AMSER Case of the Month

55-year-old female presenting with post-menopausal bleeding

Melina Diaz Pellot, OMS-IV
Lake Erie College of Osteopathic Medicine

Dr. Sarah Crafton, MD
Dr. Matthew Hartman, MD
Dr. Sharon Liang, MD
Allegheny Health Network

Patient Presentation

- HPI: 55-year-old G2P2002 post-menopausal female who initially presented to her PCP with new onset uterine bleeding. She has been using tampons frequently as a result. Associated symptoms include pelvic cramping. Denies vaginal discharge, urinary symptoms, or changes in bowel habits.
- Ob/Gyn: Abnormal pap at 20 y.o.; underwent LEEP at 21 y.o.
- Family Hx: (-) breast, endometrial, colon and ovarian cancer
- Labs: Inhibin B 257.7

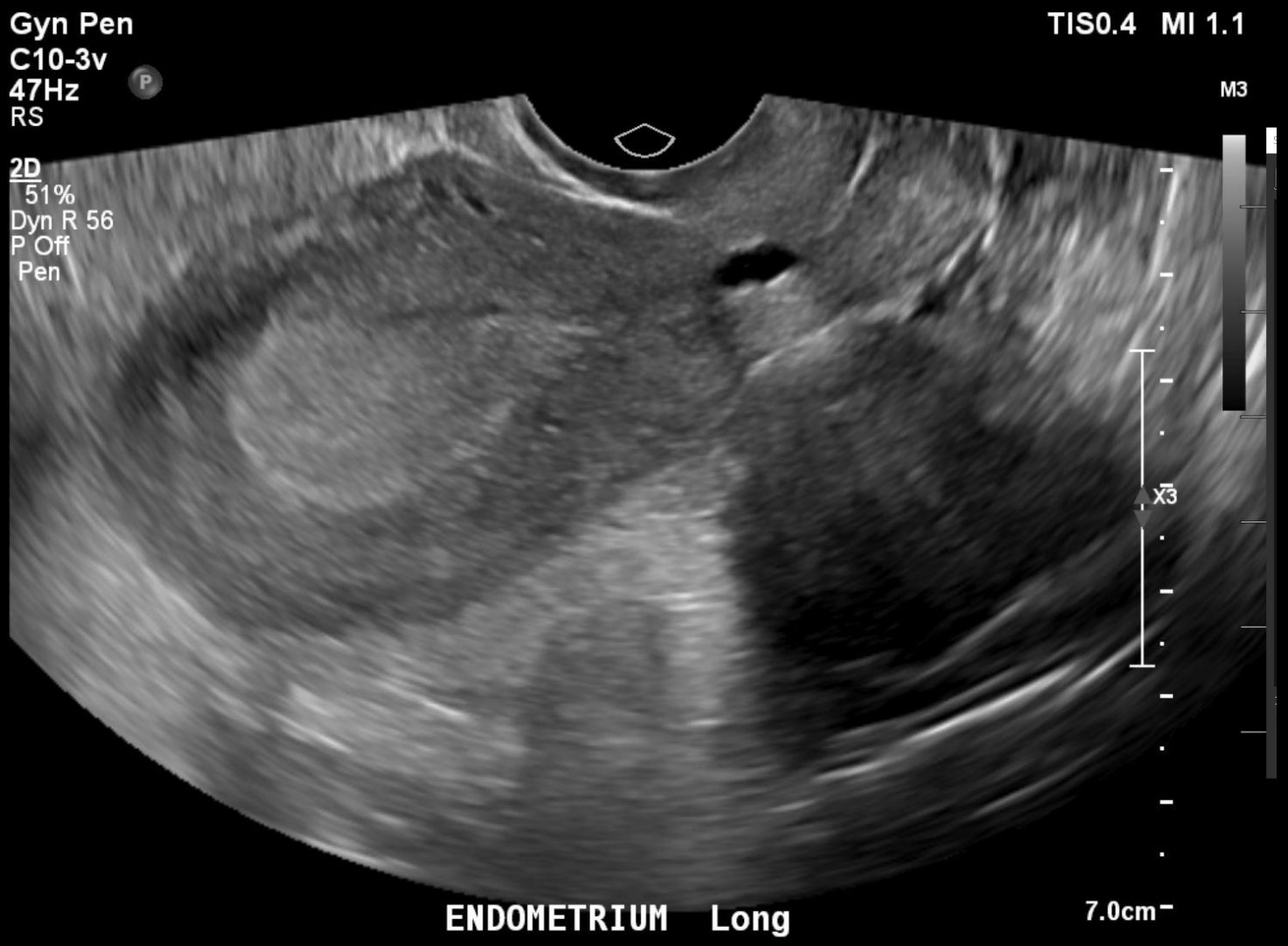
What imaging should we order?

ACR Appropriateness Criteria: Abnormal Uterine Bleeding

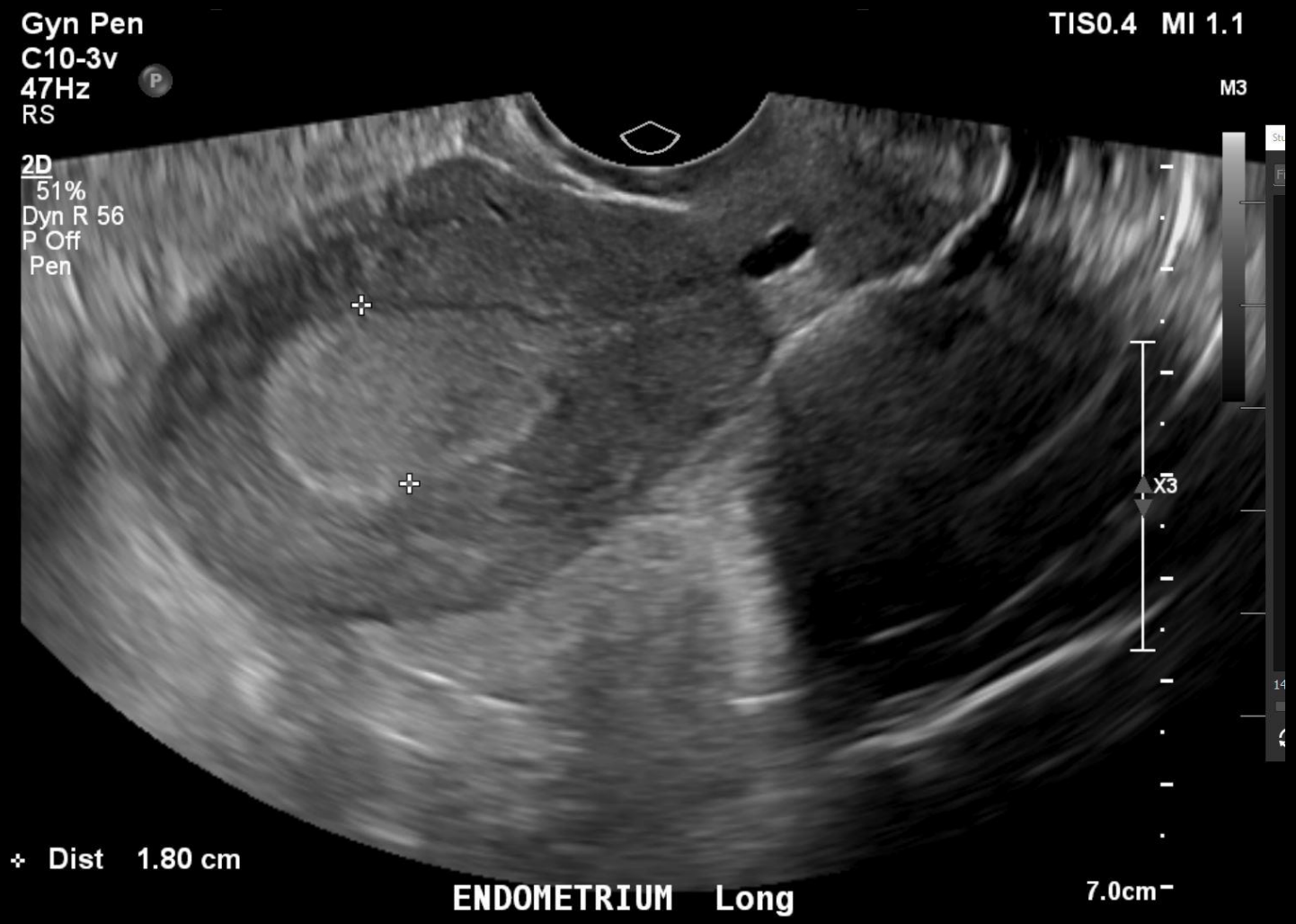
Scenario	Procedure	Adult RRL	Peds RRL	Appropriateness Category	
Uterine bleeding, abnormal, initial imaging	US sonohysterography	0 mSv O	0 mSv [ped] O	May be appropriate	
	US duplex Doppler pelvis	0 mSv O	0 mSv [ped] O	Usually appropriate	
	US pelvis transabdominal	0 mSv O	0 mSv [ped] O	Usually appropriate	
	US pelvis transvaginal	0 mSv O	0 mSv [ped] O	Usually appropriate	
	CT pelvis with IV contrast	1-10 mSv ☢☢☢	3-10 mSv [ped] ☢☢☢☢	Usually not appropriate	
	CT pelvis without and with IV contrast	10-30 mSv ☢☢☢☢	3-10 mSv [ped] ☢☢☢☢	Usually not appropriate	
	CT pelvis without IV contrast	1-10 mSv ☢☢☢	3-10 mSv [ped] ☢☢☢☢	Usually not appropriate	
	MRI pelvis without and with IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate	
	MRI pelvis without IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate	

This imaging modality was ordered by her PCP.

US Pelvis Transvaginal: Endometrium (unlabeled)

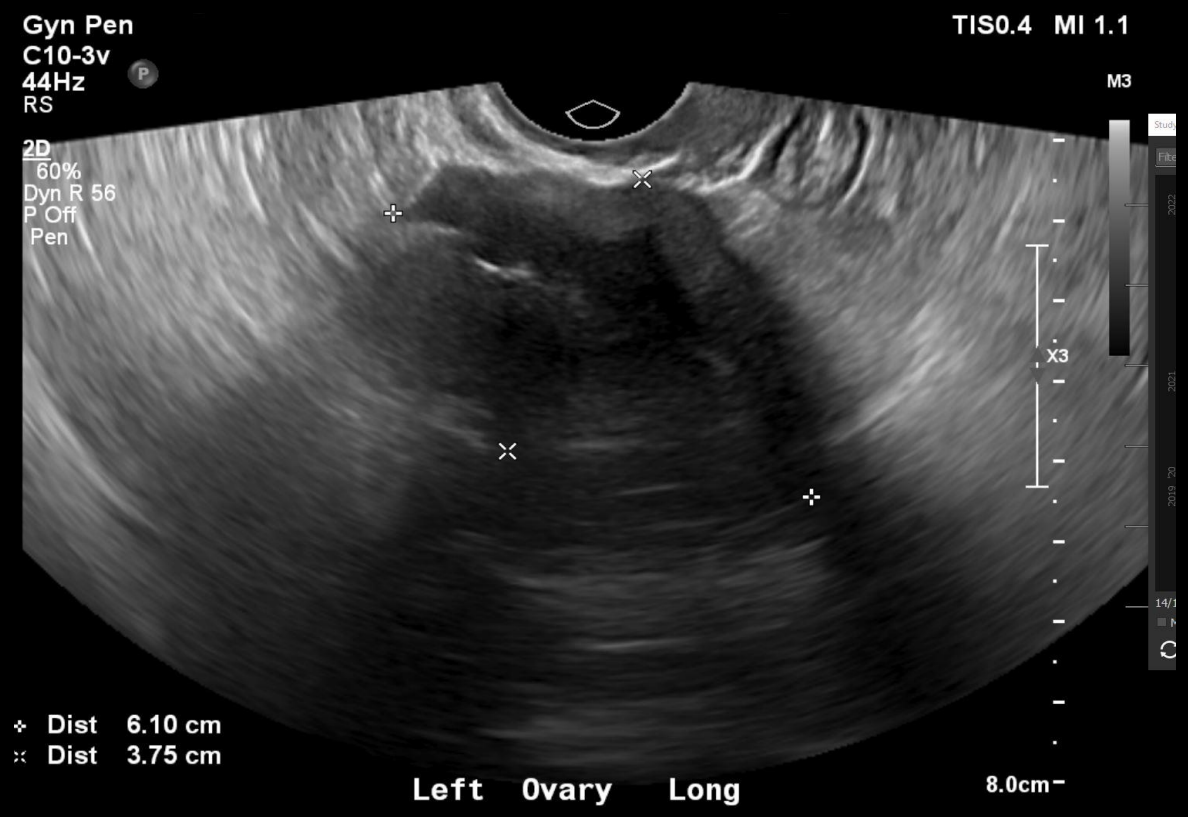


US Pelvis Transvaginal: Endometrium (labeled)

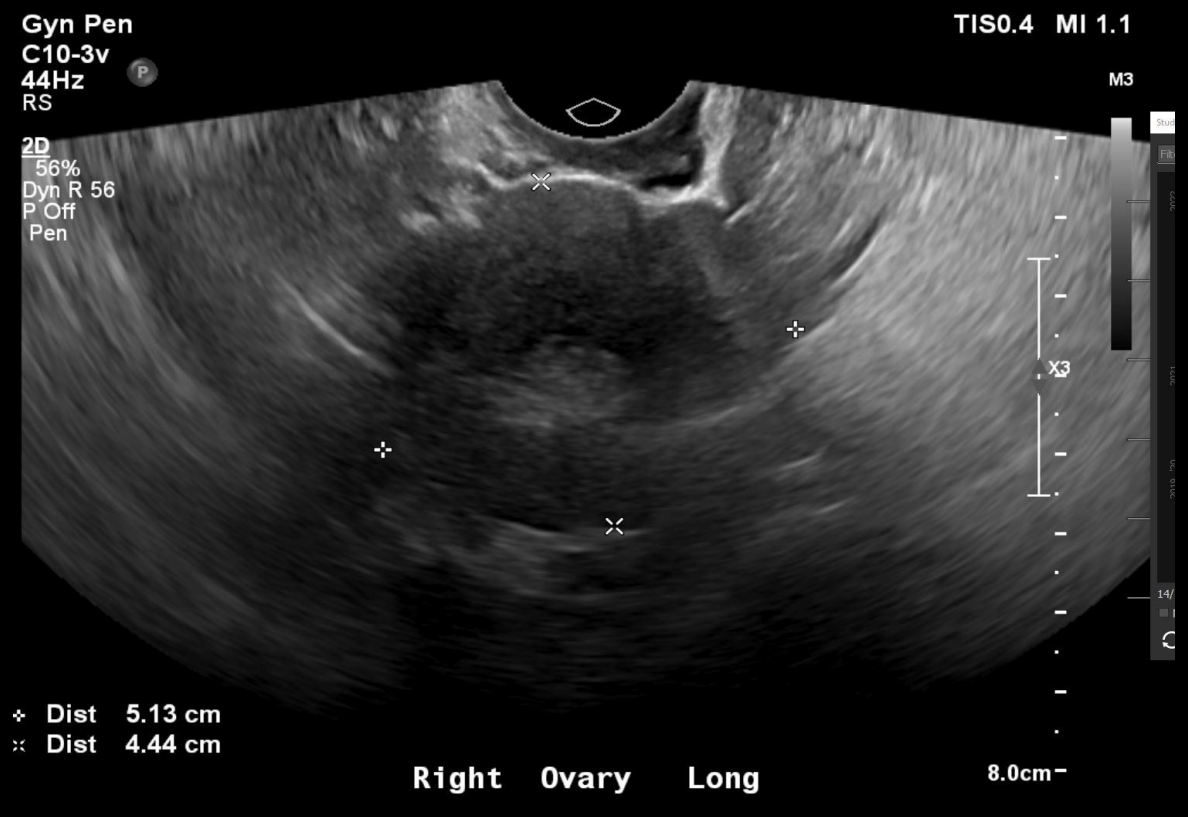


Markedly thickened endometrium measuring 1.8 cm. Small amount of abnormal vascularity with color Doppler interrogation.

US Pelvis Transvaginal: Ovaries (labeled)



Enlarged and heterogeneous solid mass replacing the left ovary, measuring 6.1 x 3.8 x 4.6 cm.



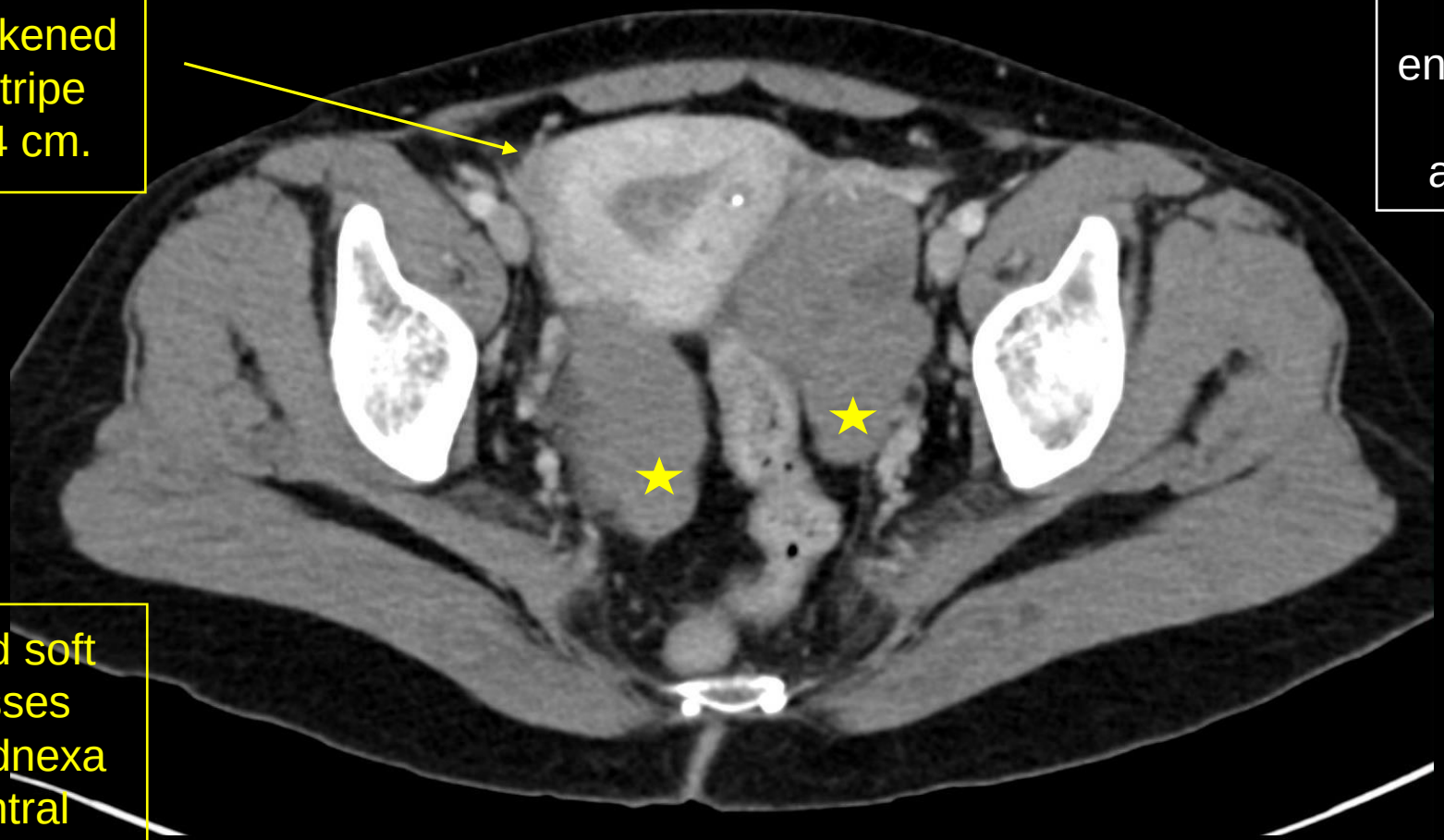
Enlarged and heterogeneous solid mass replacing the right ovary, measuring 5.1 x 4.4 x 5.0 cm.

What additional imaging was ordered?

CT Abdomen Pelvis w Contrast (unlabeled)

CT Abdomen Pelvis w Contrast (labeled)

Enlarged anteverted uterus with thickened endometrial stripe measuring 1.4 cm.



No pathologically enlarged lymph nodes identified in the abdomen or pelvis.

Large multilobulated soft tissue density masses replacing bilateral adnexa with regions of central hypodensity. Lesion in the right adnexa measures 7.2 x 4.4 cm and lesion in the left measures 8.0 x 5.7 cm.

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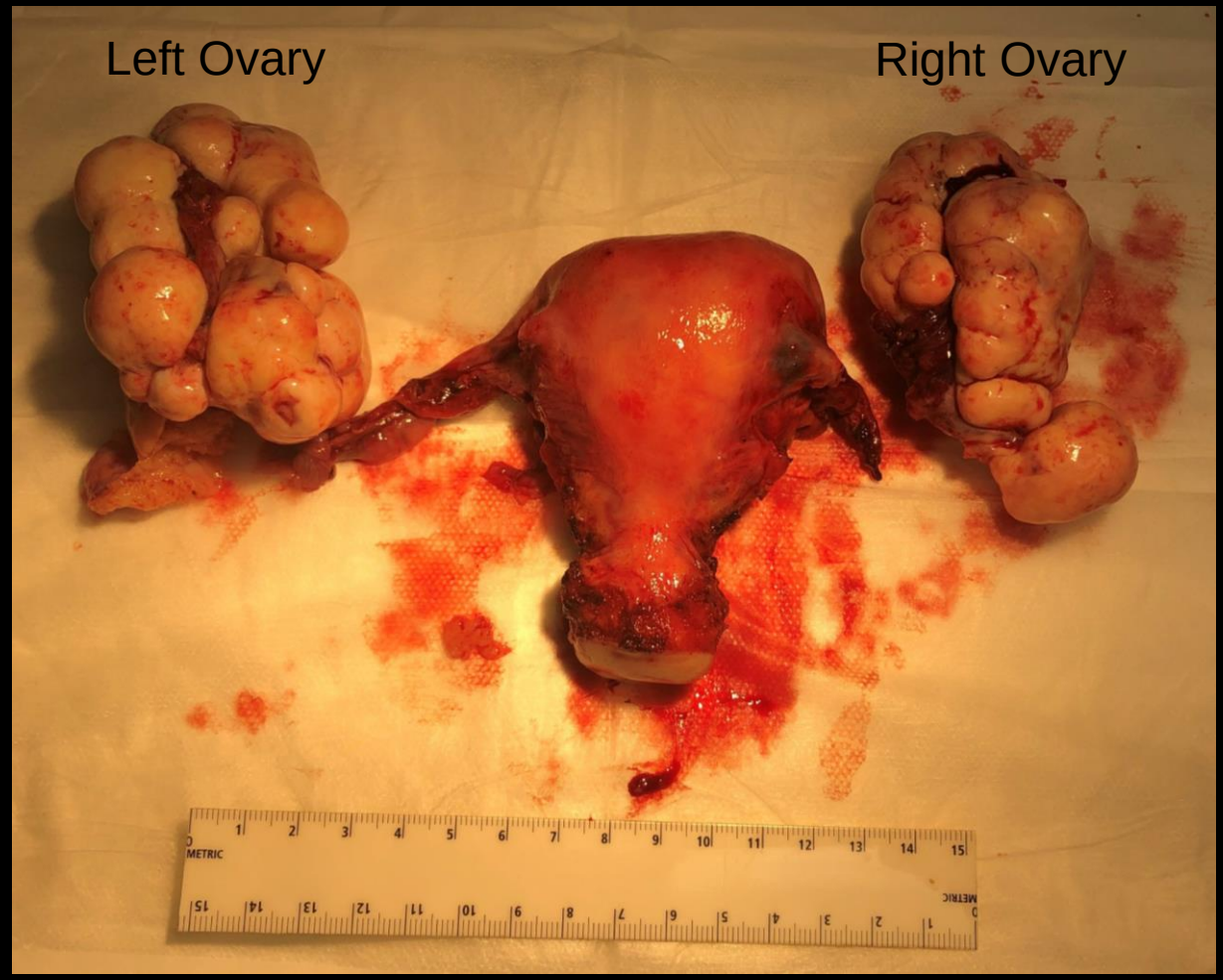
Differential based on imaging:

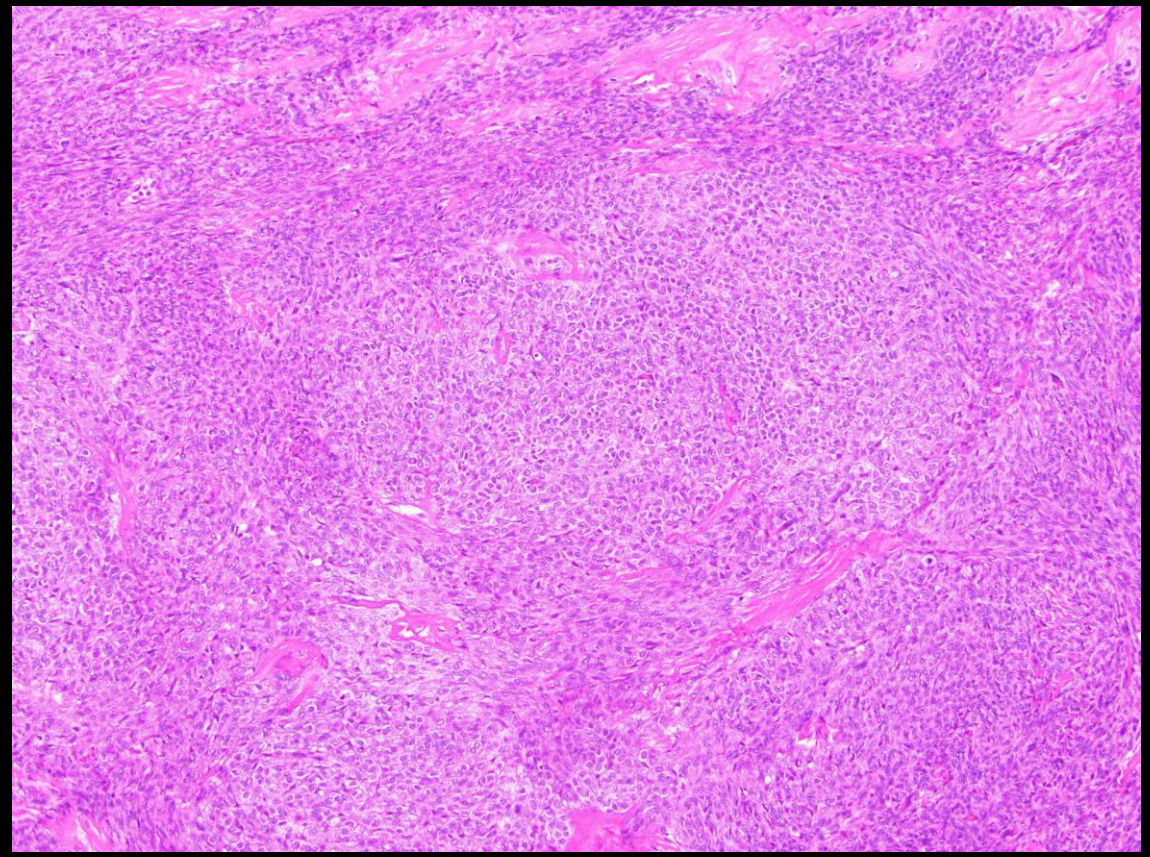
- Granulosa Cell Tumor
- Fibrothecoma
- Mets

Gross Findings

s/p robot-assisted laparoscopic hysterectomy with removal of bilateral pelvic masses

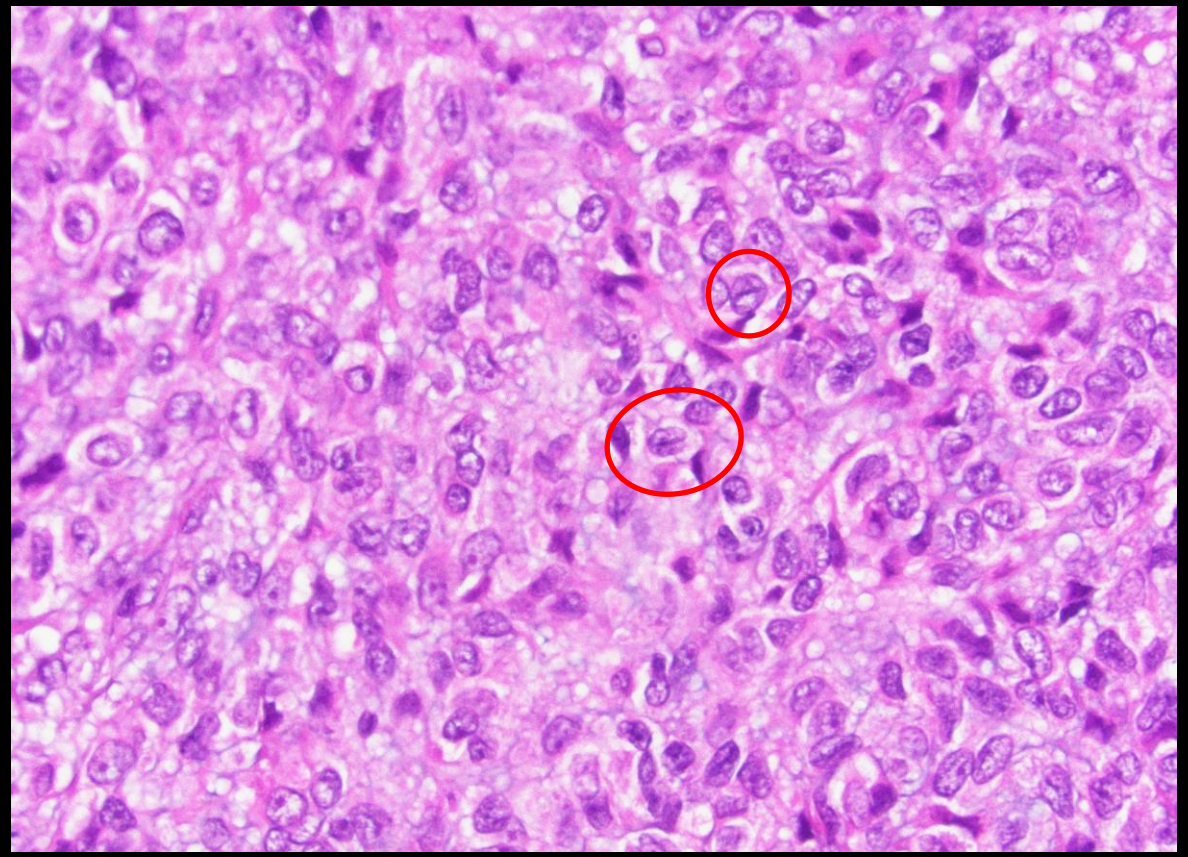


Histopathological Findings: Left Ovary



H&E Stain, Low Power

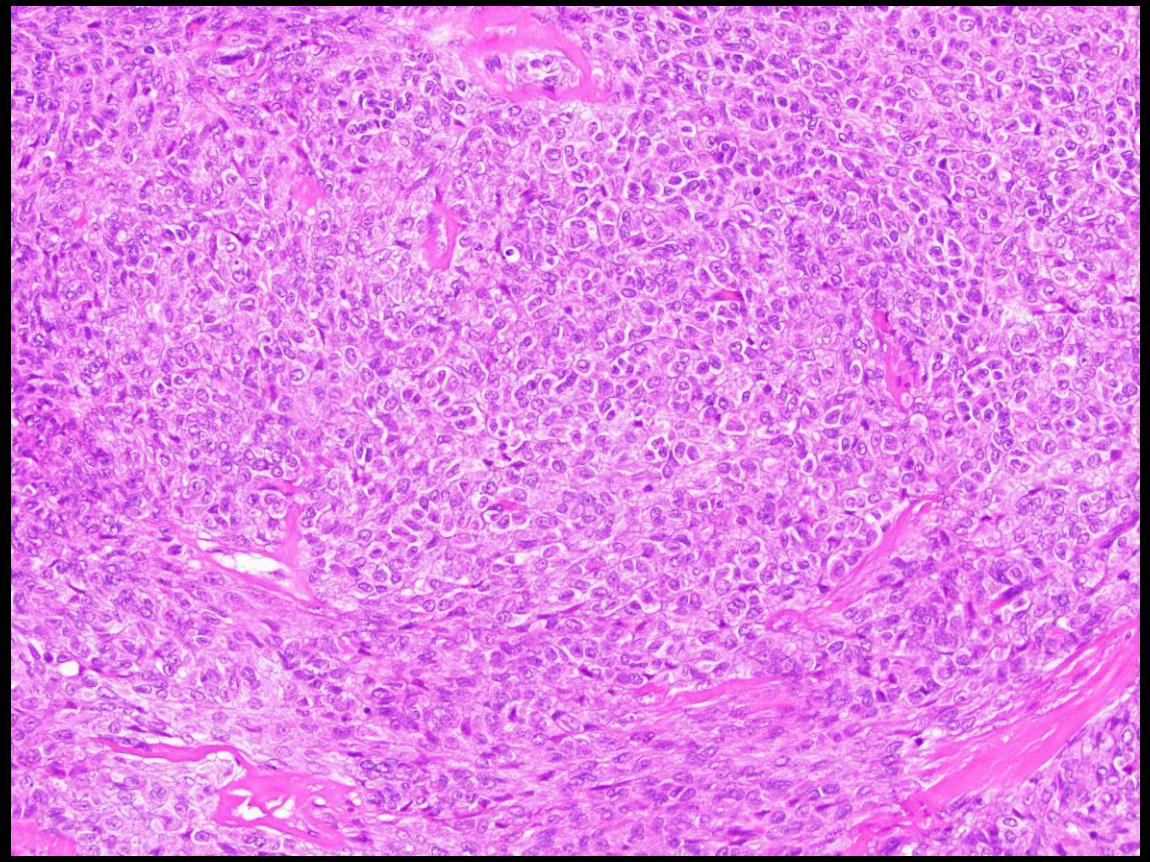
Nodular pattern separated by fibrous stromal tissue.



H&E Stain, High Power

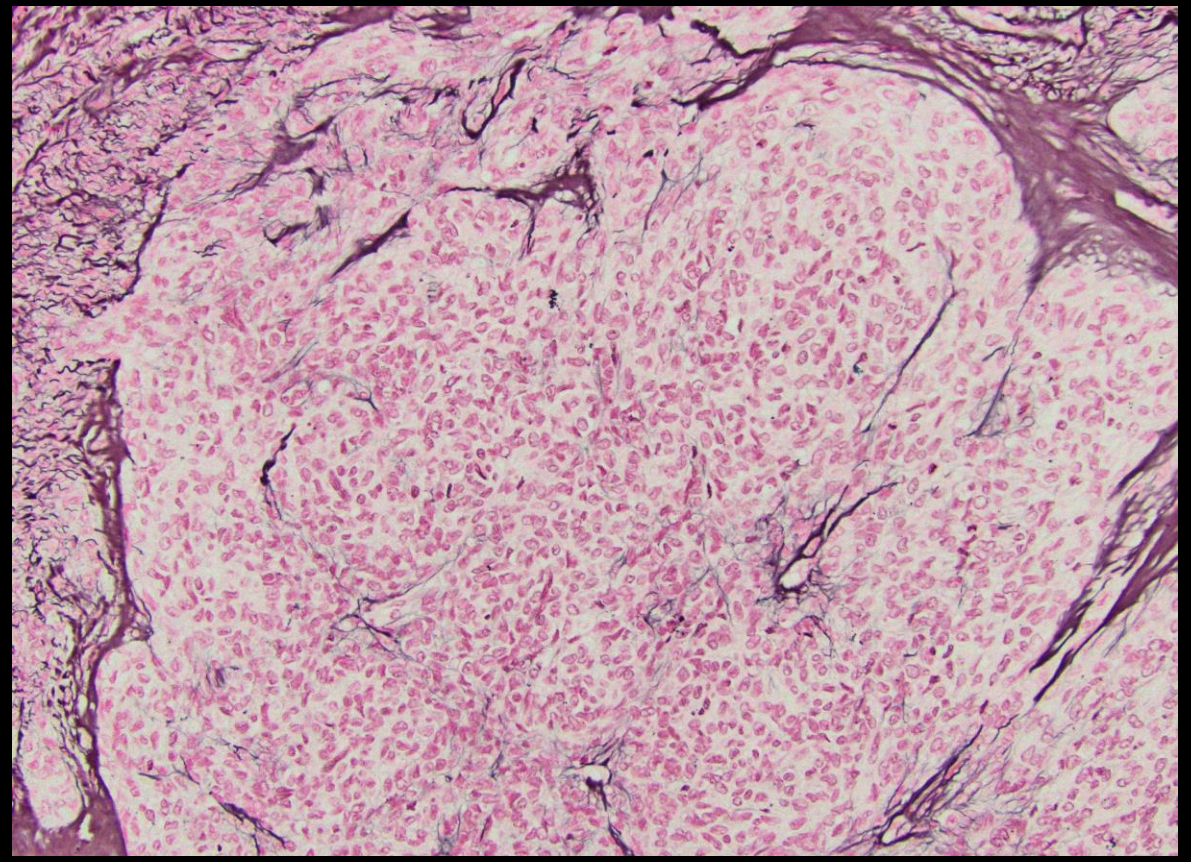
Nuclear grooves notable for their ‘coffee bean’ shape (red circle).

Histopathological Findings: Left Ovary



H&E Stain, Intermediate Power

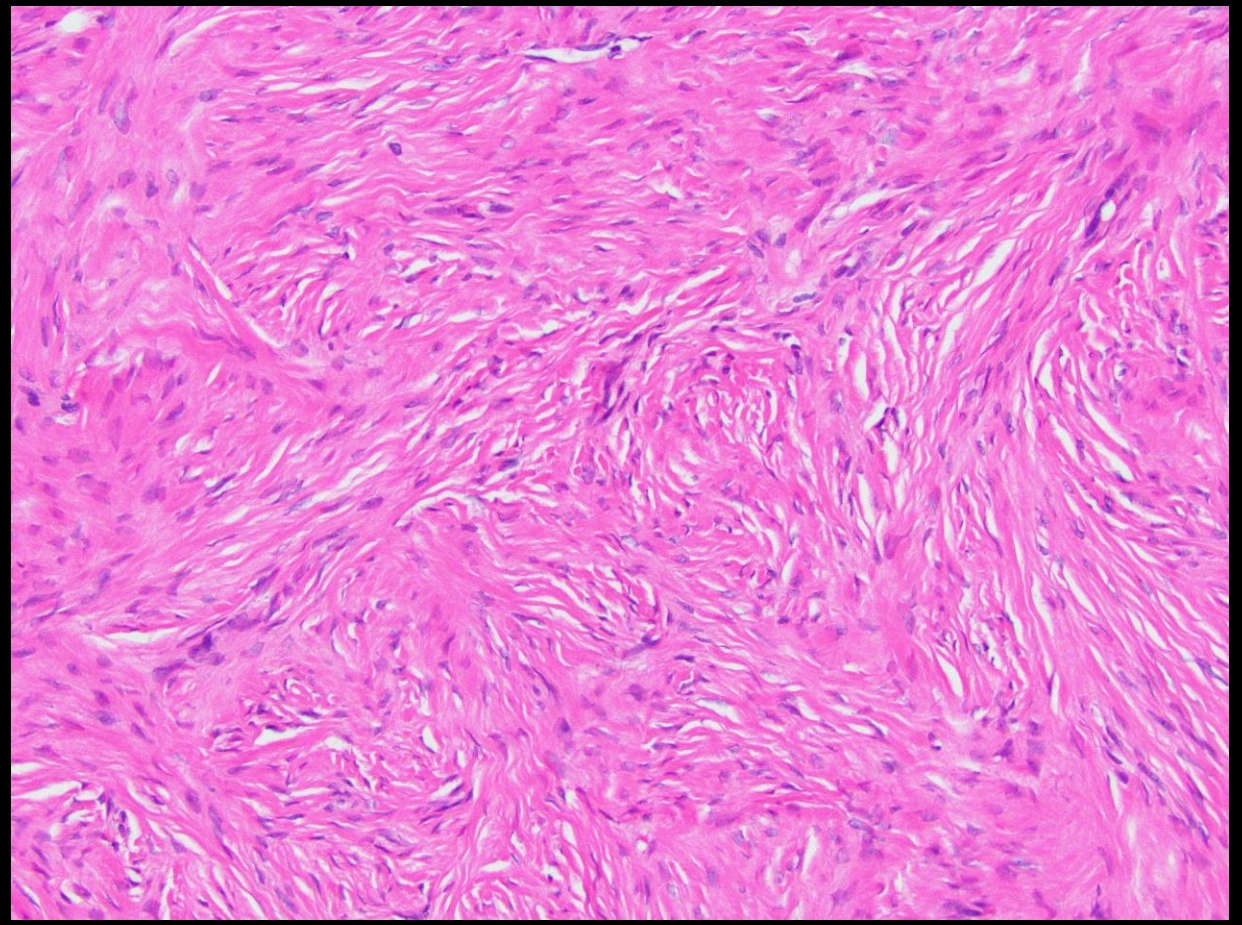
Epithelioid cells present, pale cytoplasm, no necrosis or mitotic activity seen.



Reticulum Stain, Intermediate Power

Nested pattern highlighted on this stain with no individual cell wrapping seen.

Histopathological Findings: Right Ovary



H&E Stain, Intermediate Power

Consistent with a fibroma.

Findings and Final Diagnosis:

- Pathology of the left ovarian mass revealed a cellular stromal neoplasm consisting of epithelioid appearing cells in nodular and nested pattern of growth.
- The lesional cells demonstrated oval shaped nuclei with pale/amphophilic cytoplasm with visible nucleoli and nuclear grooves.
- Final diagnosis consistent with **adult type granulosa cell tumor stage IA** of the left ovary.
- Right ovary was consistent with serous adenofibroma.
- Cytology of peritoneal washings negative.

Discussion: Adult Type Granulosa Cell Tumor Clinical Presentation

- Ovarian granulosa cell tumors (GCTs) are a class of sex cord-stromal tumors which can further be divided into two subtypes: adult and juvenile.
- The adult subtype makes up 95% of GCTs, occurring in peri- and postmenopausal women with a median age of 50 years.
- Most commonly presents as abnormal uterine bleeding and pain secondary to large tumor size.
- 25-50% of GCTs are associated with endometrial hyperplasia attributable to endogenous estrogen.
- Confinement to the ovary occurs with 80-90% of GCTs. Metastasis with ascites presents in only 10% of cases.

Discussion: Diagnosis

- A pathognomonic feature associated with GCTs is FOXL2 mutation, present in approximately 95% of cases.
- Tumor markers play a role in diagnosis, specifically Inhibin B and Anti-müllerian hormone.
- Grossly there is a lot of variation, with majority of GCTs being cystic and filled with serous fluid or clotted blood when sectioned.
- Microscopy reveals characteristic ovoid nuclei with a longitudinal groove in addition to scant pale cytoplasm, minimal cytologic atypia, and low mitotic rate.
- Specifically on US or MRI, one characteristic morphologic pattern is a solid mass with spongelike appearance.
- The role of CT is limited to assessment of metastatic disease.

Discussion: Staging

Stage I: Tumor confined to ovaries or fallopian tube(s)	**T1-N0-M0**
IA: Tumor limited to 1 ovary (capsule intact) or fallopian tube; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings	**T1a-N0-M0**
IB: Tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings	**T1b-N0-M0**
IC: Tumor limited to 1 or both ovaries or fallopian tubes, with any of the following:	
IC1: Surgical spill	**T1c1-N0-M0**
IC2: Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface	**T1c2-N0-M0**
IC3: Malignant cells in the ascites or peritoneal washings	**T1c3-N0-M0**
Stage II: Tumor involves 1 or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or peritoneal cancer	**T2-N0-M0**
IIA: Extension and/or implants on uterus and/or fallopian tubes and/or ovaries	**T2a-N0-M0**
IIB: Extension to other pelvic intraperitoneal tissues	**T2b-N0-M0**
Stage III: Tumor involves 1 or both ovaries or fallopian tubes, or peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes	**T1-3/N0-1/M0**
IIIA1: Positive retroperitoneal lymph nodes only (cytologically or histologically proven):	**T1/T2-N1-M0**
IIIA1(i) Metastasis up to 10 mm in greatest dimension	
IIIA1(ii) Metastasis more than 10 mm in greatest dimension	
IIIA2: Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes	**T3a2-N0/N1-M0**
IIIB: Macroscopic peritoneal metastasis beyond the pelvis up to 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes	**T3b-N0/N1-M0**
IIIC: Macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ)	**T3c-N0/N1-M0**
Stage IV: Distant metastasis excluding peritoneal metastases	**Any T, any N, M1**
Stage IVA: Pleural effusion with positive cytology	
Stage IVB: Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)	

Granulosa cell tumors are staged according to the FIGO classification.

- Staging procedures include peritoneal washings, biopsies, and infracolic omentectomy.
- Majority of GCTs are diagnosed at stage Ia.

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Discussion: Treatment, Follow-up, Relapse

- The gold standard treatment for GCTs is a total abdominal hysterectomy and bilateral salpingo-oophorectomy, particularly in those with advanced disease or who are postmenopausal.
- Conservative measures can be taken for those presenting with local disease (stage Ia) who wish to preserve their fertility with a unilateral salpingo-oophorectomy.
- Follow-up for at least 3-5 years, including Inhibin B and AMH serum markers. Both are elevated in relapse, correlating with disease burden.
- Relapse is typical 4-7 years from diagnosis, most commonly occurring in the pelvis.

References:

- Berek, JS, Renz, M, Kehoe, S, Kumar, L, Friedlander, M. Cancer of the ovary, fallopian tube, and peritoneum: 2021 update. *Int J Gynecol Obstet*. 2021; 155(Suppl. 1): 61-85. https://doi.org/10.1002/ijgo.13878.

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- Taylor, Erin C., et al. “Multimodality Imaging Approach to Ovarian Neoplasms with Pathologic Correlation.” *RadioGraphics*, vol. 41, no. 1, 2021, pp. 289–315., https://doi.org/10.1148/rg.2021200086.

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