Diagnostic problems in uterine smooth muscle tumors

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Leiomyosarcoma (LMS) – rare, 1/800 specimens clinically thought to be LM

- **Solitary, poorly circumscribed mass, large** (averaging 10 cm)
- If the uterus contains several tumour nodules, **LMS is usually the largest one**
- The cut surface is typically fleshy, cream or tan, with obvious areas of haemorrhage or necrosis
LMS – diagnostic criteria

1. ATYPIA
2. NECROSIS
3. MITOSES

In the **classic (spindle cell)** LMS, the malignancy is diagnosed when any 2 of the criteria are established.
At low magnification - ATYPIA must be obvious (diffuse)
At low magnification - NECROSIS – “geographic”

- coagulative necrosis of the tumour tissue that has outgrown its blood supply
- NOT A SPECIAL TYPE OF NECROSIS
- THE CONSTELATION OF FINDINGS
Leiomyosarcoma (LMS) - “TUMOUR CELL NECROSIS”

1. Abrupt transition from necrosis to non-necrotic tissue
2. Pleomorphic & hyperchromatic nuclei - frequently seen in necrotic areas
3. Perivascular preservation of viable tumour cells
TUMOUR CELL NECROSIS

GEOGRAPHIC NECROSIS
Viable cells around blood vessels

ABRUPT TRANSITION

HYALINE NECROSIS

MORE REGULAR OUTLINES
Blood vessels also necrotic

INFLAMMATION
Granulation tissue - fibrosis
“tumour cell necrosis” vs. “hyaline necrosis”
MITOSES
10 or more/10 HPFs
MITOSES

• **Misinterpretation**
  - apoptotic cells
  - pyknotic nuclei
  - lymphocytes, mast cells
  - precipitated haematoxylin or cellular debris

• **Strict mitotic count**
  - absence of nuclear membrane with discernible cytoplasm
  - presence of hairy extensions of chromatin extending from a central clotlike mass of chromosomes (single clot in metaphase or separate in telophase)
In the classic (spindle cell) LMS, the diagnosis of malignancy is established when

1. NUCLEAR ATYPIA diffuse, moderate to severe 
   AND 
2. THE MITOTIC COUNT ≥10/10 HPF

1. NUCLEAR ATYPIA diffuse or multifocal, diffuse, moderate to severe 
   AND 
2. TUMOR CELL NECROSIS 
   AND 
3. THE MITOTIC COUNT ≥10/10 HPF

UNCOMMONLY

1. NUCLEAR ATYPIA minimal or absent 
   AND 
2. TUMOR CELL NECROSIS 
   AND 
3. THE MITOTIC COUNT ≥10/10HPF
+ infiltrative margin
Ancillary methods - IHC

- LMS
  - p53: STRONG DIFFUSE POSITIVITY at least > 30%
  - Ki-67: >30% - indicative of LMS
- p16: STRONG DIFFUSE POSITIVITY
- ER, PR
Rare & very rare LMS variants – Myxoid LMS

- **Myxoid LMS**
- Grossly – gelatinous
- Micro - cells spindle or stellate, abundant ECM (Alcian blue positive)

**MARKED CYTOLOGIC ATYPIA AND/OR TUMOR CELL NECROSIS AND ANY MITOTIC COUNT**

- **NO ATYPIA**
  - **NO TUMOR CELL NECROSIS AND MITOSES: > 2/10 HPF**

 ANY OF THE FOLLOWING:

- DESTRUCTIVE INFILTRATION OF THE SURROUNDING MYOMETRIUM


**Burch DM, Tavassoli FA.** Myxoid leiomyosarcoma of the uterus Histopathology 2011;59:1144–55
Rare & very rare LMS variants – Epithelioid LMS

• More than 50% of cells have to have epithelioid appearance

CRITERIA PREDICTIVE OF MALIGNANCY ARE LESS WELL ESTABLISHED

ATYPIA
diffuse, moderate to severe
AND
TUMOR CELL NECROSIS
AND
MITOSES: ≥ 5/10 HPF

Tavassoli FA, Devilee P. Pathology and Genetics of Tumors of the Breast and Female Genital Organs, WHO Classification of Tumors. Lyon: WHO; 2003.
STUMP (Smooth Muscle Tumor of Uncertain Malignant Potential)

- Definition - WHO
- A smooth muscle tumour that cannot be diagnosed reliably as benign or malignant on the basis of generally applied criteria
- Uncertainty about the type of necrosis
- The mitotic rate is elevated but not to the level diagnostic of LMS
- Uncertainty about the histologic variant (epithelioid or myxoid)
Most follow benign clinical course recurrence? p16 & p53 positivity

Some LM variants grossly display changed colour and/or consistency, evoking suspicion of necrosis, hemorrhagic/apoplectic degeneration in pregnancy, postpartum, or with OC. In these cases, extensive sampling, especially of unusual areas of the tumour, is MANDATORY.
Cellular (highly cellular) LM

dd/EST

- thick walled arteries
- cleft-like spaces
- desmin
- CD 10

up to 4 mitoses/10 HPF
Mitotically active LM

- Typical or cellular LM (usually < 10 cm) showing an increased mitotic activity
- **4 - 20 mitoses/10 HPF** (commonly between 5 and 9)
- Usually associated with:
  - the secretory phase of the cycle
  - pregnancy
  - the use of exogenous hormones
  - 60% - submucosal localisation
    - superficial ulceration - possible reparative nuclear atypia, mitoses, necrosis (not TCN)
**LM with bizarre nuclei (symplastic, atypical, bizarre LM)**

- Atypia—usually patchy/multifocal
- Nuclear pseudoinclusions, pyknosis

Usually up to 2 mitoses/10 HPF (in the absence of TCN - 7/10 HPF)
Hydropic LM - NOT myxoid LM

- Accumulation of oedema fluid
- The smooth muscle component is reduced to thin cords
- Formation of pseudocystic spaces

dd/ Myxoid LM - myxoid areas stain basophilic with Alcian blue
LM variants - rare

- vascular (angiomatoid) LM
- lipoleiomyoma
- epithelioid LM (plexiform tumorlet)
- up to 1MF/10 HPF
Uterine artery embolisation
(polyvinyl alcohol)
• Most smooth muscle tumors of the uterus are LEIOMYOMAS
• Gross appearance is important (if unusual - extensive sampling)
• Features to be assessed:
  • ATYPIA AT LOW MAGNIFICATION
  • GEOGRAPHIC (TC) NECROSIS
  • NUMBER OF MITOSES (≥10/10HPF)
• To diagnose a LMS - at least 2 features
Remember:

• IHC can SOMETIMES be helpful

• LM
  – ER, PR – positive
  – Ki-67(MIB-1) – low (< 30%)
  – p53 – absent or minimal (< 30%)
  – p16 - negative

• Avoid the diagnosis of STUMP
Remember:

- Insist on clinical informations
  - pregnancy
  - the phase of the menstrual cycle
  - any medication (exogenous hormones, OC, GnHR)

- In a curettage specimen or intraoperative (frozen section) analysis the definitive diagnosis of malignancy should be avoided
Greetings from Zagreb!