Cutaneous Mucinoses

Nathan C. Walk, M.D.

- Mucinoses
  - Diverse group of disorders which have in common deposition of basophilic, finely granular and stringy material in the connective tissues of the dermis.
  - Predominantly hyaluronic acid
    - c/w Mucopolysaccharidoses, where predominant dermal mucin is chondroitin sulfate
  - Staining methods?
    - Alcian blue at pH 2.5
    - Colloidal iron

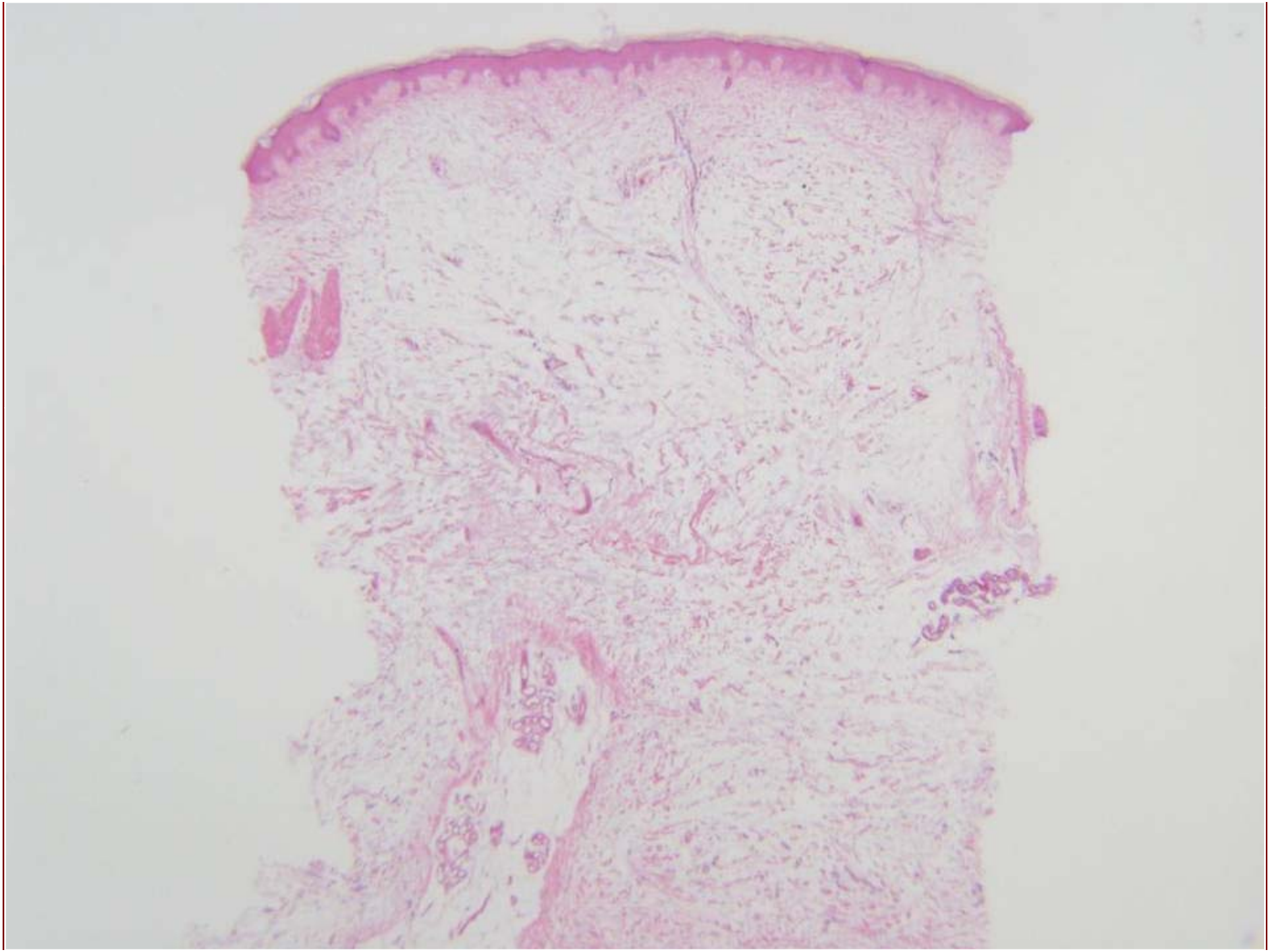
Table 47.2 Primary (distinctive) cutaneous mucinoses

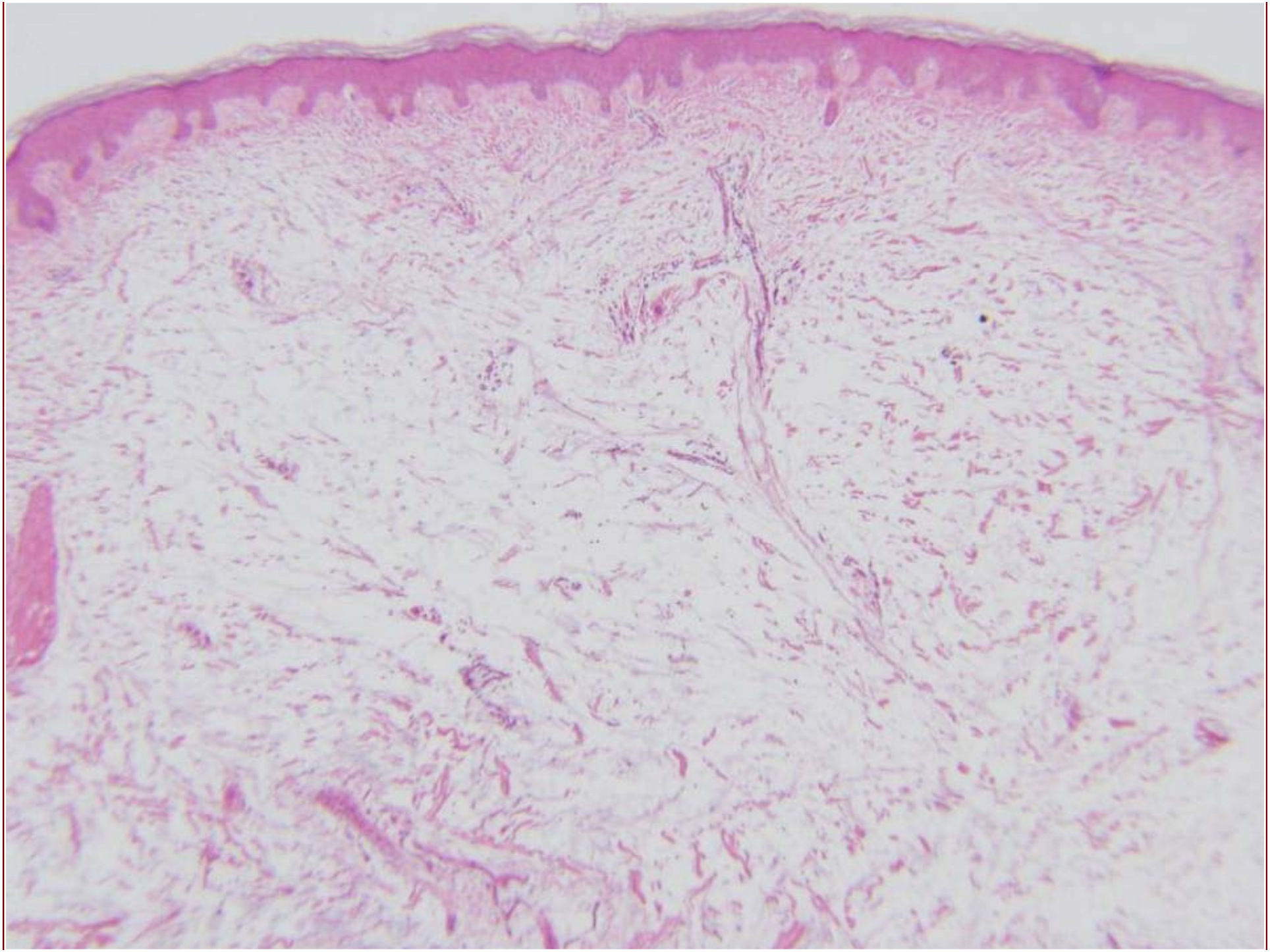
PRIMARY (DISTINCTIVE) CUTANEOUS MUCINOSES
Degenerative–inflammatory mucinoses
Dermal
Lichen myxedematosus (papular mucinosis)
• Generalized and sclerodermoid (scleromyxedema)
• Localized: discrete type, acral persistent papular mucinosis, self-healing cutaneous mucinosis, cutaneous mucinosis of infancy, nodular type
• Atypical forms
Reticular erythematous mucinosis
Scleredema
Dysthyroidotic mucinoses
• Localized (pretibial) myxedema
• Generalized myxedema
Cutaneous lupus mucinosis
Cutaneous focal mucinosis
Digital mucous cyst
Miscellaneous mucinoses
Follicular
Pinkus' follicular mucinosis
Urticaria-like follicular mucinosis
Hamartomatous–neoplastic mucinoses
Mucinous nevus
(Angio)myxoma

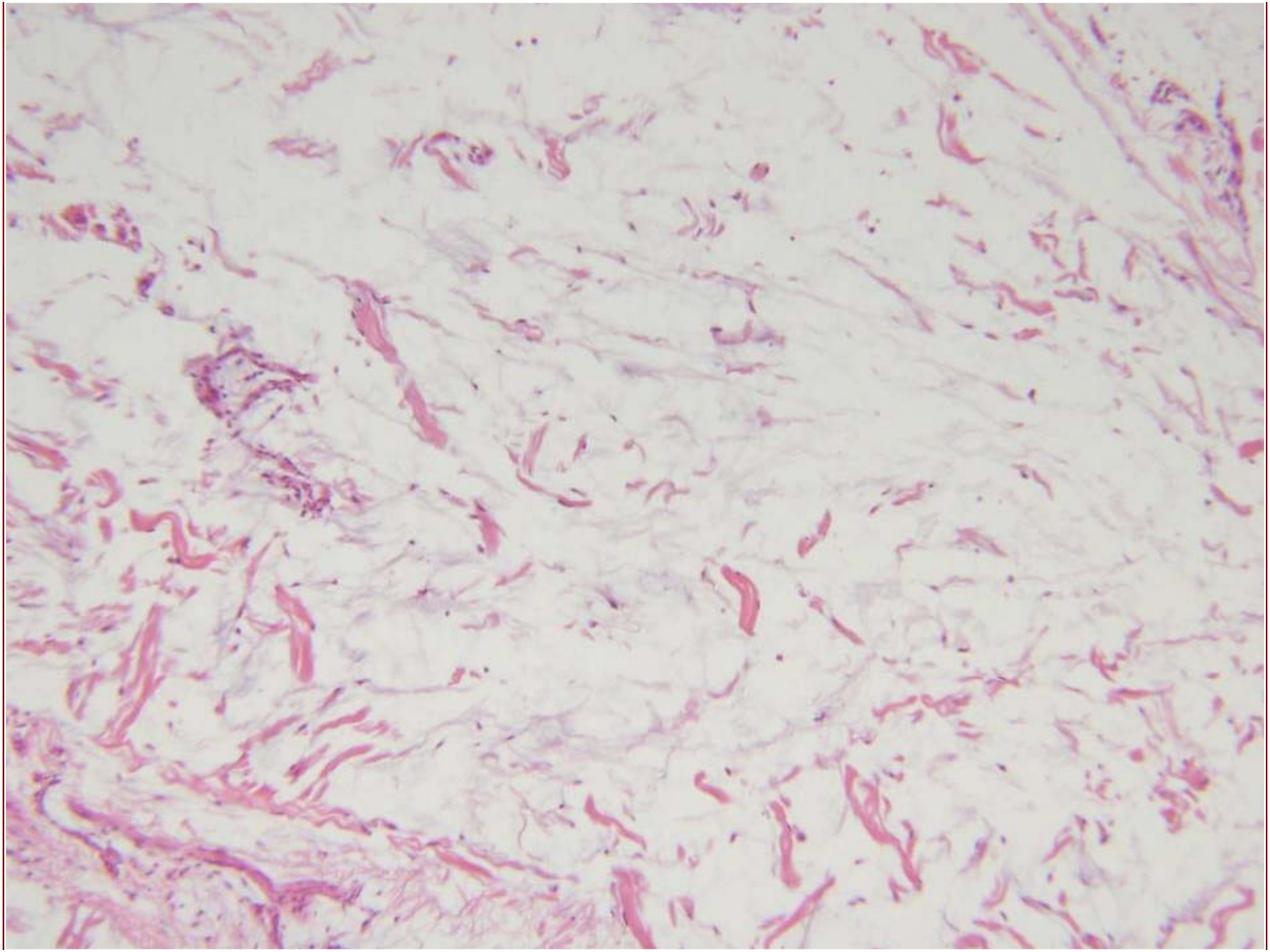
Table 47.3 Disorders associated with histologic deposition of mucin (secondary mucinoses)

DISORDERS ASSOCIATED WITH HISTOLOGIC DEPOSITION OF MUCIN (SECONDARY MUCINOSES)
Epithelial mucinosis
• Mycosis fungoides • Spongiotic dermatitis • Basal cell carcinoma • Verruca vulgaris • Keratoacanthoma • Squamous cell carcinoma
Dermal mucinosis
• Lupus erythematosus • Dermatomyositis • Scleroderma • Degos' disease • Granuloma annularePachydermoperiostosis • UV radiation and PUVA • Hypertrophic scar • Actinic elastosis • Chronic graft-versus-host disease • Hereditary progressive mucinous histiocytosis • Epithelial tumors (basal cell carcinoma, eccrine tumors) • Mesenchymal tumors (fibroma, malignant fibrous histiocytoma, myxosarcoma, lipoma) • Neural tumors (neurofibroma, neurilemoma, neuromyxoma)
Follicular mucinosis
• Lymphoma • Pseudolymphoma • Cutaneous leukemia • Spongiotic dermatitis • Lupus erythematosus • Hypertrophic lichen planus • Insect bites • Angiolymphoid hyperplasia with eosinophilia • Hodgkin's disease • Lichen striatus • Sarcoidosis • Photo-induced eruptions • Familial reticuloendotheliosis

- Case 83



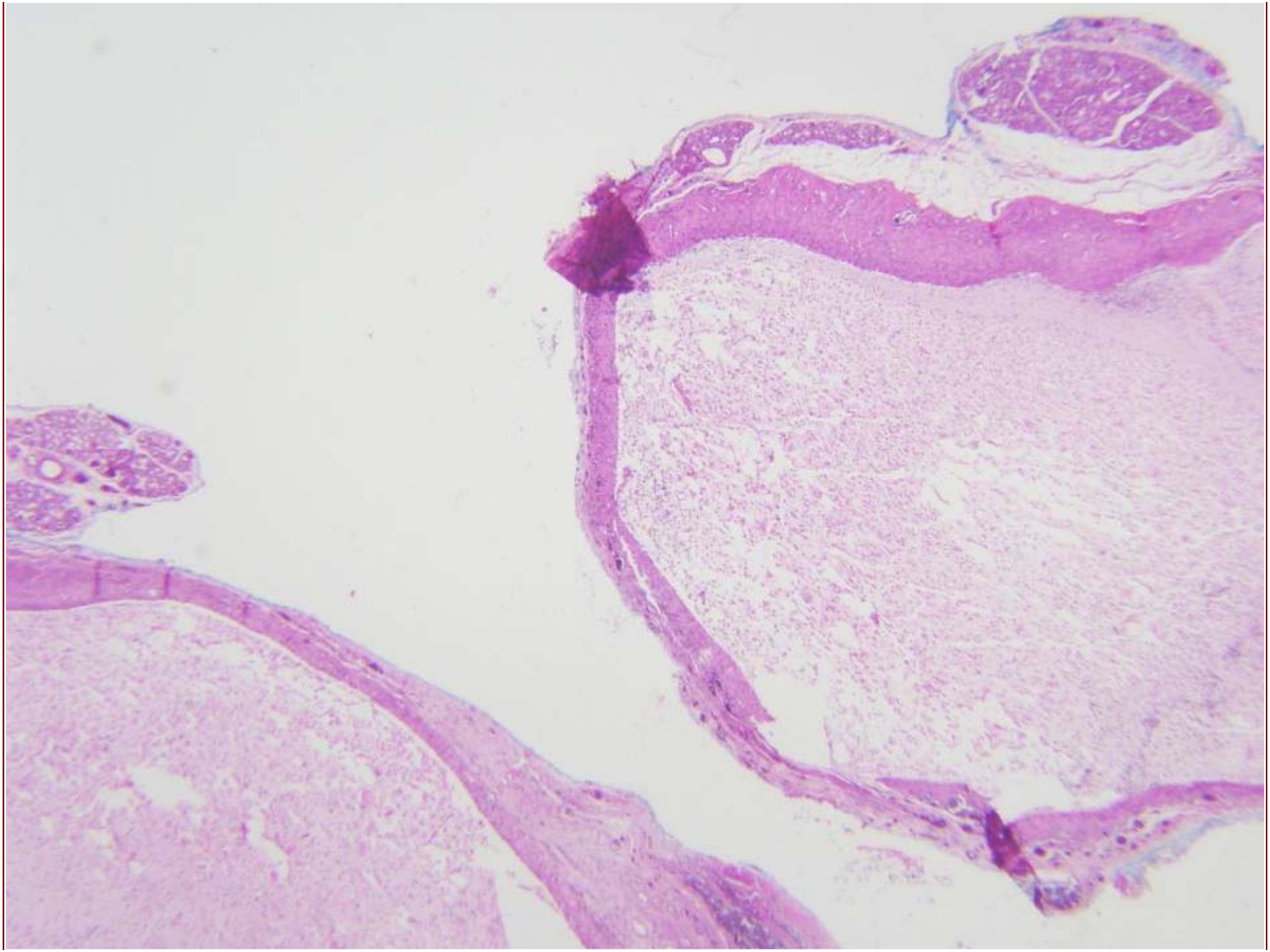


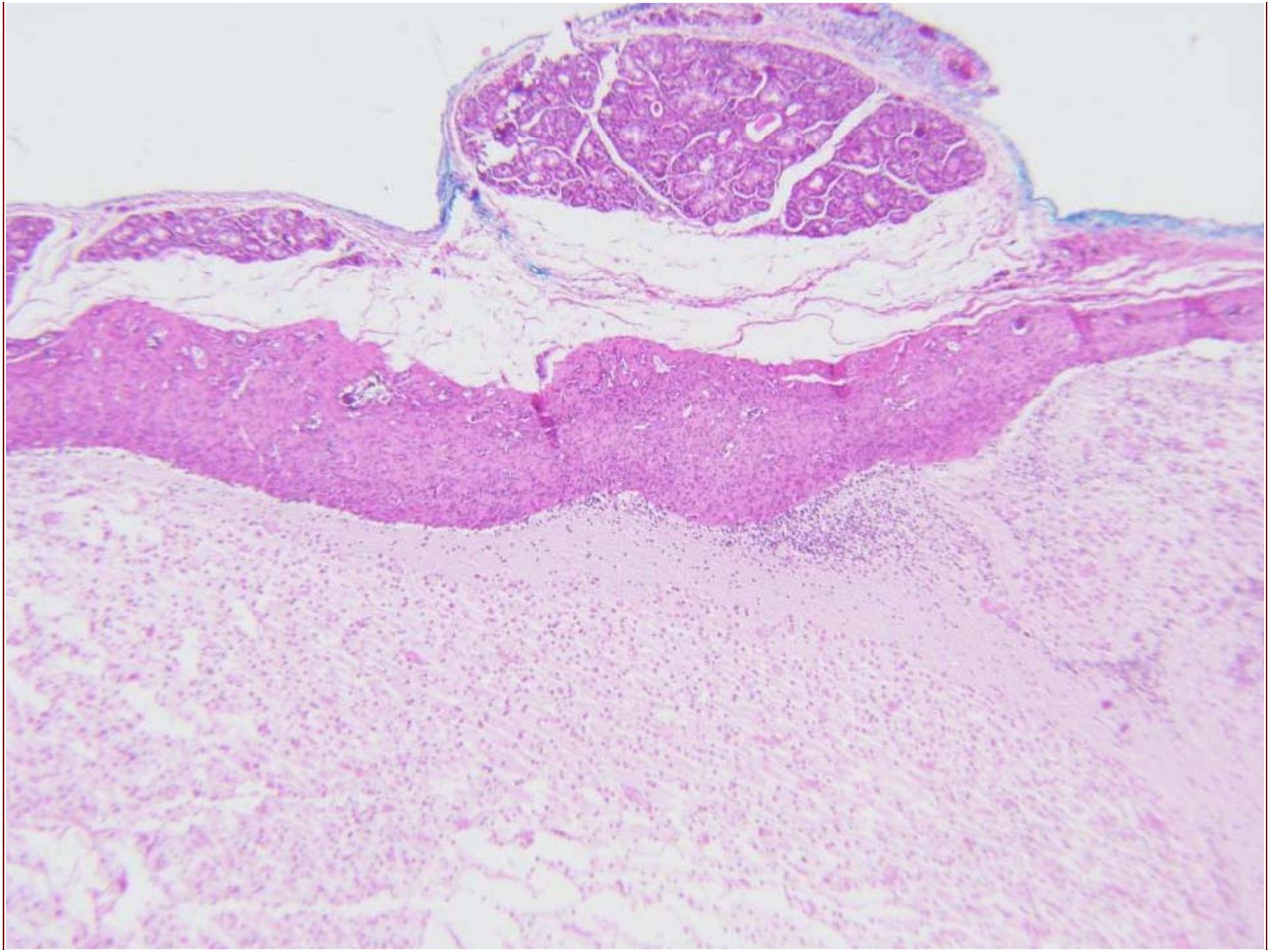


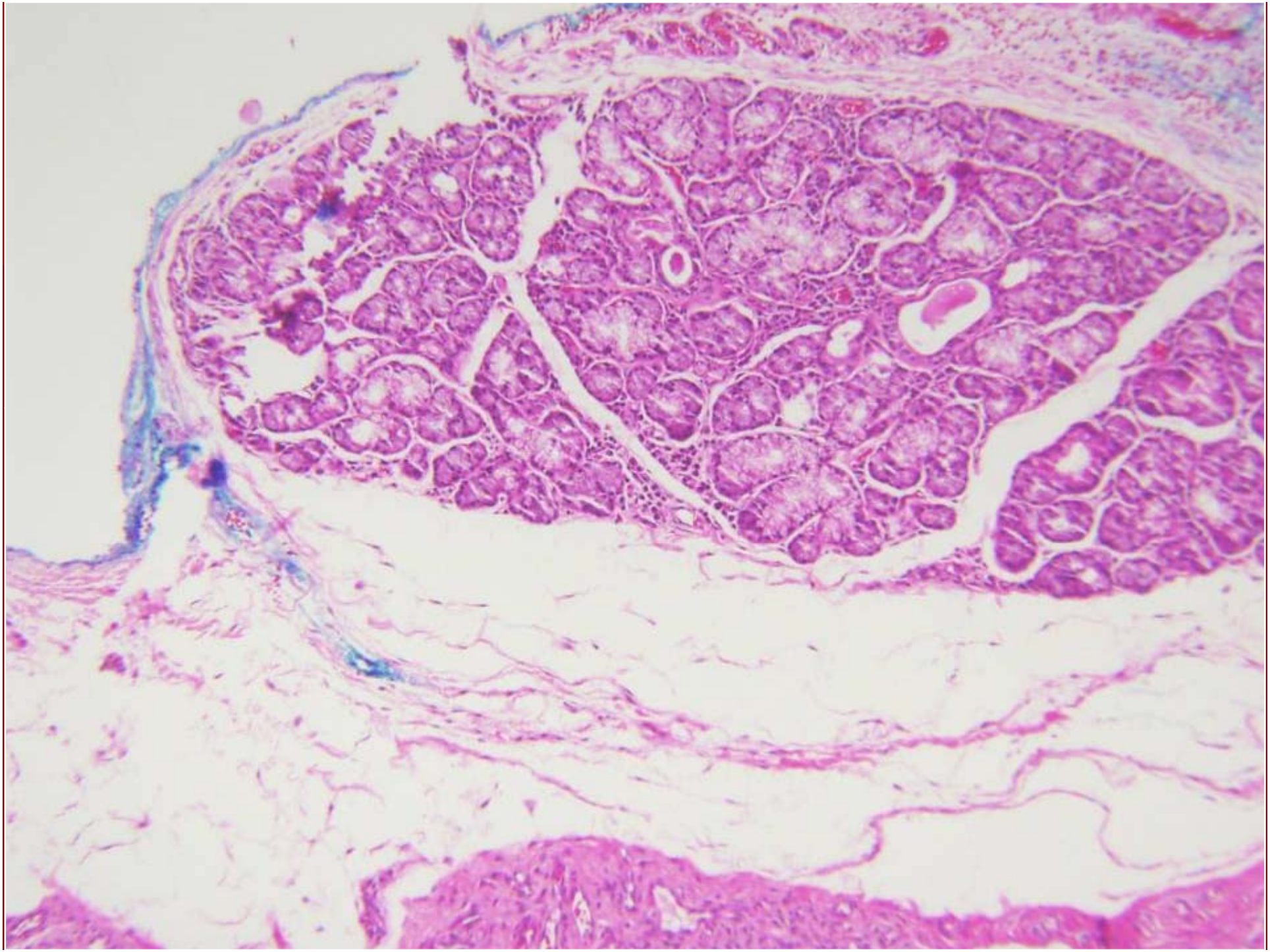
Pretibial myxedema

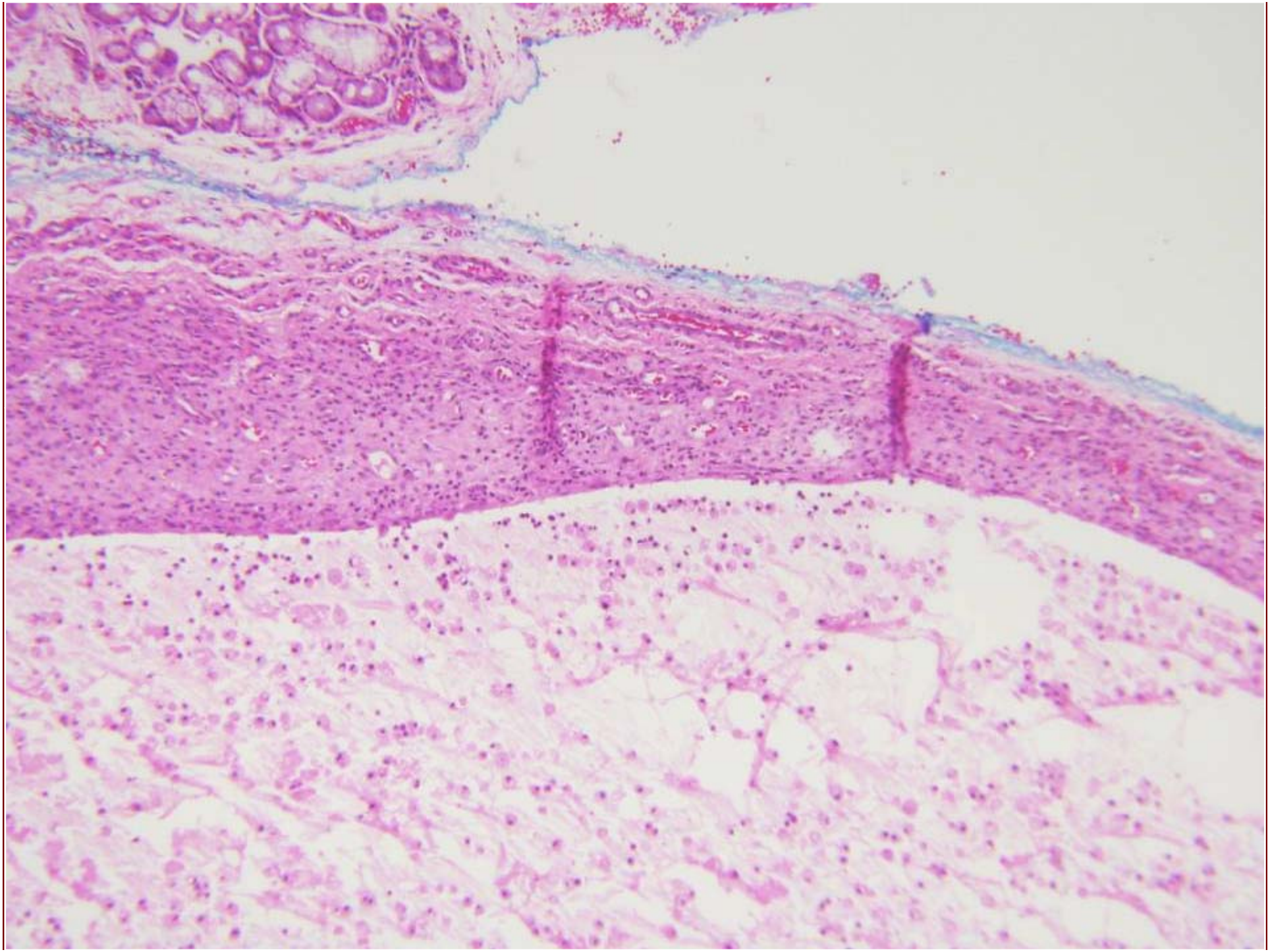
- Histology:
  - Increased mucin often localized to mid and lower dermis
    - Results in wide separation of collagen bundles
      - Why? In tissue, mucin bind lots of water, which is removed by fixation…
  - Fibroblasts NOT increased
- Clinical:
  - Occurs in 1-4% patients with Graves' disease
  - Anterior lower legs – circumscribed nodular lesions
  - Increased production of hyaluronic acid

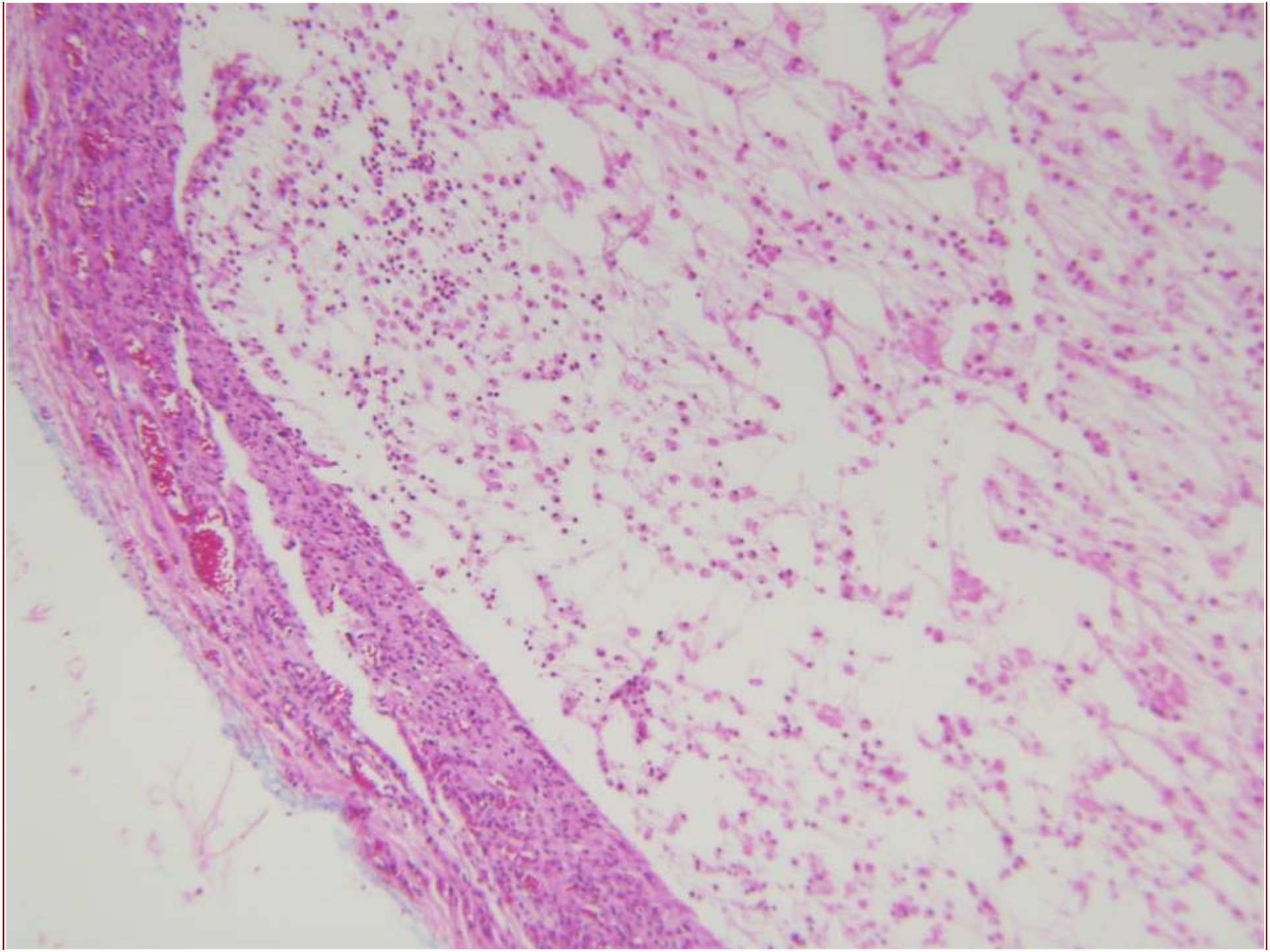
- Case 84







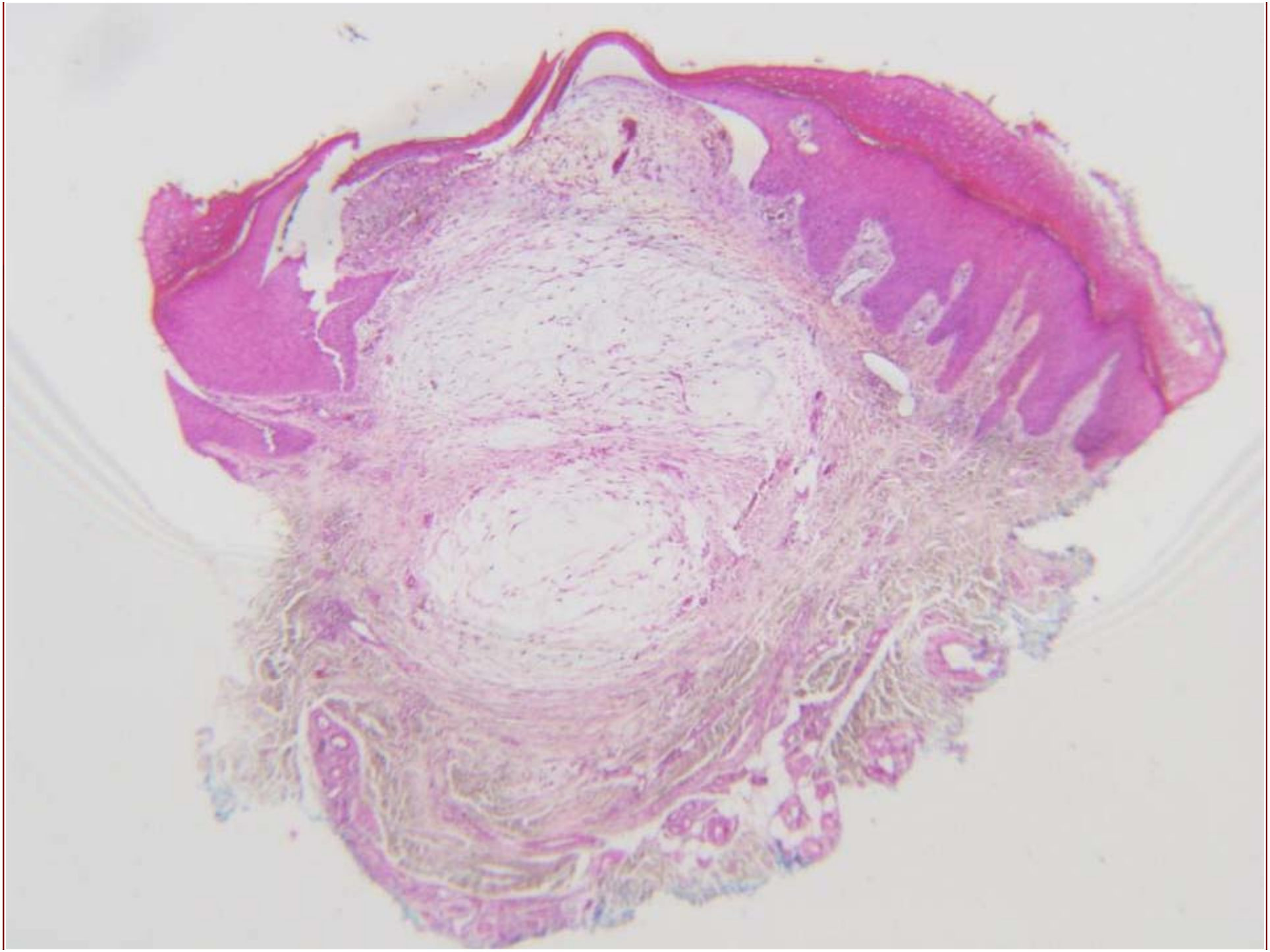


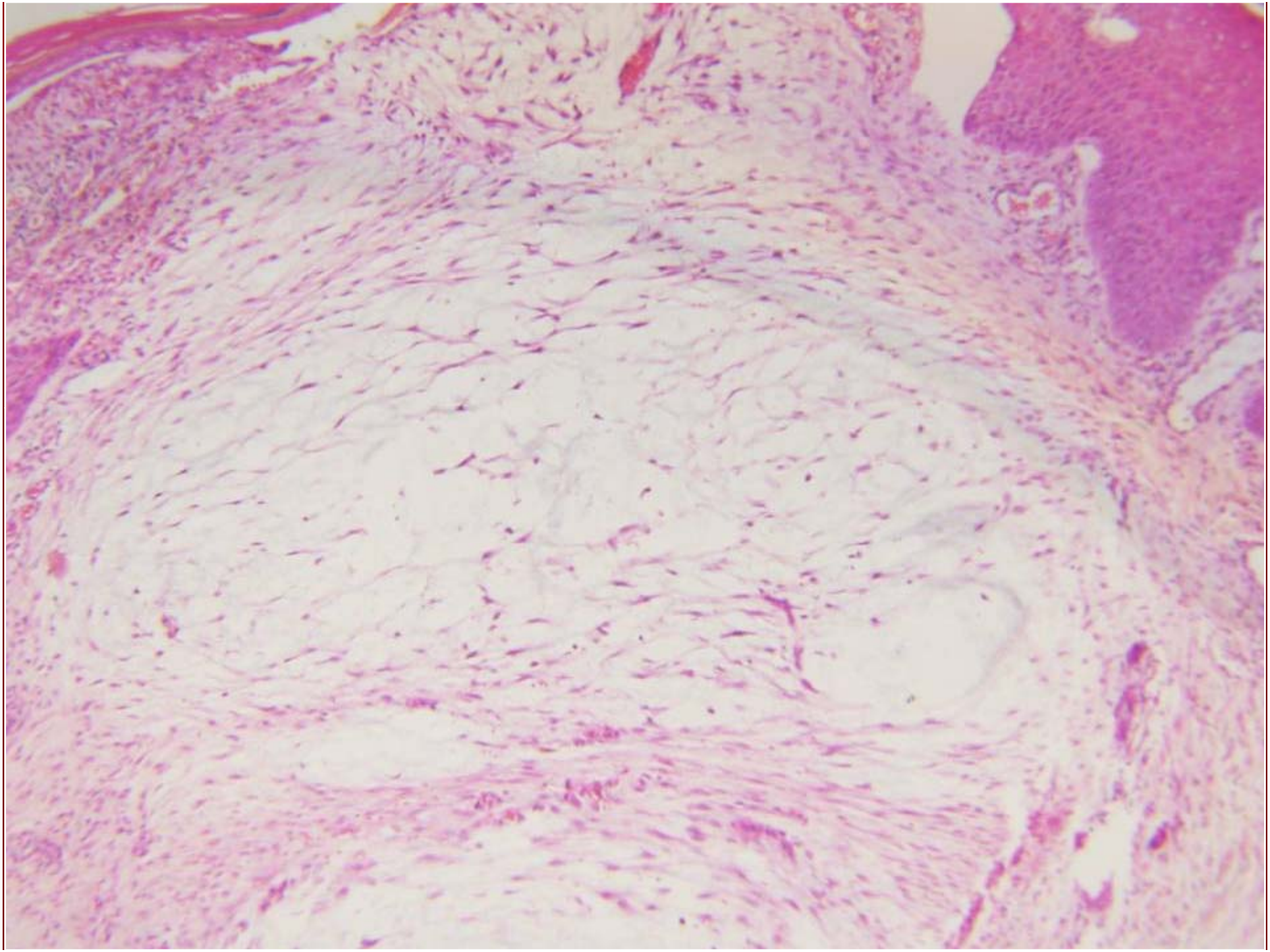


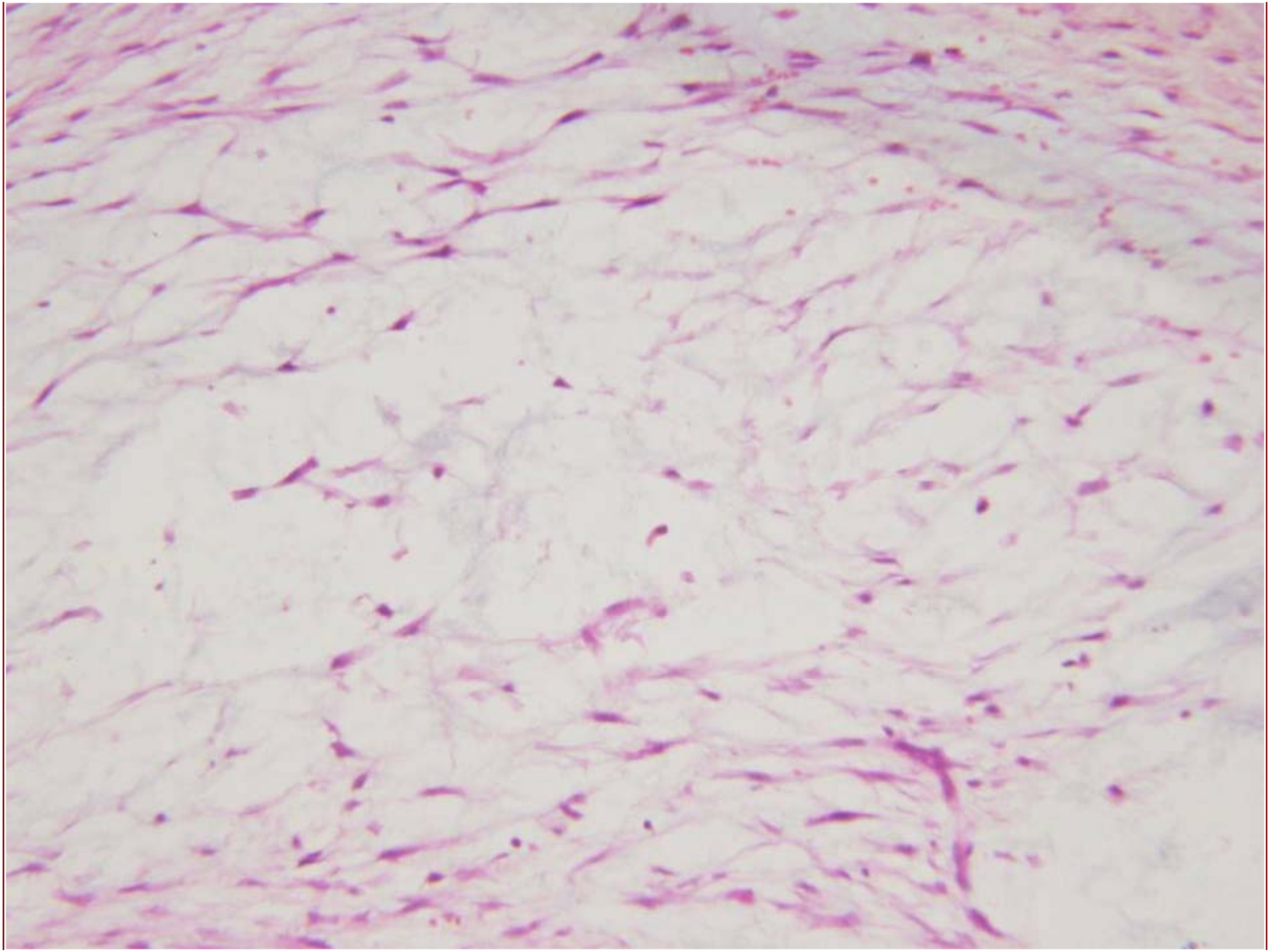
Mucocele

- Histology:
  - NO epithelial lining – actually a “pseudocyst”
  - Cystic space with surrounding granulation and fibrous tissue, poorly defined.
  - Cyst contains mucin and muciphages
- Clinical:
  - Result from rupture of a duct of a minor salivary gland with extravasation of mucus into submucosal tissues
  - White or blue nodules

- Case 85



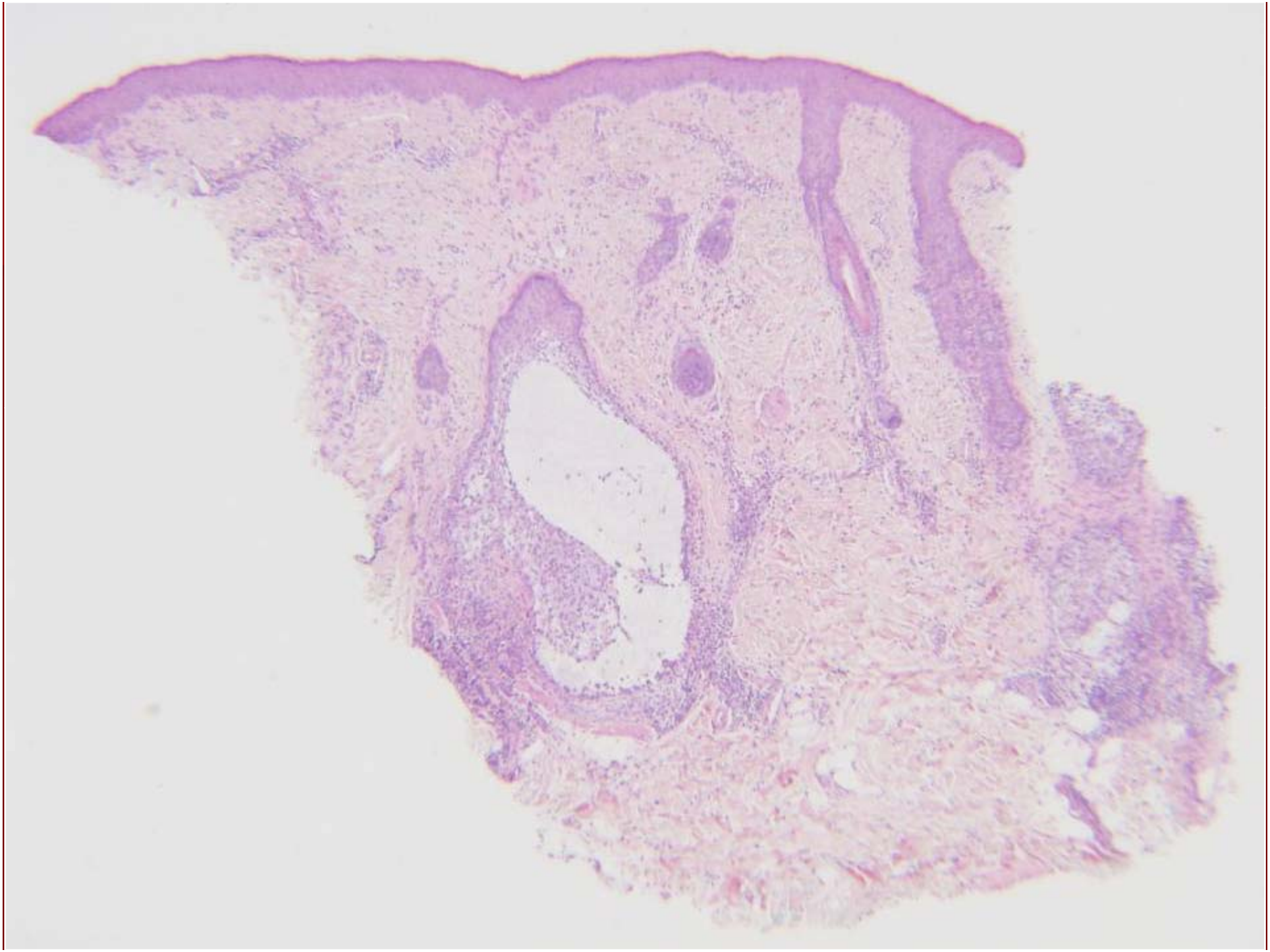


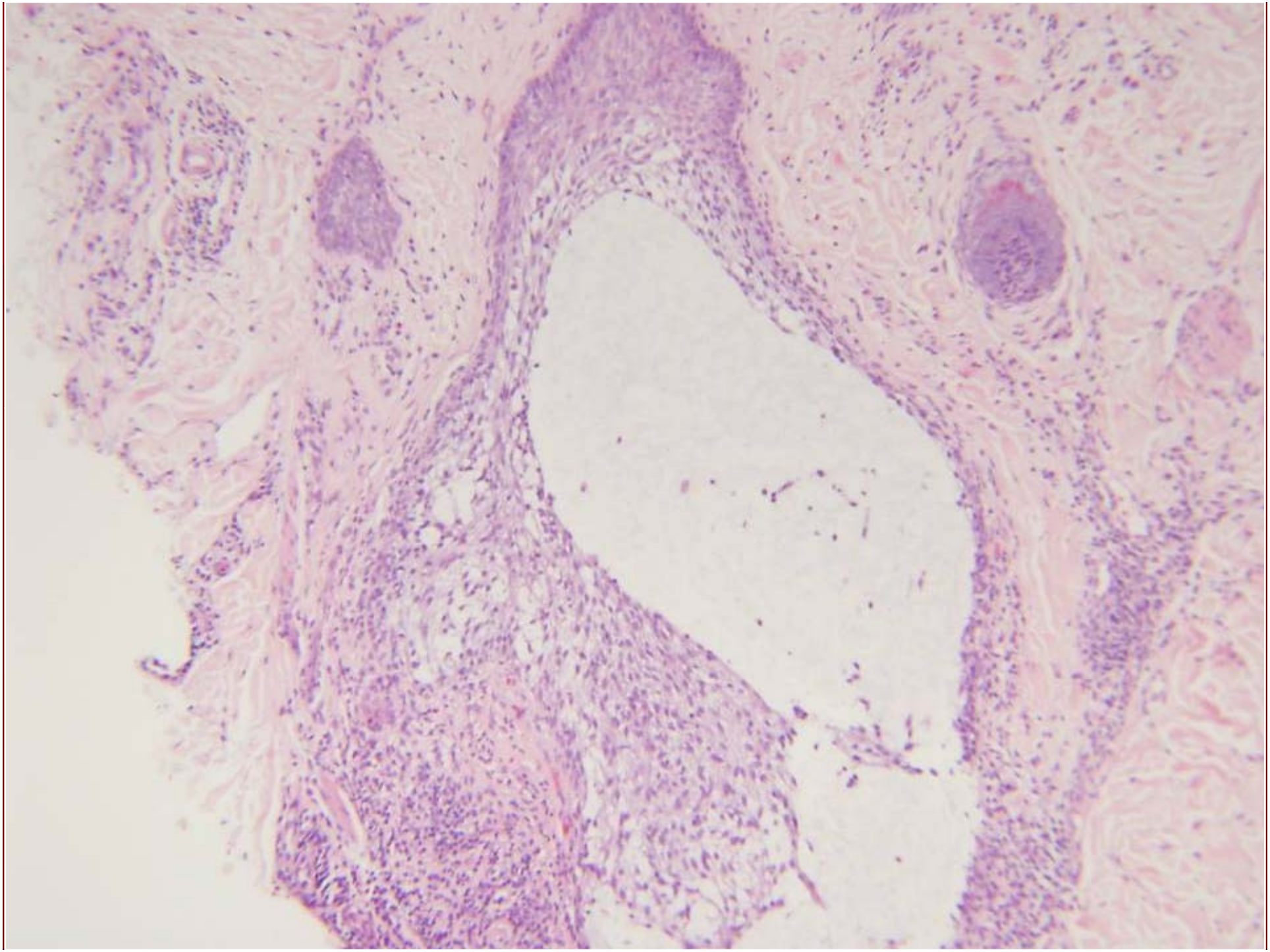


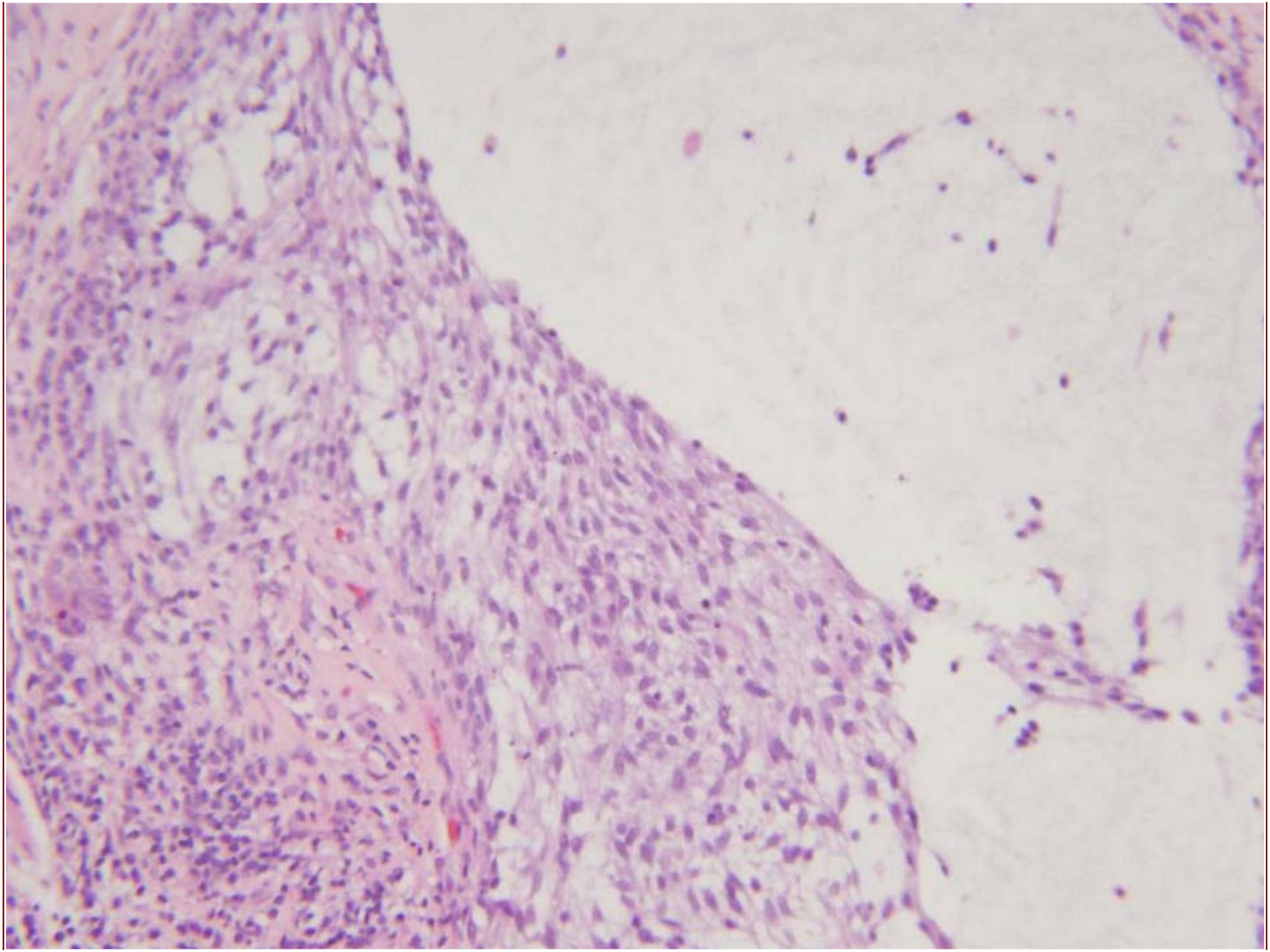
Digital mucus cyst

- Histology:
  - Resembles focal mucinosis
    - Large myxoid area containing stellate fibroblasts, sometimes with microcyst spaces
    - ‘Pool’ of mucin
- Clinical:
  - Solitary, dome-shaped, shiny, tense cystic nodule on the dorsum of the fingers.
  - On acral skin! (c/w focal cutaneous mucinosis)

- Case 86





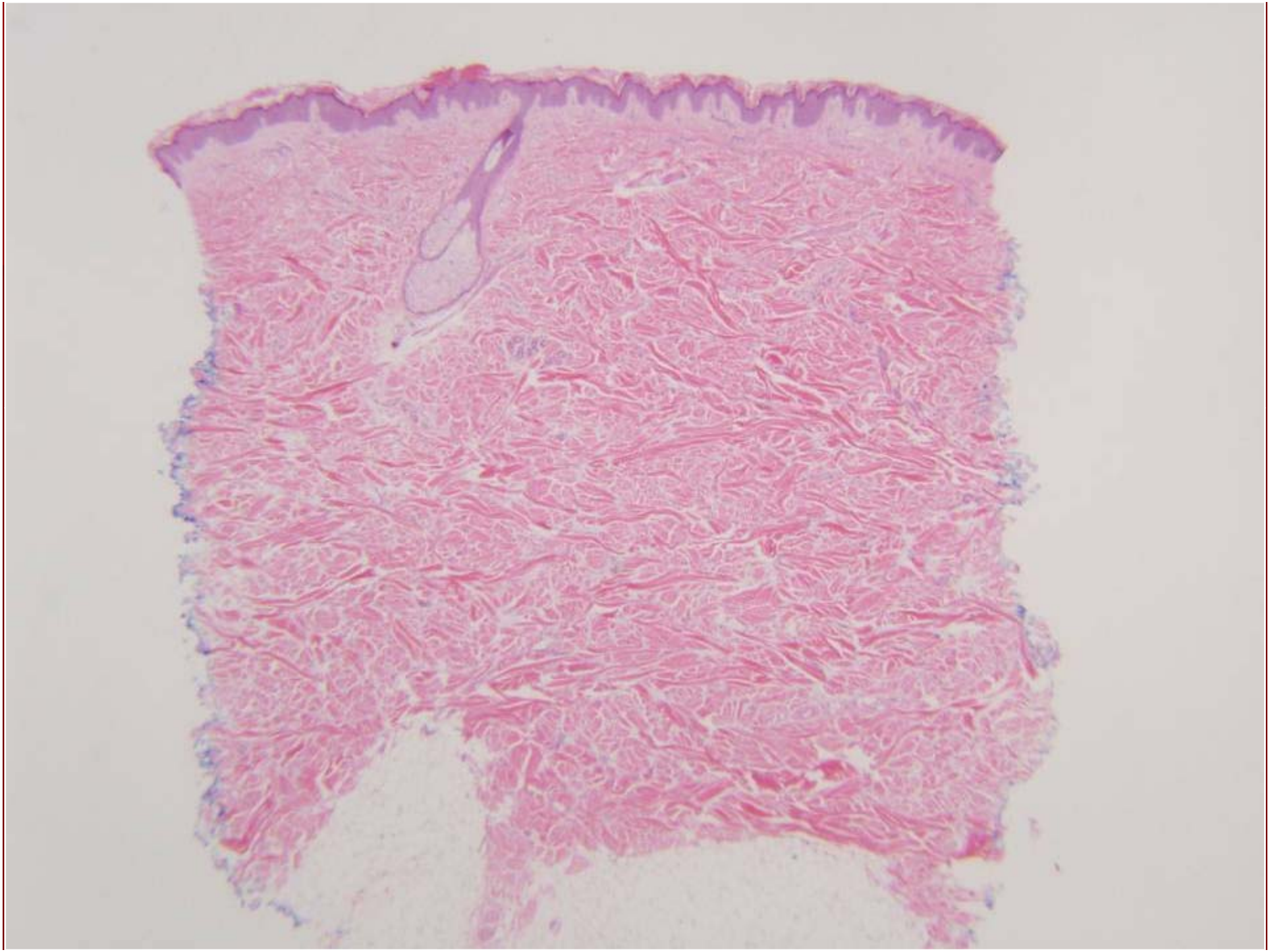


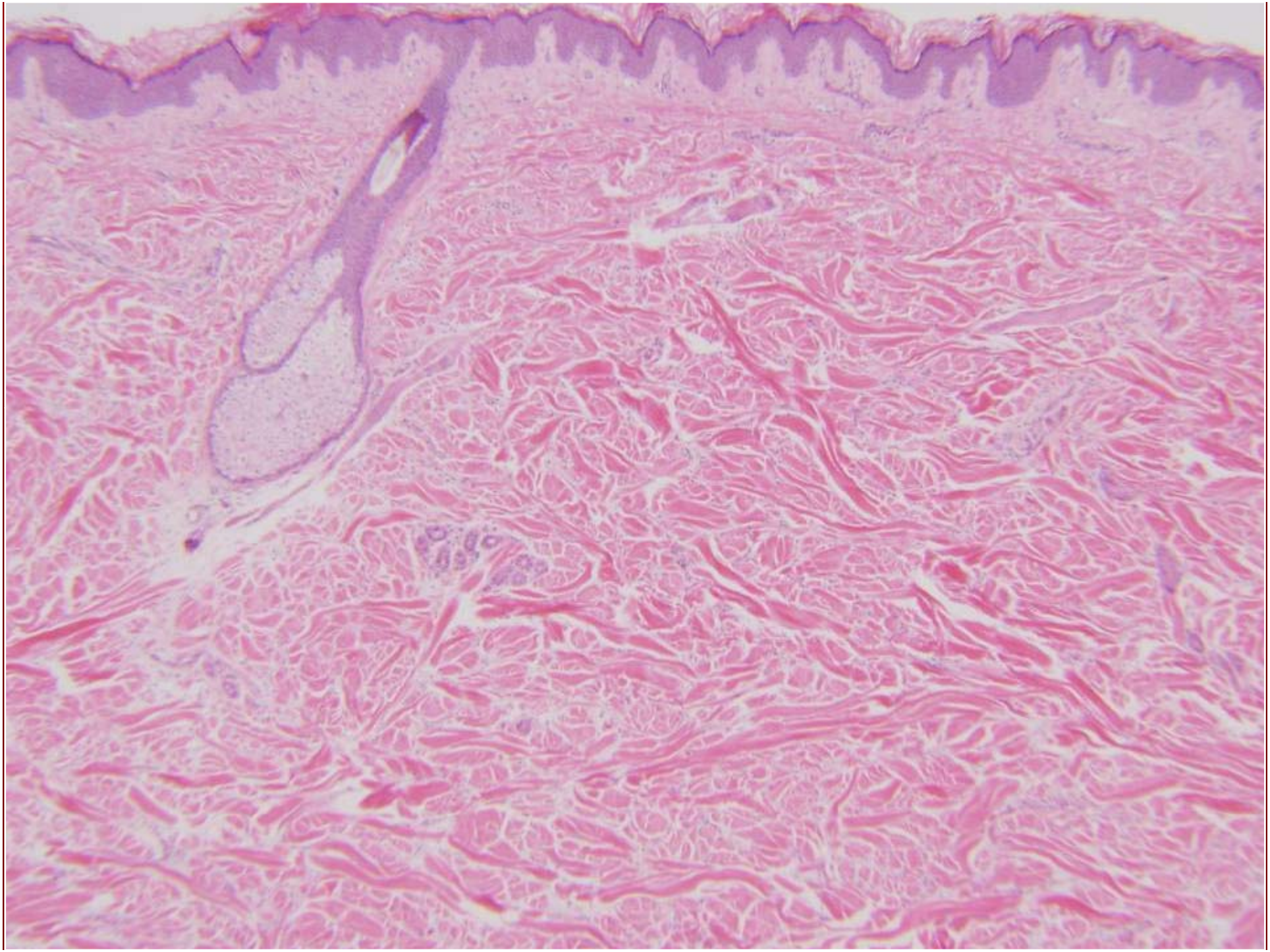
Follicular mucinoses

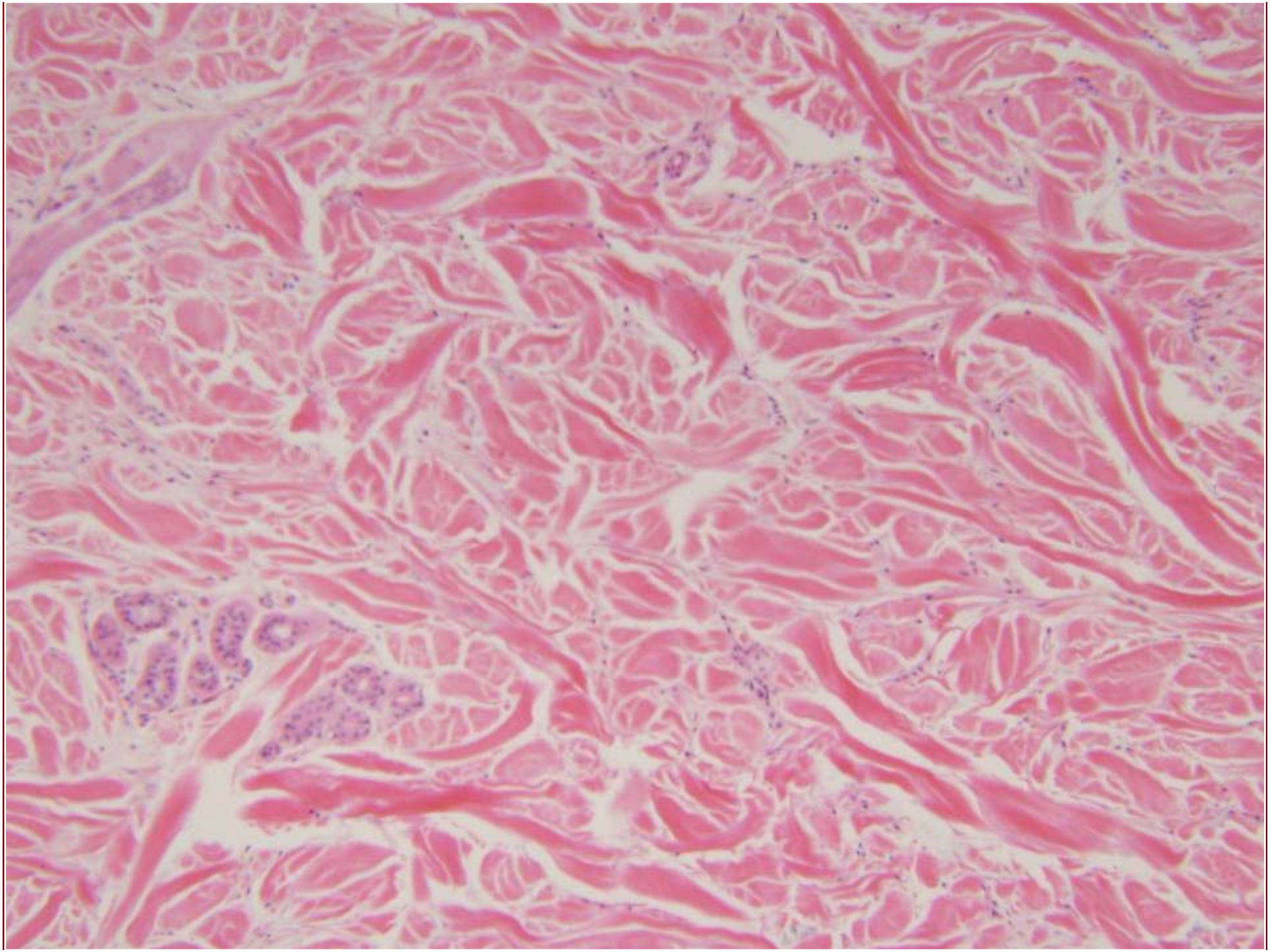
- Histology:
  - Hair follicles (+ sebaceous glands) accumulate mucin
    - Causes keratinocytes to disconnect
  - Mixed perifollicular and perivascular inflammatory cell infiltrate
  - Sometimes follicles are converted into cystic cavities

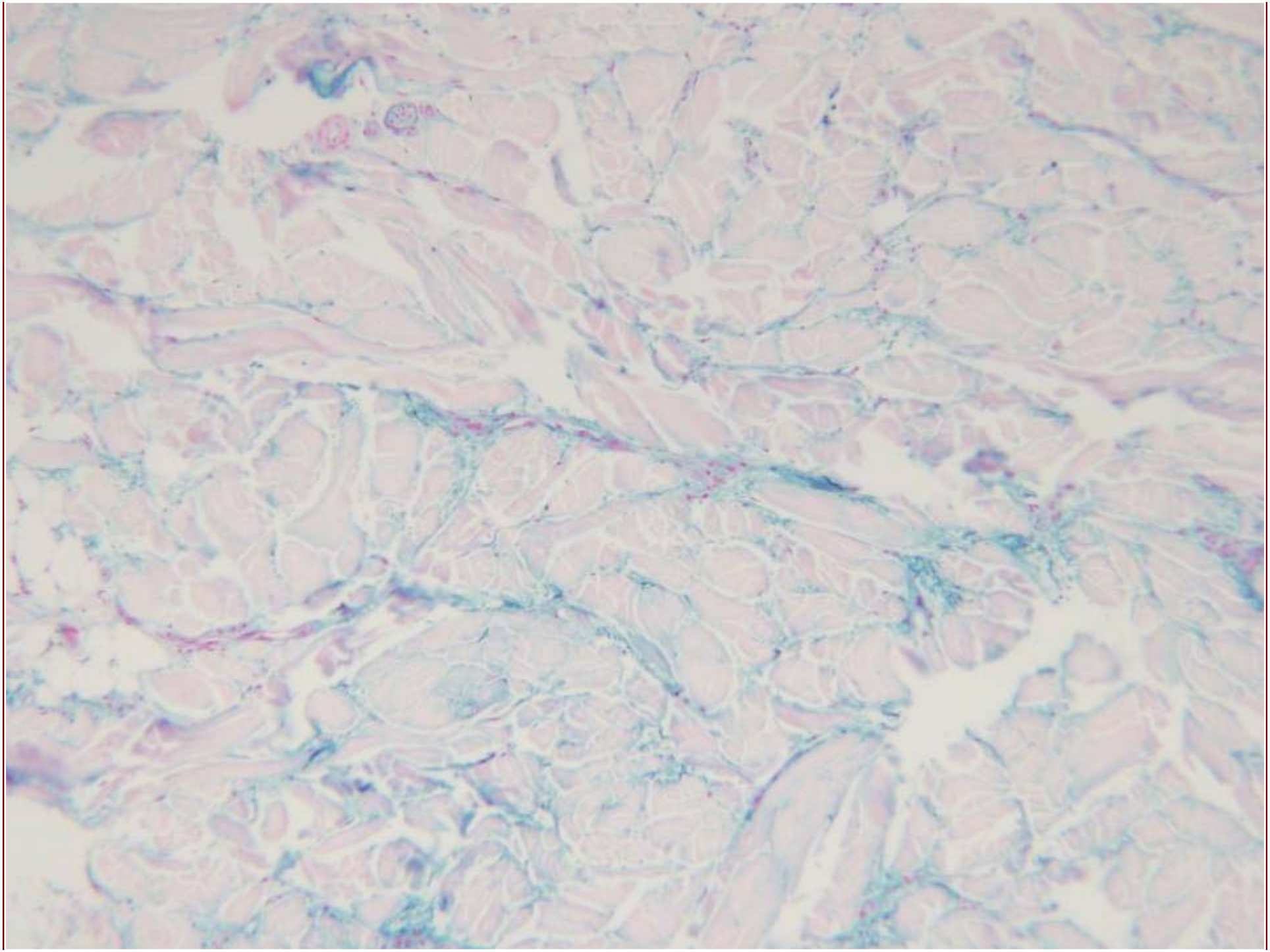
- Clinical:
  - Two primary entities
    - Pinkus' follicular mucinosis
    - Urticaria-like follicular mucinosis
  - "Tissue reaction pattern"
    - Mycosis fungoides
    - Arthropod bites
    - Lymphoma
    - Spongiotic dermatitis
    - Lupus erythematosus
    - Other

- Case 87 a & b





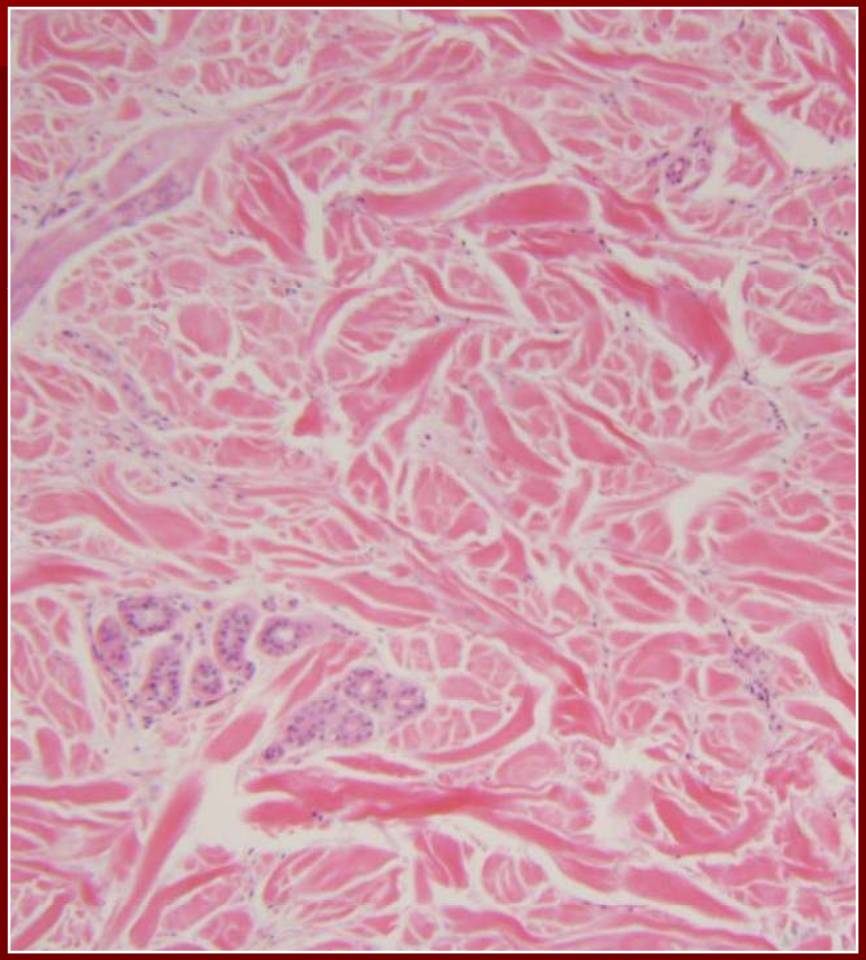


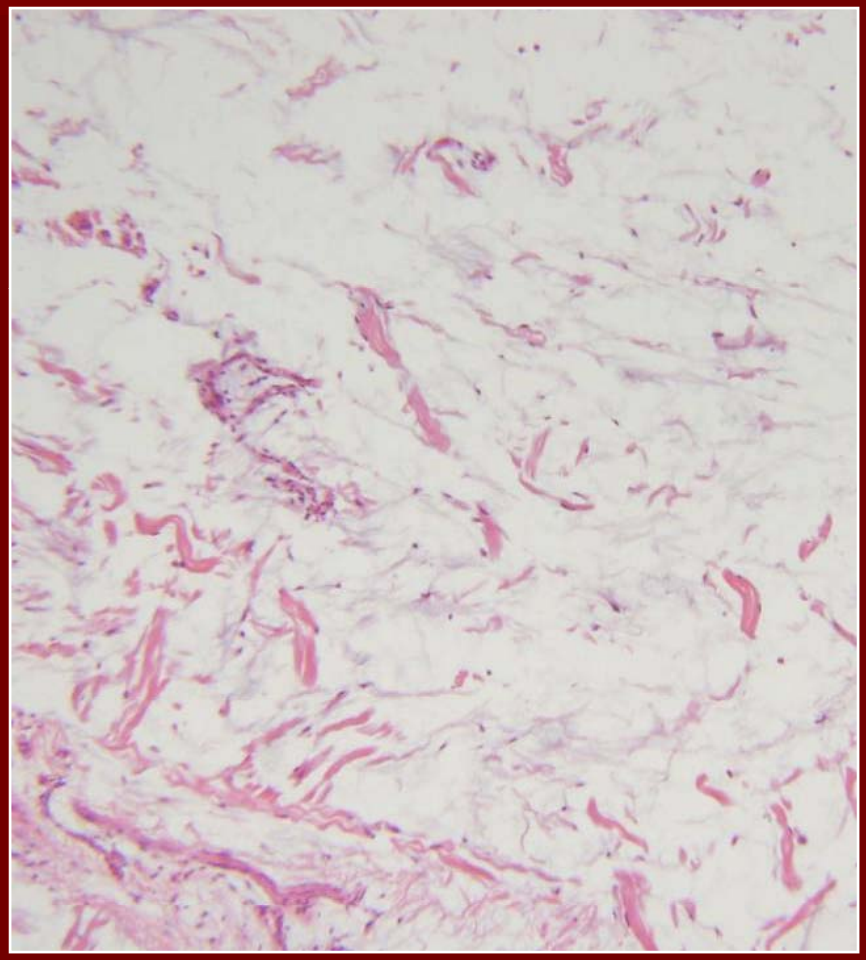


Scleredema

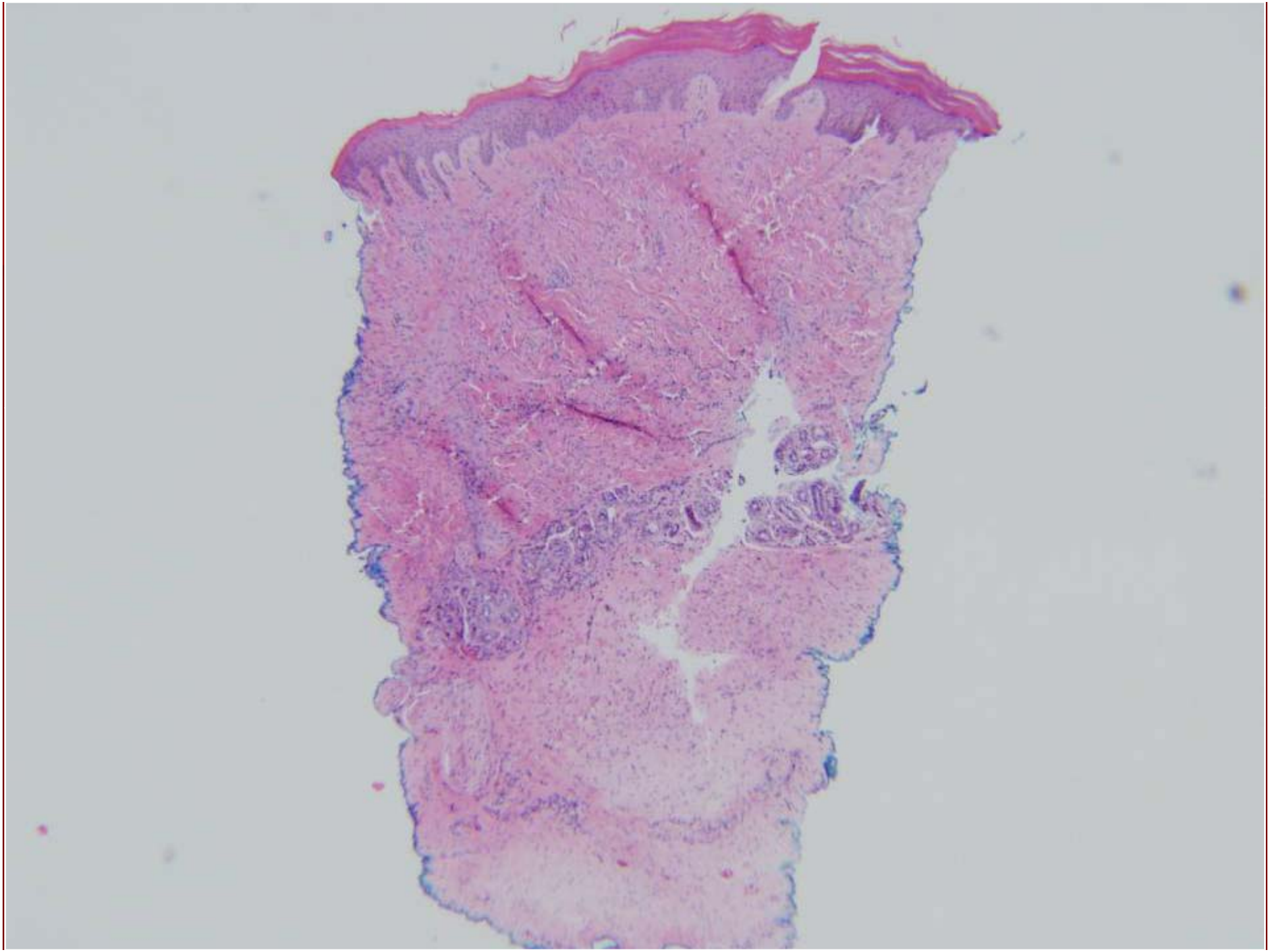
- Histology:
  - Collagen bundles swollen and separated from each other
  - Increased mucin
    - May be very difficult to definitively identify increased mucin – remember, scleredema is in differential of Normal skin biopsy
  - NO increase in cellularity

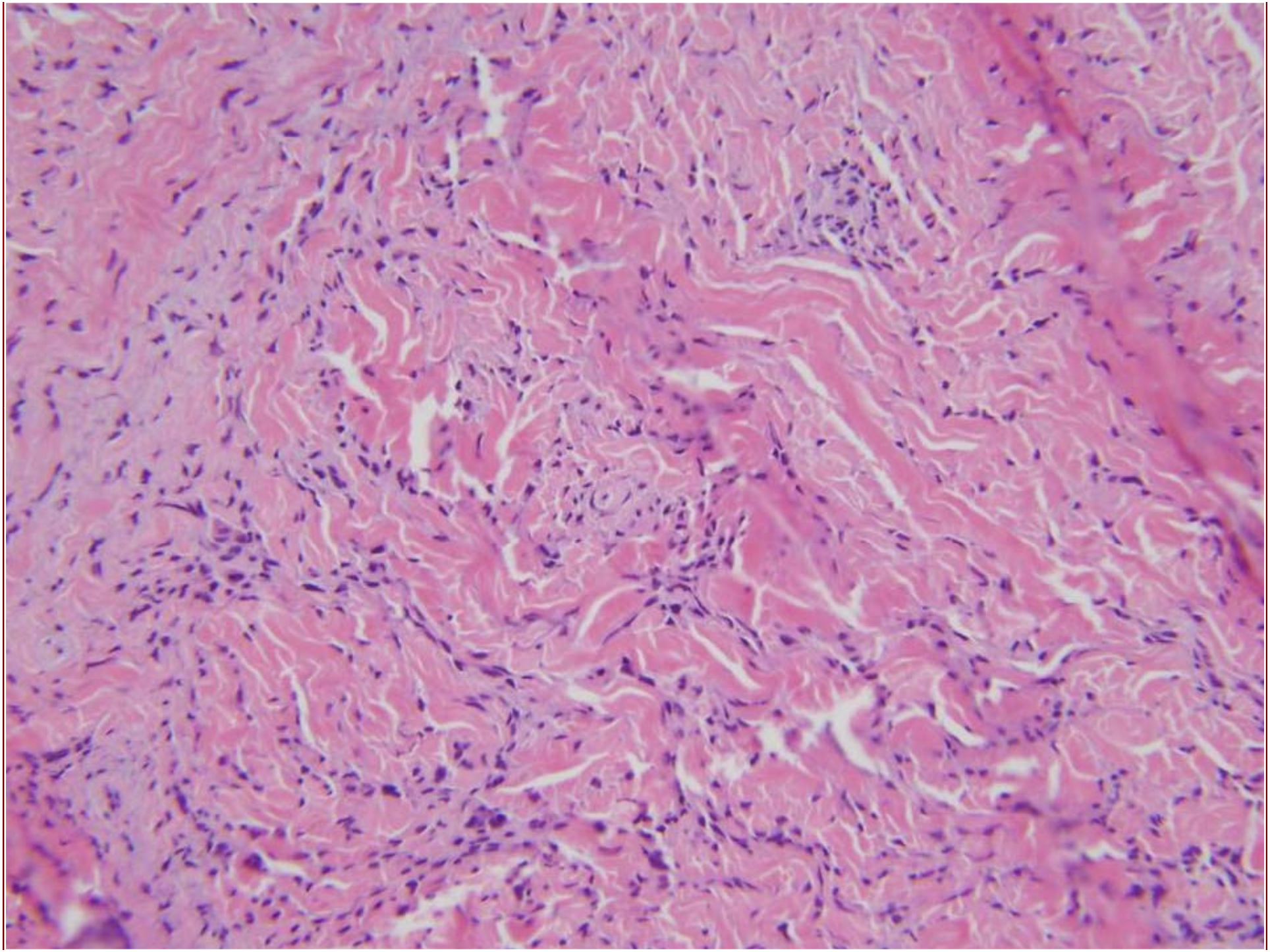
- Clinical:
  - 3 types
    1. Middle aged man, diabetes, on shoulders, upper back – erythema and induration
    2. Middle aged women/children, post strep infection of respiratory tract – skin of cervicofacial region hardens suddenly
    3. Same as #2, but no preceding infection, longer duration, a/w monoclonal gammopathy

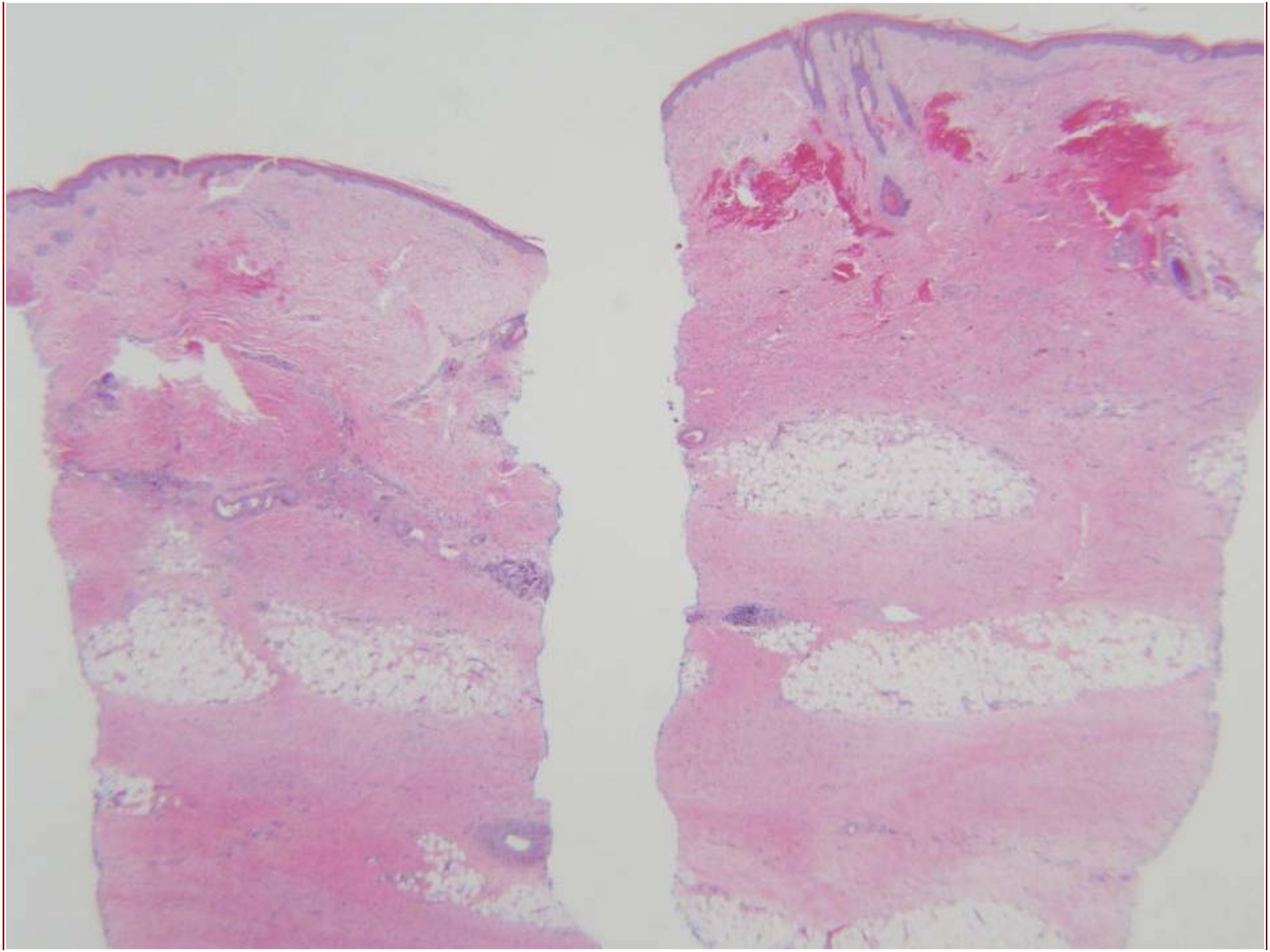


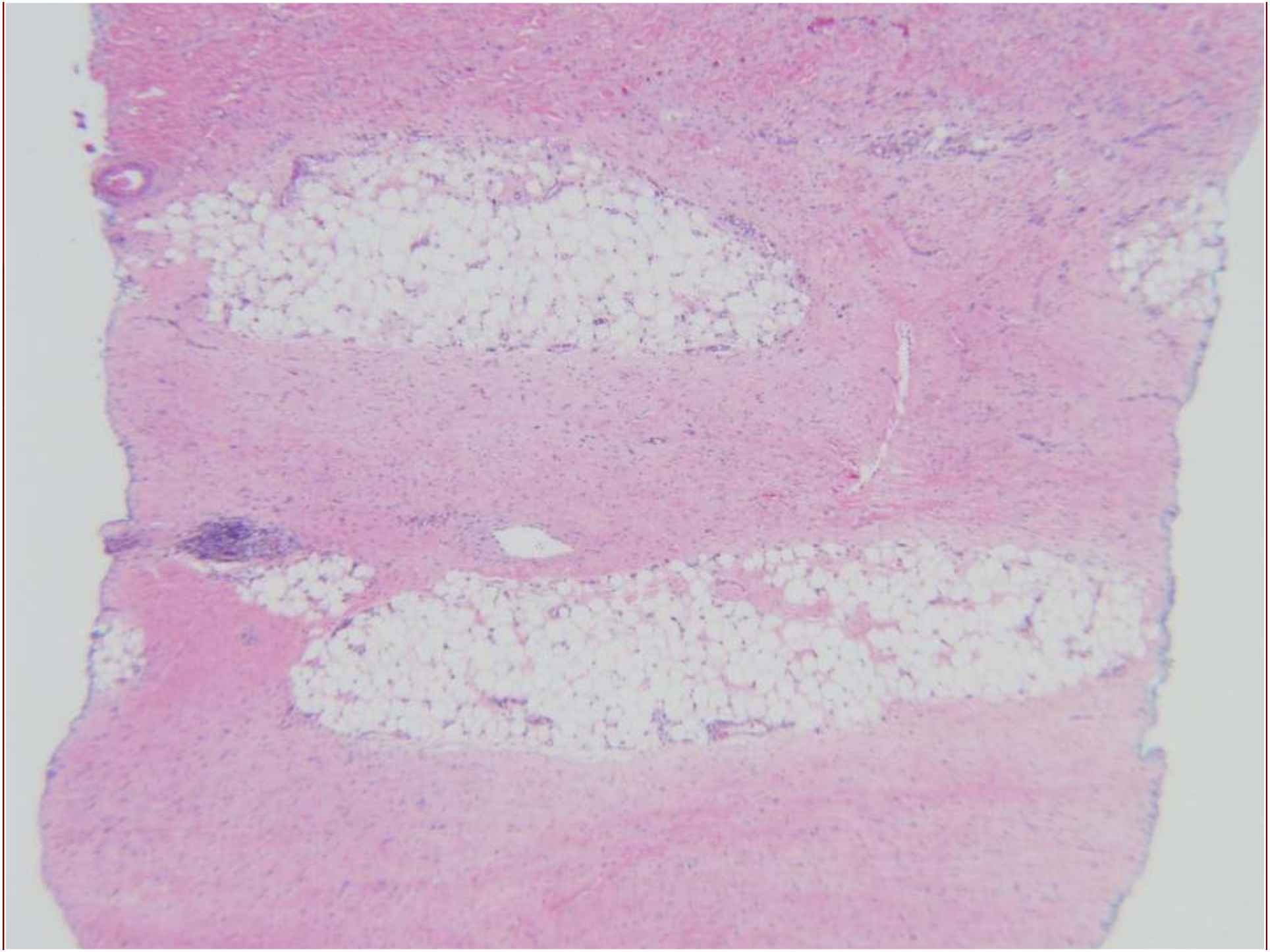


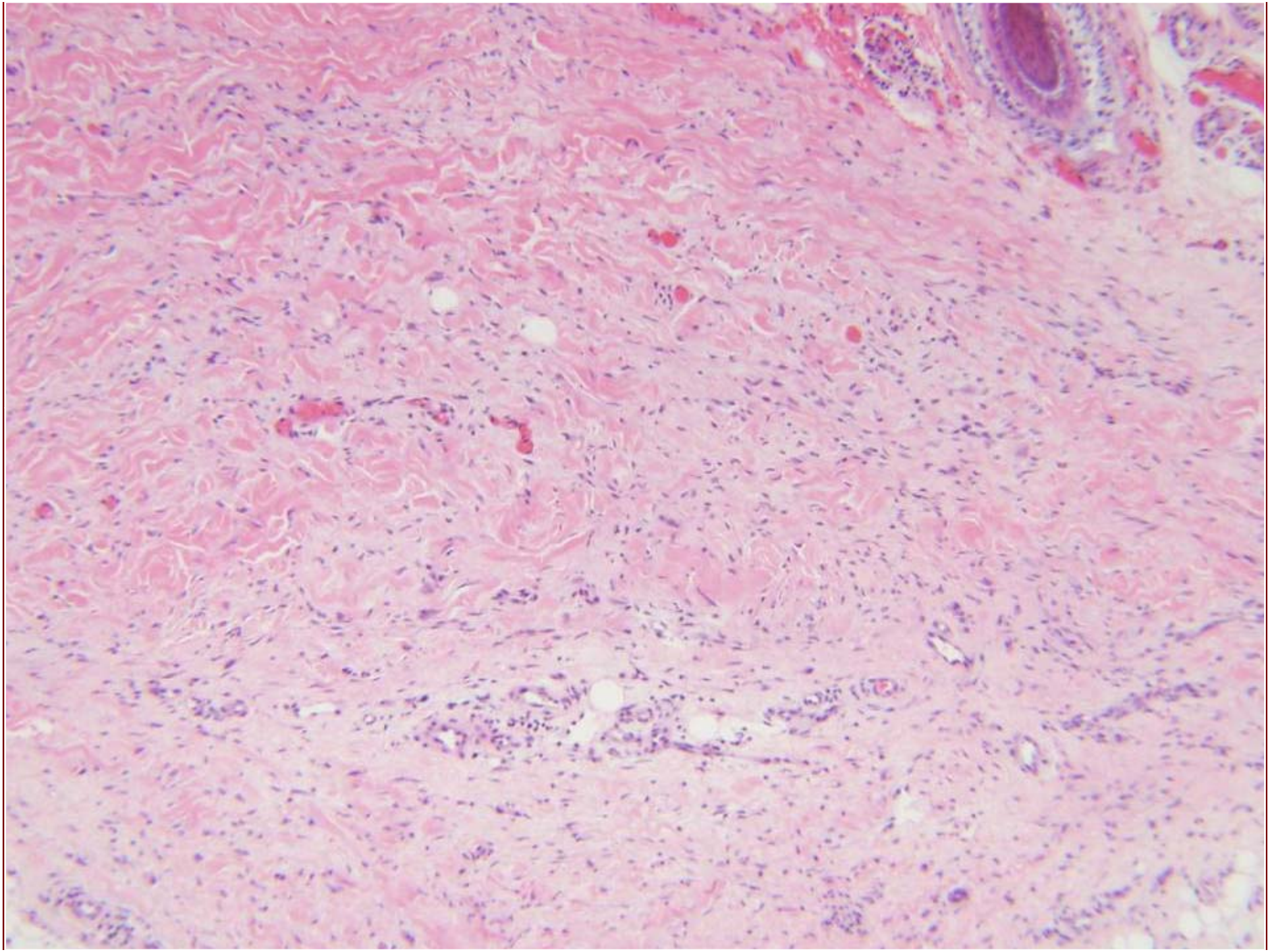
- Case 80 a & b

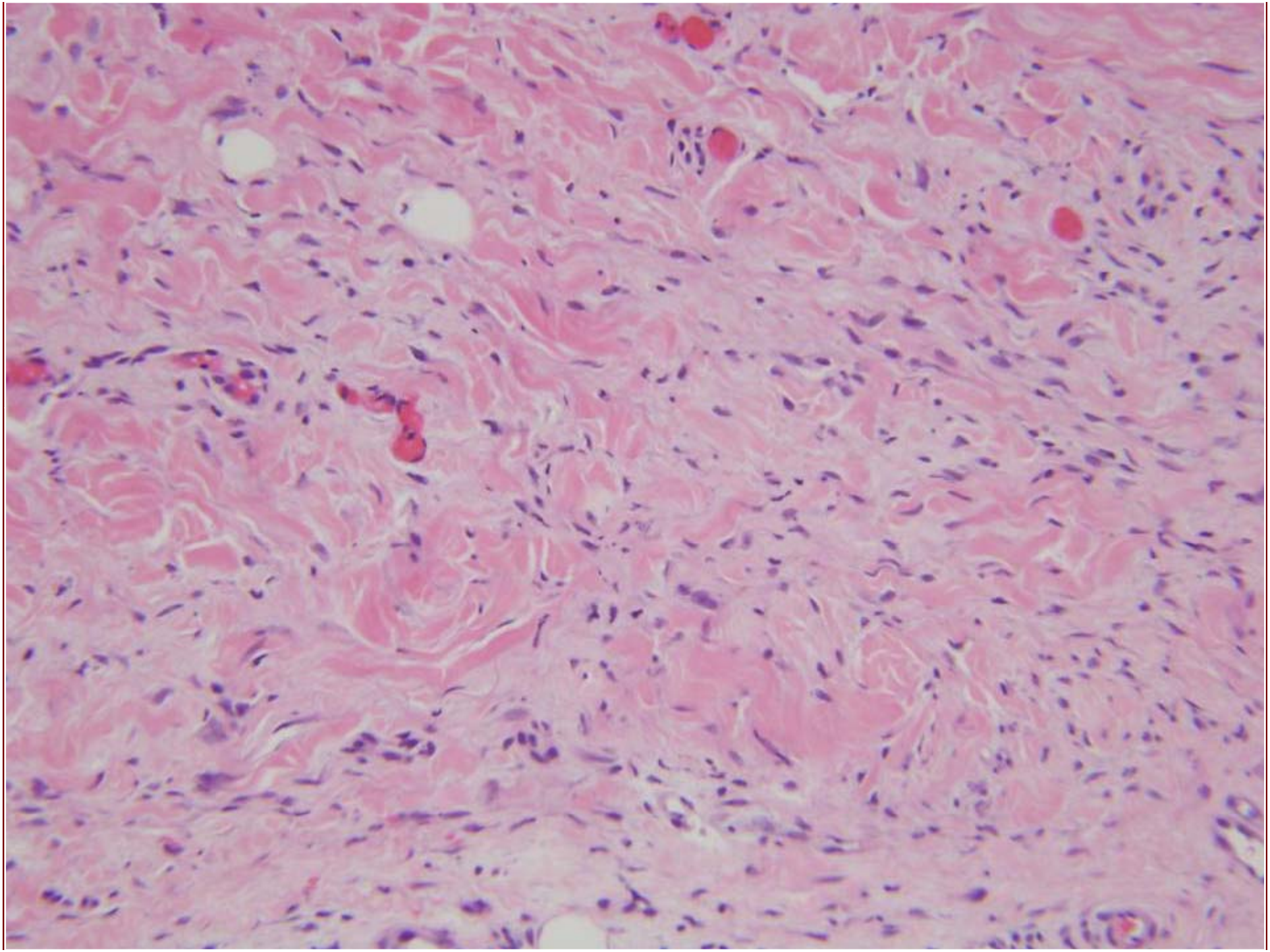


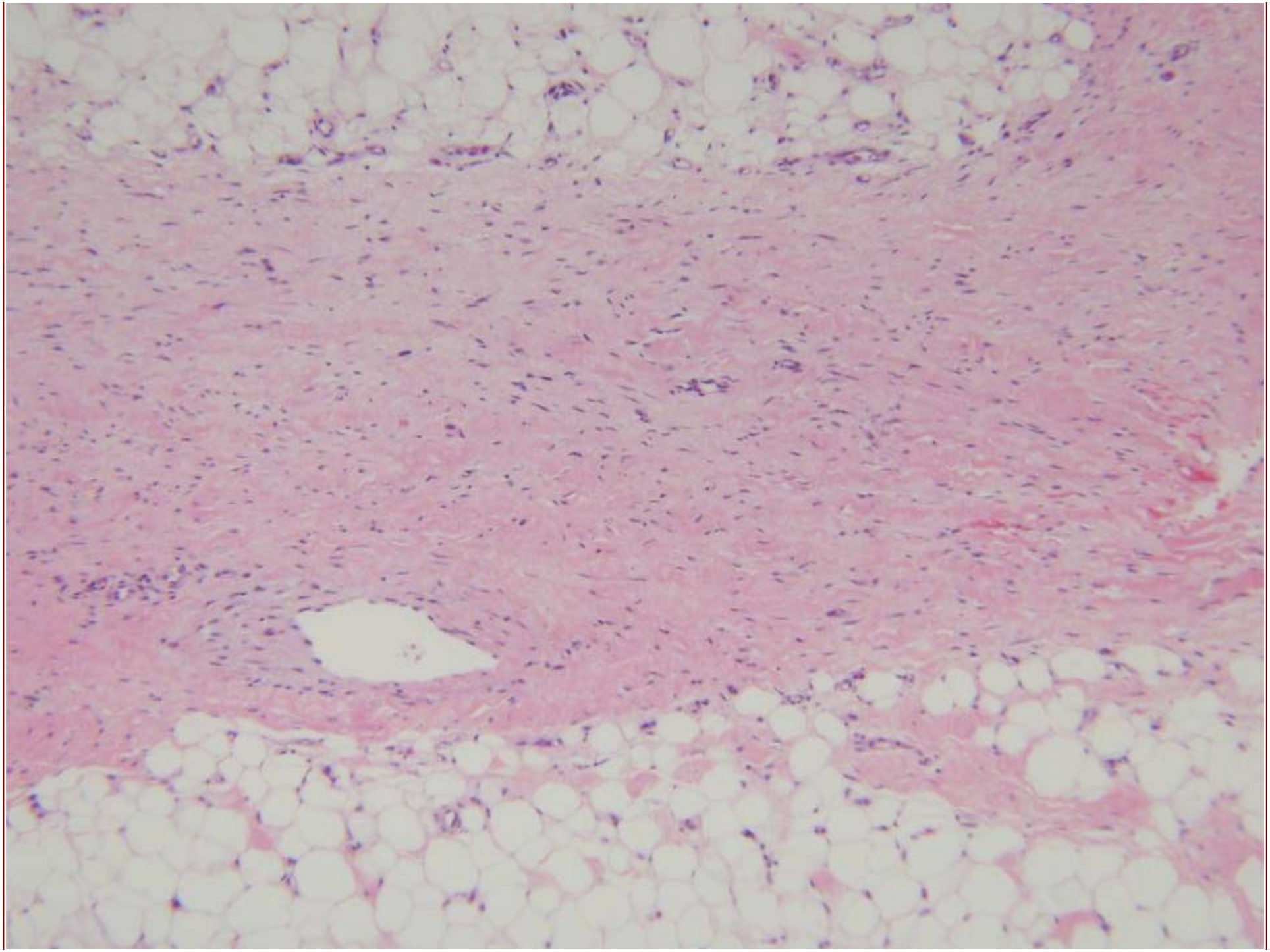












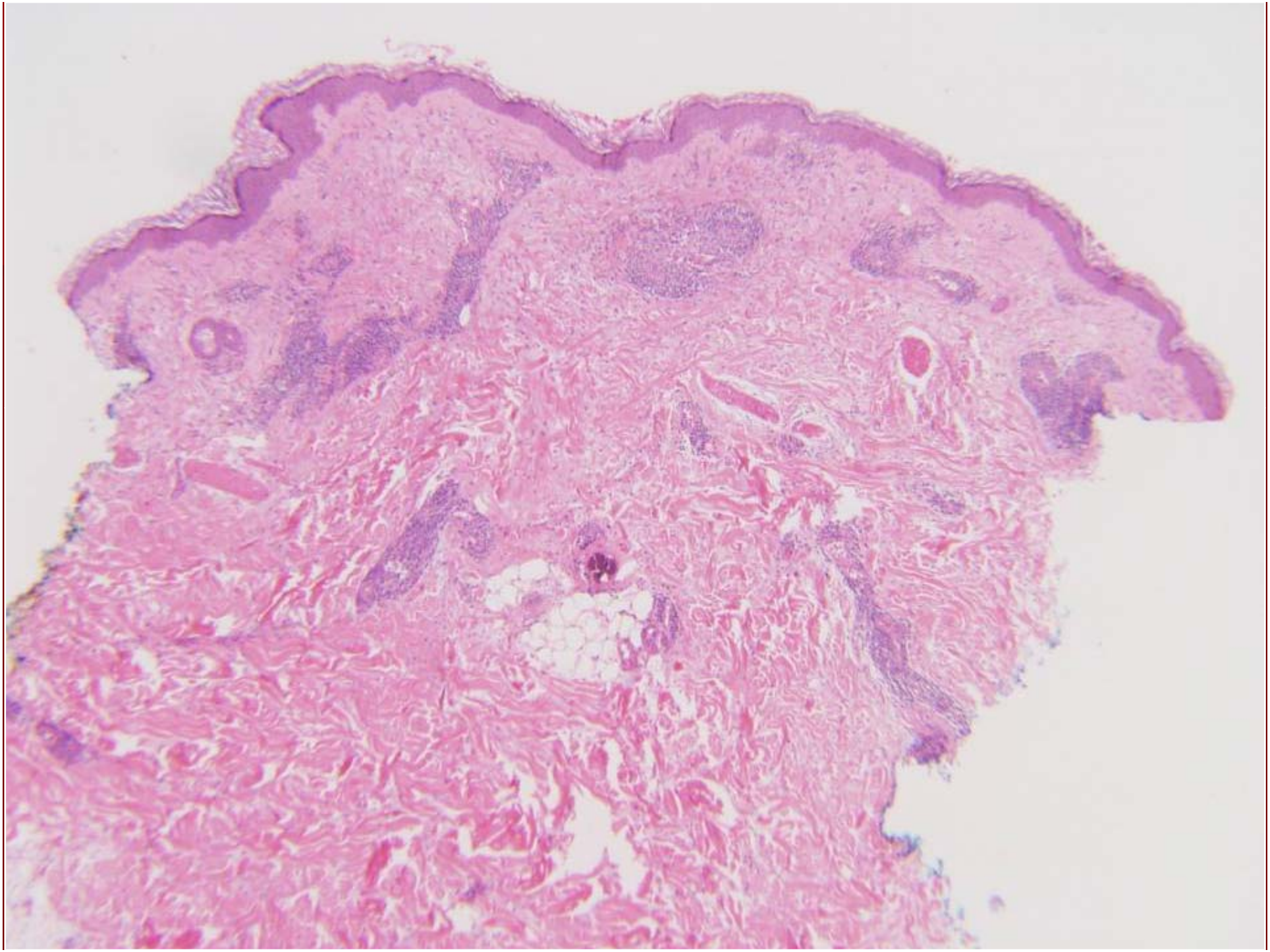
Nephrogenic systemic fibrosis

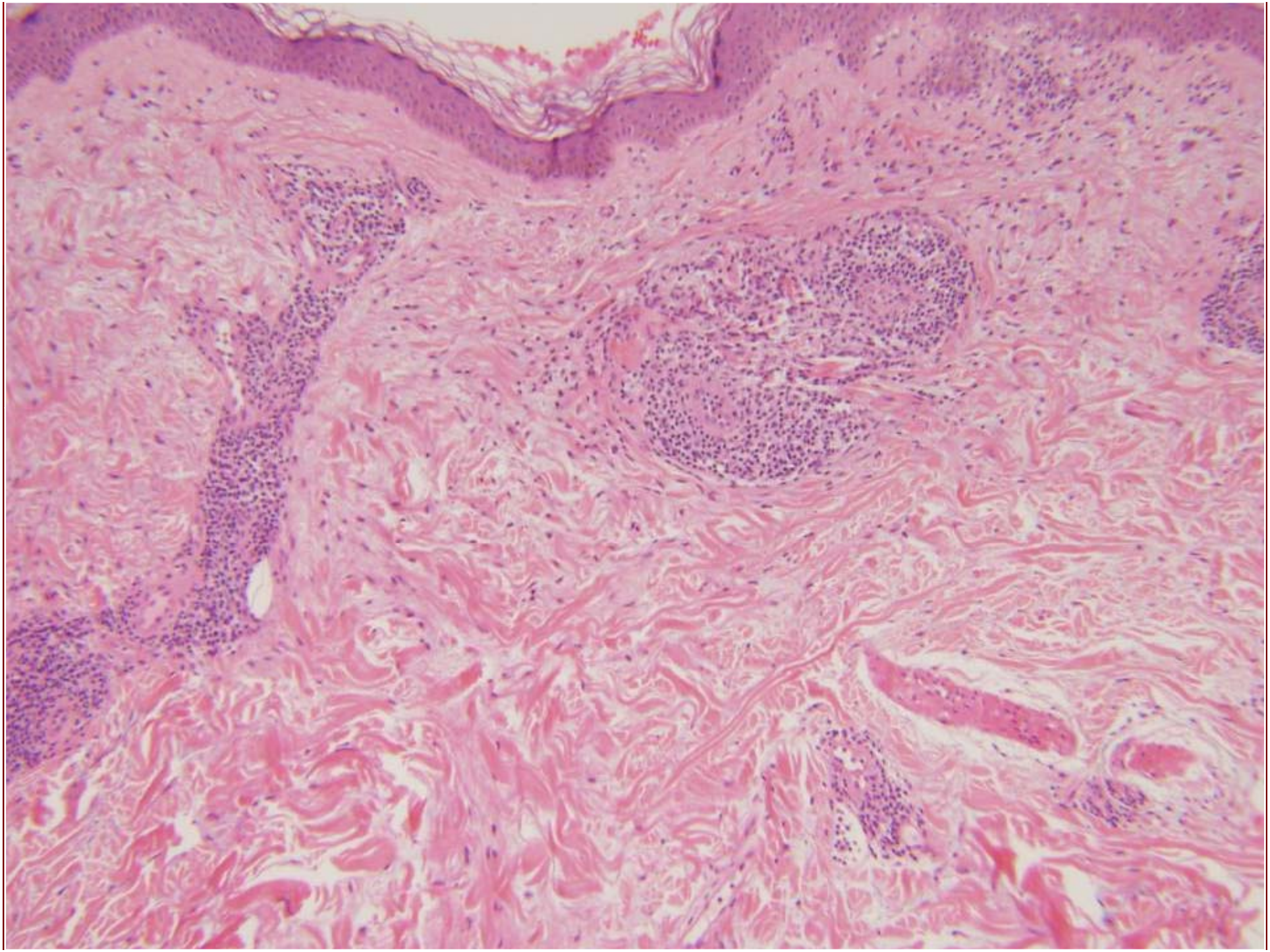
- Aka nephrogenic fibrosing dermopathy

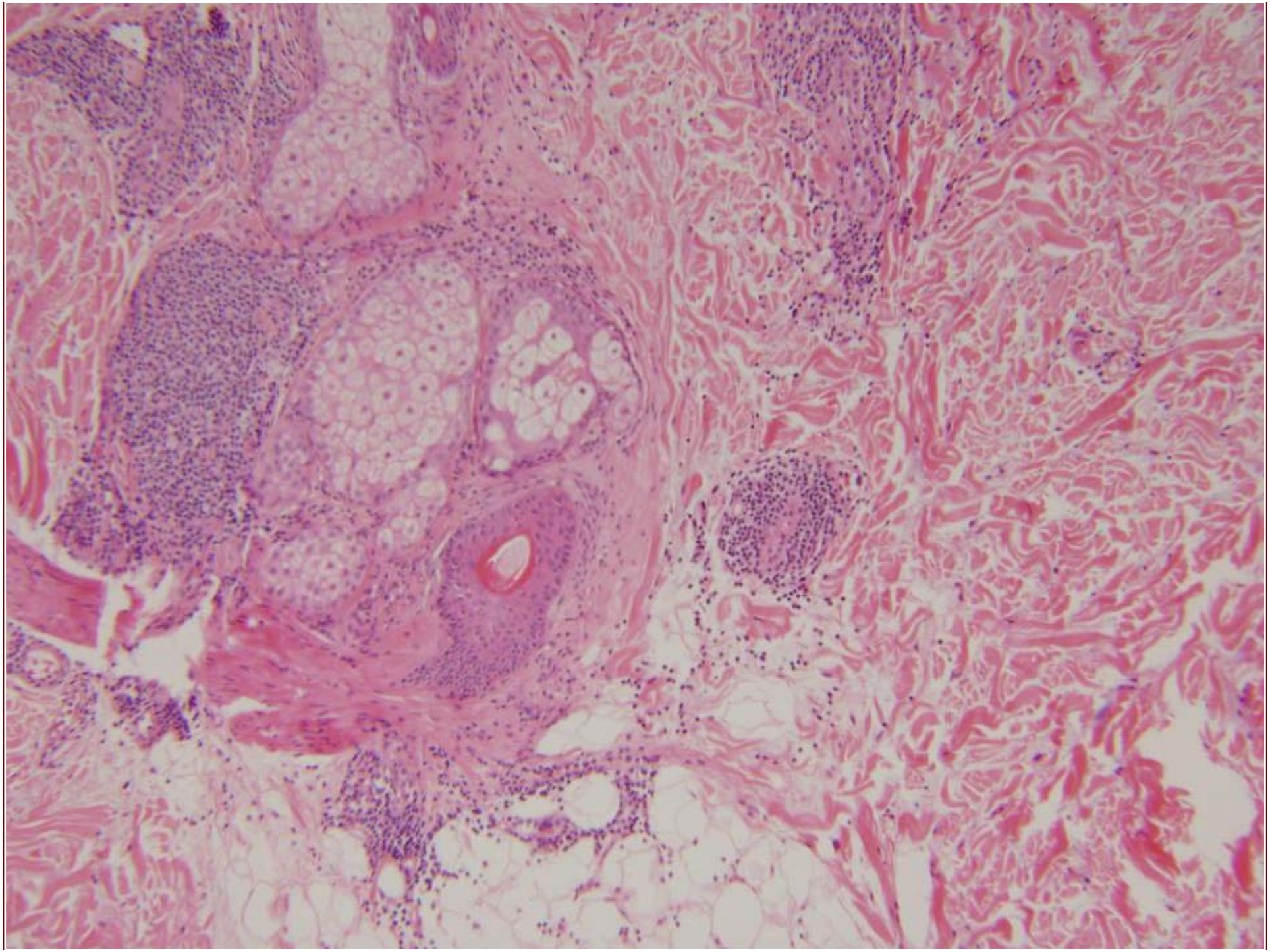
- Histology:
  - Scleredema
    - Increased mucin only
  - Scleromyxedema
    - Increased mucin AND fibroblasts early
    - Even more fibroblasts late w/ irregularly distributed thickened collagen
    - Results in THICKENED dermis
    - Mixed inflammation (+ multinucleate histiocytes)
  - NSF (sister to scleromyxedema)
    - Less mucin and inflammation than scleromyxedema

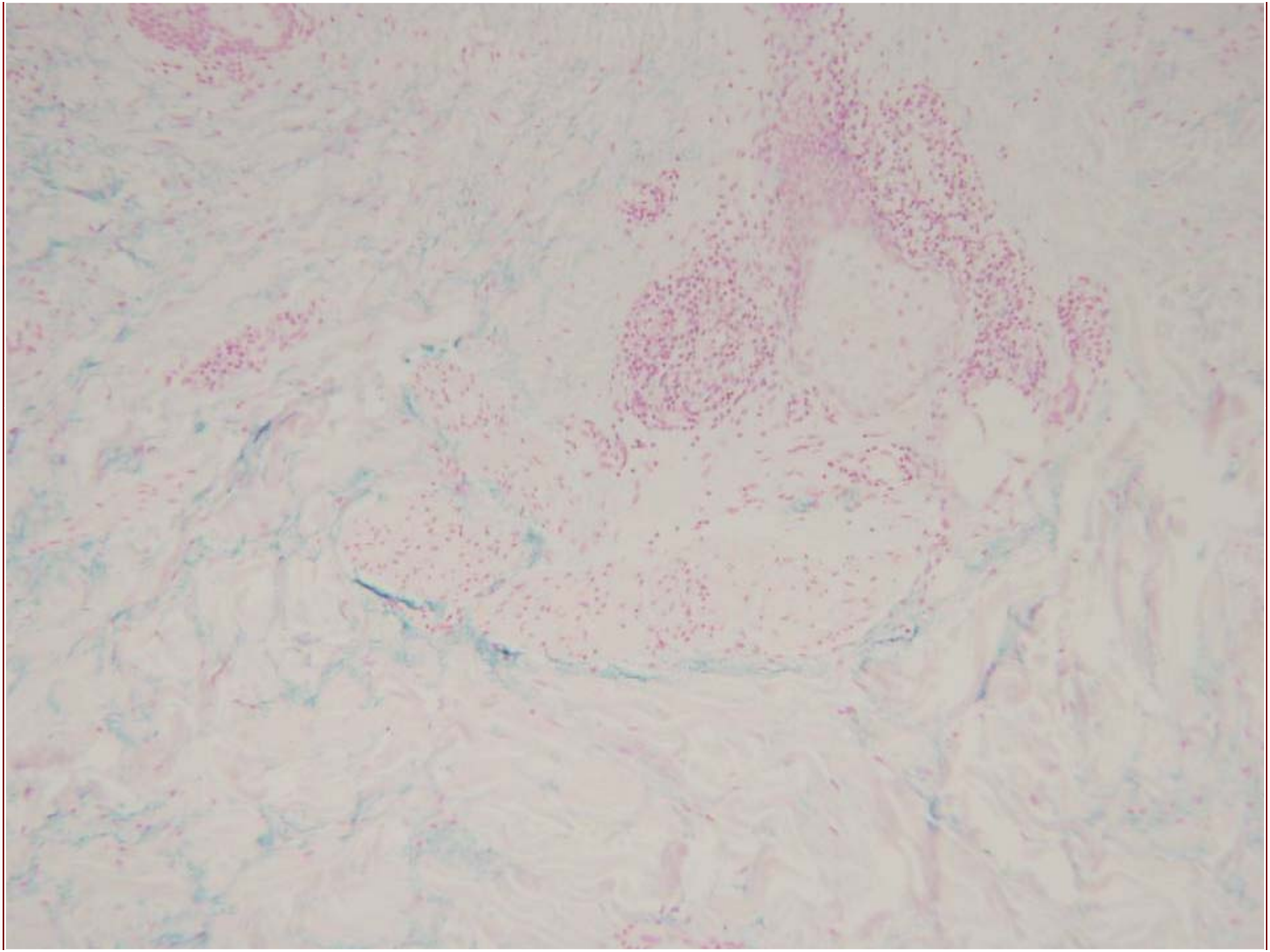
- Histology:
  - Immunohistochemistry:
    - CD34 and procollagen 1 – positive in spindled cells
      - Do not distinguish NSF from scleromyxedema (study out of Penn, J Cutan Path, Aug 2005)

- Case 88 a & b









Reticular erythematous mucinosis

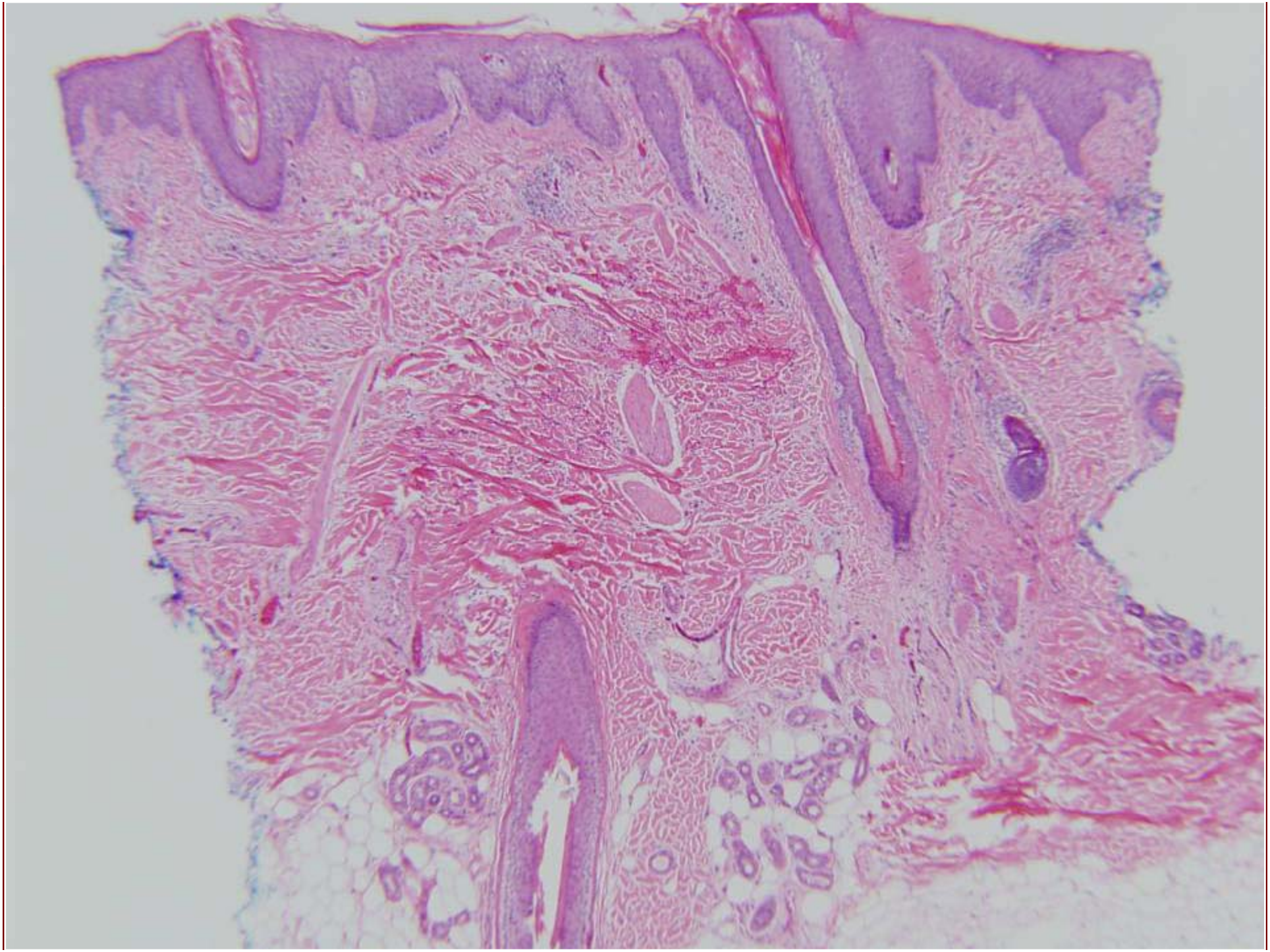
- Histology:
  - Superficial and deep perivascular lymphocytic infiltrate
    - +/- perifollicular
  - Slight vascular dilatation
  - Separation of collagen bundles, with deposition of mucin
  - Epidermis usually normal

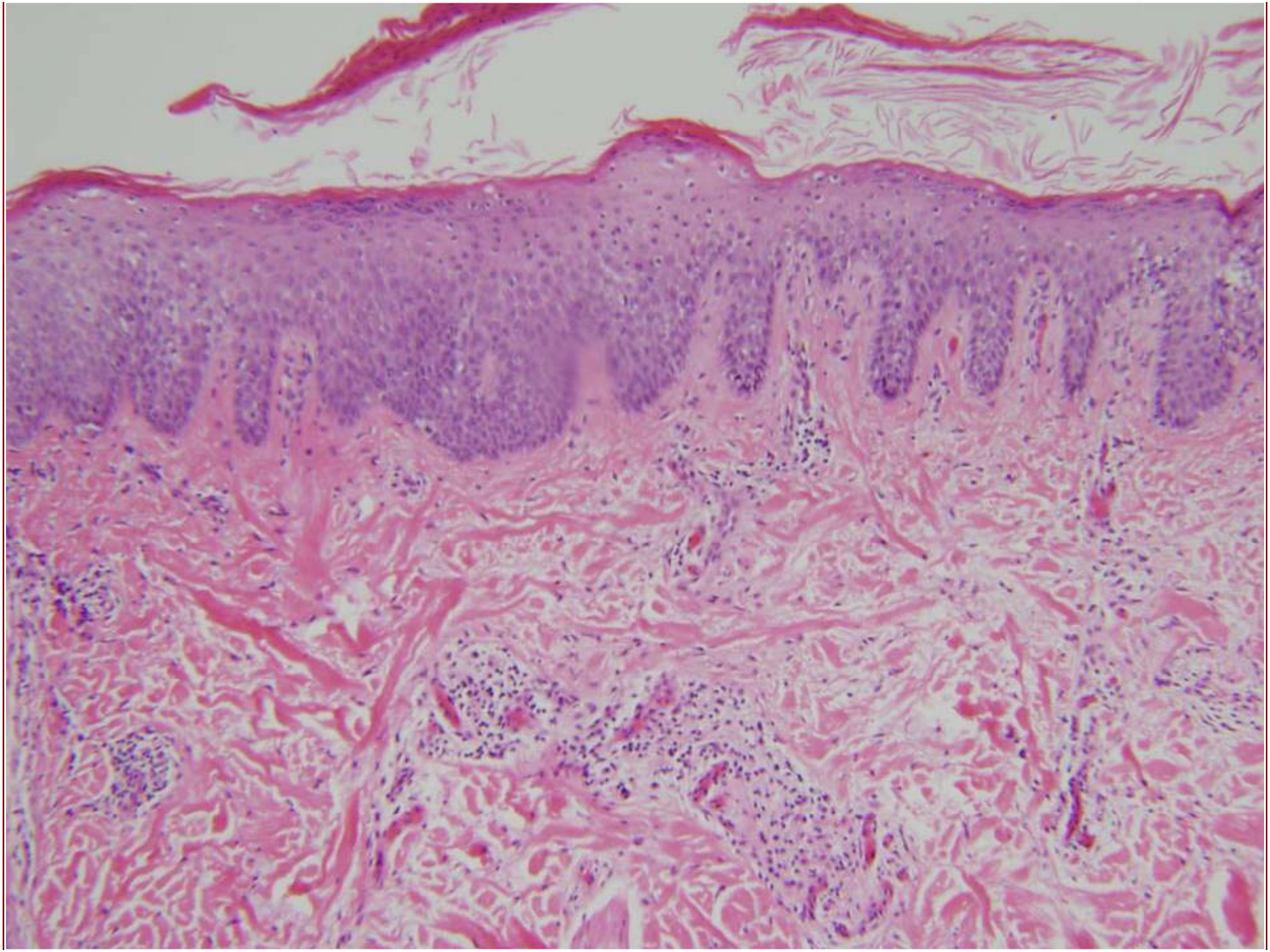
- Clinical:
  - Persistent, photo-aggravated, erythematous papular or plaque-like eruption in the midline of the back or chest.

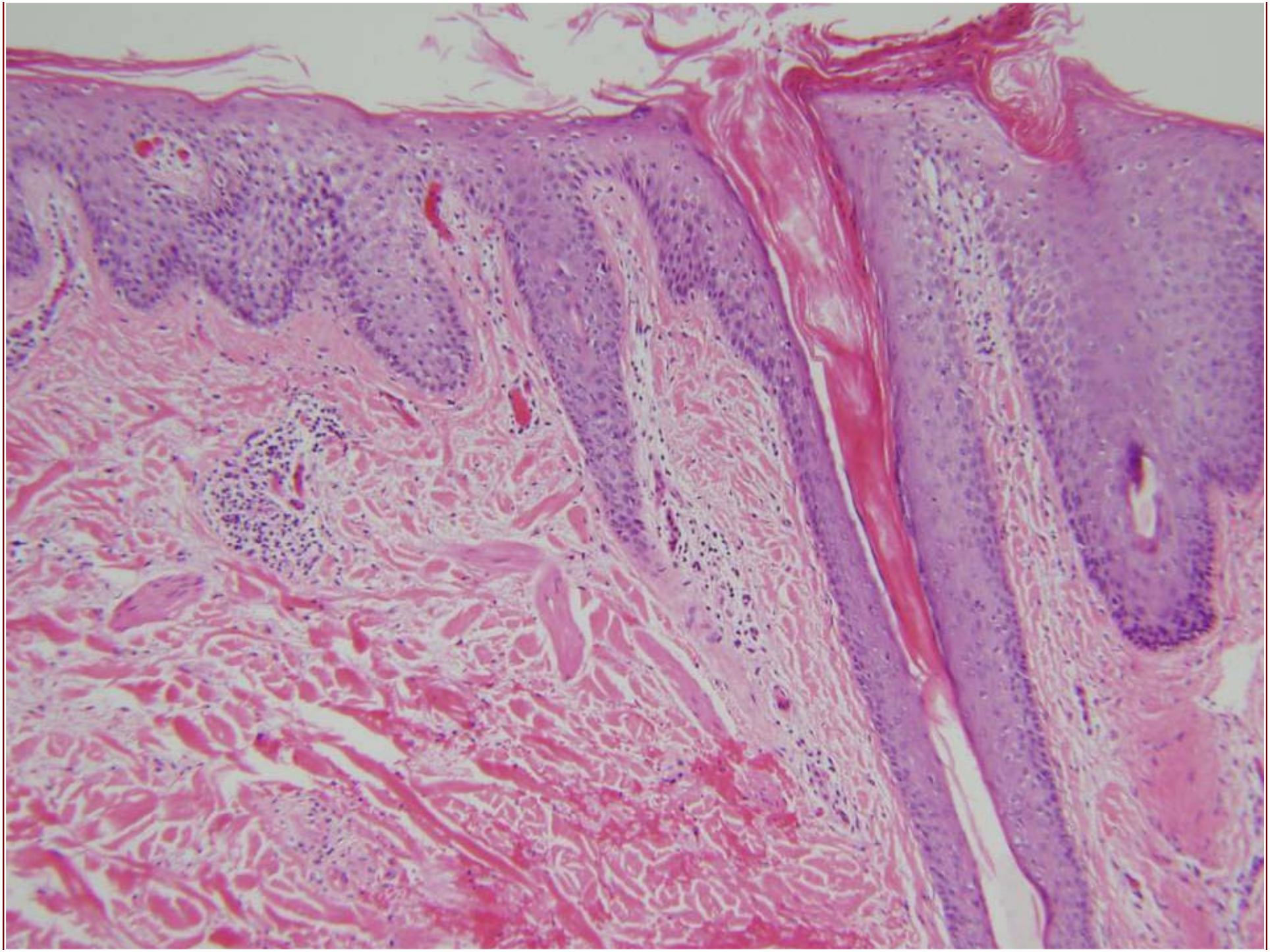
- Differential:
  - Lupus erythematosus
    - Involvement of epidermis
      - Interface changes, thick BM, follicular plugging?
    - DE-junction C3 and IgG
  - Lupus tumidus
    - Impossible to distinguish histologically
    - Clinically, scattered smooth-topped papules
  - Jessner's
    - Lacks mucin

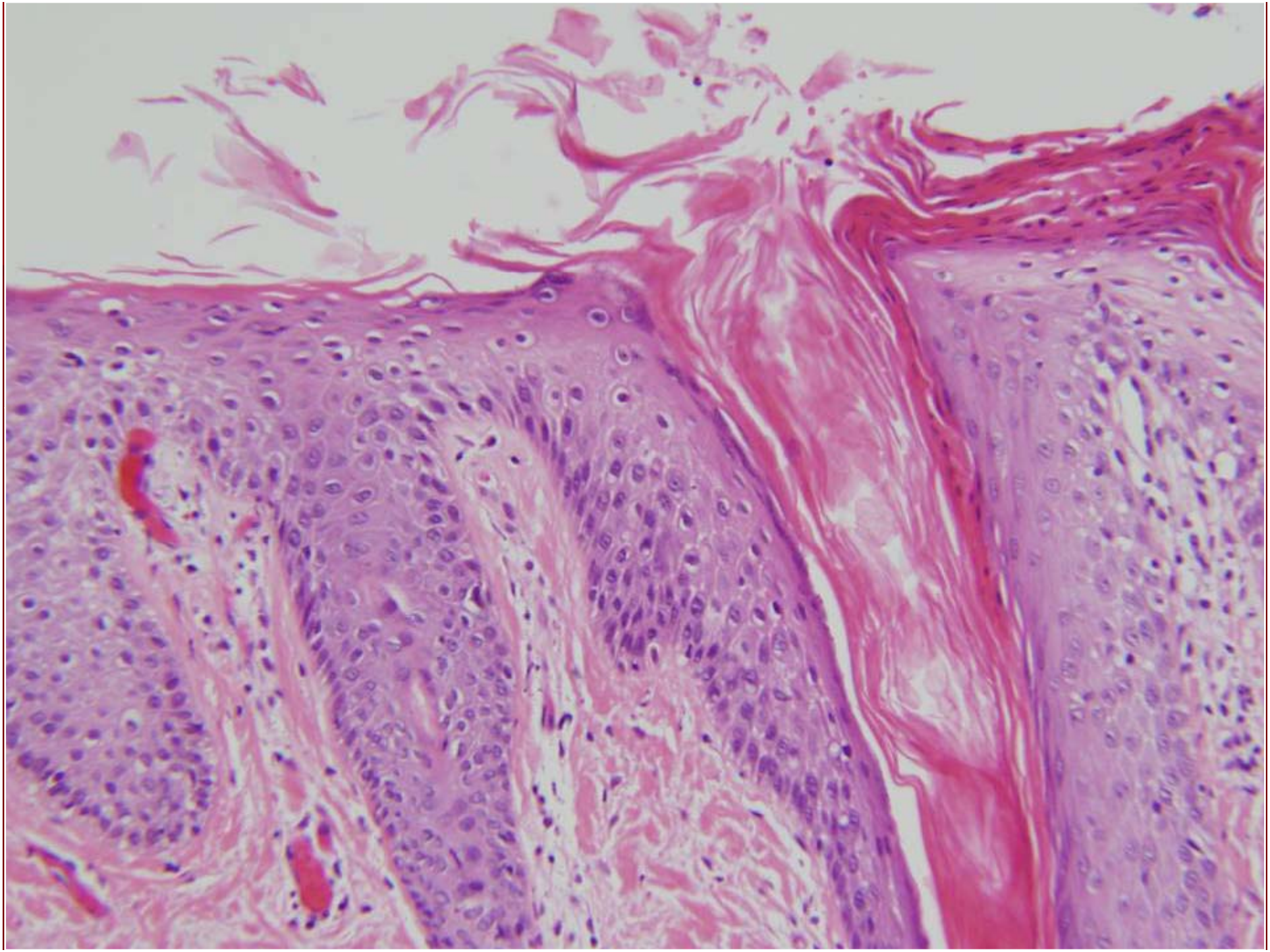
Review

- Case 8



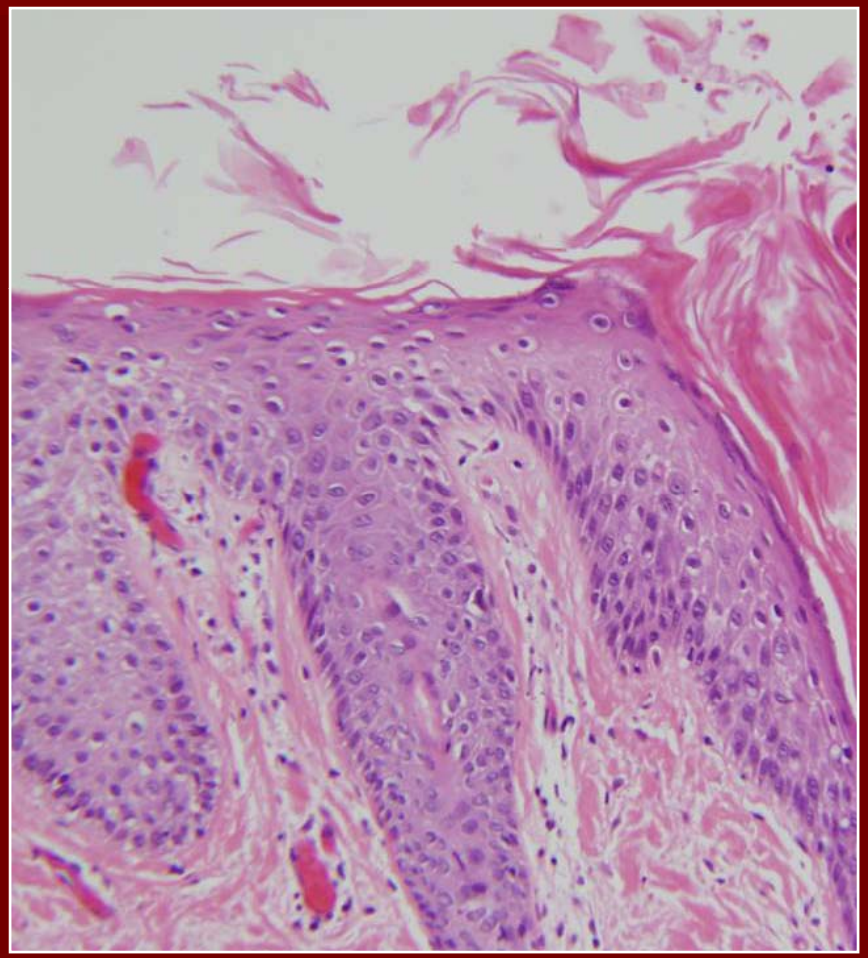






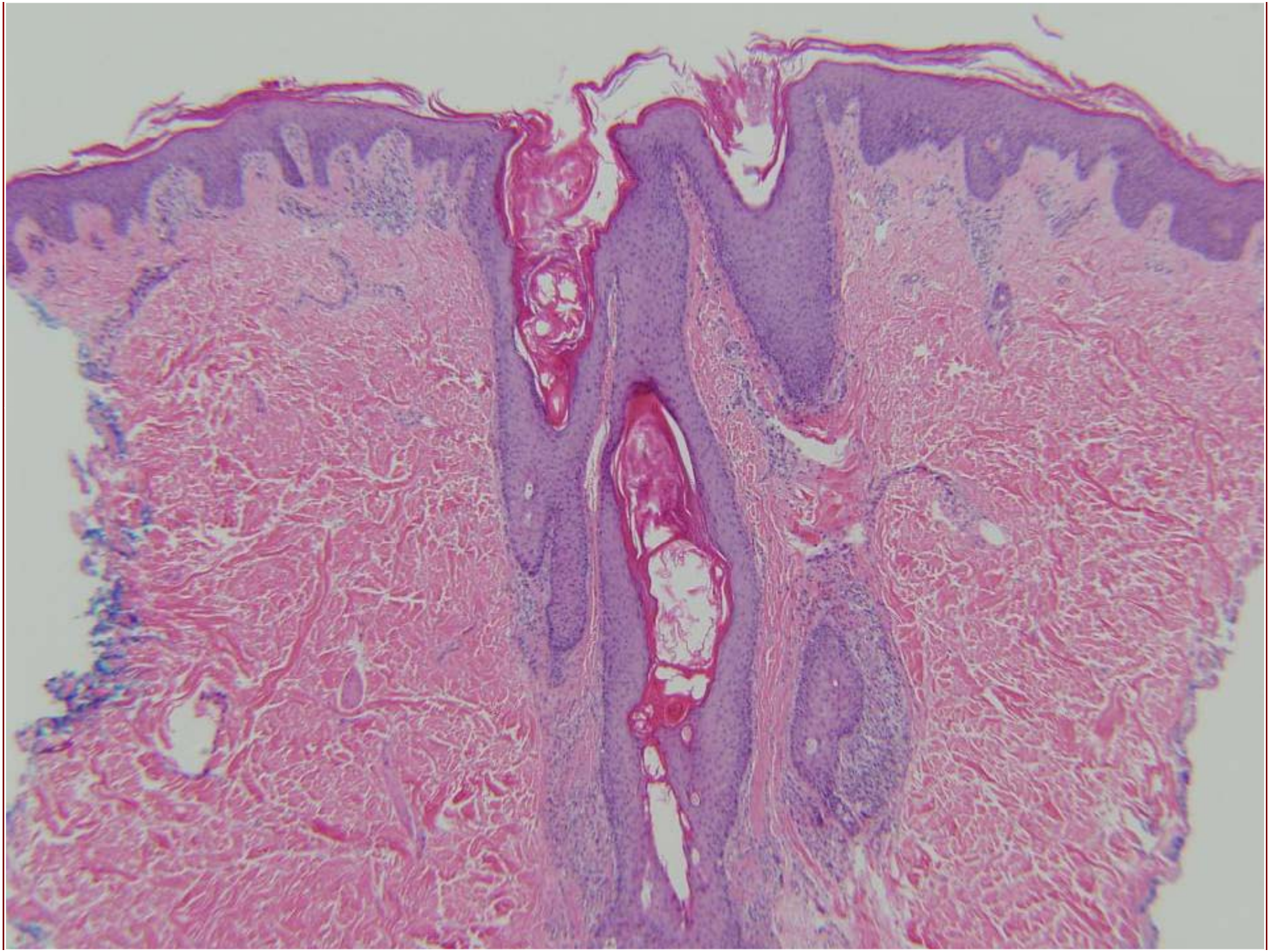
Seborrheic dermatitis

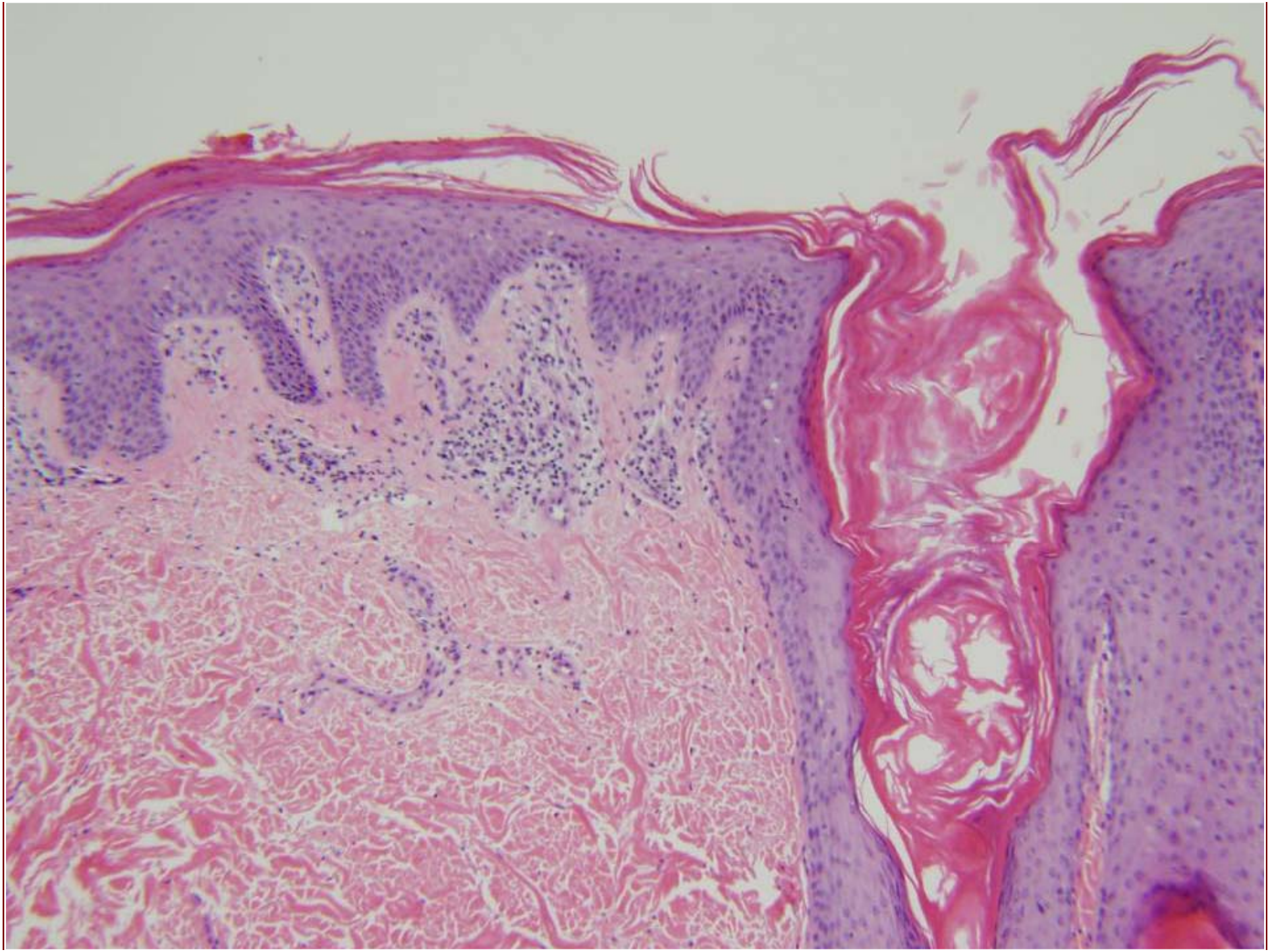
- *Histology:*
  - Spongiosis
  - Psoriasiform hyperplasia – less so than psoriasis, usually.
  - Folliculocentric parakeratosis and scale crusts
  - PVLI

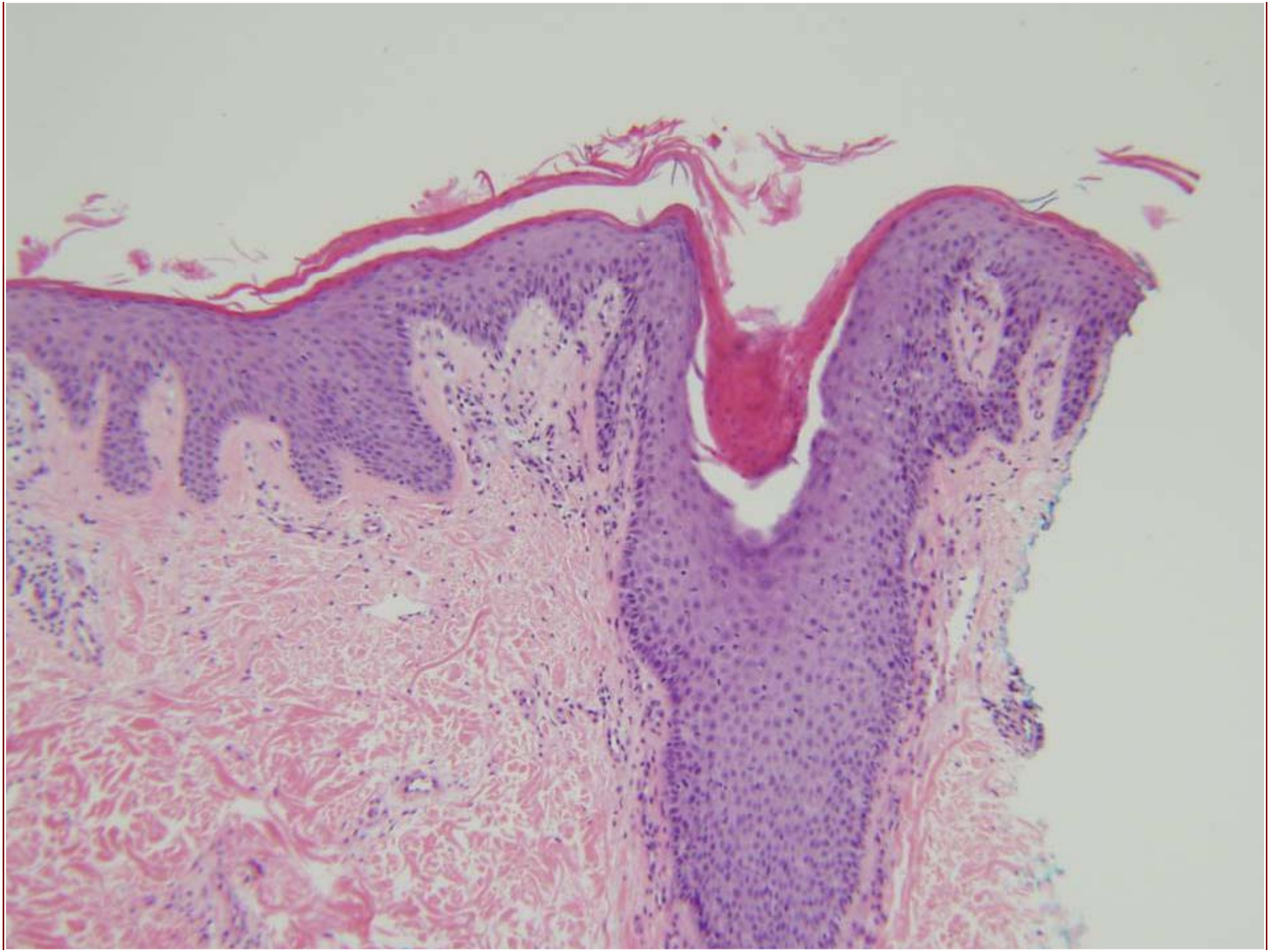


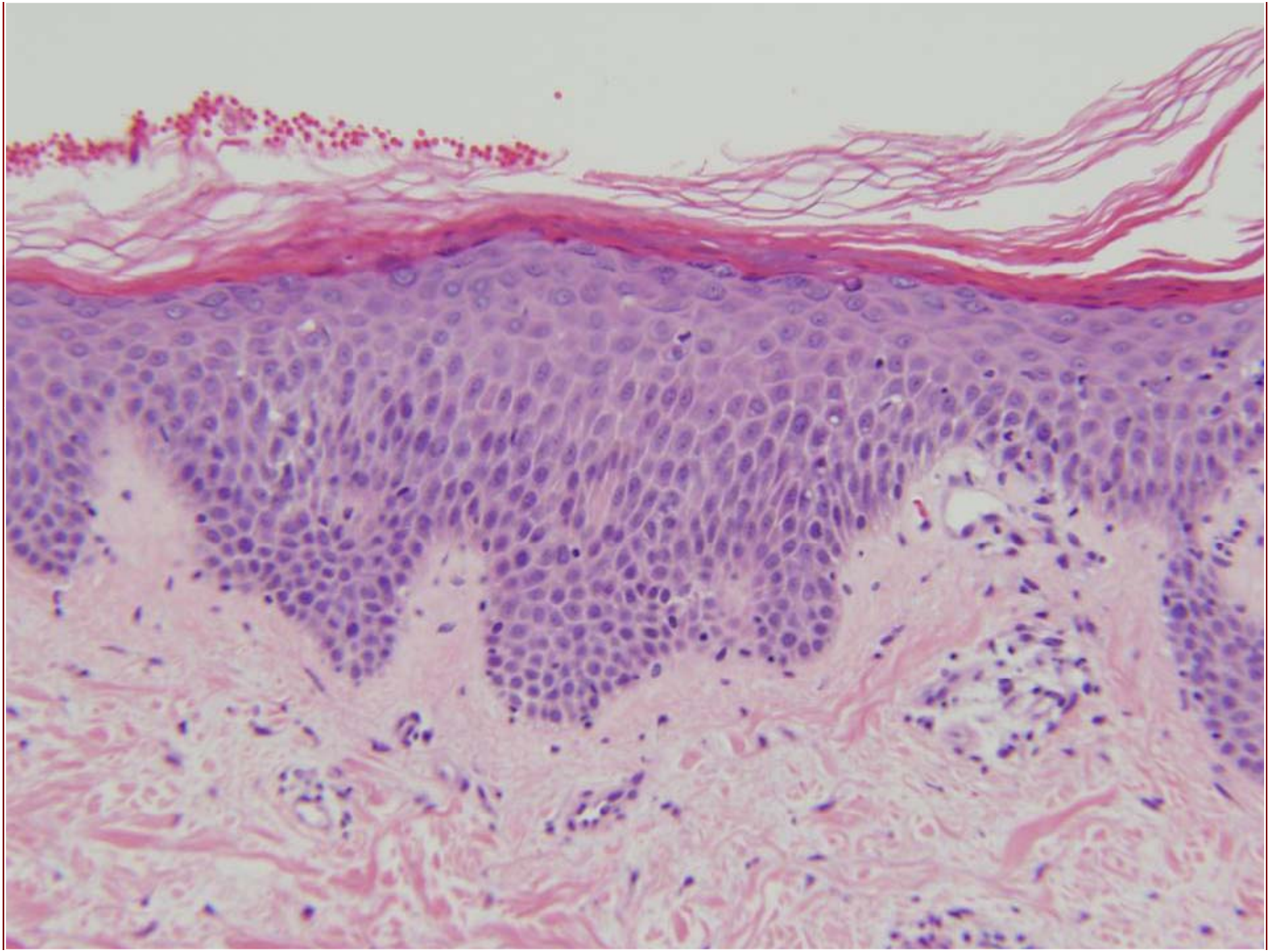
Review

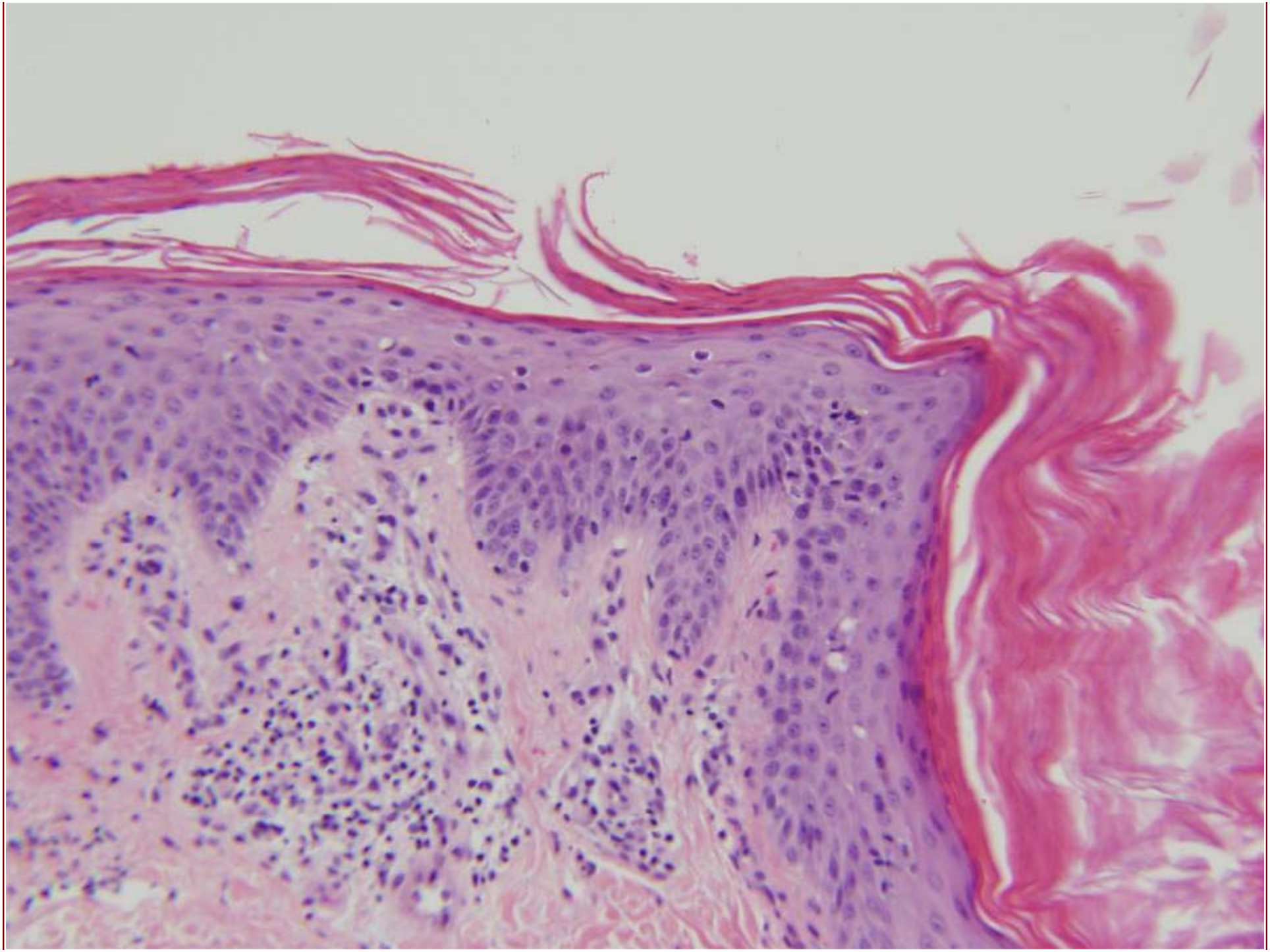
- Case 3

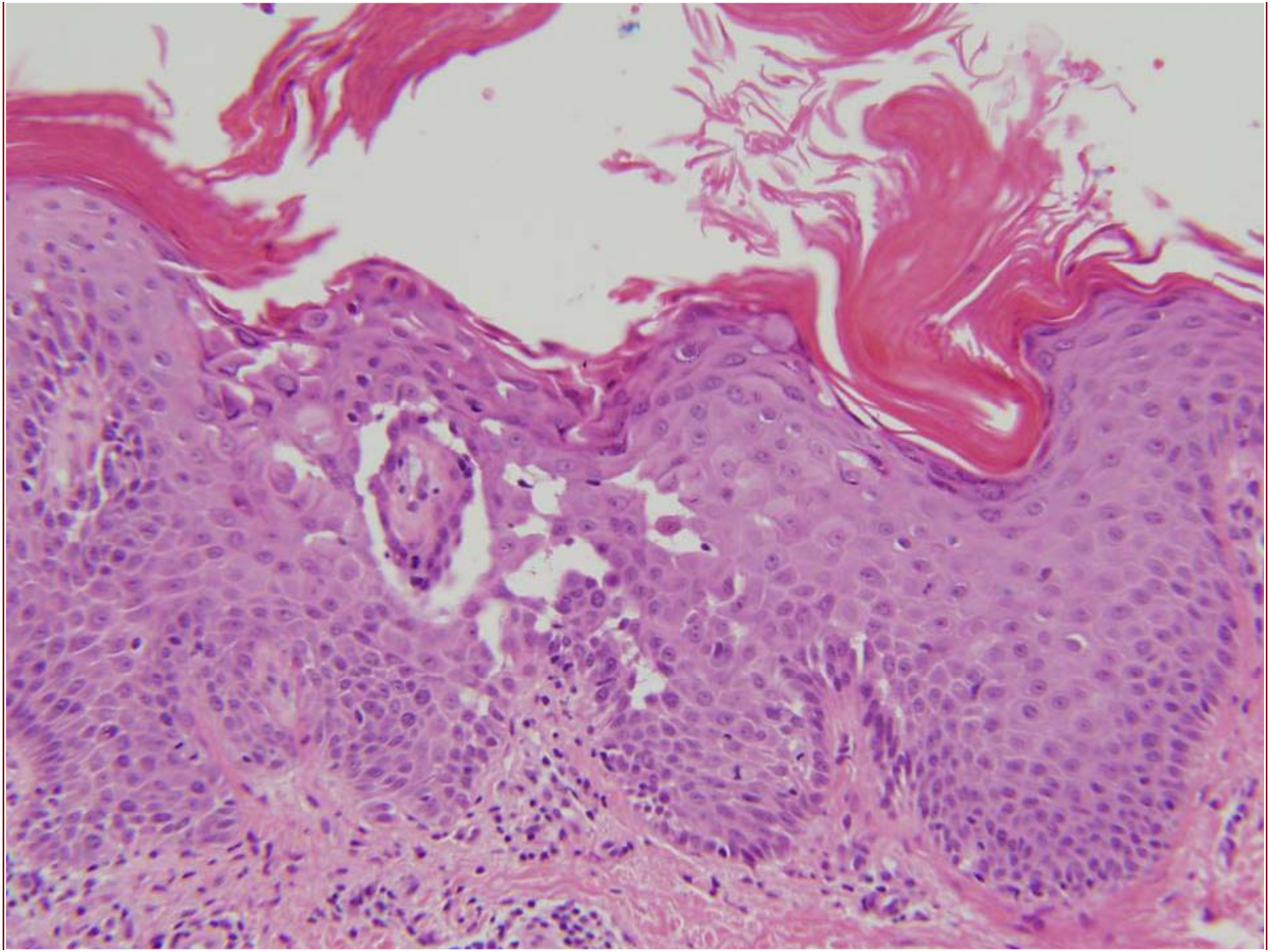


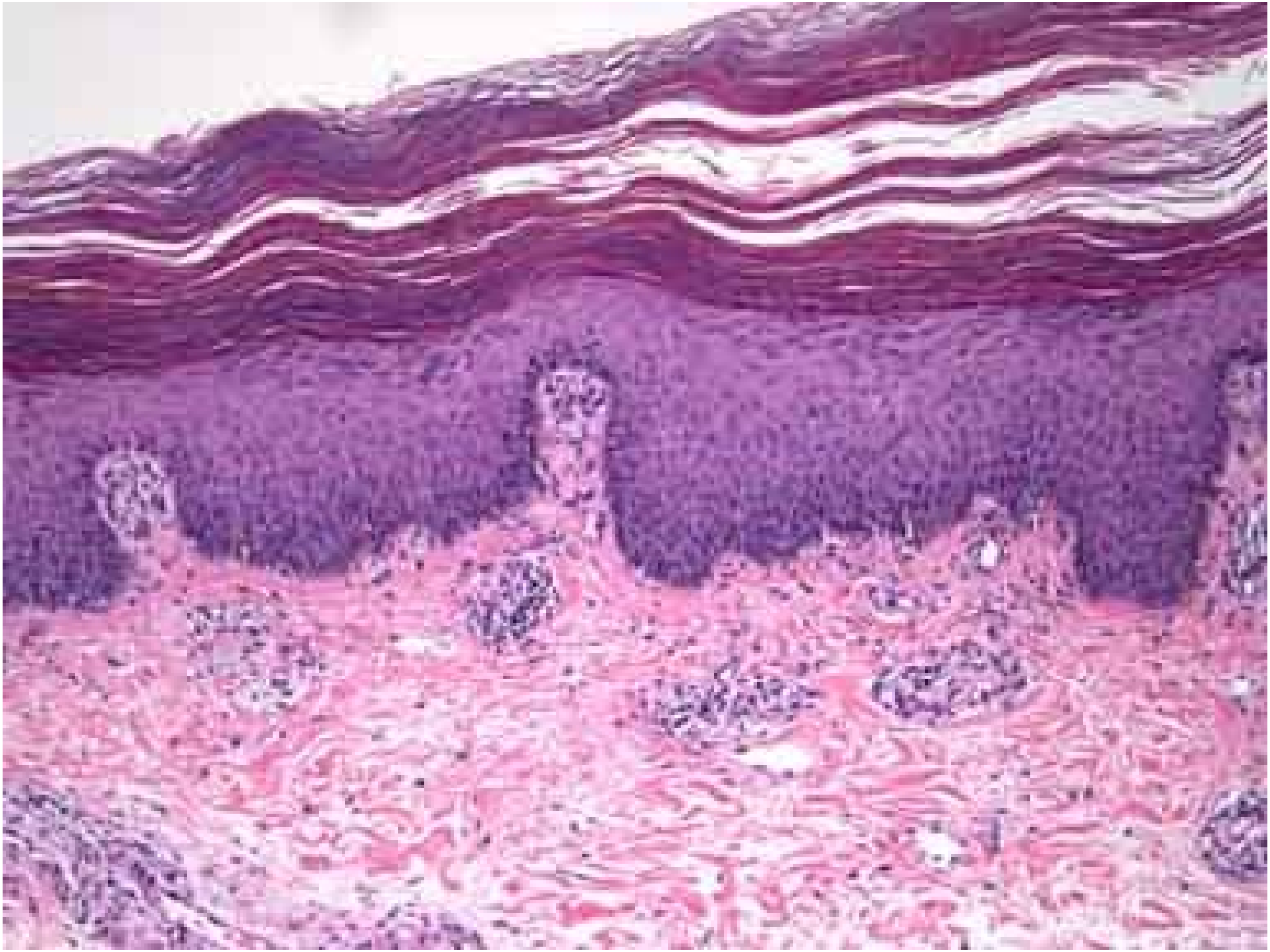






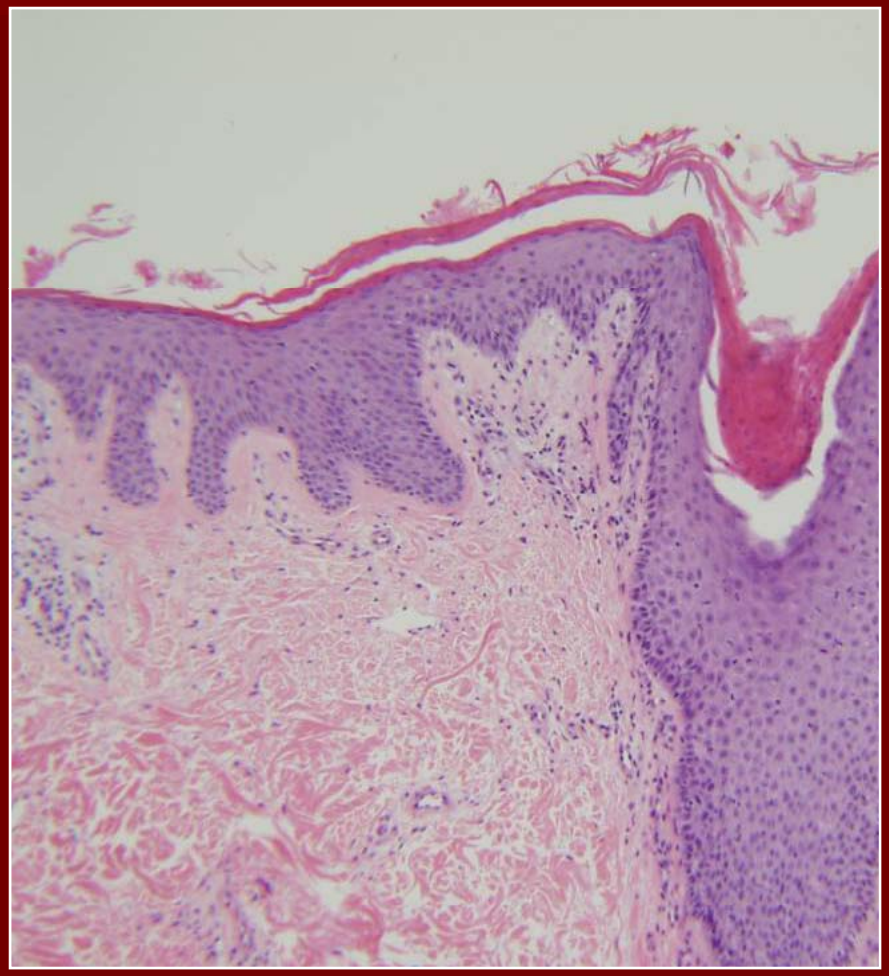




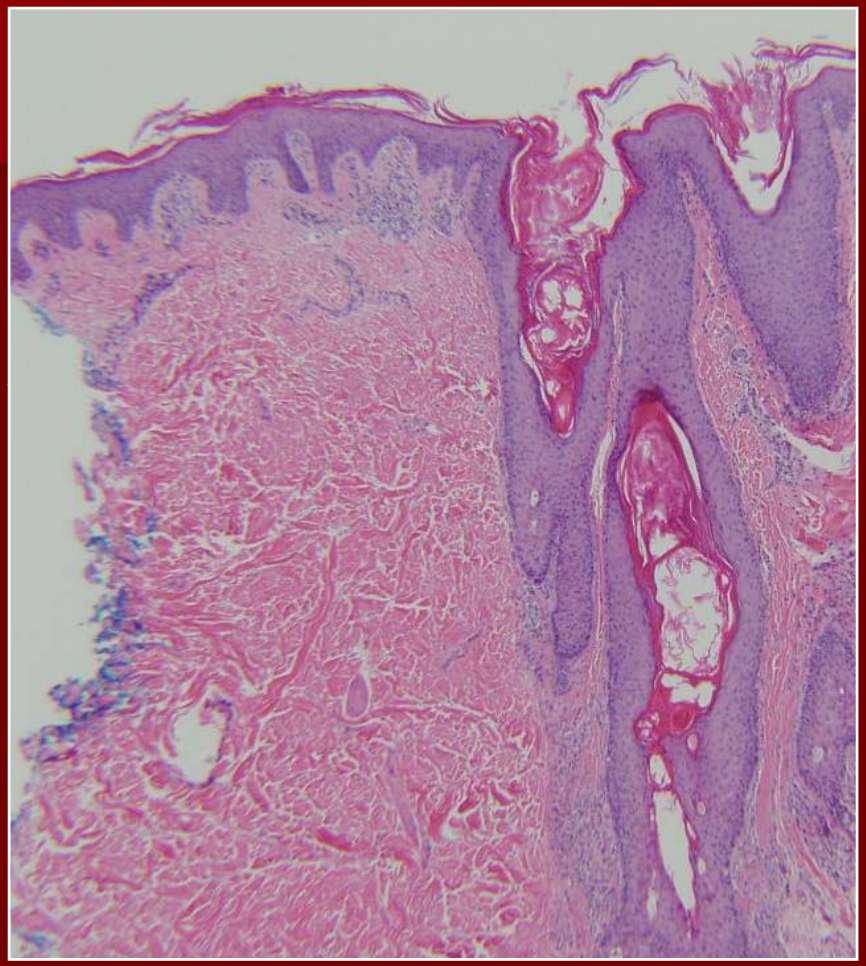


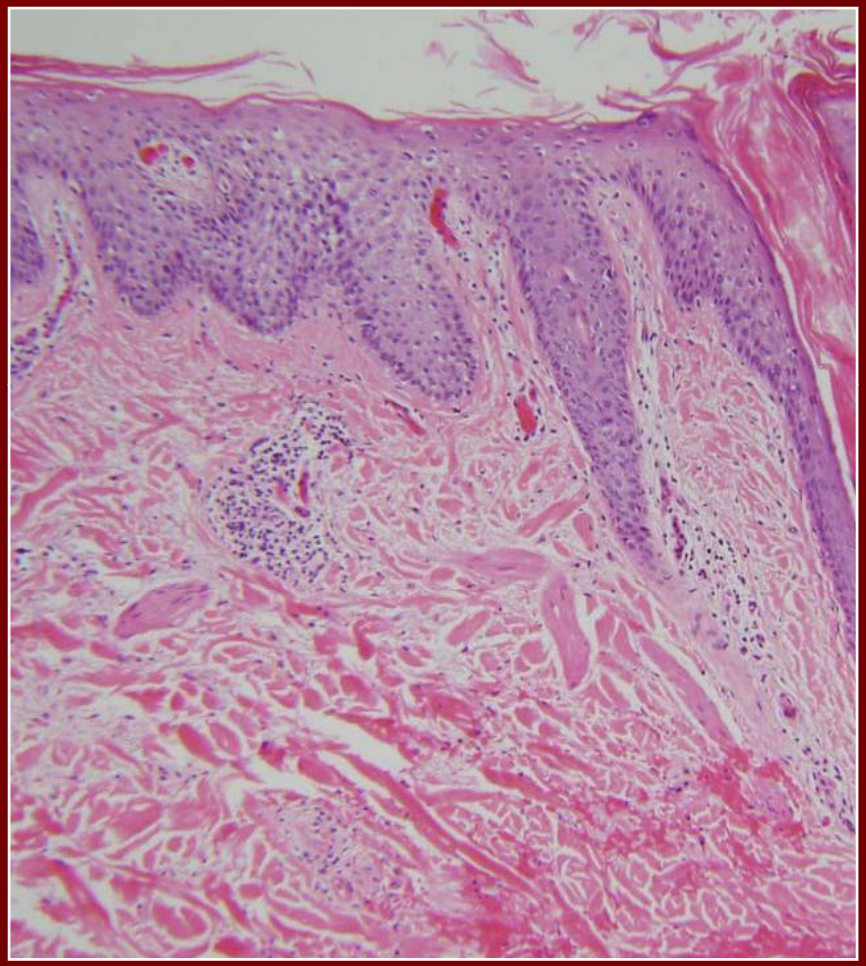
Pityriasis rubra pilaris

- *Histology:*
  - Biopsy @ site of erythema, not plugs….
  - Parakeratosis at lips of follicles, follicular plugging
  - Alternating orthokeratosis and parakeratosis in both vertical and horizontal directions
  - Irregular acanthosis
  - Irregular HYPERKERATOSIS
  - THICK suprapapillary plates
  - RETAINS granular layer, may be hypergranulosis
  - SPLI
  - May have focal acantholytic dyskeratosis**

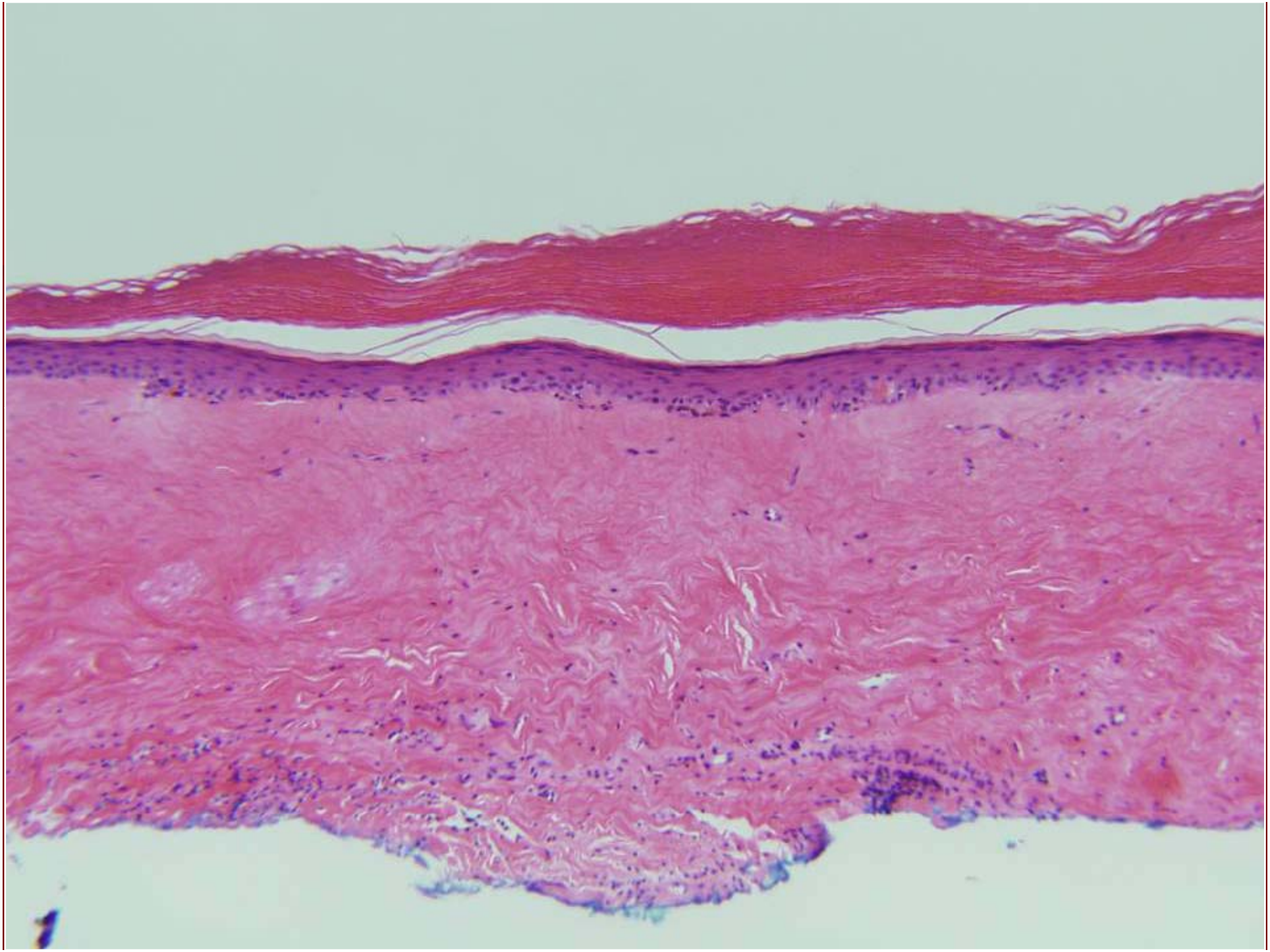


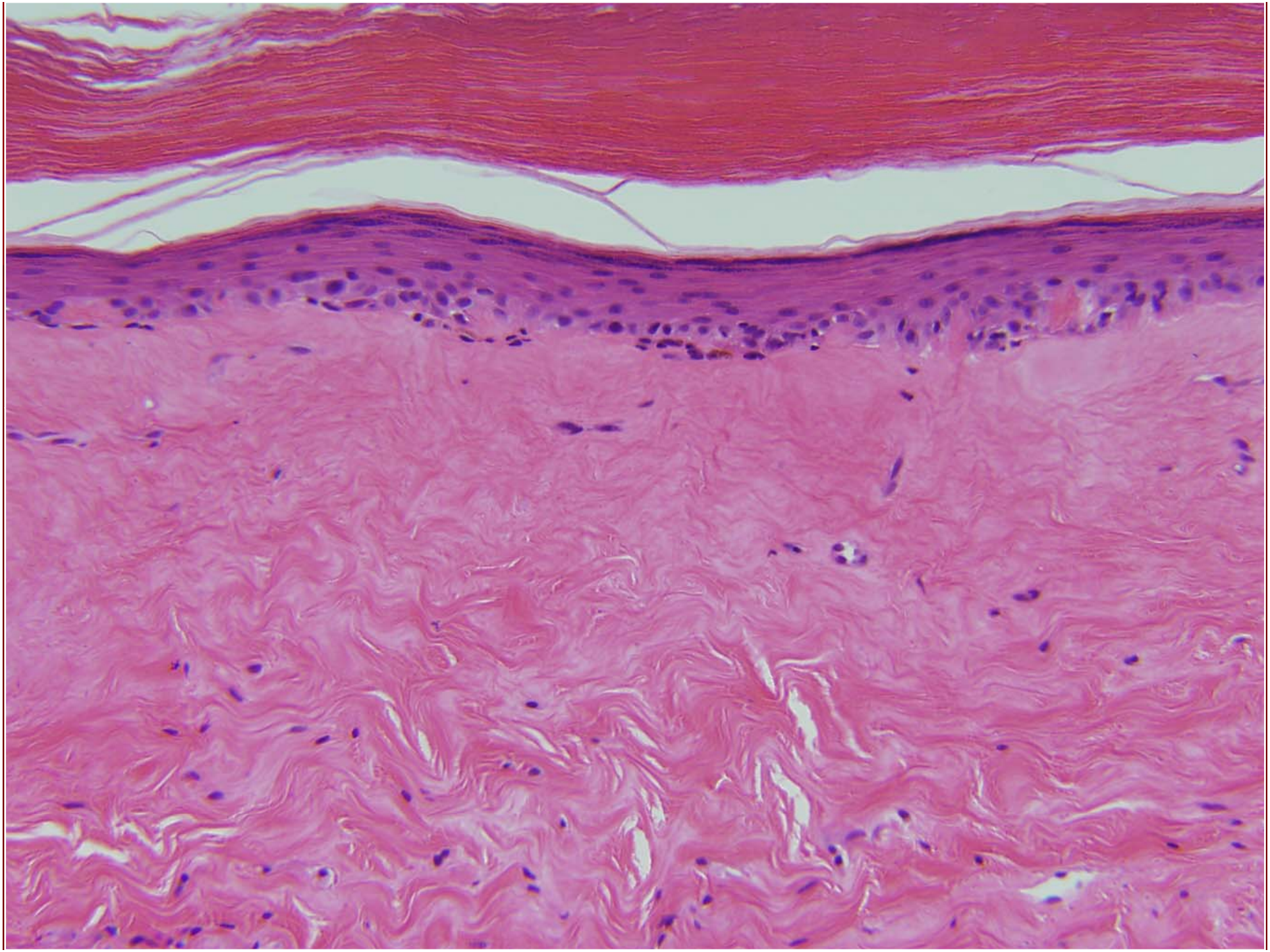
3 features help differentiate...

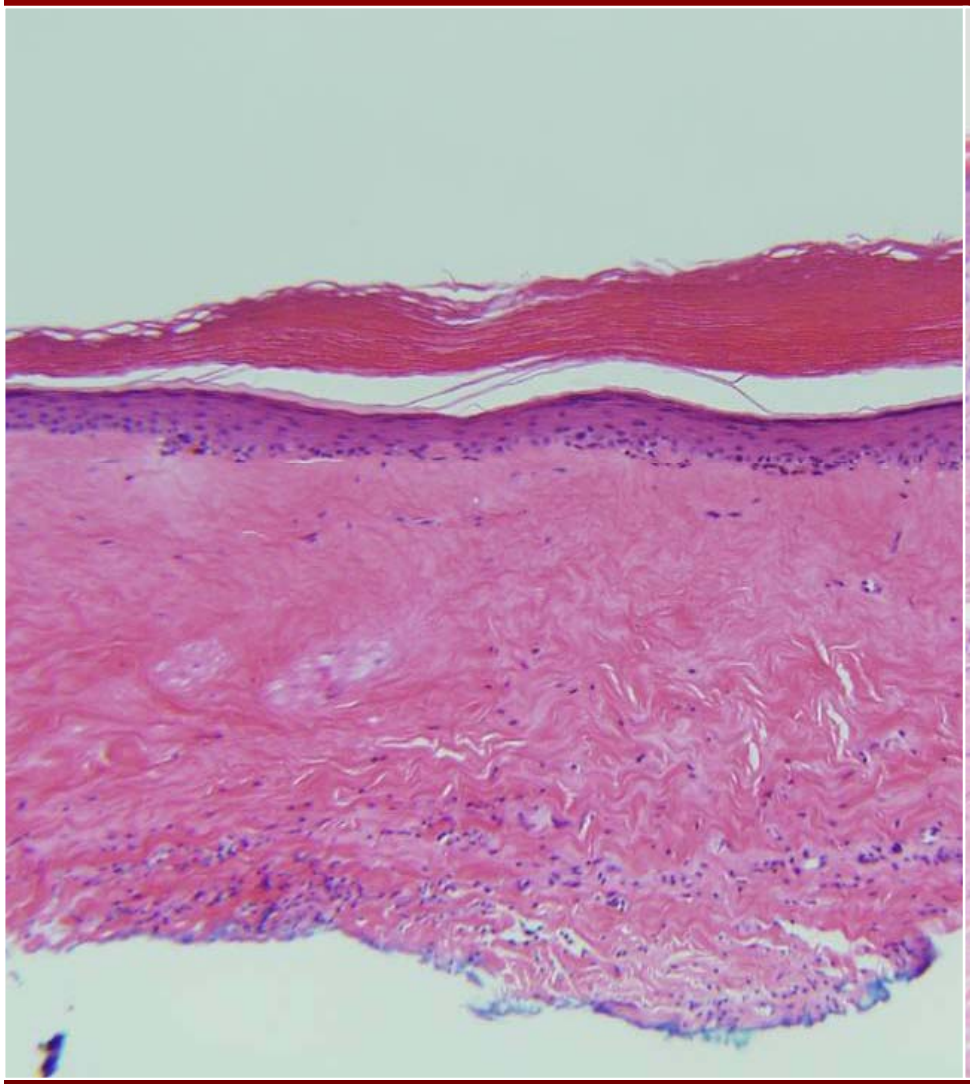


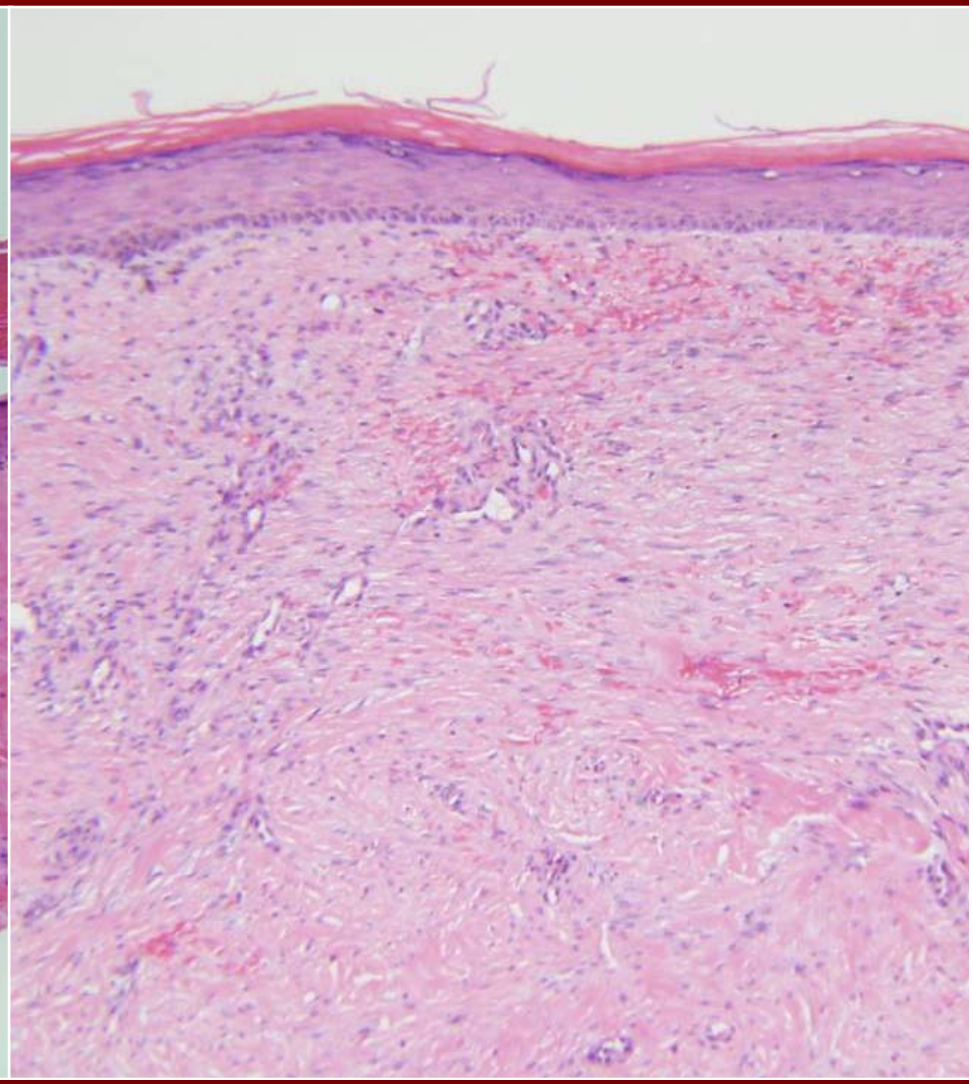


- Case 24









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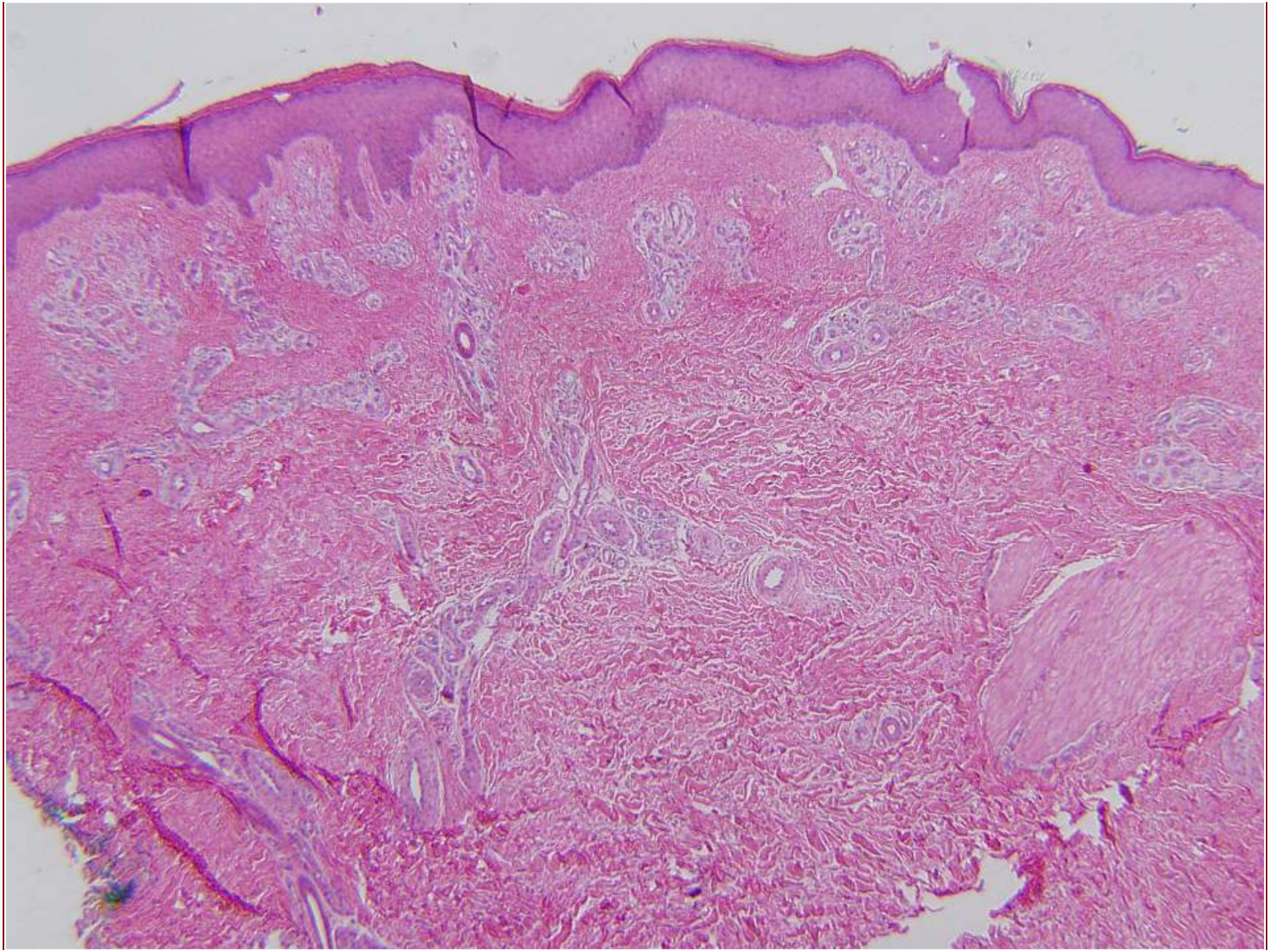
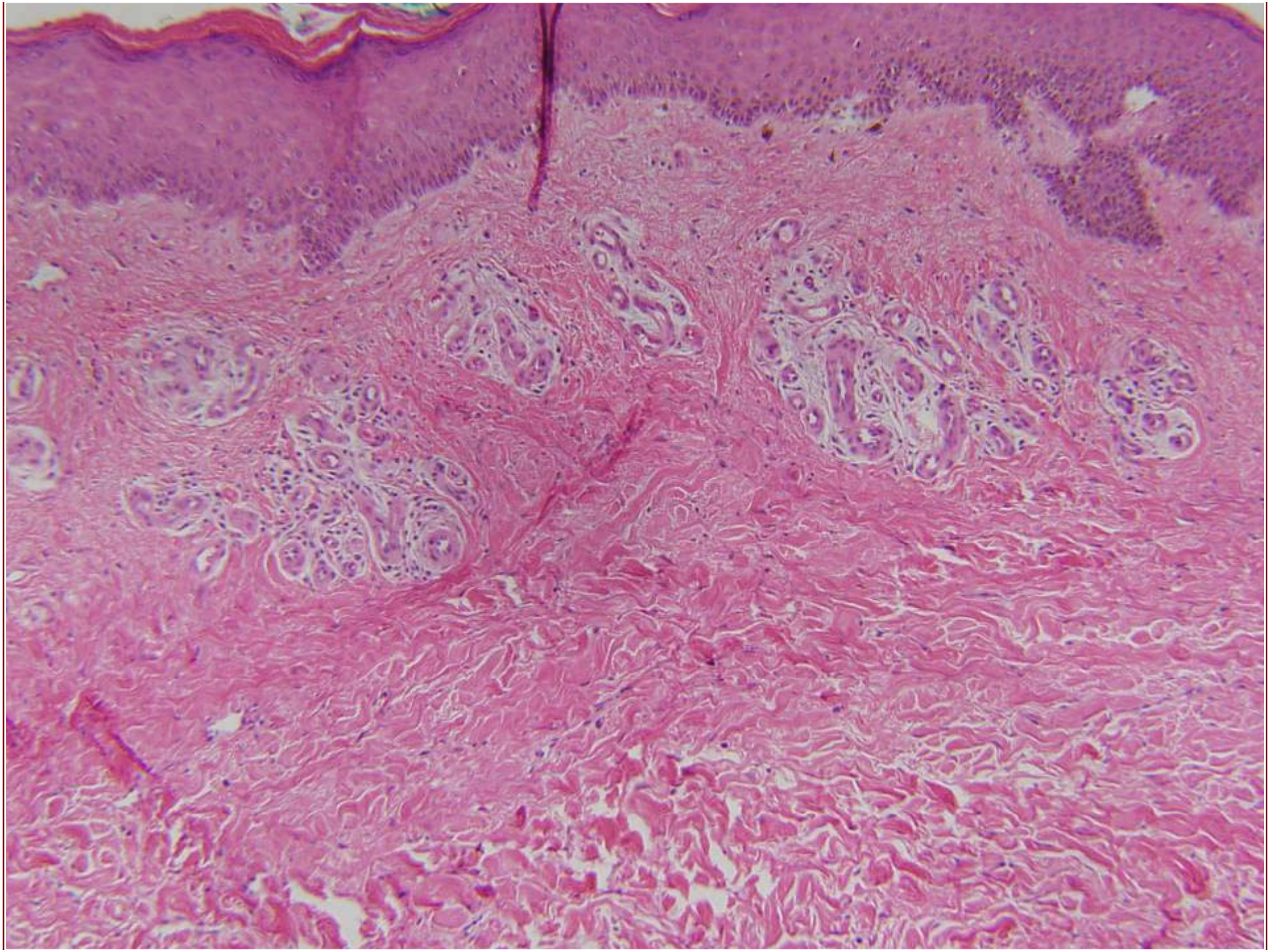
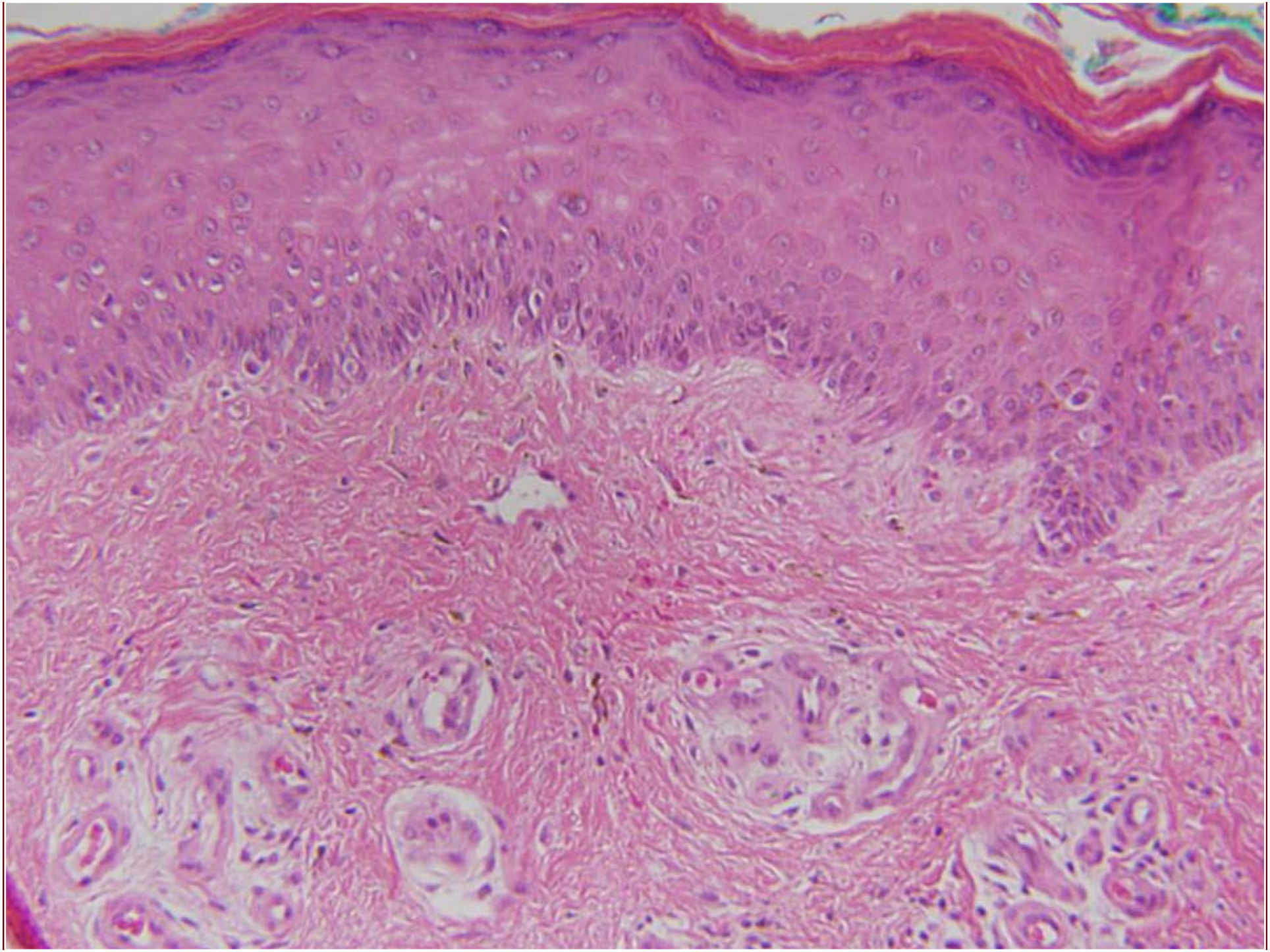
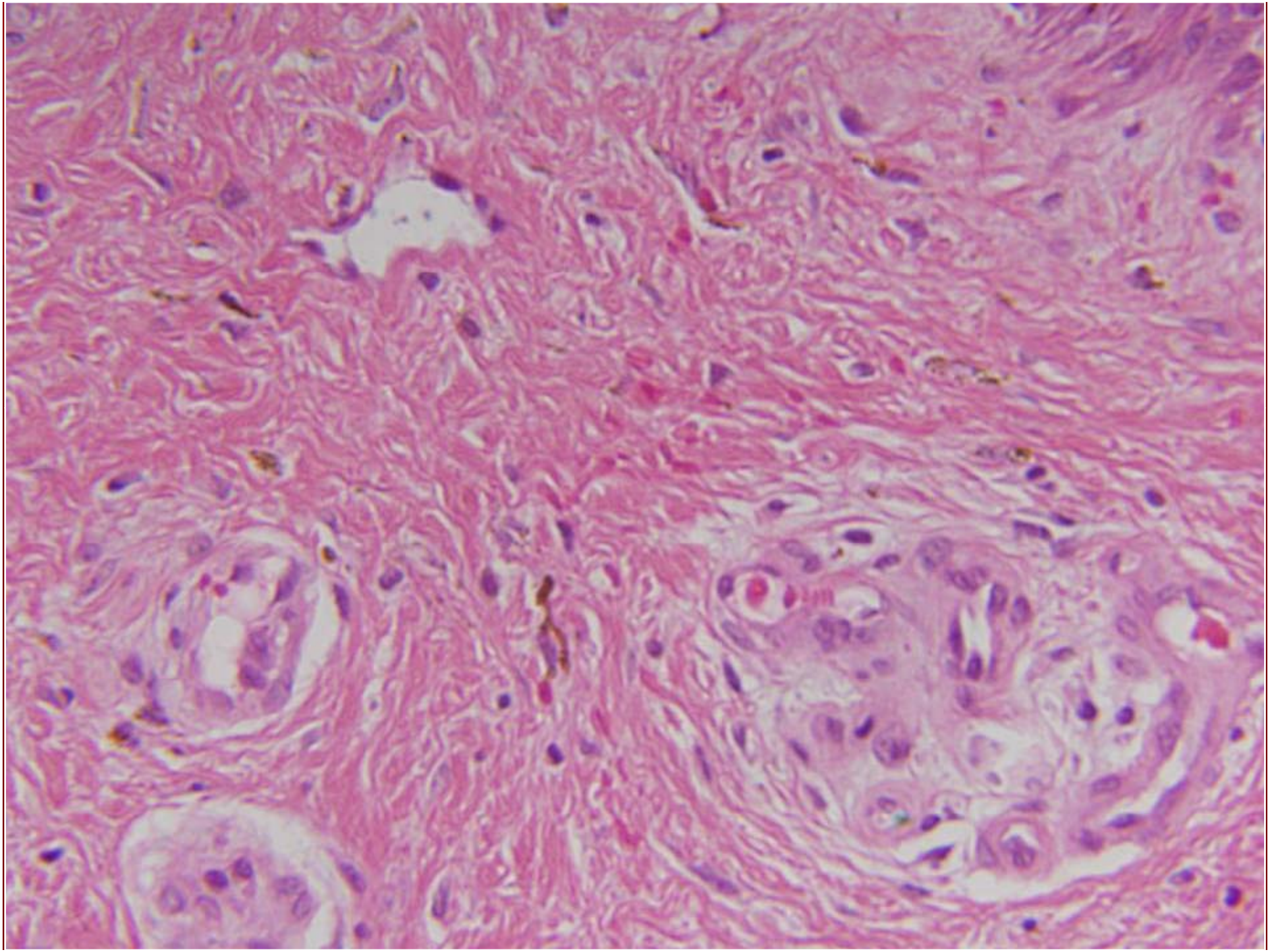


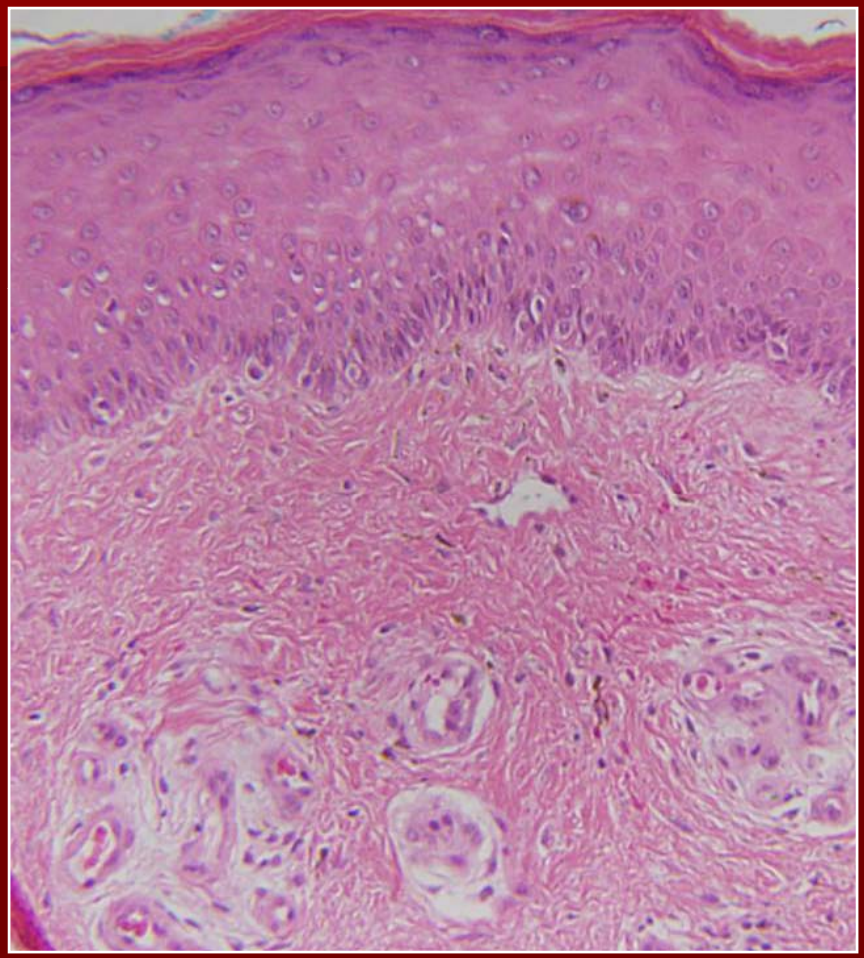


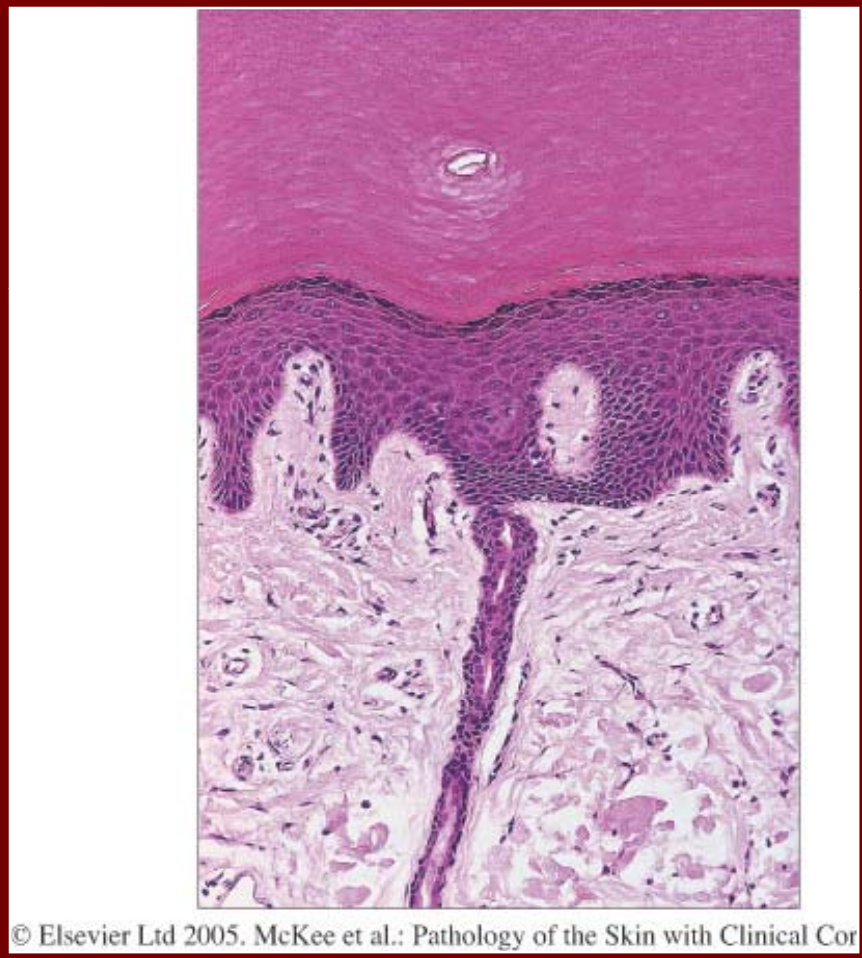




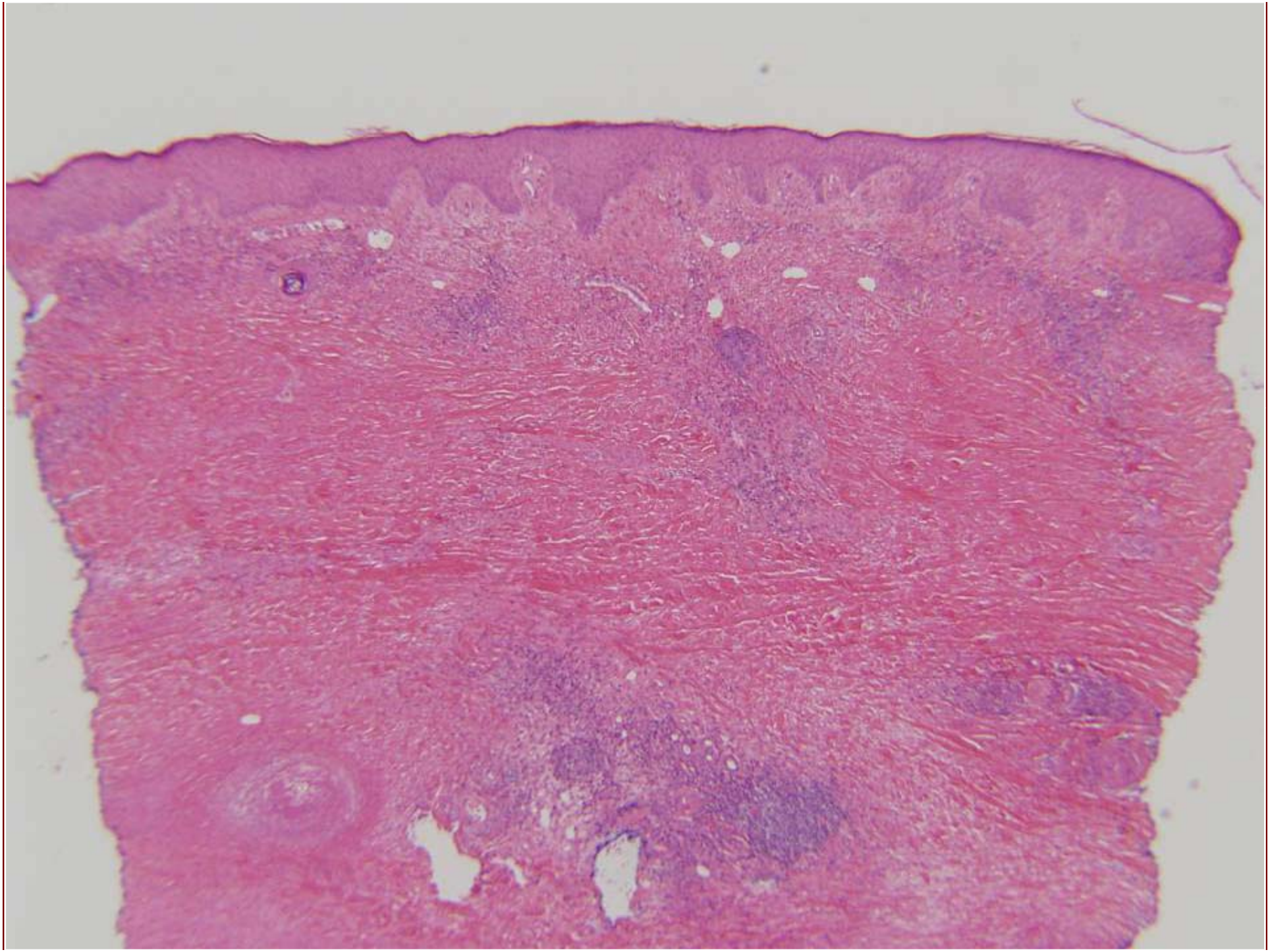
Histological features of Stasis Dermatitis

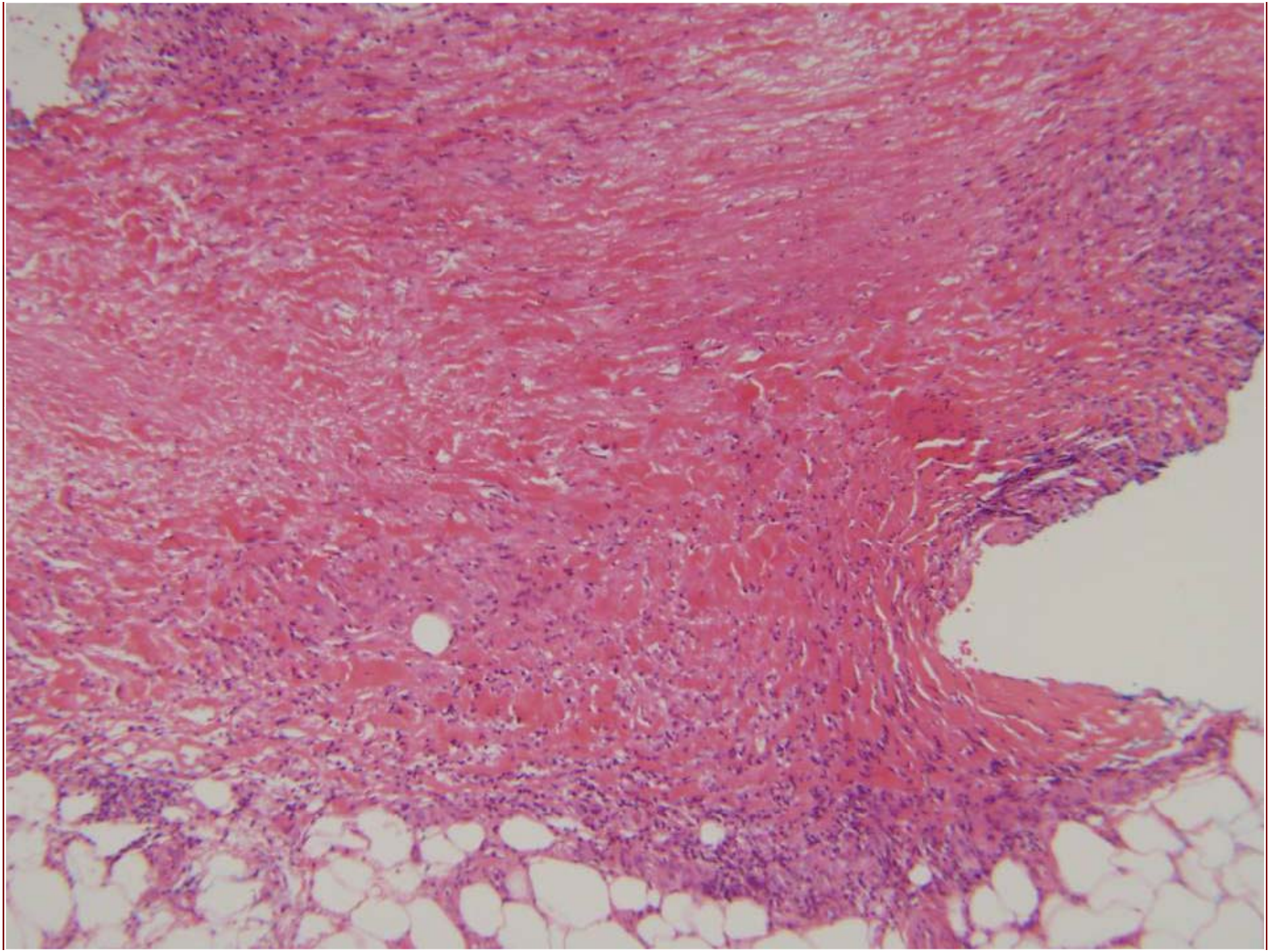
- Focal parakeratosis and serum scale crust
- Mild spongiosis
  - ?Spongiotic vesiculation…think superimposed contact dermatitis
- **Dermal changes
  - Proliferation of small blood vessels with RBC extravasation
  - Variable dermal fibrosis
  - Abundant hemosiderin present throughout the dermis
  - Thick walled veins in deep dermis or subcutis

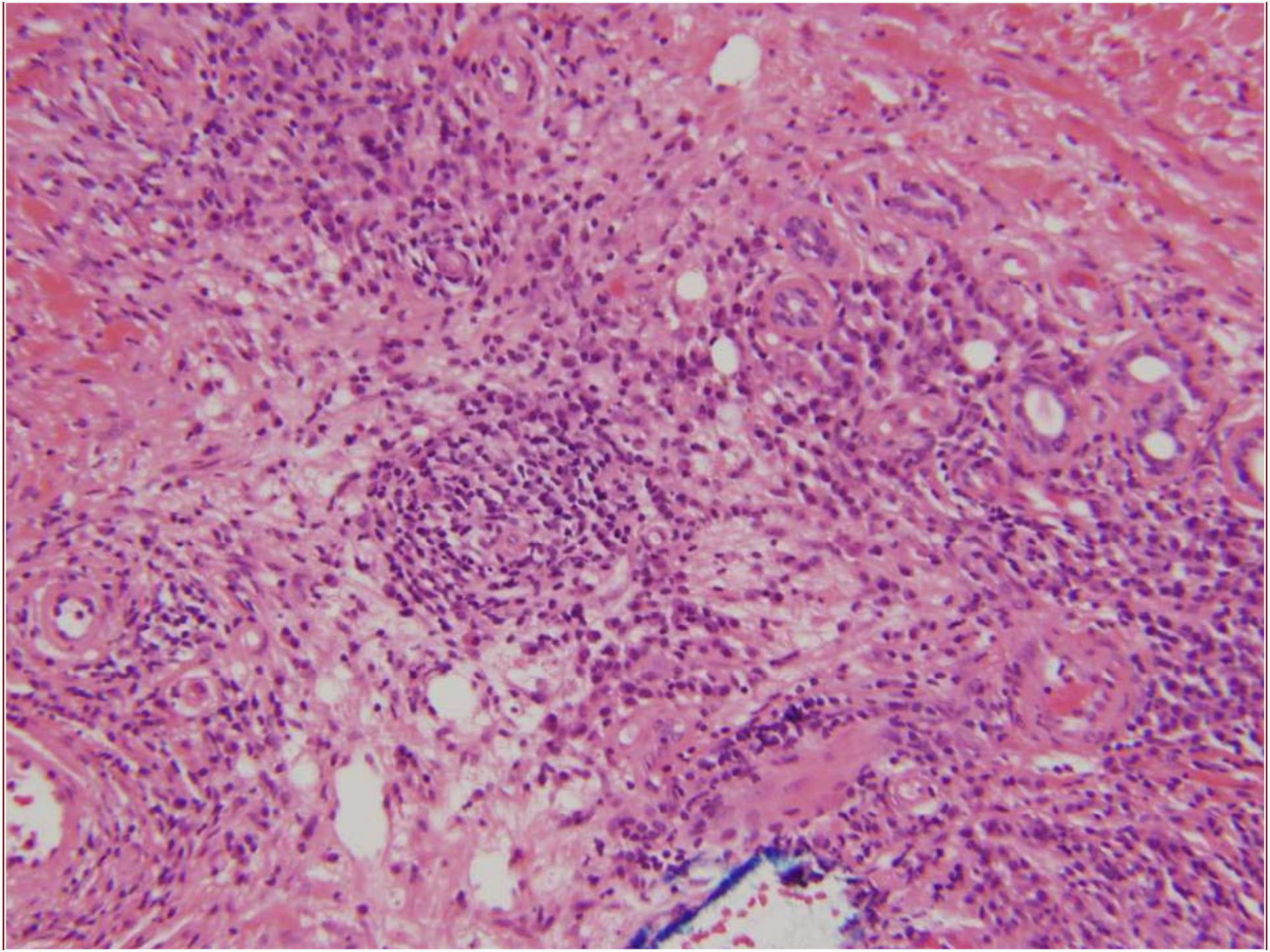


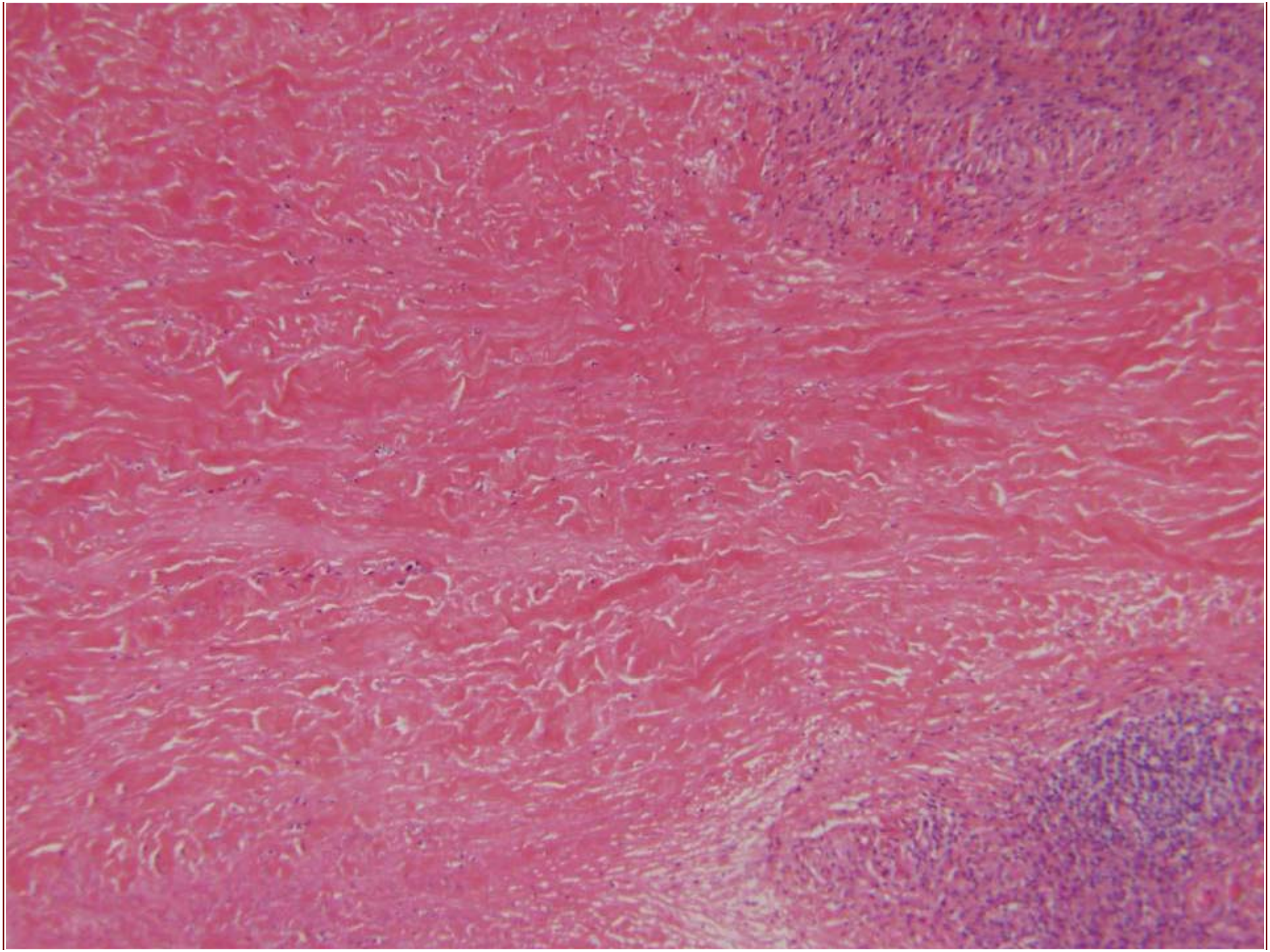


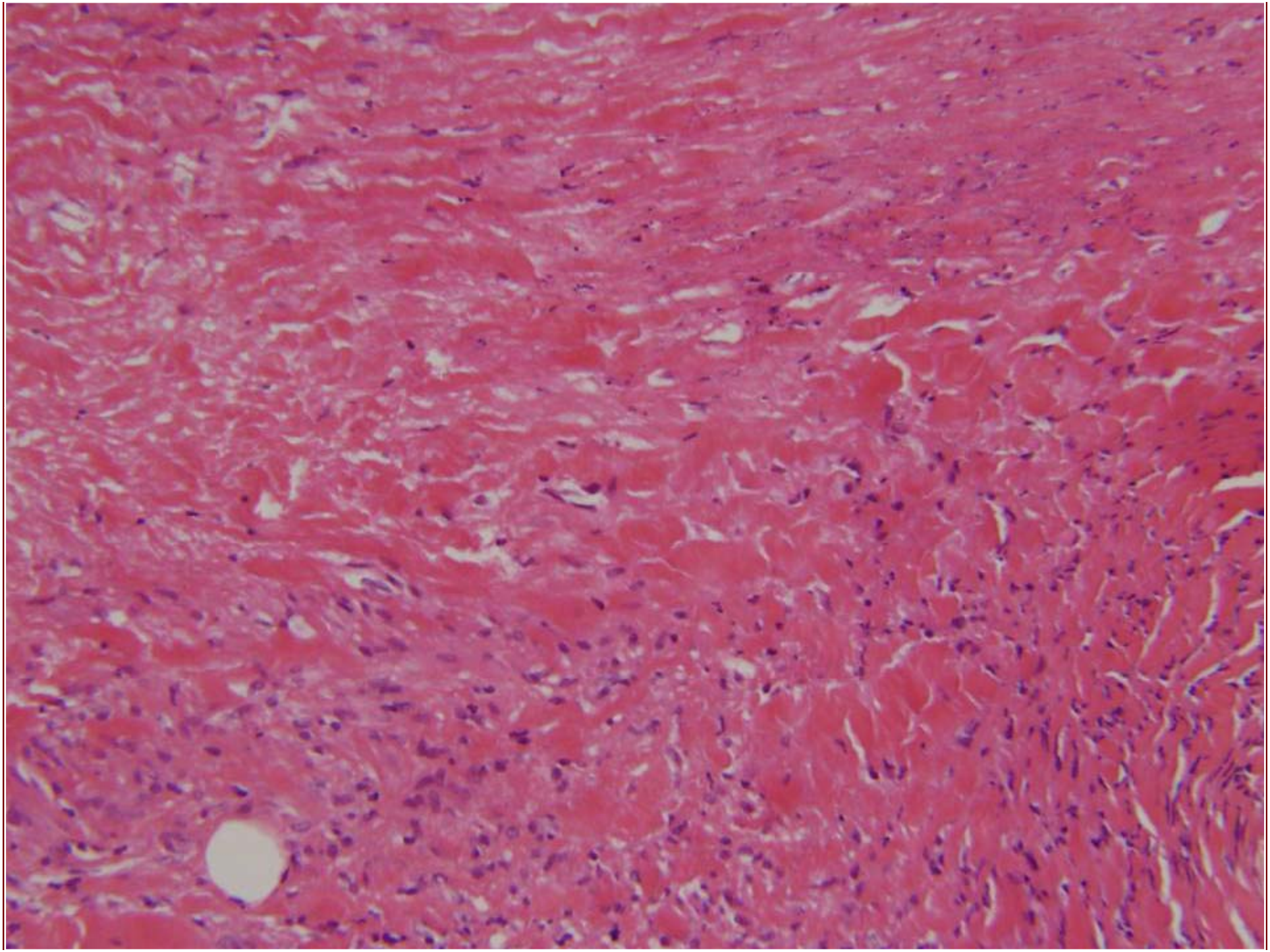
- Case 45

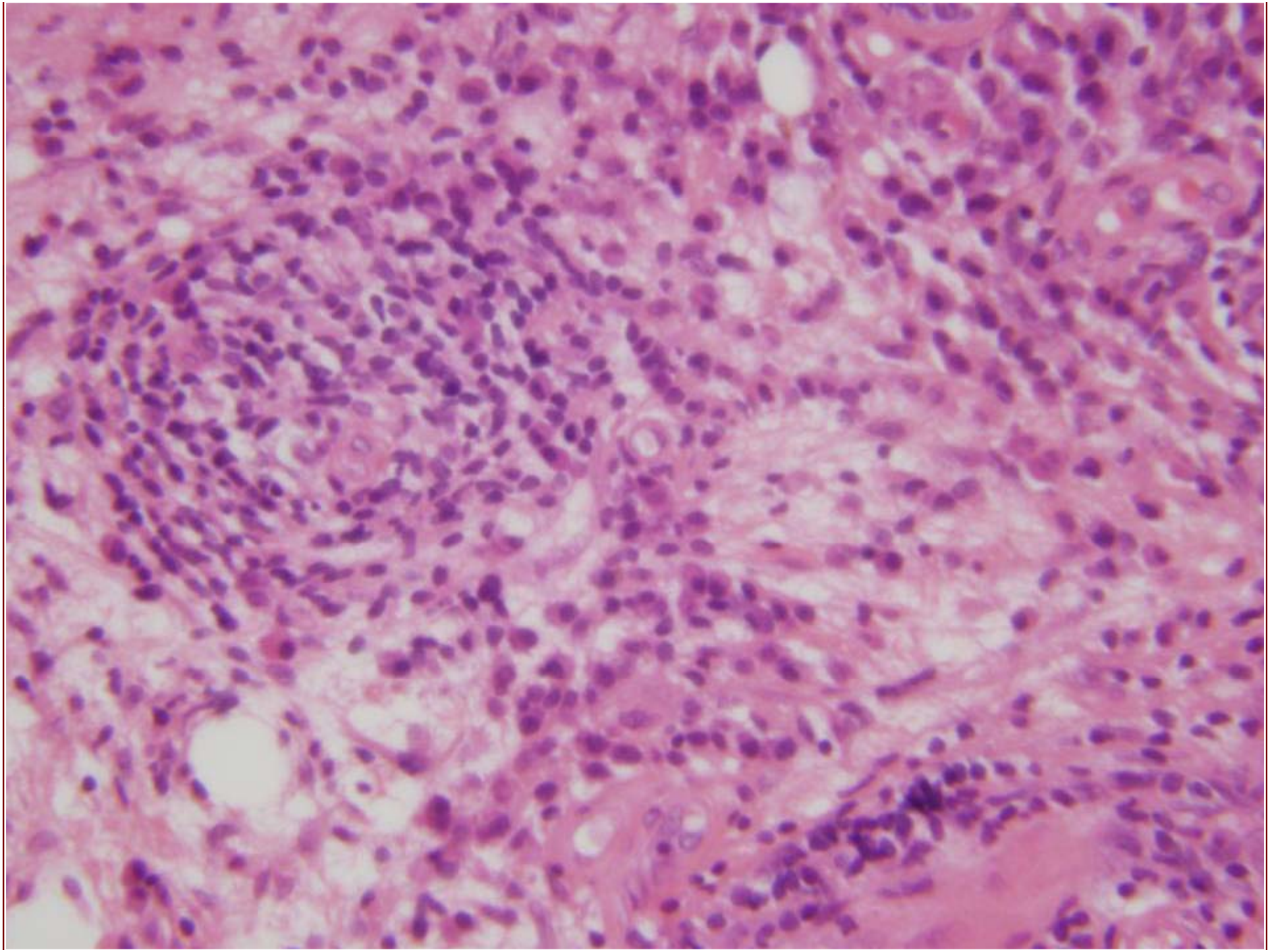








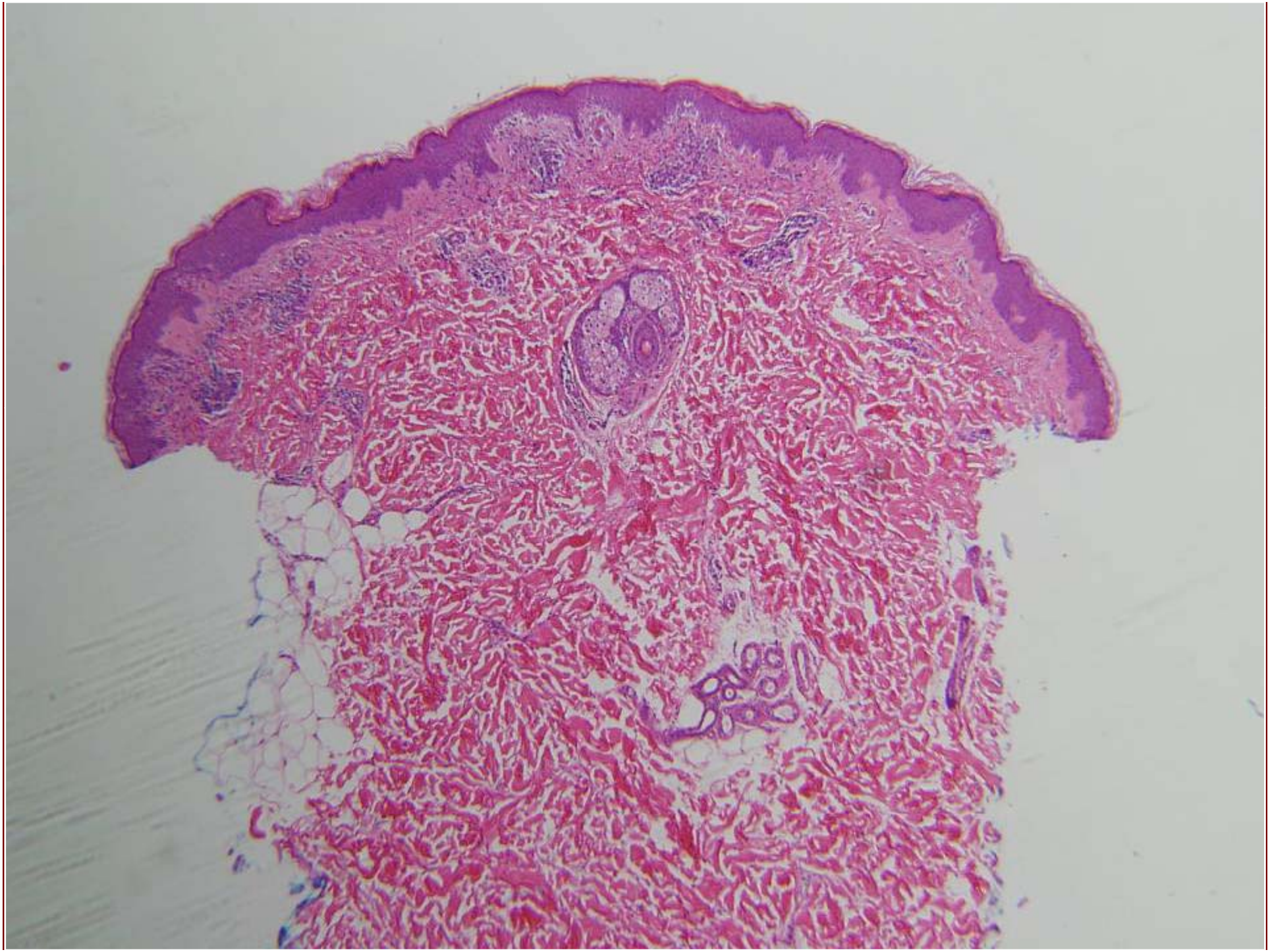


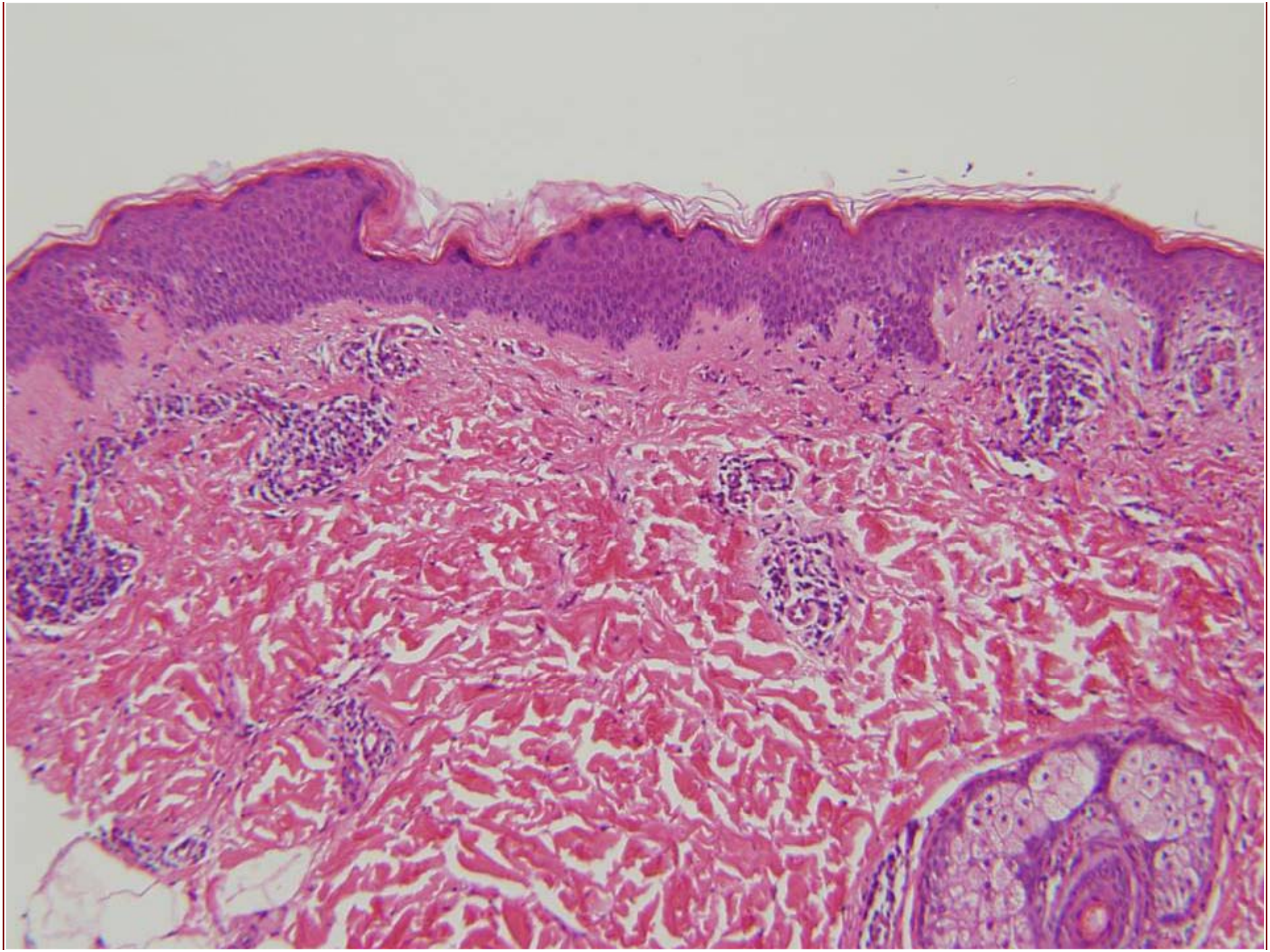


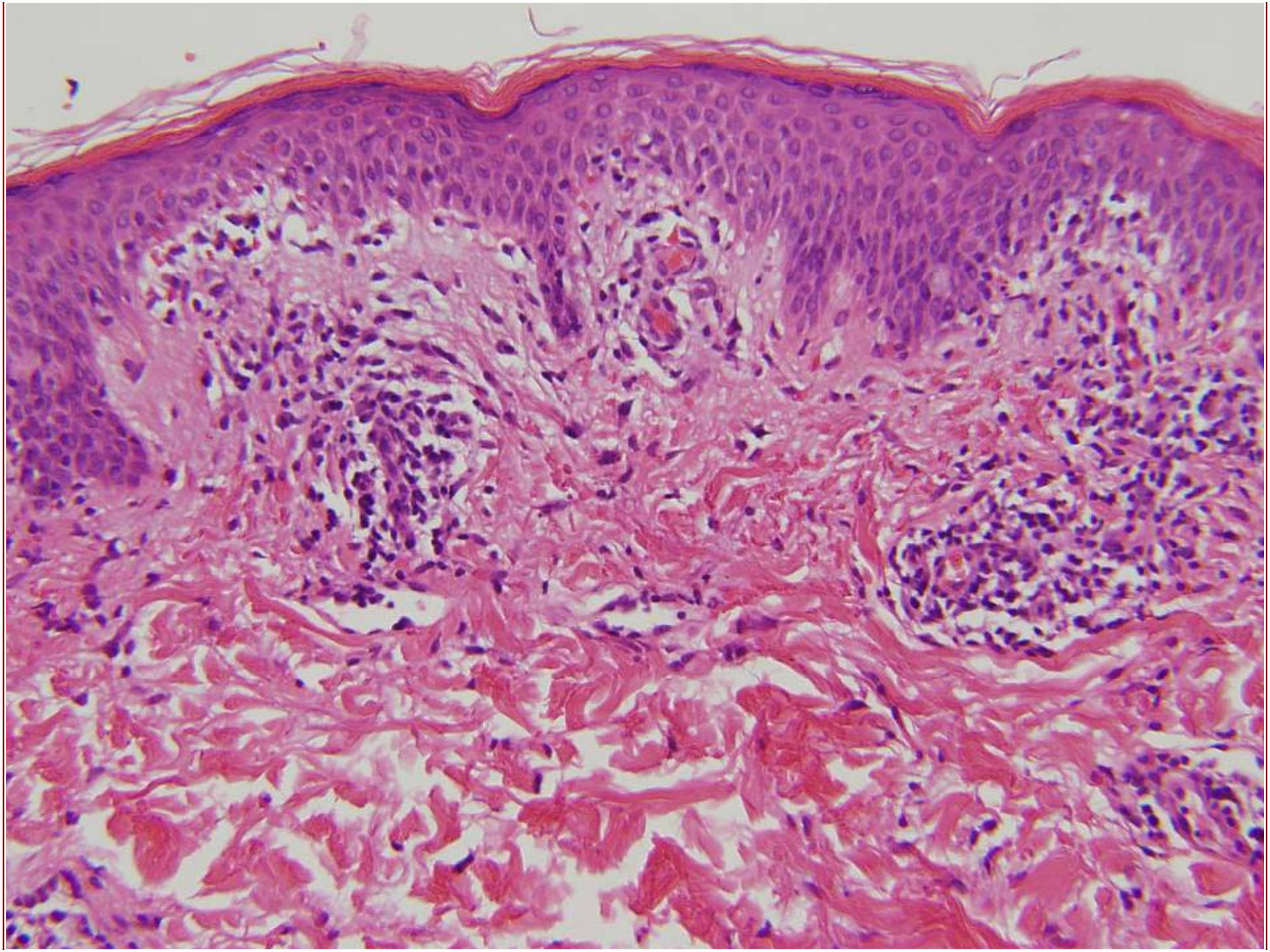
Necrobiosis lipoidica

- Histology:
  - More going on
    - Full thickness dermal involvement, sometimes with sub-Q fat (septa)
    - **Necrobiosis more extensive and less well defined than in GA
    - Layered appearance, open-ended
    - Vascular changes (particularly deep) – endothelial swelling, lymphocytic vasculitis, ?clot
  - Variable palisading of lymphocytes and histiocytes
  - Lipid in necrobiotic area, little/no mucin
  - Plasma cells

- Case 55



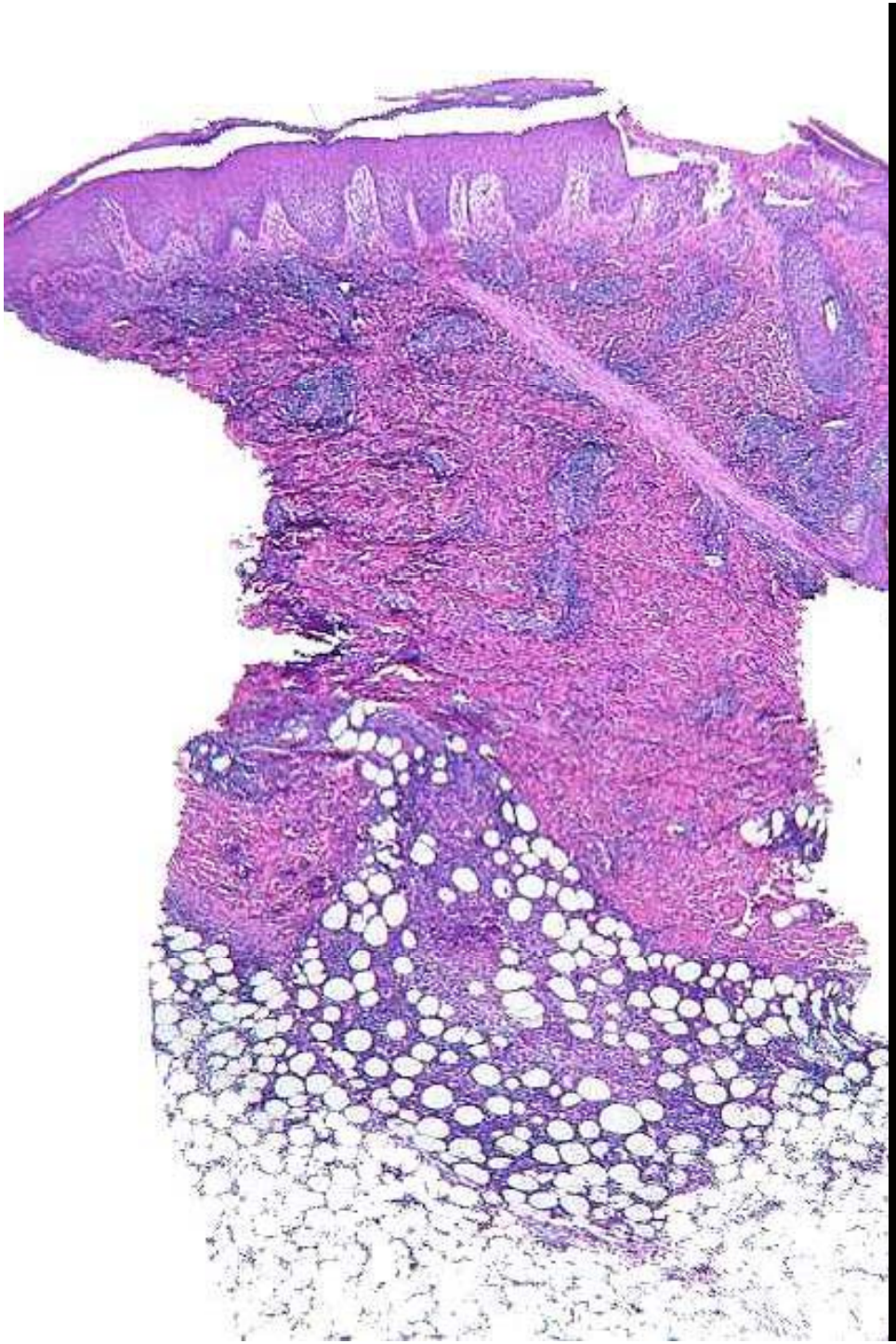


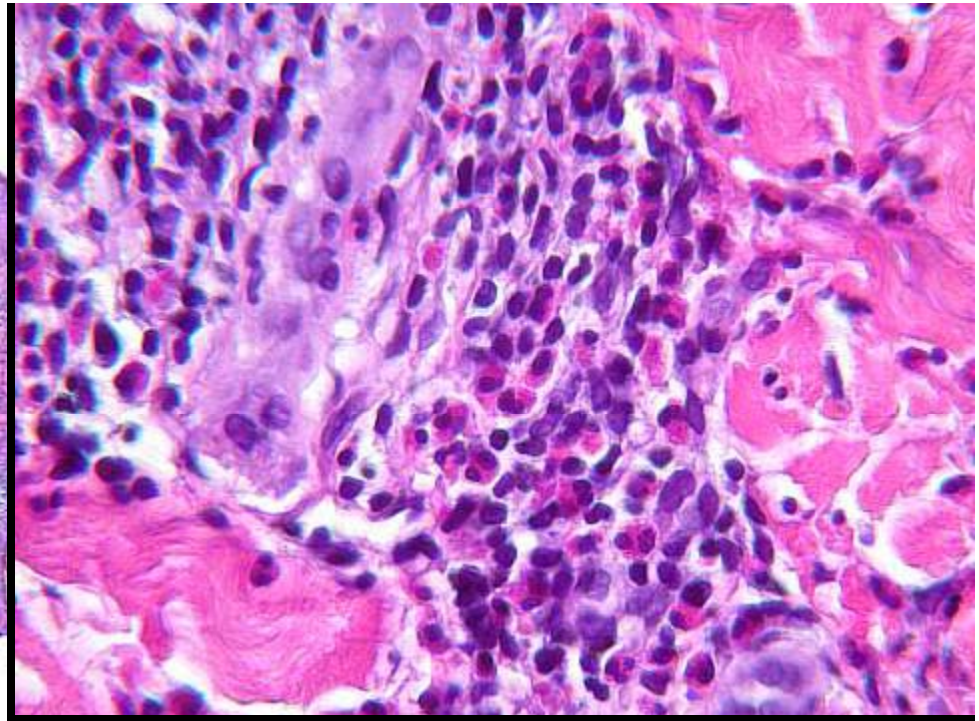


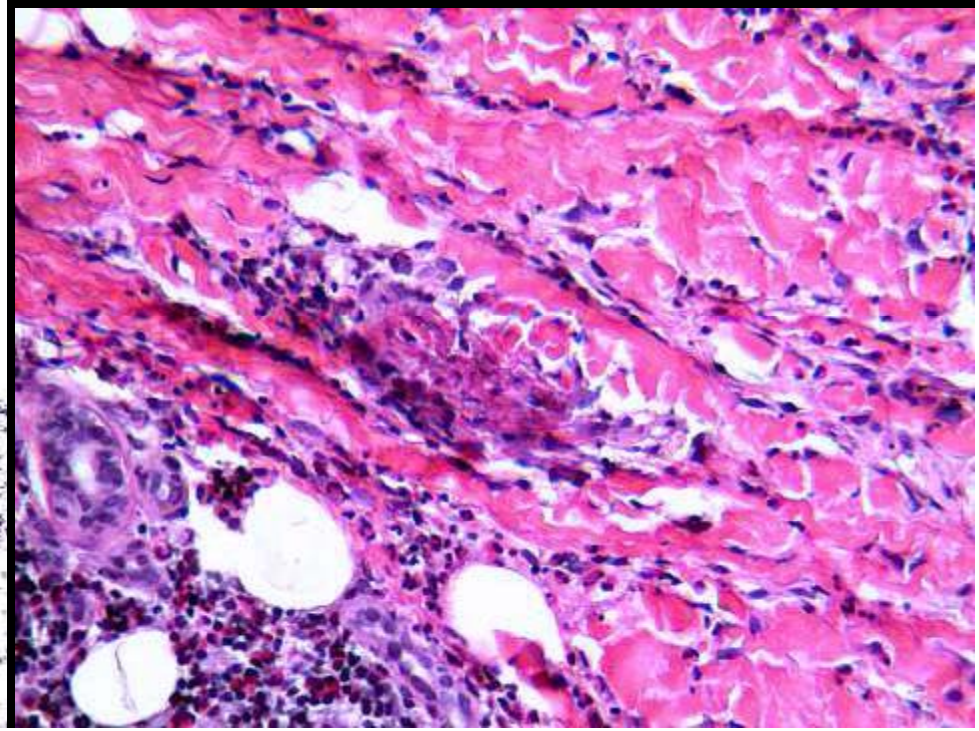
Pigmented purpuric dermatosis

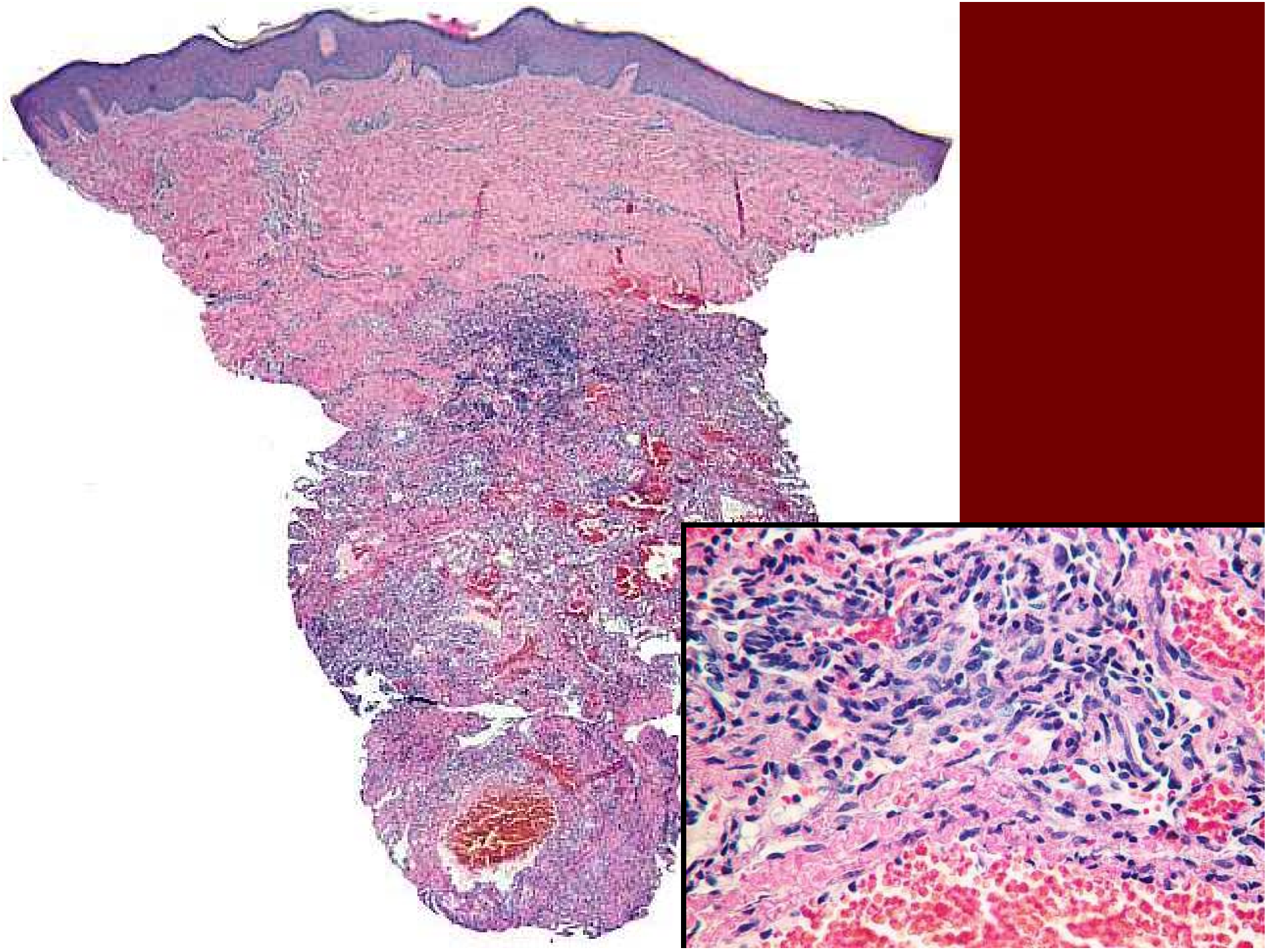
- Pigmented purpuric dermatoses
  - Lymphocytic vasculitis of upper dermis – so called "capillaritis"
    - Lymphocytes around vessels and in dermis
    - Extravasated RBCs
    - +/- exocytosis of lymphocytes and spongiosis
    - Hemosiderin in macrophages – higher than in stasis
  - Part of LUMP mneumonic...infiltrates that fill papillary dermis:
    - Lichenoid disease
    - Urticaria pigmentosa
    - Mycosis fungoides and precursors
    - Pigmented purpuric dermatoses

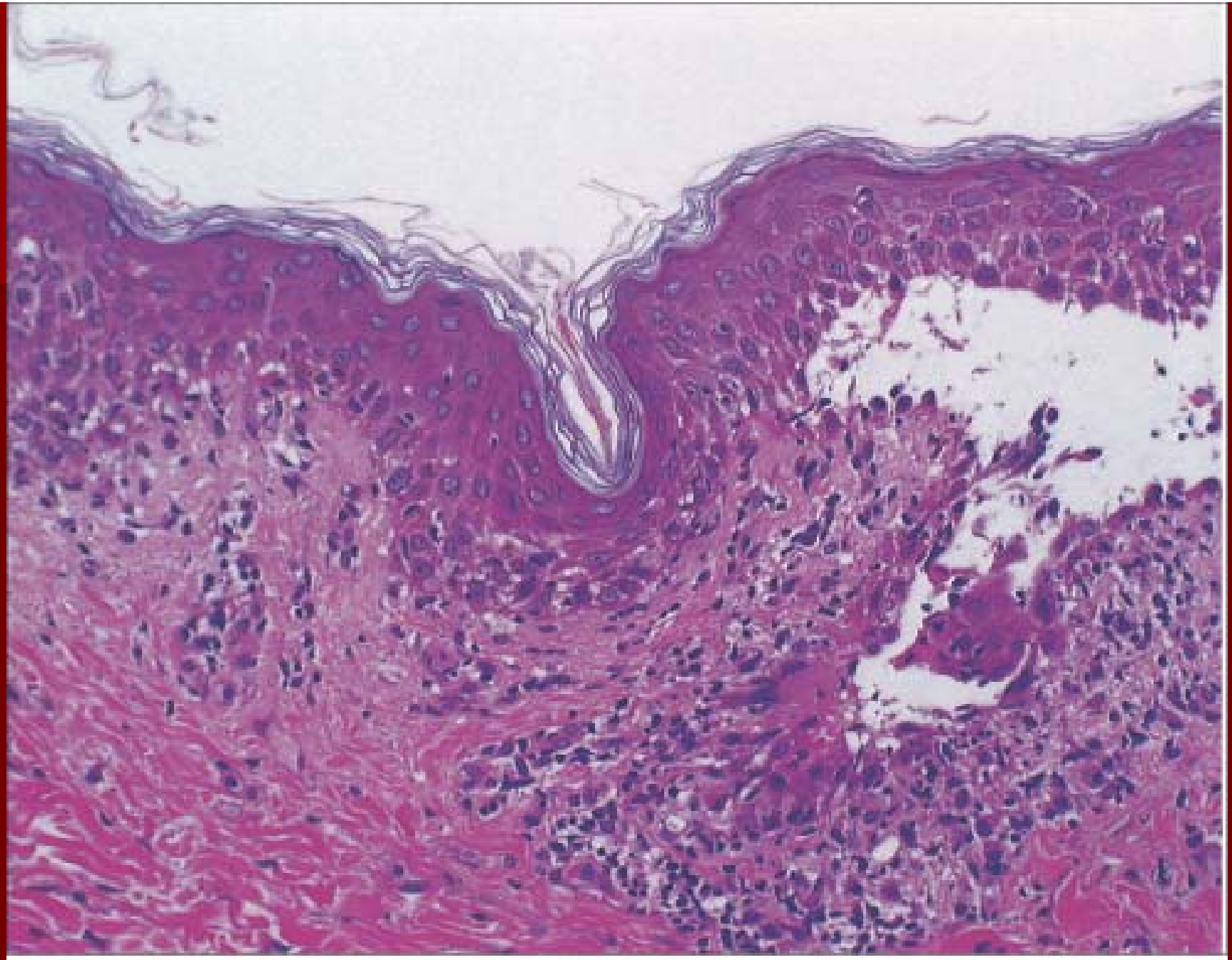
Unknowns











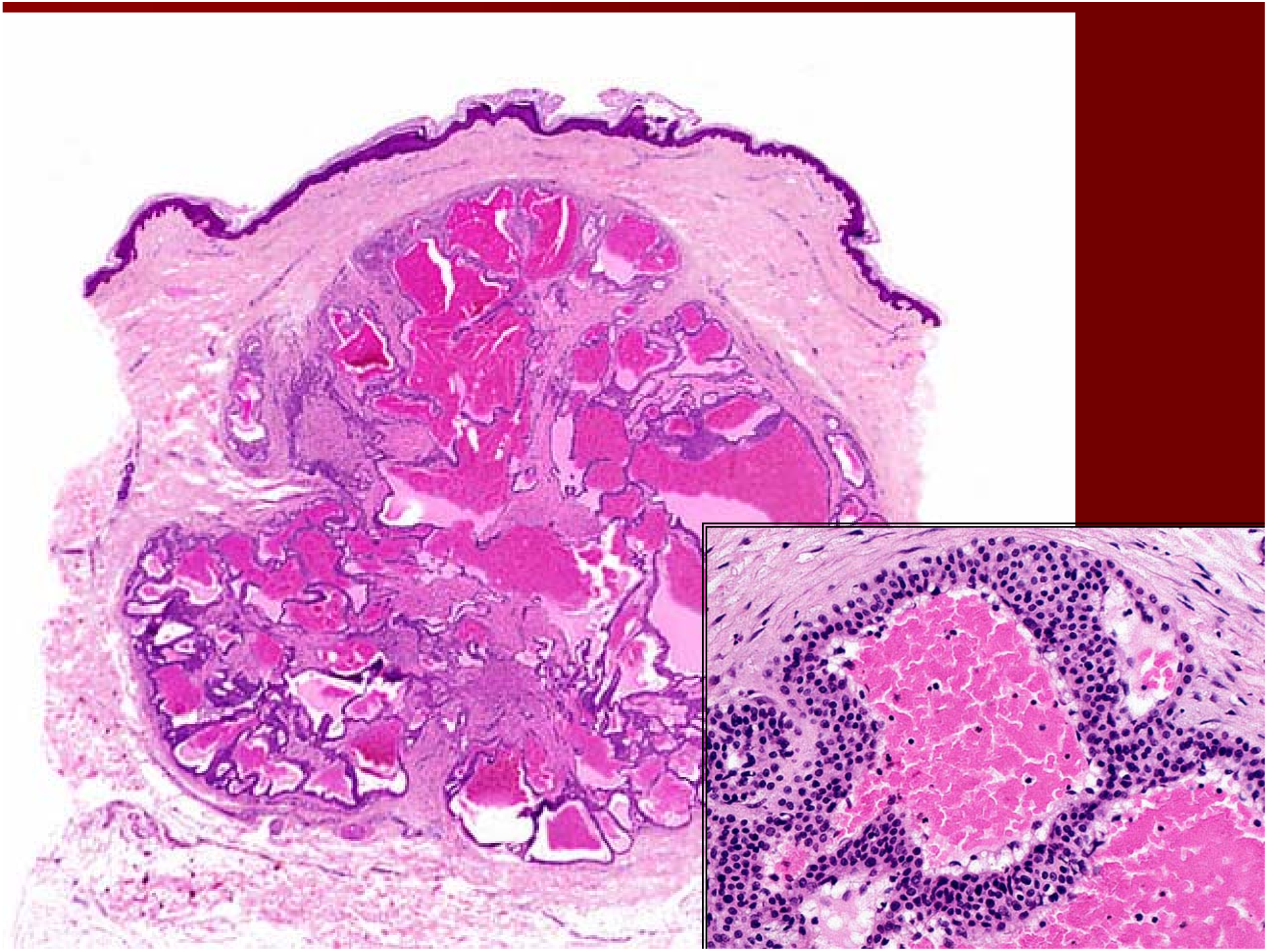
- What is the differential for eosinophilic spongiosis?

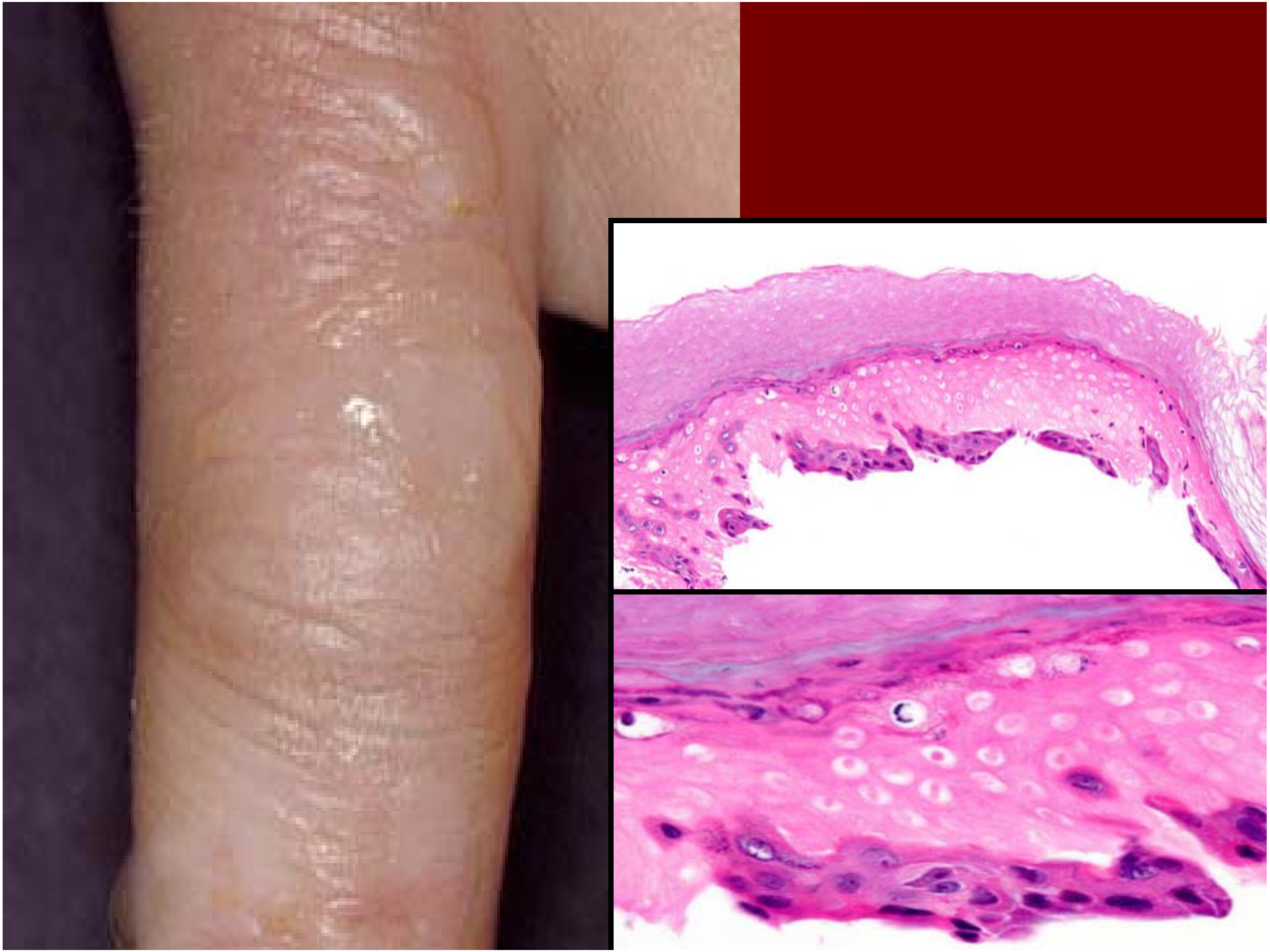
- Bullous pemphigoid
- Pemphigus
- Incontinentia pigmentosum
- Allergic contact dermatitis

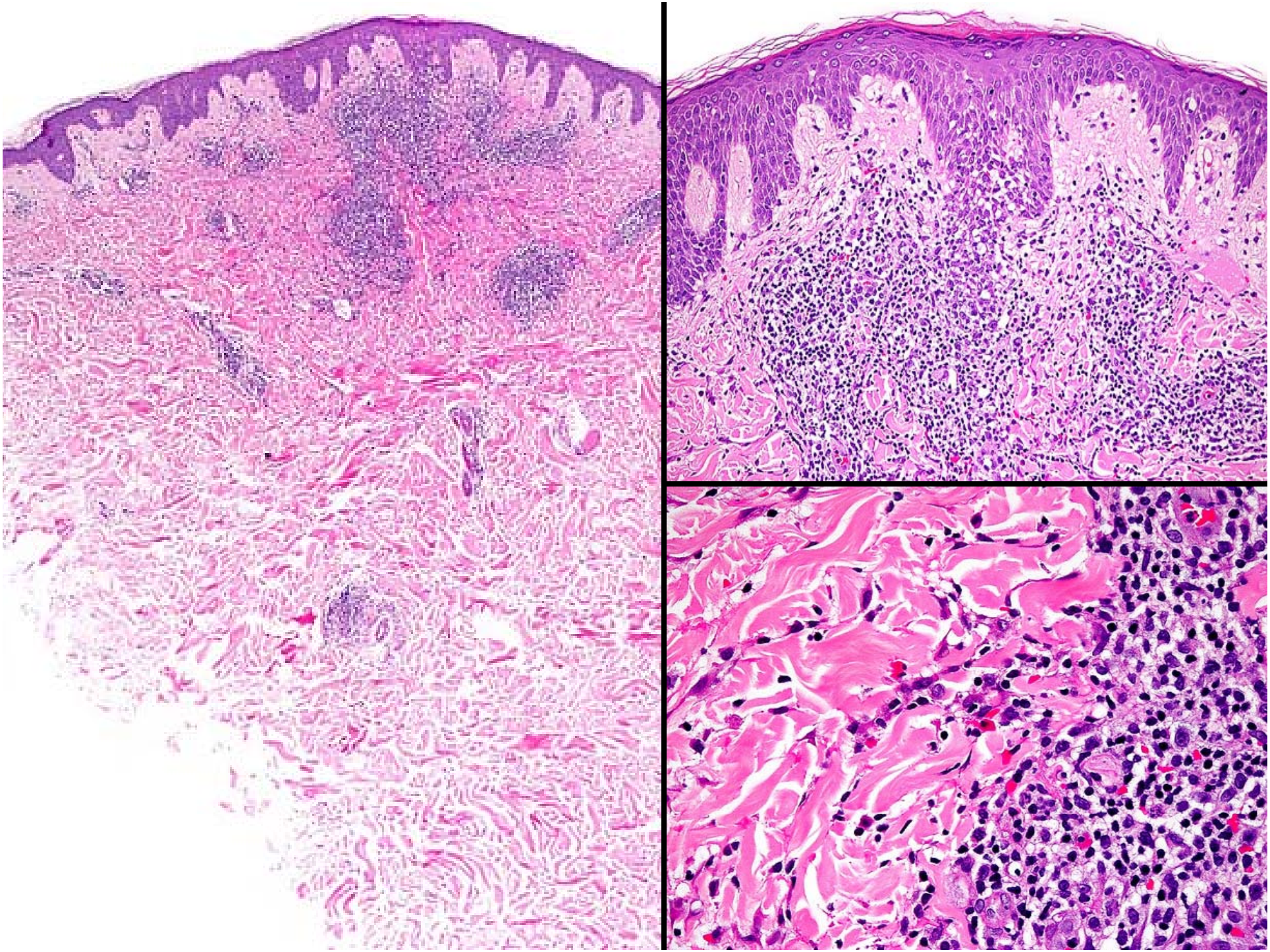
- Arthropod bite

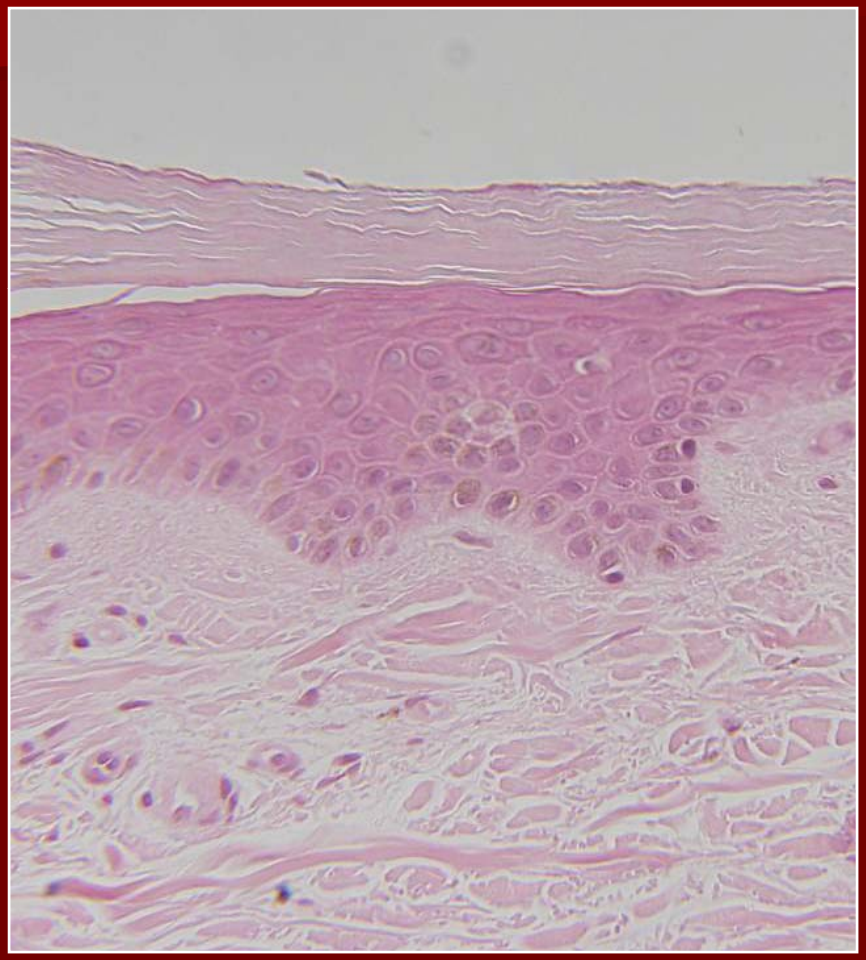
Table 31.3 Causes of eosinophilic spongiosis.

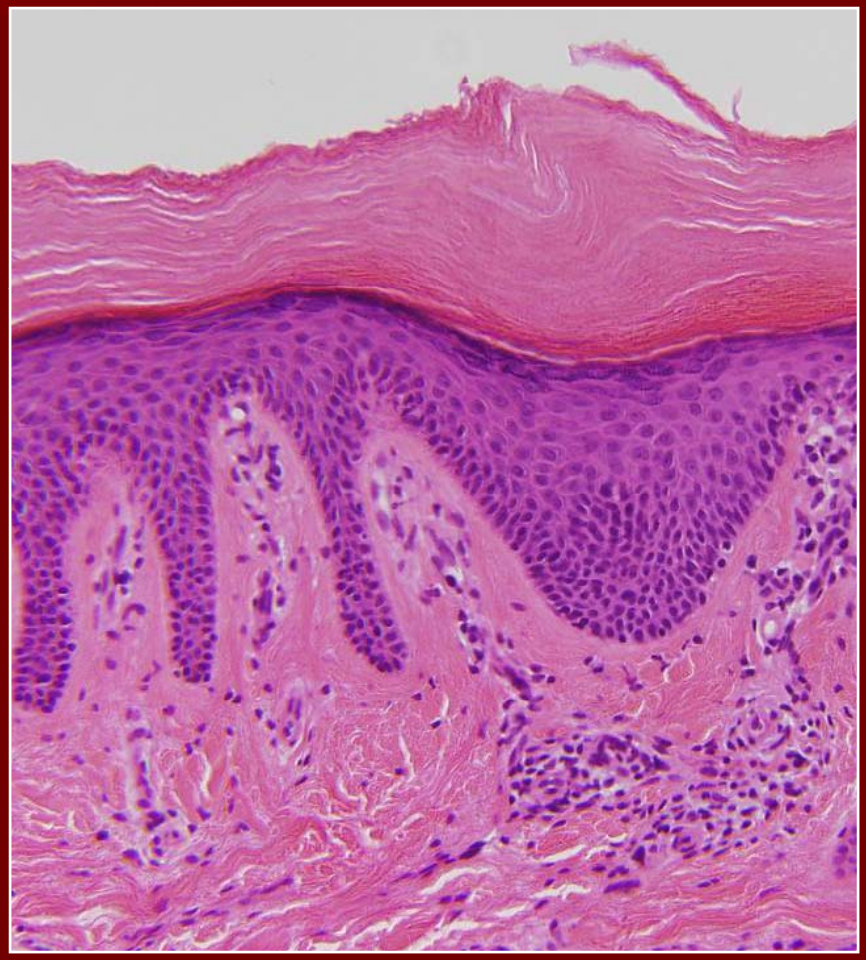
CAUSES OF EOSINOPHILIC SPONGIOSIS
Pemphigus vulgaris
Pemphigus foliaceus
Bullous pemphigoid
Gestational pemphigoid (herpes gestationis)
Linear IgA bullous dermatosis
Incontinentia pigmenti
Insect-bite reaction
Drug eruptions
Atopic dermatitis
Contact dermatitis
Transient acantholytic dermatosis (Grover's disease)











Distinguishing micro features of ichthyoses…

- Ichthyoses – all have hyperkeratosis
  - Vulgaris – AD – decreased profilaggrin
    - Decreased granular layer
    - Thin epidermis, diminished rete
    - Follicular plugging
  - X-linked – steroid sulfatase deficiency
    - Normal/thickened granular layer
    - Acanthosis
  - Lamellar – Ar – transglutaminase-1 mutation
    - Mild acanthosis, psoriasiform hyperplasia, extensive hyperkeratosis
  - Nonbullous CIE – Ar
    - Same as lamellar, but + parakeratosis, looks a lot like psoriasis w/ decr. Granular layer below parakeratosis, + neutrophils
  - Bullous CIE – AD – K1 and K10 mutations
    - Epidermolytic hyperkeratosis