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Mixed epithelial and mesenchymal uterine tumours

BAGP teaching session

24'th February 2021

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Objectives :

1. WHO 2020 classification of mixed epithelial and mesenchymal uterine tumours.
2. Diagnostic clues for each entity
3. Prognostic features
4. Differential diagnosis and
5. Mimics

Poll question :1

According to the WHO 2020 classification ,which of these are mixed epithelial and mesenchymal uterine tumours?

WHO 2014

1. Adenomyoma
2. Atypical polypoid adenomyoma
3. Adenofibroma
4. Adenosarcoma
5. Carcinosarcoma

WHO 2020

1. Adenomyoma
2. Atypical polypoid adenomyoma
3. Adenosarcoma

WHO 2020: Mixed epithelial and mesenchymal uterine tumors

	GLANDS	STROMA
Adenomyoma	Benign	Benign
Atypical polypoid adenomyoma	Atypical	Benign
Adenosarcoma	Benign	Atypical

Adenomyoma

- Benign tumour composed of admixture of benign endometroid type glands + endometrial type stroma (varying amount which can be inconspicuous) + smooth muscle

- AKA :

Adenomyomatous polyp or polypoid adenomyoma

- Sites:

Submucosal , intramural , subserosal , broad ligament

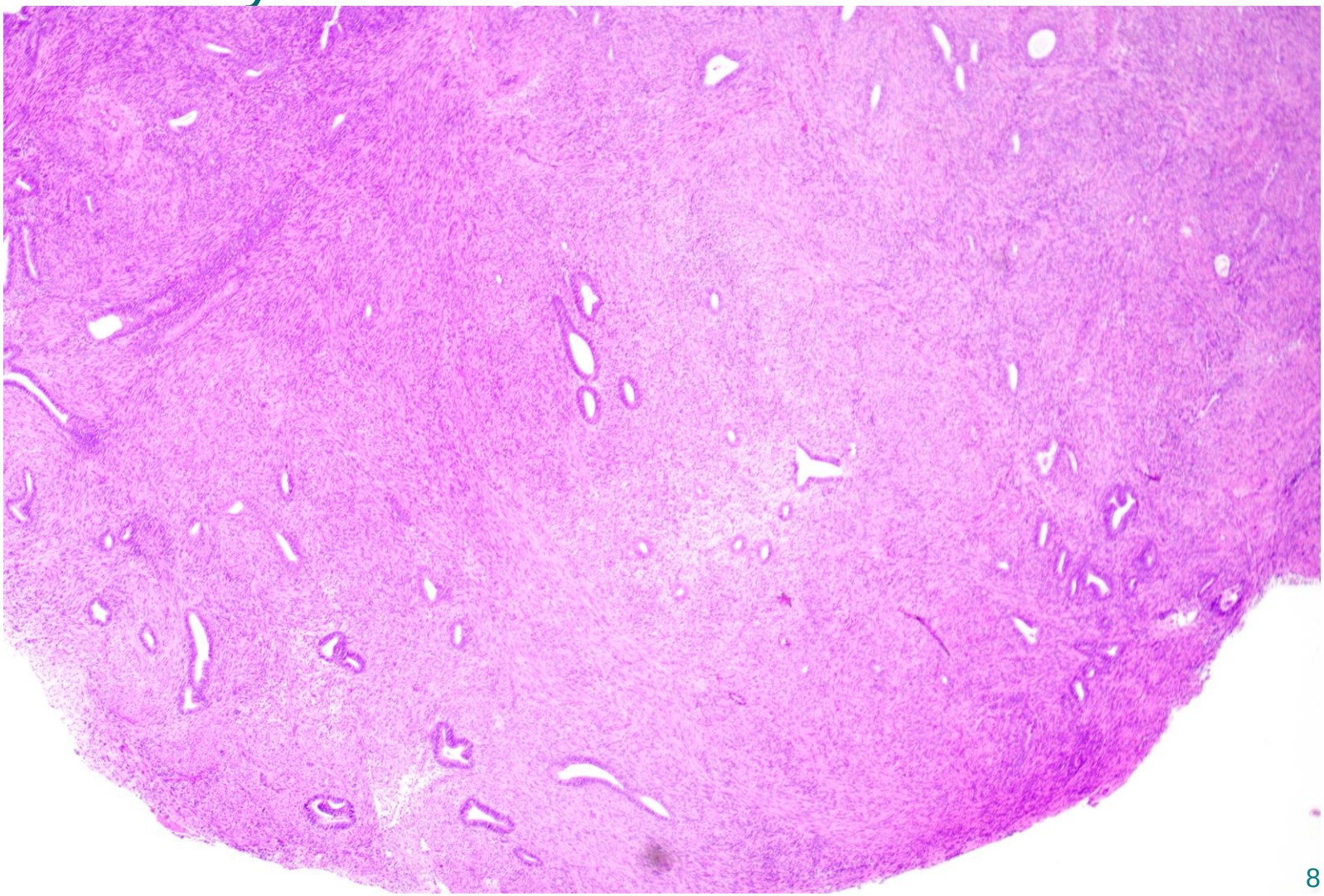
- Epithelial metaplasia :

Tubal, mucinous ,squamous

Adenomyoma



Adenomyoma



Adenomyoma

DD:

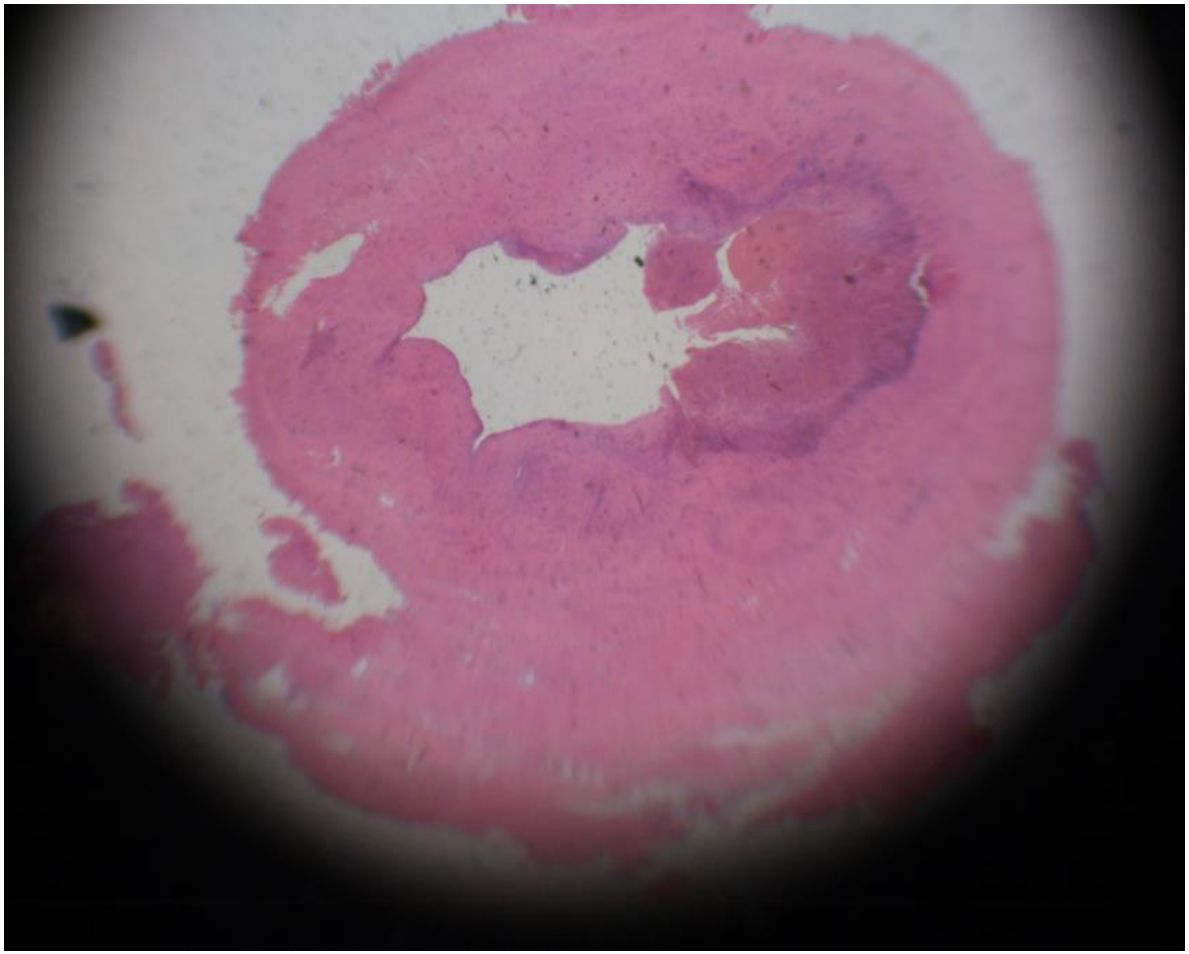
1. Accessory cavitated uterine mass (ACUM) /Juvenile cystic adenomyoma - <30 years, -/> 1cm cystic lesion, located in the lateral wall.

2. Non-communicating horn of unicornuate or bicornuate uterus.

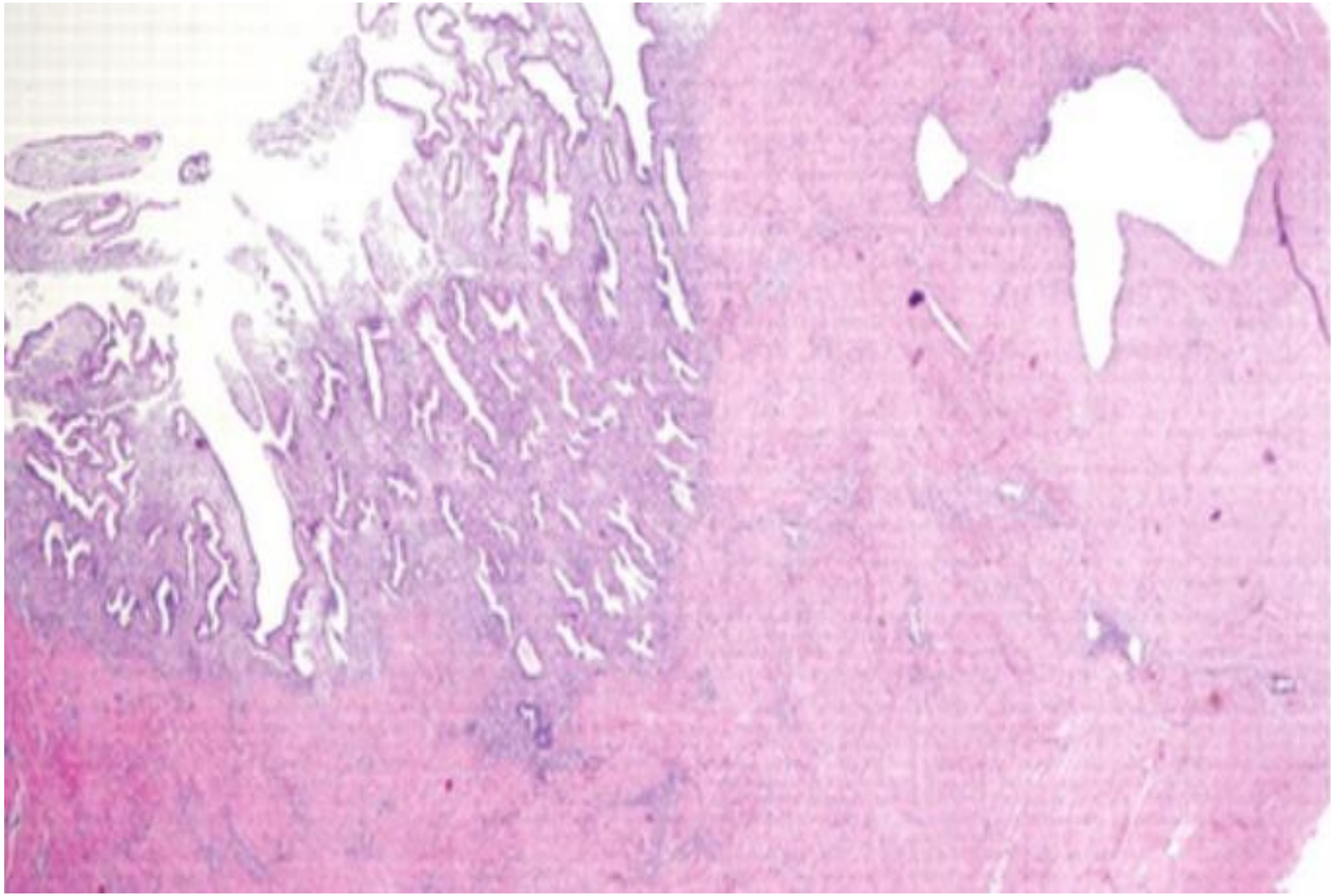
3. Endometrial polyp- not uncommon for a minor component of smooth muscle to be present in the stroma .

	ACUM	Non-communicating uterine horn	Cavitatory Adenomyoma
Definition	Mullerian anomaly without uterine malformation Isolated cavitated mass at the level of round ligament insertion.	Mullerian anomaly with uterine malformation (unicornuate uterus, bicornuate uterus)	A focal adenomyosis which is not in direct continuity with the endometrial cavity
Pathophysiology	Caused by duplication and persistence of the Mullerian duct	Due to the failure of Mullerian ducts to elongate towards the urogenital sinus	Invagination of the endometrial basalis layer into the myometrium

ACUM



Bicornuate uterus with rudimentary uterine horn



Atypical polypoid adenomyoma (APA):

- Polypoid lesion composed of cytologically atypical and architecturally complex endometrial glands set within benign fibromyomatous or myofibroblastic stroma.

- Site:

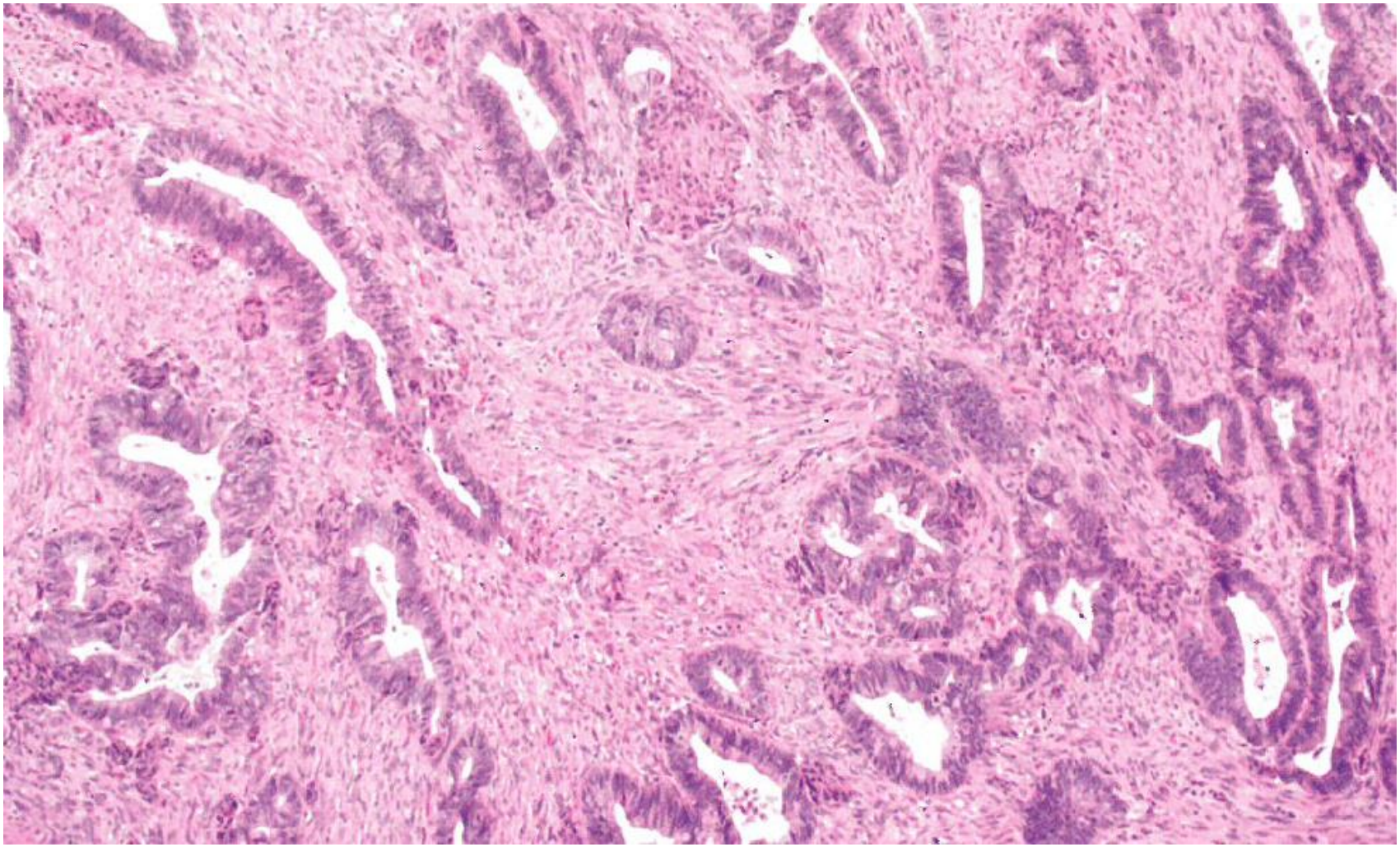
Tend to occur in LUS but may arise in corpus.

- Pathogenesis:

May arise secondary to prolonged estrogen stimulation

- IHC and molecular features similar to AH and low grade endometroid adenoca

APA



APA

Prognosis :

- Risk of recurrence for usual APA is 30%
- Risk of recurrence is higher with more complex architecture up to 60% .
- Risk of progression to adenoca is 8.8 %

APA

DD:

1. Low grade endometroid adenocarcinoma with myometrial invasion -in curettage specimens

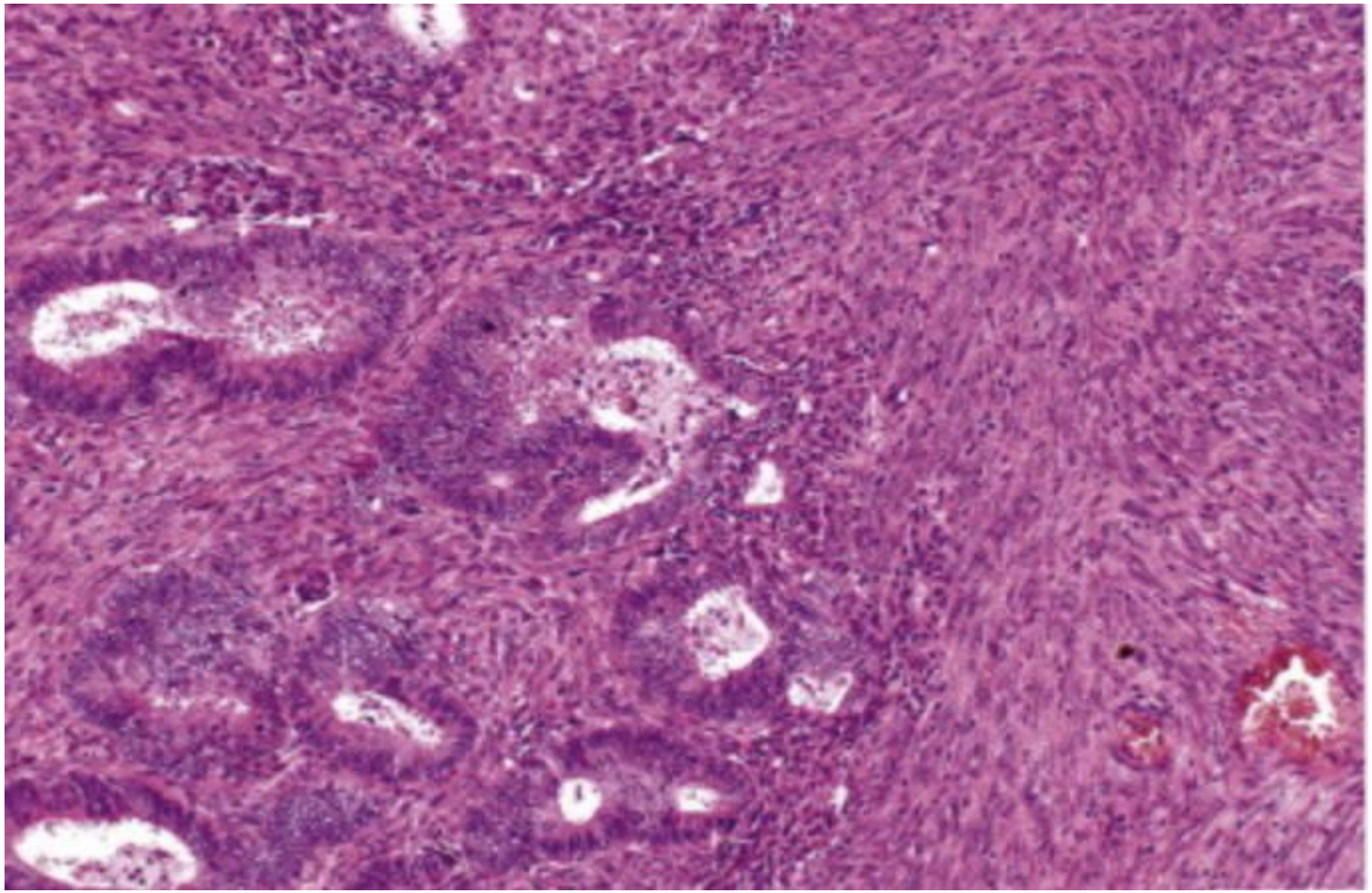
Important to be able to differentiate as conservative management is an option for APH patients wishing to retain fertility and to avoid unnecessary hysterectomy .

2. Adenomyomatous polyp : no gland crowding or atypia , absence of squamous morules.

Poll question : 2

35 year old presents with 6 month h/o menorrhagia. US detected thickened and polypoid endometrium.

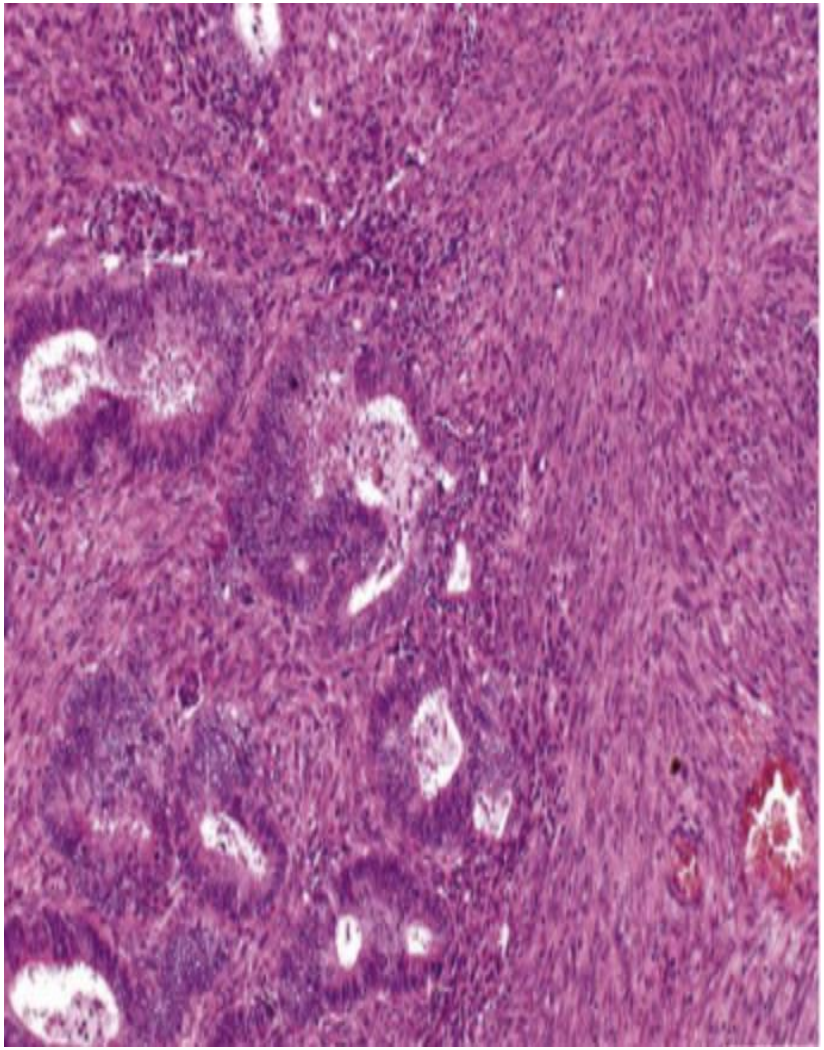
What is your diagnosis ?



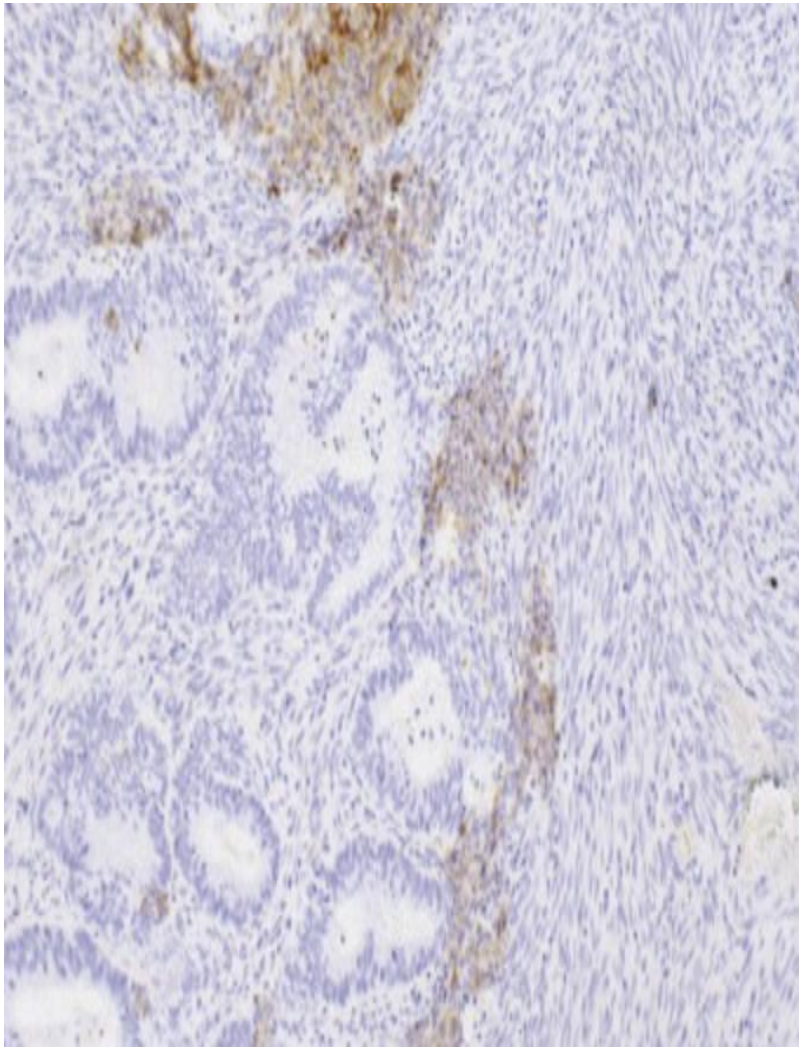
APA v/s myoinvasive carcinoma:

CD10 is usually negative or only focally positive in APA . Fringe like staining pattern of CD10 is seen in myoinvasive adenocarcinoma.

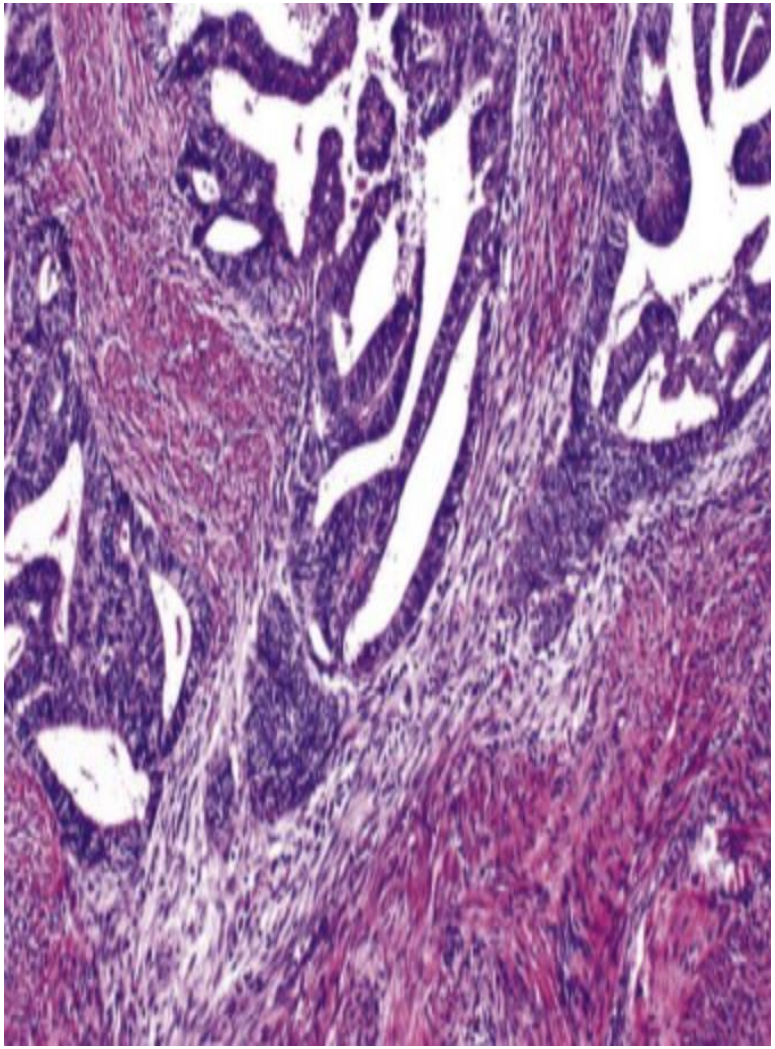
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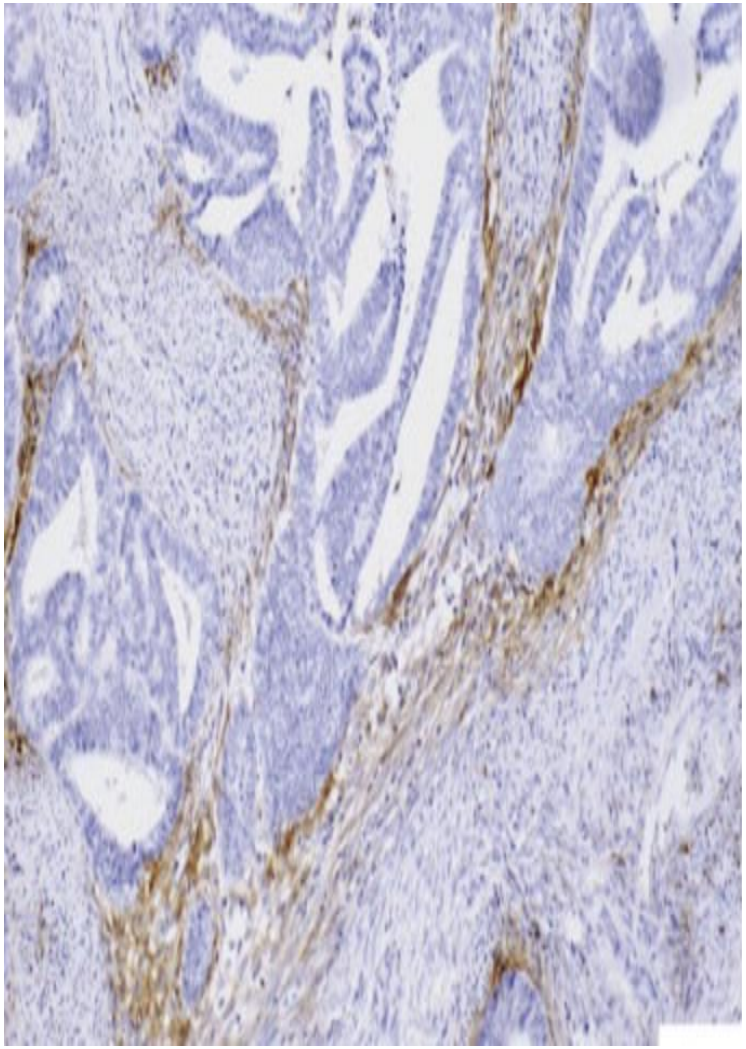


CD10



Myoinvasive adenocarcinoma with fringe pattern of CD10 staining





APA v/s myoinvasive carcinoma:

- The fibromyomatous stroma of APA is typically negative for **H-caldesmon** in contrast to myometrium in myoinvasive endometrial adenocarcinoma.

- Stromal **p16** expression is suggestive of APA than myoinvasive endometrioid carcinoma.
  (AJSP Nov19, Volume 43 (11), p 1526–1535)

- **STATB2** nuclear staining is seen in stromal cells of APA
  (Int J Gynecol Pathol. 2019 Sep;38(5):397-403)

APA – fibromatous stroma	CA- infiltrated myometrium
CD10 - / partially +	periglandular fringe-like CD10 staining
H-caldesmon - /only focally +	H-caldesmon ++
P16 +	P16 -
In glands Ki67 <15%	Ki67 >50%

Adenosarcoma:

Biphasic tumour with benign epithelial component and a malignant stromal component.

AKA Mullerian adenosarcoma

Sites:

Uterus – most common

Can also occur in cervix, vagina ,ovary, FT, peritoneal surfaces(presumably arising from endometriosis)

Adenosarcoma:

Characteristic features:

Architechture:

- Low power phyllodes like architecture
- Peri glandular condensation (subepithelial cambium layer)
- Intraglandular protrusions of cellular stroma

Epitheium:

- Benign but can show mild atypia and metaplastic changes

Stroma:

- Typically low grade but can be high grade.
- Previous criteria – 2 or more mitosis /10 hpf needed to distinguish from adenofibroma.

  Current criteria : mitotic activity can be minimal or even absent in adenosarcoma.

Adenosarcoma:

Stromal characteristic features:

- Stromal over growth when >25% of the tumour shows pure sarcoma
- Sarcoma is typically homologous but not uncommon to have heterologous elements like rabdomyosarcoma or chondrosarcoma
- Stroma can show focal sex cord differentiation

IHC:

- CD10+,ER+,PR+ but this can be lost in sarcomatous overgrowth

Worse prognosis

- Sarcomatous overgrowth
- Heterologous stromal elements
- High grade stroma
- Stage

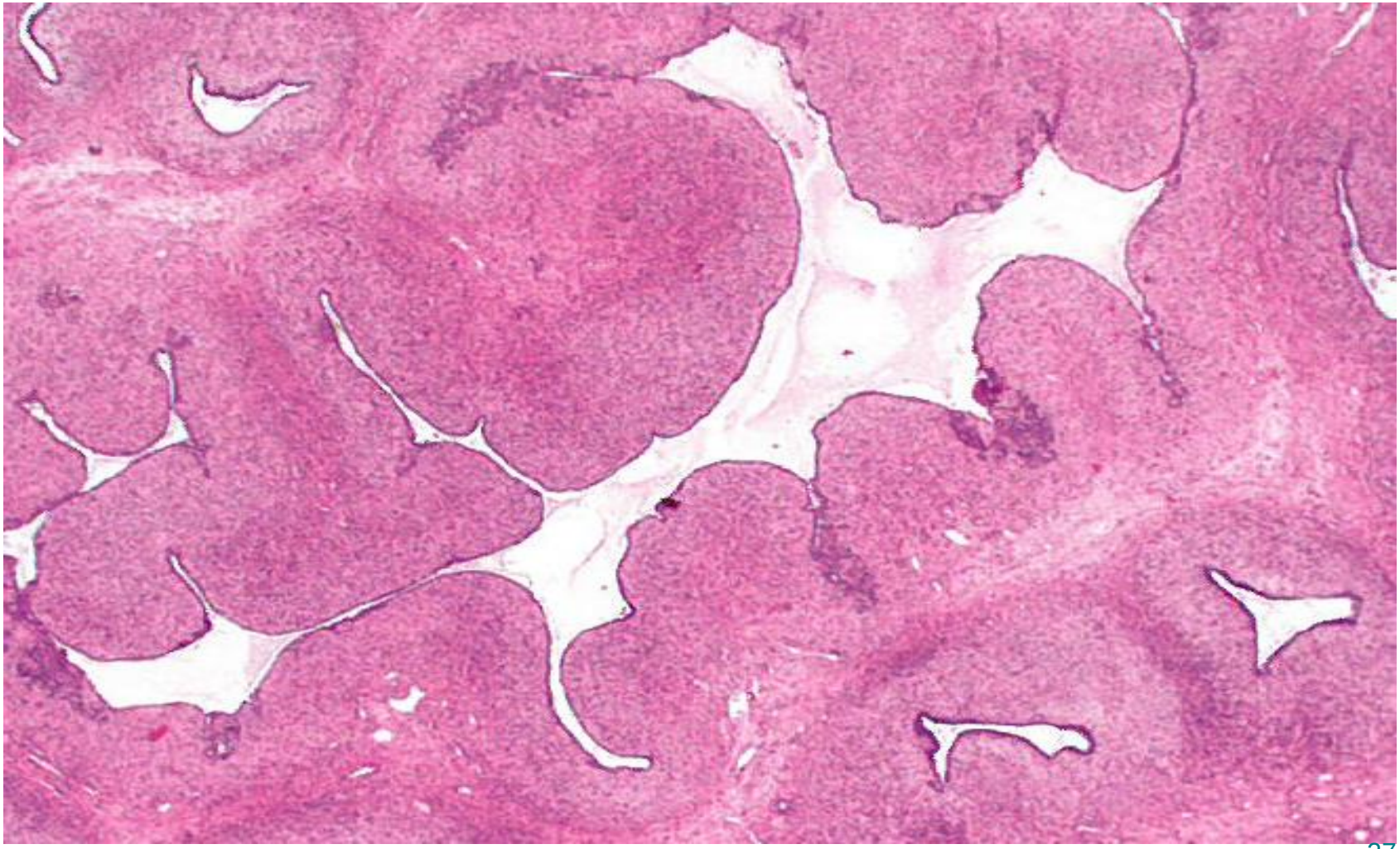
Adenosarcoma

TNM	FIGO	Description
T1a	1A	Tumour limited to endometrium/endocervix
T1b	1B	Tumour invades <50% myometrium
T1c	1C	Tumour invades <50% myometrium

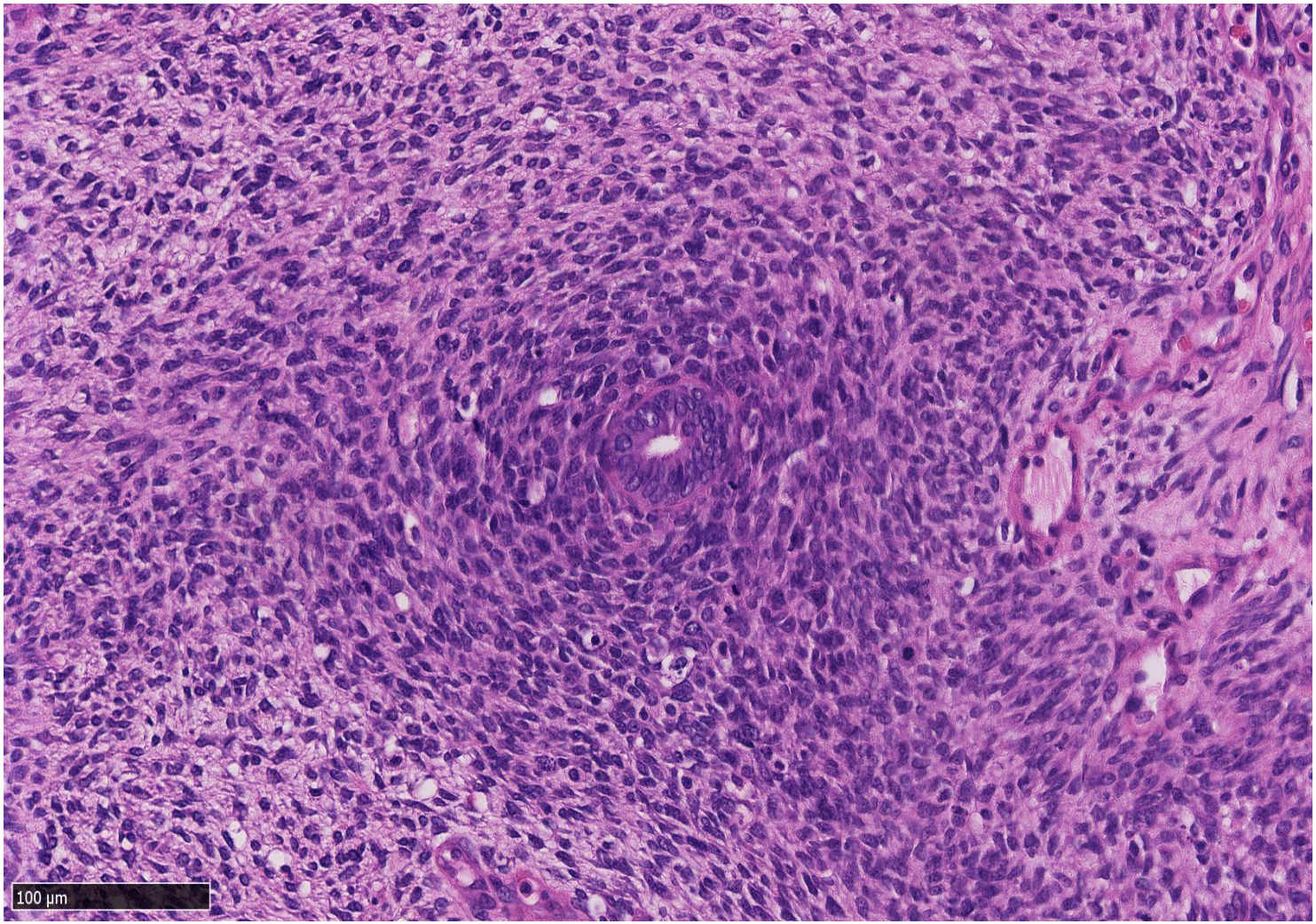
Leiomyosarcoma & Endometrial stromal sarcoma

TNM	FIGO	Description
T1a	1A	Tumour 5 cm or less in max dimension
T1b	1B	Tumour more than 5 cm

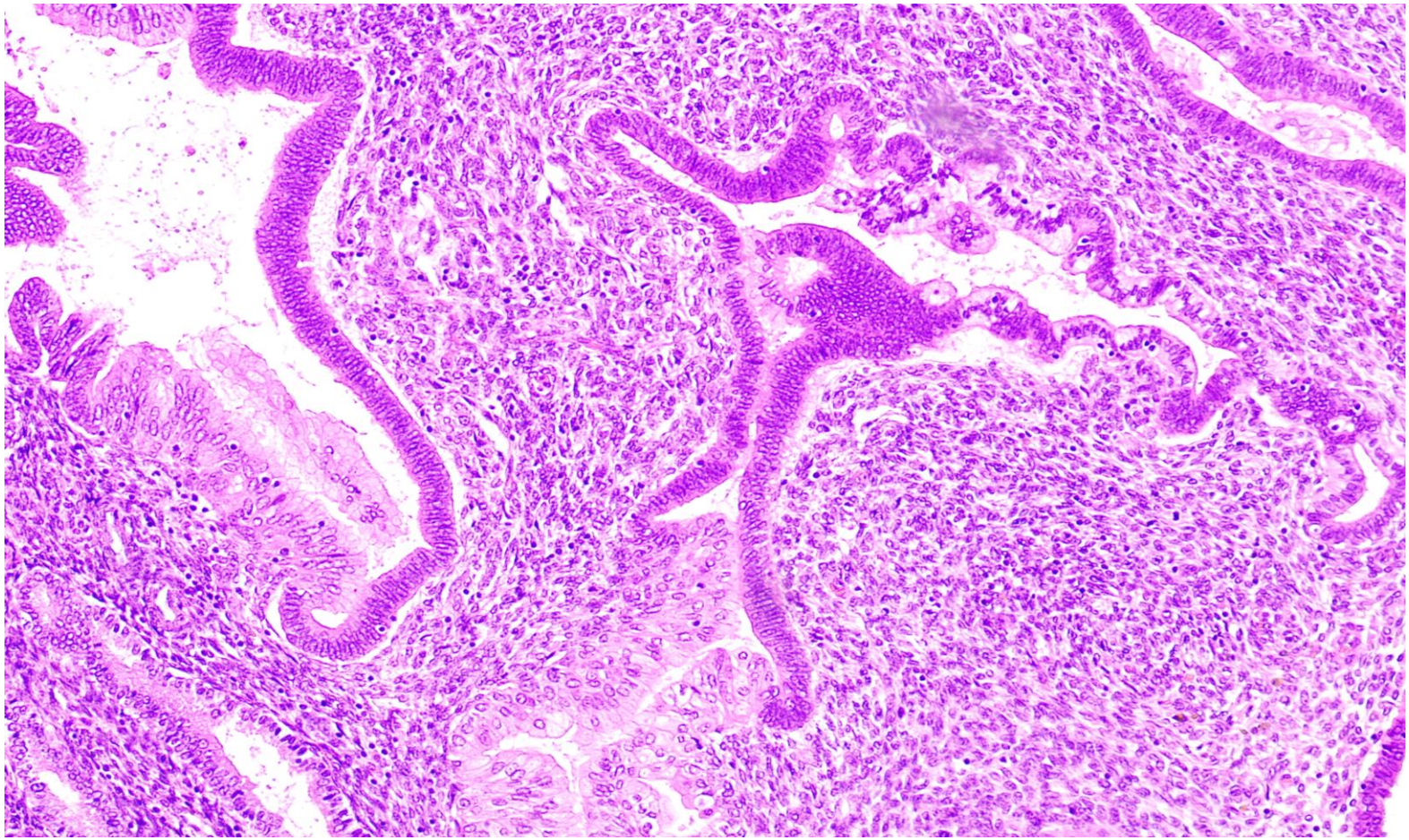
Phylloides like pattern



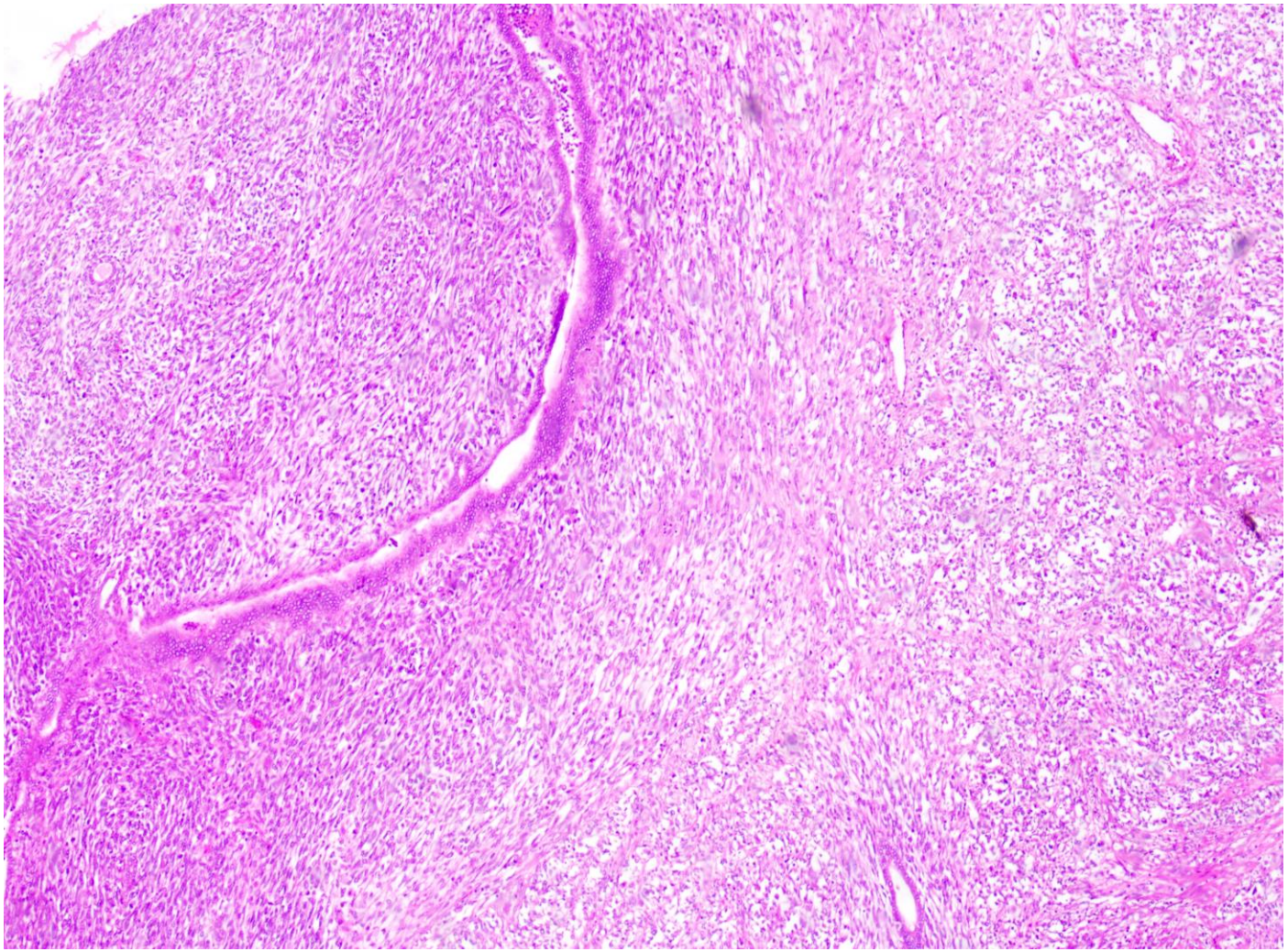
Periglandular cuffing



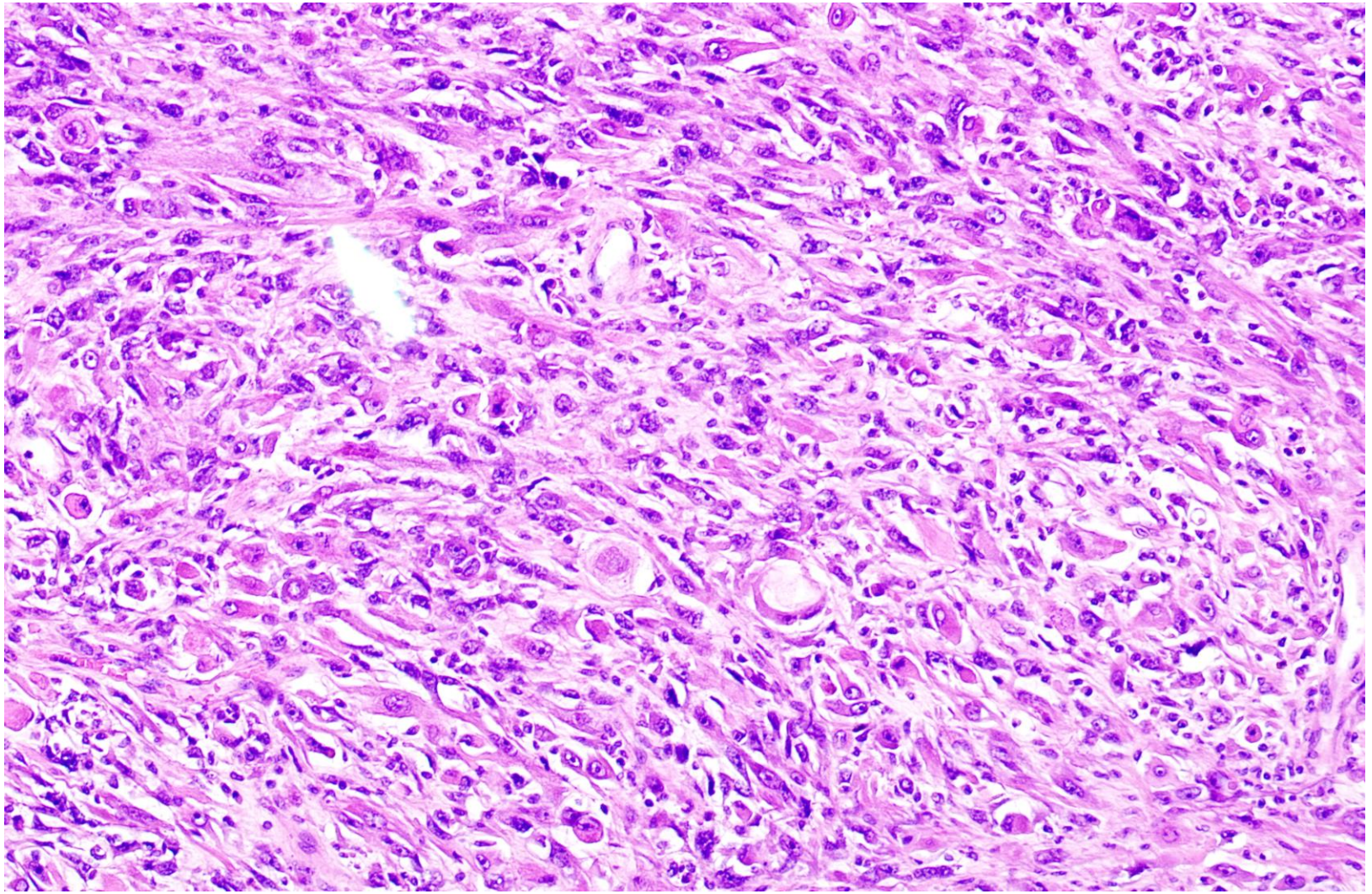
Intraglandular protrusions of cellular stroma



Adenosarcoma with sarcomatous overgrowth



Sarcomatous overgrowth with heterologous rabdomyosarcoma



Adenosarcoma:

DD:

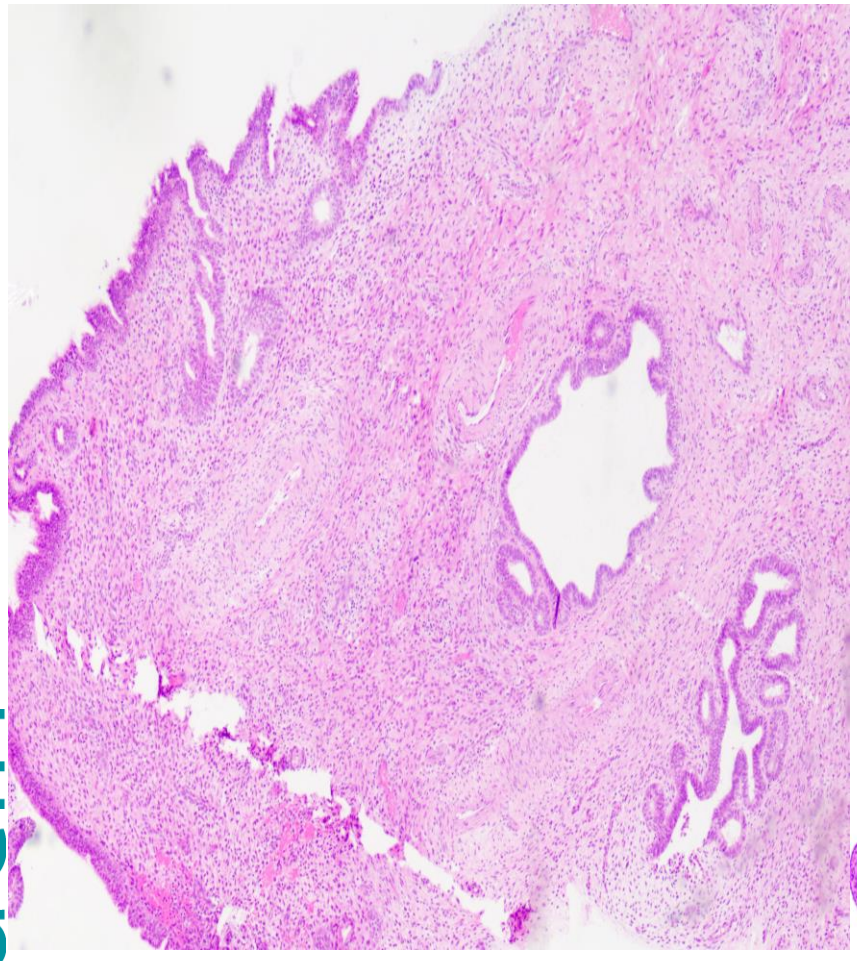
1. Endometrial polyp : lack of cambium layer, periglandular stromal cuffing , intraglandular stromal protrusion

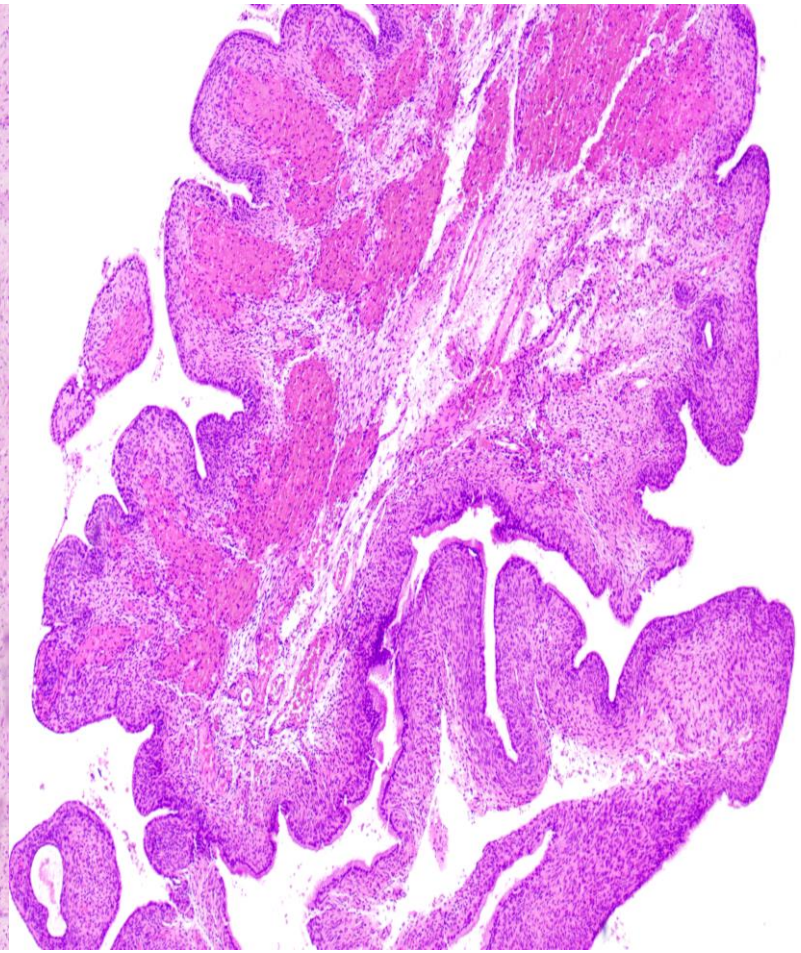
2. Carcinosarcoma : high grade epithelial component which can sometimes only be seen focally. Glandular atypia in adenosarcoma is only mild

3. Embryonal rabdomyosarcoma – Adenosarcoma with rabdomyoblastic differentiation can be difficult to distinguish. ER/PR + in adenosarcoma , lack of glandular component.

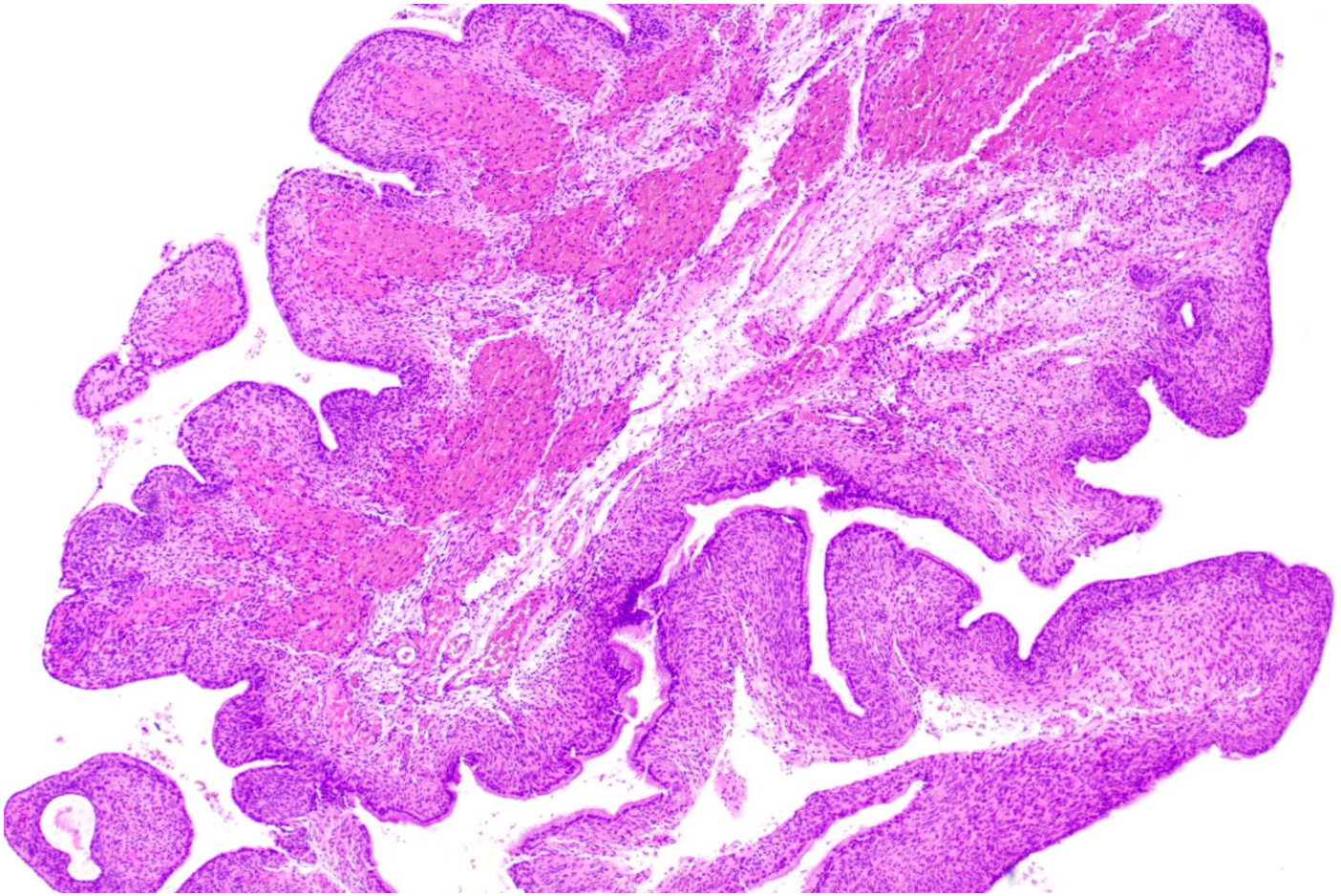
4. Endometrial stromal sarcoma: May be difficult in biopsy , similar IHC, lack of cambium layer, periglandular stromal cuffing , intraglandular stromal protrusion

Endometrial polyp vs Adenosarcoma

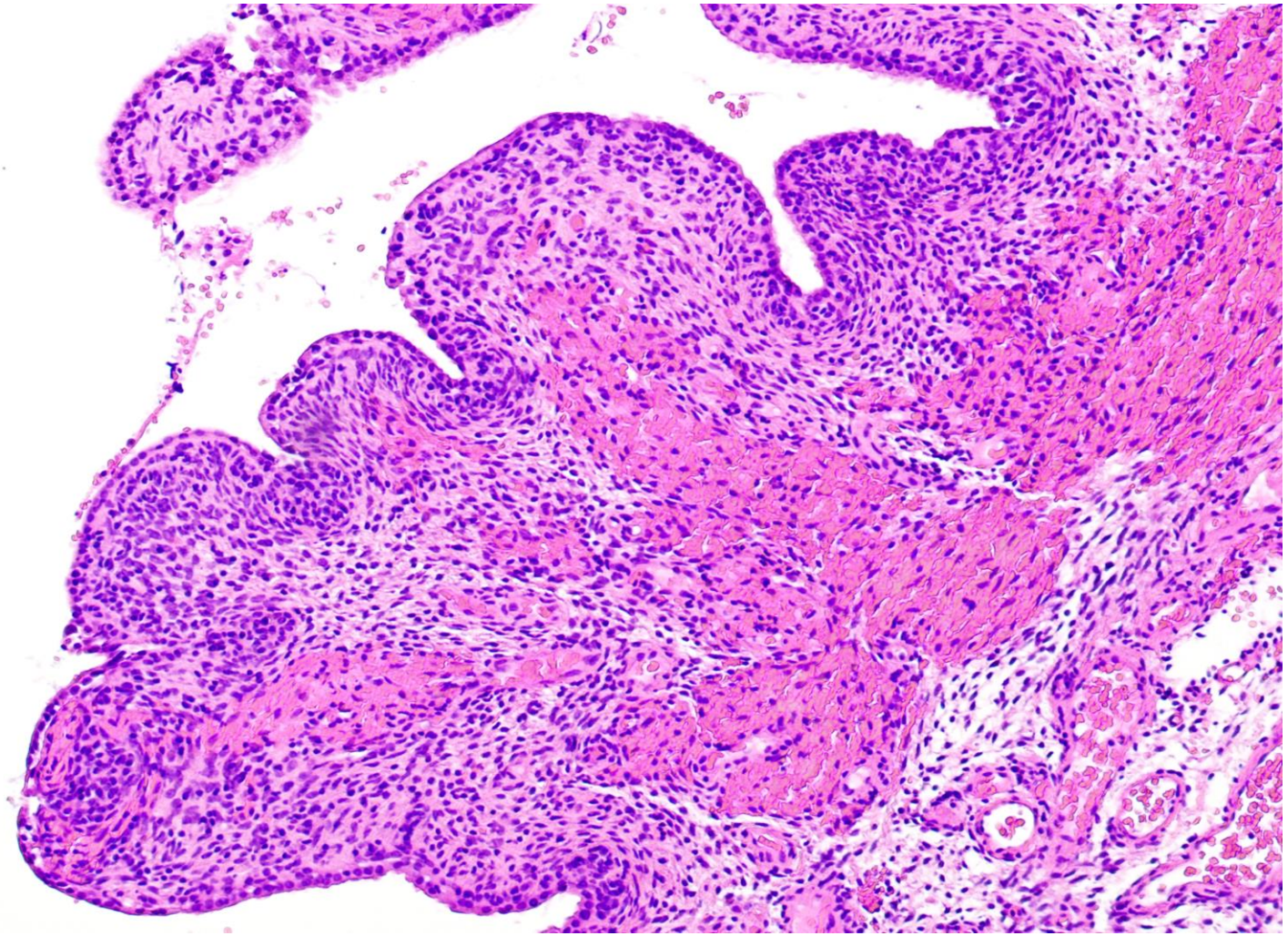




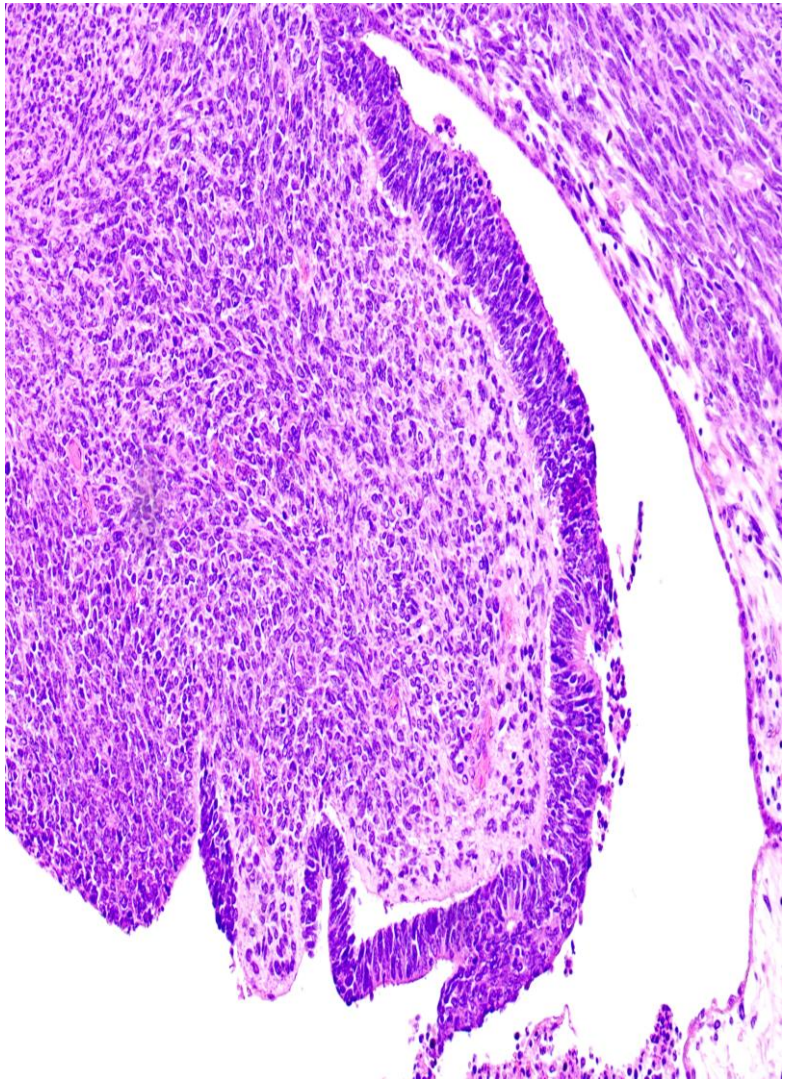
Small adenosarcoma



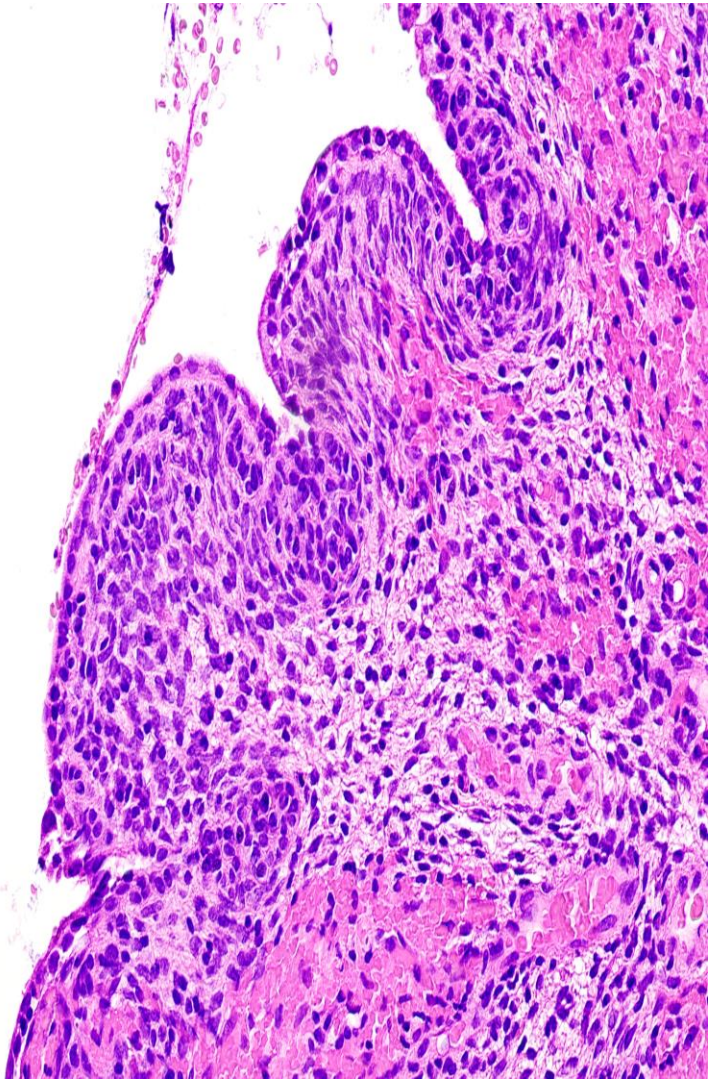
Subepithelial cambium layer



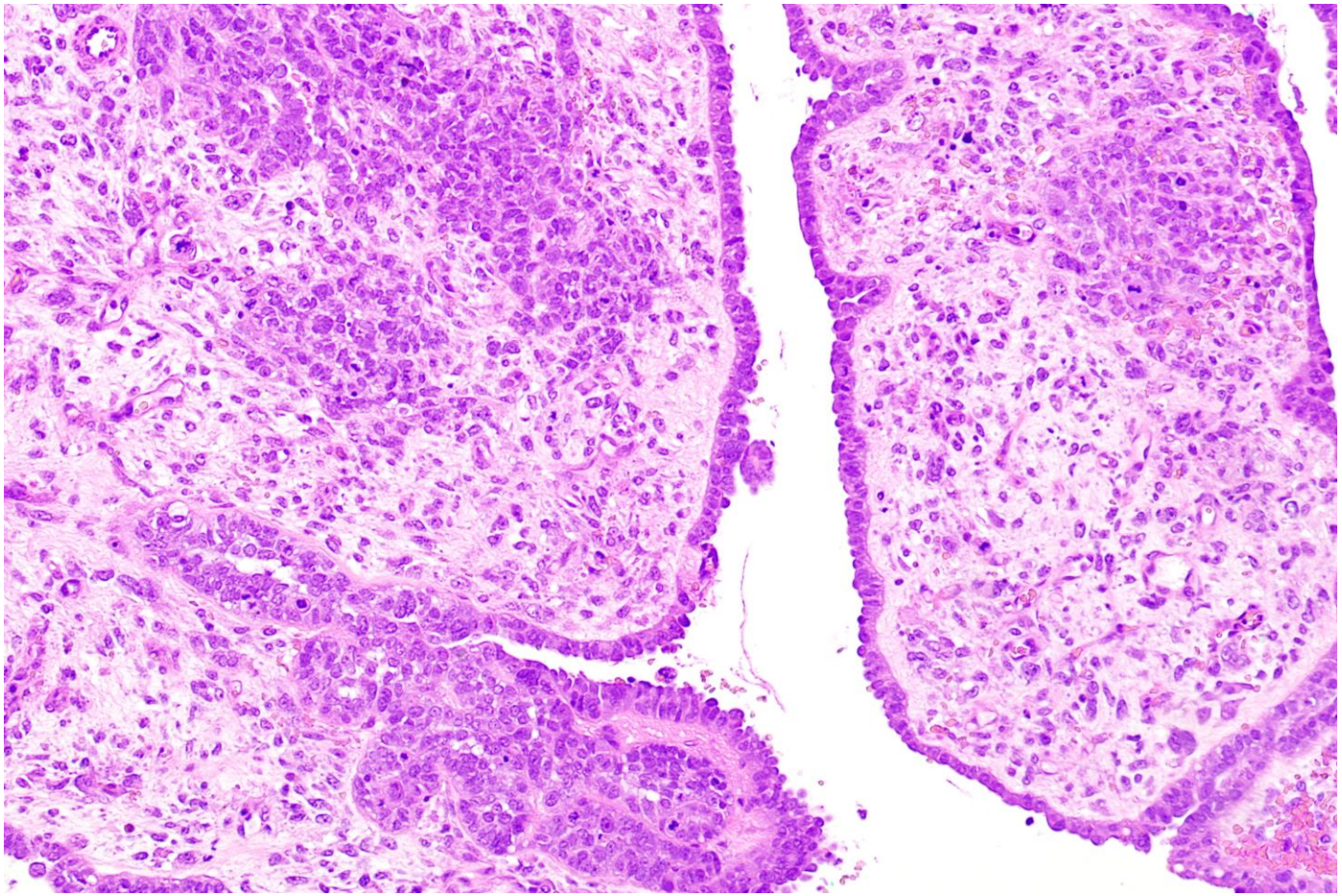
Carcinosarcoma



Adenosarcoma

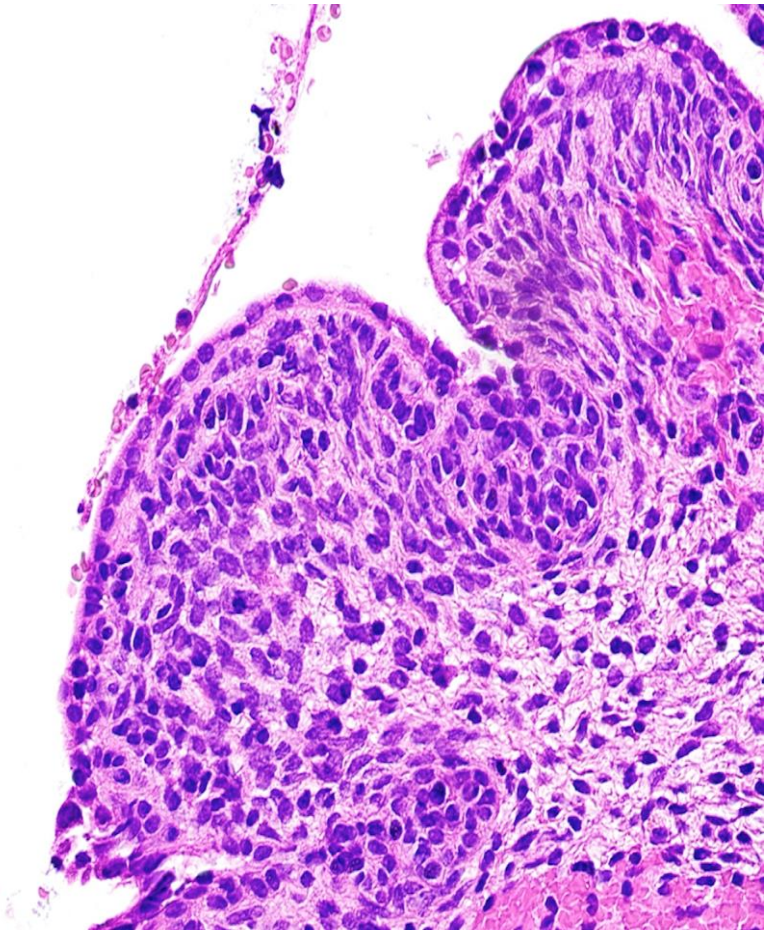


Carcinosarcoma

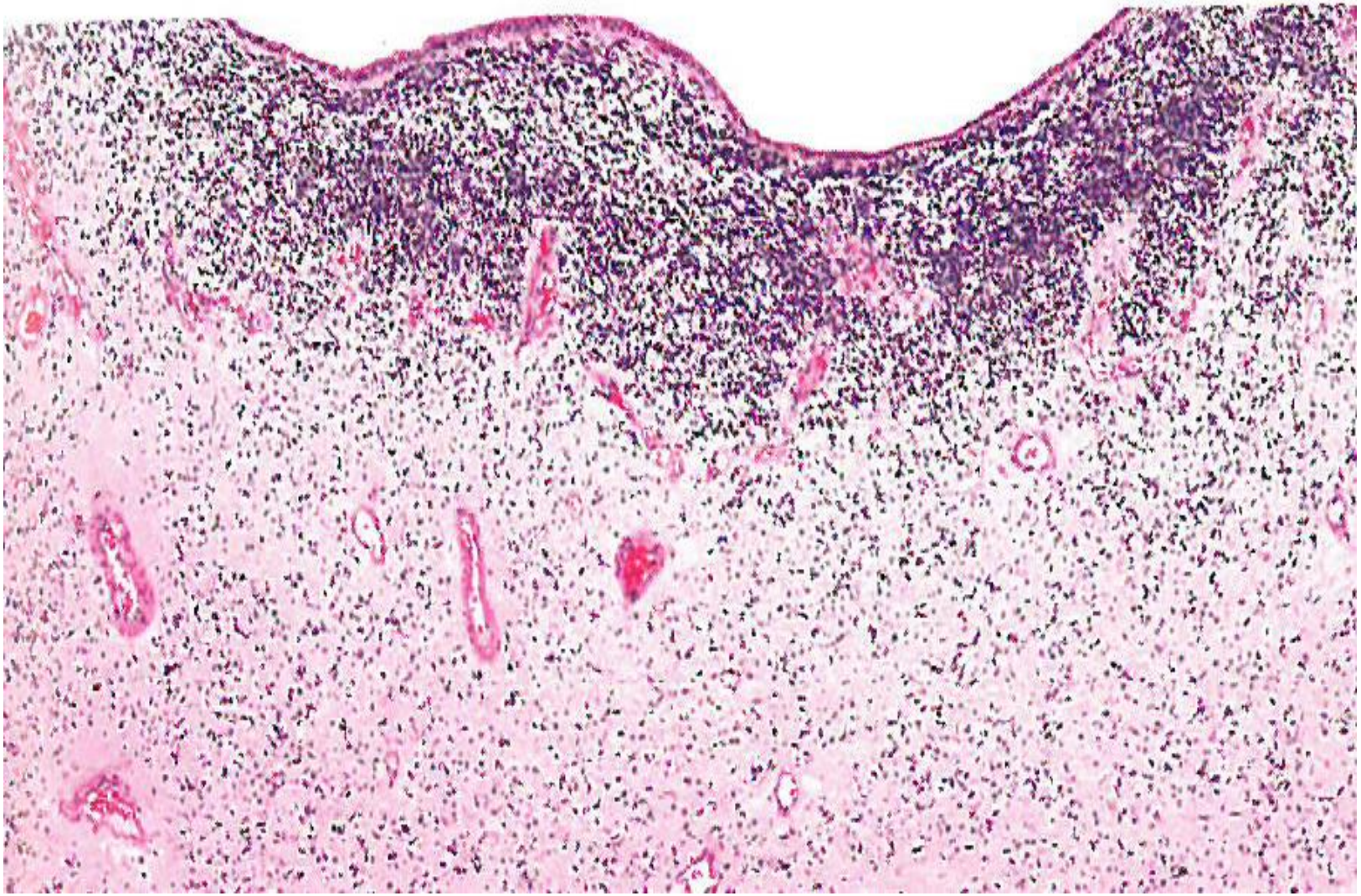


Embryonal rabdomyosaroma vs Adenosarcoma

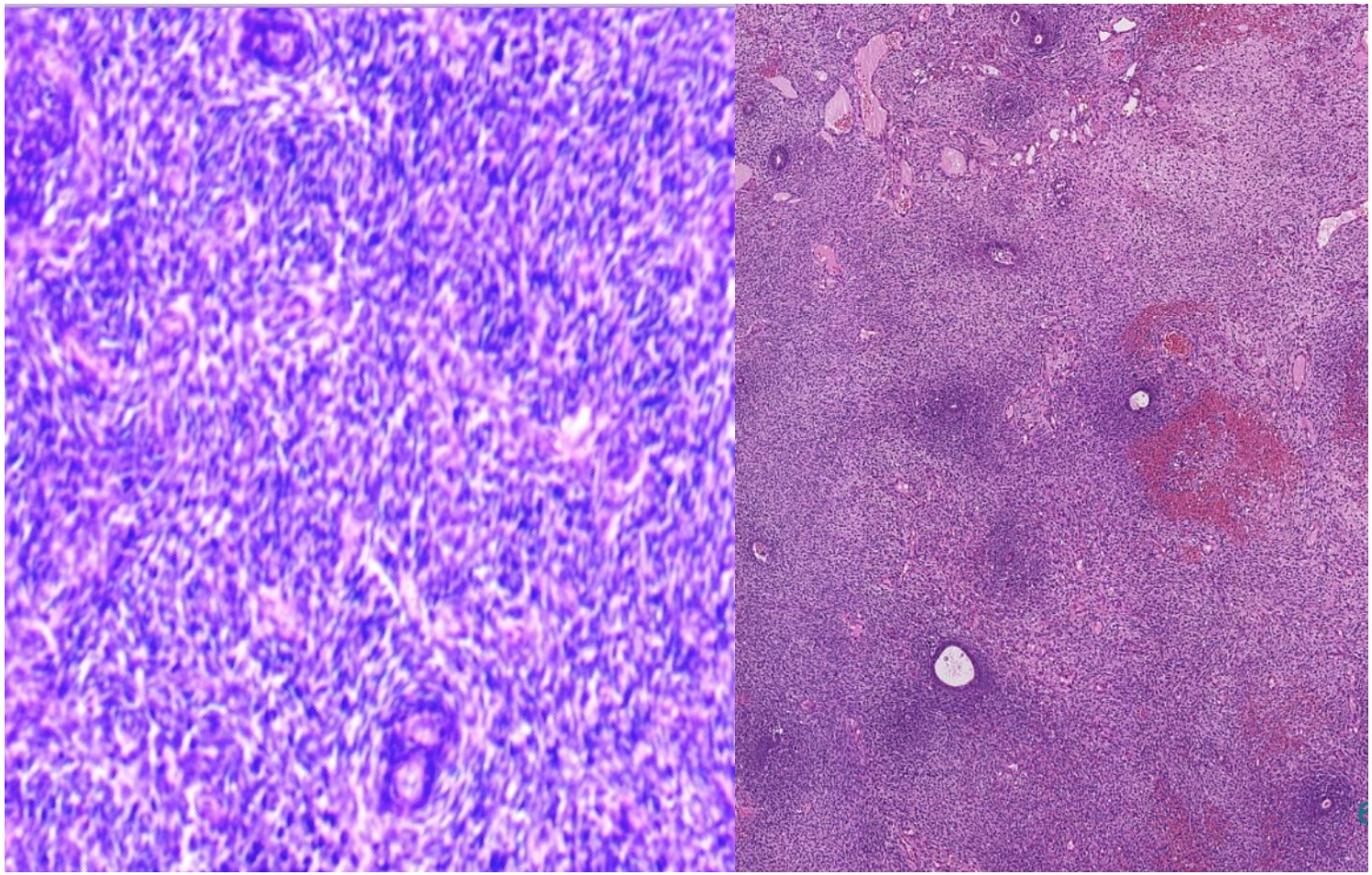




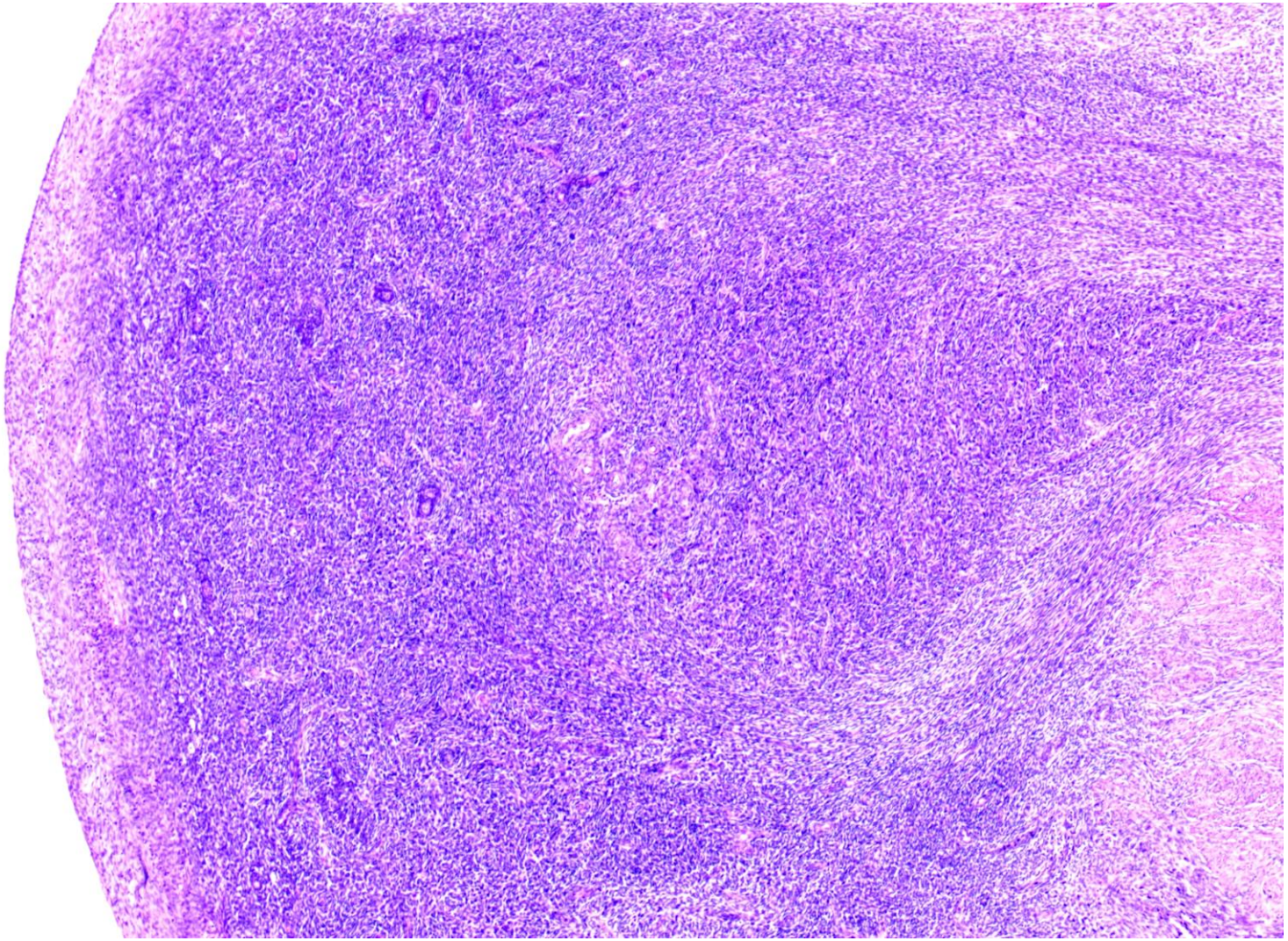
Embryonal rabdomyosaroma



Endometrial stromal sarcoma vs Adenosarcoma

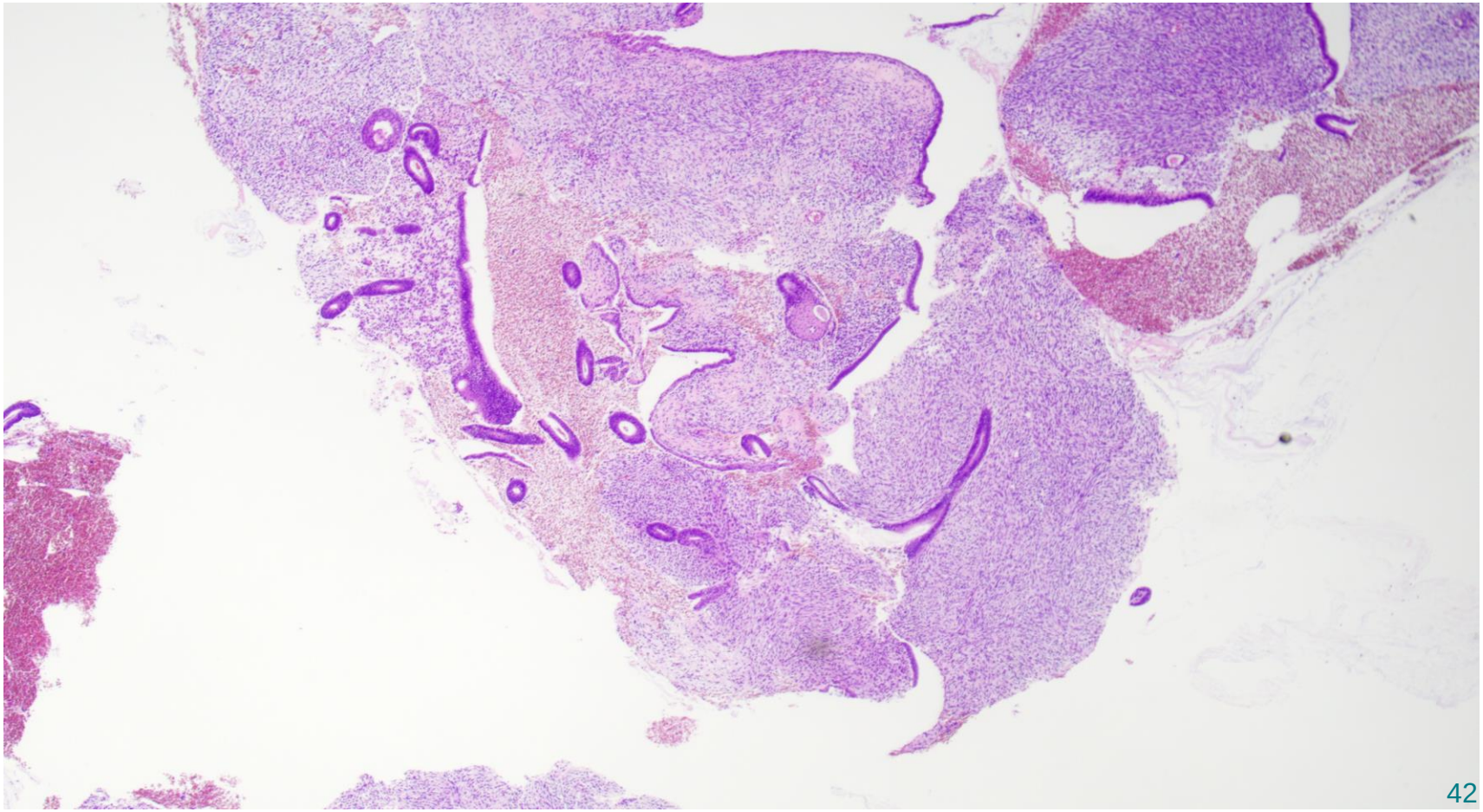


Endometrial stromal sarcoma

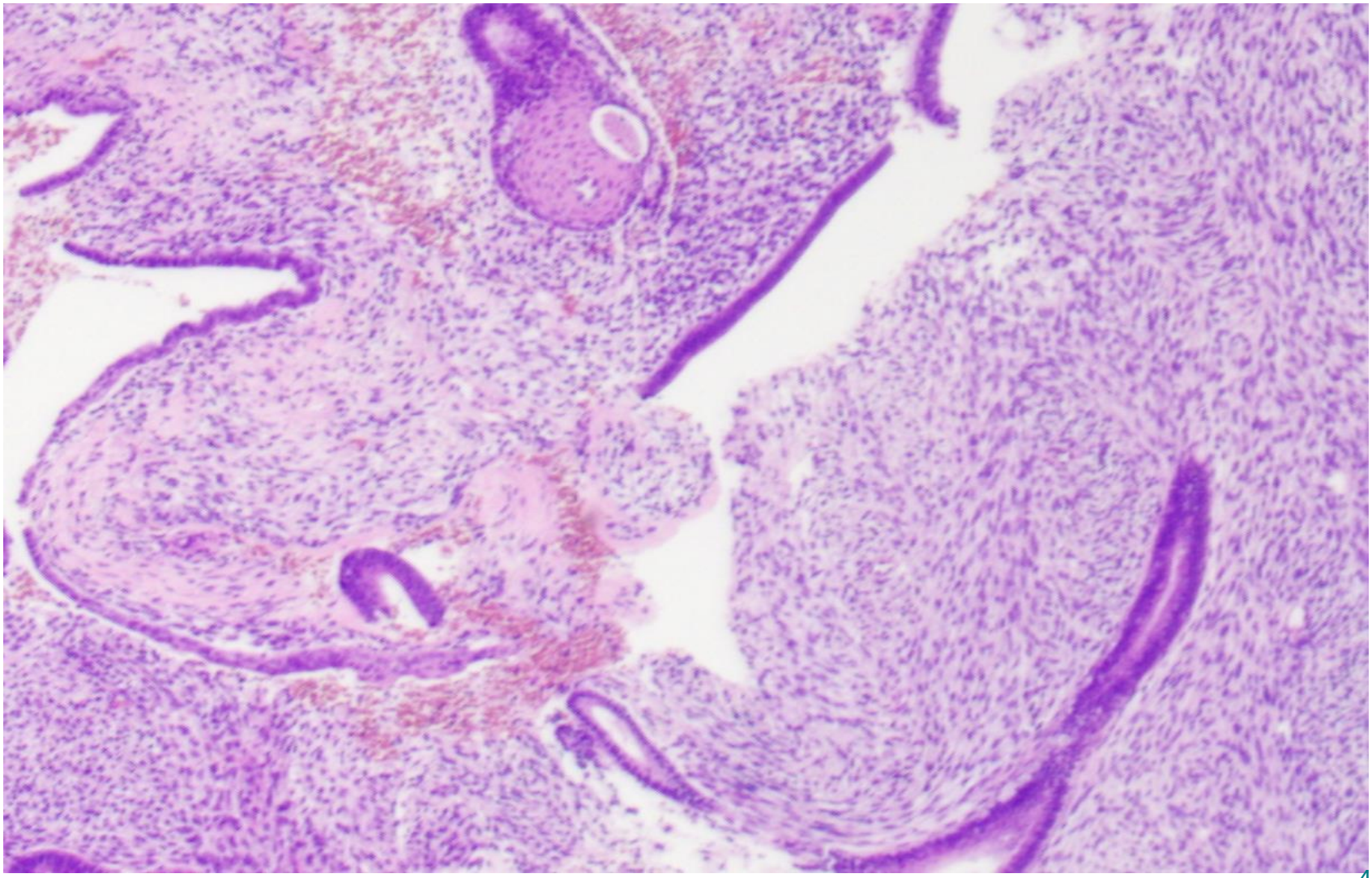


Poll question : 3

35 year old presents with 6 month h/o menorrhagia.
US detected thickened and polypoid endometrium.
What is your diagnosis ?

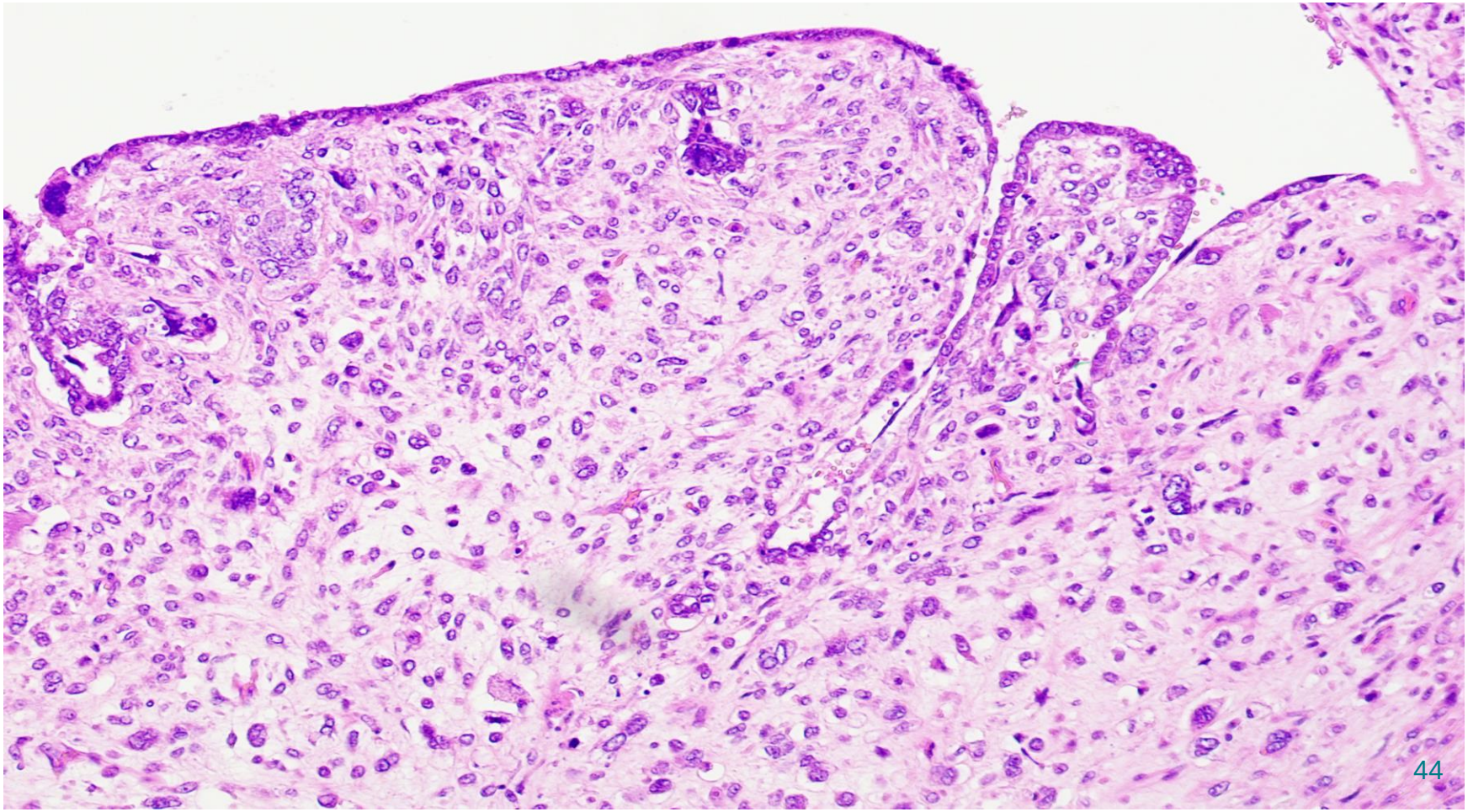


Adenosarcoma in endometrial currettings

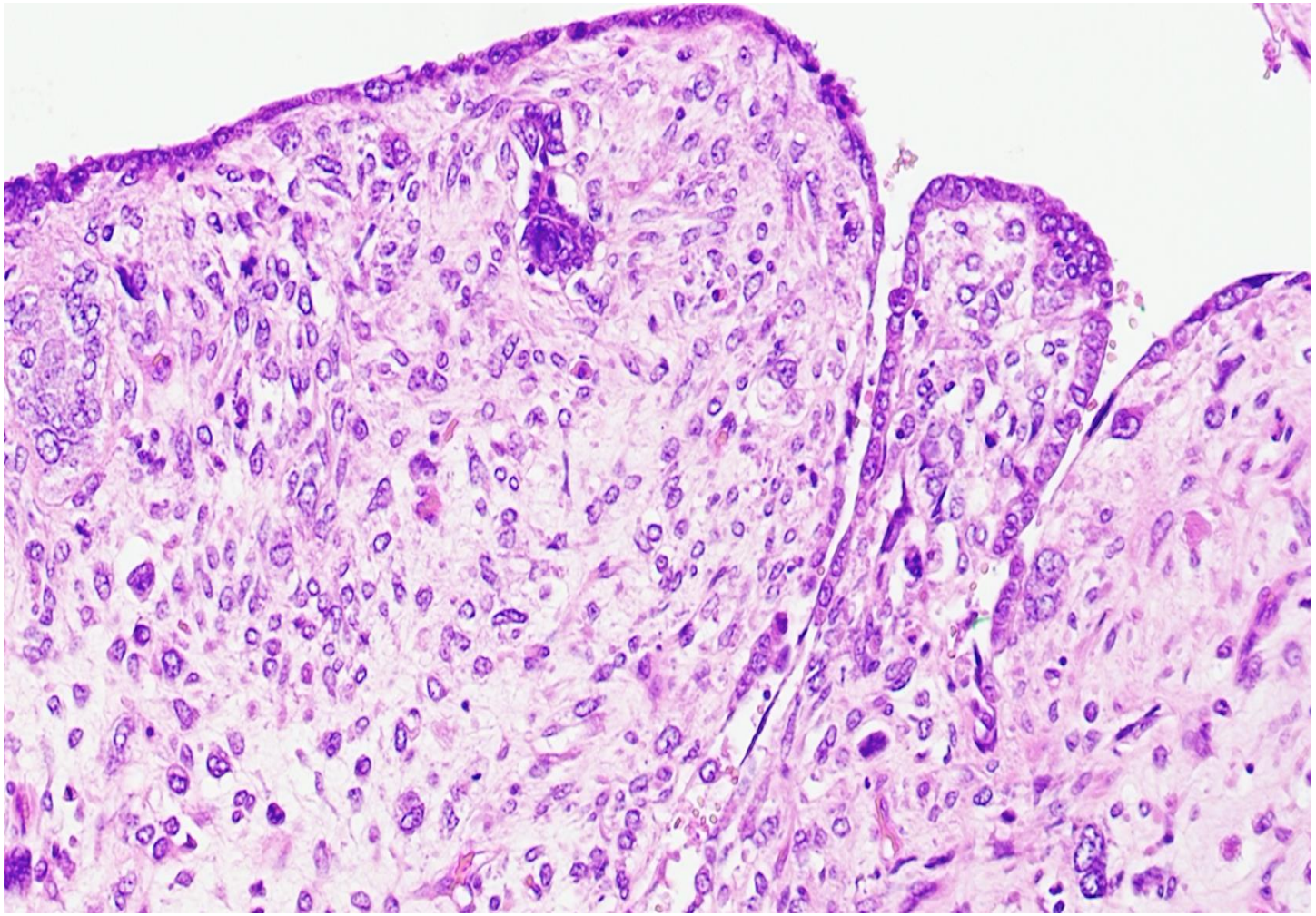


Poll question : 4

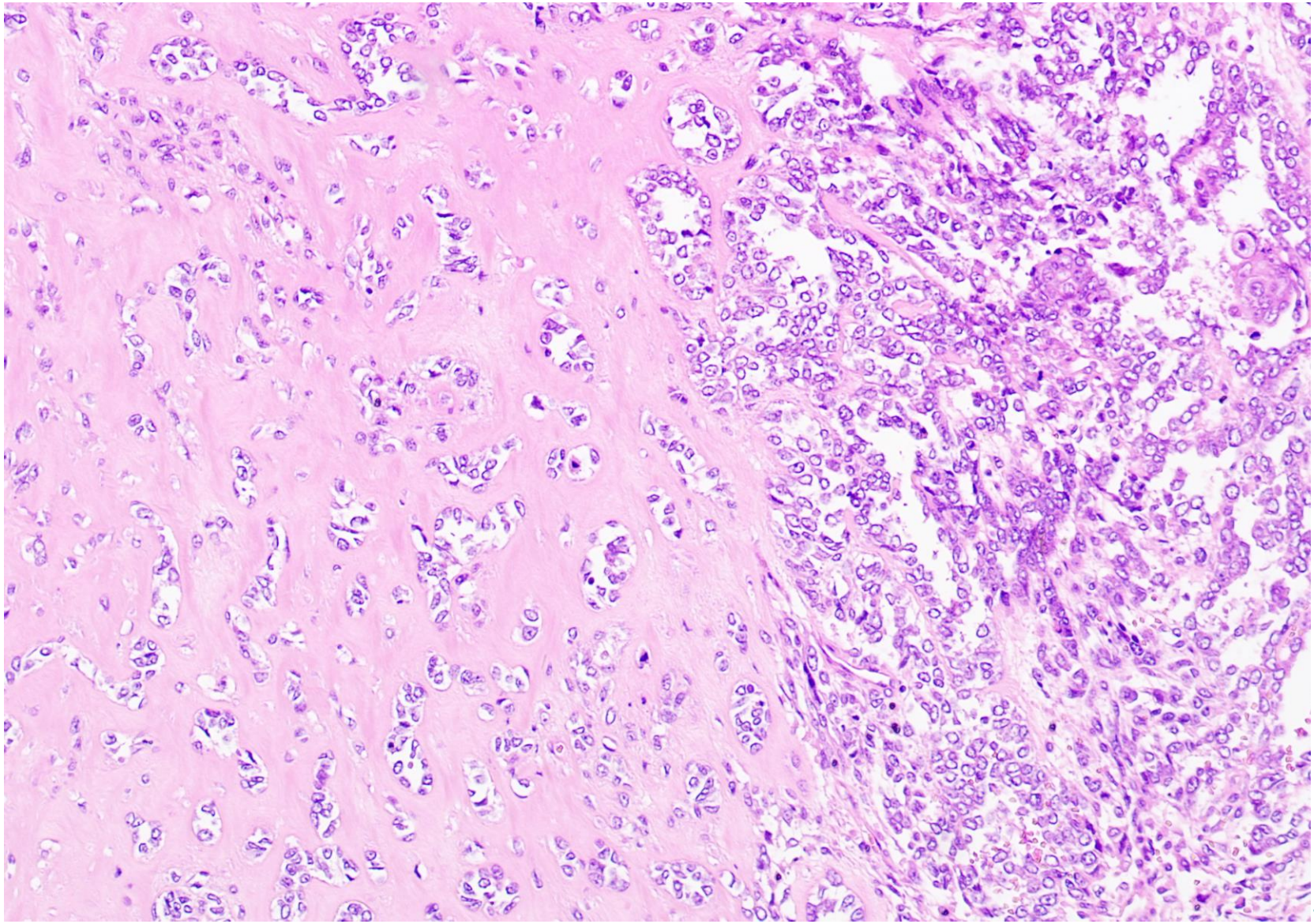
35 year old presents with 6 month h/o menorrhagia. US detected thickened and polypoid endometrium.
What is your diagnosis ?



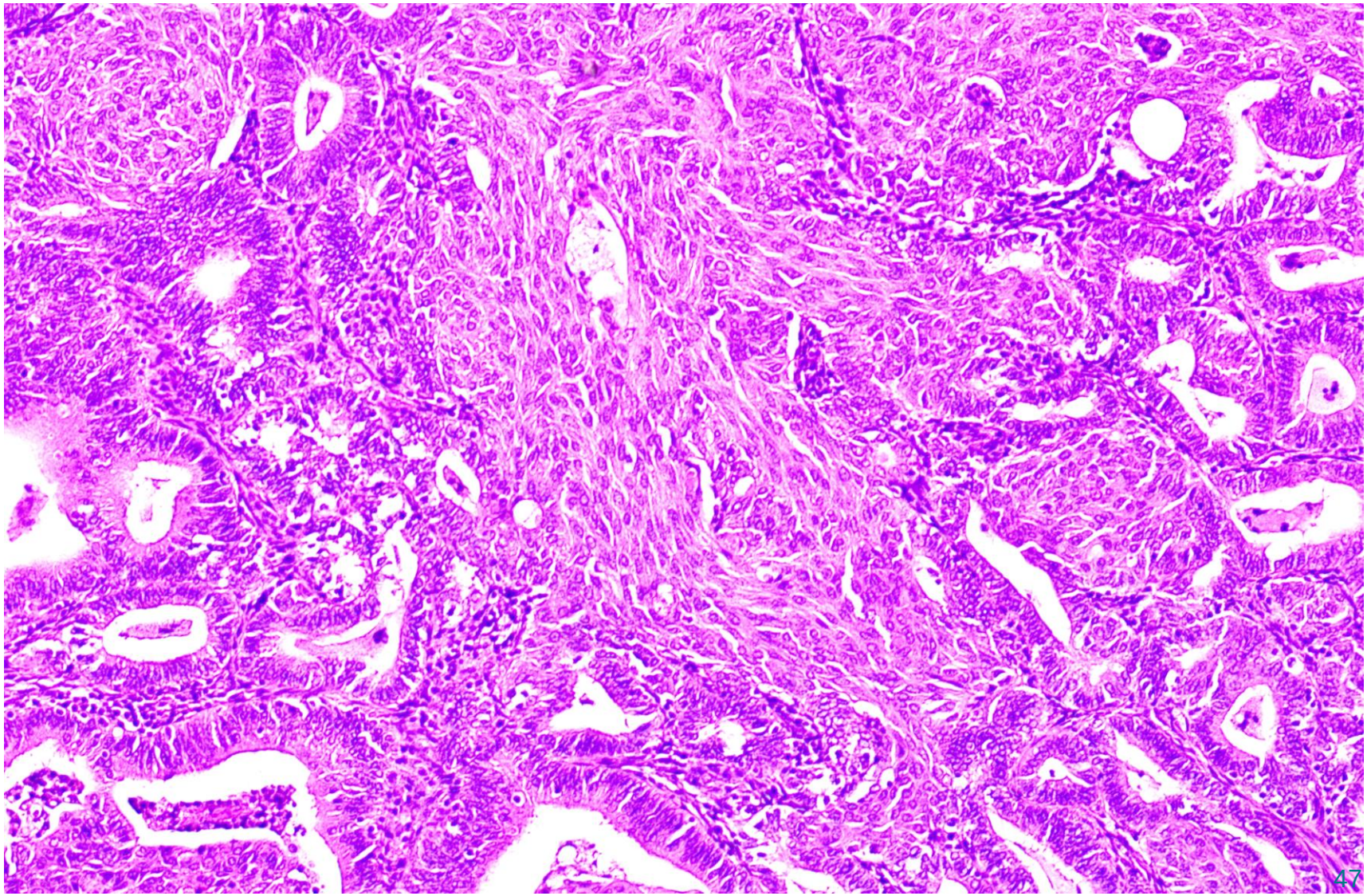
Adenosarcoma with high grade stroma



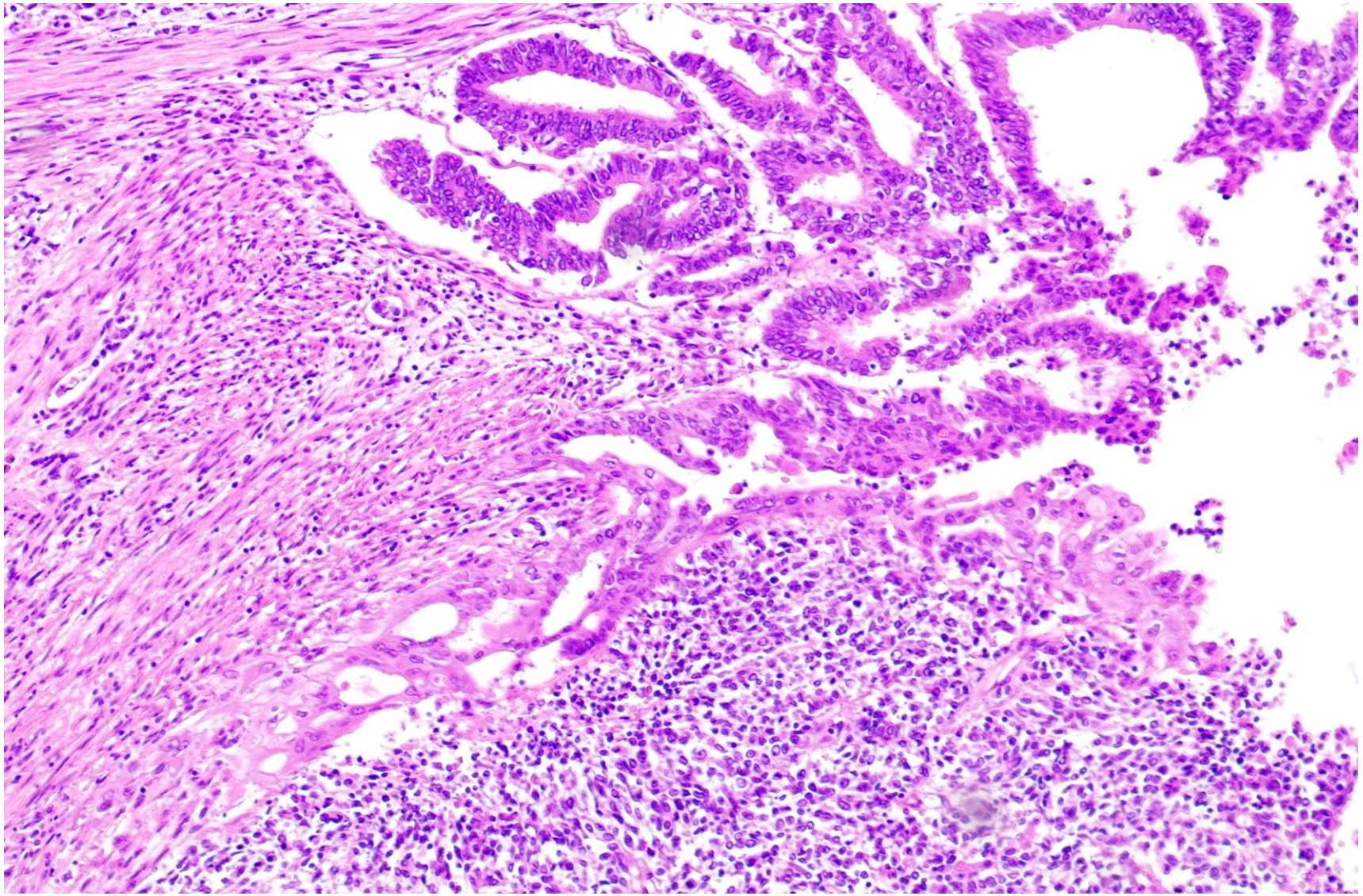
Mimic of mixed epithelial and mesenchymal tumour



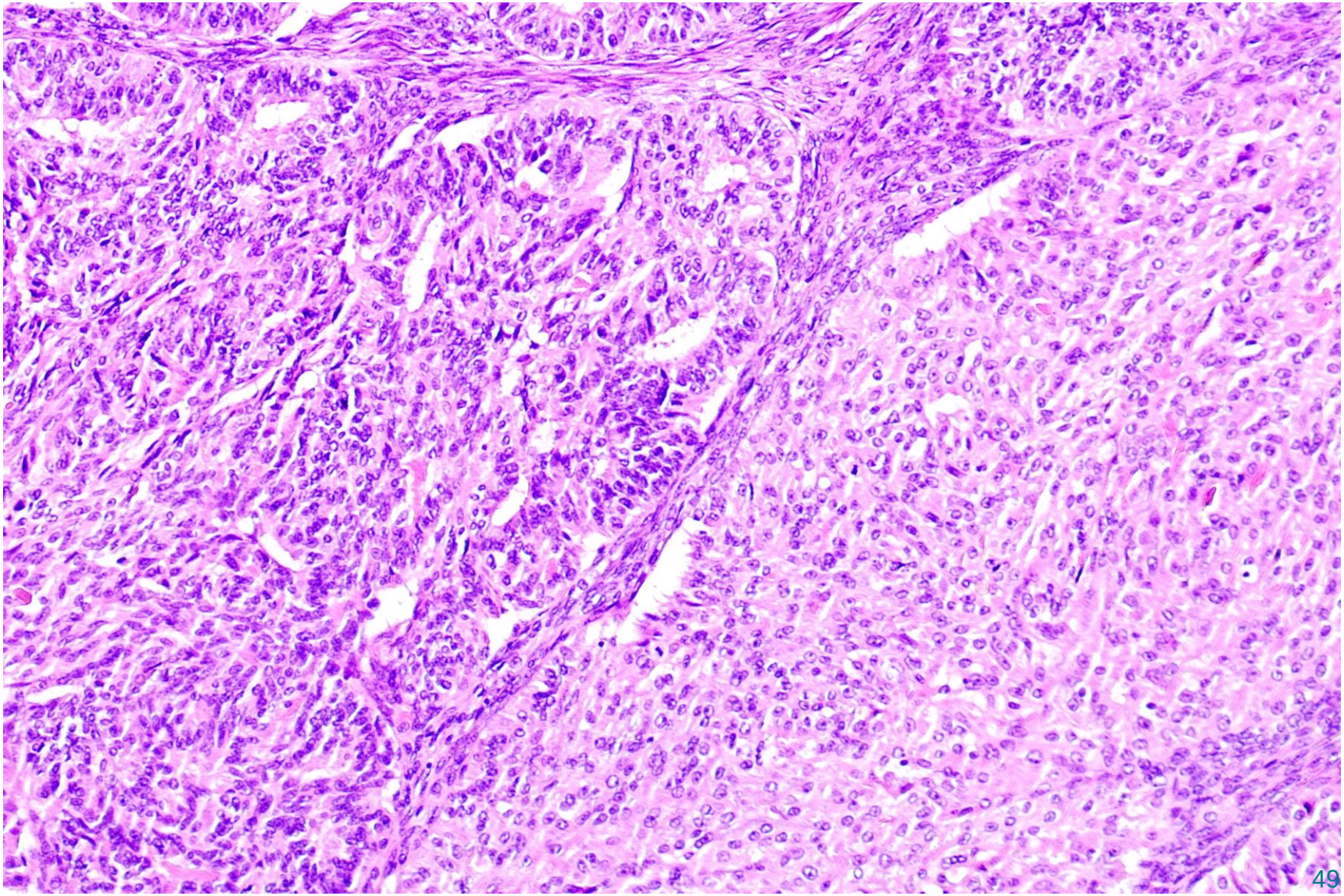
Mimic of mixed epithelial and mesenchymal tumour



Mimic of mixed epithelial and mesenchymal tumour



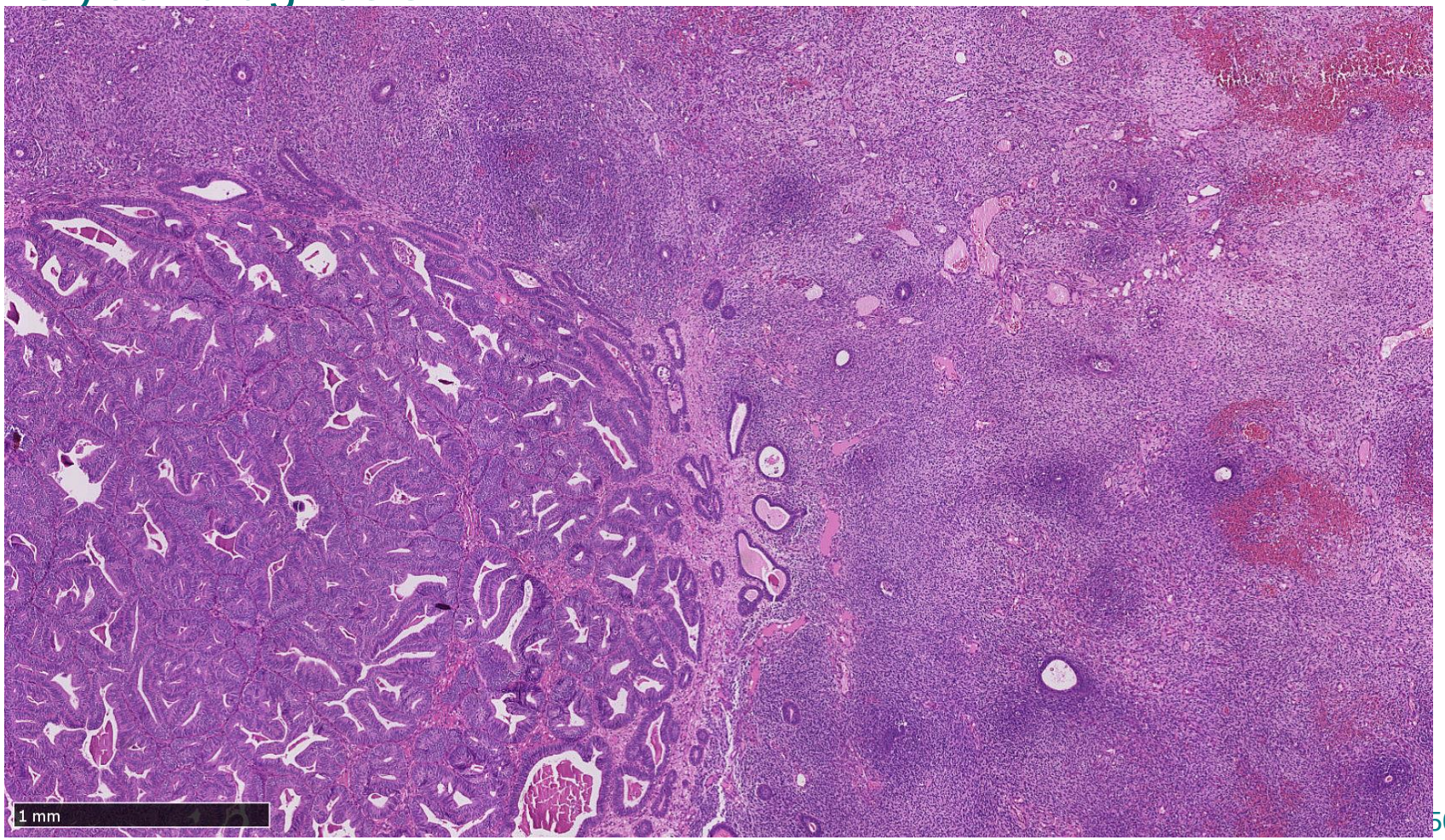
Mimic of mixed epithelial and mesenchymal tumour



Poll question : 5

35 year old presents with 6 month h/o menorrhagia. US detected thickened and polypoid endometrium.

What is your diagnosis ?



ORIGINAL ARTICLES

BCOR Expression in Mullerian Adenosarcoma

A Potential Diagnostic Pitfall

Muthukumarana, Vidarshi MD*; Fix, Daniel J. MD†; Stolnicu, Simona MD, PhD‡; Park, Kay J. MD§; Soslow, Robert A. MD§; Benayed, Ryma PhD§; Ladanyi, Marc MD§; Antonescu, Cristina R. MD§; Chiang, Sarah MD§ Author Information

The American Journal of Surgical Pathology: June 2020 - Volume 44 - Issue 6 - p 765-770
doi: 10.1097/PAS.0000000000001445

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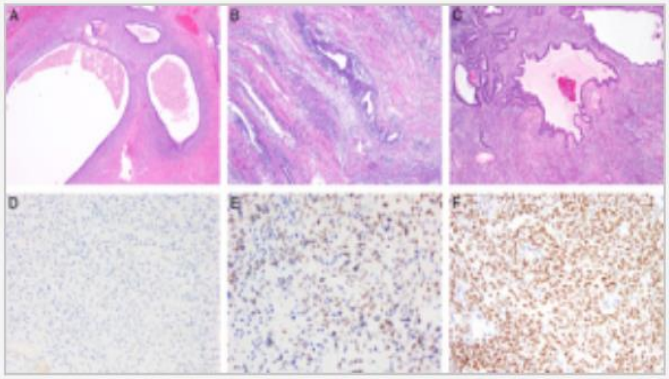


FIGURE 1
BCOR expression in adenosarcoma. Periglandular stromal condensation is seen in low-grade (A) and high-grade tumors (B, C), one which exhibited stromal overgrowth (not pictured). D, BCOR expression is absent in the low-grade tumor. E and F, Strong BCOR expression is seen in the mesenchymal component of both high-grade tumors.

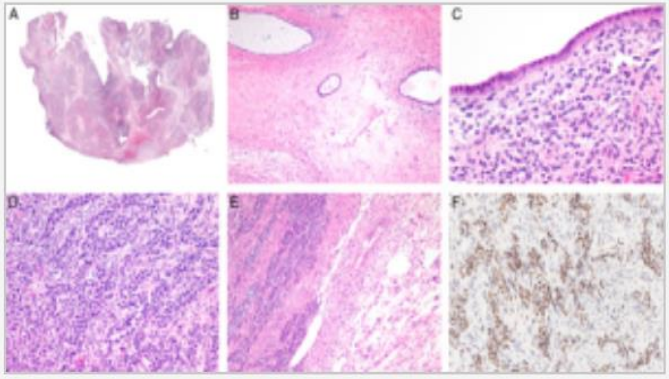
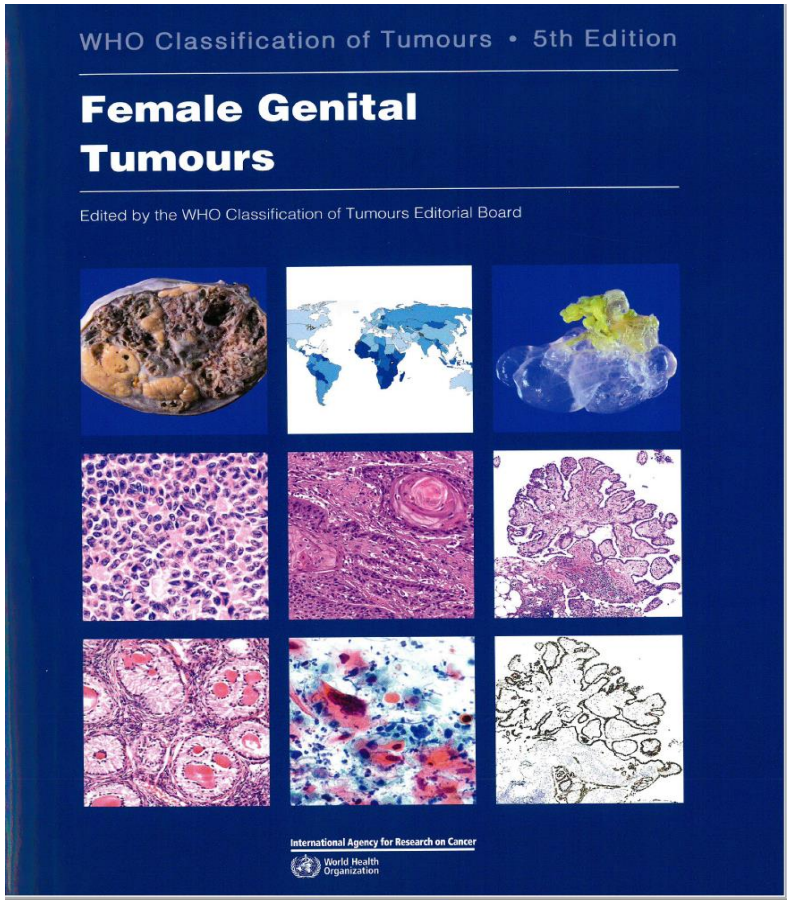


FIGURE 2
High-grade adenosarcoma with *JAZF1-BCORL1* fusion. A, Phyllodes-like growth pattern and periglandular stromal condensation are visible on low magnification. B, Periglandular stromal condensation surrounds cystically dilated glands and is associated with fibrotic stroma. C, Stromal cells adjacent to cytologically bland epithelium have mild to moderate nuclear atypia. D and E, Cells with marked cytologic atypia form cords and trabeculae adjacent to (E) a fibromyxoid spindle cell component. F, Strong BCOR expression is seen in the sex cord-like foci.

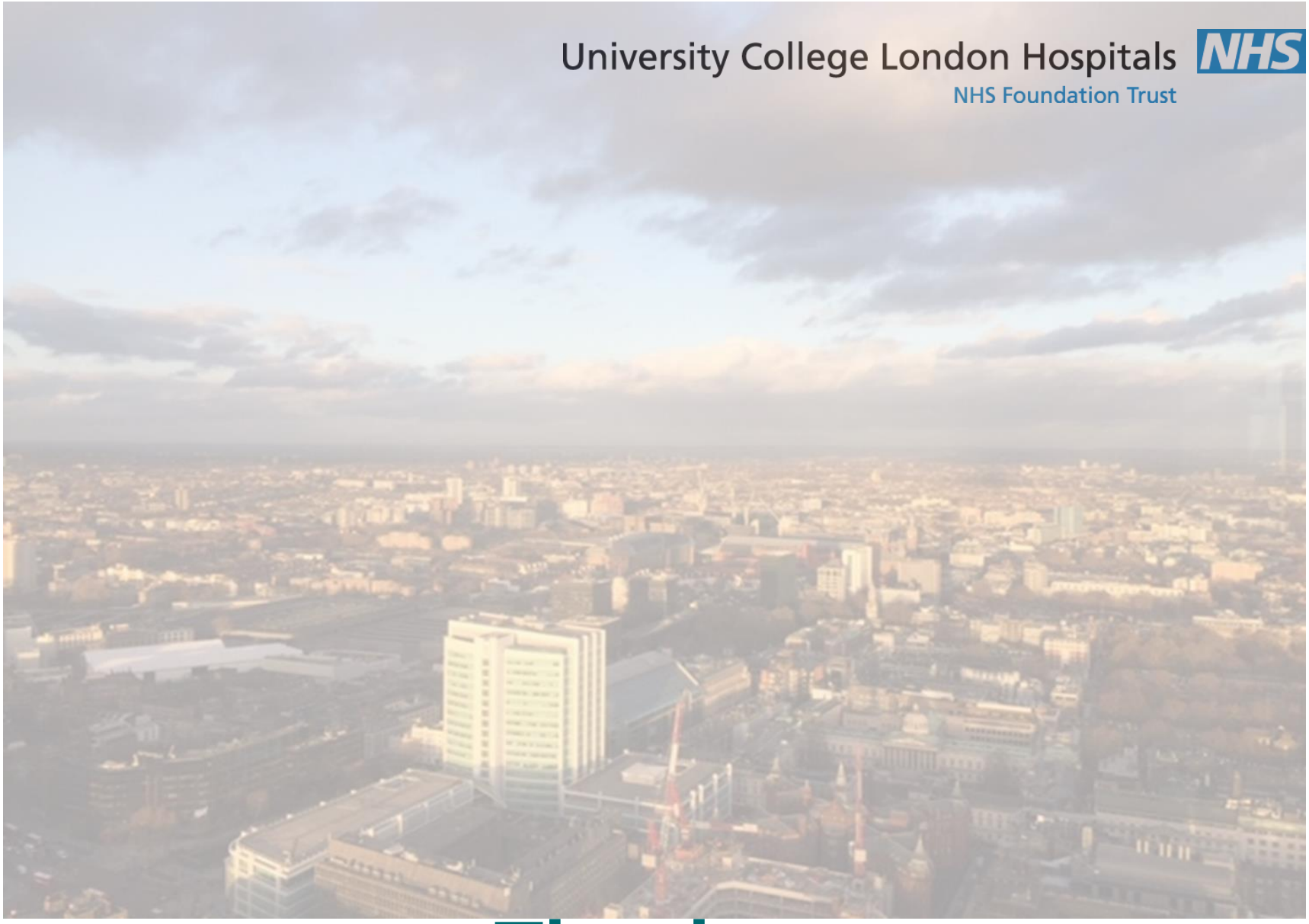
References



Seidman JD, Chauhan S . Evaluation of the relationship between adenosarcoma and carcinosarcoma and a hypothesis of the histogenesis of uterine sarcomas. *Int J Gynecol Pathol*2003;22:75–82.

Clement PB, Scully RE . Mullerian adenosarcoma of the uterus: a clinicopathologic analysis of 100 cases with a review of the literature. *Hum Pathol* 1990;21:363–381.

W.Glenn McCluggage , A practical approach to the diagnosis of mixed epithelial and mesenchymal tumors of the uterus. Modern Pathology *2016;* 29, S78–S91.



Thank you

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