Non-epithelial Uterine Tumors

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Scope

• Pure mesenchymal tumors
  - Smooth muscle tumors
    - Endometrial stromal tumors
      - Mixed endometrial stromal and smooth muscle tumor
  • Mixed Mullerian tumors
  • Miscellaneous
    - Perivascular epithelioid cell tumor
    - Adenomatoid tumor

Smooth muscle tumors

• Leiomyoma and leiomyoma variants
• Leiomyosarcoma
• Borderline smooth muscle tumor/ Smooth muscle tumor of uncertain malignant potential (STUMP)

Leiomyoma

Enlarged nodular uterus
Cut surface: Well circumscribed, firm or rubbery, grey white mass (es) with whorled appearance.
Can be “shelled out”
Micro: Interlacing fascicles of uniform spindle cells with bland looking cigar-shaped nuclei. Mitosis is rare. Necrosis is absent.

Leiomyoma, histological variants

• Leiomyoma
  - with degenerative changes
    - with hydropic change
    - with hormonal induced changes (hemorrhagic/apoplectic)
• Cellular and highly cellular leiomyoma
• Mitotically active leiomyoma
• Epithelioid leiomyoma
• Myxoid leiomyoma
• Leiomyoma with bizarre nuclei (Atypical leiomyoma, symplastic leiomyoma)
• Lipo leiomyoma

Leiomyoma with degenerative changes
Cellular and highly cellular leiomyoma

Epithelioid leiomyoma

Leiomyoma with bizarre nuclei (Atypical leiomyoma)

Lipoleiomyoma

Leiomyoma, growth pattern variants

- Diffuse leiomyomatosis
- Dissecting leiomyoma including cotyledonoid leiomyoma
- Intravenous leiomyomatosis
- Diffuse leiomyomatosis peritonealis
- Leiomyoma with vascular invasion
- Benign metastasizing leiomyoma

Diffuse leiomyomatosis

Dissecting leiomyoma including cotyledonoid leiomyoma

Diffuse leiomyomatosis peritonealis

Intravenous leiomyomatosis

Leiomyosarcoma

‘Malignant smooth muscle tumor’
- 1% of all uterine malignancies
- 0.64 cases per 100,000 women
- present later in life around or after menopause
- unsuspected or presumed to be leiomyoma before patho. exam.

Leiomyosarcoma

Micro:
- Atypia
- Mitotic figure...*Atypical mitosis*
- Necrosis: geographic coagulation necrosis
- Cellularity
- Infiltrative pattern
- Vascular invasion
- Metastasis
Leiomyosarcoma

- Types of leiomyosarcoma
  - Conventional, spindle, NOS
  - Epithelioid
  - Myxoid

Myxoid leiomyosarcoma

- Soft grey gelatinous surface, maybe well defined margin grossly hypocellular, minimal atypia, low mitotic count (mitotic count ≥ 2/10HPF, myxoid LMS)

Differential diagnoses:
  - myxoid LM
  - hydropic LM
  - myxoid EST
  - intravenous leiomyomatosis

Epithelioid leiomyosarcoma

- Round to polygonal cells in > 50% of tumor
  - Softer may lack whorled cut surface
  - Eosinophilic/clear cytoplasm
  - Round nuclei
Epithelioid leiomyosarcoma

- Any degree of cytologic atypia and ≥ 5 mf /10HPFs without necrosis
- ≥ 5 mf /10HPFs without necrosis with any degree of cytologic atypia

Epithelioid LMS

DDx
- Poorly differentiated carcinoma
- PEComa
- UTROSCCT
- PSTT /ETT
- Endometrial stromal sarcoma
- Malignant melanoma/ alveolar soft part sarcoma/ rhabdoid tumor

Borderline smooth muscle tumor / Smooth muscle tumor of uncertain malignant potential (STUMP)

- Smooth muscle tumors that are difficult to classify as benign or malignant based on generally applied criteria
  - Subtype of smooth muscle differentiation in doubt...standard/epithelioid/myxoid
  - Type of necrosis...uncertain
  - Borderline number of mitotic figures
  These interpretation will result in different criteria of justifying malignancy.

Practical classification of smooth muscle tumors

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Necrosis</th>
<th>mf/10hpf</th>
<th>Atypia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leiomyosarcoma</td>
<td>+</td>
<td>Any rate &gt;10</td>
<td>+ or - Diffuse/multifocal; moderate to severe</td>
</tr>
<tr>
<td>STUMP</td>
<td>Questionable</td>
<td>Any rate &gt;15</td>
<td>Approaching &amp;&lt;10</td>
</tr>
<tr>
<td>LM with bizarre nuclei</td>
<td>-</td>
<td>≤10</td>
<td>Diffuse/multifocal; moderate to severe</td>
</tr>
<tr>
<td>Mitotically active LM</td>
<td>-</td>
<td>≤15</td>
<td>-</td>
</tr>
</tbody>
</table>

Immunohistochemistry

- Smooth muscle markers: (variable in LMS)
  - smooth muscle actin, desmin, smooth muscle myosin, h-caldesmon
  - oxytocin, keratin, EMA (more often epithelioid variant)
  - CD10 variable positivity
  - ER, PR in nearly 100%
  - AR in 30%
  - WT-1 p53 minimal to absent in benign
  - MiB-1 (Ki-67)
**Endometrial stromal tumors (EST)**

- Composed of cells morphologically resemble nonneoplastic proliferative phase endometrial stroma and prominent spiral arteriole-like vascular component.

Cytogenetic abnormalities in low grade ESS chromosome rearrangements involving chromosomes 6, 7 and 17; most common reciprocal balanced translocation: - t(7;17)(p15;q21) (chimeric JAZF1-JJAZ1 mRNA transcripts)

**WHO 2003 Classification:**
- endometrial stromal nodule
- endometrial stromal sarcoma, low grade
- undifferentiated endometrial sarcoma

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**Endometrial stromal nodule (ESN)**

- Very rare; median age, 47; AUB; pelvic pain
- Macro: Well delineated, soft tan yellow cut surface, expansile margin; mean diameter, 7 cm; intramyometrial, subserosal, polypoid
- Micro: Endometrial stromal cells and prominent spiral arteriole-like vascular component;
  - hypercellular/hypocellular/myxoid/epithelioid;
  - mf 1-5/10HPFs.
  - Focal irregularity not exceed 3 mm; no vascular invasion

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**Mixed endometrial stromal and smooth muscle tumor**

- Stromomyoma: an admixture of endometrial stromal and smooth muscle elements...a minimum of 30% of the minor component
- Should be evaluated and reported in the same way as EST

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**Mixed endometrial stromal and smooth muscle tumor**

- Cytokeratin, Desmin, Vimentin...
**Endometrial stromal sarcoma, low grade**

- **Macro**
  - intramyometrial nodular mass
  - intracavitary polypoid mass
  - diffuse myometrial invasion
  - any combination of these patterns

Extension beyond uterus/extension involvement of parametrial vessels ('worm-like' appearance)

**Endometrial stromal sarcoma, low grade**

**Undifferentiated endometrial sarcoma**

- **Macro:**
  - one or more tan-yellow to grey fleshy intracavitary polypoid masses with hemorrhage or necrosis

**Differential diagnosis:**

- Smooth muscle tumor
- Mixed endometrial stromal-smooth muscle tumors
- Uterine tumor resembling ovarian sex cord stromal tumor (UTROSCT)
- Endometrial polyp with atypical stroma
  - Rare heterologous tumour
Mixed epithelial and mesenchymal tumors

- **Adenomyoma** - benign
- - Atypical polypoid variant
- **Adenofibroma** - benign
- **Carcinofibroma** - very uncommon
- **Adenosarcoma**
- **Carcinosarcoma**

Mixed epithelial and mesenchymal tumors

- **Adenomyoma**
  - endocervical type...arising in cervix, polyph... benign
  - endometrial type... polyph/ submucosal mass... benign
  - endometrial glands and smooth muscle
- **Atypical polypoid adenomyoma**
  - complex proliferation of glands with variable atypia admixed with cellular smooth muscle
- **Adenofibroma**
  - benign epithelial and mesenchymal components
  - much less frequent ... may be associated with tamoxifen therapy

**Adenomyoma**

- Low grade mullerian adenosarcoma... admixture of a benign or sometimes atypical) epithelial component with a low grade malignant stromal component ...8% of uterine sarcoma
- Postmenopausal ; associated risk.. Hyperestrinism (tamoxifen), prior radiation therapy
- **Macro:** endometrial lesion, cervix(9%), myometrium(4%)

**Adenosarcoma**

- Polyoid, papillary intraluminal soft to firm, spongiform from cysts and clefts reminiscent of phyllodes tumor
- ≥ 4 mf/10 HPFs (≥ 2 mf/10 HPFs with marked cellularity / significant atypia)
**Metastasis:**

The factors determining prognosis of *uterine sarcoma* (contd)

- For carcinosarcomas, predictors of metastasis
  - **Isthmic or cervical location**
  - **LVSI**
  - serous and clear cell histology, and grade 2 or 3 carcinoma

**Progression-free interval**
- adnexal spread, lymph node metastases, tumor size, peritoneal cytologic findings, and depth of myometrial invasion correlate


Perivascular epithelioid cell tumor (PEComa)

- Composed predominantly or exclusively of HMB-45 positive perivascular epithelioid cells with eosinophilic granular cytoplasm
- Age: 40-75 yrs (mean 54)/.../... uncertainty malignant potential
- Macro: mass in uterine corpus
- Micro: 1) tongue-like growth pattern of low grade ESS, abundant eosinophilic granular/clear cytoplasm (diffuse HMB-45 and variable muscle marker expressions)
  2) lesser tongue-like growth pattern of epithelioid cells with less prominent clear cytoplasm and a smaller number HMB-45 (+) cells but more extensive muscle marker differentiation
- Genetic susceptibility:
  - pelvic nodes involved by lymphangioleiomyomatosis
  - one fourth had tuberous sclerosis

Adenomatoid tumor

- Benign tumor of mesothelium forming gland like structures
- Site: uterine serosa, myometrium
- Macro: softer, less well defined than leiomyoma
- Micro: multiple small, often slit-like interconnecting spaces within the myometrium lined by cuboidal or attenuated cells, infiltrative appearance...
  - may be confused with lymphangiomata
  - little nuclear atypia, signet ring like
  - no stromal desmoplastic response
- IPX... Positive keratin and mesothelial markers

References

1. Crum CP, Lee KR. Diagnostic gynecologic and obstetric pathology. 2006
4. Olah KS, Diam JA, Gey H. Leiomyosarcoma have a poorer prognosis than mixed mesodermal tumor when adjusting for known prognostic factors; the result of a retrospective study of 62 cases of uterine sarcoma. Br J Obstet Gynaecol 99(7);1992:590-4

Any questions?

Thank You for Your Attention