

Atypical glandular cells in PAP smears



Unsolved case of
adenocarcinoma

Atypical glandular cells in PAP smears

10 years period of evaluation (01.01.2014 – 31.12.2023)

62927 PAP smears

35868 (57%) conventional PAP smears

27059 (43%) liquid based (Thin prep) smears

Atypical glandular cells in PAP smears

13061 cases (20.76%) - positive.

11841 (90.7%) - squamous cell abnormalities

1220 (9.3%) - glandular cell abnormalities.

AGC (cervical&endometrial carcinoma) - 886 (72.7%) - conventional smears

AGC (cervical&endometrial carcinoma) - 334 (27.3%) - liquid-based smears.

Histological examination was available in 265 patients (23.3%)

Negative for intraepithelial lesion or malignancy (NILM) = 49866

Histology with glandular lesions - available in 965 (1.9%) cases

Findings	Conventional Cytology	Liquid-Based Cytology	Total
Cervical Adenocarcinoma	49	35	84
Endometrial Adenocarcinoma	97	70	167
Benign Cervical Lesions	0	2	2
Benign Endometrial Lesions	10	2	12
Total AGC with Histological Evaluation	157	108	265
Negative for Intraepithelial Lesions and Malignancy (NILM)			49866
Cervical Adenocarcinoma	3	1	4
Endometrial Carcinoma	3	8	11
Benign Cervical Lesions	304	118	373
Benign Endometrial Lesions	408	135	577
Total Histological Evaluations (NILM)			965

Sensitivity, specificity, positive and negative predictive values

	Cervical		Endometrial	
	conventional	LB PAP	conventional	LB PAP
Sensitivity	0.94	0.97	0.97	0.89
Specificity	1.00	0.98	0.97	0.98
PPV	1.00	0.94	0.90	0.97
NPV	0.99	0.99	0.99	0.94

Rules in Pathology

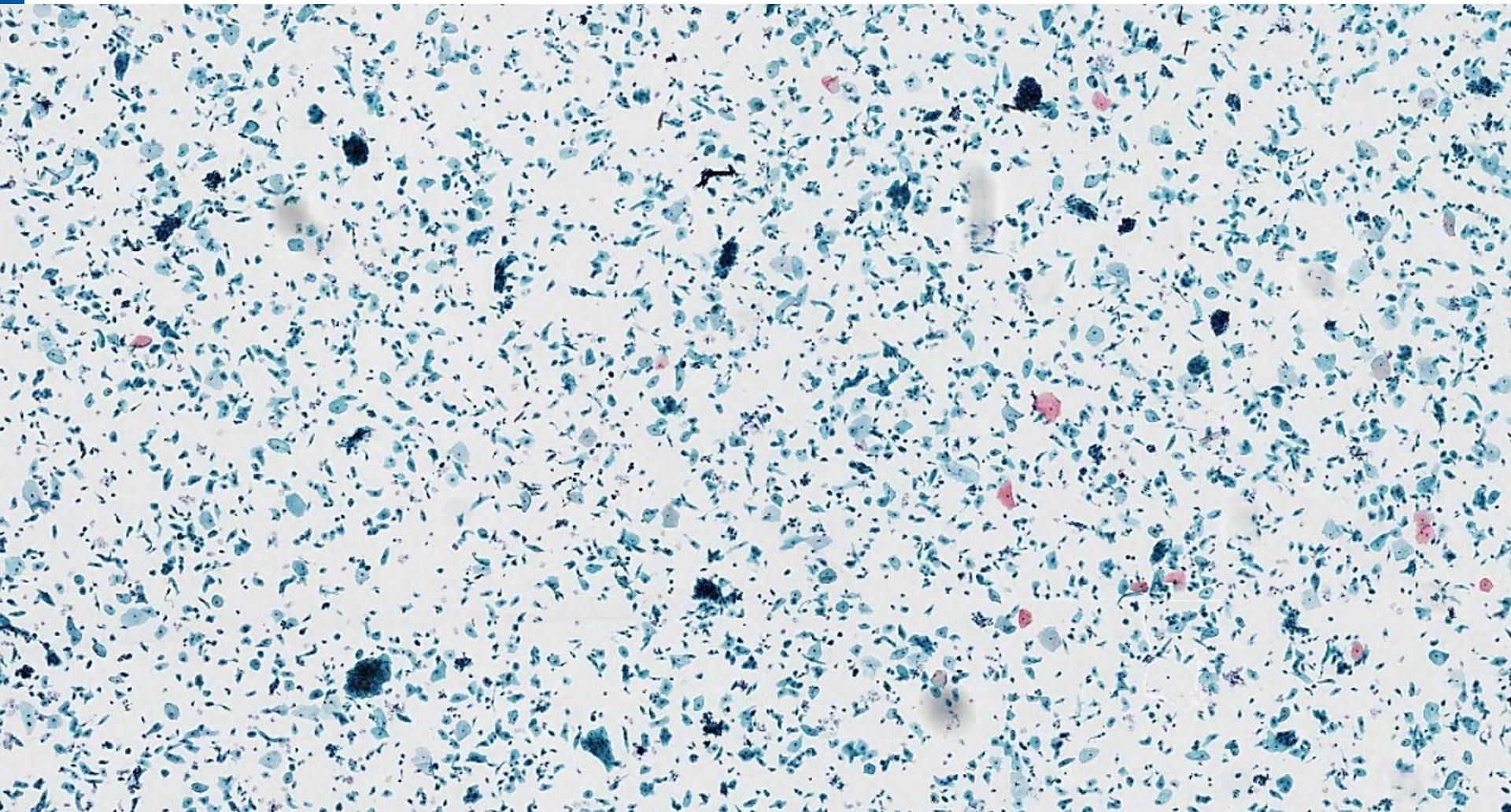
Speed (velocity) = distance /
time $v=s/t$

Pressure (P)

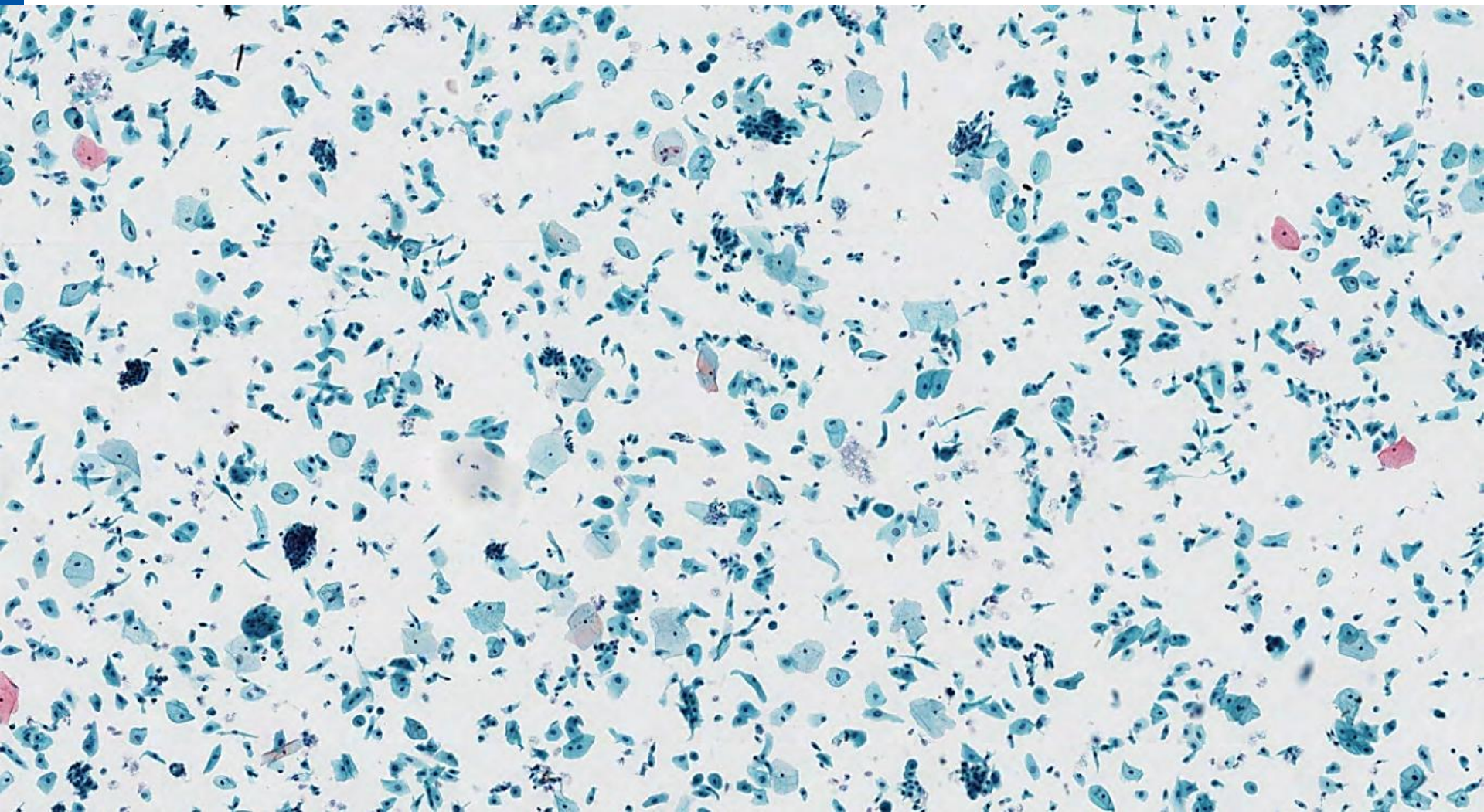
Unsolved case of adenocarcinoma

52 yrs old patient with vaginal bleeding. Anaemia

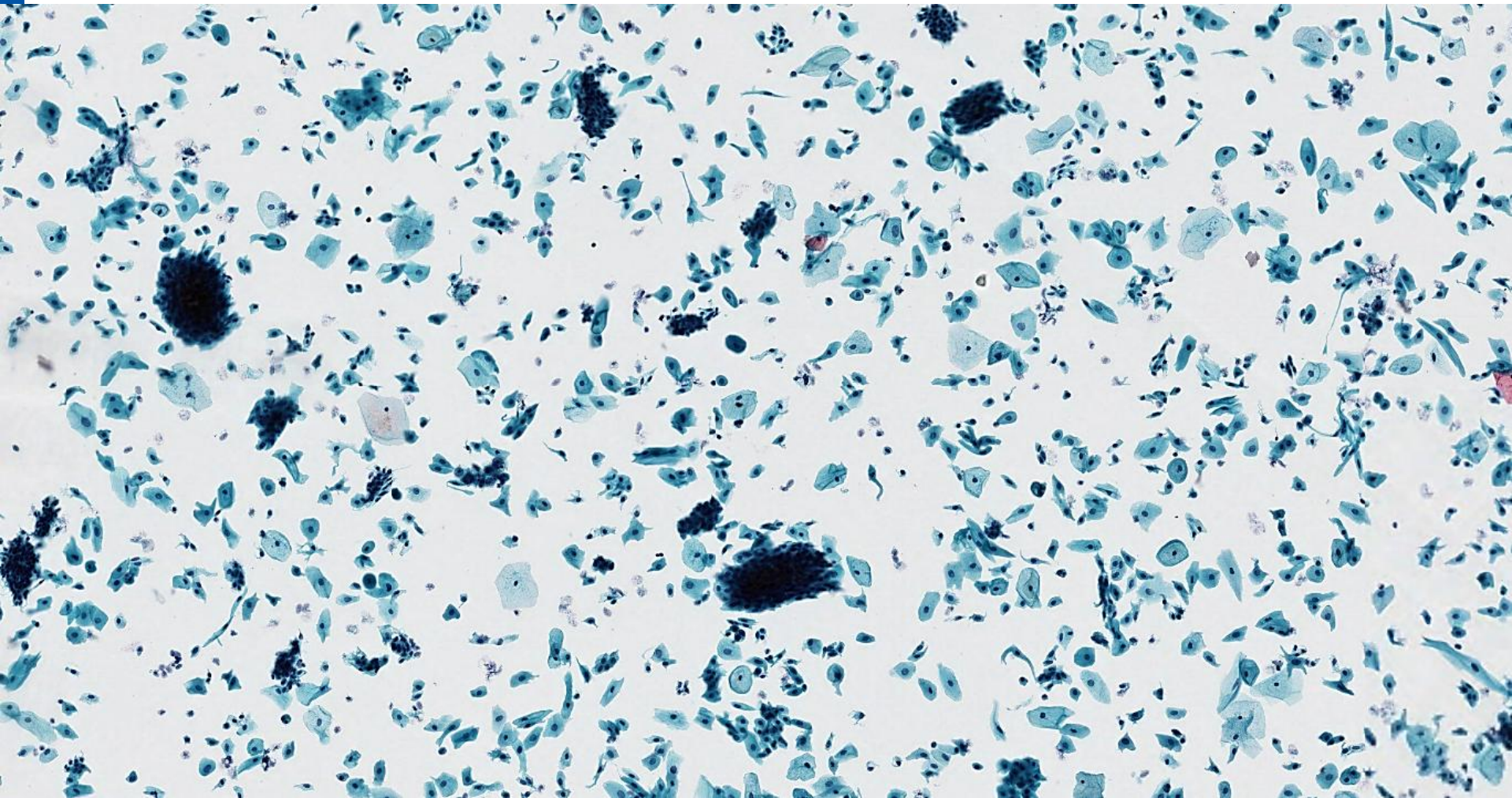
PAP smear



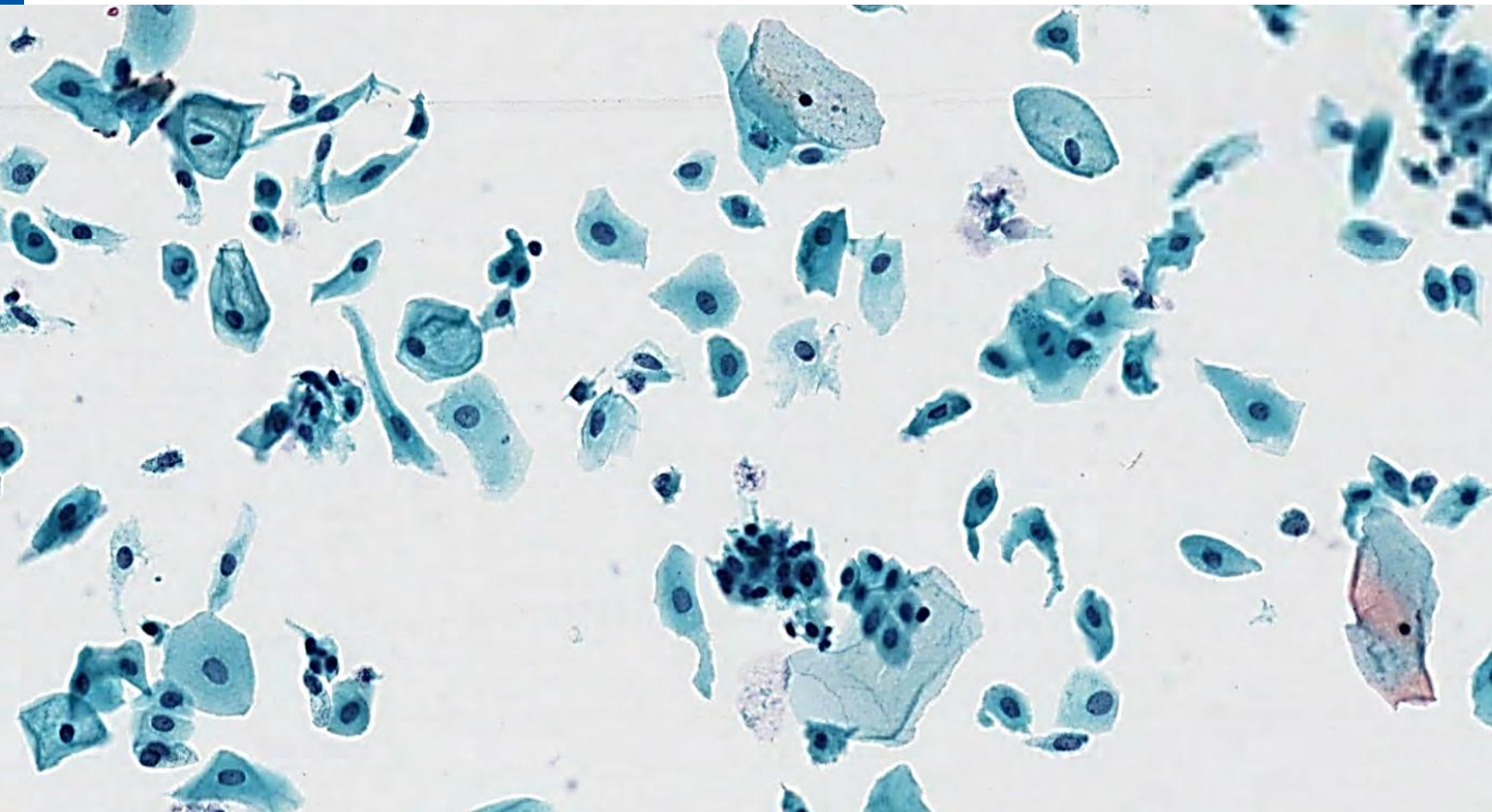
PAP smear



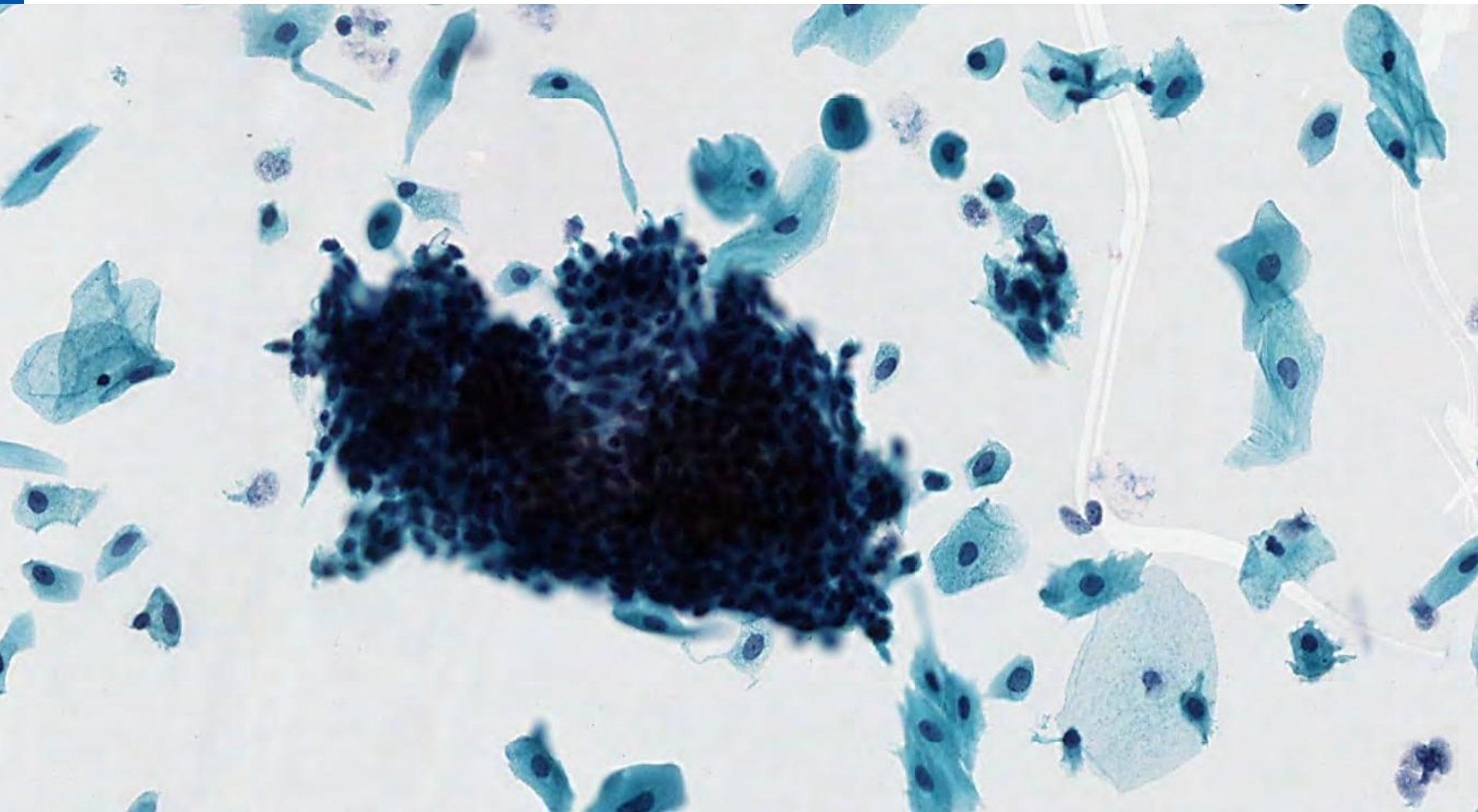
PAP smear



PAP smear



PAP smear



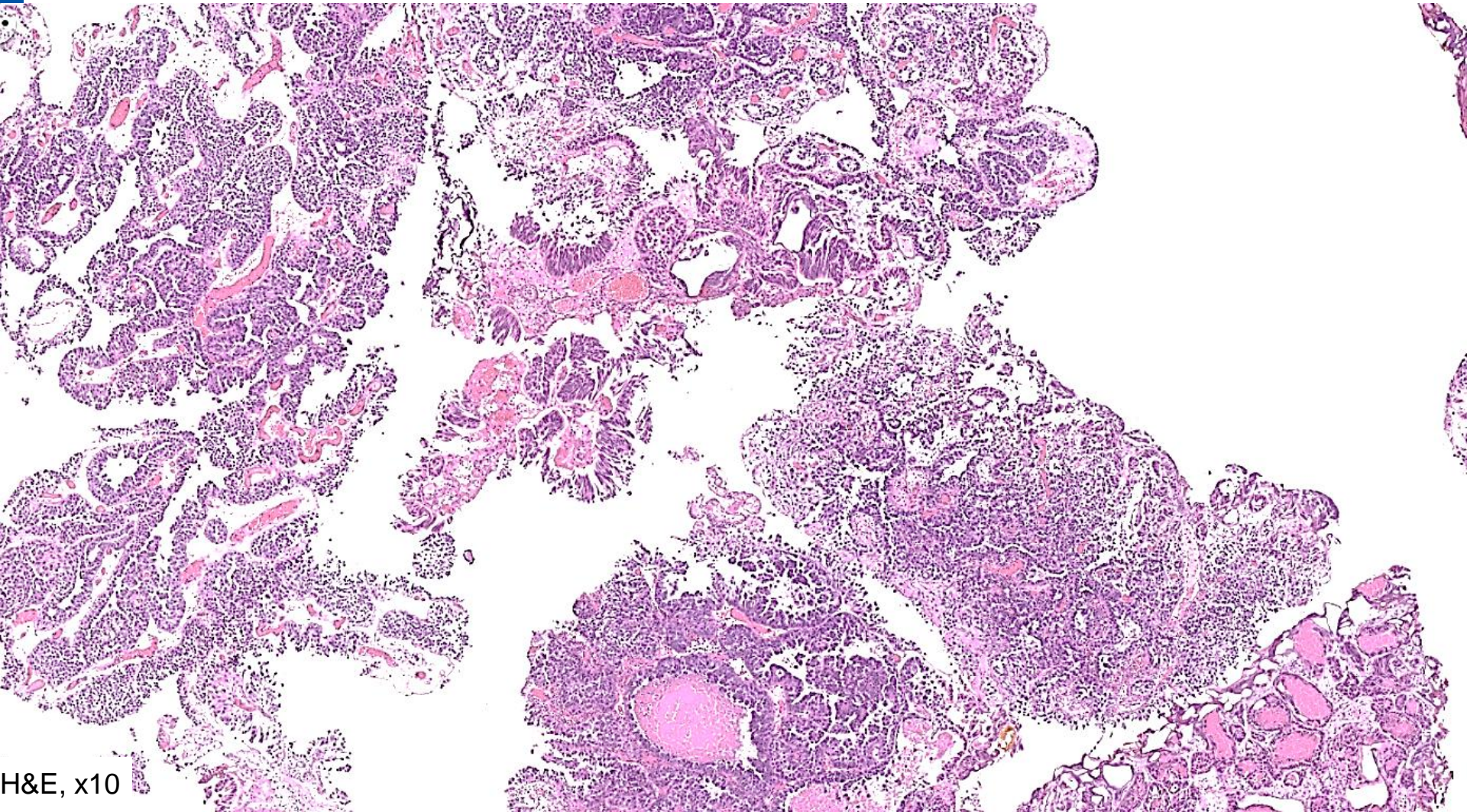
Cytological diagnosis:

AGC – atypical glandular cells

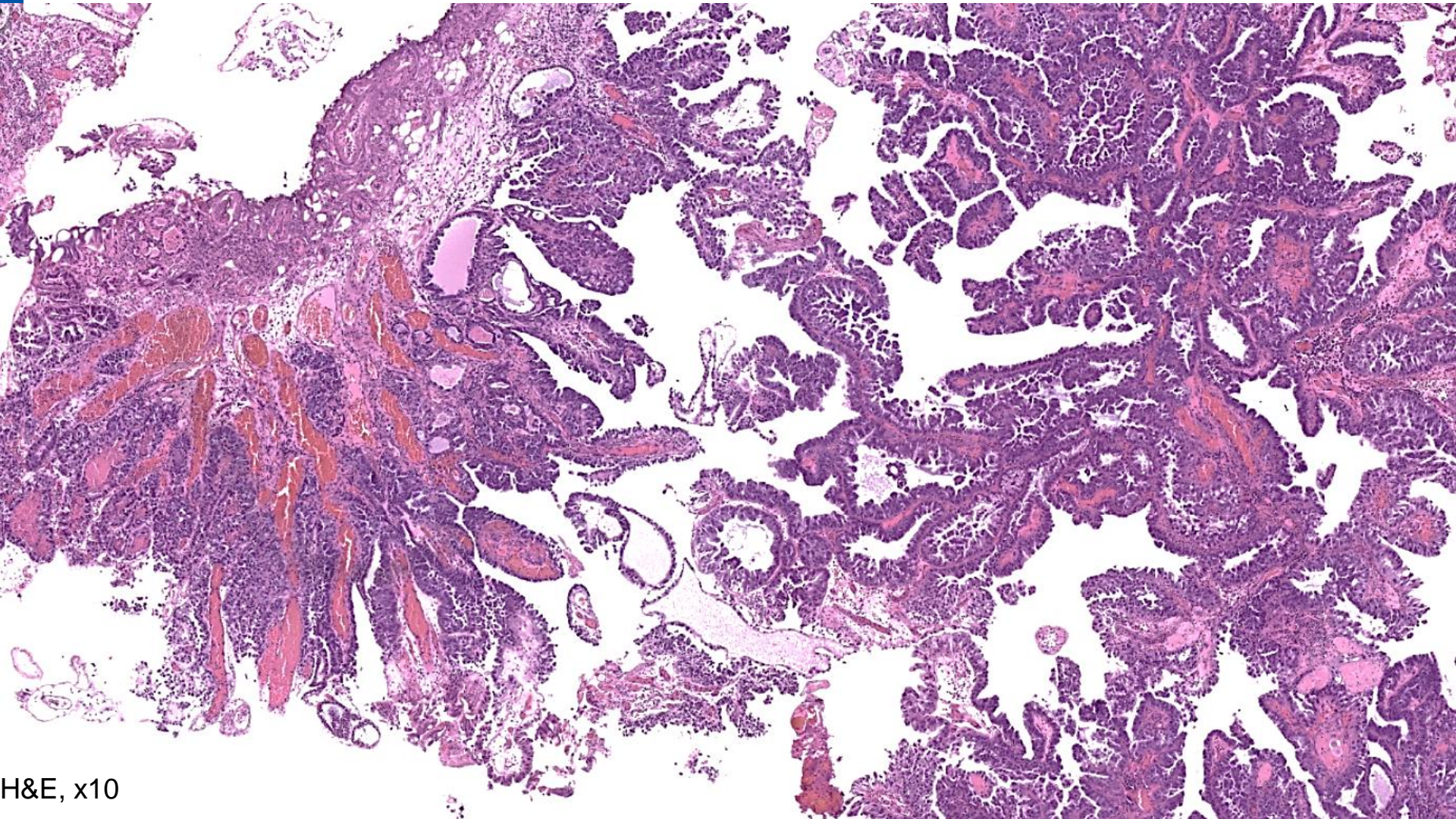
Recommendation: Biopsy /
endocervical curetting

Biopsy - tissue fragments measuring up to 1 cm.

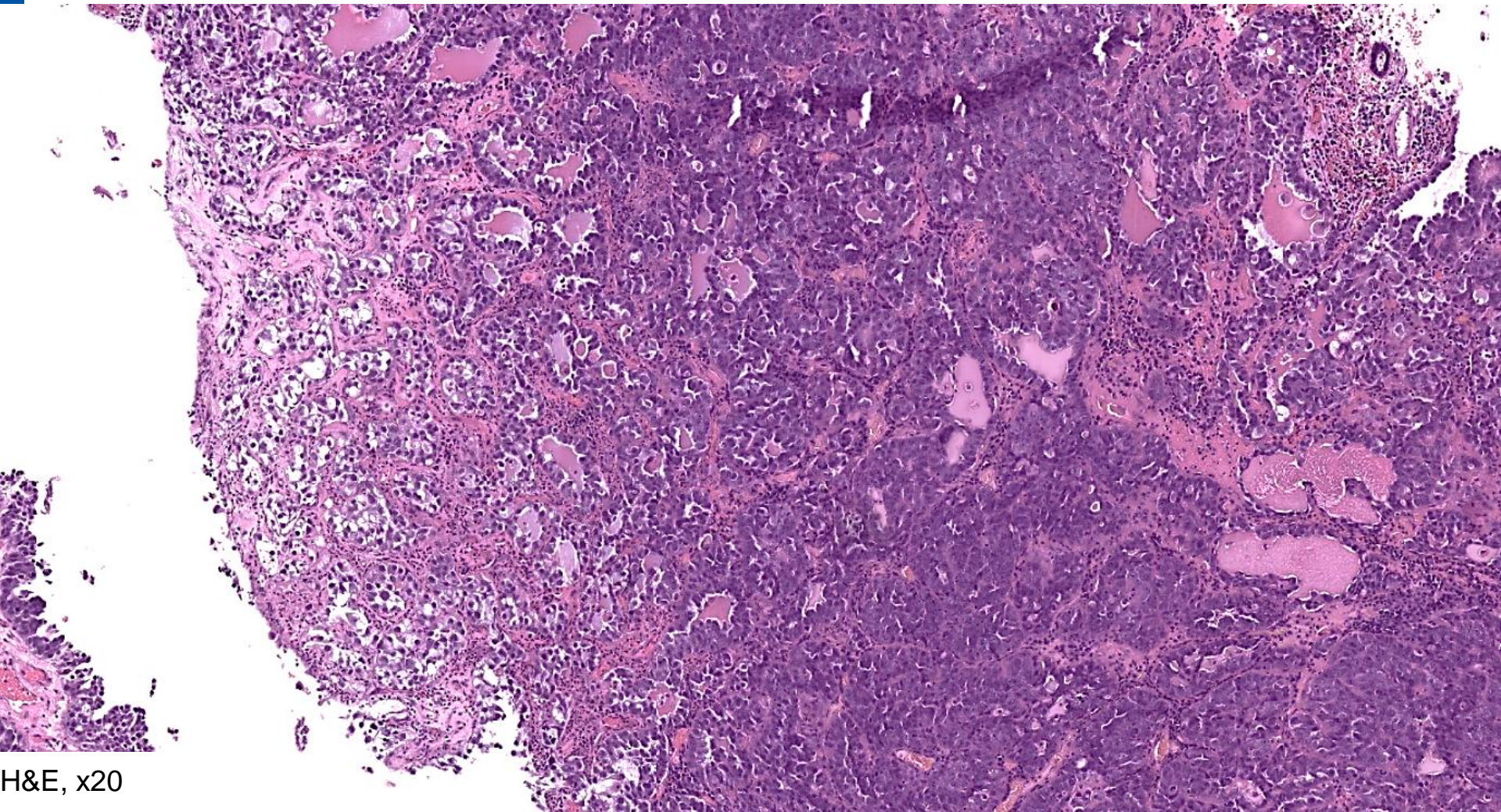
Microscopy: neoplastic tissue composed of pseudoglandular, tubular and papillary structures



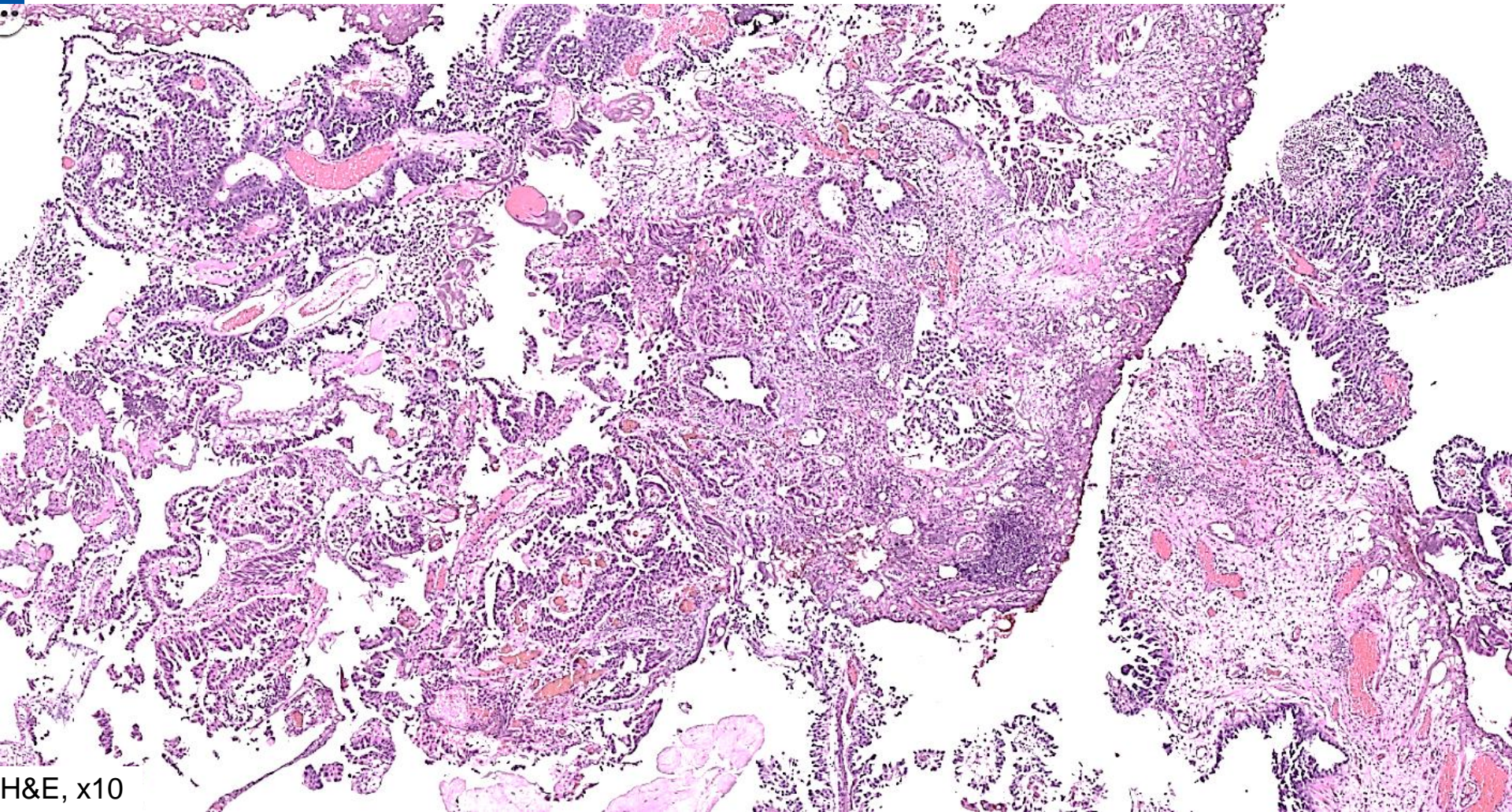
Papillary structures



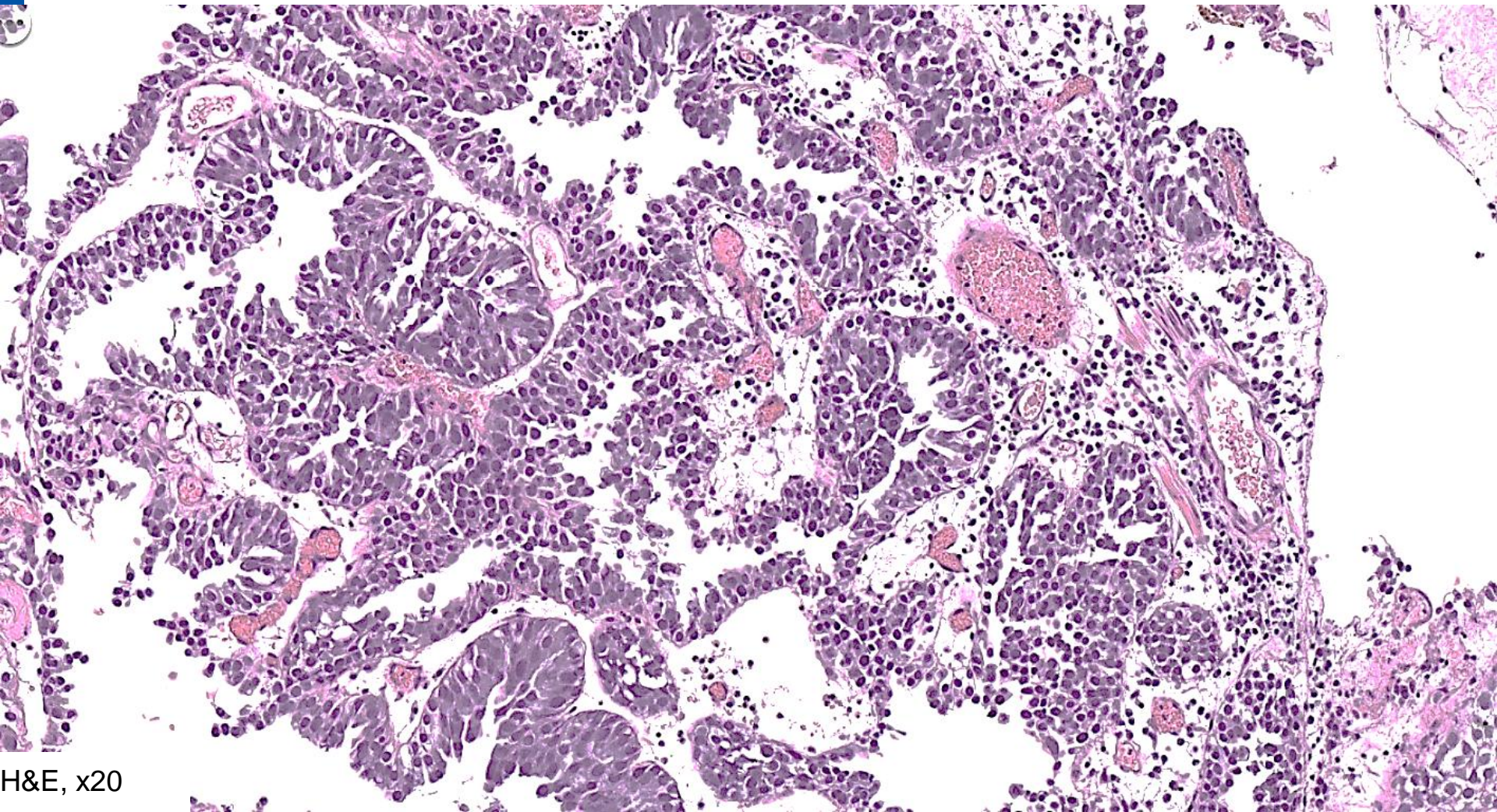
Tubular and pseudoglandular pattern



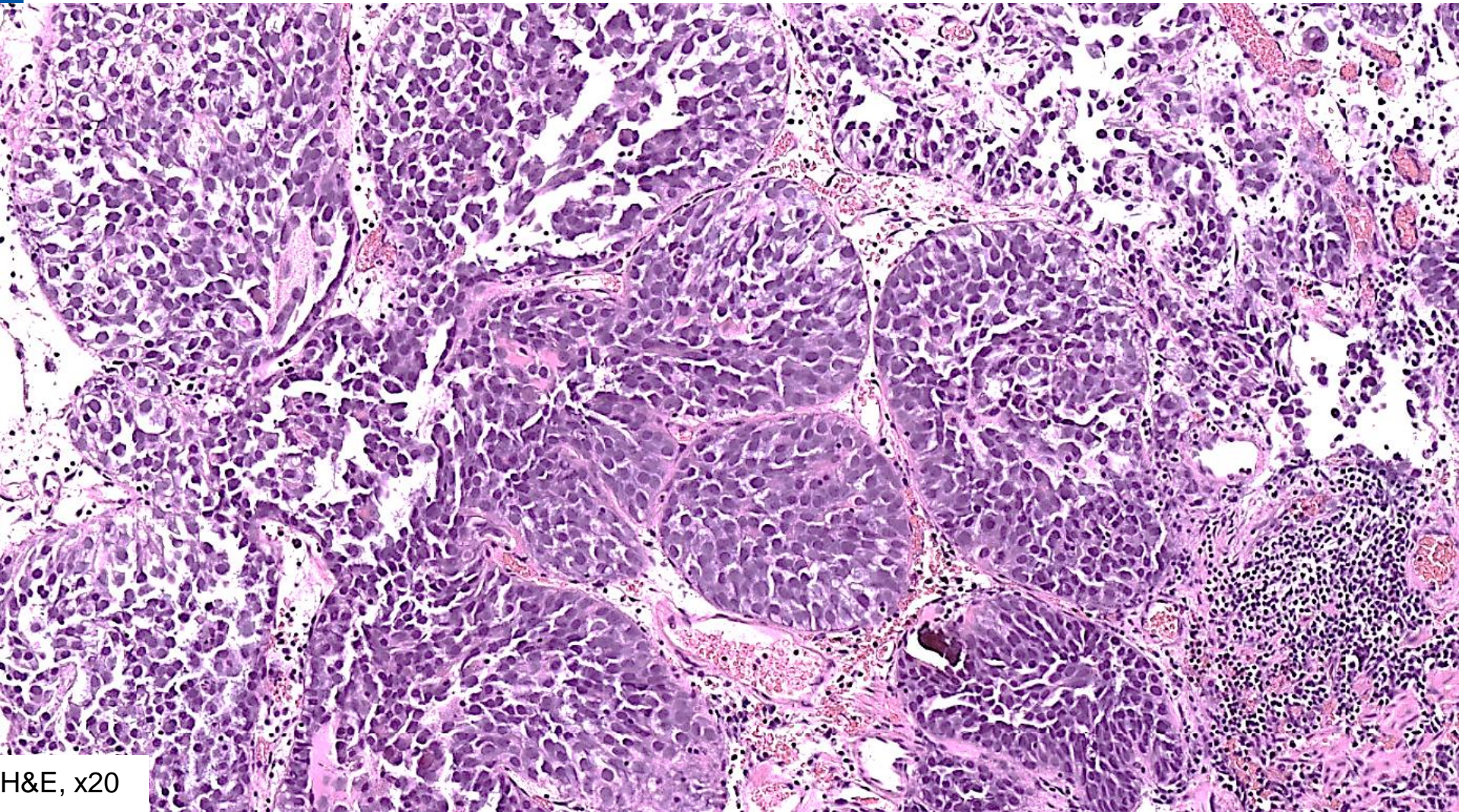
Papillary and solid zones



Pseudoalveolar and glandular pattern with high columnar amphophilic cells



Solid zones with acinic-like nests

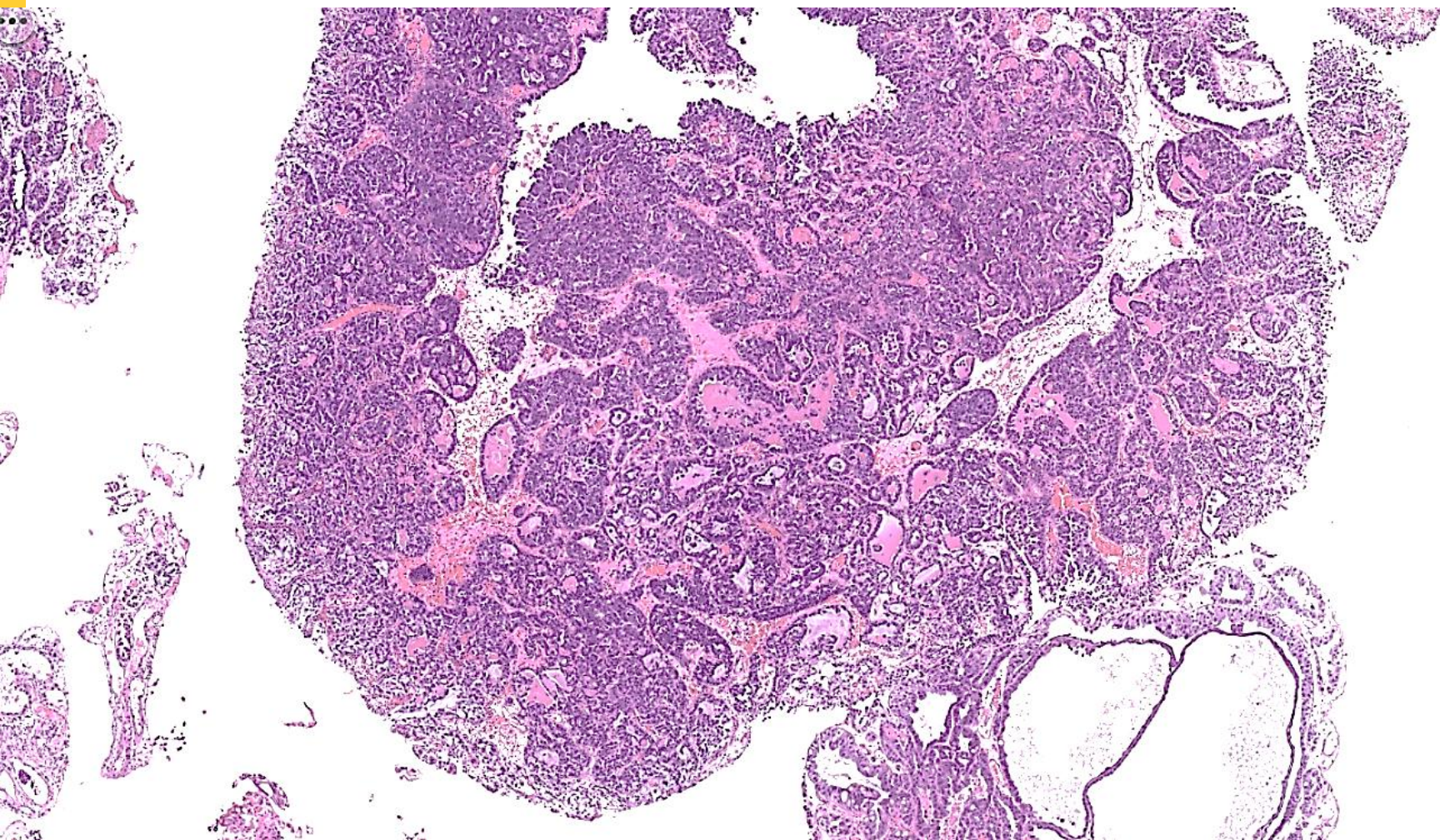


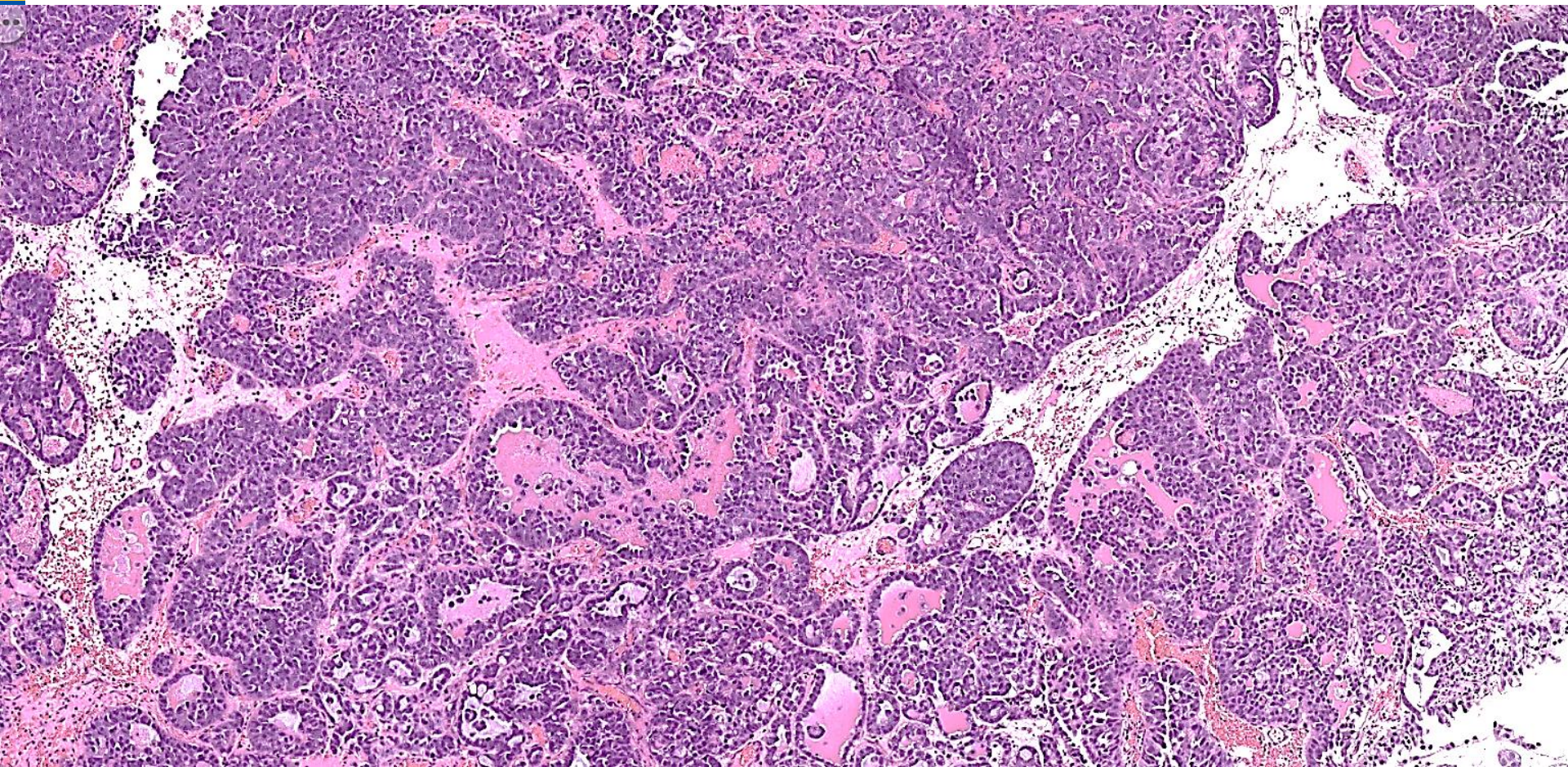
Histopathological diagnosis

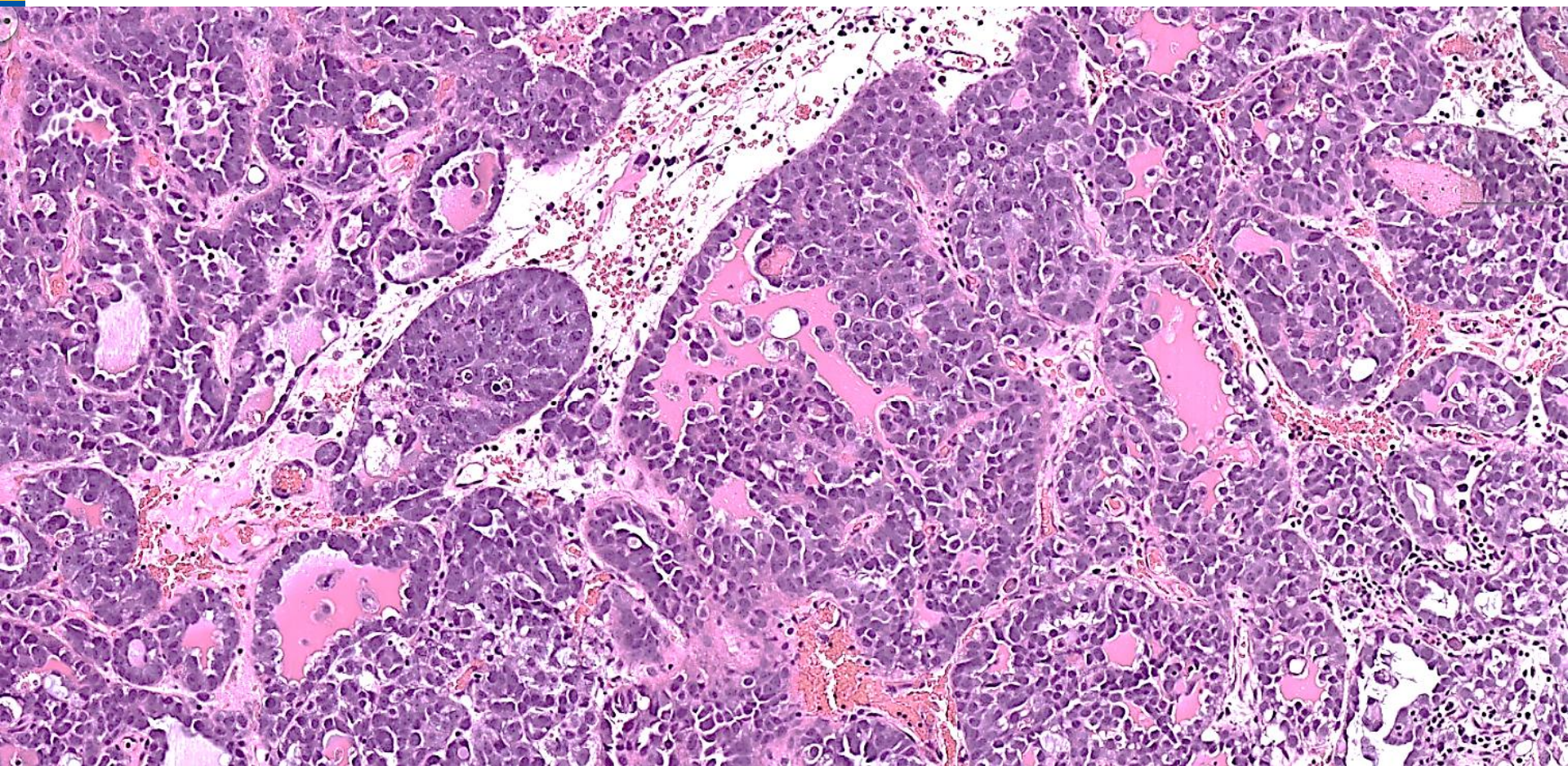
Adenocarcinoma, NOS
(endocervical, endometrial???)

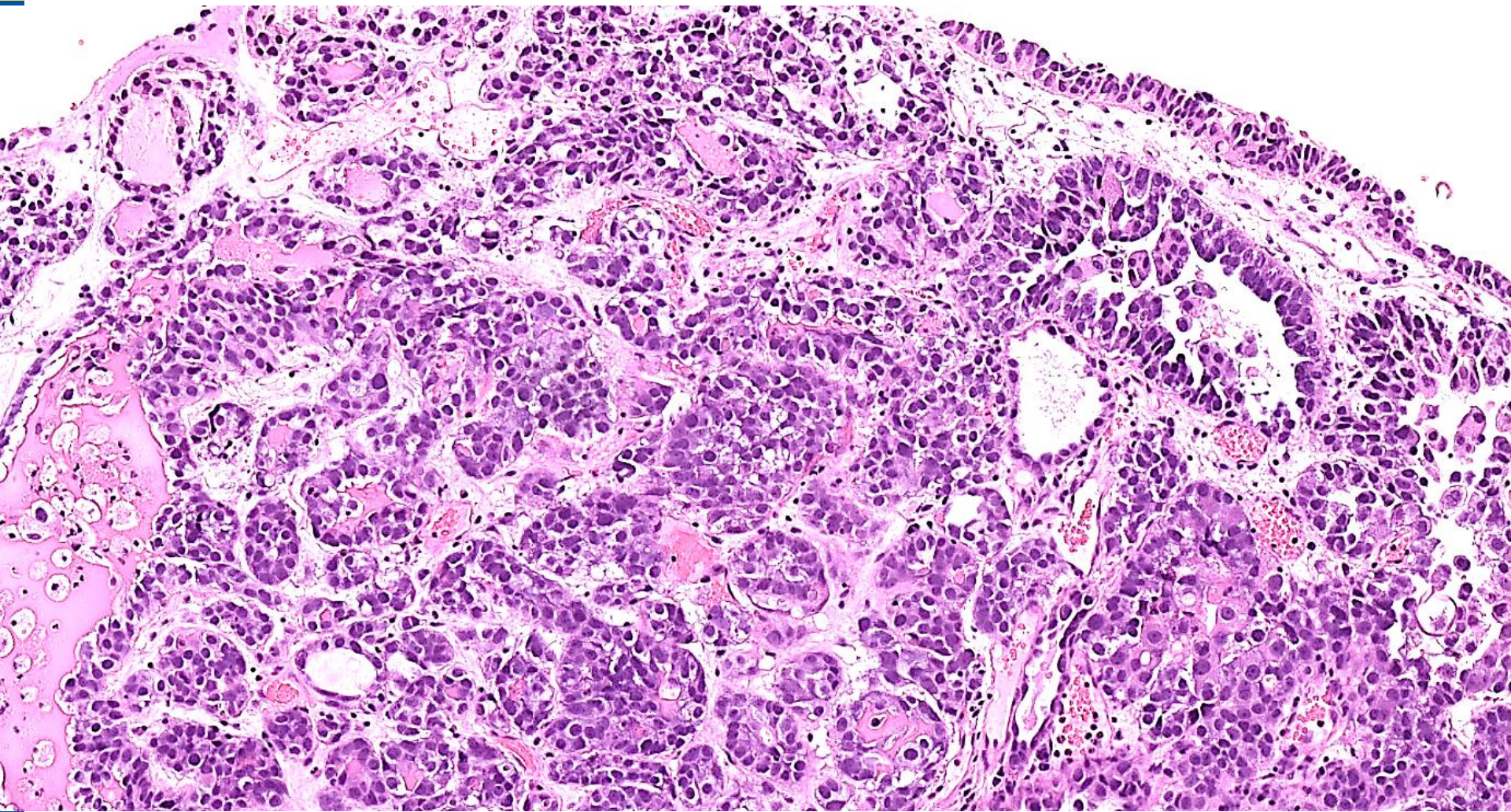
- The surgical treatment was impossible
- The paraffin block was taken for second opinion and it was never returned to our Hospital.
- Further follow-up was without results.

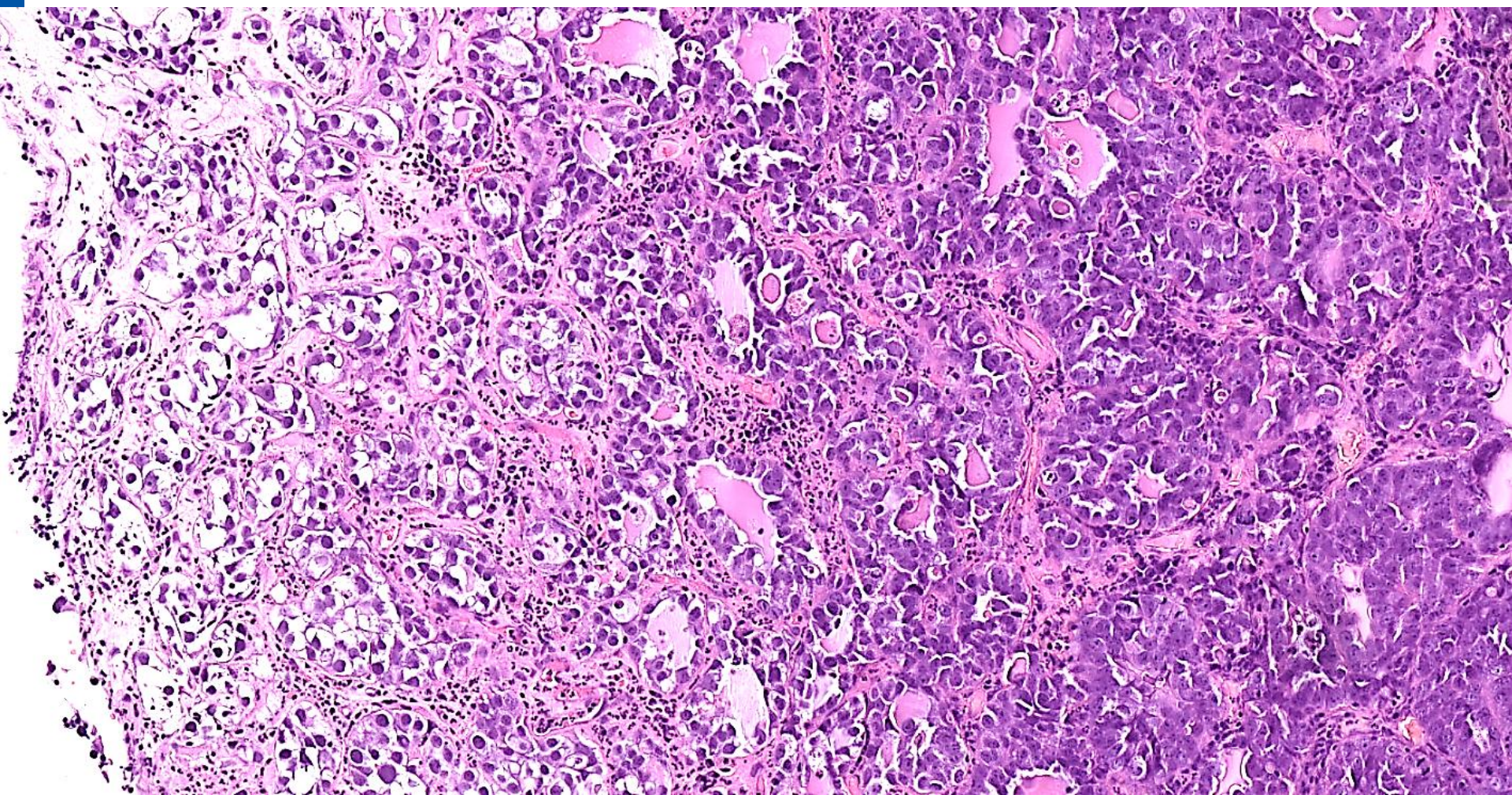


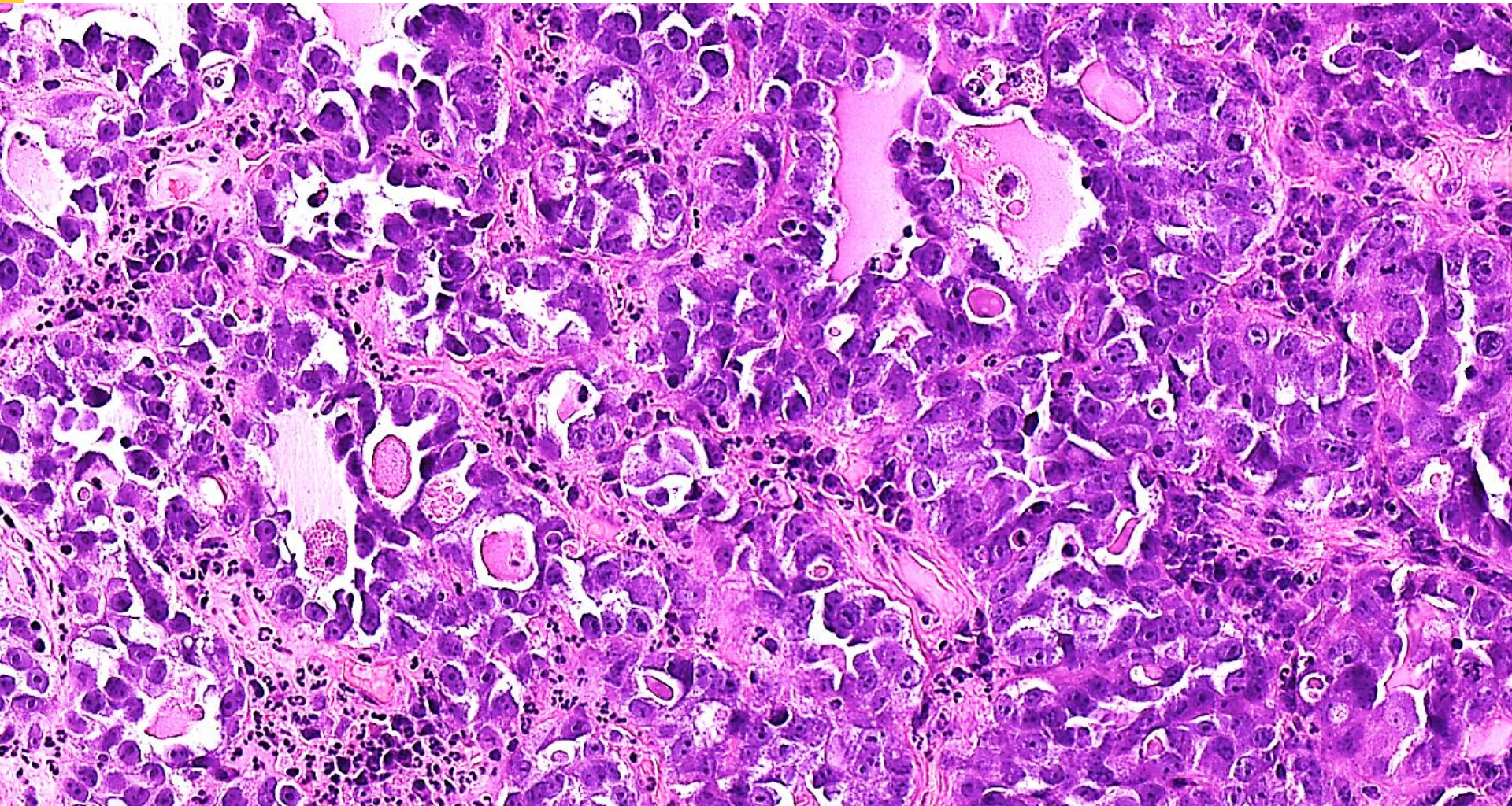


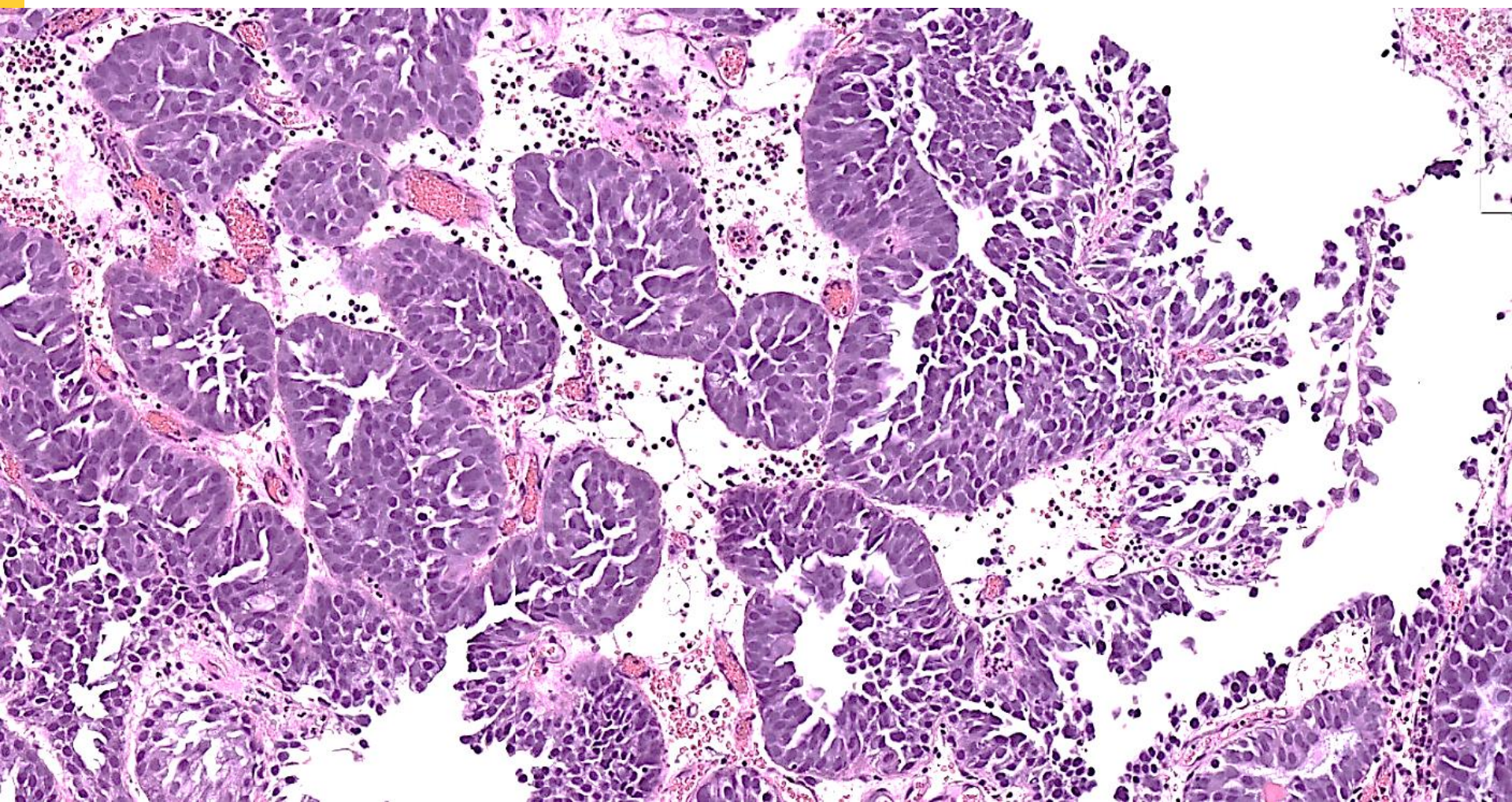


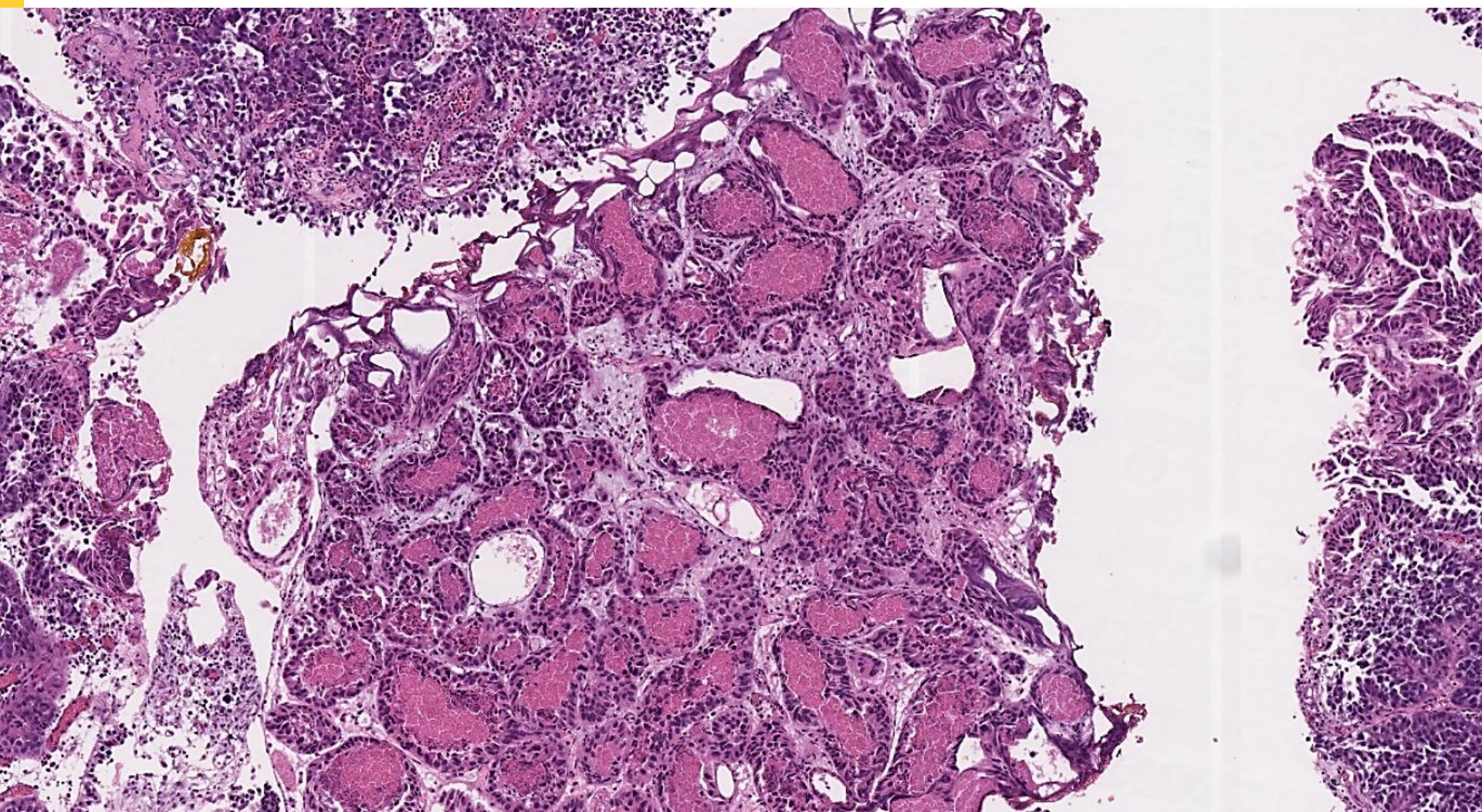


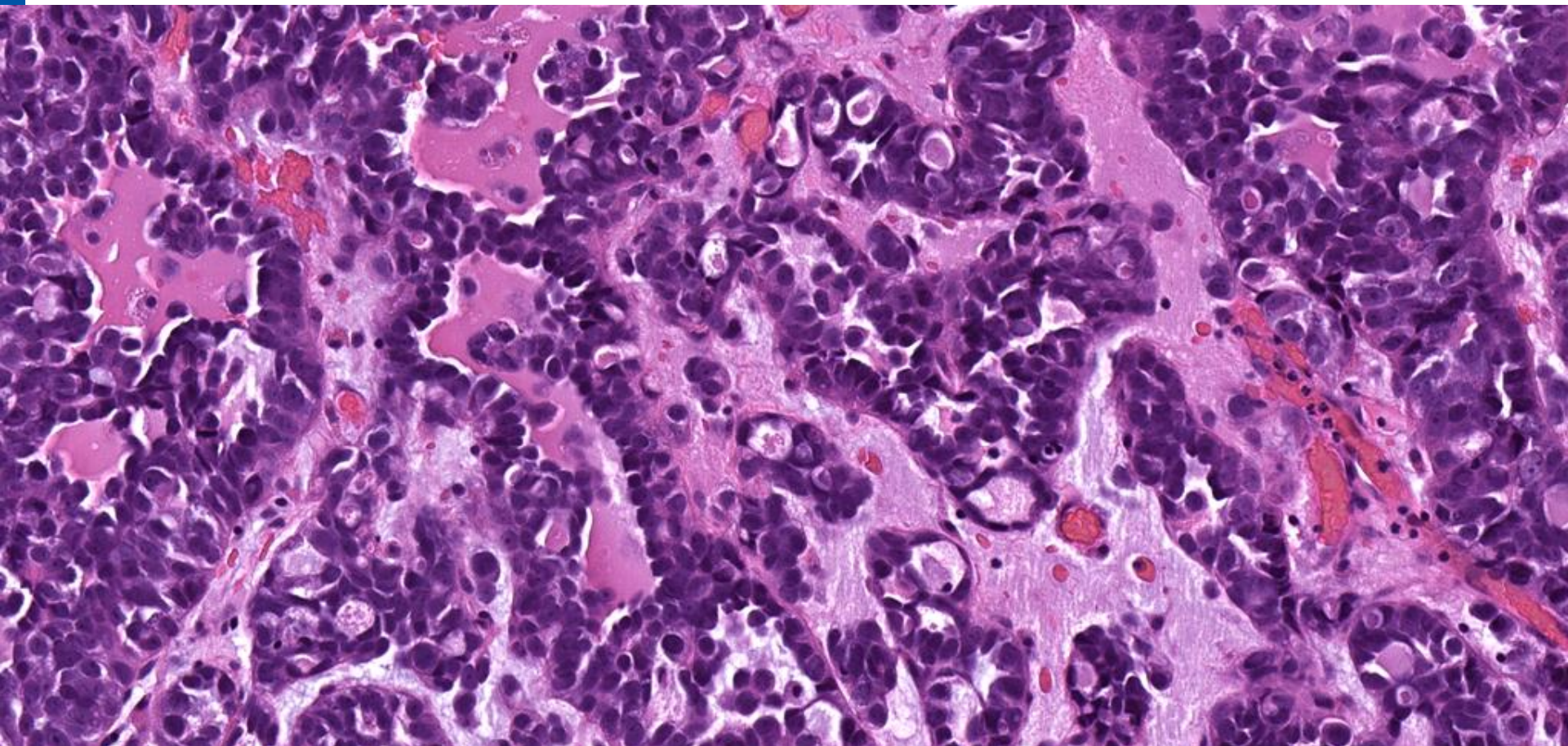


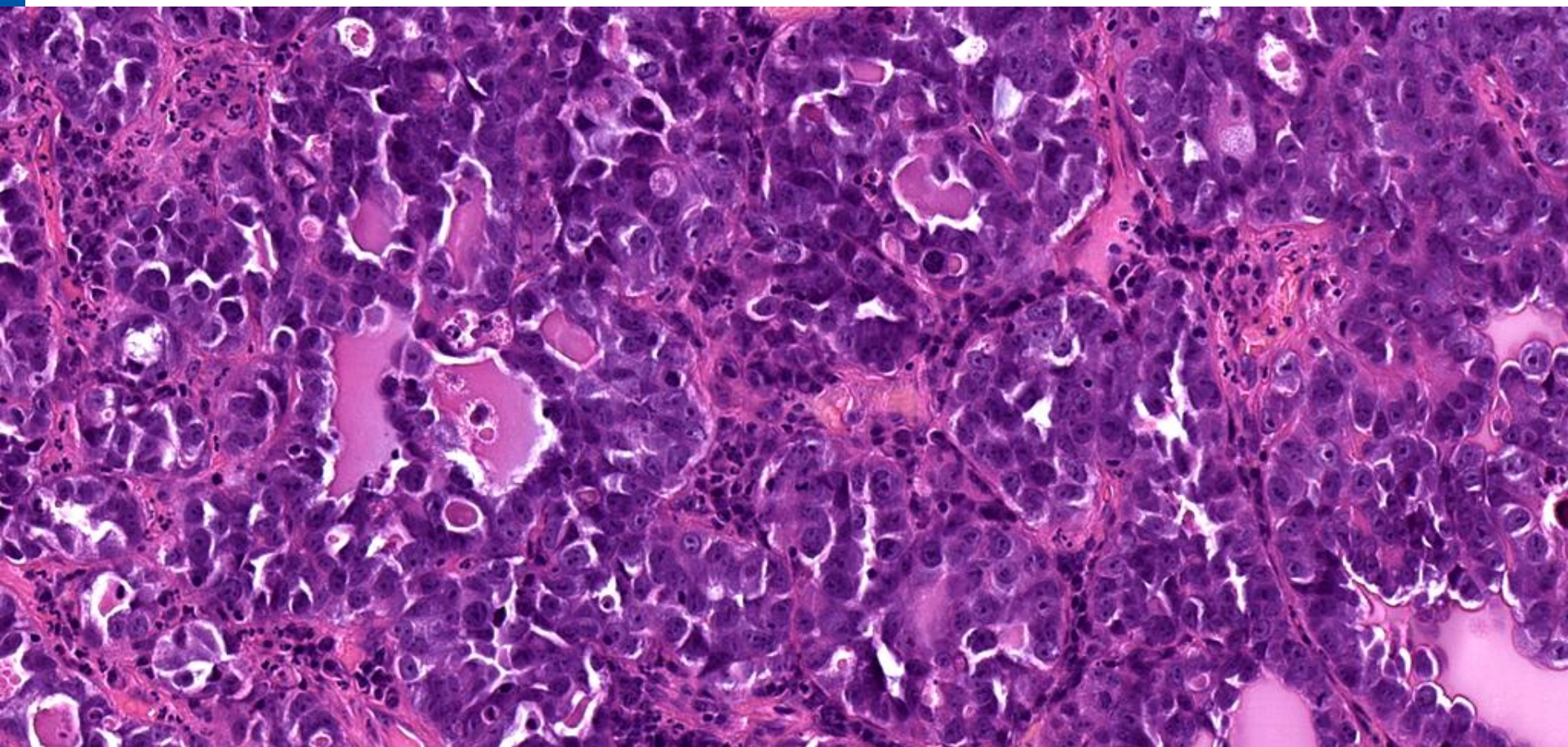


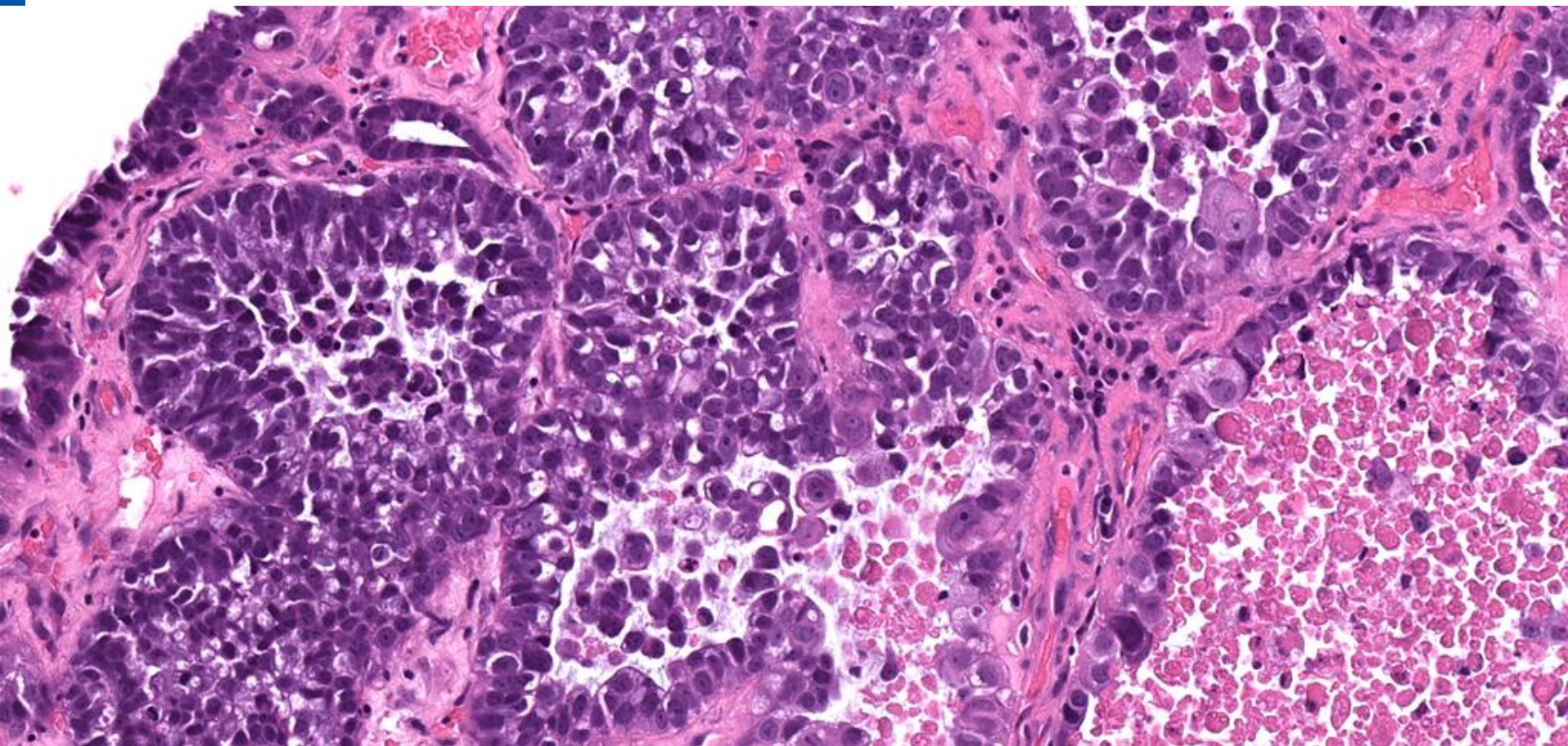


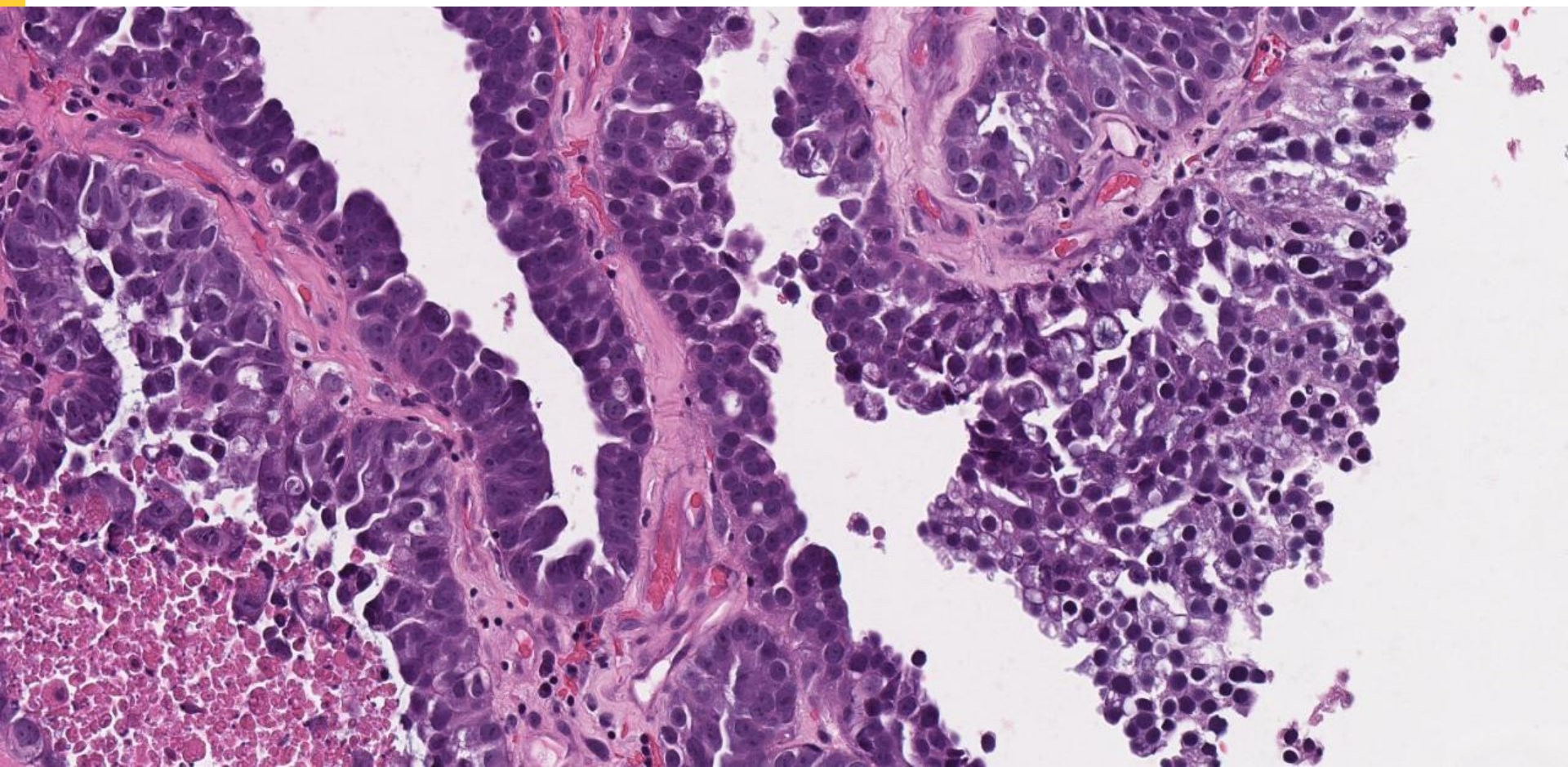


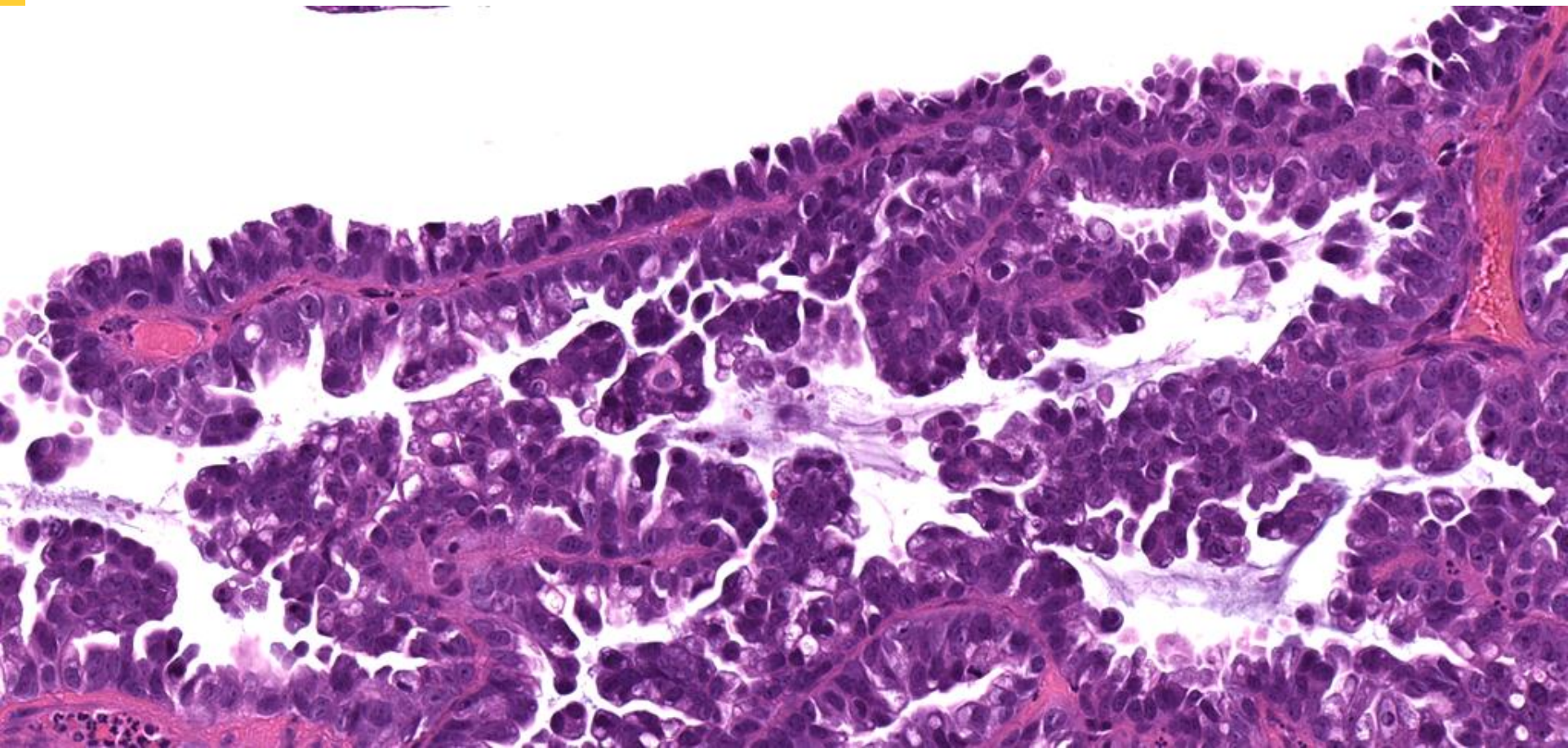


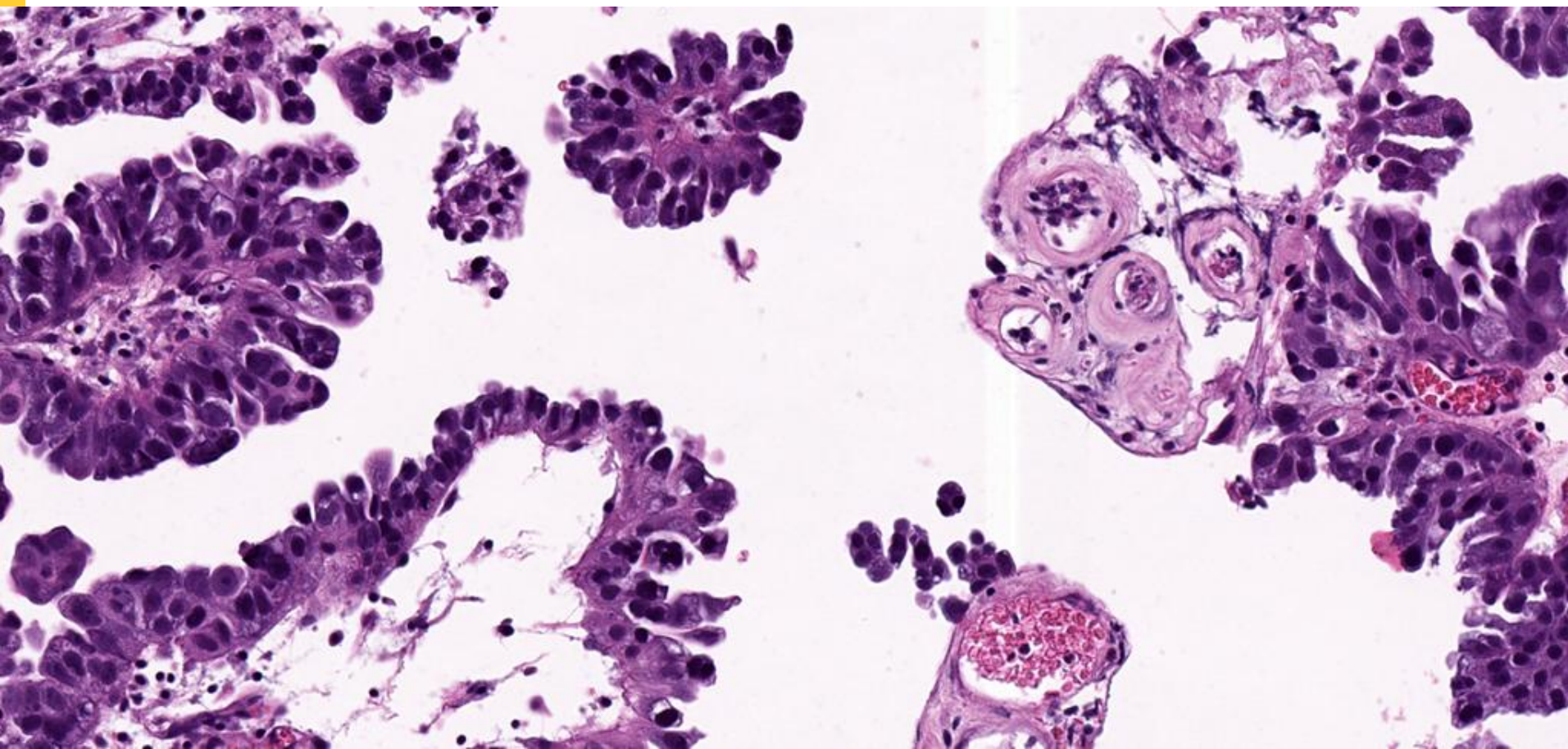






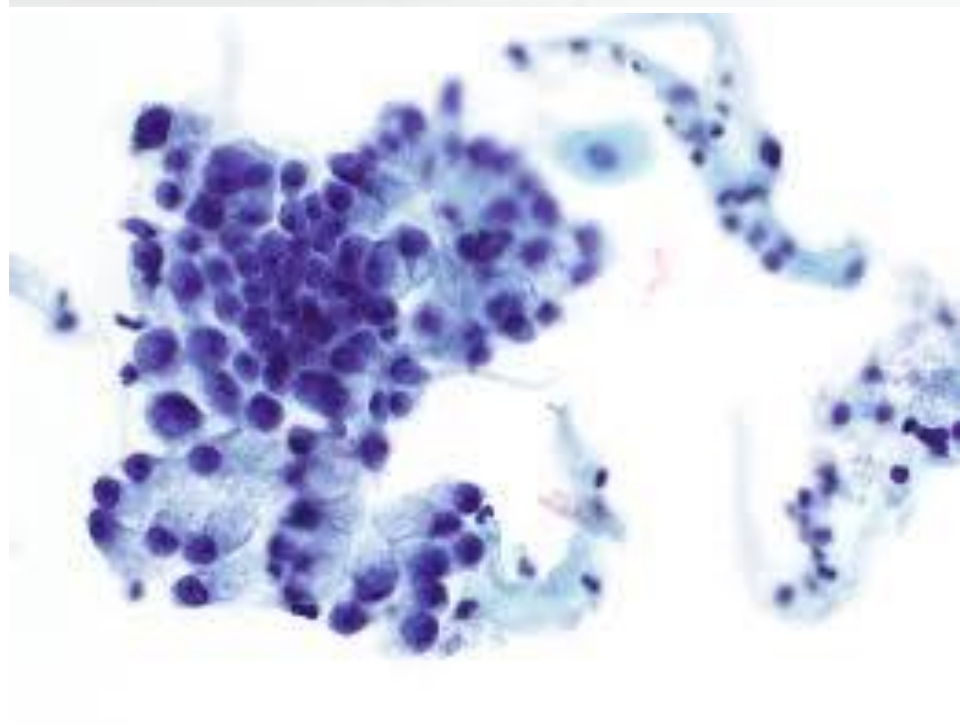
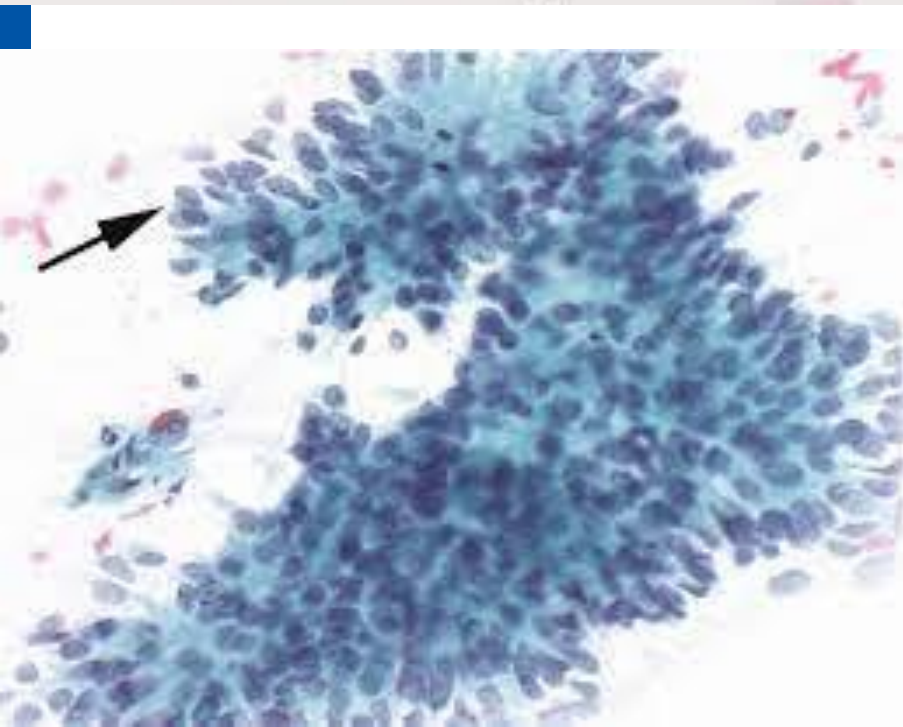
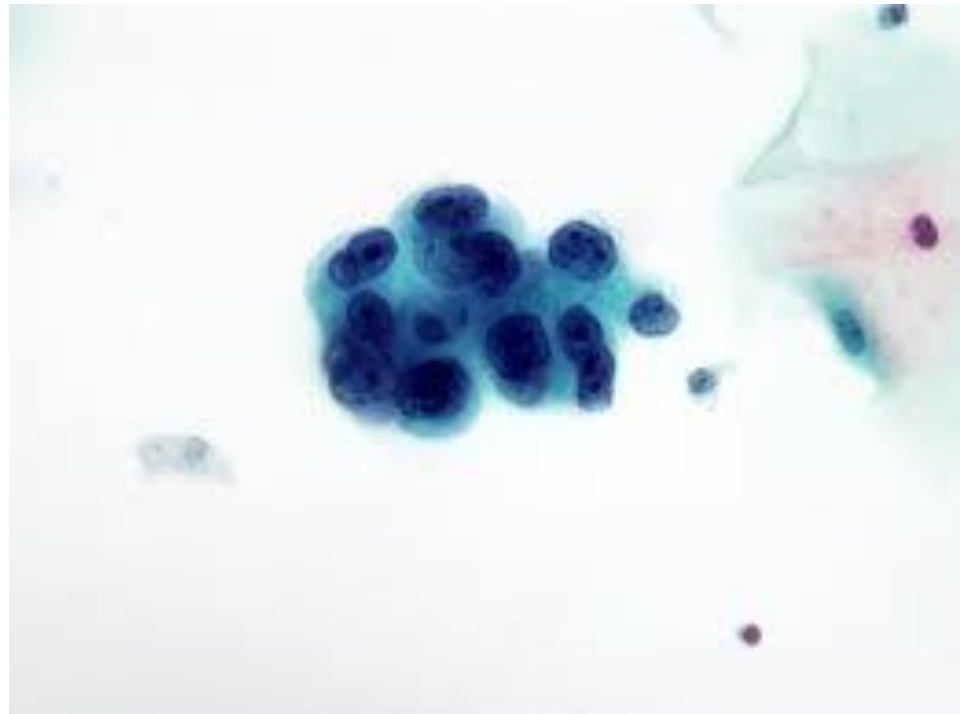
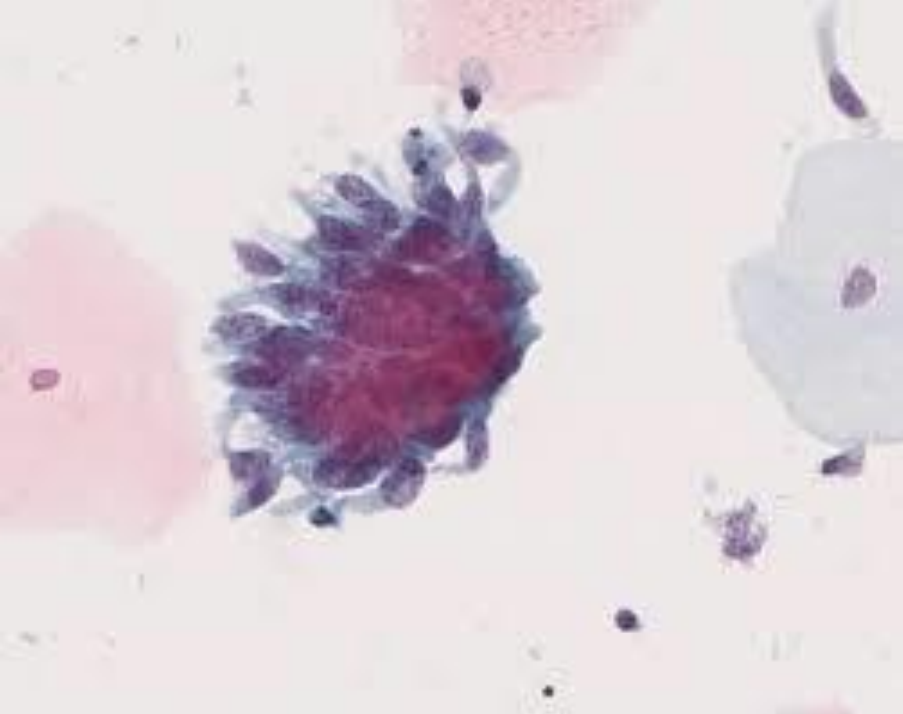


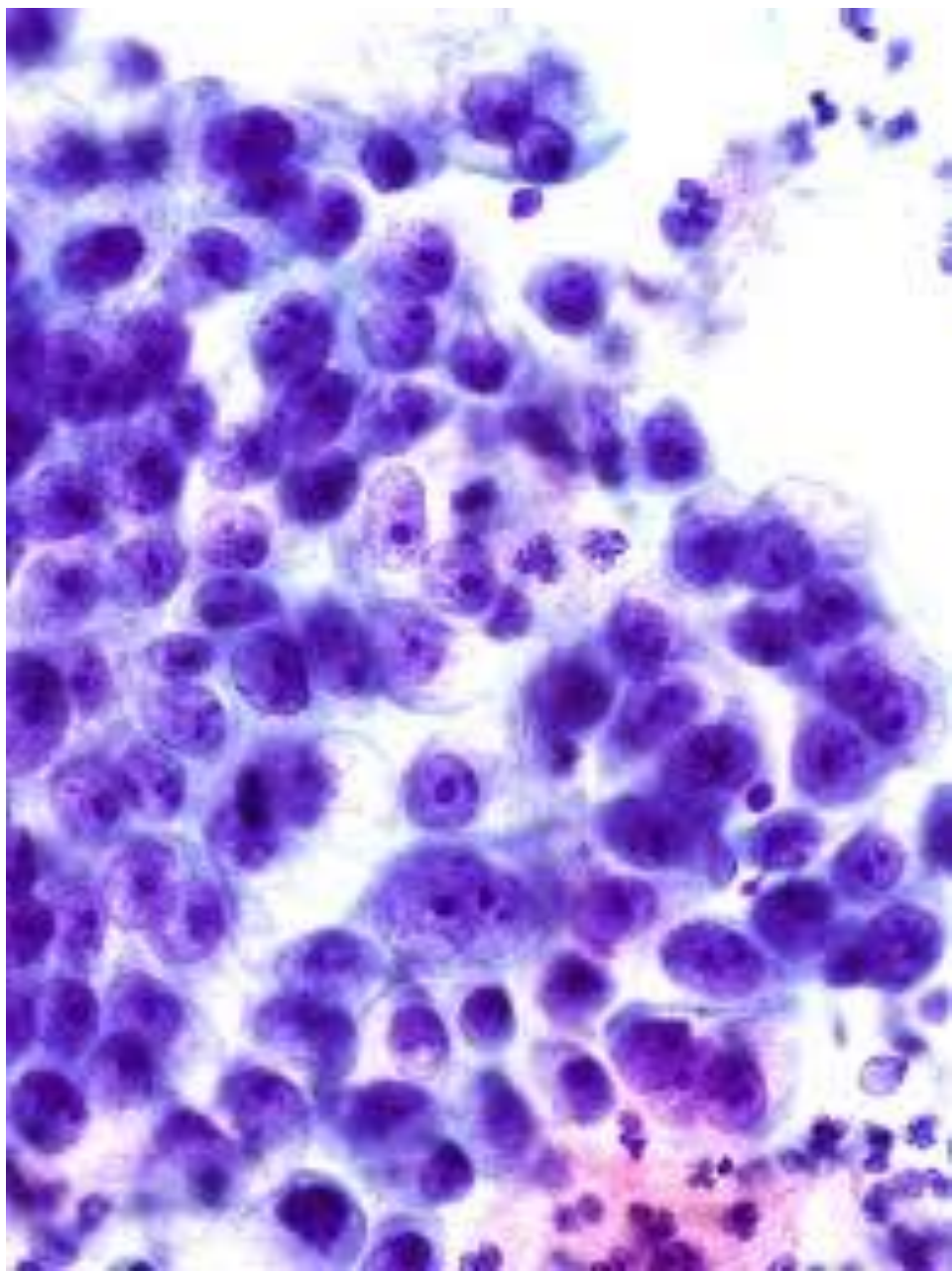
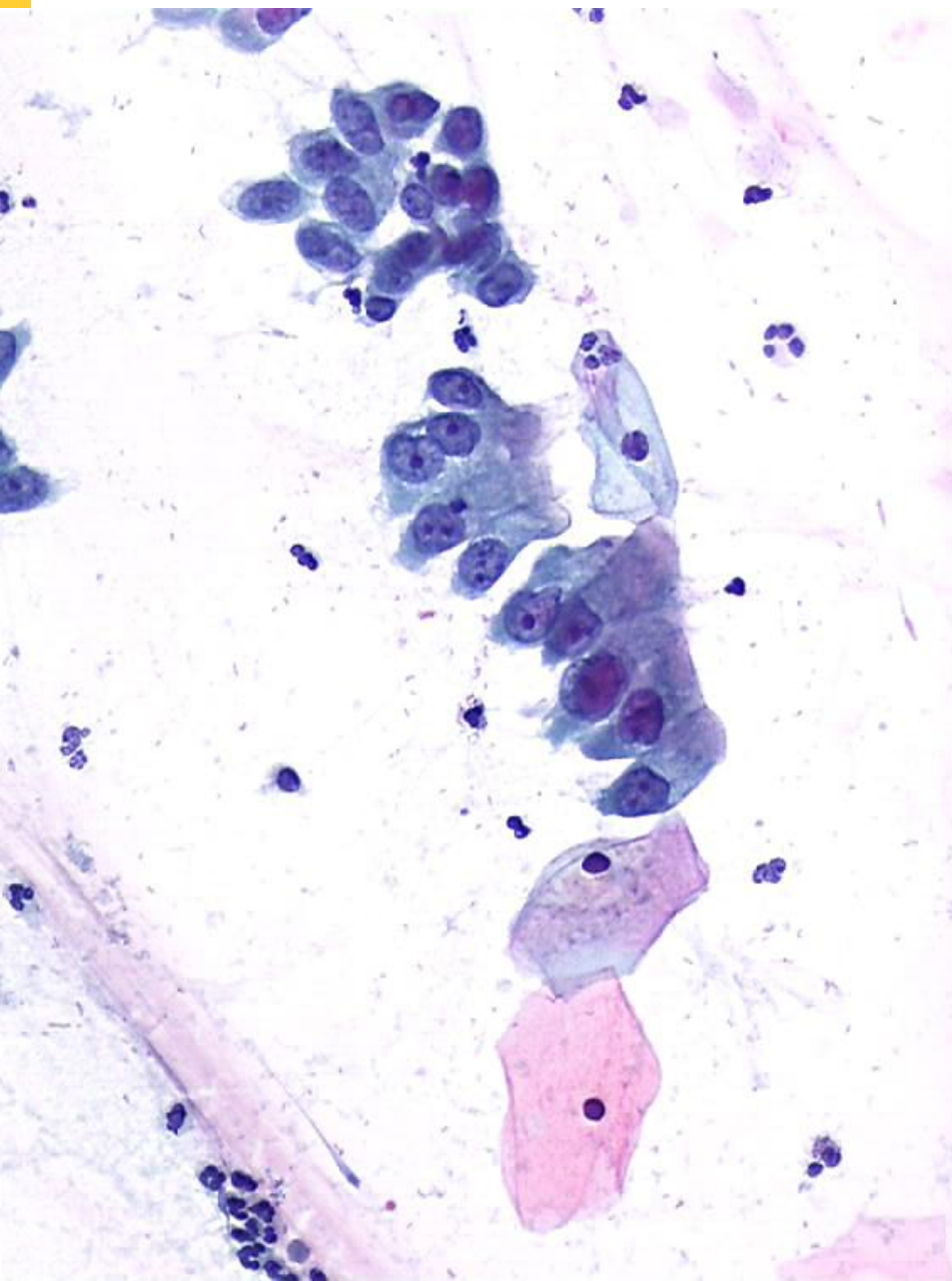


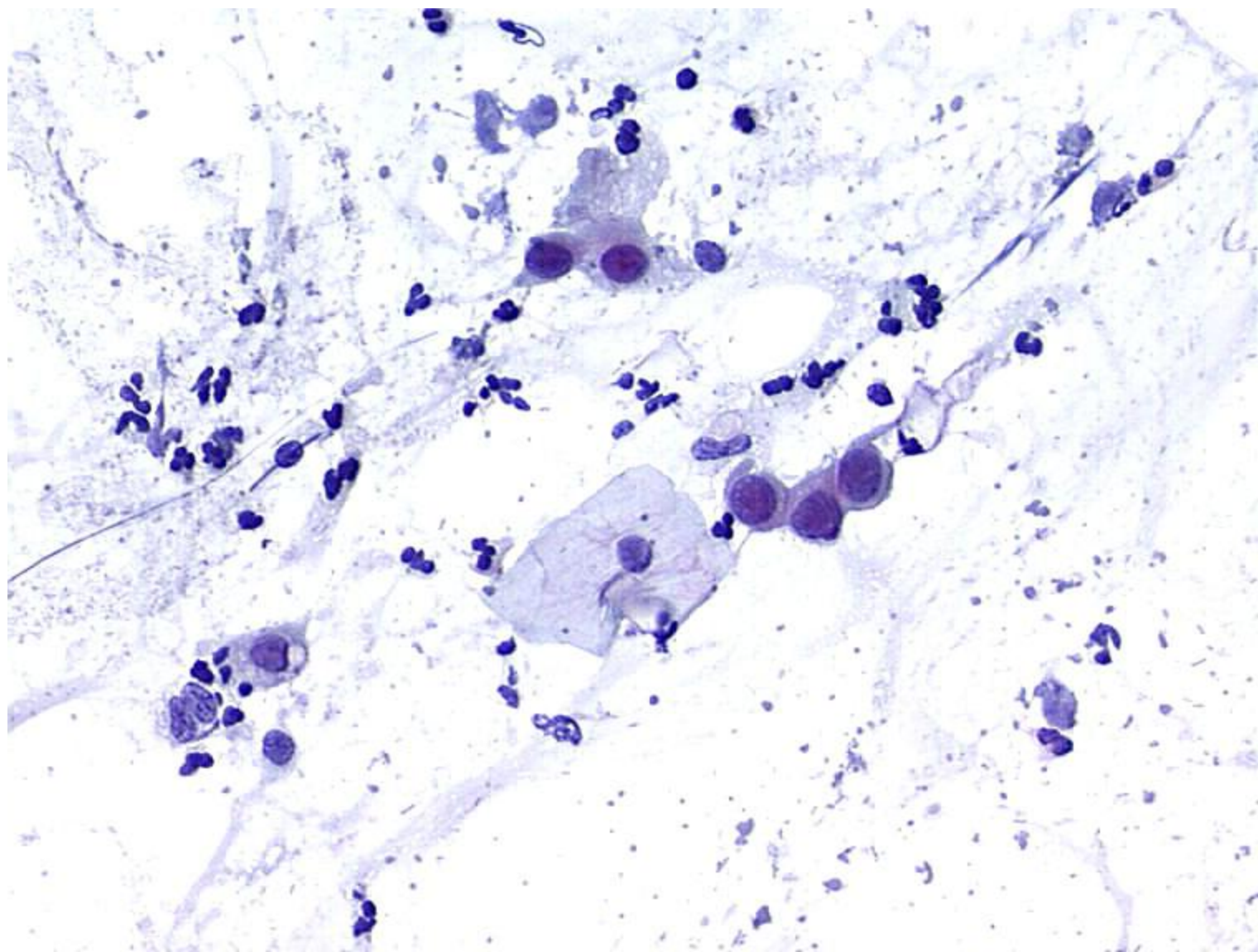


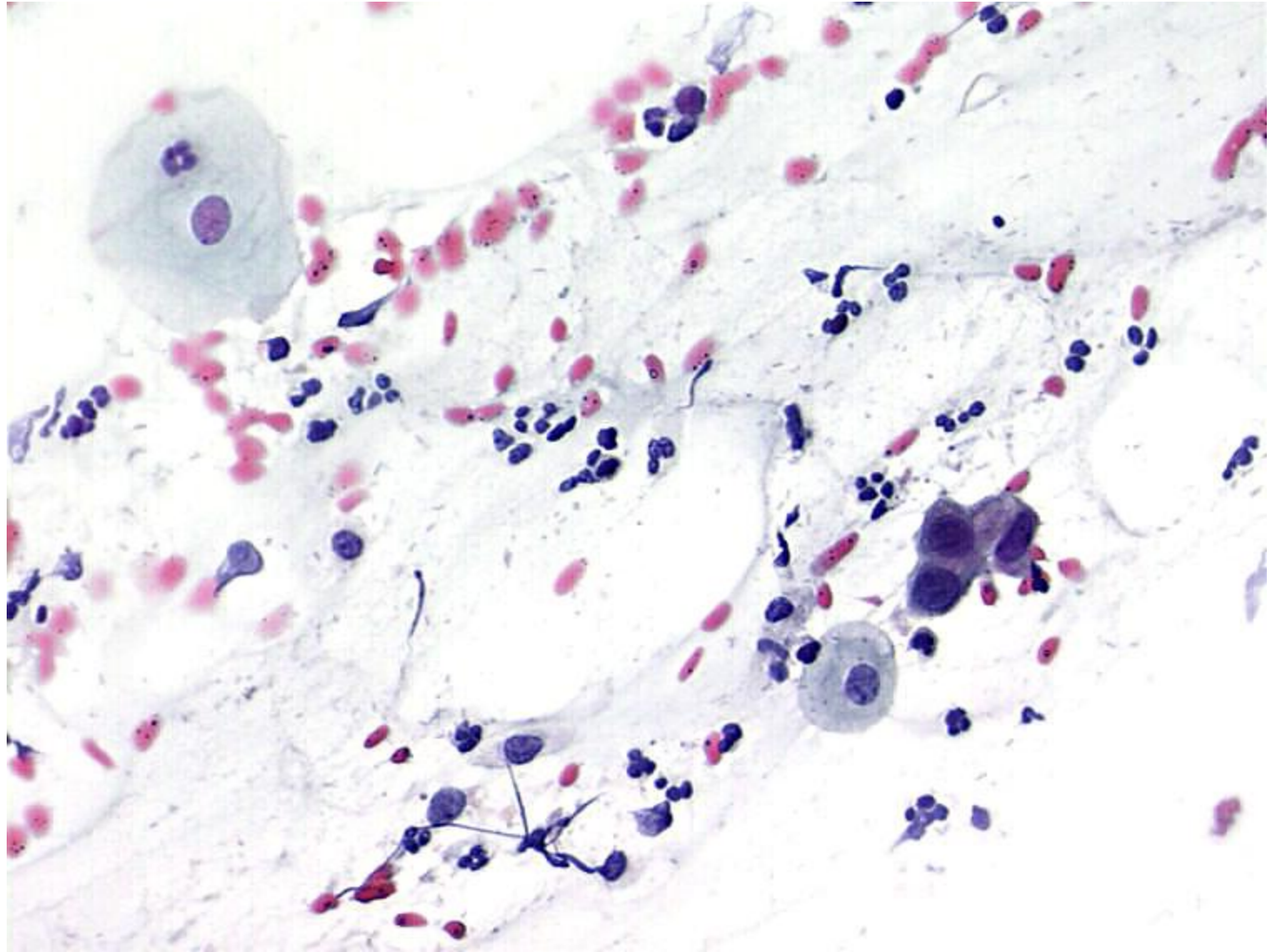
Next step

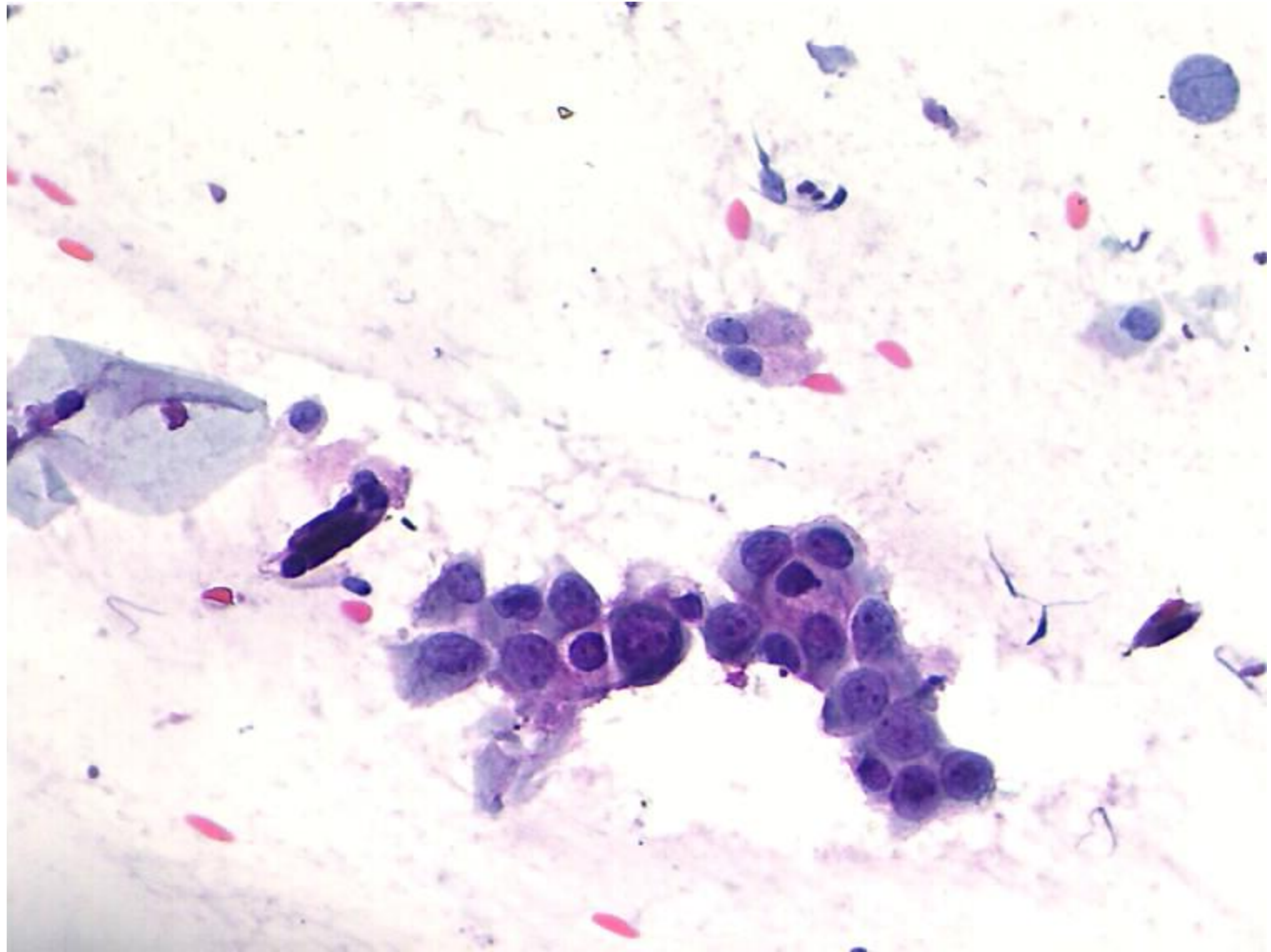
Back to cytology – what was missed in first examination?

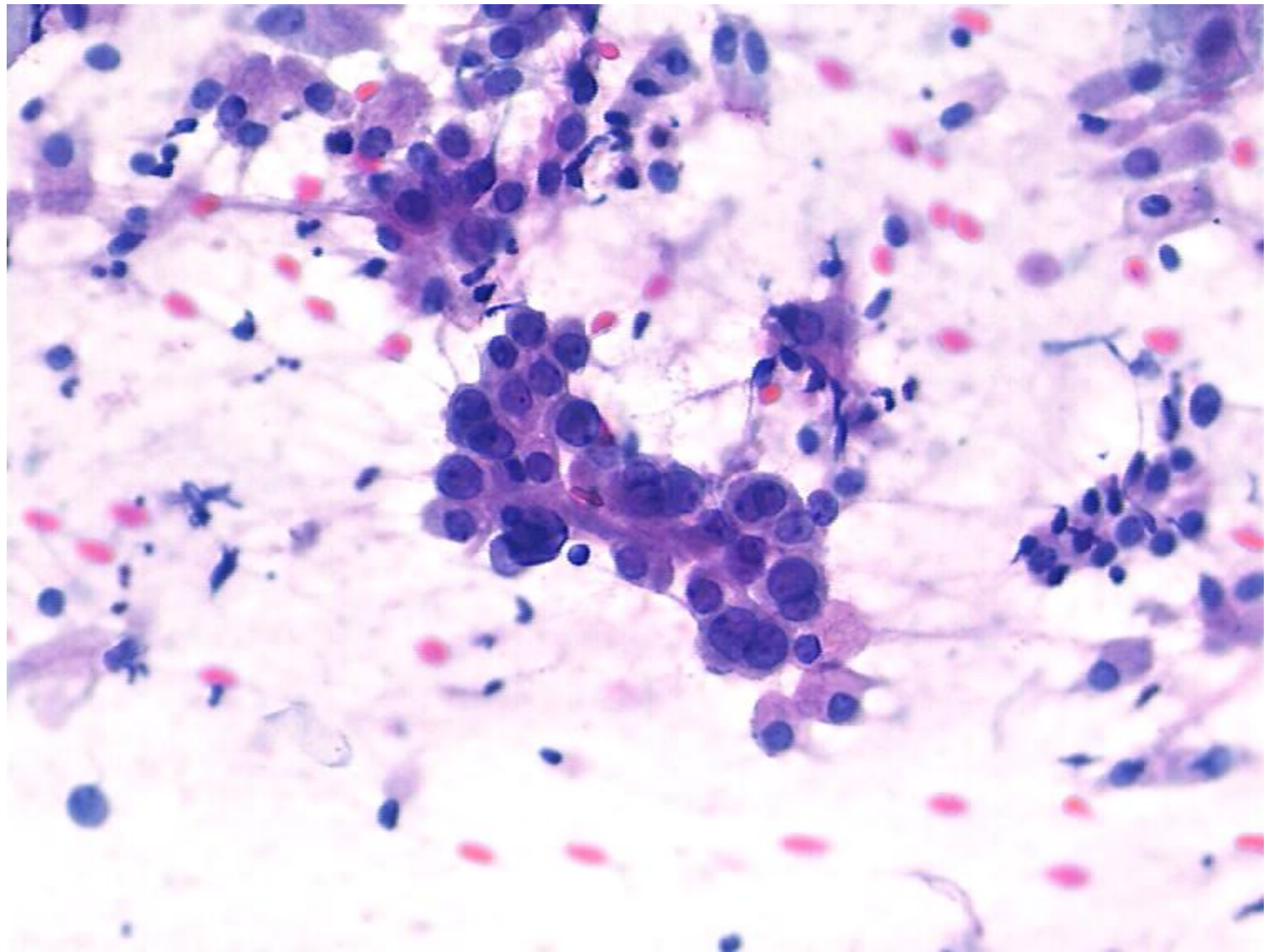






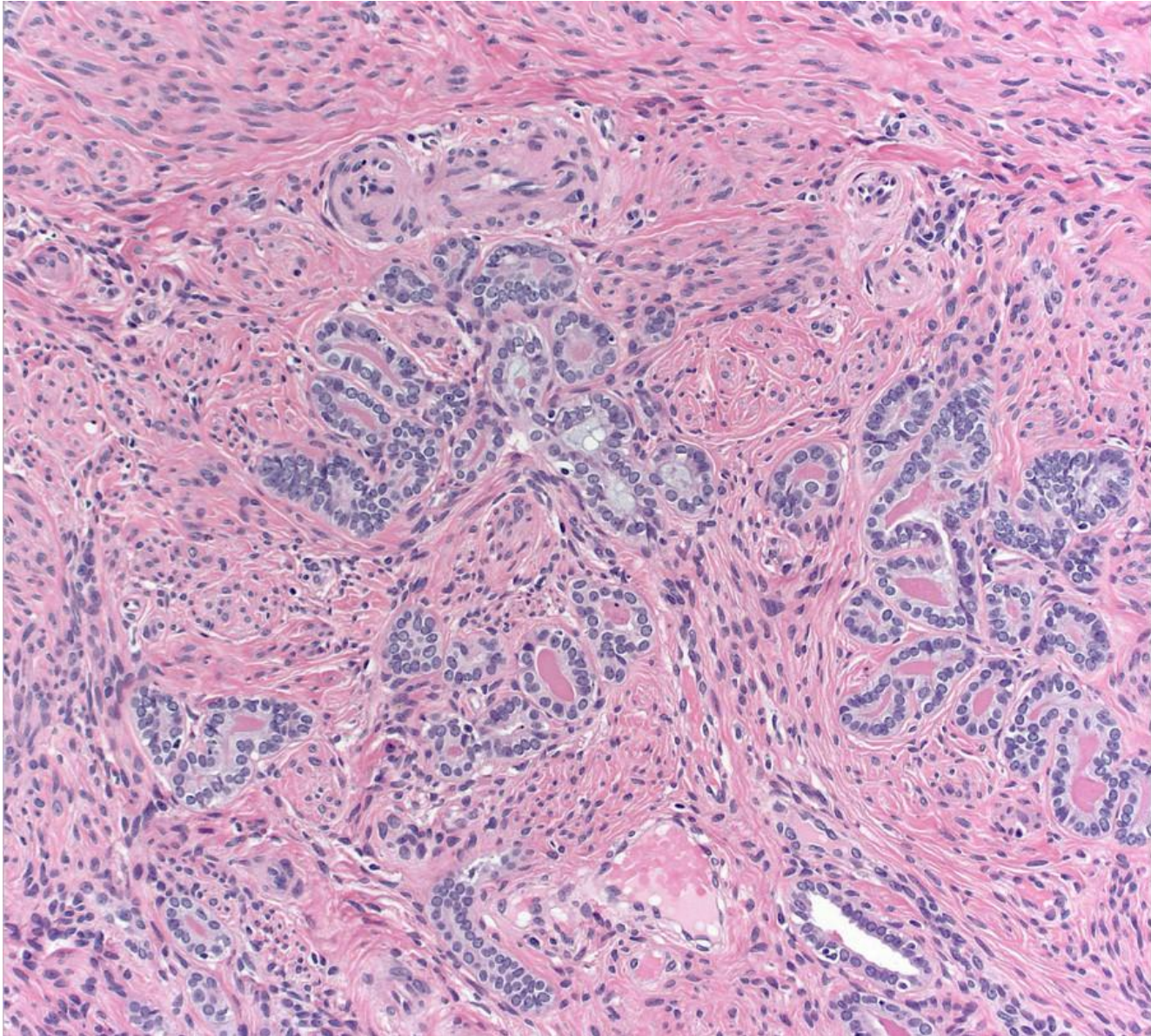






What is this?

Mesonephric remnants



Supposed diagnosis:

Mesonephric (like) adenocarcinoma

Cytology description of mesonephric cells

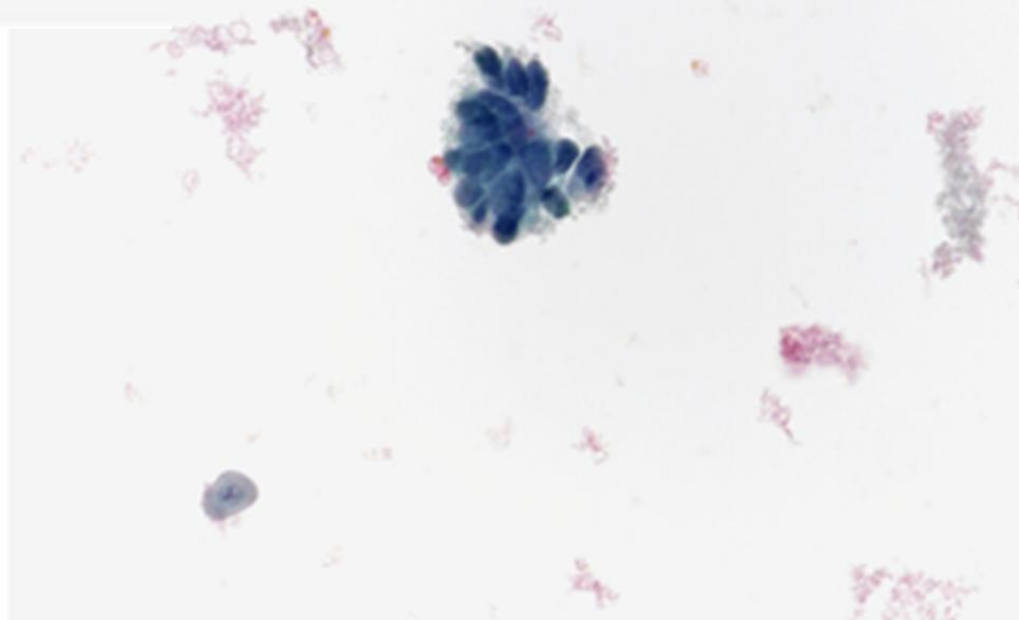
- Clusters of epithelial cells in tubular, cribriform and sheet-like proliferations (Cytopathology 2013;24:129)
- Round to oval, occasionally angulated, small to medium sized nuclei with mild to moderate atypia and increased N:C ratio (Cytopathology 2013;24:129)
- Intraluminal eosinophilic material (Cytopathology 2013;24:129)
- Infrequently detected by cervical cytology compared to cervical squamous cell carcinoma (BMJ Case Rep 2012;2012:bcr0120125632)

Cytological features:

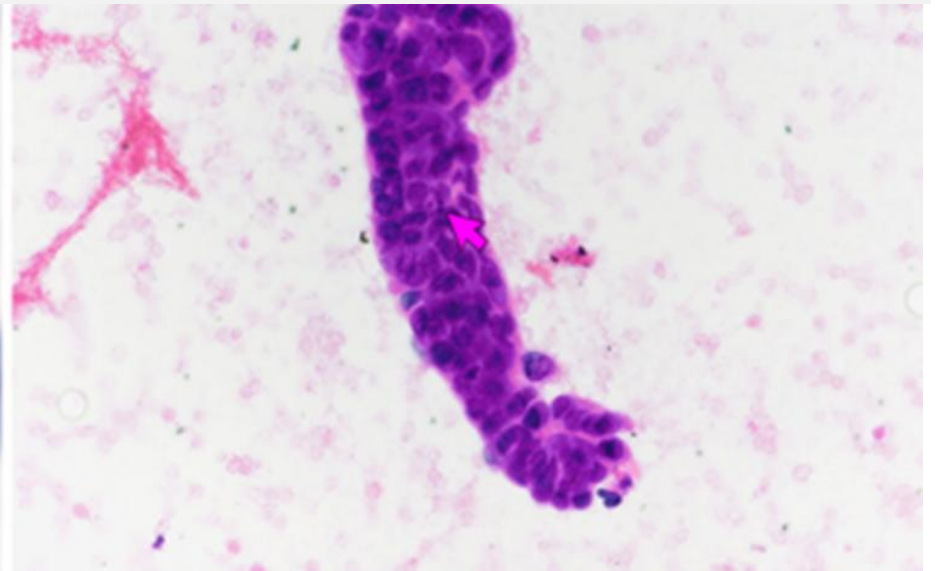
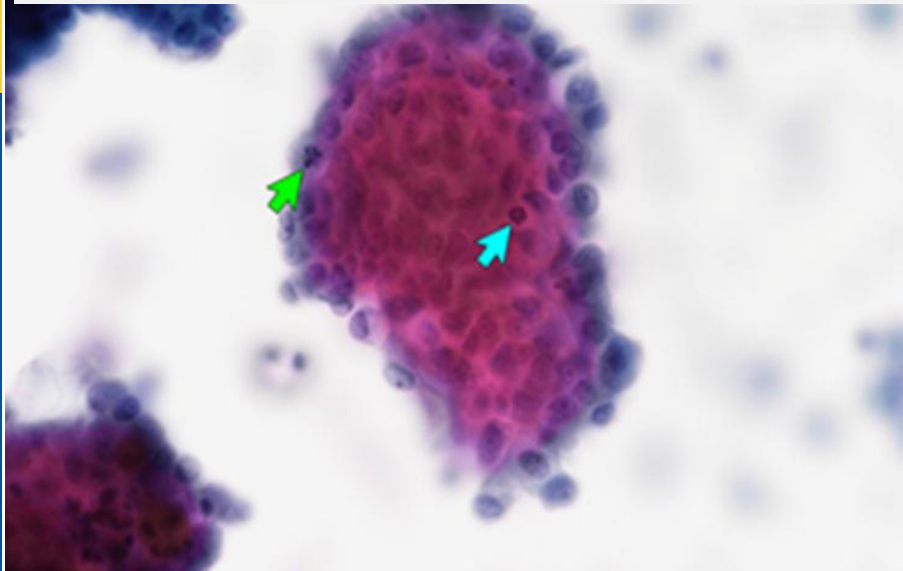
tumor cells possess relatively monotonous, round nuclei and scant cytoplasm, resulting in a *high nuclear-to-cytoplasmic ratio*. Nucleoli are indistinct.

Cytological features:

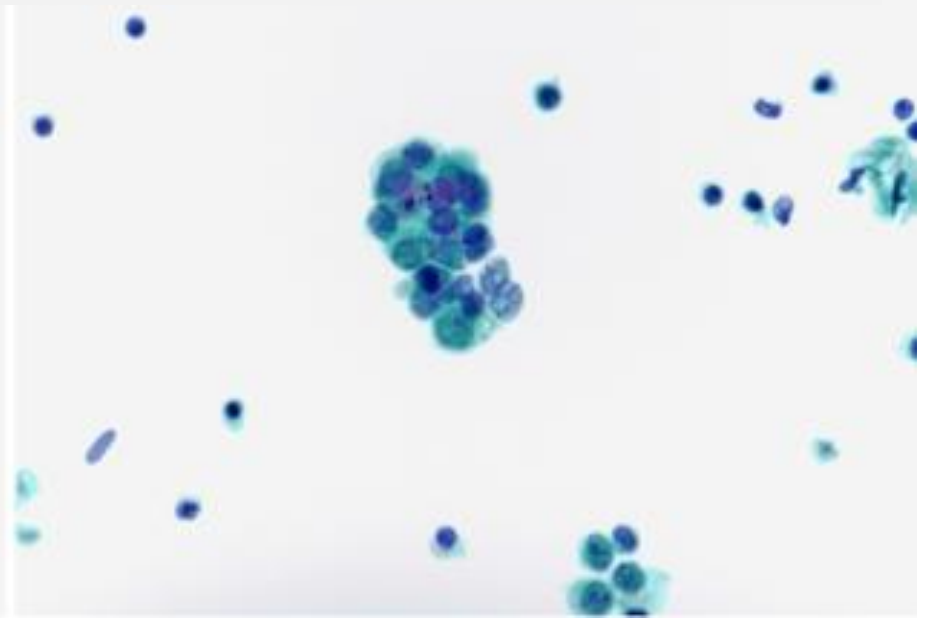
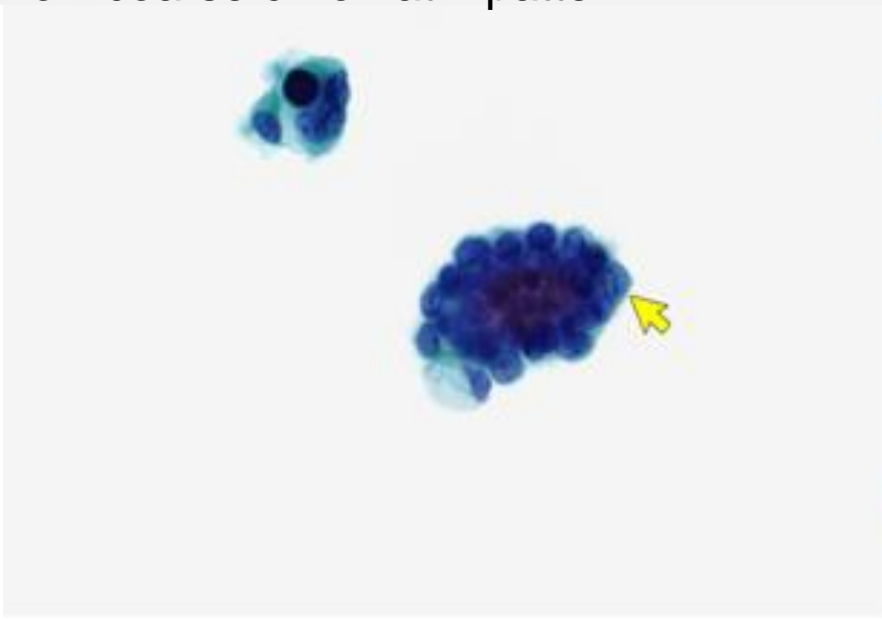
in addition to round nuclei some cells are with *fusiform shape* are also identified on the same cytology slide.



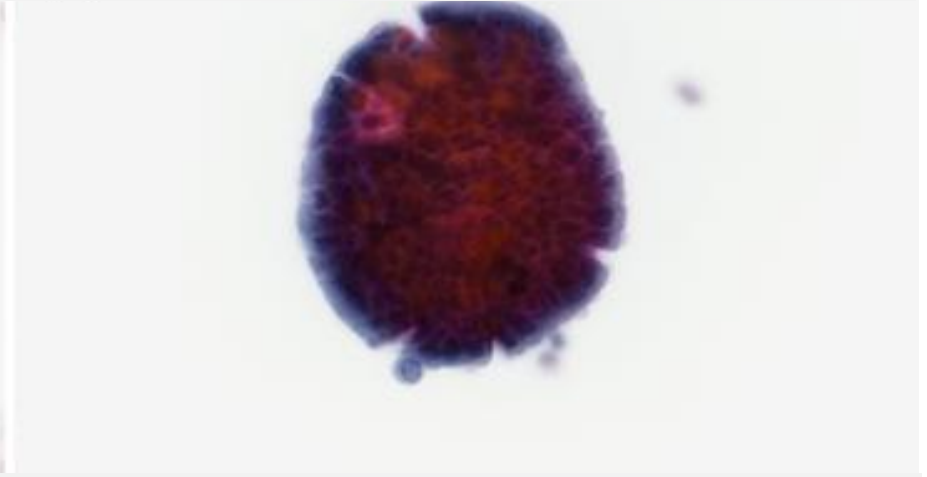
A mitotic figure (blue) and an atypical one (green) were detected within the three-dimensional cellular cluster. *Apoptotic bodies* (pink arrow)



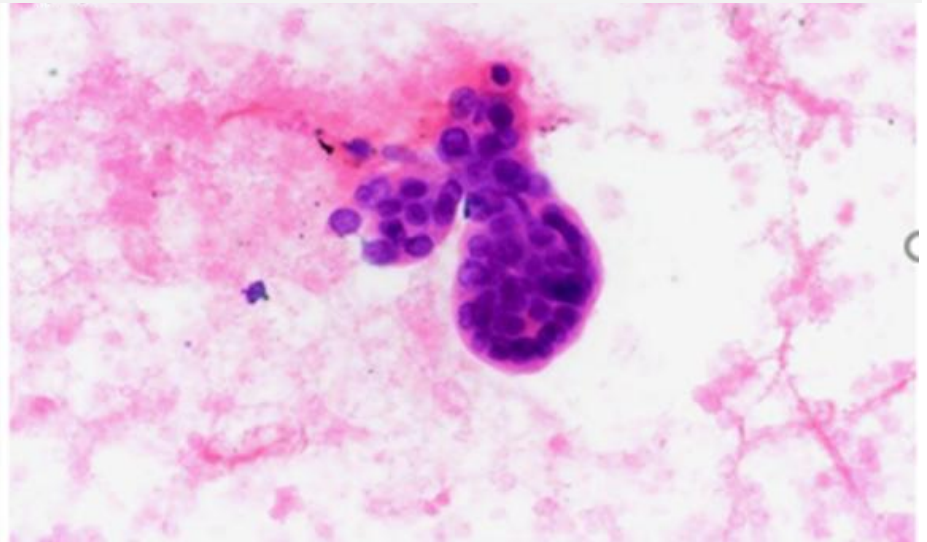
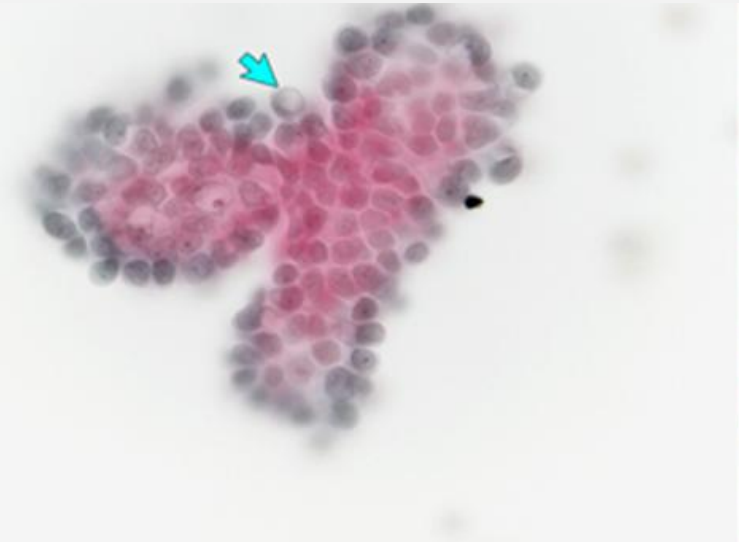
Some tumor cells exhibit *intranuclear grooves* (yellow arrow). Tumor cell nuclei show coarse chromatin pattern



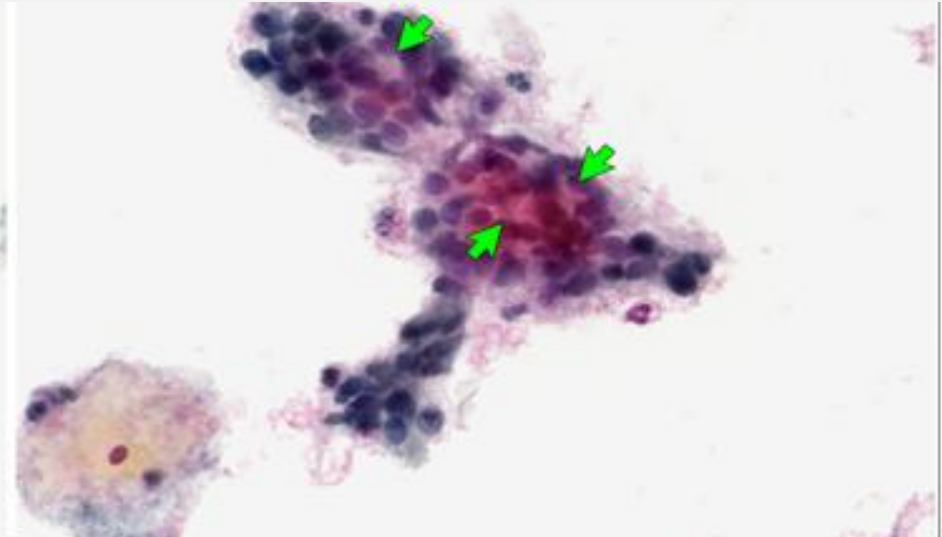
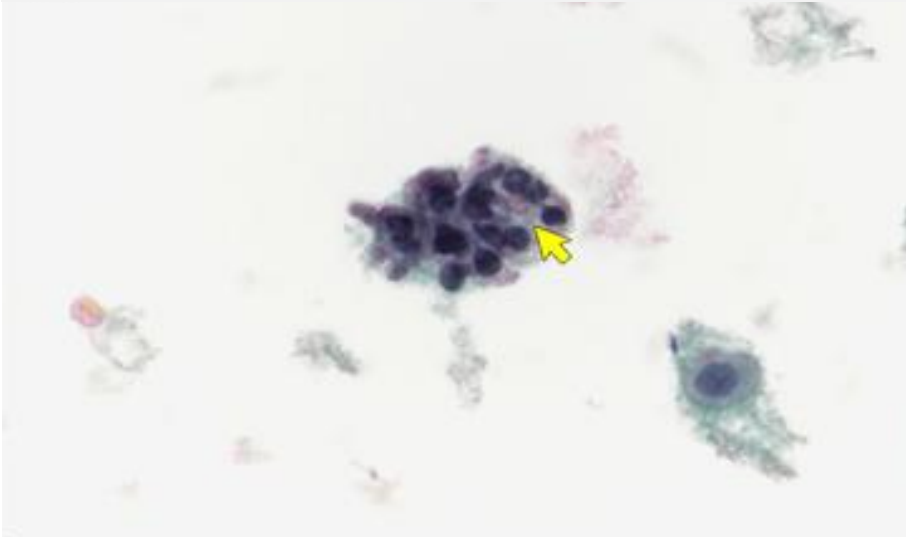
A three-dimensional cluster of tumor cells is present, with a few scattered neutrophils in the background



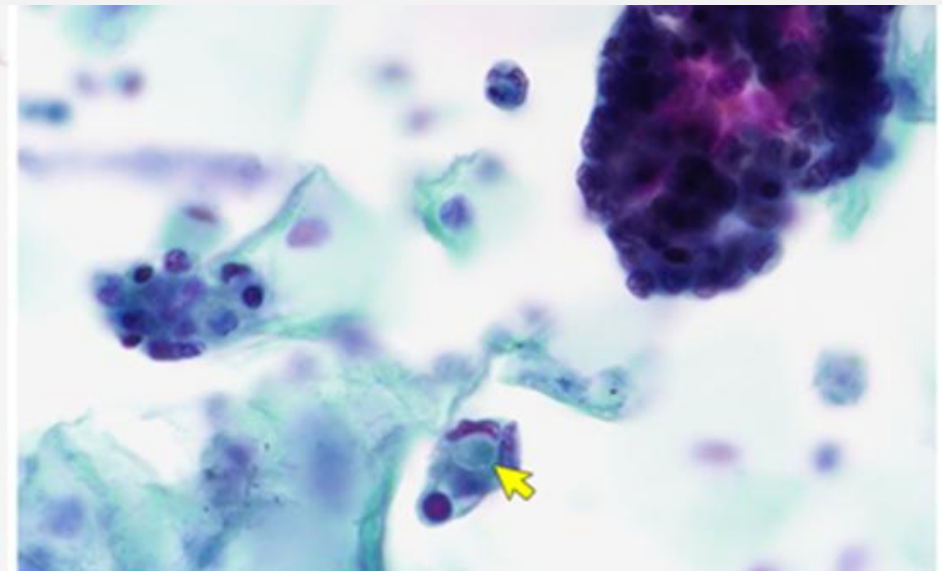
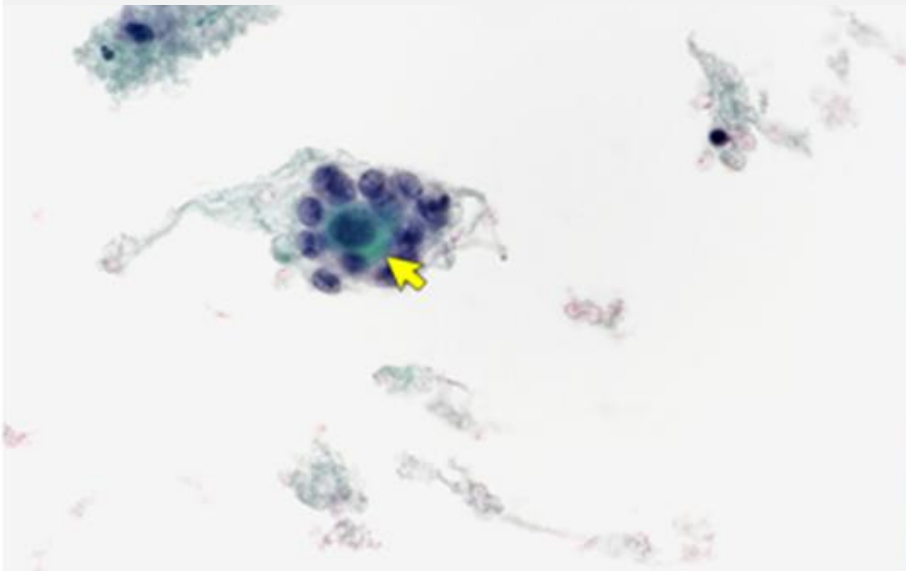
Papillary clusters with few intranuclear cytoplasmic pseudoinclusions (blue arrow). Tumor cells in the form of a tight cluster showing hyperchromatic, overlapped nuclei and cytoplasm oriented toward the periphery of the cluster



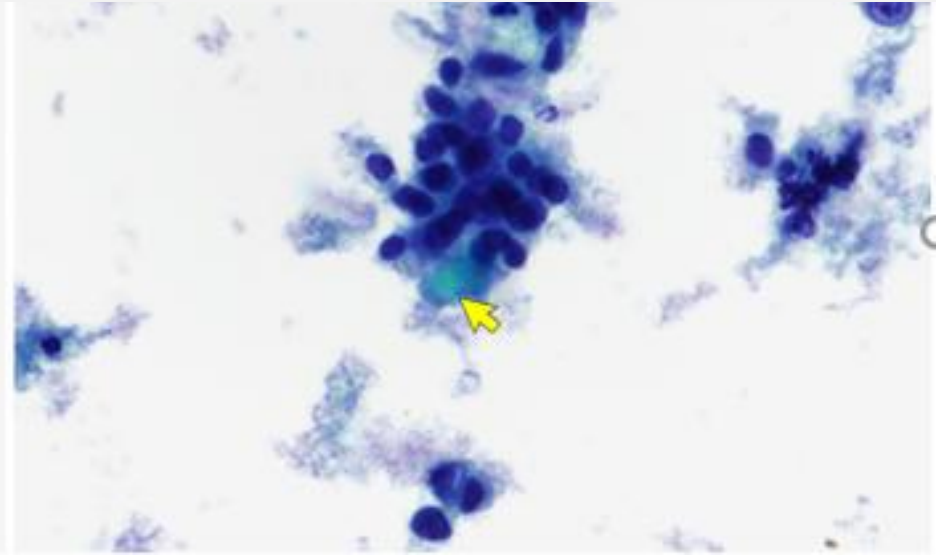
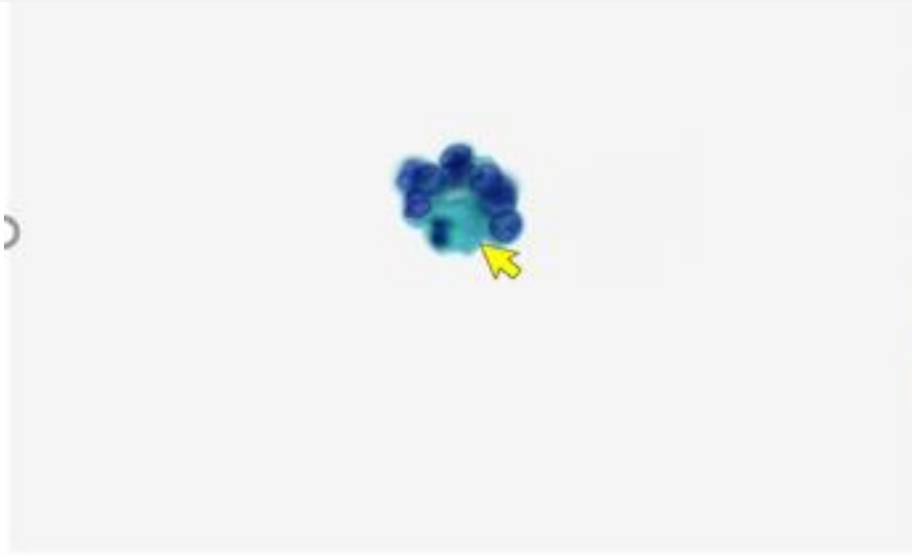
A small floating papillary tuft displays round, hyperchromatic nuclei with mild *pleomorphism and irregular membrane*: some clusters contain *tubular structures* (yellow and green arrows).



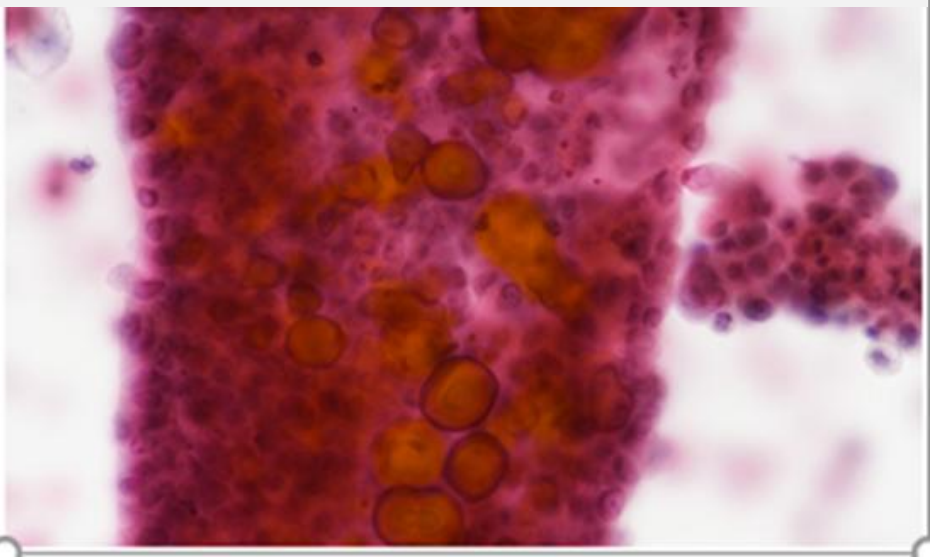
Hyaline-like globules: a hyaline-like globule appears to overlap with tumor cell nuclei or more often located in the *lumen-like spaces* between tumor cells.



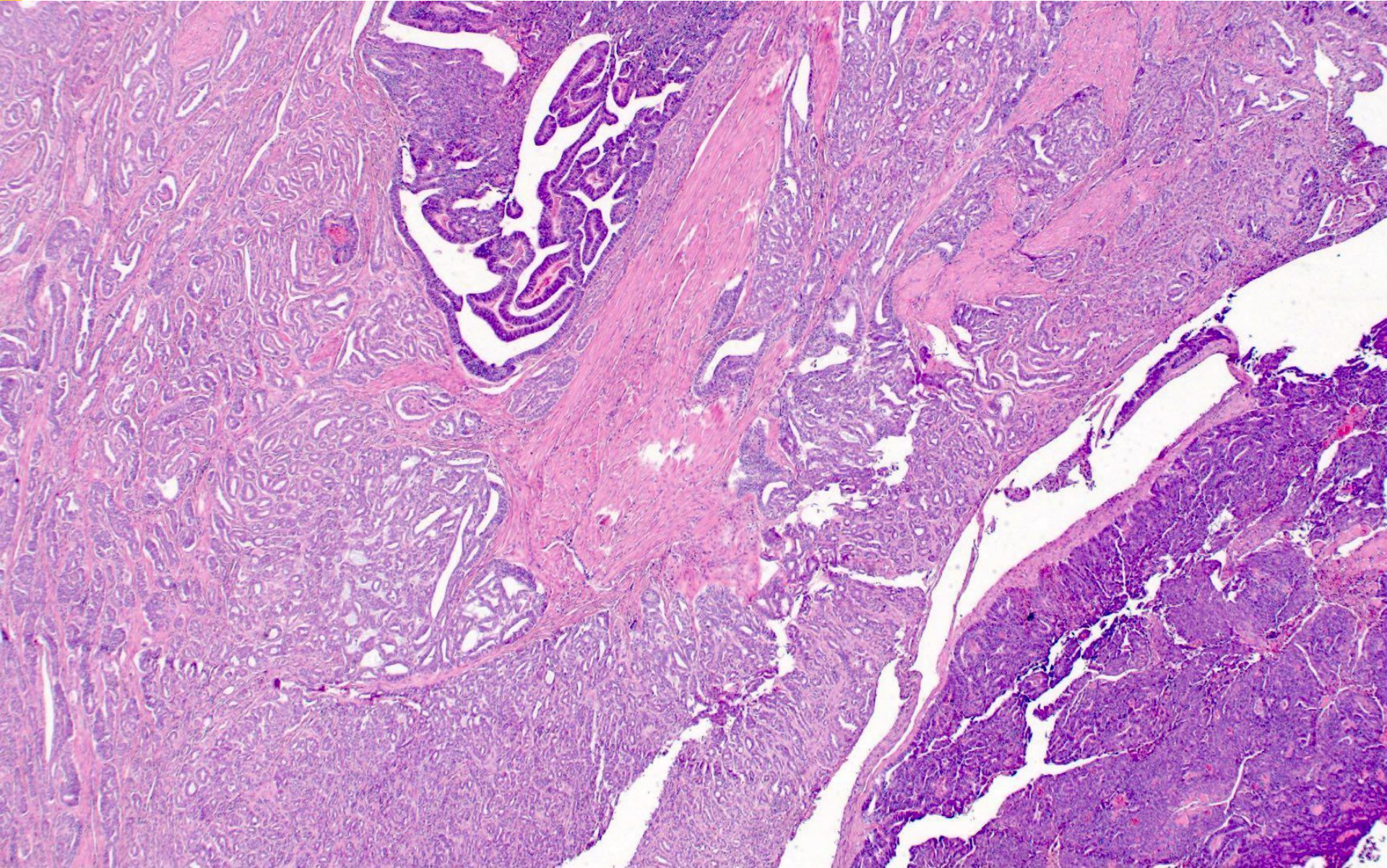
Isolated tumor cells with *hyaline globules* and hyaline globules adhered to the periphery of tumor cell clusters

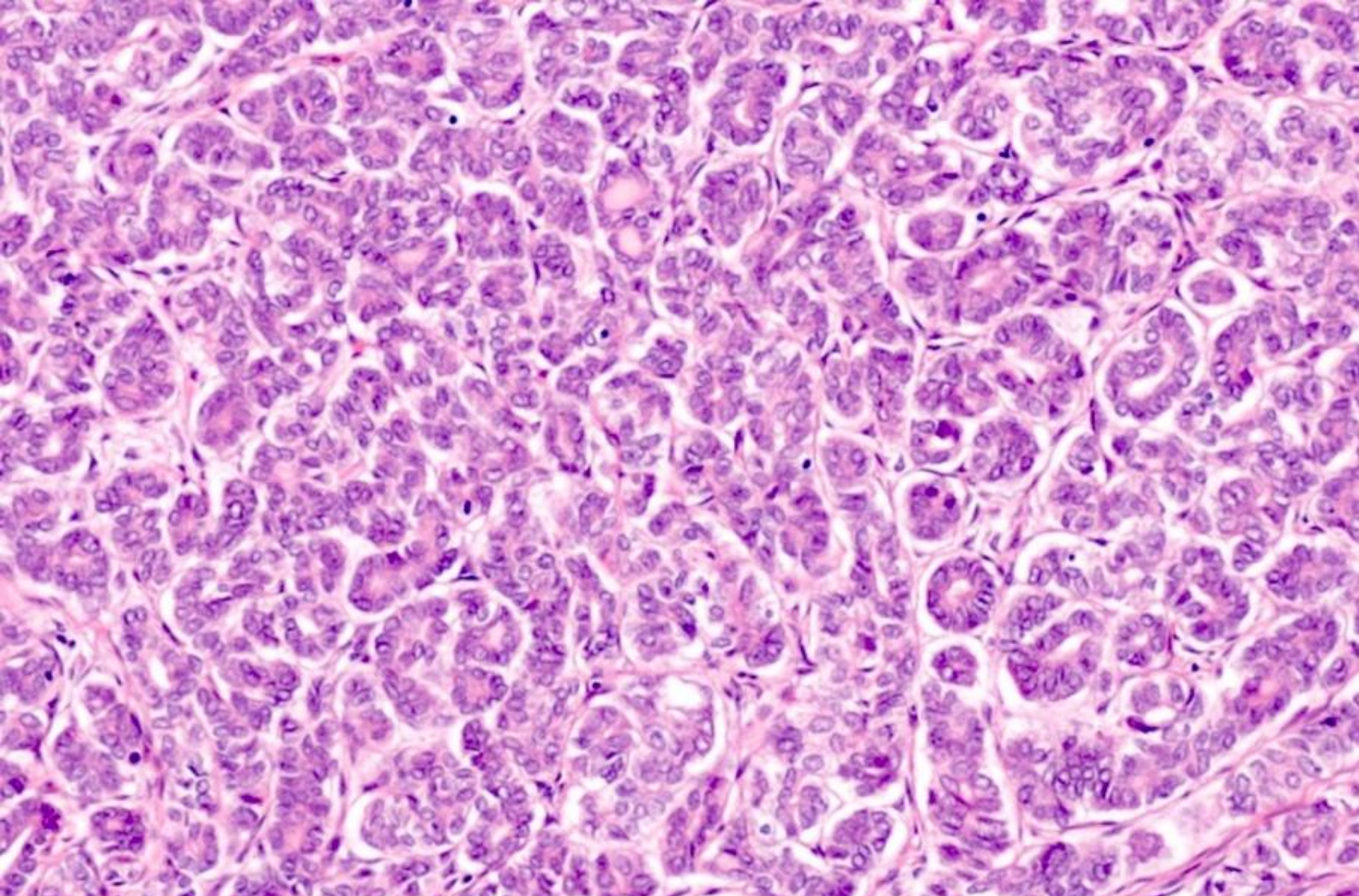


Hyaline globules inside papillary tufts and a large number of globules in three-dimensional cellular cluster (*psammomatous microcalcifications-like*)

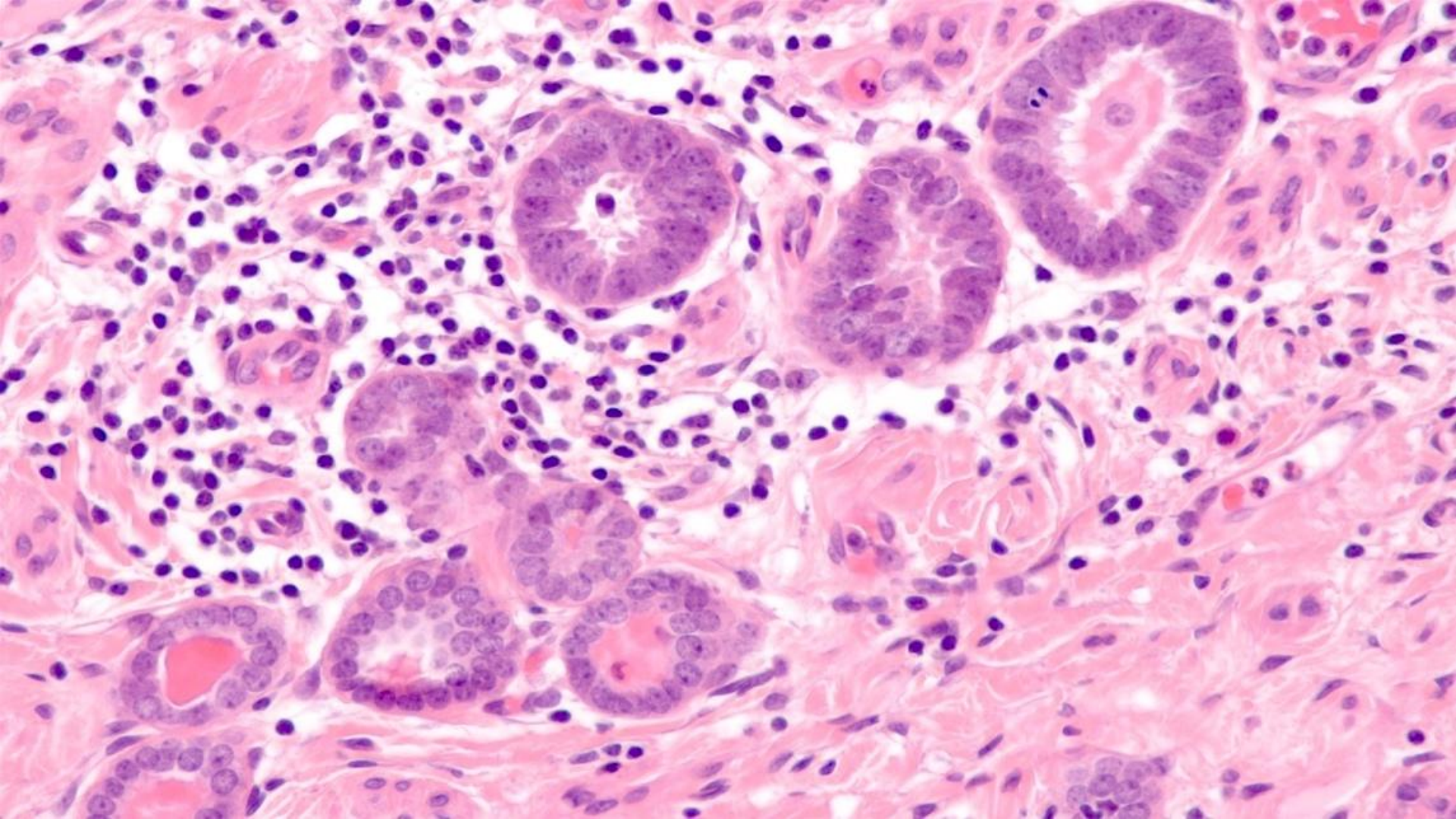


Mesonephric adenocarcinoma

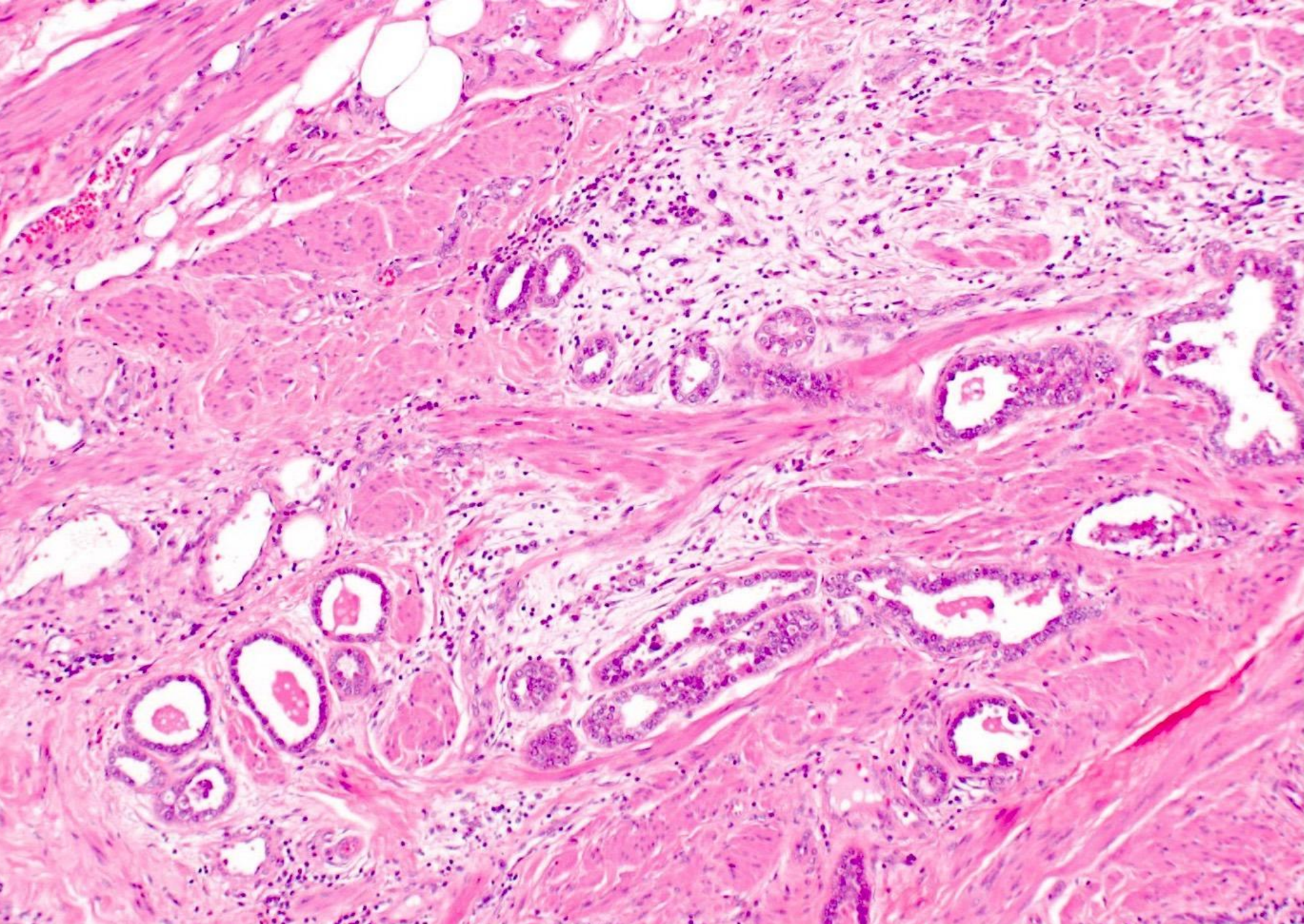




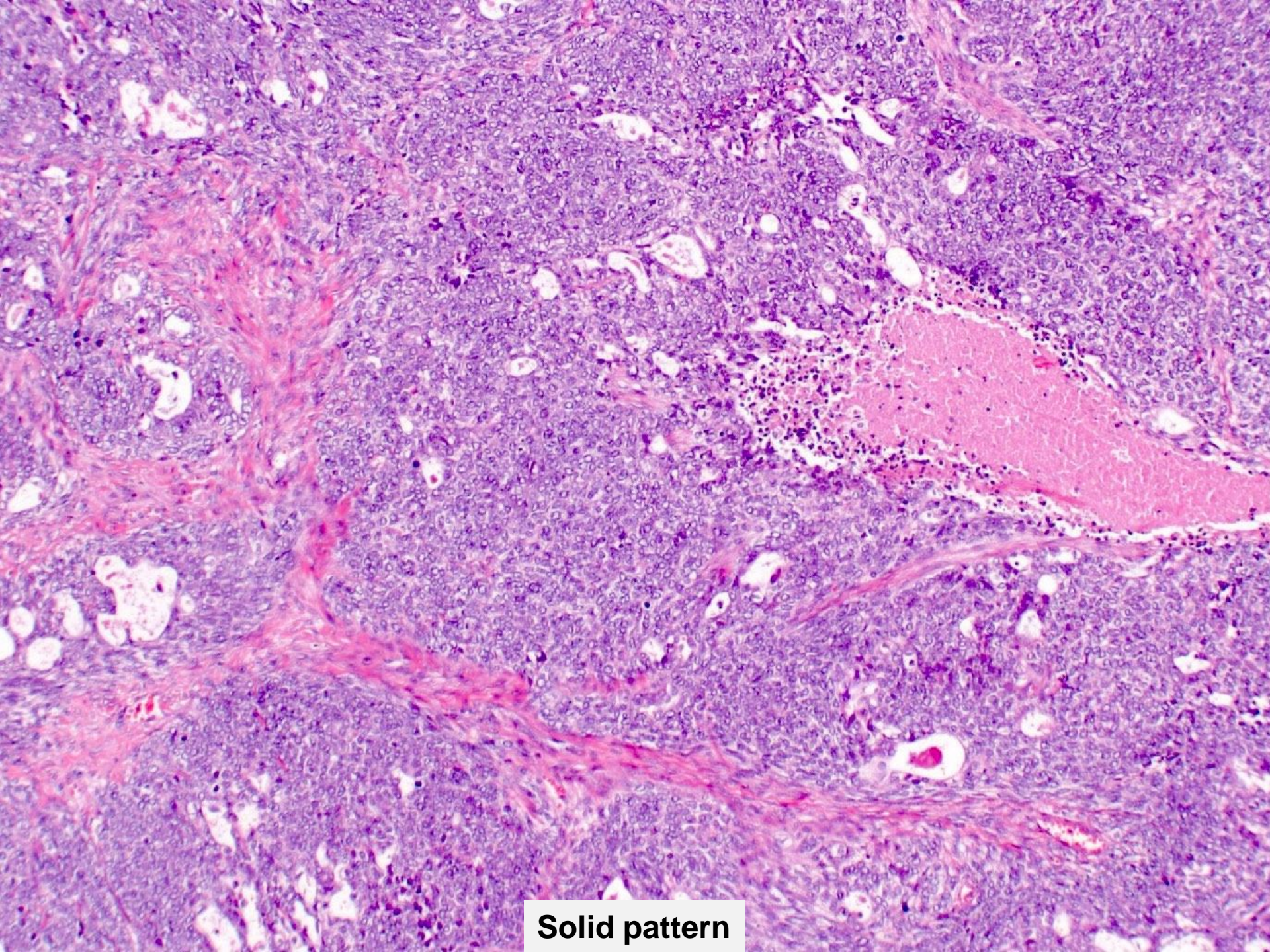
Mesonephric adenocarcinoma-tubular pattern



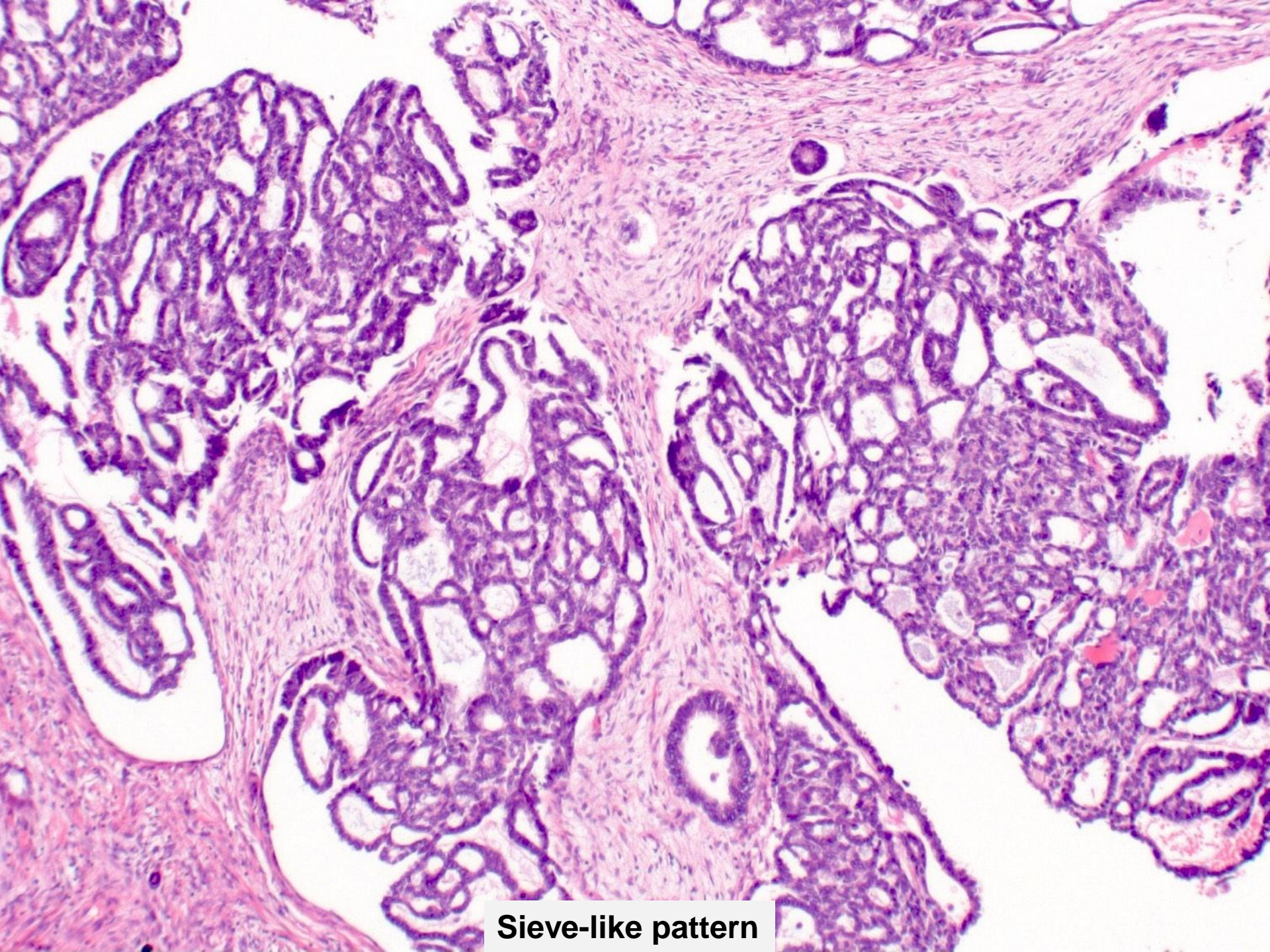
Tubular pattern with adjacent mesonephric remnants



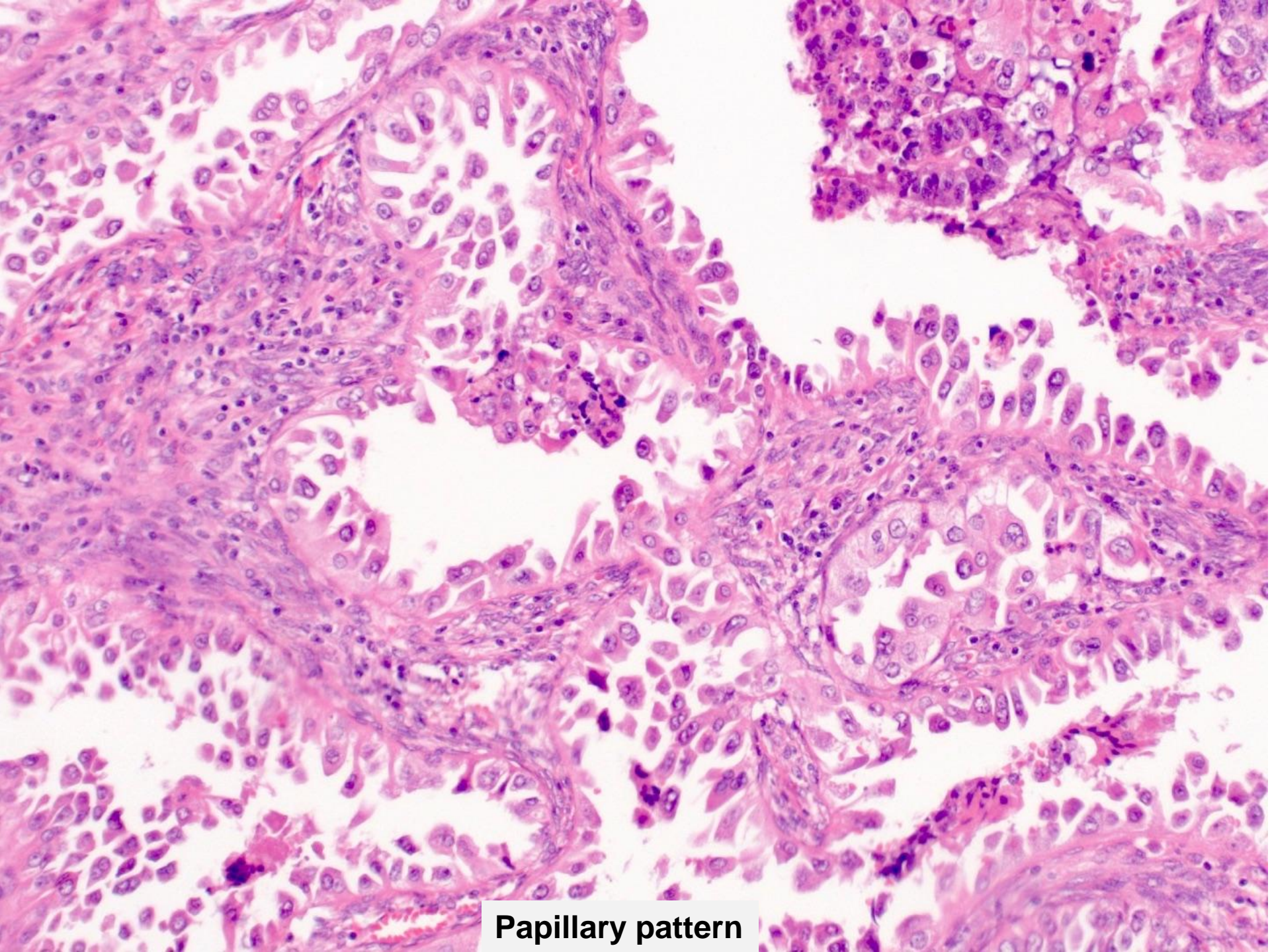
Tubular pattern with desmoplasia



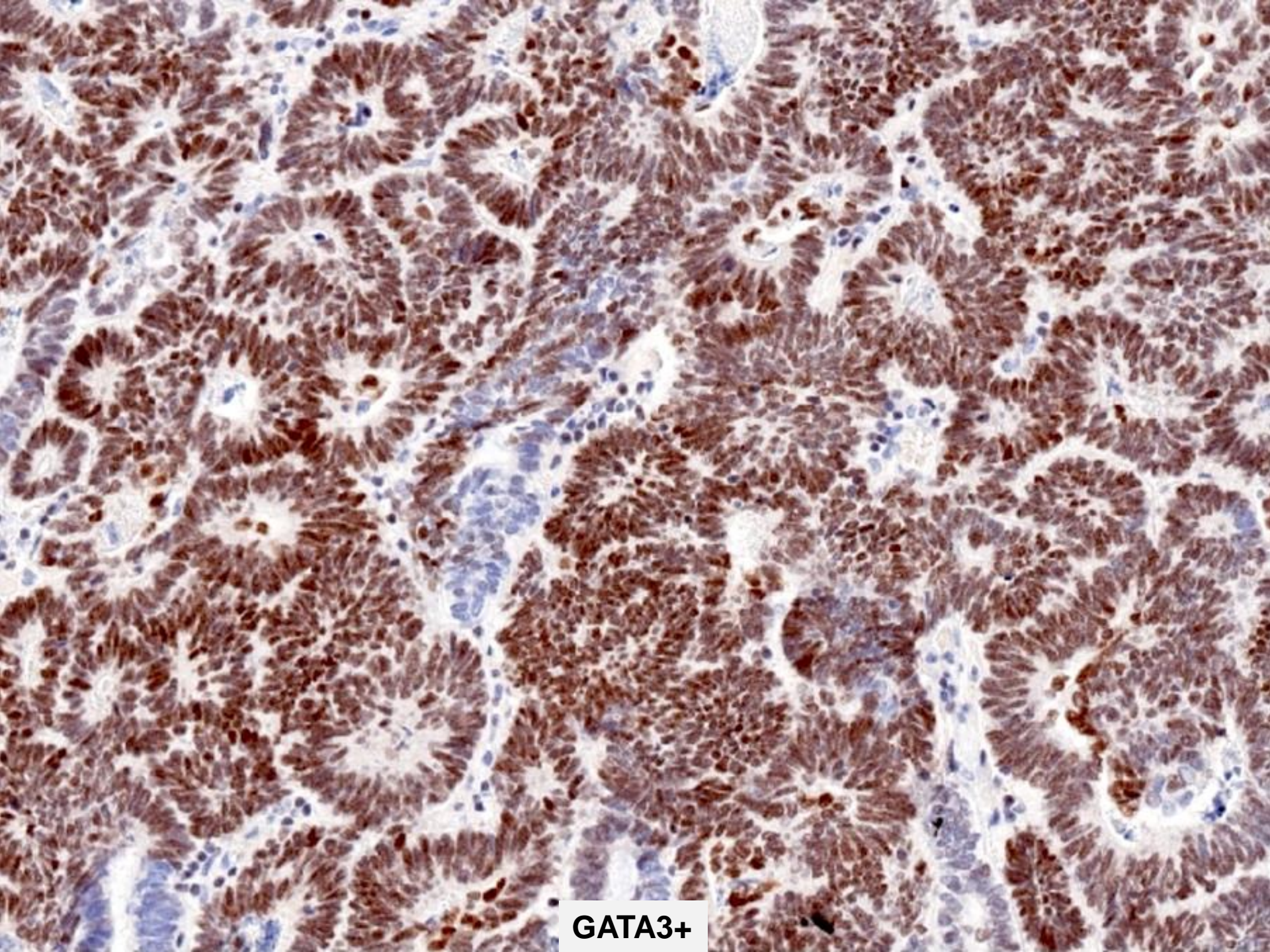
Solid pattern



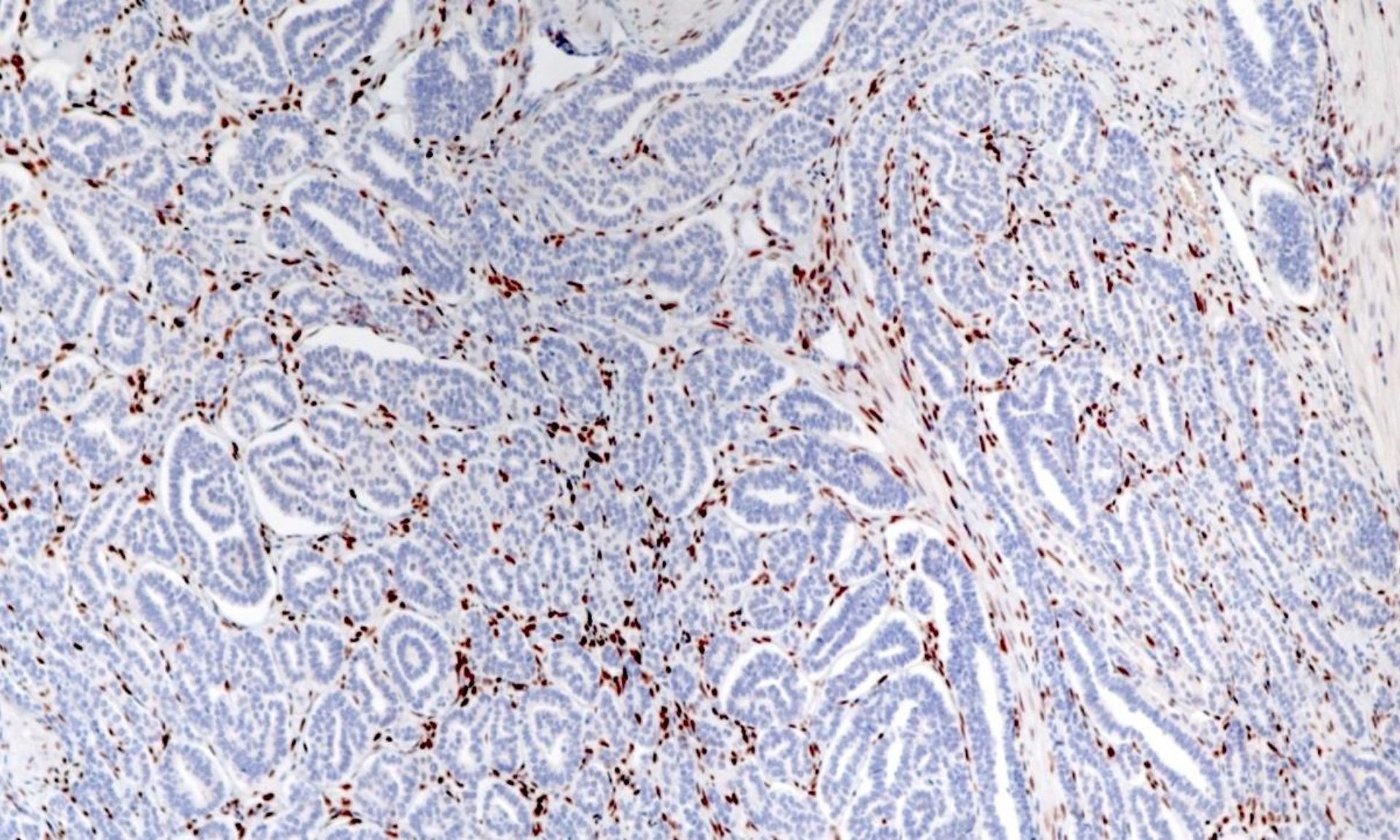
Sieve-like pattern



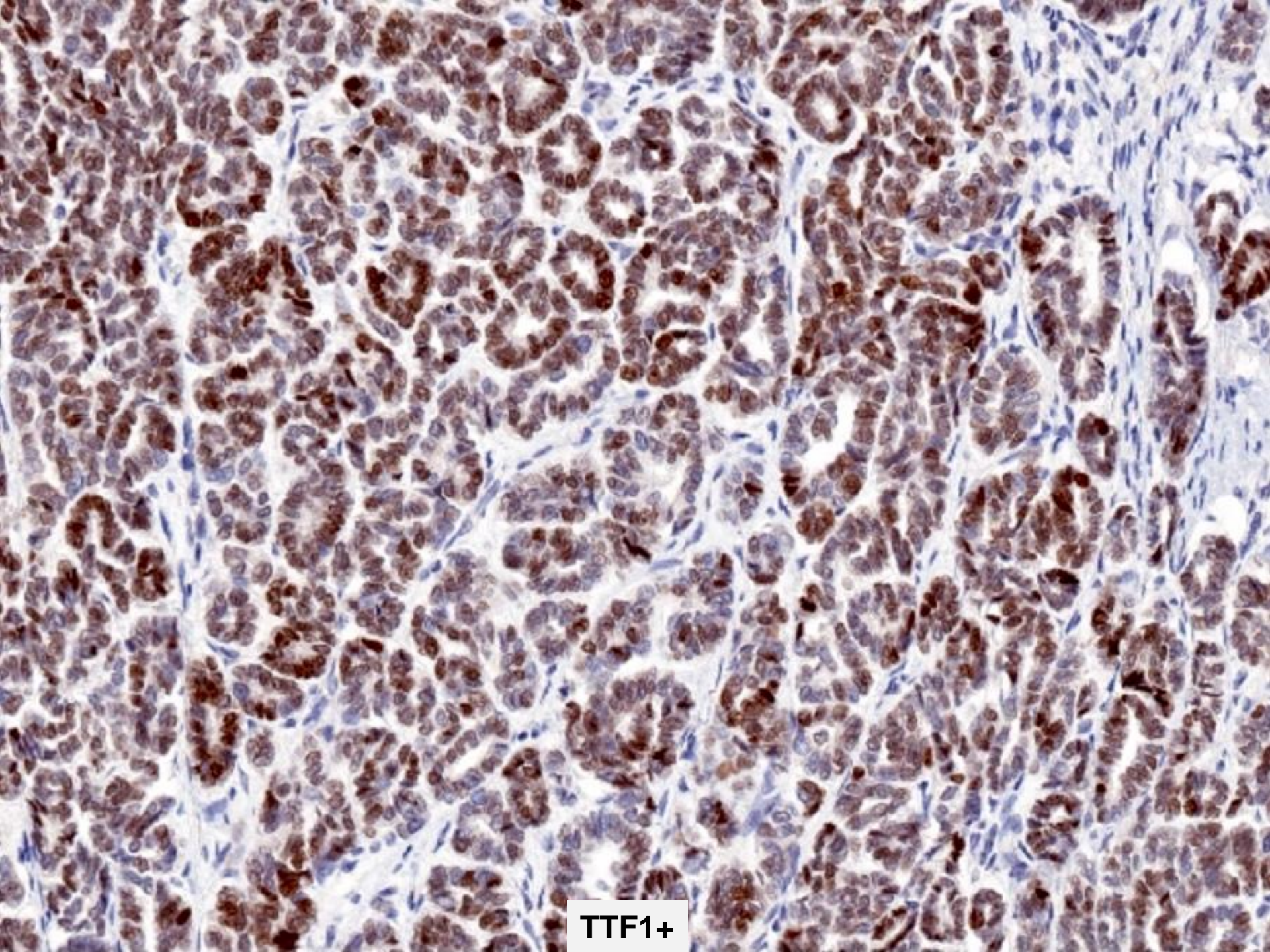
Papillary pattern



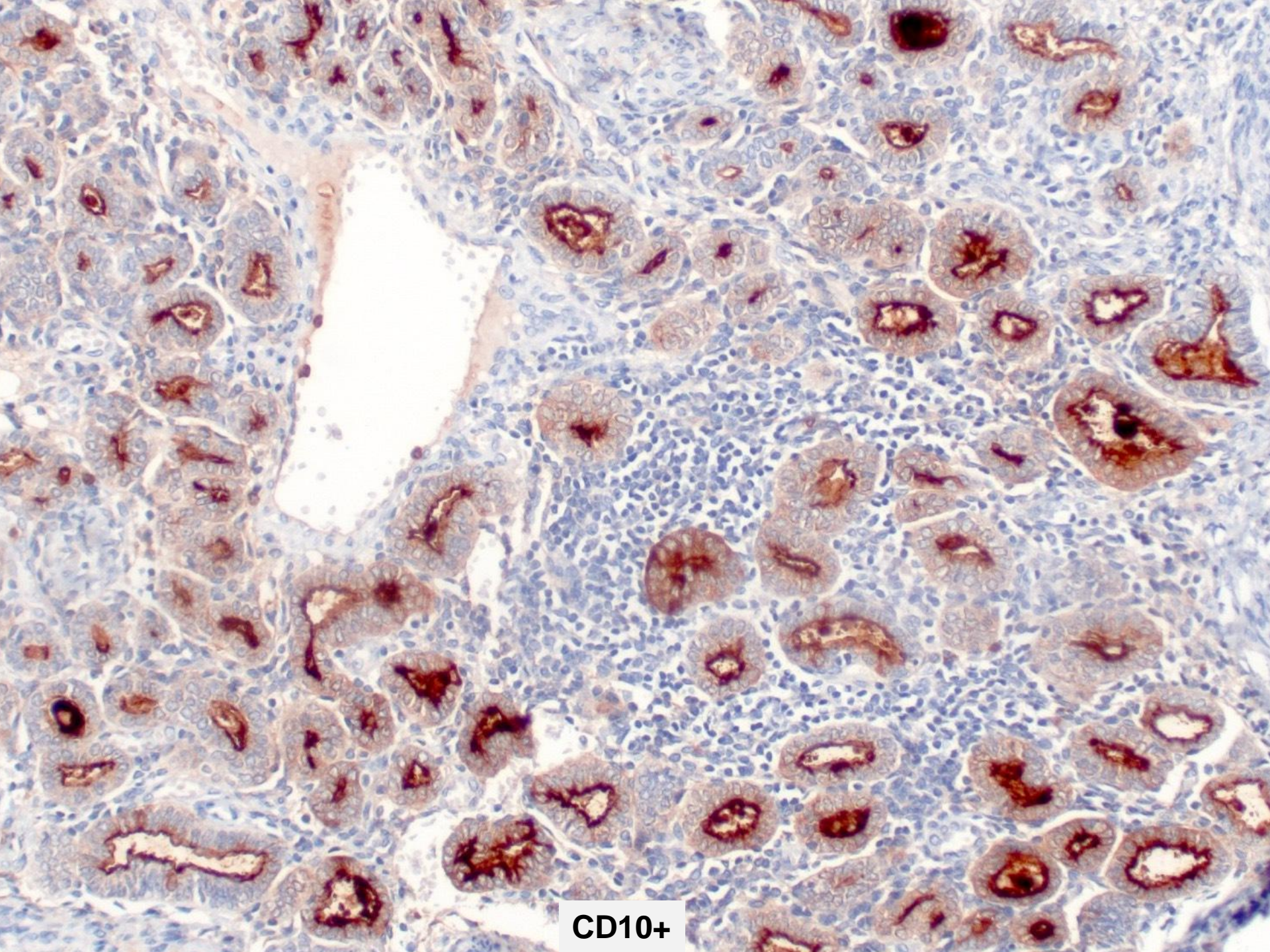
GATA3+



ER-



TTF1+

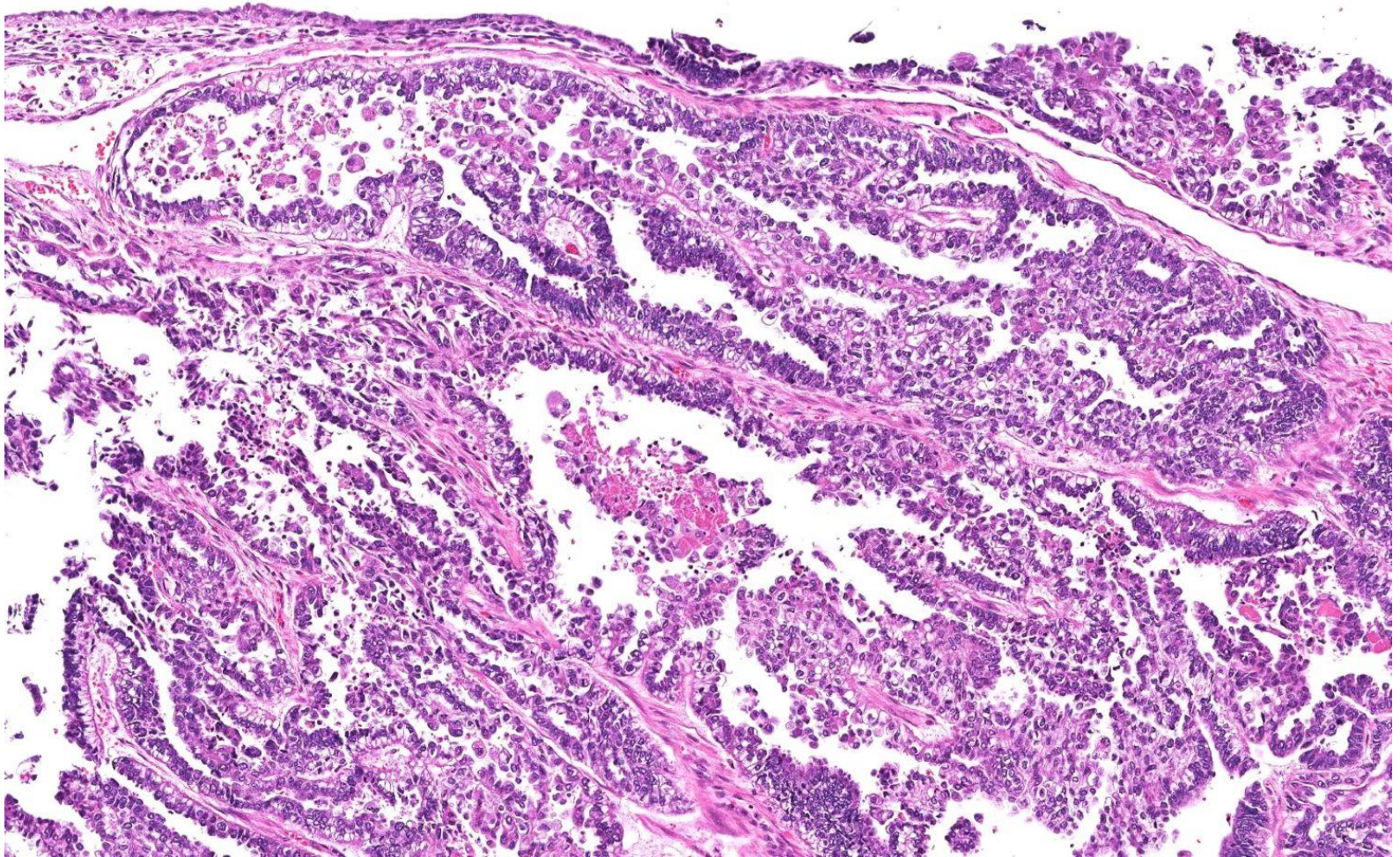


CD10+

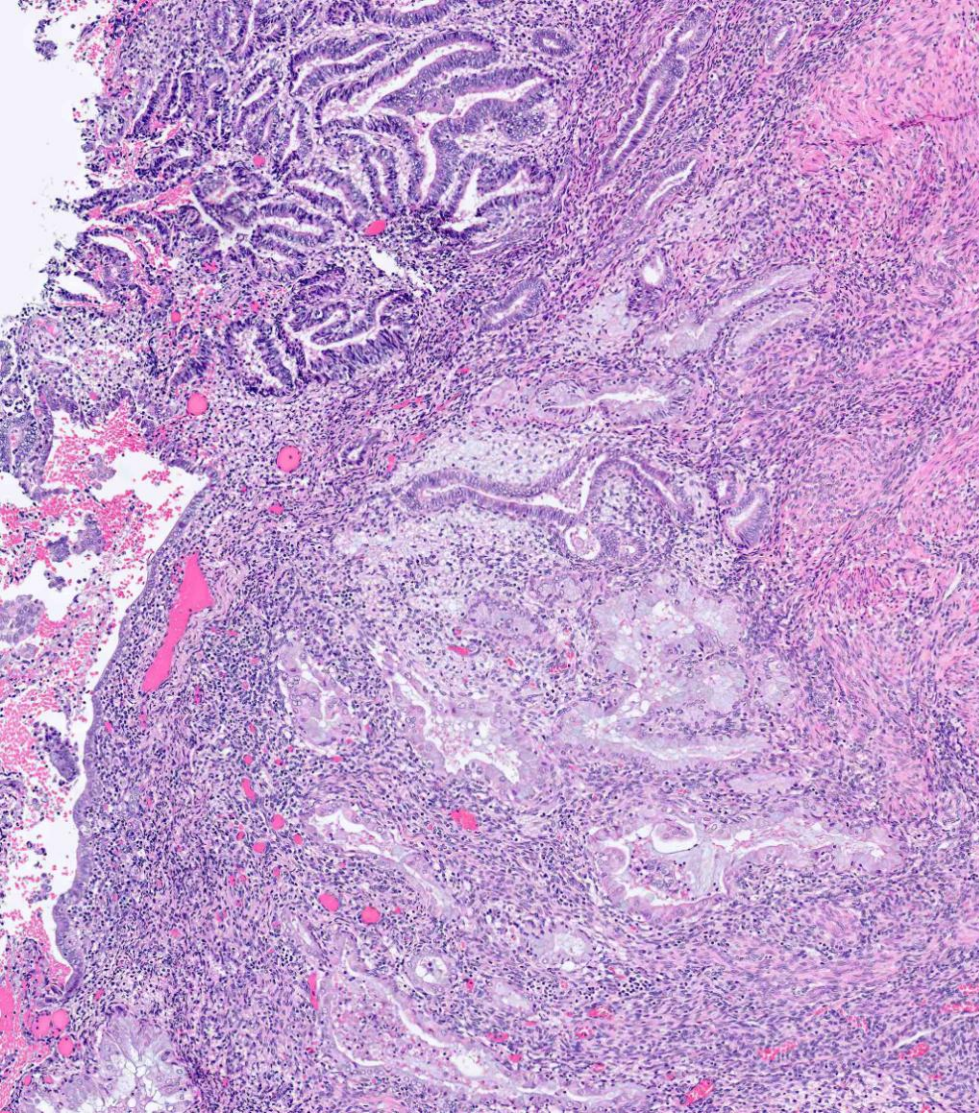
Differential diagnosis

Mesonephric-like adenocarcinoma (MLA) of the endometrium:

Bulk of tumor in uterine corpus, no associated mesonephric remnants, both are ER-, GATA3+, CD10+ and MLA more commonly TTF1+ than mesonephric adenocarcinoma of the cervix



Differential diagnosis

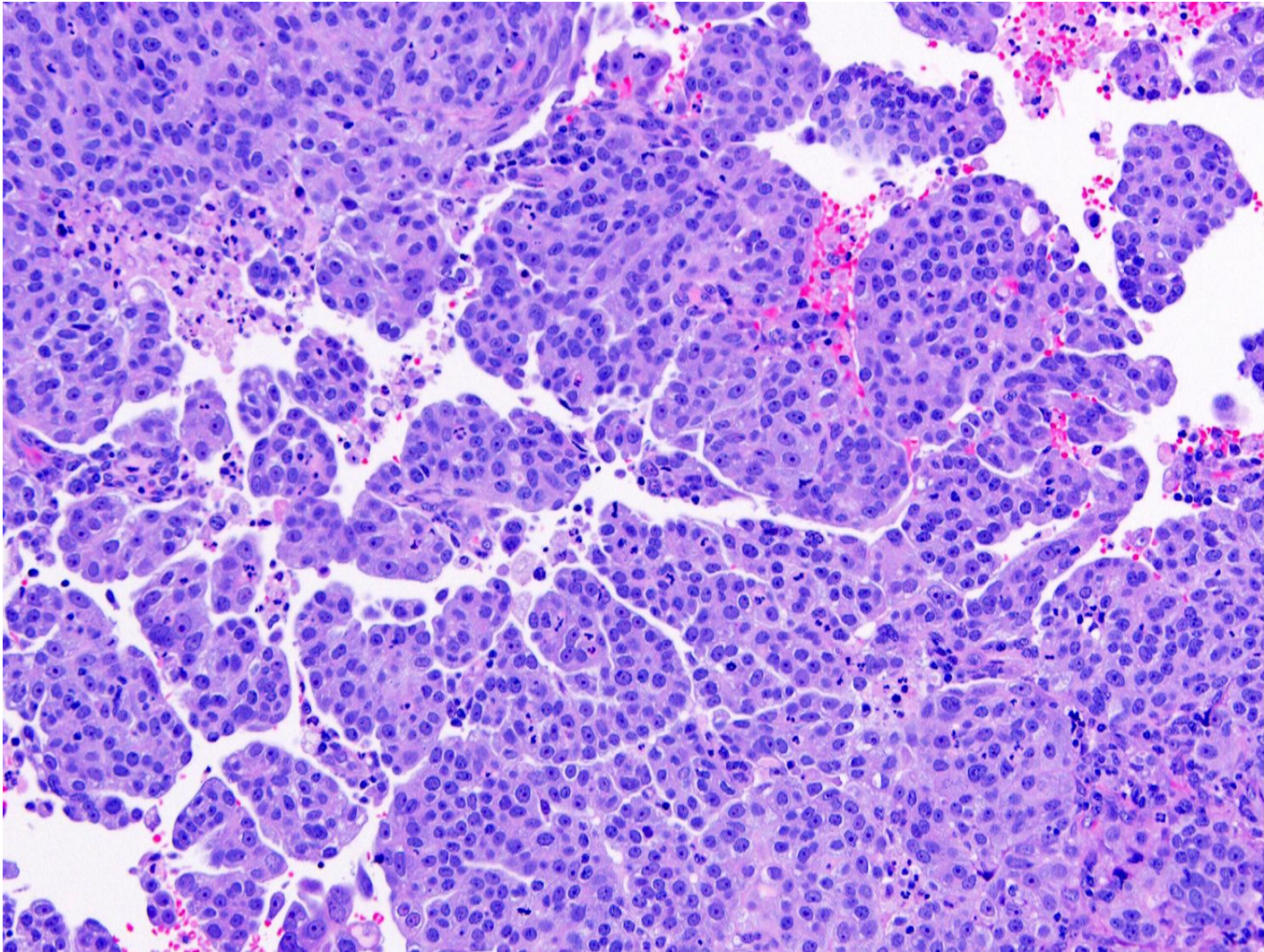


Endometrioid adenocarcinoma-

Also shows a variety of histologic patterns. Important to notify is squamous/mucinous metaplasia

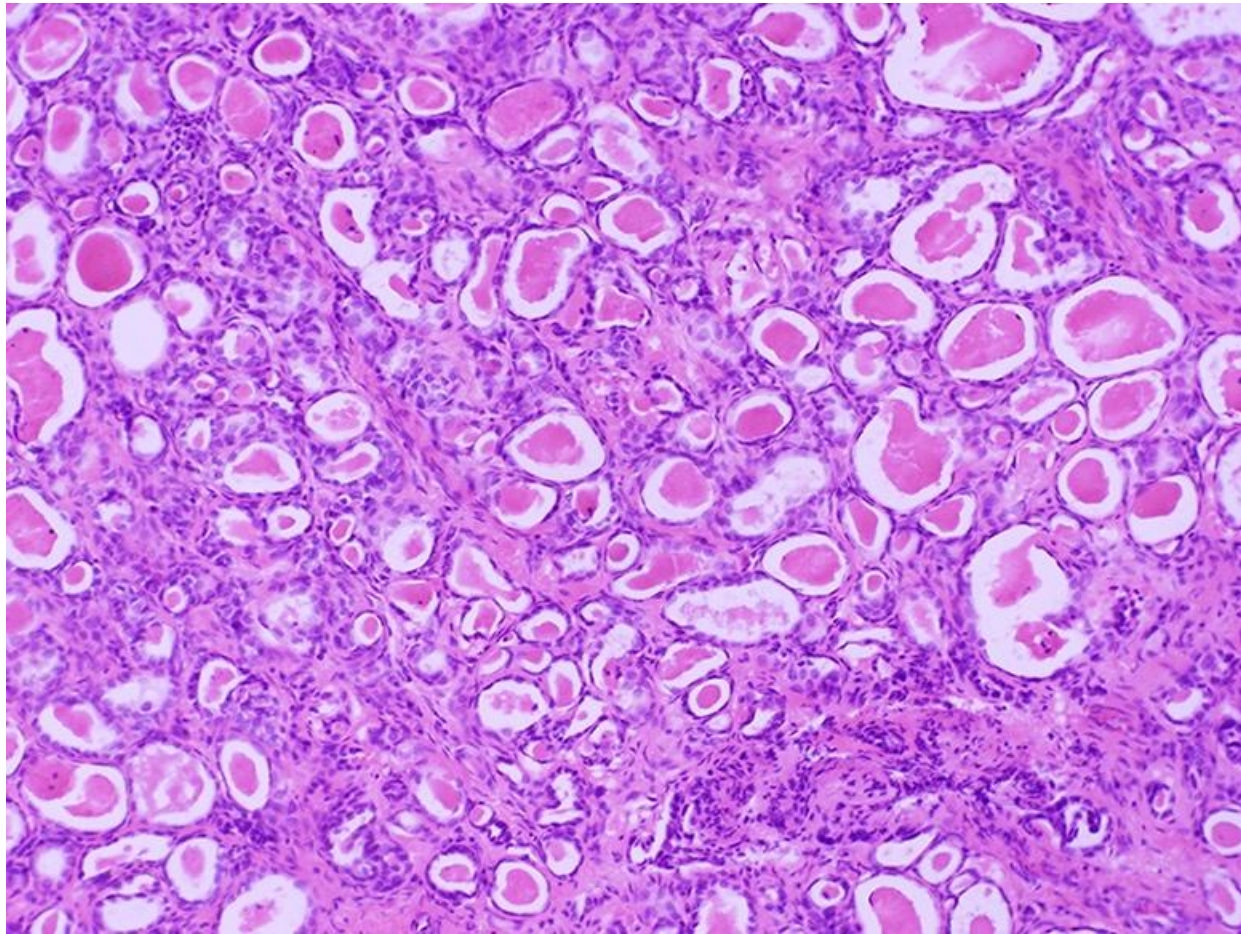
Differential diagnosis

Endometrial serous carcinoma: Mutant p53 pattern, GATA3-, CD10-



Differential diagnosis

Clear cell carcinoma: also show solid, papillary and tubulocystic morphologic patterns, cuboidal cells with clear to eosinophilic cytoplasm, in contrast to relatively blue, basophilic appearance of mesonephric carcinoma
Both are ER- and variably HNF-1B+,AMACR+, Napsin A+



Immunohistochemical profile

Type/marker	PAX-8	GATA3	ER	Napsin A	AMACR	CD10	TTF-1
Mesonephric	+	+	-	-	-	+	-/+
Endometrioid	+	-	+	-	-	-	-
Clear cell	+	-	-	+	+	-	-
Serous endometrial	+	-	-/+	-	-	-	-
Mesonephric-like endometrioid	+	+	-	-	-	-/+	+

Prognosis and outcome - cervical mesonephric adenocarcinoma

Worse overall survival, disease specific survival, and progression free survival compared to HPV endocervical adenocarcinoma

Majority present at FIGO stage IB or higher

Many cases (half in one study) are associated with recurrence, commonly to distant sites

Stage I: recurrence rate 32%, mean recurrence interval of 24 months, mean overall survival of 50 months

Spindle component may portend a worse outcome

Treatment: Mainstay of treatment is hysterectomy with or without bilateral salpingo-oophorectomy and pelvic lymph node dissection

Roles of neoadjuvant or adjuvant chemotherapy and radiation therapy remain unclear

Prognosis and outcome – mesonephric-like endometrial adenocarcinoma (MLA)

Factors associated with development of metastasis in mesonephric adenocarcinoma of the uterine corpus

Large tumor size (> 4 cm)

Ill defined tumor border

Advanced FIGO stages (III - IV)

Presence of coagulative tumor cell necrosis

High mitotic activity (> 10/10 high power fields)

Lymphovascular invasion

Associated with aggressive clinical course

Tends to present with advanced stage (FIGO II or more)

Increased risk of recurrent disease

Increased tendency to metastasize to the lungs even for tumors with stage I disease

Compared with other endometrial adenocarcinomas

Better overall survival than carcinosarcoma and serous carcinoma

Equal overall survival to endometrioid grade 3

Worse overall survival than endometrioid grade 1 - 2 carcinomas

Treatment of MLA

Surgical approach with total hysterectomy and bilateral salpingo-oophorectomy, with or without pelvic and para-aortic lymph node dissection, is the primary therapy

Adjuvant chemotherapy and radiation therapy have been used

Hormone therapy has been reported in 2 cases

No tumor specific treatment options have been elucidated for MLA



THANK
YOU

