

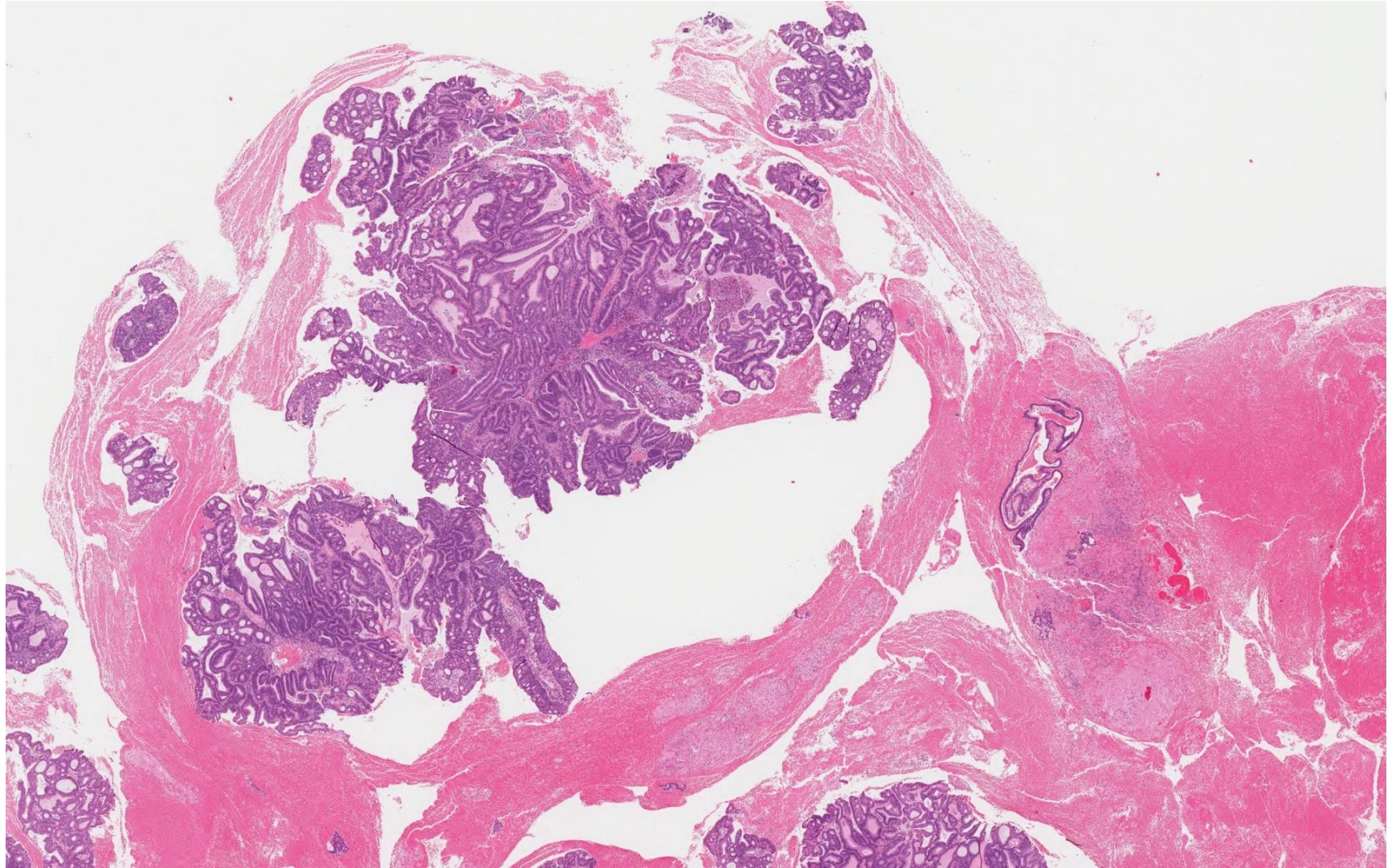
ENDOMETRIAL CARCINOMA: MIMICS AND SUBTYPES

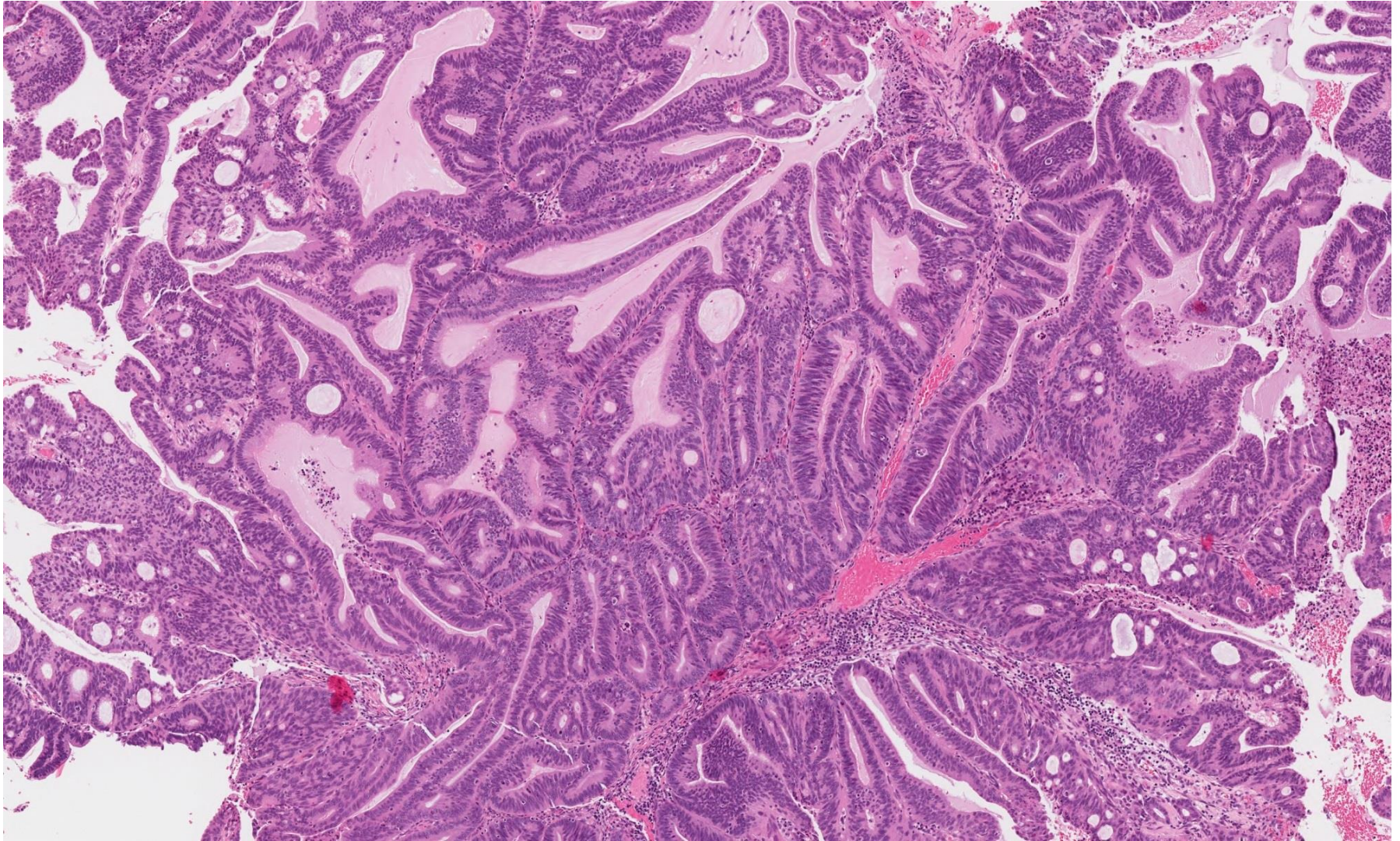
Robert Soslow, MD

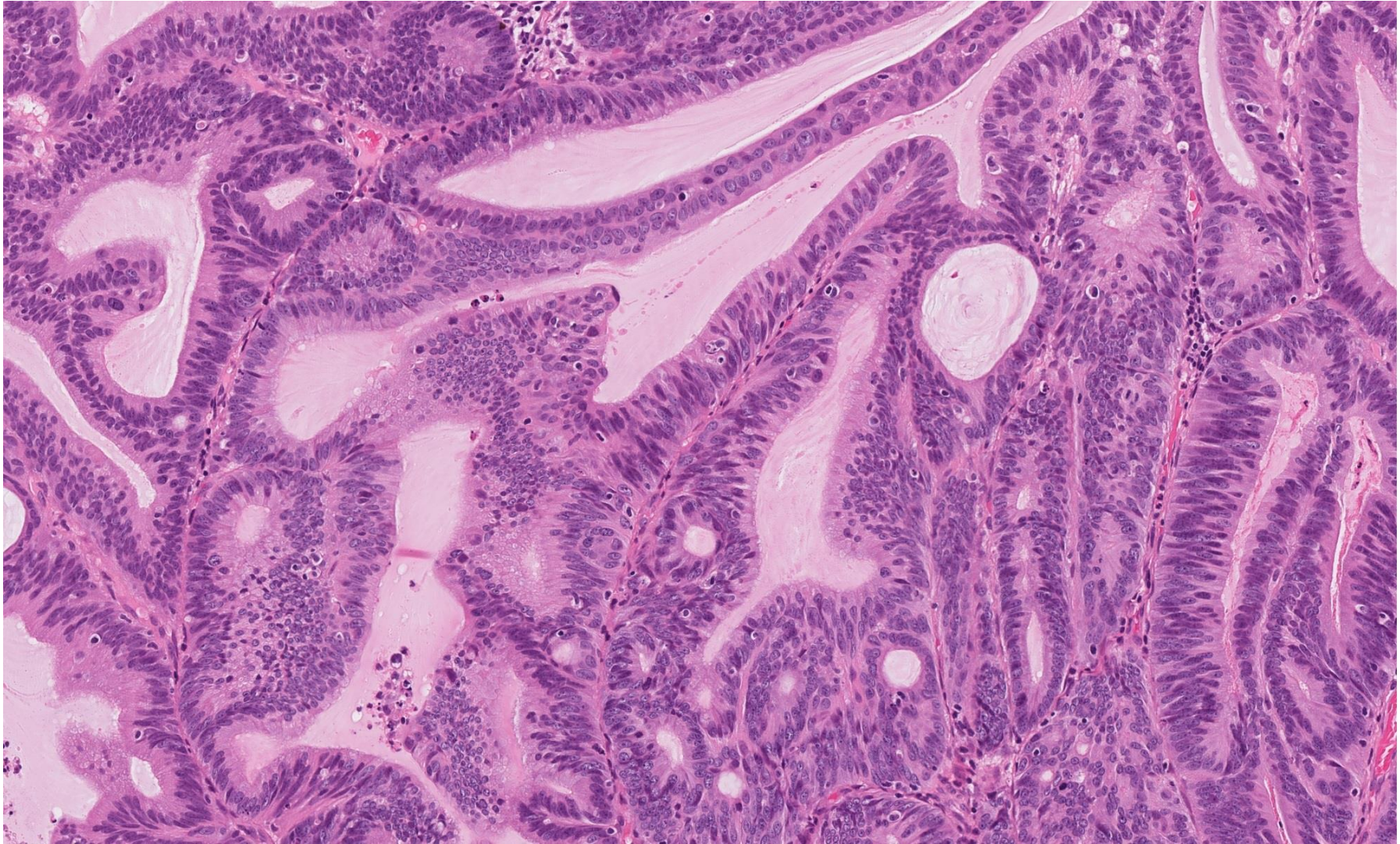
Cleveland Clinic, Cleveland, USA

Endometrioid carcinoma

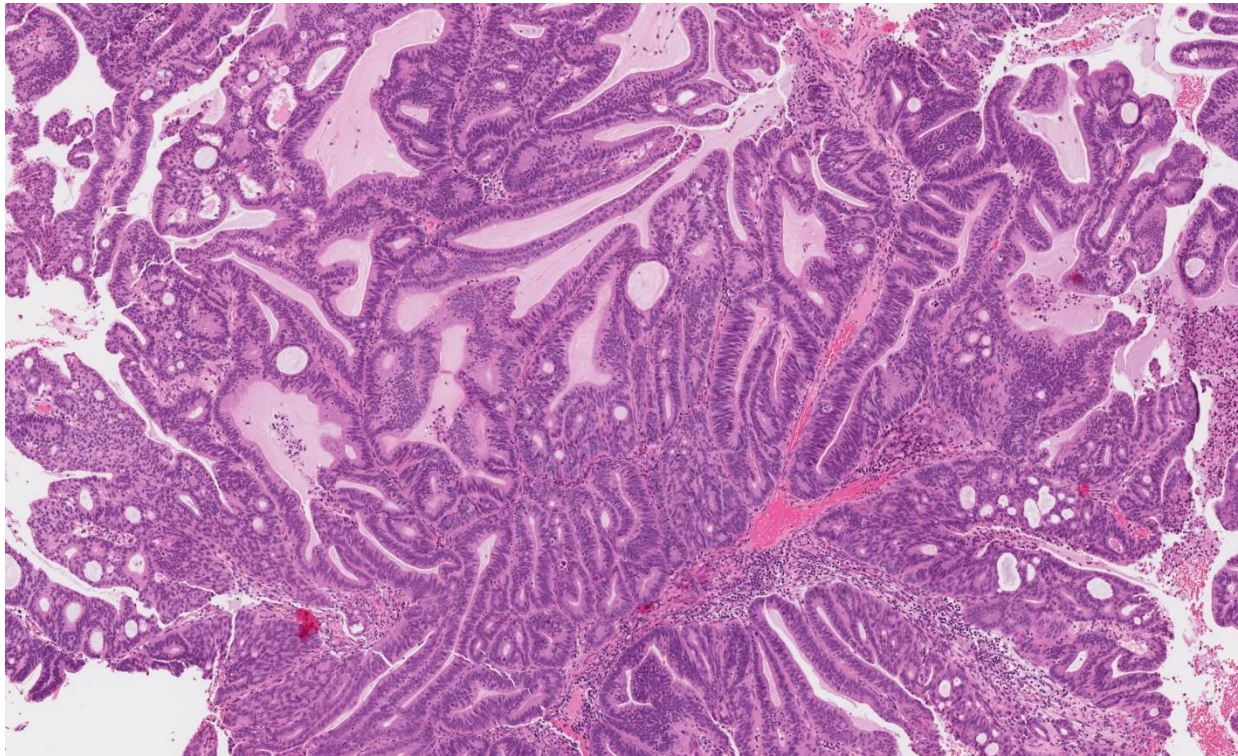
- 79-year-old woman reported vaginal bleeding and underwent endometrial curettage.

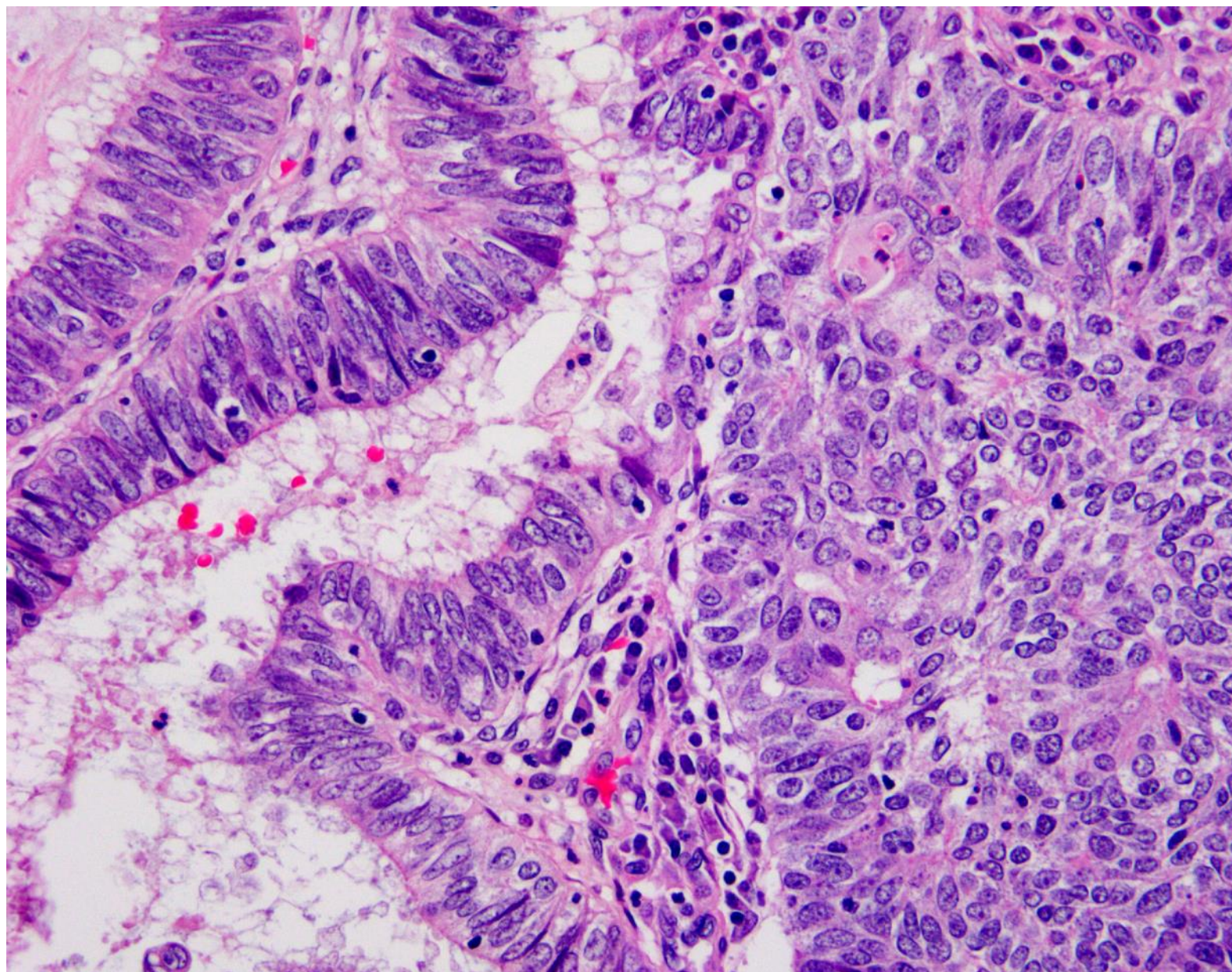


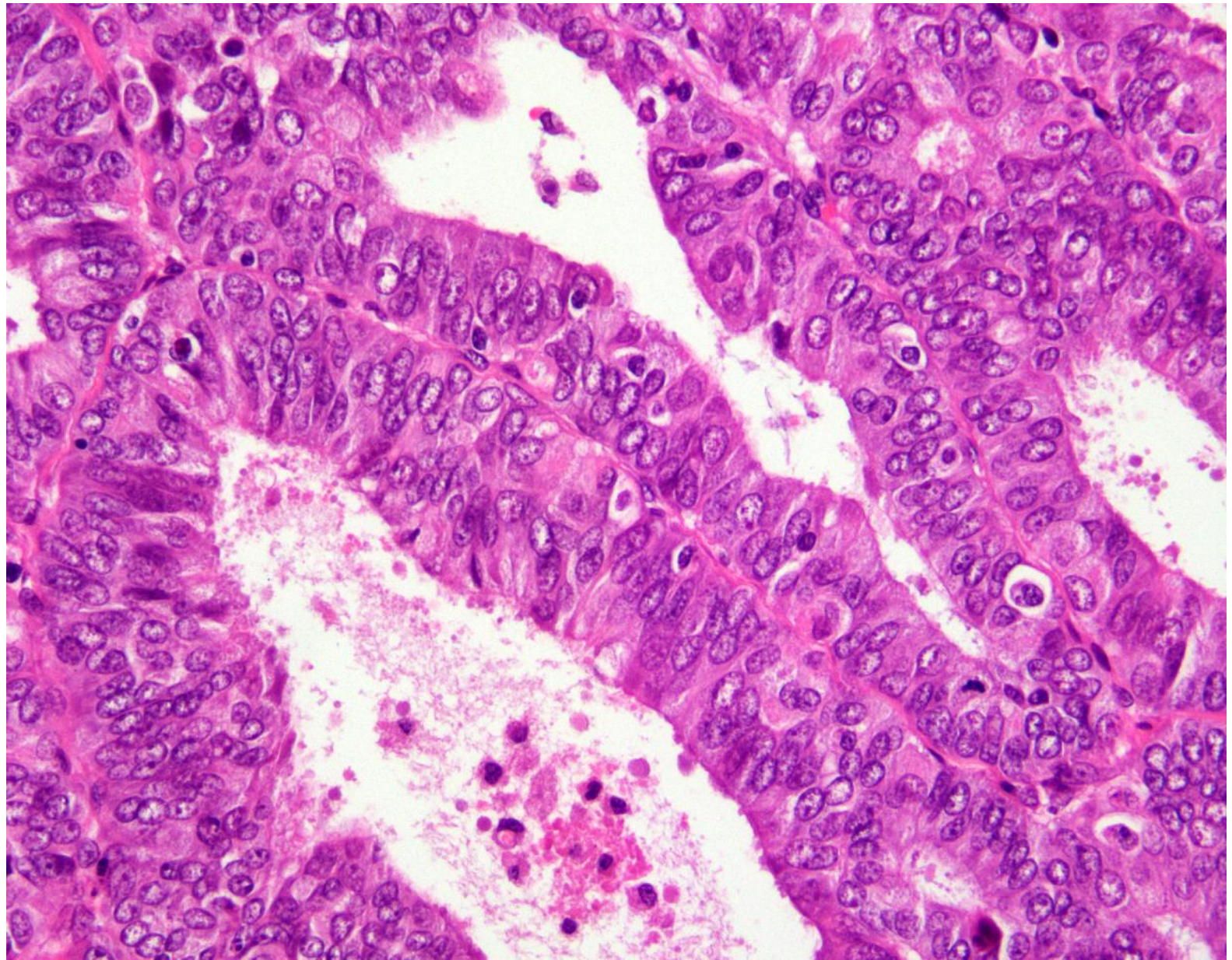




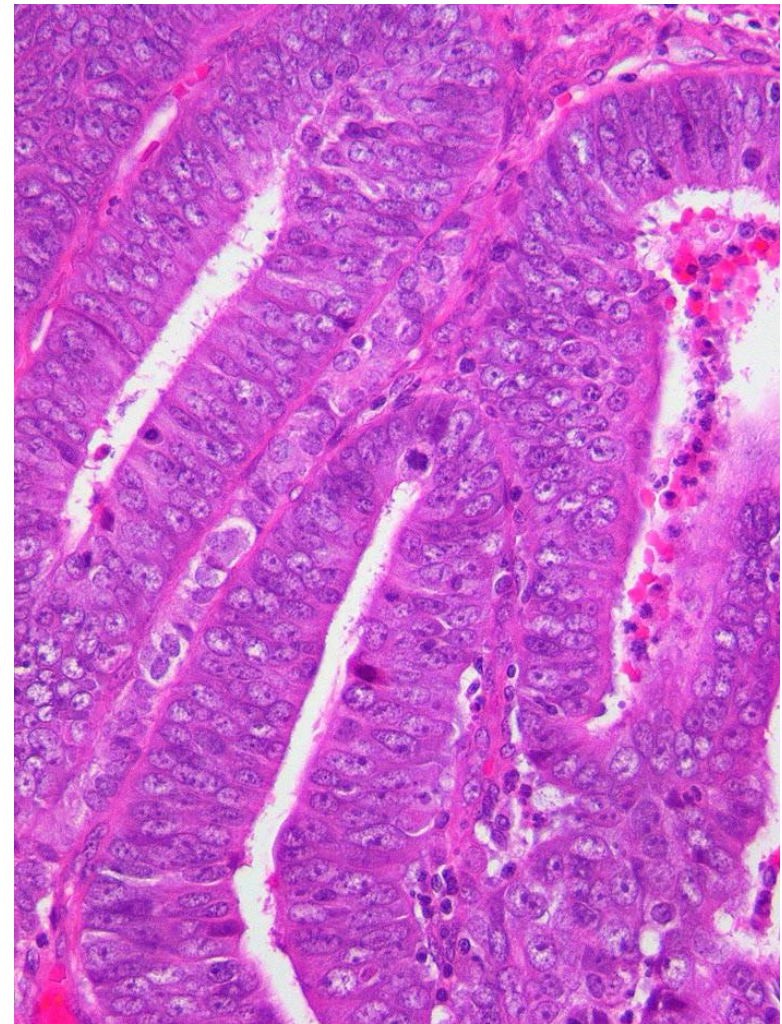
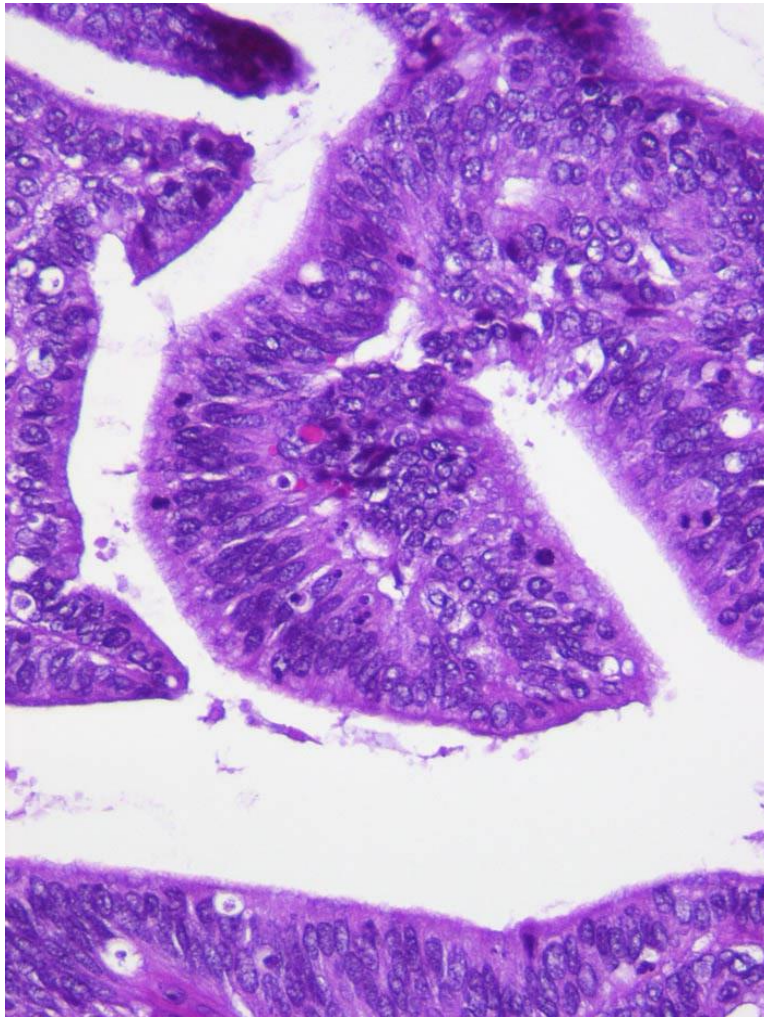
Diagnosis: Endometrioid carcinoma FIGO grade 1



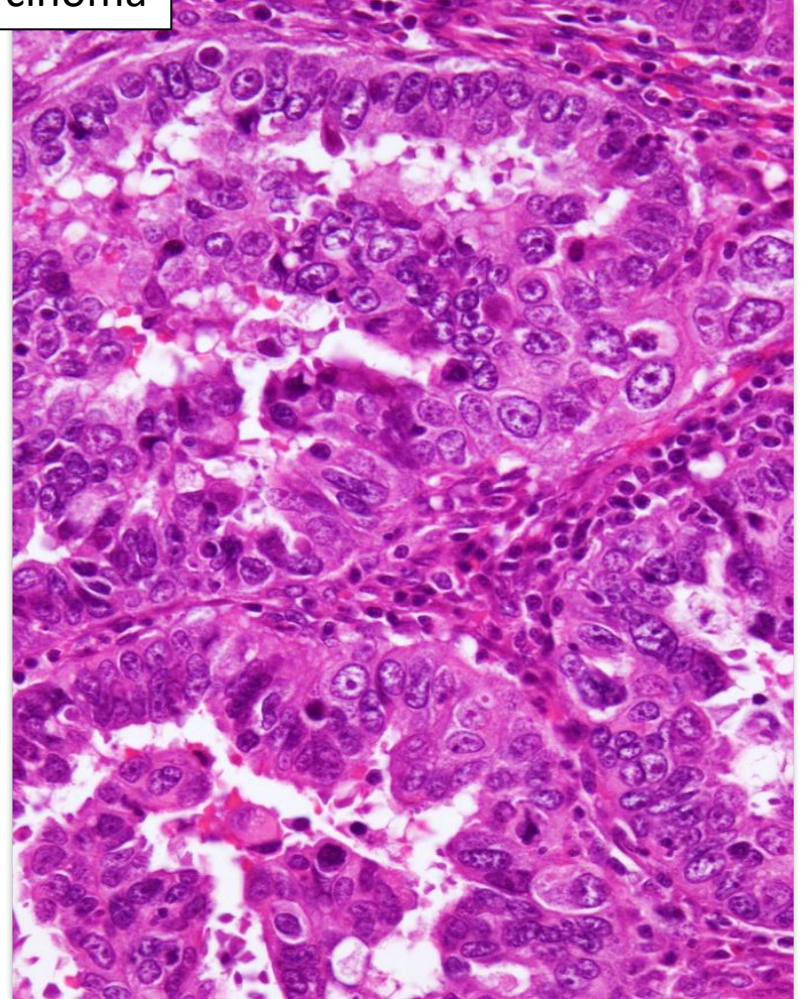
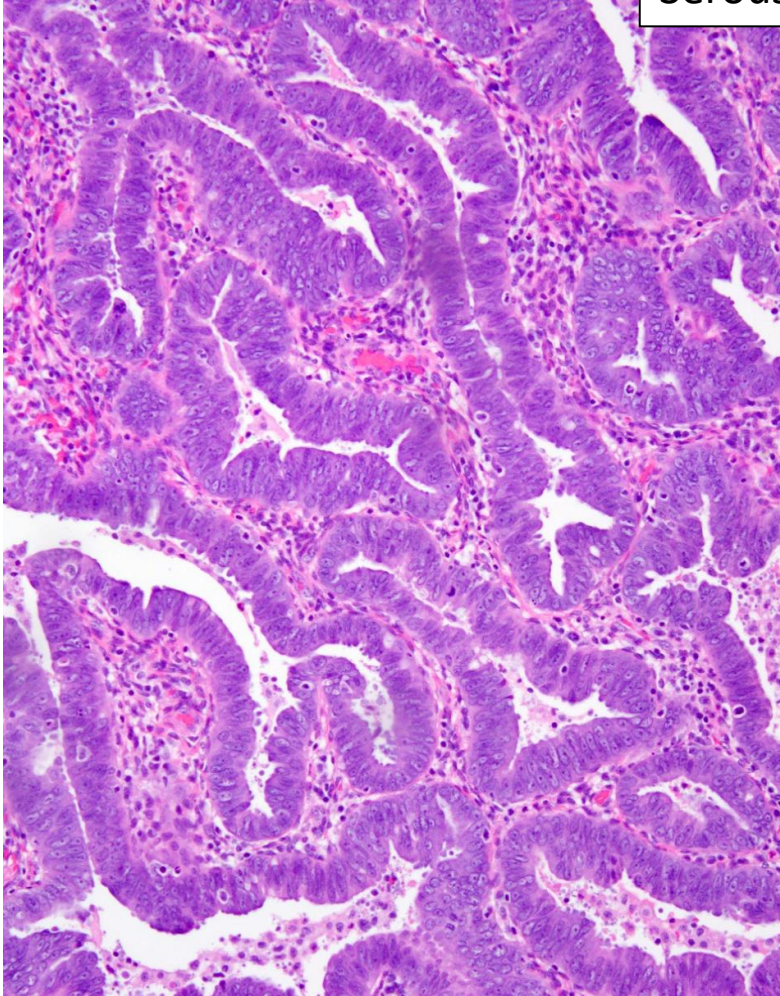




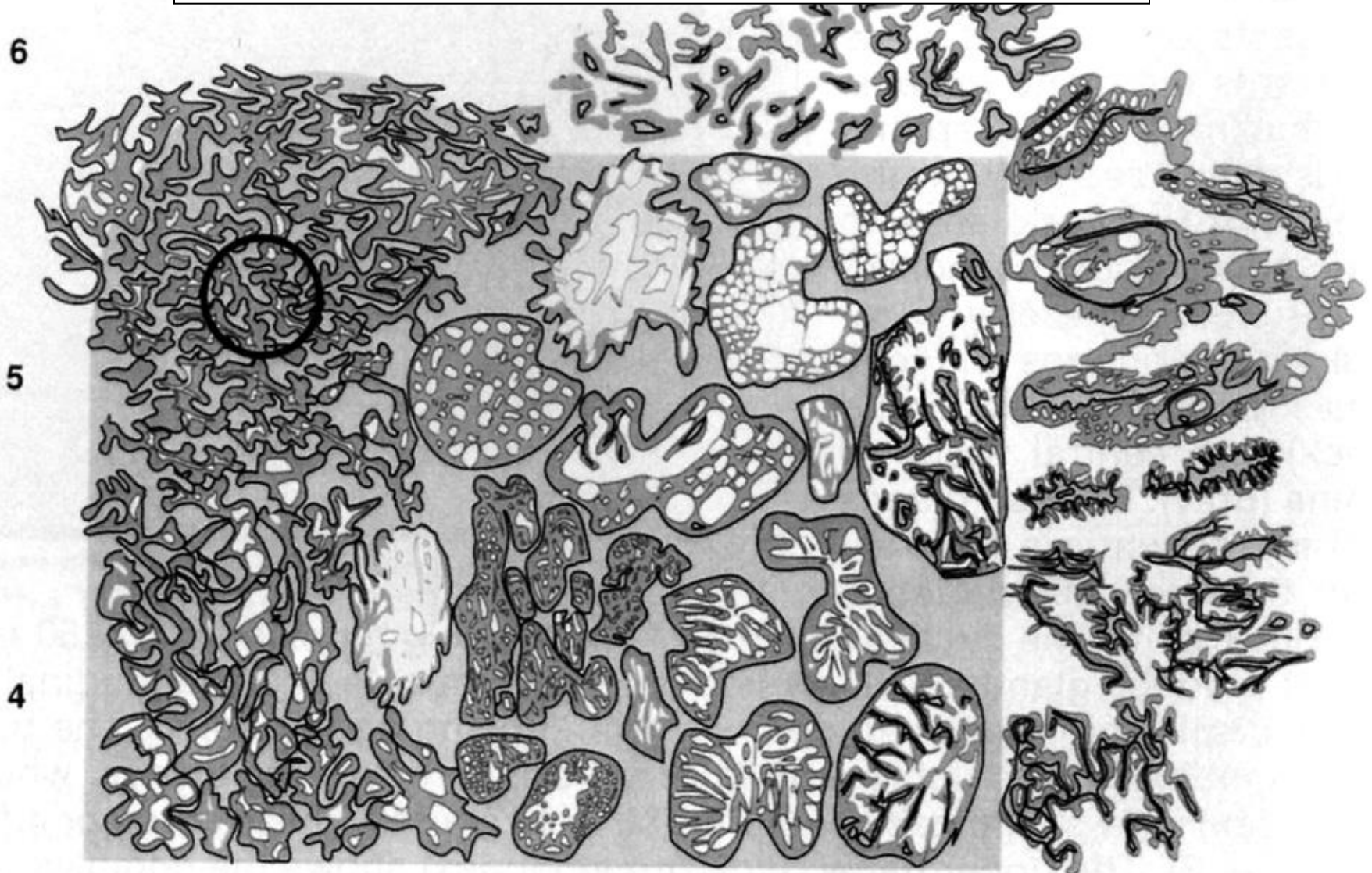
Endocervical adenocarcinoma HPVA



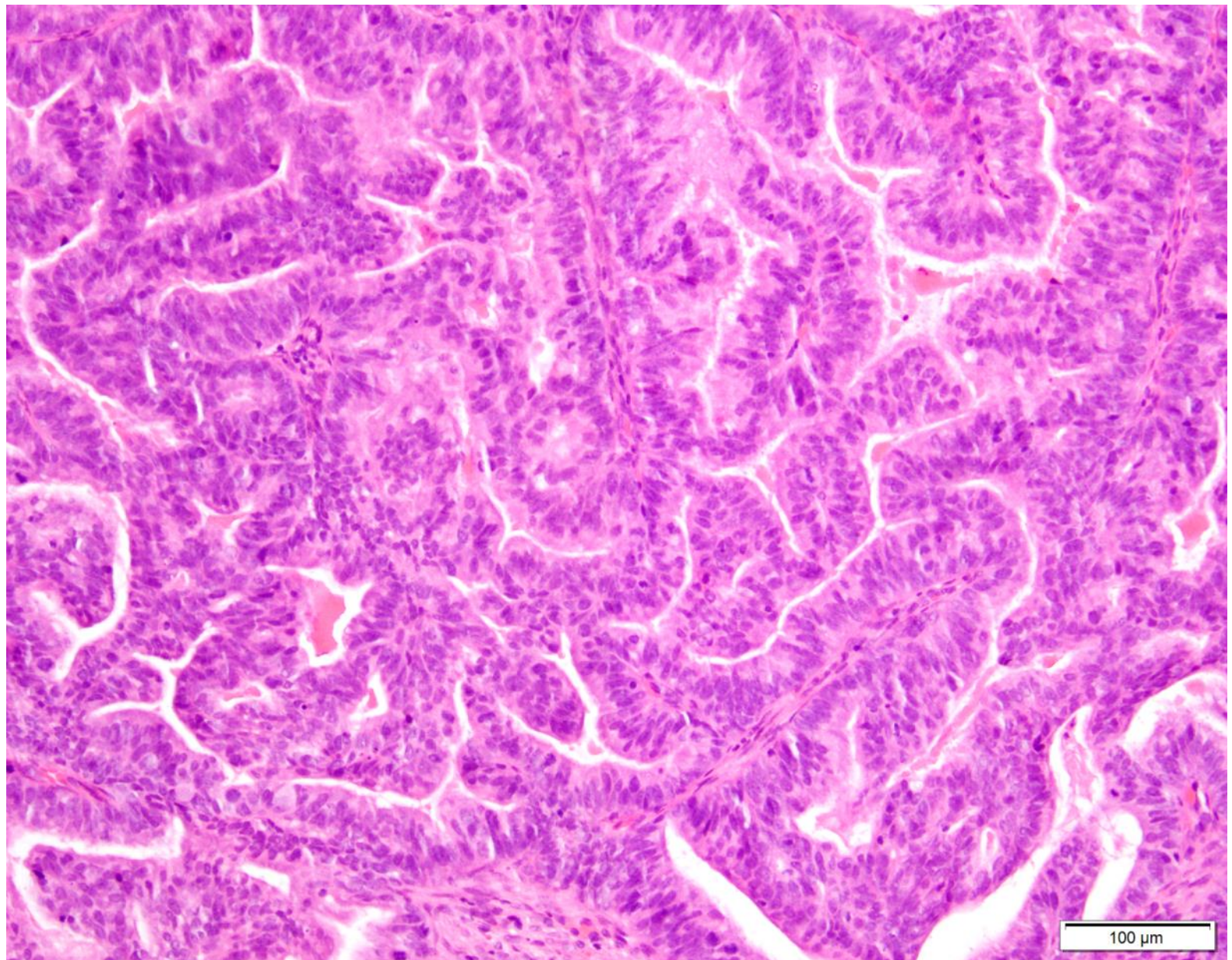
Serous carcinoma

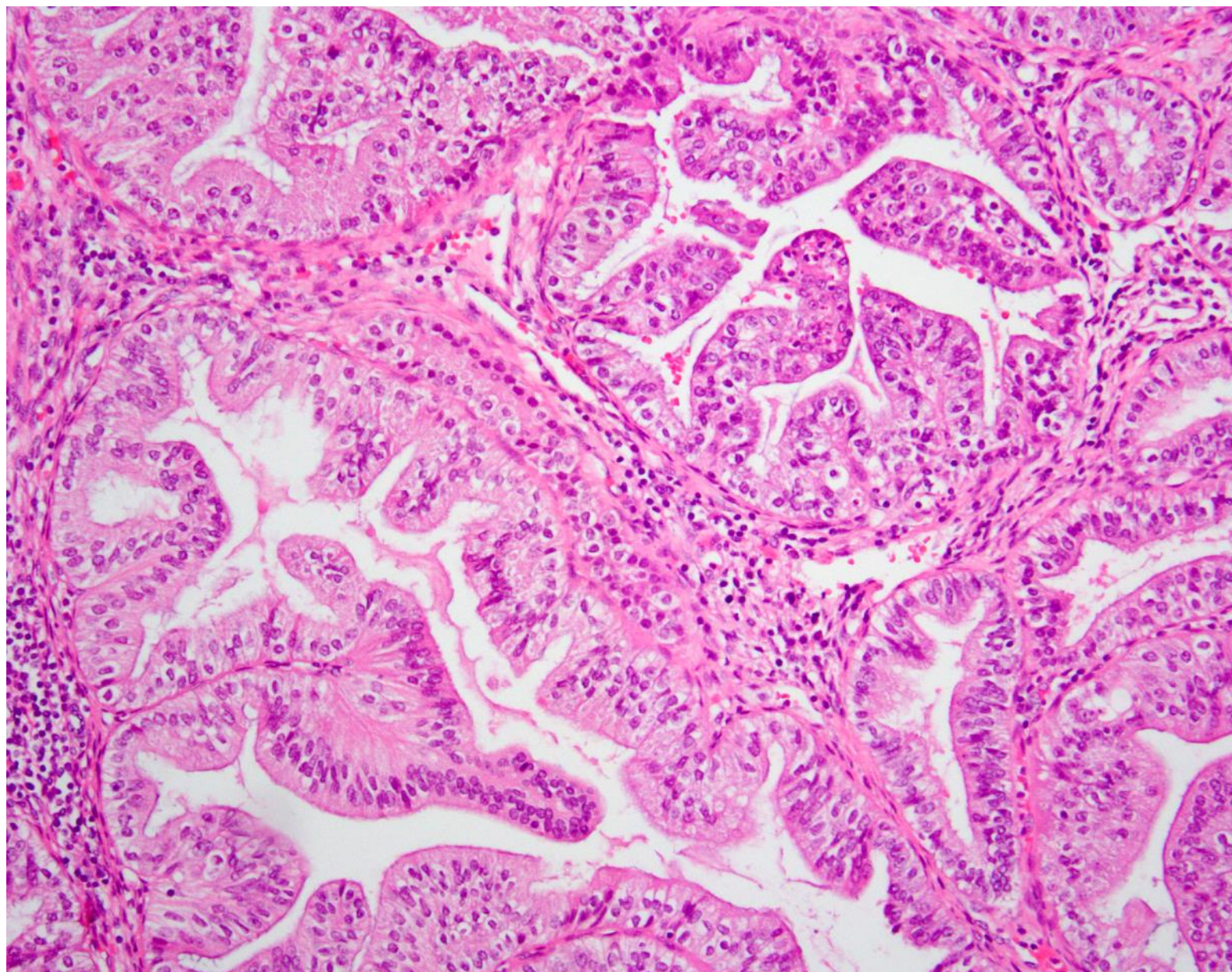


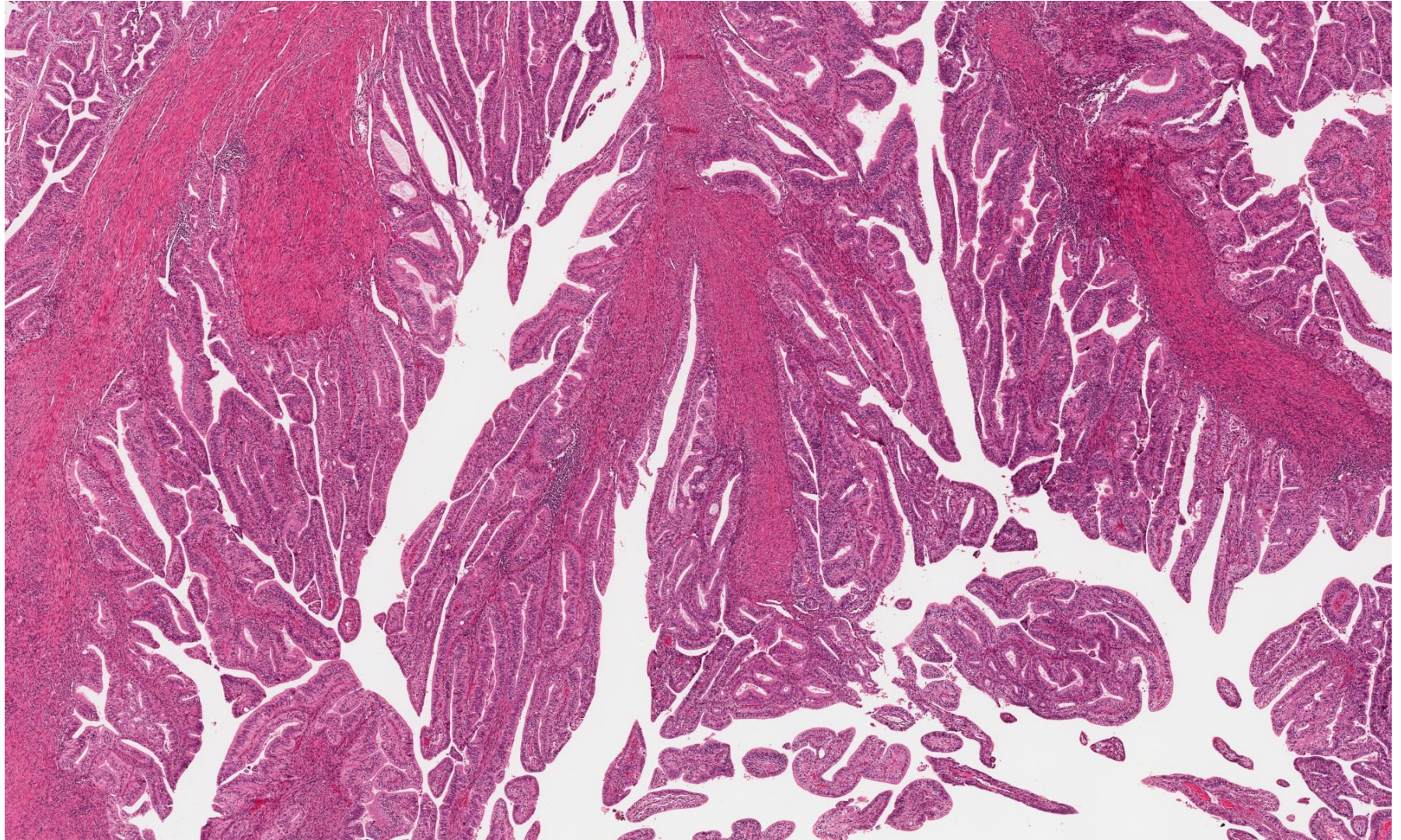
Carcinoma

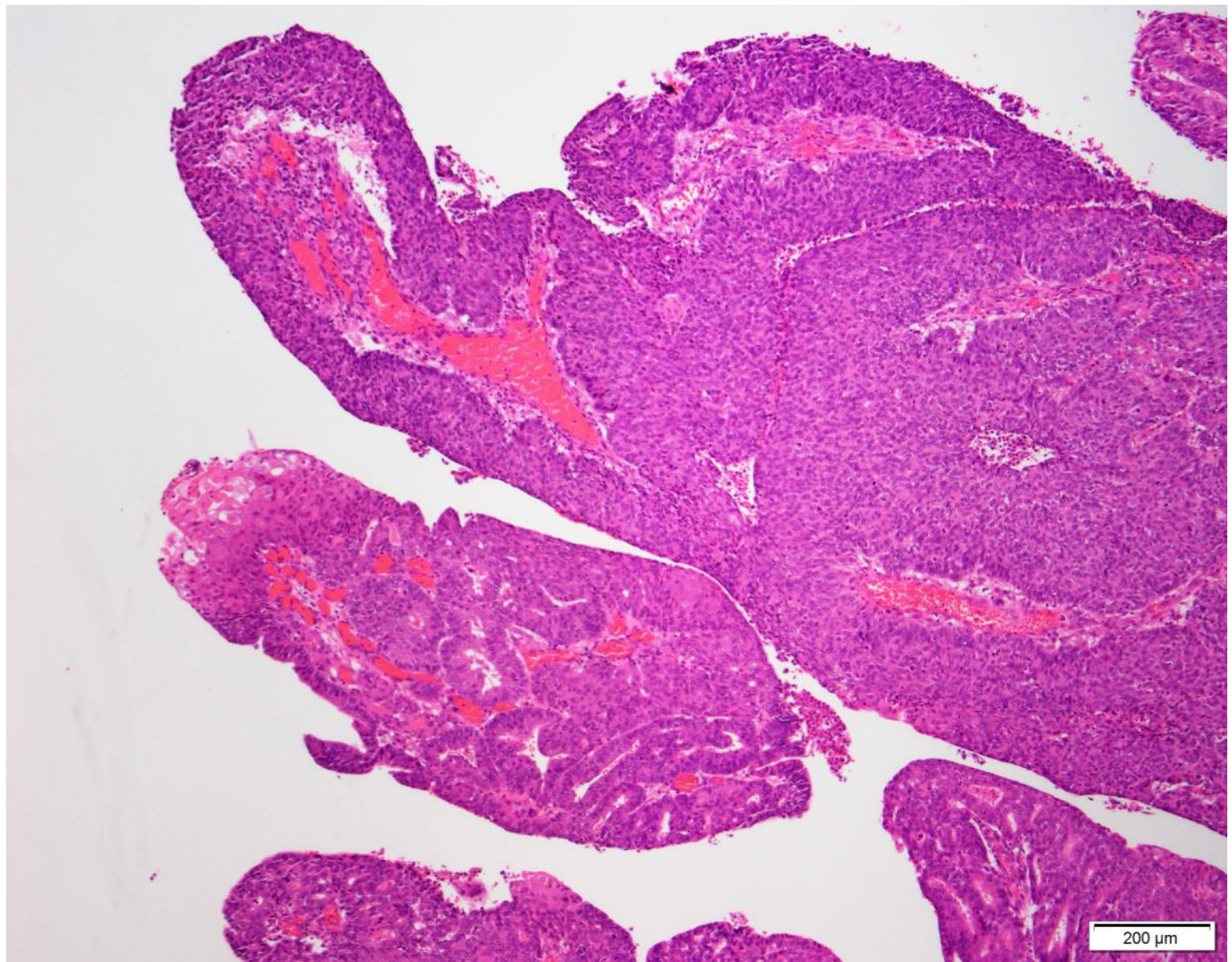


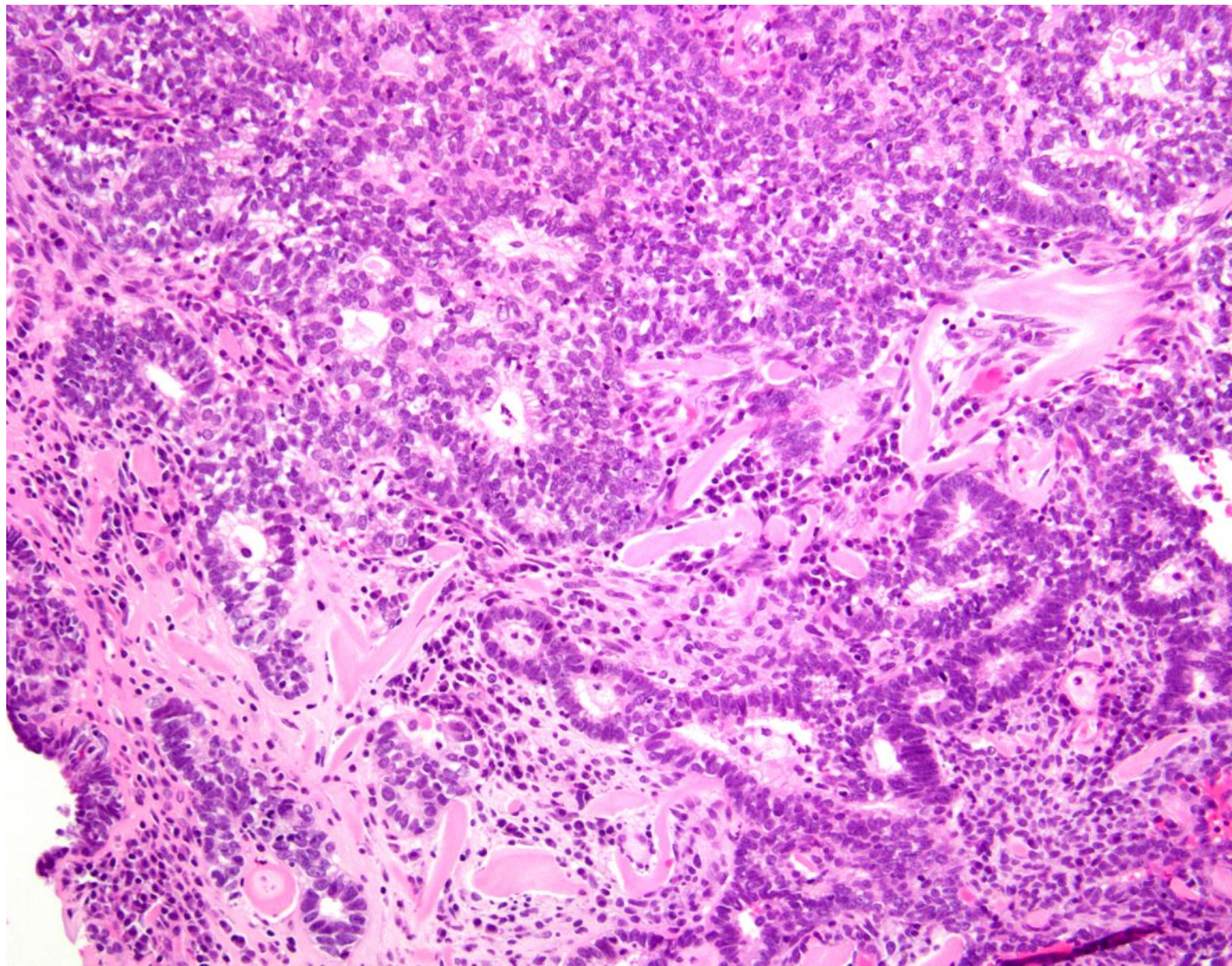
Longacre TA, et al. Am J Surg Pathol. 1995 Apr;19(4):371-406

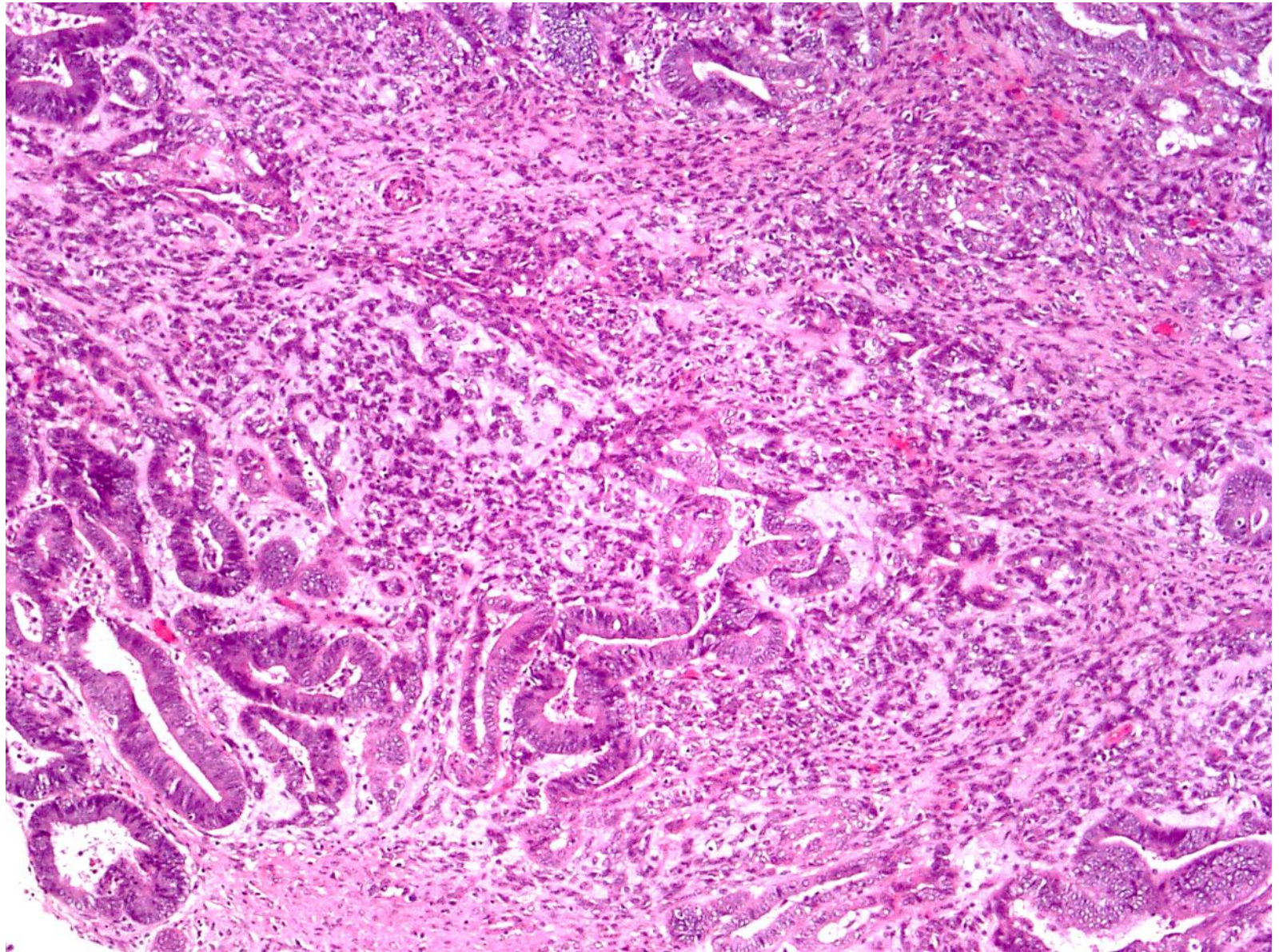


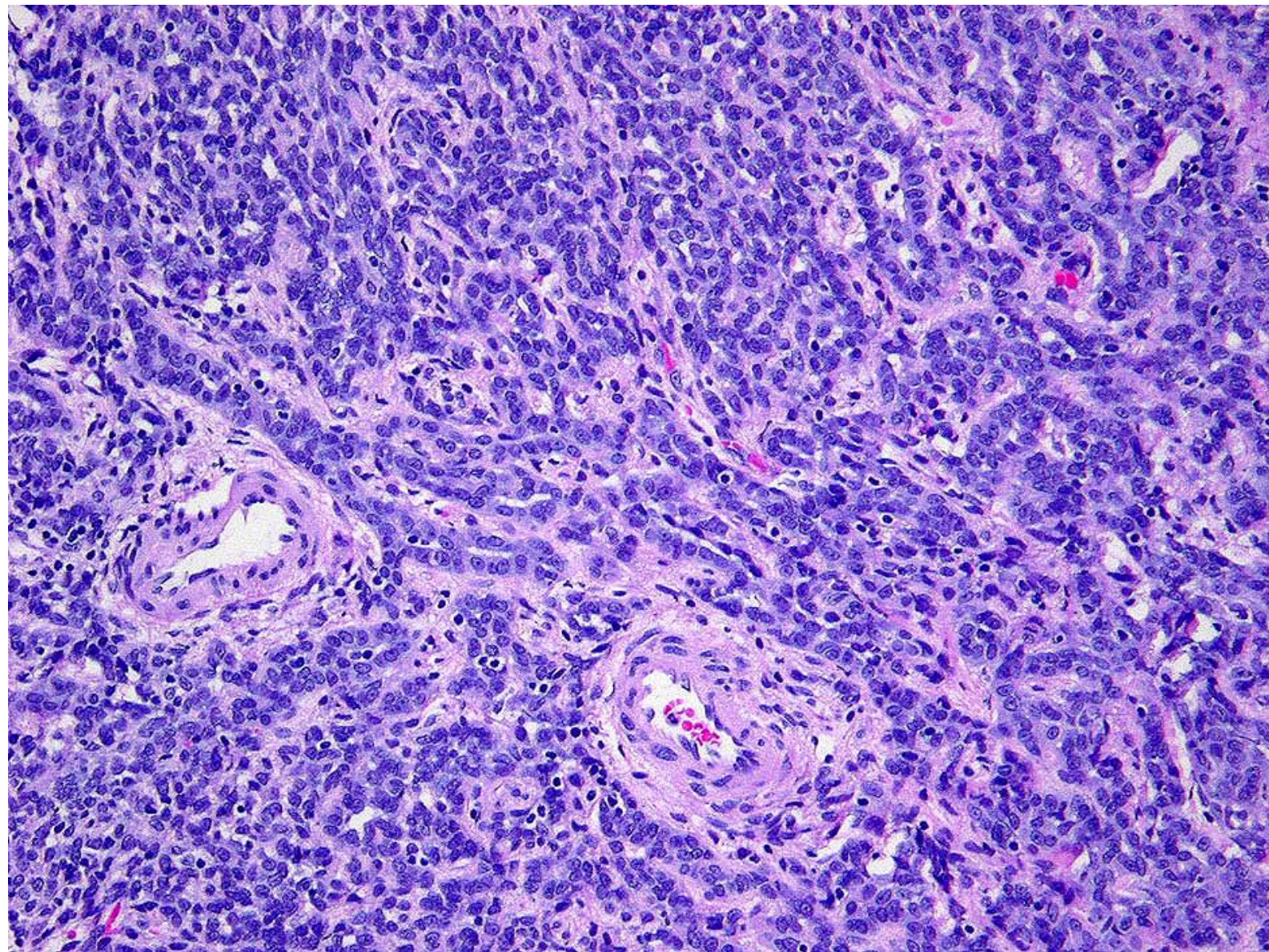


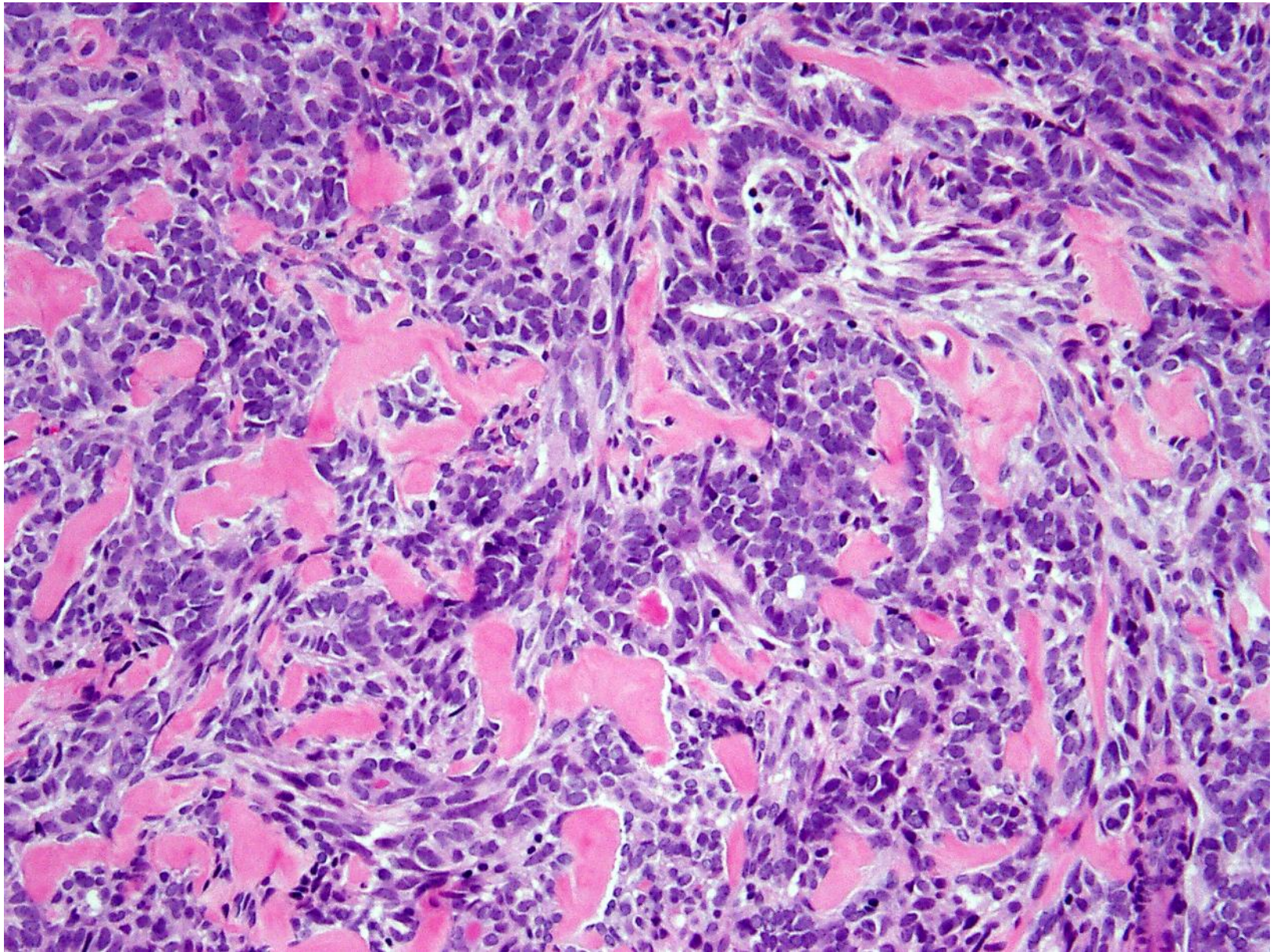


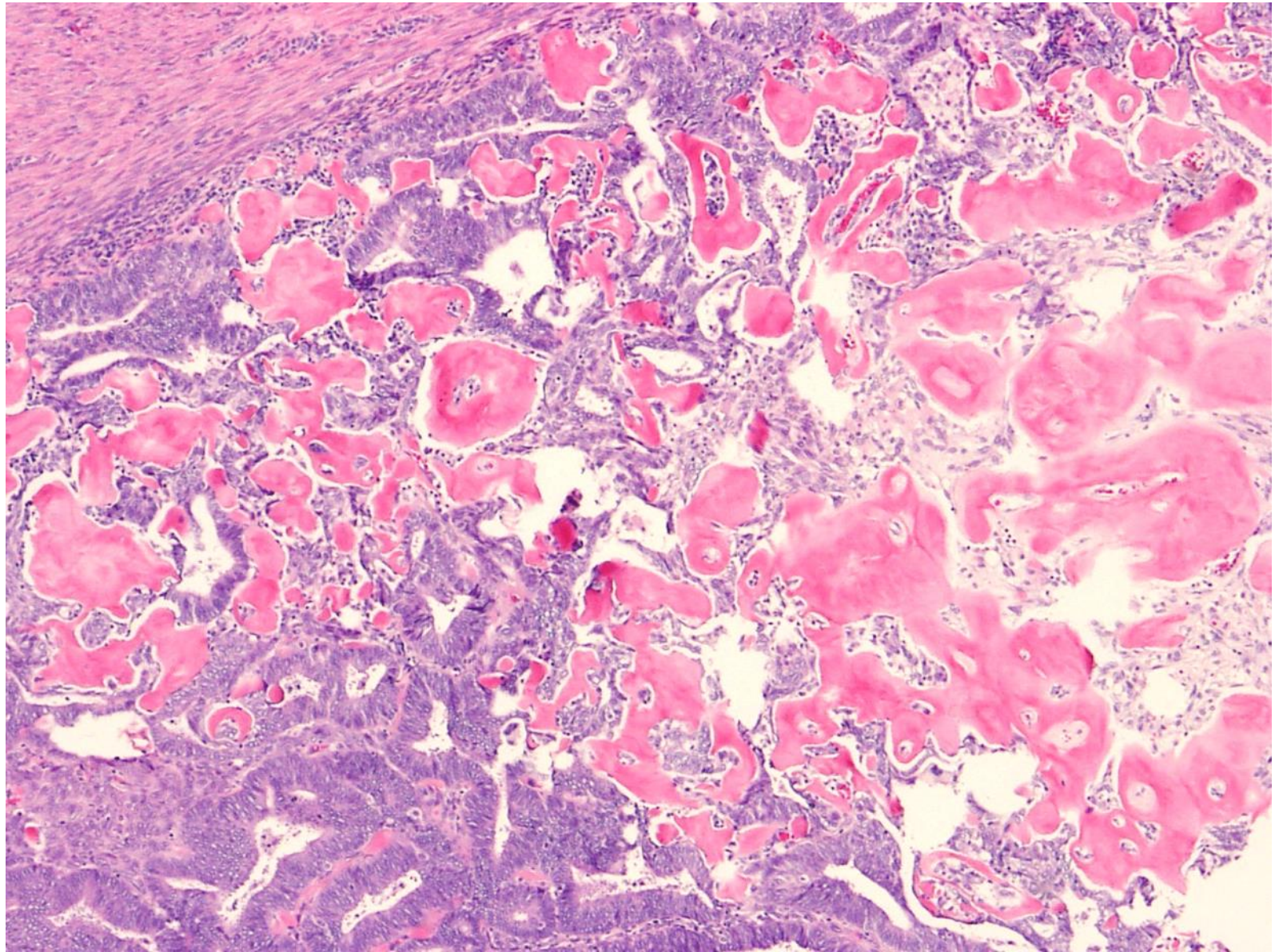


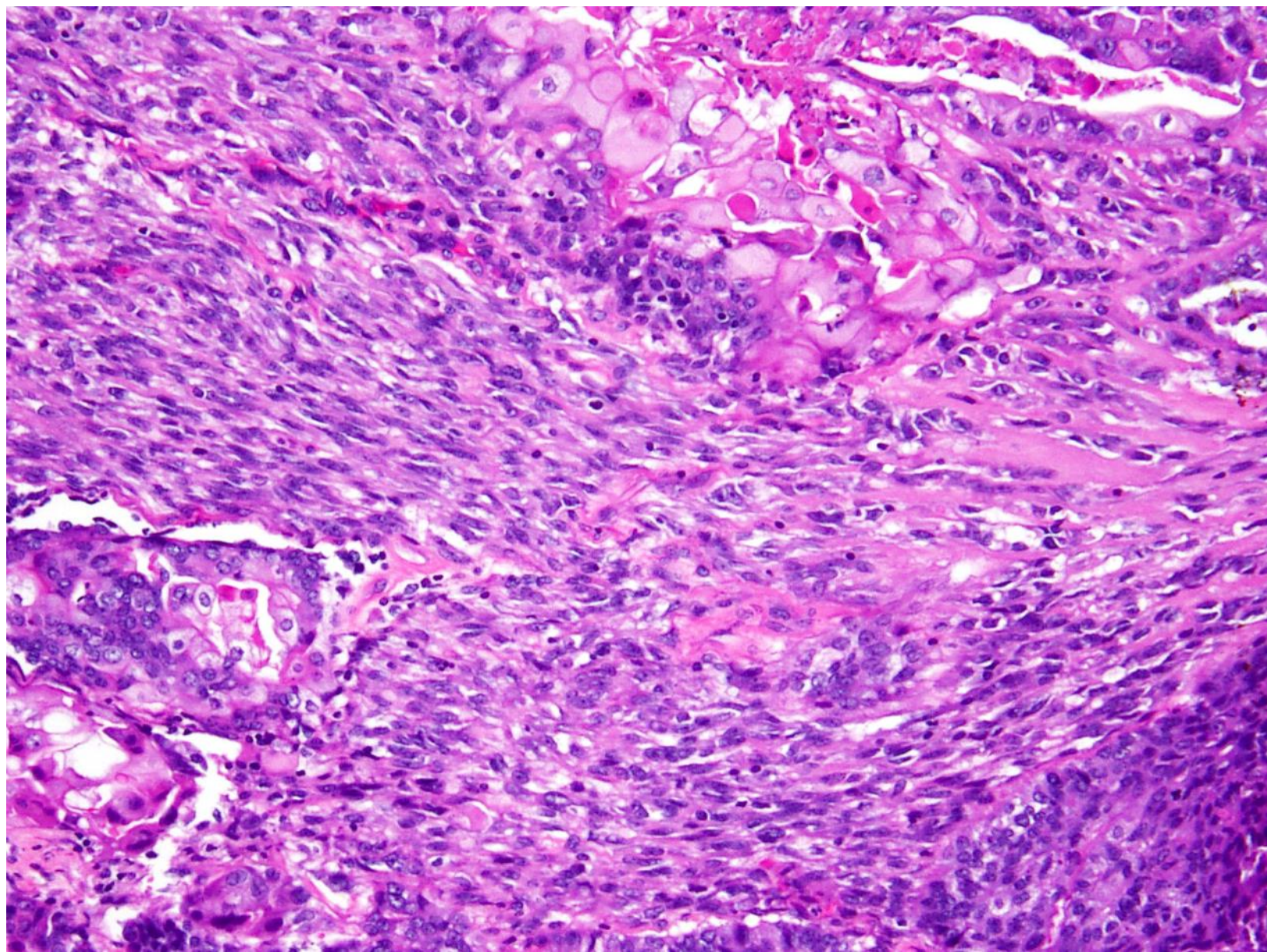


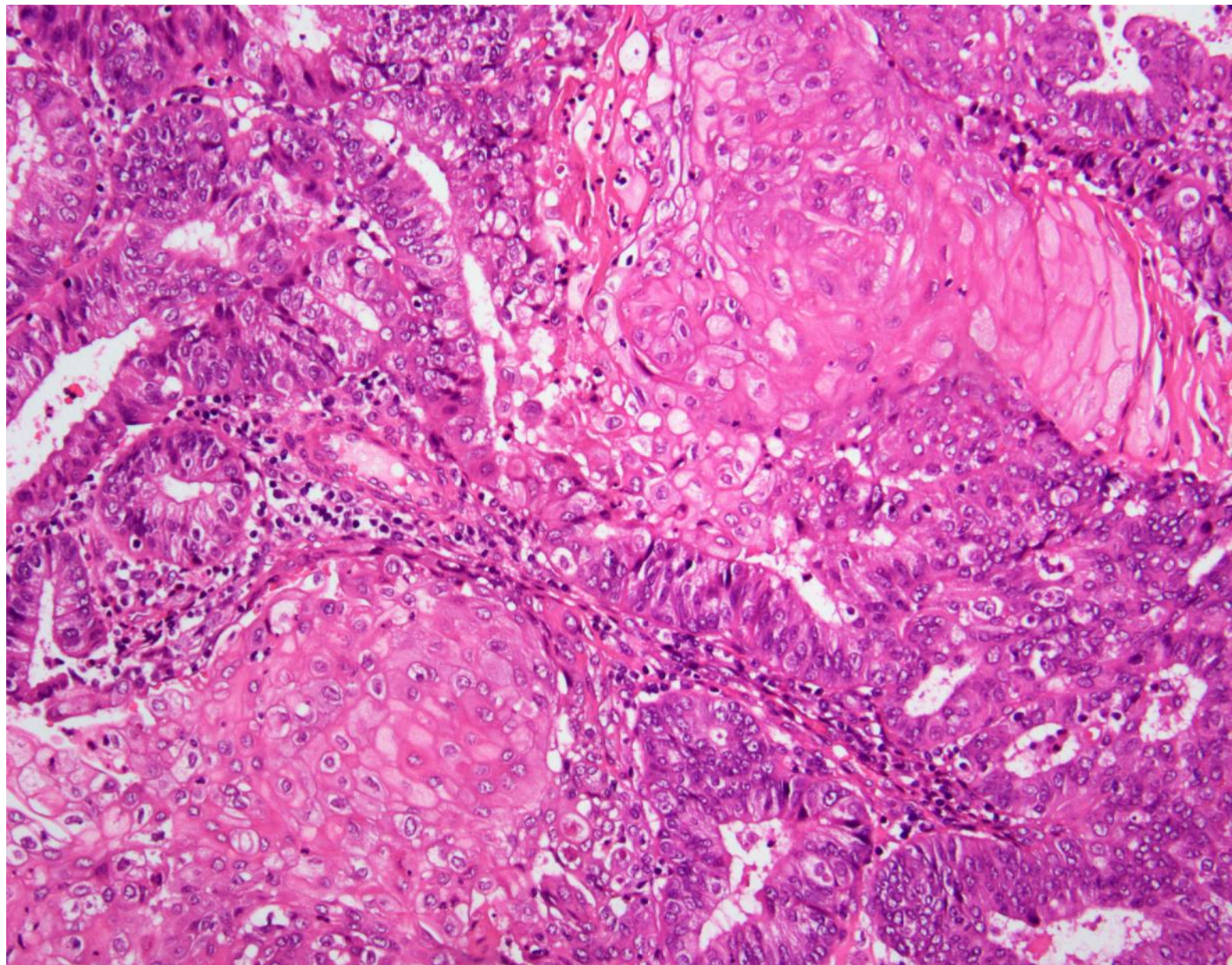


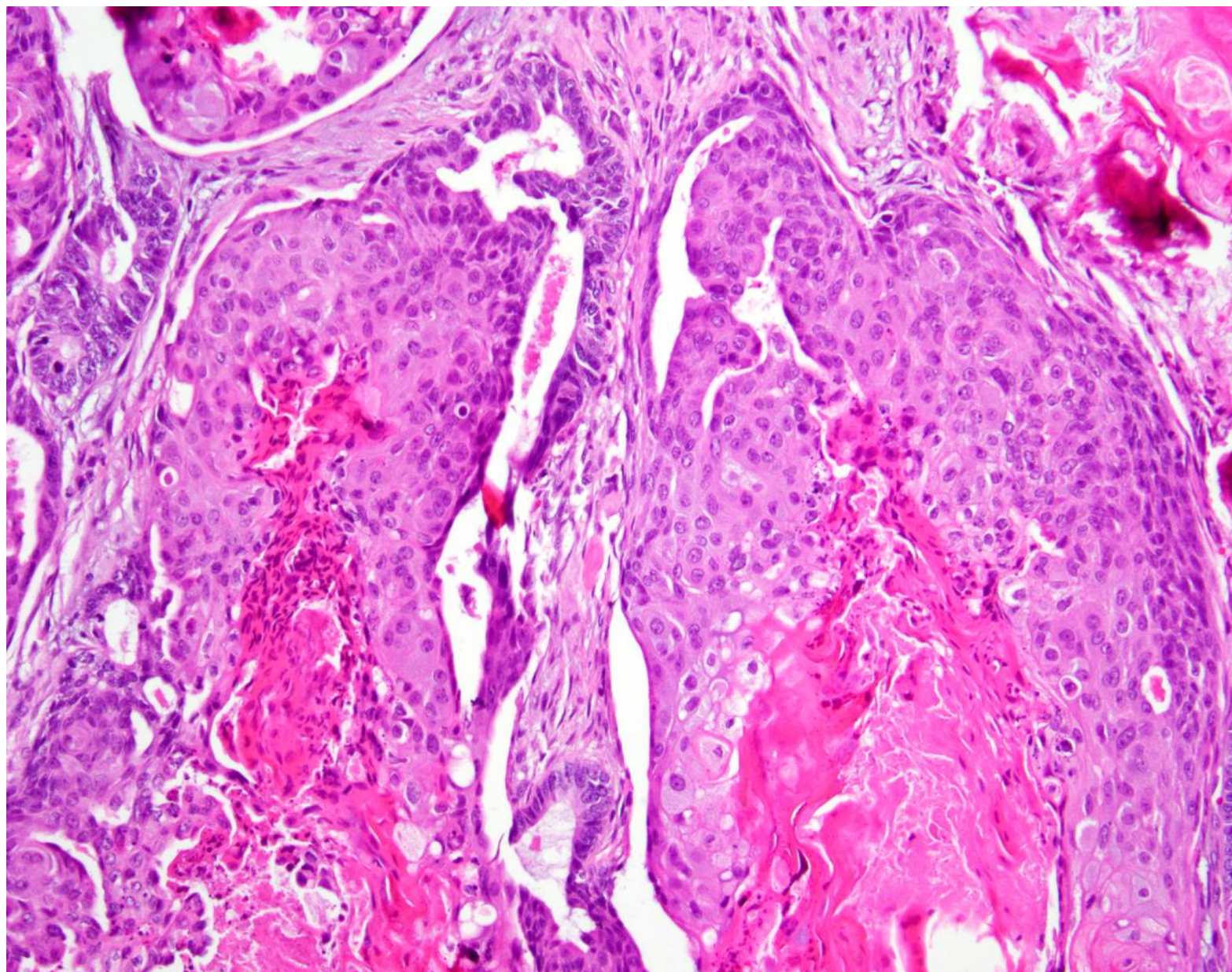


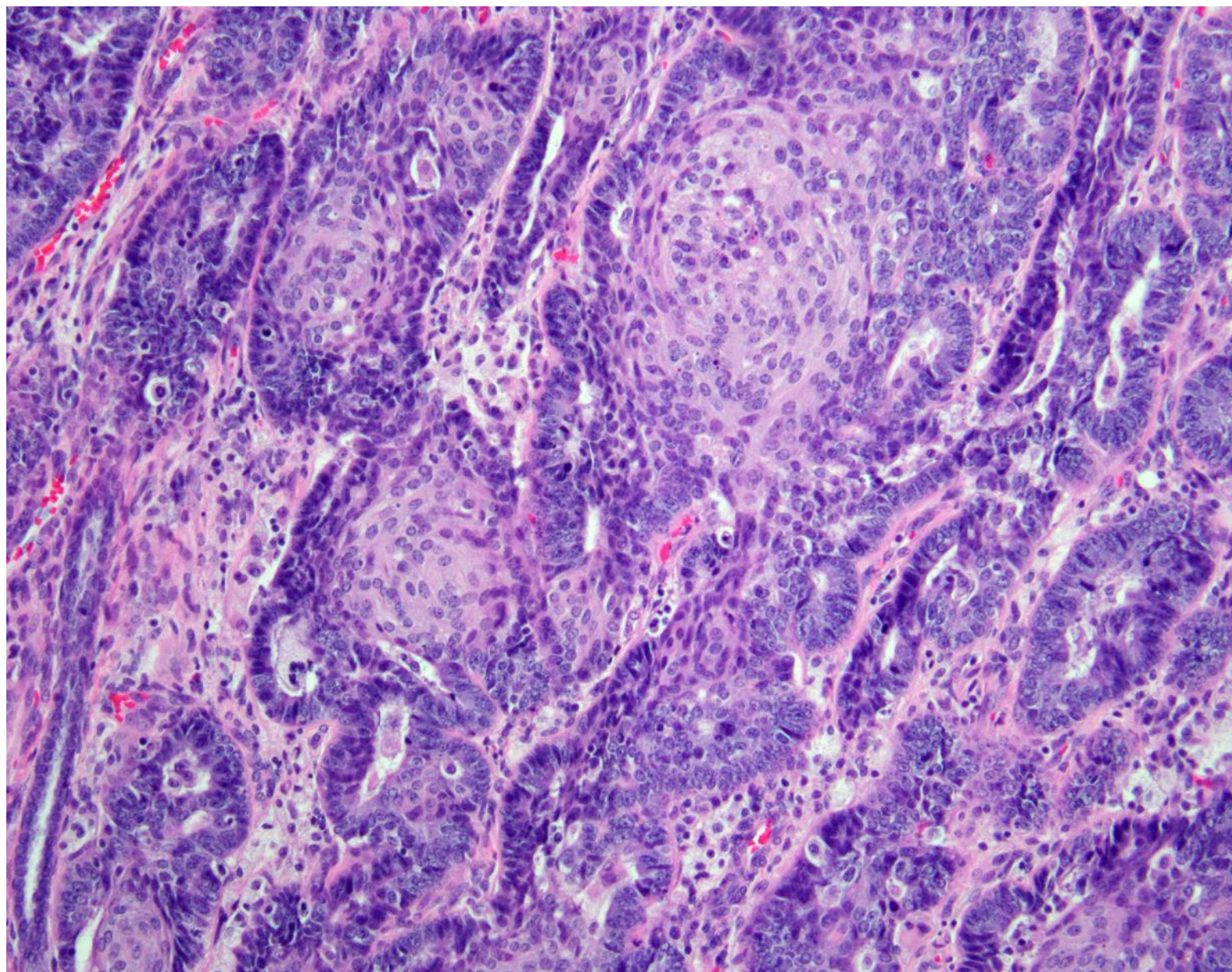


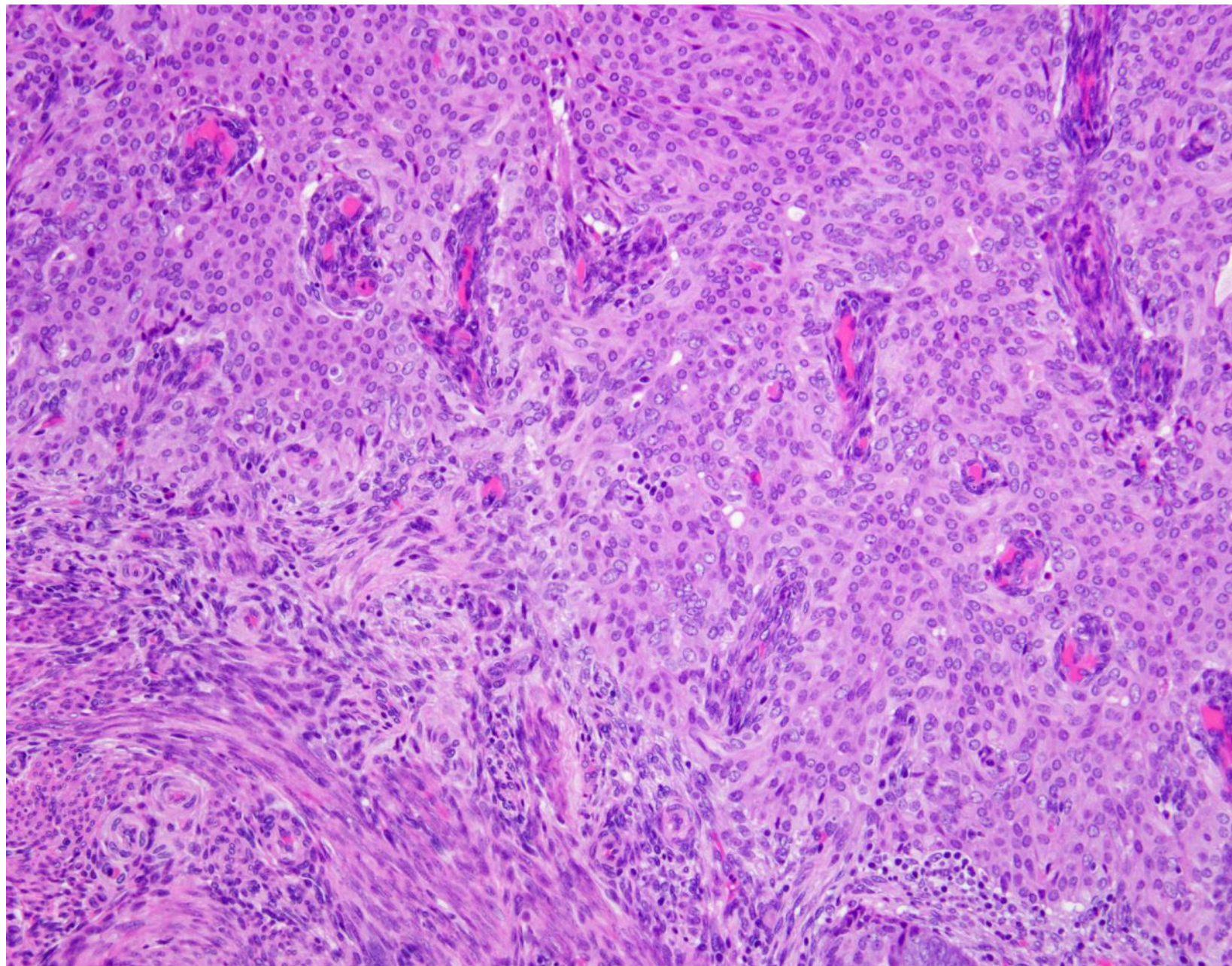


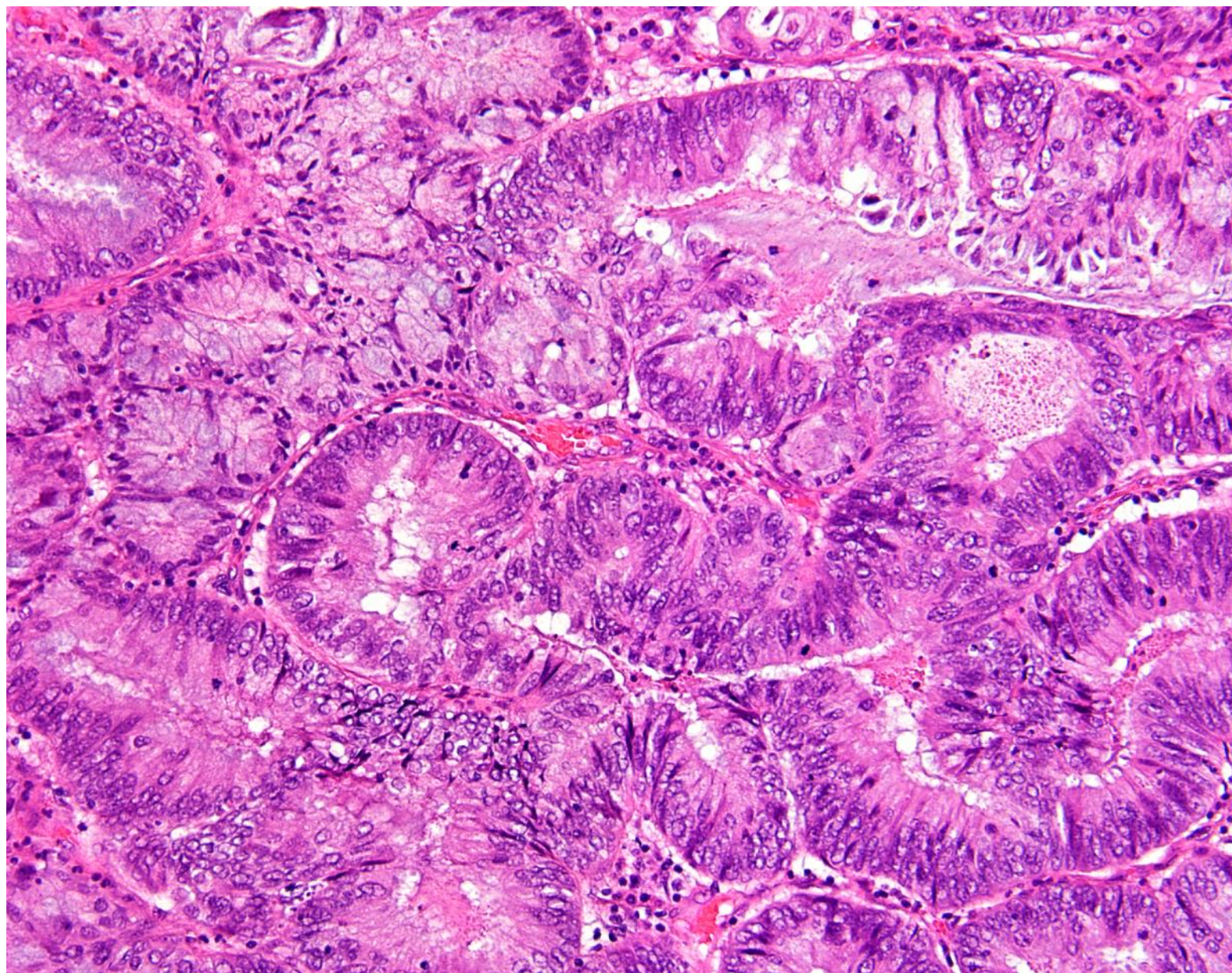


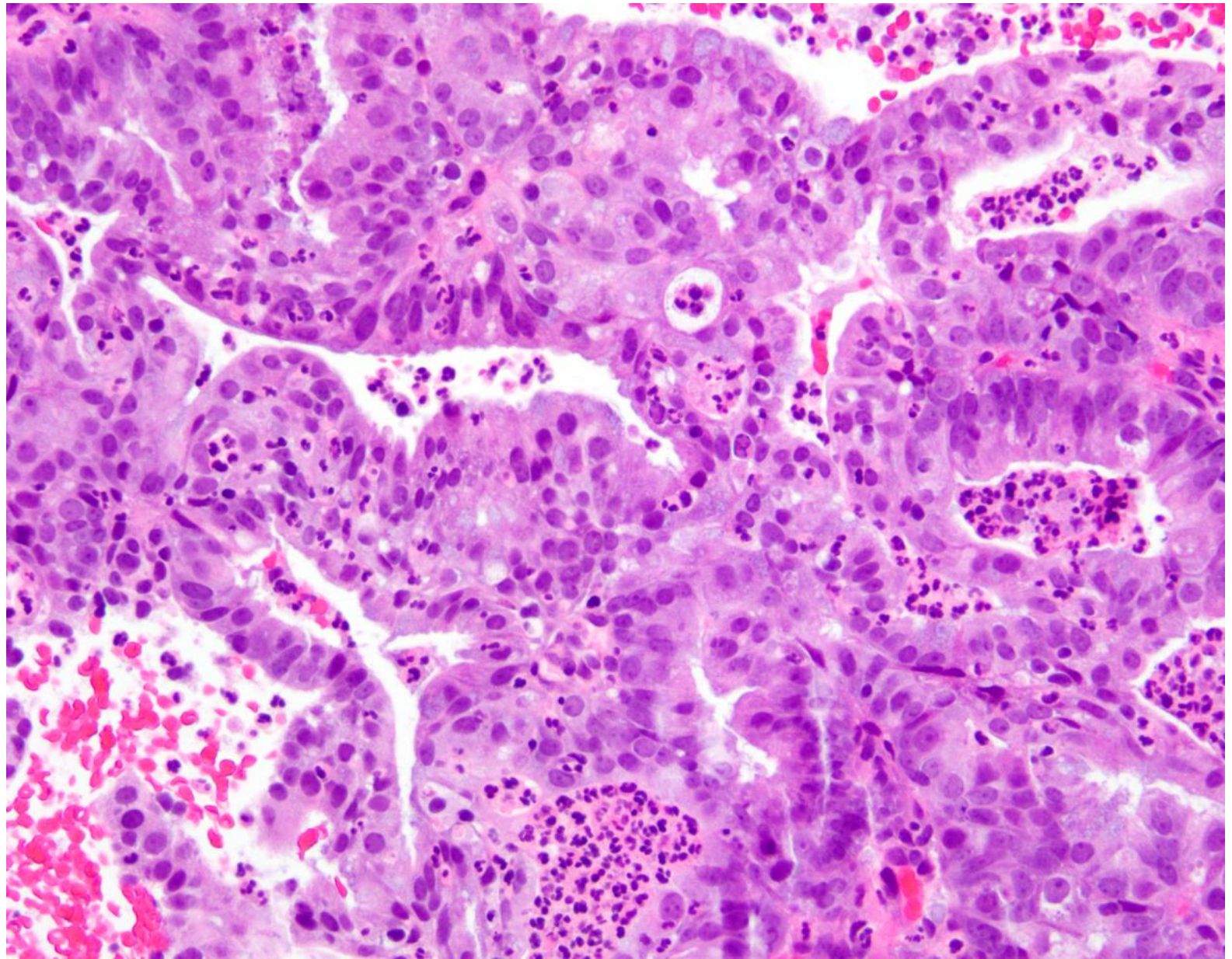


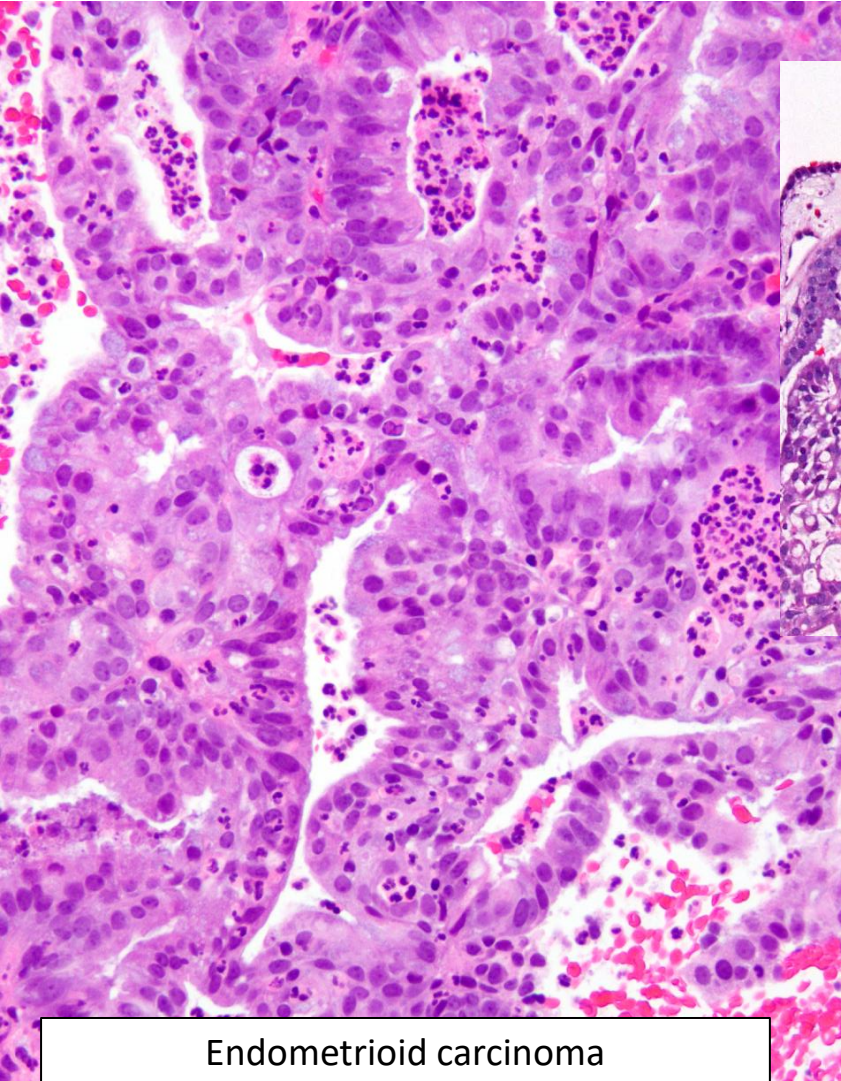






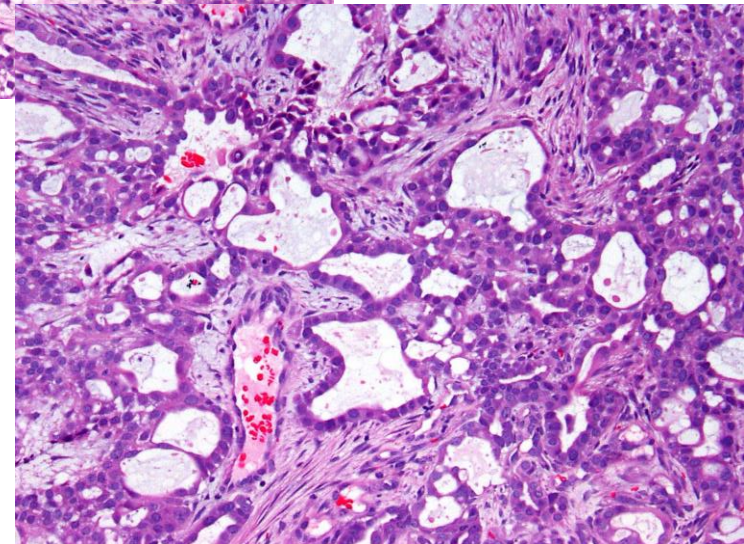
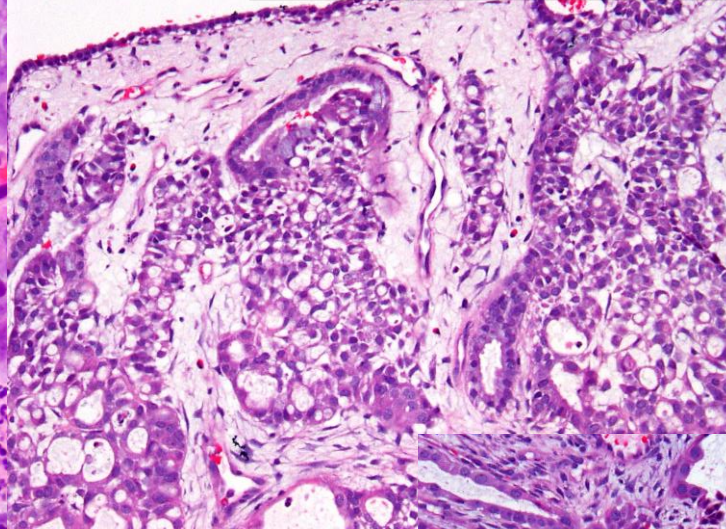


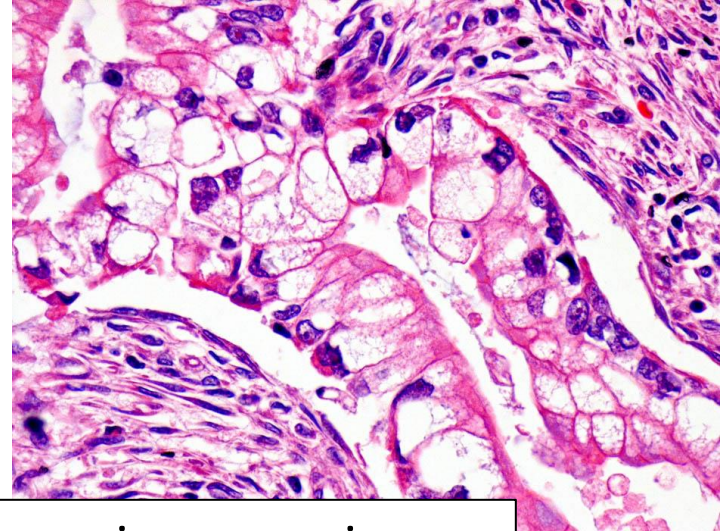
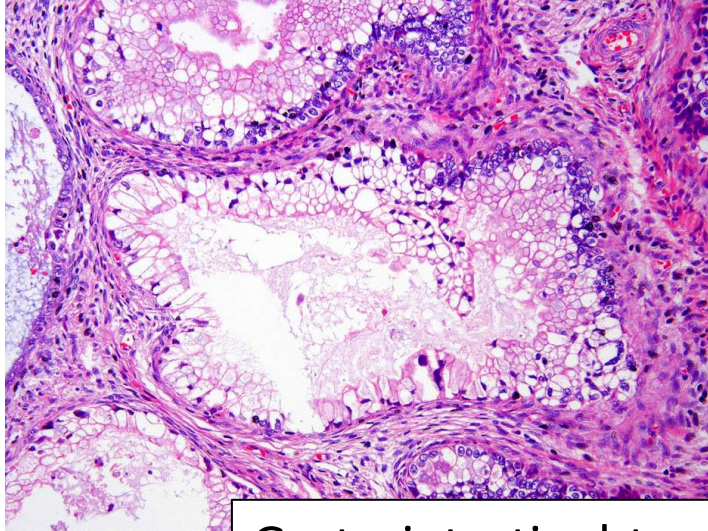




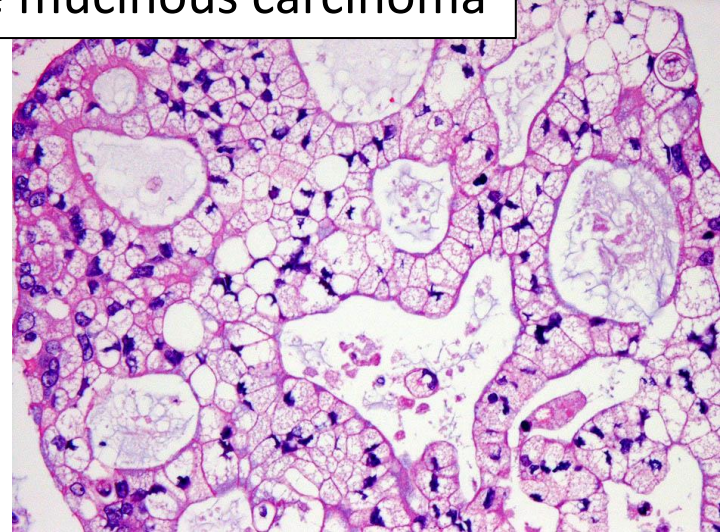
Endometrioid carcinoma

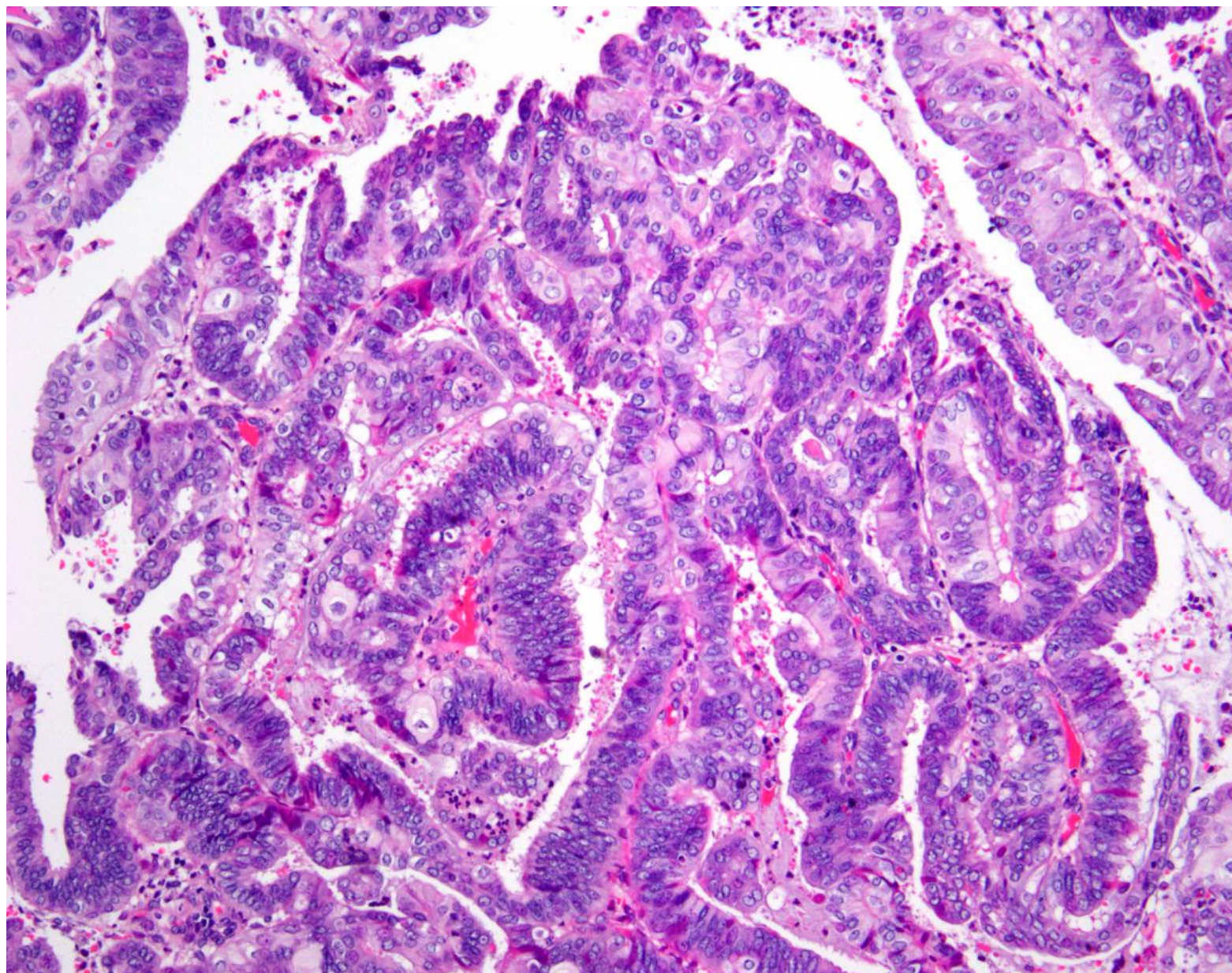
Cervical microglandular hyperplasia

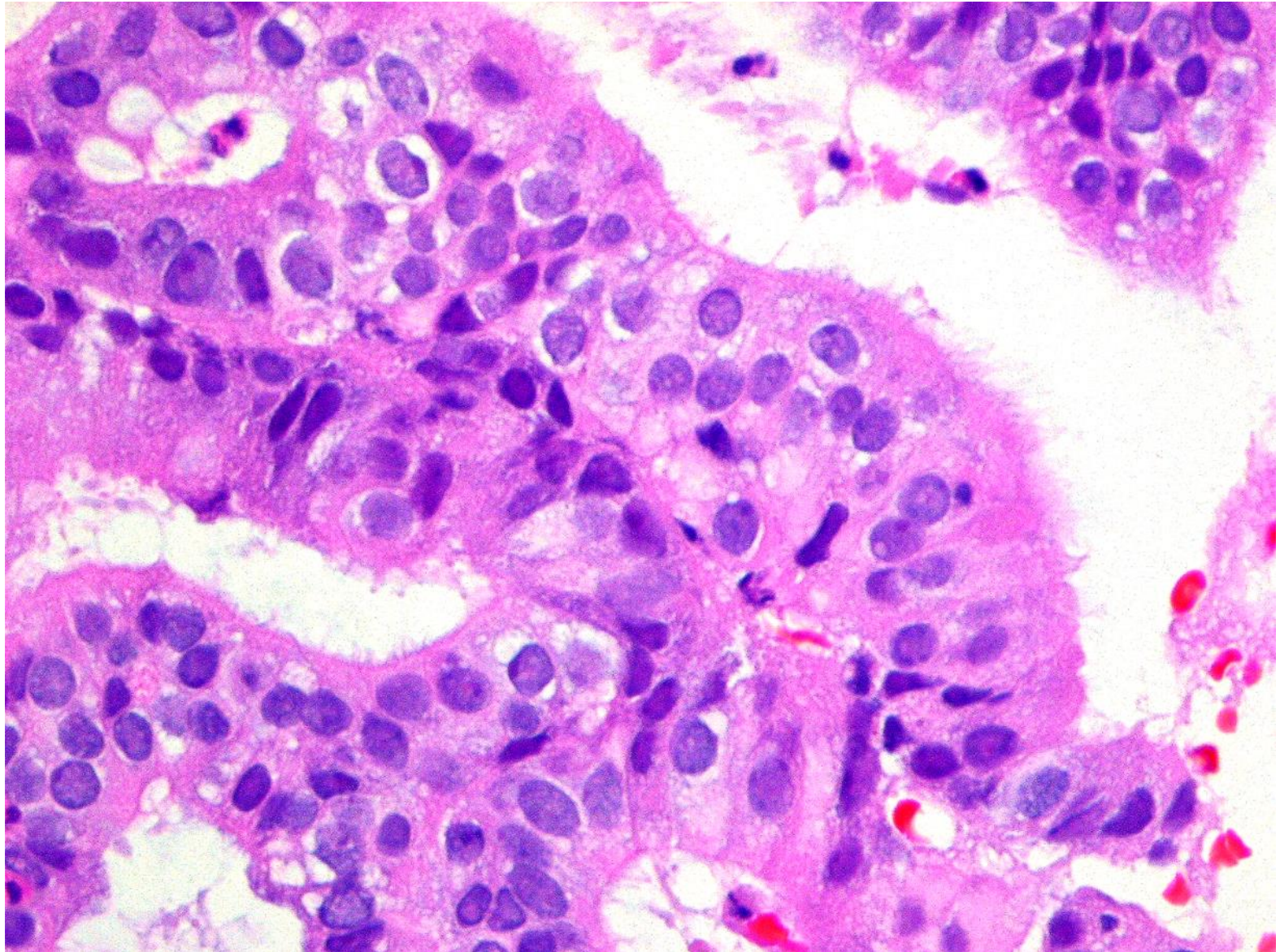


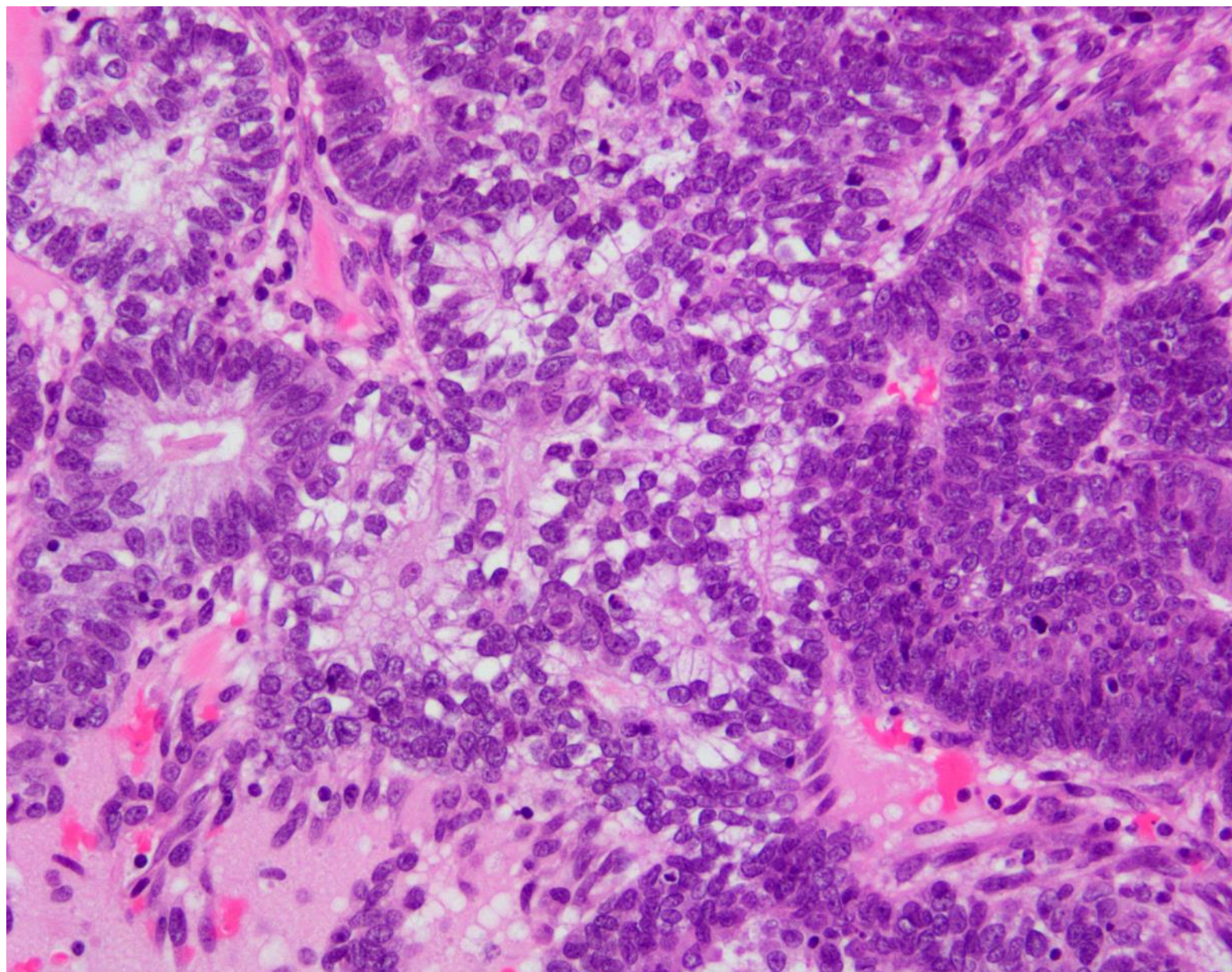


Gastrointestinal-type mucinous carcinoma

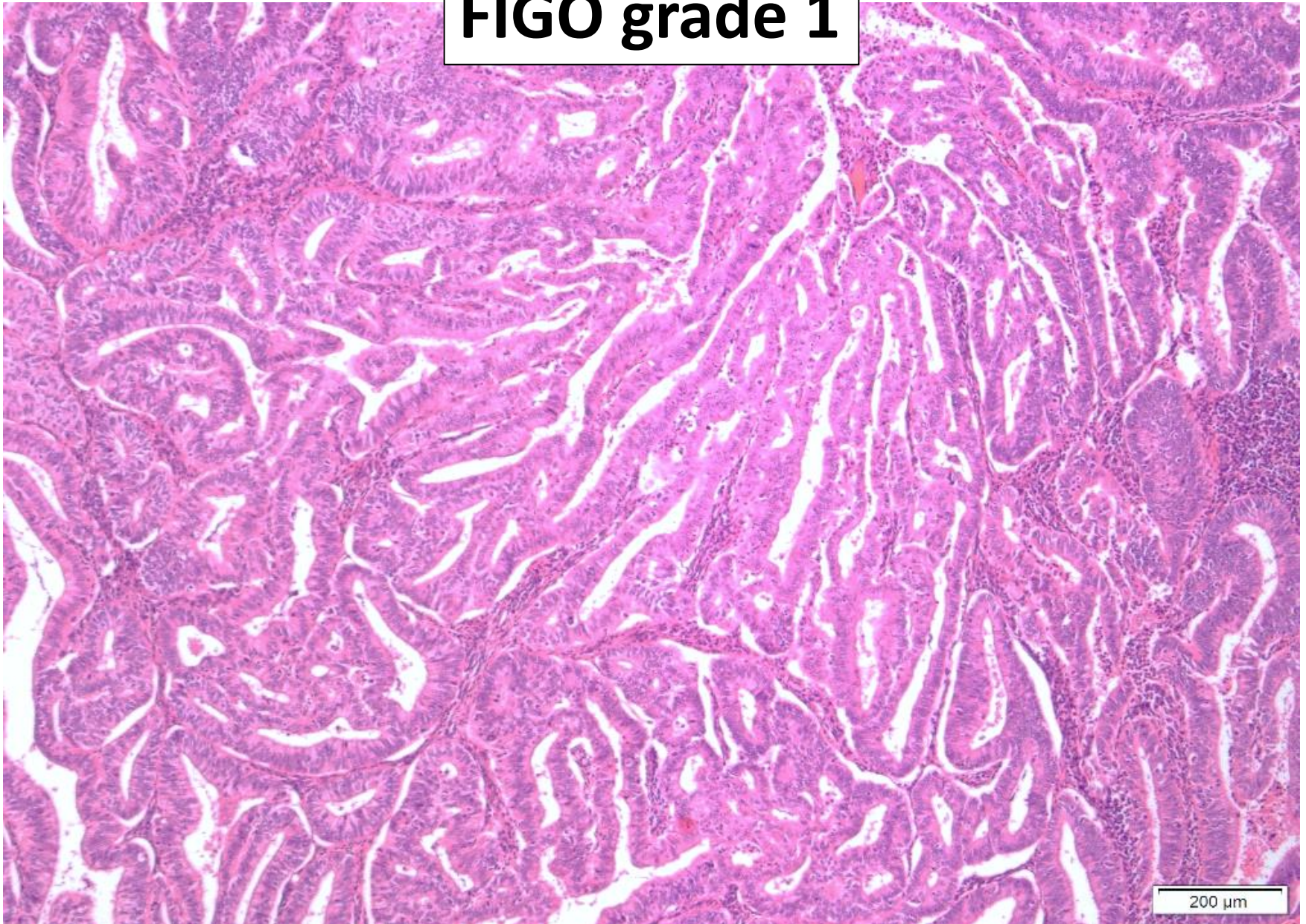




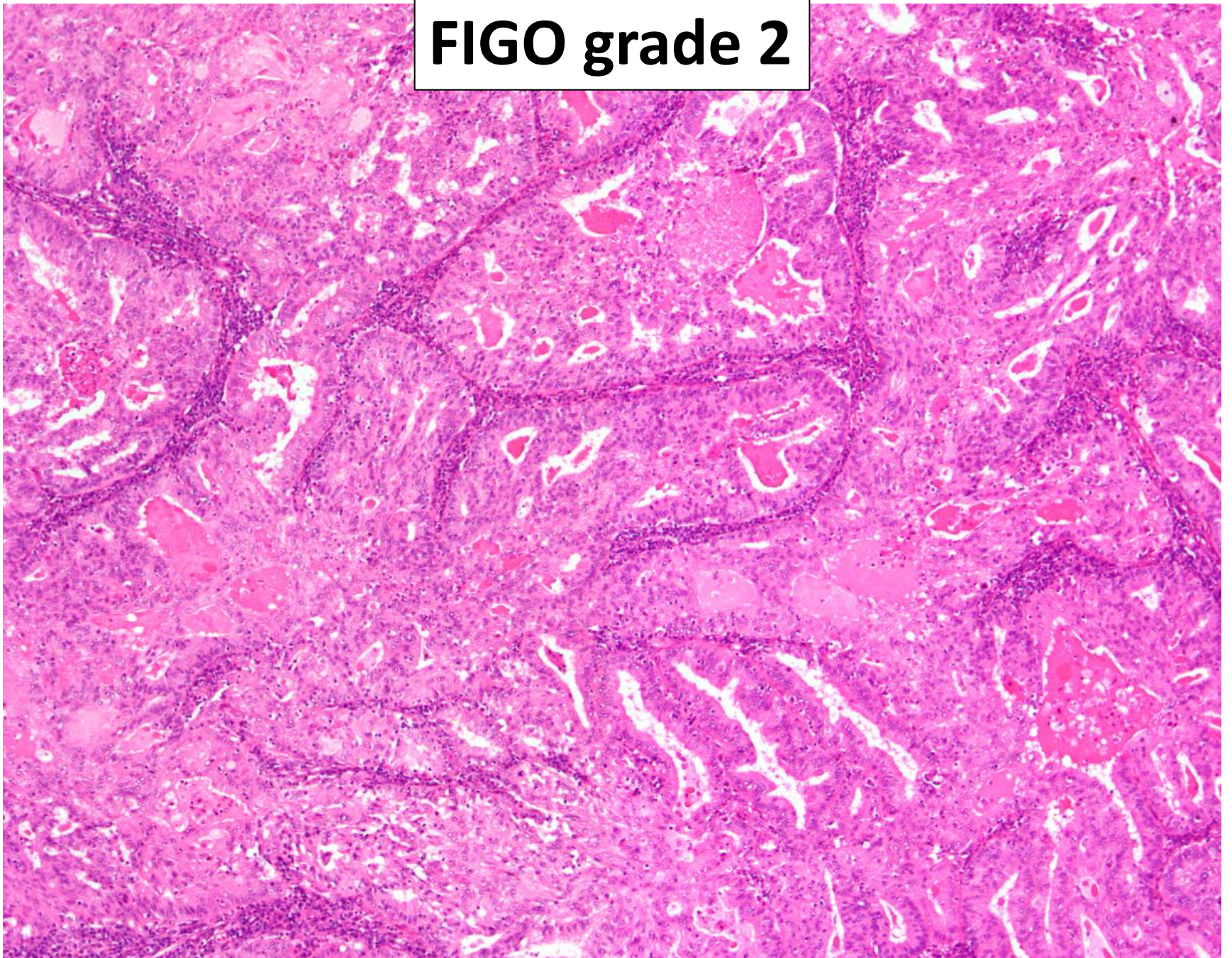




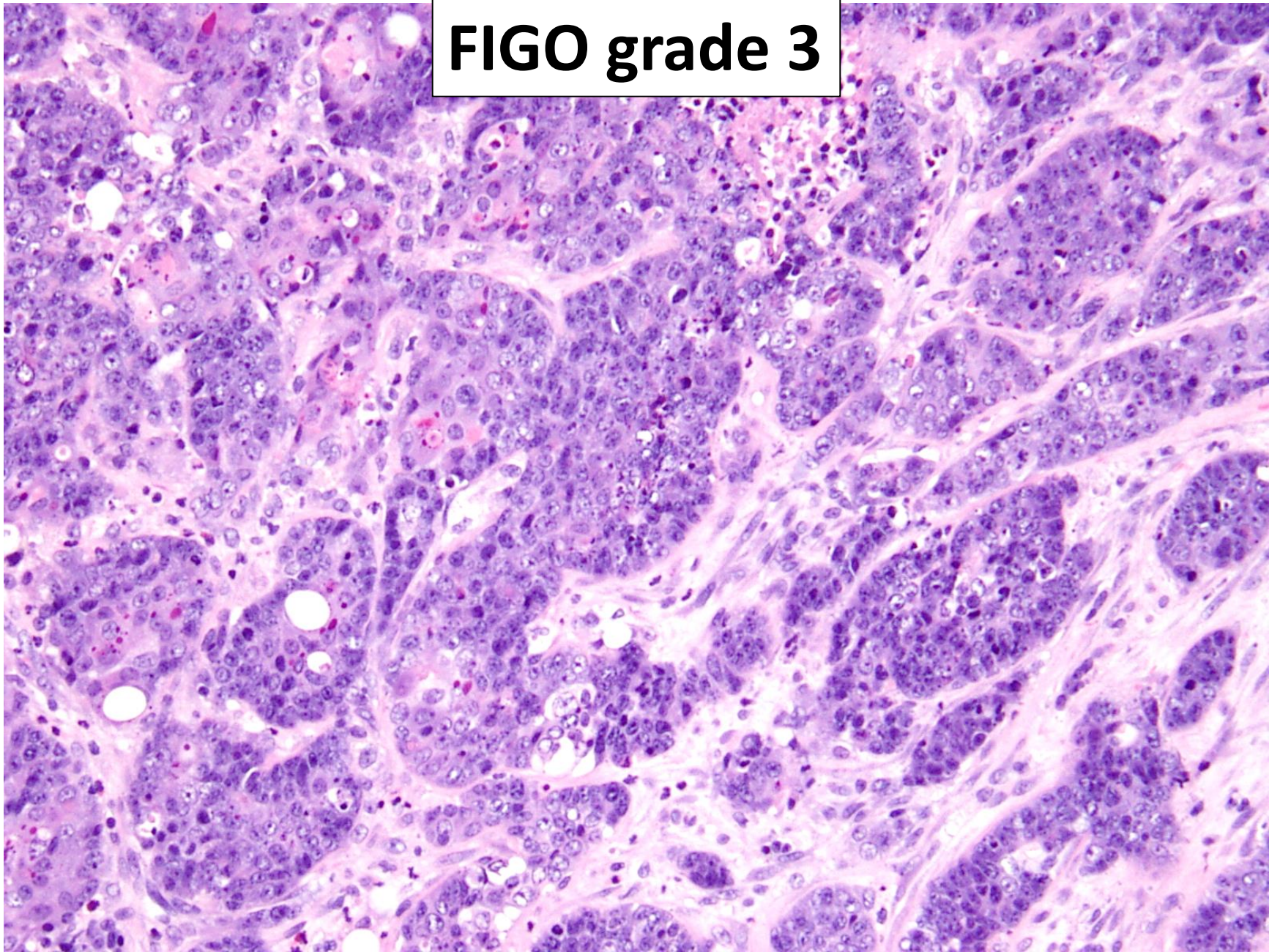
FIGO grade 1



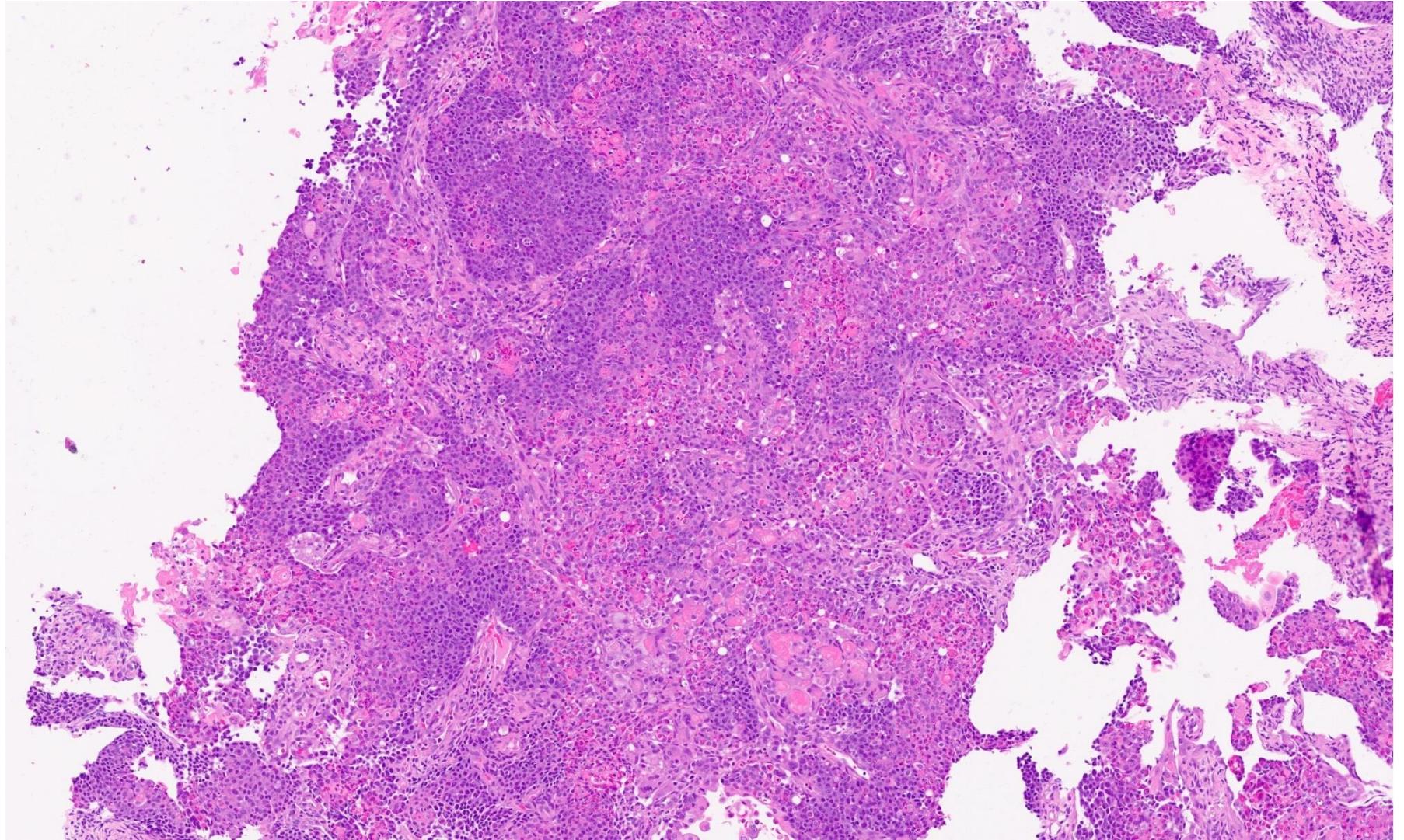
FIGO grade 2

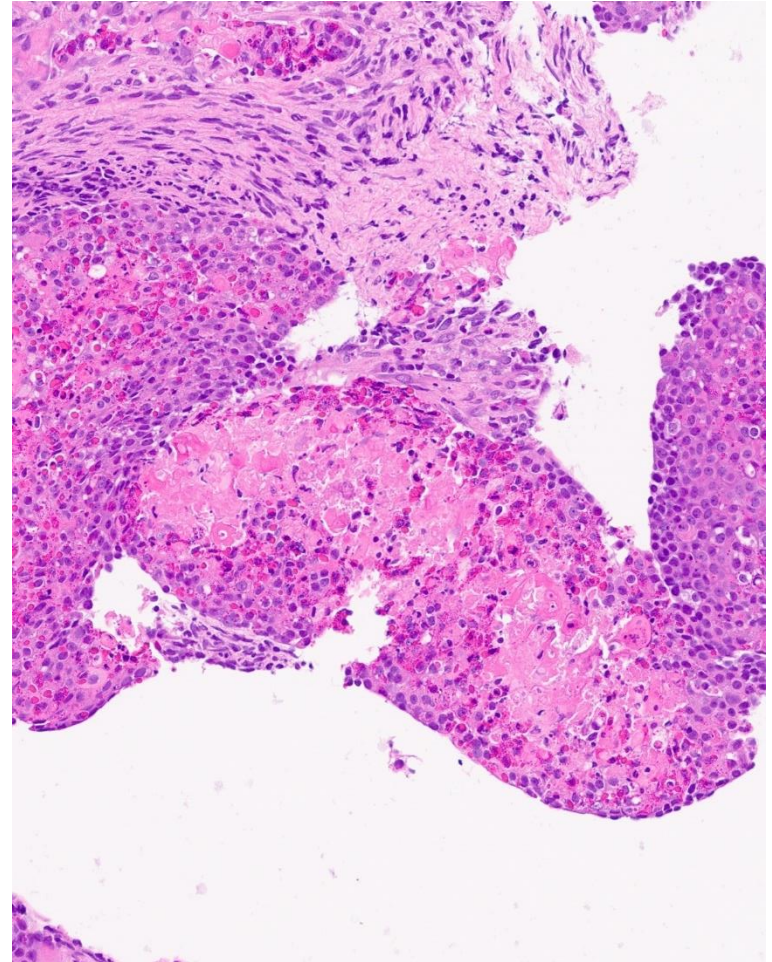
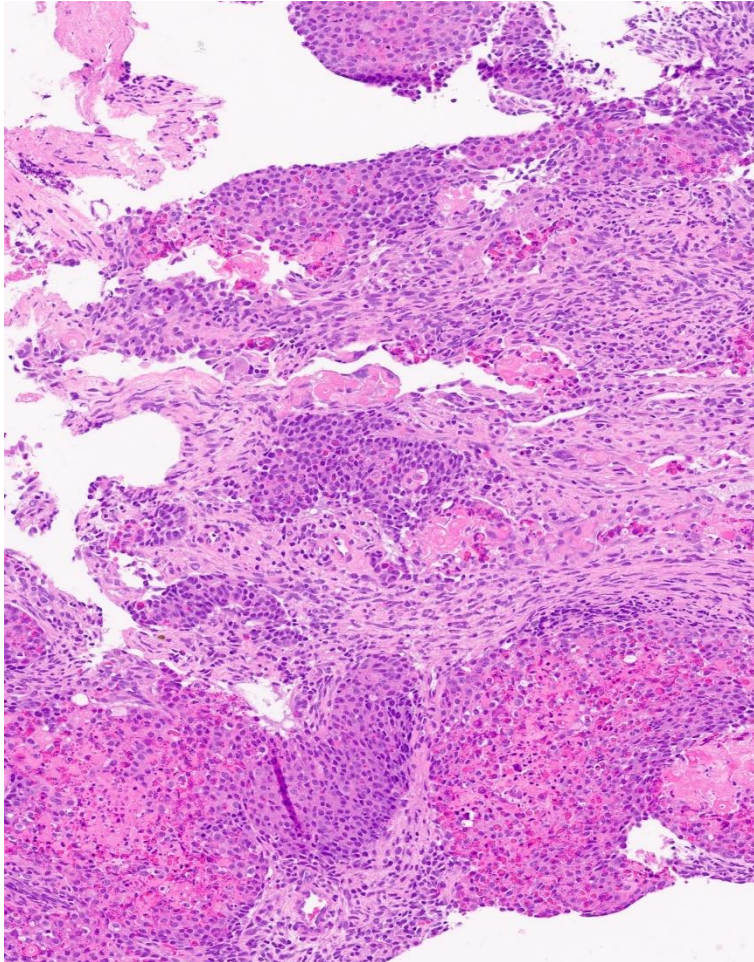


FIGO grade 3



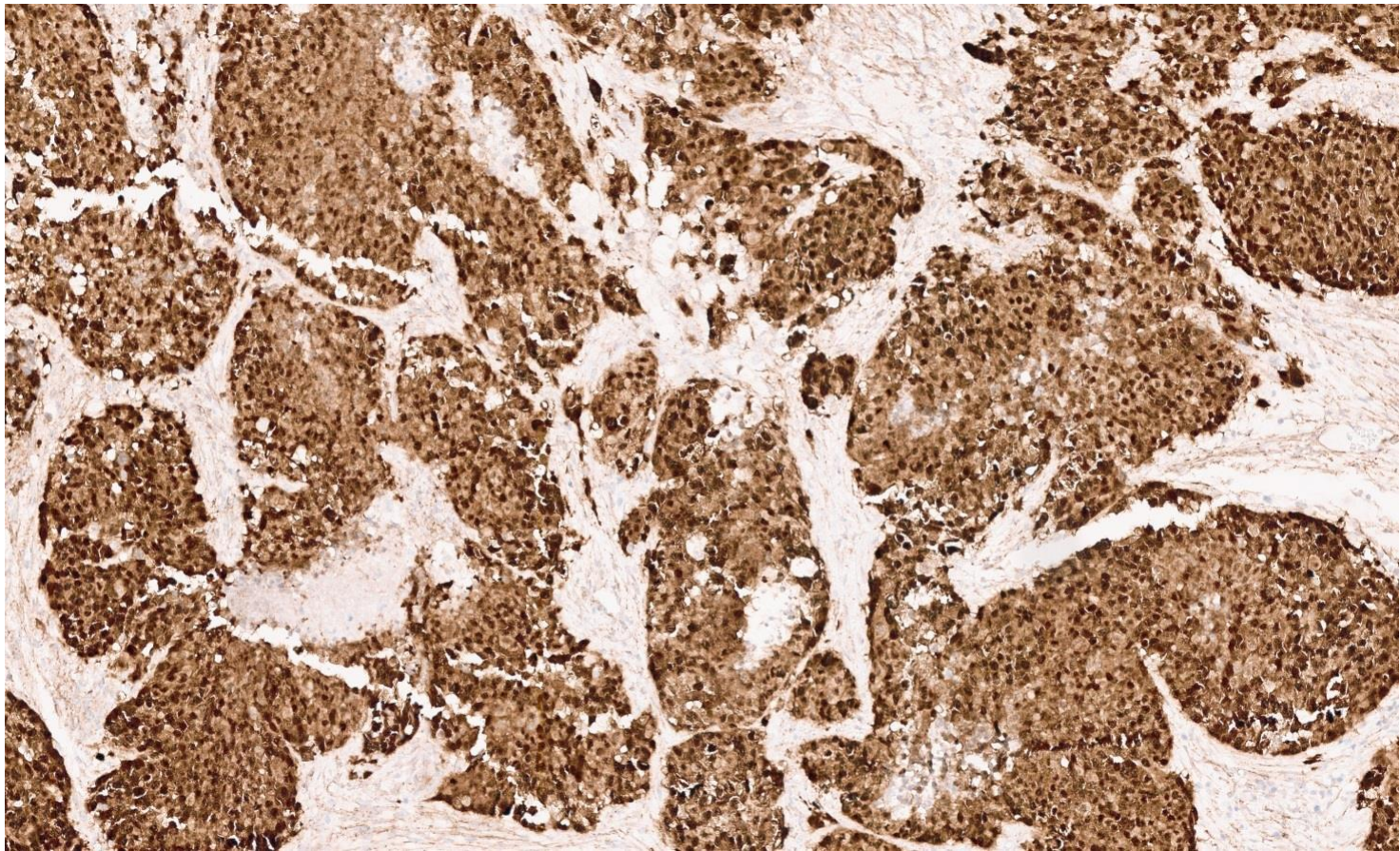
- A 63-year-old woman diagnosed with endometrioid carcinoma on endometrial curettage
- Hysterectomy: Deeply myoinvasive 4 cm tumor
- Chest CT: Multiple nodules



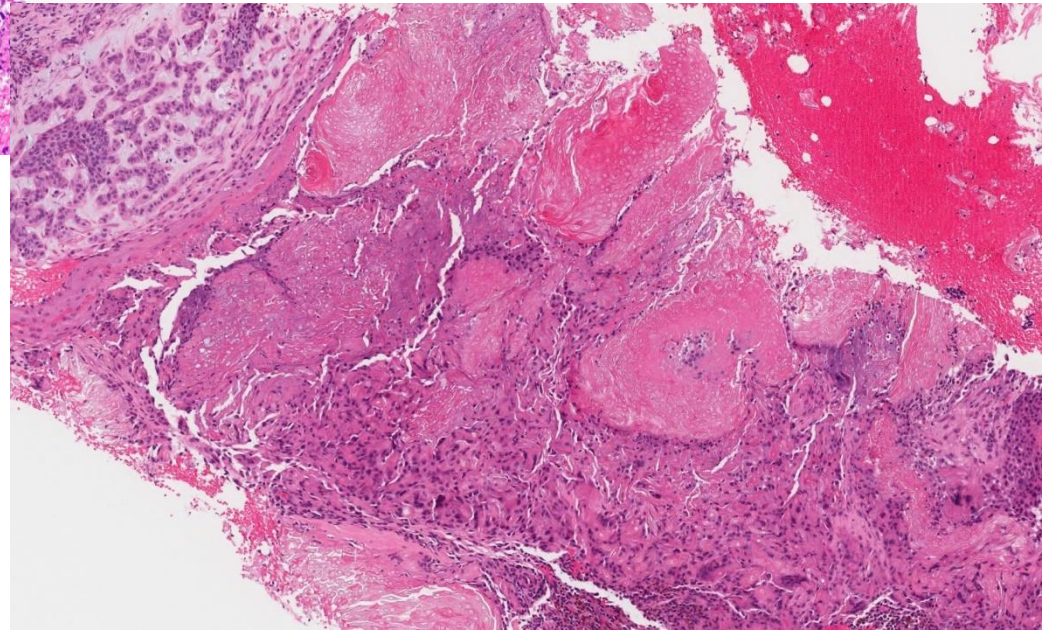
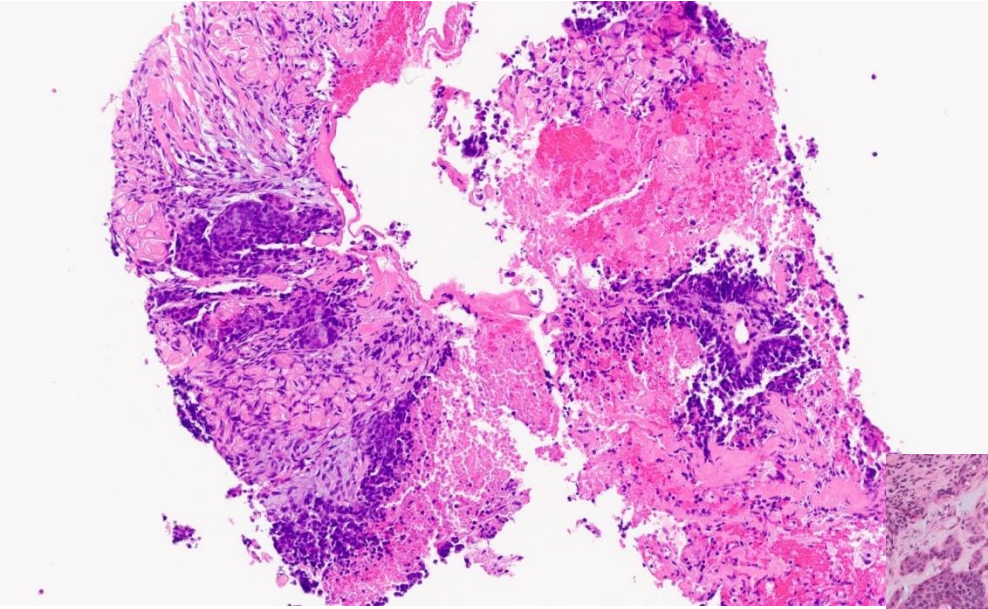


Immunohistochemistry

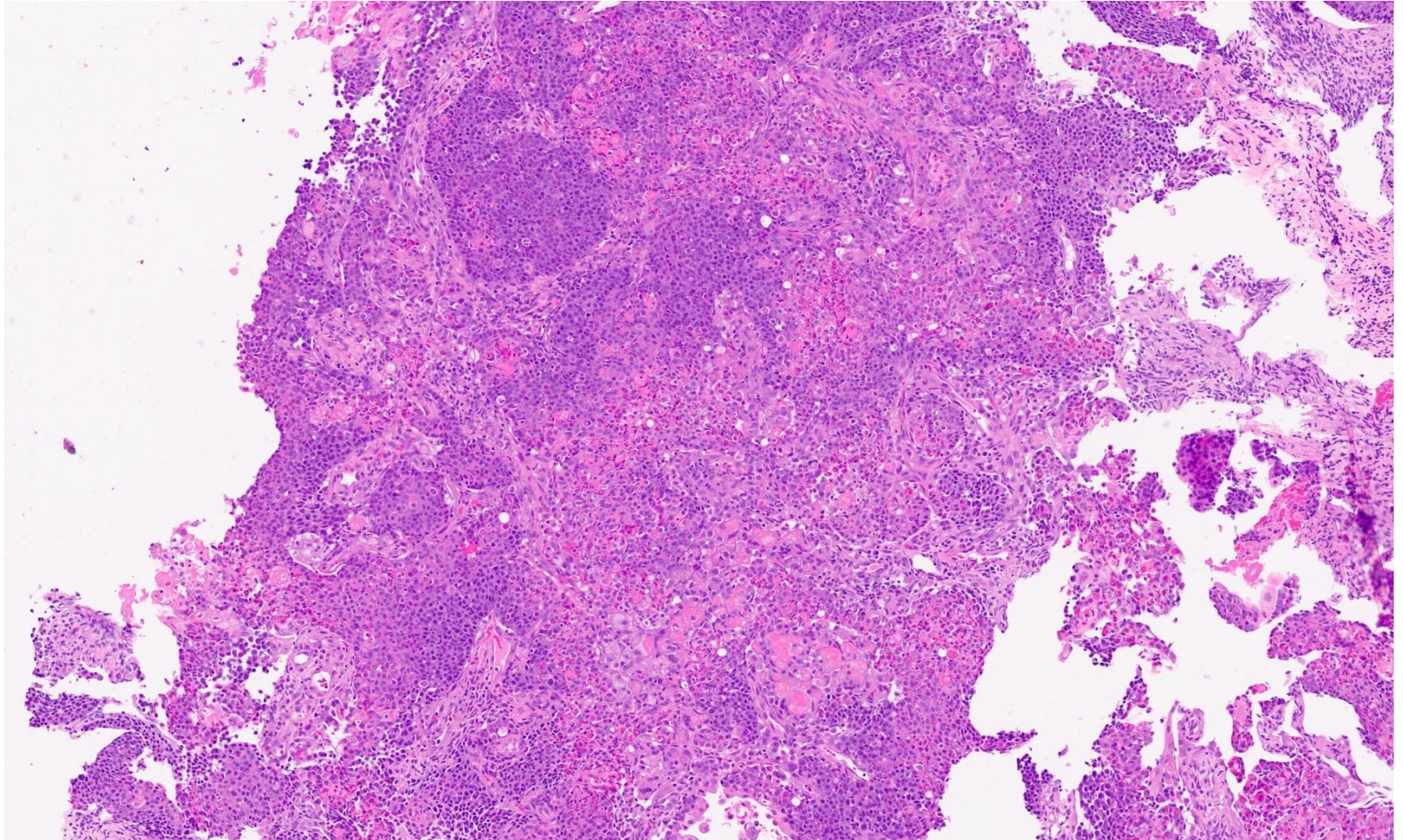
- Nuclear β -catenin expression
- PAX8, p63, ER and PR negative
- Patchy CDX2 and synaptophysin expression
- Retained DNA MMR expression
- p53 wild type pattern

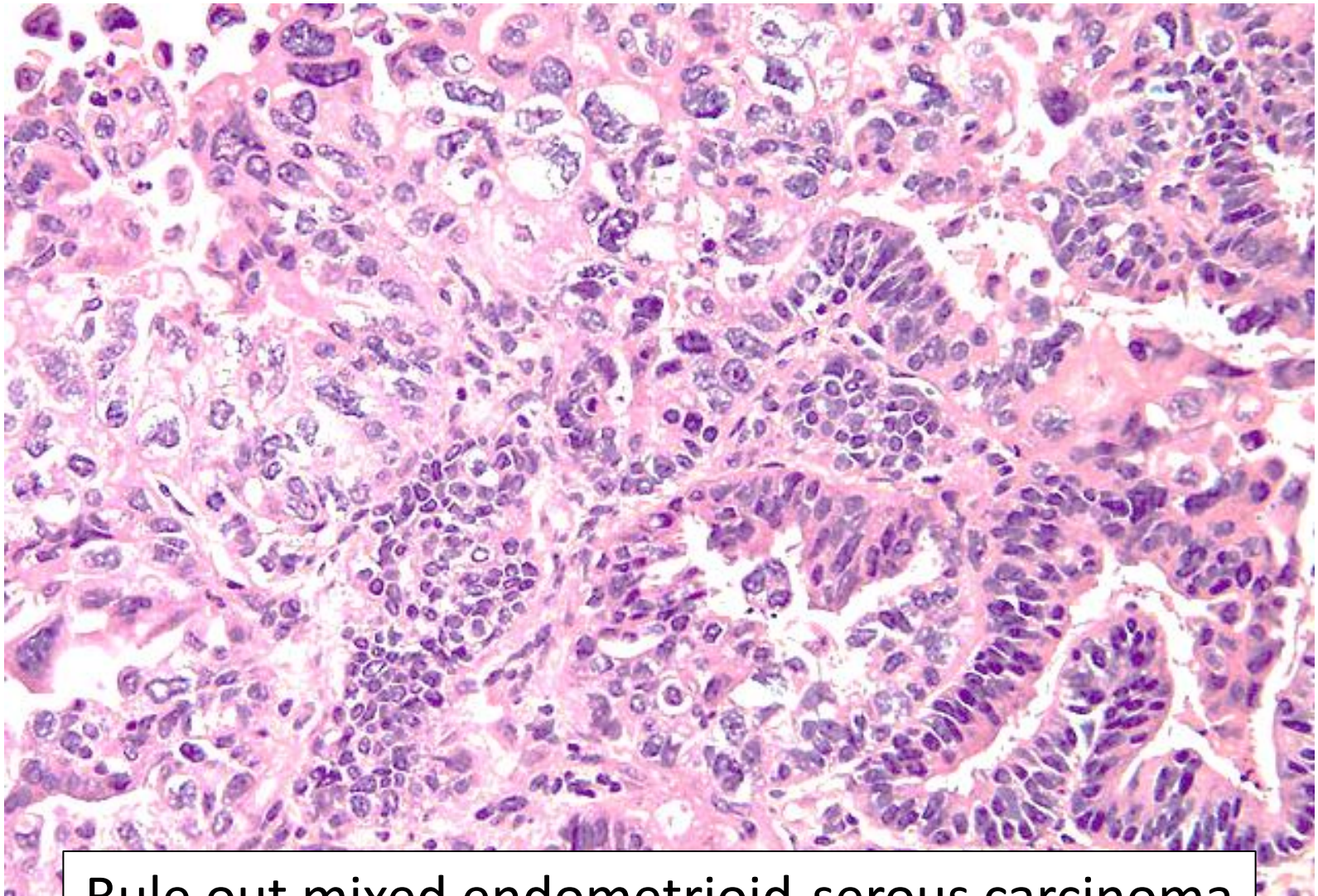


β-catenin



High-grade pilomatrix-like endometrial carcinoma





Rule out mixed endometrioid-serous carcinoma

Rule out MMRd endometrioid carcinoma

Rule out POLE endometrioid carcinoma

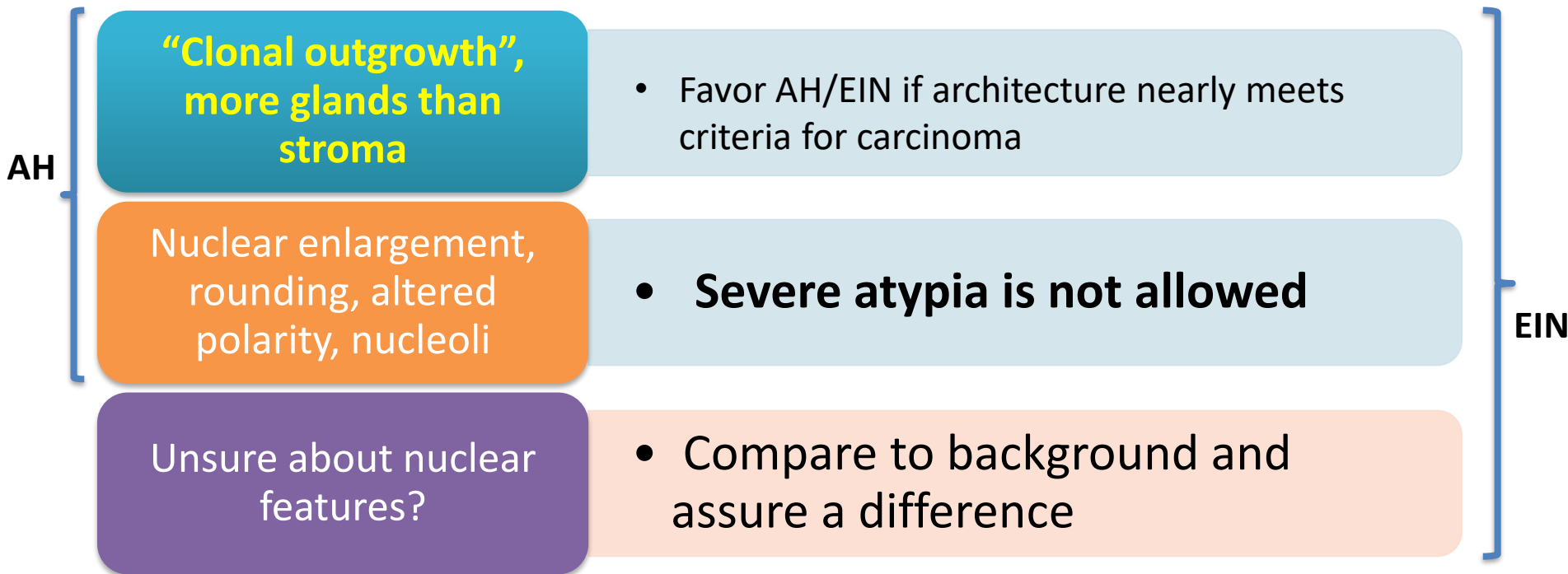
Molecular signatures and immunophenotype

- Endometrioid

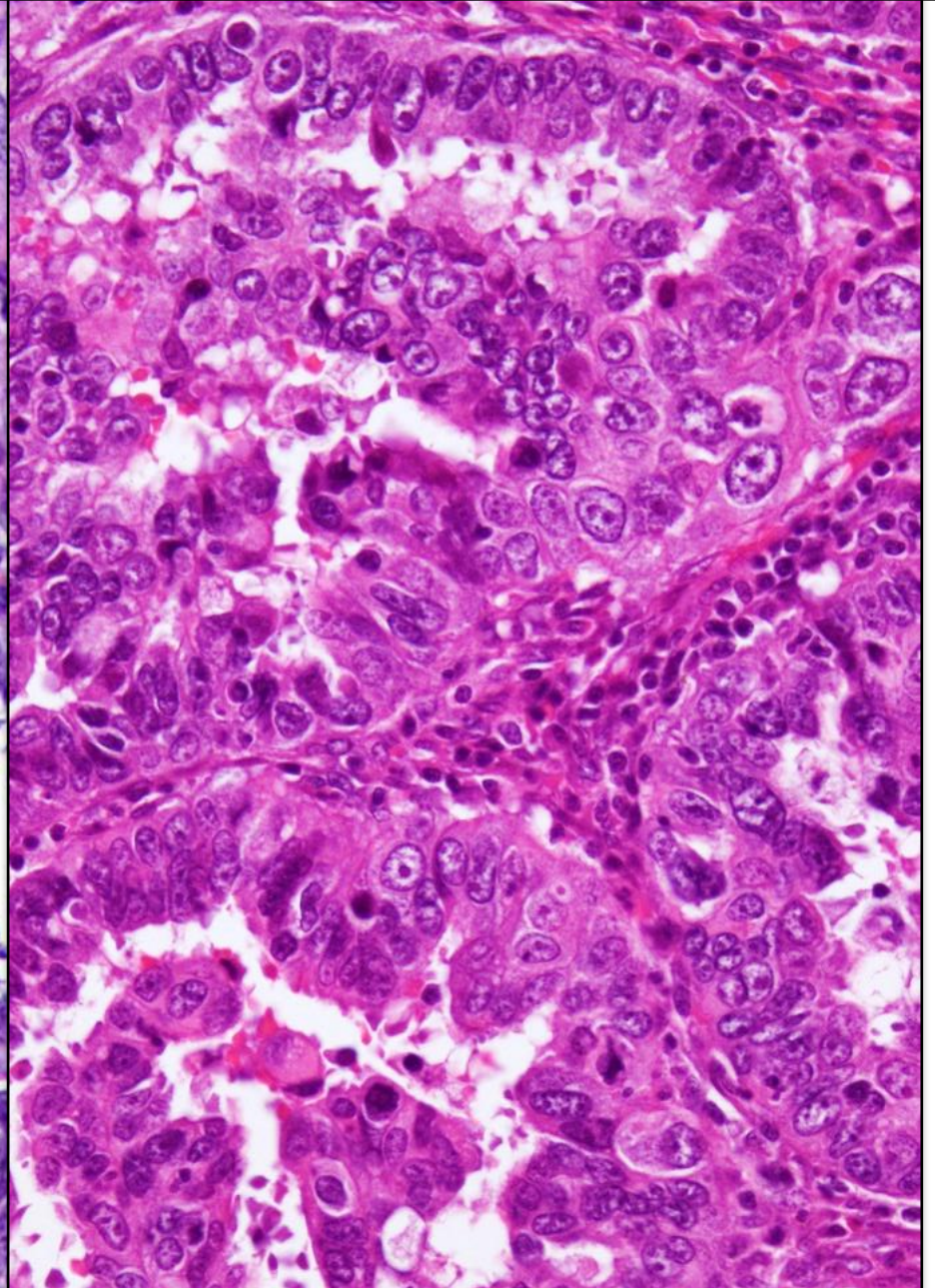
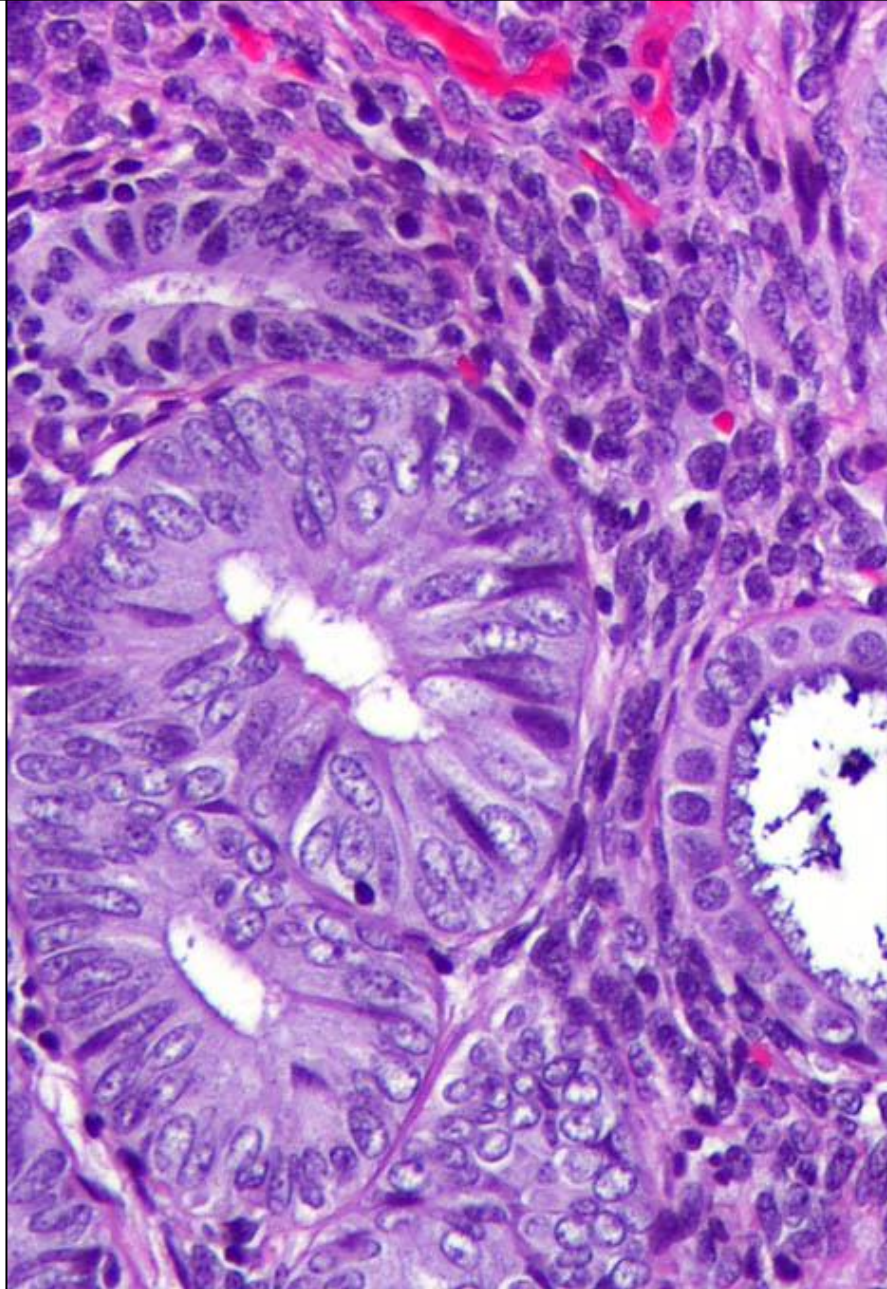
- Mutations: *PTEN, PIK3CA, ARID 1A, DNA MMR, KRAS, CTNNB1, TP53, POLE*
- IHC: aberrant PTEN, ARID 1A, DNA MMR, β -catenin, p53

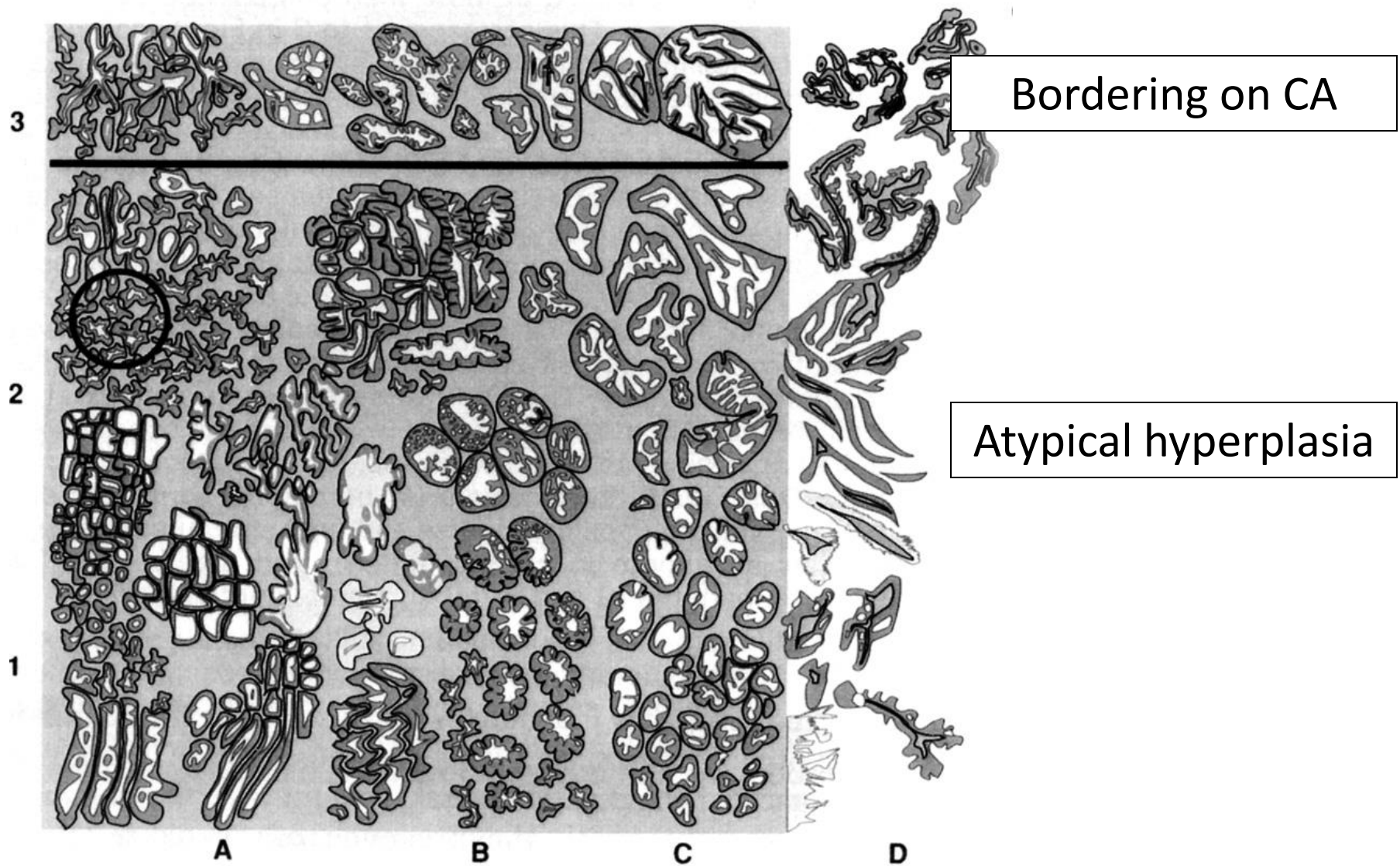
Differential diagnosis

Atypical hyperplasia/EIN

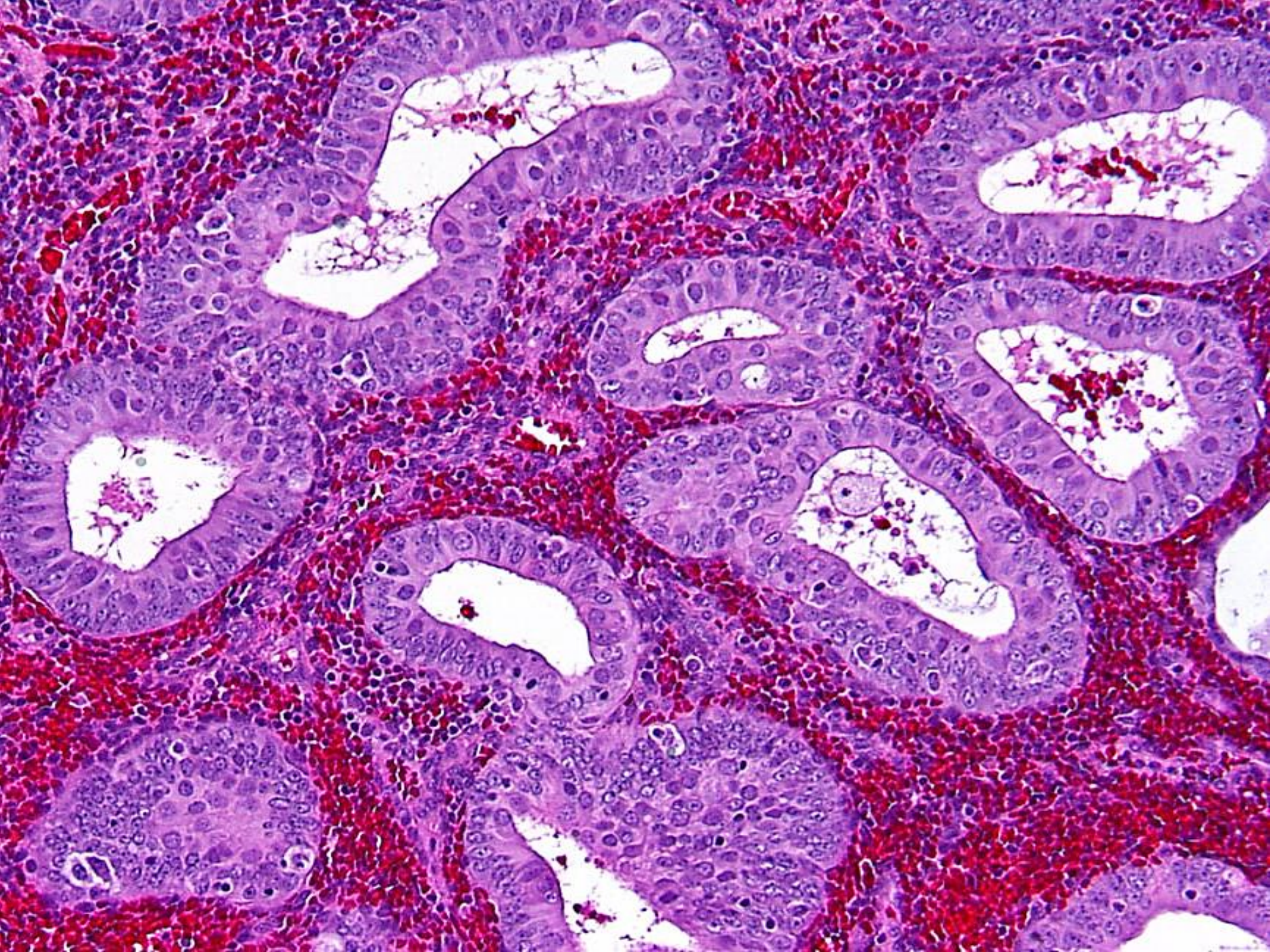


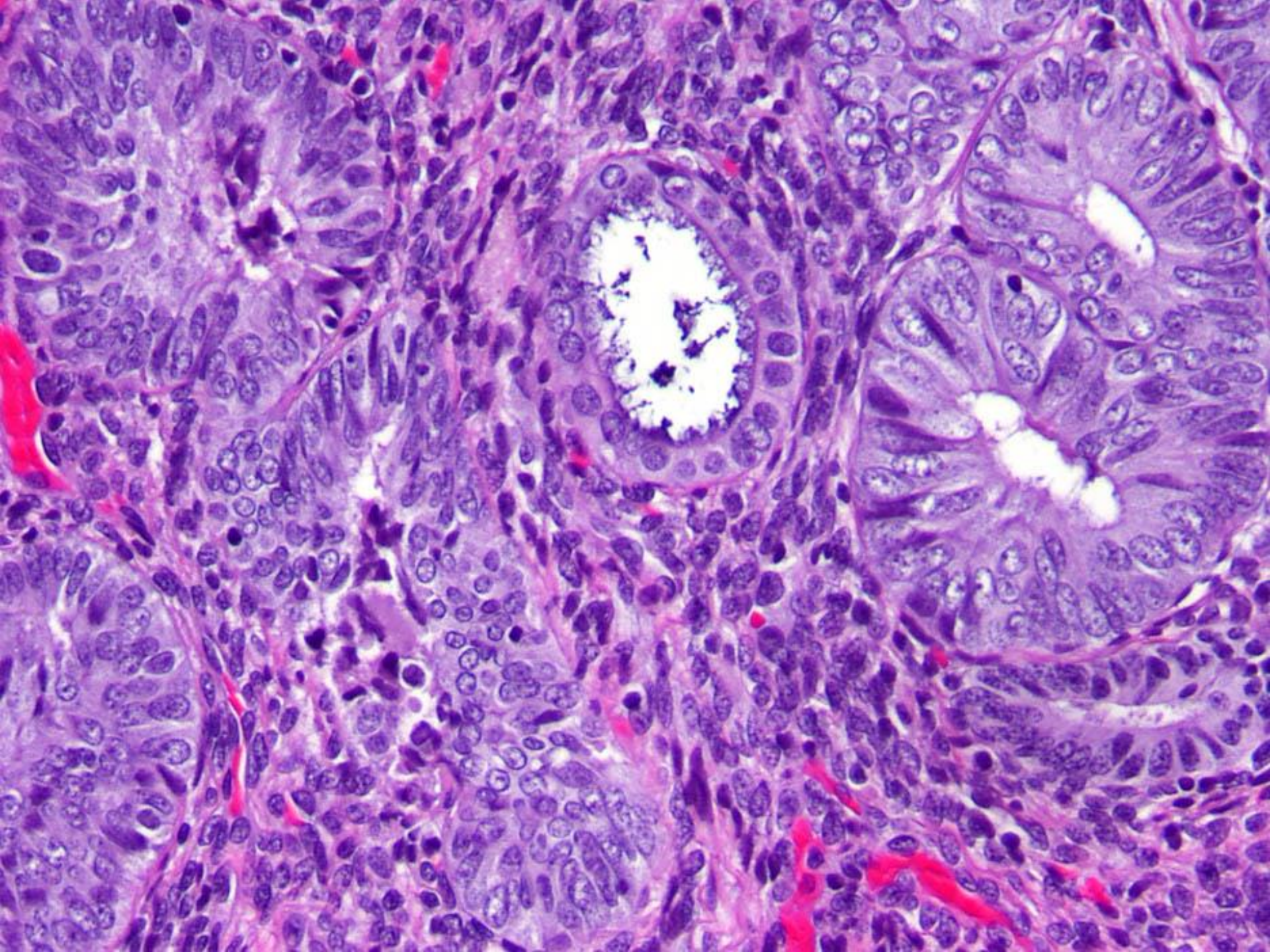
Atypical hyperplasia versus Serous carcinoma



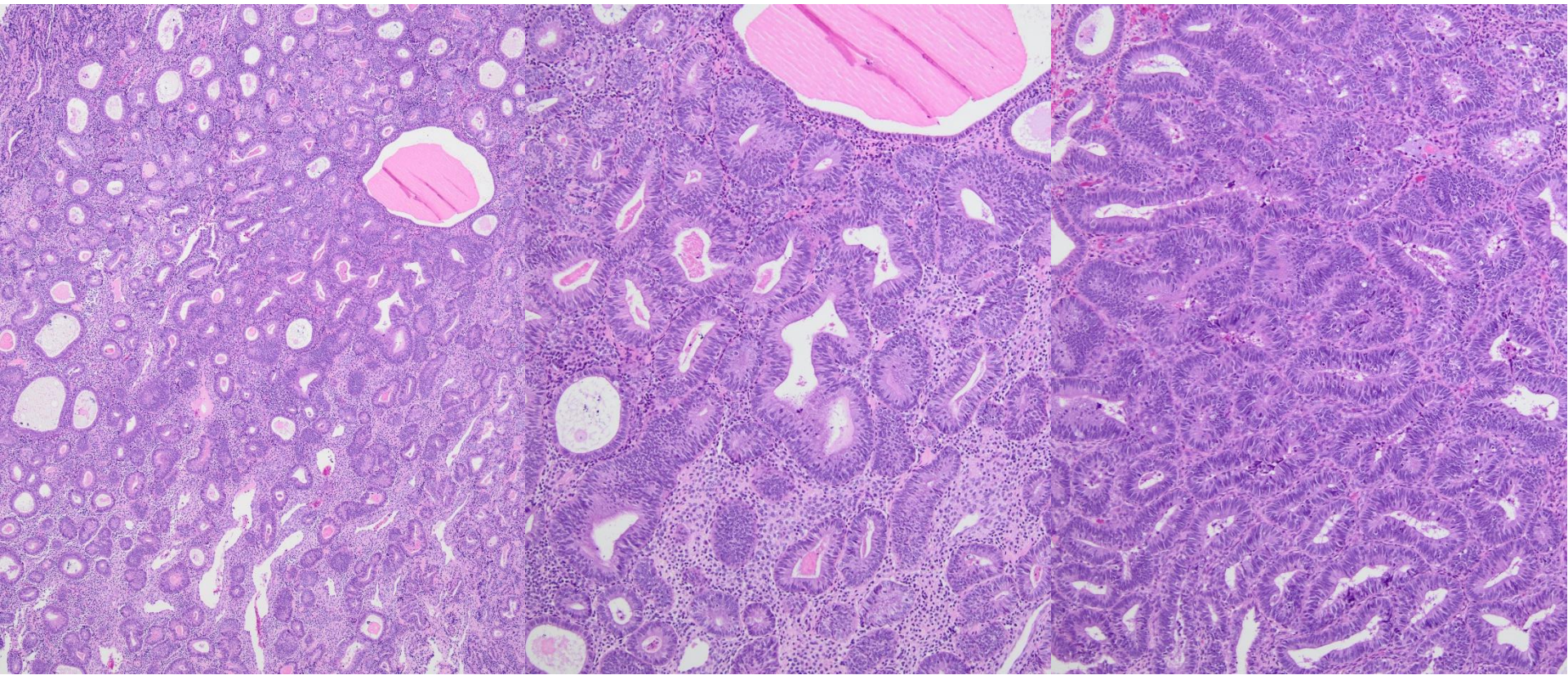


Longacre TA, et al. Am J Surg Pathol. 1995 Apr;19(4):371-406

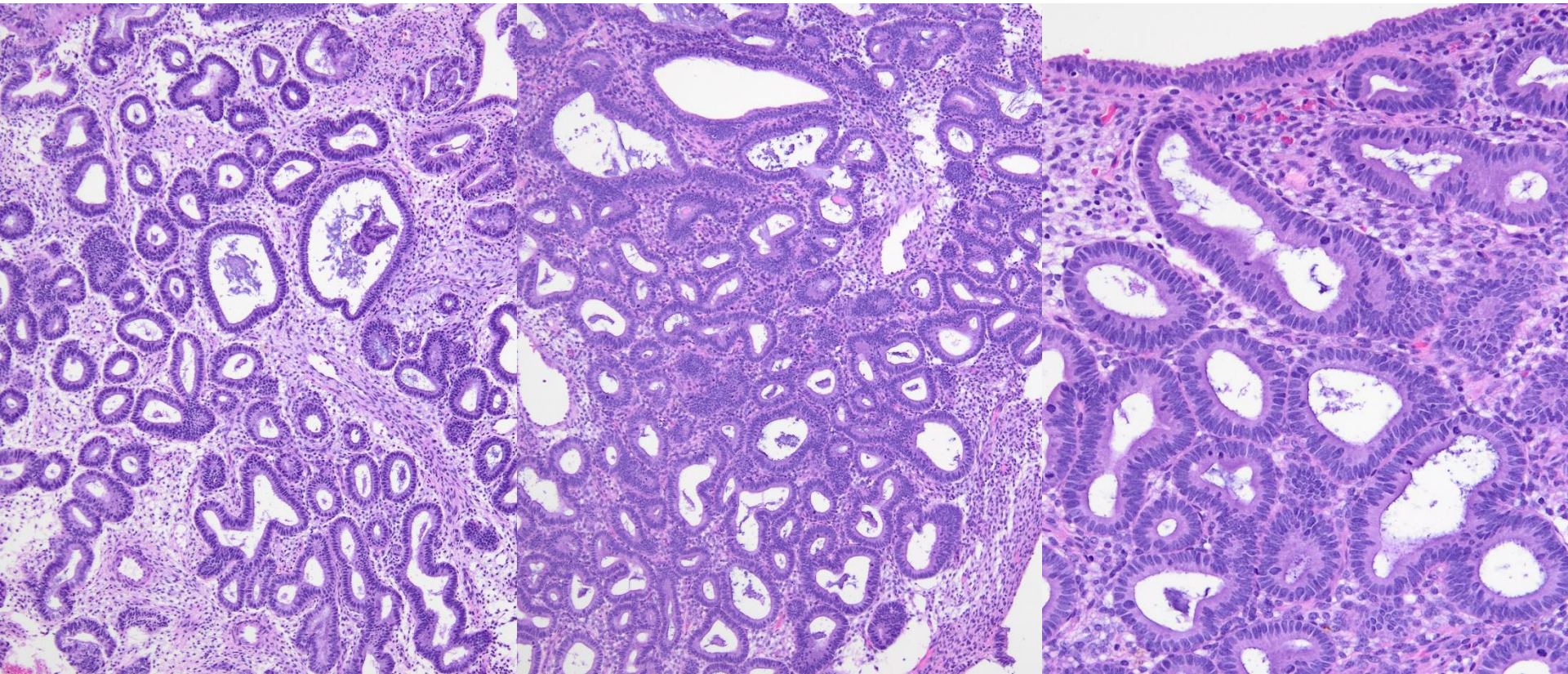




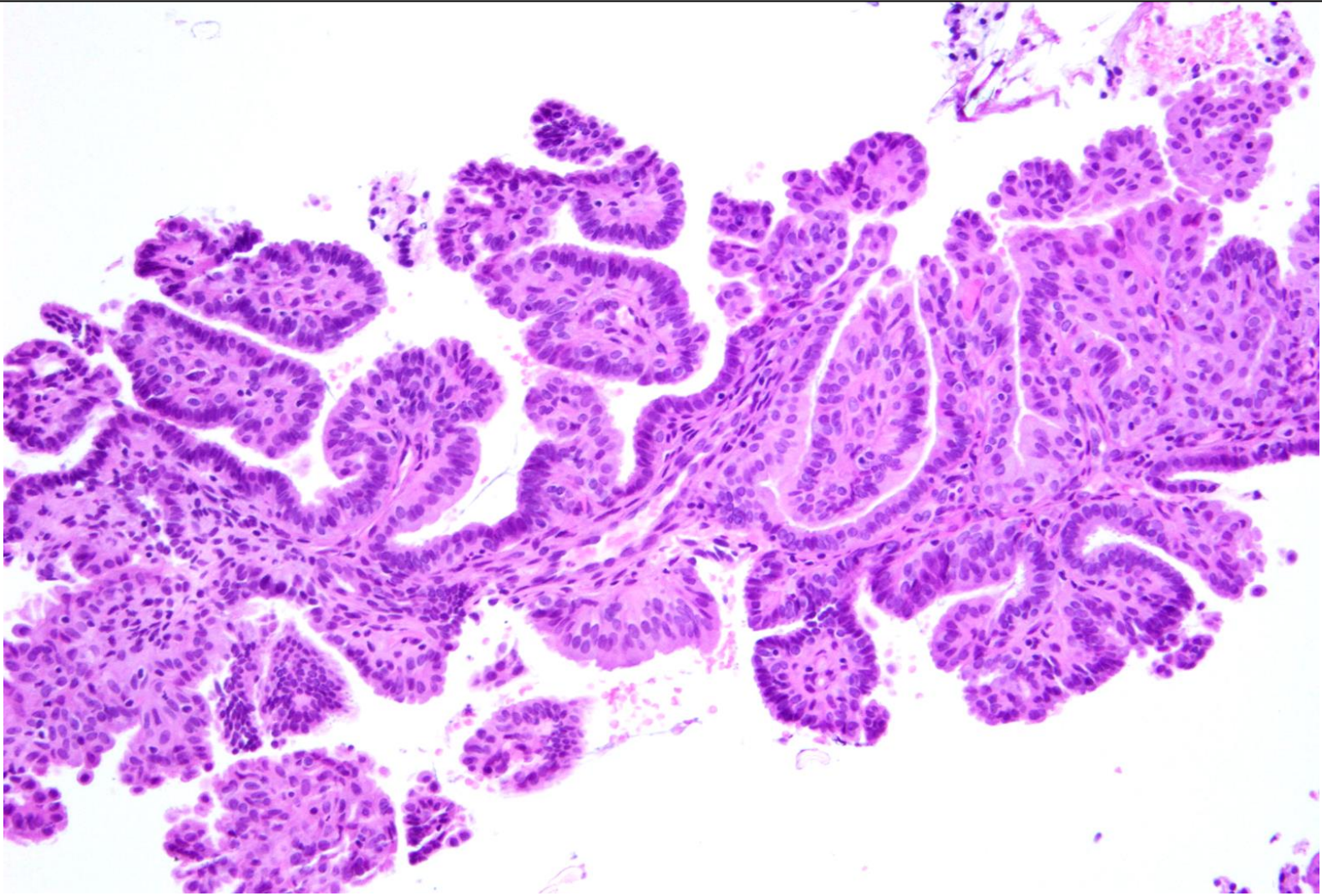
62-year-old with postmenopausal bleeding



42-year-old with a cervical polyp and post-coital bleeding



Benign papillary change “Lehman-Hart lesion” “Ip lesion”



“Ip lesion”

Benign

- Focal
- Simple papillae
- No nuclear atypia

Hyperplasia/atypical hyperplasia

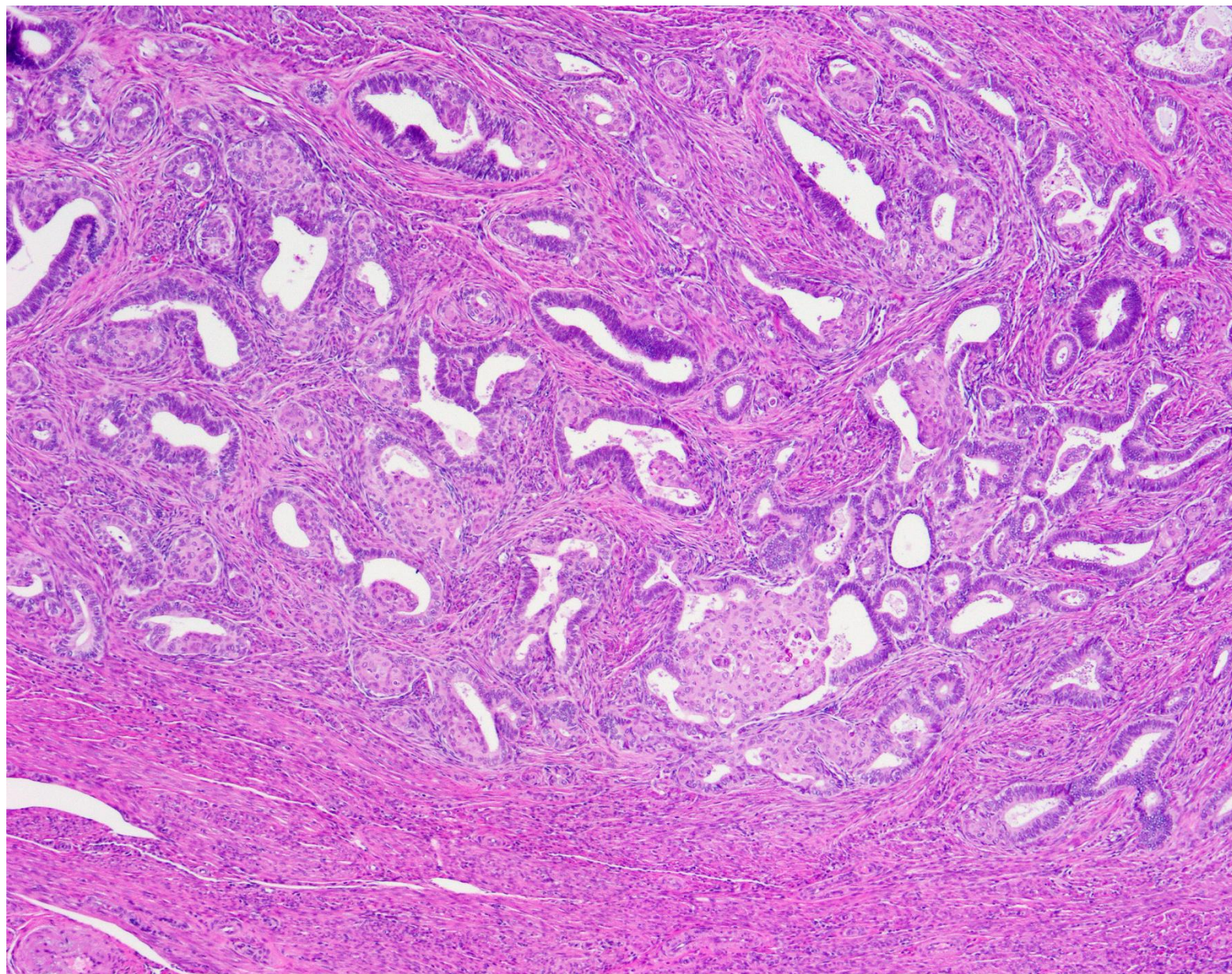
- Diffuse *and/or*
- Complex branching papillae
- Nuclear atypia
- Exclude papillary syncytial change

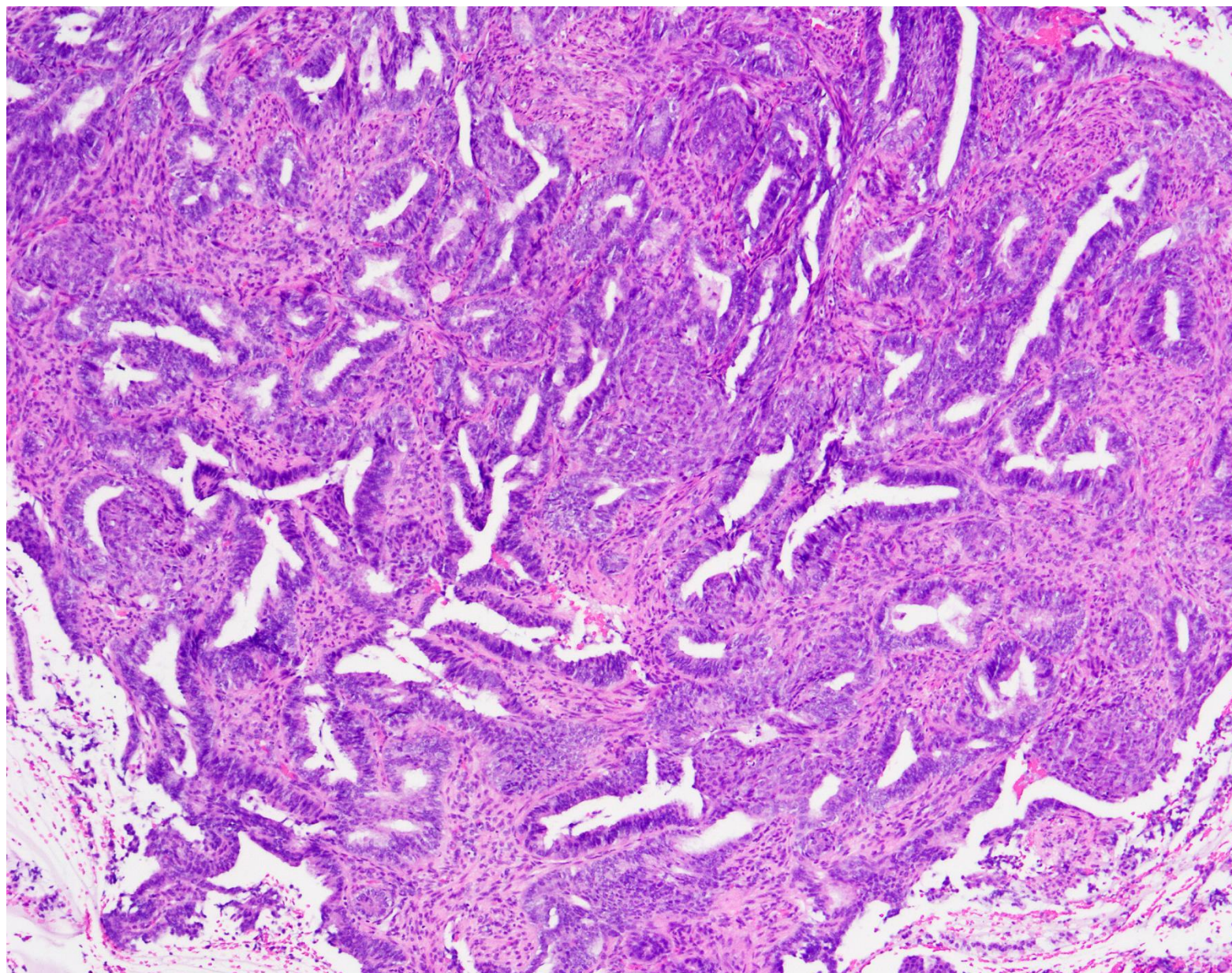
Atypical polypoid adenomyoma (APA)

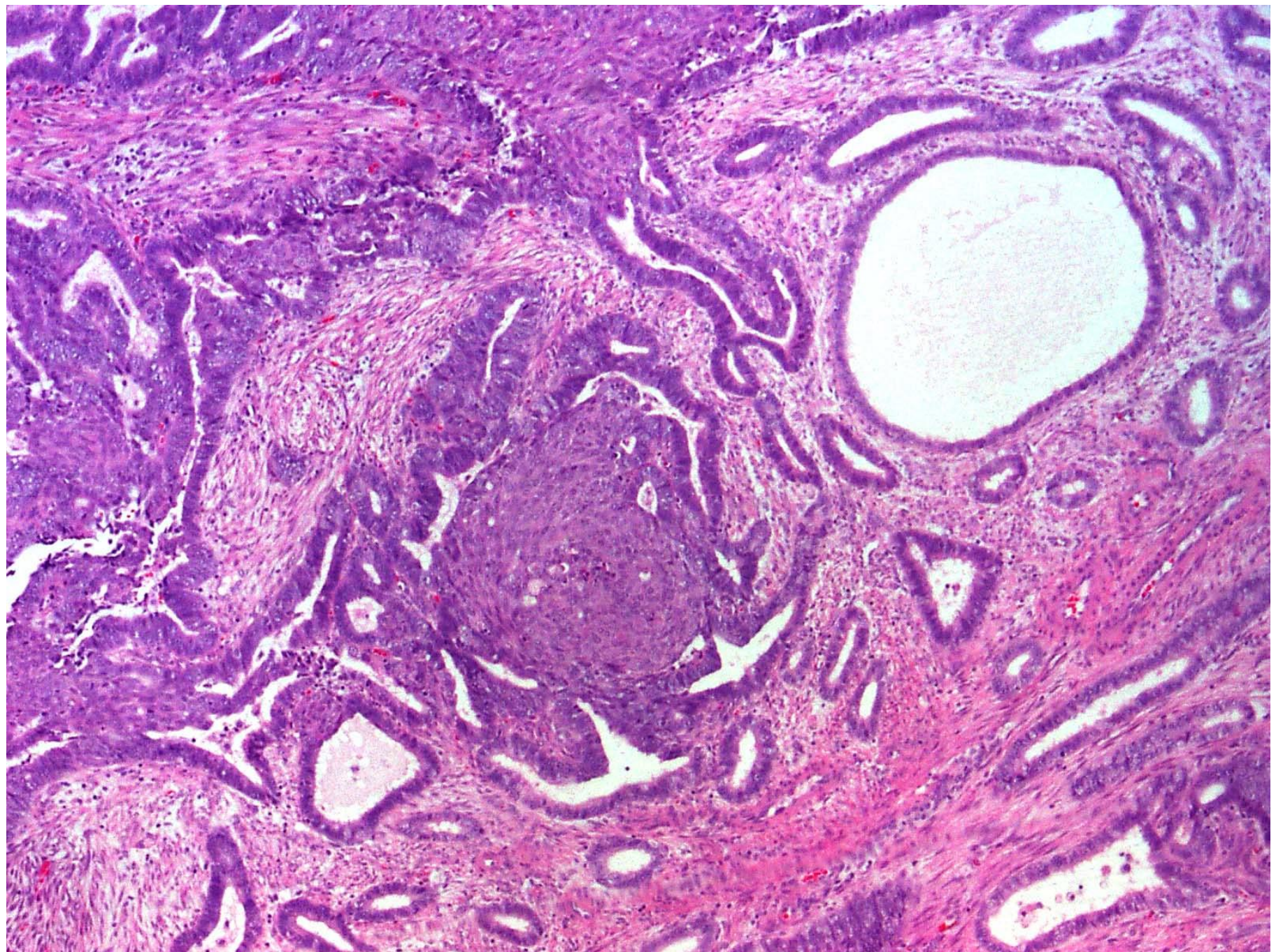
- Clinical correlates:
 - Mean age: 40 years
 - 30% infertile
 - May be managed with hysteroscopy/D&C/polypectomy
 - Very rare presence of myoinvasive CA on followup hysterectomy

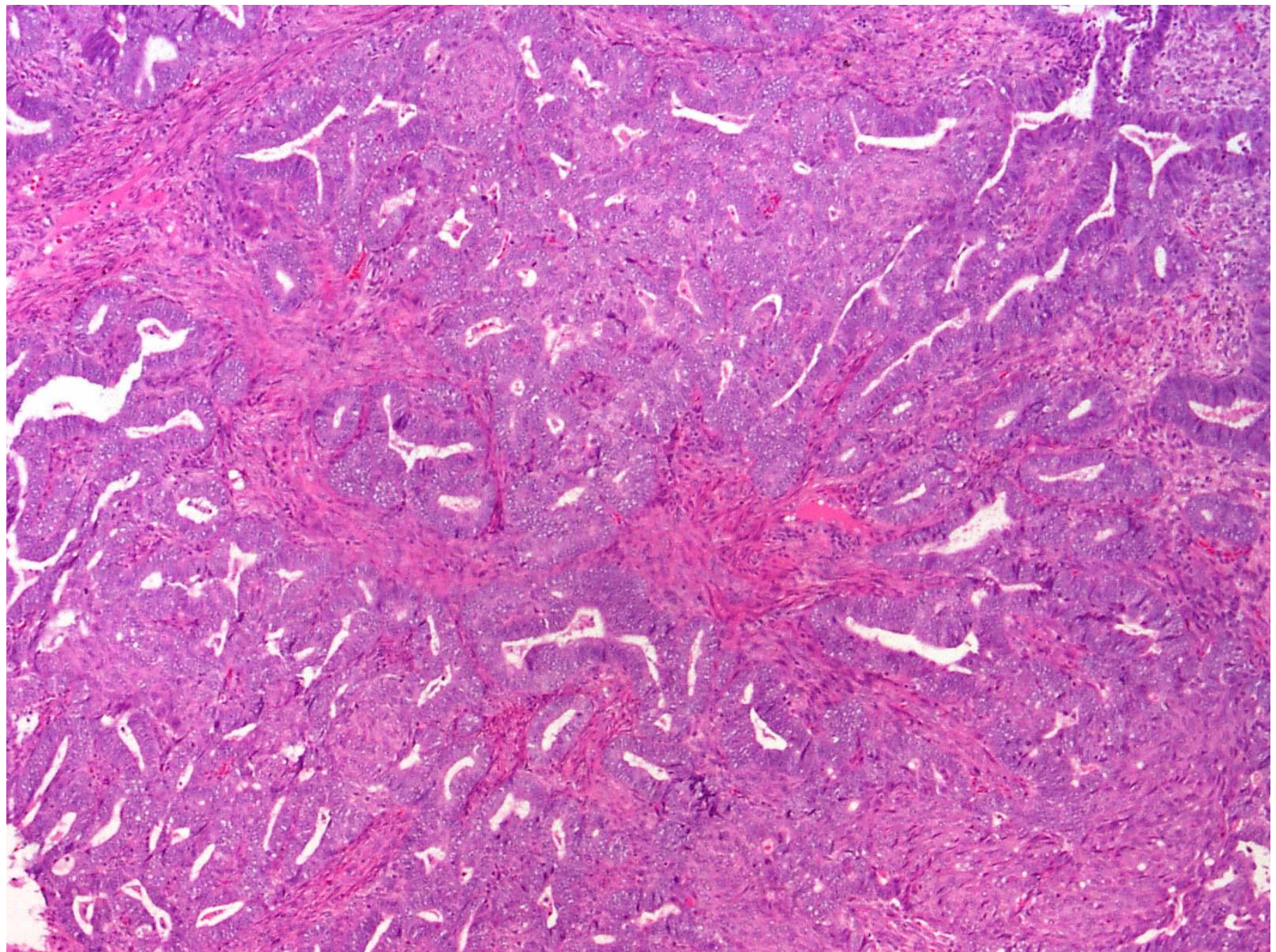










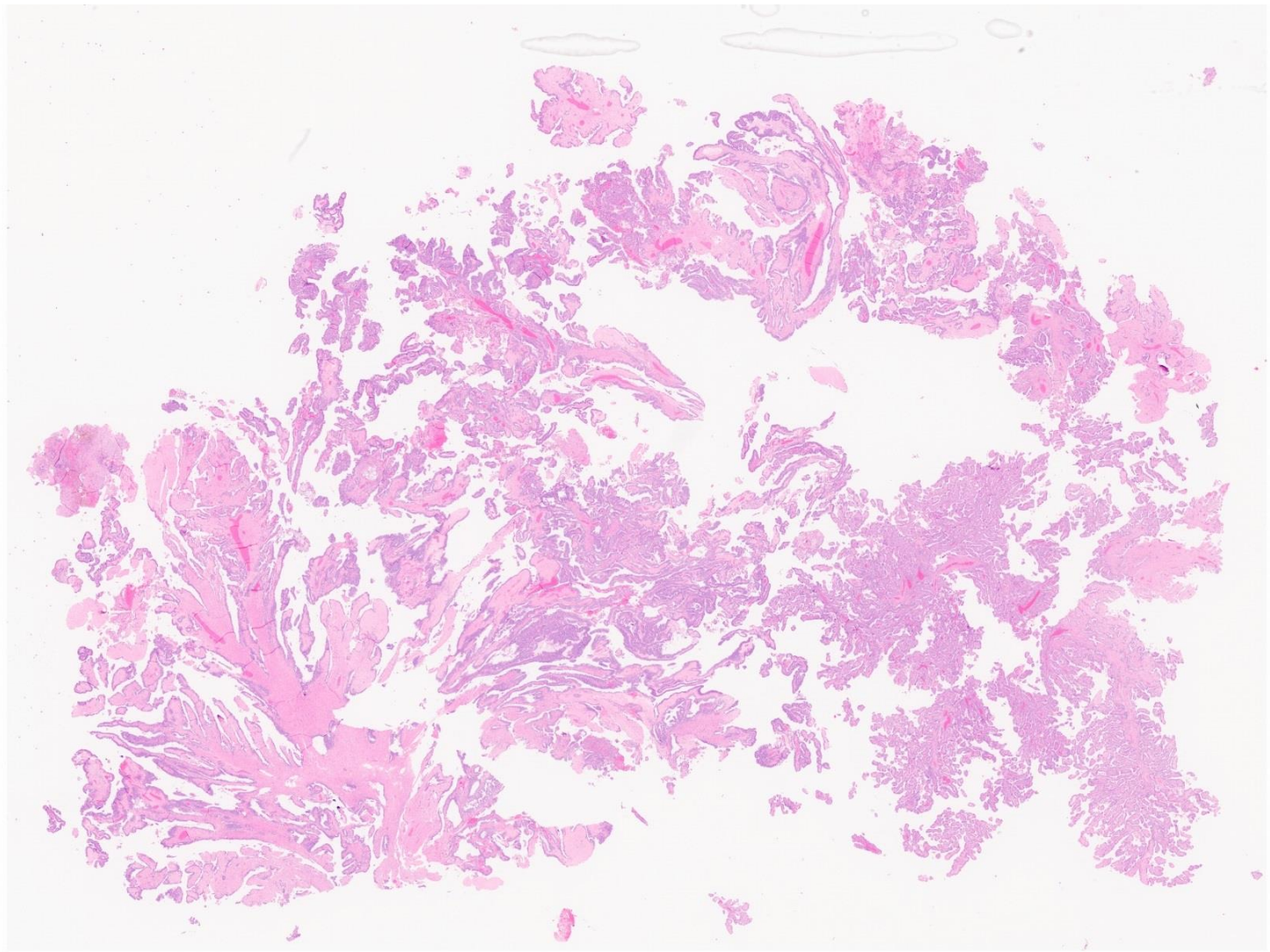


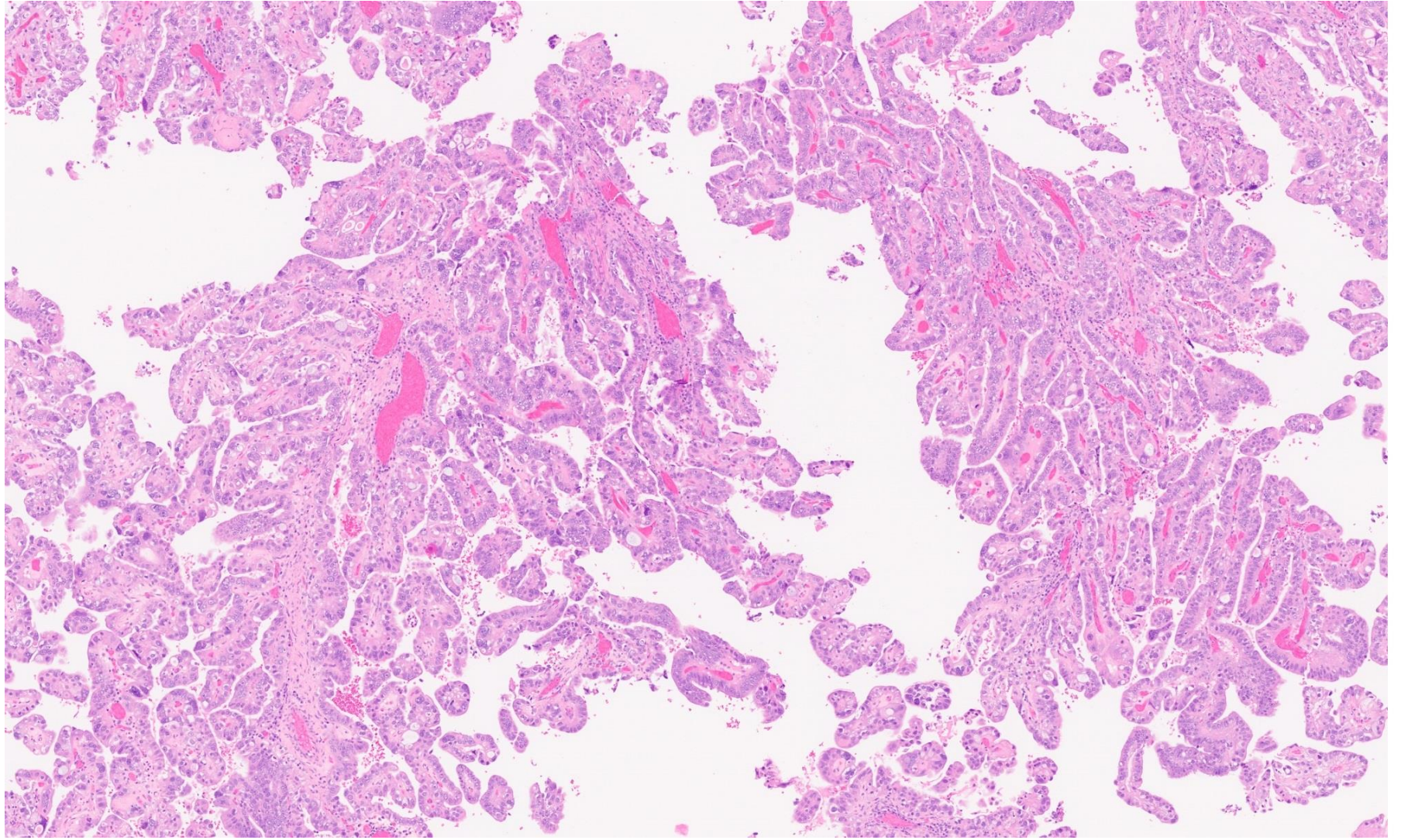
APA summary

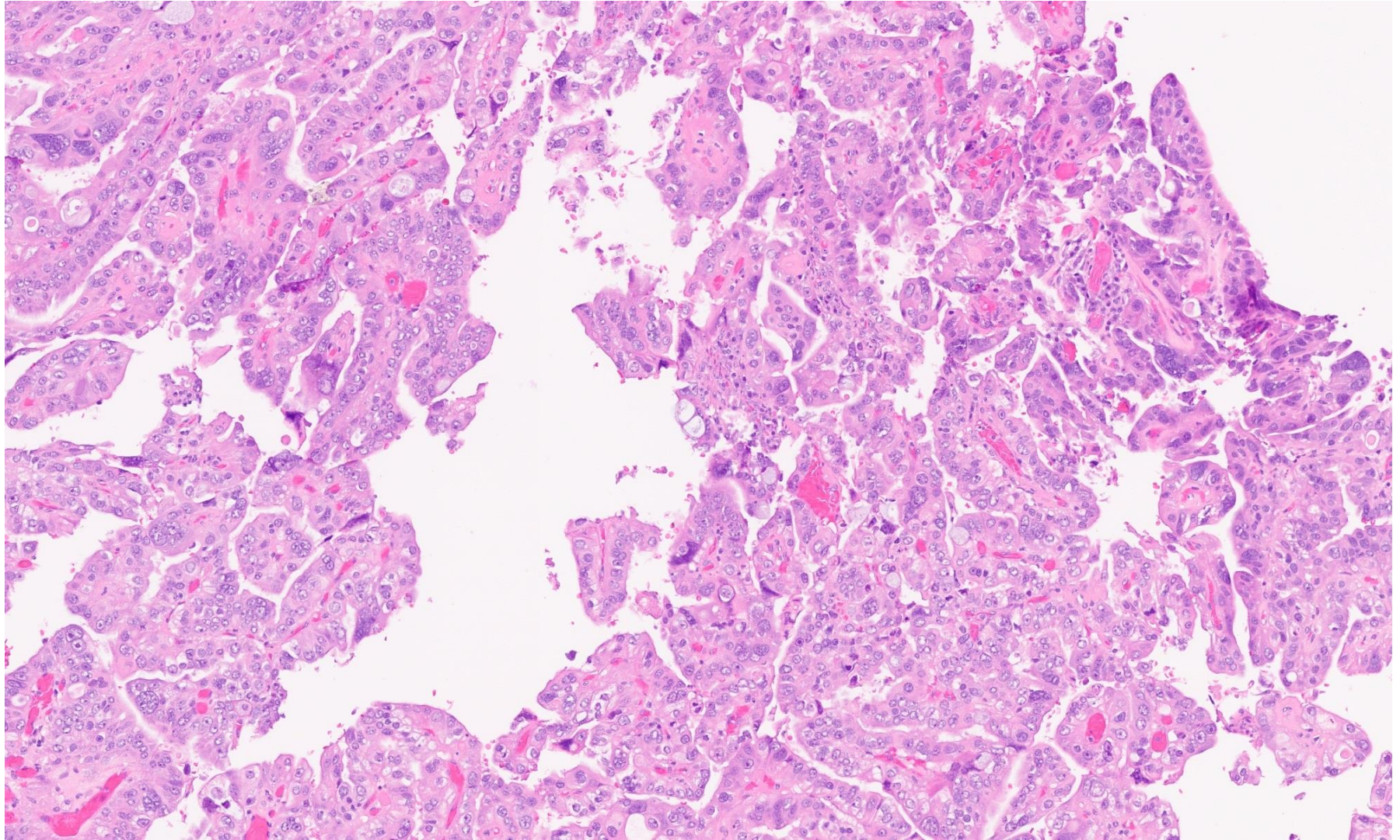
- Similar to CAH or FIGO G1 in a myomatous polyp
- Frequency of myometrial invasion (very low) is similar to that associated with CAH/FIGO1 CA confined to a polyp
- Recognition of entity
 - Minimizes overdiagnosis of invasive carcinoma
 - Allows conservative management

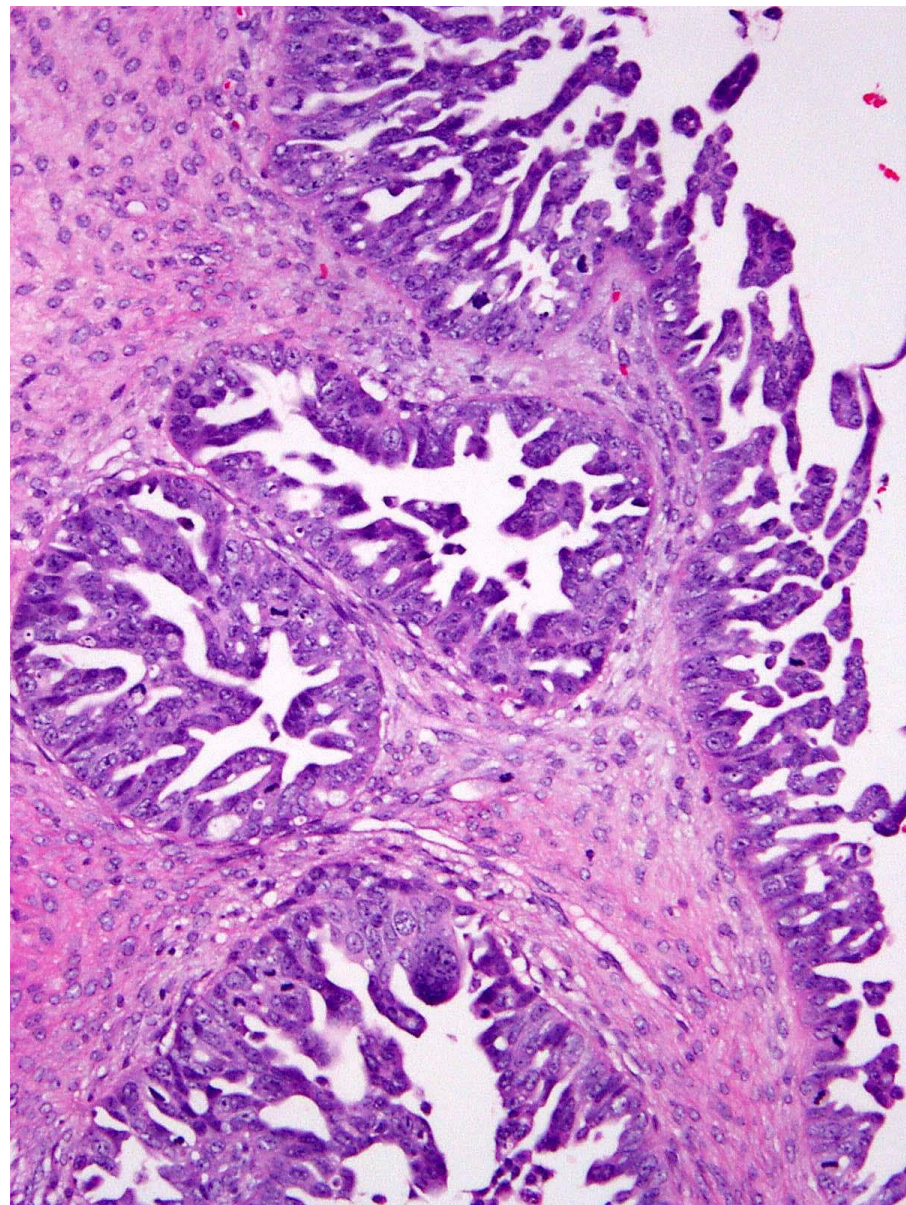
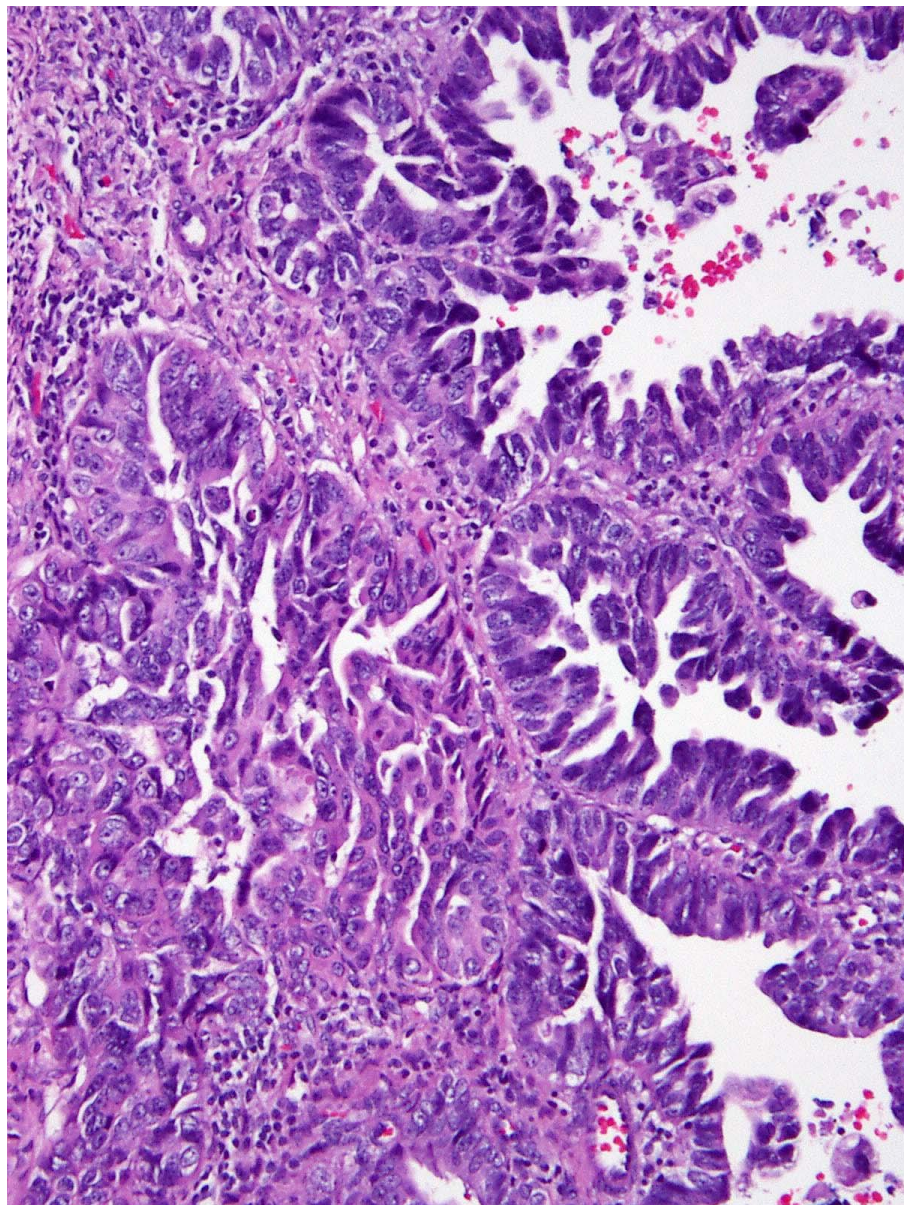
Serous carcinoma

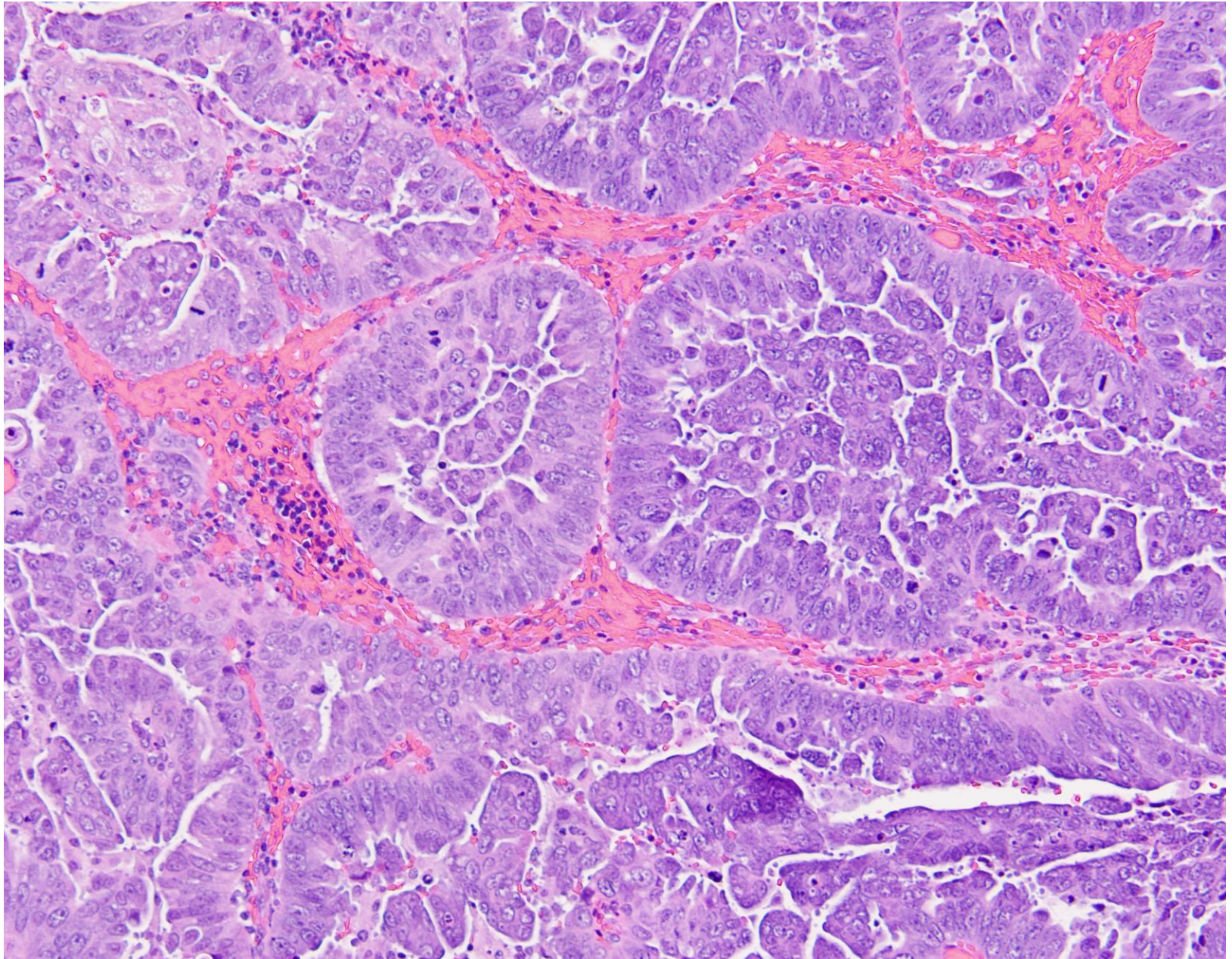
- 70-year-old woman reported a feeling of abdominal fullness.
- Physical examination, radiologic survey and biopsy: pelvic mass, a high-grade Mullerian carcinoma
- No myometrial invasion at hysterectomy, but extrauterine spread
- pT3NxM1

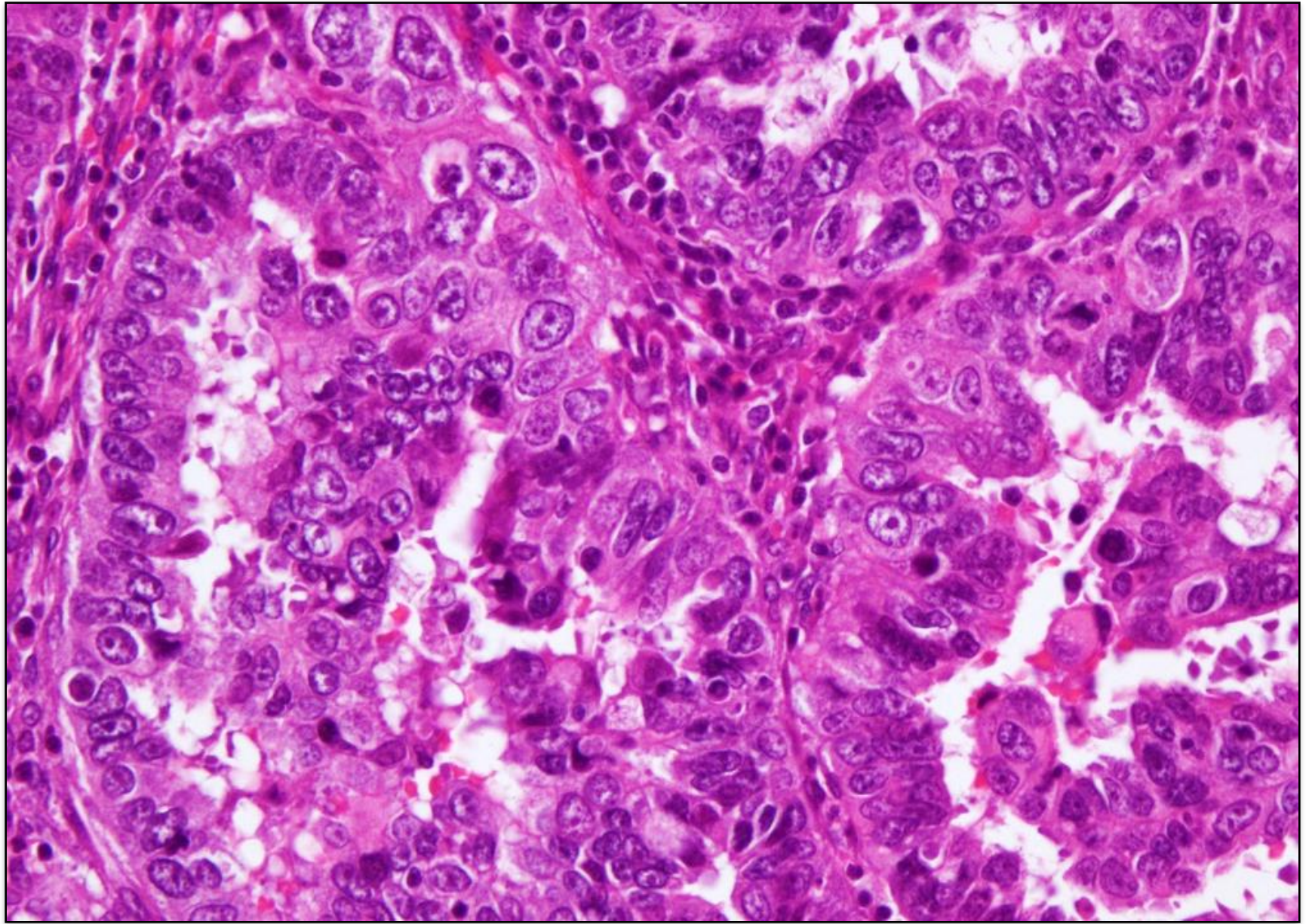


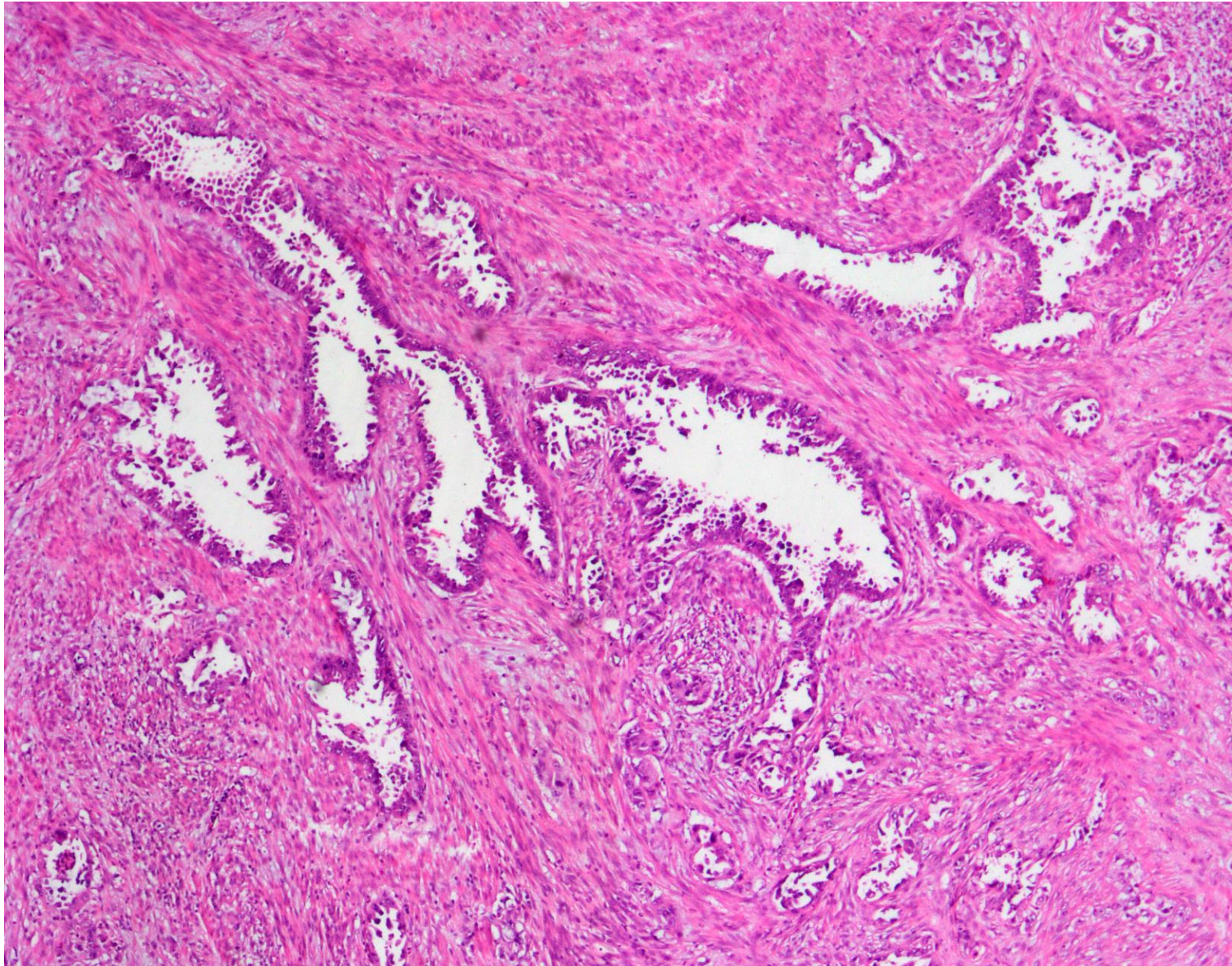




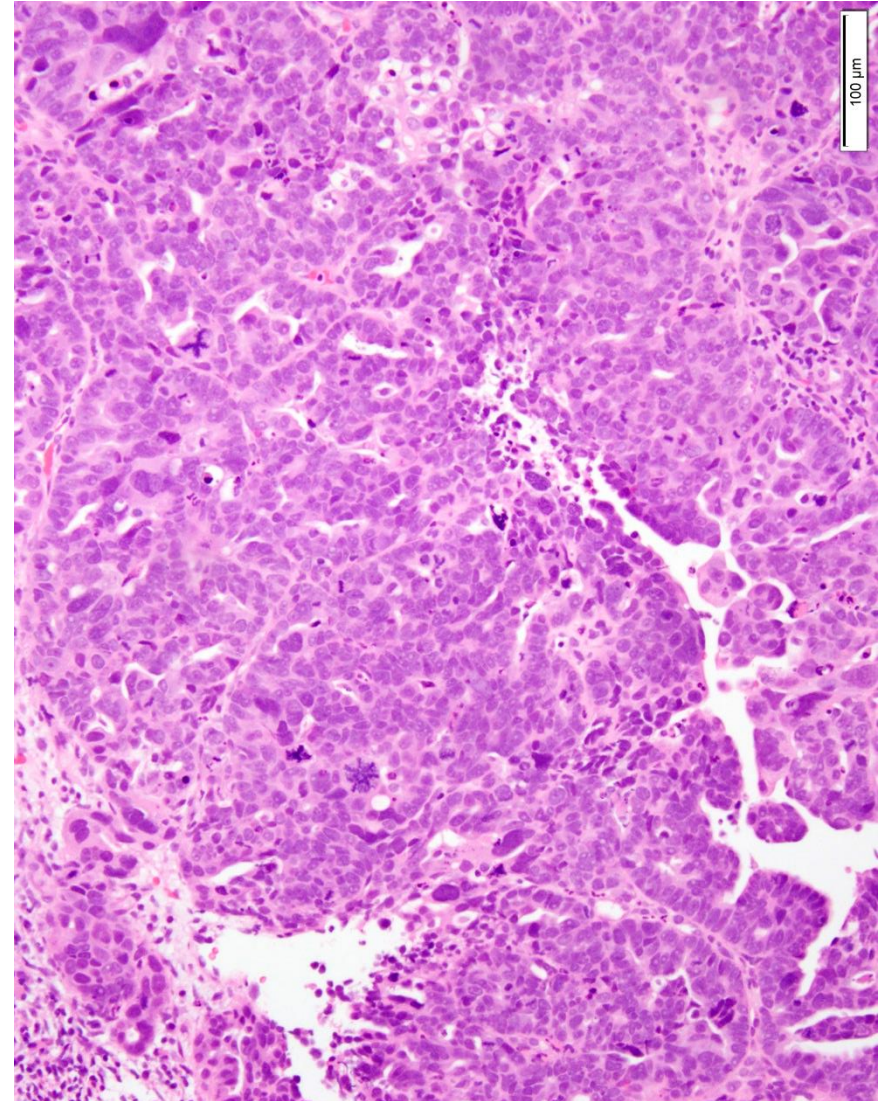
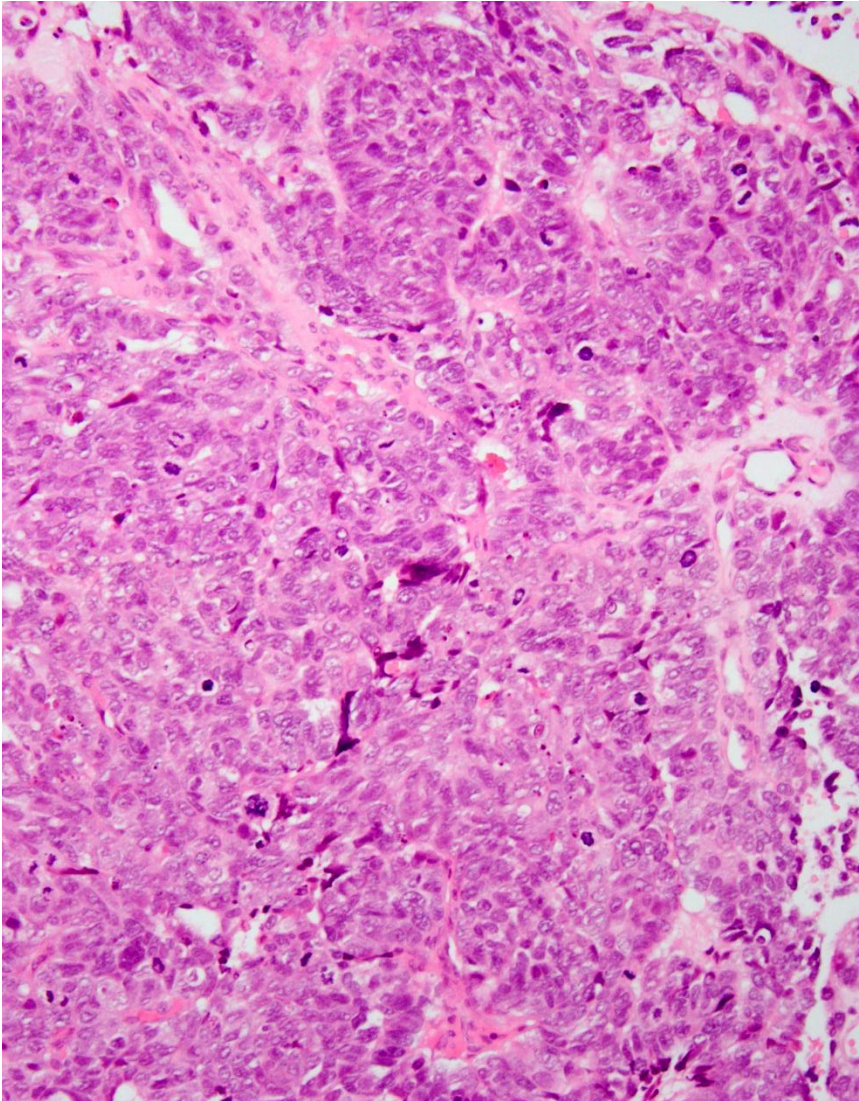




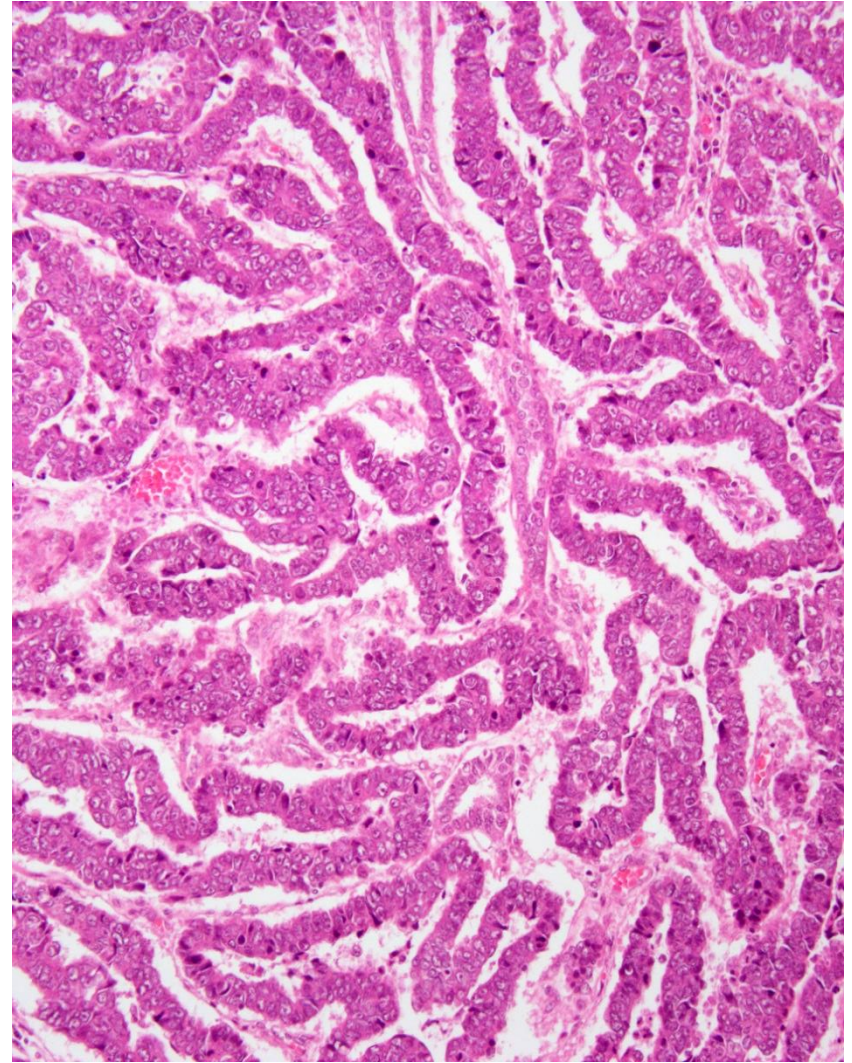
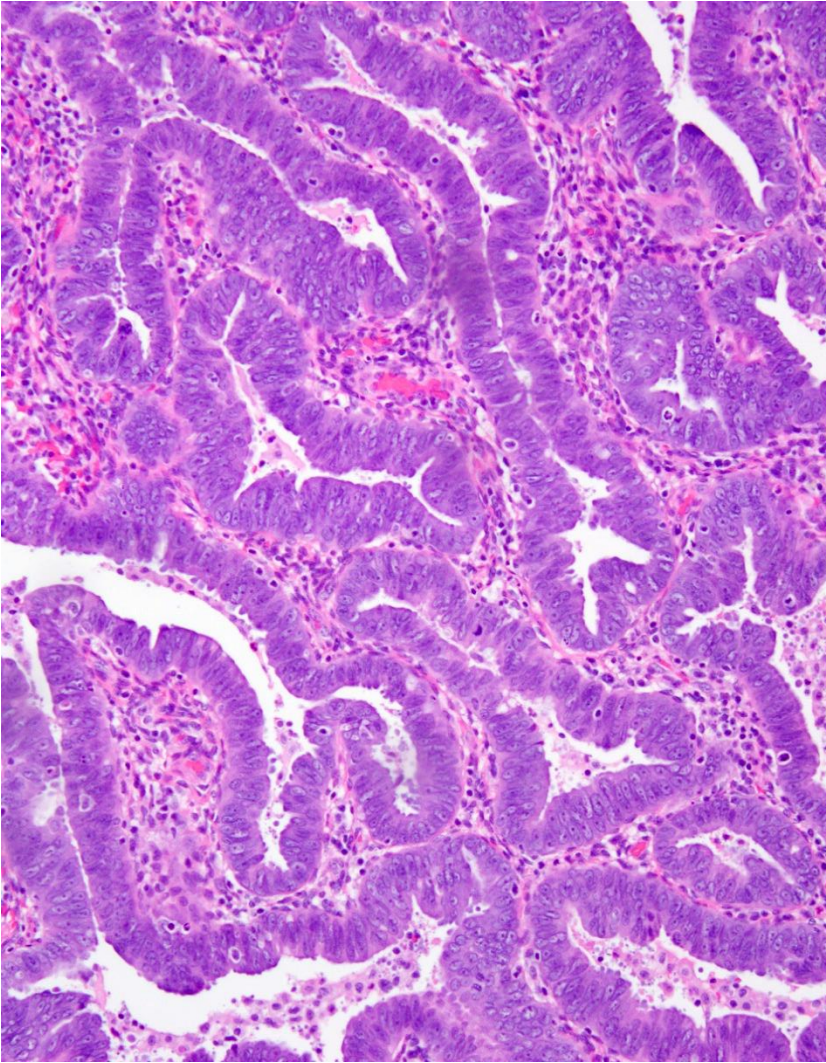




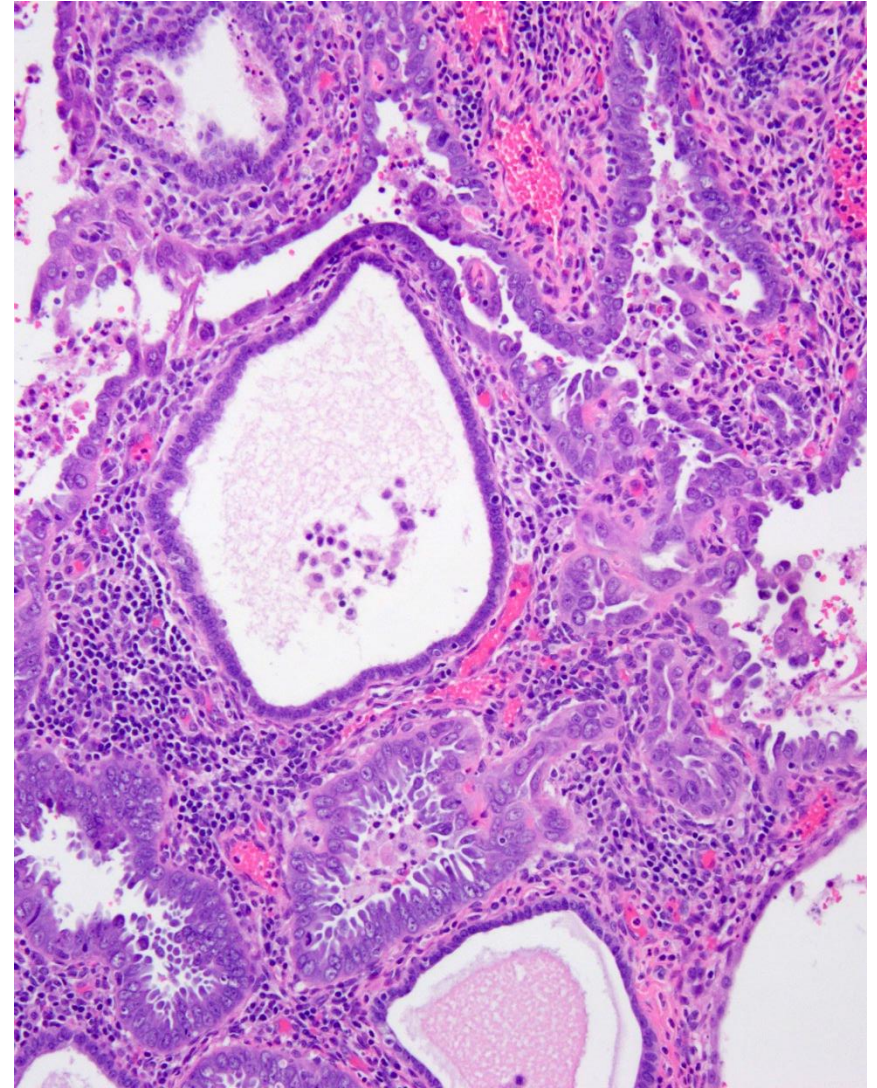
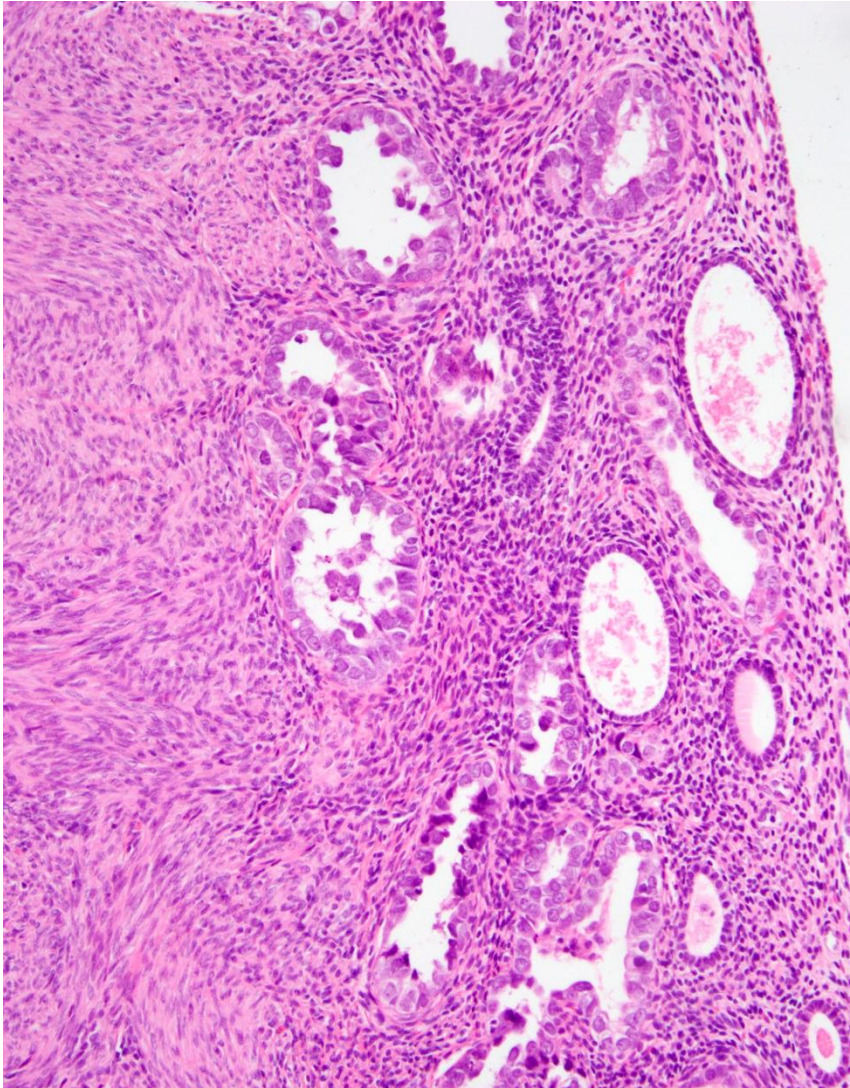
Solid serous carcinoma

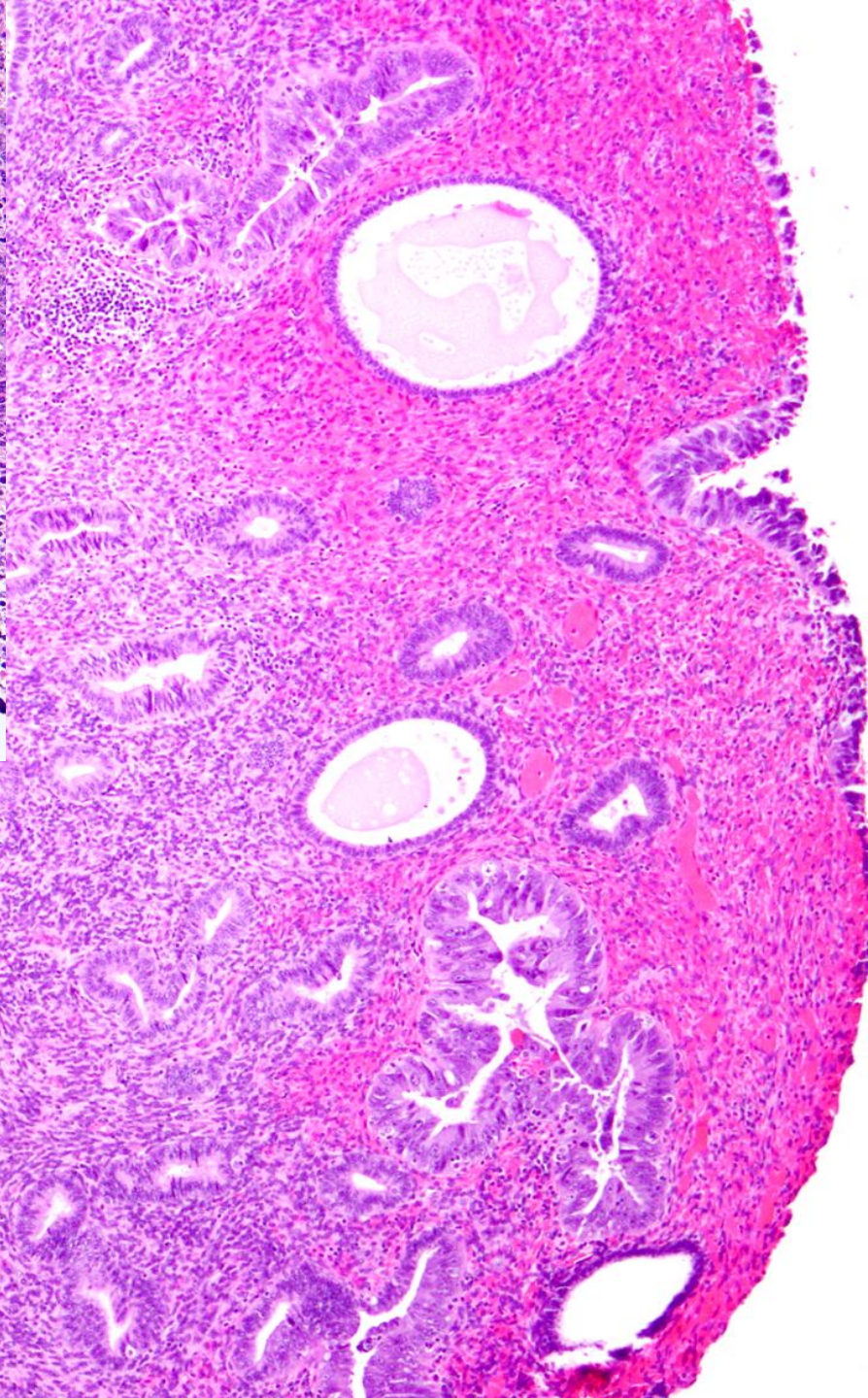
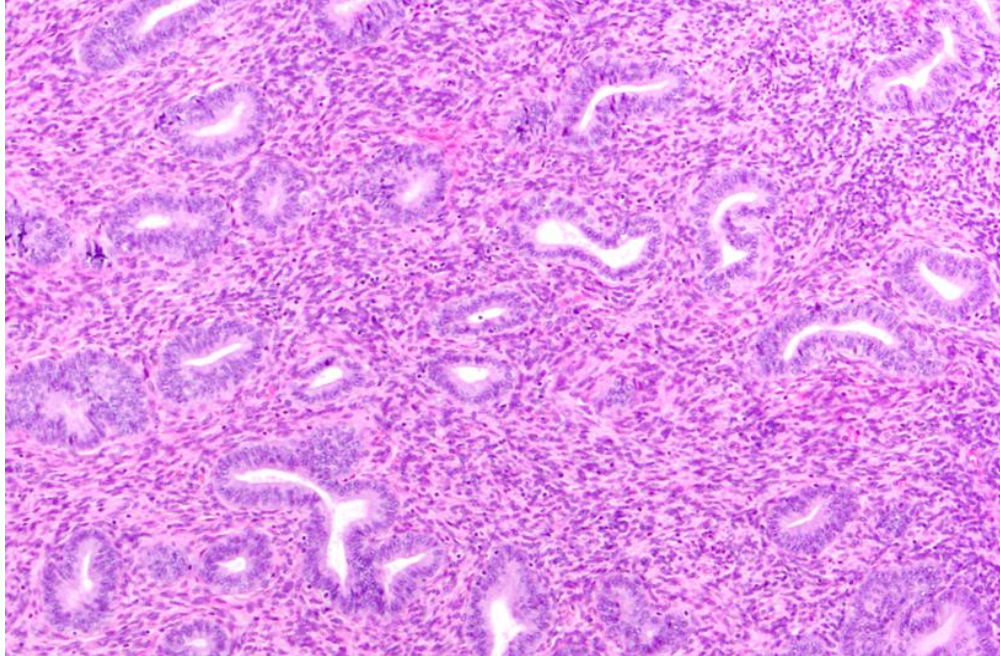
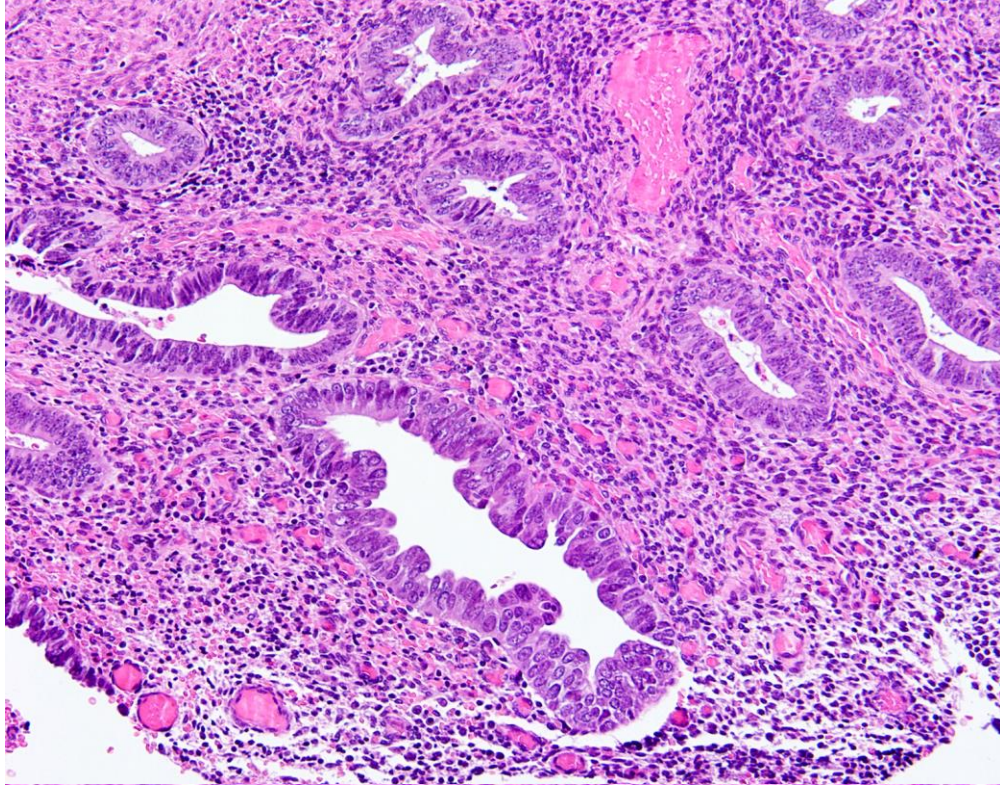


Glandular serous carcinoma

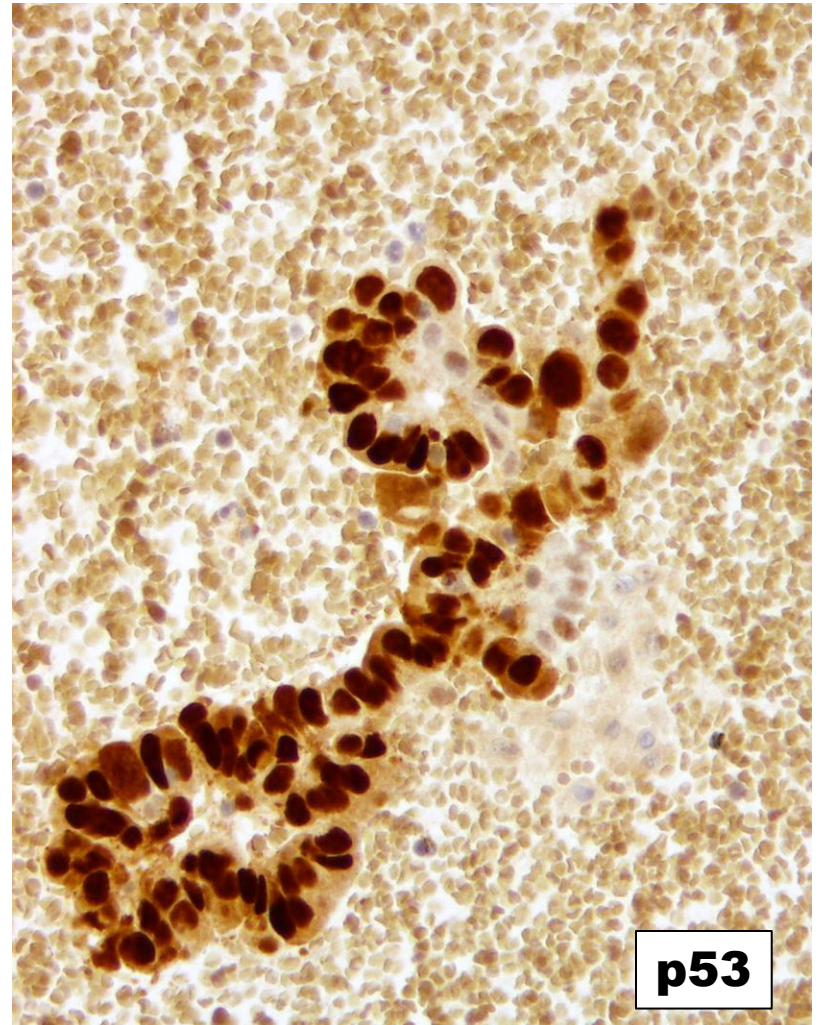
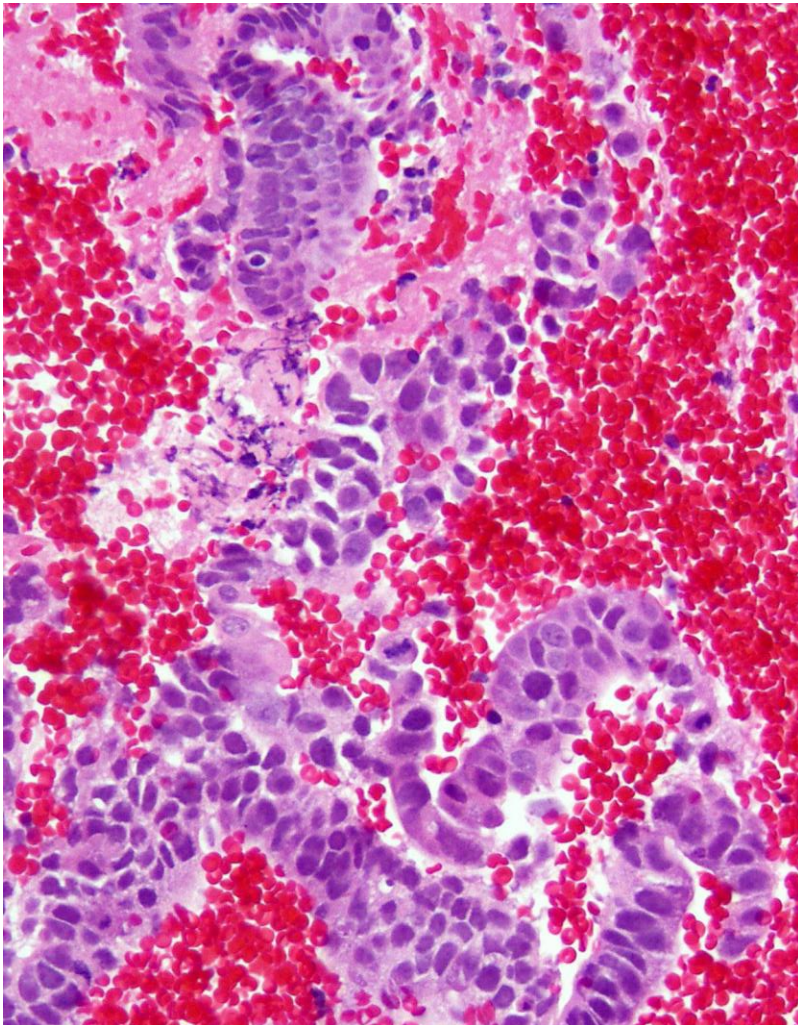


“Serous intraepithelial carcinoma”

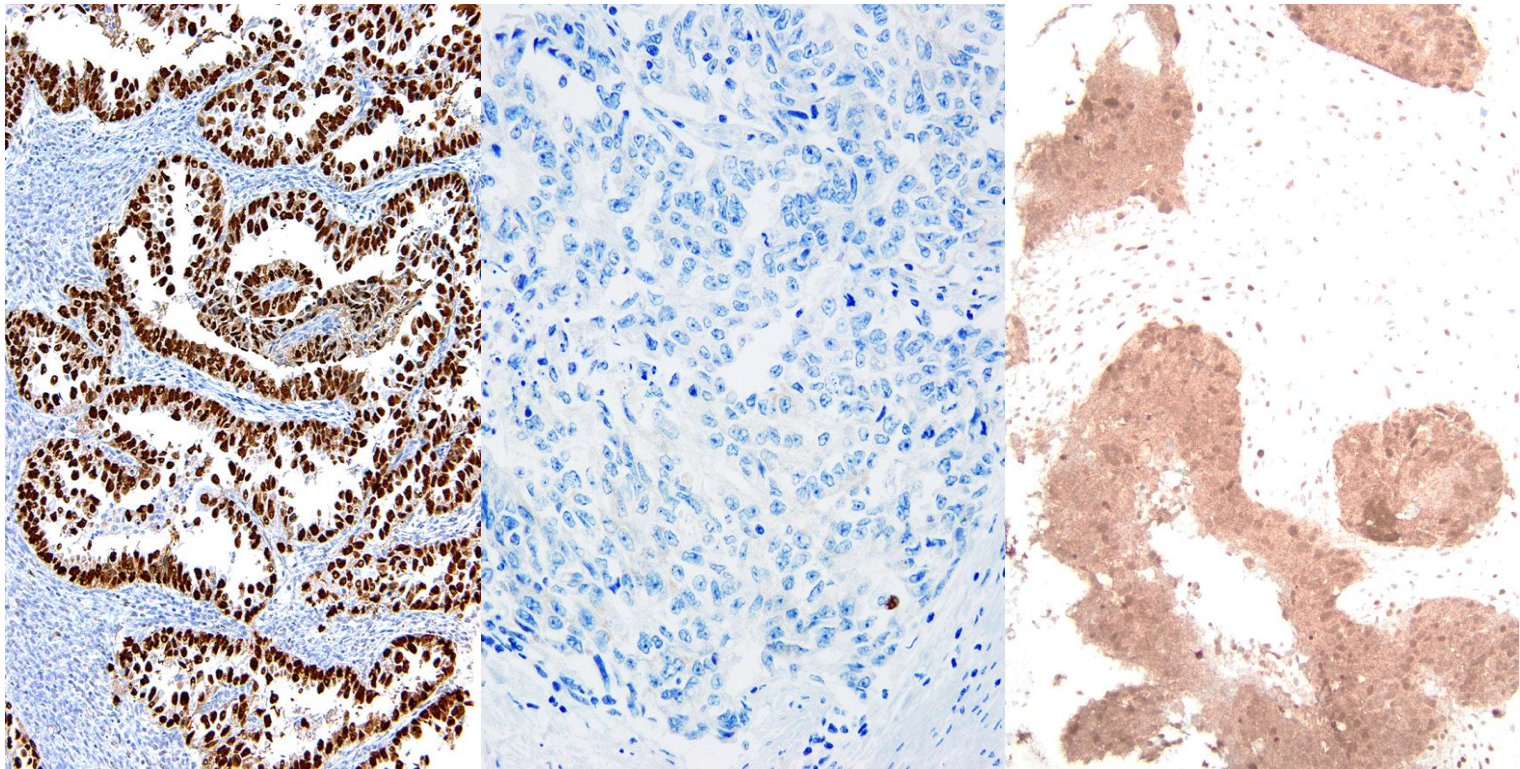




“Serous intraepithelial carcinoma” in biopsy material



Aberrant p53 staining



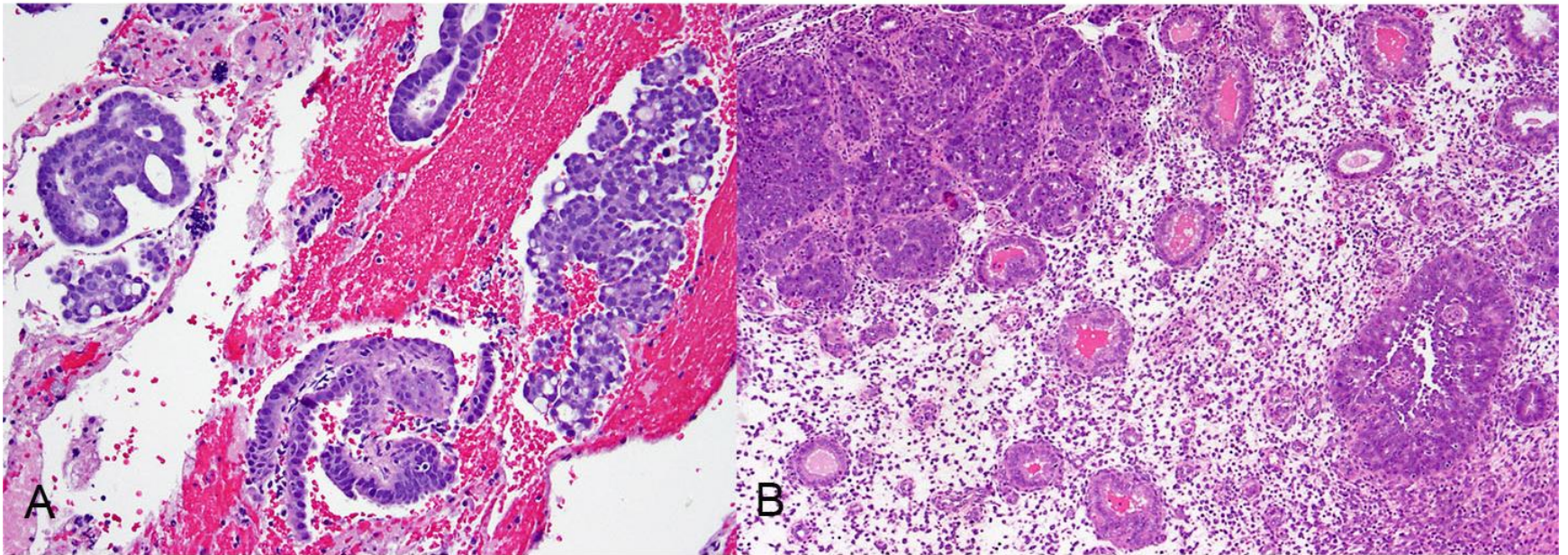
Molecular signatures and immunophenotype

- Serous
 - Mutations: *TP53*, *PPP2R1A*, *PIK3CA*
 - IHC: aberrant p53, high p16

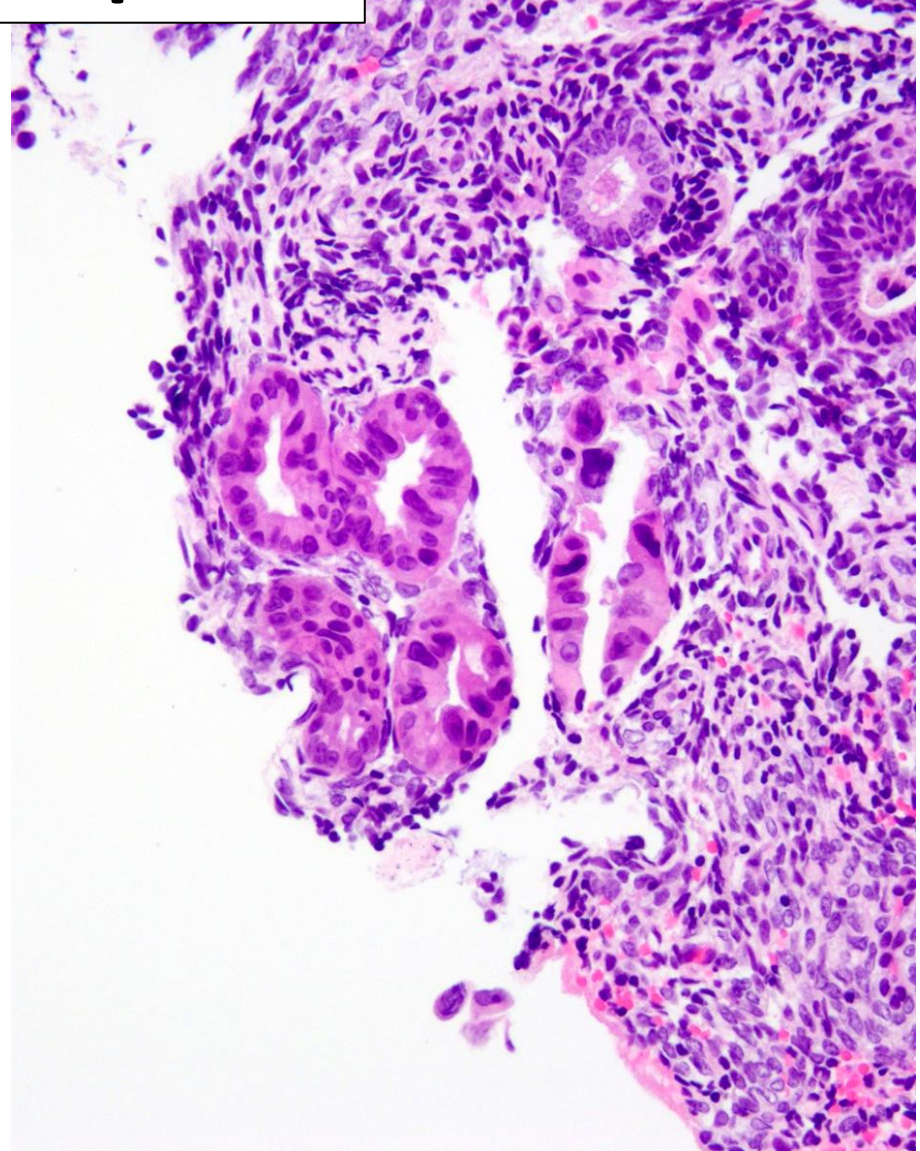
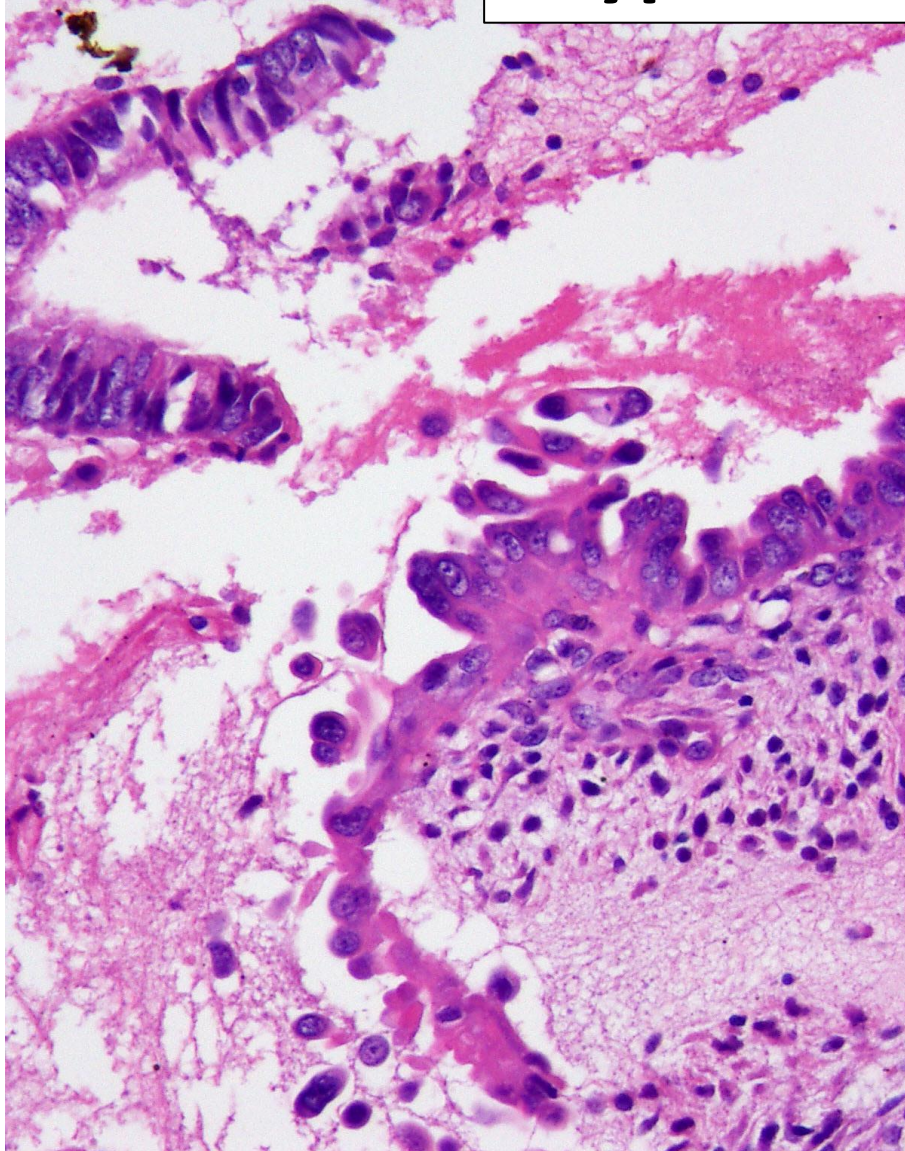
Differential diagnosis

Other p53-abnormal endometrial
carcinomas and...

Drop metastasis of tubo-ovarian serous carcinoma

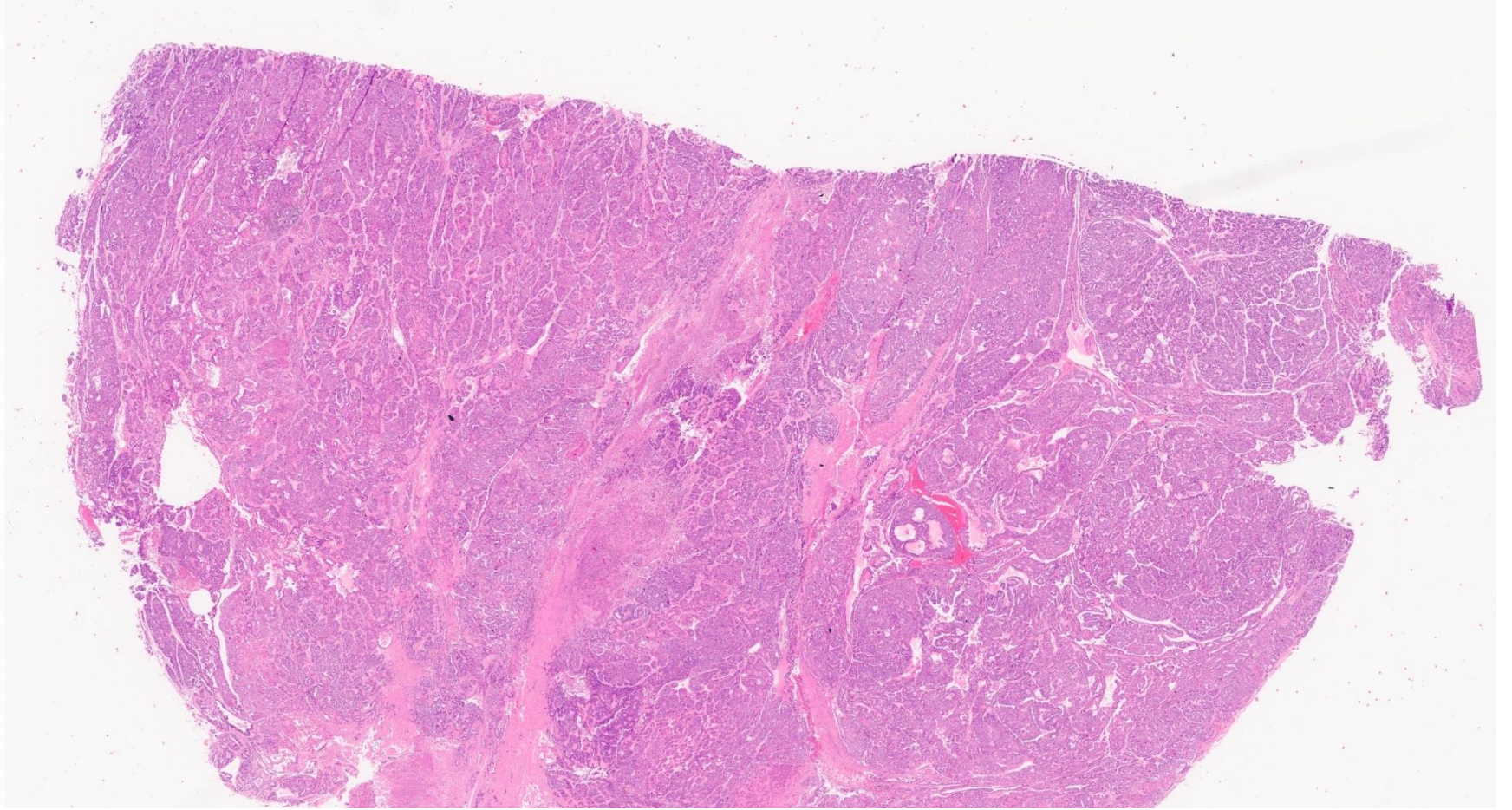


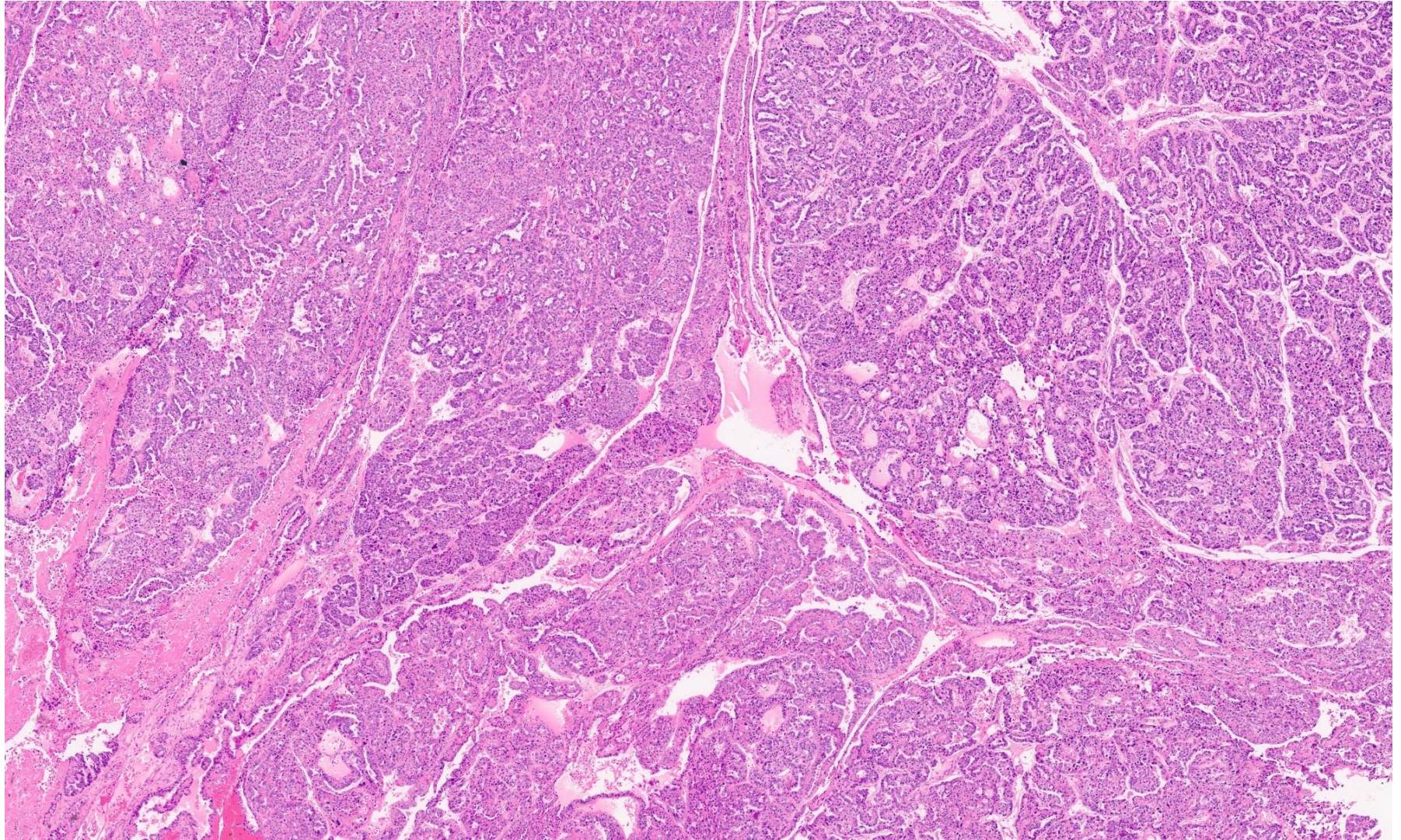
Atypical metaplasia

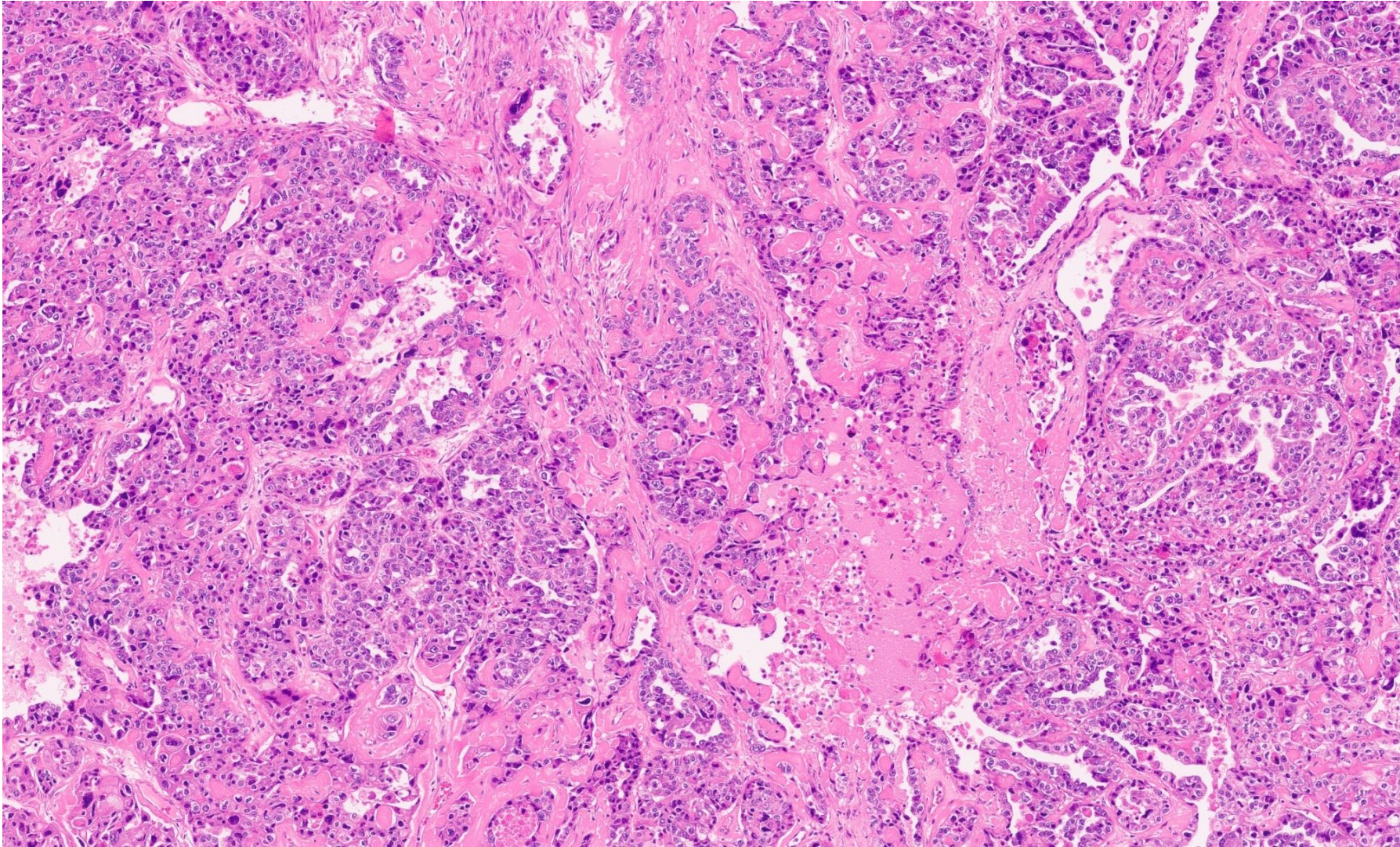


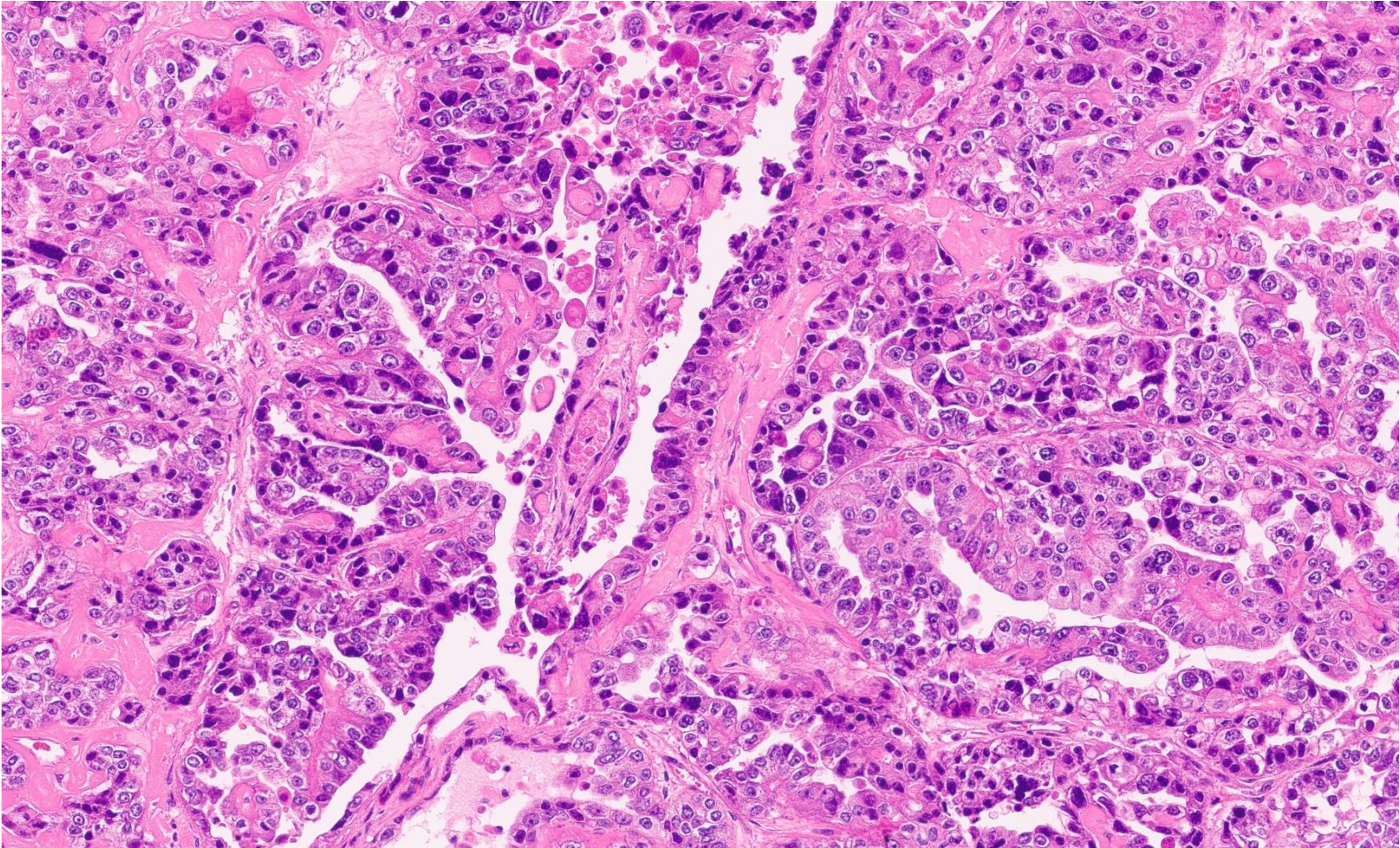
Clear cell carcinoma

- 58-year-old woman diagnosed with endometrial carcinoma who underwent hysterectomy.









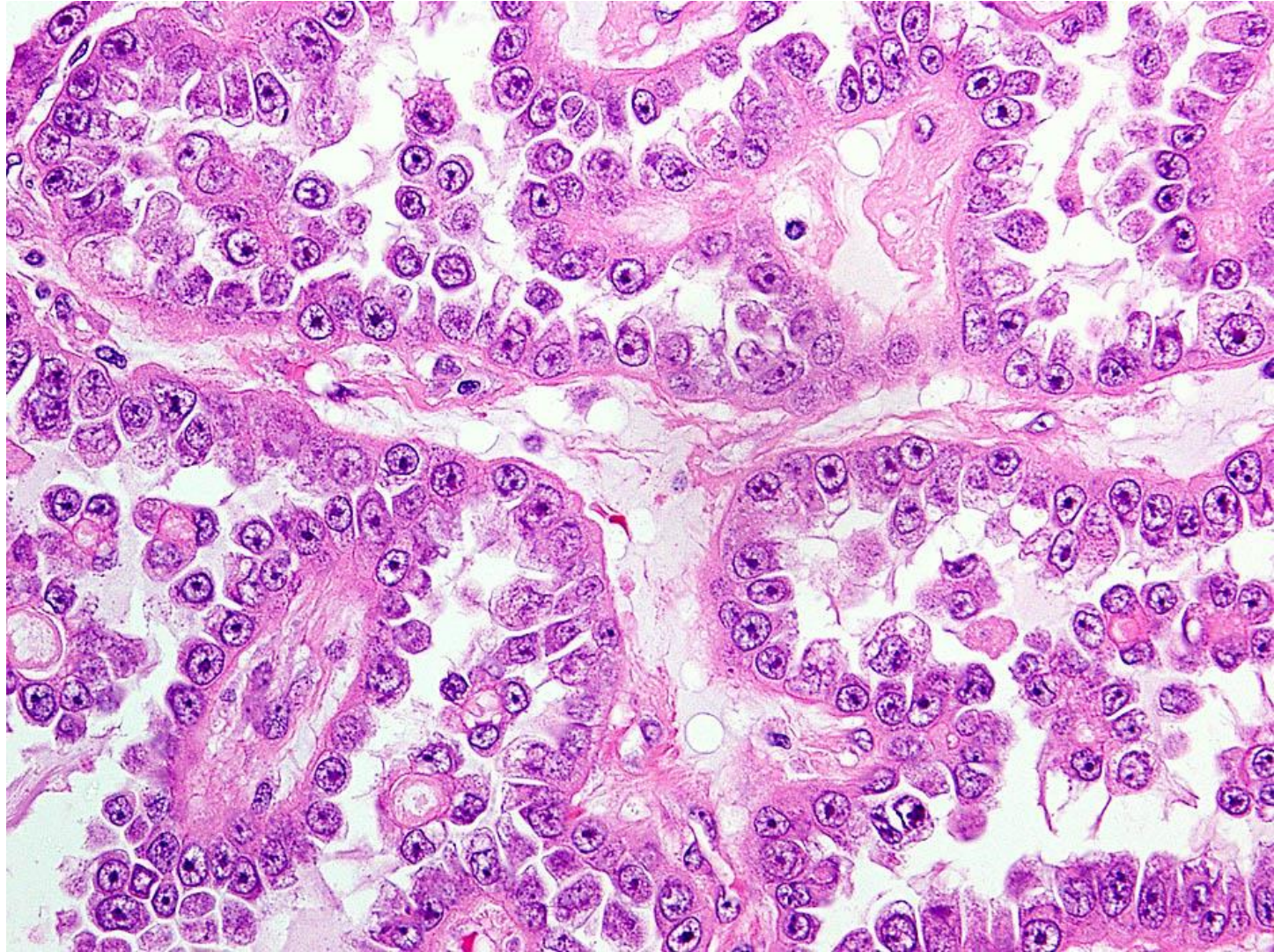
Clear cell carcinoma

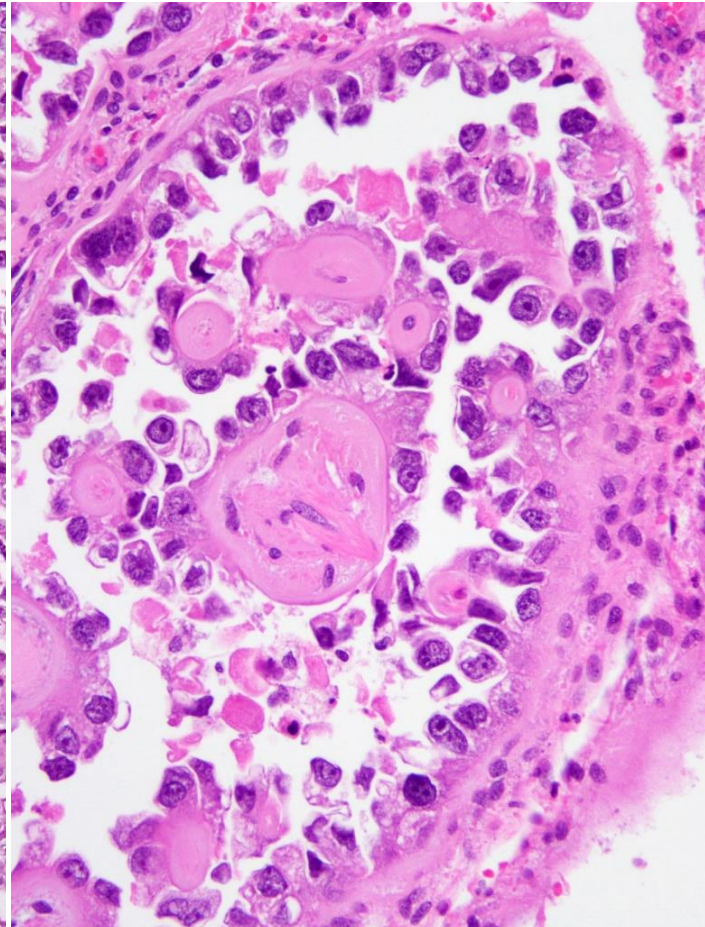
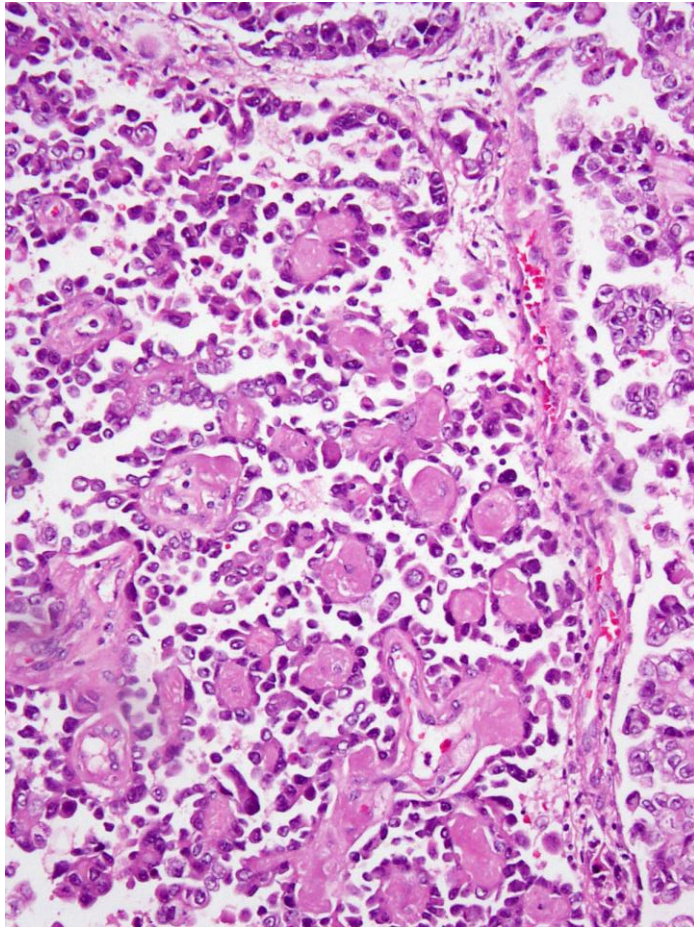
Architecture

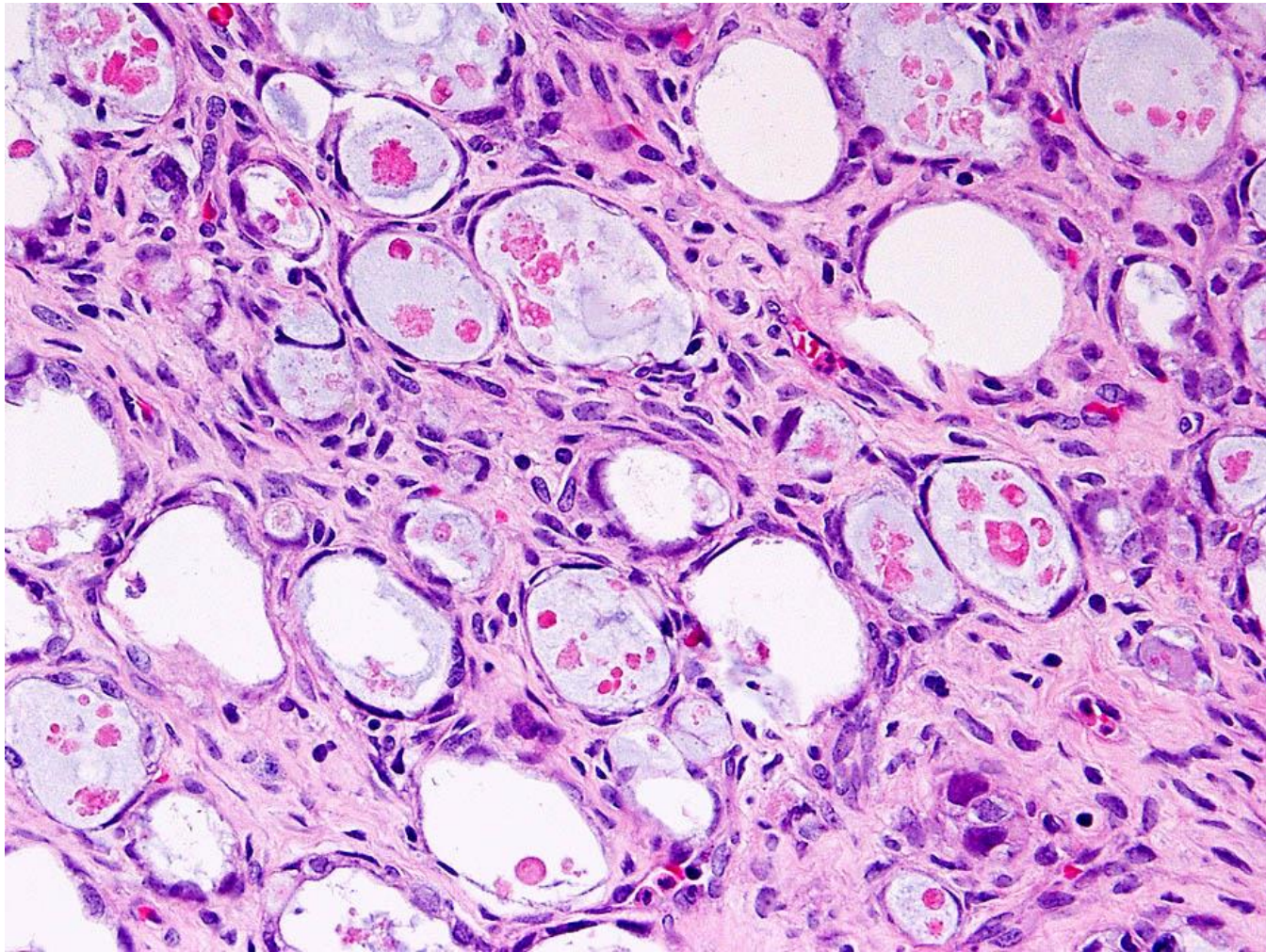
Cell shape

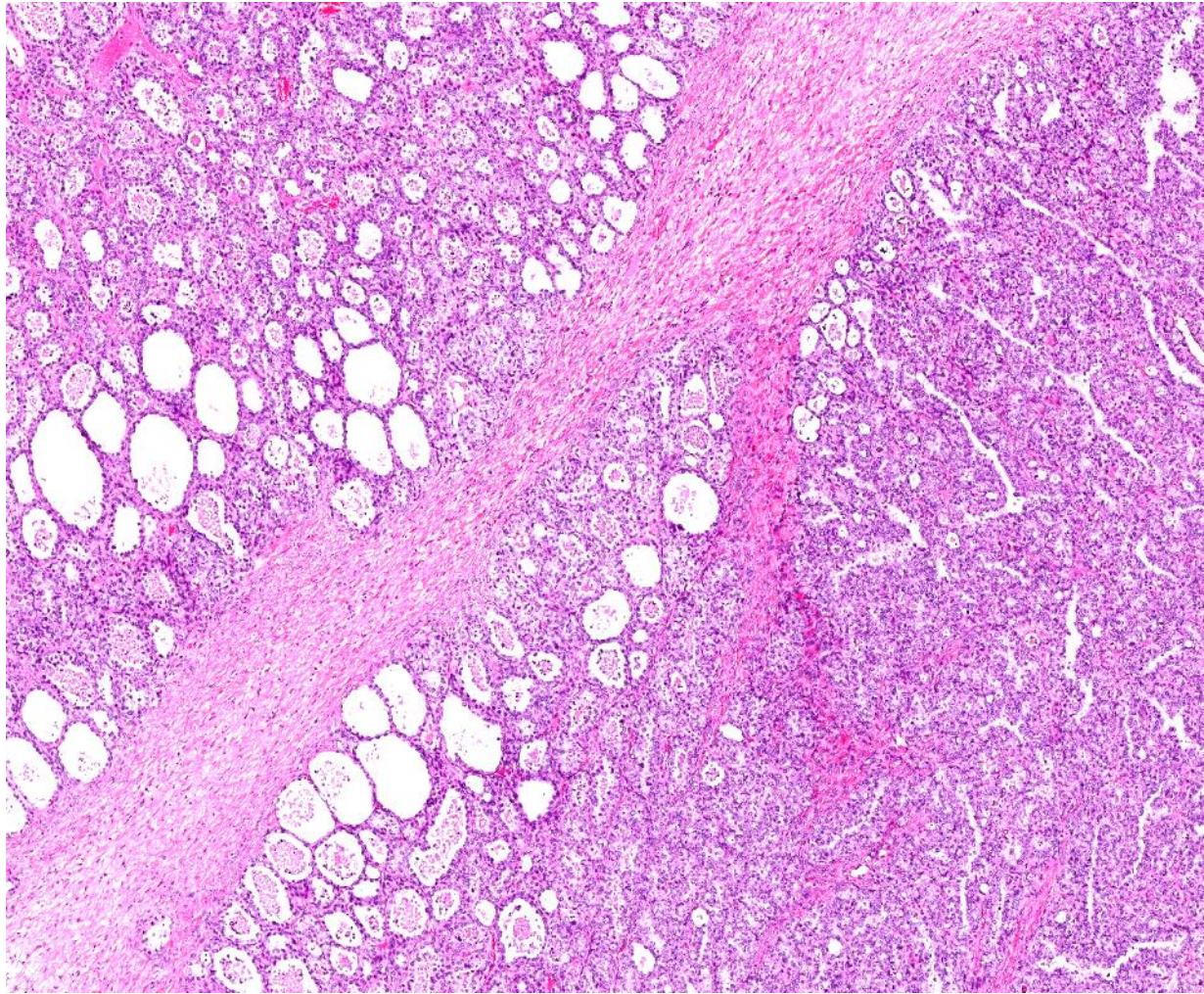
Nucleus and mitotic
count

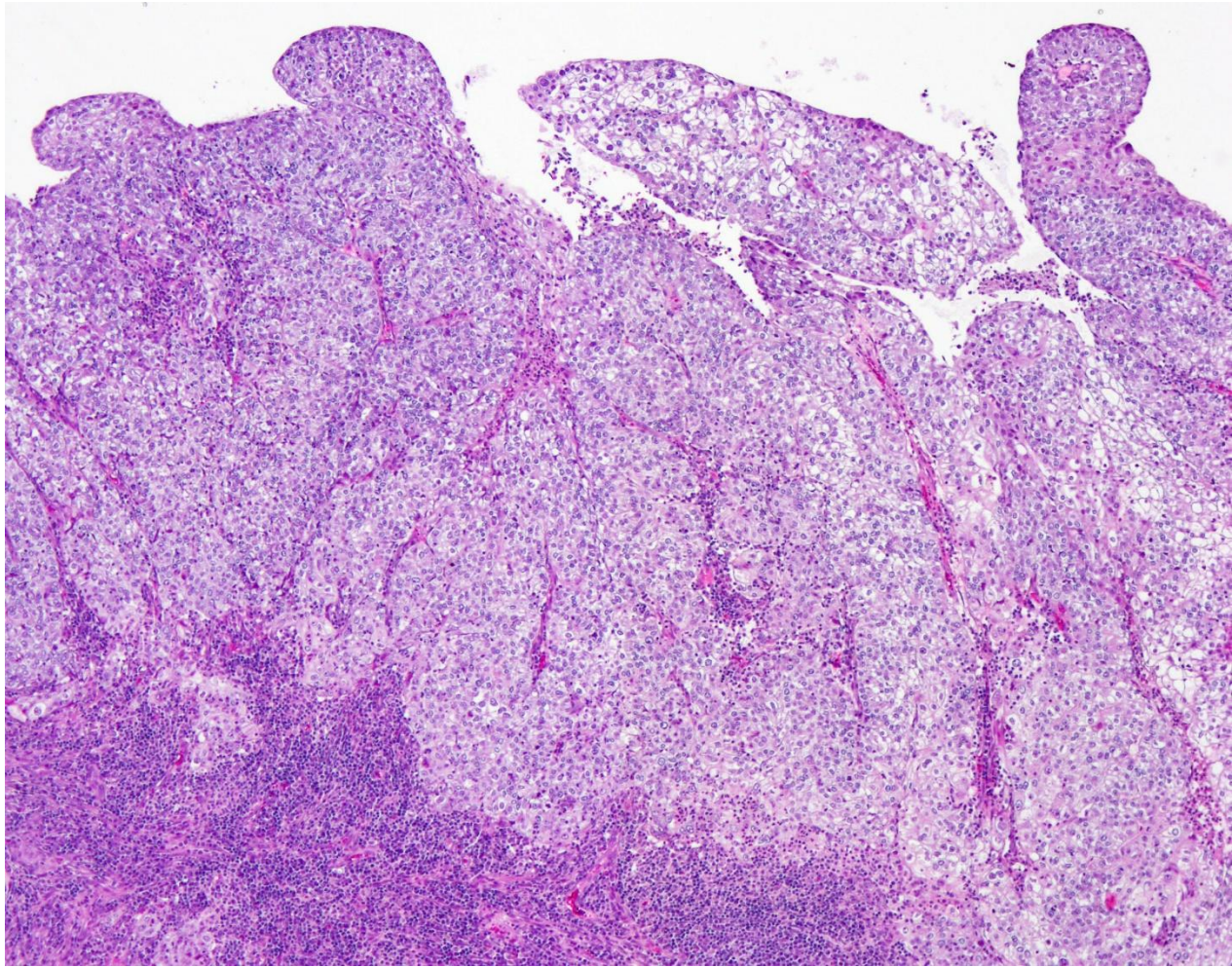
Cytoplasm

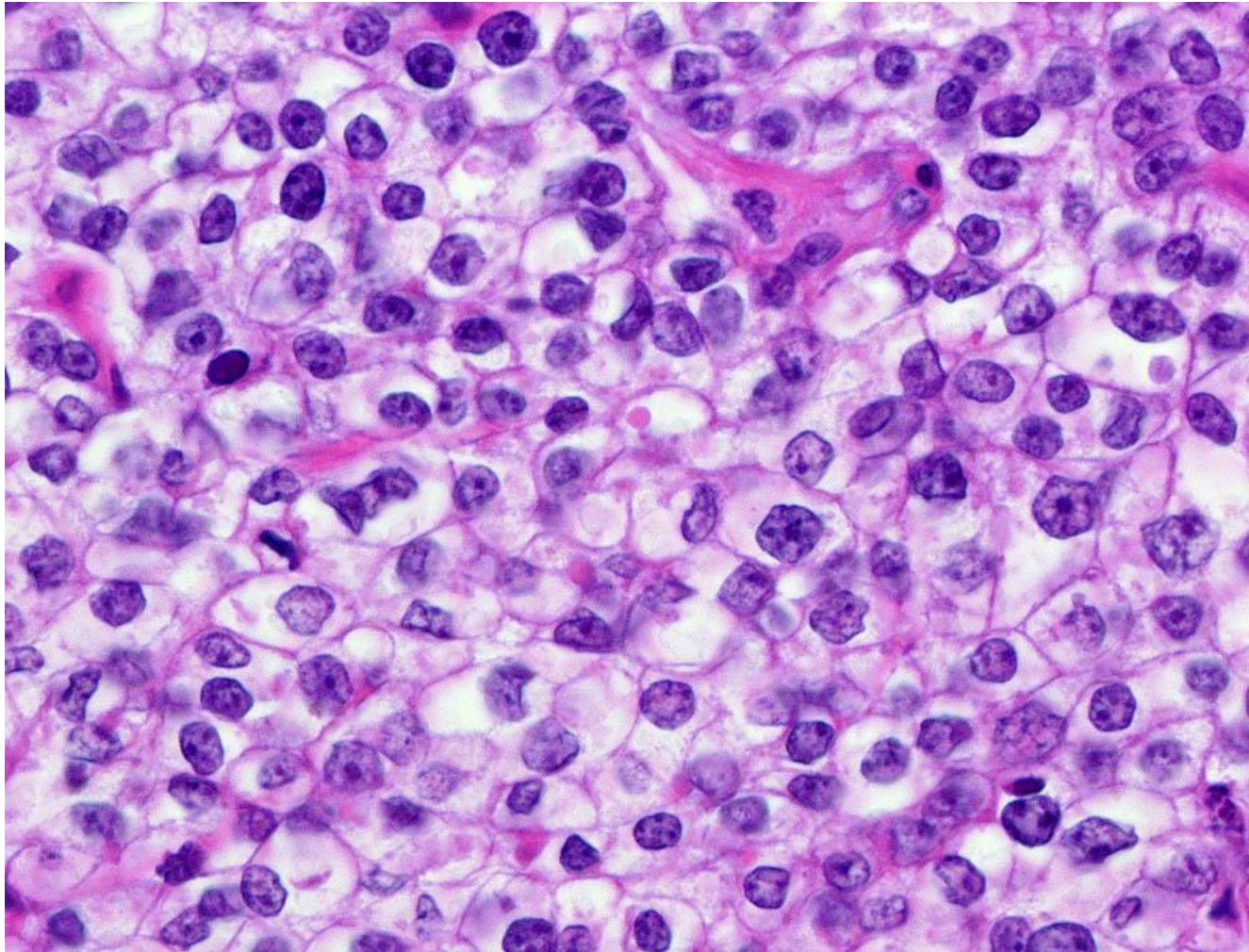


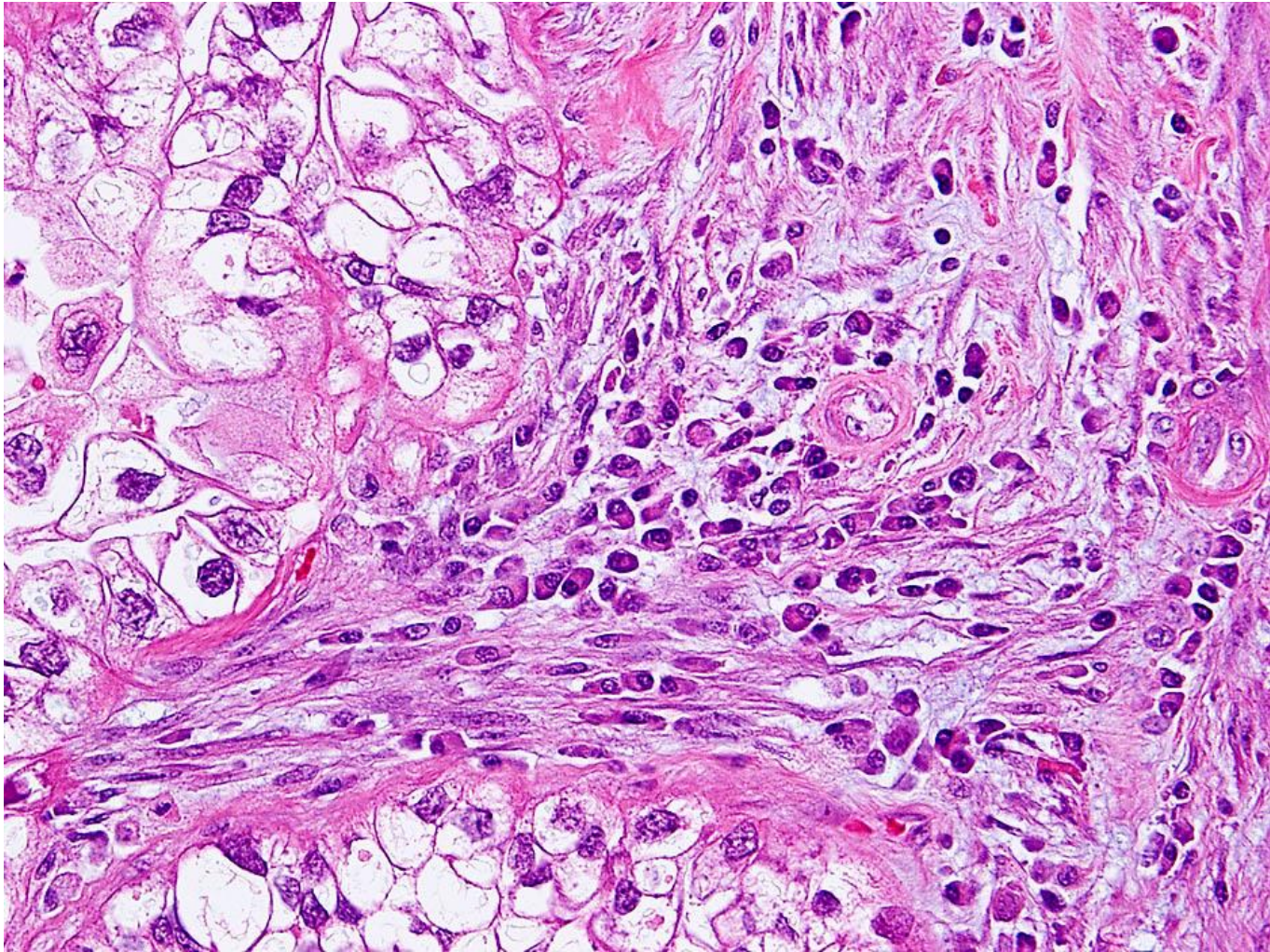


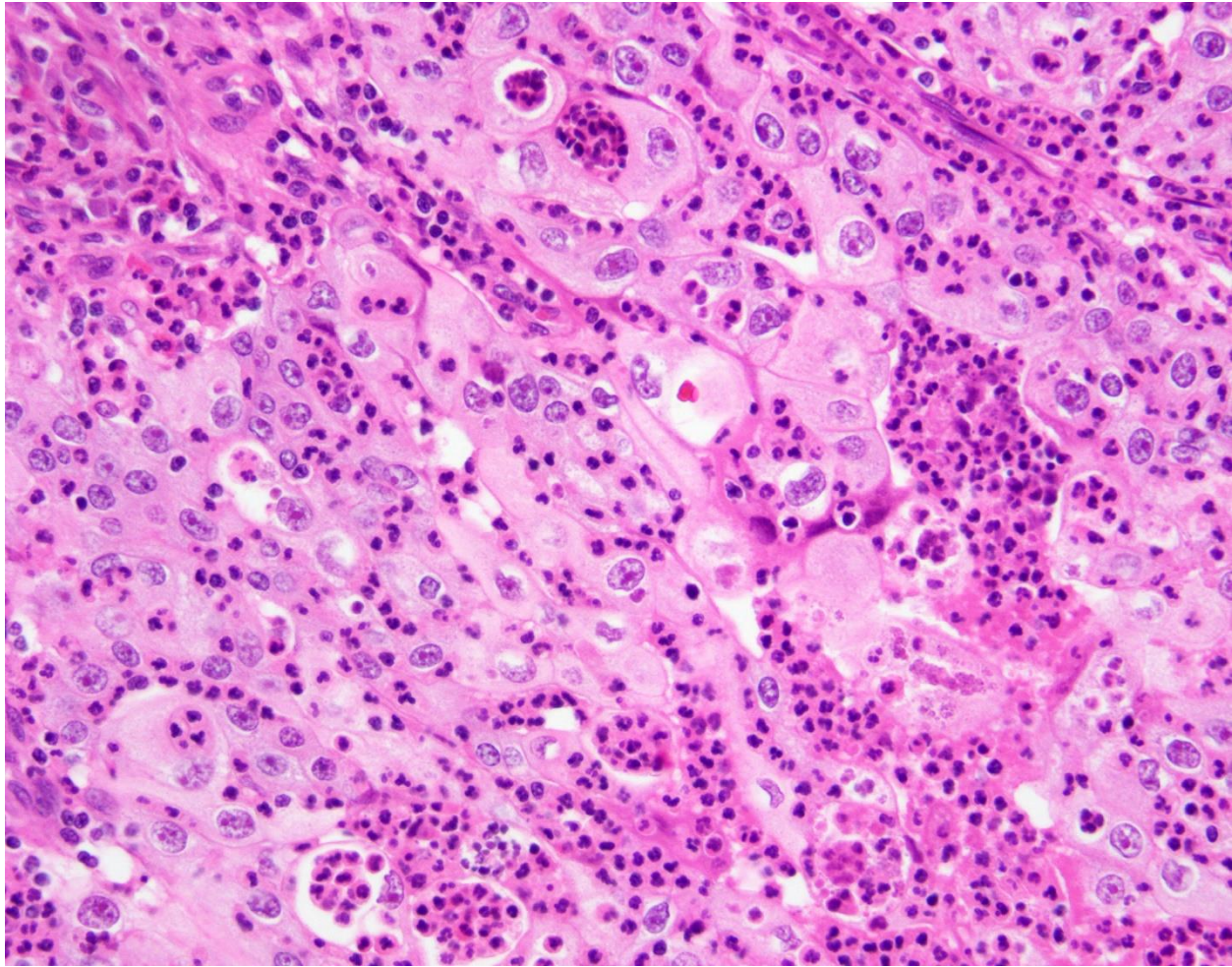






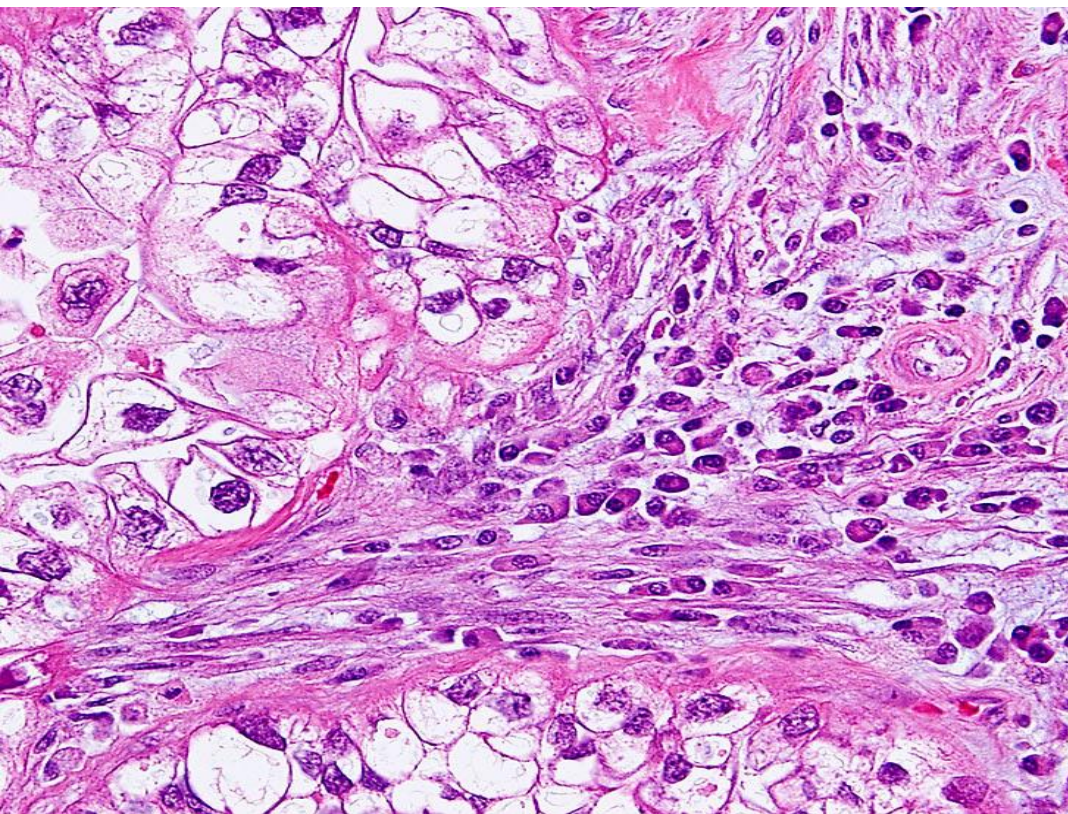




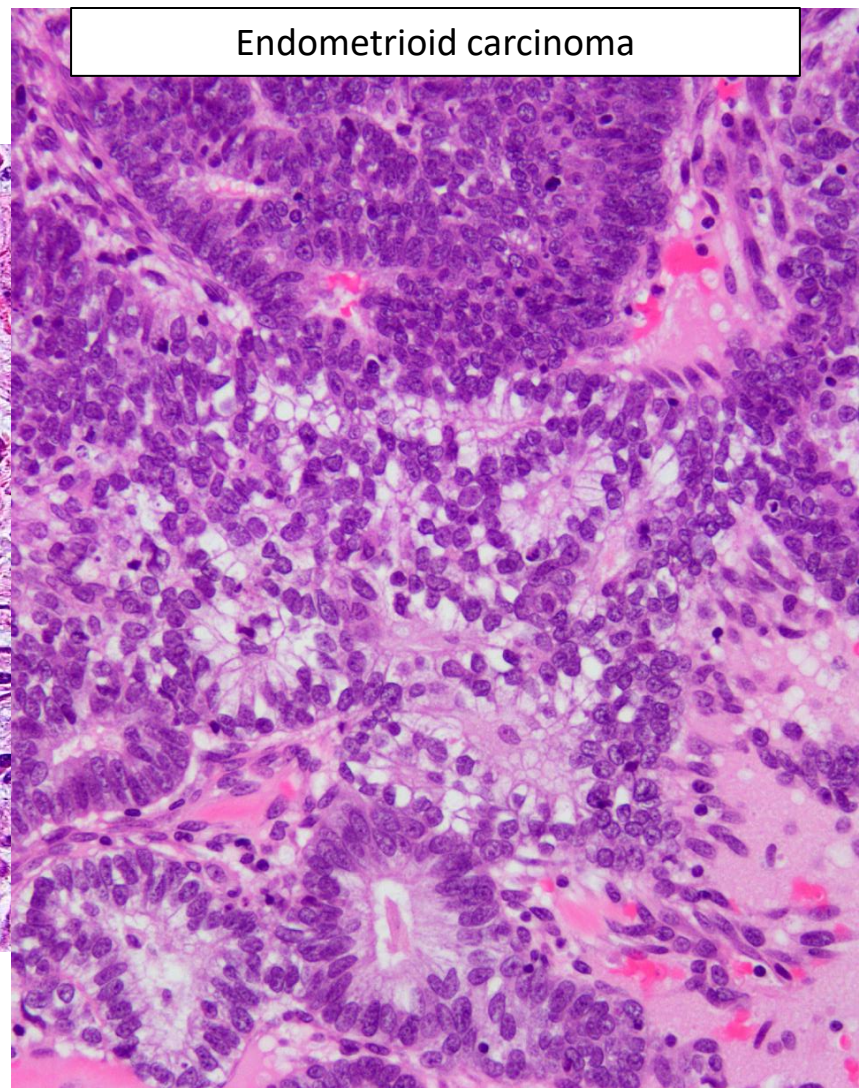


Molecular signatures and immunophenotype

- Mutations: *PIK3CA*, *ARID 1A*, *TP53*, *DNA MMR*, *POLE*
- IHC:
 - ER/PR negative
 - +/- Napsin A, racemase
- Risk stratified with p53, MMR, *POLE*

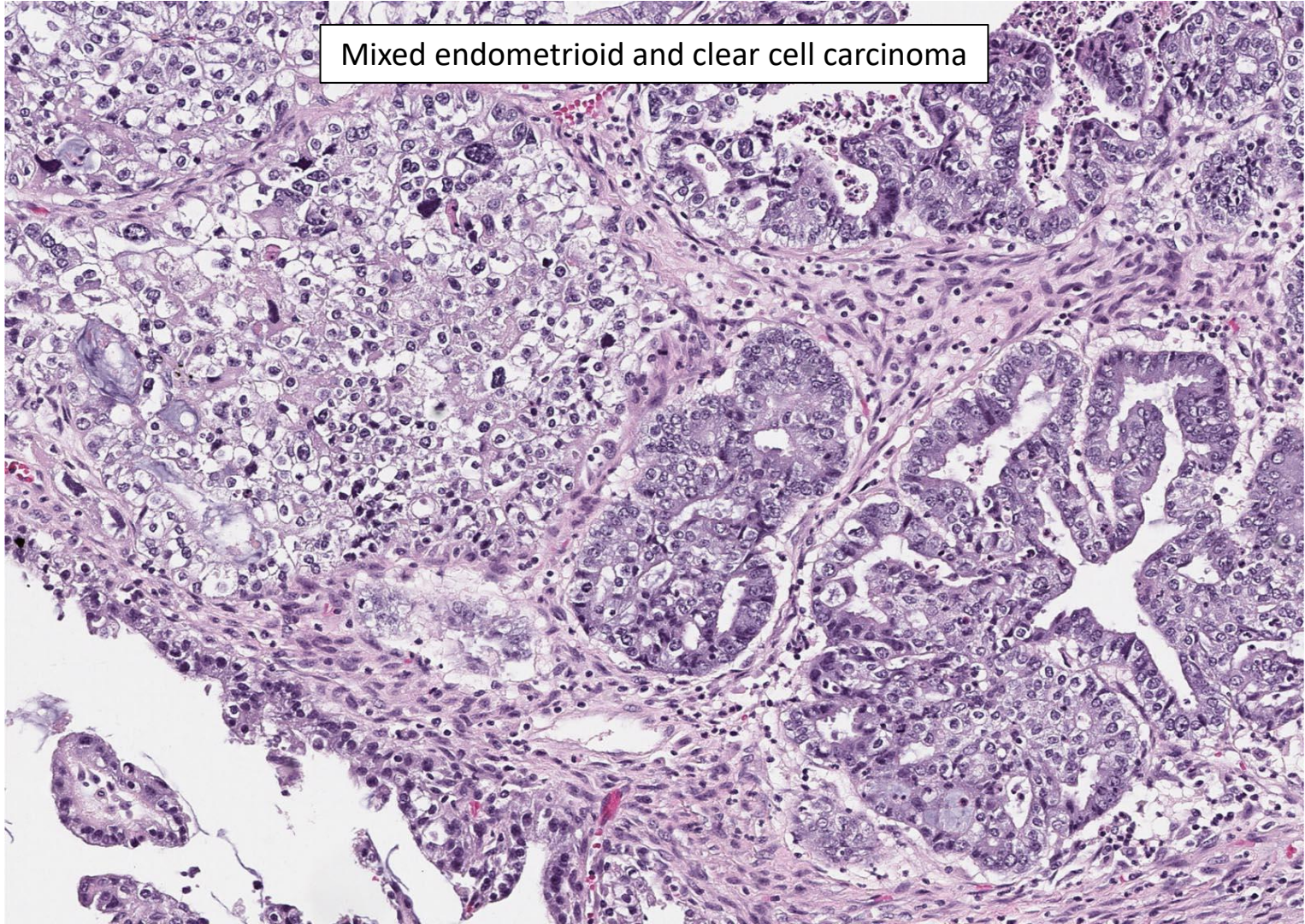


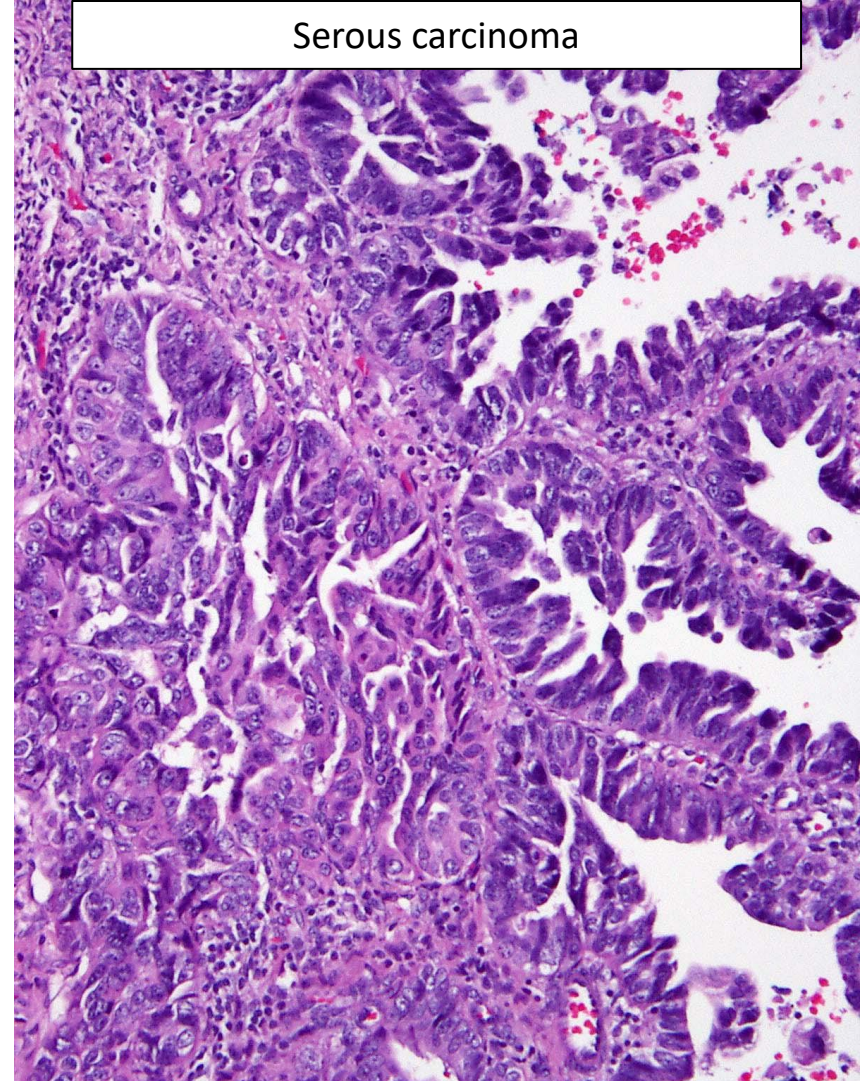
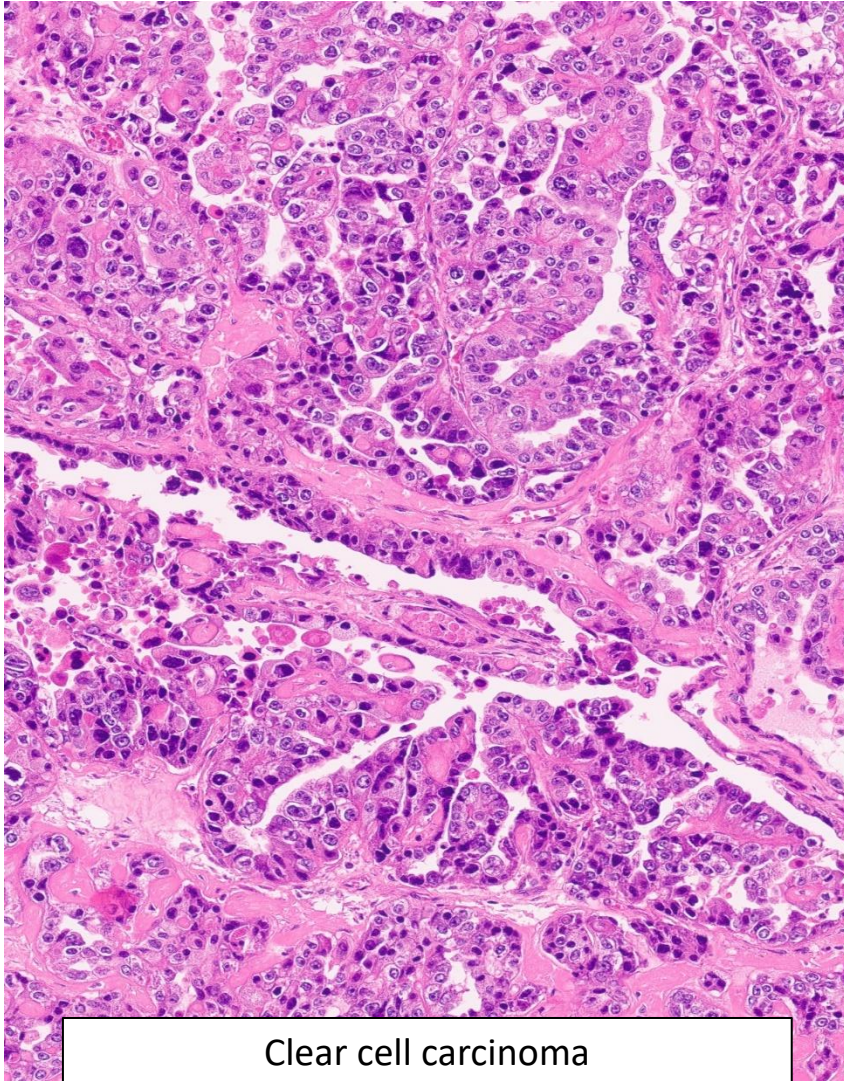
Clear cell carcinoma



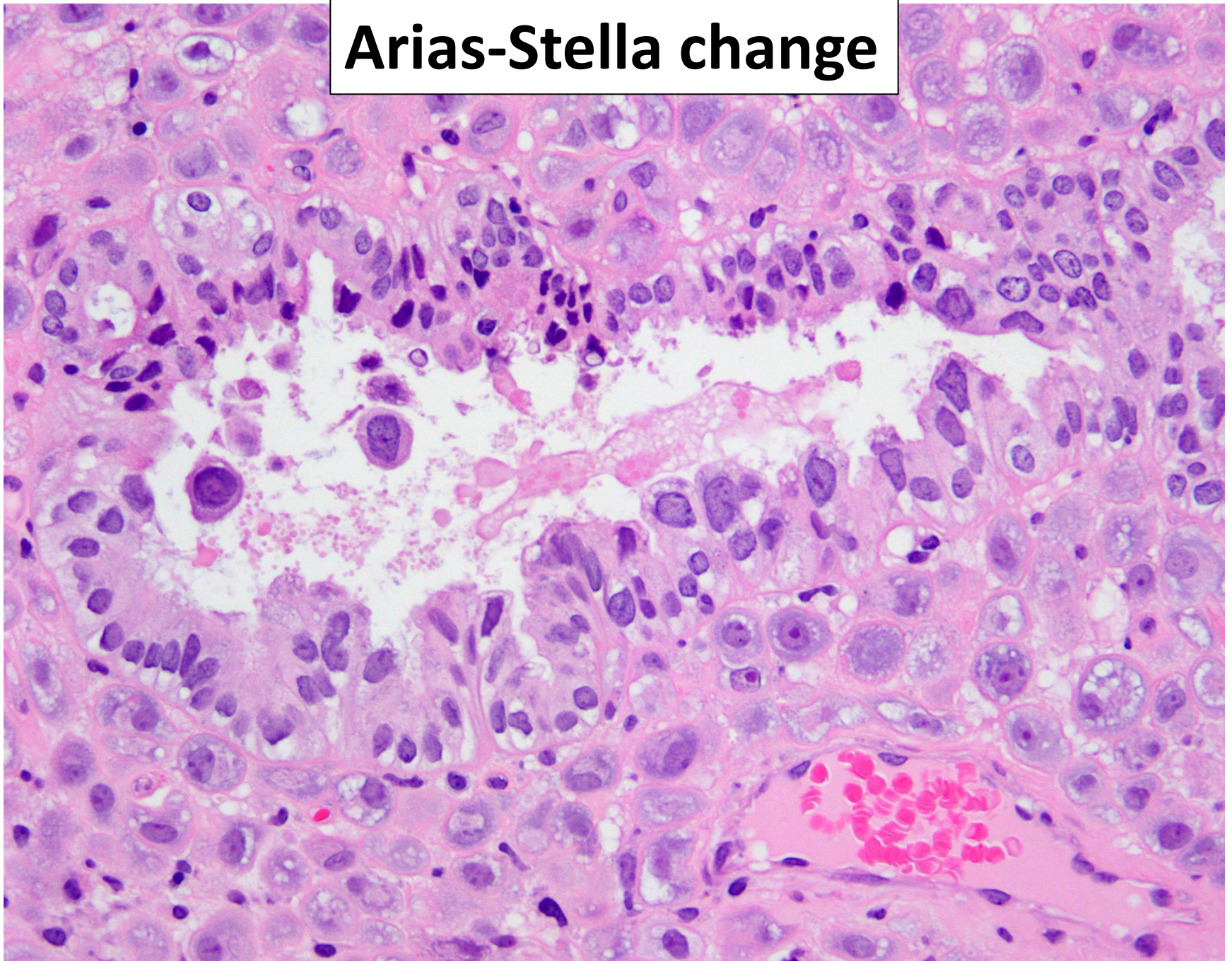
Endometrioid carcinoma

Mixed endometrioid and clear cell carcinoma

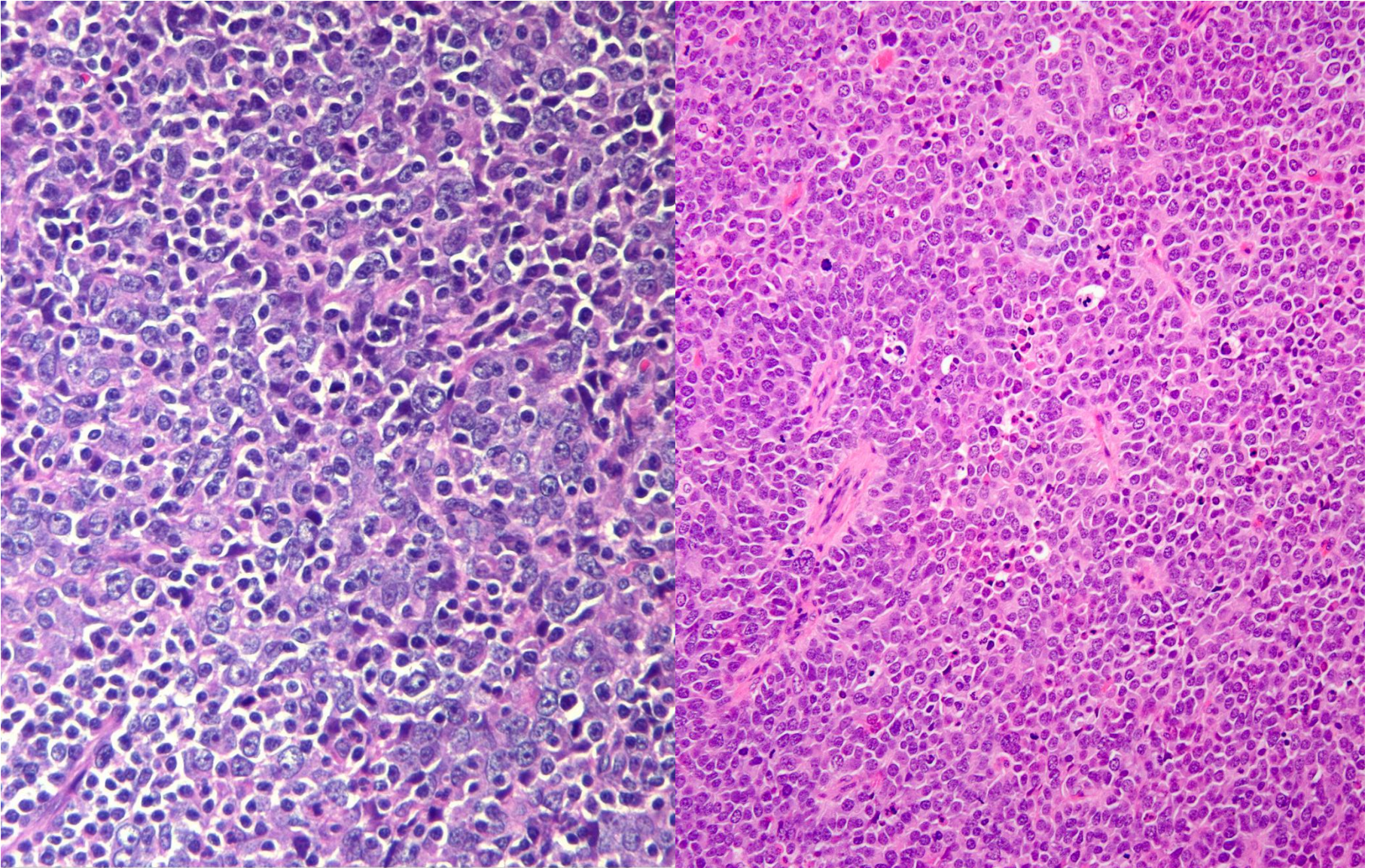


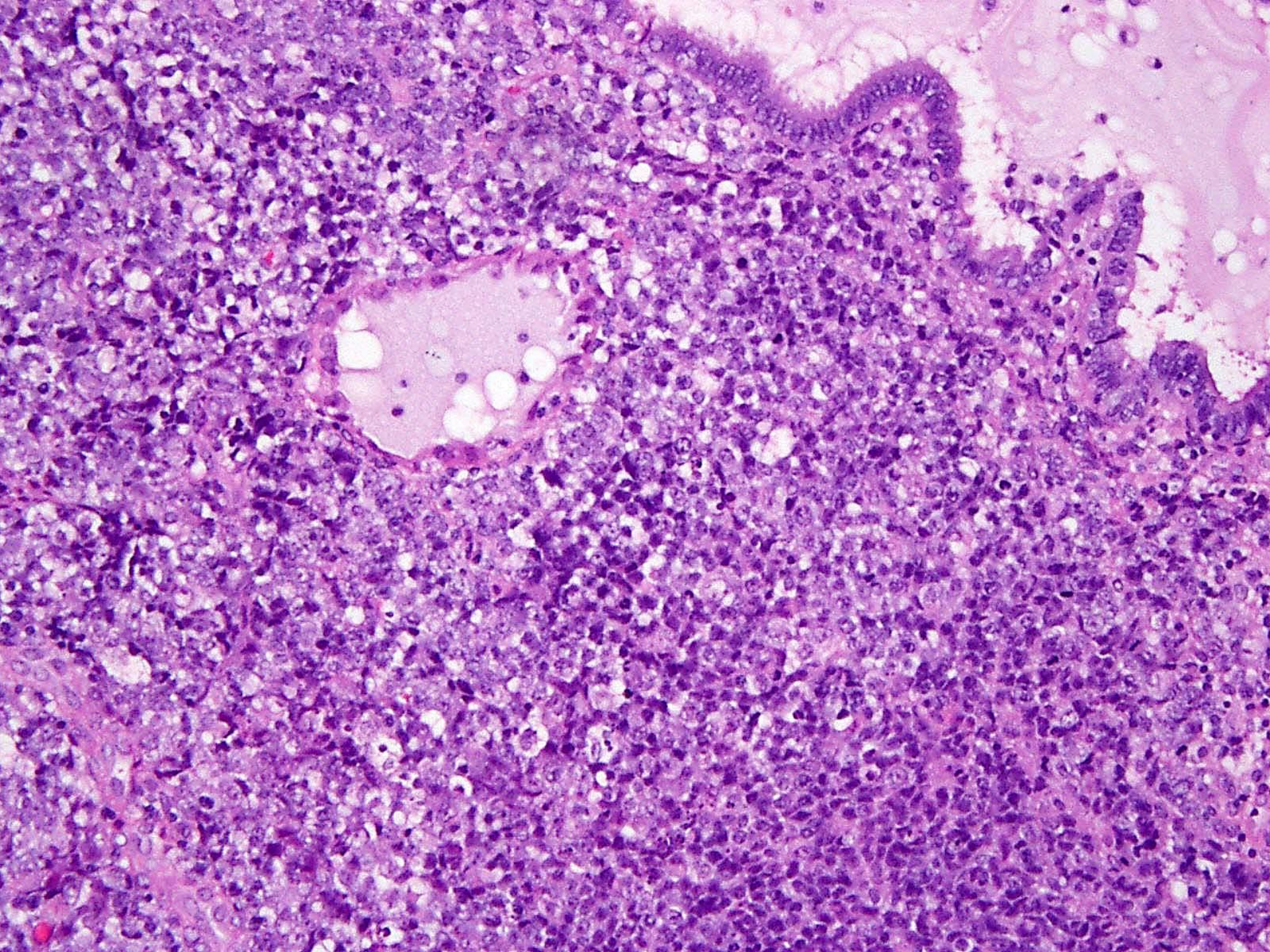


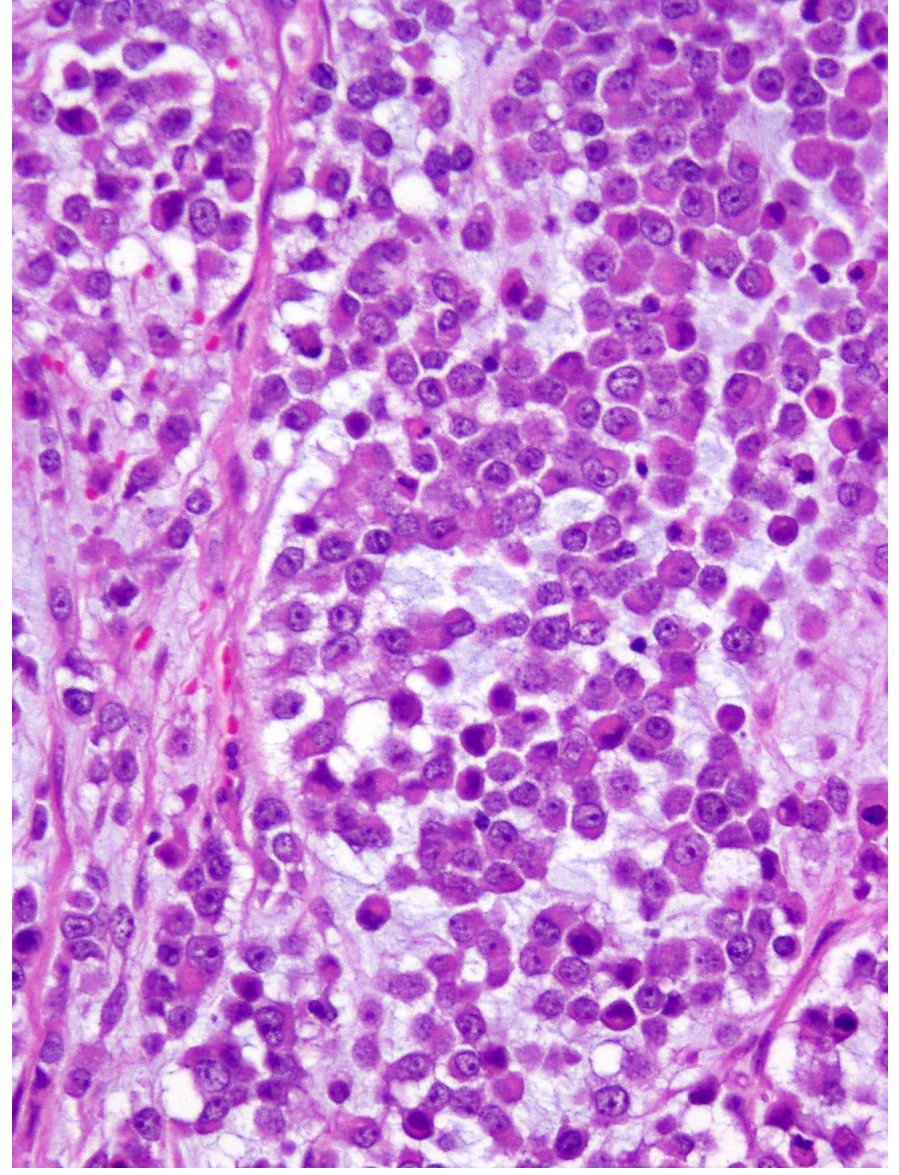
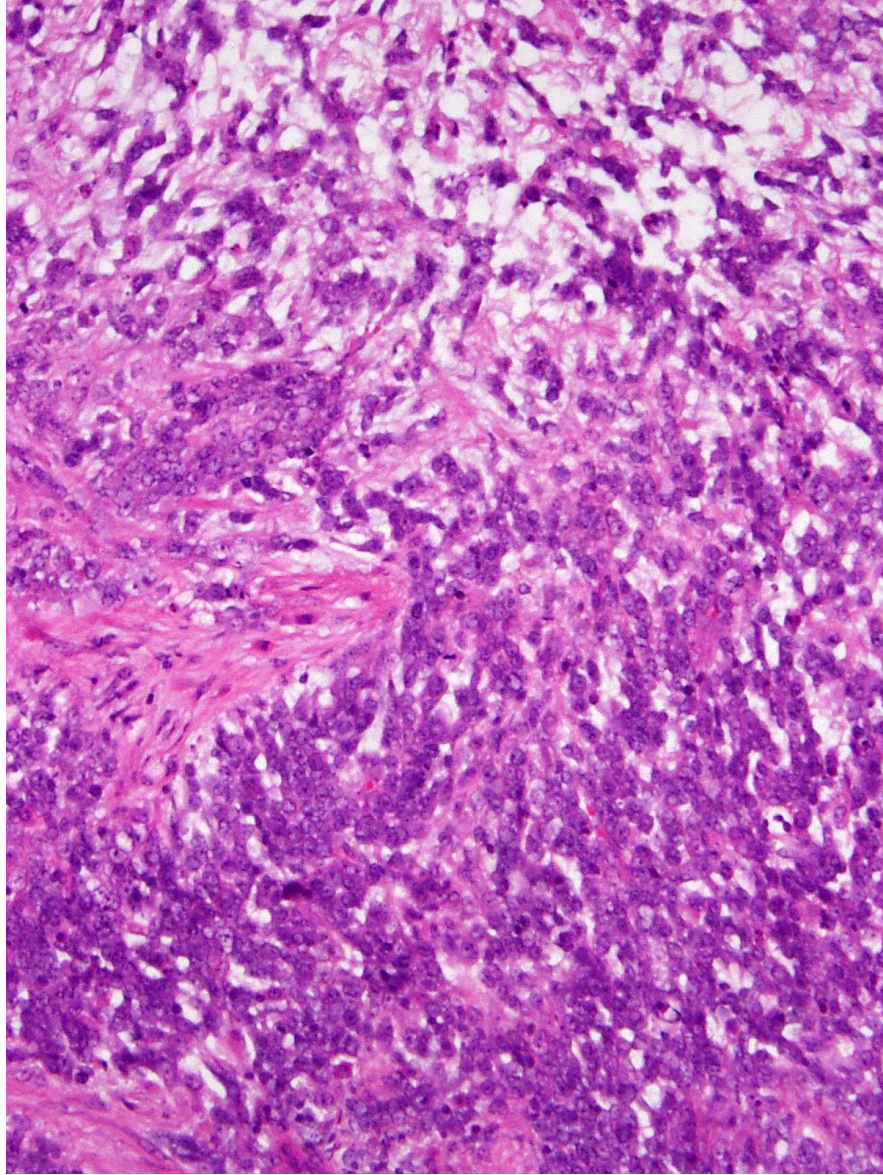
Arias-Stella change



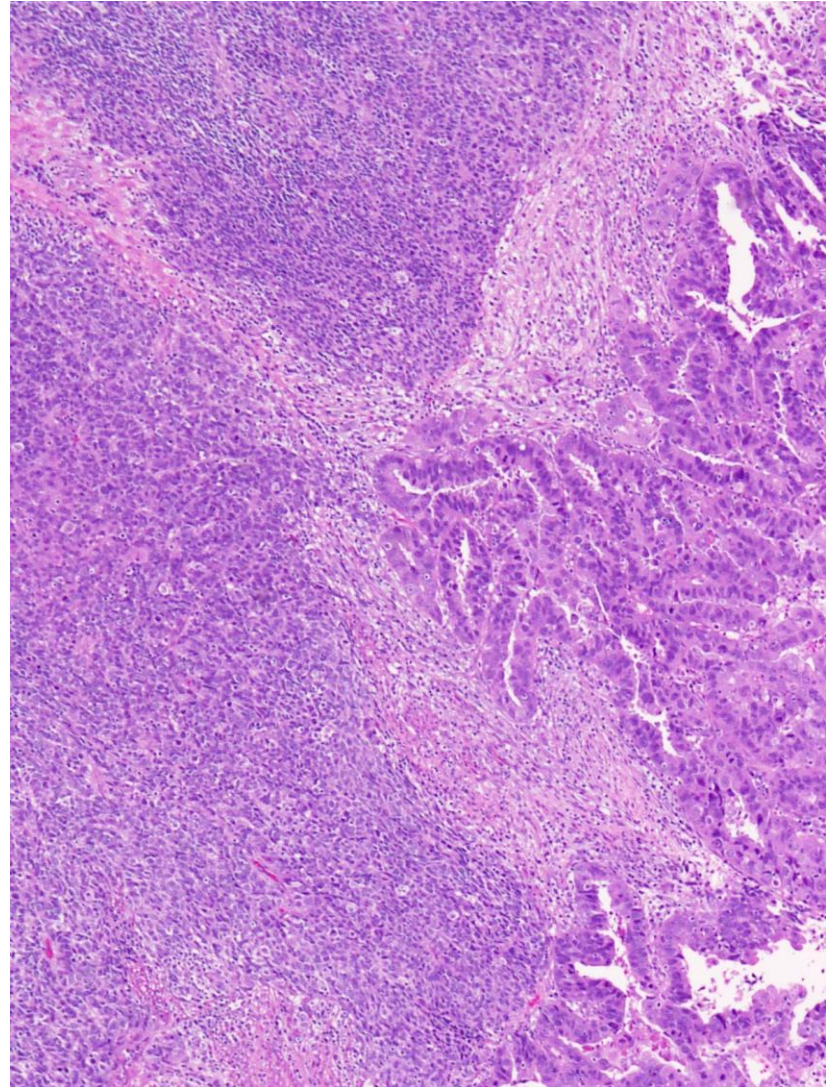
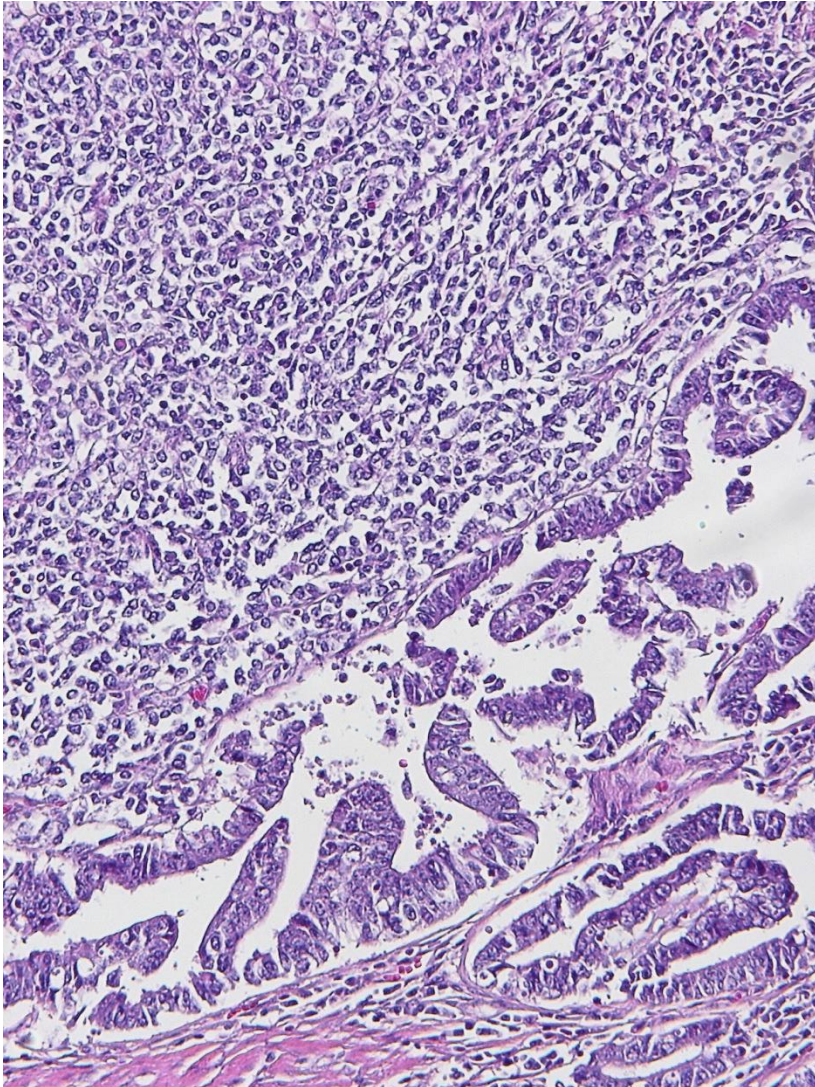
Undifferentiated carcinoma







De-differentiated carcinoma

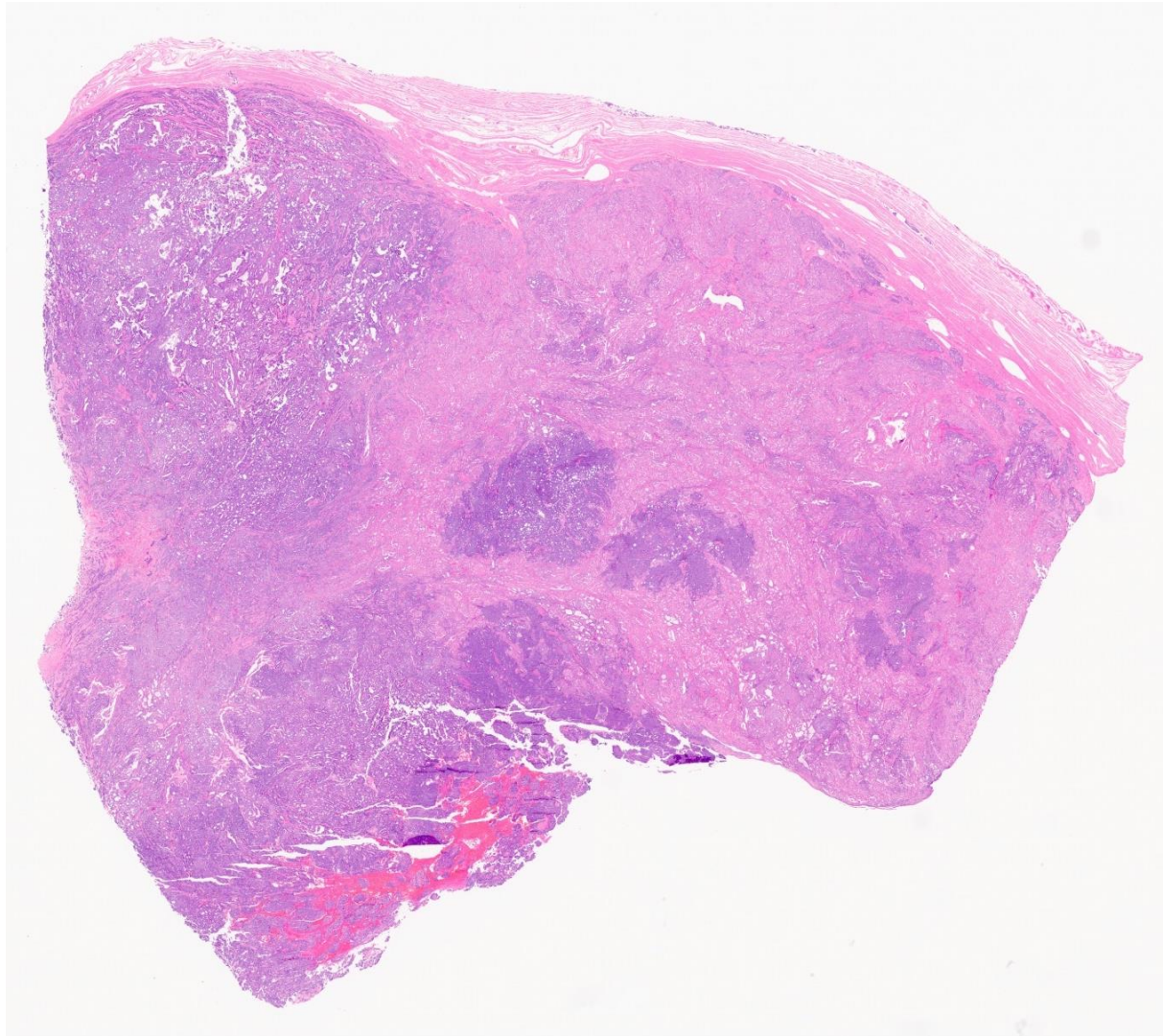


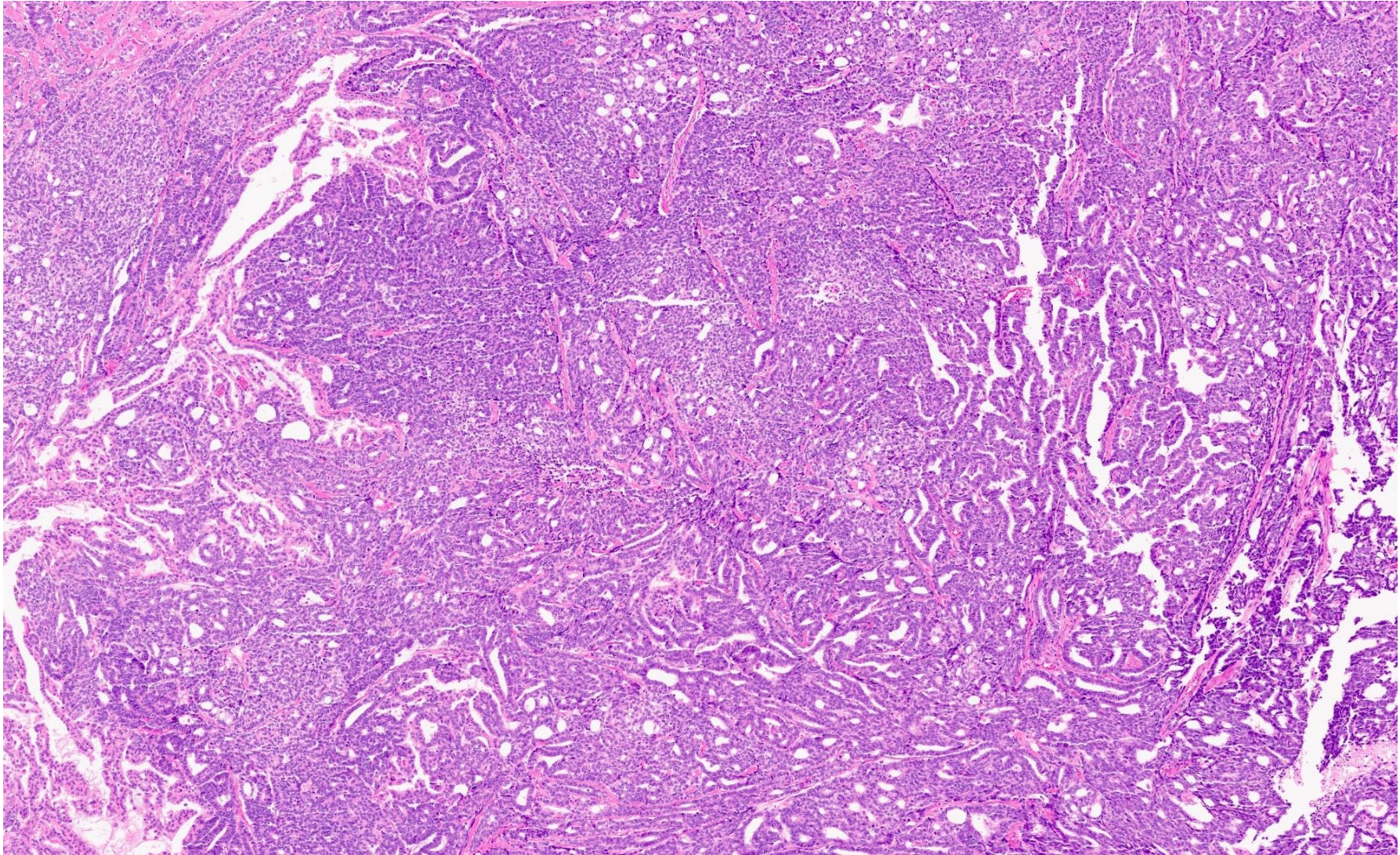
Molecular signatures and immunophenotype

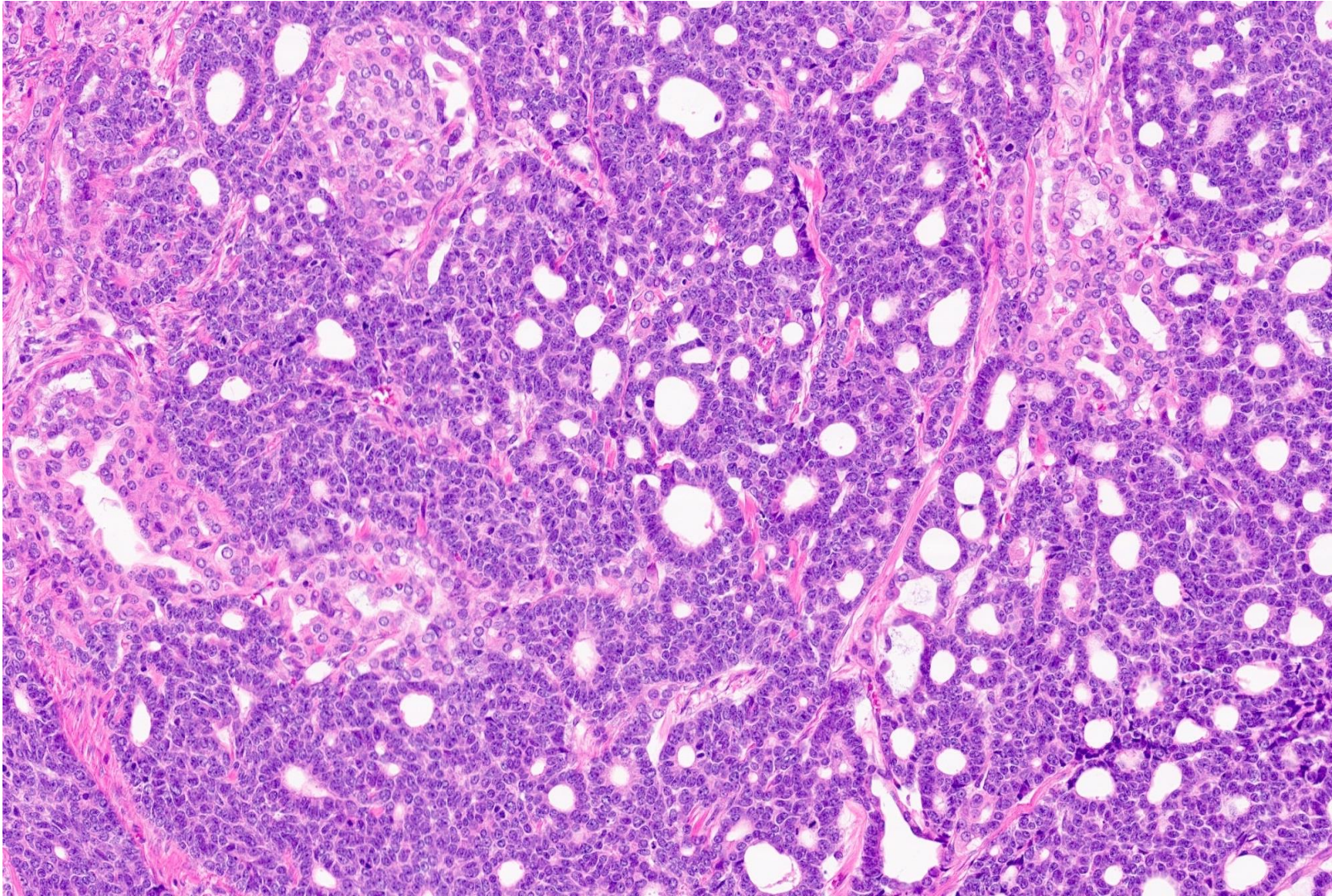
- Un- and De-differentiated carcinoma
 - Mutations: *ARID1A*, *ARID1A*, *SMARCA4*, *SMARCA2*, *SMARCB1*, *DNA MMR*, *POLE*...
- IHC:
 - Positive: vimentin, EMA (few cells), CK18 (few cells), SALL-4
 - Variable: CAM5.2, CD138, SMARCA4/B1, ARID1A, DNA MMR, synaptophysin, chromo, p53
 - Negative: **PAX8**, e-cadherin

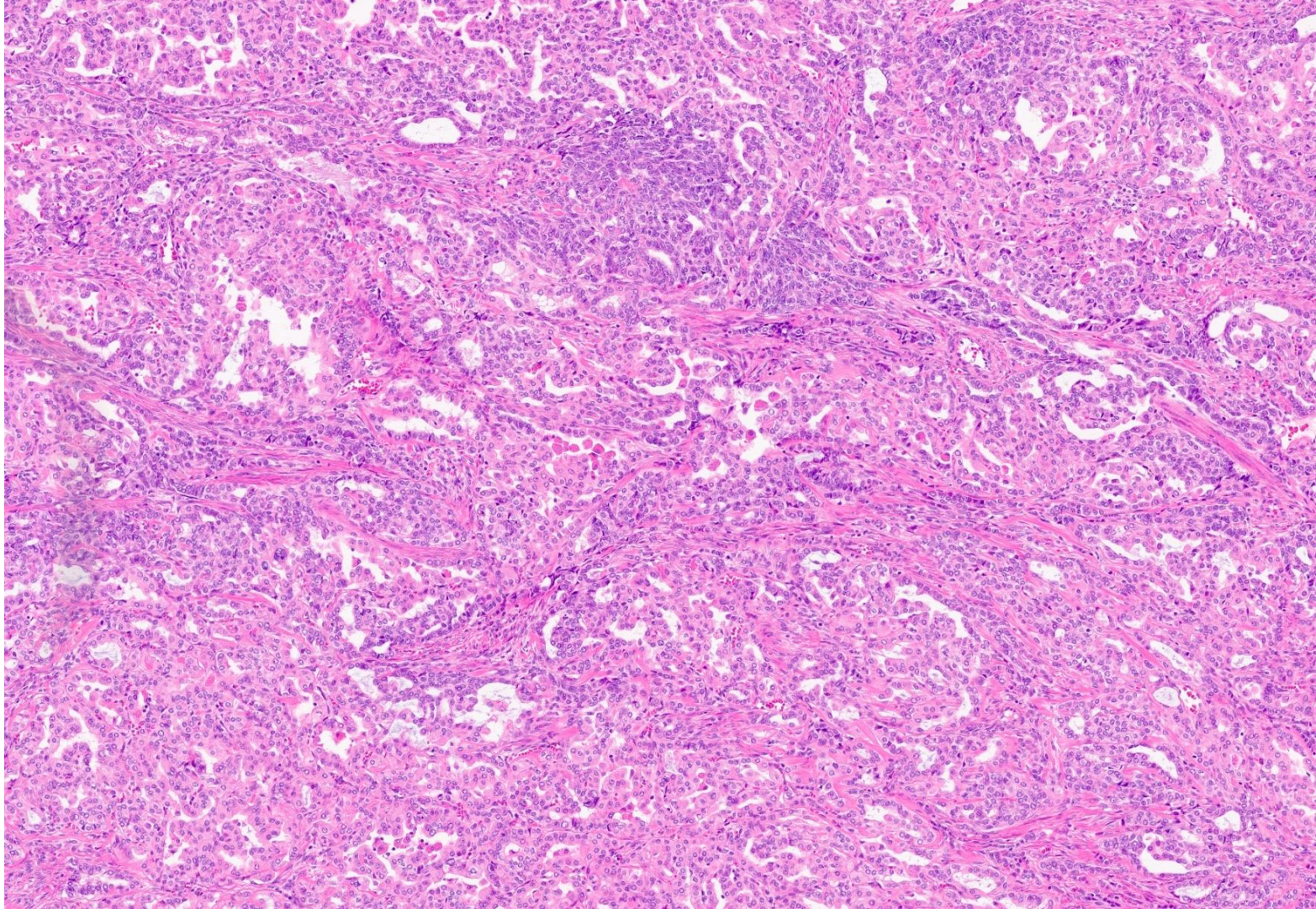
Mesonephric-like carcinoma

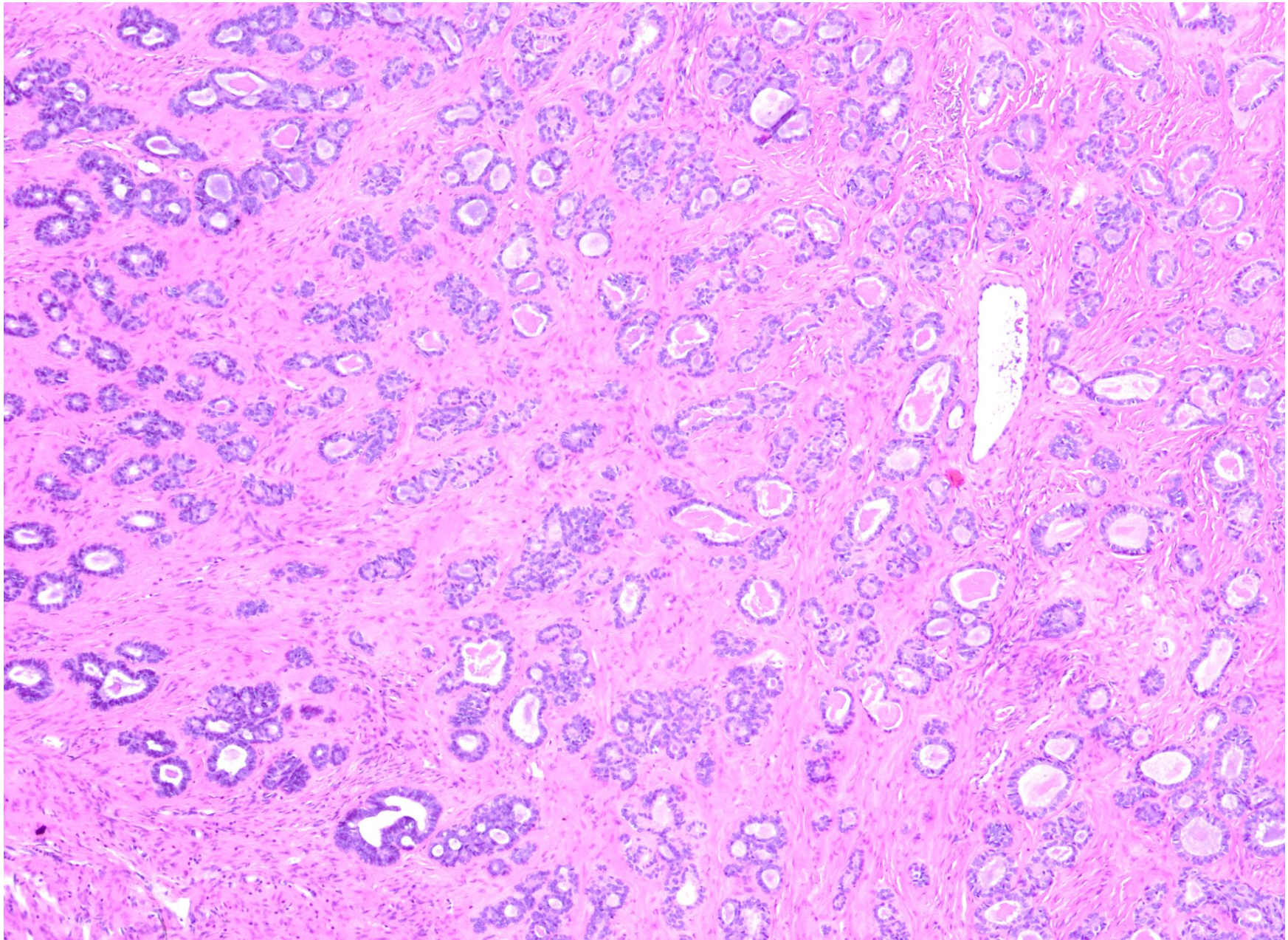
- A 78-year-old woman was diagnosed with endometrioid carcinoma on endometrial curettage.
- At hysterectomy, she was found to have a deeply myoinvasive 5.5 cm tumor.
- pT2N0i+Mx

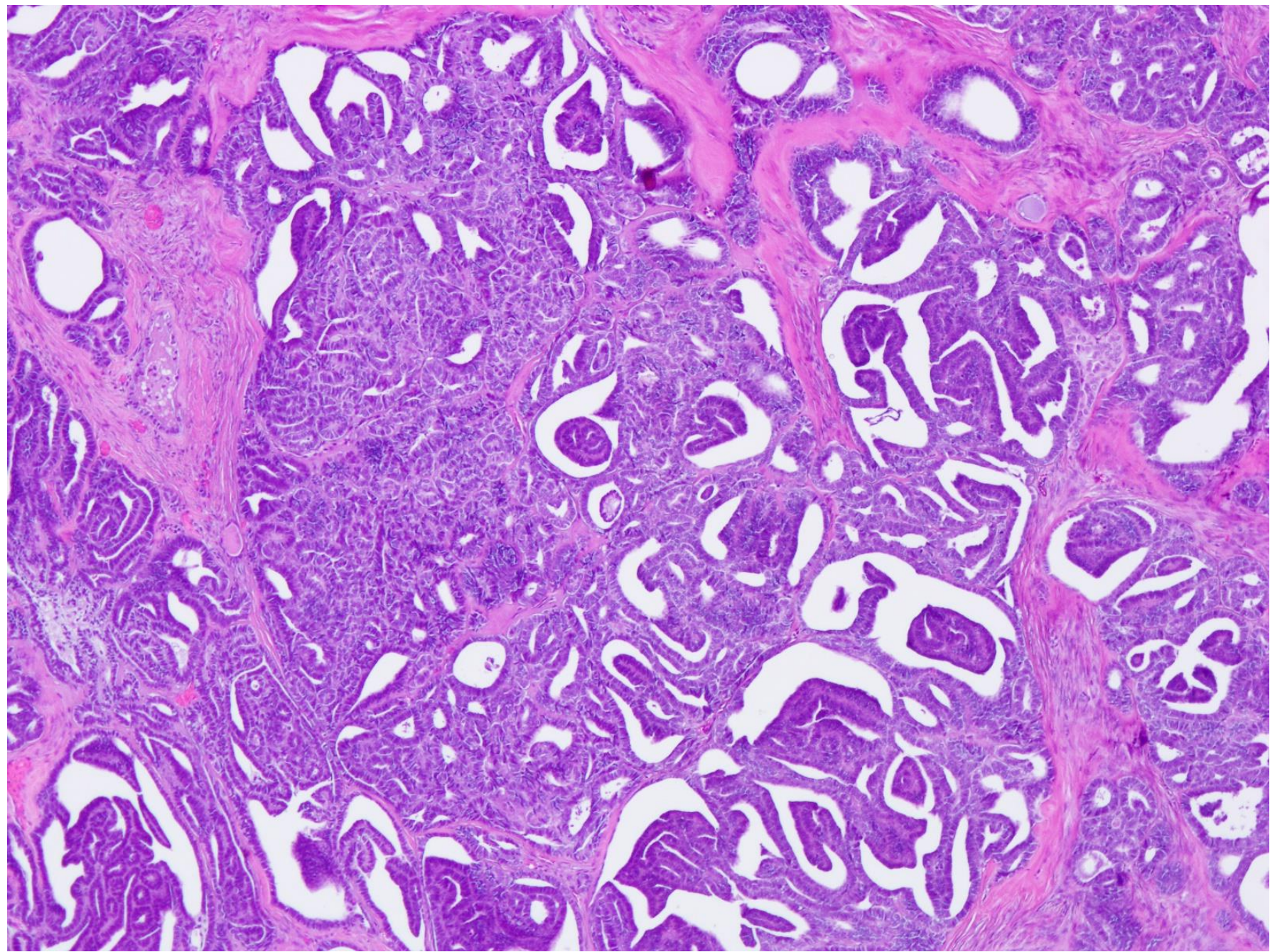


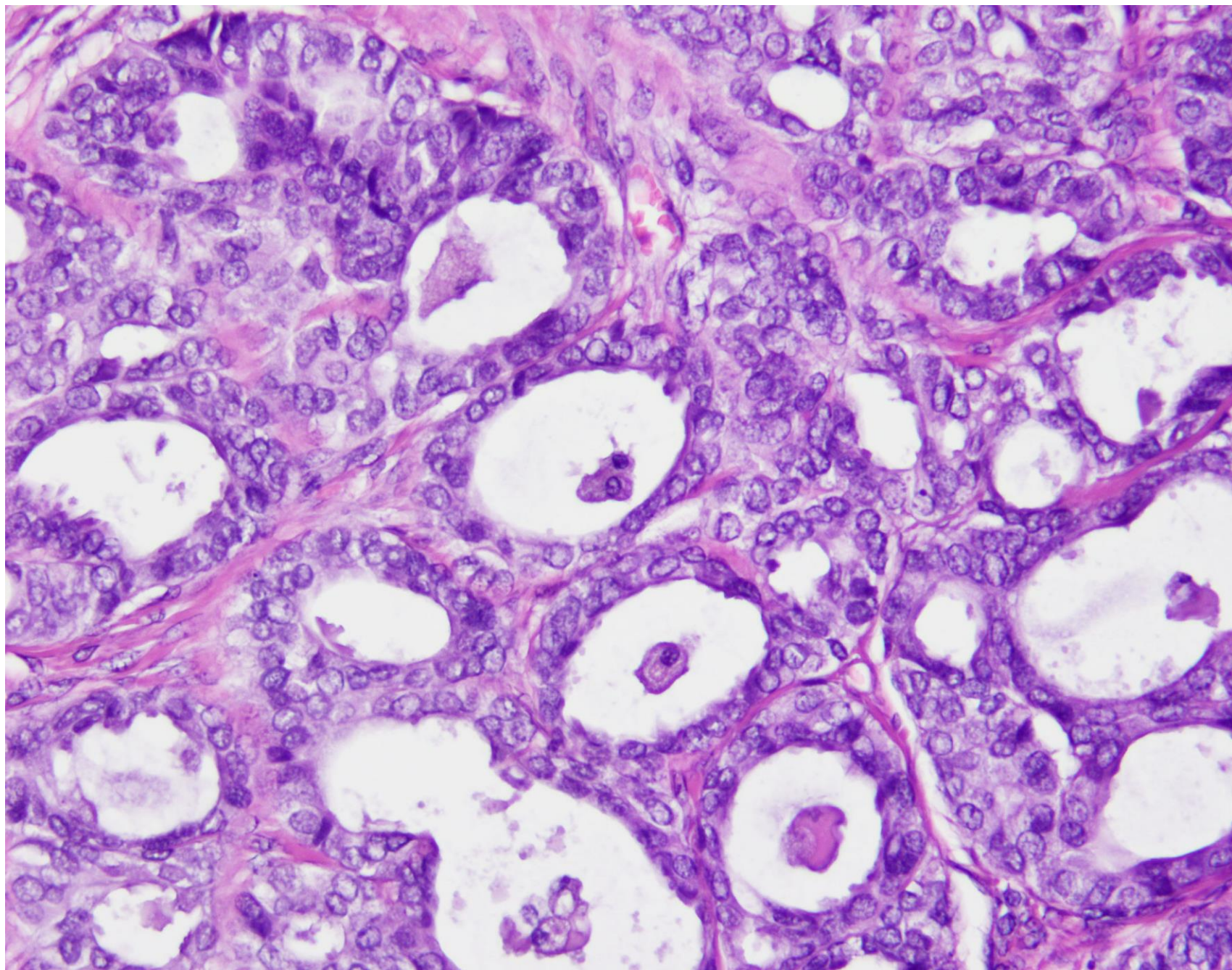


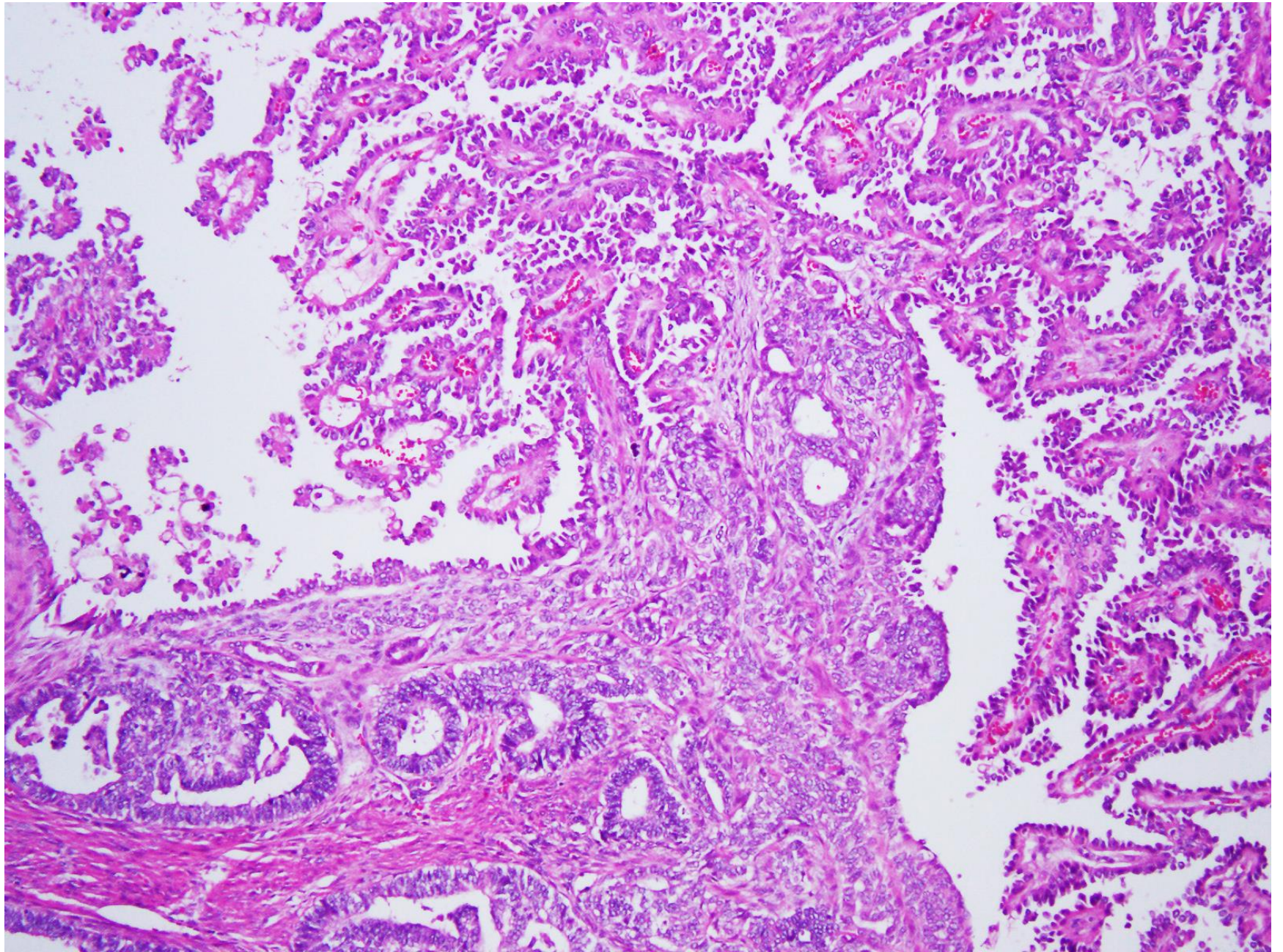


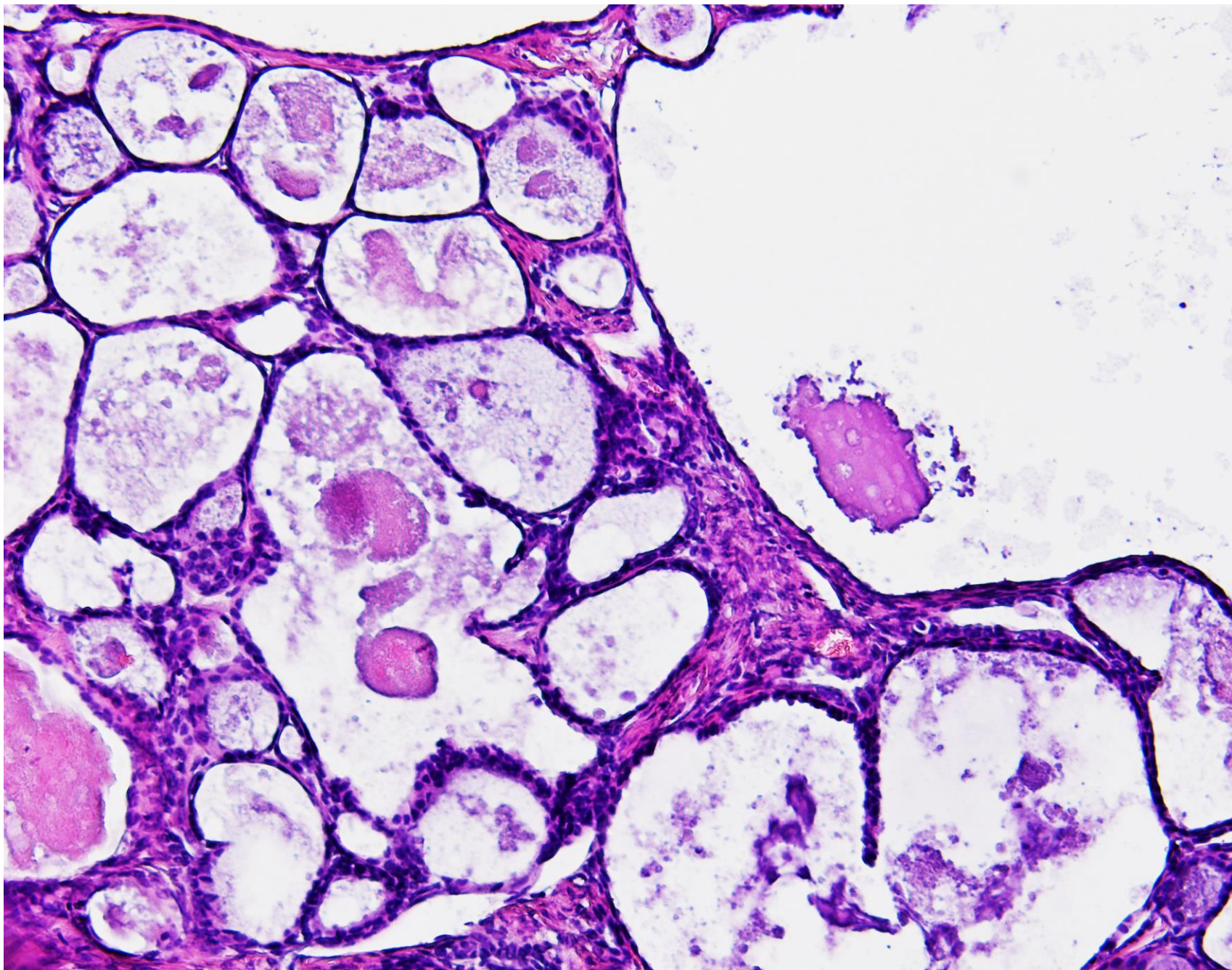


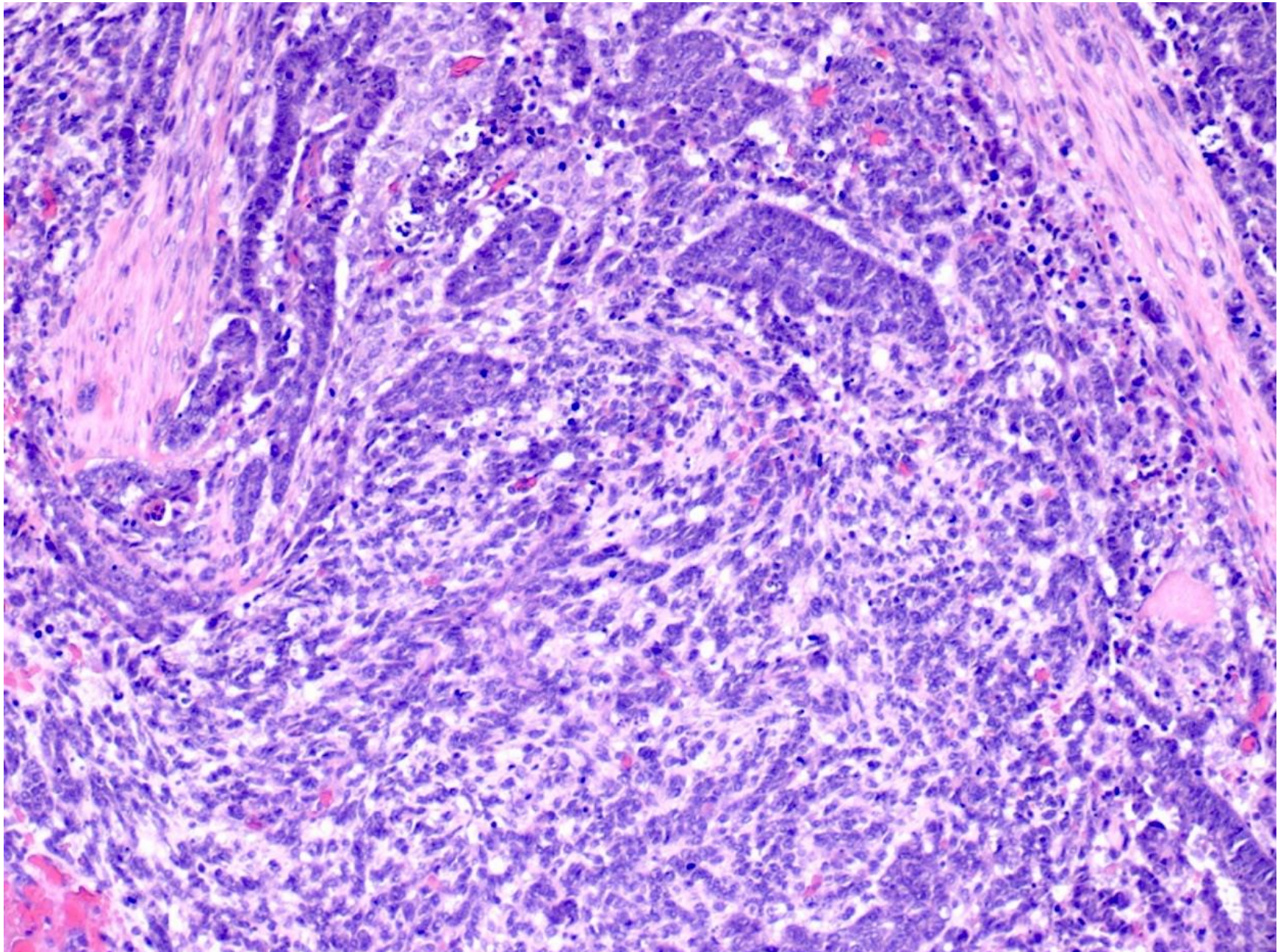




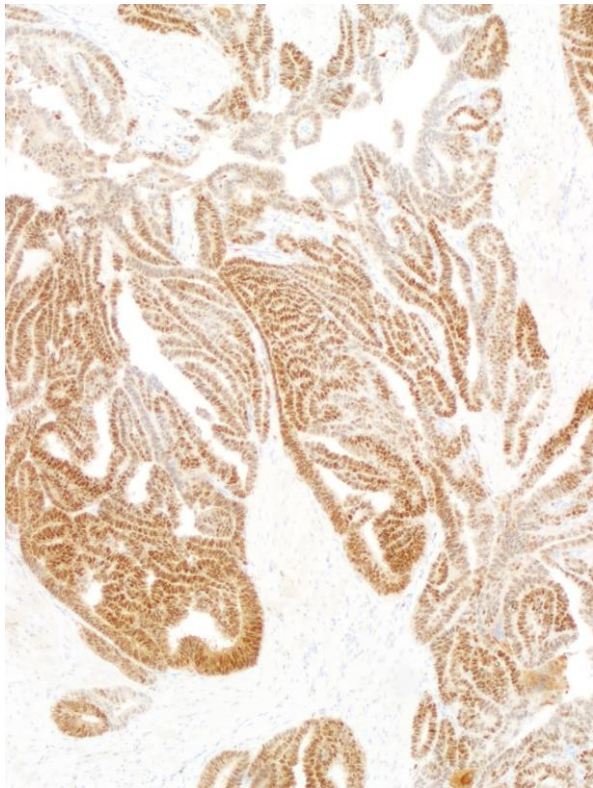




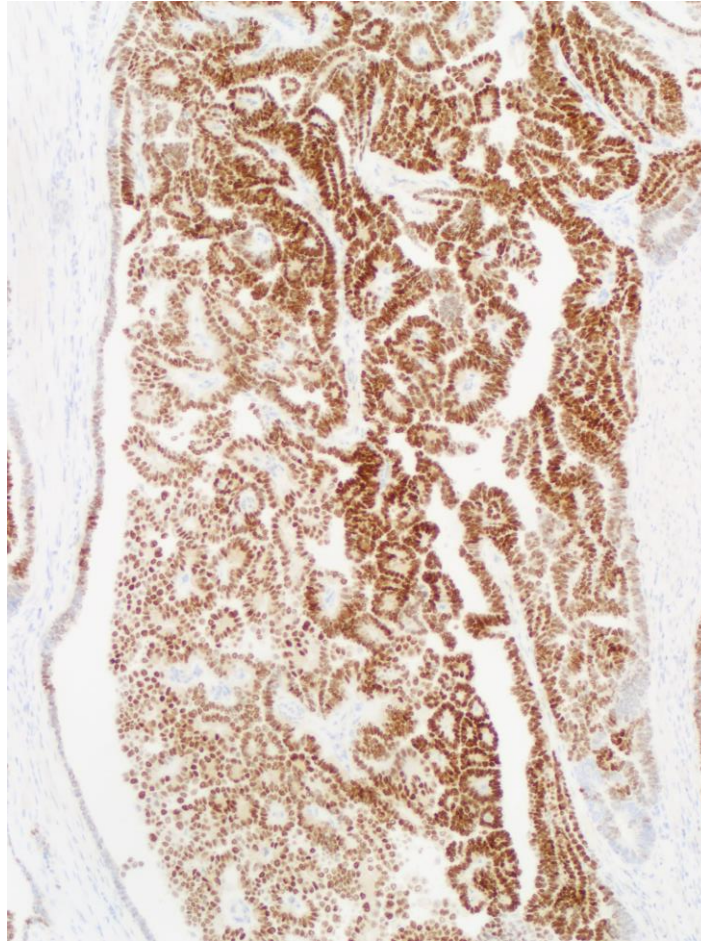




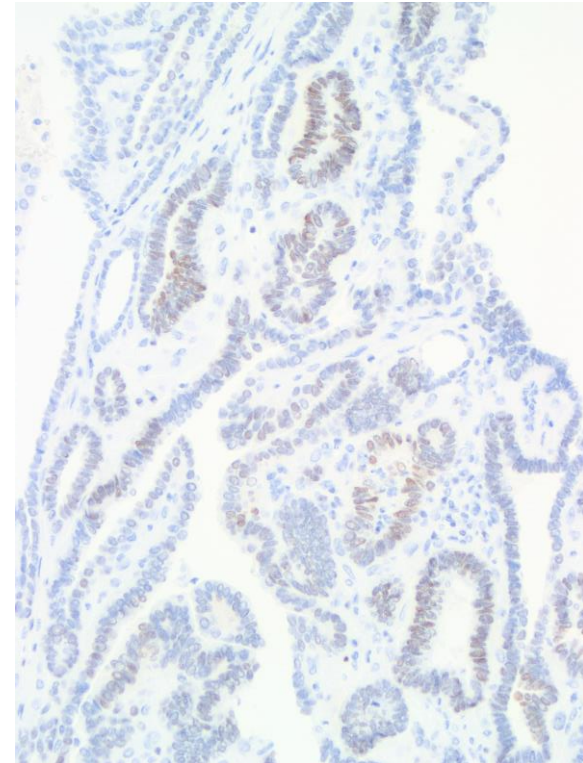
PAX8



TTF-1

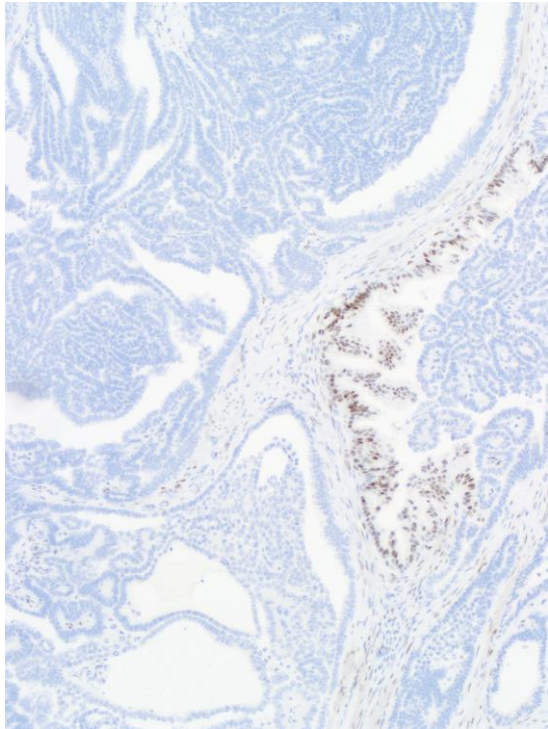


GATA3

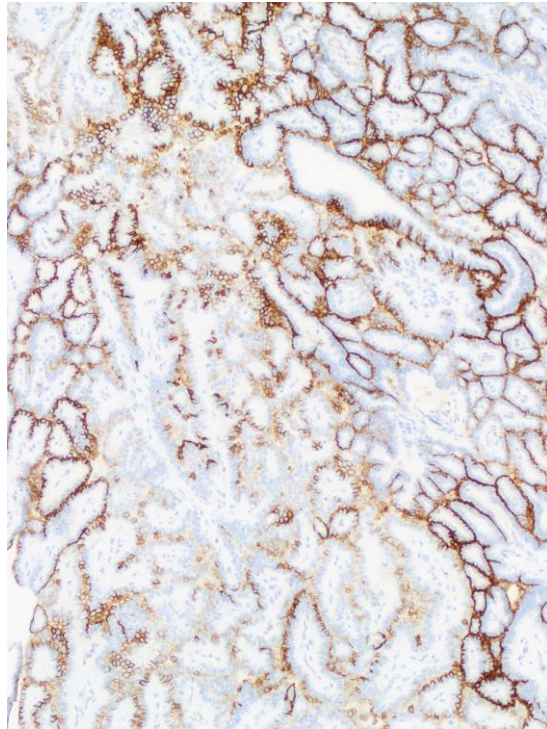


Courtesy of Natalia Buza, MD

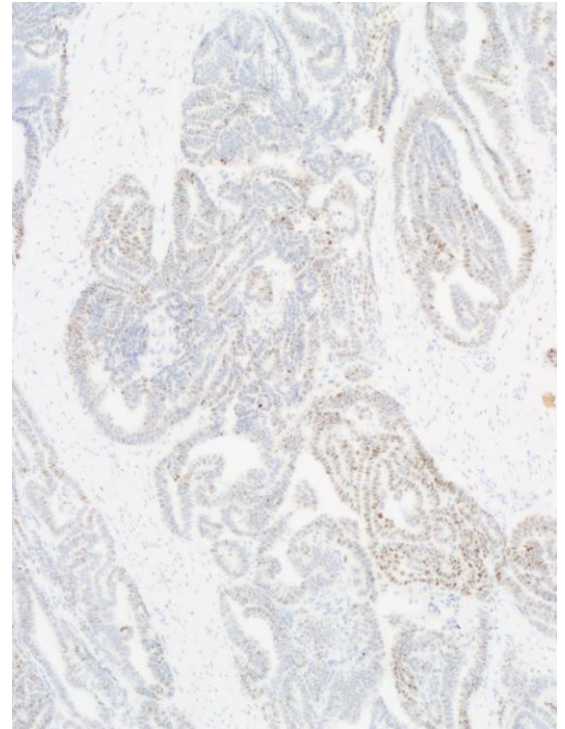
ER



CD10



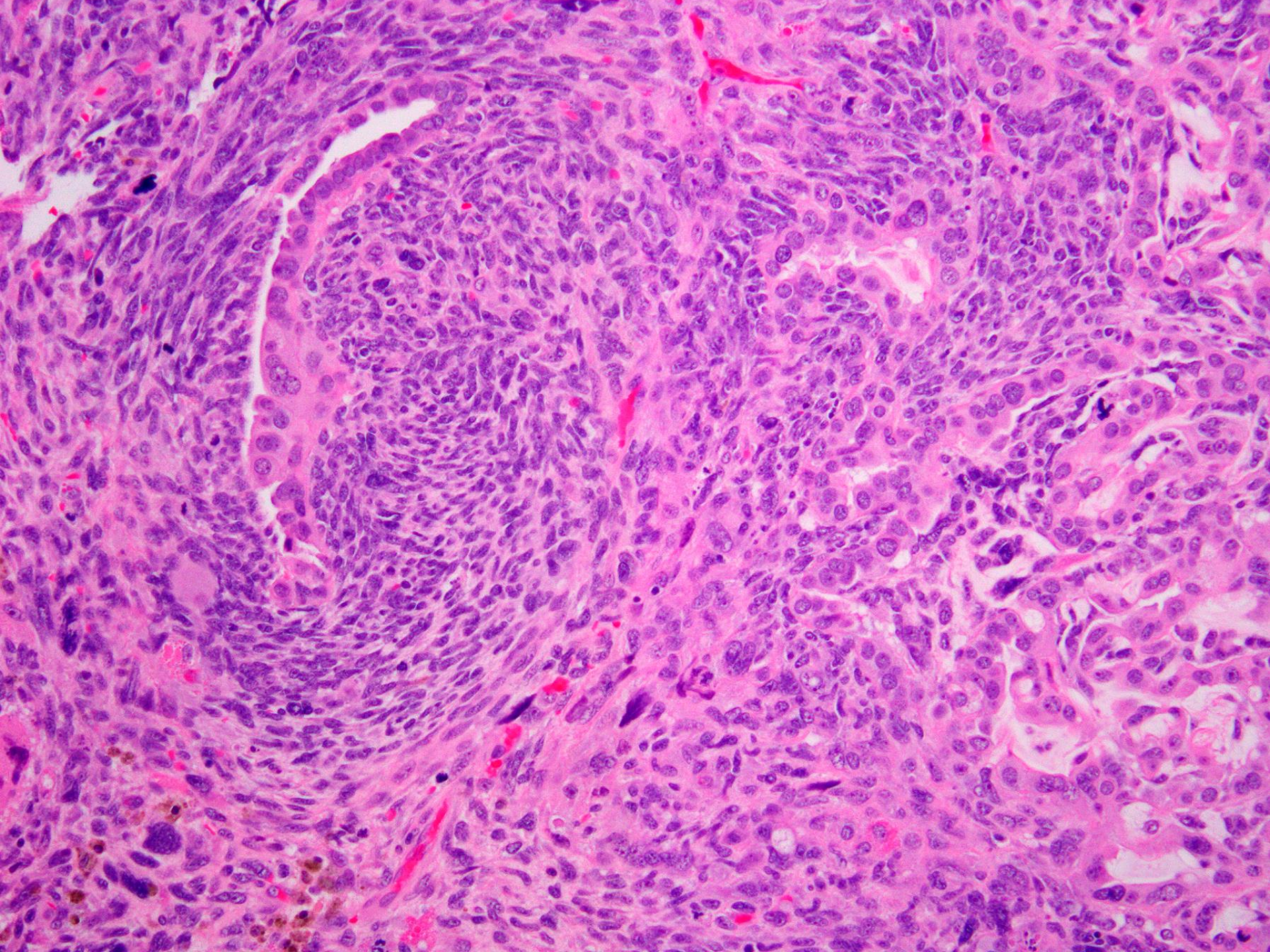
p53

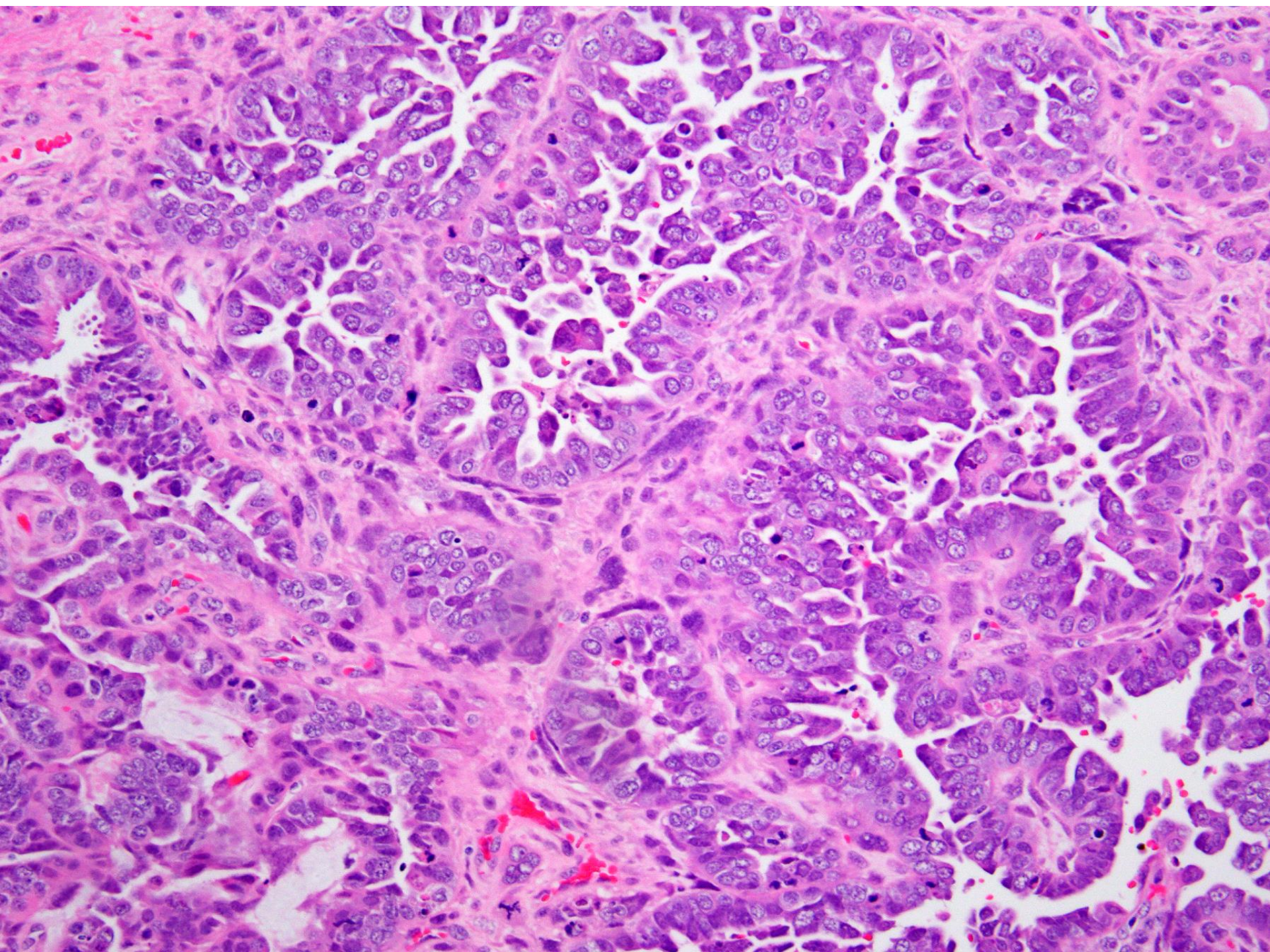


Molecular signatures and immunophenotype

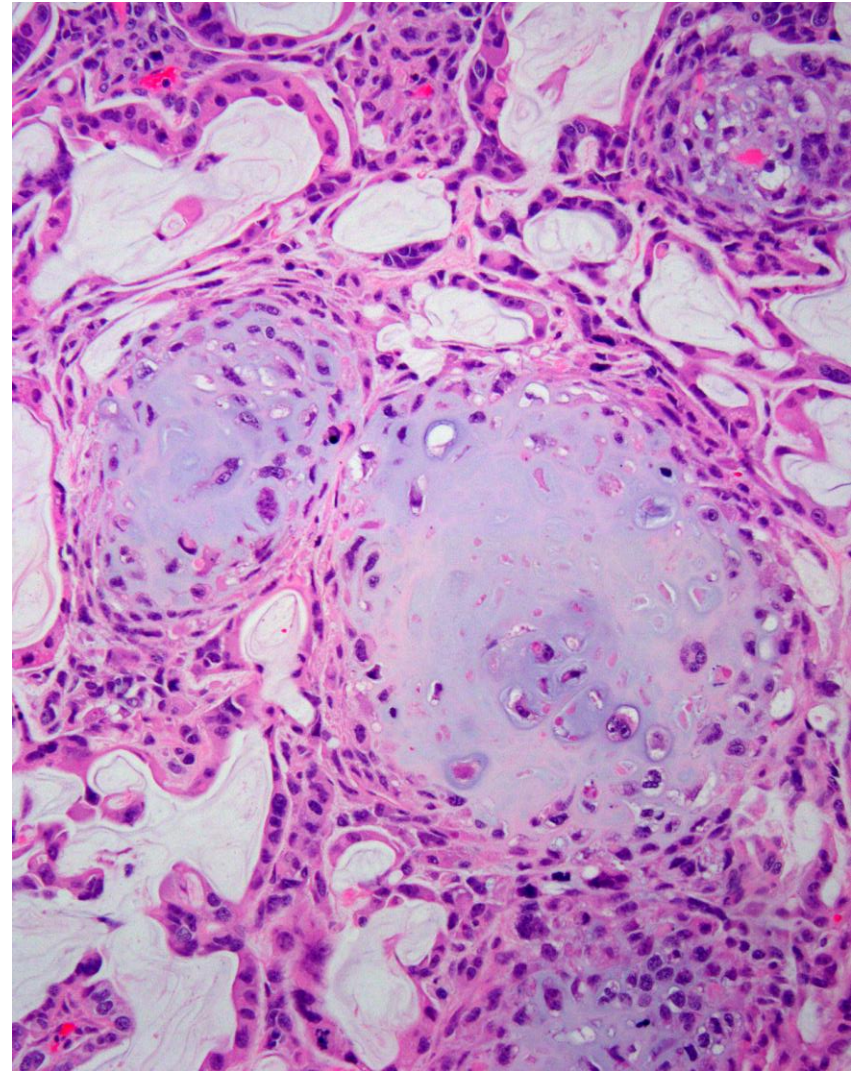
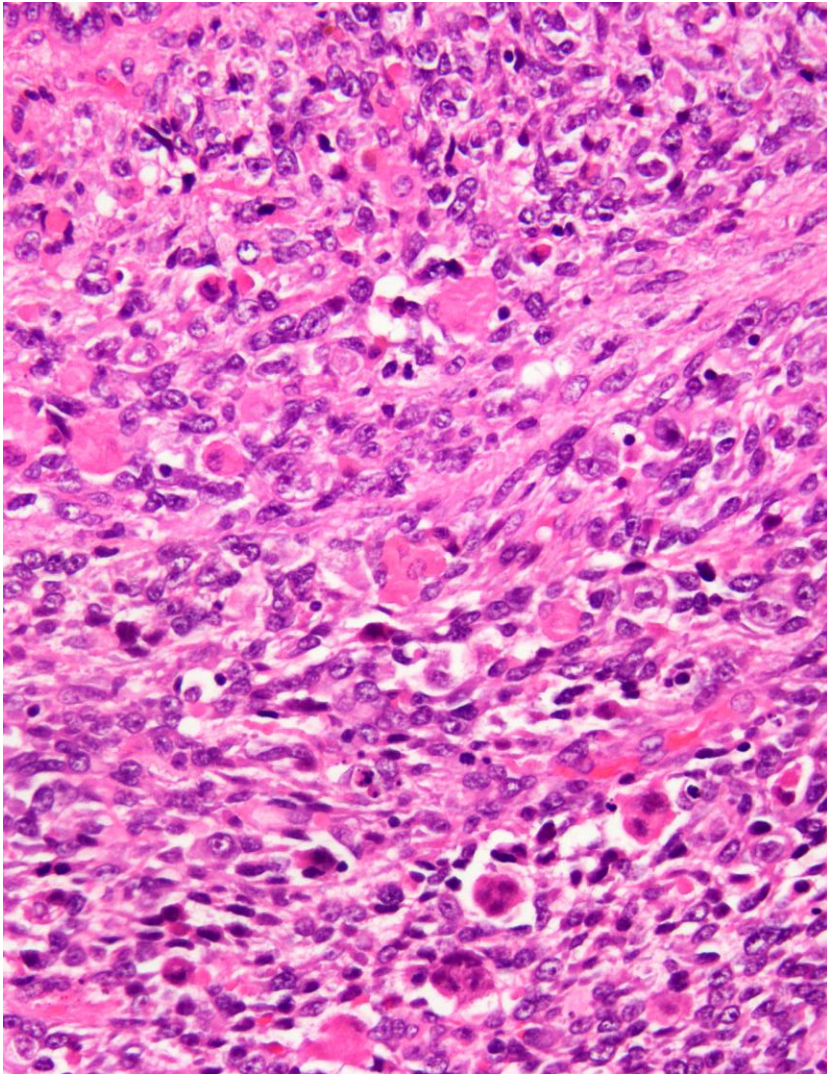
- Mesonephric-like carcinoma
 - Mutations: *KRAS*; no *PTEN* or MMRd
 - Cytogenetics: *1q* gains
 - IHC: +/- TTF1, +/- GATA3, ER/PR-

Carcinosarcoma (MMMT)

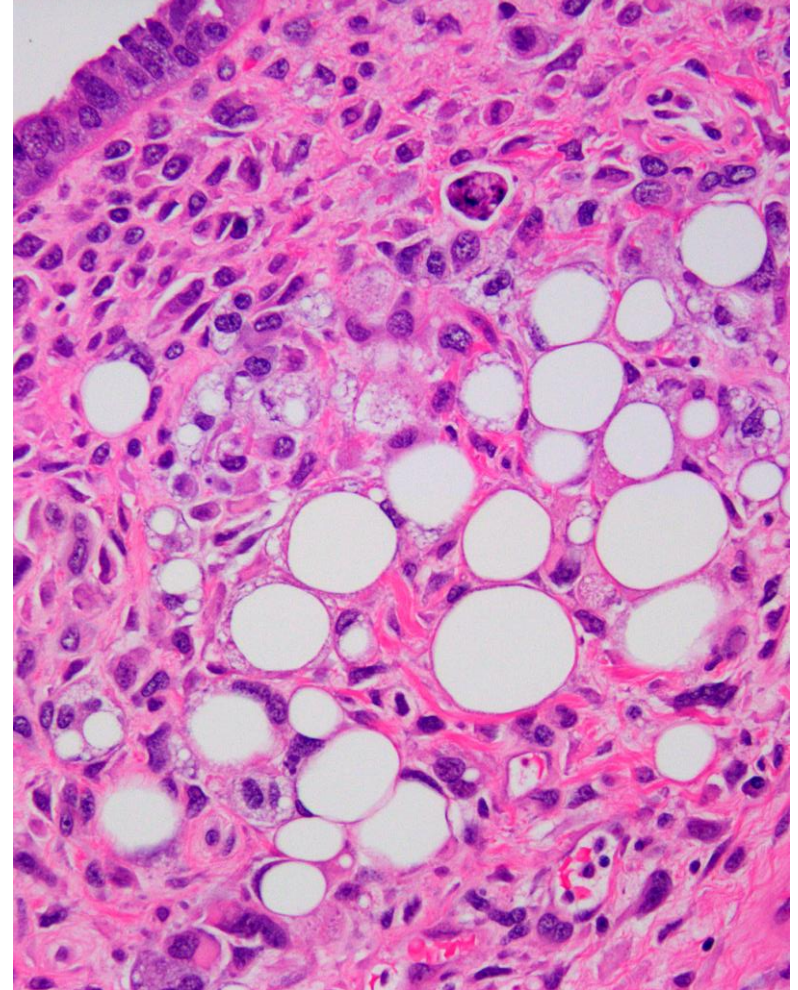
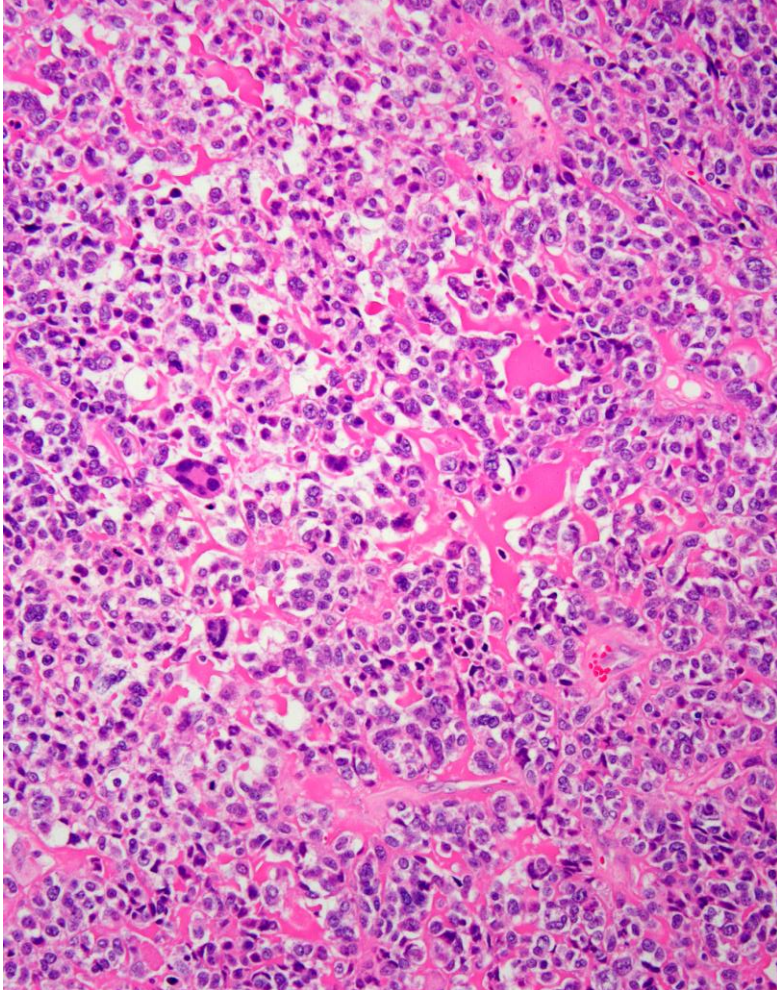




Common heterologous elements



Rare heterologous elements



Molecular signatures and immunophenotype

- Carcinosarcoma
 - Mutations: *TP53*, *PIK3CA*, *DNA MMR*, *POLE*
 - IHC: not relevant for diagnosis

SUMMARY

- Endometrial carcinomas are diverse and, when differentiated, are morphologically distinctive.
- The differential diagnosis can be extensive, but morphology and ancillary studies are often definitive.



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