

**UAB** MEDICINE

Knowledge that will change your world

**Transurethral Resections of Bladder**  
*Diagnostic Pitfalls and Mimickers*

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**University of Alabama at Birmingham**

# **Mimickers of Bladder Carcinoma**



# Mimickers of Bladder Carcinoma

- Benign Mimickers of Urothelial Carcinoma
- Benign Mimickers of Bladder Adenocarcinoma

- Malignant Mimickers of Urothelial Carcinoma
- Malignant Mimickers of Bladder Adenocarcinoma

## Benign Mimickers of Urothelial Ca

- Reactive urothelial atypia
- Polypoid/Papillary Cystitis
- X-Ray Rx/Chemo Rx Induced Changes
  - Radiation Atypia
  - Intravesical ChemoRx
  - Systemic ChemoRx: Cytosan
  - Pseudocarcinomatous Hyperplasia

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# Polypoid/Papillary Cystitis

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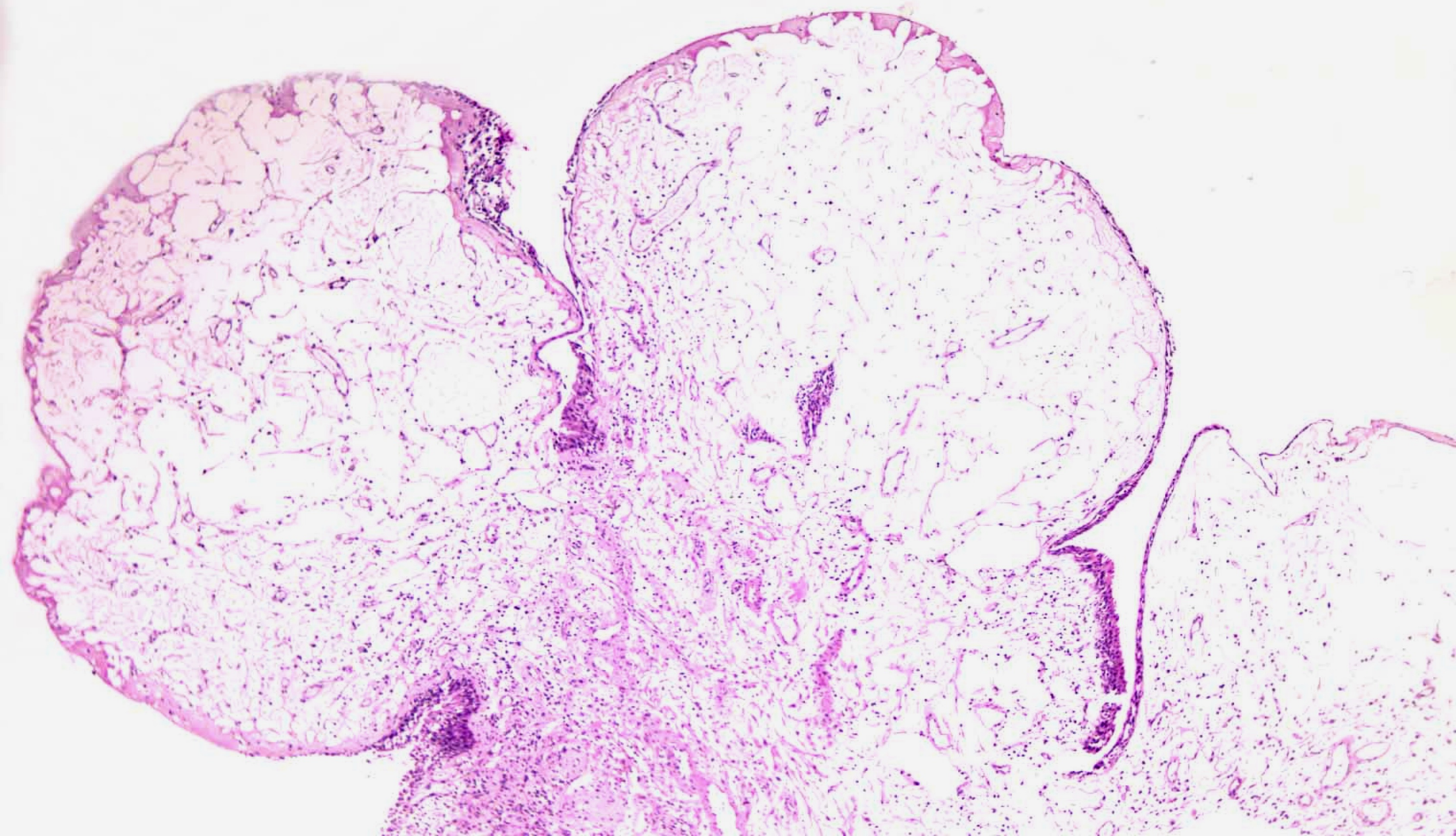
- Reaction to **injury**
- Indwelling catheters, fistula, abscess, long-standing urinary obstruction
- Often recognized as **inflammatory by urologist** at cystoscopy: bullous, polypoid, papillary

# Polypoid/Papillary Cystitis

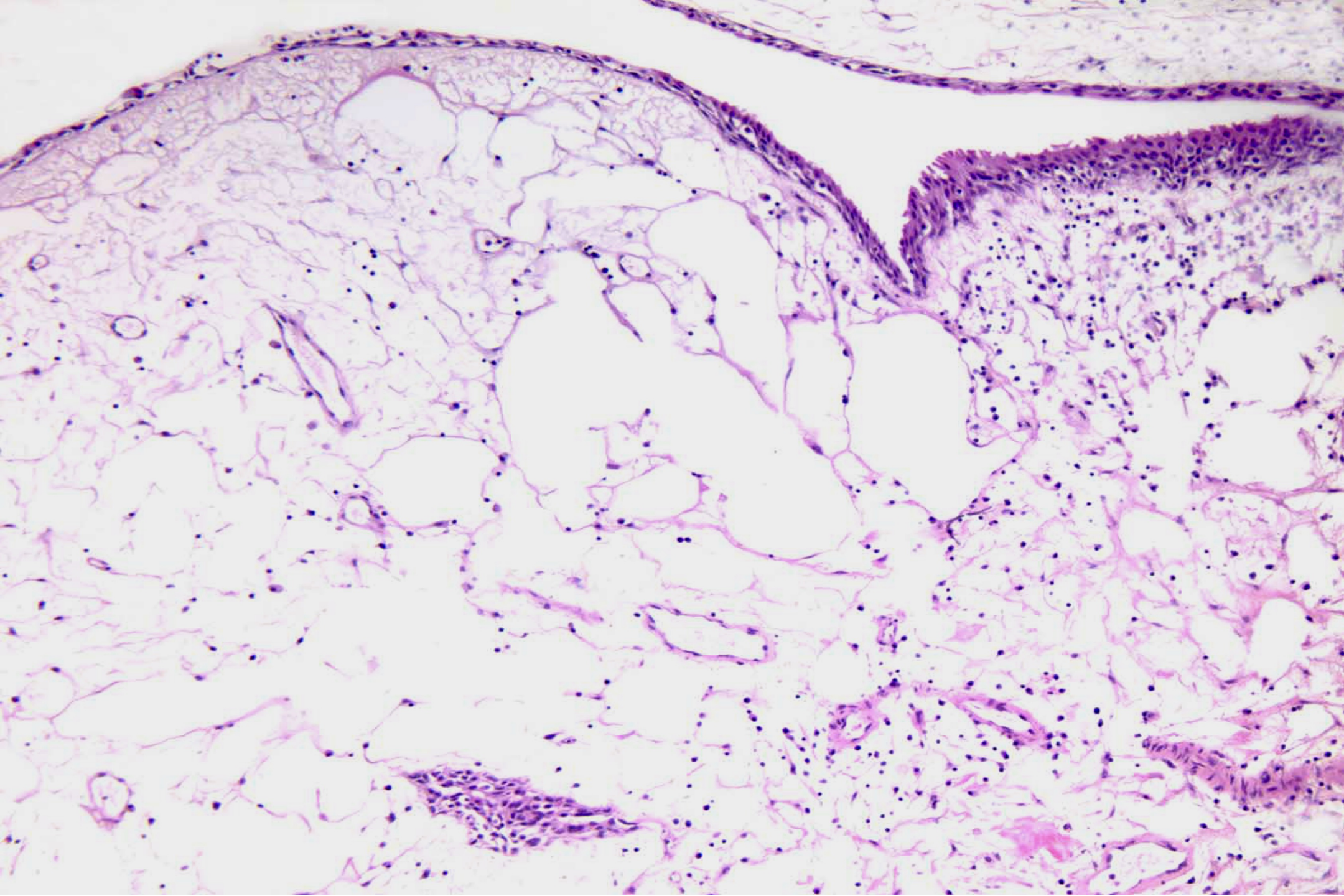
*Lane, Z et al. Am J Surg Pathol 2008*

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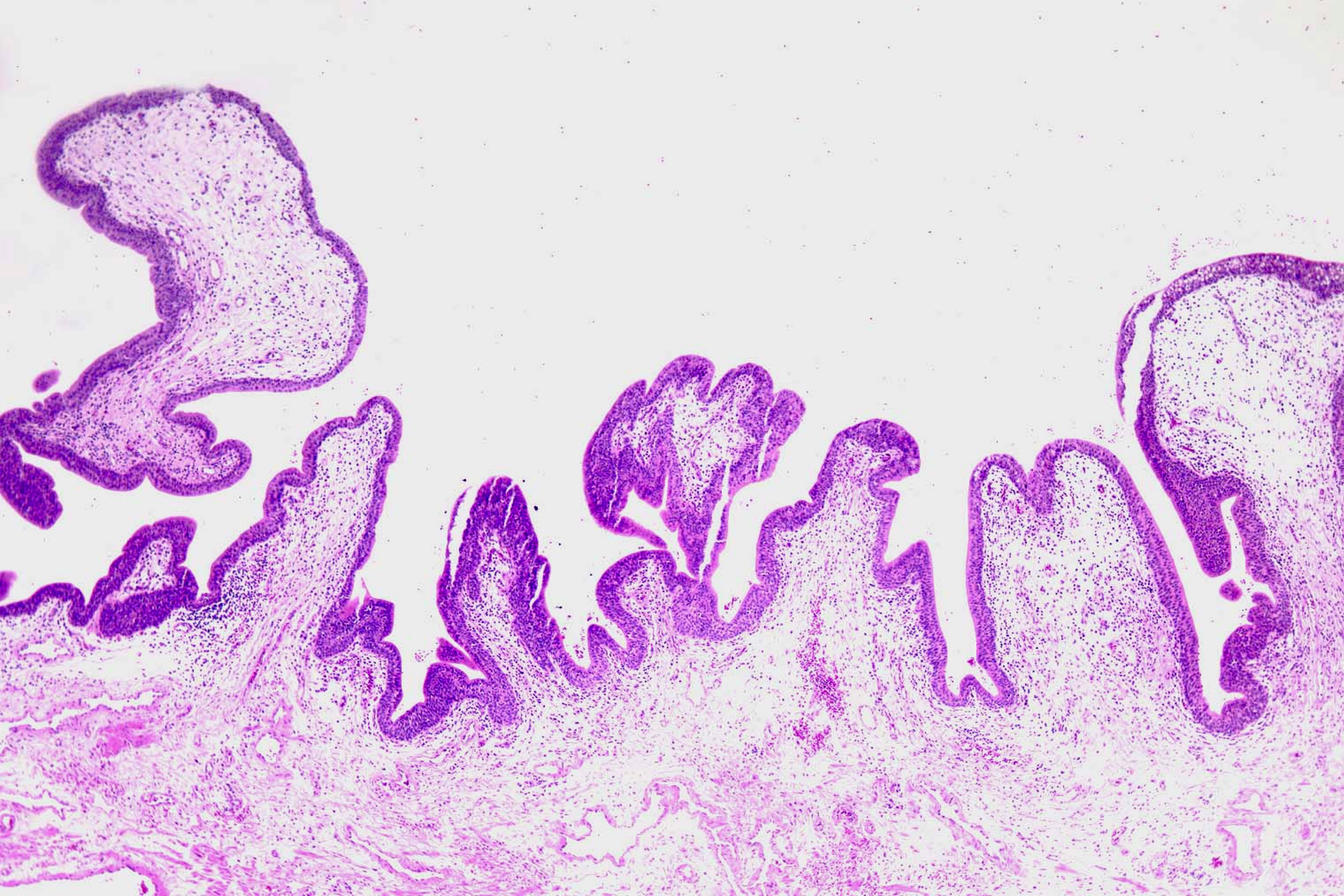
- 41/ 155 cases **misdiagnosed as UrCa** (2000-2007)
- Prior Hx: Stent, radiation Rx, fistula etc..
- The key to Dx is **low magnification** impression of reactive lesion
- **Inflamed** background: **edematous** or densely fibrous
- Predominantly **simple, non-branching**, broad-based fronds
- Relatively normal thickness urothelium
  
- ? polypoid cystitis     $\Rightarrow$  clinical history and cystoscopy impression that might suggest a reactive process.



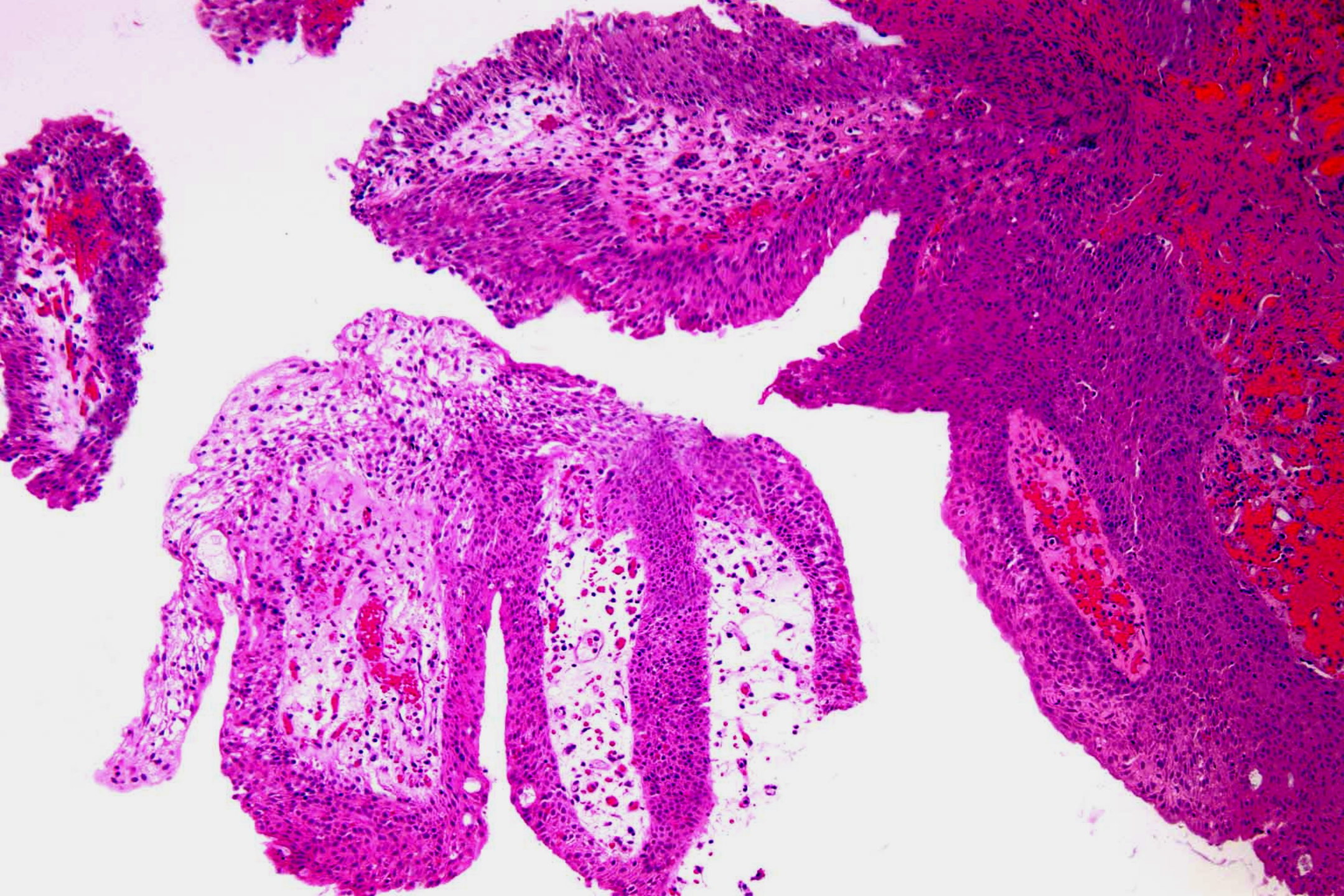




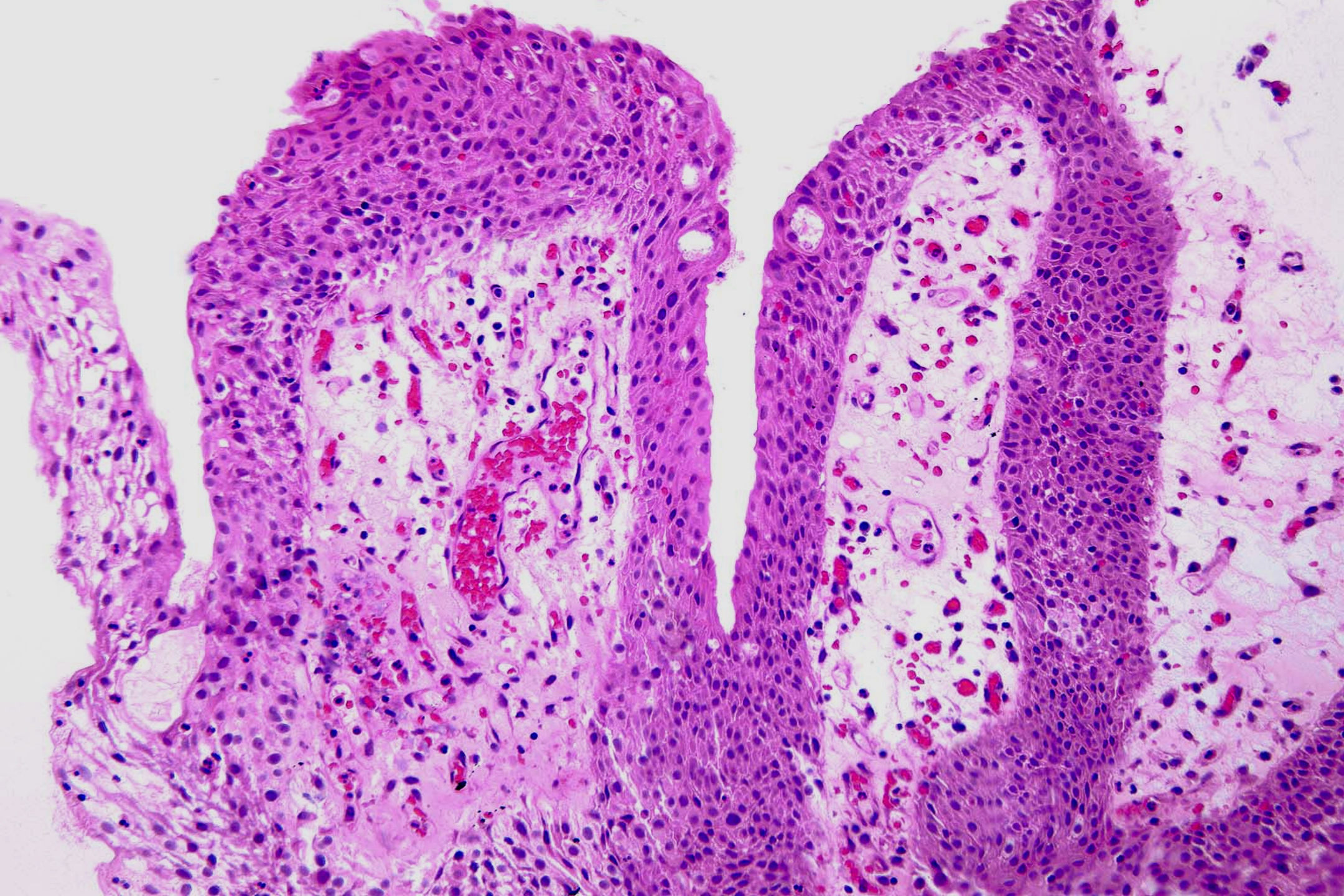




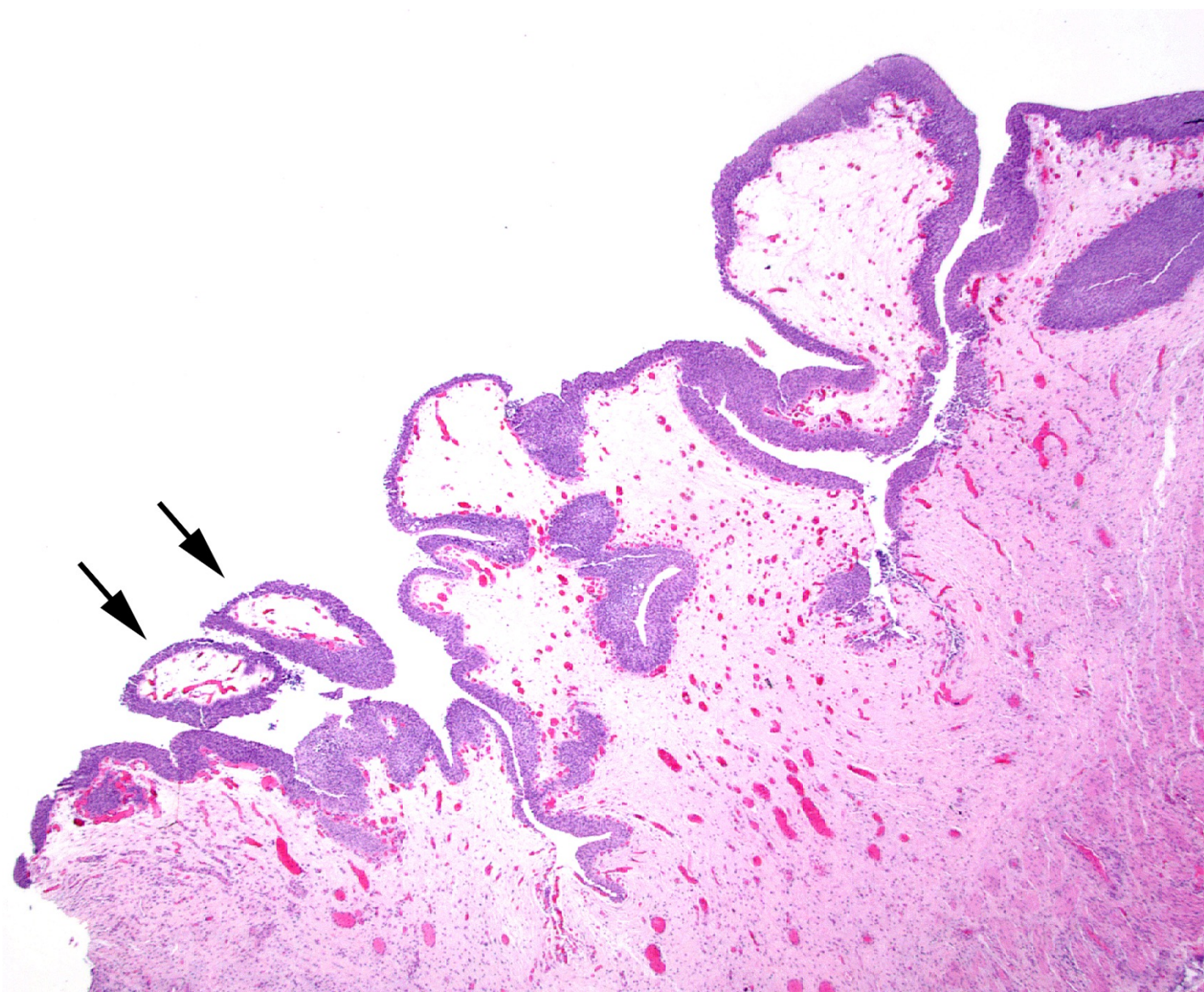




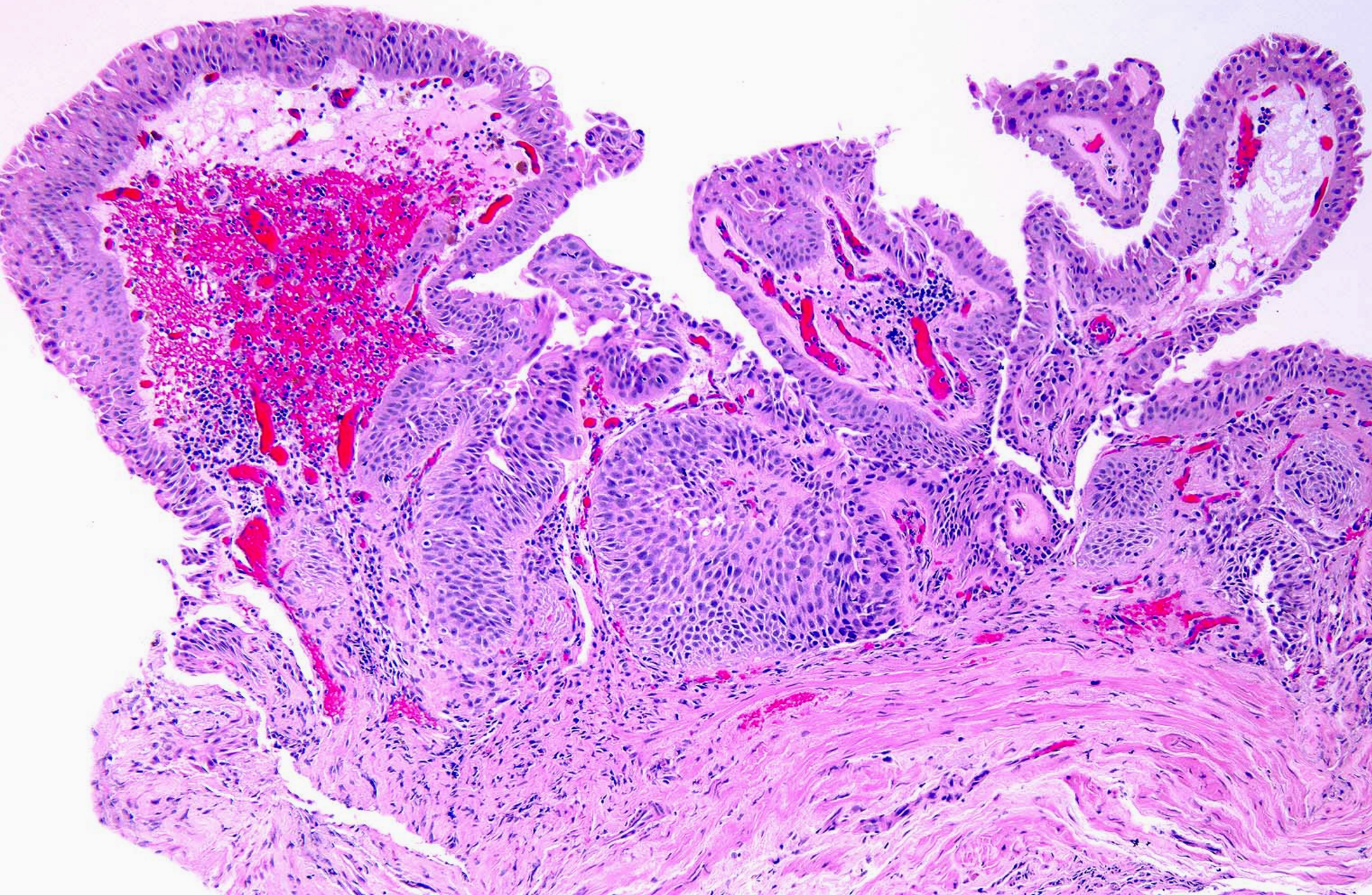














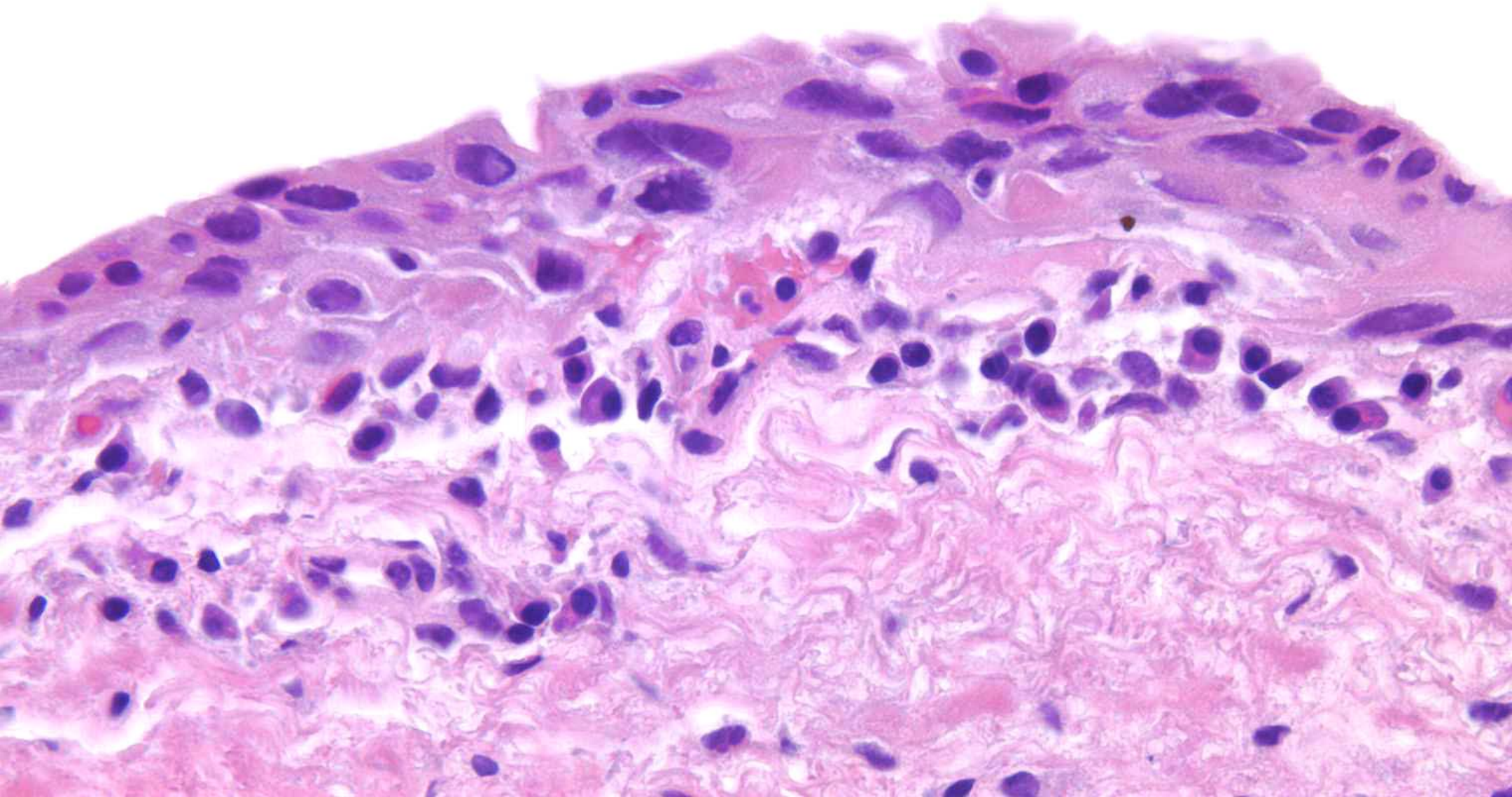
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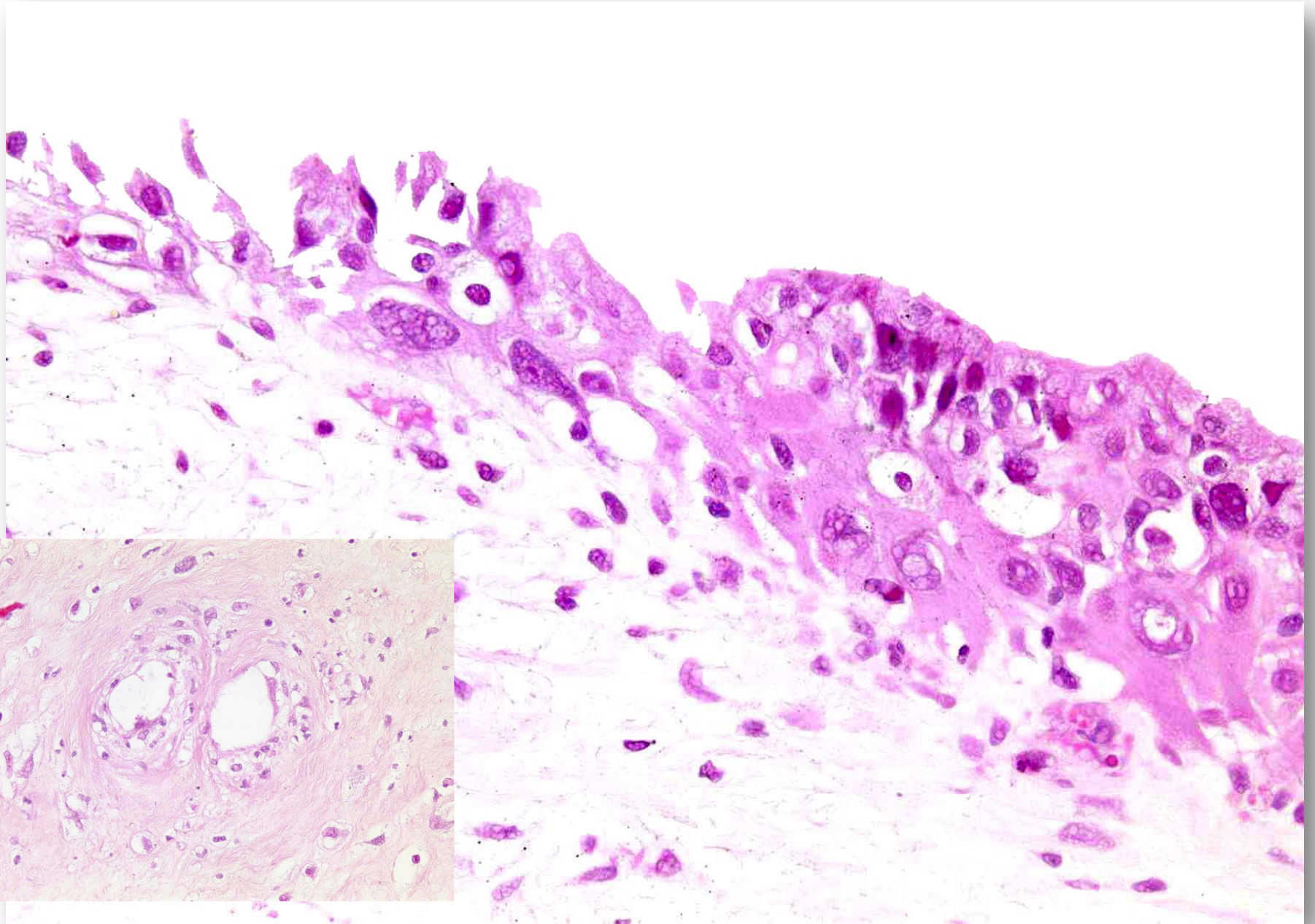
# Radiotherapy Induced Urothelial Atypia

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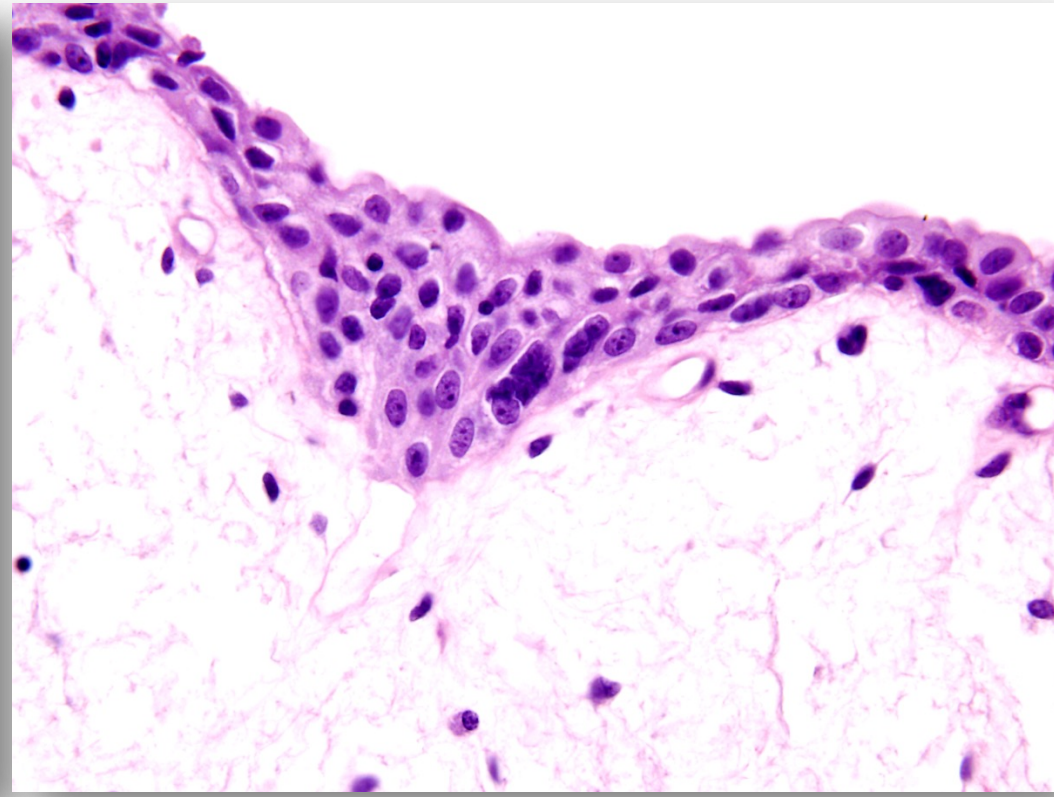
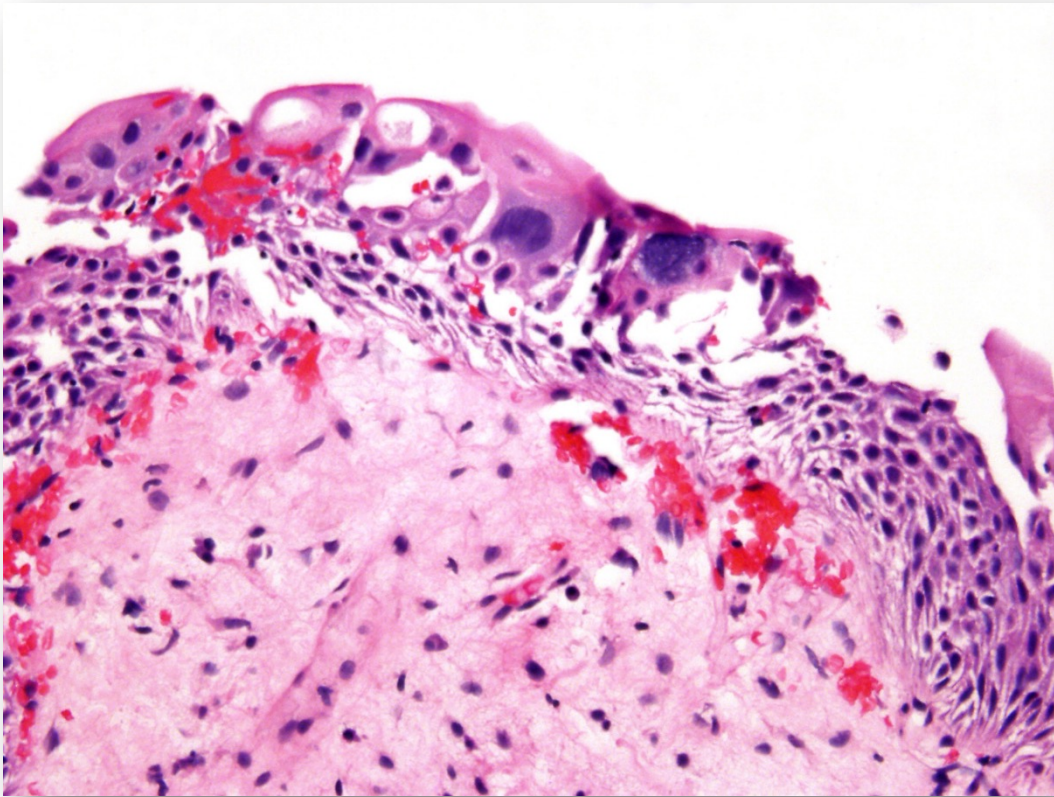
- Urothelial cell **enlargement**, **multinucleation**, and **smudgy/degenerative chromatin** pattern **vacuolization** with maintenance of abundant cytoplasm.
- Just because there is urothelial atypia with a history of radiotherapy, one cannot discount the **possibility of CIS**, as radiation is also associated with an increased risk of bladder cancer. **Mitotic figures** are more consistent with CIS.
- Atypia persisting **over 12 months** following radiation? R/O neoplastic lesion

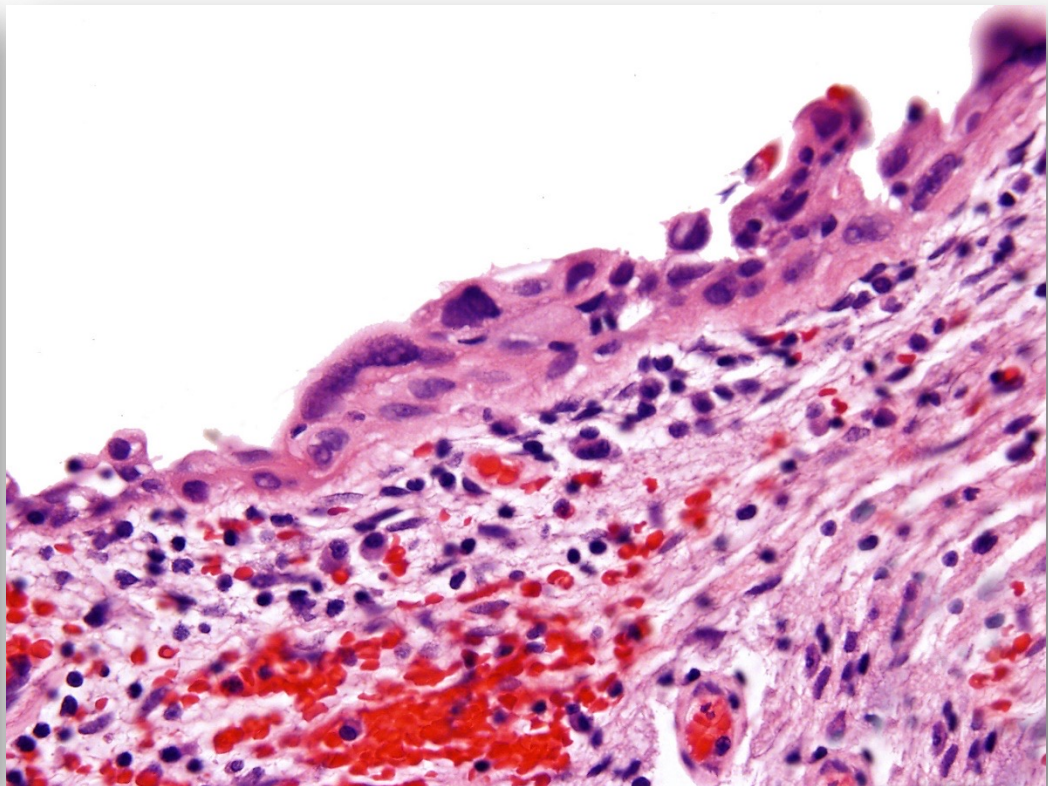
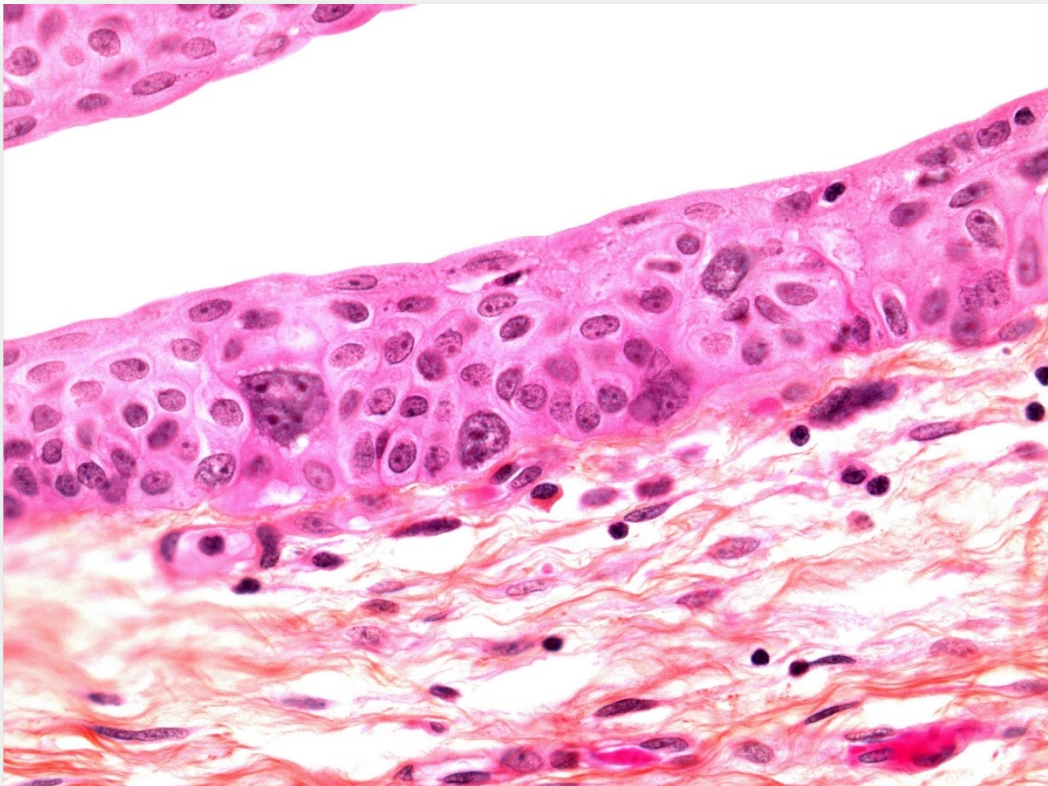












## Pseudocarcinomatous Hyperplasia of Bladder

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- Less familiar to pathologists is “radiation-induced pseudocarcinomatous hyperplasia”.
- ***Baker and Young in 2000***: first series (4 pts) to report this benign mimicker of invasive urothelial carcinoma.

# Pseudocarcinomatous Hyperplasia

*Chan, T. et al. Am J Surg Pathol 2004*

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- 20 bladder cases; either **radiation or chemotherapy** induced
- All 17 cases where follow-up available had **benign clinical course**
- All patients presented with **hematuria**
  
- Pts: 80% male; mean age 69.
  
- The mean interval from radiation 27 months. longest 79 months.



# Prior Therapy ?

## ***Chan et al. Am J surg Pathol 2004***

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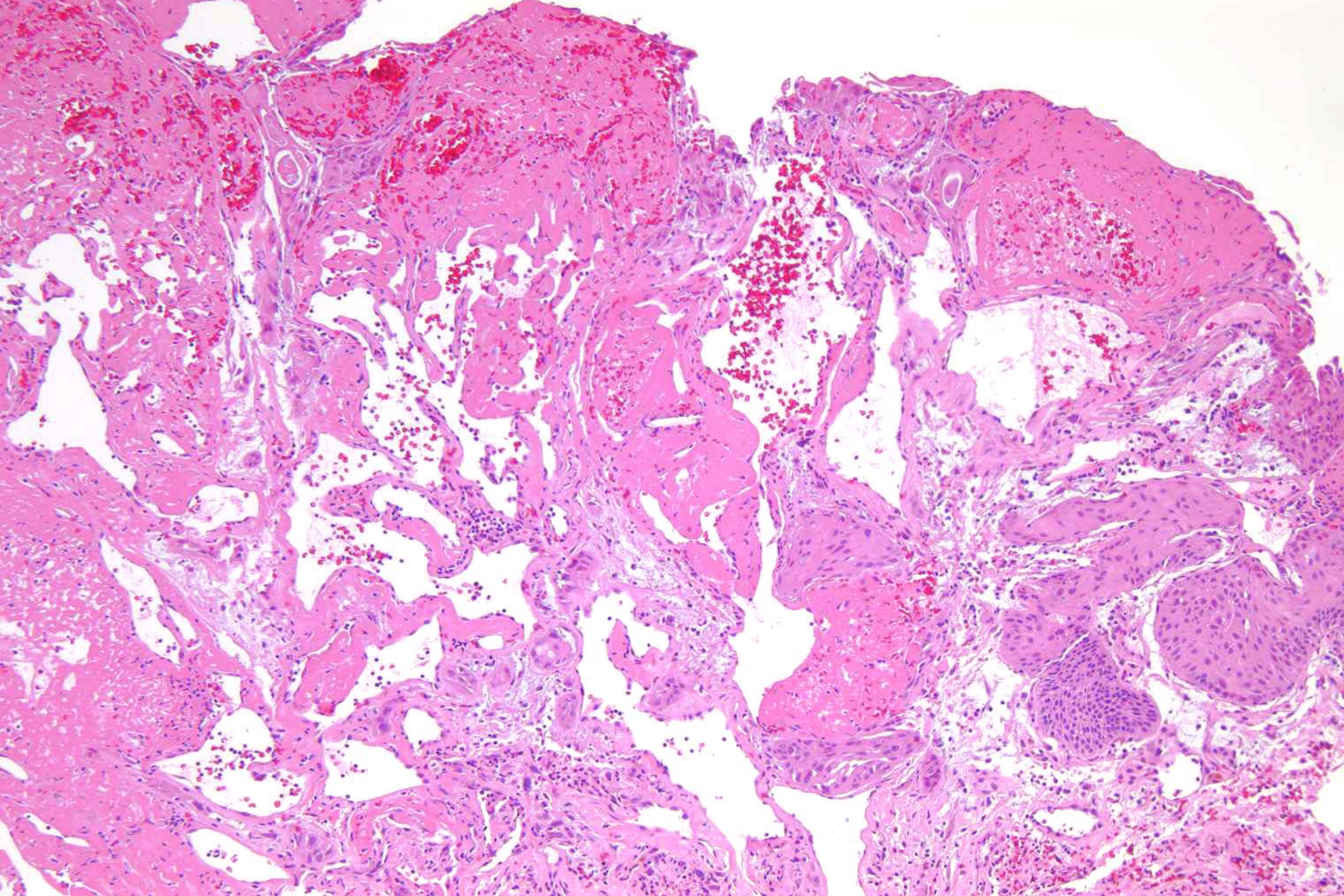
- Pelvic irradiation
  - 15 Prostate cancer
  - 2 Endometrial cancer
- Systemic chemotherapy
  - 1 Metastatic colon cancer
  - 1 Mixed connective tissue Dz
- Unknown
  - 1 Laryngeal cancer.

## ***Lane, Z et al. Am J Surg Pathol 2008***

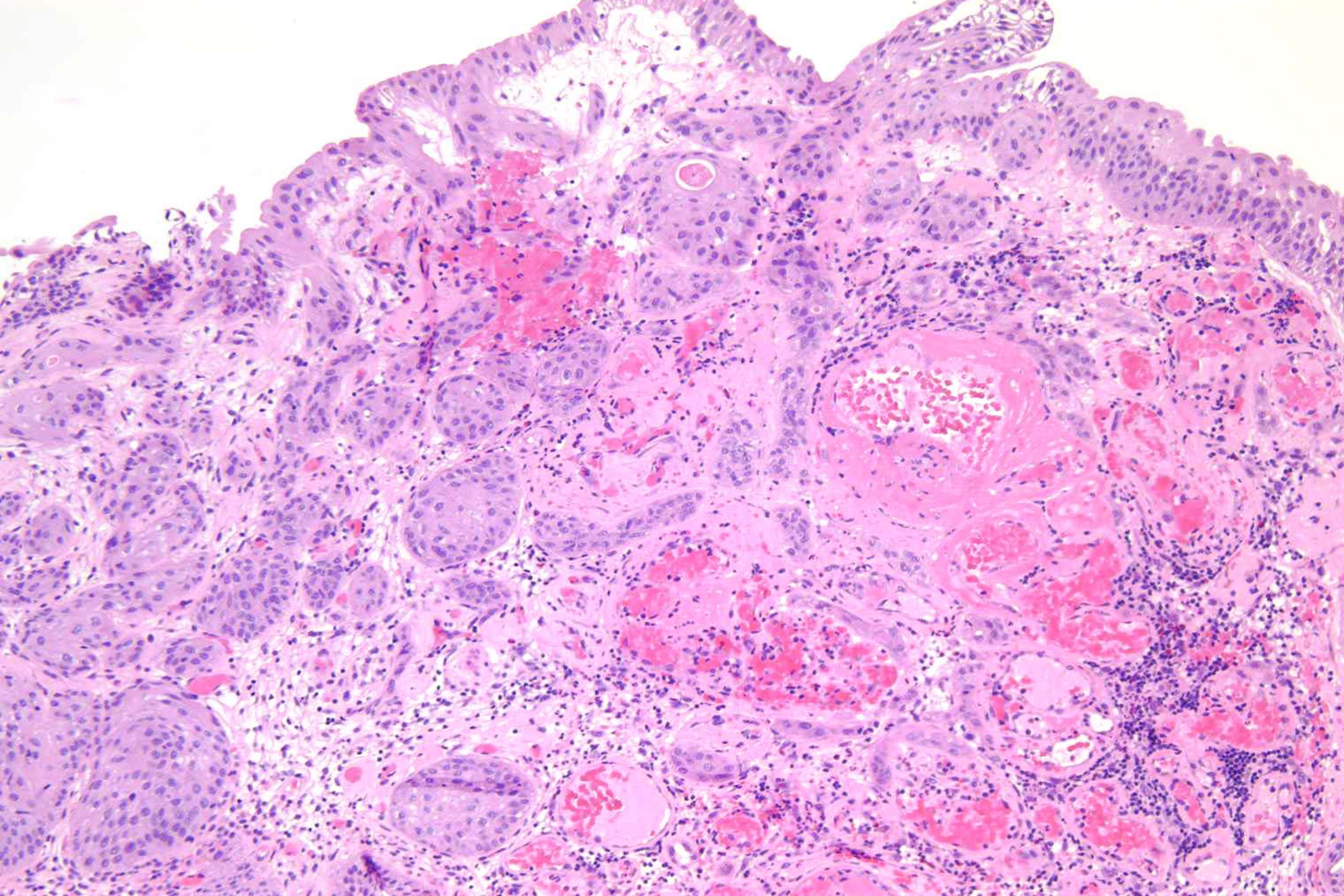
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- All 8 cases without prior X-Ray or ChemoRx
- Atrial fibrillation, hypertensionsion, hyperlipidemia, AVM of bladder, Recent GI bleeding, UB catheterization

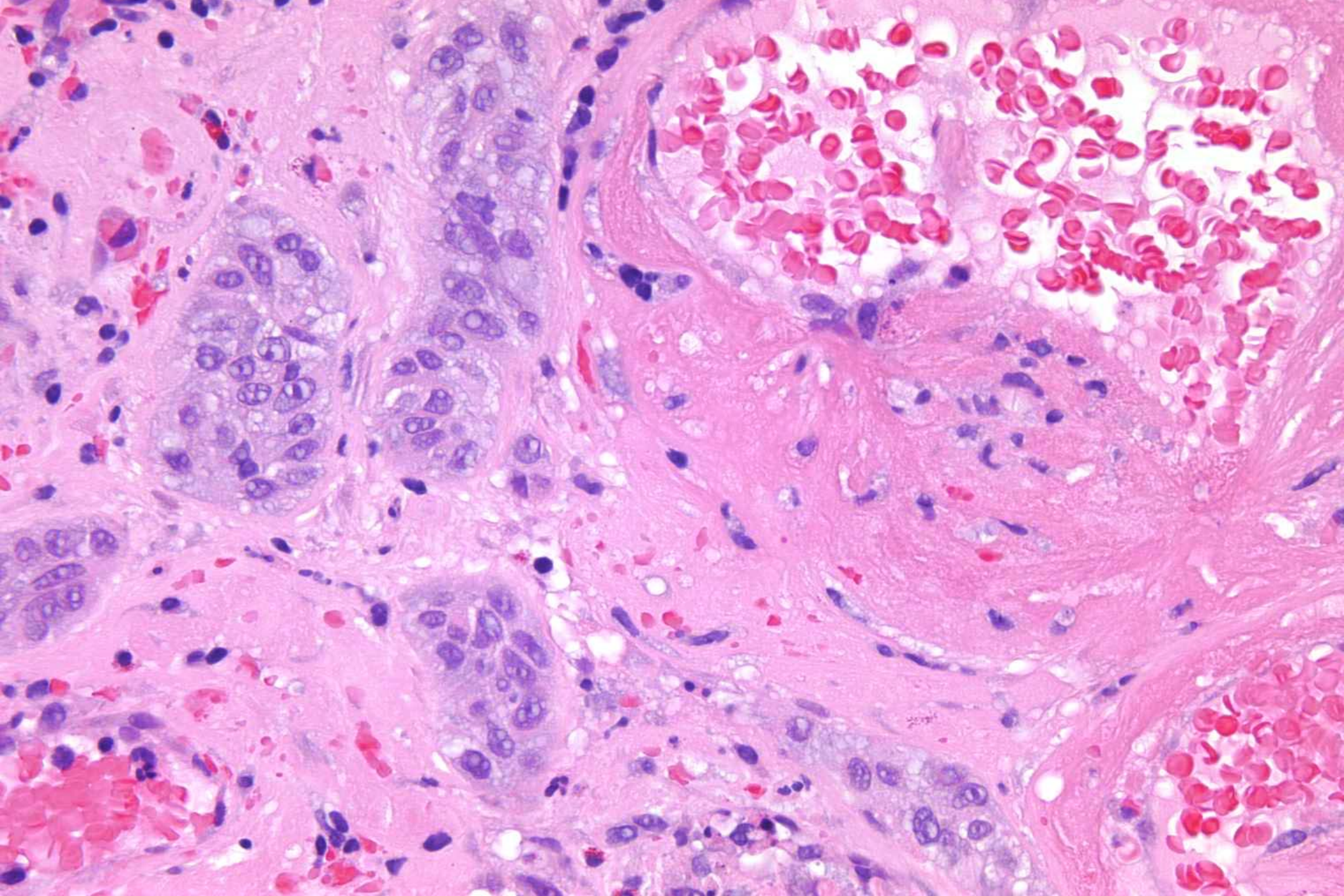




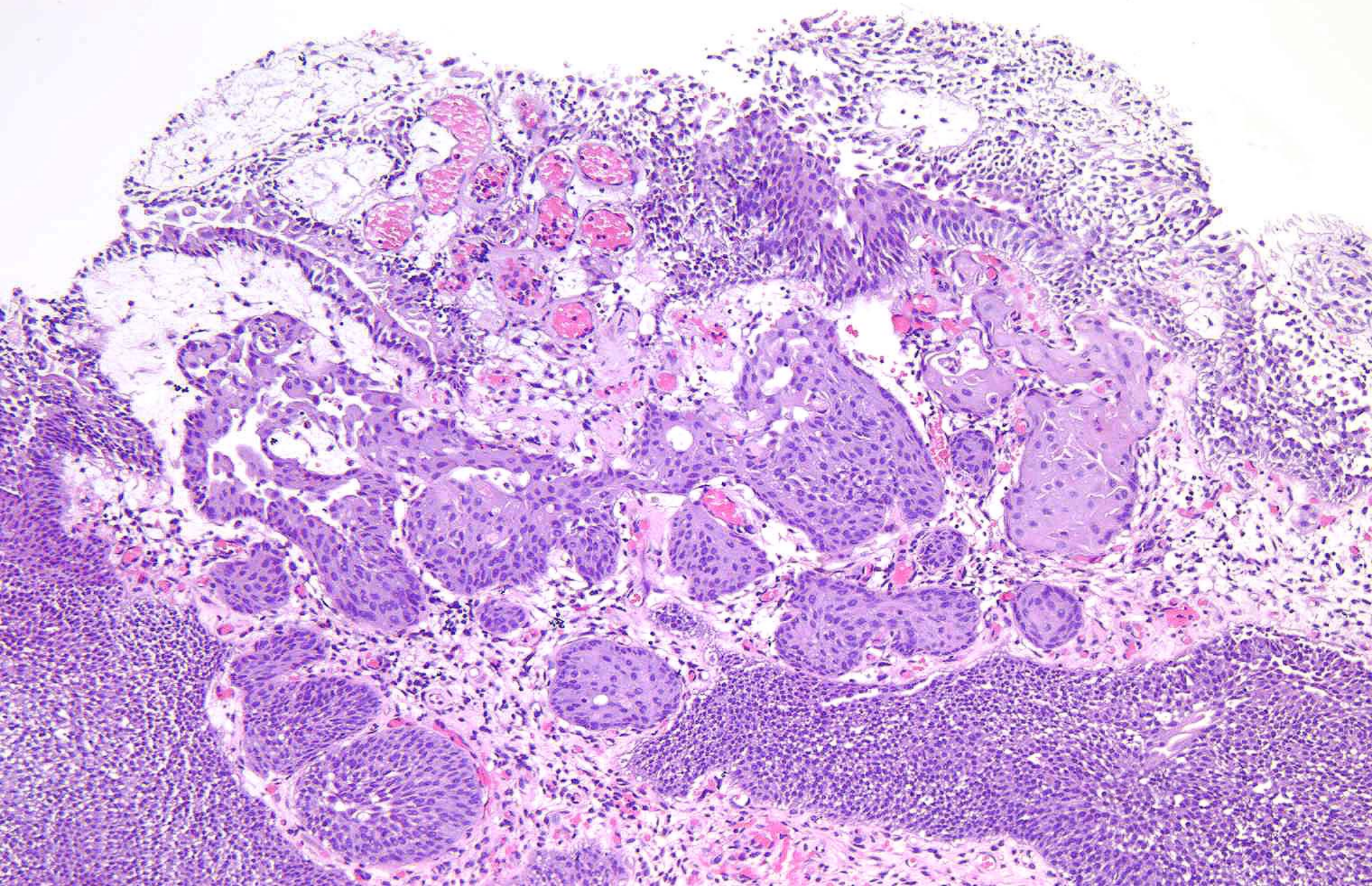




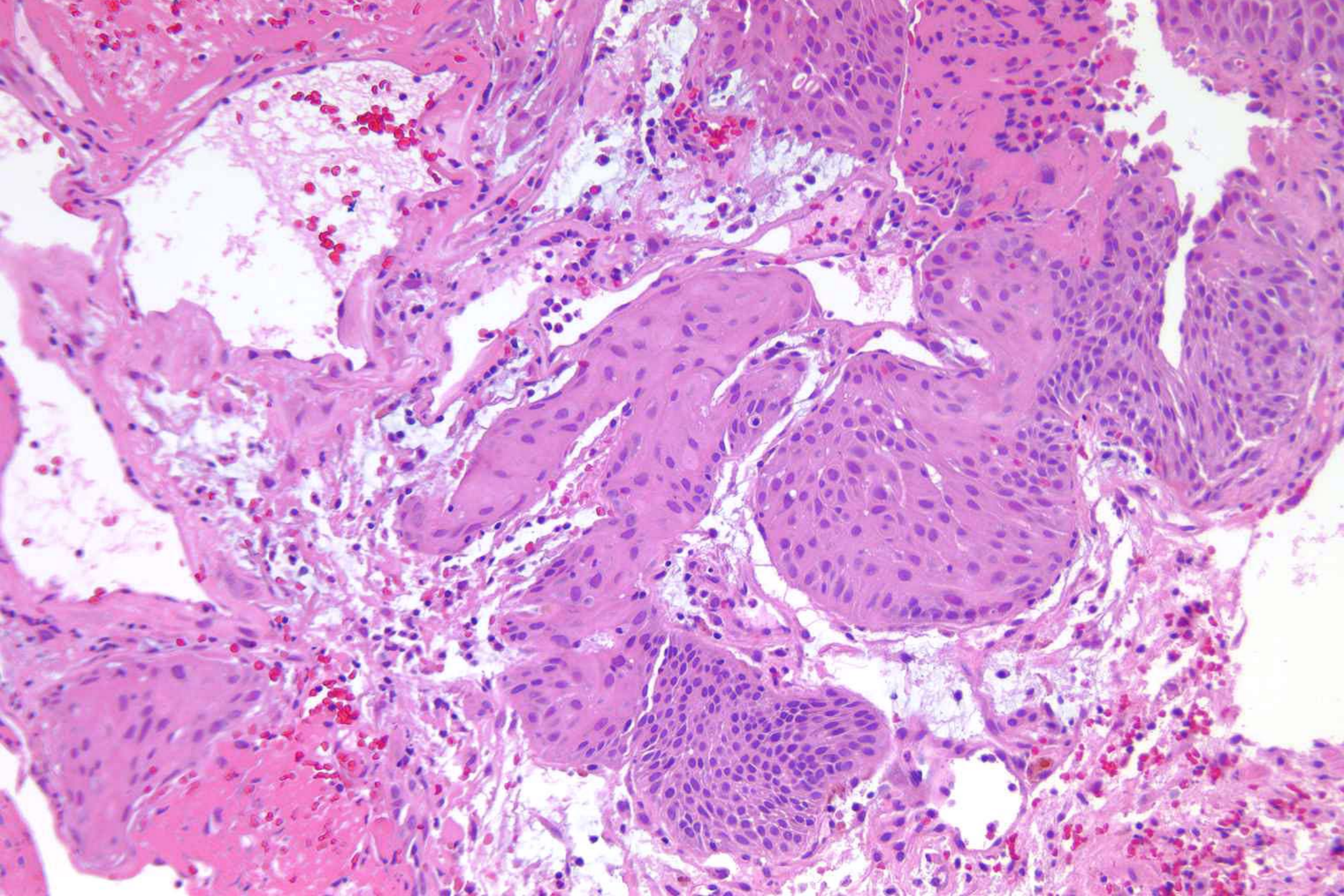




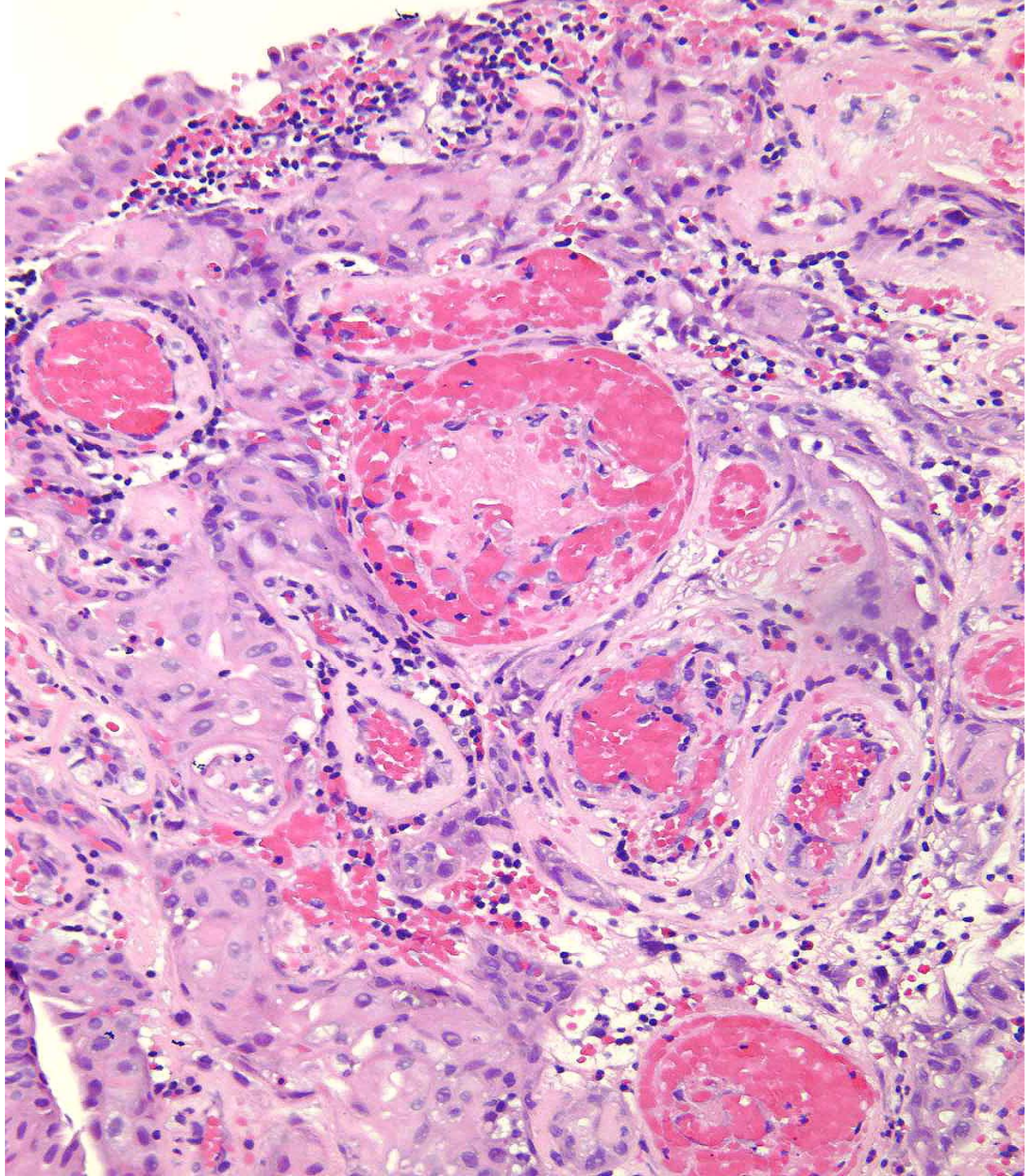




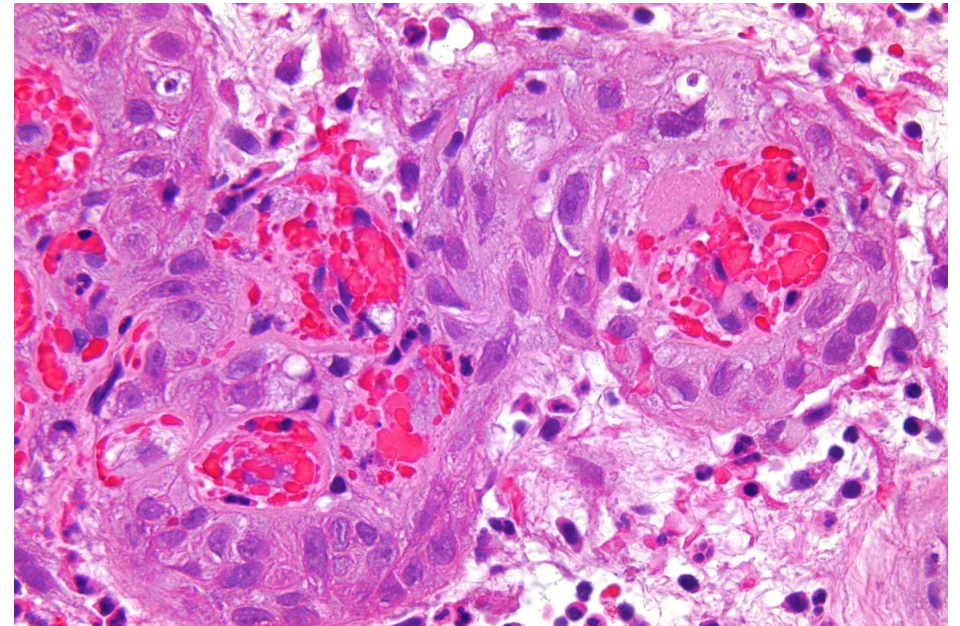
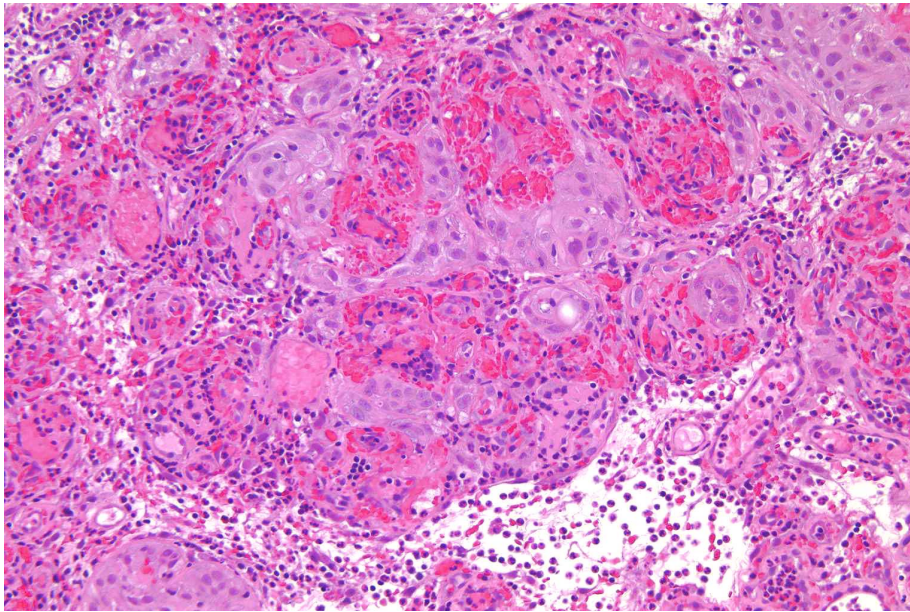












# Histologic Clues to Benign Nature

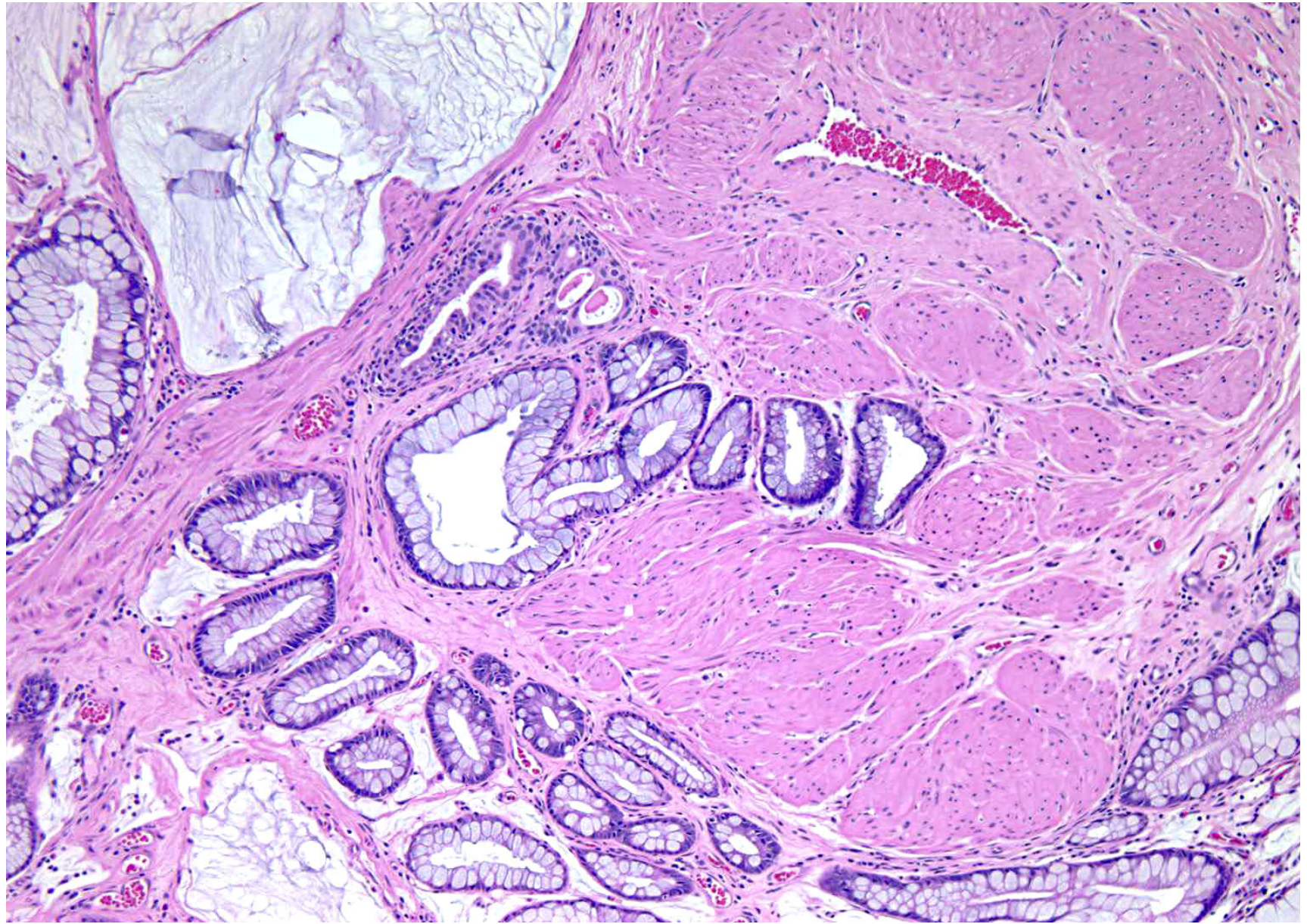
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- Edema (94%), **vascular congestion** (78%), hemosiderin (56%)
- Most importantly **fibrin deposits** with urothelial nests encircling the fibrin
- **Nests do not extend irregularly down** into the lamina propria or muscularis propria as is seen with the urothelial carcinoma
- Ulceration (39%) and **thickened vessels** (72%), which are clues to the prior irradiation

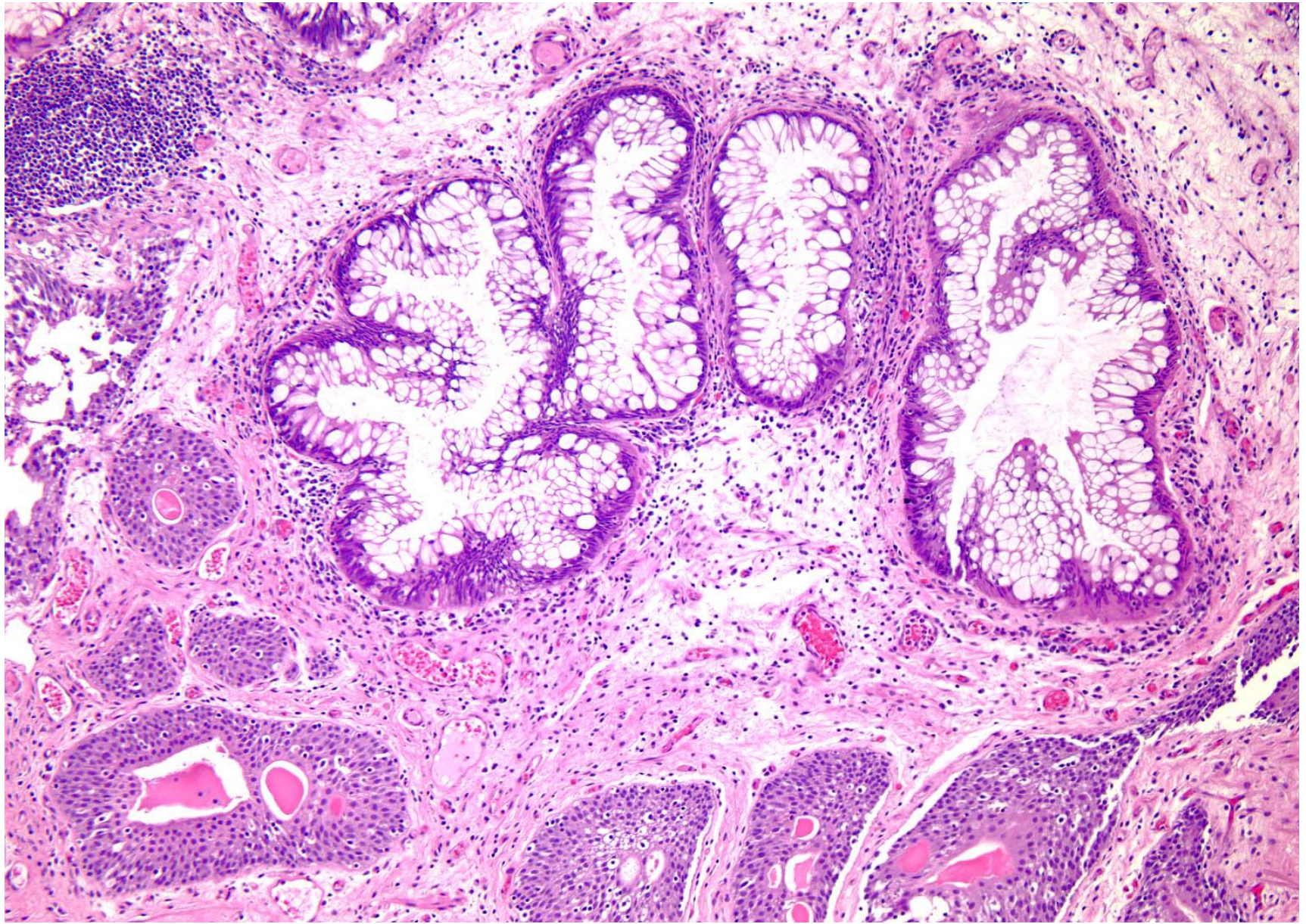
# Benign Mimickers of Bladder Adenocarcinoma

- **Florid cystitis cystica et glandularis**
- Endocervicosis/mullarianosis
- Nephrogenic adenoma (Nephrogenic metaplasia)

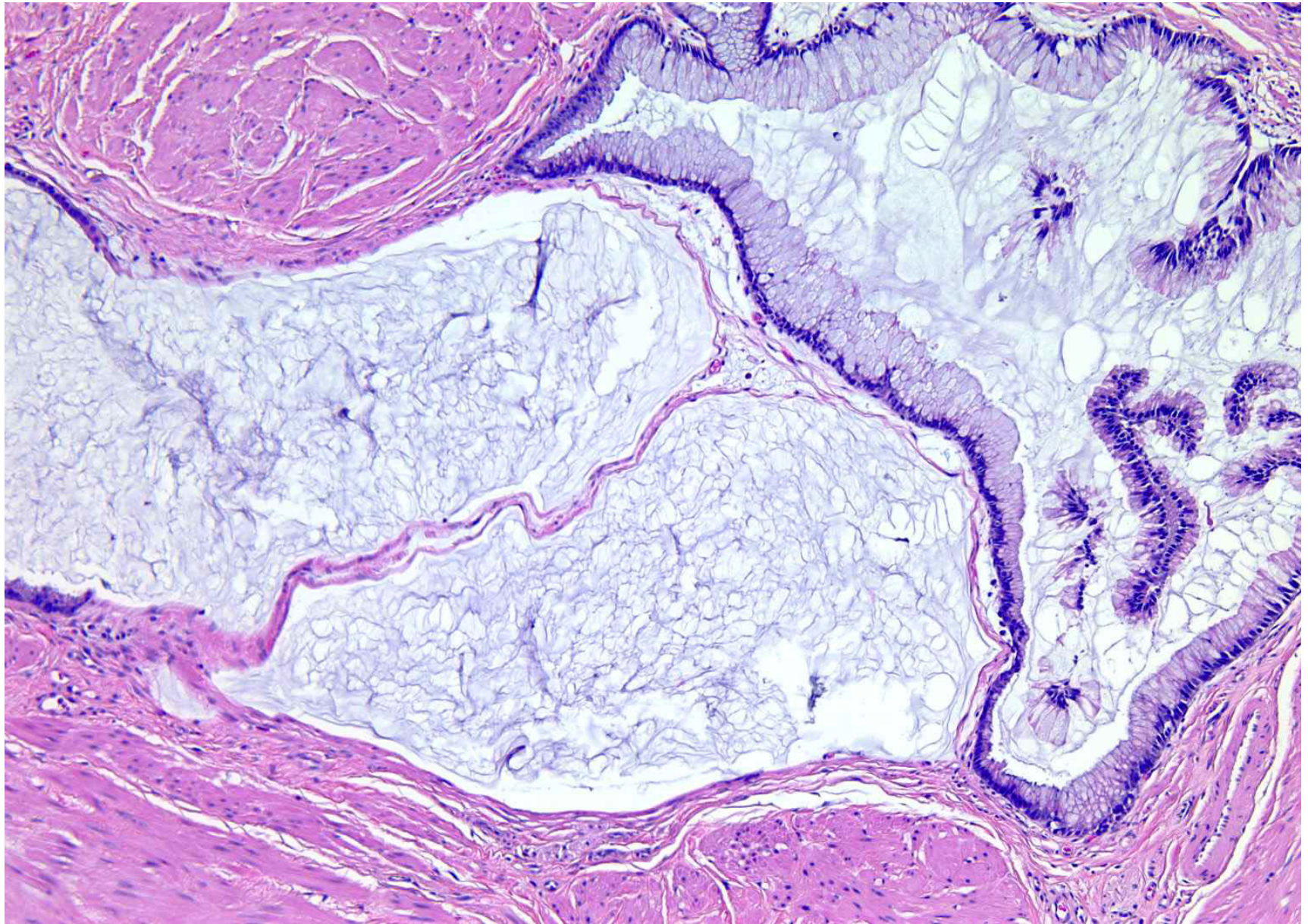




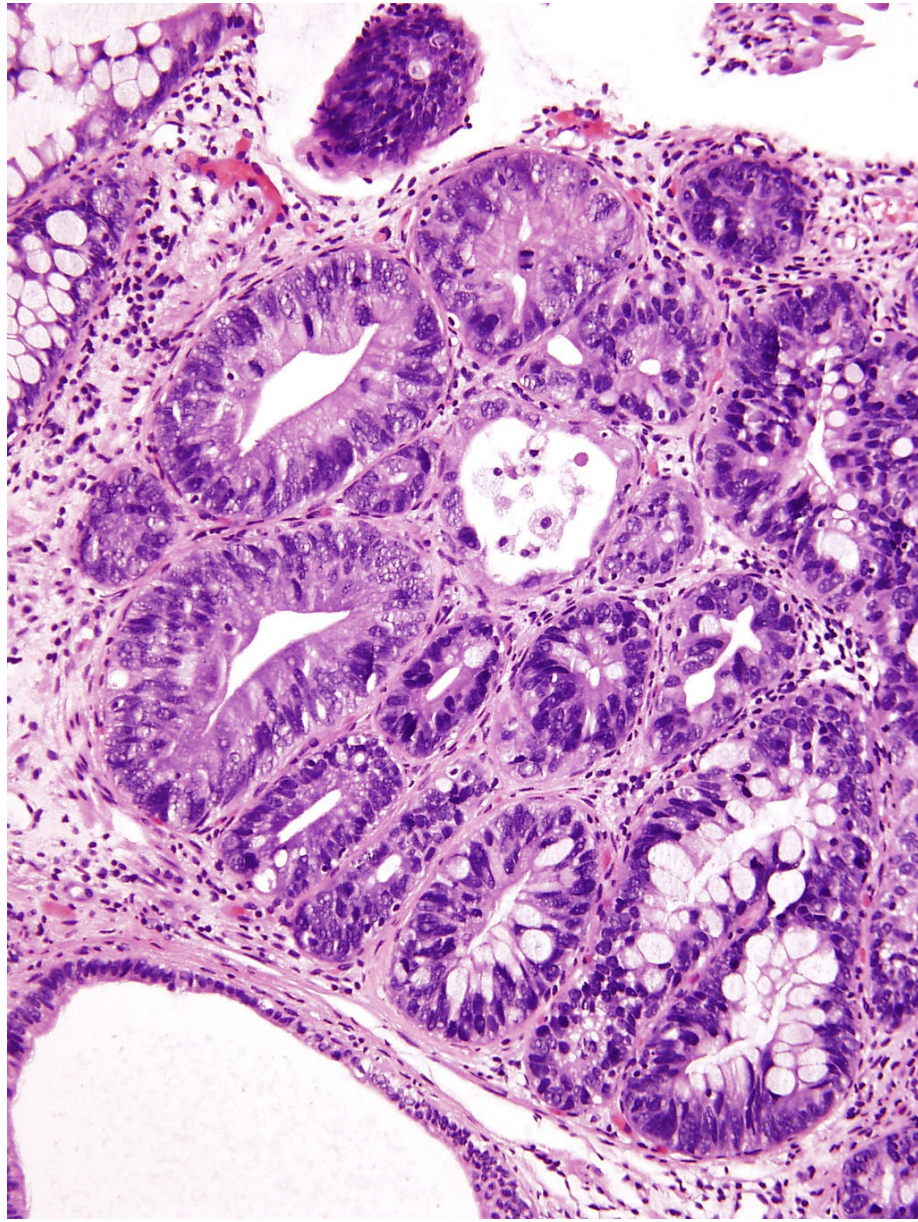












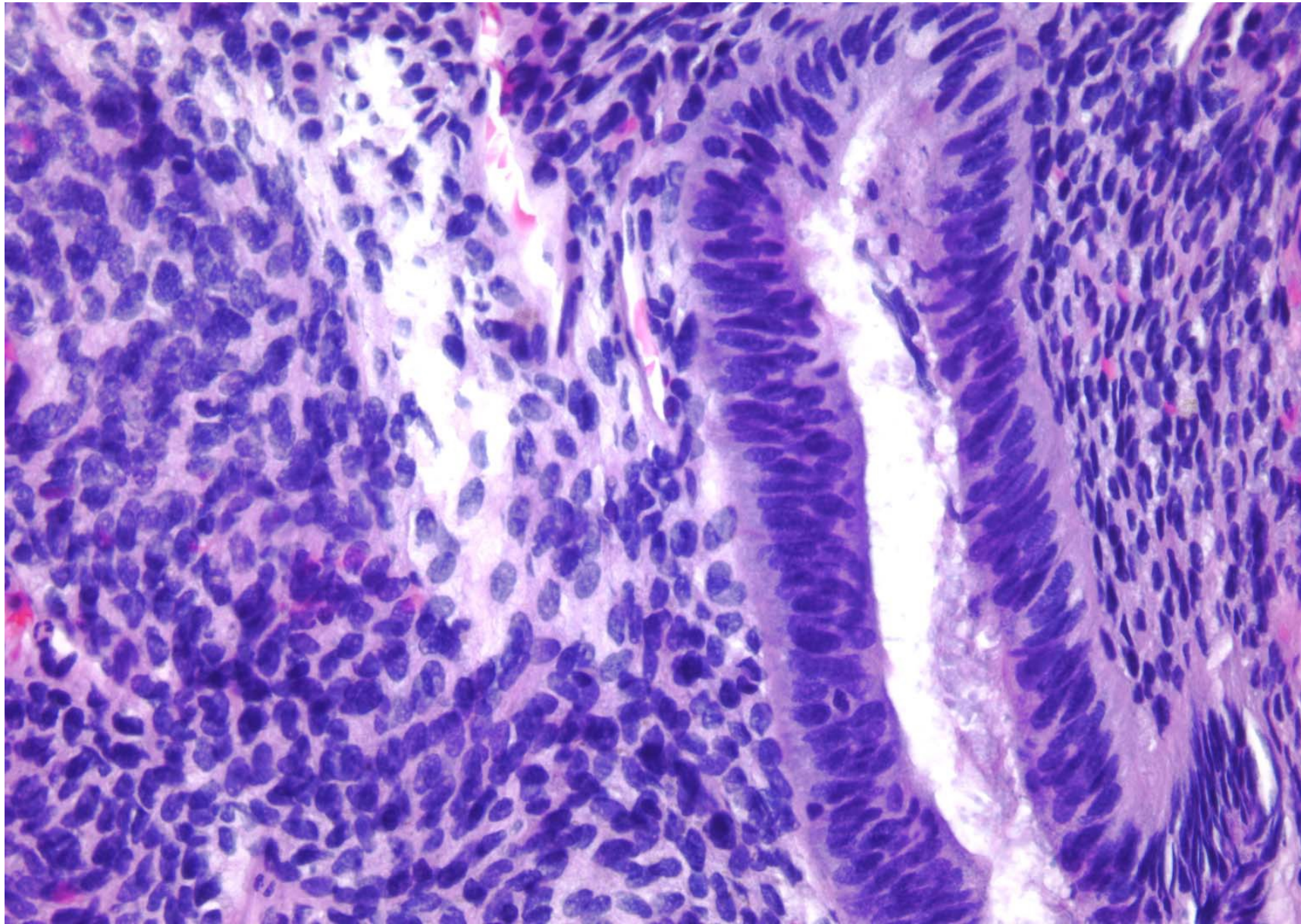
CCG with high grade glandular dysplasia !



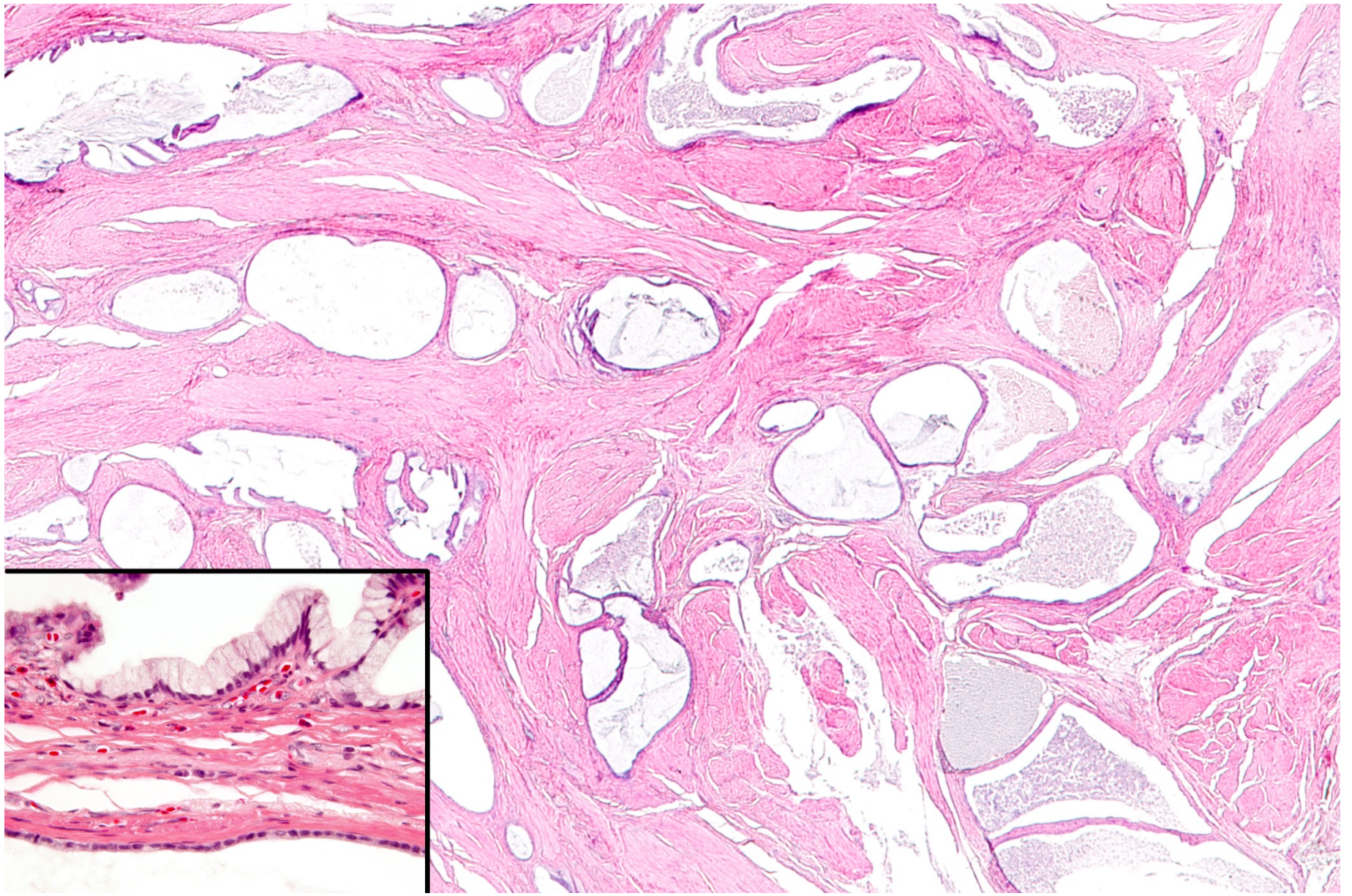
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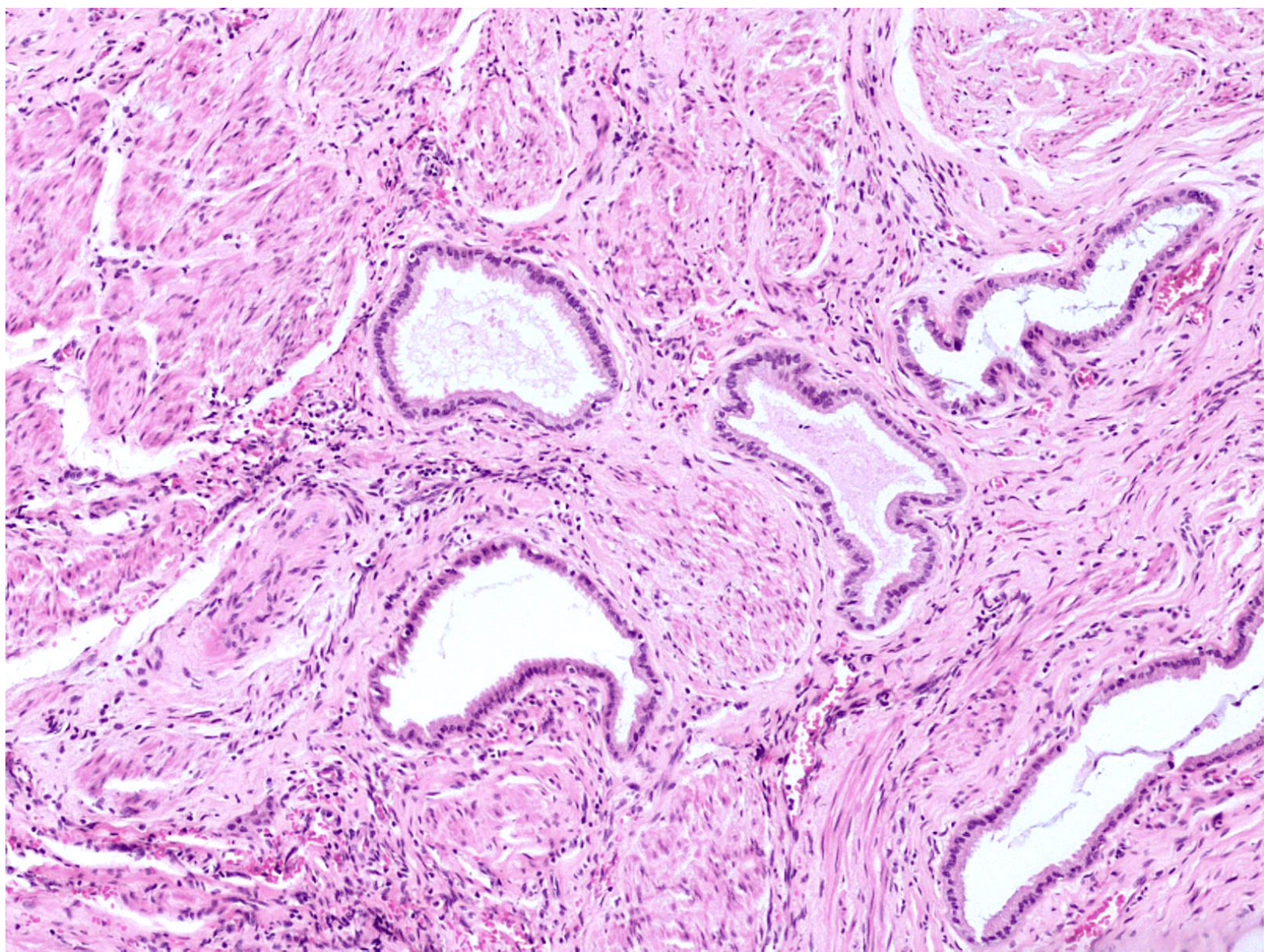




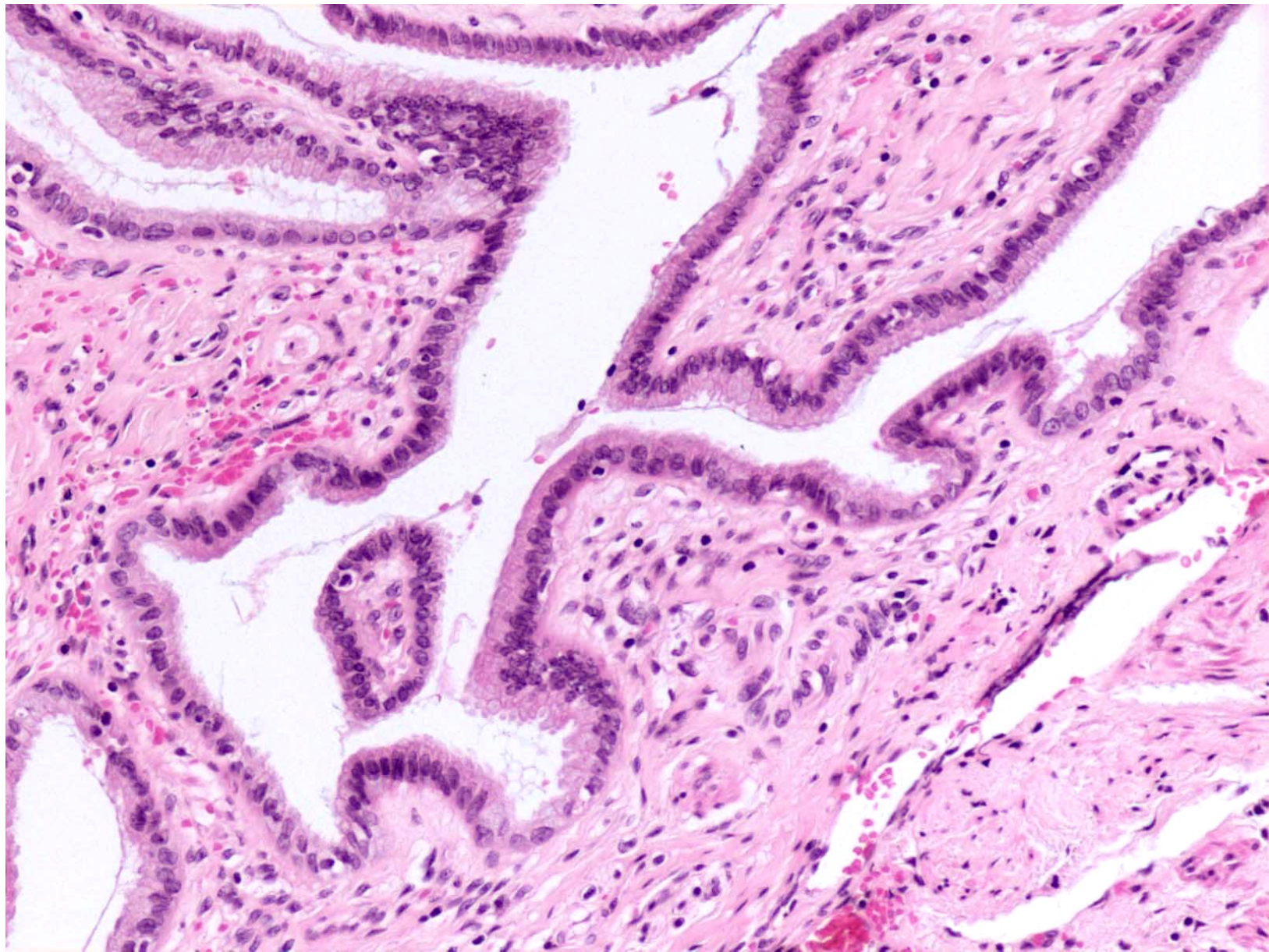




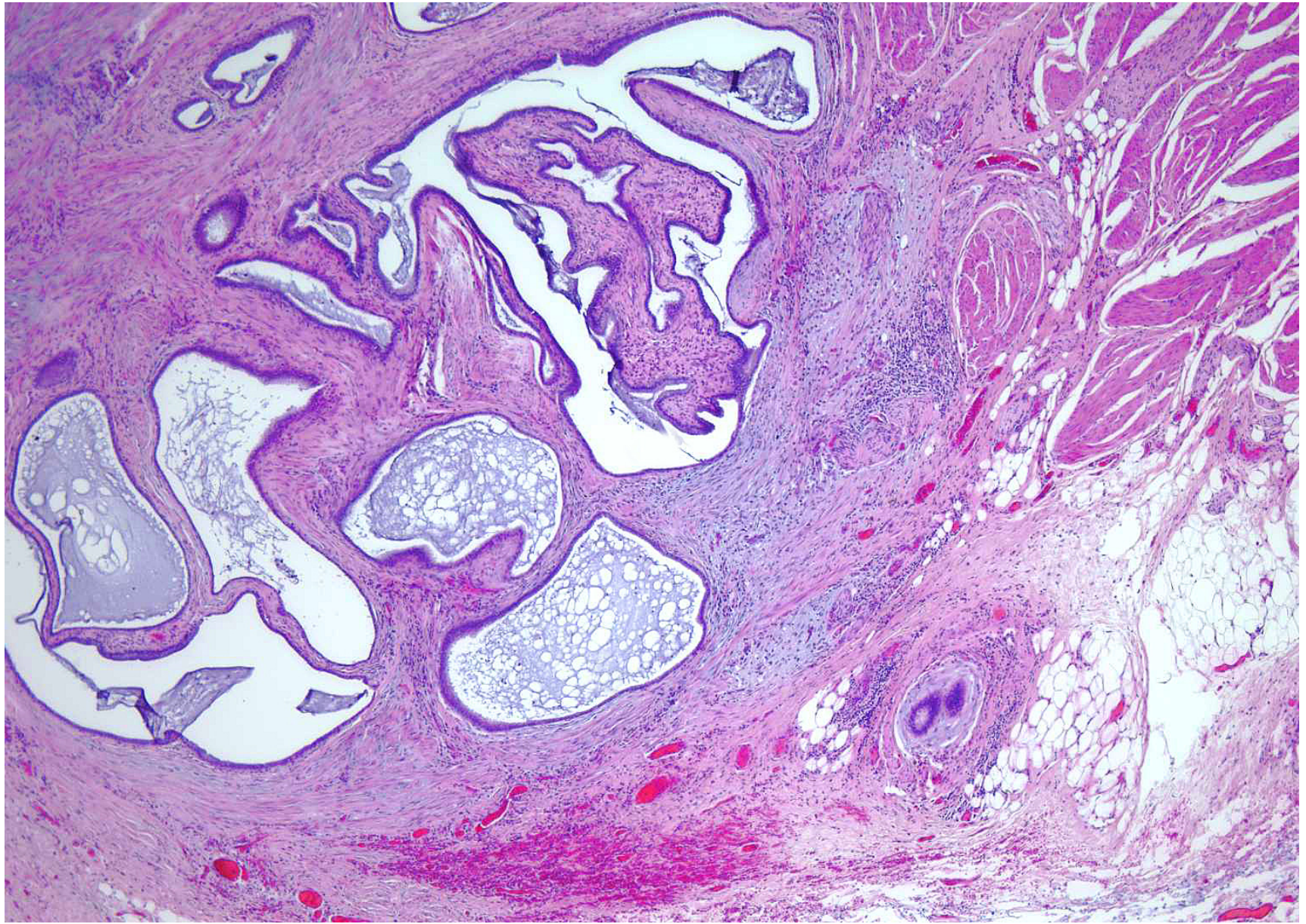




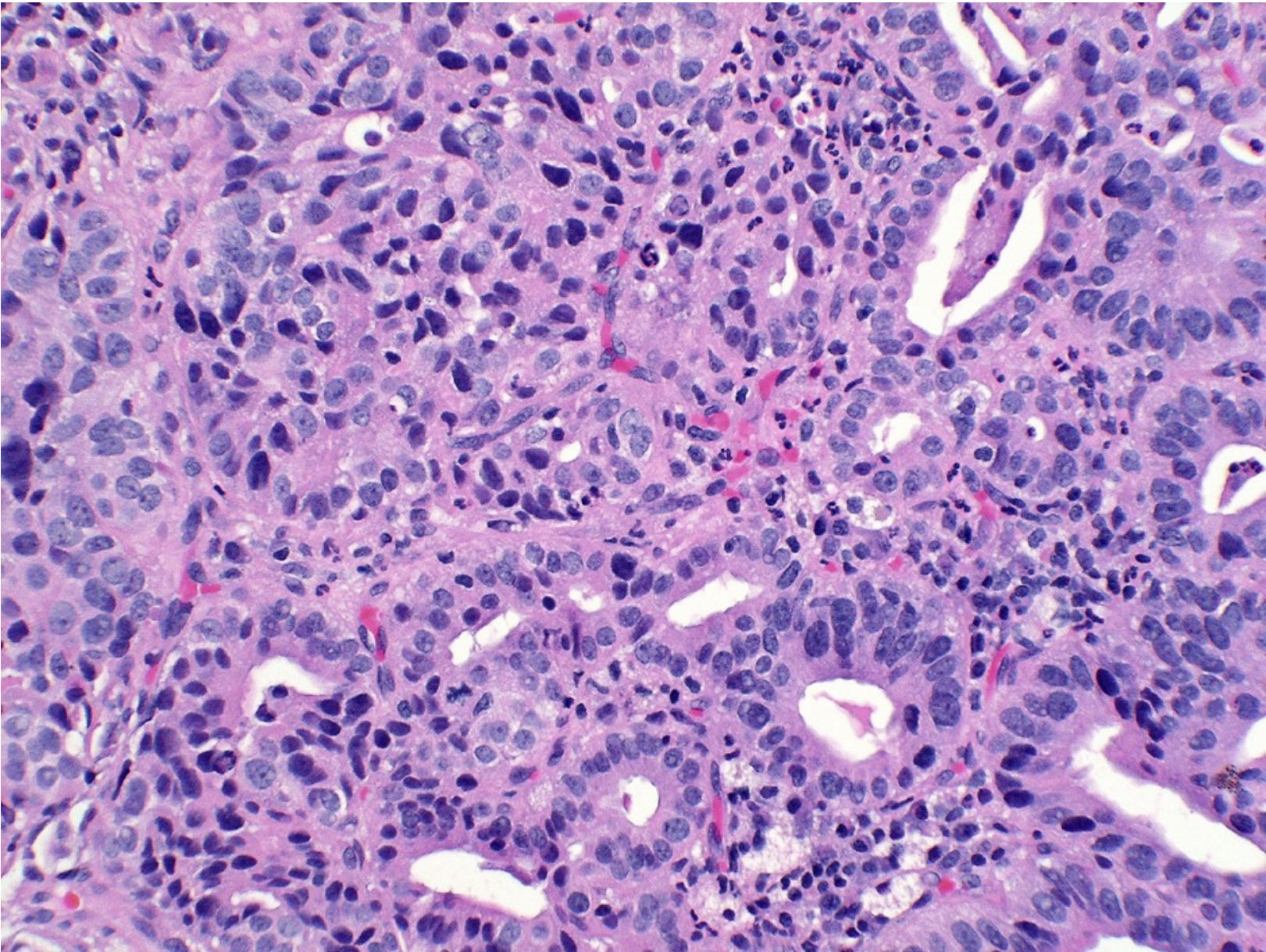












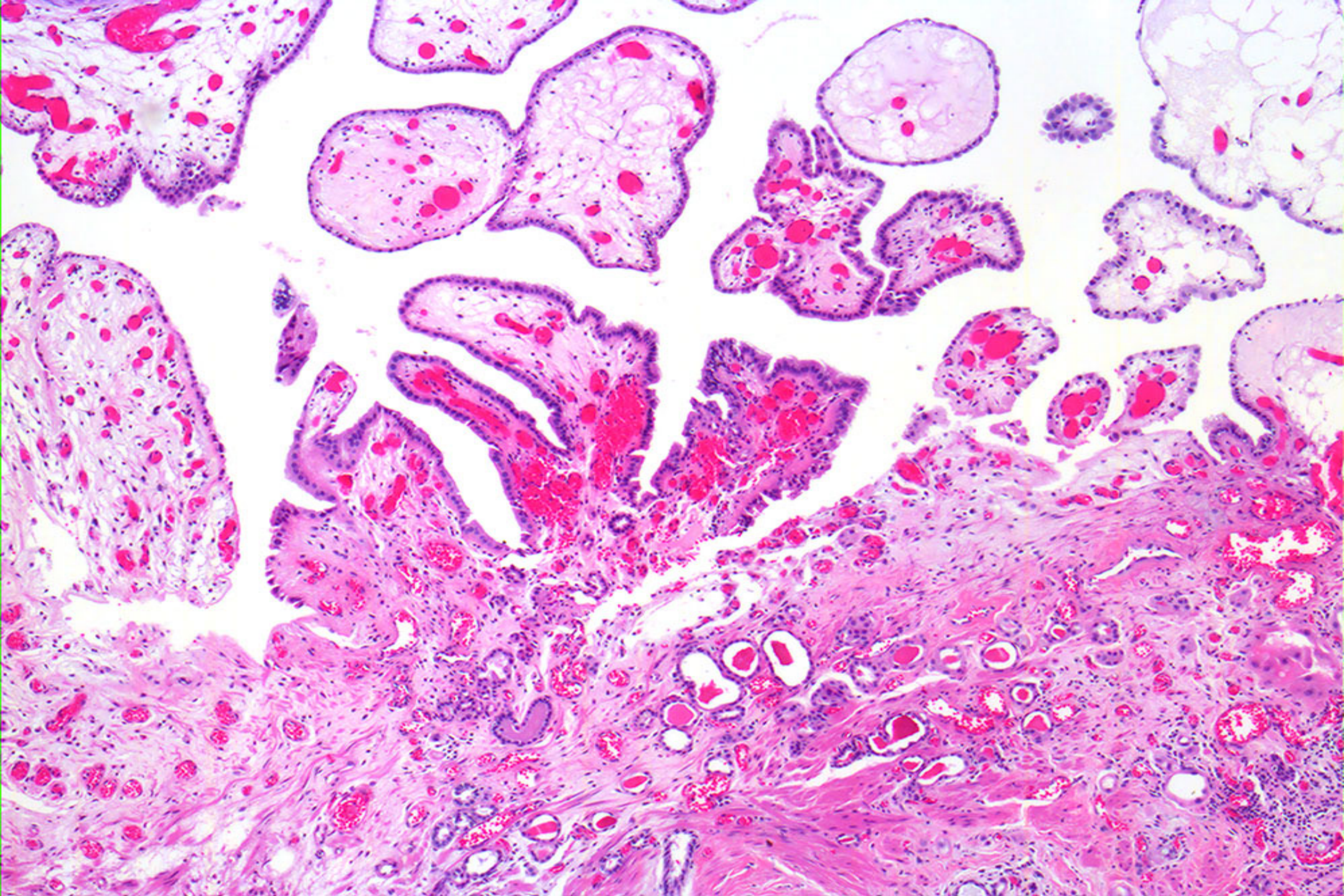
Bladder adenocarcinoma NOS!



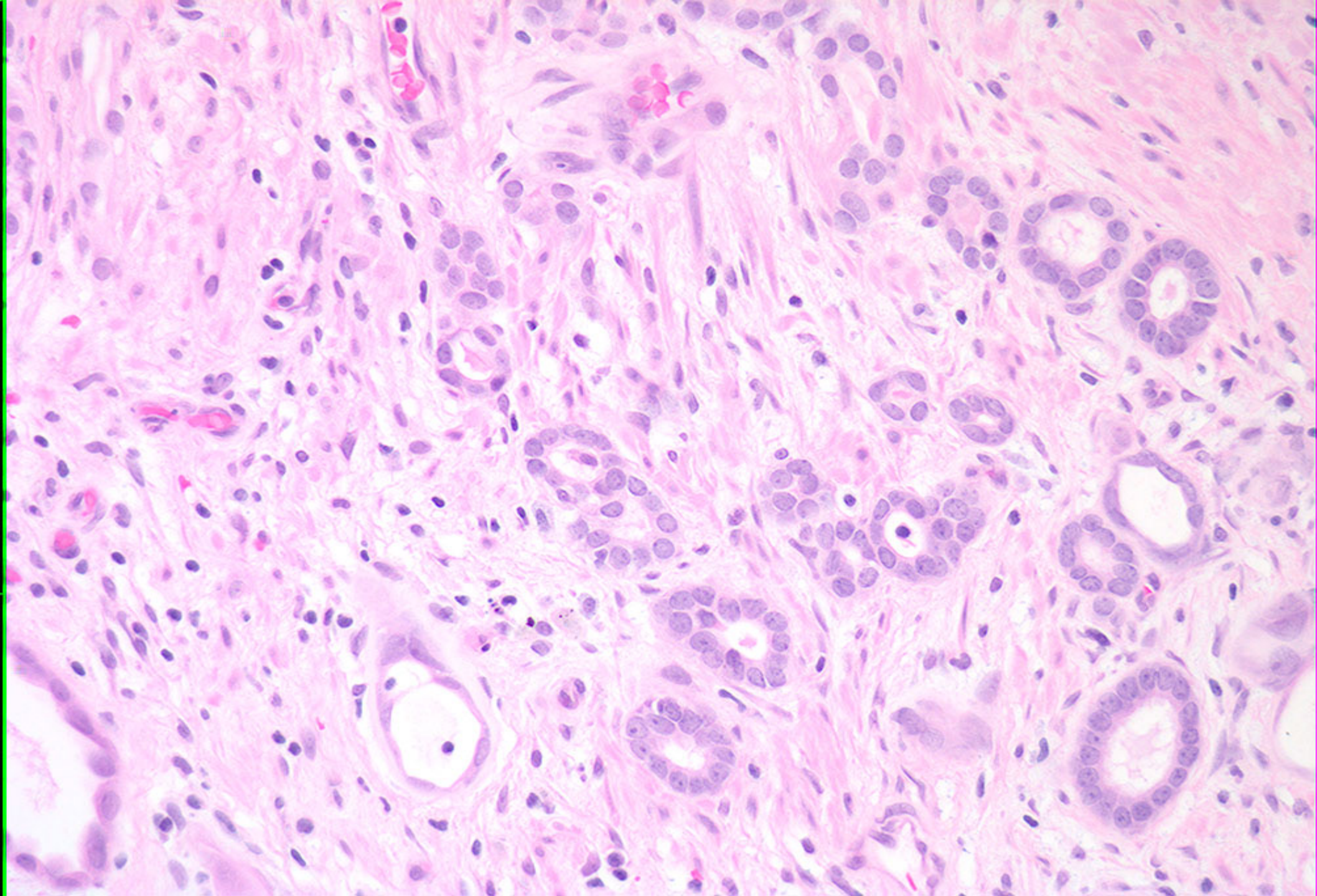
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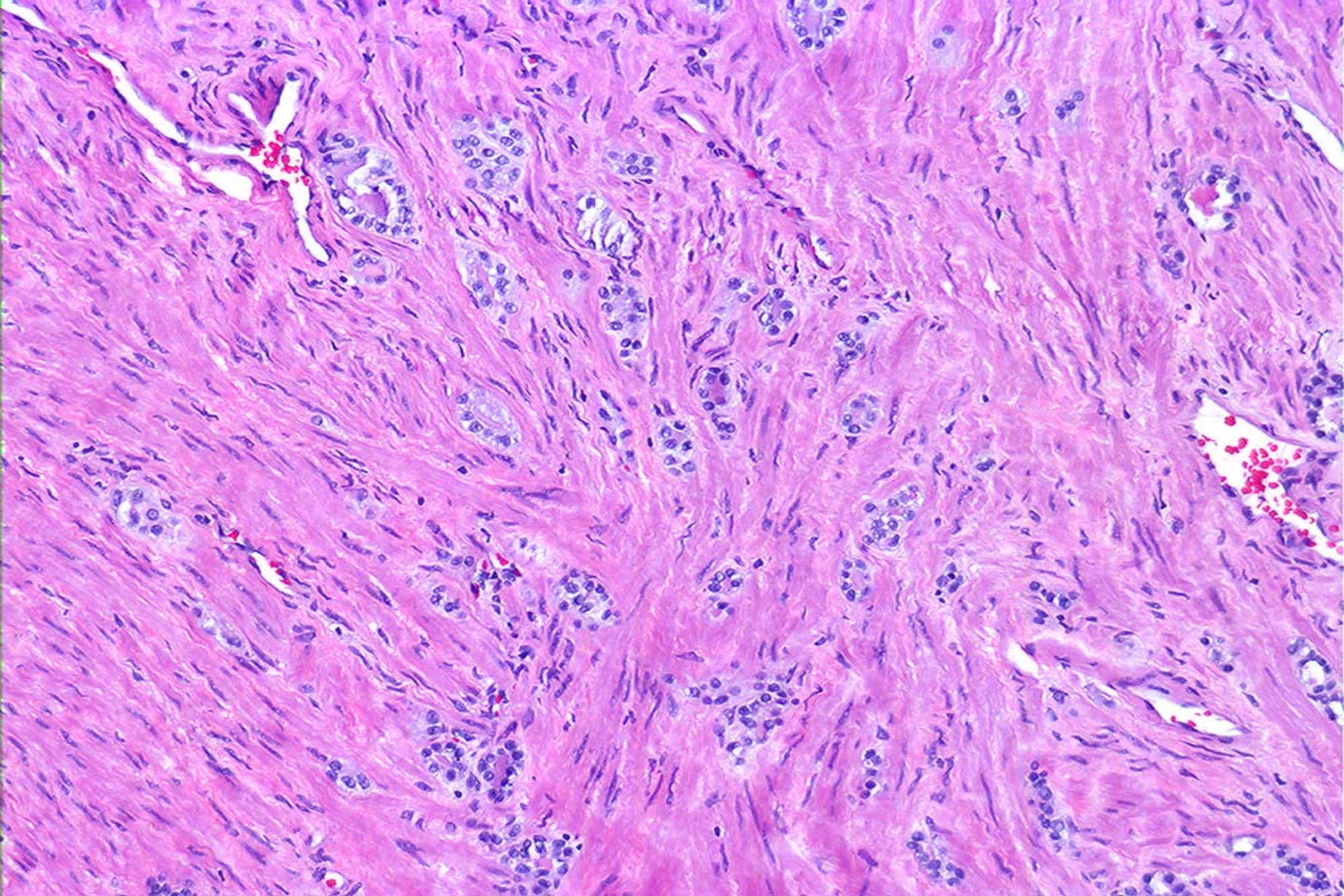




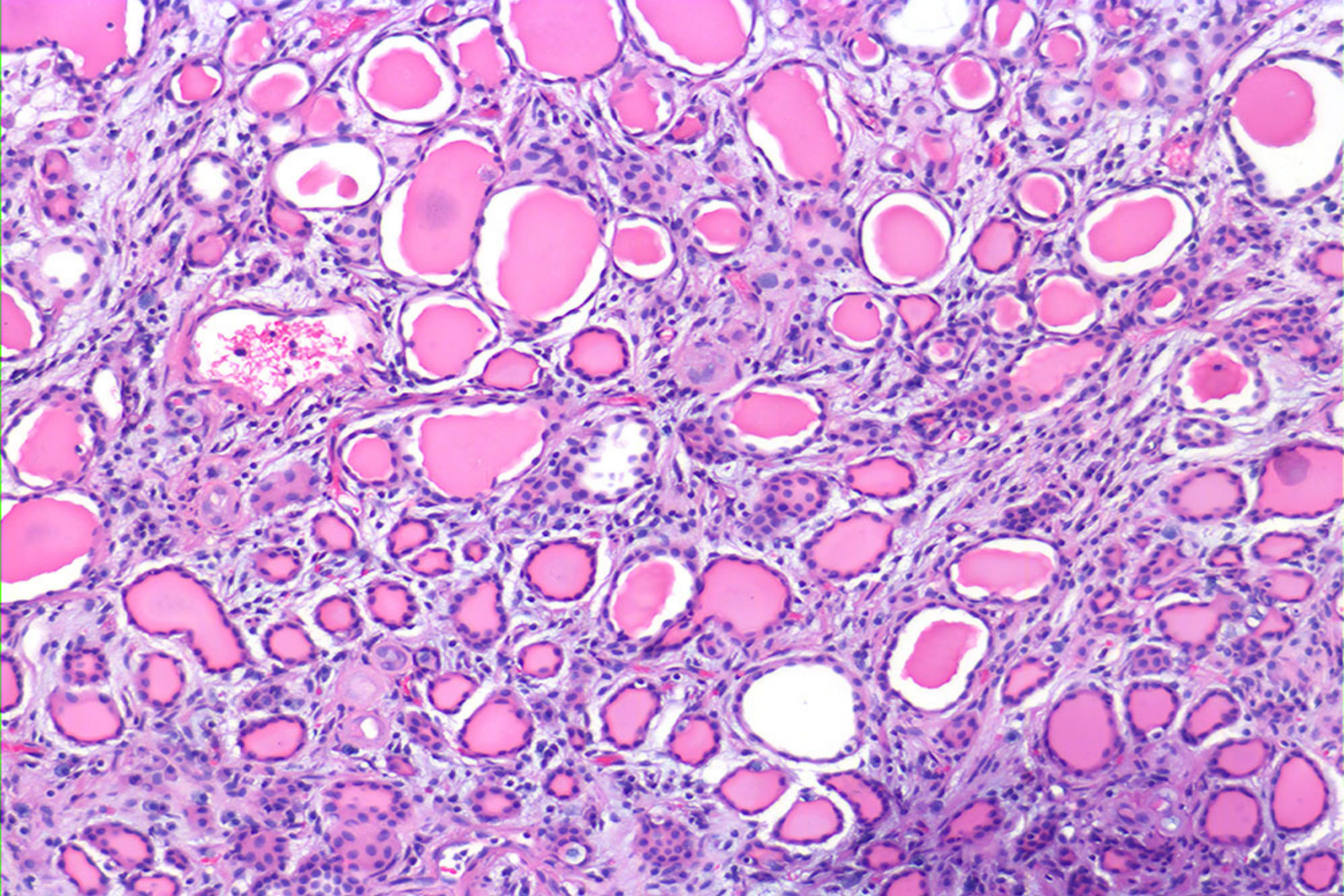




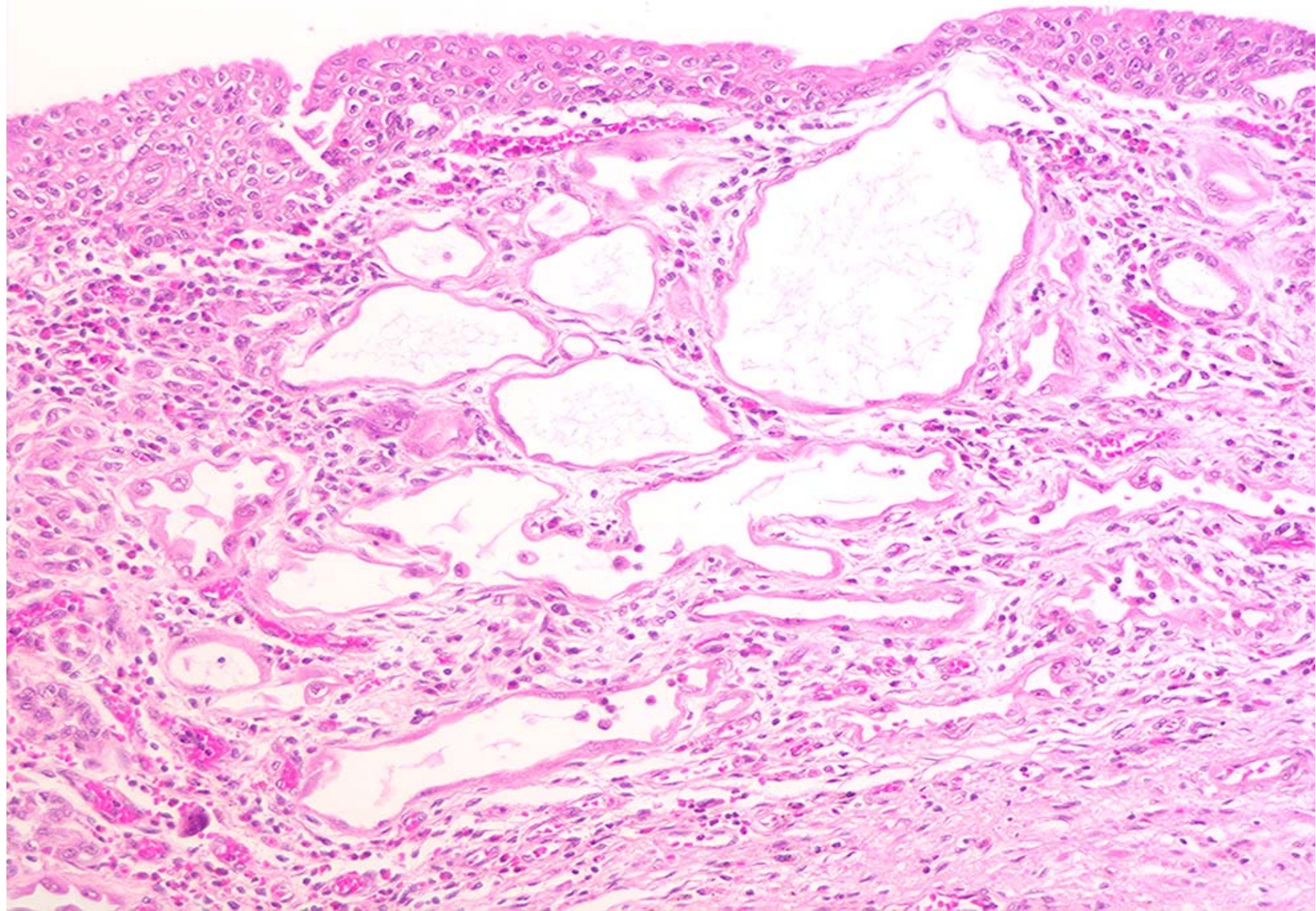




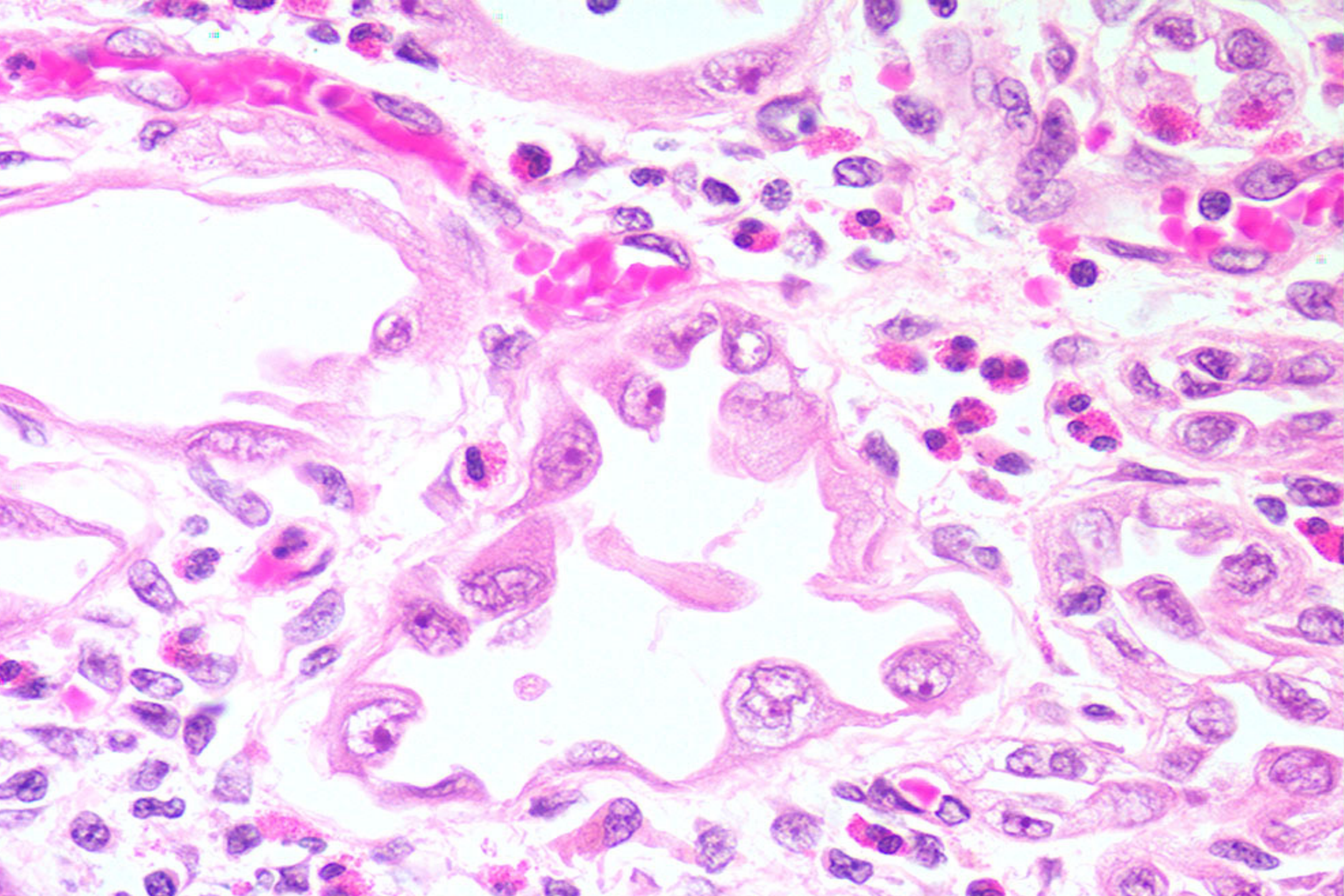




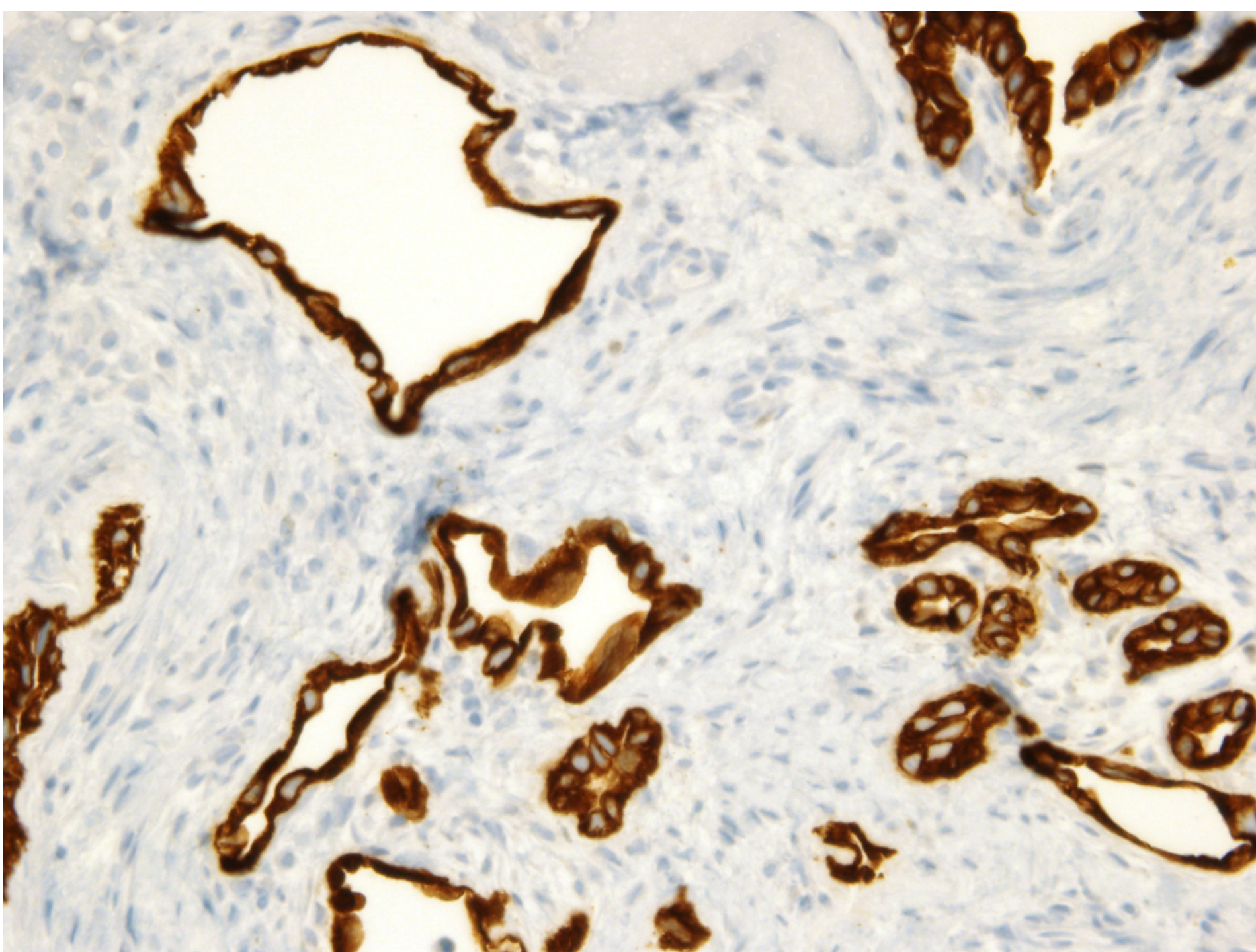




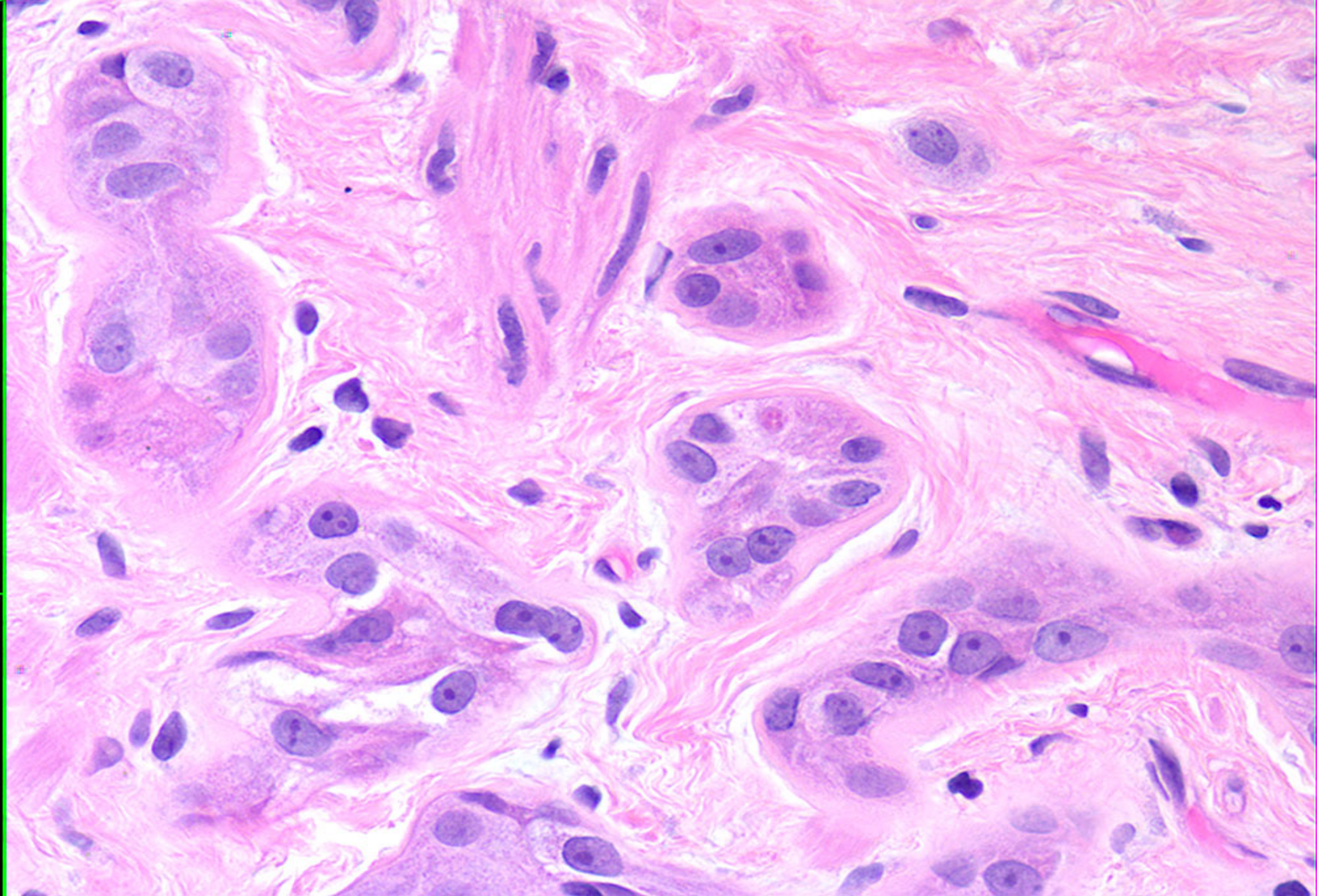




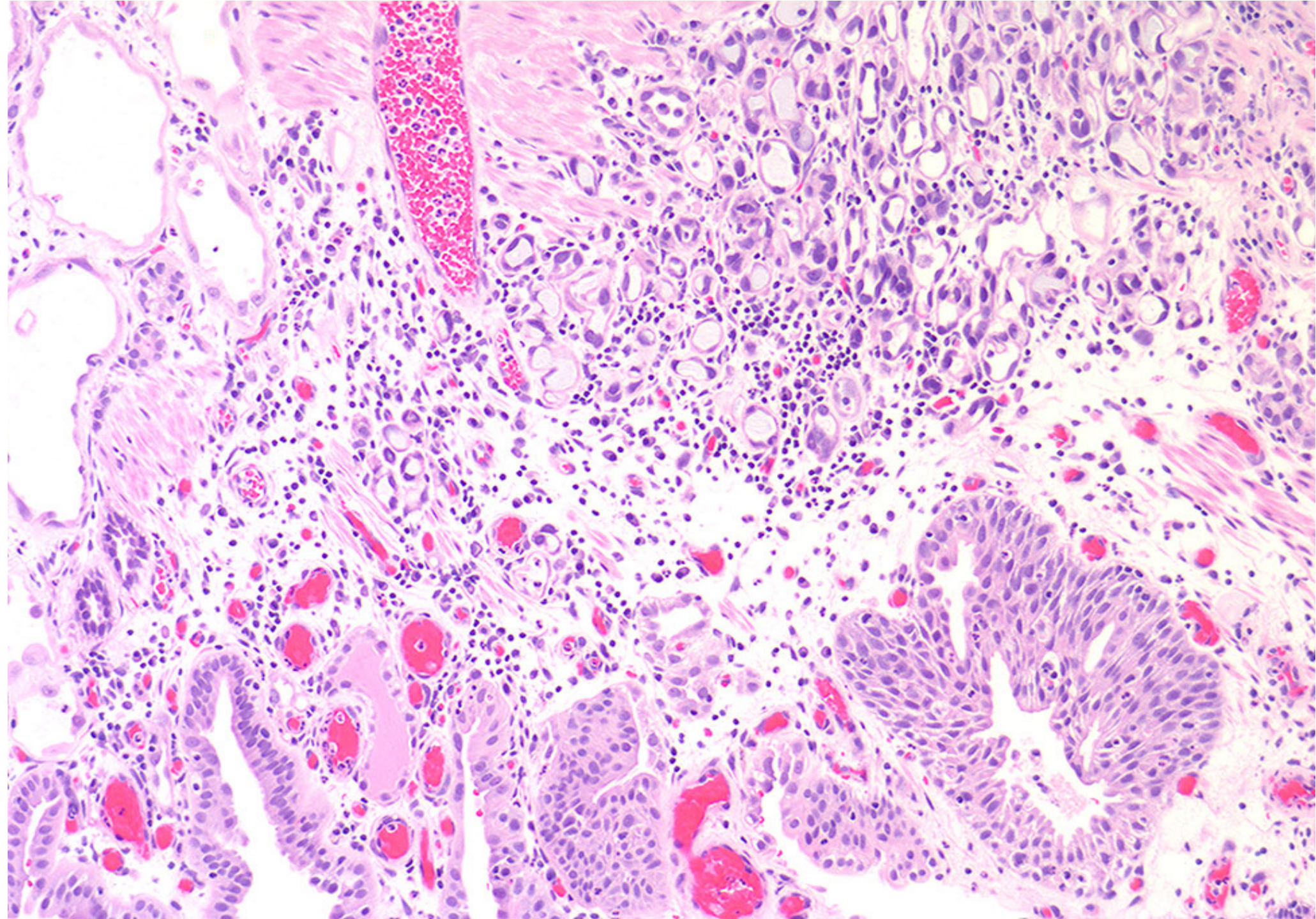




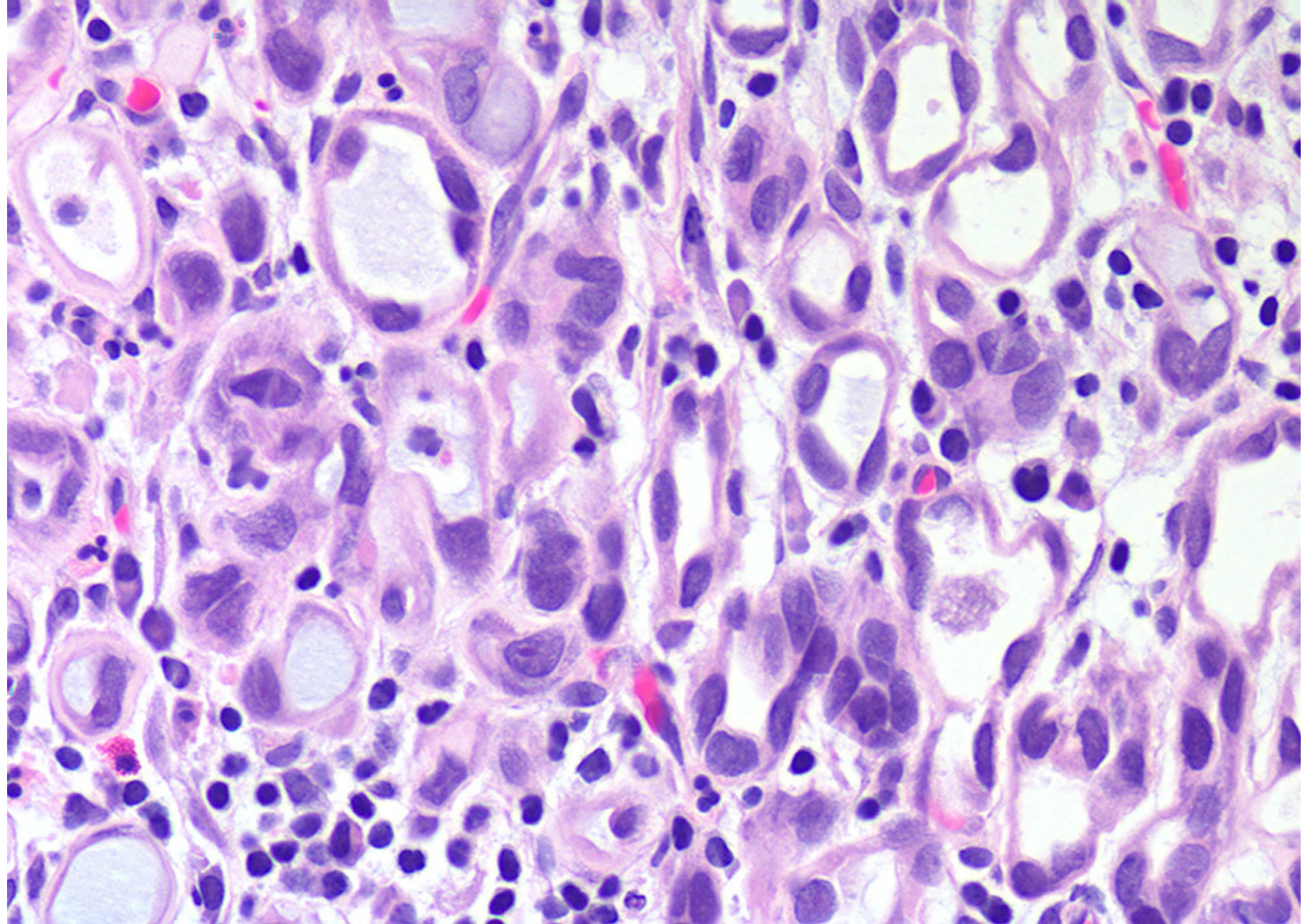




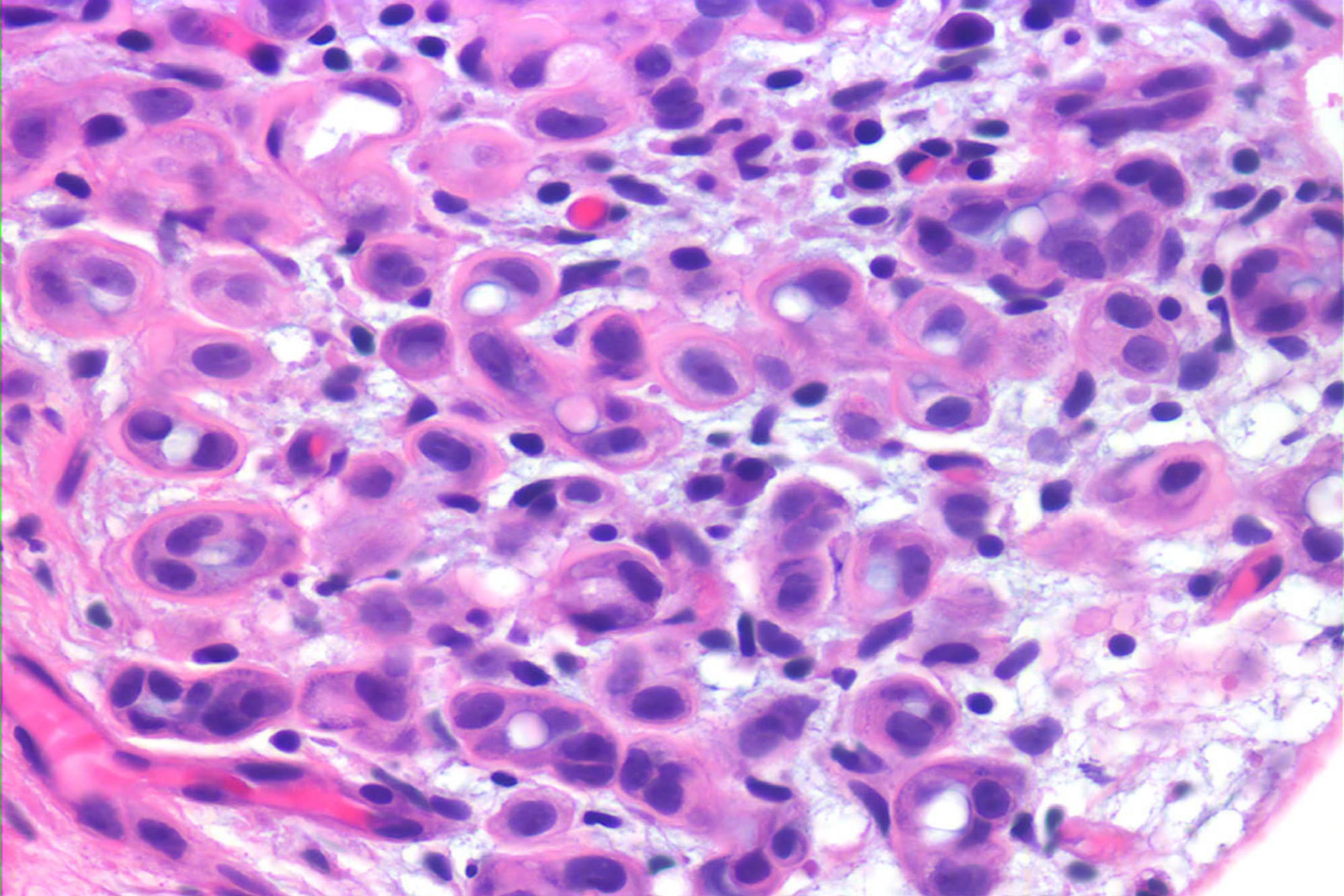














# Malignant Mimickers of Bladder Carcinoma

## Malignant Mimickers of Urothelial Carcinoma

- PCa (Gleason 5)
- Pheochromocytoma

## Malignant Mimickers of Adenocarcinoma

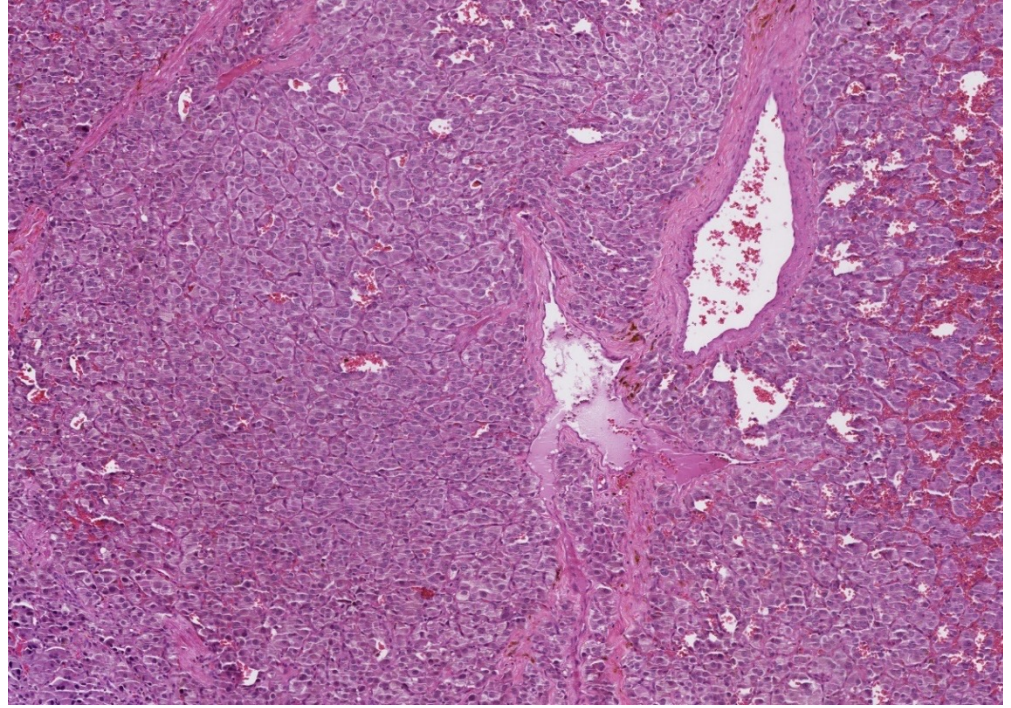
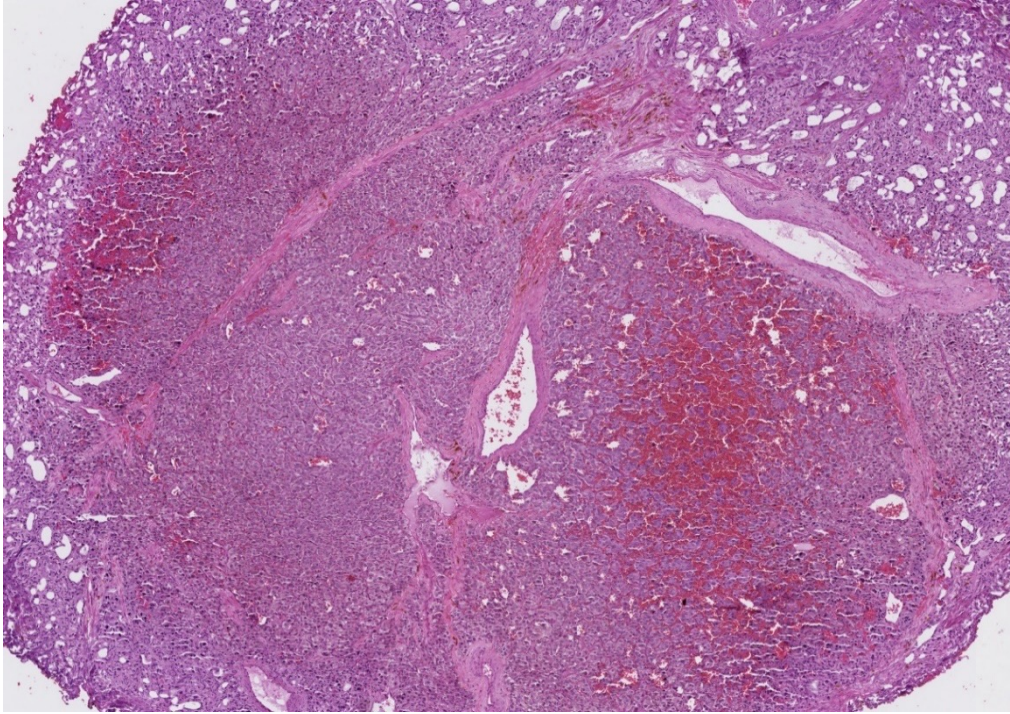
- CRCa
- PCa (Gleason 3,4)
- Other metastatic adenocarcinoma



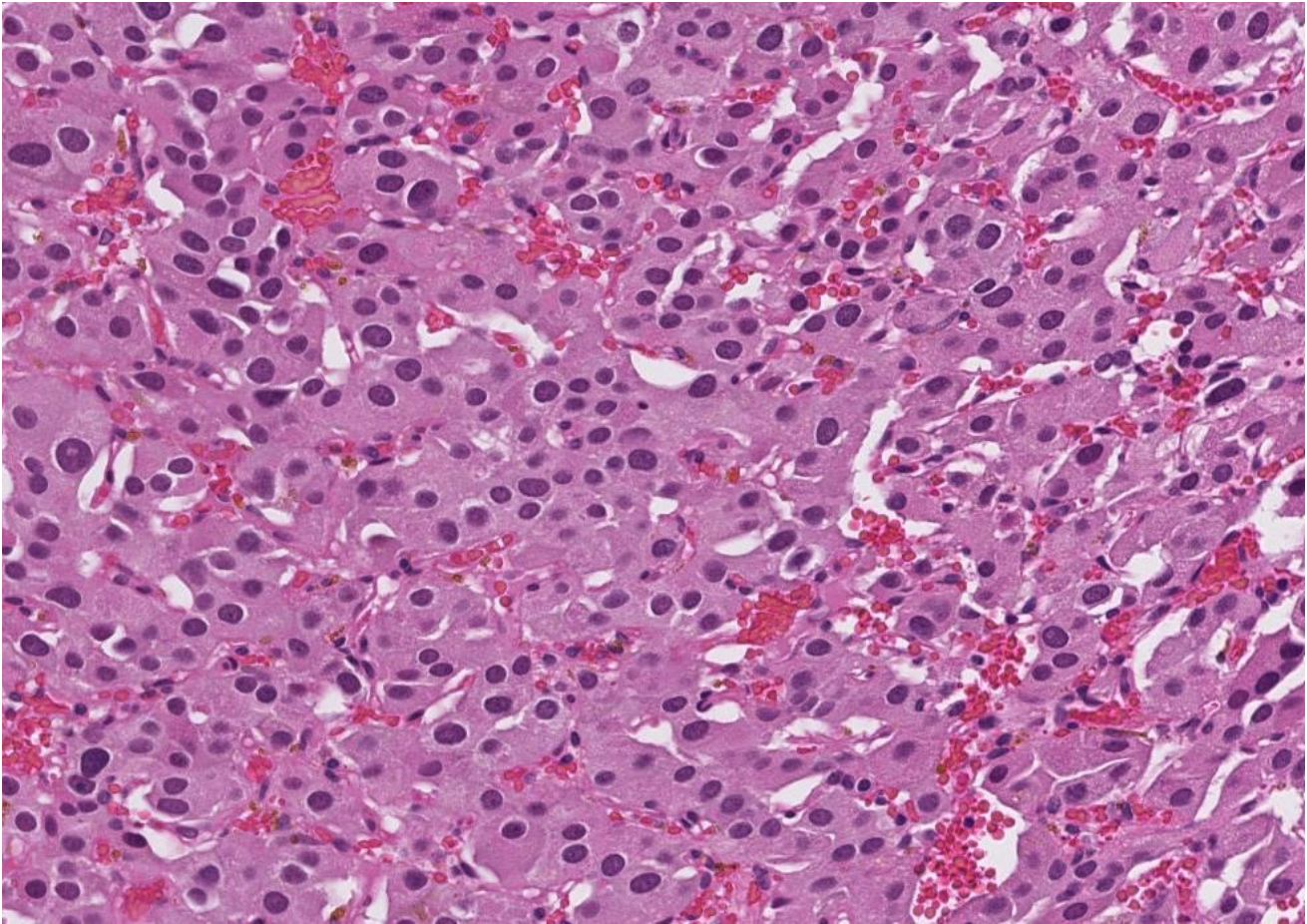
## **Case 1**

A 58 yr old male smoker presented with persistent microhematuria; a TURB was performed.











# Case # 1

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Diagnosis:

- A. Invasive Urothelial Carcinoma, High Grade
- B. Malignant Melanoma
- C. Paraganglioma
- D. Large Cell Neuroendocrine Carcinoma



# Case # 1

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## Diagnosis:

- A. Invasive Urothelial Carcinoma, High Grade
- B. Malignant Melanoma
- **C. Paraganglioma**
- D. Large Cell Neuroendocrine Carcinoma



# Paraganglioma

## Clinical Characteristics

### Clinical Features

- Rare bladder tumor (<1%); middle aged **women**
- Classic presentation
  - paroxysmal **hypertension**
  - micturition attacks (headache, palpitations, diaphoresis, blurred vision)
- Cystoscopy
  - “**submucosal**” mass

### Biologic Behavior

- 5–15% malignant behavior
- **No reliable criteria** to accurately predict



# Paraganglioma

## Immunohistochemistry & Molecular Dx

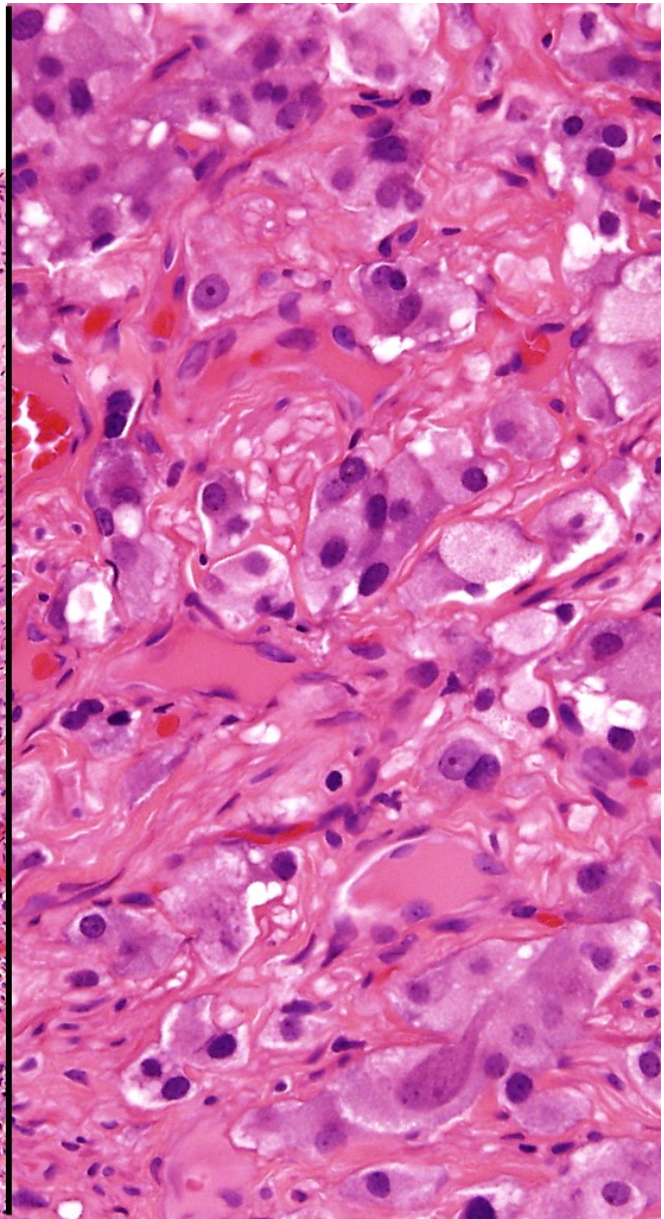
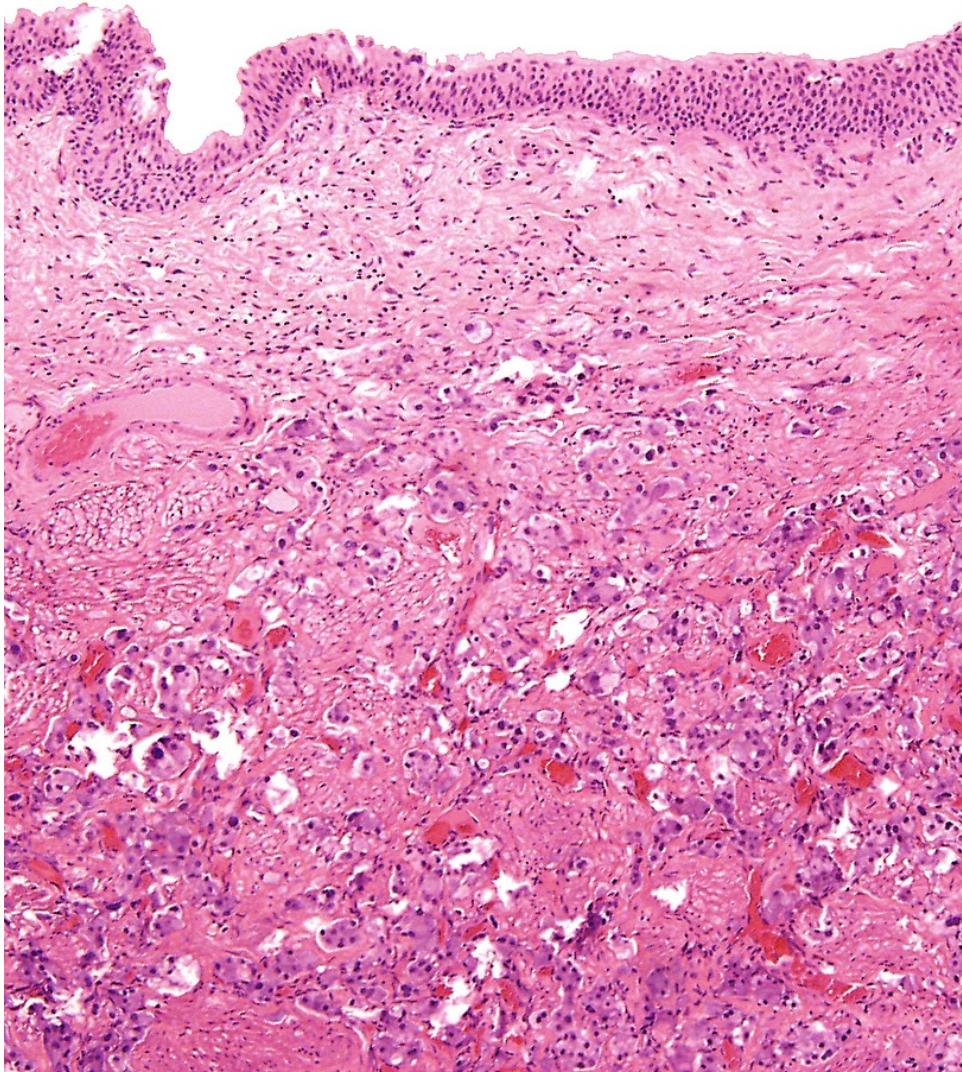
### IHC:

- Chromogranin (+) , synaptophysin (+), S100 (+) sustentacular
- Cytokeratins (AE1/AE3, CK903 , CK7 , CK20): usually (-)
- p63 (-)
- **GATA3 POSITIVE !**

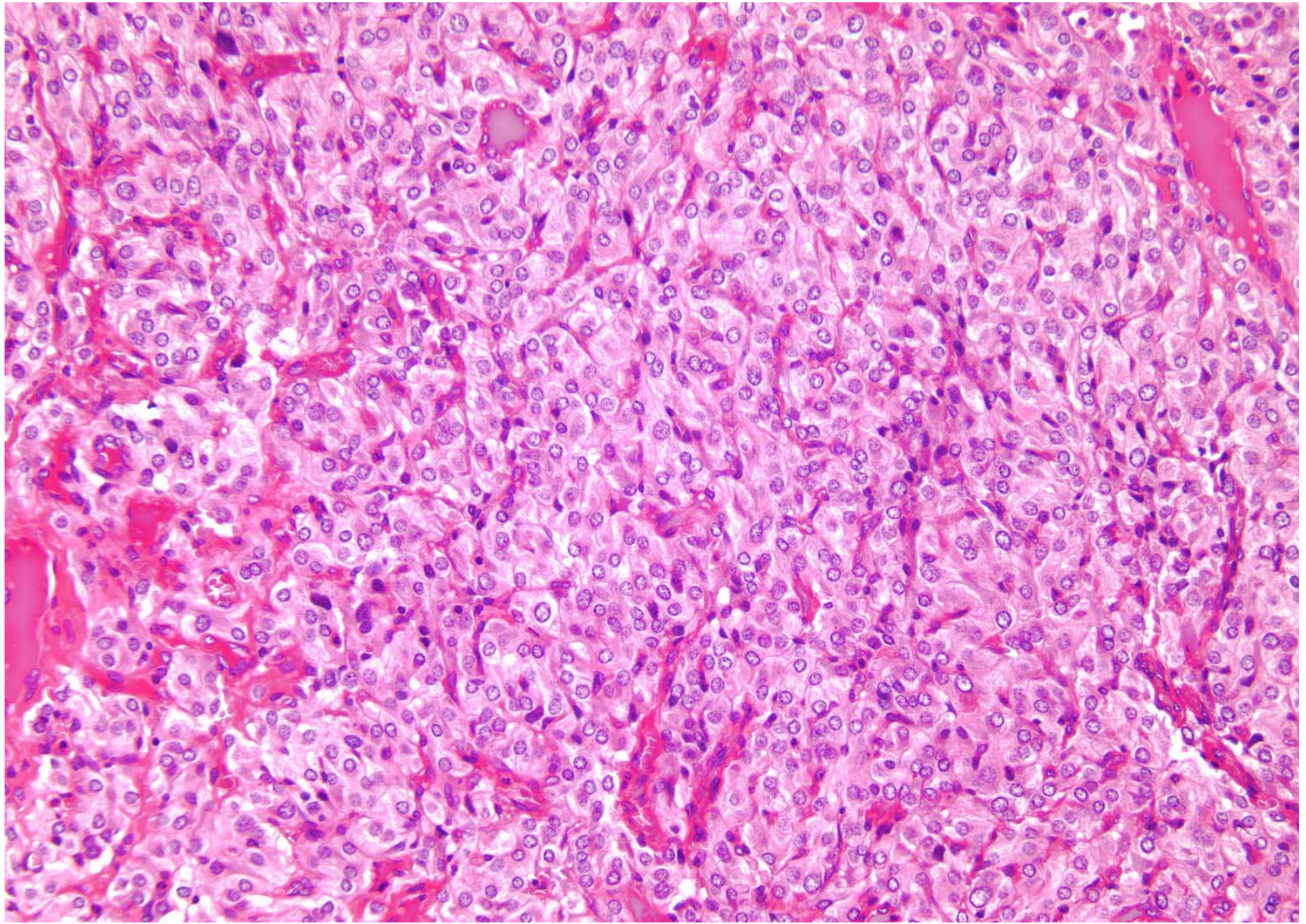
### Molecular Dx:

- MEN2: *RET*
- von Hippel-Lindau disease: *vHL*
- Neurofibromatosis 1 (NF 1)
- Paraganglioma syndromes type 1,3,4: ***SDH* subunits D, C, B**

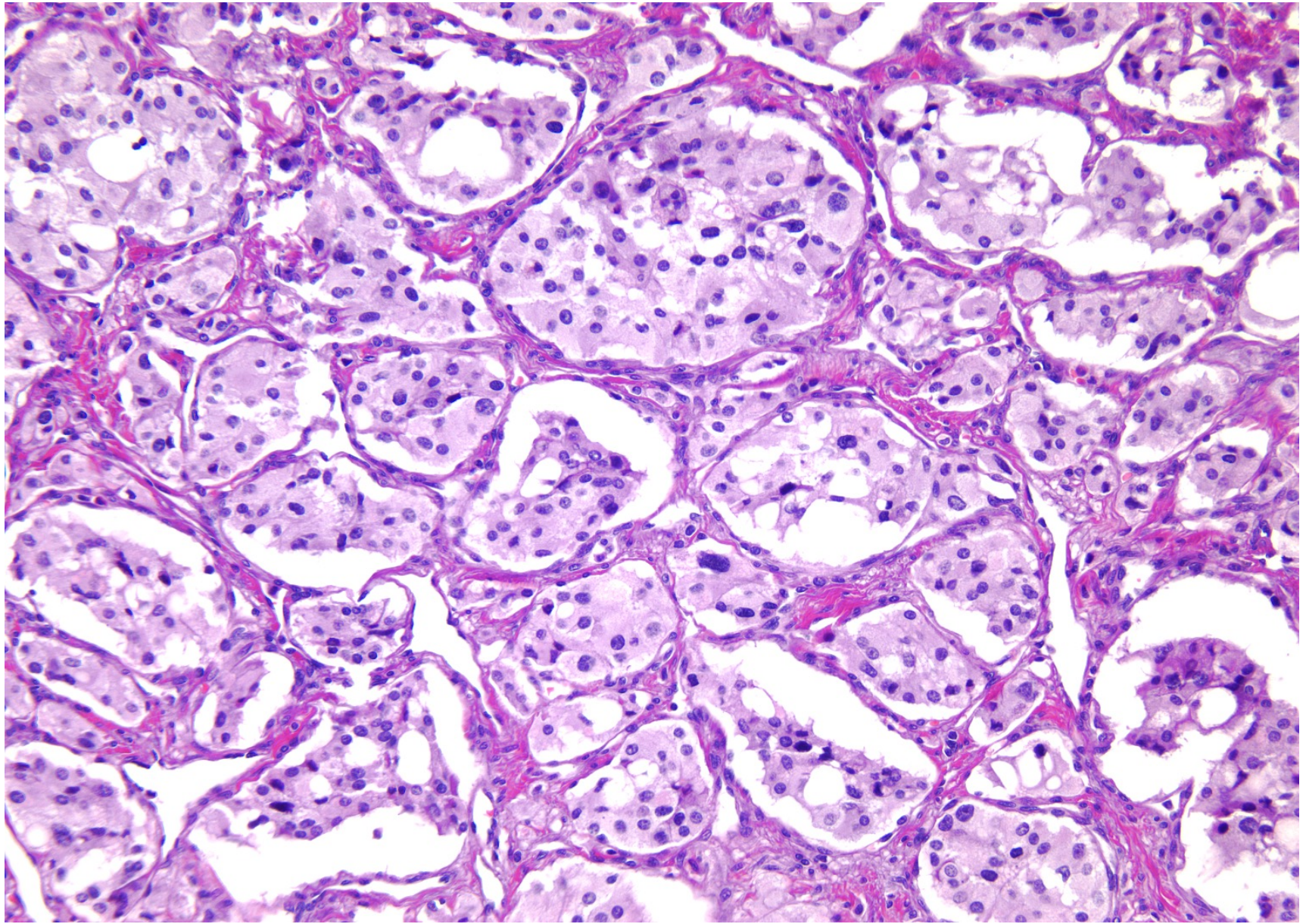




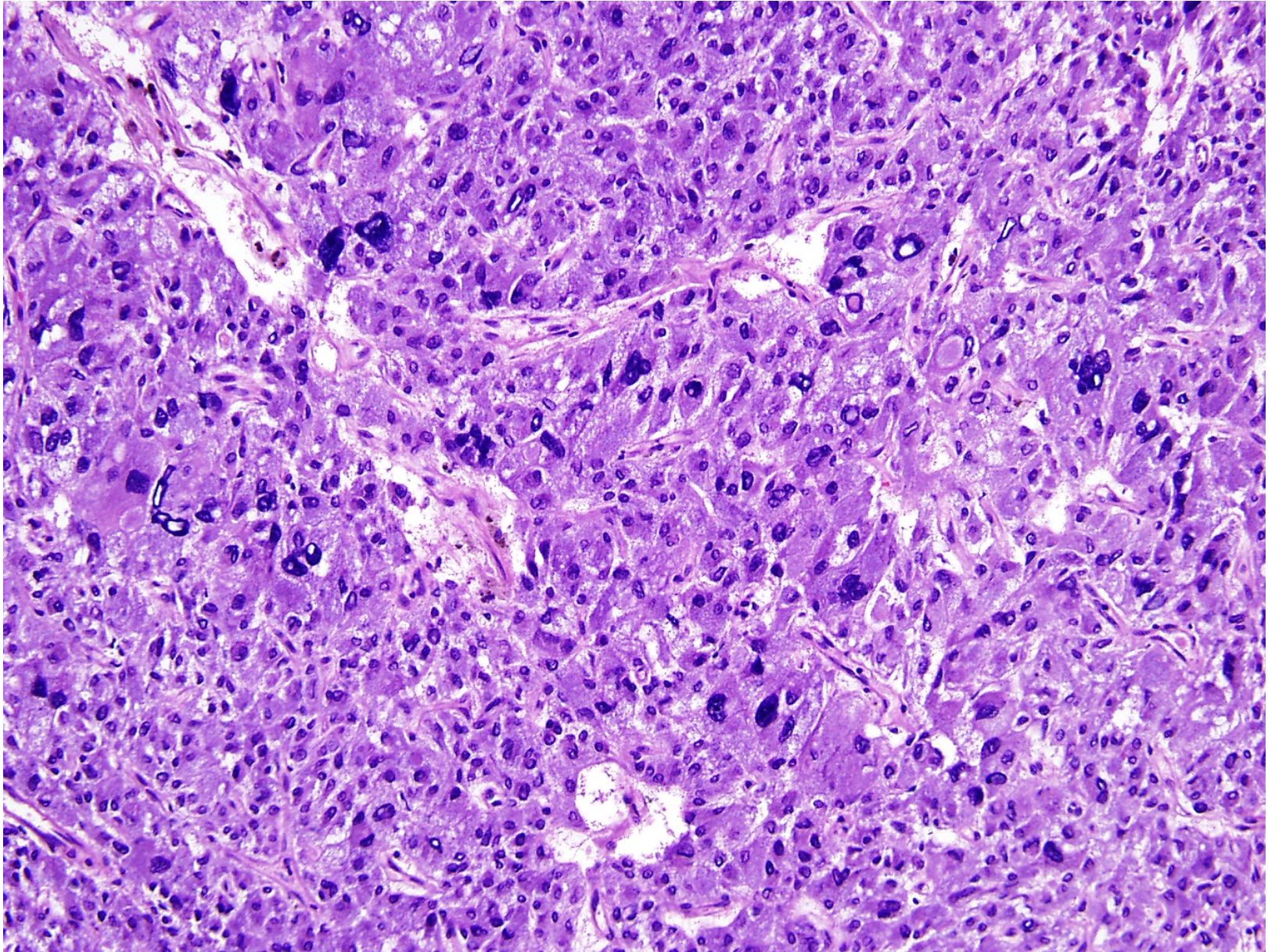




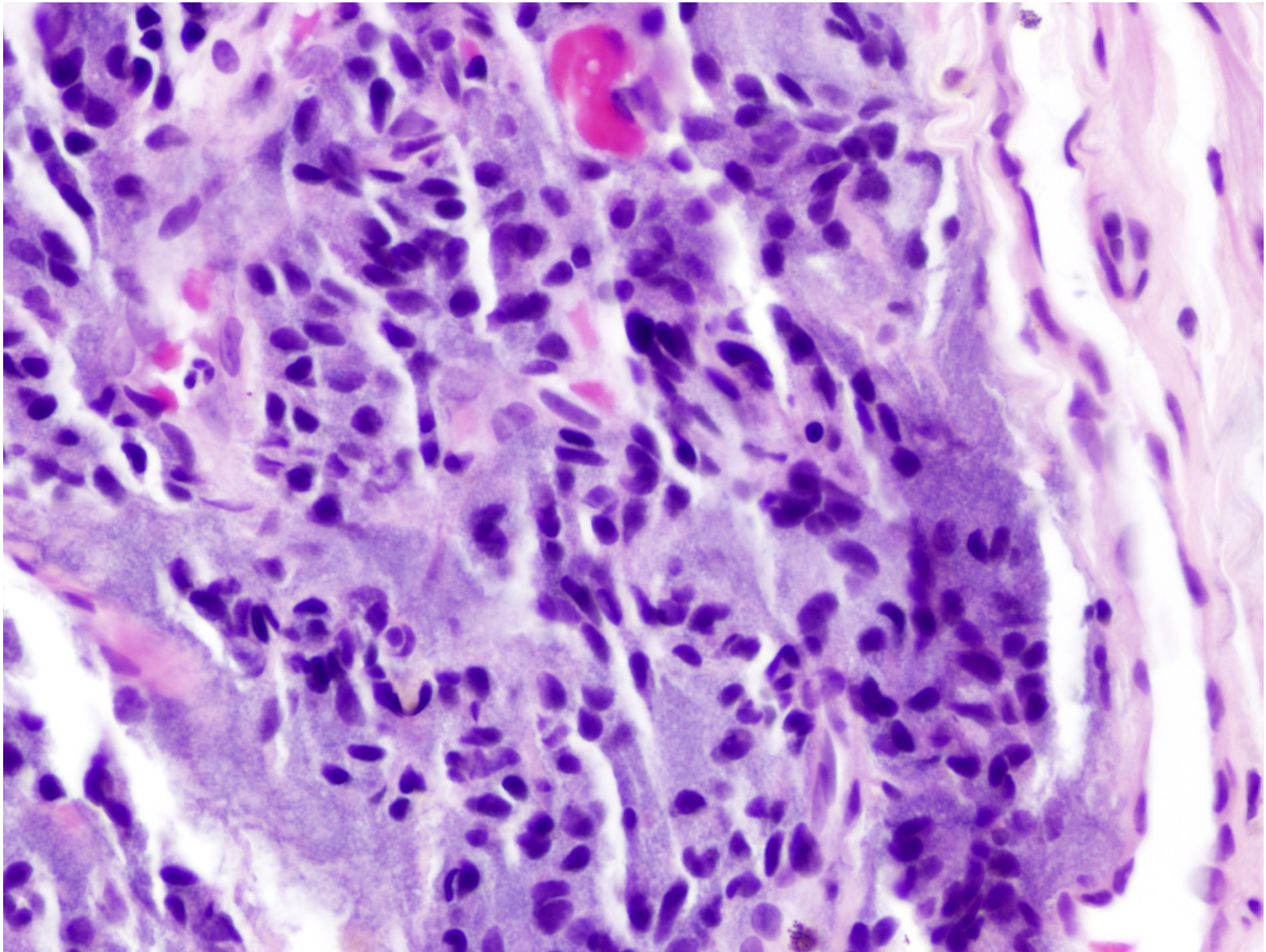




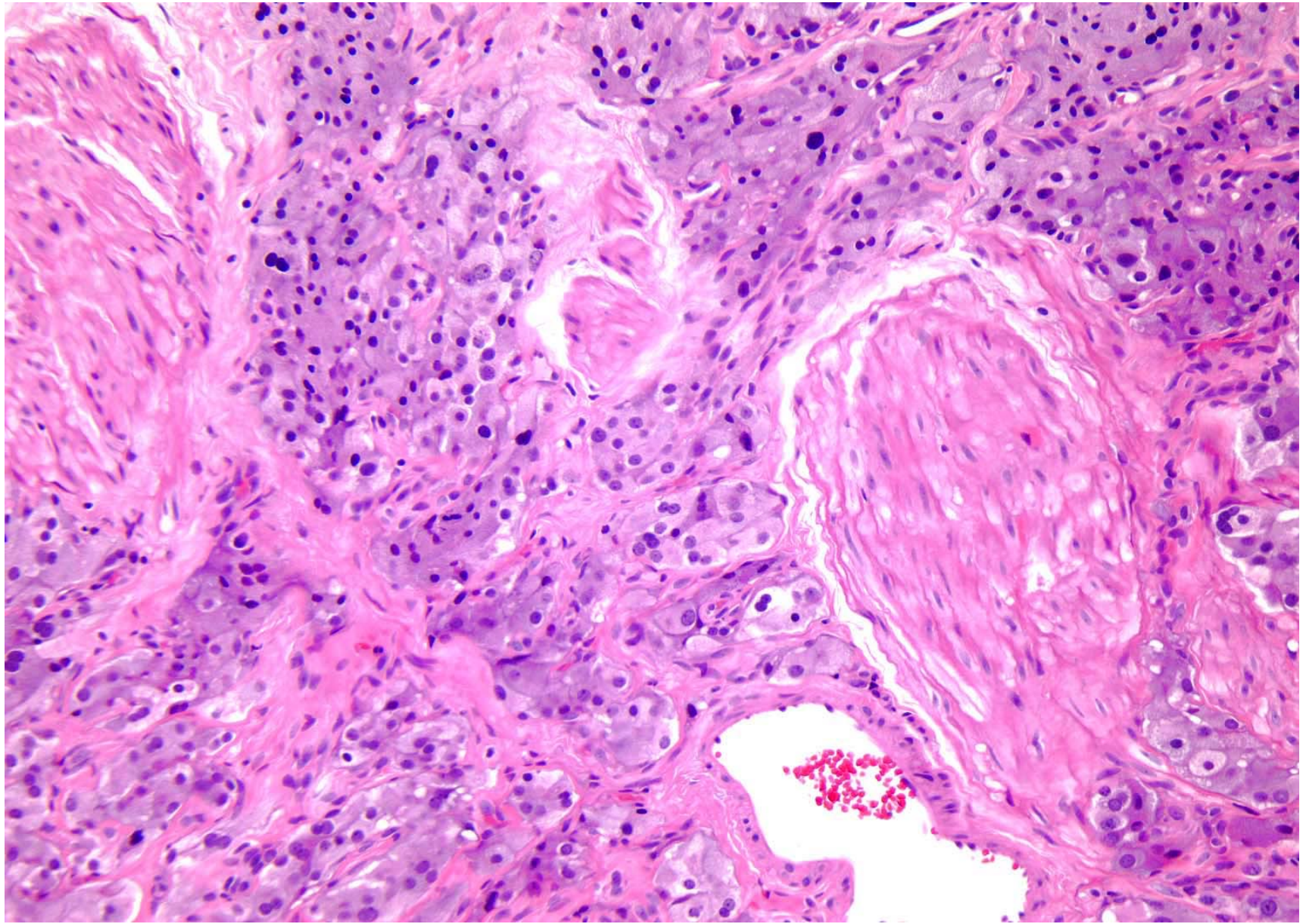




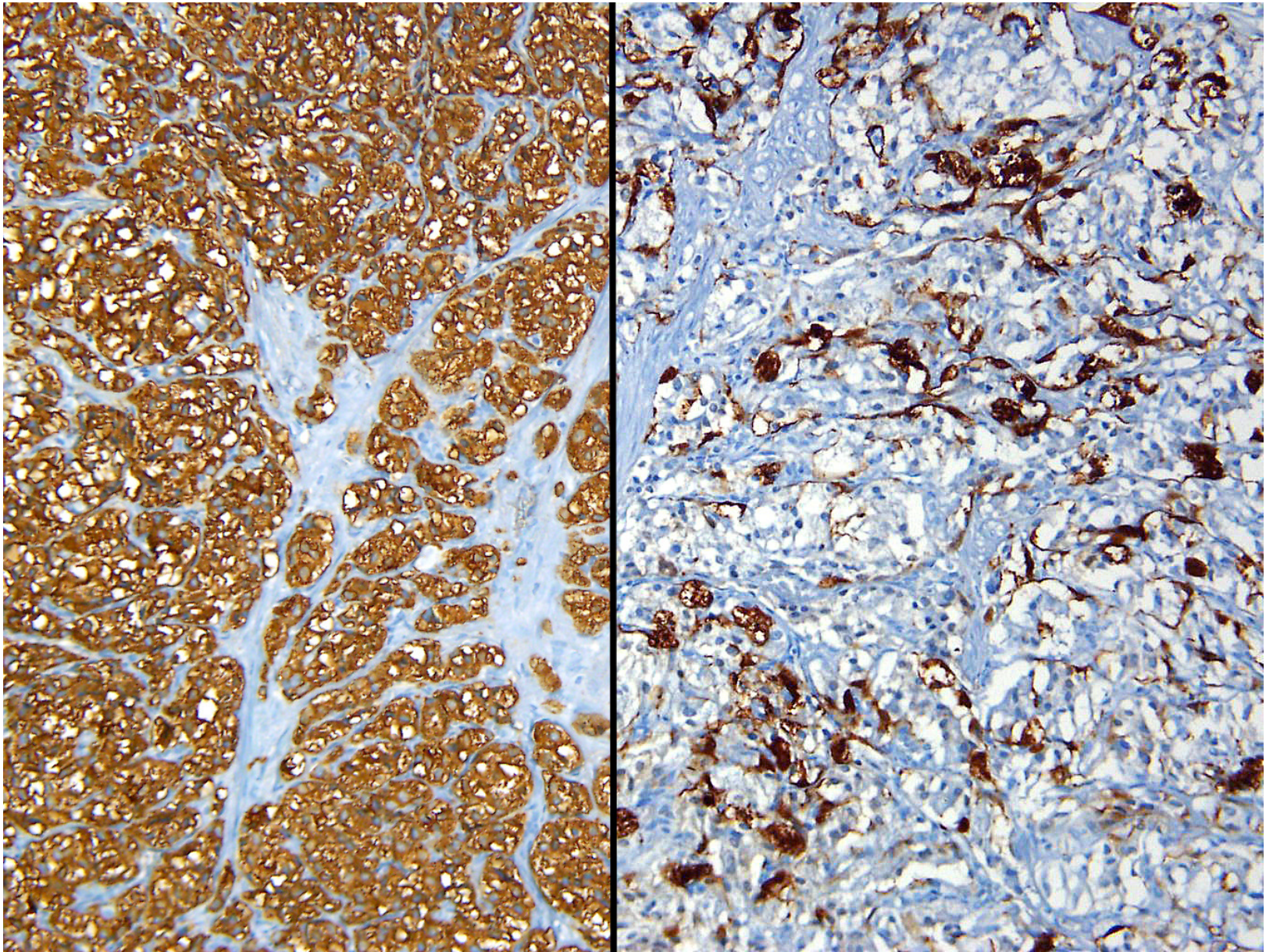












SYN

S100



# Paraganglioma

## Histologic Clues:

- Rich **vascular** pattern
- **Nested** architecture
- Large polygonal cells with abundant **amphophilic granular** cytoplasm

## DDX:

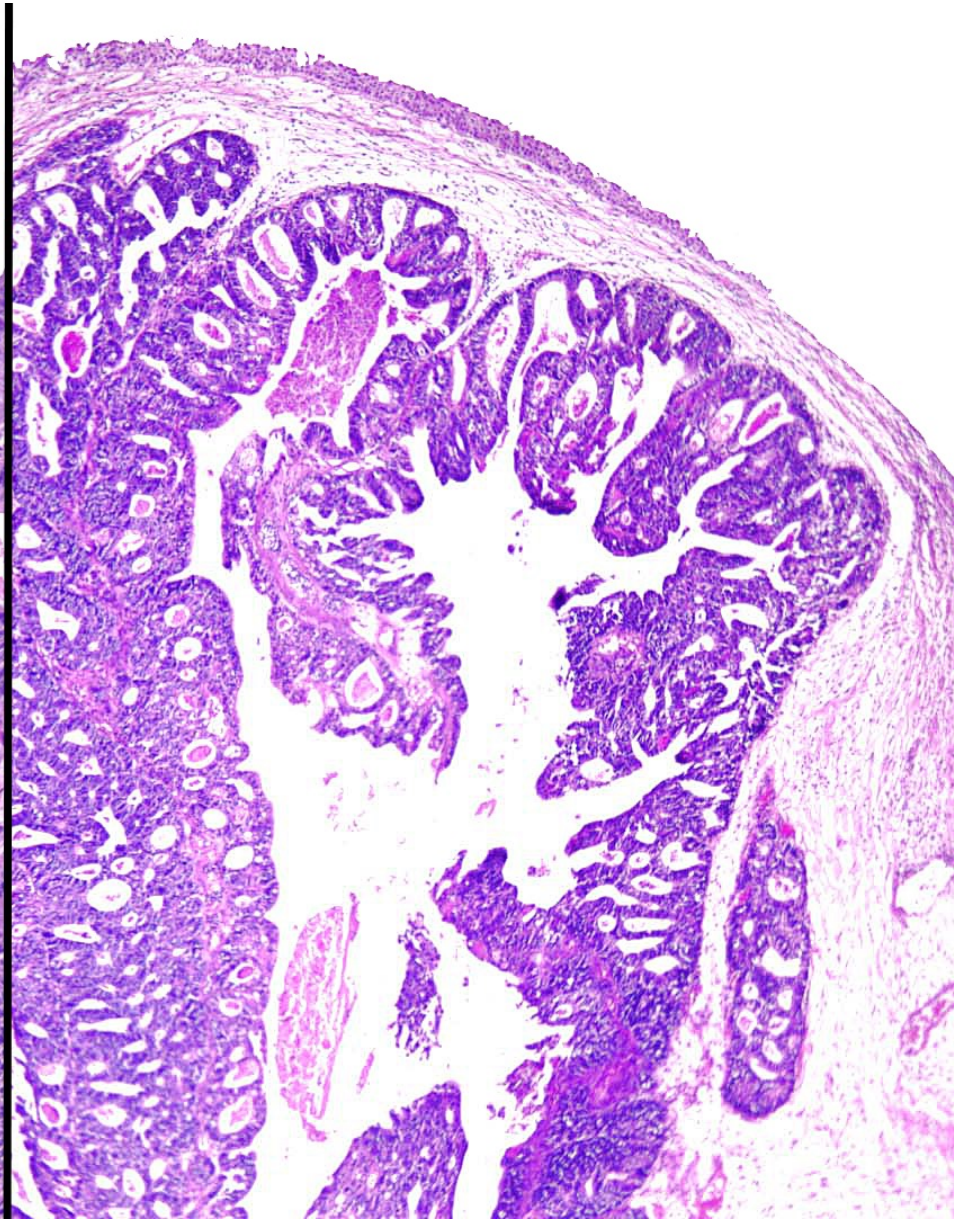
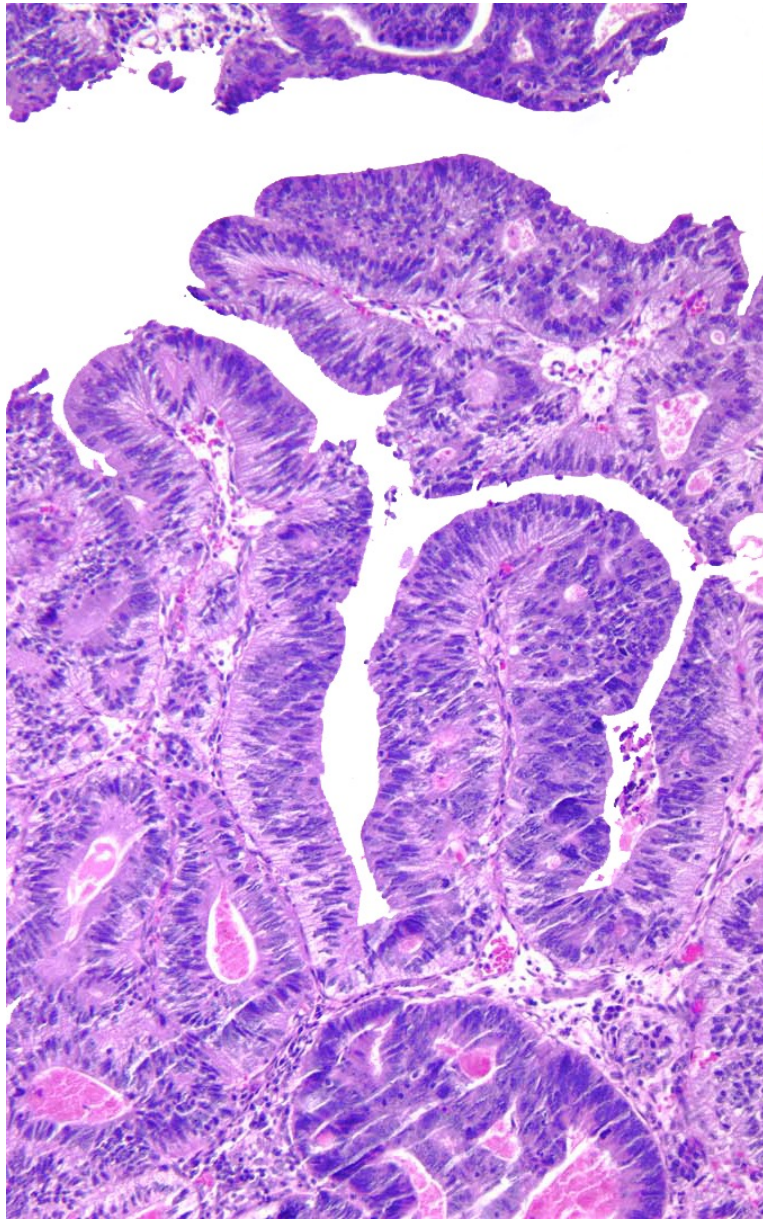
- **Cautery artifact & infiltration of detrusor muscle** → misinterpretation as URCa
- Significant clinical implications



## **Case 2**

A 59 yr old female smoker presented with gross hematuria; a TURB was performed.







## Case # 2

### Diagnosis:

- A. Villous Adenoma with Associated Invasive Adenocarcinoma of Urinary Bladder
- B. Secondary bladder involvement by Colonic Adenocarcinoma
- C. Urachal Adenocarcinoma
- D. Cystitis Cystica et Glandularis.

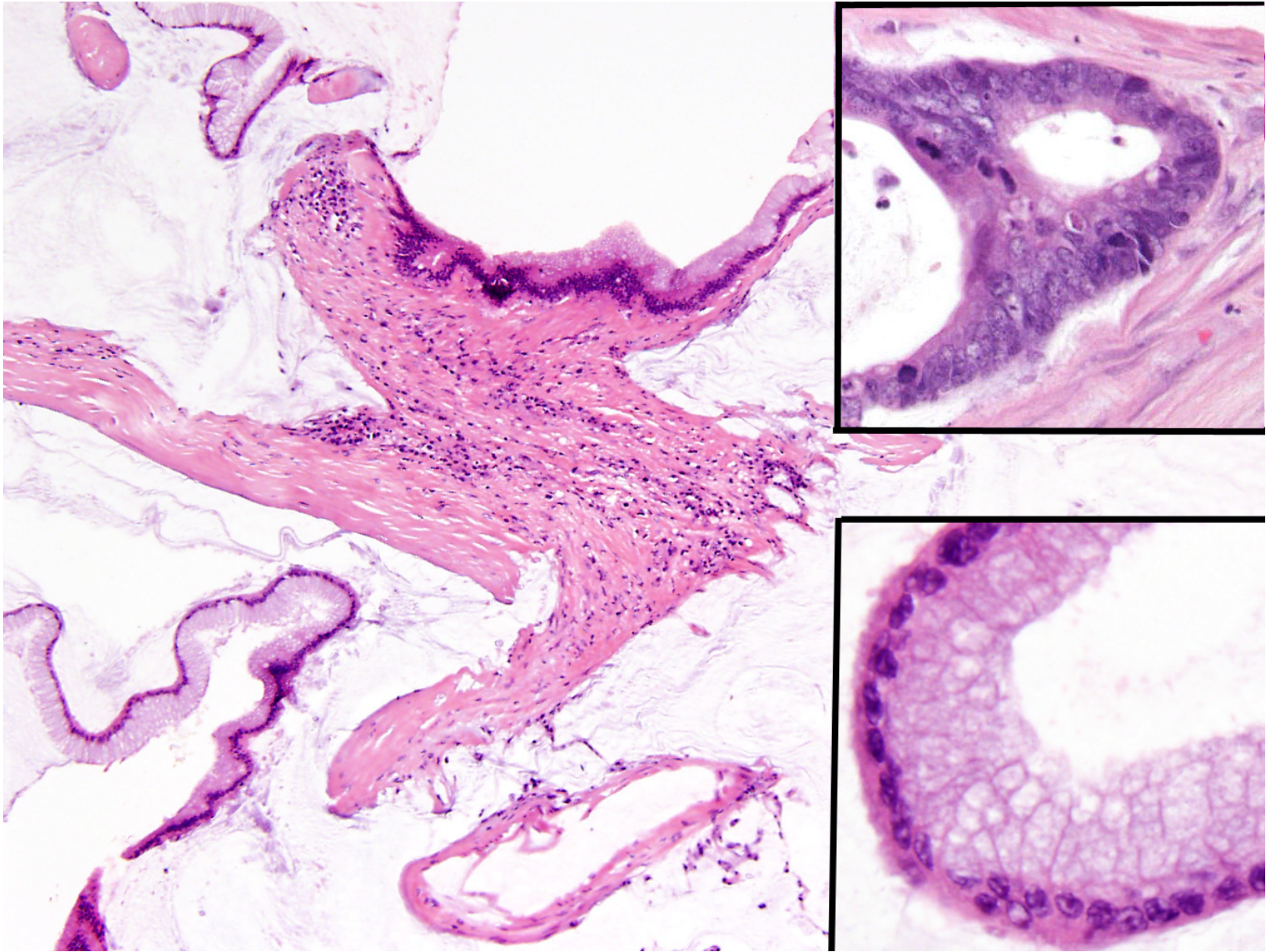


## Case # 2

### Diagnosis:

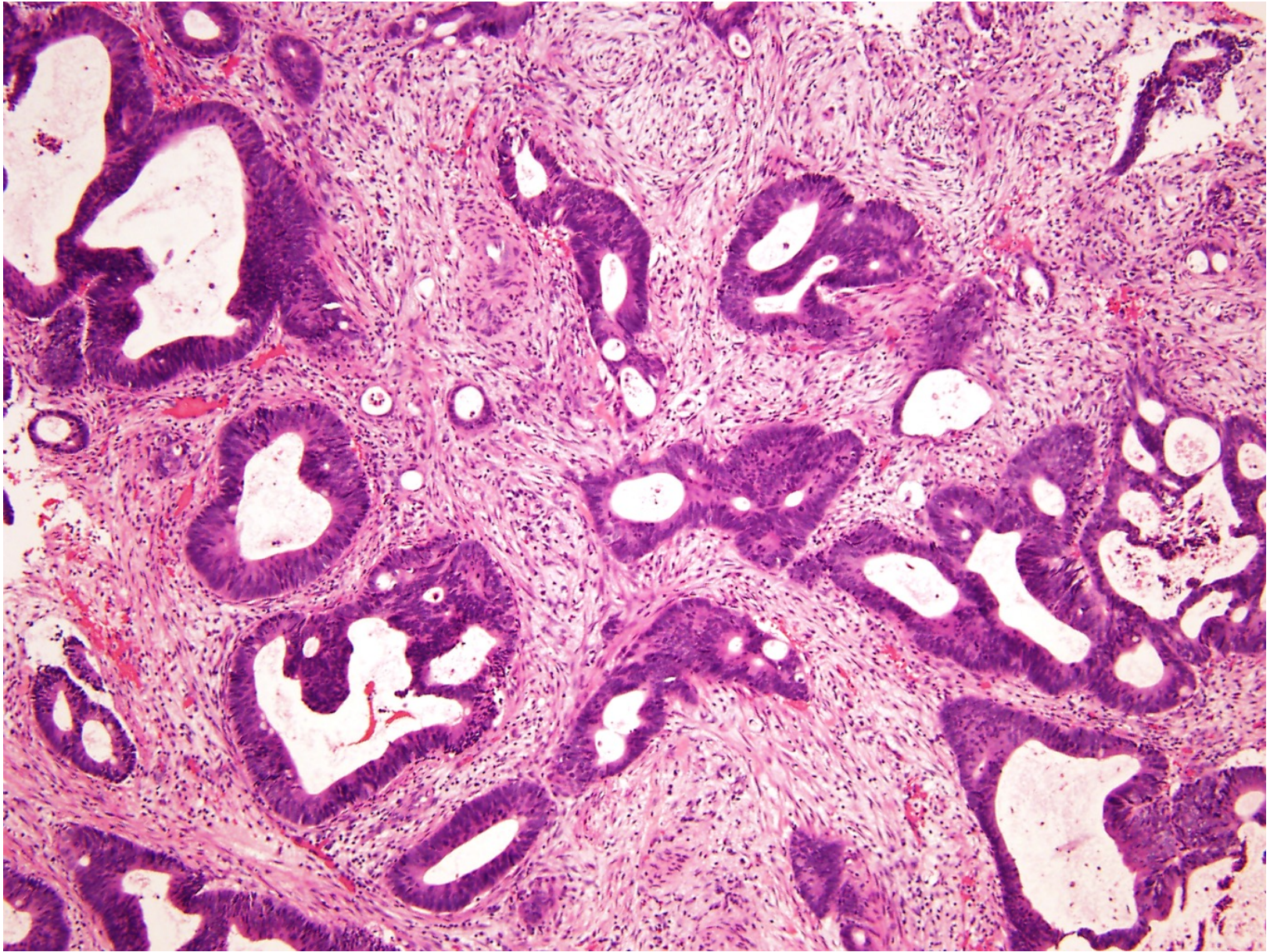
- A. Villous Adenoma with Invasive Adenocarcinoma of Urinary Bladder
- **B. Secondary bladder involvement by Colonic Adenocarcinoma**
- C. Urachal Adenocarcinoma
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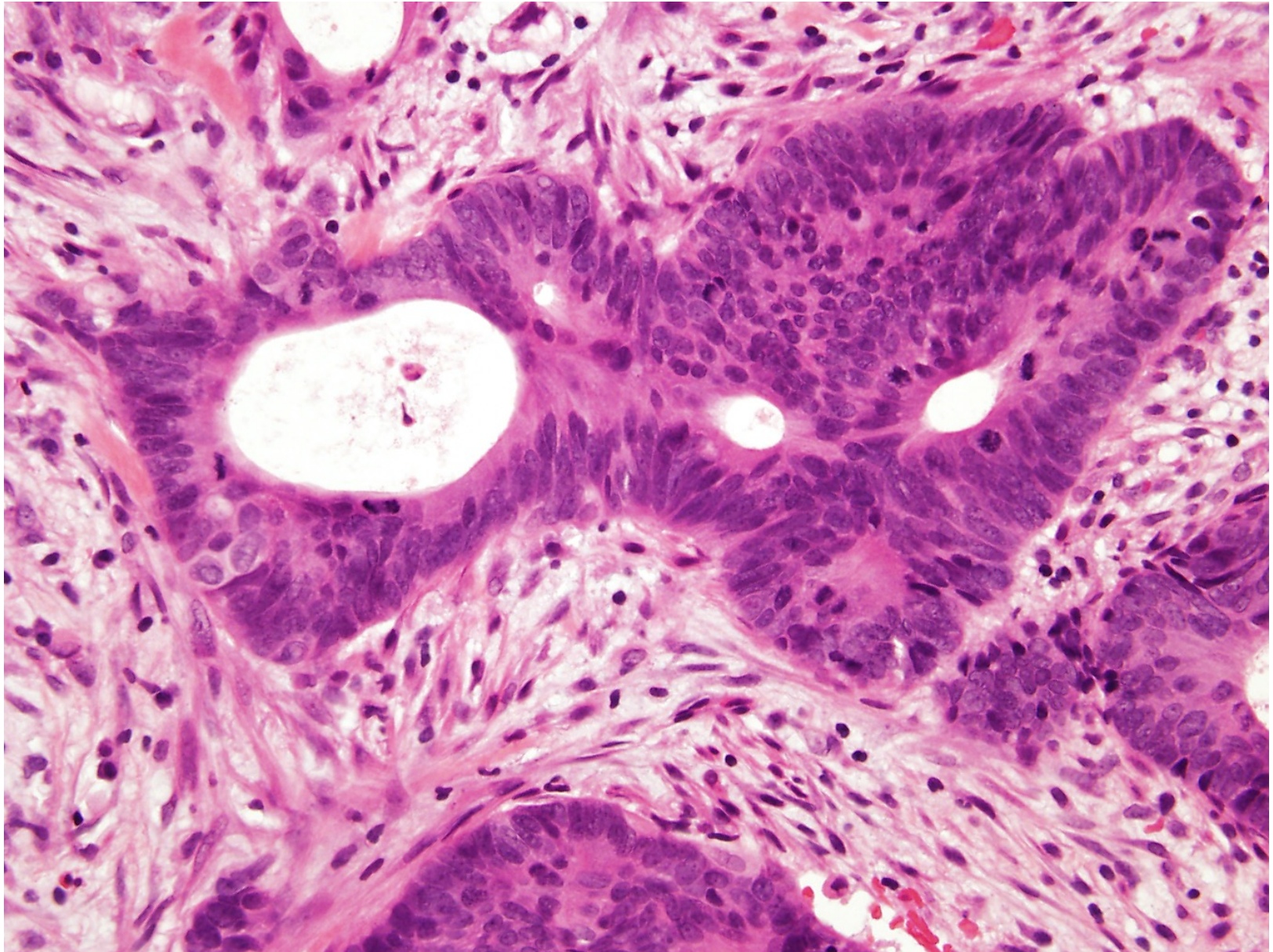
Bladder Adenocarcinoma, Intestinal type





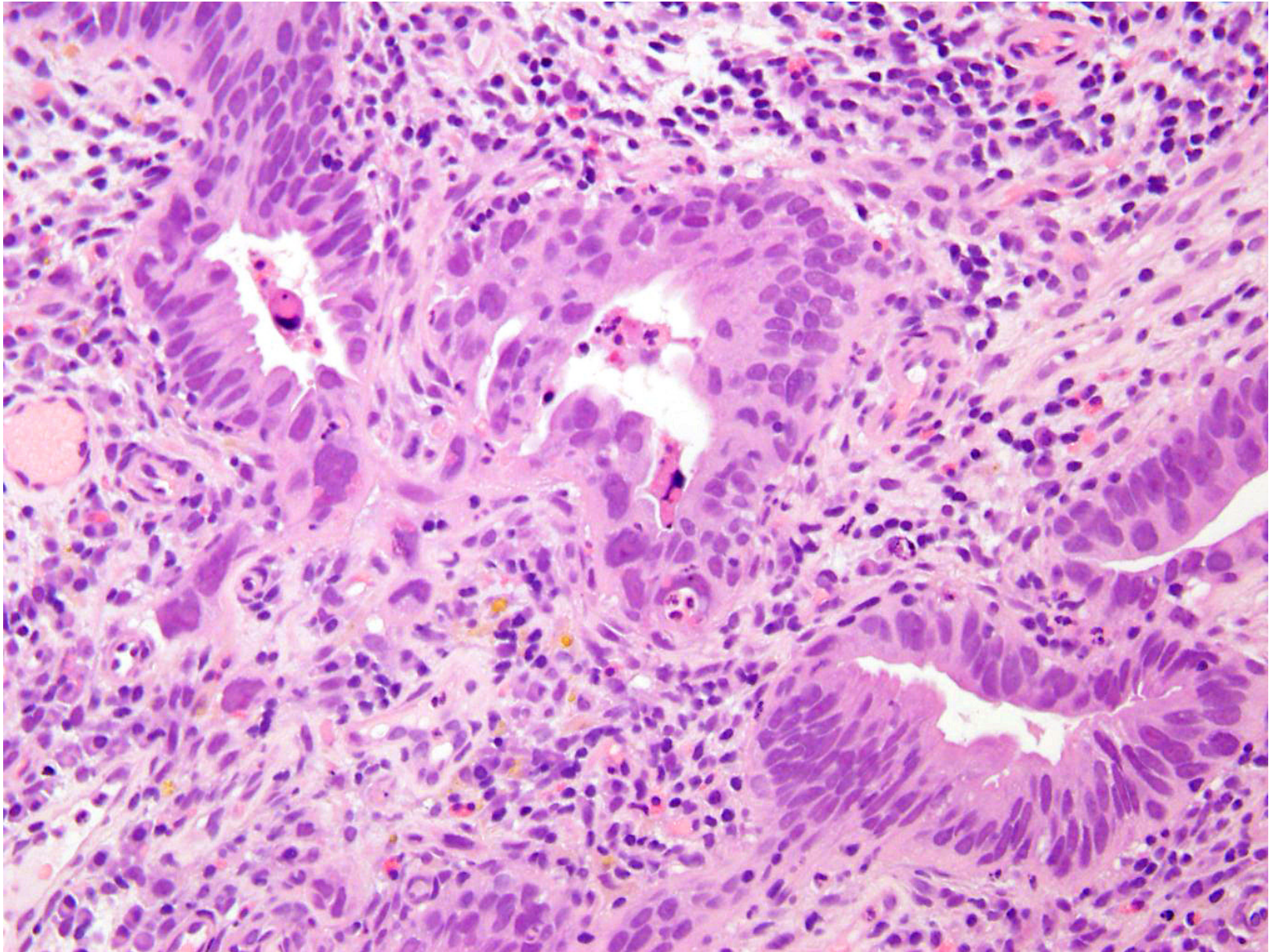
Bladder Adenocarcinoma, Intestinal type





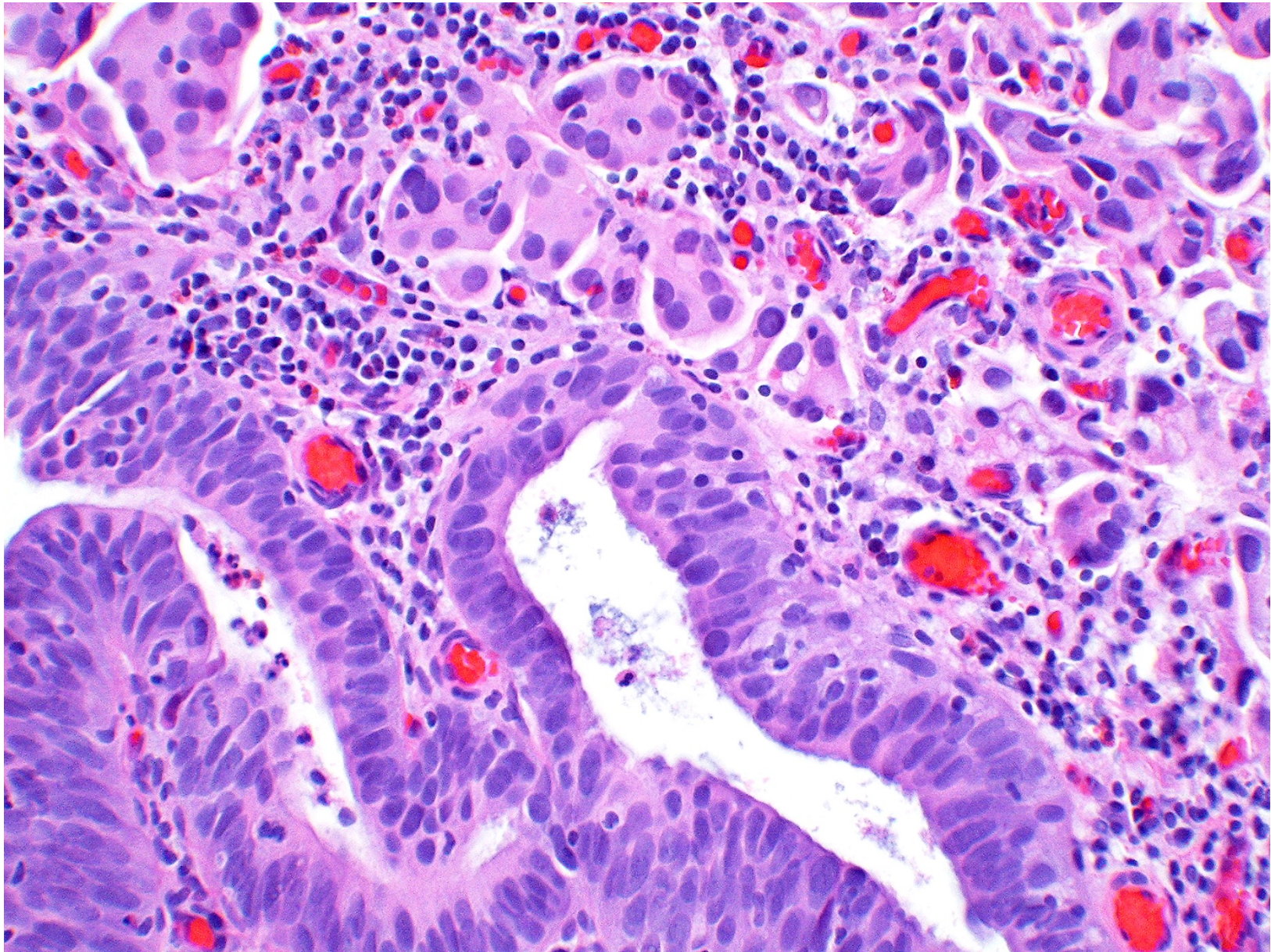
Bladder Adenocarcinoma, Intestinal type





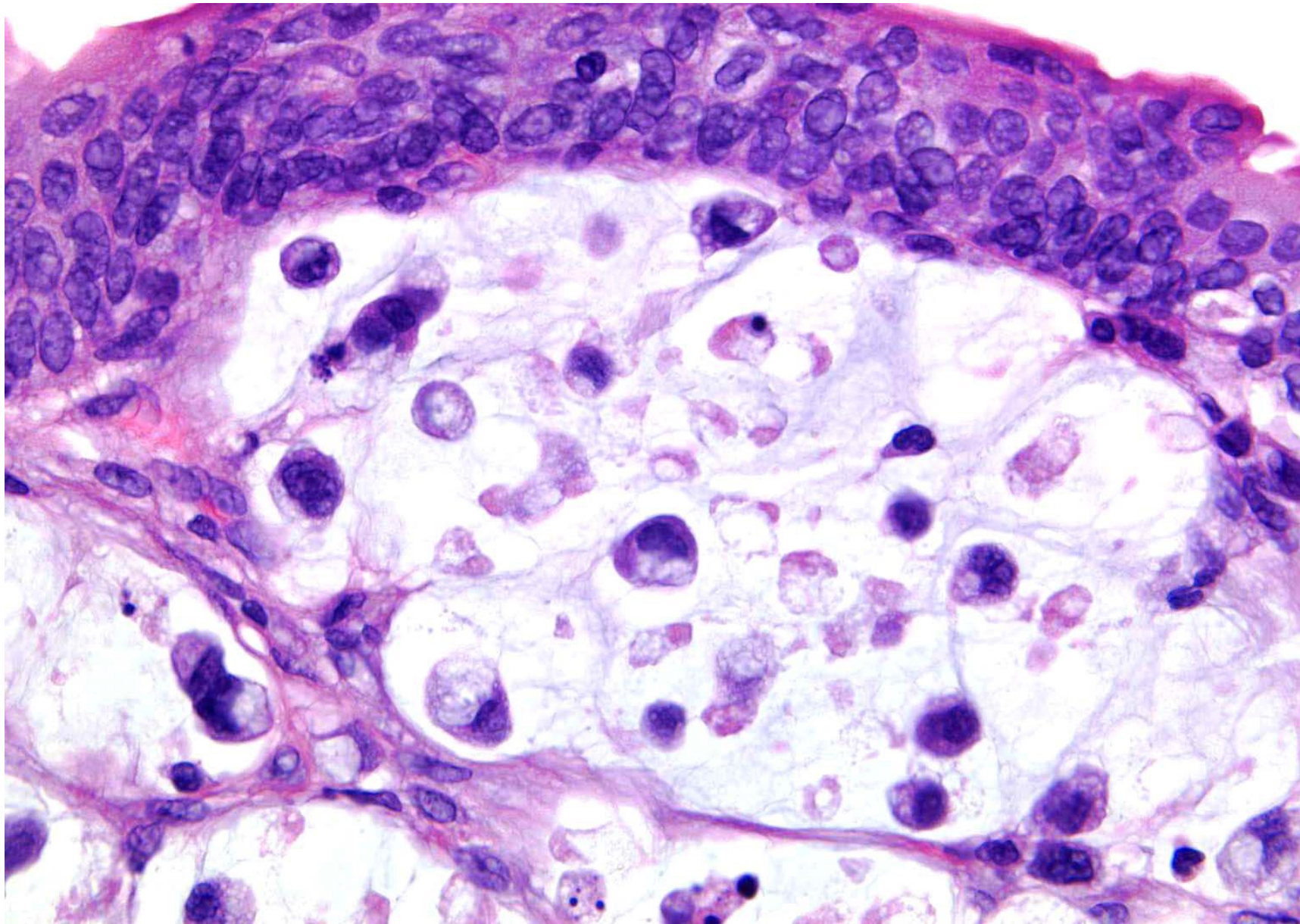
Bladder Adenocarcinoma, Intestinal type





Bladder Adenocarcinoma, Intestinal type





Bladder Adenocarcinoma, Signet Ring Mucinous



# Secondary Tumors of Urinary Bladder

## CRCa vs Primary Adenocarcinoma

- Secondary CRCa spread to bladder is **more common** occurrence
- Differentiating a CRCa spread from “intestinal type” primary **can not be made with absolute certainty**
- Presence of a **background** of intestinal metaplasia/villoglandular adenomatous dysplasia **can be mimicked by colonization** by secondary well differentiated CRCa
- **A recommendation to rule out spread** should be forwarded to avoid a potentially unjustifiable radical cystectomy



# Secondary Tumors of Urinary Bladder

## CRCa Vs Primary Bladder Adenocarcinoma

- *Wang HL et al. AJSP 2001*  
Nuclear B-catenin (-), CK7(+) 65%, CK20(+) 50%
- *Suh N et al. Mod Pathol 2005*  
CDX2 (+) 50% and Villin (+) 60%
- *Raspollini MR et al. appl immunohistochem mol morphol 2005*  
CDX2 (+) 13% , CK7 (+) 60%, CK20 (+) 60%



# IHC

## CRCa Spread Vs Primary Bladder Adenocarcinoma

MARKER	Primary Bladder Adenocarcinoma	CRCa spread to Bladder
CDX2	+ (15-50%)	+ (100%)
<b>Nuclear B Catenin</b>	-	+ (80%)
Ck 20	+ (50-60%)	+ (95%)
<b>CK7</b>	+ (60%)	+ (5%)
Villin	+ (60%)	+ (98%)
<b>GATA3</b>	+/-	-

*Wang HL et al. AJSP 2001; Raspollini MR et al. appl immuno 2005; Suh N et al. Mod Pathol 2005*

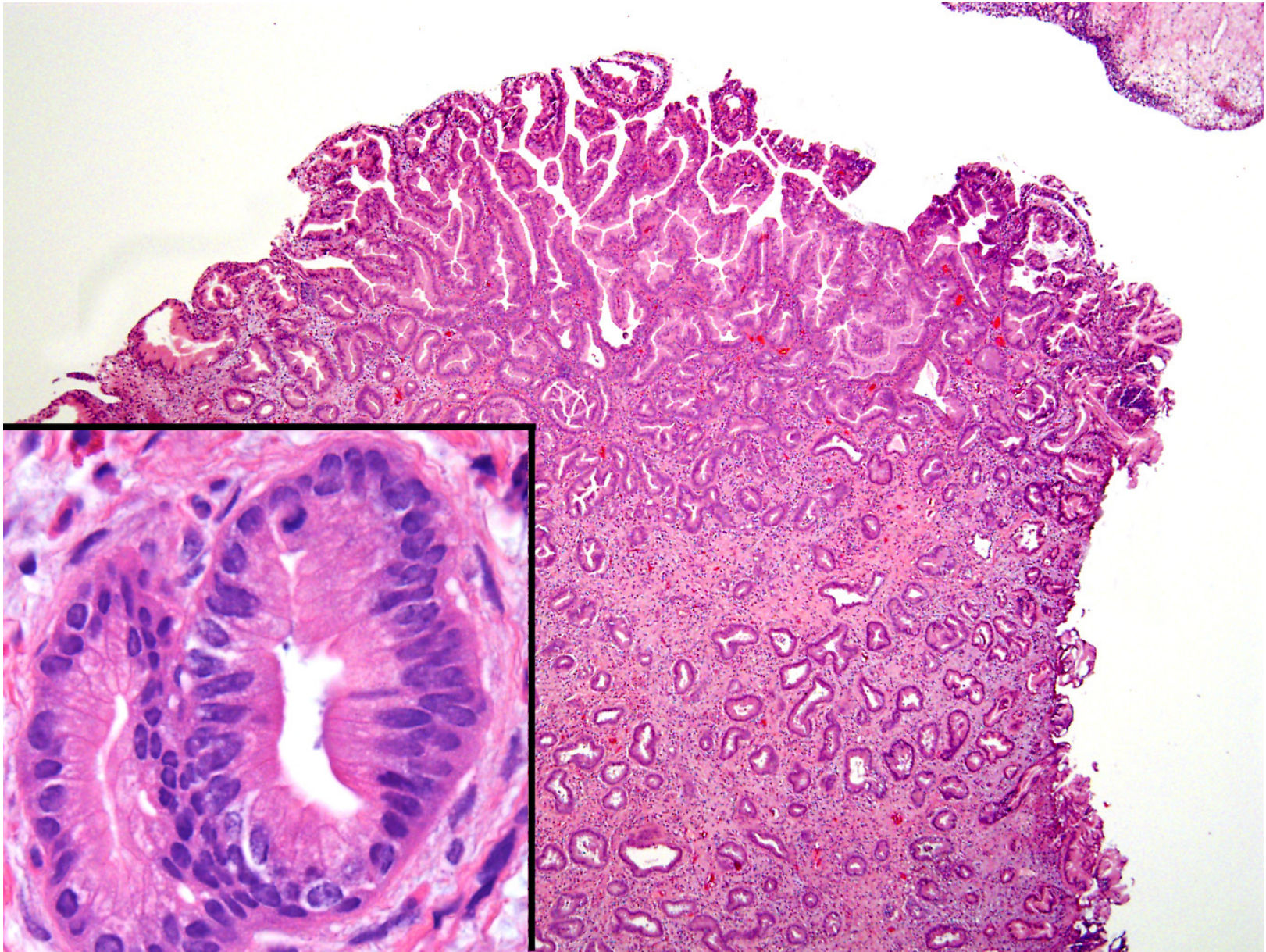


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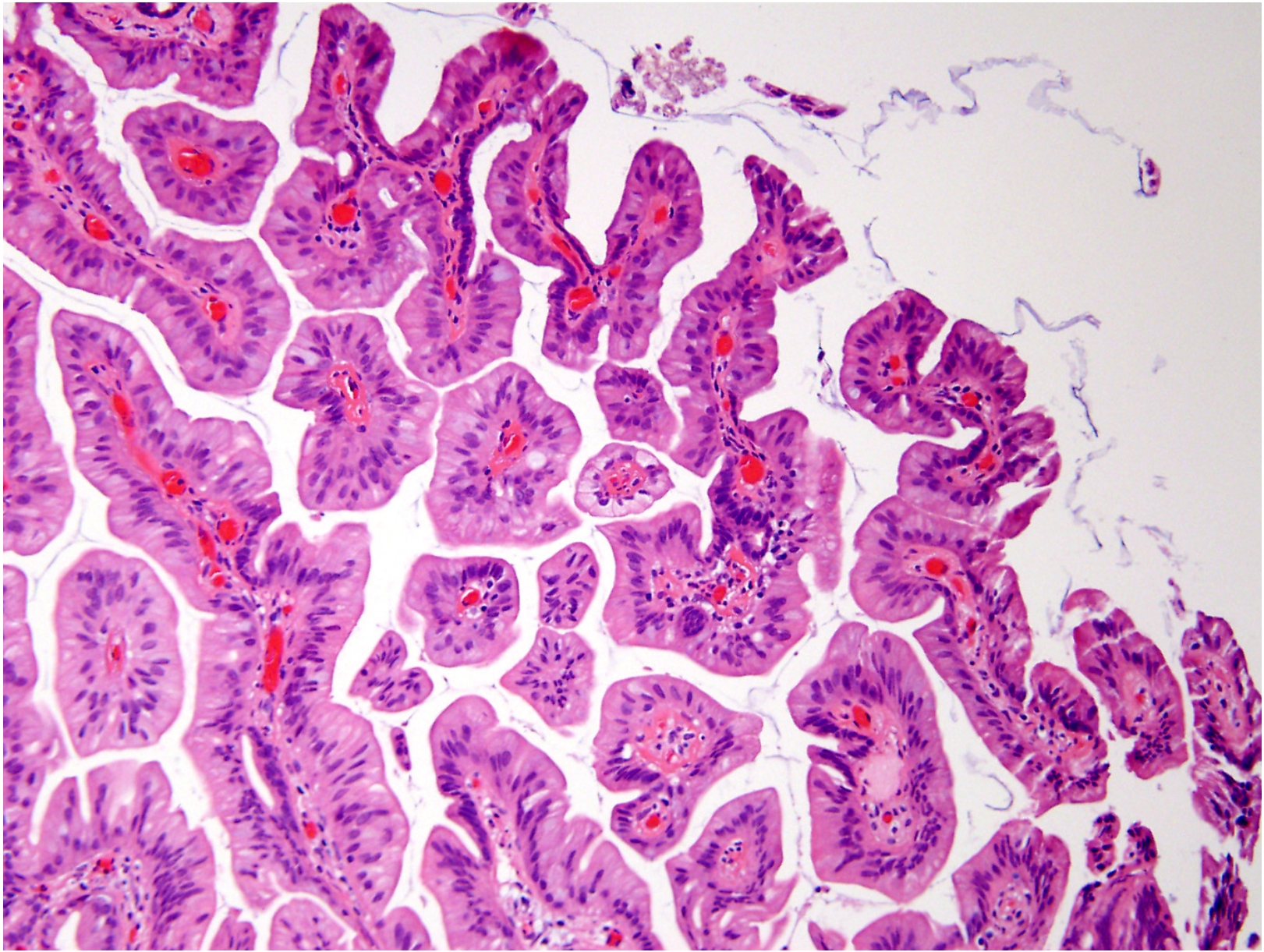
- Most common sources: colorectal (33%), prostatic (12%) and cervical (11%) sites
- Other sources include breast, stomach, lung and melanoma primaries.



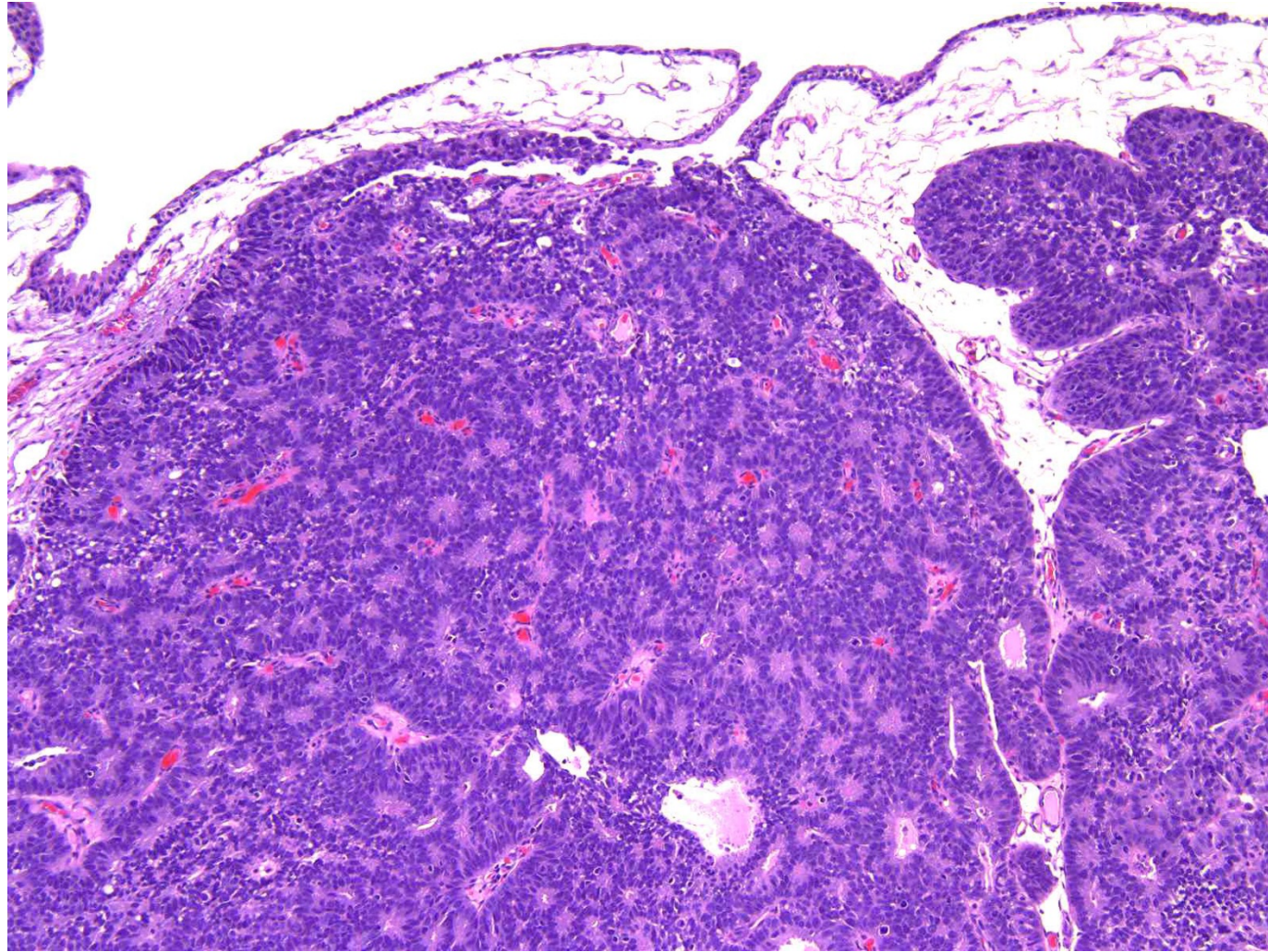


Metastatic Pancreatic Ductal Adenocarcinoma









Prostate Adenocarcinoma



# CONCLUSIONS

- Bladder cancer mimickers include benign entities as well as malignancies
- Extension or Metastases from extravesical primaries should be considered when a CIS or Non-Invasive Papillary precursor is not identifiable

Thank You !





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