AMSER Case of the Month

Postmenopausal Bleeding

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LECOM

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Patient Presentation

- 83 year old female, G5P4005, non-smoker
- Initial presentation to Urology for gross hematuria and known UTI
  - Bladder scan: incidental finding of thickened endometrium at 1.2 cm
- Consulted to Obstetrics/Gynecology for transabdominal and transvaginal ultrasounds, hysteroscopy with dilation and curettage
  - Postmenopausal bleeding revealed in history after questioning
- Dilation and curettage revealed a malignancy
  - Patient was referred to Gynecology/Oncology for additional workup and therapy

Patient Presentation

- PMHx: skin cancer, high cholesterol, hypertension, osteoporosis, degenerative joint disease, hematuria, hiatal hernia, irritable bowel
- PSHx: Ovarian cyst removal (1950), right knee surgery, colon surgery
- Family Hx: ovarian cancer and osteoporosis (mother), heart disease (father)
  - Negative: breast, uterine, and cervical cancer
- Gynecologic Hx: G5P4005, menopause at age 54, negative Pap smear in 2014, no STI hx

Physical Exam

- Blood pressure: 150/80
- Pulse: 62
- Respirations: 12
- General: negative for chills, fatigue, sleep disturbance, weight gain or loss; normal appetite
- GI: negative for abdominal pain, abdomen soft, nontender, no guarding or rebound tenderness, no masses, no hepatosplenomegaly
- GU: positive for right sided flank pain that comes and goes (evenings)
- Gyne: positive for postmenopausal bleeding 4 months prior (resolved), normal appearance of cervix with scant blood, no masses on bimanual exam
- Heme/lymph: no lymphadenopathy in supraclavicular, neck, or inguinal regions
- Labs: within normal limits

ACR Appropriateness Criteria

Clinical Condition: **Abnormal Vaginal Bleeding**

Variant 1: **Postmenopausal vaginal bleeding. First study. (Endometrial sampling may also be performed initially followed by imaging if results are inconclusive or symptoms persist despite negative findings.)**

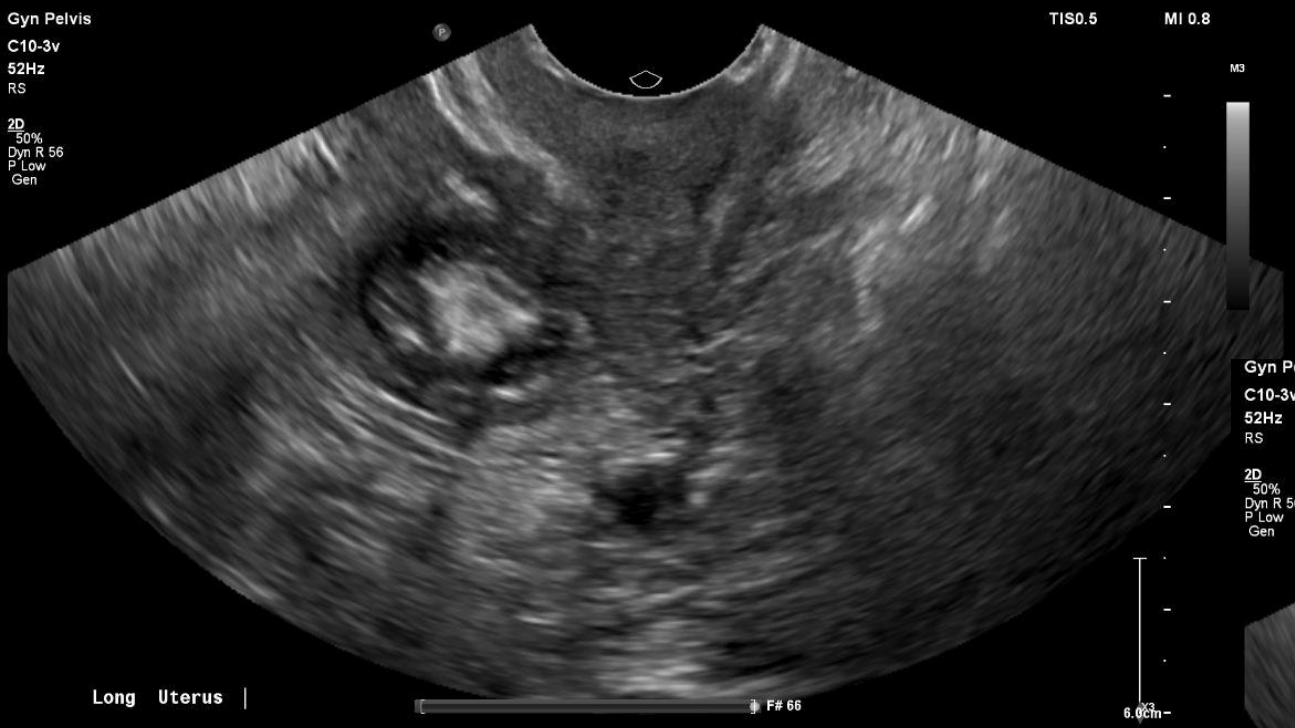
Radiologic Procedure	Rating	Comments	RRL*
US pelvis transvaginal	9	3-D imaging may be a useful adjunct to 2-D imaging to better characterize an intracavitary abnormality.	O
US pelvis transabdominal	8		O
US saline infusion sonohysterography	6	3-D imaging may be a useful adjunct to standard 2-D imaging if intracavitary abnormality is suspected.	O
US duplex Doppler pelvis	5	This procedure may be useful to better characterize a focal or diffuse endometrial abnormality.	O
CT pelvis with IV contrast	2		☢☢☢
MRI pelvis without and with IV contrast	2		O
CT pelvis without IV contrast	1		☢☢☢
CT pelvis without and with IV contrast	1		☢☢☢☢
MRI pelvis without IV contrast	1		O

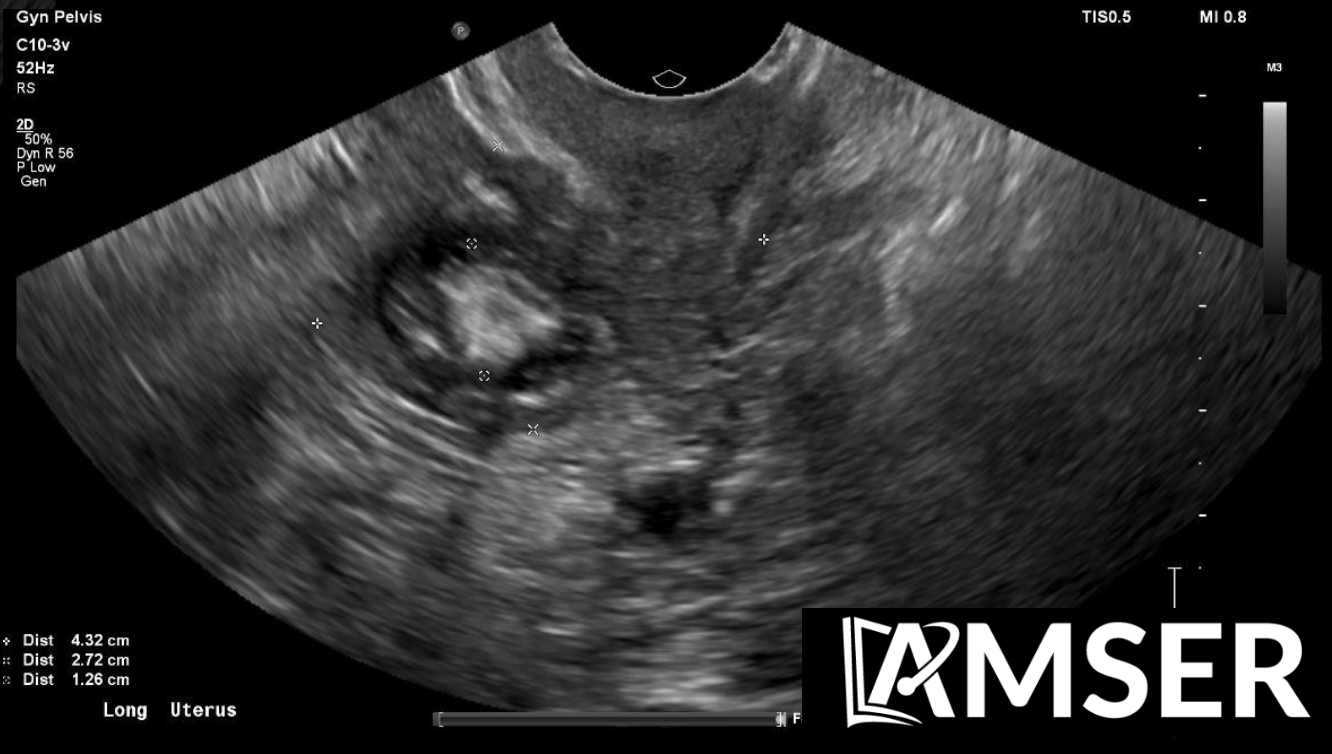
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

*Relative Radiation Level

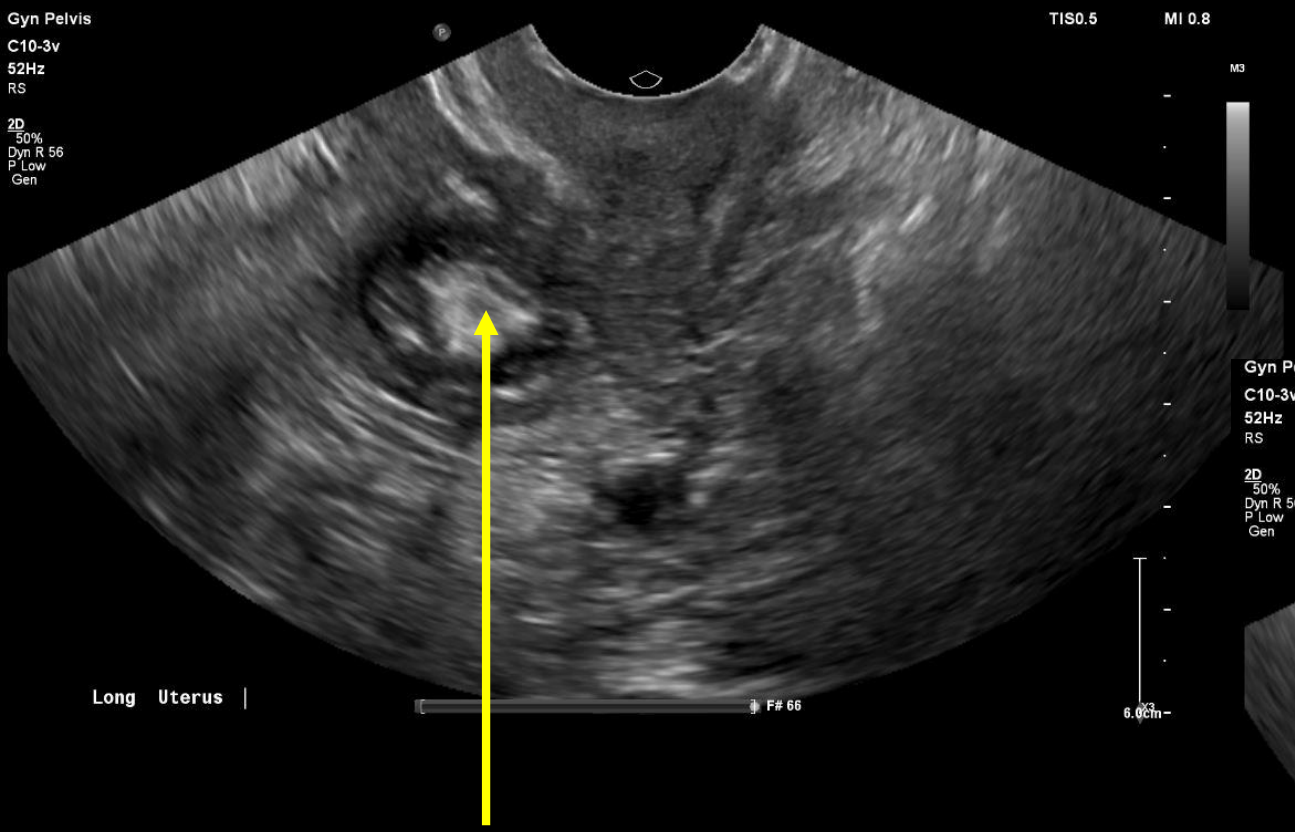
Image: American College of Radiology. ACR Appropriateness Criteria. Available at https://acsearch.acr.org/list. Accessed October 24, 2019.

Ultrasound: Transvaginal (Longitudinal) – Images Unlabeled





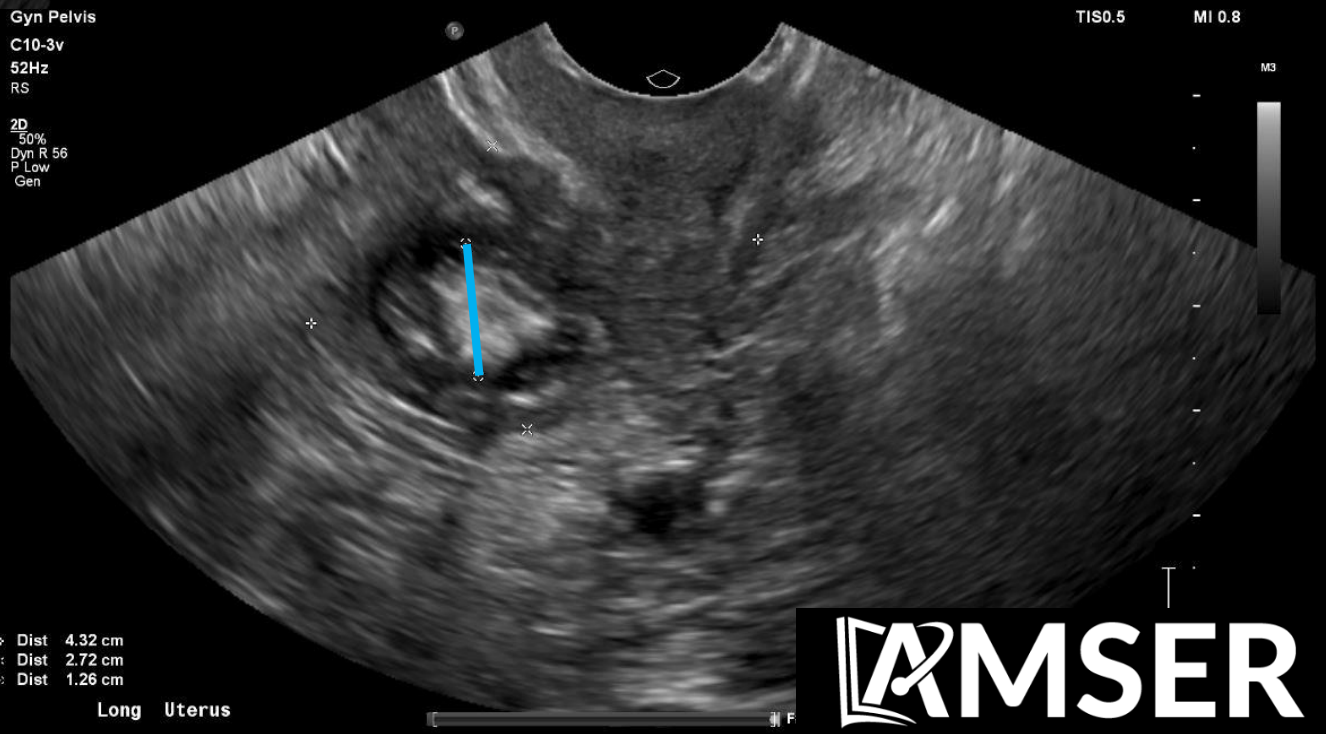
Ultrasound: Transvaginal (Longitudinal) – Images Labeled



Hyperechoic thickening in body of uterus

Measurements:

- 1.26 cm – endometrial thickness

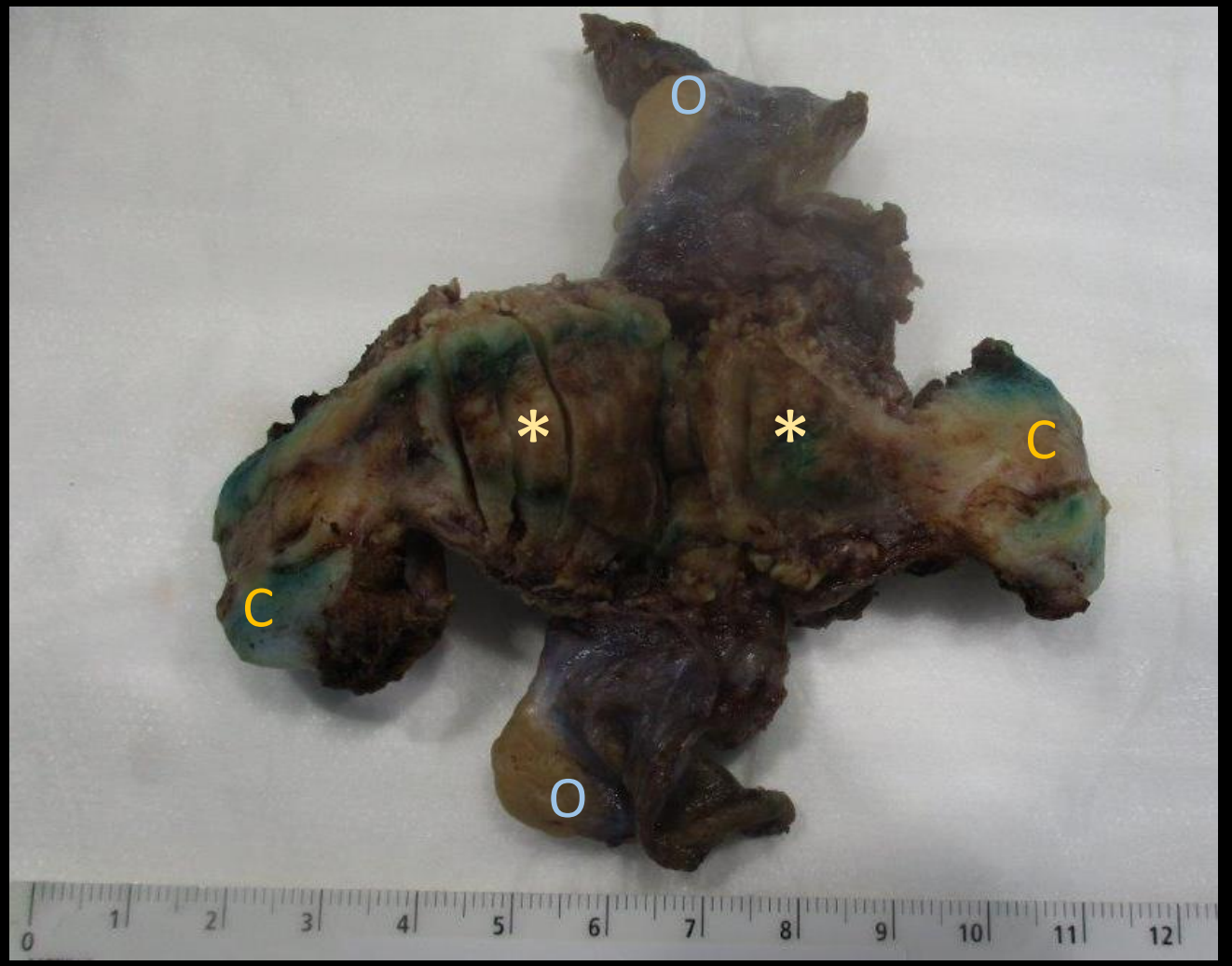


Differential Diagnosis Based on Imaging

- Endometrial Carcinoma
- Endometrial Hyperplasia
- Endometritis
- Endometrial Polyps

Pathology: Gross Specimen

- Uterus and cervix with B/L tubes and ovaries
  - Endometrium: “yellow-tan lesion approximately 2 x 2 cm” involving “less than 0.3 cm of the 1.5 cm endomyometrial thickness”
- Sentinel Lymph Nodes (1 left and 2 right): negative for tumor cells



Bivalve dissection

C - Cervix

O - Ovaries

* - Endometrial surface

Pathology: Histology

- Normal Endothelium Histology

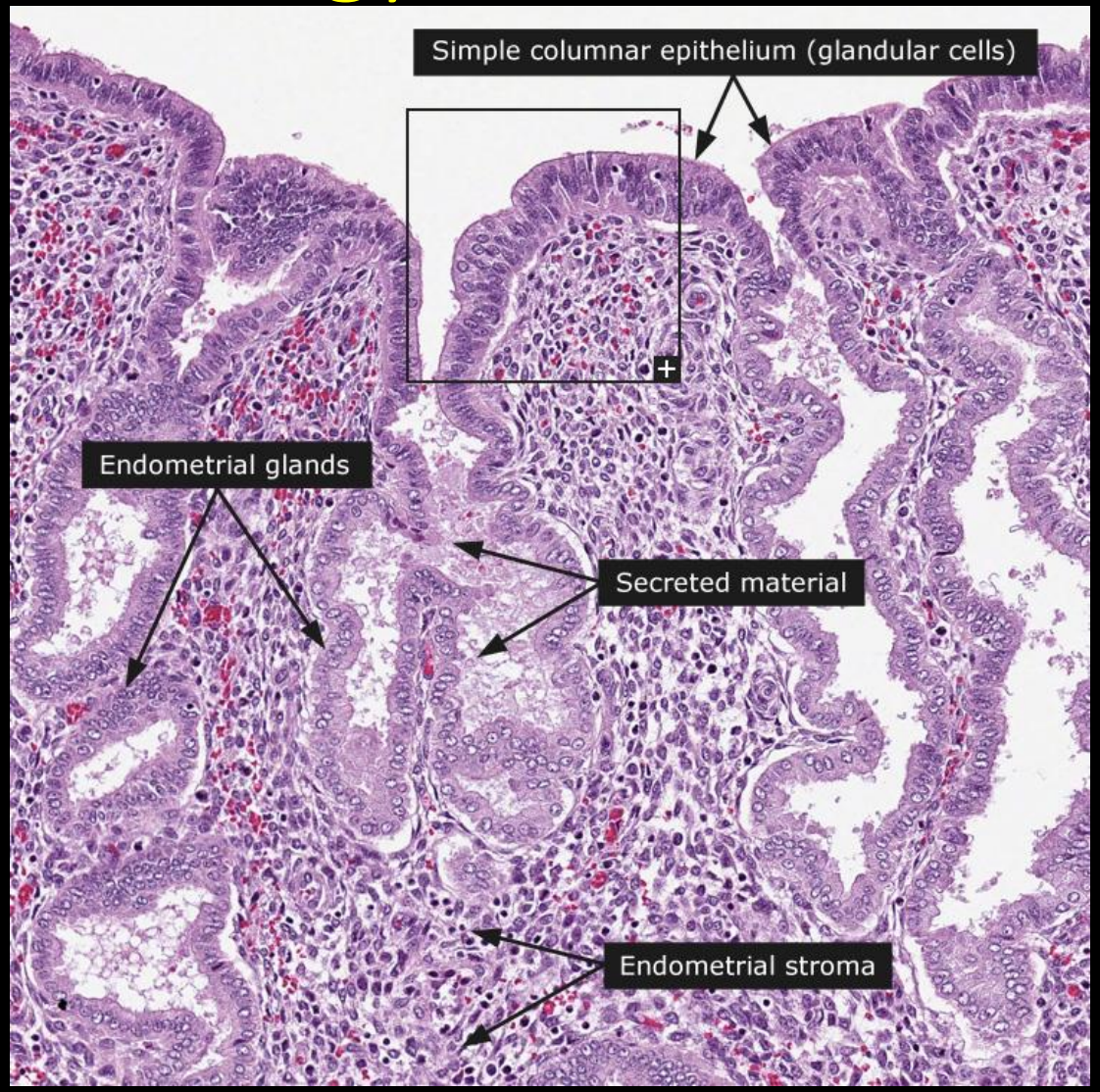
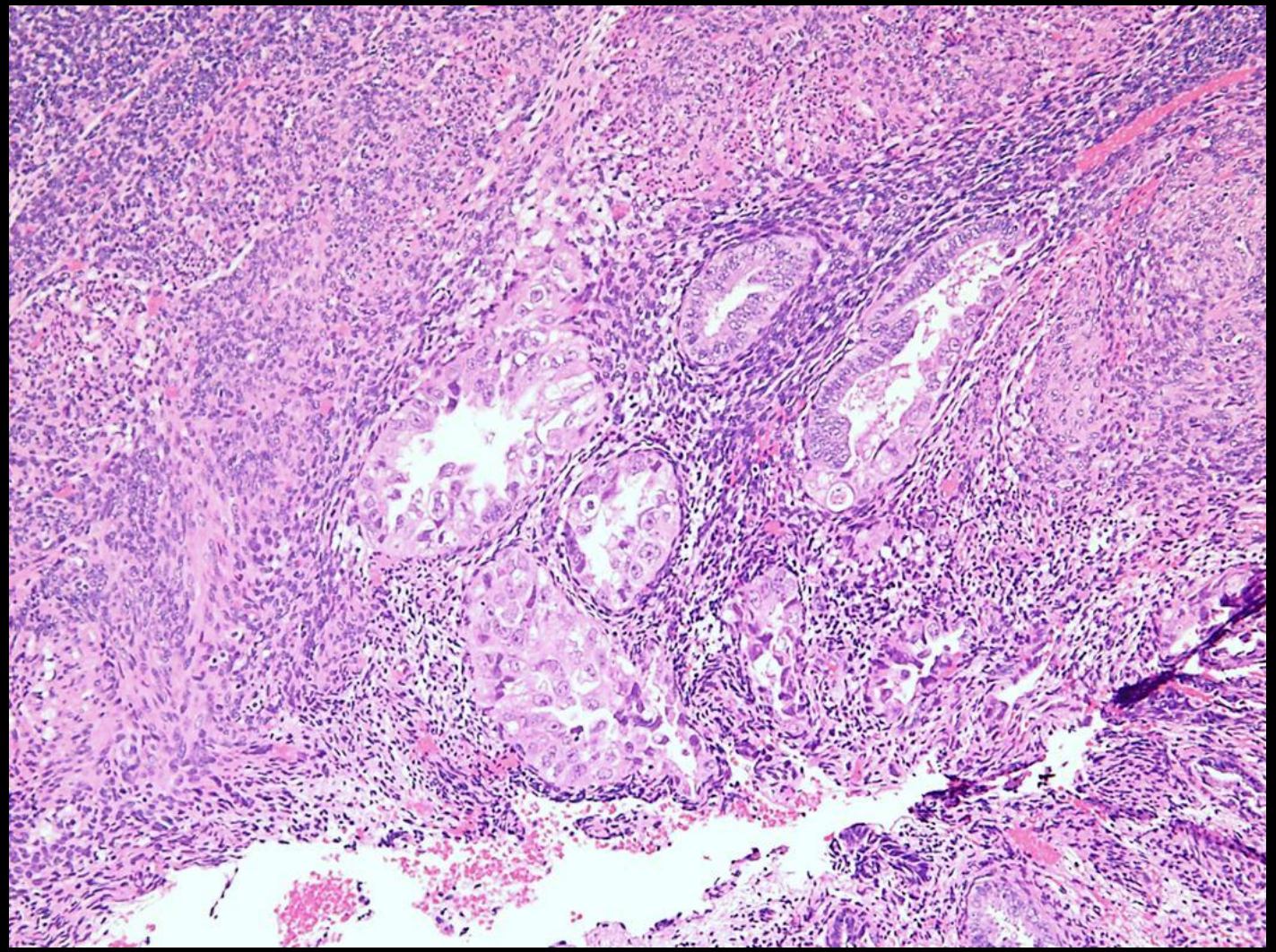


Image: Endometrium. (n.d.). Retrieved October 30, 2019, from https://www.proteinatlas.org/learn/dictionary/normal/endometrium/detail 1.

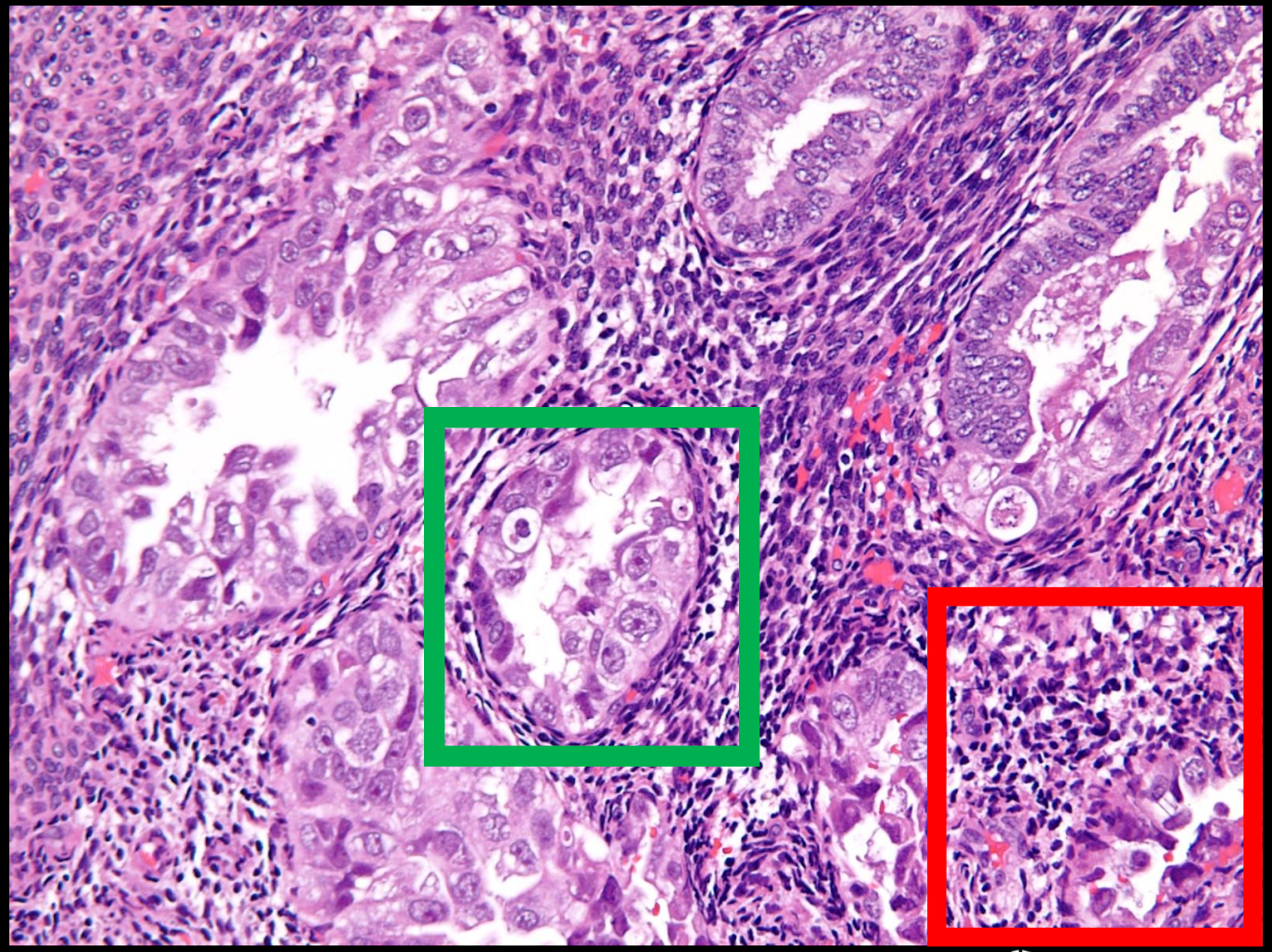
Pathology: Histology

- Patient's Histology (100x)
- Clear cell carcinoma present on Hematoxylin and Eosin (H&E) Stain



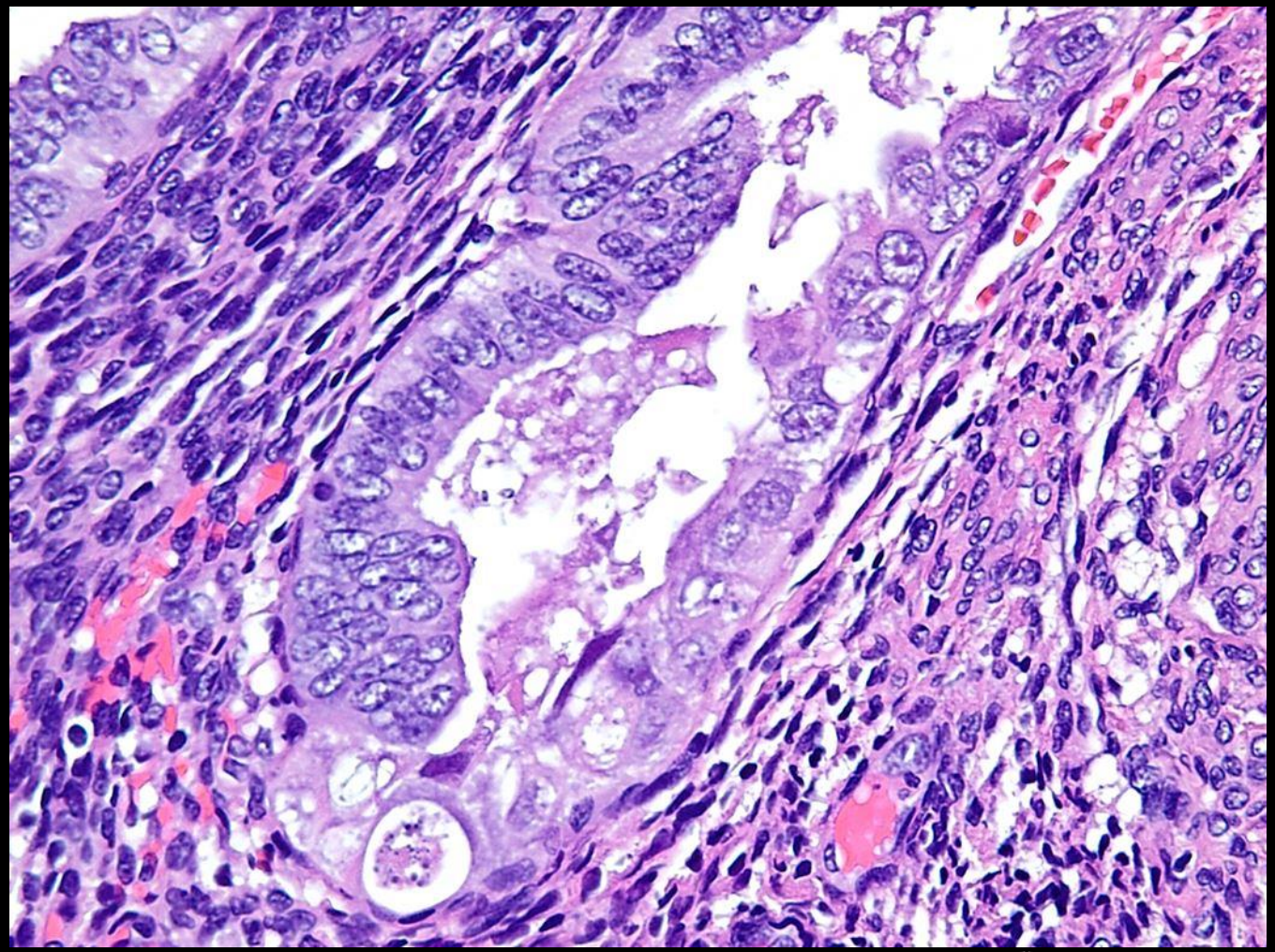
Pathology: Histology

- 200x, H&E stain
- Affected endometrial gland with clear cells with hobnailing, which is characteristic of clear cell carcinoma
- Unaffected endometrial glands and endometrial stroma



Pathology: Histology

- Endometrial gland partially involved with clear cell carcinoma
- Clear cells appear clear due to increased glycogen



Final Dx

Clear Cell Carcinoma of the Endometrium

FIGO Stage IA

Less than 50% myometrial invasion (7%)

Treatment

- Definitive therapy: hysterectomy
  - Robotic-Assisted Hysterectomy with Bilateral Salphingo-Oophorectomy was performed in this patient
- Brachytherapy
  - A type of radiation therapy
  - Insertion of radioactive implants directly into the tissue

Discussion: Endometrial Carcinoma

- Types of Endometrial Carcinomas:
  - Type I tumors: grade 1 or 2 endometrioid histology– 80%
    - Precursor lesion often present
    - Estrogen-responsive
    - Good prognosis
  - Type II tumors: grade 3 endometrioid tumors, serous, clear cell, mucinous, squamous, transitional cell, mesonephric and undifferentiated tumors – 10-20%
    - Precursor lesion rarely found
    - Not responsive to estrogen
    - High grade, poor prognosis
- Clear Cell Carcinomas of the Endometrium: <5% of all endometrial carcinomas

Discussion: Clear Cell Endometrial Carcinoma

- Epidemiology & Risk Factors:
  - Postmenopausal females*, median age 66-68 years old
  - Increased incidence with prior pelvic radiation or tamoxifen therapy
  - Current smokers
  - Non-white race
  - Multiparity*
  - Unopposed estrogen/Estrogen therapy
  - Obesity
  - Family hx – first-degree relative with endometrial or colorectal cancers

* = seen in this patient

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Discussion: Clear Cell Endometrial Carcinoma

- Signs and Symptoms:
  - Abnormal vaginal bleeding* (irregular menses, postmenopausal) – 90% of cases
  - Abdominal or pelvic pain
  - Abdominal distension
  - Bloating
  - Early satiety
  - Change in bowel/bladder function

  } Advanced Endometrial Cancer

  - Pelvic Exam:
    - Bleeding of the vagina, cervix*, urethra or rectum
    - Mass or mass effect
  - Possible coexisting adnexal ovarian tumors
  - CBC showing possible blood loss anemia – in patients with significant blood loss

* = seen in this patient

Discussion: Clear Cell Endometrial Carcinoma

- Diagnosis:
  - Transvaginal ultrasound (TVUS) or Endometrial biopsy (EMB)
    - If EMB first and inadequate → TVUS
    - If TVUS first:
      - Endometrium ≤4 mm → no EMB required
      - Endometrium >4 mm or unable to visualize thickness → hydrosonography, hysteroscopy, or EMB
  - Definitive: Histology-based (endometrial biopsy, curettage, or hysterectomy specimen)
    - Sentinel lymph node mapping indicated for women with clear cell carcinoma

Discussion: Clear Cell Endometrial Carcinoma

- Staging:
  - International Federation of Gynecology and Obstetrics (FIGO) Clinical Staging

Stage	Extent of disease	5-year survival
I	**Limited to body of uterus**	**~85%**
Ia	no myometrial invasion or <50% myometrial invasion	
Ib	>50% myometrial invasion	
II	**Limited to body of uterus and cervix**	**~75%**
III	**Extension to uterine serosa, peritoneal cavity and/or lymph nodes**	**~45%**
IIIa	Extension to uterine serosal, adnexae or peritoneal cavity (positive peritoneal washings/ascites)	
IIIb	Extension to vagina or parametrium	
IIIc1	Pelvic lymph node involvement	
IIIc2	Para-aortic lymph node involvement	
IV	**Extension to adjacent organs or beyond true pelvis**	**~25%**
IVa	Extension to adjacent organs e.g. bladder, bowel	
IVb	Distant metastases or positive inguinal lymph nodes	

Image: Watson, L. J. (2018, September 4). Endometrial and Uterine Cancer. Retrieved October 25, 2019, from https://geekymedics.com/endometrial-cancer/.

Discussion: Clear Cell Endometrial Carcinoma

- Treatment:
  - Total hysterectomy and B/L salphingo-oophorectomy with pelvic and para-aortic lymphadenectomy
    - With pelvic washings
  - Clear cell that is stage IA disease may be observed or treated with vaginal brachytherapy
    - Clear cell carcinomas are not typically chemosensitive
  - Clear cell carcinomas more likely to recur with distant spread
  - Stage III or IV clear cell and those with recurrent disease → adjuvant chemotherapy
    - Cisplatin, taxol, and/or doxorubicin (doublet or triplet combination)

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