

Dermatopathology

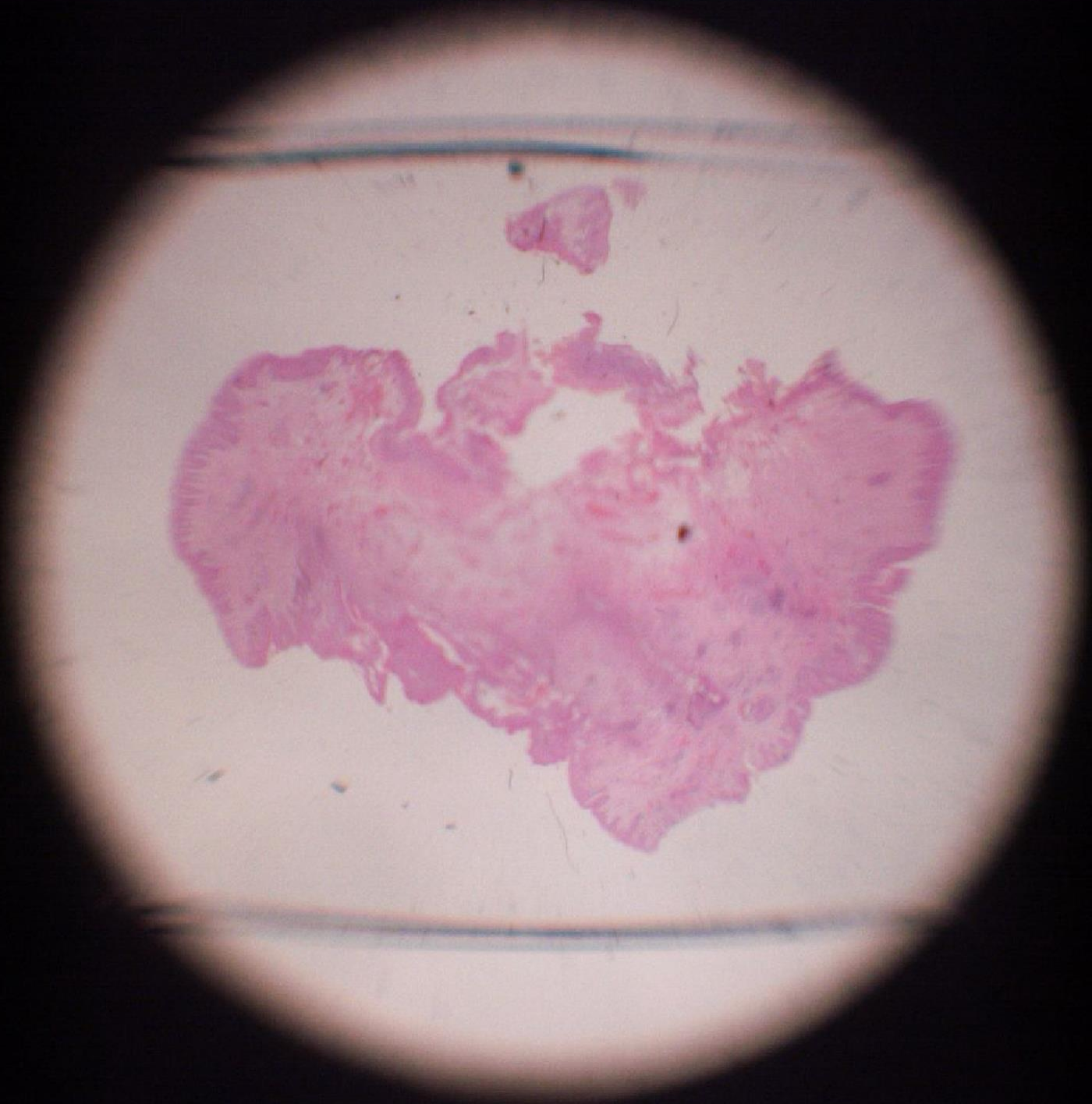
FRCPATH

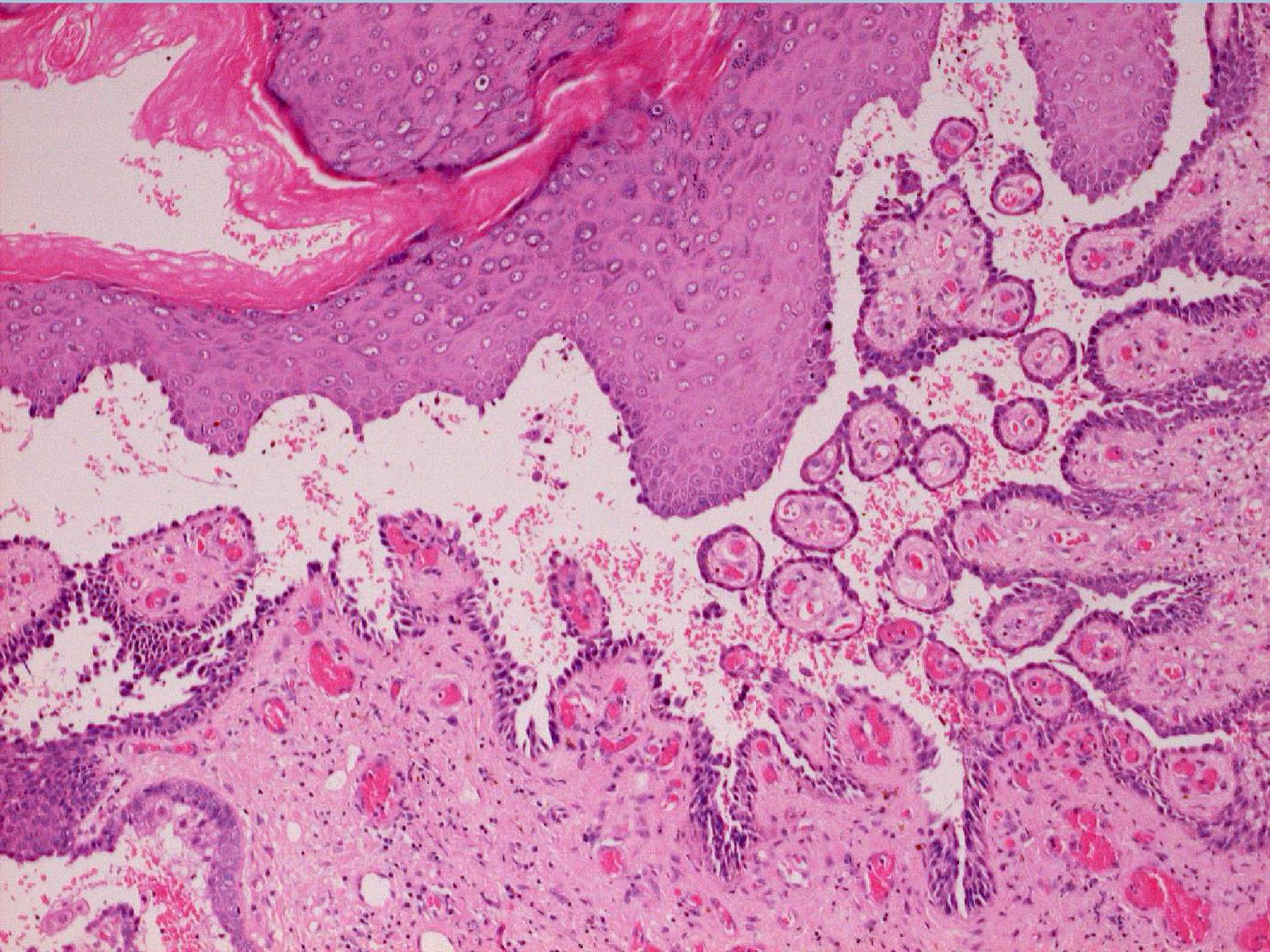
2019

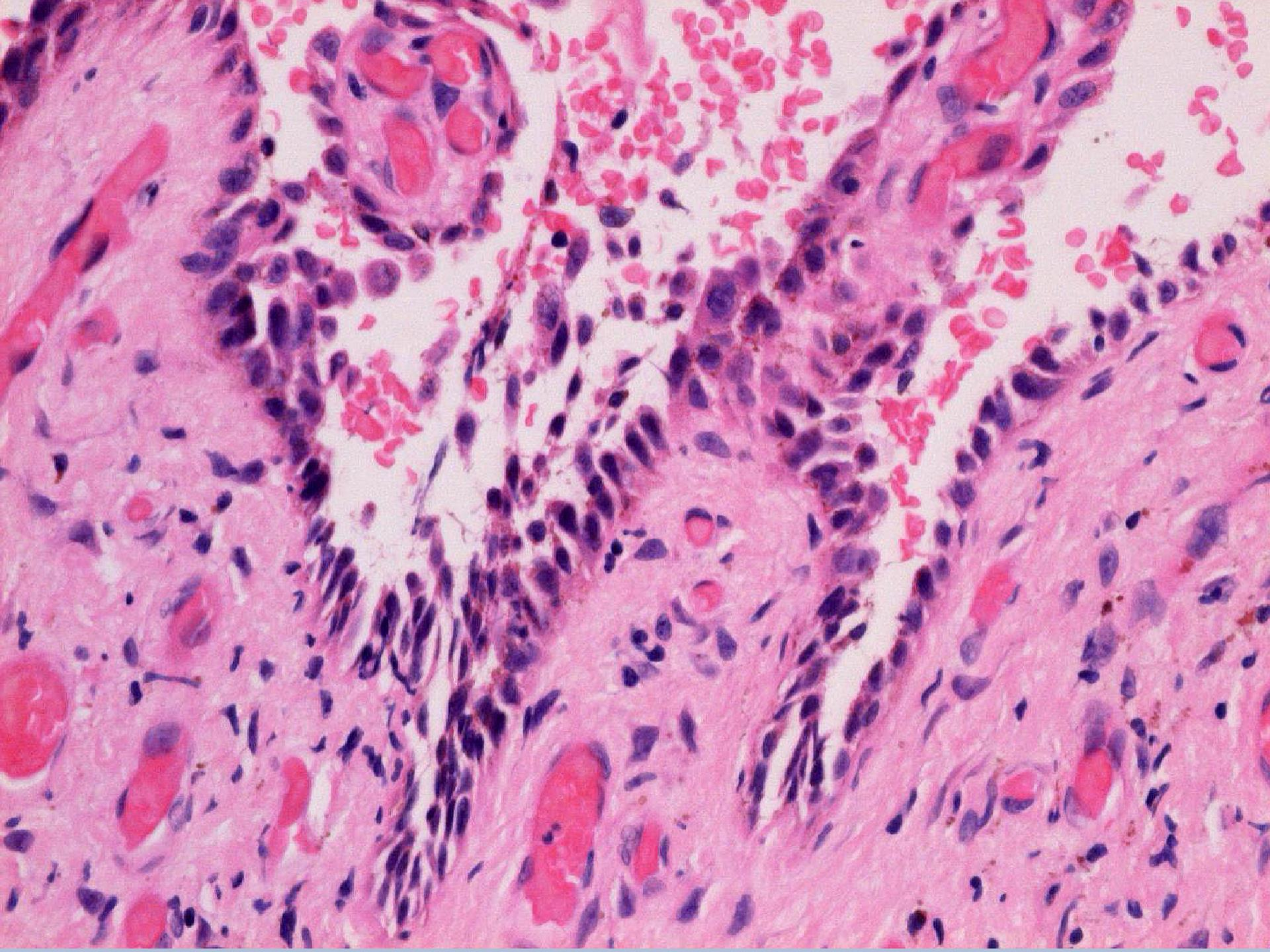
Dr Laszlo Igali

Case 1

- F45
- Anal skin tag







Case 1

Fibroepithelial anal polyp with acantholysis

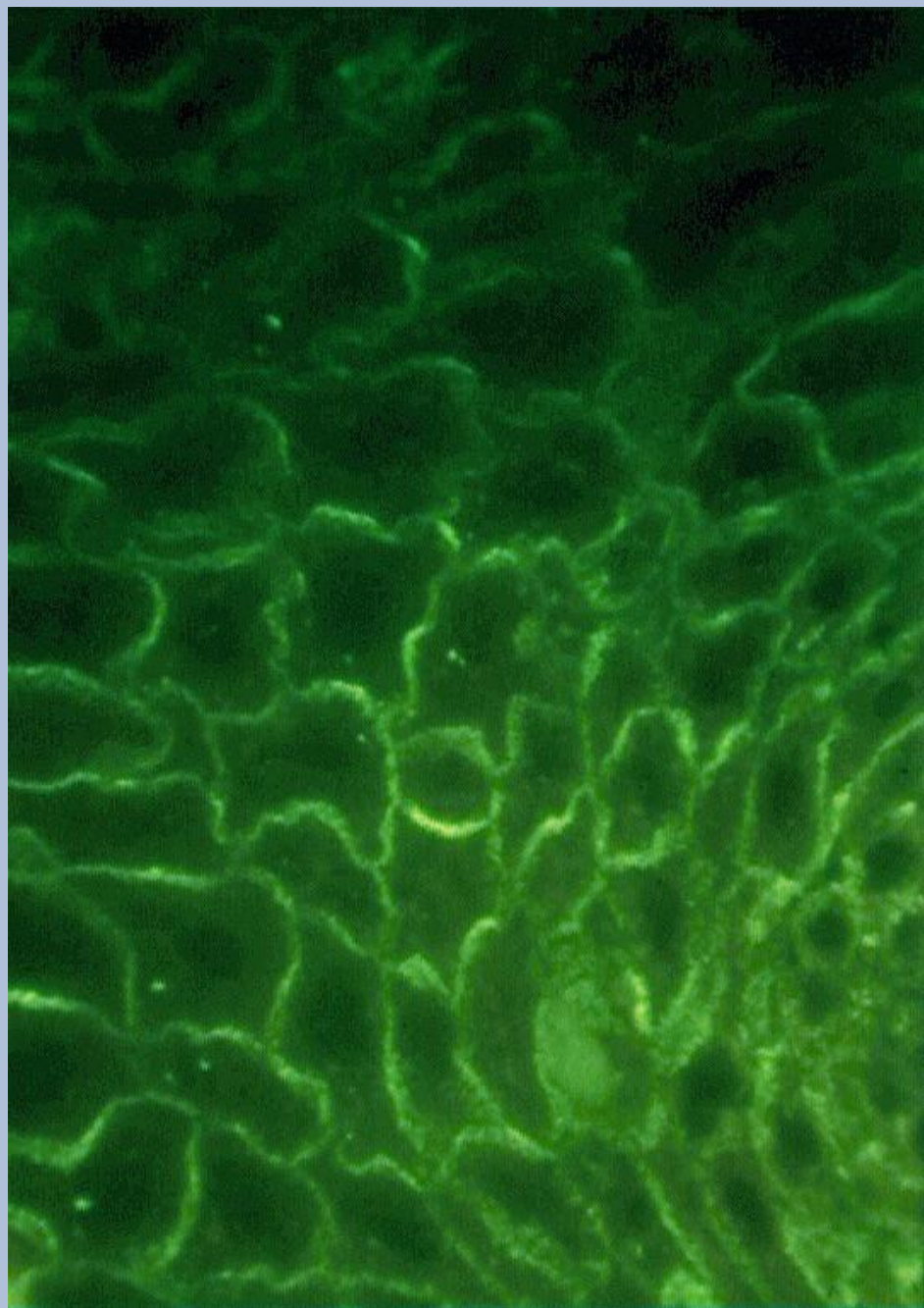
- FEP
- Acantholysis
- Suprabasal
- “tombstone” cells

Acantholysis

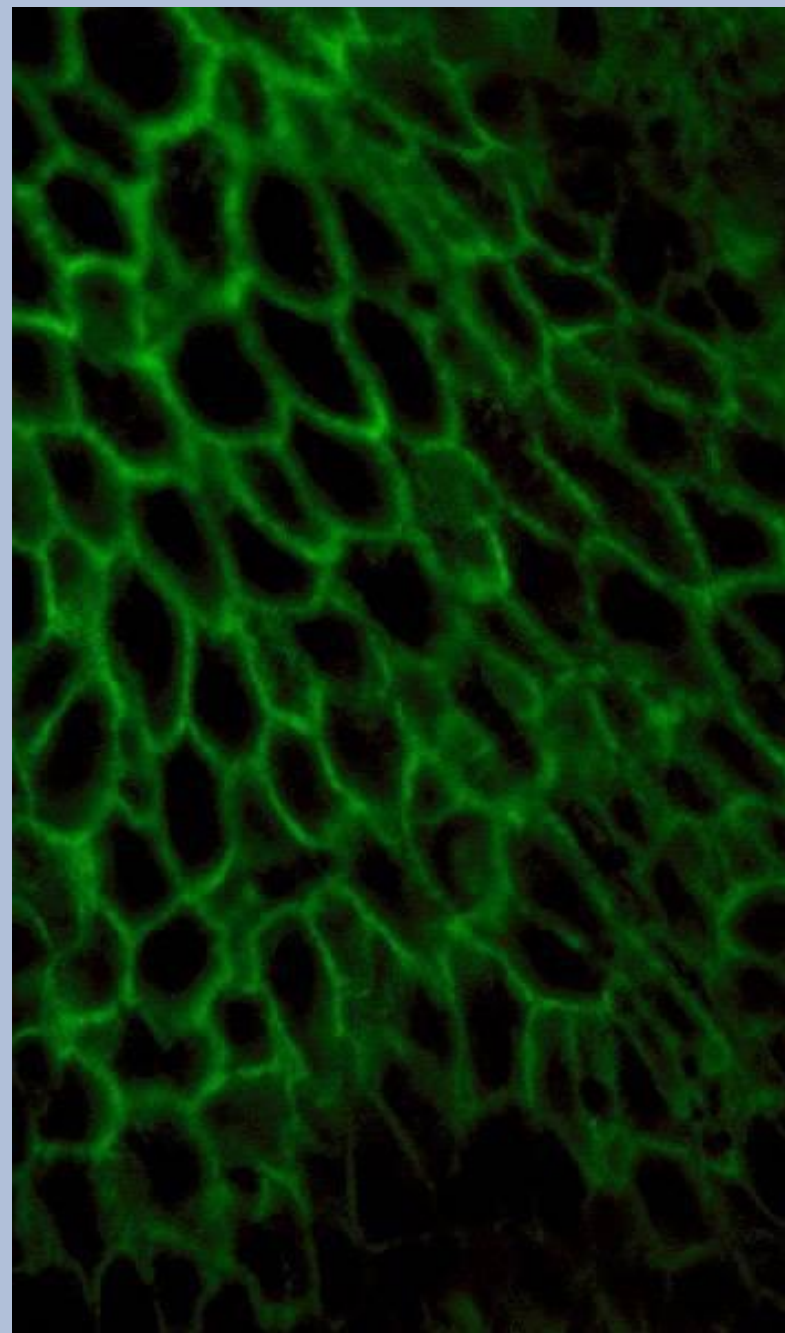
- Pemphigus
- Acantholytic dermatosis of the genitocrural area
- Grover’s disease
- Focal acantholytic dyskeratosis
- Darier’s disease
- Hailey-Hailey
- HSV

Pemphigus

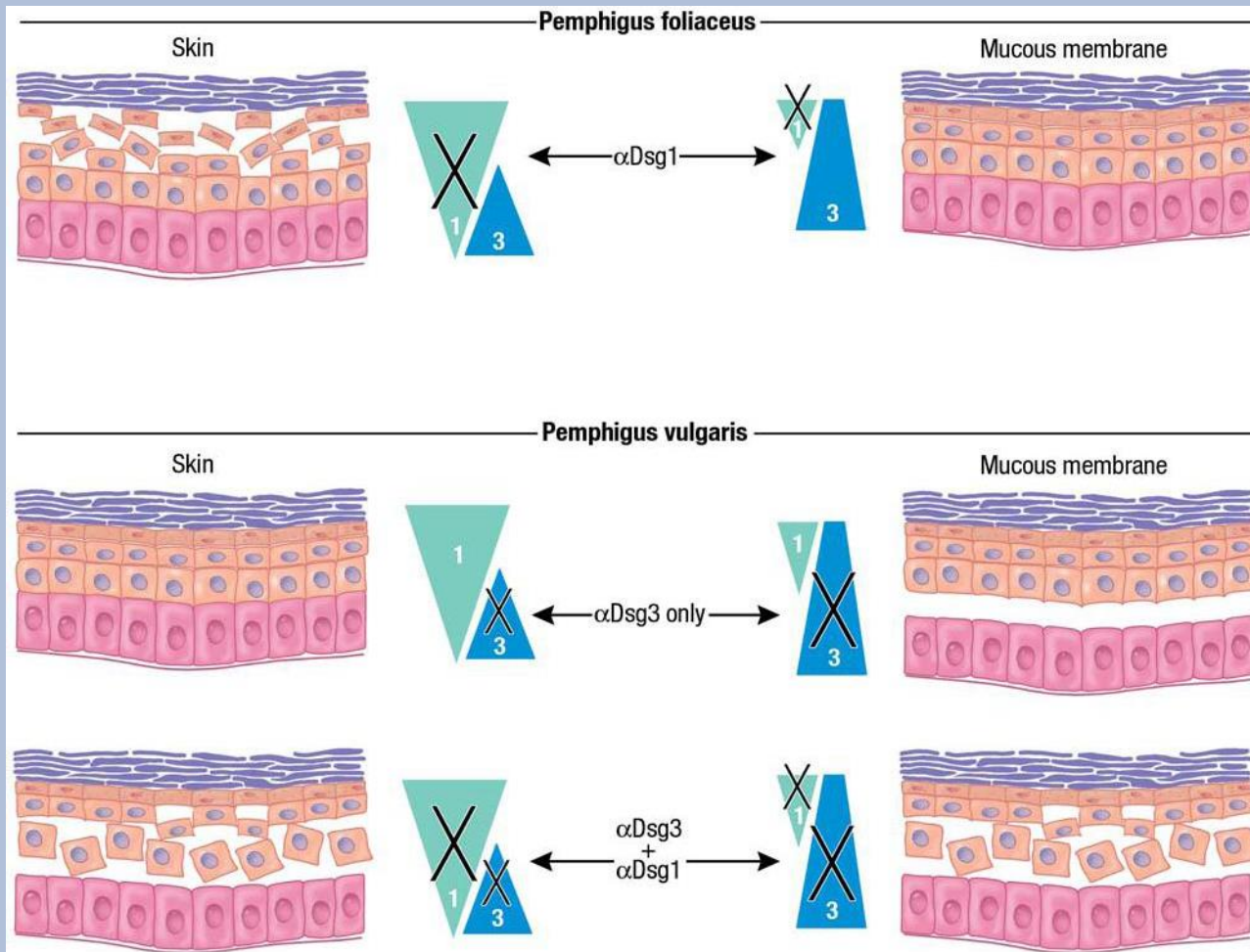
- Vulgaris
 - Suprabasal
 - No grains, parakeratin
 - Formation of villi
 - Follicular involvement
 - Prebullous - eosinophilic spongiosis



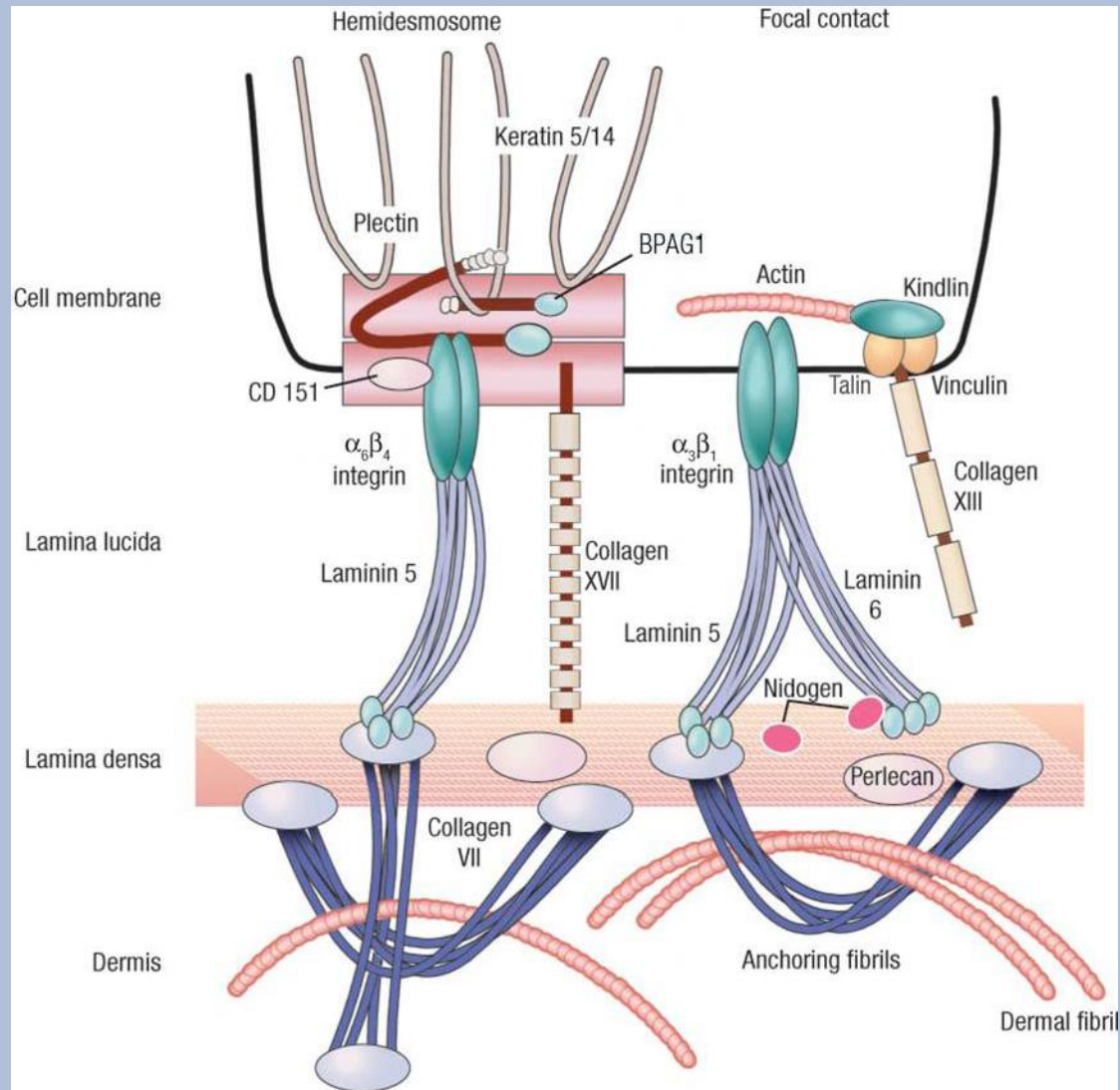
IgG



Desmoglein compensation



Basement membrane zone

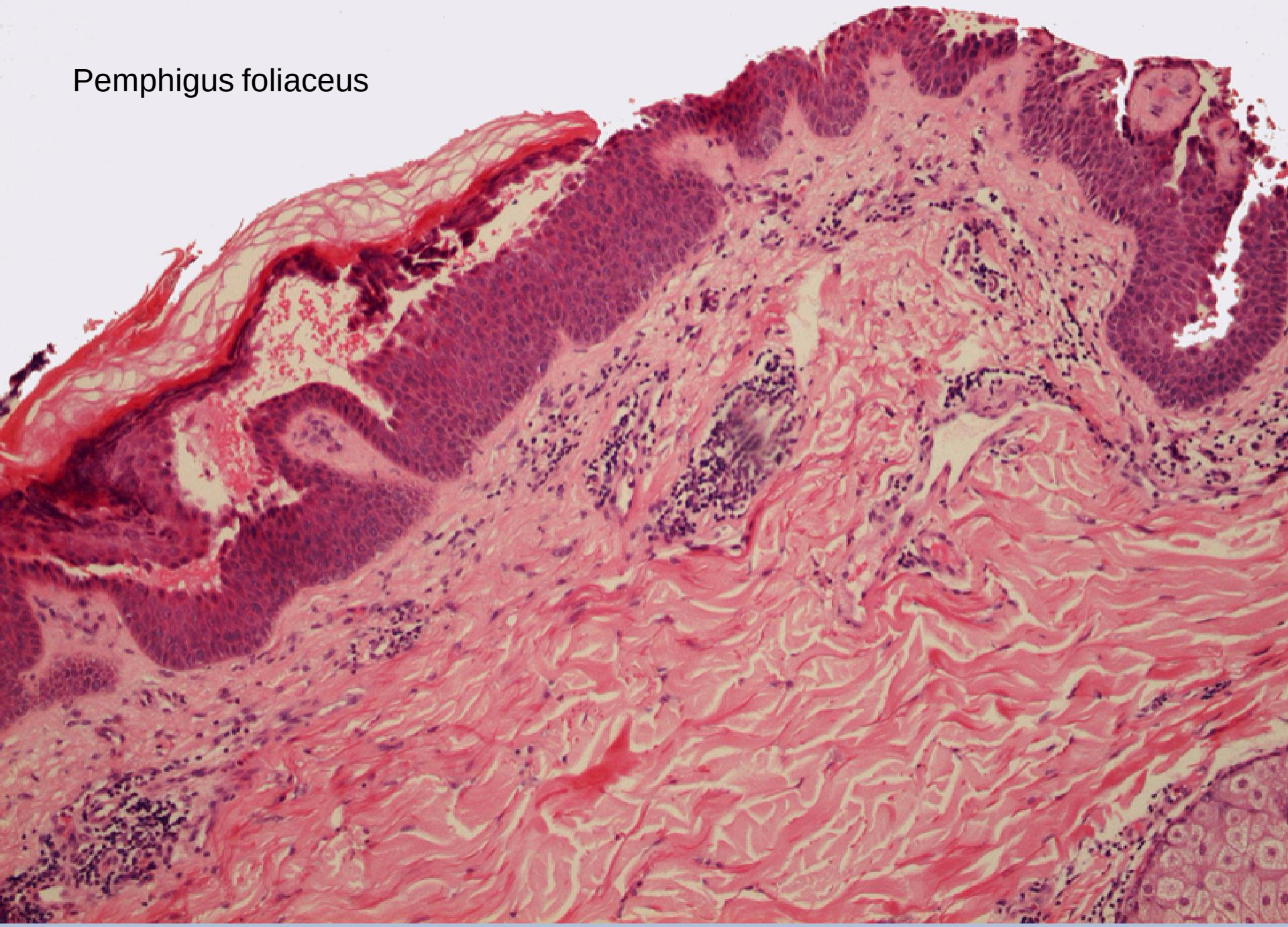


Target antigens

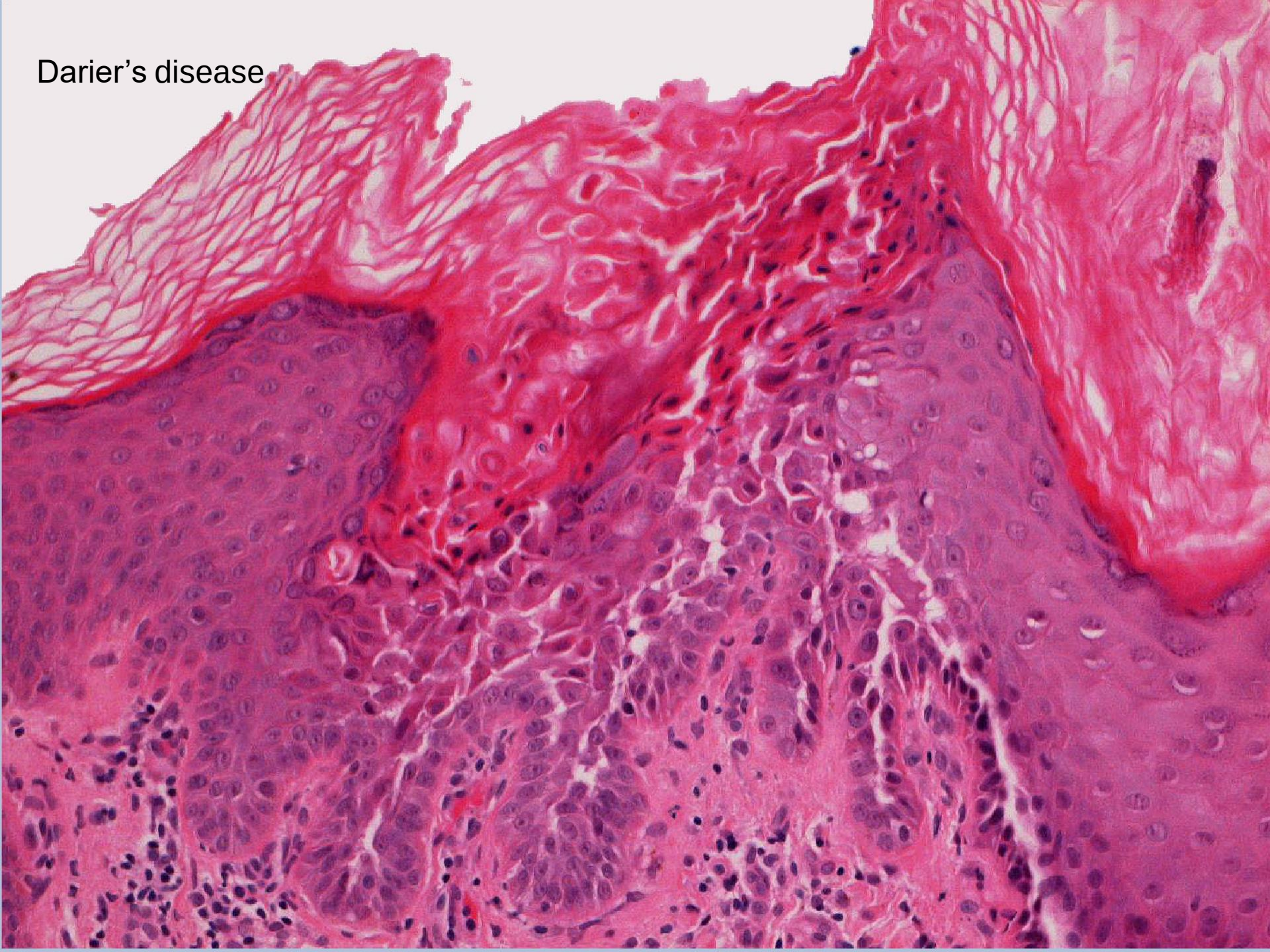
Hemidesmosomal and Basement Membrane Zone (BMZ) Targets in Skin Disease

	HEMIDESMOSOME/BMZ COMPONENT	AUTOIMMUNE TARGET	GENETIC TARGET
Cytoskeletal proteins	Keratin 5 and 14		EBS
Hemidesmosomal plaque proteins	Bullous pemphigoid antigen 1/BP230 Plectin	BP BP, CP	EBS-MD
Other intracellular adhesion complex proteins	Kindlin-1		KS
Hemidesmosomal transmembrane components	Collagen XVII/BP180 $\alpha_6\beta_4$ integrin CD151	BP, CP, LAD, PG BP, CP	JEB-non-Herlitz JEB-PA Pretibial EB, nephritis, deafness, thal thalassemia minor
Anchoring filament proteins	Laminin 332/laminin-5 Ectodomain of collagen XVII	CP LAD, BP	JEB-Herlitz JEB-non-Herlitz JEB-non-Herlitz
Anchoring fibril proteins	Collagen VII	EBA	DEB

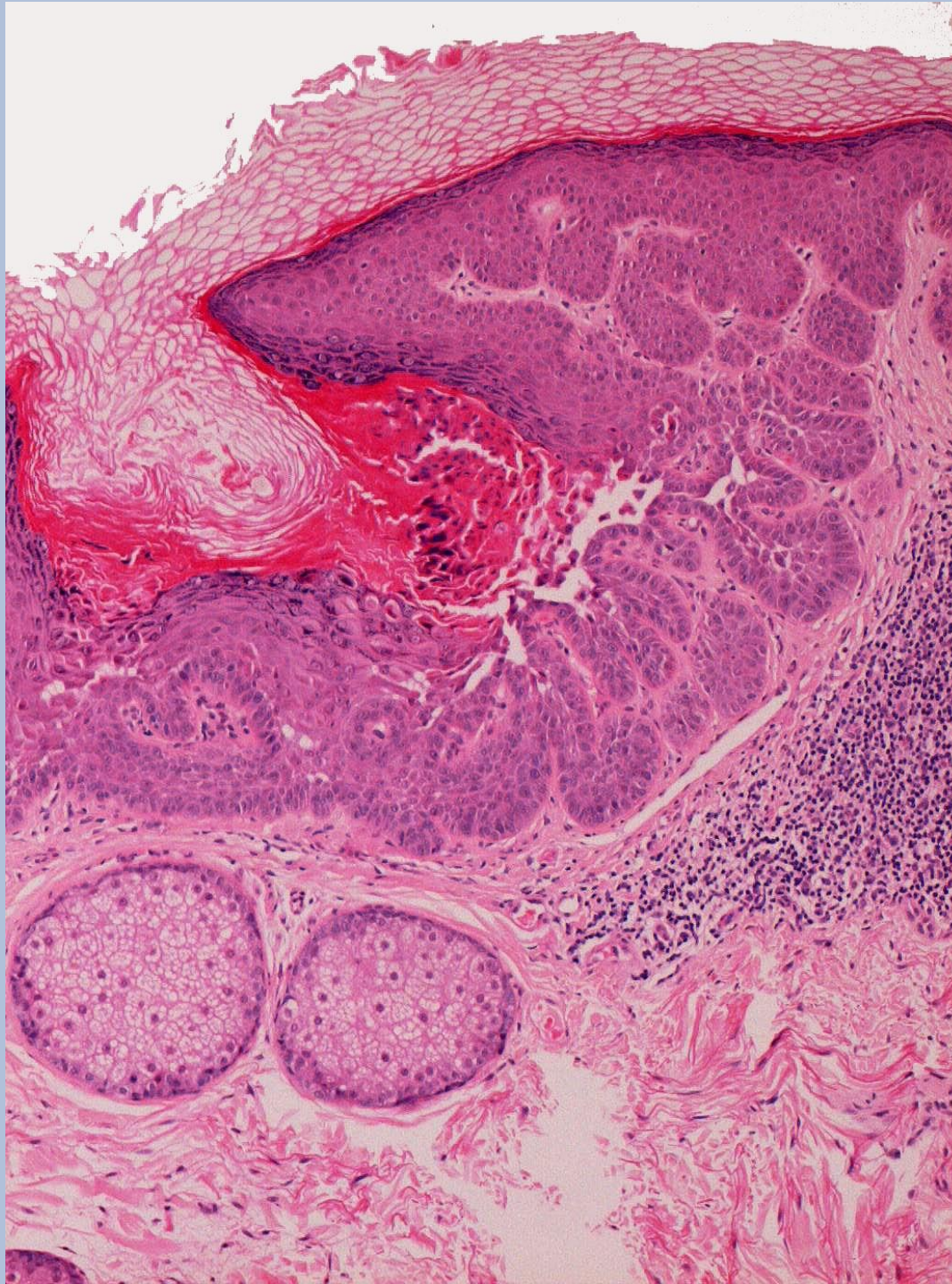
Pemphigus foliaceus



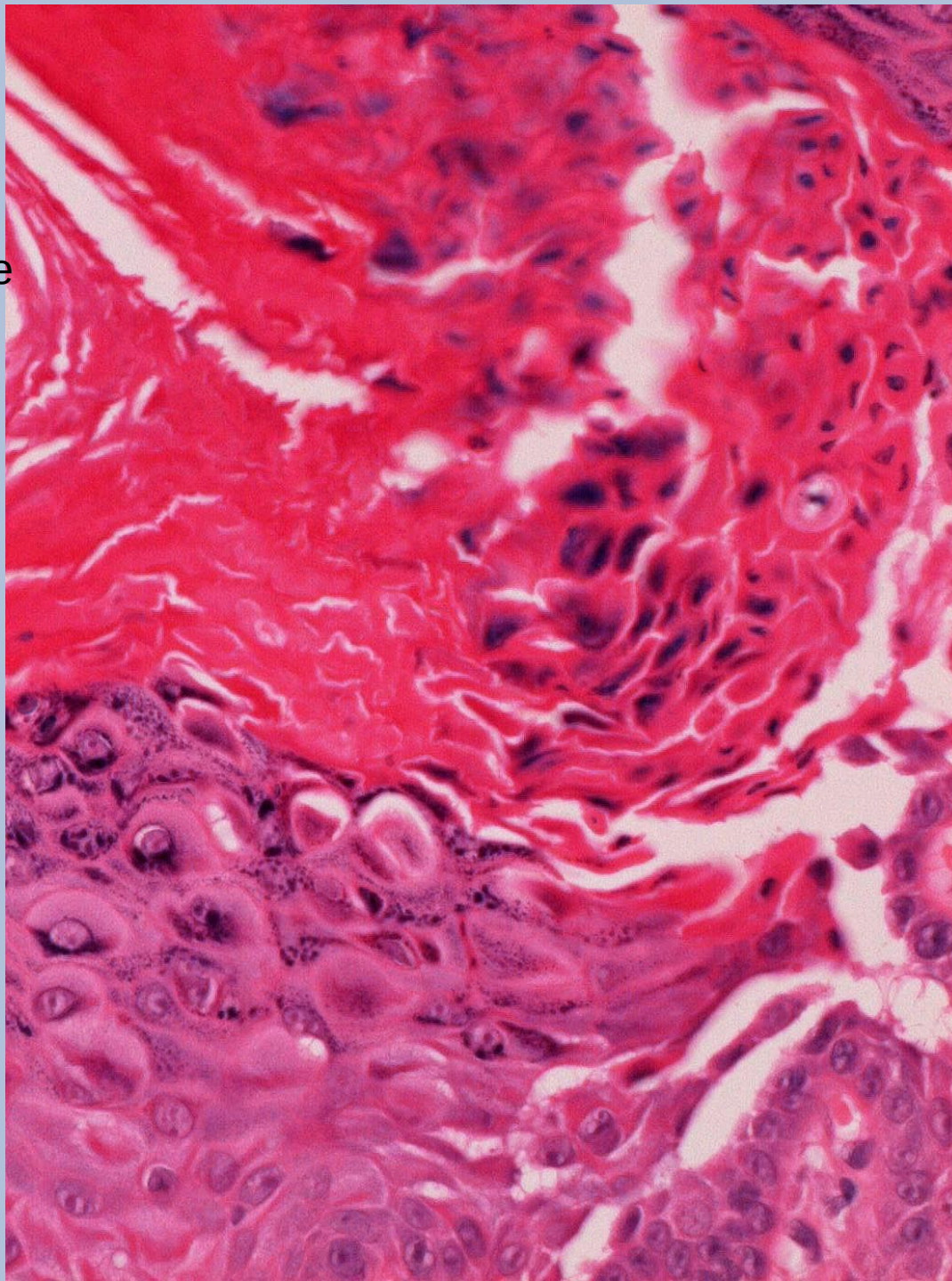
Darier's disease



Grover's disease

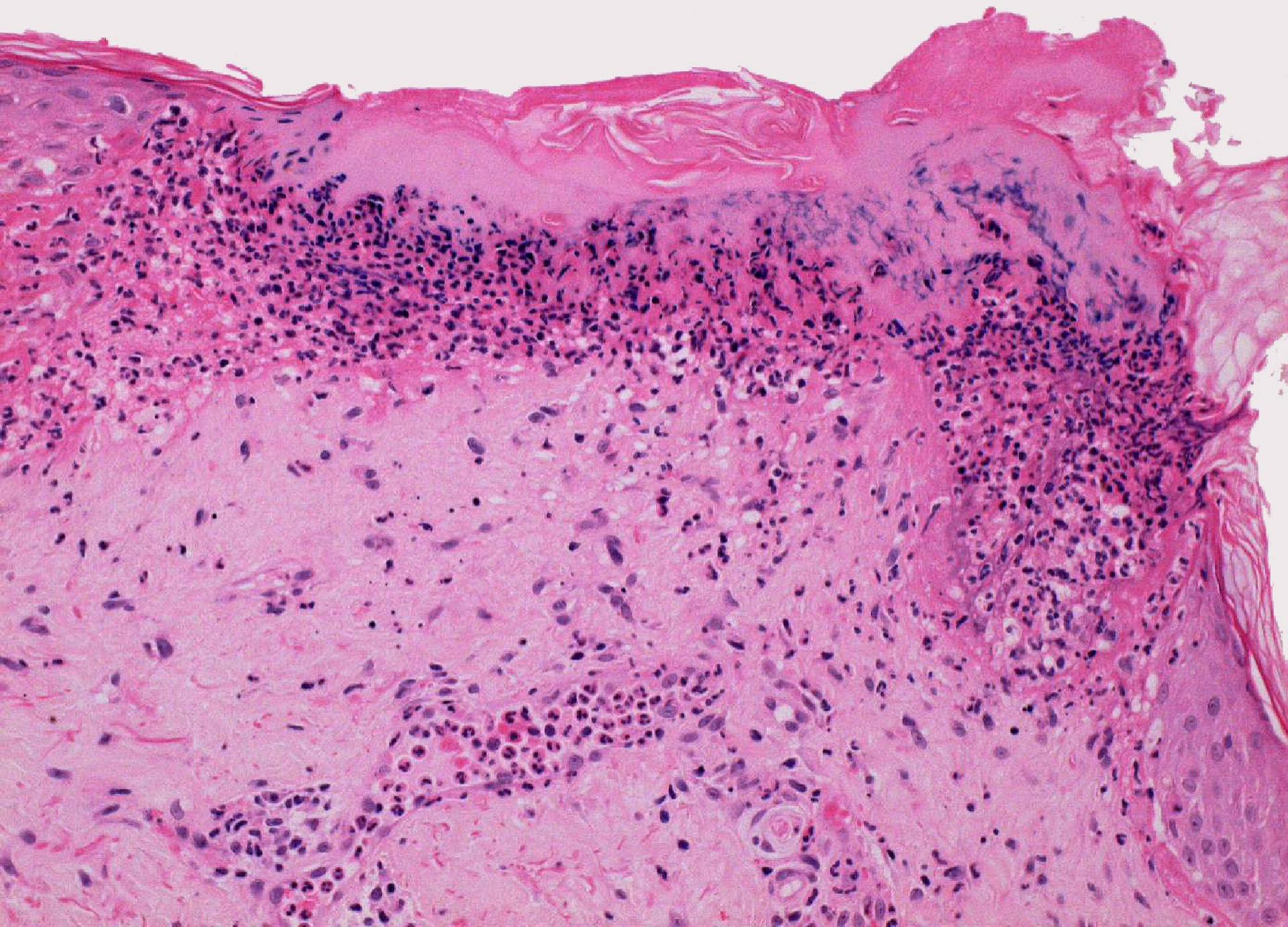


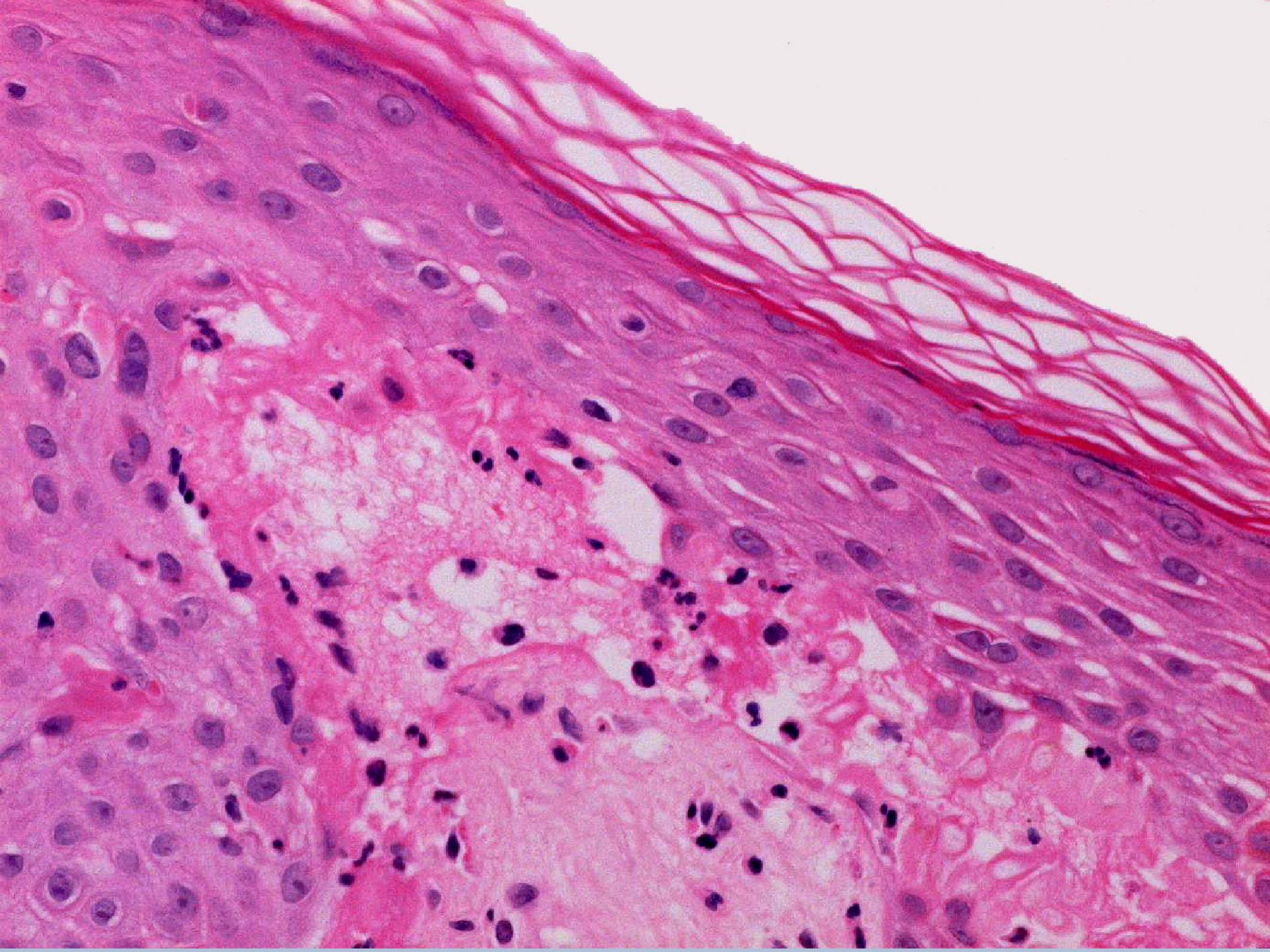
Grover's disease

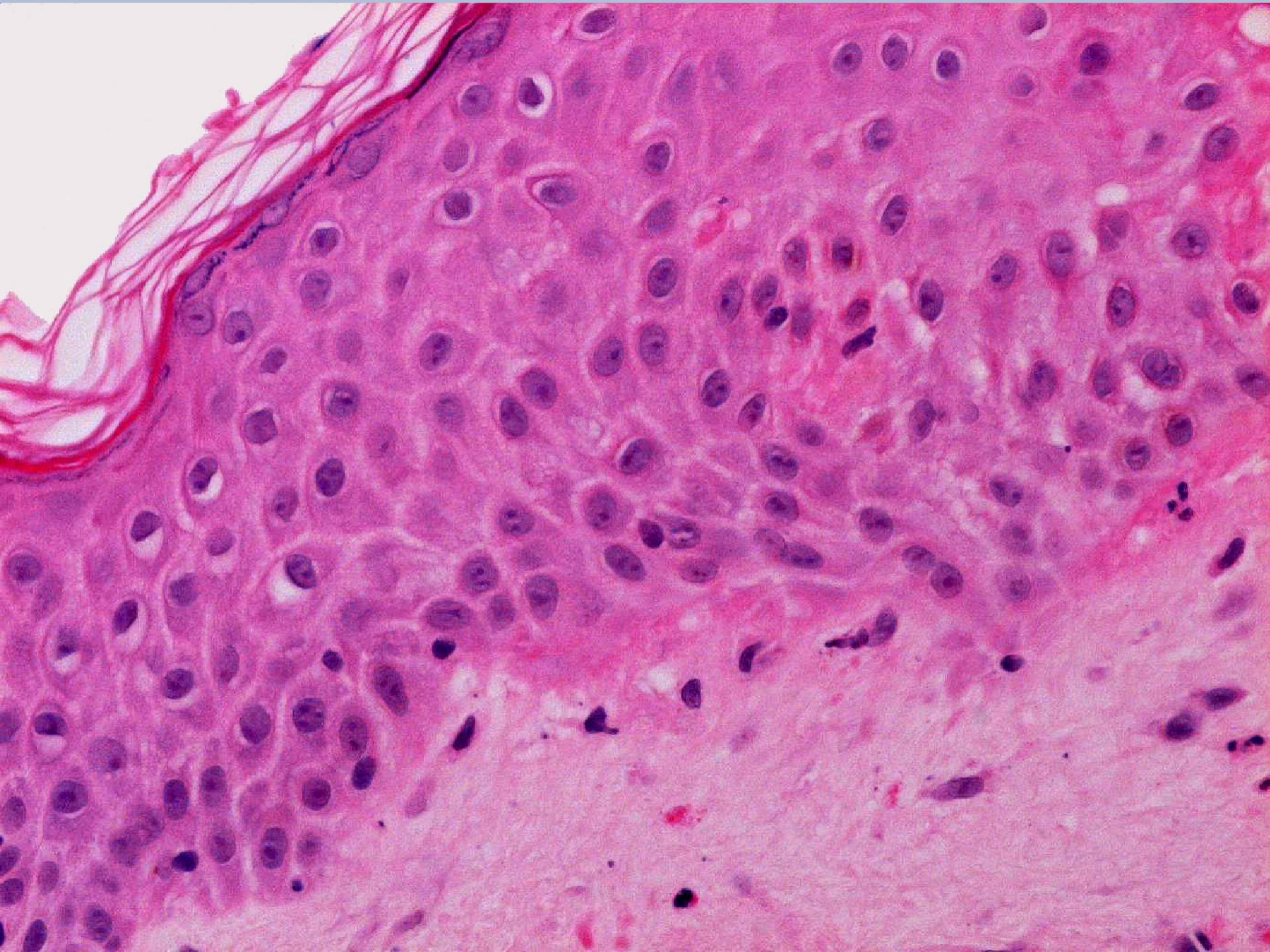


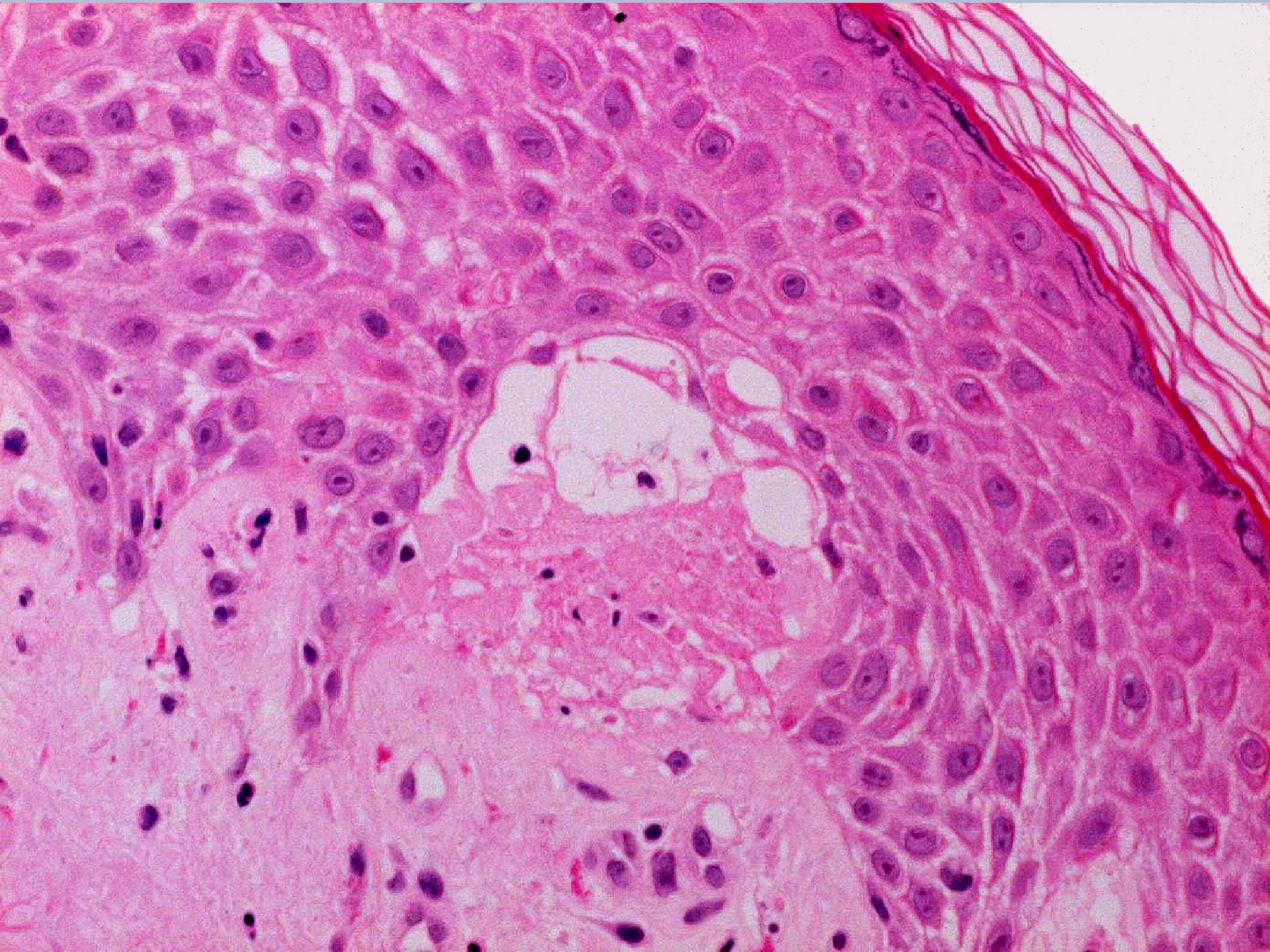
Case 2

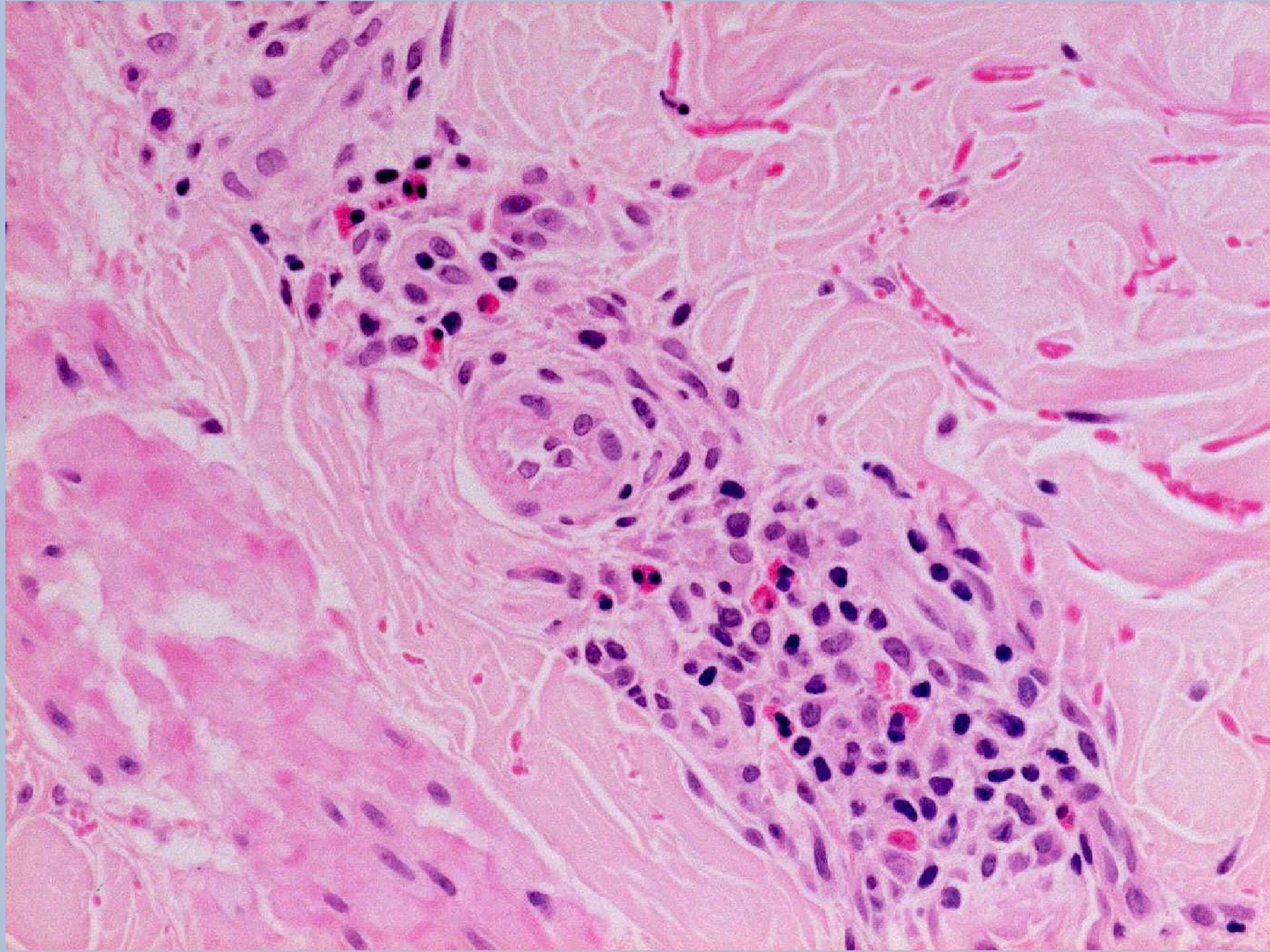
- M 46
- Anaemia
- Widespread, itchy, vesicular rash
- Elbows, lower back, buttocks











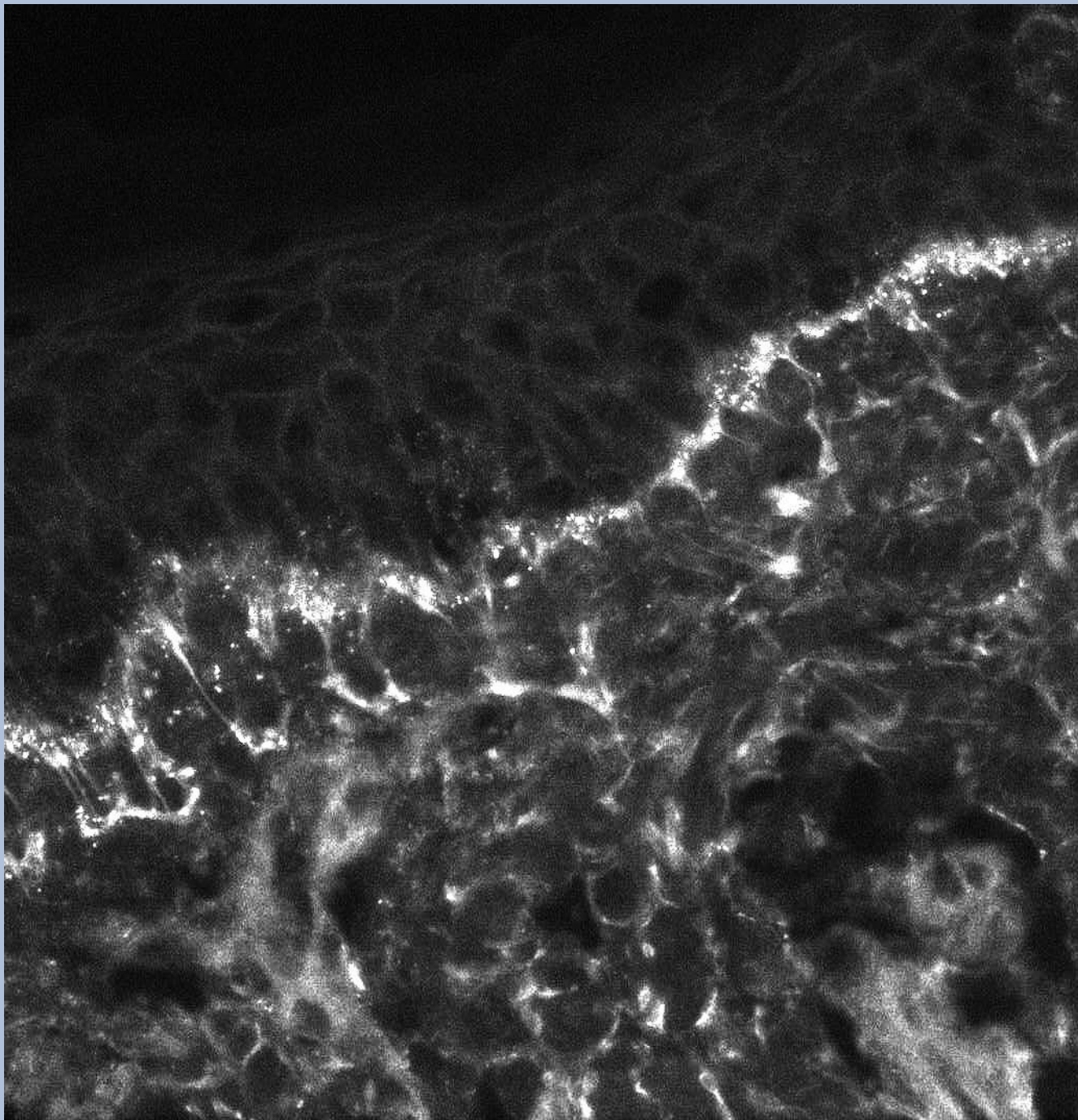
Case 2

- Subepidermal blister with eosinophils
 - Bullous pemphigoid
 - Cicatricial pemphigoid
 - Pemphigoid gestationis
 - Linear IgA disease
 - Inflammatory EBA
 - Paraneoplastic pemphigus
 - Bullous Wells' syndrome
 - Bullous fixed drug eruption
 - Dermatitis herpetiformis

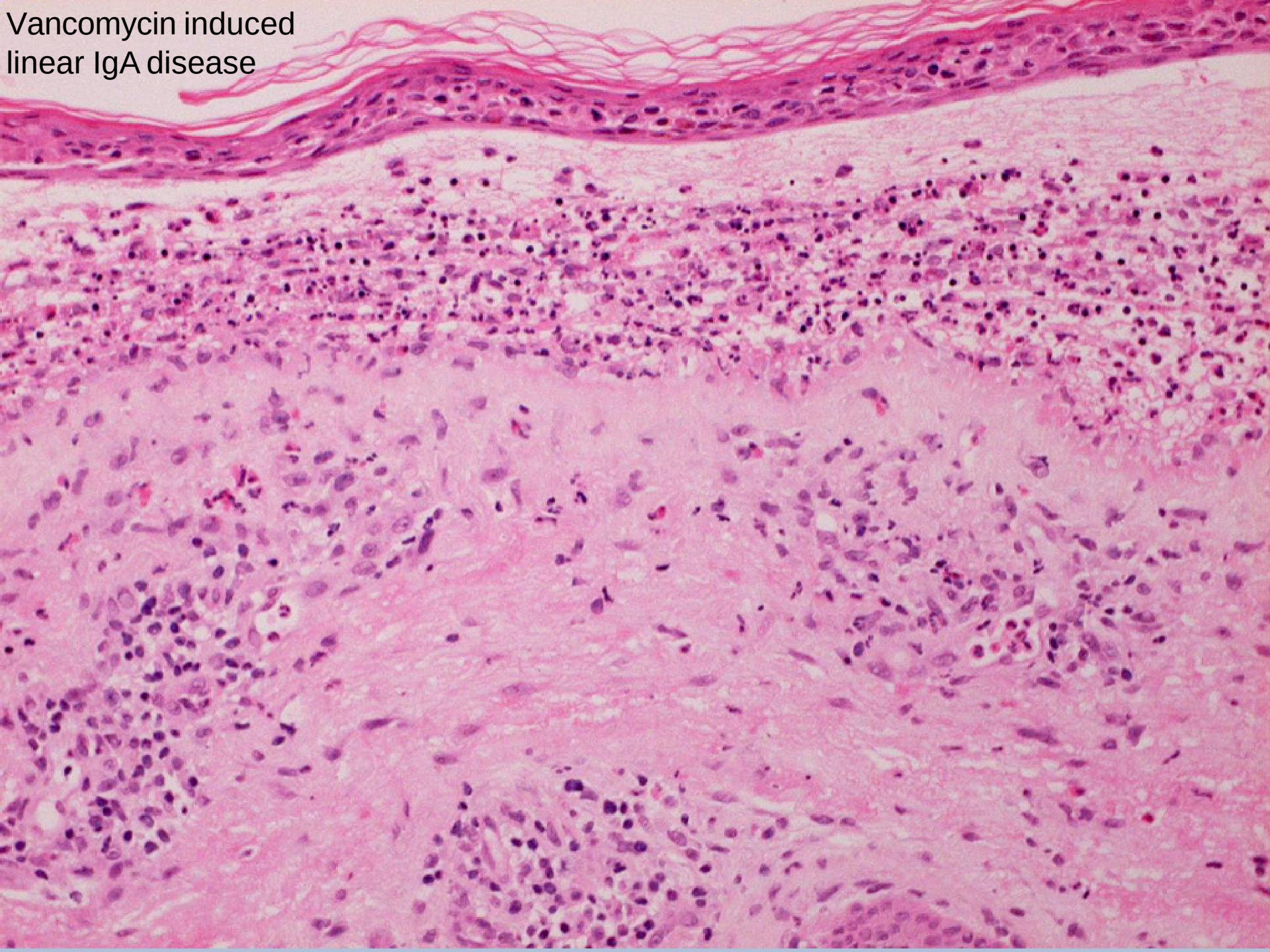
Dermatitis herpetiformis

- Neutrophil microabscesses
- Papillary degeneration
 - Also linear IgA
- May be excoriation only
- IMF

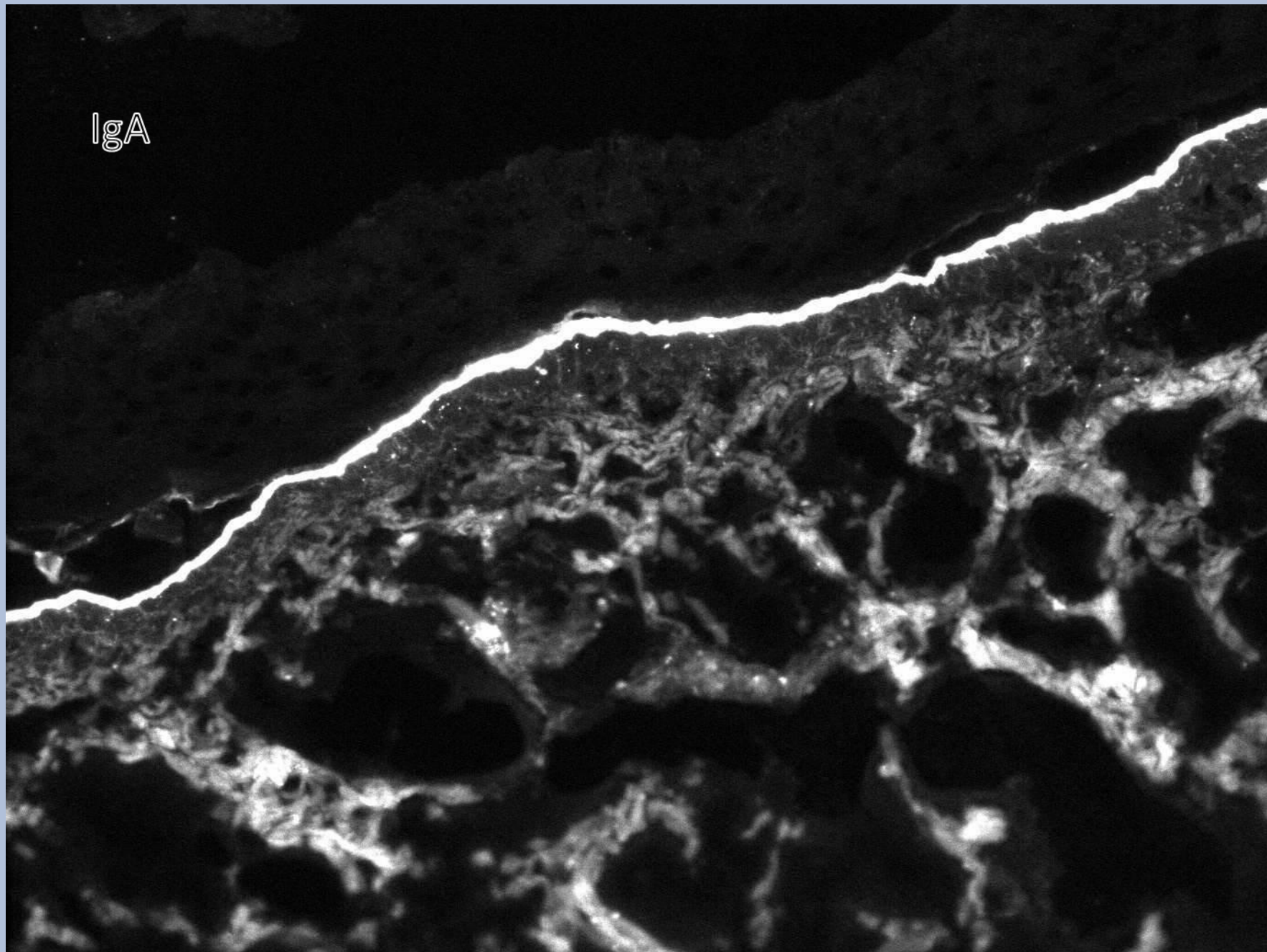
IgA



Vancomycin induced
linear IgA disease

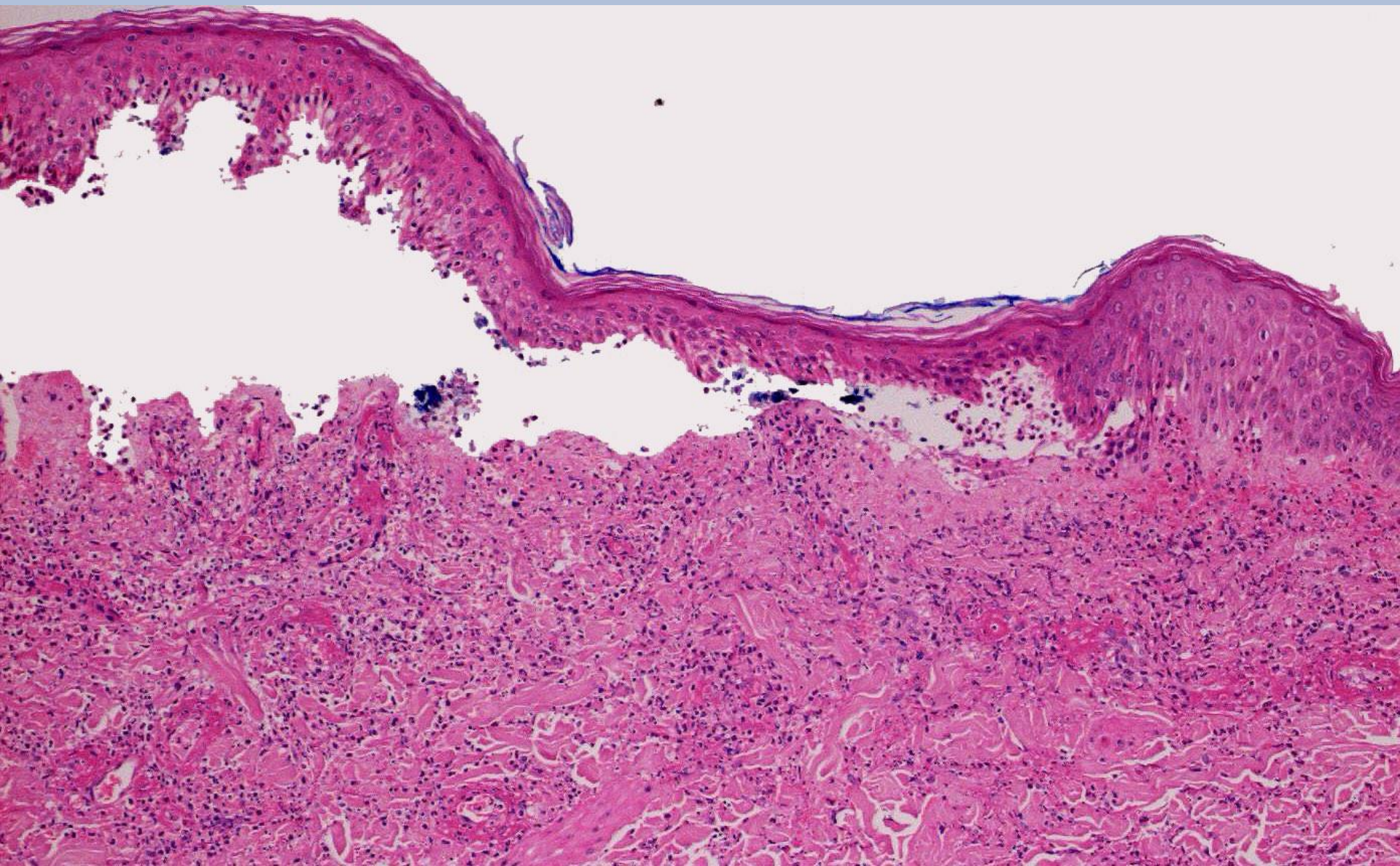


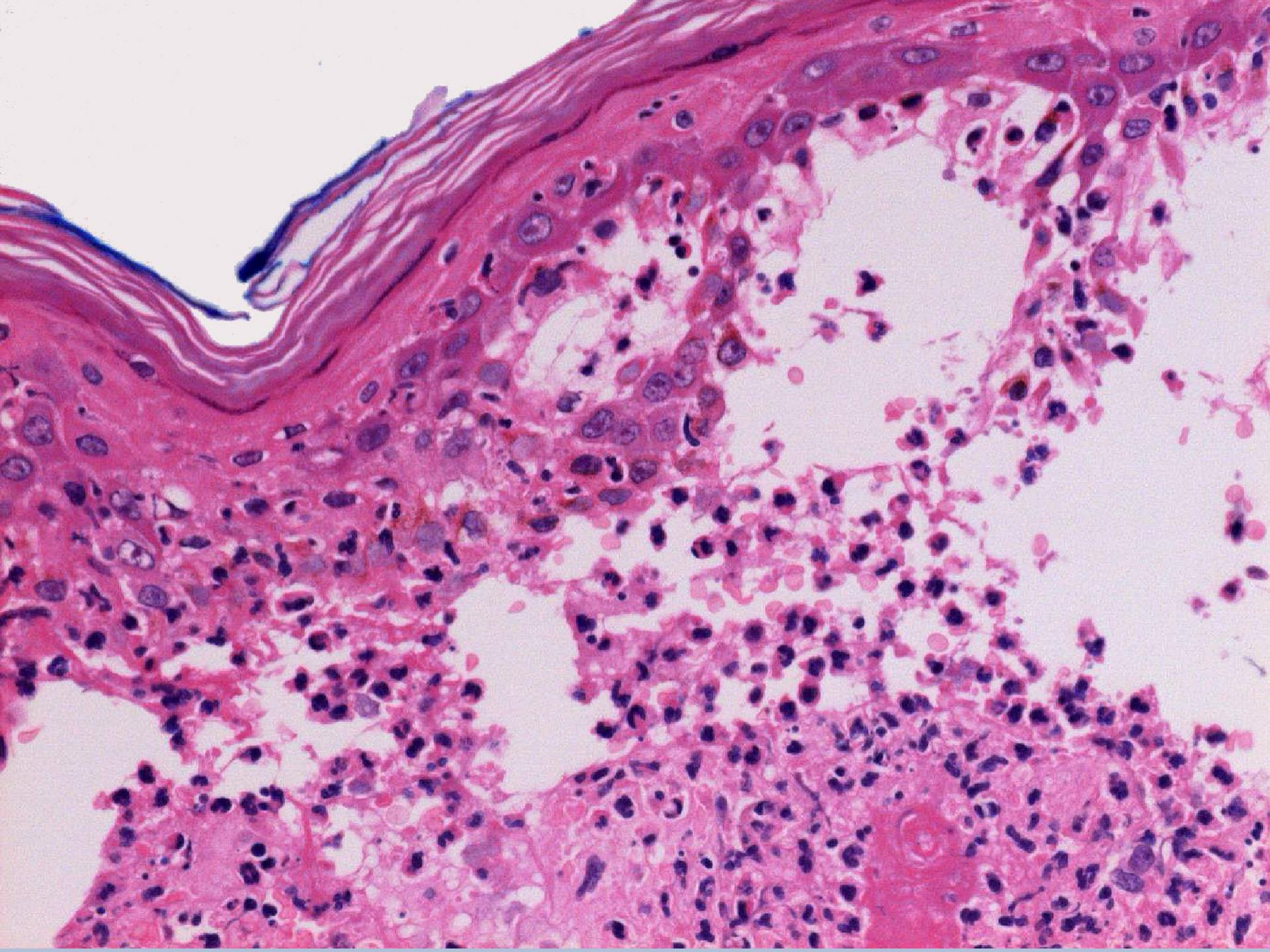
IgA

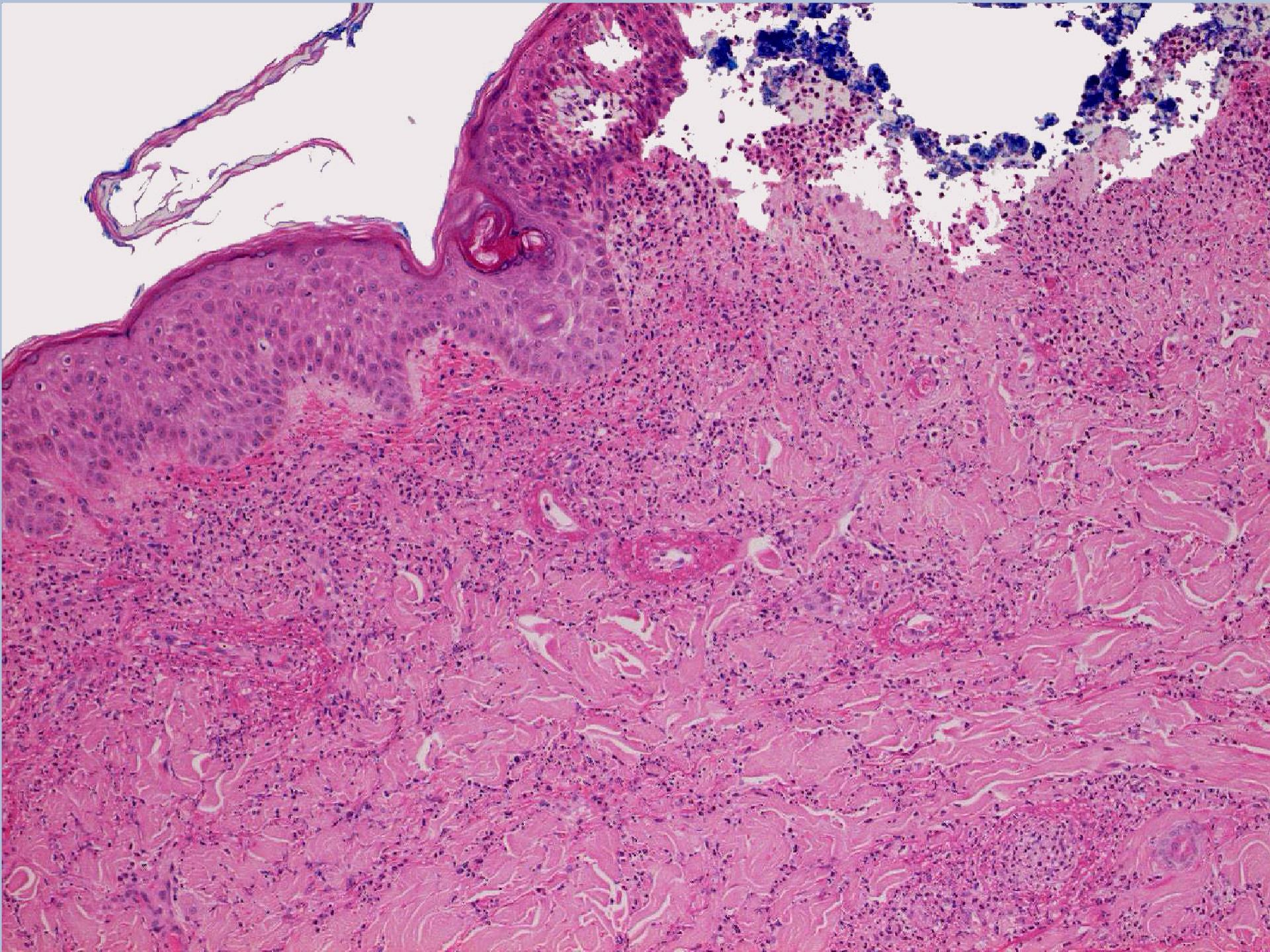


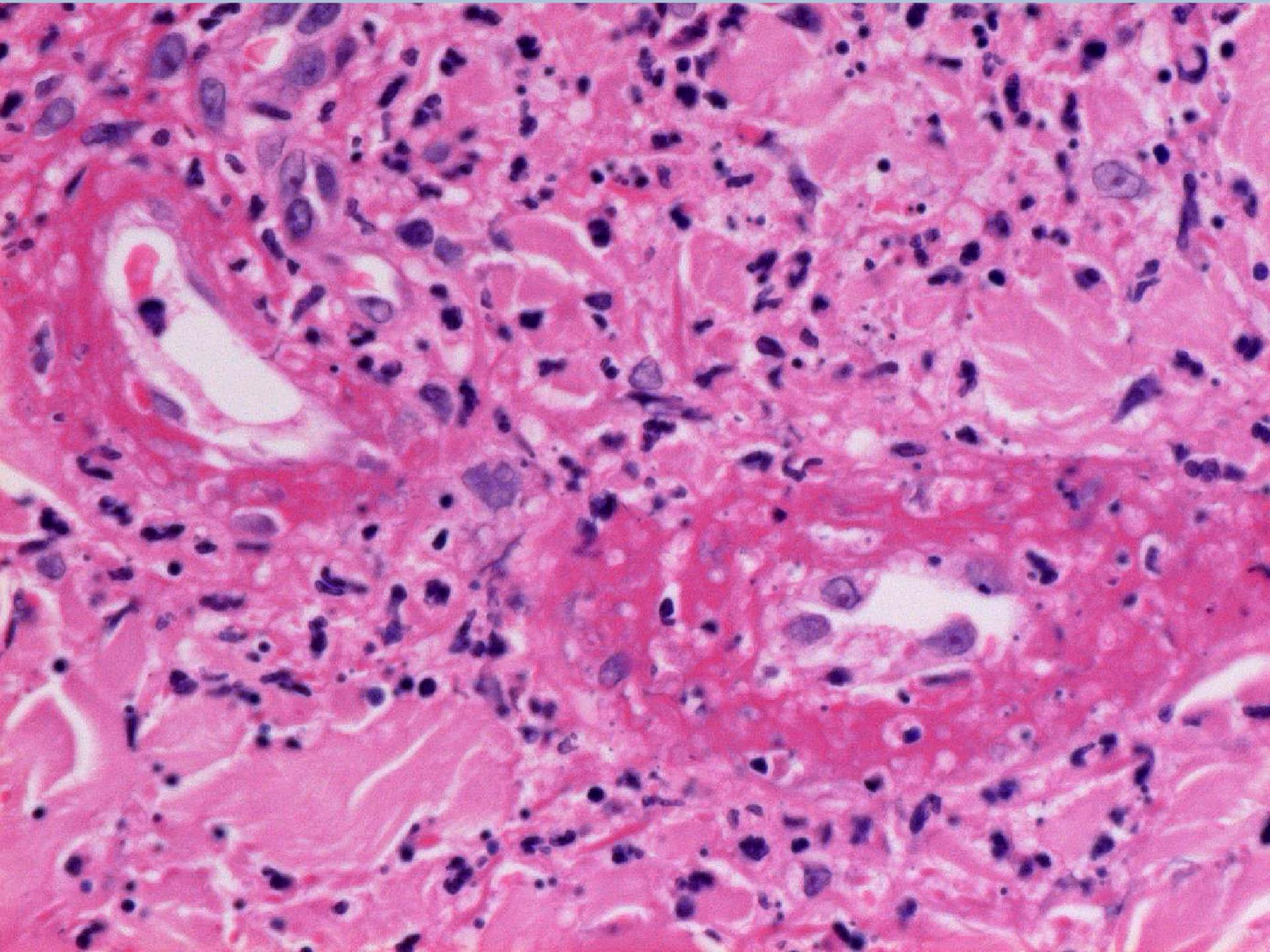
Case 3

- M 60
- Bullous rash on legs, abdomen









Case 3

- Neutrophilic subepidermal blister
 - Dermatitis herpetiformis
 - Linear IgA disease
 - Pemphigoid
 - Vesicular, polymorphic
 - Inflammatory EBA
 - Bullous lupus erythematosus
 - Bullous Sweet's syndrome
 - **Bullous leukocytoclastic vasculitis**

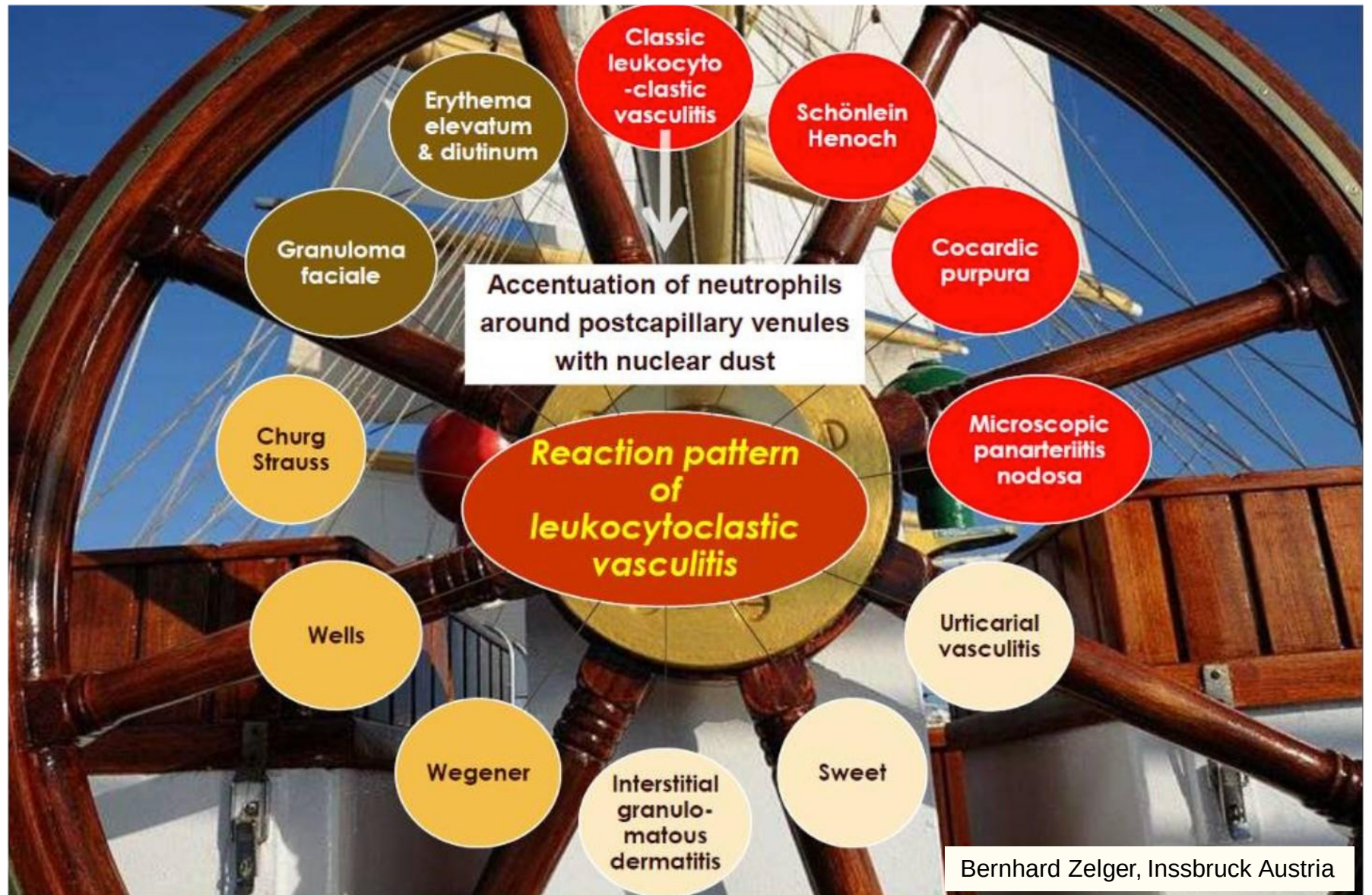
Leukocytoclastic vasculitis

- **Infiltration of small vessel walls by neutrophils**
- Neutrophils in perivascular areas and interstitium
- Oedema of vessel walls and perivascular dermis
- **Leukocytoclasia** (may be absent)
- **Fibrinoid ~~necrosis~~ change**
- **Endothelial cell swelling and necrosis**
- Red cell and fibrin extravasation
- Thrombosis
- Epidermal or dermal necrosis, subepidermal separation, perivascular fibrosis

Neutrophilic vasculitis

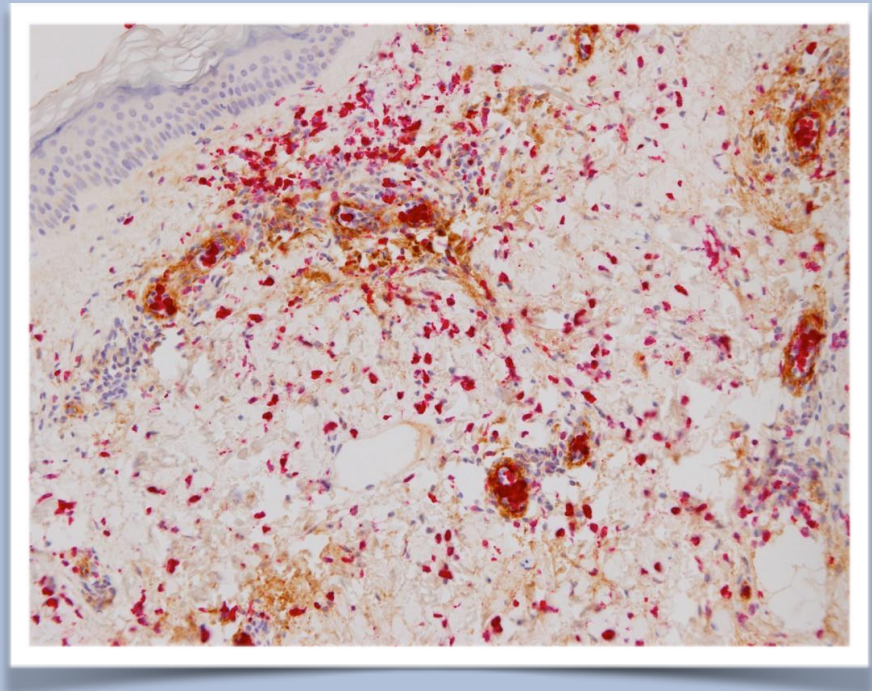
- LCV
 - Including Wegener's, C-S, CTD, chronic vasculitis syndromes
- Cutaneous polyarteritis
- Nodular vasculitis
- Polyarteritis nodosa
- Microscopic polyangiitis
- Cryoglobulinaemia
- Rheumatoid arthritis

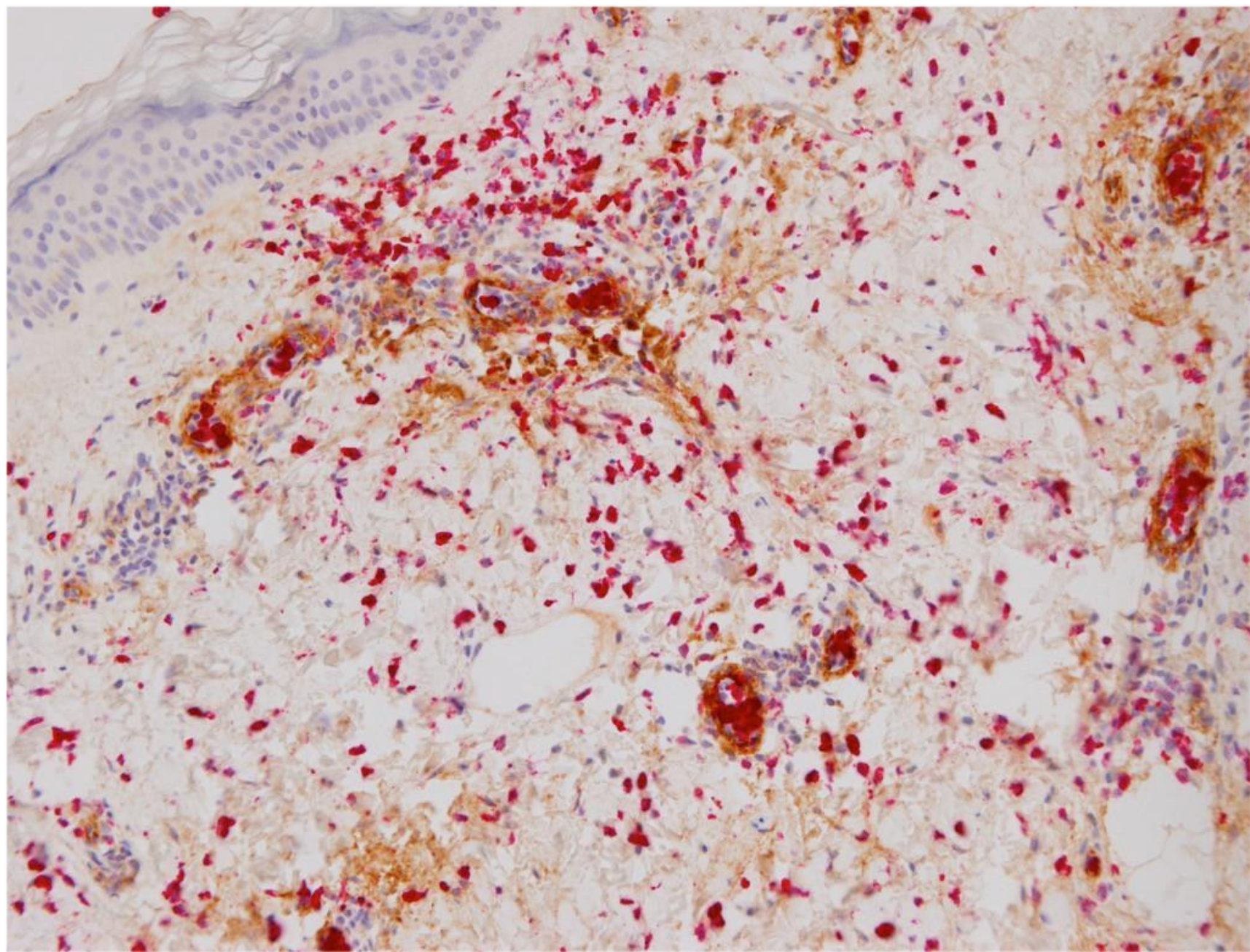
Vasculitis



Vasculitis

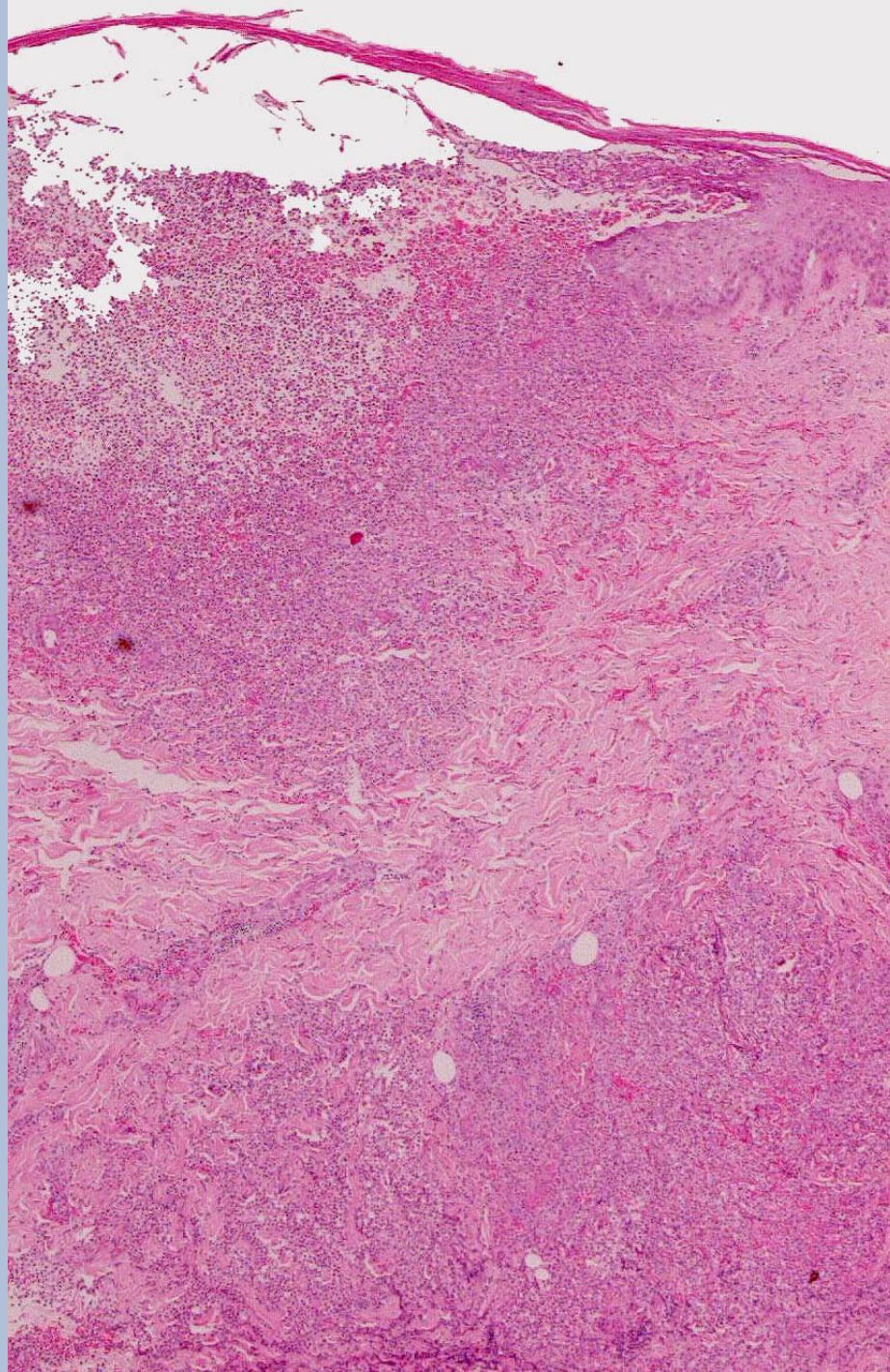
- vascular “inflammation”
- leakage - RBC extravasation
 - fibrinoid change - repair the leak!
- leukocytoclasia
- NETs

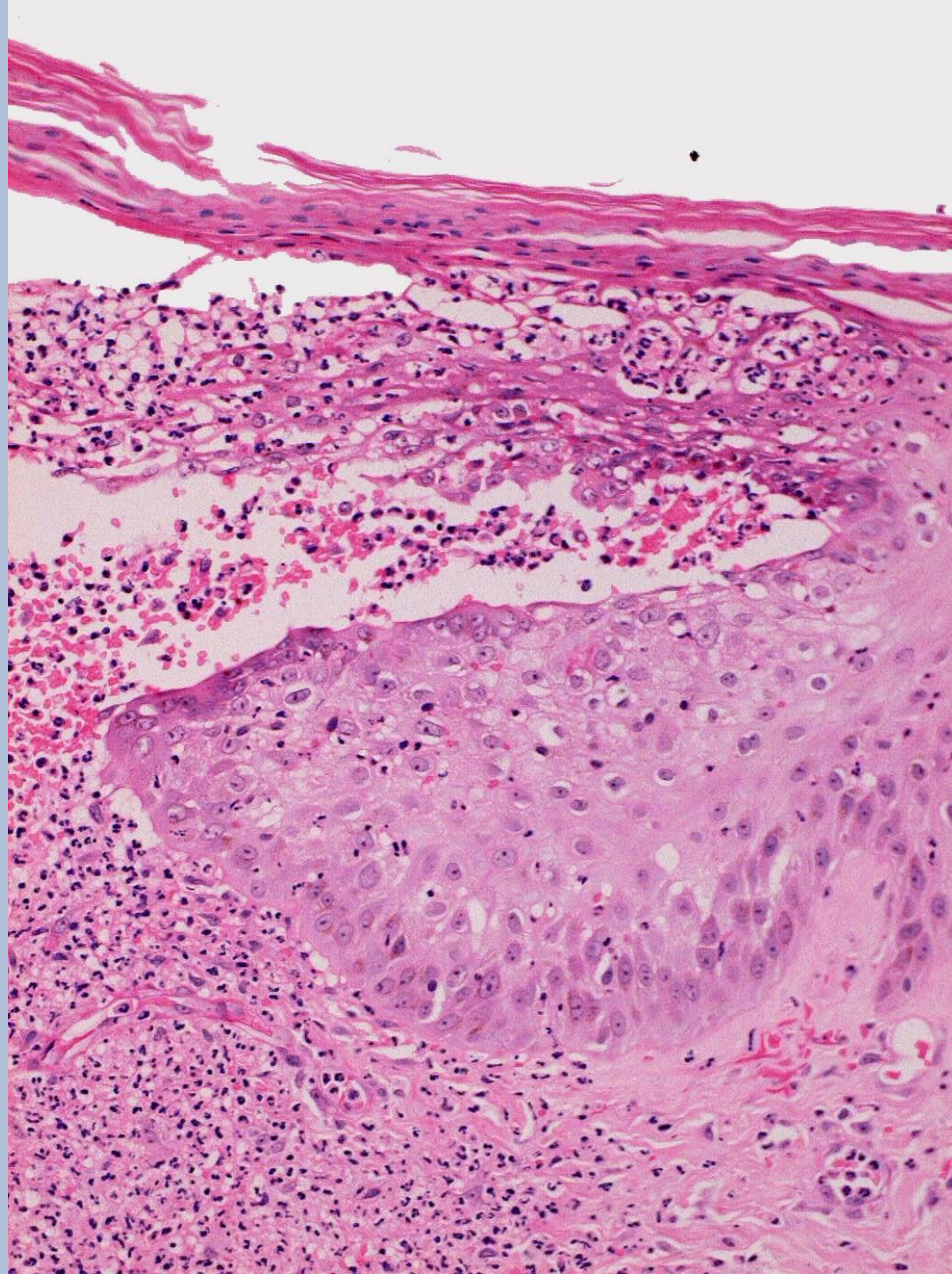


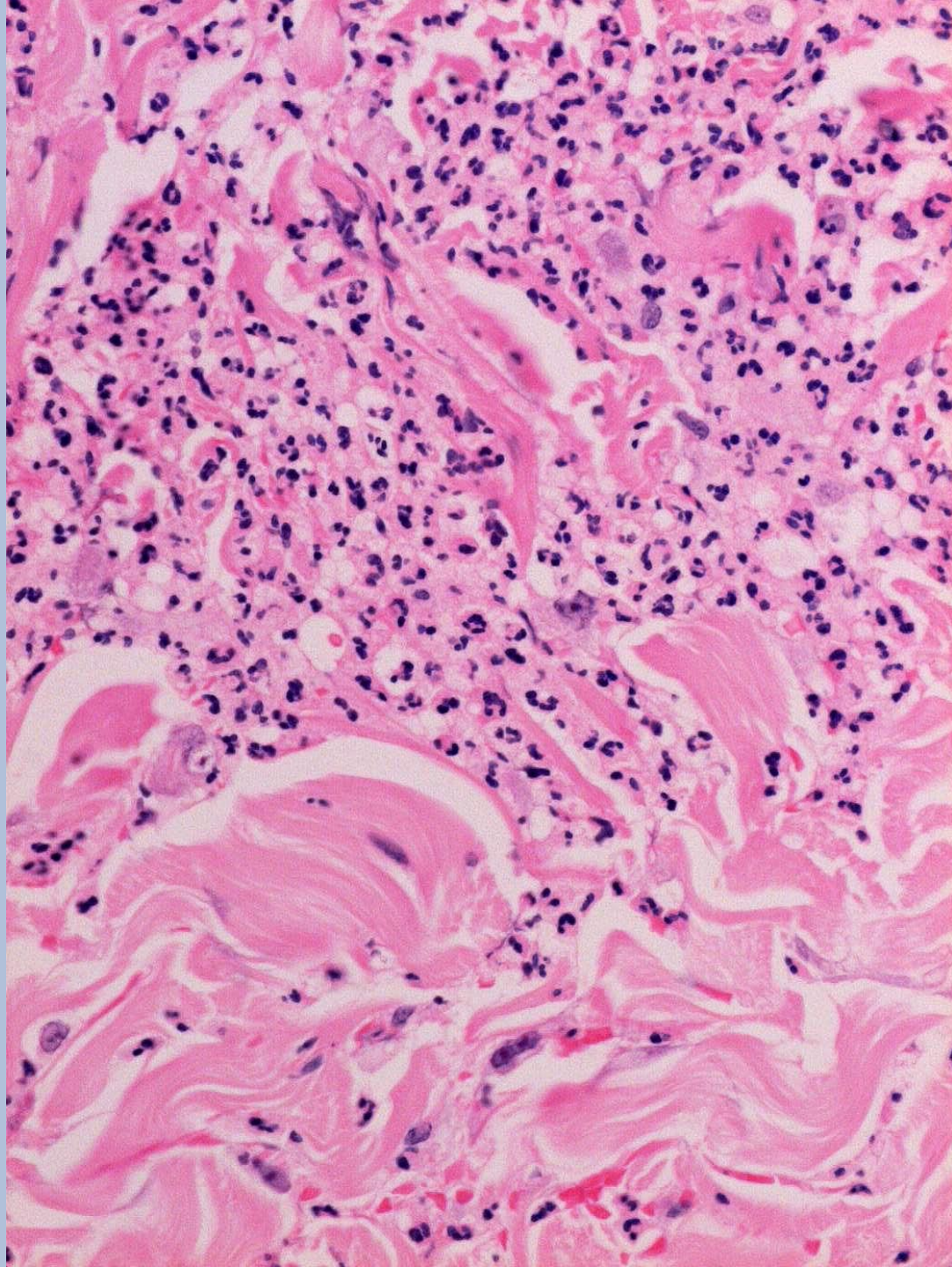


Case 4

- M 44
- UC, rapidly progressive pustulonecrotic areas on lower legs







Case 4

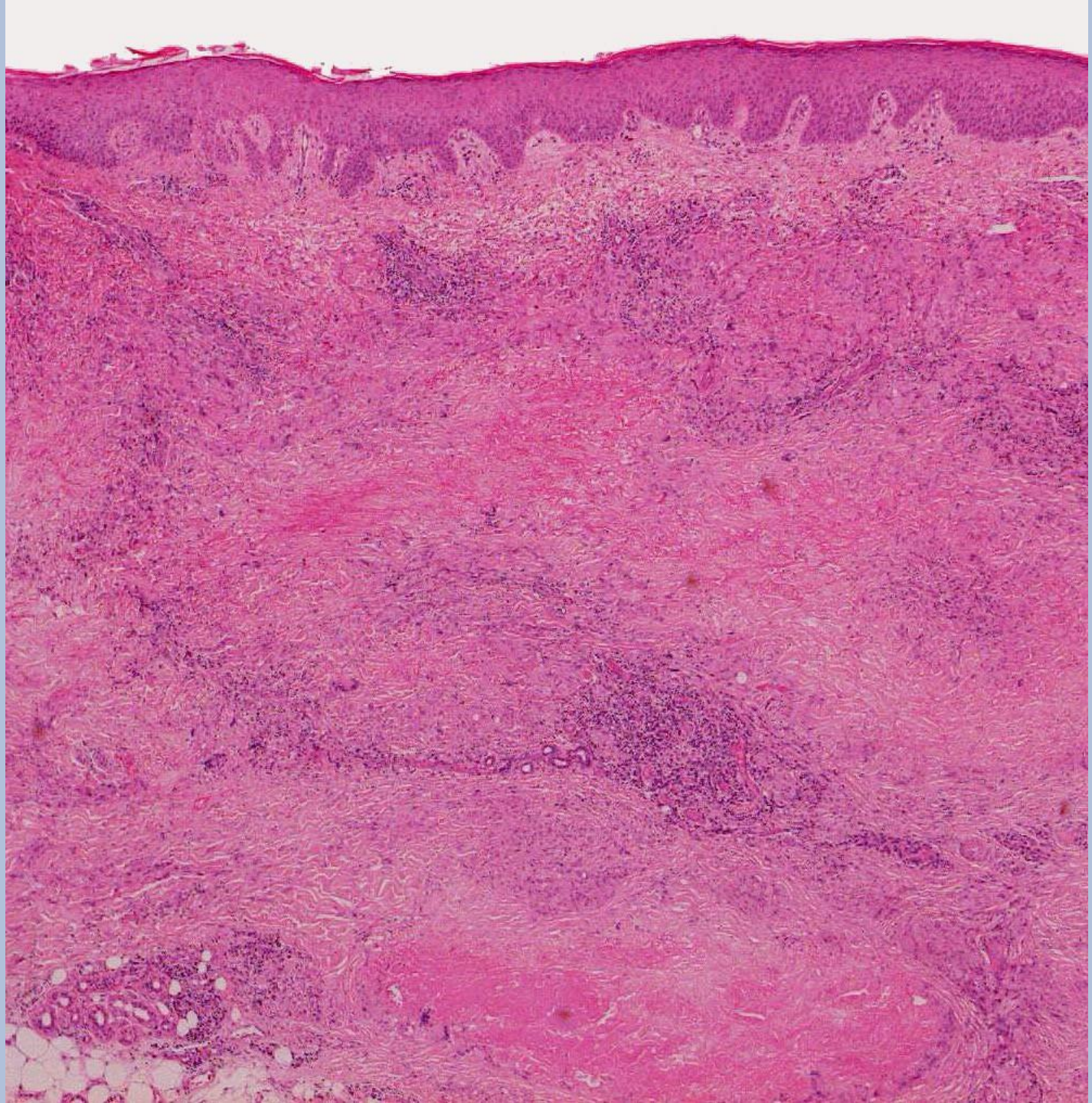
- Neutrophilic dermatosis
 - INFECTION
 - » Necrotizing fasciitis
 - Sweet's syndrome
 - » Acute febrile neutrophilic dermatosis
 - Neutrophilic dermatosis of the dorsal hands
 - Pyoderma gangrenosum
 - Rheumatoid neutrophilic dermatosis
 - Neutrophilic urticaria
 - Behcet's disease
 - Halogenoderma
 - Arthropod bites

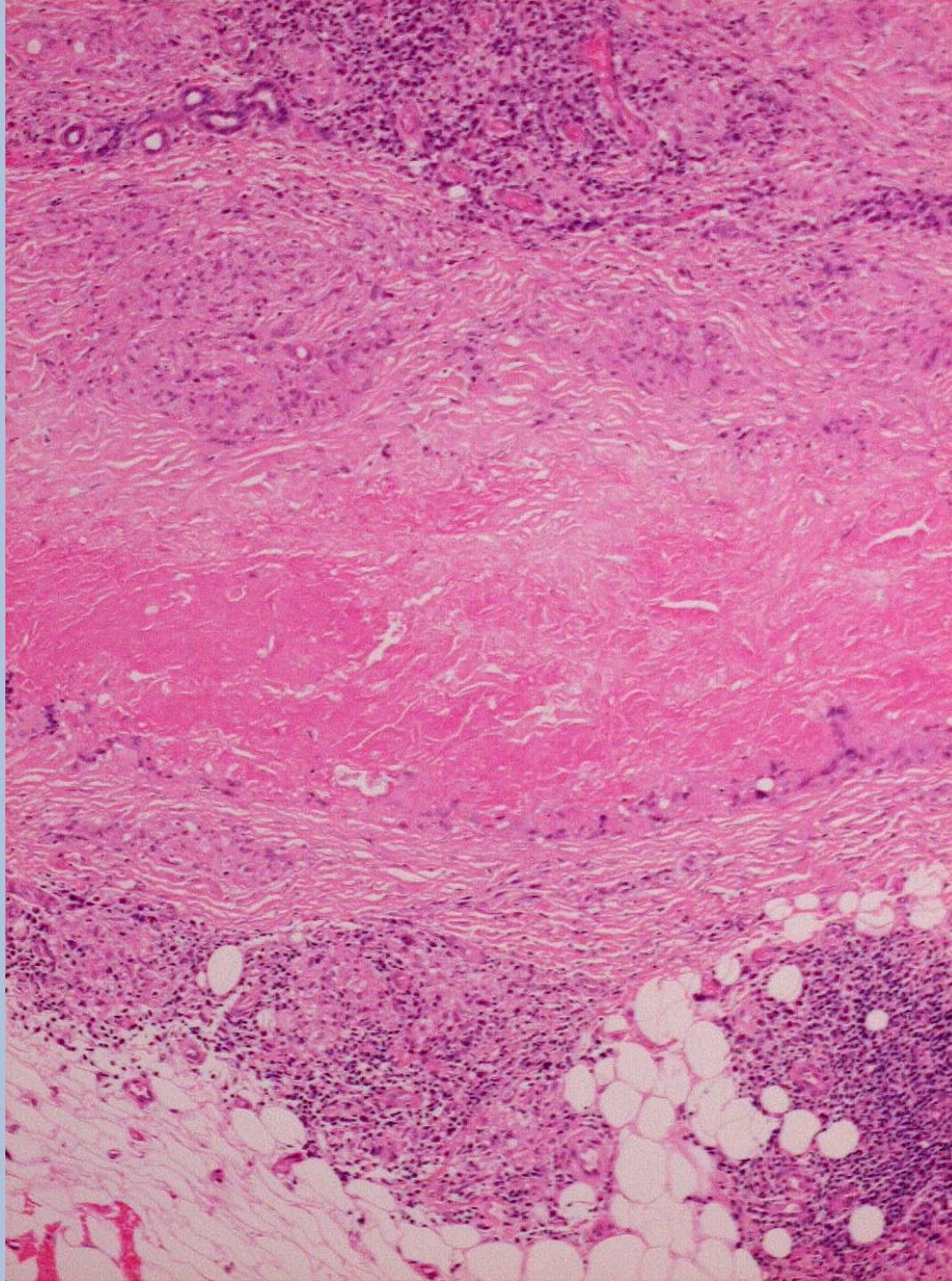
Pyoderma gangrenosum

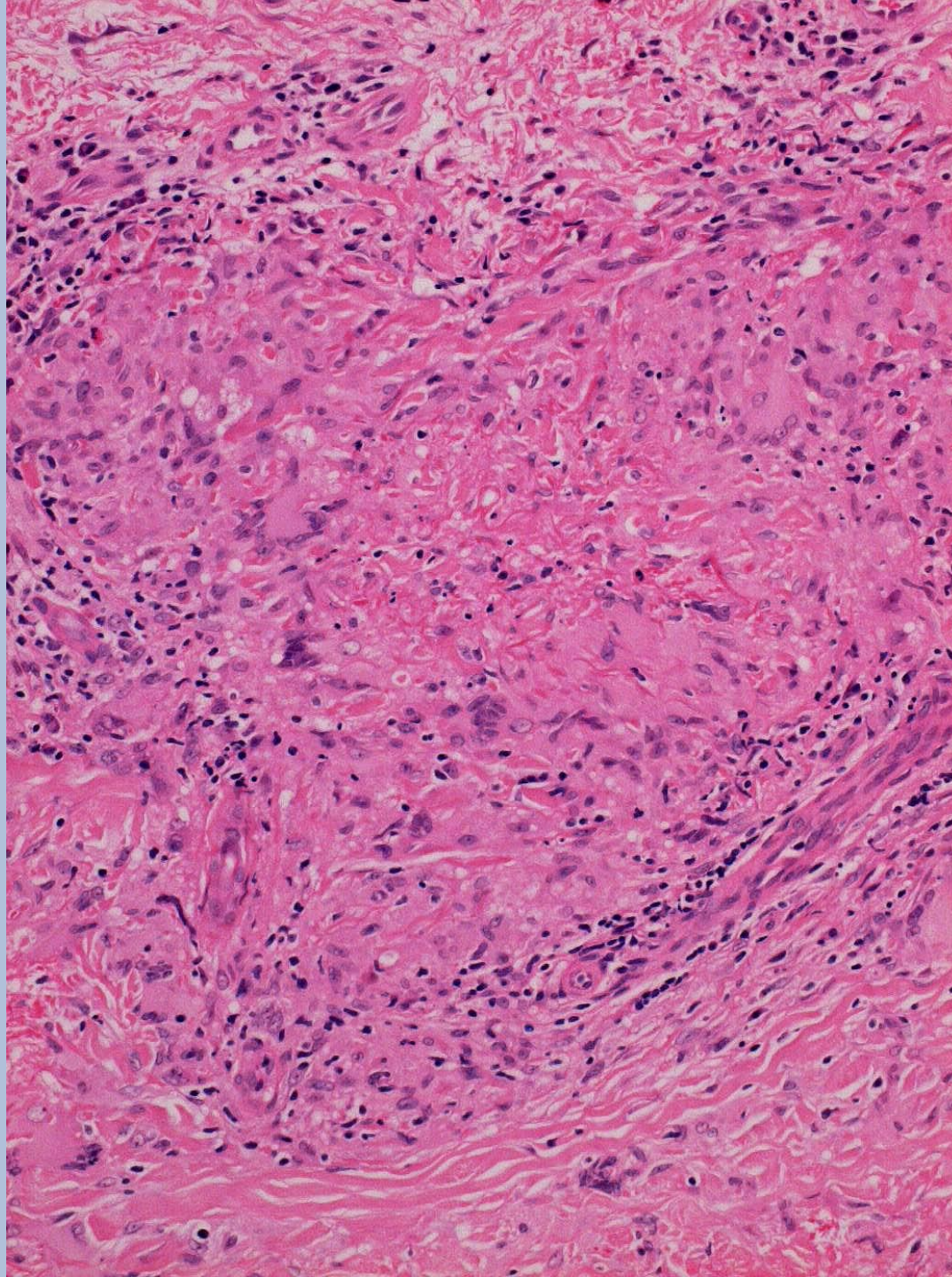
- History of pathergy, undermining ulcer
- Non-specific ulceration
- Intra-epidermal neutrophils, pustulation
- Vasculitis related to ulceration
- Giant cells
 - Crohn's disease, superficial granulomatous pyoderma

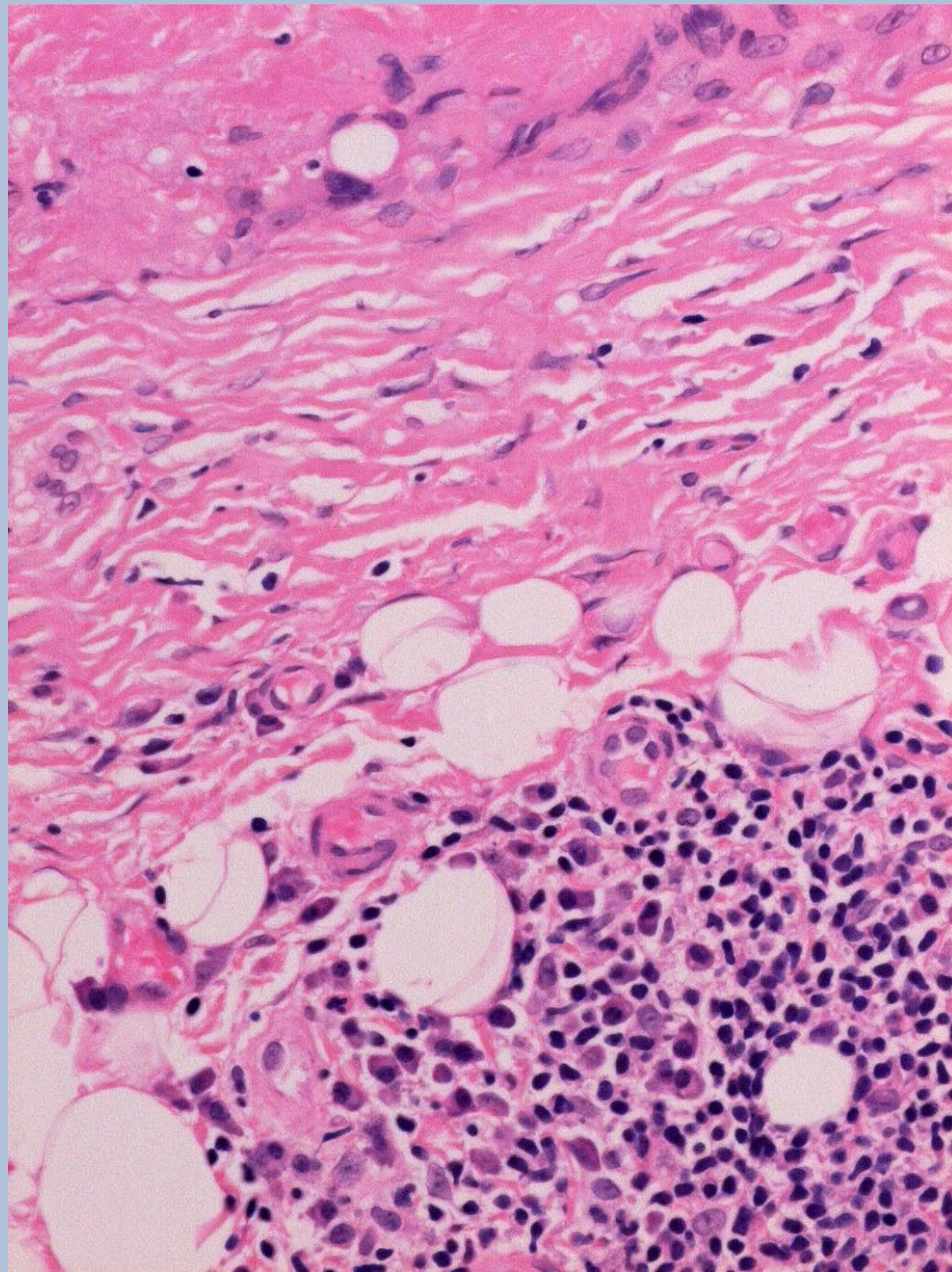
Case 5

- F53
- Multiple indurated, erythematous lesions on lower legs with yellowish edges, hypothyroidism
- ?panniculitis









Case 5

- Necrobiotic granulomas
 - Necrobiosis lipoidica
 - Granuloma annulare
 - Rheumatoid nodule
 - Elastolytic granuloma
 - Atypical facial necrobiosis lipoidica
 - Necrobiotic xanthogranuloma
 - (Palisaded neutrophilic and granulomatous dermatitis)
 - (foreign body granuloma)
 - (Crohn's)

Necrobiosis lipoidica

- CLINICAL

- Diabetes, thyroid disease, IBD
- Red/brown progressing to yellow plaques

- Plasma cells*

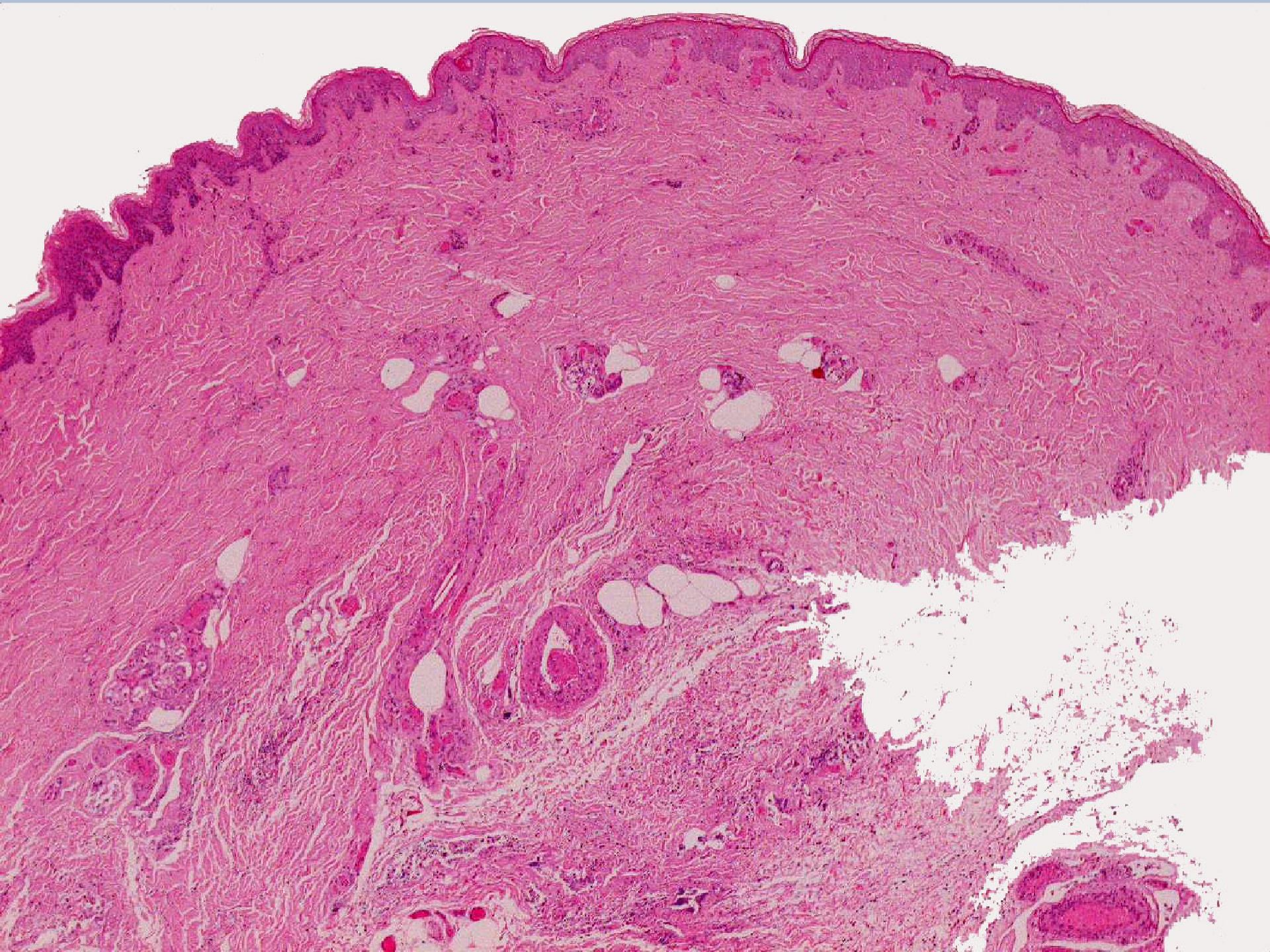
- Scarring

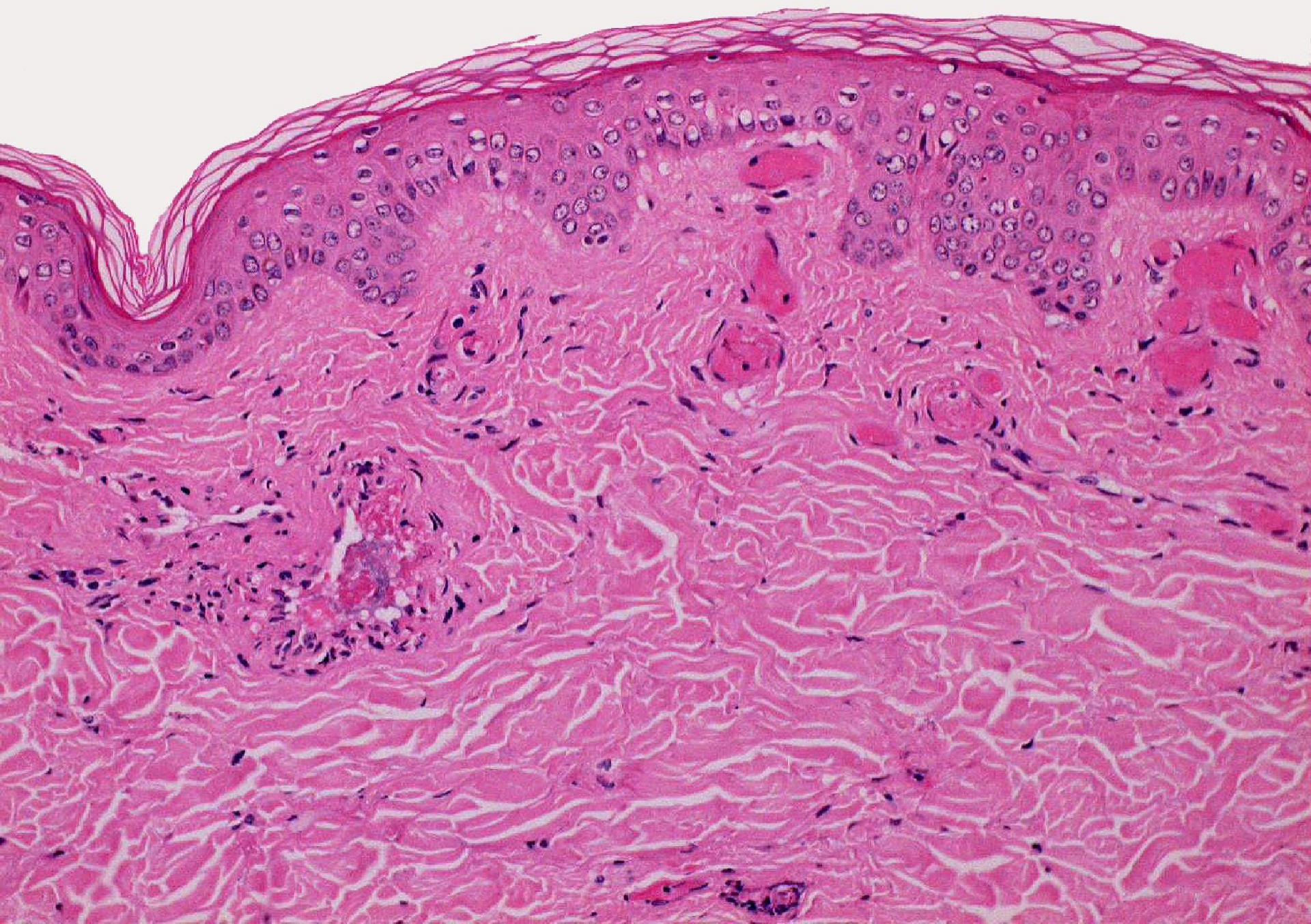
- Subcutaneous involvement

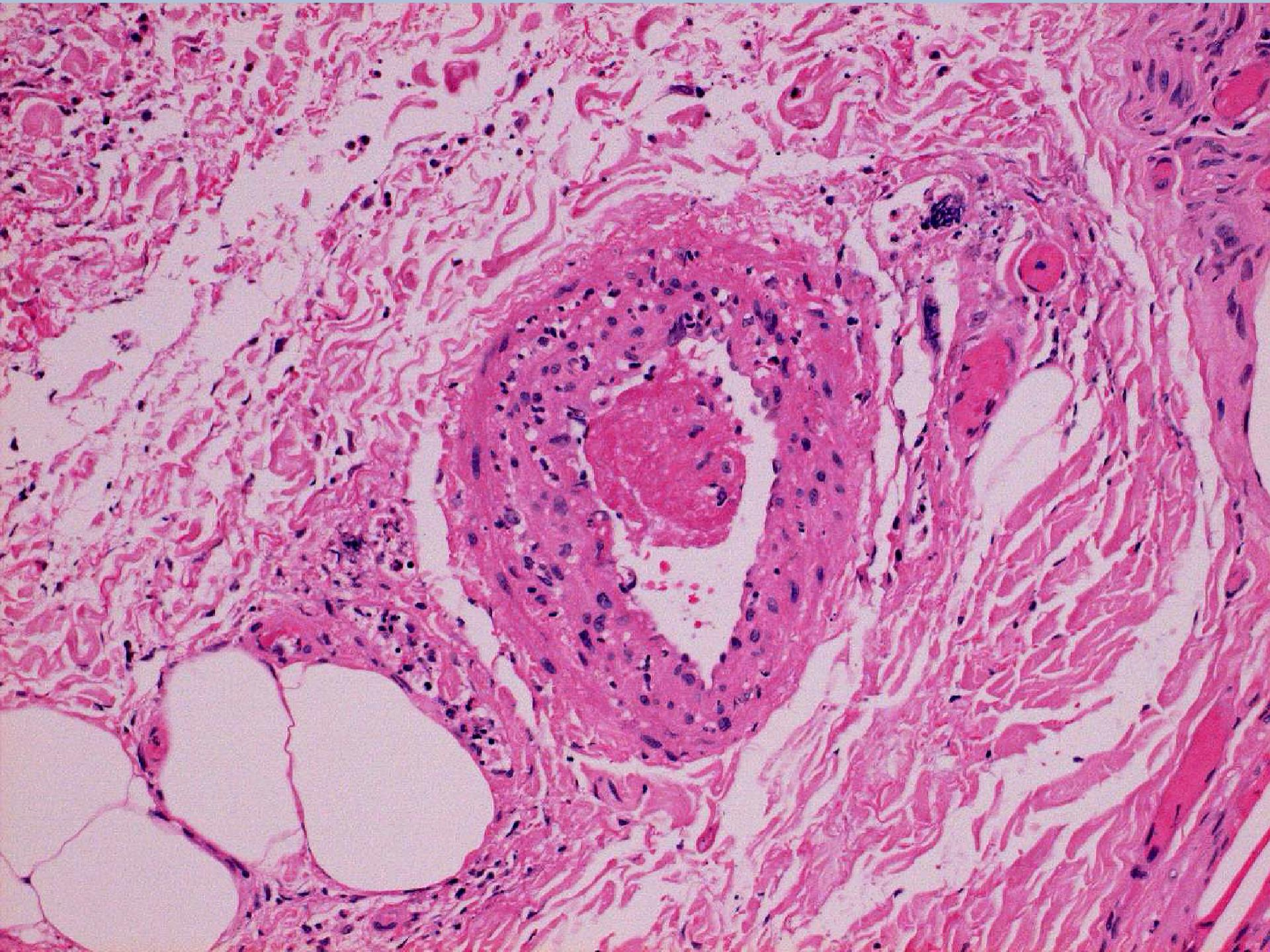
*Plasma cells in GA, consider infection – syphilis, borrelia

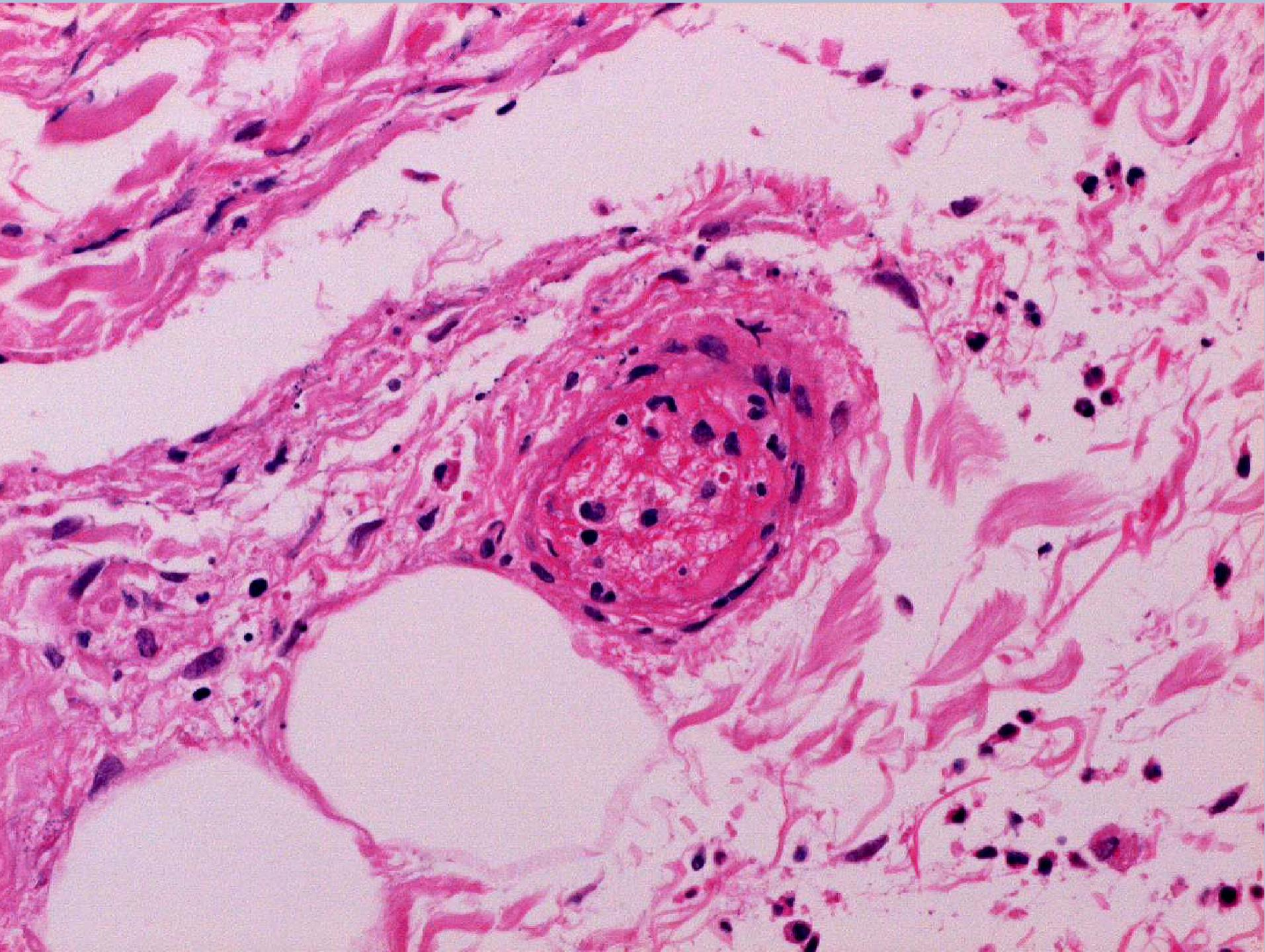
Case 6

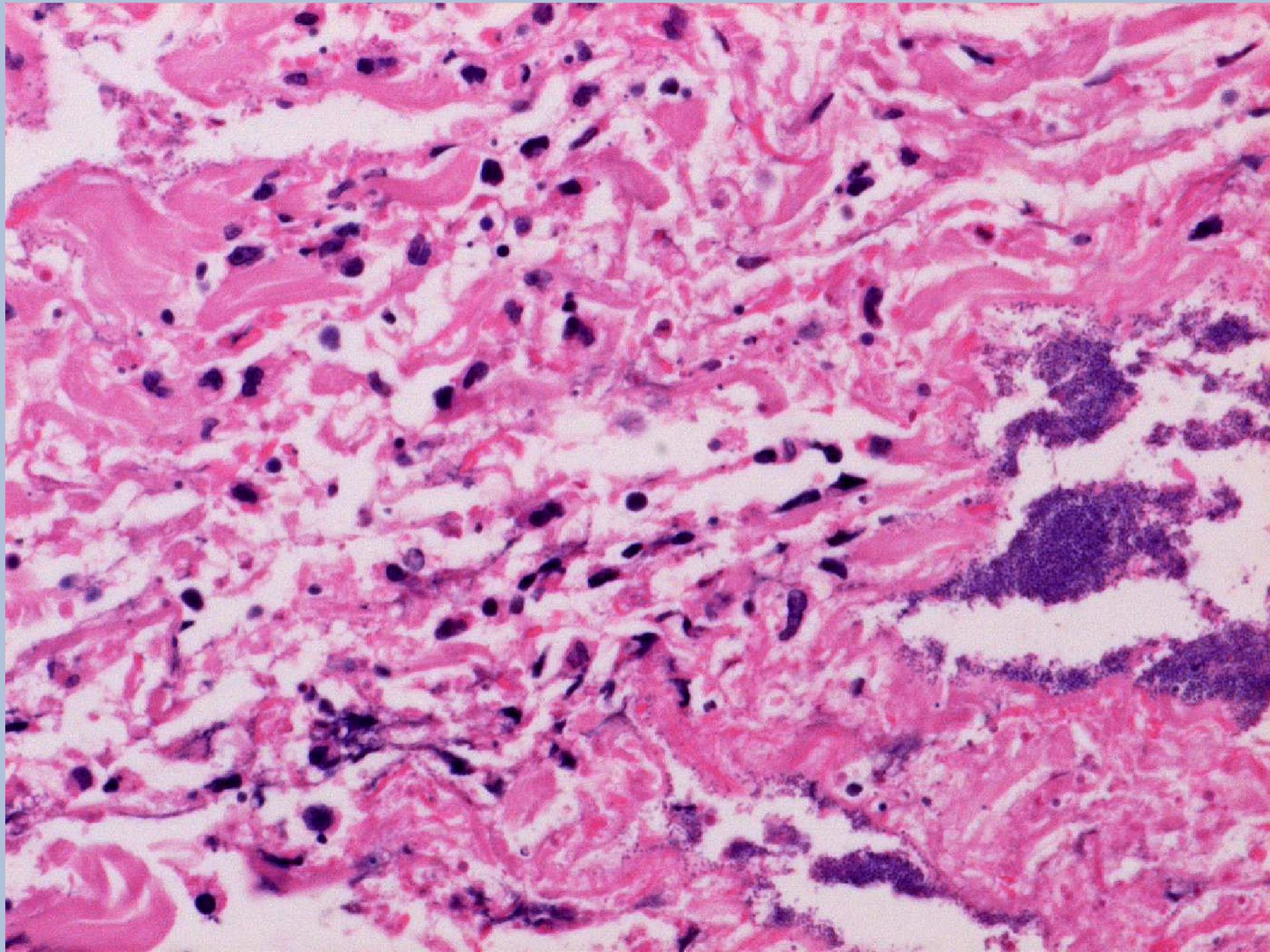
- F84
- Advancing inflammation left foot









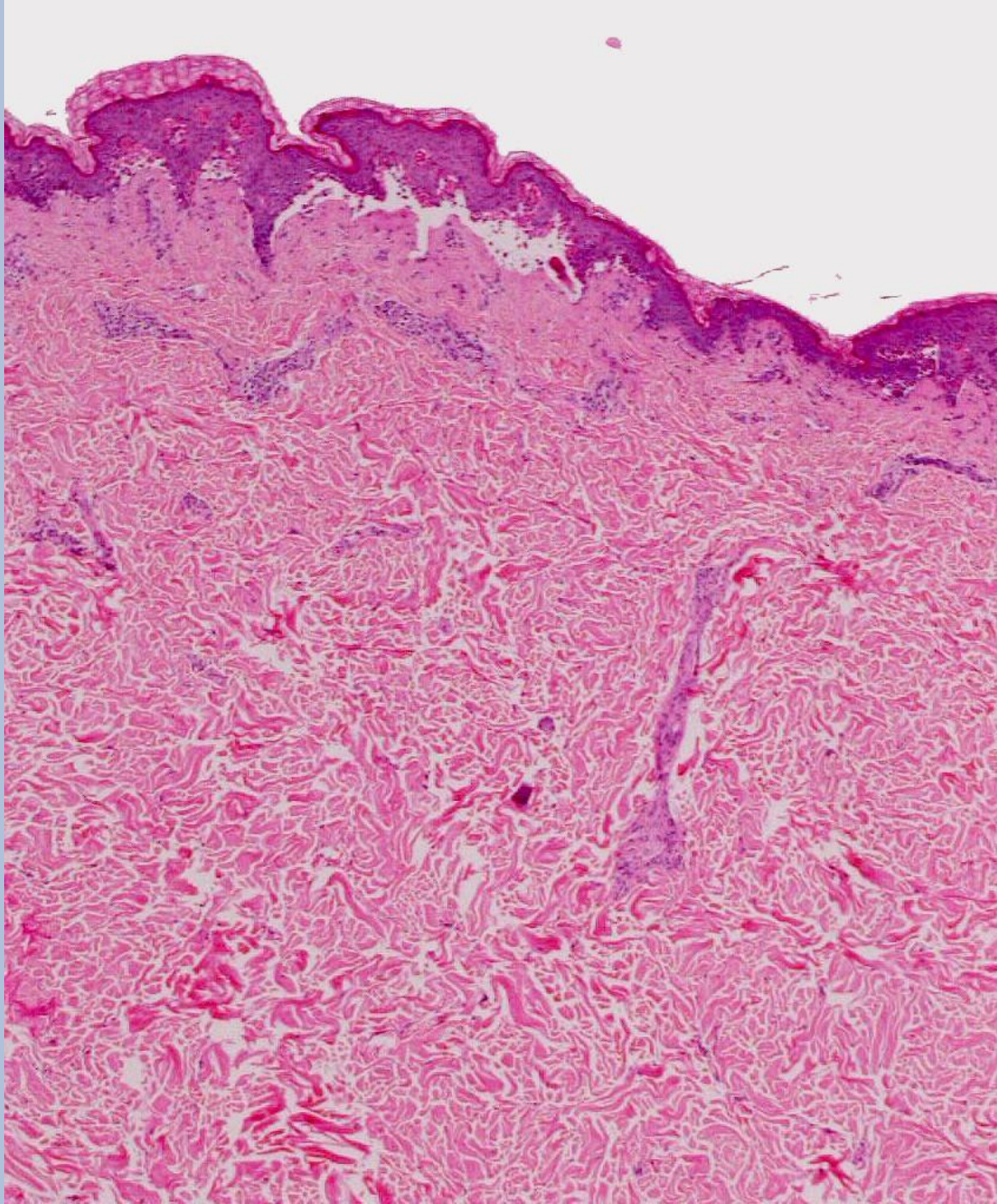


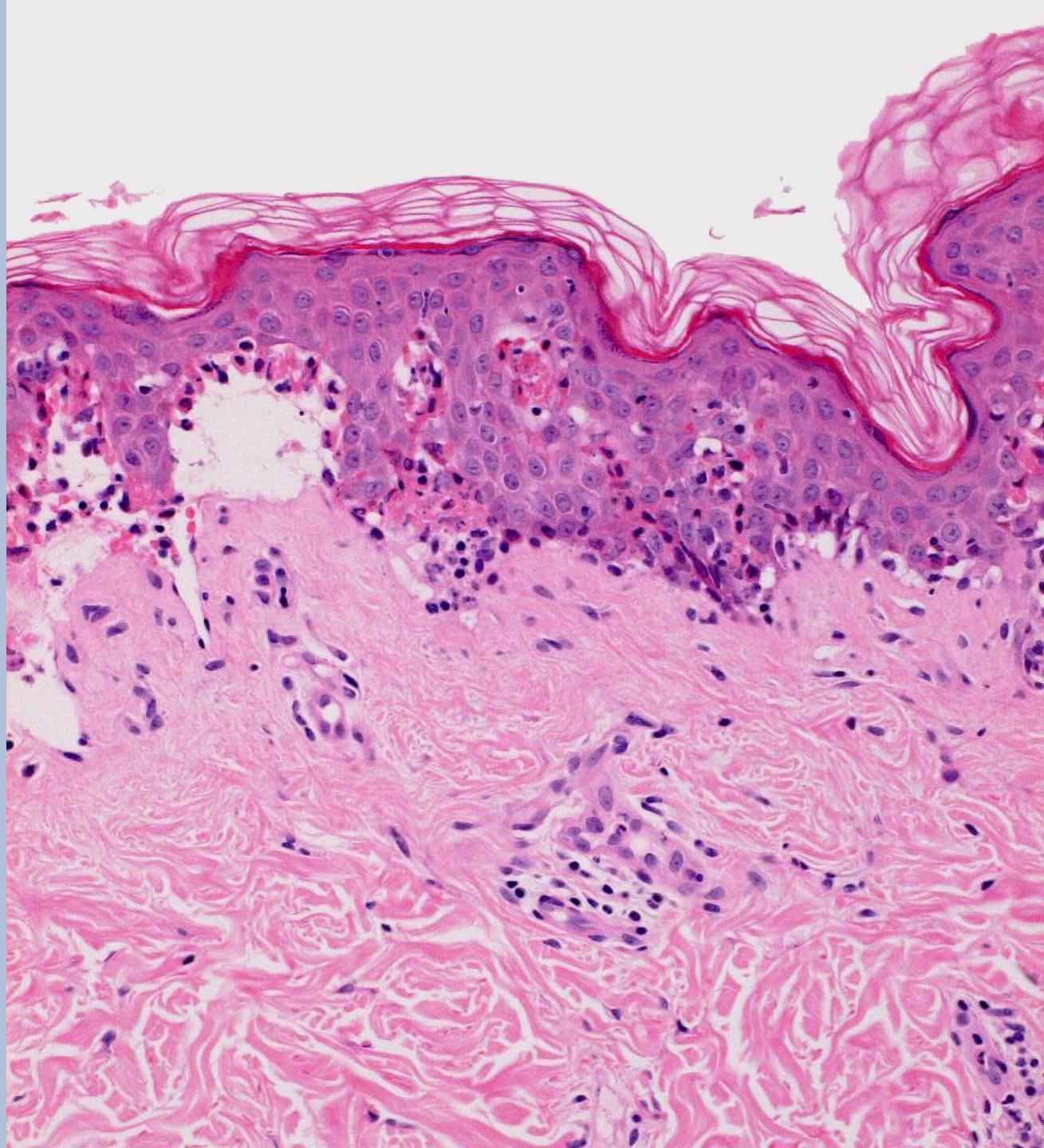
Case 6

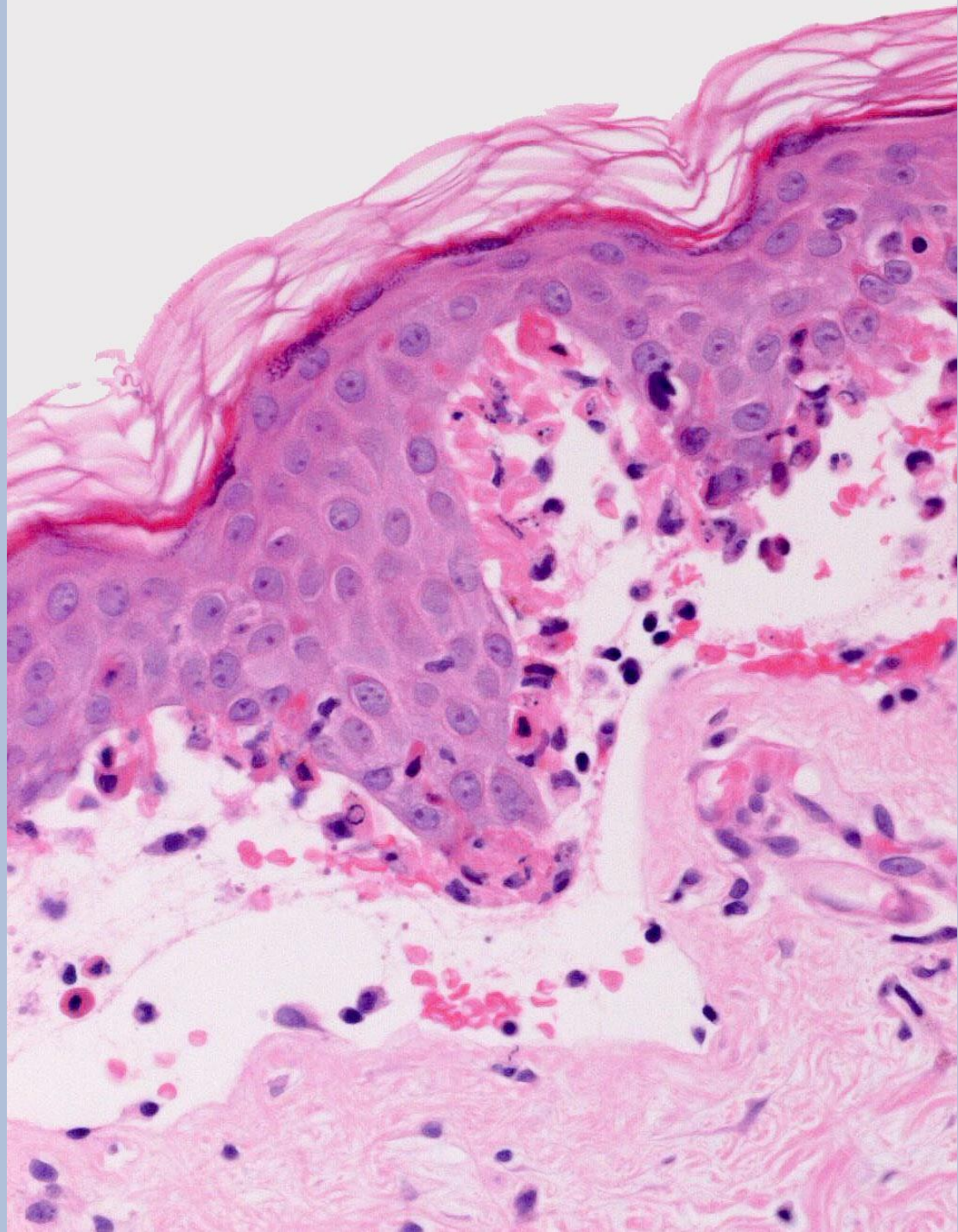
- Necrotizing fasciitis
 - Thrombosis, vasculitis
 - May precede necrosis
 - May be some distance from the clinical lesion
 - Vascular congestion
 - Perivascular neutrophils
 - Necrosis, bacterial growth
- BEAWARE - PYODERMAGANGRENOSUM

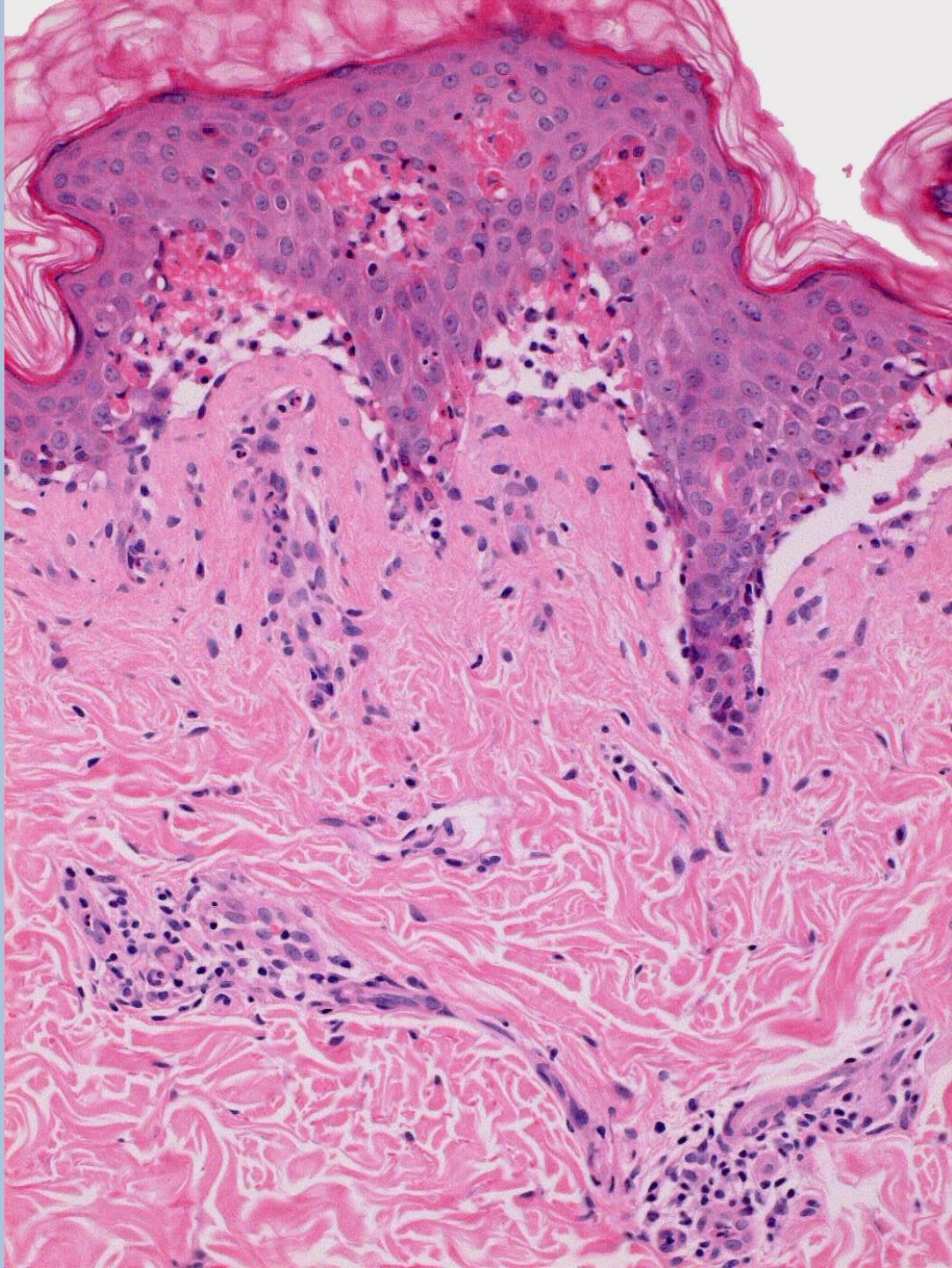
Case 7

- F17
- Trigeminal neuralgia, conjunctivitis, lip crusting









Case 7

- Bullous interface dermatitis
 - Lichen planus-like
 - Erythema multiforme-like
 - Atrophic
 - Psoriasiform
 - Hyperplastic/verrucous

EM-like interface dermatitis

- Severe vacuolopathy, subepidermal bulla
- Papillary oedema
- Red cell extravasation
- **Patchy infiltrate**

EM-like interface dermatitis

- Erythema multiforme
- Stevens Johnson syndrome
- Acute/subacute lupus erythematosus
- Dermatomyositis
- Pityriasis lichenoides
- GVHD
- Drug reactions
- Paraneoplastic pemphigus

- CLINICOPATHOLOGICAL CORRELATION

Stevens-Johnson Syndrome

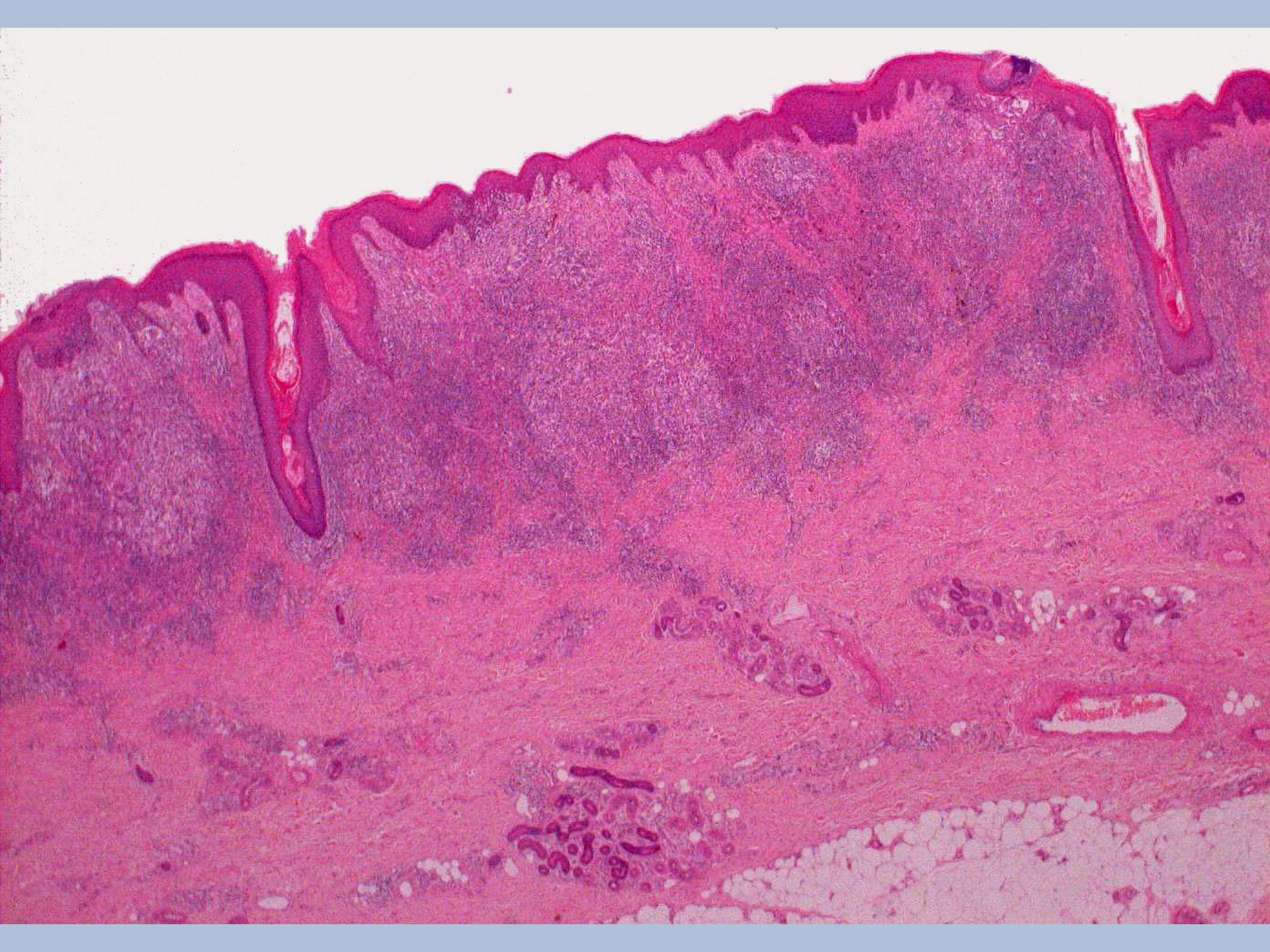
- Drug induced
- Flaccid and blood-filled blisters
- Ulceration, crusting
- Loss of skin, +ve Nikolsky
- Eyes, mouth, pharynx, mucosal
- May not be eosinophils, despite drug-induced aetiology

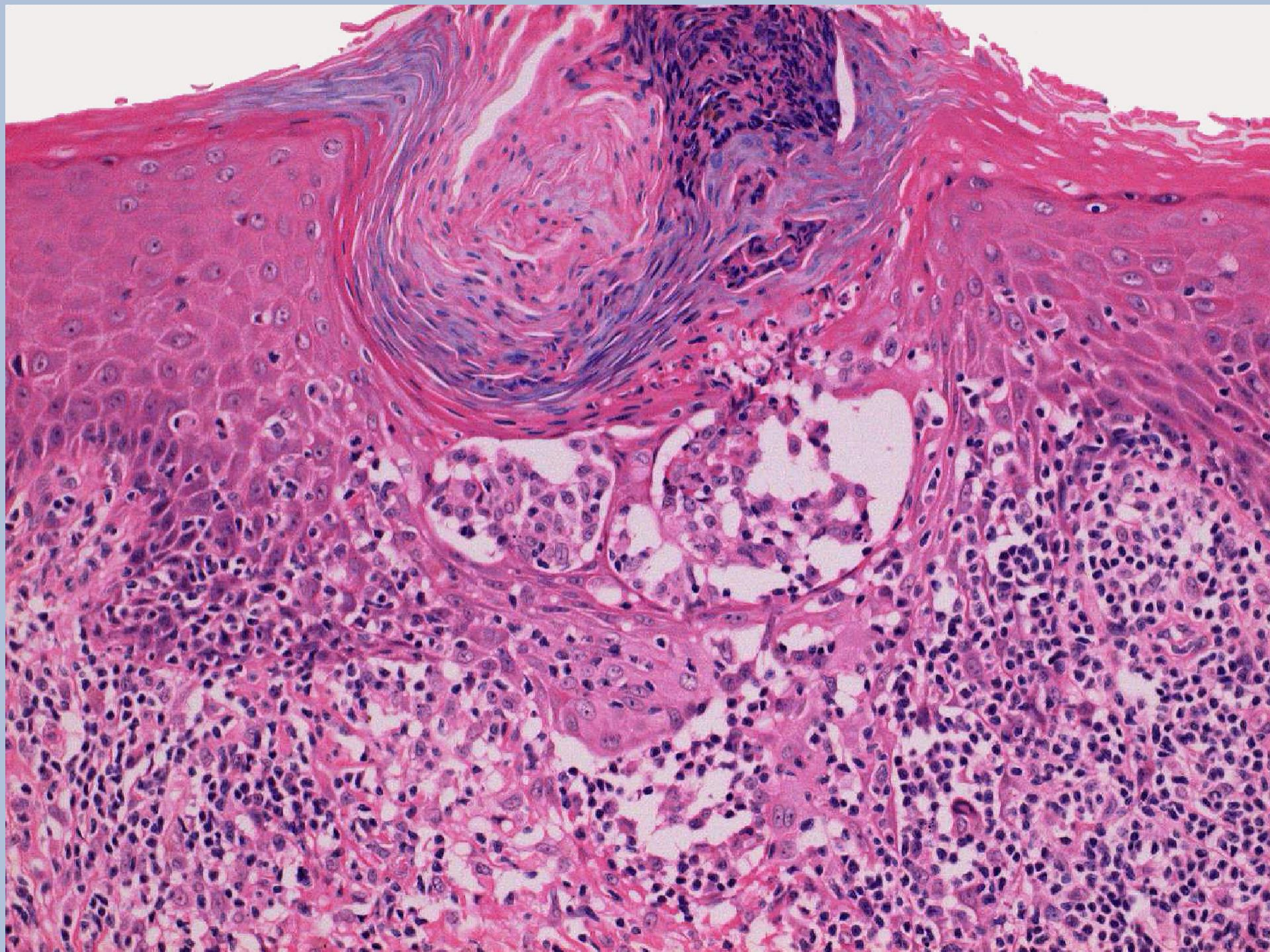
SJS/TEN

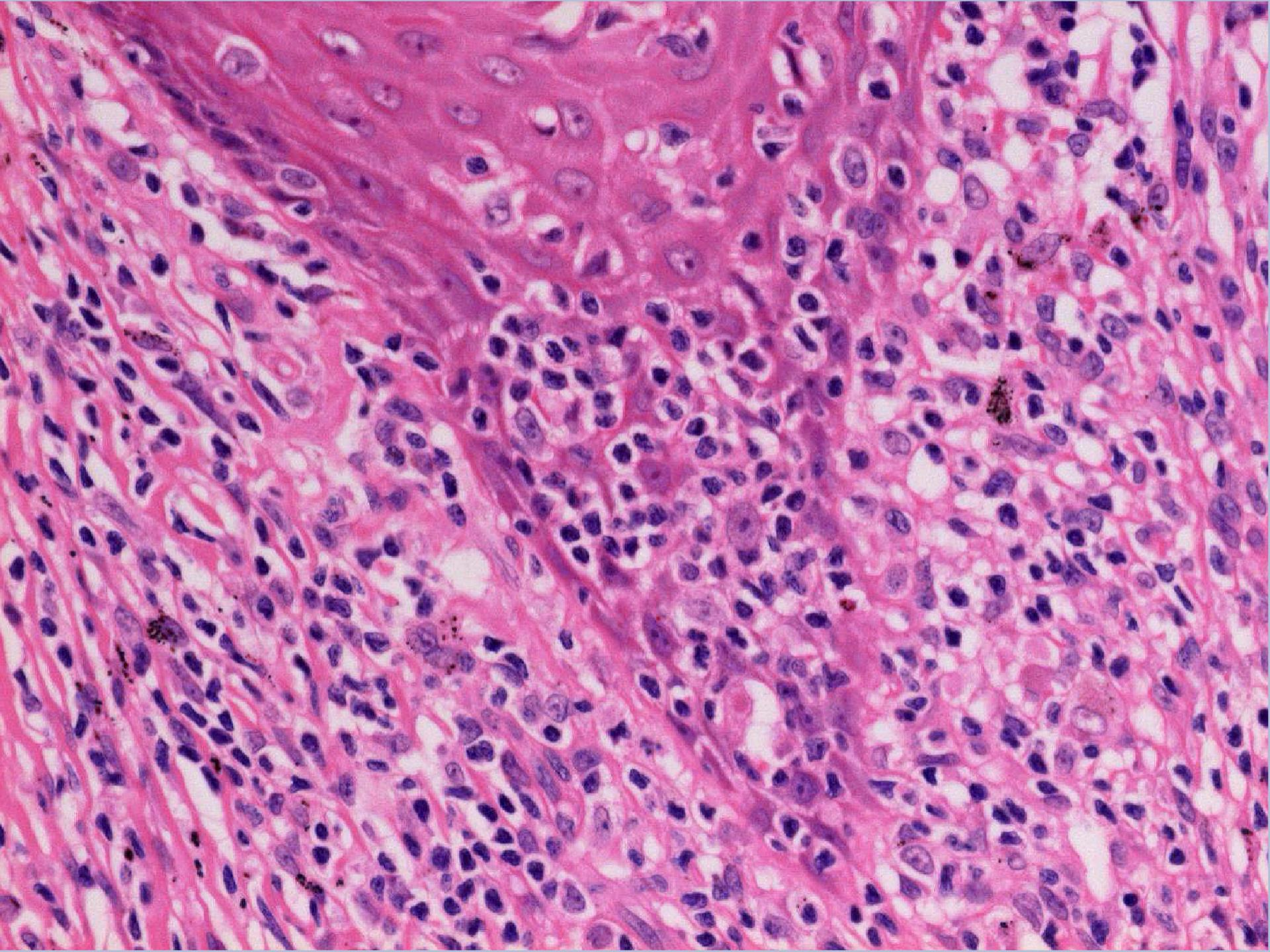
- Clinical differential may be Staphylococcal scalded skin syndrome
 - Offer frozen section of blister roof
 - Stratum corneum only
 - SSSS
 - Full epidermal thickness (necrotic)
 - TEN/SJS

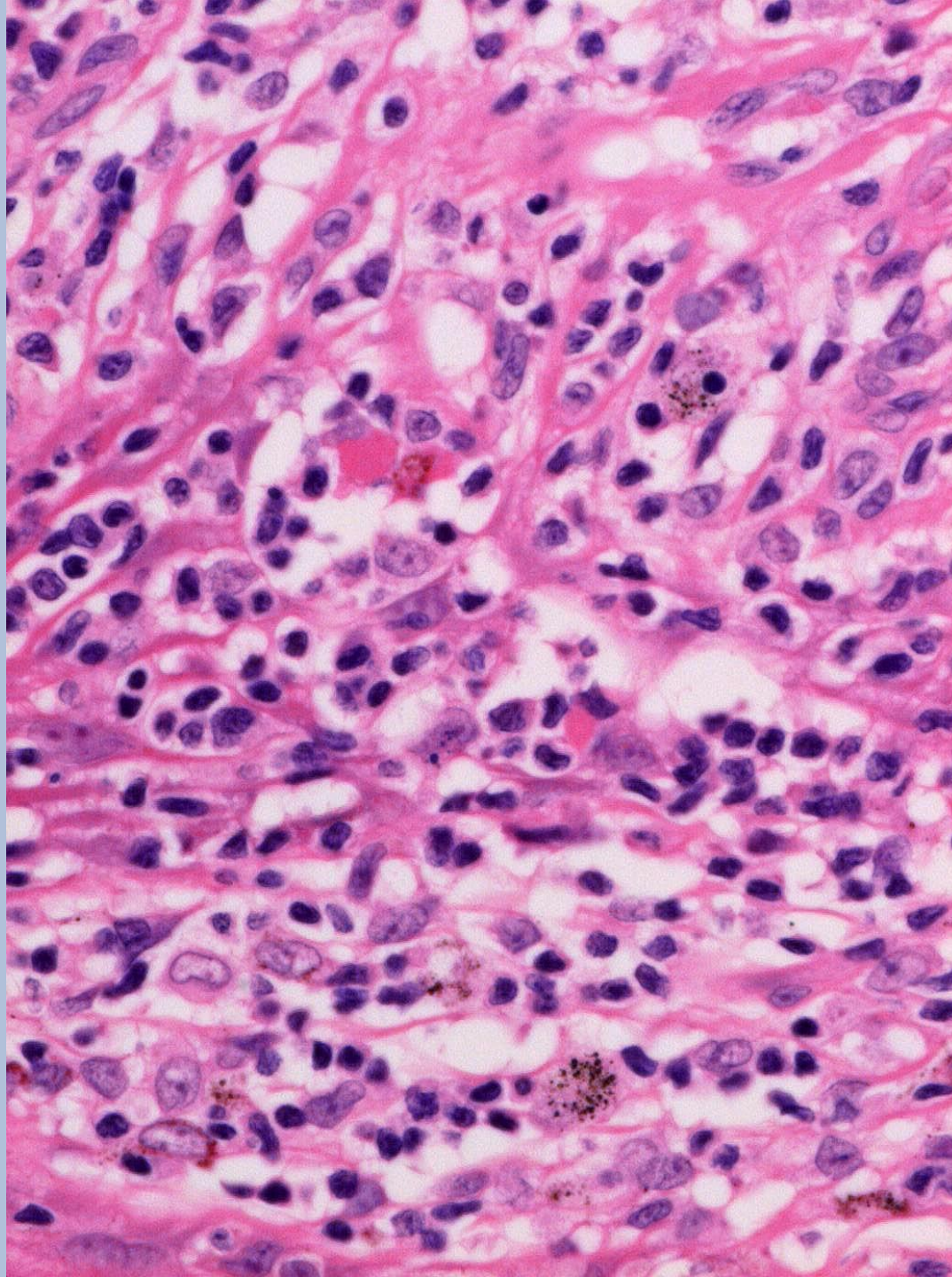
Case 8

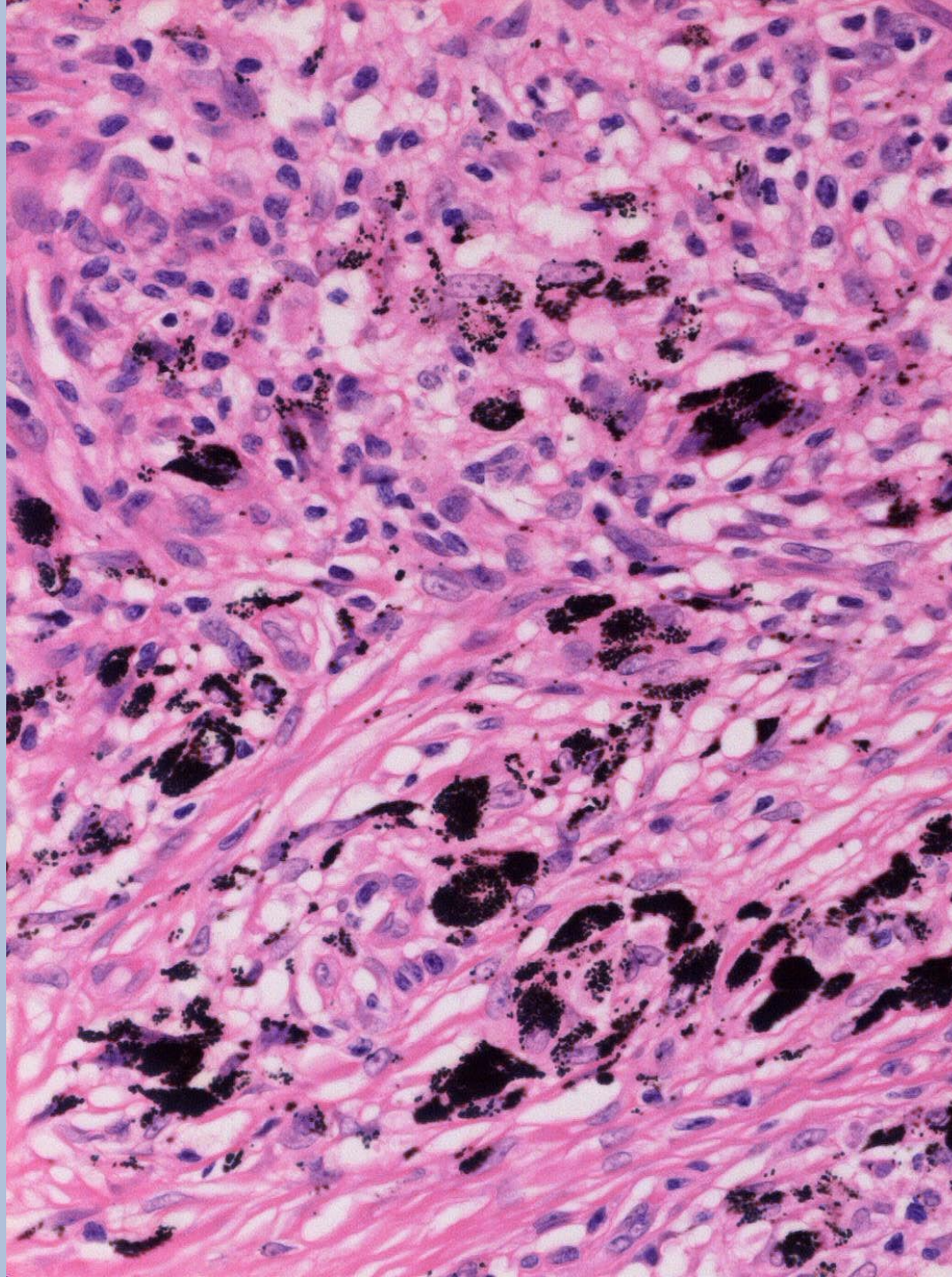
- M 29
- Red area on left forearm











Case 8

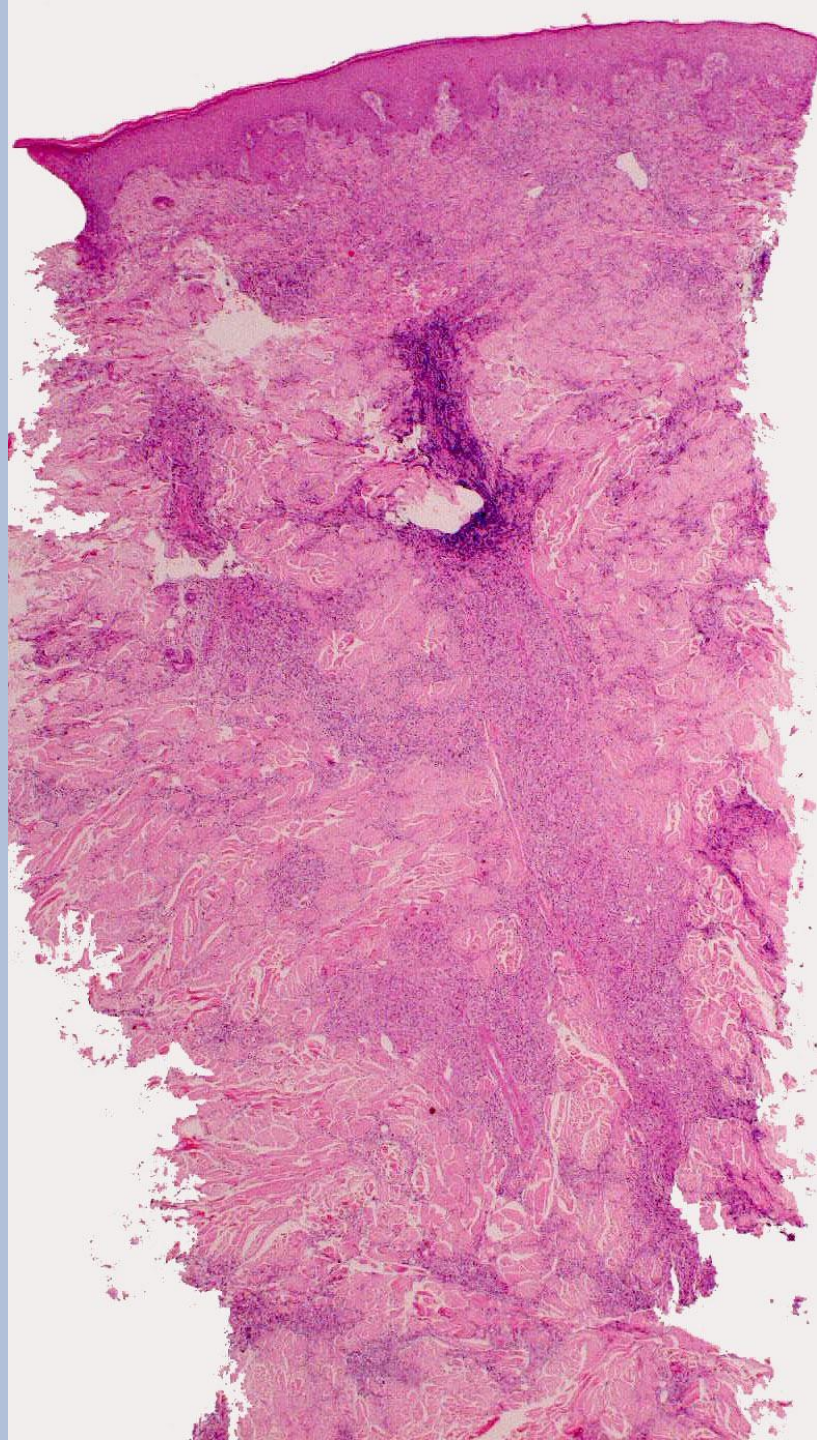
- Lichen planus-like interface dermatitis
- Lichen planus and variants
- Discoid lupus erythematosus
- Acute and chronic GvHD
- Lichenoid keratosis
- Drug eruptions
 - Parakeratosis, suprabasal apoptotic cells, rbc extravasation, eosinophils, plasma cells
- Lichen striatus

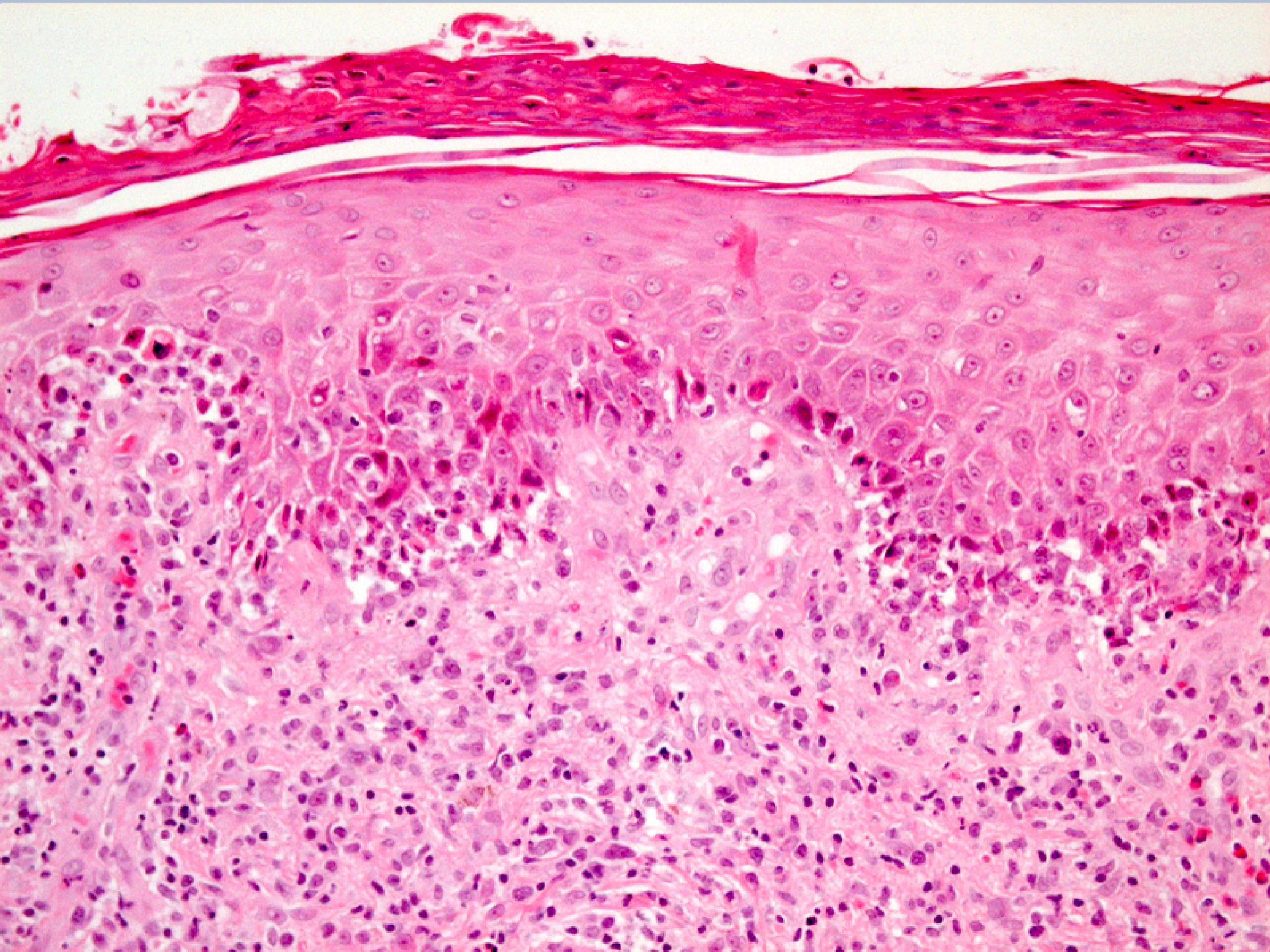
LP-like interface dermatitis

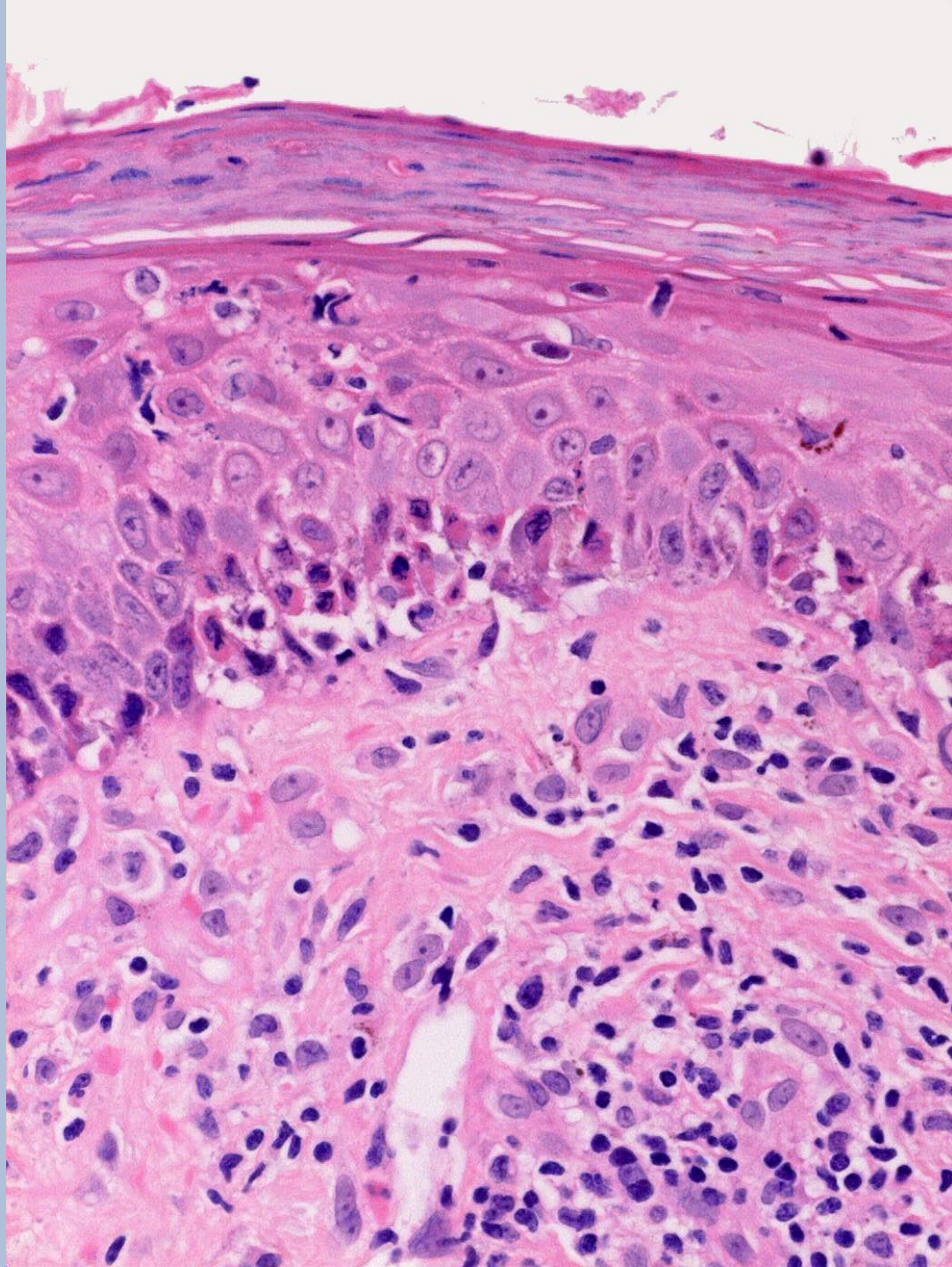
- Lichenoid tattoo reaction
 - Usually against red (mercury)
 - LP with parakeratosis, deep extension
 - May be granulomas
- Other patterns
 - Amalgam tattoo
 - Pseudolymphoma
 - Acute generalised exanthematous pustulosis

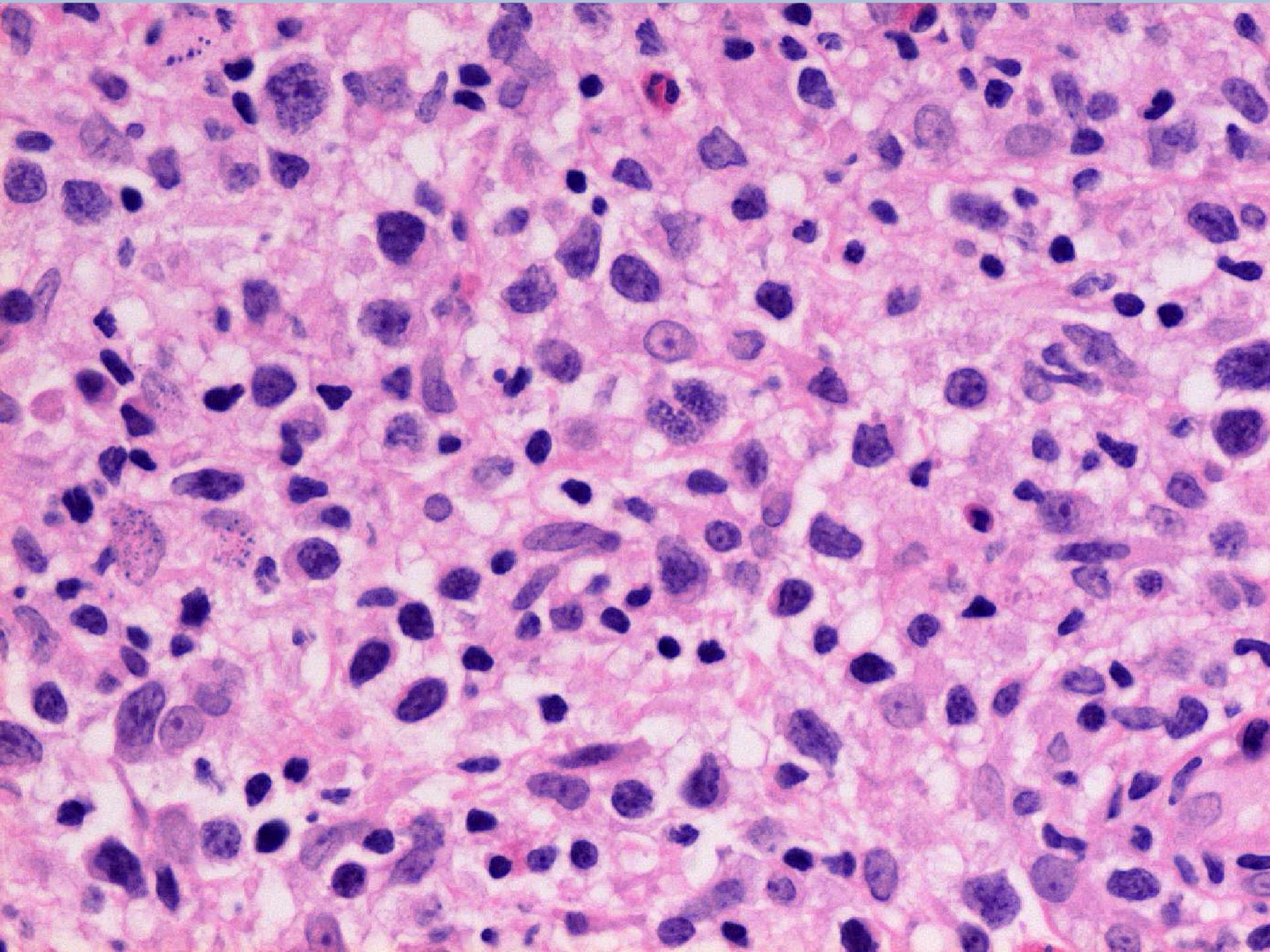
Case 9

- M 66
- Multiple erythematous plaques – back, limbs

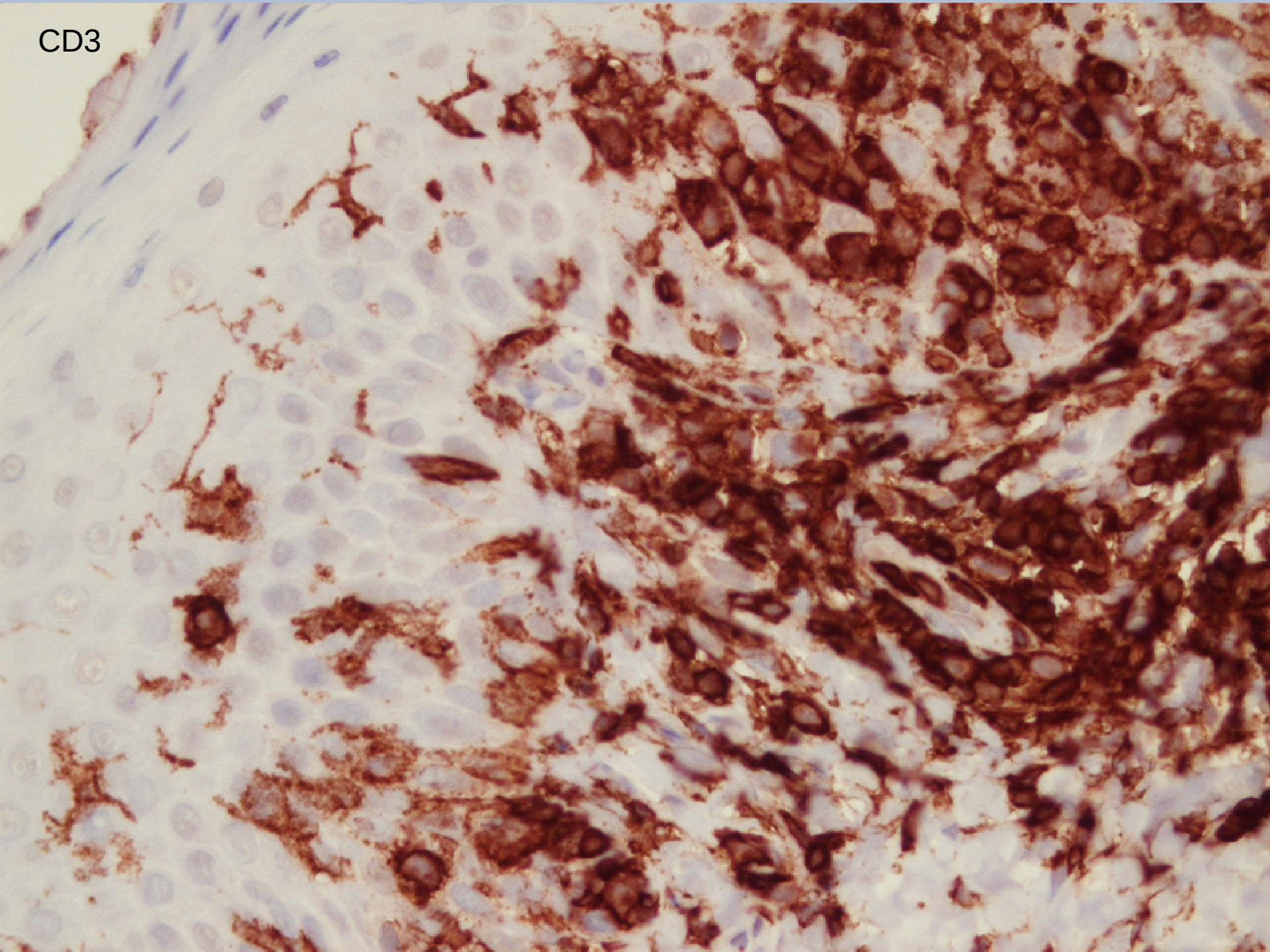








CD3



Case 9

- Epidermotropic T-cell infiltrate with interface dermatitis
 - Atypical epidermotropic T-cells
 - Mycosis fungoides
 - Sezery syndrome
 - Adult T-cell leukaemia/lymphoma
 - Primary cutaneous CD8+ve cytotoxic T-cell lymphoma
 - Epidermotropic gamma/delta cutaneous TCL
 - Lymphomatoid papulosis, type B
 - Pagetoid reticulosis
 - Pseudolymphomatous drug eruption
 - Follicular mucinosis
 - Pseudolymphomatous folliculitis

Clonal T-cell proliferations

- TCL
- Lymphomatoid Papulosis
- Drug-induced T-cell pseudolymphoma
- Follicular mucinosis
- Lichen aureus
- “Clonal dermatosis”
- LSet A
- lichen planus
- Lichenoid keratosis
- Pityriasis lichenoides
- Psoriasis

Mycosis fungoides

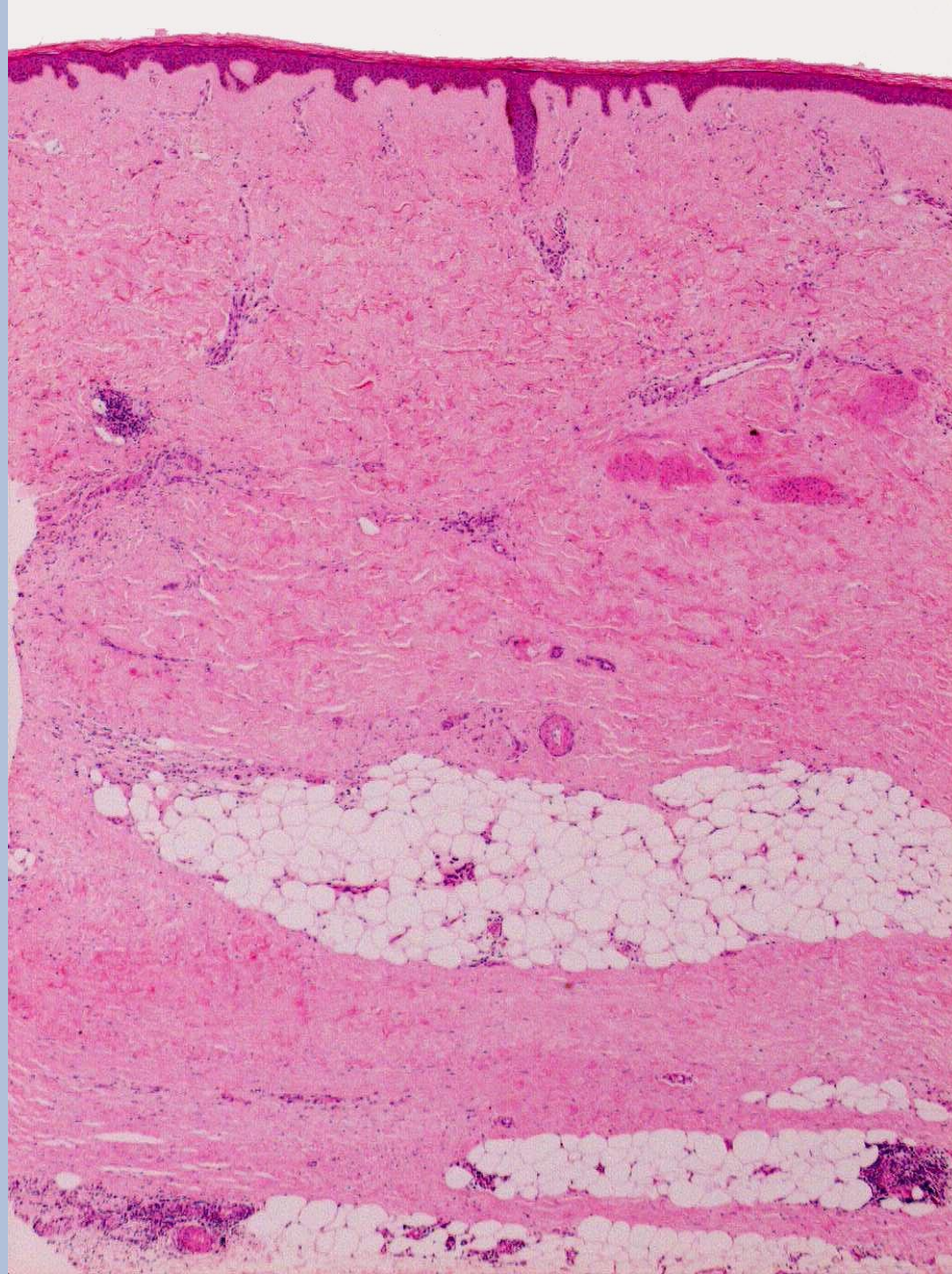
- 4% have an interface dermatitis component
- Pautrier microabscesses
- Papillary dermal fibrosis
- Epidermal atrophy, poikiloderma
- Psoriasiform hyperplasia

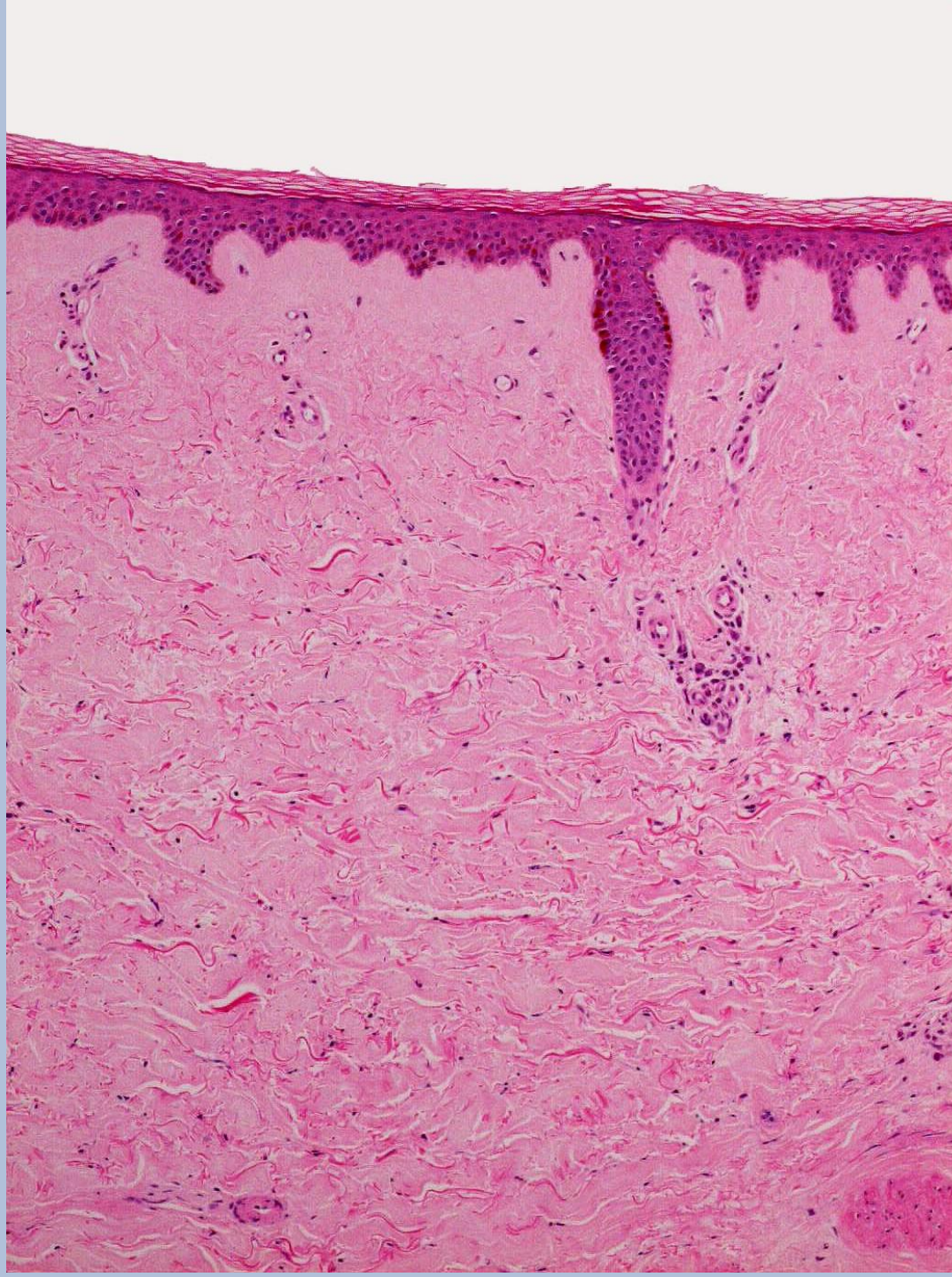
Mycosis fungoides

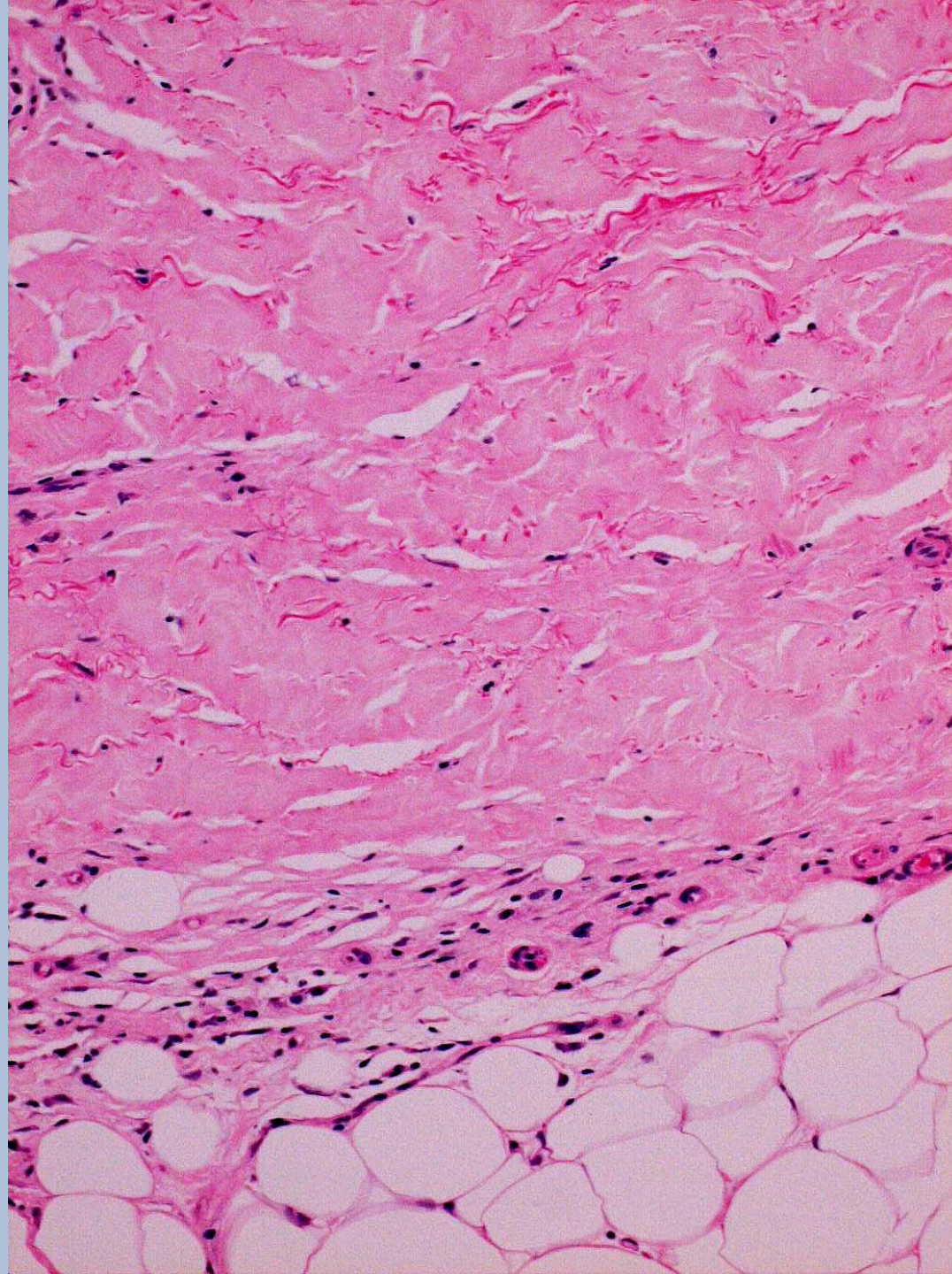
- Ask for multiple biopsies
 - Concurrent (up to 5) or over time
- Specific diagnosis of T-cell proliferations requires correlation of the **clinical**, histological, immunohistochemical and molecular findings
- Don't over-estimate the significance of clonality
- Don't make a definite diagnosis without knowing the clinical context

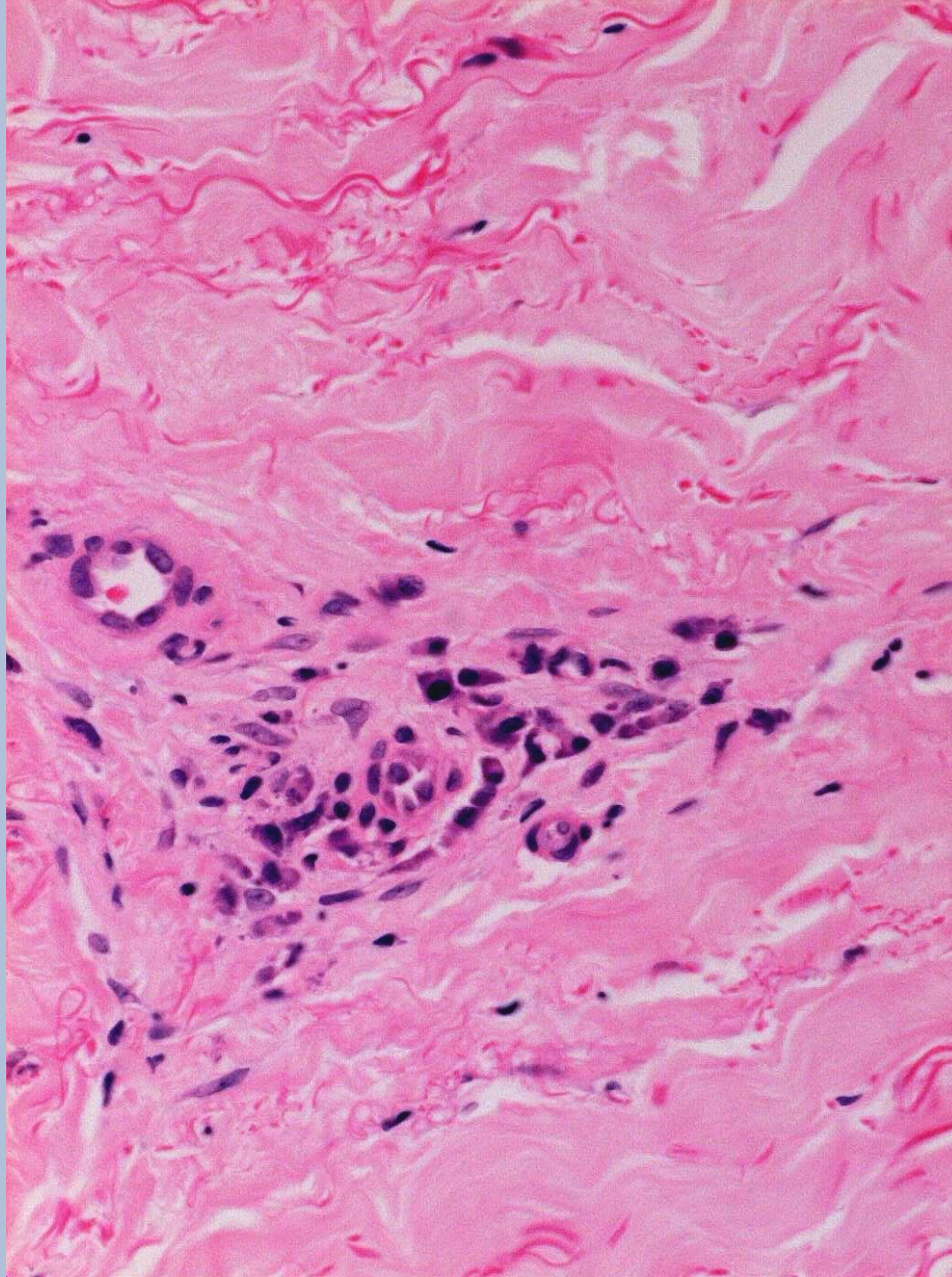
Case 10

- M 74
- Large pale area on left shin









Case 10

- Dermal sclerosis
 - Papillary dermal sparing
 - Reticular dermal sclerosis
 - Subcutaneous involvement - septa
 - Perivascular chronic inflammation with plasma cells

Dermal sclerosis

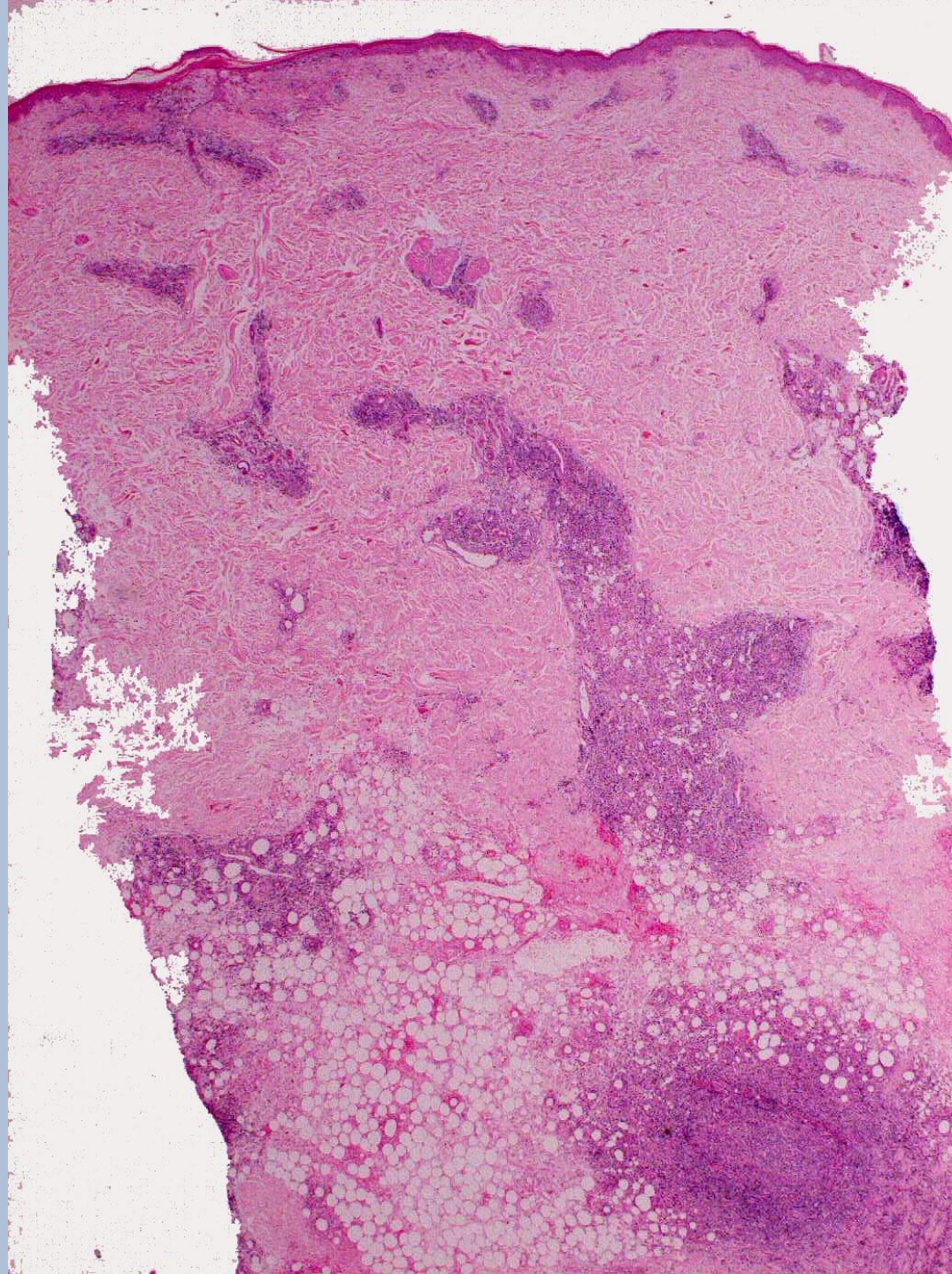
- Morphoea (localised scleroderma)
 - Superficial morphoea
 - Morphoea profunda
 - Generalised morphoea
- Systemic sclerosis
- Atrophoderma of Pasini and Pierini
- Lichen sclerosus
- Chronic GVHD
- Chronic radiation dermatitis
- Atrophie blanche
- Mixed CTD
- Porphyria cutanea tarda
- Scleredema
- Scar

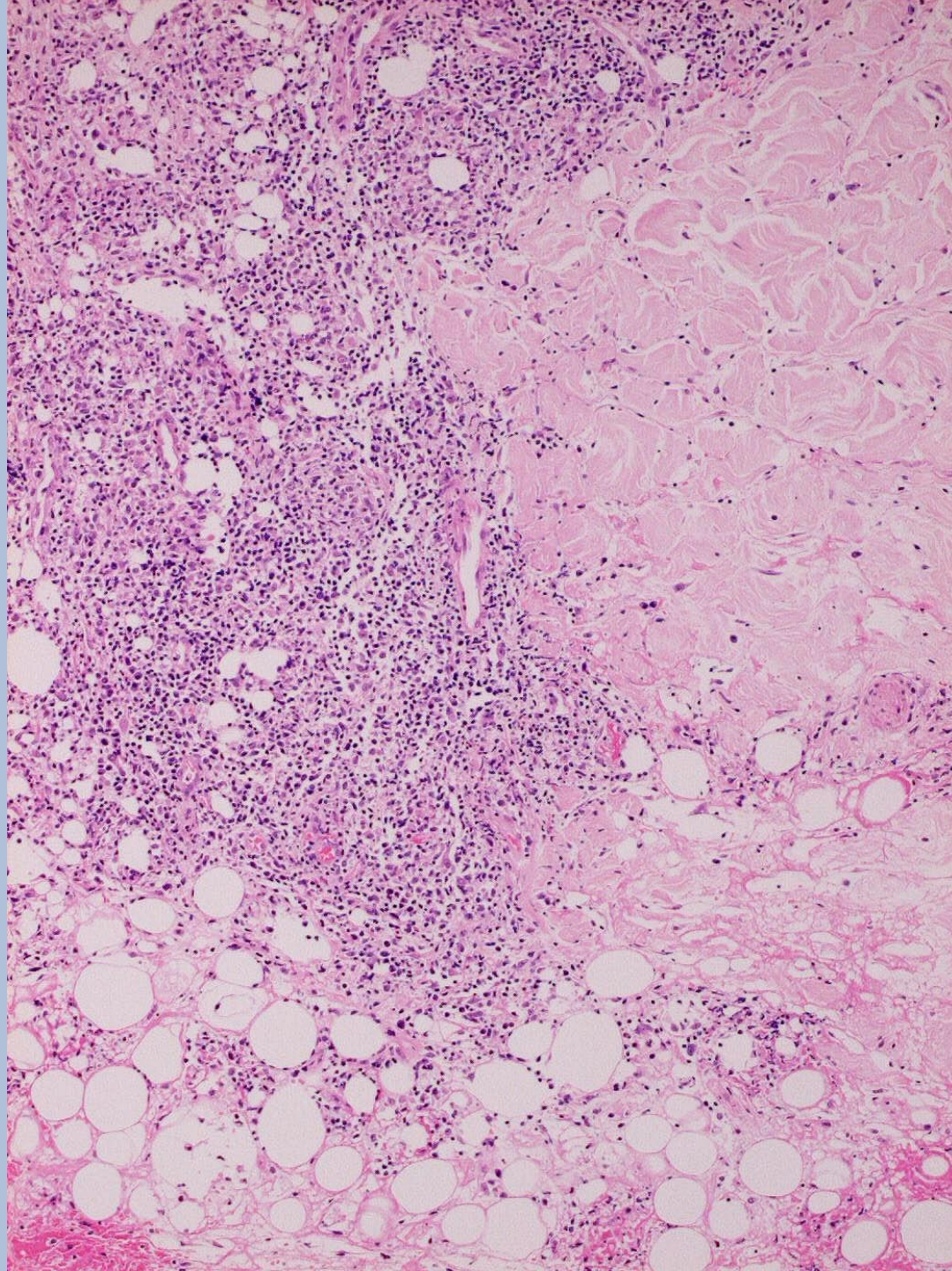
Case 10

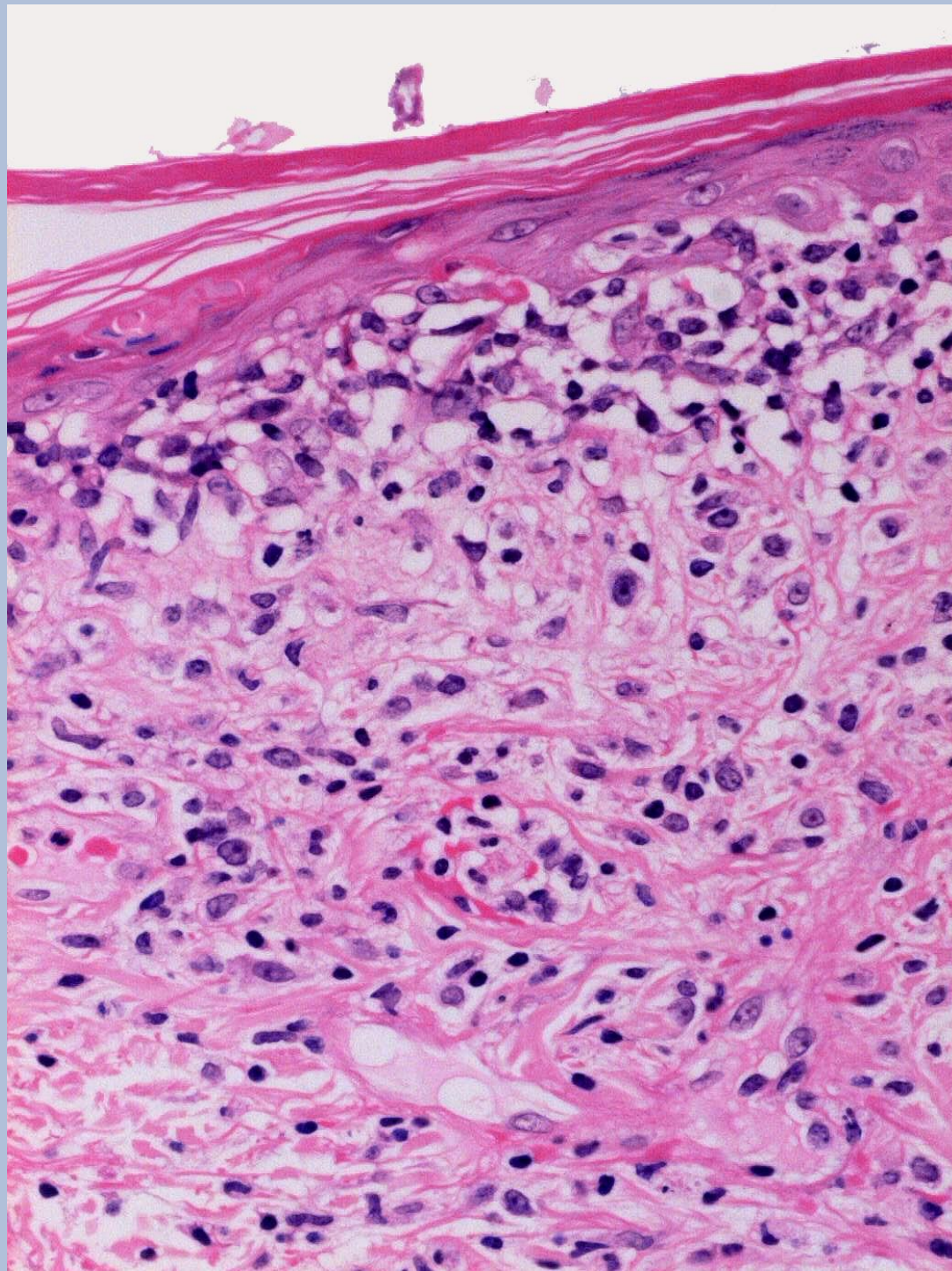
- Morphoea
 - Typical histological features

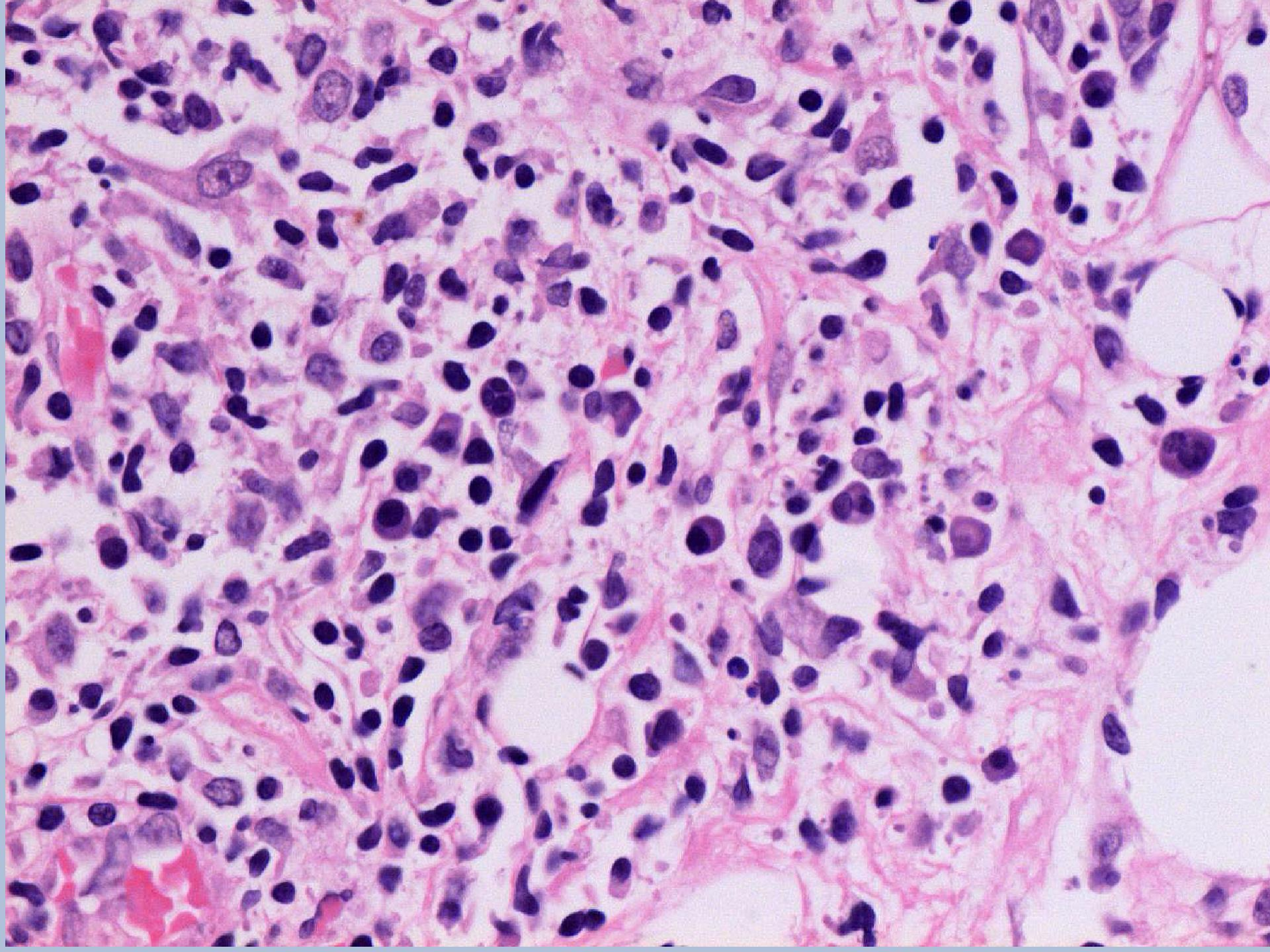
Case 11

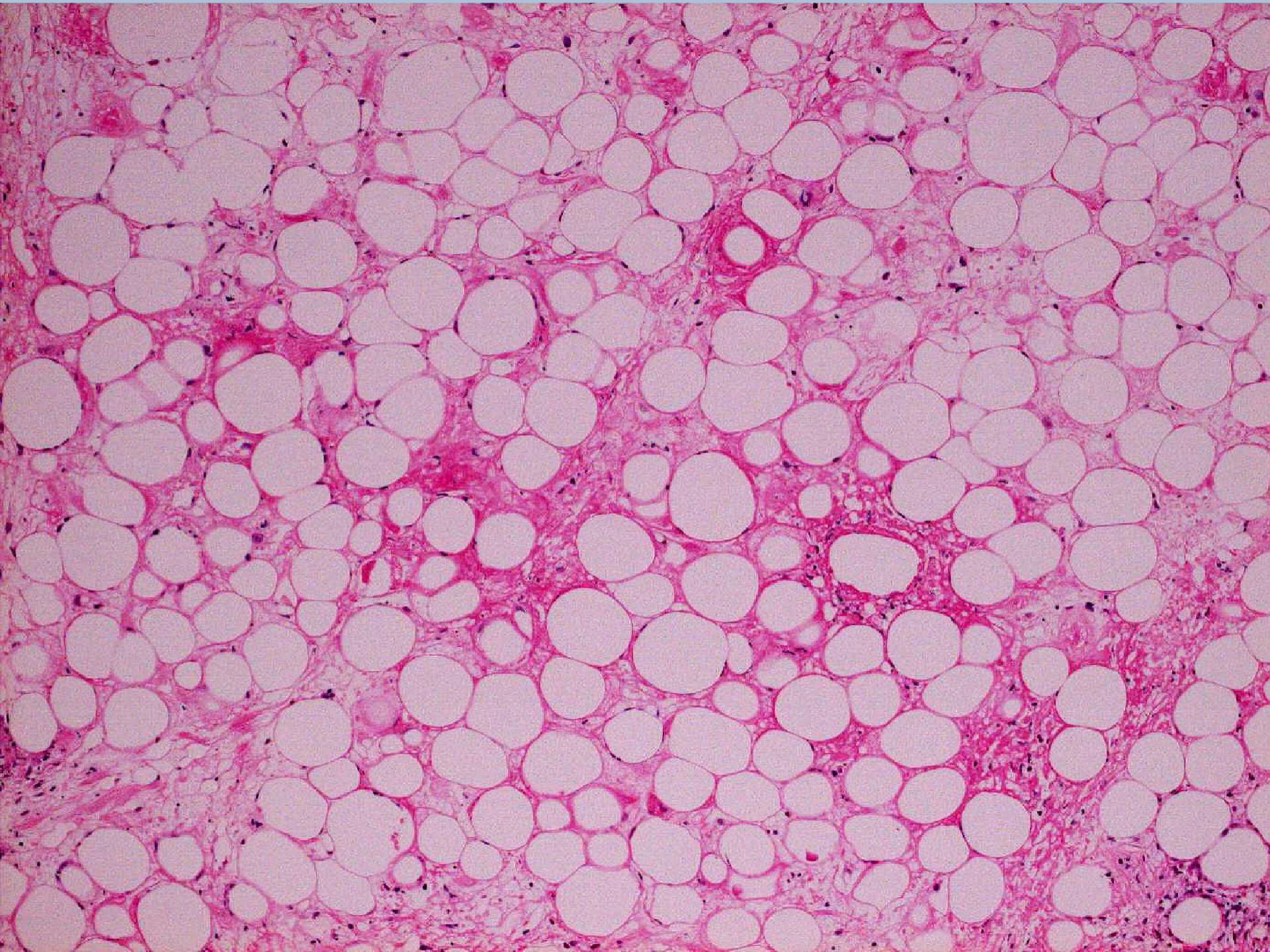
- F39
- Irregular nodular area, left upper arm











Case 11

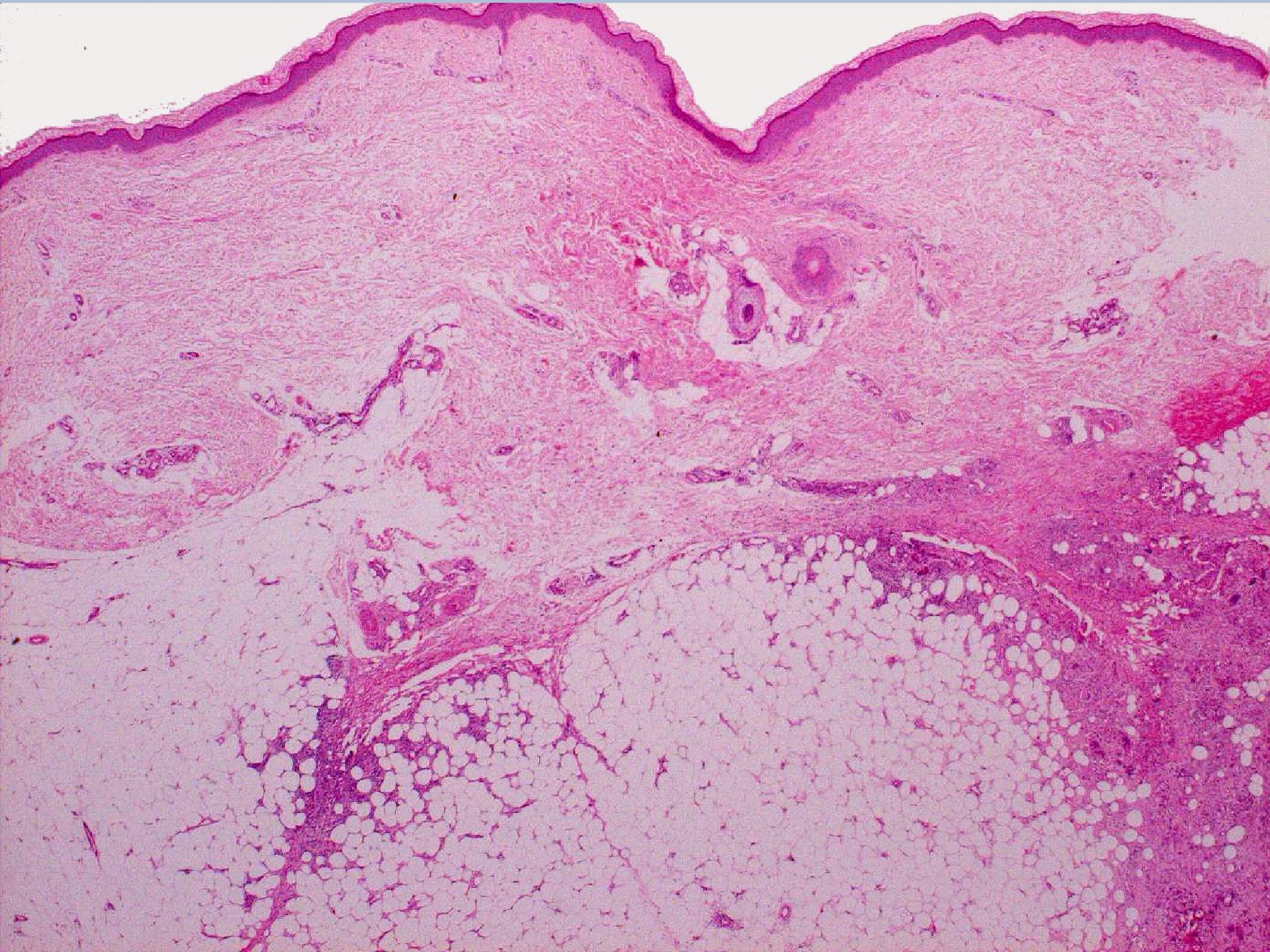
- Superficial and deep chronic inflammation
 - Plasma cells
- Interface dermatitis
- Eosinophilic fat necrosis

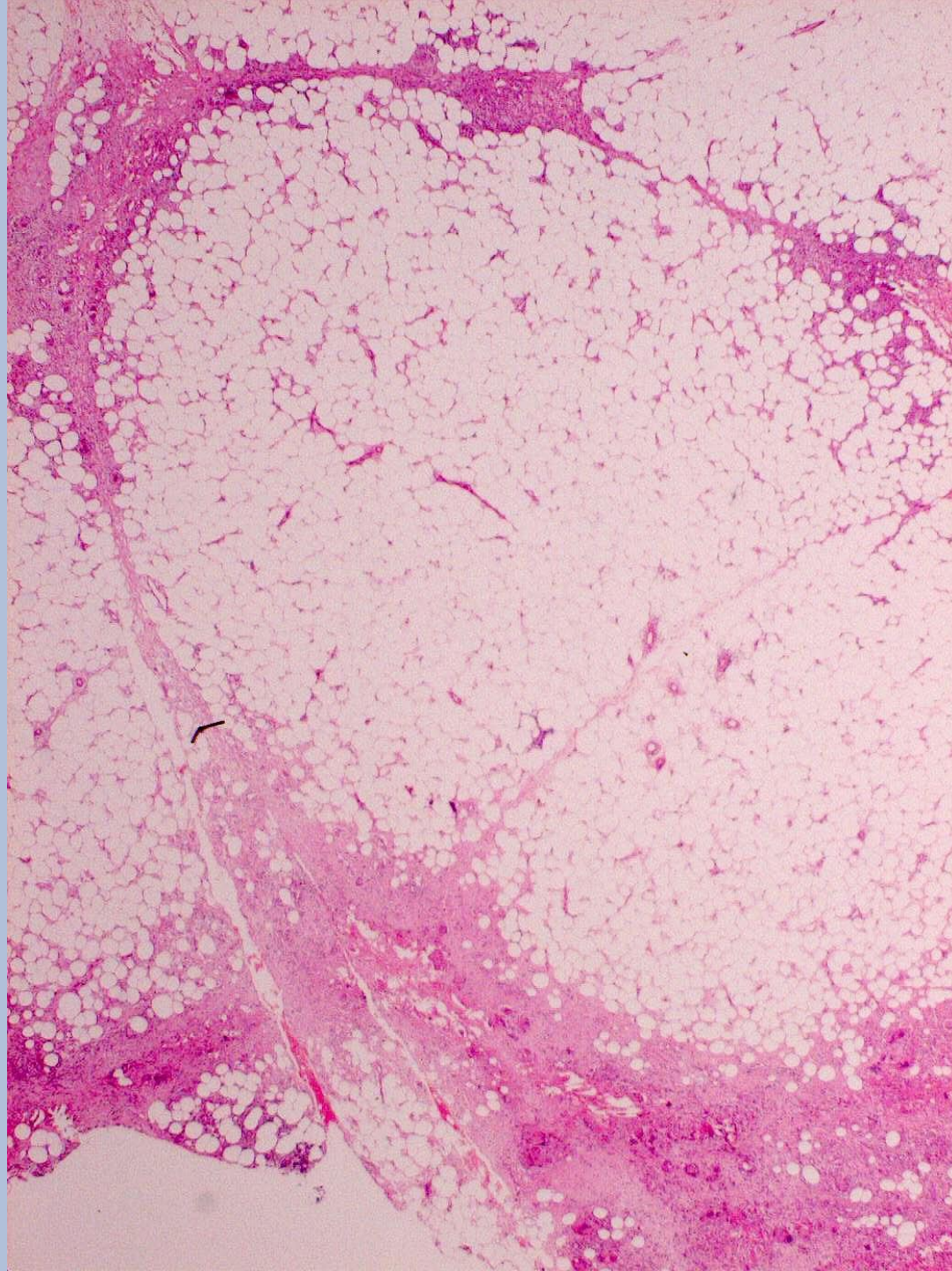
Case 11

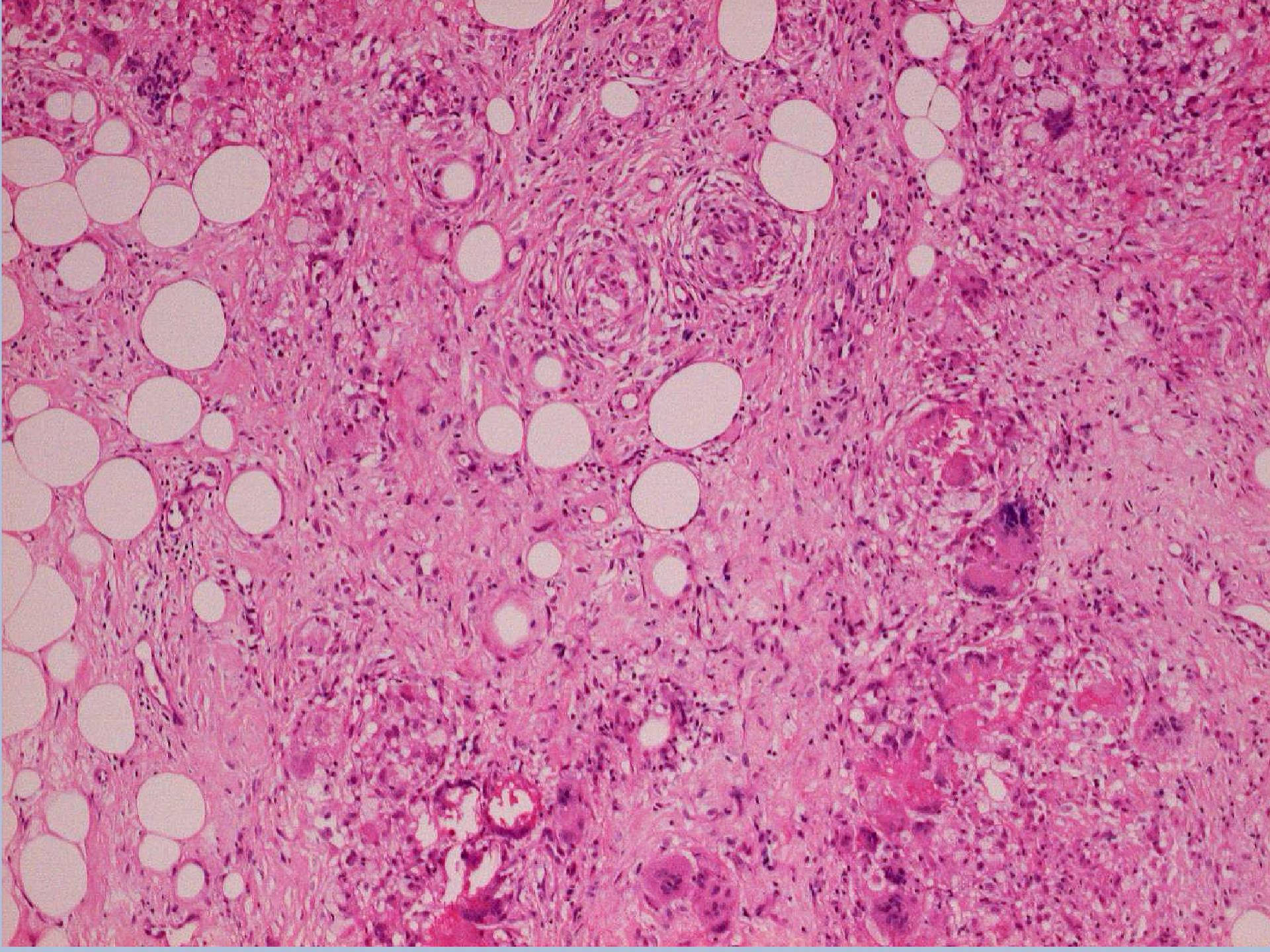
- Lupus profundus
 - Additional features:
 - Lymphocytic vasculitis
 - +/- fibrinoid necrosis
 - Lymphoid follicles
 - Increased mucin
 - Hyalinisation of vessels, fat
 - IMF – lupus band

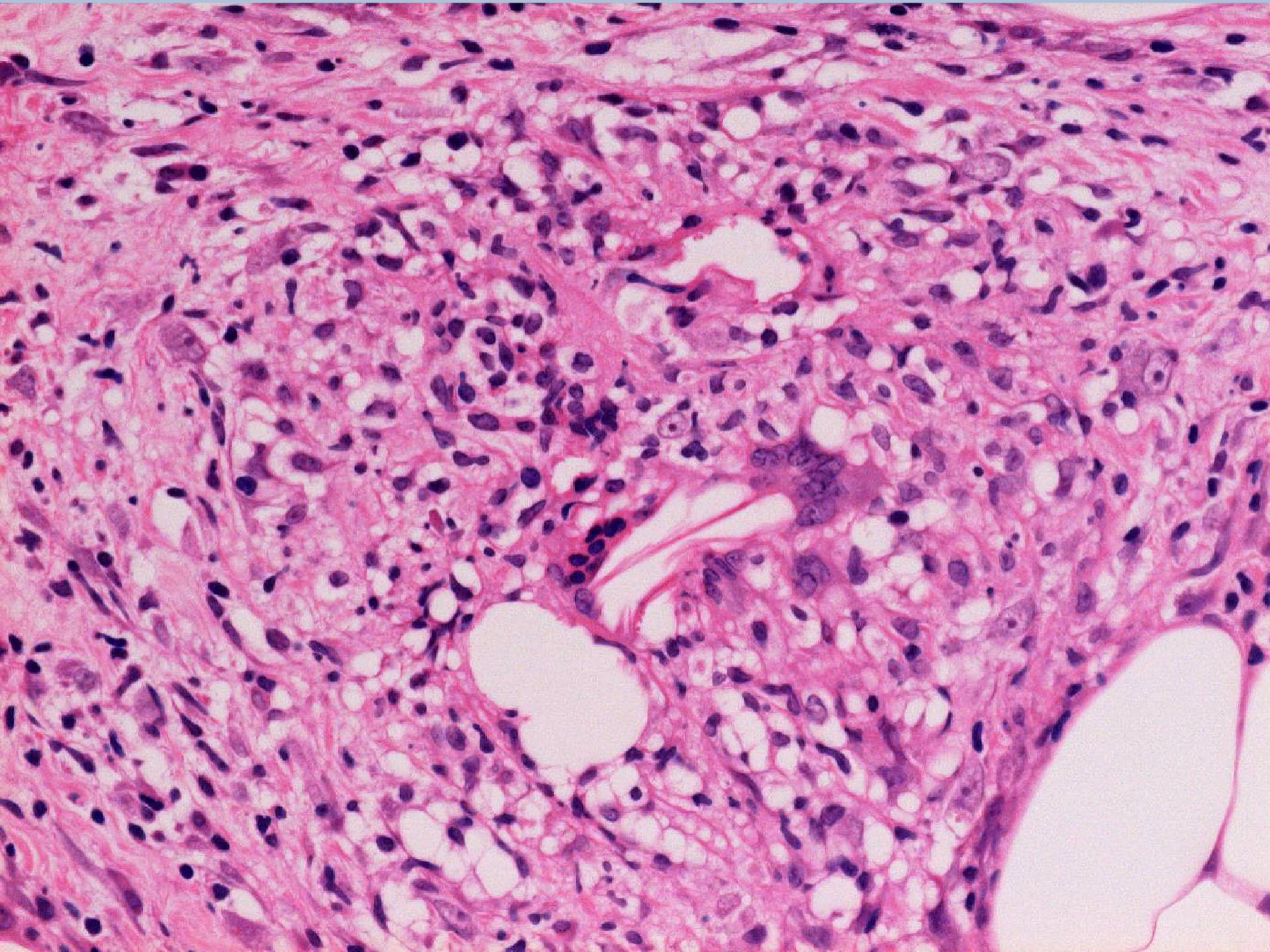
Case 12

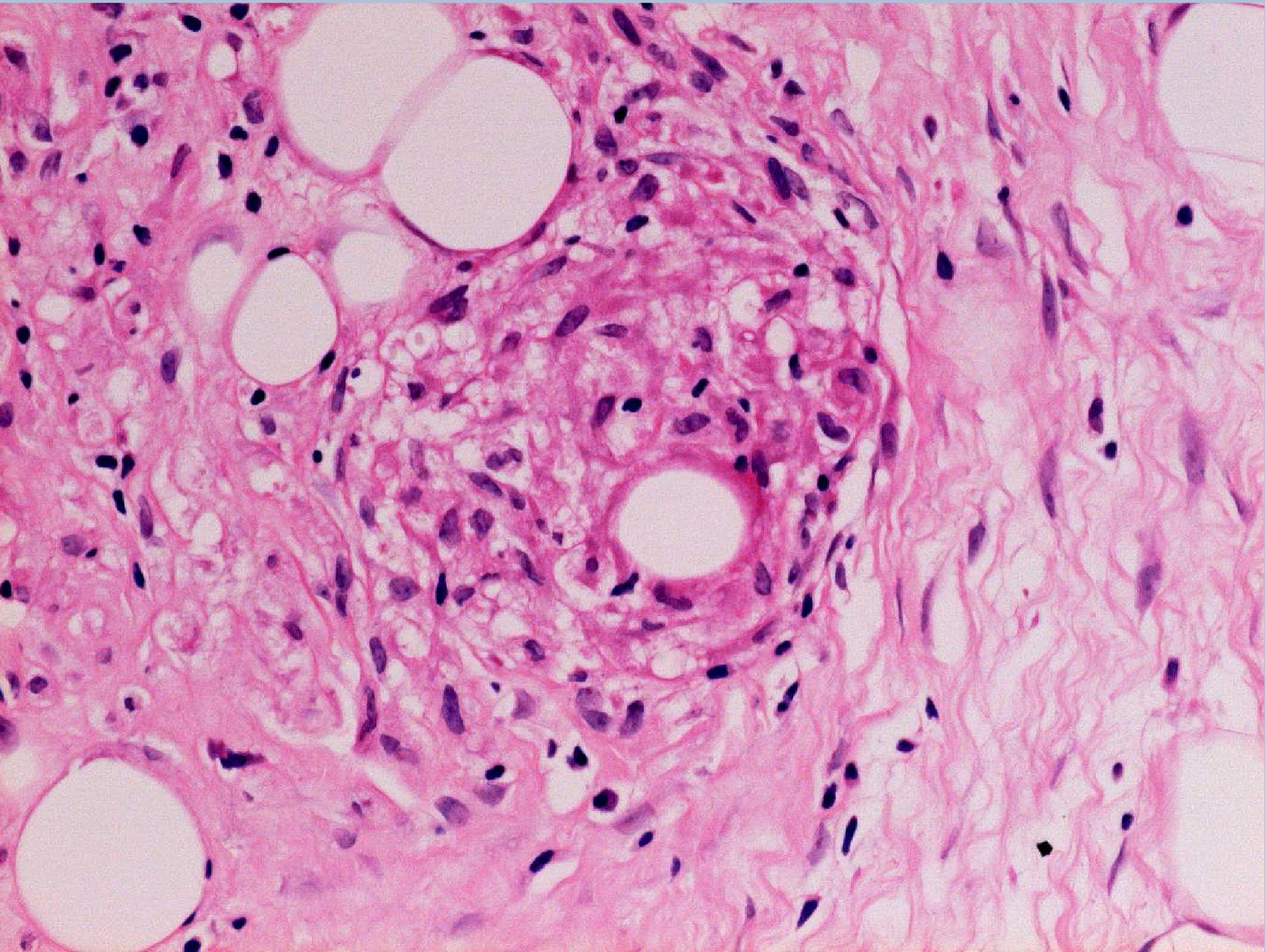
- F57
- Tender nodules on lower legs











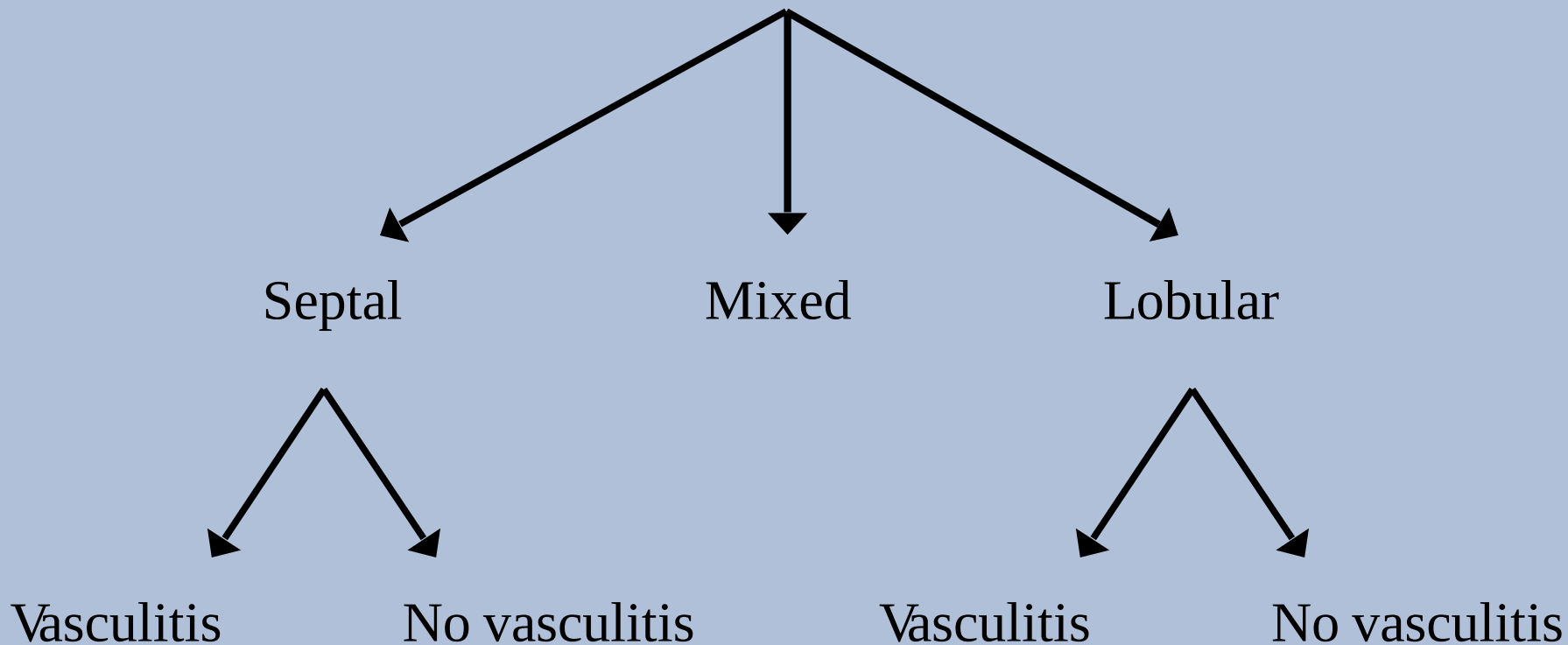
Case 12

- Septal granulomatous panniculitis

Case 12

- Panniculitis
 - All mixed - look for **predominant** pattern
 - Septal, lobular, mixed
 - 90% are erythema nodosum or nodular vasculitis
 - Clinical, adequate biopsy and levels required
 - **EXCLUDE INFECTION**

Panniculitis



Panniculitis

- Septal
 - with vasculitis
 - Leukocytoclastic
 - Cutaneous PAN
 - Thrombophlebitis
 - without vasculitis
 - **Erythema nodosum**
 - GA - mucin
 - Rh. Nodule – fibrin
 - Necrobiosis lipoidica -
Dermal fibrosis, necrobiosis
 - Scleroderma - fibrosis

Erythema Nodosum

- Clinical
 - F > M
 - Ant. and lat. lower legs
 - Arms, face, trunk
 - Tender, warm nodules
 - Bruise-like colours
 - Bilateral, symmetrical
 - Pyrexia
 - Joint pain
- Associations
 - Infections
 - Streptococcal
 - Yersinia, cat scratch, psittacosis
 - Ulcerative colitis
 - Sarcoid
 - Drugs
 - Lymphoma
 - Oestrogens
 - OCP, pregnancy
 - Neutrophilic dermatoses
 - Sweet's, Bechet's

Erythema Nodosum

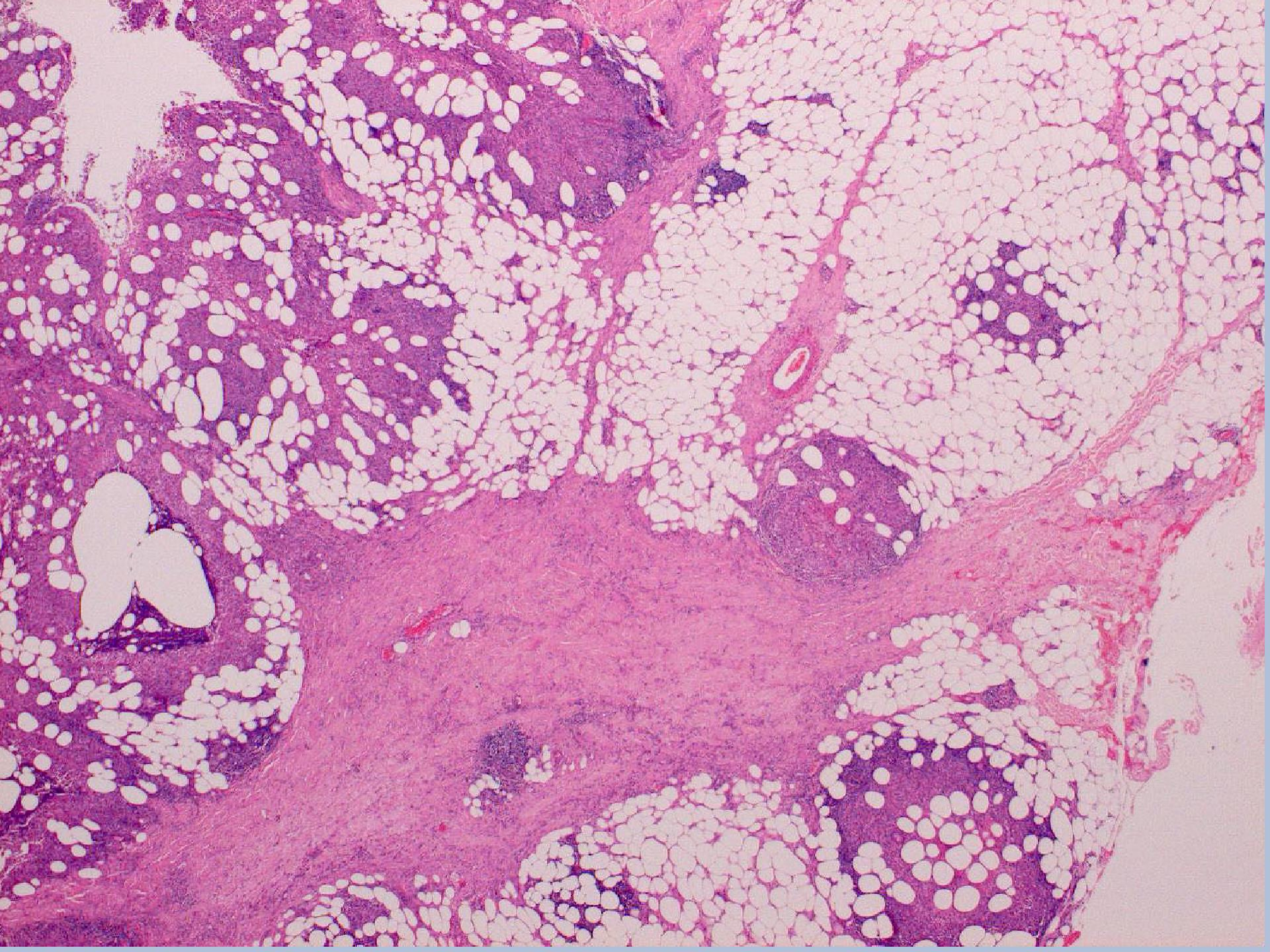
- Chronic venulitis
- Septal haemorrhage, inflammation, fibrosis
- Granulomatous – Miescher's radial
- Fat necrosis rare or focal

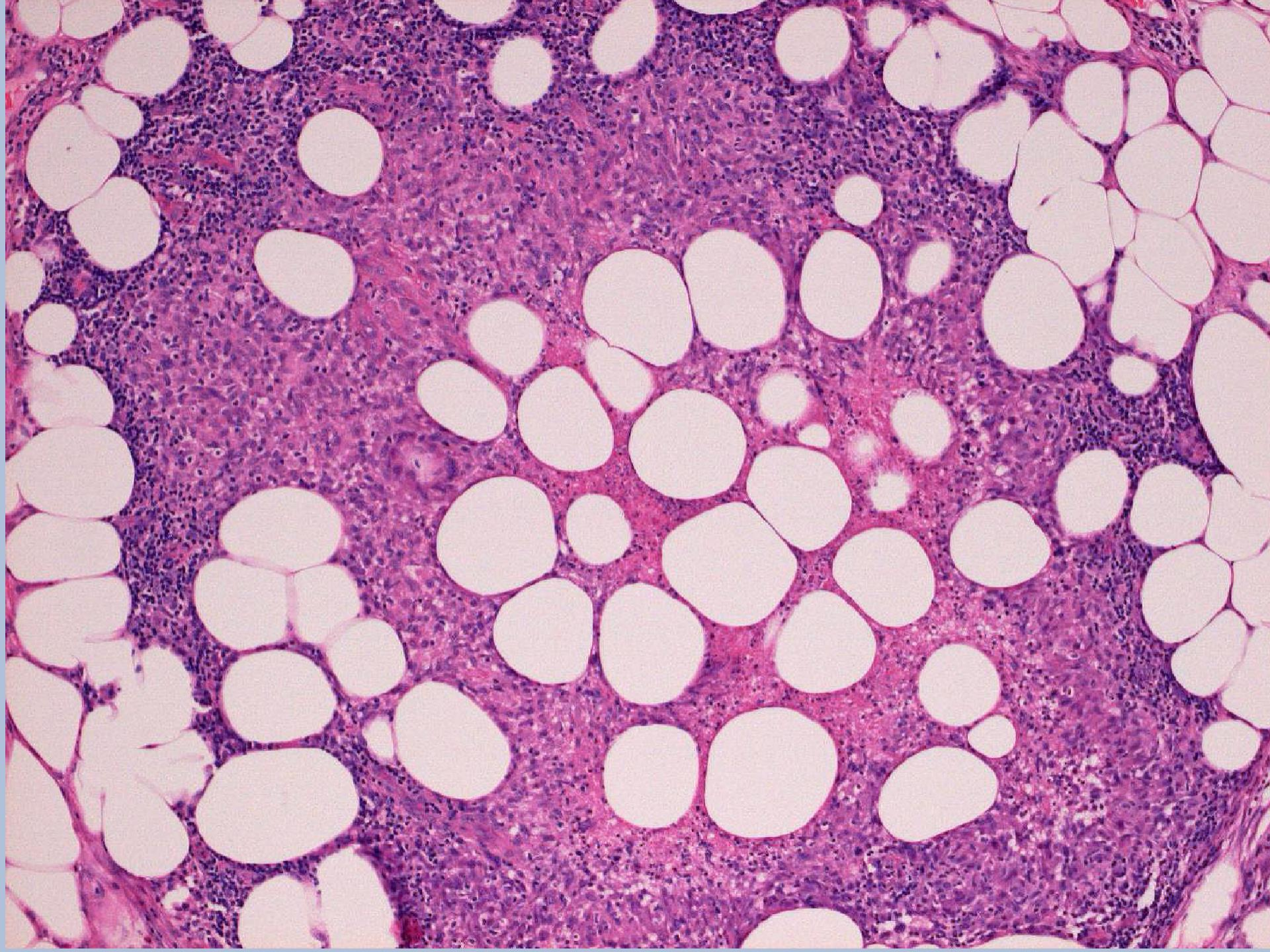
Erythema Nodosum

- Miescher's radial granuloma
 - Histiocytes round small spaces
- Neutrophils very early so NOT usually present
- Late appearances
 - Granulation tissue - neovascularisation and chronic inflammation - at septal/lobular interface

Case 13

- M 38
- Subcutaneous nodule on left arm





Case 13

- Lobular granulomatous panniculitis

Panniculitis

- Lobular

- With vasculitis

- **Nodular vasculitis**

- Erythema nodosum
leprosum
 - Lucio's phenomenon

- Without vasculitis

- LE profundus (or mixed)
 - Lipodystrophy
 - Post steroid panniculitis
 - Subcutaneous fat necrosis of the newborn
 - Scleroderma neonatorum
 - Pancreatic panniculitis
 - Infection
 - Deep fungi,
 - atypical mycobacteria
 - Alpha-1-AT deficiency
 - Factitial, trauma
 - Sarcoid, Crohn's (v. rarely with vascular involvement)

Lobular granulomatous panniculitis

- HISTORY
- Look for neutrophils
 - Vasculitic, Pancreatic, Infection, Alpha-1-AT deficiency, Factitial, Traumatic, Cold, Nodular vasculitis, rheumatoid panniculitis
- Check for foreign material
- Perls stain for haemorrhage
 - Trauma, vascular damage, stasis
- ALWAYS: gram, PASd, ZN as minimum

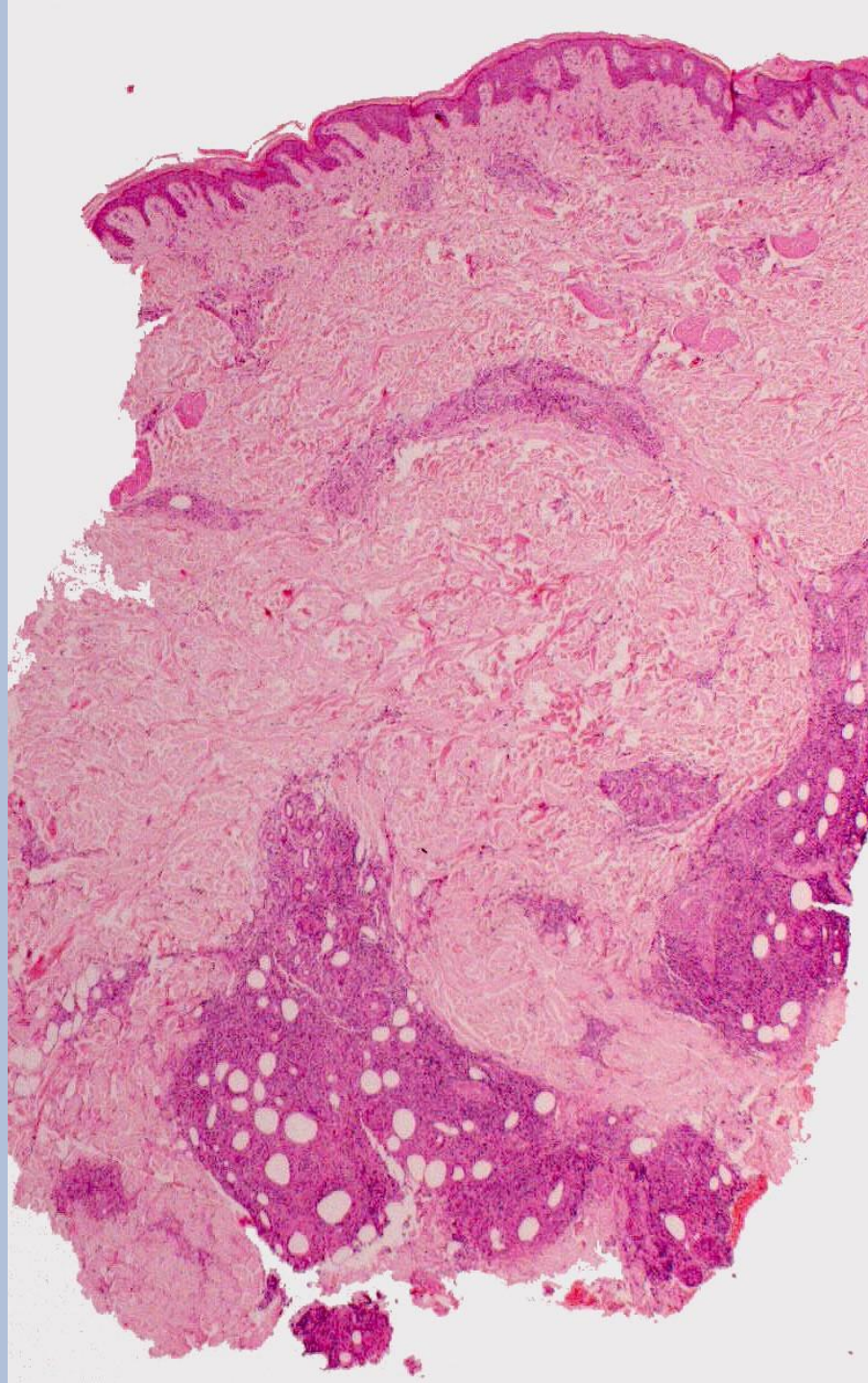
Lobular granulomatous panniculitis

- History
 - Previous vaccination site
 - can be vs aluminium – blueish histiocytes
 - May be psuedolymphomatous
 - Up to years afterwards
- Post-vaccination granulomatous panniculitis

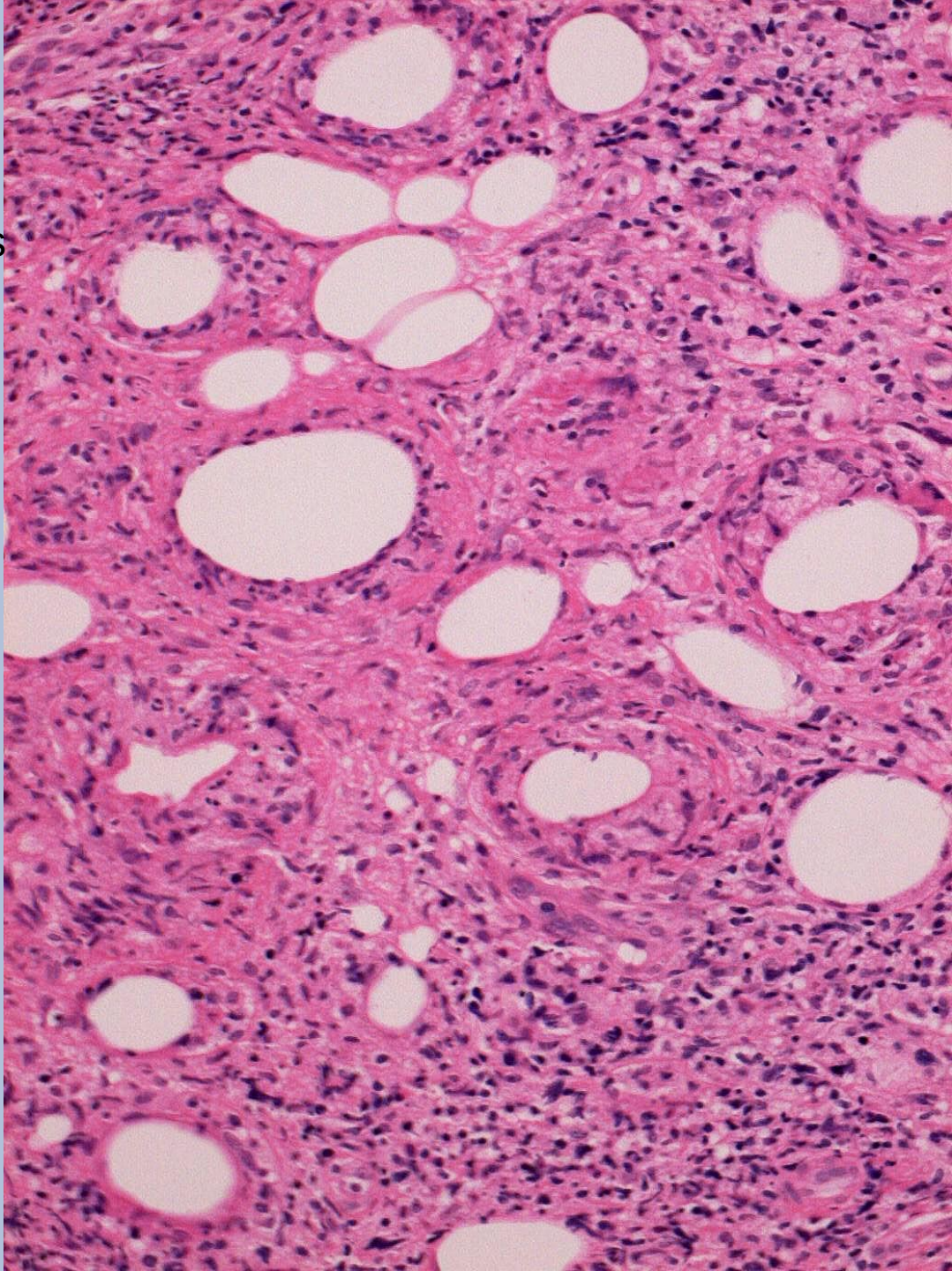
Nodular Vasculitis

- F > M
- Calves
- Ulcerated, erythematous nodules
- Scars
- Associated with cold, venous stasis
- TB - erythema induratum

Nodular vasculitis



Nodular vasculitis



Nodular Vasculitis

- Granulomatous lobular panniculitis
- Vasculitis – usually veins
 - Small vessels in the lobule are inflamed
 - This is a secondary phenomenon
- Fat necrosis
- Neutrophils
- Septal spill-over
- Around 70% are probably TB – tuberculid
- Late features
 - Tuberculoid granulomas in lobule
- **EXCLUDE INFECTION**

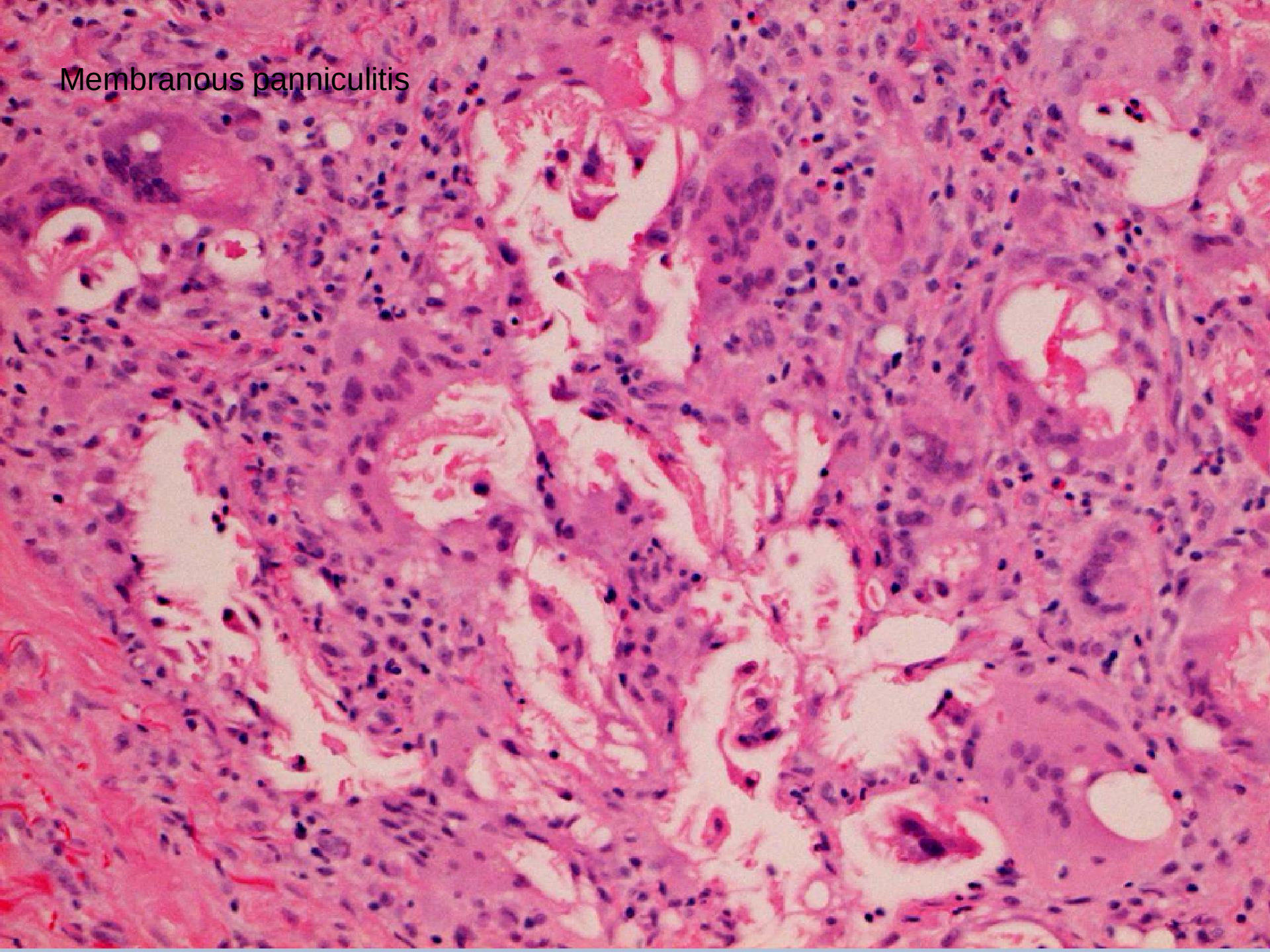
Panniculitis

- Erythema nodosum vs • Nodular vasculitis
 - Not ulcerated
 - Shins
 - Acute onset
 - Non scarring
 - Septal
- Often ulcerated
 - Calves
 - Chronic
 - Scarring
 - Lobular

Panniculitis

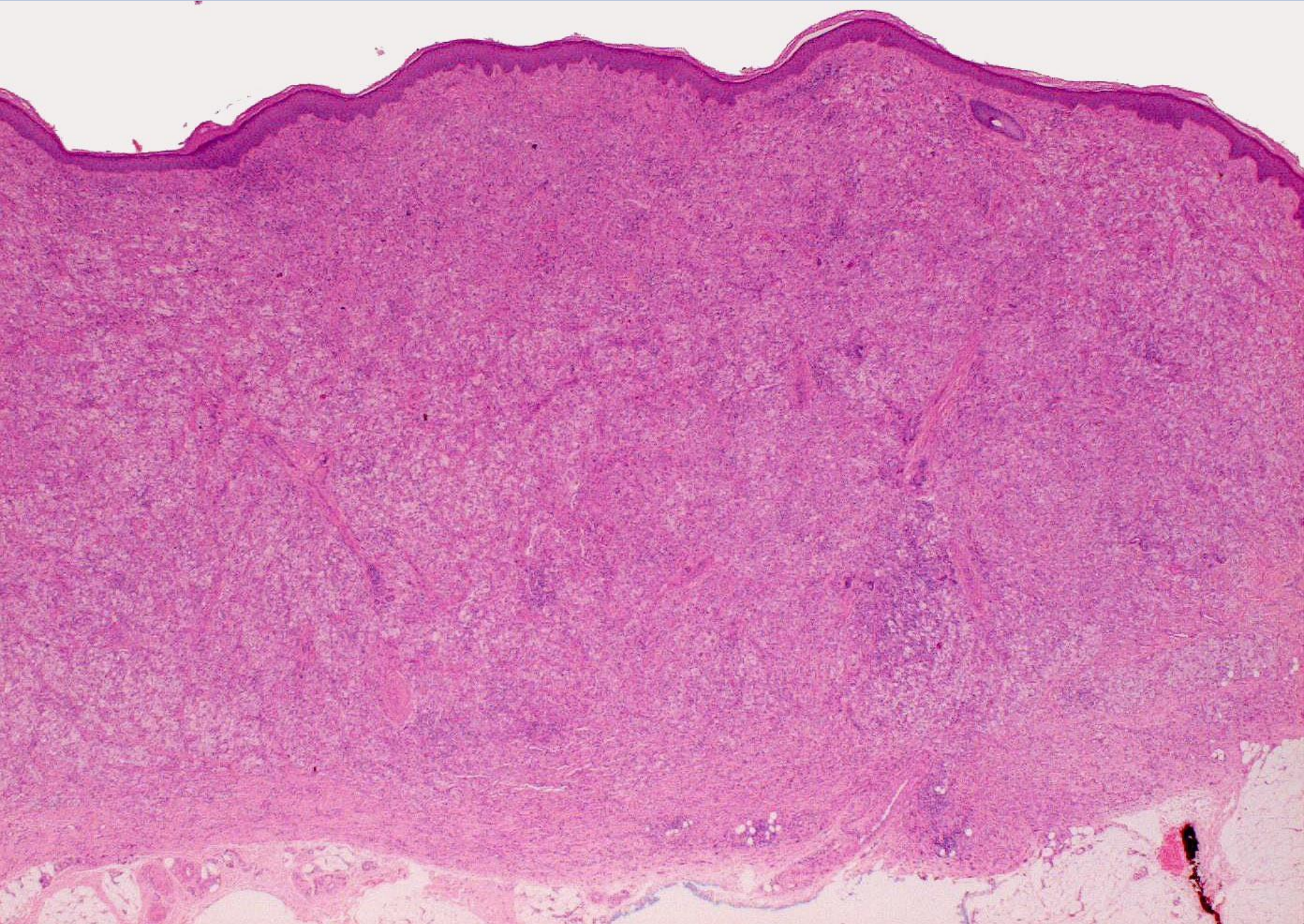
- Mixed panniculitis
 - LE profundus
 - Traumatic, factitial
 - INFECTION

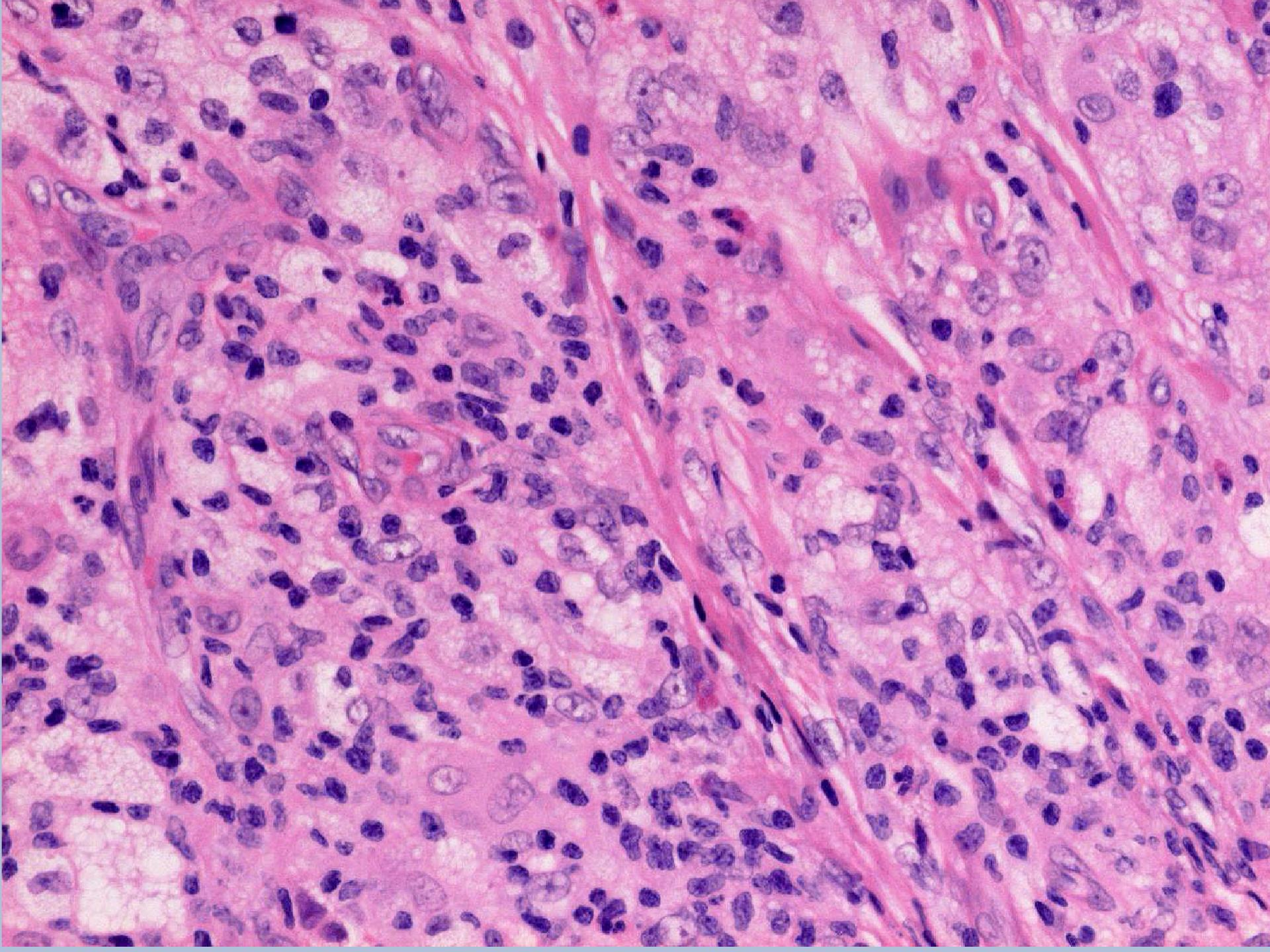
Membranous panniculitis

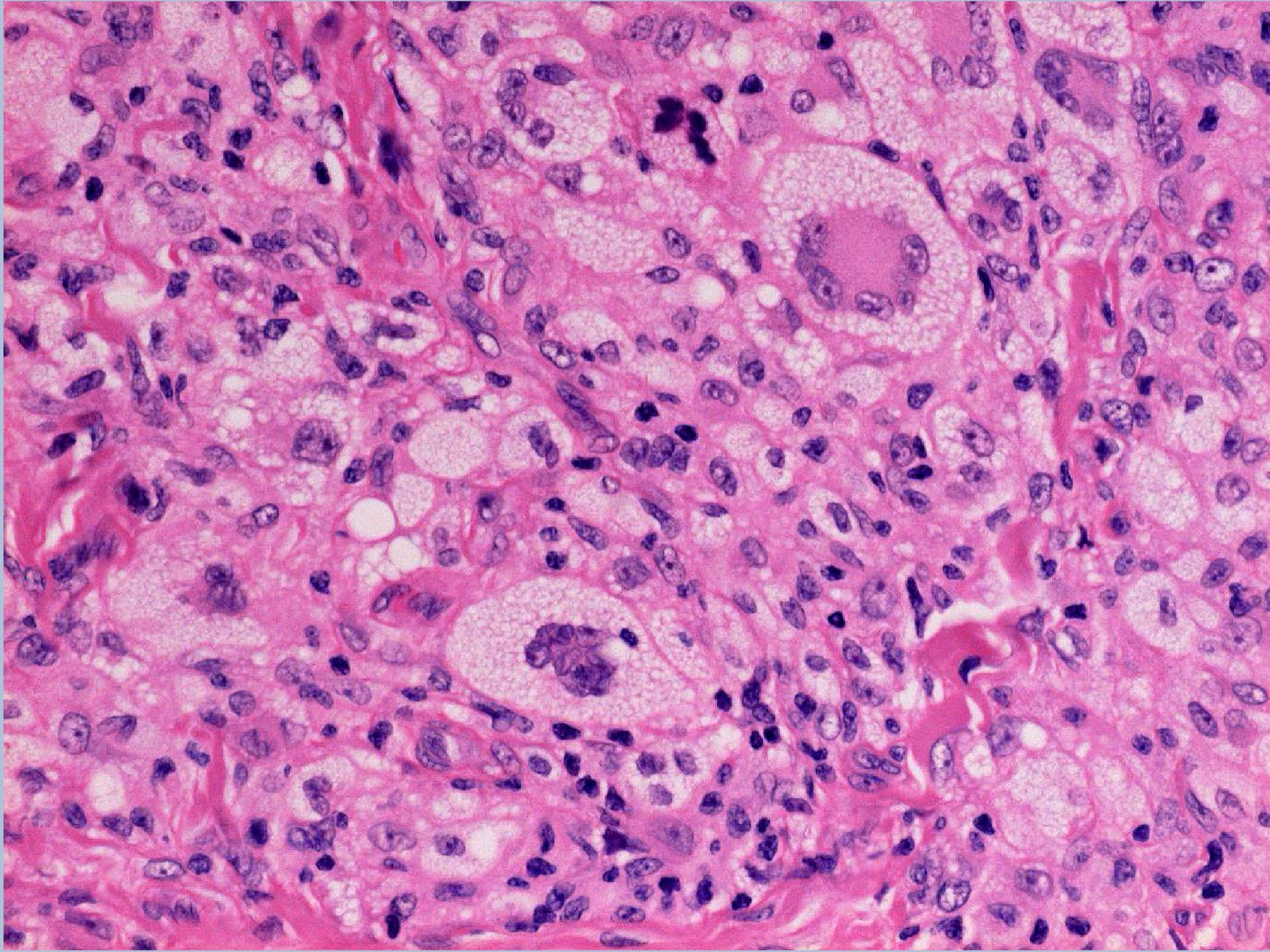


Case 14

- F6
- 15 month history of growing keratoacanthoma-like lesion, dorsum of left hand







Case 14

- Xanthogranulomatous inflammation
 - Xanthoma
 - Xanthogranuloma
 - Non-Langerhan's cell histiocytosis
 - Xanthogranulomatous necrobiosis
 - Tumours
 - eg benign fibrous histiocytoma, giant cell tumour, verruciform xanthoma
 - Fat necrosis, lipophages

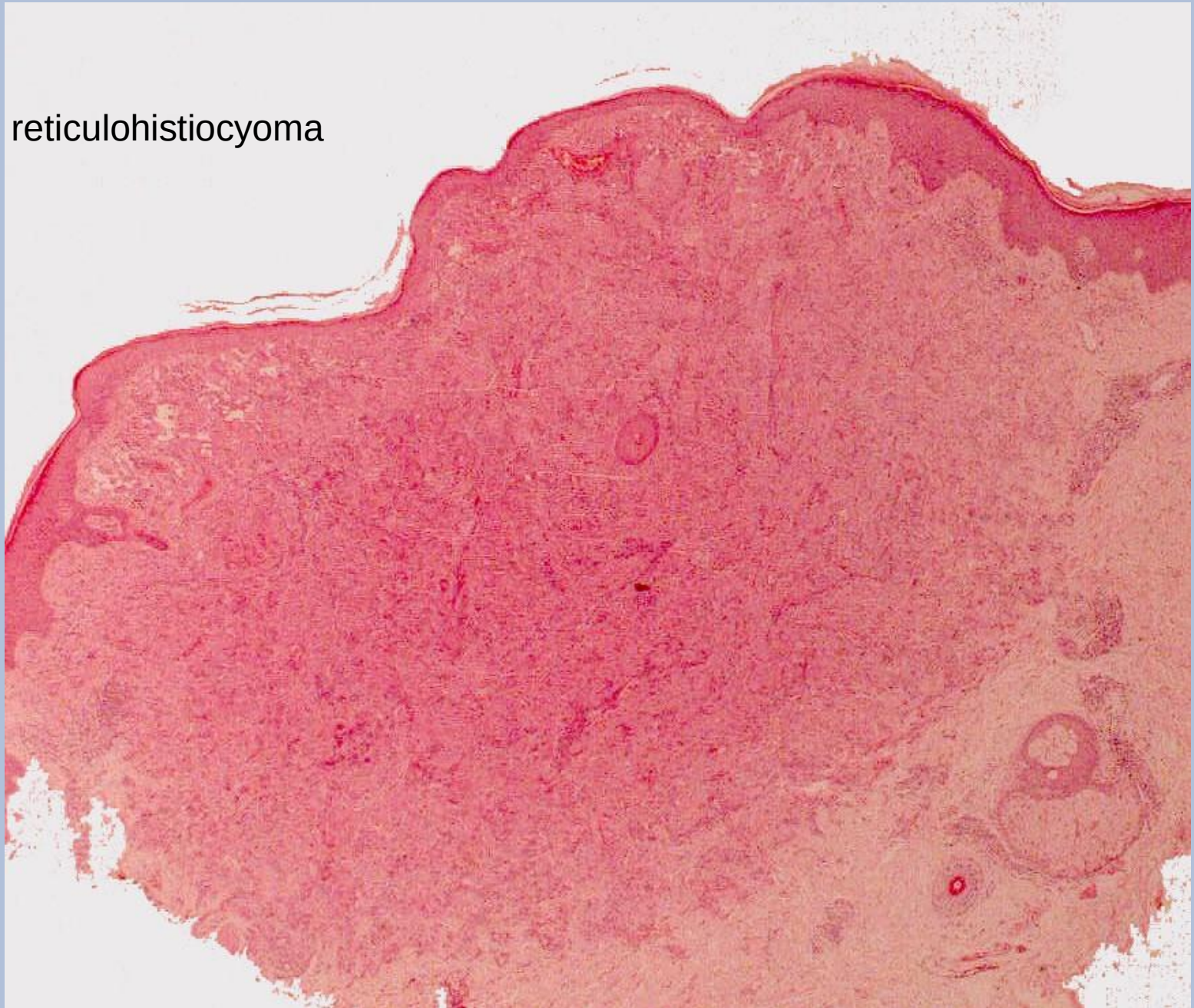
Xanthogranulomatous inflammation

- Not specific
 - Need good clinical information
 - Wedge-shaped infiltrate with
 - Lymphocytes, plasma cells, neutrophils, eosinophils
 - Epidermal sparing
 - S100 –ve
- Xanthogranuloma (juvenile type)
 - CD4 +ve, can be S100 +ve, FXIIIa+ve

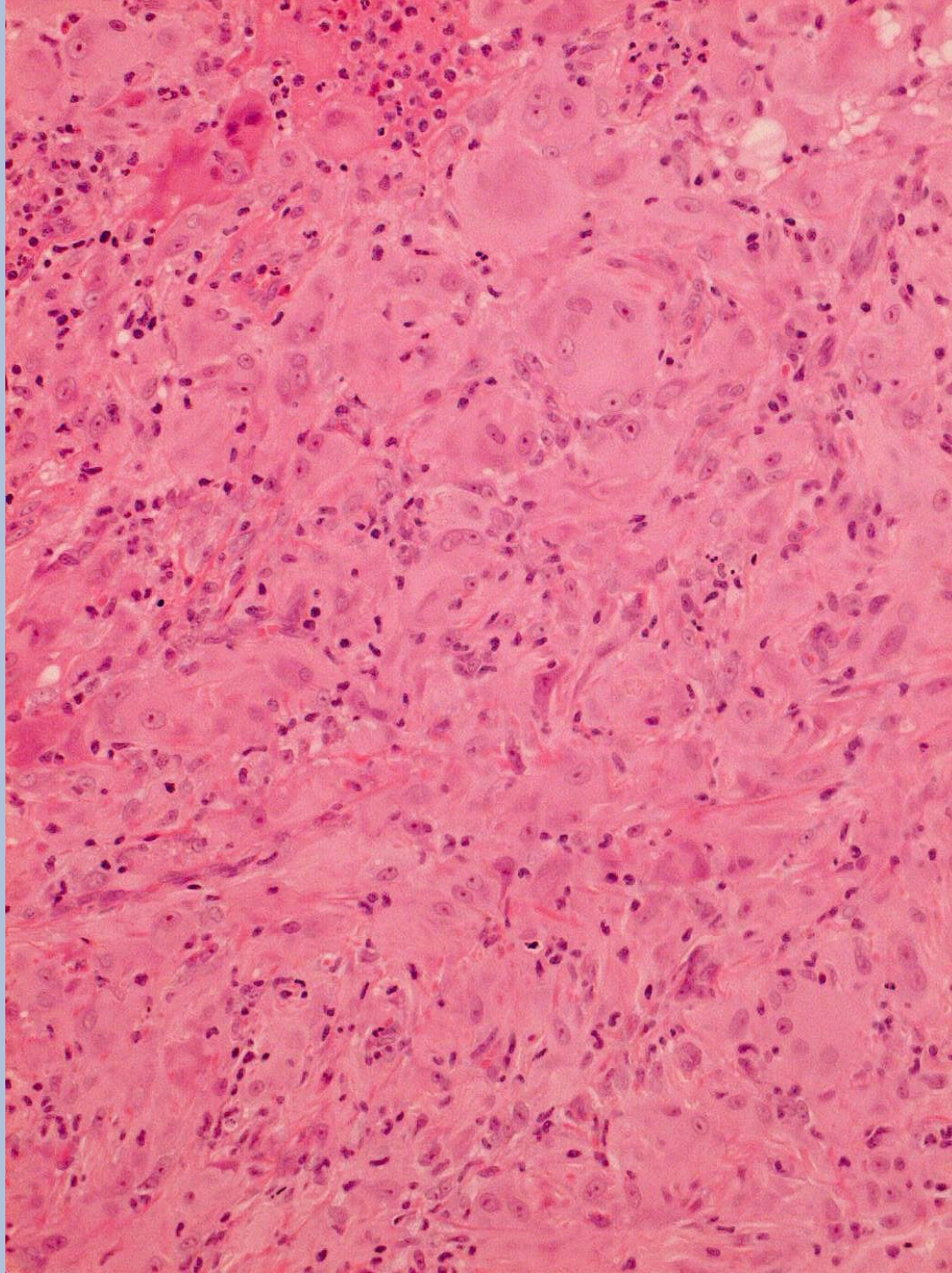
Xanthogranuloma (juvenile type)

- Can occur
 - Adults, subcutis, intramuscular, generalised, systemic
- Early
 - May not be xanthomatized
 - Diff dx – reticulohistiocytoma, histiocytoses, LCH, Rosai-Dorfman
- Late
 - Spindle cells, fibrosis, storiform
 - Diff dx – fibrous histiocytoma
- May be cytological atypia

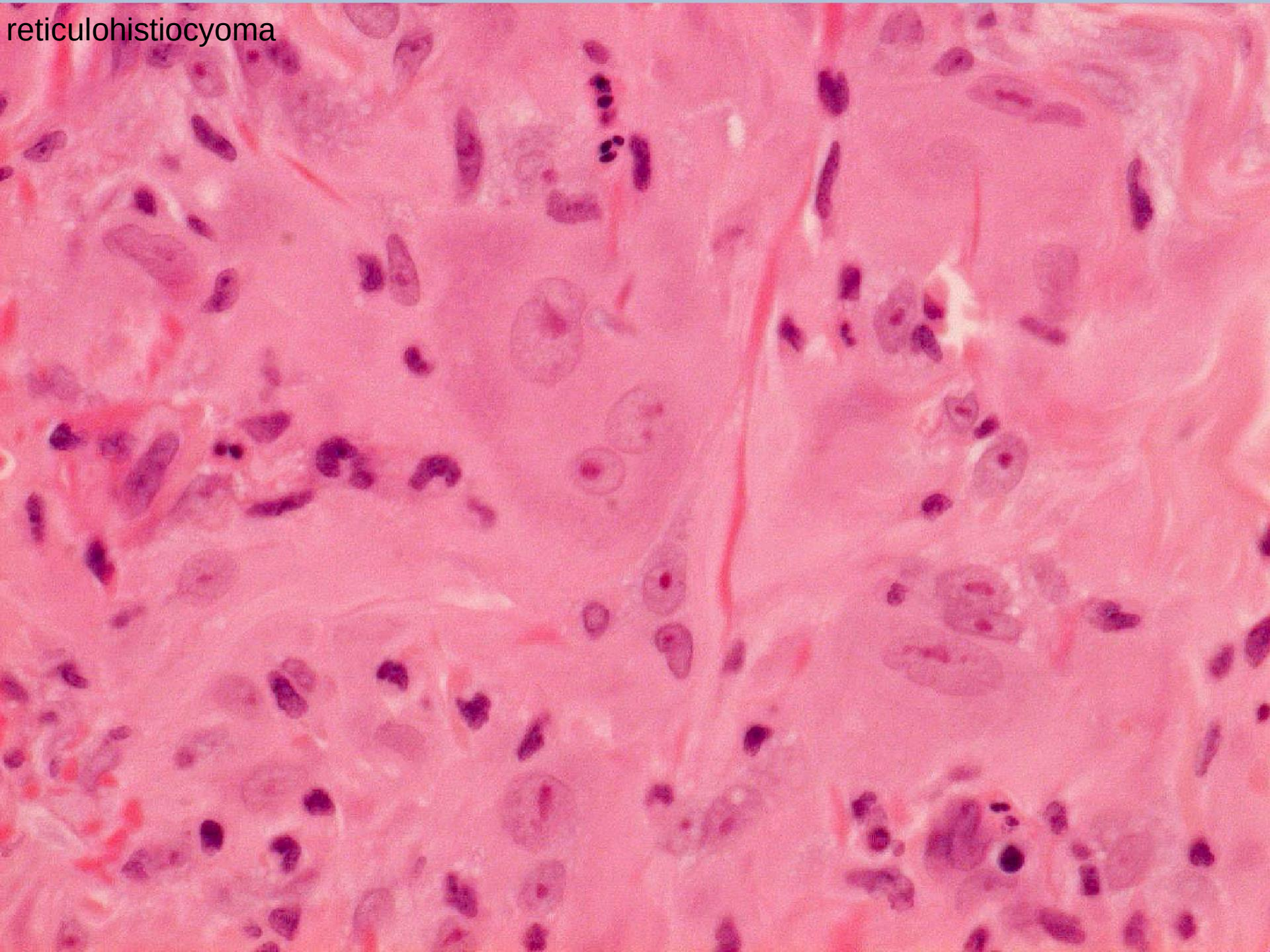
reticulohistiocytoma



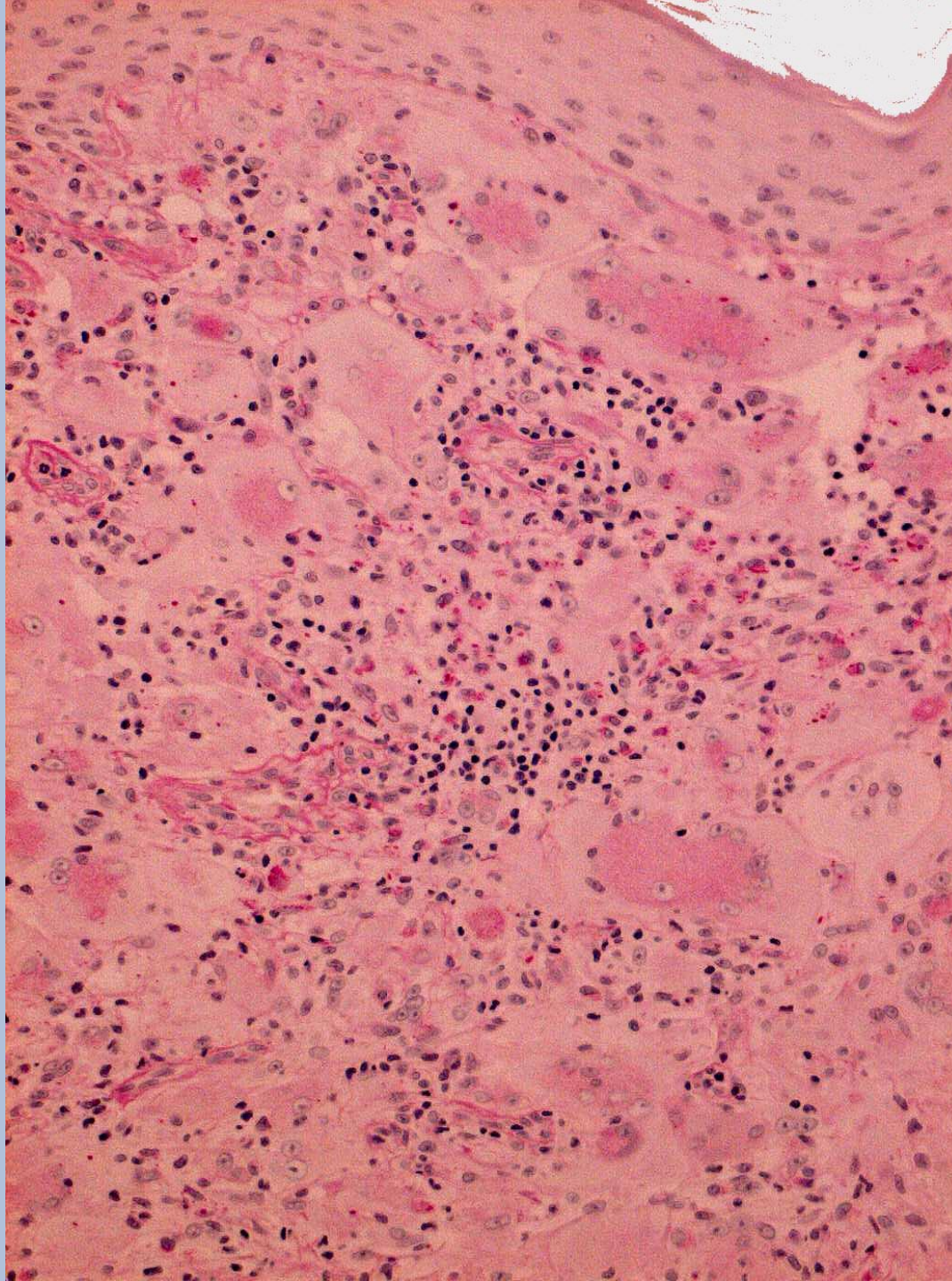
reticulohistiocytoma



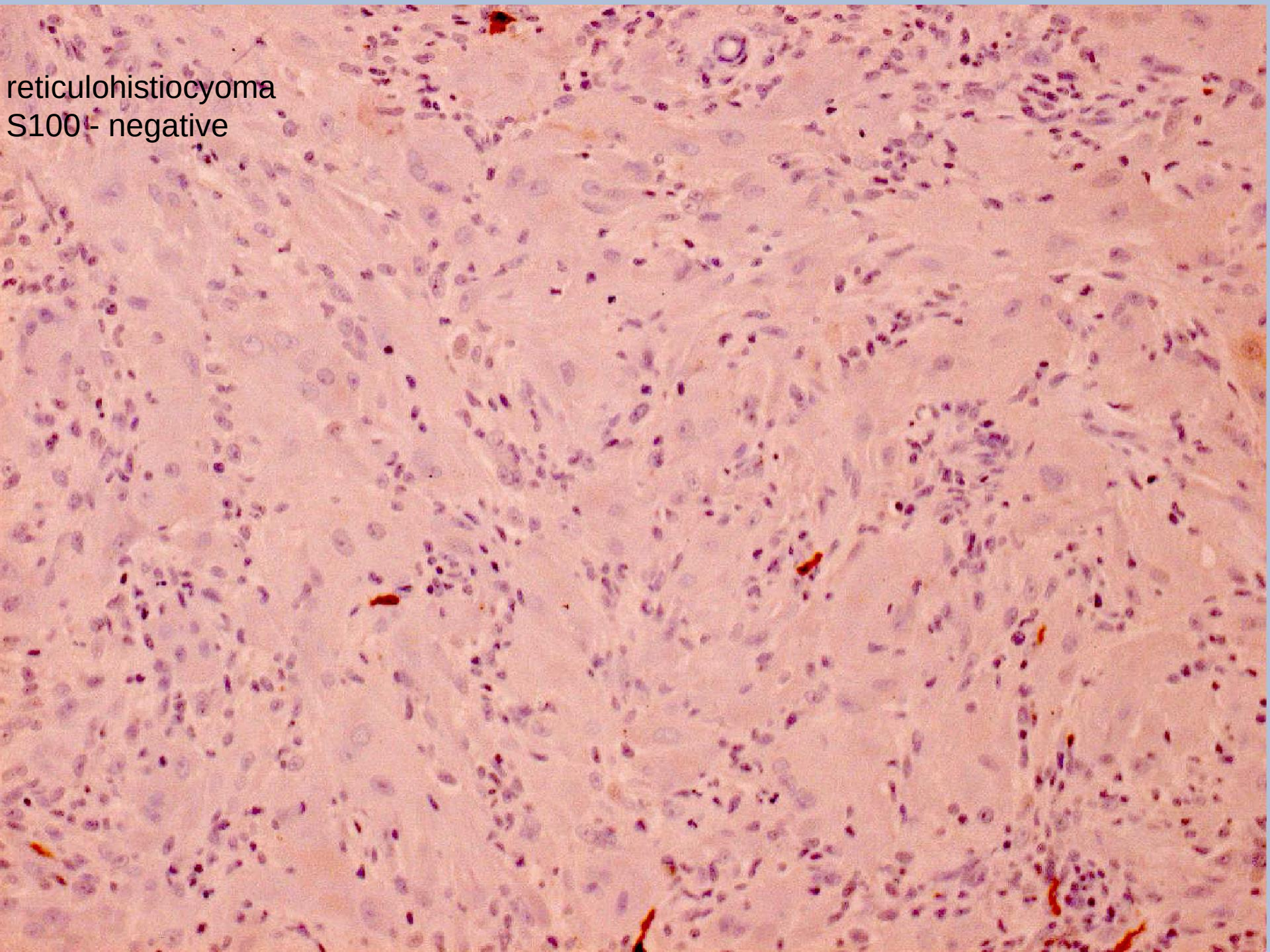
reticulohistiocytoma

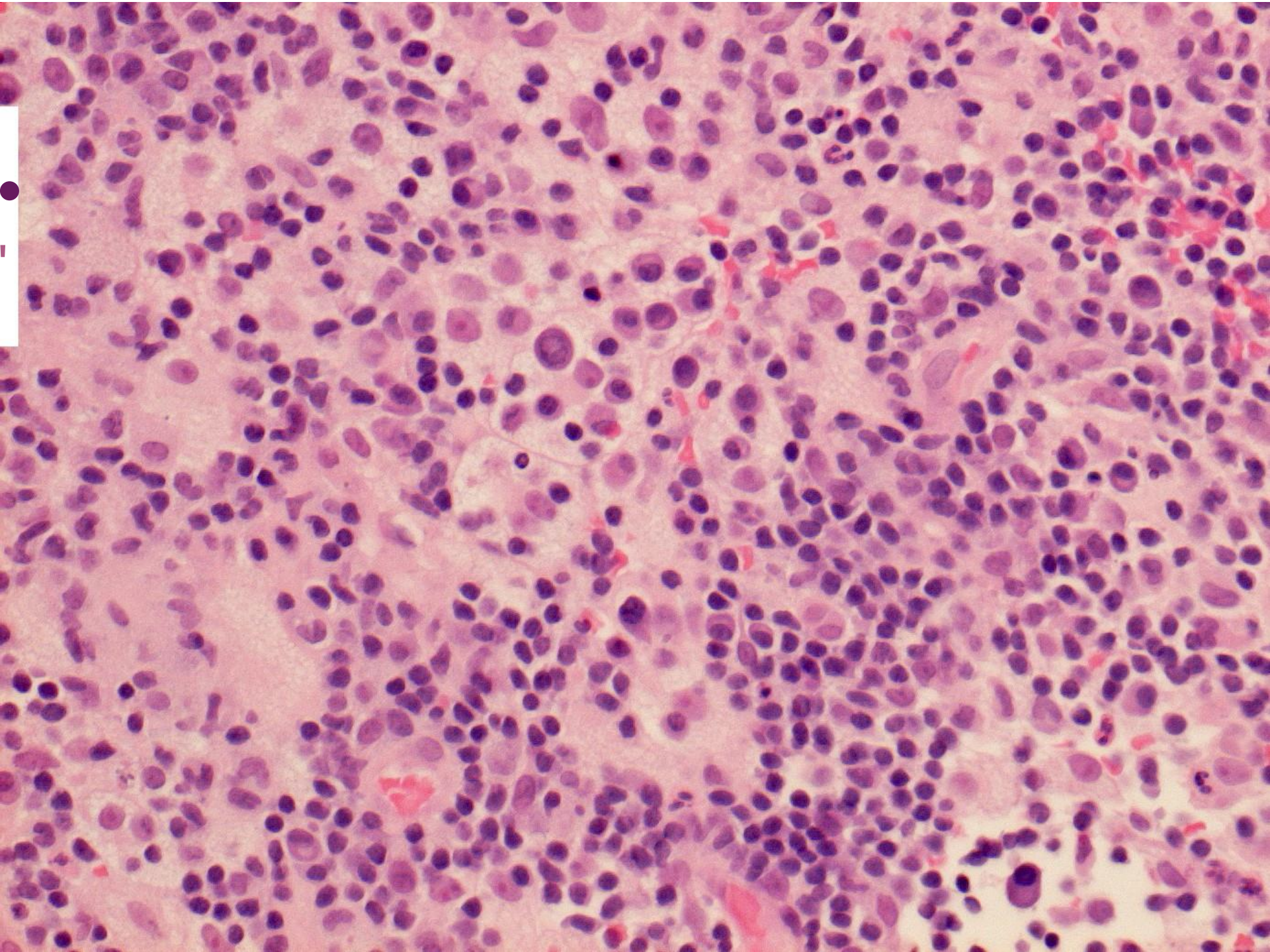


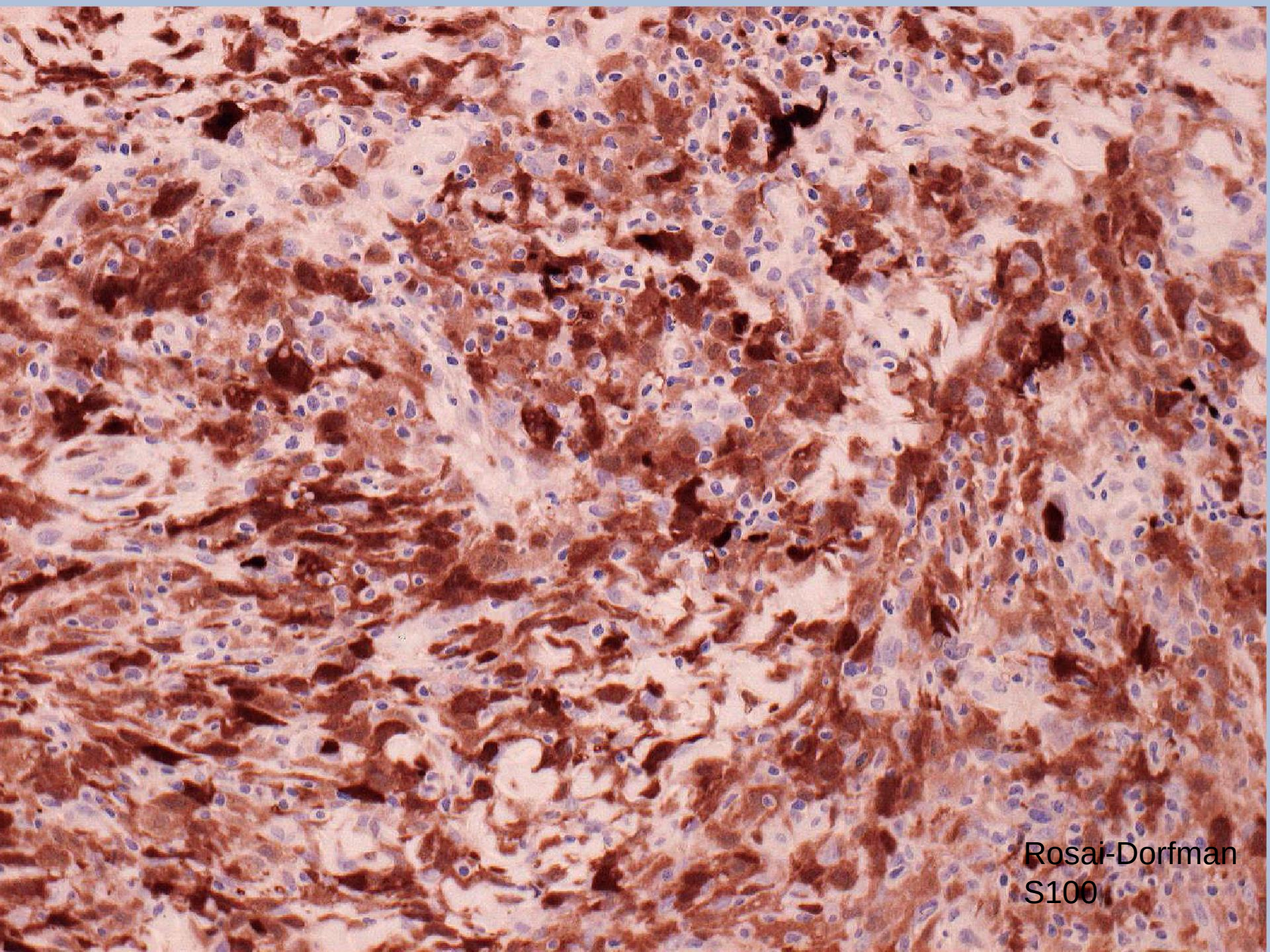
reticulohistiocytoma
PASd



reticulohistiocytoma
S100 - negative



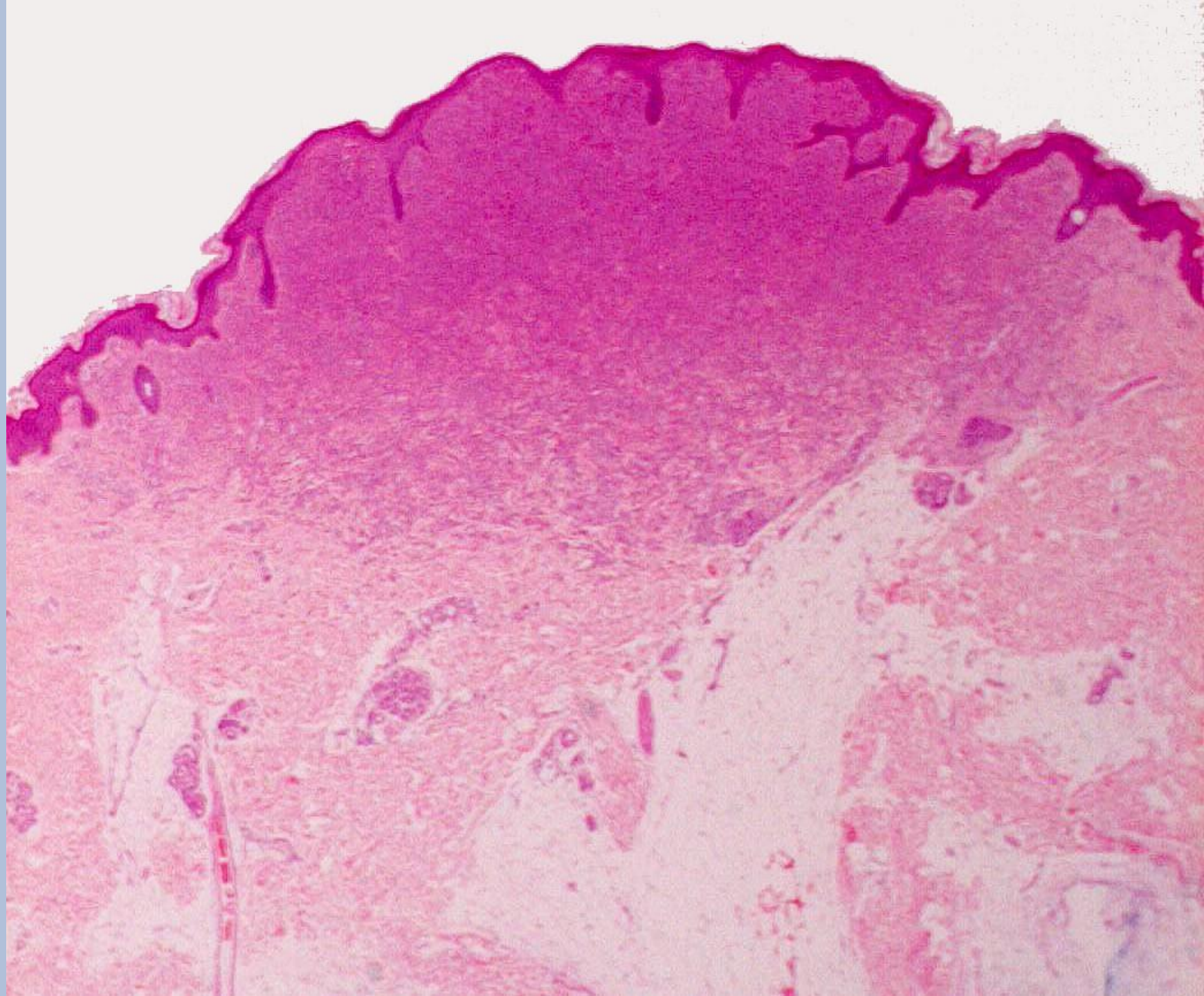


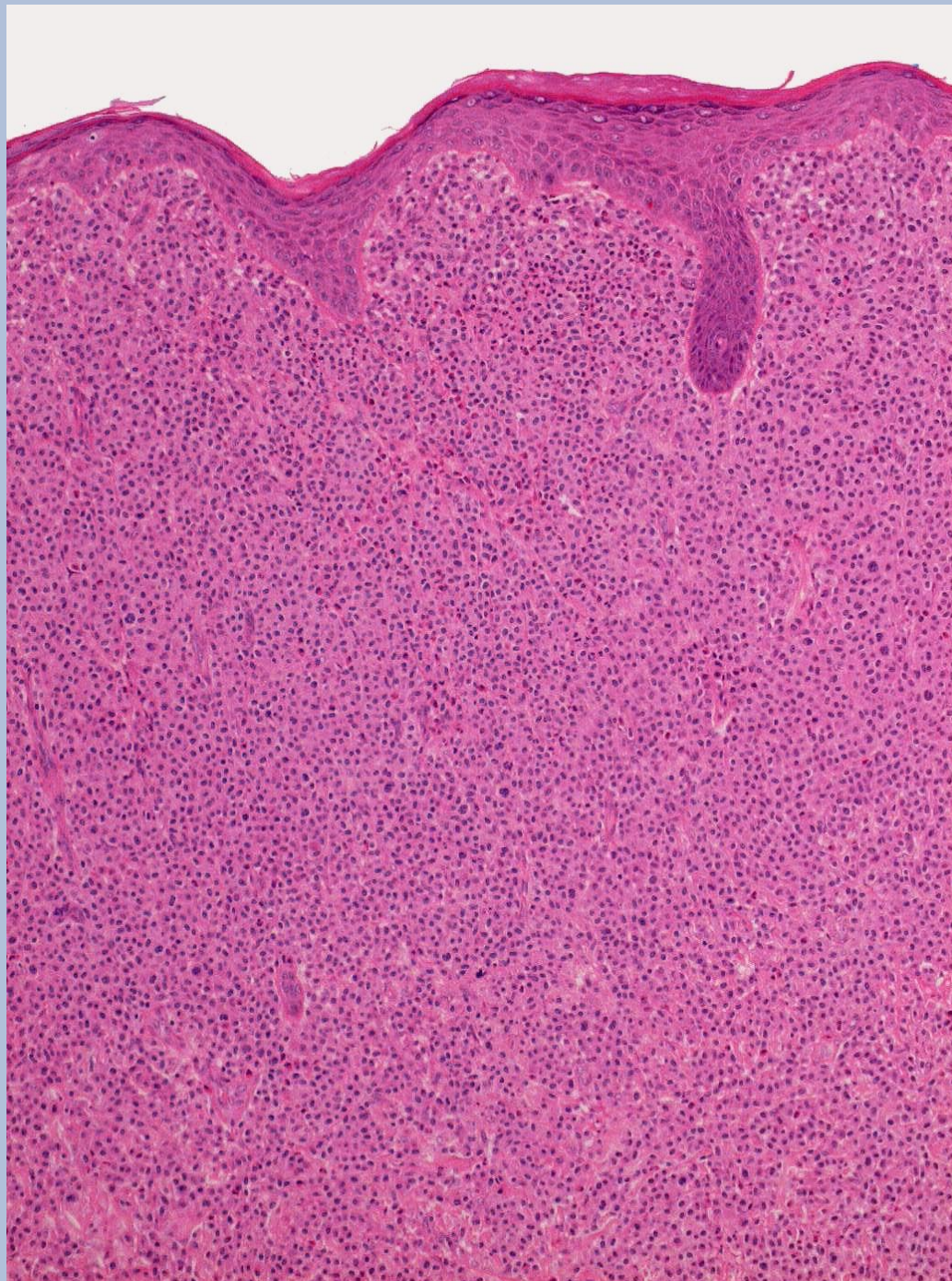


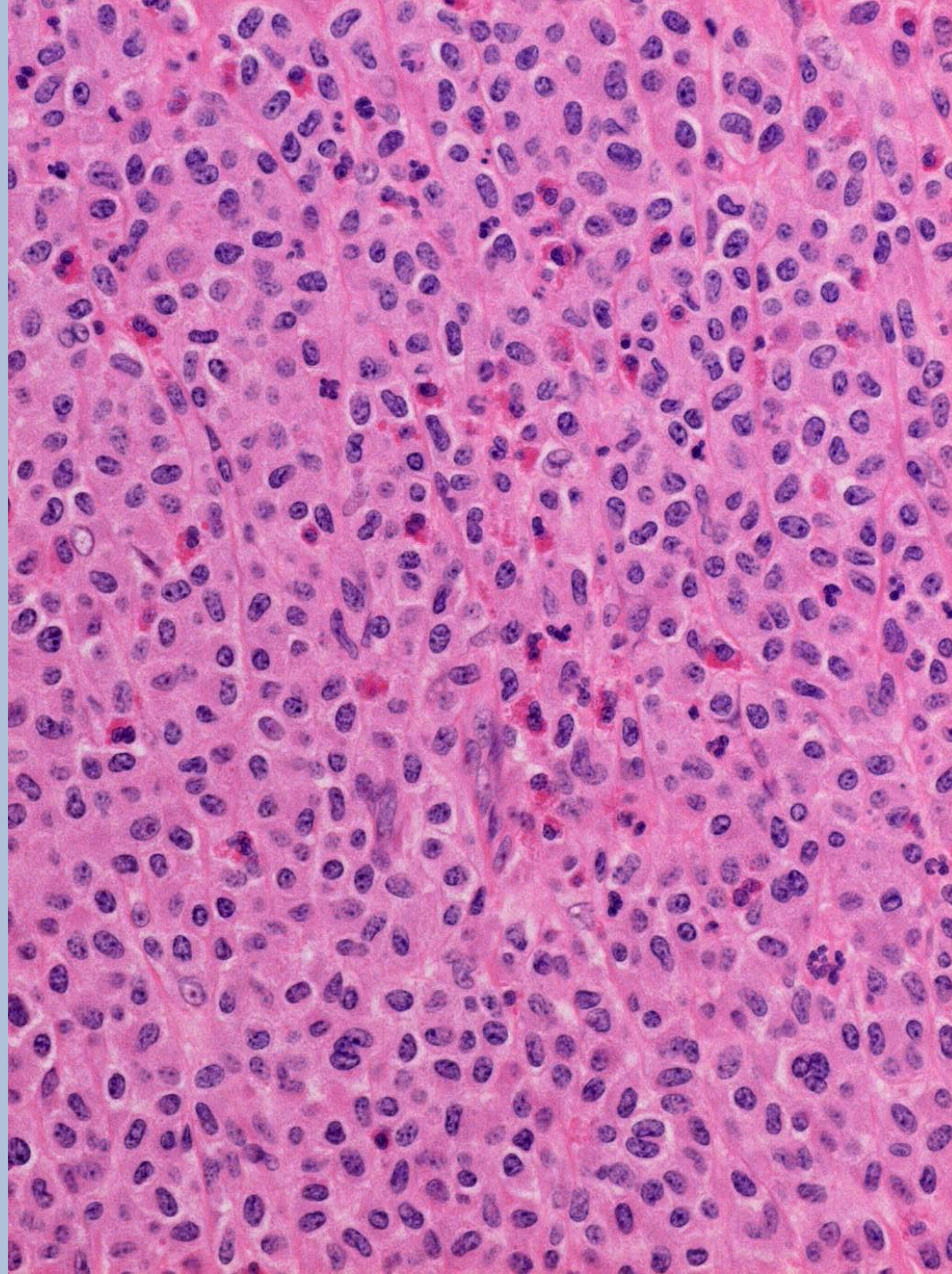
Rosai-Dorfman
S100

Case 15

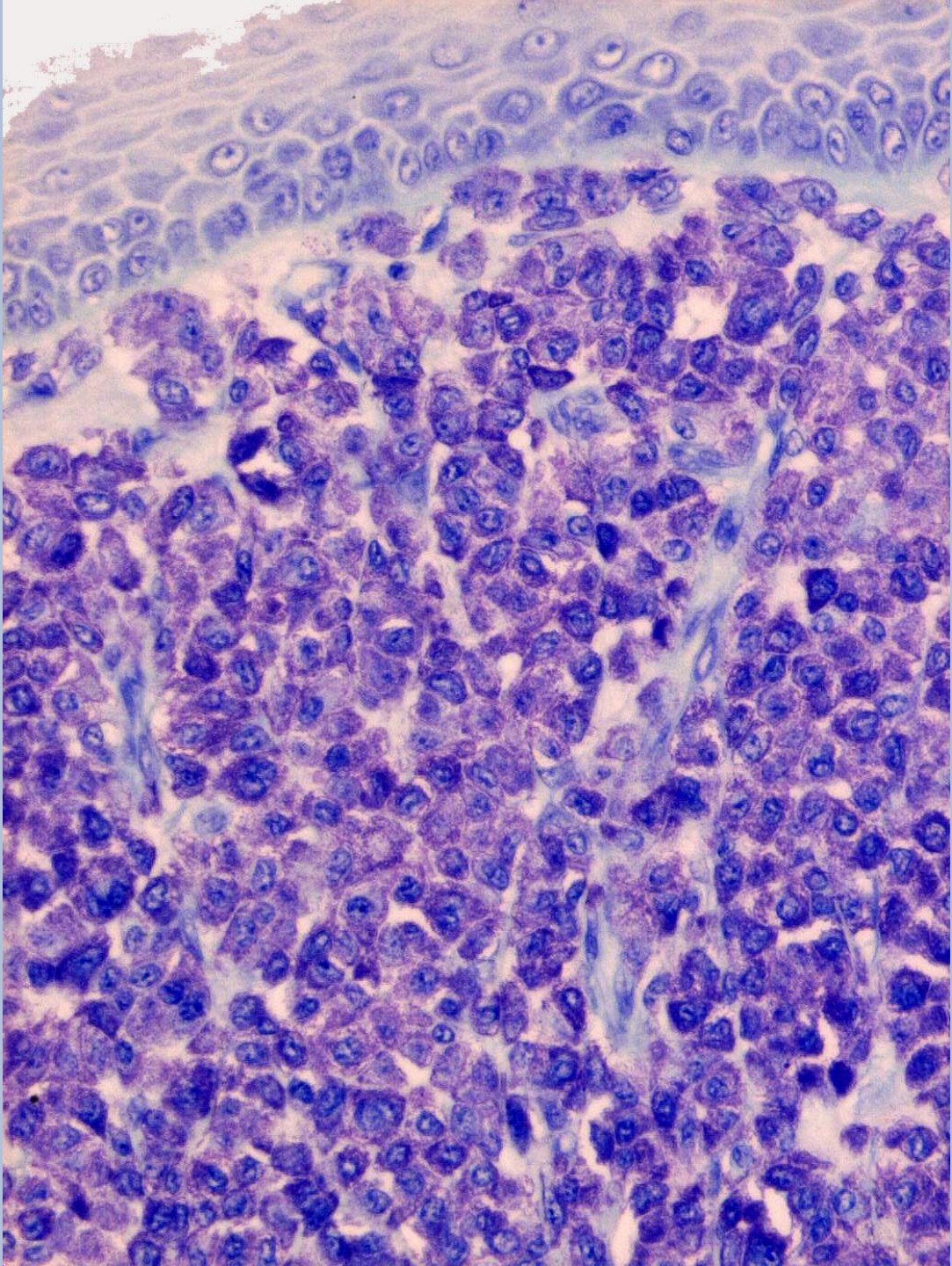
- F4
- Dermatofibroma left thigh

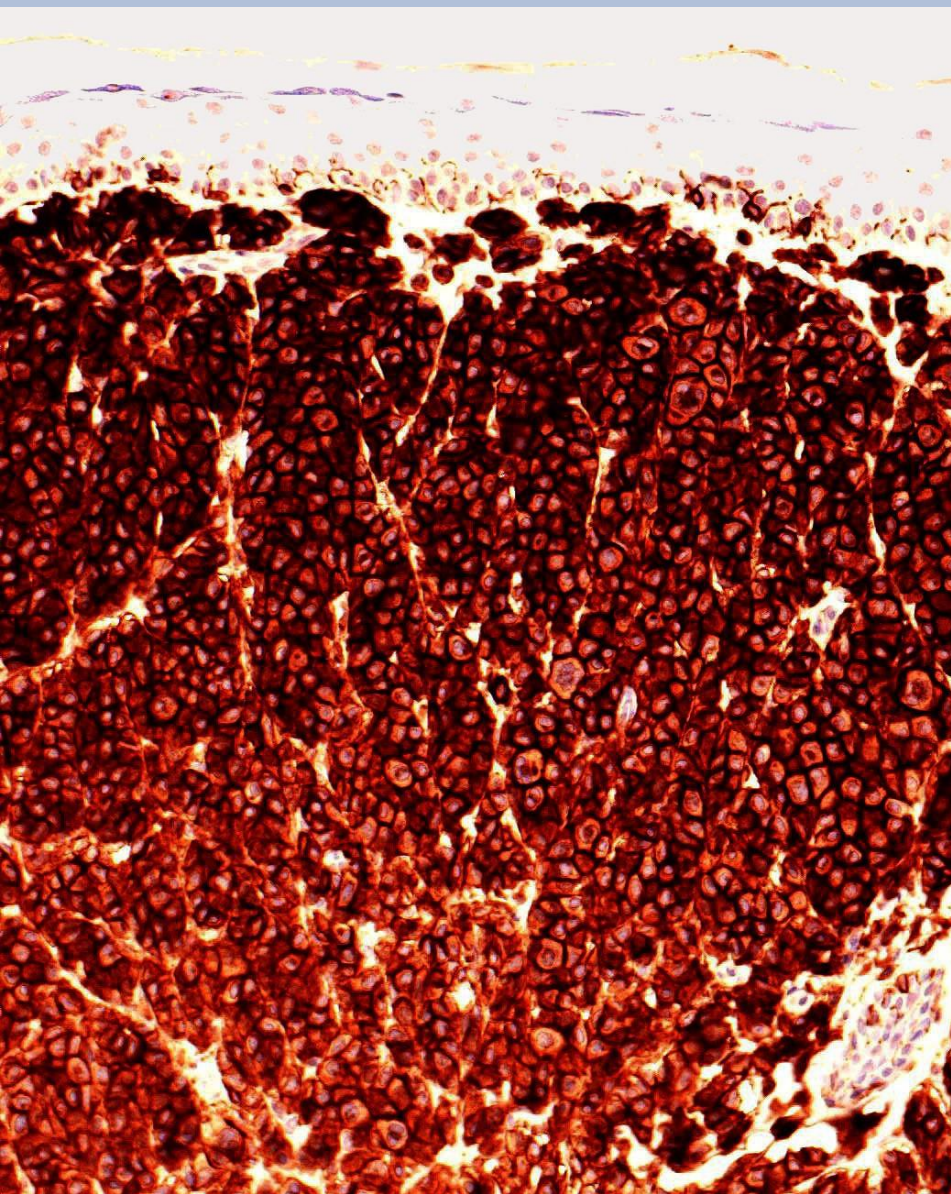




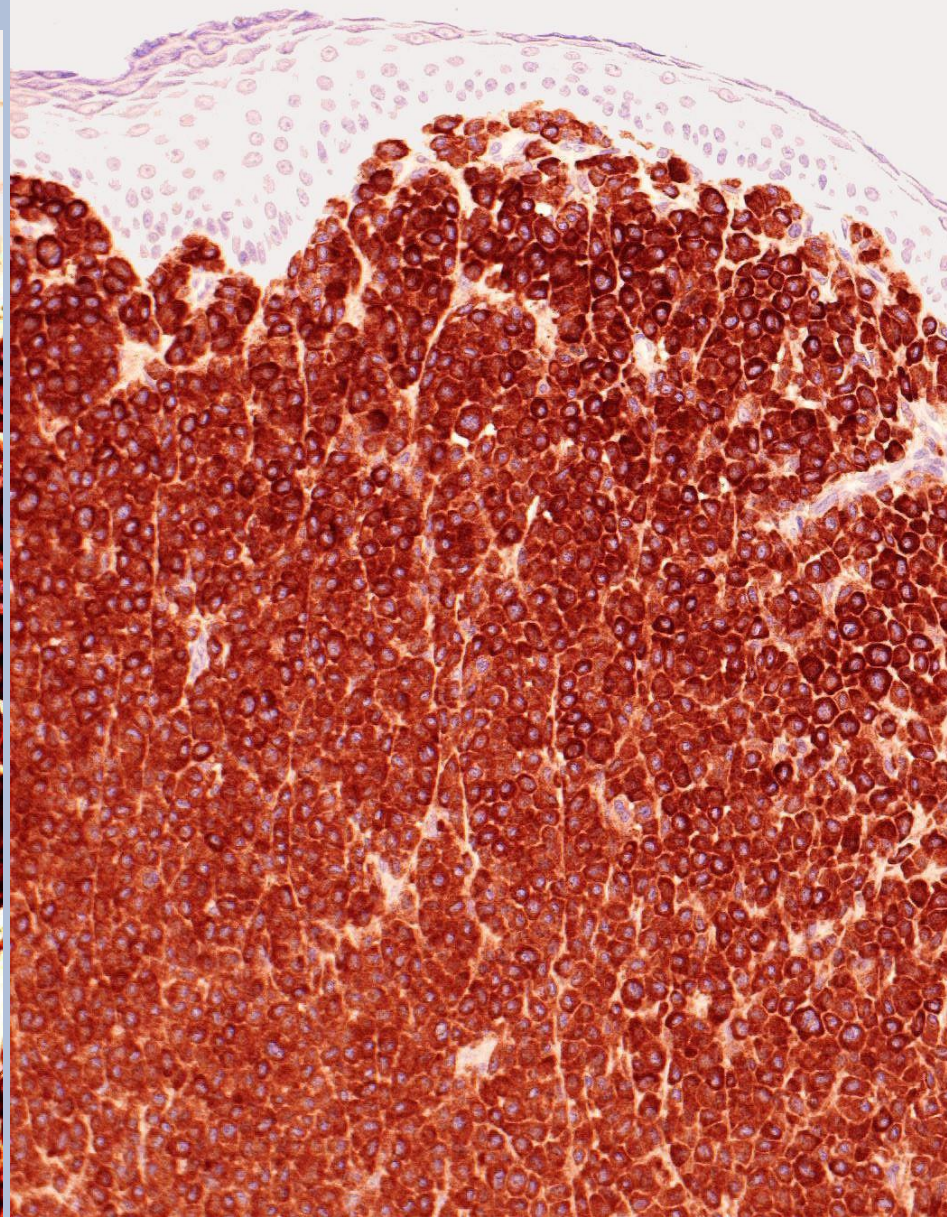


Toluidine blue





Mast cell tryptase



CD117

Case 15

- Mast cell disease

- Cutaneous

- Mastocytoma, urticaria pigmentosa, diffuse cutaneous mastocytosis, telangiectasia macularis eruptiva perstans, involvement in systemic mastocytosis

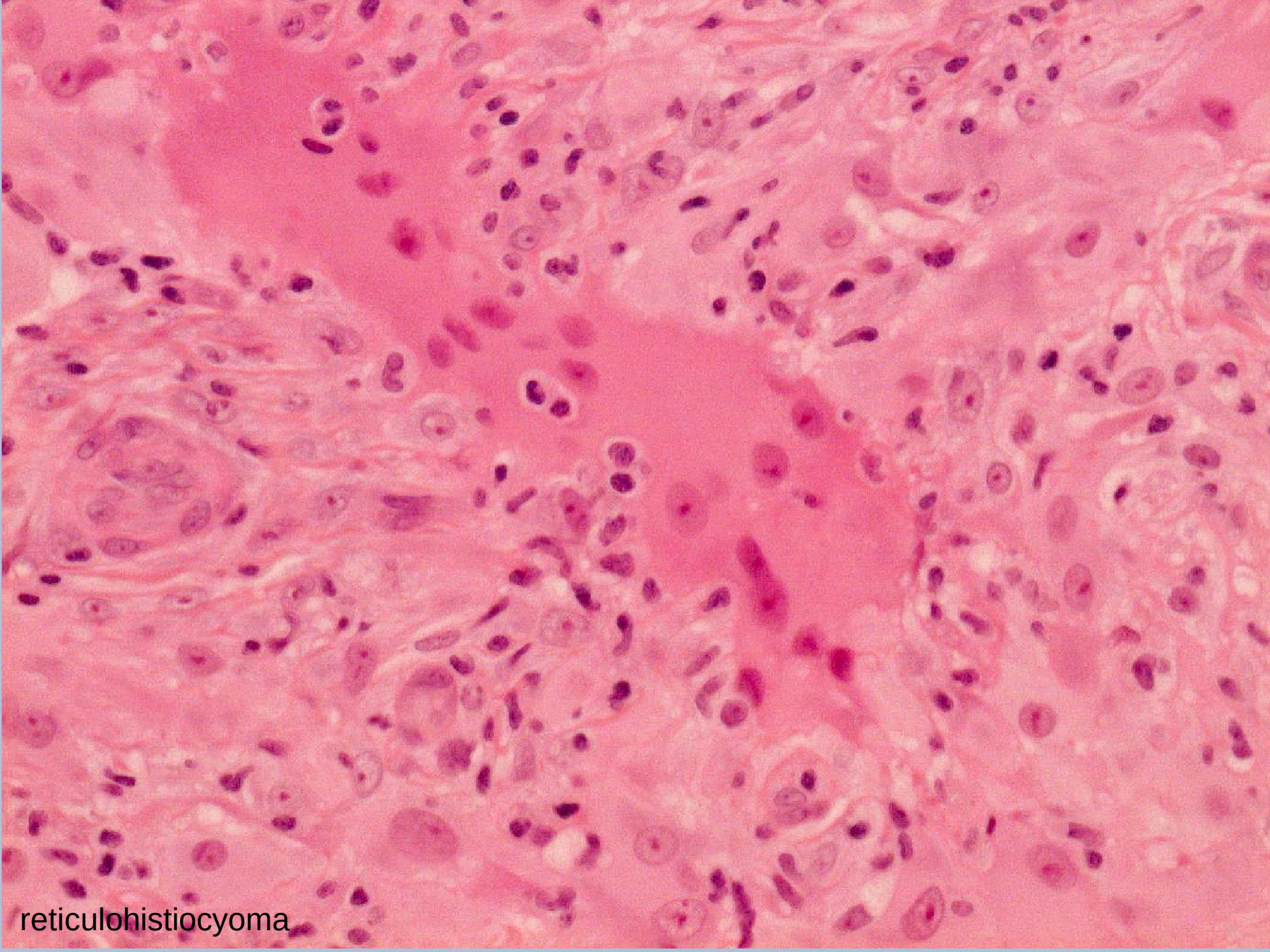
- Systemic

- Many subsets inc indolent, MC leukaemia, sarcoma

Mastocytoma

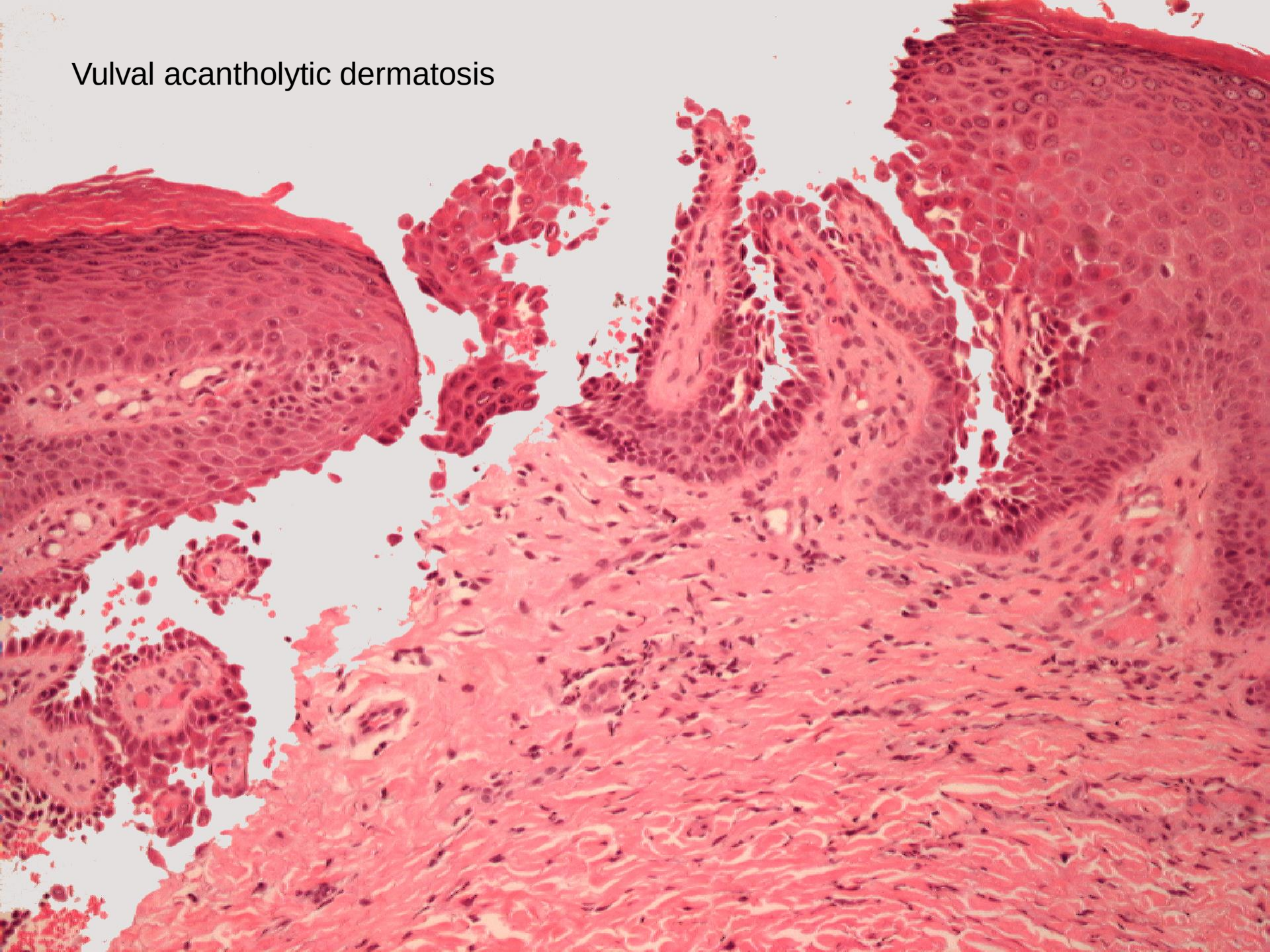
- Solitary or grouped
- Basal epidermal hyperpigmentation
- May be bullous
- Round or spindle cells
- Abundant eosinophilic granular cytoplasm
- Eosinophils

end of part one

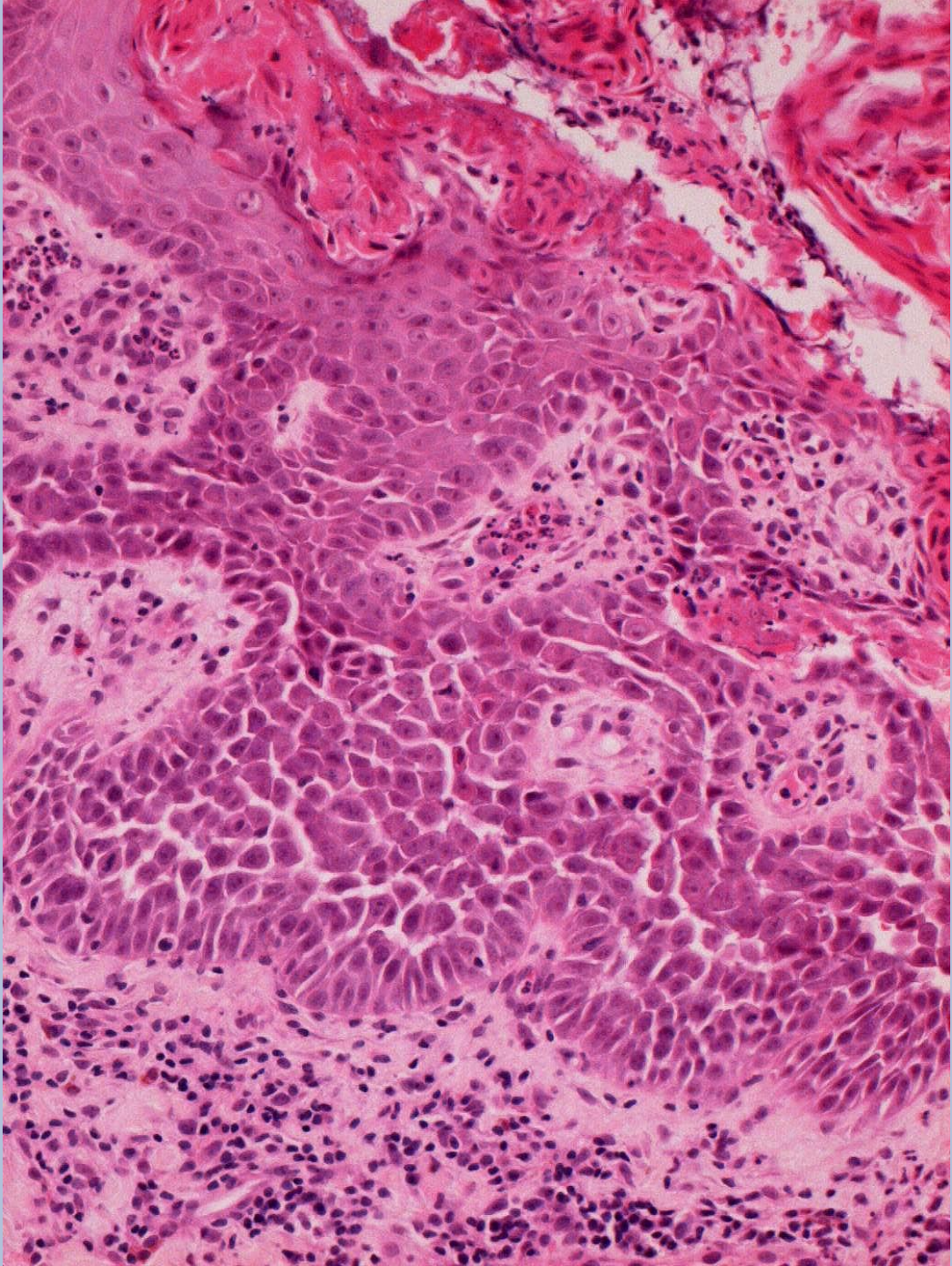


reticulohistiocytoma

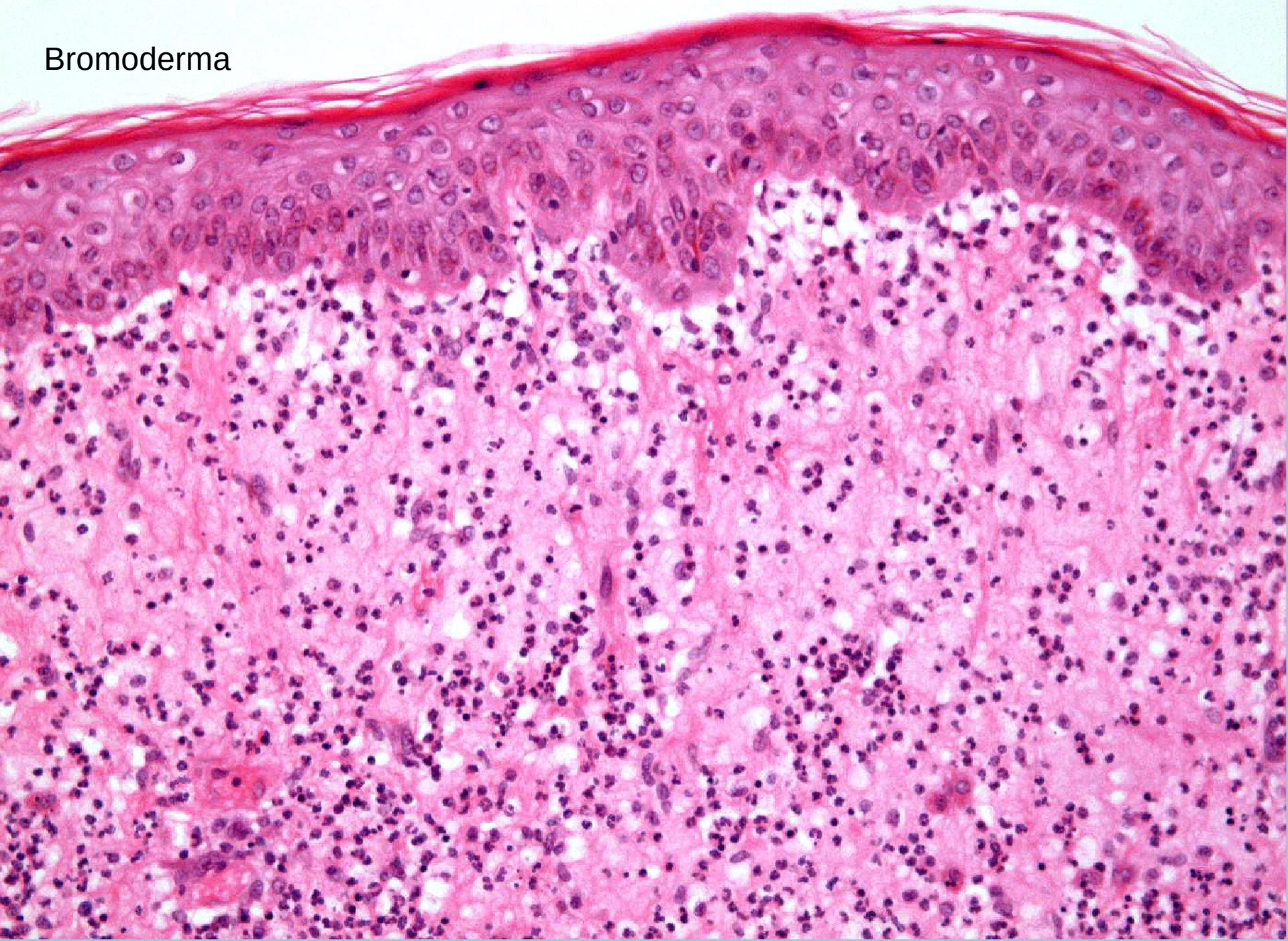
Vulval acantholytic dermatosis

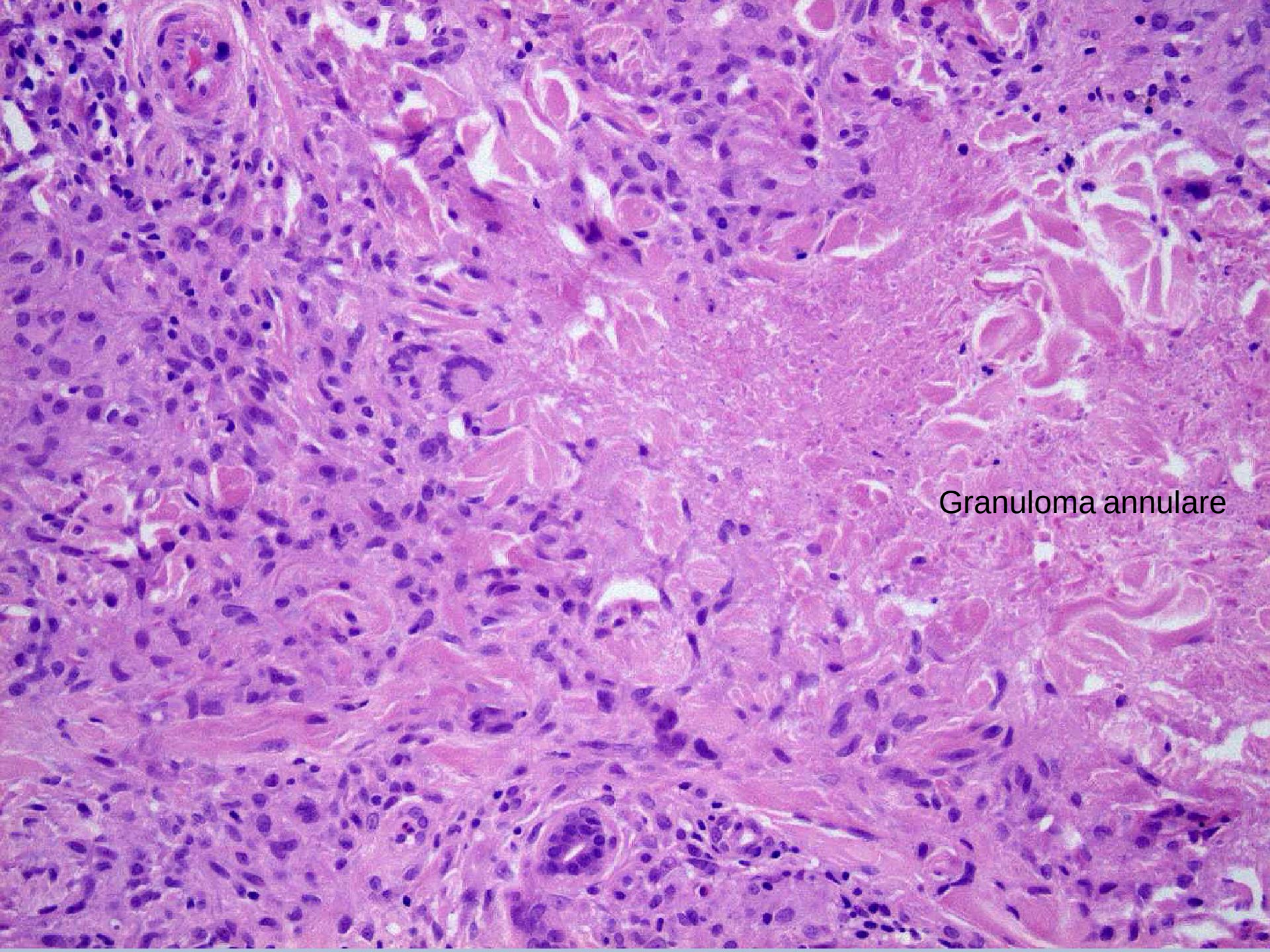


Vulval
acantholytic
dermatosis



Bromoderma





Granuloma annulare

SCLE

