

Cutaneous  
Squamous Cell Carcinoma...  
Good Grades Are Not Enough!

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# Should We Report These?

- Thickness
- Grade of differentiation
- Histologic type
- Growth pattern
- Perineural invasion
- Lymphovascular invasion

# Poor Prognostic Factors

- Thickness (Clark's level and Breslow depth)
  - Recurrence risk
    - <10% for lesions <2 cm
    - 30% for lesions >2 cm
  - Survival
    - 3 YRS was 98% if tumor <3.5 mm in depth
    - 84% >3.5 mm in depth
- Growth pattern
  - Small nests
  - Infiltrative pattern
  - Diffuse haphazard growth
  - Isolated strands
  - Clusters of cells or single cells
- Perineural invasion
  - Present in 2.4-14% of tumors
  - More frequent in recurrences
  - 2 year cure rate of only 2% if perineural invasion was found
- Degree of differentiation
- Histologic type-Acantholysis
- Recurrence after treatment



# Questionable Significance

- Location (non-mucosal surfaces excluded)
- Ulceration
- Inflammation

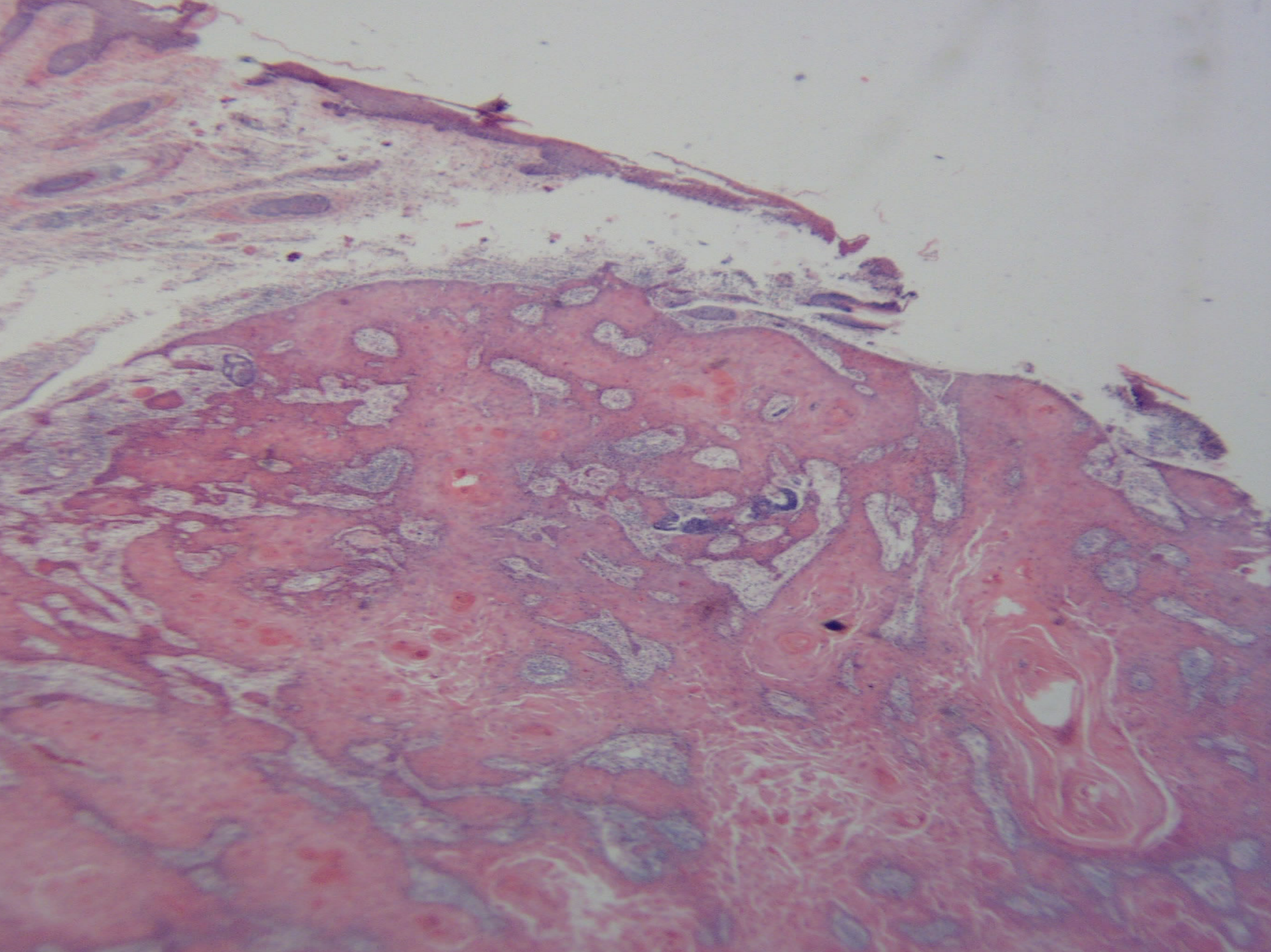
# Proposed Classification Schemes

- Low Risk of Aggressive Behavior
  - Bowen's Disease/Carcinoma in situ
    - Erythroplasia of Queyrat
  - Actinic keratosis/KIN I-III
  - Keratoacanthoma
  - Verrucous
  - Papillary
- High Risk of Aggressive Behavior
  - Marjolin's Ulcer
  - Acantholytic
  - Desmoplastic/Sarcomatoid
  - Invasive Bowenoid
  - Adenosquamous
  - Lymphoepithelioma-like carcinoma
  - Transplant related

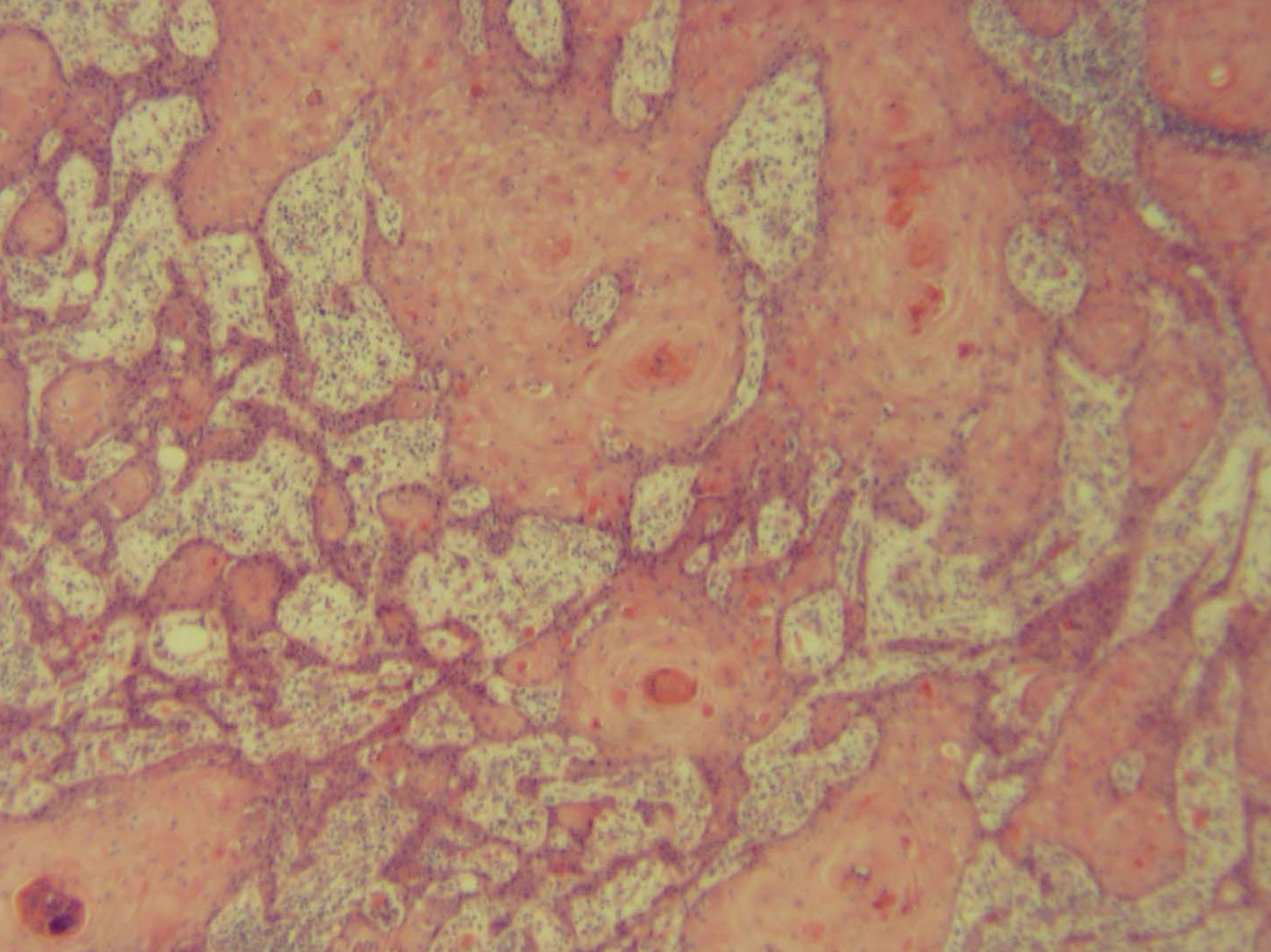
# Keratoacanthoma

- Resemble squamous cell carcinomas both clinically and histologically
- Usually nodules with a scaly central plug.
- History of rapid onset with growth to 1-2 cm over a period of 1-2 months
- Many spontaneously involute or regress after 3-6 months
- Males in their 6-7th decades.

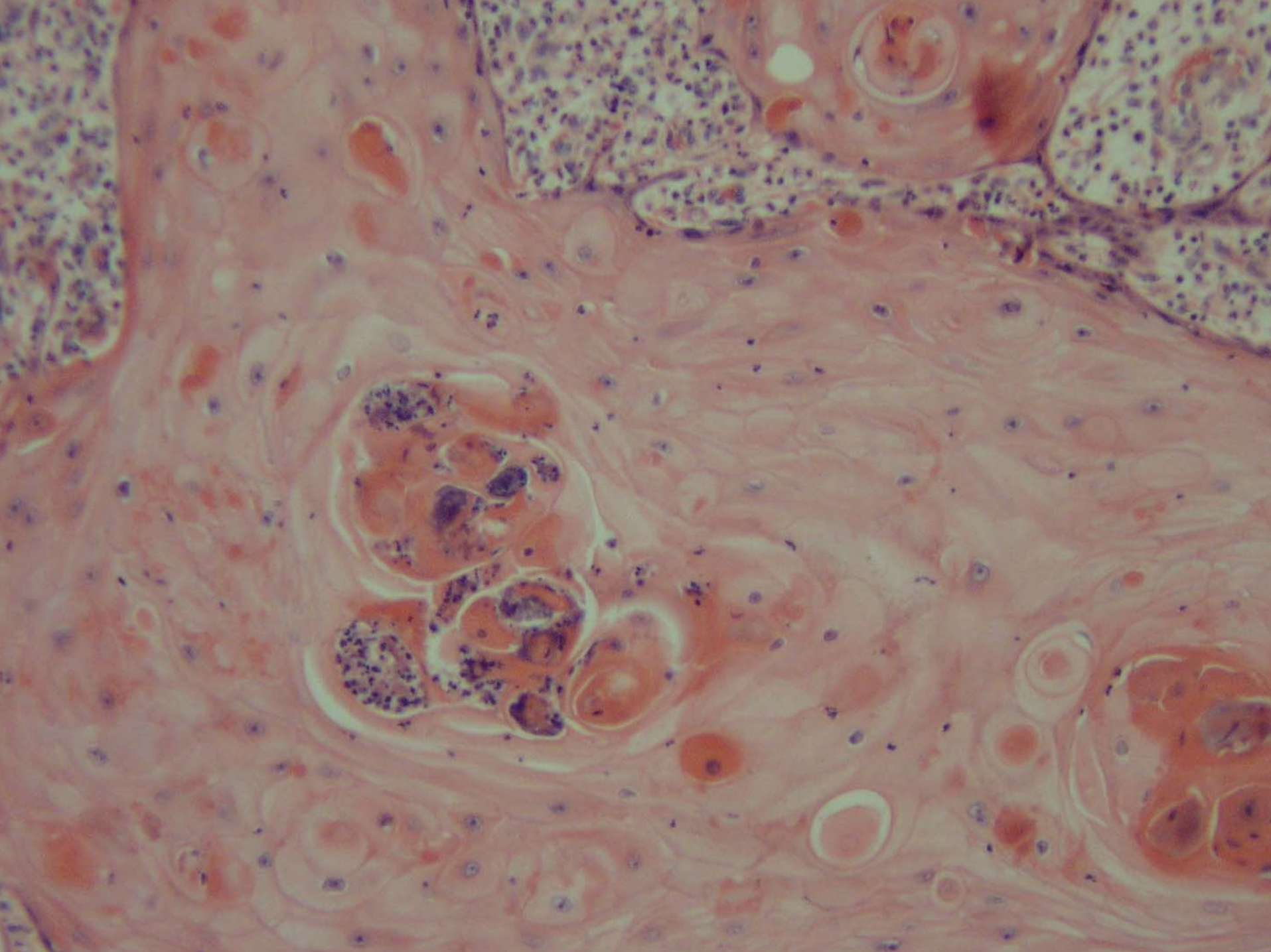




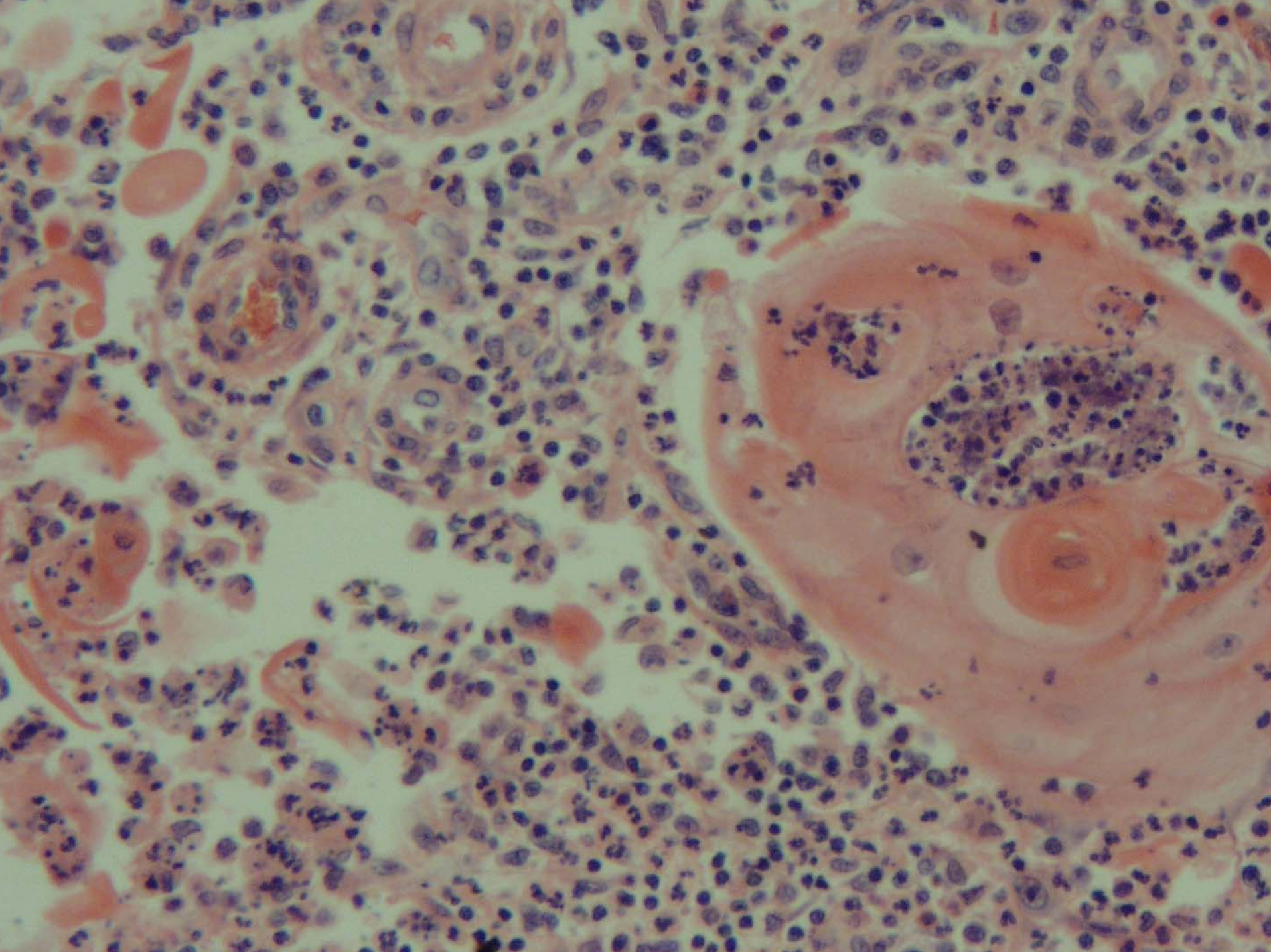




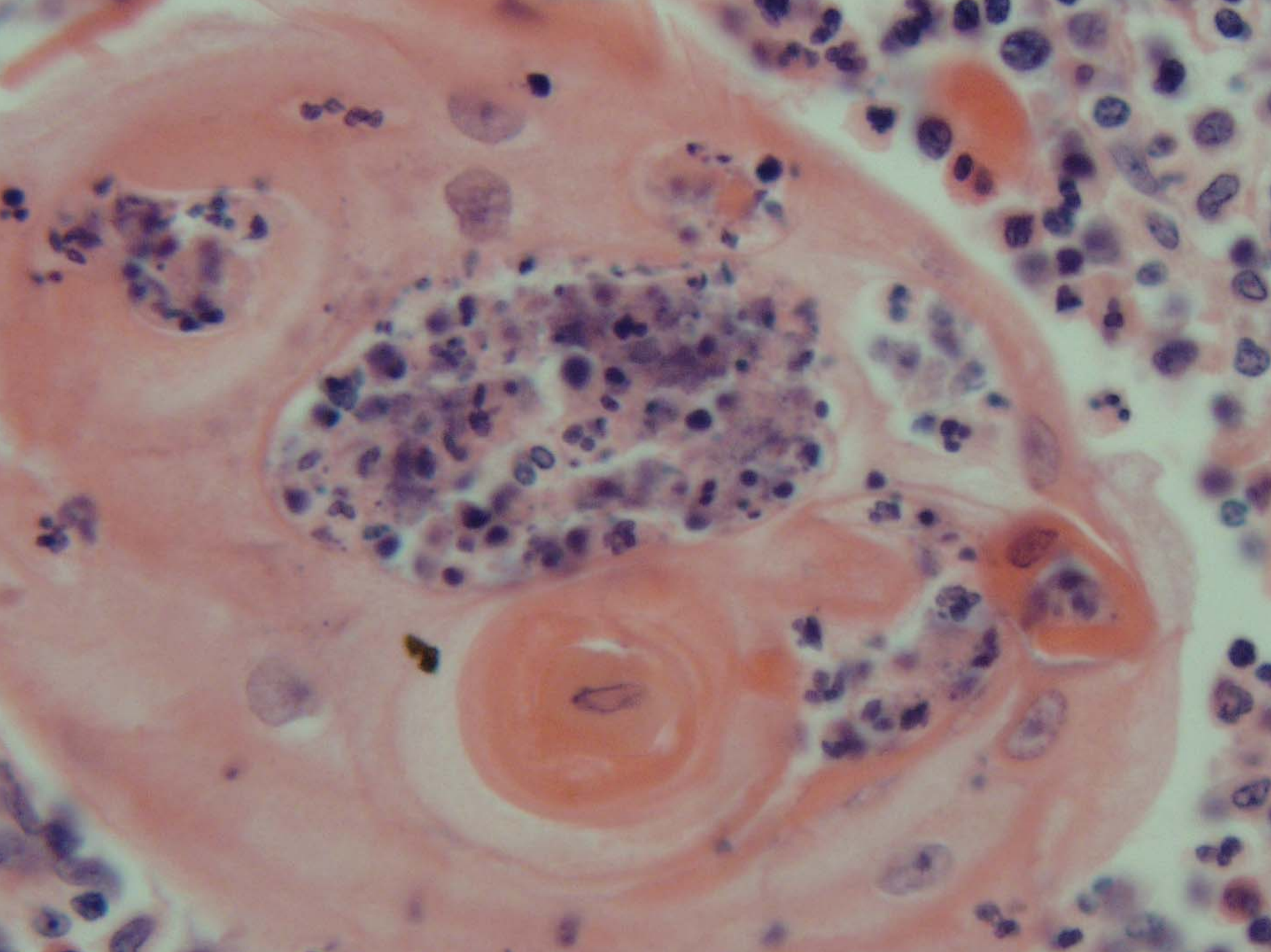




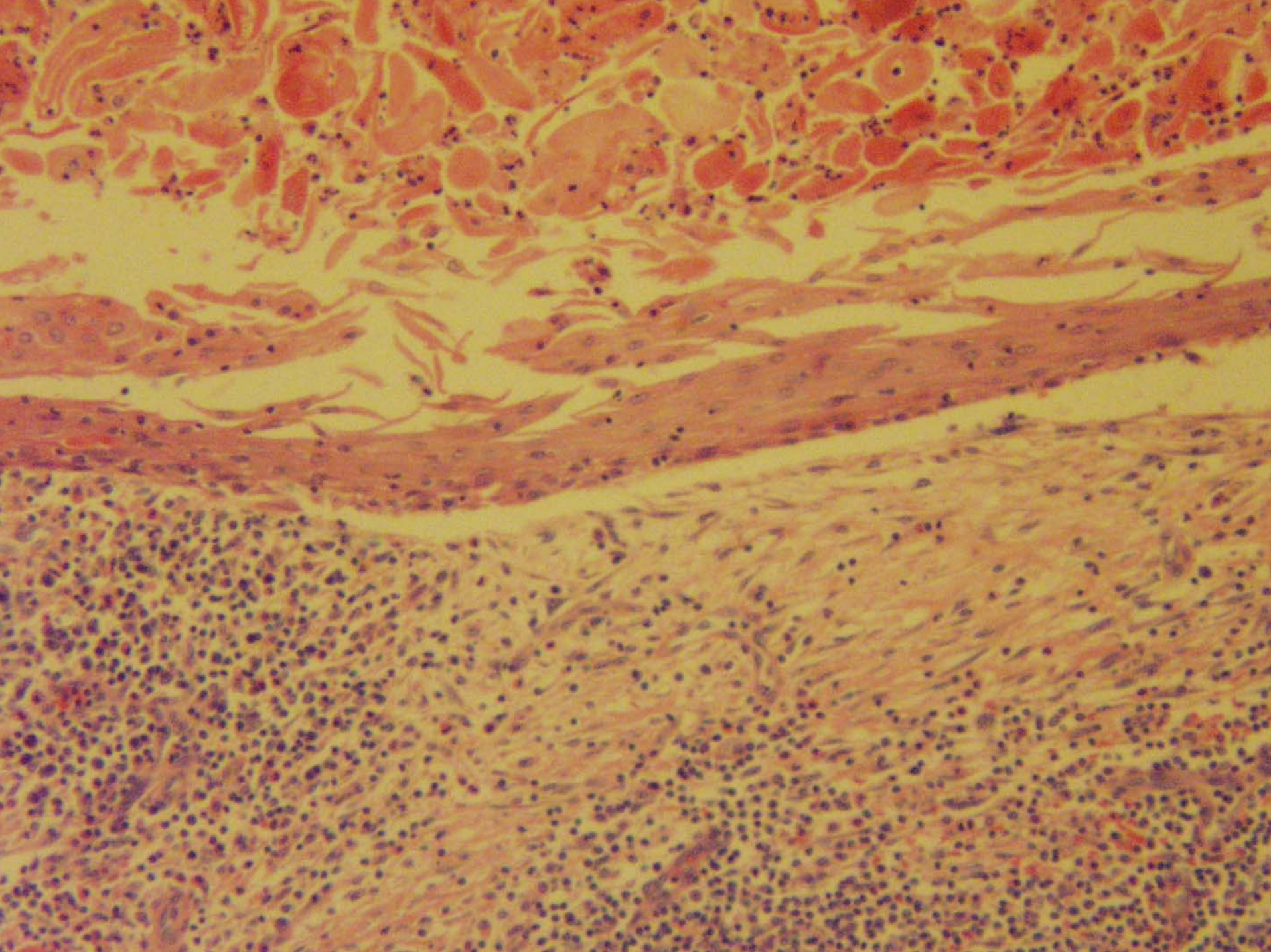












# Keratoacanthoma Clinical Variants

- Giant
- Multiple-Ferguson Smith Type
- Multiple-Grzybowski (Eruptive) Type
- Subungual



# KA-Histology

- Exoendophytic proliferation of well-differentiated keratinocytes with a large keratin filled crater. Surrounding this keratin crater are buttressing or lipping of the epidermal edges
- Keratinocytes have a distinct eosinophilic cytoplasmic appearance with a bland cytology and rare mitotic figures
- Frequent eosinophils and neutrophils

# KA-Differentiation from SCC

- ICAM (CD-54) ligand for the cell adhesion receptor LFA-1, important in immune stimulation that is upgraded in inflammatory cutaneous disorders
  - Increase in expression in the fully developed keratoacanthoma and absent in the evolving and resolved keratoacanthoma
  - Squamous cell carcinomas expression focally observed in the well-differentiated tumors, dramatic increase in poorly differentiated tumors
- VCAM (CD-106) adhesion molecule normally found in stimulated endothelium, plays a critical role in the migration of leukocytes
  - Expressed in the fully developed keratoacanthoma and was absent in the evolving and resolved keratoacanthoma
  - Moderate expression in the well-differentiated squamous cell carcinoma, and intense expression was seen in the fully developed keratoacanthoma and poorly differentiated squamous cell carcinoma.
  - Temporal related increase in expression of VCAM (CD-106) in conjunction with the evolution of keratoacanthoma
- Increased expression of both markers is seen with squamous cell carcinoma dedifferentiation.

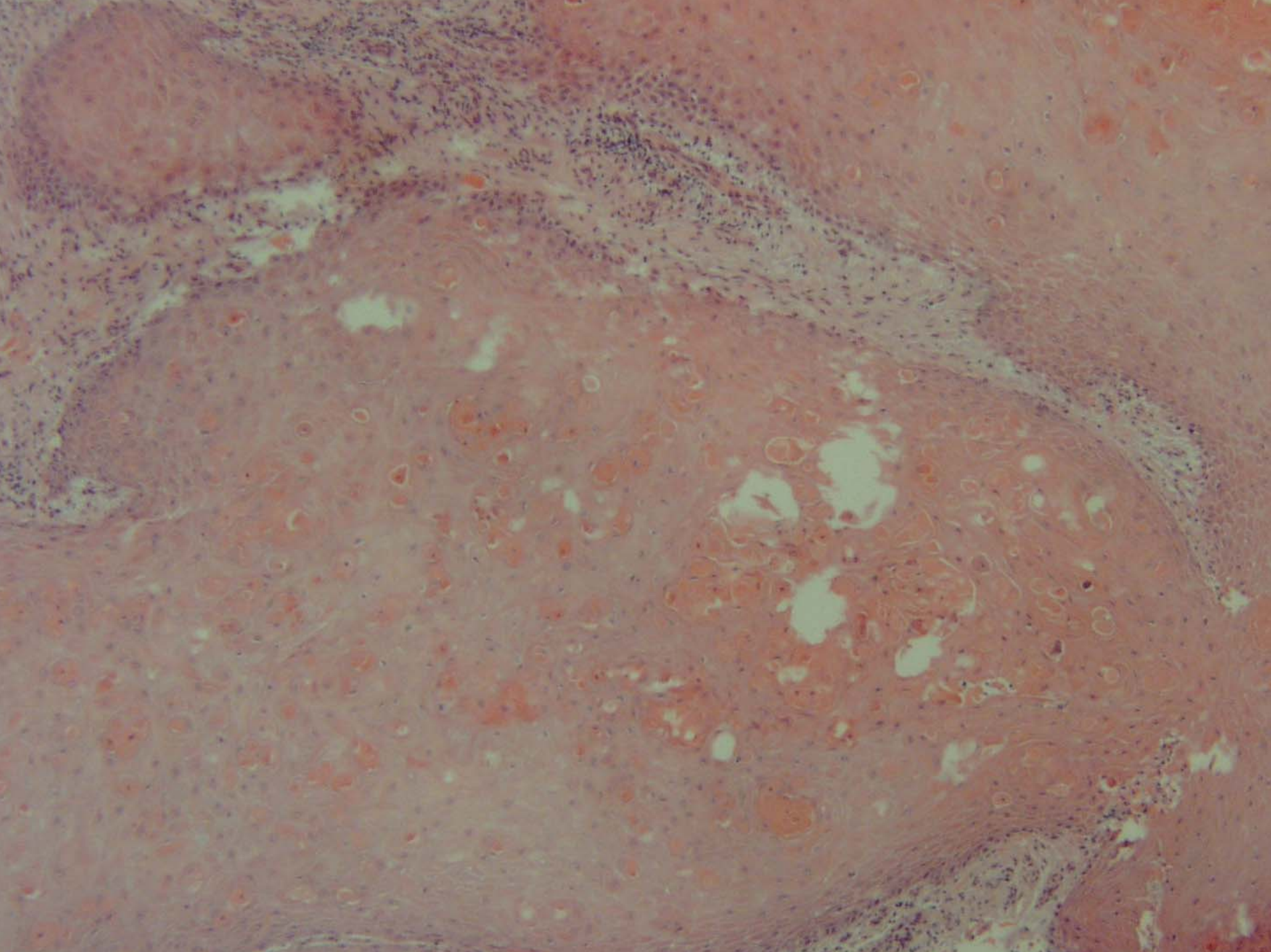
# KA-Differentiation from SCCA

- Syndecan-1, heparan sulfate proteoglycans that mediates intercellular and cell to matrix adhesion
  - Expression appears to be inversely correlated with tumor aggressiveness and invasiveness.
  - Previous studies have shown decreased levels of syndecan-1 expression in invasive cutaneous SCC, correlating with tumor de-differentiation. However, a similar study has never been done on KA.
- All 24 KAs were positive for syndecan-1 expression. Staining intensity of 18 cases was comparable with that of SCC in situ or adjacent normal epidermis
- By comparison, invasive SCC showed significantly diminished staining. Reduced staining in focal areas of cytologic atypia at the base was present in three KAs.
- Syndecan-1 expression in KA mirrors that of SCC in situ and normal epidermis, providing a molecular basis that biologically KA may be closely related to SCC in situ but distinctively different from invasive SCC.
- Mod Pathol 2002;15:45-49

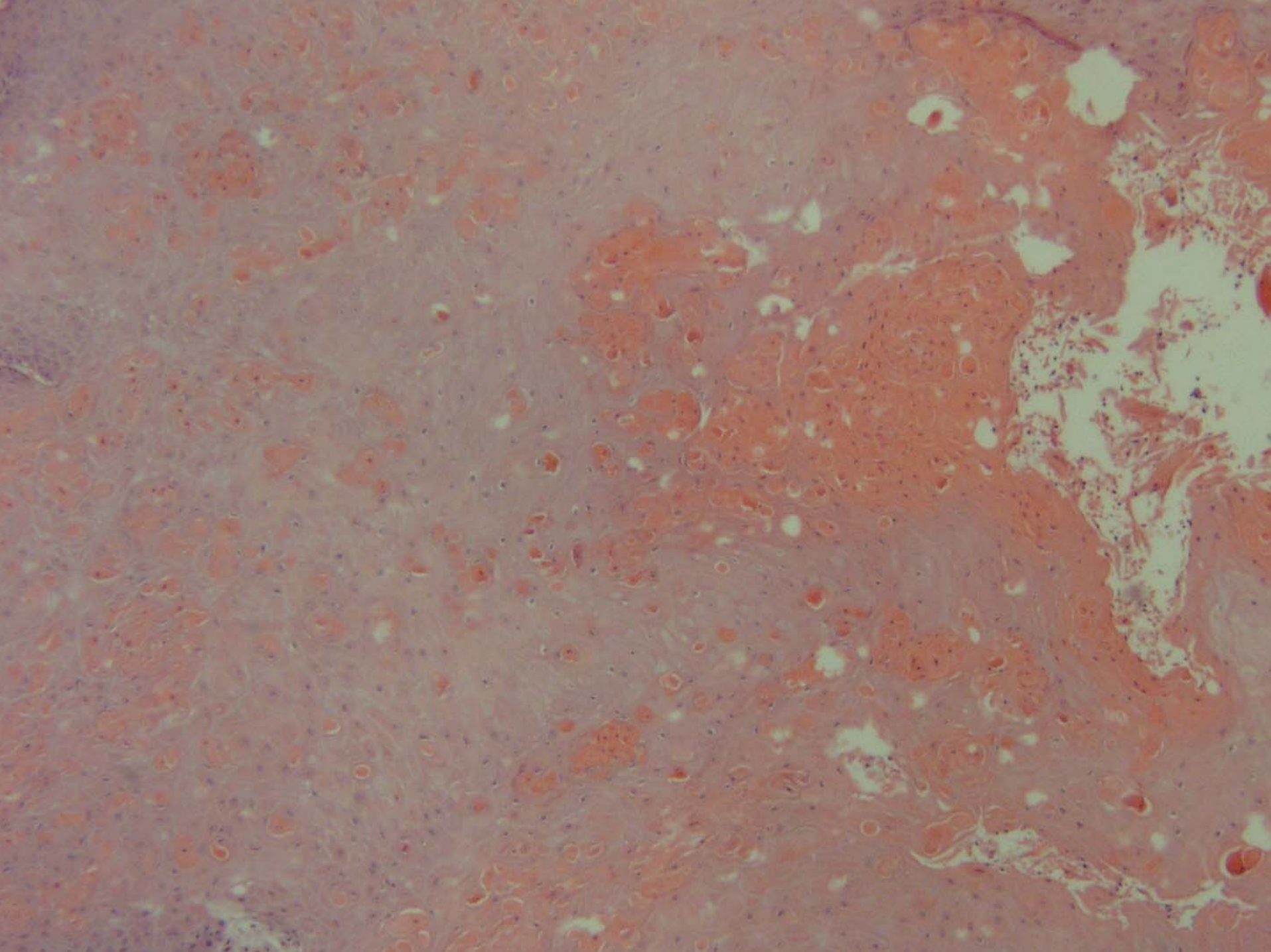


# Subungual Keratoacanthoma

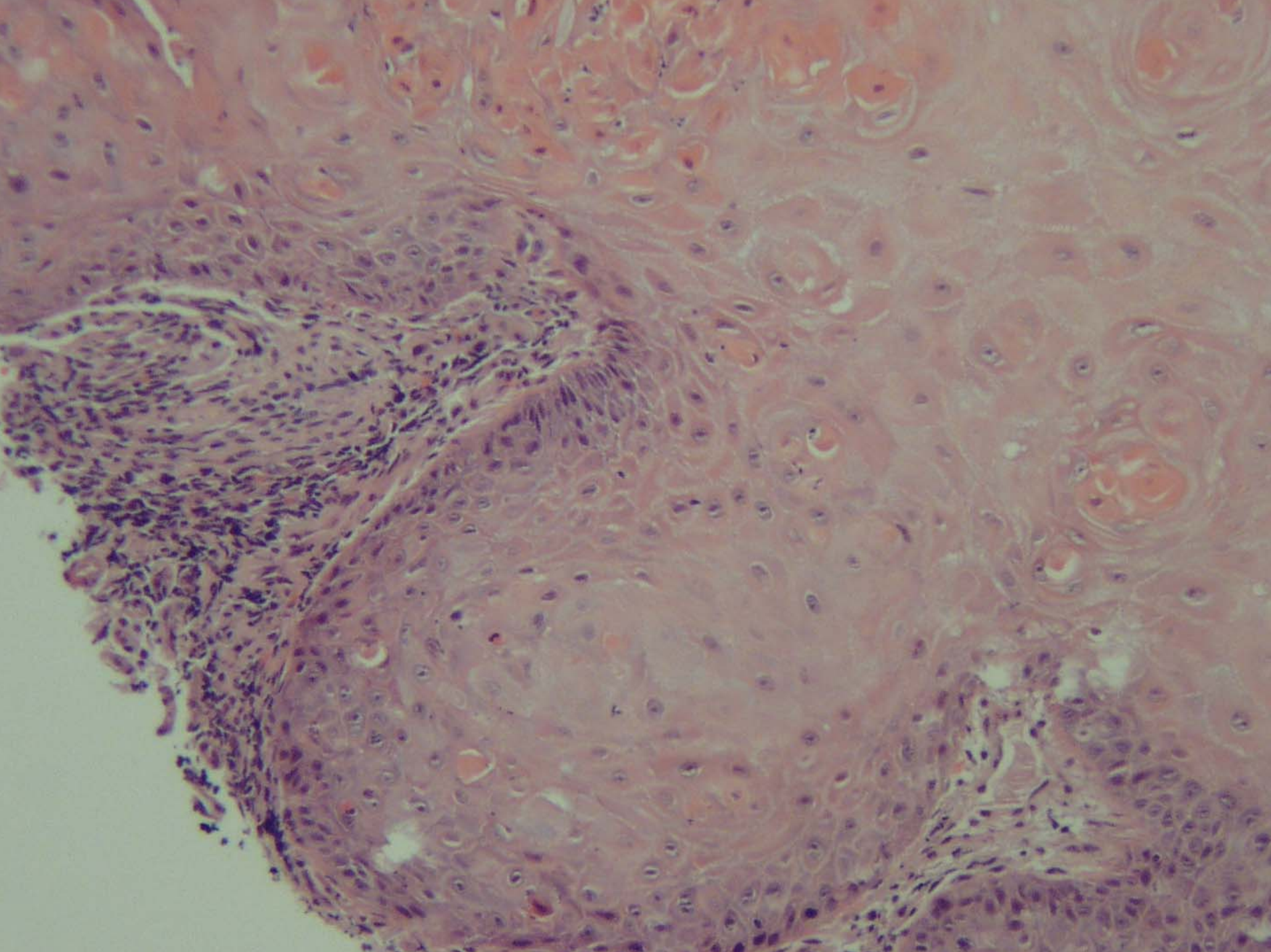
- Differs from the common solitary keratoacanthoma:
  - Clinical similarity to verruca vulgaris
  - More dyskeratotic cells and fewer neutrophils and eosinophils
  - More vertical in orientation (longer than it is broad)
  - Failure to regress spontaneously
  - Longer course
  - Tendency to destroy bone
  - Keratoacanthoma situated in the subungual region is a more destructive neoplasm than a squamous cell carcinoma there



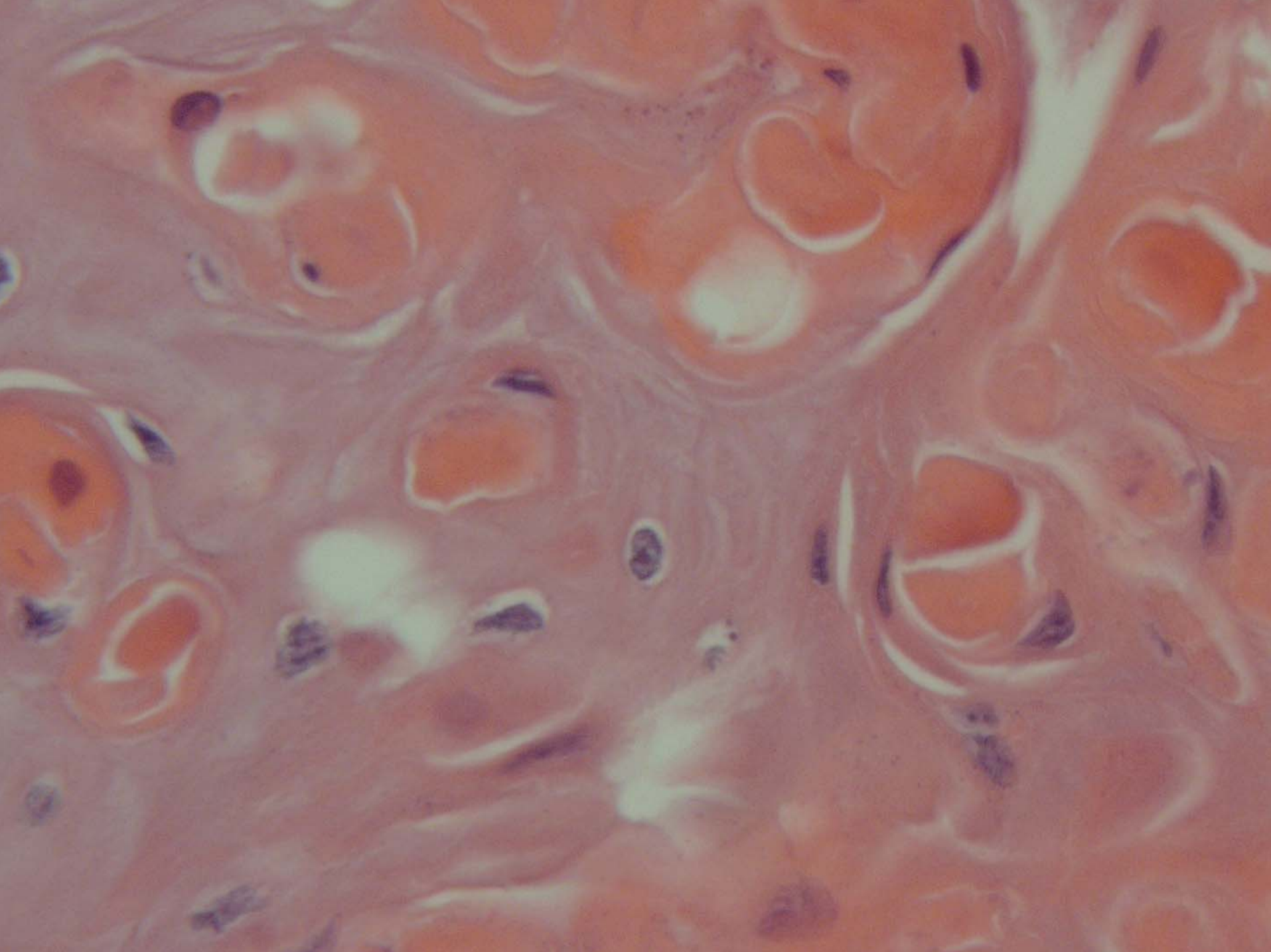








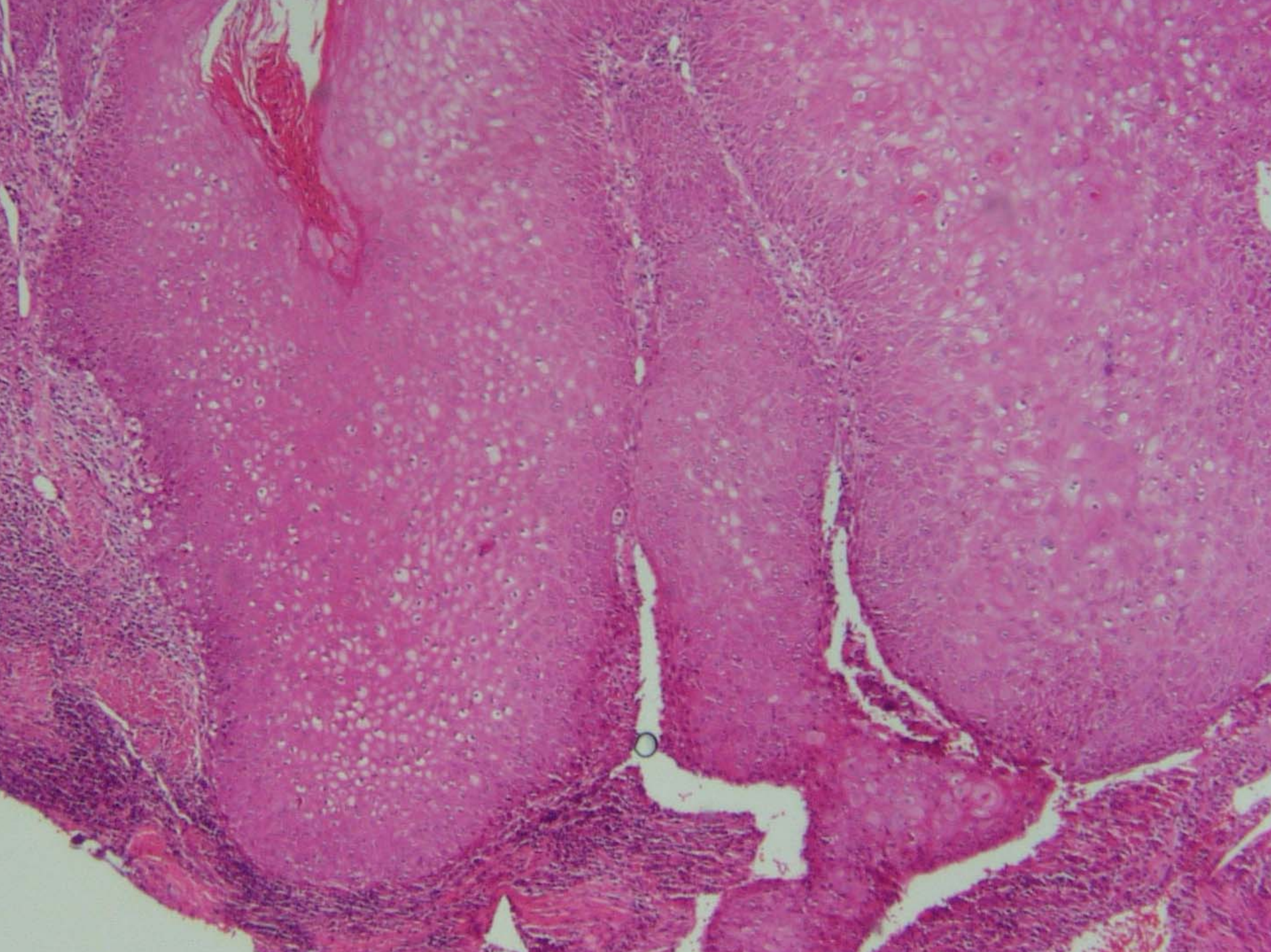




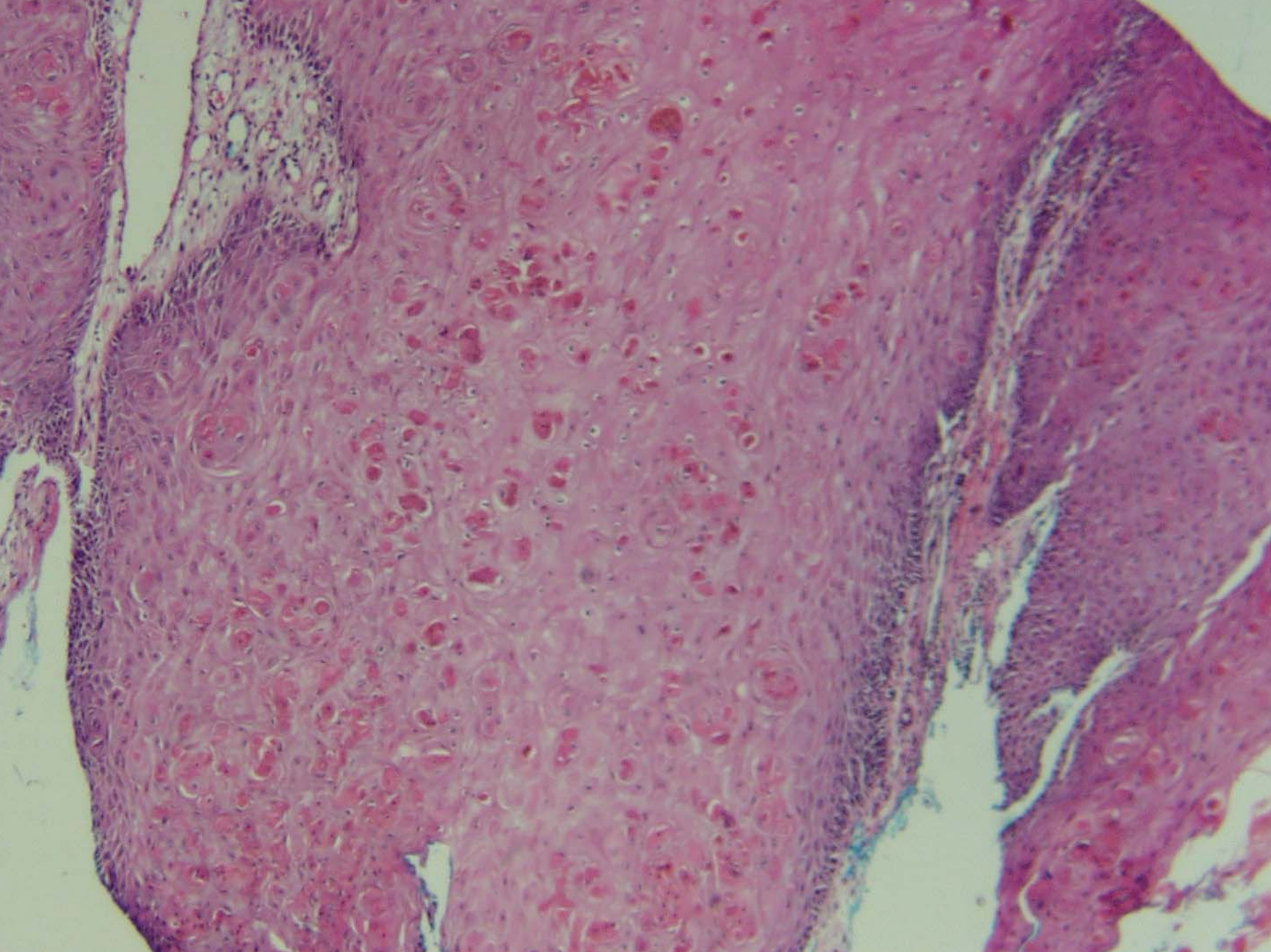
# Verrucous Carcinoma

- Exo or endophytic tumors often growing at sites of chronic irritation
- Classified based upon location
  - Oral
  - Plantar
  - Buschke-Lowenstein tumors

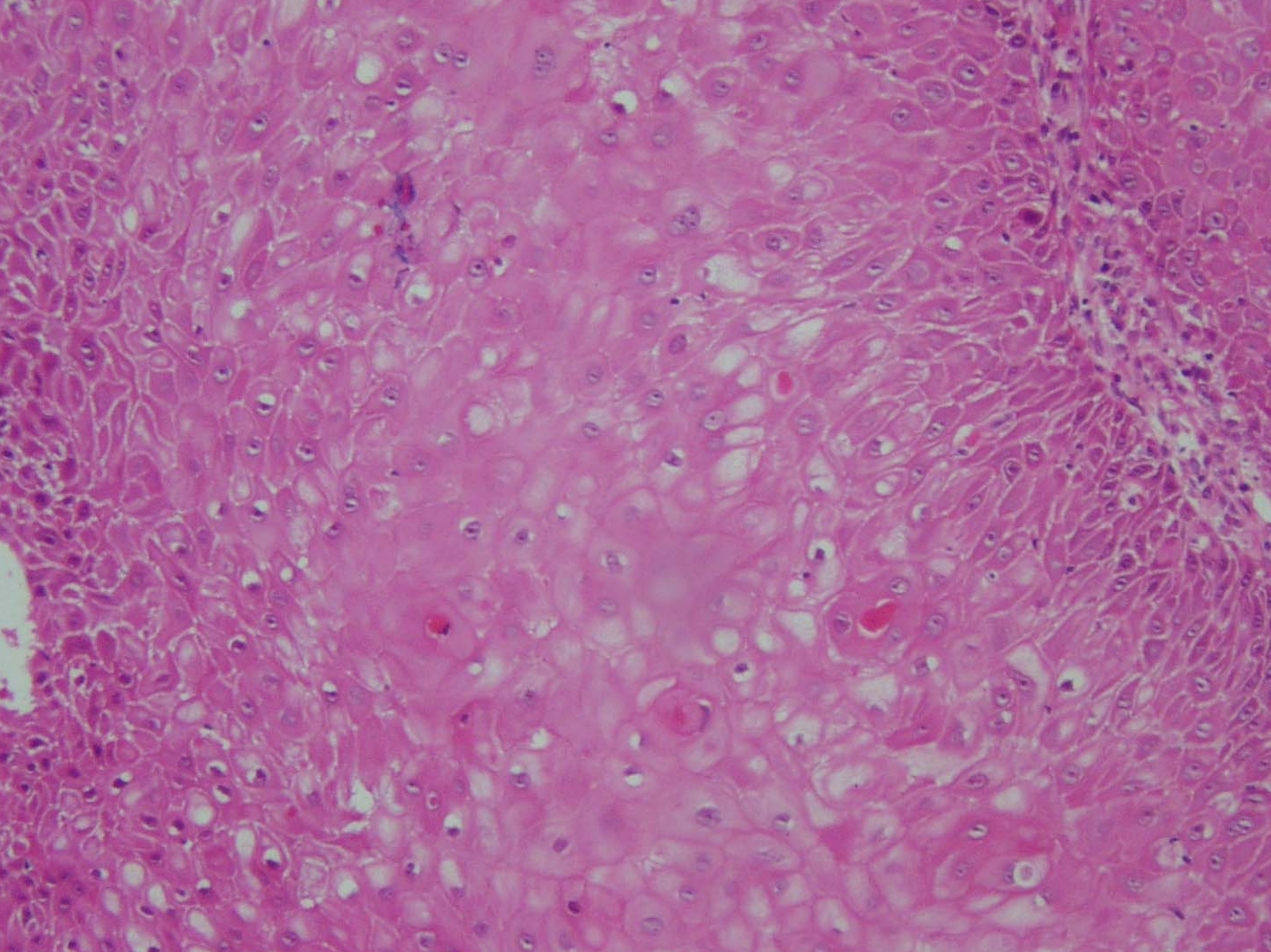




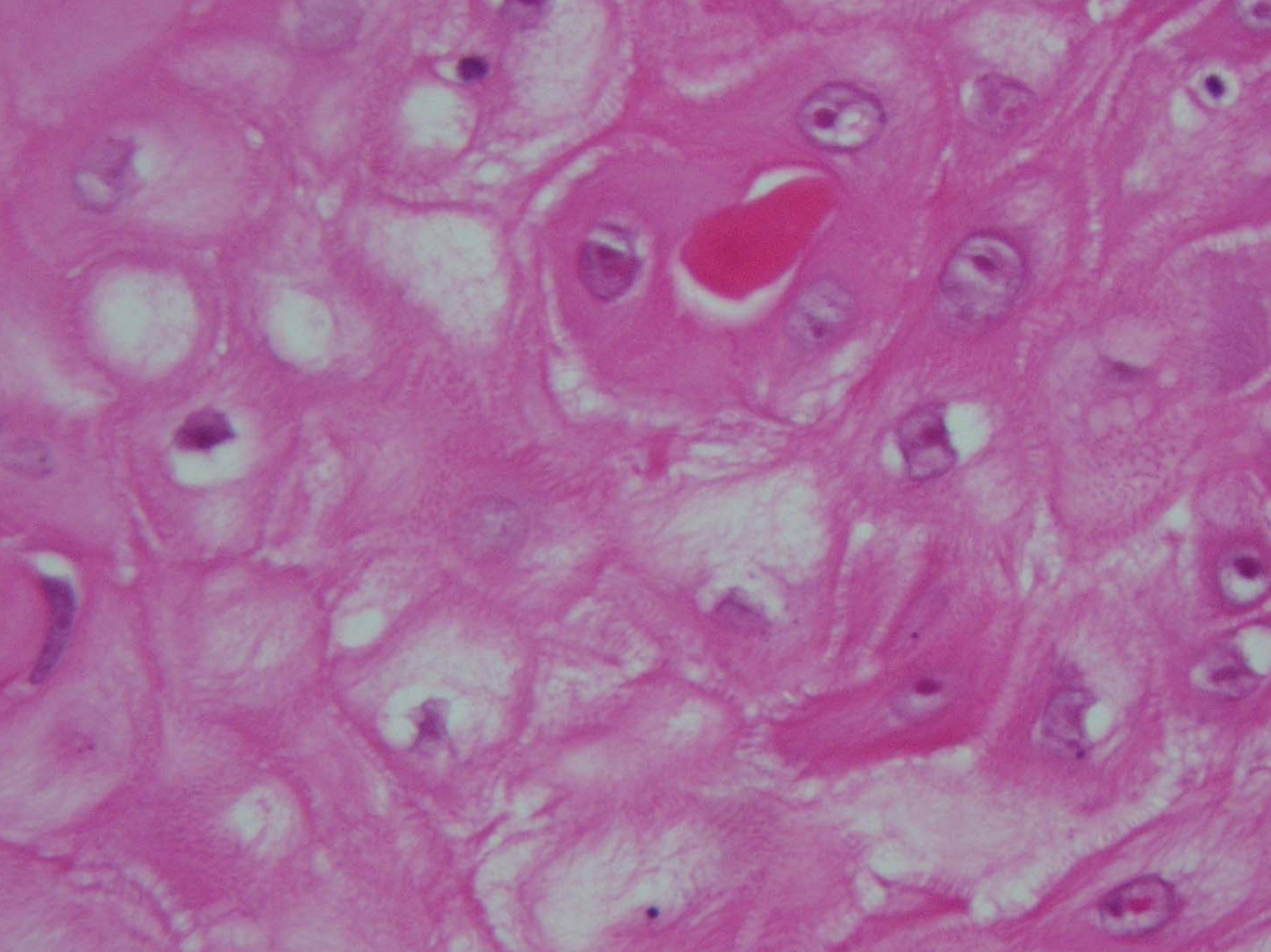








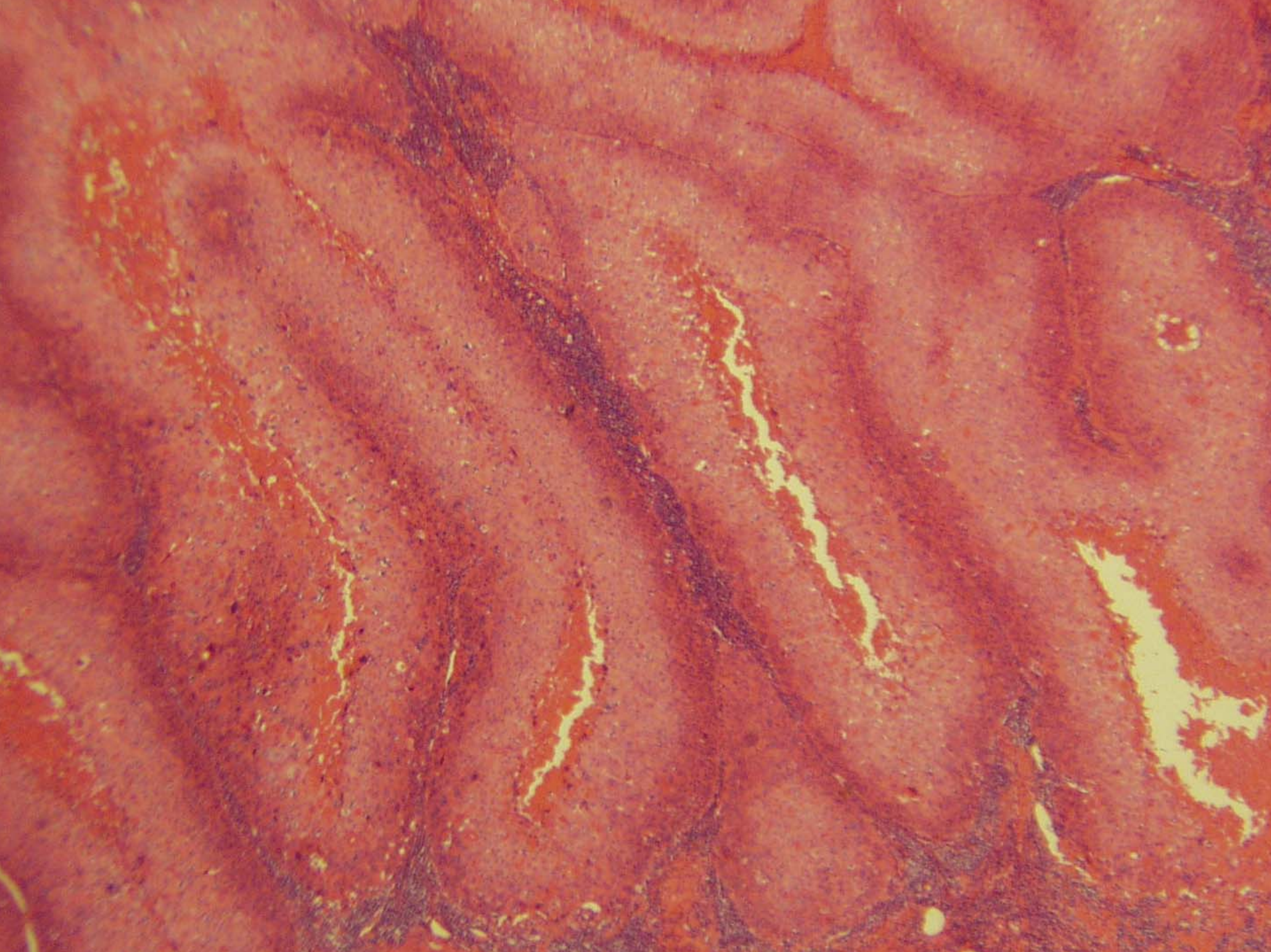




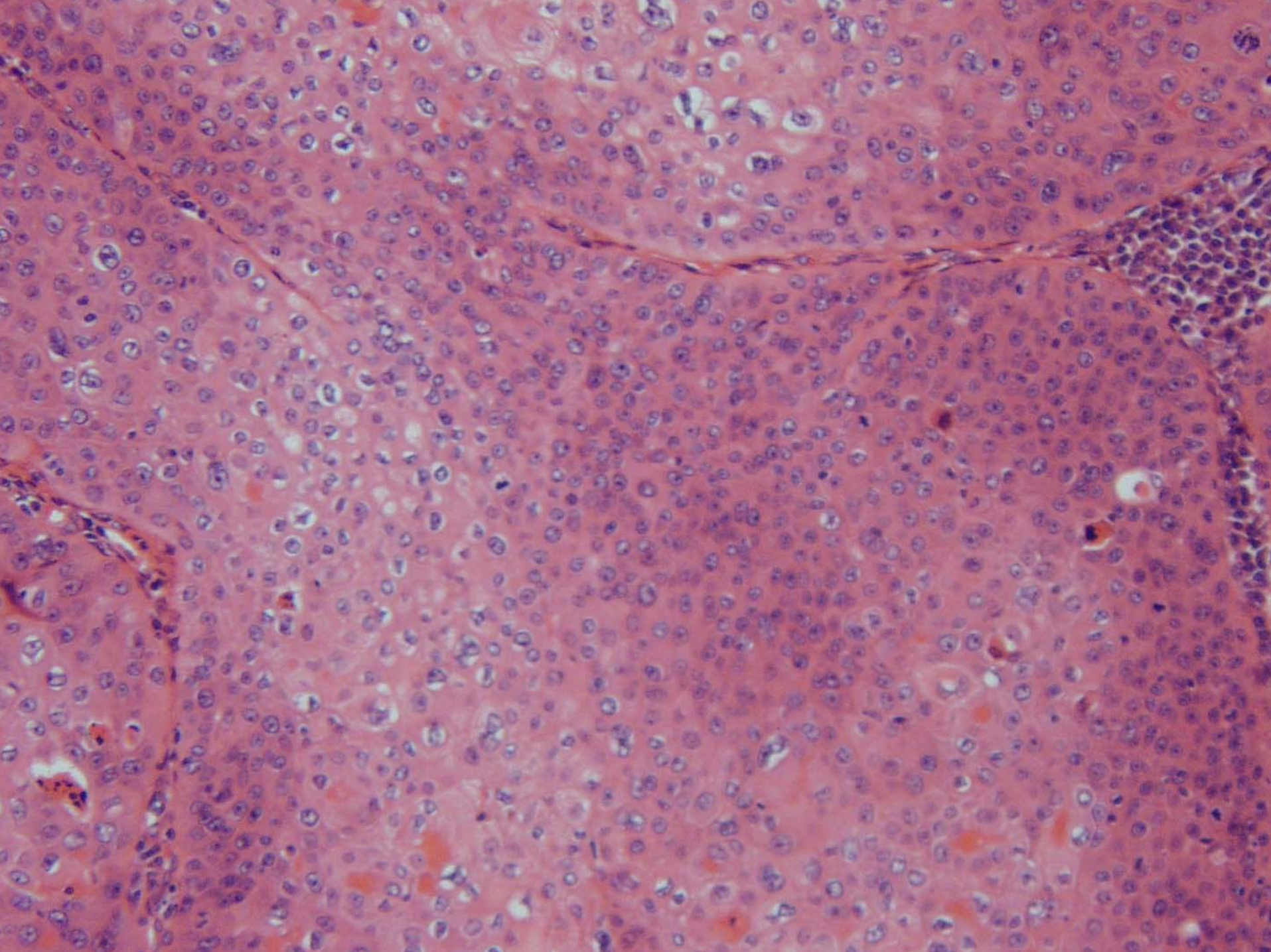


# Papillary SCCA

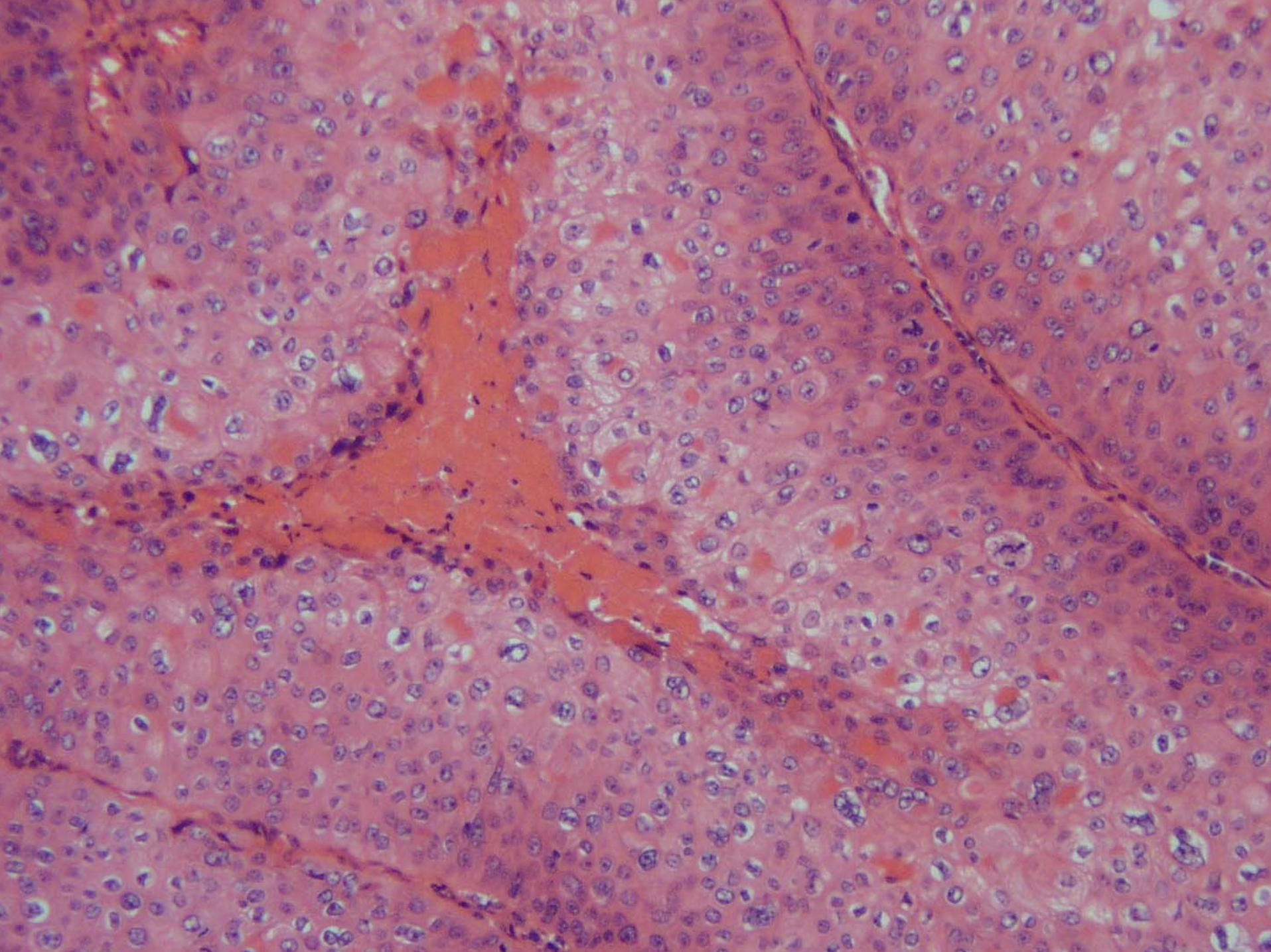
- Exophytic verrucous growth
- High grade nuclear changes
- Prominent papillary growth pattern with several layers of notably atypical squamous epithelium overlying a fibro-vascular core in both cases
  - Mitoses were frequent
  - Lack deep invasion although focal invasion of the stalk may occur
  - These tumors were histologically distinct from verrucous carcinoma, verrucous Bowen's disease, and previously described adnexal carcinomas. The lack of deep invasion and the absence of local recurrence or metastatic disease after 18 months follow-up suggest that this histologic variant is a low-grade malignancy, although study of more cases and longer follow-up will be necessary to accurately assess the biology of this papillary variant of SCC.



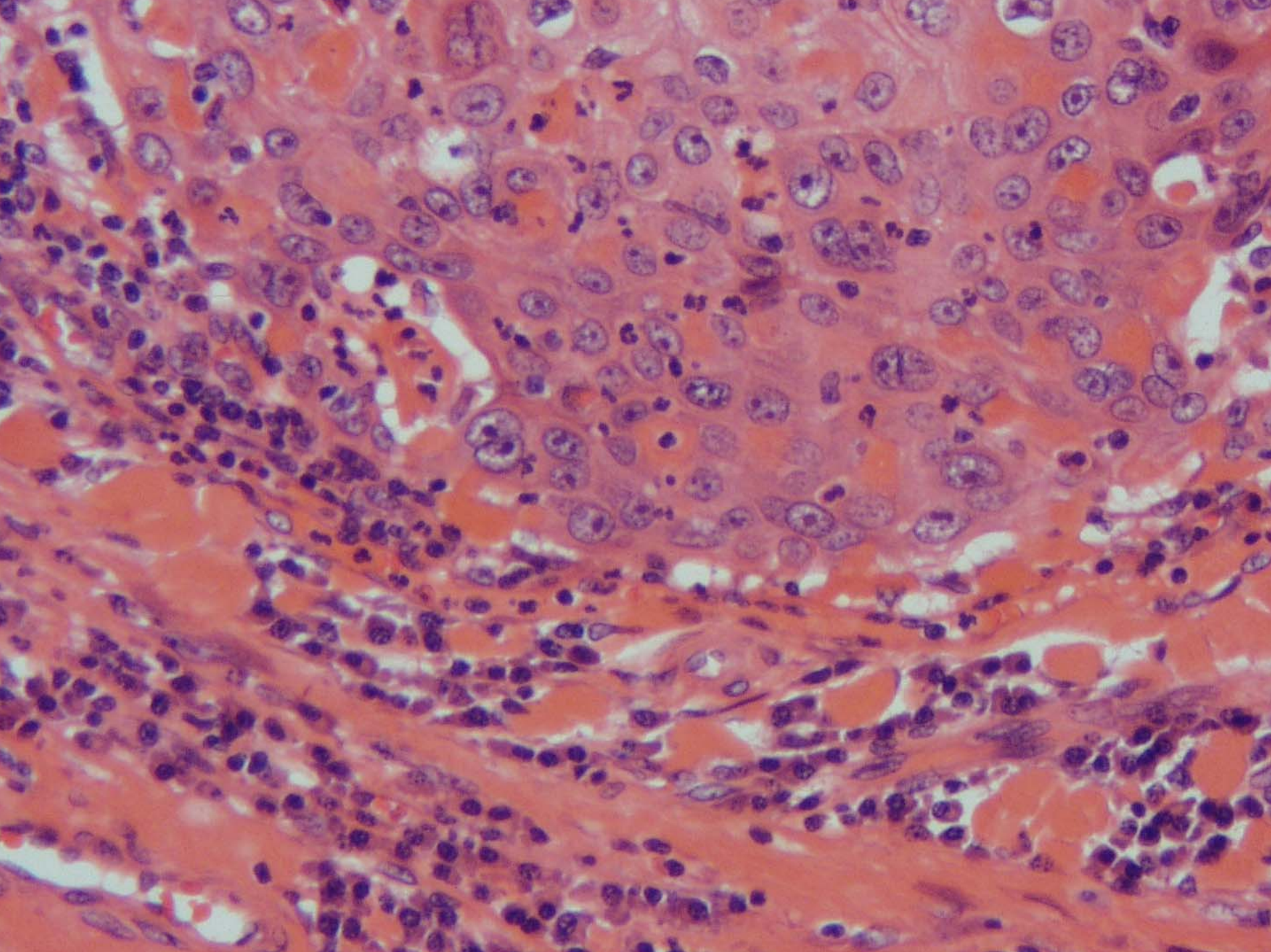




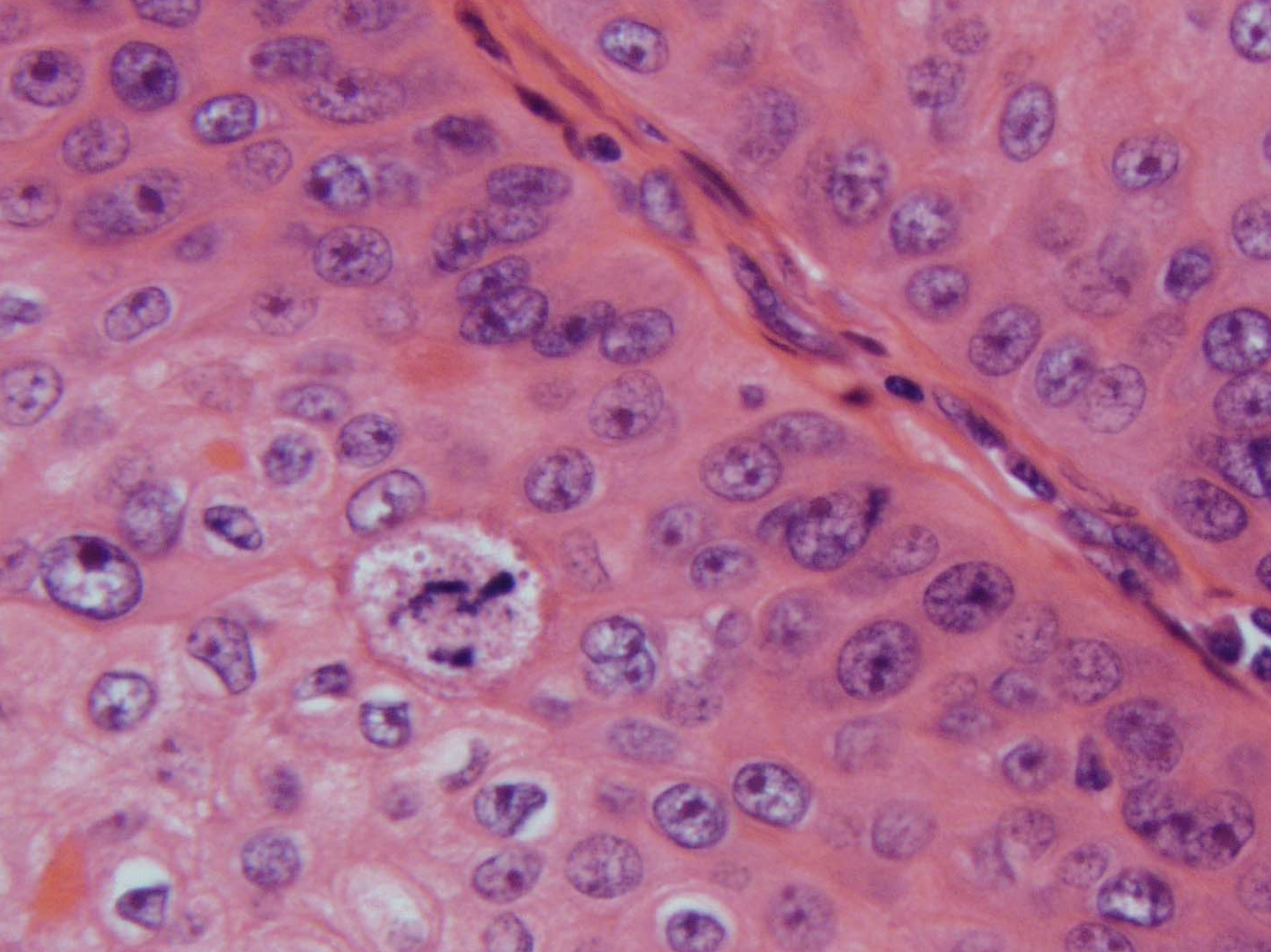














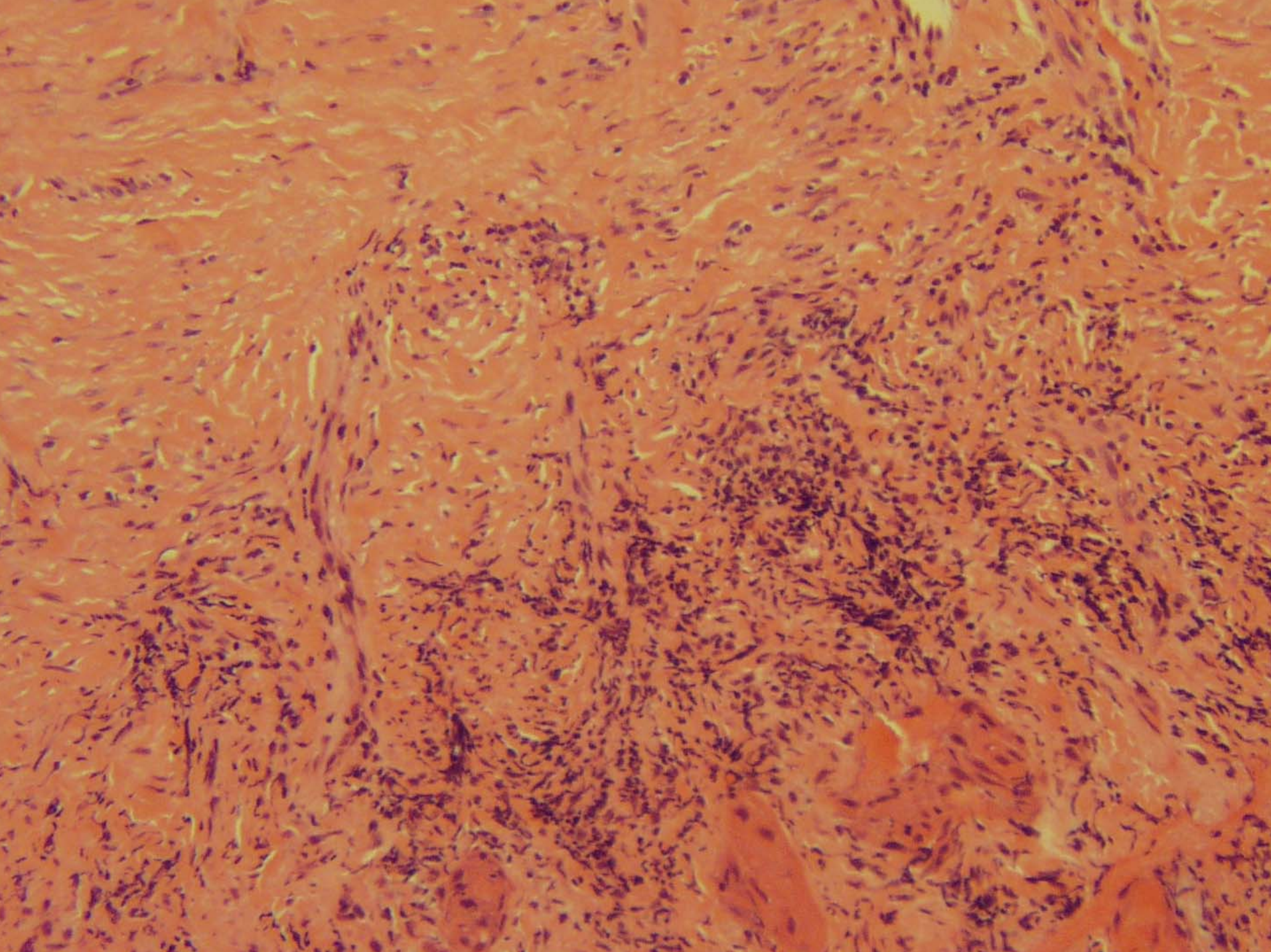
# Aggressive Variants

- Marjolin's Ulcer
- Acantholytic
- Sarcomatoid (Adenoid, Pseudovascular)
- Invasive Bowenoid
- Adenosquamous

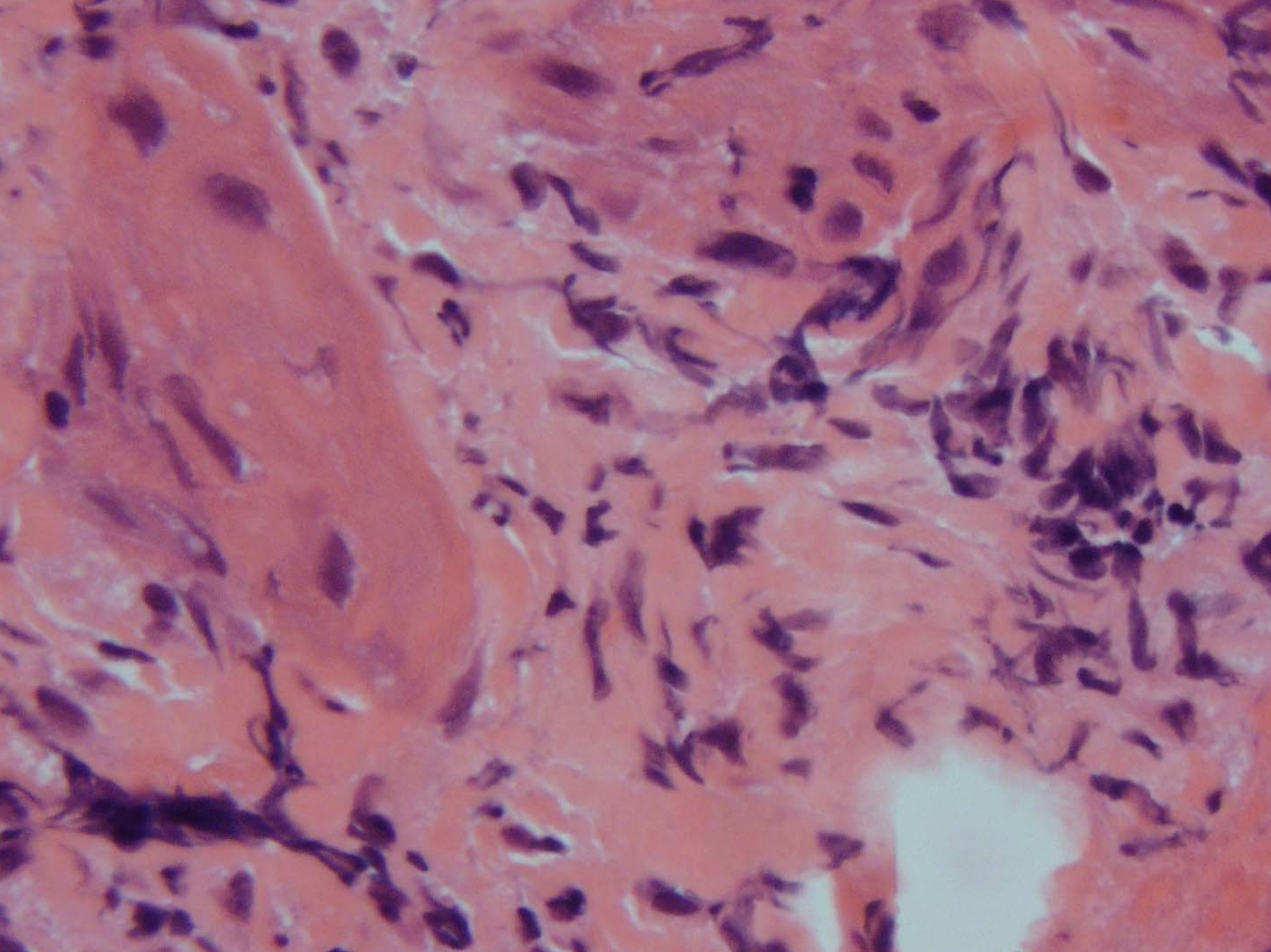
# Marjolin's Ulcer

- Aggressive form of squamous cell carcinoma that arises from sites of chronic injury, scars, burns, or irradiation sites





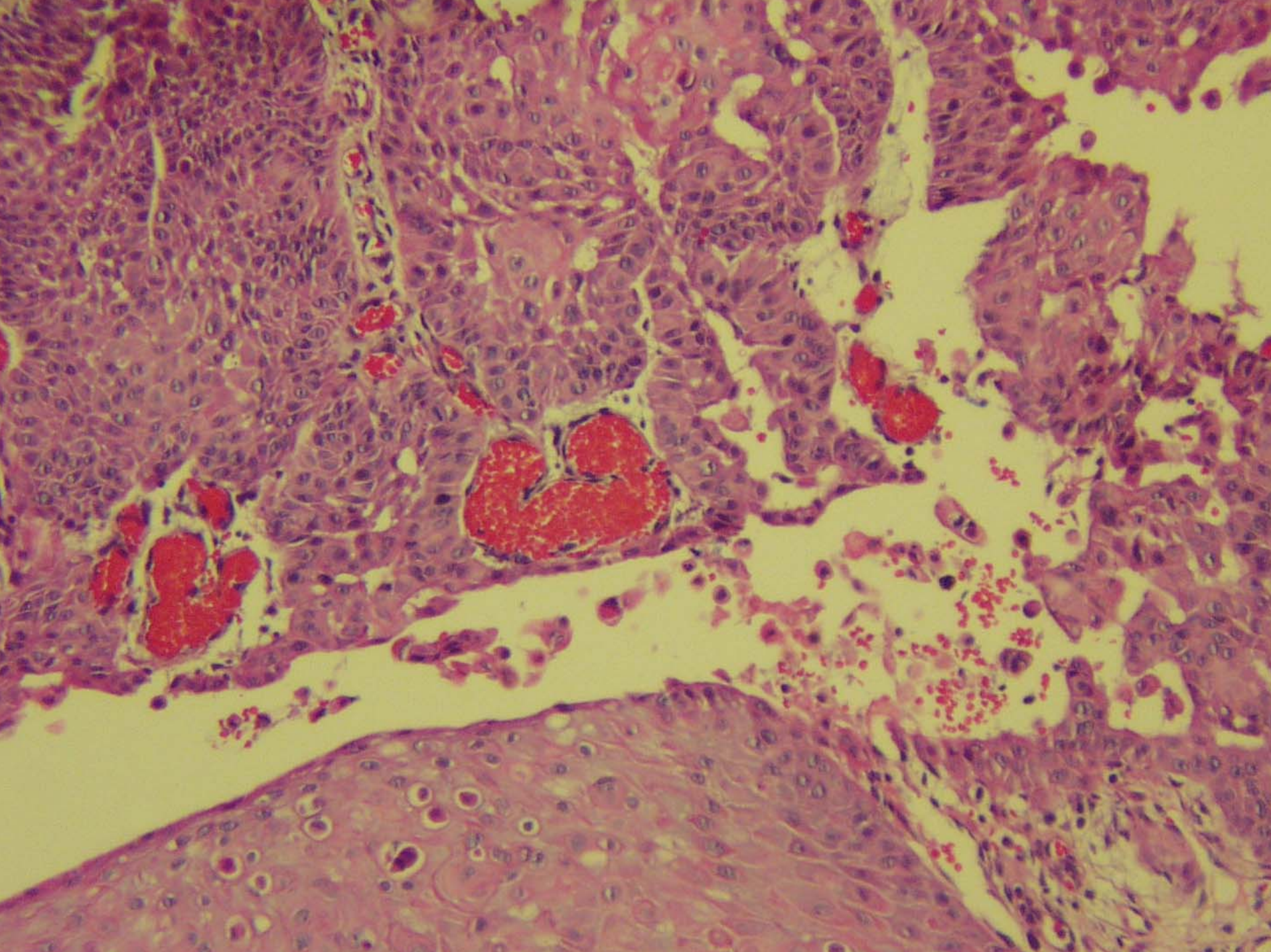




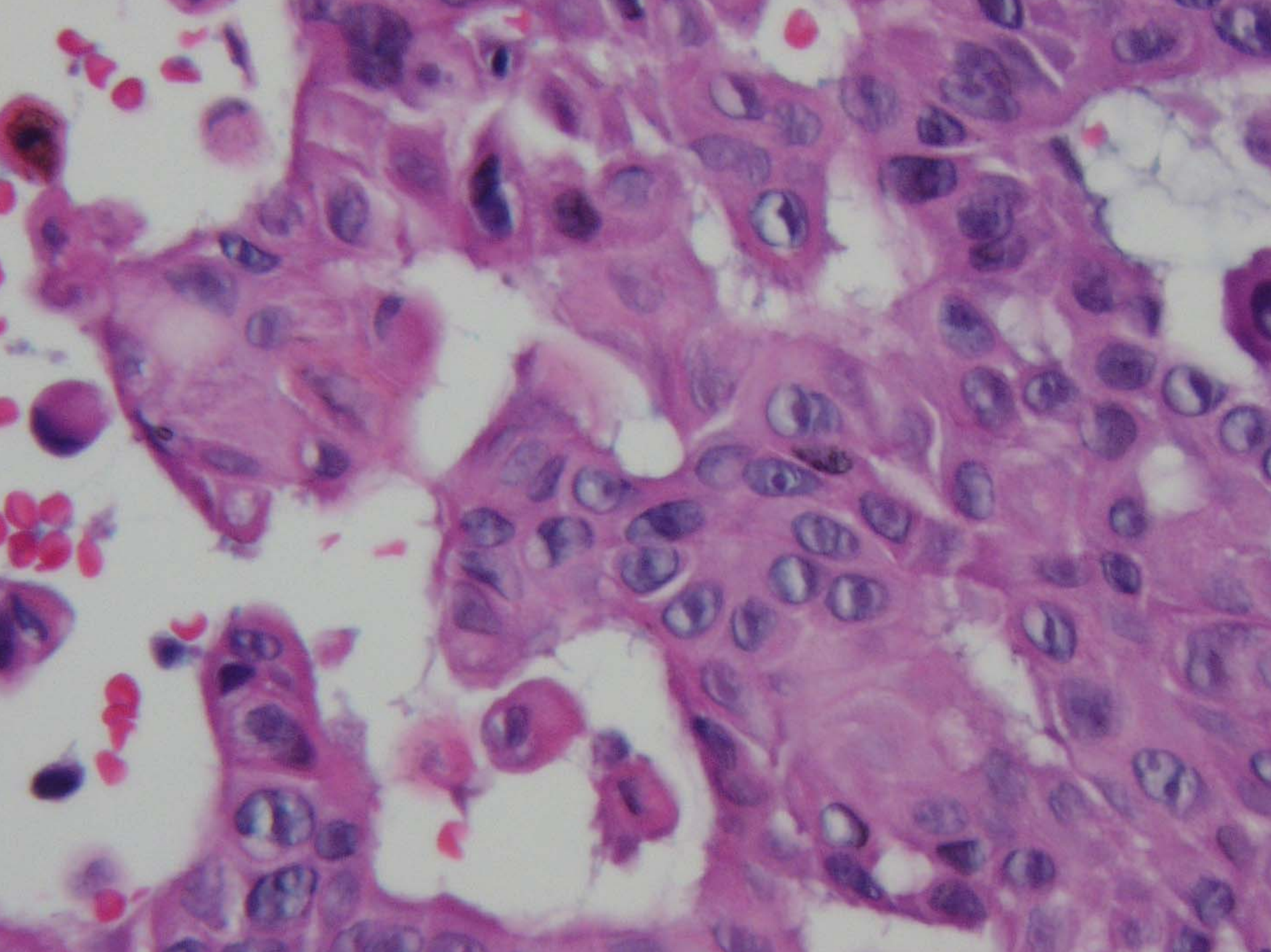


# Acantholytic SCCA (Pseudovascular)

- Usually present as ulcer on the head and neck of men in 5-6th decade
- Has been associated with recurrences following radiation therapy
- Pseudoglandular acantholytic changes
  - Interanastomosing cordlike arrays of polygonal or flattened tumor cells, with internal pseudolumina that contained detached tumor cells
  - Connection between the dermal neoplasm and the epidermis was apparent in three cases, but it was focal
  - Erythrocytes were seen in pseudovascular spaces
- IPOX
  - Positive for CK and EMA
  - Negative for FVIII and CD34



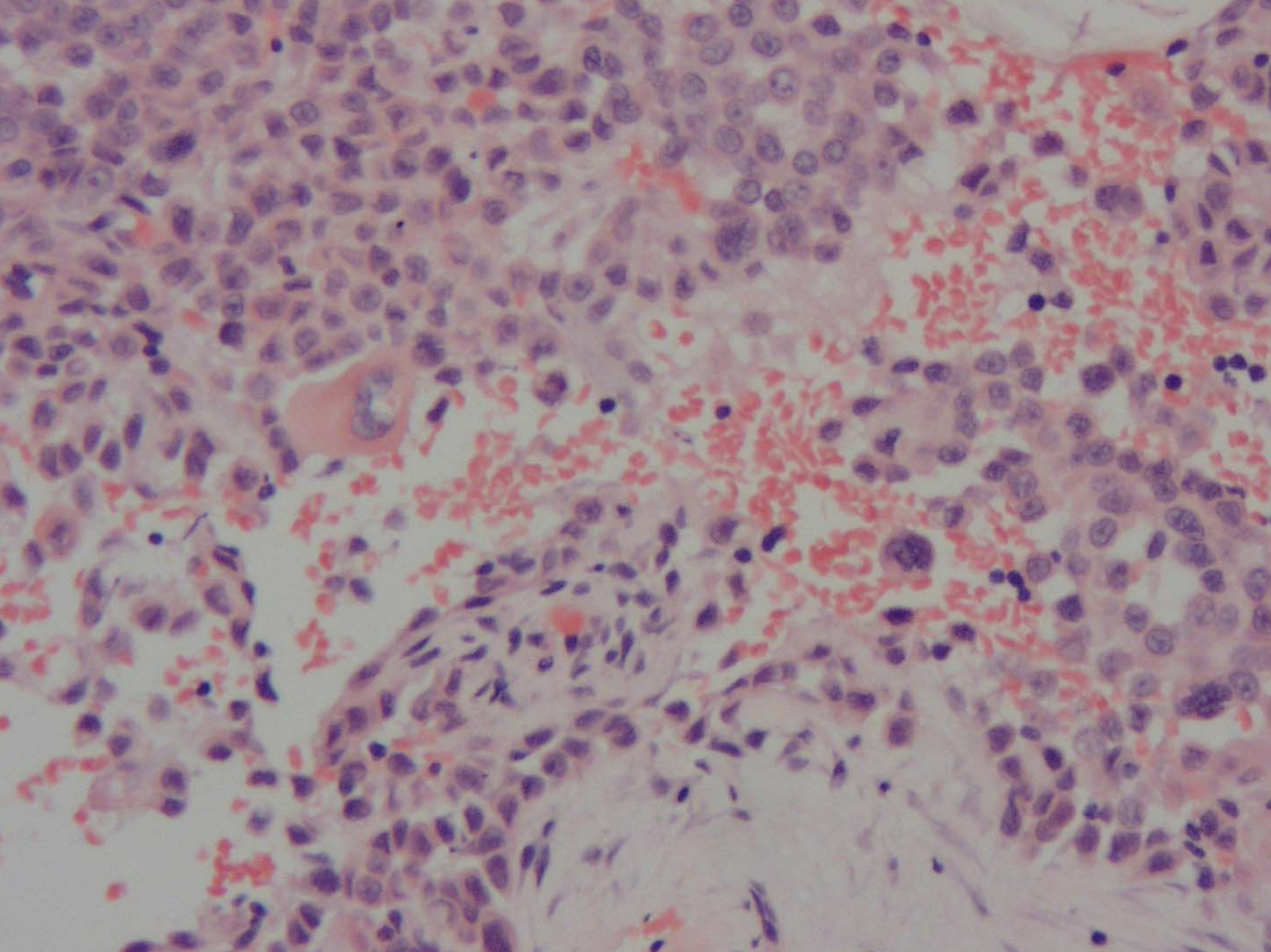




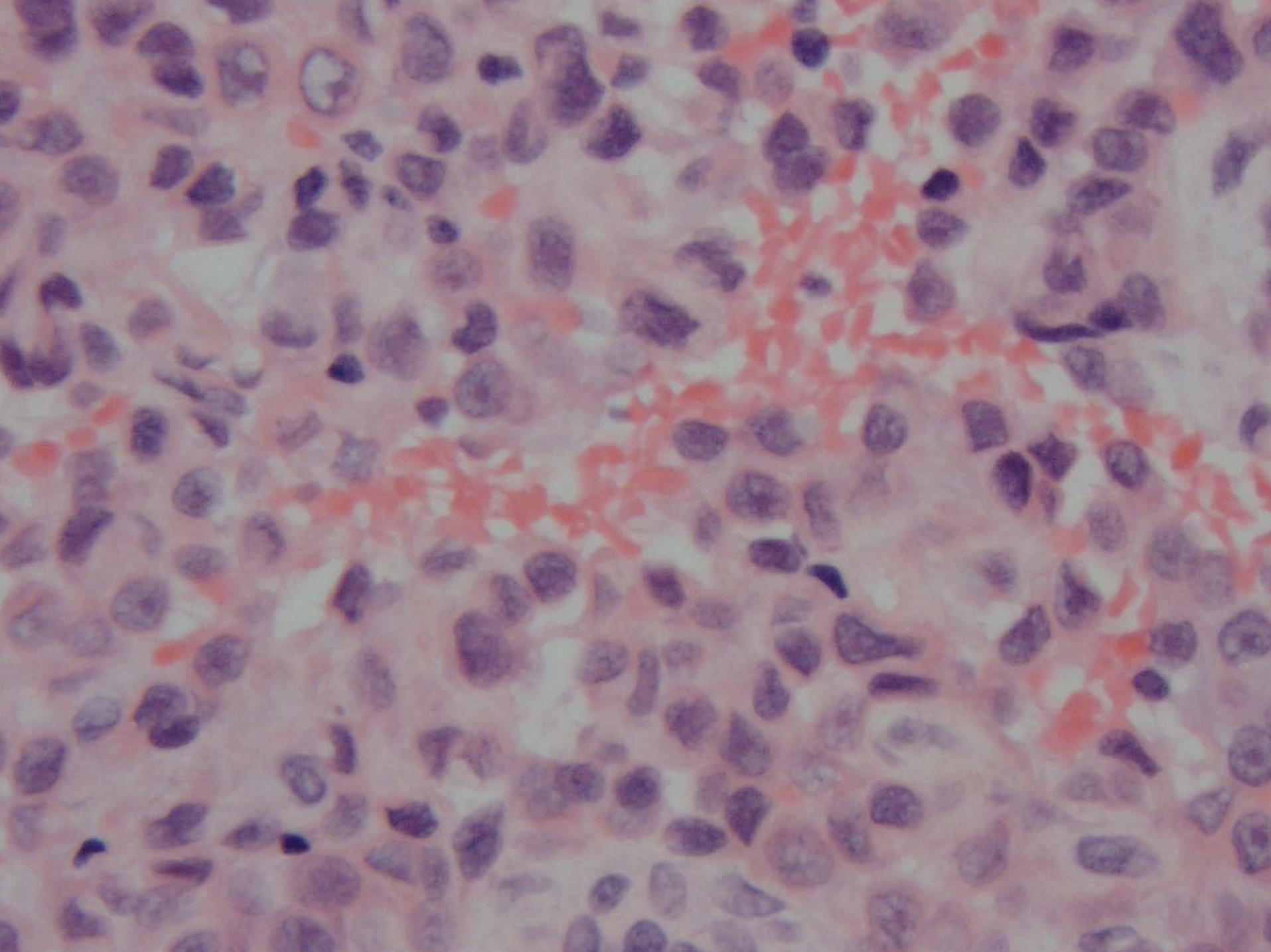
# Poorly Differentiated/Sarcomatoid SCCA

- Spindle cell
- Desmoplastic
- Carcinosarcoma





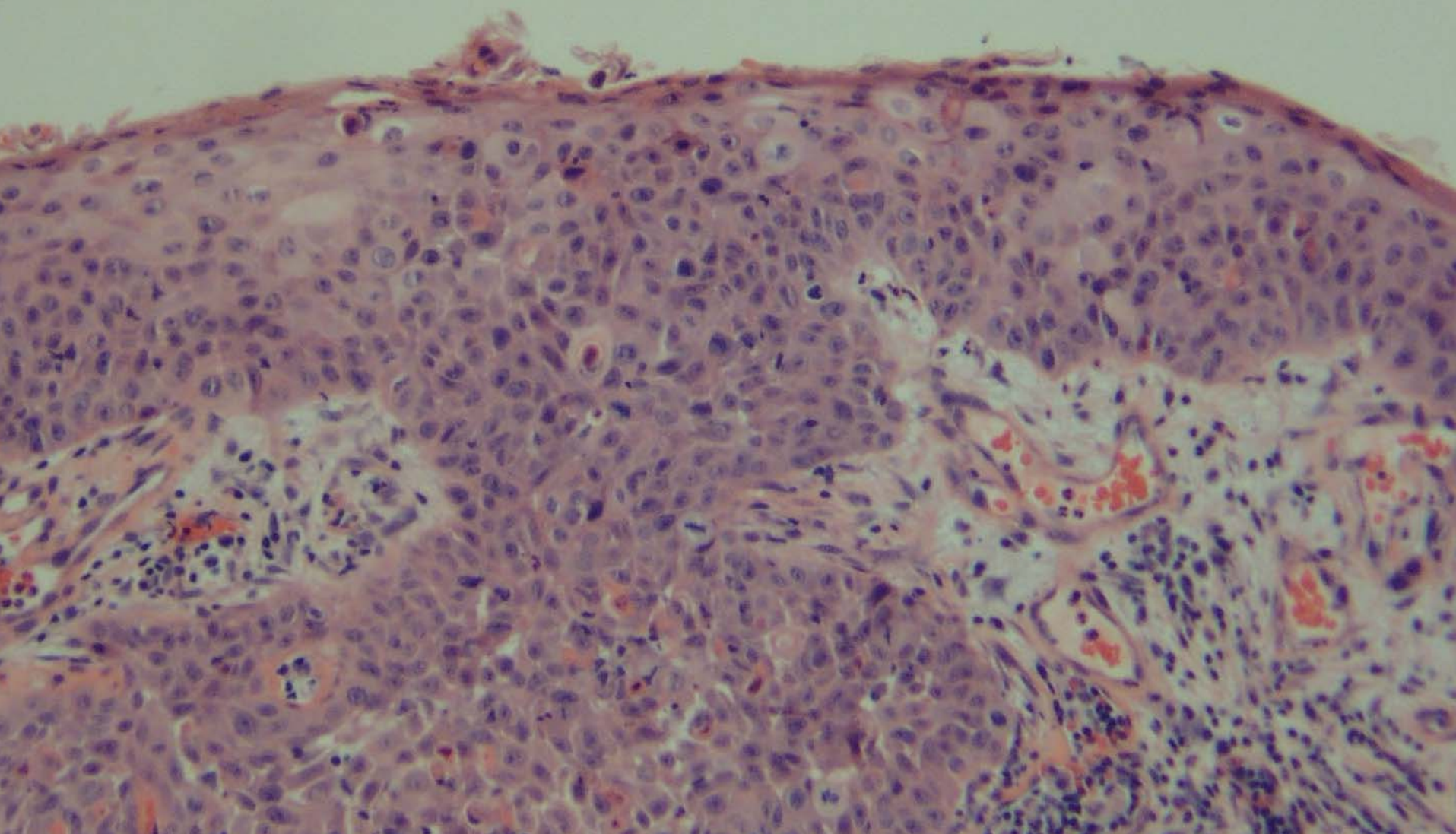




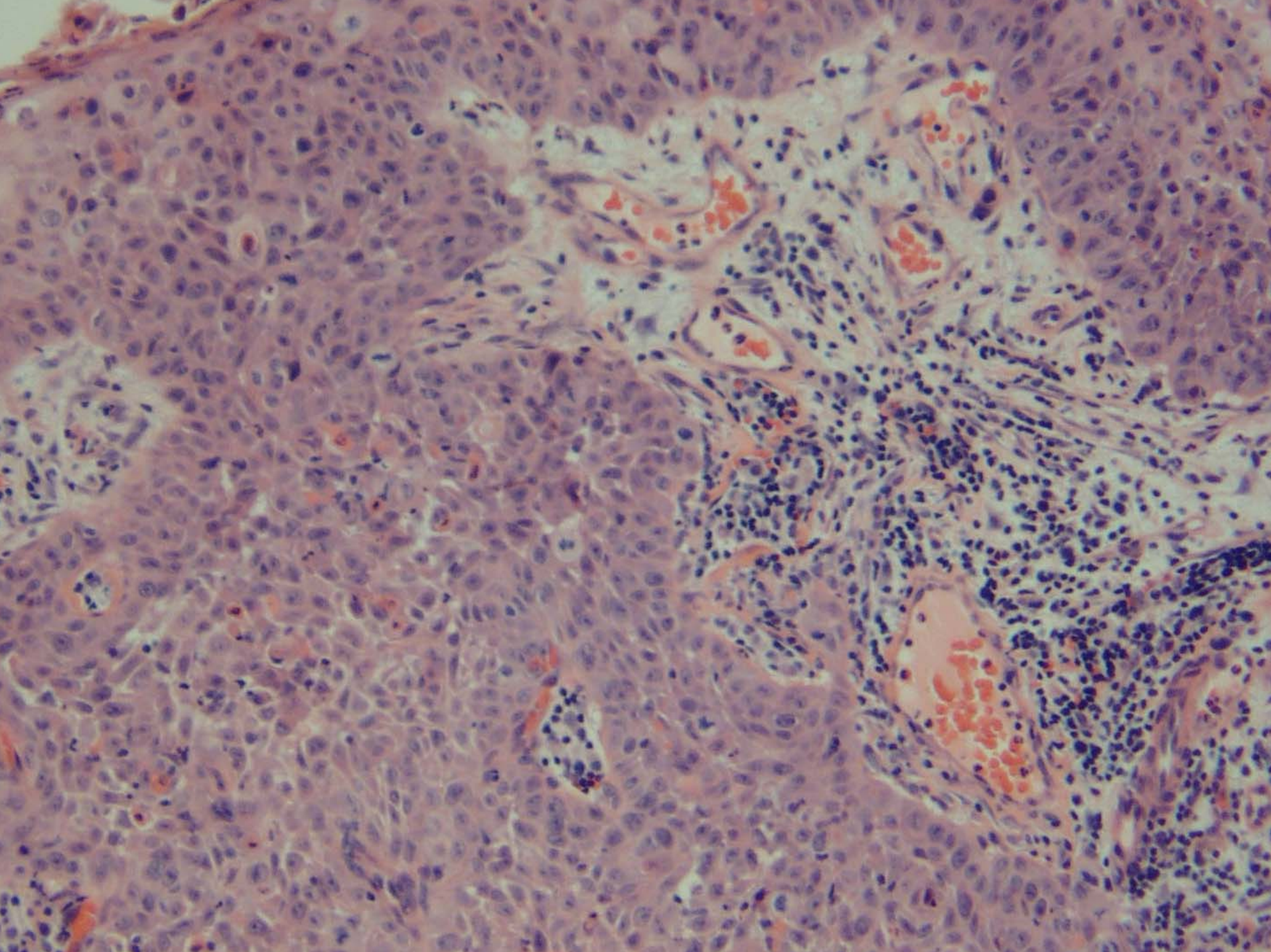


# Bowenoid SCCA

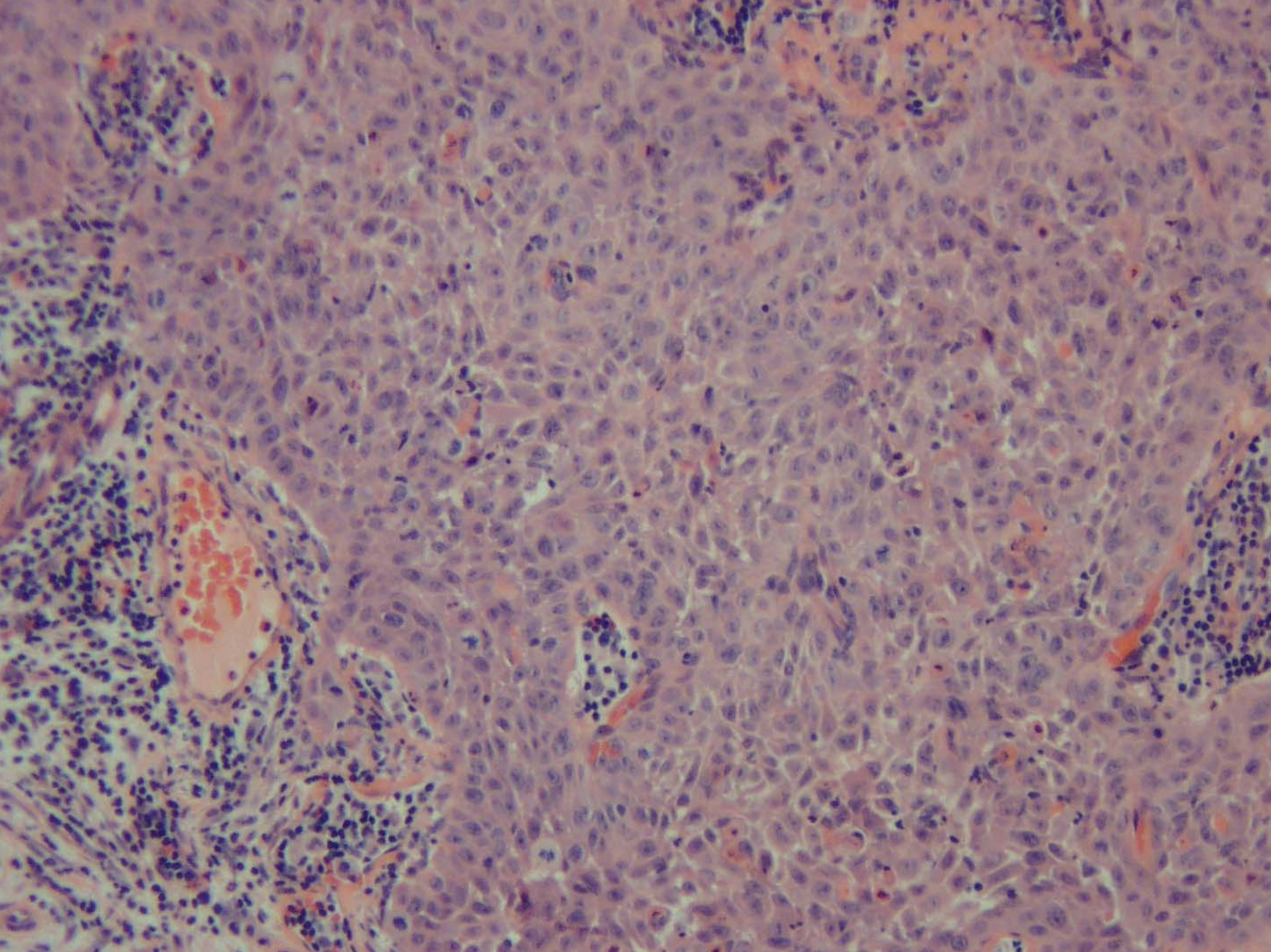
- In situ carcinoma with neoplastic keratinocytes invade the dermis
- HPV 2 associated in extragenital lesions  
HPV 16 most common in genital lesions



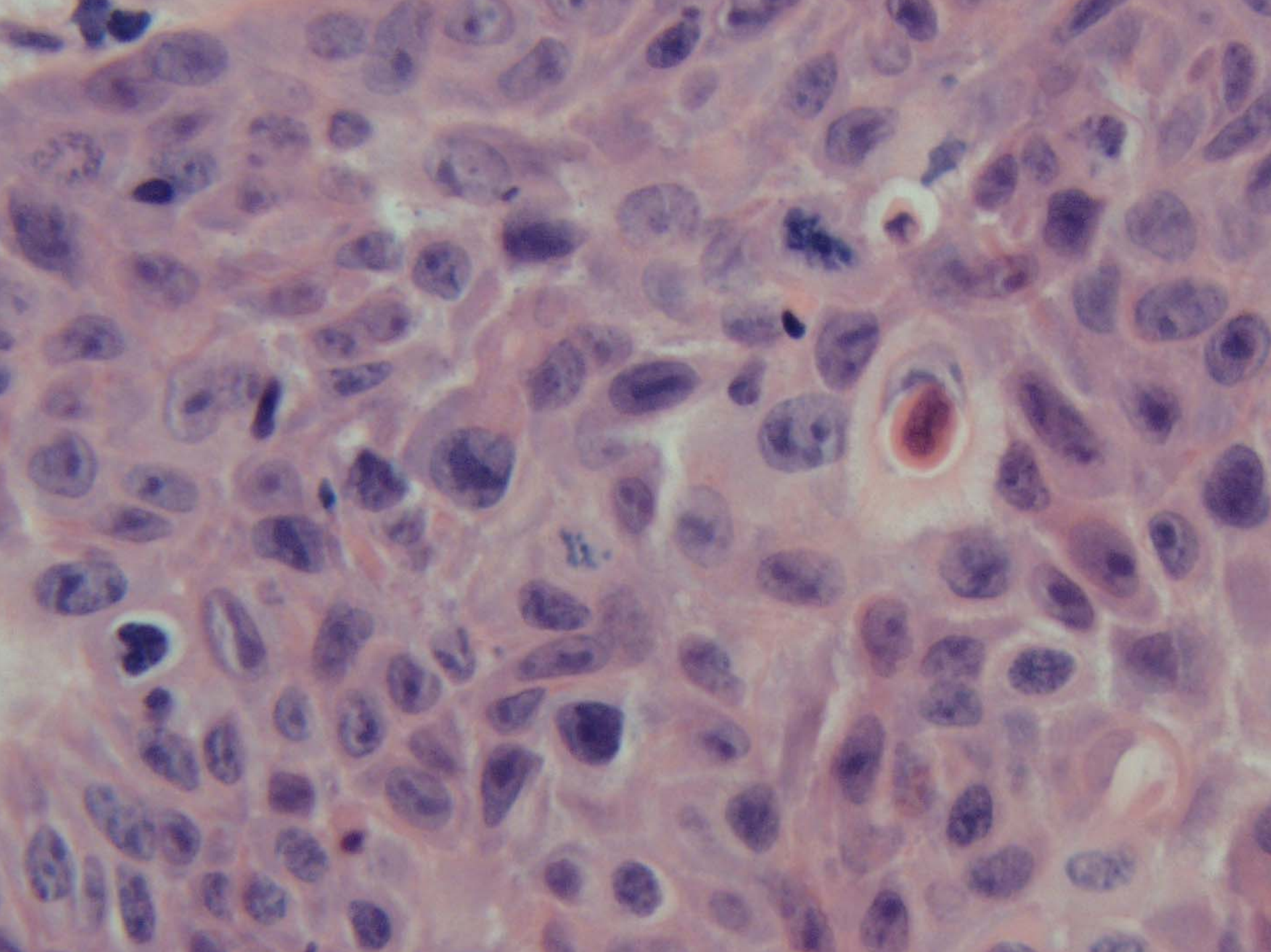












# Adenosquamous CA

- Rare
  - Less than 15 well-documented
  - Term such as mucoepidermoid carcinomas and acantolytic squamous cell carcinomas have been used
- Two components
  - Conventional squamous cell carcinoma merging with adenocarcinoma
- Prognosis
  - Local recurrence with later lymph node metastases
  - No evidence of disease 8 months later
- Always exclude metastases to skin
- Journal of Cutaneous Pathology 2001;28 (10), 542-545



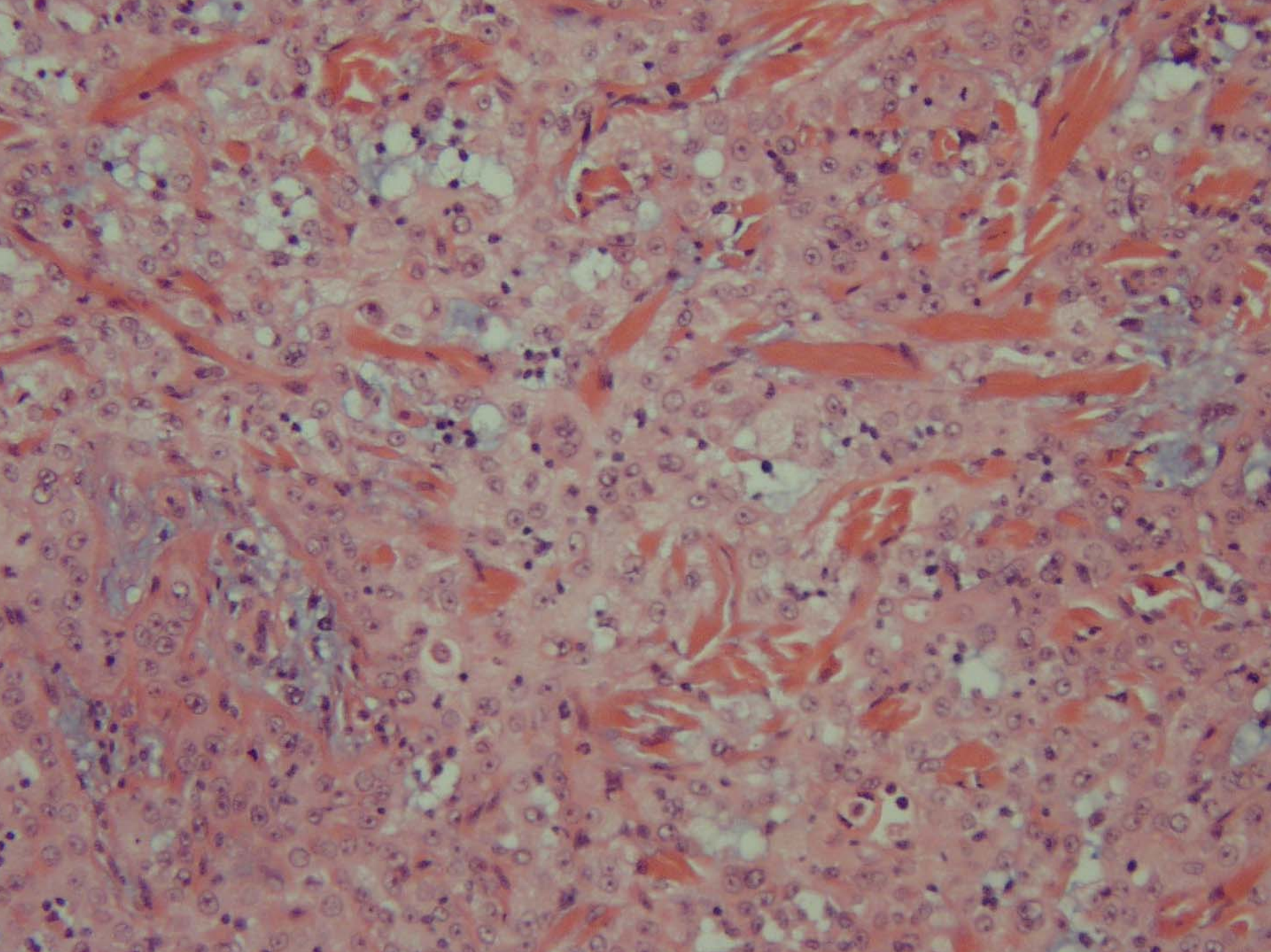
# Unusual Variants

- Mucinous
- Pigmented

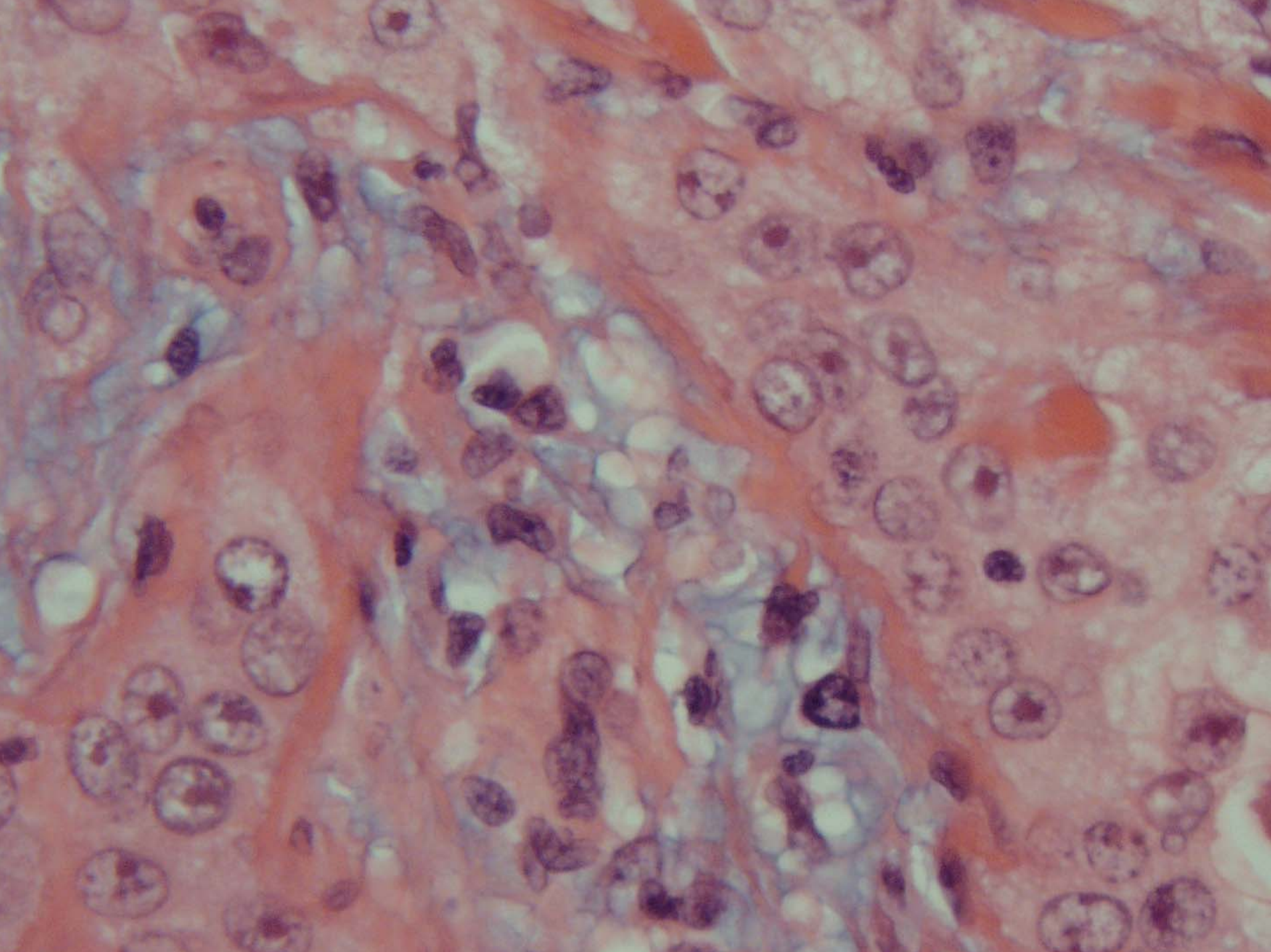
# Mucinous SCCA

- Mucinous change
- Differentiate from basosquamous CA
- Rule out metastatic adenocarcinoma

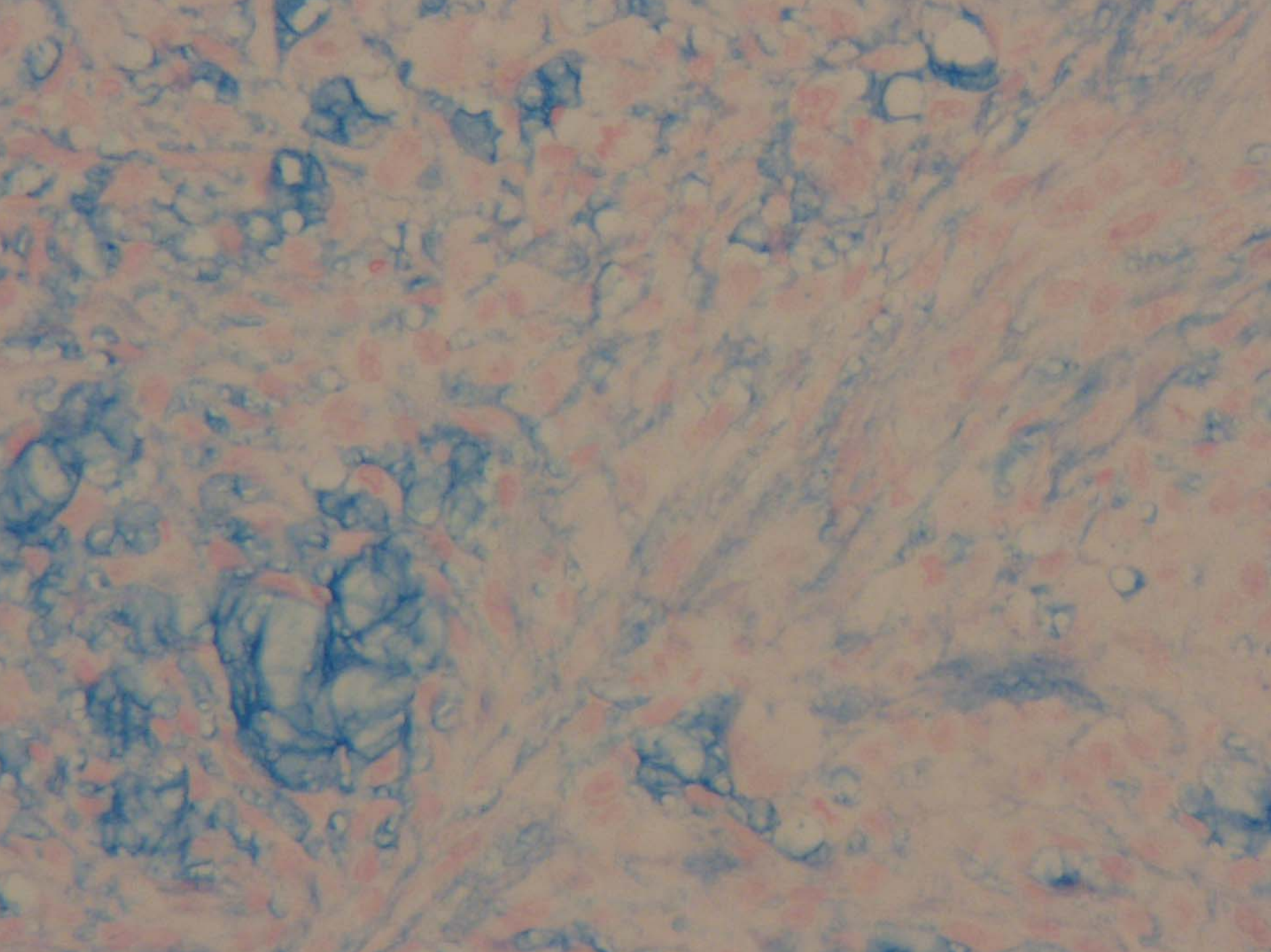












# Pigmented SCCA

- Rare
  - 5/46,791 archived cases
  - Relative frequency of approximately 0.01%
- Rapidly growing crusted papule on actinic damaged skin of the face
- Mixture of keratinized squamous cells and melanin-producing dendritic melanocytes.
- IPOX
  - Squamous cells stained for epithelial membrane antigen, low and high molecular keratins
  - Melanocytes stained for S-100 and HMB-45
  - Matched series of 31 SCCs failed to show intratumoral melanocytes.



# Treatment

- Surgery
- MOHS
- Radiation
- Sentinel lymph node excision

# Metastasis

<b>Risk Factor</b>	<b>Percentage</b>
Acantholytic histology	2-19%
Arising in Bowen's disease	2-5%
Non-sun exposed skin	2-3%
Lip	2-16%
Arising in Marjolin's ulcer	10-30%
Perineum and penis	30-80%



# Survival

- Estimated 1200 deaths a year occur from basal cell and squamous cell carcinomas
  - Majority occurring with Squamous cell carcinomas
- Survival 3 Years
  - 98% if tumor <3.5 mm in depth
  - 84% >3.5 mm in depth

# References

J Eur Acad Dermatol Venereol 1998;11:37-44

J Am Acad Dermatol 1992;26:976-990

J Dermatol Surg Oncol 1982;8:589-600

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