AMSER Case of the Month

Postmenopausal Bleeding

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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
### 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.)

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

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

*Relative Radiation Level*
Ultrasound: Transvaginal (Longitudinal) – Images Unlabeled
Ultrasound: Transvaginal (Longitudinal) – Images Labeled

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

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
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
  • 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 → hydersonography, 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

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


