ENDOMETRIAL HYPERPLASIA

Week 78

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SDH slide by Chloé Alutchek, MS4

Reading Assignment:
ACOG Committee Opinion #631
Endometrial Intraepithelial Neoplasia
LEARNING OBJECTIVES

• To review the most up to date nomenclature for endometrial hyperplasia

• To understand the risk of progression to and concurrent diagnosis of endometrial cancer in patients diagnosed with endometrial intraepithelial neoplasia

• To be able to counsel patients on the management of endometrial intraepithelial neoplasia
CASE VIGNETTE

• A 58 y.o. G2P2 woman presents to your office complaining of vaginal bleeding. She reports having 2-3 episodes of vaginal spotting over the past 1 year. She is worried she could have cancer.

  • She reports her LMP was at age 54.
  • She has no other complaints.
FOCUSED HISTORY

What elements of this patient’s history are most relevant?

• OBHx: FT NSVD x 1, FT C/S x 1
• GYNHx: No menses in ~ 4 years
  Denies h/o fibroids, ovarian cysts, abnormal paps
  SA with her husband only
• PMHx: HTN, obesity
• PSHx: Laparoscopic appendectomy, cesarean delivery
• MEDS: HCTZ
• ALL: NKDA
• SocHx: 20 pack year smoking history, occasional ETOH, denies use of illicit drugs
PERTINENT PHYSICAL EXAM FINDINGS

What elements of this patient’s physical exam are most relevant?

- **Vitals:** BP 149/86, 278lbs, 5’6”, **BMI 45**
- **Abd:** Obese, non-distended, soft, nontender, **no masses palpated**
- **Pelvic:**
  - **Vulva:** Normal external female genitalia. No lesions.
  - **Vagina:** Atrophic vaginal tissue. No discharge.
  - **Cervix:** Parous os. No lesions. No discharge. No CMT.
  - **Uterus:** NT. Anteverted. Not enlarged.
  - **Adnexa:** NT. No masses palpable.
After completing a thorough history and directed exam, the patient asks you why she is having this bleeding.

What are the differential diagnoses for AUB?
- Vaginal or endometrial atrophy
- Structural lesions
- Endometrial intraepithelial neoplasia
- Endometrial cancer

What are the differential diagnosis for PMB?
- Vaginal or endometrial atrophy
- Structural lesions
- Endometrial intraepithelial neoplasia
- Endometrial cancer

Fig. 1. Basic PALM—COEIN classification system for the causes of abnormal uterine bleeding in nonpregnant reproductive-aged women. This system, approved by the International Federation of Gynecology and Obstetrics, uses the term "abnormal uterine bleeding" paired with terms that describe associated bleeding patterns ("heavy menstrual bleeding" or "intermenstrual bleeding"), a qualifying letter (or letters) to indicate its etiology (or etiologies), or both. Abbreviation AUB indicates abnormal uterine bleeding. (Data from Munro MG, Critchley HO, Broder MS, Fraser IS. FIGO classification system [PALM-COEIN] for causes of abnormal uterine bleeding in nongravid women of reproductive age. FIGO Working Group on Menstrual Disorders. Int J Gynaecol Obstet 2011;113:3–13. [PubMed] [Full Text]  "

Abnormal uterine bleeding:
- Irregular bleeding (AUB-IB)
- Intermenstrual bleeding (AUB-IMB)
She then asks what the next steps are in diagnosing the cause of her PMB

- **Imaging**
  - Transvaginal ultrasound
  - Saline infusion sonohysterography

- **Endometrial sampling** (See Endometrial Biopsy AudubonBon for more information)
  - Office endometrial biopsy
  - Hysteroscopy directed endometrial sampling (office or operating room)

- **Making the distinction between hyperplasia, precancerous lesions or neoplasia has significant clinical implications**
  - Allows for appropriate interventions
  - Avoid under or overtreatment
PATHOPHYSIOLOGY

- Endometrial hyperplasia is defined histologically as abnormal overgrowth of endometrial glands

- Prolonged, unopposed stimulation of the endometrium by estrogen causes proliferative glandular epithelial changes

- Endometrial hyperplasia is clinically significant because it can be a precursor to adenocarcinoma of the endometrium
RISK FACTORS AND REDUCTION

• Obesity 
  🡪 Diet, exercise, weight loss
• Nulliparity and infertility
• Chronic anovulation 
  🡪 Progestin therapy
• Early menarche
• Late onset of menopause
• Diabetes 
  🡪 Lifestyle modifications, pharmacologic intervention
• Unopposed estrogen therapy 
  🡪 Addition of progestins
• Tamoxifen
## Endometrial Hyperplasia Classification

Currently, there are 2 systems of endometrial pre-cancer nomenclature:

<table>
<thead>
<tr>
<th>Nomenclature System</th>
<th>Risk of Concurrent Endometrial Ca</th>
<th>Risk of Progression to Endometrial Ca</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WHO94 schema</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple hyperplasia</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Complex hyperplasia</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Simple hyperplasia with atypia</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>Complex hyperplasia with atypia</td>
<td>42%</td>
<td>29%</td>
</tr>
<tr>
<td><strong>Endometrial intraepithelial neoplasia schema</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign (benign endometrial hyperplasia)</td>
<td>43% (10% high-risk uterine carcinoma)</td>
<td>40%</td>
</tr>
<tr>
<td>Premalignant (endometrial intraepithelial neoplasia)</td>
<td>43% (10% high-risk uterine carcinoma)</td>
<td>40%</td>
</tr>
<tr>
<td>Malignant (endometrial adenocarcinoma, endometrioid type, well differentiated)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
# ENDOMETRIAL INTRAEPITHELIAL NEOPLASIA CRITERIA

<table>
<thead>
<tr>
<th>Nomenclature</th>
<th>Topography</th>
<th>Functional Category</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign endometrial hyperplasia</td>
<td>Diffuse</td>
<td>Prolonged estrogen effect</td>
<td>Hormonal therapy, symptomatic</td>
</tr>
<tr>
<td>Endometrial intraepithelial neoplasia</td>
<td>Focal progressing to diffuse</td>
<td>Precancerous</td>
<td>Hormonal therapy or surgery</td>
</tr>
<tr>
<td>Endometrial adenocarcinoma, endometrioid type, well differentiated</td>
<td>Focal progressing to diffuse</td>
<td>Malignant</td>
<td>Surgery, stage based</td>
</tr>
</tbody>
</table>

*Previously known as atypical endometrial hyperplasia.

# Endometrial Intraepithelial Neoplasia Criteria

**Table 2.** Definitions of Endometrial Intraepithelial Neoplasia* Criteria

<table>
<thead>
<tr>
<th>Endometrial Intraepithelial Neoplasia* Criteria</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Architecture</td>
<td>Area of glands greater than stroma (volume percentage stroma less than 55%)</td>
</tr>
<tr>
<td>Cytology</td>
<td>Cytology differs between architecturally crowded focus and background</td>
</tr>
<tr>
<td>Size greater than 1 mm</td>
<td>Maximum linear dimension exceeds 1 mm</td>
</tr>
<tr>
<td>Exclude mimics</td>
<td>Benign conditions with overlapping criteria (ie, basalis, secretory, polyps, repair)</td>
</tr>
<tr>
<td>Exclude cancer</td>
<td>Carcinoma if maze-like glands, solid areas, or appreciable cribriforming</td>
</tr>
</tbody>
</table>

*Previously known as atypical endometrial hyperplasia.

Primary goals in patients diagnosed with endometrial intraepithelial hyperplasia are:

- Ruling out concurrent adenocarcinoma
- Design a treatment plan that can accommodate delayed discovery of an occult carcinoma
- Preventing progression to endometrial cancer

**Total hysterectomy** is an effective means of treating a biopsy diagnosis of endometrial intraepithelial neoplasia

- Supracervical hysterectomy, morcellation, and endometrial ablation are unacceptable for treatment of endometrial intraepithelial neoplasia.
MEDICAL MANAGEMENT

Is there a role for medical management for our patient?

• Nonsurgical management of endometrial intraepithelial neoplasm is acceptable for certain patient populations:
  • Patients desiring future fertility
  • Patients with medical comorbidities precluding surgical management
• If endometrial intraepithelial neoplasia is present, there is a higher incidence of failure of medical management and subsequent development of cancer

<table>
<thead>
<tr>
<th>Hormonal Agent</th>
<th>Dosage and Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medroxyprogesterone acetate</td>
<td>10–20 mg/d, or cyclic 12–14 days per month</td>
</tr>
<tr>
<td>Depot medroxyprogesterone</td>
<td>150 mg intramuscularly, every 3 months</td>
</tr>
<tr>
<td>Micronized vaginal progesterone</td>
<td>100–200 mg/d or cyclic 12–14 days per month</td>
</tr>
<tr>
<td>Megestrol acetate</td>
<td>40–200 mg/d</td>
</tr>
<tr>
<td>Levonorgestrel intrauterine system</td>
<td>52 mg in a steroid reservoir over 5 years</td>
</tr>
</tbody>
</table>

Regression of hyperplasia (simple, complex, and atypical) has been observed in 80-90% of patients receiving either of these 2 agents for 3 months.

*Previously known as atypical endometrial hyperplasia.

Black women are approximately twice as likely to die from uterine cancer as women in other racial/ethnic groups.

Black women are 2x more likely to be diagnosed with distant stage uterine cancer than women of other racial/ethnic groups for each histologic type.

Black women are more likely to have aggressive histologic types than other women, including carcinosarcomas, and sarcomas.

Improving access to health care among low-SES women to facilitate earlier diagnosis and optimal treatment may serve to diminish the racial/ethnic difference in endometrial cancer survival.
Description: Endometrial hyperplasia workup and management

Given the presence of [AUB, postmenopausal bleeding, results of transvaginal ultrasound], the need for further evaluation with both imaging and endometrial tissue sampling to determine whether carcinoma or premalignant lesions are present was discussed with the patient. Recommendations were made to proceed with transvaginal ultrasound and office endometrial biopsy.

Results of the endometrial biopsy were discussed.

A diagnosis of [endometrial intraepithelial neoplasia] was made.

Management options were discussed with patient including expectant vs medical vs surgical management. R/B/A of each were discussed in detail. Pt opted for ***.
CODING AND BILLING

• Diagnostic Codes (ICD-10)
  • N93.9    AUB
  • N95      PMB
  • N85.02   Endometrial intraepithelial neoplasia
### CODING AND BILLING – NEW PATIENT

<table>
<thead>
<tr>
<th>HISTORY</th>
<th>EXAM</th>
<th>MEDICAL DIAGNOSIS MAKING</th>
<th>CODE</th>
<th>APPLICABLE GUIDELINES</th>
</tr>
</thead>
</table>
| Problem focused:  
  - Chief complaint  
  - HPI (1-3) | Problem focused:  
  - 1 body system | Straight forward:  
  - Diagnosis: minimal  
  - Data: minimal  
  - Risk: minimal | 99201 | - Personally provided  
- Primary care exception  
- Physicians at teaching hospitals |
| Expanded problem focused:  
  - Chief complaint  
  - HPI (1-3)  
  - ROS (1-3) | Expanded problem focused:  
  - Affected areas and others | Straight forward:  
  - Diagnosis: minimal  
  - Data: minimal  
  - Risk: minimal | 99202 | - Personally provided  
- Primary care exception  
- Physicians at teaching hospitals |
| Comprehensive  
  - Chief complaint  
  - HPI (4)  
  - ROS (2-9)  
  - Past, family, social history (1) | Detailed:  
  - 7 systems | Low:  
  - Diagnosis: limited  
  - Data: limited  
  - Risk: low | 99203 | - Personally provided  
- Primary care exception  
- Physicians at teaching hospitals |
| Comprehensive  
  - Chief complaint  
  - HPI (4+)  
  - ROS (10+)  
  - Past, family, social history (3) | Comprehensive:  
  - 8 or more systems | Moderate:  
  - Diagnosis: multiple  
  - Data: moderate  
  - Risk: moderate | 99204 | - Personally provided  
- Physicians at teaching hospitals |
| Comprehensive  
  - Chief complaint  
  - HPI (4+)  
  - ROS (10+)  
  - Past, family, social history (3) | Comprehensive:  
  - 8 or more systems | High:  
  - Diagnosis: extended  
  - Data: extended  
  - Risk: high | 99205 | - Personally provided  
- Physicians at teaching hospitals |
# CODING AND BILLING – ESTABLISHED PATIENT

<table>
<thead>
<tr>
<th>HISTORY</th>
<th>EXAM</th>
<th>MEDICAL DIAGNOSIS MAKING</th>
<th>CODE</th>
<th>APPLICABLE GUIDELINES</th>
</tr>
</thead>
</table>
| Expanded problem focused:  
- Chief complaint  
- HPI (1-3) | Problem focused:  
- 1 body system | Straight forward:  
- Diagnosis: minimal  
- Data: minimal  
- Risk: minimal | 99212 | - Personally provided  
- Primary care exception  
- Physicians at teaching hospitals |
| Expanded problem focused:  
- Chief complaint  
- HPI (1-3)  
- ROS (1) | Expanded problem focused:  
- Affected area and others | Low:  
- Diagnosis: limited  
- Data: limited  
- Risk: low | 99213 | - Personally provided  
- Primary care exception  
- Physicians at teaching hospitals |
| Detailed  
- Chief complaint  
- HPI (4+)  
- ROS (10+)  
- Past, family, social history (3) | Detailed:  
- 7 systems | Moderate:  
- Diagnosis: multiple  
- Data: moderate  
- Risk: moderate | 99214 | - Personally provided  
- Physicians at teaching hospitals |
| Comprehensive  
- Chief complaint  
- HPI (4+)  
- ROS (10+)  
- Past, family, social history (2) | Comprehensive:  
- 8 or more systems | High:  
- Diagnosis: extended  
- Data: extended  
- Risk: high | 99215 | - Personally provided  
- Physicians at teaching hospitals |
EVIDENCE

• References