Uterine Pathology & Case Presentations

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Chief
In a galaxy far away, years ago!
Conflict of Interest

None
Objectives

- To review the most common histologic conditions/tumors of the uterus
- Apply pathologic knowledge to the clinical management of the most common presentations
Case # 1

34 year old G0P0 provides a history “irregular periods” occurring every four months or so. She is sexually active, but not trying to get pregnant and not using contraception.

P.E.

146/94, Wt. 249#, Ht. 62”

Coarse hair over chin, breasts and abdomen.

Uterus is palpably irregular, size undermined.

She wants you to fix the bleeding.

Next???
Case # 1

- Pregnancy test Negative.
- TV sono, endometrial biopsy or both ??
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TV Sono:
Uterine size is 11x9x8 cm, irregular contour with multiple mural masses ranging from 1-3 cm.
Endometrium is 28 mm in thickness.
Ovaries are 3x4 cm bilaterally, with multiple cysts.

Endometrial biopsy is performed and the Medical Student asks you what is causing the bleeding and what you think the pathology report will show??
Case # 2

88 year old G3P3 with menopausal bleeding. Weight is 98 #. Uterus is only slightly enlarged on pelvic exam.

Sonogram shows a 8x9x7 cm uterus with a 9mm endometrial stripe and no enlargement of the adnexa. Hysteroscopy with D&C is performed.

The same Medical Student wants your best guess as to what the histology report will show.
Case # 3

49 year old G3P3 with perimenopausal symptoms. You have been performing annual exams for the past 15 years. Her pelvic exam is consistent with a mobile, irregular, 12 cm uterus. Compared to previous exams the uterus is enlarged.

The same Medical Student wants to know what you will do next.

???
Abnormal Uterine Pathology

**Benign**

Associated with Bleeding
- Anovulatory endometrium
- Proliferative → Hyperplasia
- Endometrial polyps
- Submucosal myoma

**Pre-malignant & Malignant**

Mass Effect
- Leiomyoma
Benign Endometrial Histology

- **Proliferative Endometrium**
  - Estrogen induced gland proliferation with tubular glands, pseudostratified epithelium and increased mitotic activity.
Benign Endometrial Histology

- Anovulatory Endometrium
  - Usually due to persistent estrogen stimulation. Characterized by cystic glandular proliferation, regularly irregular gland distribution, and patchy stromal breakdown.
Benign Endometrial Histology

- Endometrial polyp
  - Monoclonal neoplastic proliferation of stromal cells incorporating a non-neoplastic glandular component. Usually with central thick walled vessels, +/- a connecting stalk.
Benign Endometrial Histology

Endometrial stromal tumors

Endometrial stromal nodule

- Usually well circumscribed intramural or submucosal lesions with a pushing interface to the surrounding myometrium. Cells resemble proliferative phase endometrial stroma and seem to whorl around prominent spiral arterioles.
Tumors of the Myometrium

Leiomyoma

- Unicellular clonal neoplasm secondary to inactivation of the X chromosome.
- The most common human tumor. Present in 77% of hysterectomy specimens regardless of the indication for surgery.
- Fascicles of bland smooth muscle cells, usually well circumscribed. Normal (non-atypical) mitoses are seen variably especially in the luteal phase.
# Abnormal Uterine Pathology

## Benign

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## Malignant

Epithelial
- AEH/EIN
- Endometrioid
- Clear Cell
- Papillary Serous
- Carcinosarcoma

Mesenchymal
- Leiomyosarcoma
- Low Grade Stromal Sarcoma
- Undifferentiated
Endometrial Cancer Precursors
Estrogen Dependent

- Proliferative endometrium
  - Hyperpalsia
    - Hyperplasia with atypia (EIN)
      - Cancer
Proliferative Endometrium

Complex Endometrial Hyperplasia

Atypical Endometrial Hyperplasia
Endometrial Intraepithelial Neoplasia (EIN)

- **Clonal** proliferation of architecturally and cytologically altered premalignant endometrial glands, prone to malignant transformation to endometrioid (Type I) endometrial adenocarcinoma.

- Non-invasive, genetically altered neoplasms that arise **focally** and may convert to malignant phenotype upon acquisition of additional genetic damage.
Endometrial Intraepithelial Neoplasia (EIN)

- EIN is conceptually similar to Complex Atypical Hyperplasia (CAH).
- The majority of EIN overlaps with CAH.
- EIN is not exclusive to CAH.
- Not all CAH are EIN.
- Specific to Type I endometrial cancer precursors.
AEH or EIN

- GOG 167

- Post-hysterectomy findings in women with atypical endometrial hyperplasia.
- 123/289 (42.6%) women found to have endometrial carcinoma on final pathology.
- 43/123 (34%) demonstrated myometrial invasion or Grade 2 or Grade 3 carcinomas.

Cancer 2006;106:812-819.
## Endometrial Cancer

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Type I</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Factors</td>
<td>Unopposed estrogen</td>
<td>Age</td>
</tr>
<tr>
<td>Race</td>
<td>White &gt; Black</td>
<td>White = Black</td>
</tr>
<tr>
<td>Differentiation</td>
<td>Well differentiated</td>
<td>Poorly differentiated</td>
</tr>
<tr>
<td>Histology</td>
<td>Endometrioid</td>
<td>Non-endometrioid</td>
</tr>
<tr>
<td>Stage</td>
<td>I/II</td>
<td>III/IV</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Favorable</td>
<td>Not favorable</td>
</tr>
<tr>
<td>Ploidy</td>
<td>Diploid</td>
<td>Aneuploid</td>
</tr>
</tbody>
</table>
Endometrioid Adenocarcinoma

Grade 1

Grade 2

Grade 3
Uterine Papillary Serous Carcinoma

Carcinosarcoma

Clear Cell Carcinoma
Uterine Leiomyosarcoma

Histologic characteristics

The diagnosis is made when any of the following conditions are satisfied:
1) geographic tumor necrosis is definitely present; or 2) both proliferative activity greater than or equal to 10 mitotic figures/10 high powered fields and moderate to severe, diffuse or multifocal atypia are present.
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Geographic Tumor Necrosis</th>
<th>Mitotic Rate per 10 High Powered Fields</th>
<th>Atypia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leiomyosarcoma</td>
<td>Present</td>
<td>Any Rate ≥ 10</td>
<td>Present or absent Diffuse or multifocal; moderate to severe</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STUMP (smooth muscle tumor of uncertain malignant potential)</td>
<td>Questionable</td>
<td>Any rate &gt;15 Approaching but less than 10</td>
<td>Present or absent None Diffuse or multifocal; moderate to severe</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atypical leiomyoma</td>
<td>Absent</td>
<td>≤10</td>
<td>Diffuse or multifocal; moderate to severe</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leiomyoma with increased mitotic activity</td>
<td>Absent</td>
<td>≤ 15</td>
<td>Absent</td>
</tr>
</tbody>
</table>
Low Grade Endometrial Stromal Sarcoma

Previously distinguished from high grade ESS. A tumor composed of cells that morphologically resemble non-neoplastic proliferative phase endometrial stroma that infiltrates the surrounding myometrium with a “finger-like” permeative fashion and typically invades vascular or lymphatic spaces.
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Questions??