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Mimics of Bladder Neoplasia

- **Adenocarcinoma**
- **Urothelial Carcinoma**

Mimickers of Bladder Adenocarcinoma

- **Florid cystitis glandularis**
- **Endocervicosis**
- **Nephrogenic metaplasia (adenoma)**

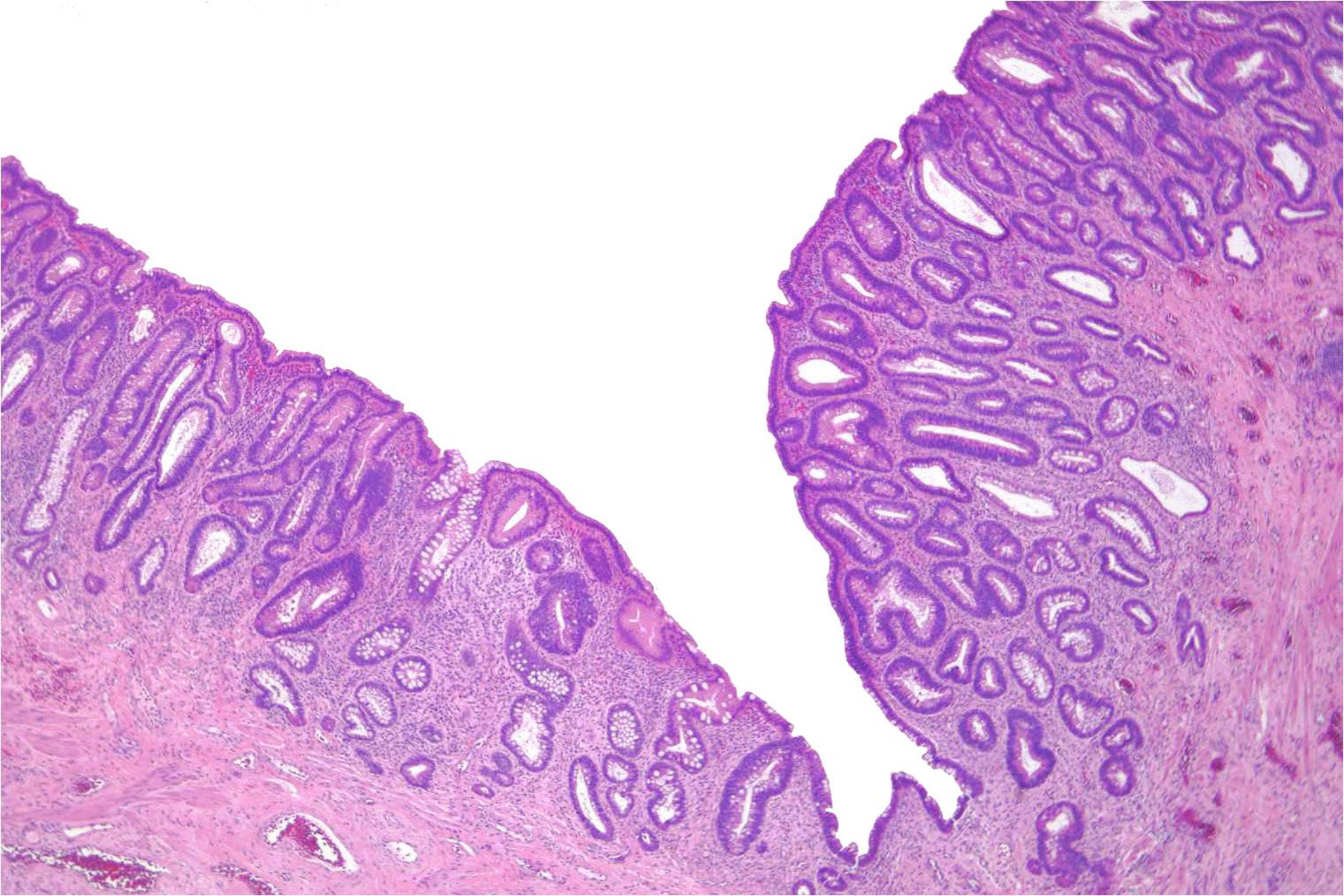
Cystitis Glandularis (Intestinal Type)
Colonic Metaplasia

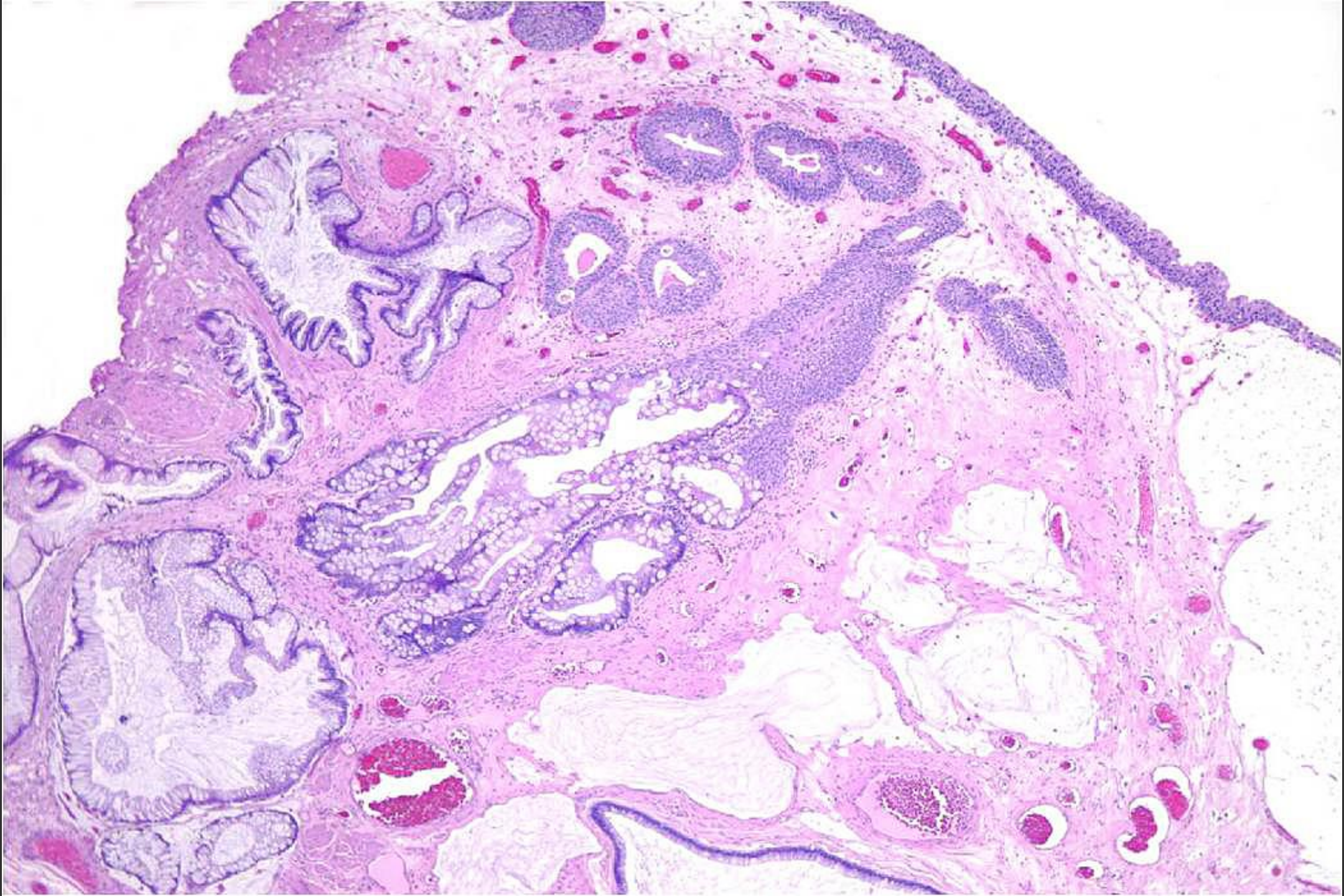
Features Mimicking Adenocarcinoma

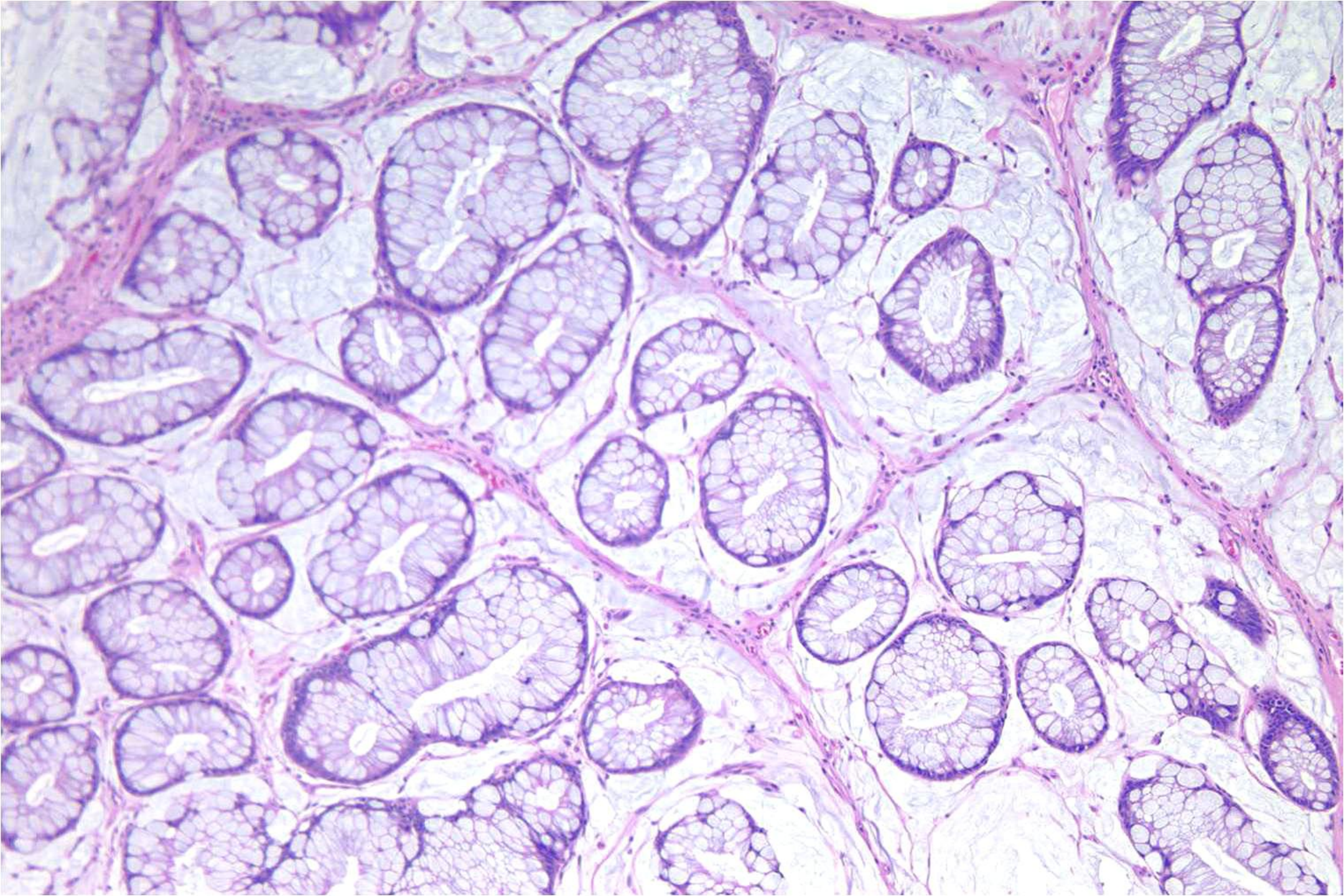
- Mucinous extravasation
- Rare involvement of muscle

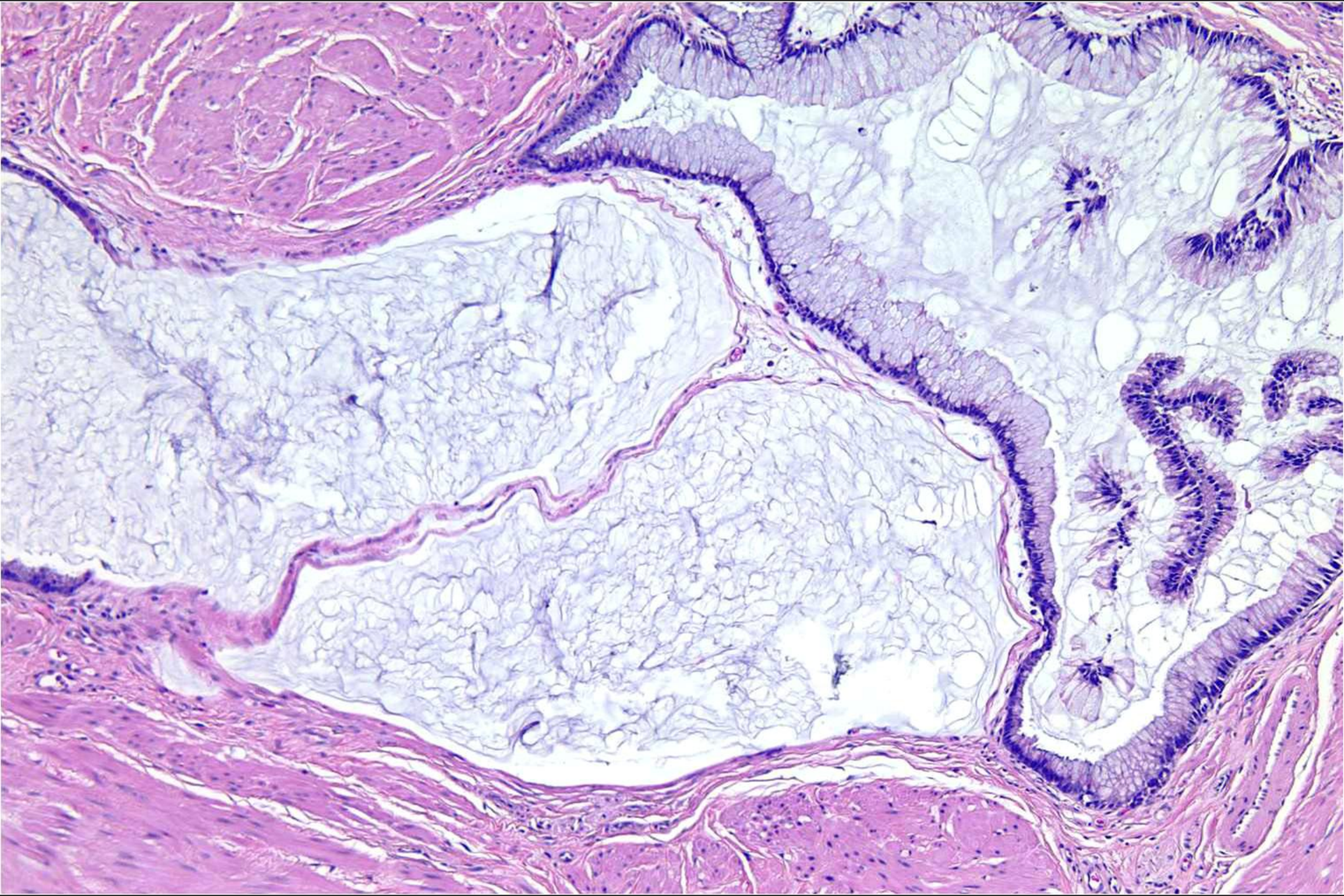
Distinguishing Features from Adenocarcinoma

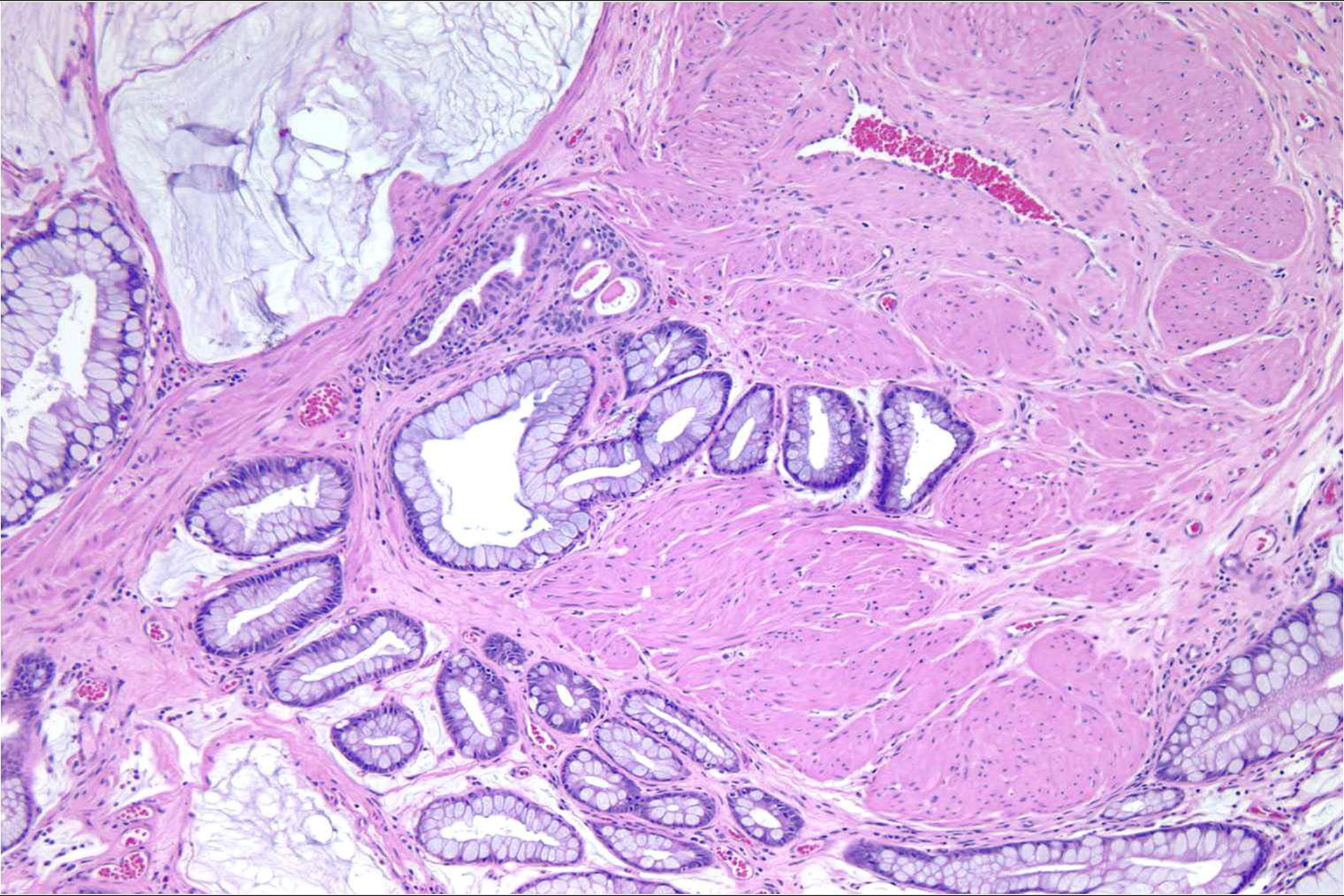
- Lack of cytologic atypia
- Lack of necrosis
- Lack of signet cells

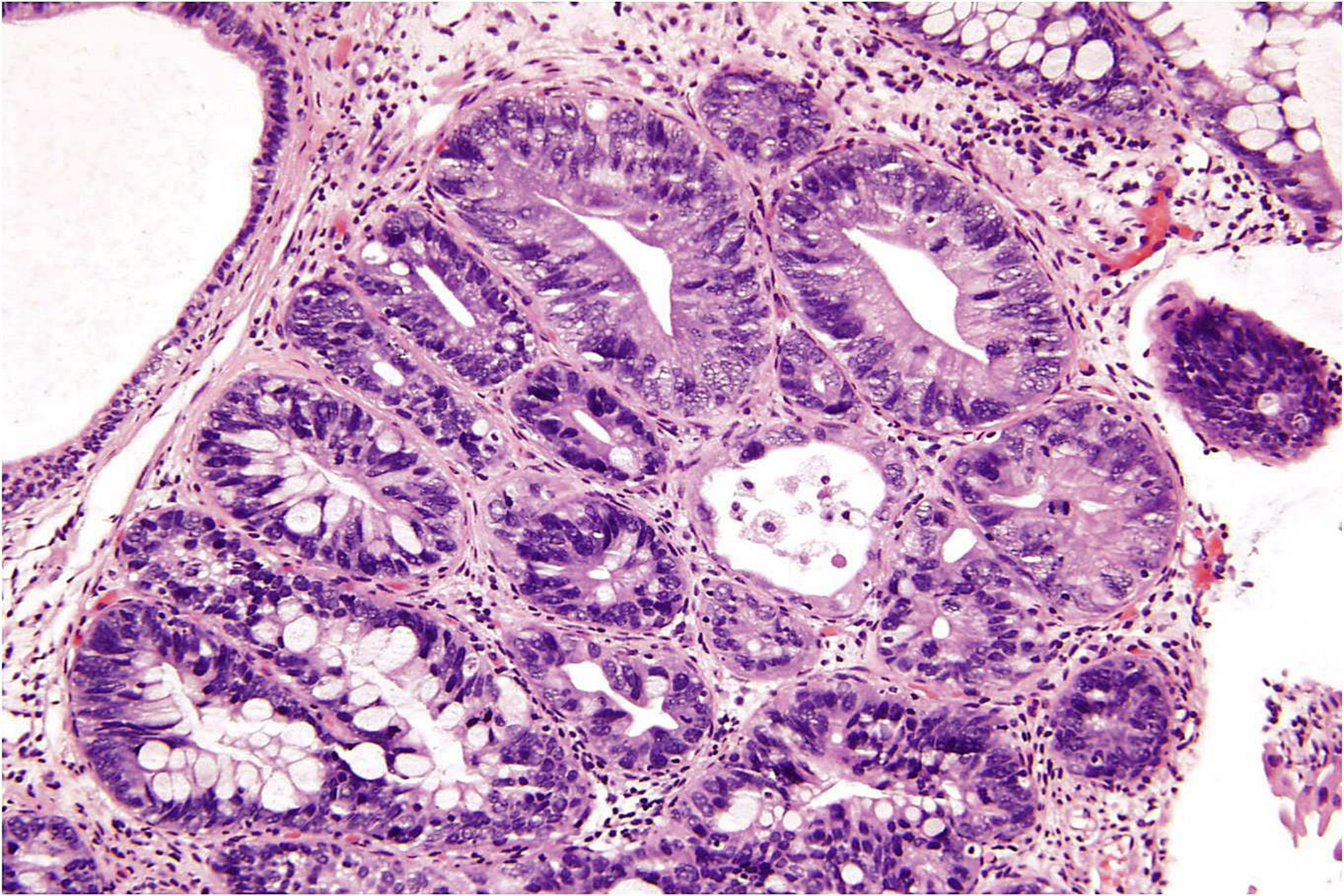








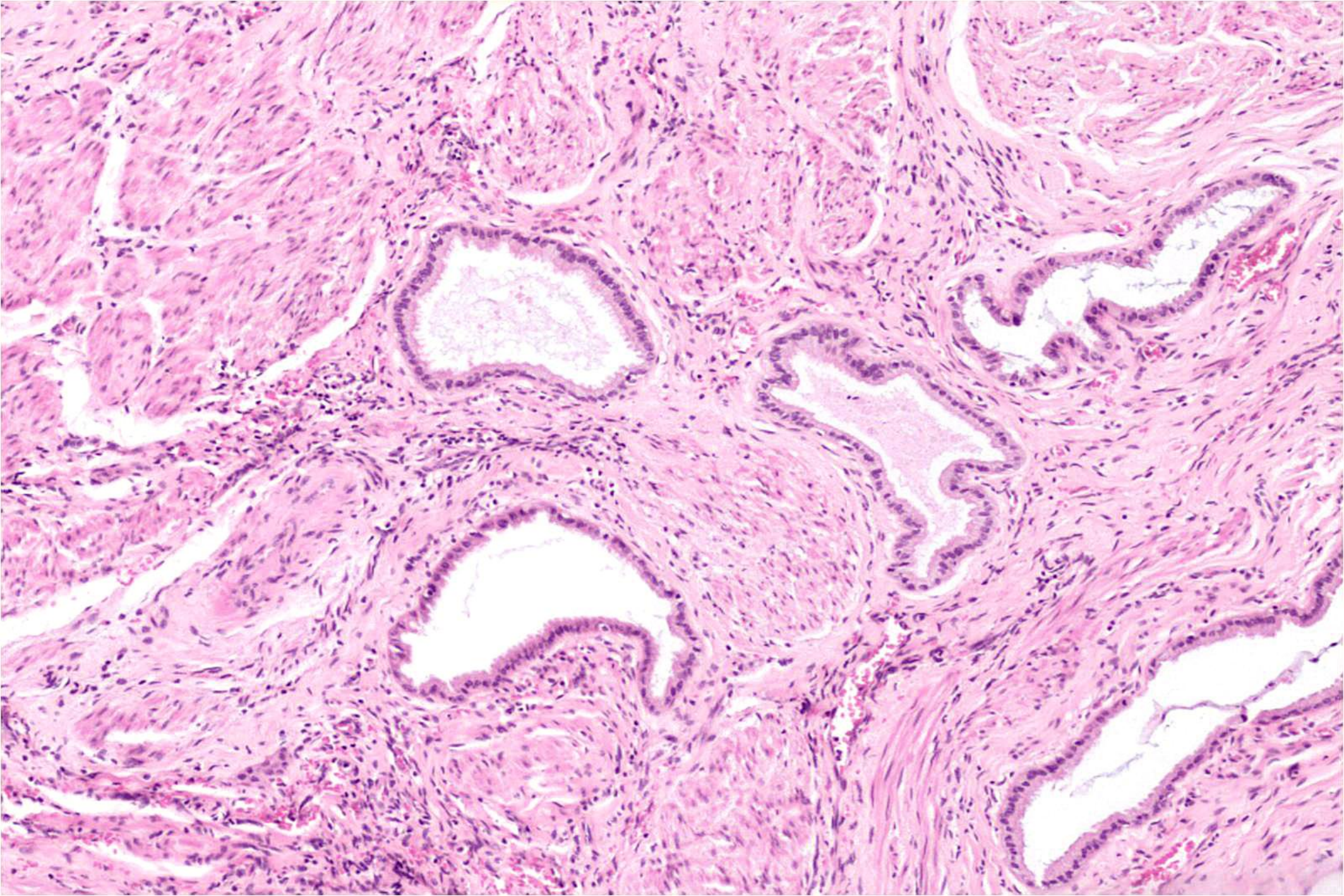


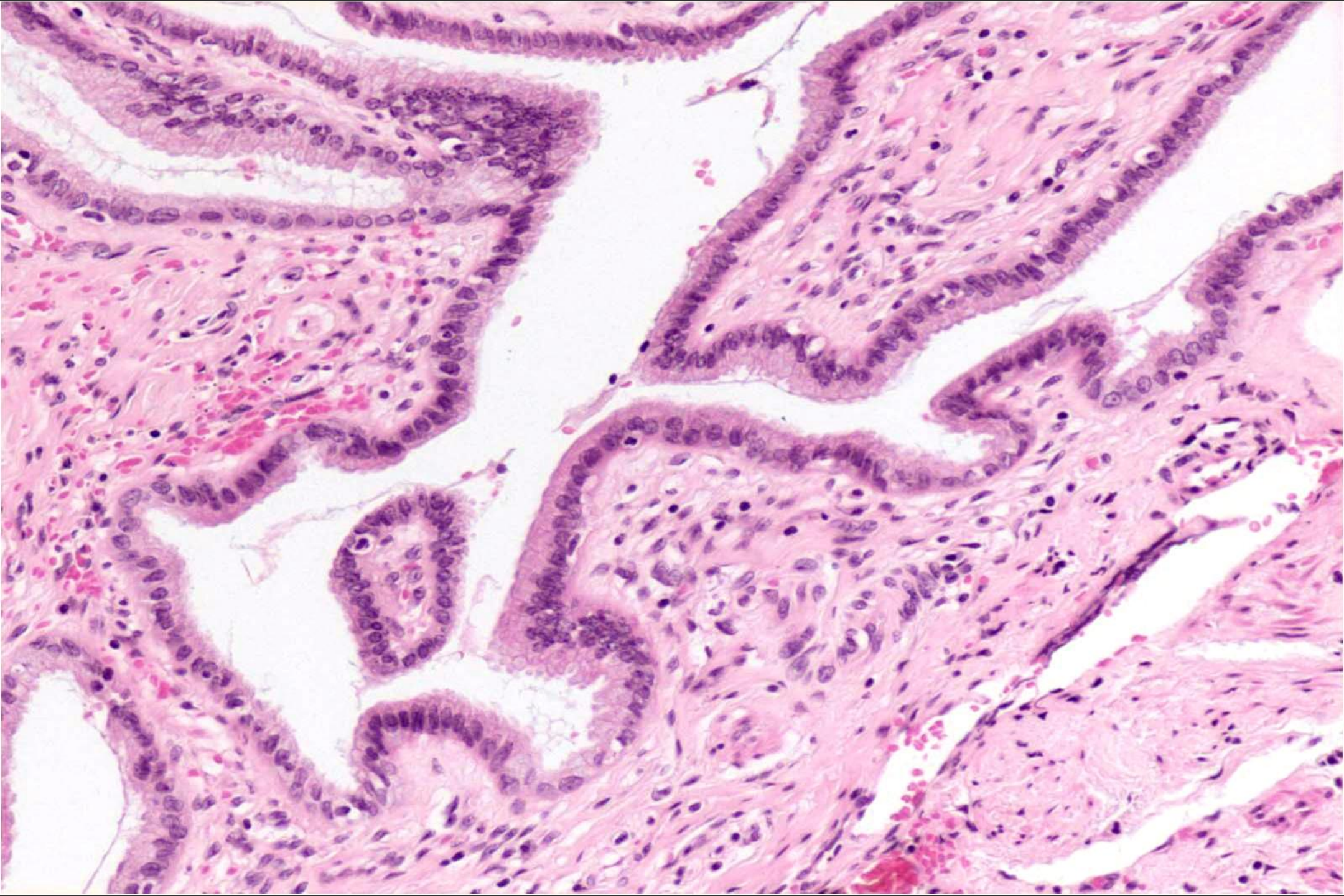


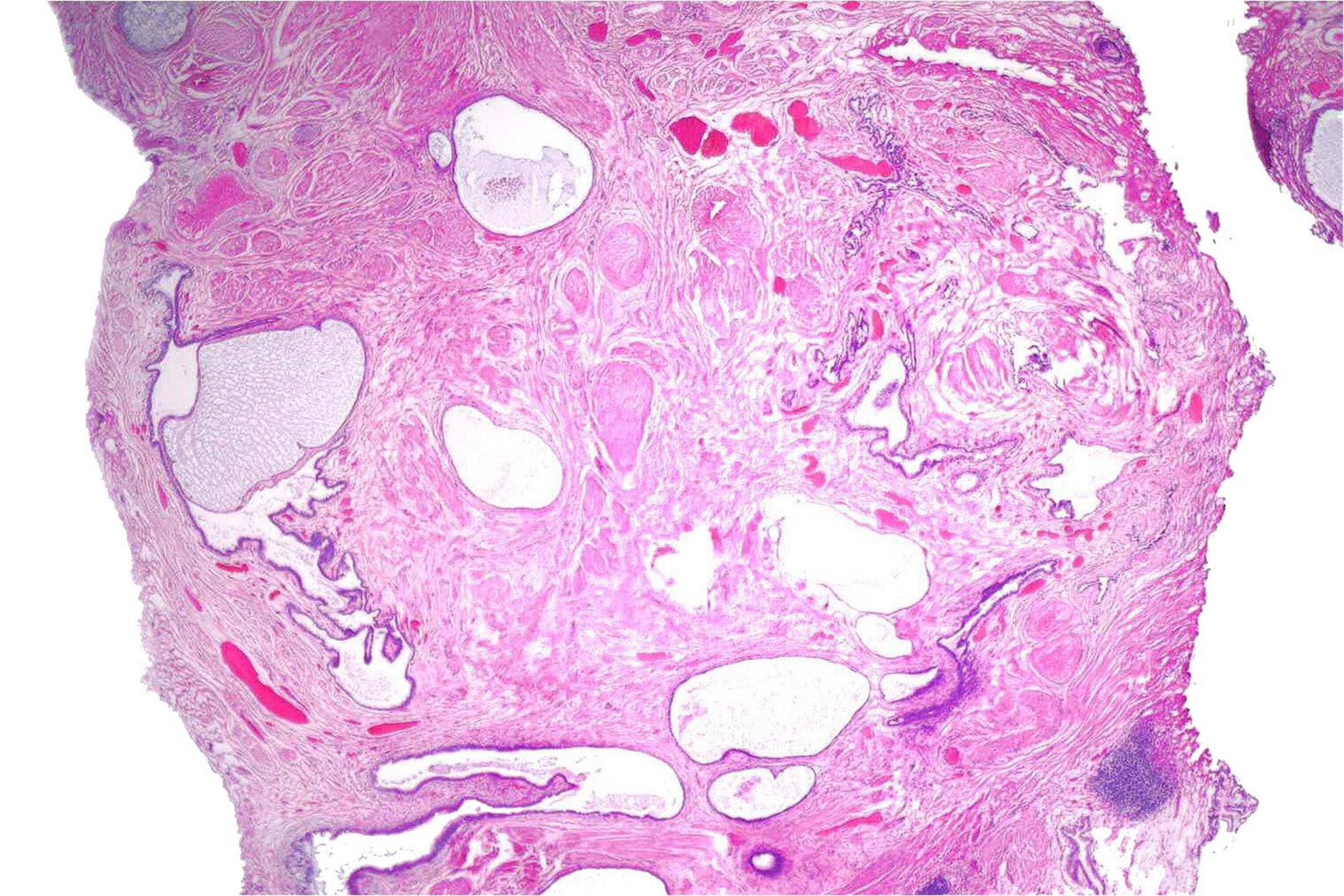
Endocervicosis

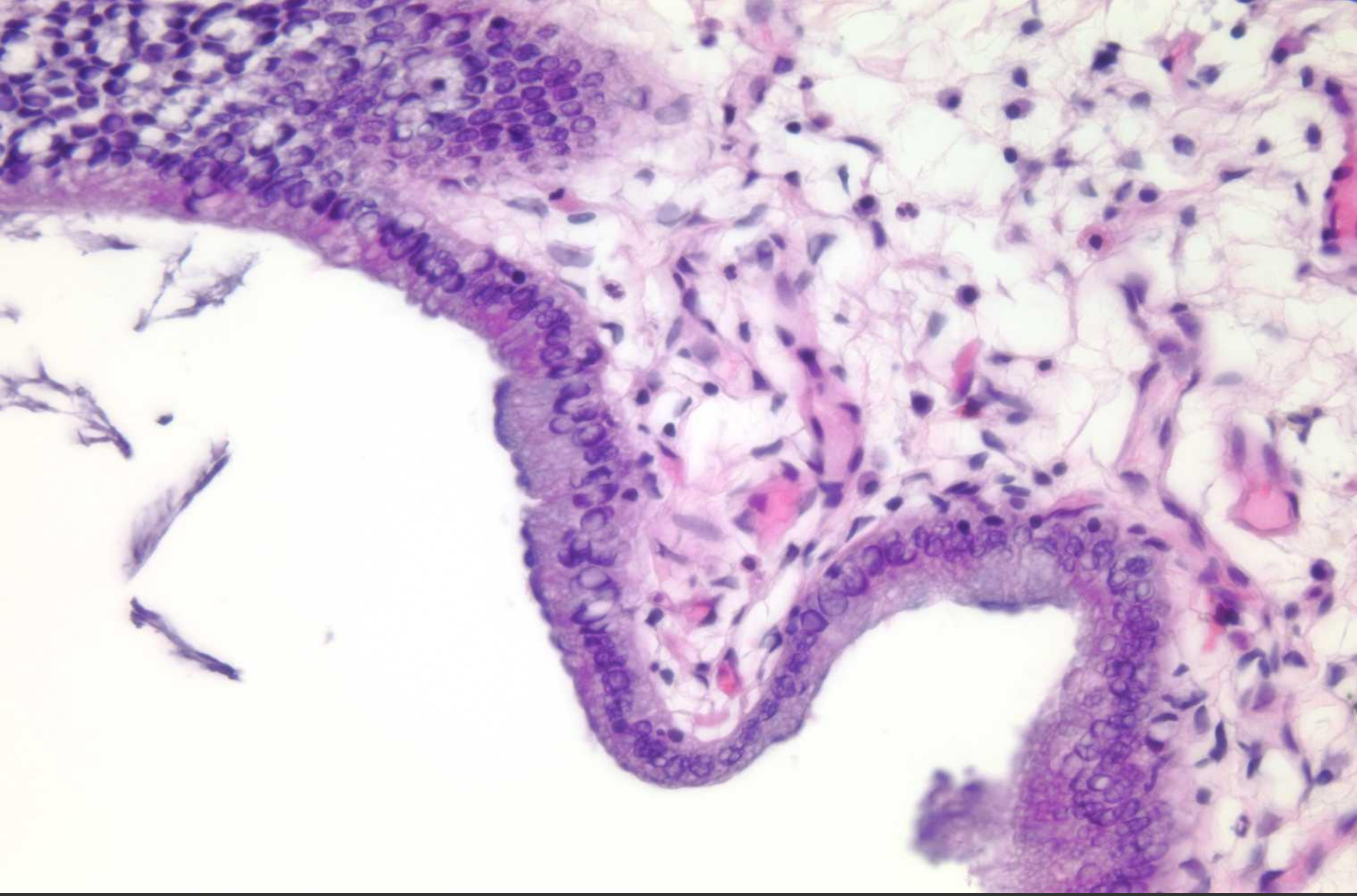
Endocervicosis

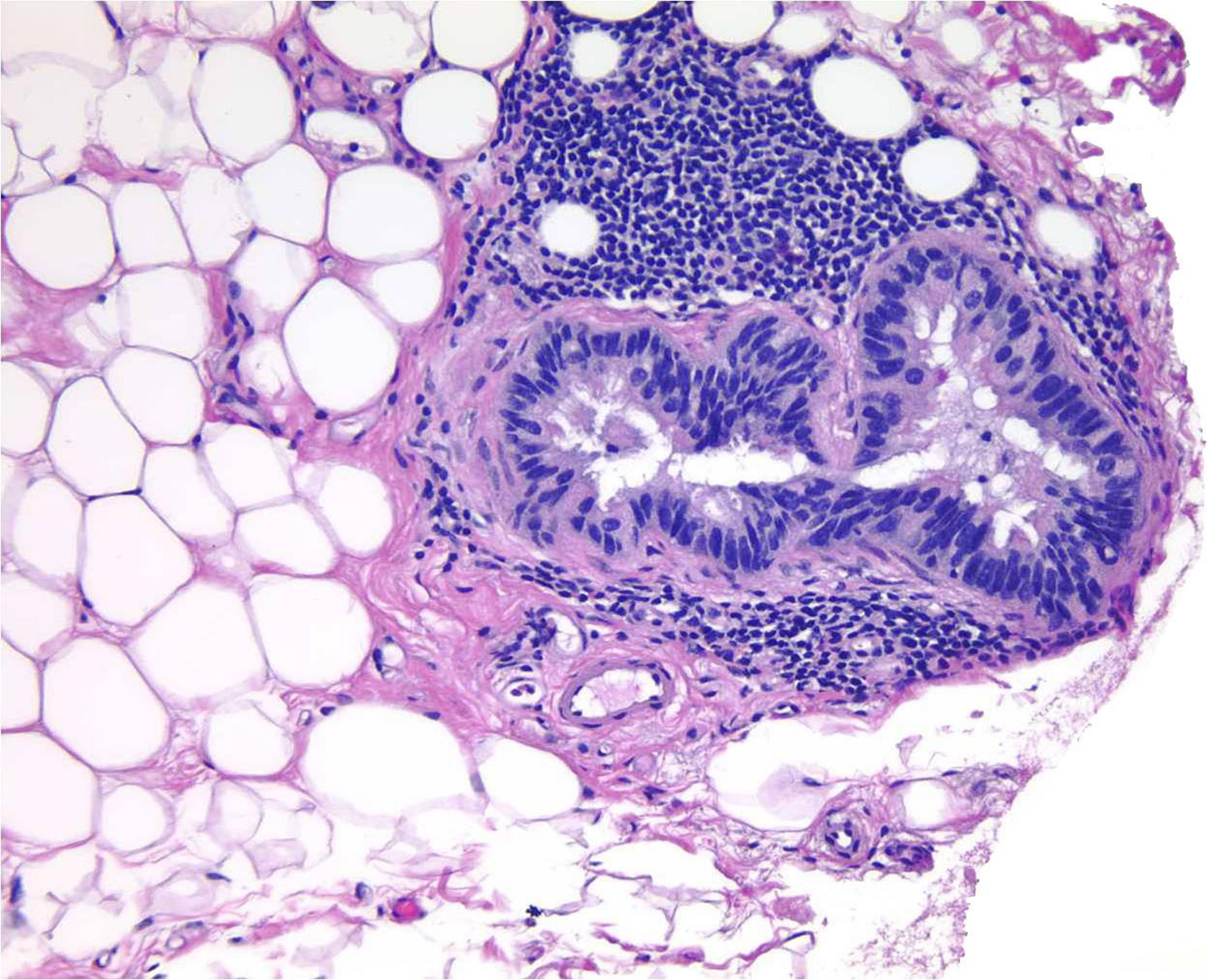
- Typically in women in their 30s and 40s
- Symptoms of pelvic pain, frequency, dysuria, hematuria, dyspareunia, dysmenorrhea
- Most common in bladder. Also seen in uterine cervix, vagina
- Mass (up to 5 cm) seen in posterior bladder wall with occasional extravesical involvement



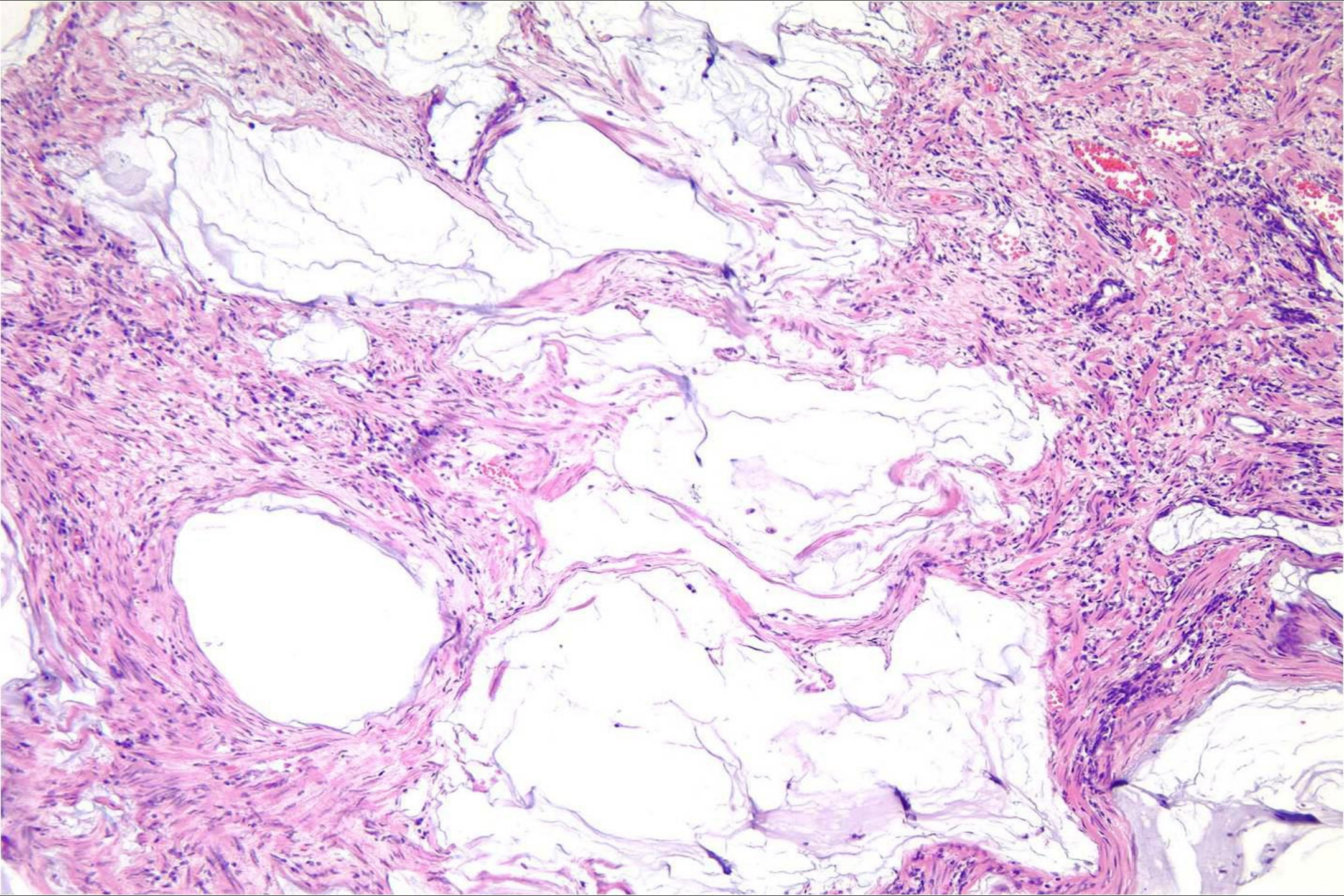


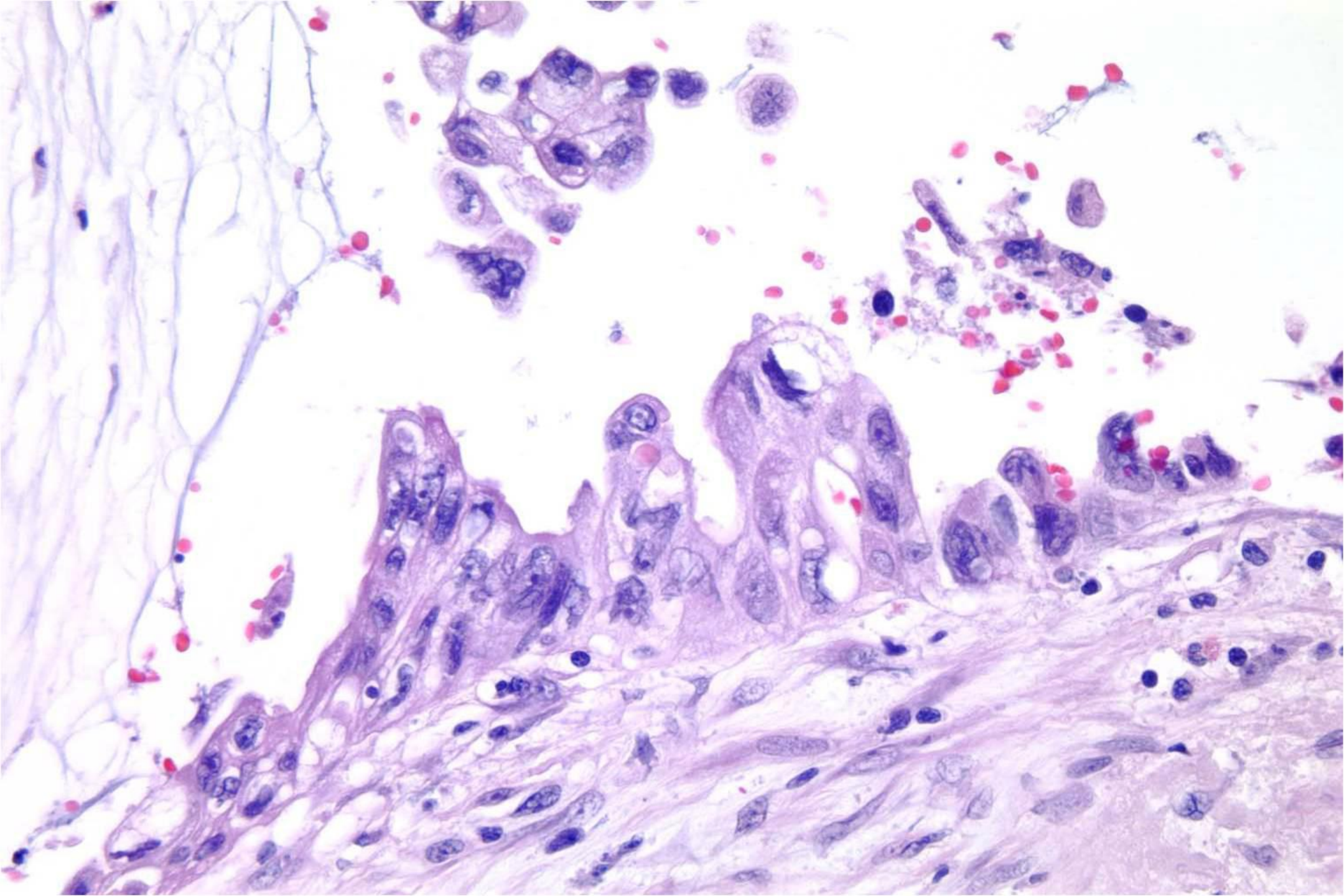


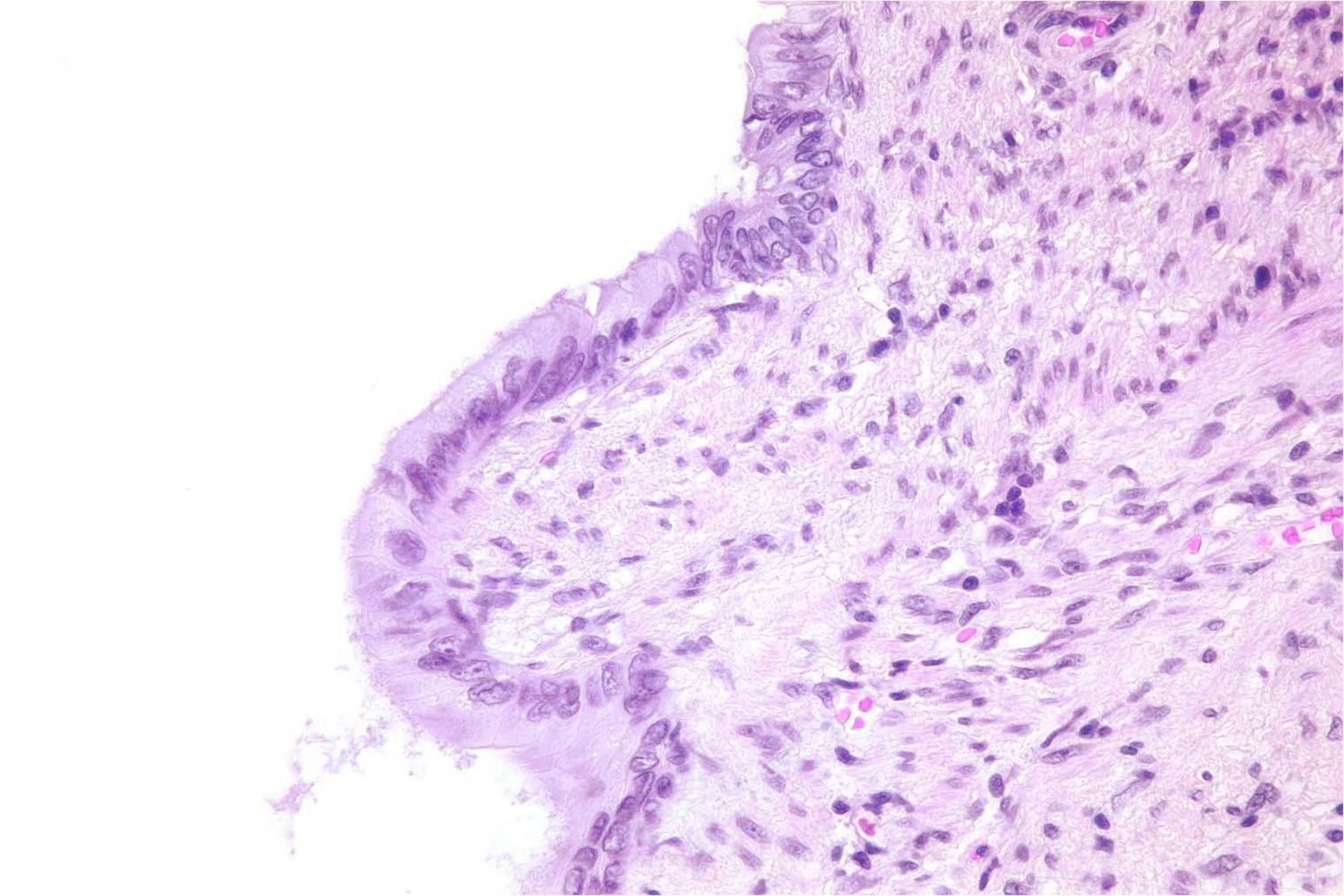


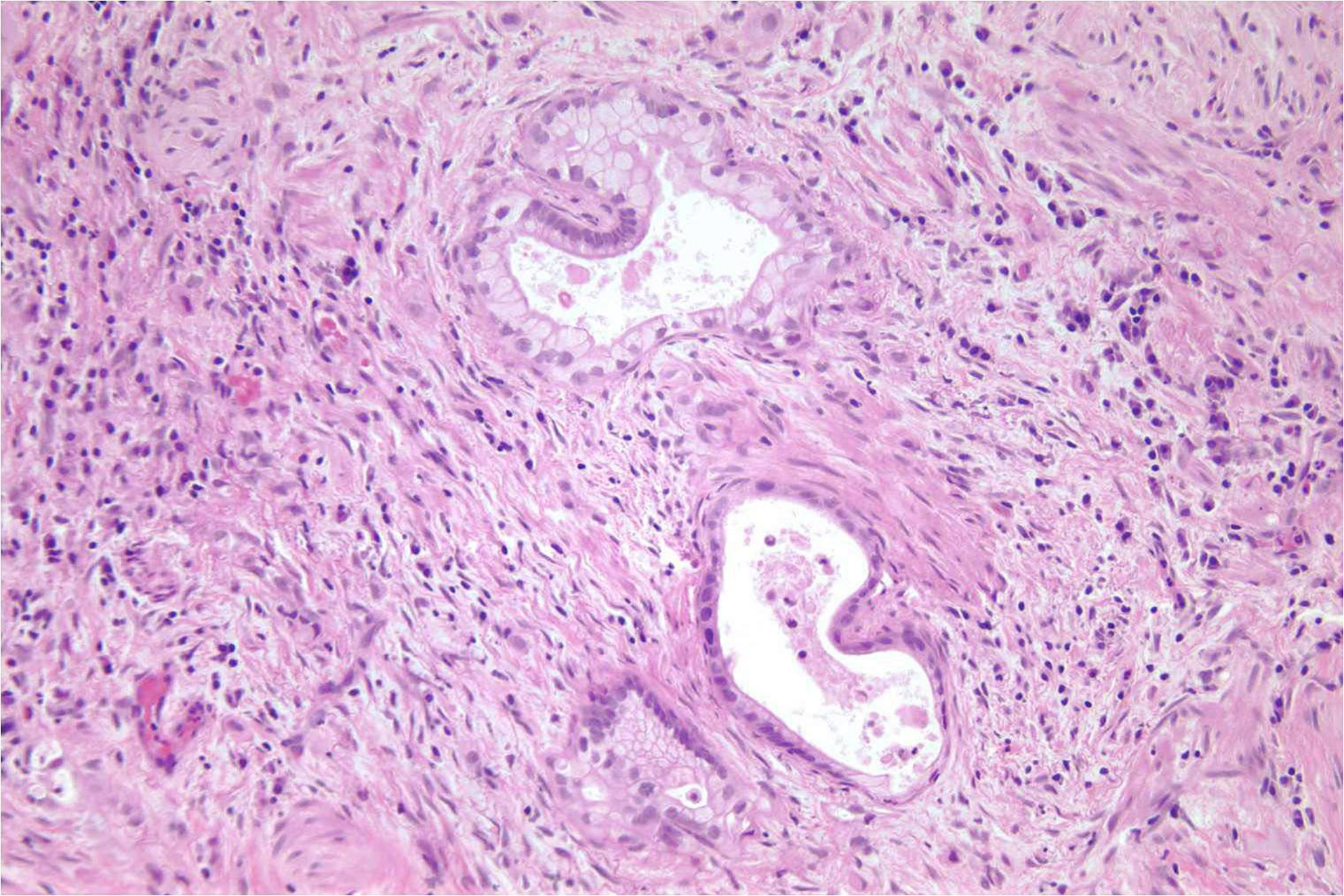


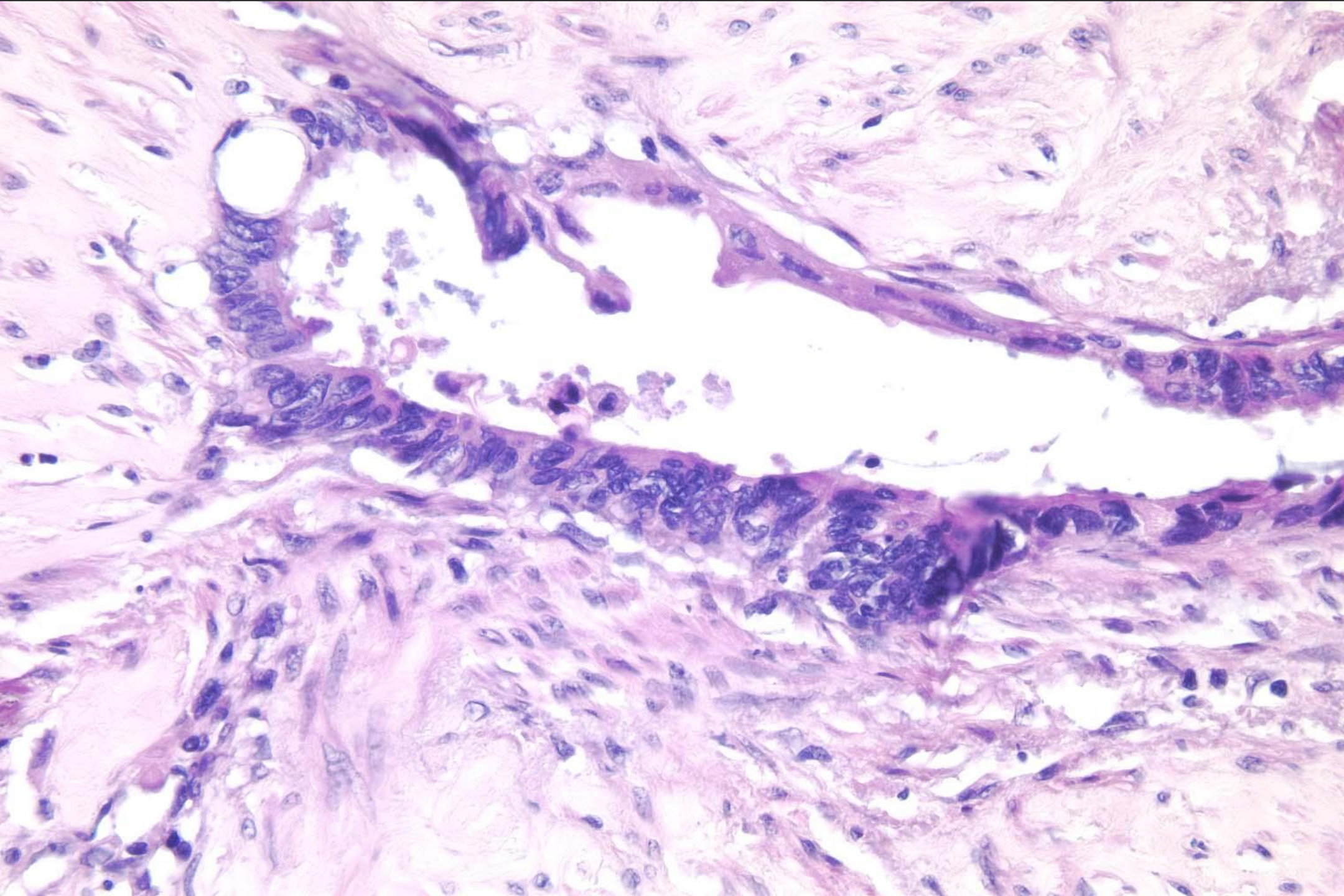
Infiltrating Adenocarcinoma of the Bladder

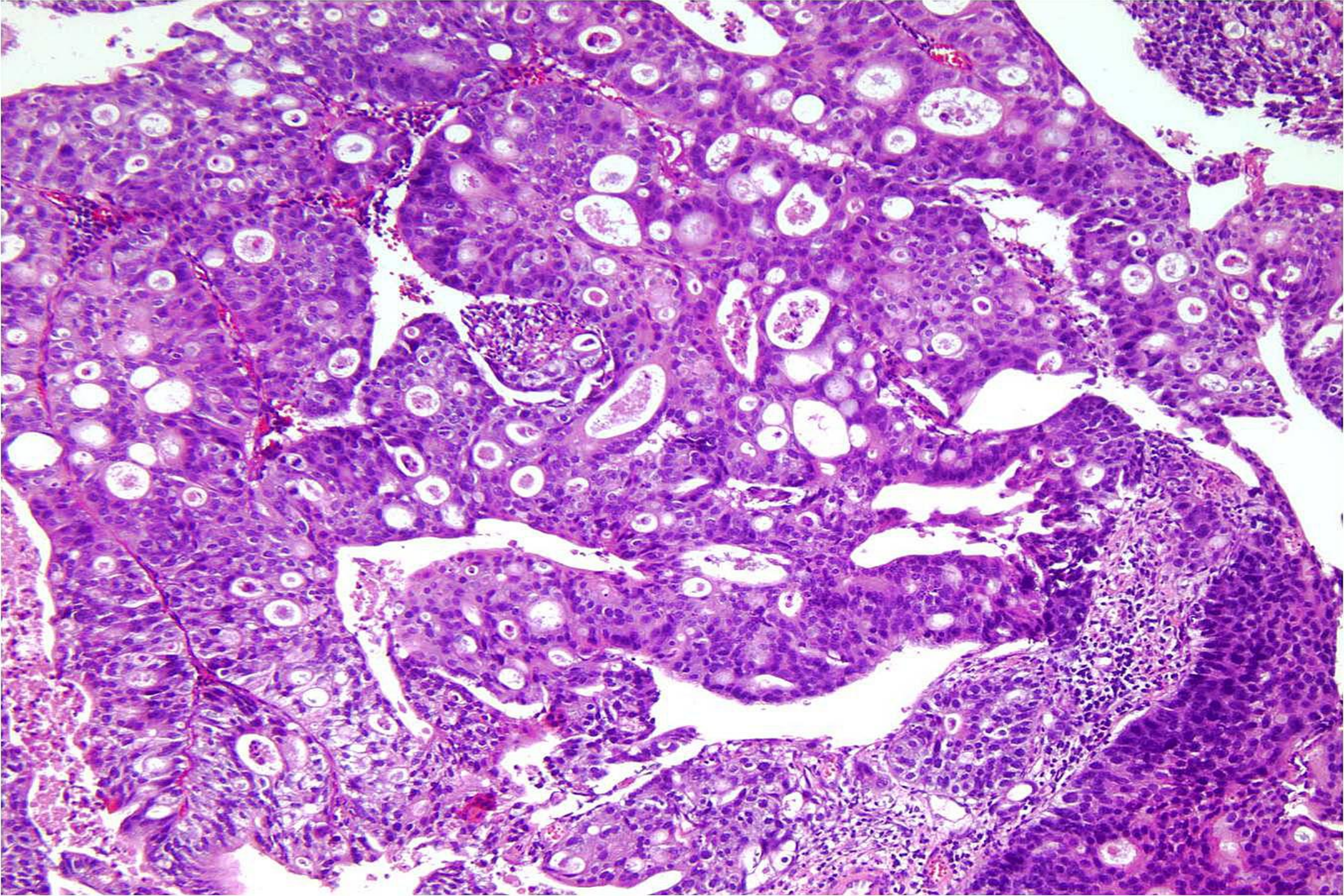


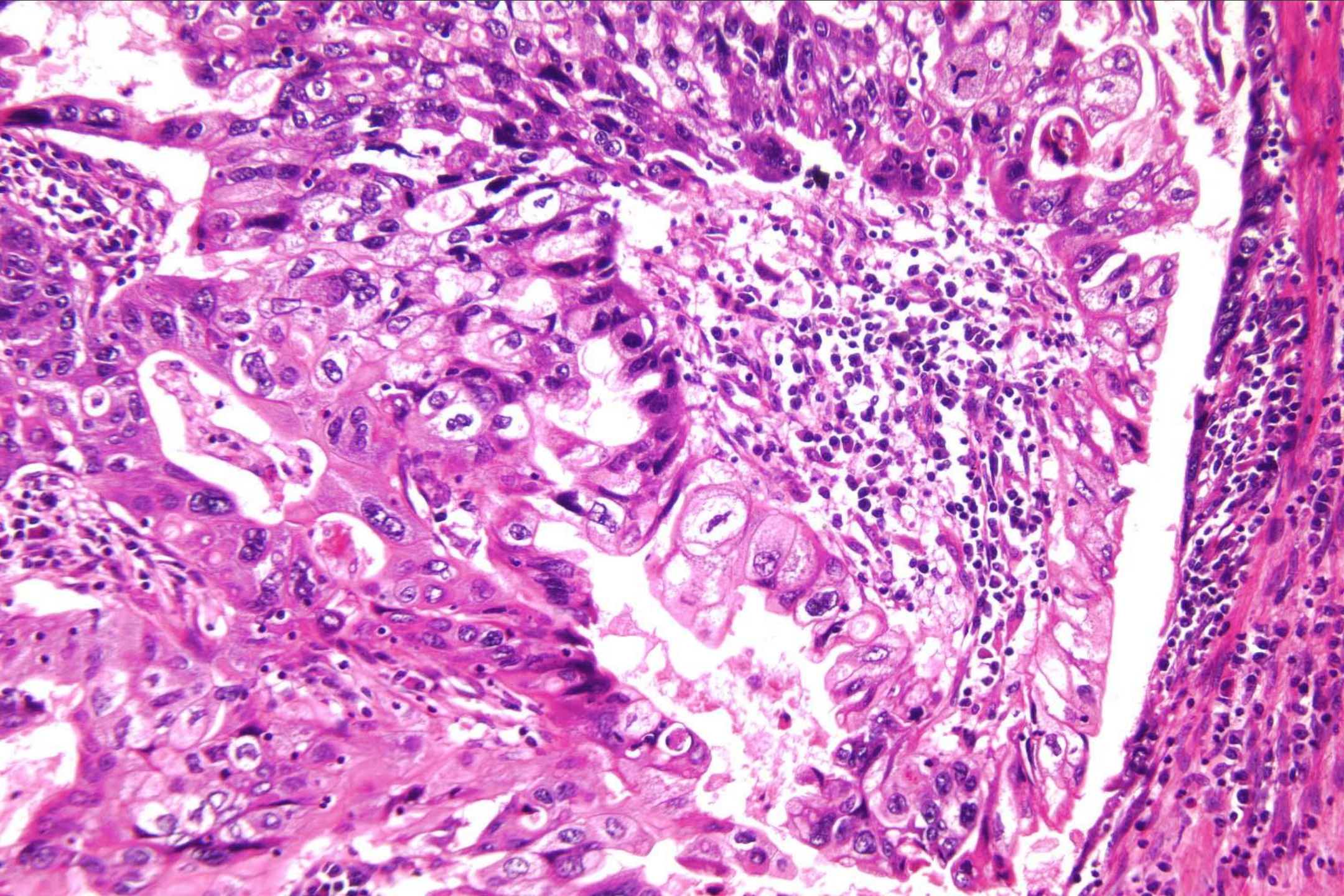


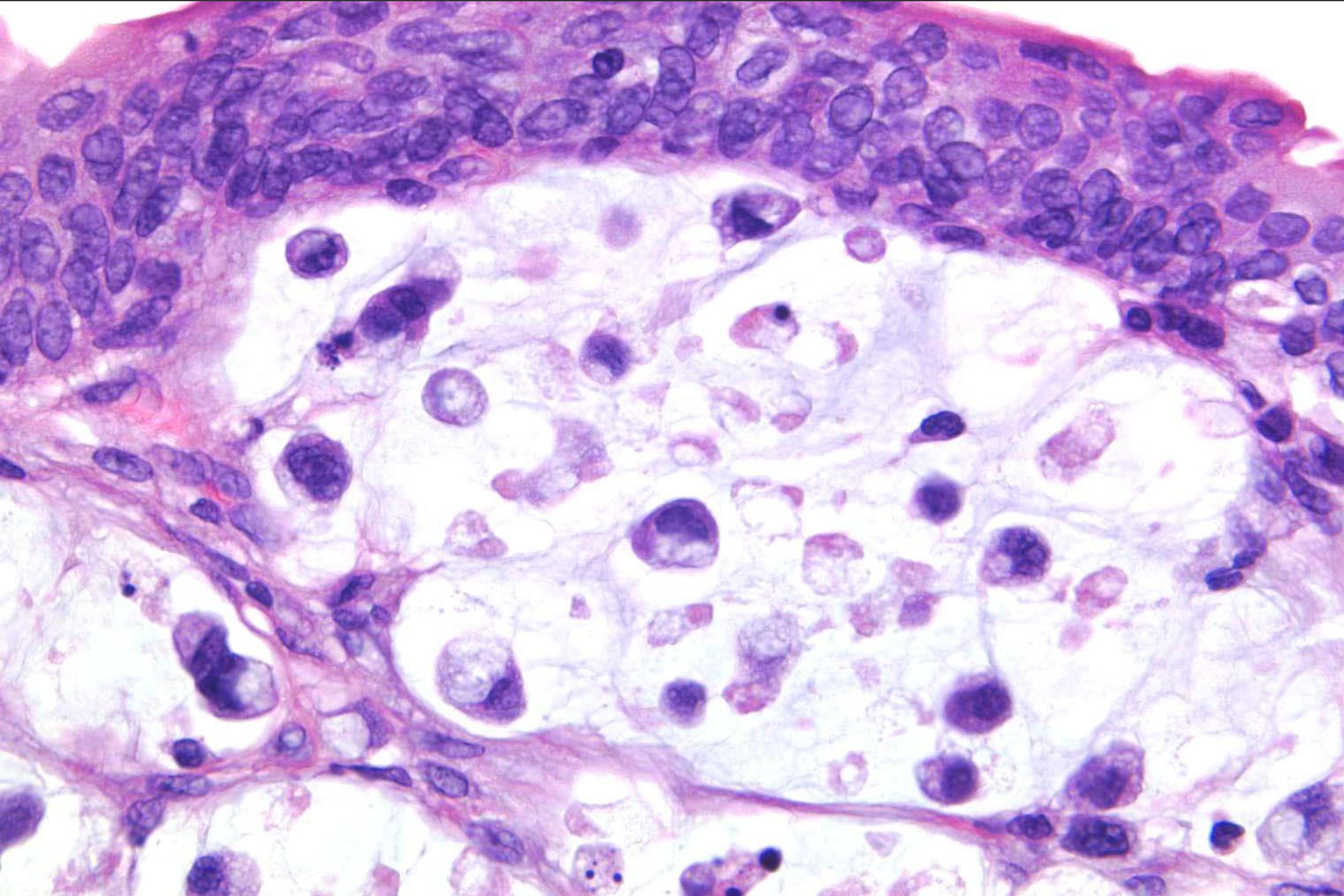






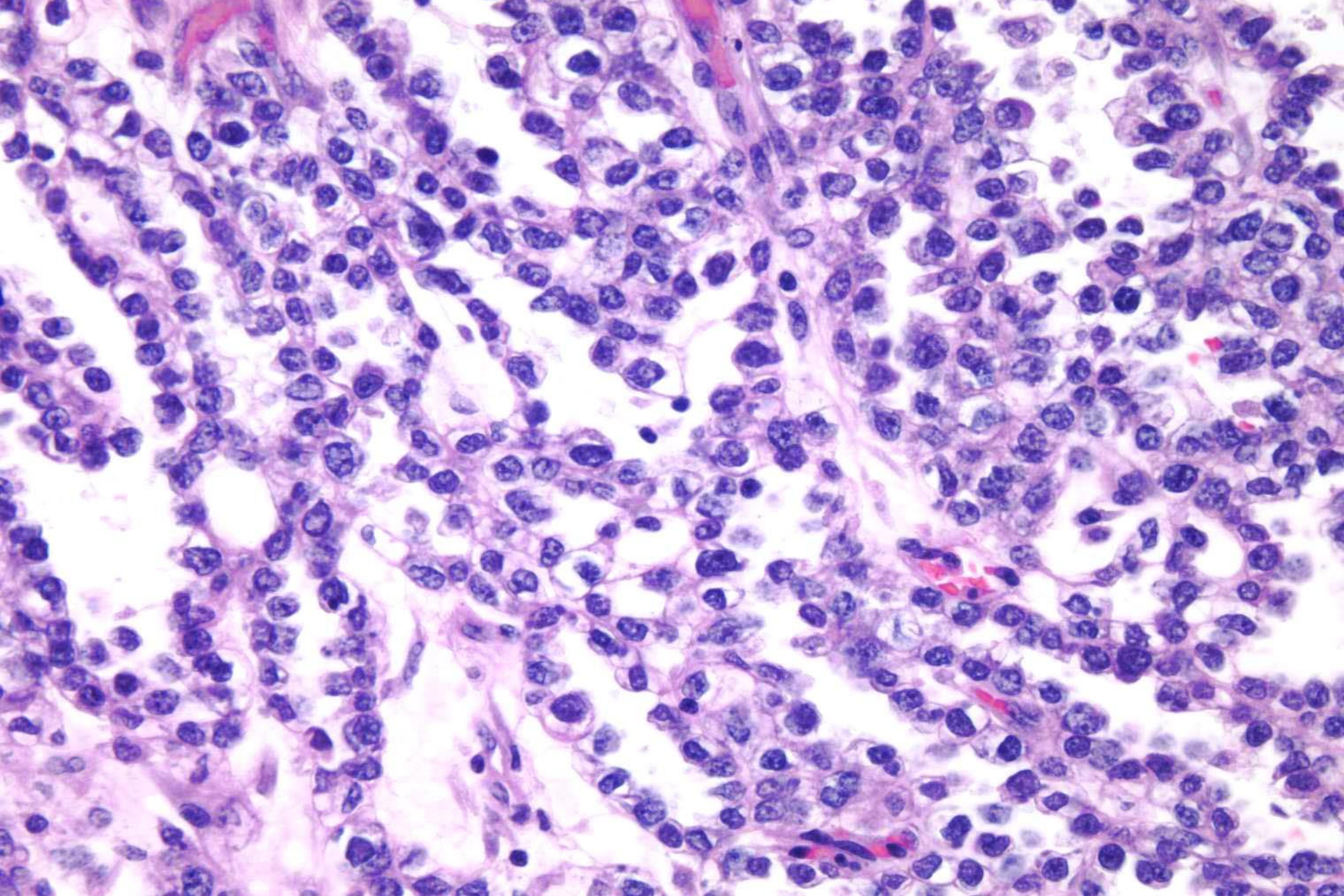


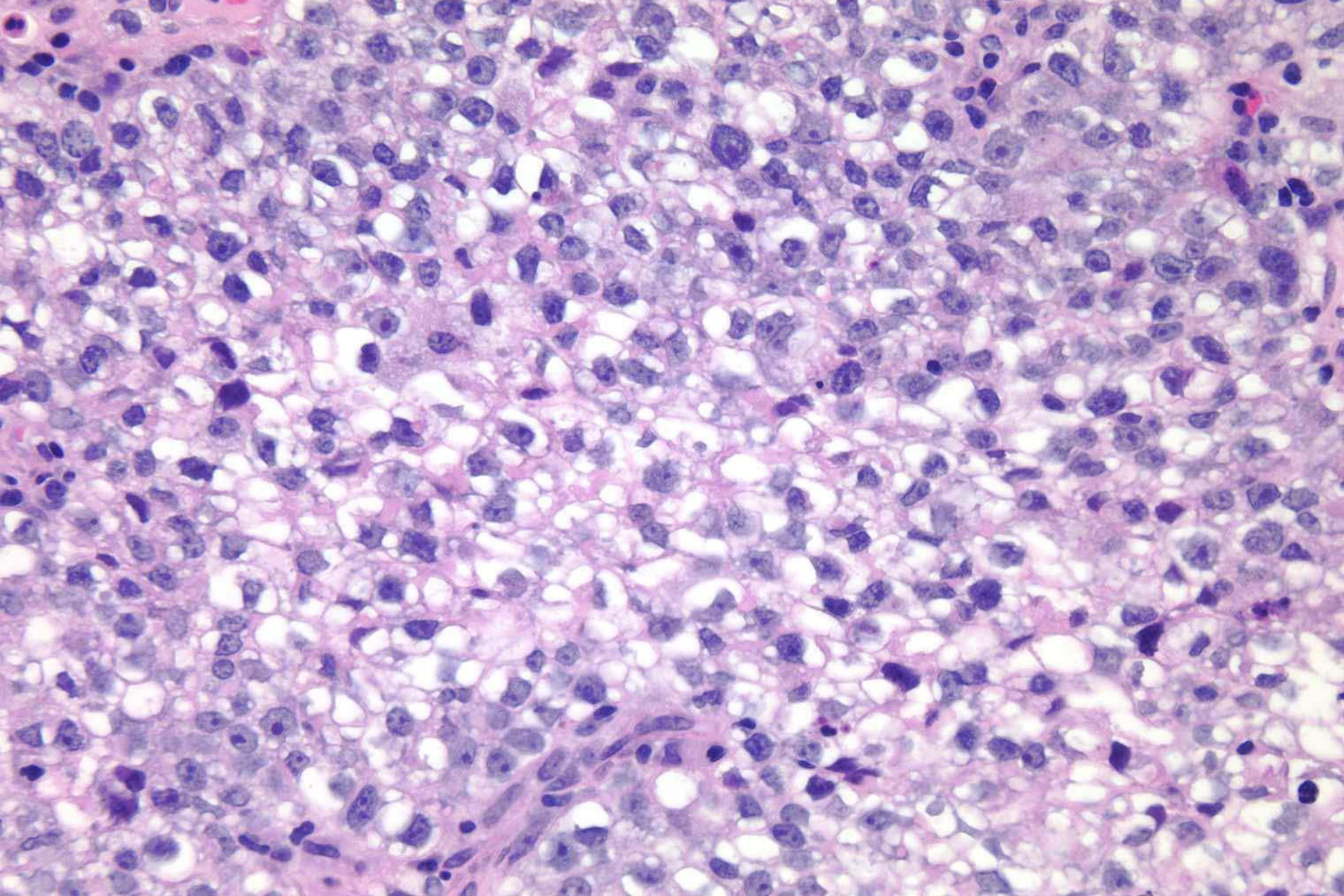


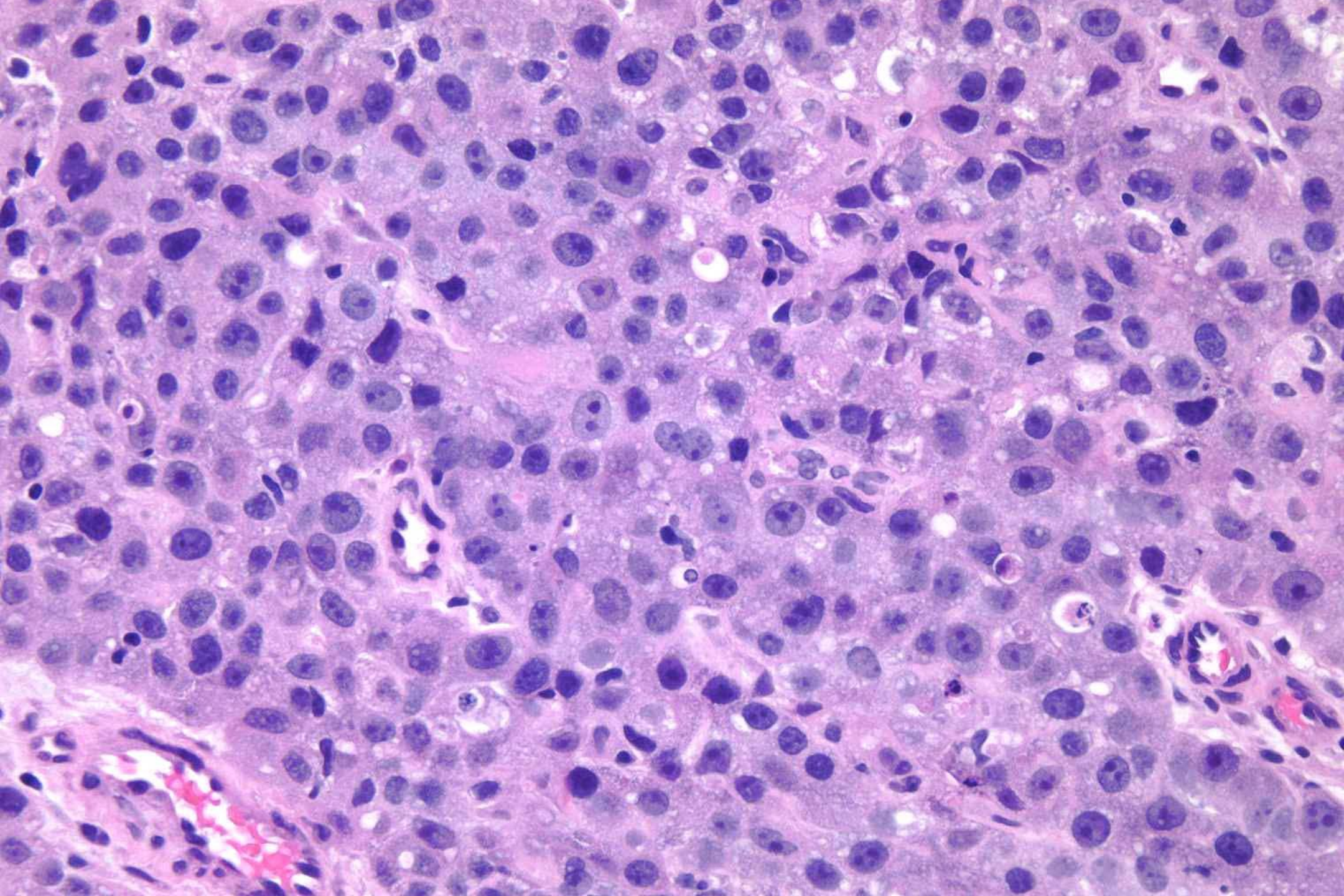


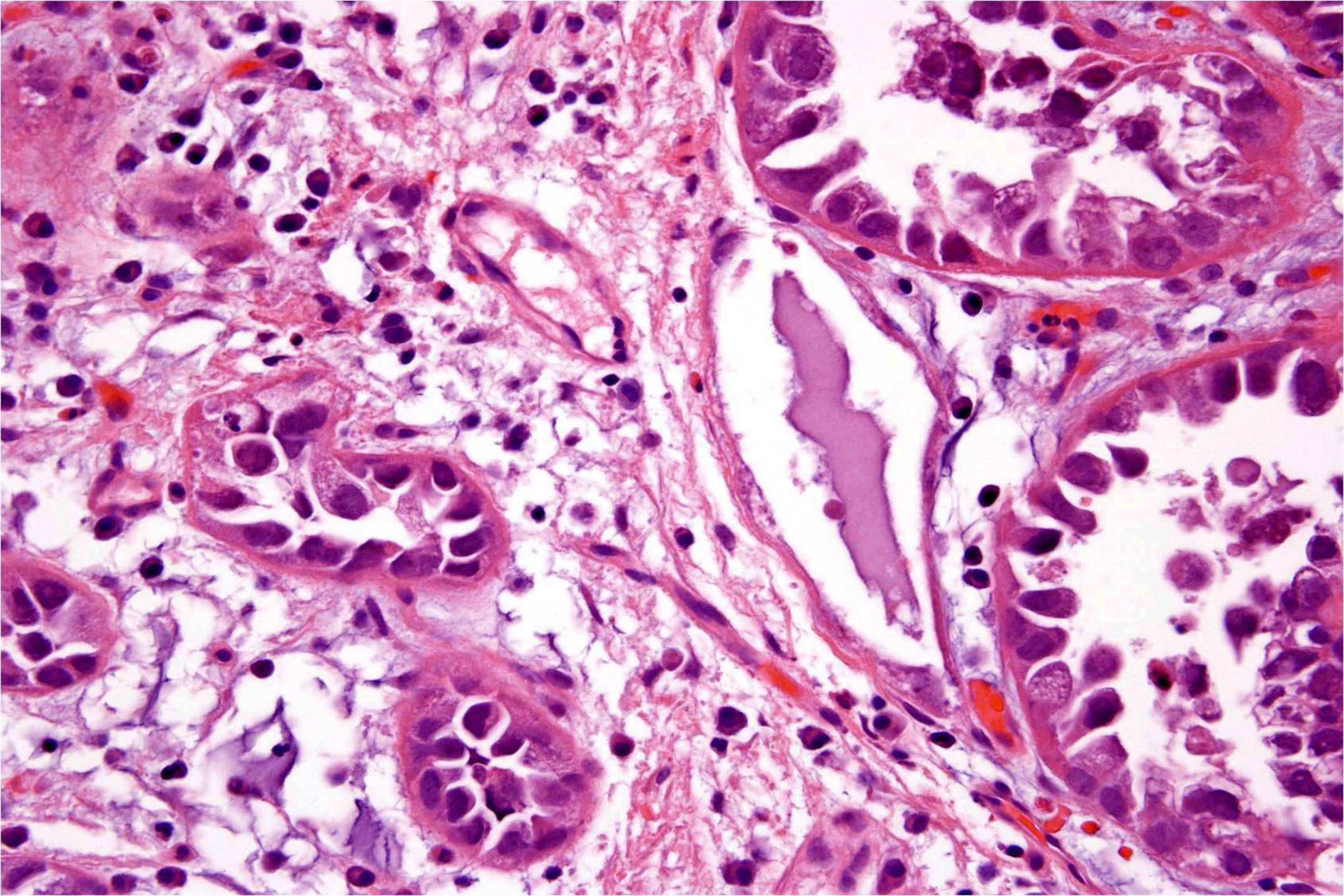
Clear Cell Adenocarcinoma

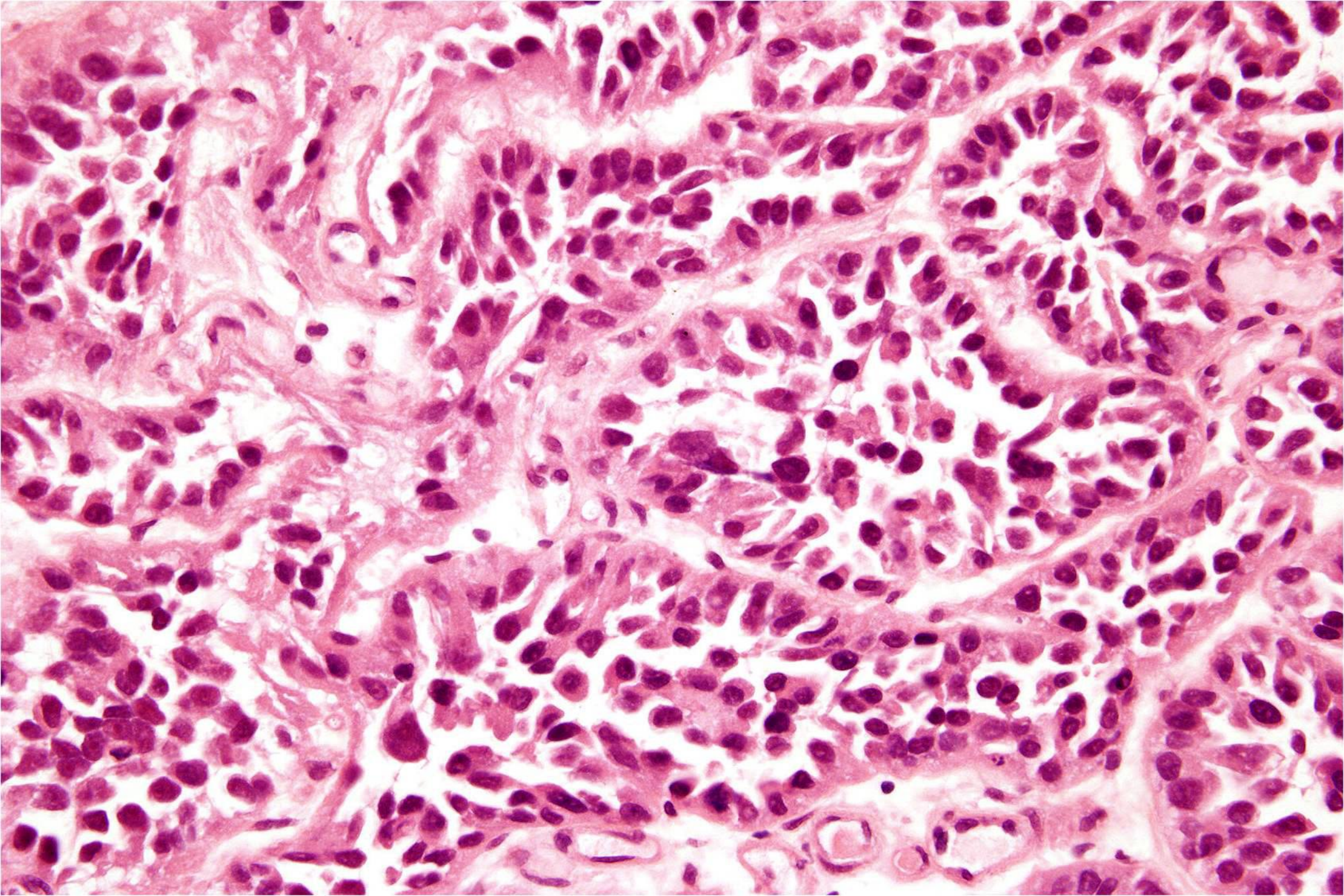
(Mesonephroid Adenocarcinoma)

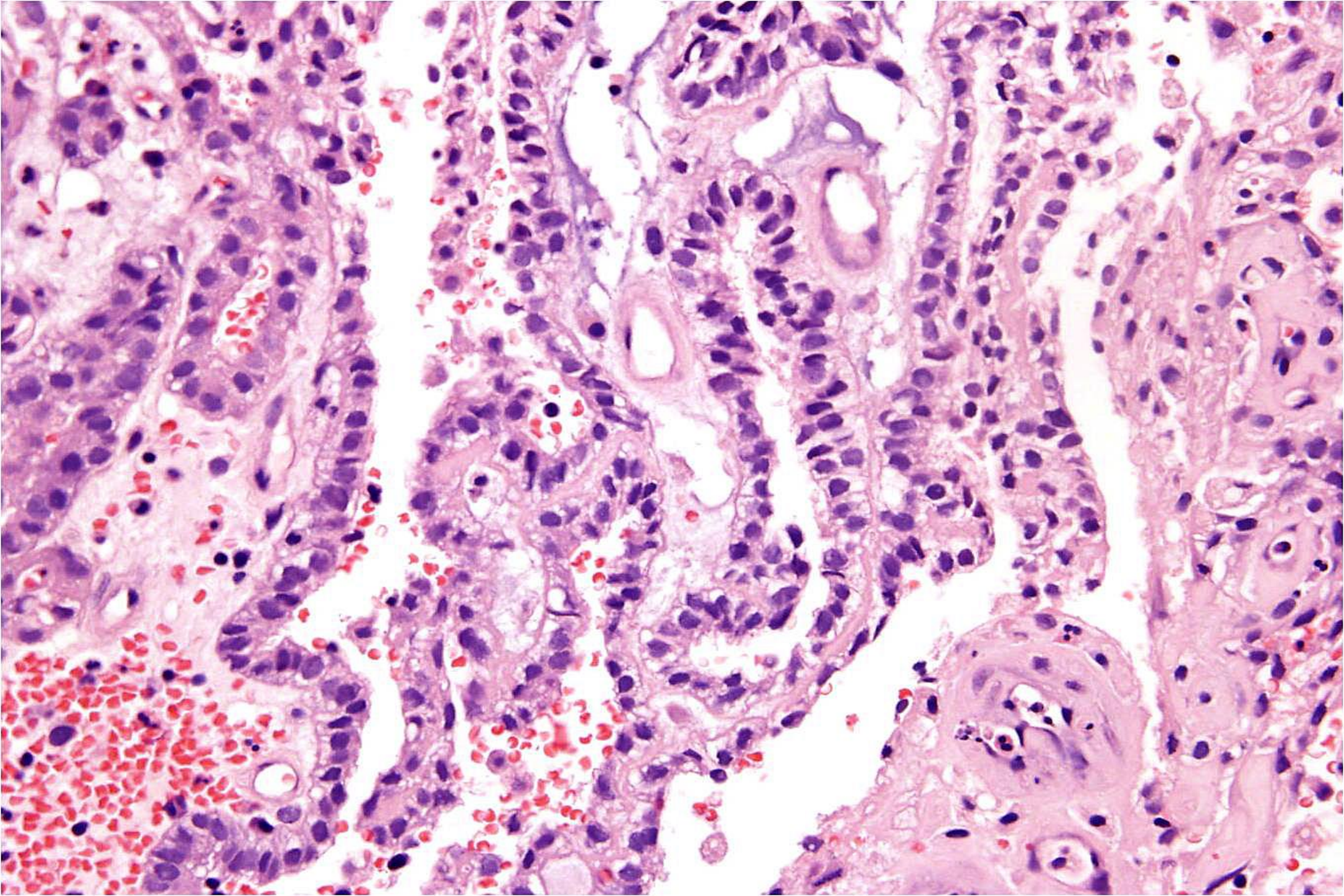




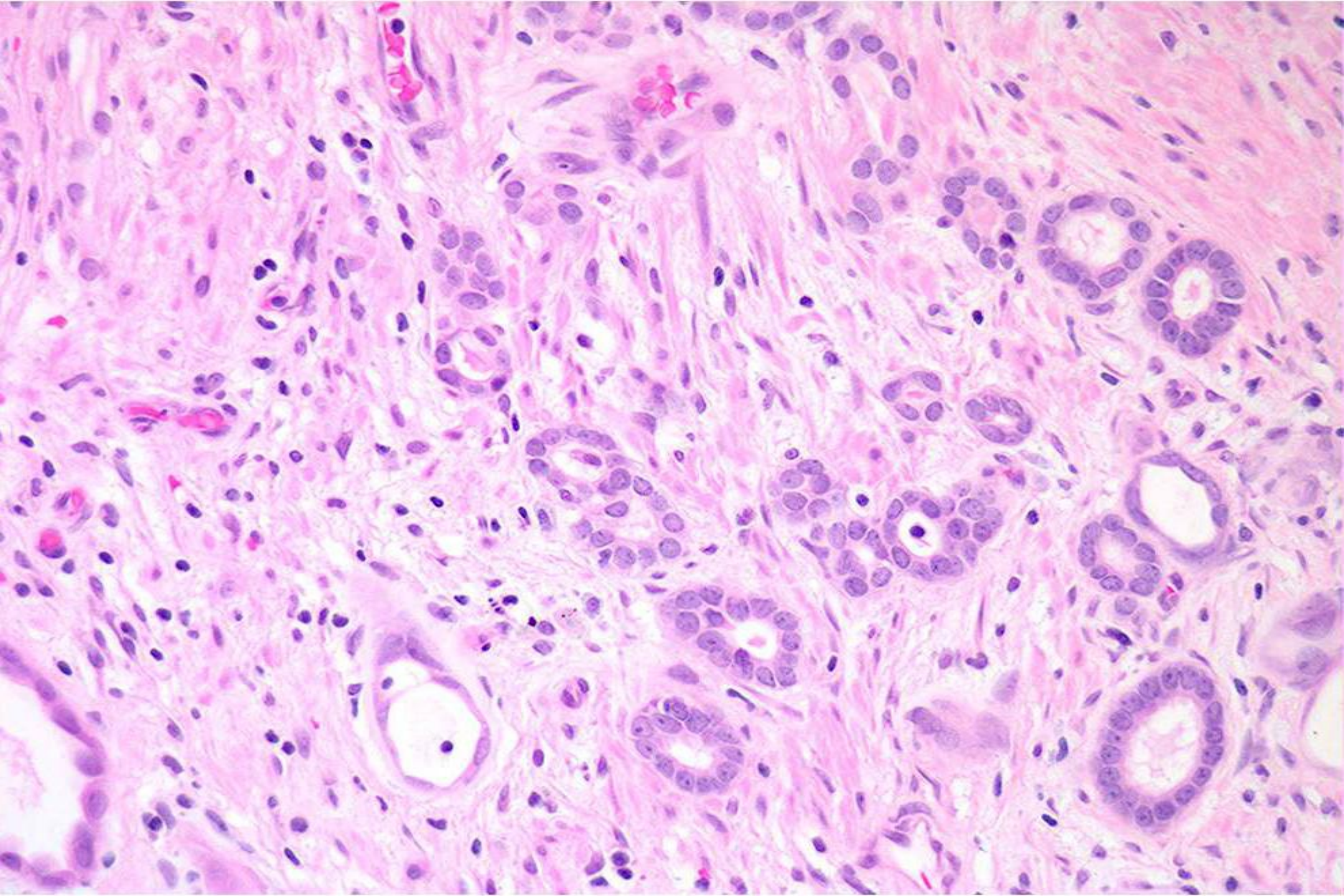


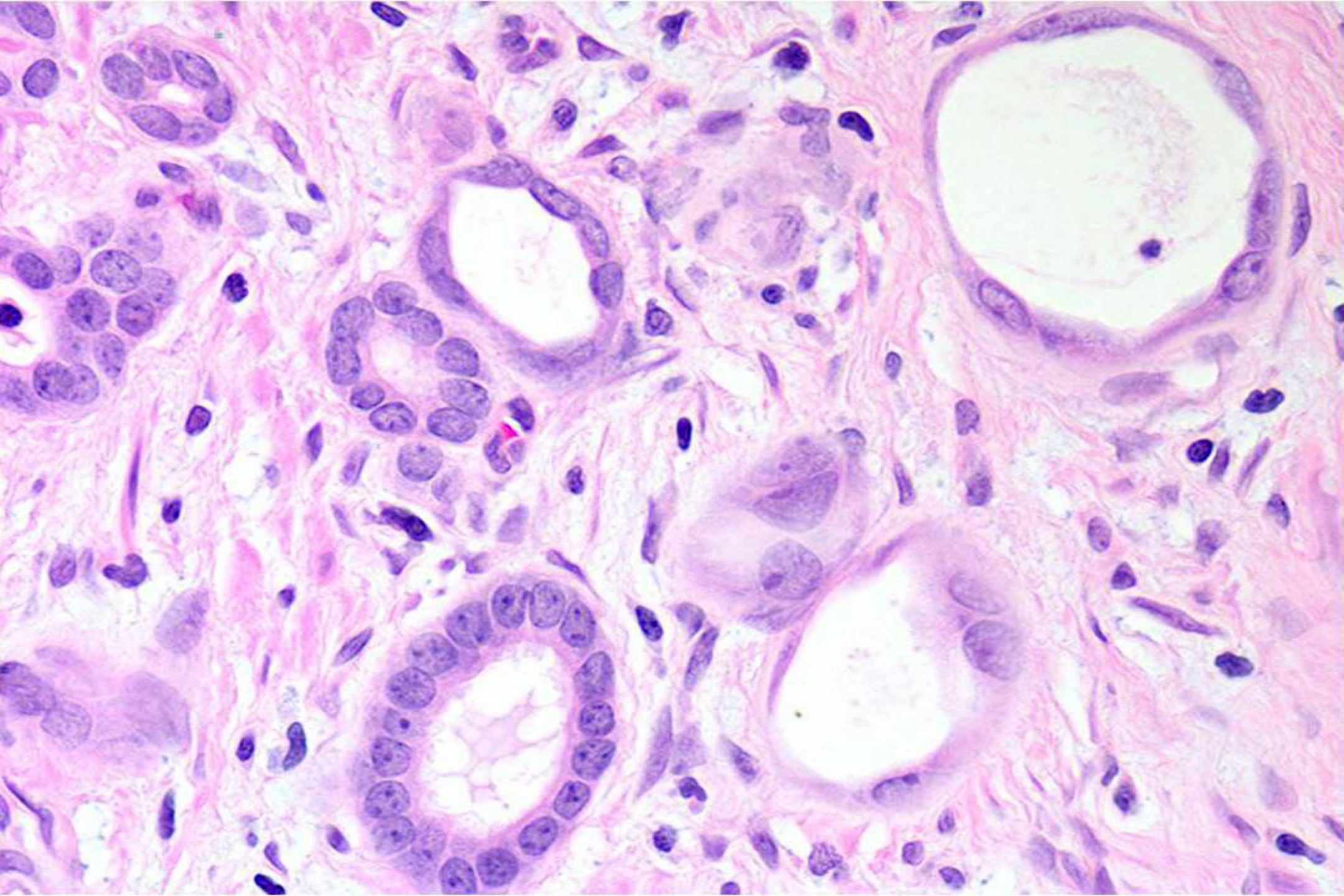


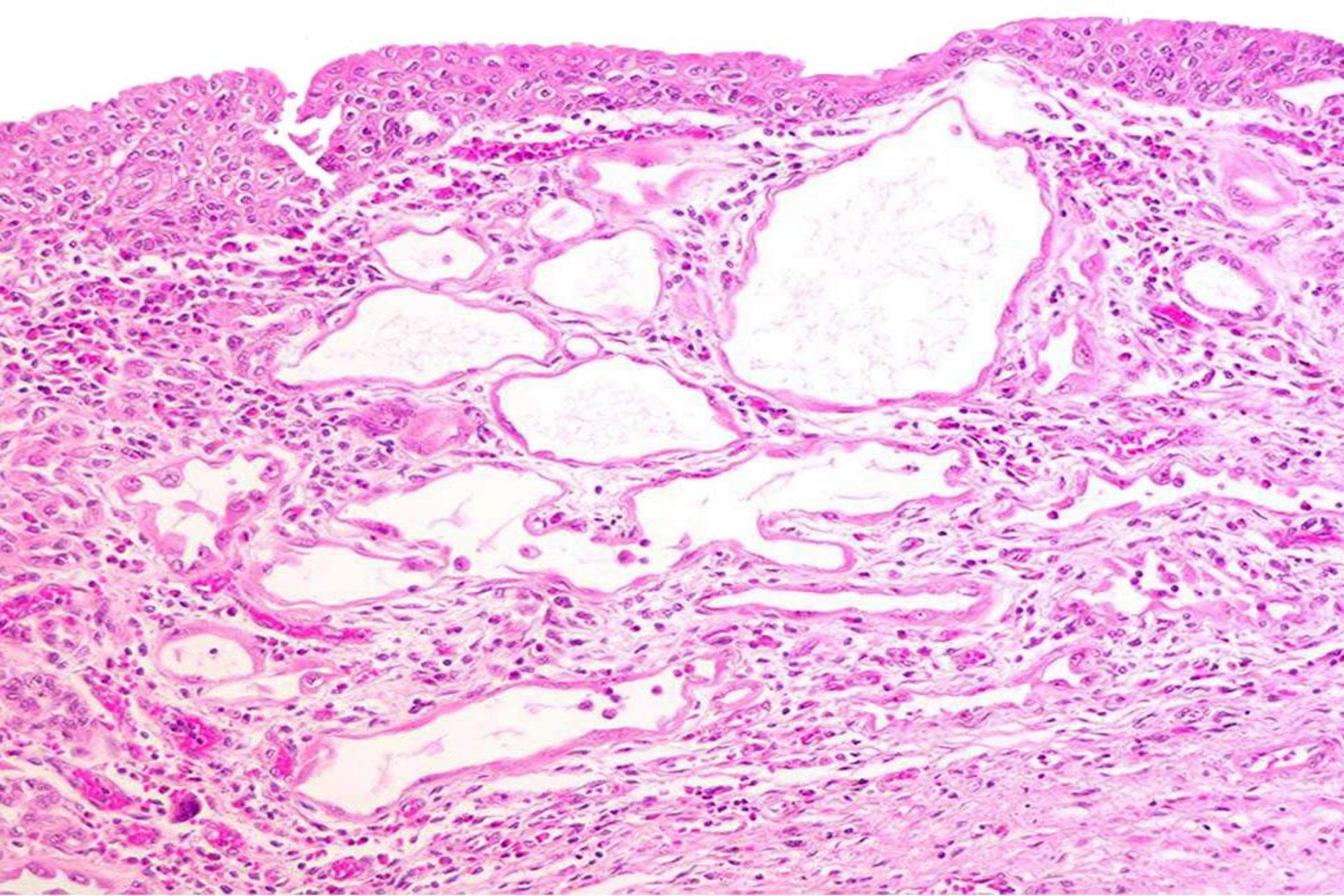


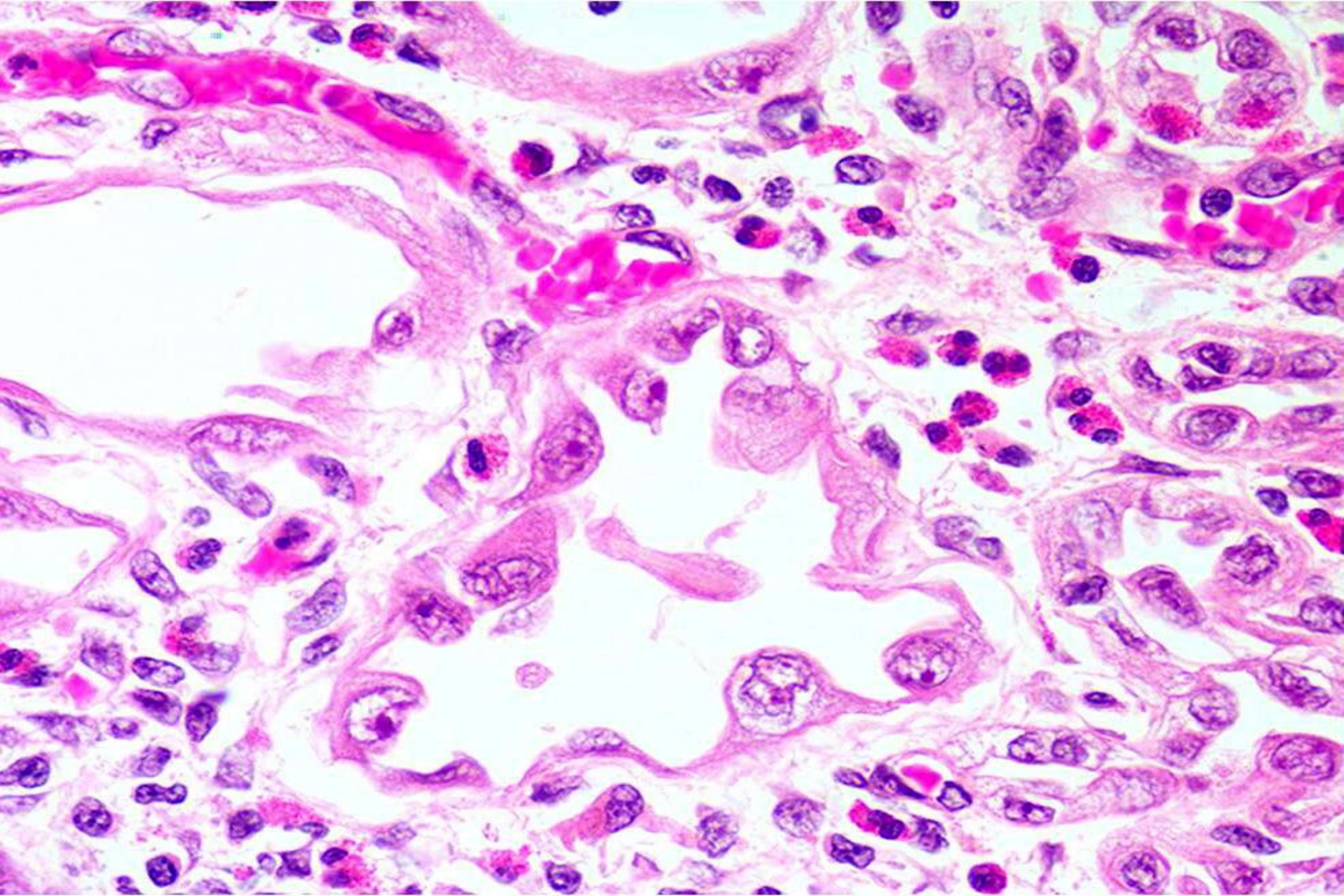


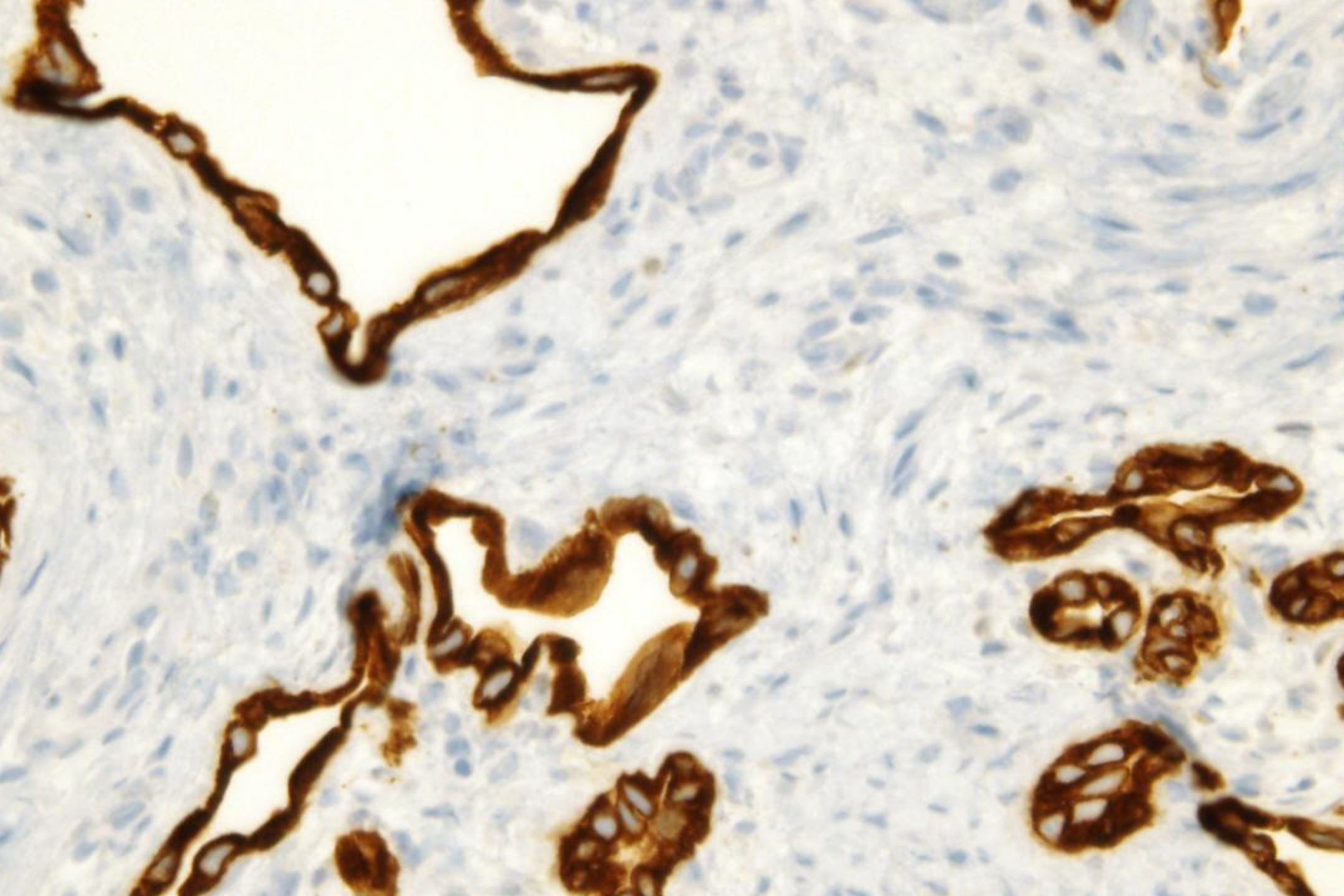
Nephrogenic Adenoma

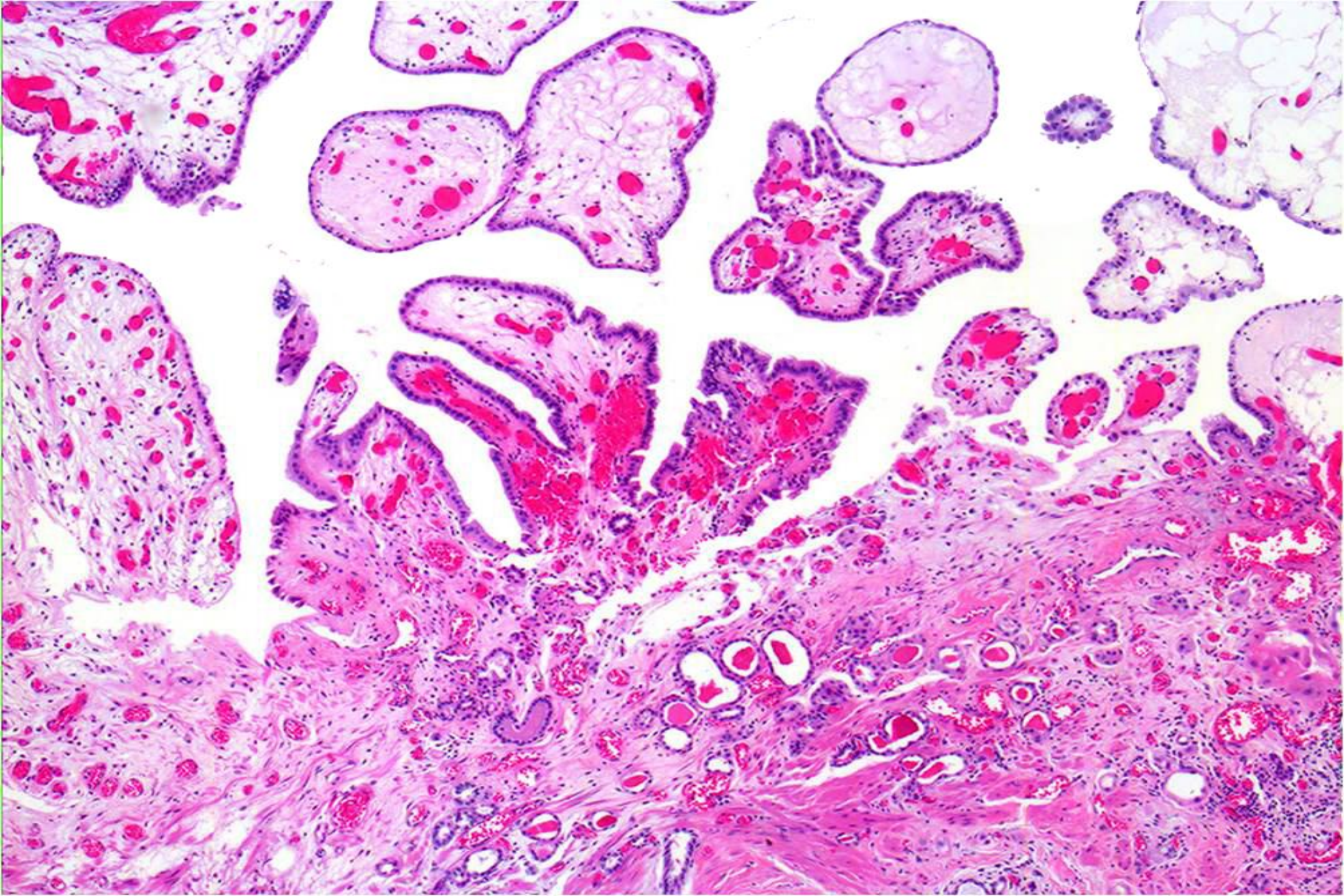


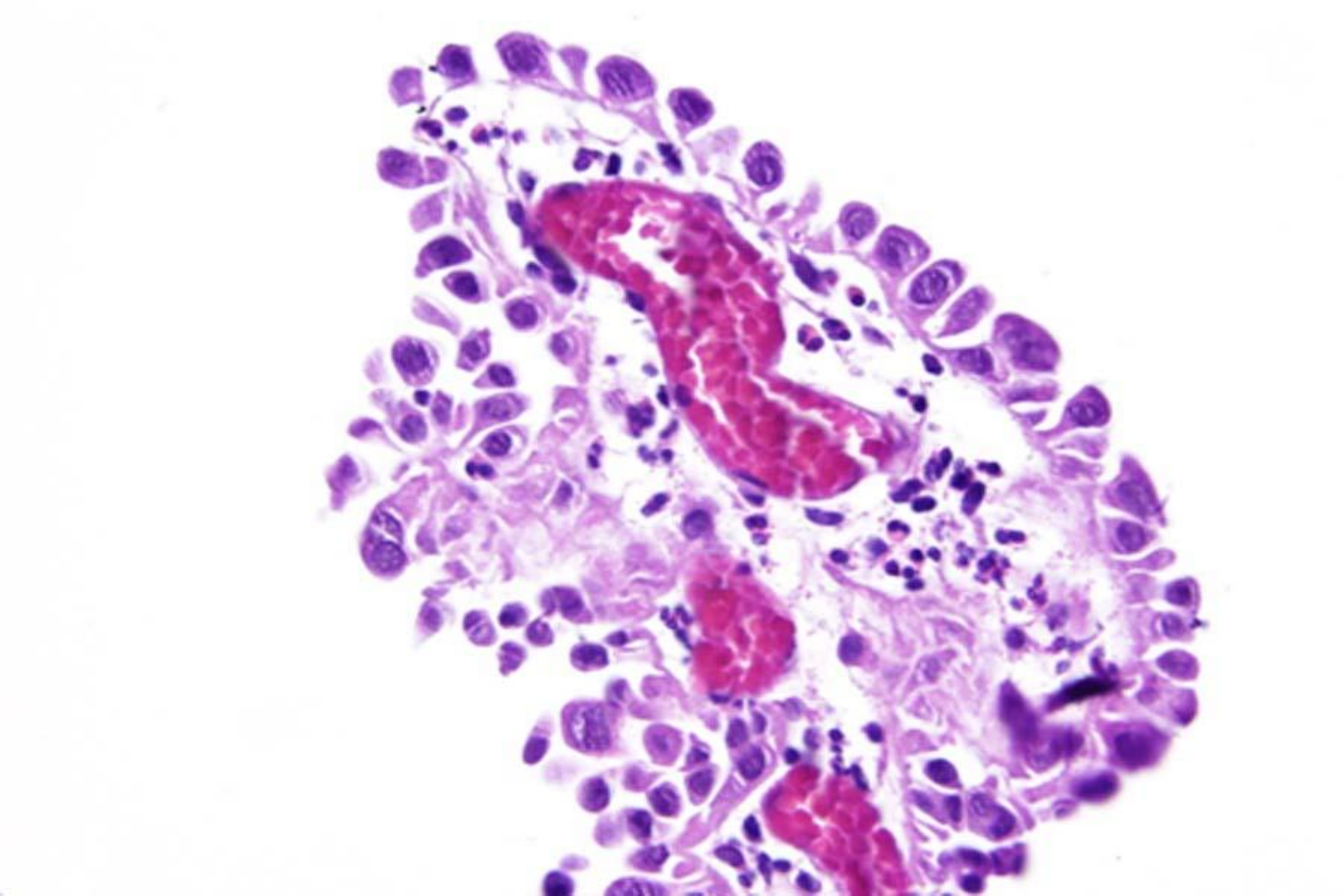


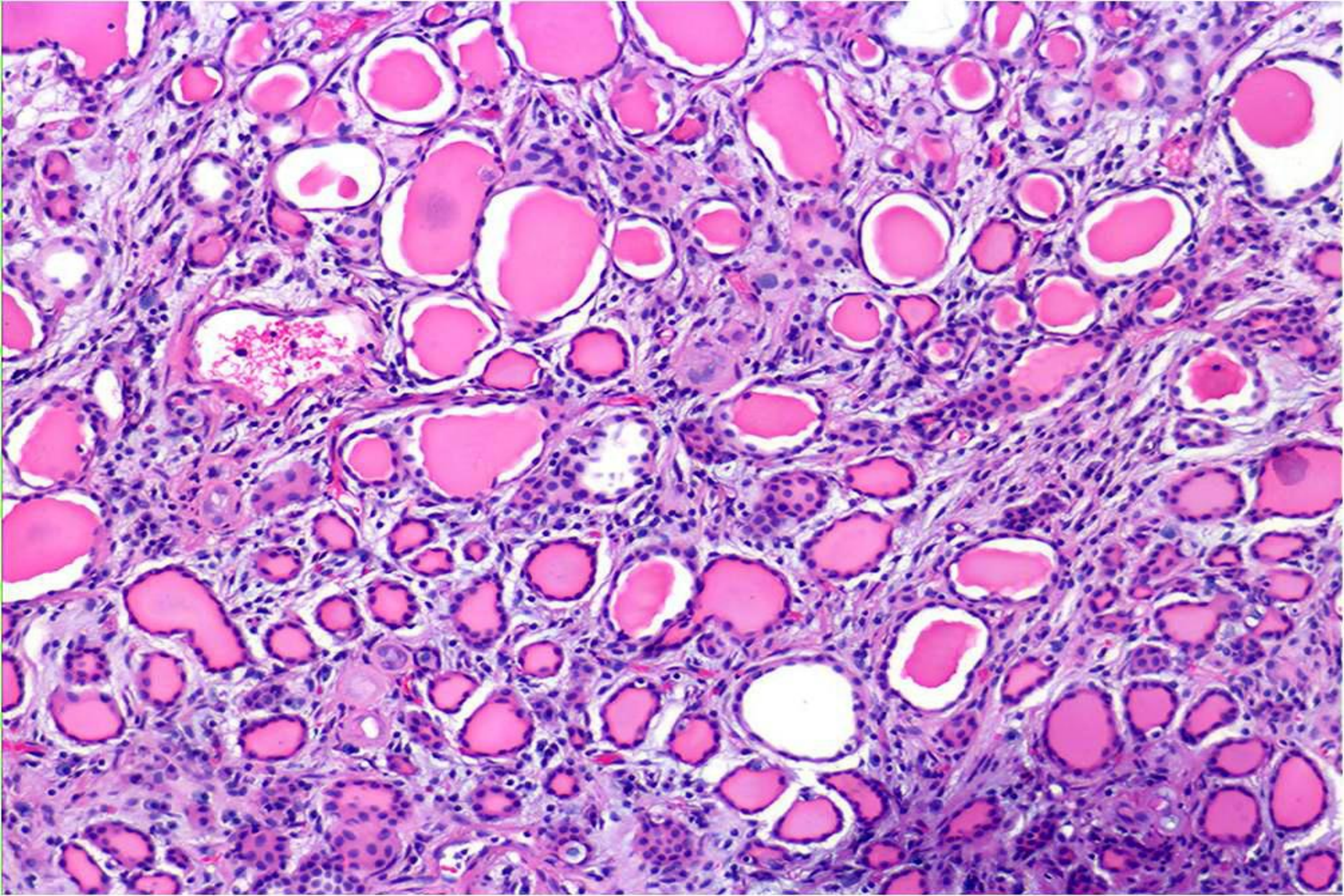


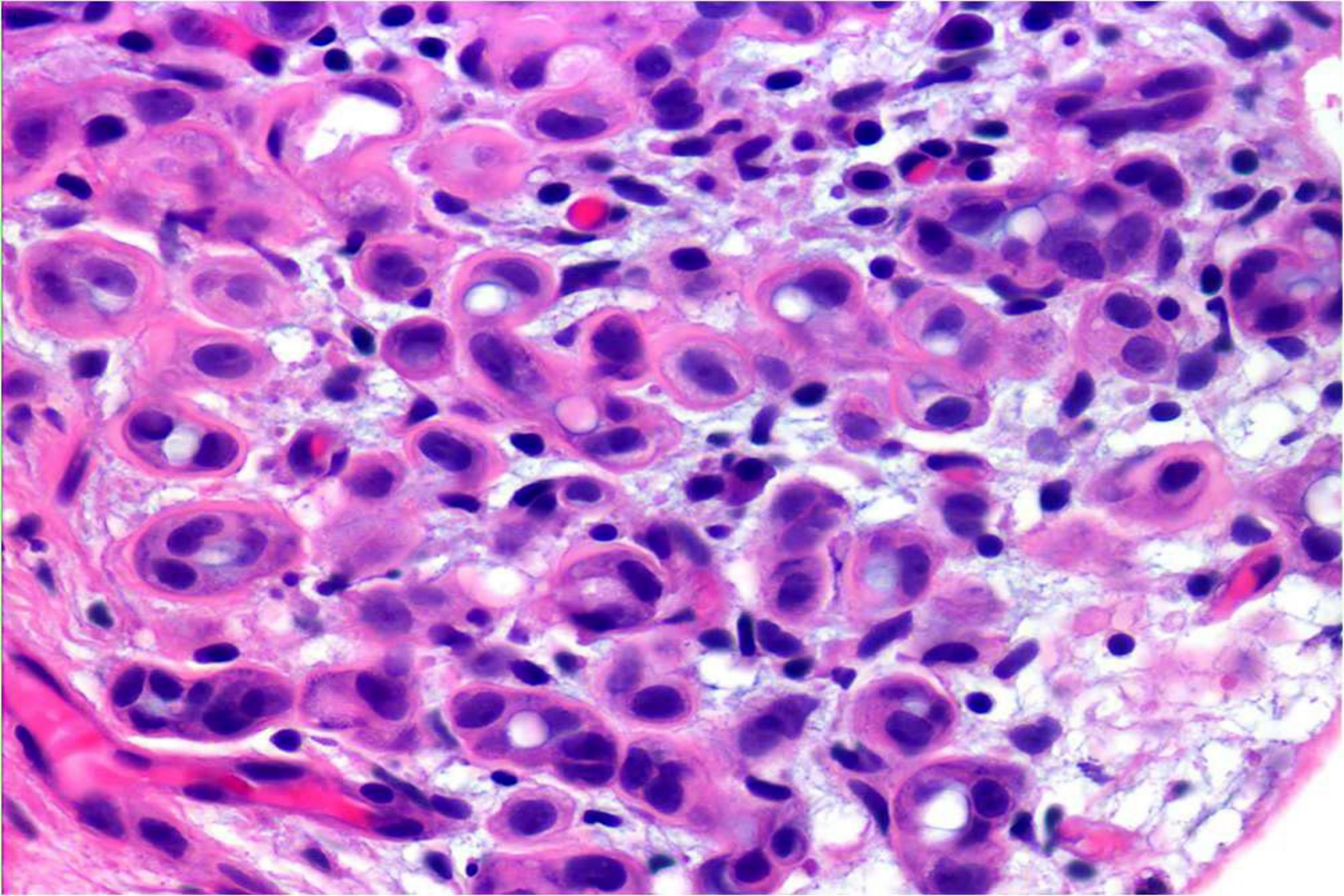


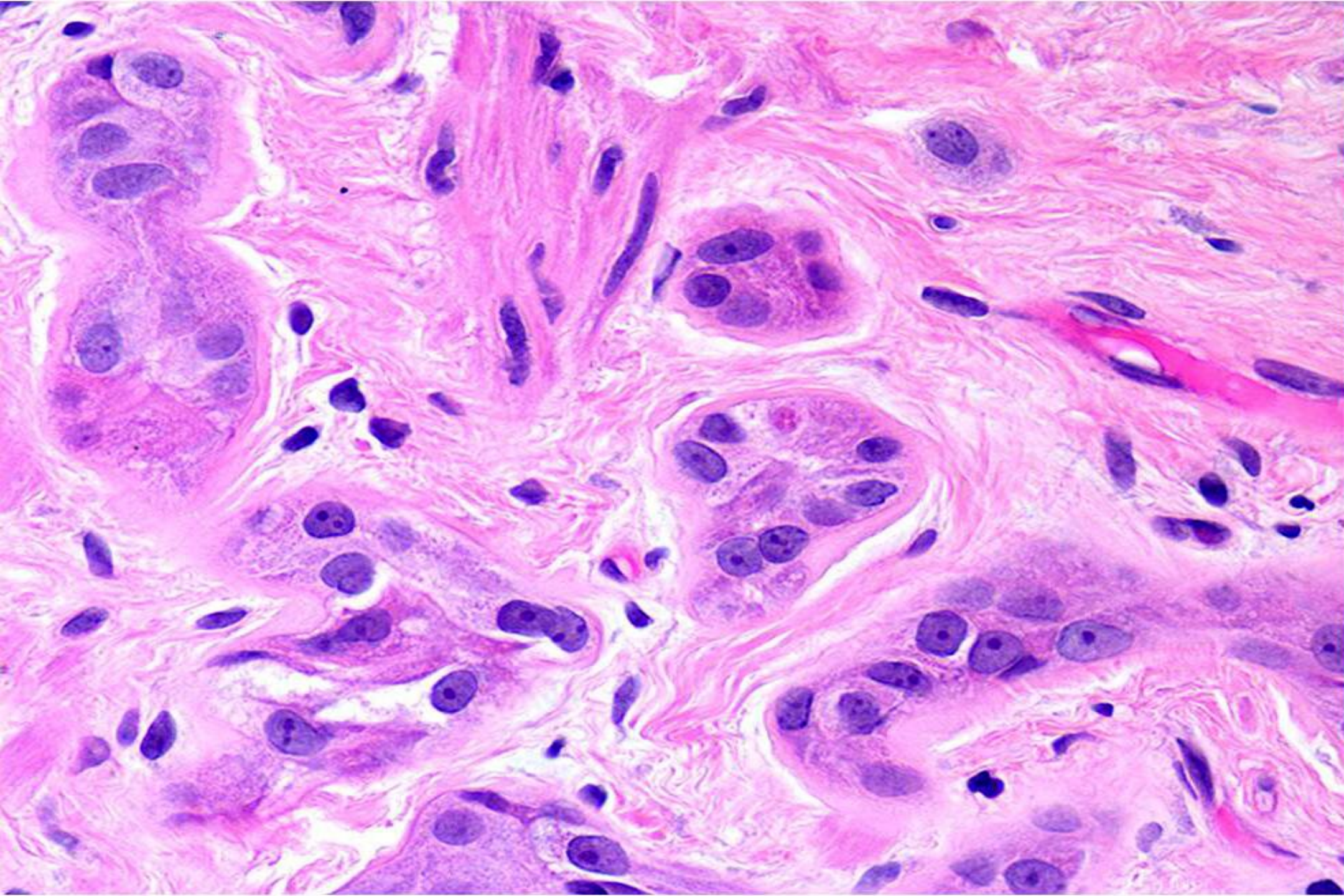


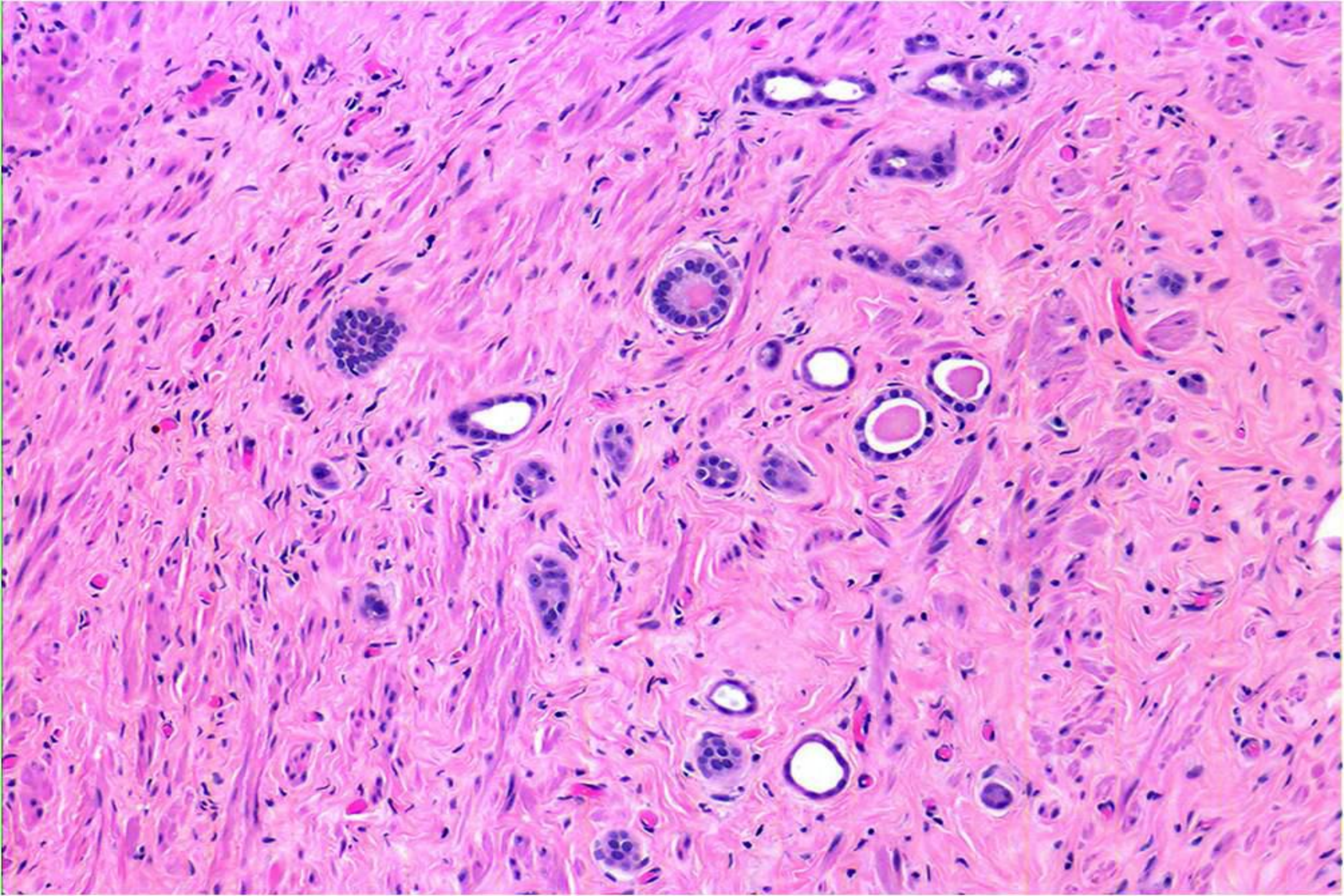


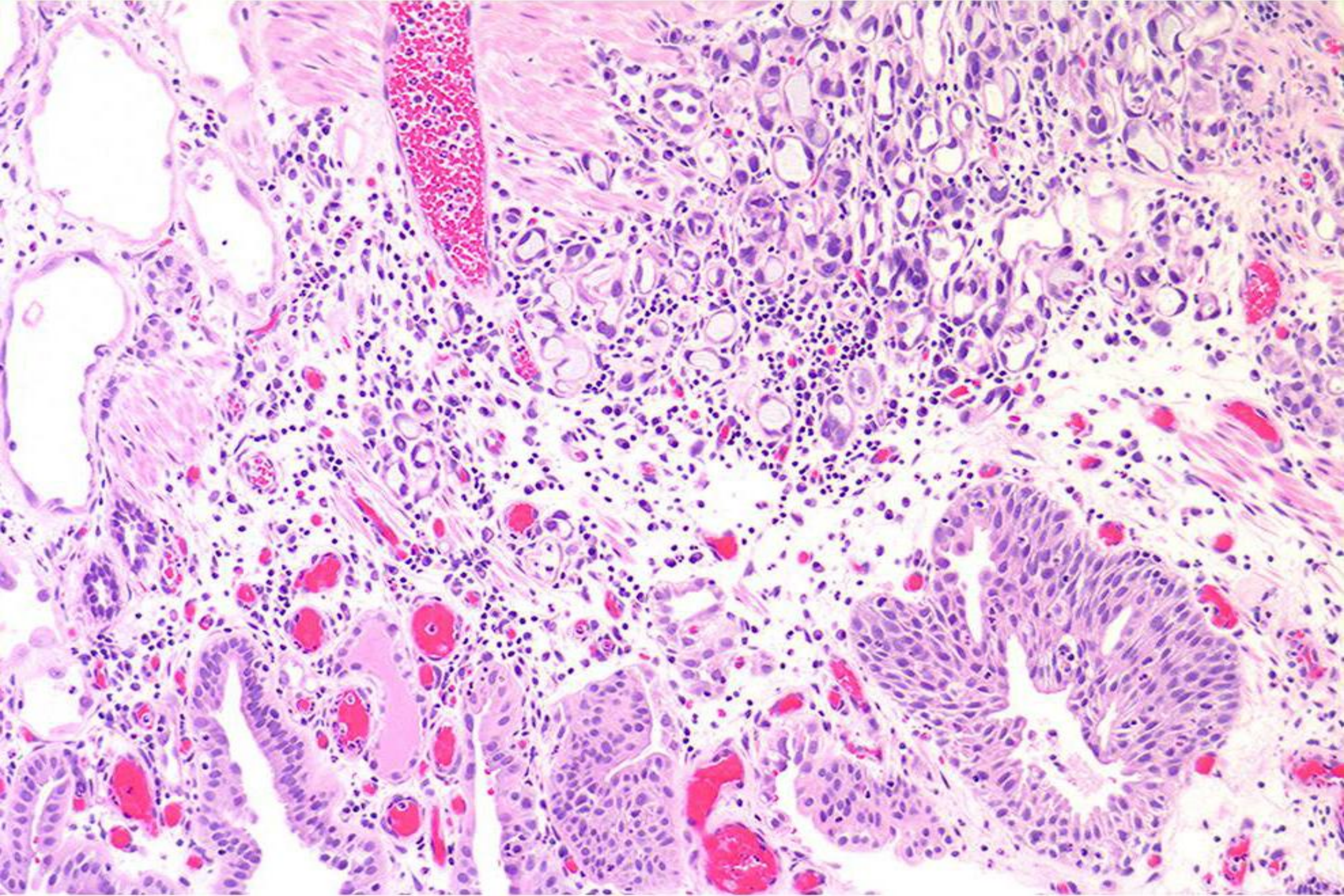


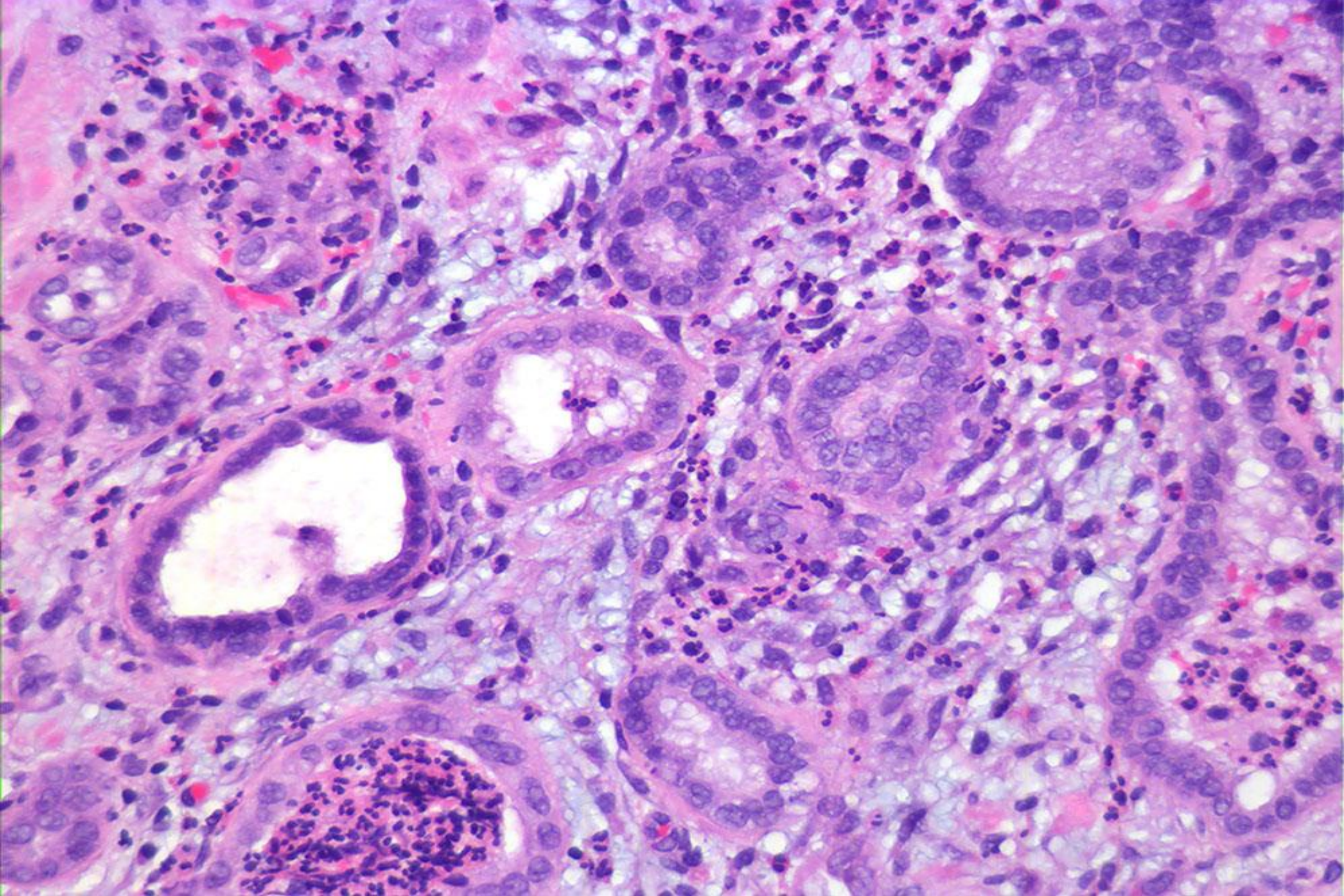


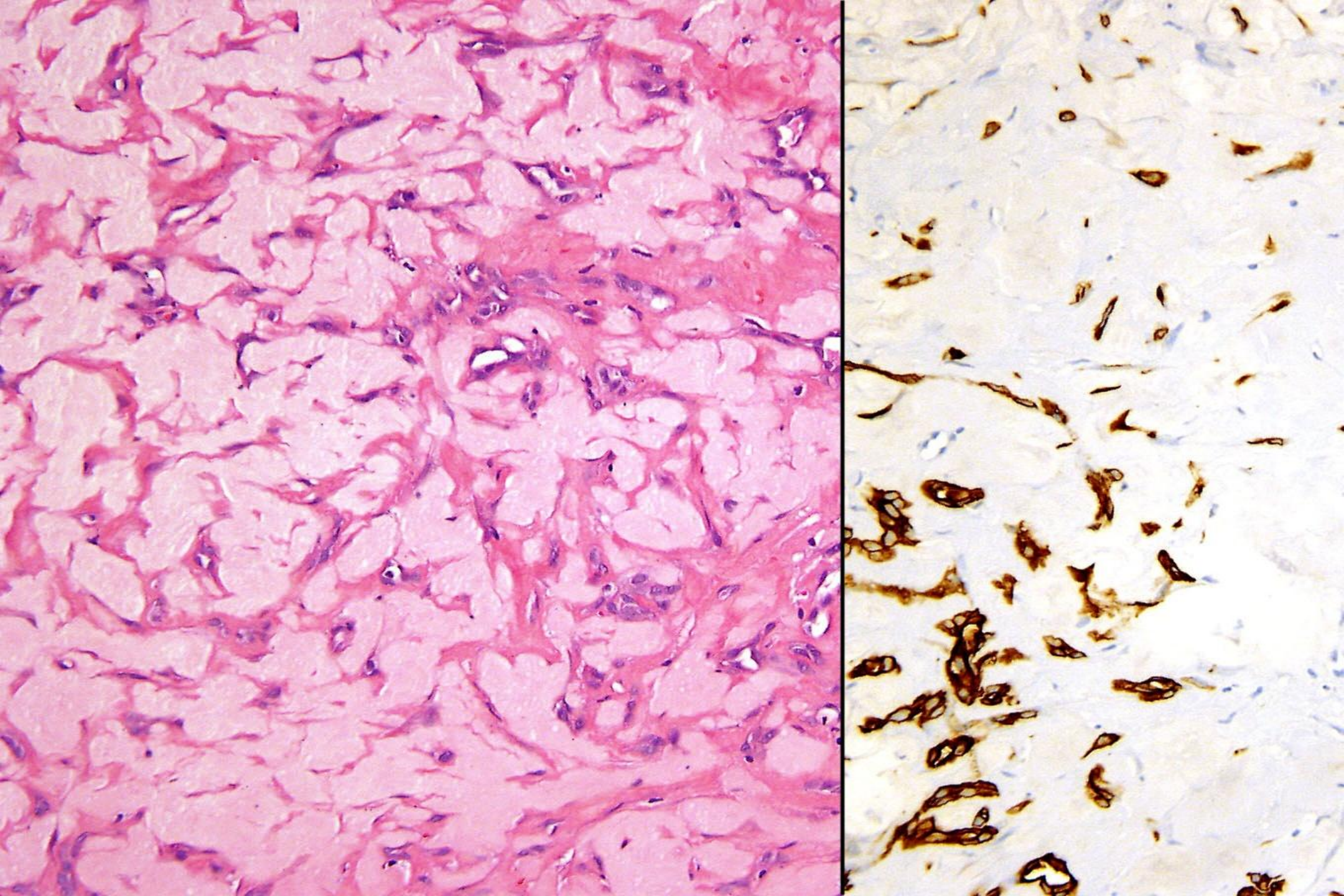












Nephrogenic Adenoma vs. Clear Cell Adenocarcinoma

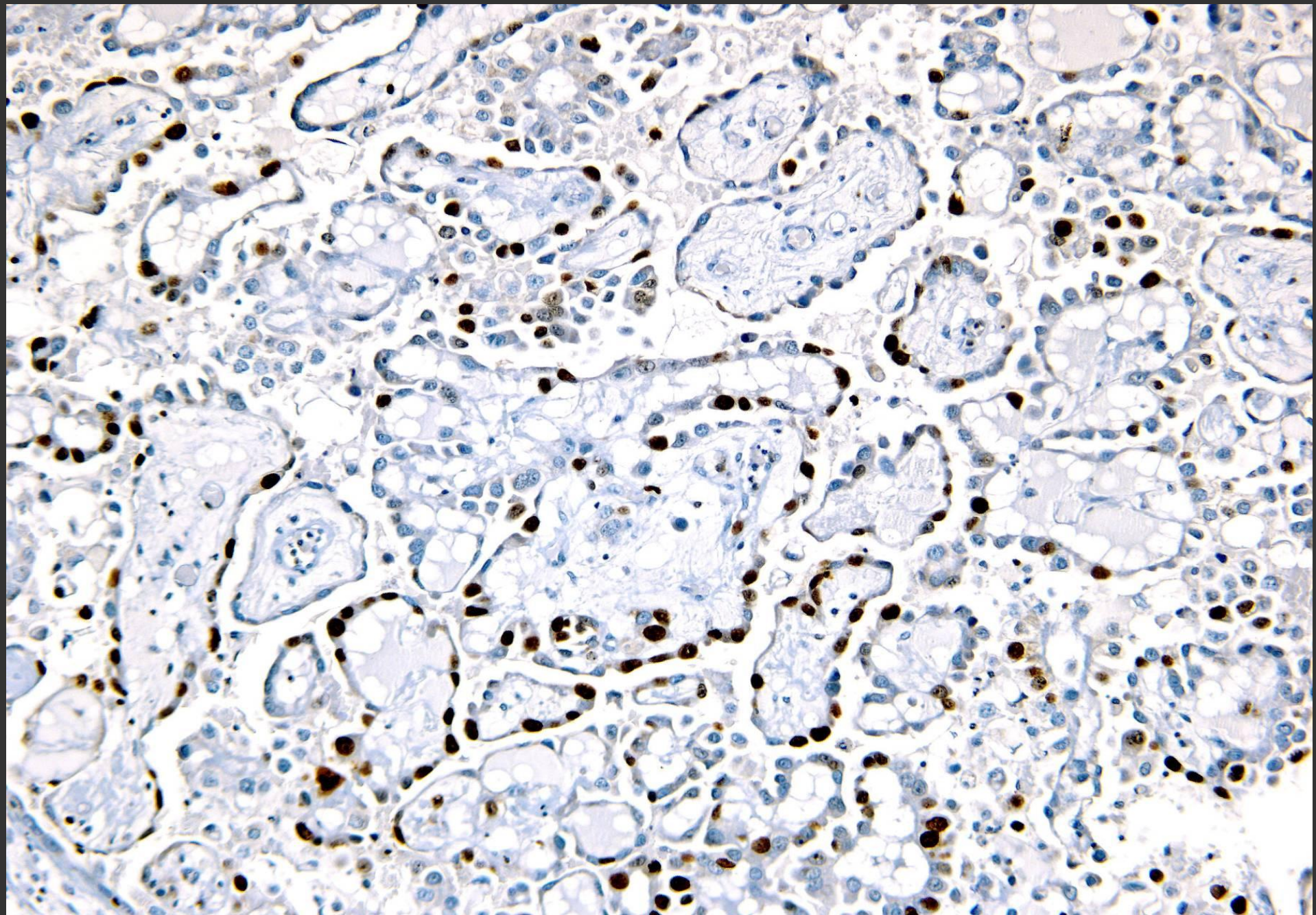
Nephrogenic Adenoma

- Usually < 1cm. Can be large.
- 20% multifocal
- M:F 2:1
- Prior injury
- Solid – rare, focal
- No mitoses
- No clear cells
- PAX2 positive

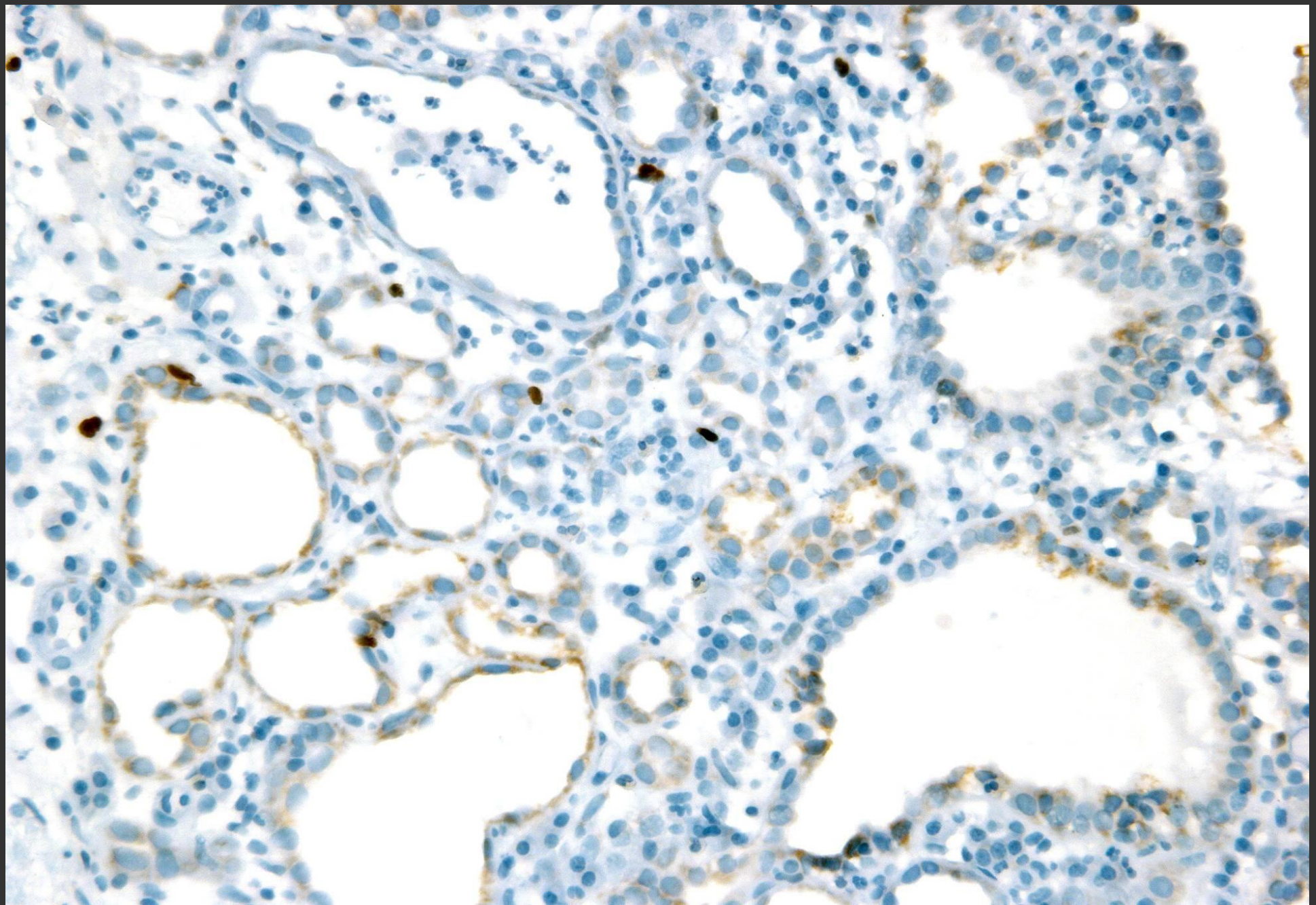
Clear Cell Adenocarcinoma

- Typically large
- Unifocal
- Rare in men
- No prior injury
- Solid areas common
- Mitotic figures common
- Typically clear cells
- PAX2 positive

Ki67 in Clear Cell Adenocarcinoma



Ki67 in NA



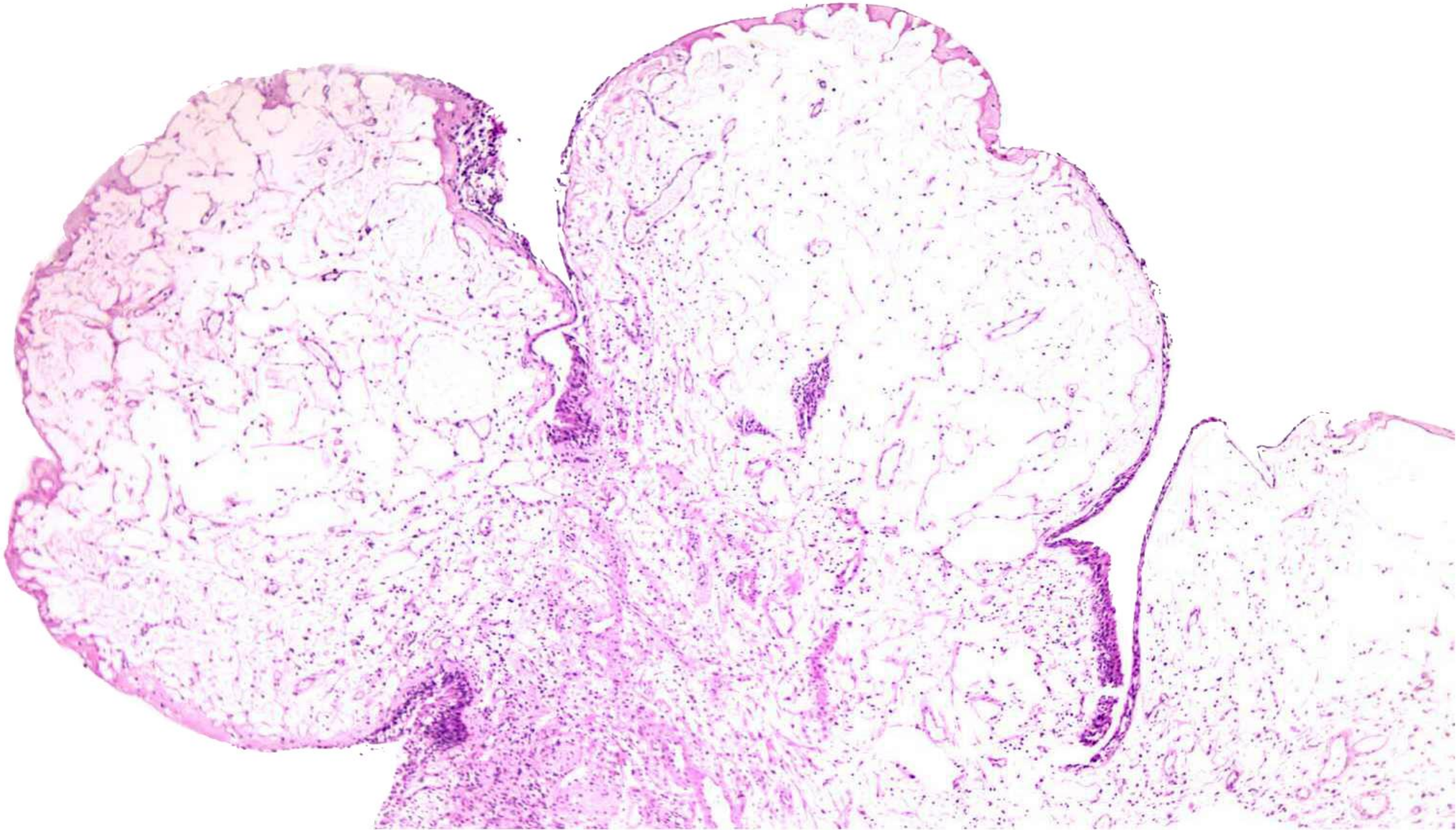
Mimics of Urothelial Cancer

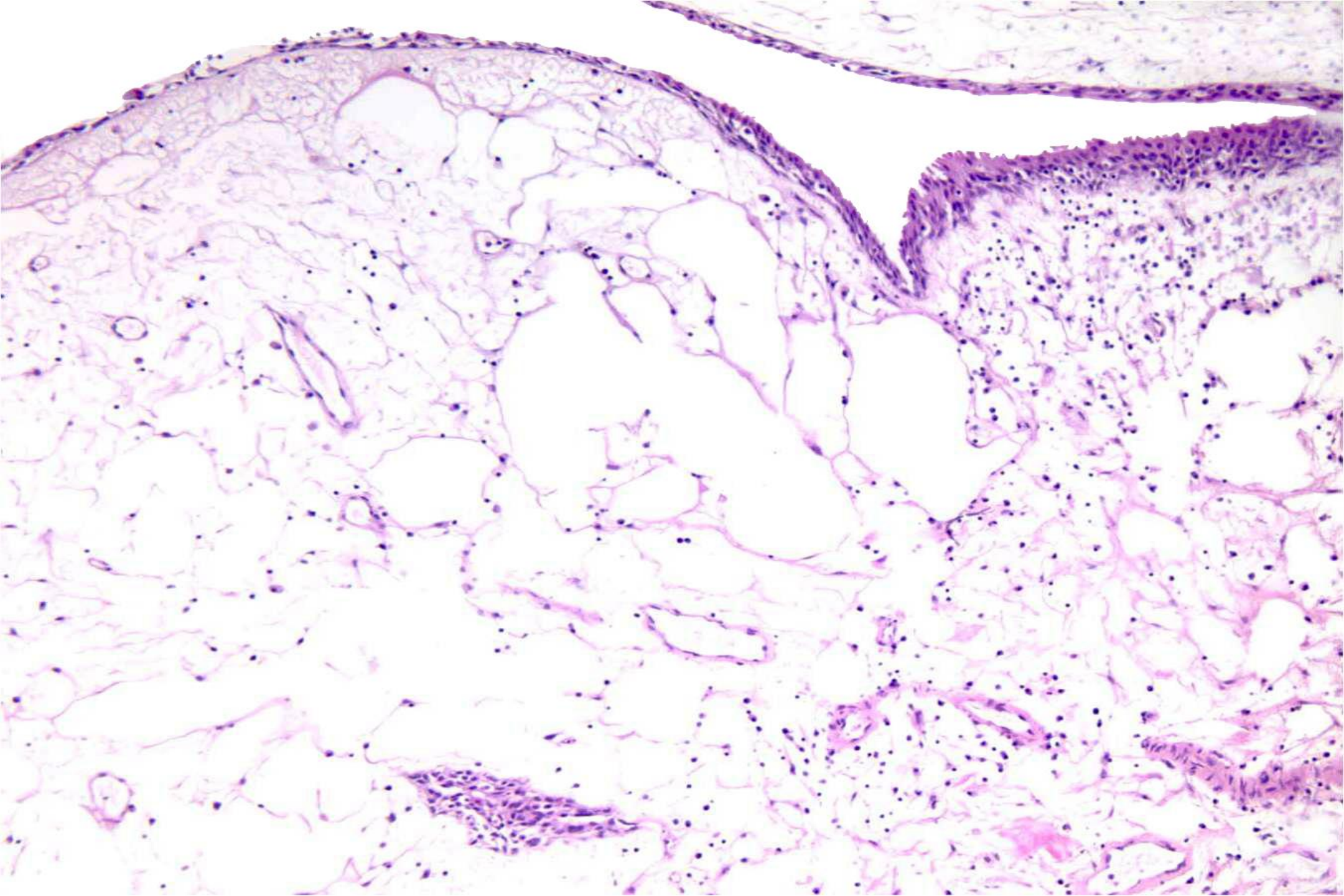
Polypoid Cystitis

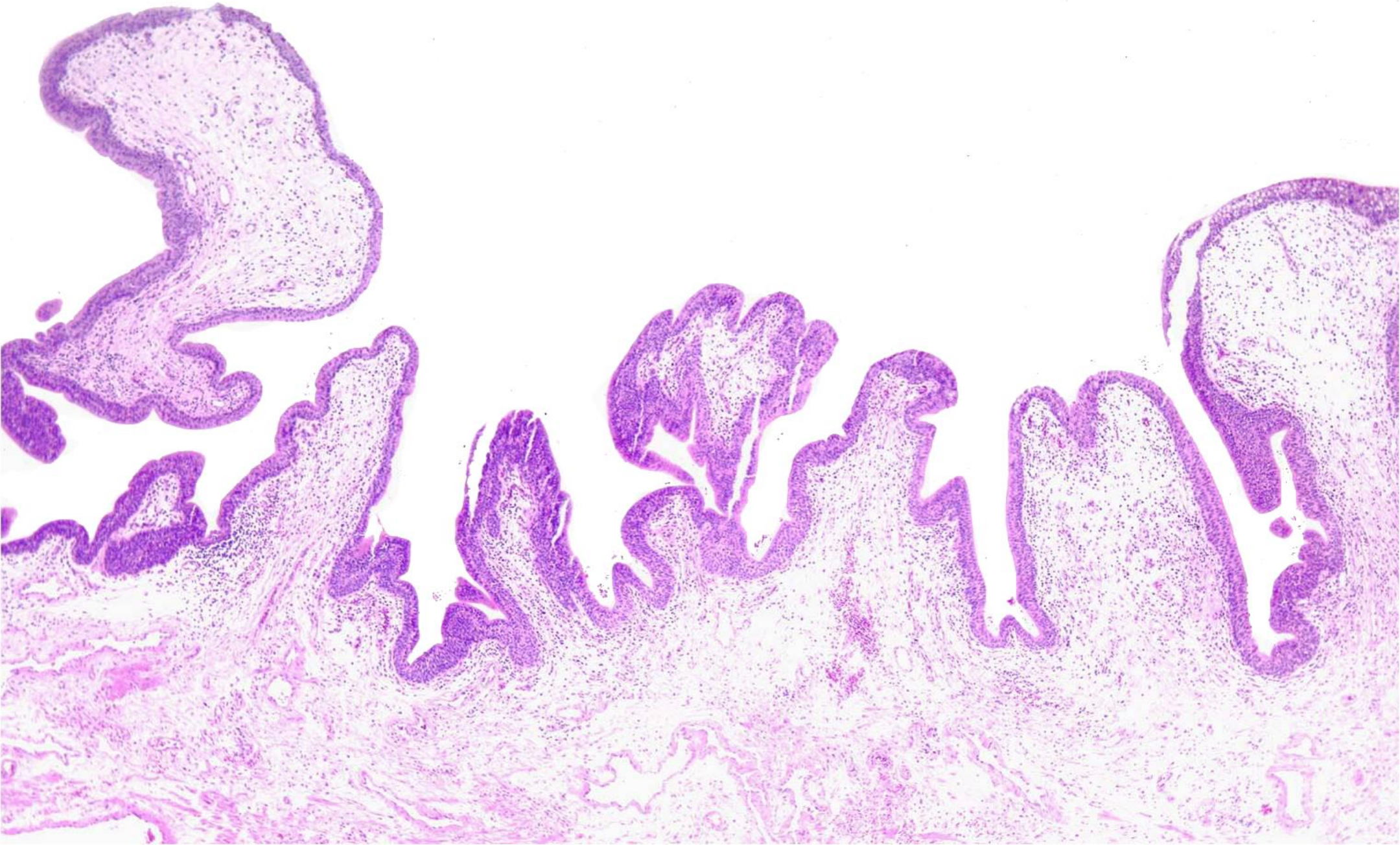
- **Reaction to injury**
- **Indwelling catheters, fistulae, abscesses, long-standing urinary obstruction**
- **Often recognized as inflammatory by urologist at cystoscopy**
- **Spectrum: bullous, polypoid, papillary**

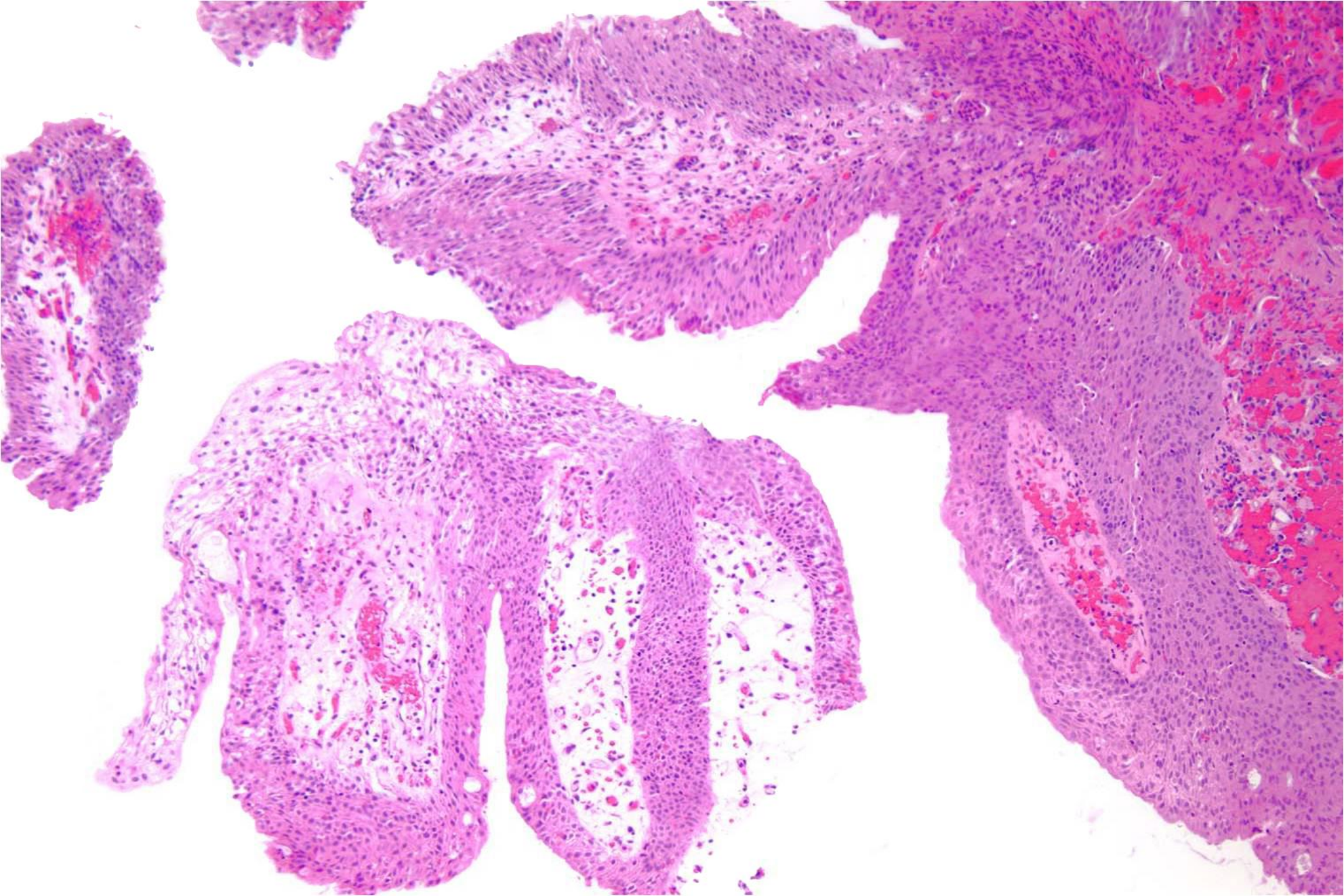
Mimic of Urothelial Carcinoma

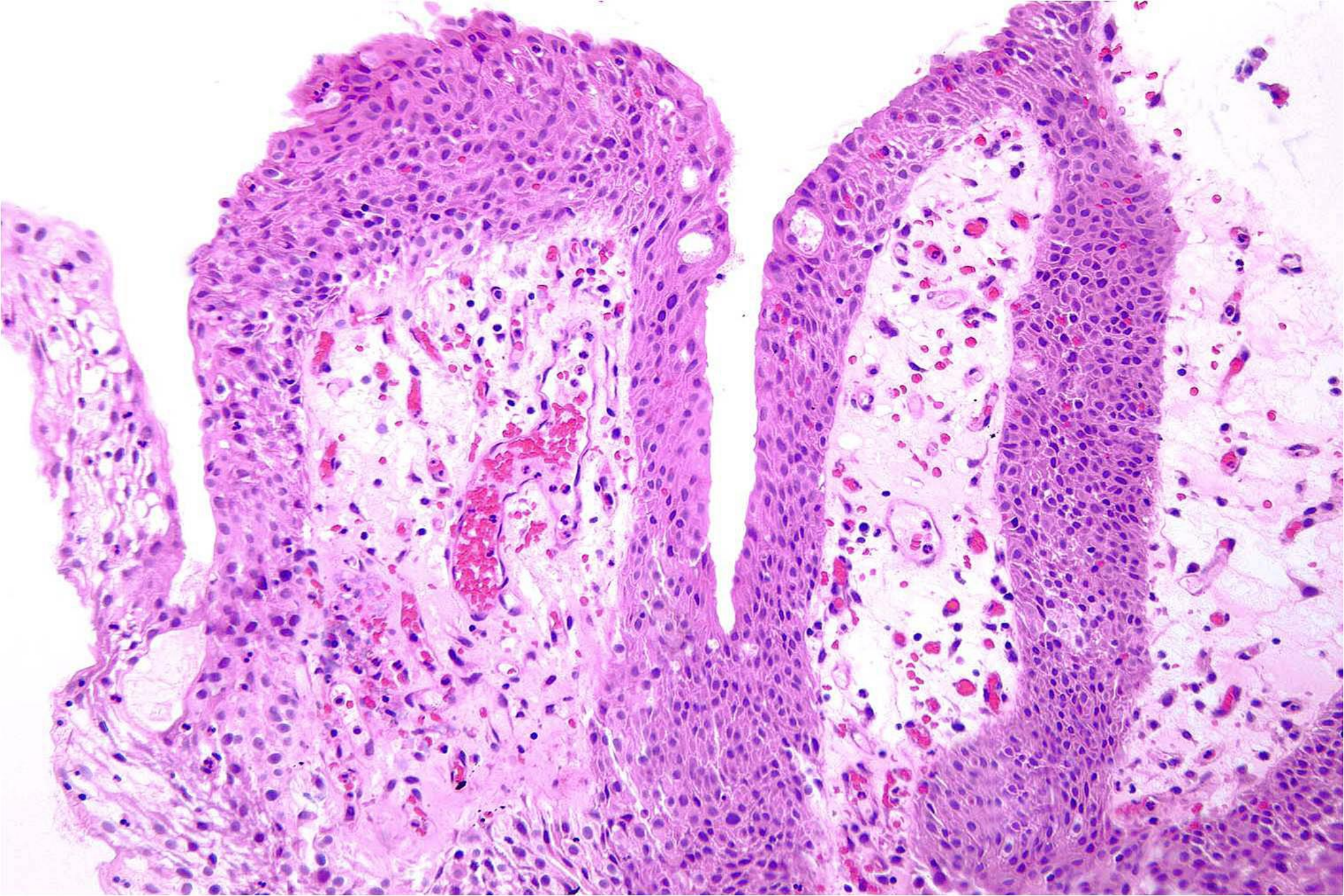
- Can have isolated papillary fronds rarely branching papillae
- Base of the papillary stalks typically both broad and narrow yet uncommonly can be only narrow
- Urothelium diffusely and focally thickened in some cases
- Reactive urothelial atypia often present
- Rare mitotic figures not uncommon
- Fibrosis (not edema) within polypoid stalks in some cases

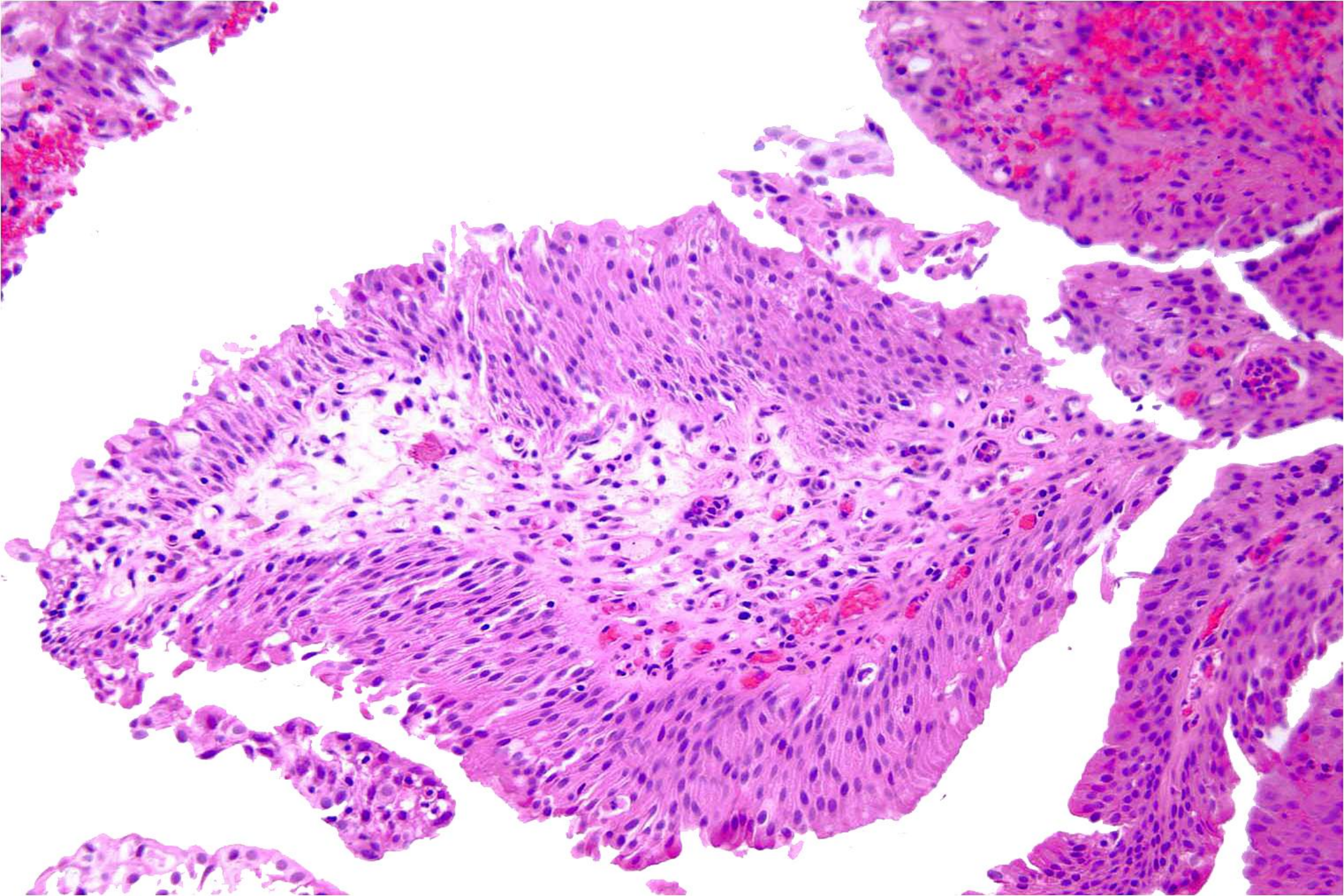


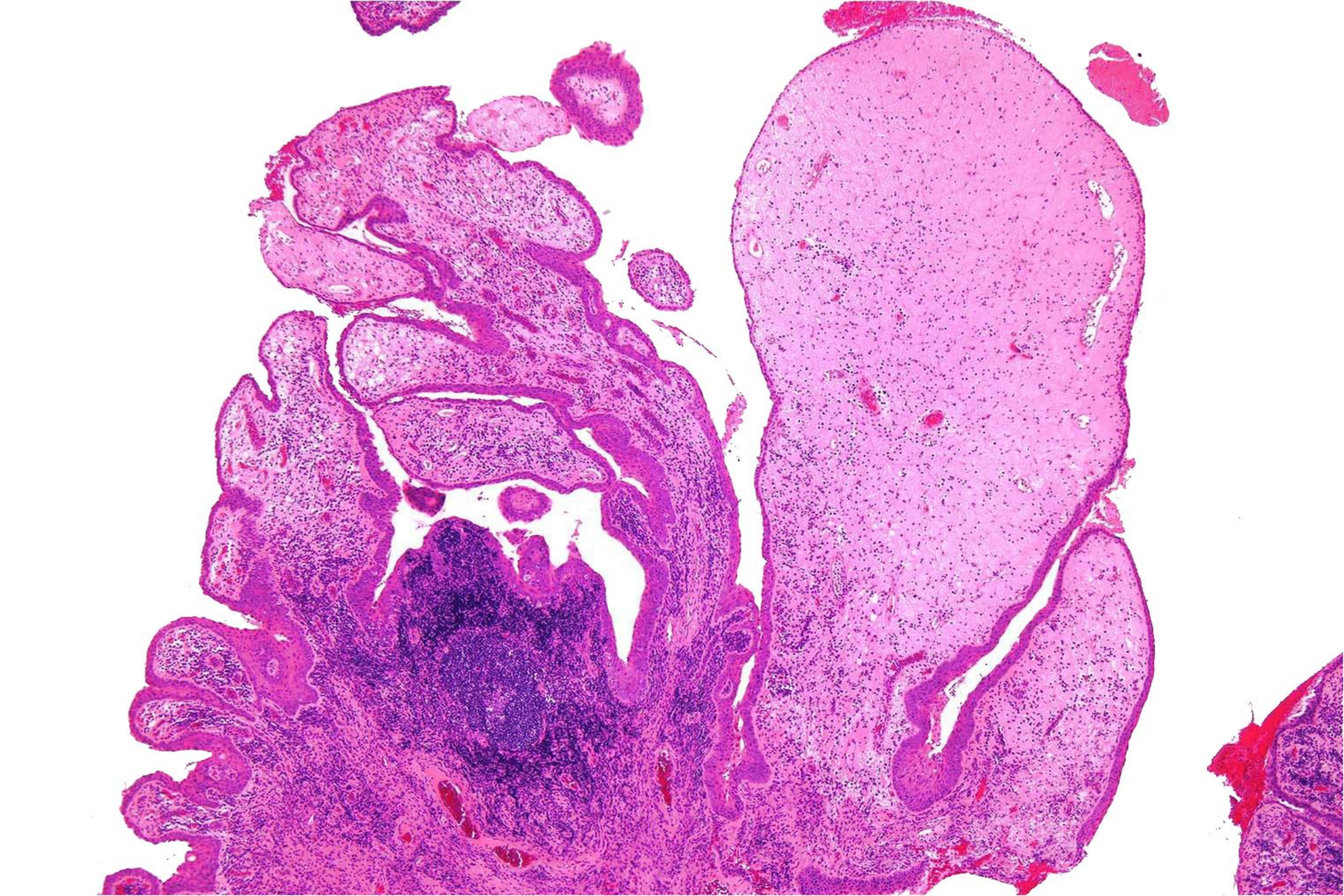


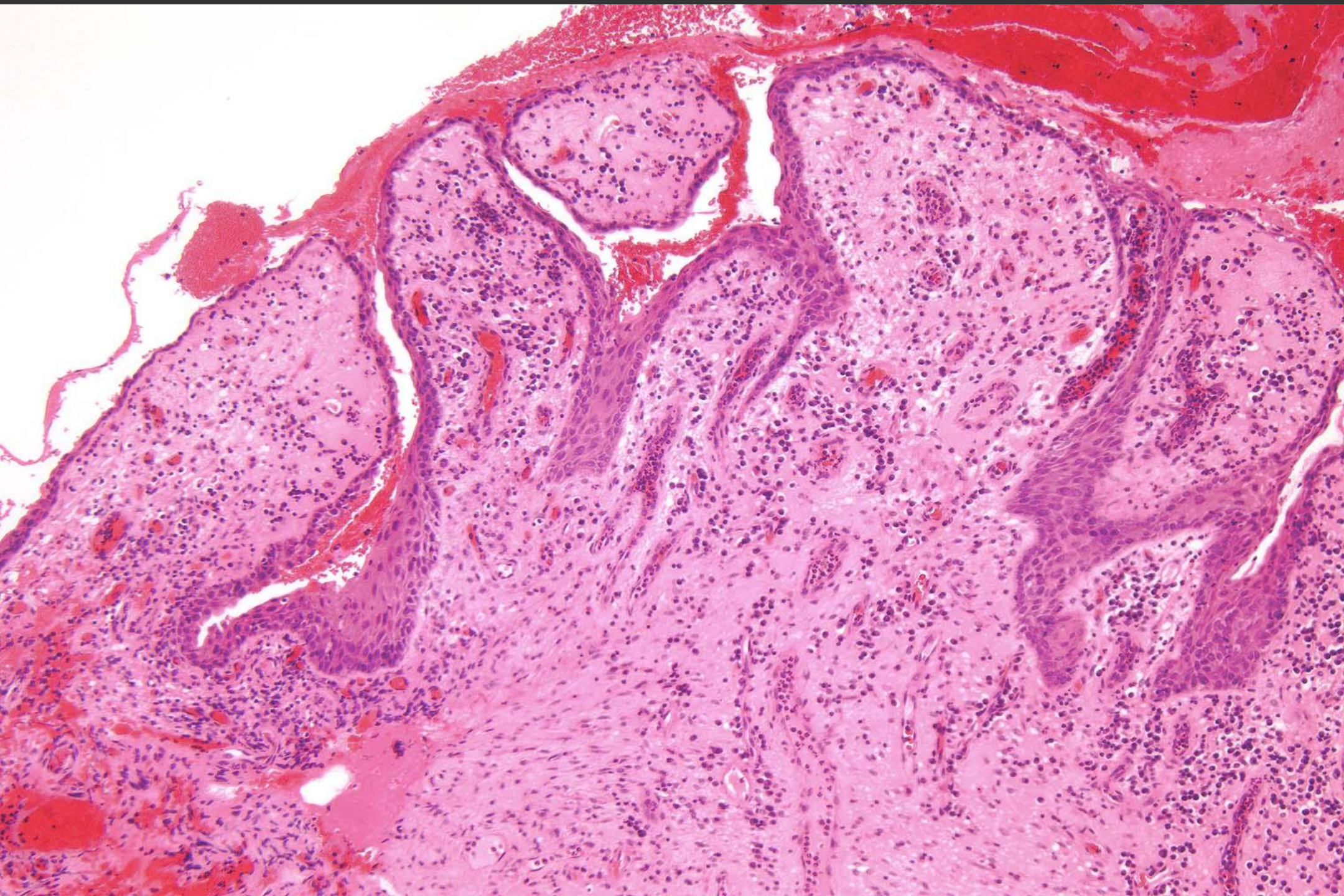


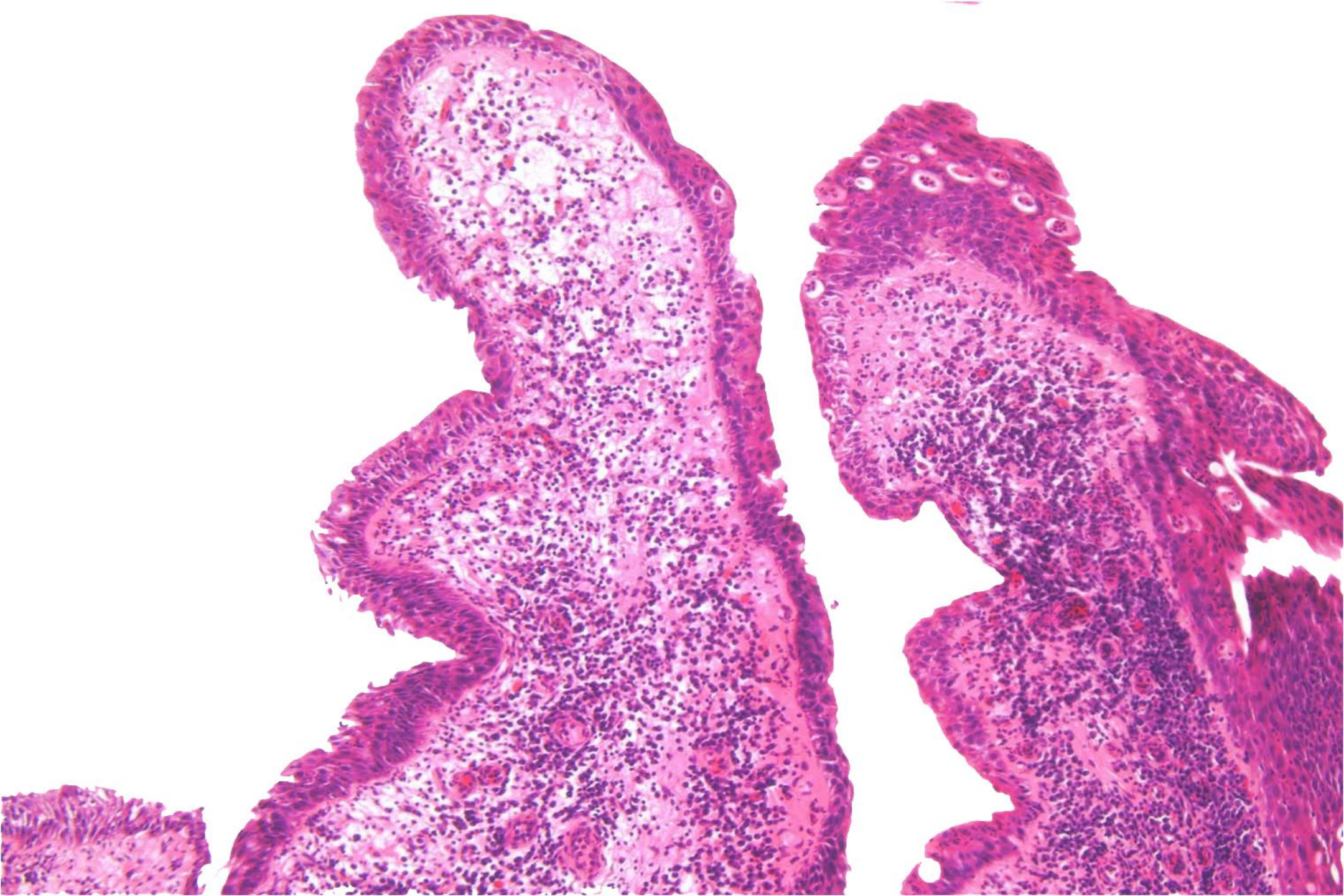


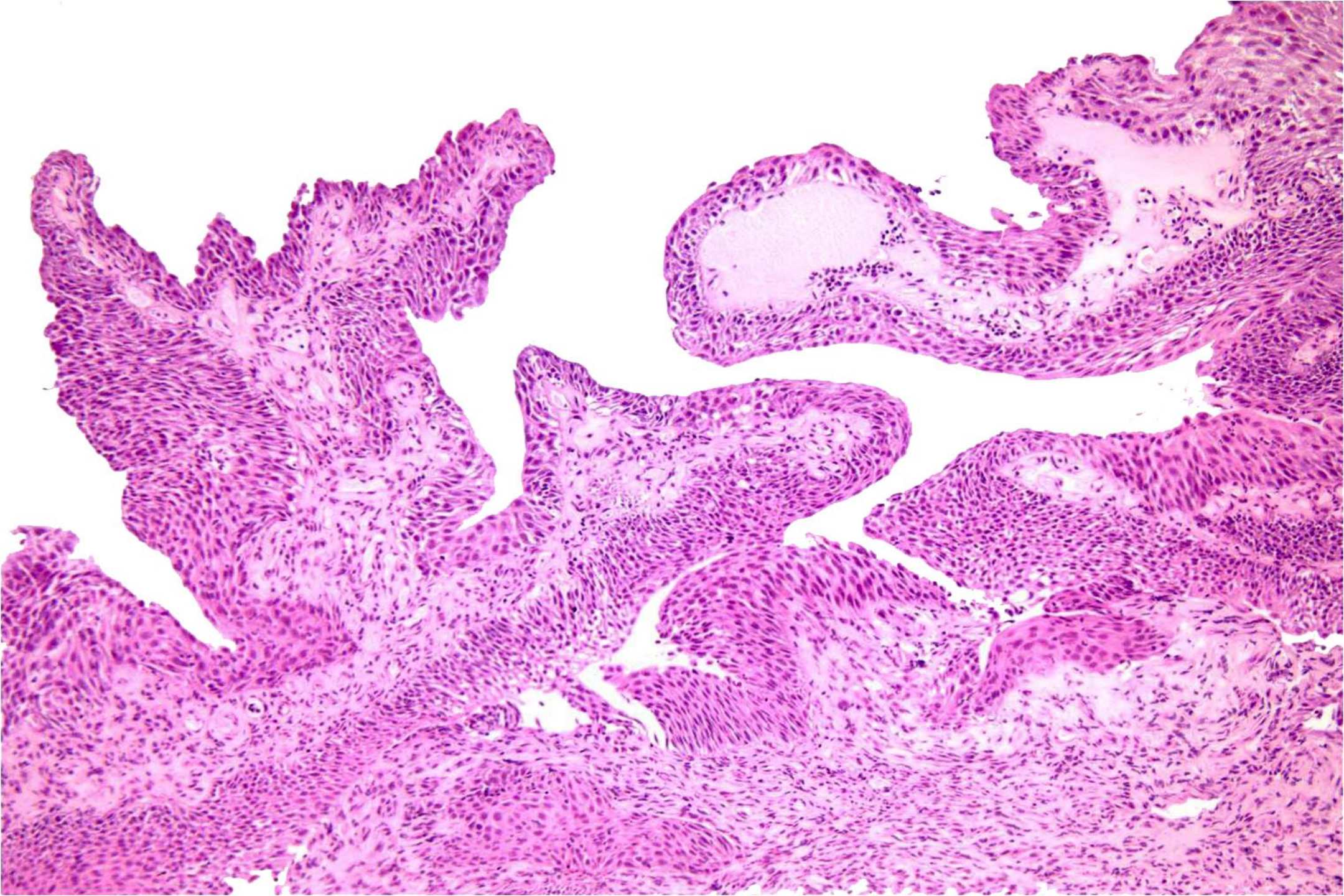


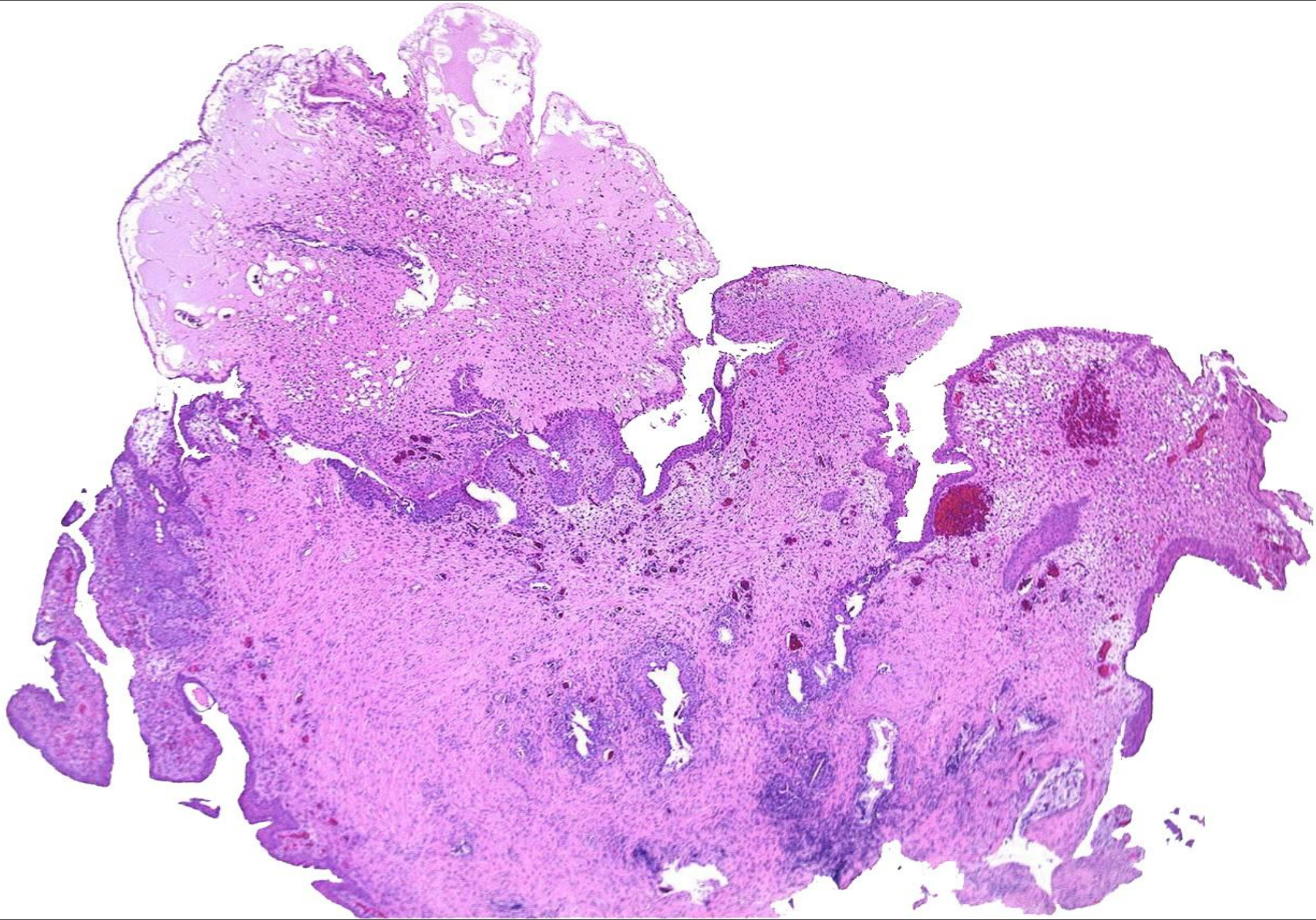


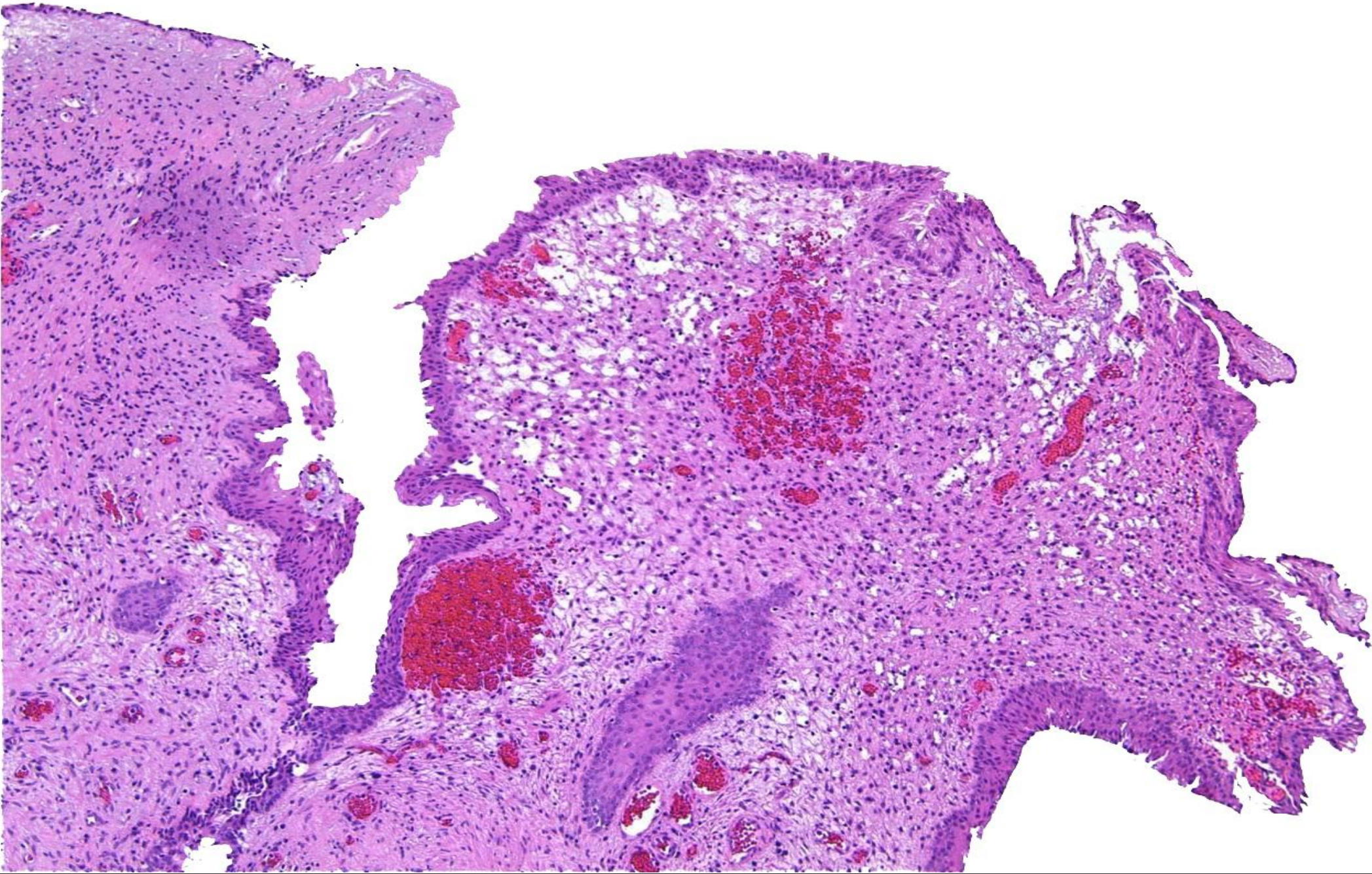


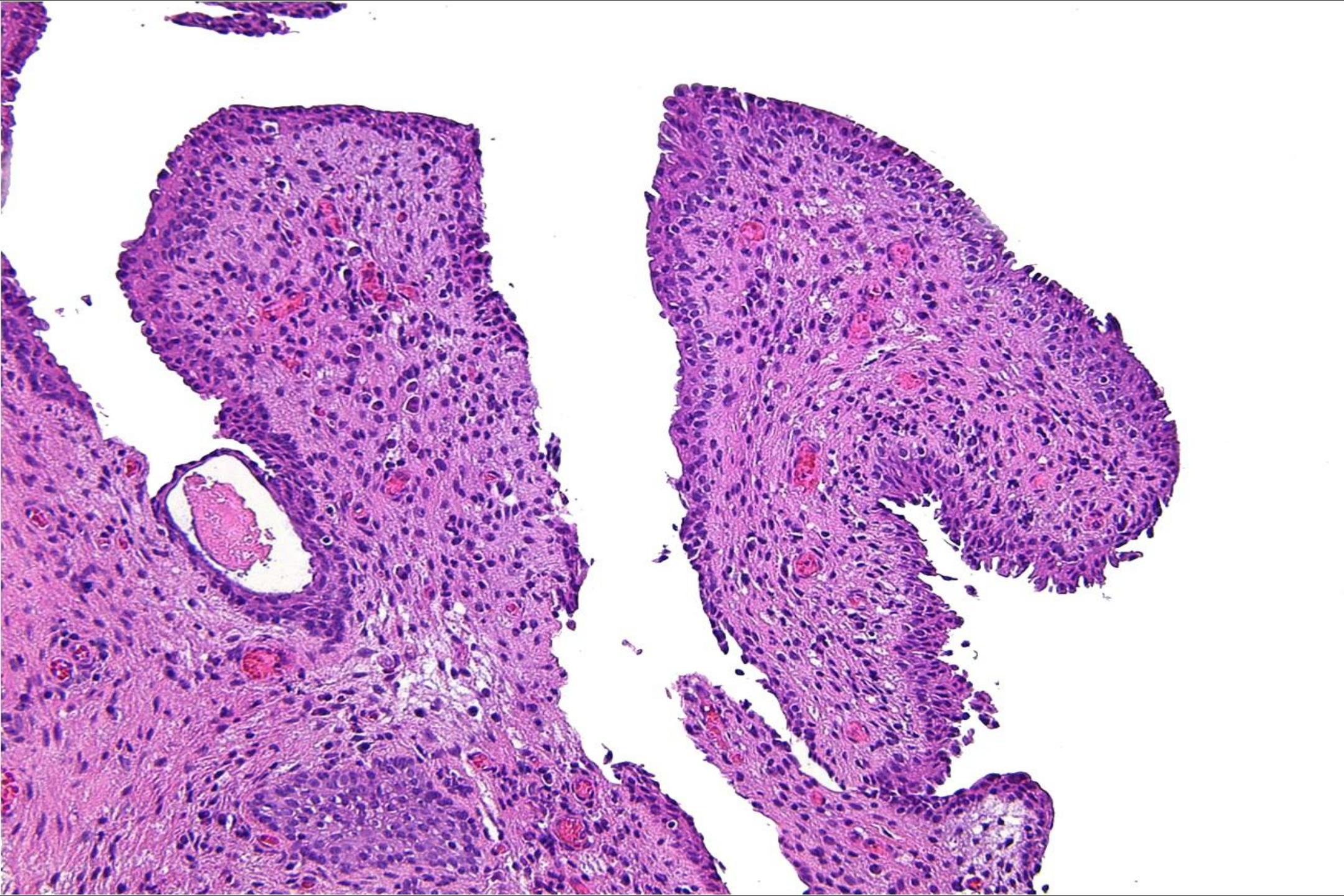












Radiotherapy of the Bladder: Pseudocarcinomatous Hyperplasia

Less familiar to pathologists is radiation-induced pseudocarcinomatous hyperplasia.

The first series to report this mimicker of invasive urothelial carcinoma was by Baker and Young in 2000 (2). Four cases were described, with follow-up available in one patient, which was benign.

Pseudocarcinomatous Hyperplasia

18 cases with either radiation or chemotherapy induced pseudocarcinomatous hyperplasia in the bladder

All 17 cases where follow-up information is available have had a benign clinical course.

All patients presented with hematuria.

Clinical Features

15 (83%) of the patients were male with an age range of 40 years to 85 years (mean 68).

The mean interval from radiation to clinical presentation was 24 months.

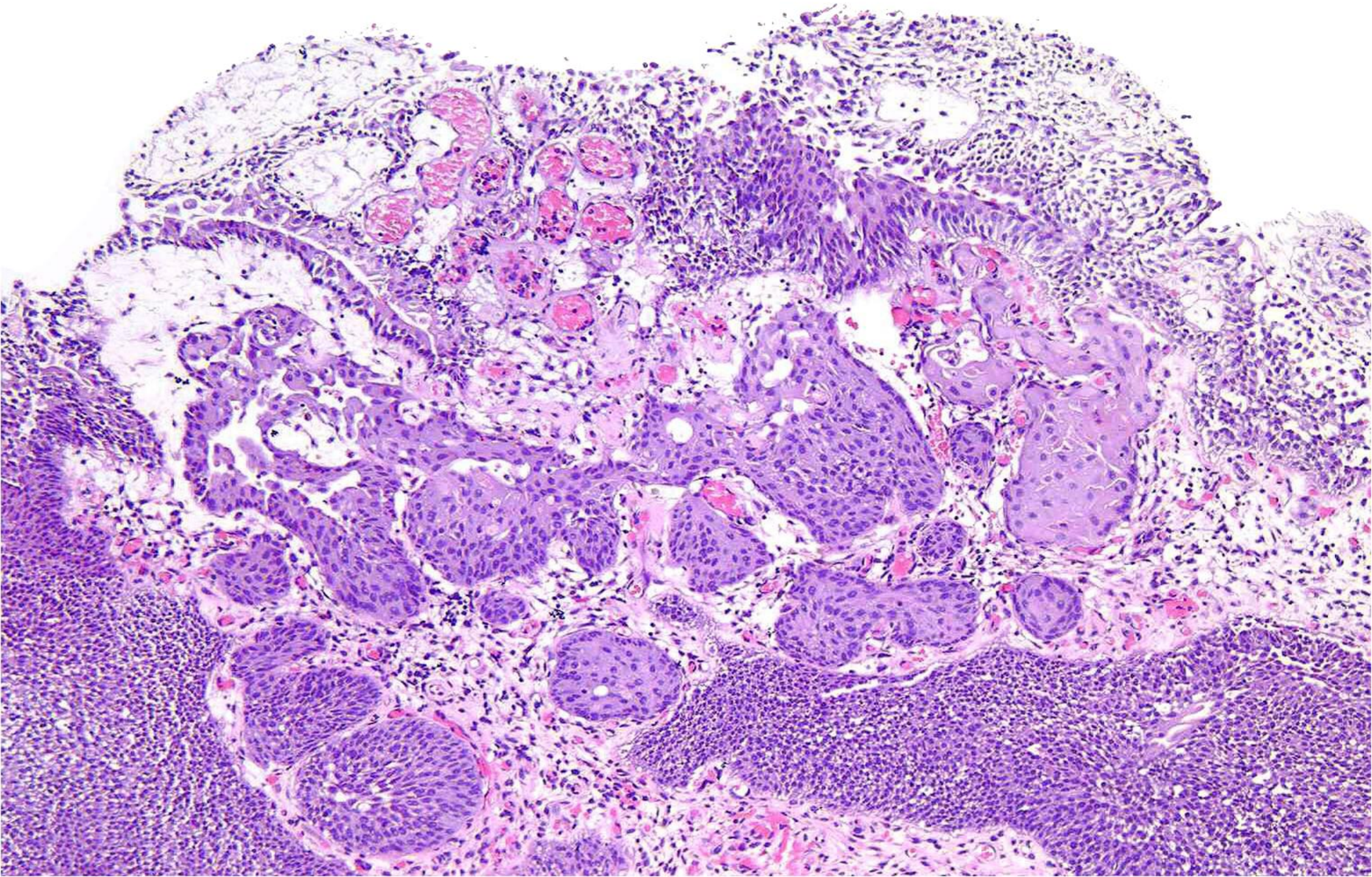
The longest interval in our study was 79 months and in the study by Baker and Young 96 months.

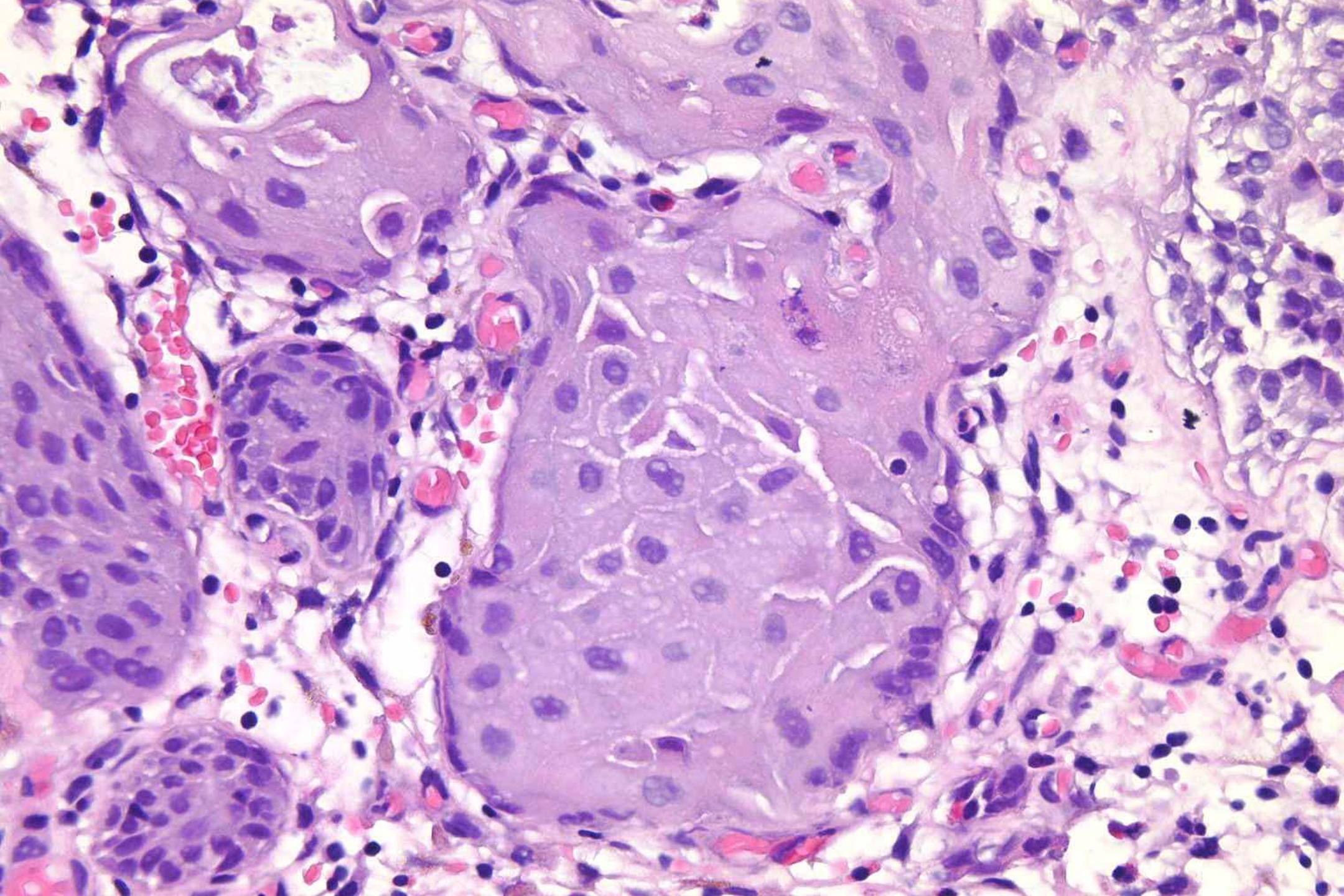
Prior Therapy

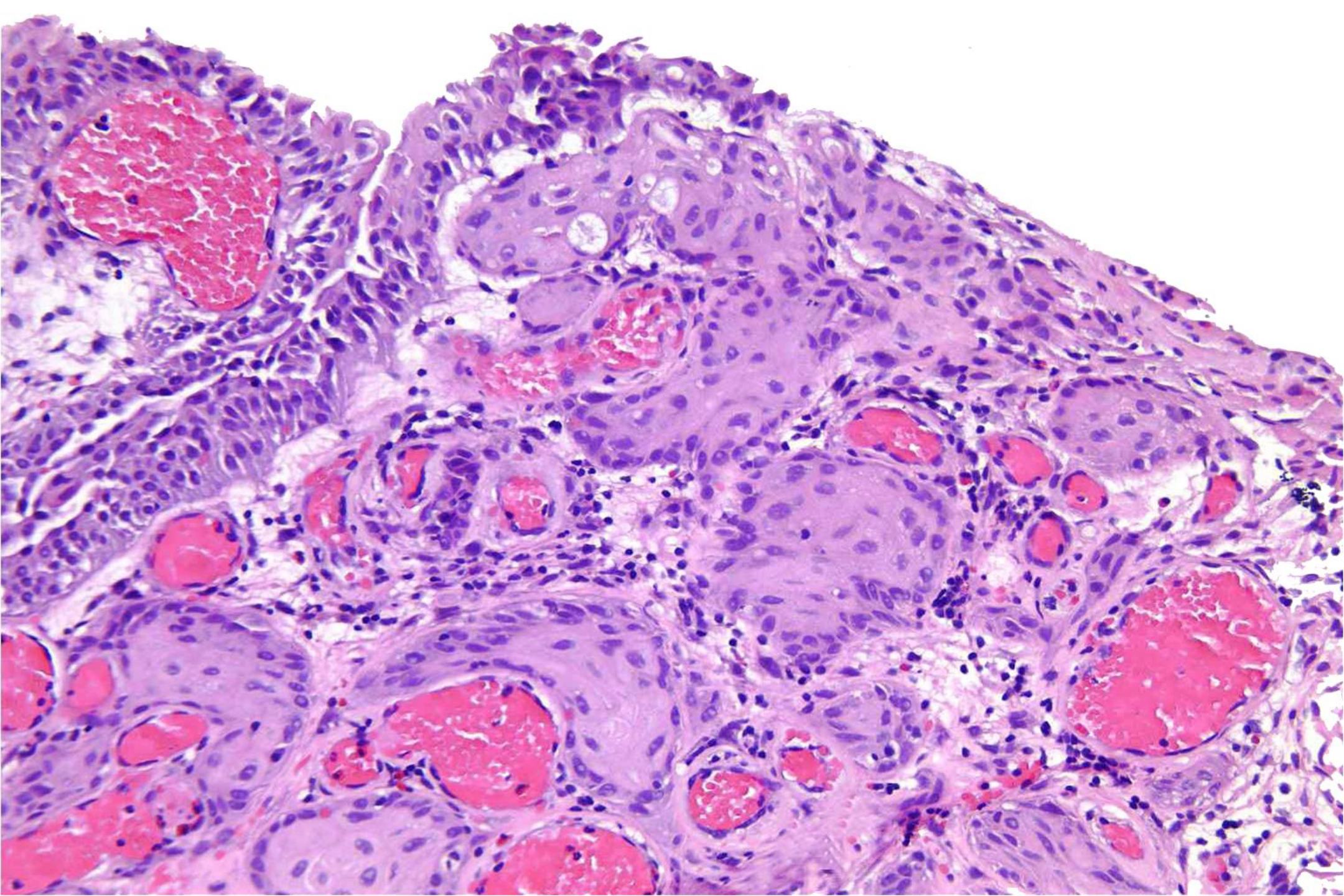
• Pelvic irradiation	14 – Prostate cancer
• Systemic chemotherapy	1 – Metastatic colon cancer 1 – Mixed connective tissue disease
• Pelvic irradiation and systemic chemotherapy	1 – Endometrial cancer
• Unknown	1 – Laryngeal cancer.

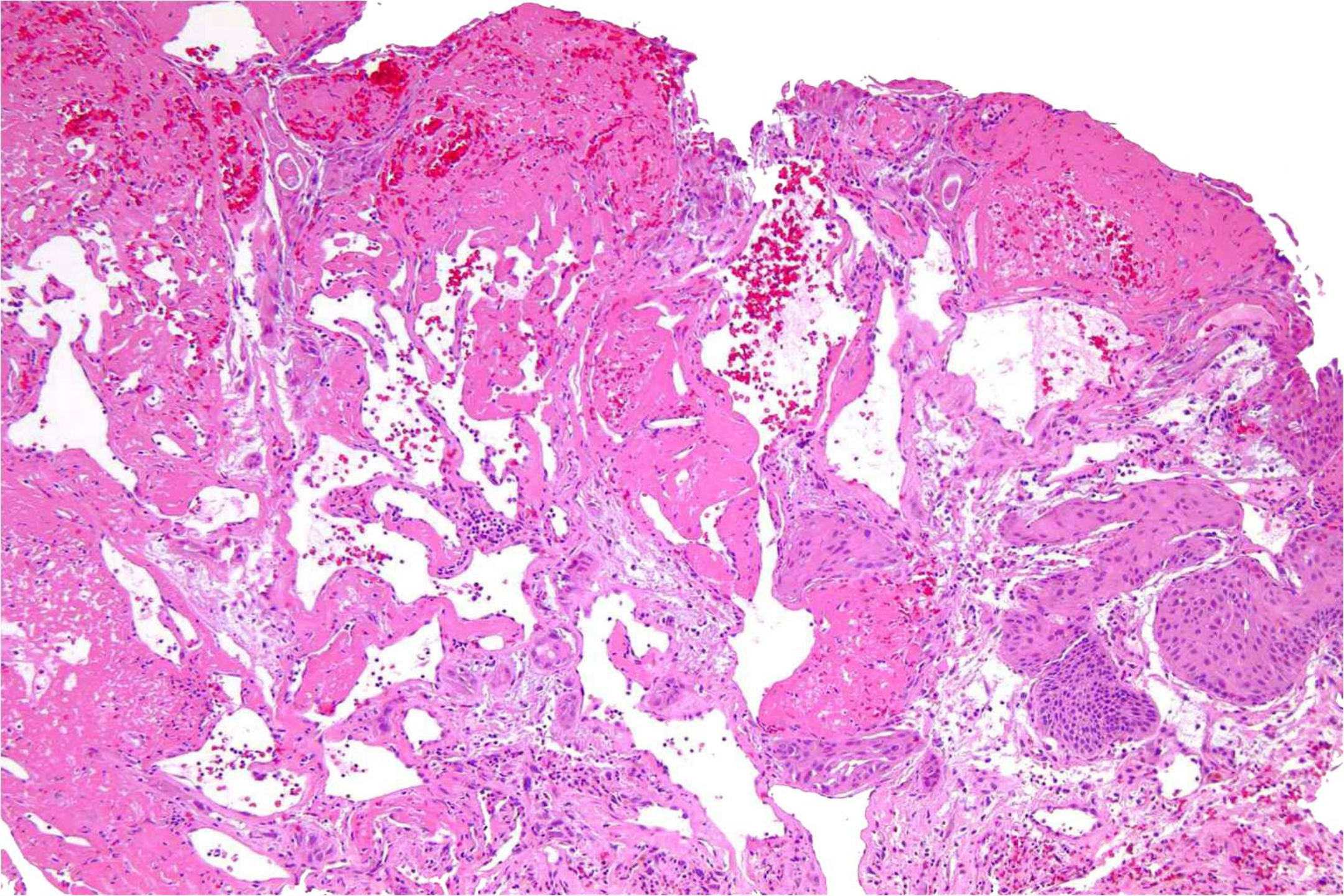
Pseudocarcinomatous Epithelial Hyperplasia in the Bladder Unassociated with Prior Irradiation or Chemotherapy

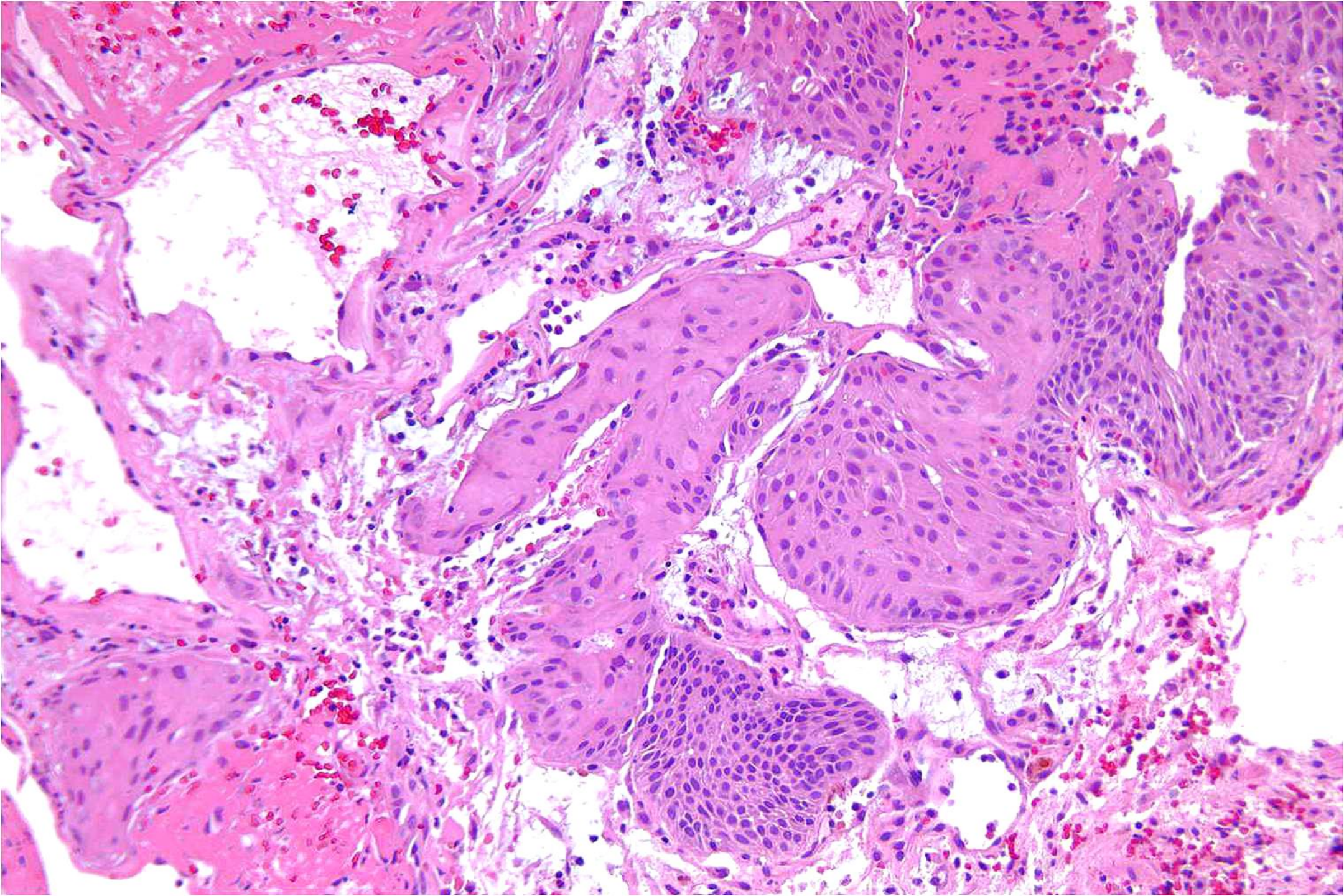
- **8 cases**
- **Severe ischemia**
- **Long-standing irritation to the bladder**

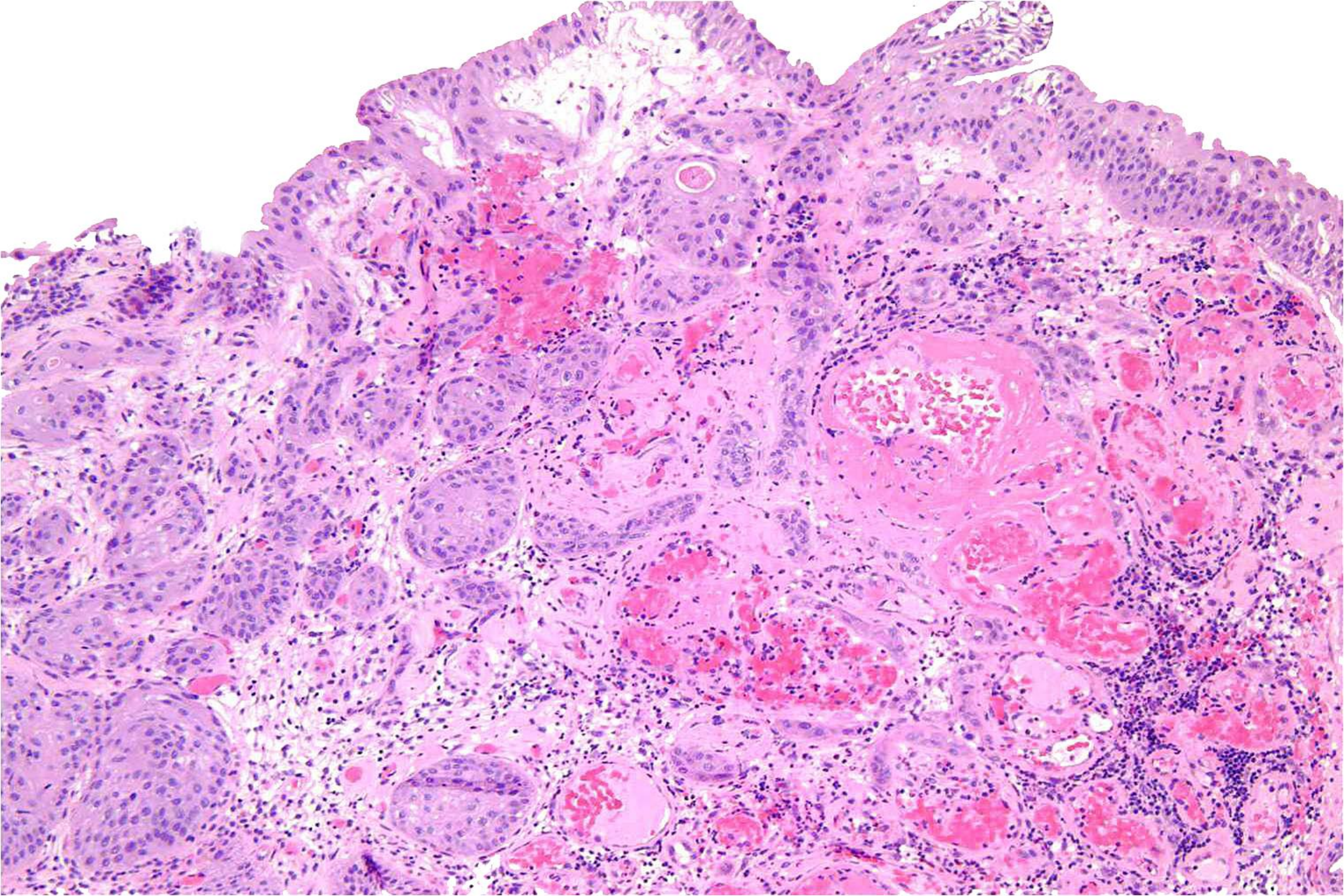


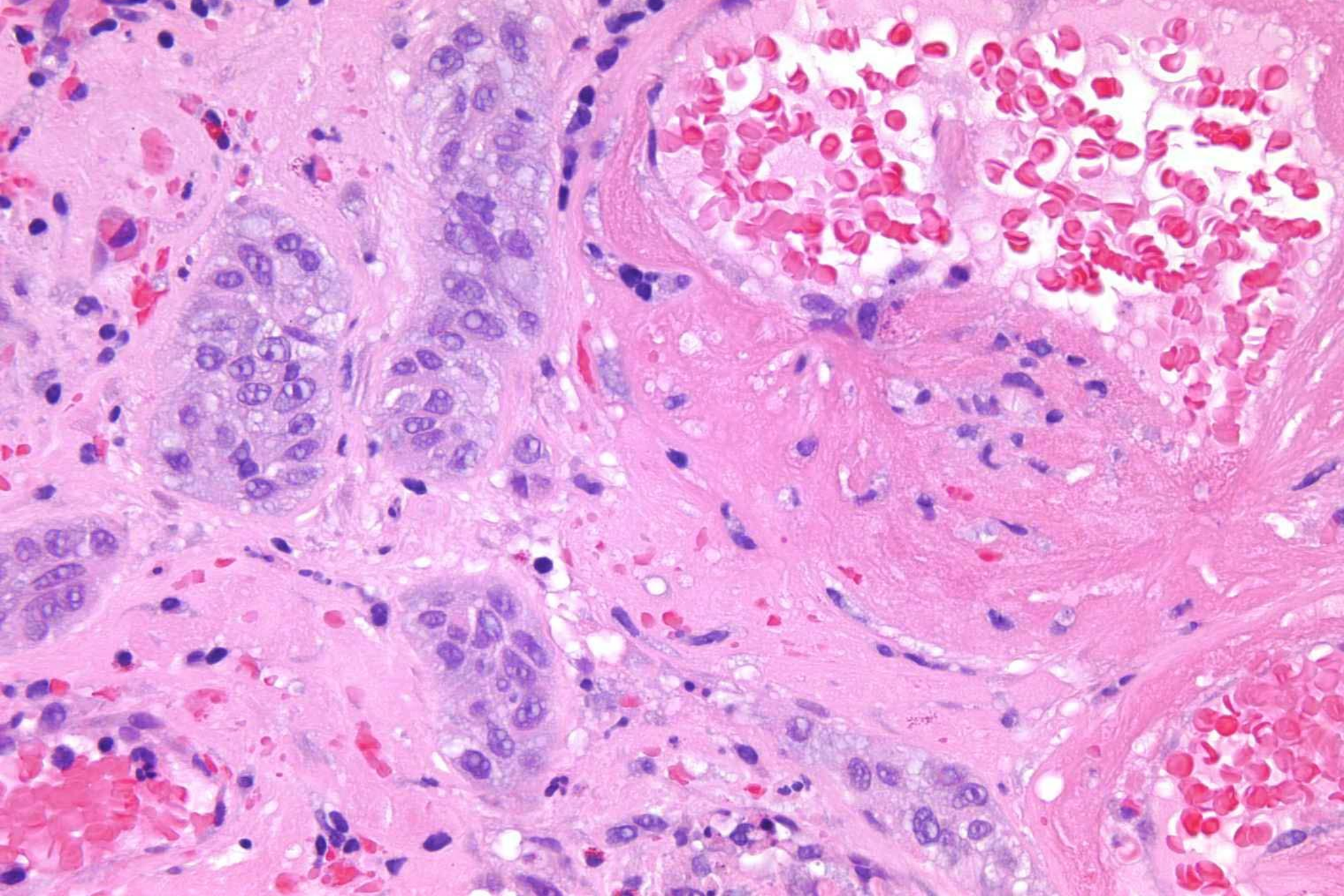


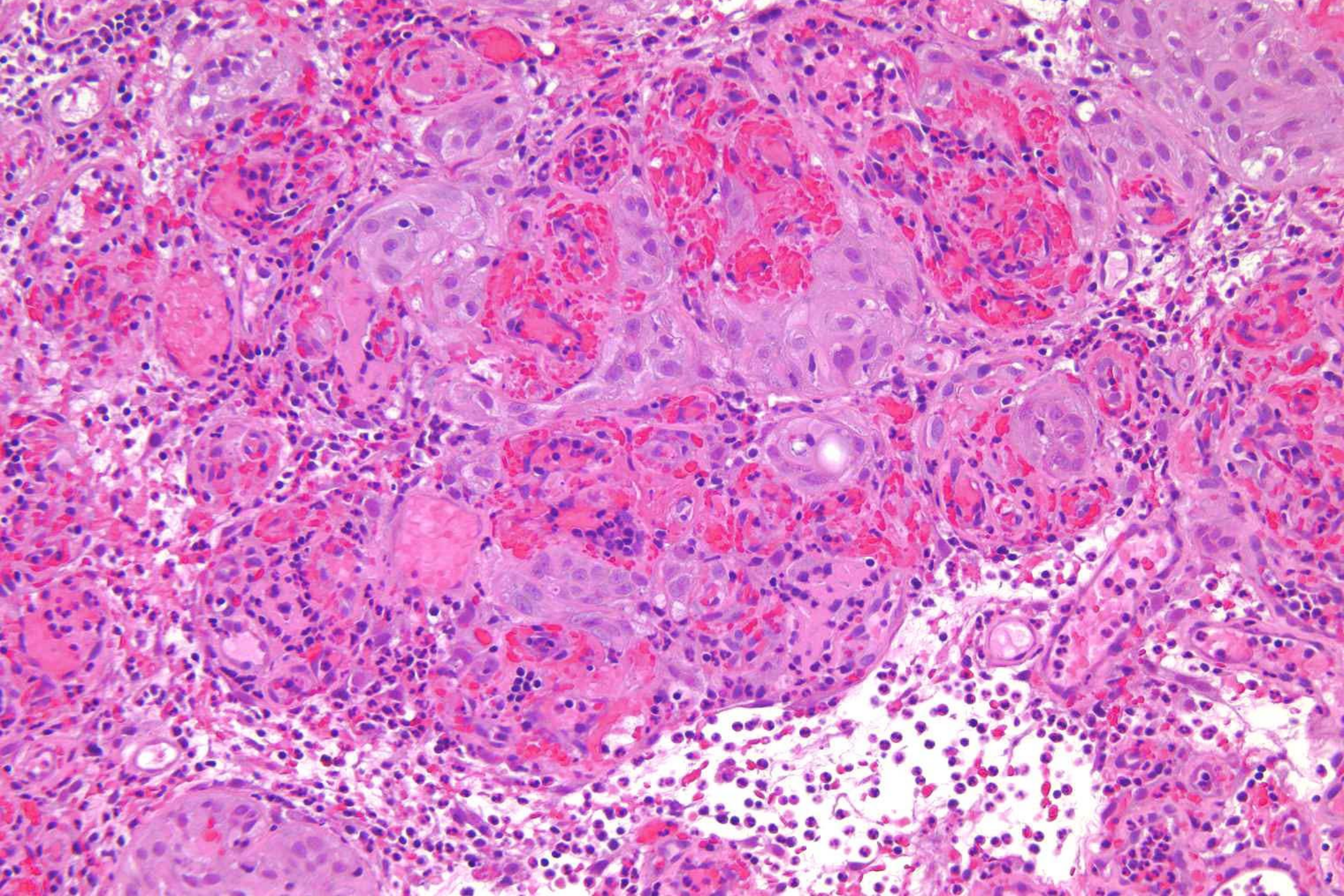


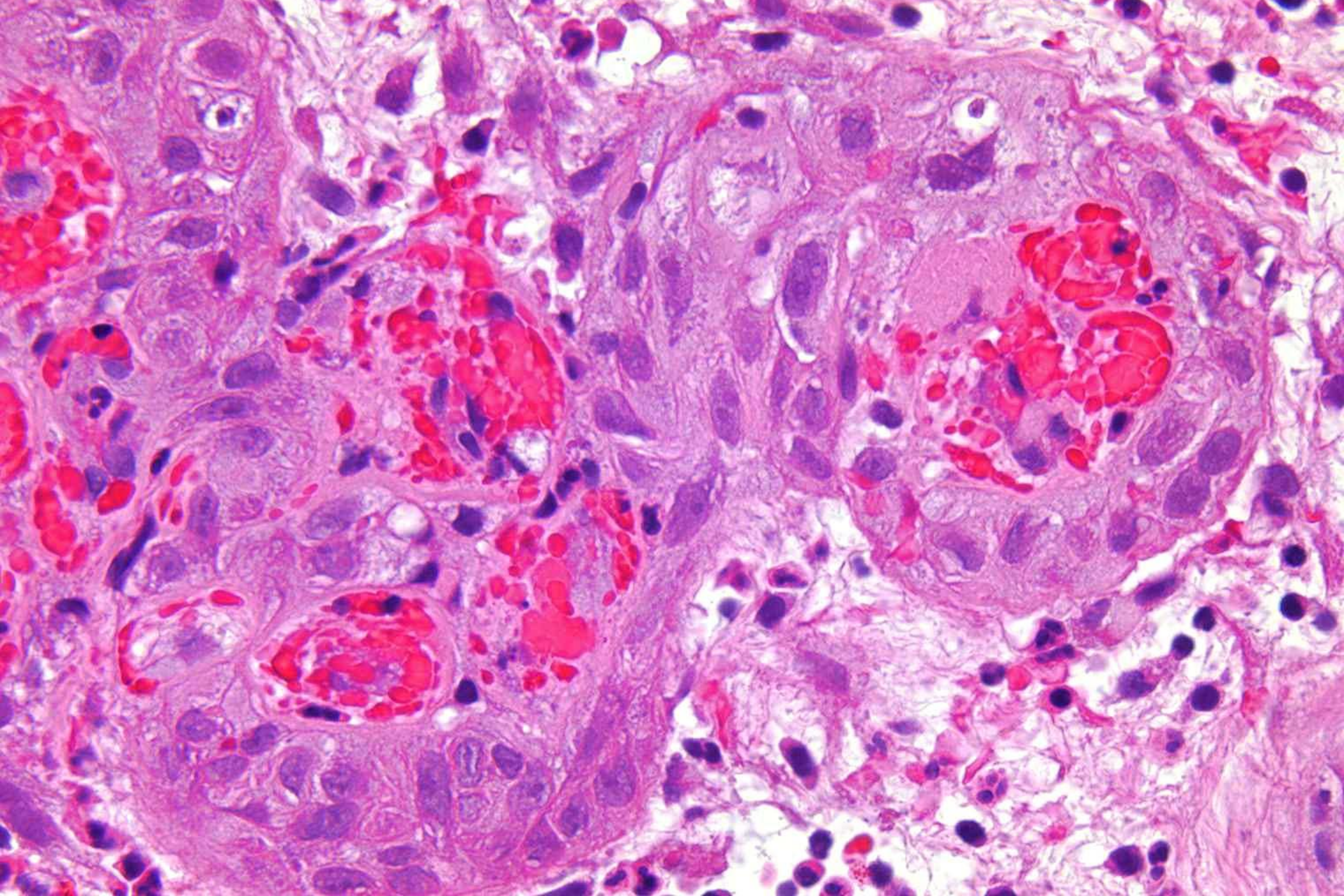












Histology: Resemblance to Cancer

- **Architectural pattern mimicking cancer: 44% with >50% involvement of LP**
- **Most cases (61%) had prominent nucleoli**
- **All had mild to moderate pleomorphism**
- **28% with mitotic figures (1-8/10HPF)**

Histologic Clues to Benign Nature

- **Edema (94%), vascular congestion (78%), hemosiderin (56%)**
- **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.**
- **Most importantly fibrin deposits with in many cases the urothelial nests encircling the fibrin.**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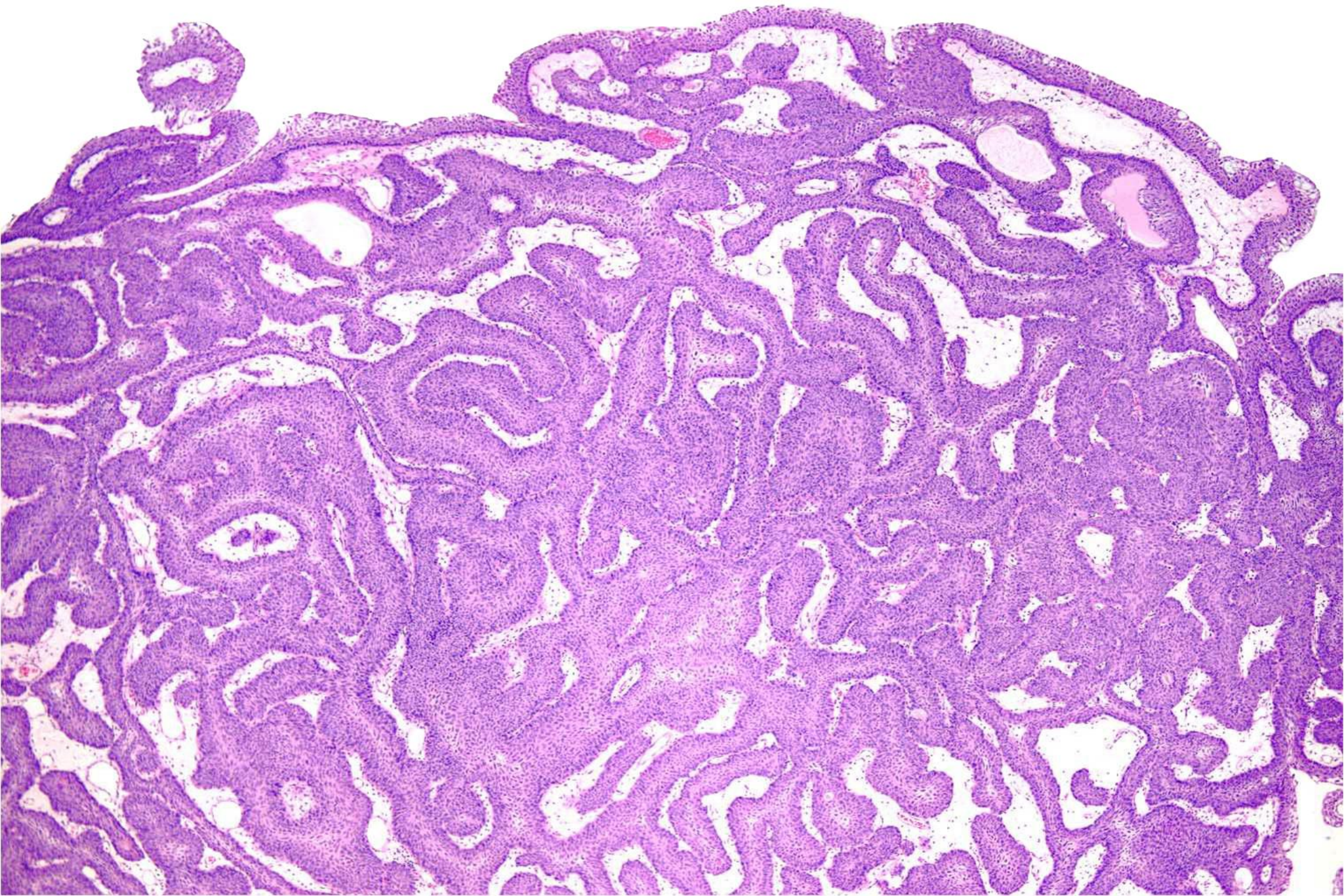
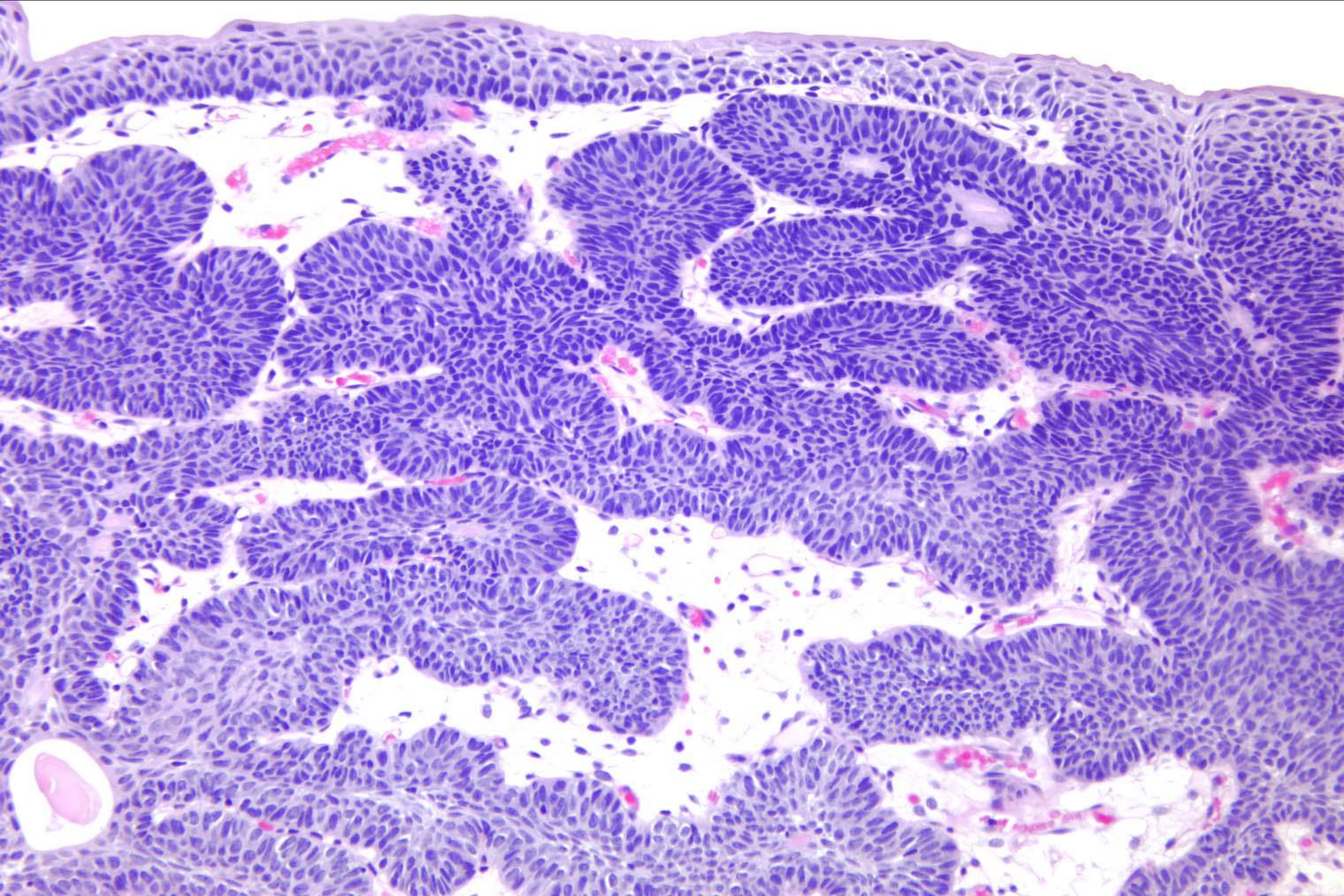
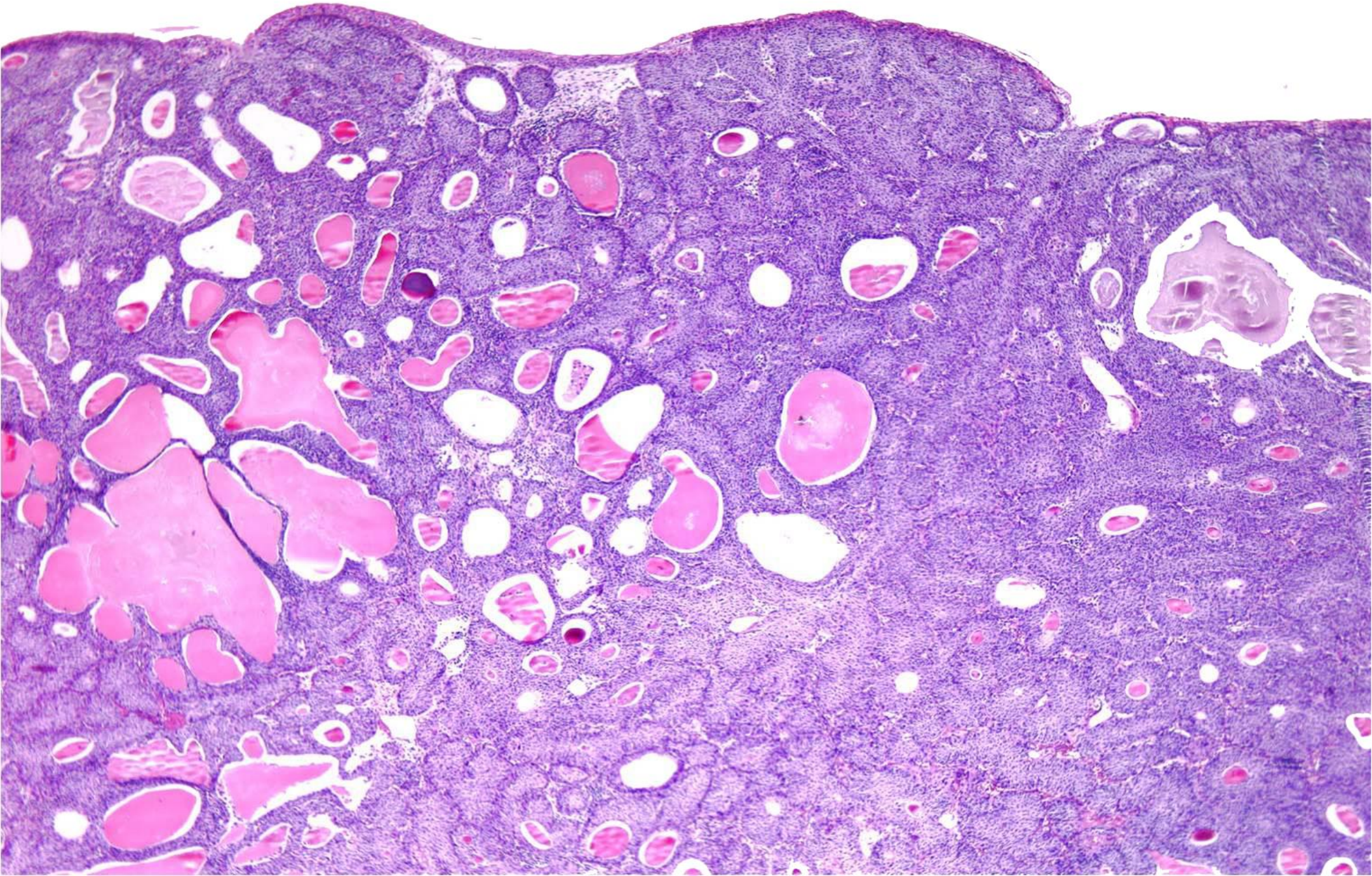
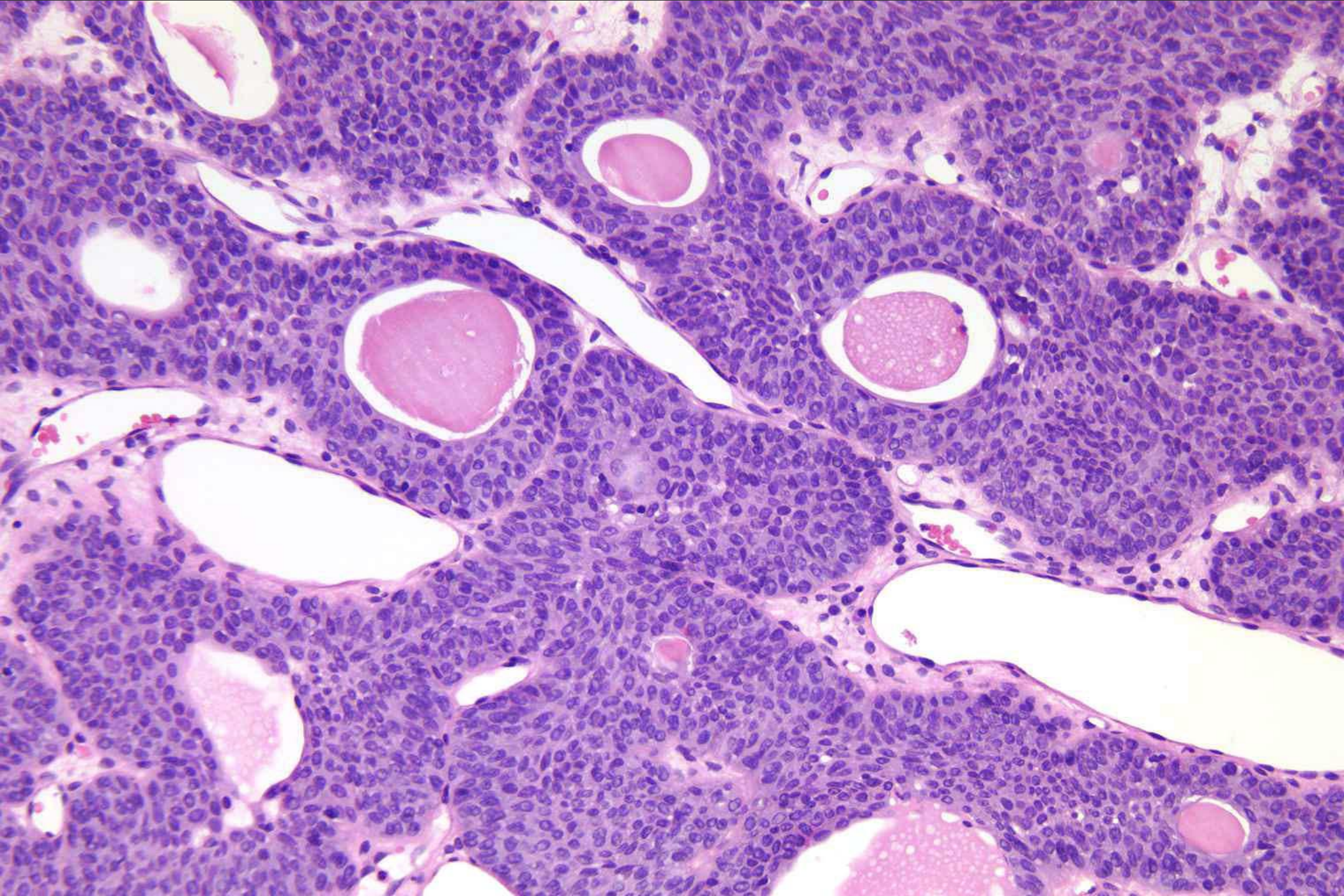
Inverted Urothelial Papilloma

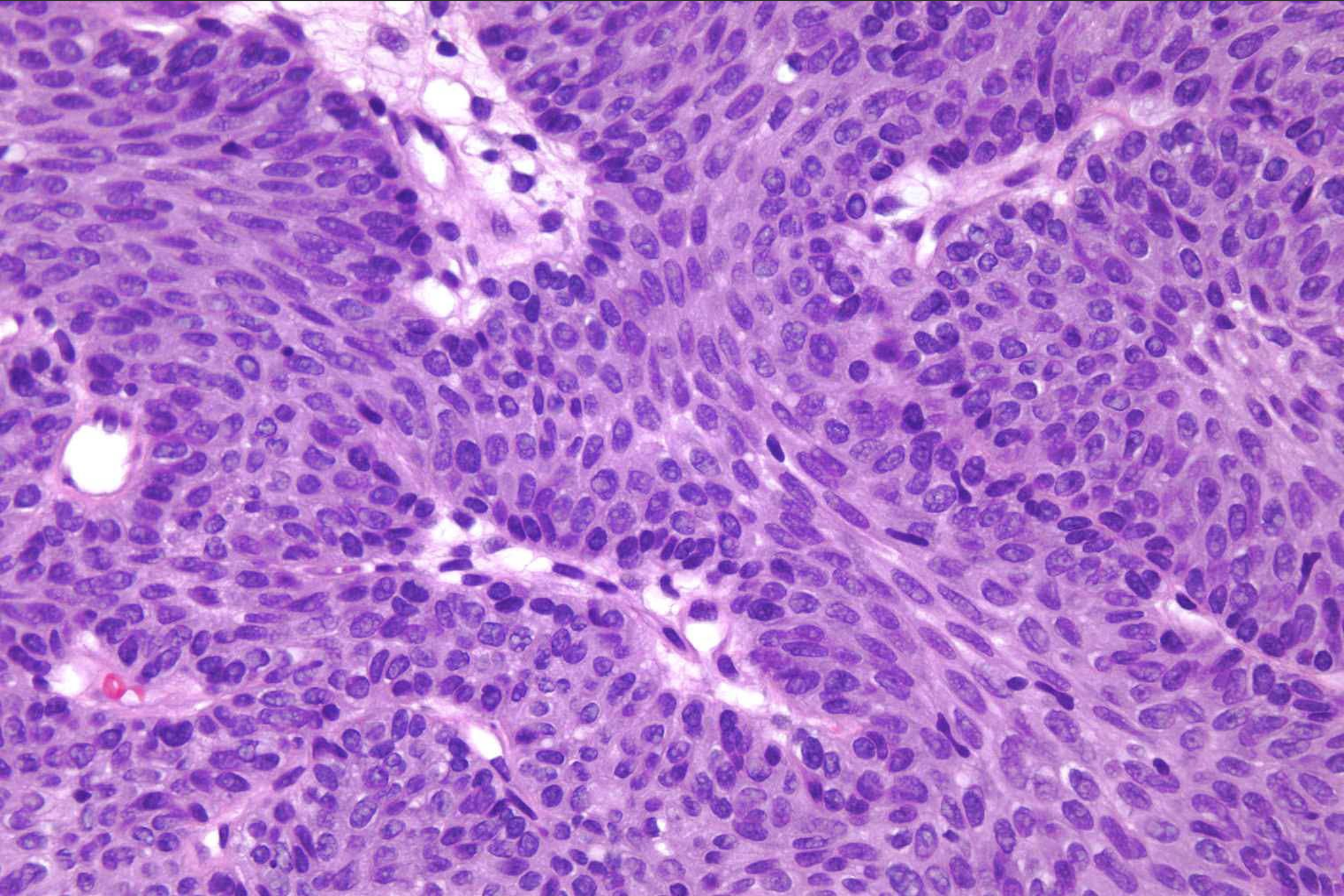
- **Most commonly seen at trigone, yet may be anywhere urothelium present.**
- **Usually solitary (3% multiple).**
- **Polypoid or sessile with smooth surface**
- **Wide size range**
- **Not related to increased risk of subsequent urothelial carcinoma**

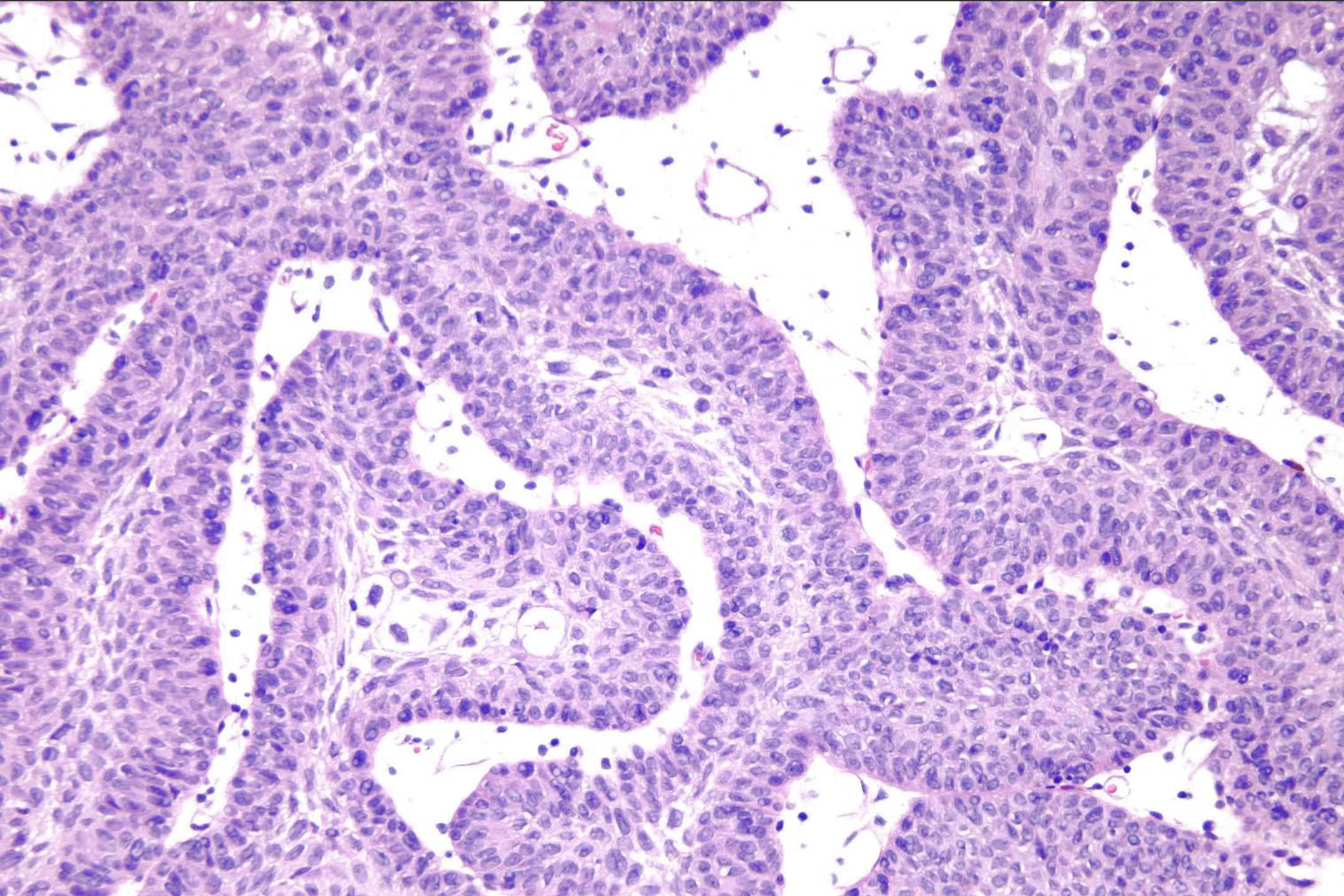


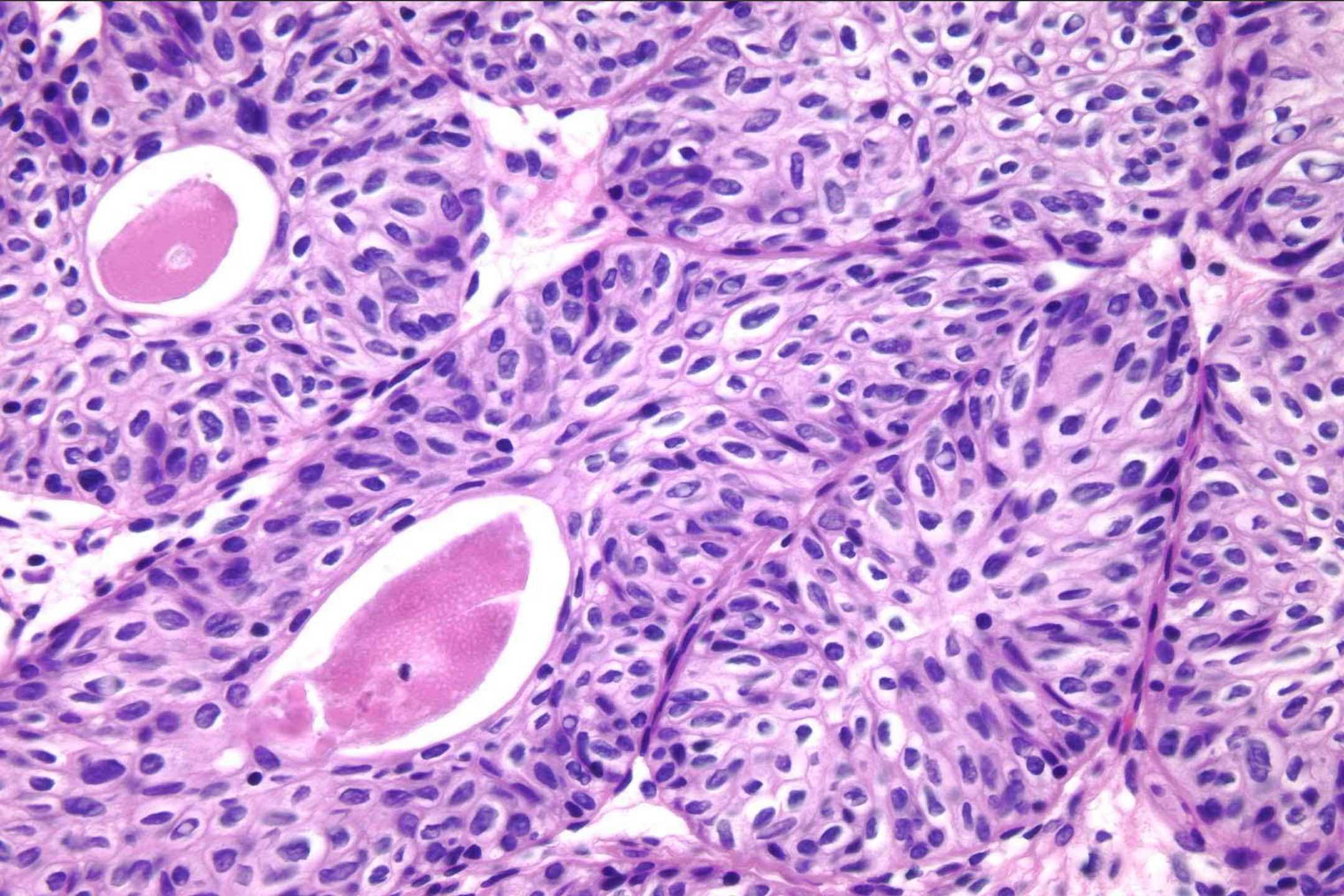


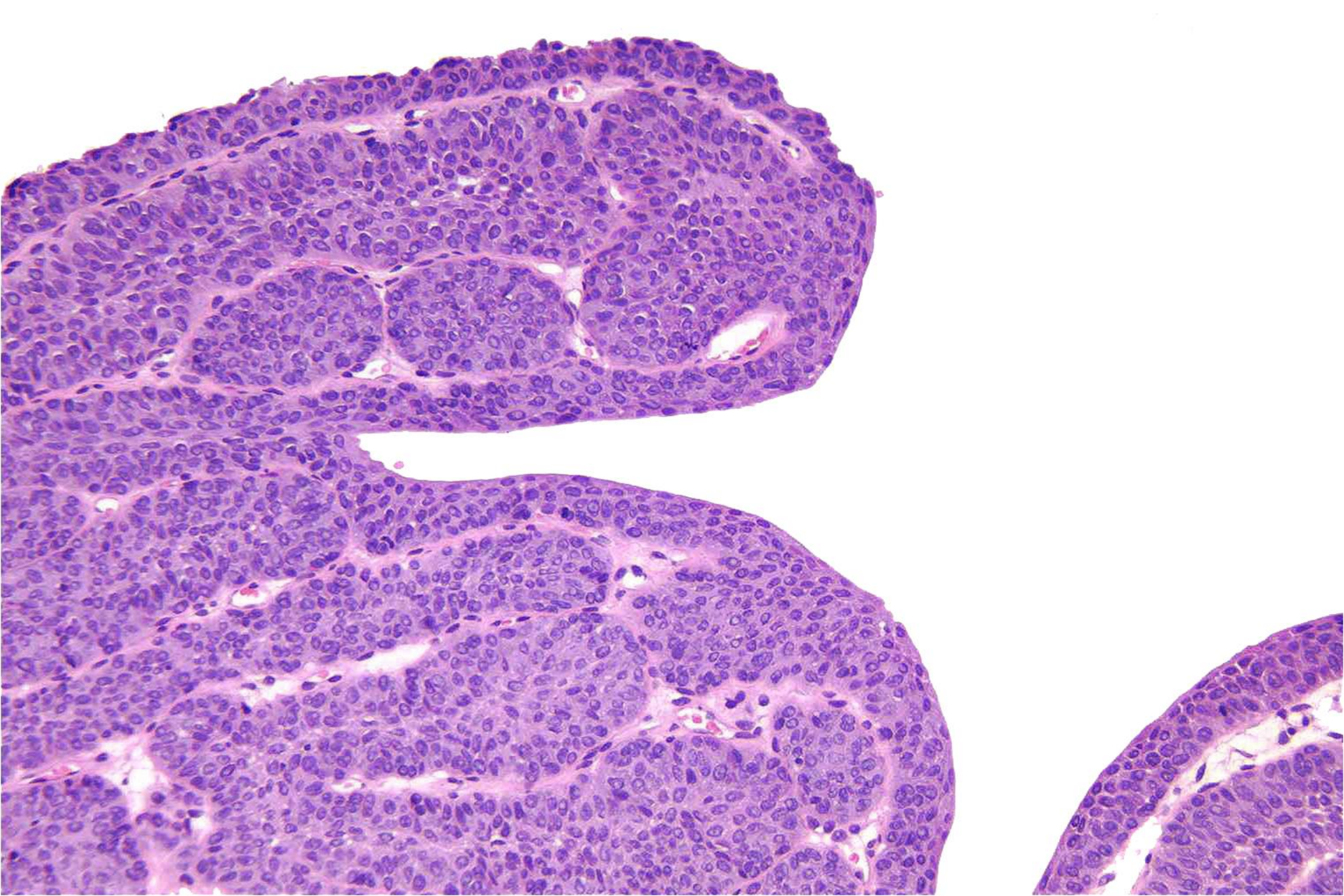


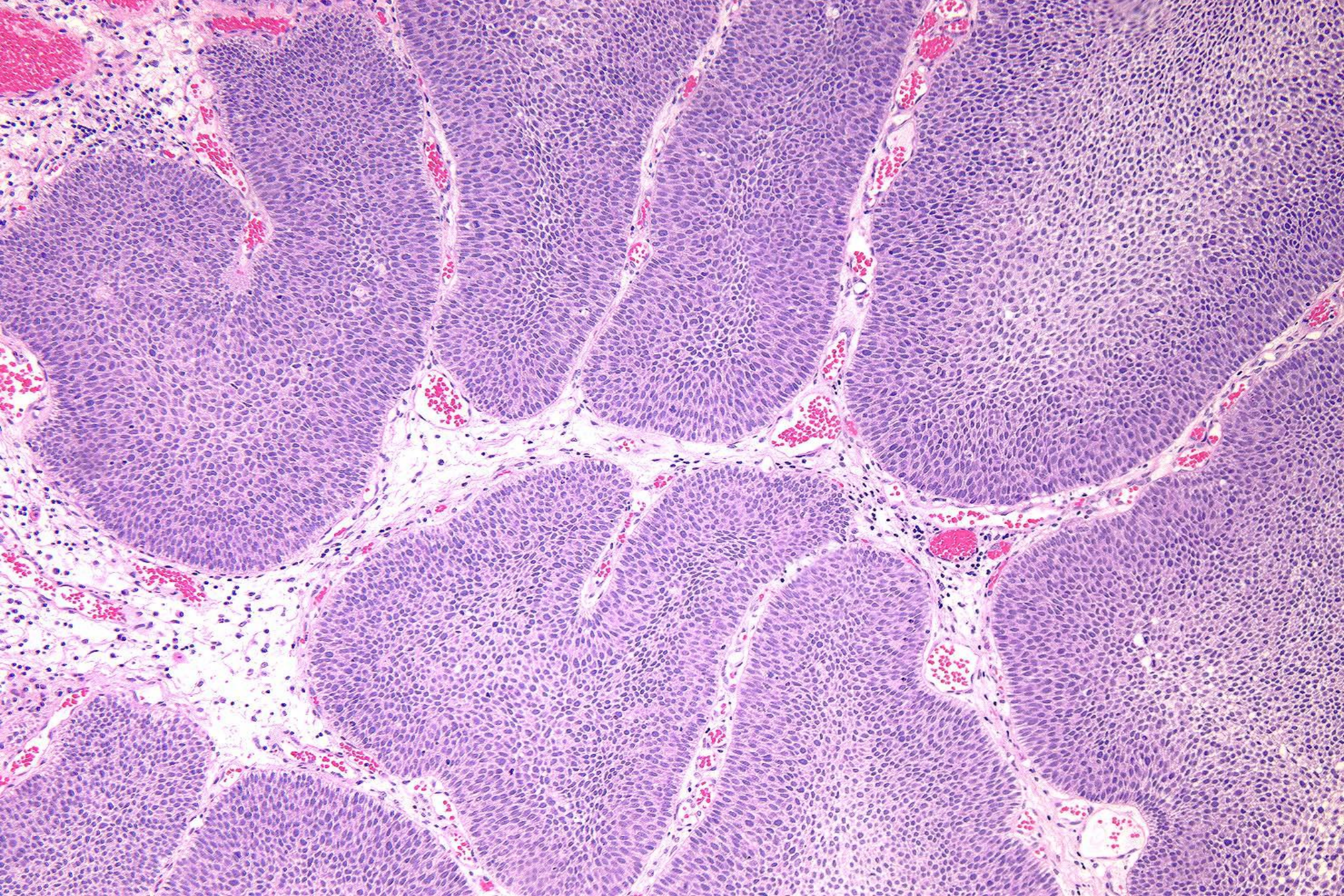


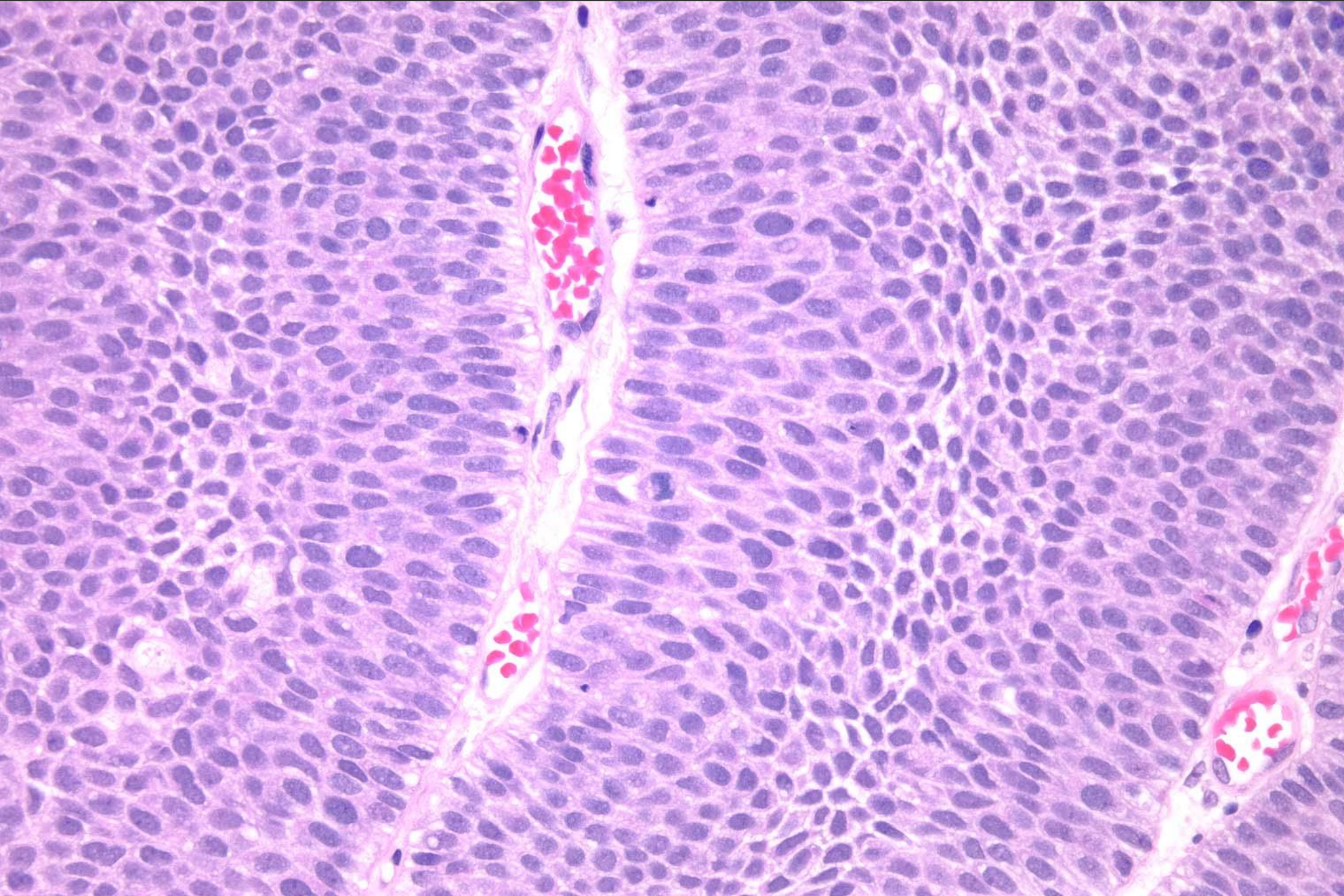


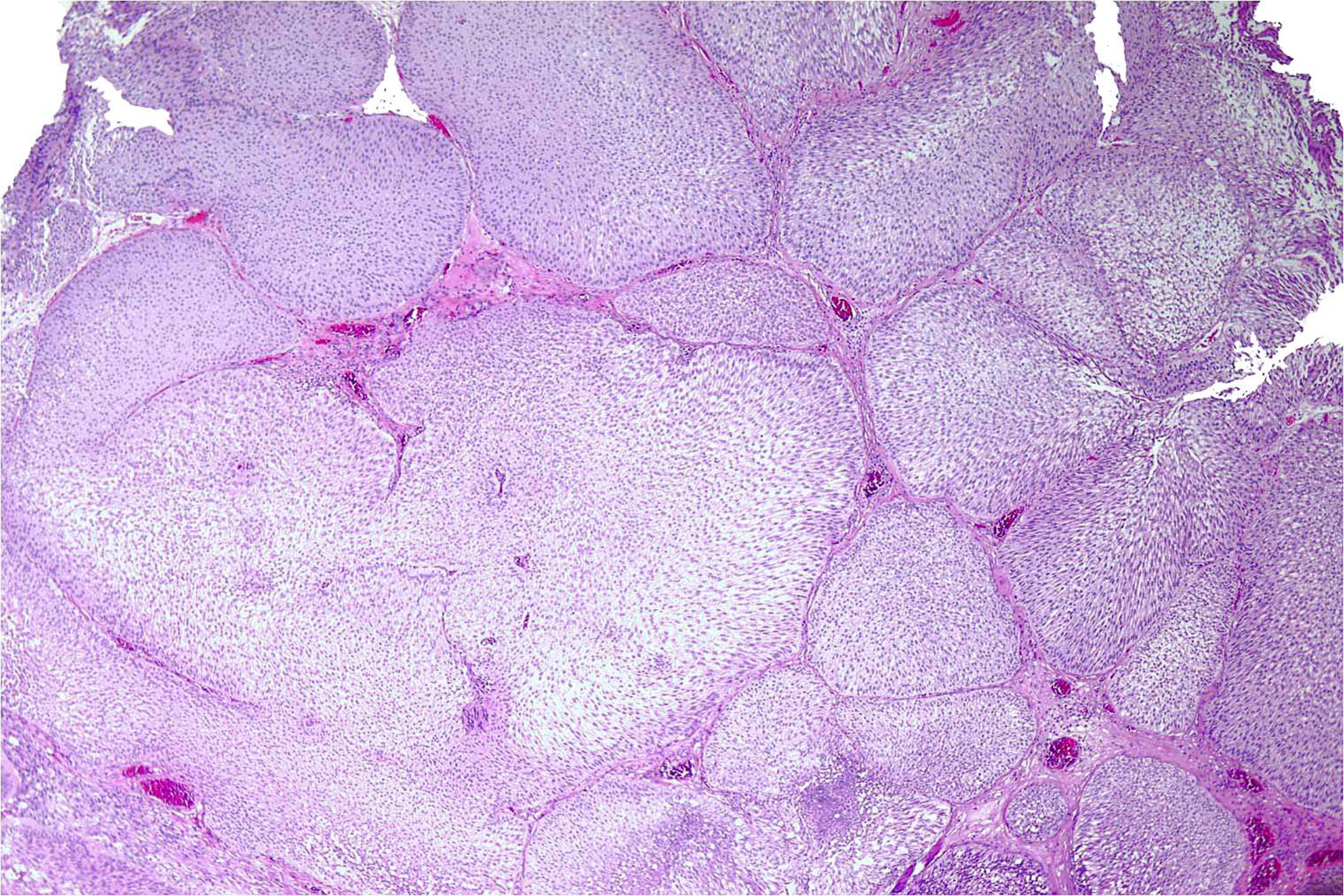


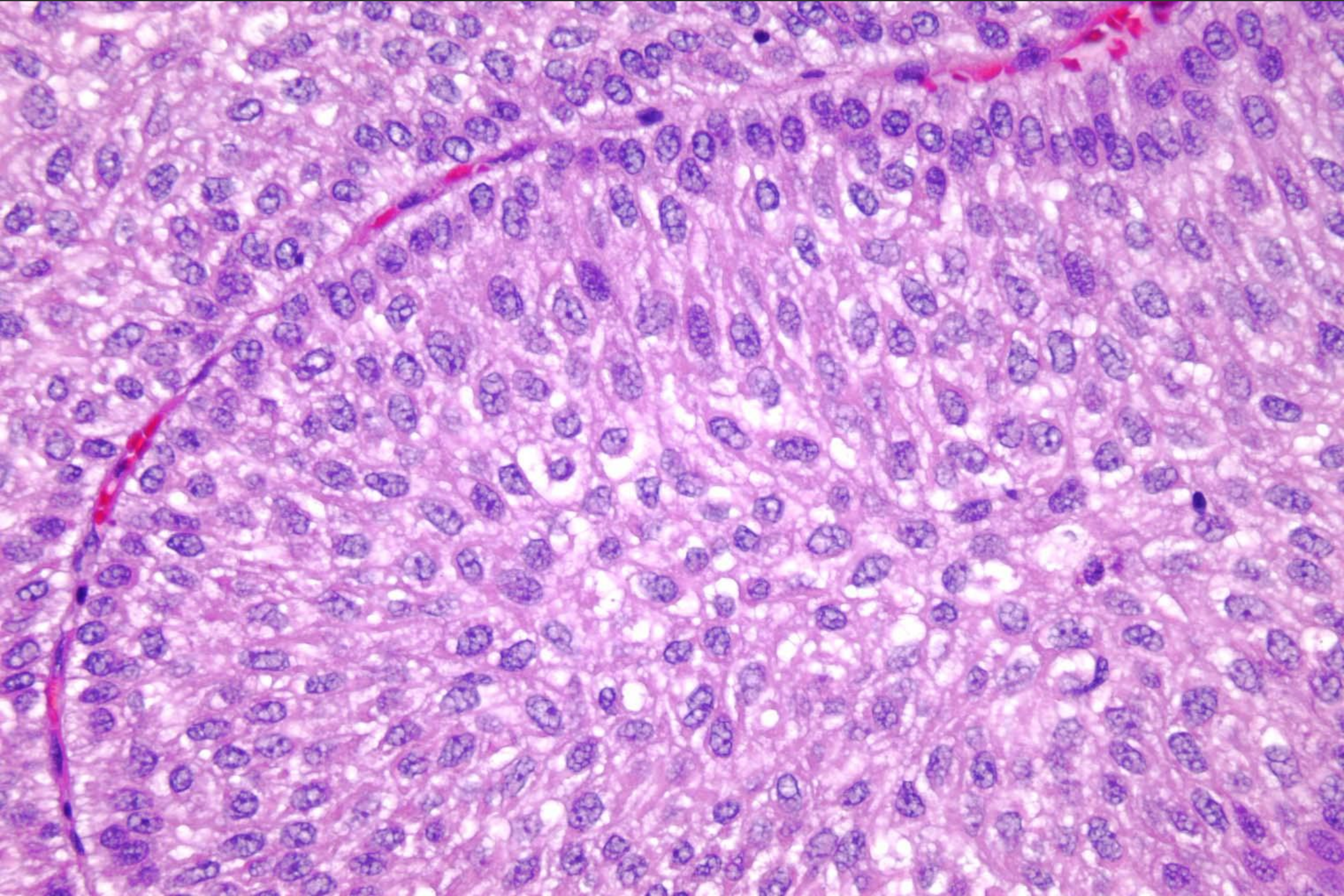












Comparison to Urothelial Carcinoma

- Lacks cytological atypia
- Mitotic activity limited to basal cell layer
- Lacks inflammation and reactive stroma
- Squamous metaplasia lacks keratin formation
- Lacks muscularis propria invasion

Nested Variant
Urothelial Carcinoma

- **Murphy WM, Deana DG. The nested variant of transitional cell carcinoma: a neoplasm resembling proliferation of Brunn's nests. *Mod Pathol* 1992;5:240-3**

Clinical Features

- **Older male patients**
- **To date, nested variant of urothelial carcinoma has been reported in only 4 women**
- **Typically present with hematuria**

Location

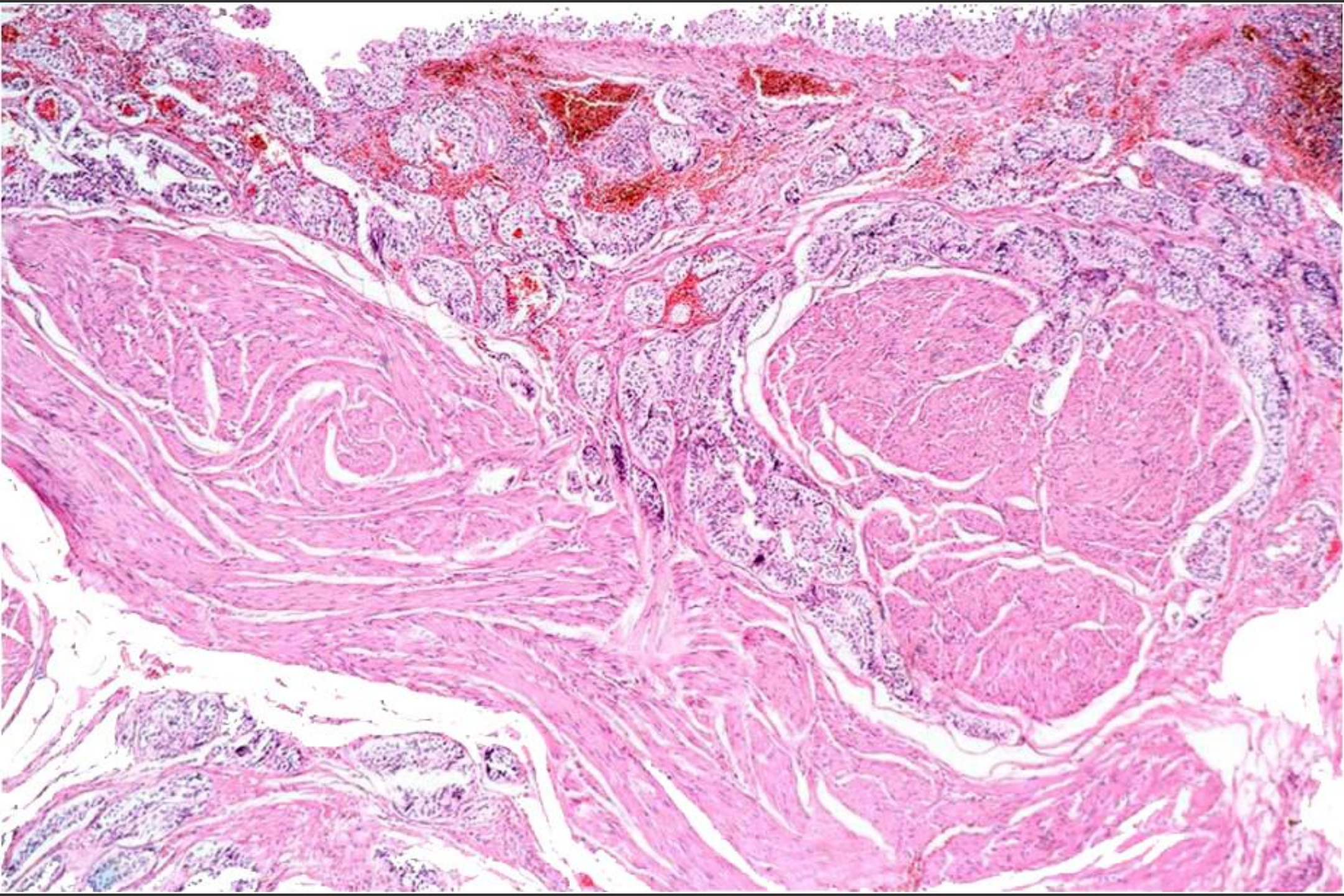
- **Anywhere in the bladder**
- **Only two cases of nested variant of urothelial carcinoma in the ureter**

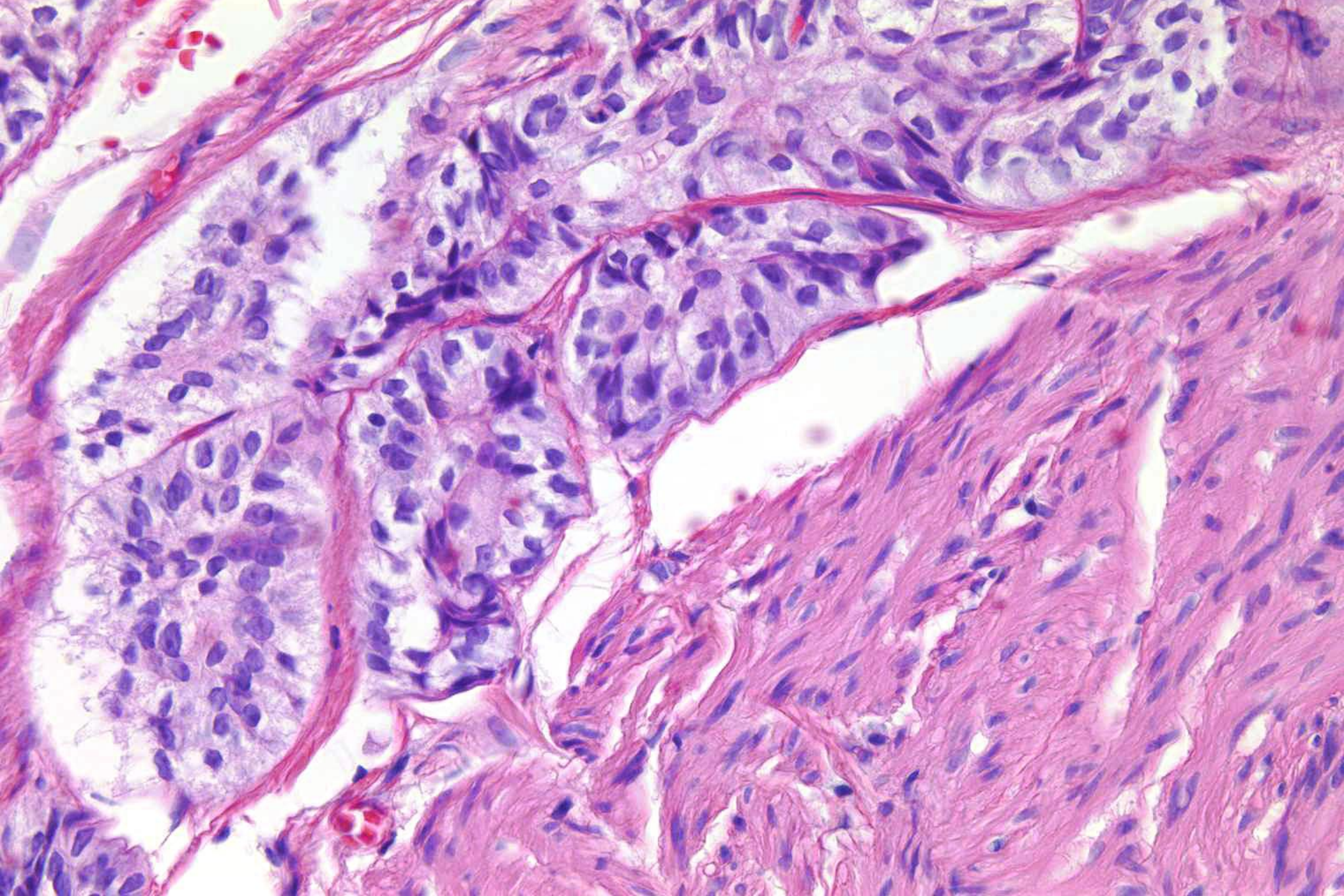
Histology – Difficult to Diagnose as Cancer

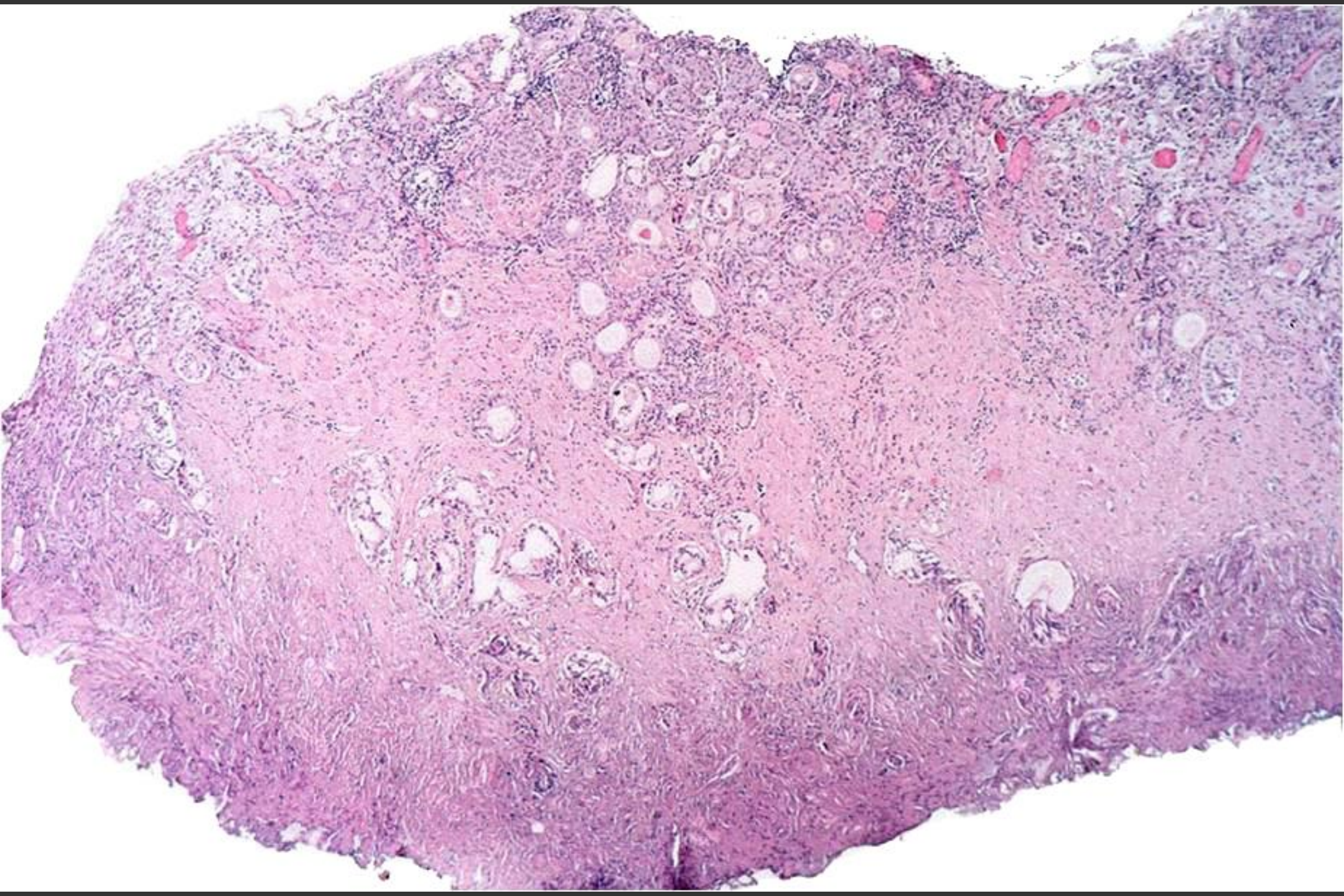
- Cytologically, may show very uniform, bland cells with only focal moderate atypia
- Nucleoli may be prominent and mitoses may be seen, but are usually not numerous
- Lymphatic invasion uncommon
- Overlying urothelium may be normal in appearance

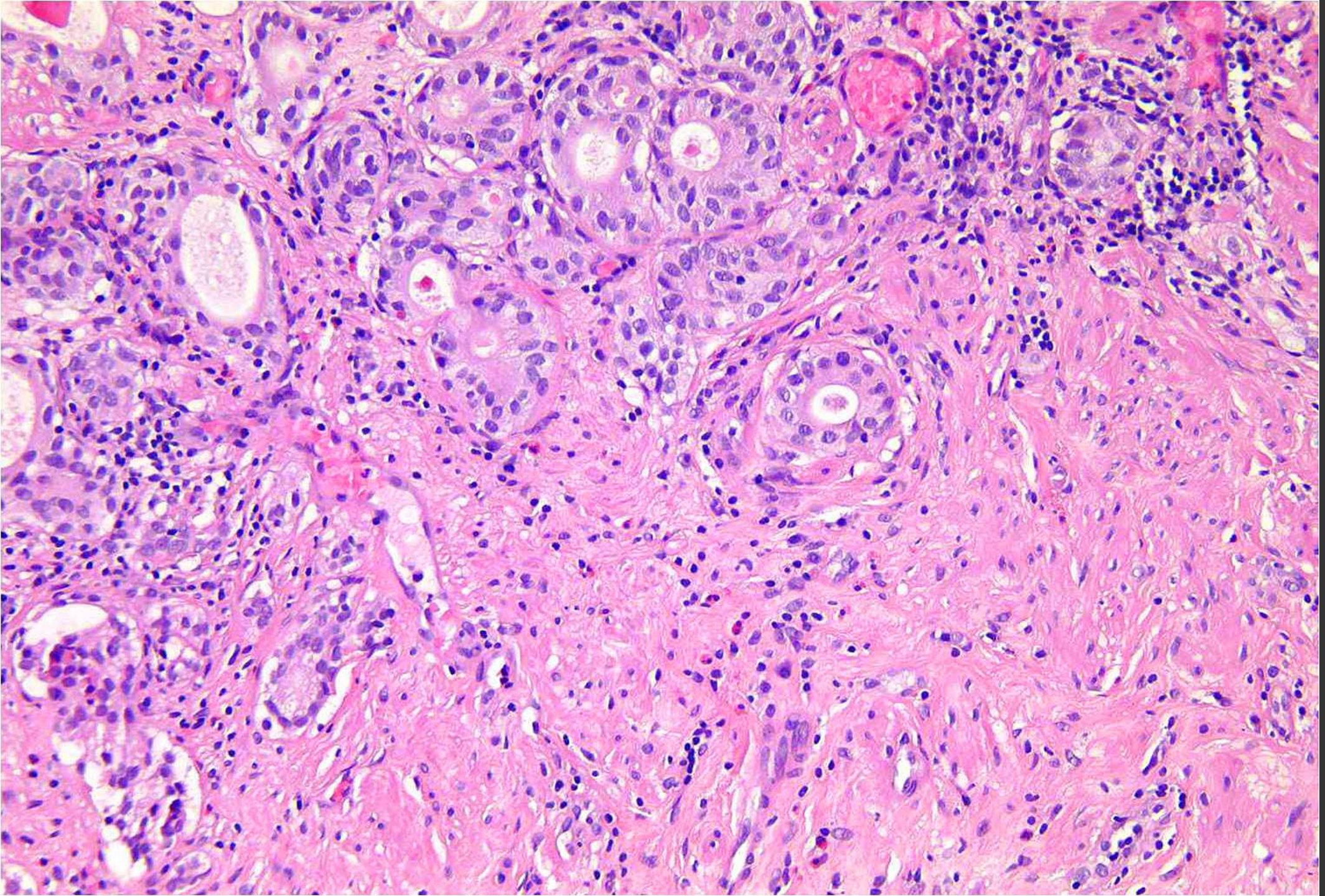
Prognosis

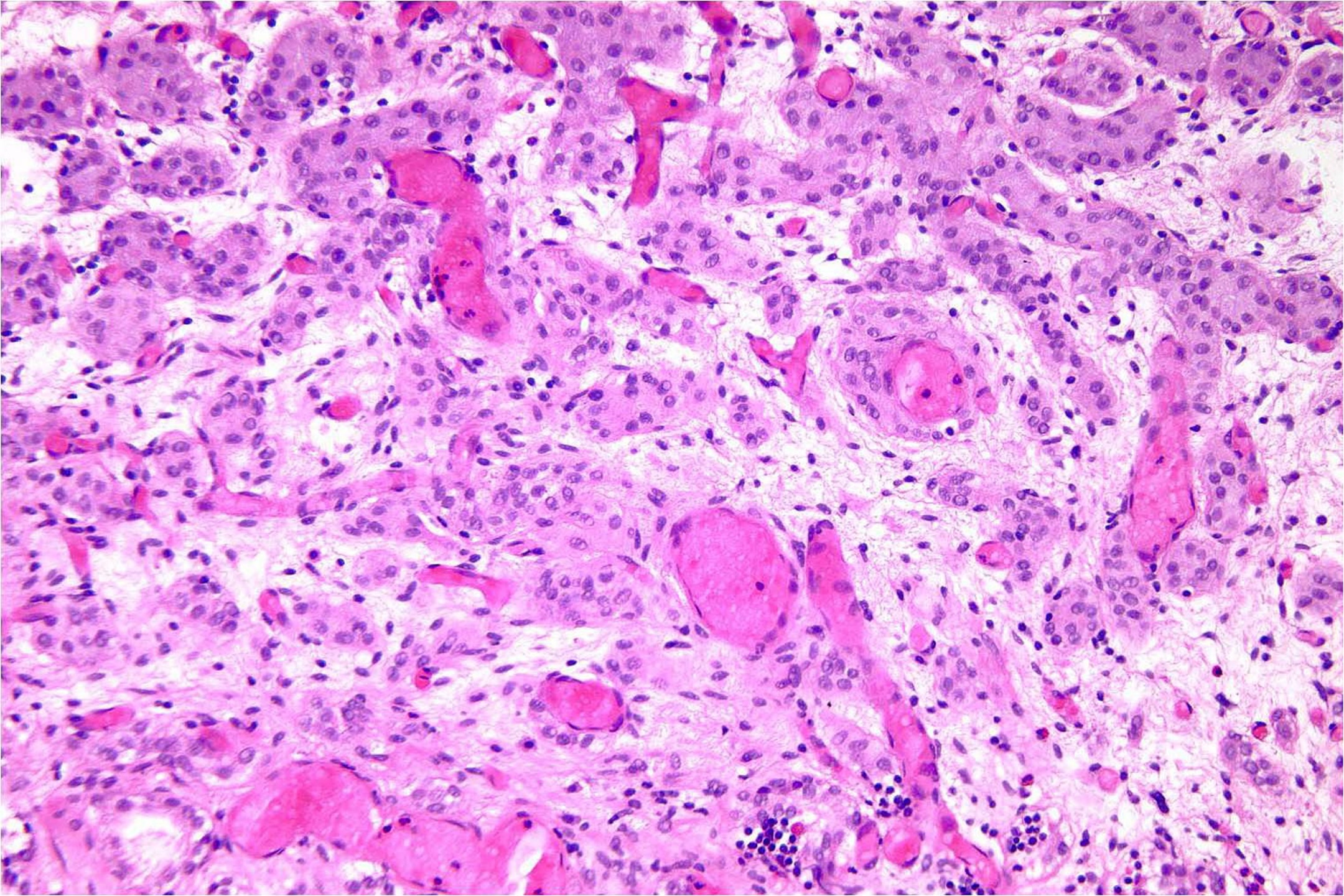
- **Clinical course generally aggressive**
- **In a review of 24 cases, Drew reported 55-60% of the tumors to show aggressive behavior, with mortality rates similar to high grade conventional urothelial carcinoma**
- **The same study showed only 3/12 nested variant of urothelial carcinoma patients to be alive without disease at an average of 16 months follow-up**

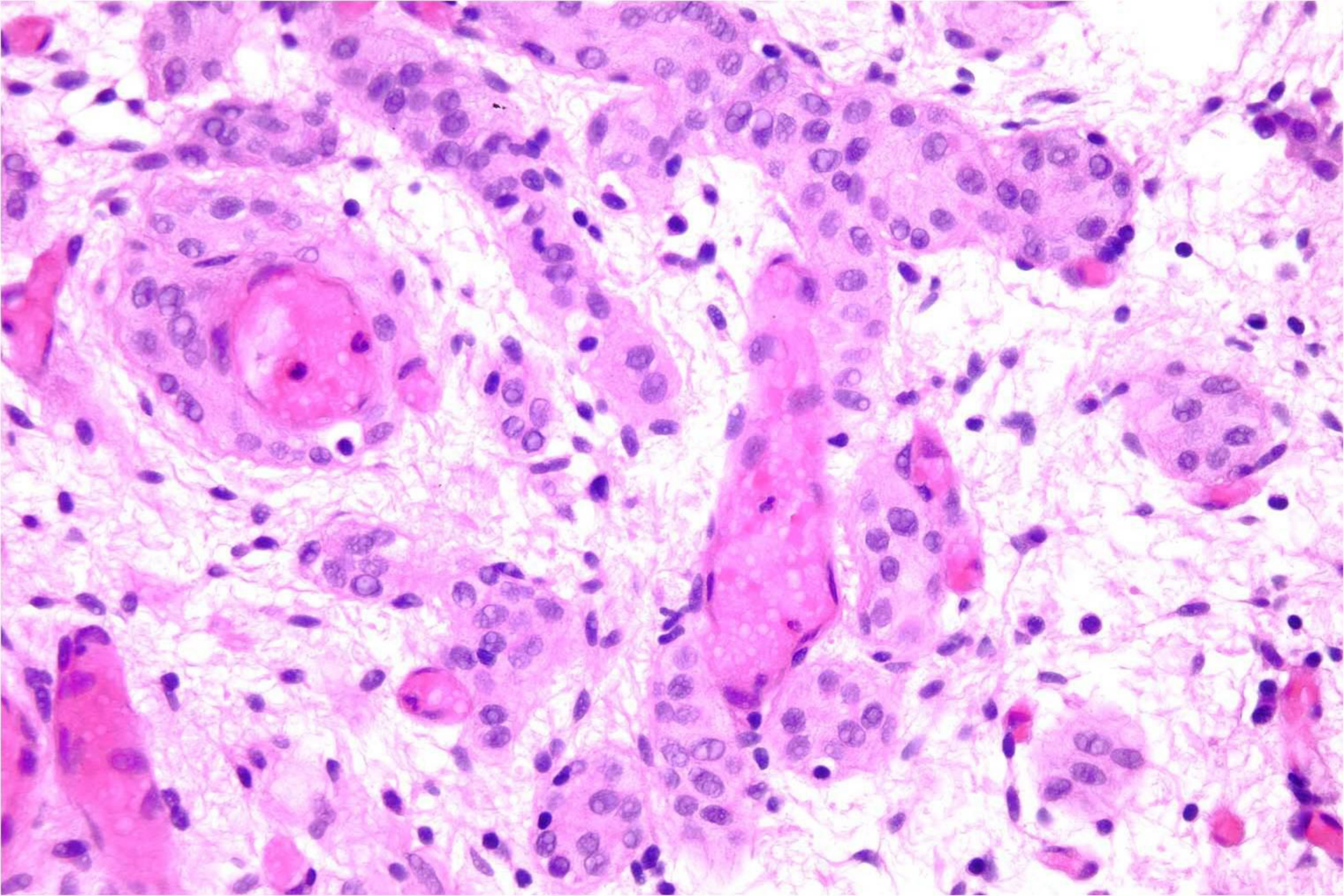


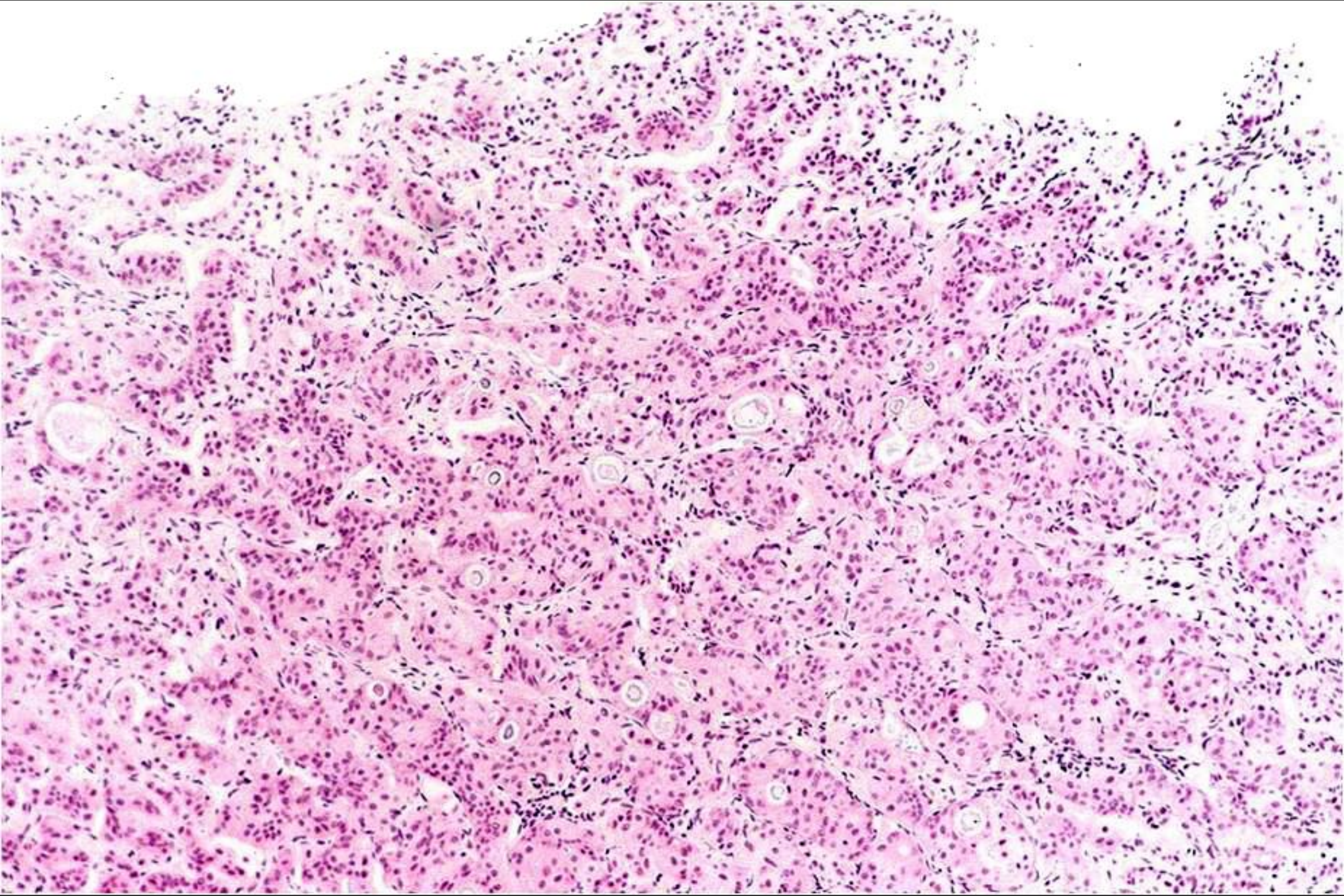


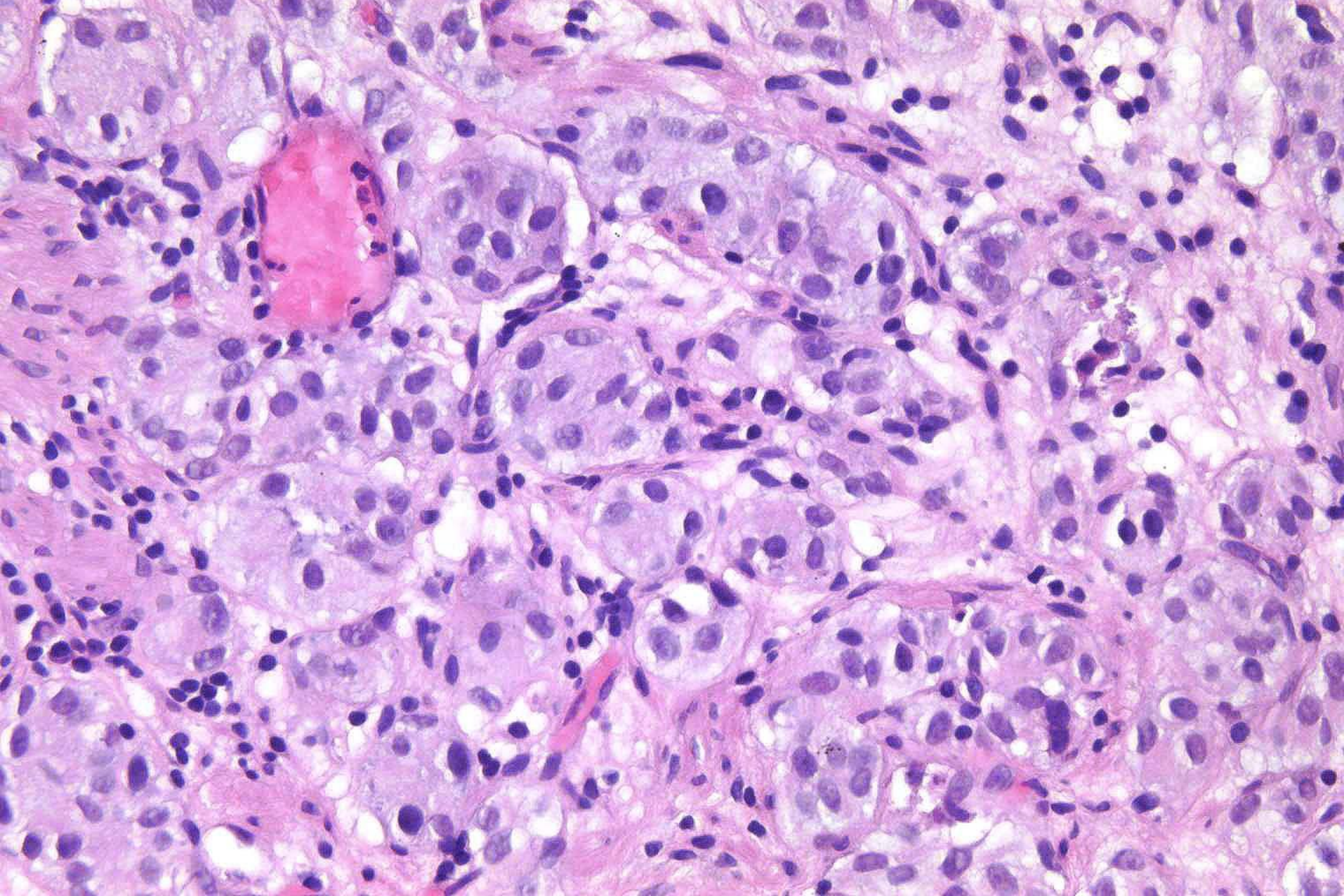


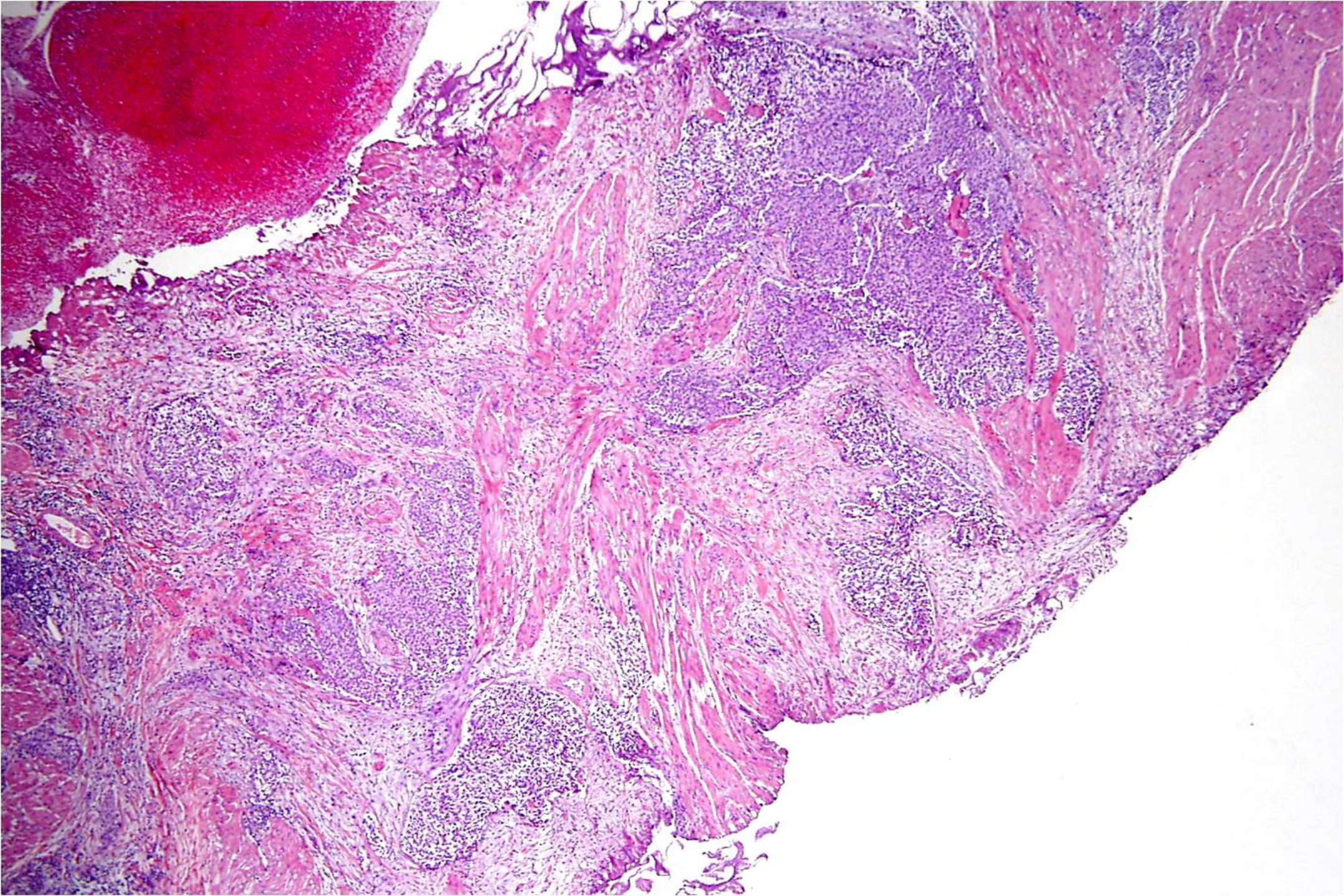


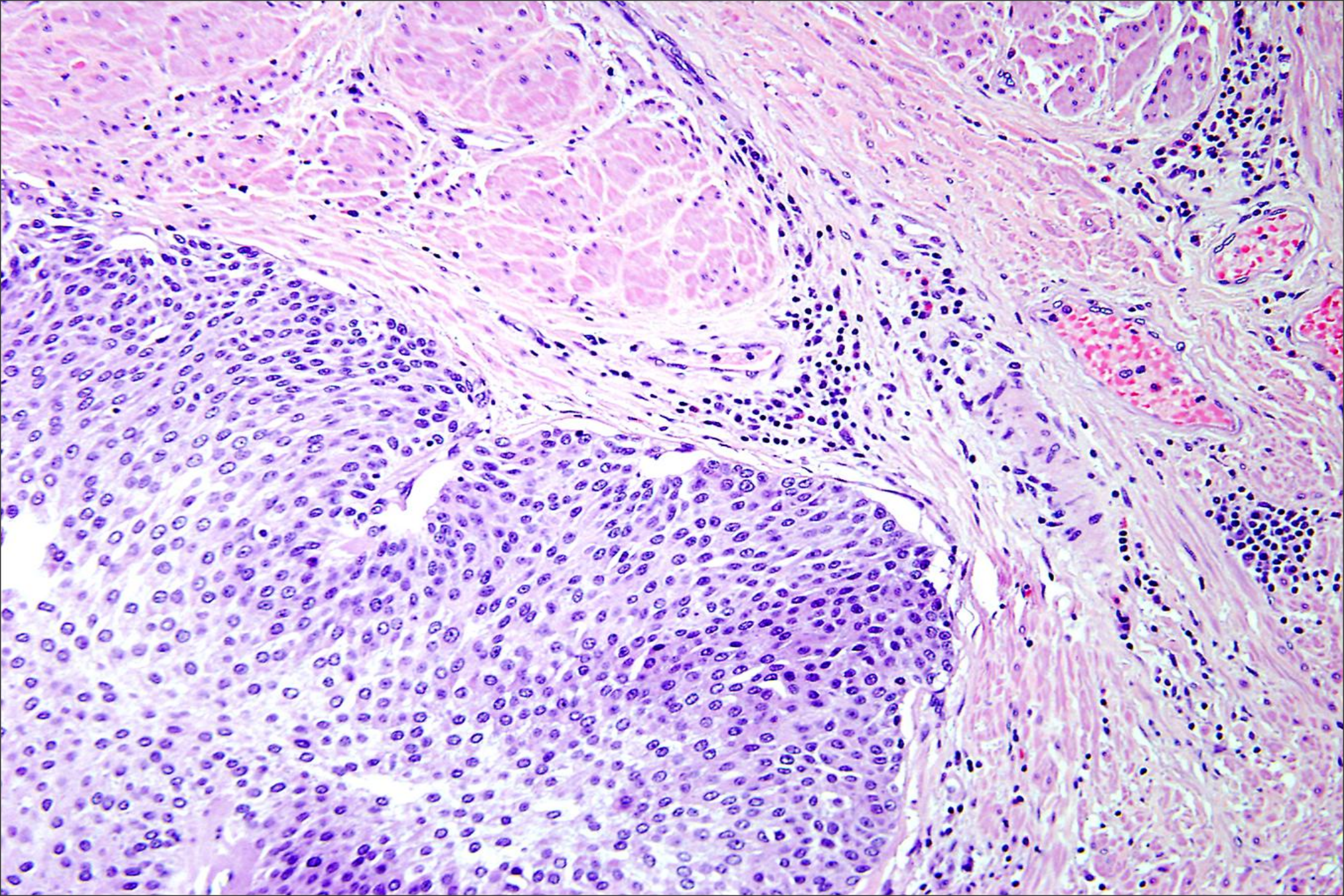


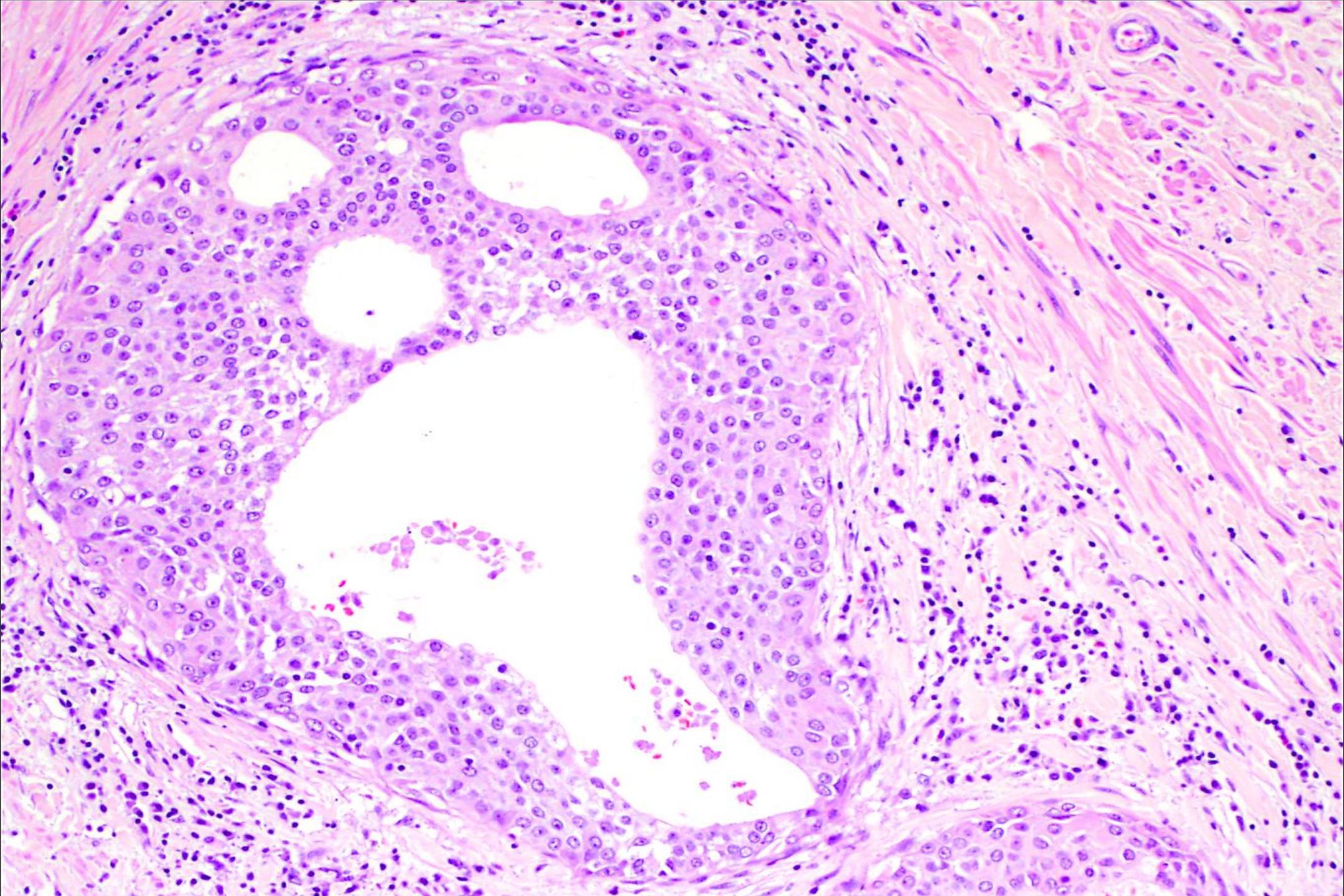


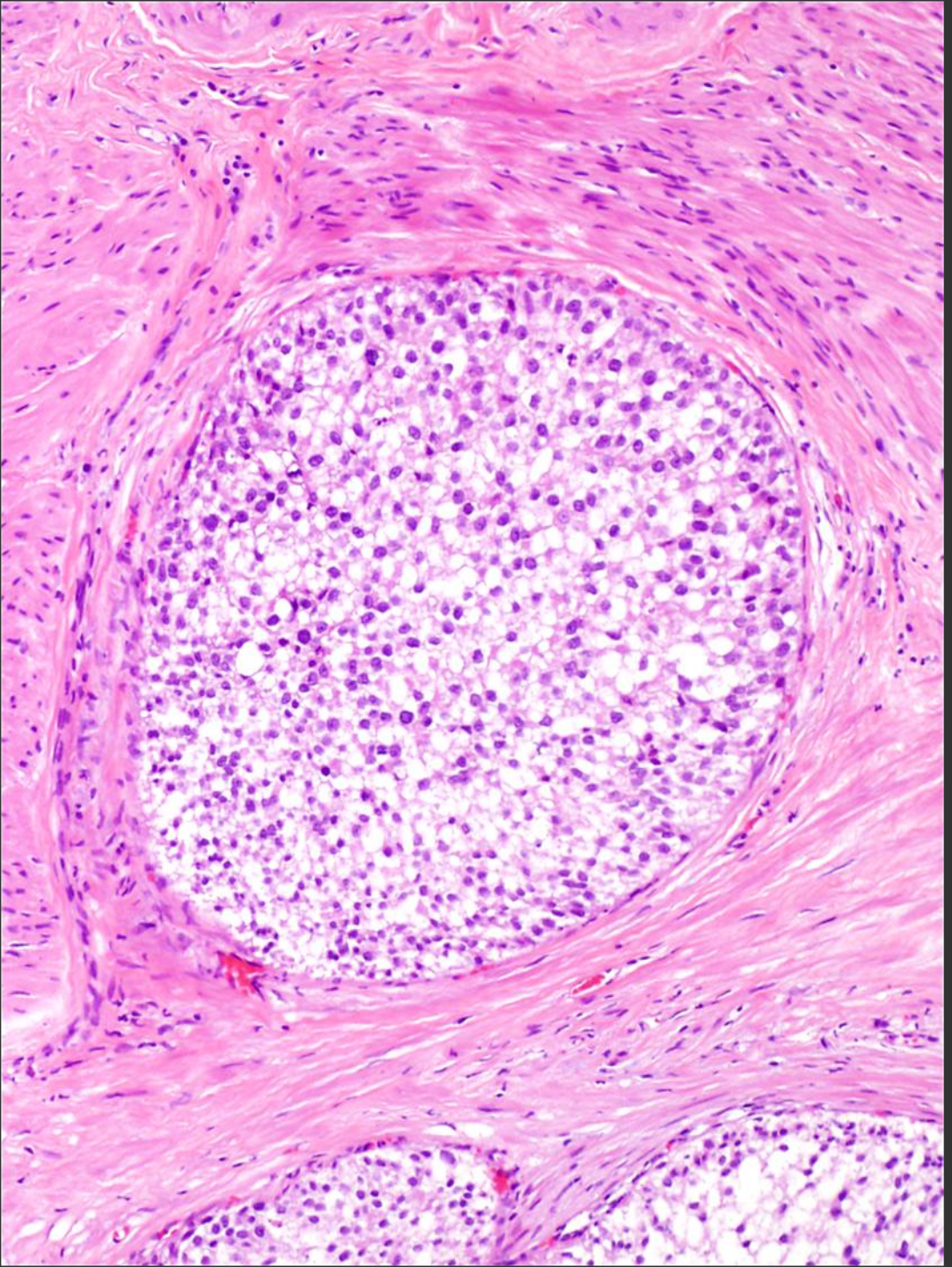
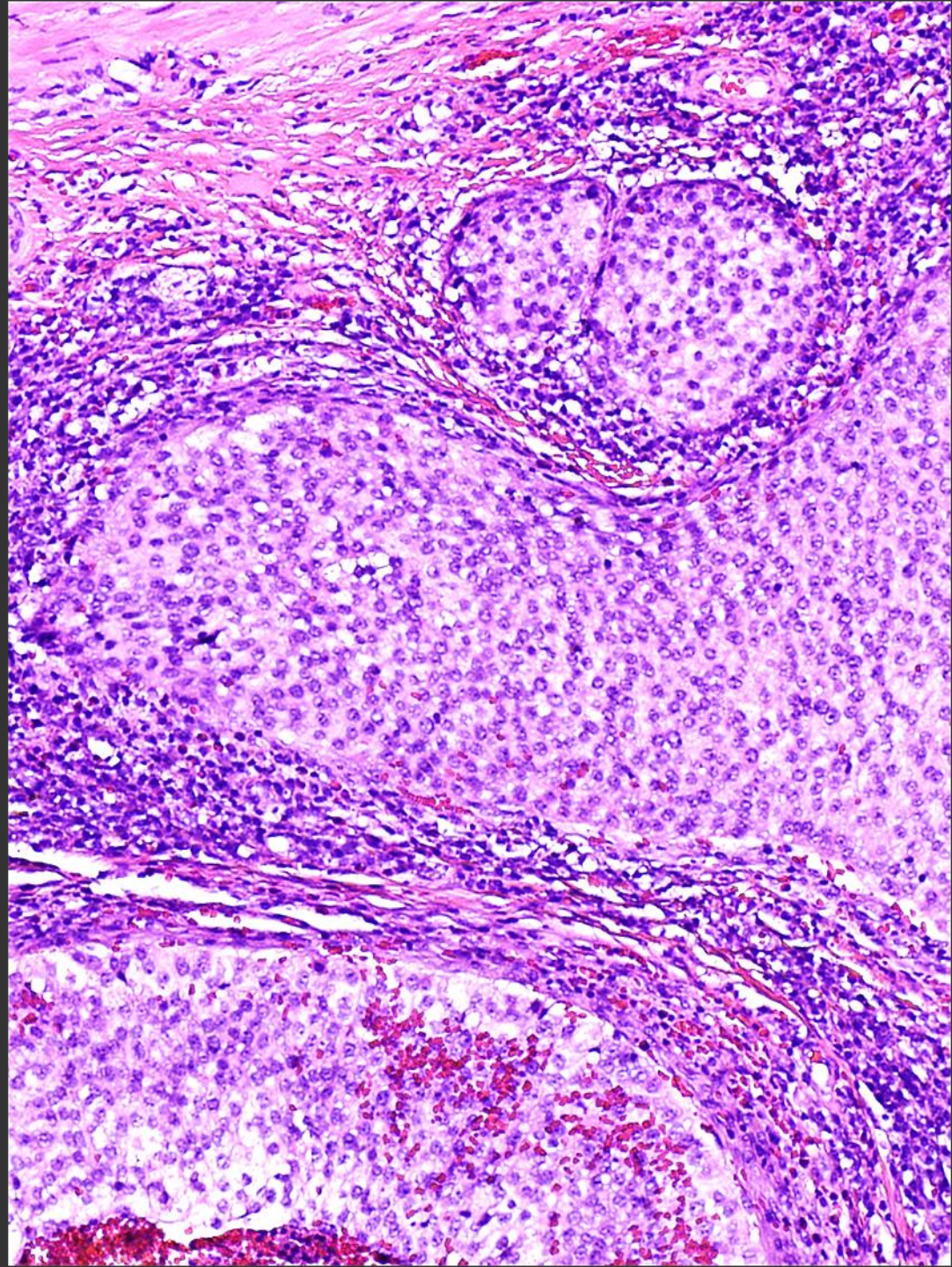










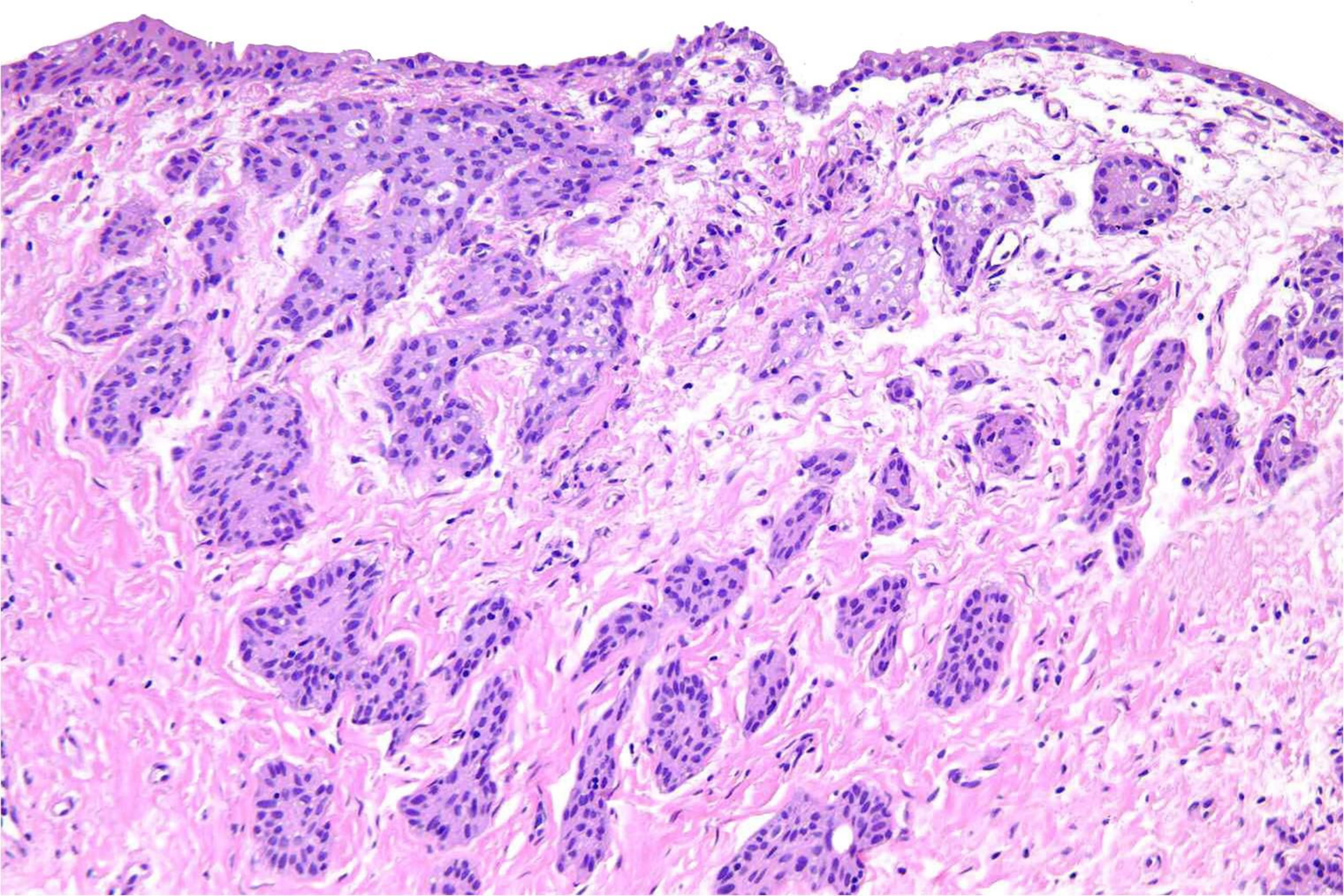



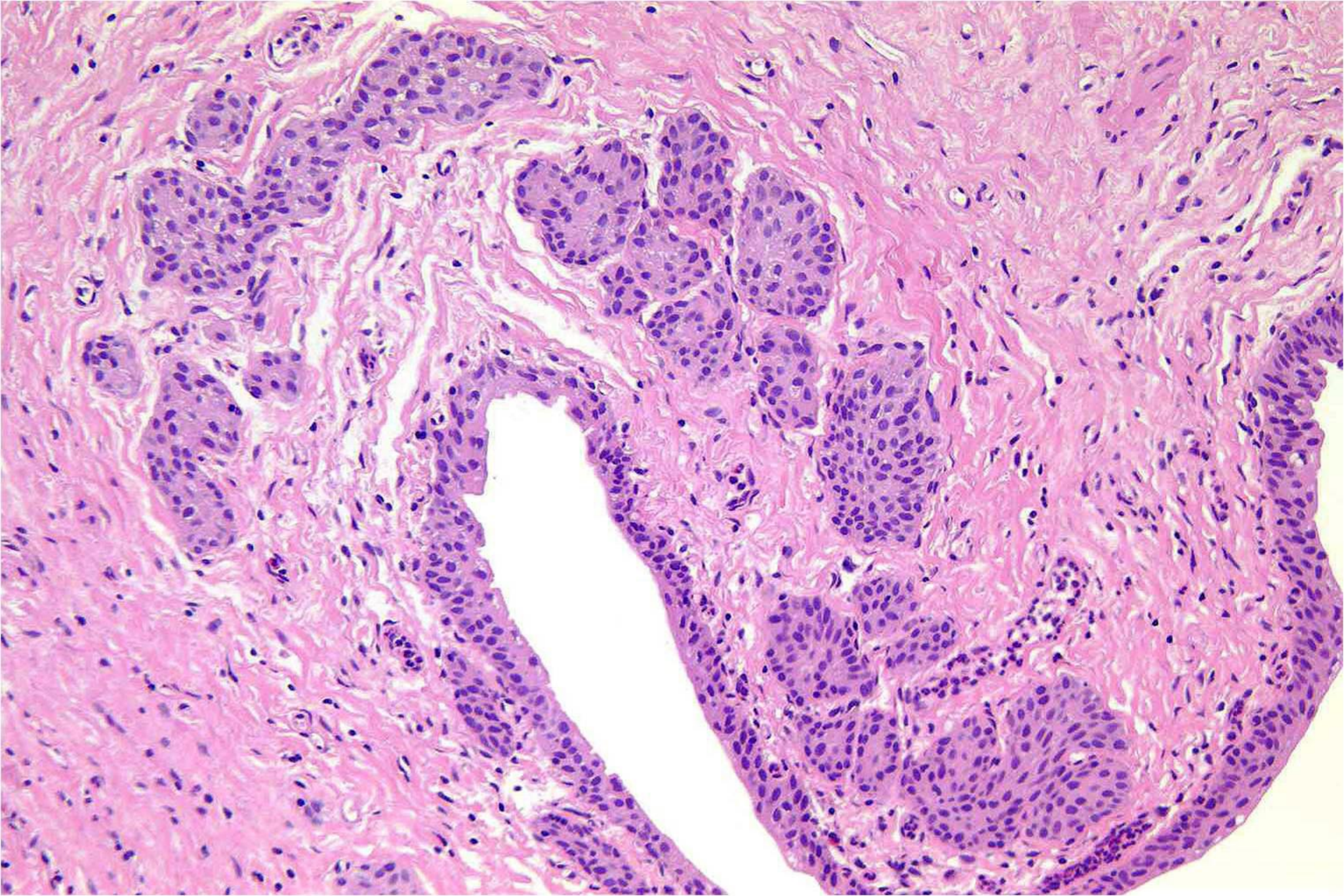
Architecture - Nests

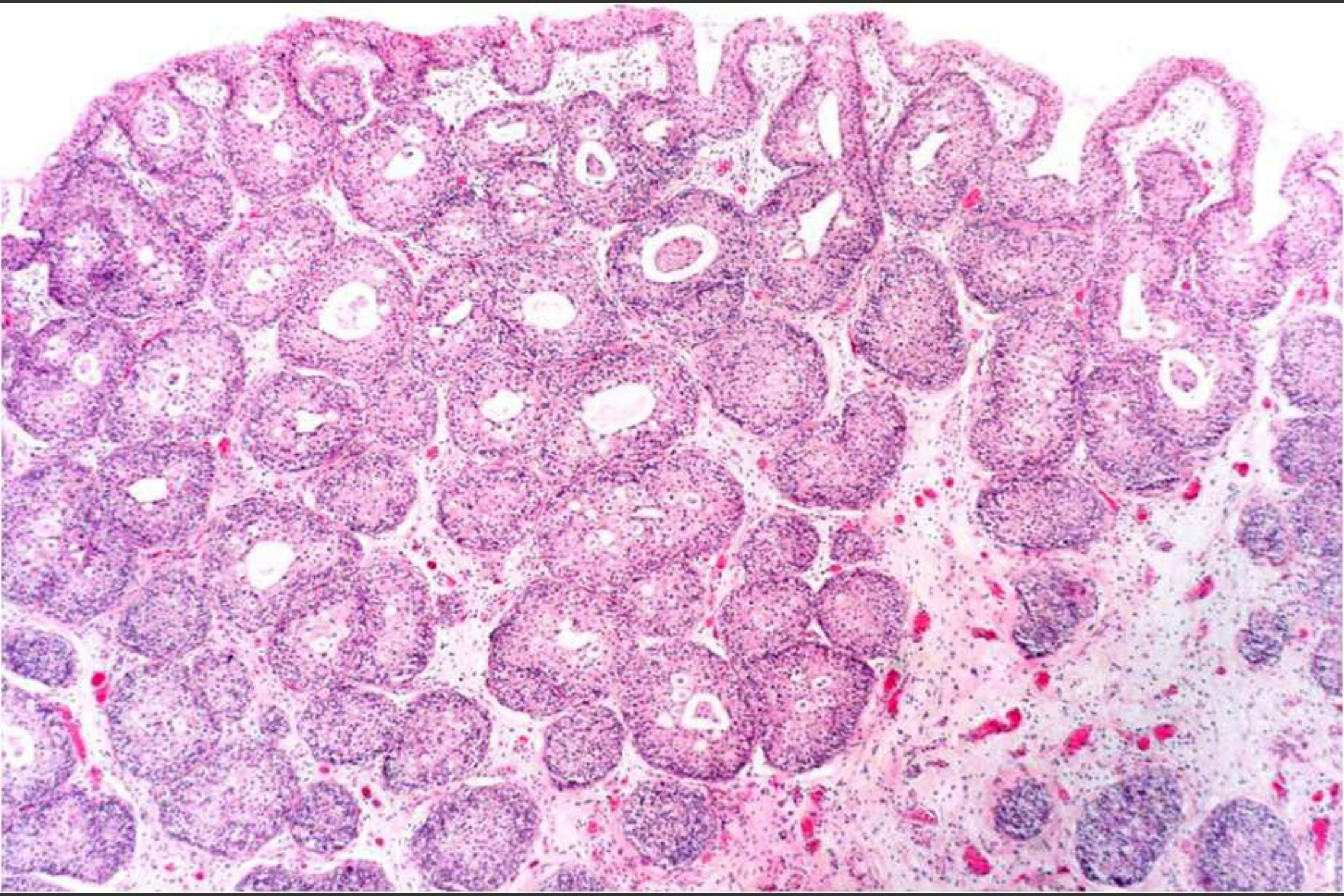
Bladder VBN	Ureter VBN	Nested TCC
Larger, more uniform with even spacing	Small crowded nests with linear or lobular arrangement	Small crowded nests with variable shape and spacing
Even base - LP	Even base - LP	Irregular base - MP

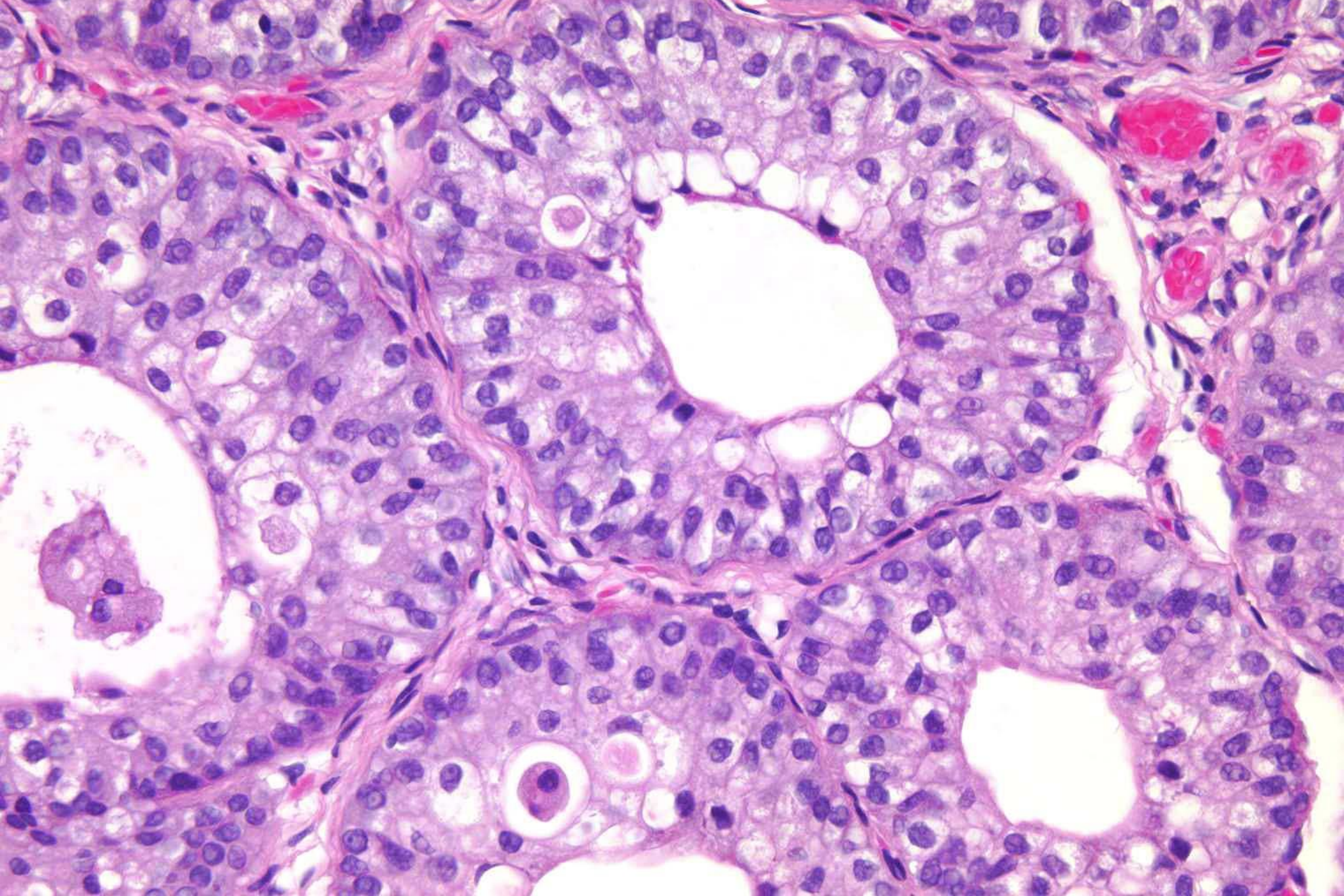
Architecture - Cysts

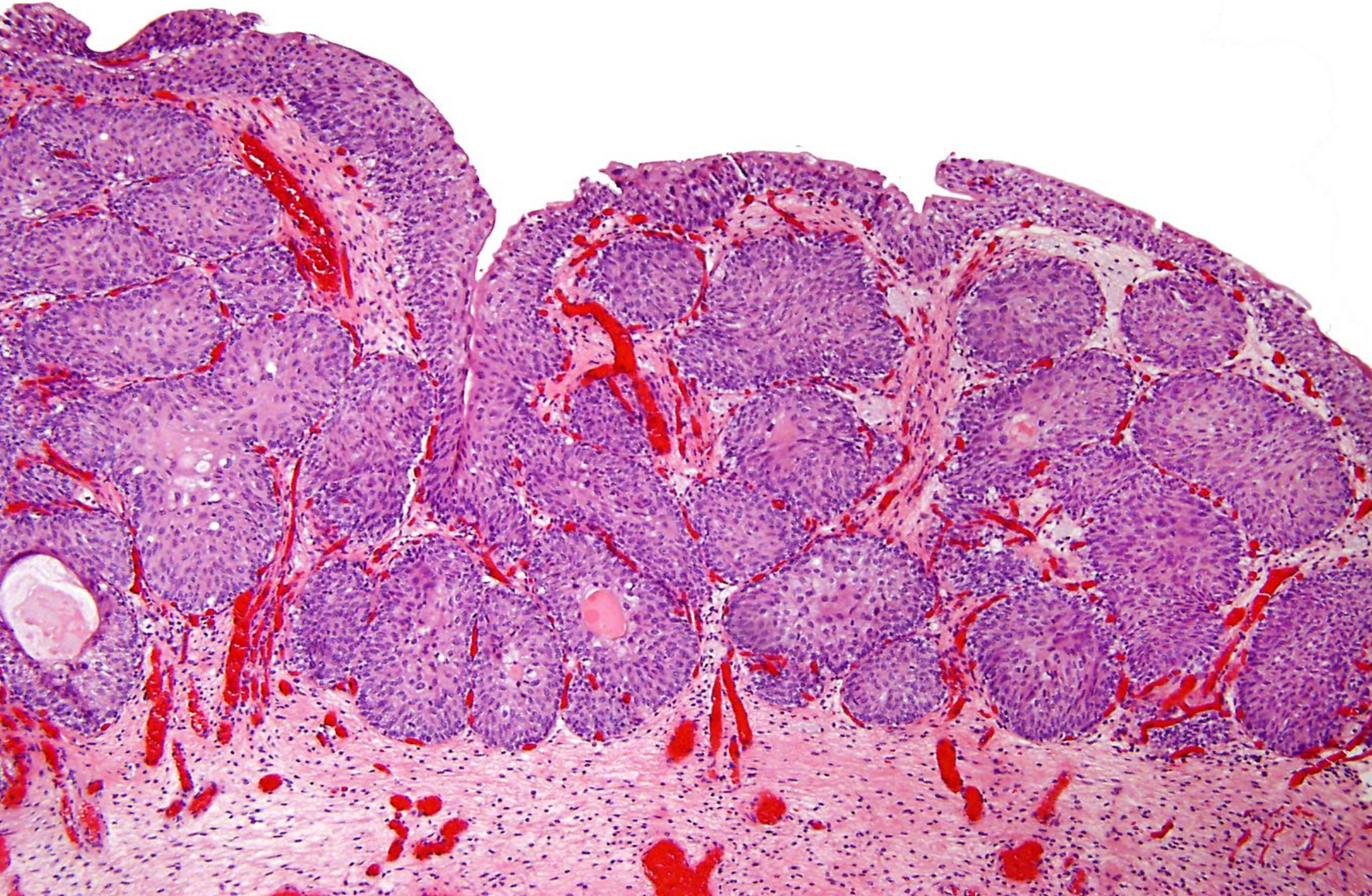
Bladder VBN	Ureter VBN	Nested TCC
Large cysts	Small cysts	Small cysts
Often involving	rare, less than	involving
70% of nests	10% of nests	20% of nests

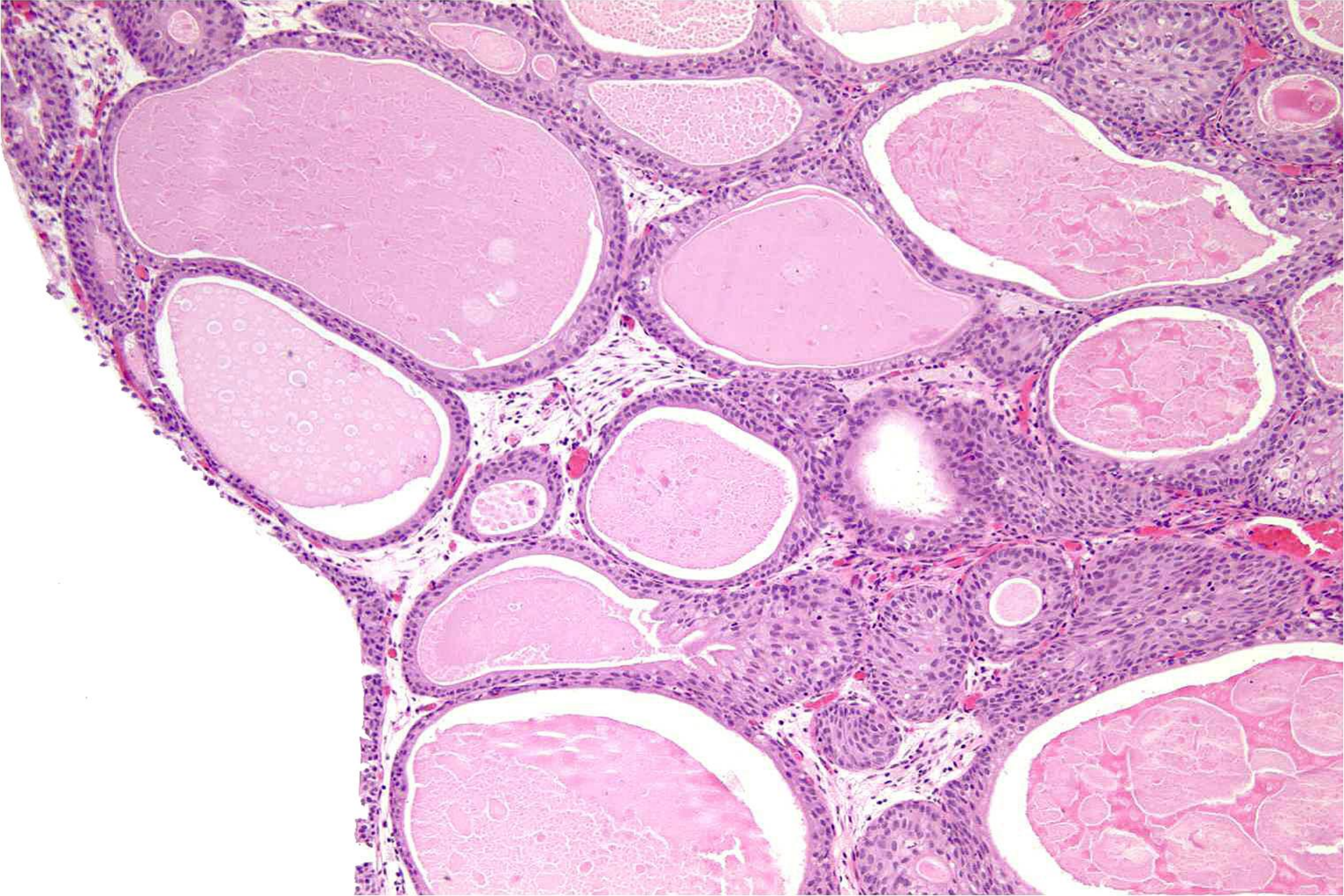












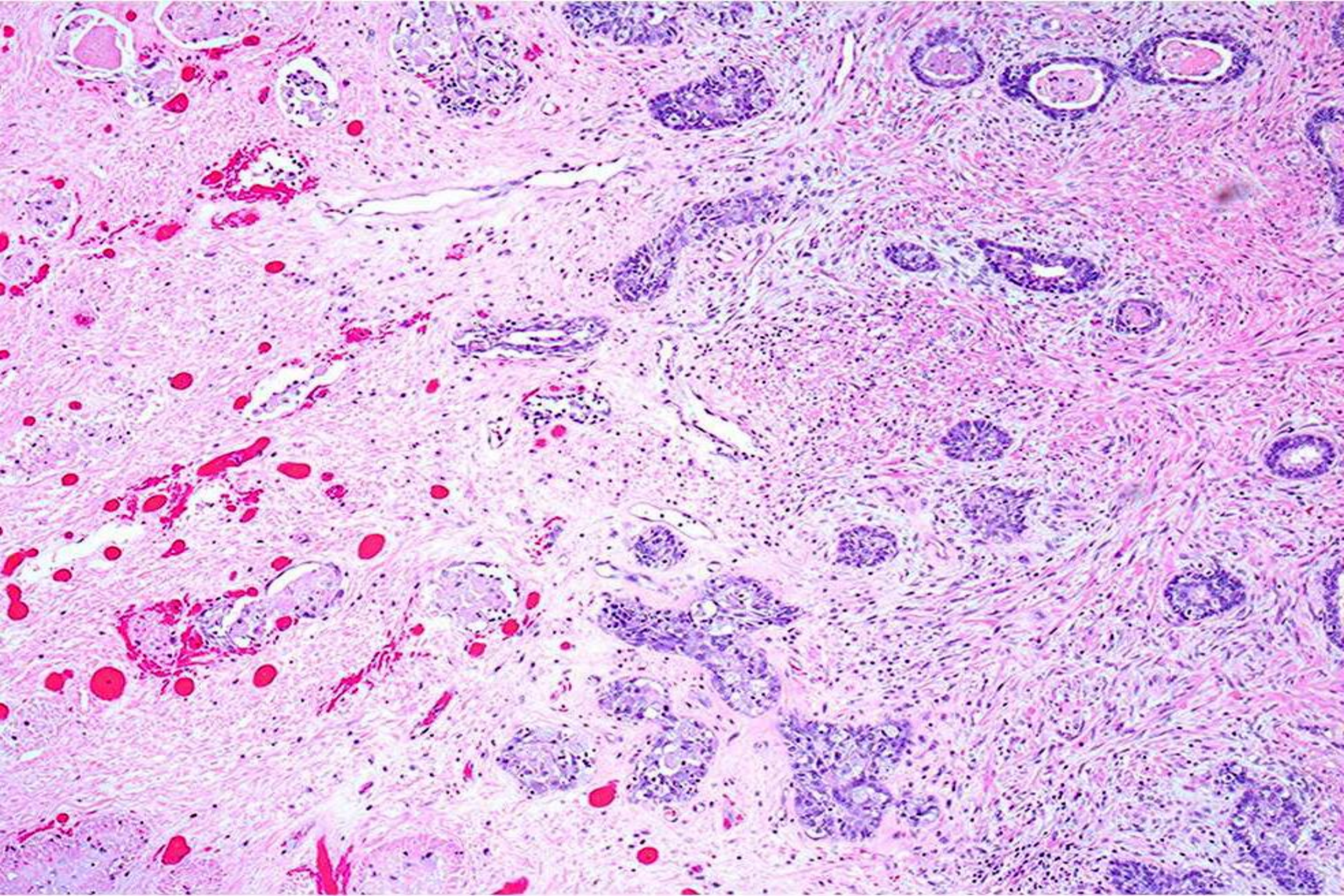
- **Nested variant of urothelial carcinoma is critical to recognize given its aggressive biology despite its deceptively bland cytology**

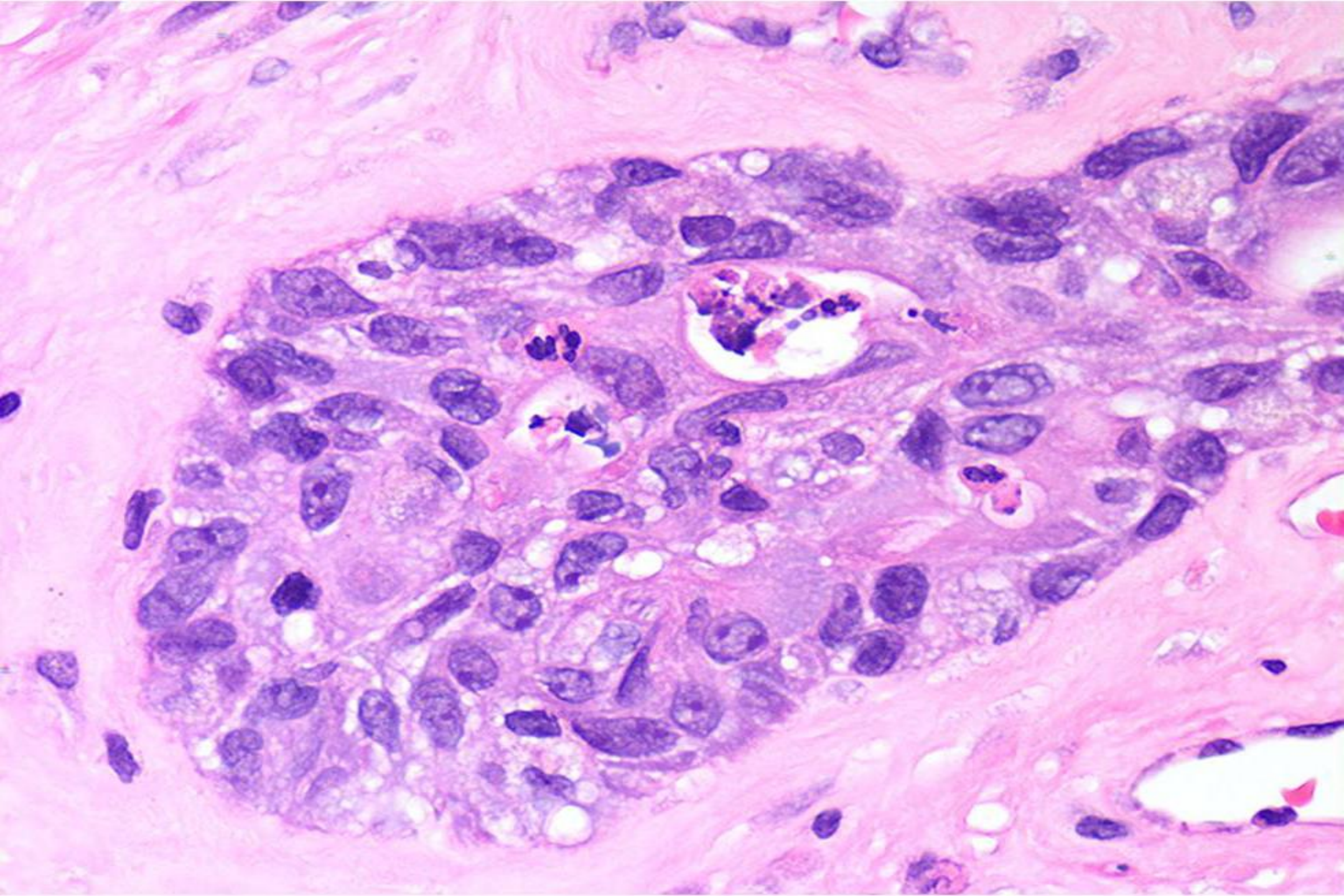
- **The diagnosis is based on the H&E appearance**

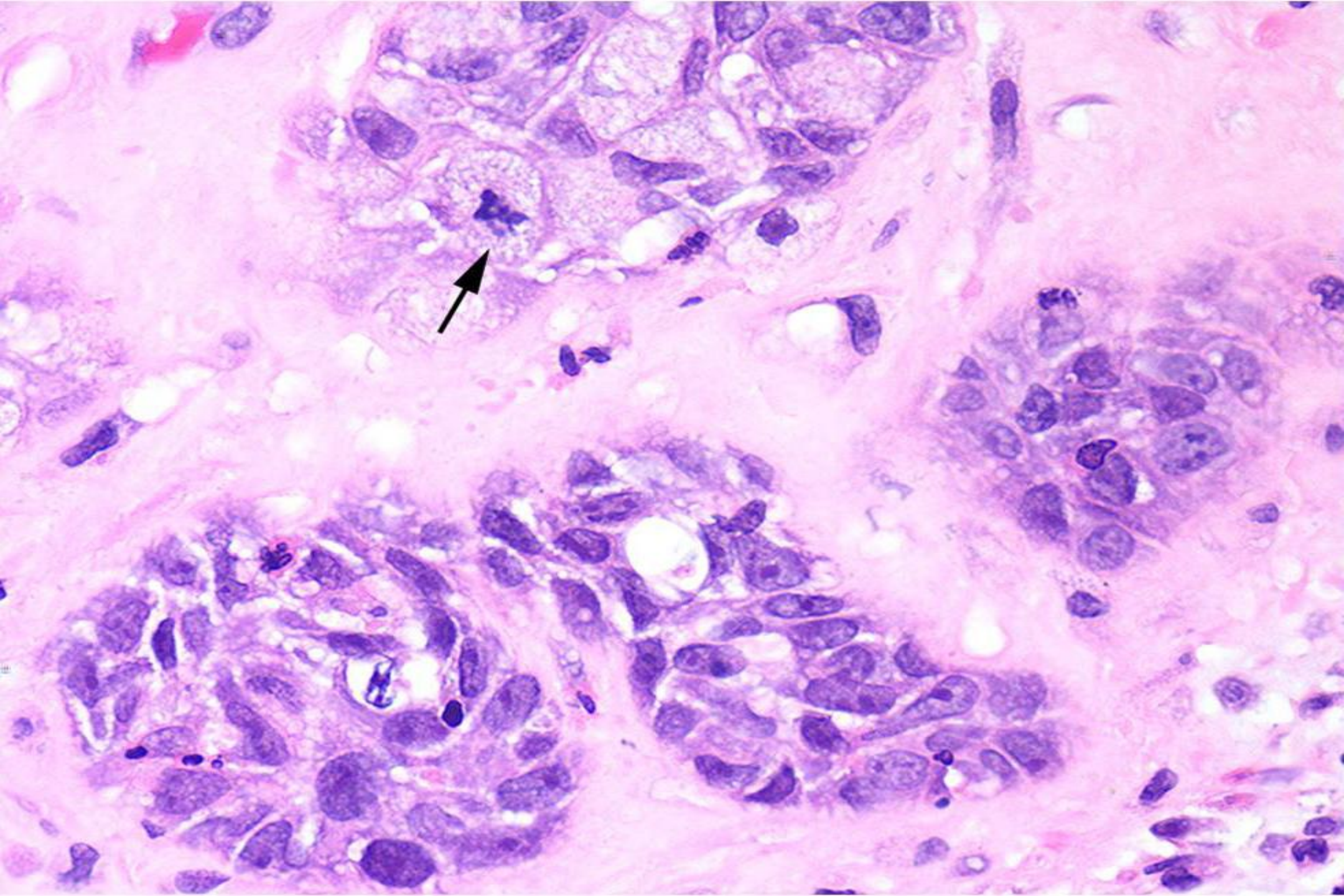
- **In cases of diagnostic uncertainty or a superficial biopsy, convey your uncertainty to the urologist and request additional tissue sampling**

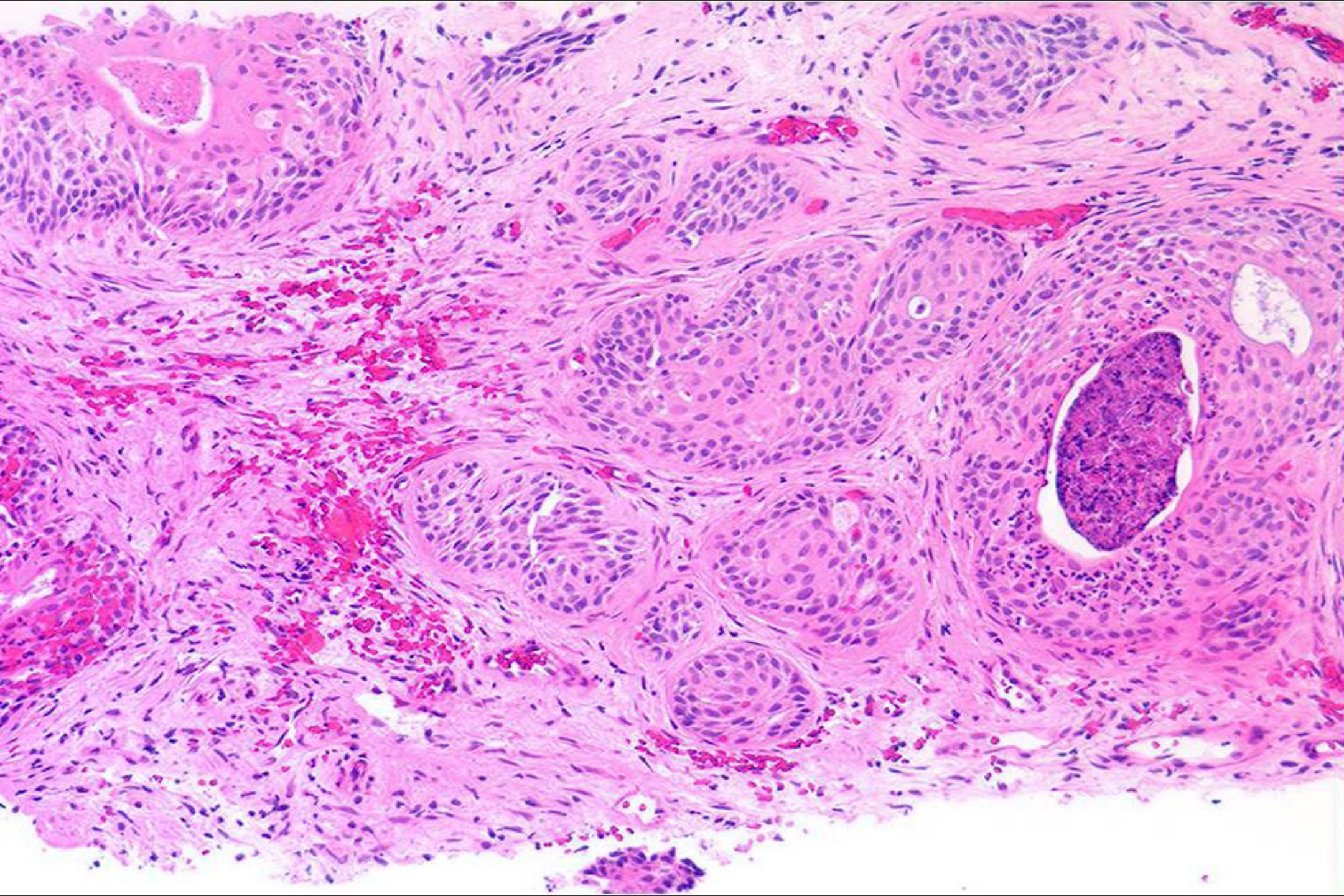
Prostatic Infarct

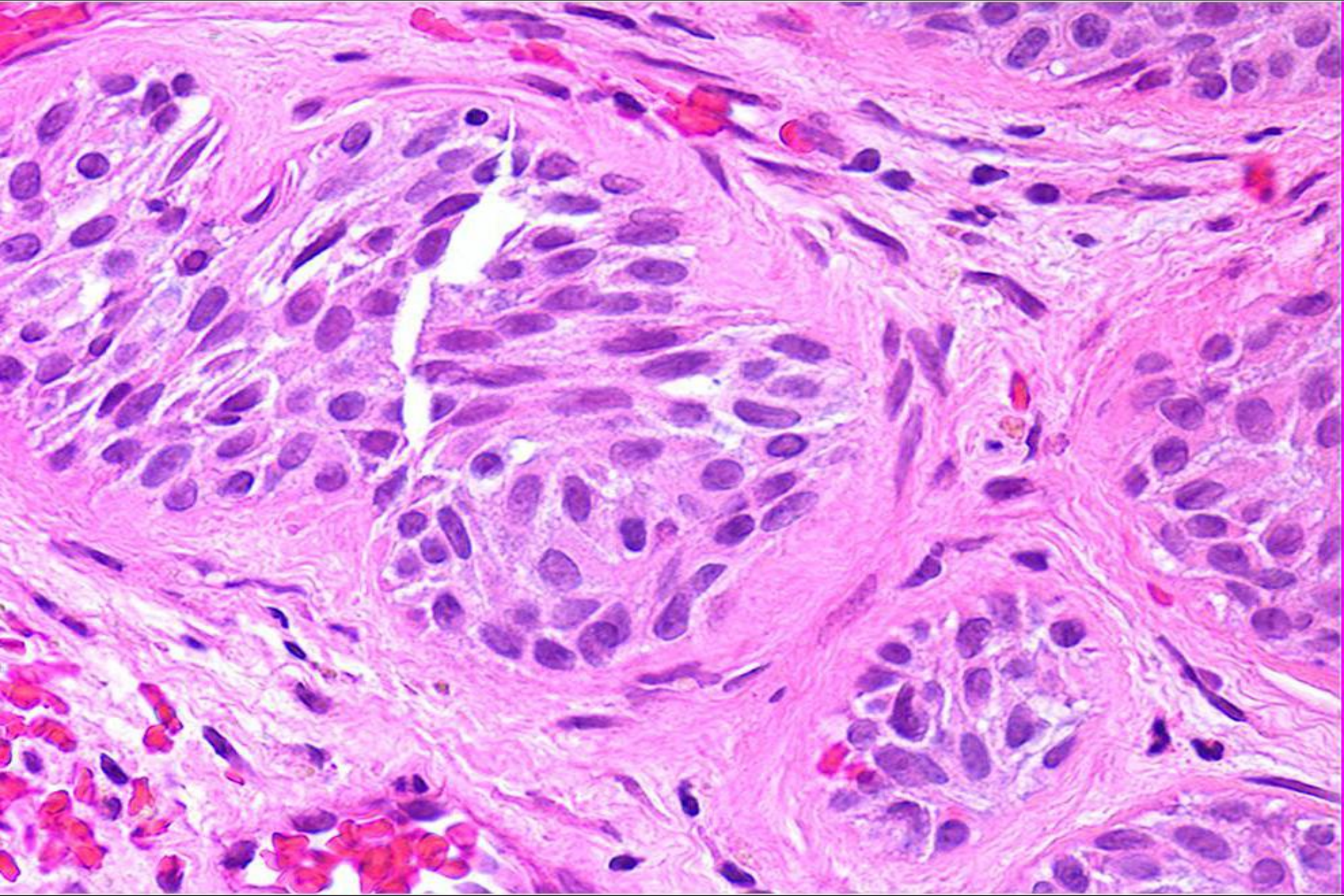
- **Associated with BPH, systemic atherosclerosis.**
- **Occasionally gives rise to spike in PSA.**
- **Mostly incidental finding on TUR and occasionally on needle .**
- **Organized from central necrosis to peripheral immature squamous (urothelial) metaplasia which can have atypia & mitoses mimicking urothelial cancer.**

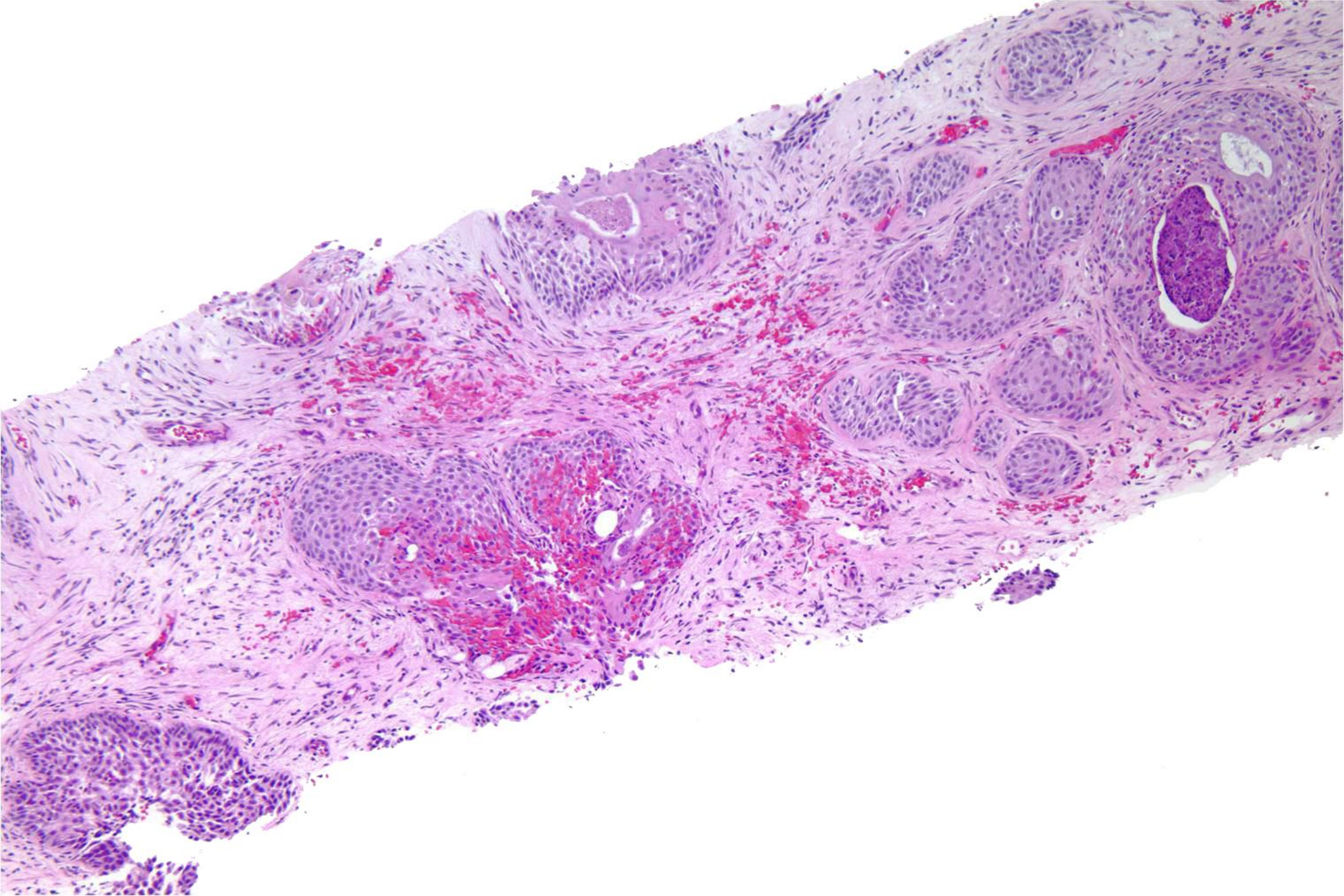


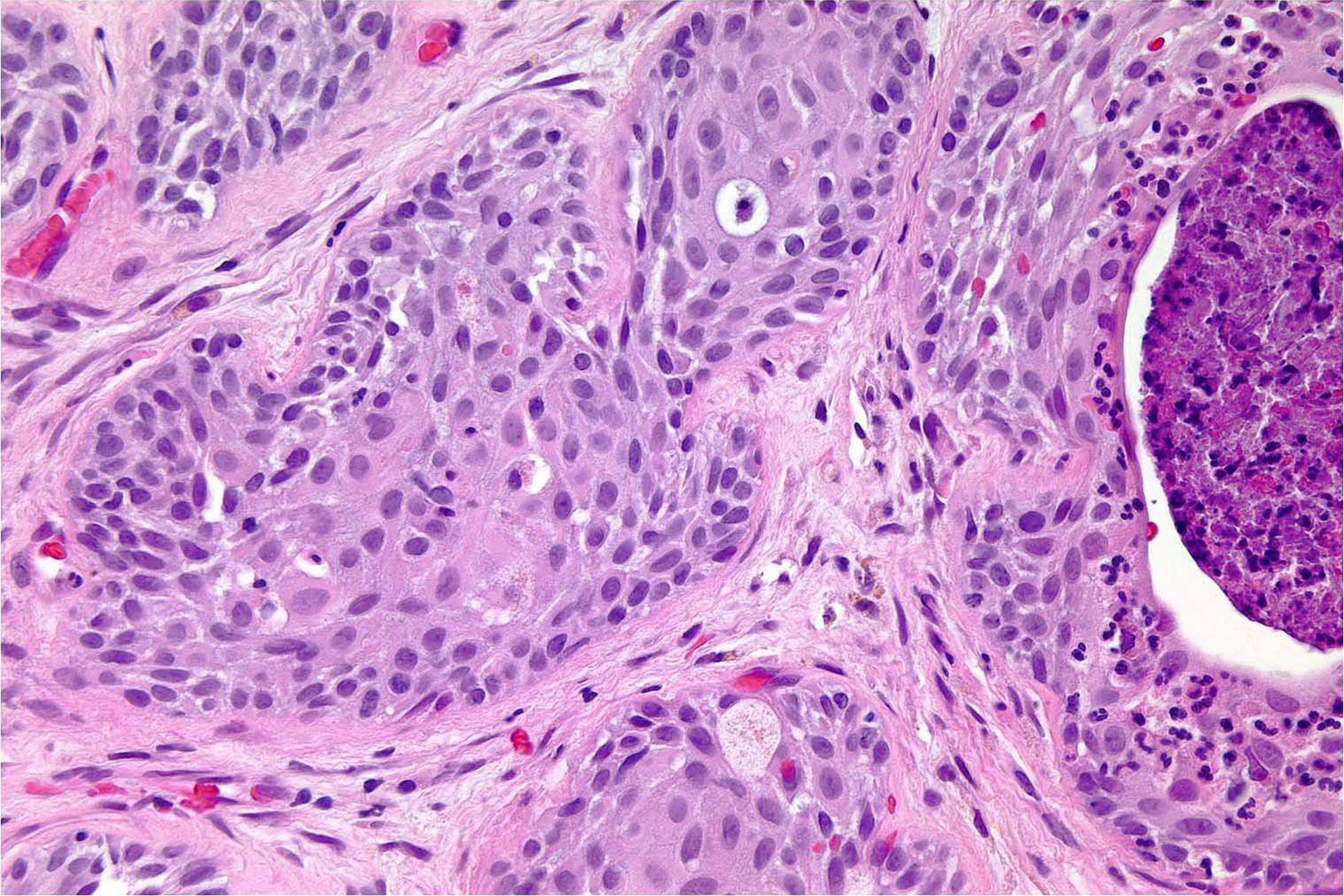












Summary

- **Wide range of benign mimickers of both adenocarcinoma and urothelial carcinoma.**
- **Important to get the impression of the urologist in certain differential diagnoses.**
- **In other entities, critical to look at the overall histology, rather than focus on isolated features that out of context may be indistinguishable from cancer.**
- **If any doubt of a diagnosis, request more tissue.**