Mesenchymal tumors of the uterus

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Pathologie
Mesenchymal tumors

1. Leiomyoma
2. STUMP
3. Leiomyosarcoma
4. Undifferentiated uterine sarcoma
5. Rhabdomyosarcoma
6. PEComa

(Endometrial stromal tumors)
Leiomyoma

- Most common uterine neoplasm
- Found in 70% of hysterectomy specimens
- >40% in women >40 years
Diagnostic challenge

- 90-95% are typical

  BUT

- The rest aren’t!

- Heavy management implications if diagnosed incorrectly
«Usual» leiomyoma
«Usual» leiomyoma
Diagnostic difficulties

• Unusual morphology

• Unusual growth pattern

• Treated leiomyoma
Diagnostic difficulties

- Nuclear atypia
- Mitosis
- Increased Cellularity
Unusual morphology

- Leiomyoma with bizarre nuclei

Bizarre nuclei
**NO** mf (typically 1-2/hpf) or tumor cell necrosis
Unusual morphology

• Cellular leiomyoma

«significant»
increased cellularity
NO cytological atypia
or mf
Unusual morphology

• Mitotically active leiomyoma

10-15 mf/10hpf
NO cytological atypia
or tumor cell necrosis

Cave: myxoid morphology!
Cutoff ≥2 mf/10hpf
Unusual morphology

- Hydropic
- Apoplectic
- Lipomatous
- Epitheloid (50%)
- Myxoid
Unusual growth pattern

- Intravenous leiomyomatosis
Unusual growth pattern

- Benign metastasizing leiomyoma
Unusual growth patterns

- Diffuse peritoneal leiomyomatosis
typically pregnancy/post-partum
Treated leiomyoma

- GnRH therapy → apoplectic changes
Treated leiomyoma

• Uterine artery embolization
STUMP

Smooth Muscle Tumor of Uncertain Malignant Potential (vs. Leiomyoma Variants)
Diffuse atypia and 5-9 mitoses/10 HPF
Tumor cell necrosis or necrosis of uncertain type
If > 15 mitoses/10 HPF, but no atypia or necrosis

• Recurrence rate 7-29%
• Clinical management remains controversial
• STUMP category should be avoided!
Table 5.1. Uterine smooth-muscle tumours with spindle-cell differentiation of uncertain malignant potential.

<table>
<thead>
<tr>
<th>Tumour cell necrosis</th>
<th>Moderate-to-severe atypia</th>
<th>Mitotic count (per 10 HPF)</th>
<th>Mean mitotic count in tumours with recurrence (per 10 HPF)</th>
<th>Cases with recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>Focal/multifocal</td>
<td>&lt; 10</td>
<td>4 (range 3–5)</td>
<td>13.6% (3 of 22 cases)</td>
</tr>
<tr>
<td></td>
<td>Diffuse</td>
<td>&lt; 10</td>
<td>4.3 (range 2–9)</td>
<td>10.4% (7 of 67 cases)</td>
</tr>
<tr>
<td>Present</td>
<td>None</td>
<td>&lt; 10</td>
<td>2.8 (range 1–4)</td>
<td>26.7% (4 of 15 cases)</td>
</tr>
<tr>
<td>Absent</td>
<td>None</td>
<td>≥ 15</td>
<td>Not applicable</td>
<td>0% (0 of 39† cases)</td>
</tr>
</tbody>
</table>

*One of the four tumours also had epithelioid cells
†Three had ≥20 mitotic figures per 10 HPF; an unknown proportion also had counts between 10 and 14 (129).
Necrosis in smooth muscle tumors

Hyaline necrosis

Tumor cell necrosis
Genetic aberrations in leiomyomas

• ~40% associated with clonal cytogenetic aberrations
  – t(12;14) best studied in intravenous leiomyomatosis
    • Balanced translocation between $HMGA2$ and $RAD51B$

• Renal carcinoma-leiomyomatosis syndrome (HLRCC)
  – Germline heterozygous loss-of-function mutation of fumarate hydratase gene, $FH$ (1q43)
    • Not seen in sporadic leiomyoma
Leiomyosarcoma

- ~ 45% of uterine sarcomas
- Leiomyoma:Leiomyosarcoma= 800:1
- Typically > 40 years with peak at 50 years
- Overall 15-25% 5-year survival rate
Leiomyosarcoma

Environmental Exposure
• May be related to prior radiation therapy
• History of oral contraceptives, tamoxifen
• Body mass index > 27

Genetic Susceptibility
• Increased incidence in patients with retinoblastoma, or hereditary leiomyomatosis and renal cell carcinoma

Precursor Lesion
• Rarely malignant transformation of leiomyoma (<3%)
Leiomyosarcoma
Leiomyosarcoma

Combination of any 2 of these features

• Diffuse moderate to severe atypia
• >10 mitoses/10hpf
• Tumor cell necrosis
Leiomyosarcoma
Diagnostic criteria

<table>
<thead>
<tr>
<th>Diagnostic Criteria (Based on Histologic Subtype)</th>
<th>Spindle LMS</th>
<th>Epithelioid LMS*</th>
<th>Myxoid LMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytologic atypia</td>
<td>Moderate to severe</td>
<td>Moderate to severe</td>
<td>Mild to severe</td>
</tr>
<tr>
<td>Tumor cell necrosis</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Mitoses</td>
<td>$\geq 10$ per $10$ HPF</td>
<td>$\geq 5$ per $10$ HPF</td>
<td>$\geq 2$ per $10$ HPF in the absence of tumor cell necrosis or cytologic atypia, especially if infiltrative margins*</td>
</tr>
</tbody>
</table>

*Only tumors with $< 3$ mitoses and no cytologic atypia should be regarded as leiomyoma.
Leiomyosarcoma

- Spindle cell
- Epithelioid
- Myxoid
IHC

- Desmin, Caldesmon, SMA
- May be CD10+, Keratin+
- ER/PR+ in 40%
- CD117+ and DOG1+ (no c-kit mutations)
- Strong p53+ and p16+ favors leiomyosarcoma (DD Leiomyoma with bizarre nuclei!)
Leiomyoma vs. Leiomyosarcoma

• typical gross but worrisome microscopic appearance \[\rightarrow\] leiomyoma with bizarre nuclei

• worrisome gross but typical microscopic appearance \[\rightarrow\] hydropic or apoplectic leiomyoma

• worrisome gross and microscopic features \[\rightarrow\] leiomyosarcoma
Undifferentiated uterine sarcoma

• Fascicular or patternless growth
• High-grade nuclear features; either uniform atypia (UUS-U) or pleomorphic (UUS-P)
• Prognosis dismal with mean survival < 2 years
Undifferentiated uterine sarcoma

CD10

p53
Rhabdomyosarcoma

• Embryonal and pleomorphic most frequent types
• MYOD1, myogenin, myoglobin, myosin, muscle specific actin, and desmin positive
• CD10 often positive; CD99 and WT1 may be positive
Rhabdomyosarcoma
Rhabdomyosarcoma
PEComa

• Family of tumors showing perivascular epithelioid cell (PEC) differentiation
• Associated with tuberous sclerosis complex (TSC)
• PEComa: Uterus one of most frequent locations; corpus > cervix
• PEComa: Aggressive behavior if tumor > 5 cm, infiltrative growth, hypercellularity, high-grade nuclei, mitoses > 1/50HPF, or necrosis
PEComa

[Image: Microscopic image of PEComa cells with arrows indicating specific areas]
PEComa
PEComa
PEComa

HMB-45

Melan-A
IST
DOCH
GANZ
EINFACH