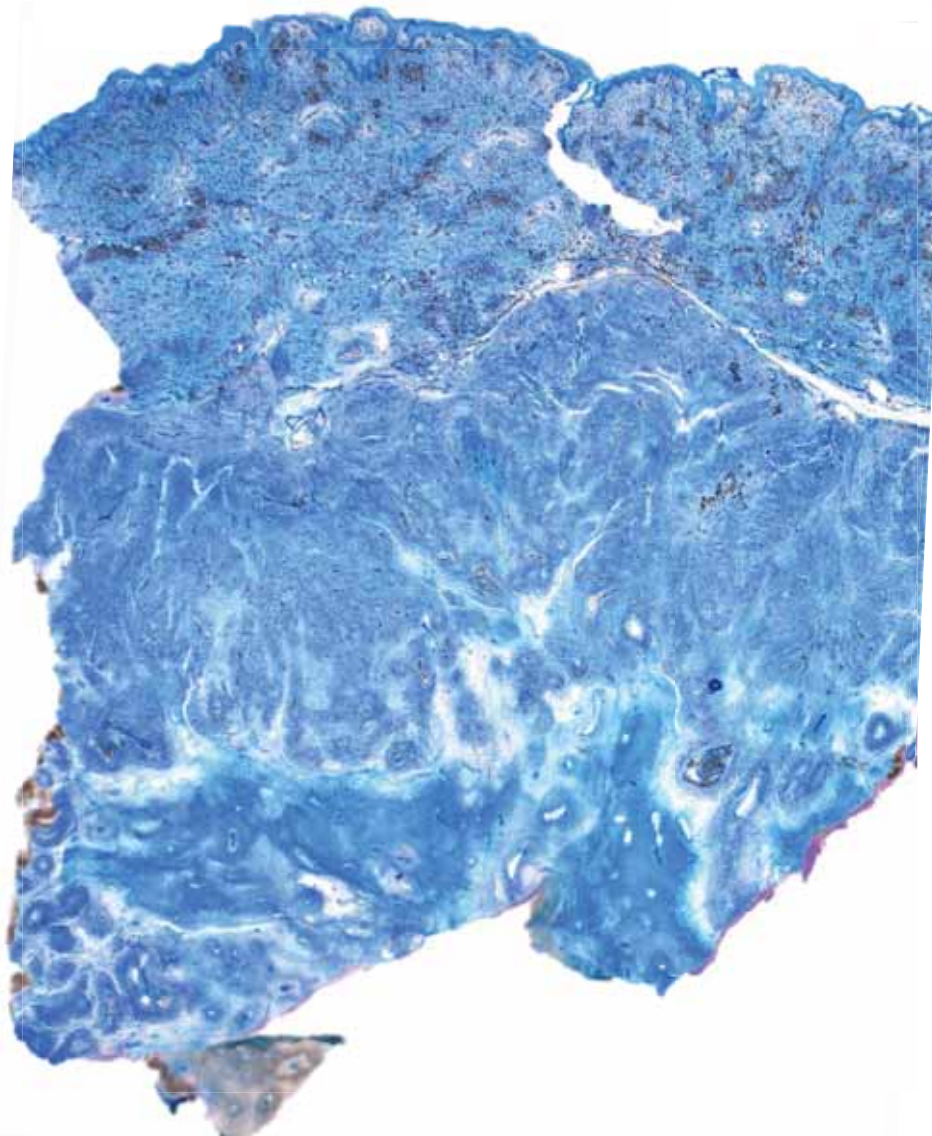
# Reactive angiomatosis

CD34



# Dx: Angiomatosis hiding a metastatic melanoma

SID001



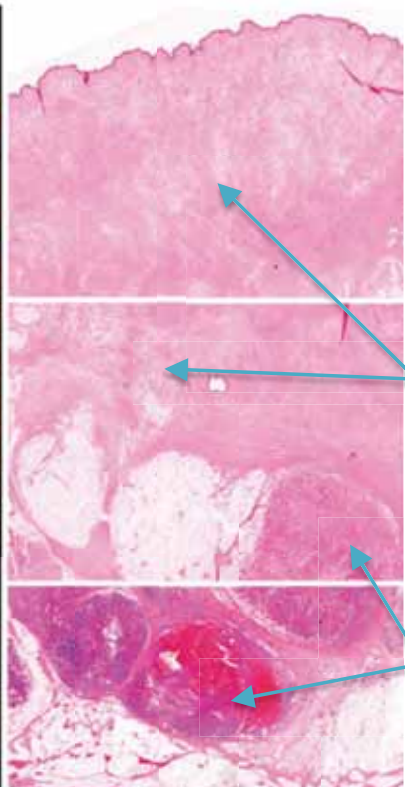
Angiomatosis

Melanoma

# When Biopsy Alone Is Not Enough for the Diagnosis: Angiomatous Florid Proliferation Hiding a Merkel Cell Carcinoma

Simonetta Piana, MD,\* Elisabetta Froio, MD,\* Cinzia Ricci, MD,† Fabio Castagnetti, MD,‡  
and Elvira Moscarella, MD†

*Am J Dermatopathol* 2015;37:78–82



Angiomatosis

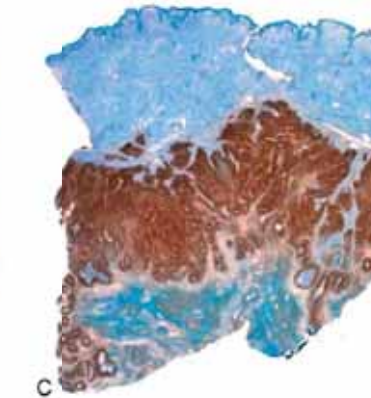
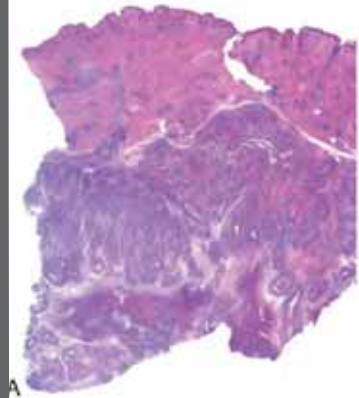
Merkel cell carcinoma

Vascular Changes in Merkel Cell Carcinoma Based on  
a Histopathological Study of 92 Cases  
*Am J Dermatopathol* 2008;30:106–111

# Angiomatous Proliferation Hiding a Metastasis of Melanoma

Noelia Rivera, MD\*  
Aram Boada, MD\*  
Carlos Ferrándiz, PhD\*  
Aurelio Ariza, PhD†  
Maria Teresa Fernández-Figueras,  
PhD†

*Am J Dermatopathol.* 2016 May;38(5):394-5



A

B

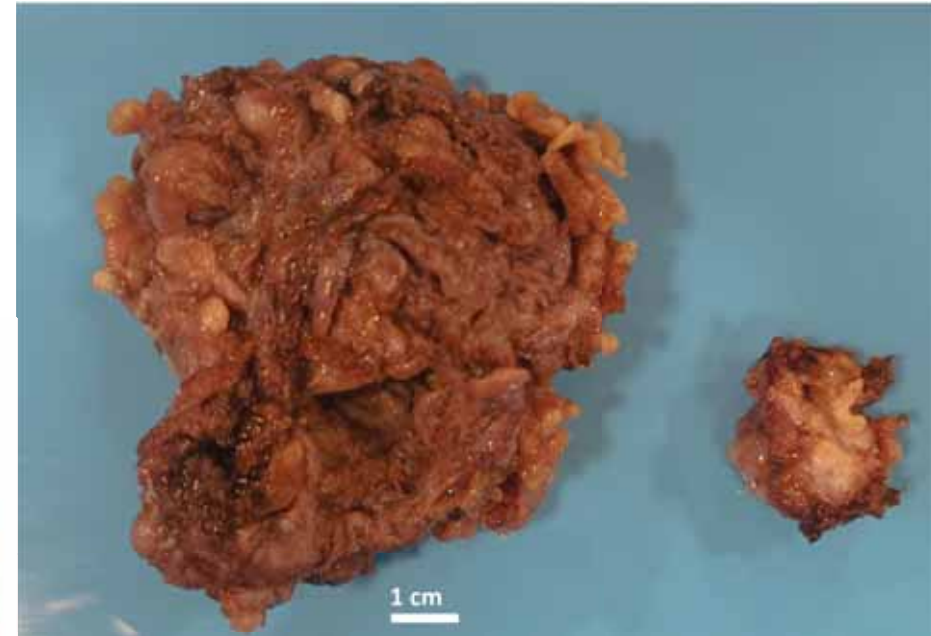
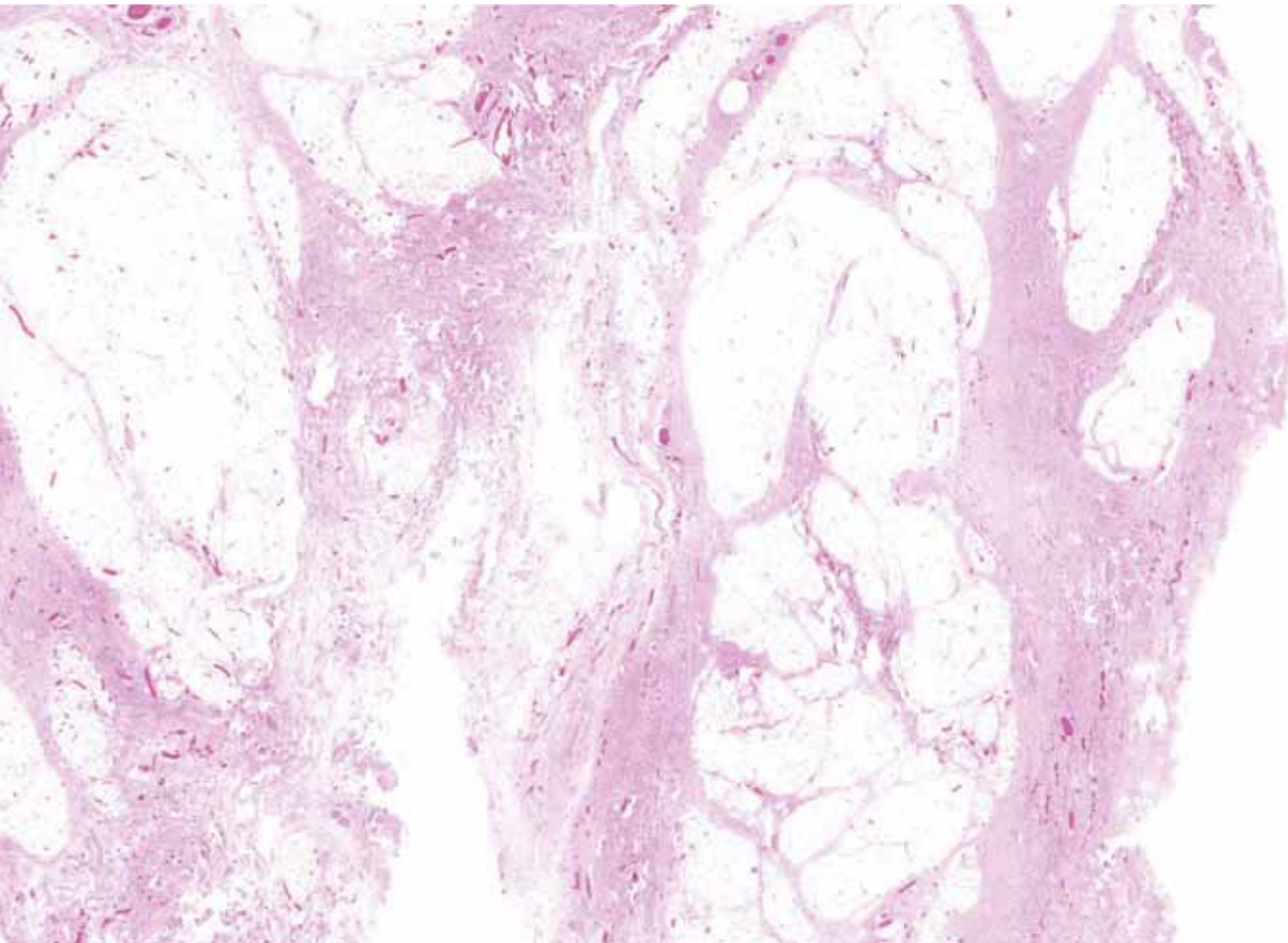
C

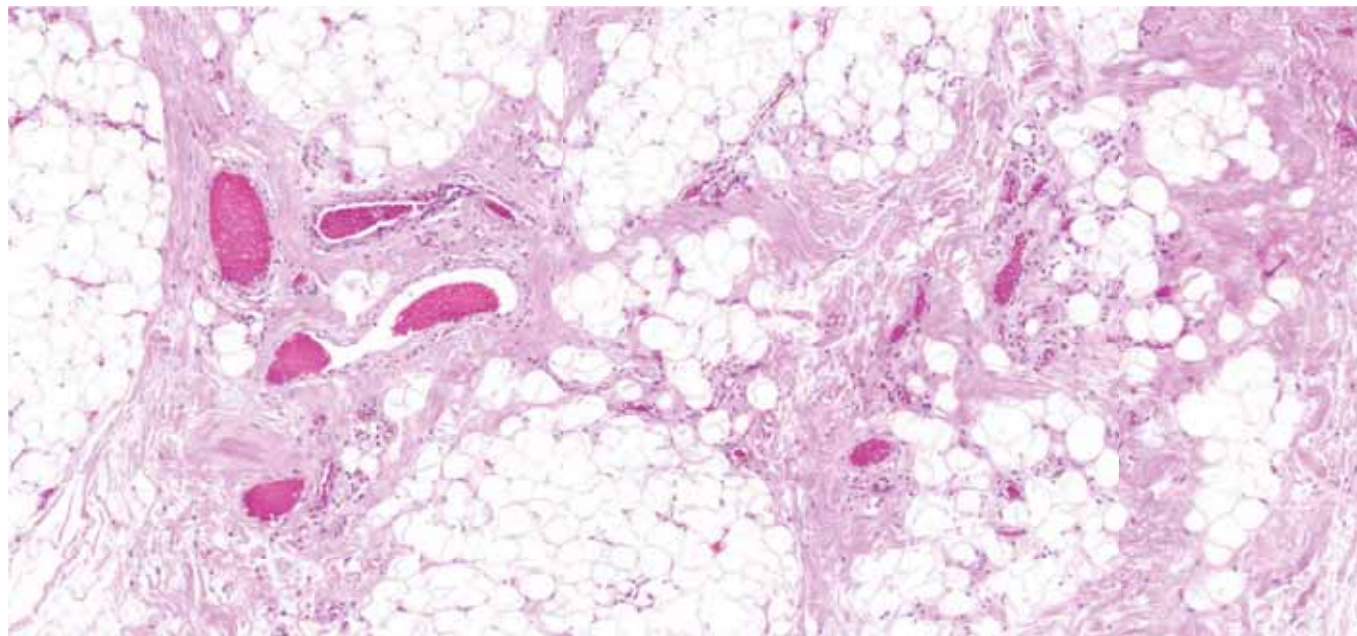
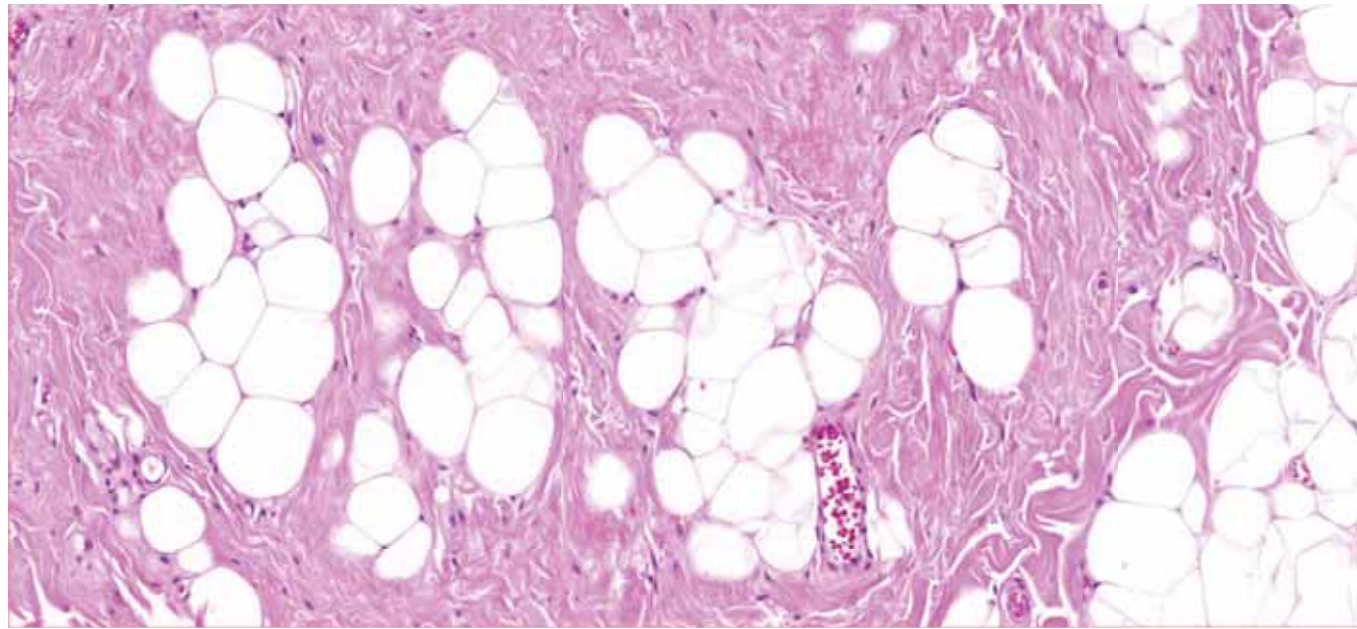
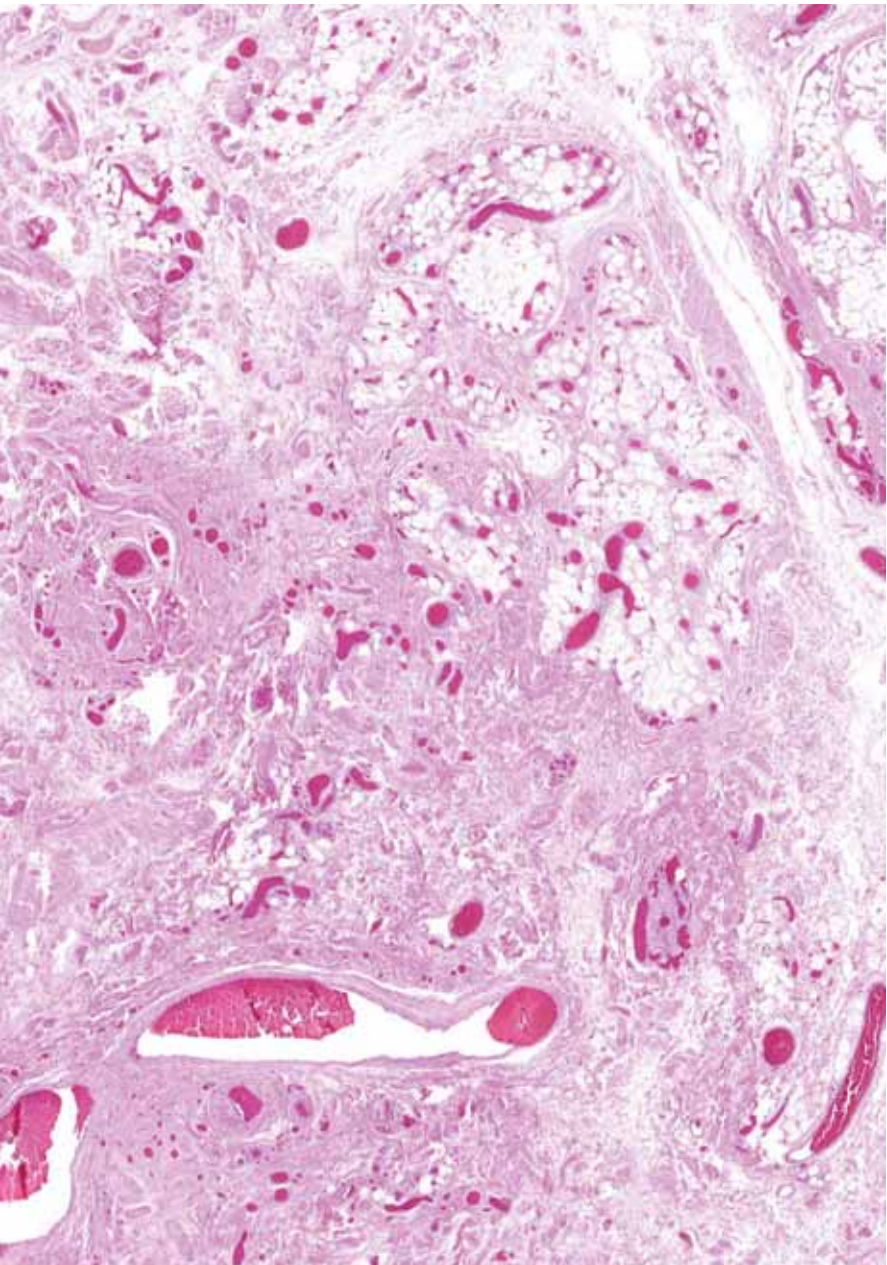
# LL 10

The missing piece of the puzzle may come from the patient



- 57-year-old man
- Perineal tumor (7 cm)
- Clinical Dx: lipoma





Do you  
cycle a lot?

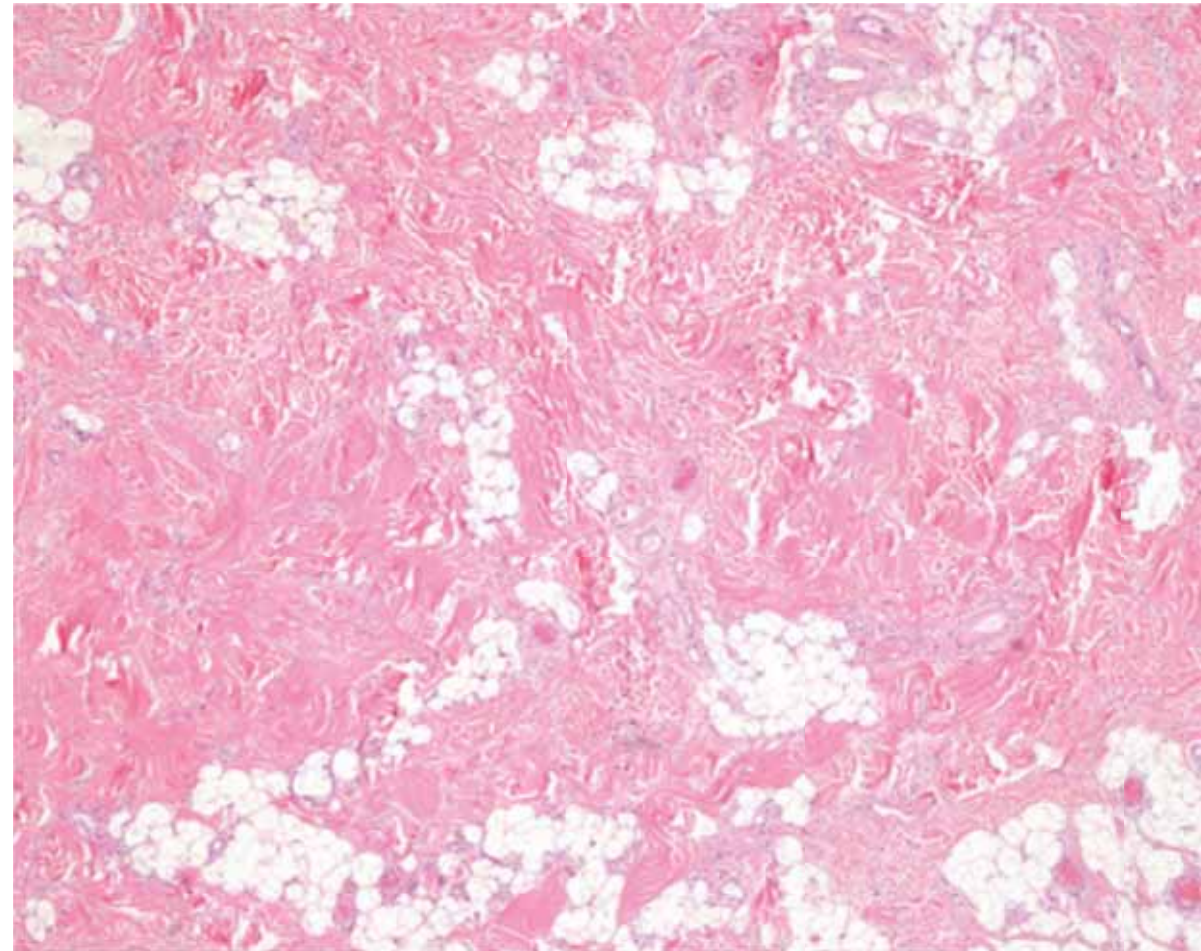


# Perineal Nodular Induration (“Biker’s Nodule”): Report of Two Cases With Fine-Needle Aspiration Cytology and Immunohistochemical Study

International Journal of Surgical Pathology  
2014. Vol. 22(1) 71–75

Radia Khedaoui, MD<sup>1</sup>, Luz M. Martín-Fragueiro, MD<sup>1</sup>,  
and Juan C. Tardío, MD, PhD<sup>1</sup>

- Fibroblastic pseudotumor
- Perineal, usually “avid” male cyclists
- Rarely > 3 cm
- Paucicellular fibroblastic proliferation with:
  - ✓ Thick collagen bundles
  - ✓ Entrapped groups of mature fat cells
  - ✓ Numerous blood vessels
  - ✓ CD34-reactive spindle and epithelioid cells
  - ✓ Small foci of fibrinoid degeneration

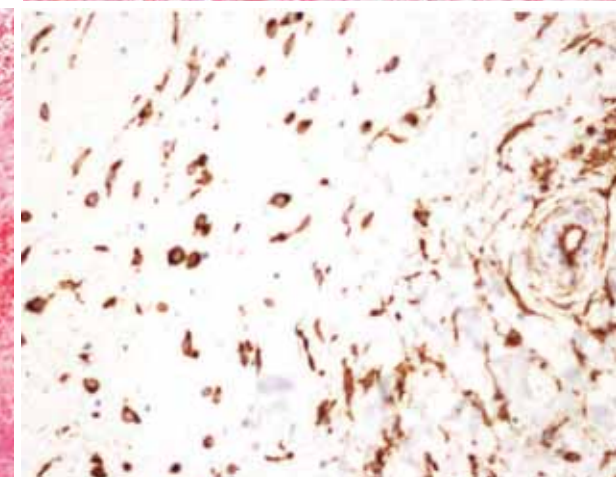
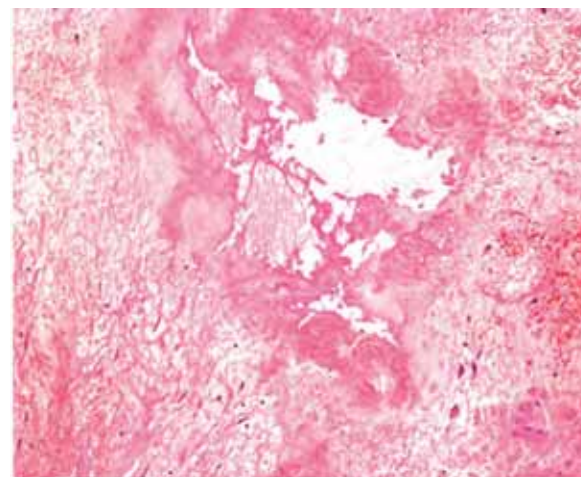
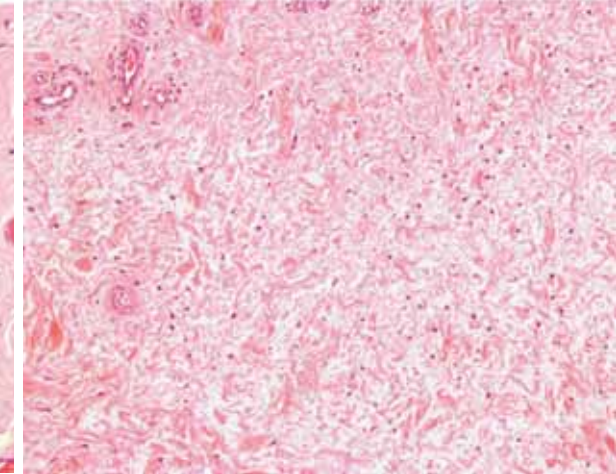
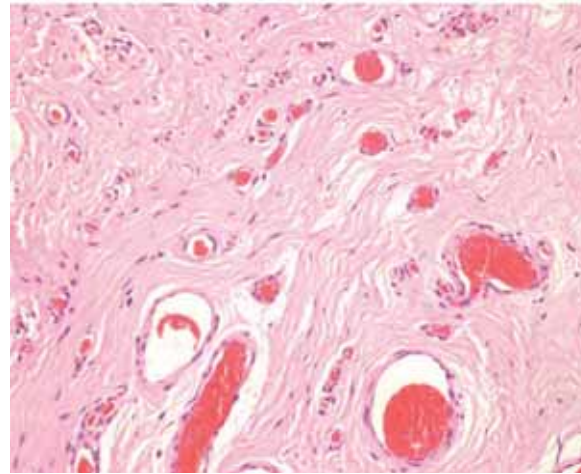


# Perineal Nodular Induration (“Biker’s Nodule”): Report of Two Cases With Fine-Needle Aspiration Cytology and Immunohistochemical Study

International Journal of Surgical Pathology  
2014. Vol. 22(1) 71–75

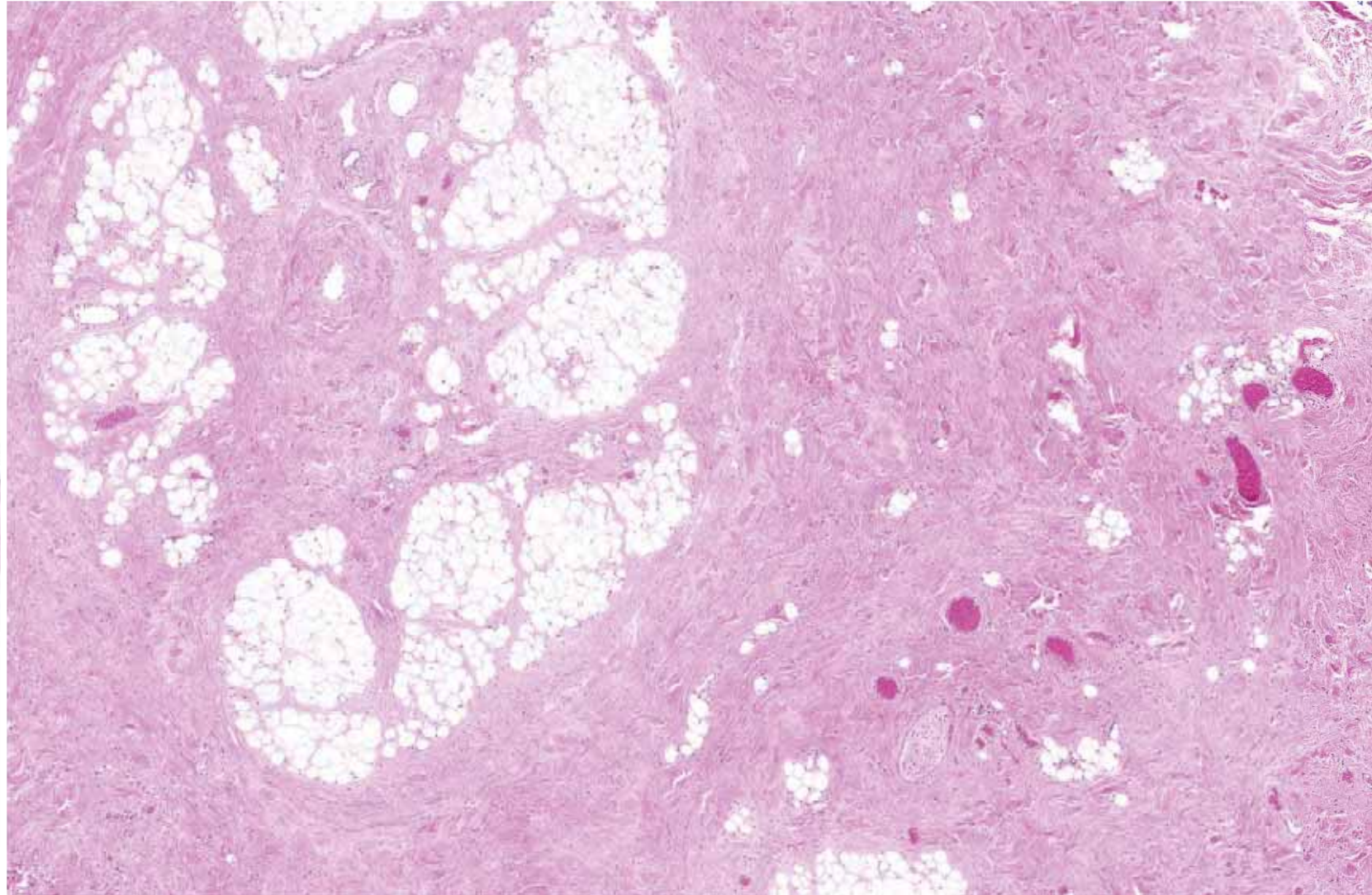
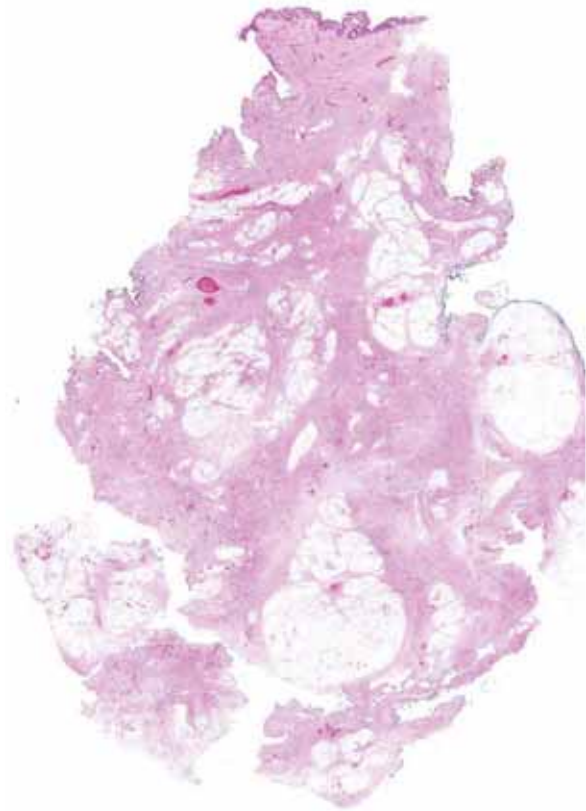
Radia Khedaoui, MD<sup>1</sup>, Luz M. Martín-Fragueiro, MD<sup>1</sup>,  
and Juan C. Tardío, MD, PhD<sup>1</sup>

- Fibroblastic pseudotumor
- Perineal, usually “avid” male cyclists
- Rarely > 3 cm
- Paucicellular fibroblastic proliferation with:
  - ✓ Thick collagen bundles
  - ✓ Entrapped groups of mature fat cells
  - ✓ Numerous blood vessels
  - ✓ CD34-reactive spindle and epithelioid cells
  - ✓ Small foci of fibrinoid degeneration



- 48-year-old man
- Perineal tumor (6 cm)
- Clinical Dx: lipoma

## Perineal nodular induration (Biker's nodule)



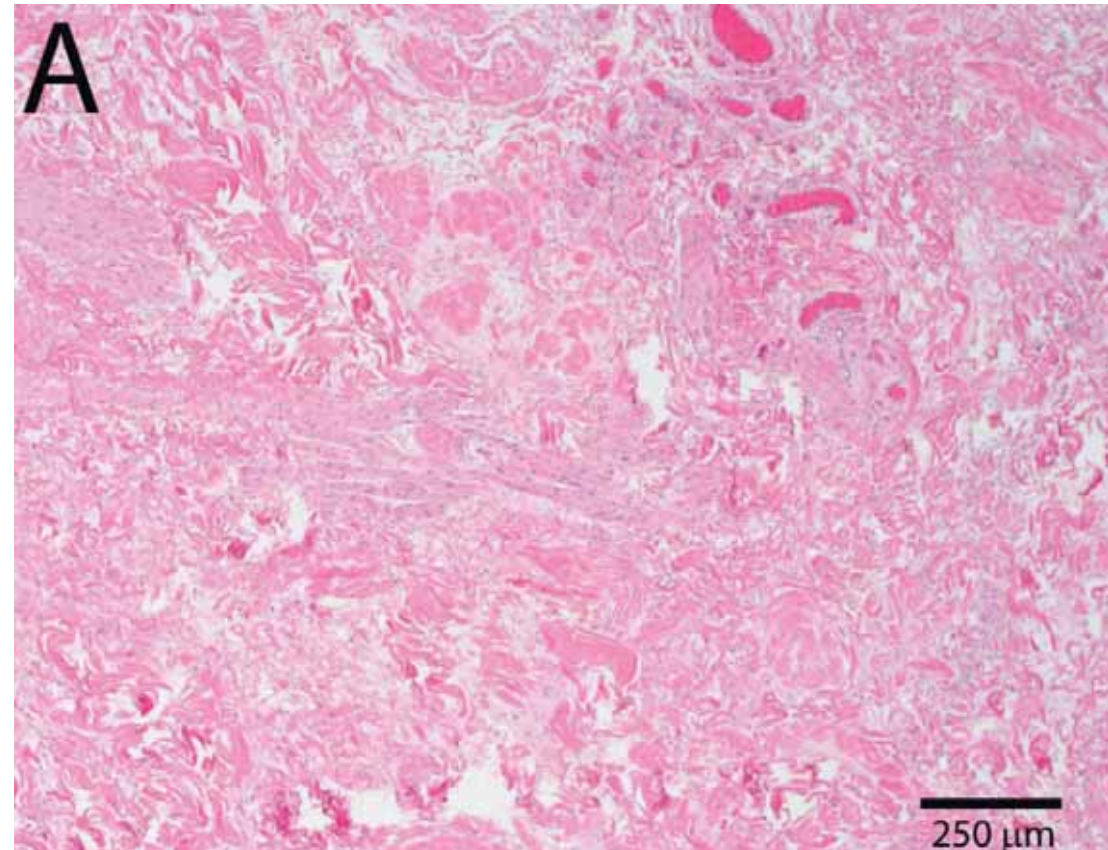
# Surgical excision of perineal nodular induration: A cyclist's third testicle

*Can Urol Assoc J* 2017;11(5):E244-7

Mohannad A. Awad, MD<sup>1,2</sup>; Gregory P. Murphy, MD<sup>1</sup>; Thomas W. Gaither, MD<sup>1</sup>; E. Charles Osterberg, MD<sup>3</sup>;  
Thomas A. Sanford, MD<sup>1</sup>; Andrew E. Horvai, MD<sup>4</sup>; Benjamin N. Breyer<sup>1,5</sup>



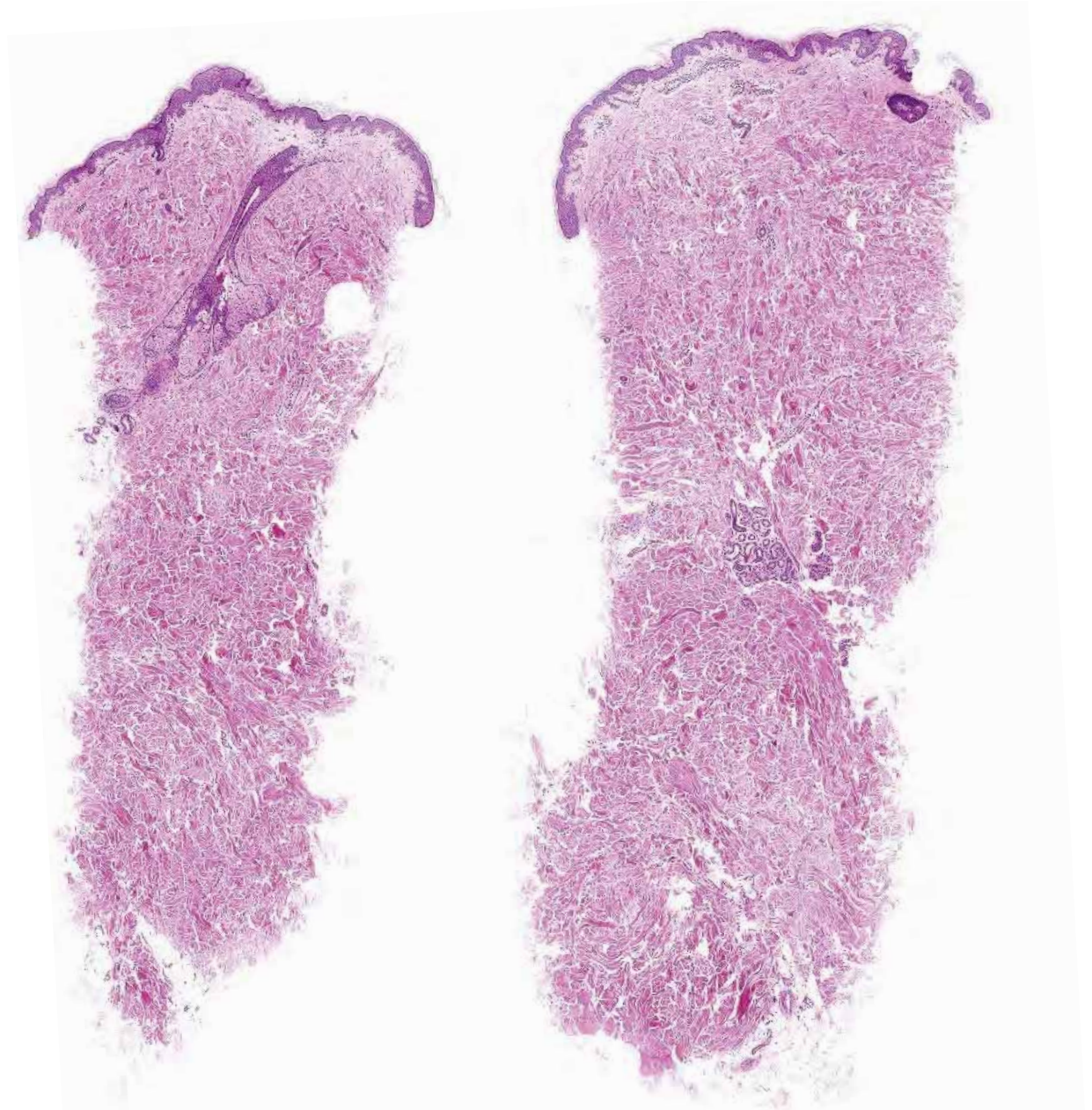
**Fig. 1.** Large, perineal fat posterior to the scrotum with redundant tissue resembling an accessory testicle (arrow).

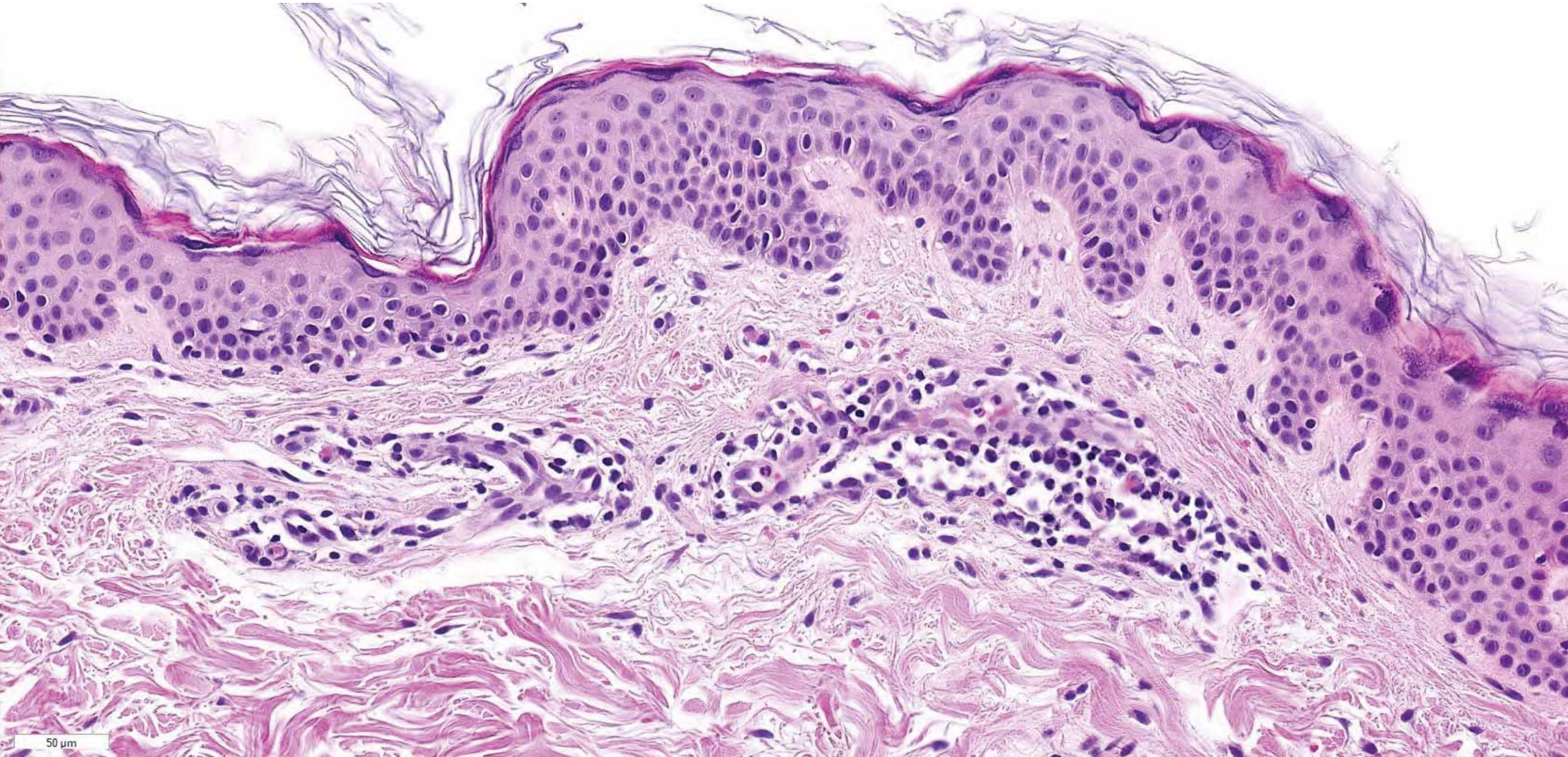


- 34-year-old man
- Asymptomatic macules for 2 weeks preceded by mild pruritus.
- Initially with a slight purple-bluish hue, but later become greyish
- Clinical Dx: Ashy dermatosis, MF, residual lesions secondary to vasodilation

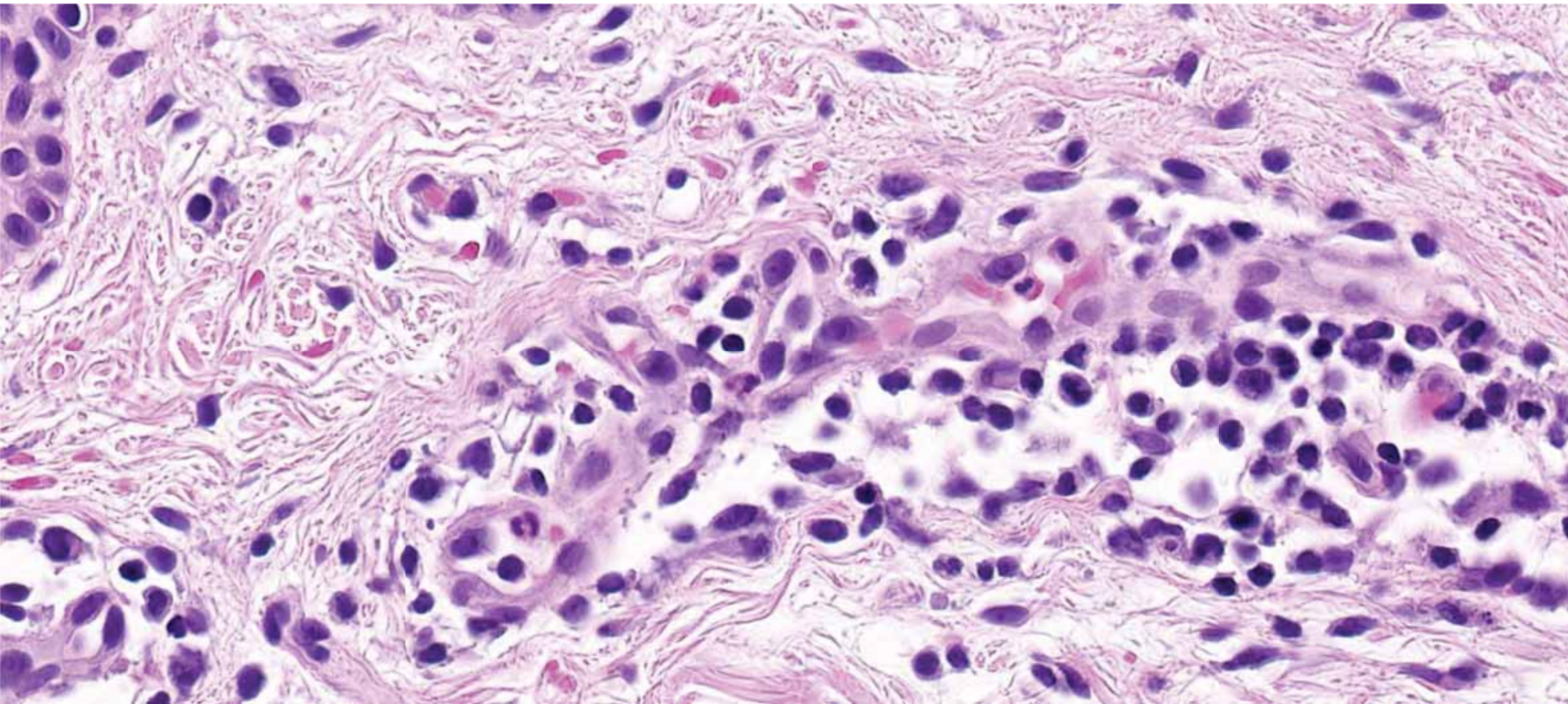


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## Maculae caeruleae

- Rare in adults.
- More common in children, due to the absence of pubic hair.  
The parasite is usually found on the eyelashes or hairline
- Anticoagulant saliva that causes purpuric dermatitis
- Dermal hypersensitivity reaction to saliva and feces

Sexually Transmitted Diseases • October-December 1979

*Pediculosis Pubis in a Clinic for Treatment of Sexually Transmitted Diseases*

THOMAS A. CHAPEL, MD, THOMAS KATTA, MD, THADDEUS KUSZMAR, PA, AND DOMINIC DeGIUSTI, PhD

121 patients ( ♂/♀: 102/19 )

Pruritus: 104 patients (86%)

Maculae cerulae 1 (< 1%) chest and flank

# Life lessons : the Barcelona experience

1. Any tumor can be painful. Specially in the subungual region
2. Pay attention to the stroma and learn how to interpret it
3. The simplest explanation is not always the correct one!
4. Don't stop at the initial diagnosis, hidden pathologies may creep around
5. Do not theorize before you have all the evidences. It biases your judgment
6. Be aware of the absence of specificity of patterns and cytological features
7. The devil lies in the details; be meticulous!
8. Success is not assured by perfect clinicopathological correlation
9. Do not dare to ask for a new/larger biopsy
10. Patients may have the missing piece of the puzzle

Stay humble, **we keep learning everyday**

