



PEACE

Partnership of Emory and Africa for Cancer and Education

Urinary Tract Pathology Part II

LARA HARIK, MD

EMORY UNIVERSITY

DEPARTMENT OF
PATHOLOGY

Recap of last presentation: Urinary Tract Part 1

- ▶ Non-neoplastic lesions
- ▶ Metaplasia
- ▶ Non-invasive neoplasms
 - ▶ CIS
 - ▶ Papillary neoplasms

Agenda



- ▶ Invasive carcinoma
- ▶ Subtypes of invasive urothelial carcinoma
- ▶ Divergent differentiation
- ▶ Non-epithelial tumors

Pathologic Staging Primary tumor (pT)

<https://www.cap.org/protocols-and-guidelines/cancer-reporting-tools/cancer-protocol-templates>

pT: Cannot be assigned

pT0: No evidence of primary tumor

pTa: Papillary noninvasive carcinoma

pTis: Carcinoma in situ

pT1: Tumor invades subepithelial connective tissue (lamina propria)

pT2a: Tumor invades superficial muscularis propria (inner half)

pT2b: Tumor invades deep muscularis propria (outer half)

pT3a: Tumor invades perivesical soft tissue microscopically

pT3b: Tumor invades perivesical soft tissue macroscopically (extravesicular mass)

pT4a: Extravesical tumor invades directly into prostatic stroma, uterus, or vagina

pT4b: Extravesical tumor invades pelvic wall, abdominal wall

Invasive Urothelial Carcinoma

Invasive tumor outcome depends on stage

Superficial (pTa, pTis, pT1)

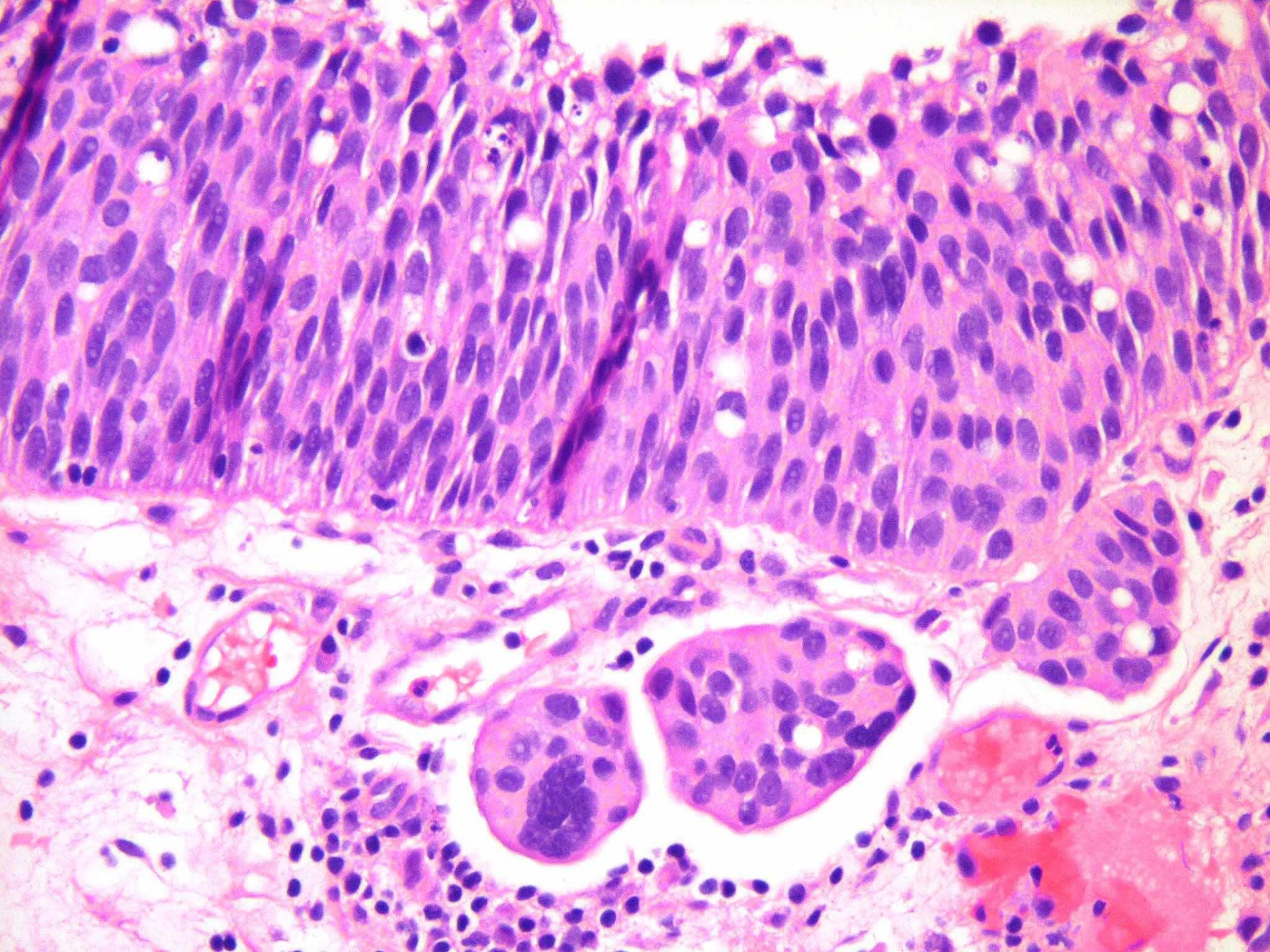
- Conservative management

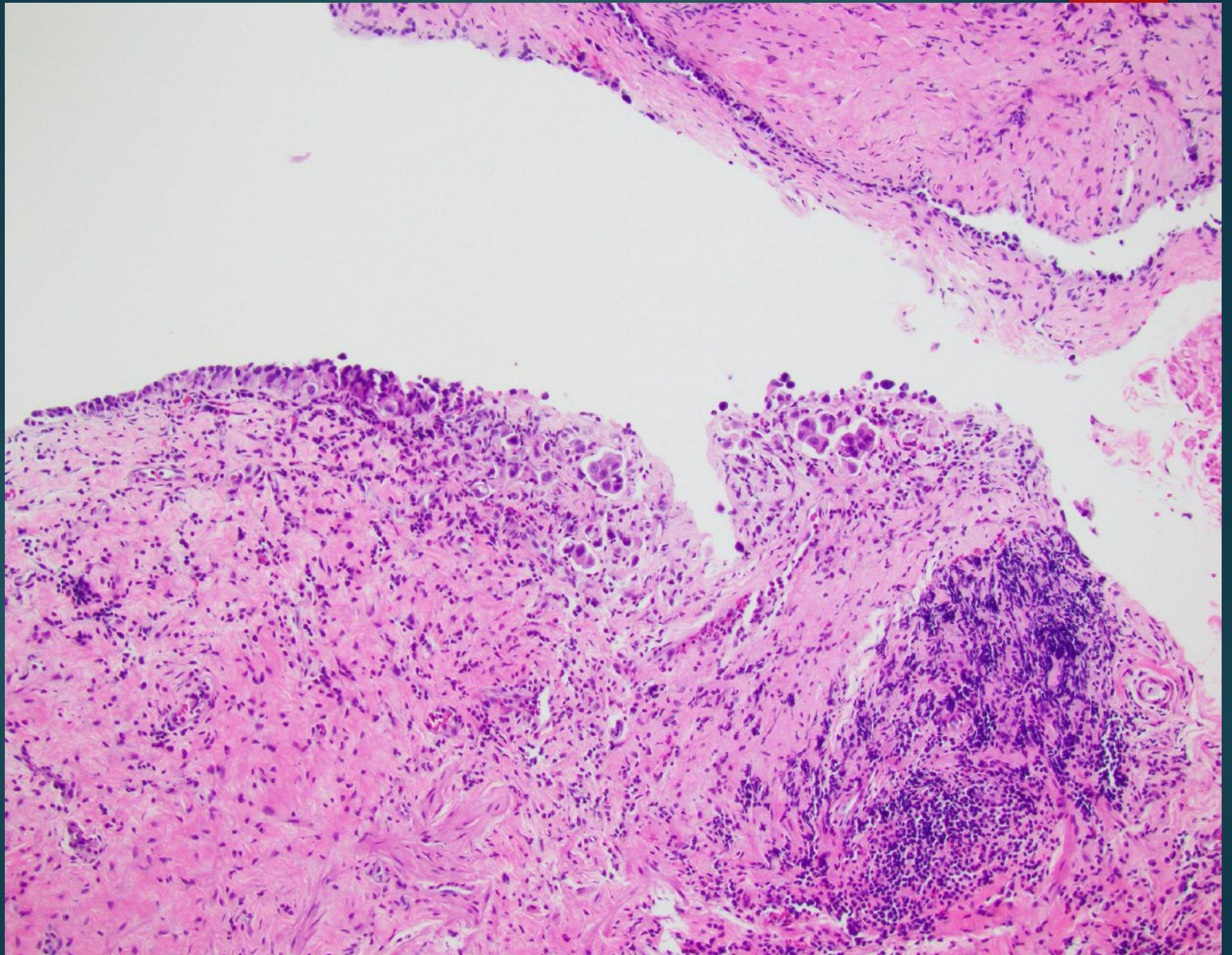
Muscularis propria invasion or greater

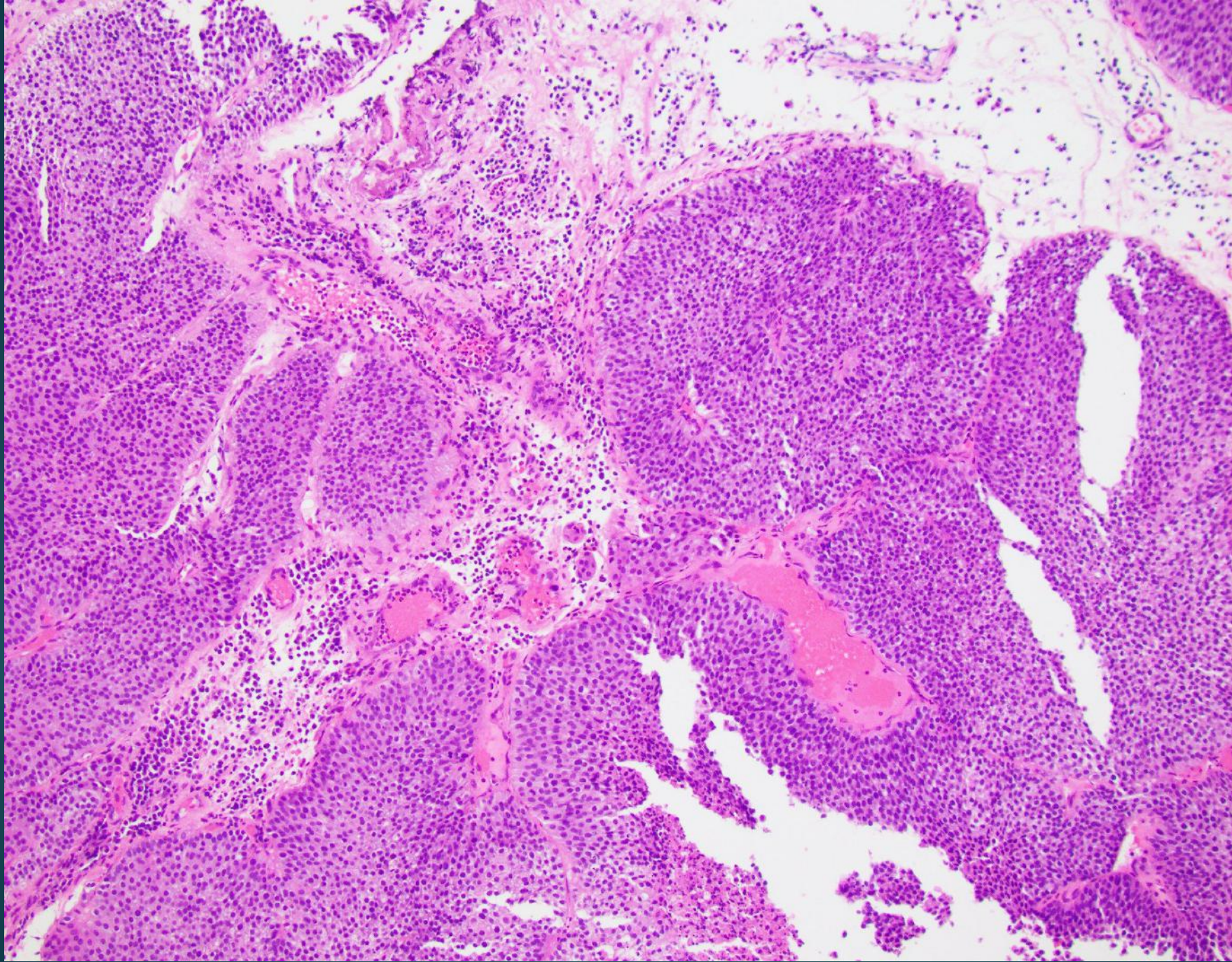
- Half have occult metastases at presentation
- A big percentage will develop metastases within 1 year

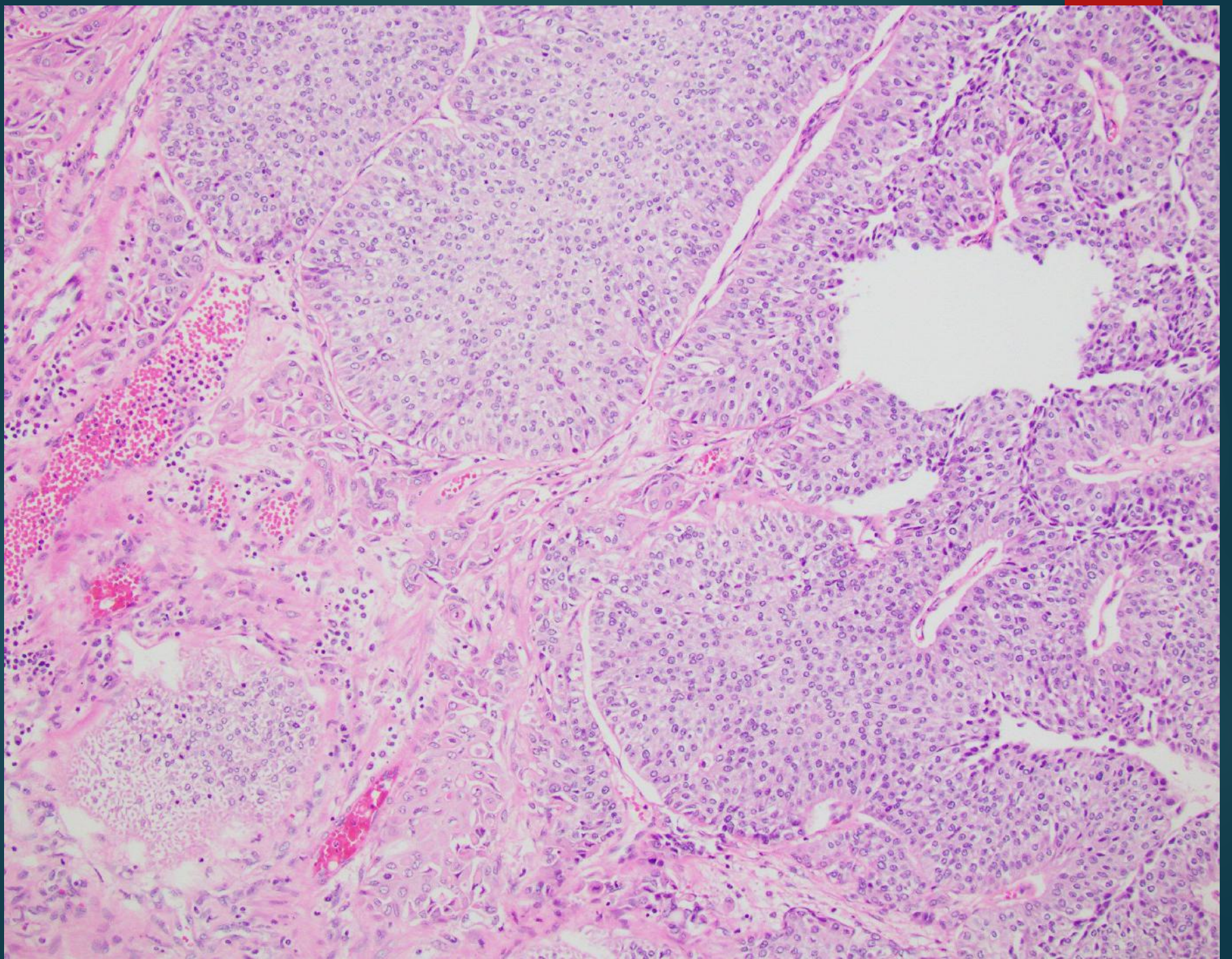
Lamina Propria Invasion

- ▶ pT1
- ▶ Quantifying pT1 extent
 - ▶ Microinvasion: <2 mm in length
 - ▶ Anatomic extension
- ▶ Features:
 - ▶ Small nests or clusters/single cells
 - ▶ Paradoxical differentiation
 - ▶ Irregular, jagged tongues
 - ▶ Clefing artifact
 - ▶ Lack of tangential capillary network





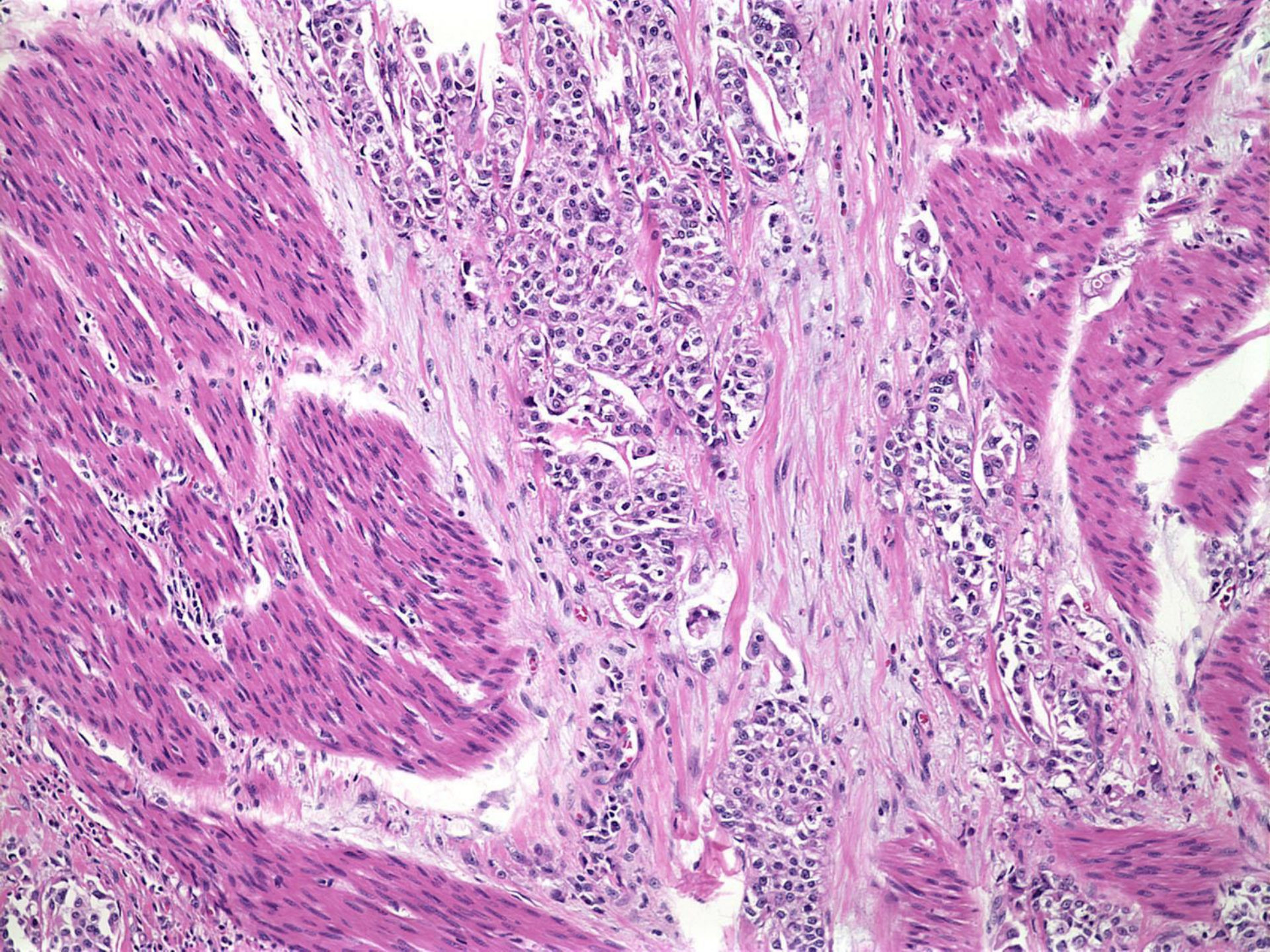


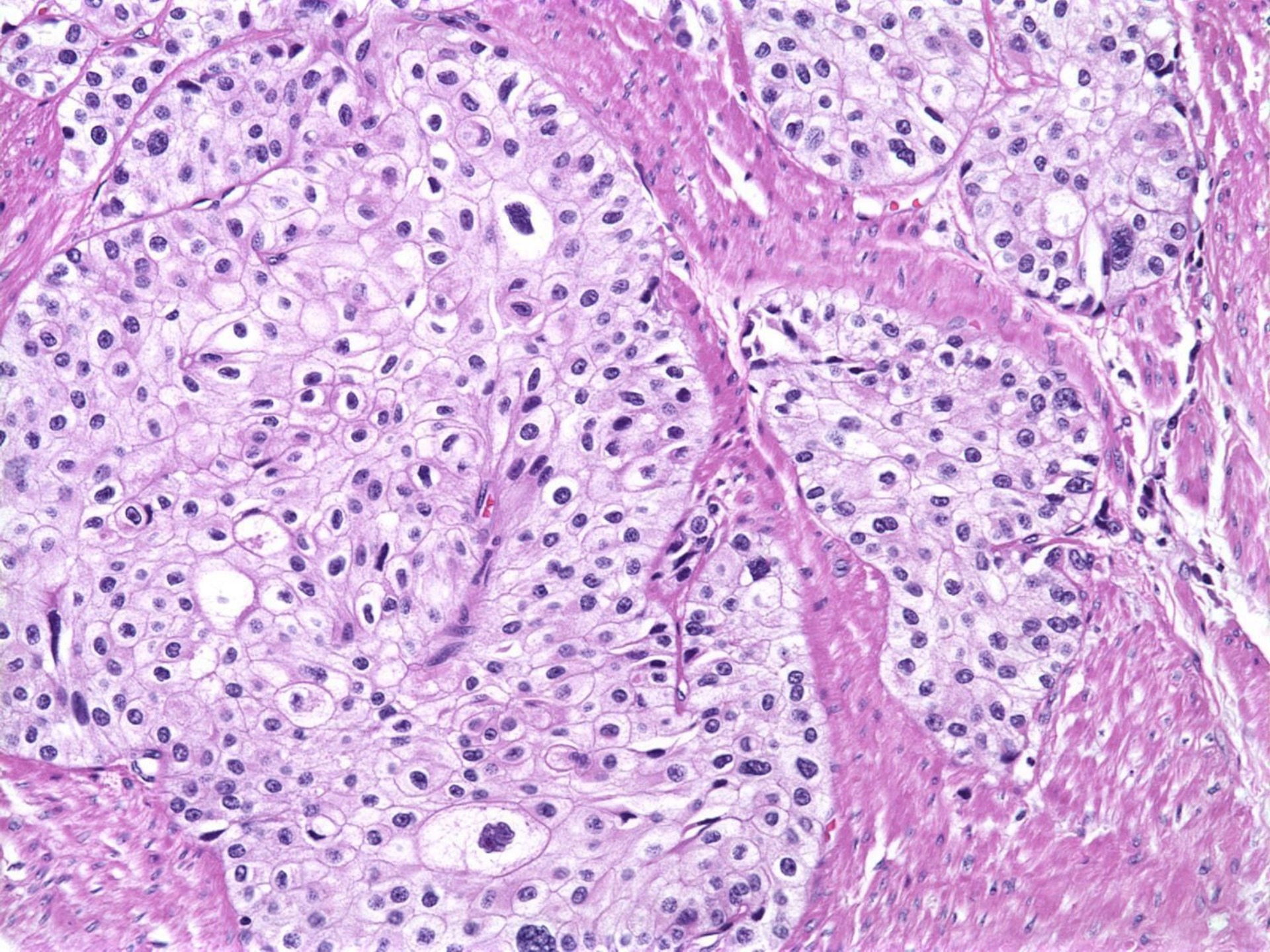


Muscularis Propria Invasion

Importance

- ▶ Therapeutic
- ▶ Diagnostic
- ▶ Prognostic





Muscularis- word of caution

- ▶ There are 2 muscularis in the bladder:
 - ▶ Muscularis mucosae and muscularis propria
 - ▶ Avoid the term muscle invasive: very confusing...

Invasive Urothelial Carcinoma- Beyond NOS

Urothelial Carcinoma

- NOS
- Subtypes of UCA
- Divergent differentiation

Pure Divergent tumors

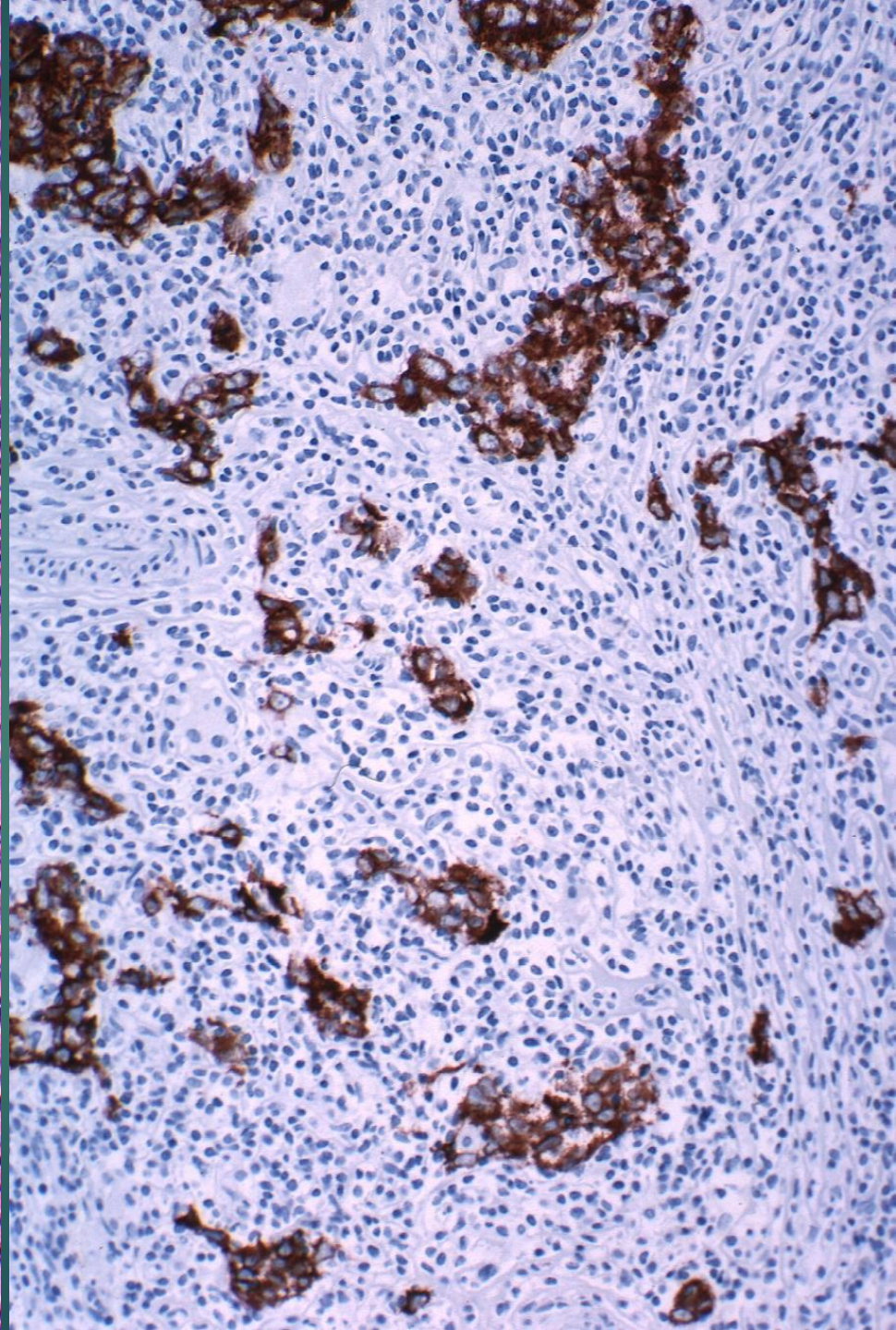
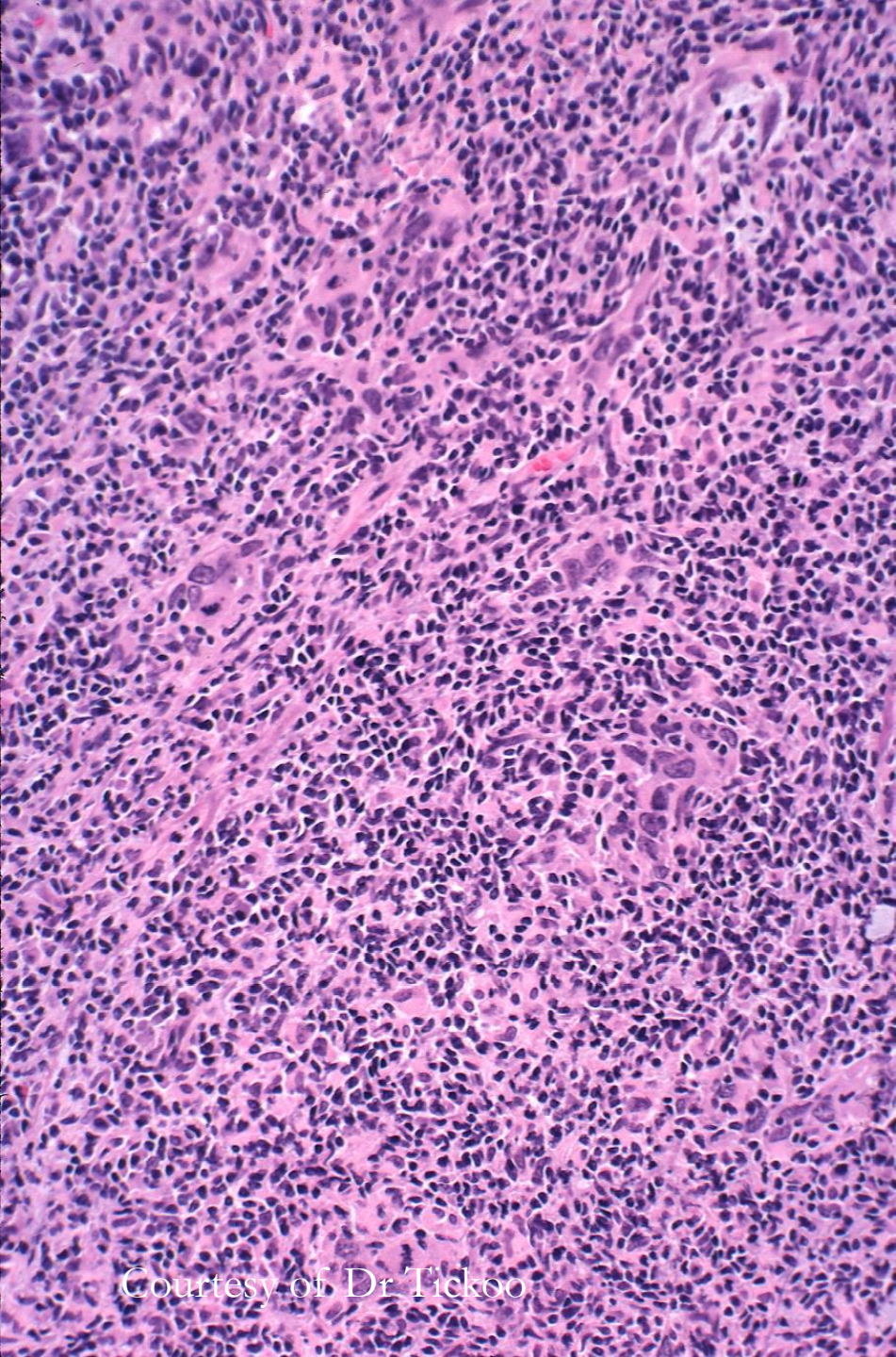
- Adenocarcinoma
- Squamous cell carcinoma

Subtypes of invasive urothelial carcinoma

- ▶ Lymphoepithelioma like carcinoma
- ▶ Nested carcinoma
- ▶ Tubular and Microcystic carcinoma
- ▶ Plasmacytoid carcinoma
- ▶ Micropapillary carcinoma
- ▶ Small cell carcinoma
- ▶ Sarcomatoid carcinoma

Lymphoepithelioma-like Urothelial Carcinoma

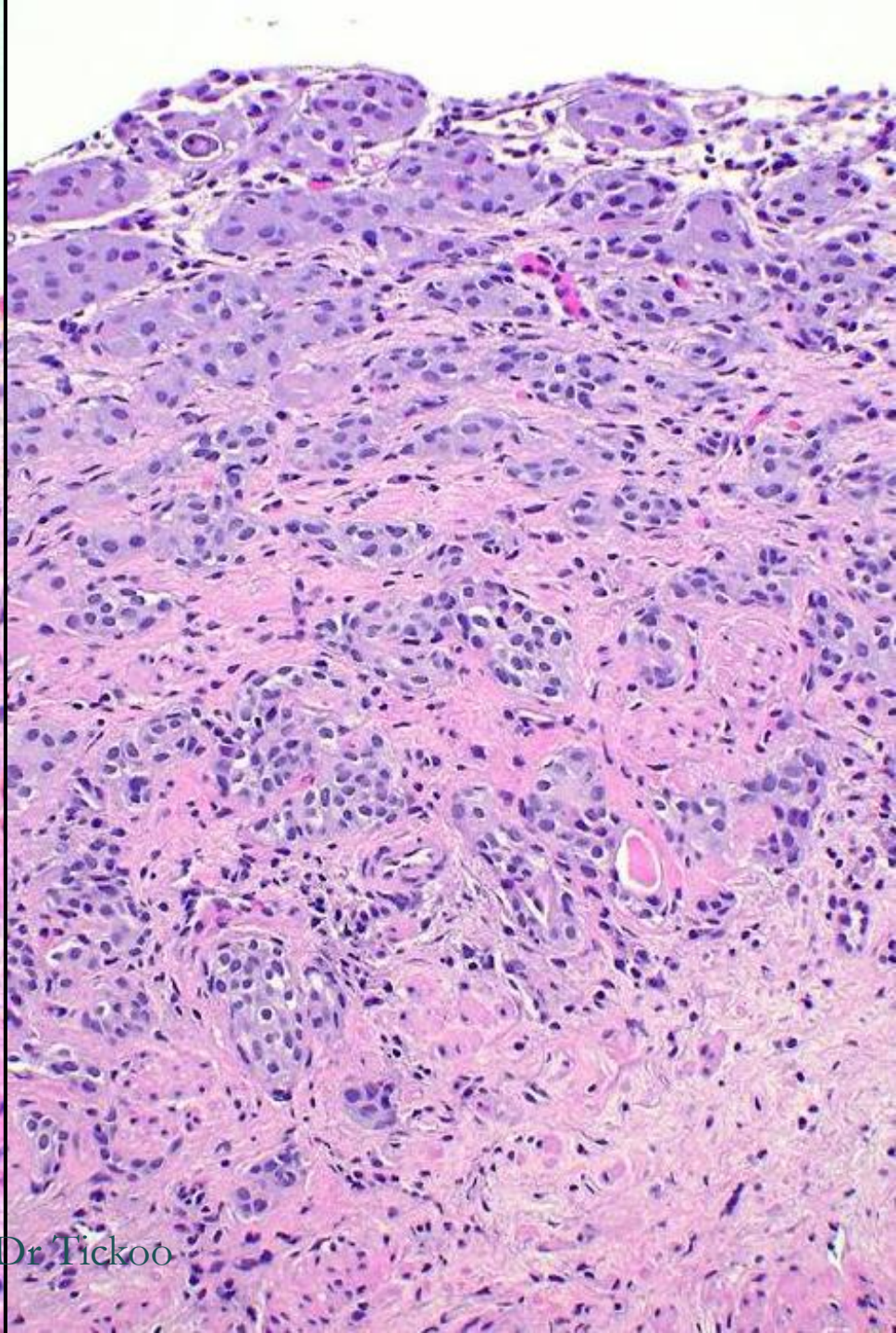
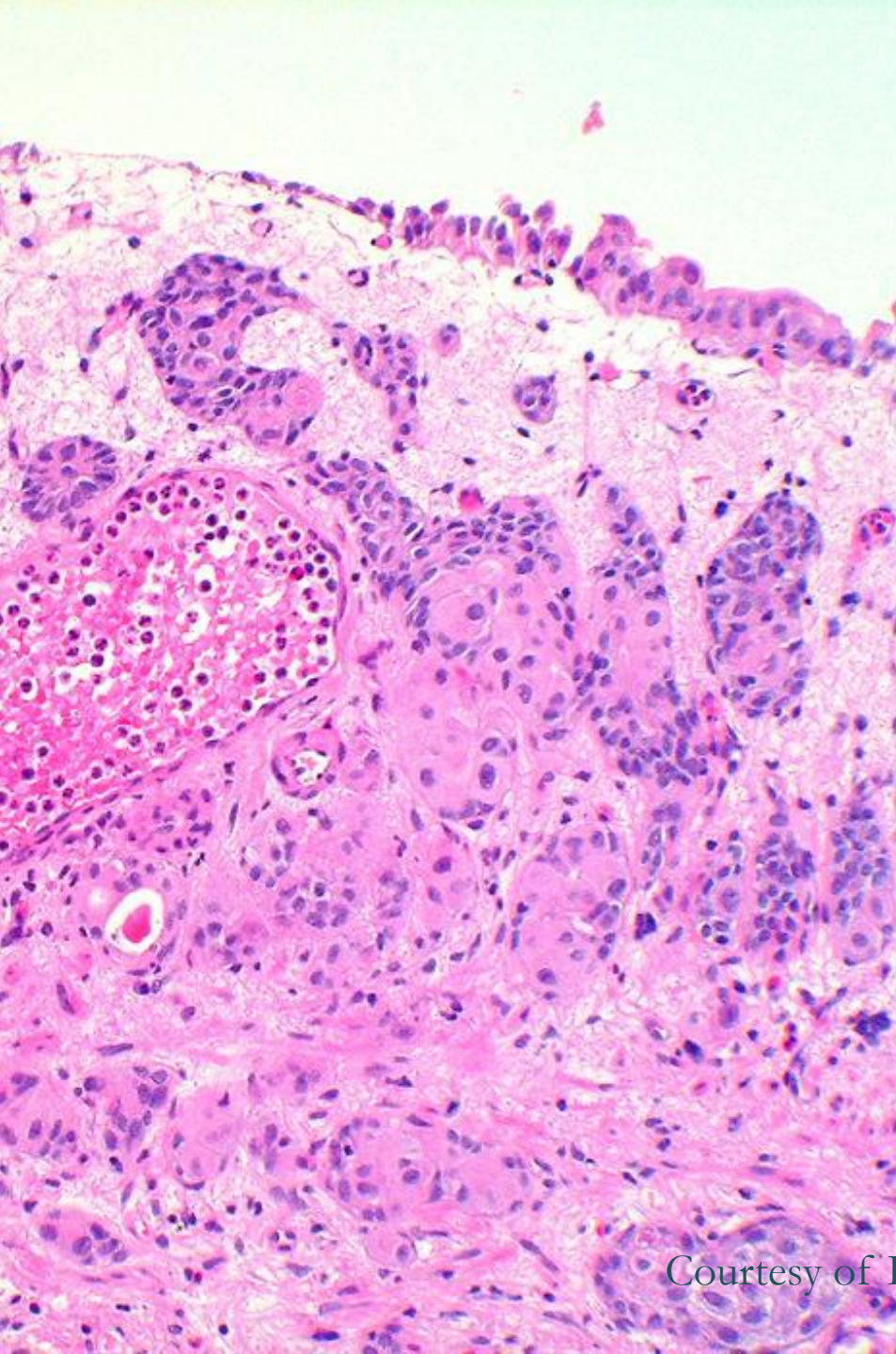
- ▶ Rare
- ▶ Need at least 50% of this component to qualify
- ▶ ? better prognosis
- ▶ Thought to respond better to therapy
- ▶ Need more studies to confirm
- ▶ Not associated with EBV or HPV



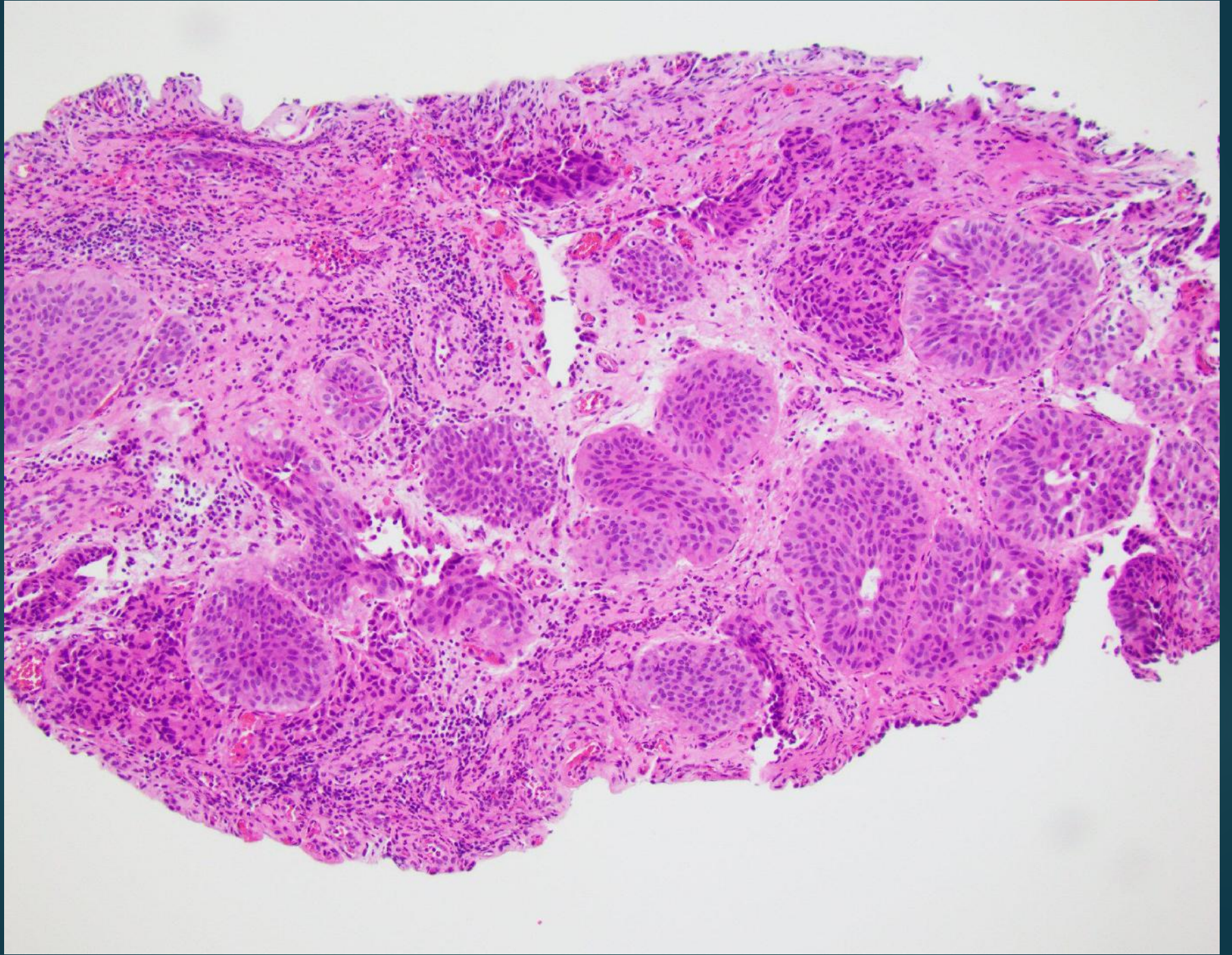
Courtesy of Dr. Tickoo

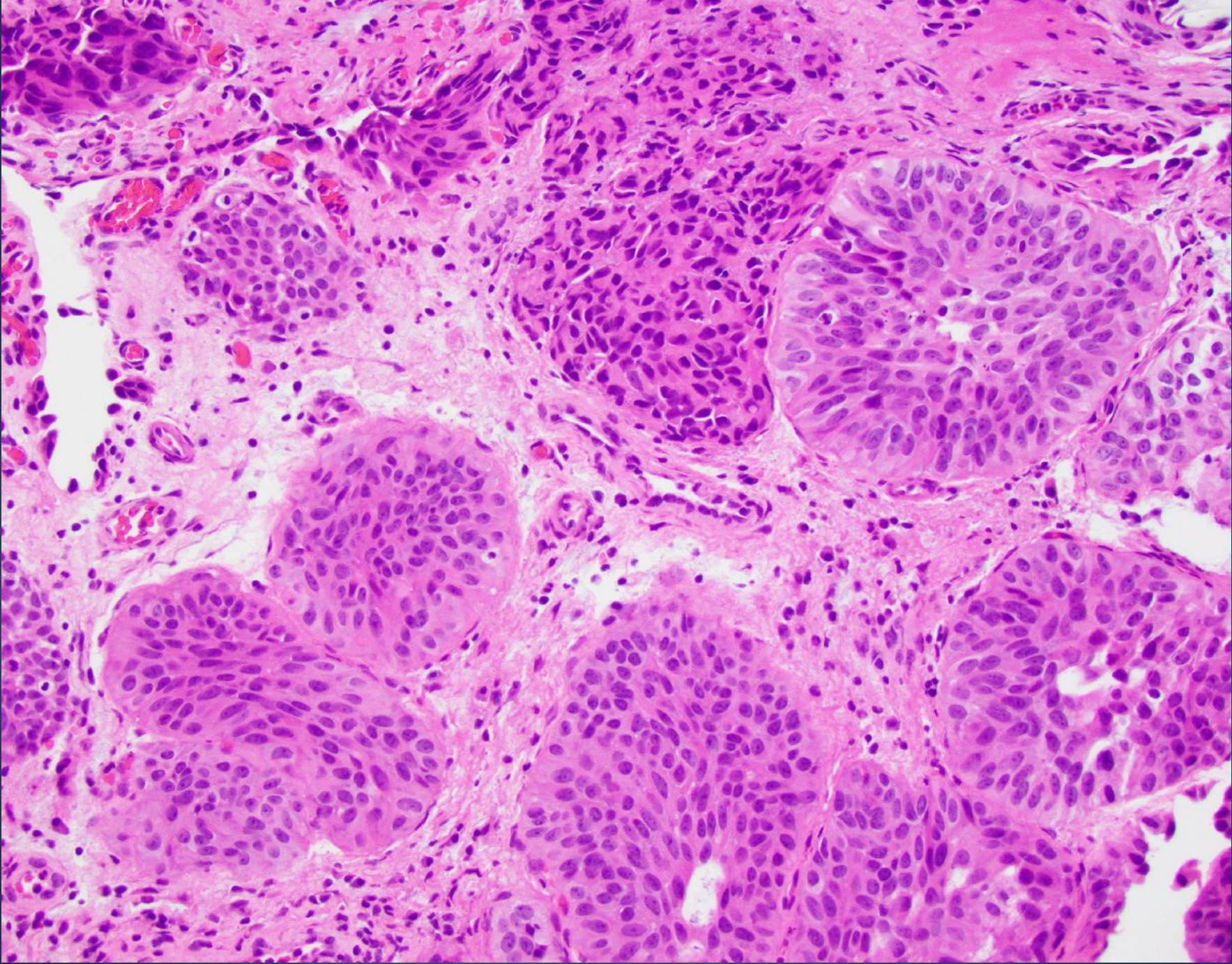
Nested Urothelial Carcinoma

- ▶ Rare
- ▶ Male predominance
- ▶ Can be multifocal
- ▶ The overlying urothelium could be histologically normal
- ▶ Minimal atypia
- ▶ Thought to be an aggressive variant: studies comparing stage by stage still need to be performed



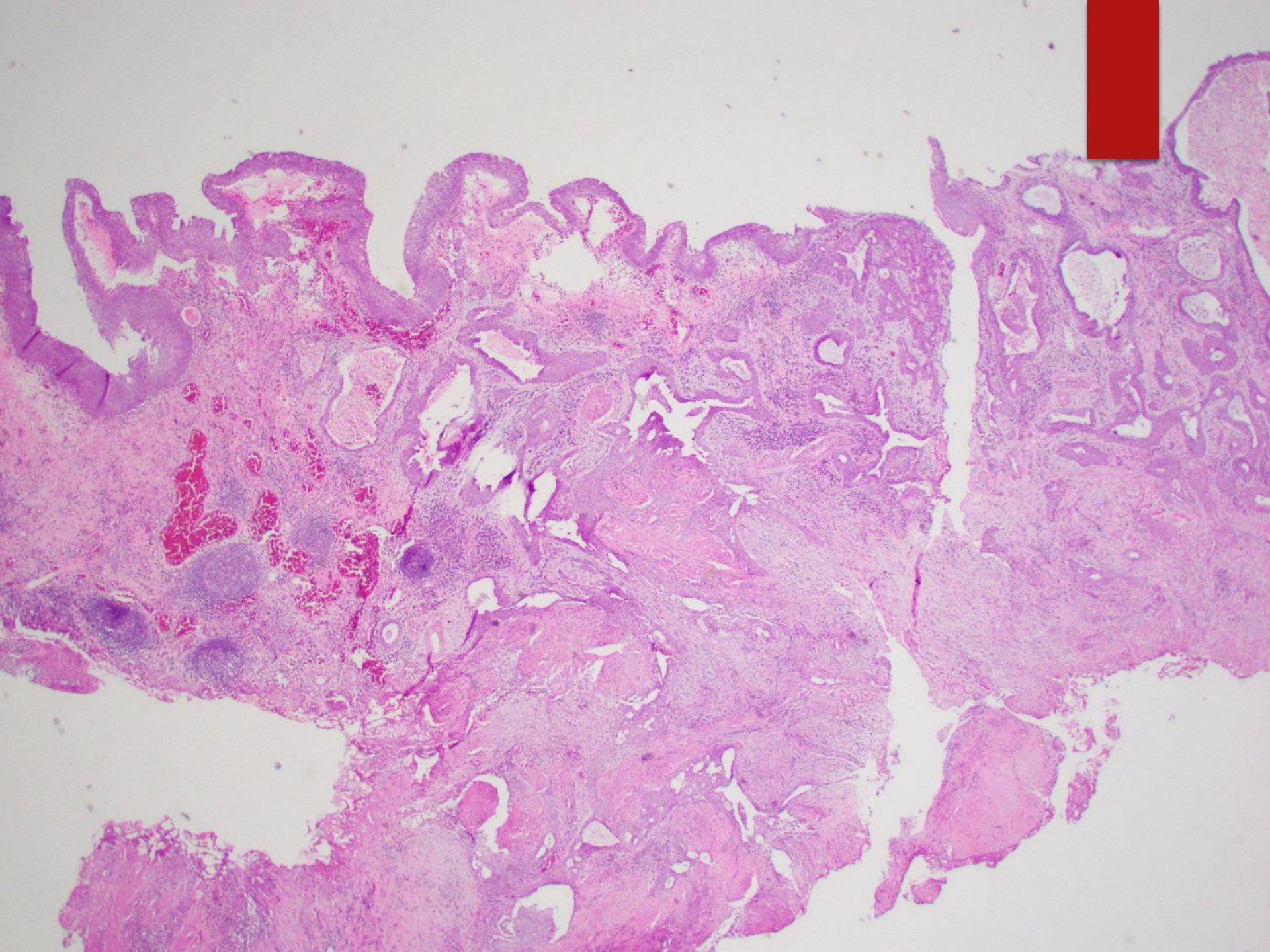
Courtesy of Dr Tickoo

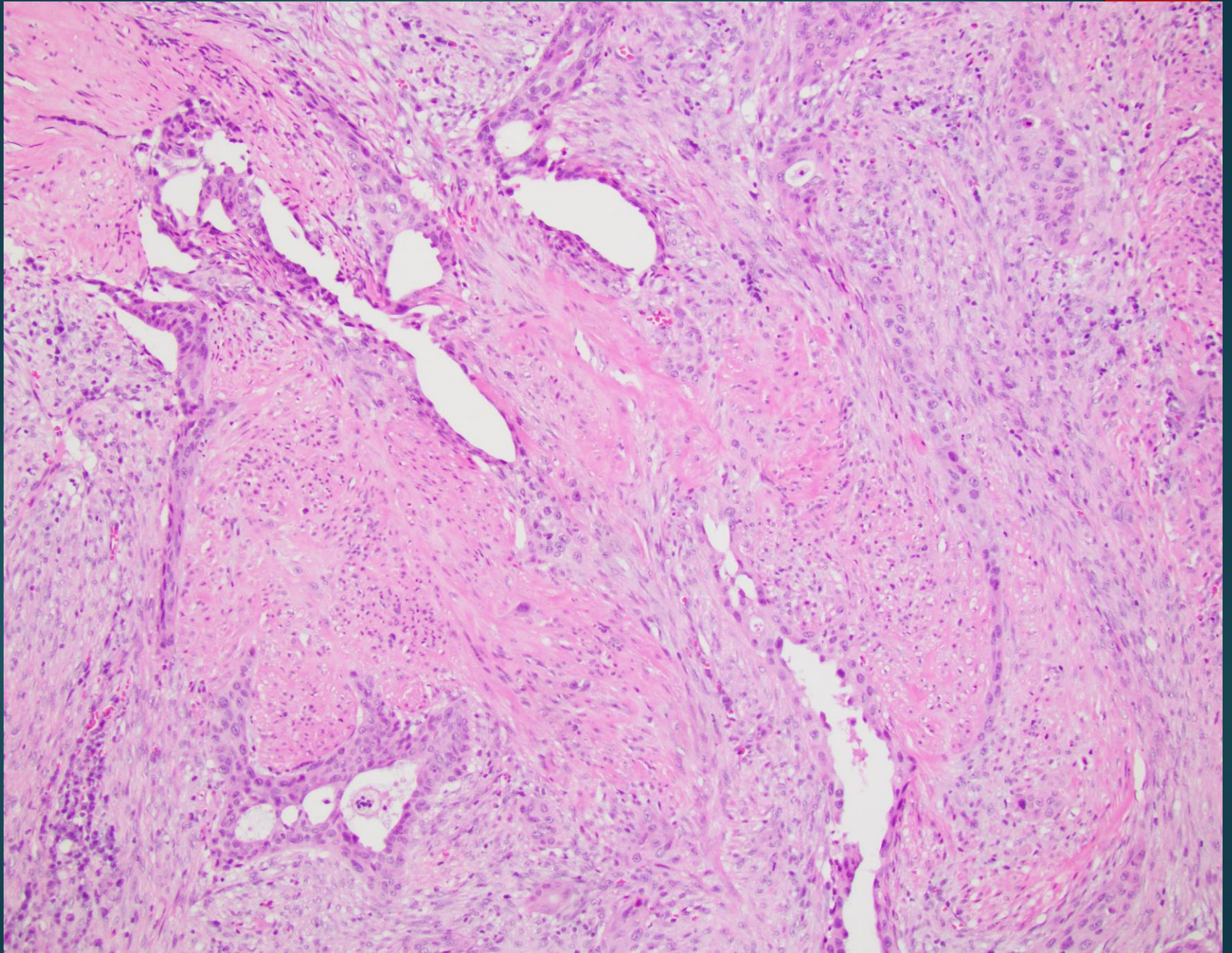




Tubular and Microcystic Urothelial Carcinoma

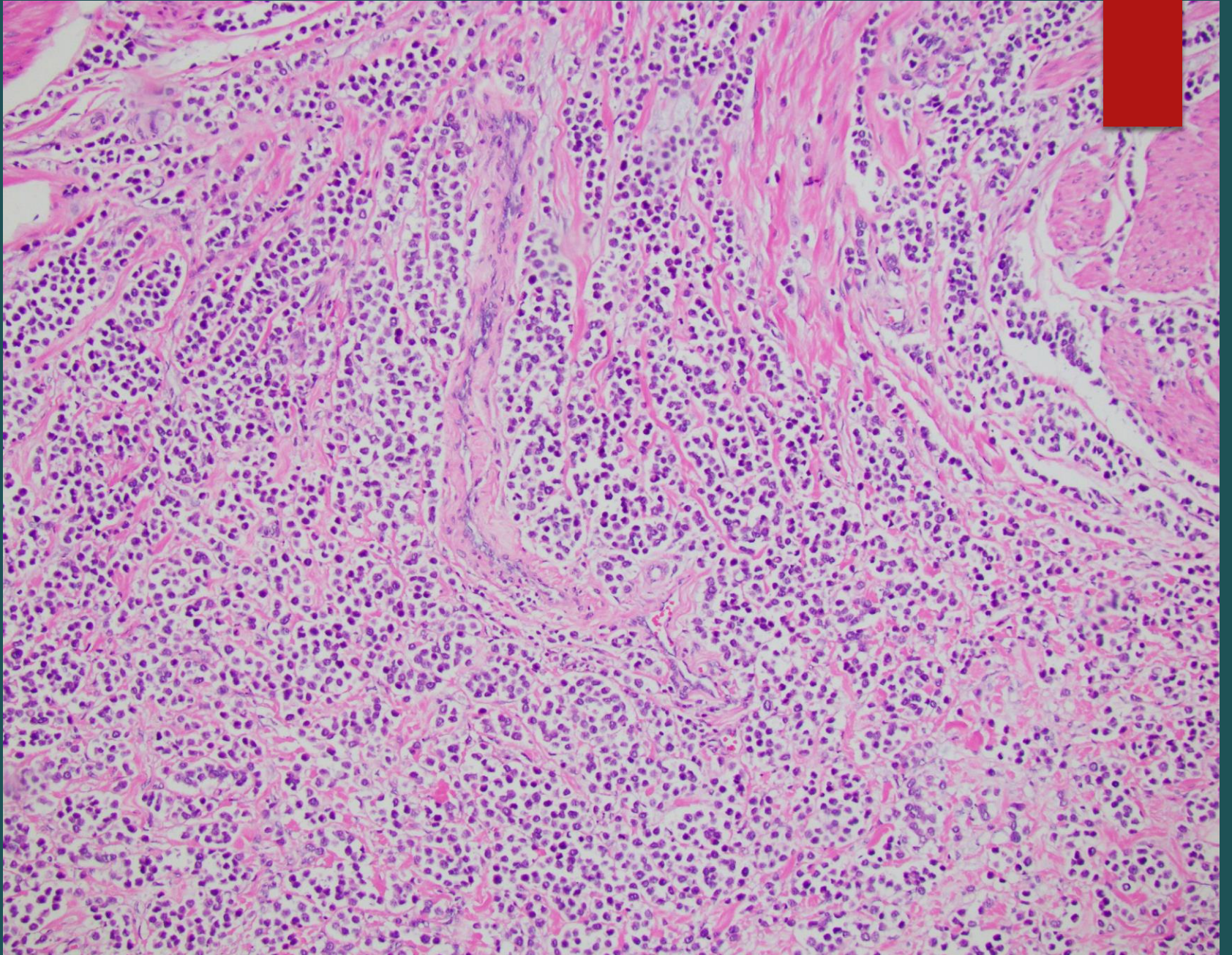
- ▶ May be related to nested variant
- ▶ Minimal desmoplasia / stromal reactions
- ▶ DDX: cystitis cystica





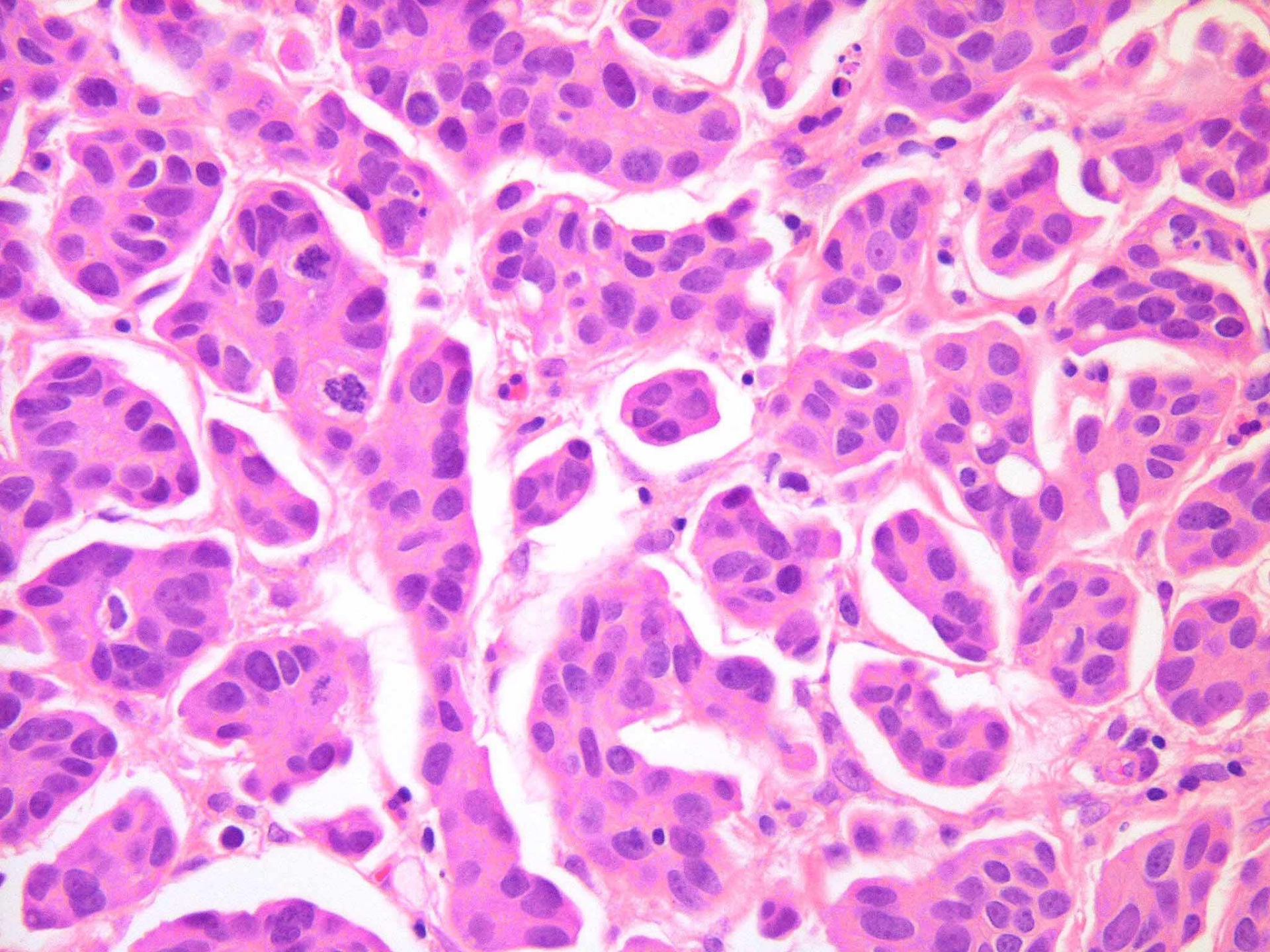
Plasmacytoid Urothelial Carcinoma

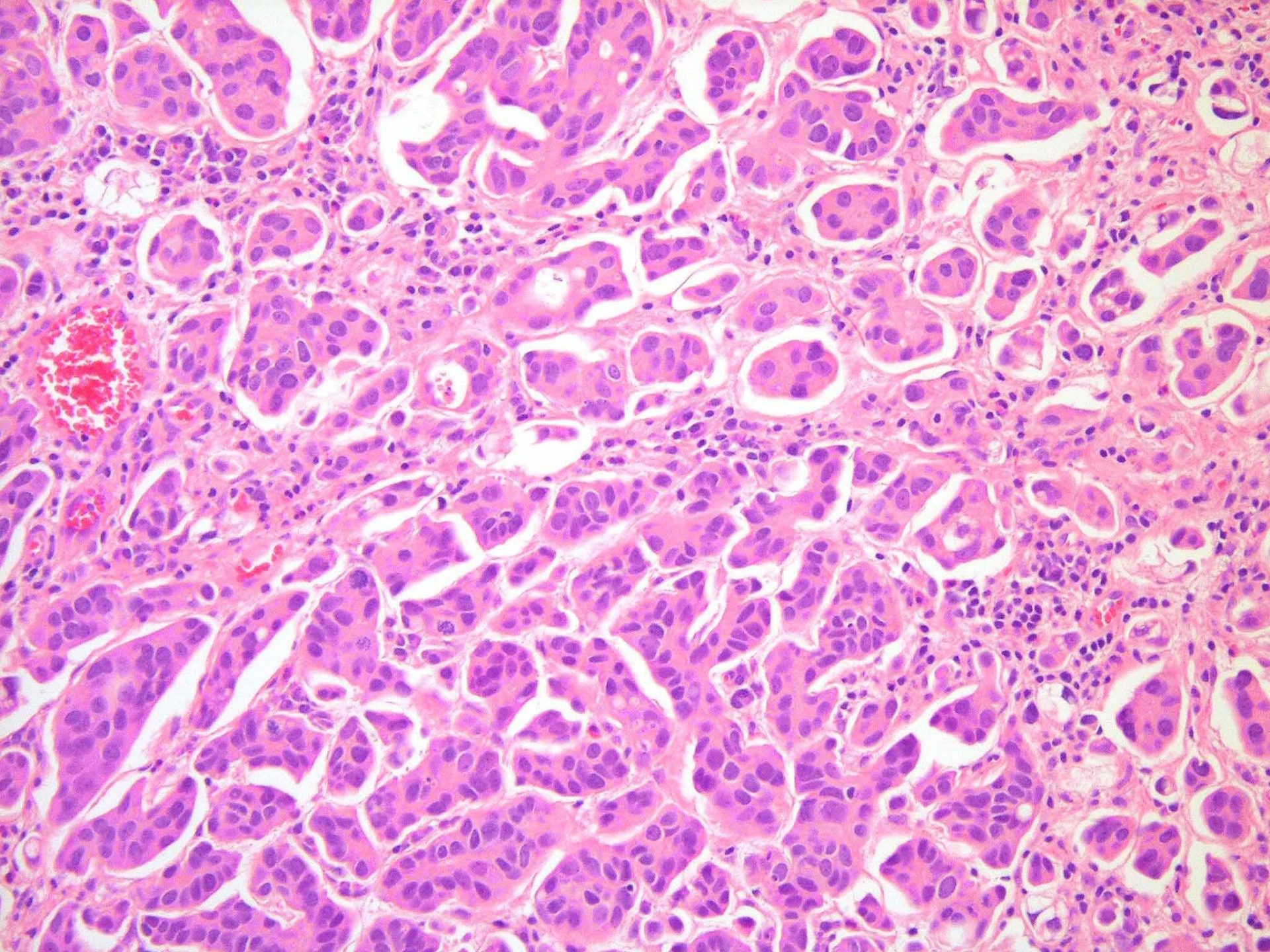
- ▶ Aggressive subtype
- ▶ Discohesive cells, small size/inconspicuous
 - ▶ Possible signet morphology, no extra-cellular mucin
- ▶ Is not always associated with in situ component
- ▶ Differential diagnosis includes
 - ▶ Metastatic carcinoma such as lobular carcinoma of the breast and gastric signet ring cell carcinoma
- ▶ Spreads along tissue planes and surfaces



Micropapillary Urothelial carcinoma

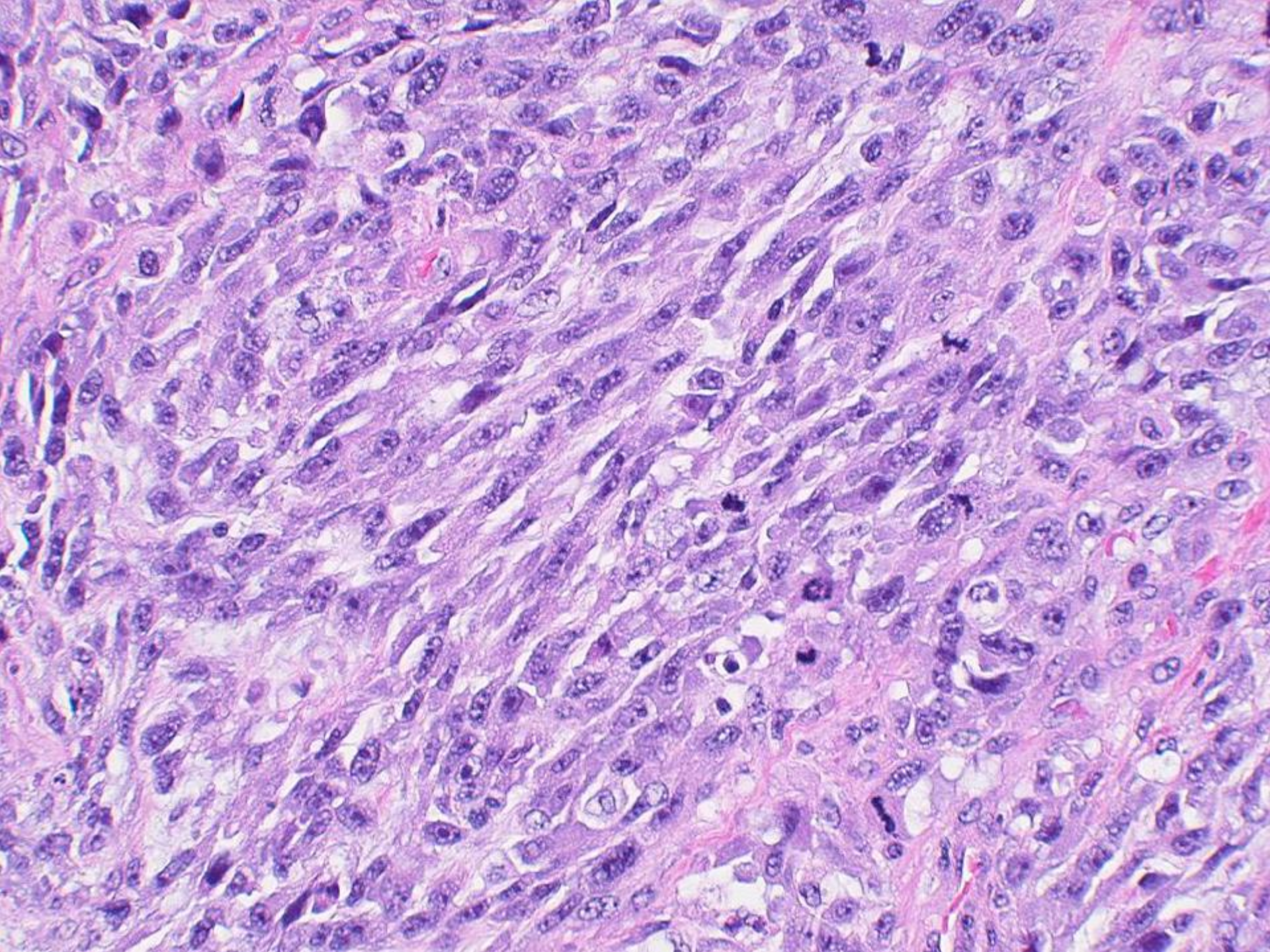
- ▶ Aggressive nature
- ▶ Usually presents at a higher stage and has poor prognosis
- ▶ Not very responsive to treatment
- ▶ Vascular invasion is common
- ▶ A big portion associated with CIS
- ▶ Diagnostic criteria needs refining

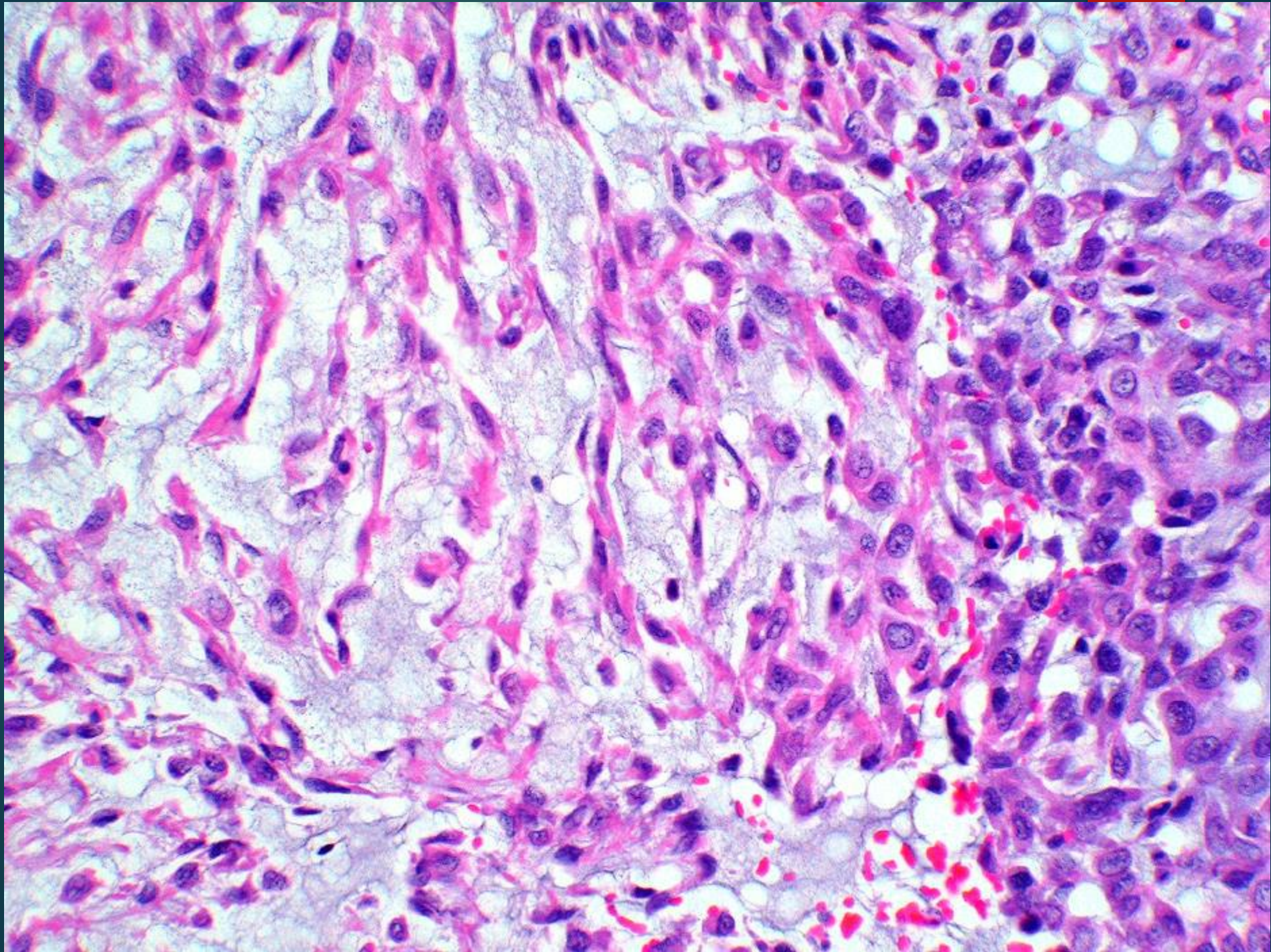


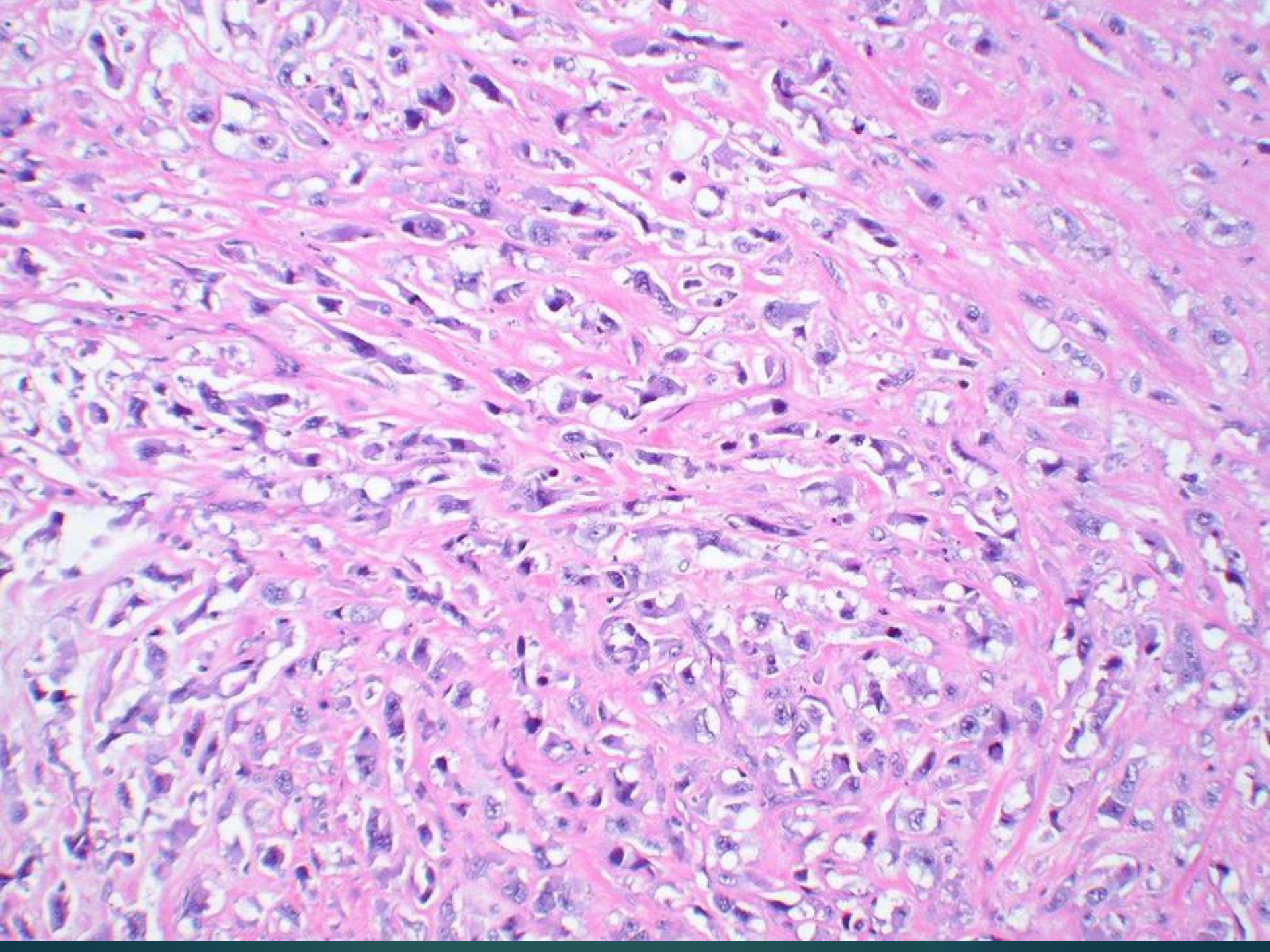


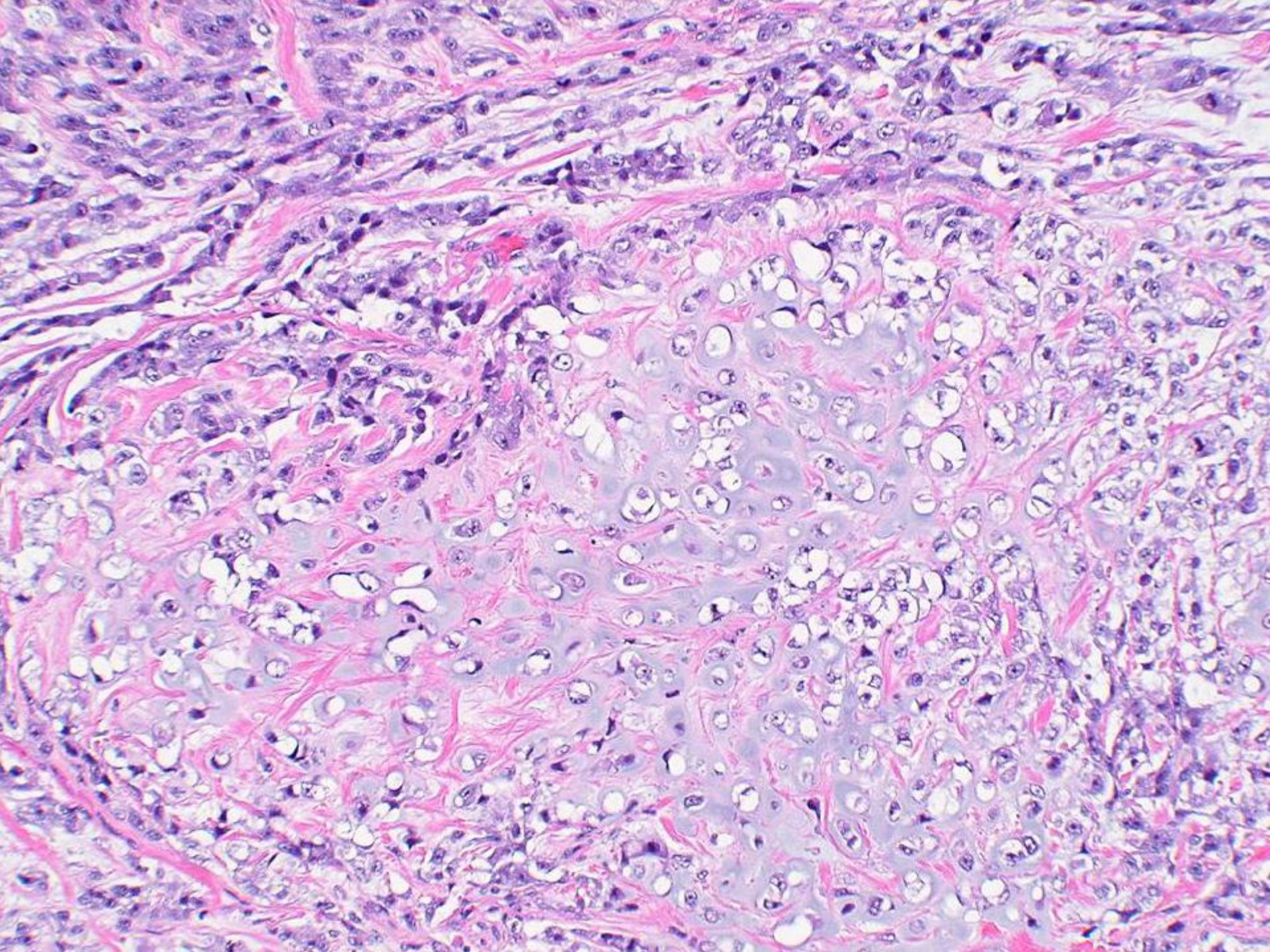
Sarcomatoid Urothelial Carcinoma

- ▶ Should be differentiated from sarcoma
 - ▶ Look for epithelial component
 - ▶ Cytokeratin positive
- ▶ Sarcomatoid carcinoma with heterologous elements
 - ▶ ? Worse prognosis
- ▶ High stage at presentation
- ▶ 5 year survival is <30%



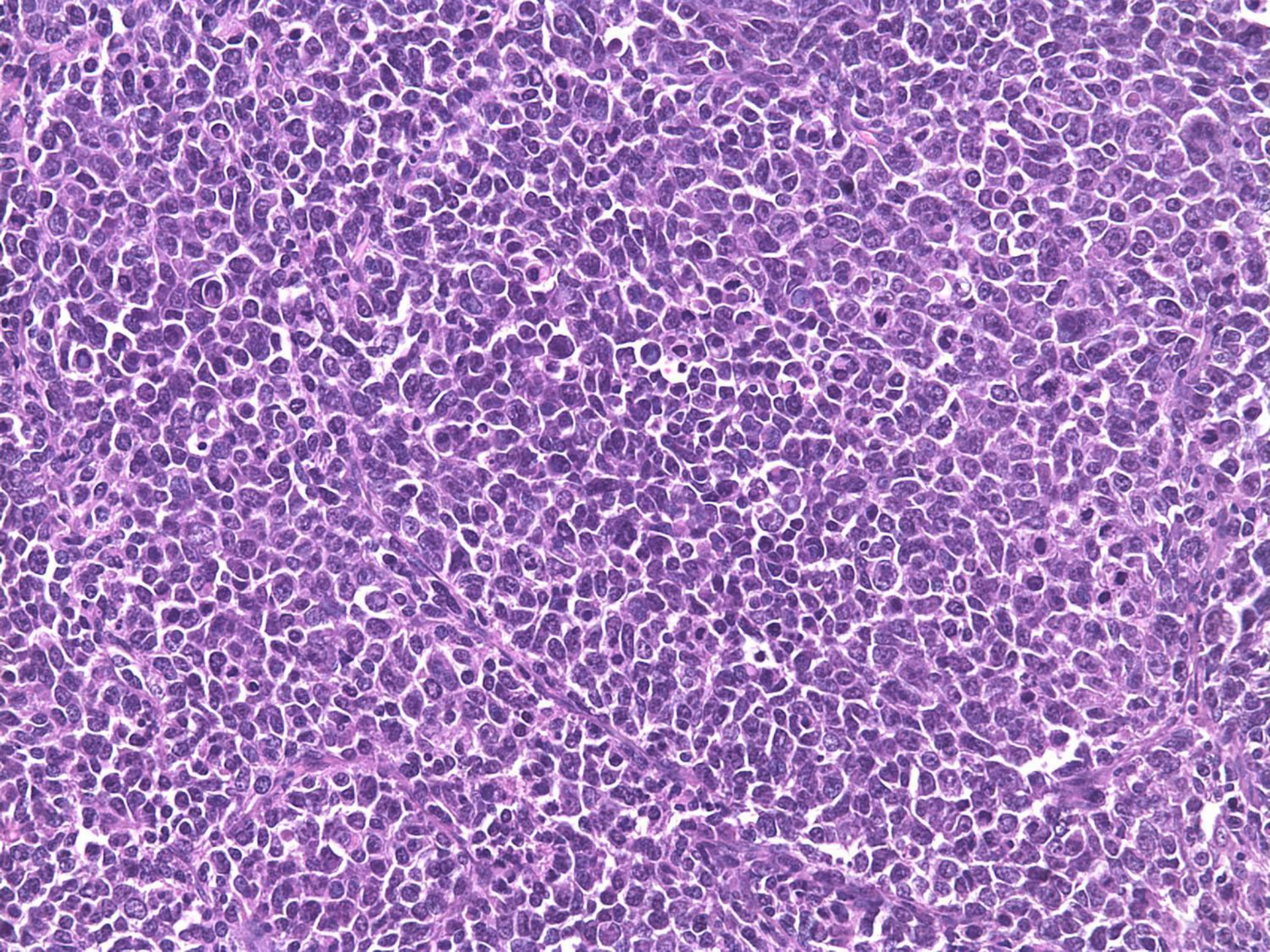


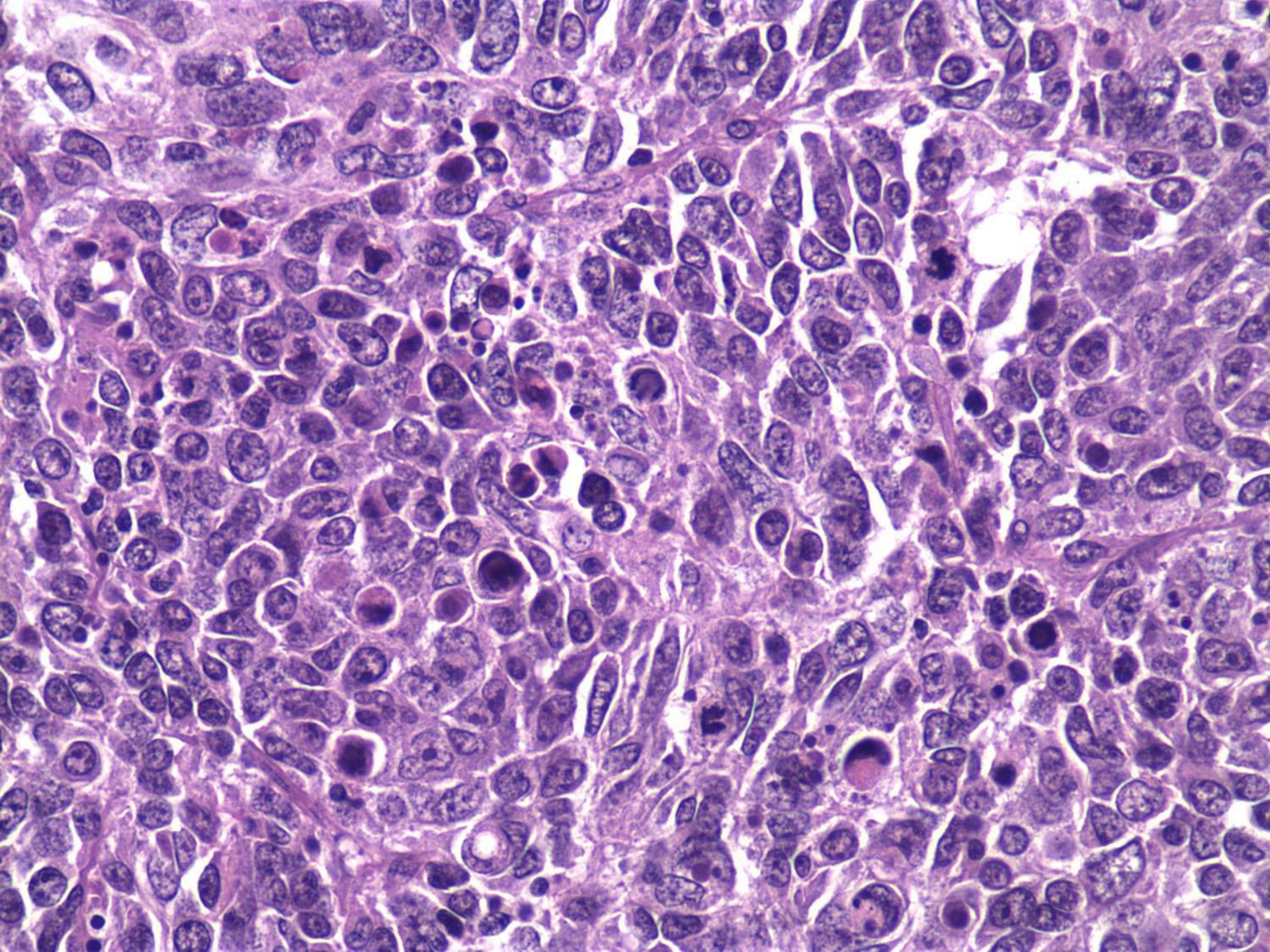


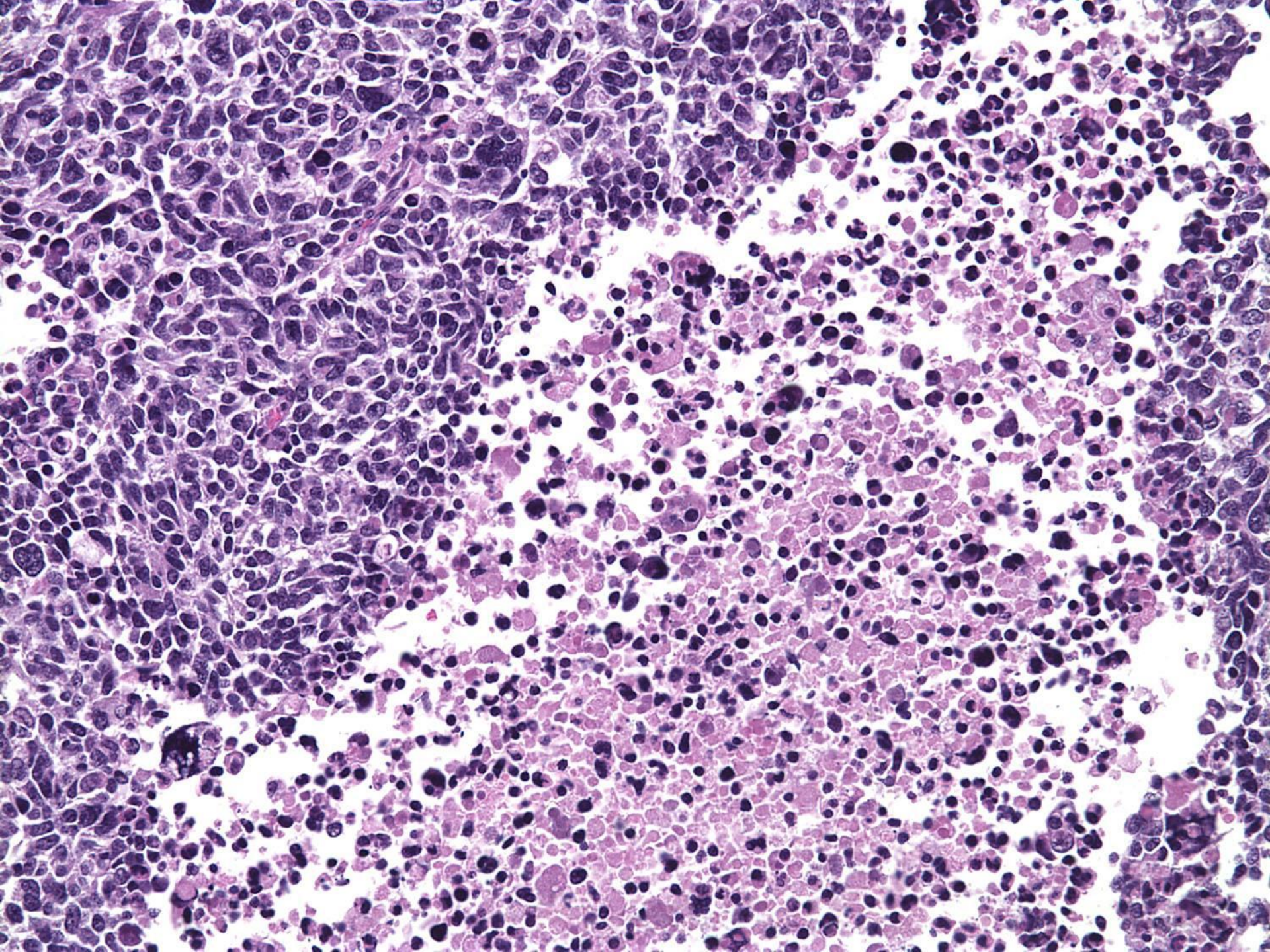


Small Cell Neuroendocrine Carcinoma

- ▶ Rare
- ▶ Present at advanced stages
- ▶ Bad prognosis, despite mixed elements
- ▶ Different chemotherapeutic agents
- ▶ When pure, cannot distinguish from small cell at other sites

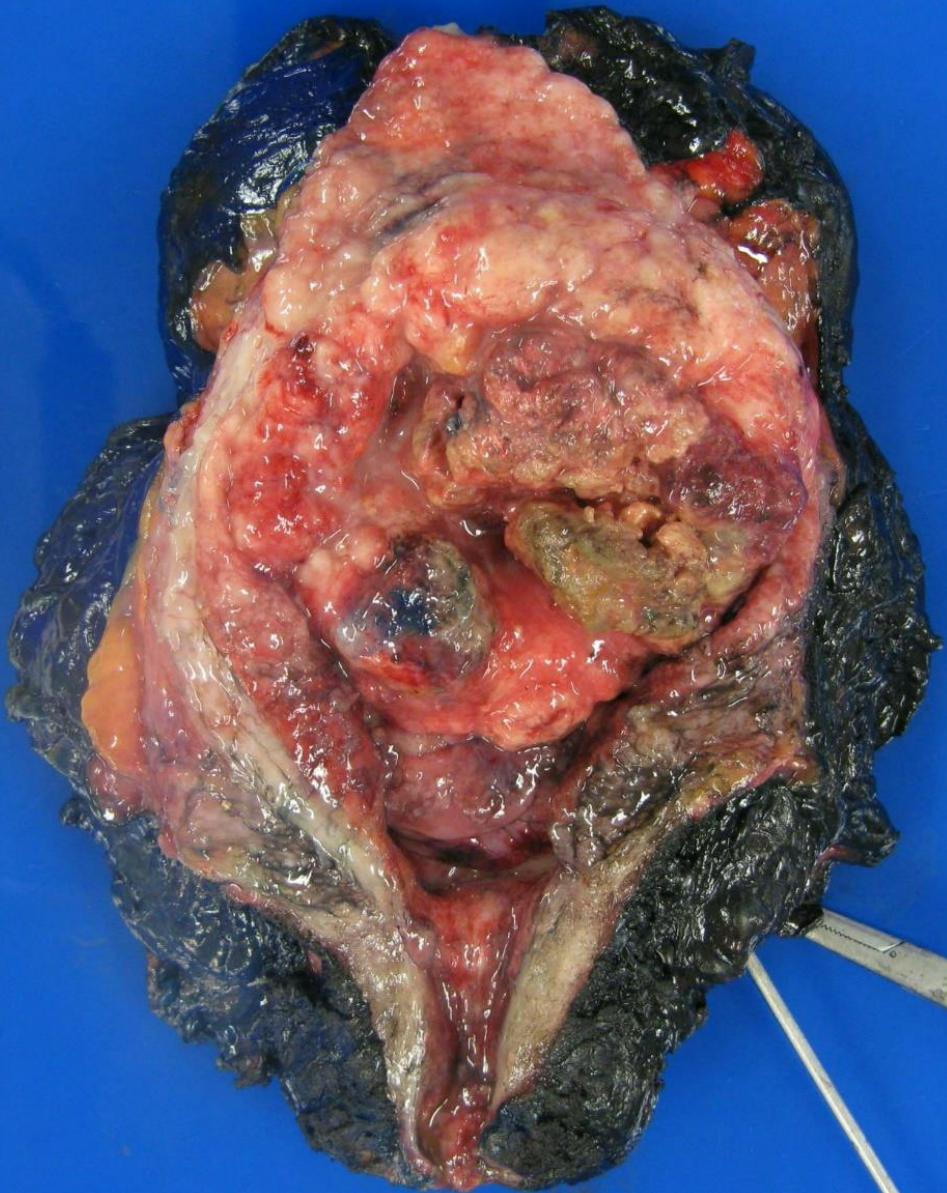






Invasive Urothelial Carcinoma- Divergent Differentiation:

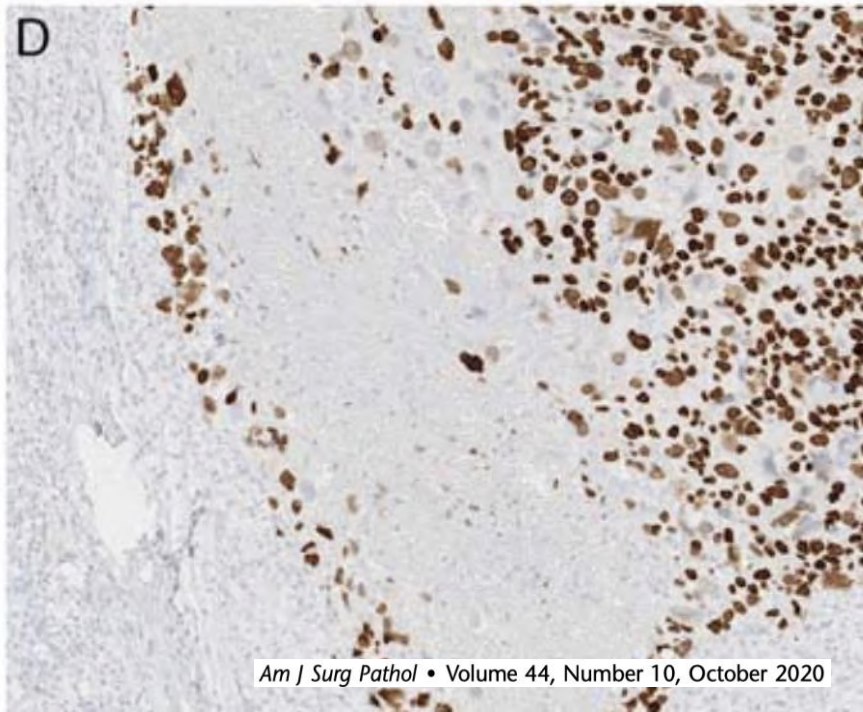
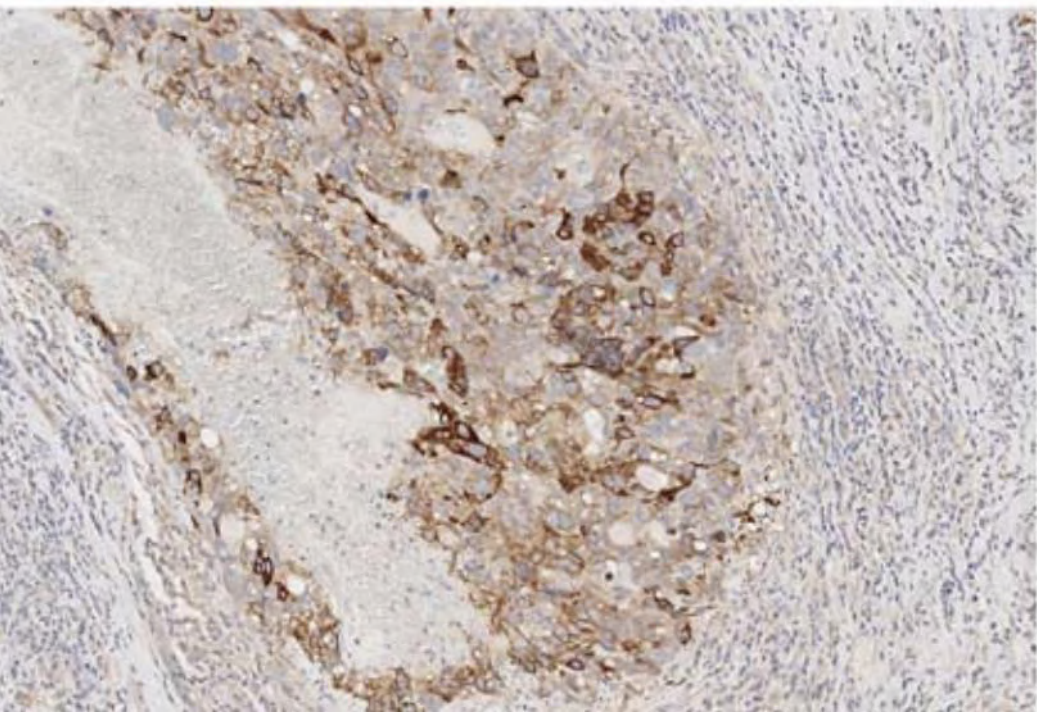
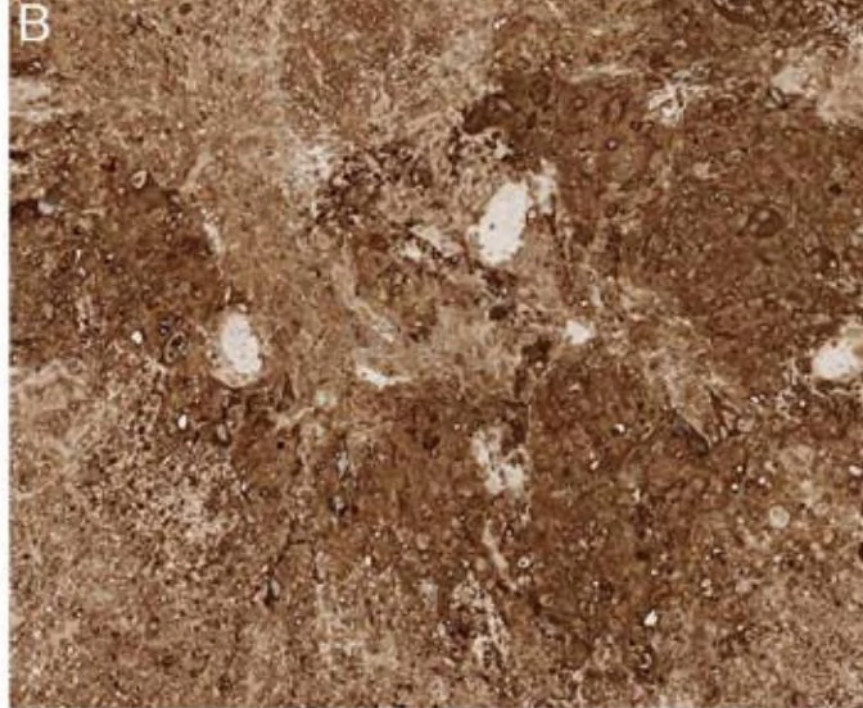
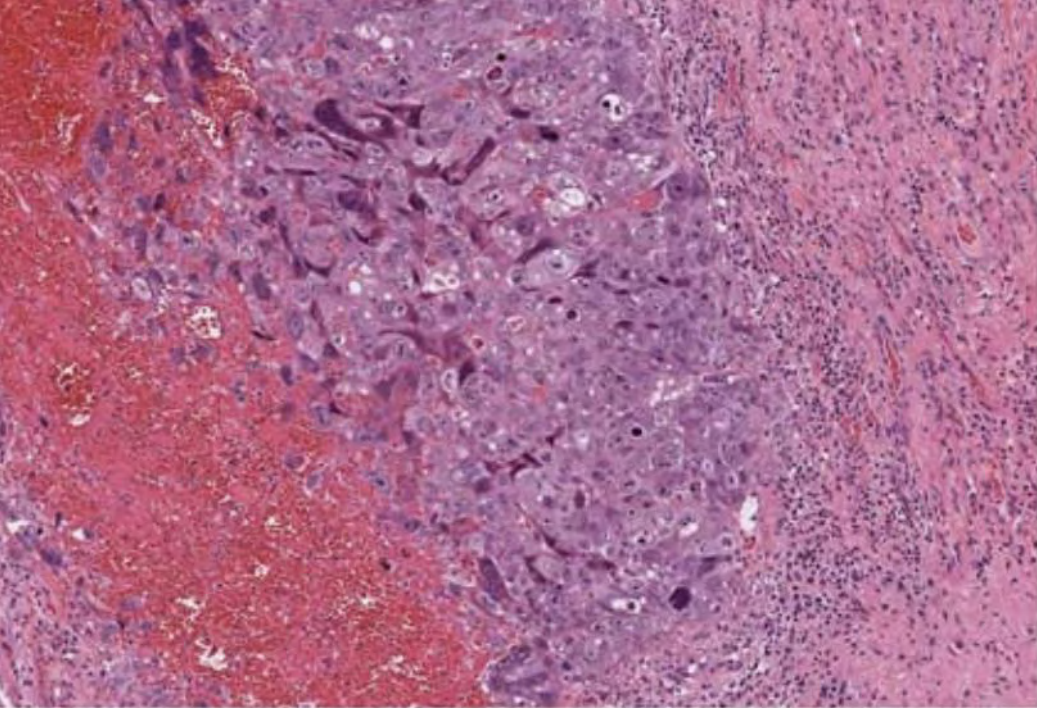
- ▶ Contains urothelial carcinoma NOS, either in situ or invasive
- ▶ In addition, can contain any one or more than one of:
 - ▶ Squamous differentiation: keratinization or intercellular bridges
 - ▶ Glandular differentiation: glandular component
 - ▶ Trophoblastic differentiation: syncytiotrophoblasts or choriocarcinoma

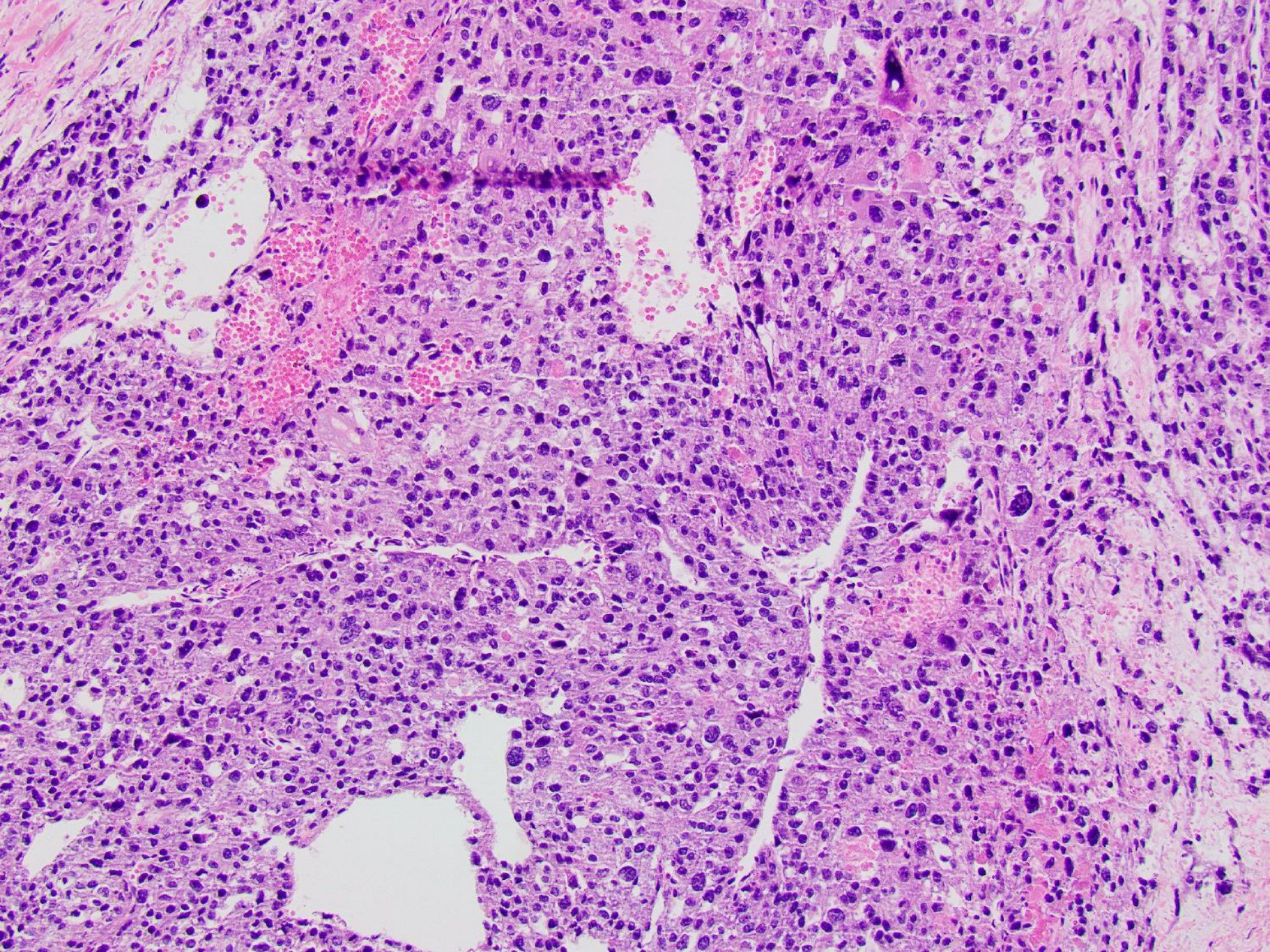




SAKURA RULES

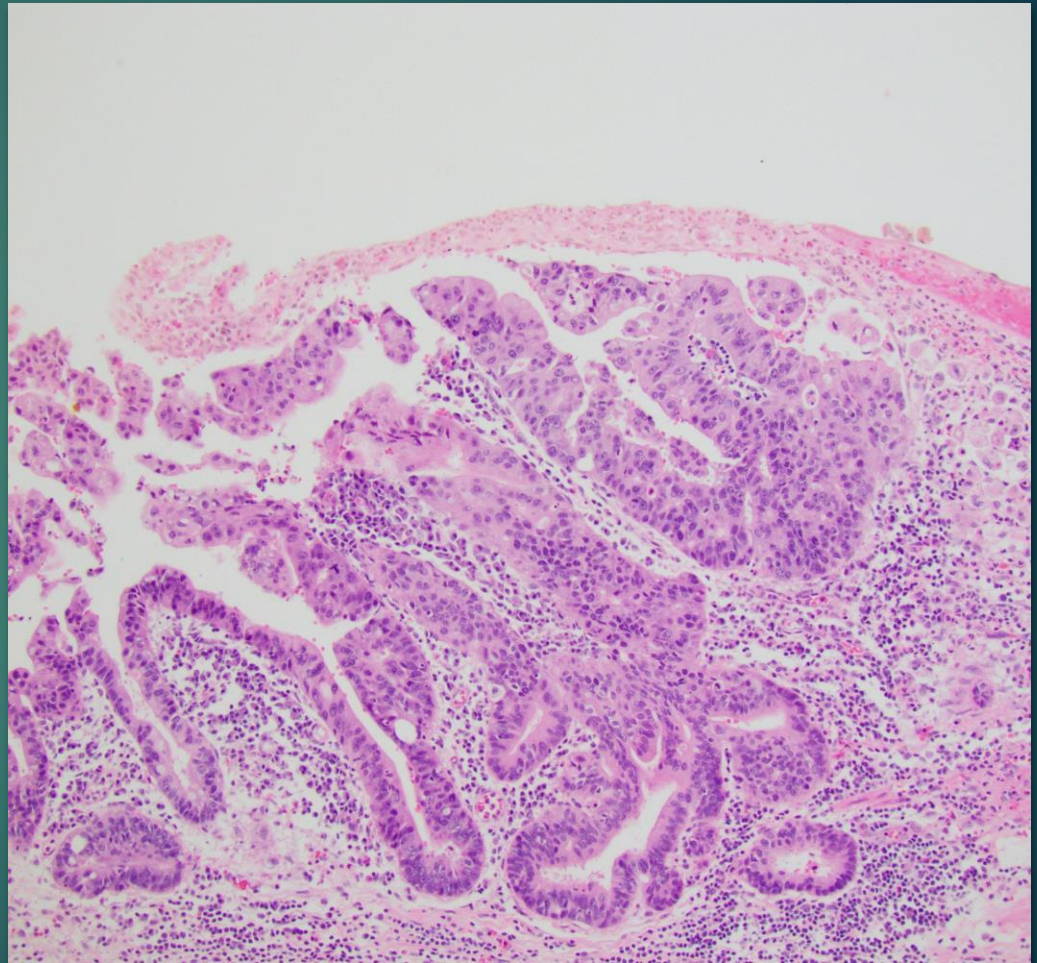
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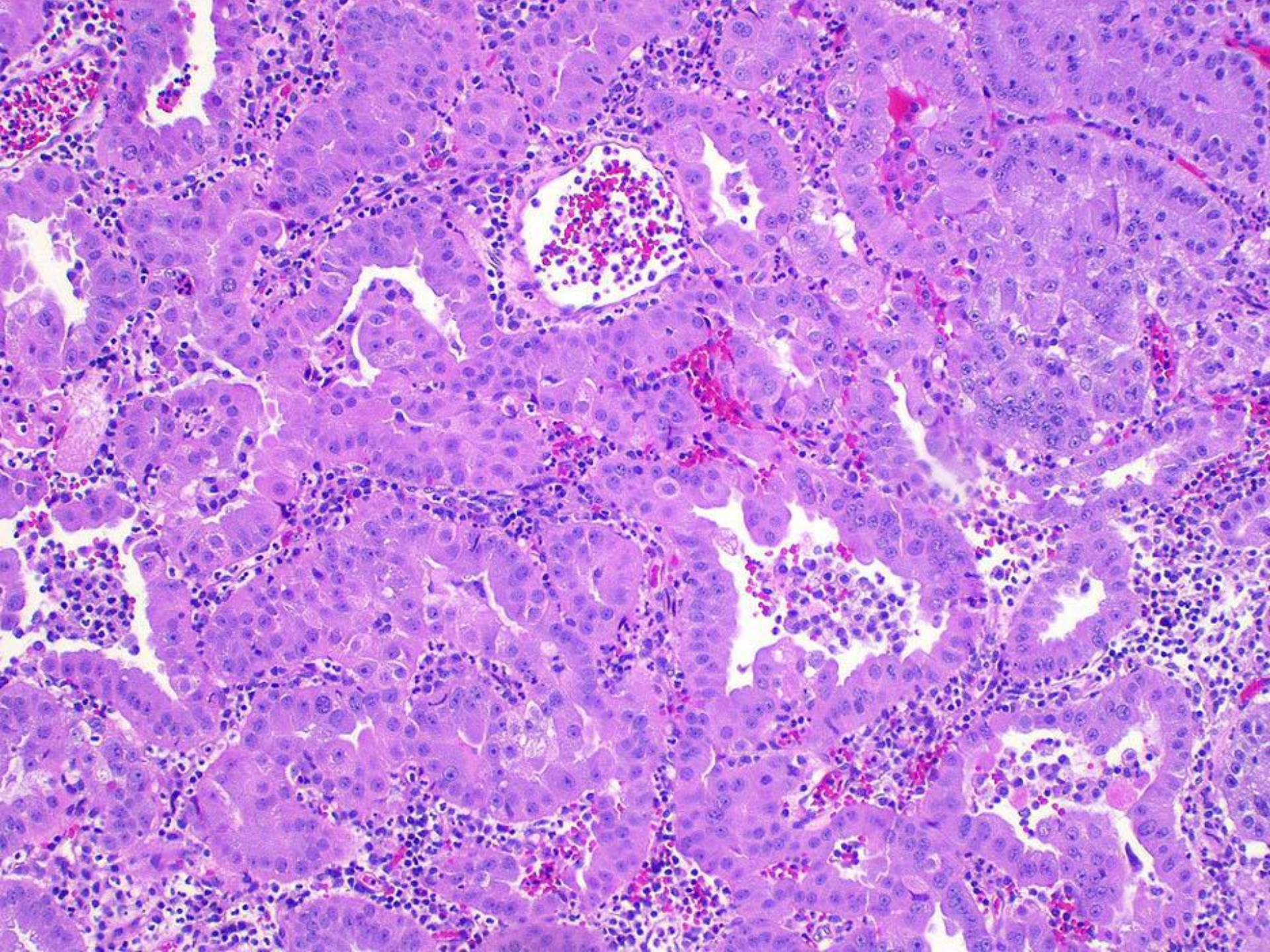
Glandular Neoplasms of the Bladder

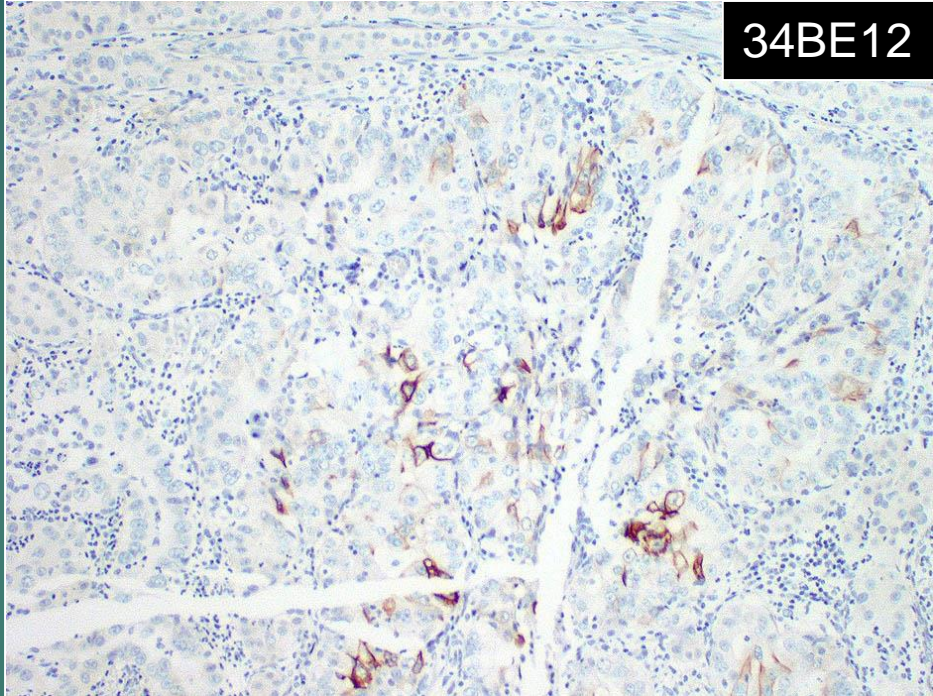
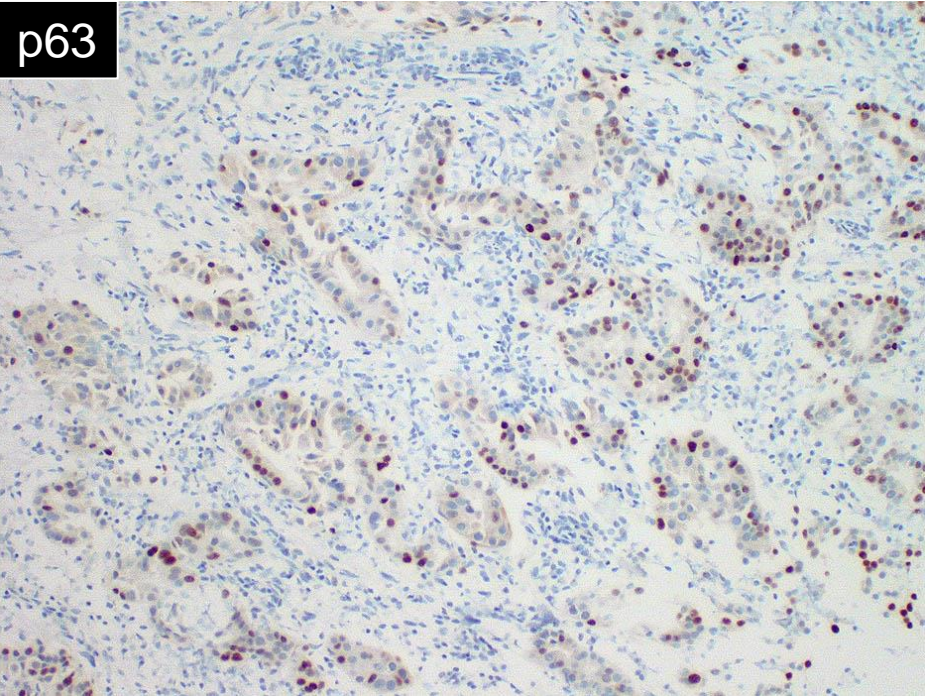
- ▶ Villous adenoma
- ▶ Adenocarcinoma in situ
- ▶ Invasive adenocarcinoma
 - ▶ 0.5-2%

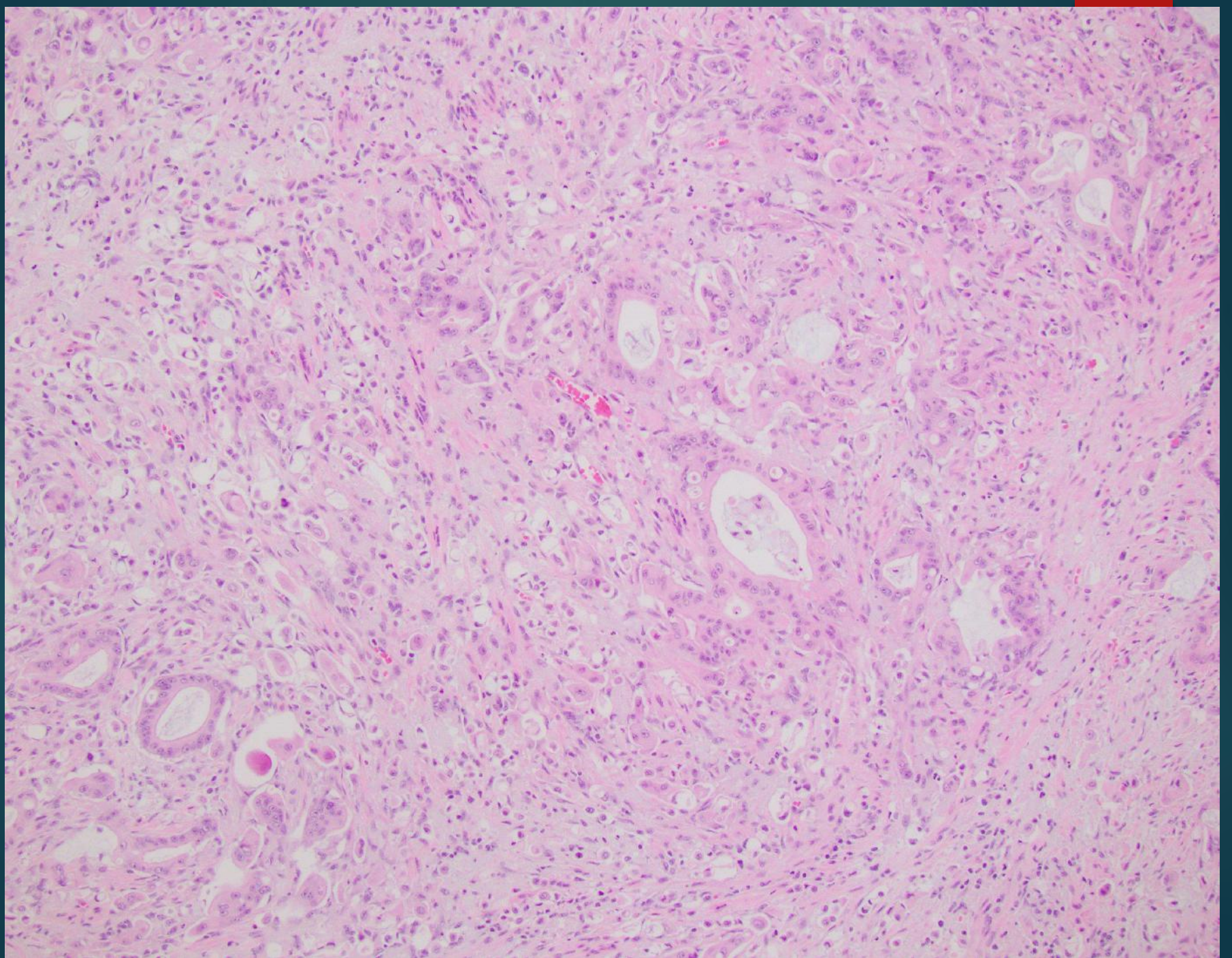


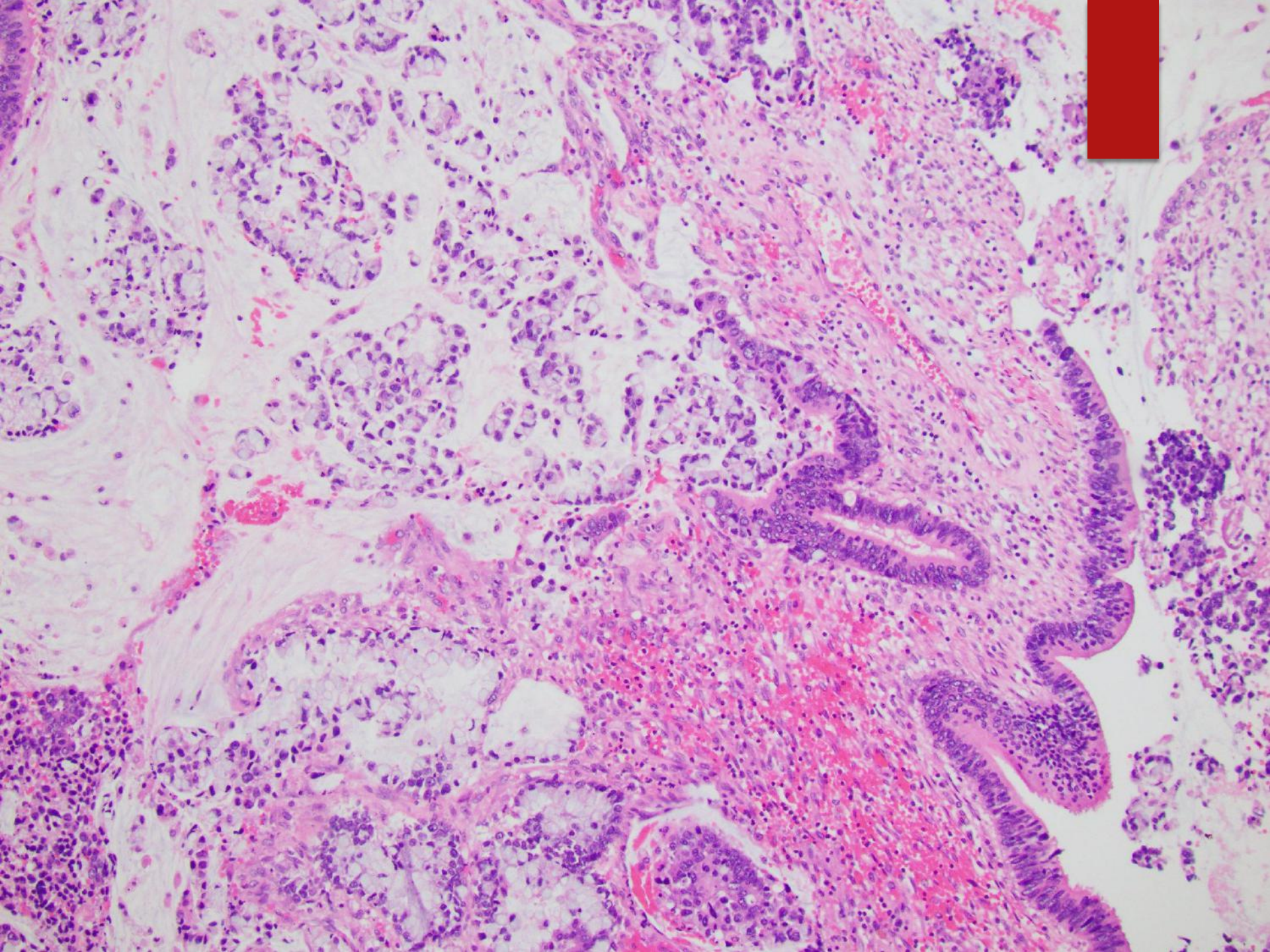
Invasive Adenocarcinoma

- ▶ Bladder extrophy and urachal remnants (dome) are risk factors
- ▶ Prognosis depends on stage.
- ▶ Signet ring cell carcinoma thought to have a worse prognosis.
- ▶ Distinction between secondary and primary tumors might pose a problem.



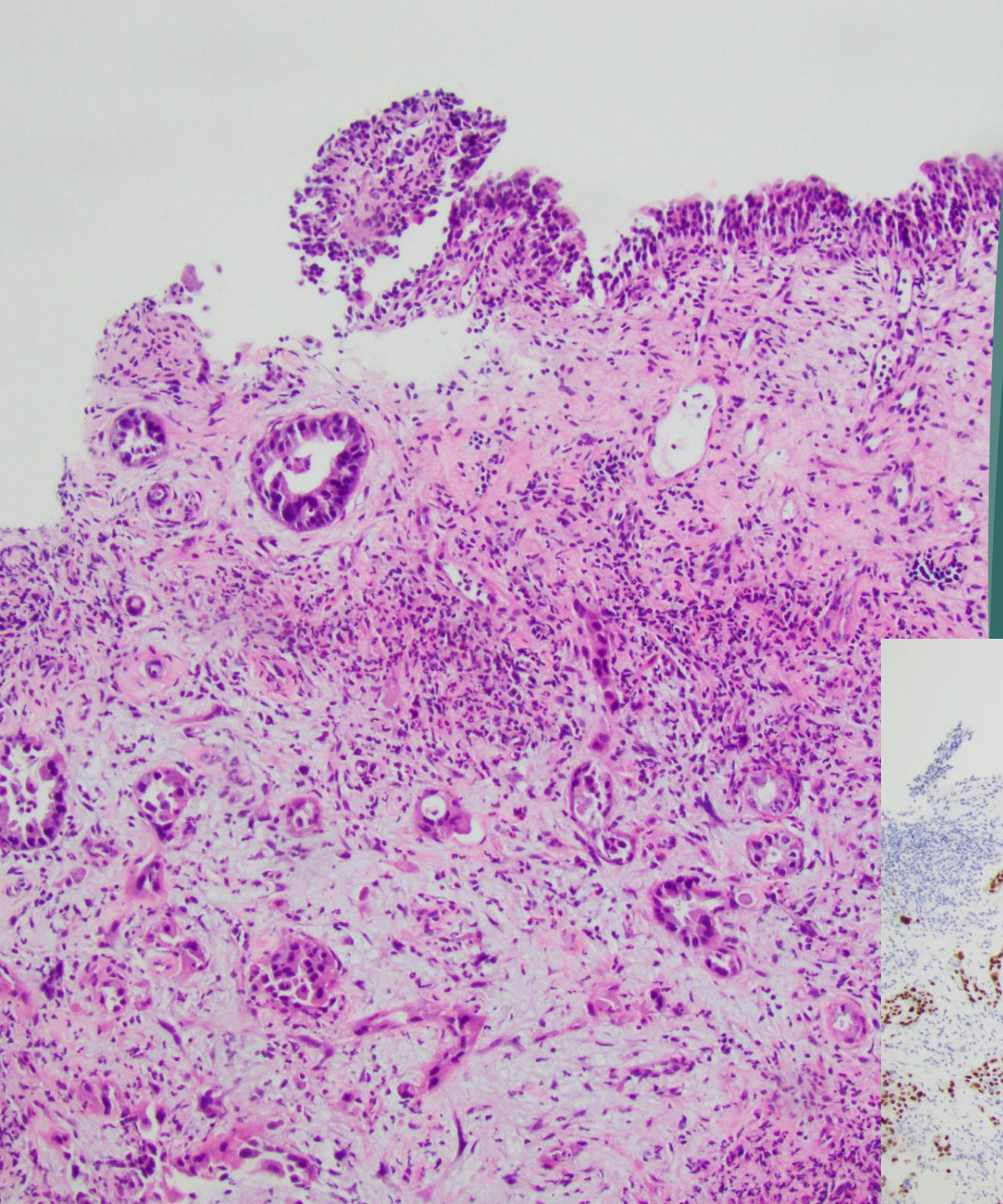






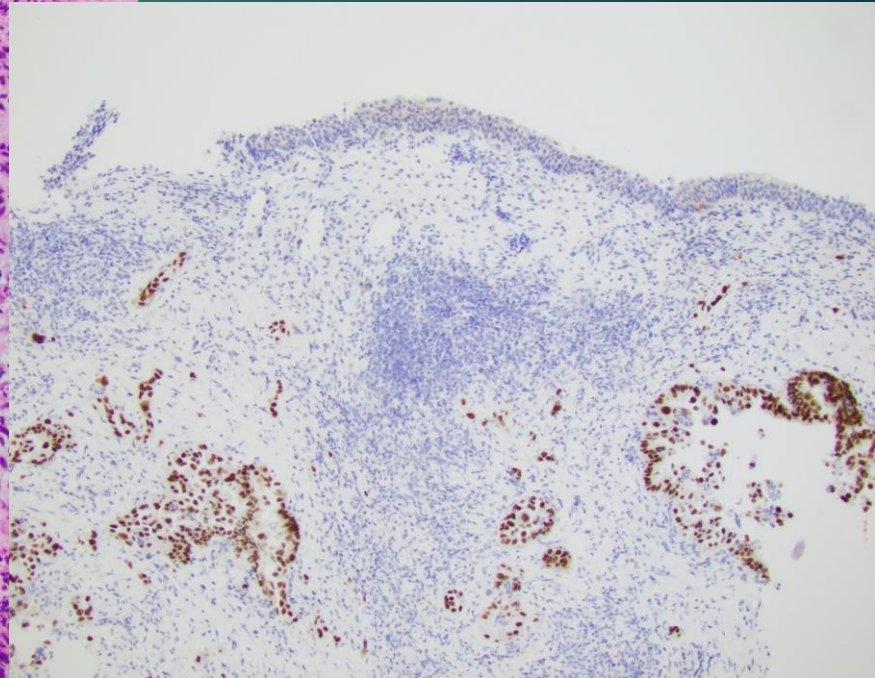
ENTERIC-TYPE ADENOCARCINOMA IMMUNOHISTOCHEMISTRY

	Bladder	Colon
CK7+/CK20-	41%	almost 0%
β -catenin	cytoplasm	nuclear



Secondary tumors/ Mullerian

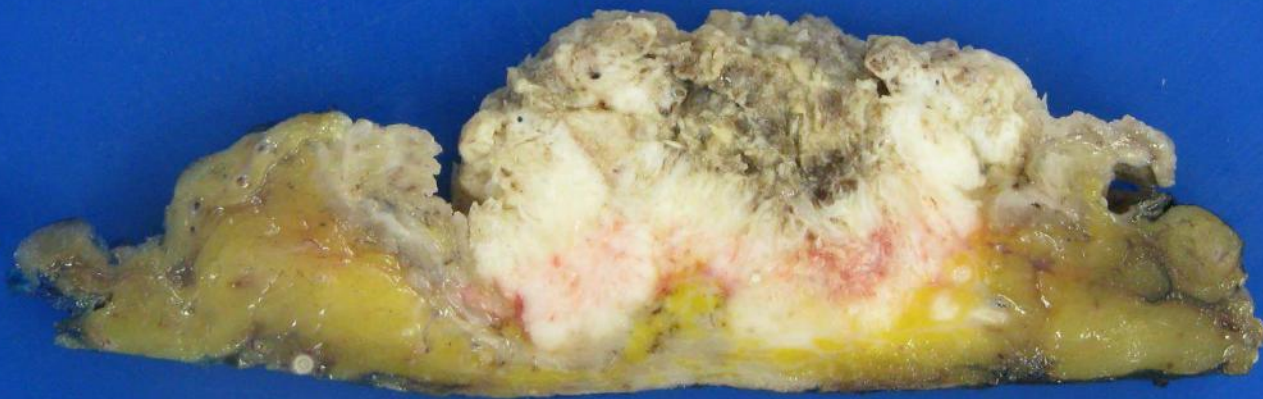
PAX8

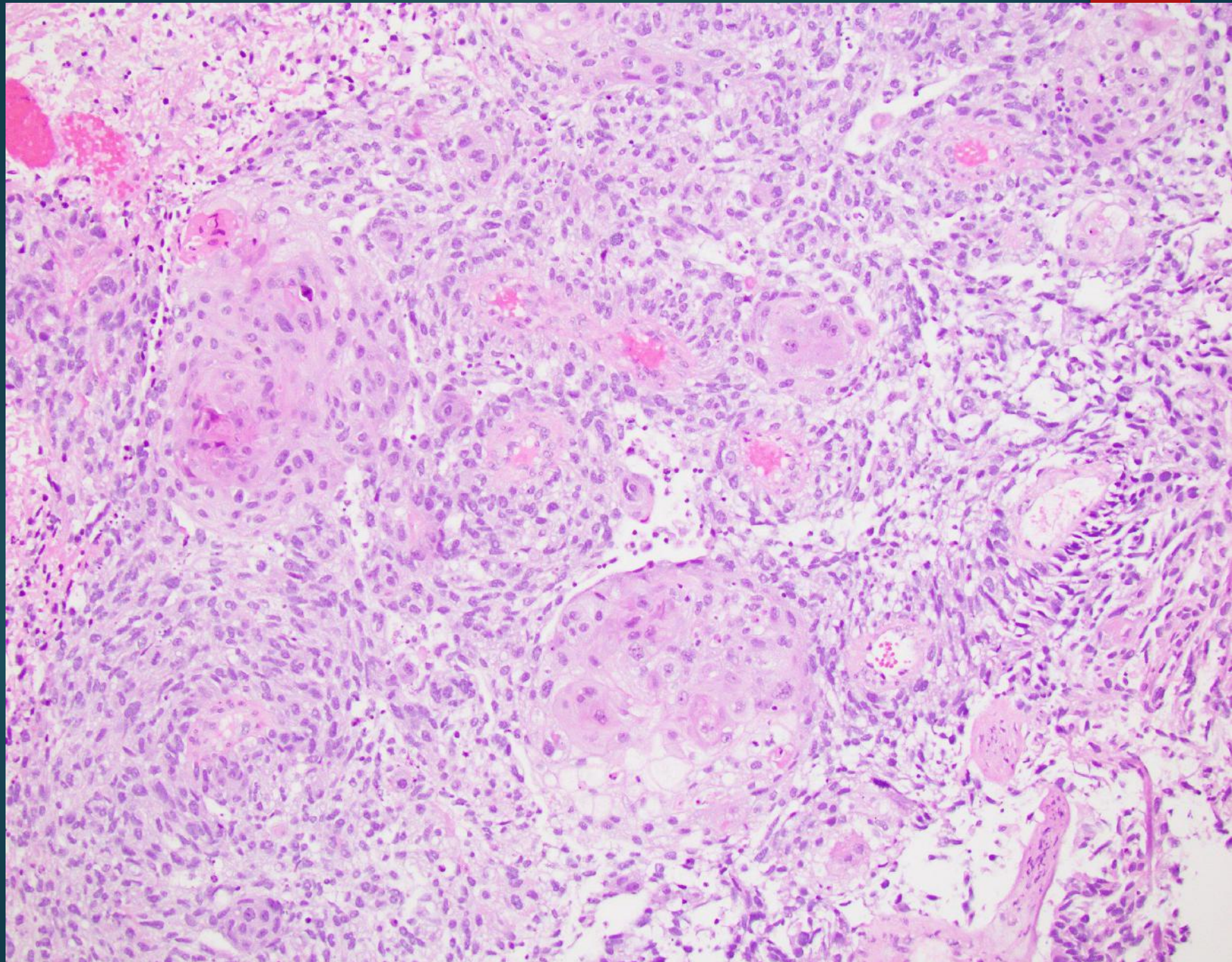


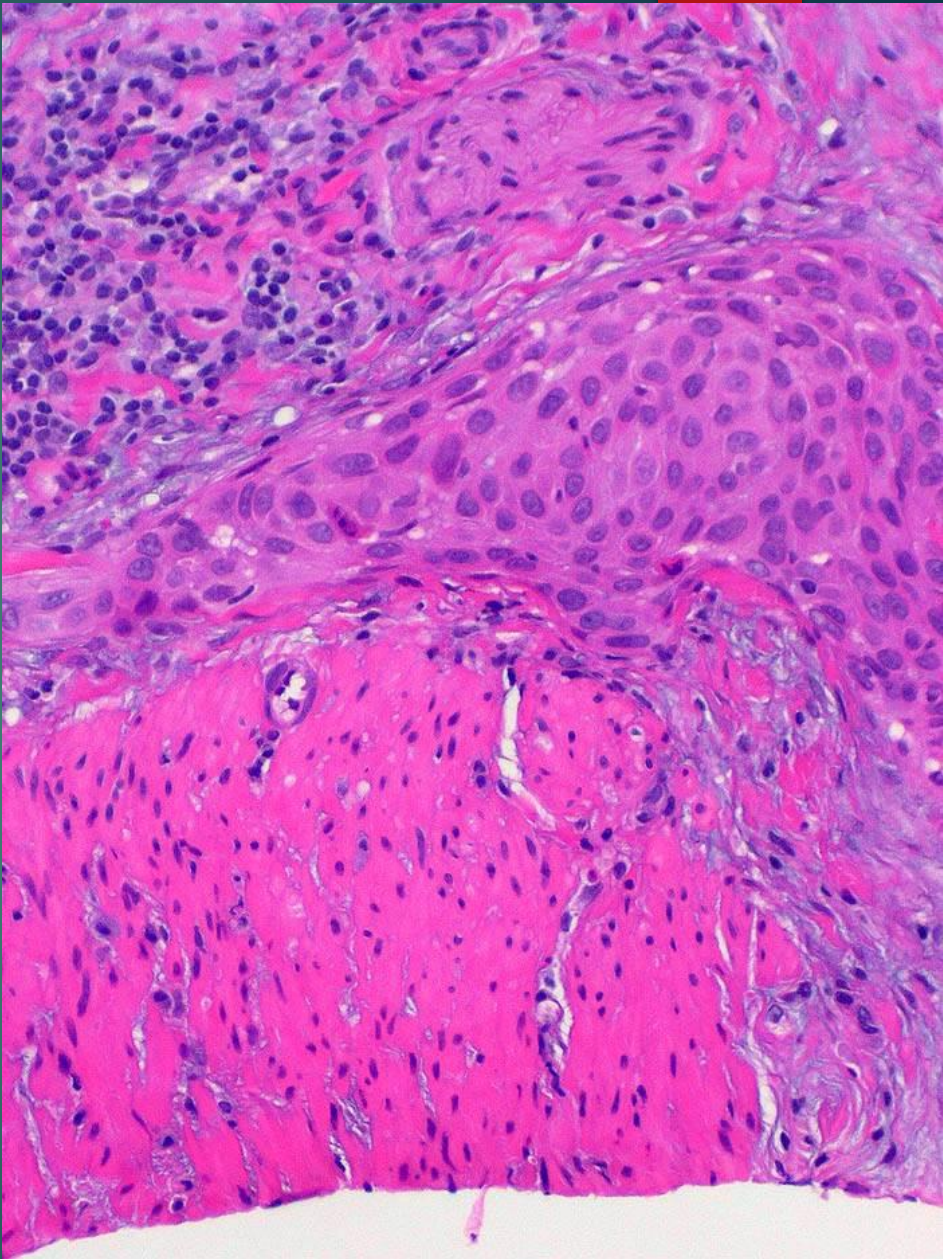
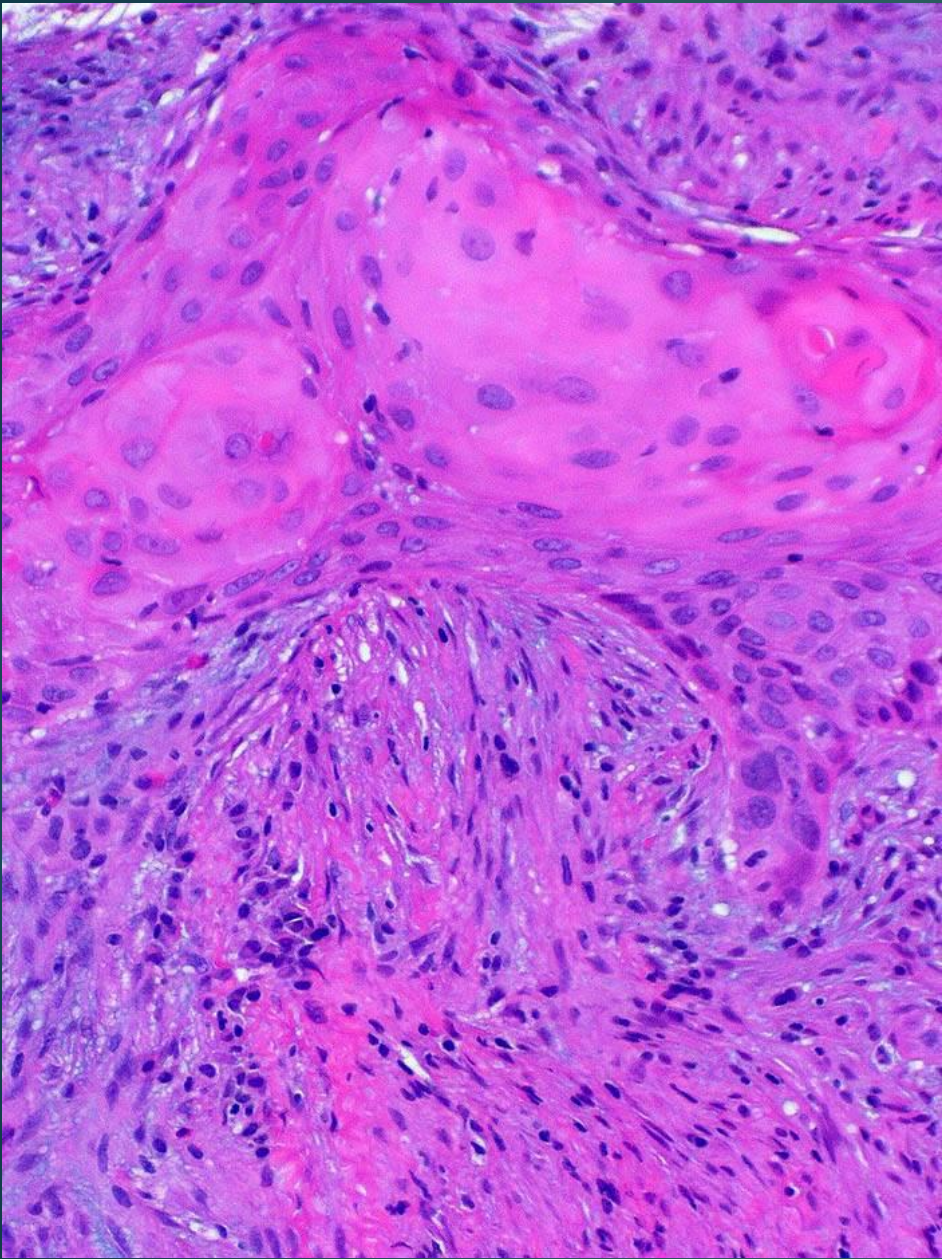
Squamous cell carcinoma

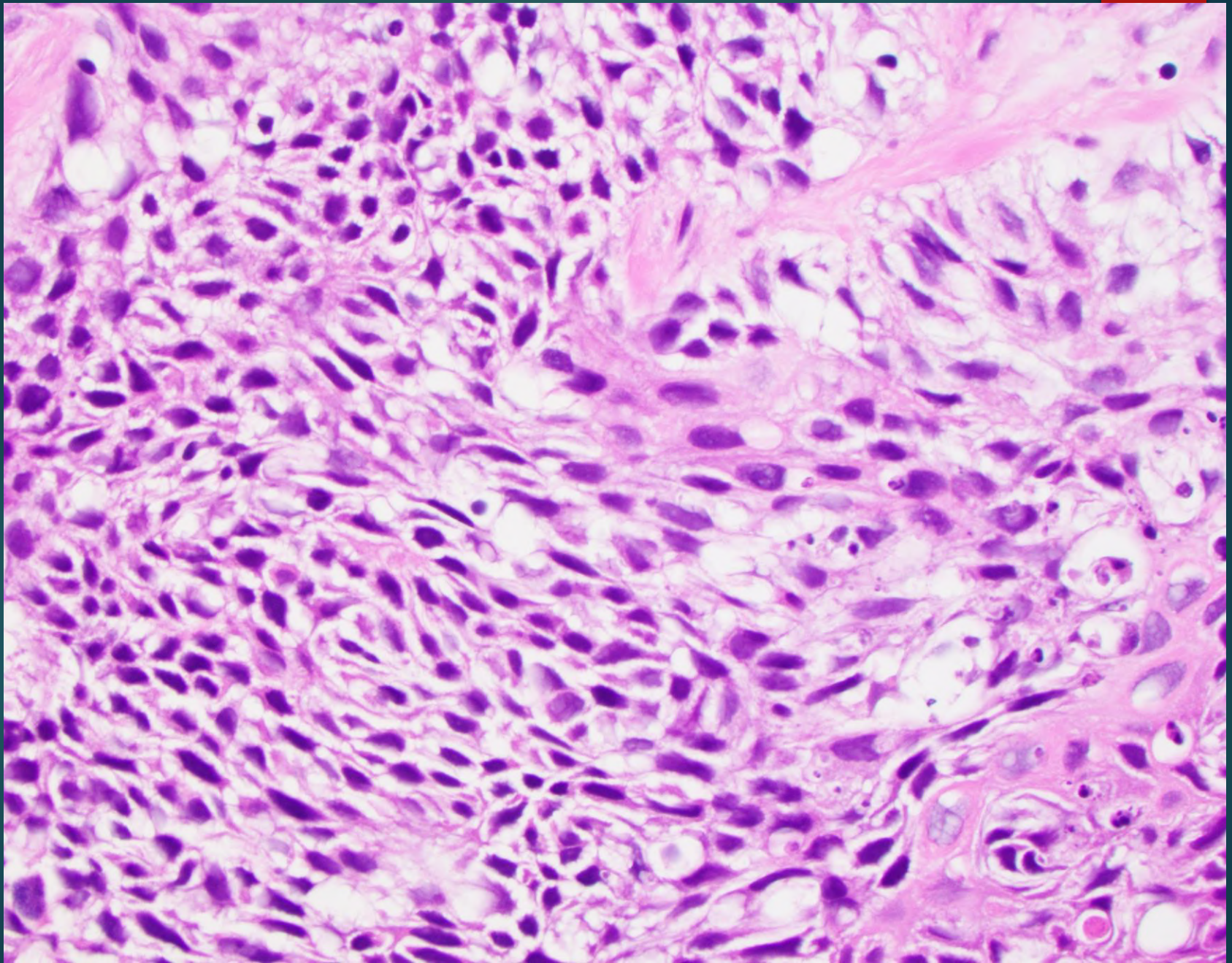
- ▶ Pure squamous cell carcinoma 5%
- ▶ Poor prognosis
- ▶ Usually presents with higher stages
- ▶ 25% metastatic at presentation
- ▶ Different therapy
- ▶ DDX: secondary SCC

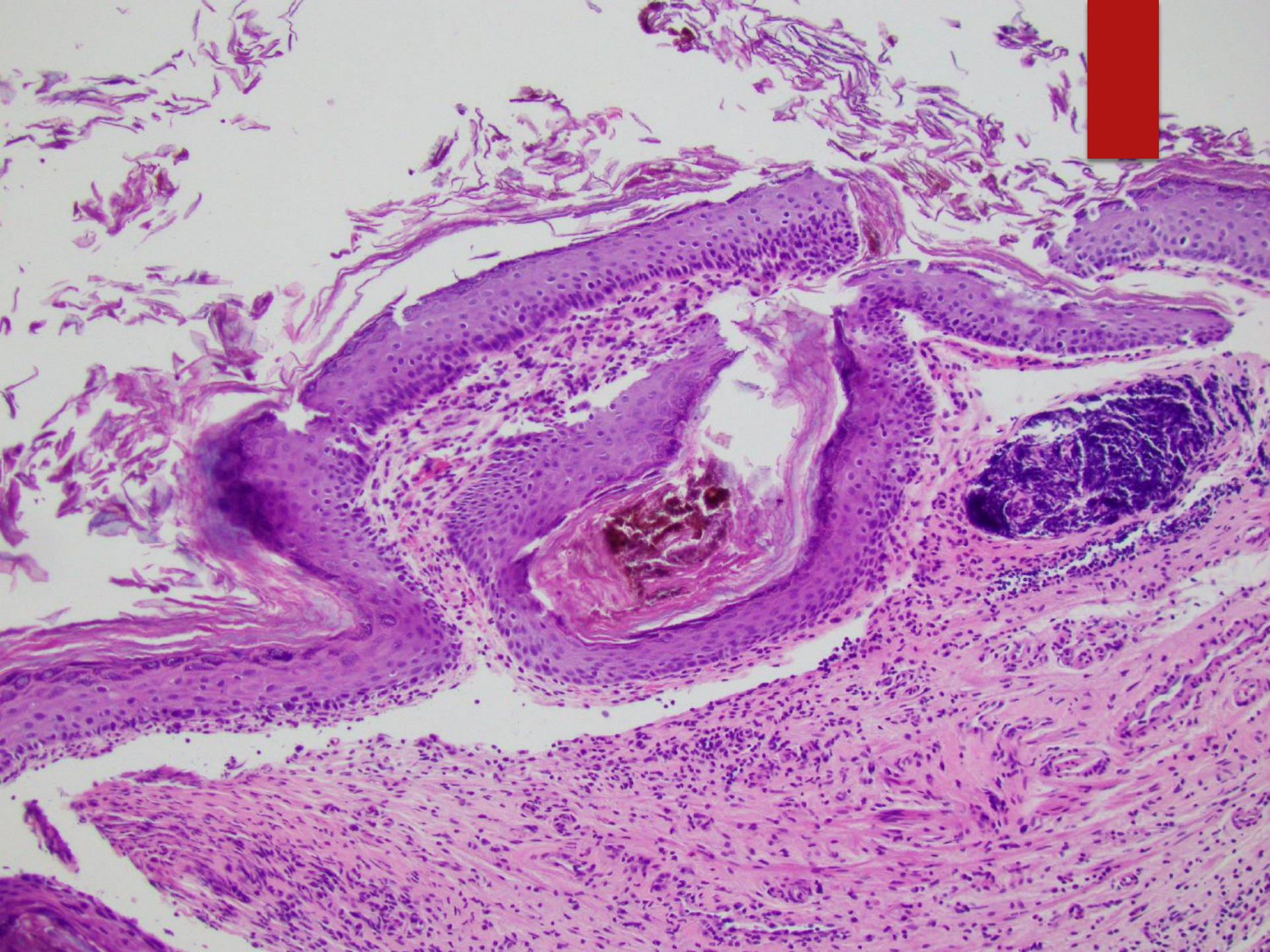






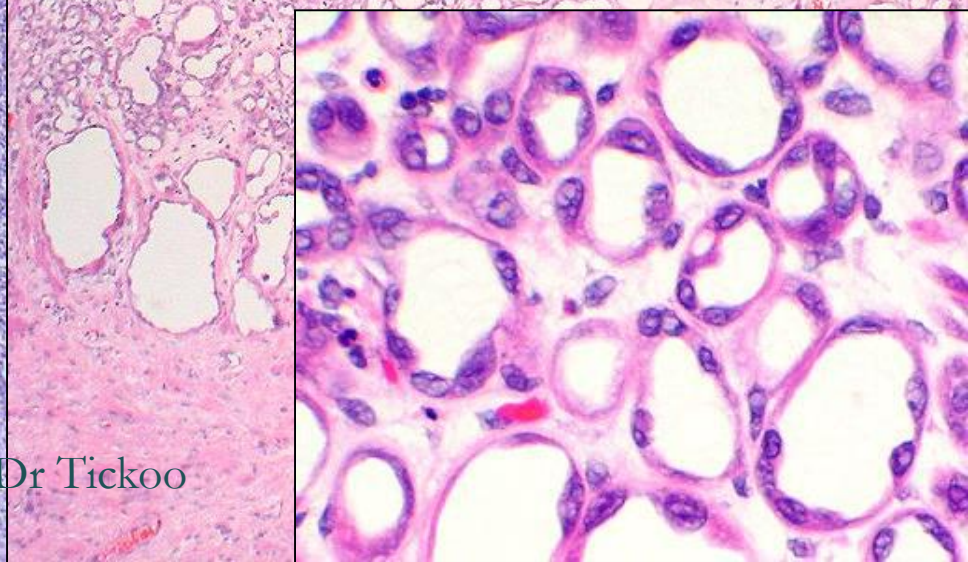
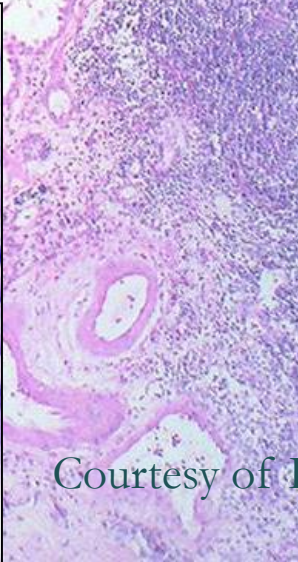
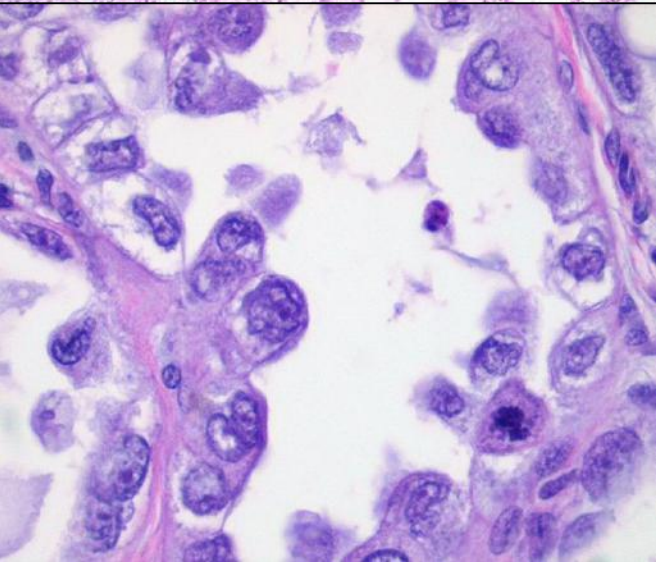
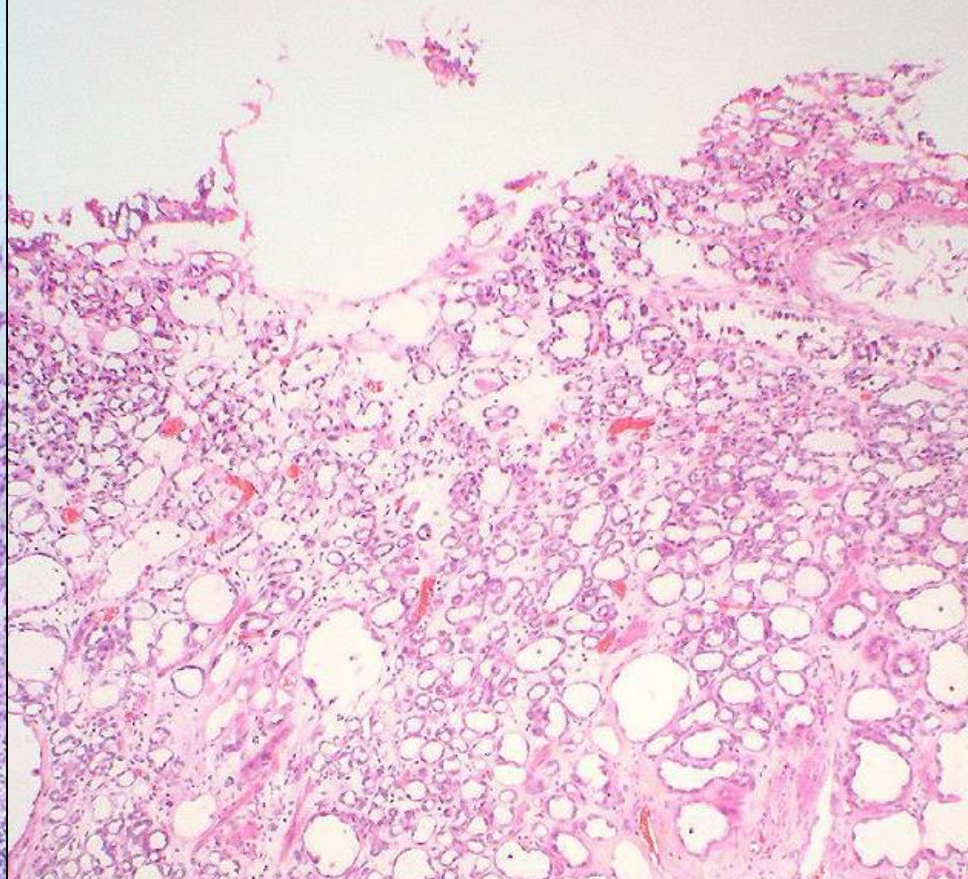
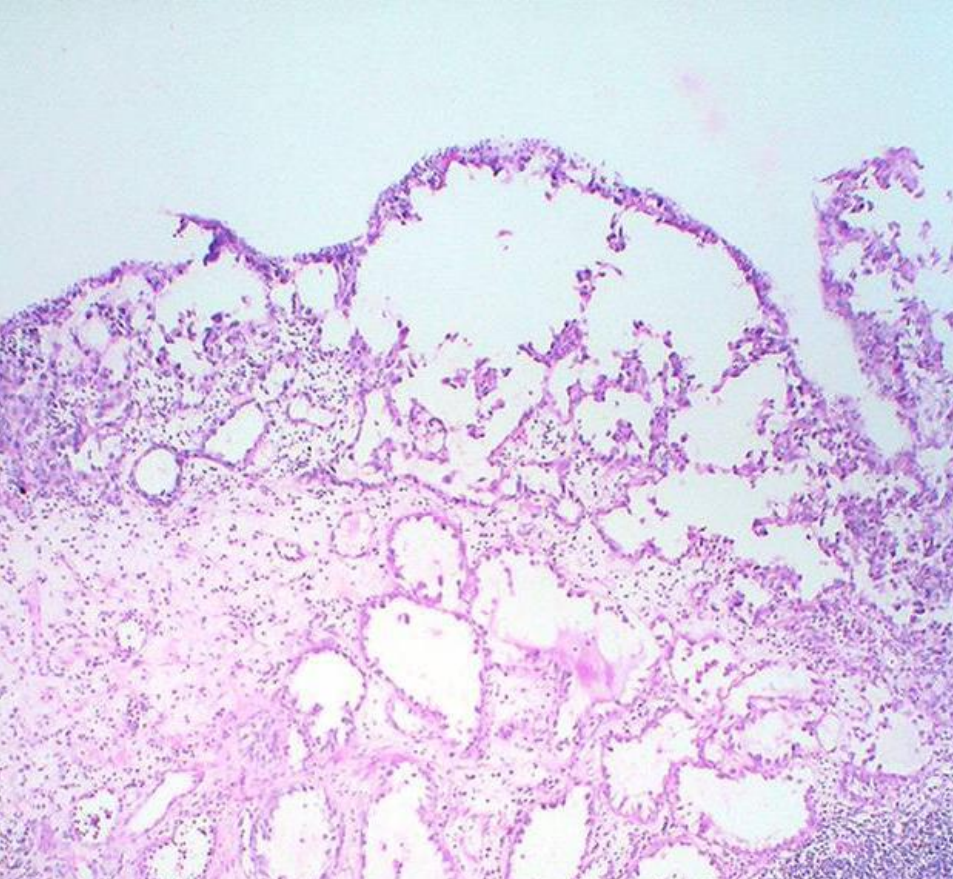






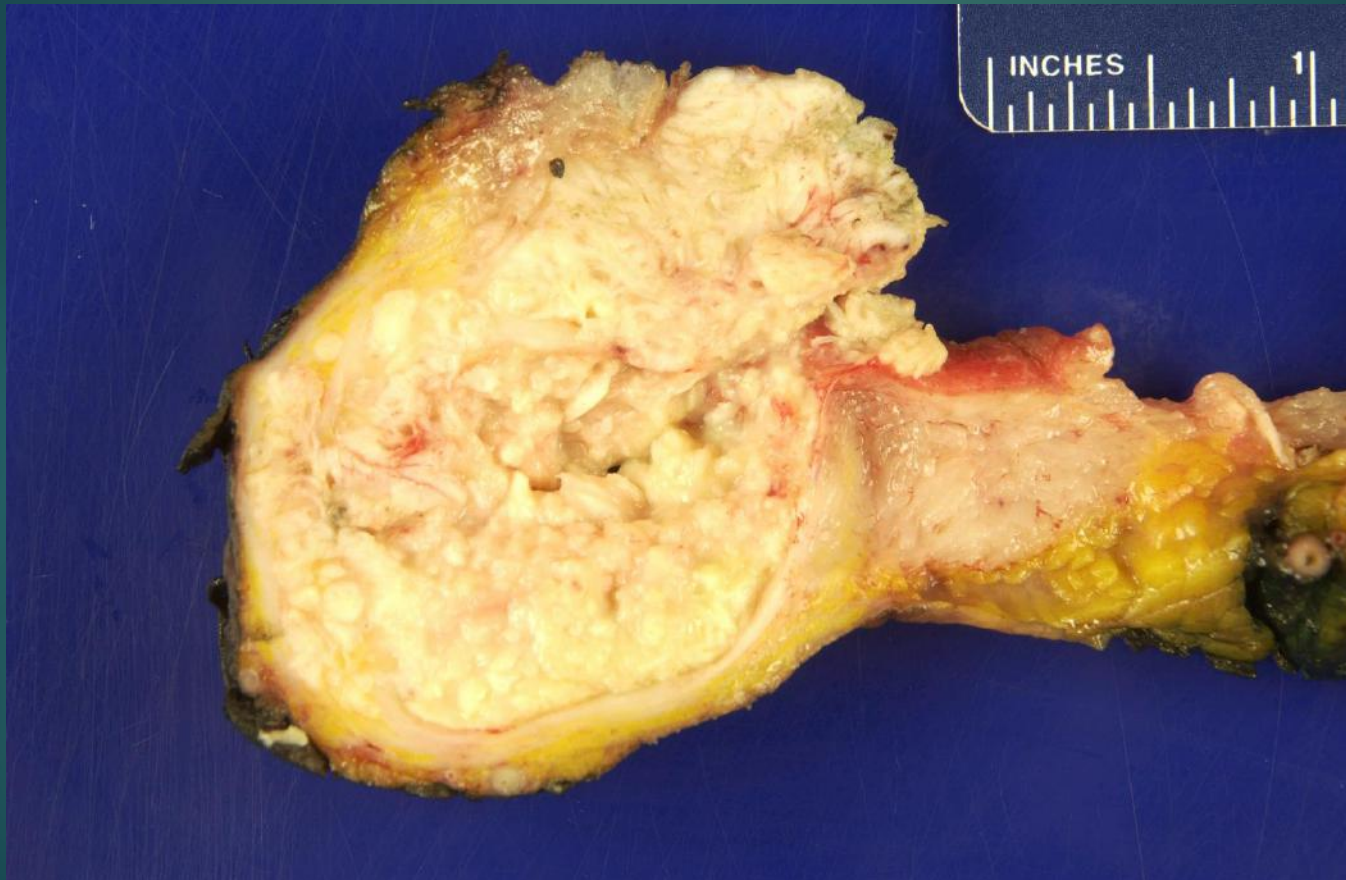
Clear Cell Carcinoma

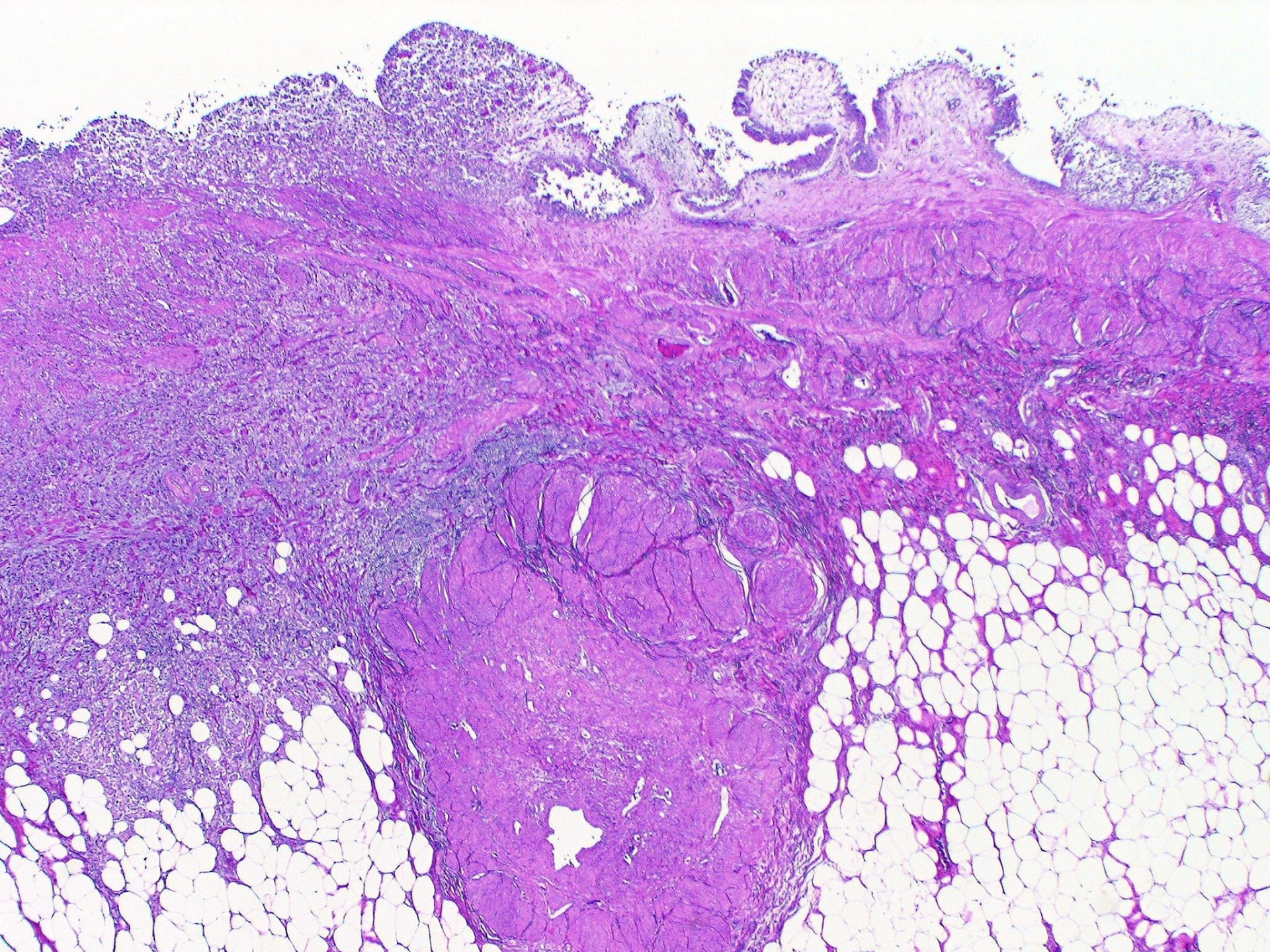
- ▶ Rare
- ▶ More common in urethra with female predominance
- ▶ Thought to be of Mullerian origin
- ▶ CK, CA125, PAX2 and 8 positive



Courtesy of Dr Tickoo

Diverticula





Non-epithelial neoplasms

▶ Benign

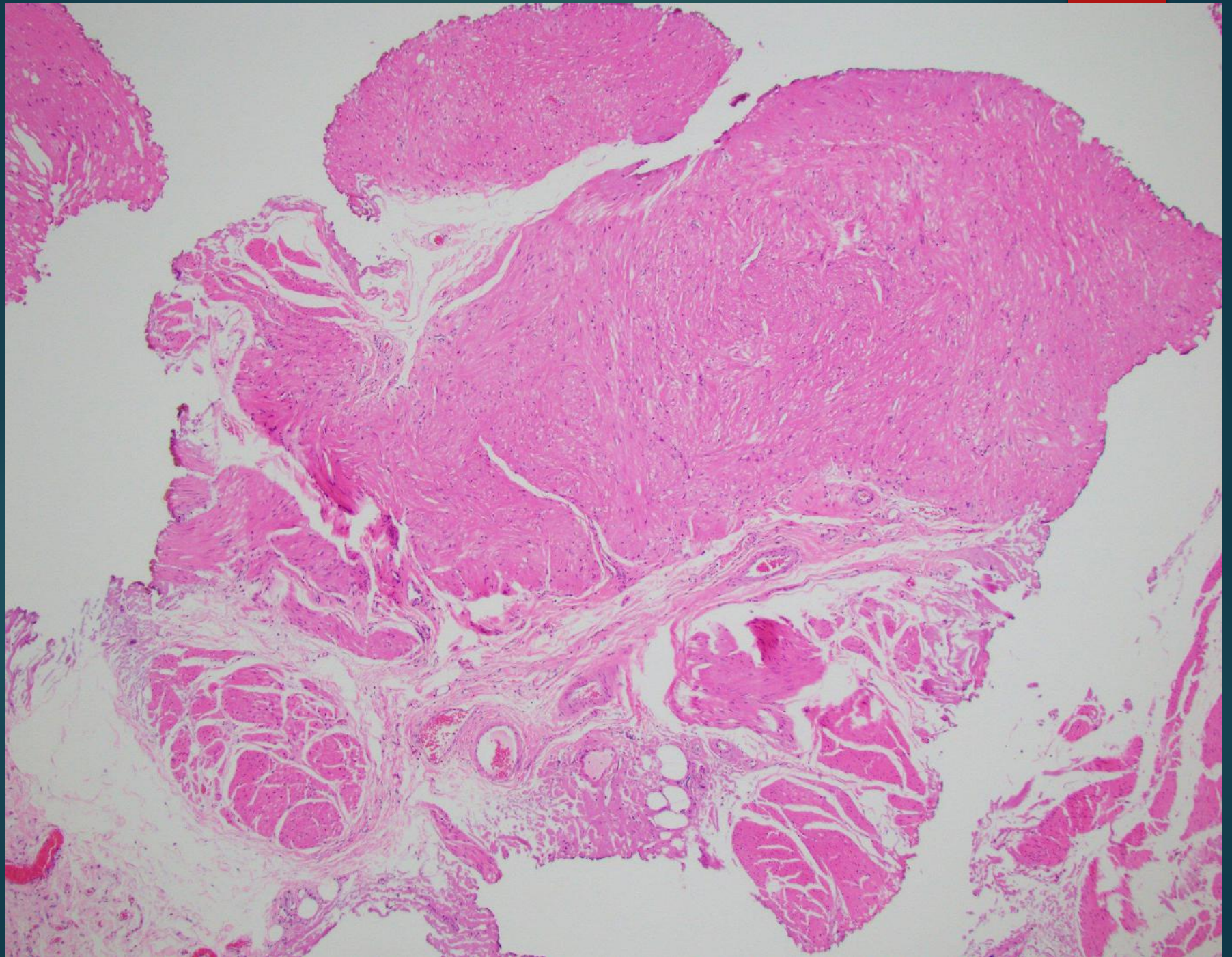
- ▶ Leiomyoma
- ▶ Pseudosarcomatous myofibroblastic proliferations

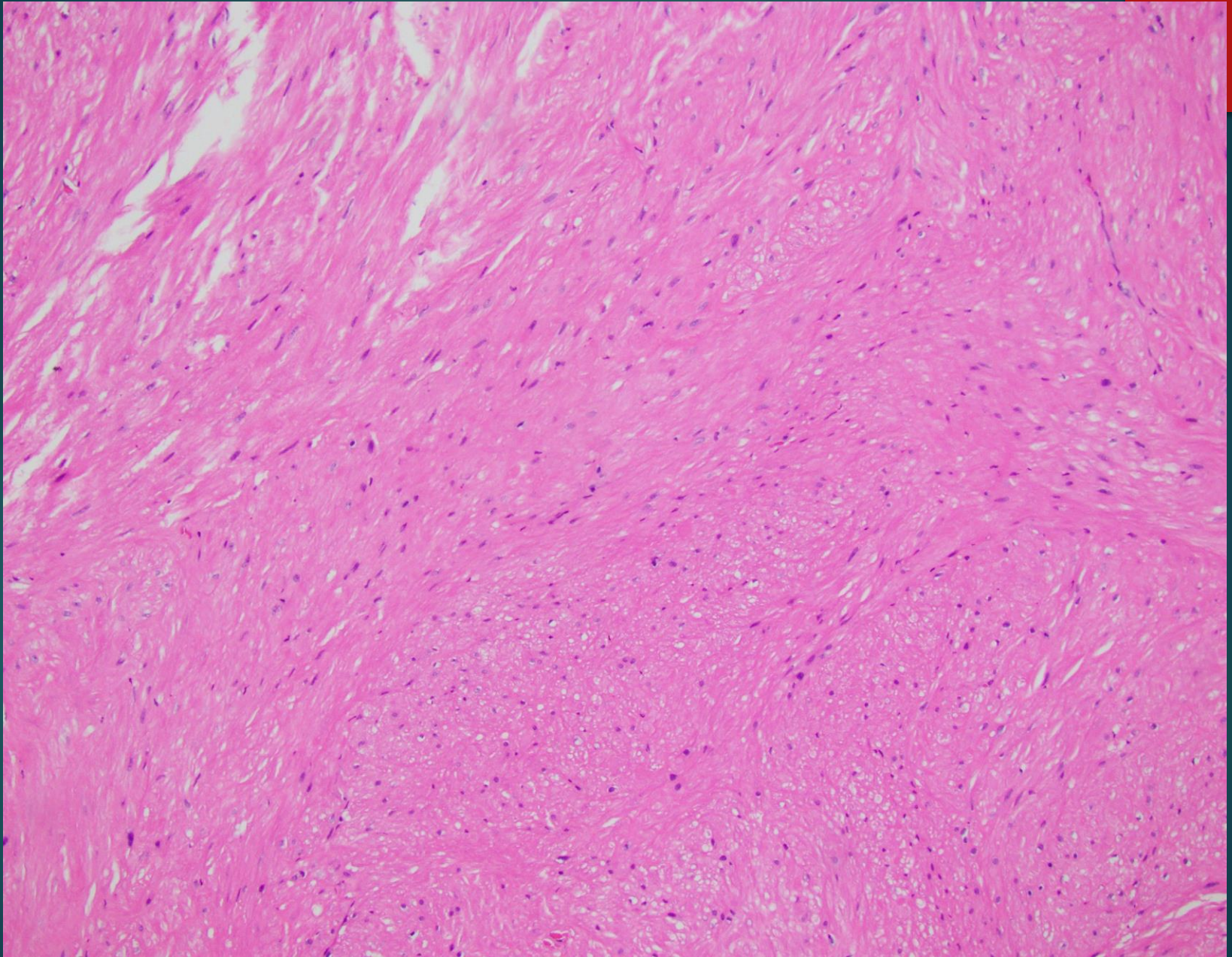
▶ Malignant

- ▶ Leiomyosarcoma
- ▶ Rhabdomyosarcoma
- ▶ Melanoma

Leiomyoma

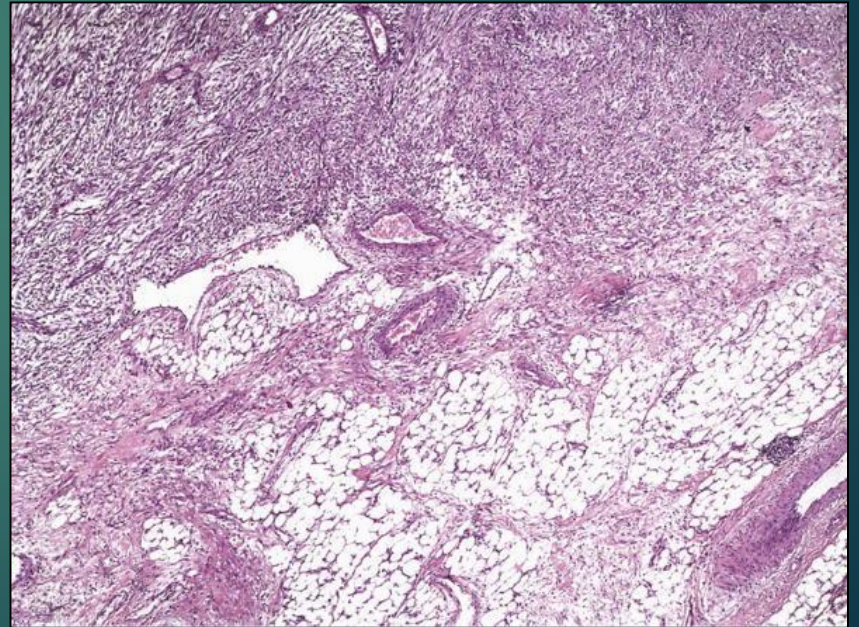
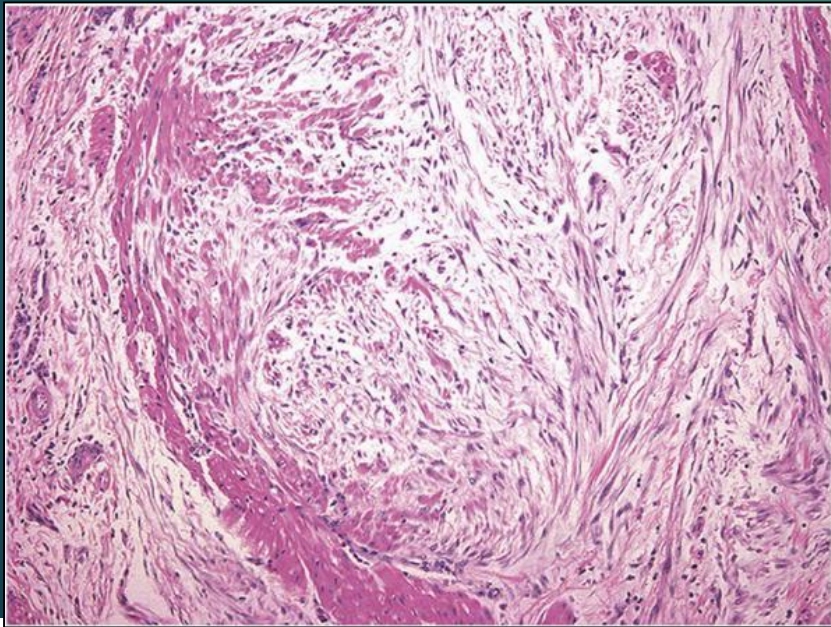
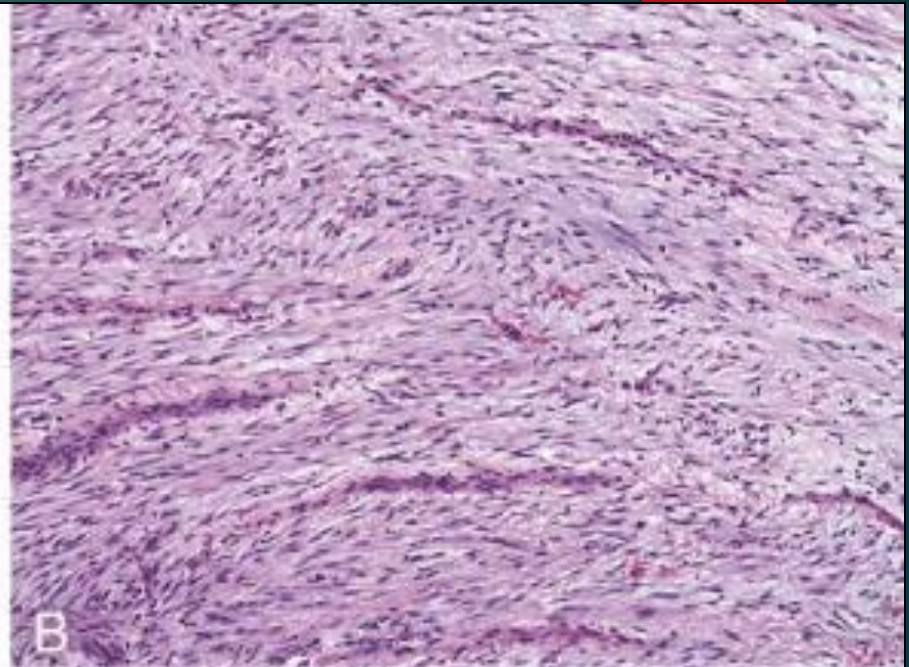
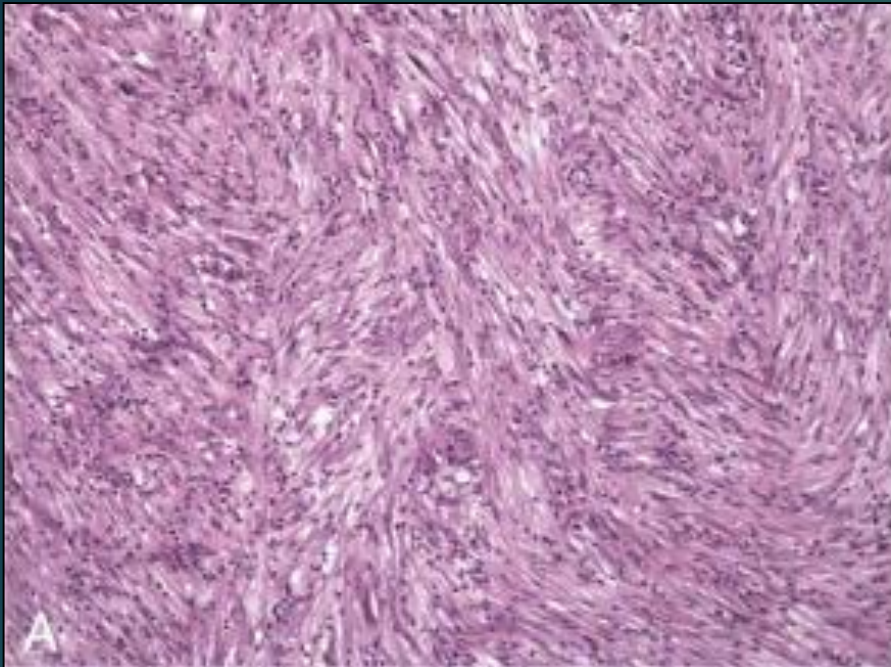
- ▶ Most common benign mesenchymal tumor
- ▶ Female predilection
- ▶ No mitoses, pleomorphism or necrosis
- ▶ Excision is curative





Pseudosarcomatous Myofibroblastic Proliferations

- ▶ Rare lesion
- ▶ Identical to post operative spindle cell nodule
- ▶ Can locally recur but usually don't metastasize
- ▶ Spindle cells with reactive vessels
 - ▶ Can have a myxoid stroma
 - ▶ No atypia, or abnormal mitotic figures
- ▶ CK, Desmin, SMA and ALK positive

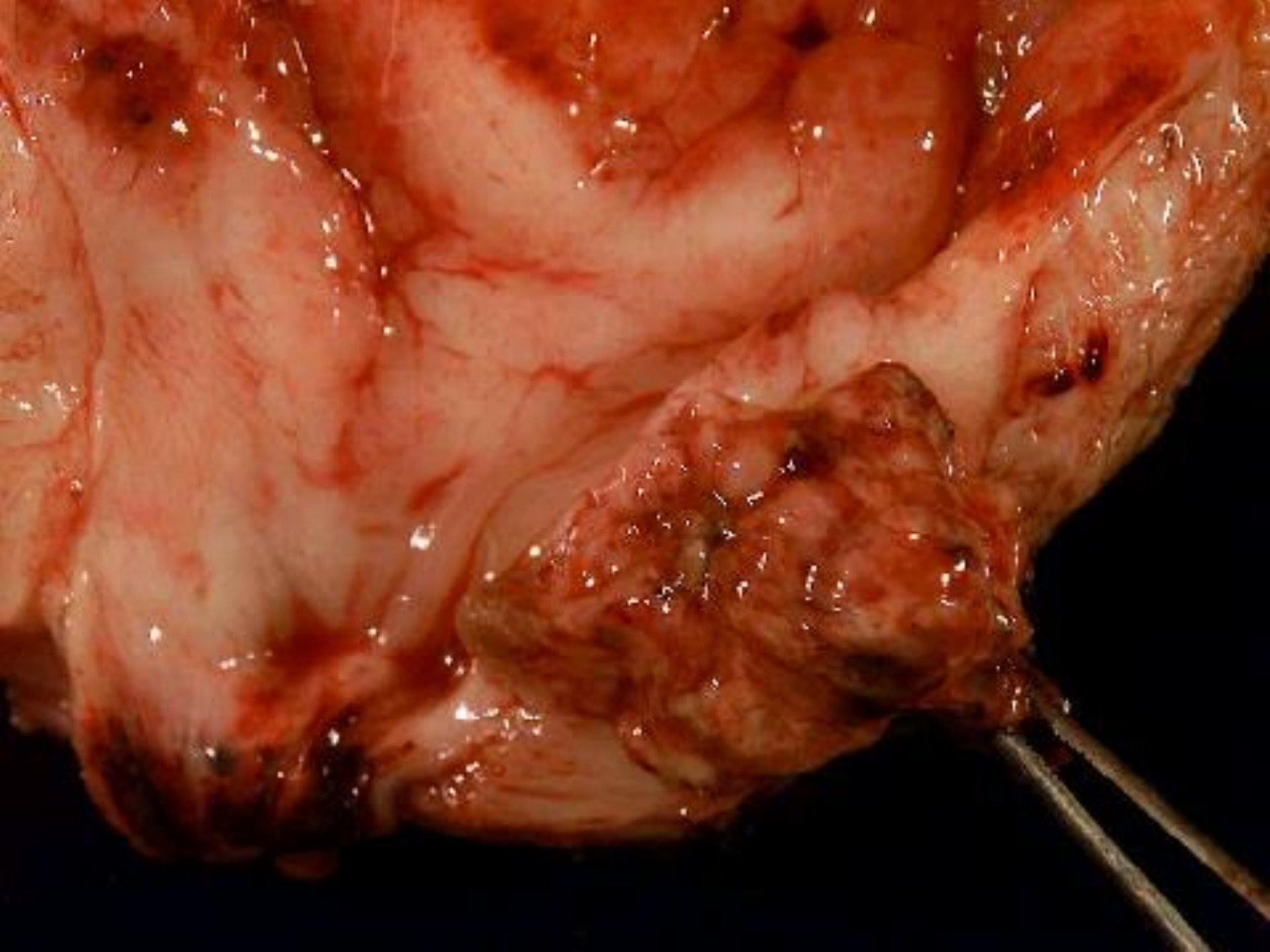


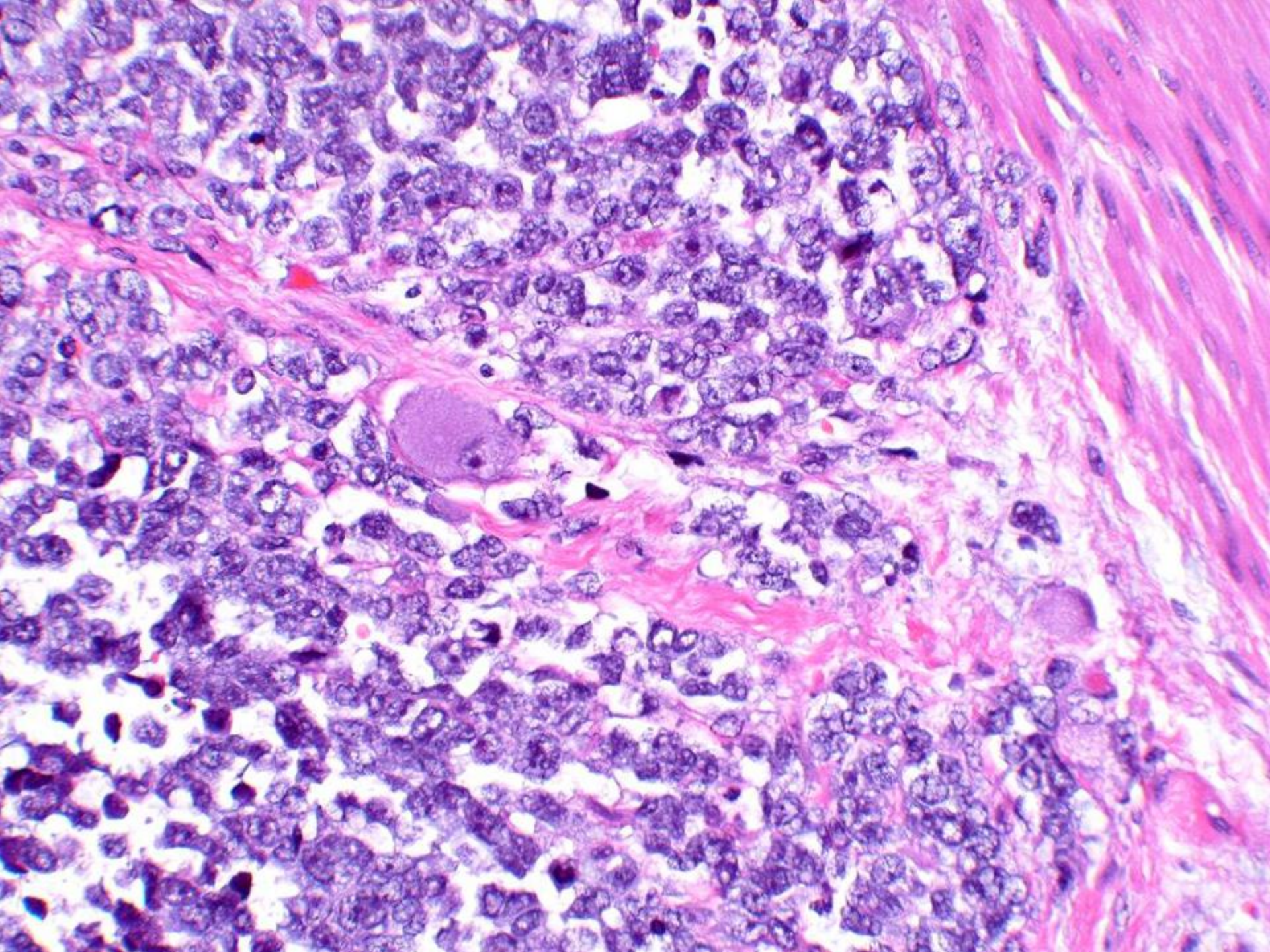
Leiomyosarcoma

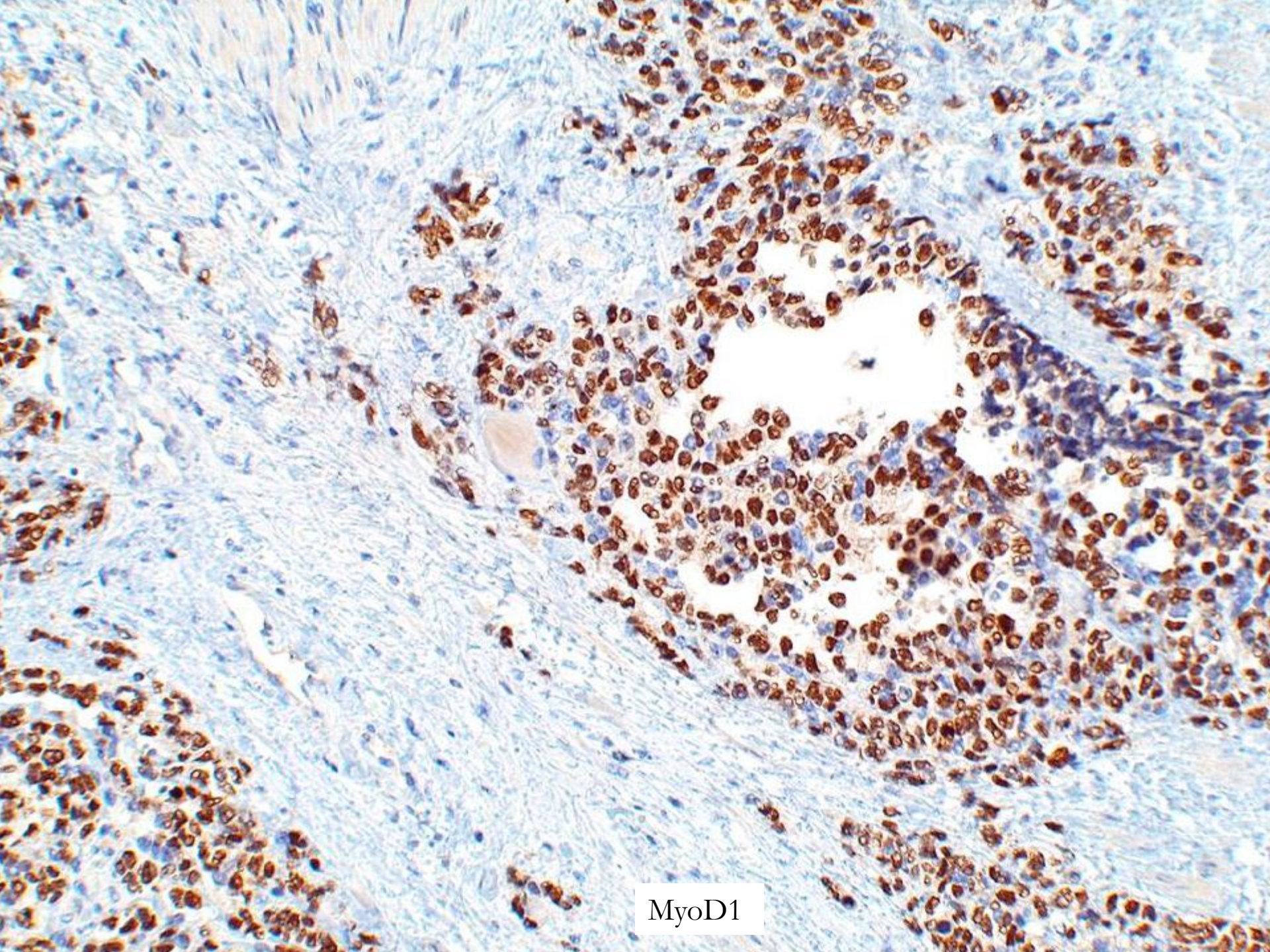
- ▶ Most common sarcoma in adults
- ▶ Male predominant
- ▶ High recurrence/metastatic rate
- ▶ Cellular, nuclear atypia and pleomorphism, mitotically active and necrotic
 - ▶ ≥ 1 mitosis/mm²
 - ▶ Infiltrative pattern

Rhabdomyosarcoma

- ▶ Most common bladder tumor of childhood
- ▶ Excellent prognosis with current therapeutic regimens
- ▶ Similar subtypes to elsewhere:
 - ▶ Embryonal
 - ▶ Alveolar
- ▶ Desmin, myogenin, MyoD1 positive
- ▶ Alveolar RMS: t(2;13), t(1;13)







MyoD1

Summary

- ▶ Diagnosing invasive urothelial carcinoma on small biopsies and TURBT is important
- ▶ Specific subtypes and divergent differentiation in urothelial carcinoma have prognostic and therapeutic implications and should be mentioned
- ▶ Secondary tumors and non-epithelial tumors are rare
 - ▶ Should be on radar when dealing with unusual case



Thank you!

QUESTIONS