

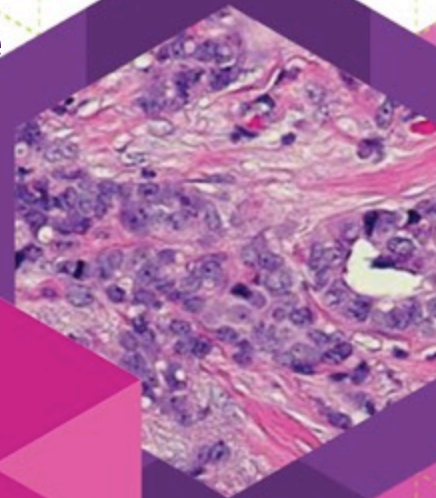
**CS05 NEW DEVELOPMENTS IN  
GASTROINTESTINAL PATHOLOGY-GIPS  
FUNNY FORMS OF ESOPHAGITIS: BEYOND  
GERD AND EOSINOPHILIC ESOPHAGITIS**

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***IN THE PAST 12 MONTHS, I HAVE NOT  
HAD A SIGNIFICANT FINANCIAL  
INTEREST OR OTHER RELATIONSHIP  
WITH THE MANUFACTURER(S) OF THE  
PRODUCT(S) OR PROVIDER(S) OF THE  
SERVICE(S) THAT WILL BE DISCUSSED IN  
MY PRESENTATION.***

## CASE 1

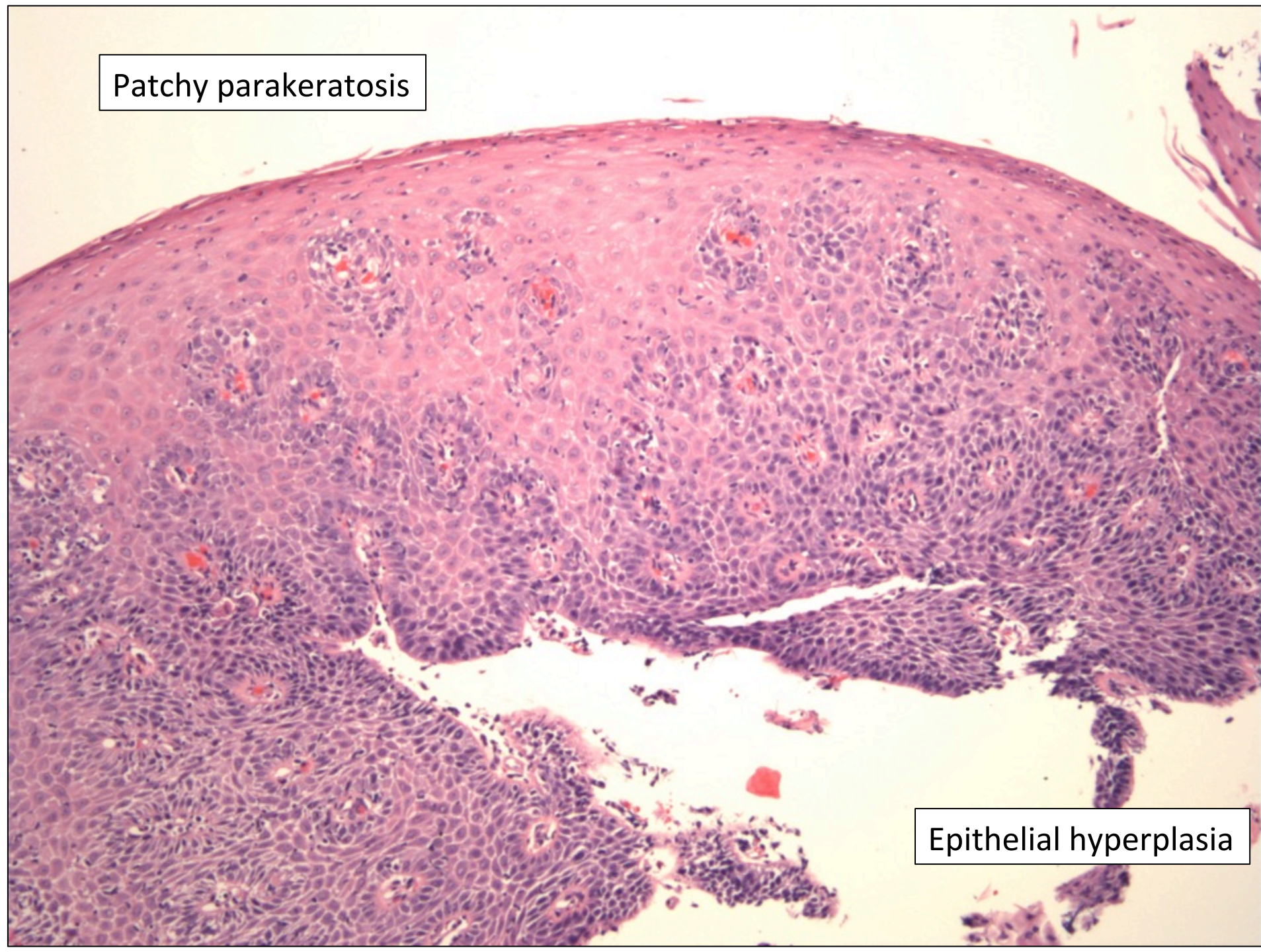
- 30-year old woman with dysphagia
- History of psoriasis



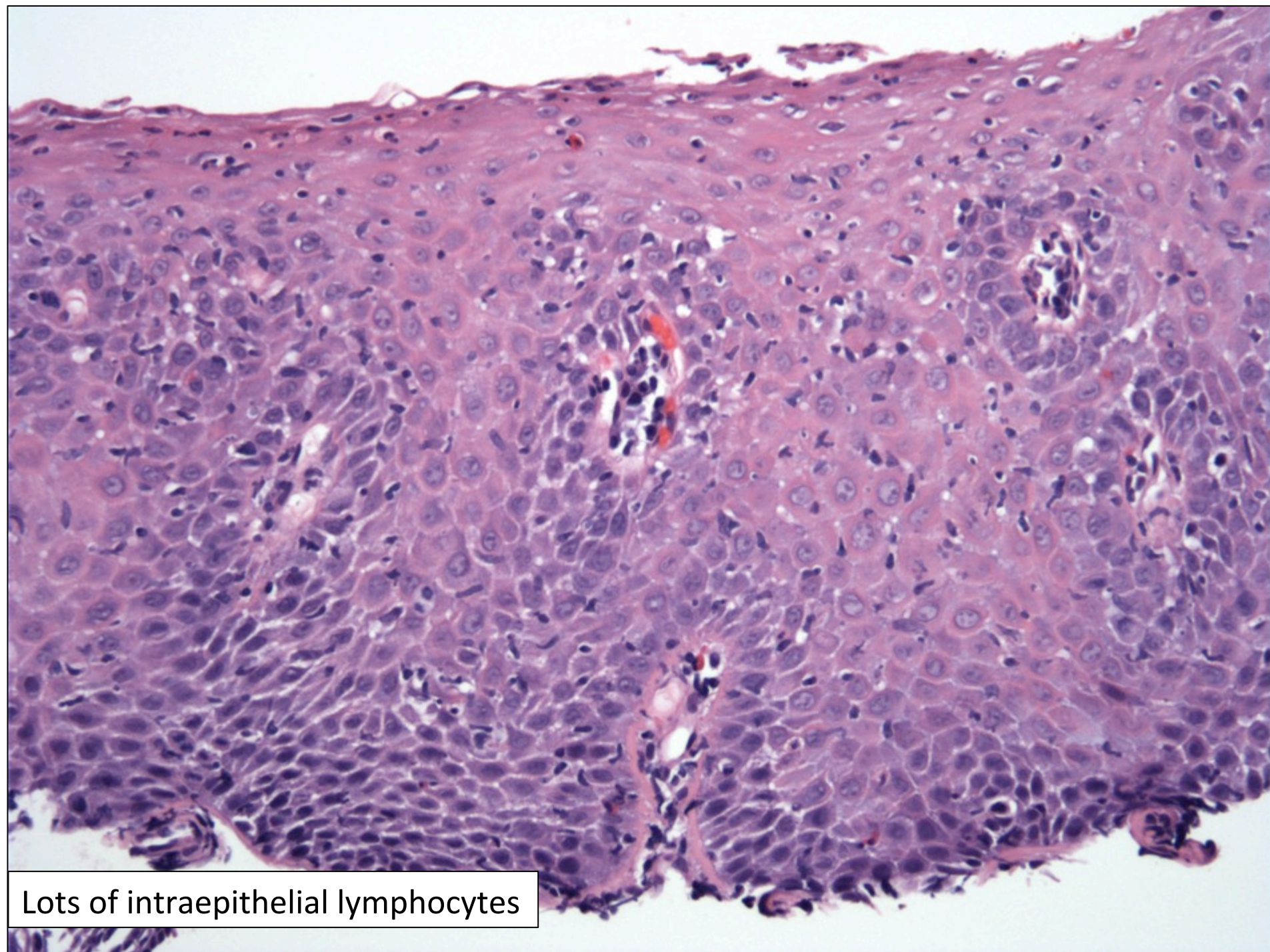


Patchy parakeratosis

Epithelial hyperplasia

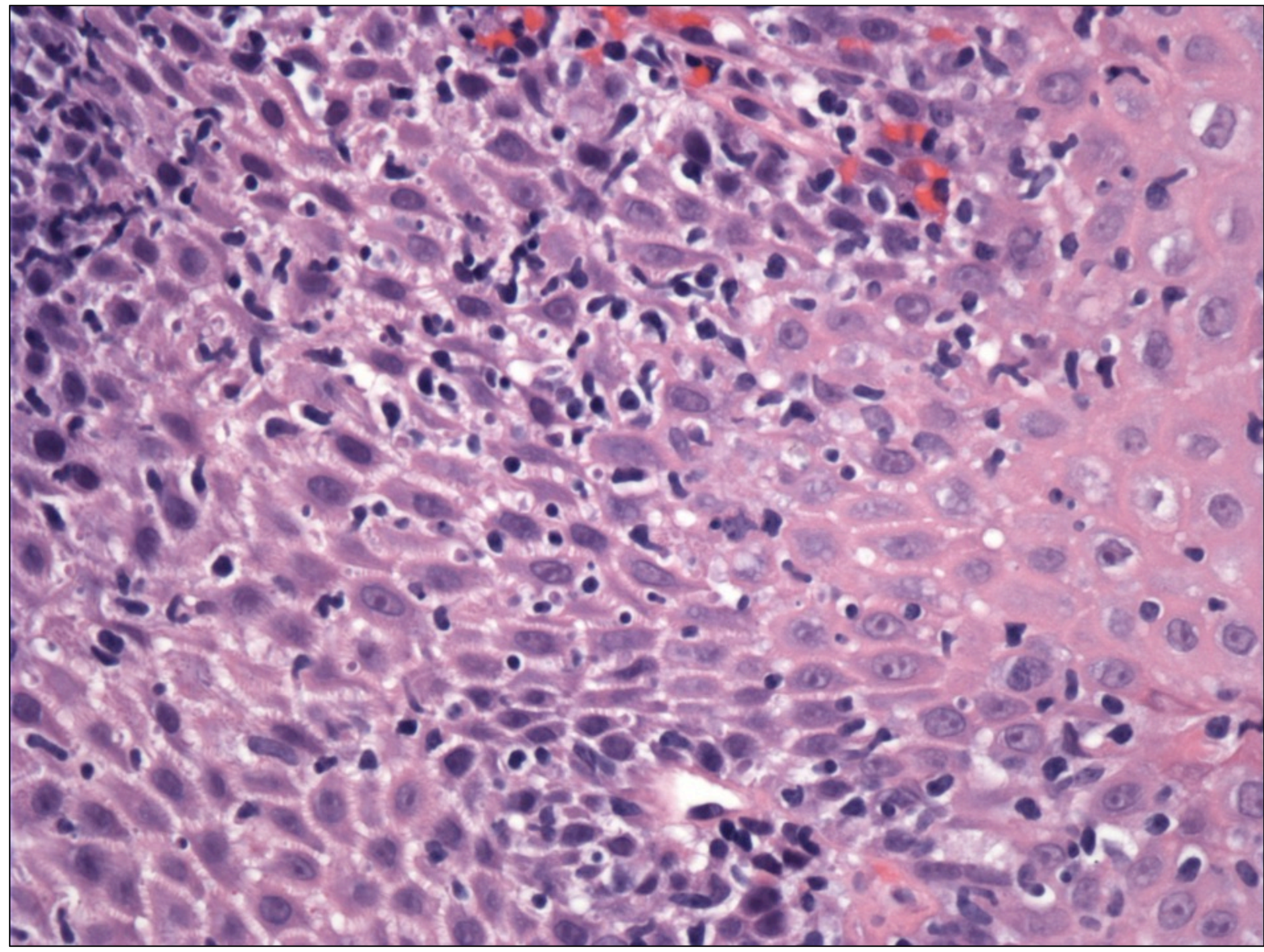






Lots of intraepithelial lymphocytes









## OUTCOME

- Case shown to dermatopathology
- Psoriasis of the esophagus
- The esophagus is lined by squamous epithelium, but it isn't the skin
- Patterns of cutaneous inflammation generally don't mean the same thing in the esophagus



# LYMPHOCYTIC ESOPHAGITIS

- Increasingly recognized as more patients undergo biopsy of proximal esophagus for eosinophilic esophagitis
  - 80% of cases identified in past 5 years
- Females affected more than males, older adults
- Manifestation of Crohn disease in children
- May be associated with other immune-mediated disorders
- Dysphagia, odynophagia, dysmotility
- Endoscopy
  - 30% normal
  - Plaques, rings, furrows simulating eosinophilic esophagitis
- Histology
  - 20-100 lymphocytes/high-power field
  - Granulocytes should be infrequent, or absent



A histological section of the esophagus stained with hematoxylin and eosin (H&E). The image shows the peripapillary epithelium, which is the layer of cells surrounding the papillae. This area is densely populated with small, dark-staining lymphocytes, indicating an inflammatory response. The underlying connective tissue of the lamina propria also shows some inflammatory cell infiltration. The overall architecture of the esophageal mucosa is visible, with the papillae extending upwards.

Lymphocytes most numerous in peripapillary epithelium

Lymphocytic esophagitis





Mucosal injury with edema and cellular necrosis

This histological image shows a cross-section of esophageal tissue. The upper portion displays the mucosal layer, which is characterized by a thickened, pink-stained area indicating edema and cellular necrosis. Below this, the lamina propria is densely infiltrated with numerous small, dark-staining lymphocytes, a hallmark of lymphocytic esophagitis. The overall architecture shows significant inflammatory damage to the mucosal lining.

Lymphocytic esophagitis





This histological slide shows a section of esophageal tissue. The background is composed of pink-stained connective tissue and muscle fibers. Numerous dark purple, oval-shaped nuclei are scattered throughout, representing lymphocytes. In the center, there is a cluster of cells with dark, hyperchromatic nuclei and some eosinophilic (pink) cytoplasm, identified as dyskeratotic cells. The overall appearance is consistent with lymphocytic esophagitis.

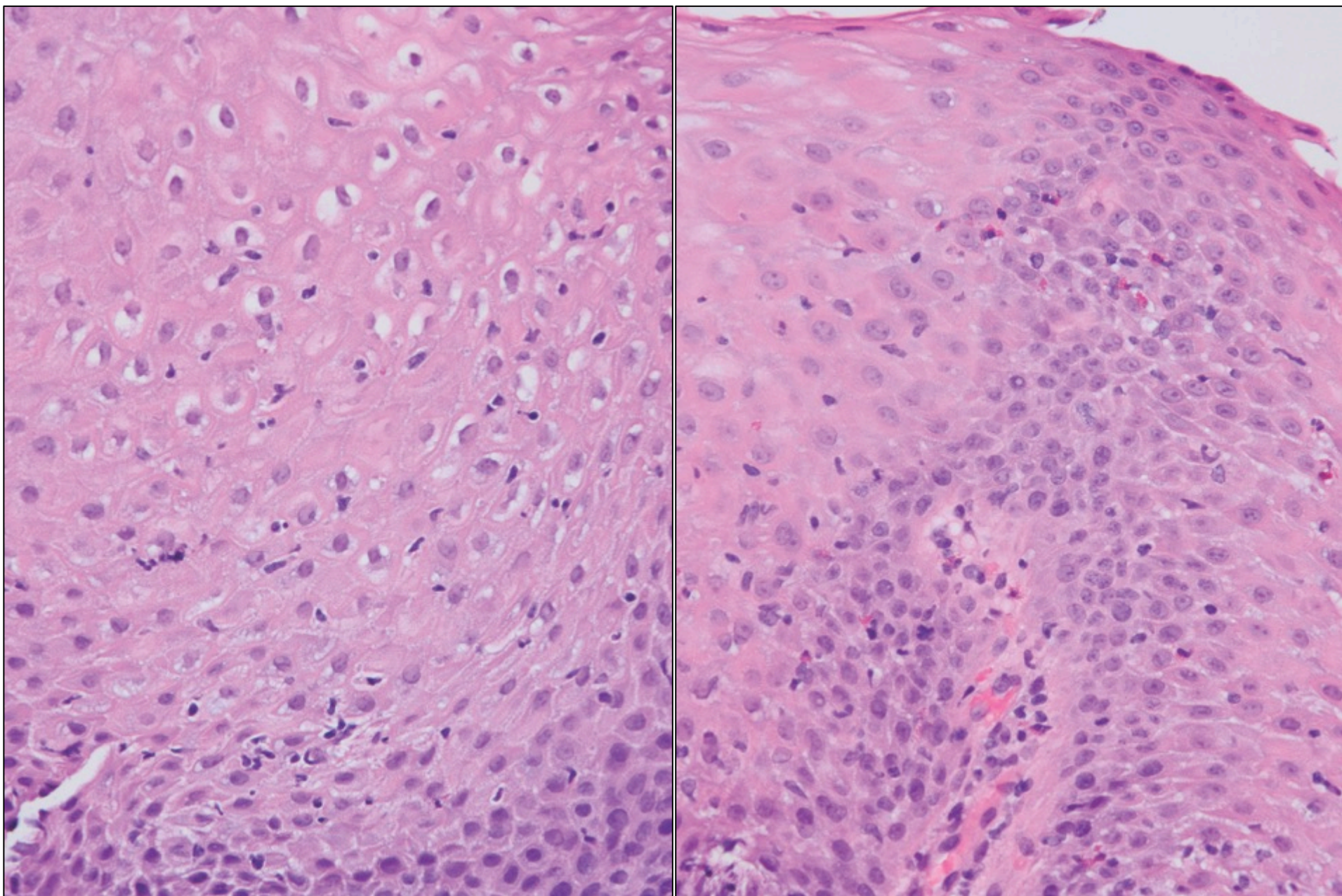
Clustered in epithelium

Dyskeratotic cells

Lymphocytic esophagitis

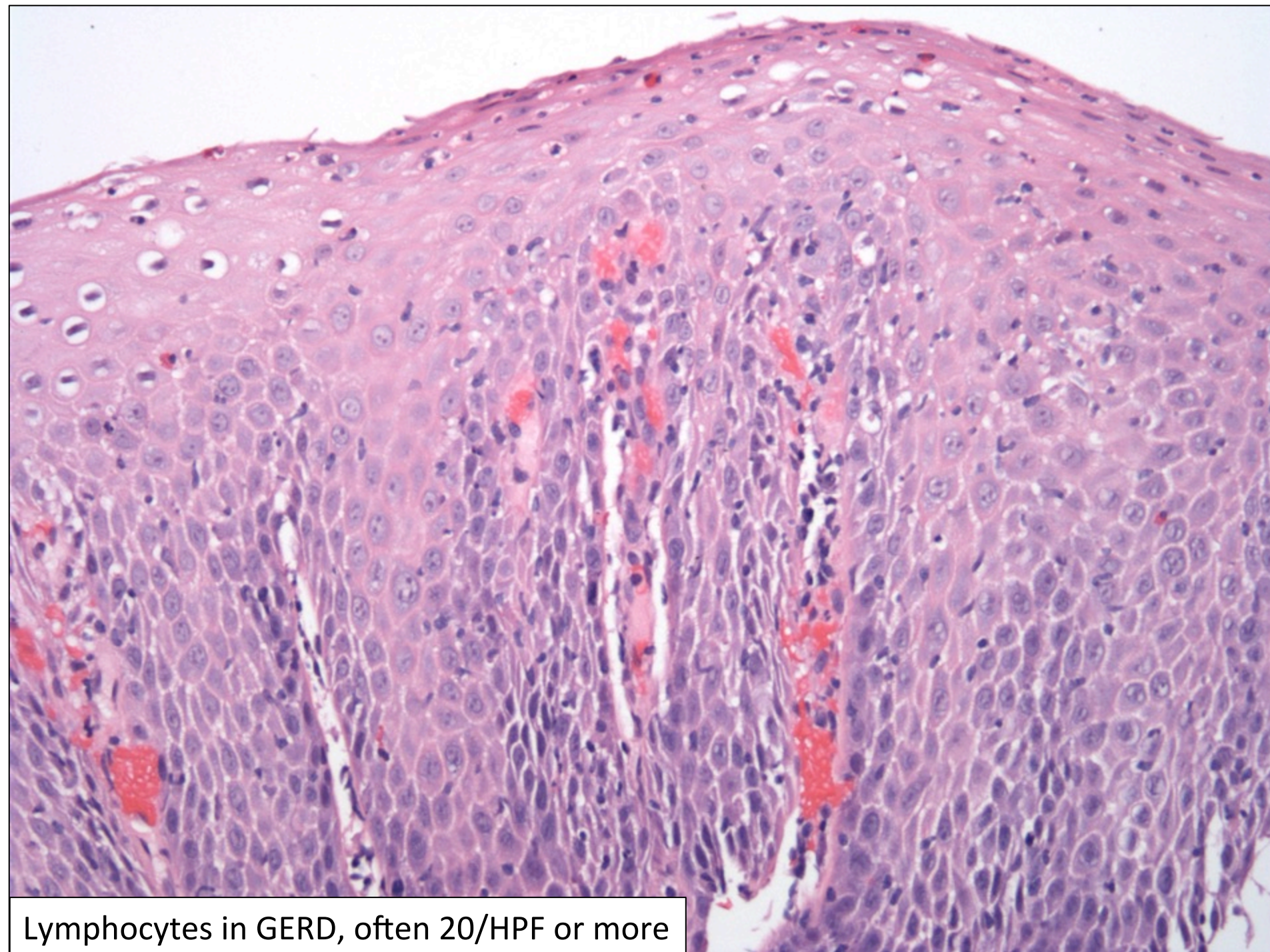


How about this one?



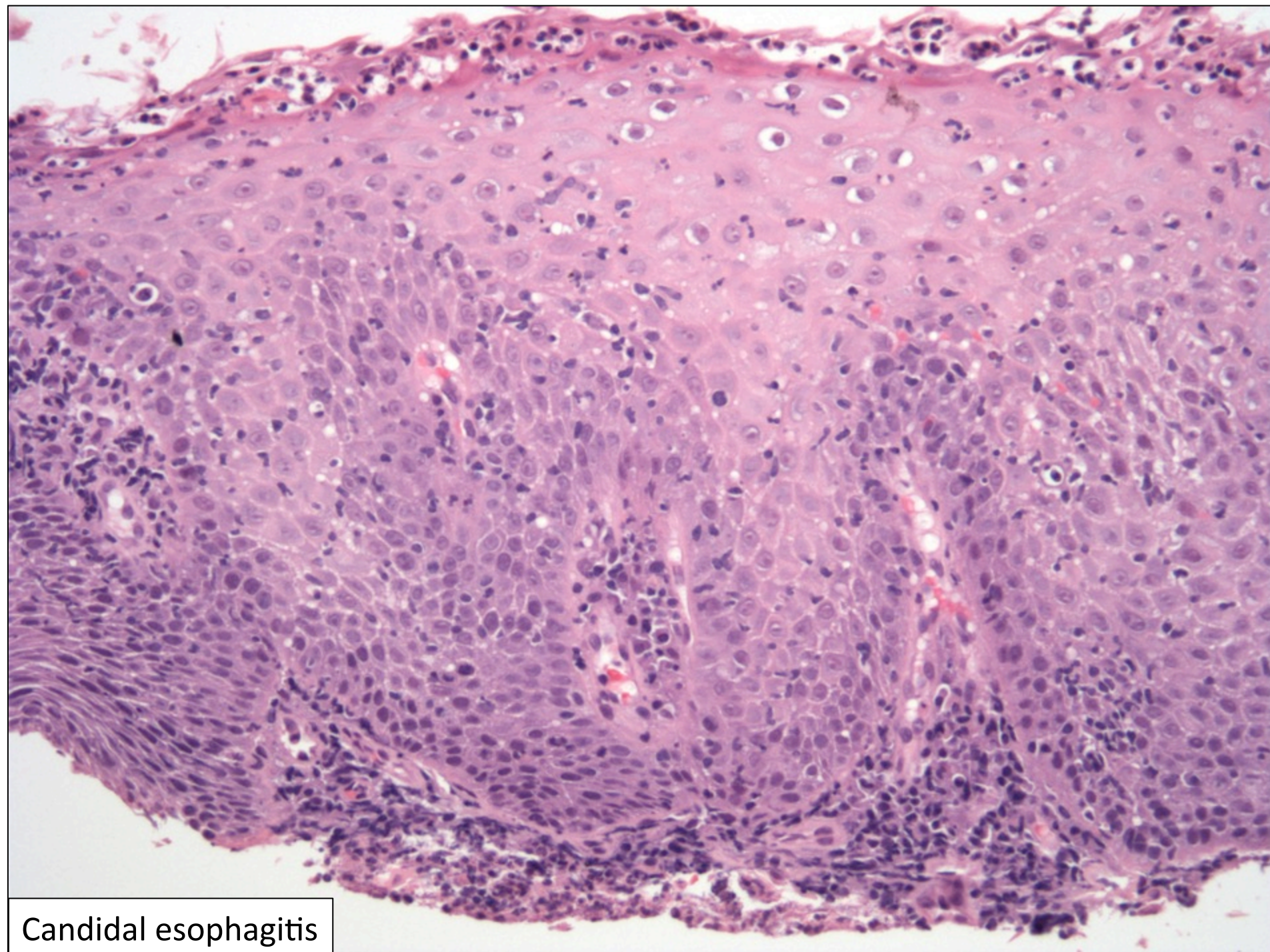
60-year old female with dyspepsia





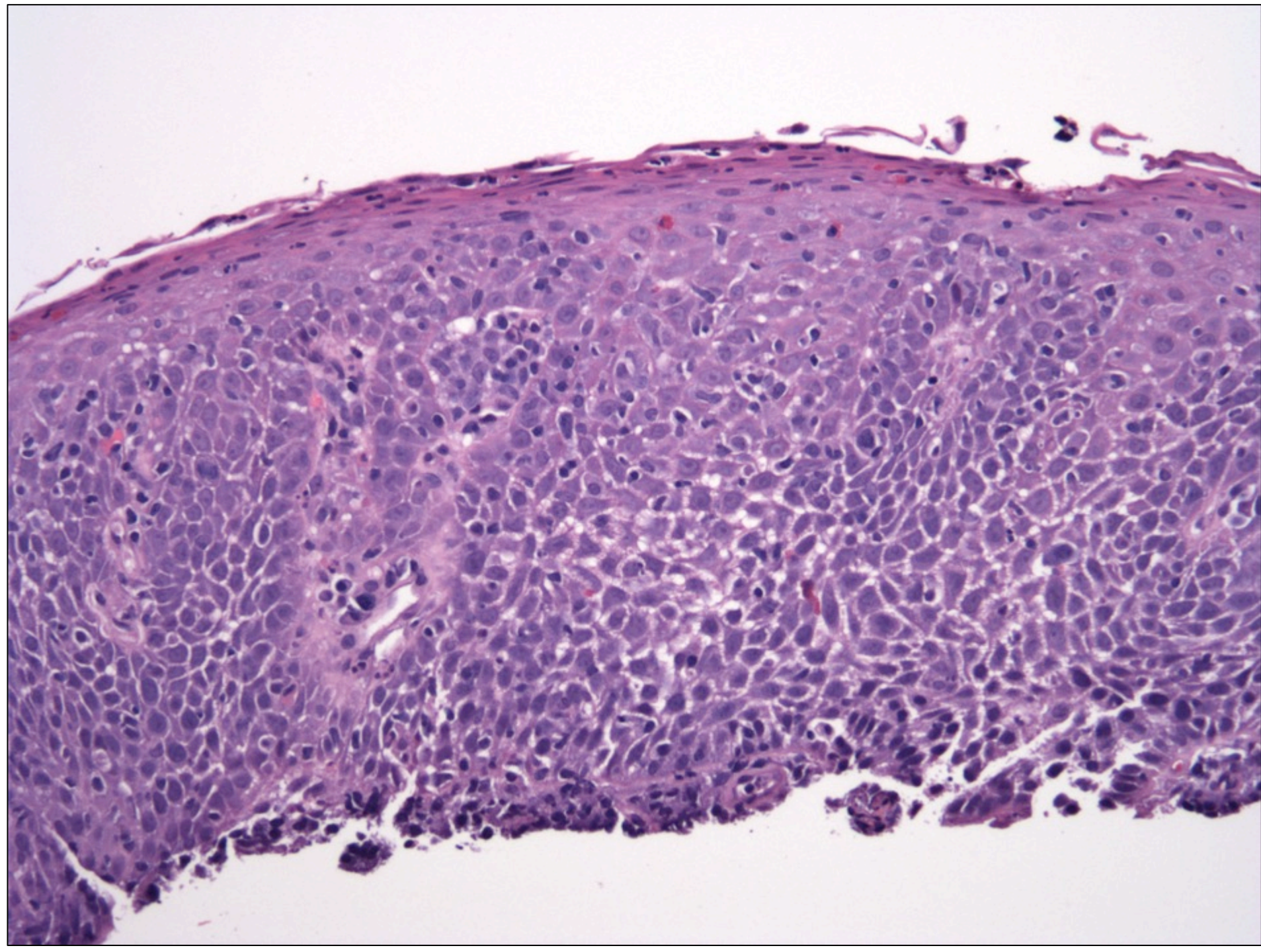
Lymphocytes in GERD, often 20/HPF or more



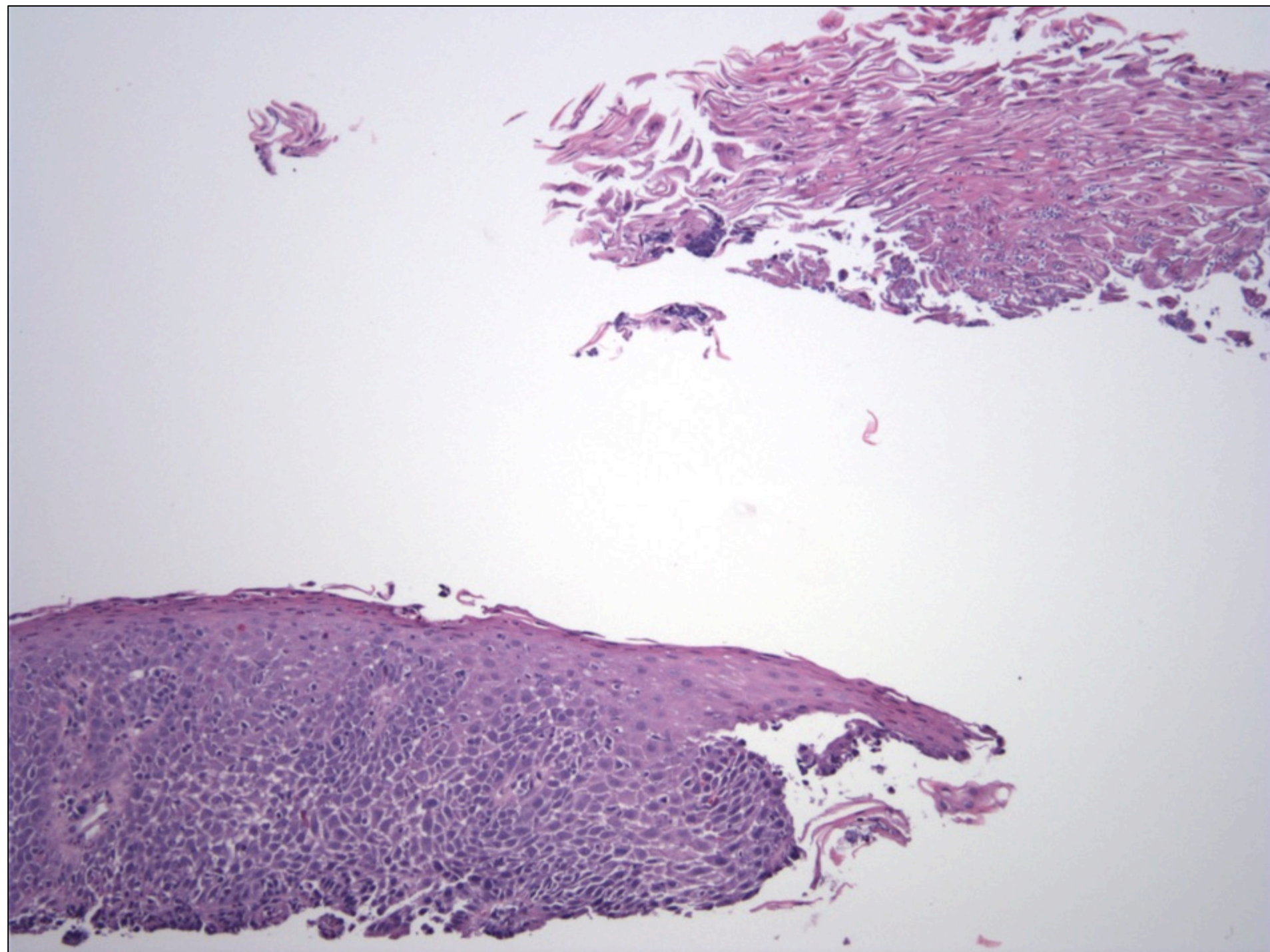


Candidal esophagitis

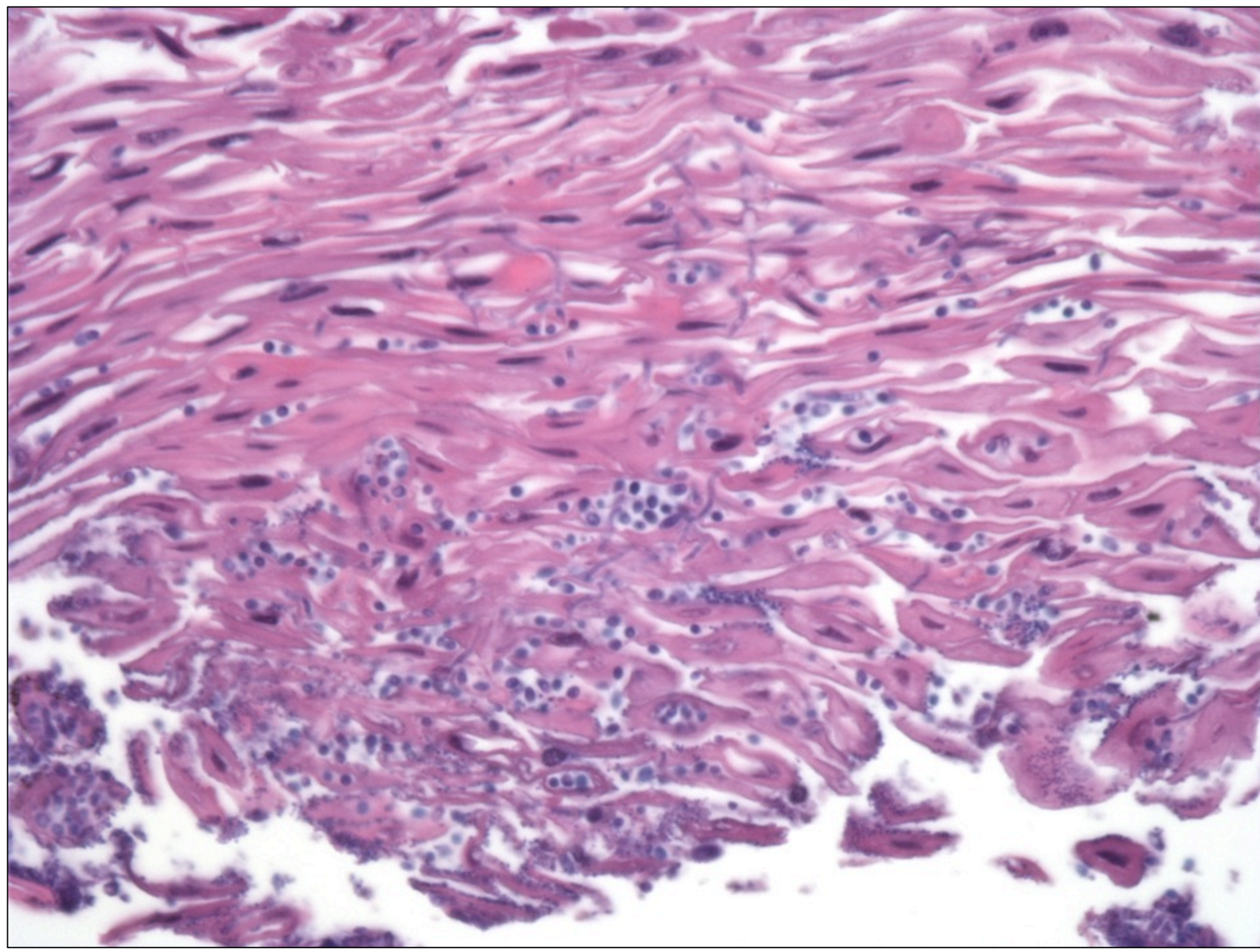






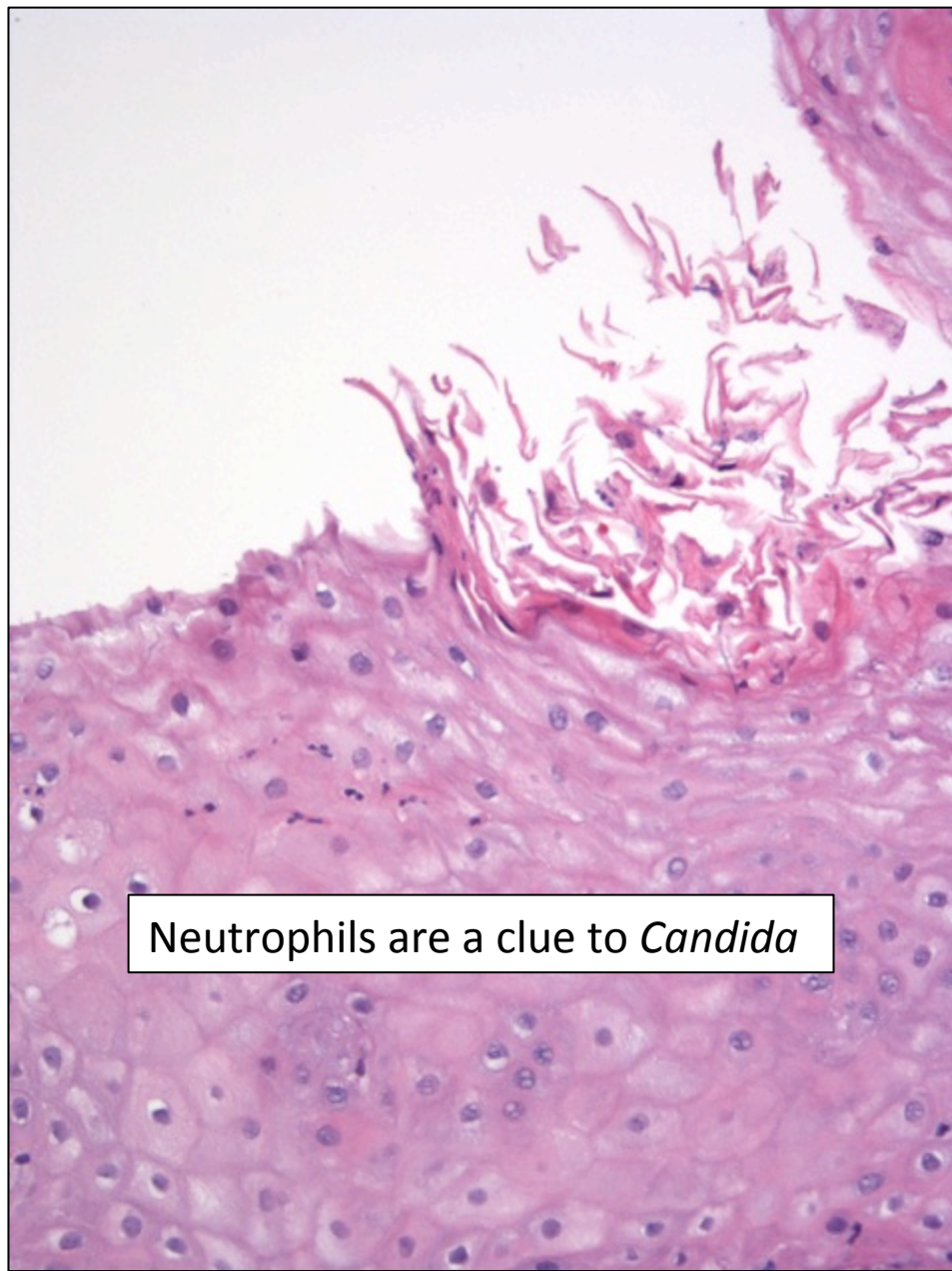




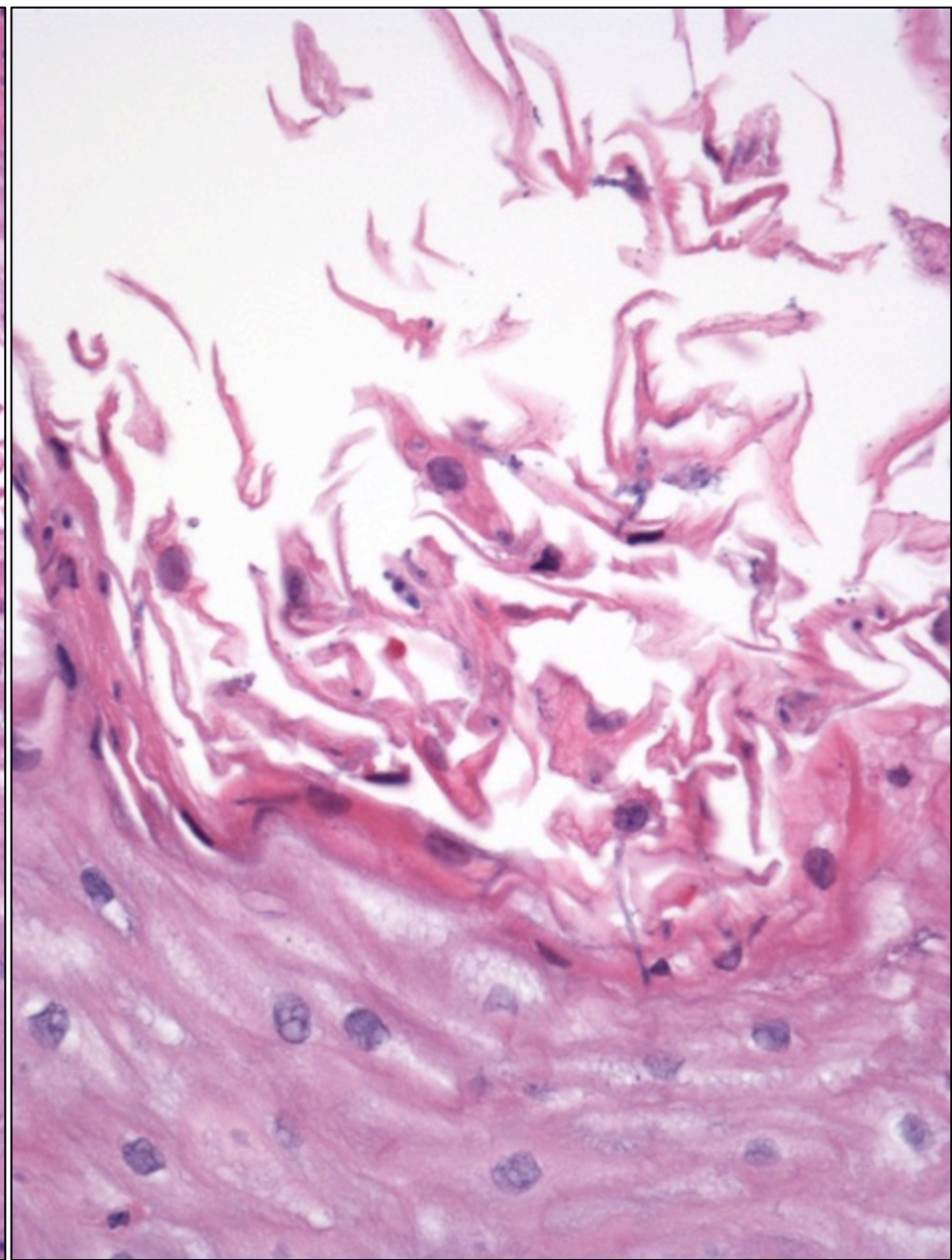








Neutrophils are a clue to *Candida*





***THERE ARE MANY CAUSES OF  
ESOPHAGEAL LYMPHOCYTOSIS....A  
DIAGNOSIS OF LYMPHOCYTIC  
ESOPHAGITIS REQUIRES CLINICAL  
CORRELATION***





## LYMPHOCYTIC ESOPHAGITIS DIAGNOSTIC CRITERIA

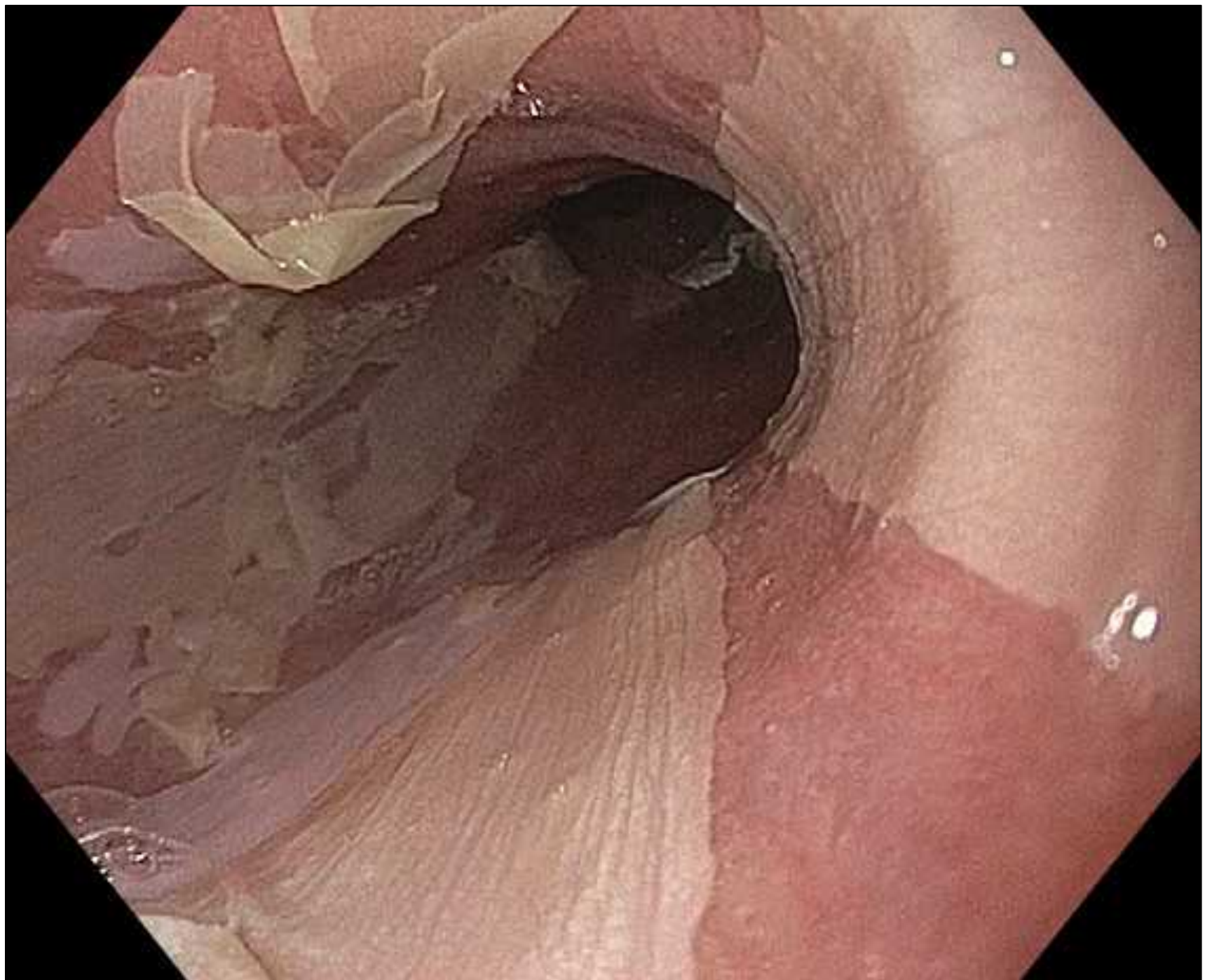
- I generally don't make this diagnosis unless
  - There are numerous intraepithelial lymphocytes with clustering and evidence of injury
    - Dyskeratotic epithelial cells
    - Intercellular edema
  - Other etiologies (GERD, eosinophilic esophagitis, candidiasis, stasis) rigorously excluded
  - Endoscopic findings suggest a diffuse mucosal abnormality (not just near the GE junction)
- Restricted definition likely identifies a group of patients with immune-mediated or drug-related injury similar to lymphocytic “itis” of the remaining GI tract



## CASE

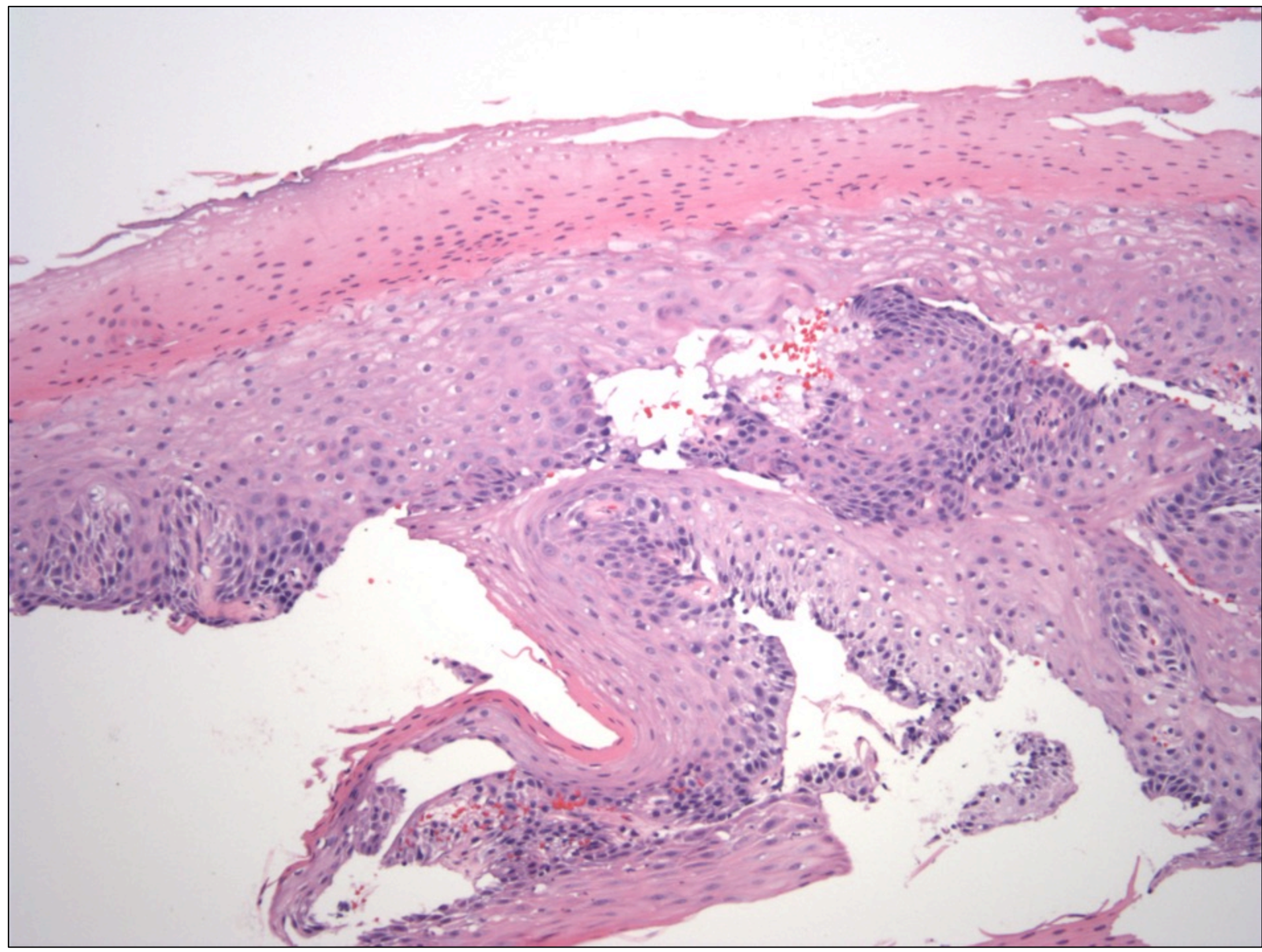
- 82-year old woman with CHF, COPD, recent fall
- Admitted to evaluate iron deficiency anemia



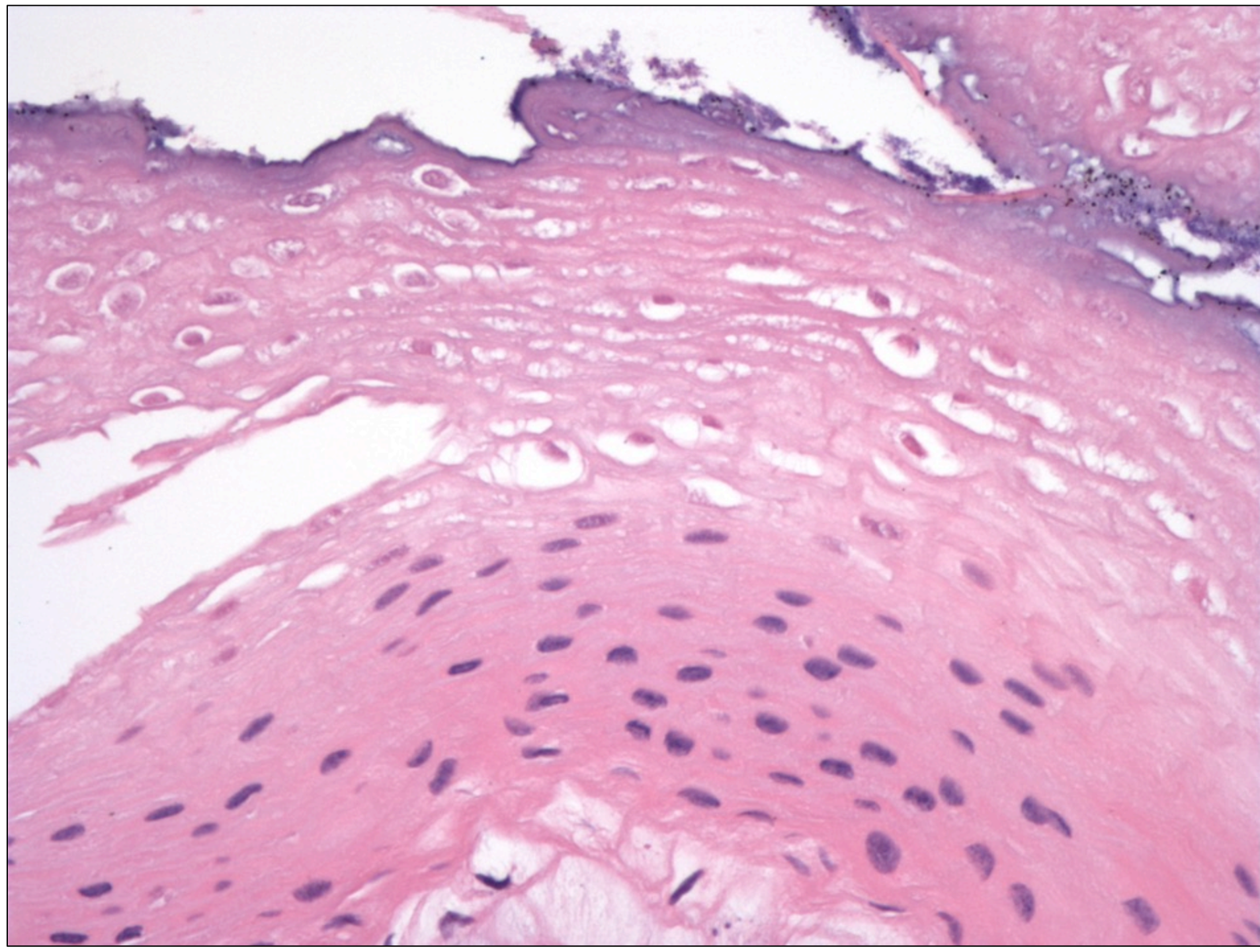
















# ESOPHAGITIS DISSECANs SUPERFICIALIS SLOUGHING ESOPHAGITIS

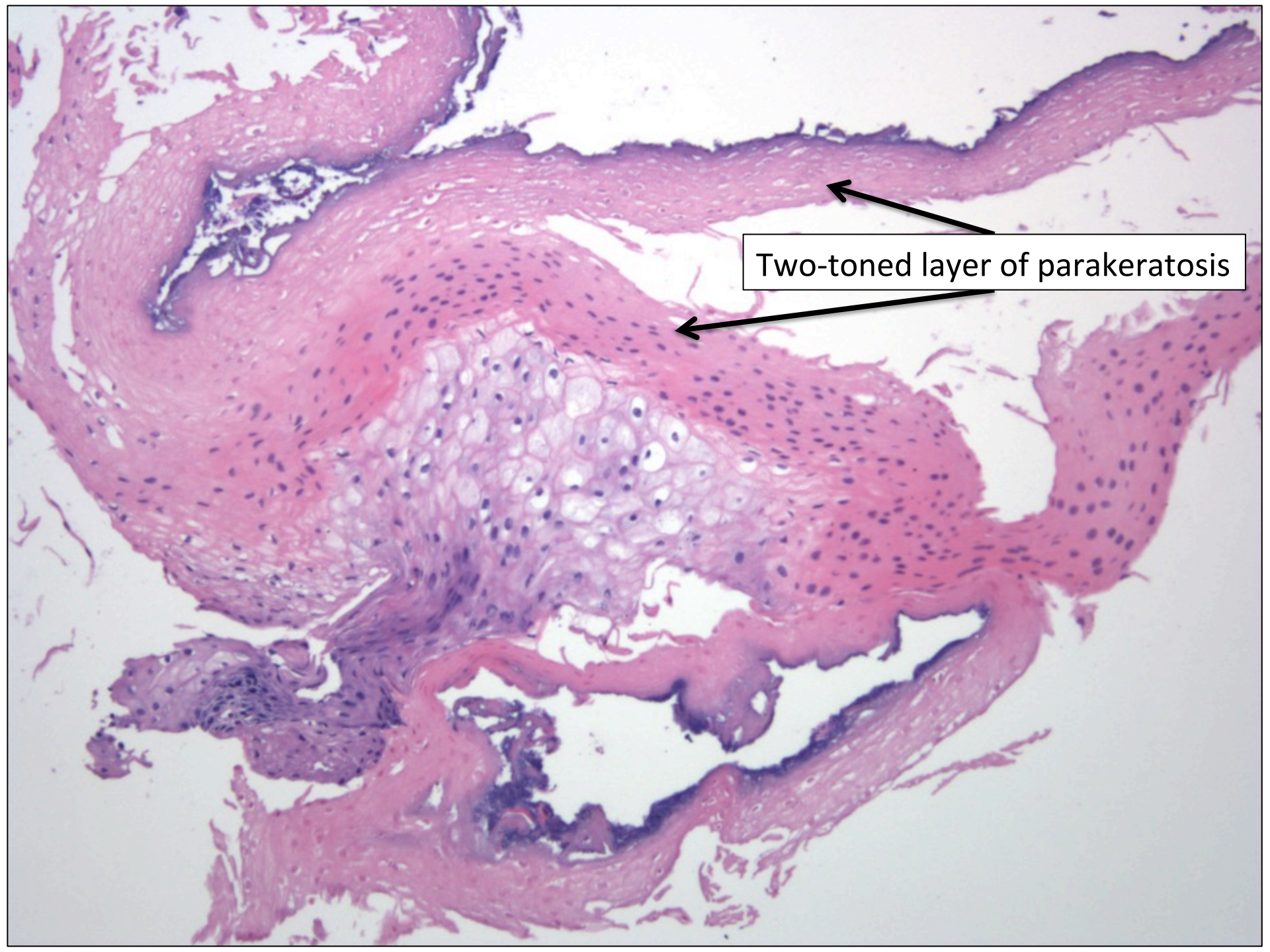
- Elderly patients
- Men and women equally affected
- Asymptomatic, dysphagia
- Self-limited with endoscopic resolution
- Chronic debilitating diseases
- Medications
  - NSAIDs, bisphosphonates, potassium chloride
  - CNS depressants
  - Medications that cause dry mouth (opioids, SSRIs)

An endoscopic photograph showing a reddish, mucosal surface. A large, dark, ulcerated lesion is visible in the center. The surrounding mucosa appears relatively normal. There are some yellowish, desquamated areas on the left side of the image. Two small, white, circular markers are visible on the right side of the mucosa.

Underlying mucosa essentially normal

Desquamation

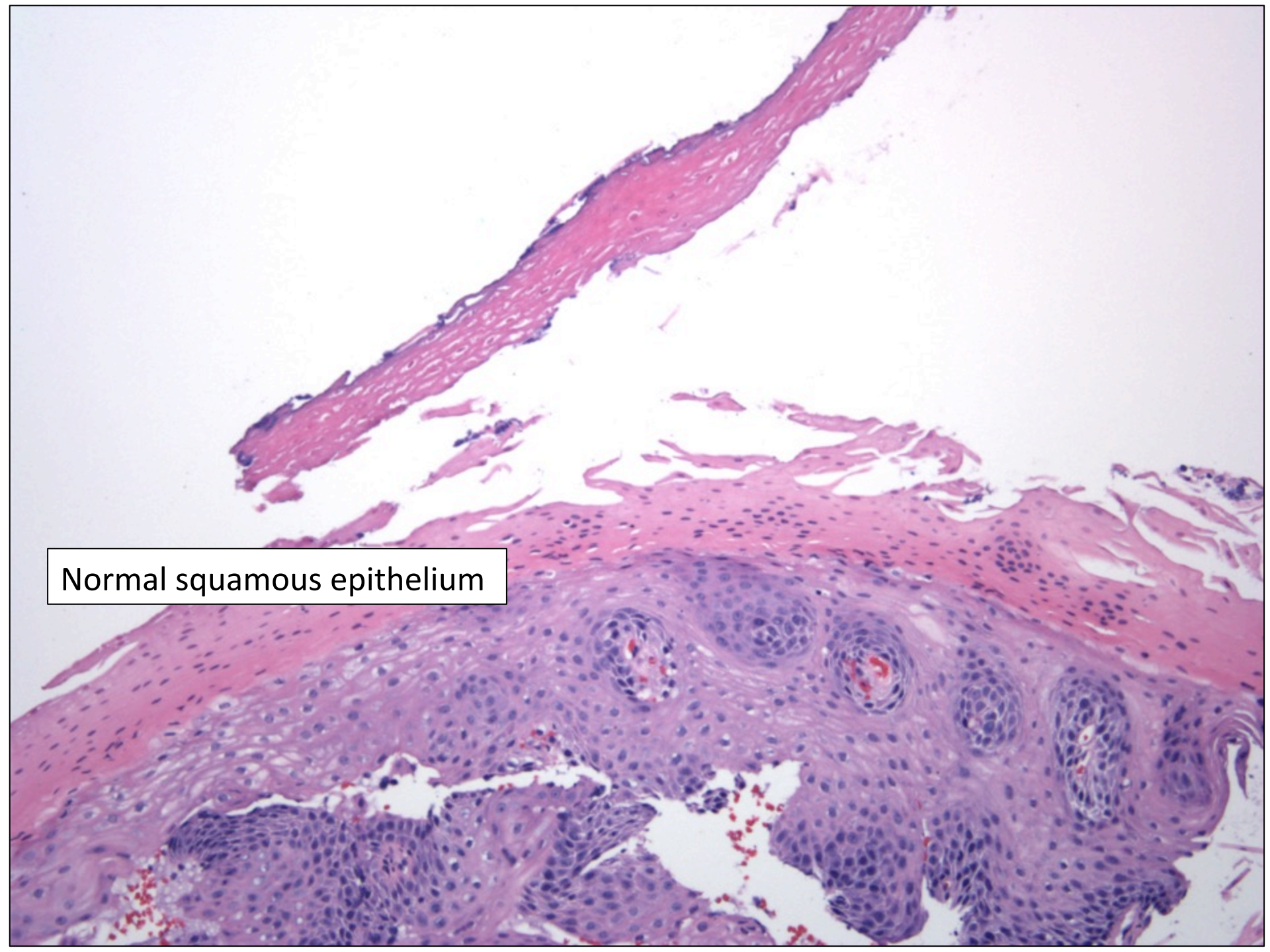




This histological image shows a section of skin with a prominent feature of parakeratosis. The epidermis is thickened, and the stratum corneum is composed of multiple layers of cells. A specific layer within this stratum corneum is highlighted by two arrows and a text box, showing a 'two-toned' appearance where the superficial layer is more eosinophilic (pink) and the underlying layer is more basophilic (purple) due to the presence of nuclei. This is characteristic of parakeratosis, often seen in conditions like psoriasis.

Two-toned layer of parakeratosis

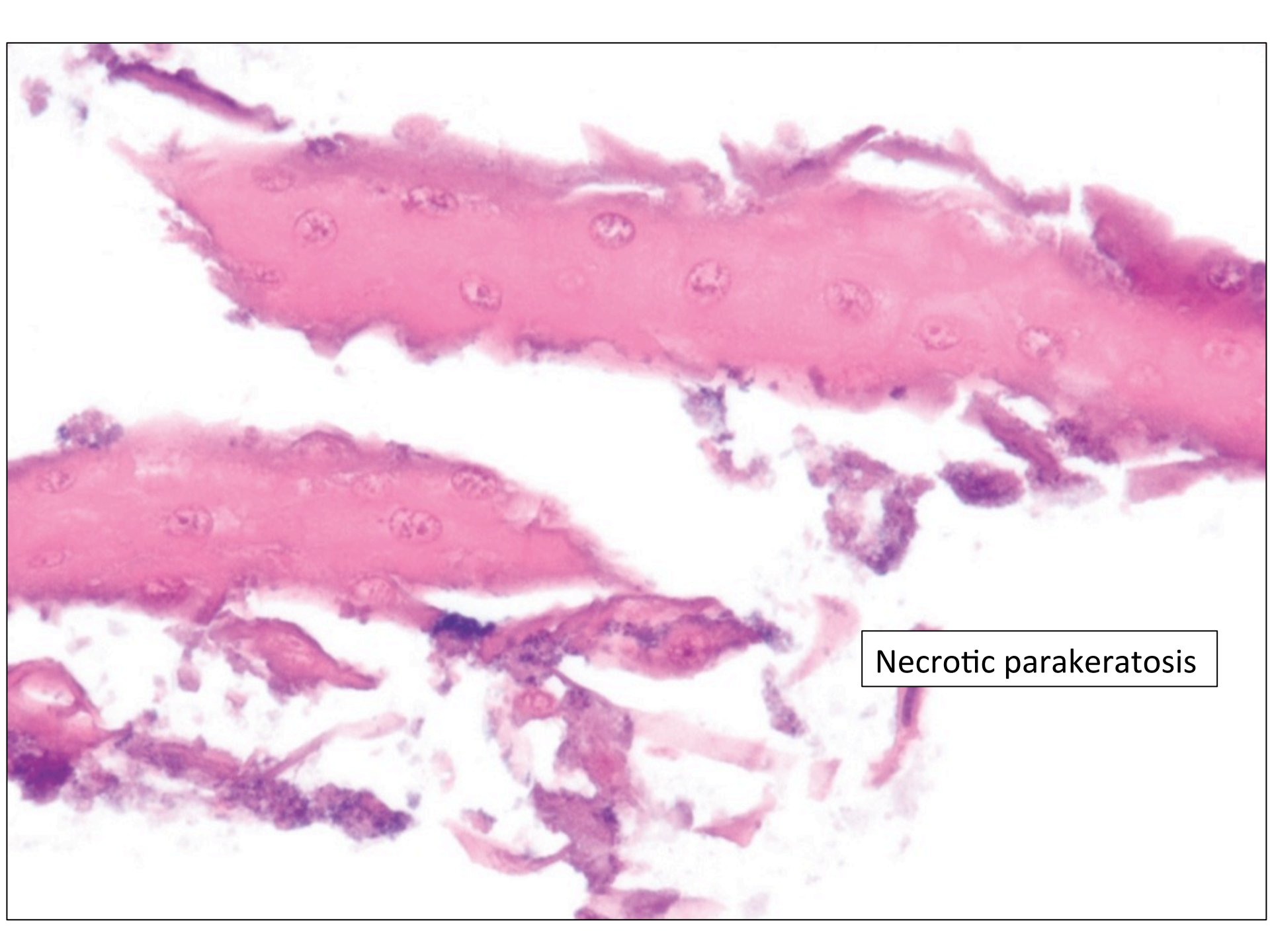




This histological image shows a section of normal squamous epithelium. The tissue is stained with hematoxylin and eosin (H&E). The upper portion of the image shows a thick, pink-stained layer of keratin. Below this, the epithelial layer is visible, characterized by multiple layers of cells. The basal layer at the bottom consists of a single layer of cells. The overall structure is organized into a stratified pattern, typical of normal squamous epithelium.

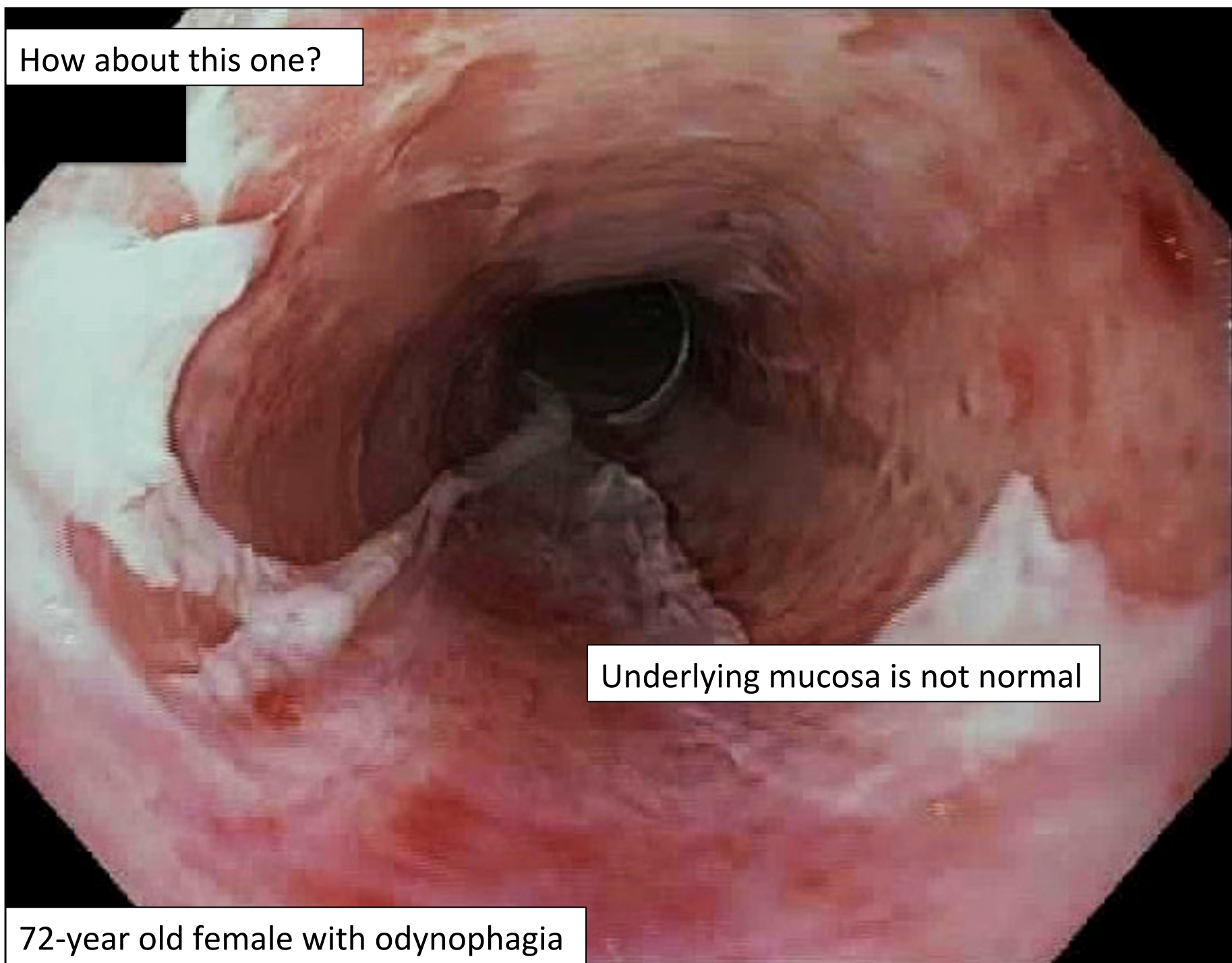
Normal squamous epithelium





Necrotic parakeratosis

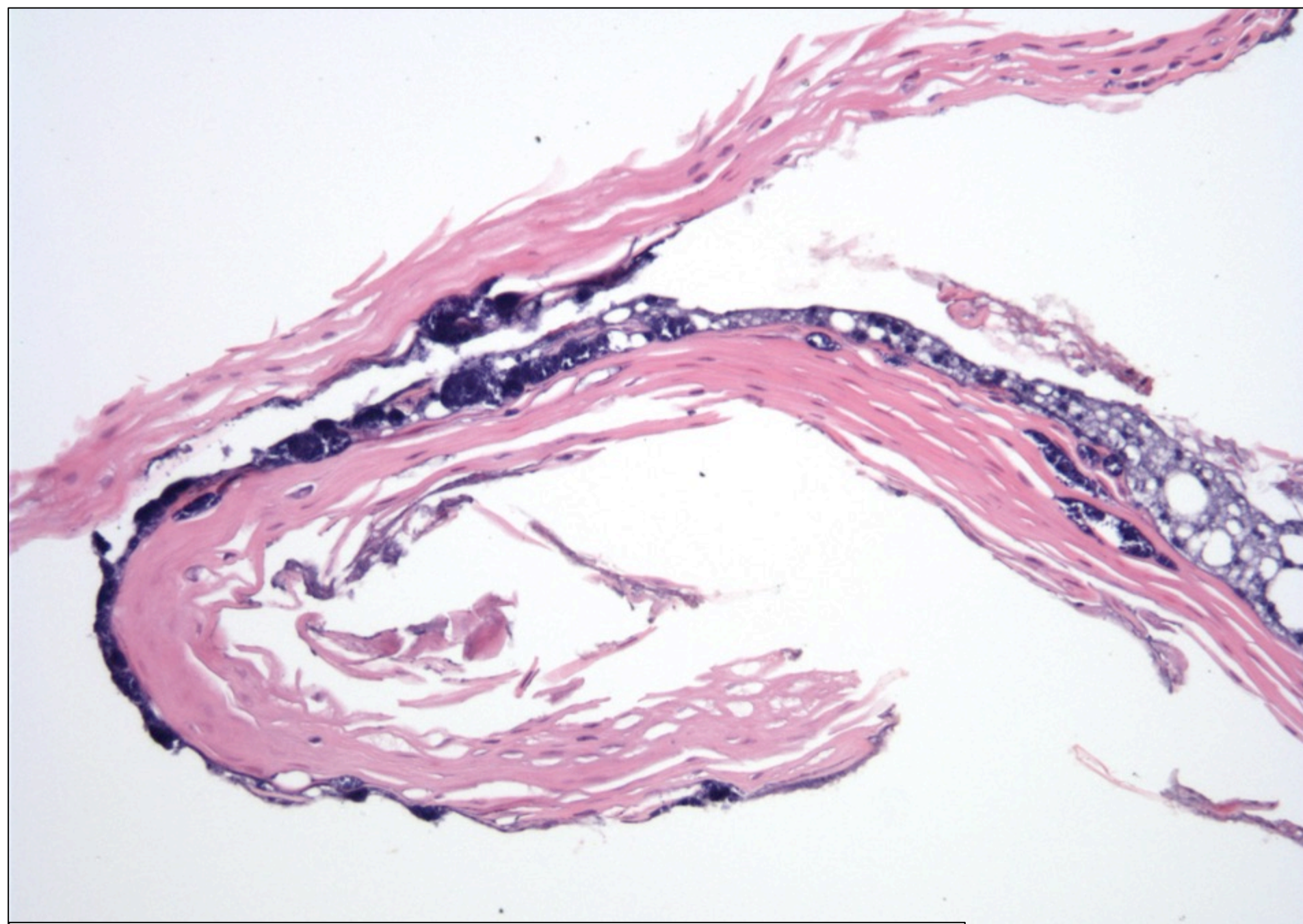
How about this one?



Underlying mucosa is not normal

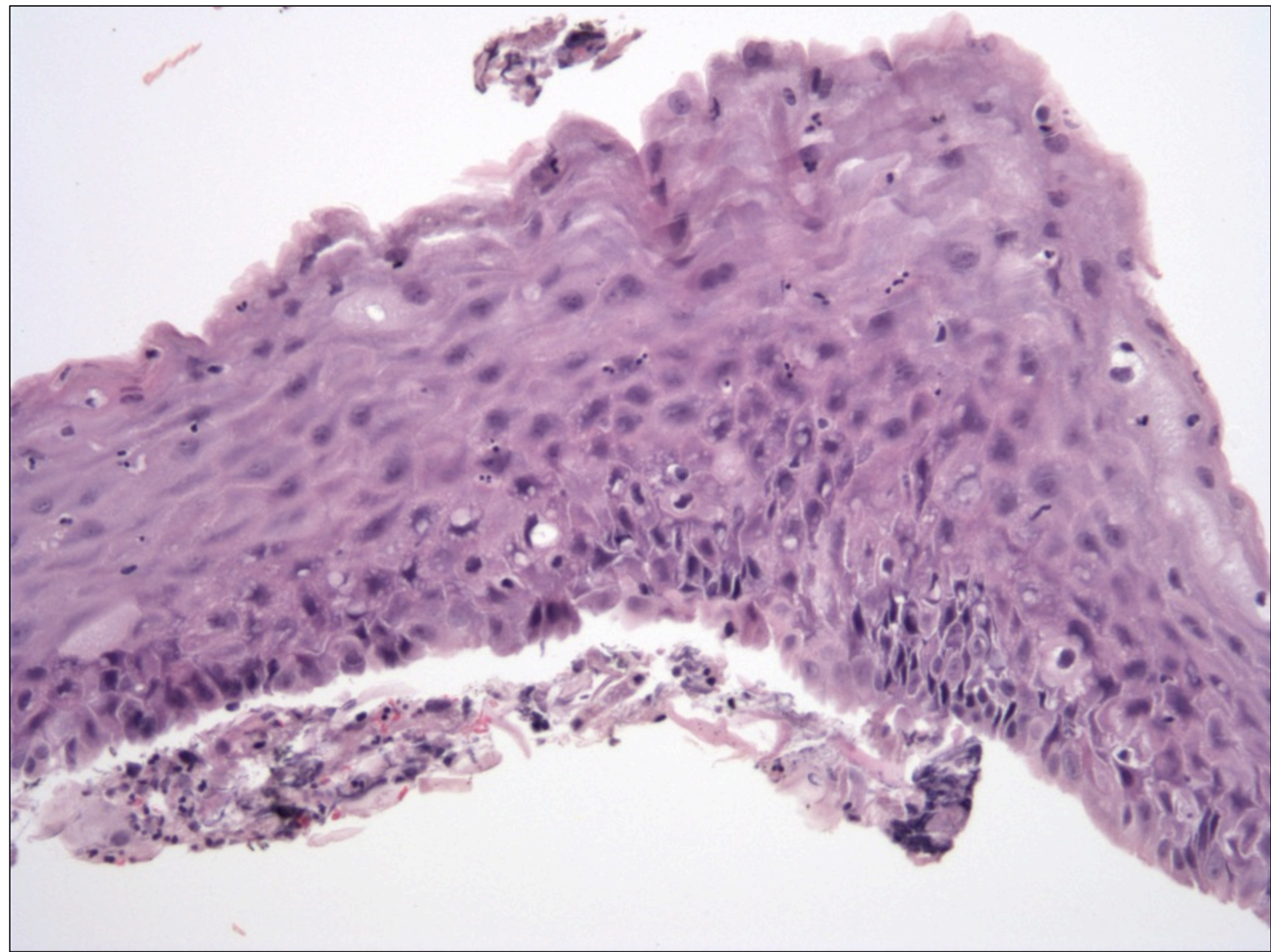
72-year old female with odynophagia



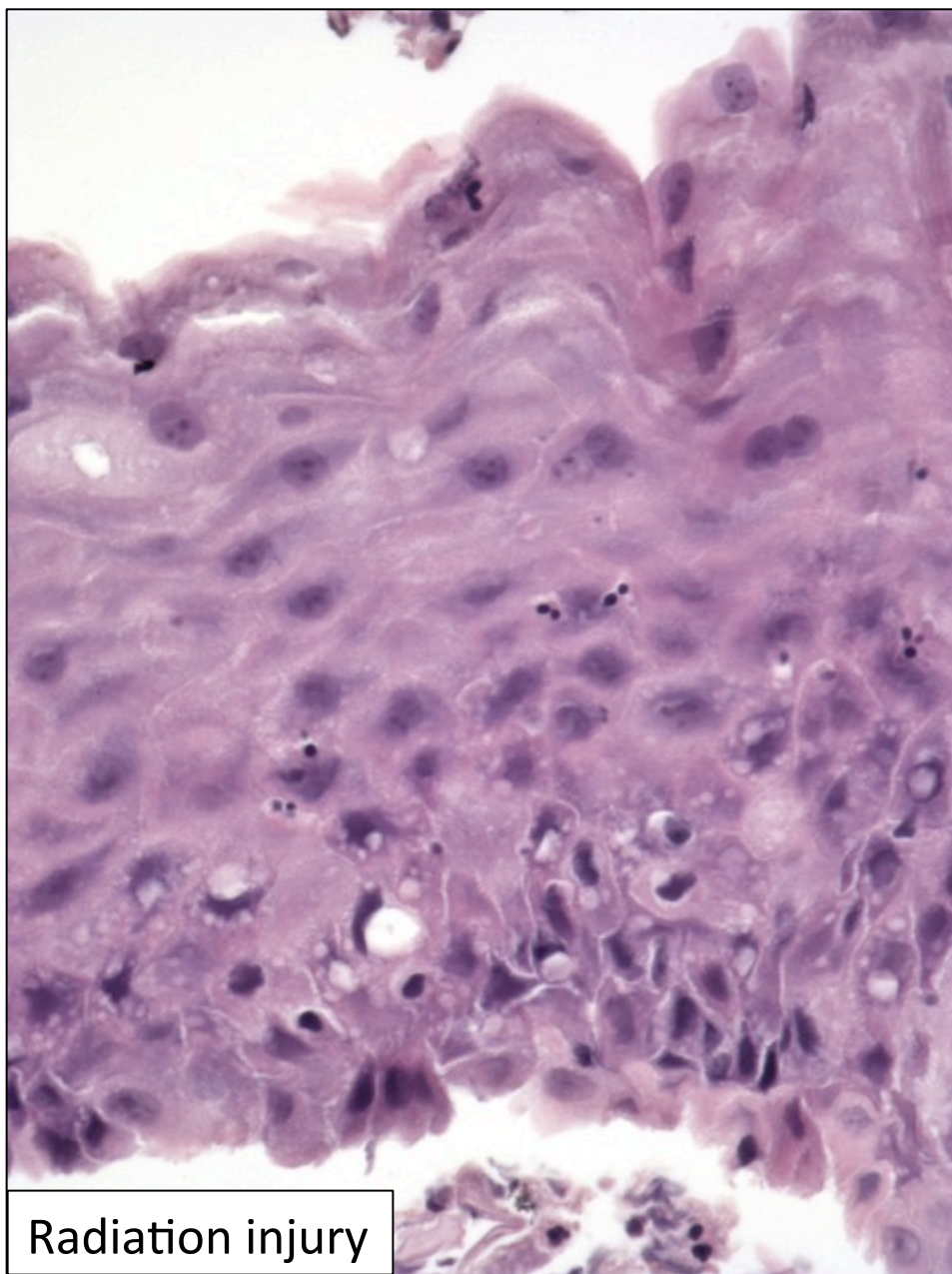


Thin strips of parakeratotic material; not dead or "two-toned"









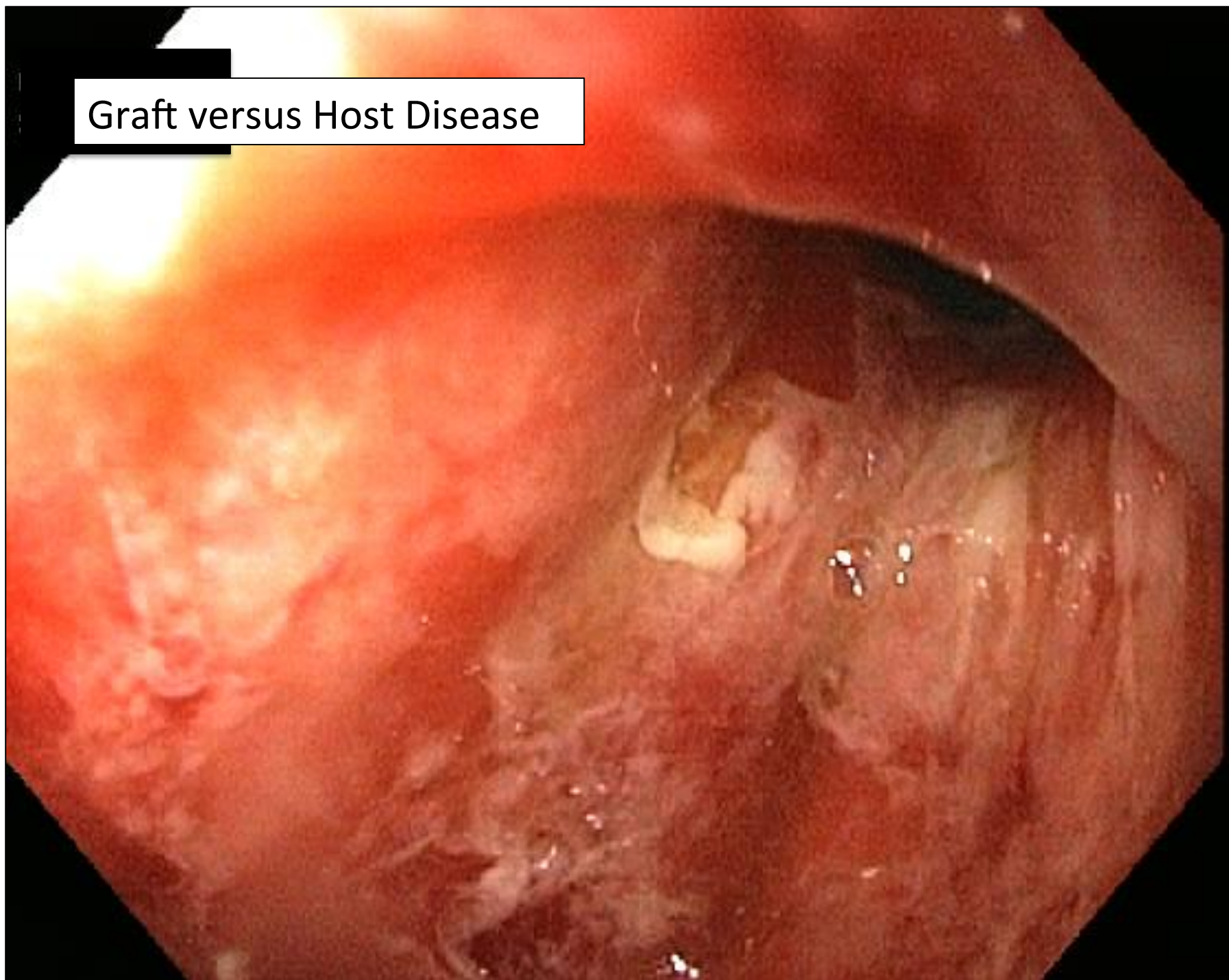
Radiation injury



Thin mucosa

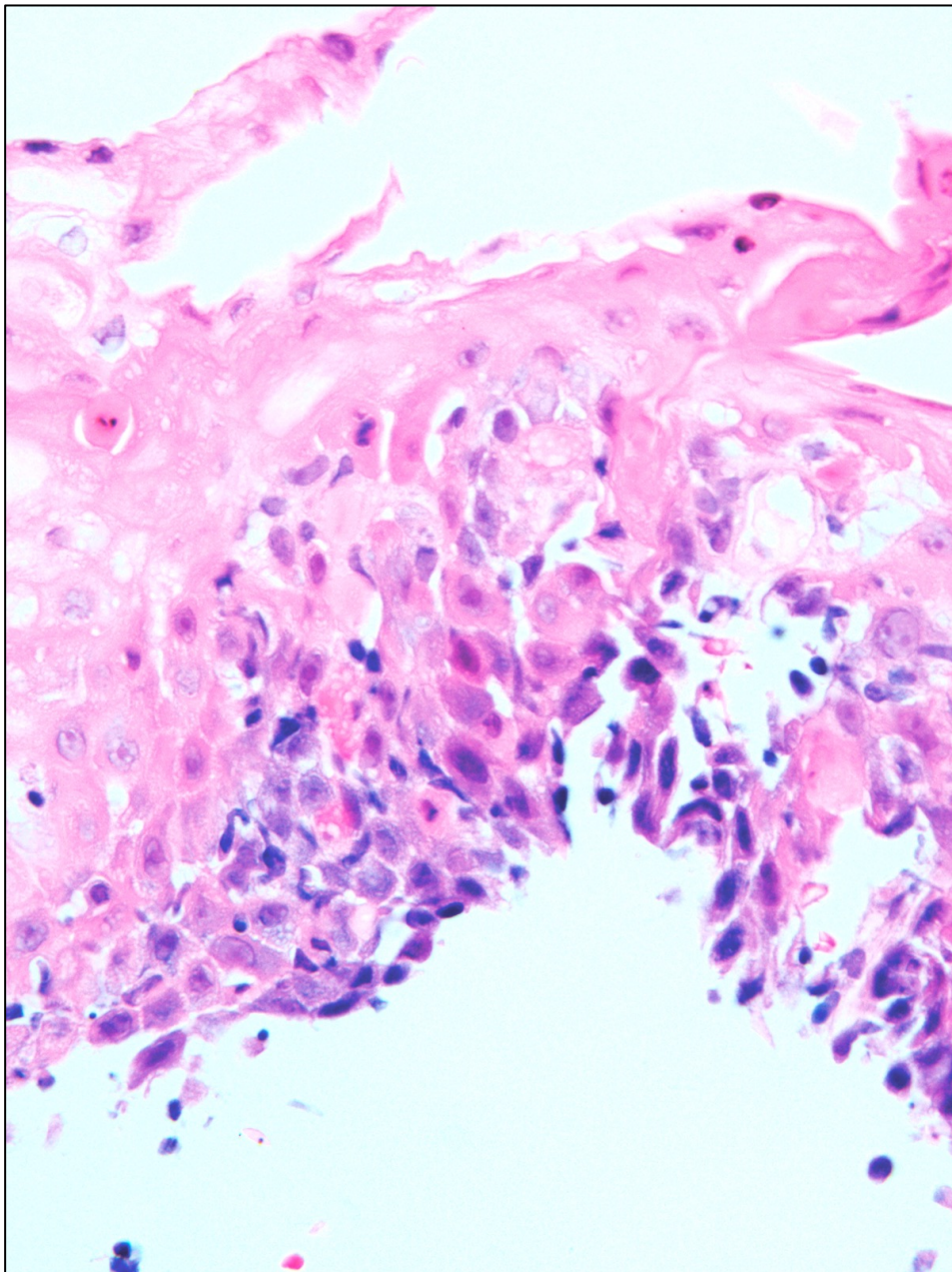
Vacuolated weird cells in basal zone

## Graft versus Host Disease

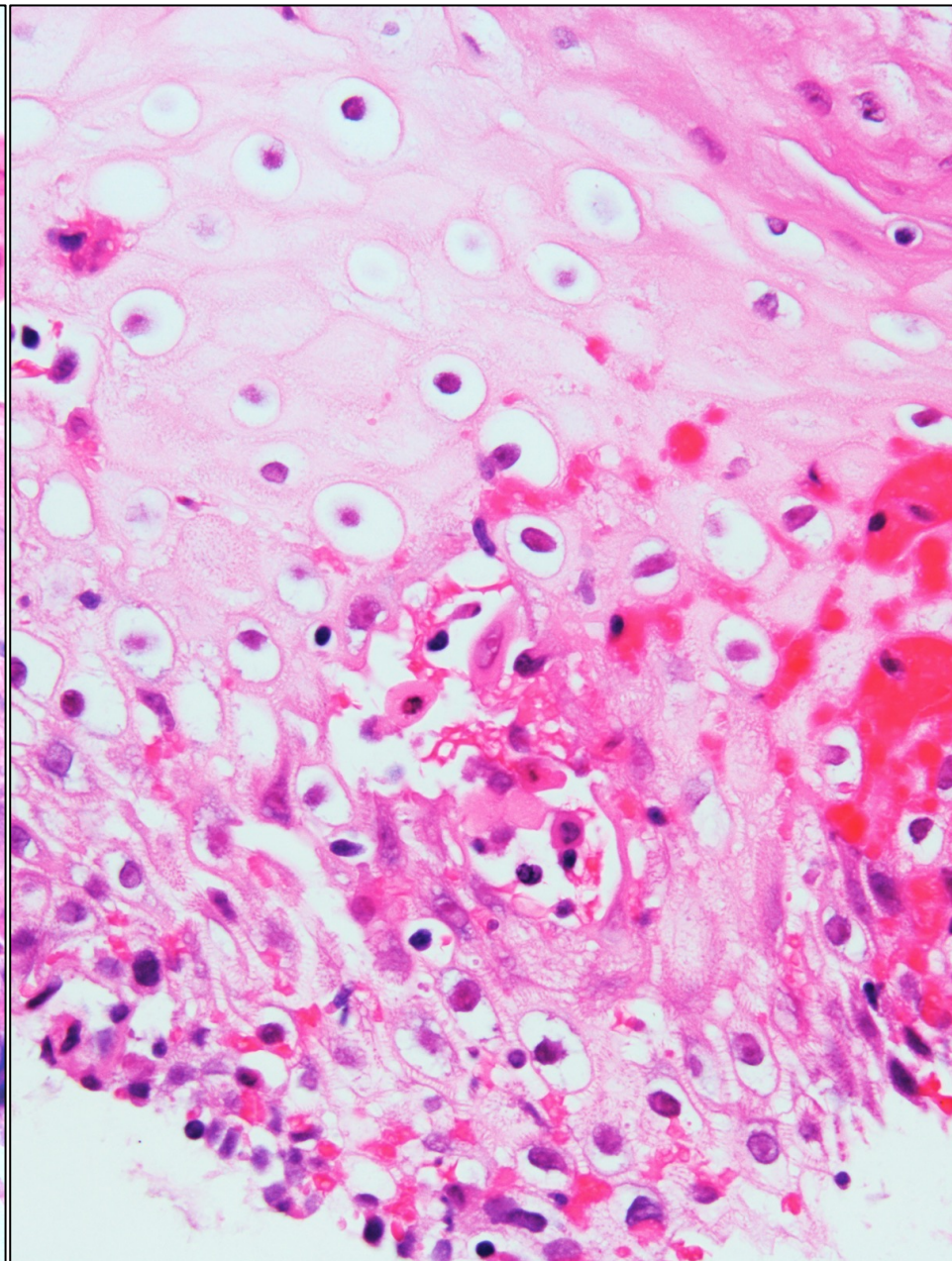




# Graft versus Host Disease

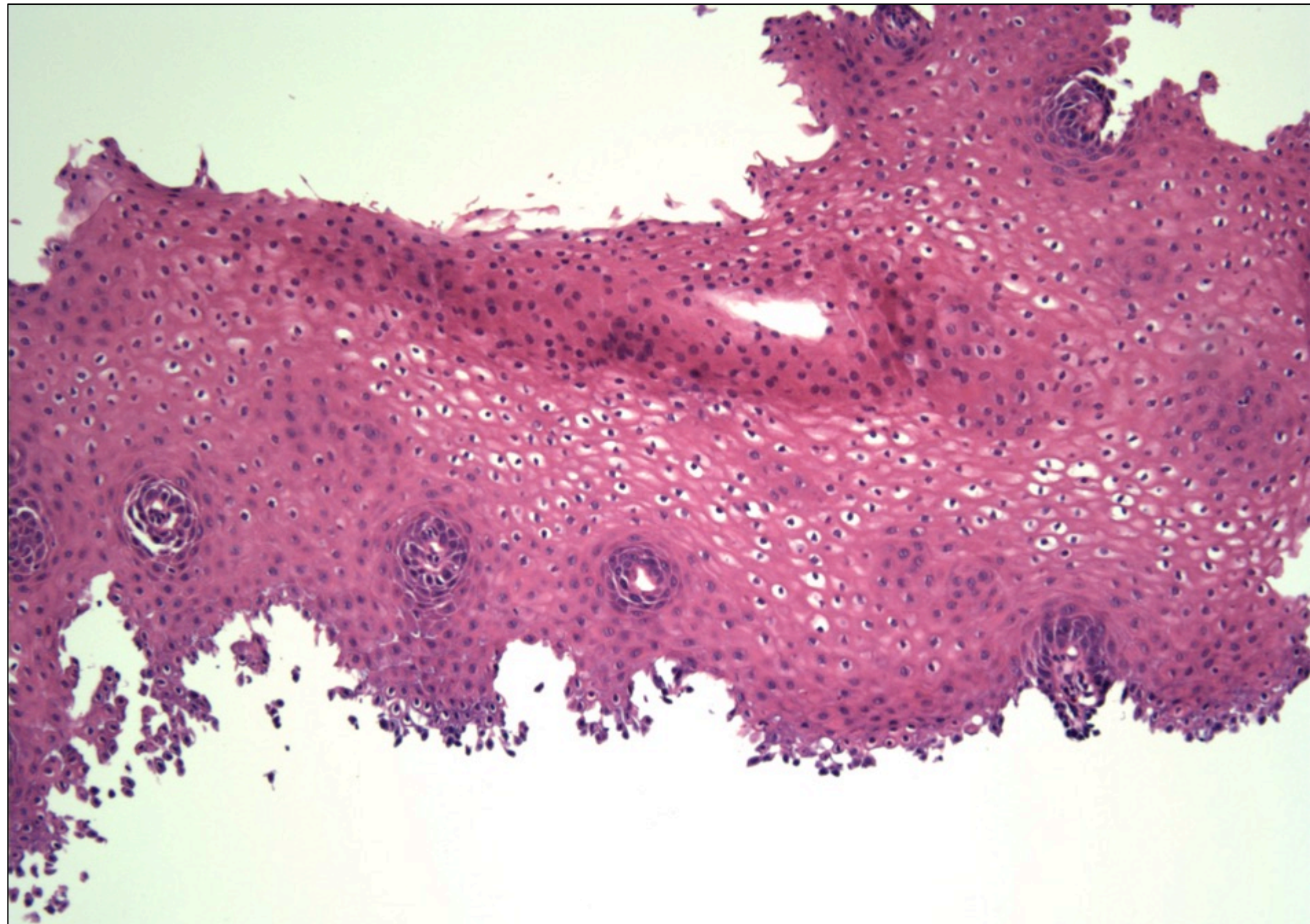


Apoptotic keratinocytes



Degenerated basal keratinocytes

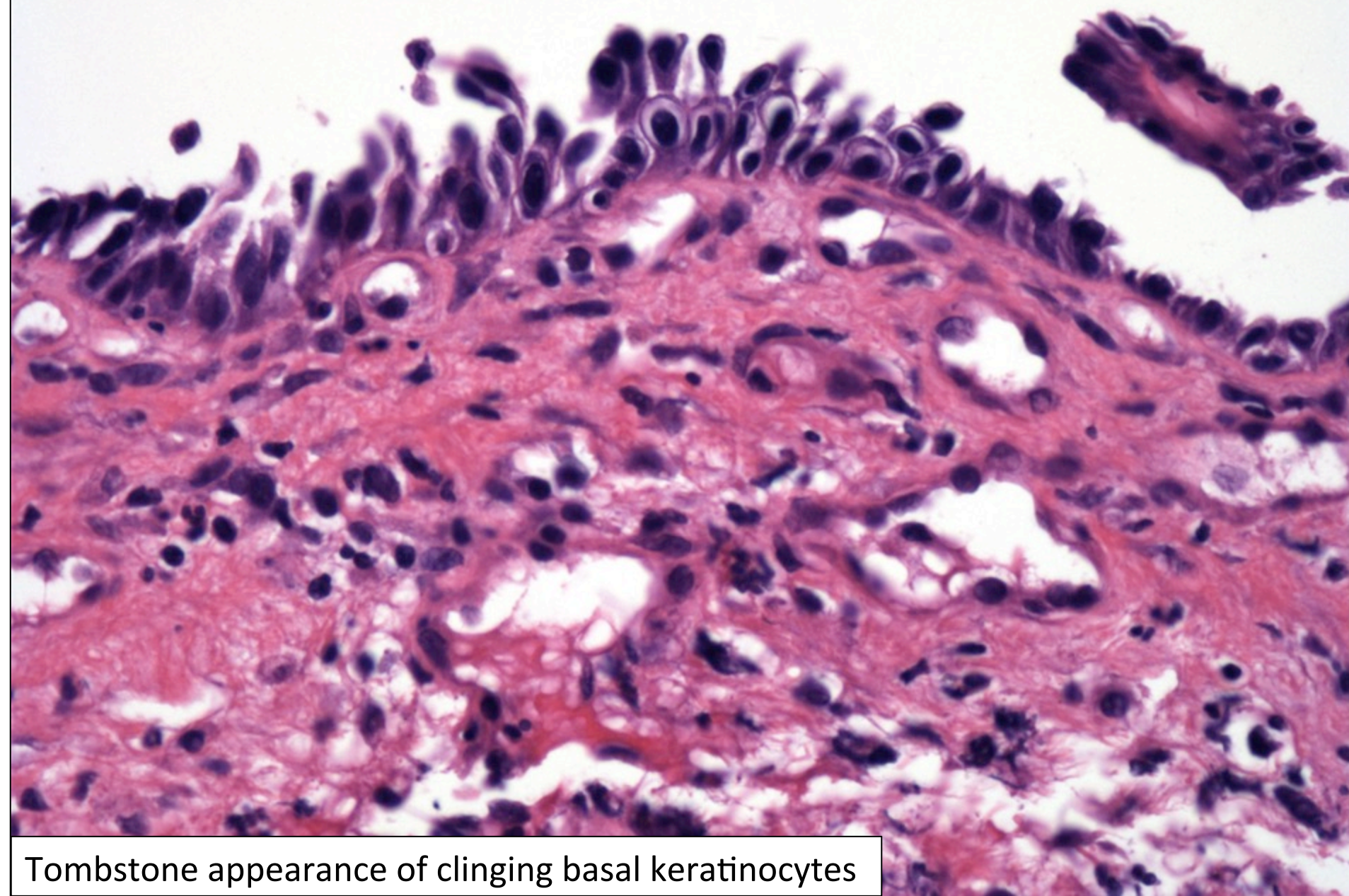




Pemphigus vulgaris; esophageal desquamation, but subtle histologic findings

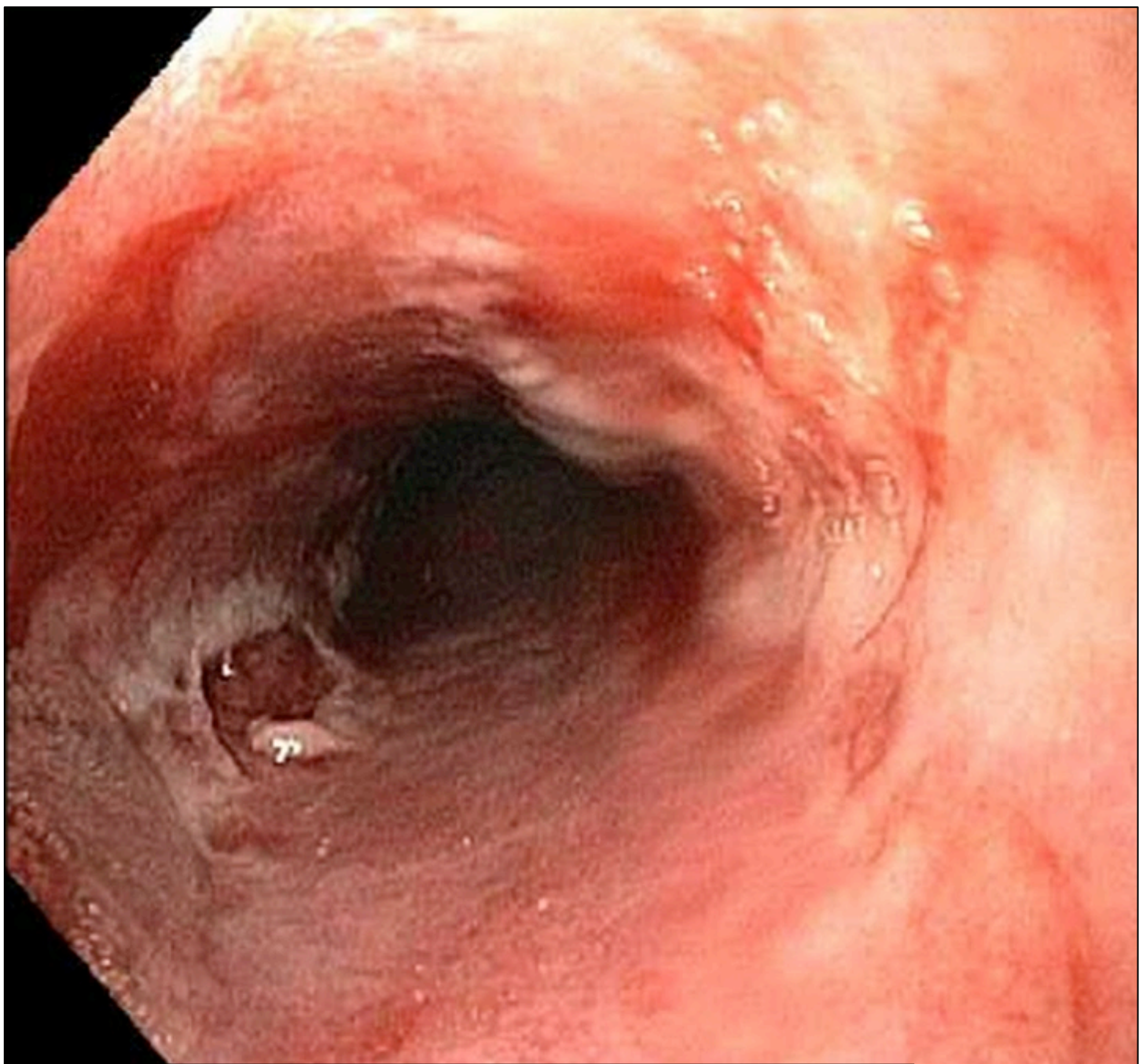


Bullae are flaccid, so may be disrupted or desquamative;  
confirm with DIF for intercellular IgG and C3 deposits



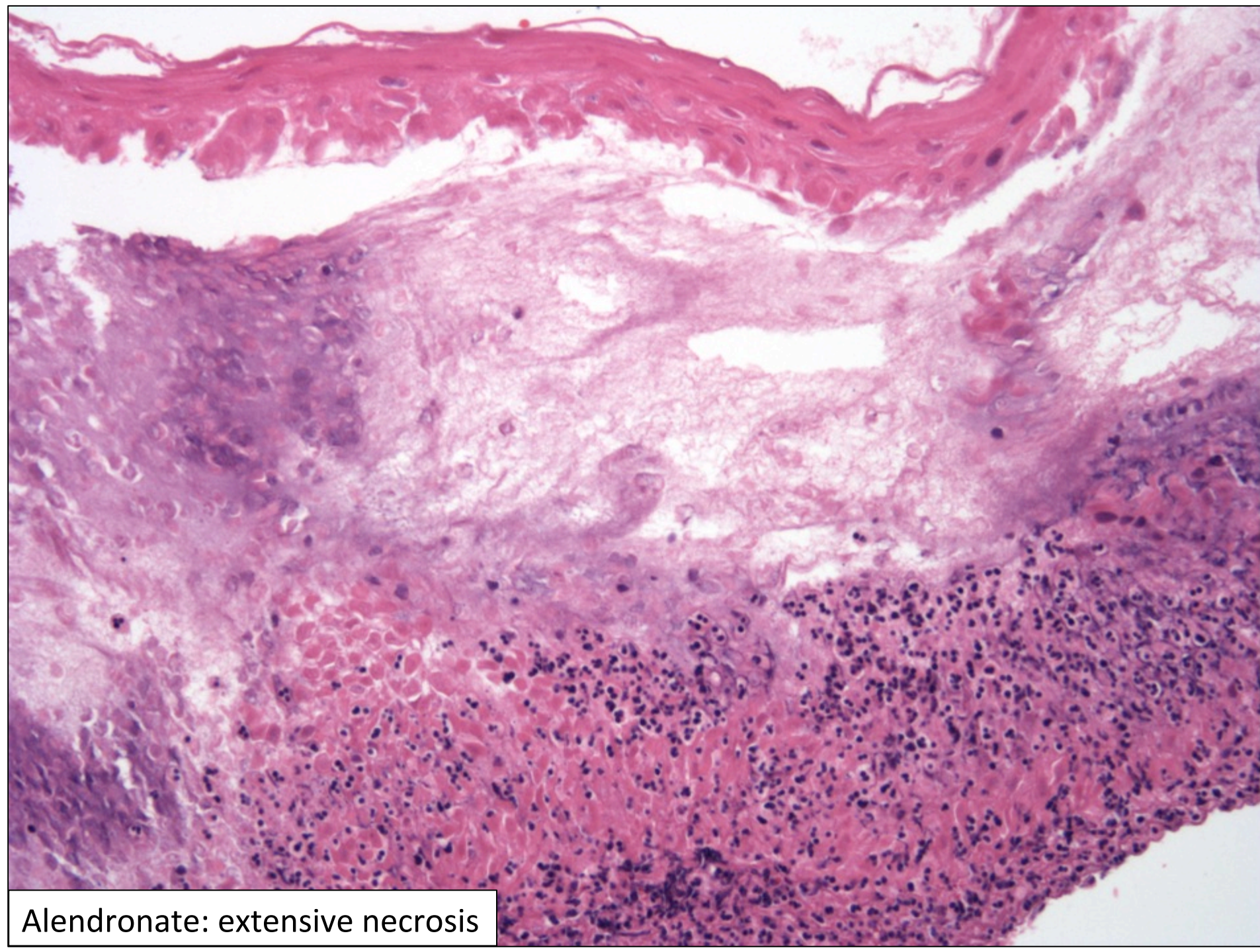
Tombstone appearance of clinging basal keratinocytes





Alendronate: severe injury, may completely desquamate





Alendronate: extensive necrosis

***THERE ARE MANY MIMICS OF  
SLOUGHING ESOPHAGITIS....THE  
HISTOLOGIC DIAGNOSIS REQUIRES  
CLINICOPATHOLOGIC CORRELATION***



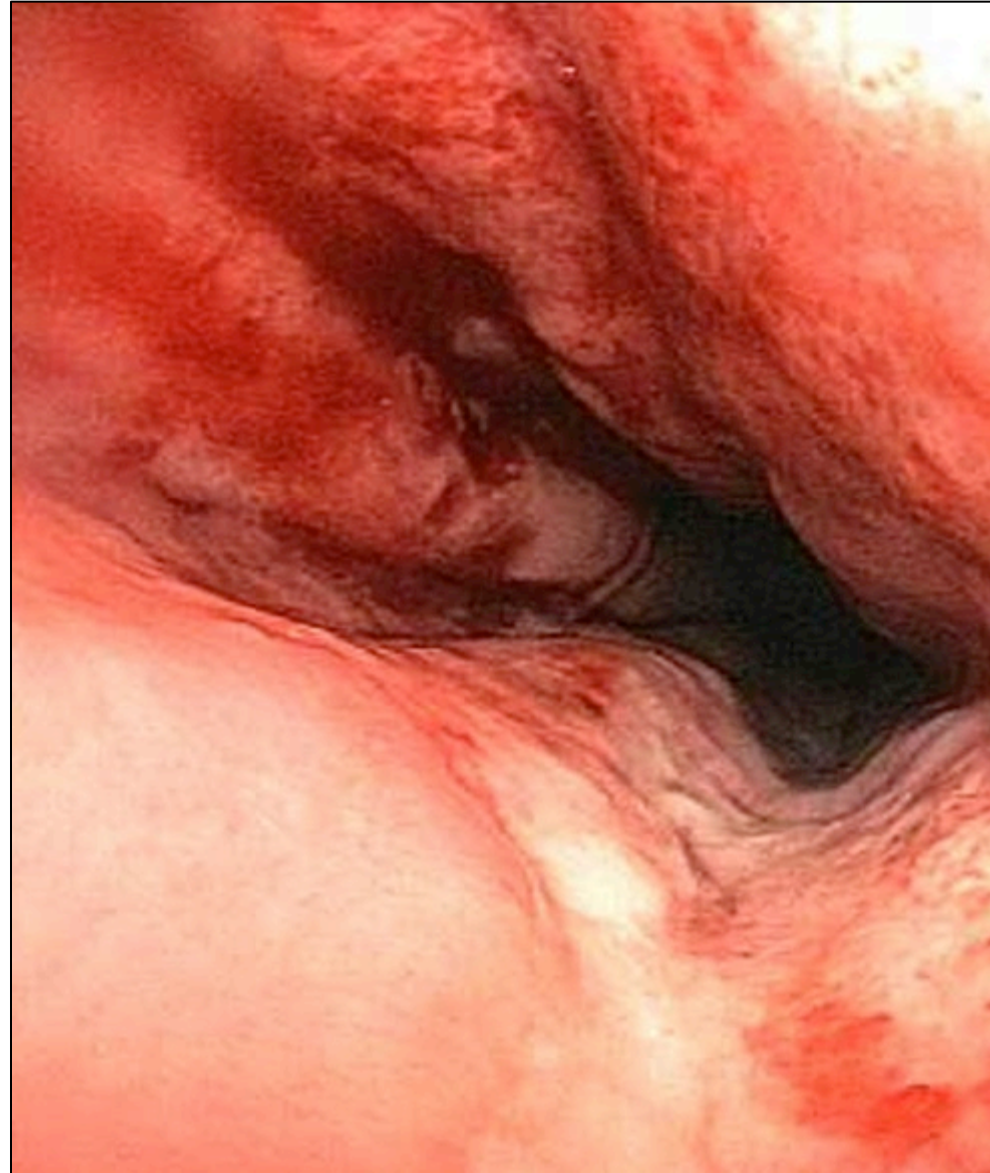


# ESOPHAGITIS DISSECANANS SUPERFICIALIS DIAGNOSTIC CRITERIA

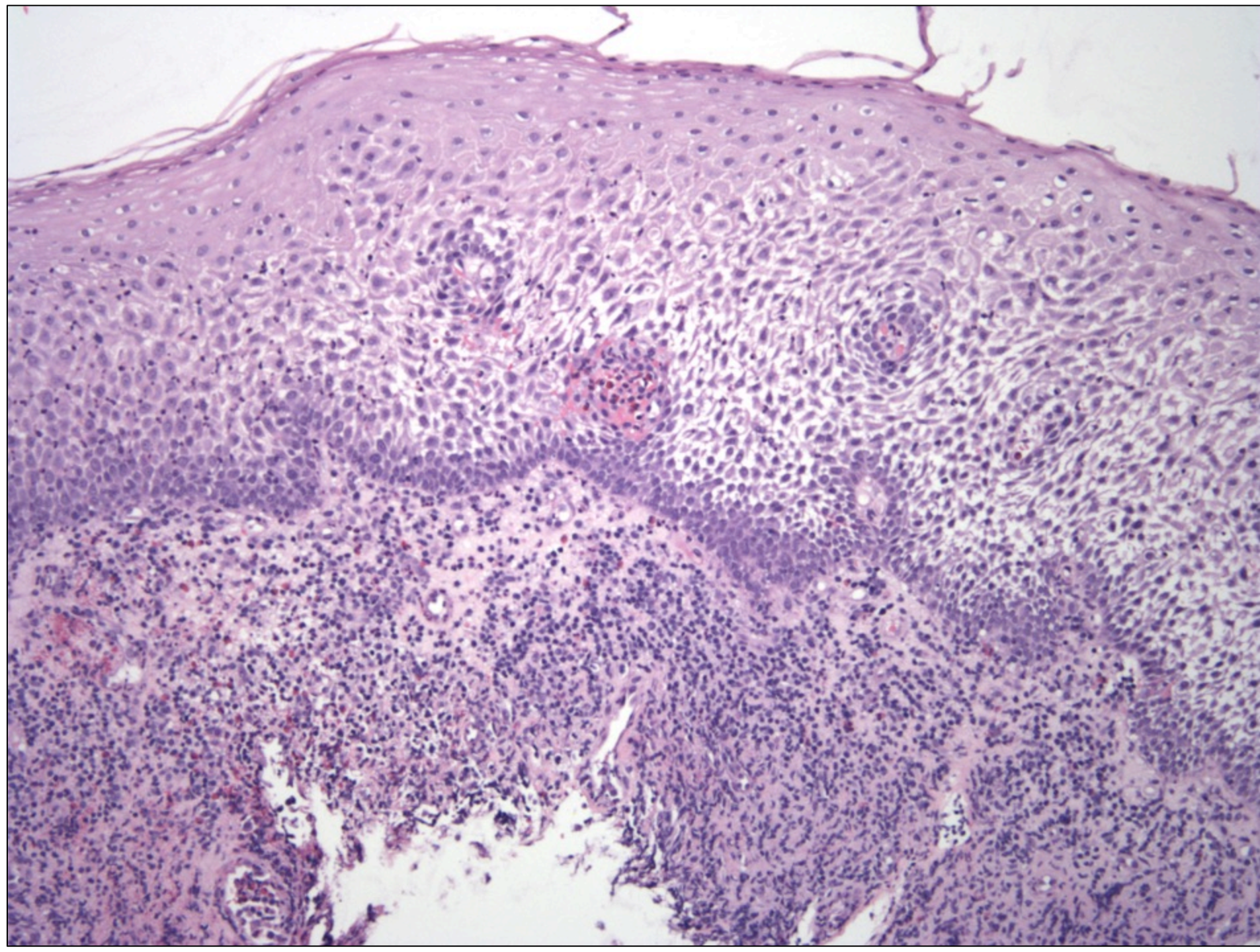
- I generally don't make this diagnosis unless
  - There is two-toned parakeratosis with necrosis of superficial layer
  - The epithelium under parakeratosis is normal
  - The clinical picture fits
    - Endoscopy shows diffuse desquamation with normal underlying mucosa
  - Other etiologies are excluded
    - Radiation
    - Graft versus host disease
    - Bullous disorders
    - Drugs (bisphosphonates)

## CASE

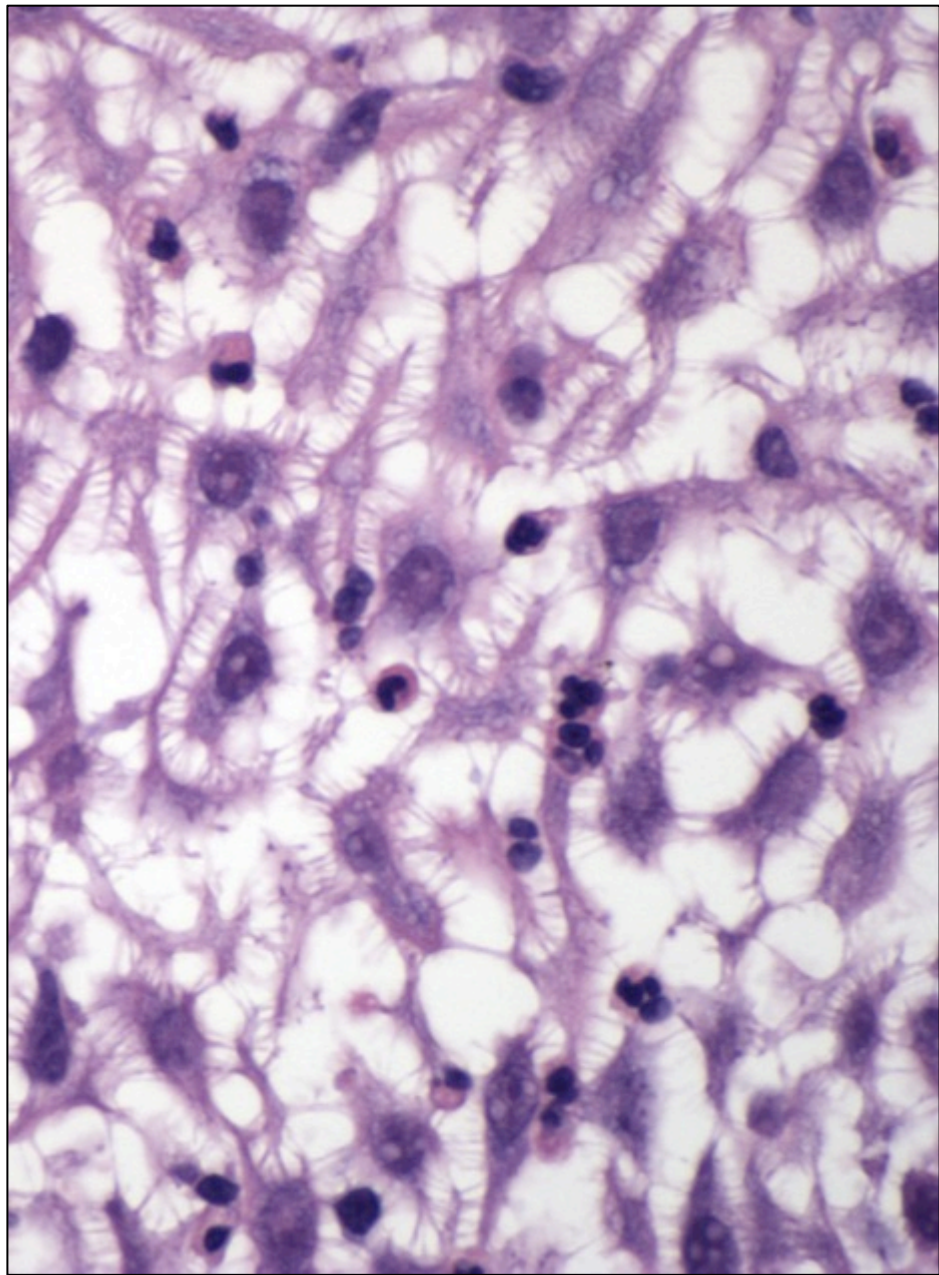
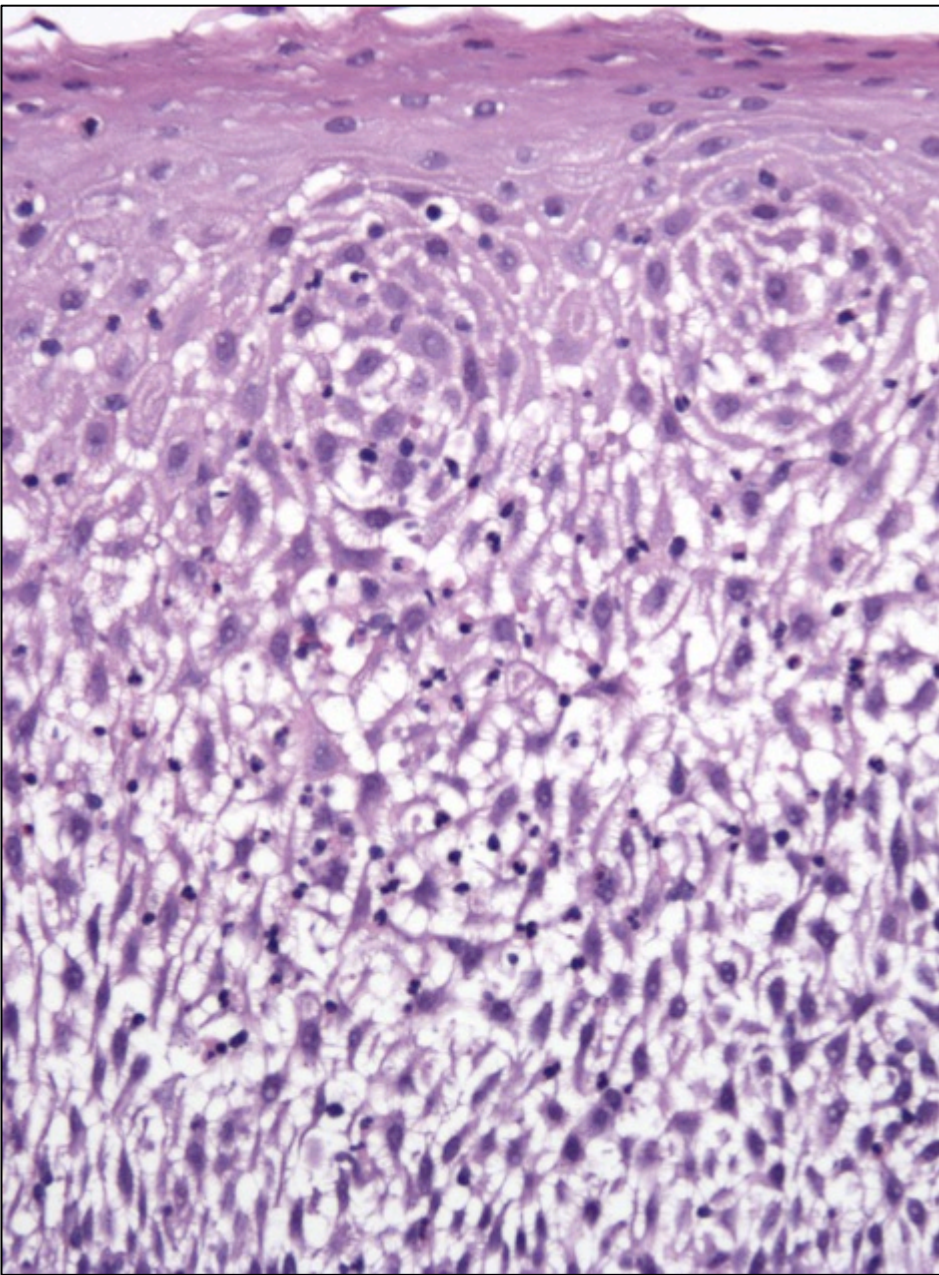
- 30-year old woman with odynophagia
- Otherwise well











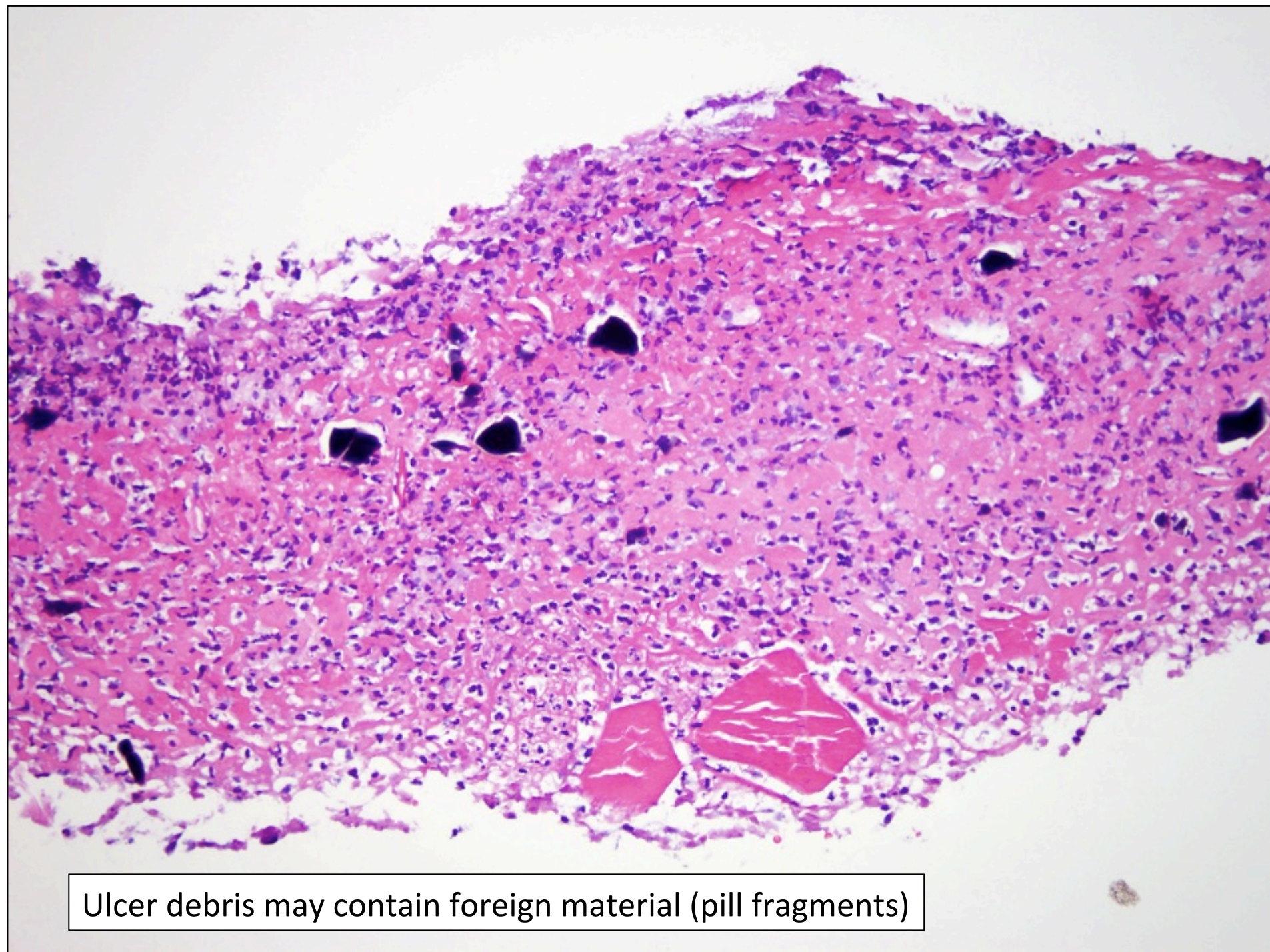
Patient was receiving doxycycline for acne treatment





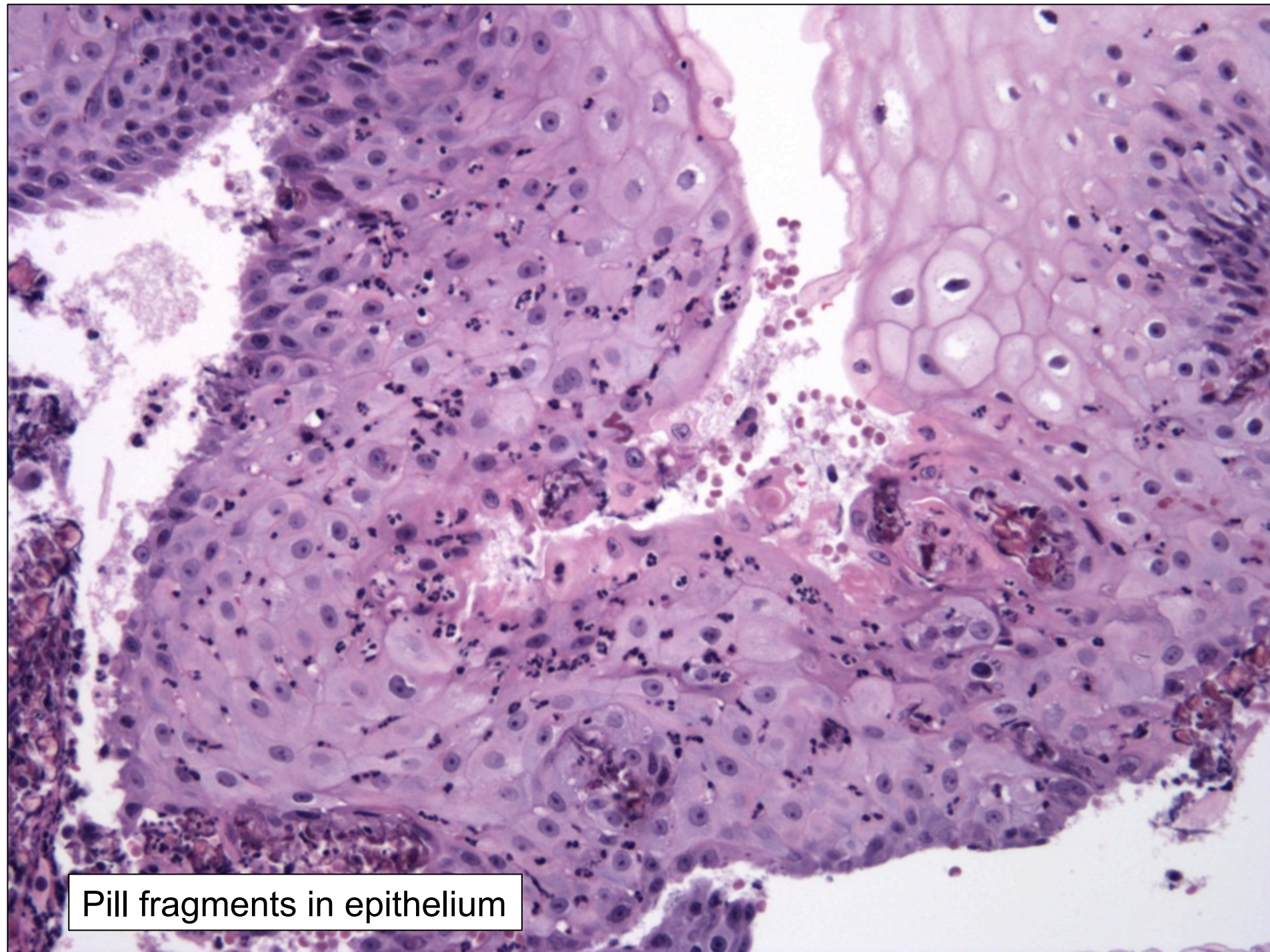
## PILL ESOPHAGITIS

- More common among older patients
- Sites of luminal narrowing (GE junction, extrinsic compression)
- Many medications can cause injury, but the big offenders are
  - Tetracyclines (treatment of acne)
    - Tetracycline, doxycycline, minocycline, oxytetracycline
  - Bisphosphonates (alendronate)
  - Iron
  - Kayexelate



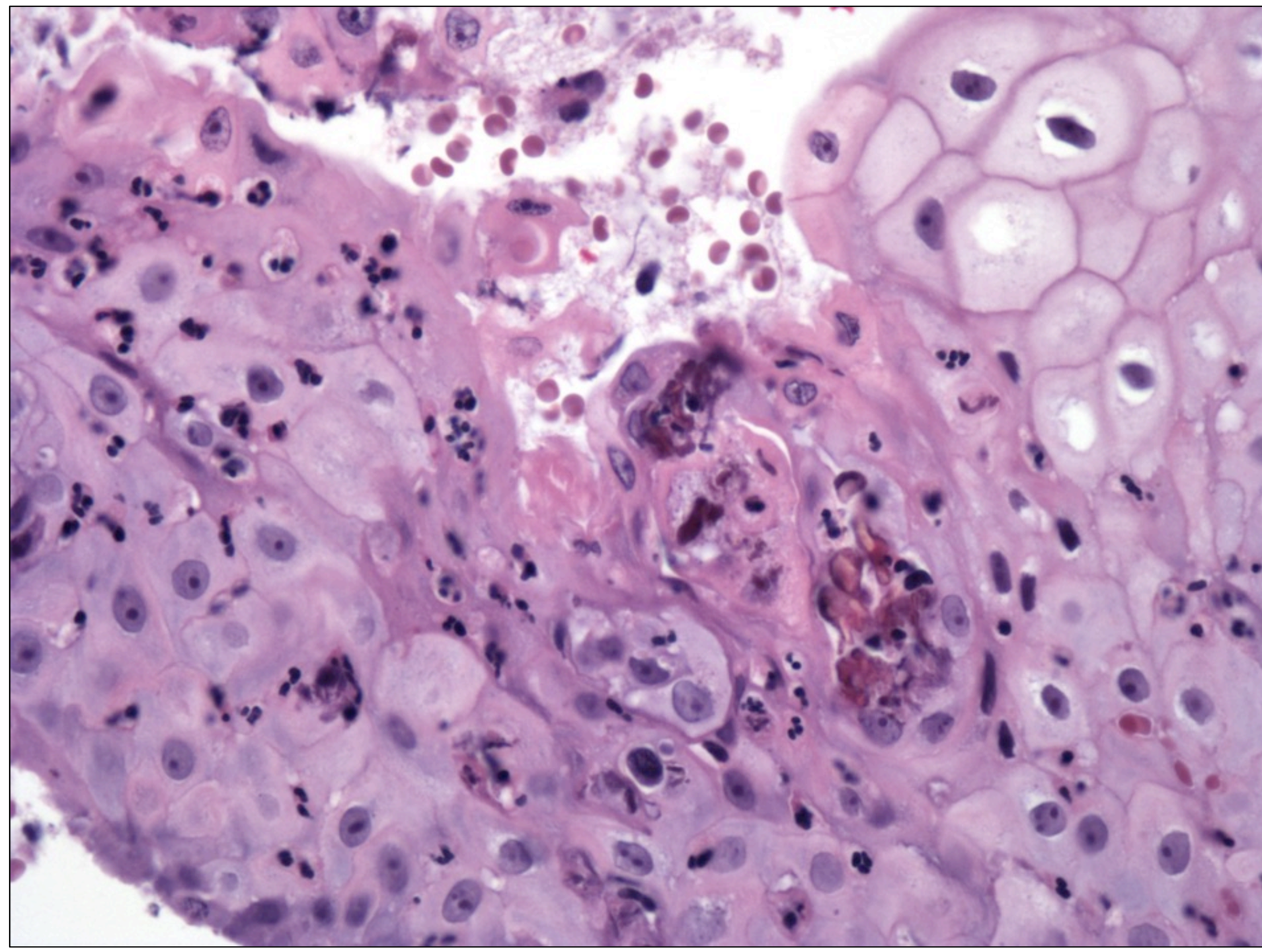
Ulcer debris may contain foreign material (pill fragments)



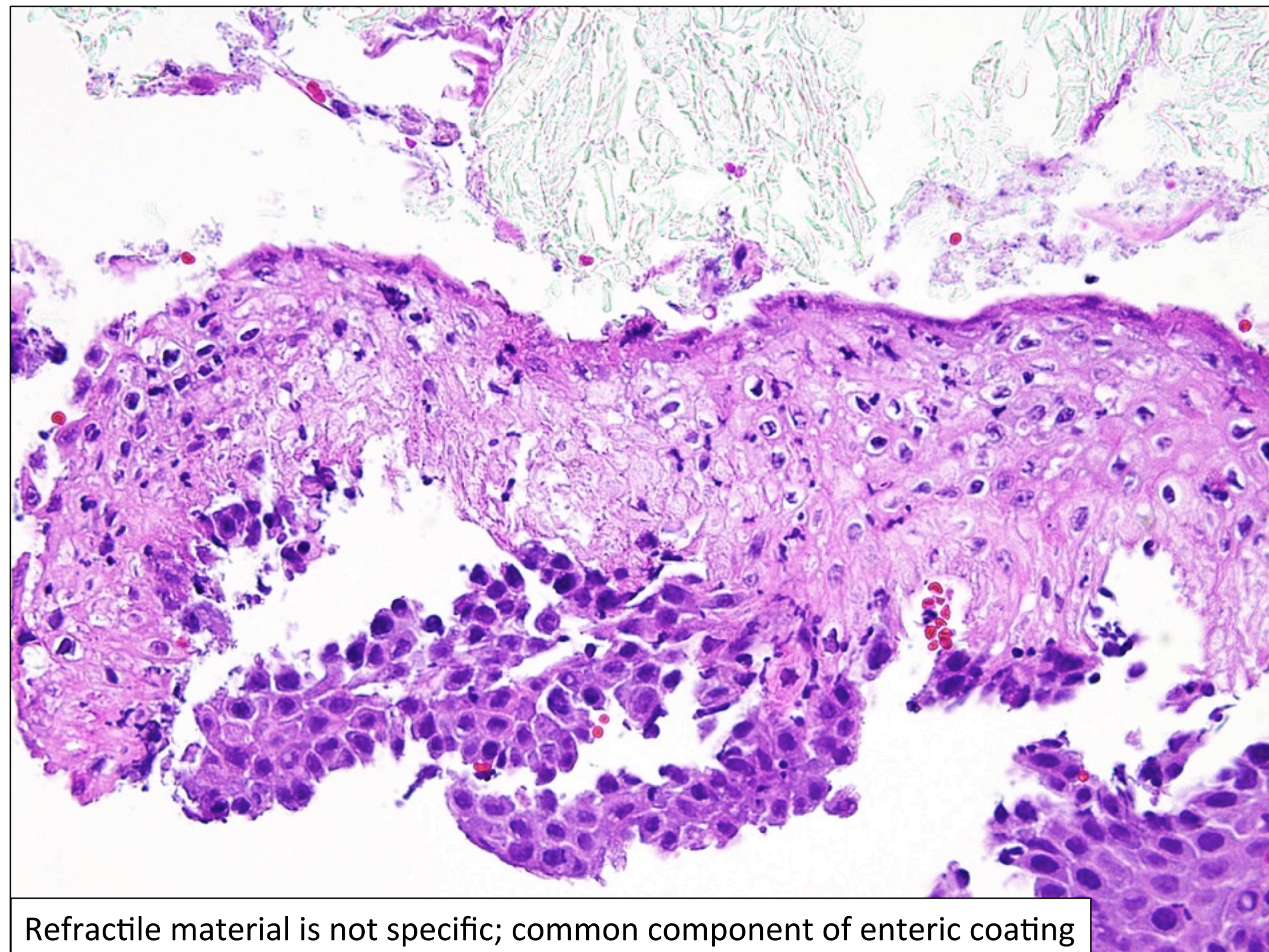


Pill fragments in epithelium



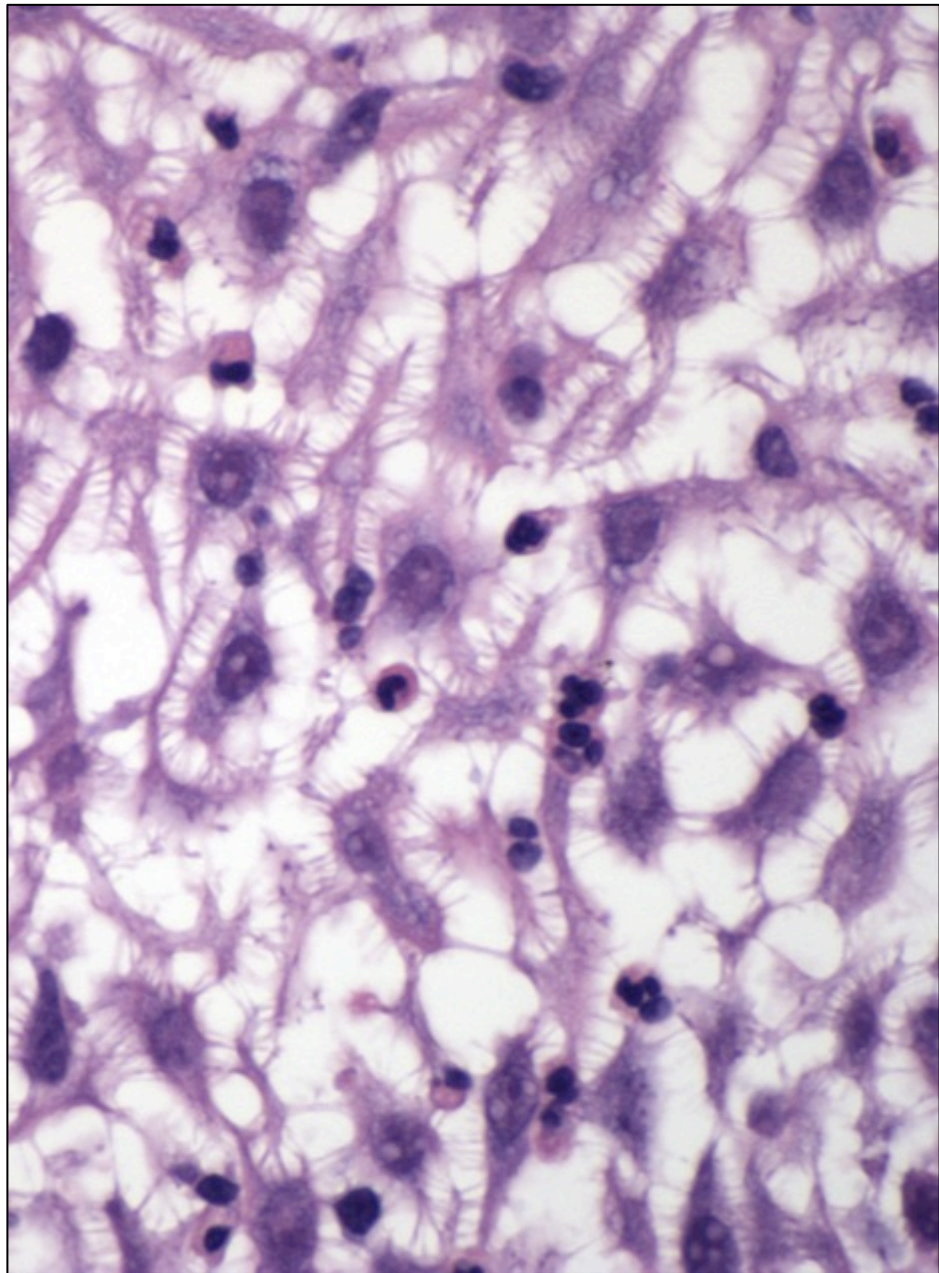
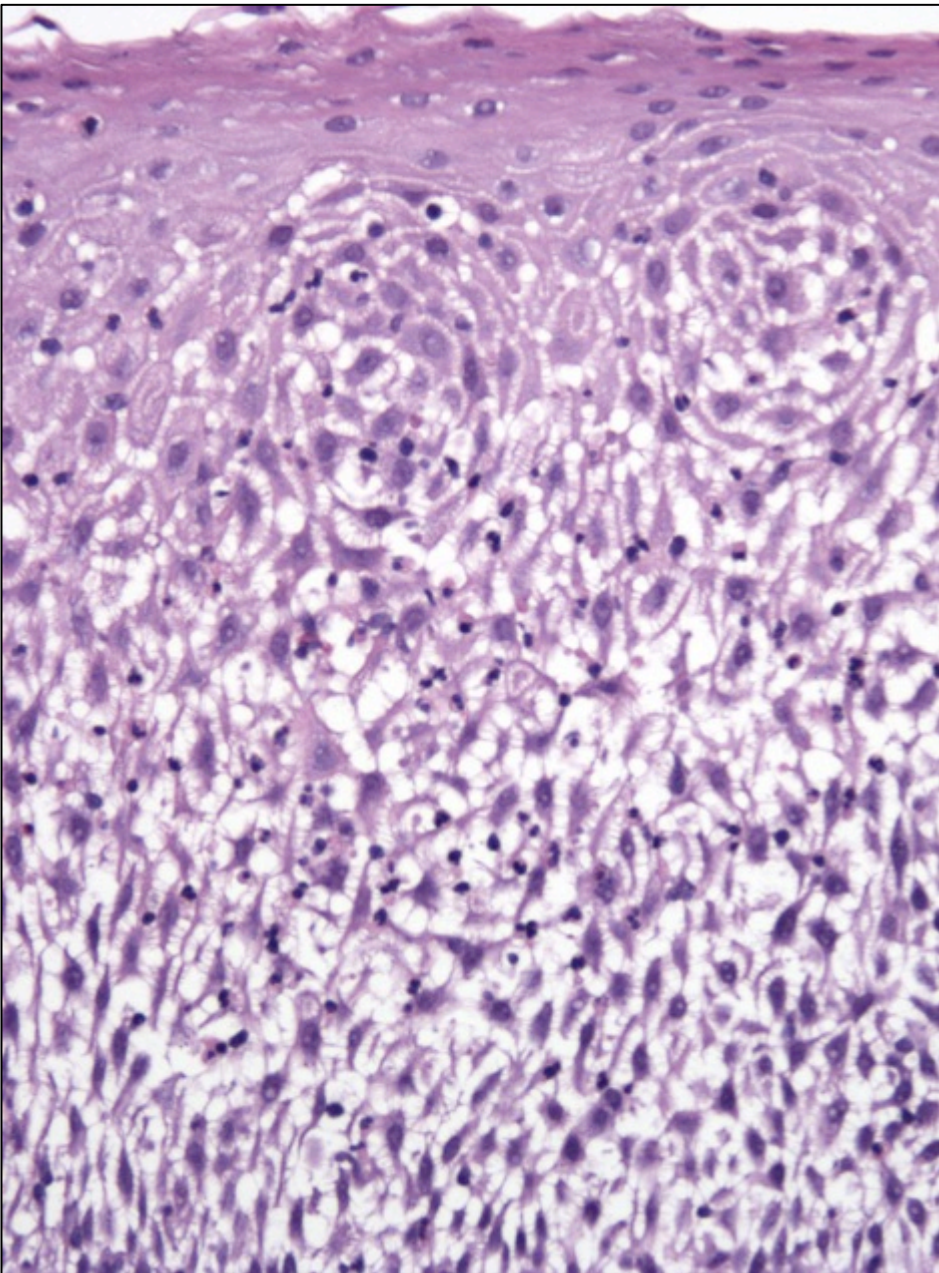






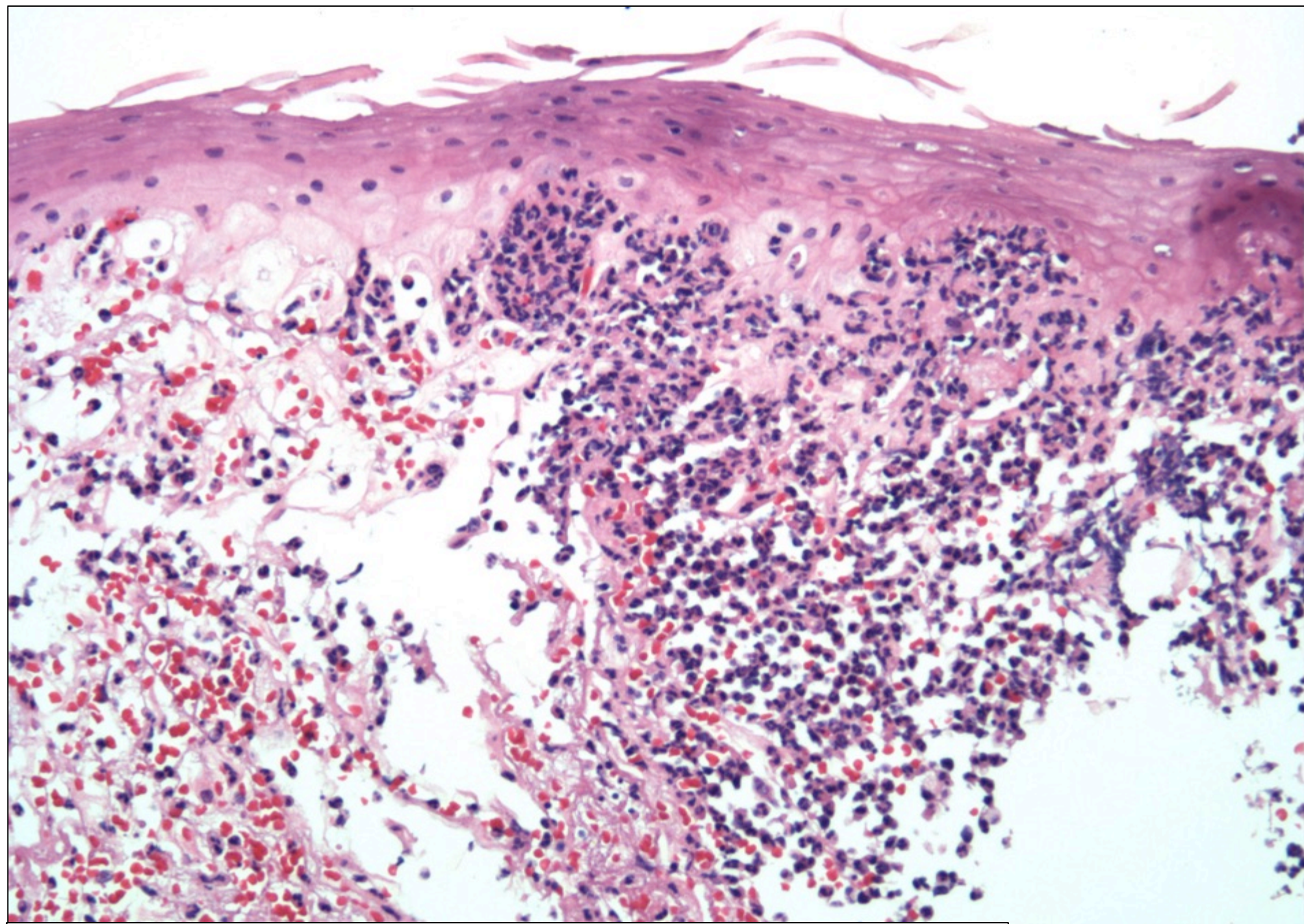
Refractile material is not specific; common component of enteric coating





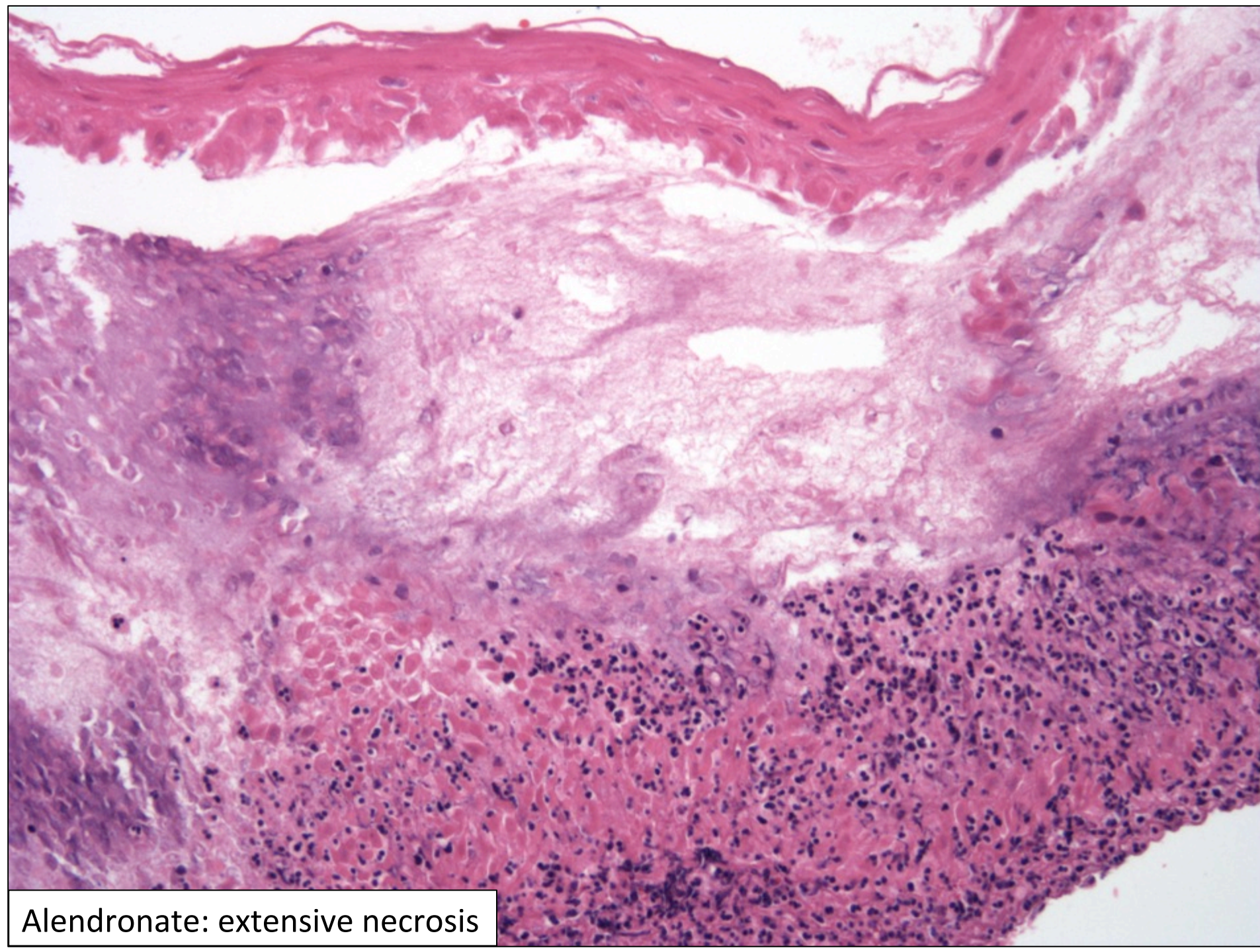
Tetracyclines: striking mucosal edema or bullae with neutrophils





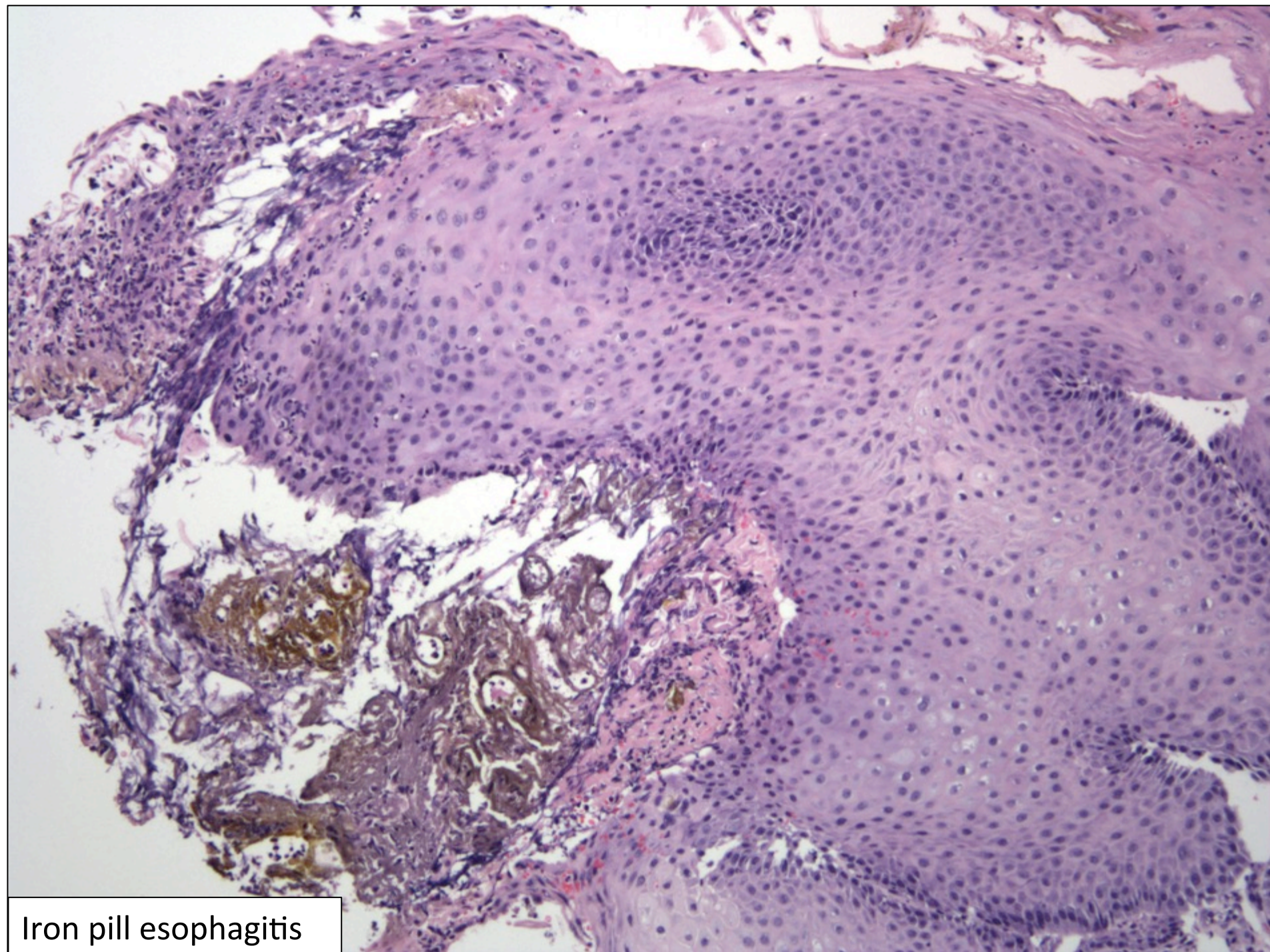
Tetracyclines: striking mucosal edema or bullae with neutrophils





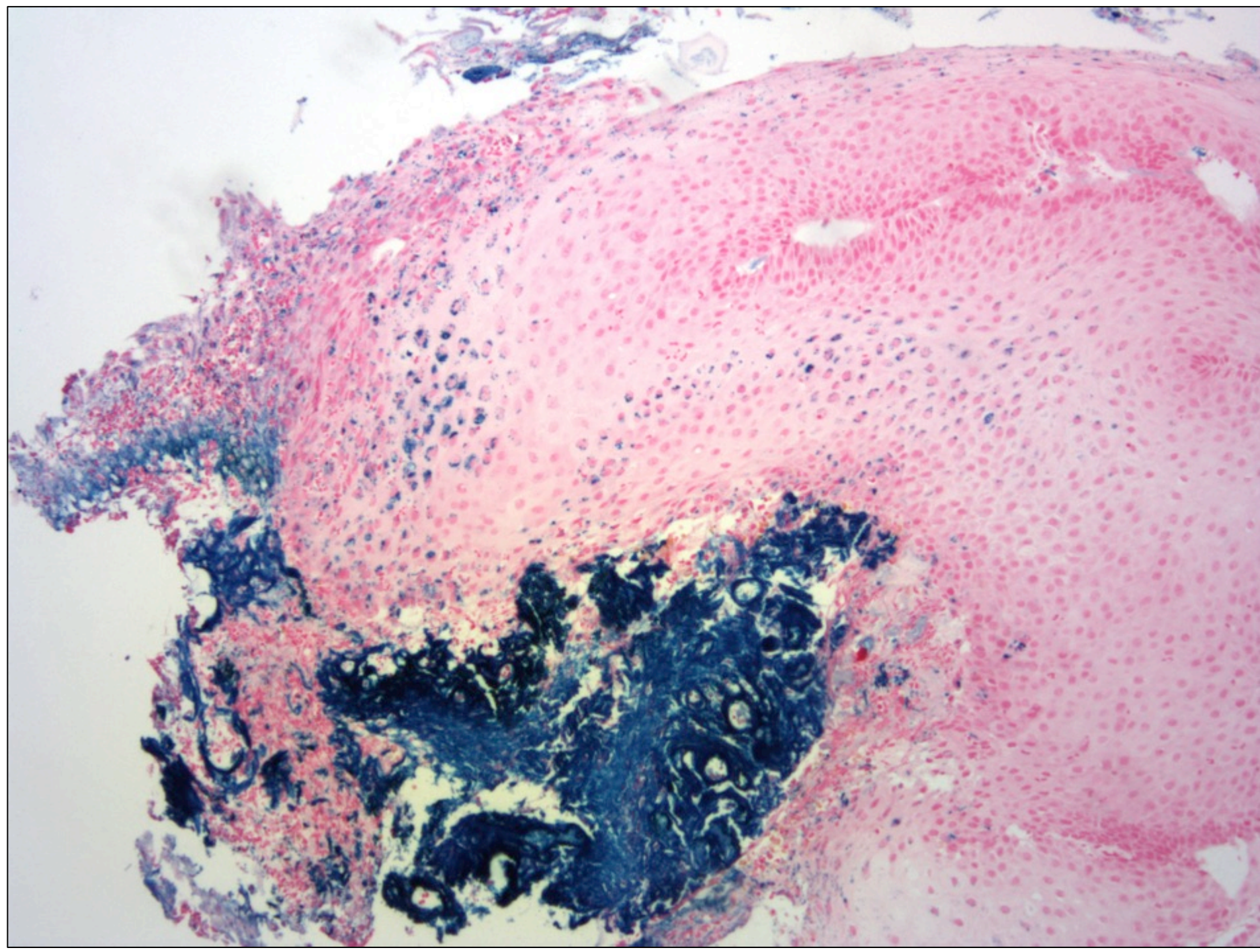
Alendronate: extensive necrosis



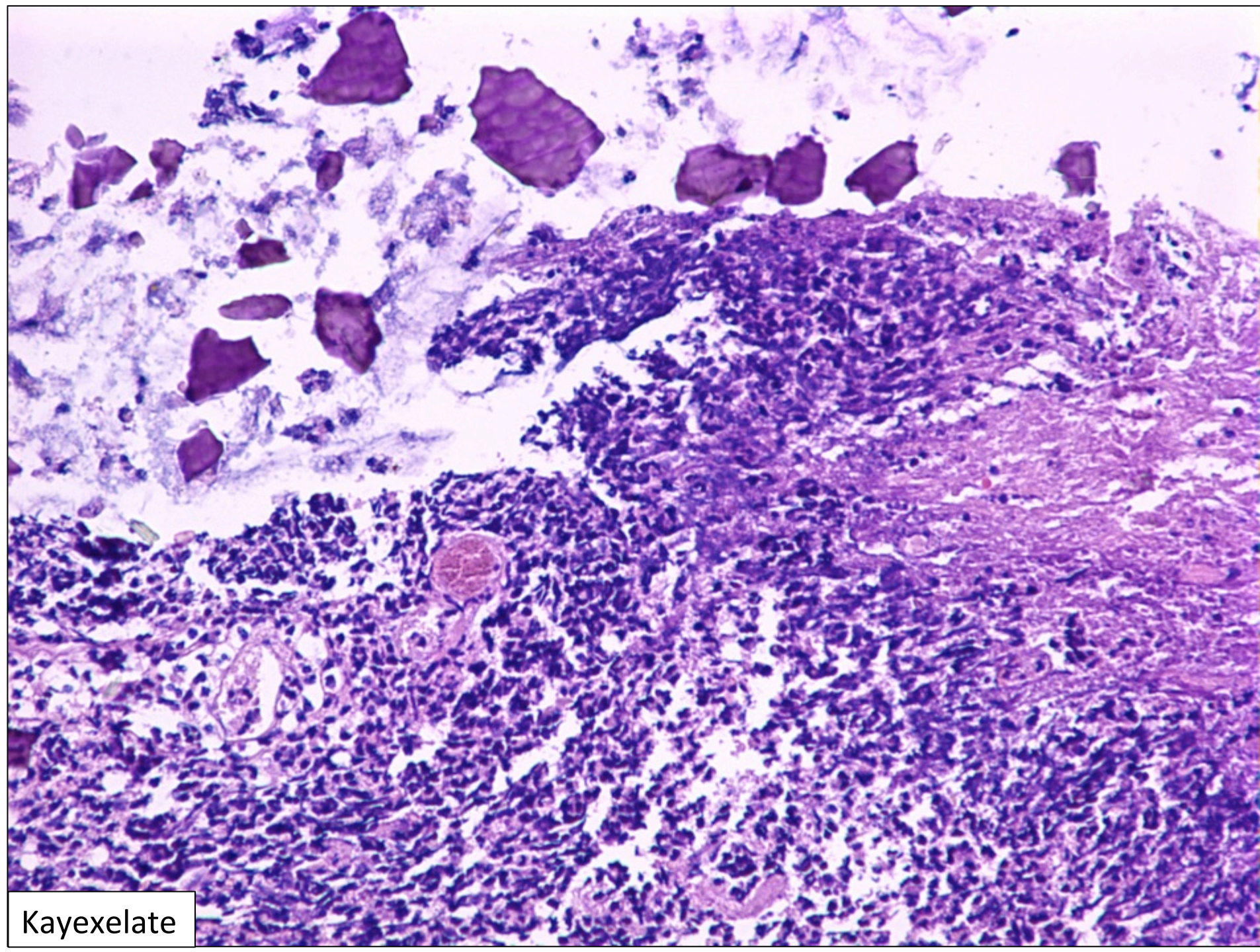


Iron pill esophagitis



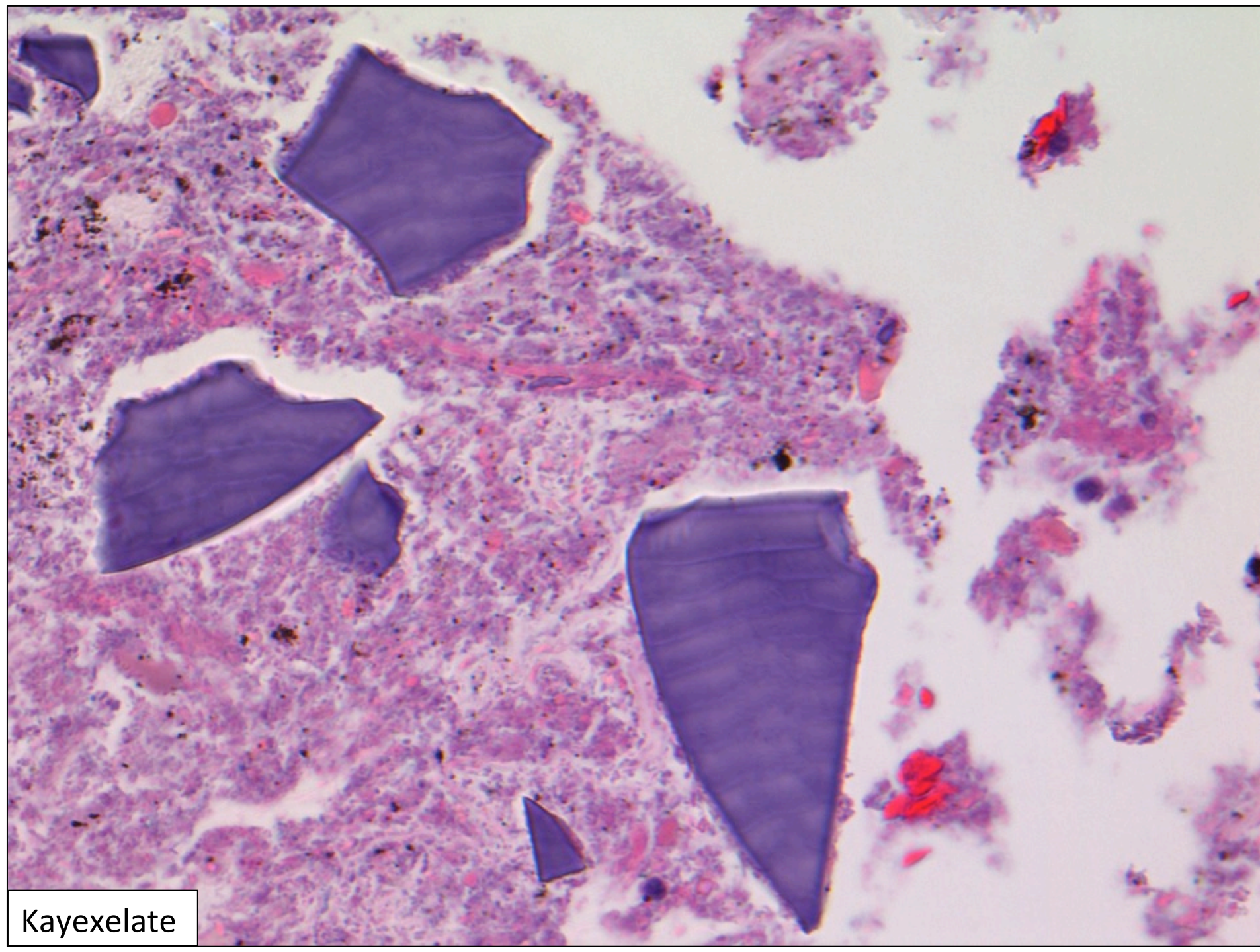






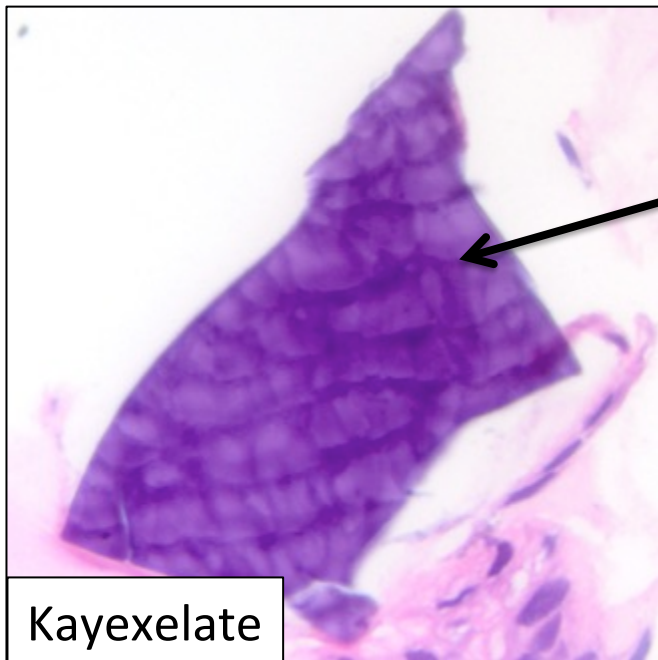
Kayexelate





Kayexelate

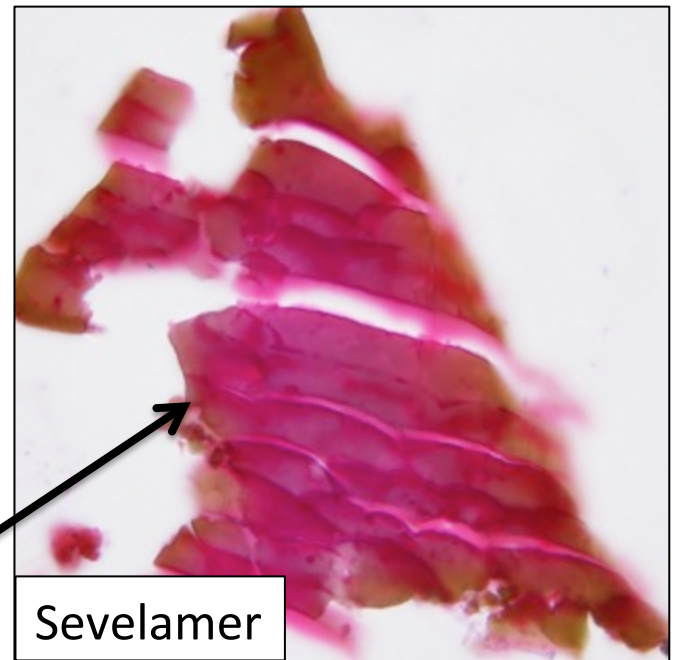




Kayexelate

“Fish scales”  
Purple, jagged

Pink with yellow edge  
“two-toned”  
Cracked scales

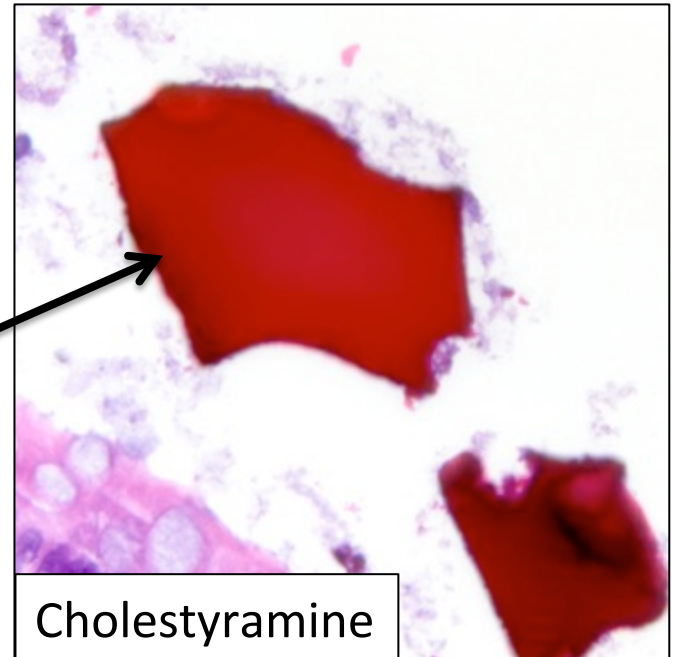


Sevelamer



None of these

Bright red, purple  
No internal structure



Cholestyramine





## MEDICATION-RELATED ESOPHAGEAL INJURY

- Consider a drug injury when
  - Foreign material is embedded in inflammatory foci (recognize kayexelate and iron)
  - Mucosal necrosis
  - “Bottom heavy” pattern of injury with edema and inflammation (neutrophils)
  - Disease is discontinuous with gastroesophageal junction
  - Ulcers in mid/upper esophagus





## LESS COMMON CAUSES OF ESOPHAGITIS TAKE HOME POINTS

- Diverse types of injury can produce similar histologic changes
- Clues to classification
  - Distribution of injury in mucosa
  - Nature of inflammatory infiltrate
  - Severity of epithelial injury
- Correlation with clinical history, medication list, and endoscopy
- The best ancillary test is often a phone call



