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Mesenchymal Tumors of the Uterus

Smooth Muscle Tumors

Stain with: Desmin, SMA, Caldesmon

Leiomyoma

Benign smooth muscle tumor. Most common uterine tumor.
If tons, particularly at a young age, consider hereditary leiomyomatosis and renal cell carcinoma (HLRCC) syndrome.
    Classically these have staghorn vessels, eosinophilic nucleoli with halos, and rhabdoid inclusions.
    Show loss of fumarate hydratase
Still have metastatic potential—"Benign metastasizing leiomyoma"

Variants:
Cellular leiomyoma—significantly increased cellularity compared to normal myometrium
Leiomyoma with bizarre nuclei—bizarre nuclei (smudged, hyperchromatic, pleomorphic) in an otherwise normal leiomyoma (no mitoses or tumor necrosis)
Mitotically active leiomyoma—increased mitoses, but no atypia or tumor necrosis

Smooth Muscle Tumor of Uncertain Malignant Potential ("STUMP")

Smooth muscle tumor whose features preclude a definitive diagnosis of leiomyoma vs. leiomyosarcoma
(Either equivocal mitoses or necrosis often; Many IMT's were previously mistakenly Dx'd as this!)
Relatively low risk of recurrence

Leiomyosarcoma

Malignant smooth muscle tumor. Typically spindle cell, but can be epithelioid.
Want to see: 1) High-grade cytologic atypia, 2) Increased mitoses (typically >2/10 HPF), and 3) Tumor-type necrosis
Genetically complex chromosomal aberrations
Very poor prognosis

Endometrial Stromal Tumors

Low-grade/benign tumors stain like normal endometrial stroma with CD10 and ER/PR; High-grade stains with Cyclin-D1

Endometrial Stromal Nodule

Benign tumor resembling proliferative endometrial stroma with a relatively well-circumscribed margin

Low-grade Endometrial Stromal Sarcoma

Malignant tumor composed of cells resembling proliferative endometrial stroma with infiltrative growth into myometrium and/or lymphovascular invasion—Often have "tongue-like" growth
Fusion of JAZF1 and SUZ12 *(think "Jazzy Suzie")*
Intermediate prognosis, mostly depending on stage

High-grade Endometrial Stromal Sarcoma

Malignant tumor derived from endometrial stromal cells with high-grade round cell morphology. Frequently myxoid.
Typically confluent, permeative, destructive growth. Usually high mitotic activity, necrosis, and LVI.
Fusions: YWHAE-associated or BCOR-associated

Other Tumors

Undifferentiated Uterine Sarcoma

Malignant tumor arising in the endomyometrium with high-grade cytologic atypia and no specific line of differentiation.
Destructive invasion. Marked cytologic atypia and brisk mitotic activity. Diagnosis of exclusion.
IHC: Variable CD10, Often Cyclin-D1 (+). May see focal SMA.
Complex genetically
Most patients present at high stage. Poor prognosis.

Uterine Tumor Resembling Ovarian Sex Cord Tumor ("UTROSCT")

Neoplasms resembling ovarian sex cord tumors without endometrial stromal component
Usually well-circumscribed.
IHC: Frequently WT-1 positive, variable expression of Inhibin, calretinin, and Melan-A
Recurrent *NCOA* translocations
Benign course typically.

Rhabdomyosarcoma

Malignant tumor showing skeletal muscle differentiation (like rhabdomyosarcomas elsewhere)
IHC: (+) desmin, myogenin, MyoD1

Perivascular Epithelioid Cell Tumor (PEComa)

Mesenchymal tumor containing epithelioid cells with clear to eosinophilic, granular cytoplasm demonstrating melanocytic and smooth muscle differentiation, thought to be derived from so-called "Perivascular Epithelioid Cells."
Mixture of spindled and epithelioid cells, many with granular cytoplasm.
IHC: (+) HMB45, Melan-A, and Cathepsin K; Variable smooth muscle markers
Some have TFE3 fusions→ clear nested epithelioid morphology
Features to evaluate malignancy: 1)≥5cm, 2)High-grad atypia, 3)>1 mitoses/50HPF, 4)Necrosis, 5)LVI
<3→ Benign/Uncertain malignant potential
≥3→Malignant

Inflammatory Myofibroblastic Tumor (IMT)

Spindled to polygonal cells growing in fascicles. Often have myxoid stroma.
IHC: ALK1 positive; variable smooth muscle markers
ALK molecular rearrangements.
Features that predict aggressive behavior: Size >7cm, Necrosis, Moderate to severe cytologic atypia, Mitoses, LVI.

NTRK-Rearranged Cervical Spindle Cell Neoplasm

Spindled cells with variable architecture, brisk mitotic activity, and often prominent lymphocytic infiltrate.
IHC: (+)CD34, S100

Tumors with a Glandular Component

Carcinosarcoma

Biphasic tumor with malignant carcinomatous and sarcomatous elements.
Usually old women with a mass prolapsing out of the cervix
Carcinoma: Often serous, sometimes endometrioid
Sarcoma: Often high-grade non-specific sarcoma, but can make heterologous elements (osteosarcoma, chondrosarcoma, rhabdosarcoma, etc…)
Often advanced stage and poor prognosis

Adenosarcoma

Mixed epithelial and mesenchymal tumor with a benign epithelial component and stroma is low-grade malignant.
(Think phyllodes tumor)
Papillary/polypoid projections of cellular stroma (often with condensation, "cuffing" around glands).
Can show heterologous elements and sarcomatous overgrowth.

MDM2/CDK4 and TERT gene amplifications.

Misc.

Adenomatoid tumor

Benign tumor of mesothelial origin.
Inter-anastomosing pseudo glands with variably sized tubules (sometimes with a signet ring appearance) with associated smooth muscle hypertrophy (so can be mistaken for a mesenchymal tumor!)
IHC: Tumor cells express CK AE1/AE3 and Mesothelial markers (D2-40, WT-1, Calretinin)