Endometrial Adenocarcinoma, Endometrioid Type, FIGO Grade 1 in a 22-Year-Old Female

Kelllynn McClennen PA-S, Cindy Rossi MHS, PA-C
Quinnipiac University Physician Assistant Program

Introduction
- Endometrial adenocarcinoma is the most common gynecologic malignancy in females and is diagnosed by endometrial biopsy.1
- This malignancy usually presents with abnormal uterine bleeding and is found in the post-menopausal population at age 40.2
- Risk factors include conditions with excess endogenous or exogenous hormones such as obesity, diabetes, nulliparity, early menarche and late menopause.3
- Polycystic ovarian syndrome (PCOS) previously was thought to increase the likelihood of women to develop endometrial carcinomas, but there is no proven correlation other than that both PCOS and endometrial carcinomas share common risk factors.4
- Type I endometrial adenocarcinoma has a better prognosis than type II.5
- Type I consists of low-grade histology, usually endometrioid, which responds well to hormone therapy and has a five-year survival rate of 96% with no lymph node metastasis and 67% with lymph node metastasis.5
- Type II is made up of high-grade histology including serous cell carcinomas which are estrogen independent and often metastasizes to lymph nodes and surrounding organs. It has a five-year survival rate of 33%.5,6
- Treatment is surgical with a hysterectomy either transabdominally, as an open surgery, or transvaginal, laparoscopically. The five-year survival rate is equivalent for both procedures, but the recovery time is less with less morbidity due to the procedure if done laparoscopically.5
- Adjuvant chemotherapy is initiated for high grade endometrial cancers and includes regimes such as paclitaxel or doxorubicin or docetaxel.4
- Table 1 includes the Federation of Gynecology and Obstetrics (FIGO) staging system to classify endometrial carcinomas.5

Table 1. 2009 FIGO Staging System for Endometrial Carcinoma5

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor confined to uterine corpus</th>
<th>Tumor invades uterine corpus and cervical stroma</th>
<th>Tumor invades uterine corpus and cervical stroma and tumor invades parametrial pelvis</th>
<th>Tumor invades bladder/bowel and/or distant metastases</th>
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<tbody>
<tr>
<td>IA</td>
<td>0 to &lt;50% myometrial invasion</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>IB</td>
<td>50% or greater myometrial invasion</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>IIIB</td>
<td>Vaginal and/or parametral invasion</td>
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<tr>
<td>IIIC1</td>
<td>Lymph nodes metastases</td>
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<td></td>
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<tr>
<td>IIIC2</td>
<td>Metastases to para-aortic lymph nodes</td>
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<tr>
<td>IV</td>
<td>Tumor invades bladder/bowel and/or distant metastases</td>
<td>Tumor invades bladder/bowel and/or distant metastases and tumor invades abdominal cavity</td>
<td>Tumor invades bladder/bowel and/or distant metastases and tumor invades abdominal cavity and metastases to para-aortic lymph nodes</td>
<td>Tumor invades bladder/bowel and/or distant metastases and tumor invades abdominal cavity and metastases to para-aortic lymph nodes and distant sites</td>
</tr>
</tbody>
</table>

Case History
- A 22-year-old Black female patient presents to her gynecologist for evaluation of abnormal uterine bleeding. She denies any risk factors including obesity, diabetes, nulliparity, early menarche and late menopause. She has no prior endometrial biopsy, and has had regular follow up bi-annually for a 2-year period. She has been on oral contraceptives for a total of 11 years. She has had no other prior gynecologic surgery.
- She states she has had major bleeding for the last 2 months, followed by spotting. Her presenting symptoms include weight loss, loss of appetite, fatigue, and night sweats.
- After a thorough Papanicolaou (Pap) smear, hCG <5mIU/mL, normal rectal examination, and normal endometrial biopsy, she was referred to gynecologic oncology for further evaluation.

Case Physical Exam
- Abdominal exam: soft, non-tender, no masses, normoactive bowel sounds
- Speculum exam: cervix visualized with papillary exophytic lesion
- Vaginal walls: non-tender and within normal limits
- Urinary mobile, non-tender, antverted
- Adnexa non-palpable
- Rectovaginal exam: no cul-de-sac nodularity or tenderness
- No inguinal, suprapubic, or submandibular lymphadenopathy

Differential Diagnosis
- Endometrial polyps
- PCOS related menorrhagia
- Congenital disorder
- Leiomyoma
- Malignancy - endometrial, cervical, or ovarian cancer

Diagnostic Testing and Results
- CBC: abnominal, low hemoglobin and hematocrit consistent with anemia 7.2 g/dL and 24.9%, slightly elevated white blood count 16.8 thou/ul.
- Chemistry studies: elevated glucose 128mg/dL and ALT 54 IU/L.
- ECG: no ischemic changes, sinus tachycardia.
- Cancer antigen 125 positive
- Normal pit, sup, axilla, and pelvic lymph nodes.
- Transvaginal ultrasound revealed a thickened endometrial stripe measuring 18mm.
- Hysteroscan: abnormal uterine cavity with polyoid endometrium
- Endometrial biopsy revealed final diagnosis of FIGO grade I endometrioid type, ER positive endometrial adenocarcinoma with atypical endometrial hyperplasia
- Genetic testing completed, and results were negative

Patient Management
- Patient was admitted to hospital, hysteroscopy dilation and curettage was performed and endometrial biopsy was done, and diagnosis was given.
- Bleeding was controlled and patient was discharged with follow up to outpatient gynecology oncology provider.
- Options for treatment were discussed and patient decided to have a hysterectomy due to her PCOS history, social history and being adamant about never becoming pregnant.
- Genetic testing was done due to family history of cancer, but it returned negative therefore ovaries were preserved during the procedure to avoid inducing menopause.
- Robotic laparoscopic hysterectomy, bilateral salpingectomy and lymphadenectomy was performed and completed successfully without complications.
- Patient was discharged with close follow up with gynecology oncology provider to determine need for adjuvant therapies.
- Pathology report returned as benign, and no further treatment was necessary.
- Patient was cleared for all activities two months post-op.

Discussion
- Abnormal uterine bleeding can stem from structural or nonstructural causes and can be remembered using the acronym PALM-COEIN.1-3
- Structural causes include polyps, adenomyosis, leiomyomata or malignancy and hyperplasia (PALM)
- Nonstructural causes include coagulopathies, ovarioly dysfunction, endometrial, iatrogenic or causes not yet specified (COEIN).
- Structural causes can be seen on imaging including transabdominal or transvaginal ultrasound, or pelvic MRI where a thickened endometrial stripe is present.
- A normal endometrial stripe at any point in the menstrual cycle is 14mm or less, but if an endometrial stripe is greater than or approaching 20mm there should be concern for malignancy.
- Endometrial stripe greater than 11mm is normal in post-menopausal women. Since approximately 95%-98% of endometrial carcinomas occurs in post-menopausal women, it is not often high on a differential for abnormal uterine bleeding in a 22-year-old female.

Conclusion
- Endometrial adenocarcinoma is uncommon in younger women but should be on a differential to be ruled out as a cause of abnormal uterine bleeding.
- A total hysterectomy with bilateral salpingo-oophorectomy is the most successful treatment but is not the only option for pre-menopausal women who want to preserve reproductive organs.
- Genetic testing helps to determine whether ovaries can be preserved. If so, hormones can continue to cycle and there is a possibility for preservation of eggs for future in-vitro fertilization.
- Adjuvant chemotherapy is used if there is high risk of recurrence, or the pathology report ends with a high-grade carcinoma.

References