

# Interesting Cases in Gynecologic Pathology

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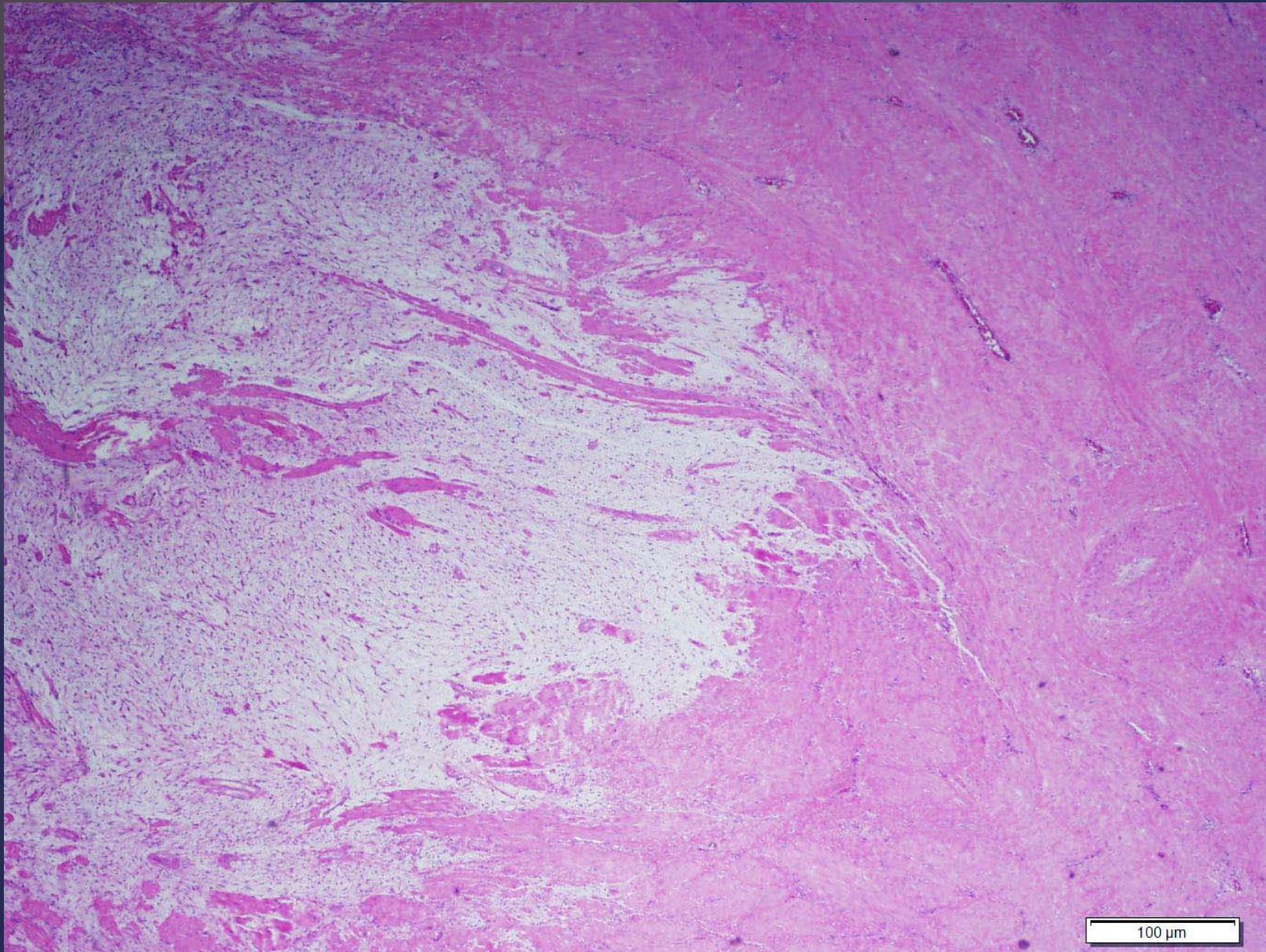
UNIVERSITY OF UTAH  
HEALTH CARE

# Case 1

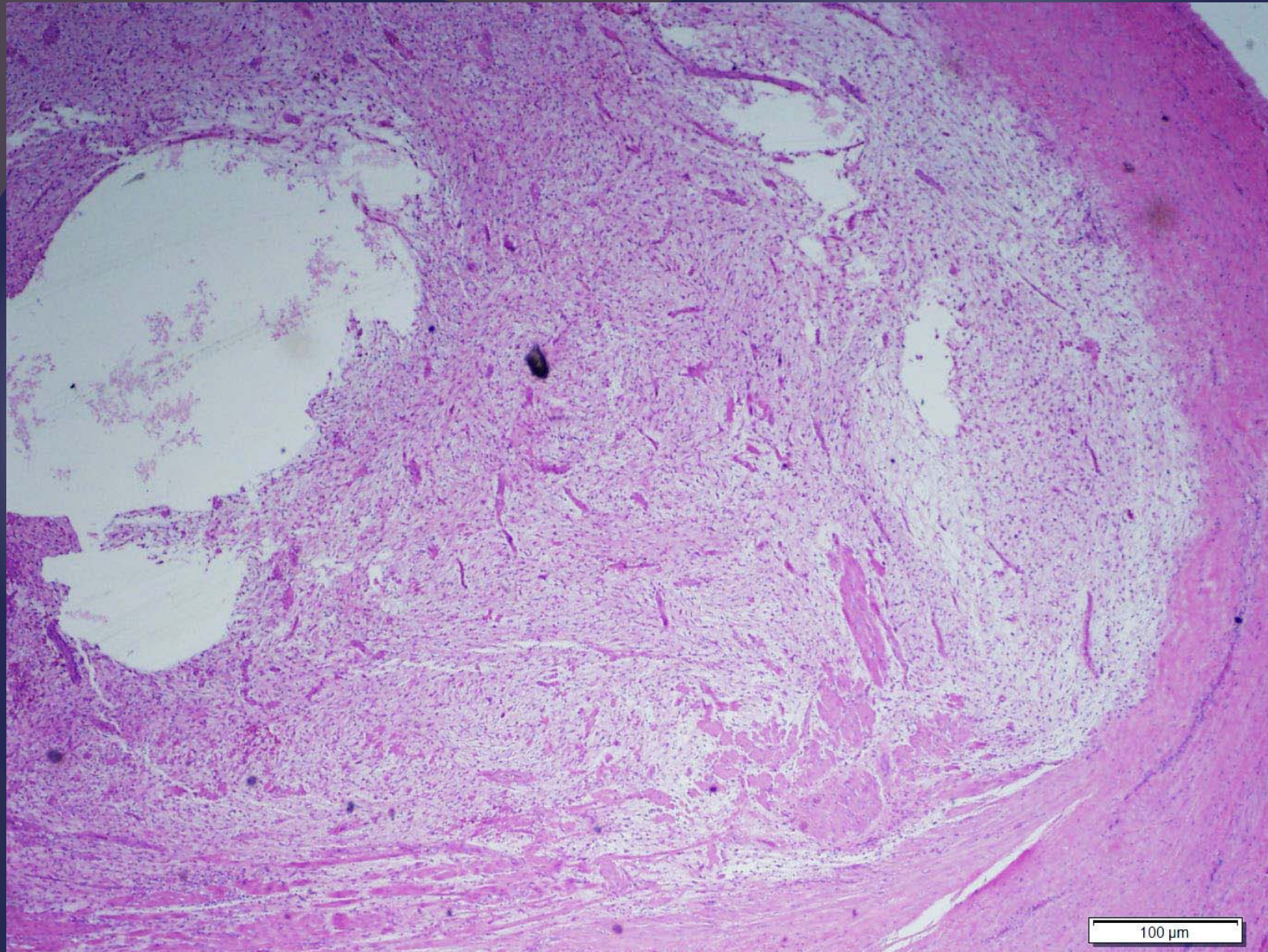
## History:

- 50 year old woman with a uterine mass
- Hysterectomy and BSO
- 11 cm yellow-white, gelatinous tumor

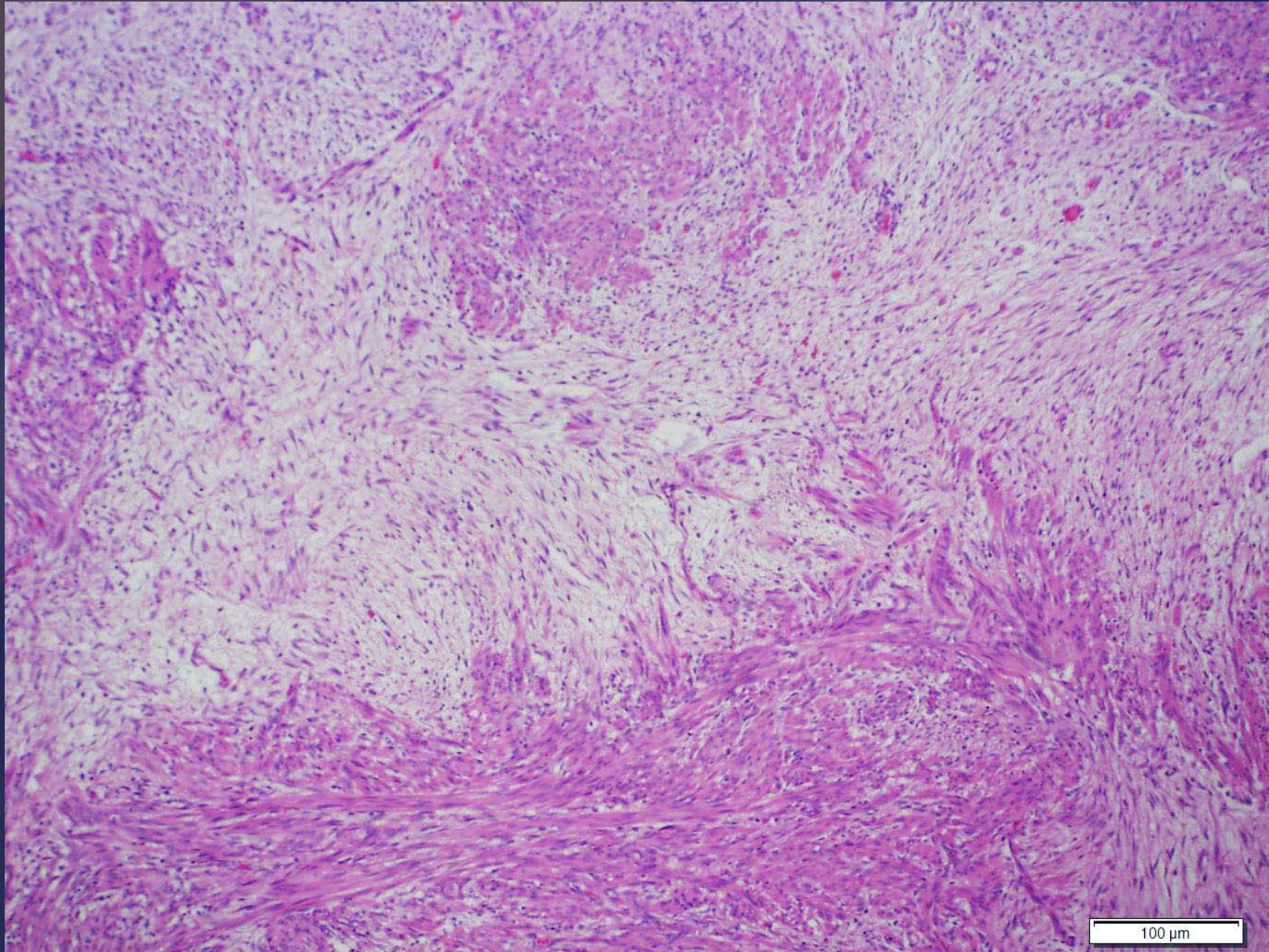
# Case 1 – Uterine Mass



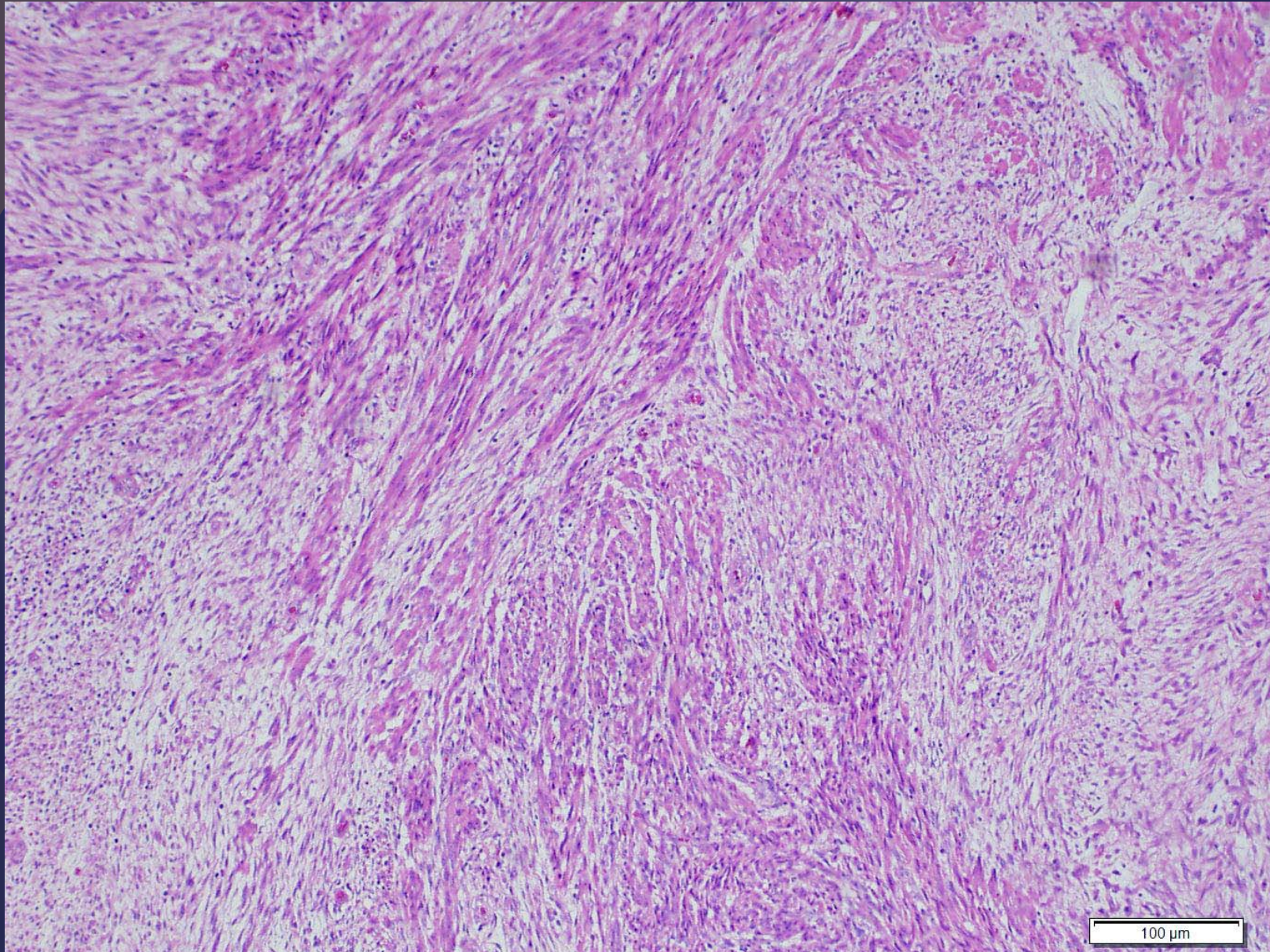
# Case 1 – Uterine Mass



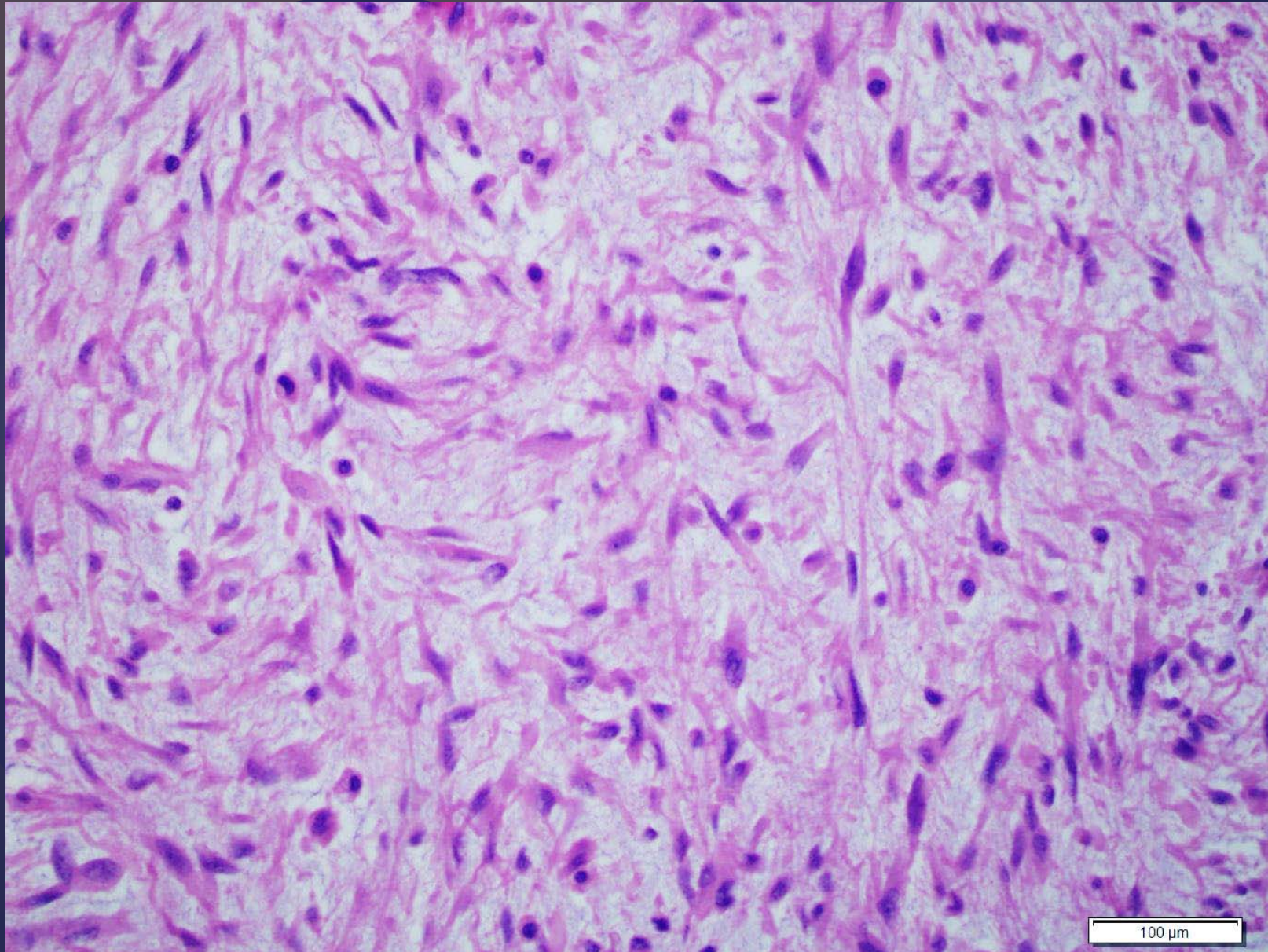
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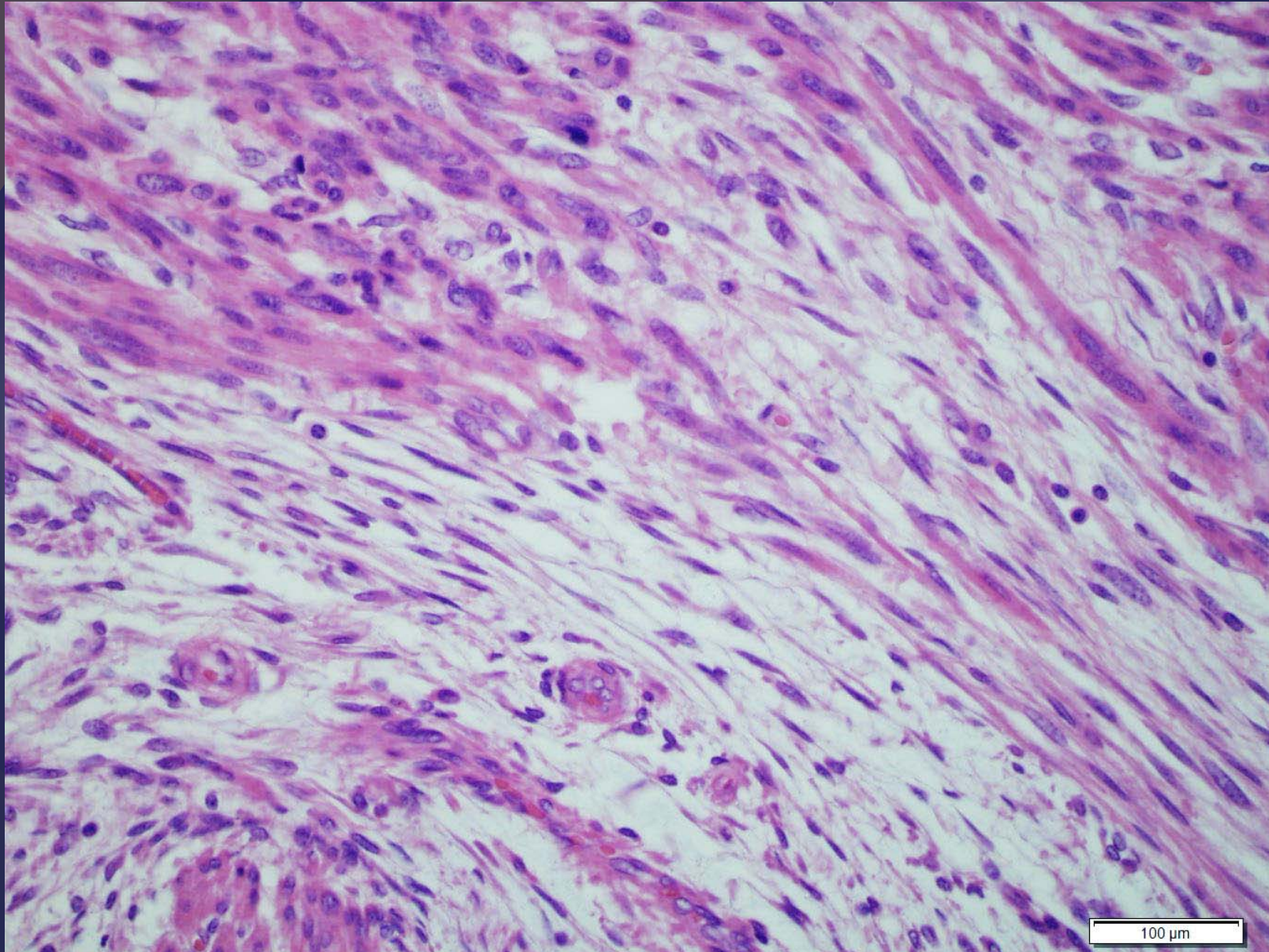
# Case 1 – Uterine Mass



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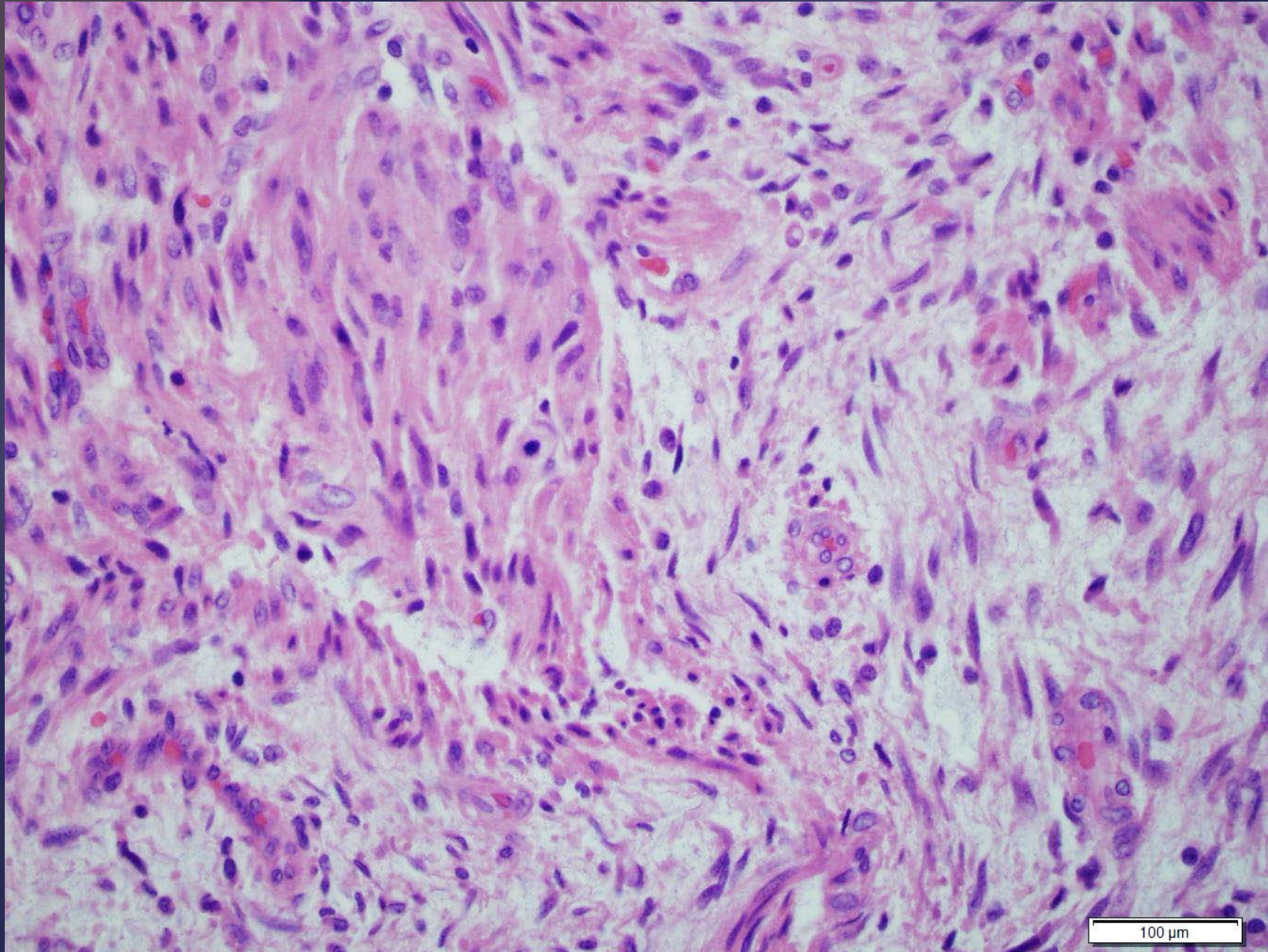


# Case 1 – Uterine Mass





# Case 1 – Uterine Mass



# Case 1- Differential Diagnosis

- Myxoid leiomyosarcoma
- Inflammatory myofibroblastic tumor
- Leiomyoma with degeneration or hydropic change
- Myxoid endometrial stromal sarcoma

# Case 1- Immunohistochemistry

- Smooth Muscle Actin (+)
- ALK (-)

# Case 1- Final Diagnosis

- MYXOID LEIOMYOSARCOMA

Dr. Esther Oliva, MGH, Boston, MA

# Case 1- Myxoid Leiomyosarcoma

A rare and distinct malignant tumor



# Case 1- Myxoid Leiomyosarcoma

A rare and distinct malignant tumor:

- Doesn't conform to the conventional leiomyosarcoma diagnostic features
- Worse prognosis
- Good recent paper :

Carlos Parra-Herran et al, Myxoid Leiomyosarcoma of the Uterus A Clinicopathologic Analysis of 30 Cases With Reappraisal of Its Distinction From Other Uterine Myxoid Mesenchymal Neoplasma, (2016).

# Case 1- Myxoid Leiomyosarcoma

## Gross Features:

- Large (average size 11 cm)
- Gelatinous, mucoid or myxoid
- Infiltrative growth pattern



# Case 1- Myxoid Leiomyosarcoma

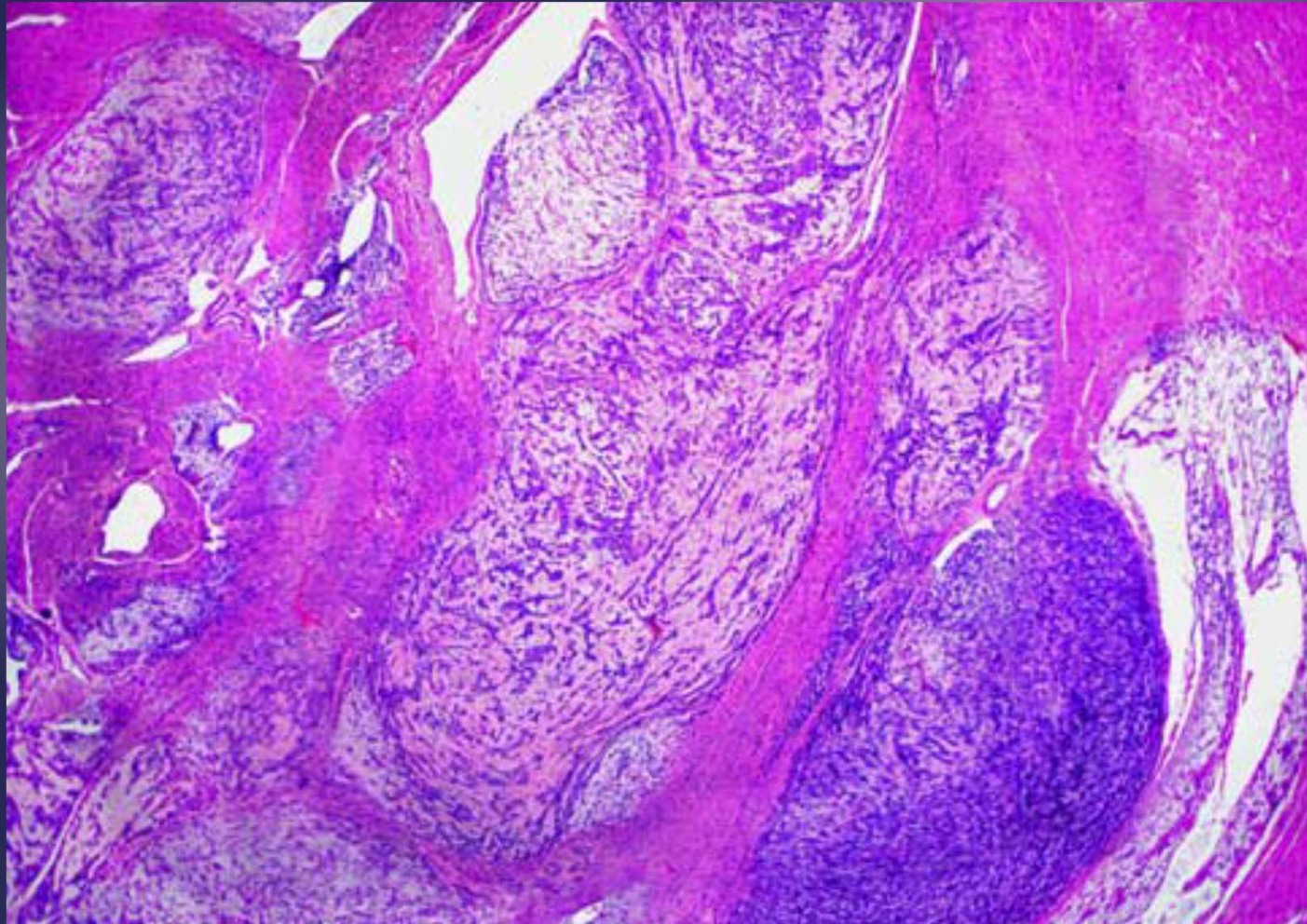
## Histology:



- Spindle cell tumor arranged in a myxoid matrix
- Variable mitotic activity (may be as low as 2/10hpf)
- Variable necrosis
- Variable atypia
  
- What's Not Variable?
  - Infiltrative border
  - Retained positivity for at least 1 smooth muscle marker

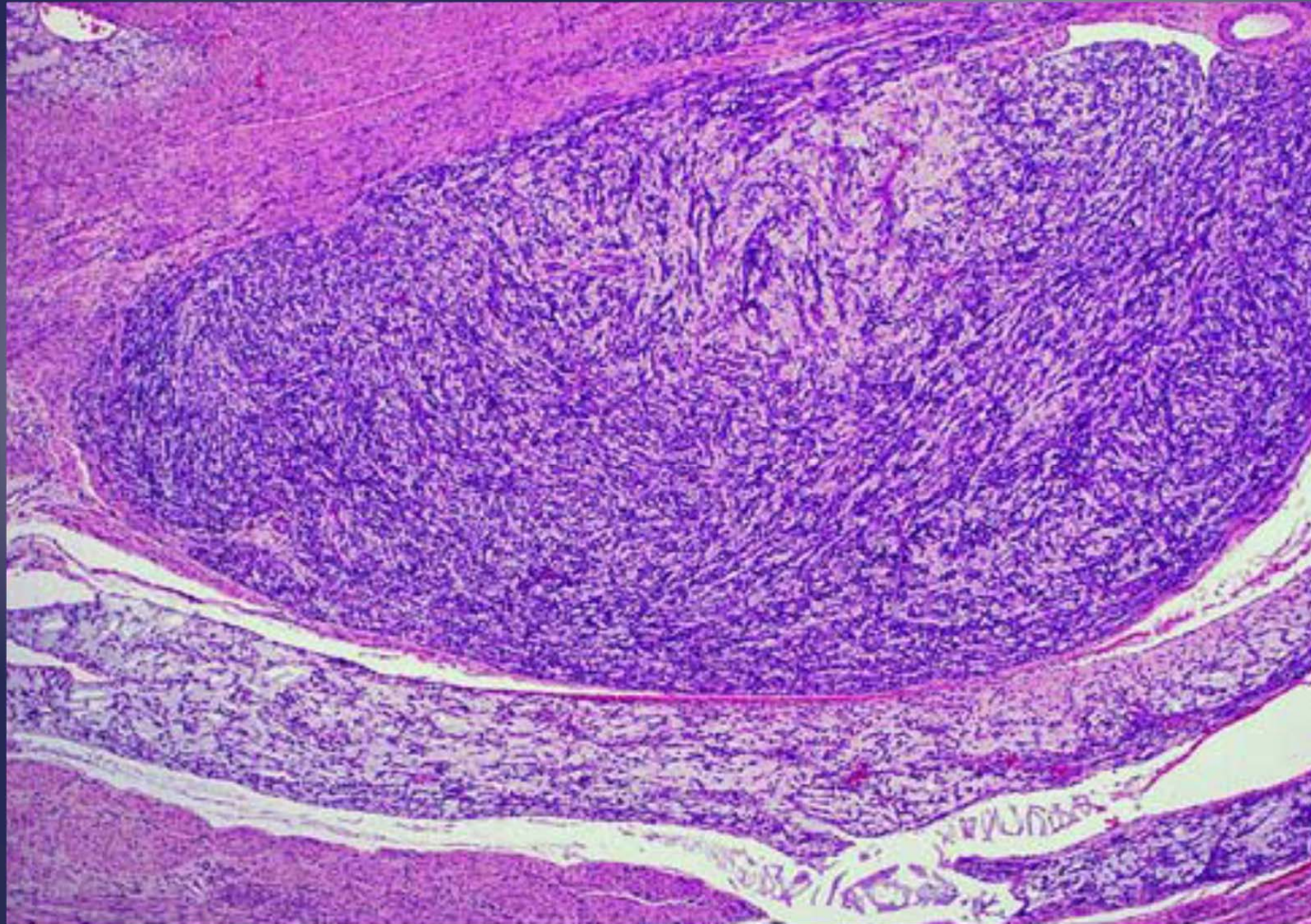


# Case 1- Myxoid Leiomyosarcoma



Parra-Herran et al, (2016)

# Case 1- Myxoid Leiomyosarcoma



Parra-Herran et al, (2016)

# Case 1- Myxoid Leiomyosarcoma

## Immunohistochemistry:

- SMA, Desmin are most sensitive
- CD10 (+) in 66%
- KI-67 of little utility
- Alcian Blue stains myxoid LMS (negative in edema/hydronic change)

# Case 1- Myxoid Leiomyosarcoma

## Treatment:

- Surgery
- Chemo/radiation have little effect

## Prognosis:

- Poor prognosis
- Worse than conventional LMS



# Practical Classification of Smooth Muscle Tumors with Typical Spindle Cell Differentiation

Diagnosis	Geographic Tumor Necrosis	Mitotic Rate (per 10 HPF)	Atypia
Leiomyosarcoma	Present	Any	Present or absent
Leiomyosarcoma	Absent	>10	Moderate to severe
STUMP	Absent	>15	Absent
Atypical Leiomyoma	Absent	<10	Moderate to severe
Leiomyoma with increased mites	Absent	<15	Absent

Table adapted from textbook: Crum et Al, Diagnostic Gynecologic and Obstetric Path, 2011

# Case 1- Myxoid Leiomyosarcoma

## Diagnostic Features:

1. >50% myxoid matrix
2. Infiltrative border, plus any one of the following:
  - 2 or more mitoses /10 hpf
  - Unequivocal coagulative tumor necrosis
  - Moderate to severe nuclear atypia

# Strange things growing on walls...



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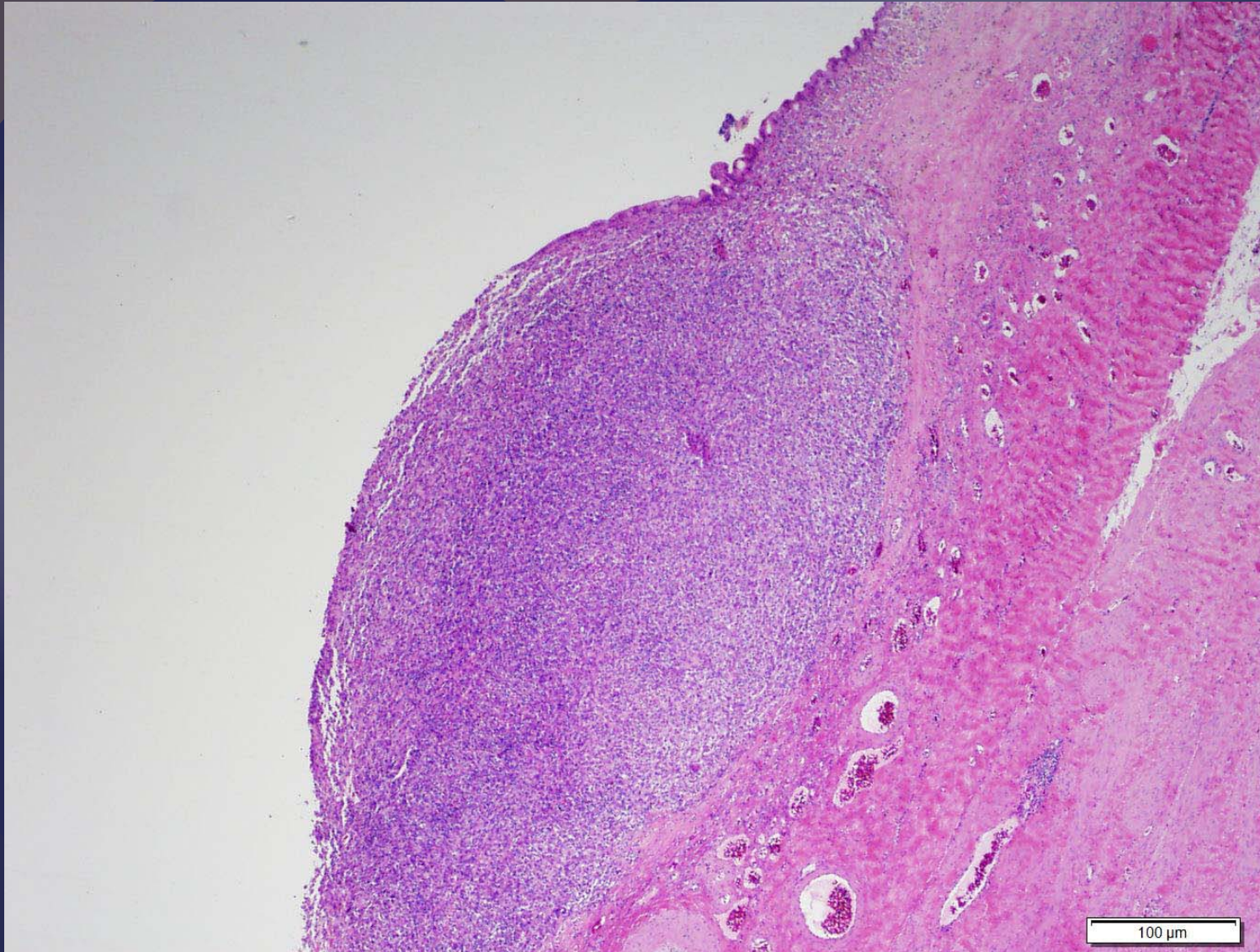
# Case 2

## History:

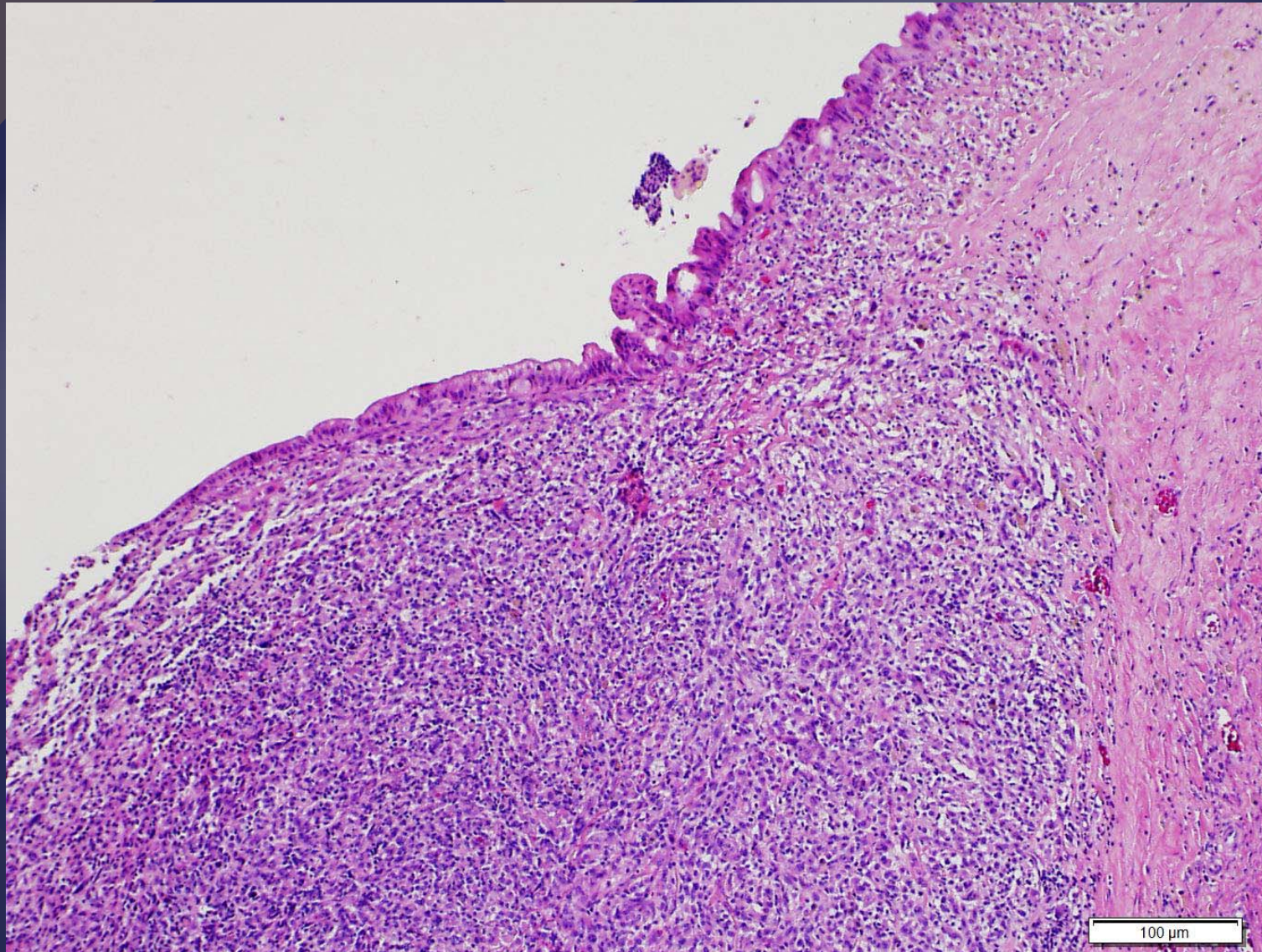
- 74 year old woman, cystic intra abdominal mass
- Hysterectomy and BSO
  - 35 cm cystic ovarian mass
  - 12.0 cm mass involving the fallopian tube



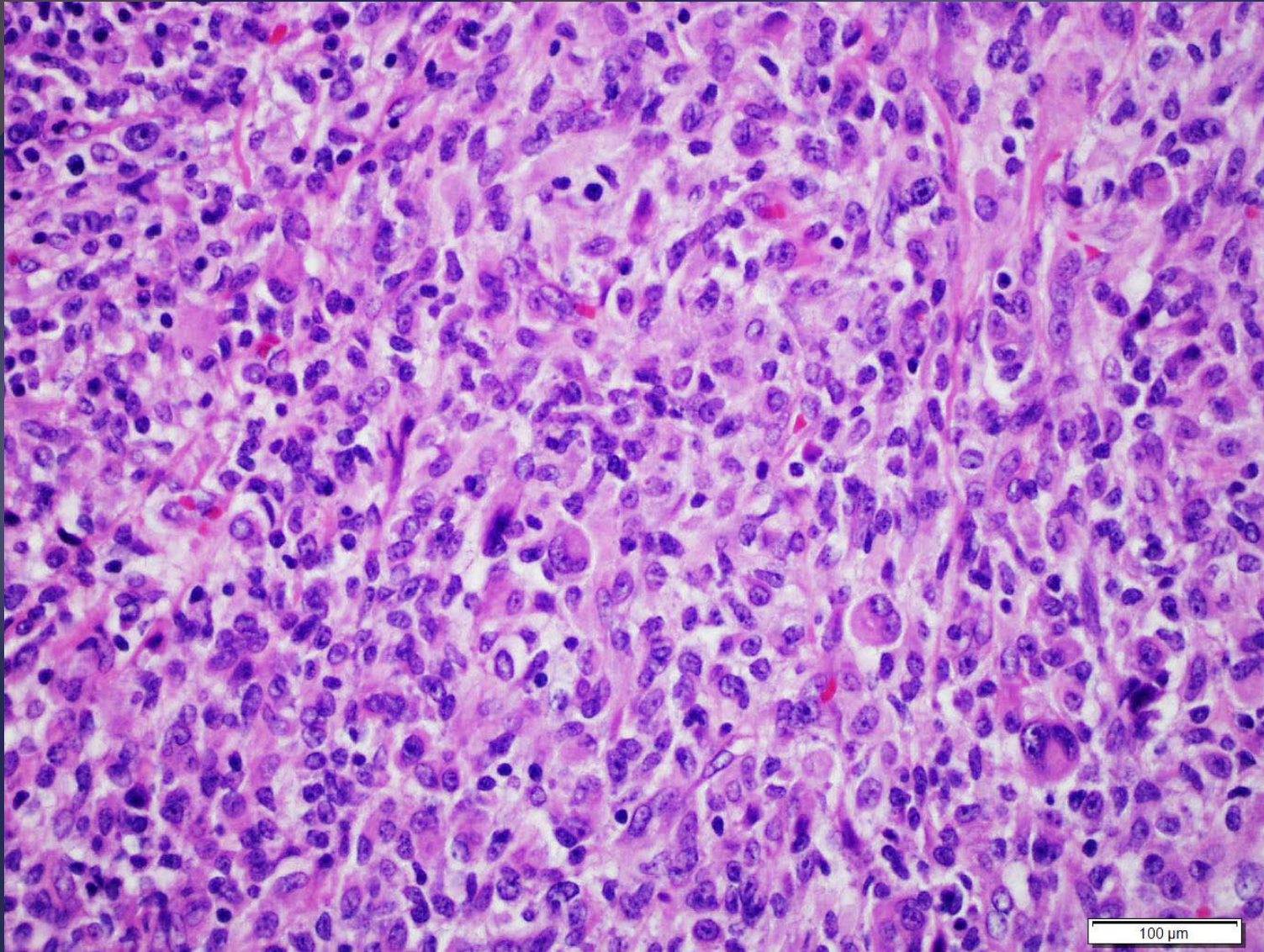
## Case 2 – Ovarian Cyst with Nodule



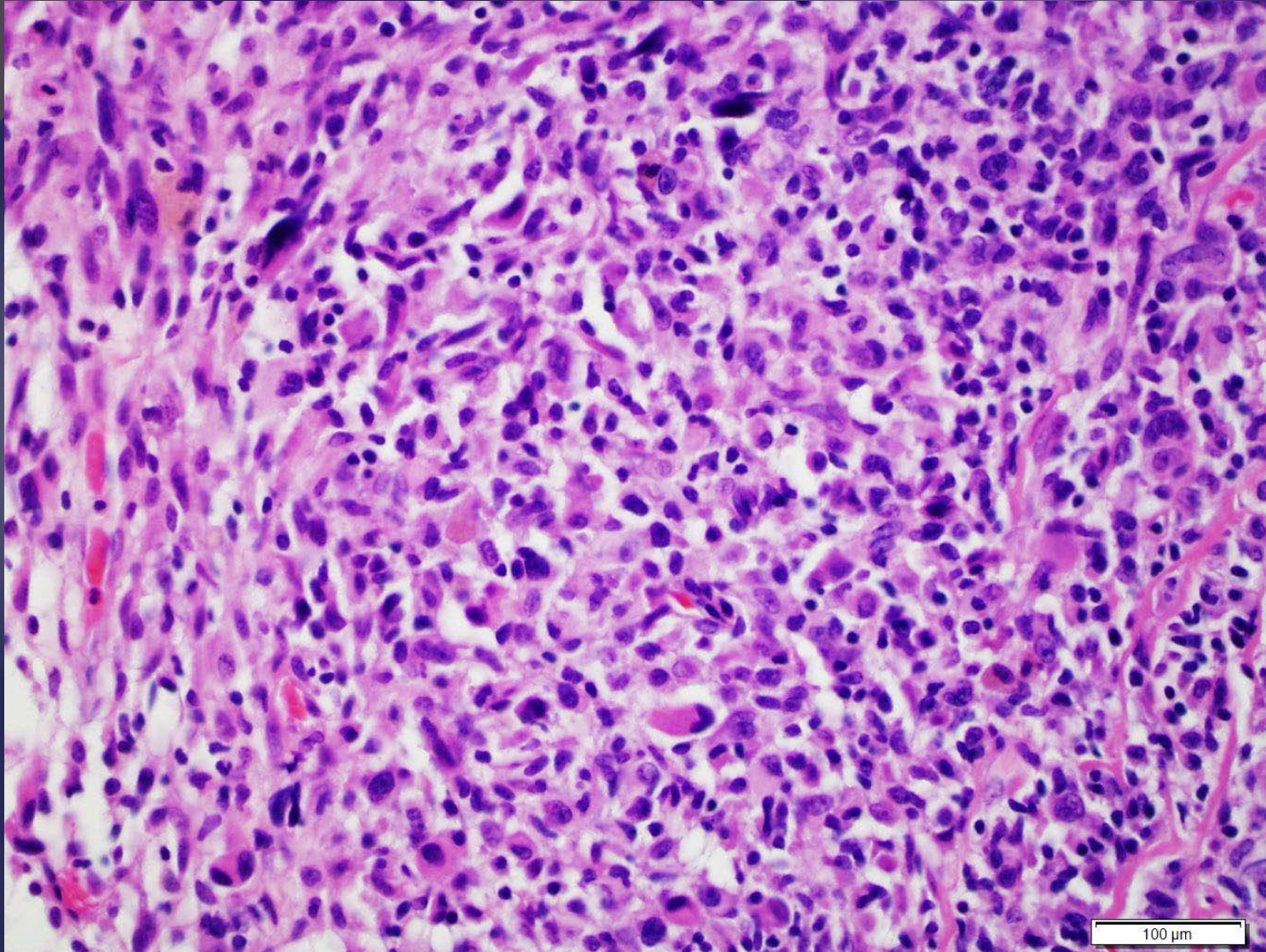
## Case 2 – Ovarian Cyst with Nodule



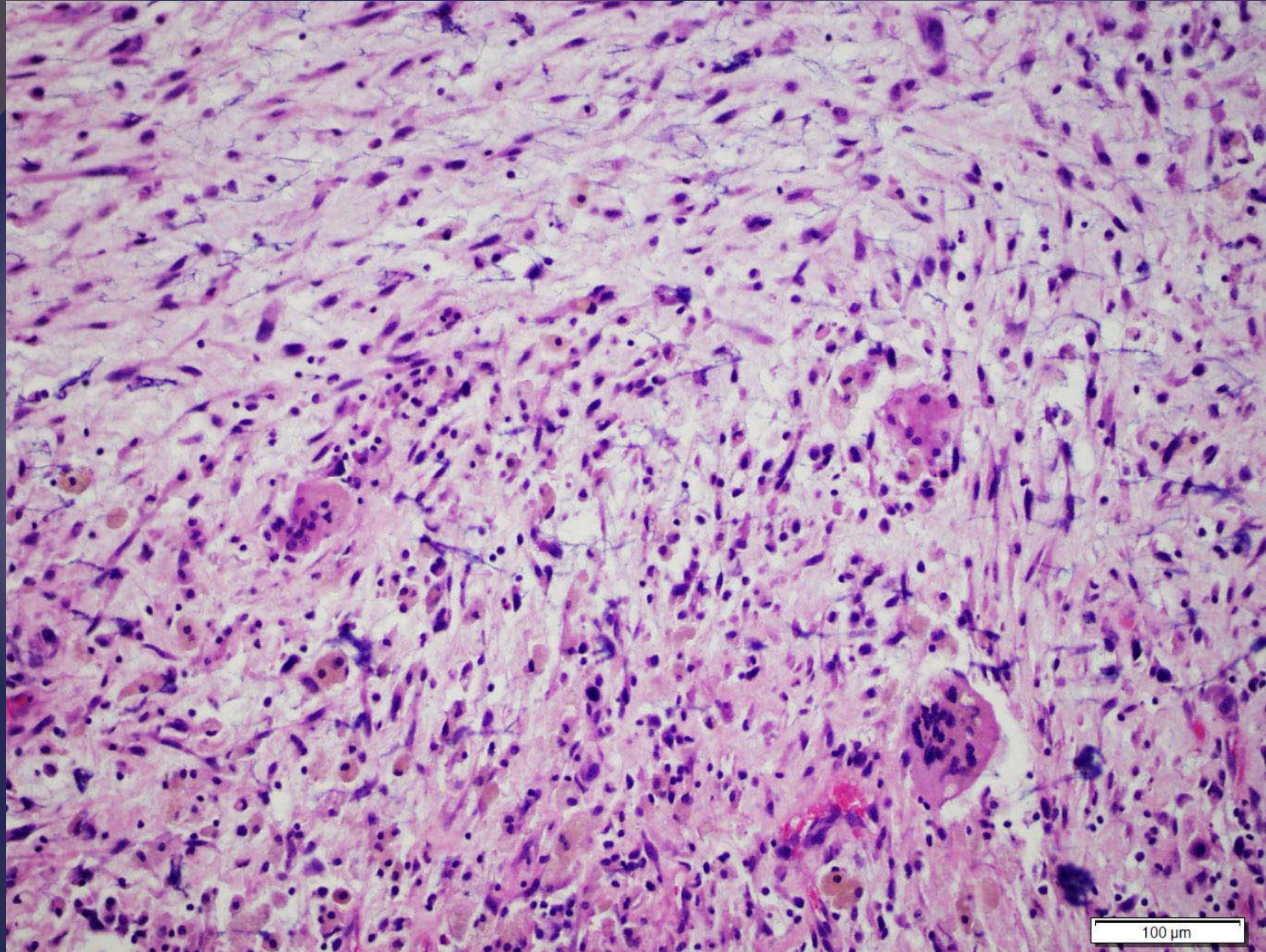
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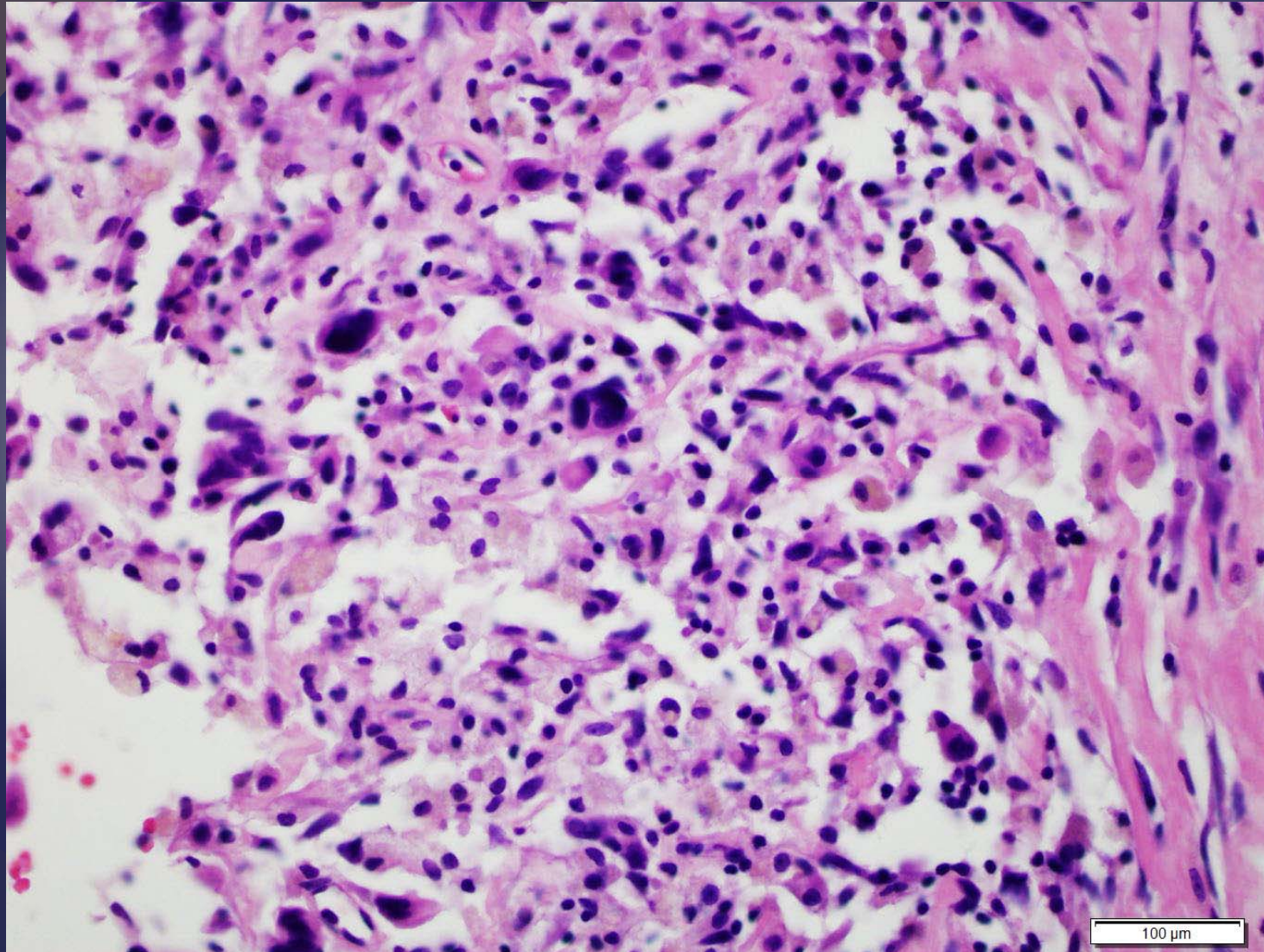
## Case 2 – Ovarian Cyst with Nodule



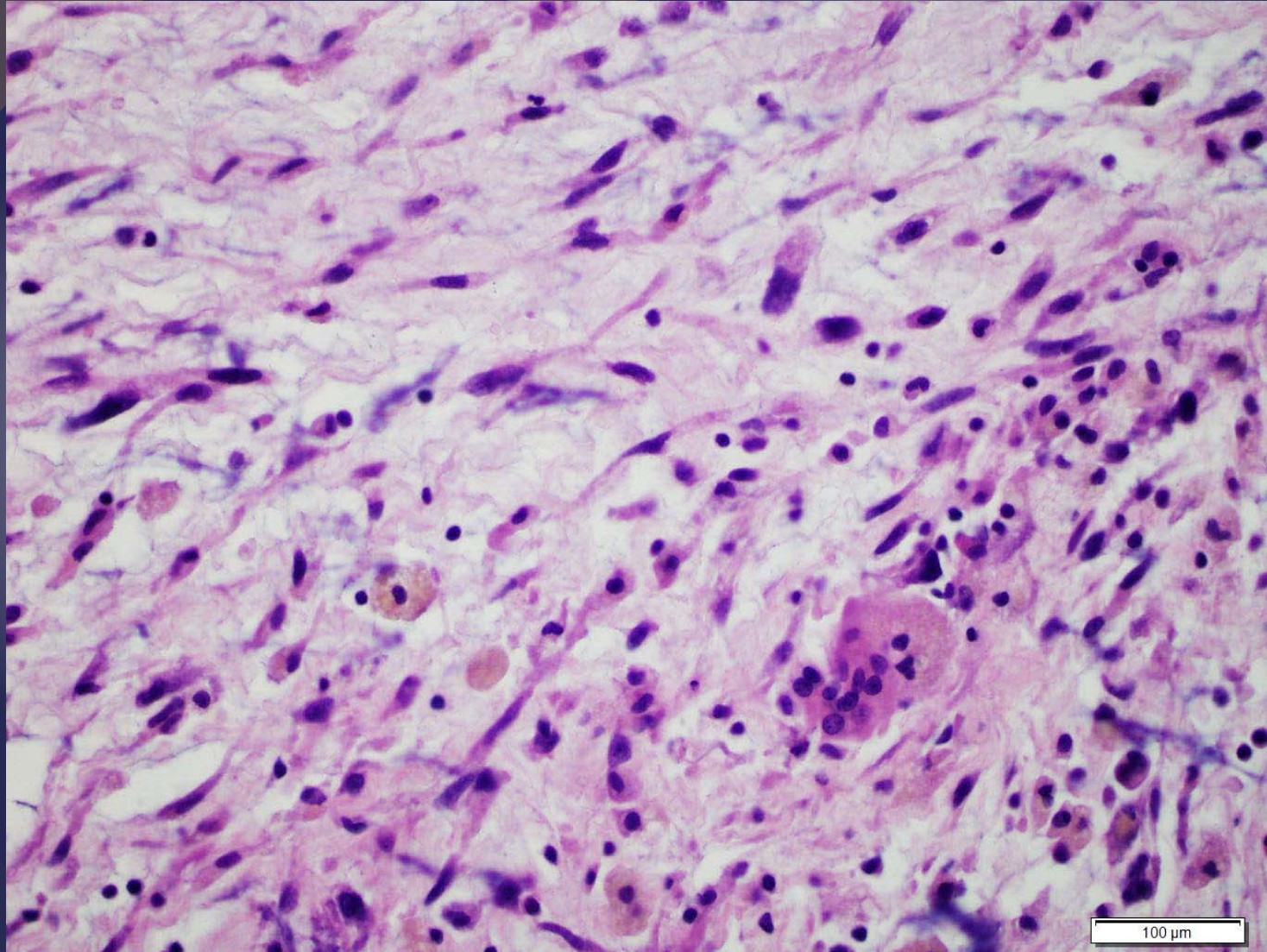
## Case 2 – Ovarian Cyst with Nodule



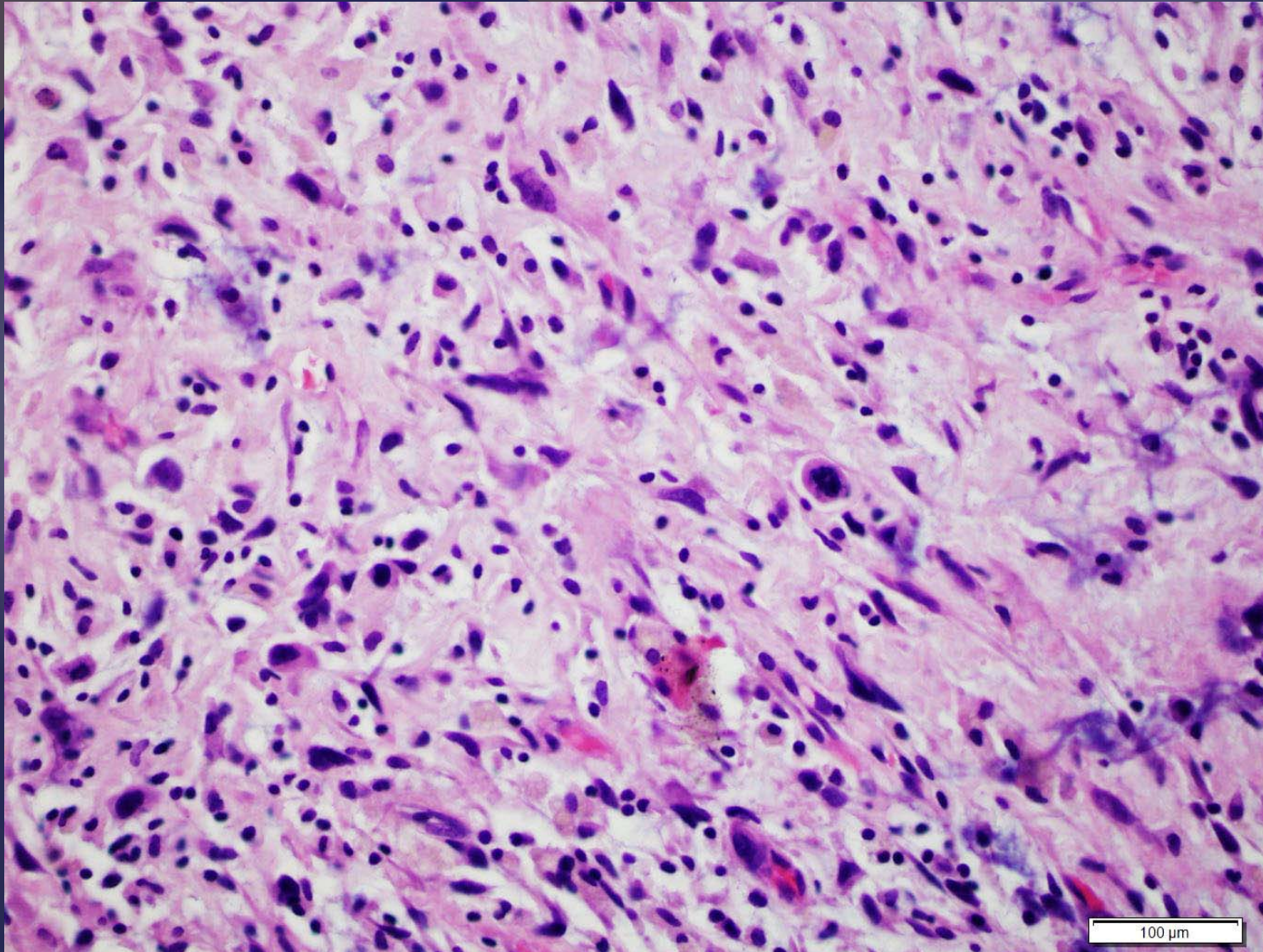
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## Case 2 – Ovarian Cyst with Nodule

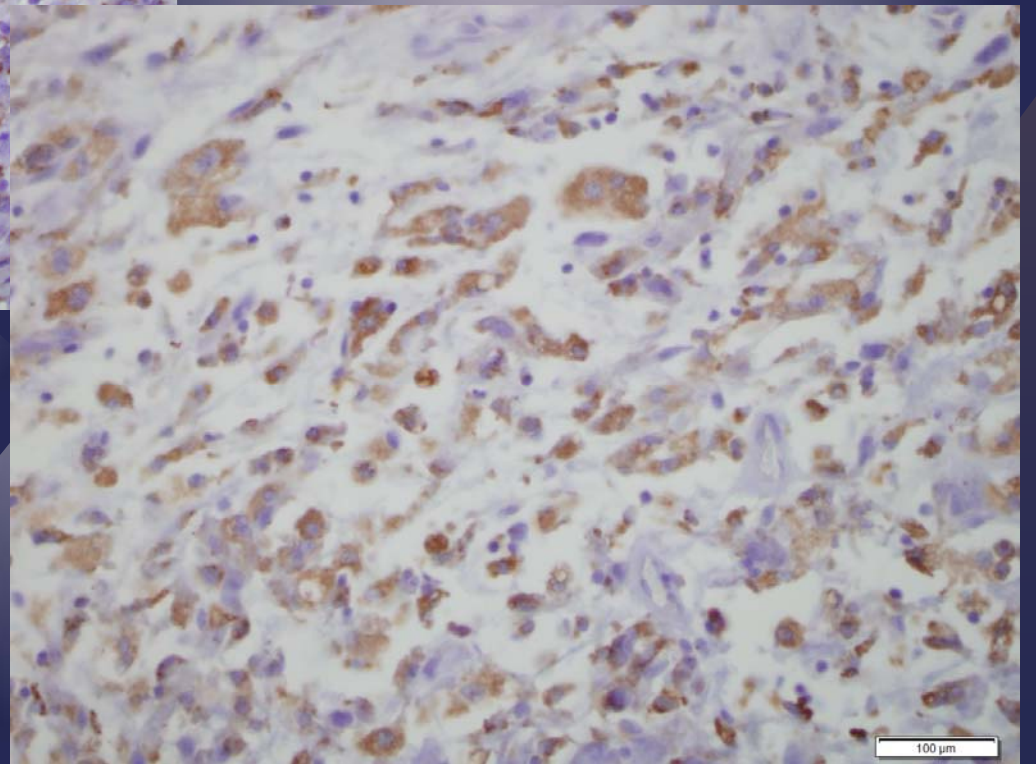
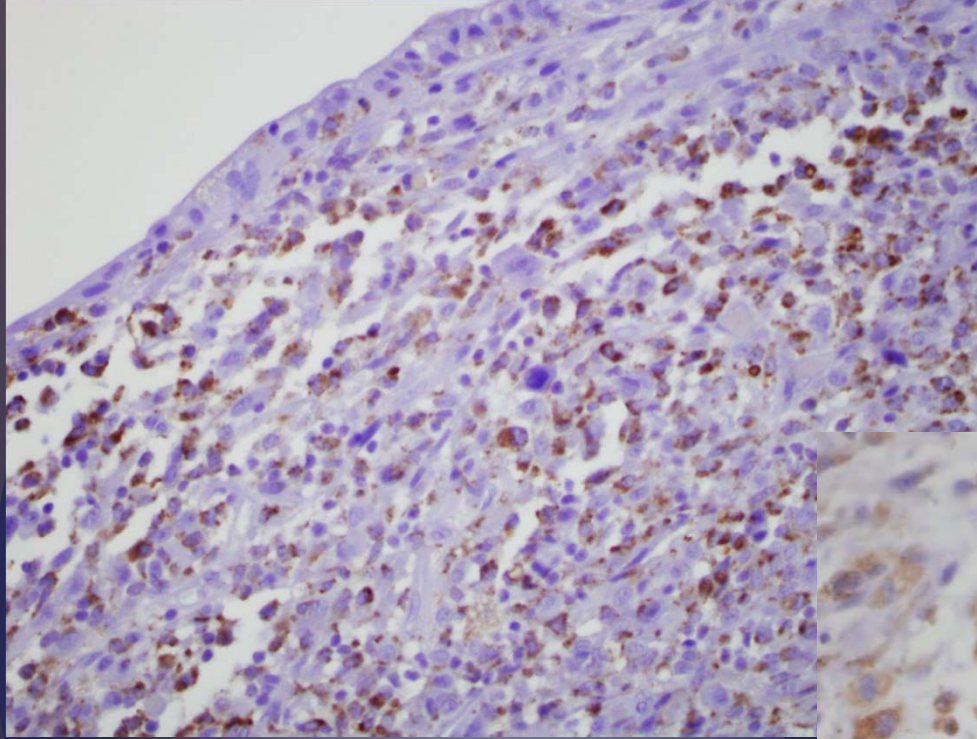




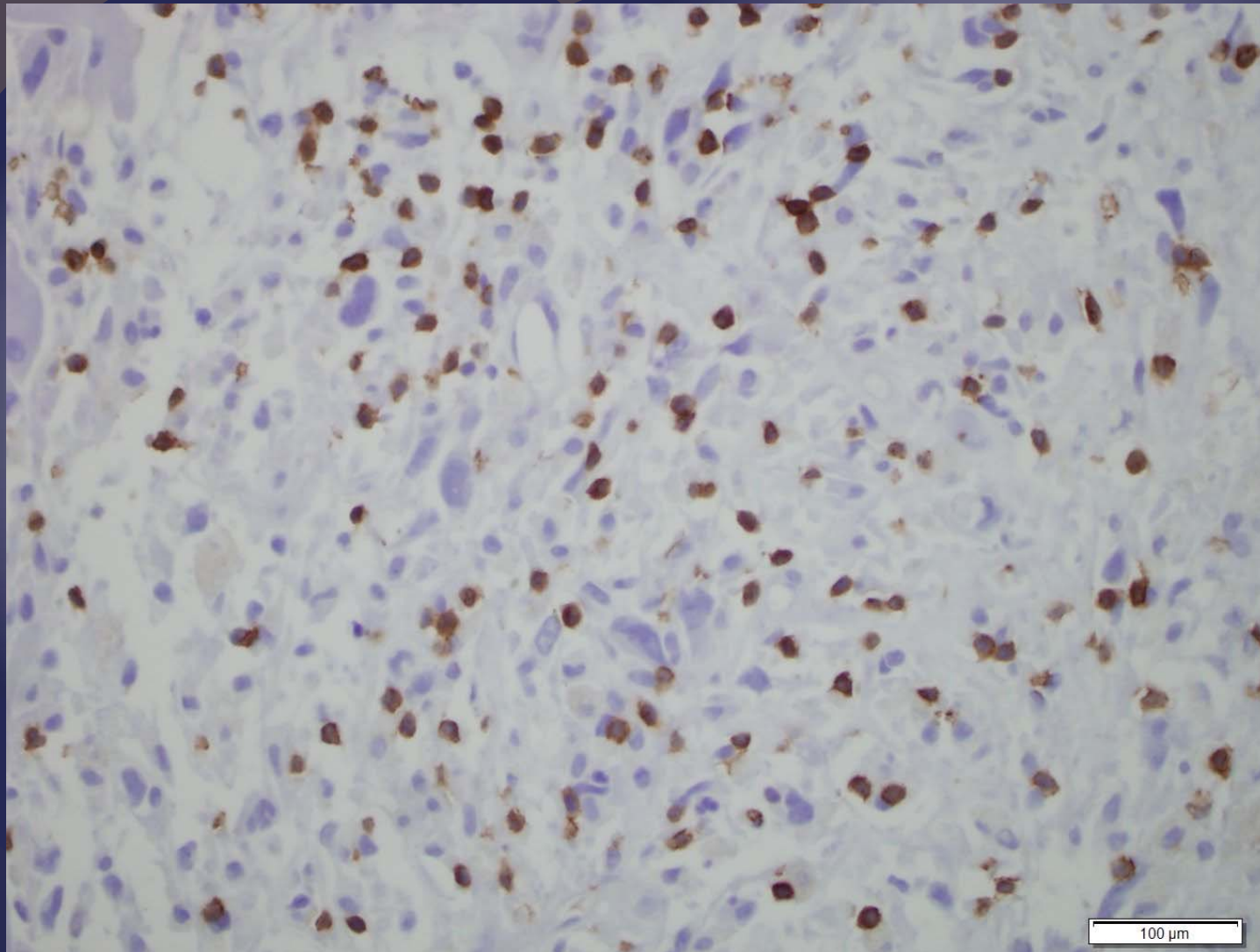
# Case 2 - Differential Diagnosis

- Sarcoma
- Carcinoma
  - Metastasis
  - Focus of anaplastic carcinoma
- Lymphoma
- Sarcoma-like mural nodule

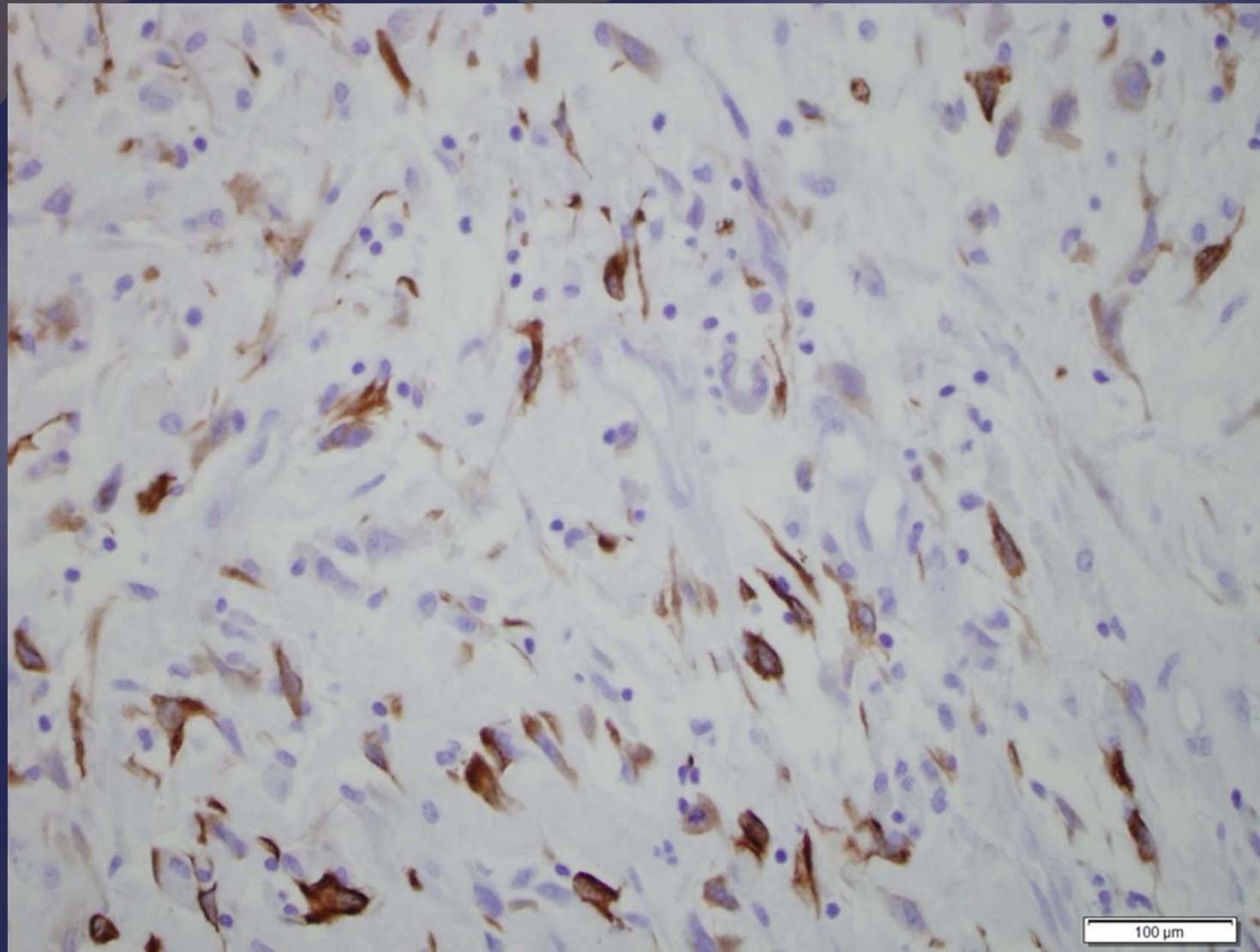
# CD 68



# CD 3



AE1/3



# Case 2 - Immunohistochemistry

- CD68 (+)
- CK7 (+ patchy)
- AE1/3 (+ patchy)
- ER (-)
- CD10 (-)
- CD3 (+ small scattered lymphocytes)
- CD20 (-)

# Case 2 - Final Diagnosis

- MUCINOUS CYSTADENOMA  
WITH A SARCOMA-LIKE MURAL  
NODULE

Dr. Robert Young, MGH, Boston

## Case 2- Mural Nodules

Strange things can be found growing in the wall of cystic ovarian neoplasms...



Which ones are benign?



Which ones are more problematic?

## Case 2- Mural Nodules

### General Features:

- Well demarcated nodule or plaque in the wall of an ovarian cyst
- Variable appearance:
  - Yellow, pink, red, hemorrhagic, necrotic
  - Single or multiple
- 1 to 20 cm
- Benign or malignant



# Case 2- Mural Nodules

## Types of mural nodules:

- Benign:
  - “Sarcoma-like mural nodule”
- Malignant:
  - Sarcomatous mural nodule
  - Mural nodule with anaplastic carcinoma

## Case 2- Mural Nodules

### Benign:

- Younger
- Smaller (<6cm)
- Sharply demarcated
- Heterogeneous cell population (giant cells, spindle cells and inflammation)

### Malignant:

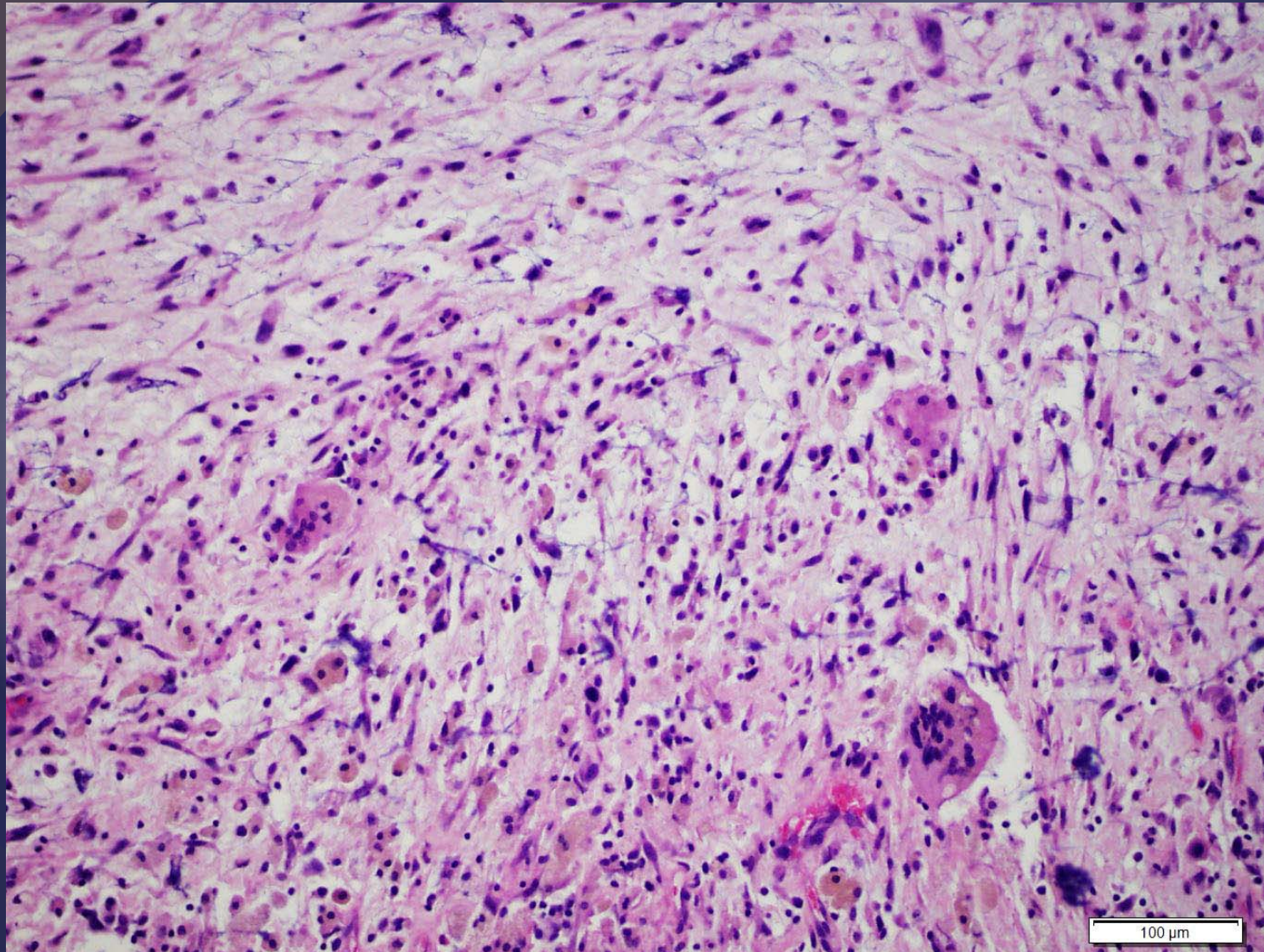
- Older
- Larger
- Infiltrative/vascular invasion
- Uniform cell population (spindled or carcinoma)

# Case 2- Sarcoma-Like Mural Nodule

## Histology:

- Shows mix of MNGCs, spindle cells and inflammation
- WITH significant pleomorphism, mitoses, atypical mitoses

## Case 2 – Sarcoma-Like Mural Nodule

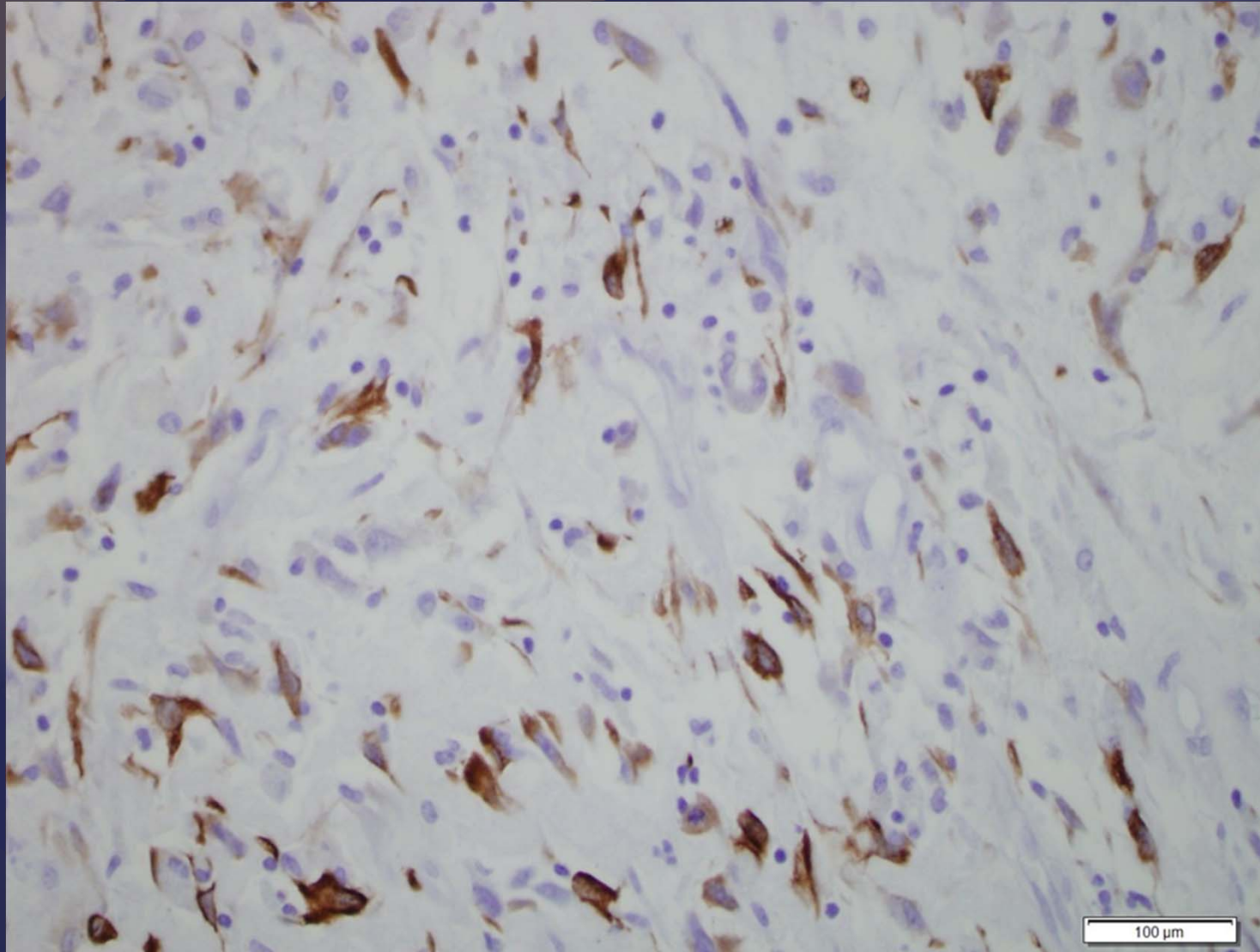


# Case 2- Sarcoma-Like Mural Nodule

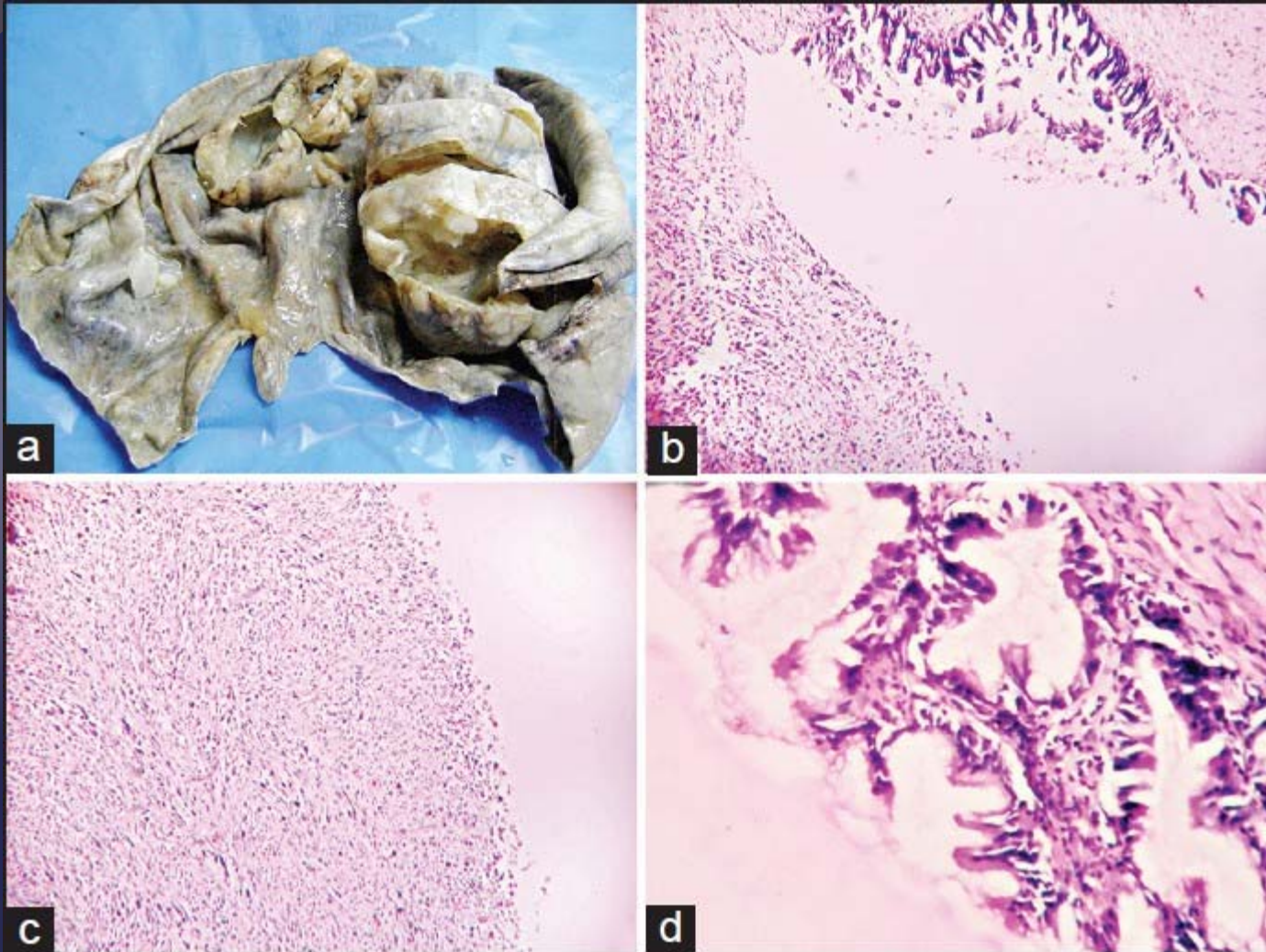
## Immunohistochemistry:

- Cytokeratin
  - Negative or patchy in sarcoma-like mural nodules
  - Strong and diffuse in anaplastic carcinoma

# Case 2- Sarcoma-Like Mural Nodule

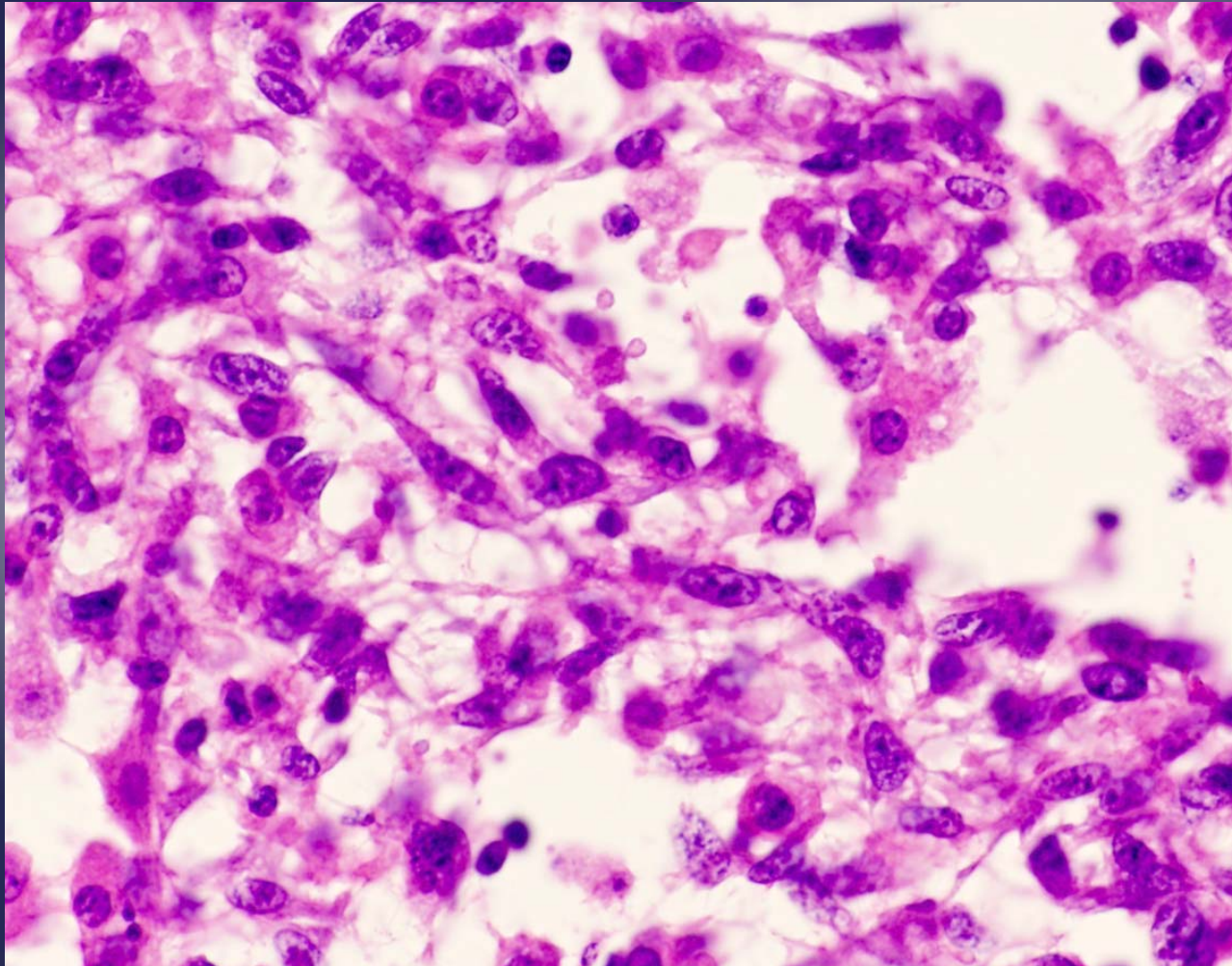


# Case 2- Sarcoma-Like Mural Nodules



Prithwijit et al, (2014)

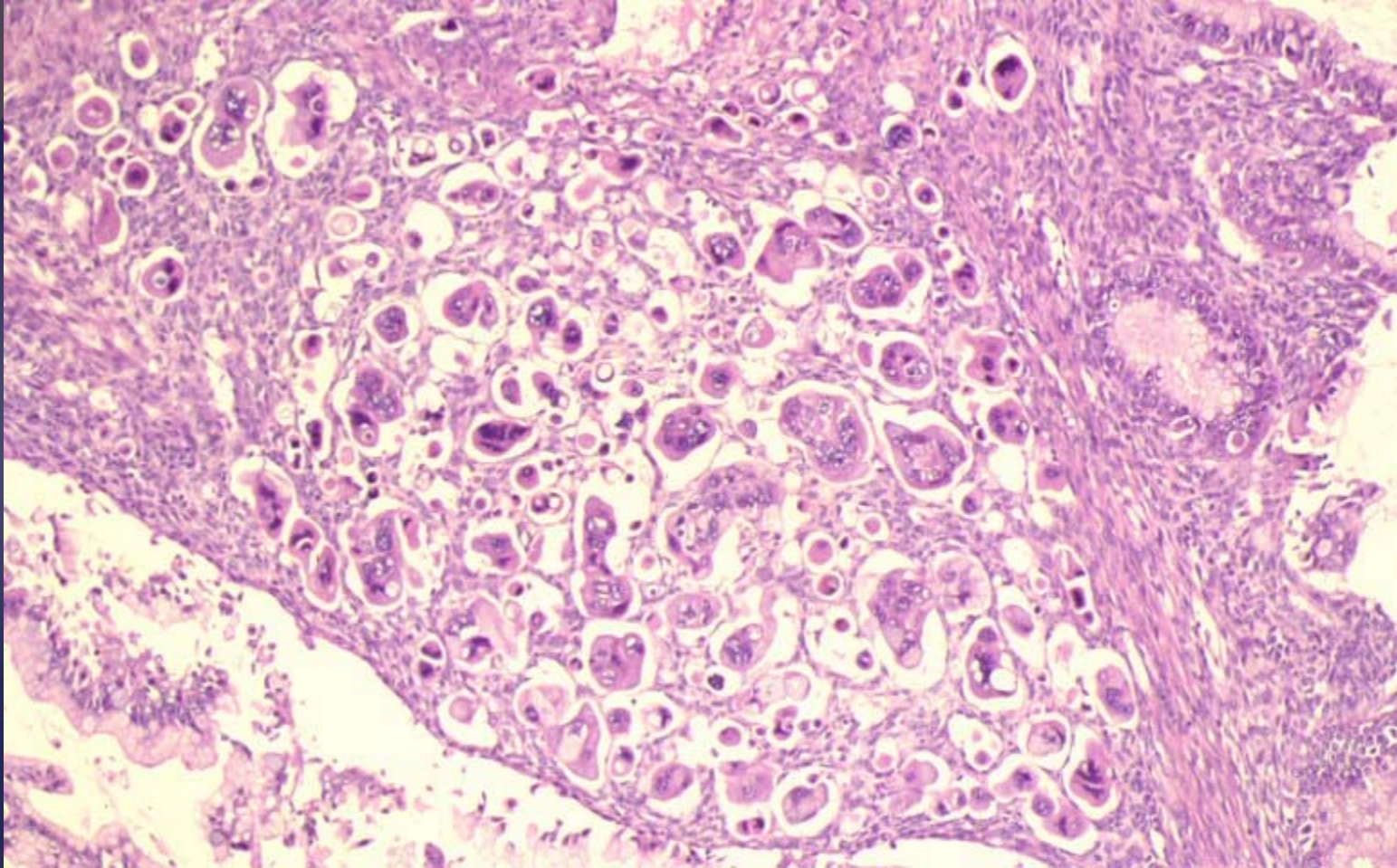
# Sarcomatous nodule



Hitoshi et al, (2013)



# Anaplastic Mucinous Carcinoma



Prat: [www.bdiap.org/Belf02/Prat/8-MucinAnapl-Ca.jpg](http://www.bdiap.org/Belf02/Prat/8-MucinAnapl-Ca.jpg)



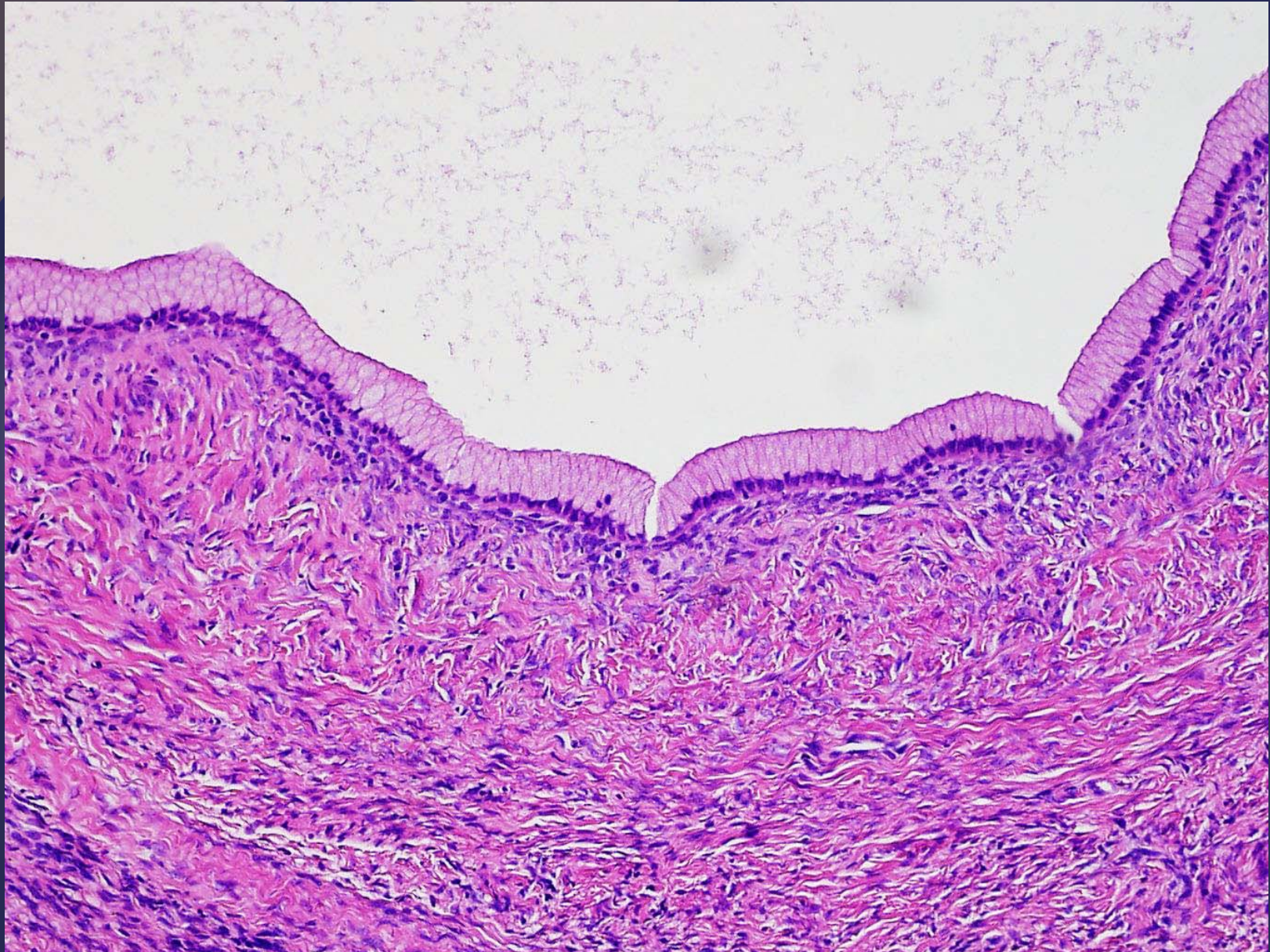
*Cueva de los cristales, Chihuahua, Mexico*

# Case 3

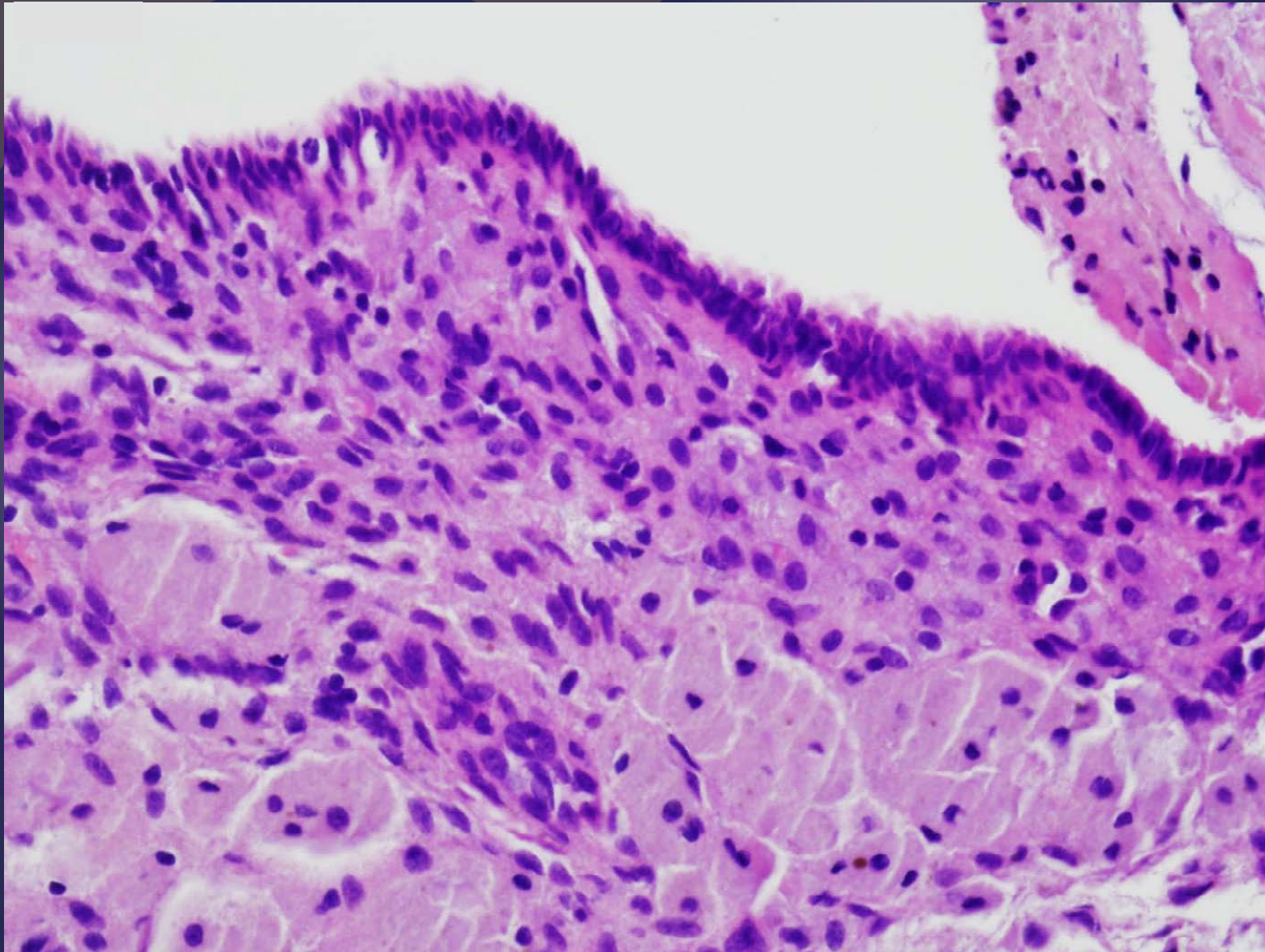
## History:

- 62 year old woman with pain and vaginal bleeding
- Anemic
- Ultrasound showed fibroid uterus
- Hysterectomy
  - Simple ovarian cyst
  - Endometriosis

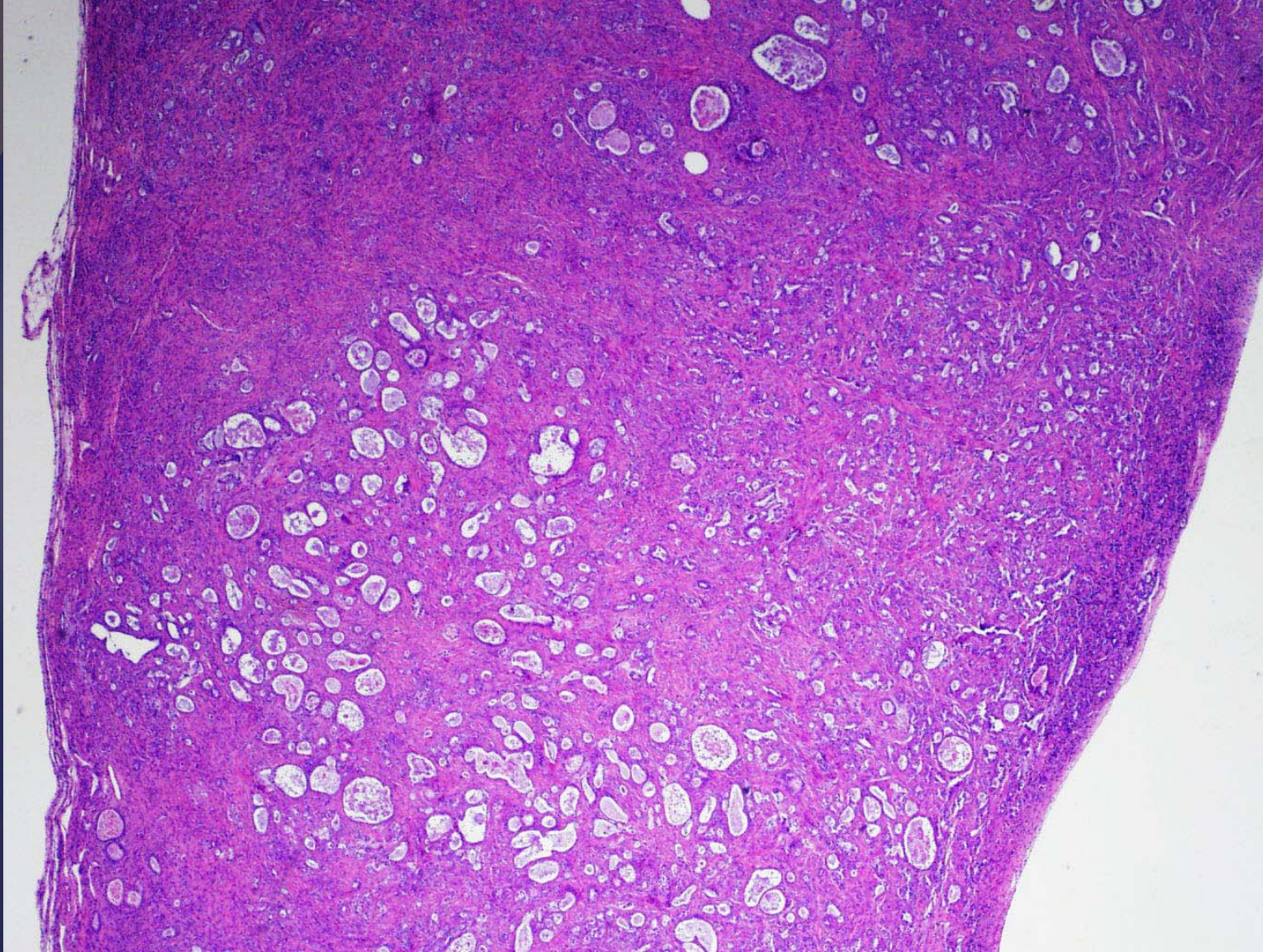
## Case 3 – Ovarian Cyst



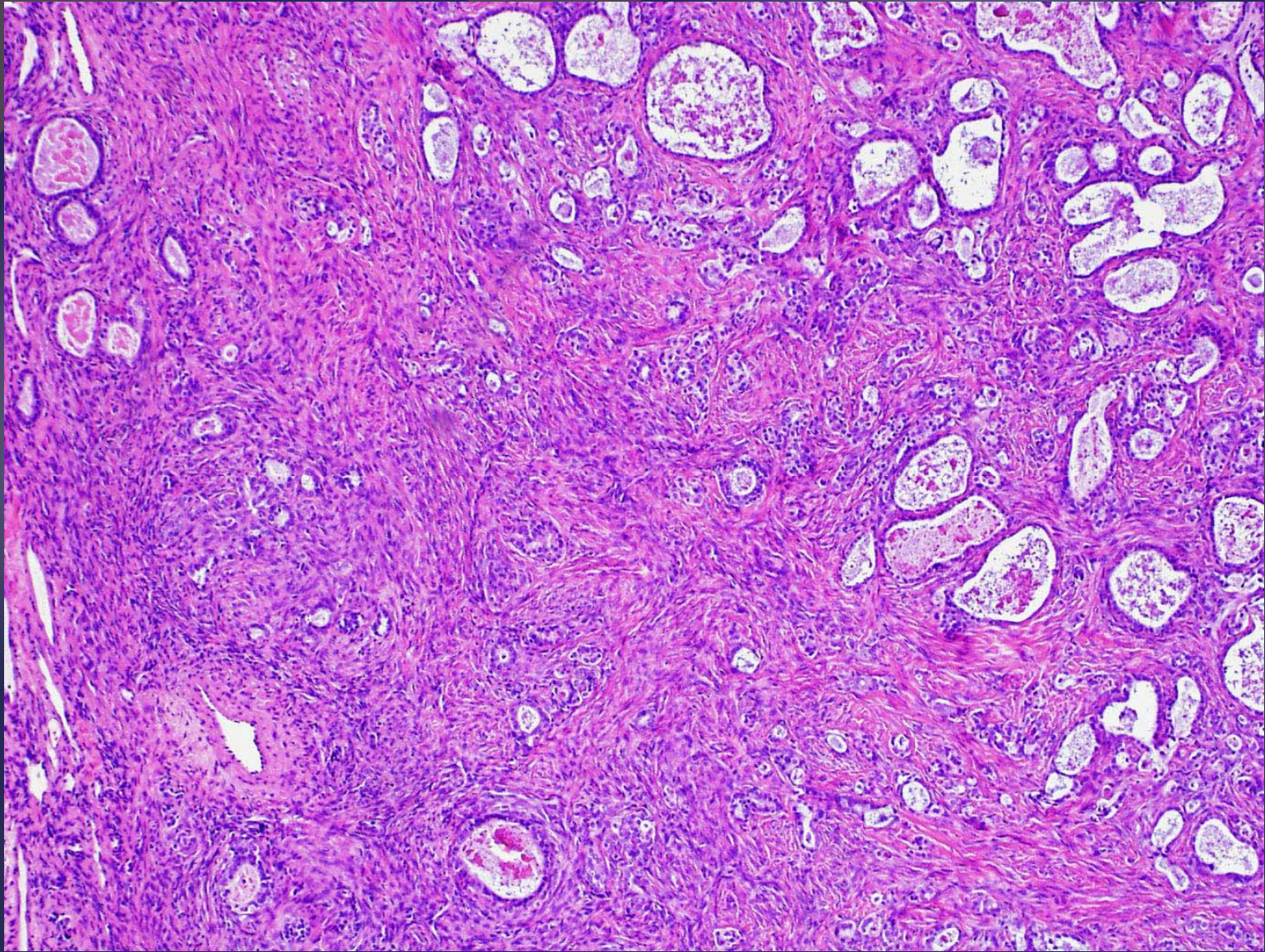
## Case 3 – Endometriosis



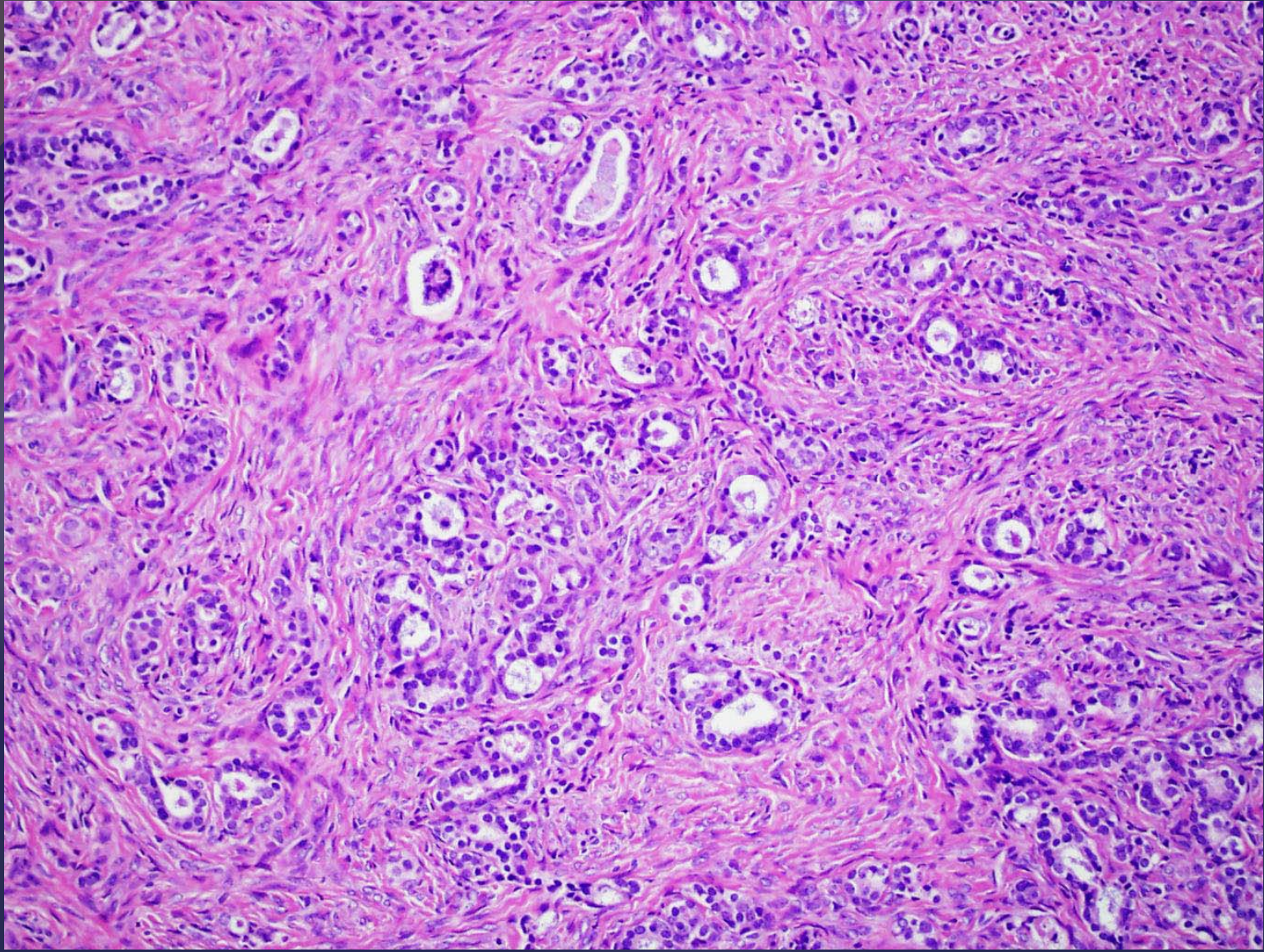
# Case 3



# Case 3

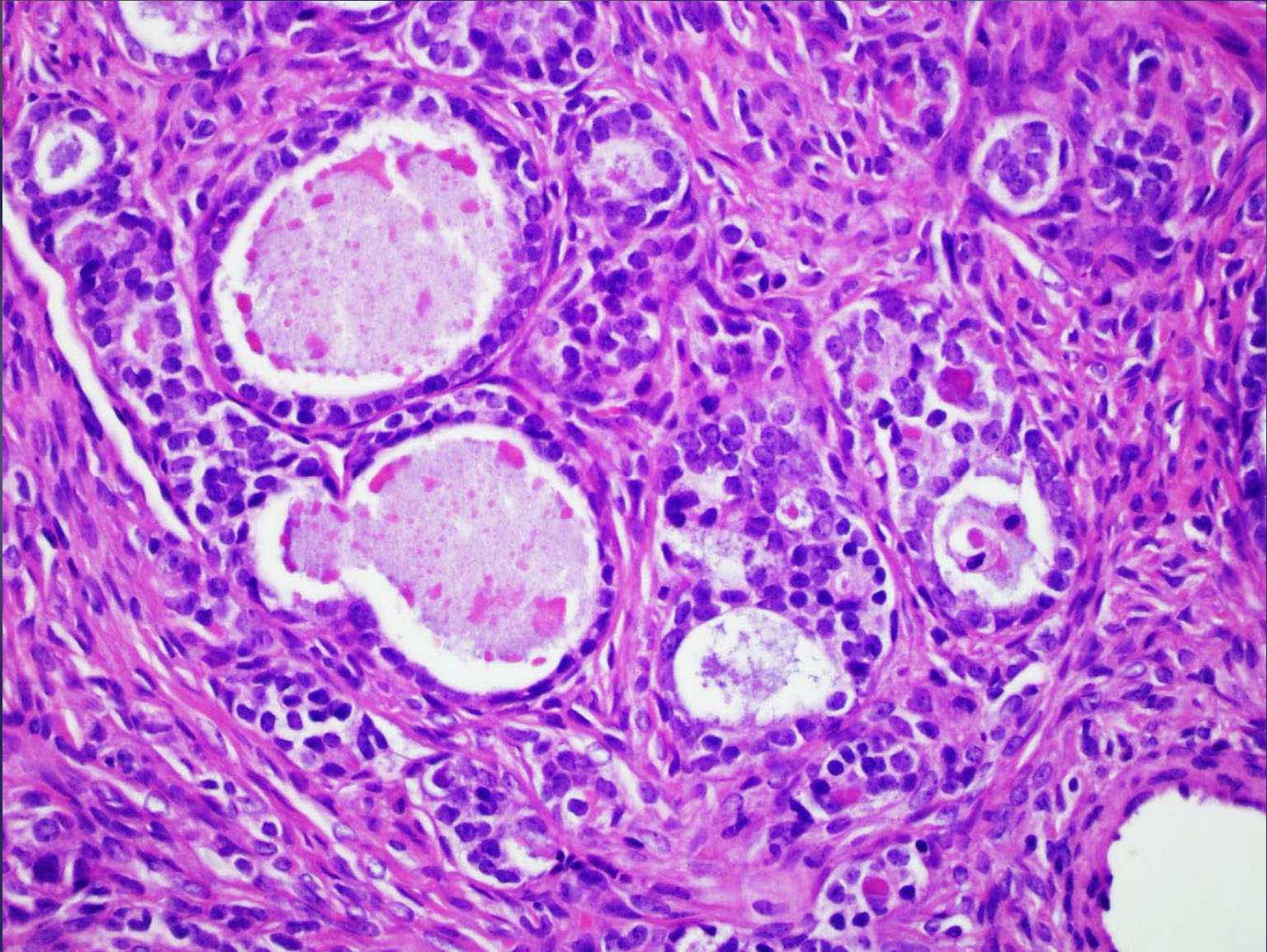


# Case 3

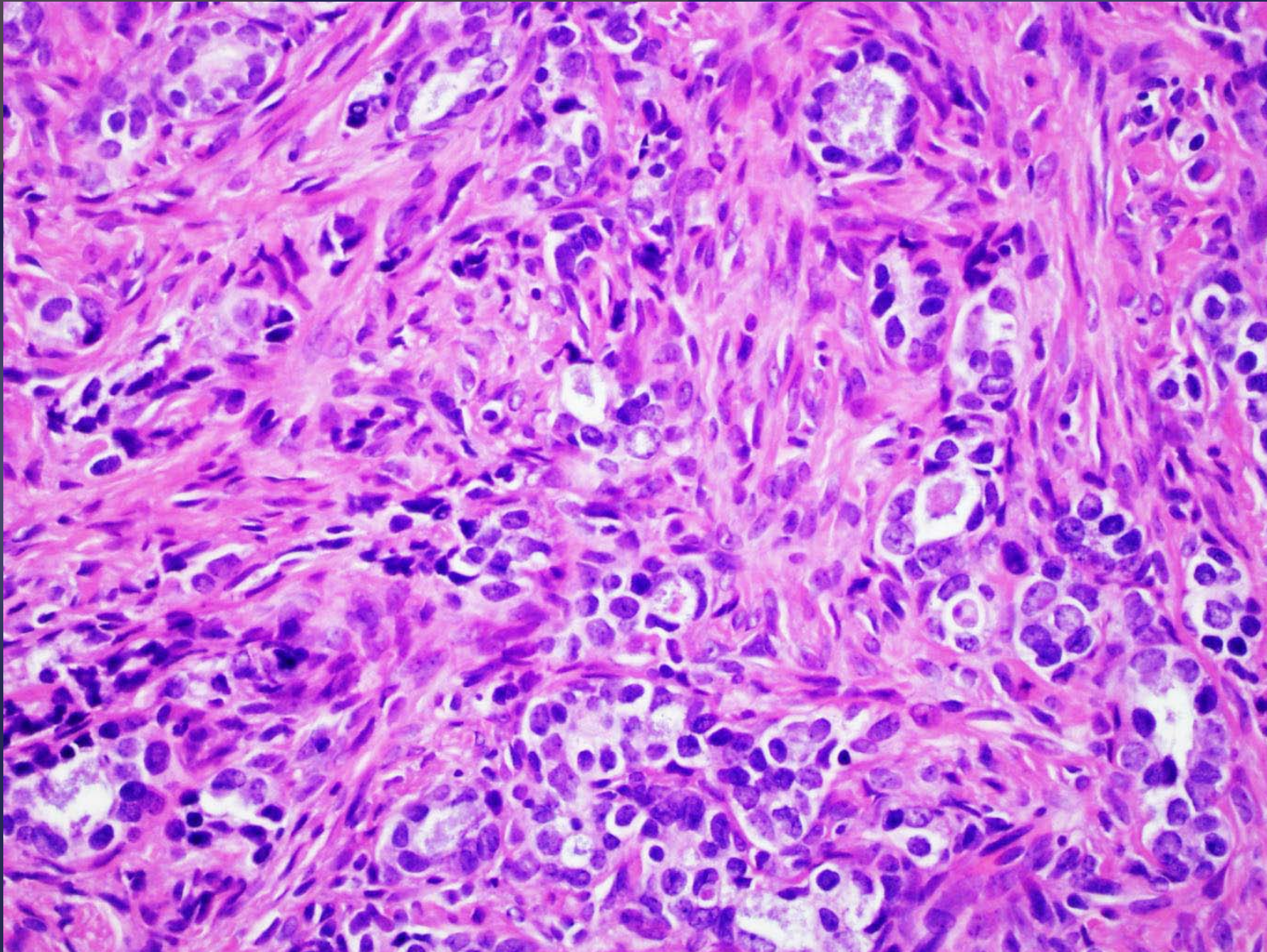




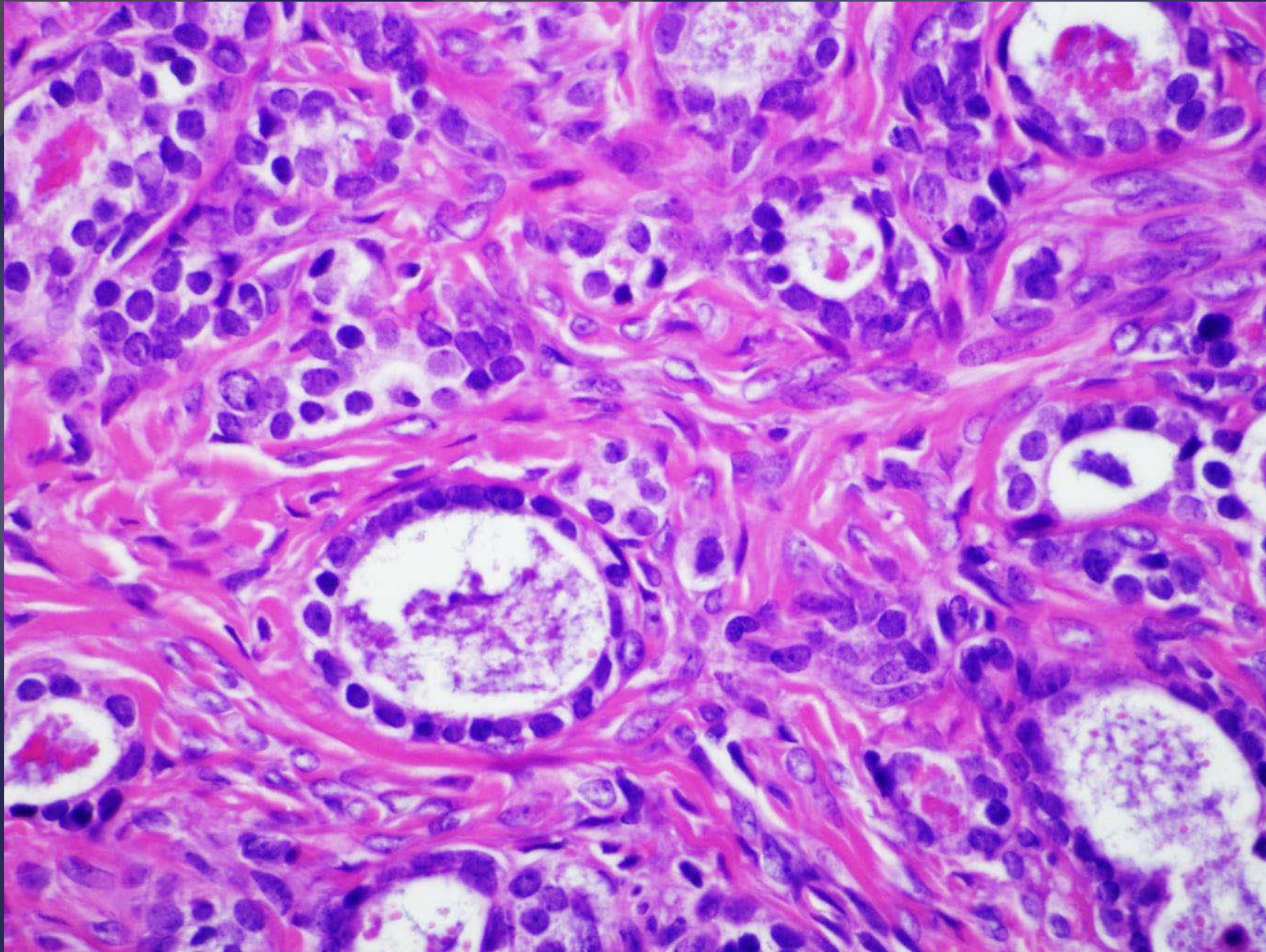
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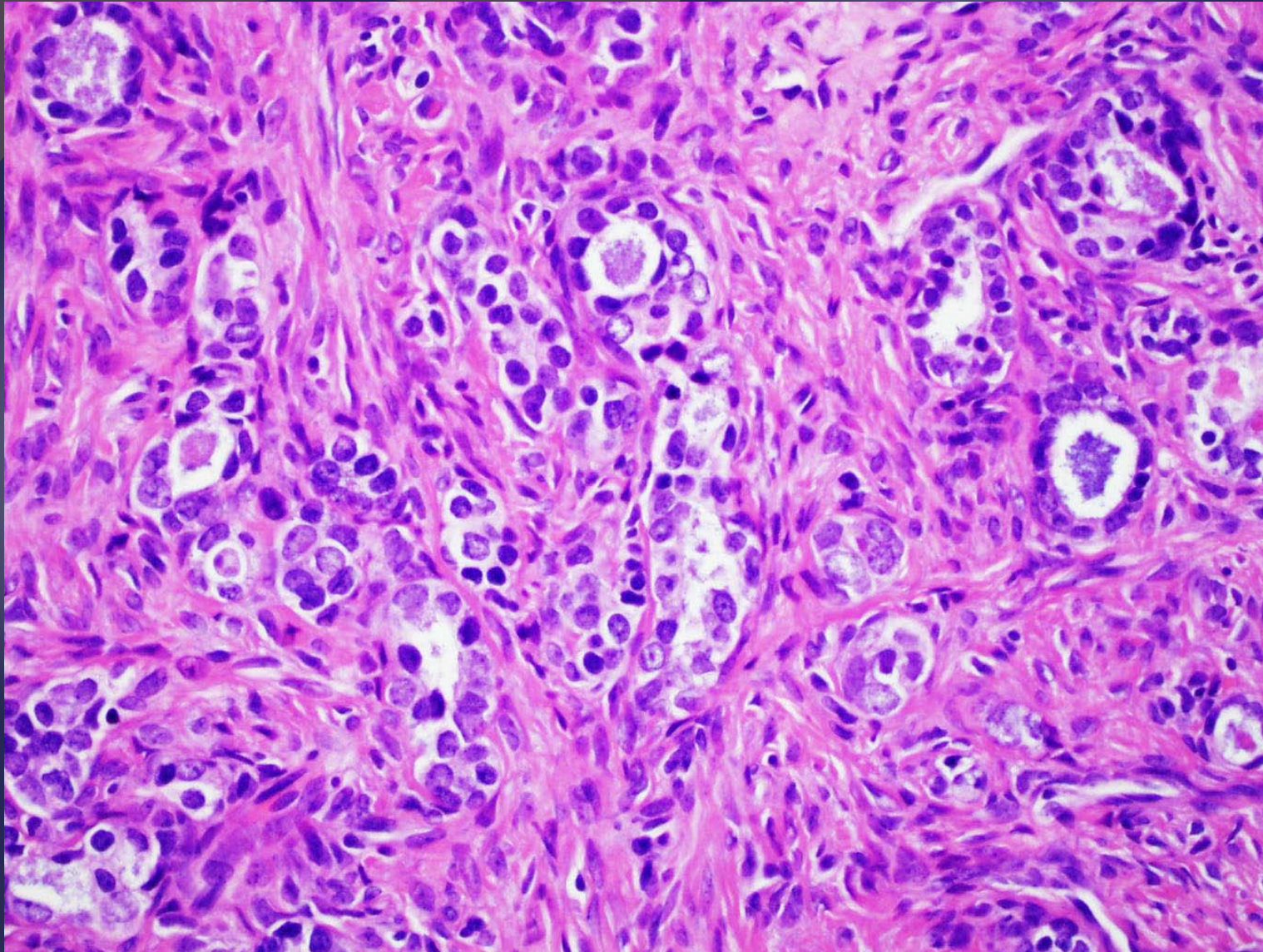
# Case 3



# Case 3



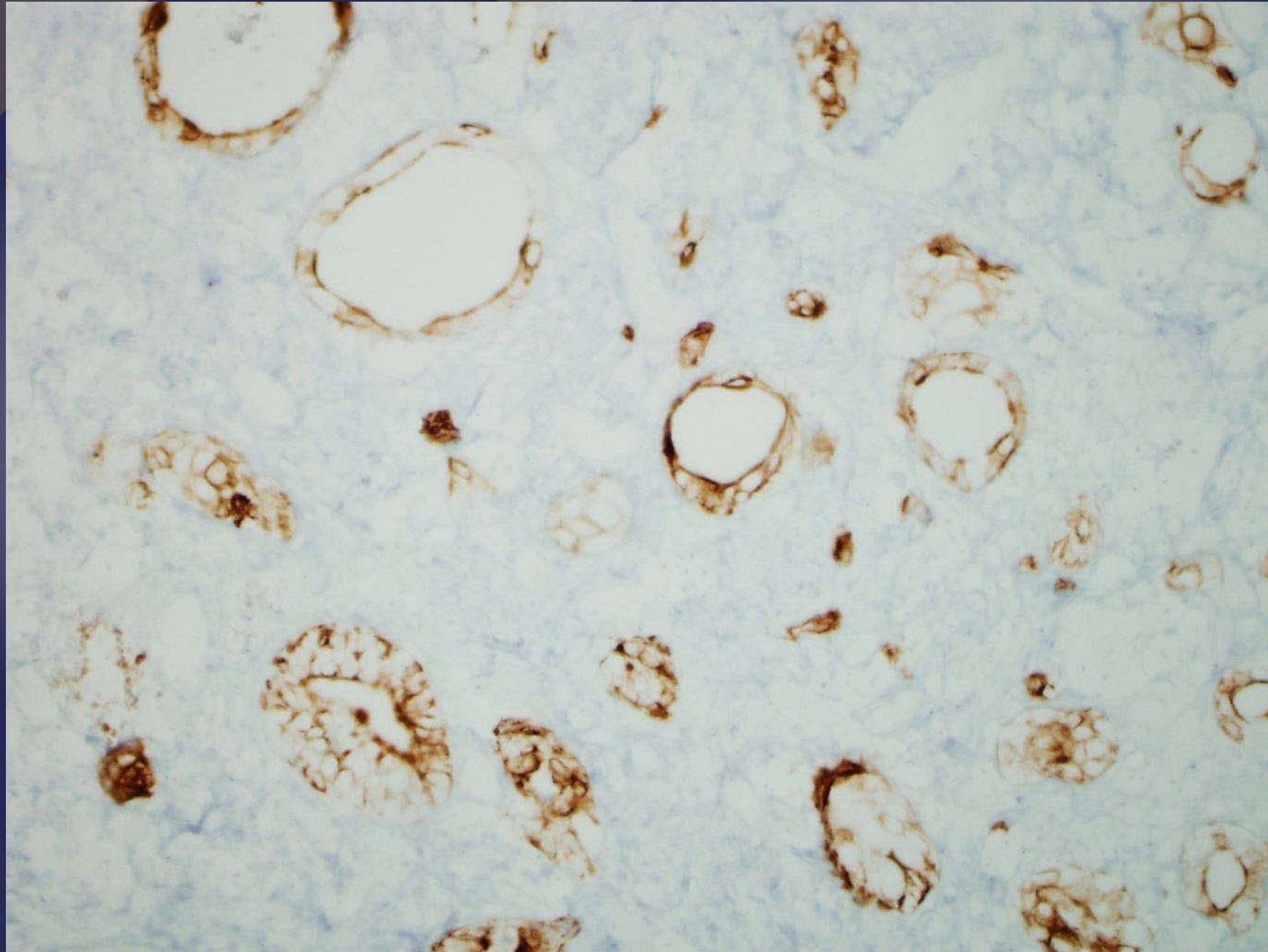
# Case 3



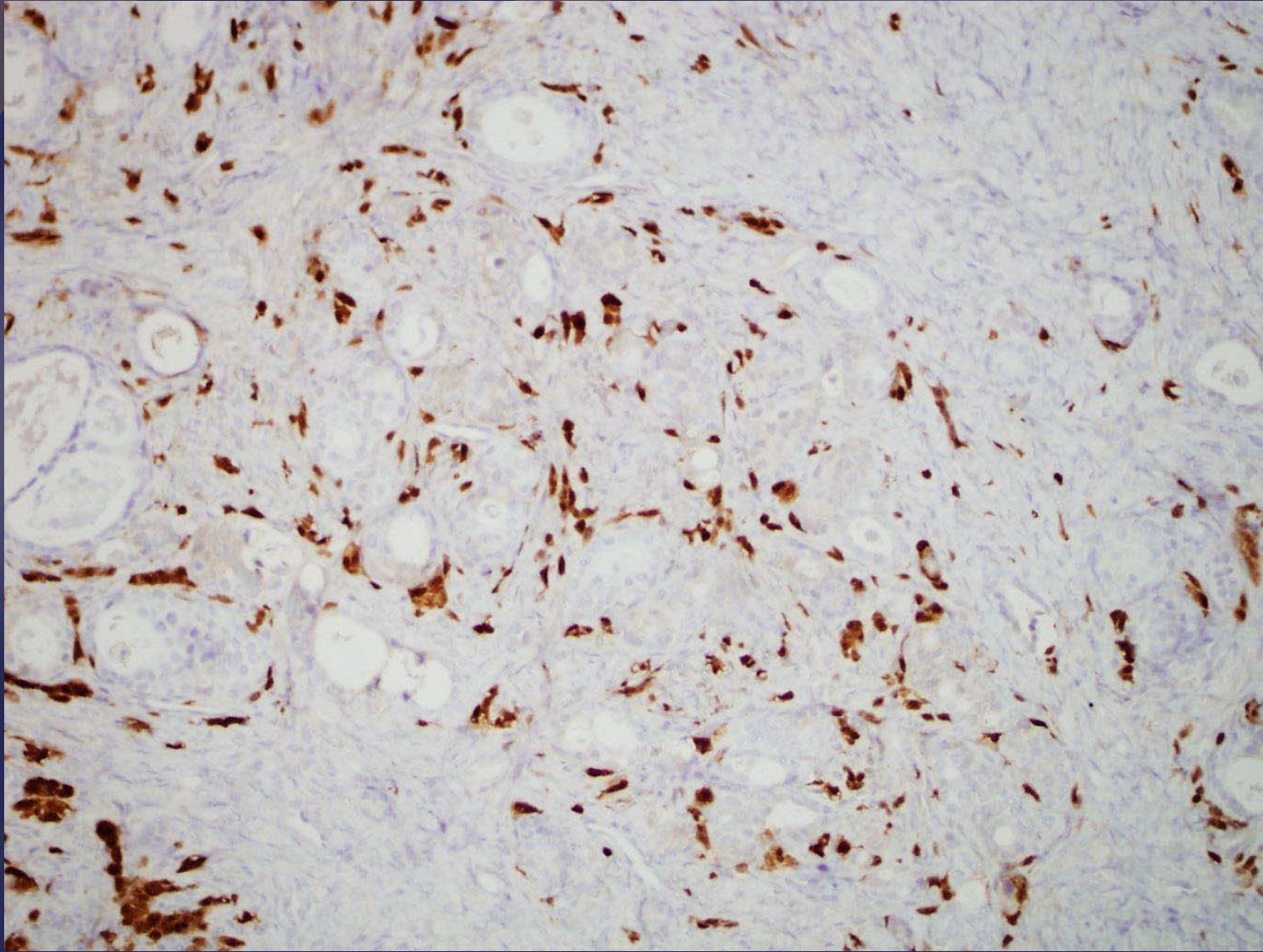
# Case 3 - Differential Diagnosis

- Carcinoma
- Metastasis
- Sex cord stromal tumor
- Mesonephric remnants
- Adenomatoid tumor
- Monodermal teratoma
  - Struma ovarii
  - Carcinoid

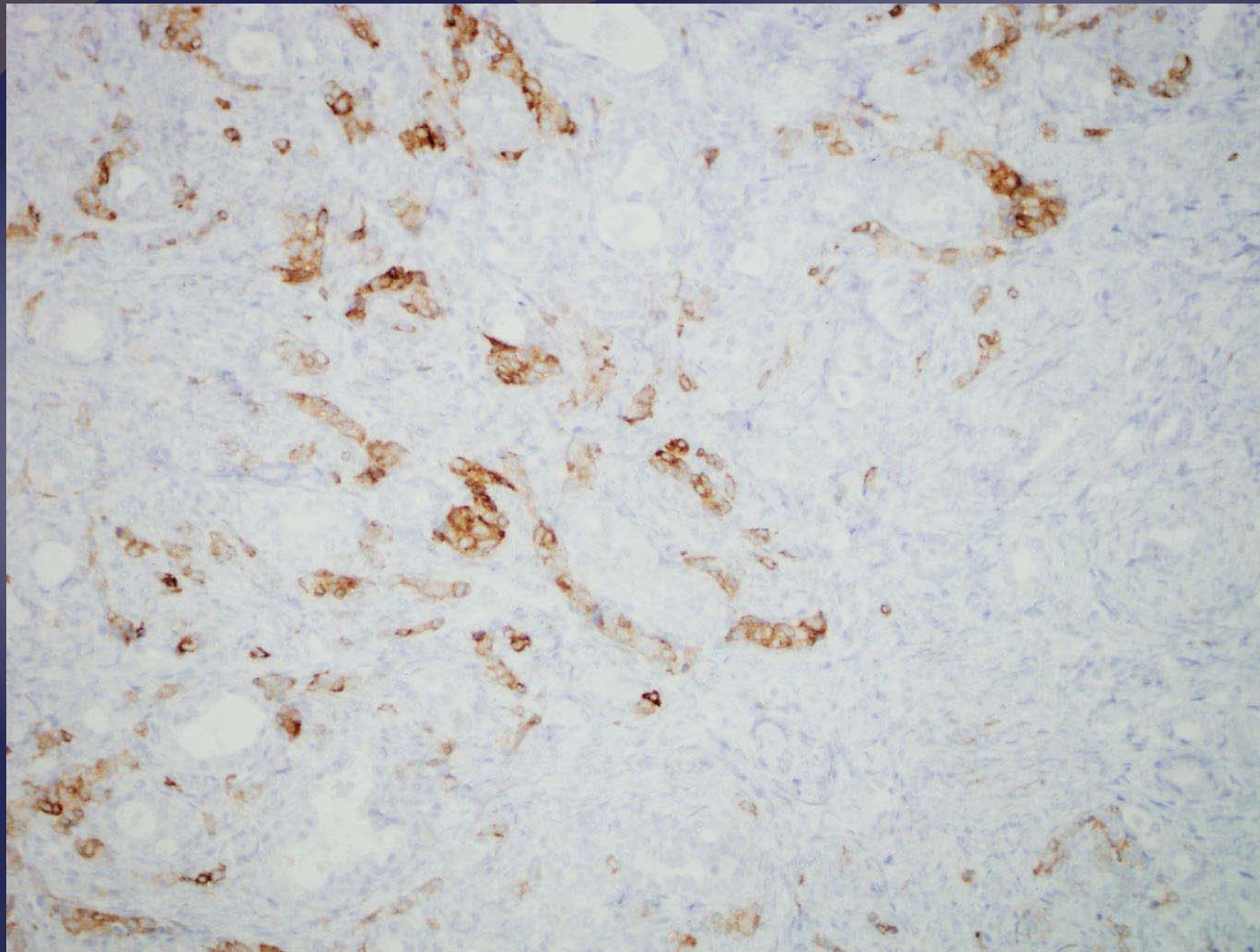
CK7 (+)



# Calretinin



# Inhibin (Focally +)





## Other Stains:

- PAX 8 (weak focal +)
- CD10 (-)
- ER (-)
- Chromogranin (-)
- Synaptophysin (-)
- TTF-1 (-)

# Case 3 - Final Diagnosis

“In my opinion, the diagnosis here is endometrioid adenocarcinoma, grade 1 of 3, arising out of the background of a mucinous cystadenoma. The mucinous cystadenoma is of mullerian mucinous type, and of course that cell type is very closely related to endometriosis. As is so typical, there is a background of endometriosis. That a carcinoma arising on the background of a mucinous cystadenoma should be endometrioid is no surprise. I think one has to call it endometrioid because there is simply no mucinous nature to the low-grade carcinoma...”

Dr. Robert Young, MGH, Boston

# Case 3 - Mucinous Ovarian Tumors

## General Features:

- Second most common epithelial-stromal neoplasm of the ovary
- 80% benign
- 10% borderline
- 10% malignant

# Case 3 - Mucinous Ovarian Tumors

## Clinical Features:

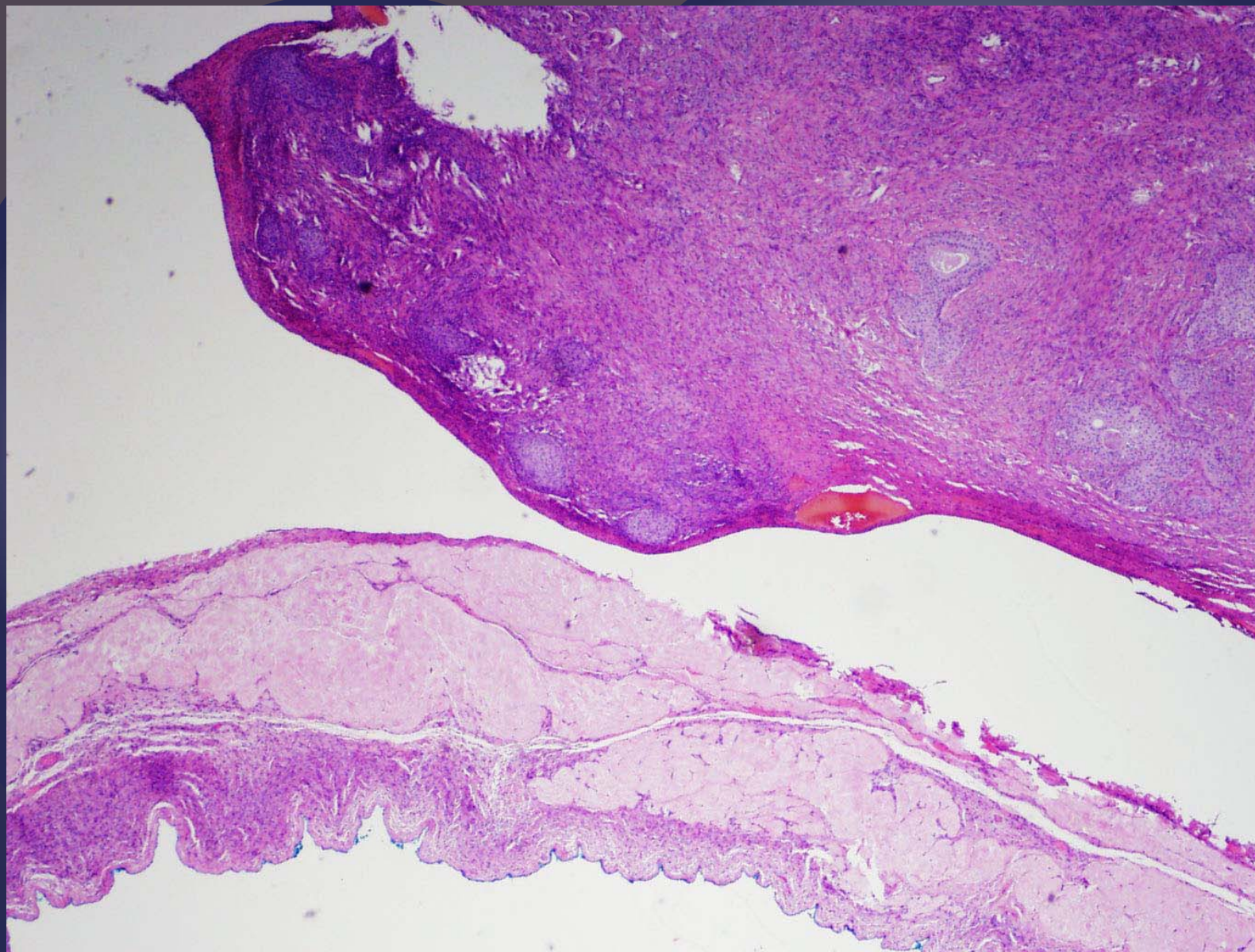
- Age at presentation
  - Benign tumors - younger women
  - Borderline and malignant tumors - average 50's
- Commonly accompanied by hormone manifestations (androgen or estrogen)
- CA-125 is less sensitive for mucinous tumors

# Case 3 - Mucinous Ovarian Tumors

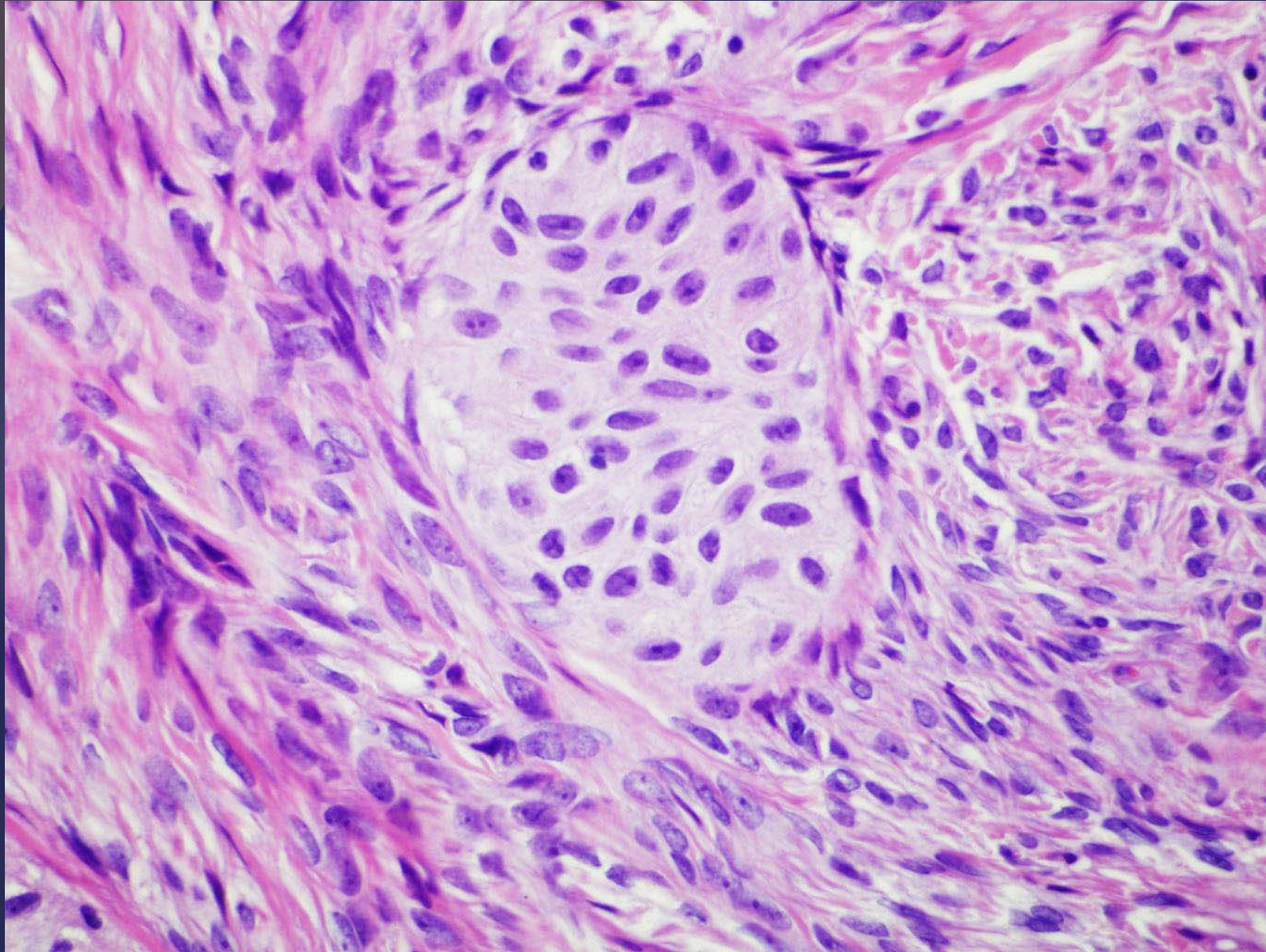
Other common cyst wall findings:

- 5% have a mature teratoma component
- Not uncommonly associated with Brenner tumor

# Case 3 – Ovarian Cyst with Brenner Tumor



## Case 3 – Ovarian Cyst with Brenner Tumor



# Case 3 - Endometrioid Ovarian Tumors

## General Features:

- Benign endometrioid tumors of the ovary are rare
- Second most common ovarian malignancy after serous



# Case 3 - Endometrioid Ovarian Tumors

## Clinical Features:

- Postmenopausal
- Mid 50's
- Discovered at earlier stage than serous
  - (stage for stage, same prognosis)
- Frequently associated with endometriosis
- Often bilateral

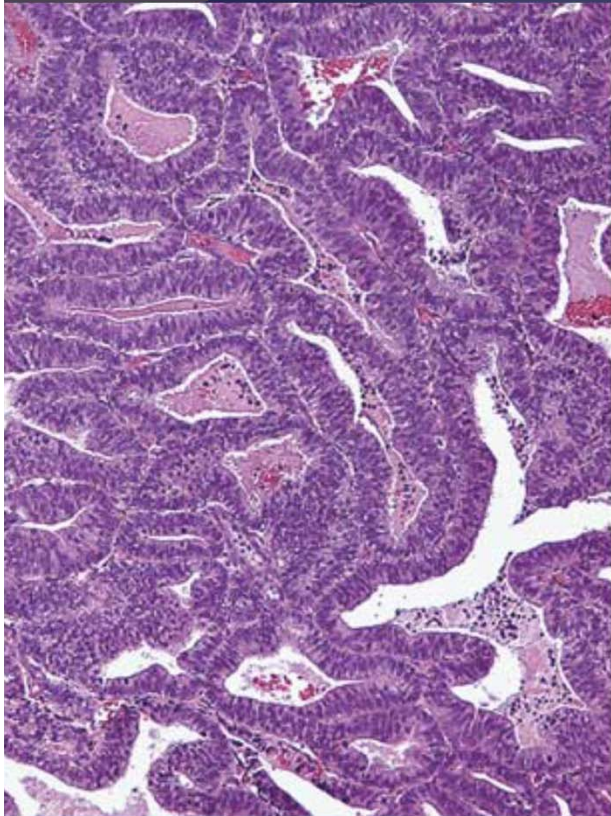
# Case 3 - Endometrioid Ovarian Tumors

## Classic Histology:

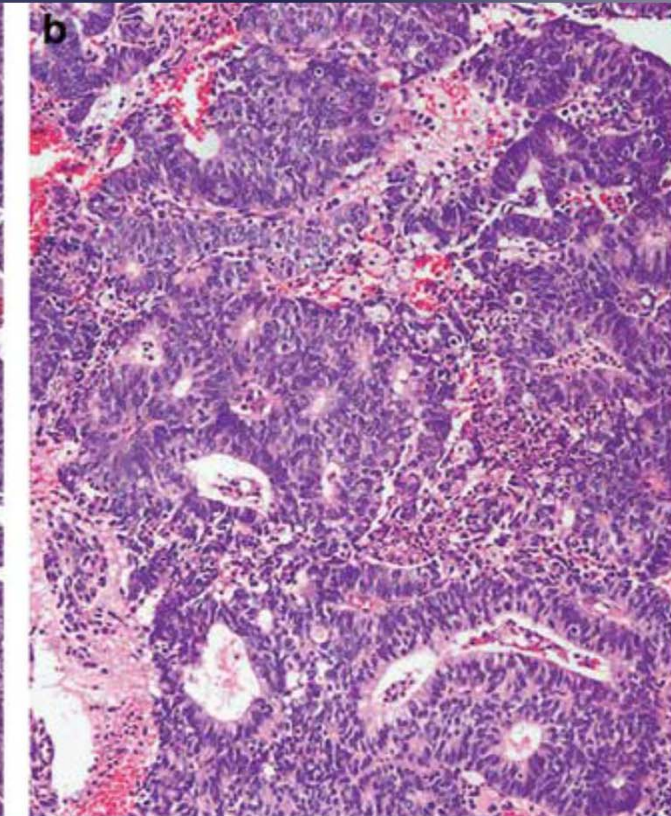
- Back to back glands, fibrotic stroma
- Stratified epithelial cells
- Squamous morules
- May be villous or papillary
- Grading in ovary same as for uterine tumors

# Case 3 - Endometrioid Ovarian Tumors

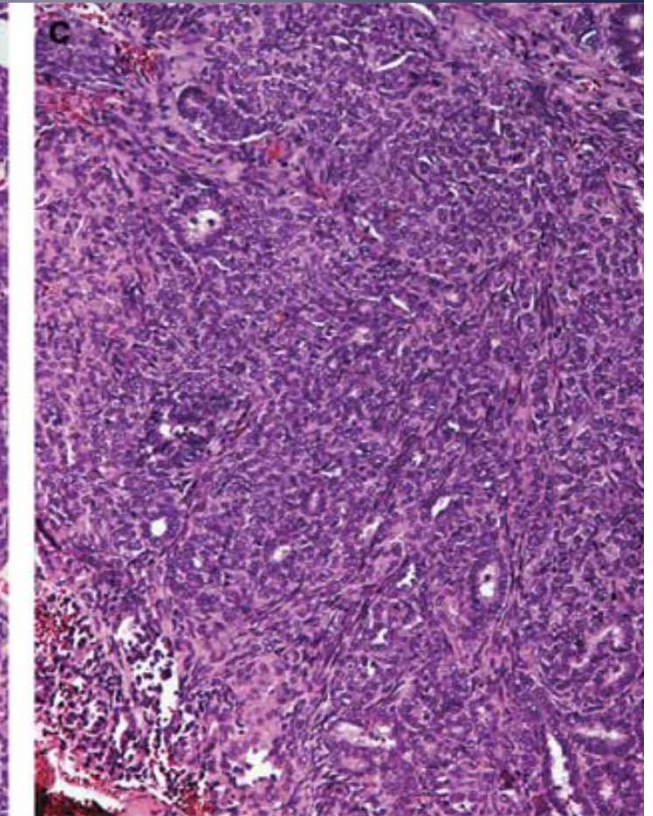
## Classic Endometrioid Histology



FIGO grade I



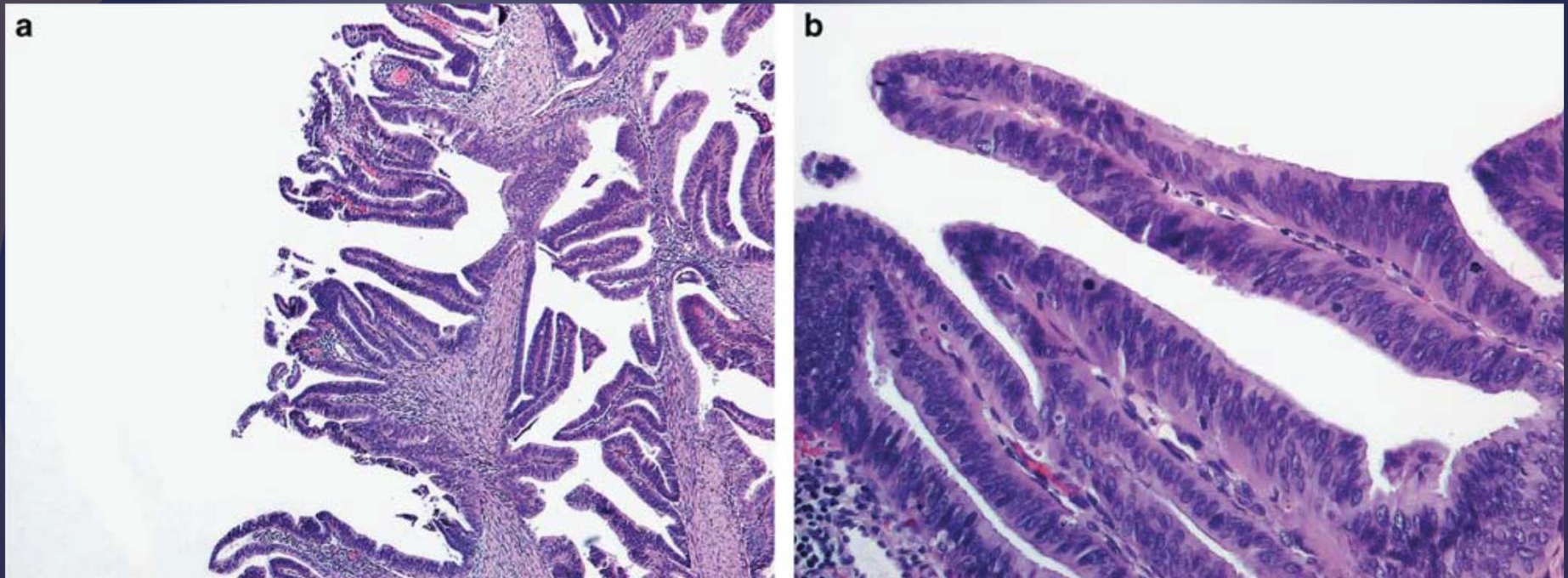
FIGO grade II



FIGO grade III

# Case 3 - Endometrioid Ovarian Tumors

Endometrioid carcinoma with villoglandular pattern



# Case 3 - Endometrioid Ovarian Tumors

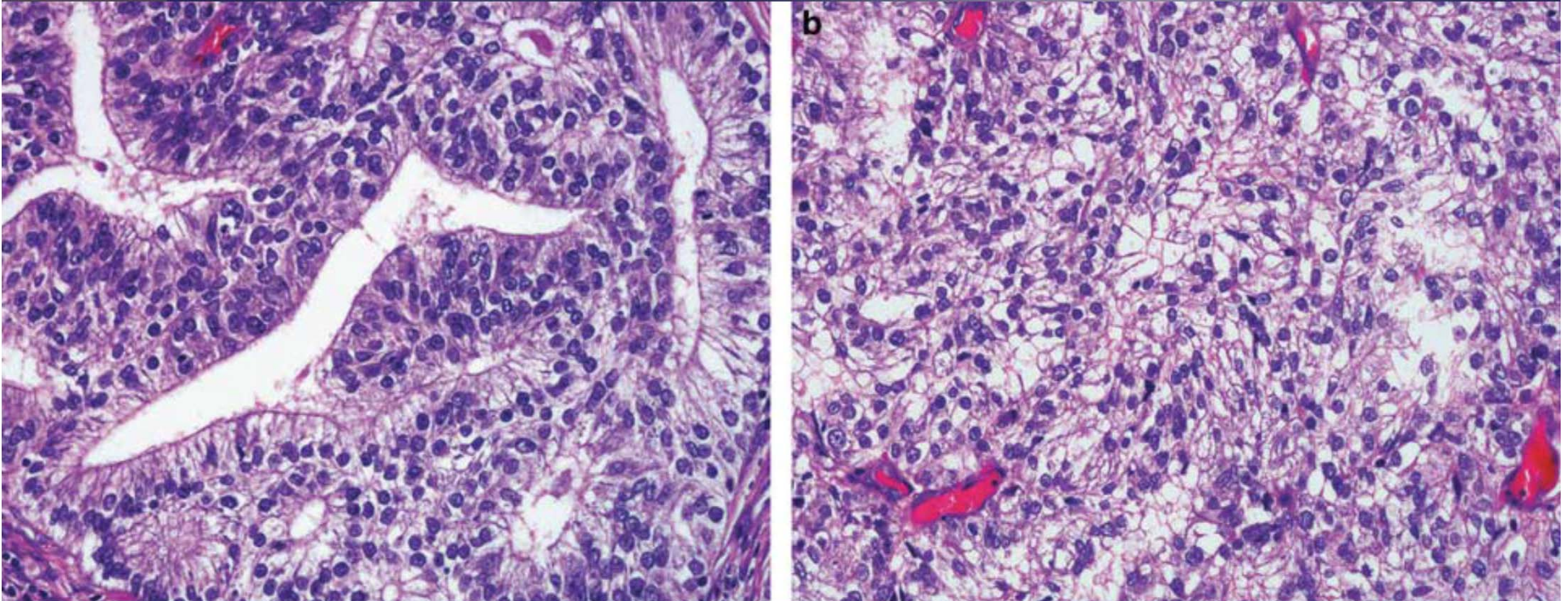
## Variant Histology:

- Secretory
- Oxyphilic
- Ciliated
- Balloon Like
- Spindle Cell
- Mimics
  - Clear cell
  - Sex cord stromal
  - Sertoli-leydig

\* In each, finding a focus of typical endometrioid carcinoma facilitates a correct interpretation

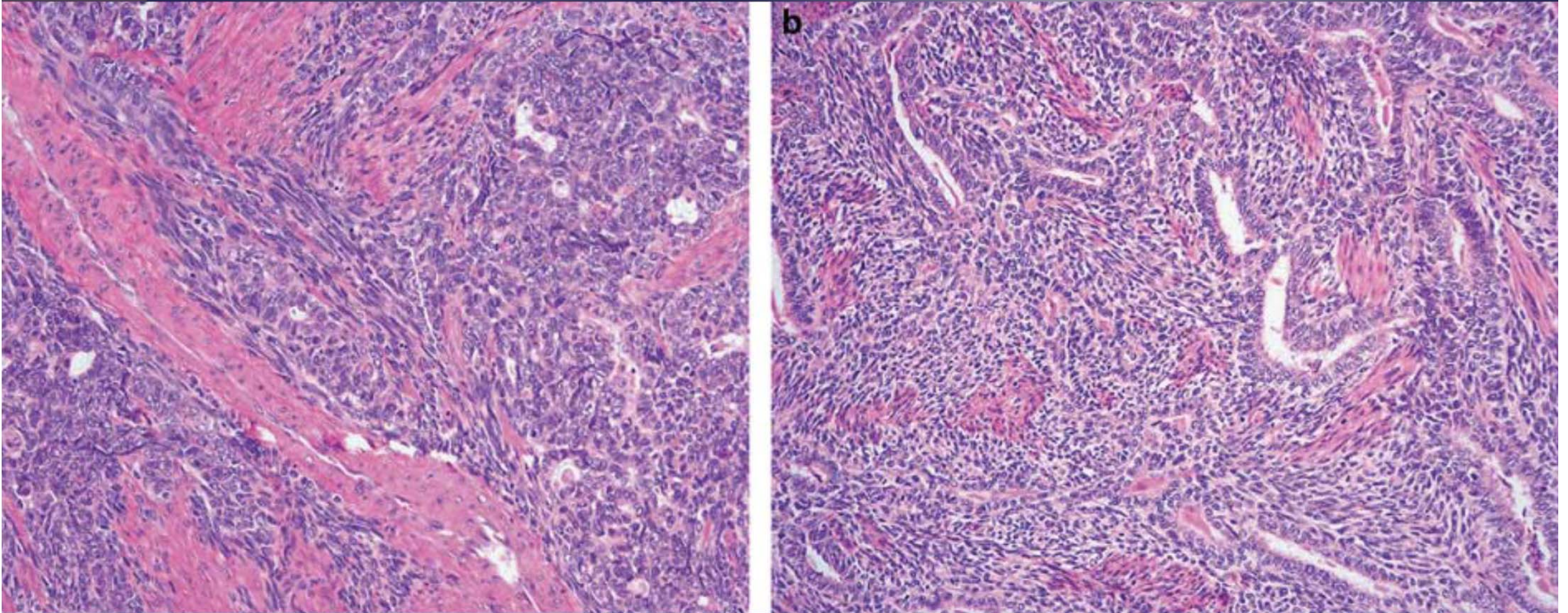
# Case 3 - Endometrioid Ovarian Tumors

## Endometrioid carcinoma with secretory changes



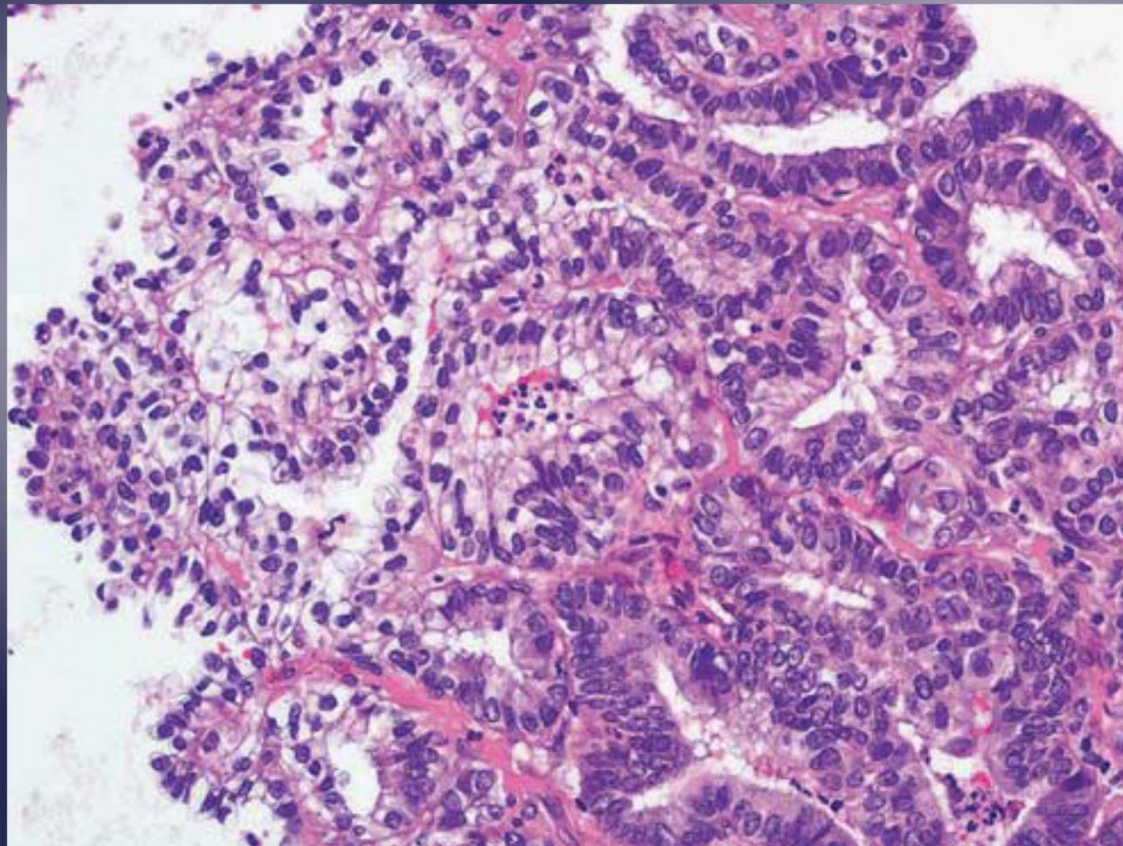
# Case 3 - Endometrioid Ovarian Tumors

## Endometrioid carcinoma with spindle cells



# Case 3 - Endometrioid Ovarian Tumors

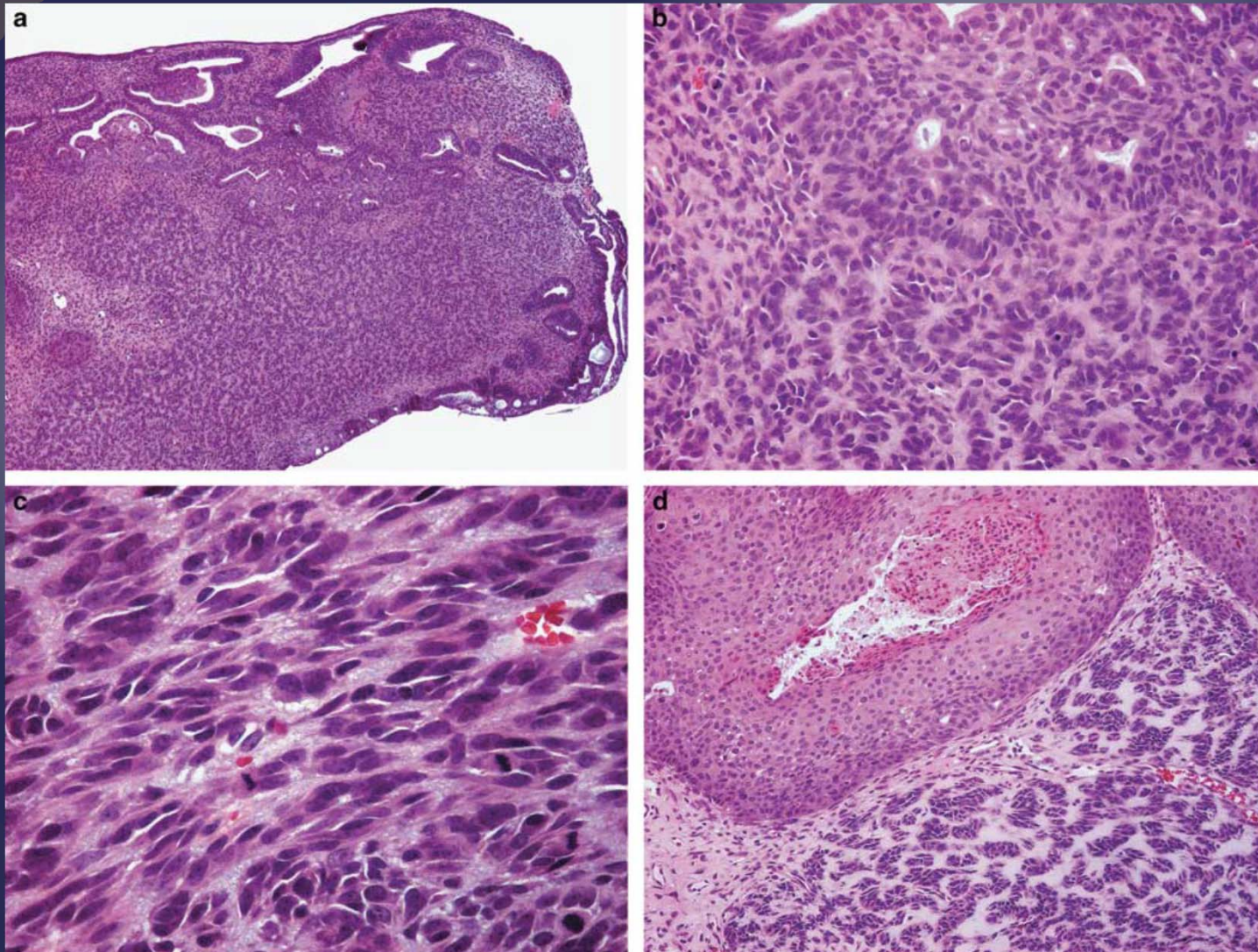
Endometrioid carcinoma with clear cell changes





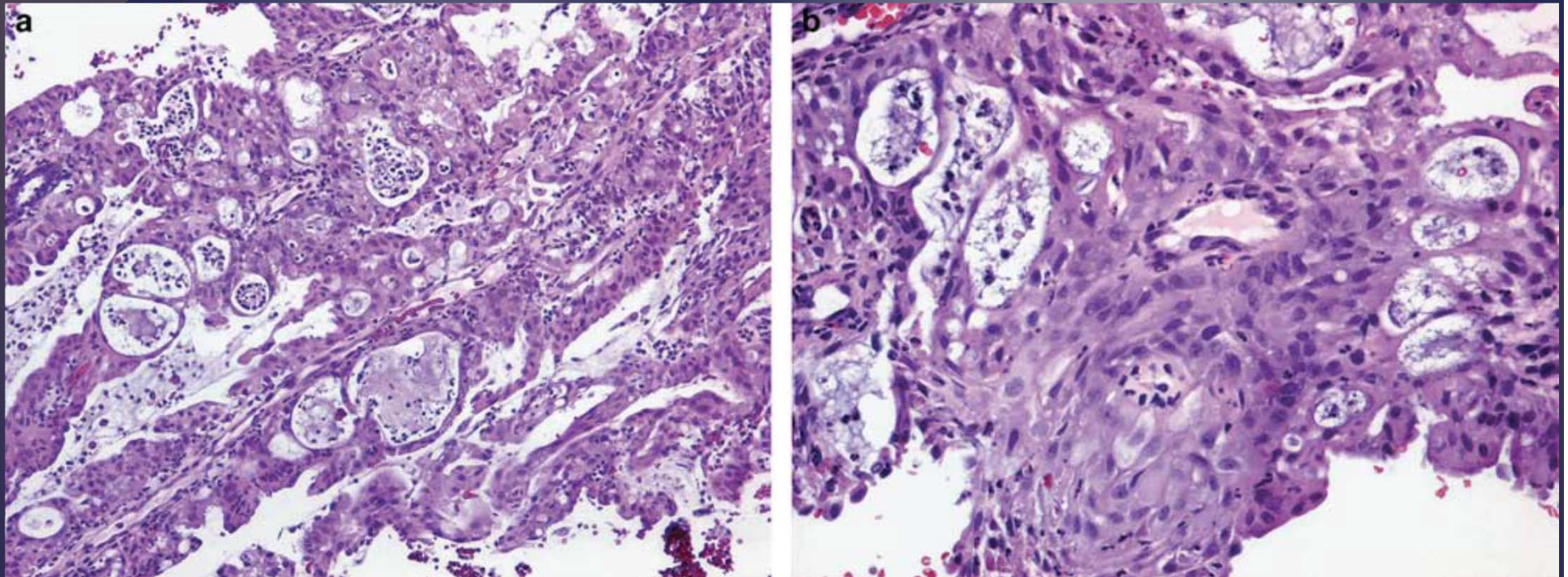
# Case 3 - Endometrioid Ovarian Tumors

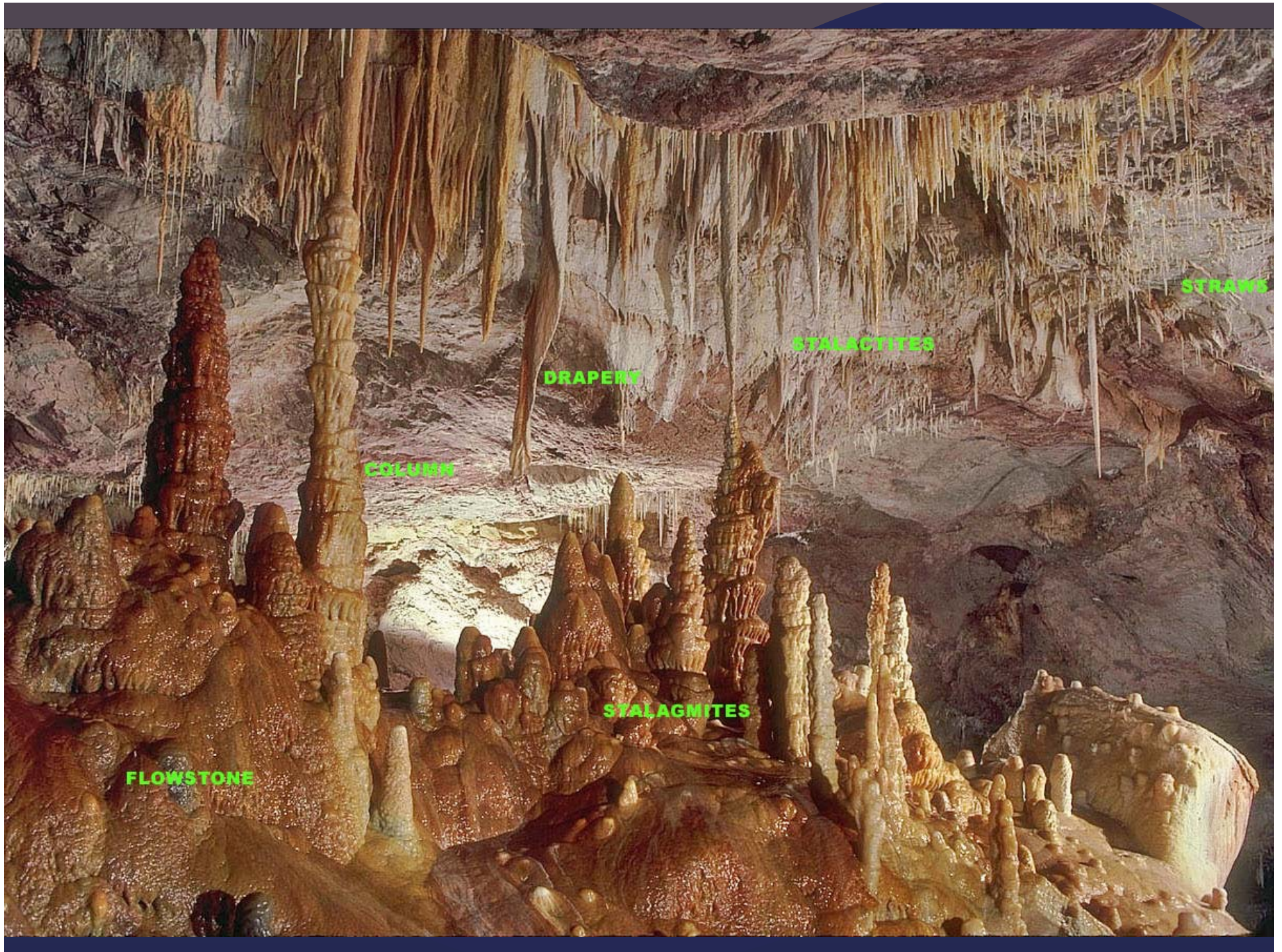
## Endometrioid carcinoma with sex cord stromal pattern



# Case 3 - Endometrioid Ovarian Tumors

Endometrioid carcinoma with microglandular pattern



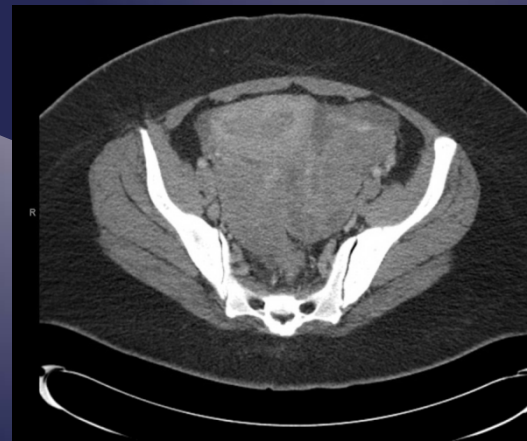
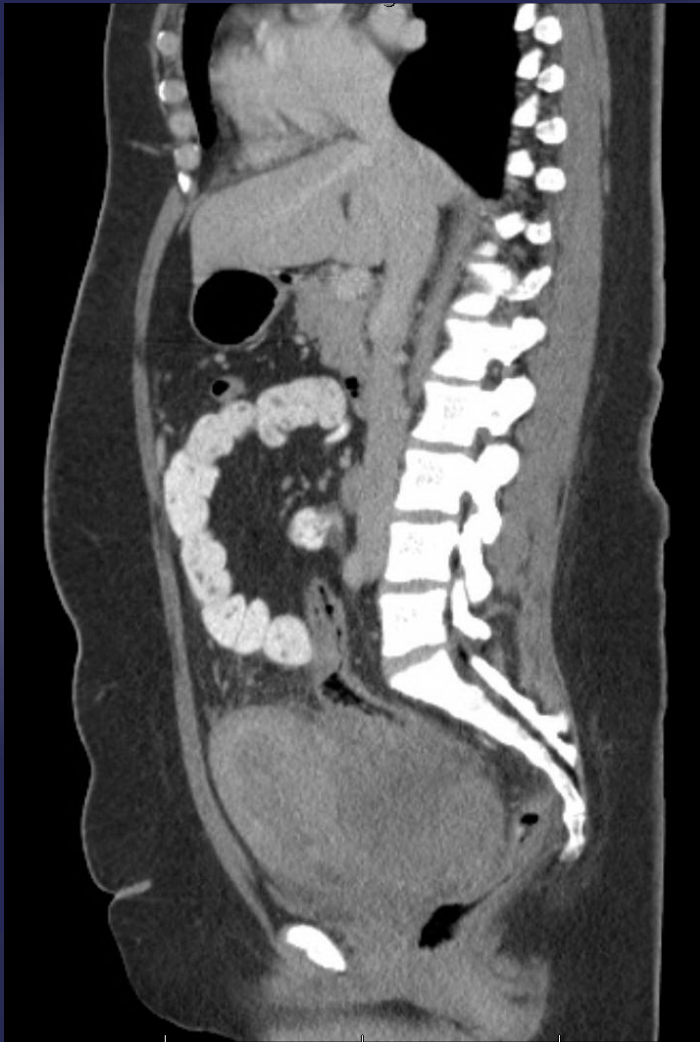


# Case 4

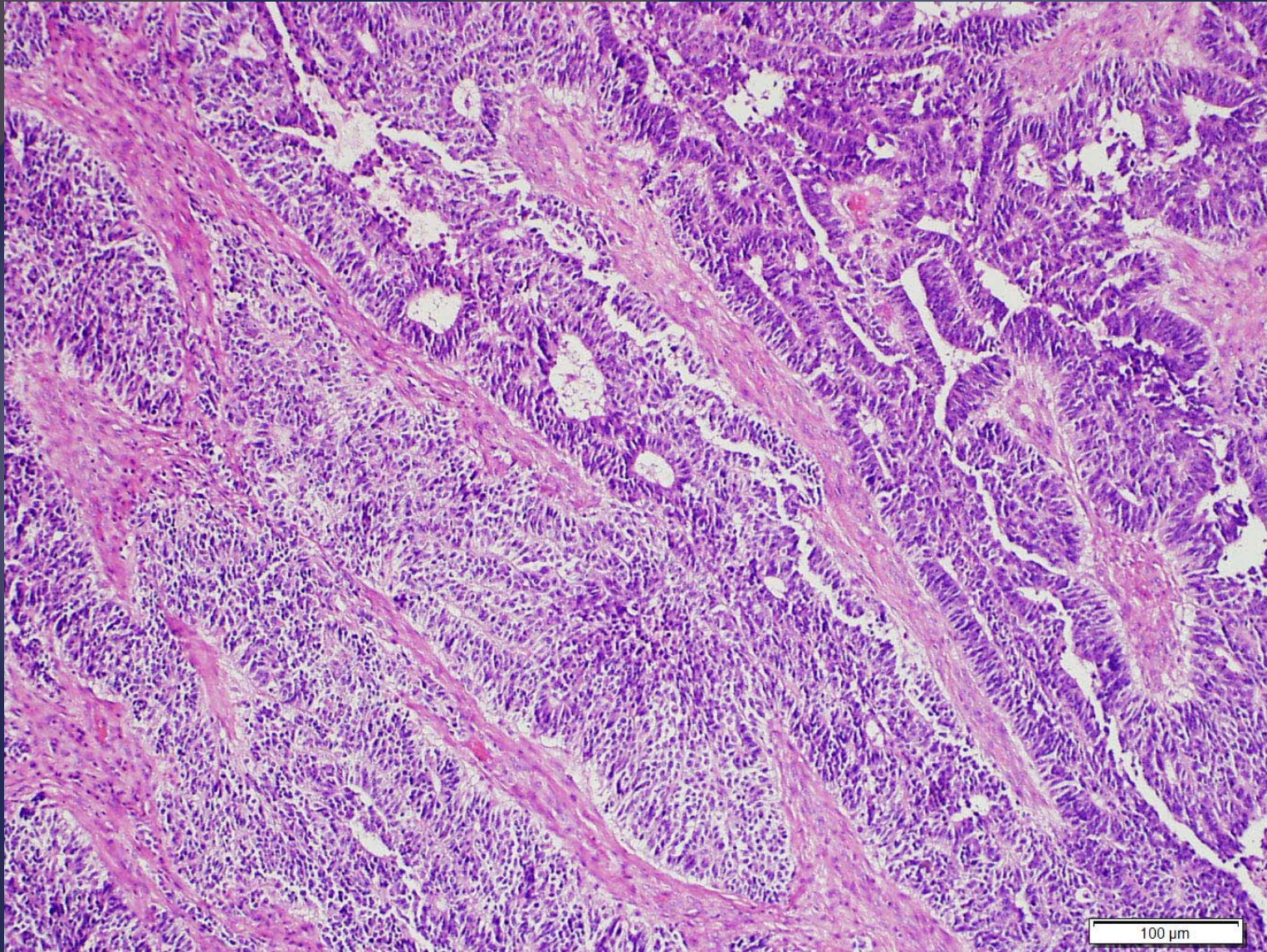
## History:

- 30 year old woman
- 10 month history of heavy vaginal bleeding
- Endometrial biopsy at outside hospital

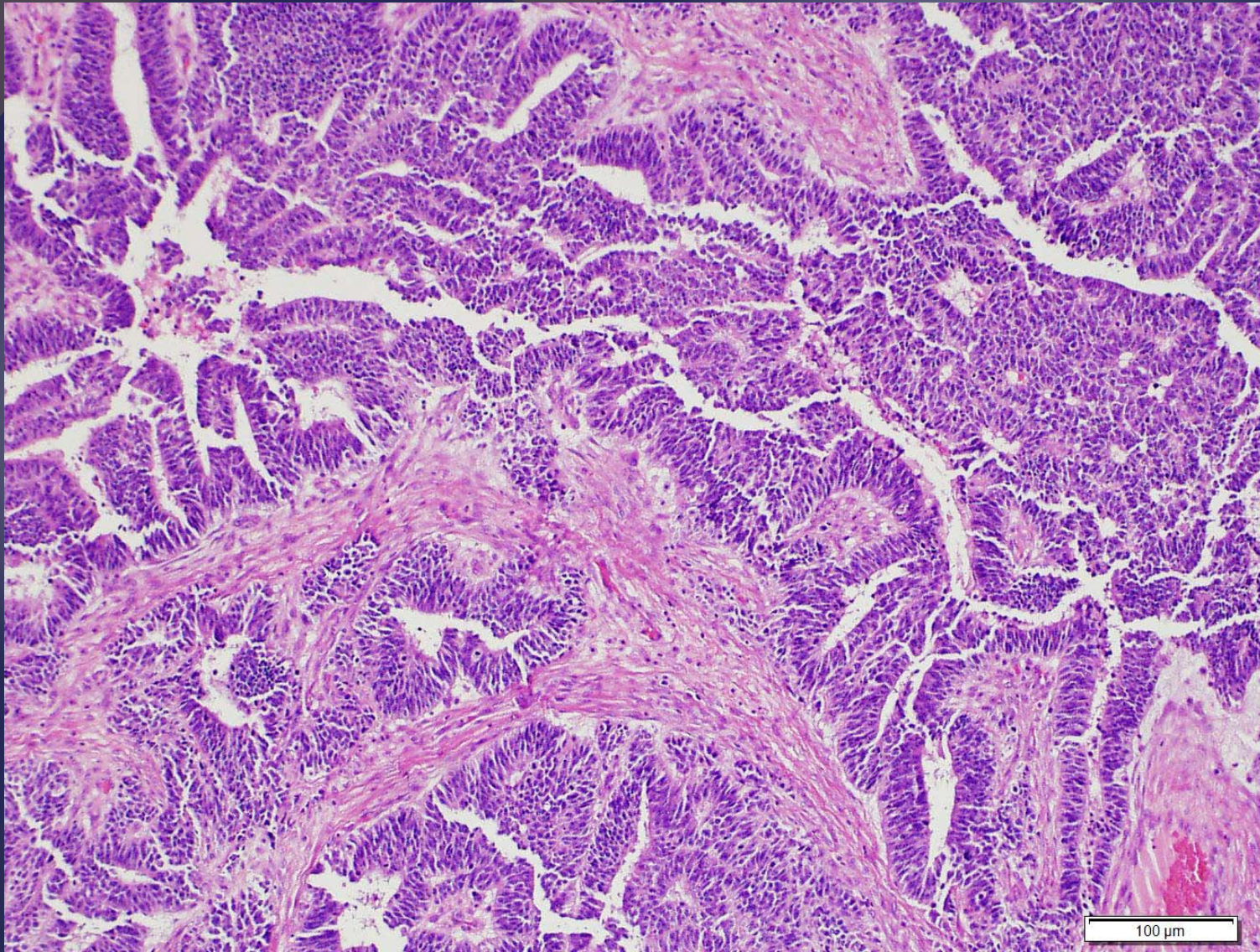
# Case 4 - CT Scan



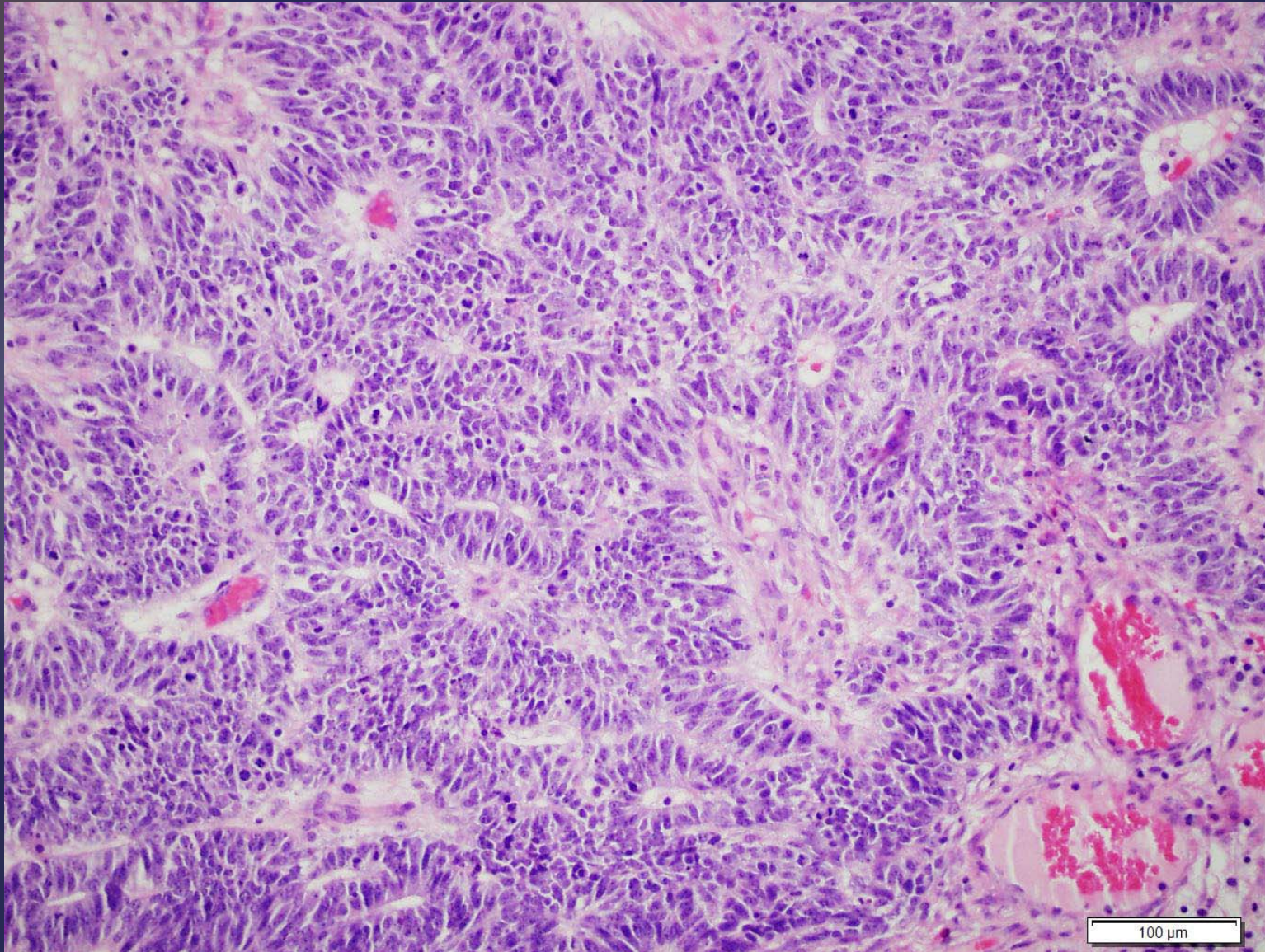
# Case 4 – Uterine Mass



## Case 4 – Uterine Mass

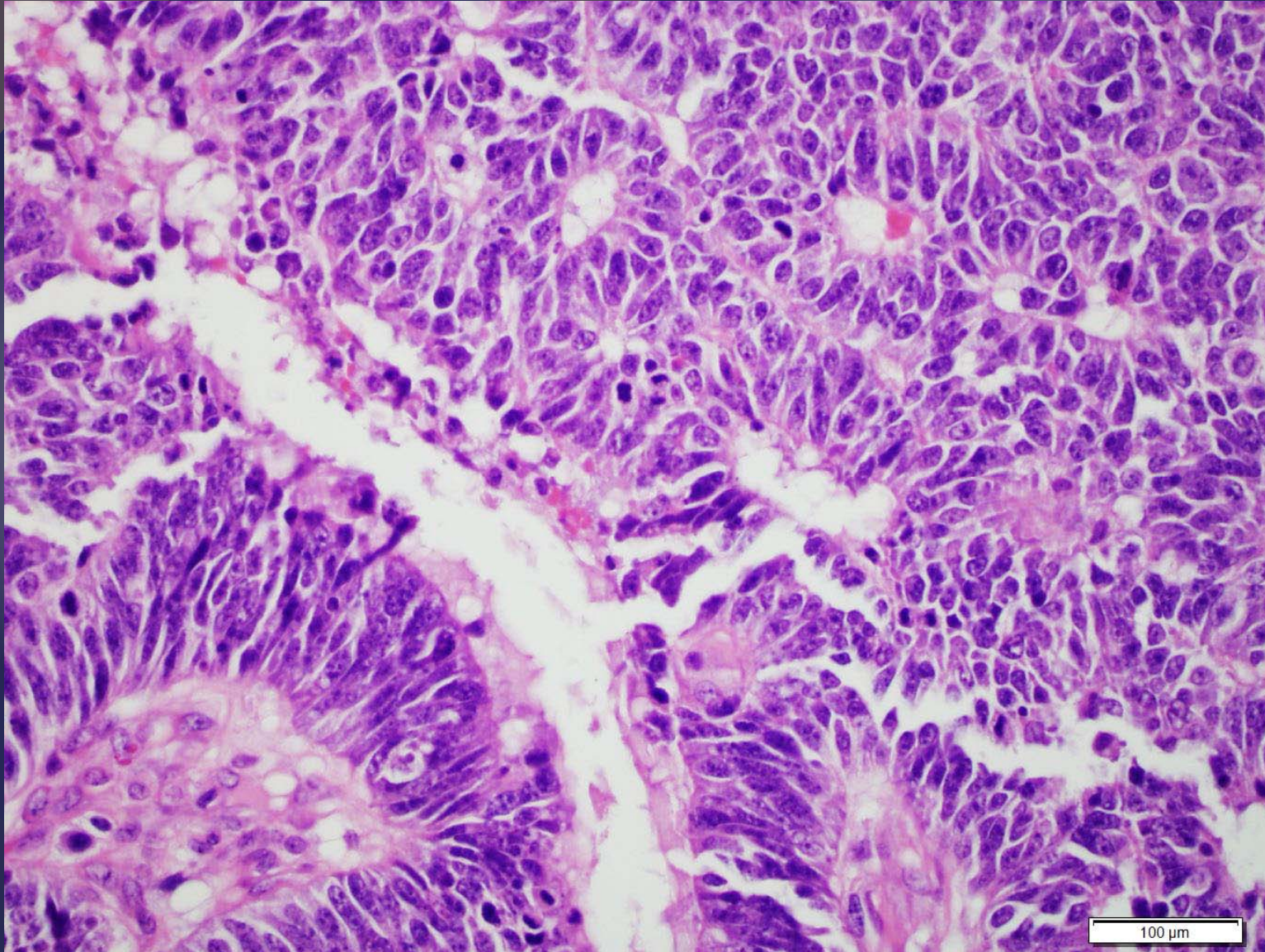


## Case 4 – Uterine Mass

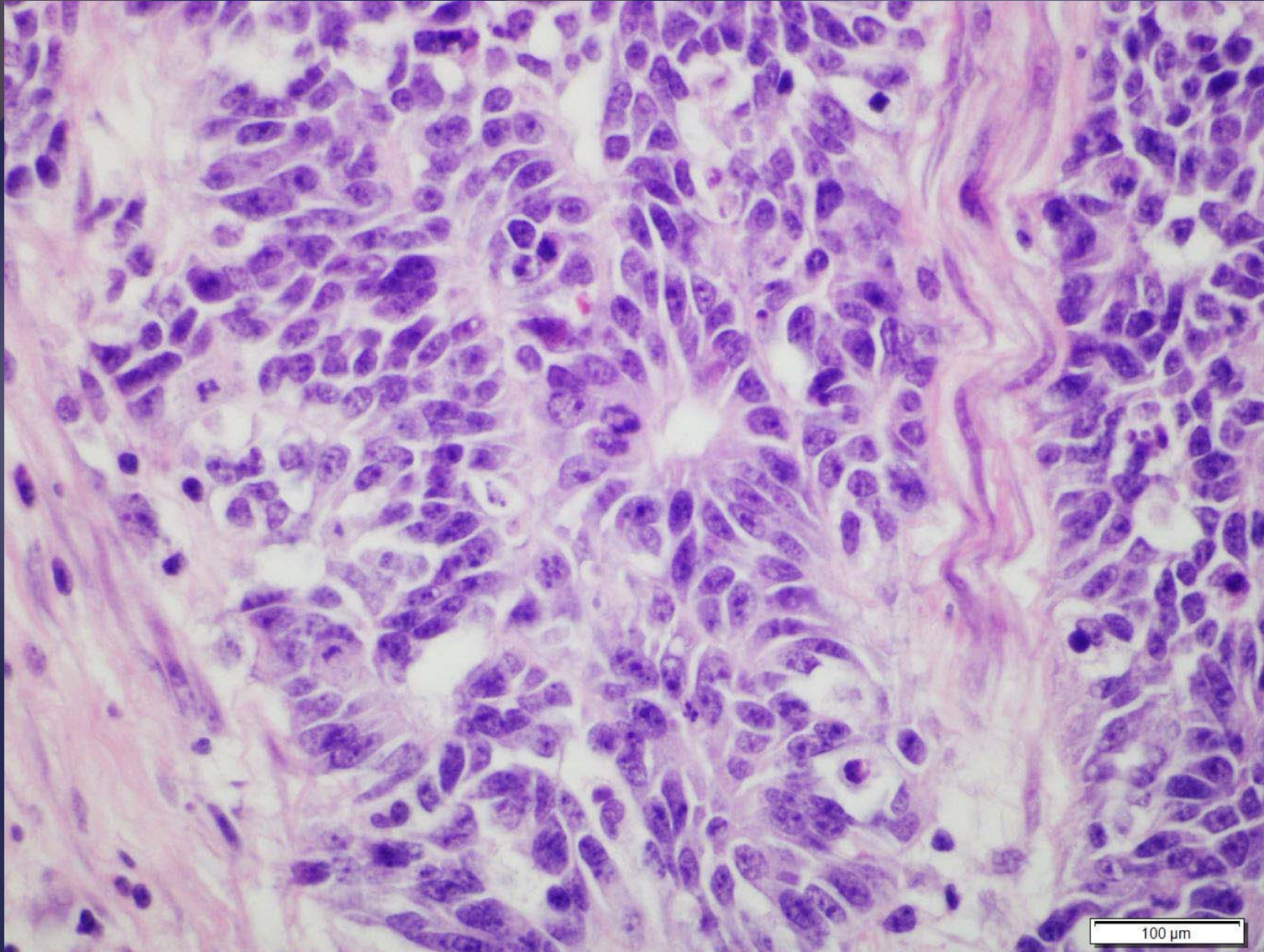




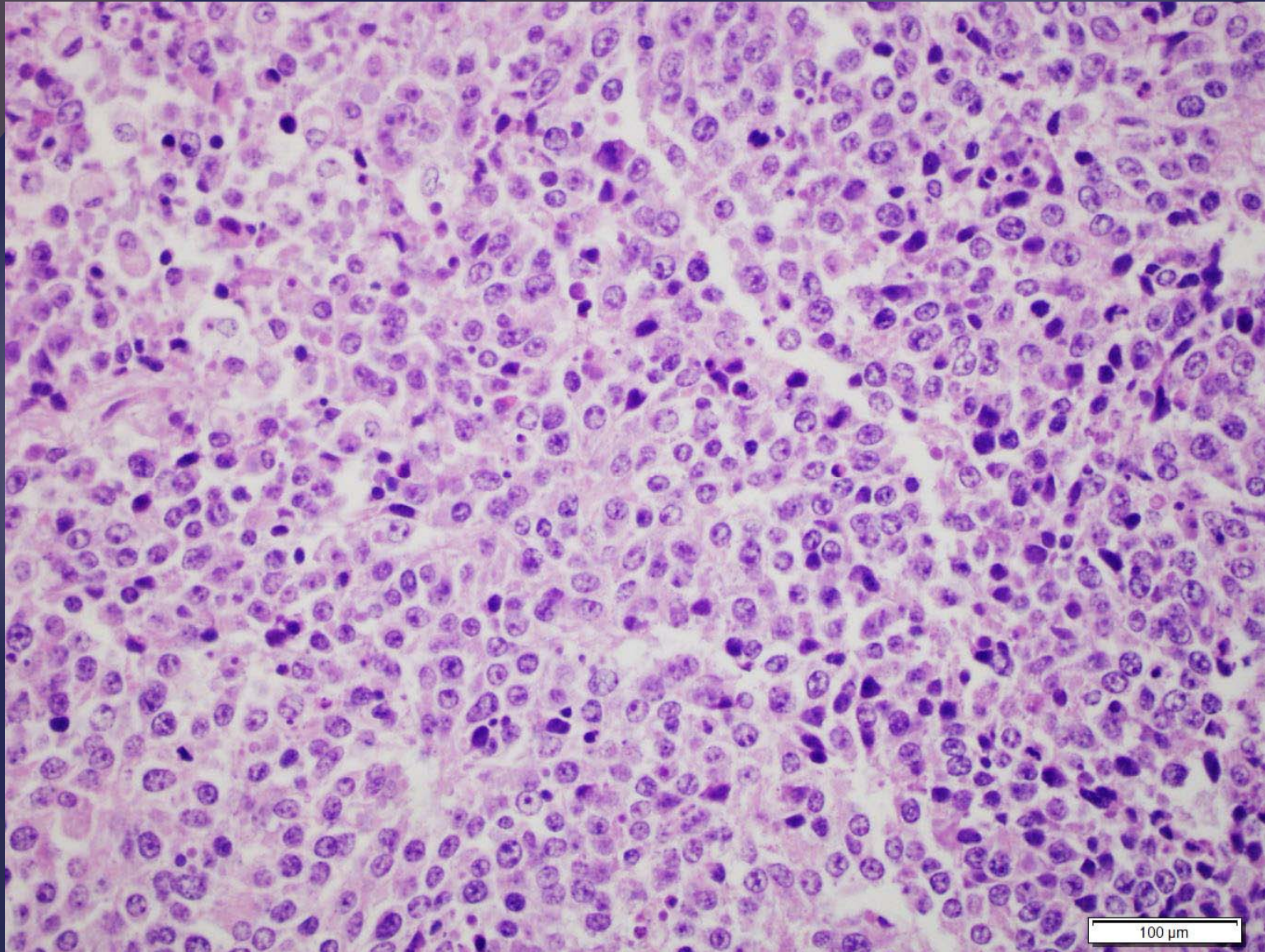
## Case 4 – Uterine Mass



## Case 4 – Uterine Mass



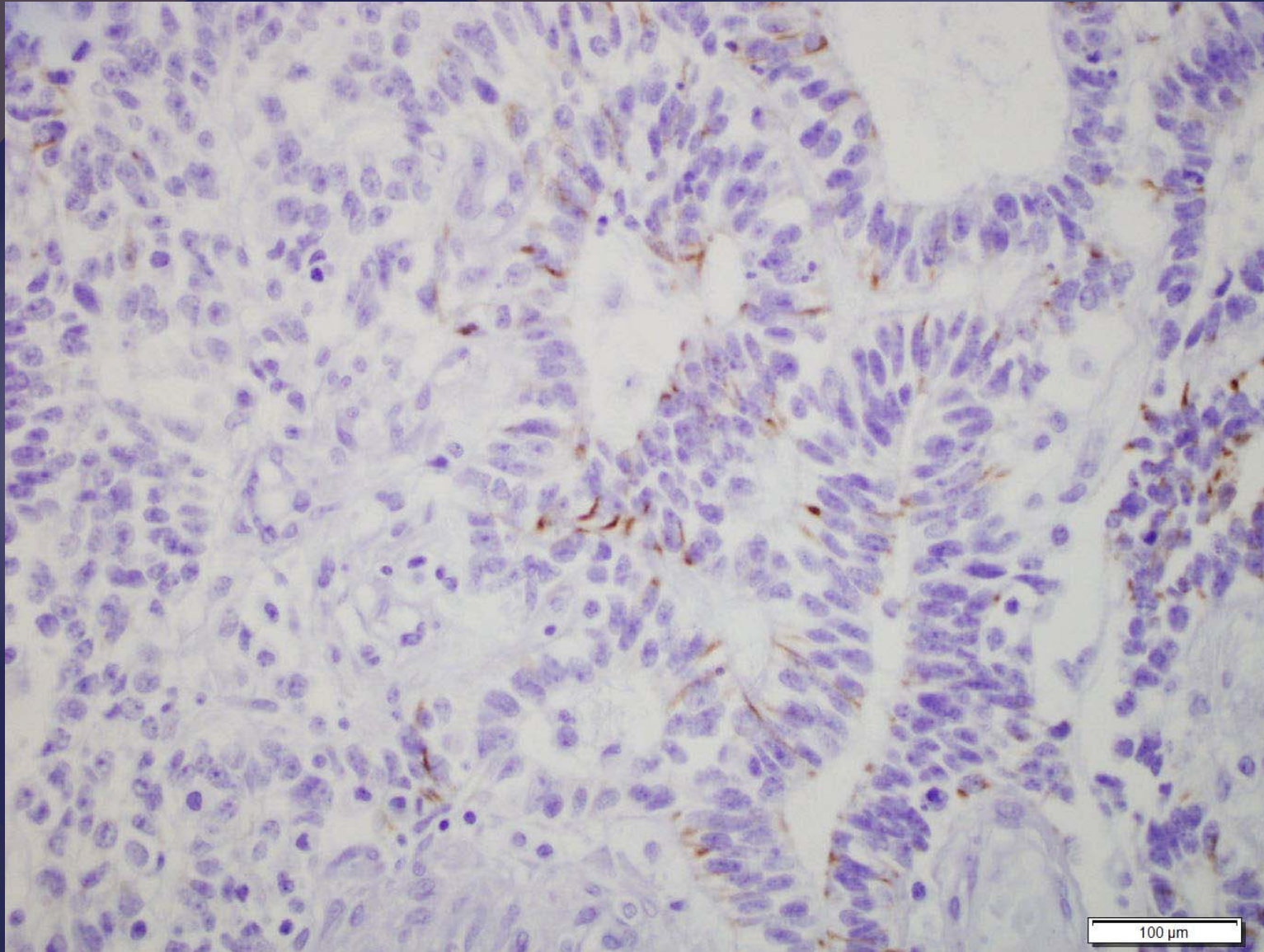
# Case 4 – Uterine Mass



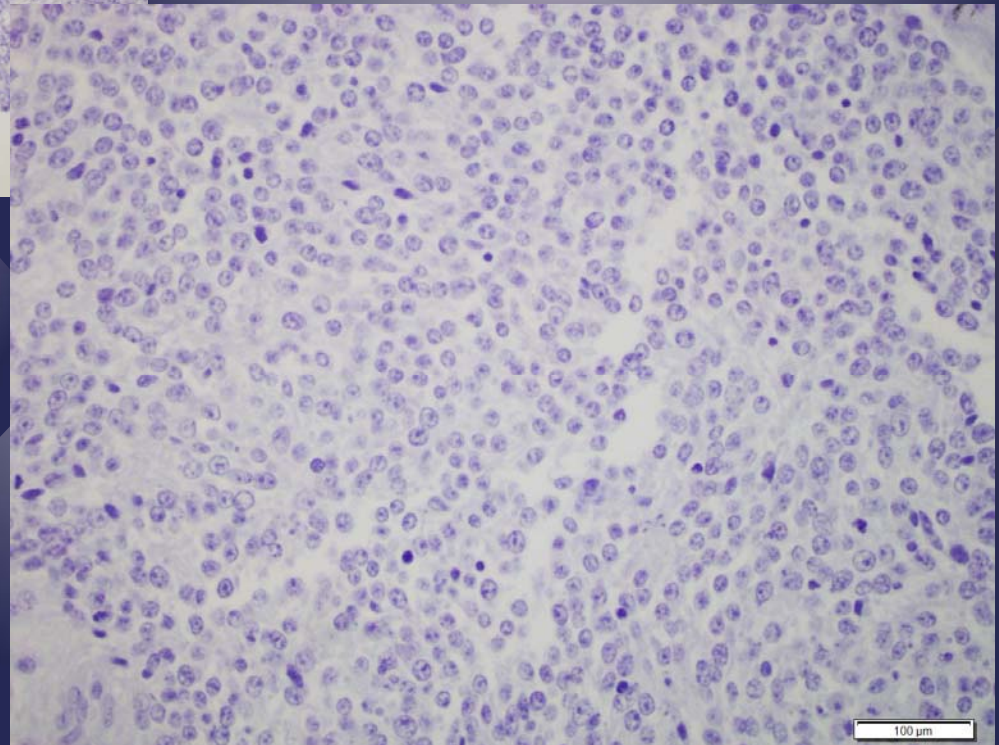
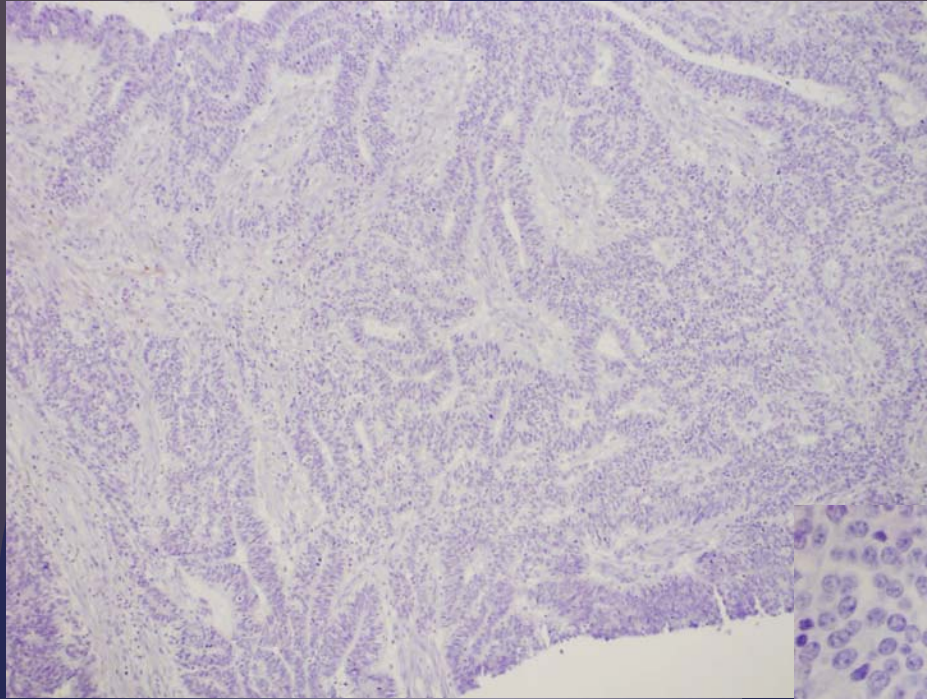
# Case 4 - Differential Diagnosis

- Endometrioid Adenocarcinoma
- Carcinosarcoma
- Metastasis
- Sex Cord Stromal Tumor
- Ewing's/PNET
- Small Cell
- Rhabdomyosarcoma
- Germ Cell Tumor

# Cam 5.2



AE1/3



## Stains:

- CAM5.2 Patchy (+)
- Vimentin (+)
- AE1/3 (-)
- CK7 (-)
- PAX8 (-)
- ER (-)
- Chromogranin (-)
- Synaptophysin (-)
- Desmin (-)
- Myf4 (-)
- Inhibin (-)
- AFP (-)
- CD99 (-)
- FLI1 (-)
- EWSR1 FISH (-)

# Case 4 - Diagnosis

- HIGH GRADE ADENOCARCINOMA



# Case 4 - History Cont.

- One month later, increasing abdominal pain
- Rapid recurrence and peritoneal carcinomatosis
- Urgently started on carboplatin/paclitaxel
- Showed little response



# Case 4 - History cont.

- Pathology sent for consultation:
- Dr. Robert Young offered another diagnosis and 2 weeks later her chemo was changed to VIP (etoposide/ifosfamide/cisplatin)
- 6 Cycles, near complete response

# Case 4 - Final Diagnosis

“ I feel this is a primitive neuroectodermal tumor (PNET)... of course we use the term primitive neuroectodermal tumor for the central-type morphology one sees in the ovary and uterus more commonly than one sees in the peripheral (Ewing's) variant. ”

Dr. Robert Young, MGH, Boston, MA

# Case 4 - Uterine PNET

## General Features:

- Small round blue cell tumors
  - Ewing family of tumors (a spectrum)
    - Characteristic translocations  $t(11:22)$  *EWSR1/FLI1*

Ewing <-----> PNET

-Small round cell morphology

- Neural differentiation

- PNET further Divided into:
  - Central-type PNET
  - Peripheral-type PNET

# Case 4 - Uterine PNET

- Peripheral-type PNET / Ewing Sarcoma
  - Usually have EWSR1 translocations
  - Neural crest derived
  - Occur outside the CNS
- Central-type PNET / Neuroblastoma
  - Usually don't have EWSR1 translocations
  - Develop from / Involve CNS
  - Most uterine and ovarian tumors are cPNET

# Case 4 – Uterine PNET

## Clinical Features:

- Rare in the Gyn tract
  - Ovary most common, then uterus
- Postmenopausal or adolescent women, abnormal vaginal bleeding and uterine mass
- Presents in advanced stage, rapidly progressive
- Associated with VHL disease

# Case 4 – PNET

## Histology:

- EWING and PNET have similar morphology
  - Uniform, small round cells, powdery chromatin, small nucleoli
  - May have rosettes, fibrillary background
  - Numerous mitoses, necrosis
  - Pure form or admixed with other uterine tumors

# Case 4 – Uterine PNET

## IHC:

- CD99 ( usually +) (7/9 + in case series)
- FLI-1 (usually +)
- Vimentin (+)
- May express keratins, chromogranin, synaptophysin, NSE and S100
- FISH:
  - Usually negative for EWSR1 rearrangements



# Case 4 – Uterine PNET

## Prognosis:

- Very few case reports of uterine PNET
- Poor prognostic factors
  - Older age
  - Higher stage
  - Tumor >8 cm
  - Poor chemo response
  - Absence of EWSR1 translocation

# Case 4 – Uterine PNET

## Treatment:

- Patients without mets at presentation respond well to intense multi-modal treatment
- Case reports of long disease free survival with platinum based chemo and etoposide

# Case 4 – Uterine PNET

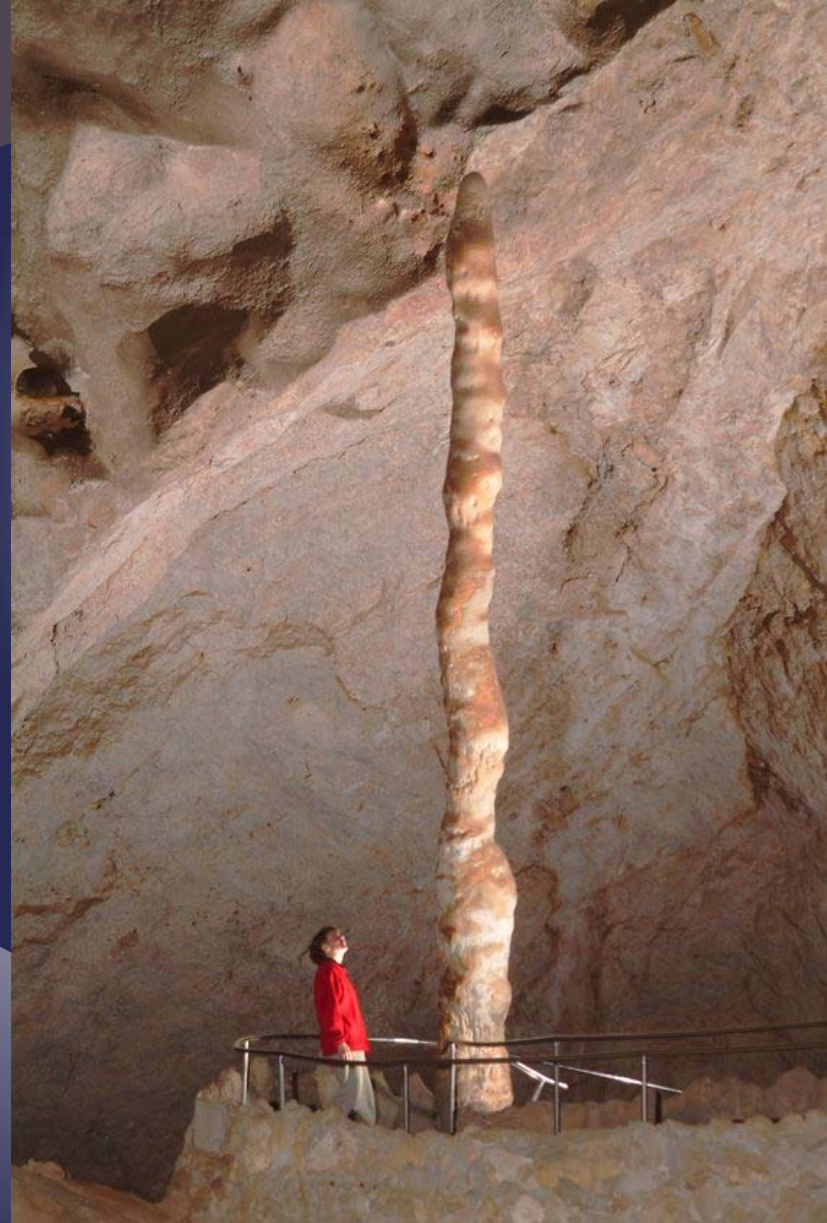
## Take Home:

- Rapid diagnosis important
- Keep in mind that Ovarian and Uterine PNET tends to be of the central type
  - No EWSR1 translocation
  - May not express CD99 or FLI1

## Follow up on our patient:

- Currently, no evidence of disease

Thank  
You



*Witches Finger, Carsbad Caverns, NM*

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## IMAGES:

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