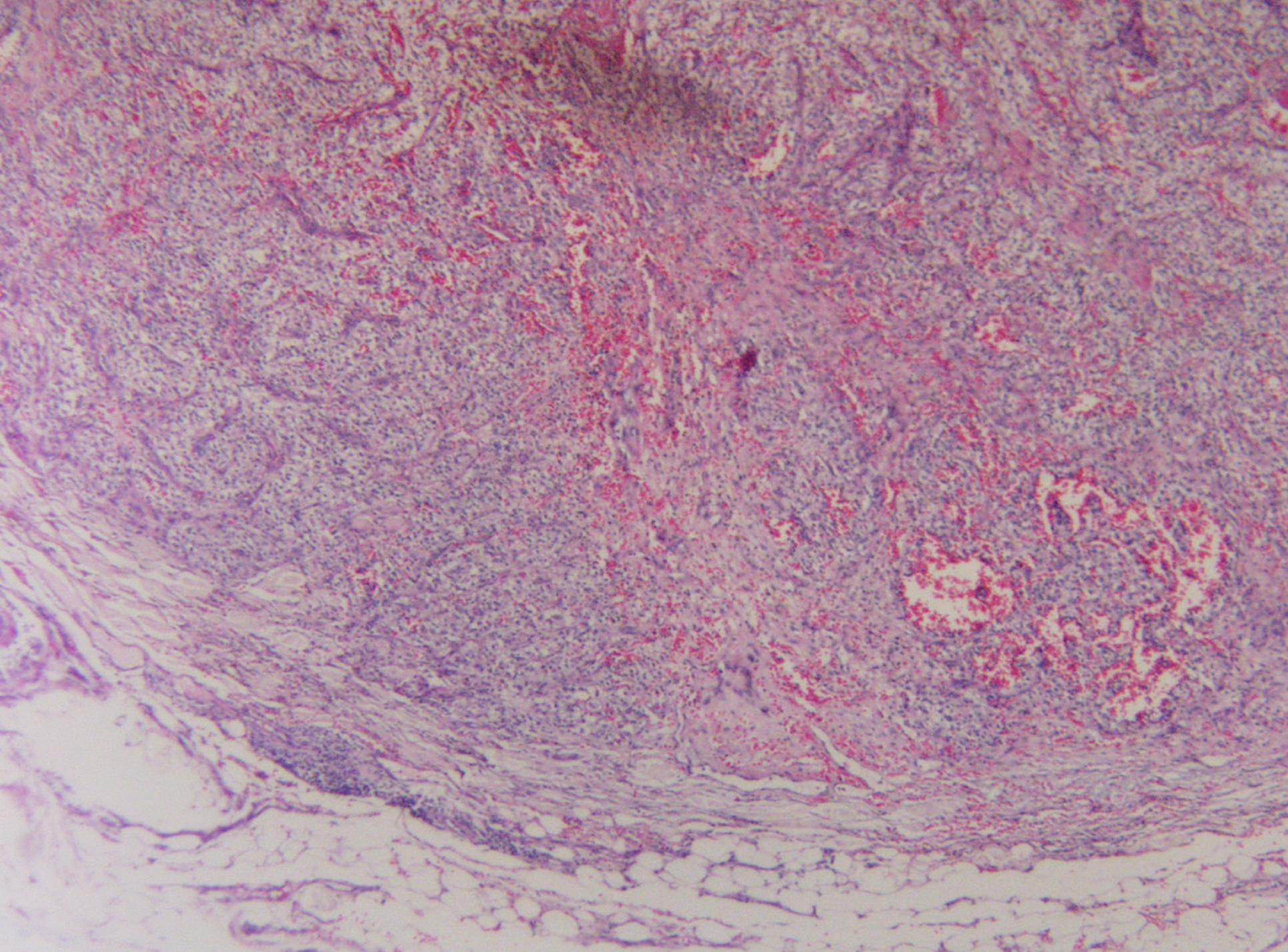


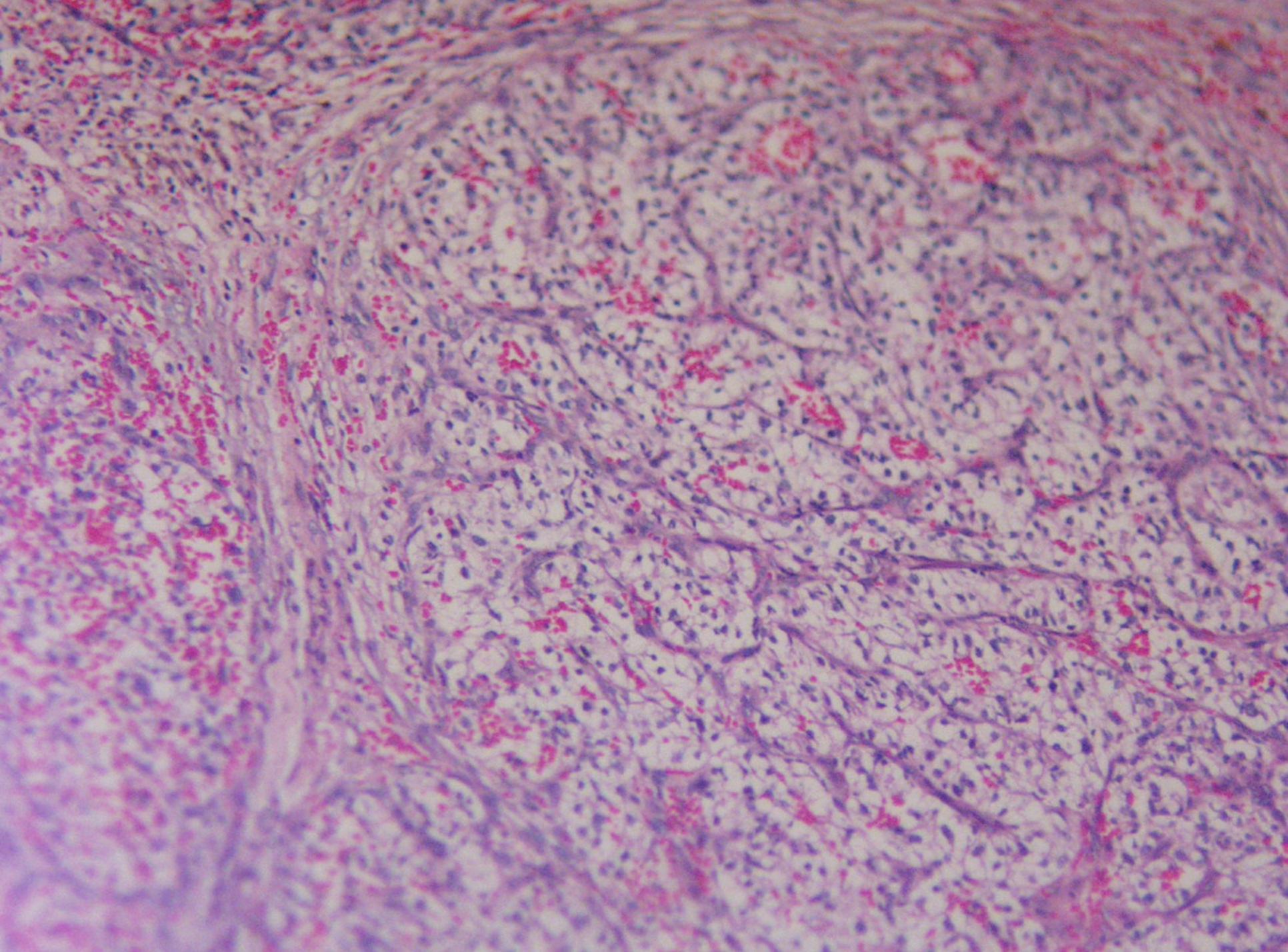
# Dermatopathology Slide Review Part 6

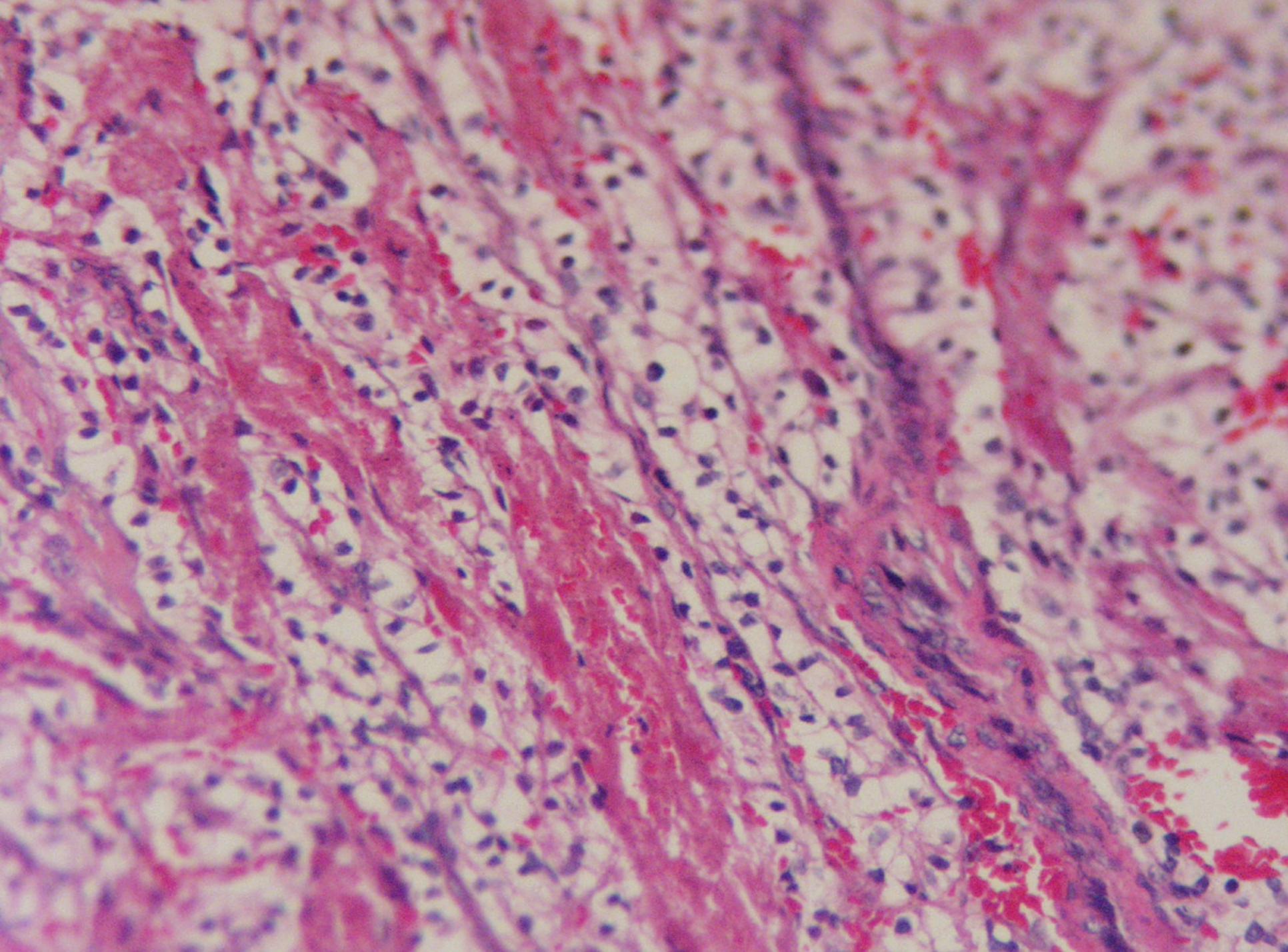
Paul K. Shitabata, M.D.

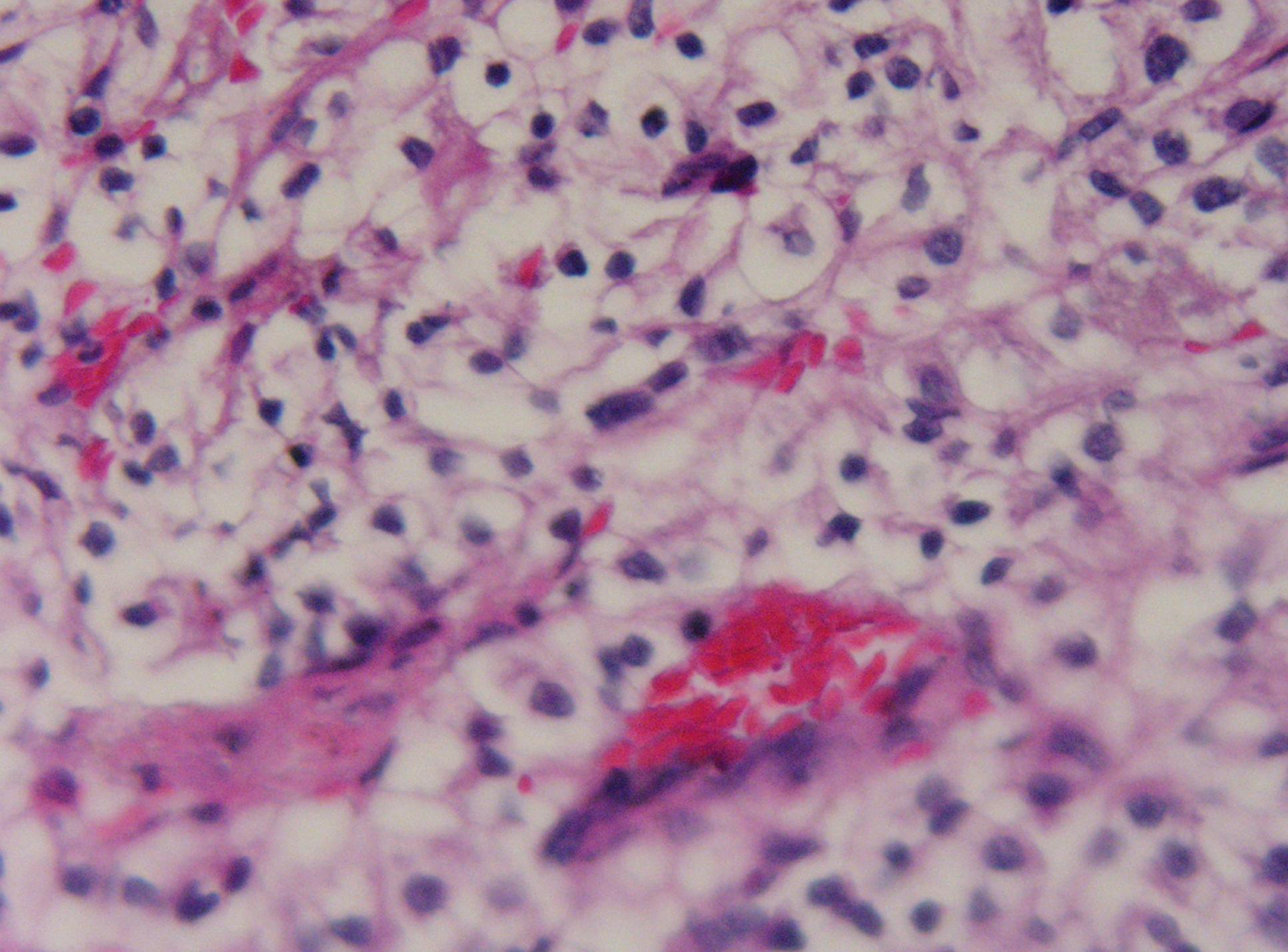
Dermatopathology Institute

89 y.o. M with nodule  
at base of right thumb





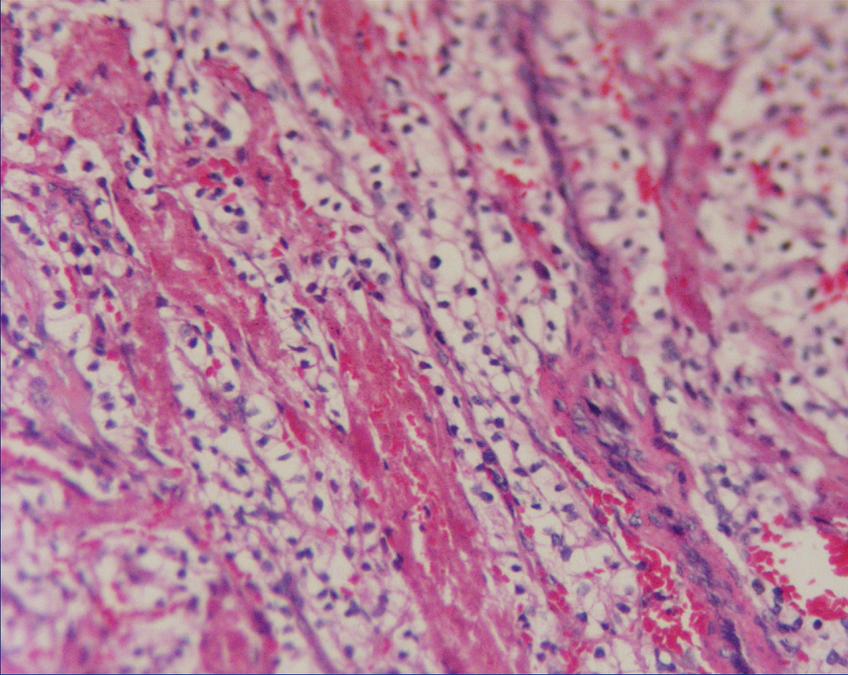




**What is your differential  
diagnosis and what stains/IHC  
would you order?**

# Metastatic Renal Cell Carcinoma

# Histopathology



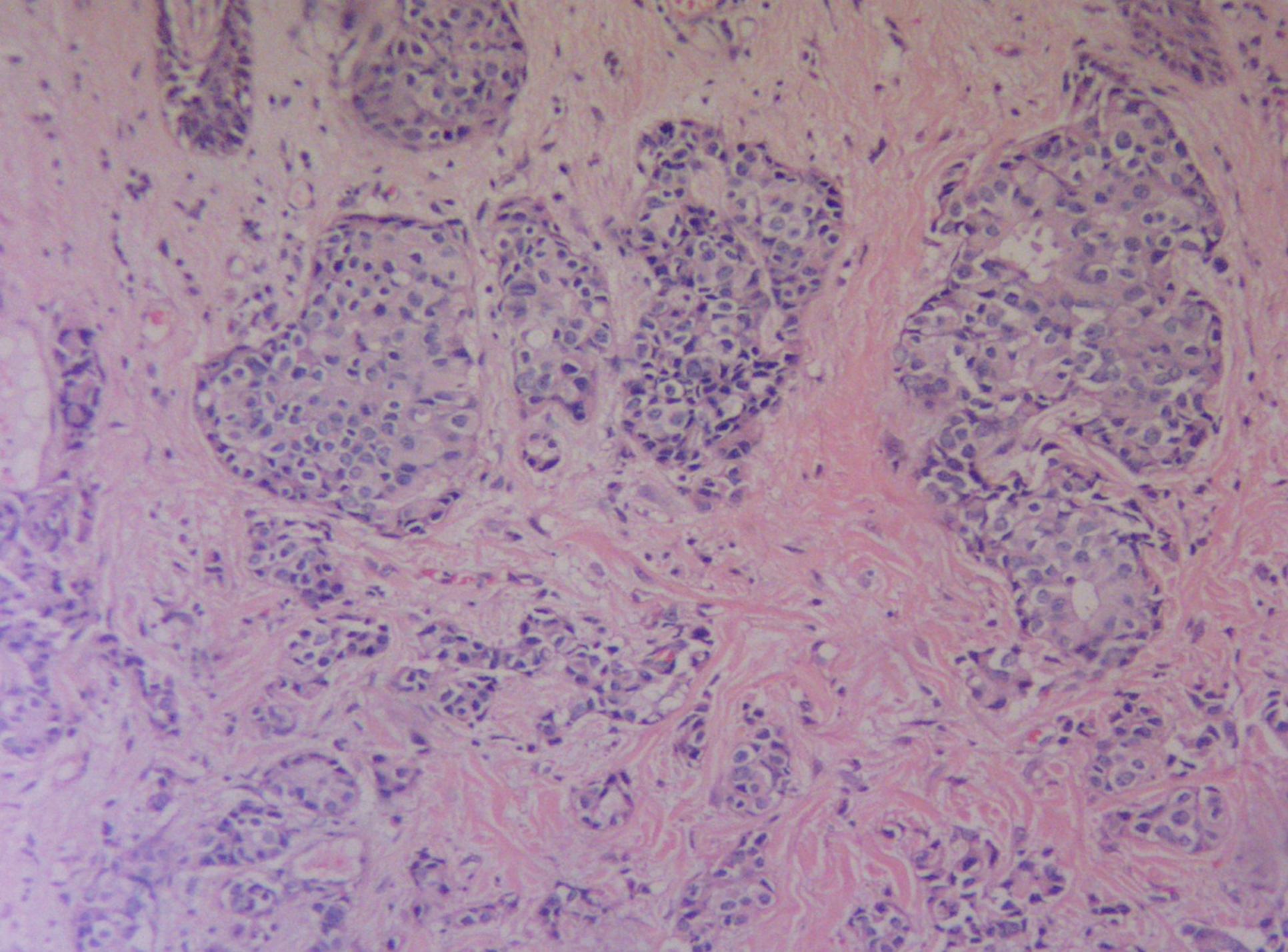
- Nested or in diffuse sheets
- Clear cells with centrally placed nuclei
- Increased vascularity-lakes of blood

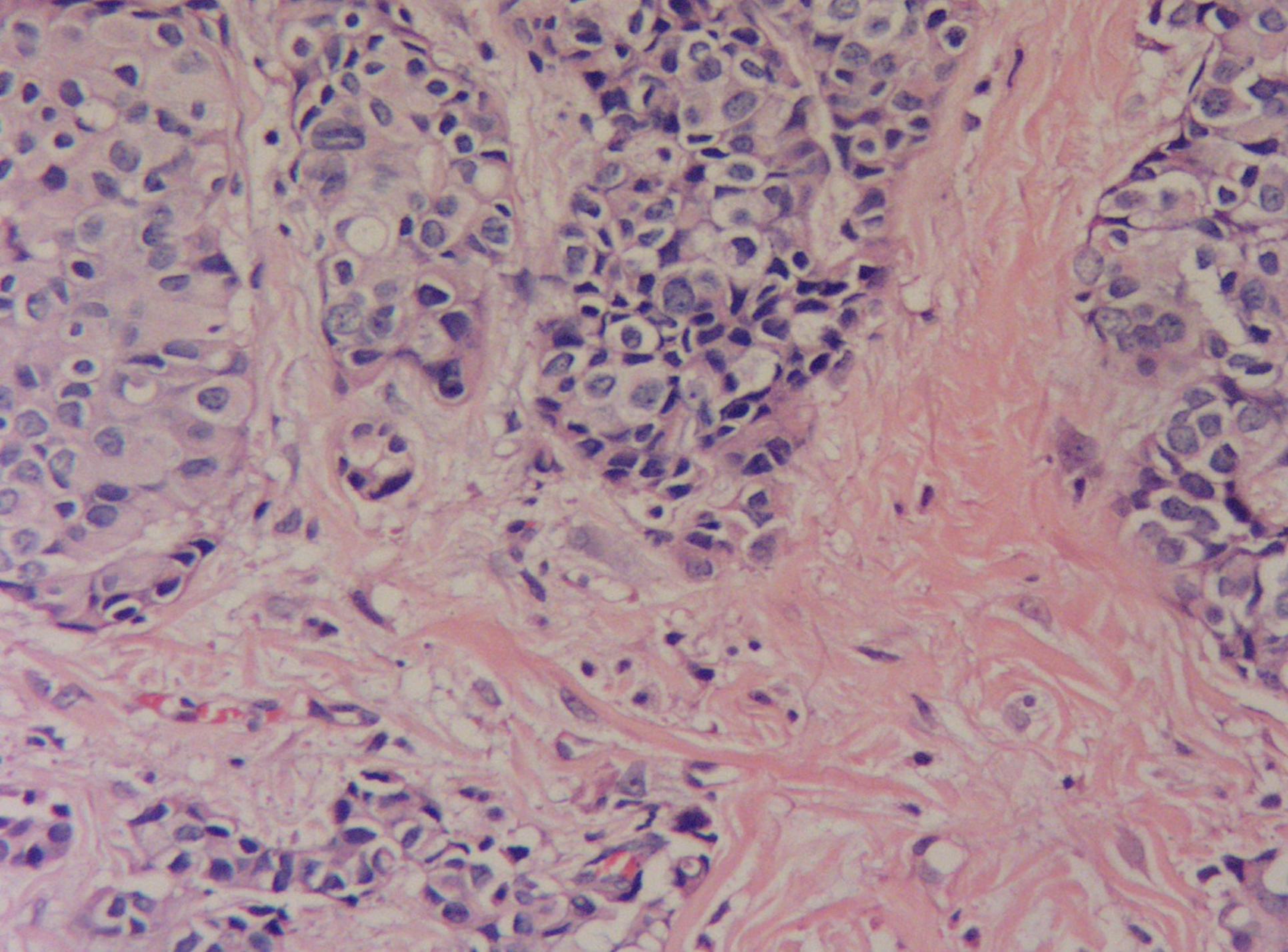
# What is the pathogenesis of these clear cytoplasmic changes?

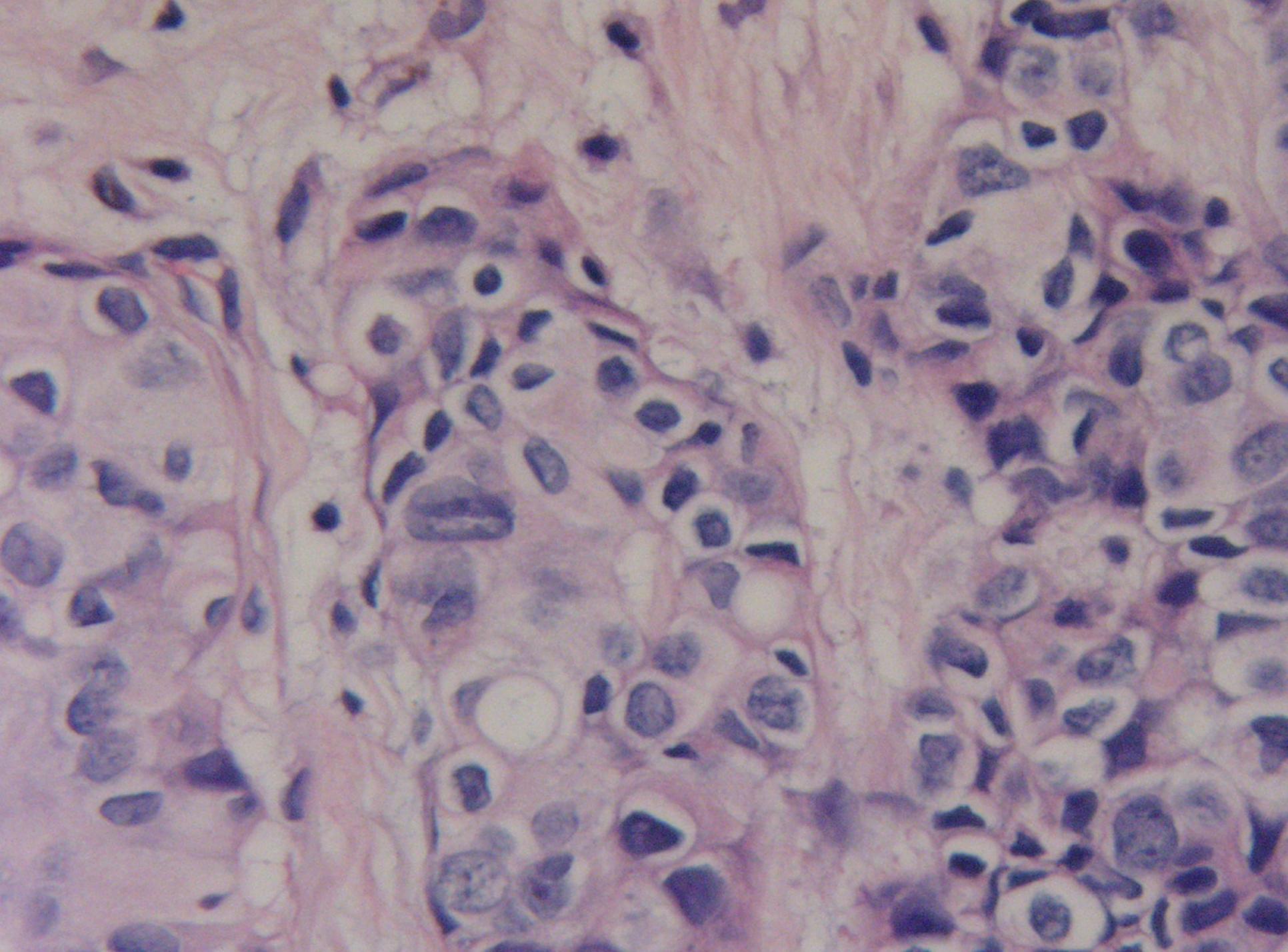
- Renal cell carcinoma
- Balloon cell melanoma
- Basal cell carcinoma with clear cell changes
- Granular cell tumor
- Clear cell Syringoma

# What is the pathogenesis of the following clear cytoplasmic changes?

- Renal cell carcinoma-lipid and glycogen
- Balloon cell melanoma-lysozymes
- Basal cell carcinoma with clear cell changes-glycogen
- Granular cell tumor-lysozymes
- Clear cell Syringoma-glycogen



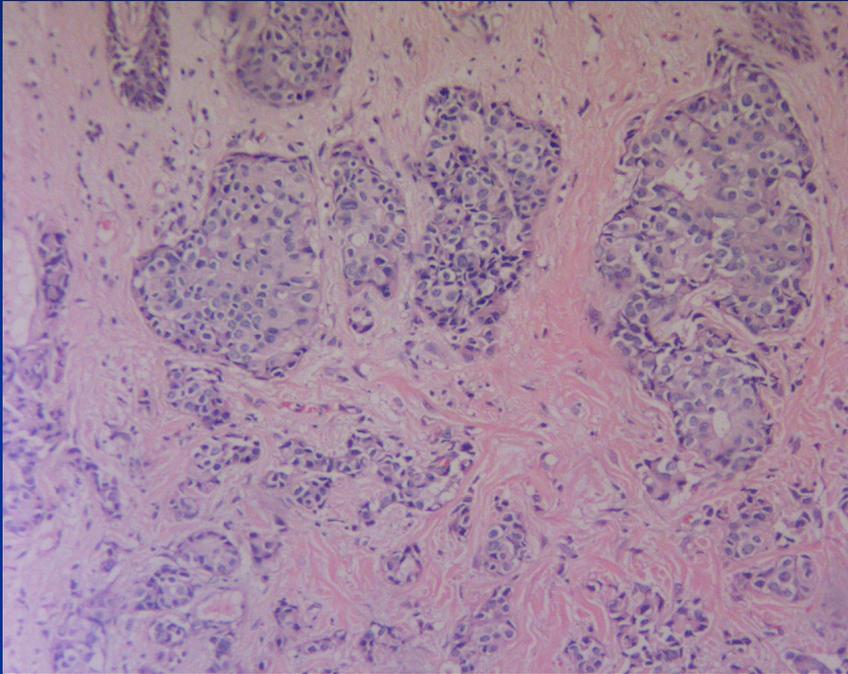




**What is your differential  
diagnosis and what stains/IHC  
would you order?**

# Metastatic Prostate Carcinoma

# Histopathology



- Glandular formation dependent upon initial grade
- May have glands with clear cytoplasmic changes
- Pleomorphic nuclei with MF
- Serum and tissue PSA

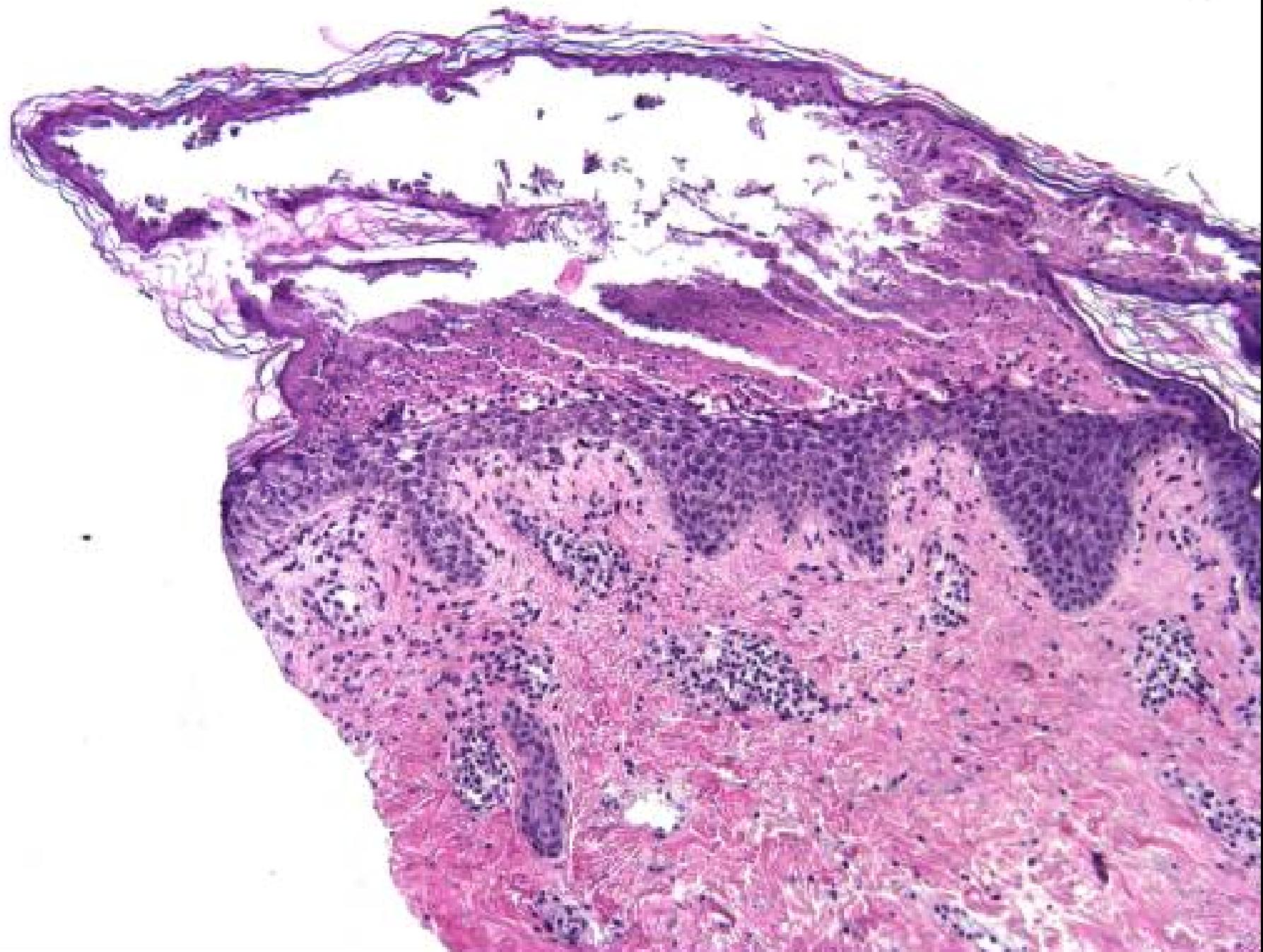
What are some names of clinical variants of metastatic malignancies to the skin?

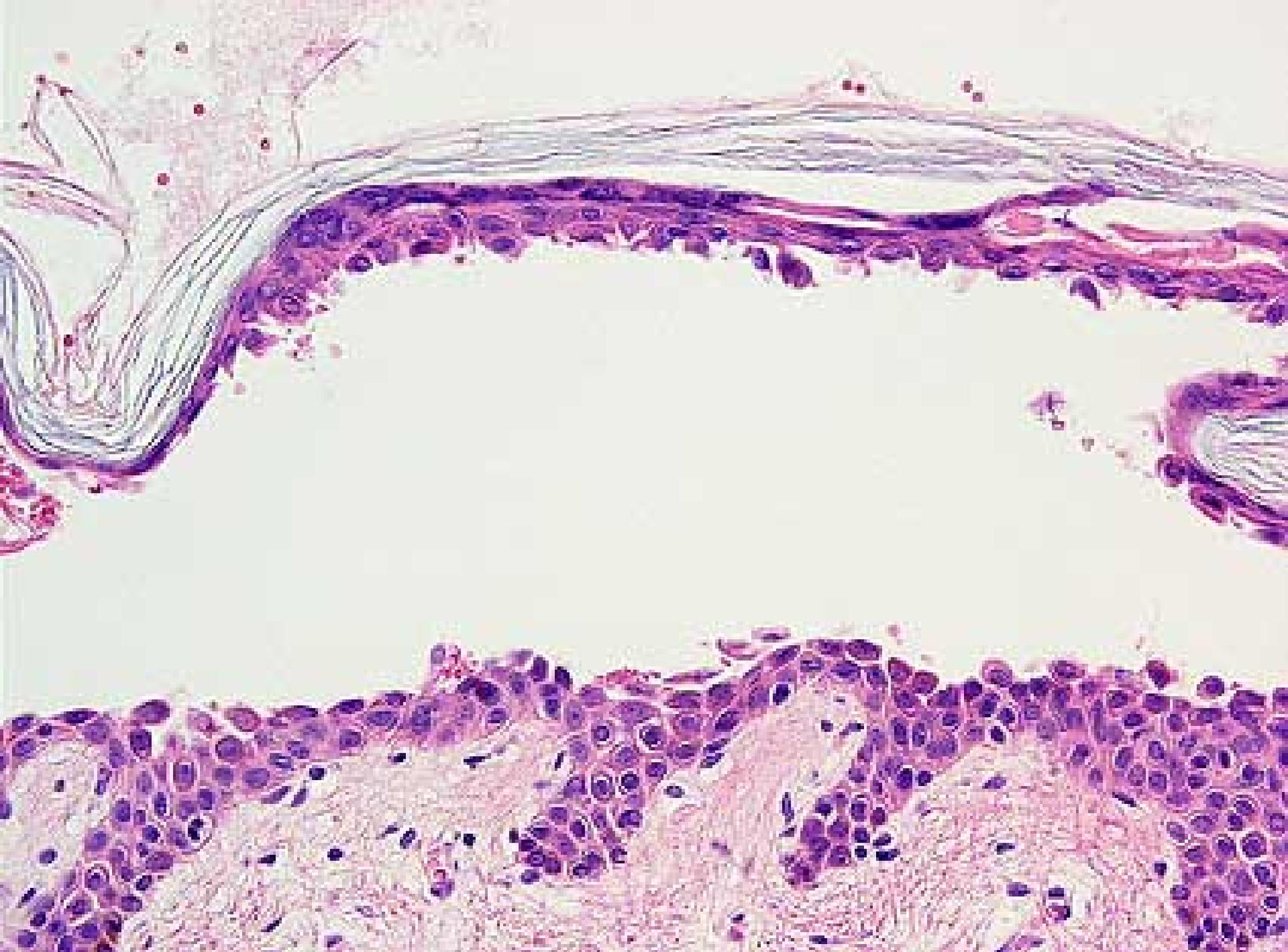
(For example-*peau d'orange* and breast cancer)

# Clinical Variants of Metastatic Malignancy to the Skin

- Paget's disease of the nipple
- Extra-mammary Paget's disease
- Peau d'orange
- Carcinoma en cuirasse
- Sister Mary Joseph's nodule
- Alopecia neoplastica
- Carcinoma erysipelatoides

66 y.o. M with  
eroded lesions and bullae

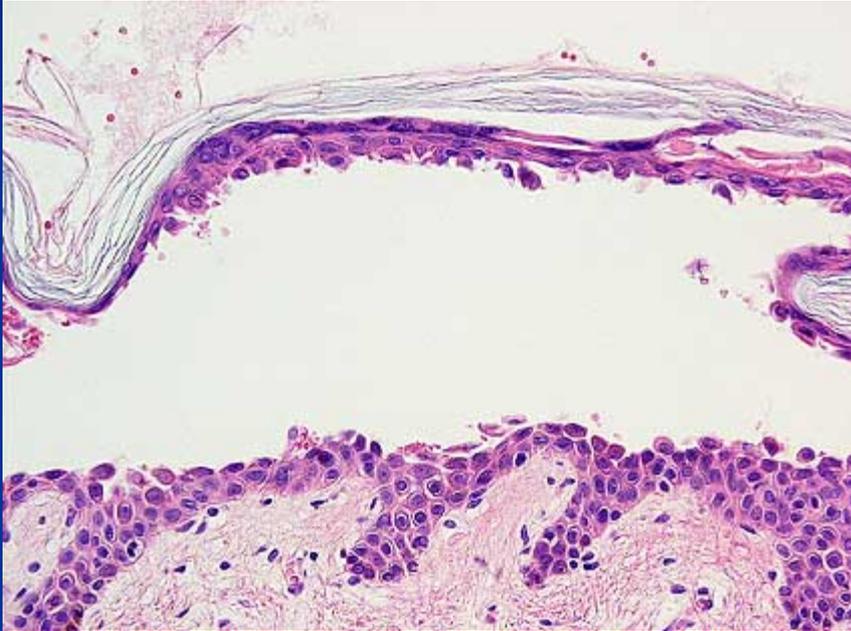




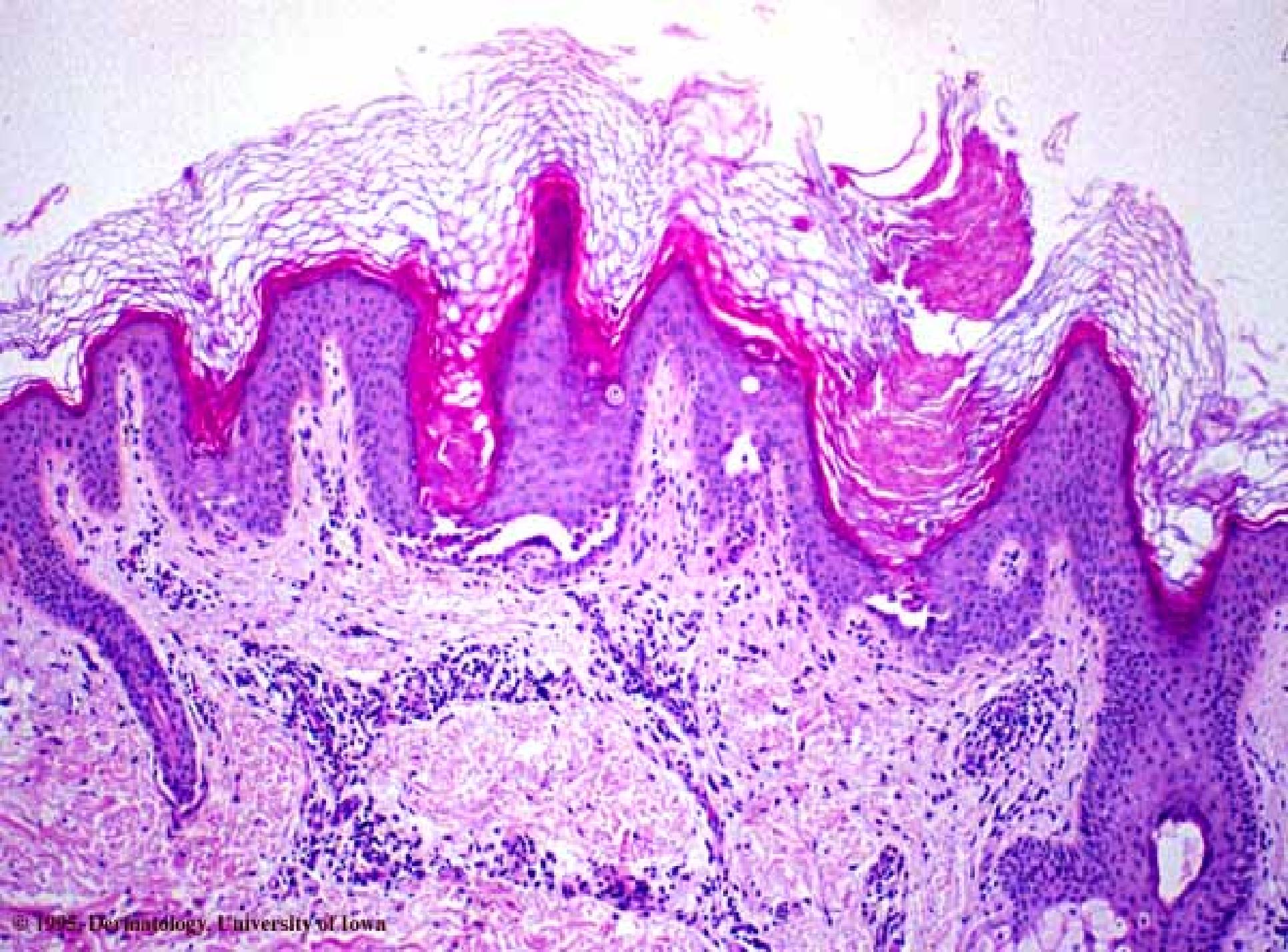
**What is your differential  
diagnosis and what stains/IHC  
would you order?**

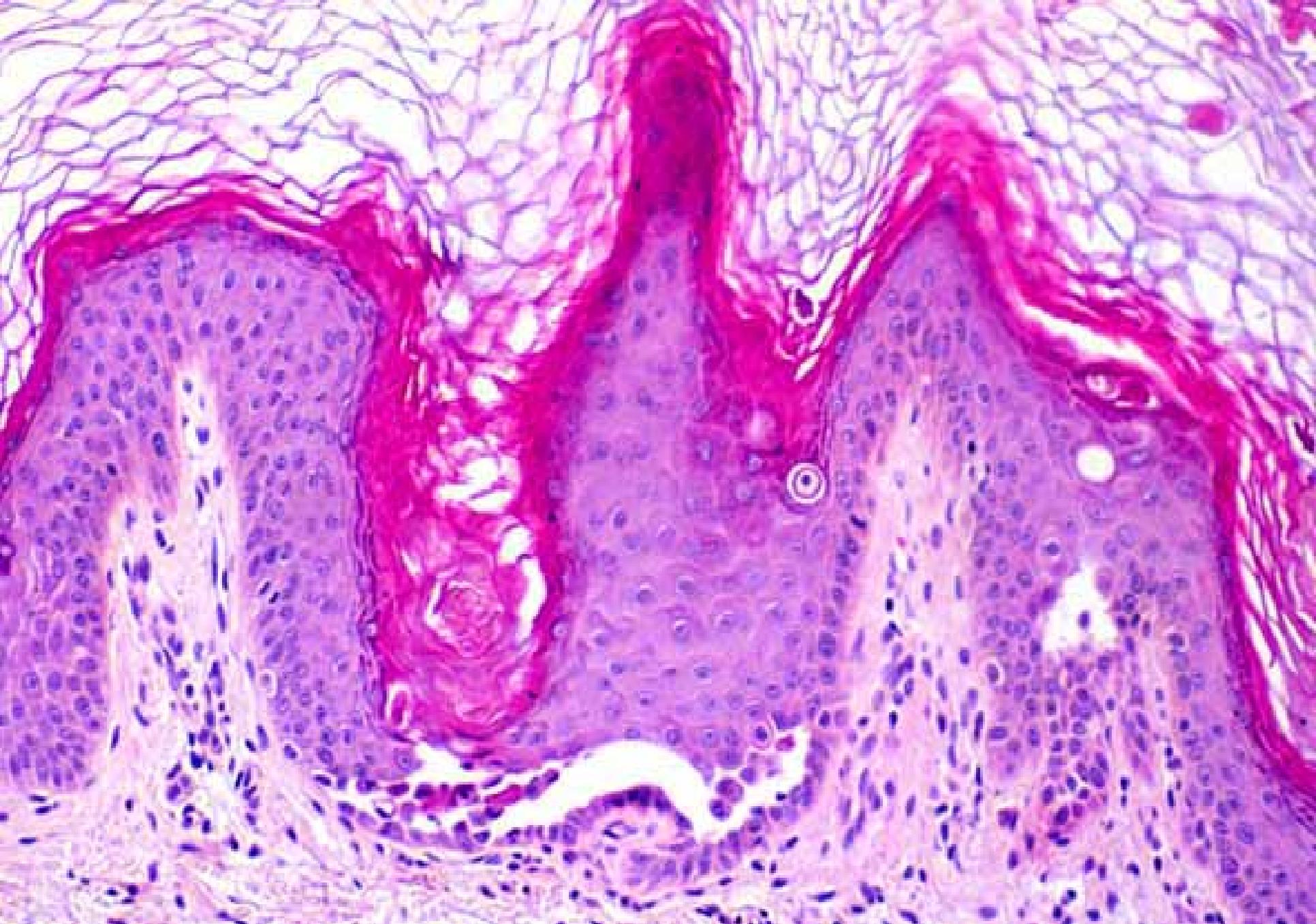
# Pemphigus Foliaceus

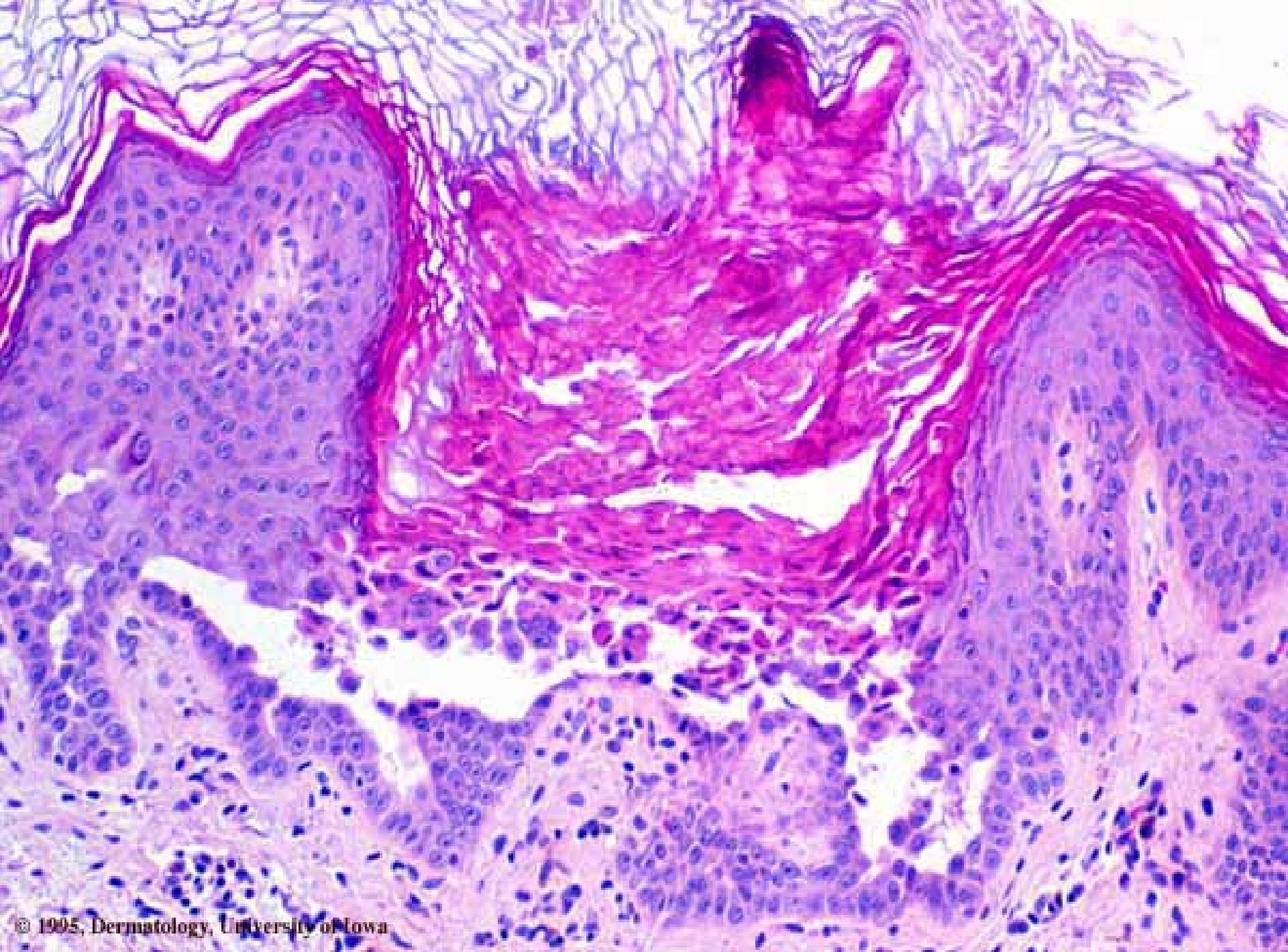
# Histopathology



- Subcorneal acantholysis (“Klingons”)
- Variable eosinophils
- DIF-Intercellular IgG
- DDX: Pemphigus erythematosus, Grover’s disease, bullous impetigo







**What is your differential  
diagnosis and what stains/IHC  
would you order?**

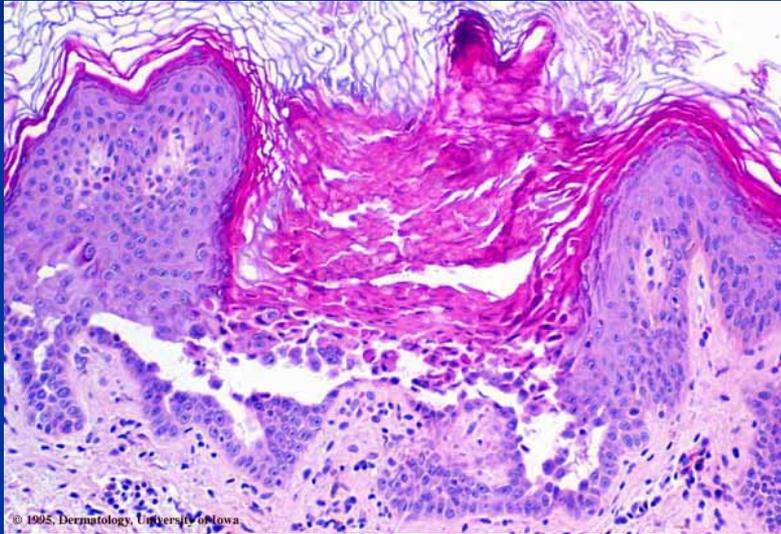
# Darier's Disease

What is the inheritance pattern  
and genetic abnormality for  
Darier's disease?

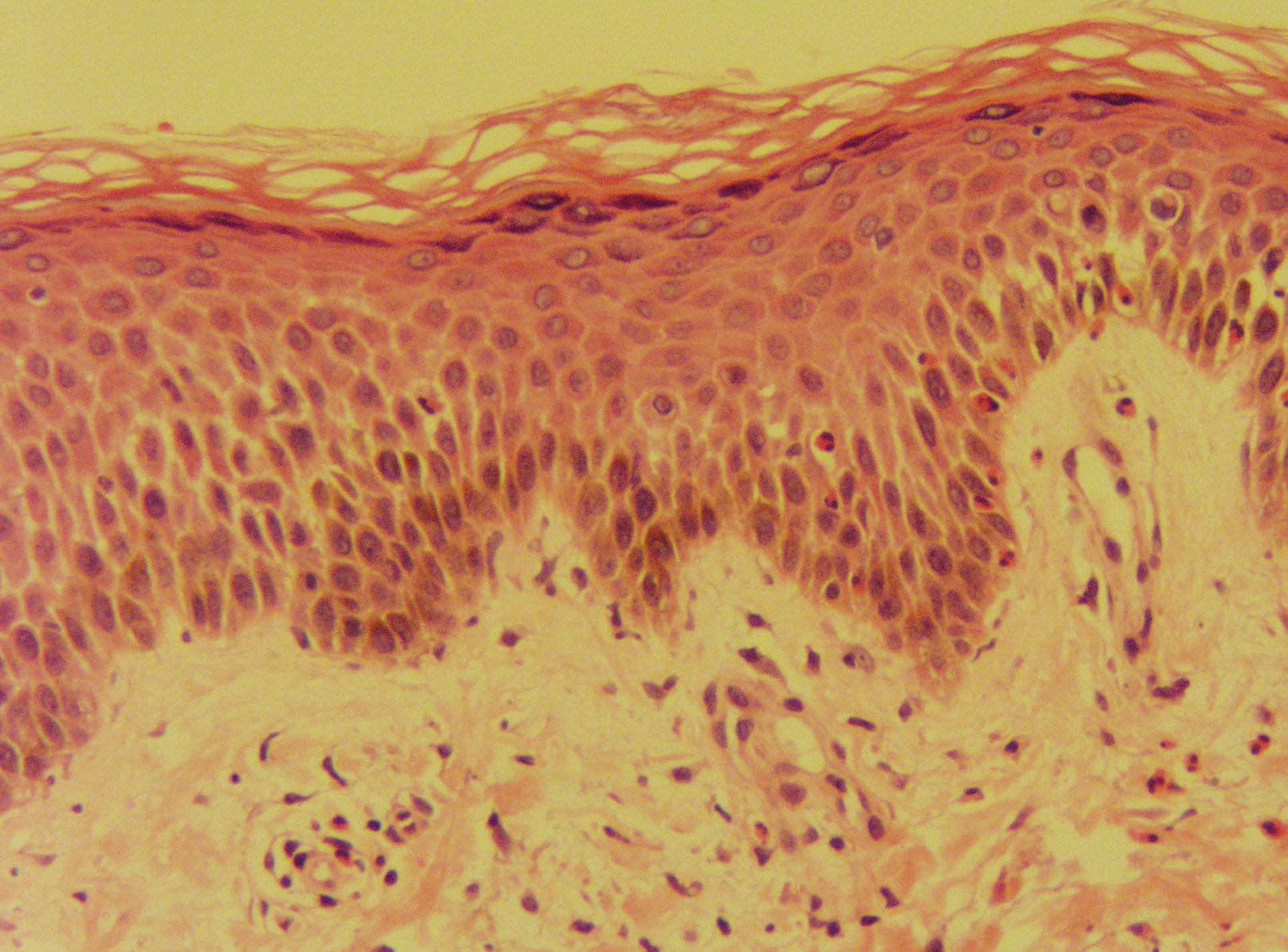
# Darier's Disease Genetic Analysis

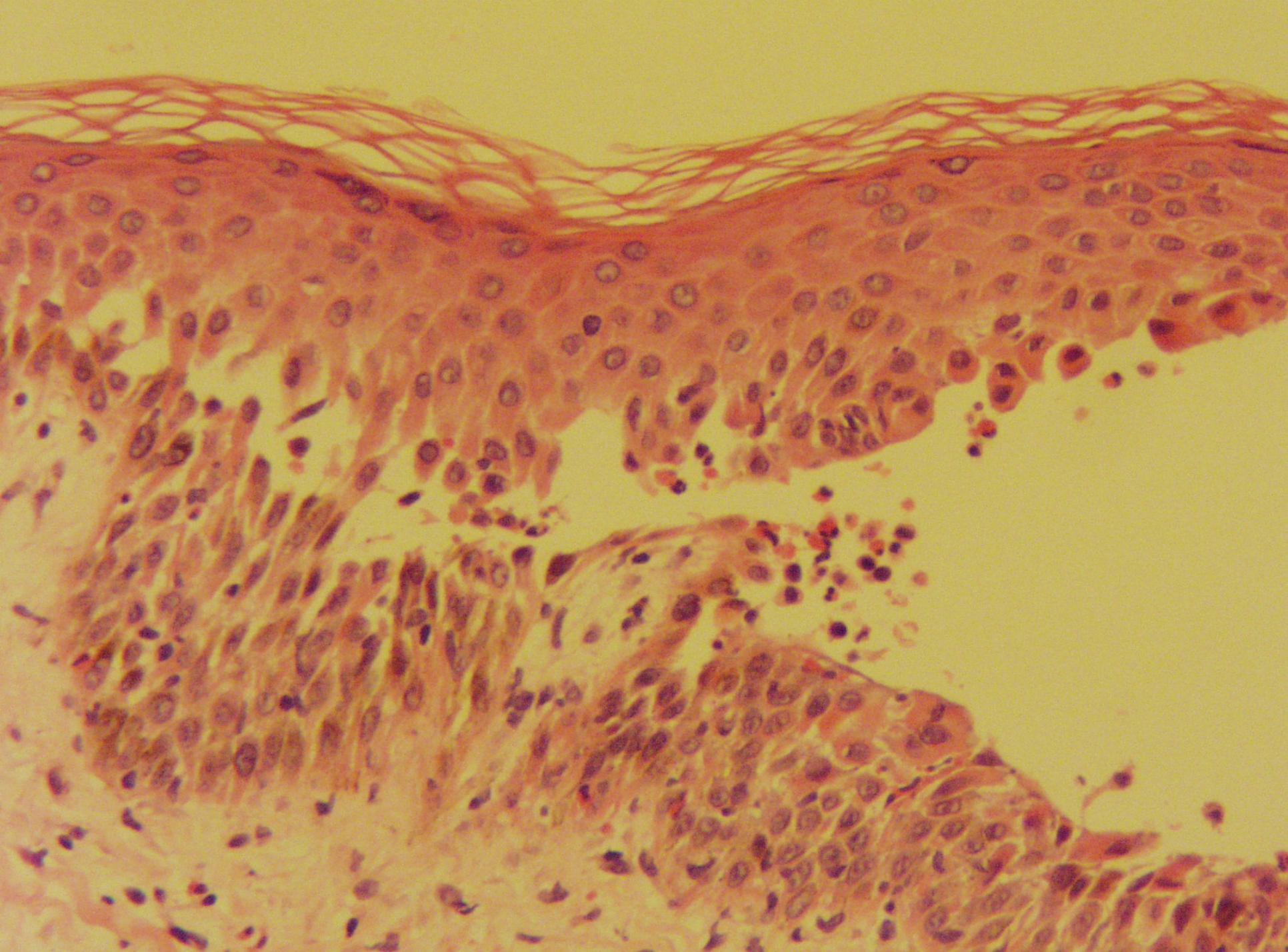
- Autosomal dominant
- Abnormal gene *ATP2A2* (12q23-24.1)
  - Gene normally encodes for the SERCA enzyme or pump (SarcoEndoplasmic Reticulum Calcium-ATPase)
  - Required to transport calcium within the cell

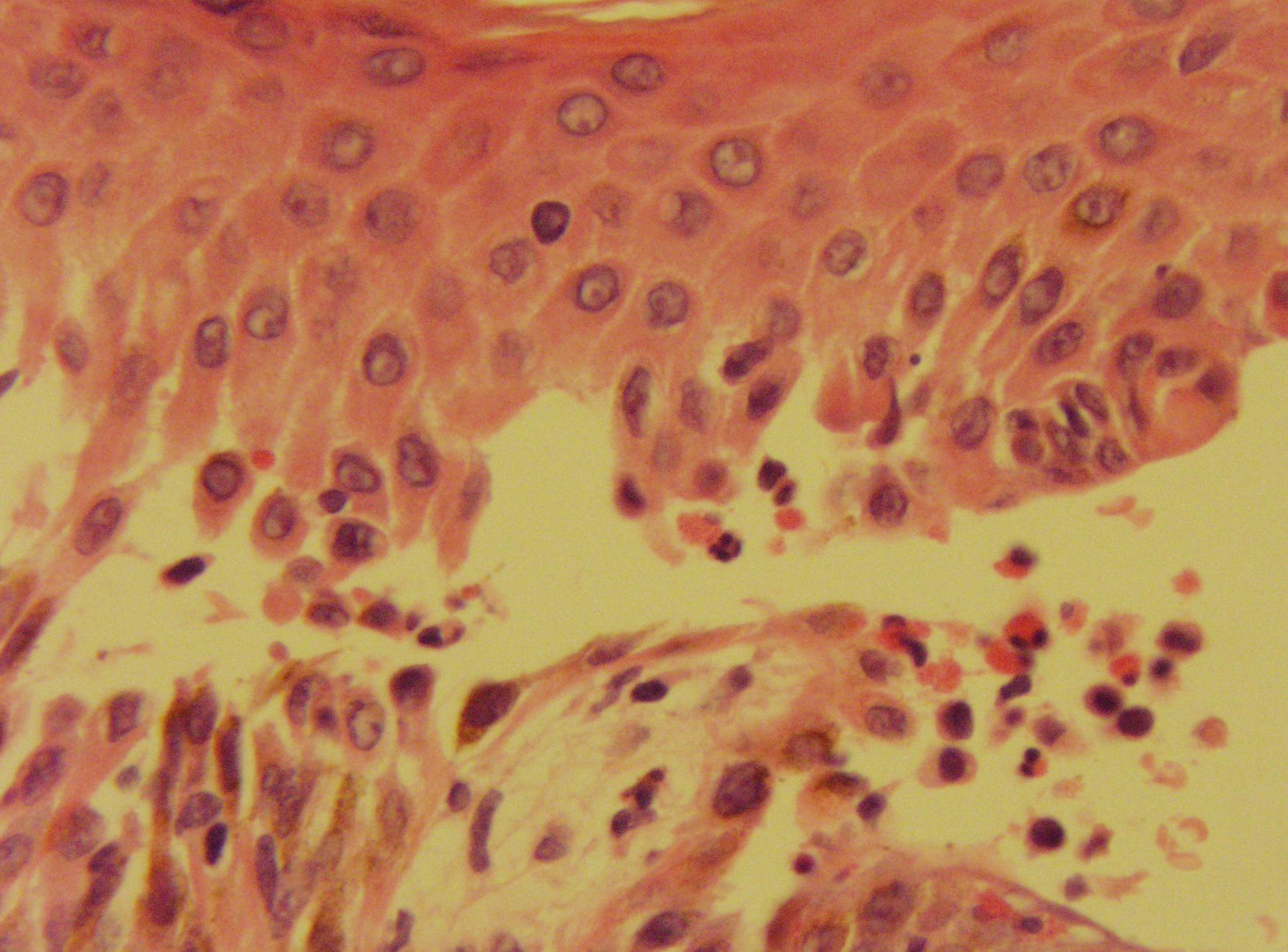
# Histopathology



- Intraepidermal acantholysis
- Corp ronds
- Corp grains
- Clinical correlation-rule out Grover's disease
- DIF negative



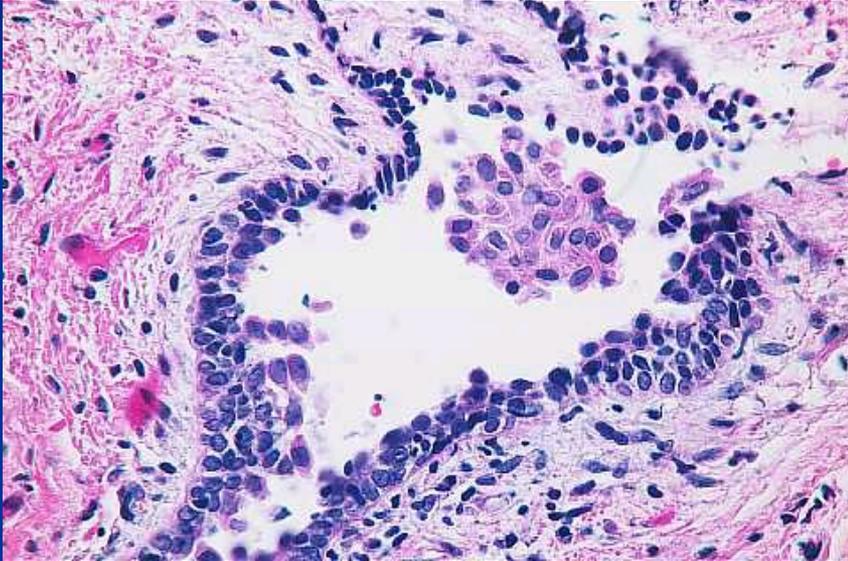




**What is your differential  
diagnosis and what stains/IHC  
would you order?**

# Pemphigus Vulgaris

# Histopathology



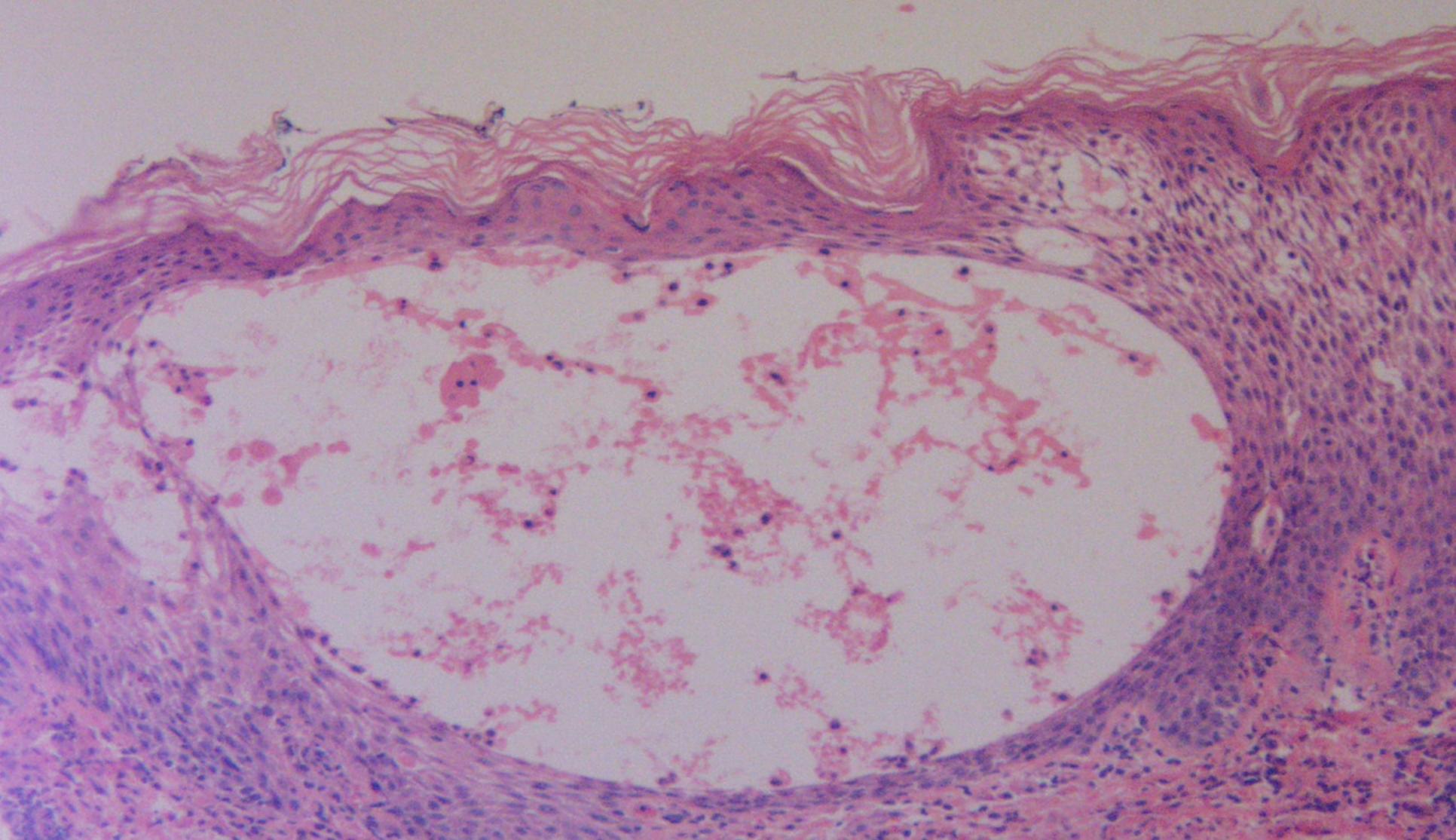
- Early lesions may have only eosinophilic spongiosis
- Intraepidermal acantholysis with suprabasilar preservation
- Eosinophilia
- Adnexal involvement
- Confirm with DIF/IIF

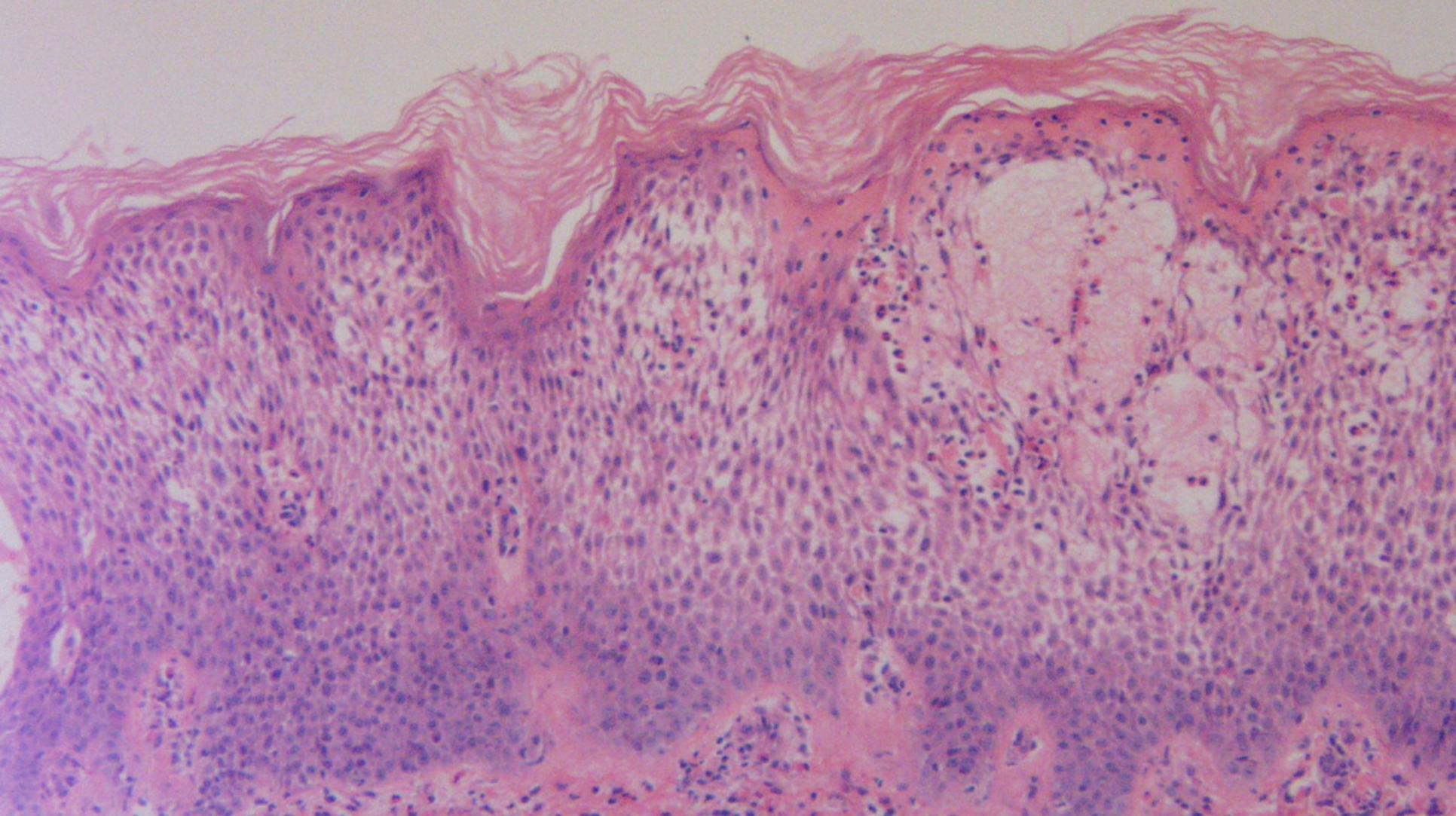
# What are the expected INDIRECT IF findings?

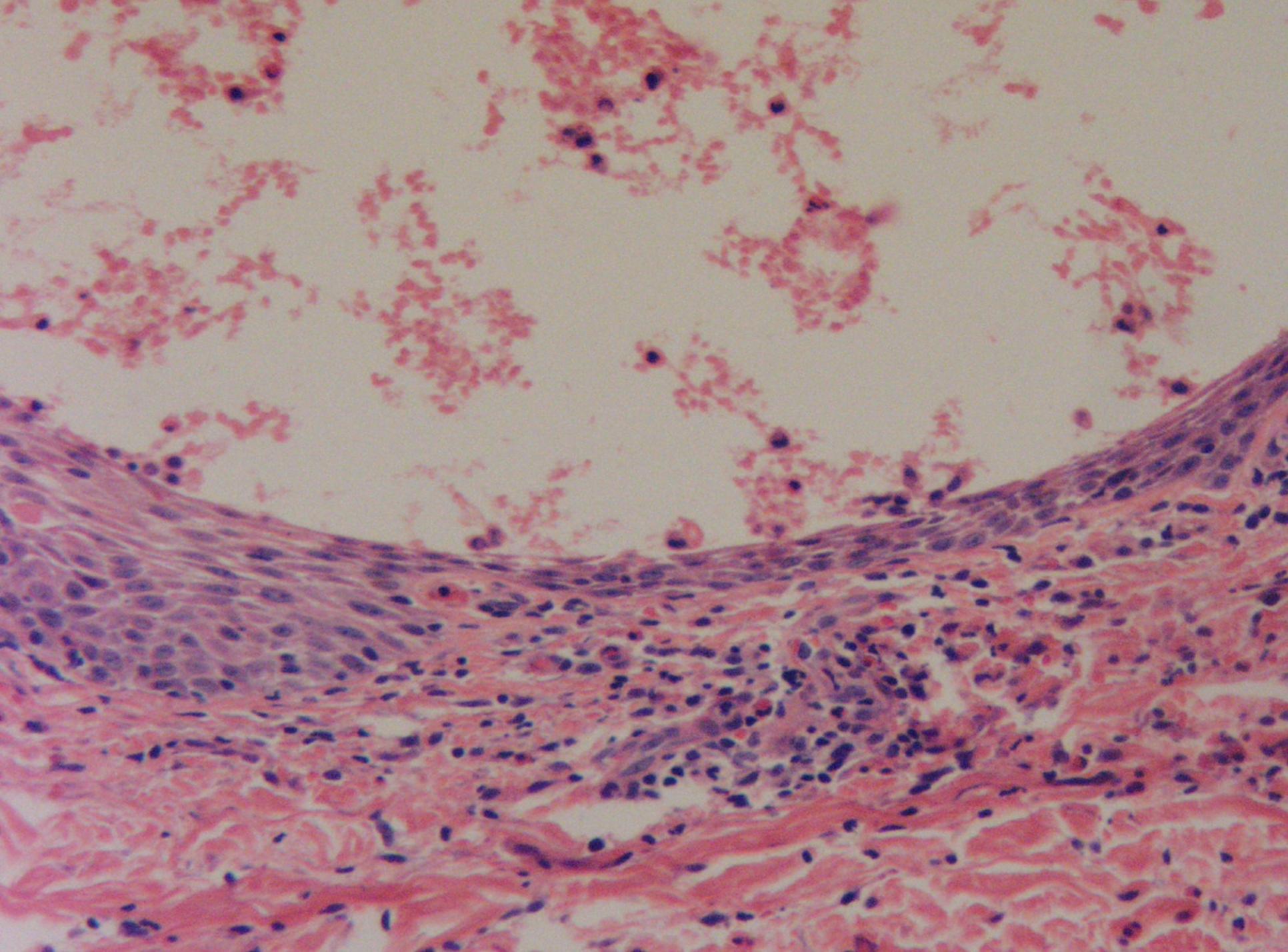
- Pemphigus vulgaris
- Paraneoplastic pemphigus
- Pemphigus foliaceus
- Pemphigus erythematosus

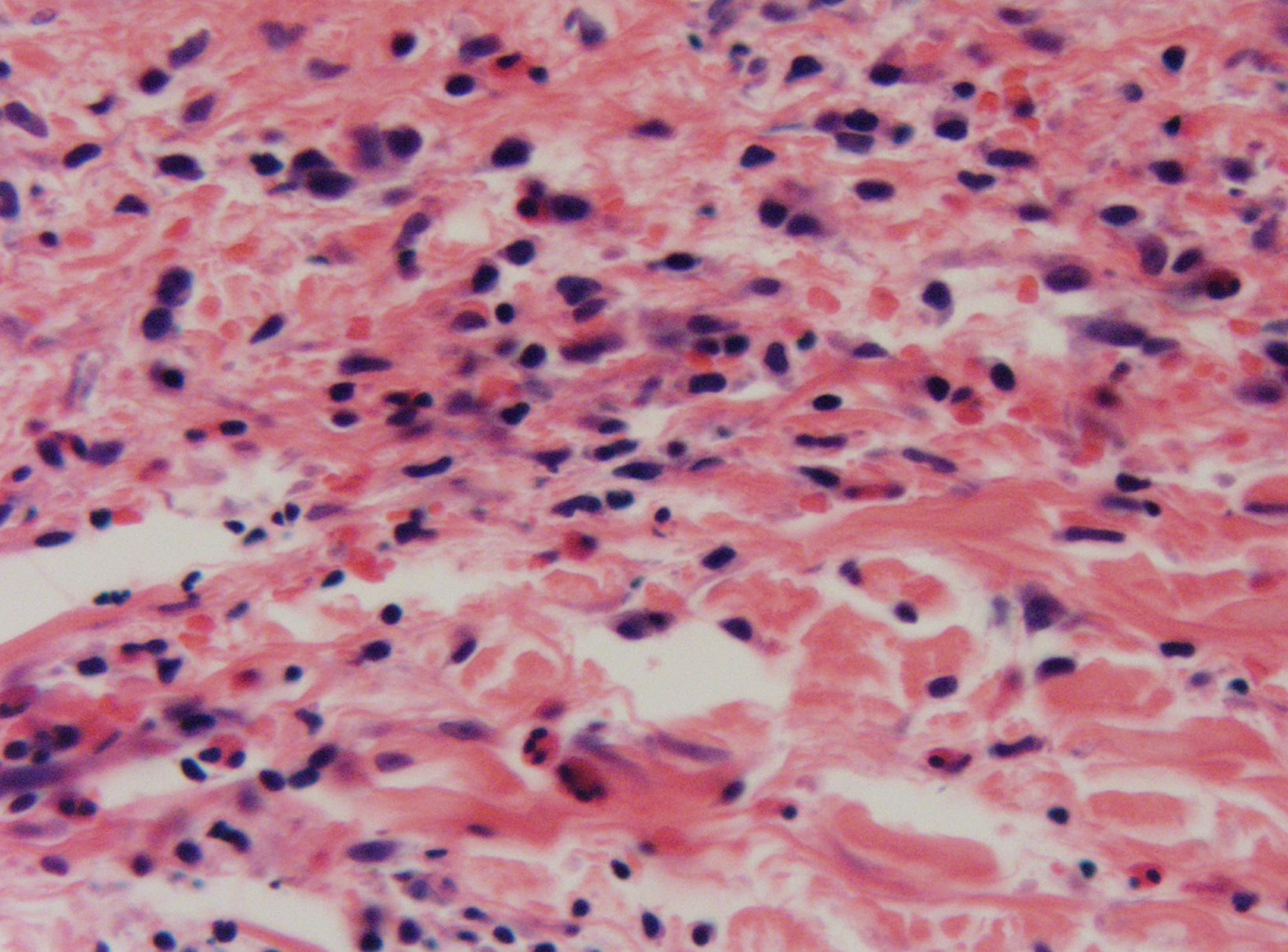
# What are the expected INDIRECT IF findings?

- Pemphigus vulgaris
- Paraneoplastic pemphigus
- Pemphigus foliaceus
- Pemphigus erythematosus
- Ab to dsg1 and dsg3
- P.V. and Antibodies to
  - Envoplakin
  - Periplakin
  - A2ML1
  - BP230
- IgG4 to dsg1
- Overlap with P.F.
  - Ab to dsg1
  - ANA for Ro, La, Sm, and DS DNA





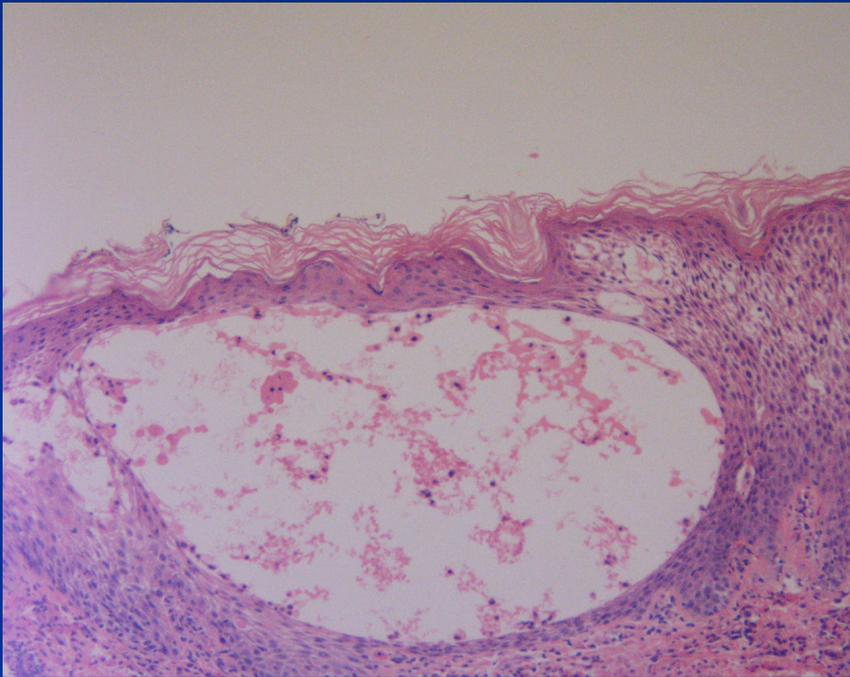




**What is your differential  
diagnosis and what stains/IHC  
would you order?**

# Bullous Drug Eruption

# Histopathology

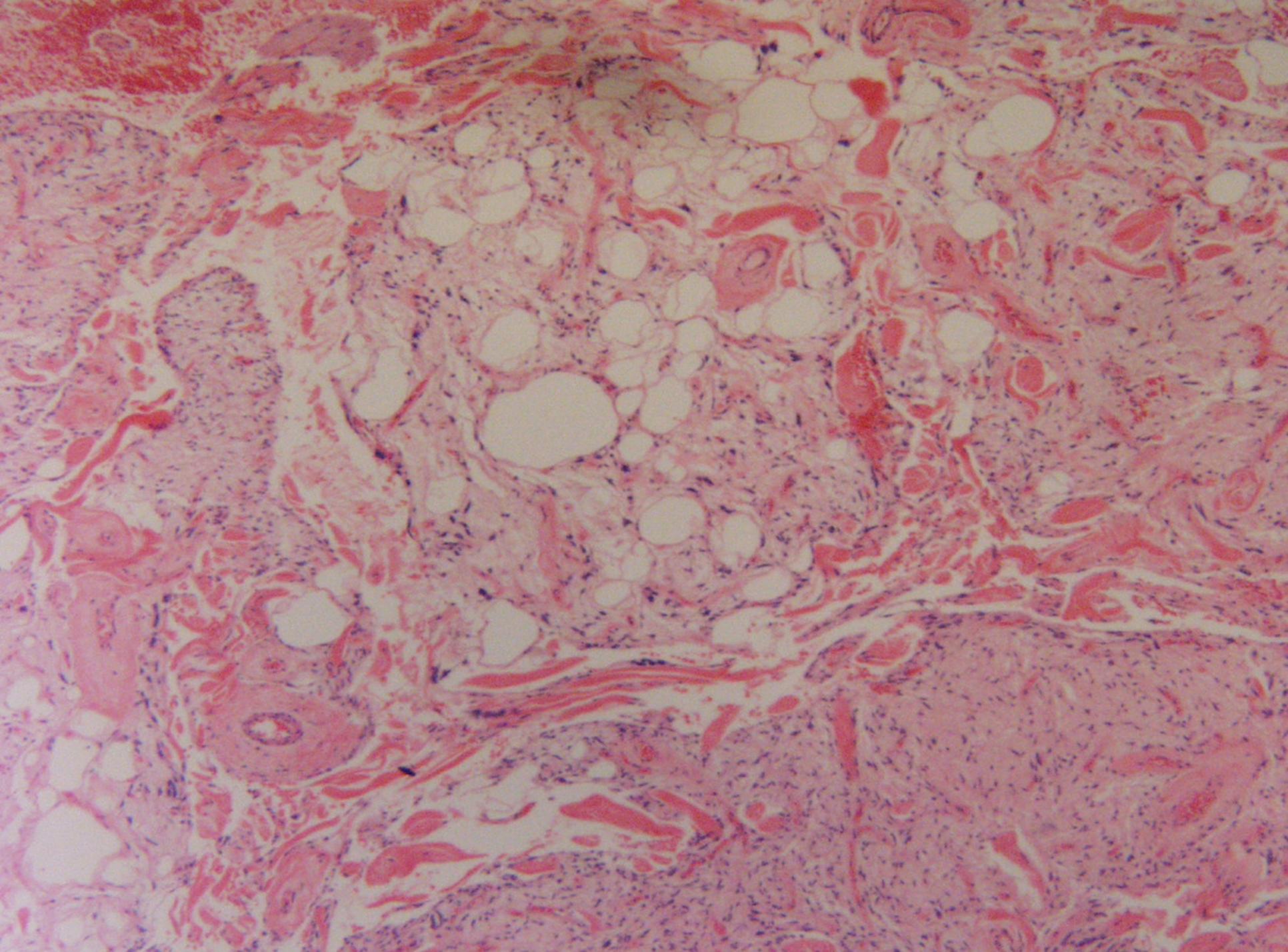


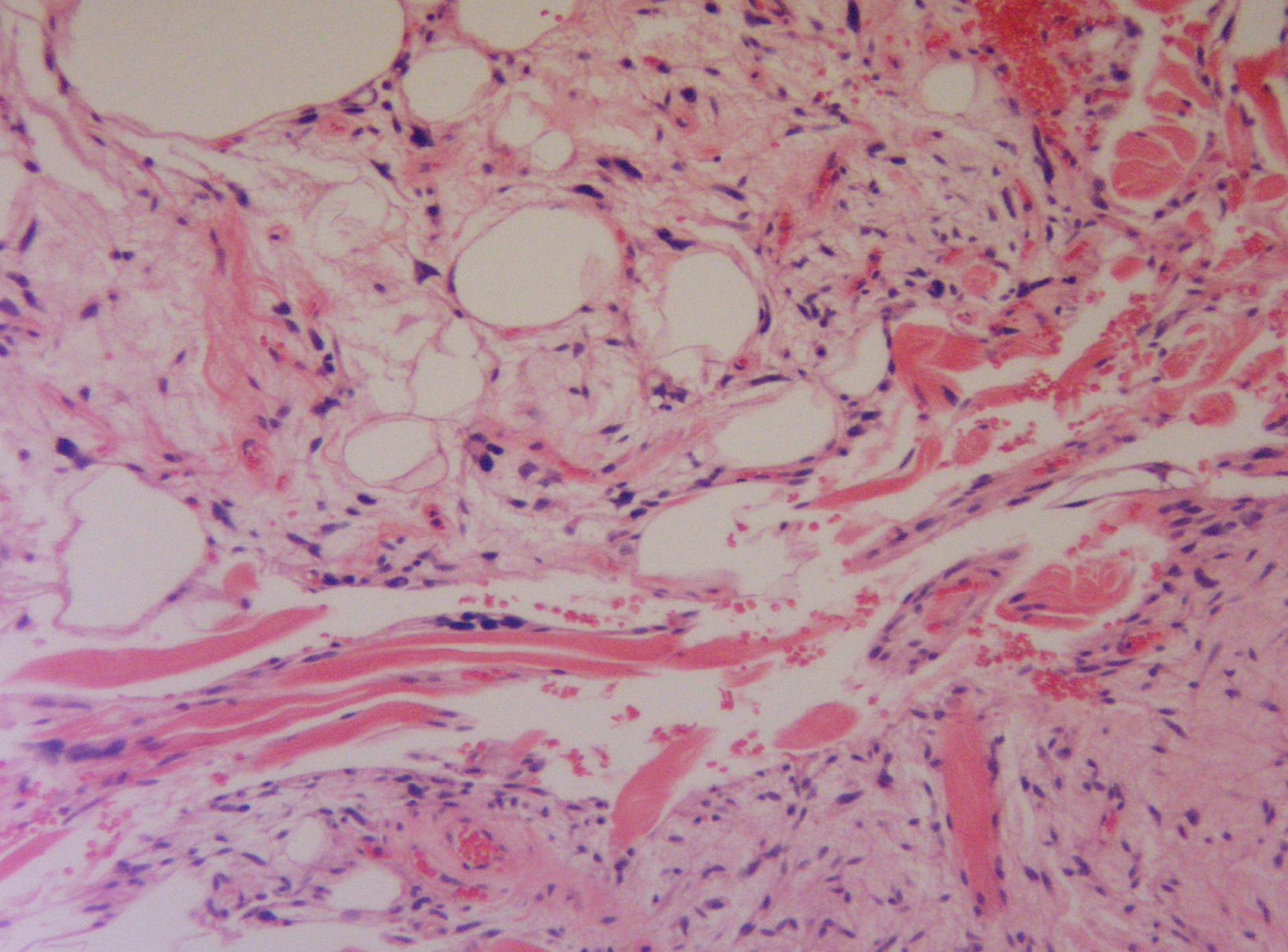
- Intraepidermal bulla with spongiosis
- Eosinophilia variable
- Rule out bullous pemphigoid or pemphigus vulgaris
- Rule out tinea
- DIF?

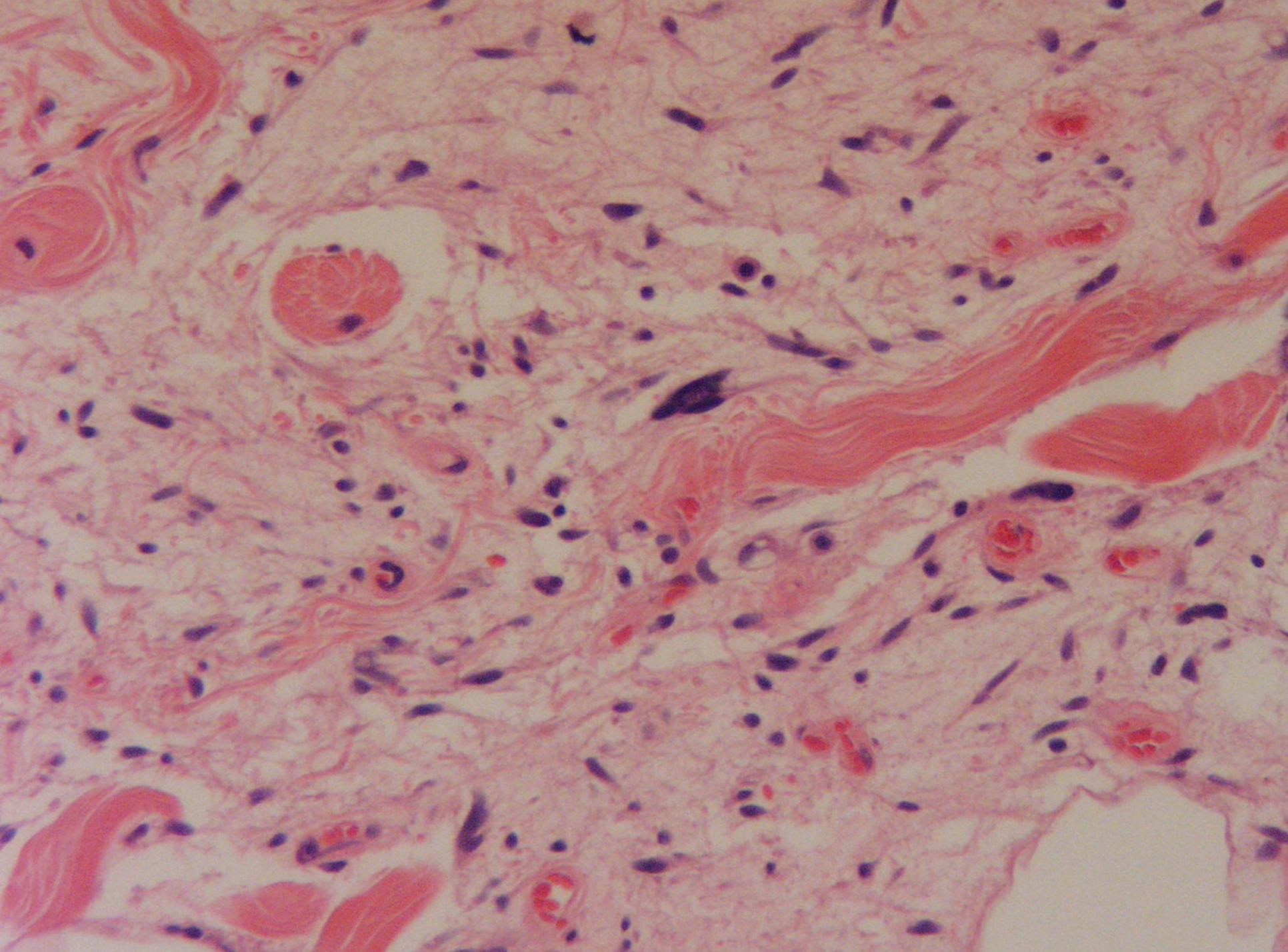
**Name some medications  
associated with bullous eruptions**

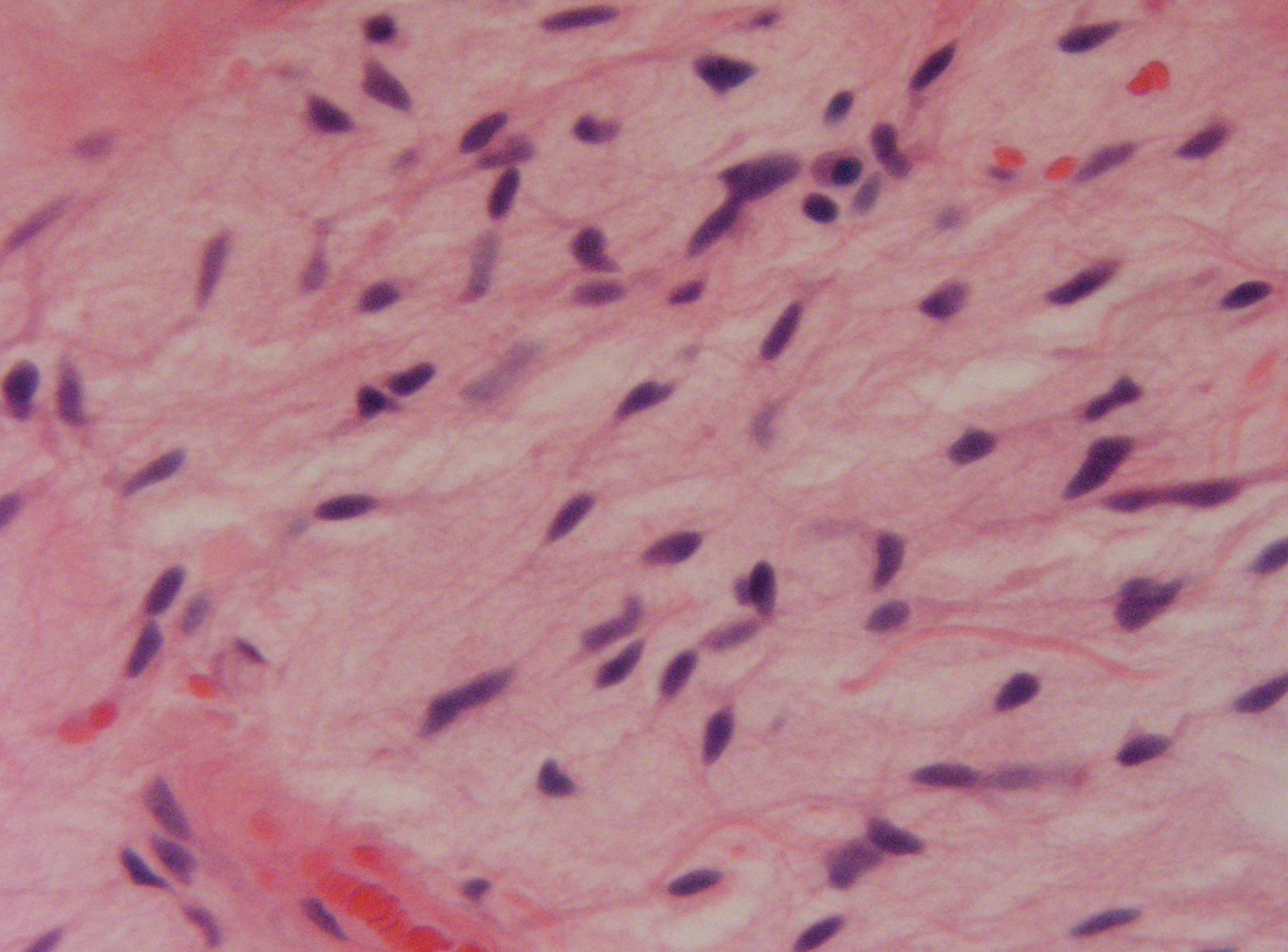
# Drugs Associated with Bullous Eruptions

- NSAIDS
- ABX
  - Tetracycline, Sulfonamides, Penicillin, Cephalosporins, Vancomycin
- Diuretics (Thiazides, Calcium channel blockers)
- Chemotherapy (5-FU, doxorubicin)
  - Hand foot syndrome
  - PD-1 inhibitors





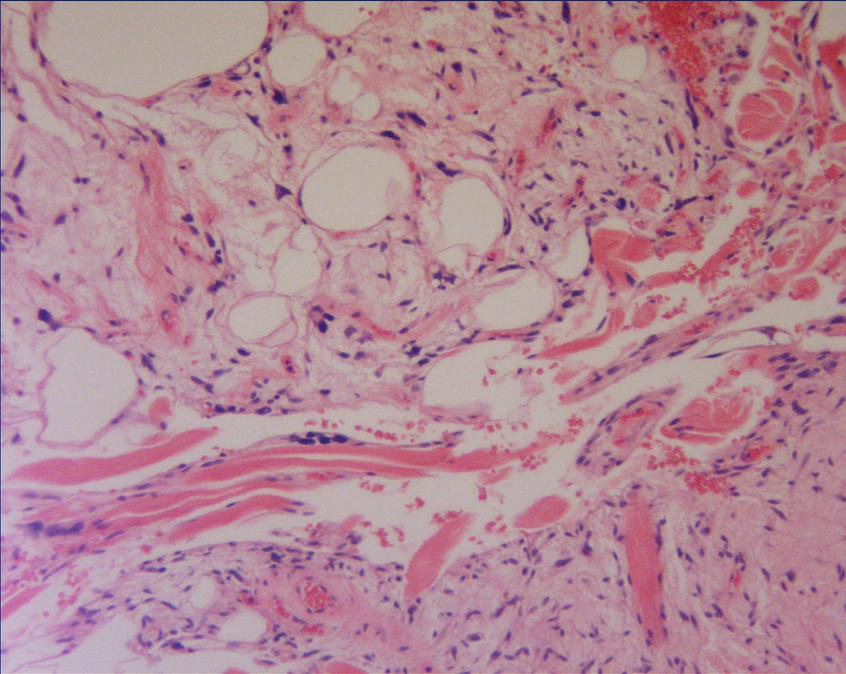




**What is your differential  
diagnosis and what stains/IHC  
would you order?**

# Spindle Cell Lipoma

# Histopathology

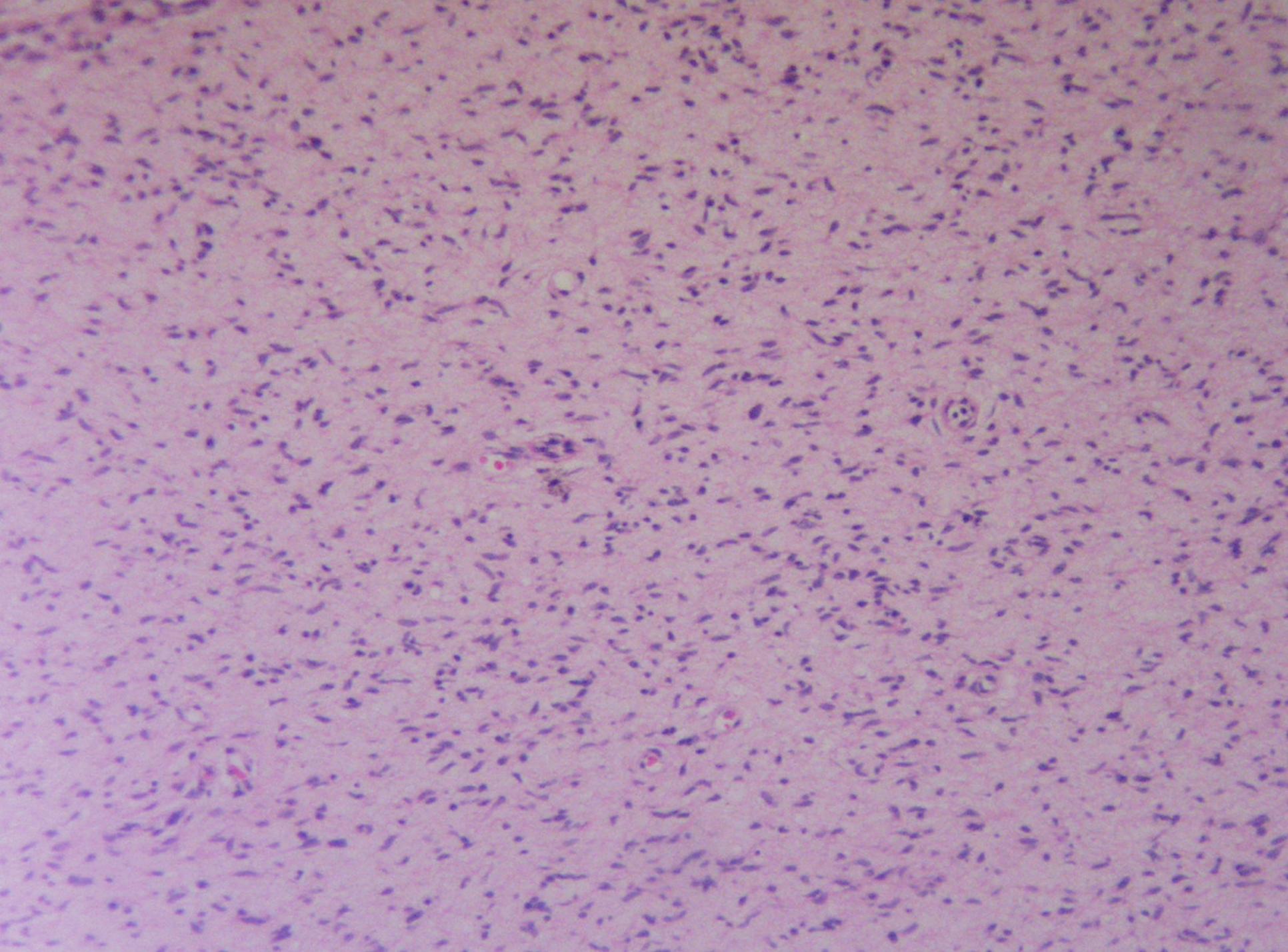


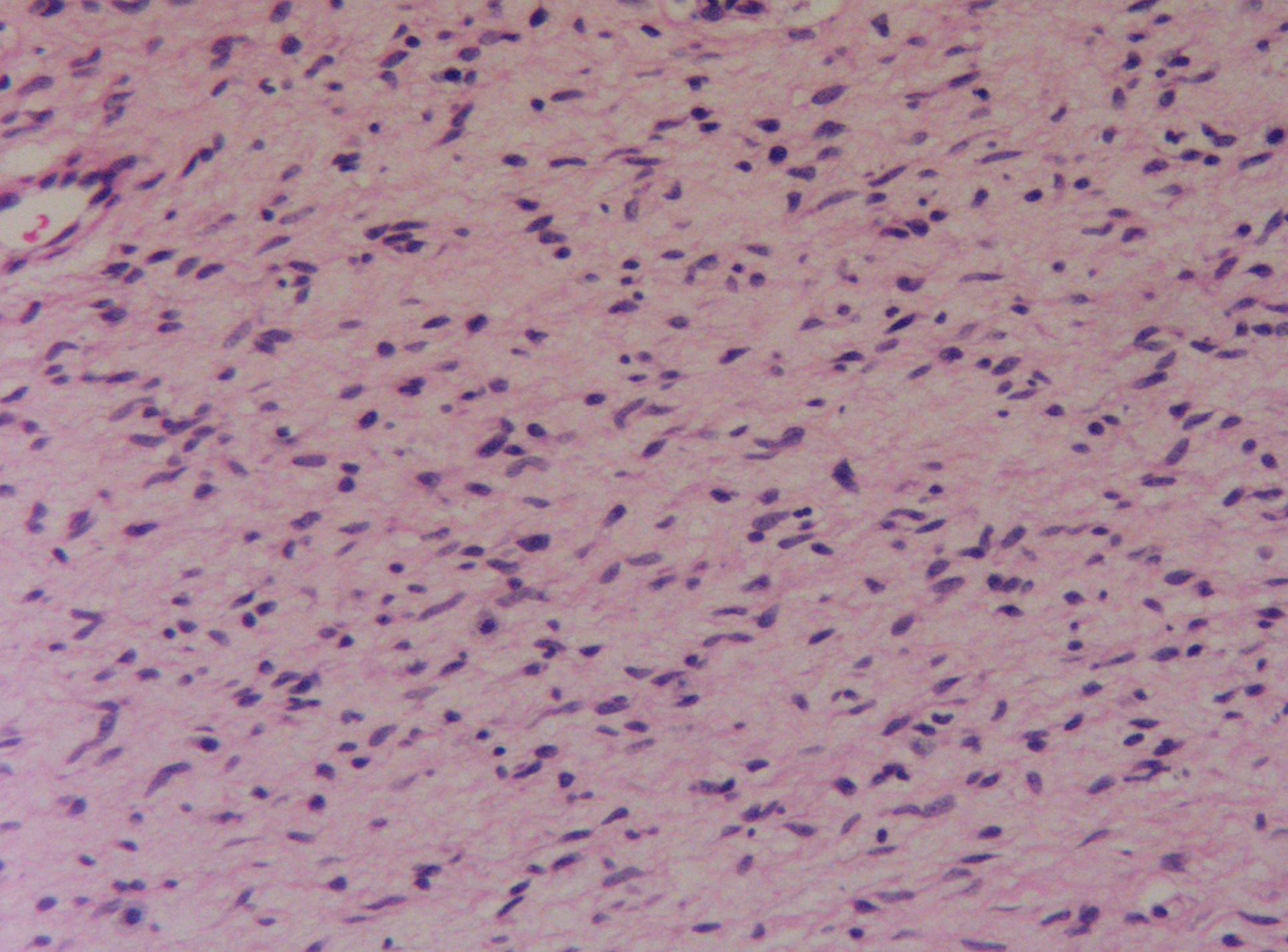
- Ropy collections of spindle cells admixed with mature adipocytes
- Myxoid background
- Clinical location

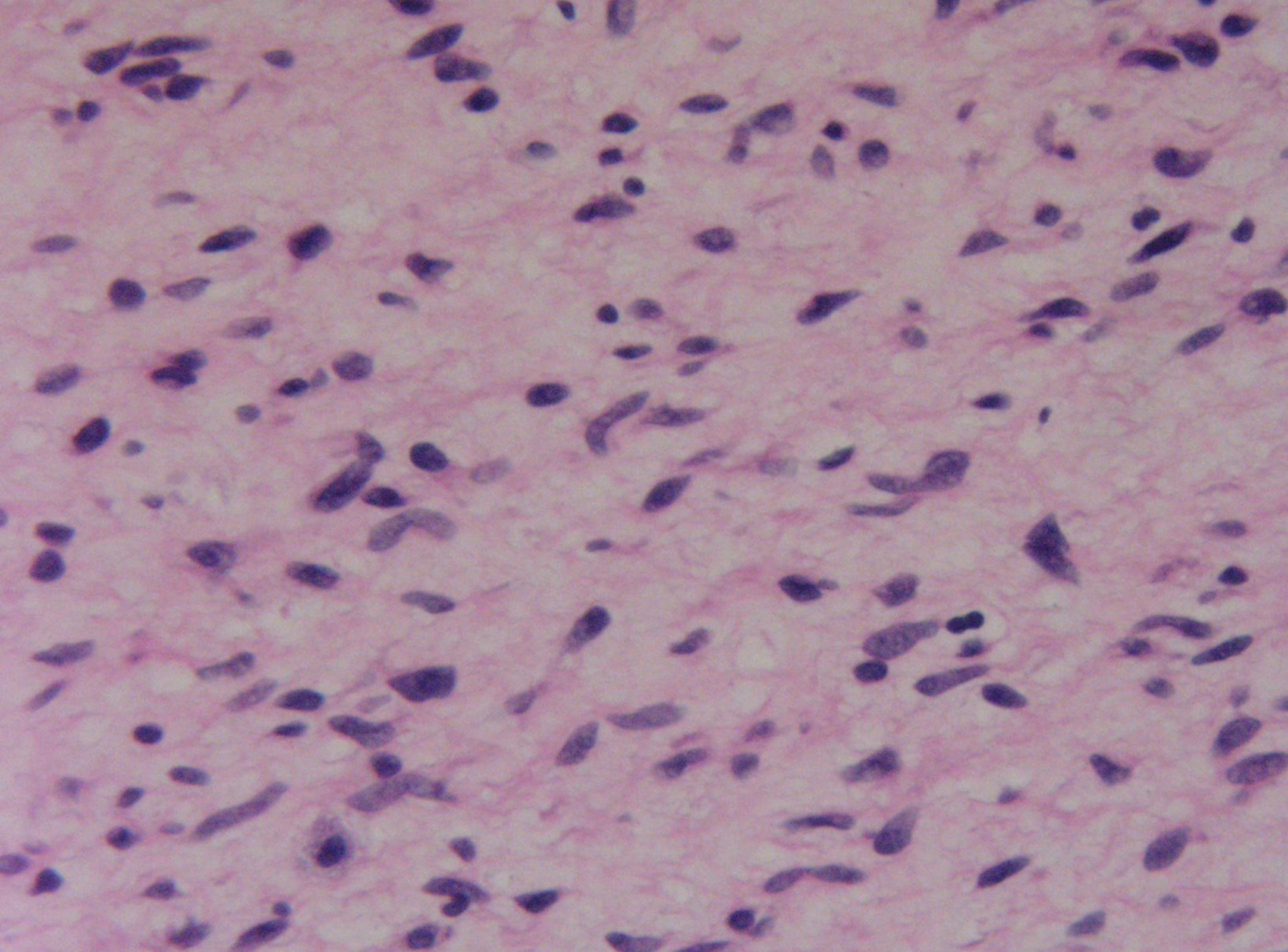
**What are some clinical syndromes associated with multiple cutaneous lipomas?**

# Syndromes of Multiple Lipomas

- Familial multiple lipomatosis
- Dercum disease (Adiposis dolorosa)
- Bannayan-Riley-Ruvalcaba/Bannayan-Zonana
- Cowden syndrome
- MERRF / Ekbom syndrome
  - MERRF (myoclonus, epilepsy and ragged-red fibers)
- MEN 1
- Proteus syndrome



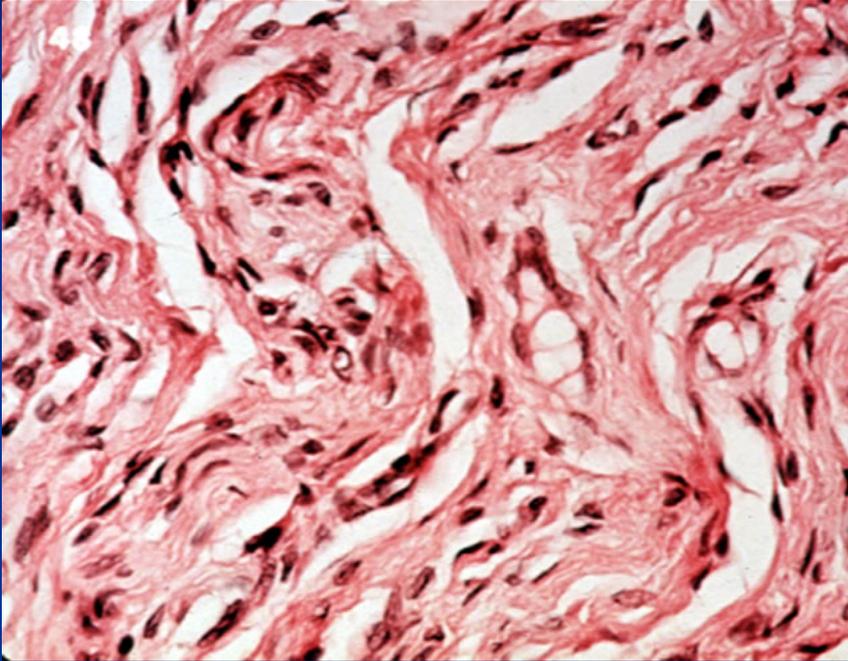




**What is your differential  
diagnosis and what stains/IHC  
would you order?**

# Neurofibroma

# Histopathology



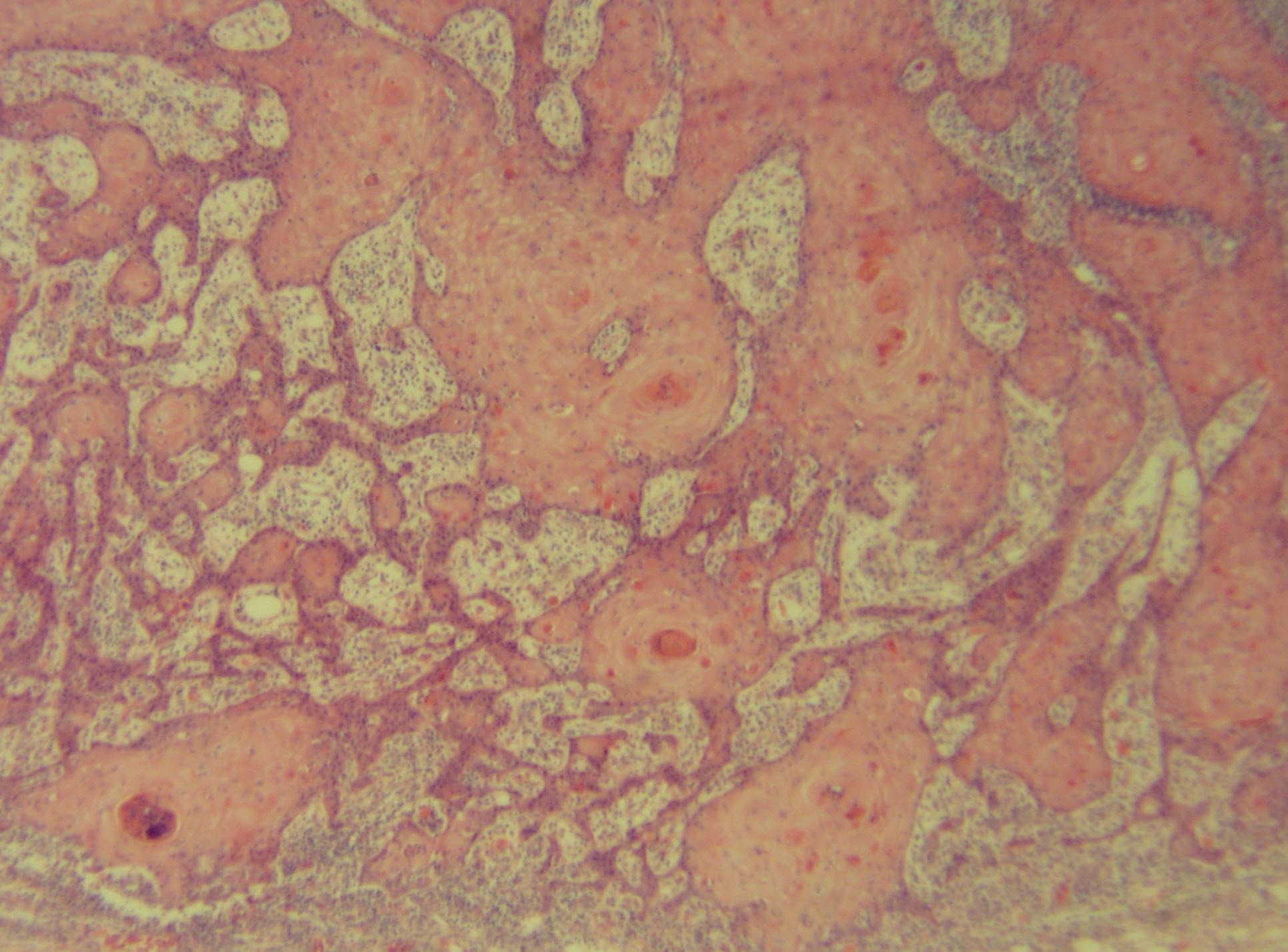
- Partly circumscribed proliferation of wavy bland nuclei
- Myxoid background
- Nerve roots

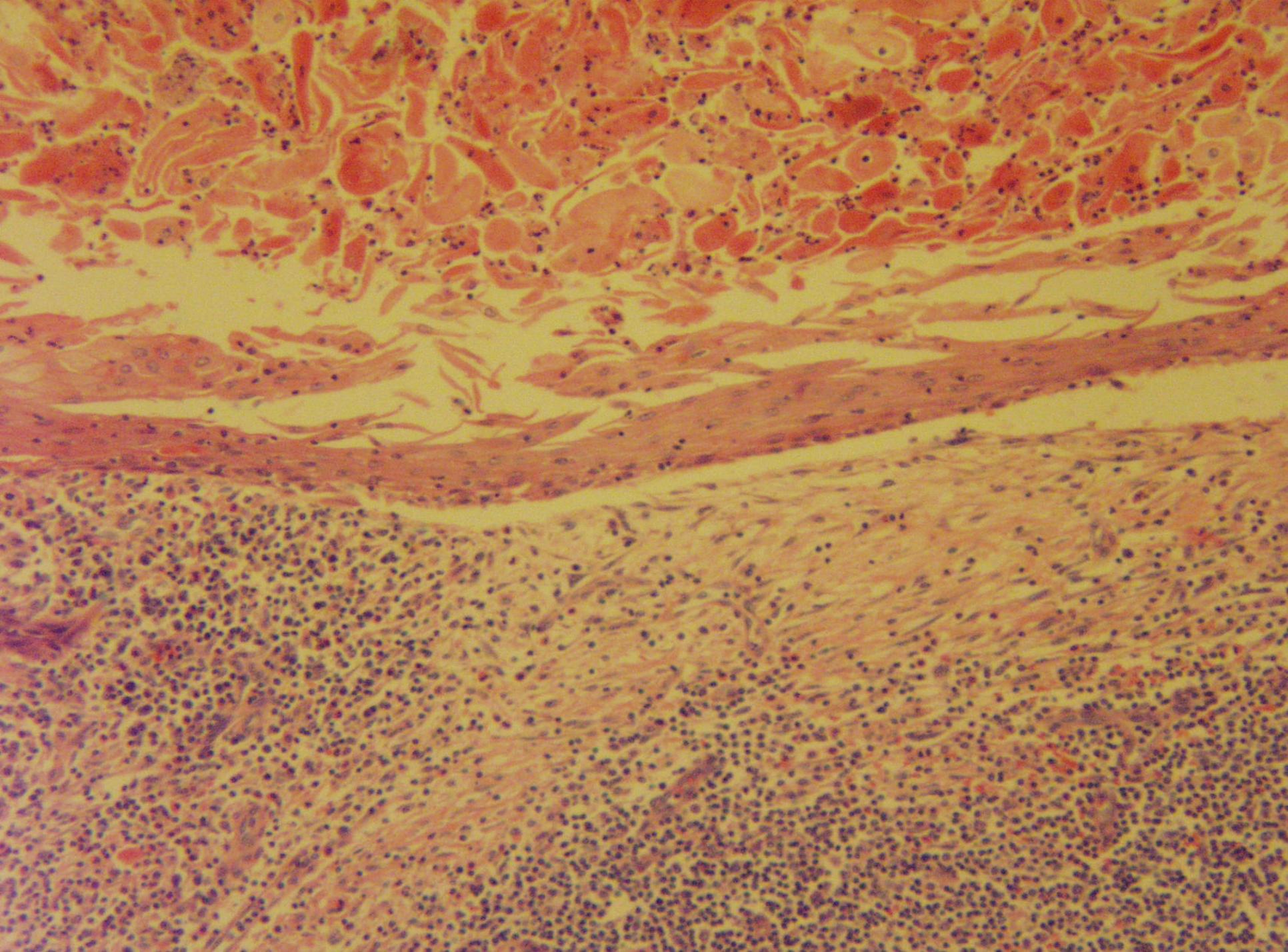
# What is Legius Syndrome?

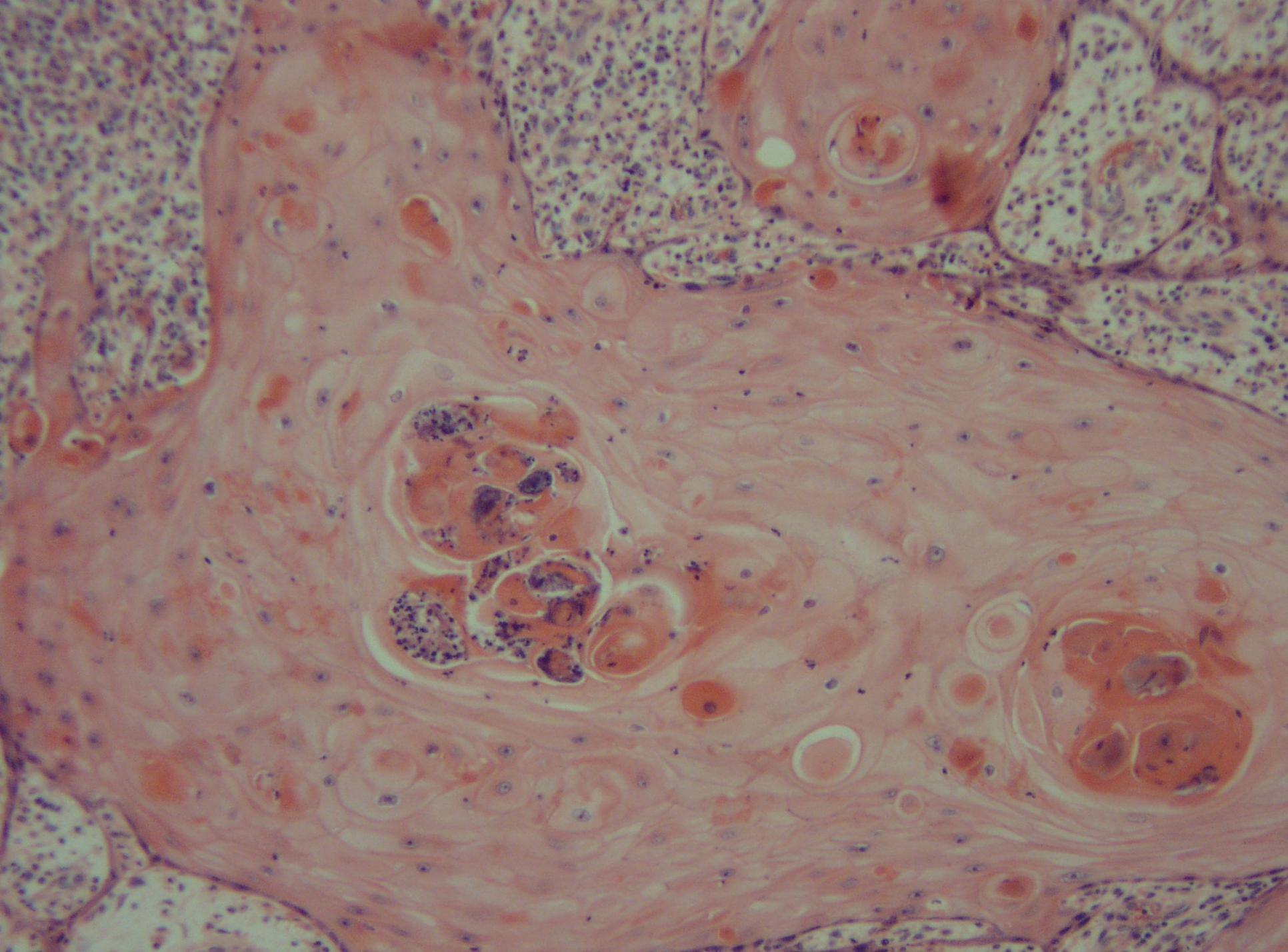
# Legius Syndrome

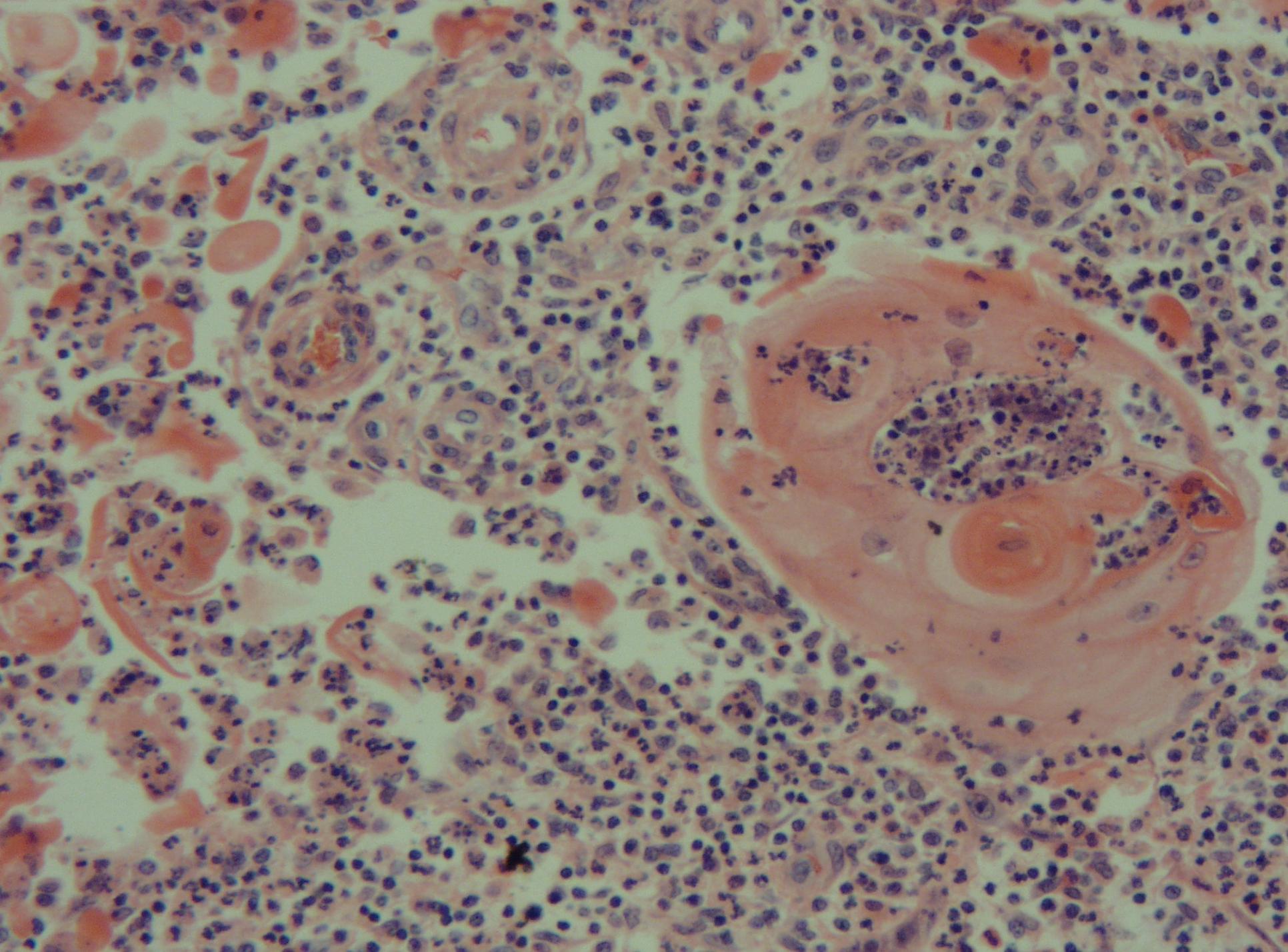
- Neurofibromatosis Type 1-like syndrome (NFLS)
- Mutations in the SPRED1 gene (mutations in chromosome 15)
- AD
- Multiple café-au-lait macules, freckles, lipomas, macrocephaly, learning delays
- LACKING
  - Lisch nodules, bone abnormalities, neurofibromas, optic pathway gliomas and malignant peripheral nerve sheath tumors

77 y.o. F with rapidly enlarging  
nodule on right arm





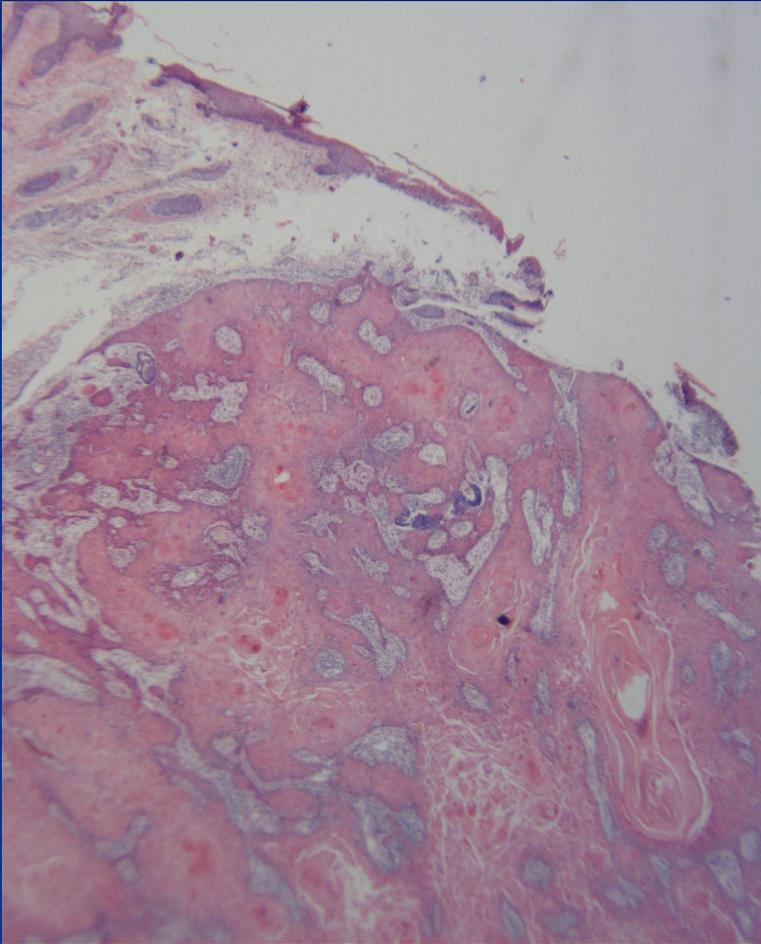




**What is your differential  
diagnosis and what stains/IHC  
would you order?**

# Squamous Cell Carcinoma- Keratoacanthoma type

# Histopathology

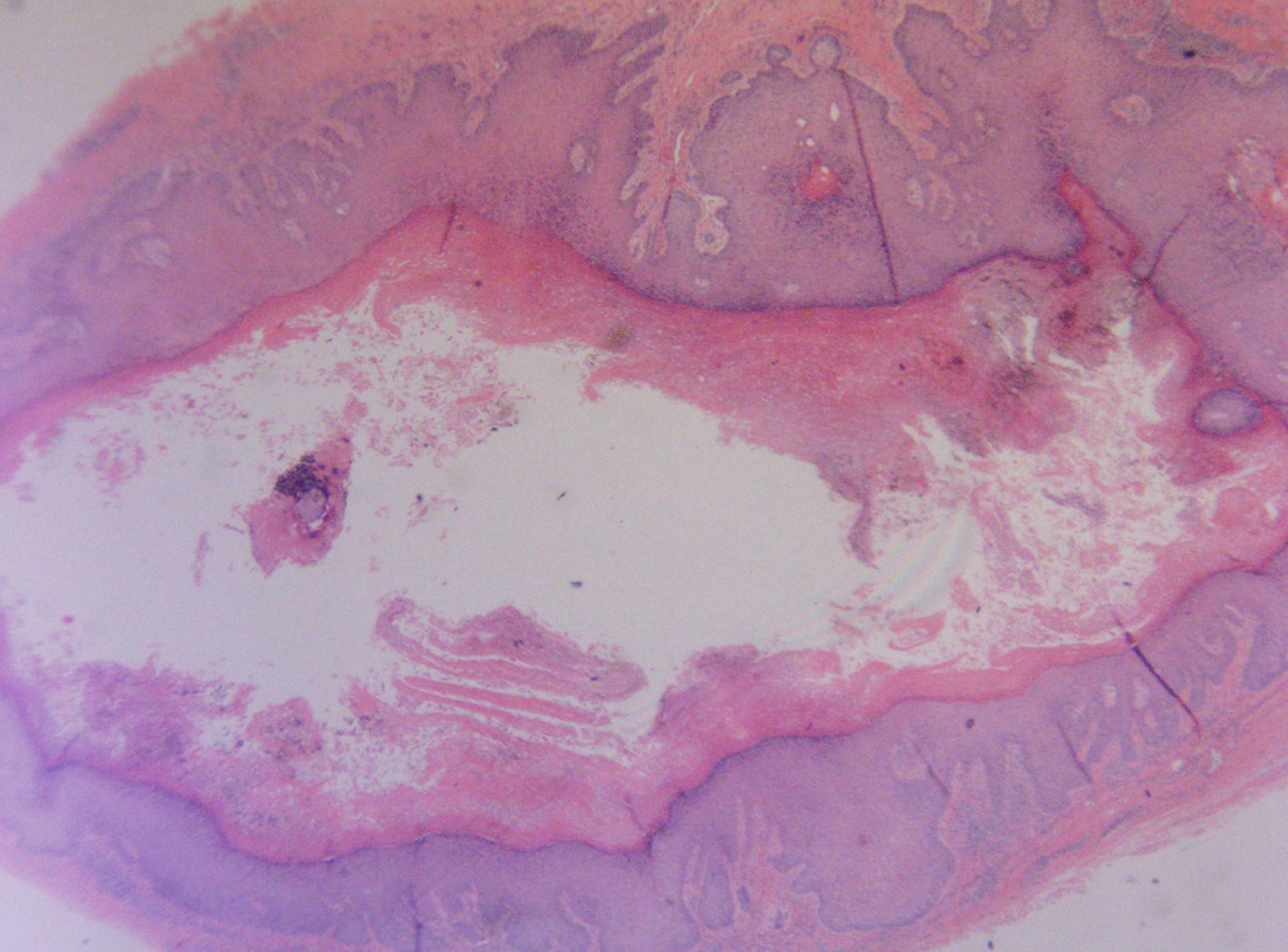


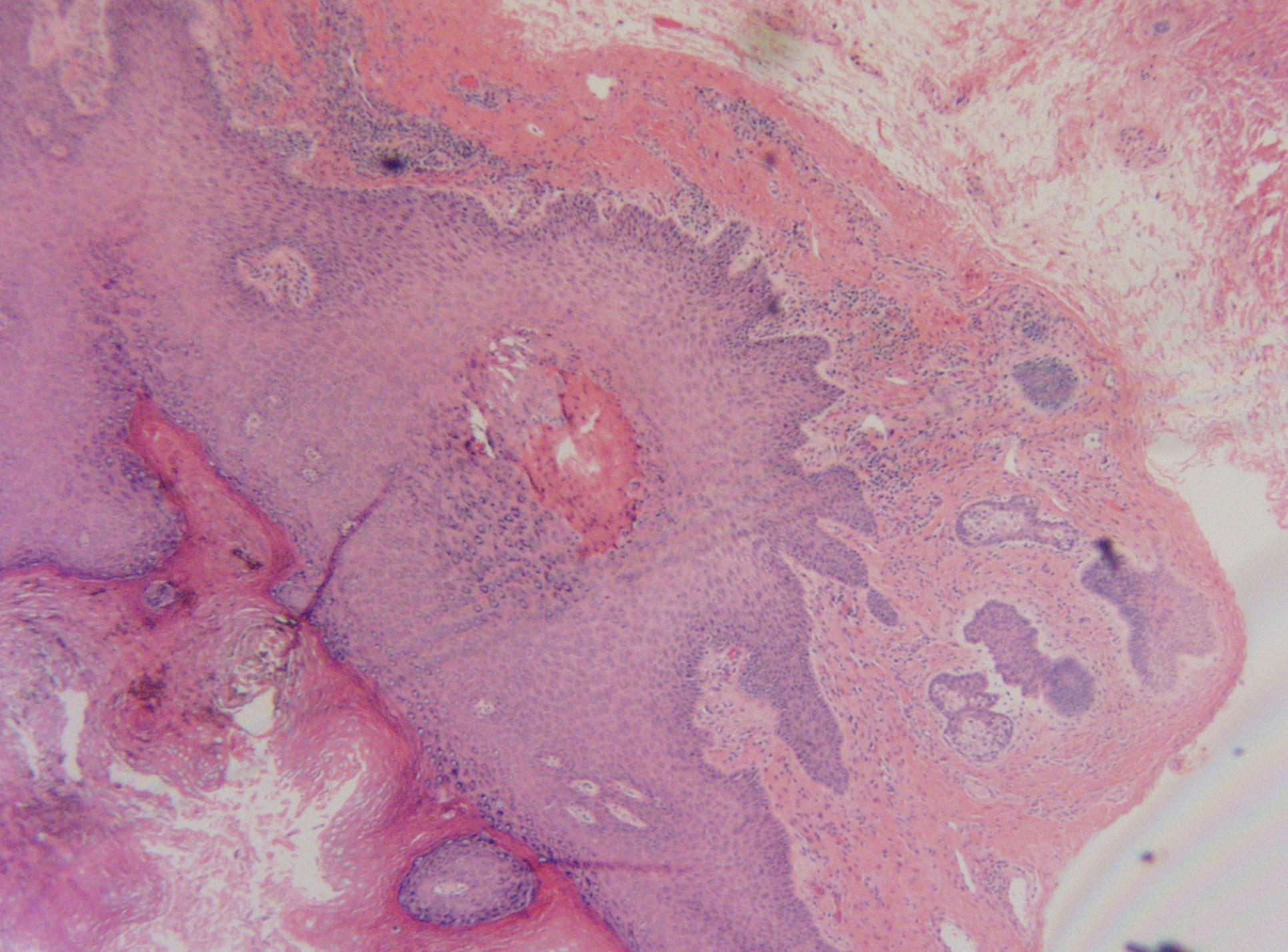
- Crateriform proliferation of glassy keratinocytes
- Epidermal buttress
- Minimal atypia
- May show regression

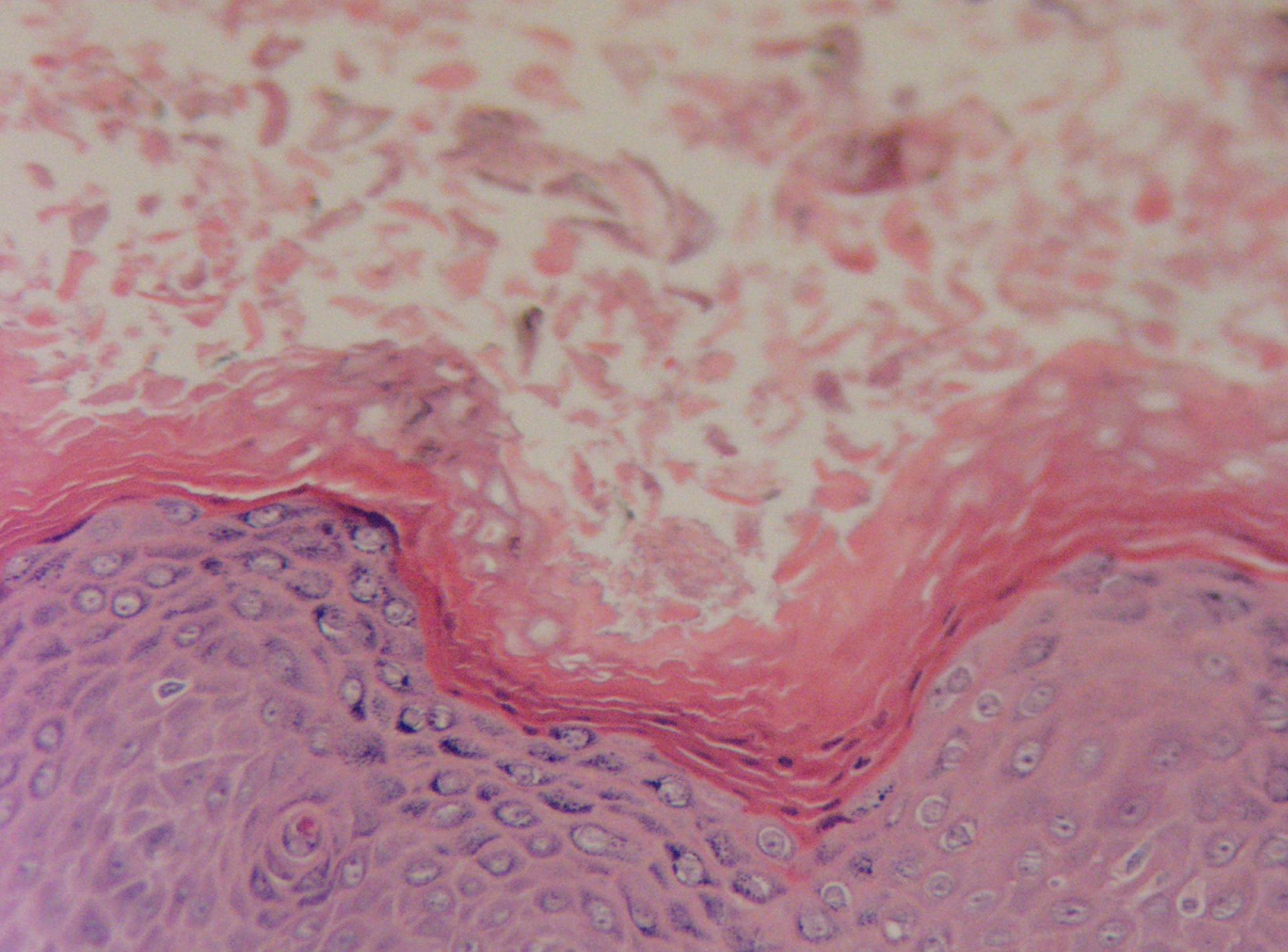
**What are some clinical syndromes associated with multiple Keratoacanthomas?**

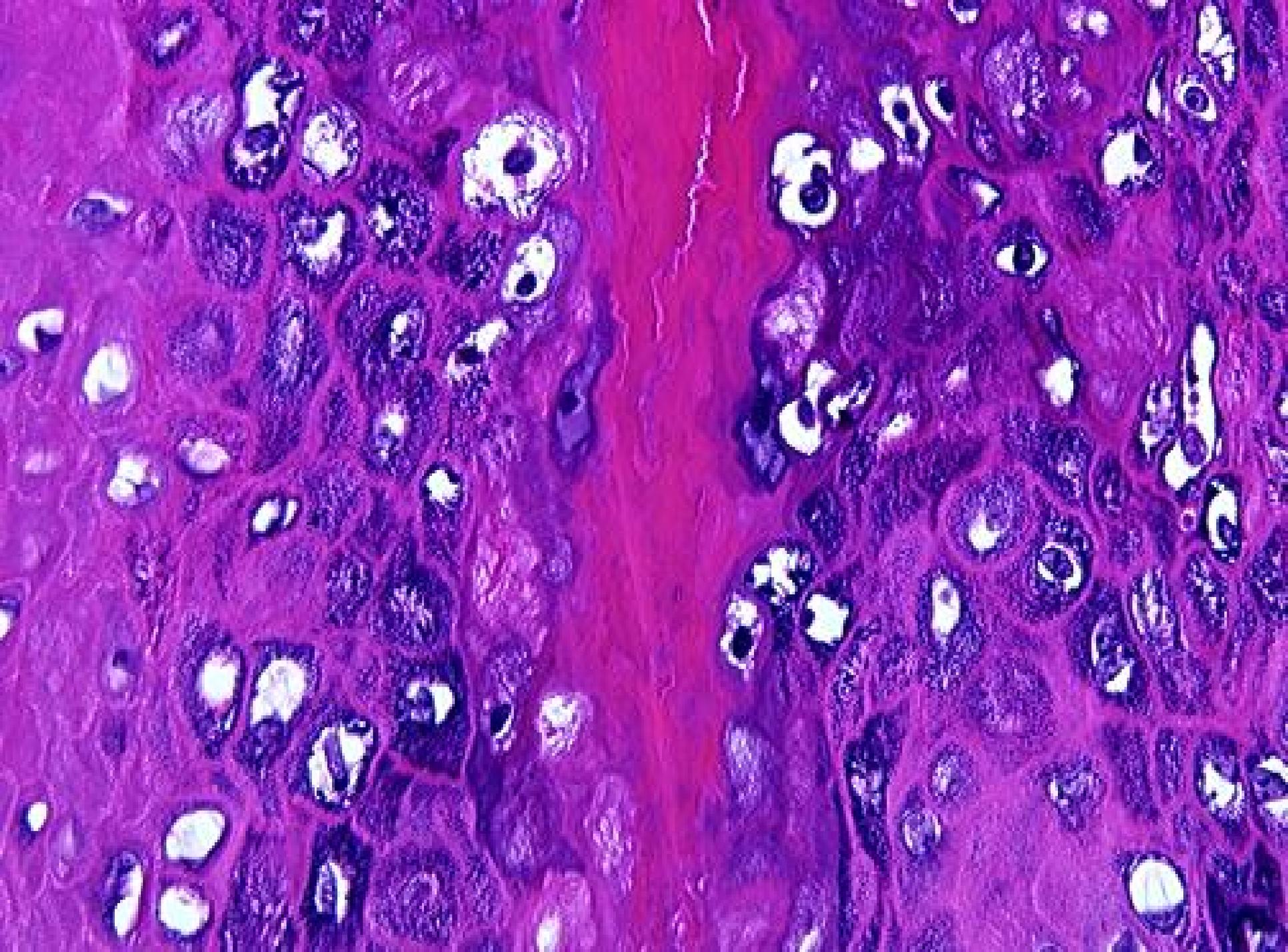
# Multiple Keratoacanthoma Syndromes

- Grzybowski eruptive keratoacanthomas
- Multiple self-healing squamous epitheliomas of Ferguson-Smith (AD with variable penetrance)
- Muir-Torre syndrome
- Drug-induced
  - BRAF inhibitors (vemurafenib, dabrafenib)
  - Checkpoint inhibitors (pembrolizumab, nivolumab, leflunomide, vismodegib, imiquimod)





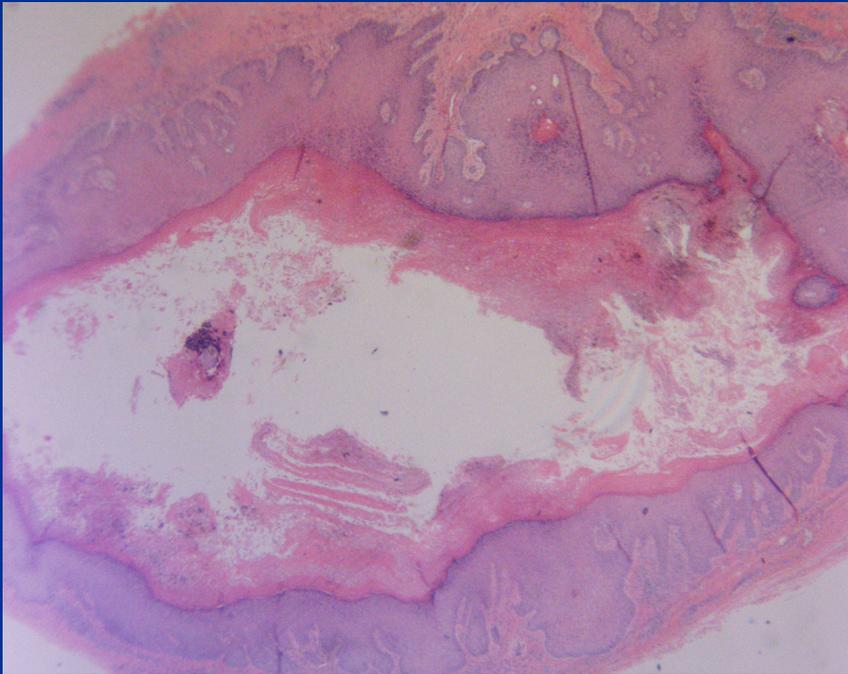




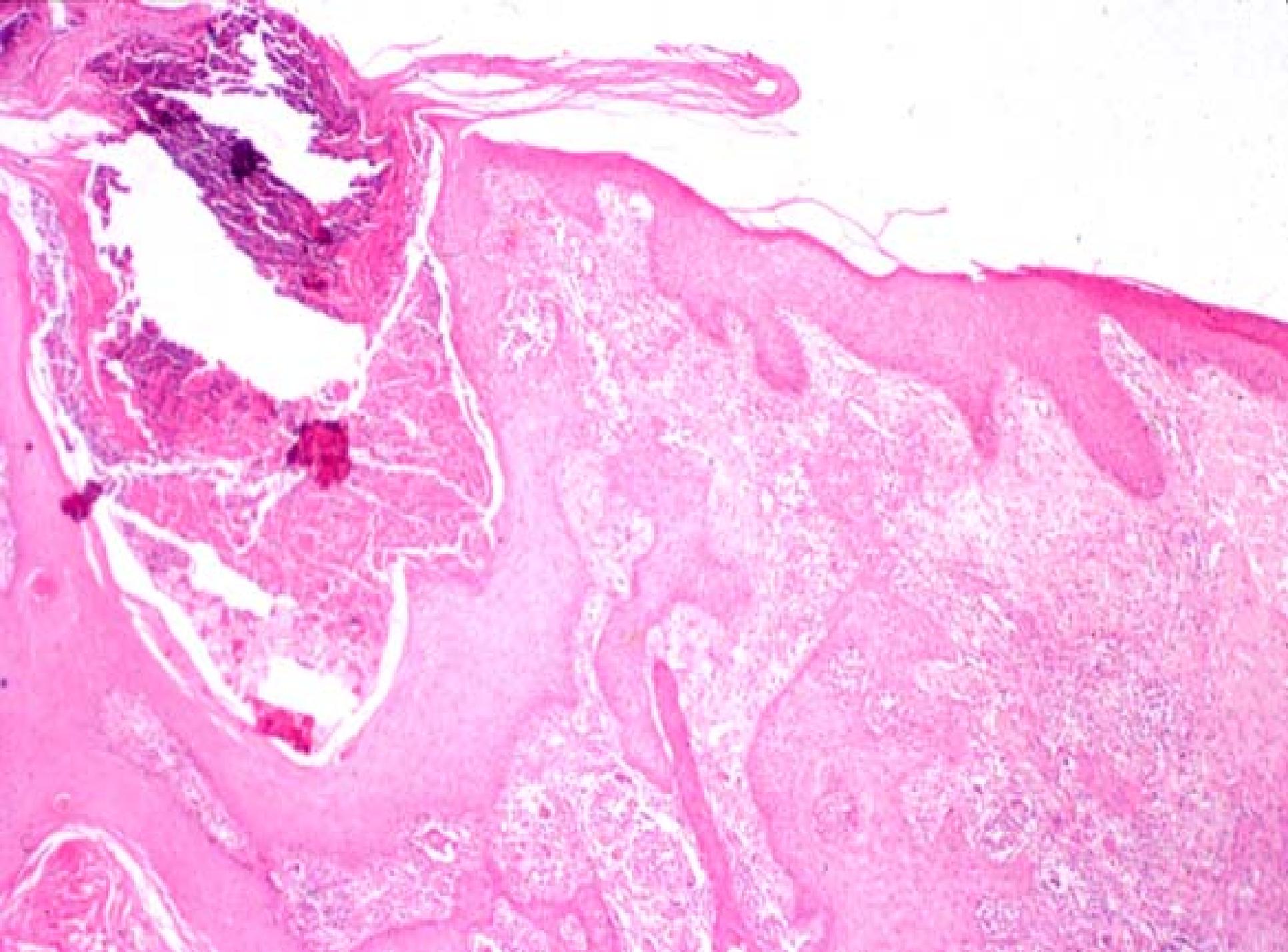
**What is your differential  
diagnosis and what stains/IHC  
would you order?**

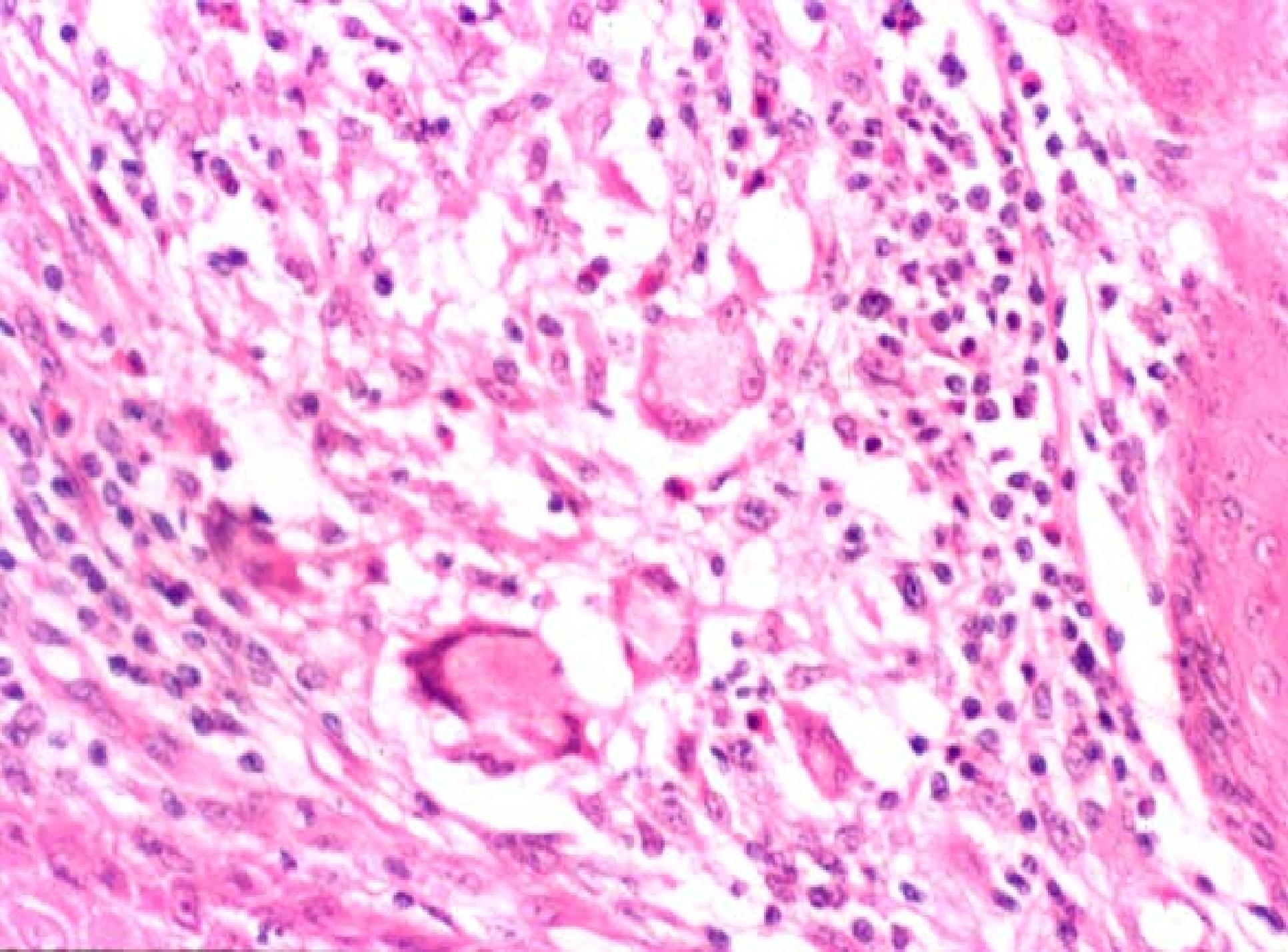
# Endophytic *Verruca Vulgaris*

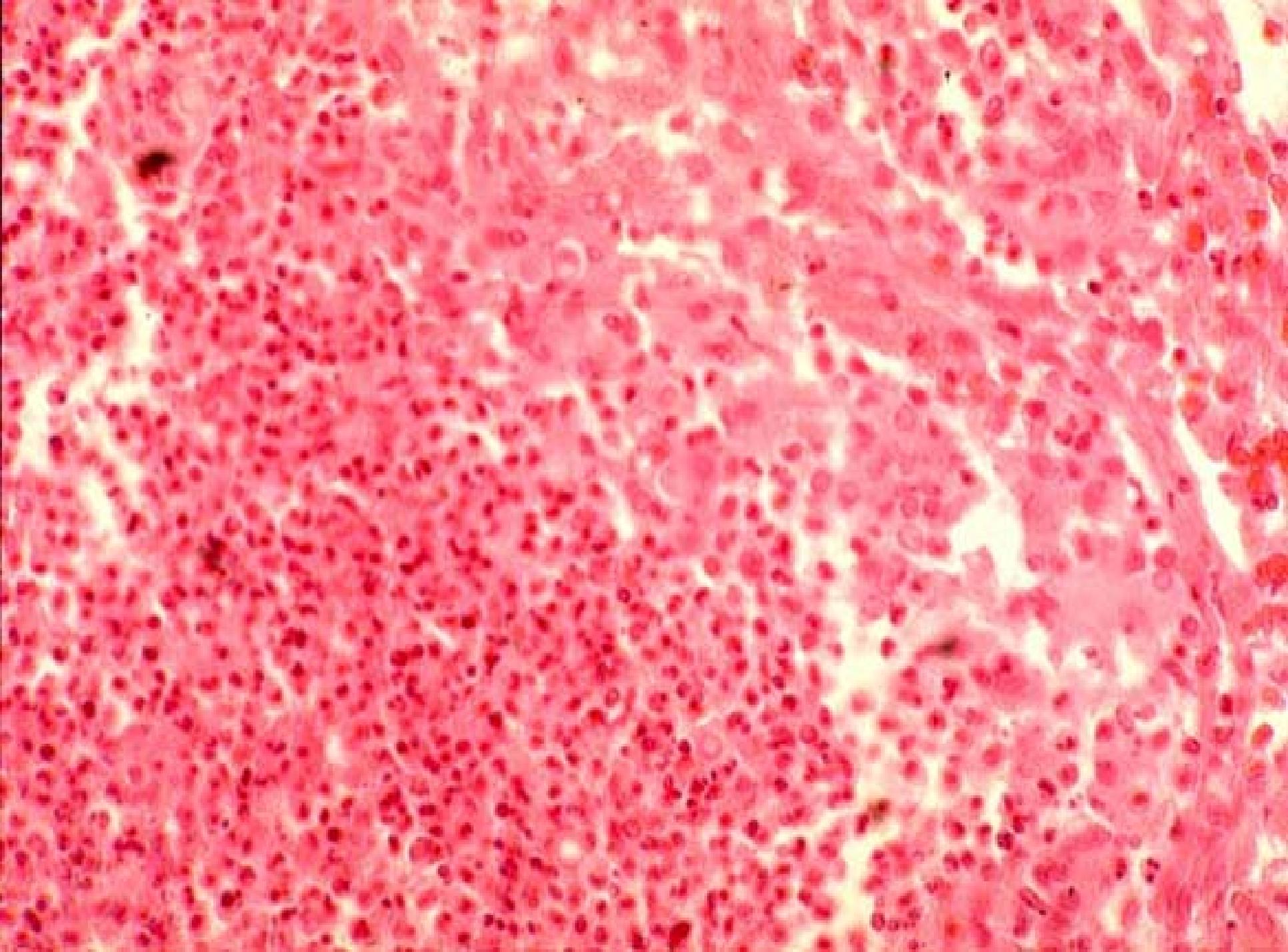
# Histopathology

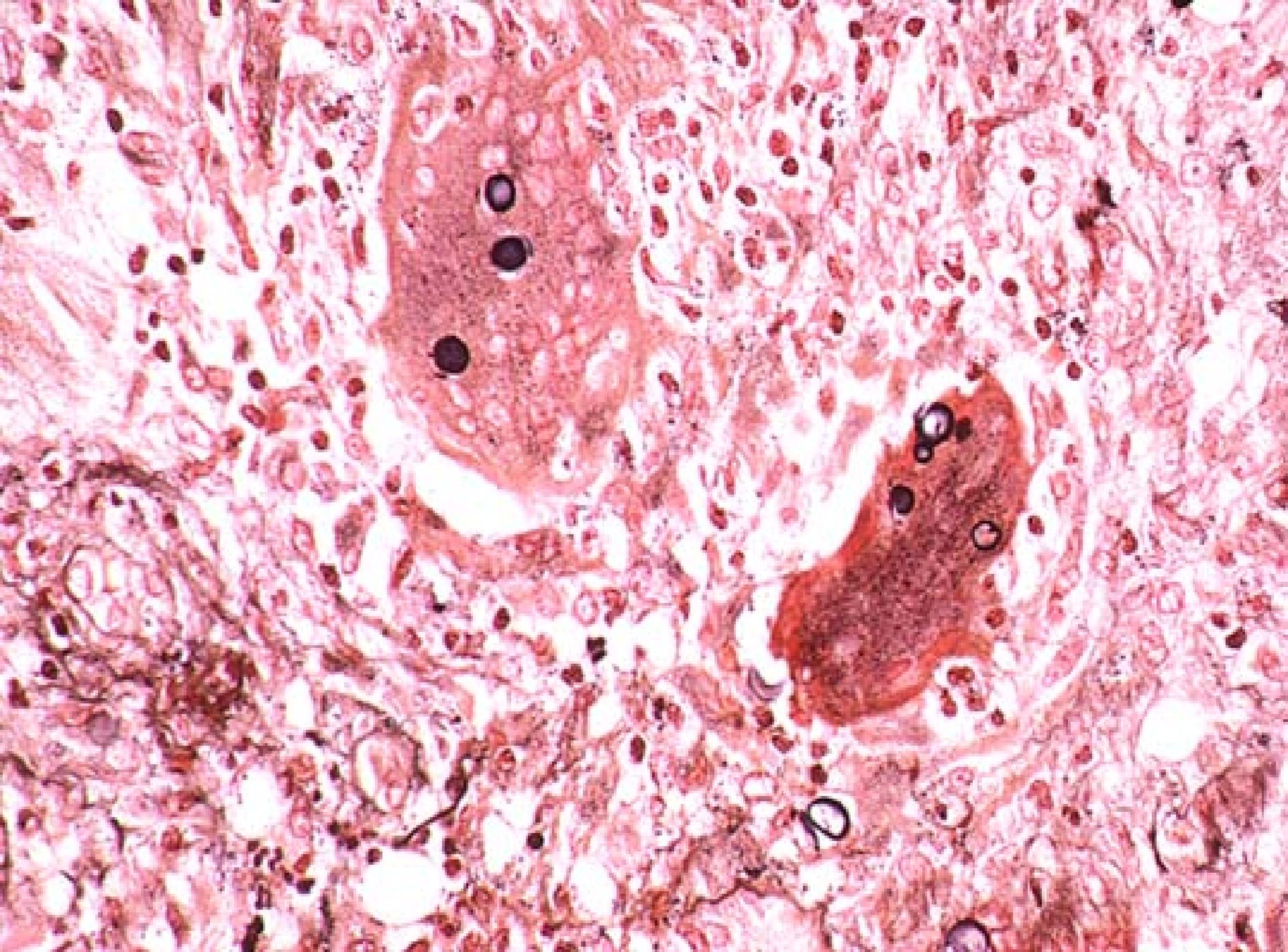


- Circumscribed appearance
- Downward invagination
- May form cyst
- Papillomatous features with koilocytes





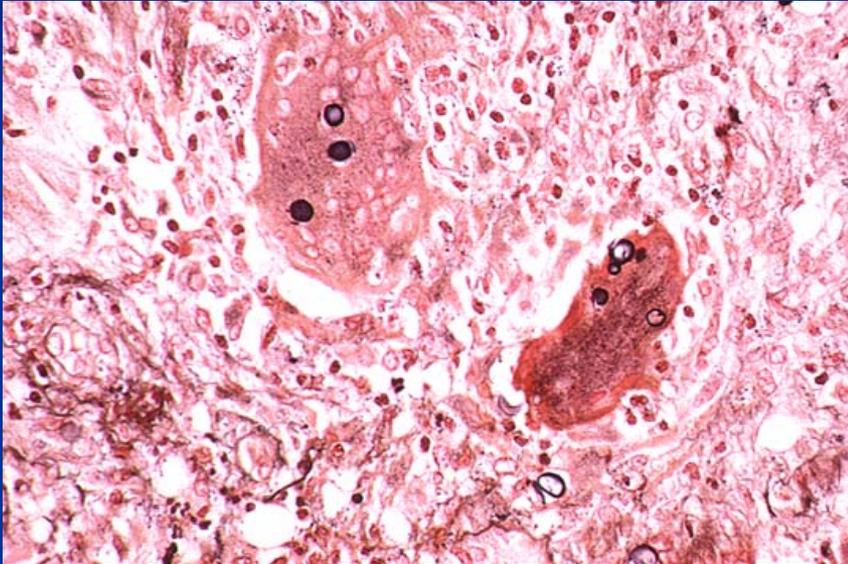




**What is your differential  
diagnosis and what stains/IHC  
would you order?**

# North American Blastomycosis

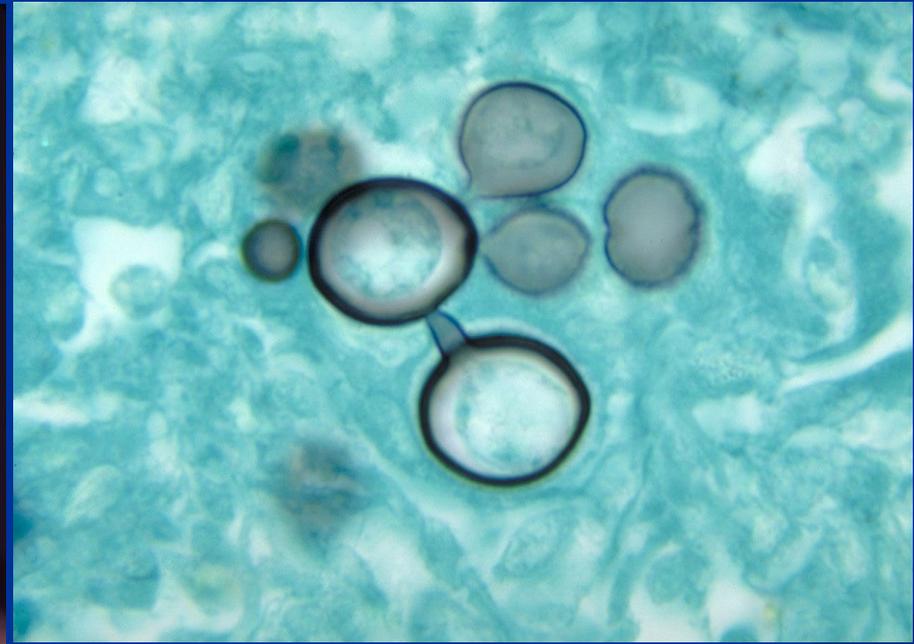
# Histopathology

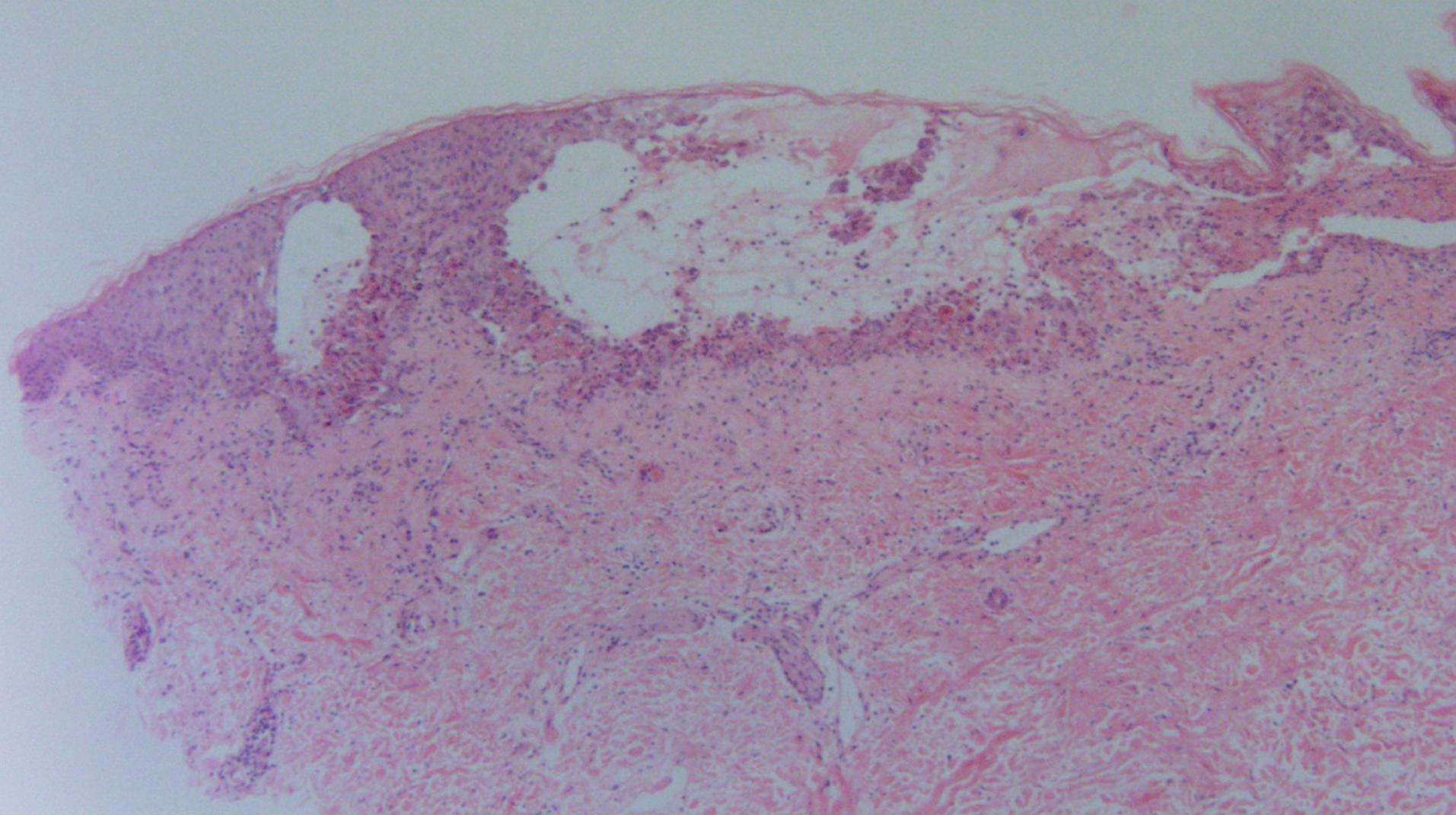


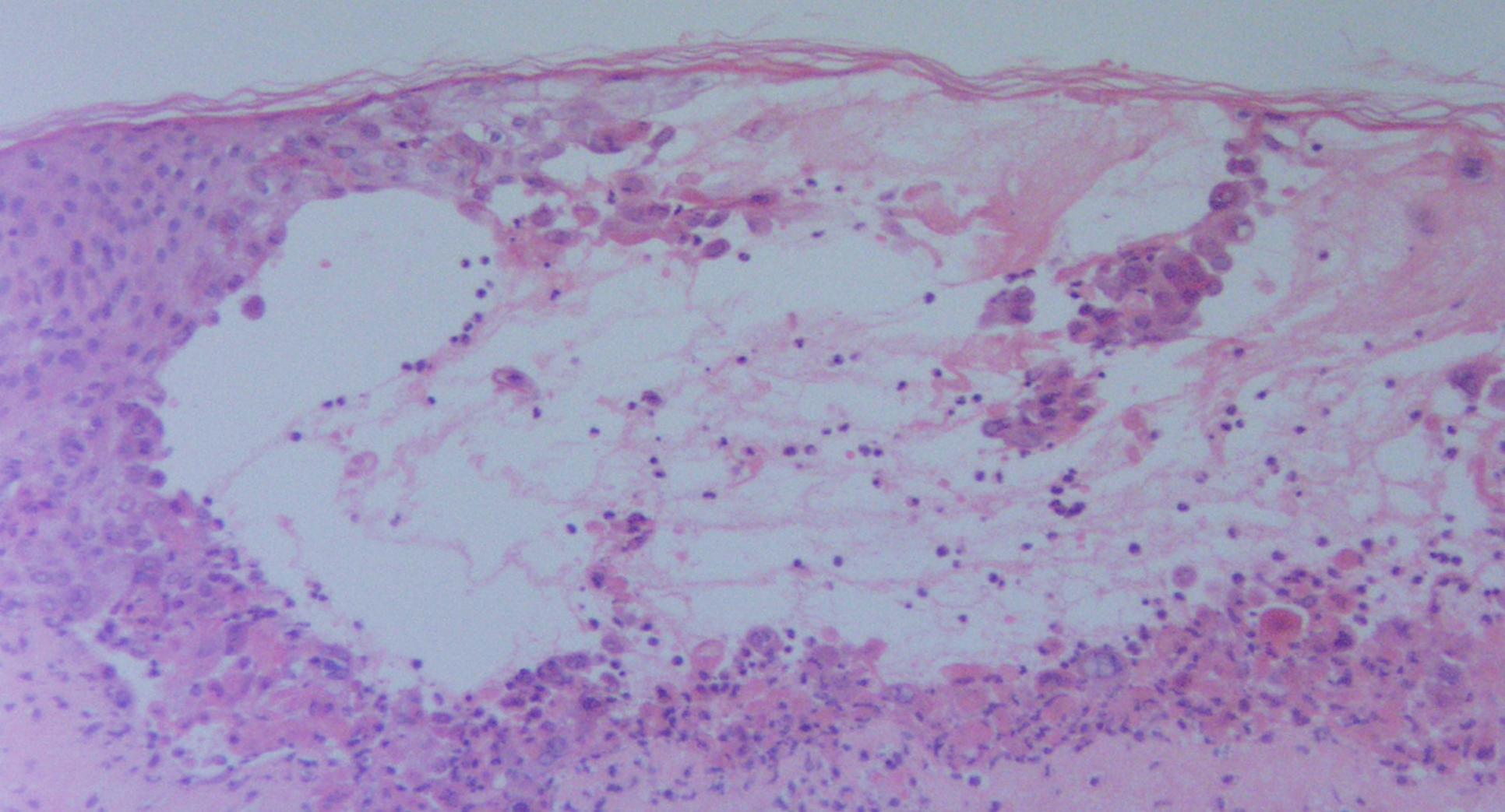
- Broad based budding of yeast organisms
- Giant cell reaction with granulomas, often caseating
- Verrucous epidermal hyperplasia

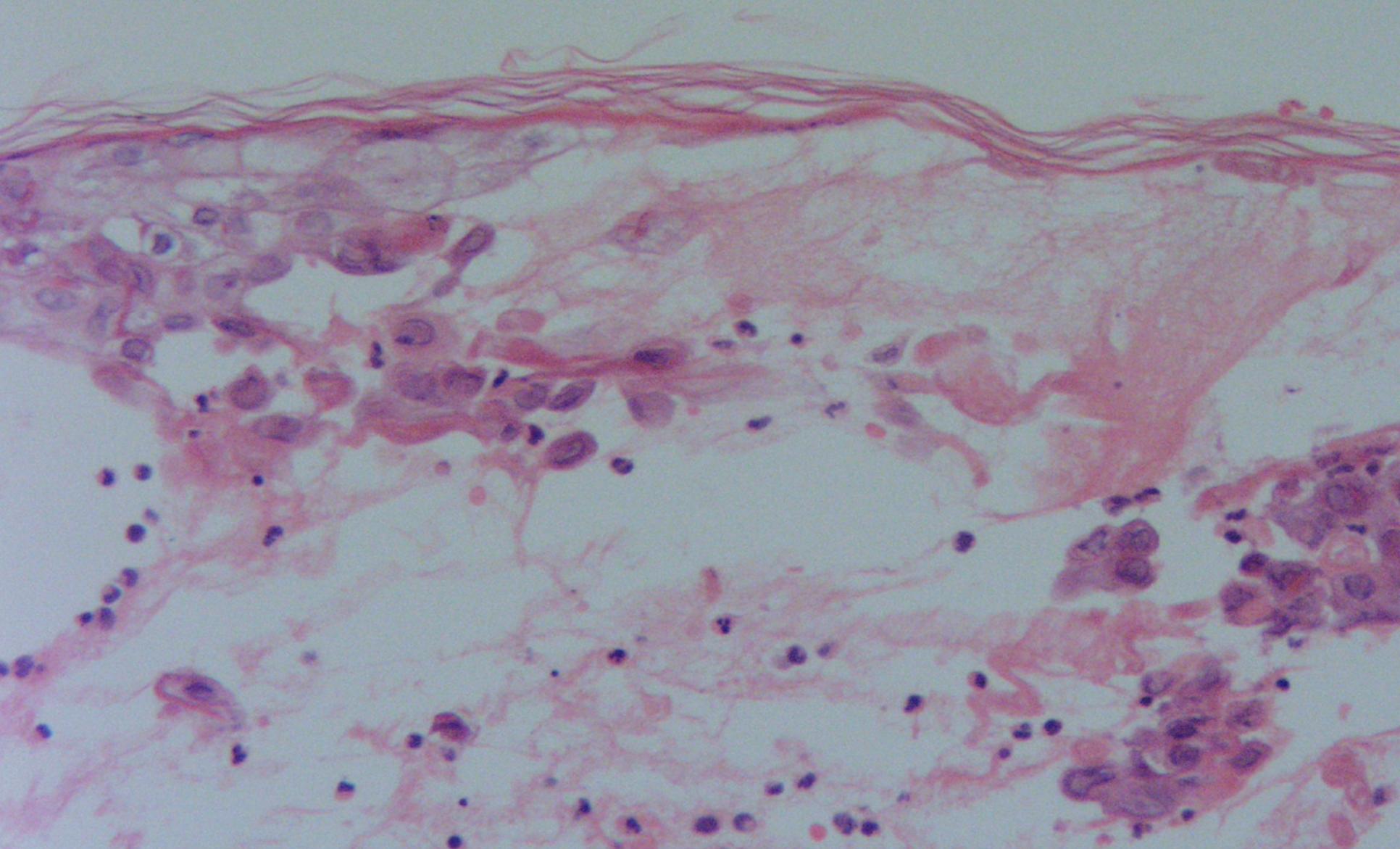
# What is South American Blastomycosis?

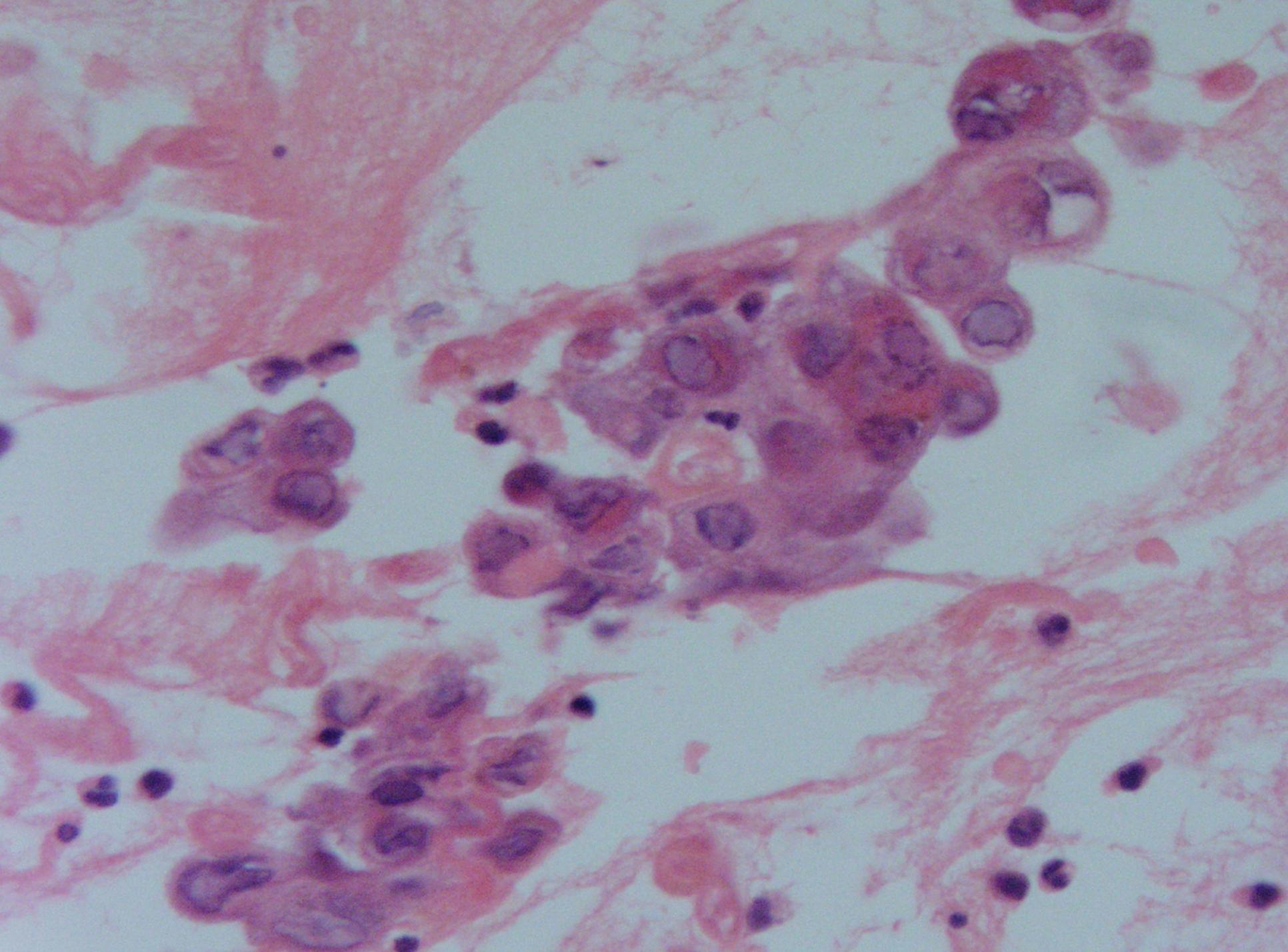
# Paracoccidioides (*brasiliensis*, *lutzii*)







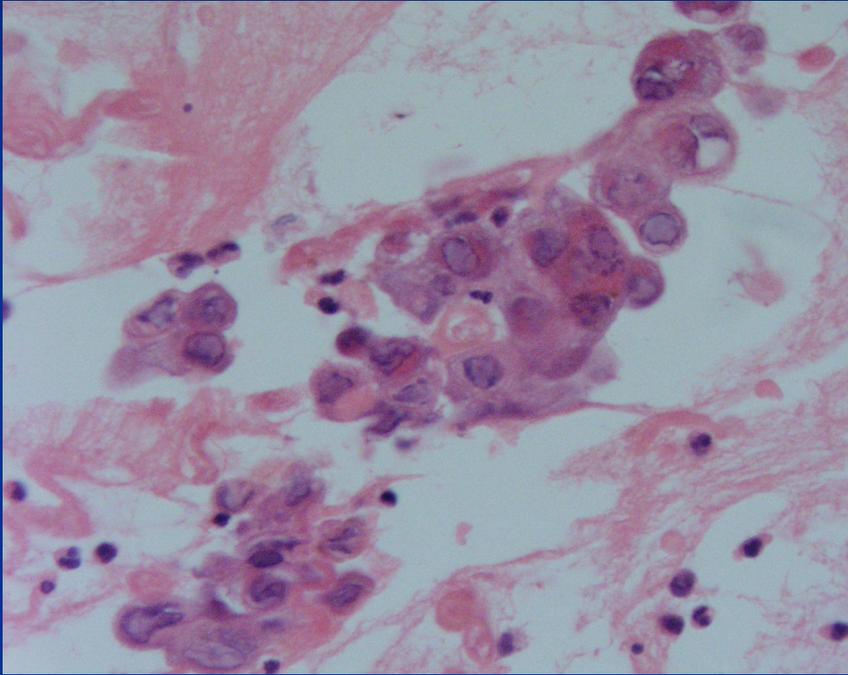




**What is your differential  
diagnosis and what stains/IHC  
would you order?**

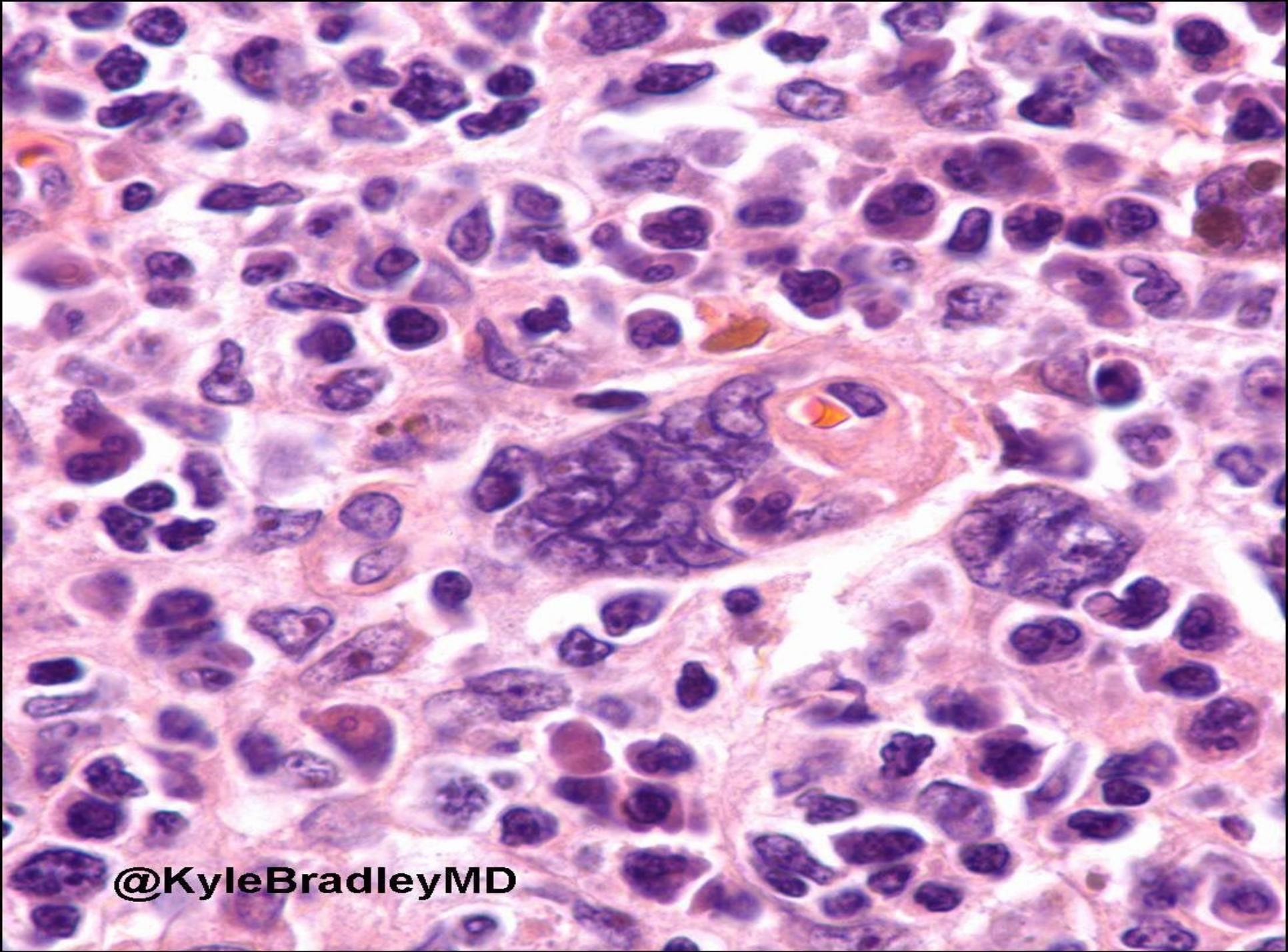
# Herpes Virus Infection

# Histopathology



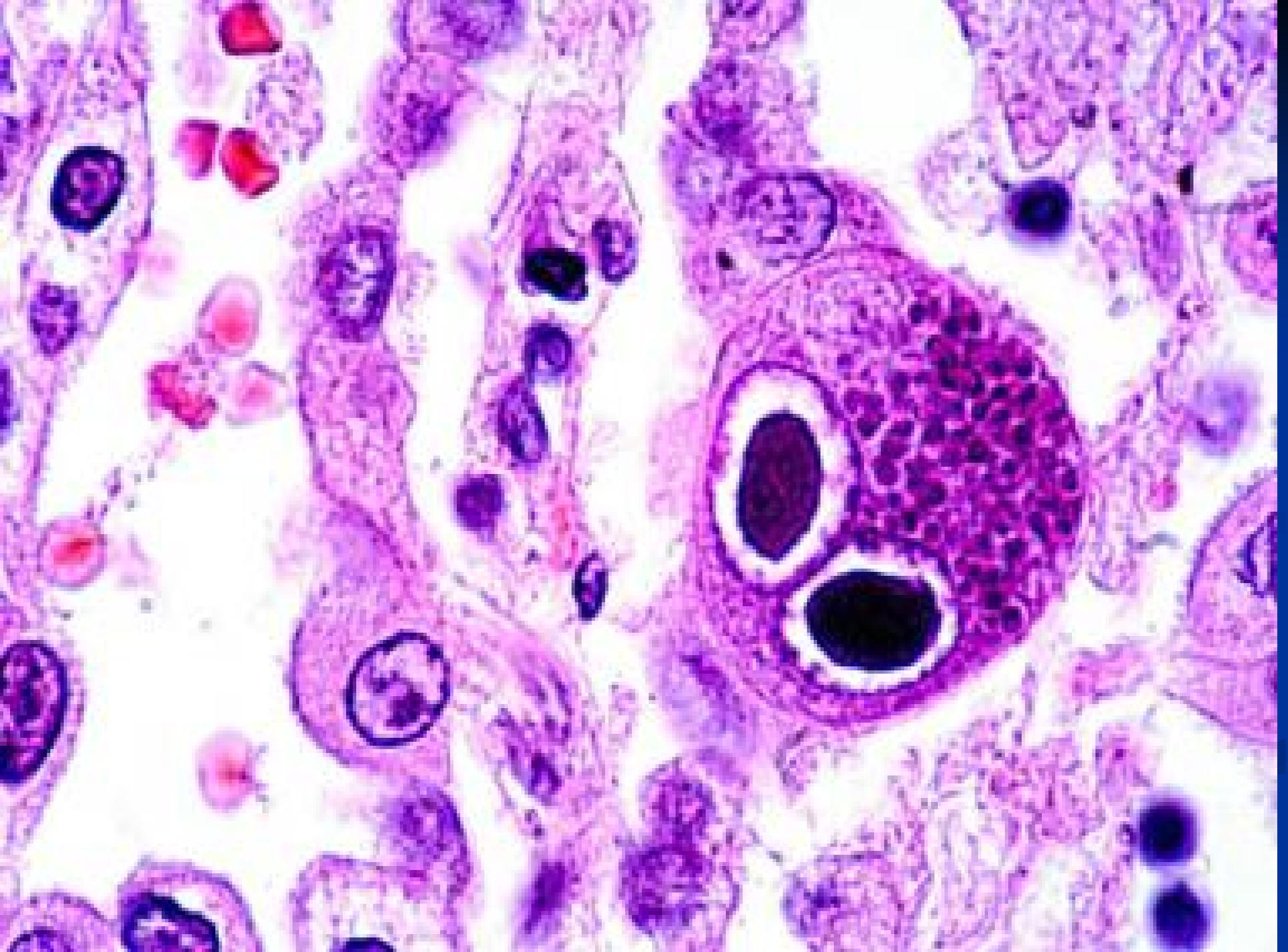
- Intraepidermal bulla with acantholysis
- Necrosis variable
- Characteristic ground glass chromatin and multinucleation

**What is the name of  
these viral inclusions?**

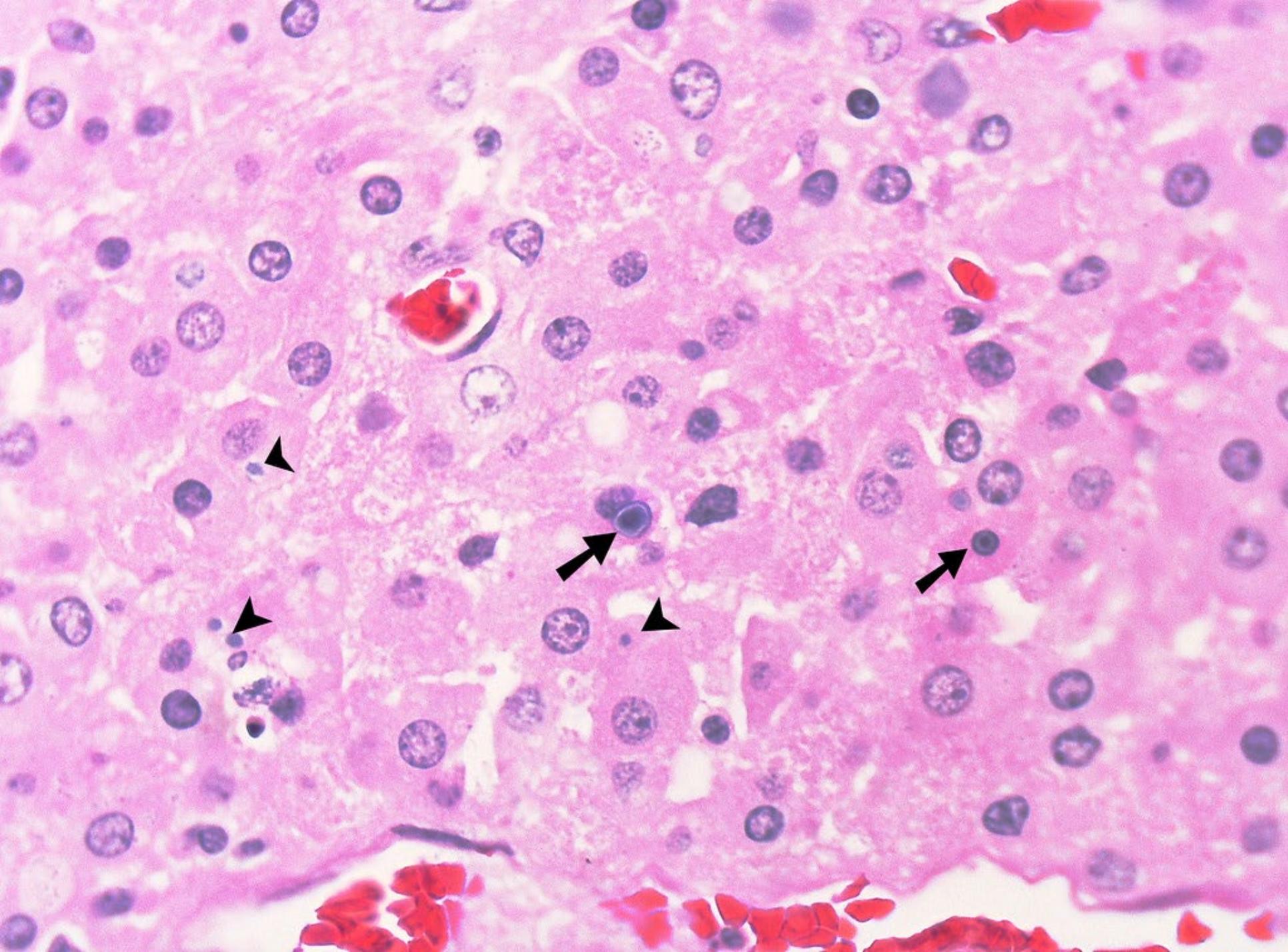


@KyleBradleyMD

# Warthin-Finkeldey Giant Cell of Measles



# Owl Eye Inclusions of CMV



# Michaelis-Gutman Bodies of Malakoplakia

# Dermatopathology Slide Review Part 6

Paul K. Shitabata, M.D.

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