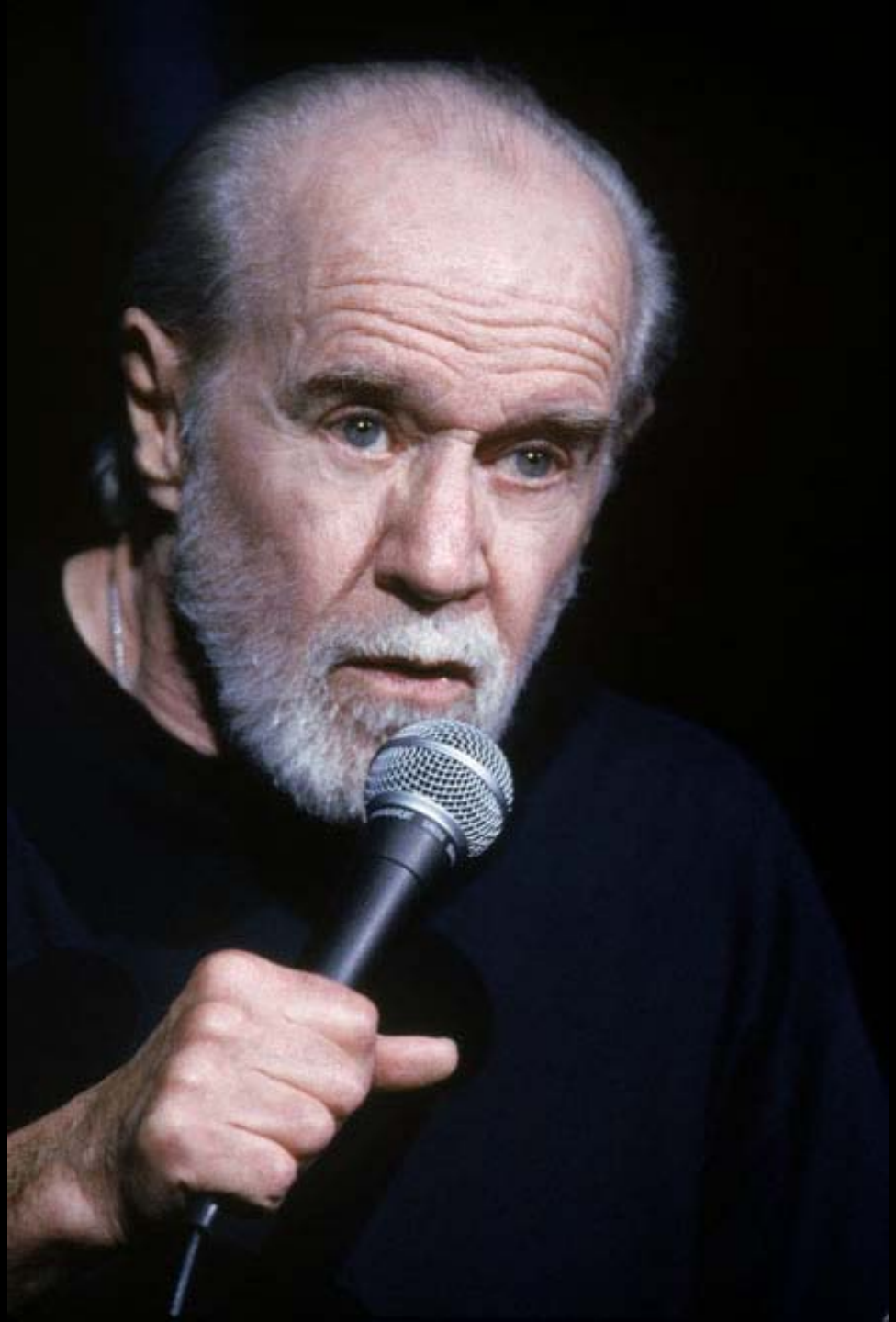

Seven Things You Should Not Say At a Dermatopathology Conference

Presented to Kaiser Woodland Hills
Dept. of Pathology
February 17, 2009

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Dermatopathology Institute
Director of Dermatopathology, Harbor-UCLA Dermatology
Associate Clinical Professor
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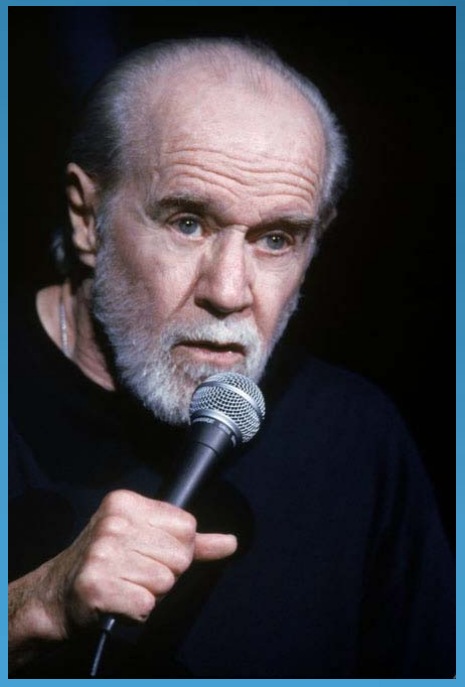
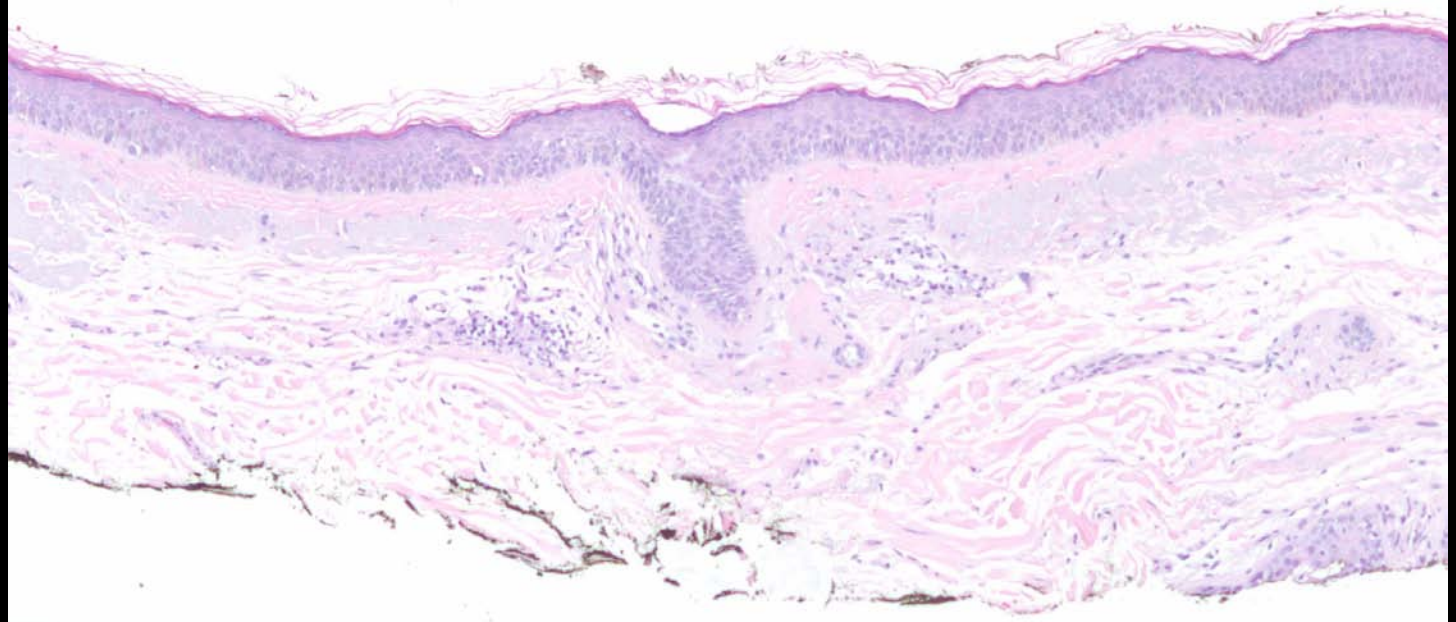
The Seven Things

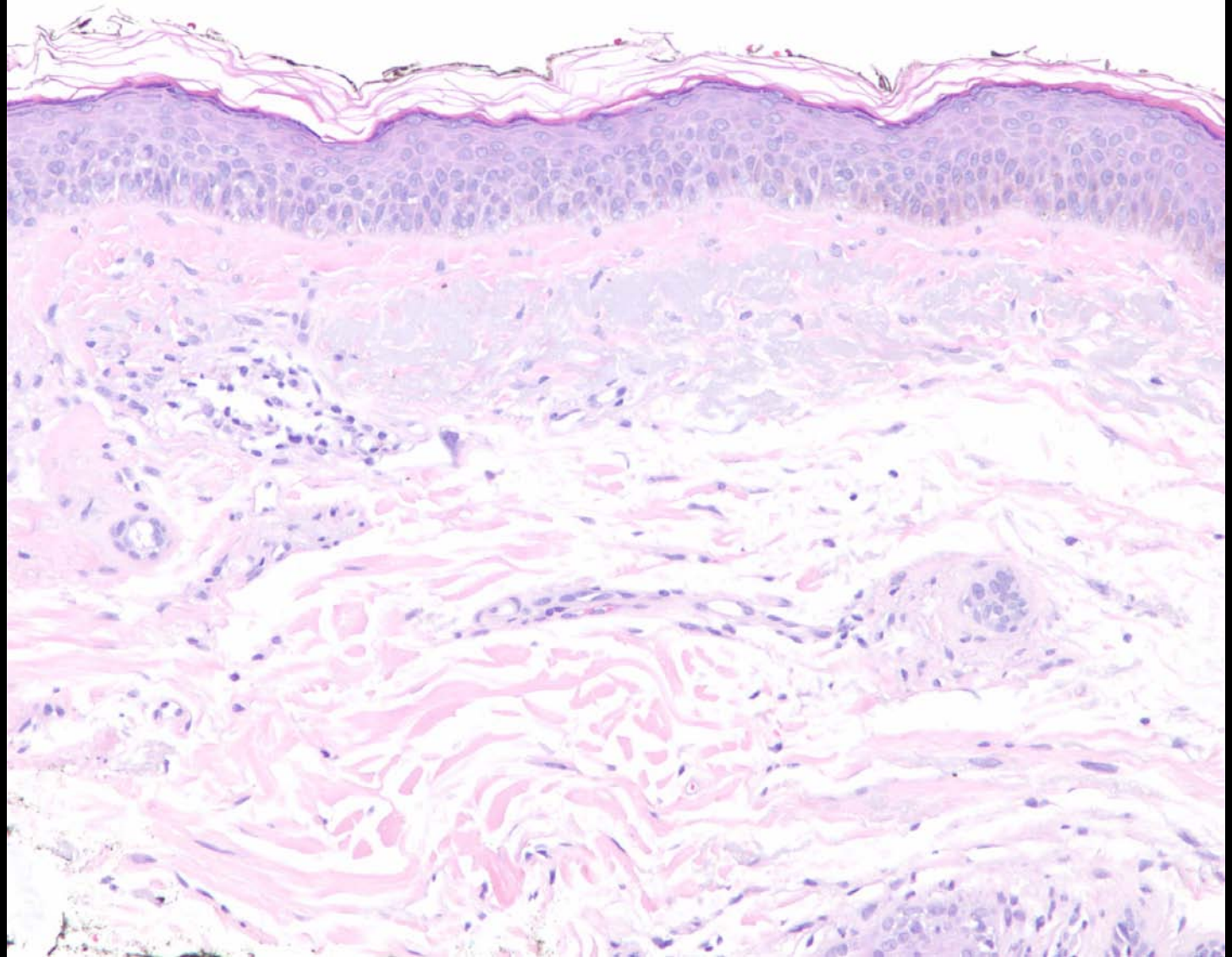
- Low Power Objective-High Power Pathologist
- Measuring a Melanoma
- The Best Special Stain
- Margins on a Punch or Shave biopsy
- Lymphocytic Vasculitis
- IHC is the Magic Bullet
- Consultant Confloption

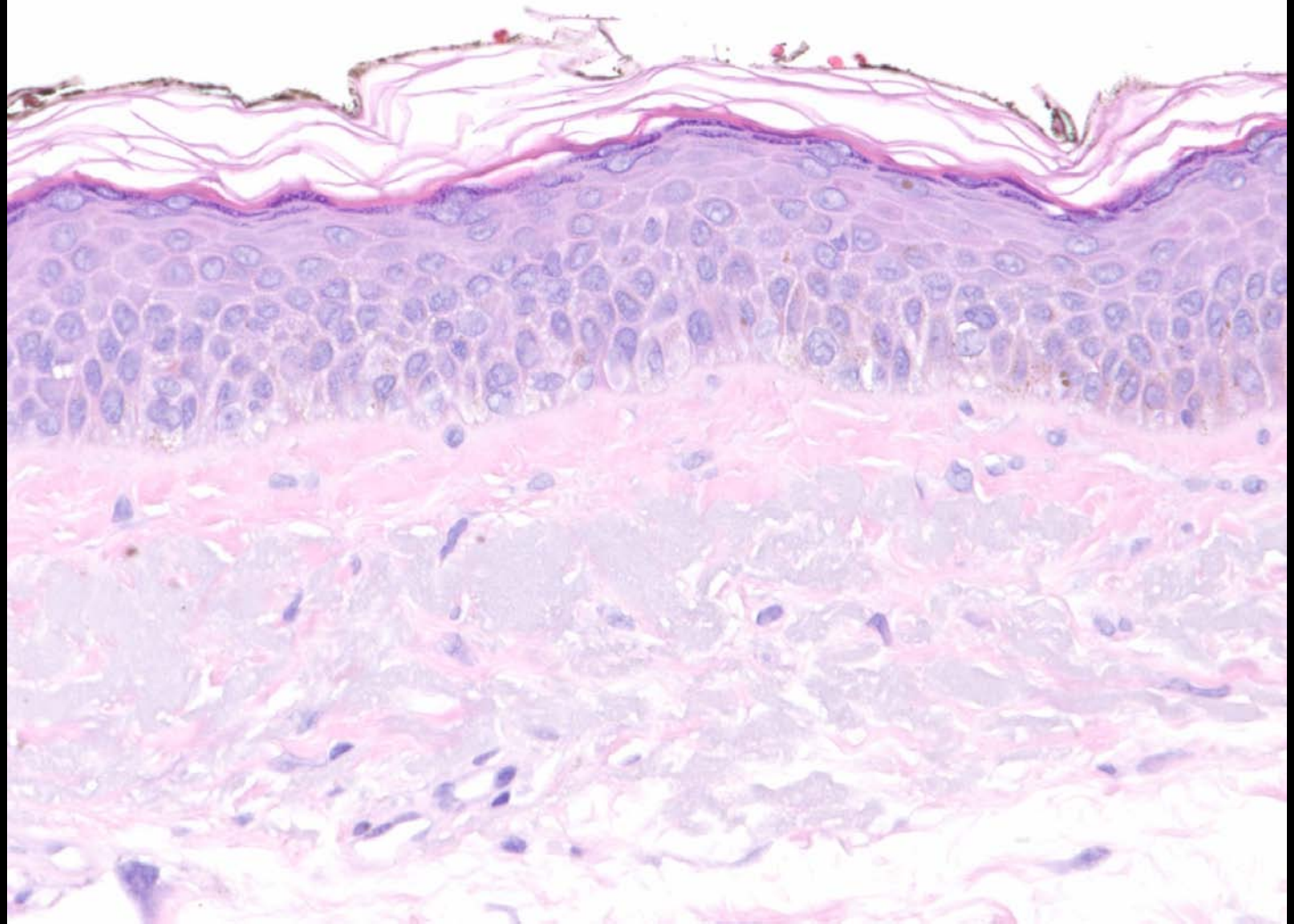
The Seven Things

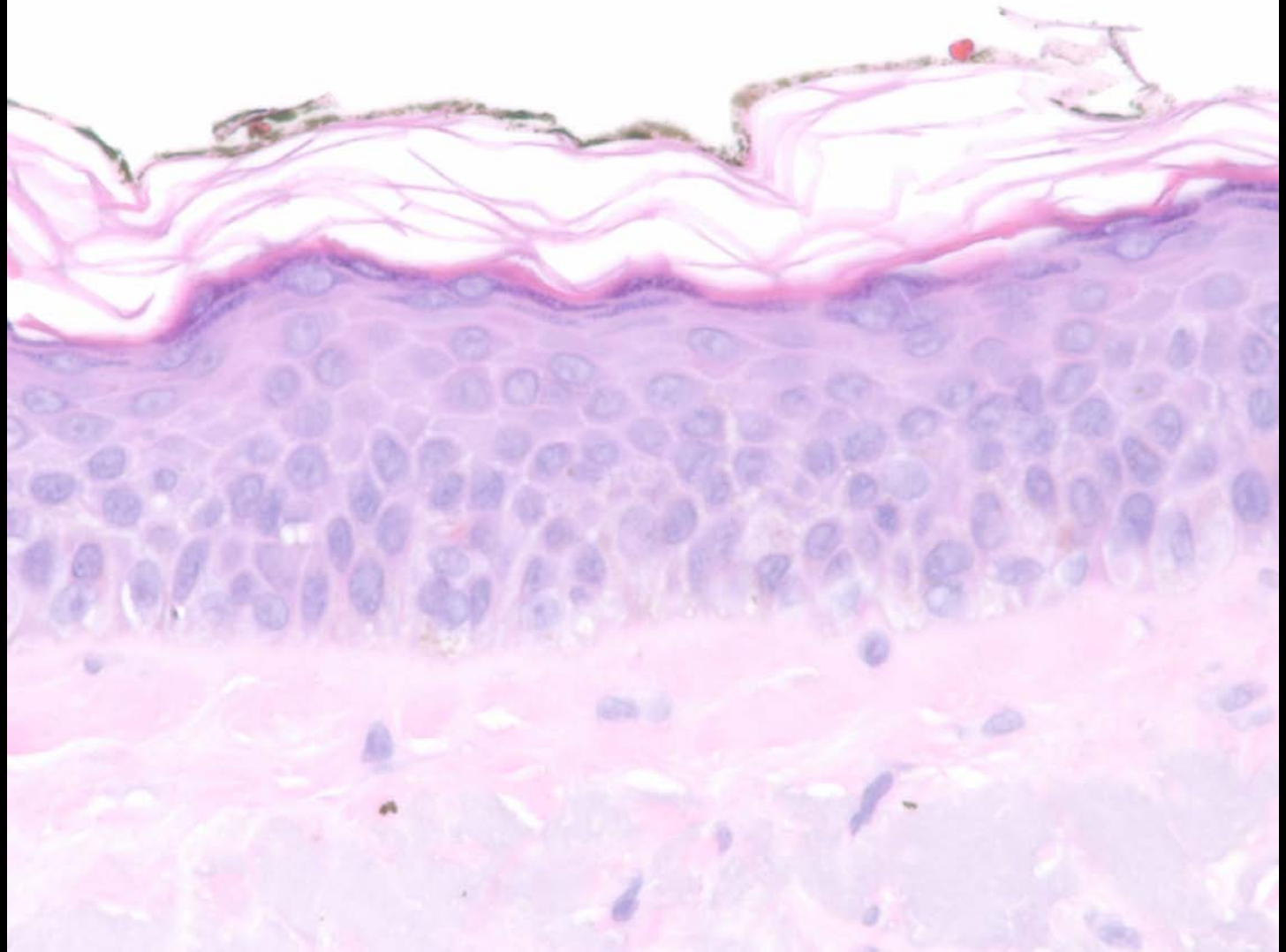
- Low Power Objective-High Power Pathologist



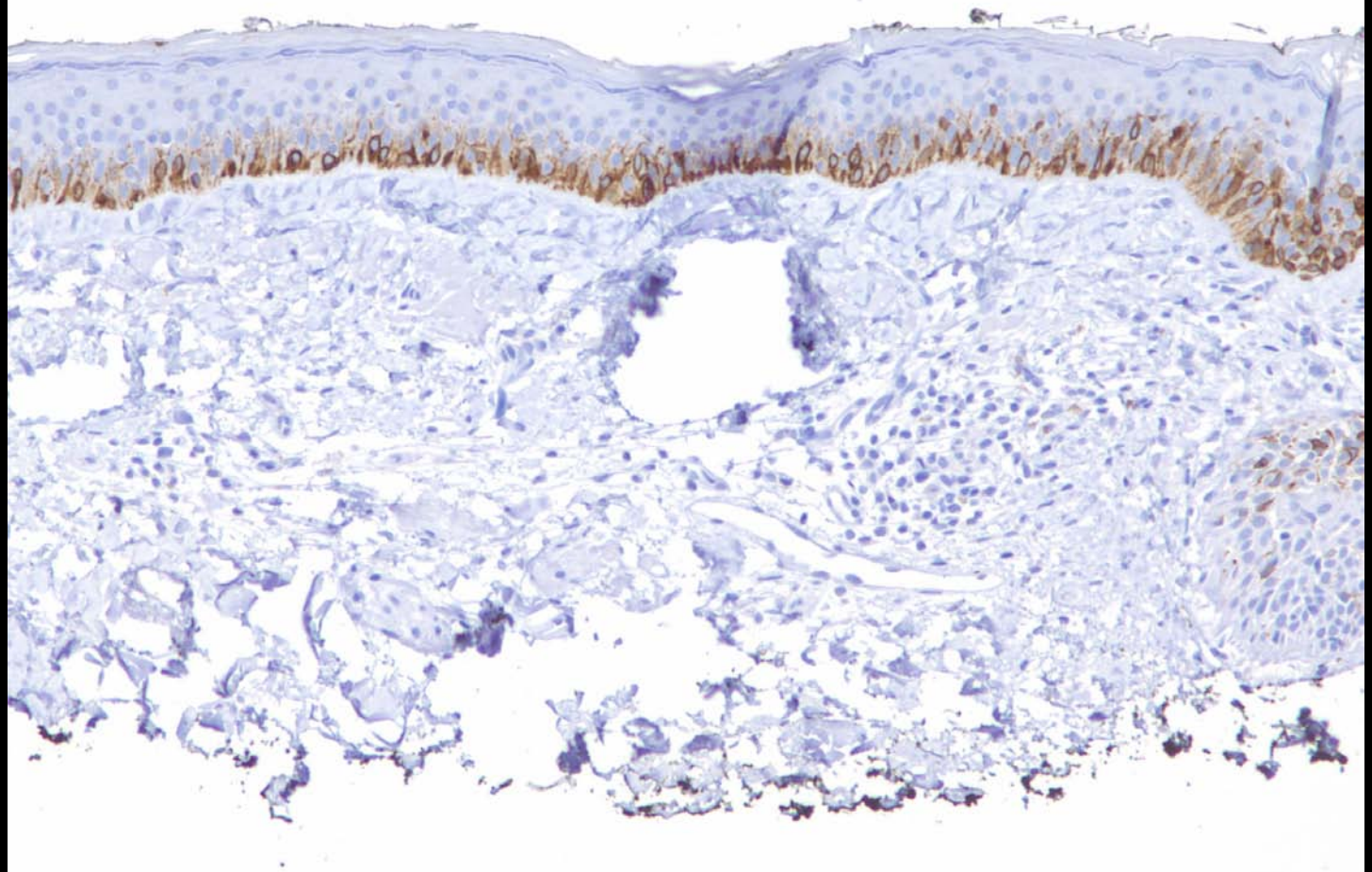






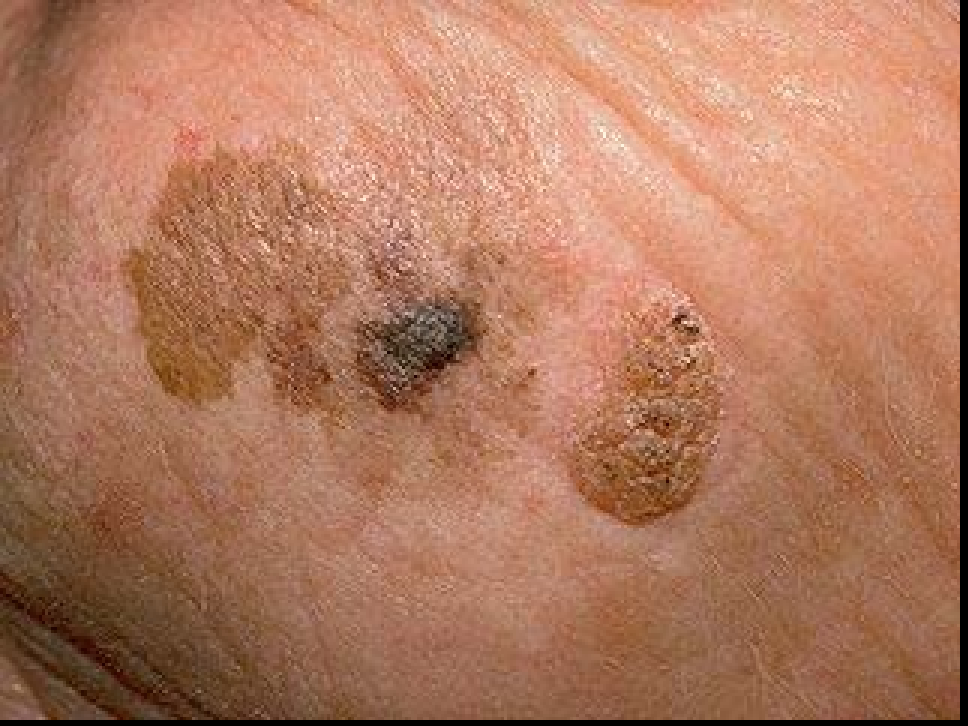


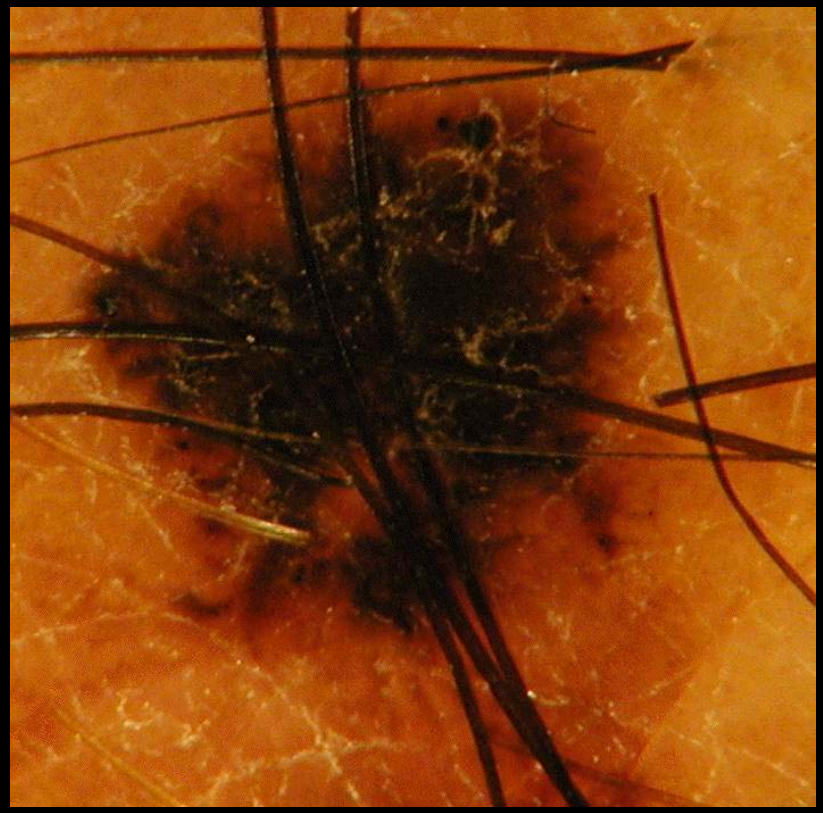
Melan-A

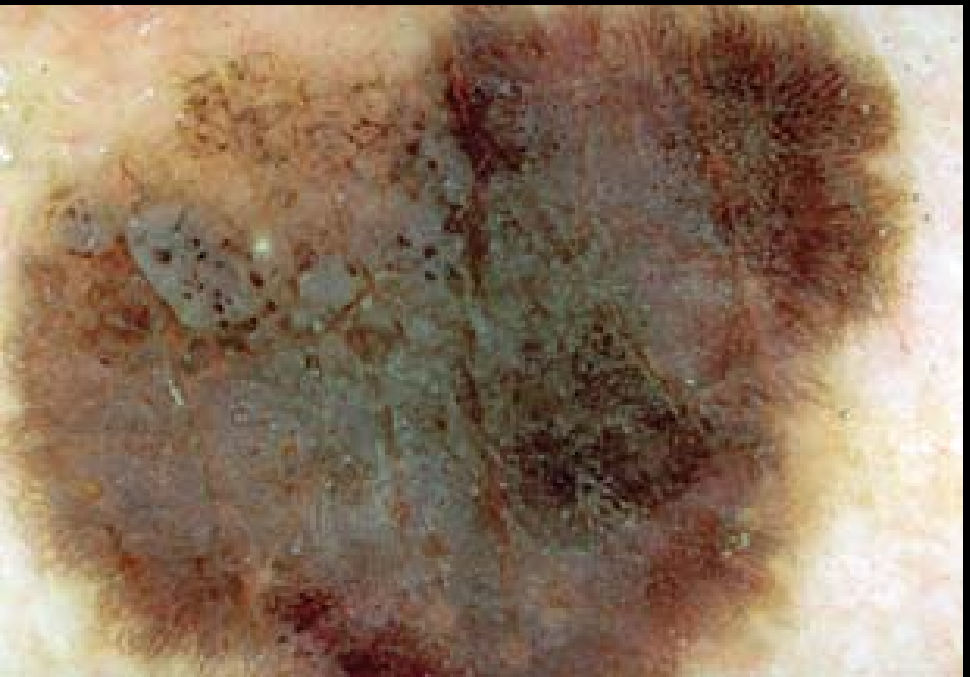


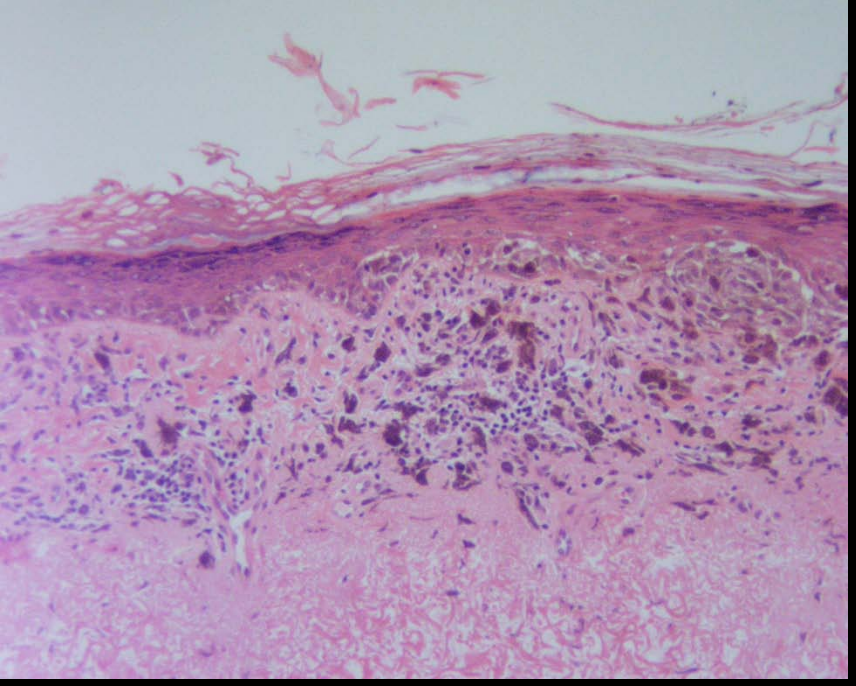
Amelanotic Melanoma in Situ: A histopathologic mimic of benign lesions

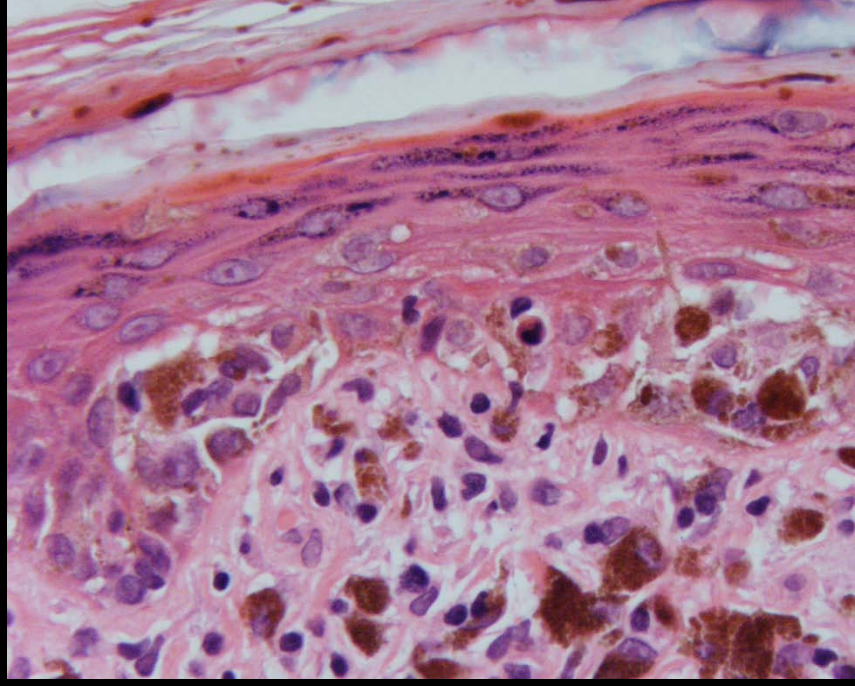
Tan BH and Shitabata PK

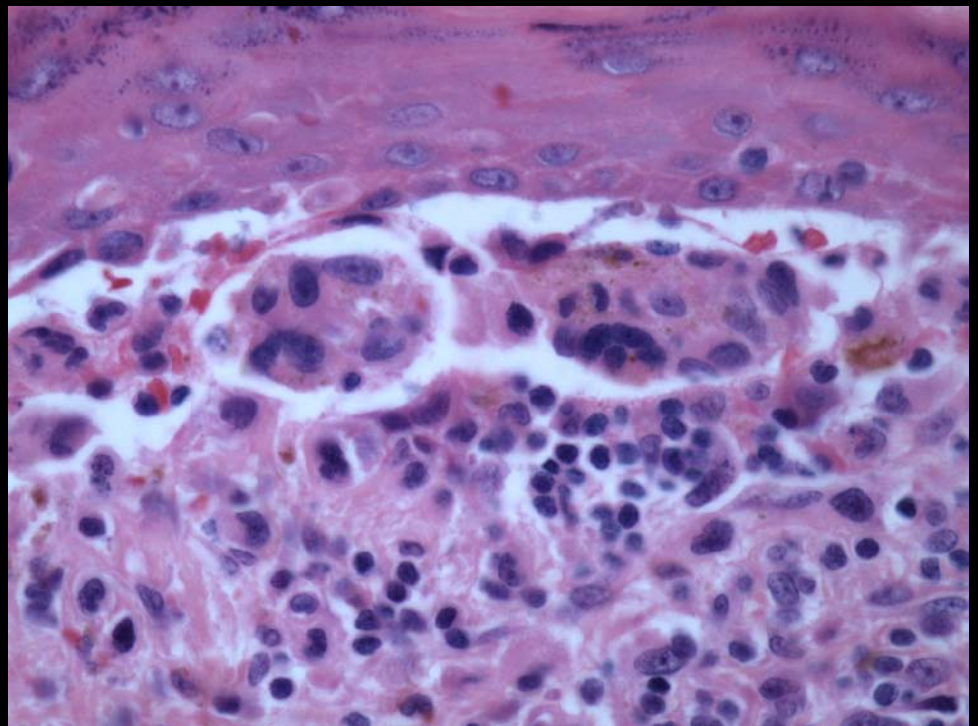








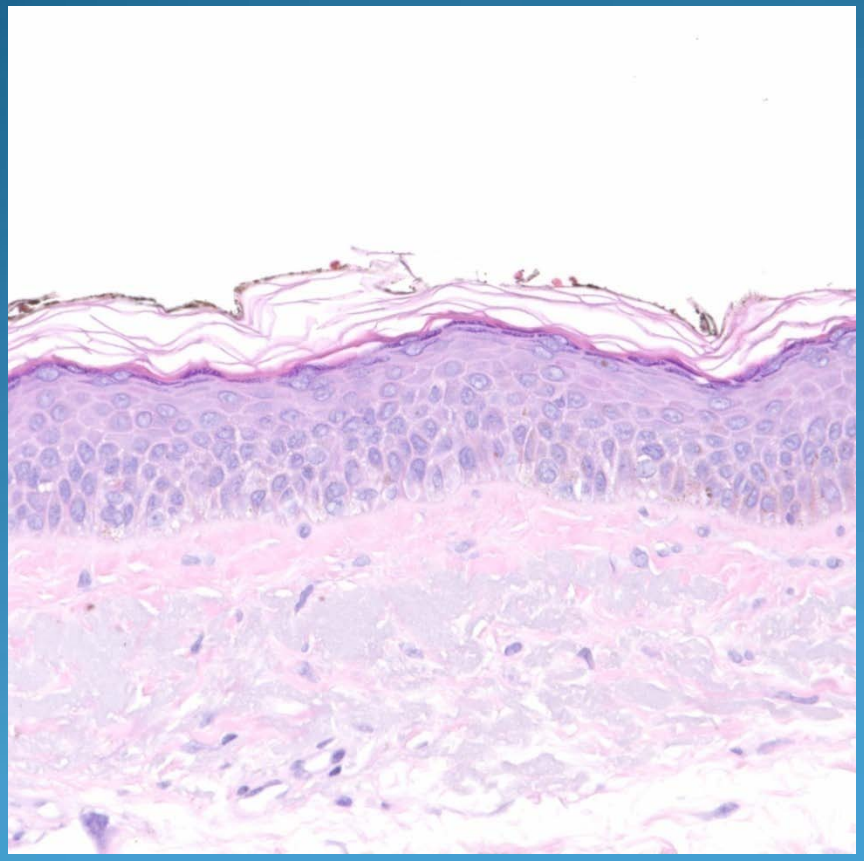




Retrospective Review

- Retrospective review of 444 cases of MMIS
- Ten cases identified
- MF 8:2
- Mean age 67 years (53-79 yrs)
- Location-Head and neck/upper trunk
- Clinical impression:
  - Atypical nevus 5/10
  - LM 3/10
  - Lentigo 1/10
  - BCC 1/10

Histopathology



- Low power architecture of sun damaged skin or lentigo
- No epidermal atrophy
- No bridging nests or discohesive clefting
- Junctional melanocytes small with minimal atypia
- Confirm by Melan-A staining

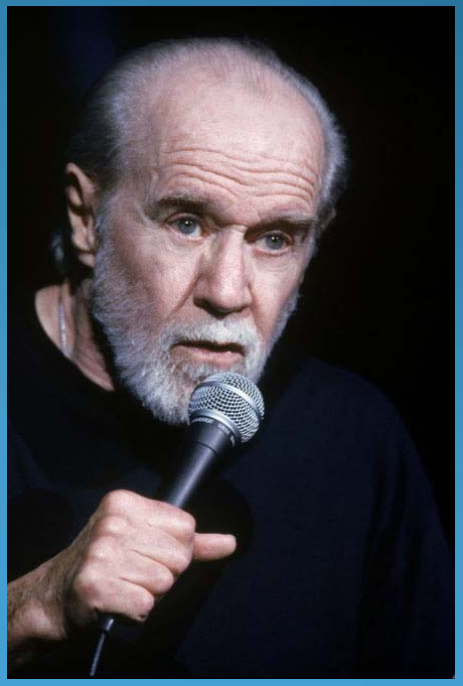
Characteristic	MMIS	AMMIS
Sun damaged skin	+	+
Epidermal atrophy	+	
Bridging/dyscohesive melanocytic nests	+	
Severe melanocytic atypia	+	
Starburst melanocytes	+/-	
Extension along adnexal epithelium	+	+

Low Power Objective may lead to a High Power Error!

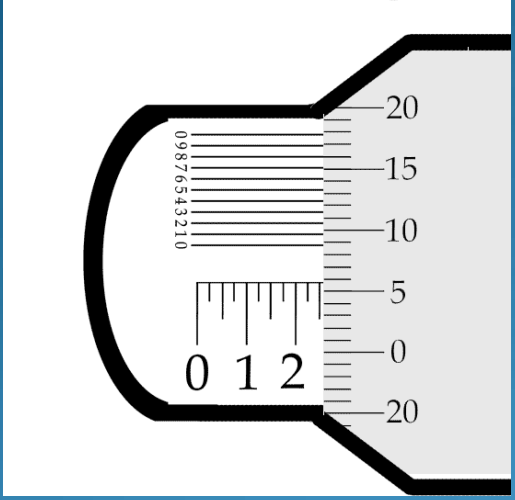
Amelanotic MMIS must be diagnosed by High Power Examination

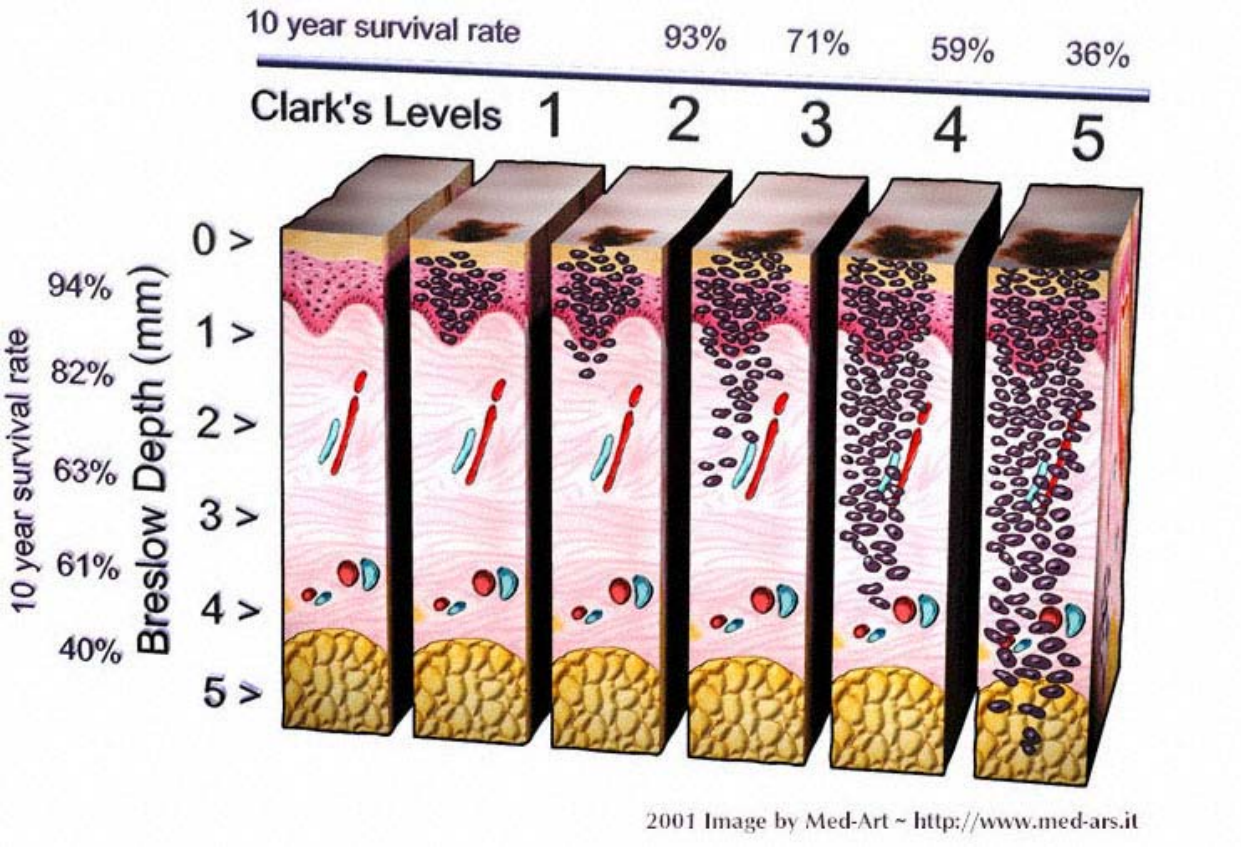
The Seven Things

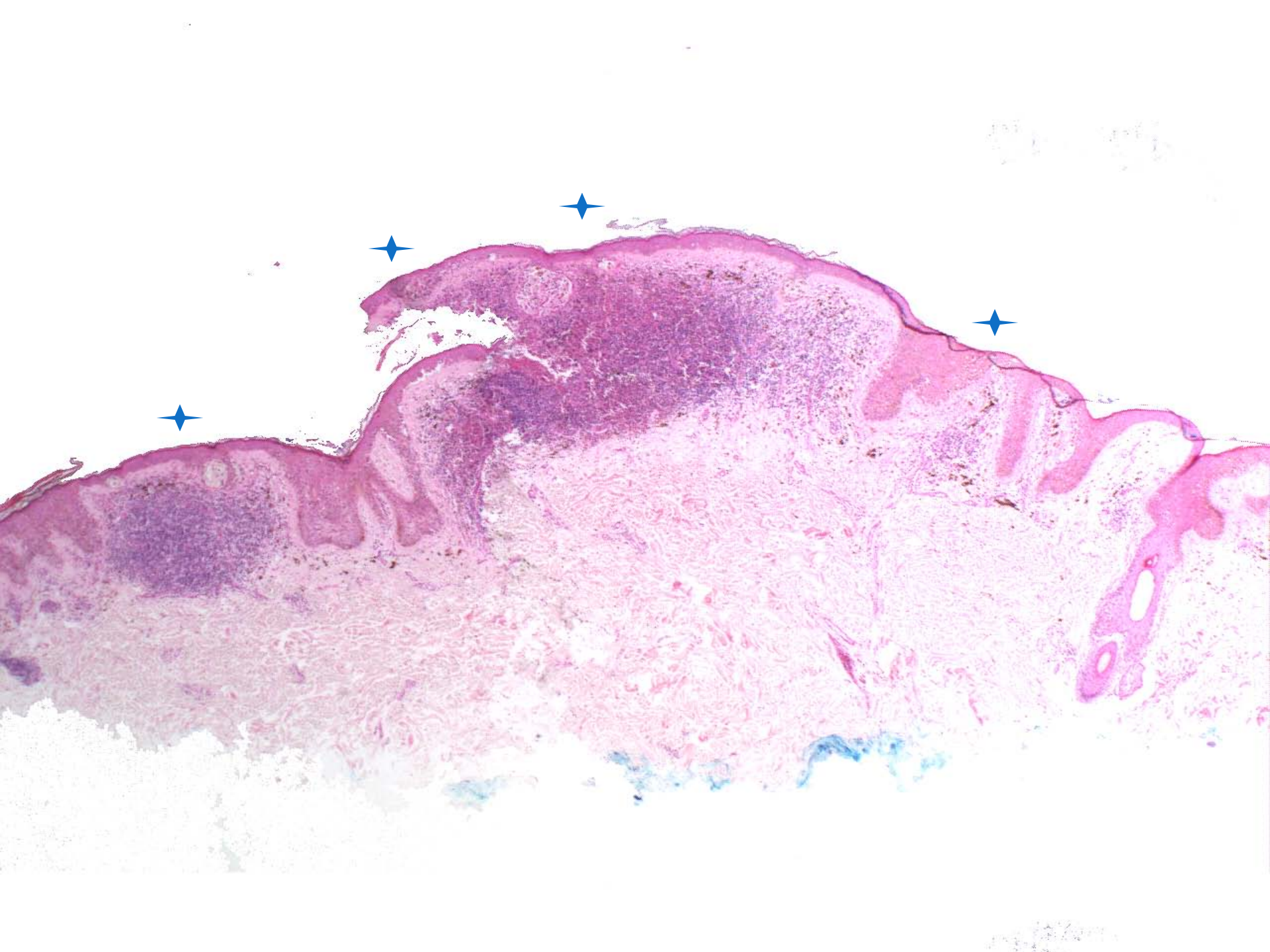
- Low Power Objective-High Power Pathologist
- **Measuring a Melanoma**

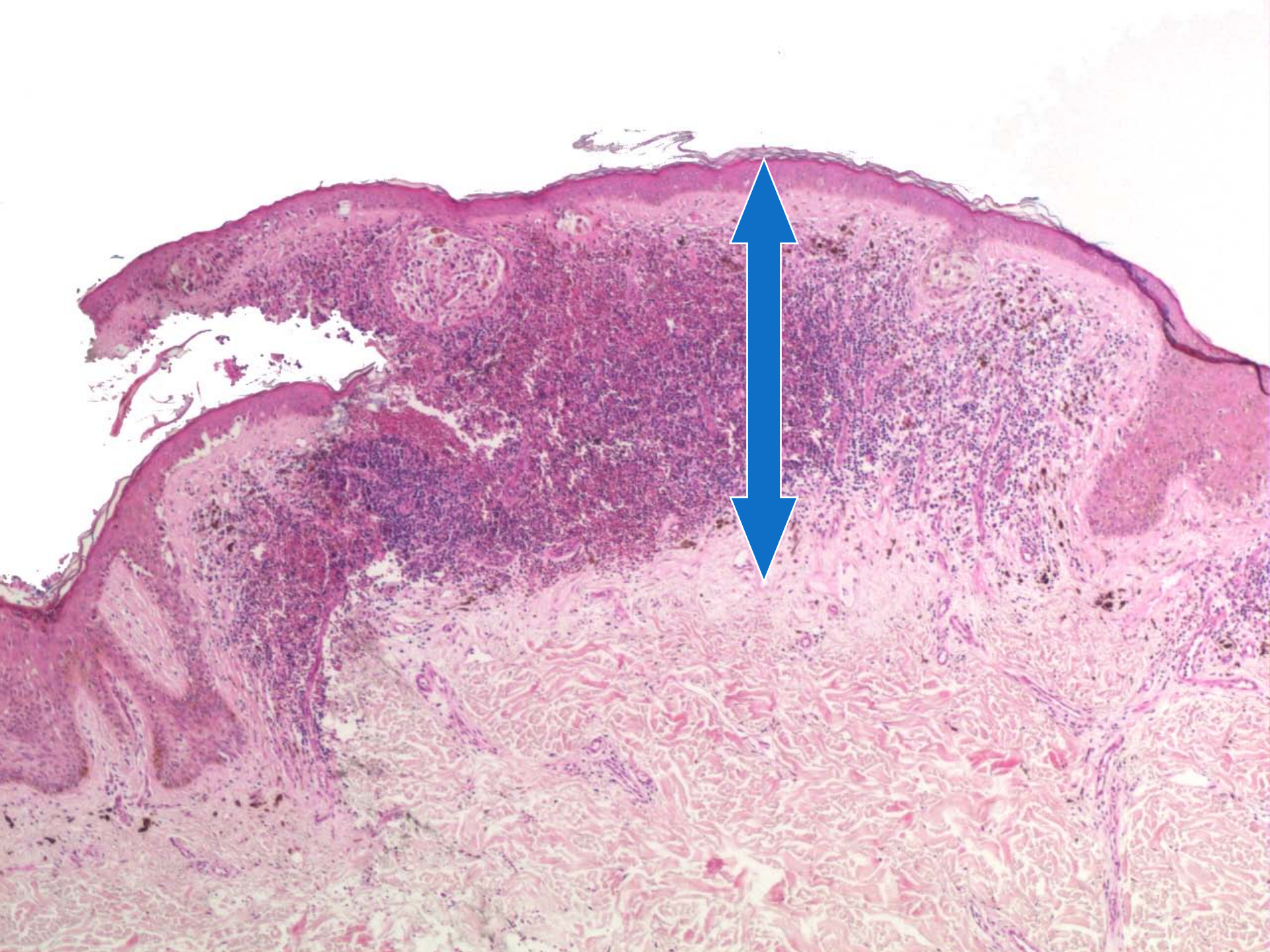


Measuring the Melanoma



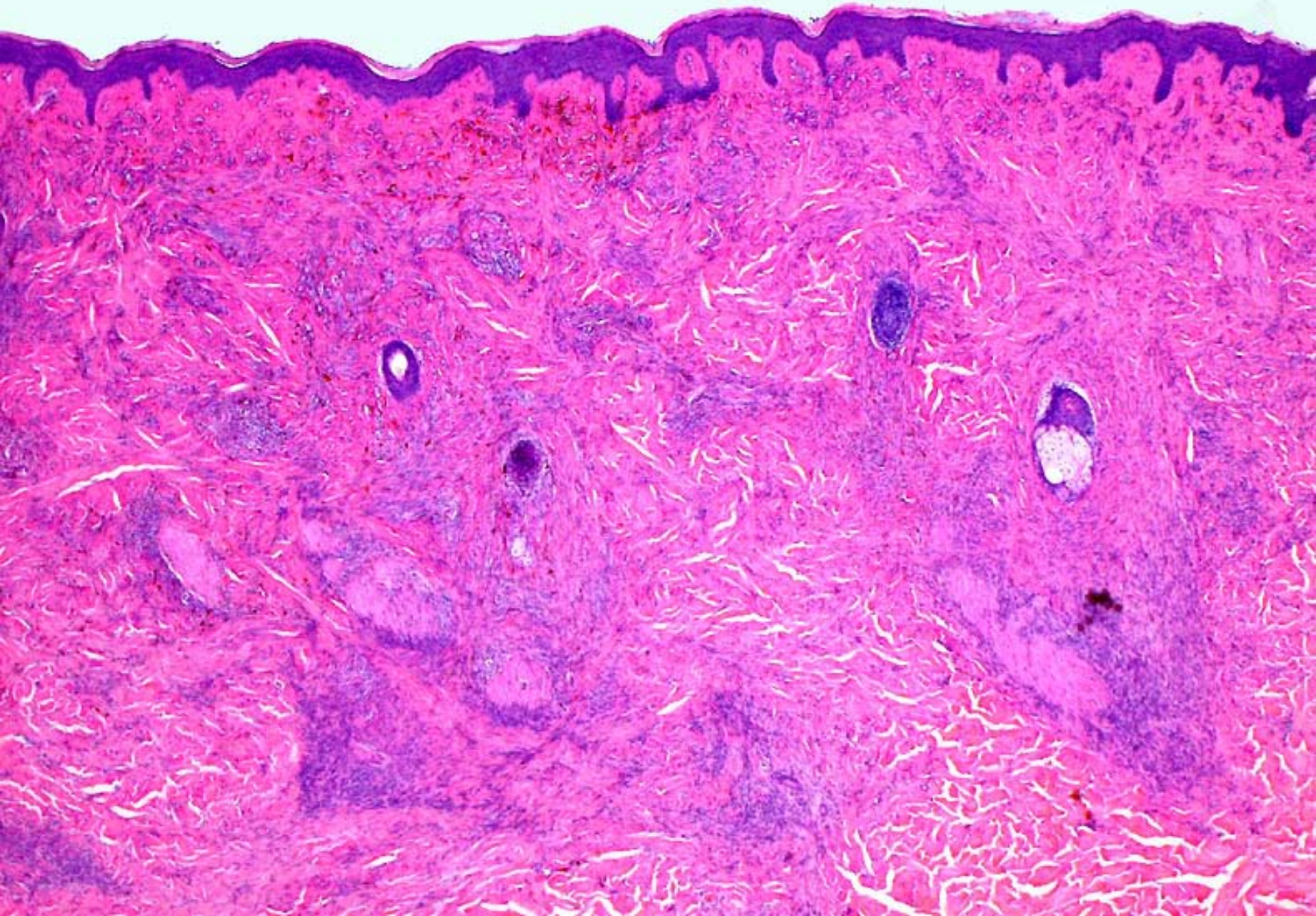


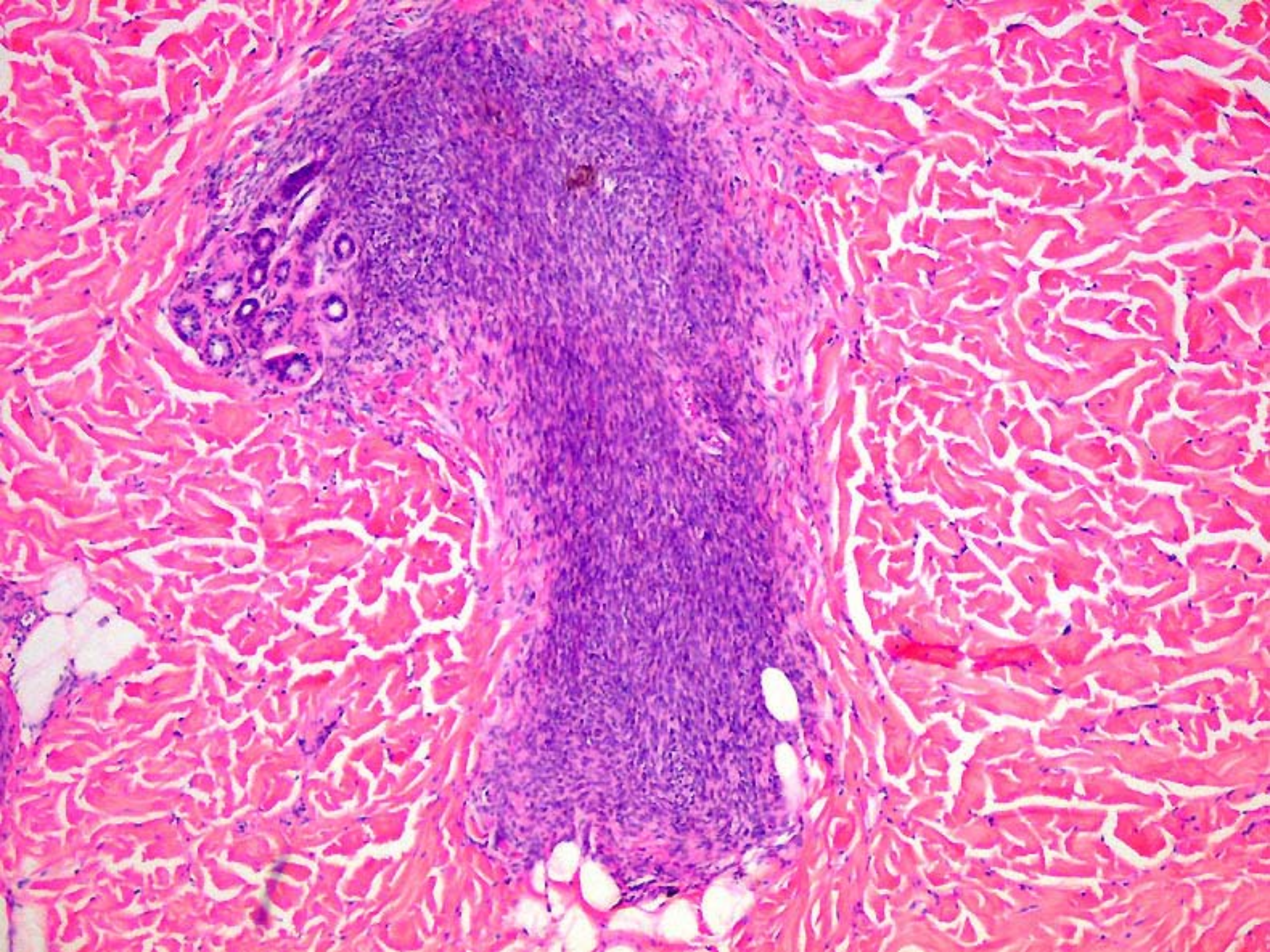


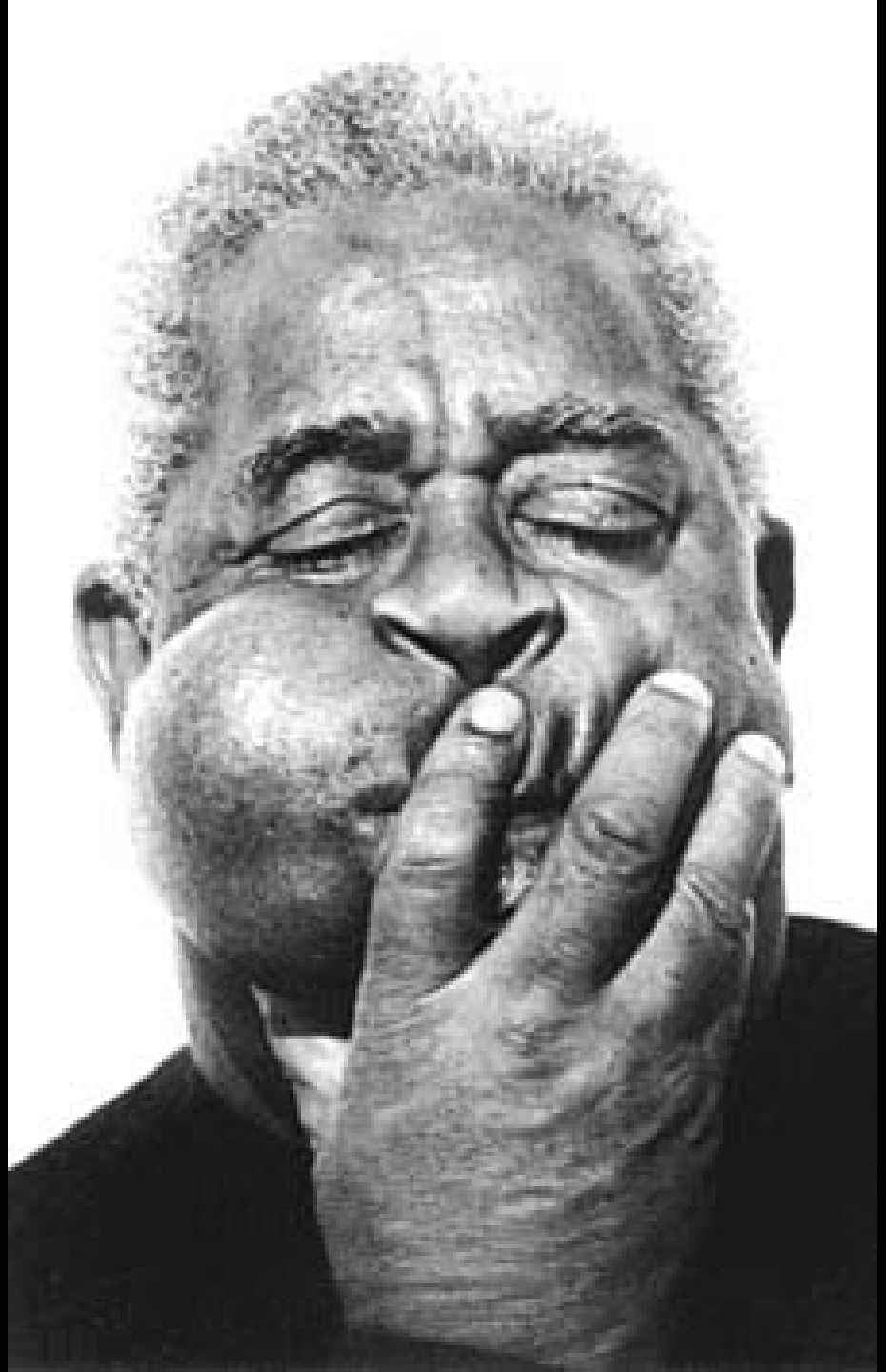


Measuring the Melanoma

- Measure from granular layer to the deepest extent of the dermal component
- Measure at right angles to surface of skin above tumor, avoid tangential sections
- Avoid hair follicles/adnexal structures
  - Atypical melanocytes in a column perpendicular to the epidermis are probably periappendageal
- Take at least 3 measurements

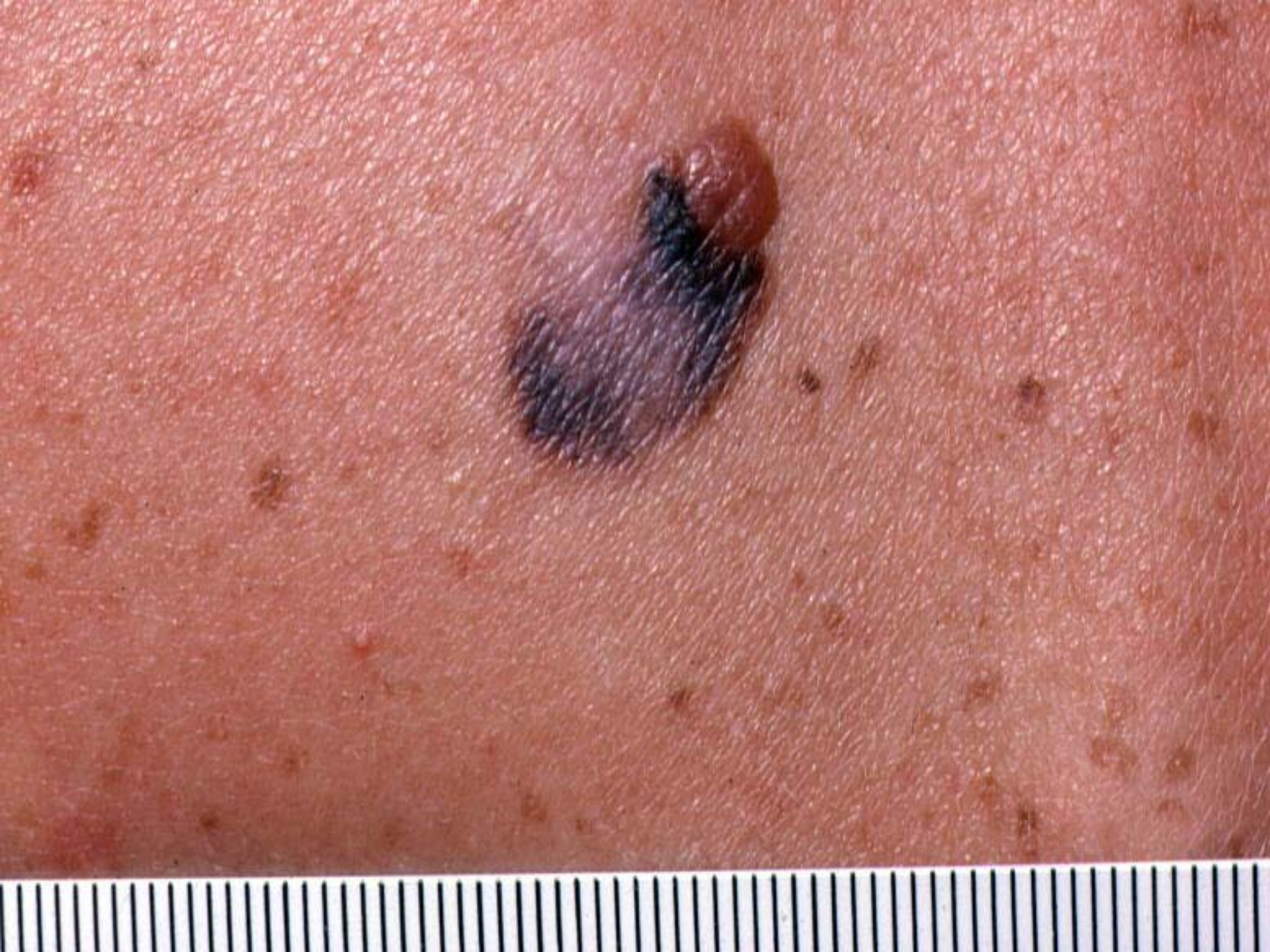


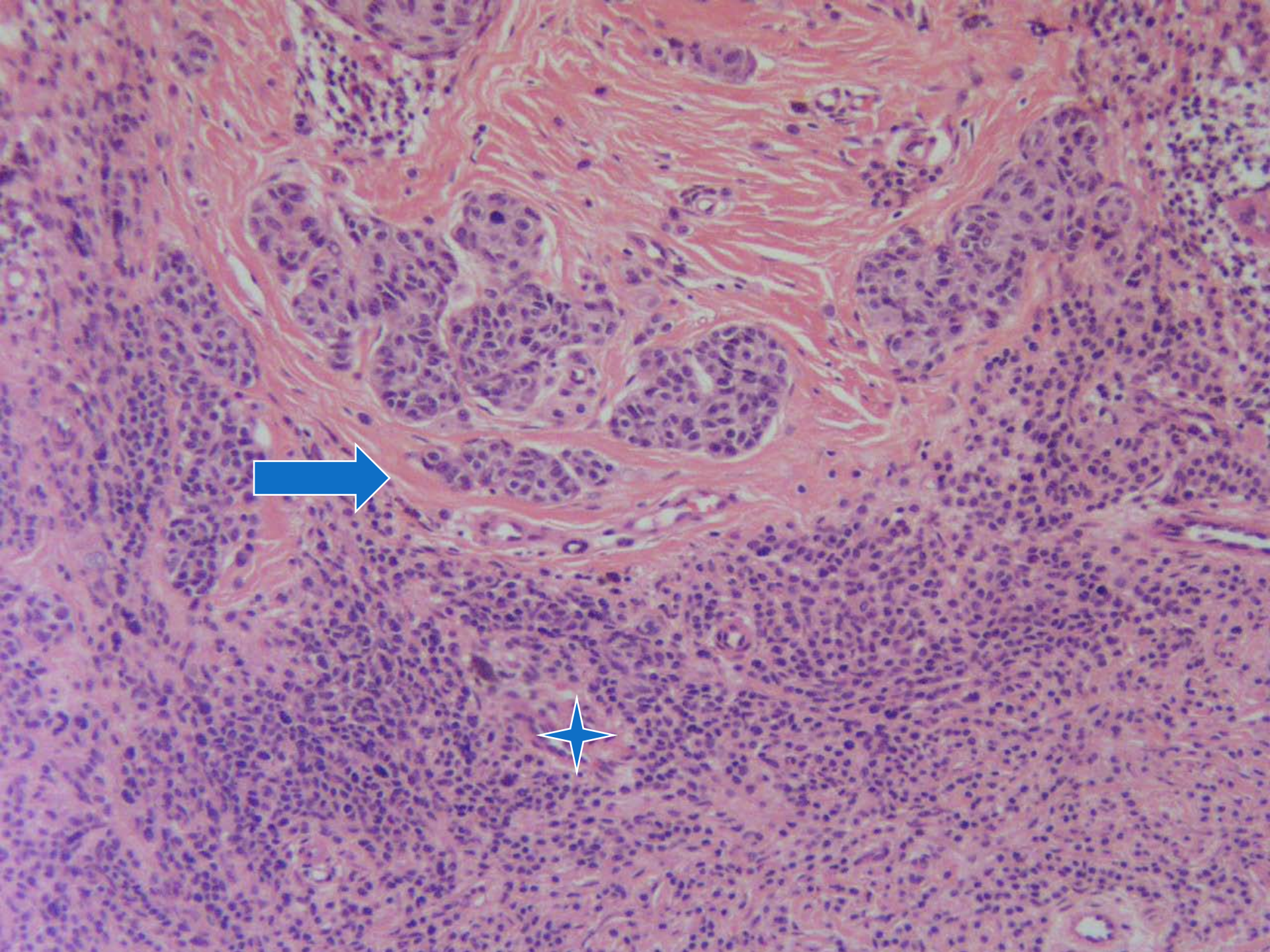


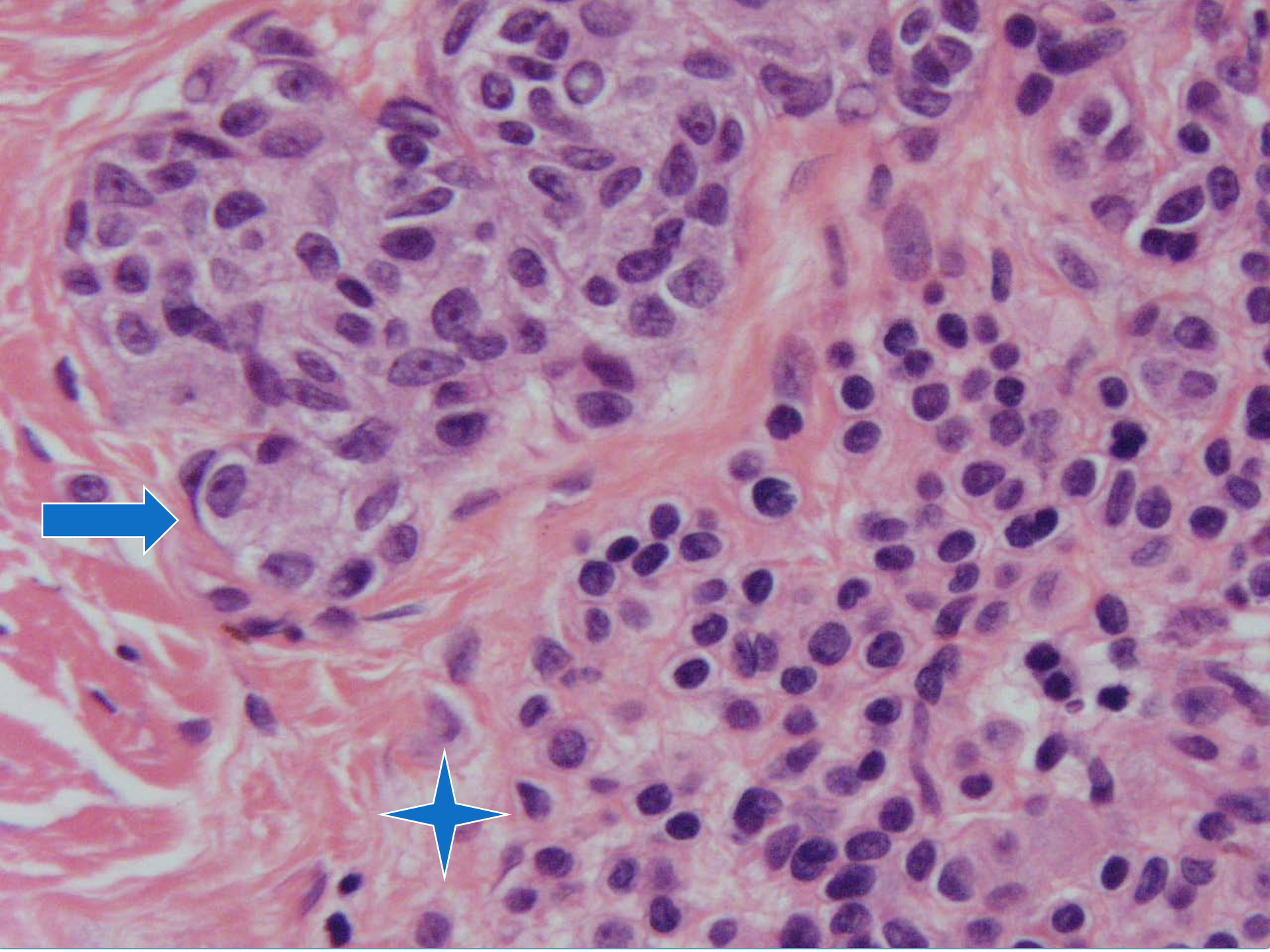


Special Situations

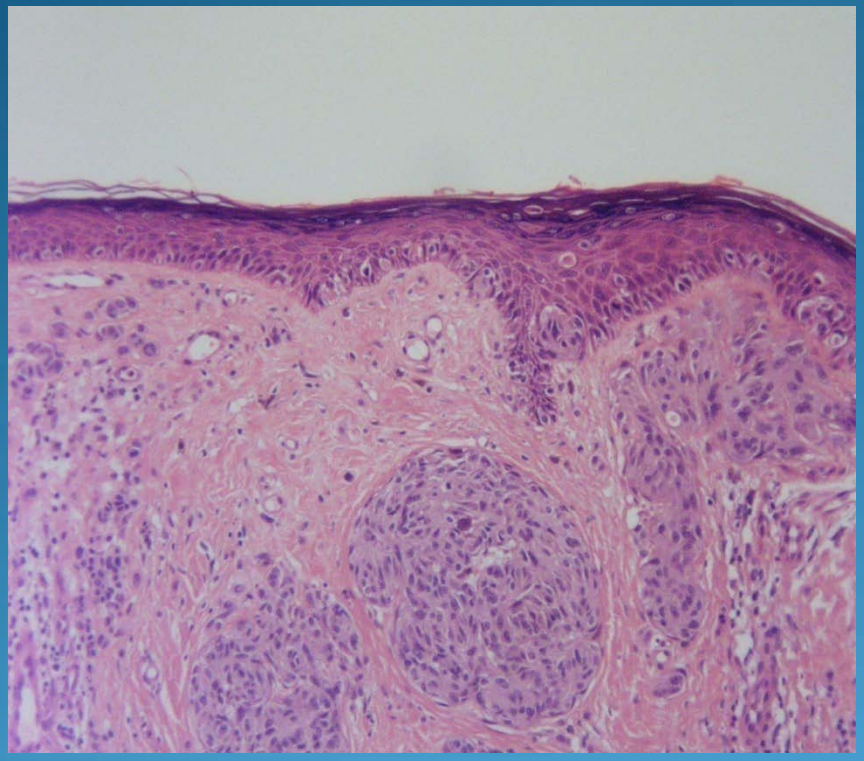
- Arising with pre-existing melanocytic nevus
- Prior biopsy or excision
- Ulceration
- Epidermal thickness
- Polypoid melanomas
- Verrucous melanomas
- Perineural invasion
- Mucosal melanomas
- Melanomas in soft tissue



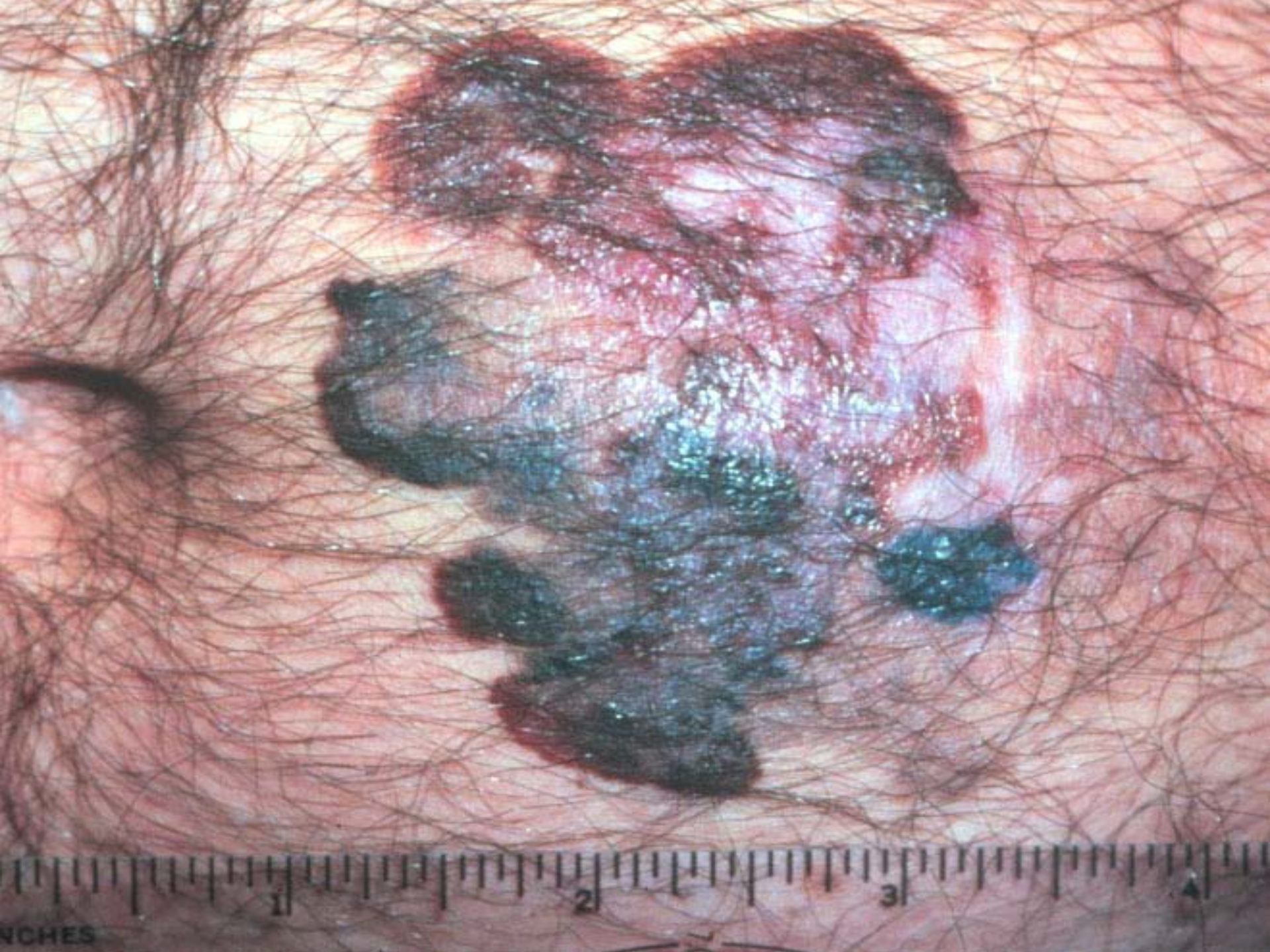




Melanoma Arising with Melanocytic Nevus

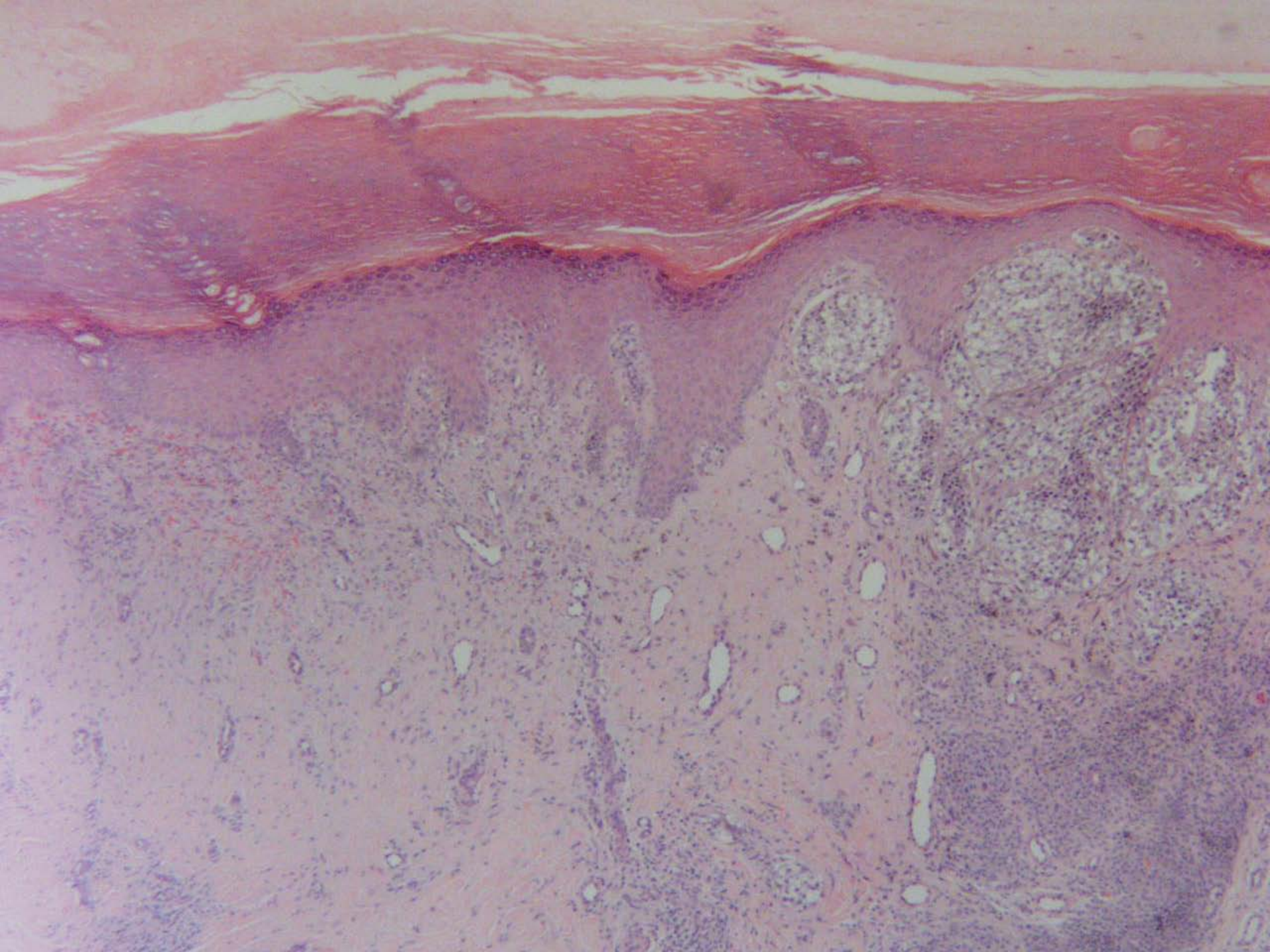


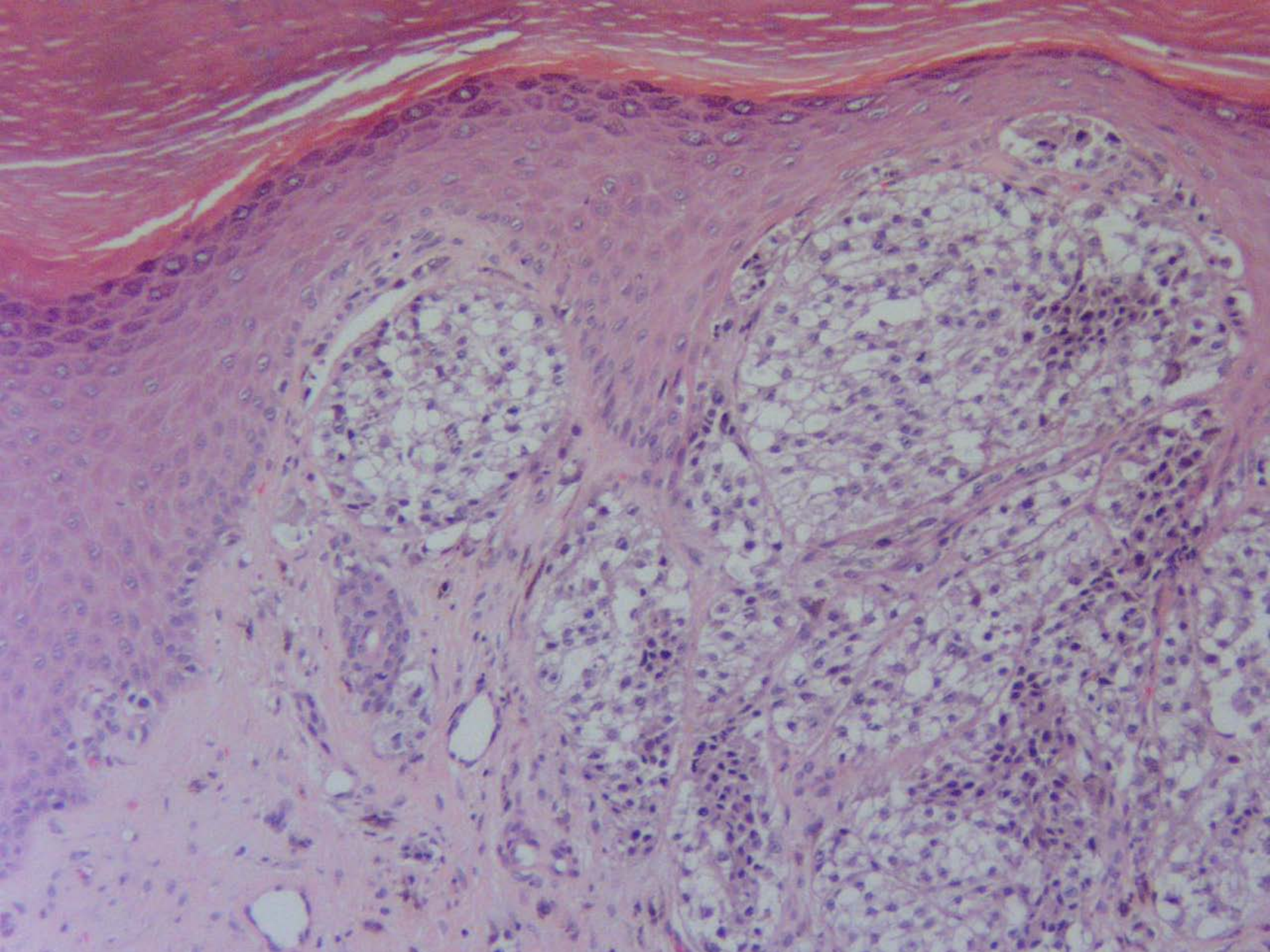
- Common problem
- Morphology
- p53, Ki67-marginally helpful
- Disclaimer about the true biological potential


1
2
3
4
NCHES

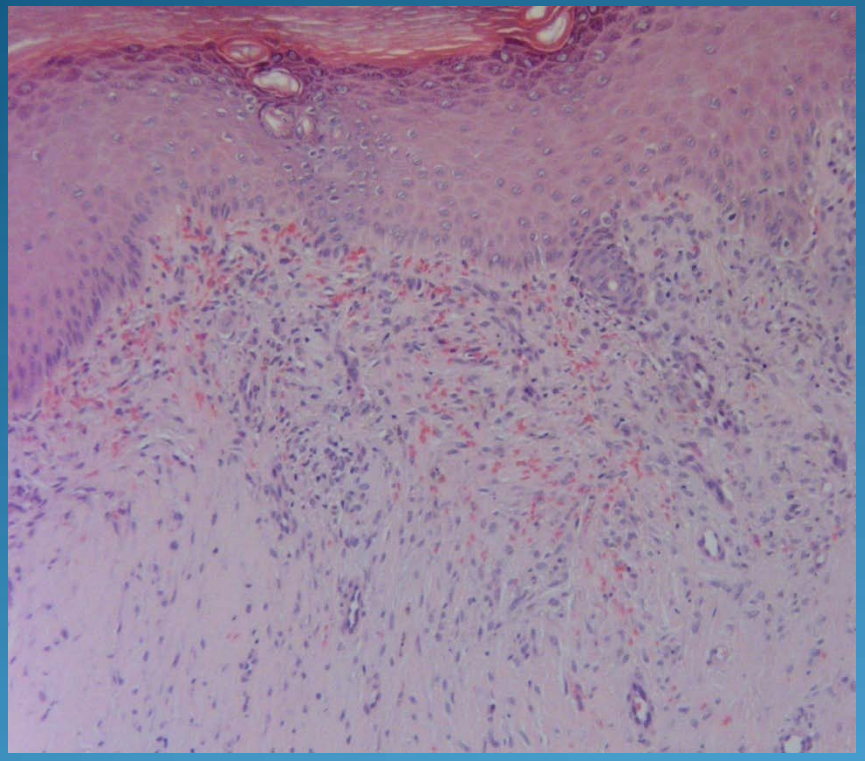
Initial Punch Biopsy

Melanoma
Level II
Thickness 0.47 mm
Extending to the punch margins
Recommend Complete Excision

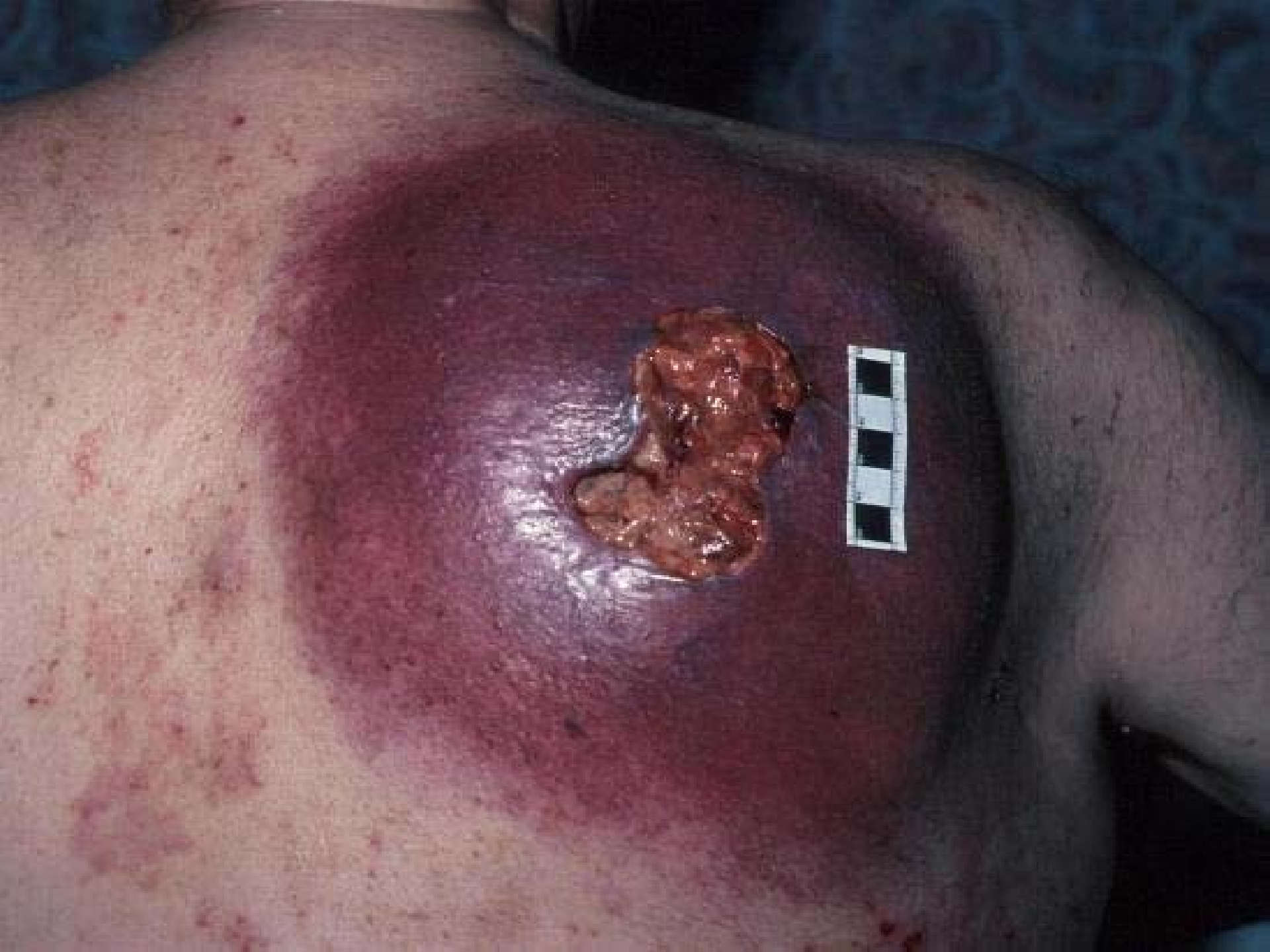




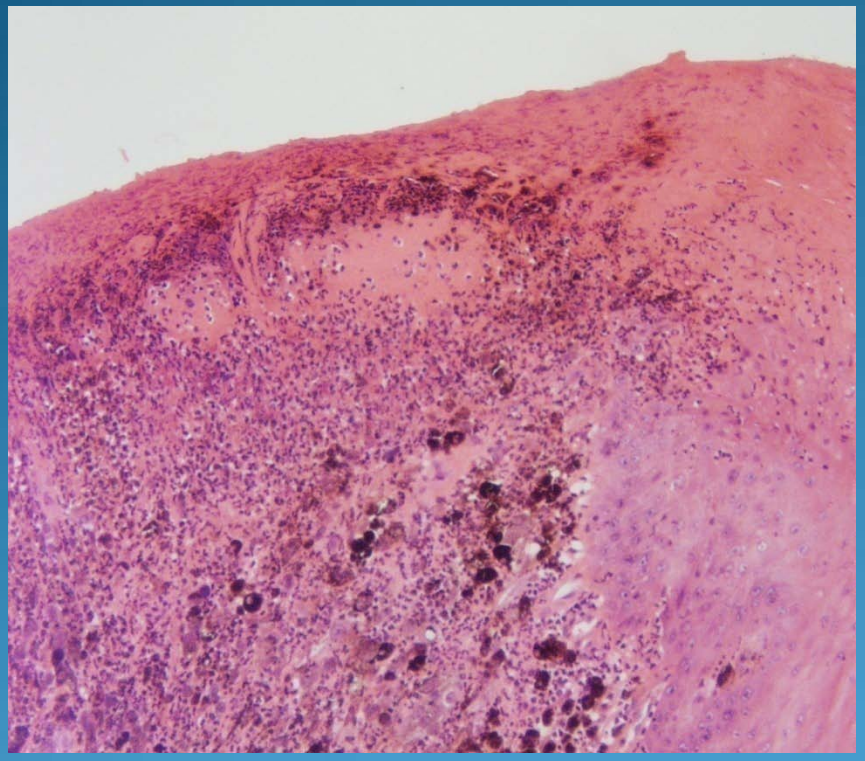
Prior Biopsy or Excision



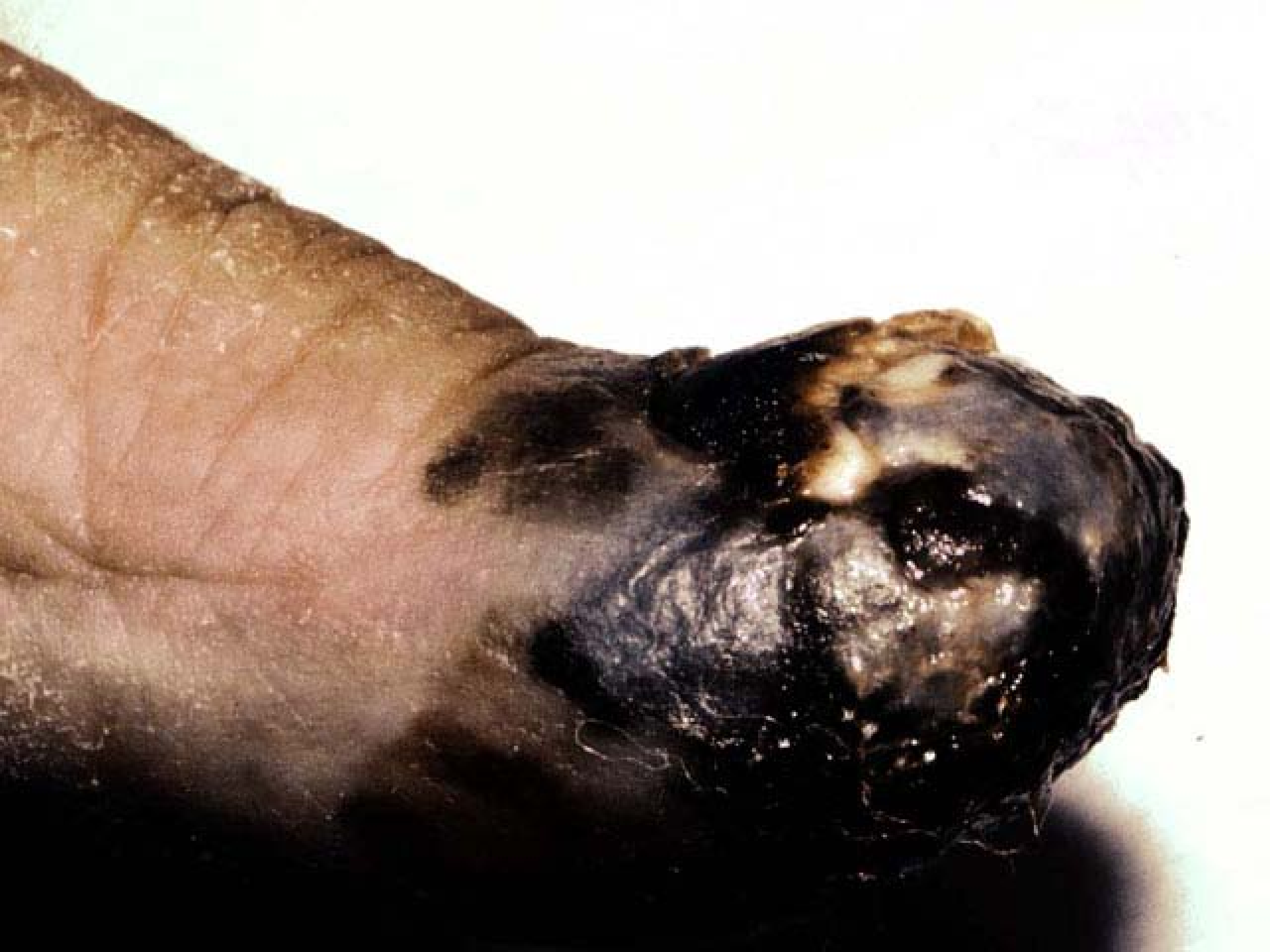
- Clark's Level II or IV?
- Depths are not additive
- Measure melanoma away from prior biopsy site

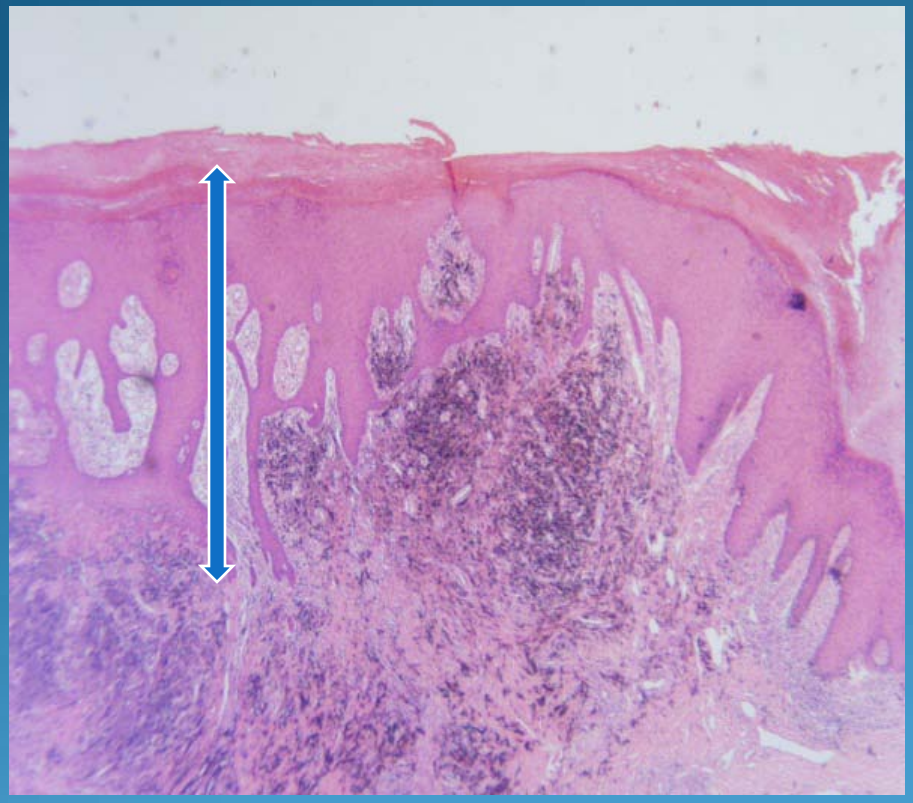


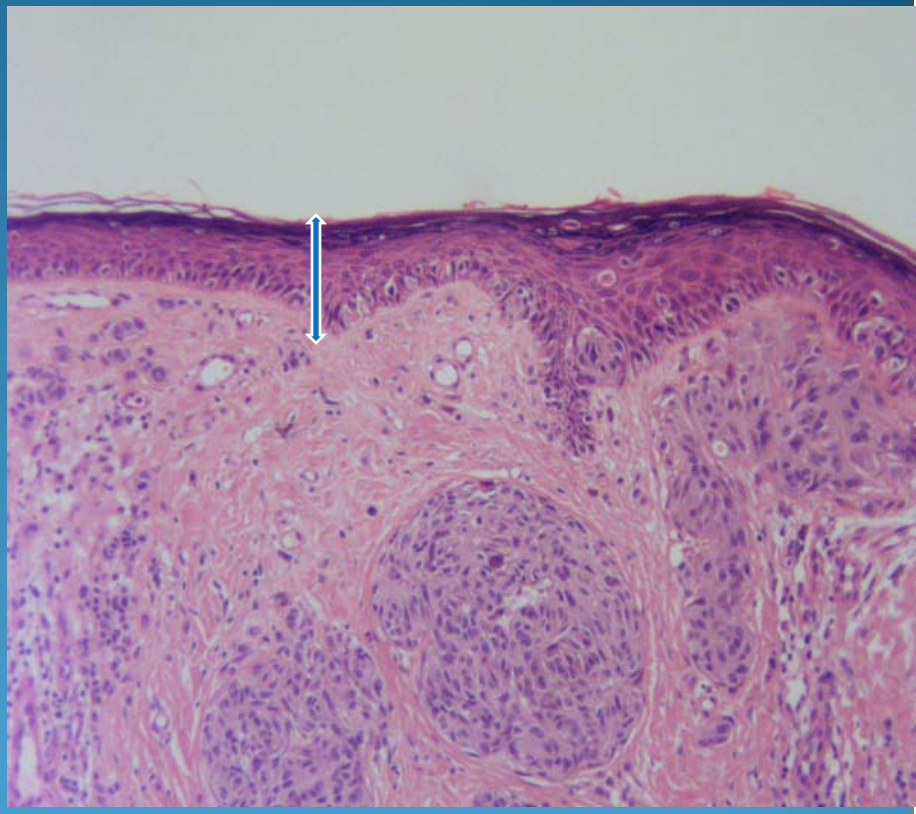
Ulceration



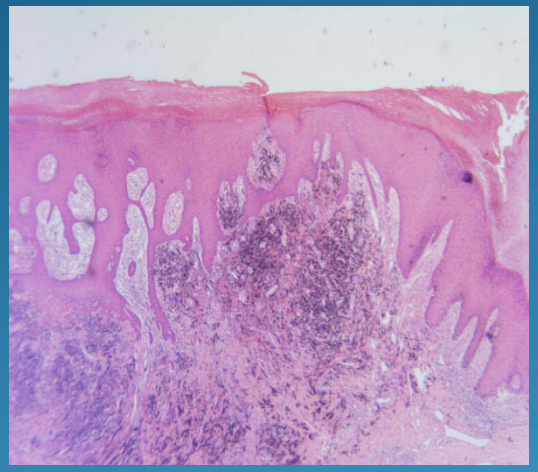
- Measure from base of ulcer to deepest dermal invasion
- Disclaimer that measurement may underestimate true thickness

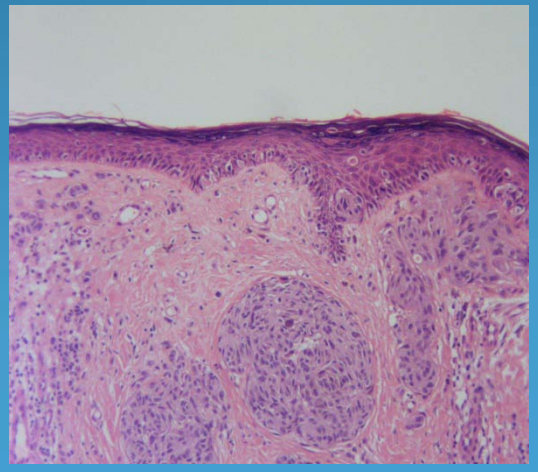






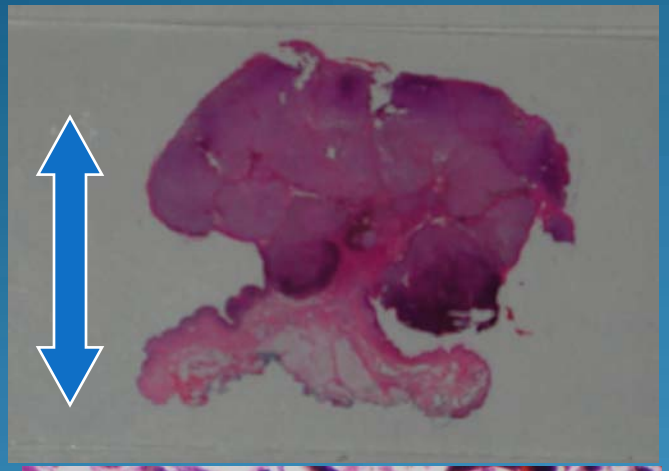
Epidermal Thickness

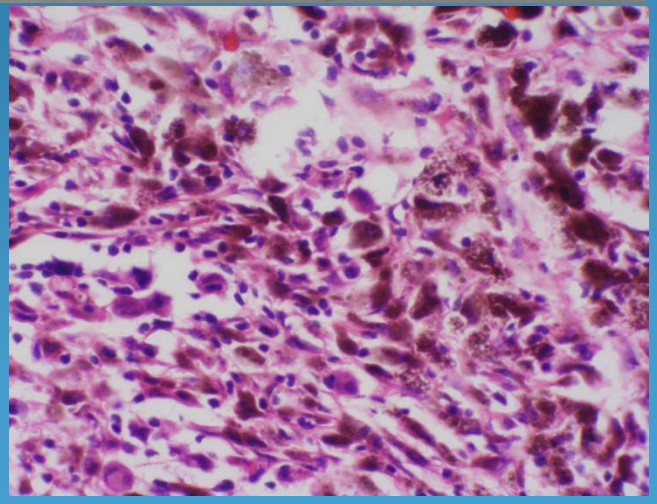




- Acral melanomas increased in Asians and African-Americans
- Melanomas of acral skin may have epidermal hyperplasia twice as thick as non-acral skin
- If epidermis is thickened, should note that much of measured thickness is due to epidermal hyperplasia

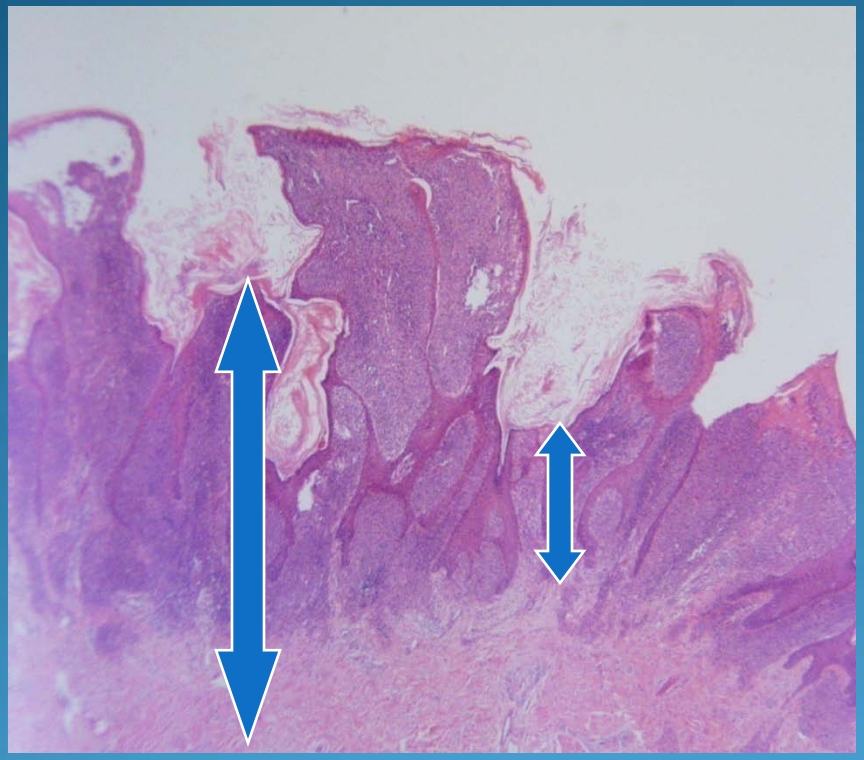
Polypoid Melanomas





- Clark's levels break down
- Measure thickness
- Consider multiple measurements

Verrucous Melanomas



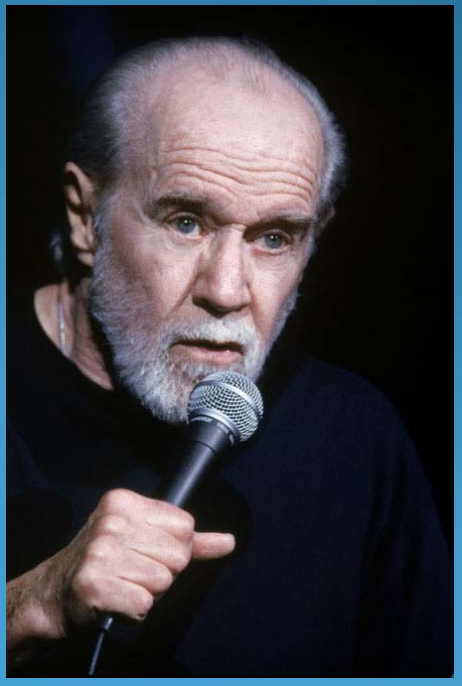
- Take an average of peak to trough
- Report maximal, minimal, and mean

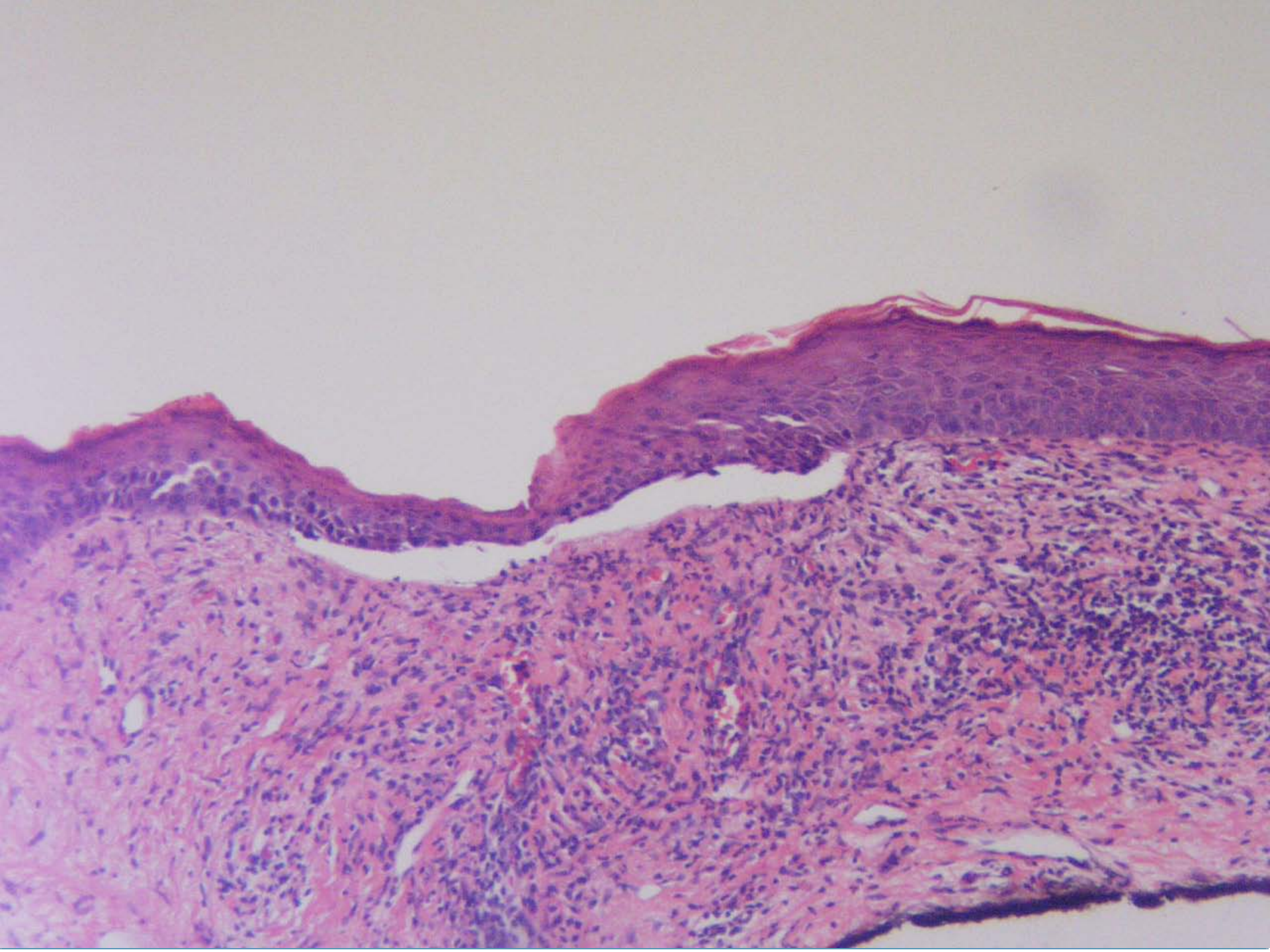
Although measuring a melanoma is the most critical component of the diagnosis,
there are several important special situations which may confound the measurement including:

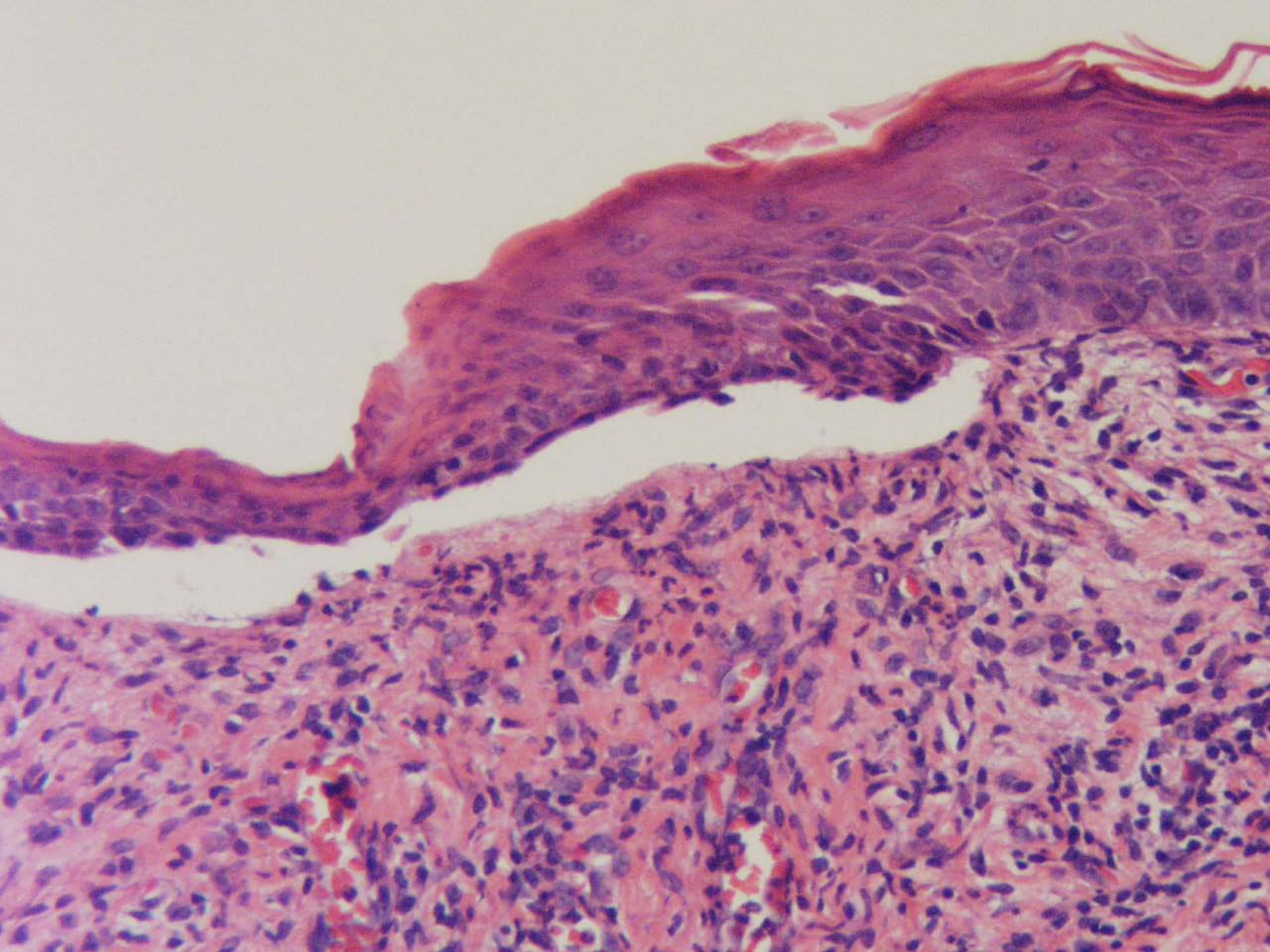
Anatomic Location
Epidermal Thickness
Unusual Variants

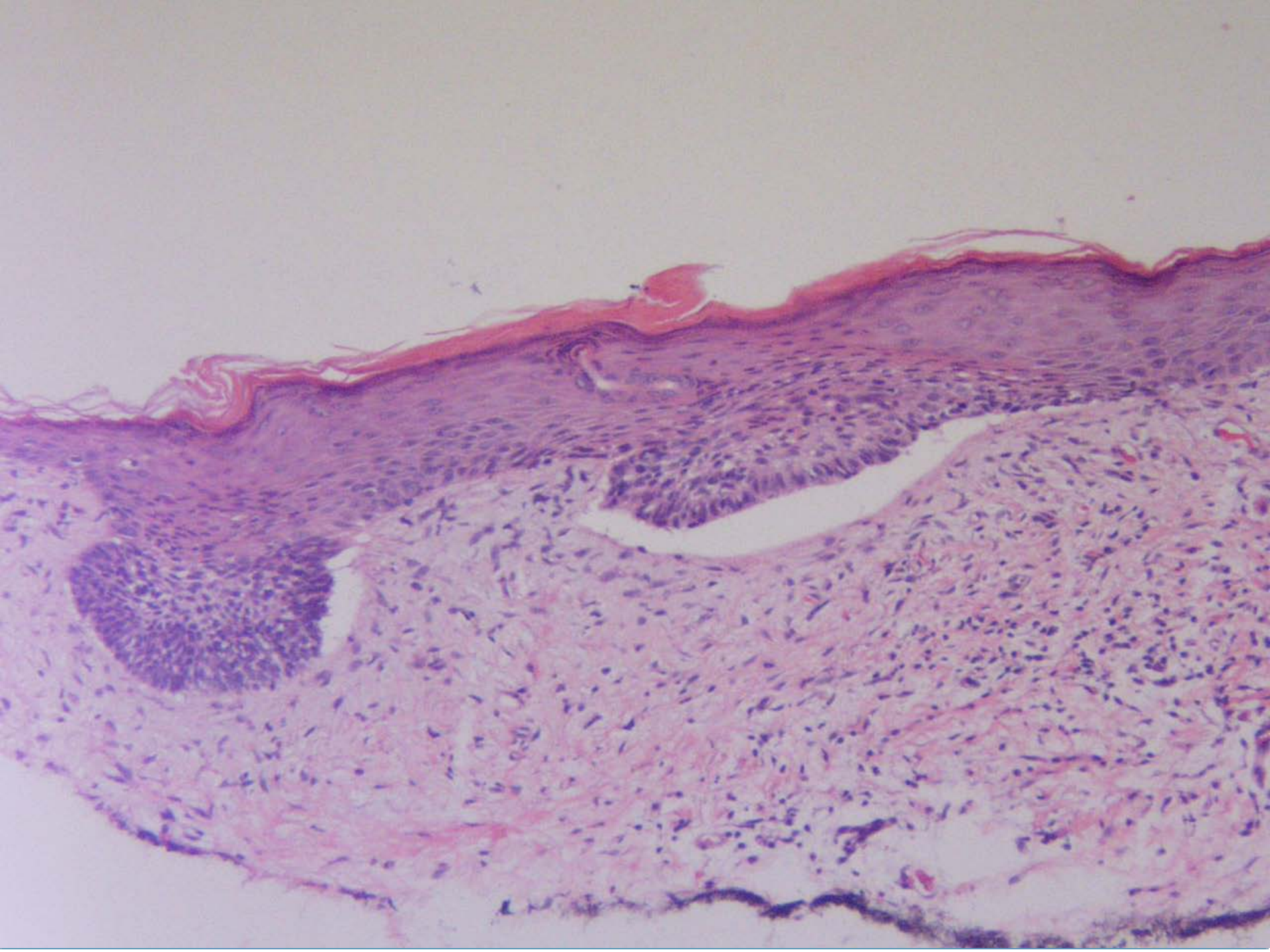
The Seven Things

- Low Power Objective-High Power Pathologist
- Measuring a Melanoma
- **The Best Special Stain**









When Do I Order Deepers?

Clues for Deeper Sections

Ulceration

Focal epidermal atypia

Equivocal adnexae

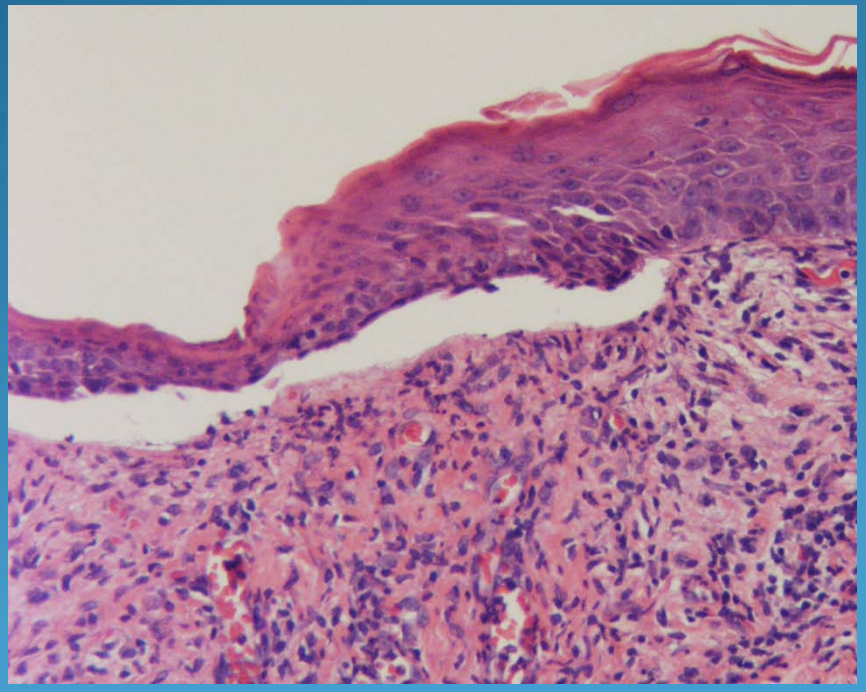
Stromal fibrosis

Empty dermal space

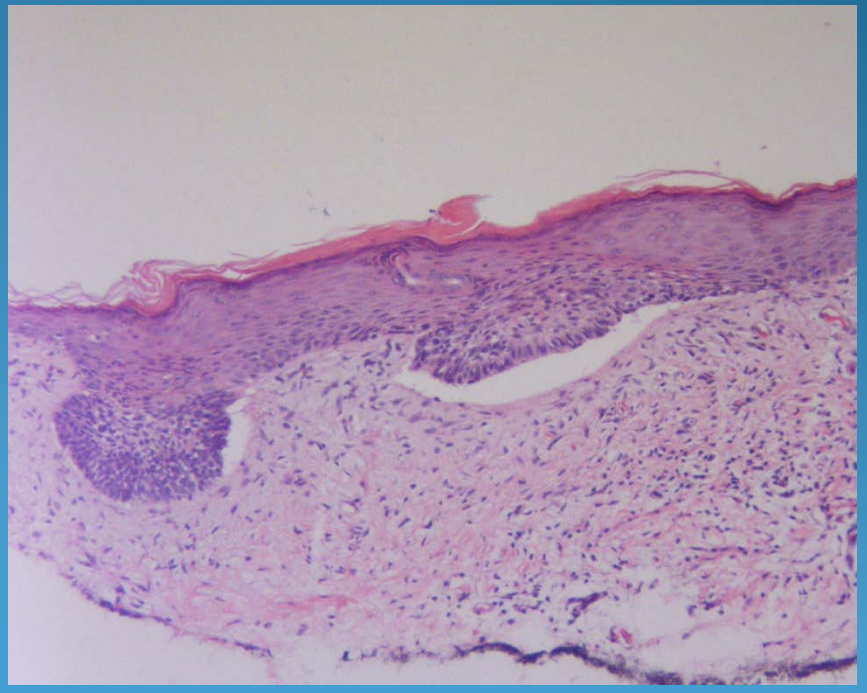
Microcalcifications

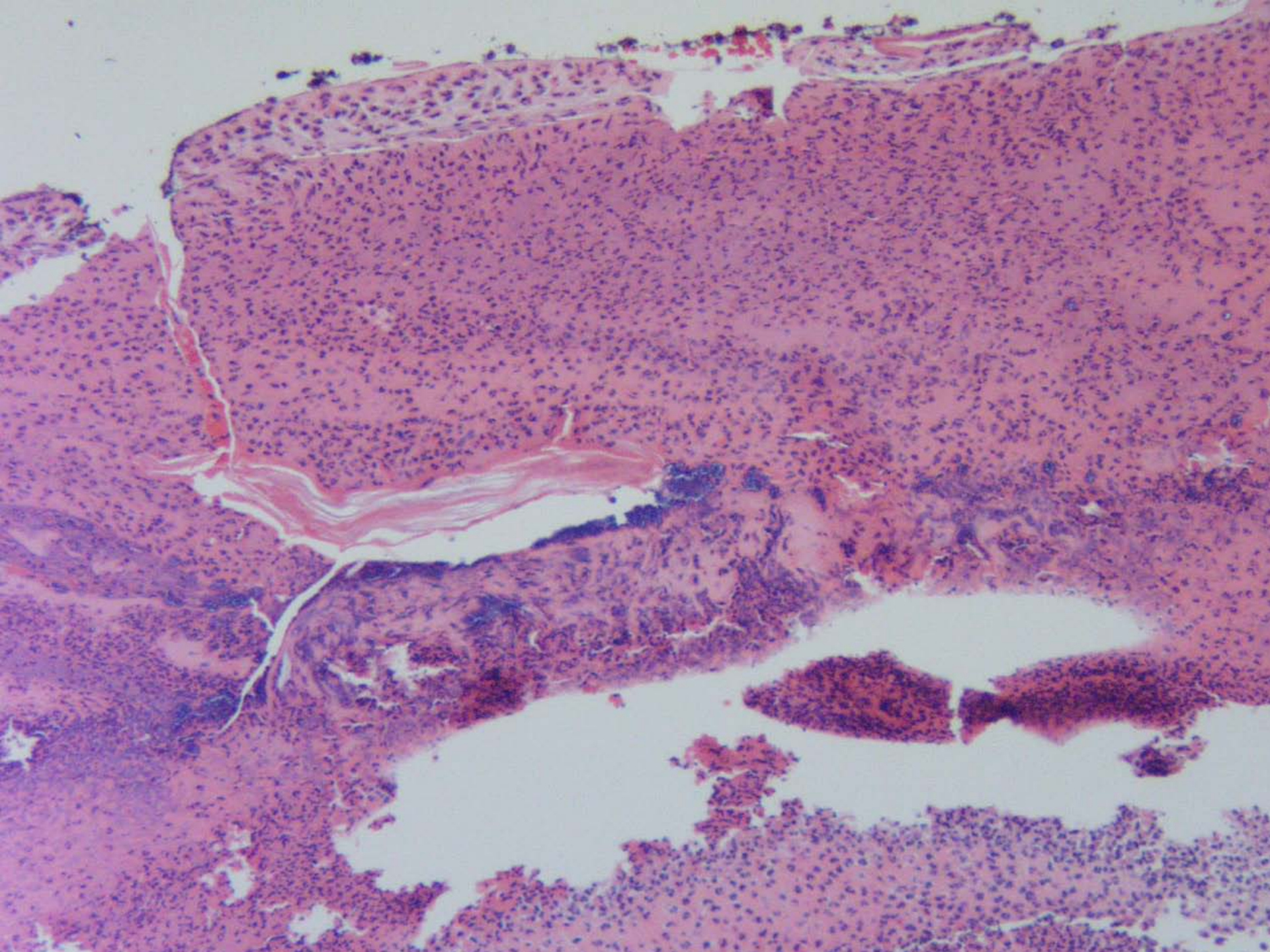
Am J Surg Pathol. 2000 Sep;24(9):1291-4.
Arch Dermatol. 2000 Apr;136(4):471-5.

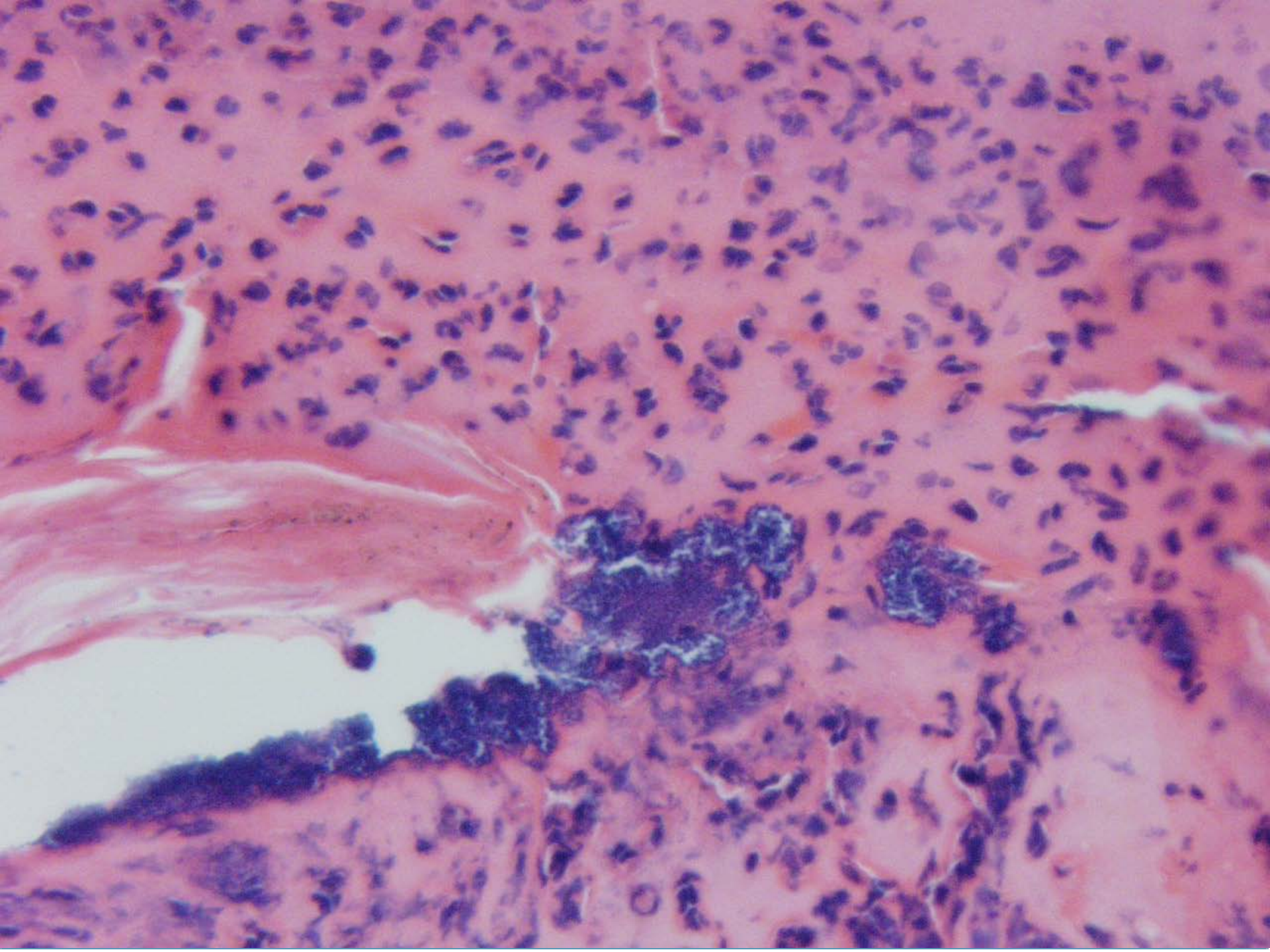
Initial Section

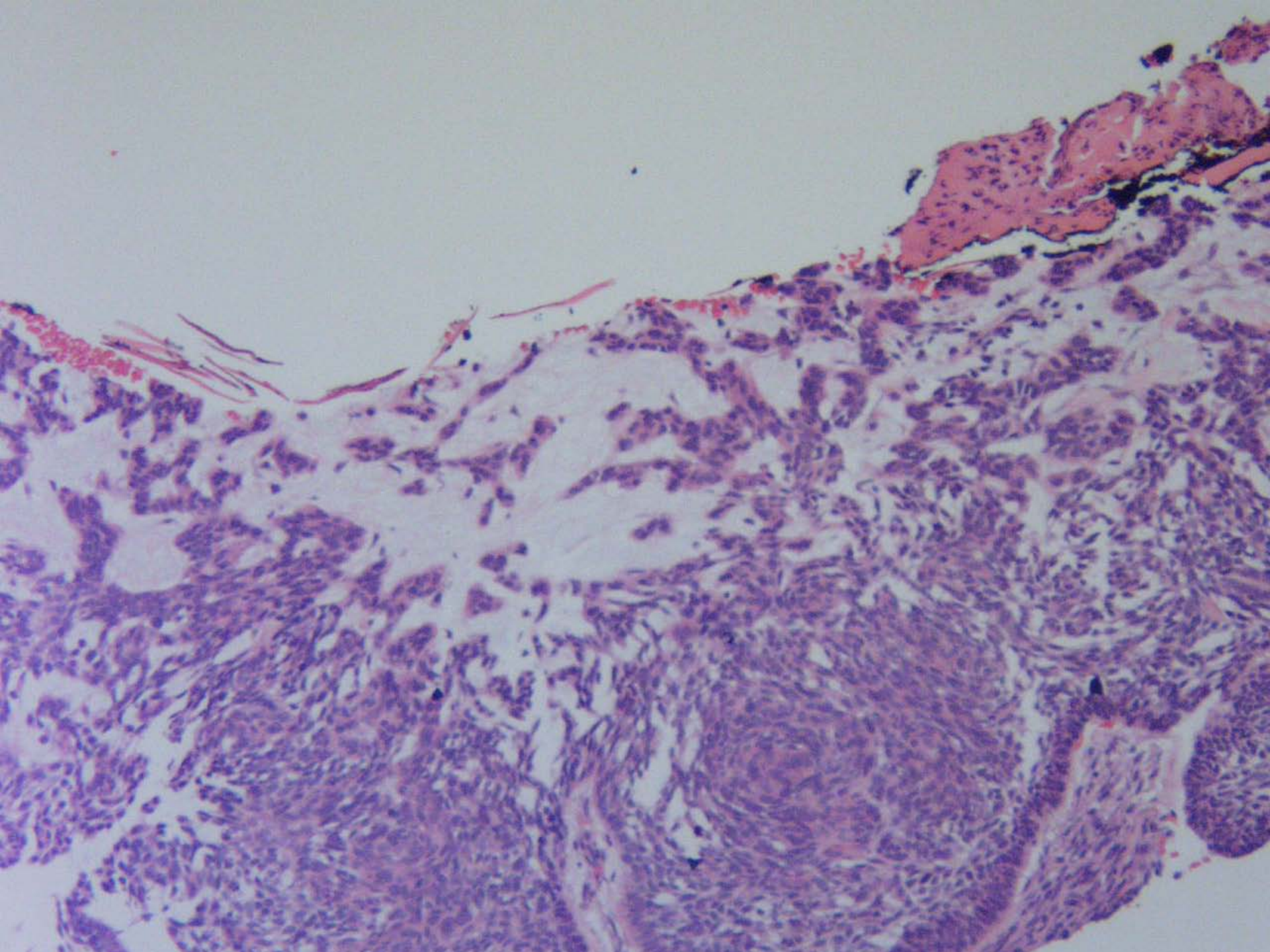


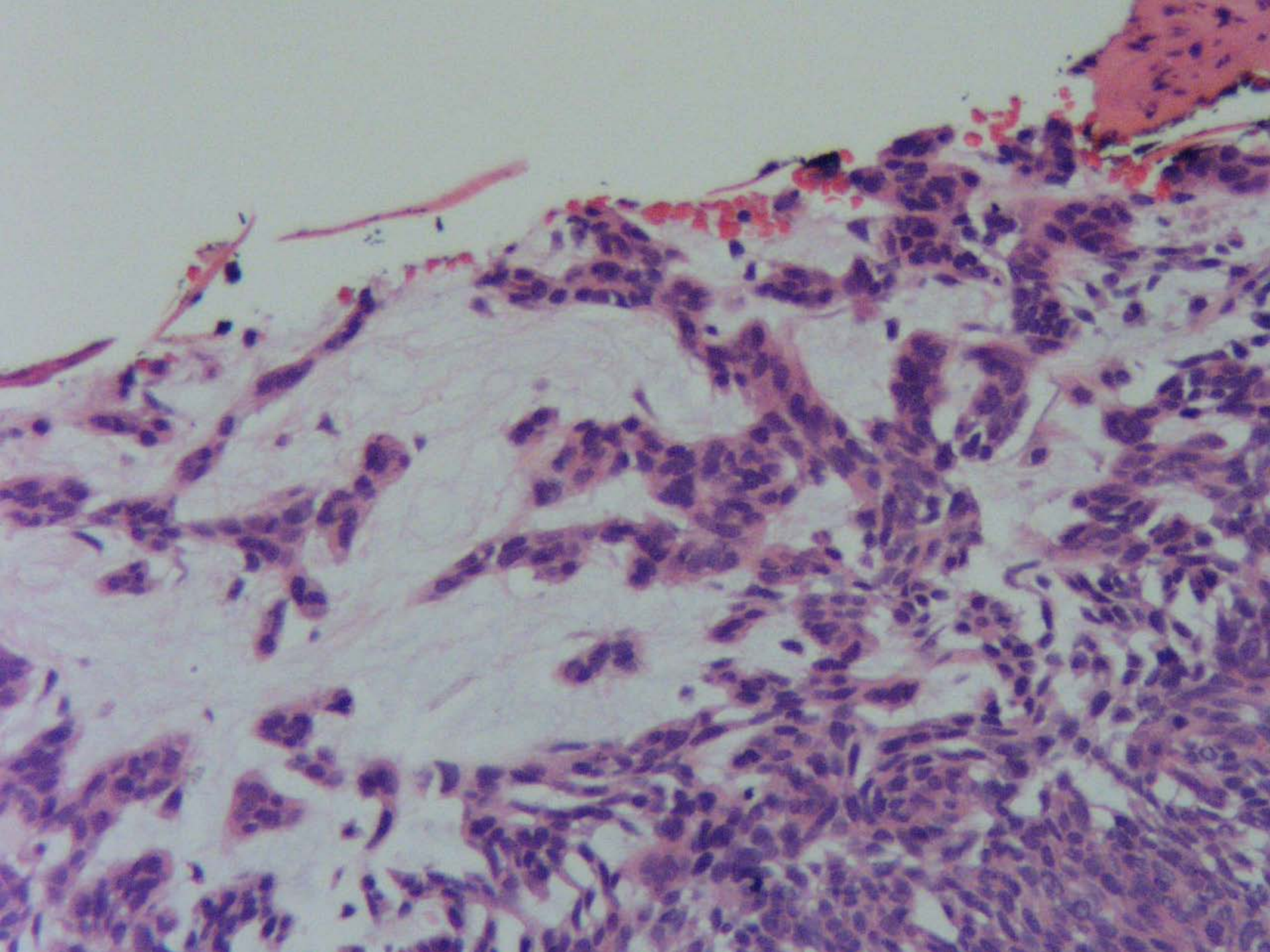
Deeper Section



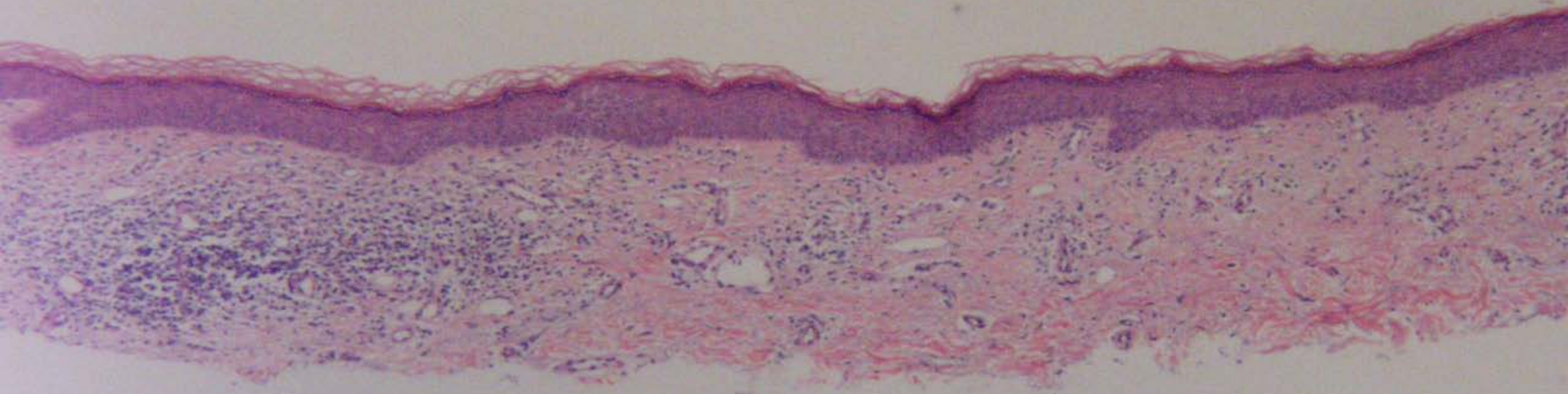


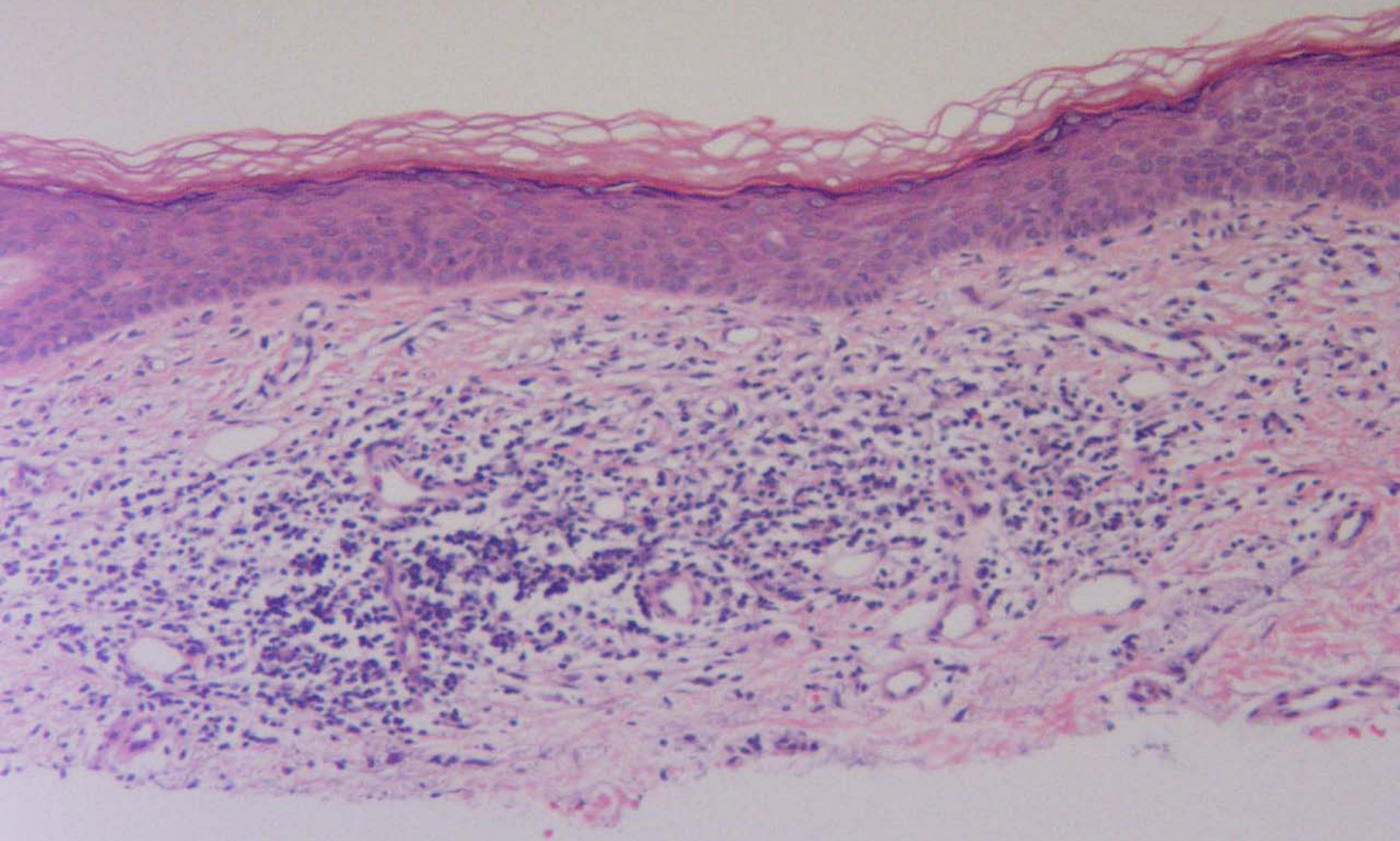


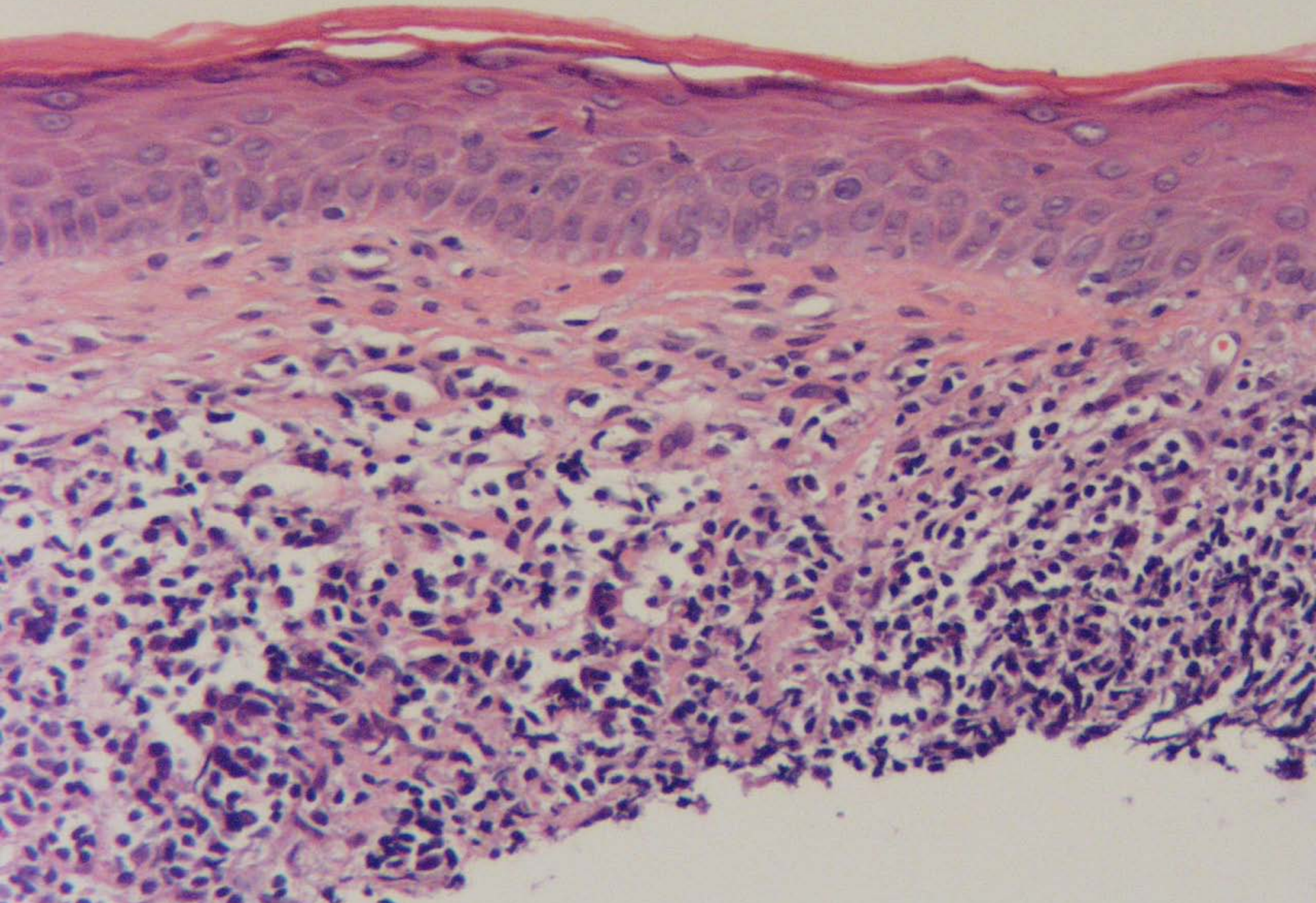


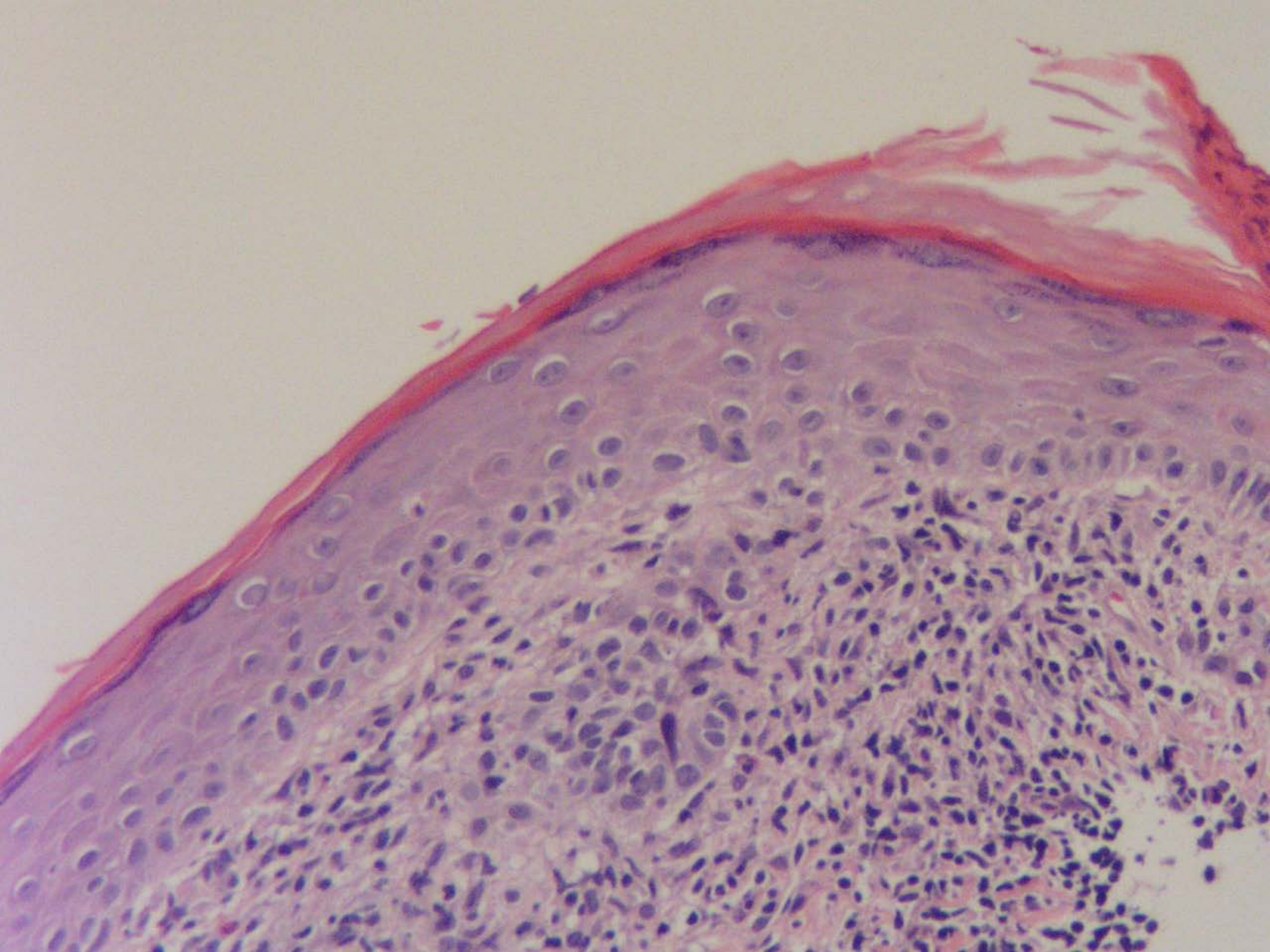


Basal Cell Carcinoma Arising with Initial Ulceration

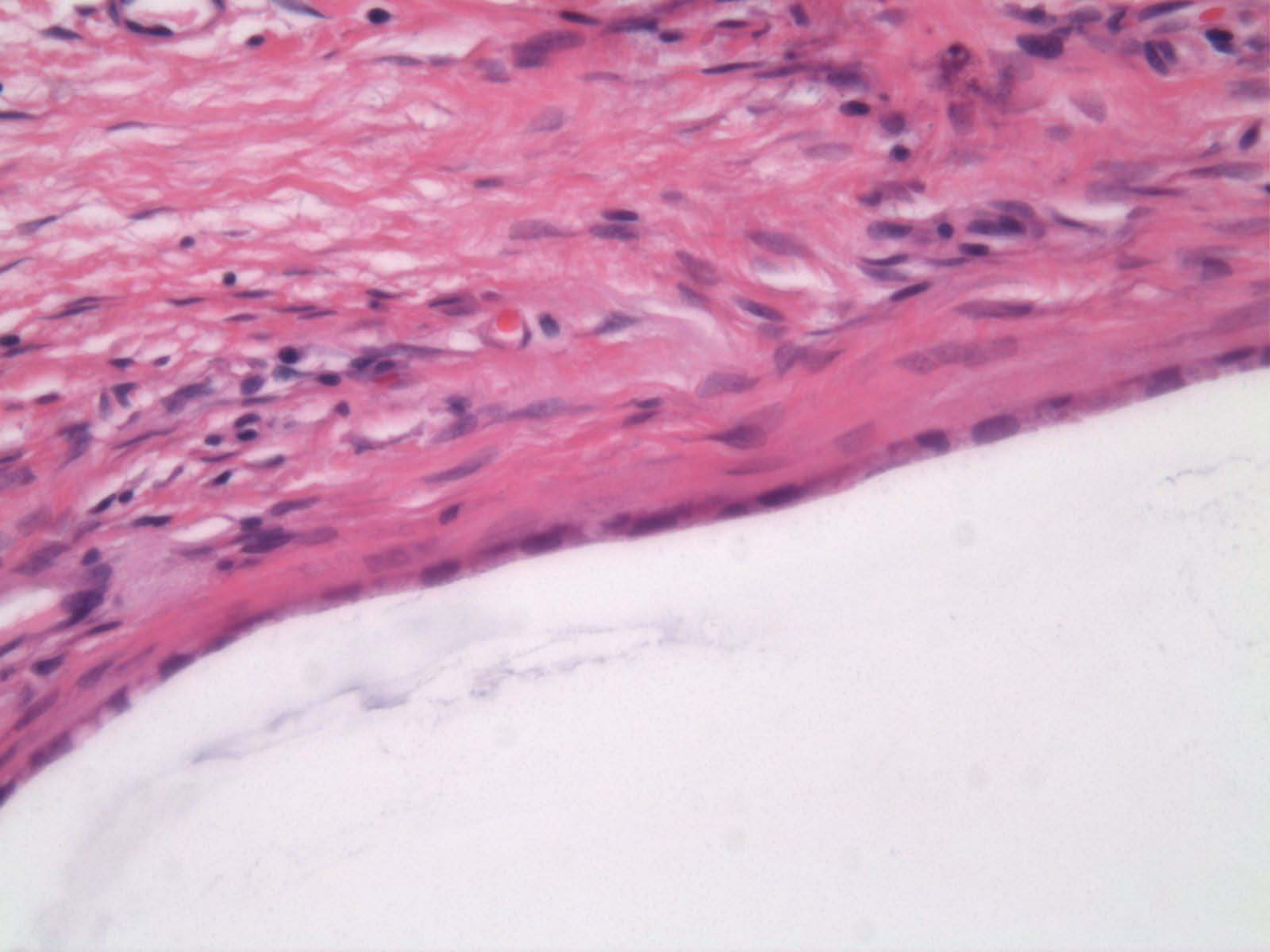


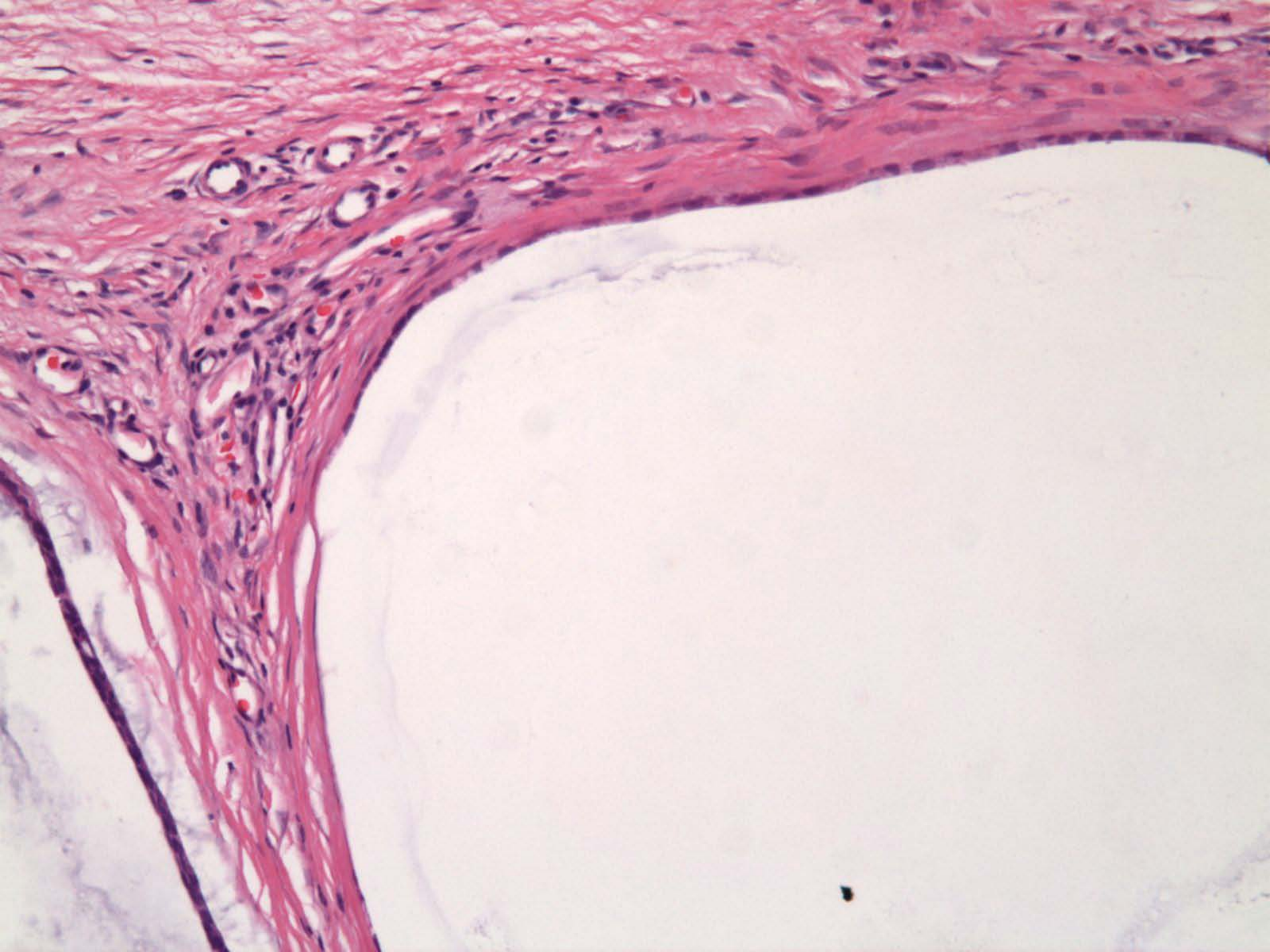


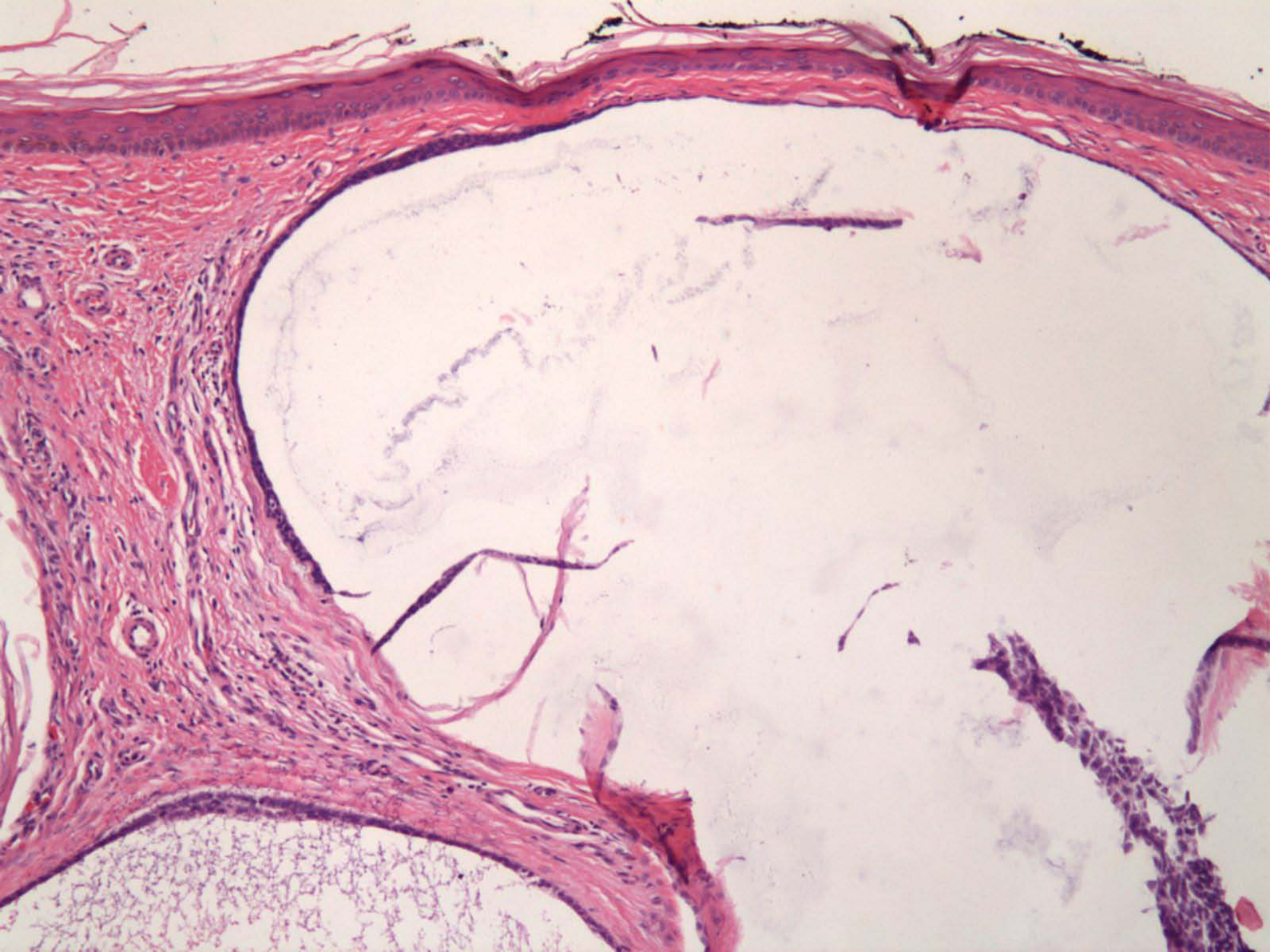


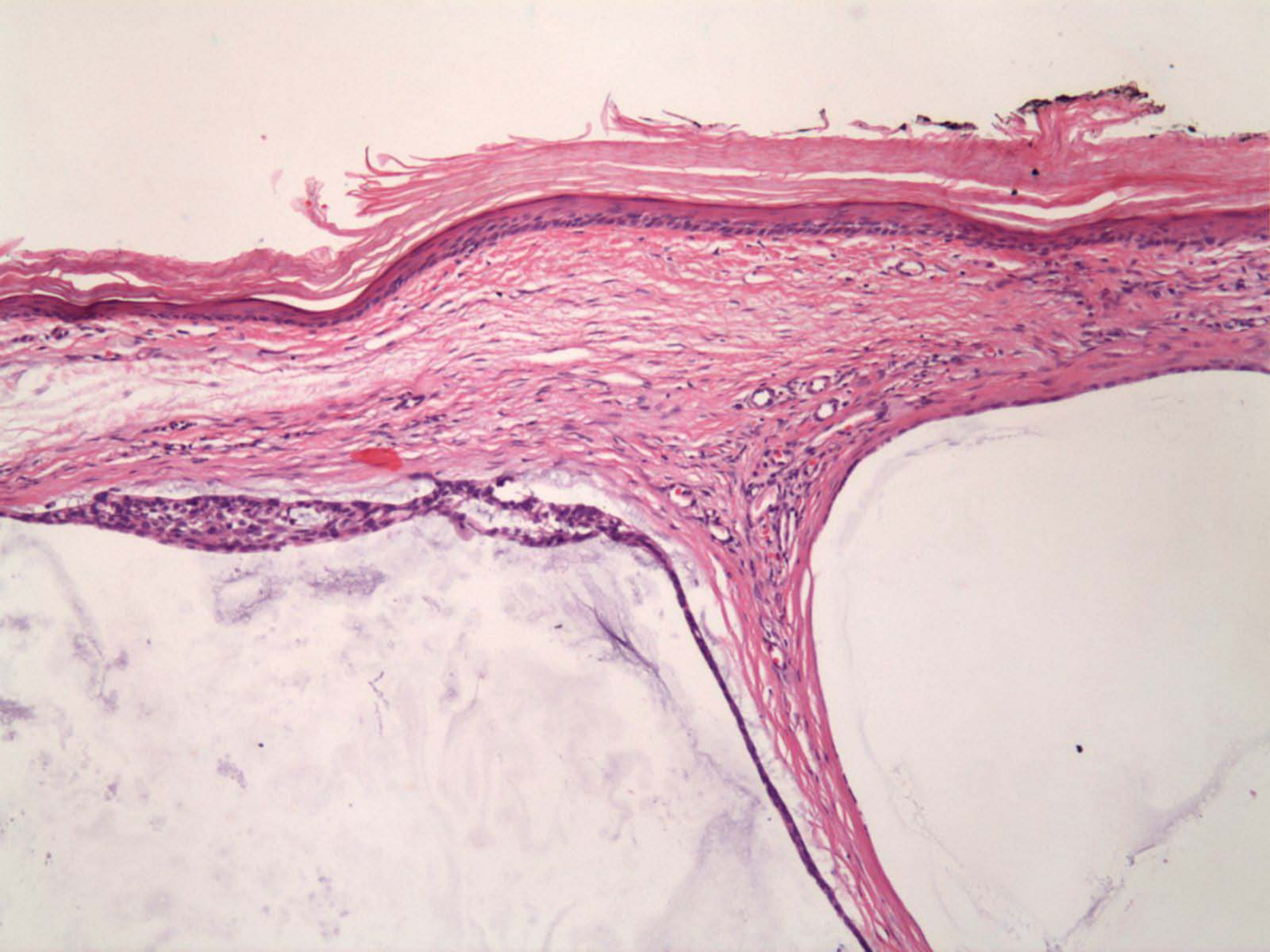


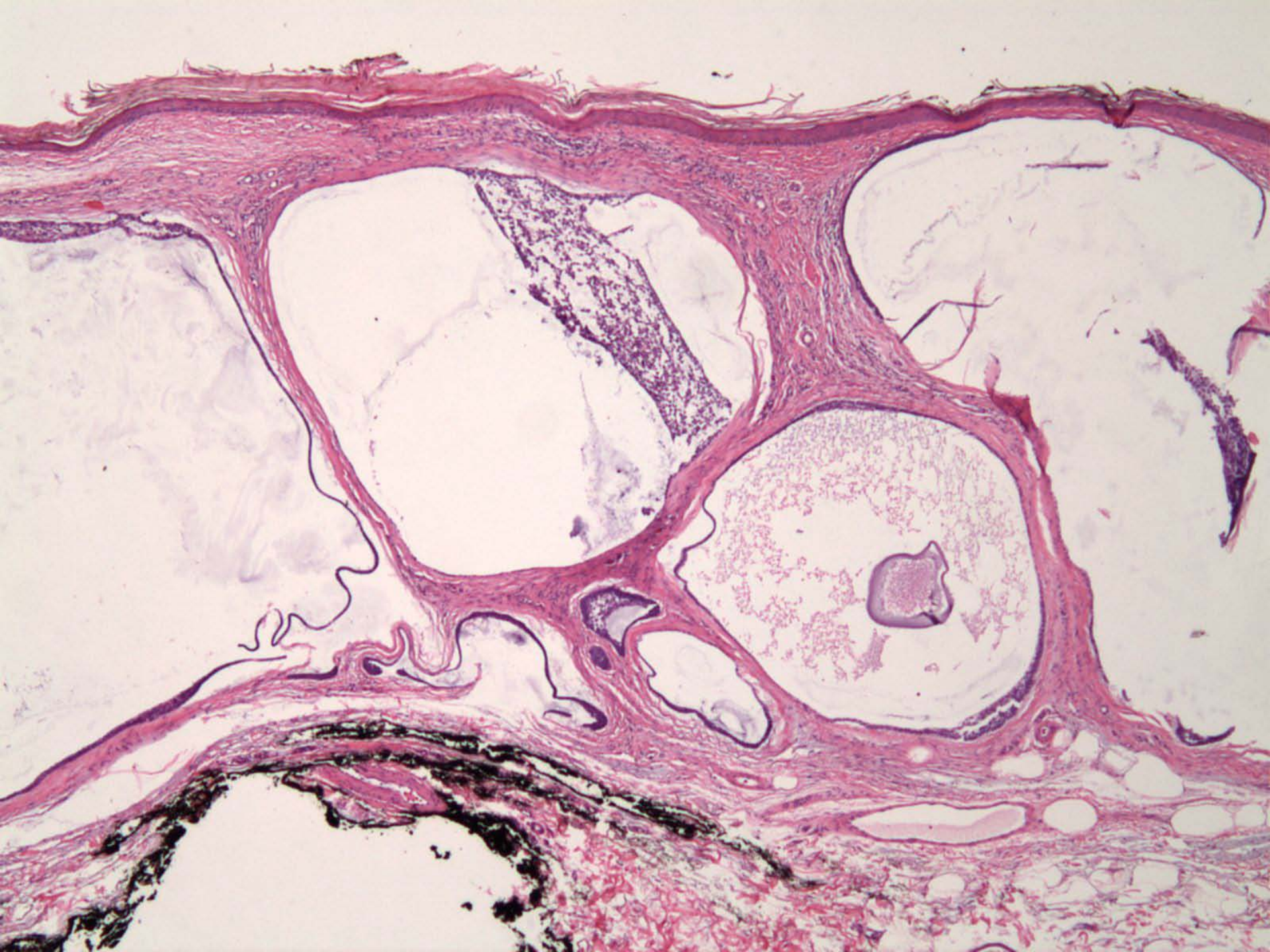
Basal Cell Carcinoma arising with stromal fibrosis

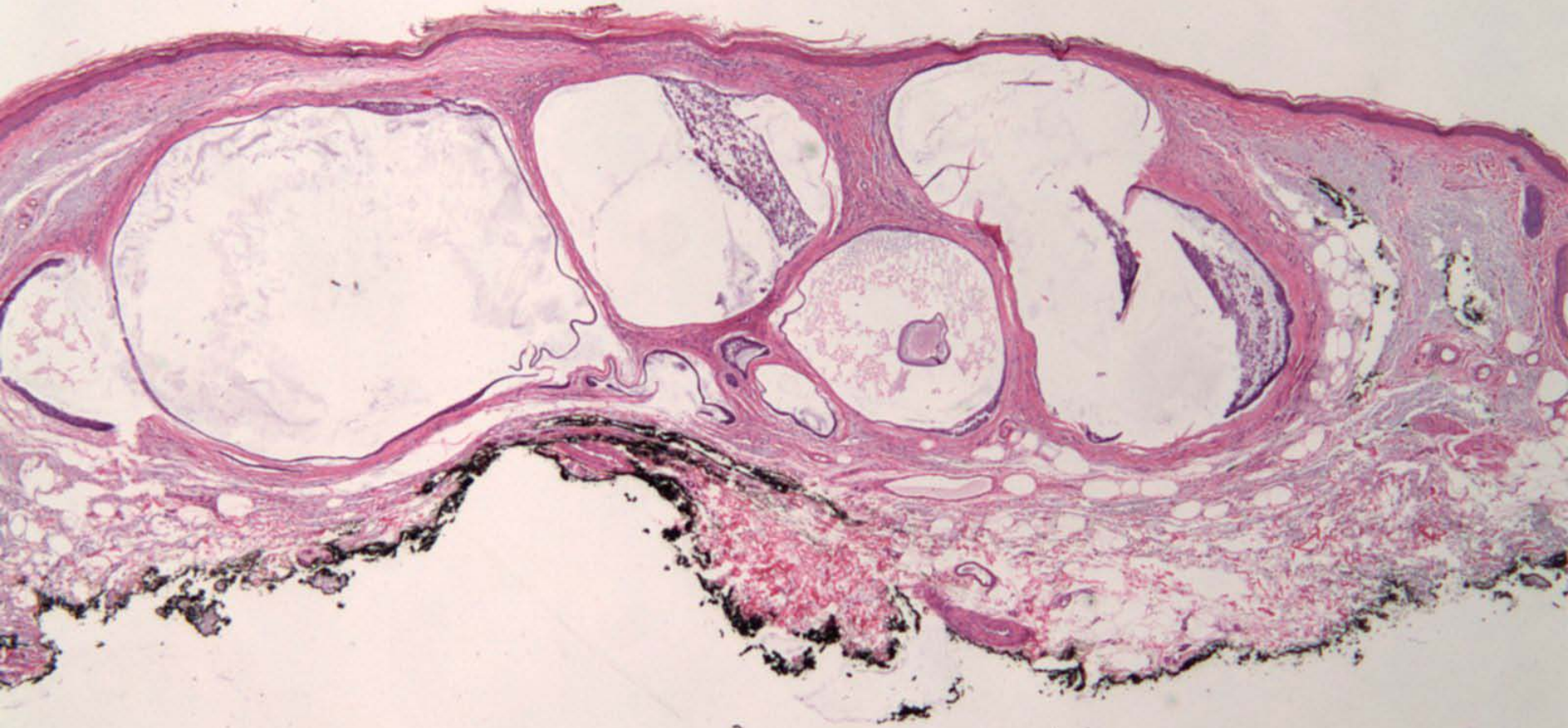




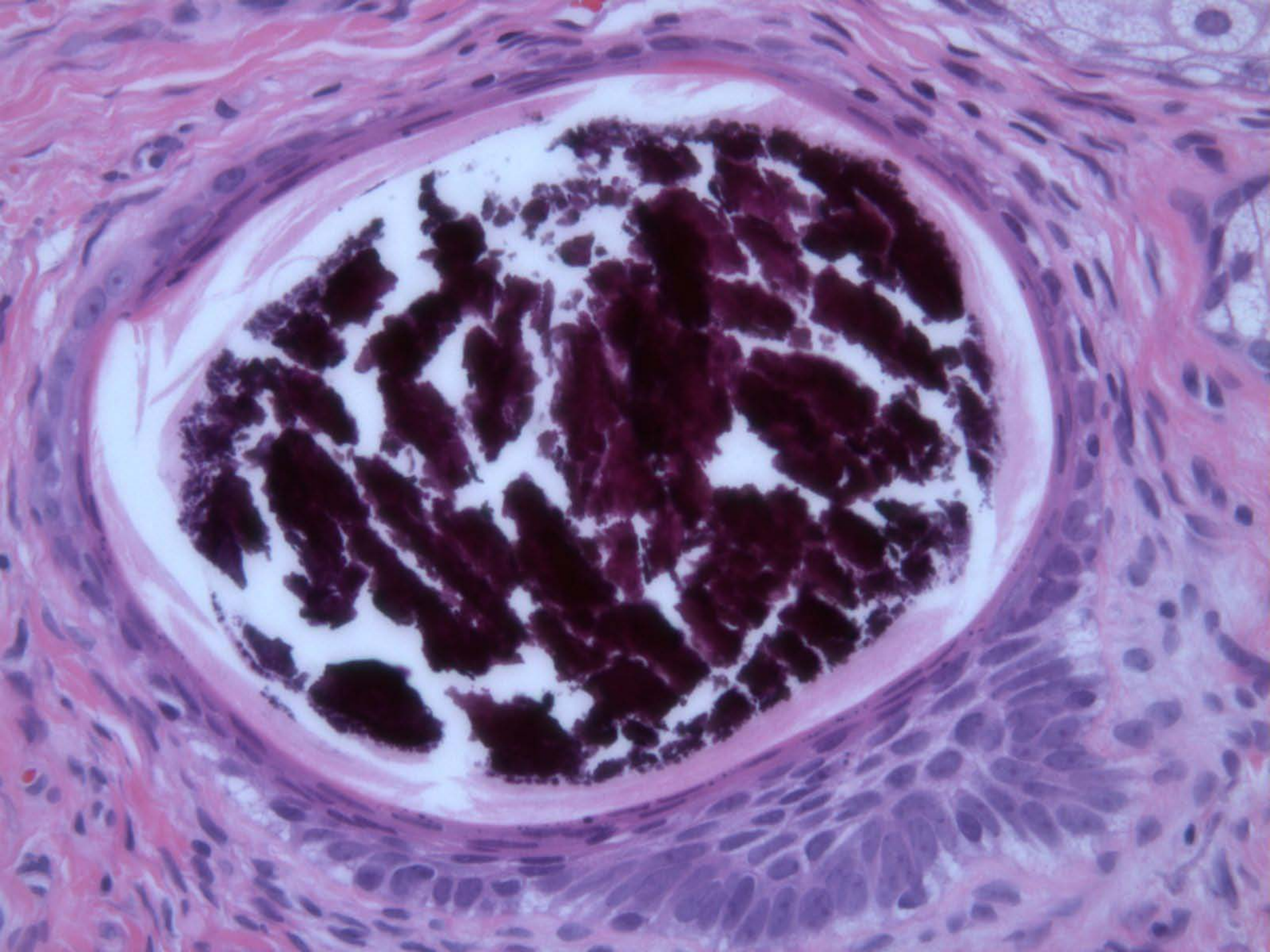


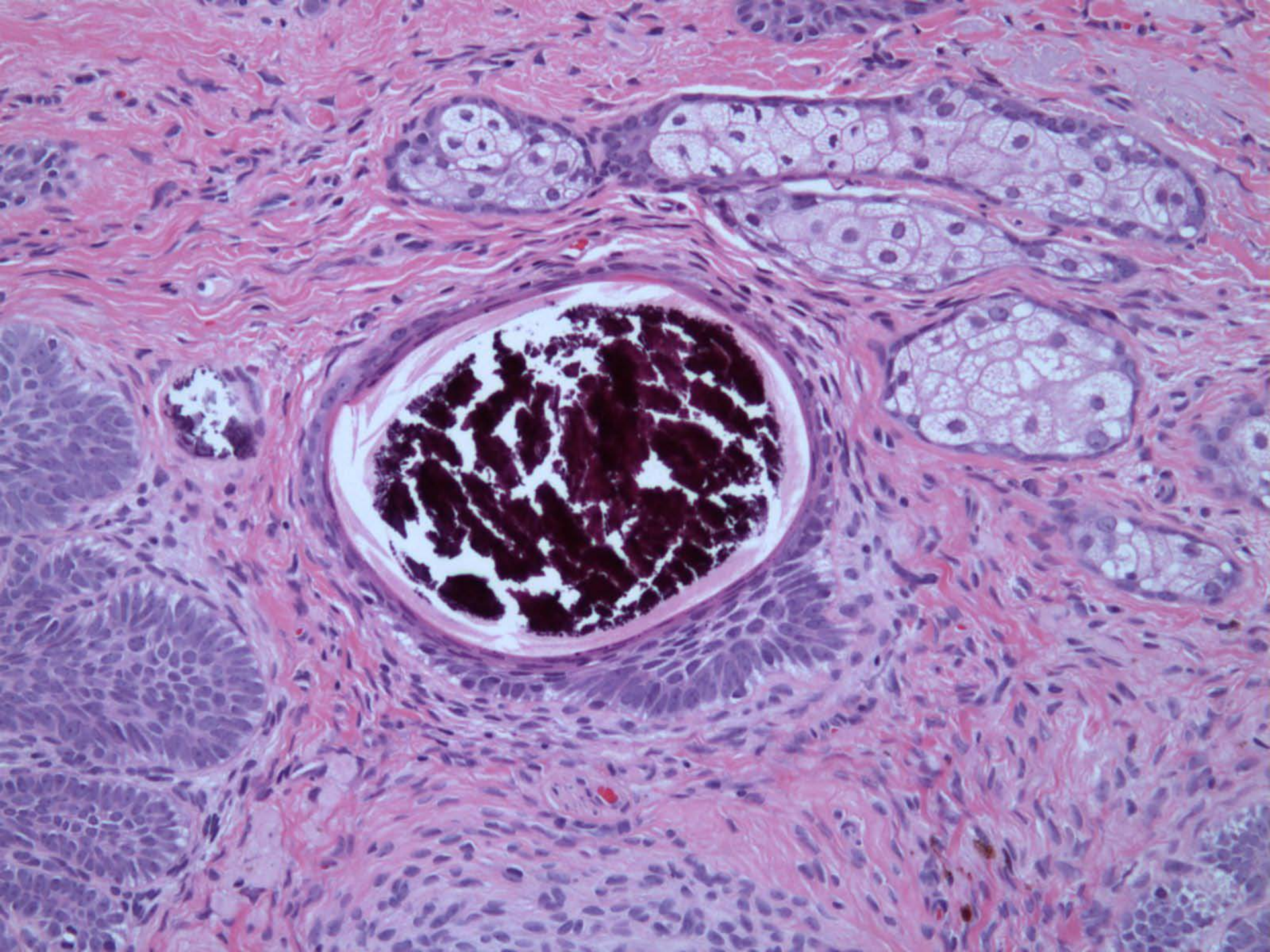


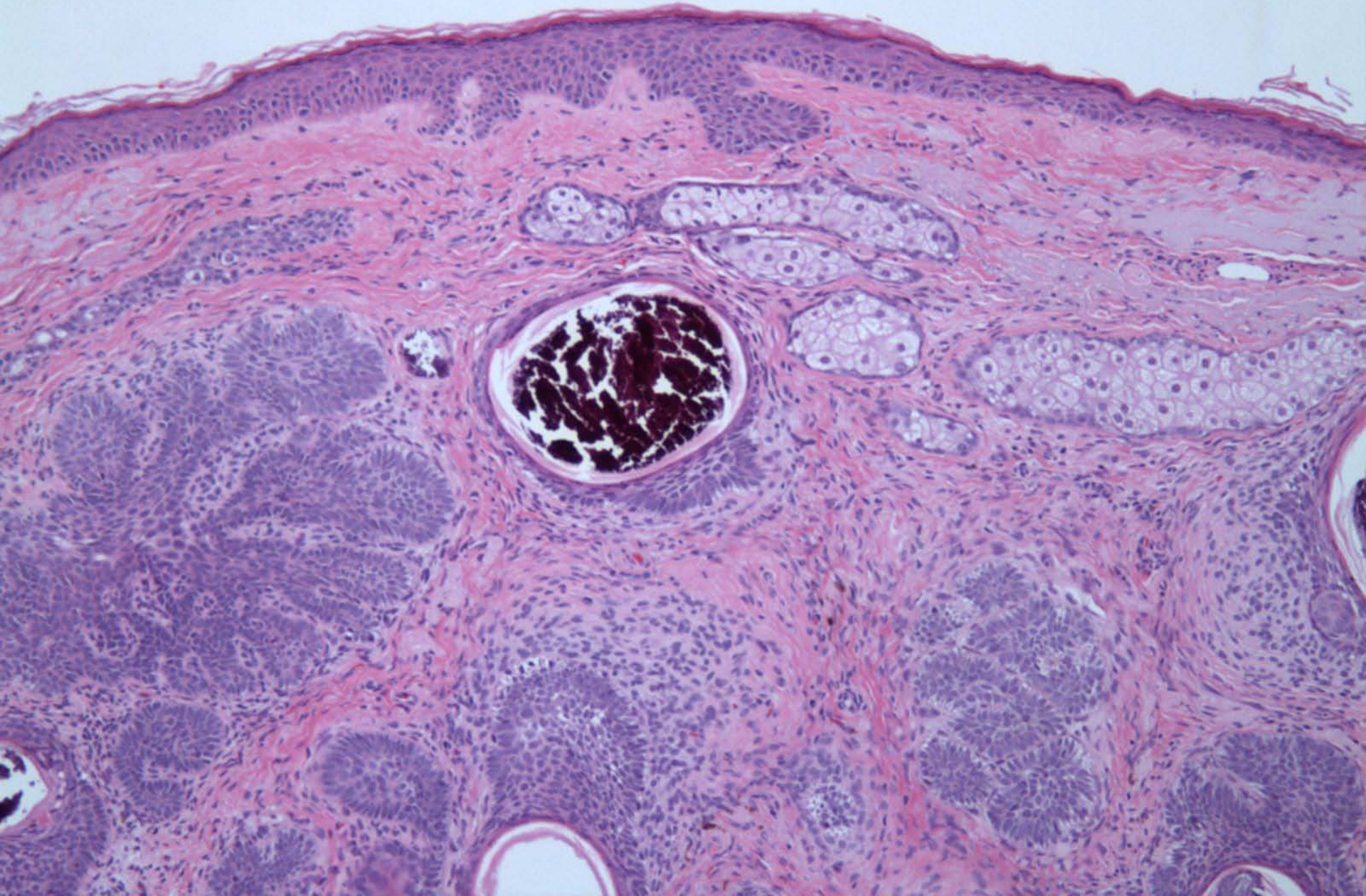


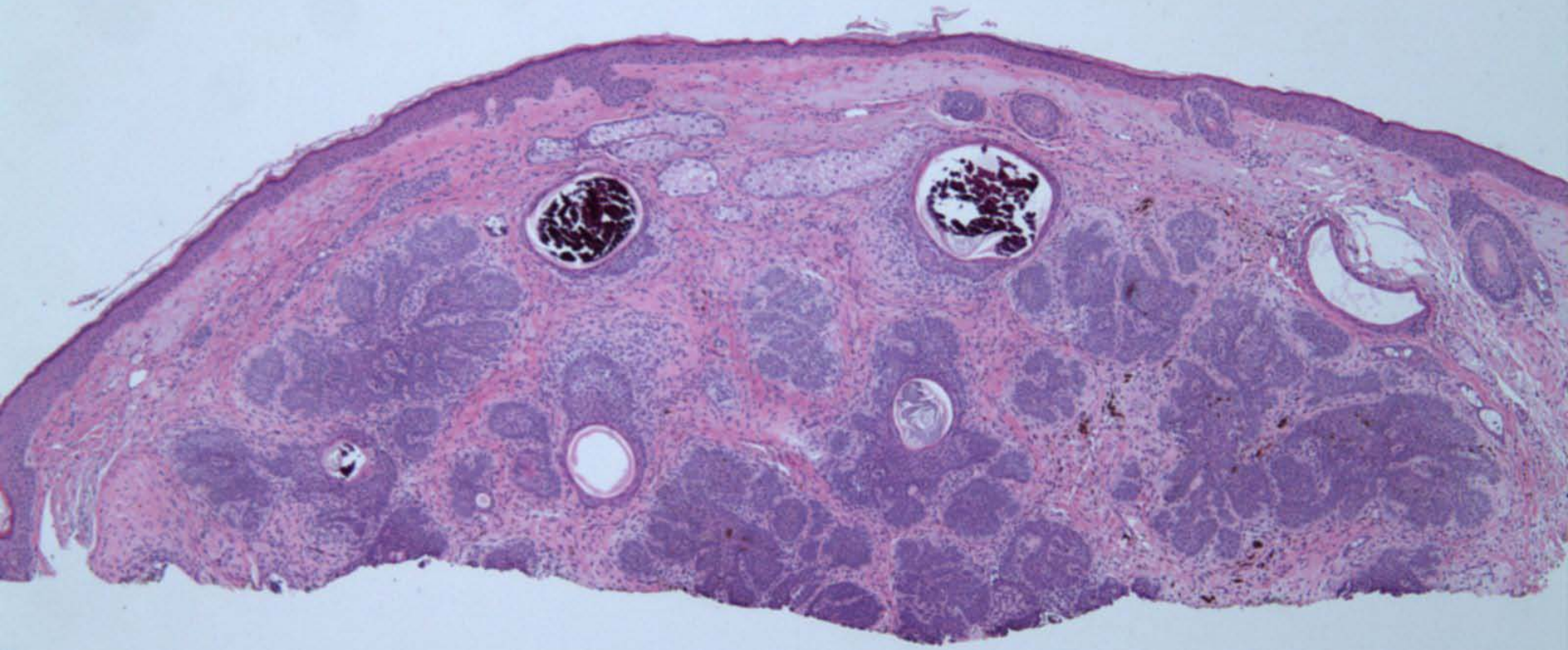


Basal Cell Carcinoma
Arising with Cystic Spaces









Basal Cell Carcinoma
Arising with Microcalcifications

Clues for Deeper Sections

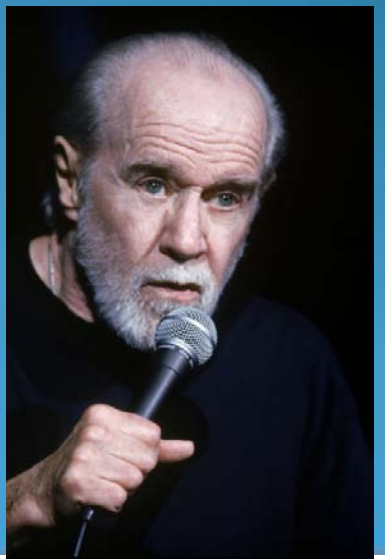
- Ulceration on initial sections
- Focal epidermal atypia
- Equivocal adnexae
- Stromal fibrosis
- Empty dermal space
- Microcalcifications

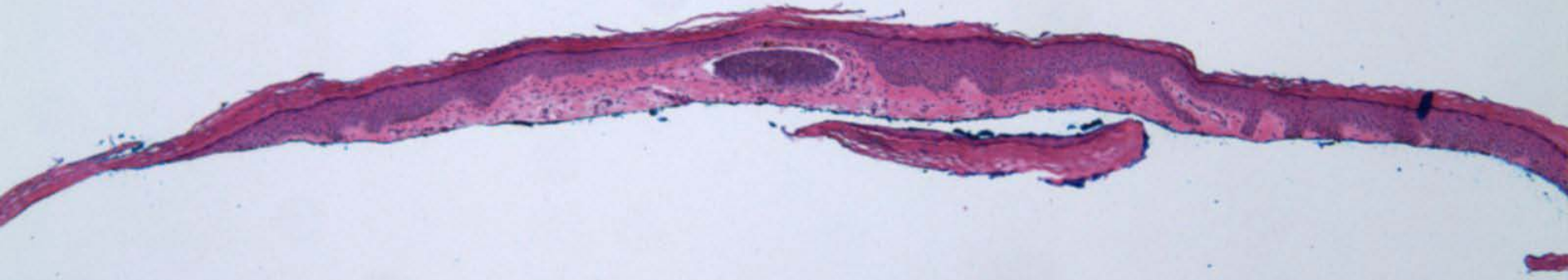
- BCC on deeper sections (3 additional slides) in 53% (50/94 cases)
- AK on initial section led to deeper sections and changed dx in 33% (23/69) including SCCIS, SCC, and BCC
  - Hx of skin cancer, clinical dx of cancer, and ulceration most important predictors

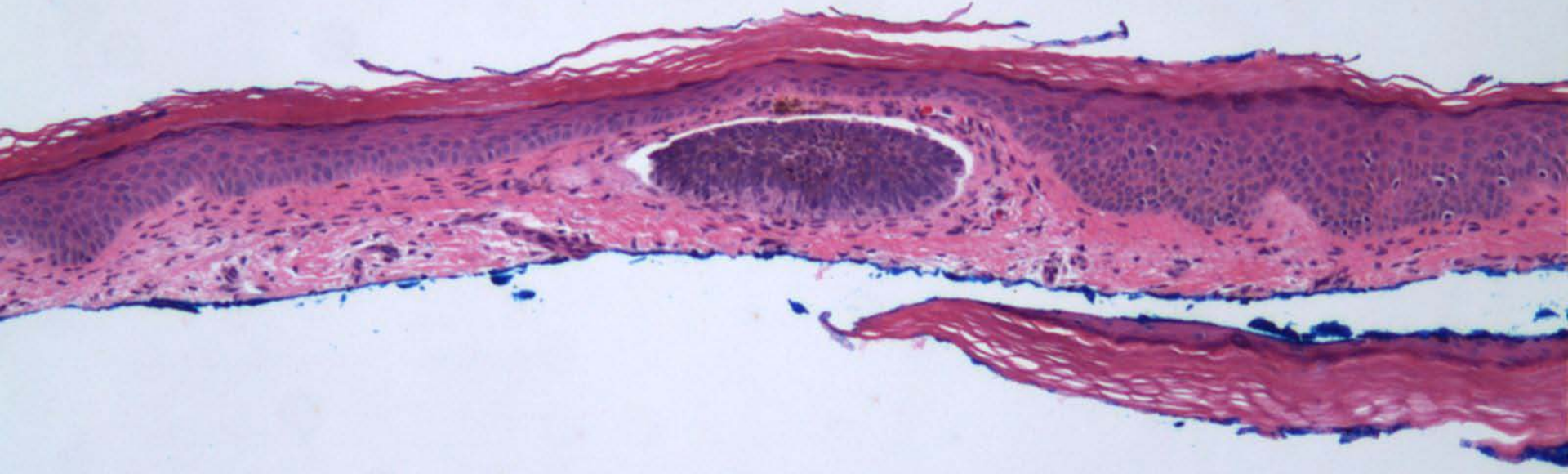
The best special stain in many instances is an H & E deeper section.

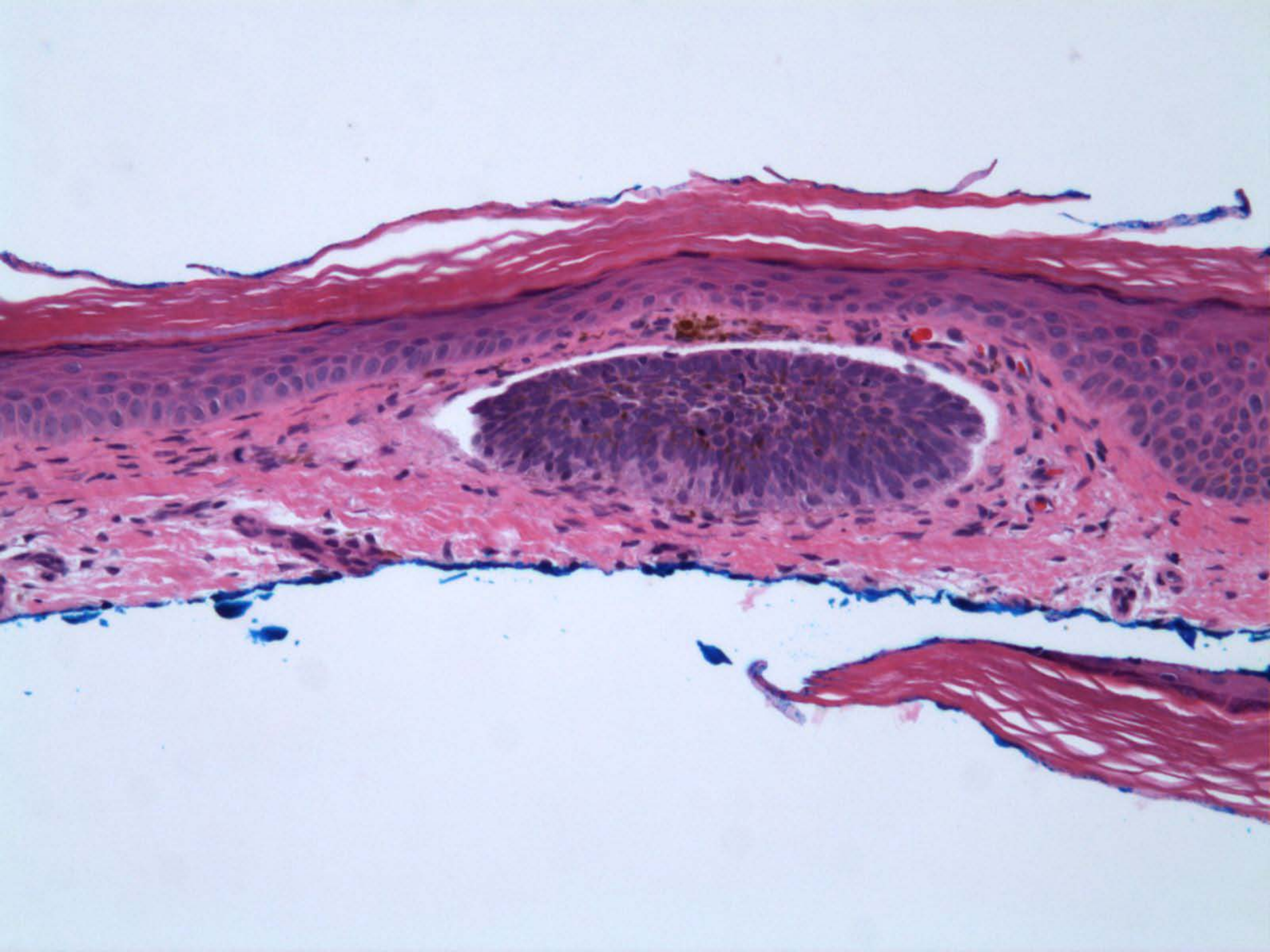
The Seven Things

- Low Power Objective-High Power Pathologist
- Measuring a Melanoma
- The Best Special Stain
- **Margins on a Punch or Shave biopsy**



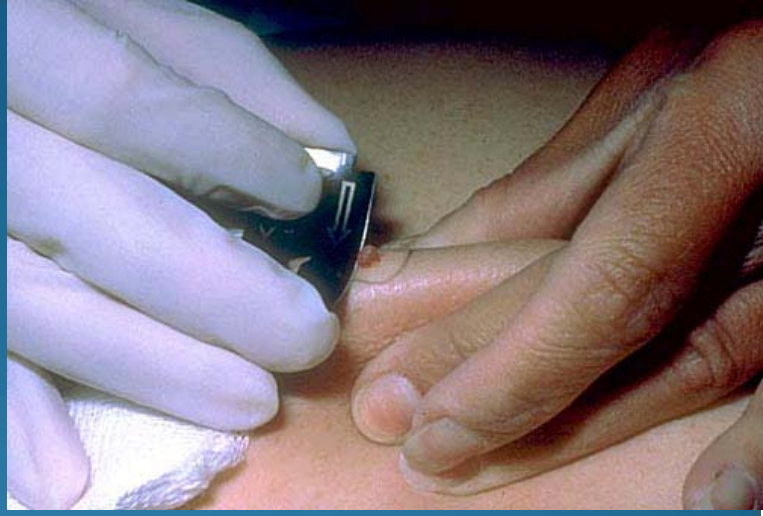






Basal Cell Carcinoma

Margins Positive or Negative?



Should I comment on margins on a punch or shave biopsy?

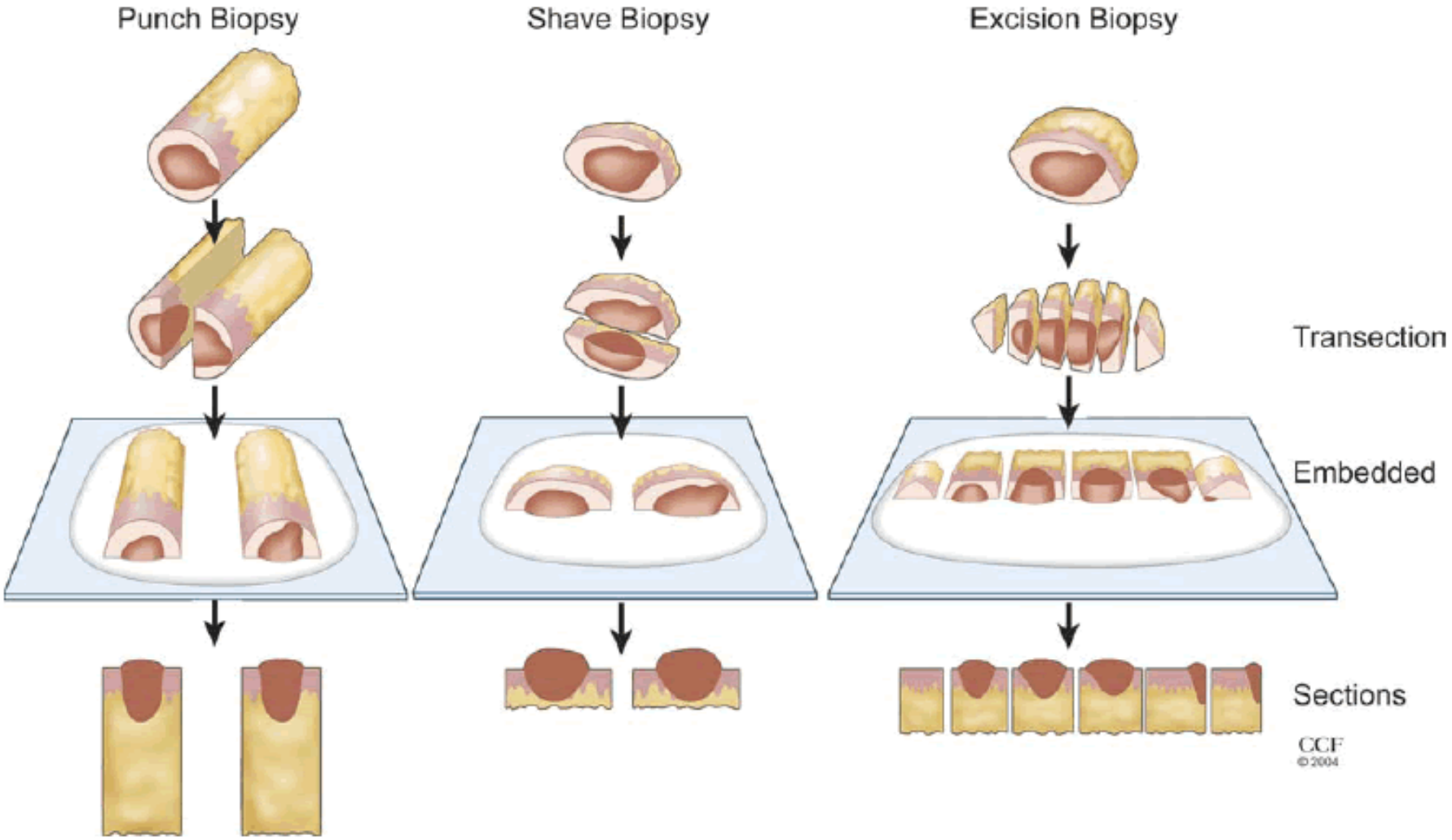
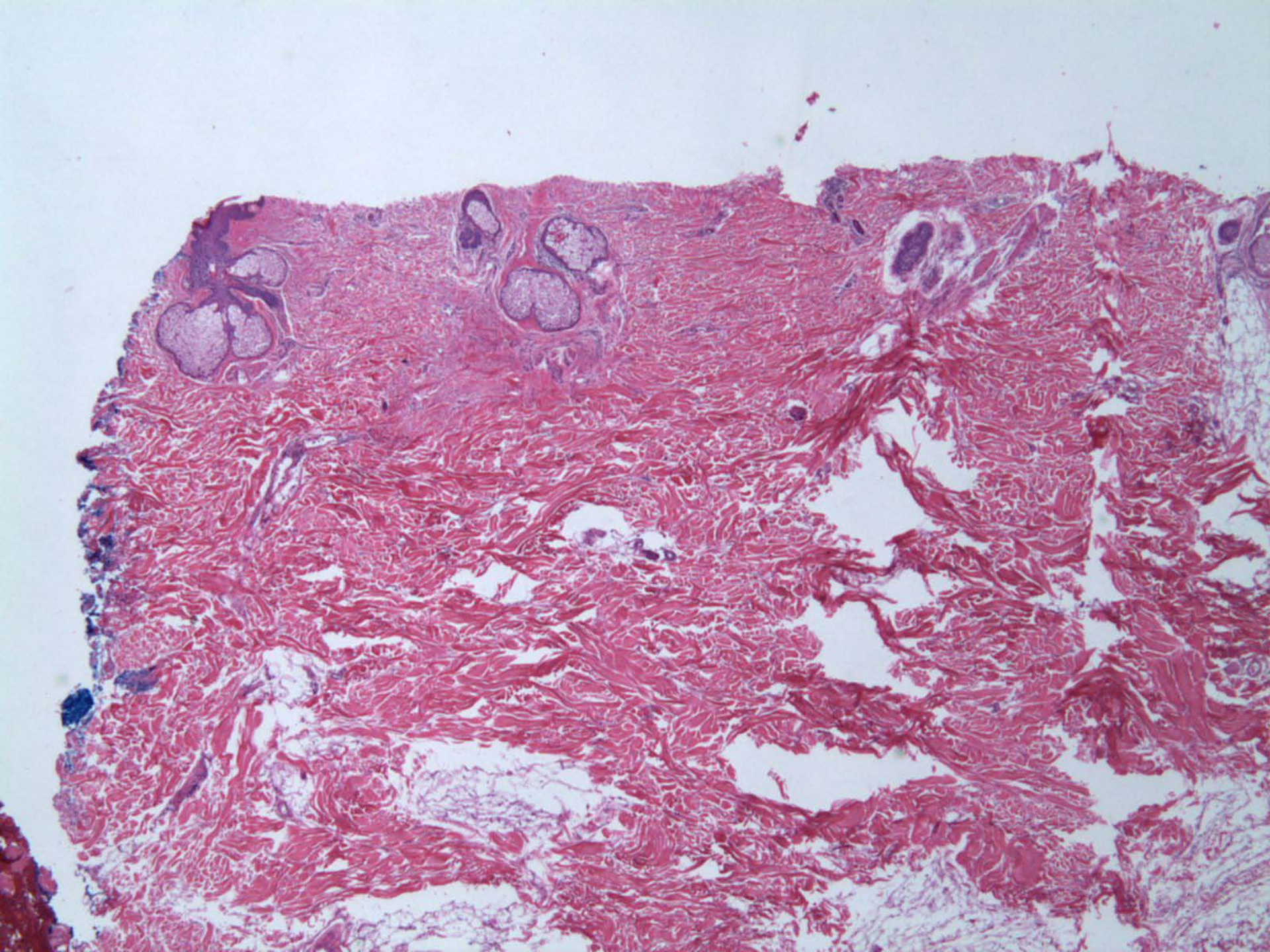
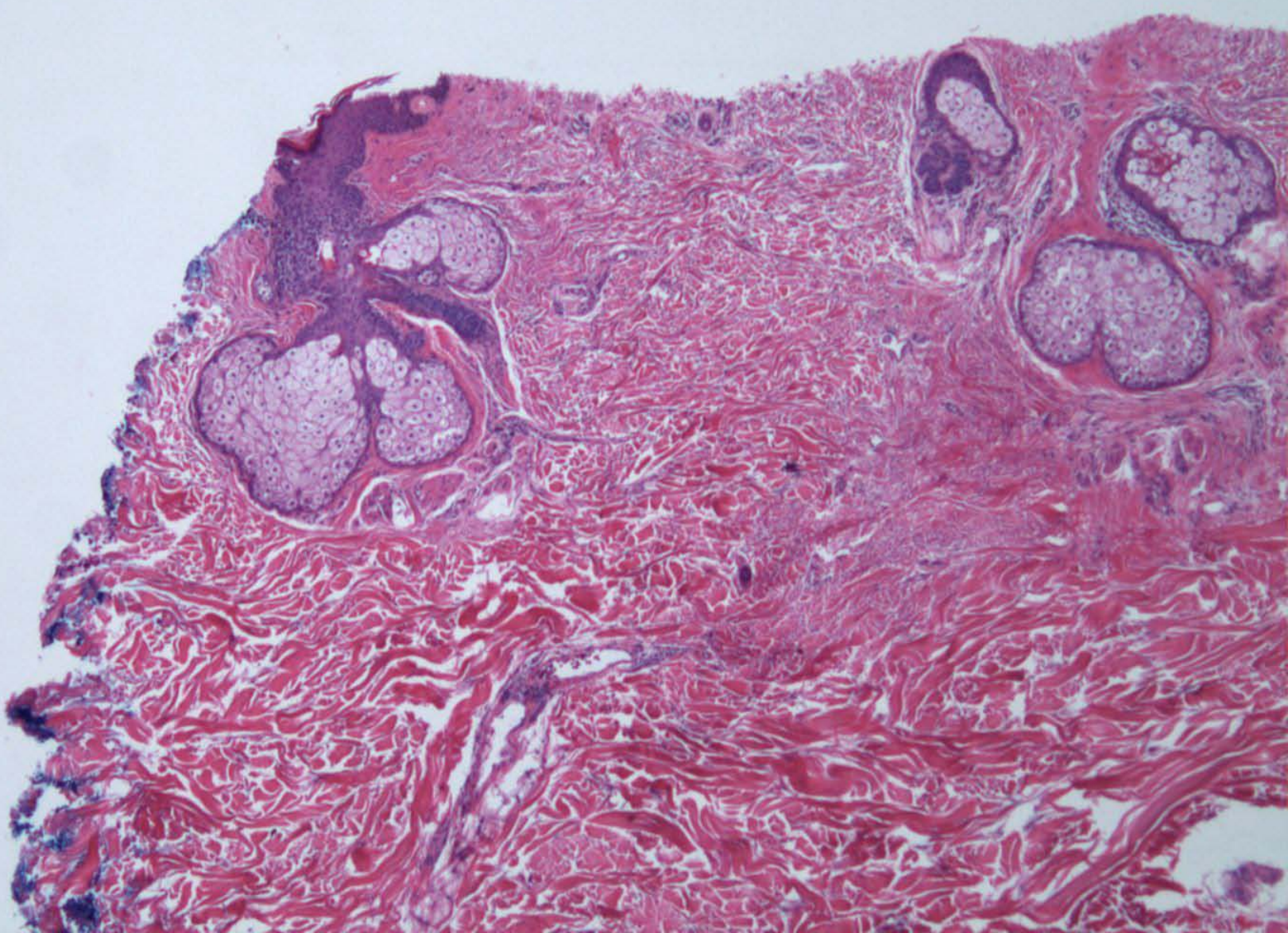


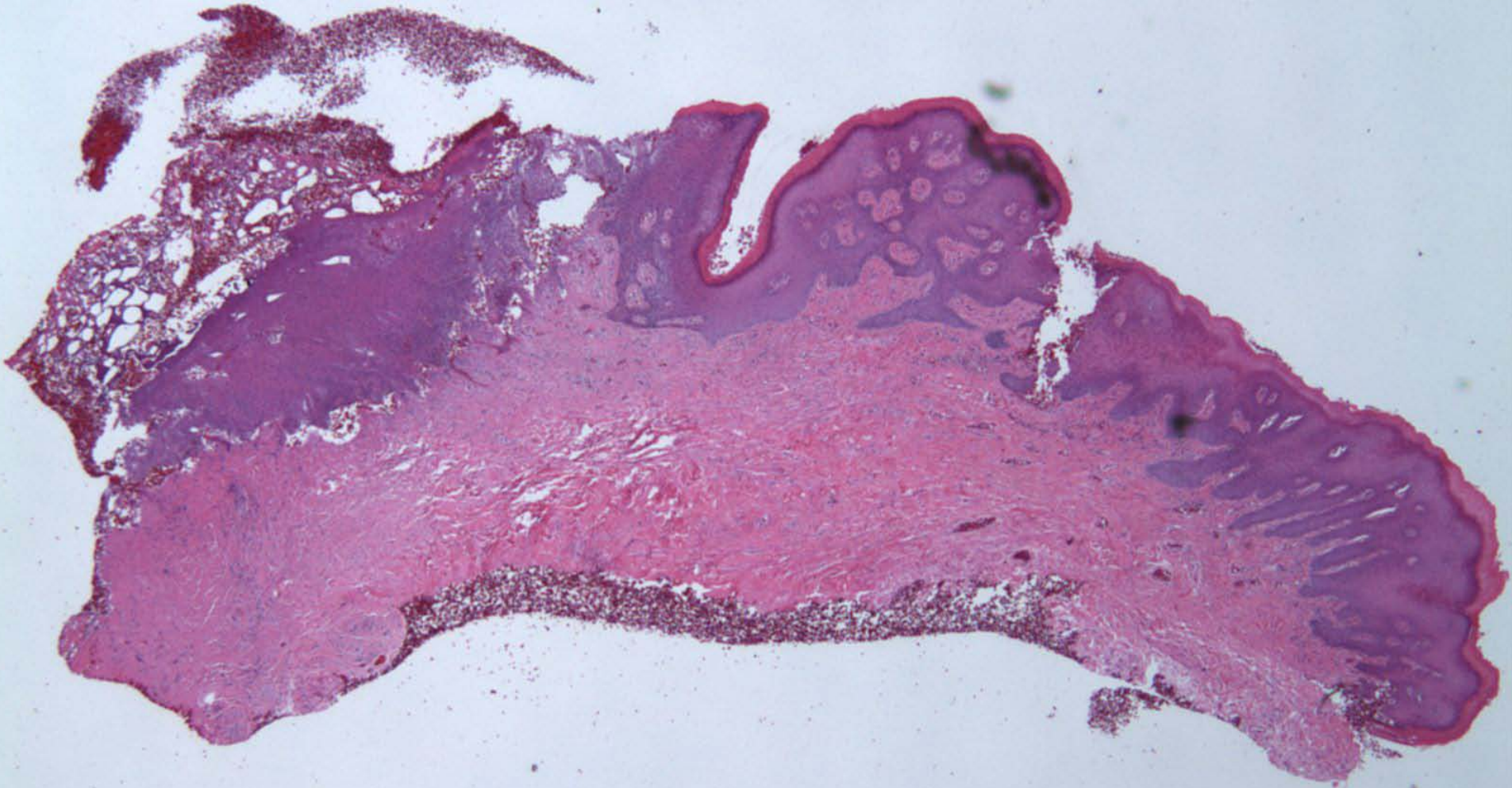
Fig 1. Comparison of a punched, shaved, and excised melanocytic lesion and the histologic steps of processing demonstrates that elliptical excisions are best suited for adequate margin evaluation. On gross examination (*top*), the nevus is present at the surgical margin in all three types of biopsies. Upon sectioning (*bottom*), however, involved surgical margins are only noted in the nevus, which was removed by an elliptical excision.

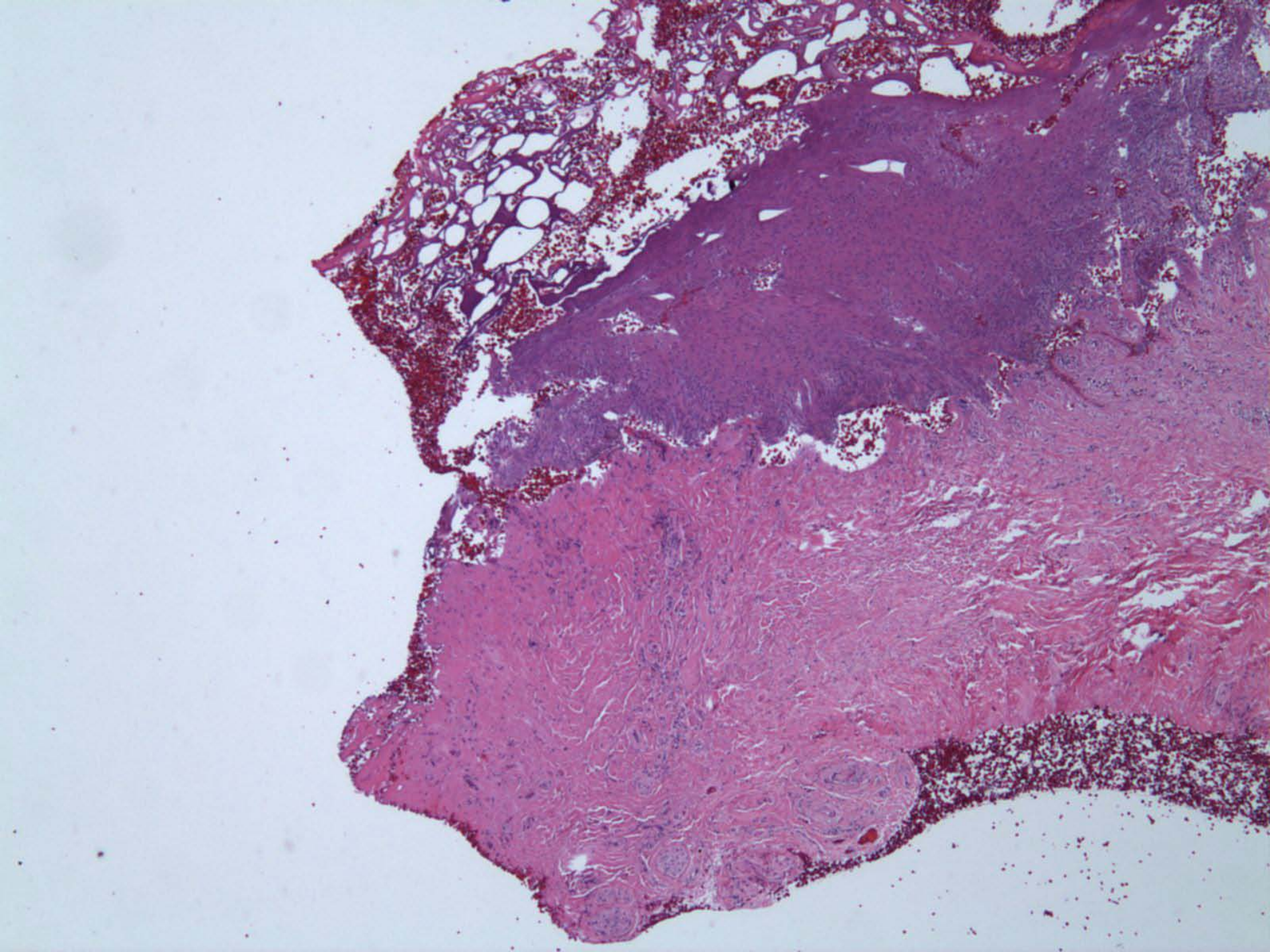
Positive or Negative Margins?

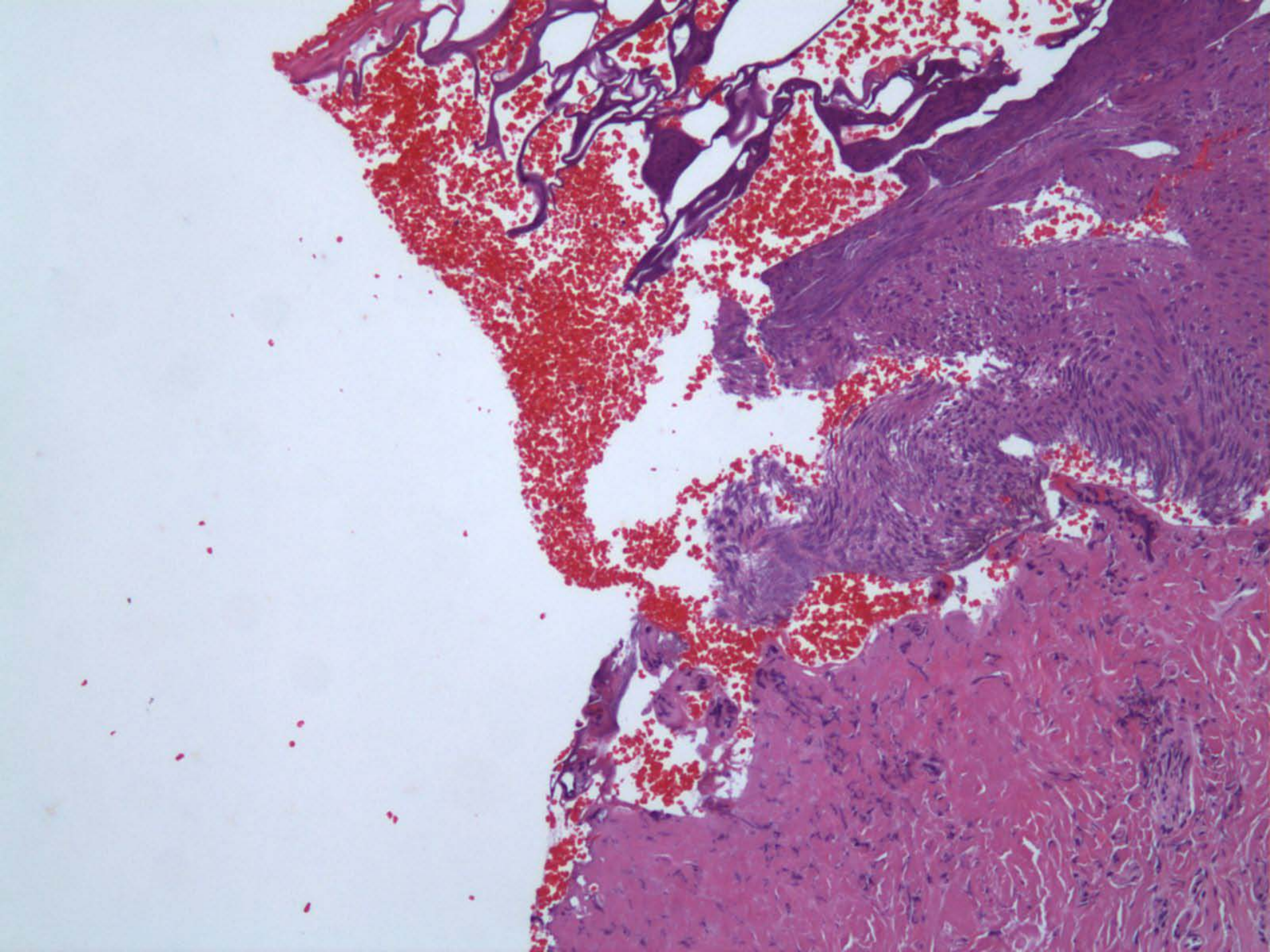
- The neoplasm extends close to the edge of the specimen, and the area of the margin is obscured by electrocautery or other artifact.
- The neoplasm extends close to the edge of the specimen, and part of the tissue at the margin is out of the plane of section.
- The neoplasm extends close to the edge of the specimen, and a scar is present between the neoplastic cells and the margin

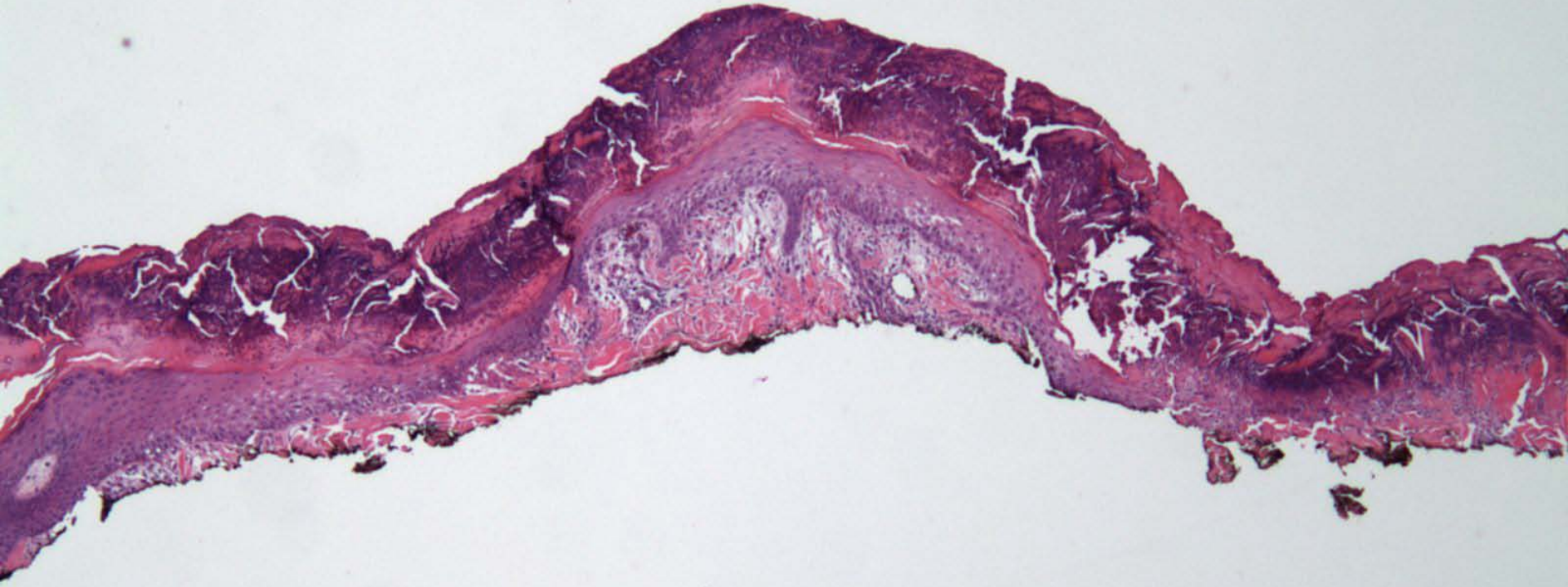


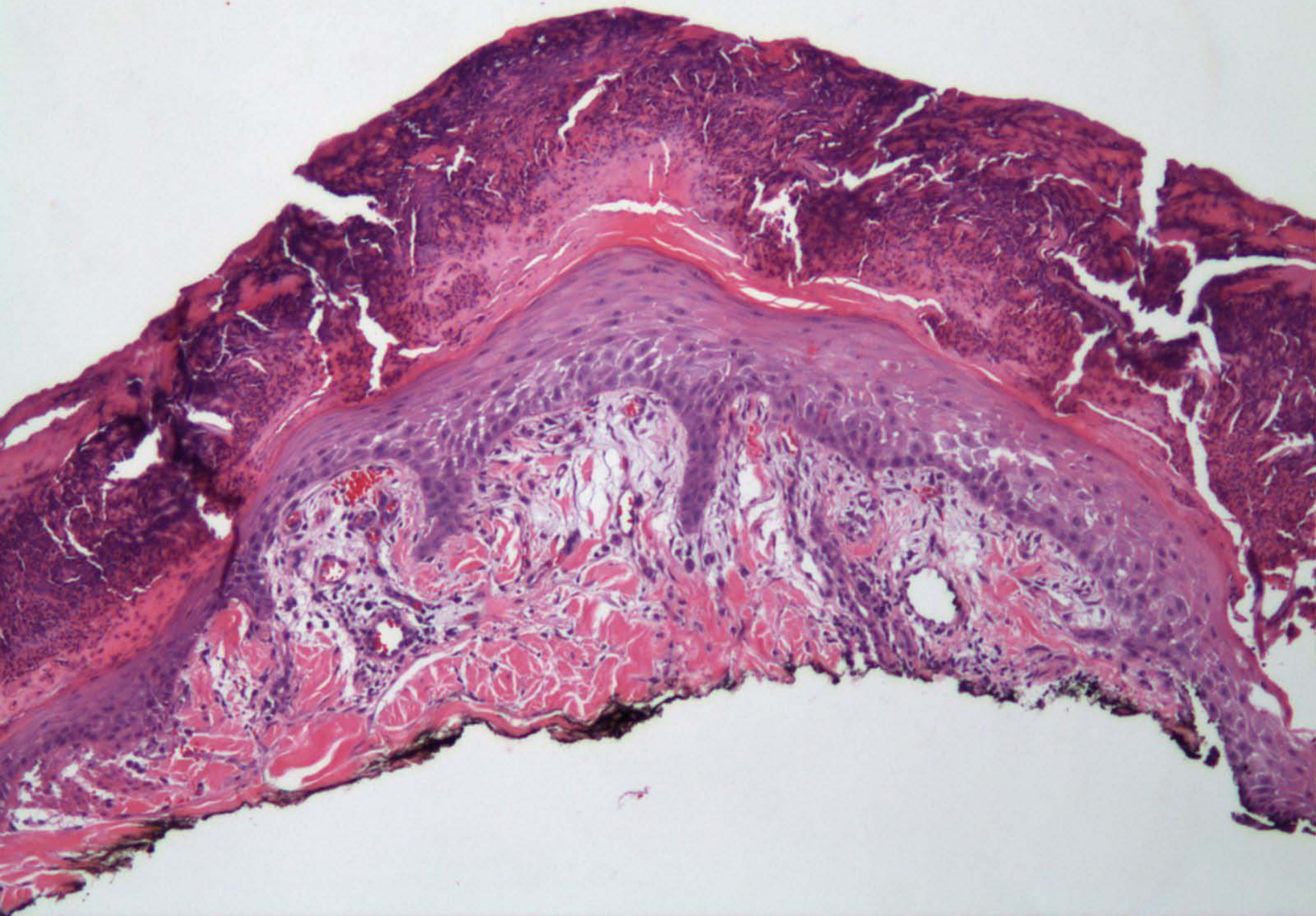


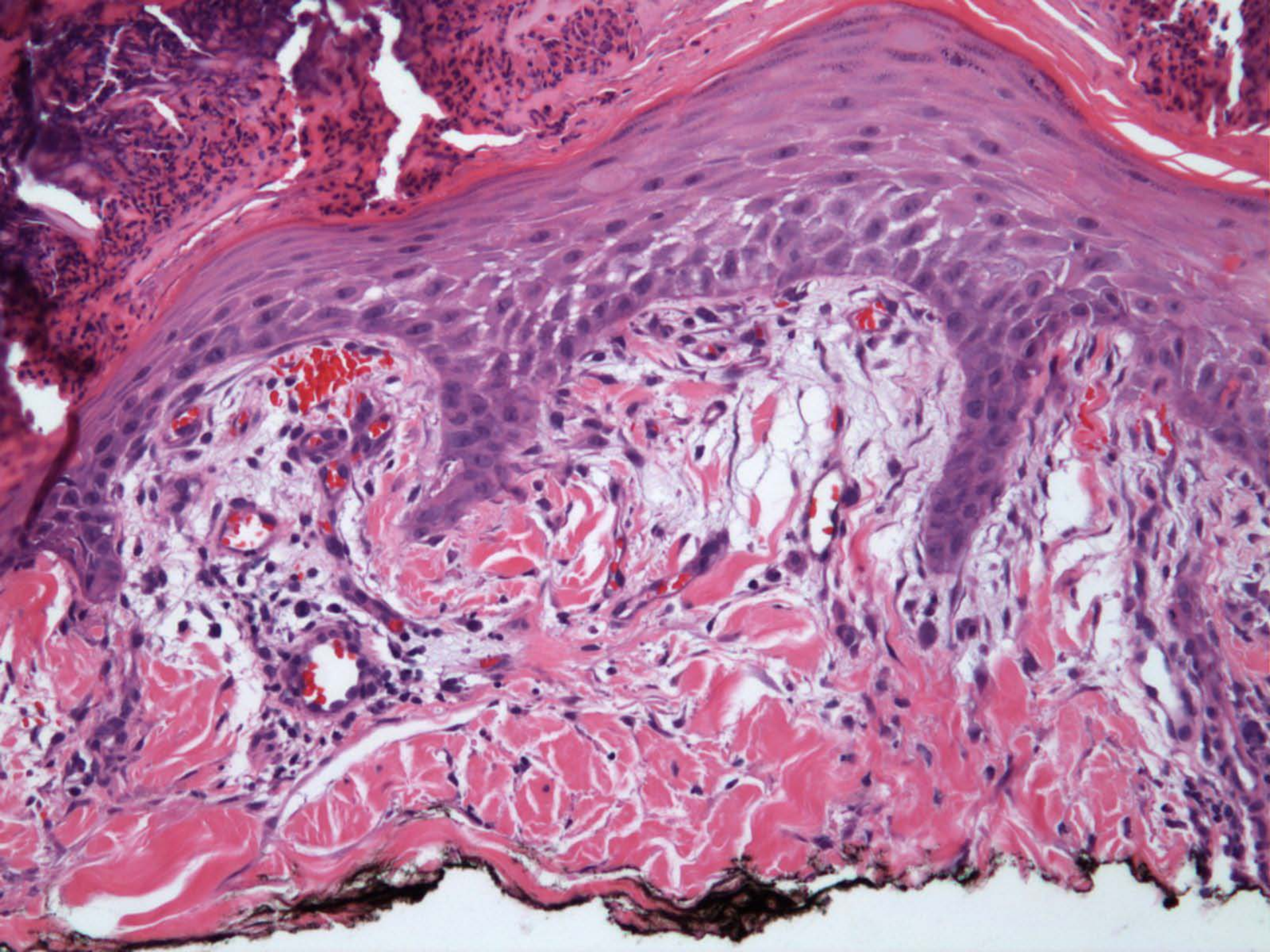












- Stroma seen between the nests of a neoplasm (e.g. the fibrosing granulation tissue-like stroma of a superficial basal cell carcinoma) is present between a nest of neoplastic cells and the margin.

- Perineural invasion is present anywhere close to a margin.

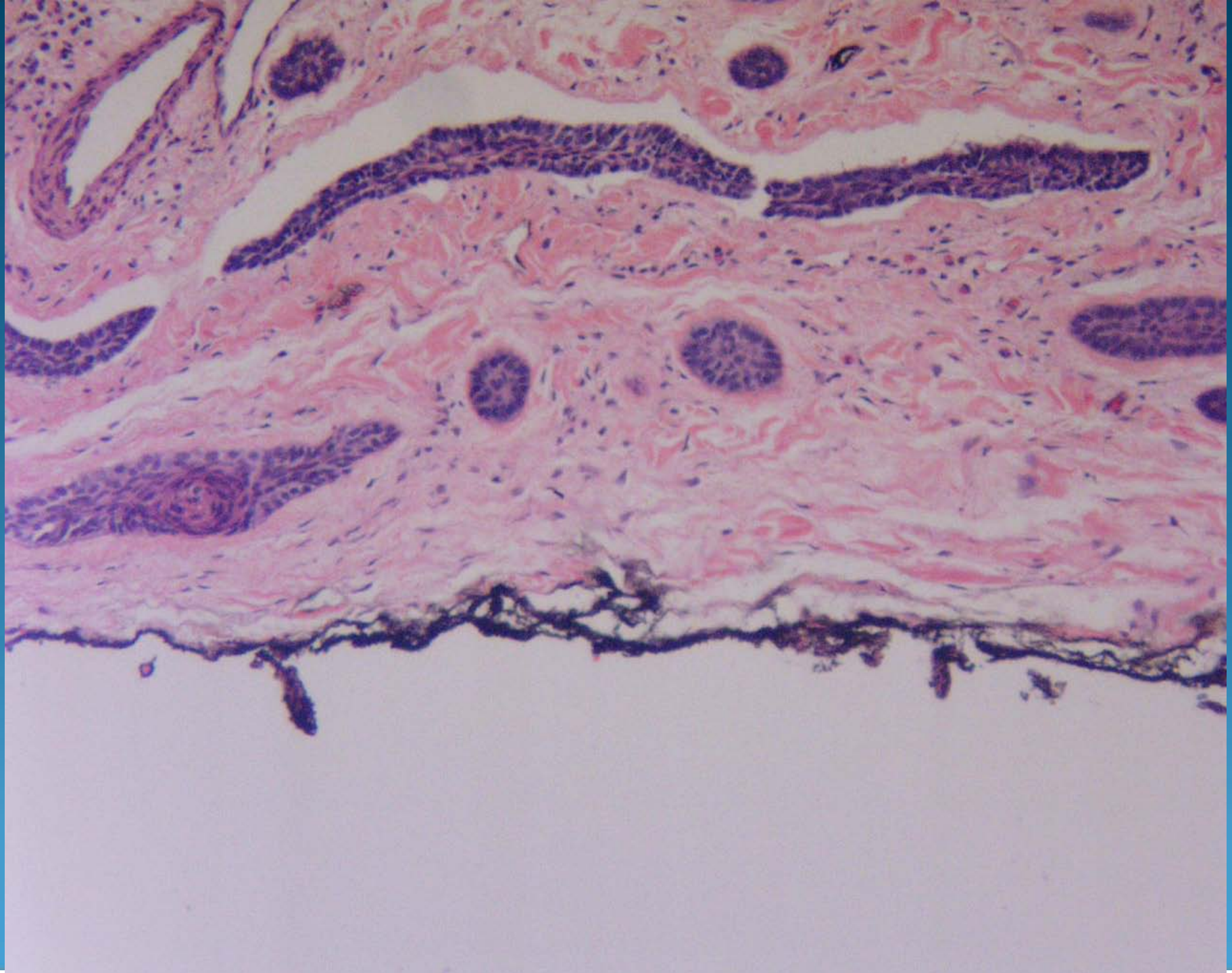
A neoplasm is so subtle (e.g. desmoplastic melanoma) that immunoperoxidase staining should be employed to distinguish between fibrosis around a biopsy site and residual neoplasm.

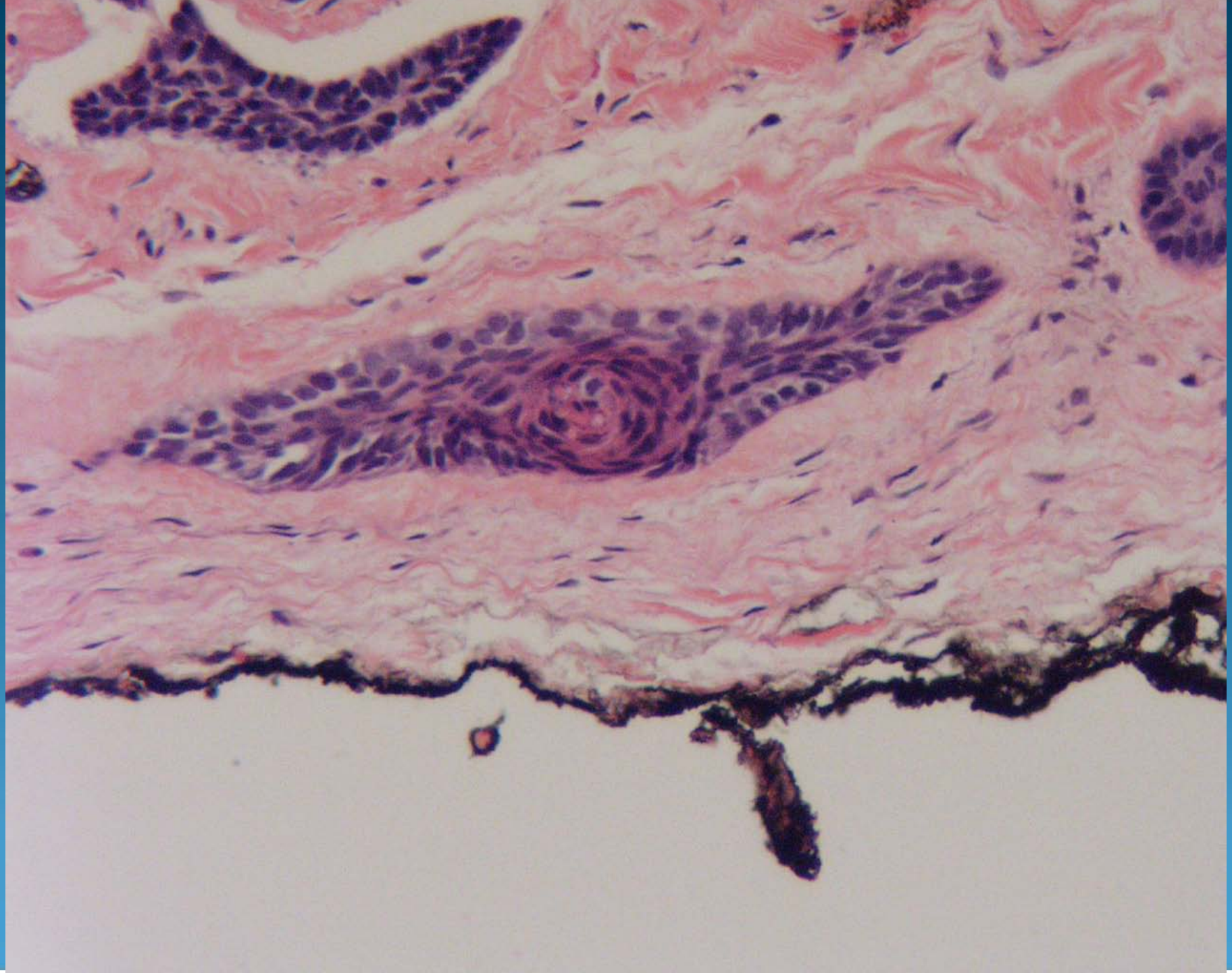
An ulcer produced by curettage (to determine the size of a subsequent excision) extends to the edge of the specimen.

LeBoit, PE. Am J Dermatopathol 2004;26:259-262.

The distance between nests of a dermal neoplasm (e.g. a basal cell carcinoma) is anywhere close to that between the most lateral, or deepest nest and the margin.

As a rule of thumb, there should be about double the distance between the last nest and the margin as the greatest gap between nests in the neoplasm.

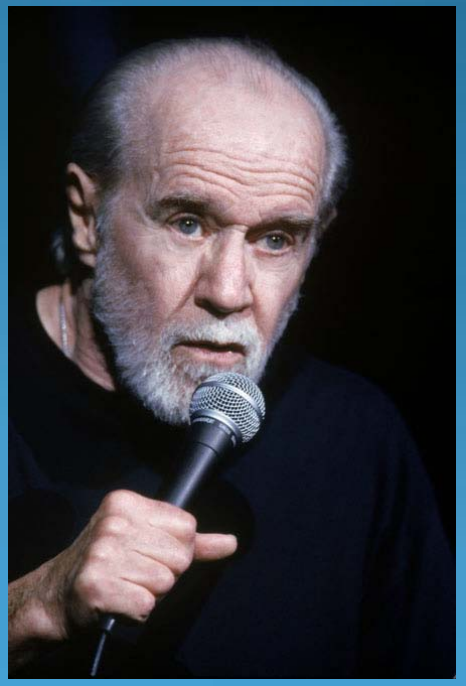




Caution is warranted in interpreting a negative margin especially in the setting of a punch/shave biopsy and equivocal margins.

The Seven Things

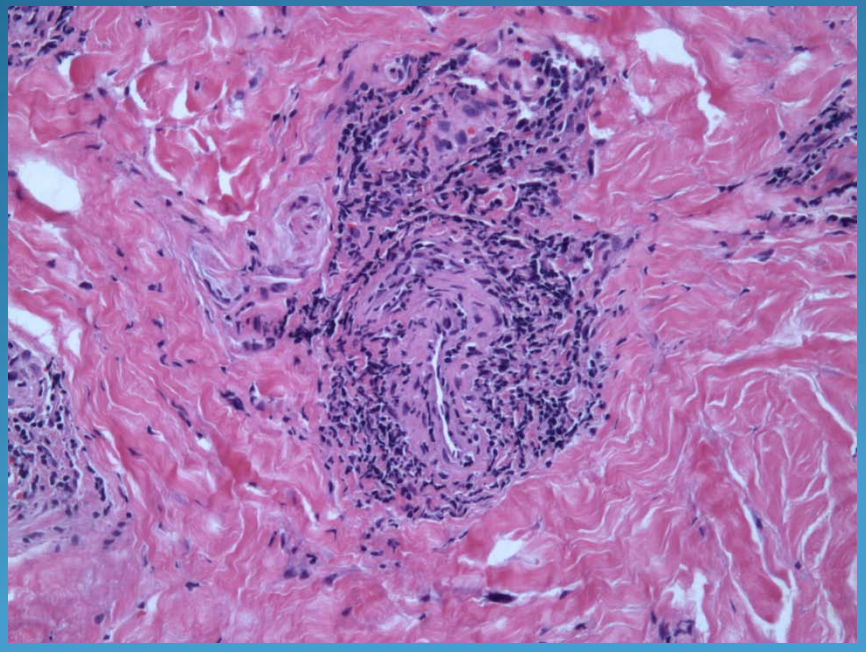
- Low Power Objective-High Power Pathologist
- Measuring a Melanoma
- The Best Special Stain
- Margins on a Punch or Shave biopsy
- **Lymphocytic Vasculitis**



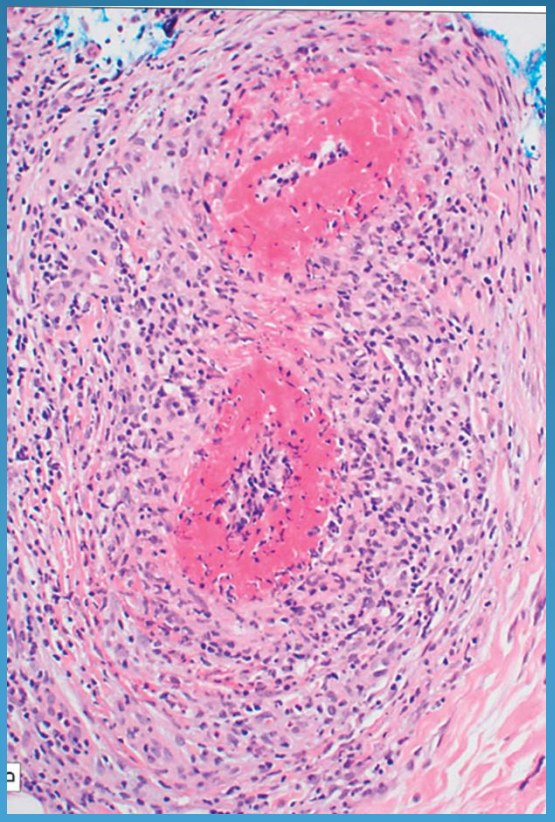
What is a lymphocytic vasculitis?

Which is the True Lymphocytic Vasculitis?

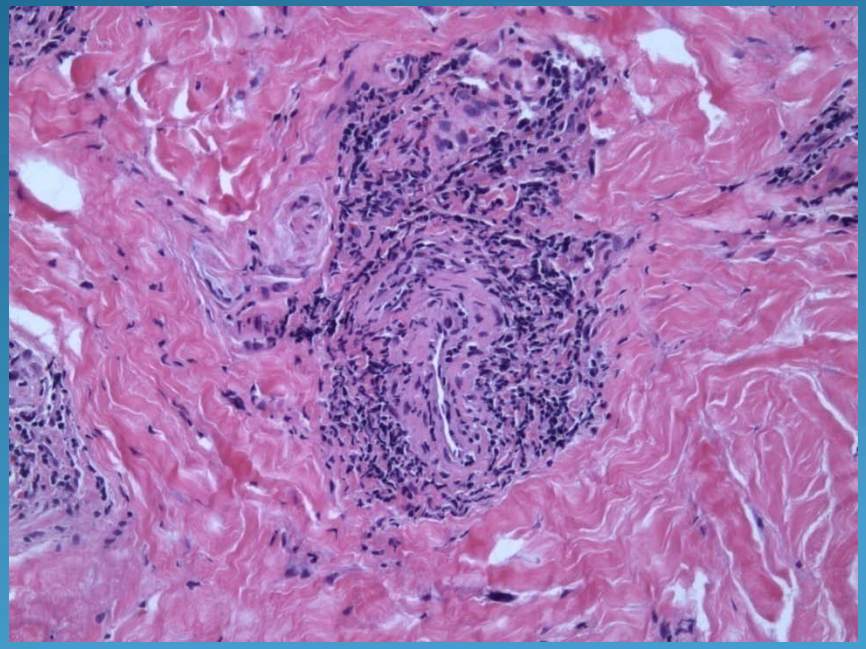
Lymphocytic Cuffing



Fibrinoid Necrosis

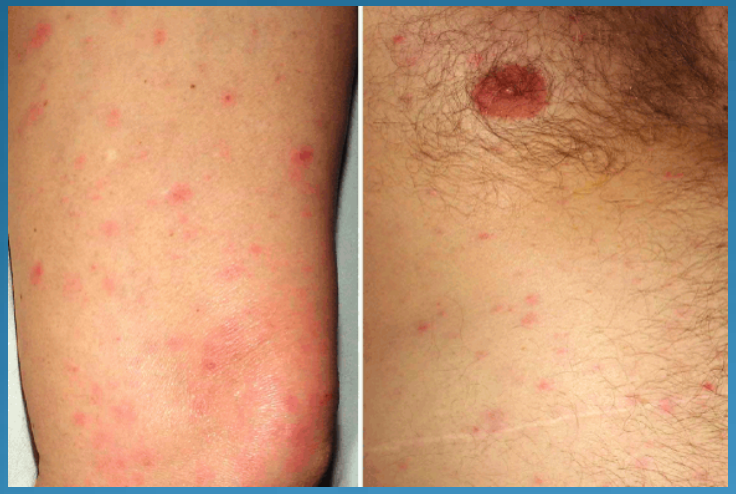


Working Definition

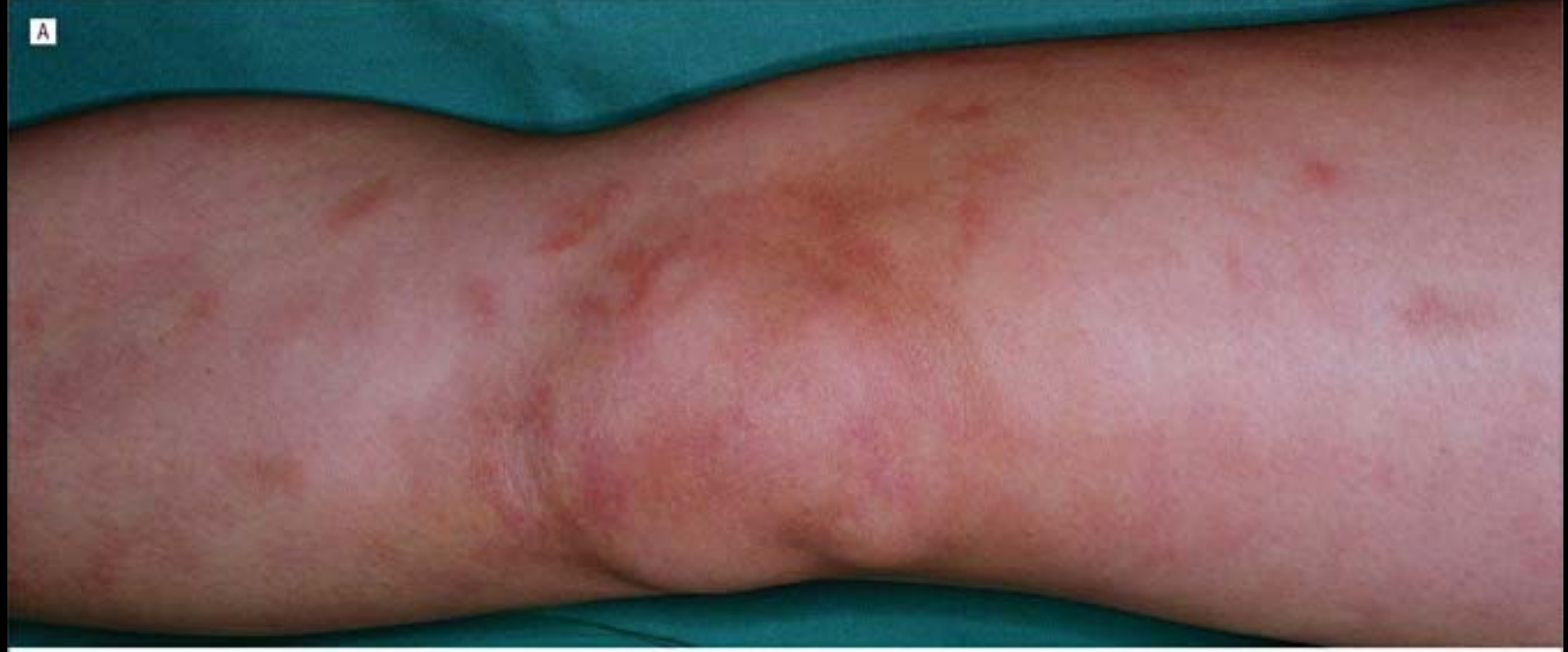


- Diapedesis of lymphocytes does not occur in muscular vessels
- Fibrin deposition in vessel wall or lumen or lamination of vessel wall
- Histopathology looking for a disease?

A Rare Event?



- PLEVA
- Rickettsia
- Lupus
- Perniosis
- Viral infections
- Drug reactions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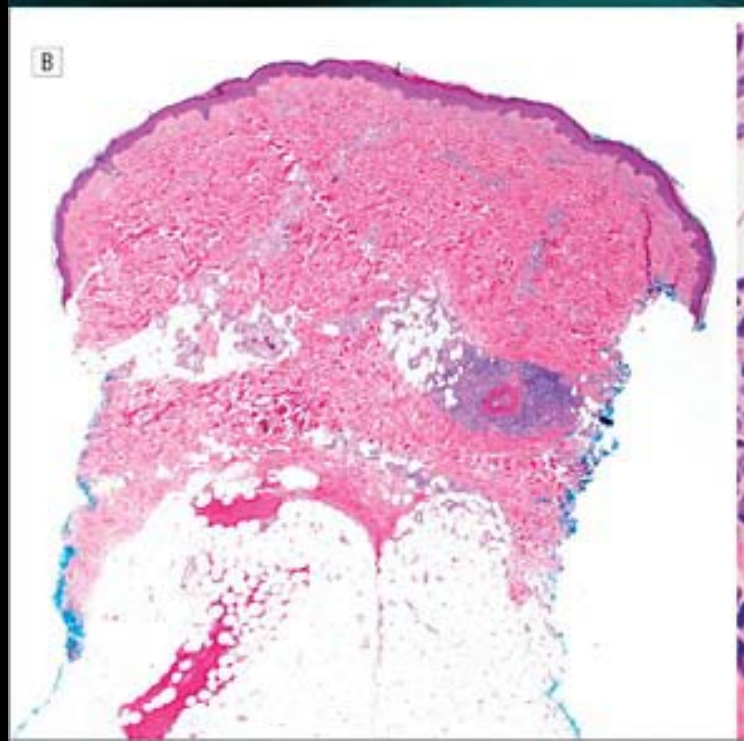
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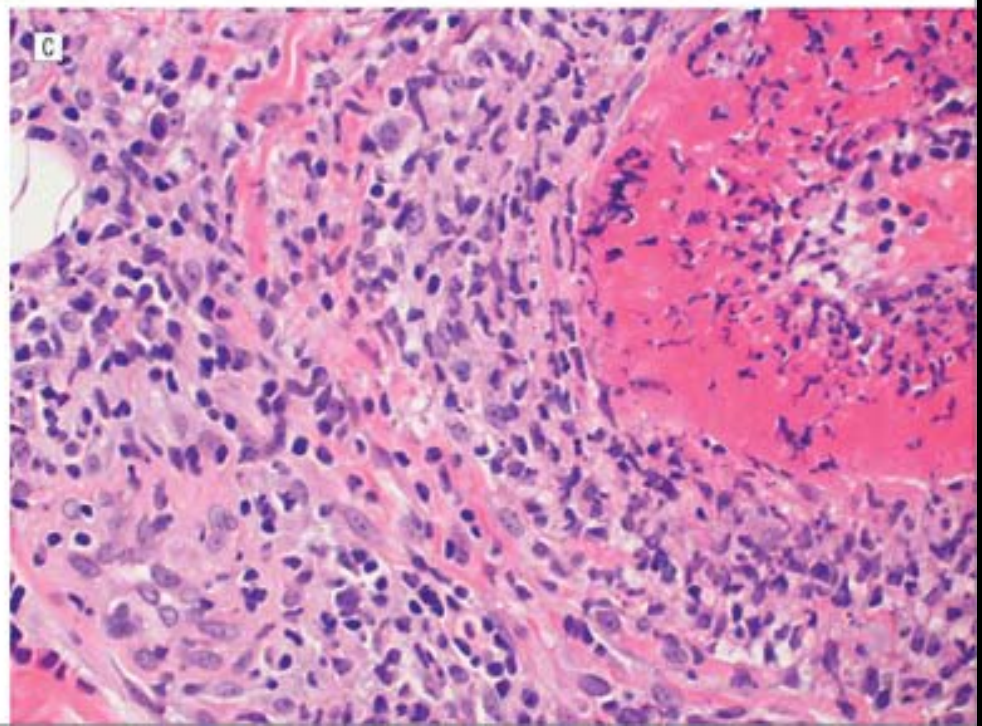
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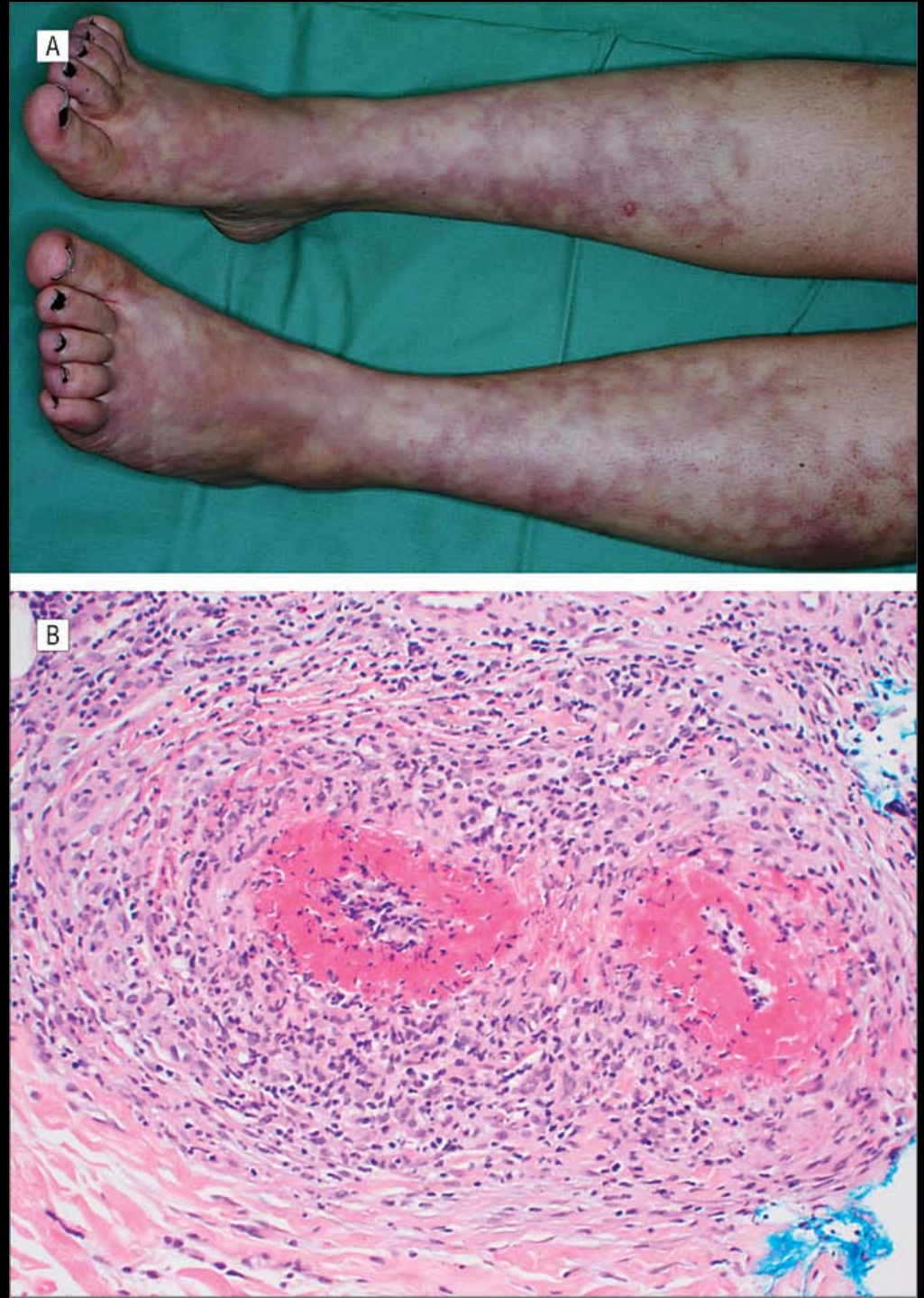
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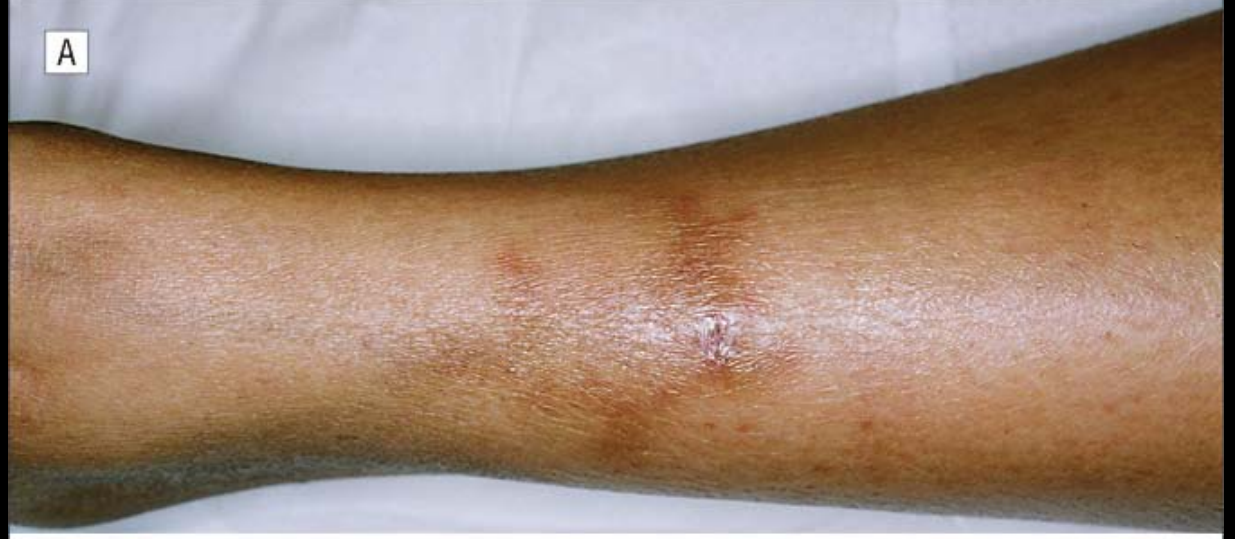
B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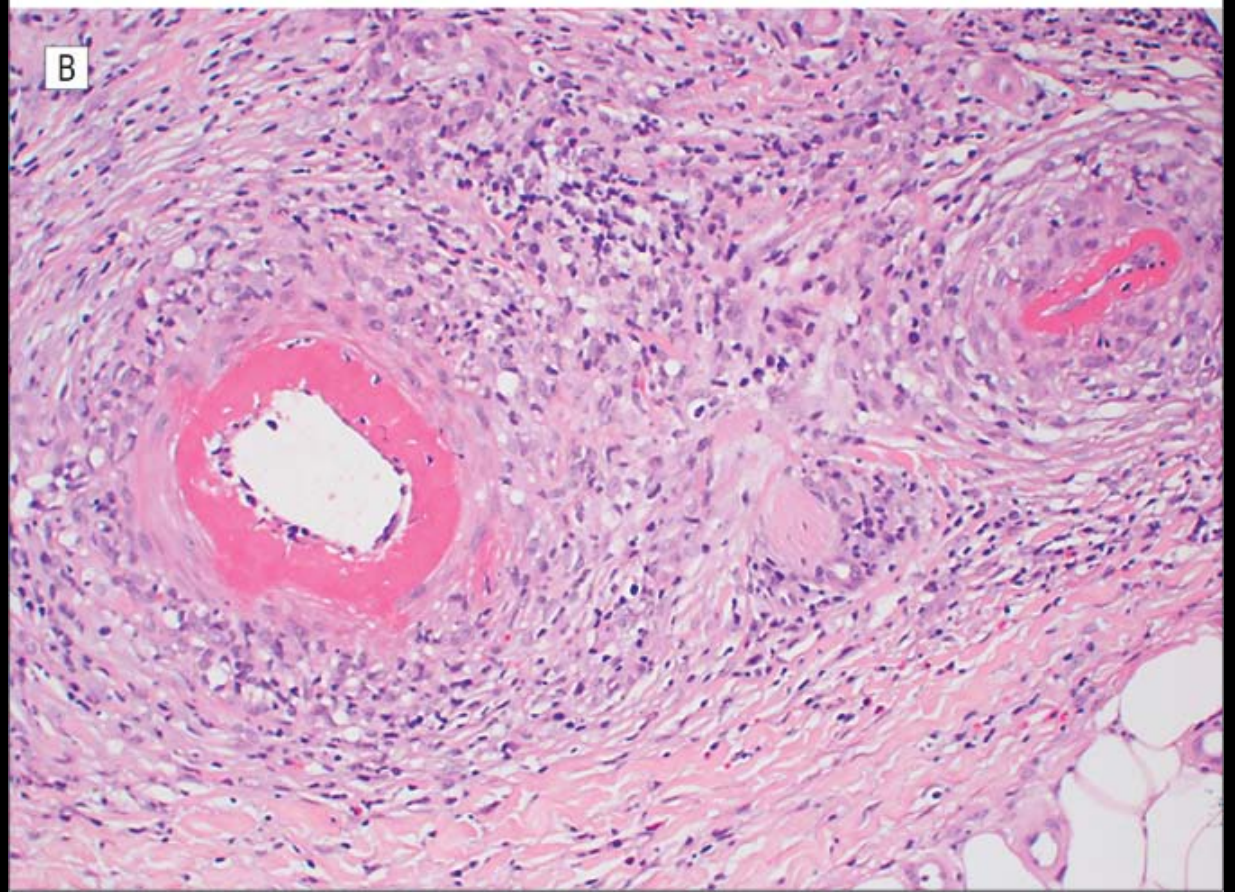
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Lymphocytic Thrombophilic Arteritis
A Newly Described Medium-Sized Vessel Arteritis of the Skin

Joyce Siong-See Lee, MMED(UK), FAMS; Steven Kossard, FACD; Michael A. McGrath, MD, FRACP

Arch Dermatol. 2008;144(9):1175-1182.

Table 4. Clinical Characteristics of Patients With Cutaneous Polyarteritis Nodosa, Lymphocytic Thrombophilic Arteritis, Livedoid Vasculitis, and APS

Clinical Characteristic	Patients With Cutaneous Polyarteritis Nodosa	Patients With Lymphocytic Thrombophilic Arteritis	Patients With Livedoid Vasculitis	Patients With APS
Sex	F>M[a]	F>M	F>M	F>M
Livedo racemosa	++	++	+	++
Nodules	++	+	–	+
Purpura	++	–	++	+
Ulceration	++	–	++	+
Atrophie blanche	+/–	–	++	+
Pain	++	–	++	+
Site of involvement	LL>UL[b]	LL>UL	LL	Any site
Constitutional symptoms	+/–	–	–[c]	+
Systemic involvement	–	–	–[c]	+ (eg, thrombocytopenia, fetal loss, and recurrent thrombosis in any organ system)
Associated systemic diseases	Inflammatory bowel disease in 6%	–	Often associated with chronic venous insufficiency and less commonly with SLE, APS, scleroderma	Secondary APS associated with SLE, other autoimmune diseases, malignancy, infections, and drugs
Disease course	Chronic, relapsing, and benign	Chronic and persistent	Chronic and relapsing	Variable, may have a fatal course (eg, catastrophic APS)

Abbreviations: APS, antiphospholipid syndrome; LL, lower limbs; SLE; systemic lupus erythematosus; UL, upper limbs; –, usually not present; +/–, infrequently or rarely present; +, sometimes present; ++, often present.

[a] Indicates females affected more often than males.

[b] Indicates LL affected more commonly than UL, or predominantly LL involvement.

[c] Generally nil, unless associated with secondary causes, such as SLE or APS.

Table 5. Histologic Characteristics of Patients With Cutaneous PAN, Lymphocytic Thrombophilic Arteritis, Livedoid Vasculitis, and Antiphospholipid Syndrome

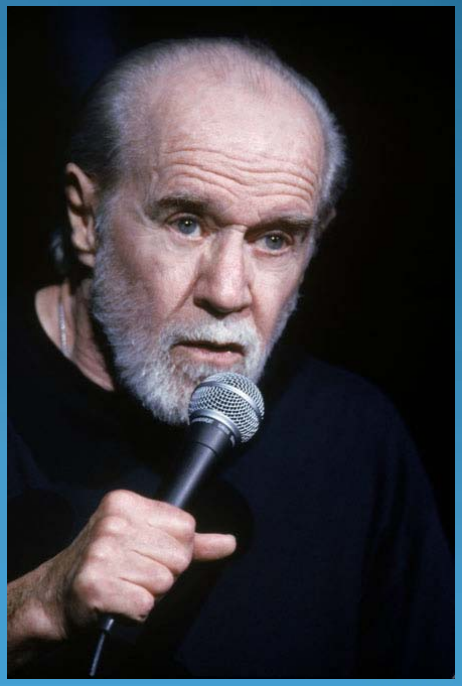
Histologic Characteristic	Patients With Cutaneous PAN	Patients With Lymphocytic Thrombophilic Arteritis	Patients With Livedoid Vasculitis	Patients With Antiphospholipid Syndrome
Involvement of small dermal blood vessels	–	–	++	+
Involvement of medium-sized arterioles	++	++	+/–	+
Presence of a fibrin ring around the vessel lumina	–	++	++	–
Presence of thrombi	+/–	+	++	++
Degree of inflammation in vessel wall	++	++	+	–
Neutrophils in vessel wall	++ (Less with older lesions)	+/– (Few even in active lesions)	–	–
Mononuclear cells in vessel wall	+ (More with older lesions)	++	+	–
Eosinophils in vessel wall	+	+/–	–	–
Nuclear dust	++	++	–	–

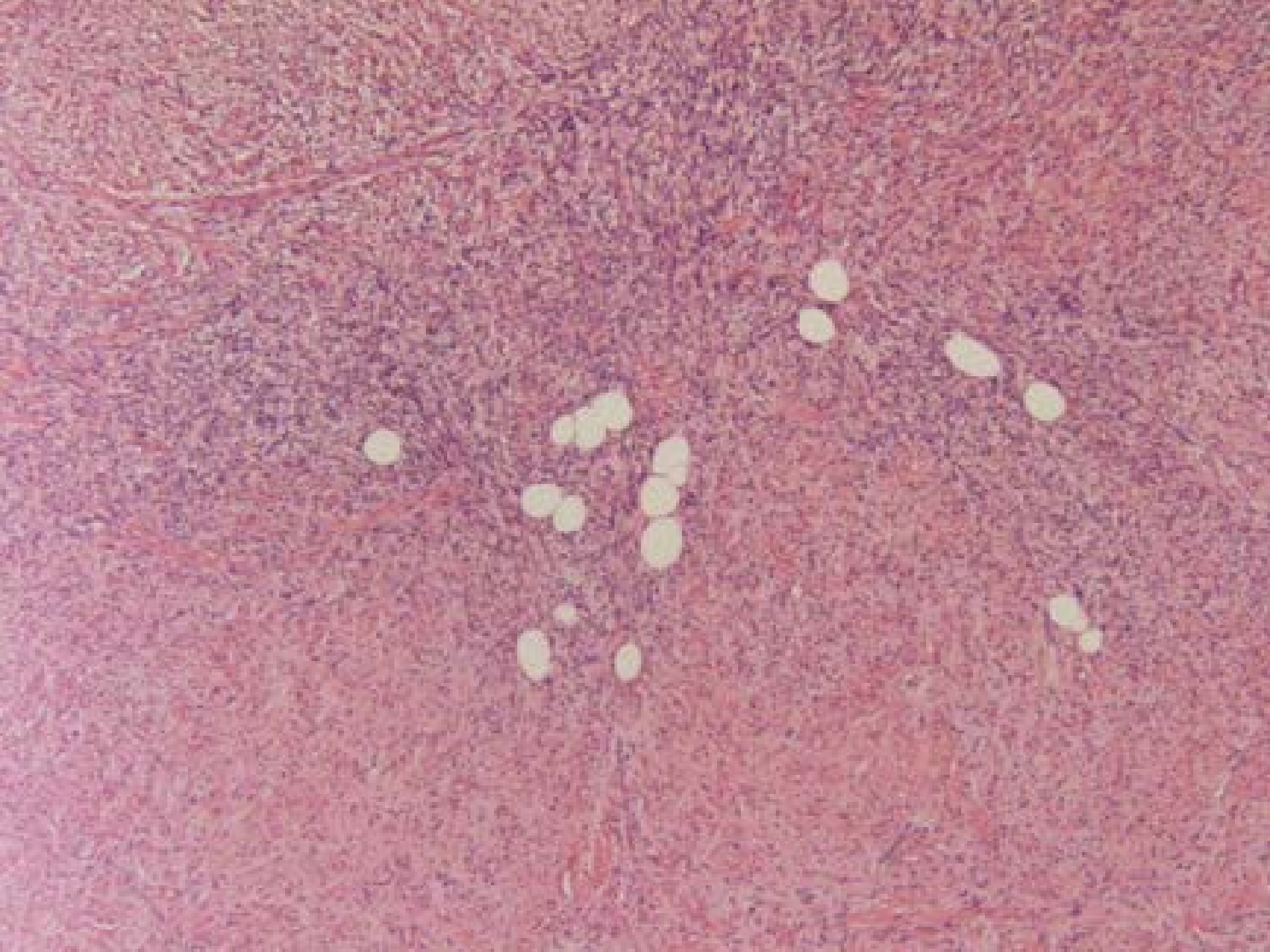
Abbreviations: PAN, polyarteritis nodosa; –, usually not present; +/–, infrequently or rarely present; +, sometimes present; ++, often present.

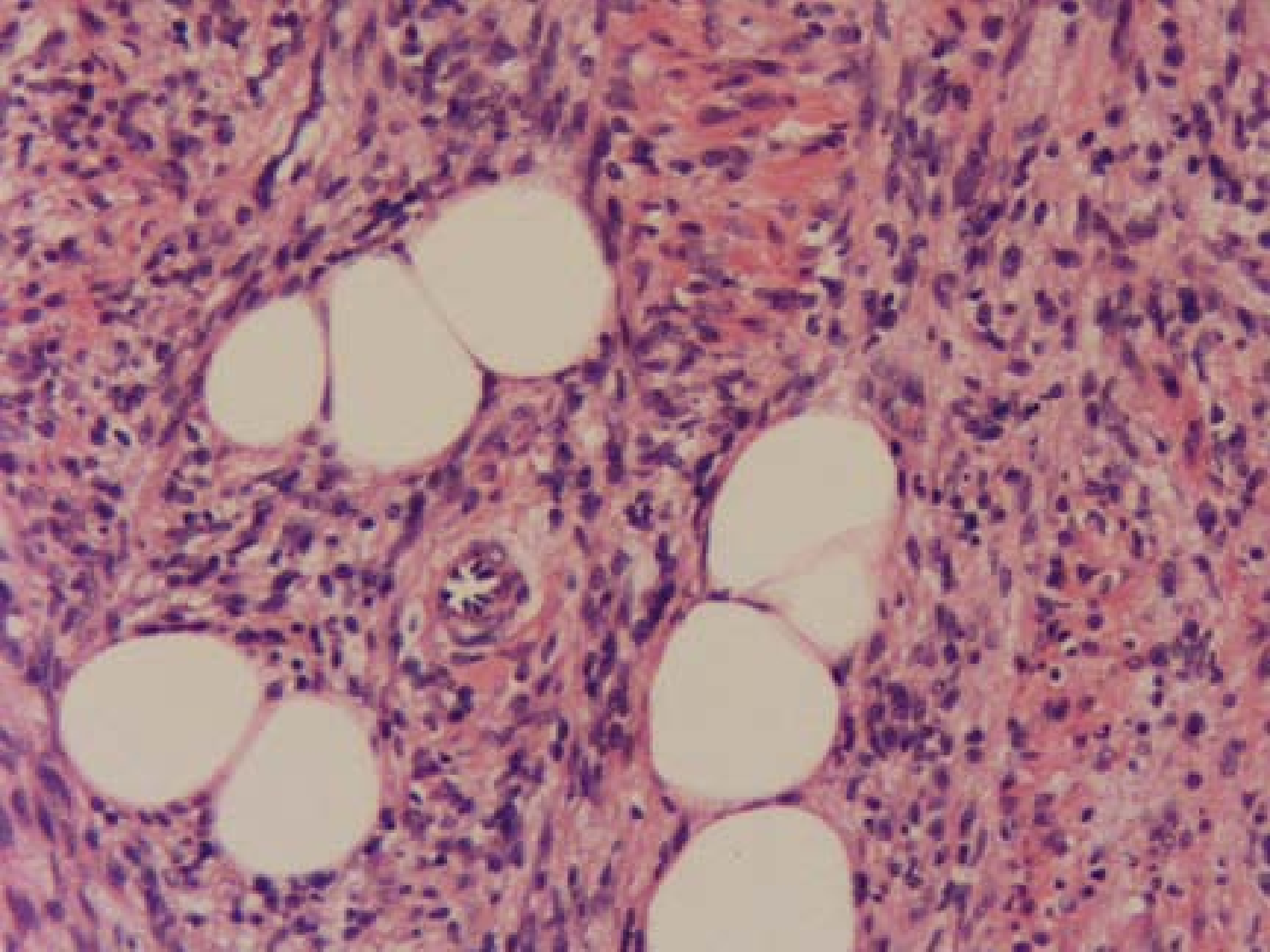
A true lymphocytic vasculitis is very rare and is now associated with a definitive clinical disease.

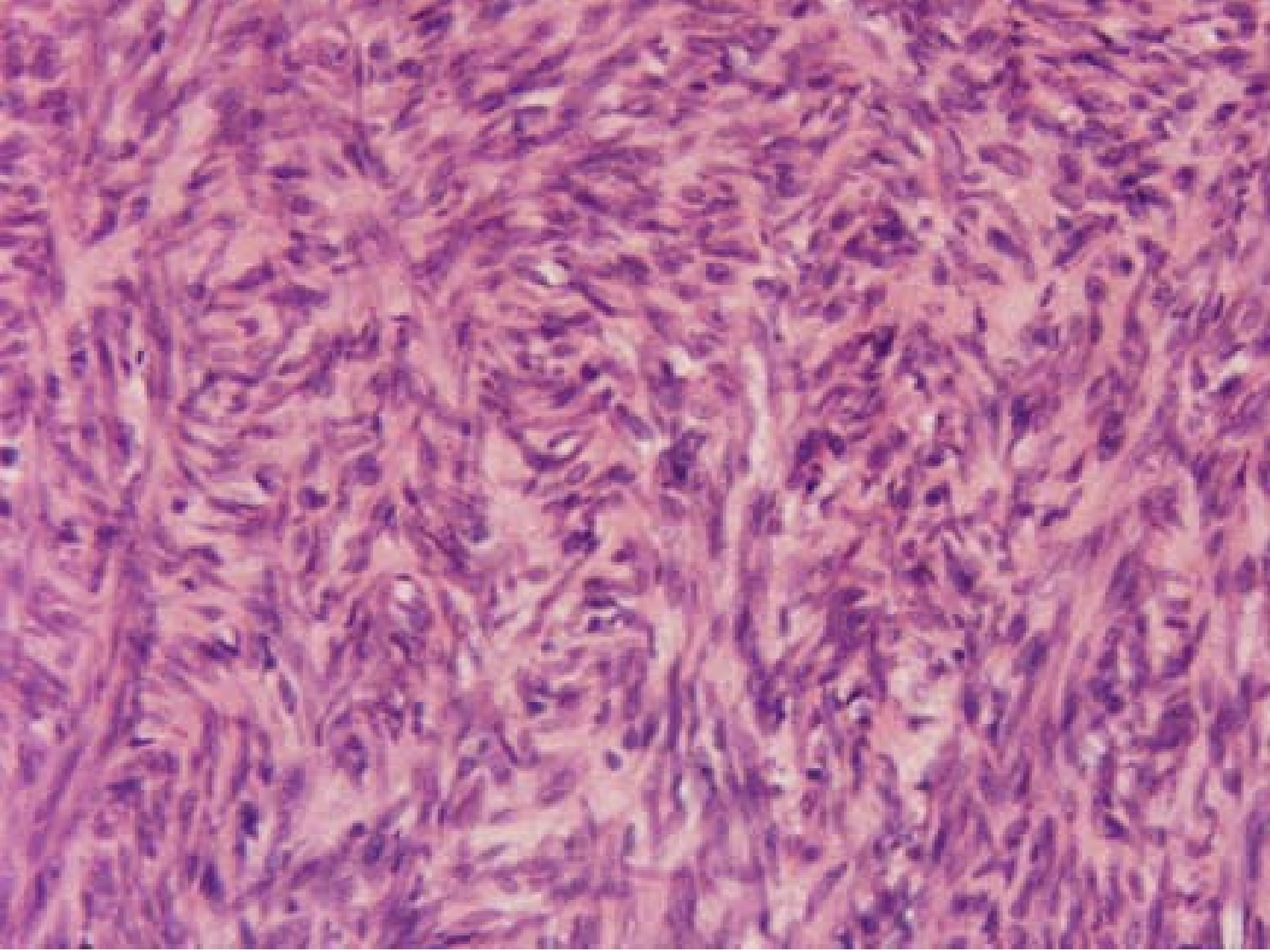
The Seven Things

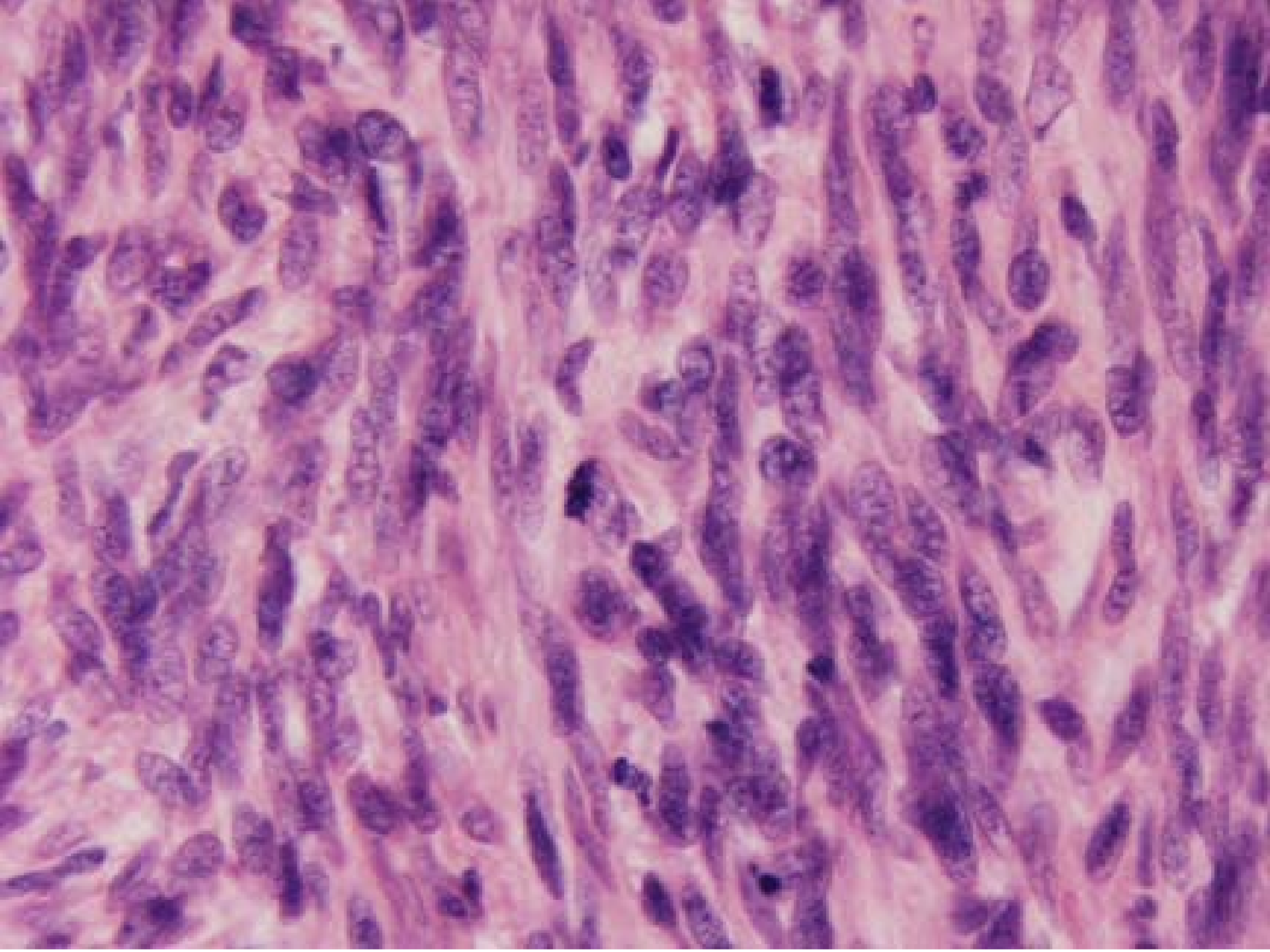
- Low Power Objective-High Power Pathologist
- Measuring a Melanoma
- The Best Special Stain
- Margins on a Punch or Shave biopsy
- Lymphocytic Vasculitis
- **IHC is the Magic Bullet**

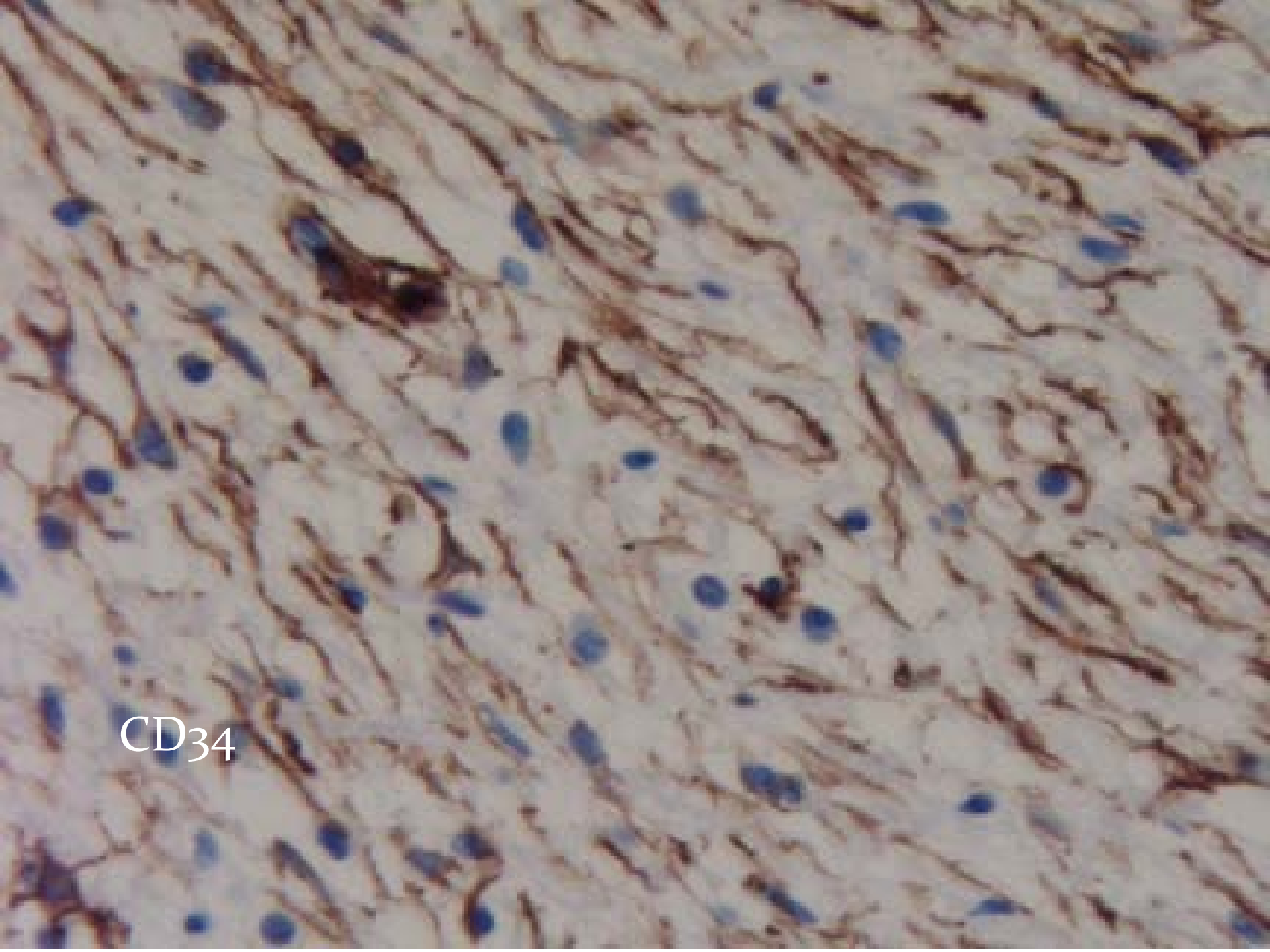








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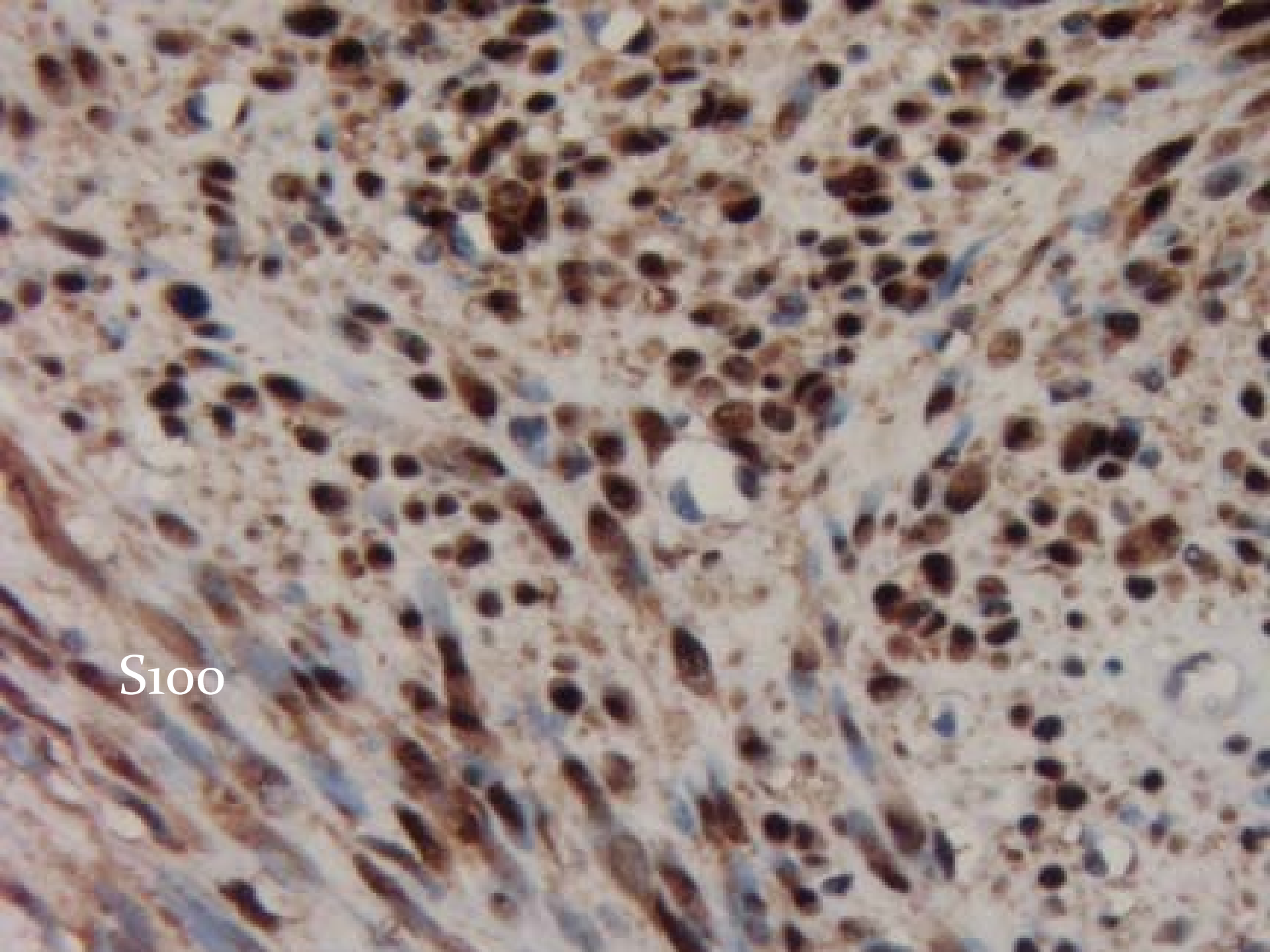
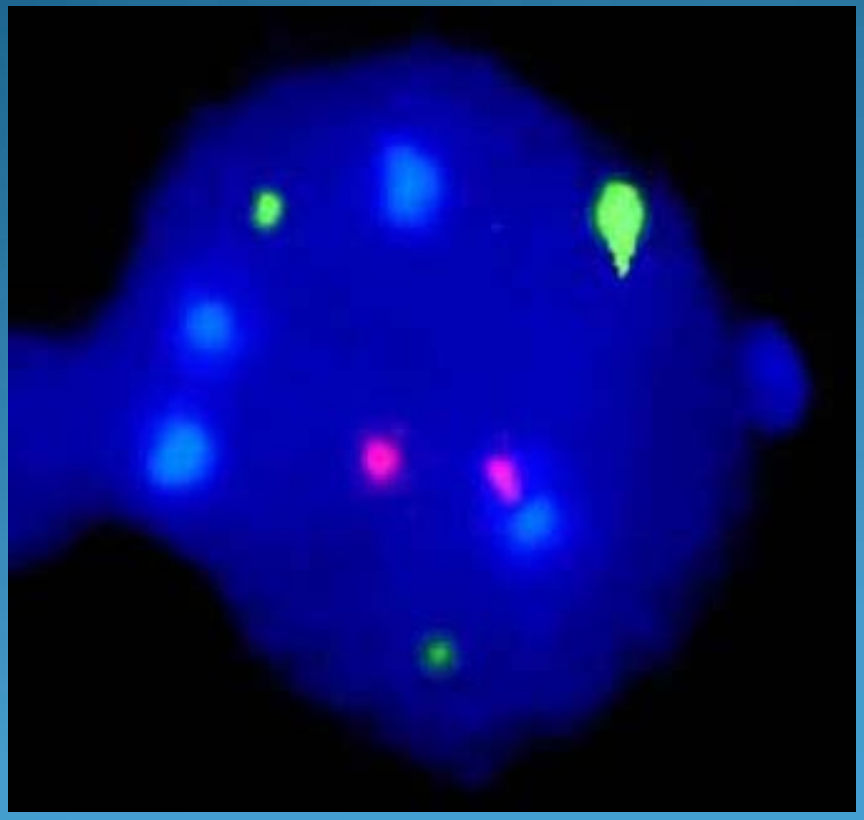

S100

Ancillary Studies



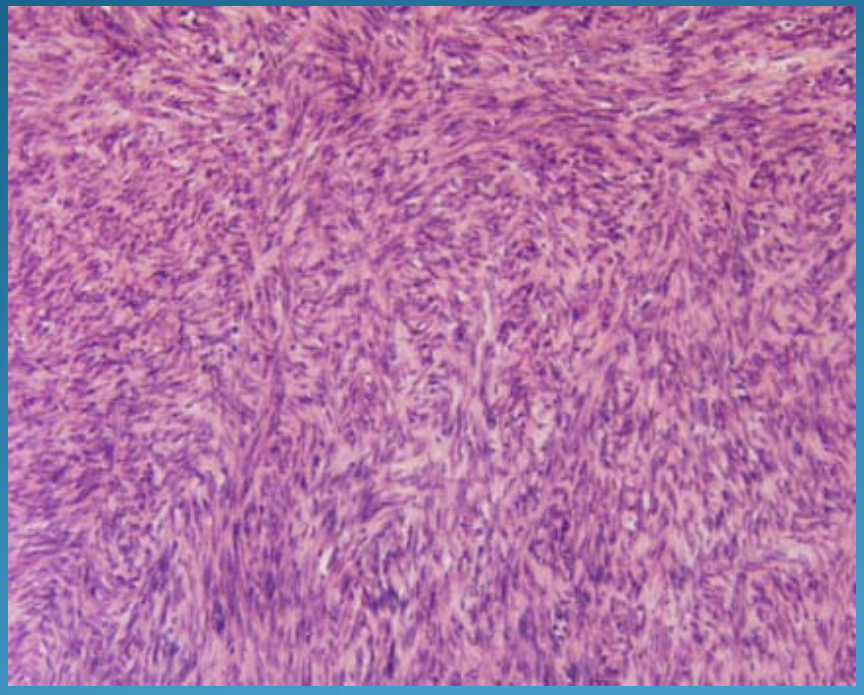
- *Negative for genomic gains of t(17;22) (COL1A1-PDGFB)
- **Amplification of 17q23.2-q25.3 (topoisomerase II-alpha (TOP2A)

*Hum Pathol. 2008 Feb;39(2):184-93.

**J Clin Pathol. 2004 Nov;57(11):1172-8.

Malignant Peripheral Nerve Sheath Tumor with CD34 co-expression

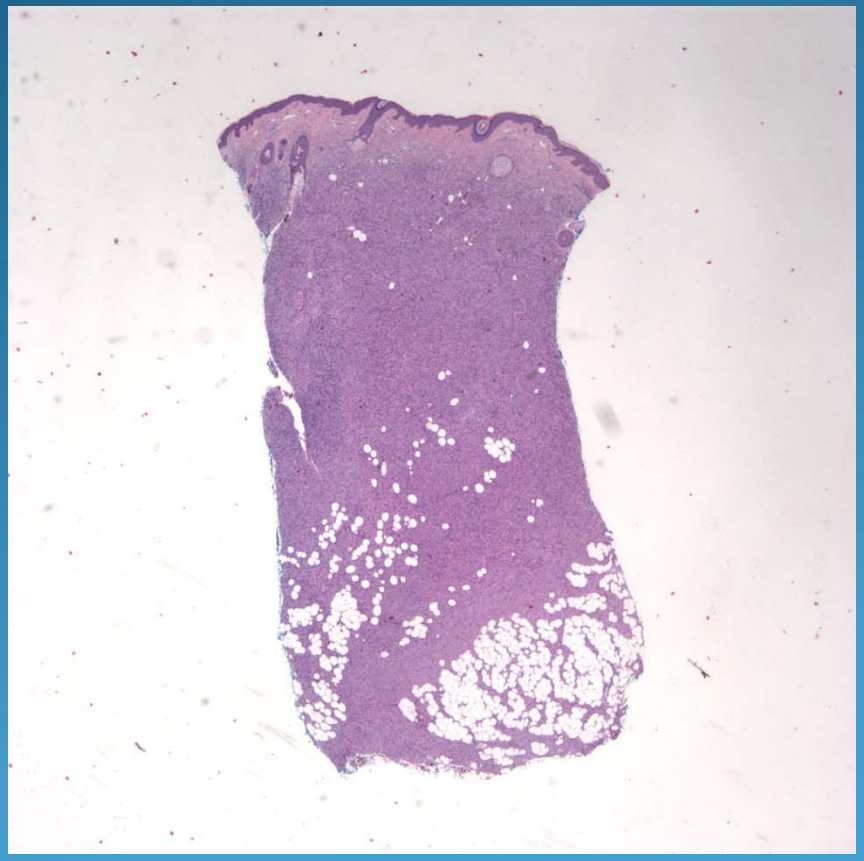
MPNST



- LG MPNST
  - 80% diffuse CD34+
- HG MPNST
  - 9% diffuse CD34+

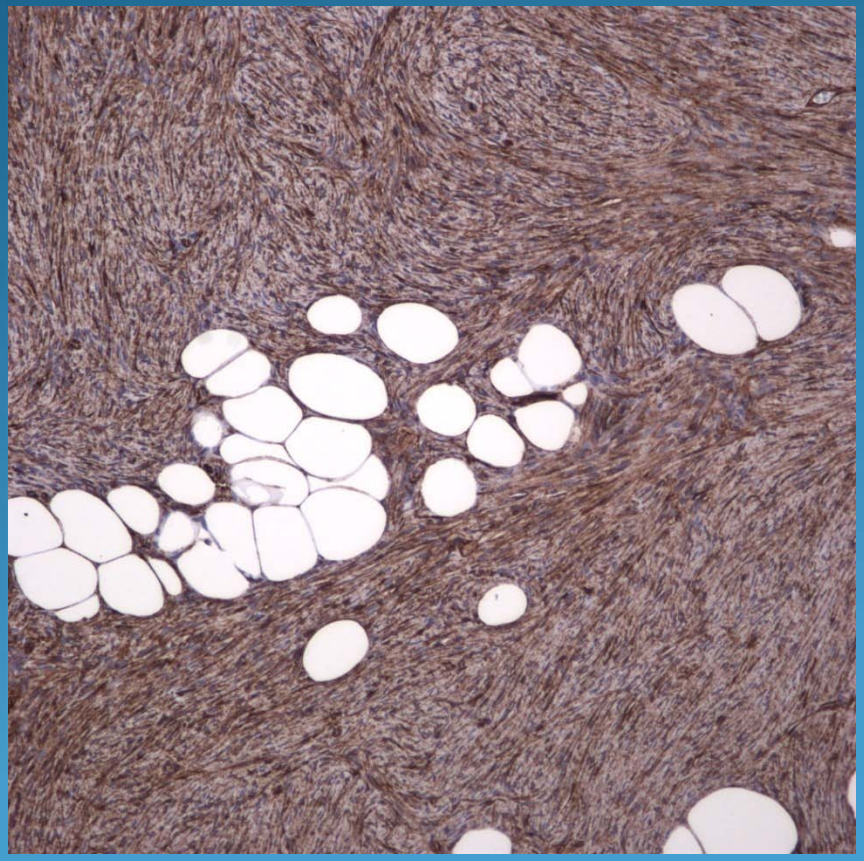
Am J Surg Pathol. 2003 Oct;27(10):1337-45.

DFSP



- CD34 diffusely expressed
- May also express bcl-2
- Pattern of Staining
- Factor XIIIa on periphery
  -

CD34



- Sialomucin cell-cell adhesion factor (1q32)
- Hematopoietic and vascular associated tissue

CD34 Positive Benign Tumors of Skin

Angiomyofibroblastoma
Superficial and Deep angiomyxoma
Acral fibromyxoma
Cellular digital fibroma
Eruptive fibromas
Glomus tumors
CD34-reactive fibrous papule of the nose
CD34-reactive trichodiscoma
Perineurioma

CD34 Positive Benign Tumors

Dendrocyte hamartoma

Medallion-like dendrocyte hamartoma

Myxoid dendrocytoma

Sclerotic fibroma

Pacinian collagenoma

Spindle cell lipoma

Pleomorphic lipoma

CD34 Positive Benign Tumors

Giant cell fibroblastoma
Fibrofolliculoma
Solitary fibrous tumor
Giant cell angiofibroma
Cellular angiofibroma
Pleomorphic hyalinizing angiectatic tumor of soft parts
Pleomorphic fibroma
Trichilemmoma

Malignant CD34+ Tumors of the Skin

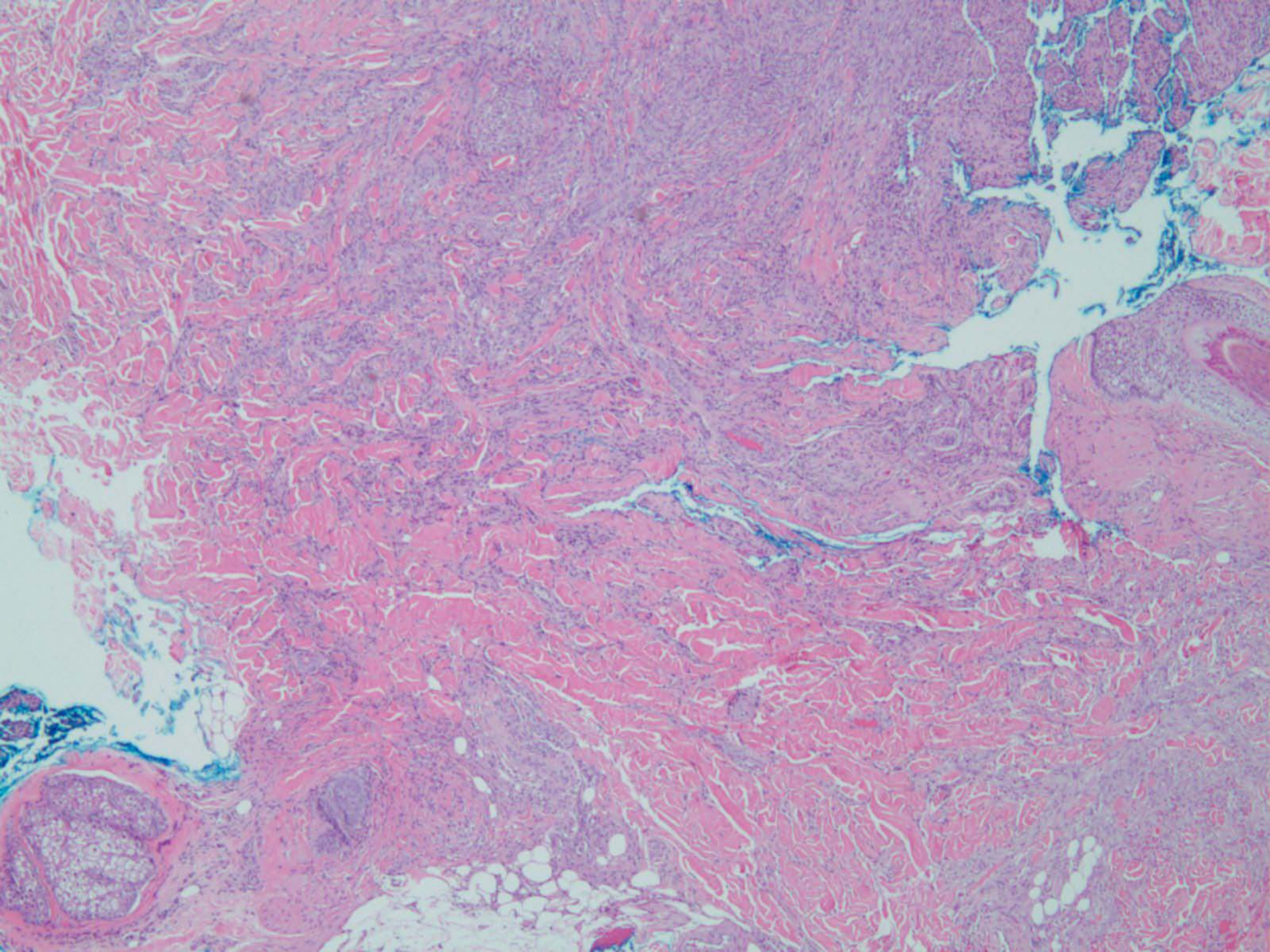
Dermatofibrosarcoma protuberans

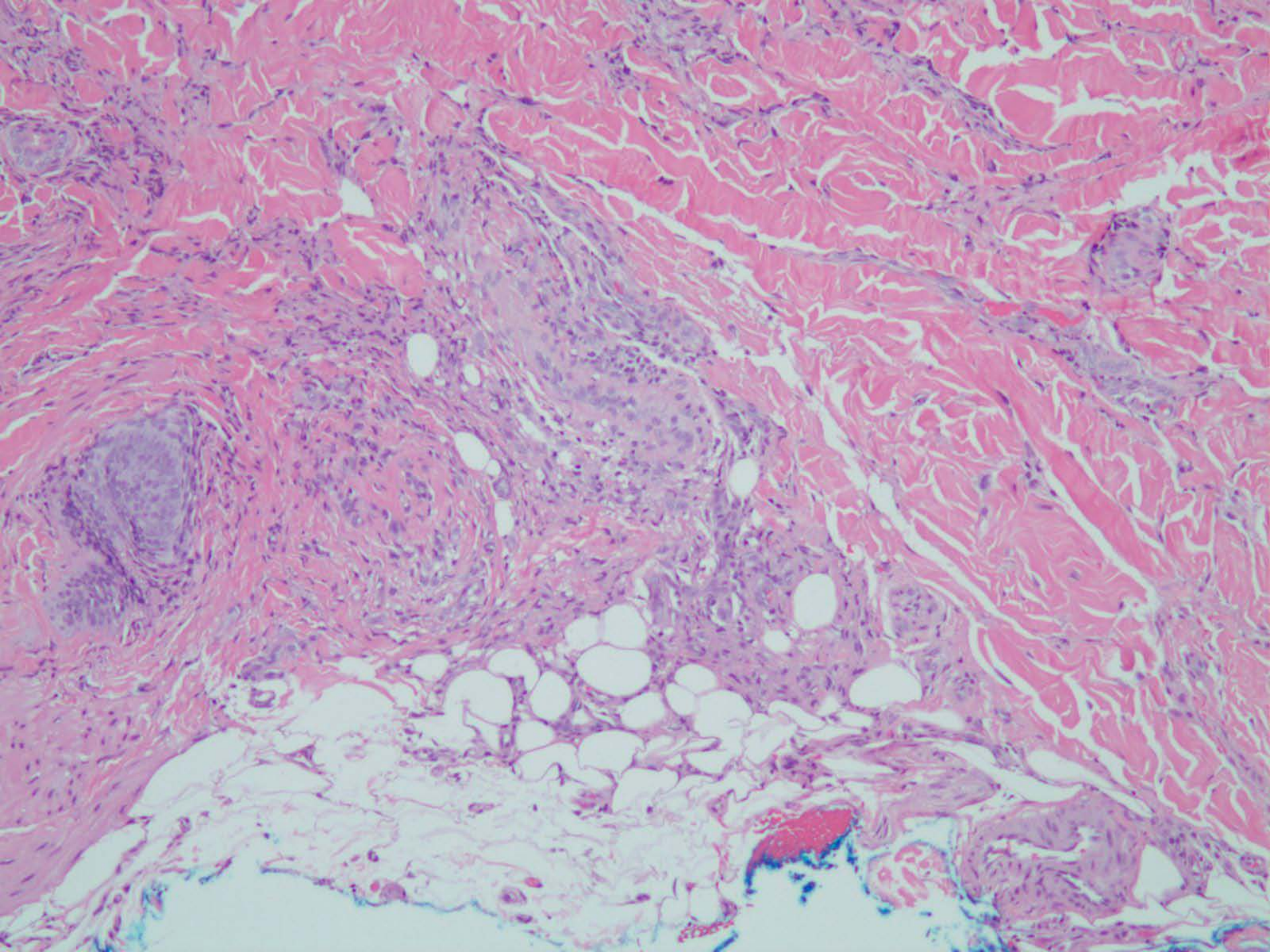
Epithelioid sarcoma

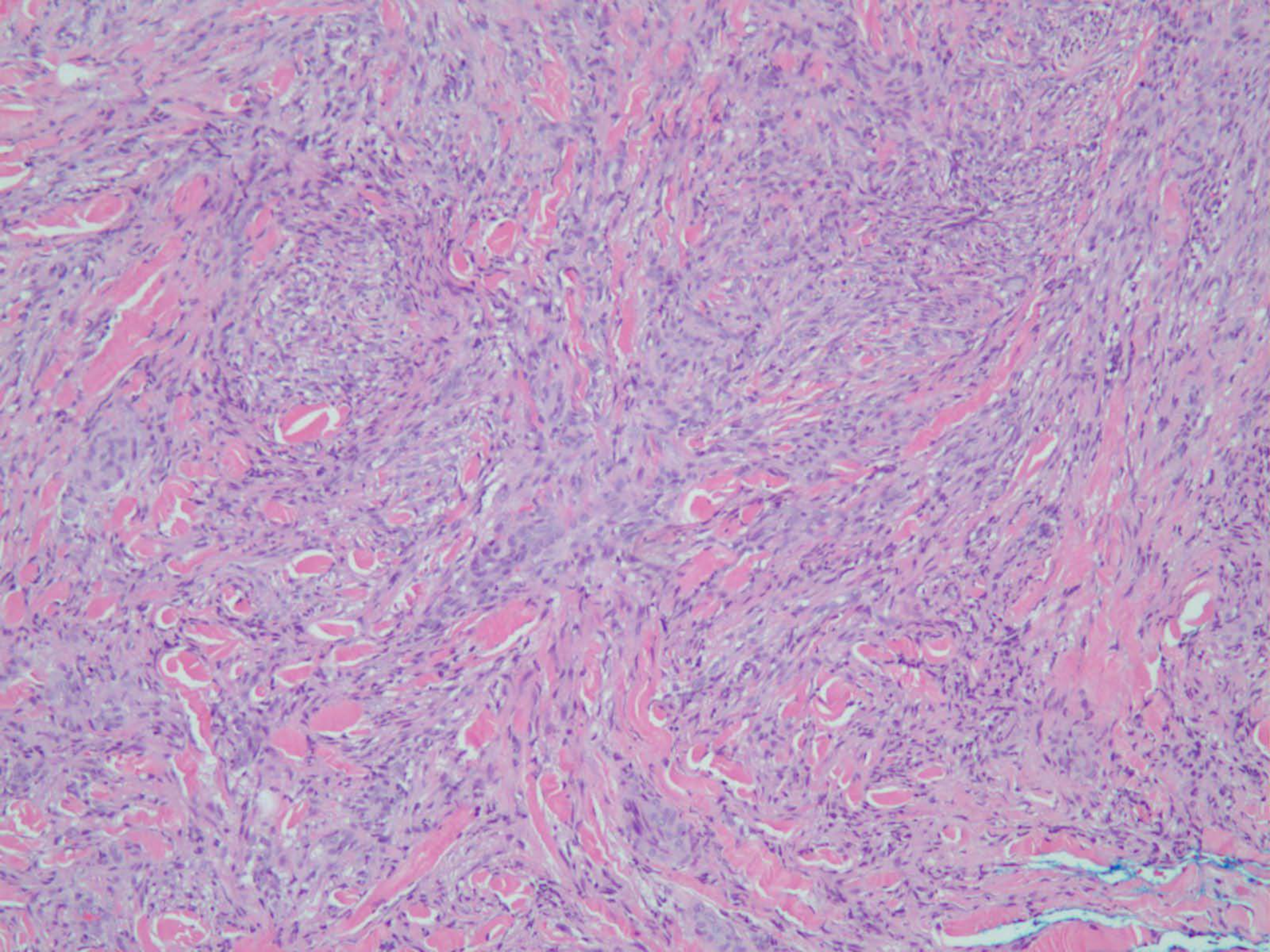
Malignant Solitary Fibrous Tumor

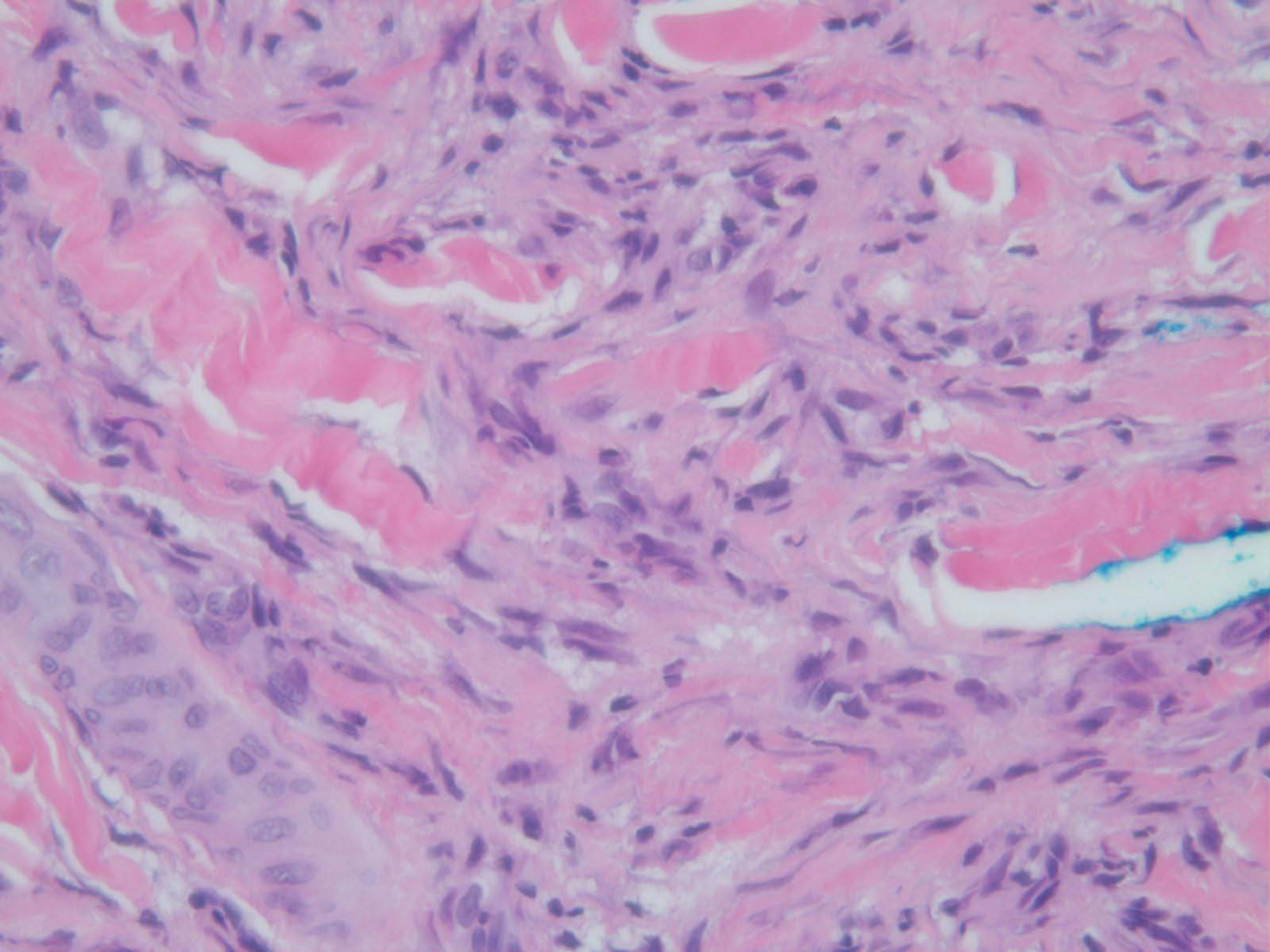
Malignant Peripheral Nerve Sheath Tumors

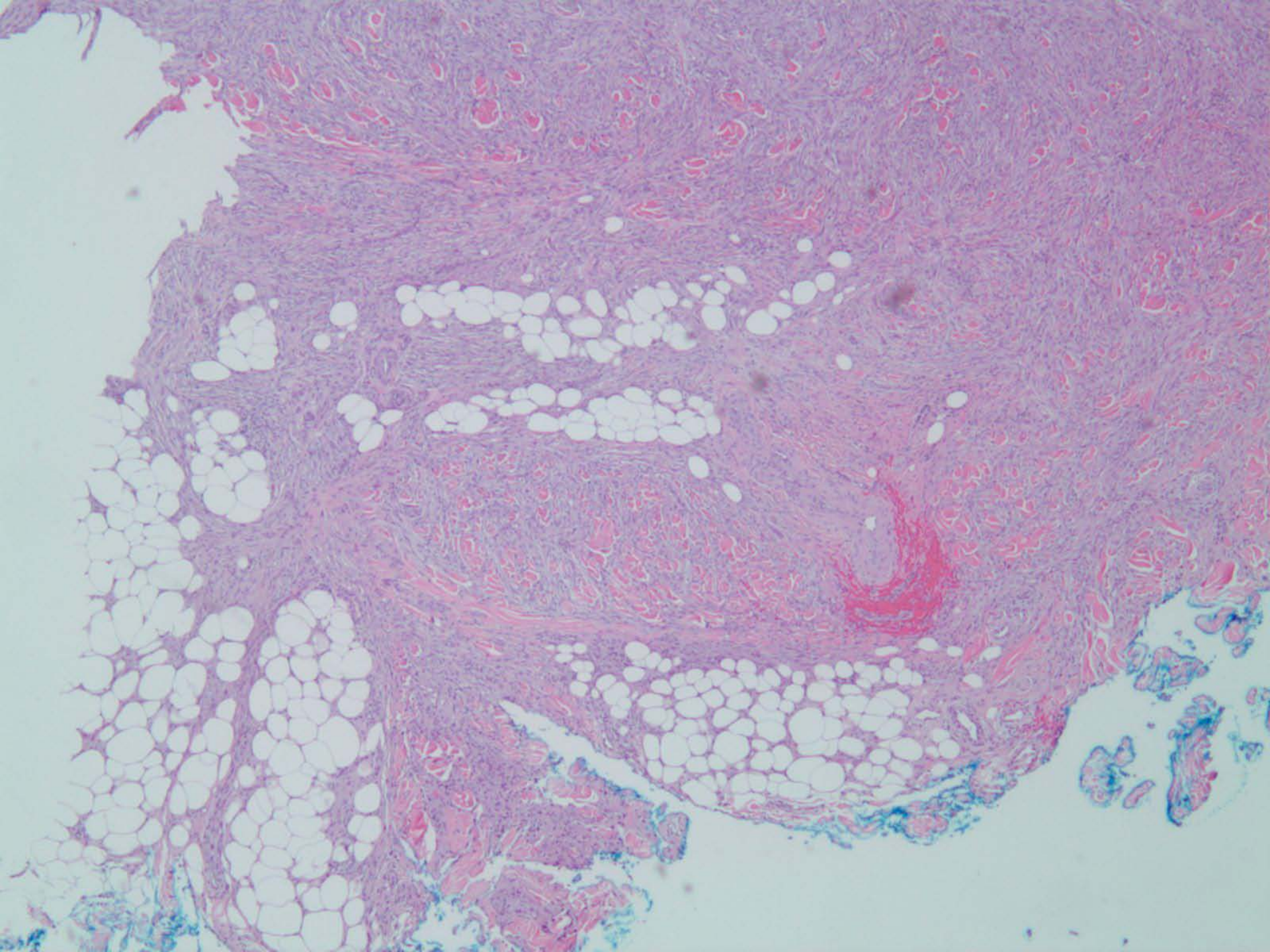
J Cutan Pathol 2009;36:89-102.

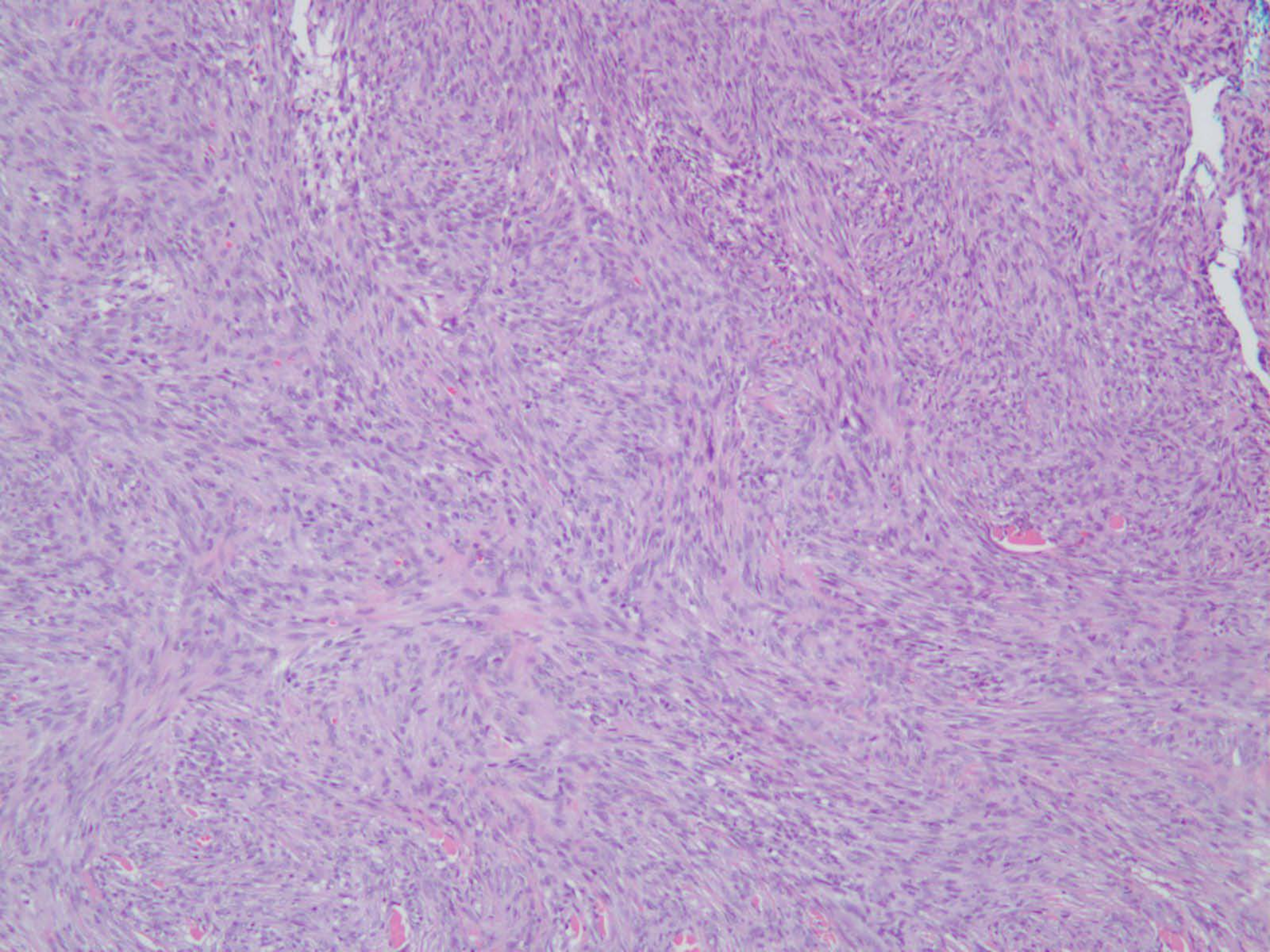


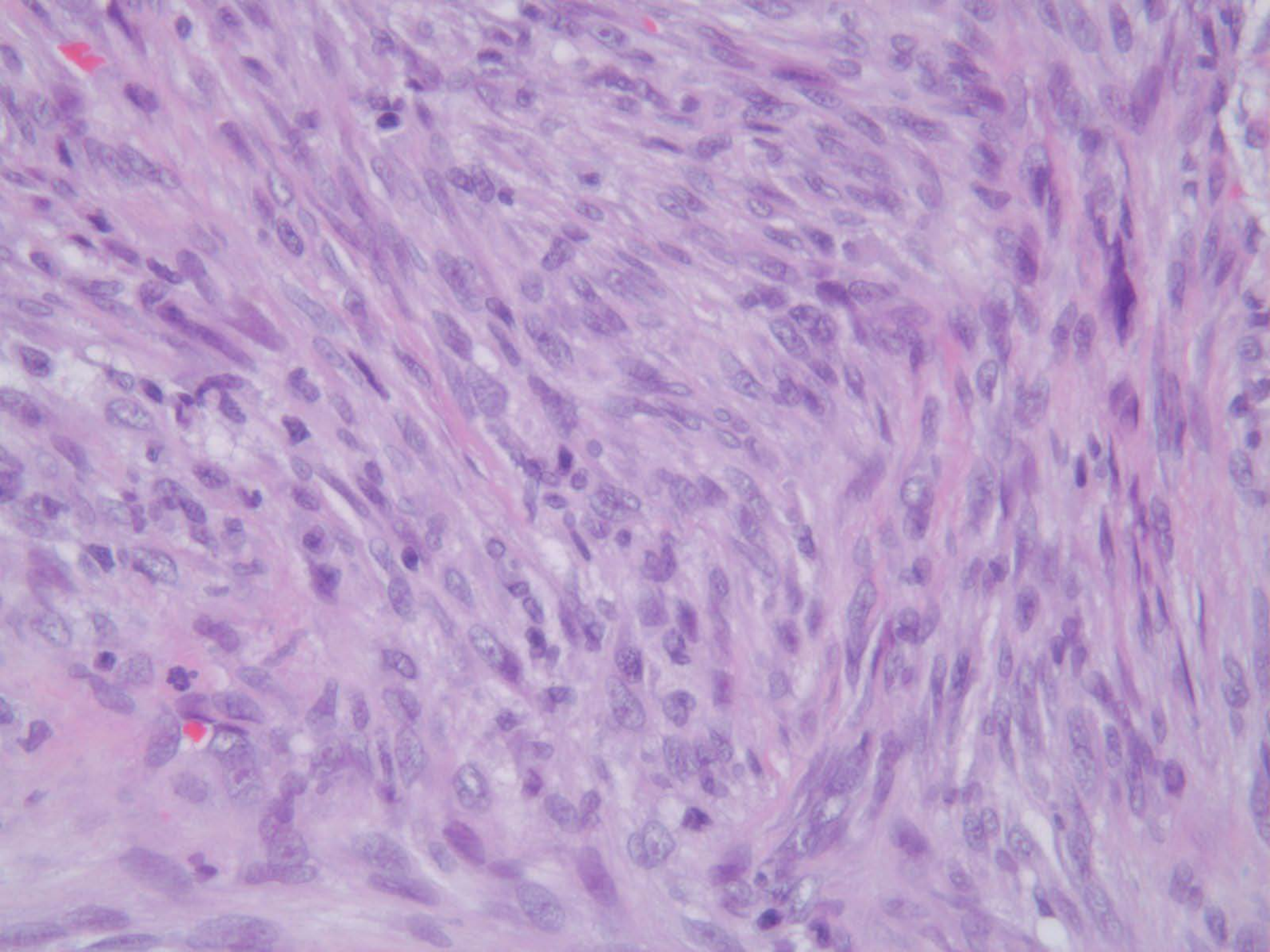


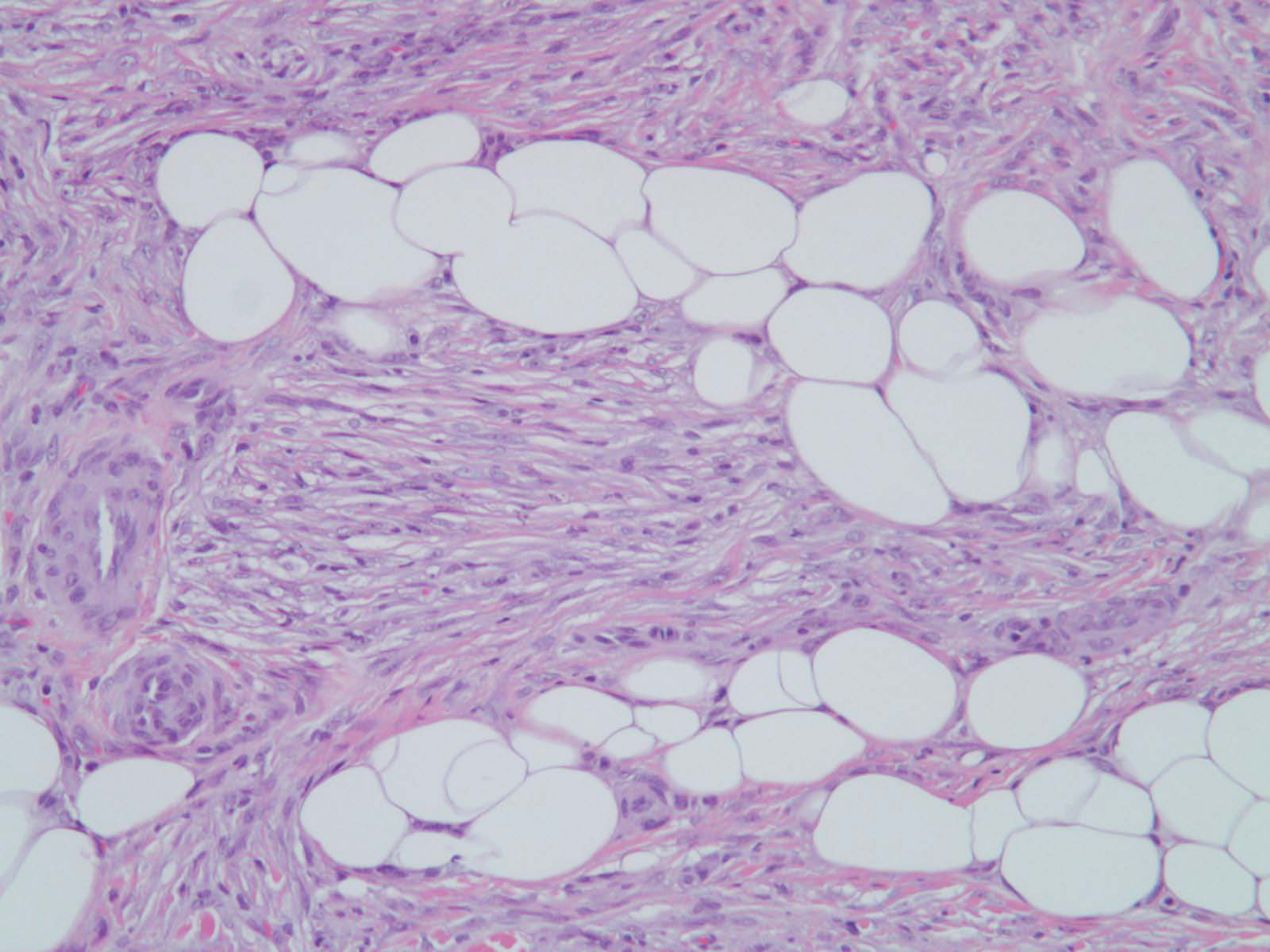


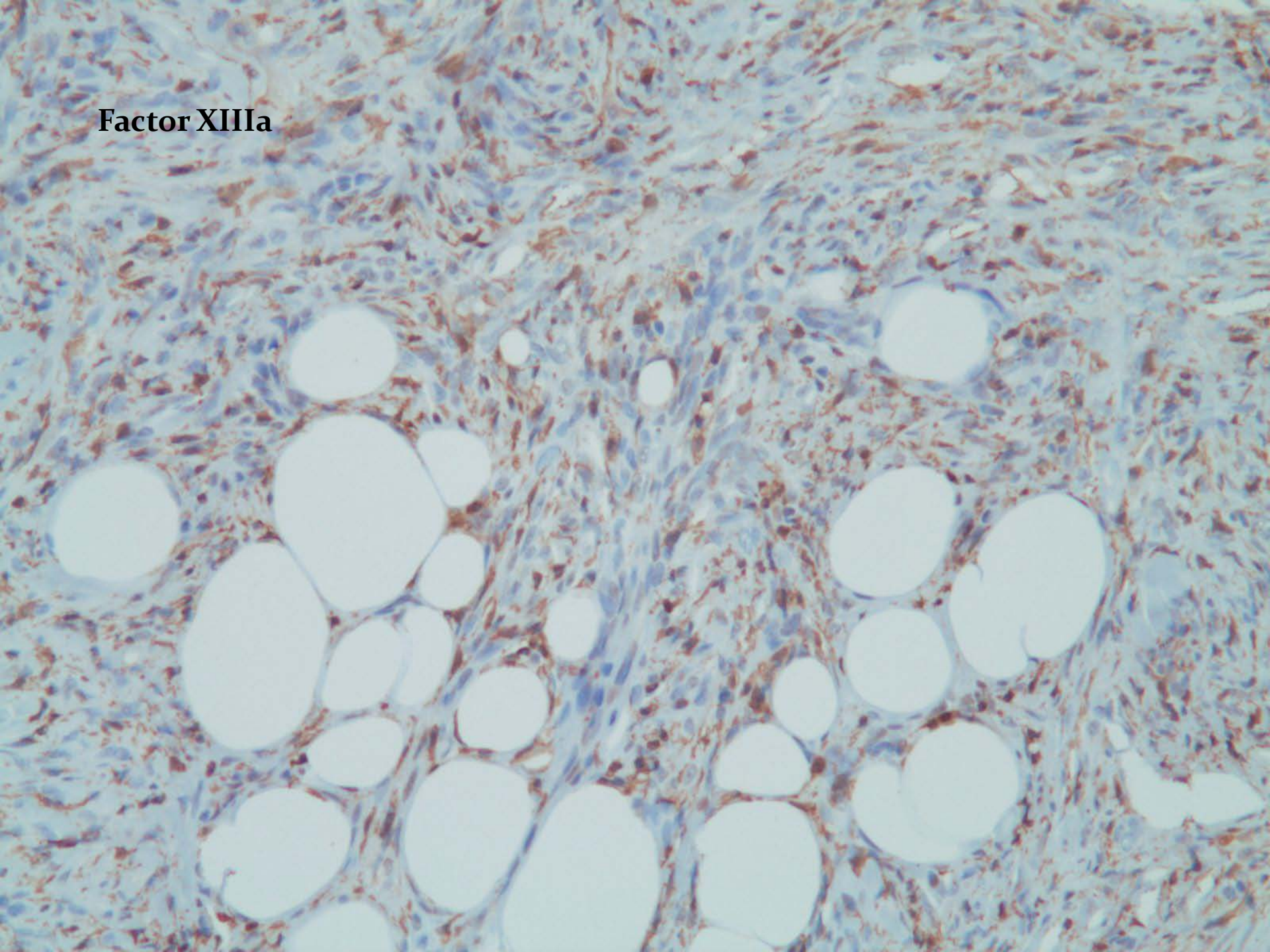


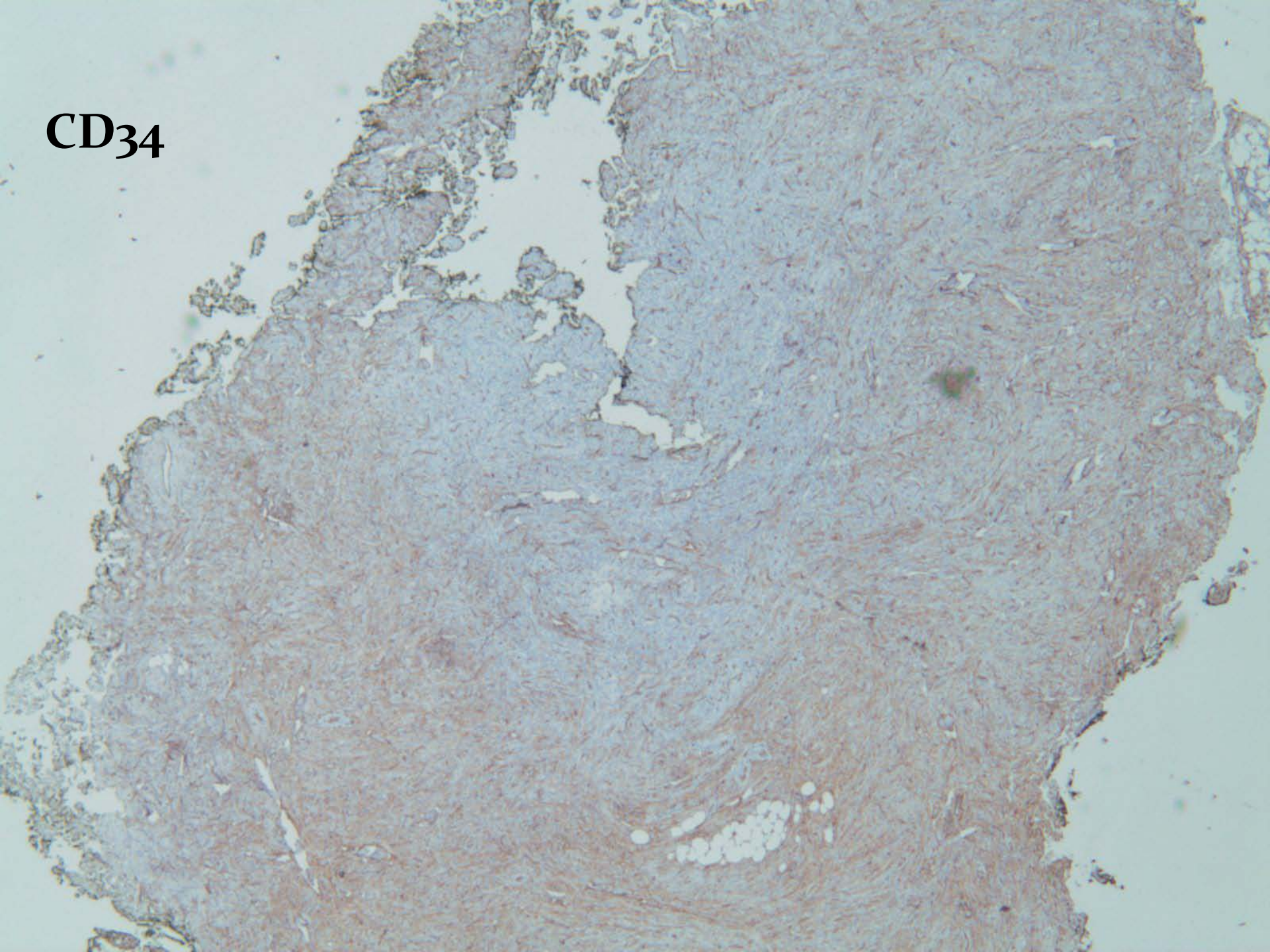


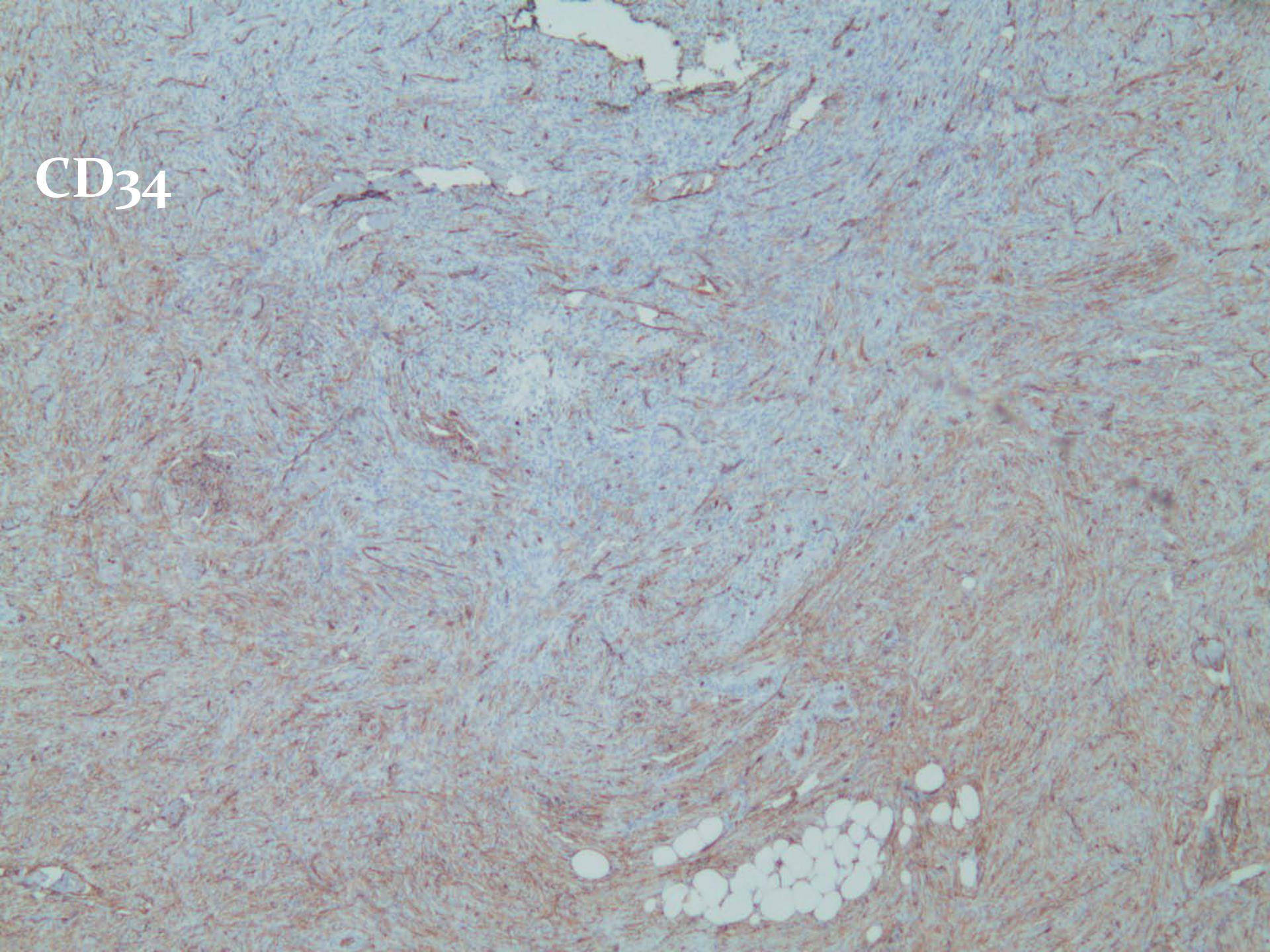


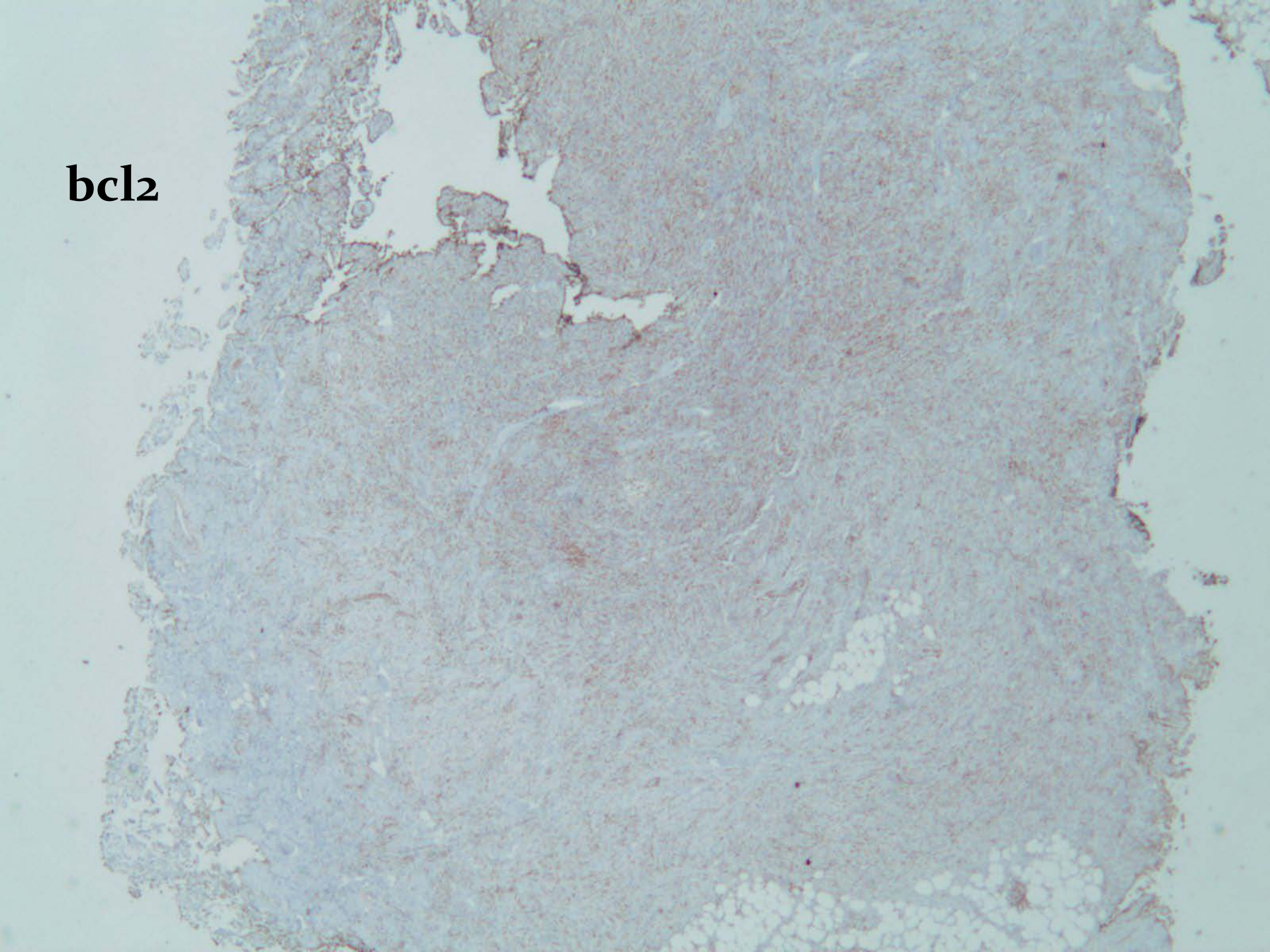


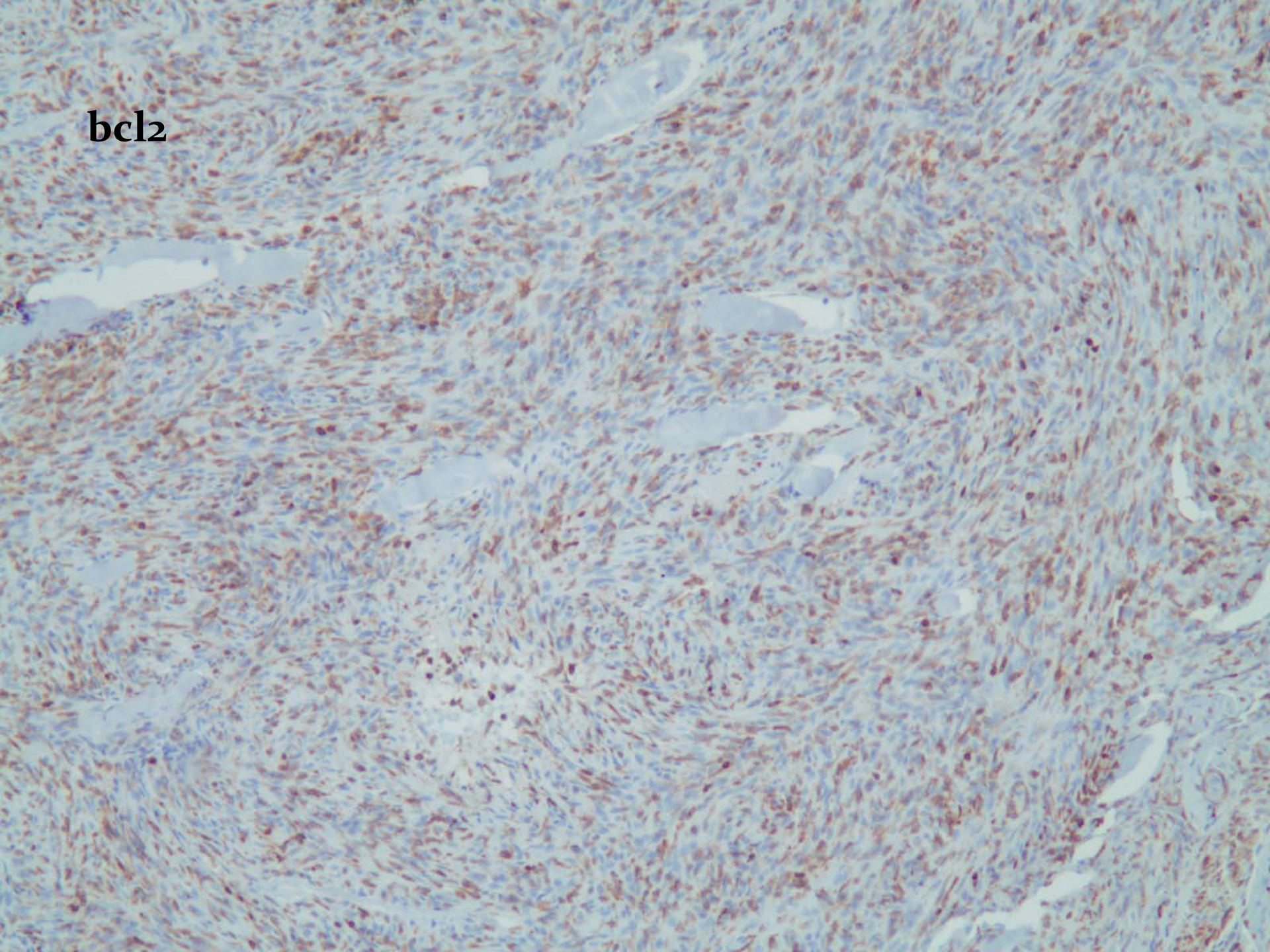



Factor XIIIa


CD34

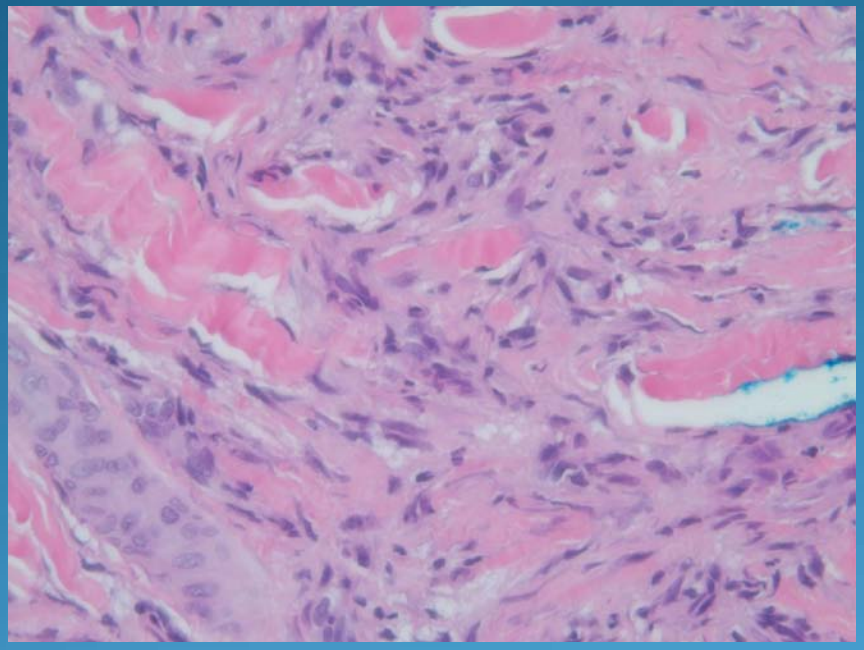

CD34


bcl2


bcl2

DFSP with DF overlap features
Confirmation: FISH

Overlap DFSP/DF

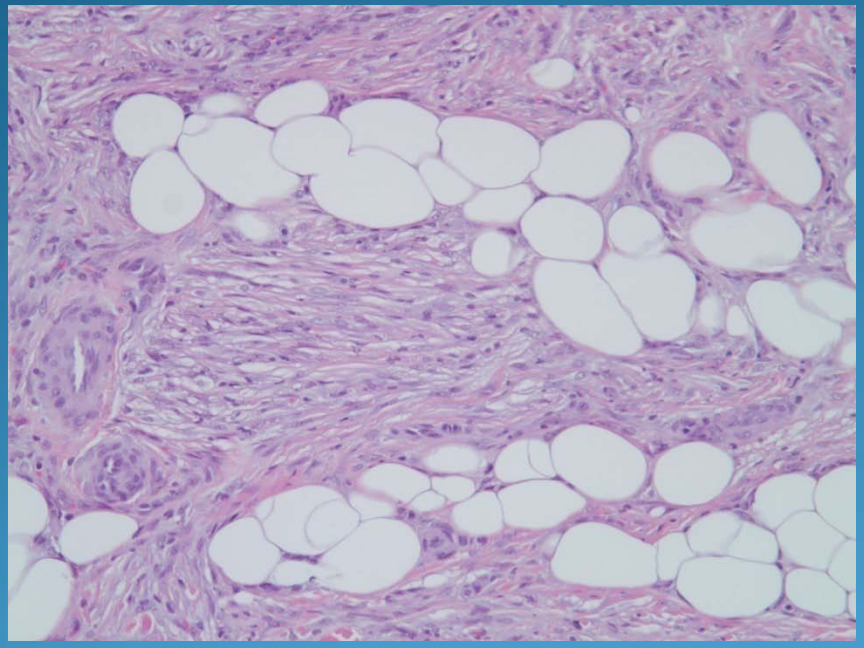


- Rare
- Overlap features-no consistent pattern
- Mixed IHC pattern
- Confirm with FISH

t(17;22) (COL1A1-PDGFB)

Am J Dermatopathol. 2008 Oct;30(5):484-7.

FXIIIa and CD34-Magic Bullets?



- FXIIIa positivity usually localized to periphery (10-15% of DFSP)
- CD34 (>90% of DFSP) diffuse
- Bcl-2 negative in DF, co-expressed with CD34 (>90% DFSP)

Am J Dermatopathol. 1993 Oct;15(5):429-34.

Am J Dermatopathol. 1997 Apr;19(2):147-53

Am J Surg Pathol. 1998 Jul;22(7):863-72.

Additional Helpful IHC Stains

IHC Stain	DF	DFSP
*Stromelysin-3	+	
**HMGA1/HMGA2	+	
***CD163	+	
*****CD44	+	

*Br J Dermatol. 2007 Aug;157(2):319-24.

**Am J Dermatopathol. 2004 Aug;26(4):267-72

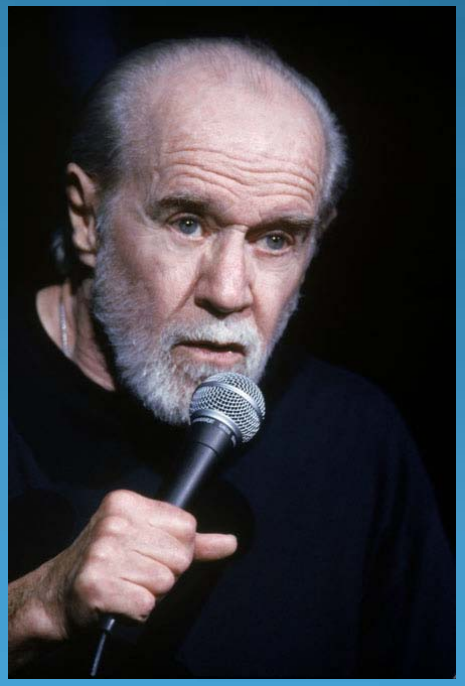
***J Cutan Pathol. 2006 May;33(5):353-60.

****J Cutan Pathol 2003; March;30(3):185-189

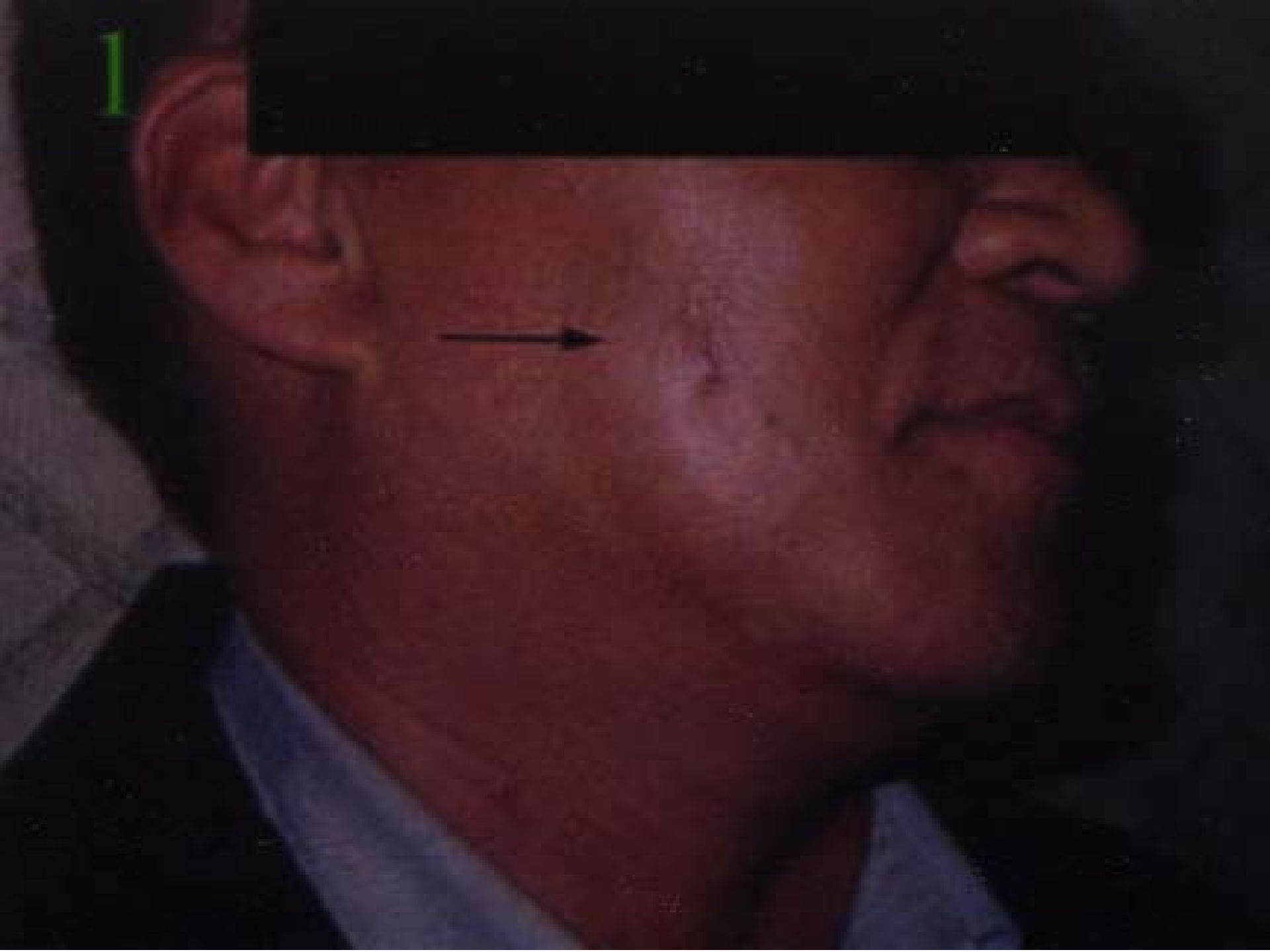
IHC may be a magic bullet for many diagnostically difficult tumors but beware of immunohistochemical mimics.

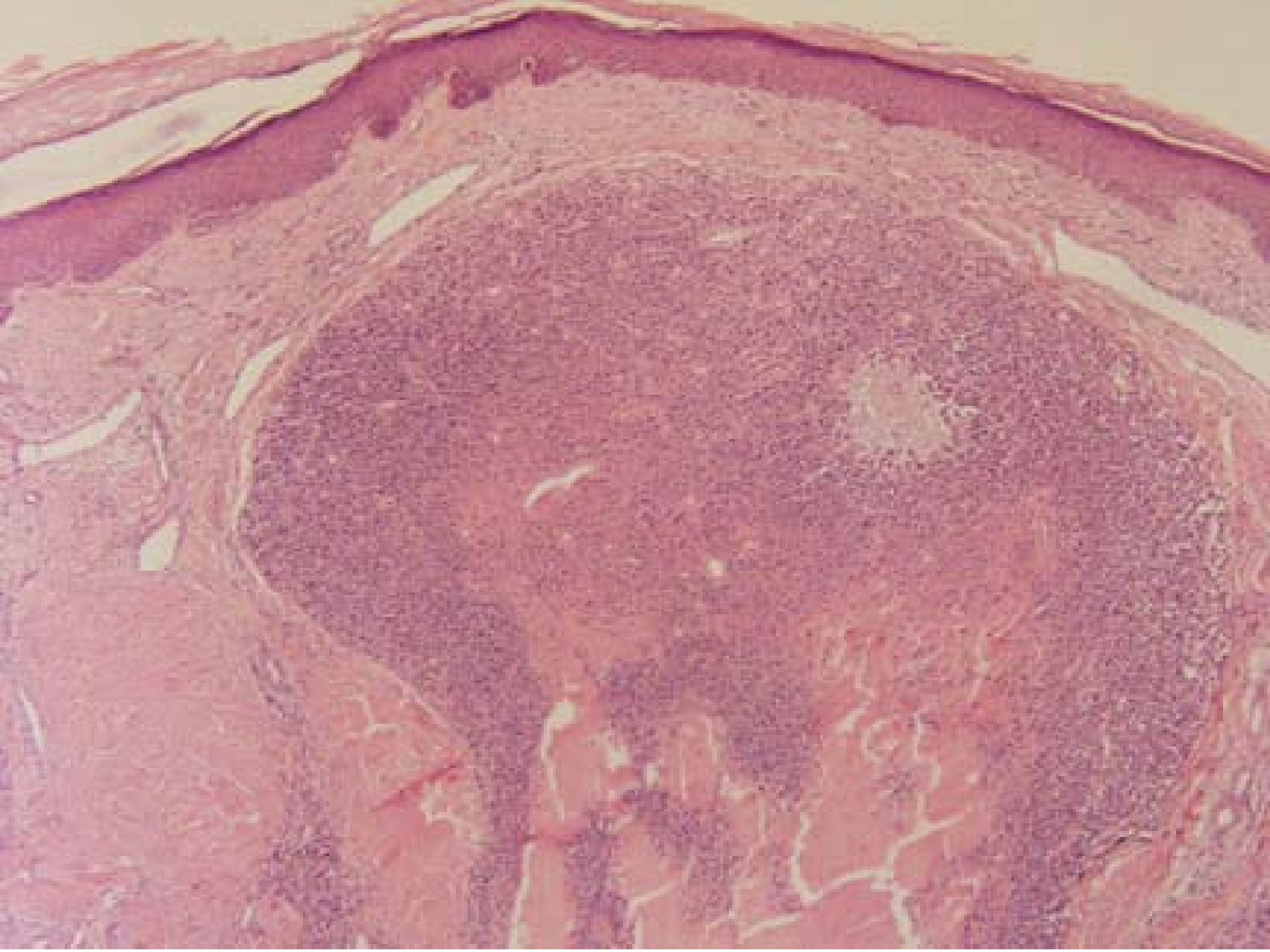
The Seven Things

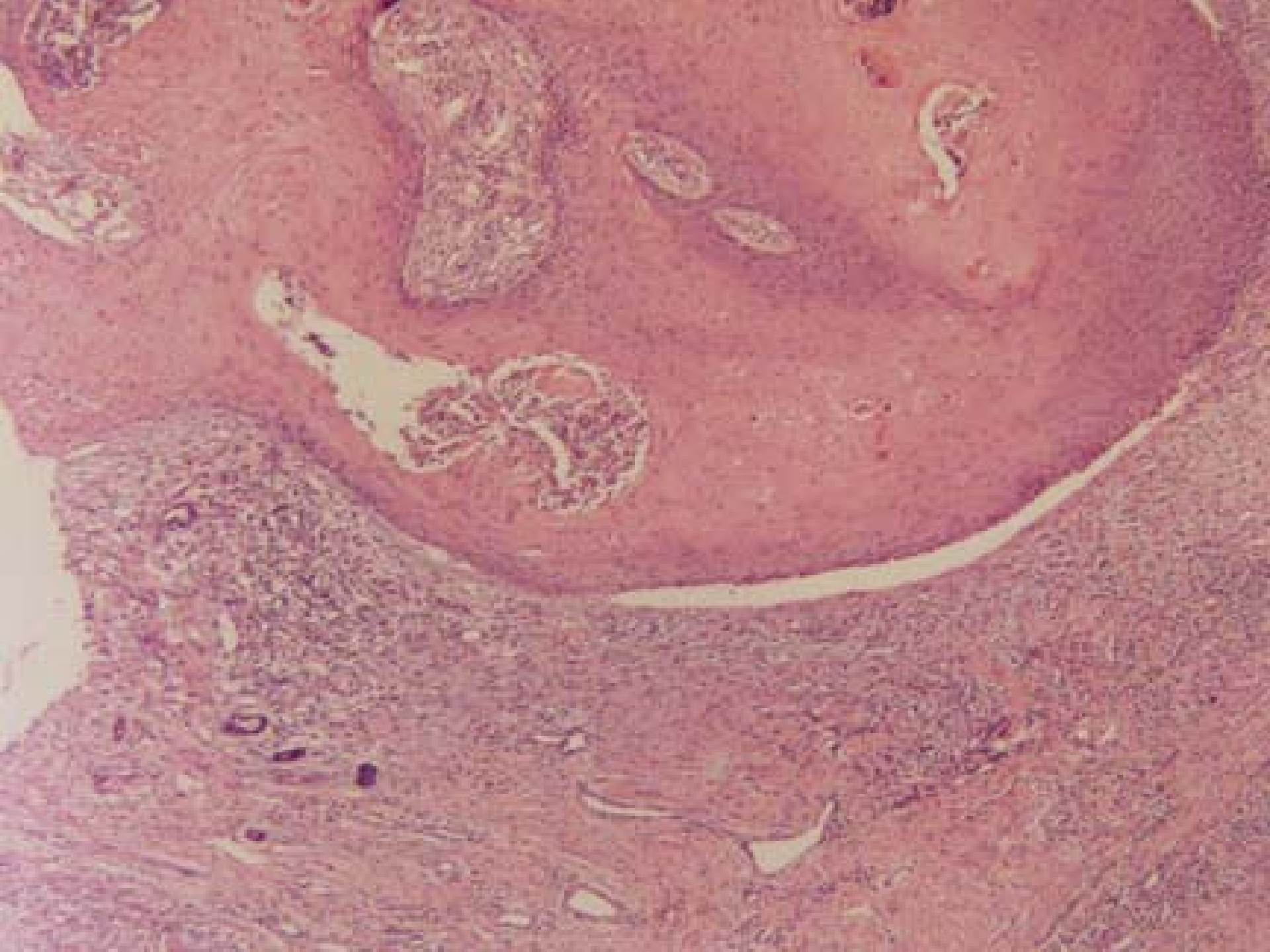
- Low Power Objective-High Power Pathologist
- Measuring a Melanoma
- The Best Special Stain
- Margins on a Punch or Shave biopsy
- Lymphocytic Vasculitis
- IHC is the Magic Bullet
- **Consultant Confloption**

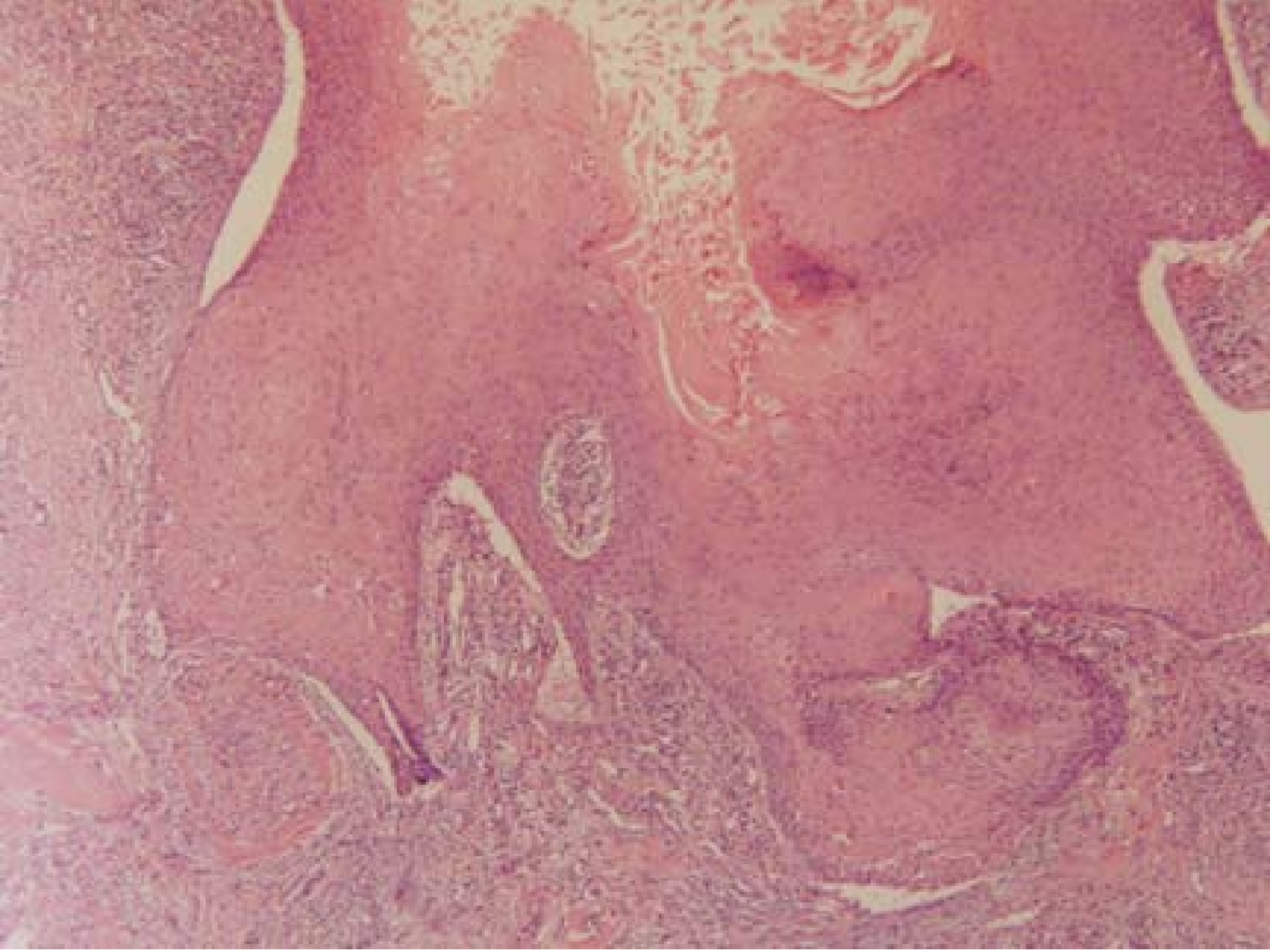


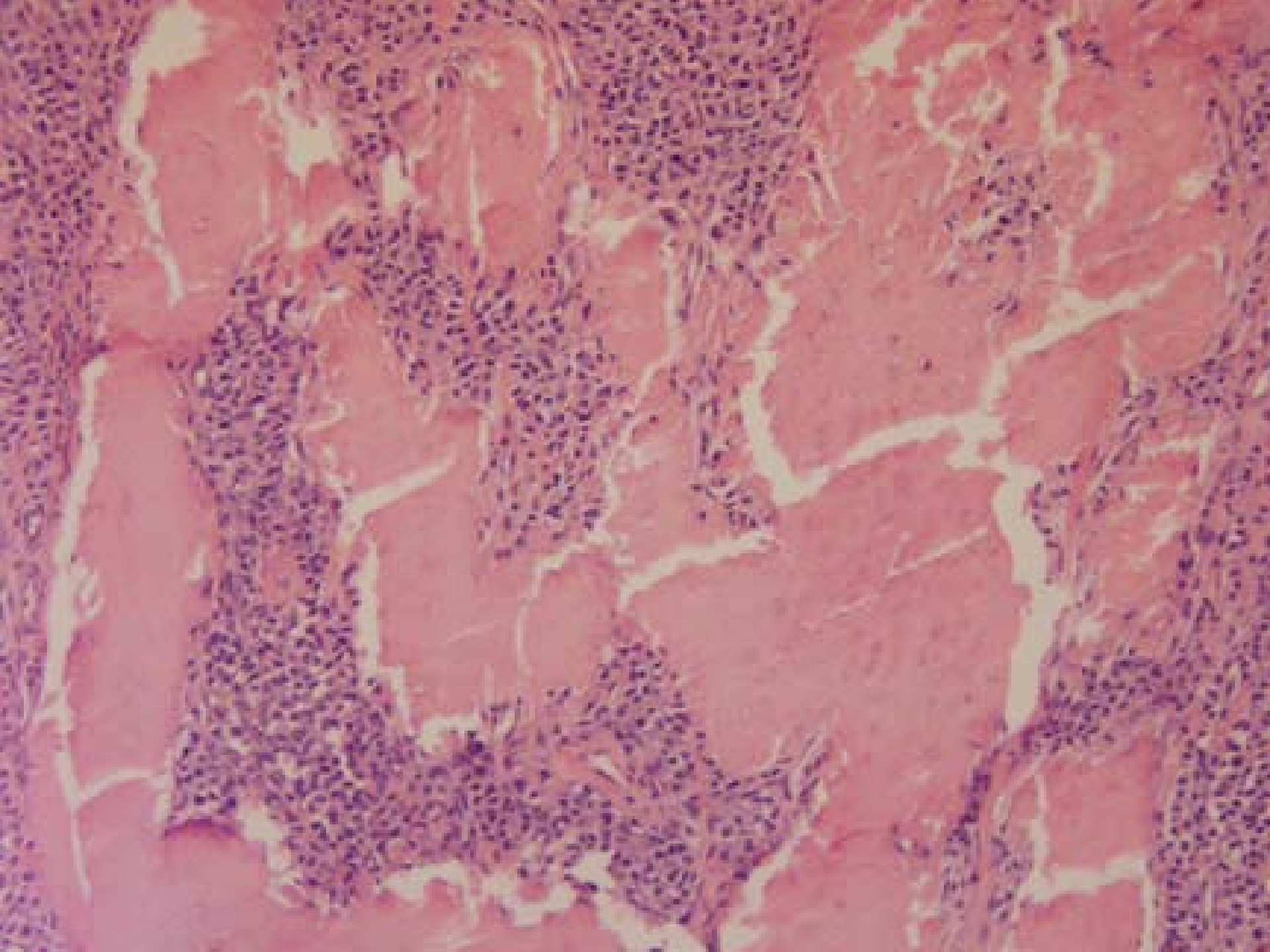
55 year old Korean man in otherwise good health presents with a slightly painful nodule on the right cheek for approximately 1 month duration

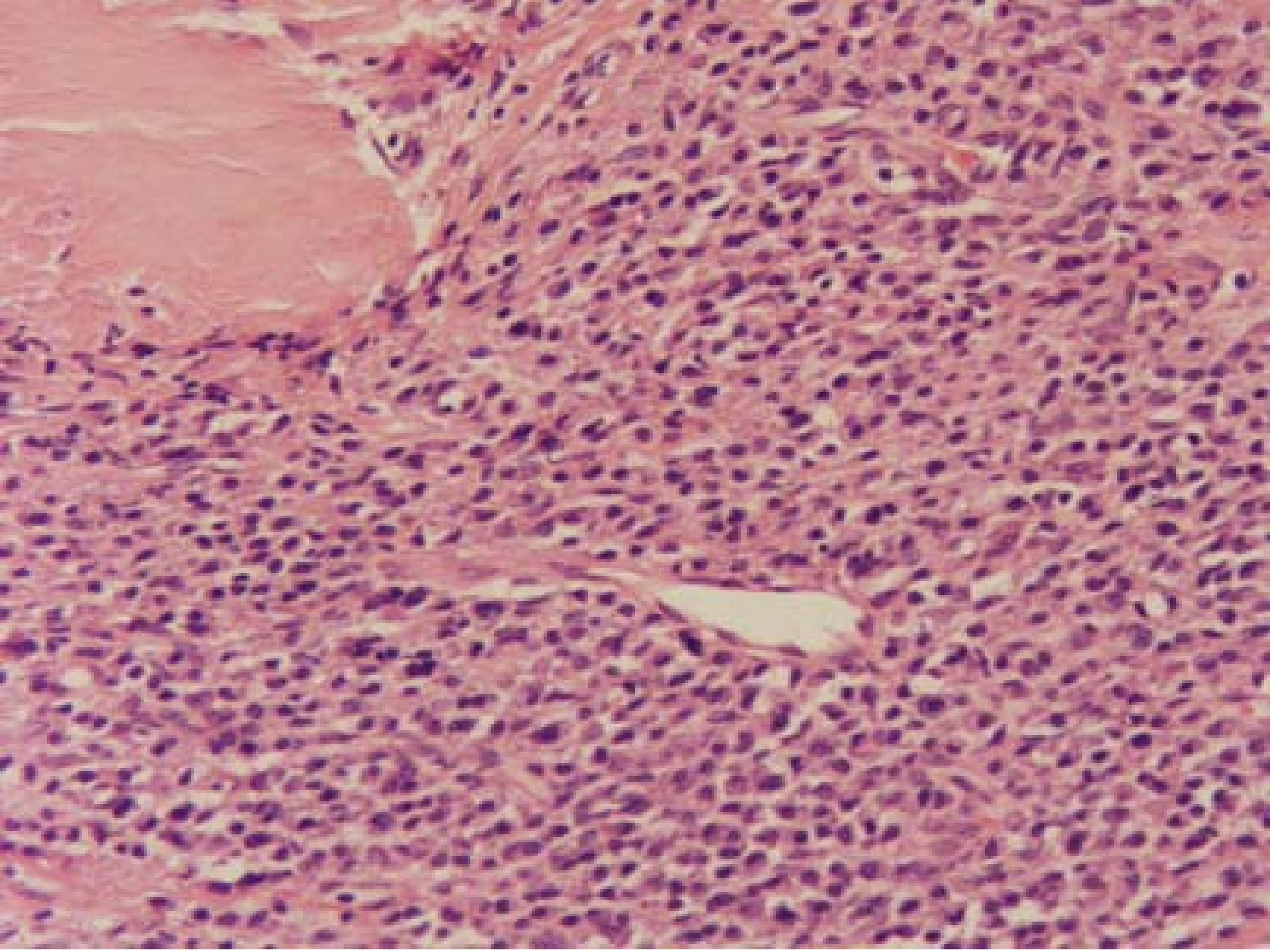


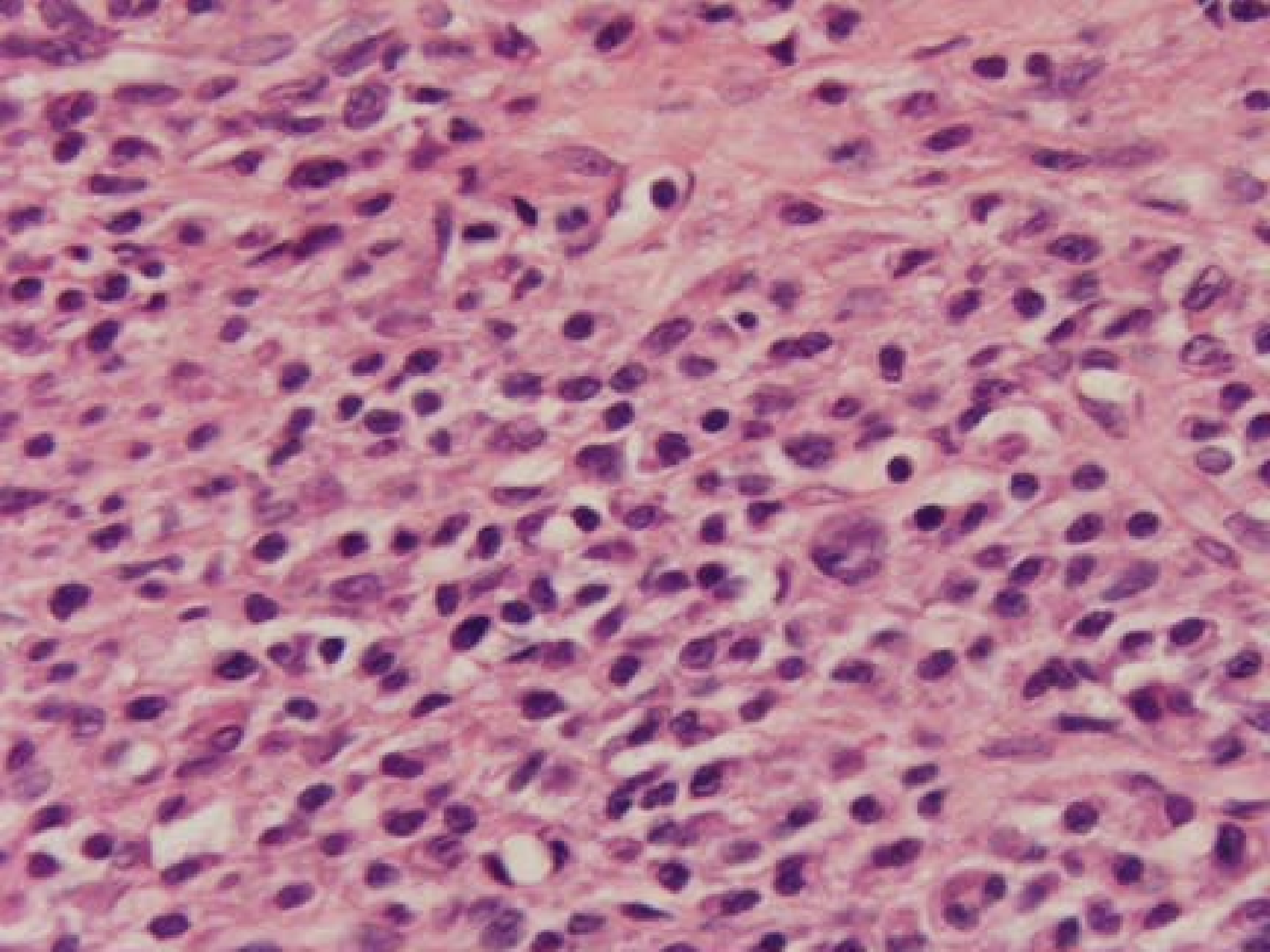


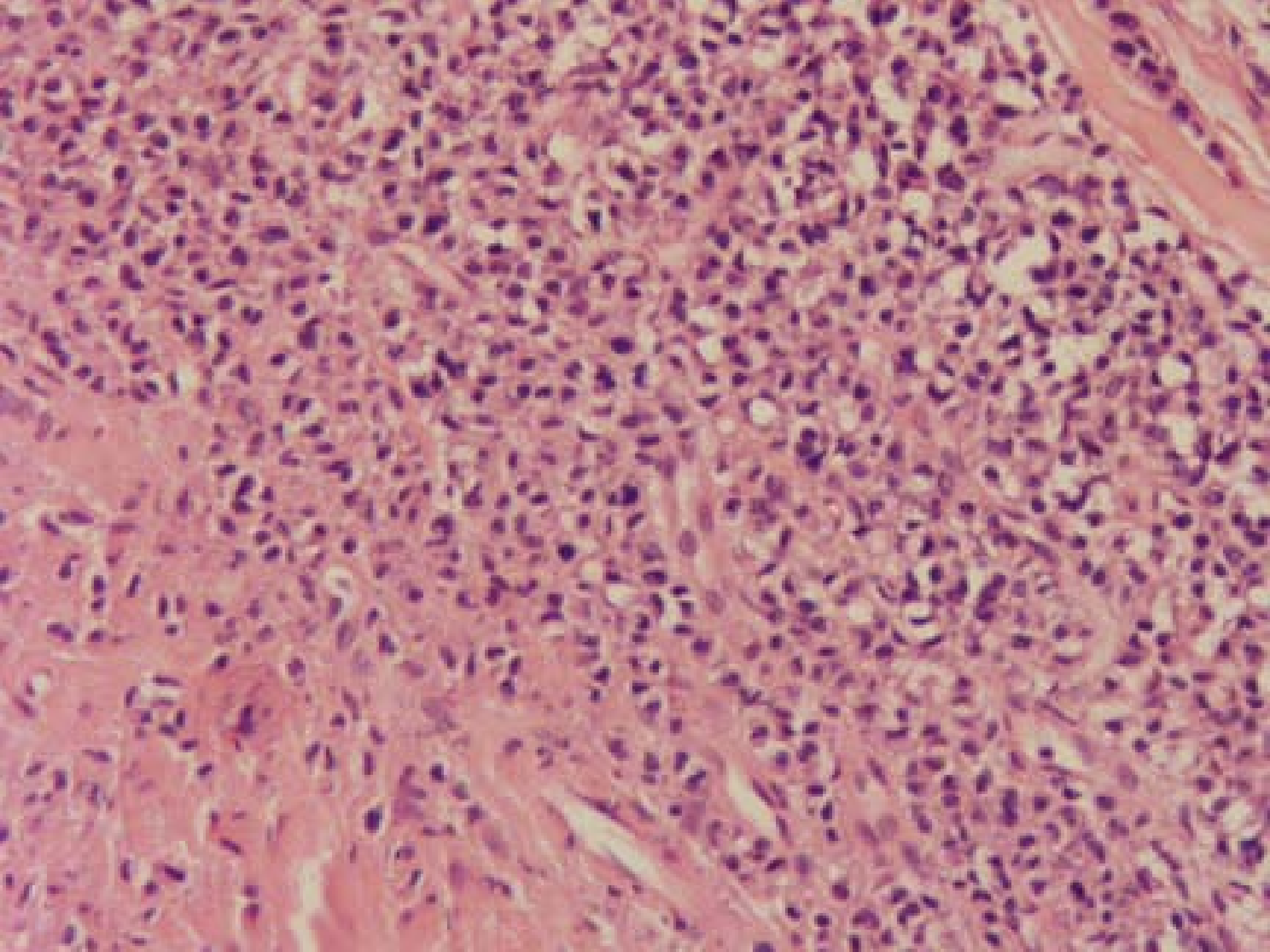


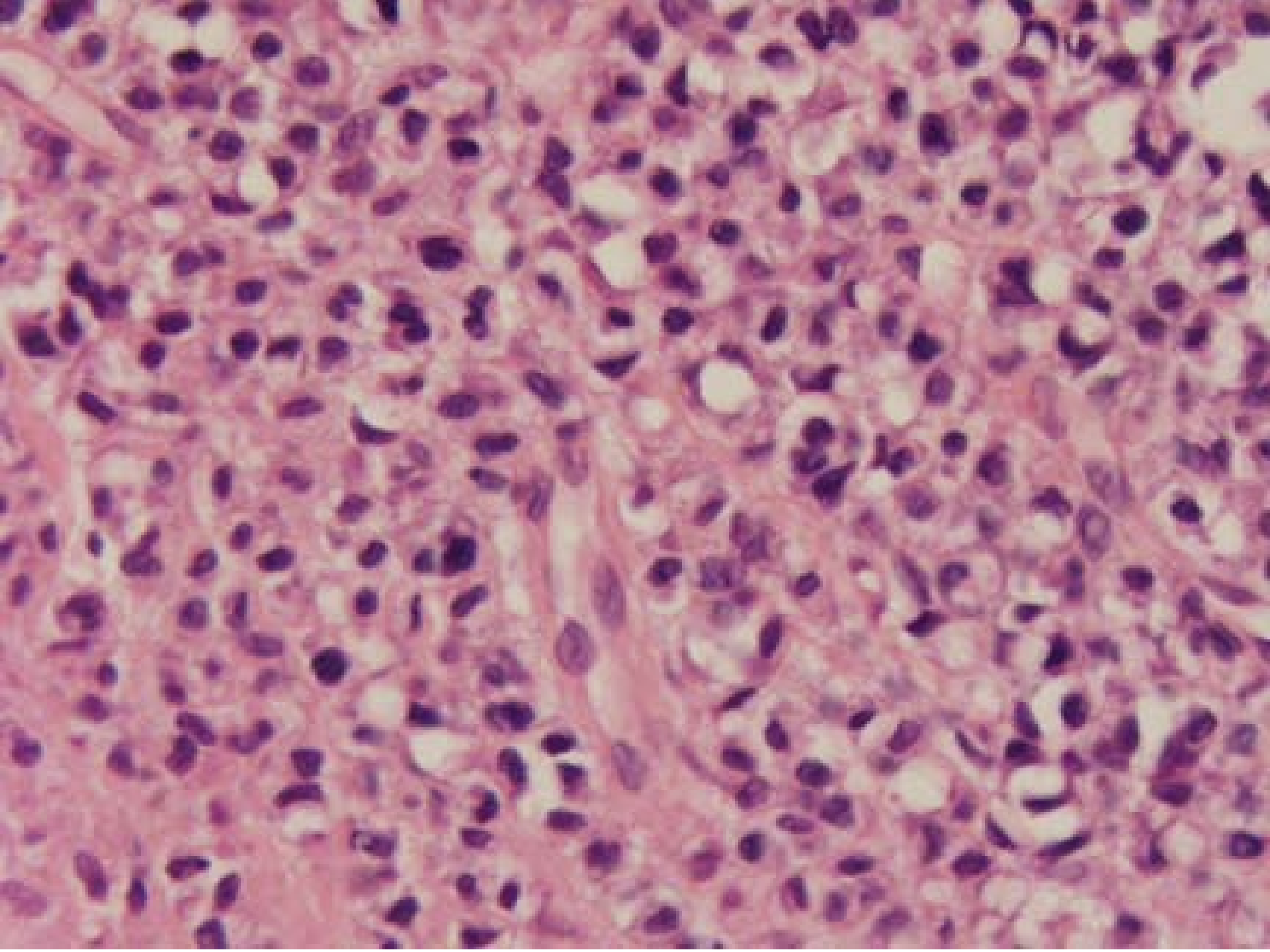






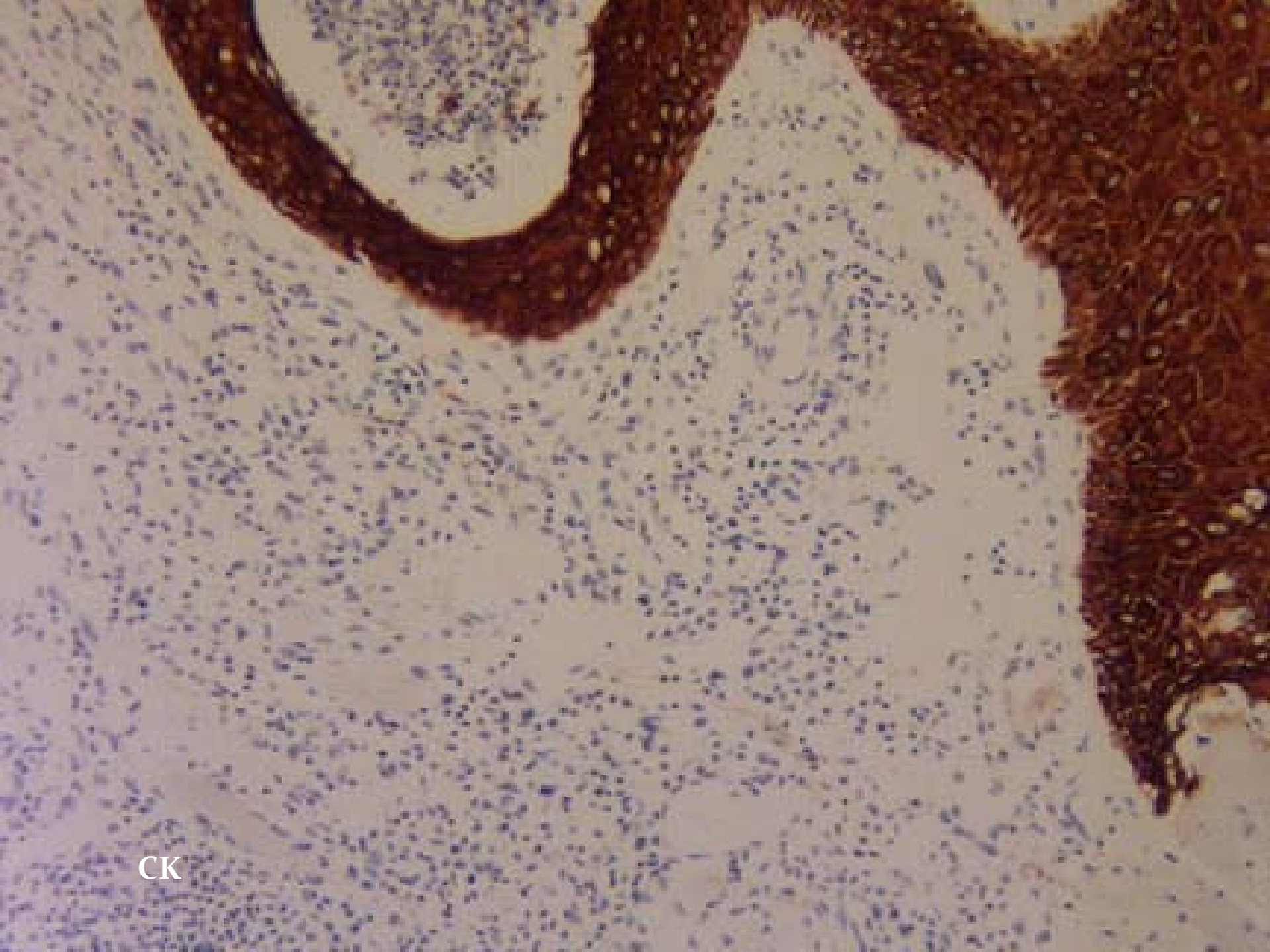


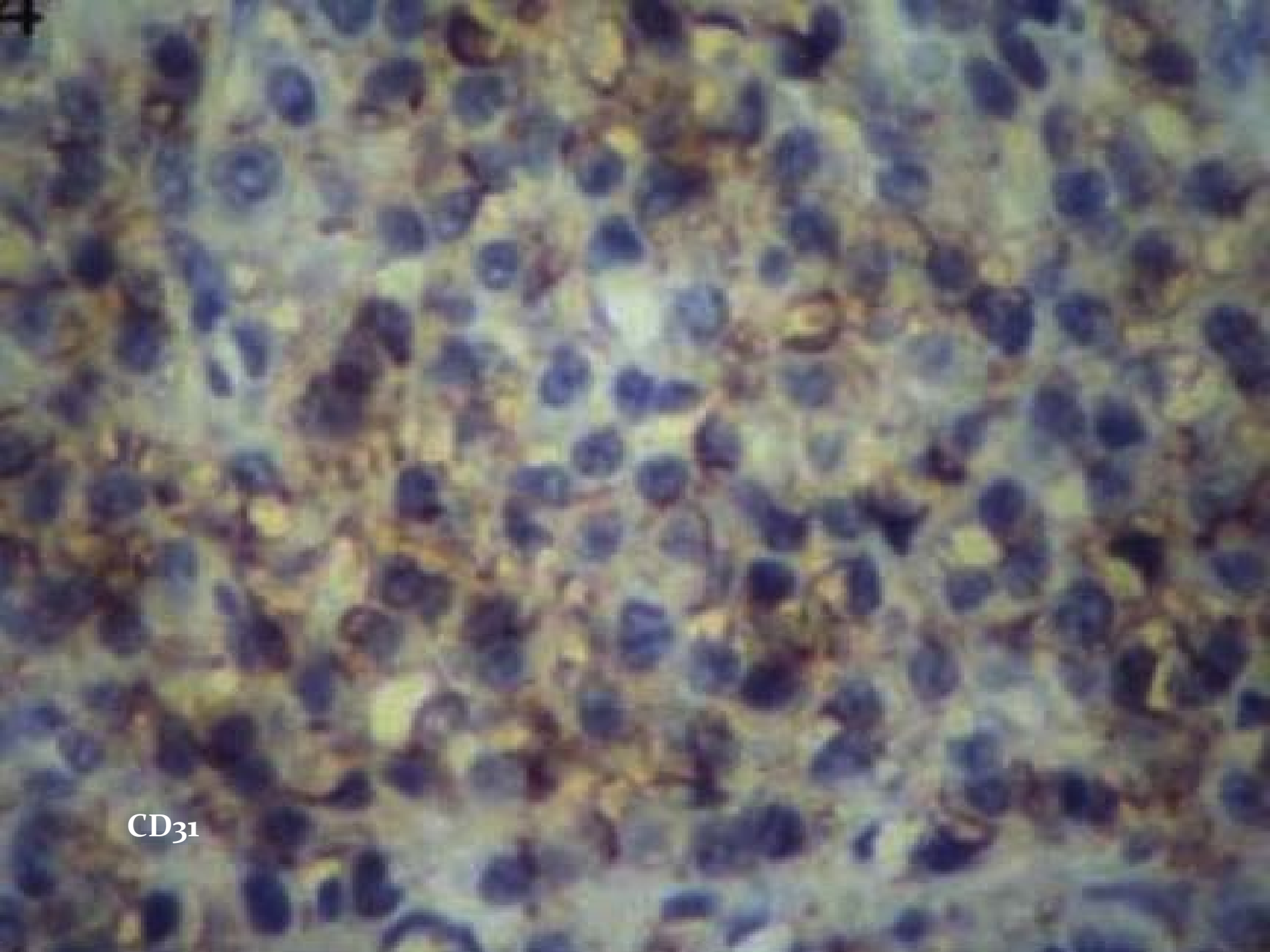




Initial Studies

- Negative for:
  - AFB, Fite, PAS, GMS, Gram, Giemsa, and mucicarmine
- Negative for:
  - SMA, Desmin, S100, Mart1, HMB45, CK


CK


CD31

Atypical Cellular Infiltrate with Signet Ring Features-
Suspicious for Malignancy

Consultant 1

Atypical cellular infiltrate, CD31 positive-Pseudoepitheliomatous hyperplasia with atypical mononuclear cells probably representing a malignant neoplasm. Doubt angiosarcoma.

Consultant 2

Pseudocarcinomatous hyperplasia with suppuration. Differential diagnosis is between an infectious process such as a deep fungus or atypical mycobacterium, collagenoderma, or even squamous cell carcinoma.

He suggested the hyalinzed material could represent bovine collagen (Zyderm) and queried whether the patient received any injections (he didn't).

Consultant 3

Atypical cells probably of vascular-endothelial origin with florid pseudo-epitheliomatous hyperplasia and peculiar eosinophilic material interpreted as keratin.

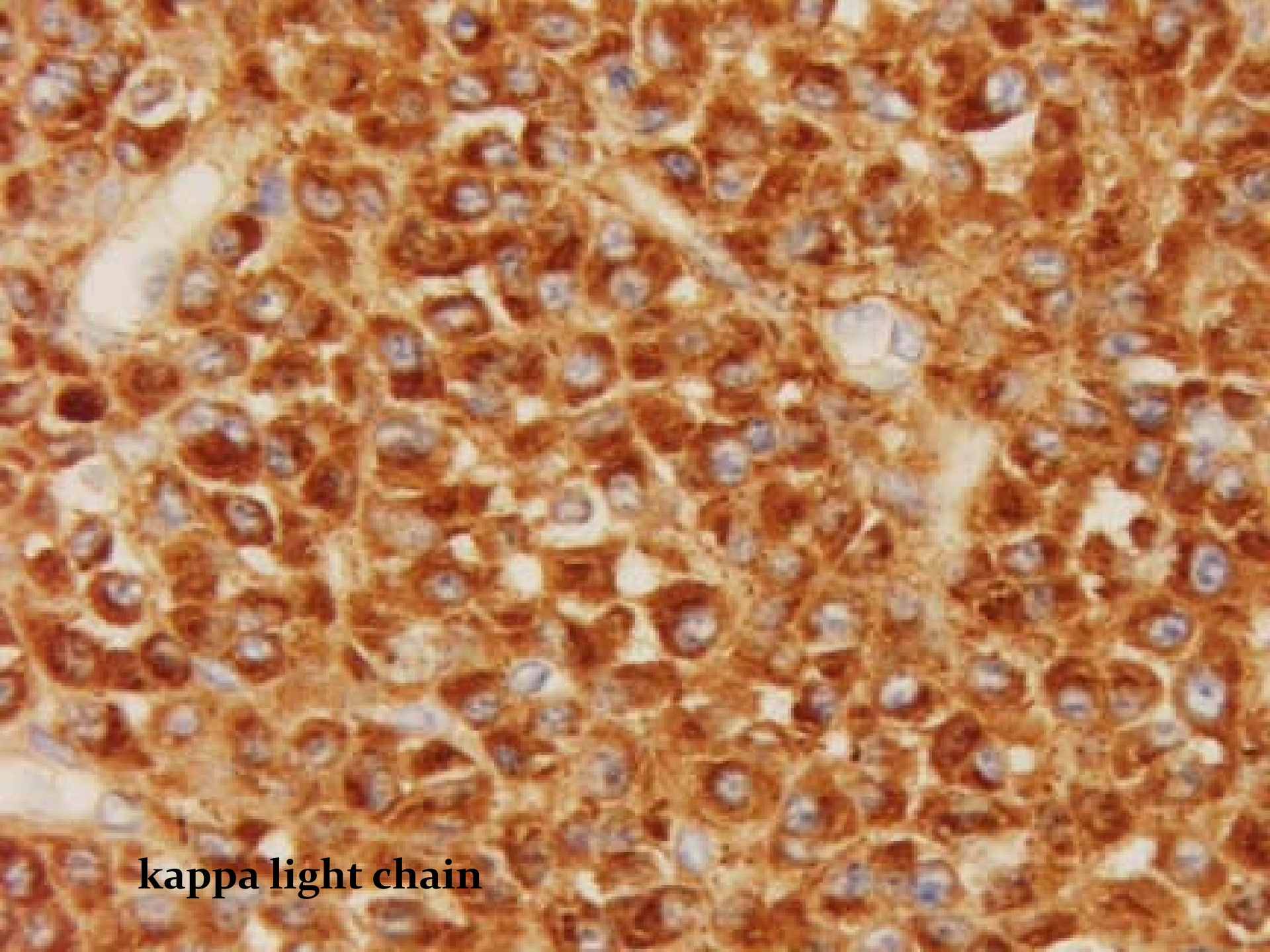
(This consultant, in turn, had the case reviewed by *two* additional dermatopathologists who were equally stymied by the case! He frankly admitted that neither he nor his other colleagues had any idea what this case might represent. He was not even sure if it was benign or malignant.)

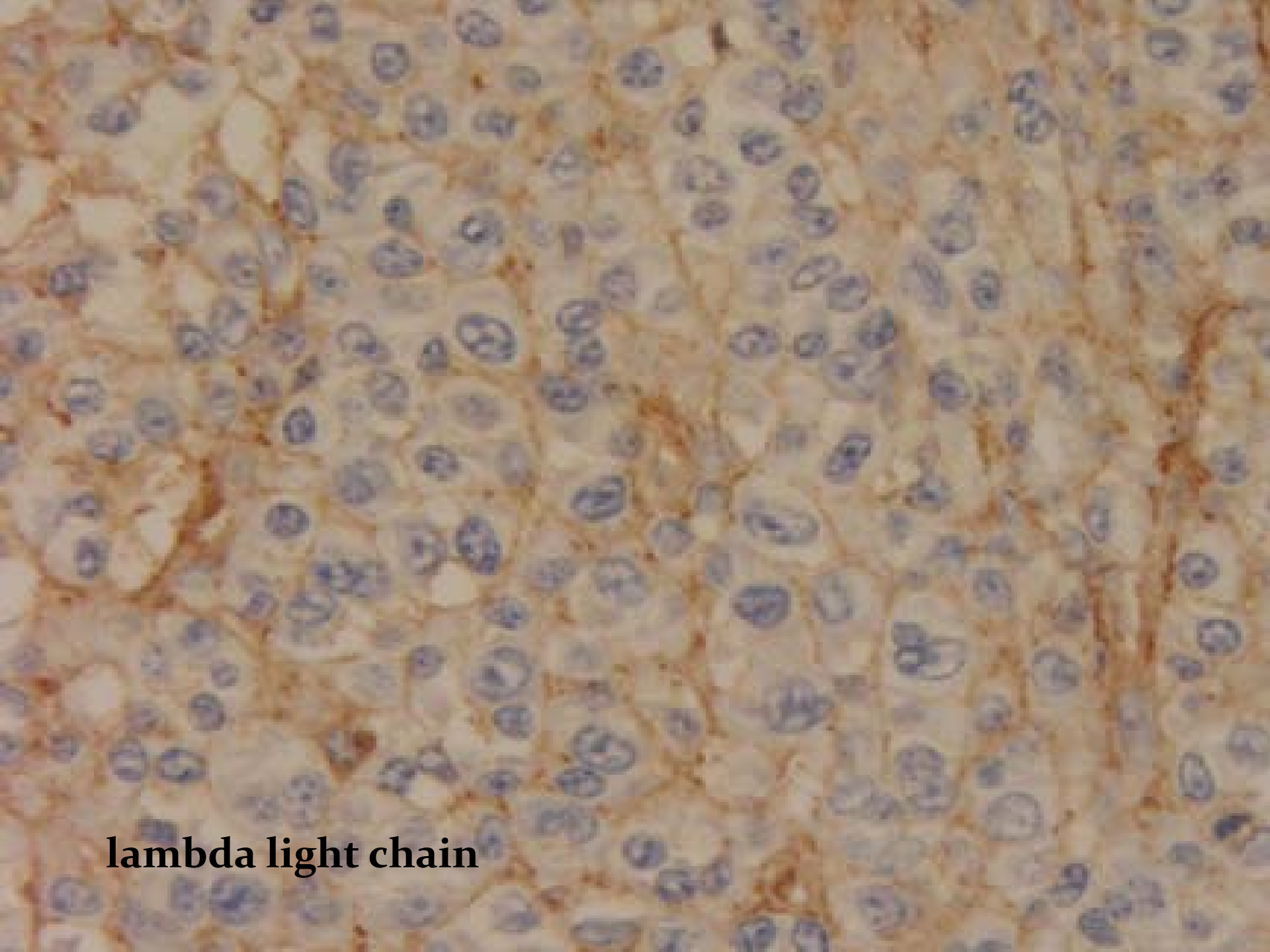
LA Metro Derm Society

February 1998

confloption

n-flurry, confusion;
State of confusion; mishap, misfortune.


kappa light chain

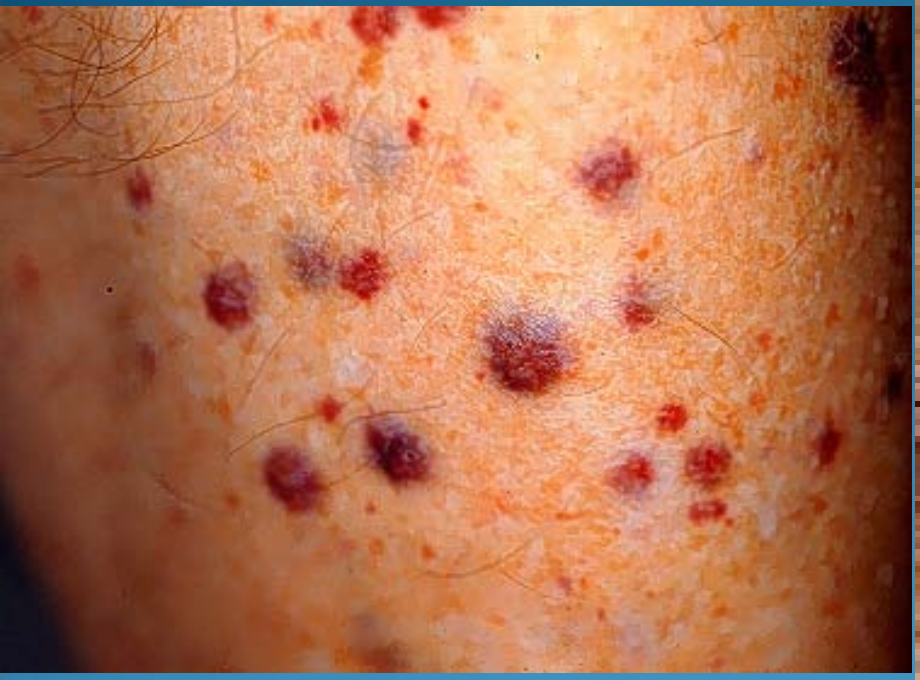

lambda light chain

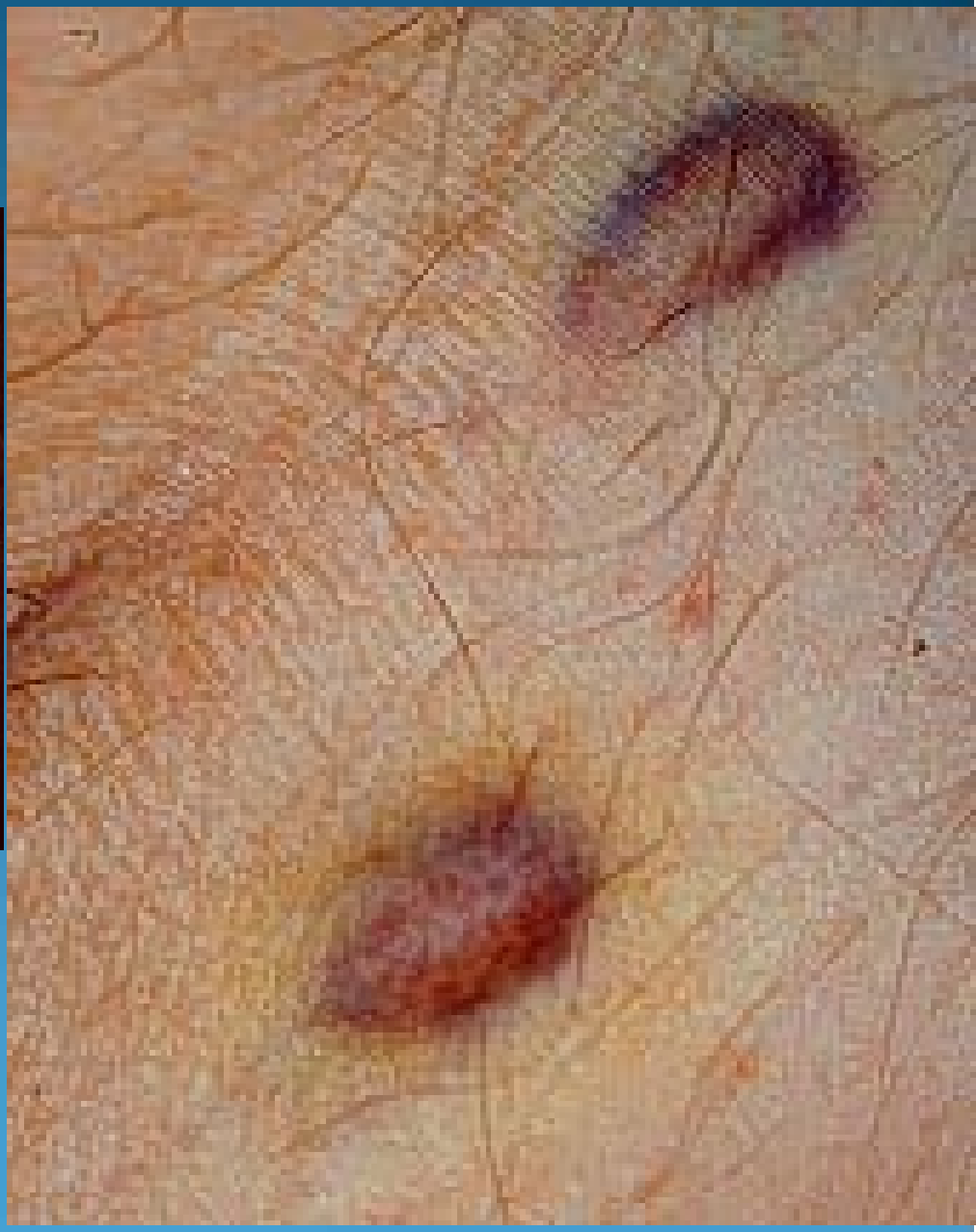
Cutaneous Plasmacytoma with kappa light chain restriction

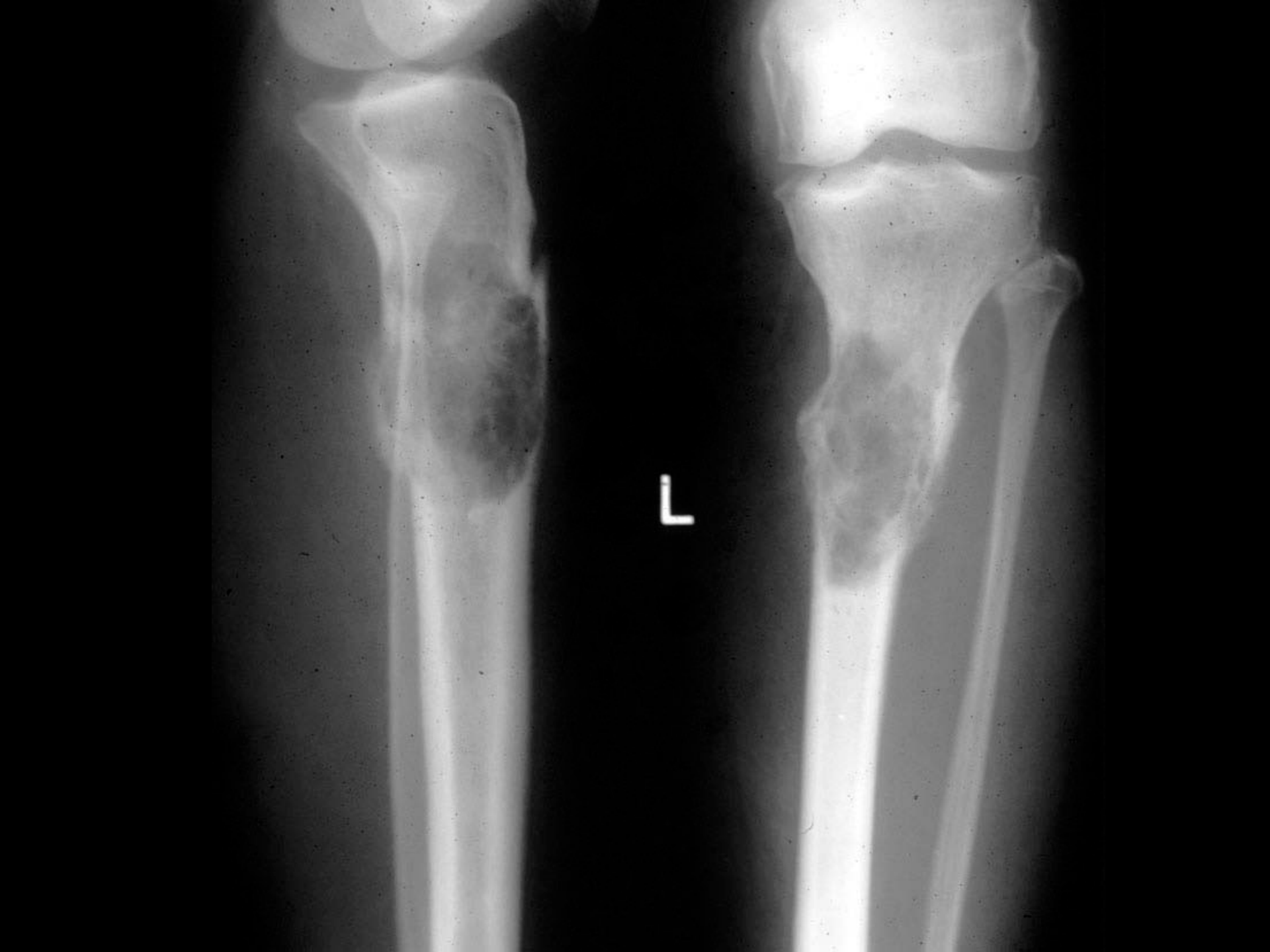
Cutaneous Plasmacytoma with kappa light chain restriction

Follow Up

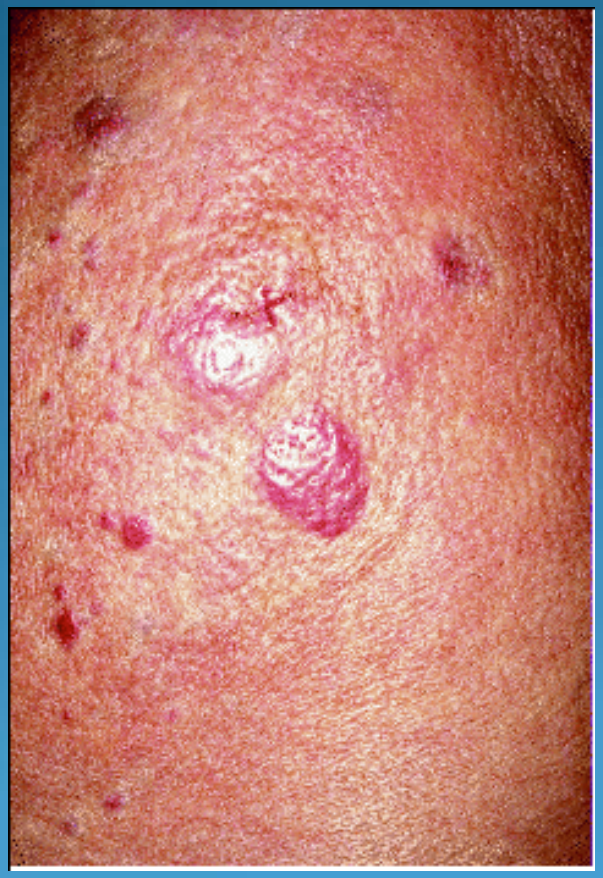
- Bone marrow negative
- Serum chemistries negative
- SPEP/UPEP negative
- Bone survey negative





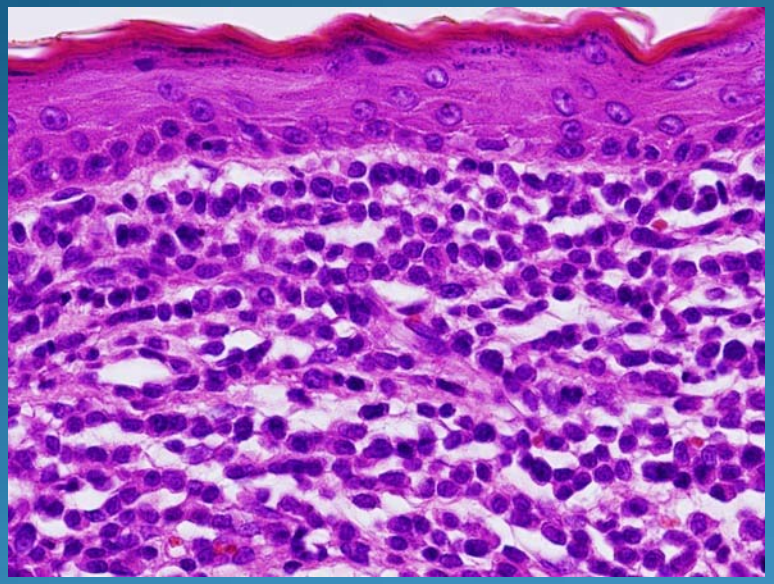

L

Clinical



- Rare
- Erythematous nodules or papules
- Monoclonal proliferation of plasma cells
- Frequent association with multiple myeloma
- Primary cases indolent course
- MM cases with secondary skin involvment-poor prognosis

Histopathology



- Dense infiltrate of plasma cells
- Maturity variable
- Light chain restriction
- DDX:
  - Infection
  - Reactive to trauma

CD31 (JC70) expression in plasma cells: an immunohistochemical analysis of reactive and neoplastic plasma cells

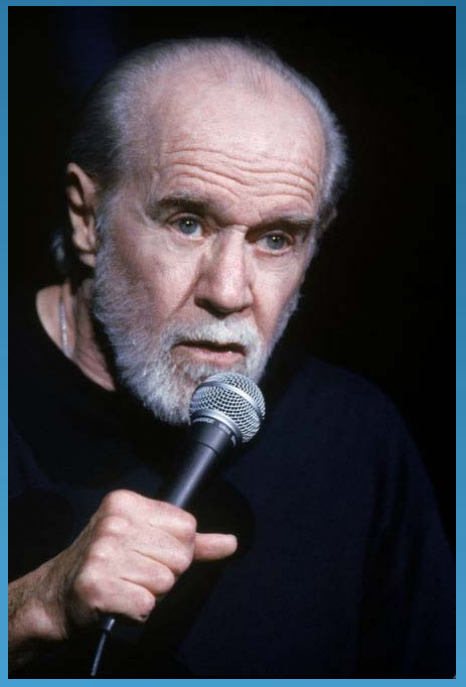
Govender D, Harilal P, Dada M, Chetty R.
J Clin Pathol. 1997 Jun;50(6):490-3.

Chose Your Consultants Wisely!

(Corollary: Choosing an odd number of consultants does not guarantee a consensus diagnosis)

The Seven Things

- Low Power Objective-High Power Pathologist
- Measuring a Melanoma
- The Best Special Stain
- Margins on a Punch or Shave biopsy
- Lymphocytic Vasculitis
- IHC is the Magic Bullet
- Consultant Confloption



Thank you!


Tan Lines From Typical Summer Activities
Waterskiing
Mountain Biking
SCUBA Diving
Rollerblading
Computer Programming
Tennis

Seven Things You Should Not Say At a Dermatopathology Conference

Paul K. Shitabata, M.D.

Presented to Kaiser Woodland Hills
Dept. of Pathology
February 17, 2009