



ZAVOD ZA PATOLOGIJU
Sveučilište u Zagrebu
Medicinski fakultet

2ND PANNONIA
CONGRESS OF
PATHOLOGY
AND 80TH ANNIVERSARY OF THE
SOCIETY OF HUNGARIAN PATHOLOGISTS
Organized by the Pathology Societies
and IAP Divisions of
AUSTRIA · CROATIA · CZECH REPUBLIC
HUNGARY · SLOVAKIA · SLOVENIA
SIÓFOK, HUNGARY, 17-19 MAY 2012
SECOND ANNOUNCEMENT

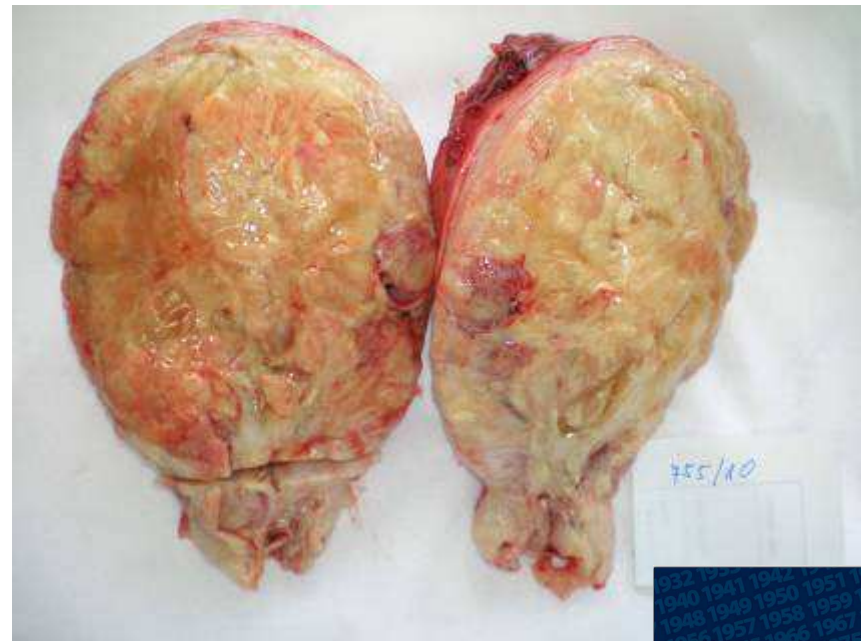
Diagnostic problems in uterine smooth muscle tumors

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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

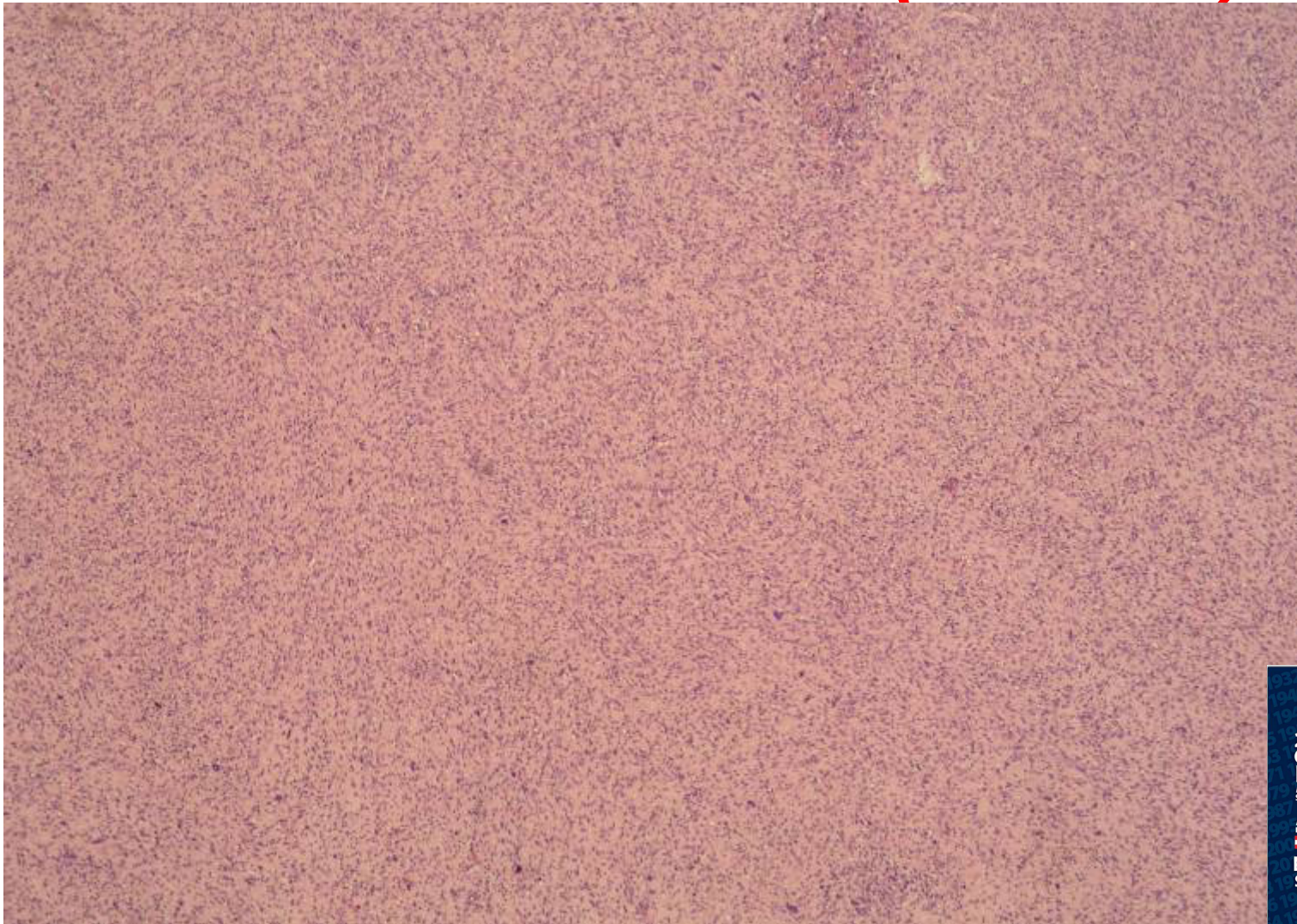
3. MITOSES

*In the **classic (spindle cell) LMS**, the malignancy is diagnosed when*

any 2 of the criteria are established



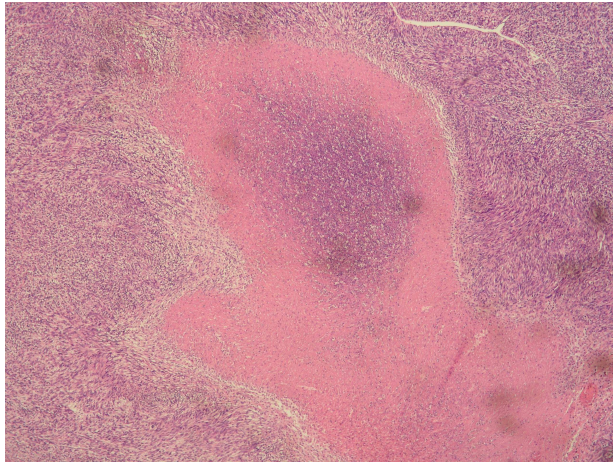
*At low magnification - ATYPIA
must be obvious (diffuse)*



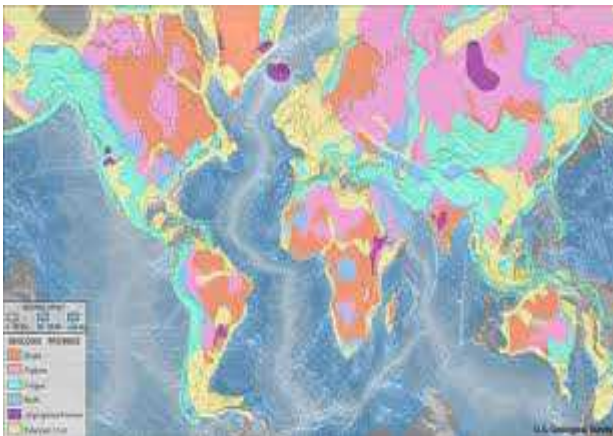
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At low magnification - NECROSIS – **“geographic”**

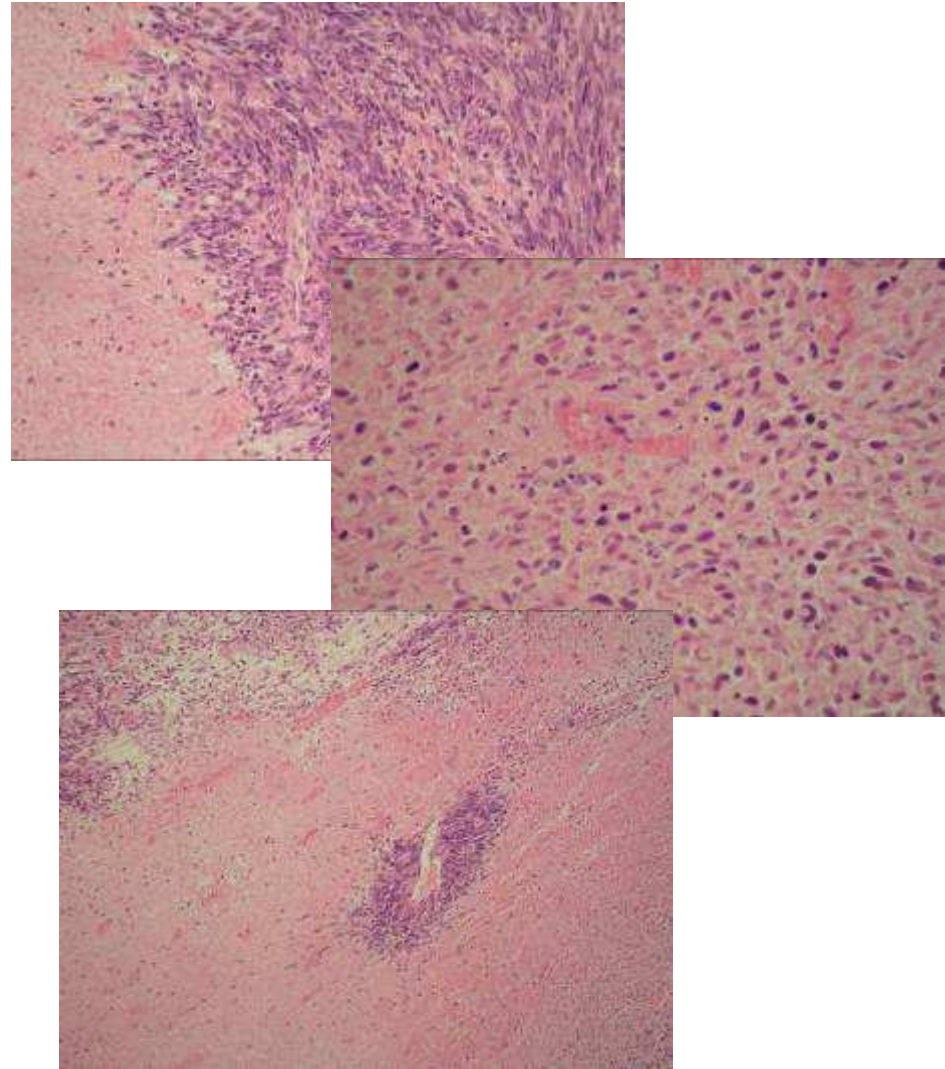


- coagulative necrosis of the tumour tissue that has outgrown its blood supply
- NOT A SPECIAL TYPE OF NECROSIS
- THE CONSTELATION OF FINDINGS



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

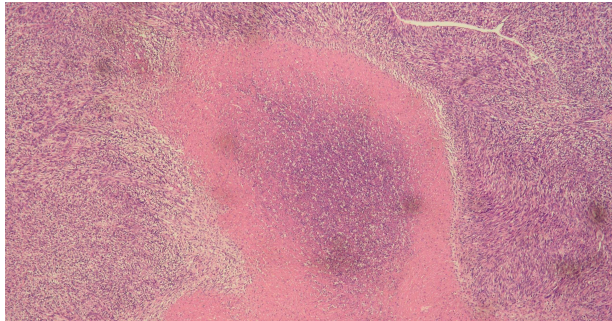


TUMOUR CELL NECROSIS

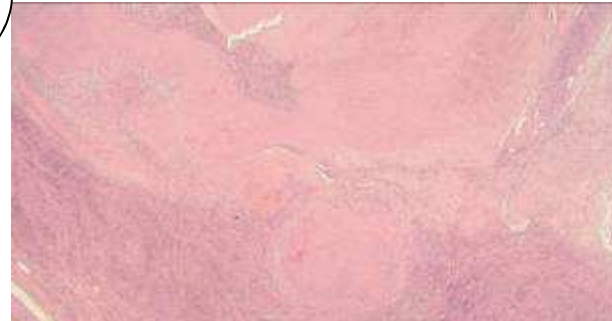
HYALINE NECROSIS

VS.

LMS

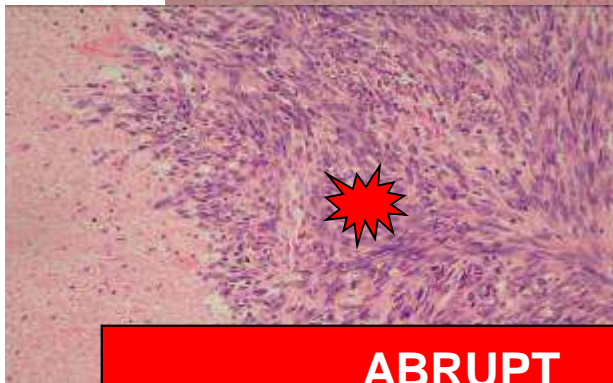
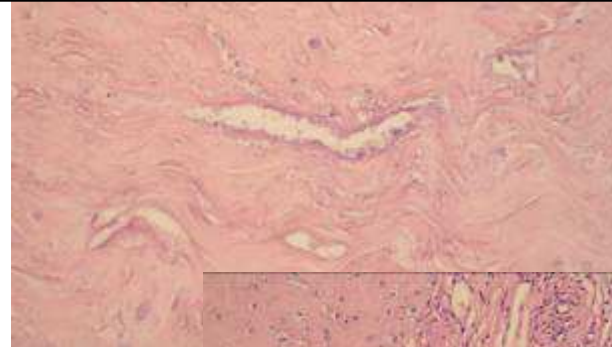
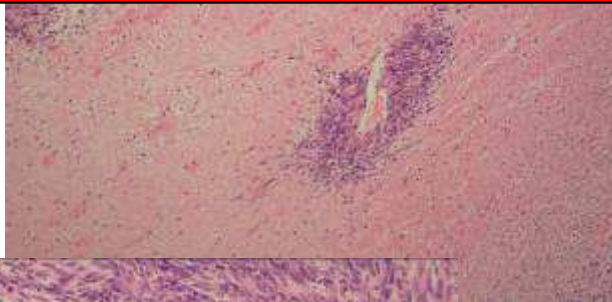


LM



**GEOGRAPHIC NECROSIS
VIABLE CELLS
AROUND BLOOD VESSELS**

**MORE REGULAR OUTLINES
BLOOD VESSELS ALSO NECROTIC**

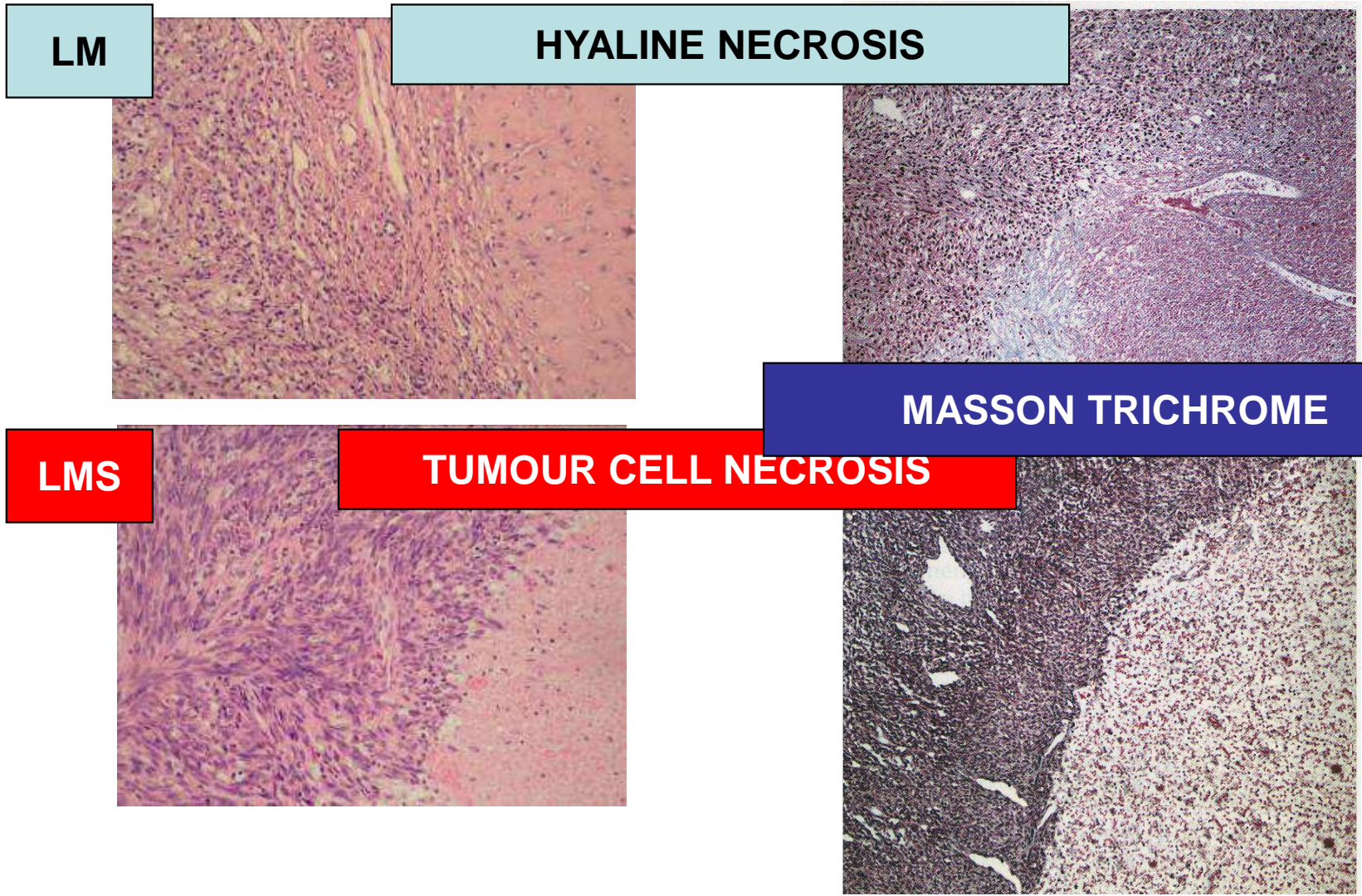


**ABRUPT
TRANSITION**



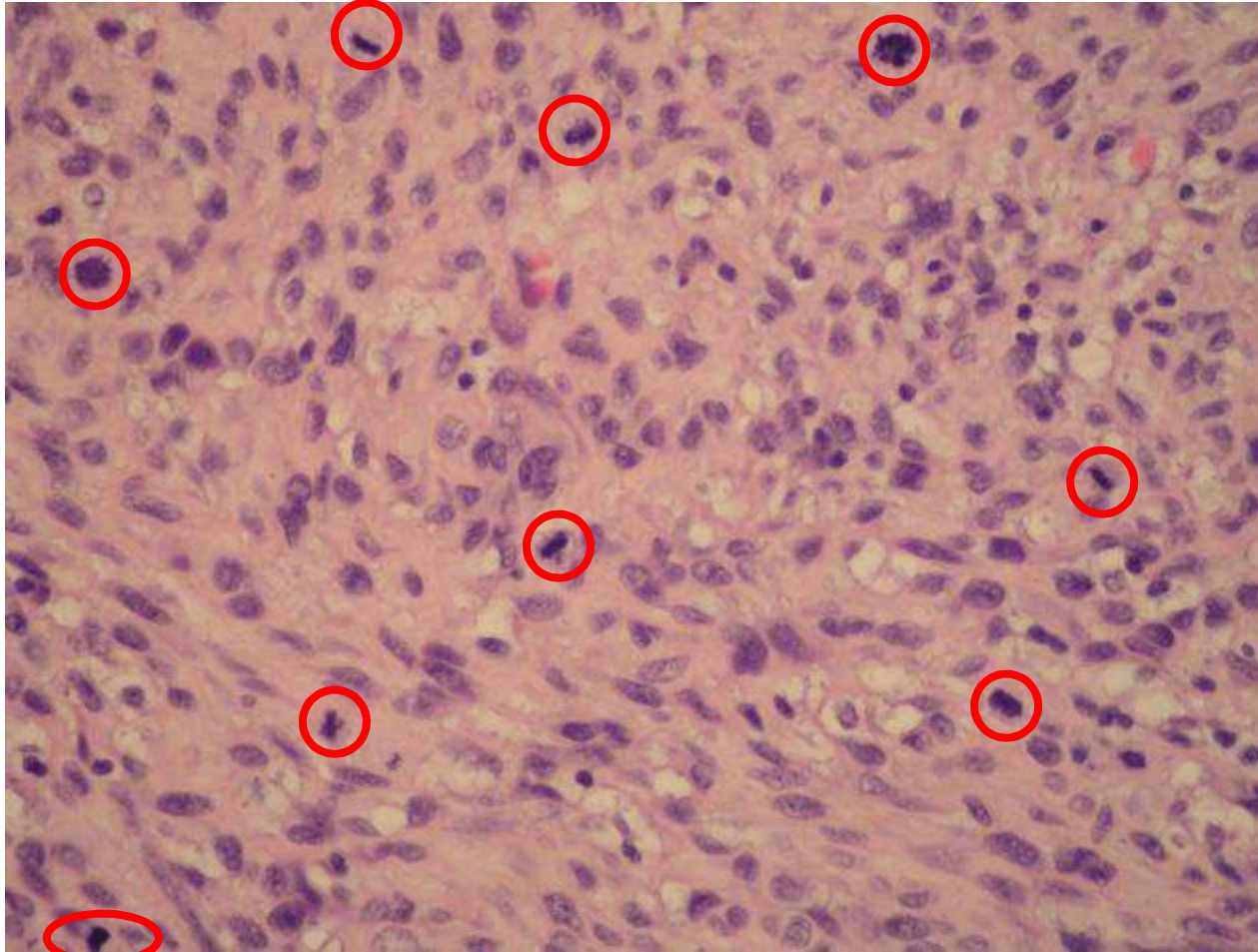
**INFLAMMATION
GRANULATION TISSUE - FIBROSIS**

“tumour cell necrosis” vs. “hyaline necrosis”



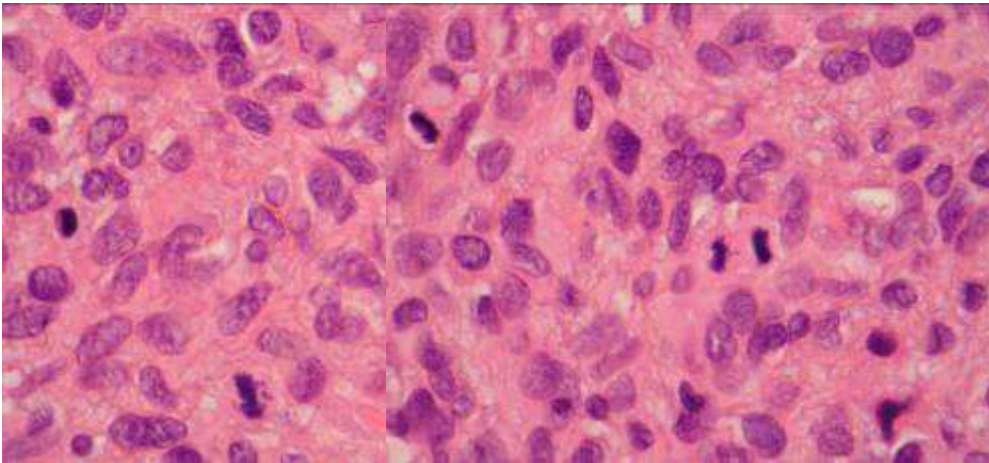
MITOSES

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

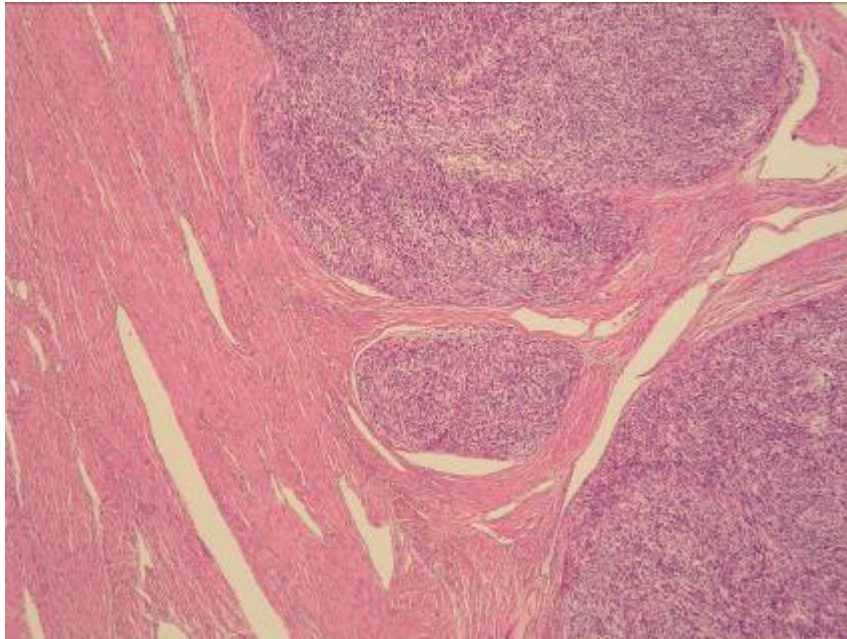
1. NUCLEAR ATYPIA
diffuse, moderate to severe
AND
2. THE MITOTIC COUNT
≥10/10 HPF

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

UNCOMMONLY

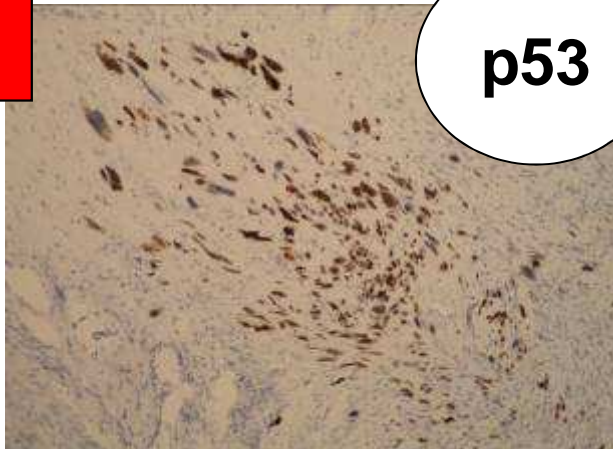
1. NUCLEAR ATYPIA
minimal or absent
AND
2. TUMOR CELL NECROSIS
AND
3. THE MITOTIC COUNT ≥10/10HPF

+ *infiltrative margin*



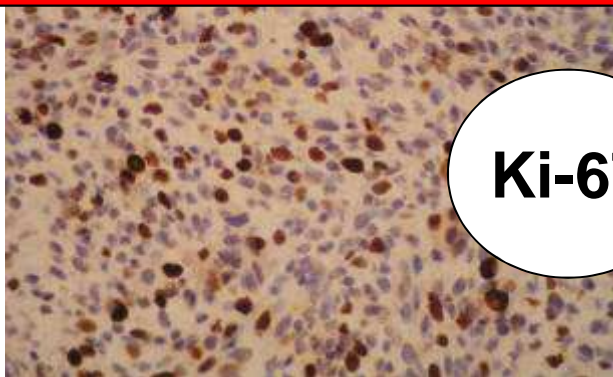
Ancillary methods - IHC

LMS



p53

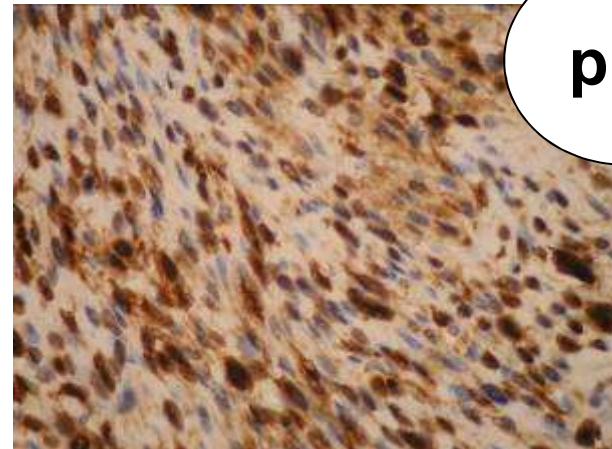
**STRONG DIFFUSE POSITIVITY
at least > 30%**



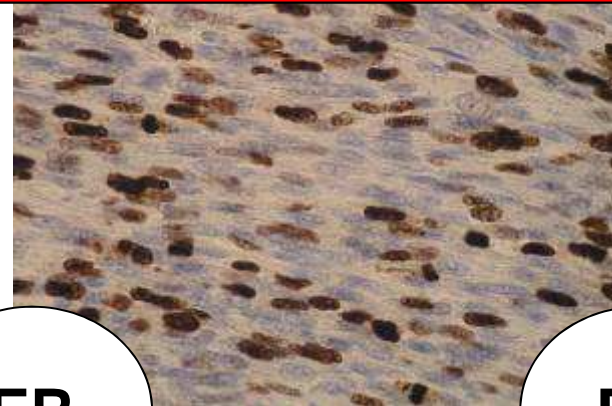
Ki-67

>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)

**ANY OF THE
FOLLOWING:**

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

**NO ATYPIA
NO TUMOR CELL NECROSIS
AND
MITOSES: \geq 2/10 HPF**

**DESTRUCTIVE
INFILTRATION OF THE
SURROUNDING MYOMETRIUM**

Toledo G, Oliva E. Smooth muscle tumors of the uterus: a practical approach. Arch Pathol Lab Med 2008;132:595-605
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: \geq 5/10 HPF

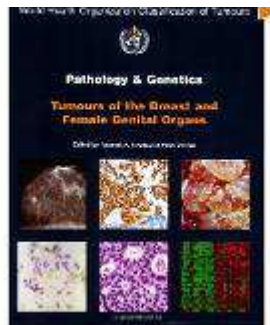
Atkins K, Bell S, Kempson R, et al. Epithelioid smooth muscle tumors of the uterus.

Mod Pathol 2001;14:132A

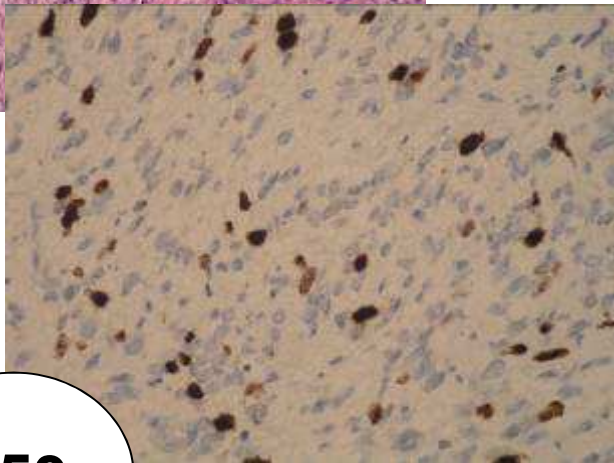
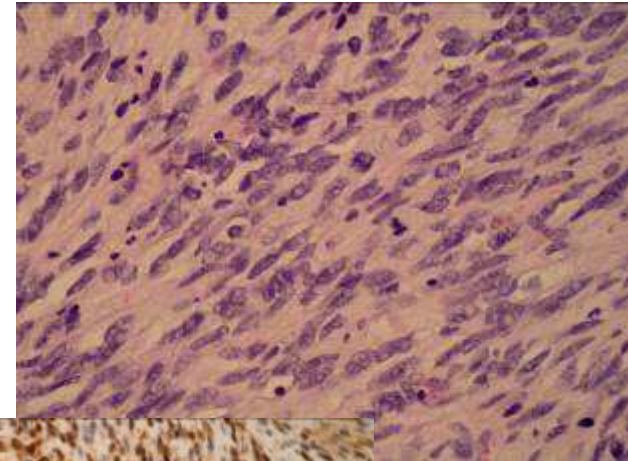
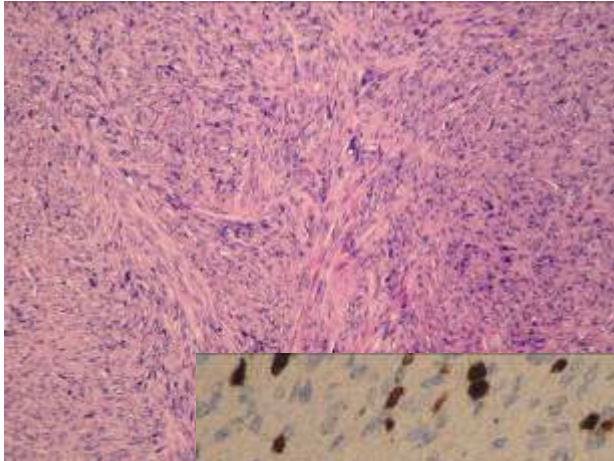
Tavassoli FA, Devilee P. Pathology and Genetics of Tumors of the Breast and Female Genital Organs, WHO Classification of Tumors. Lyon: WHO; 2003.

STUMP (Smooth Muscle Tumor of Uncertain Malignant Potential)

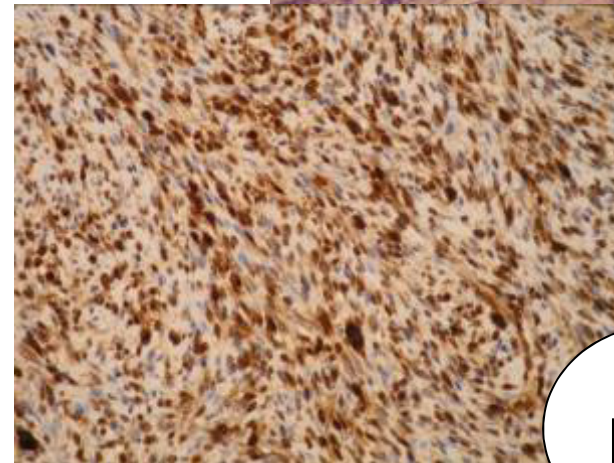
- Definition - WHO
- A smooth muscle tumour that cannot be diagnosed reliably as benign or malignant on the basis of generally applied criteria
- Uncertainty about the type of necrosis
- The mitotic rate is elevated but not to the level diagnostic of LMS
- Uncertainty about the histologic variant (epithelioid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



STUMP



p53



p16

**Most follow benign clinical course
recurrence? p16 & p53 positivity**

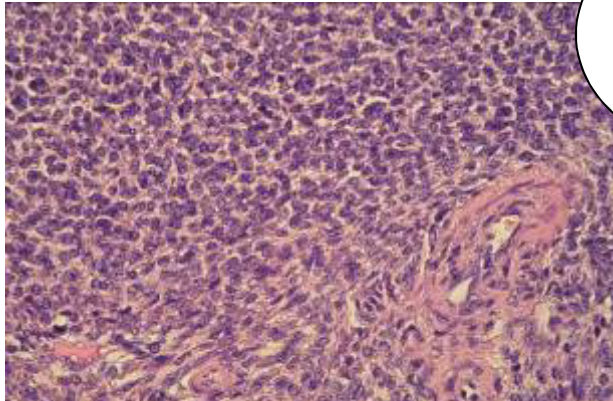
Ip P, Cheung A, Clement P. Uterine smooth muscle tumors of uncertain malignant potential (STUMP): a clinicopathologic analysis of 16 cases. Am J Surg Pathol 2009; 33: 992-1005

Some LM variants grossly display changed colour and/or consistency, evoking suspicion

**In these cases,
extensive sampling,
especially of
unusual areas of the tumour,
is MANDATORY**

Cellular (highly cellular) LM

dd/EST

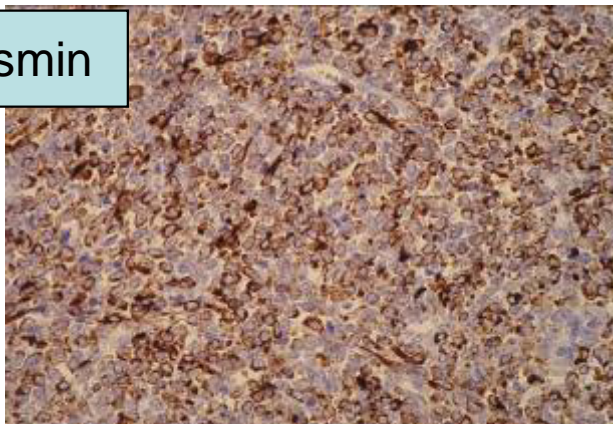


thick walled arteries

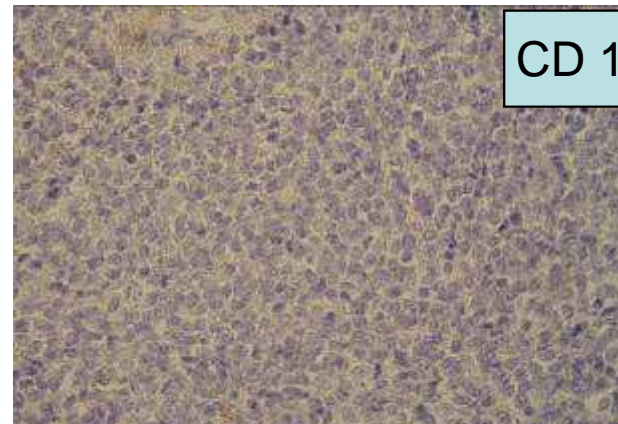


cleft-like spaces

desmin



CD 10



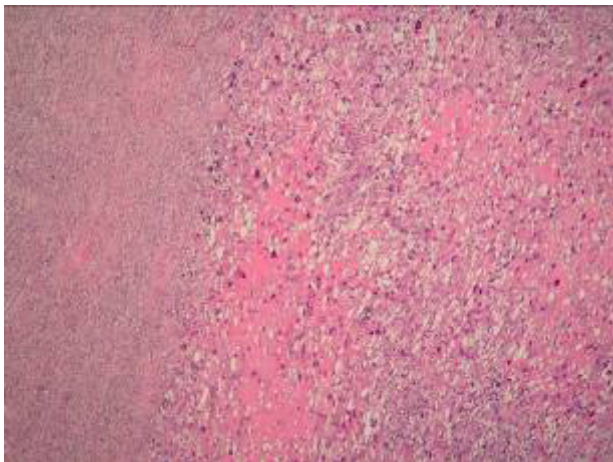
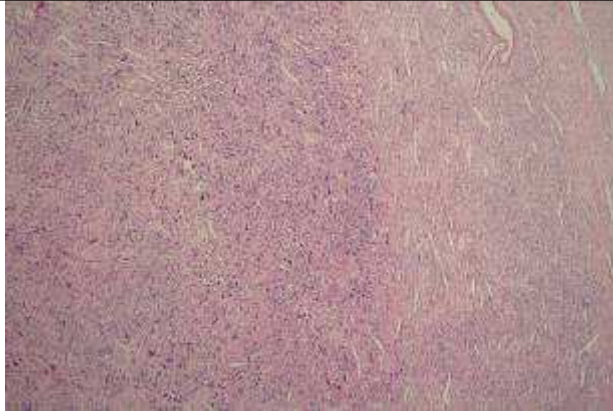
up to **4 mitoses/10 HPF**

Mitotically active LM

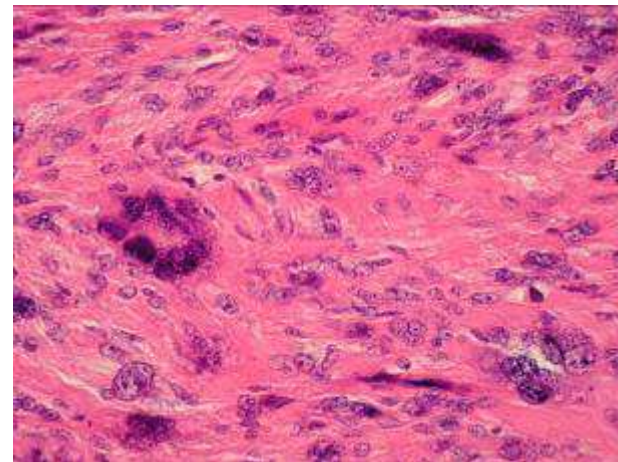
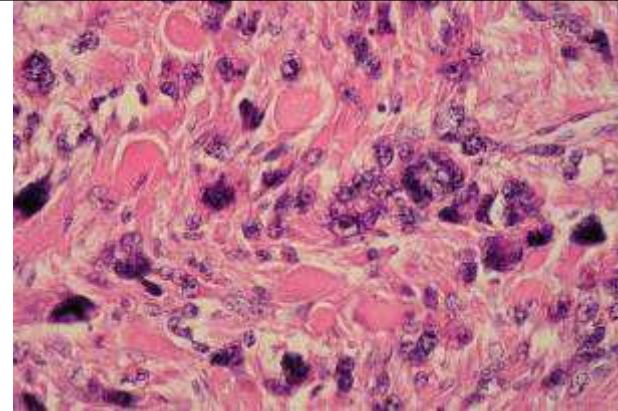
- Typical or cellular LM (usually < 10 cm) showing an increased mitotic activity
- **4 - 20 mitoses/10 HPF** (commonly between 5 and 9)
- Usually associated with:
 - **the secretory phase of the cycle**
 - **pregnancy**
 - **the use of exogenous hormones**
 - **60% - submucosal localisation**
 - superficial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

LM with bizarre nuclei (symplastic, atypical, bizarre LM)

atypia– usually patchy/multifocal



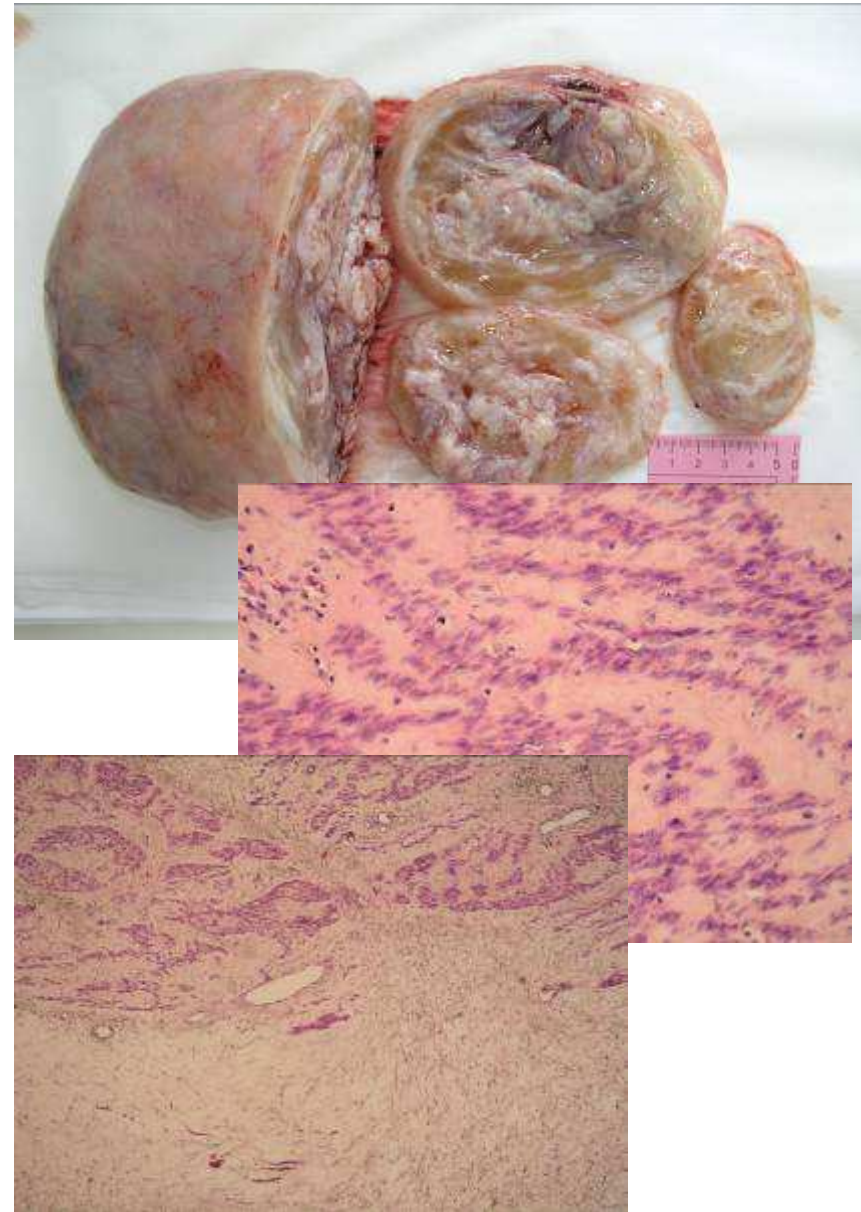
nuclear pseudoinclusions, pyknosis



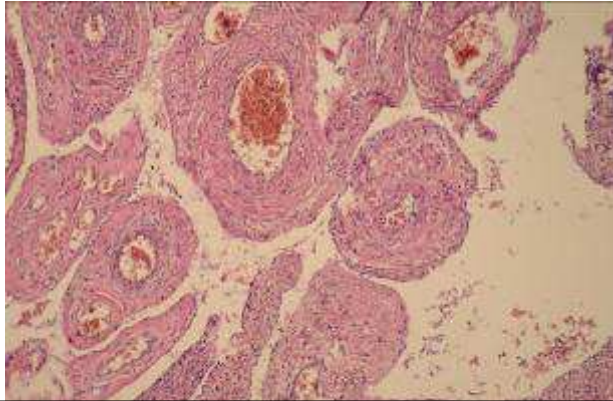
usually **up to 2 mitoses/10 HPF** (in the absence of TCN - 7/10 HPF)

*Hydropic LM - **NOT** myxoid LM*

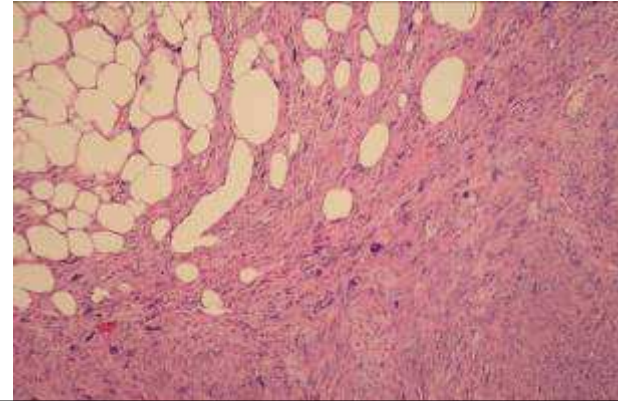
- Accumulation of oedema fluid
- The smooth muscle component is reduced to thin cords
- Formation of pseudocystic spaces
- **dd/ Myxoid LM** - myxoid areas stain basophilic with Alcian blue



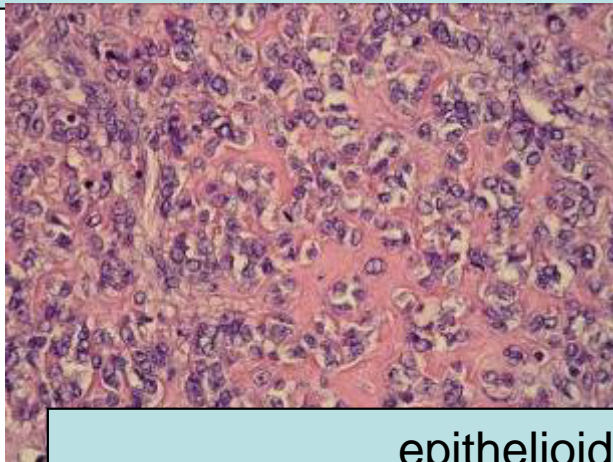
LM variants - rare



vascular (angiomatoid) LM



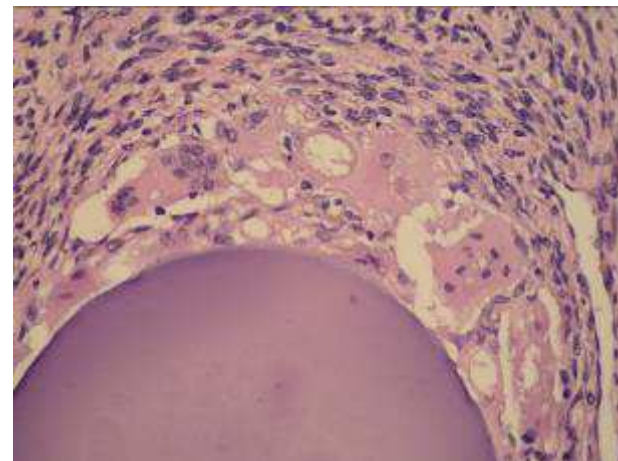
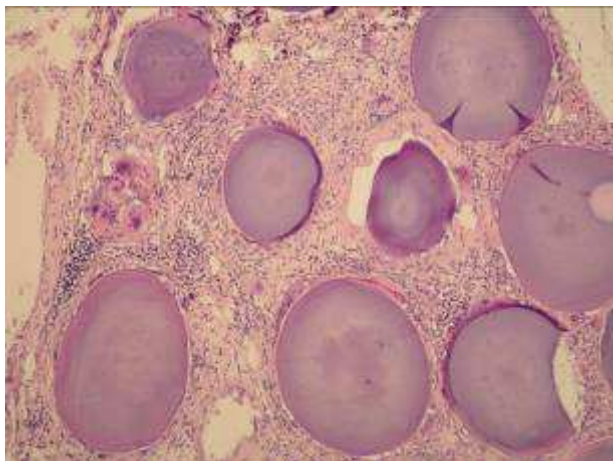
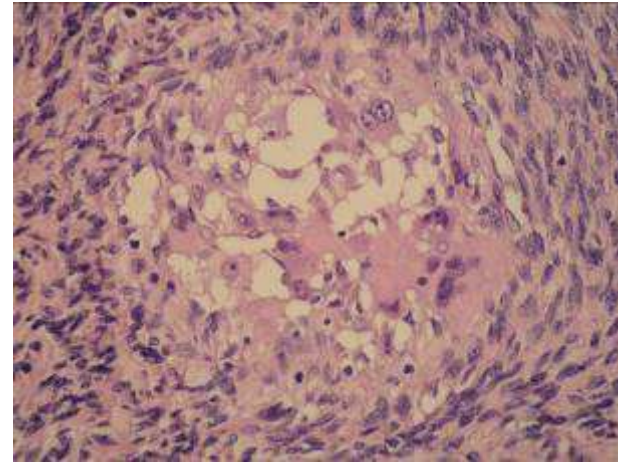
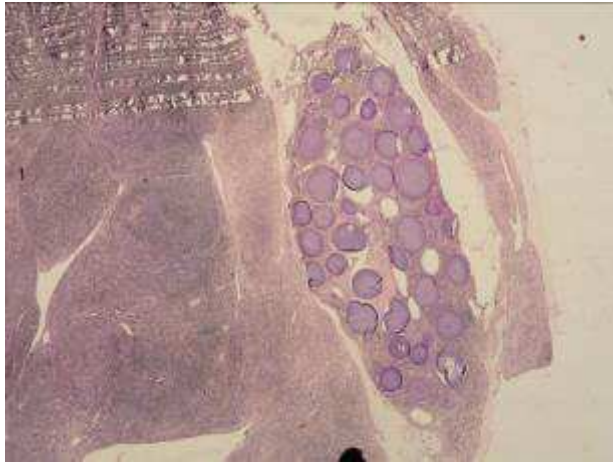
lipoleiomyoma



epithelioid LM (plexiform tumorlet)

up to 1MF/10 HPF

Uterine artery embolisation (polyvinyl alcohol)





Remember:

- 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 ($\geq 10/10$ HPF)**
- 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!