Recent Developments in Surgical Pathology of the Uterine Corpus

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DIAGNOSTIC CHALLENGES IN UTERINE SMOOTH MUSCLE TUMORS

Histology of USMT

- Distinguished by using conventional morphologic criteria (Stanford criteria):
- nuclear atypia, mitotic index, and presence of coagulative tumor cell necrosis.
- However, interpretation of these diagnostic criteria can be subjective or affected by hormonal status of the patient, delay in tissue fixation, or other nonhormonal treatments.

STUMP

- “smooth muscle tumor of uncertain malignant potential”
- has been established for those tumors that cannot be categorized confidently as benign or malignant owing histologic features

STUMP

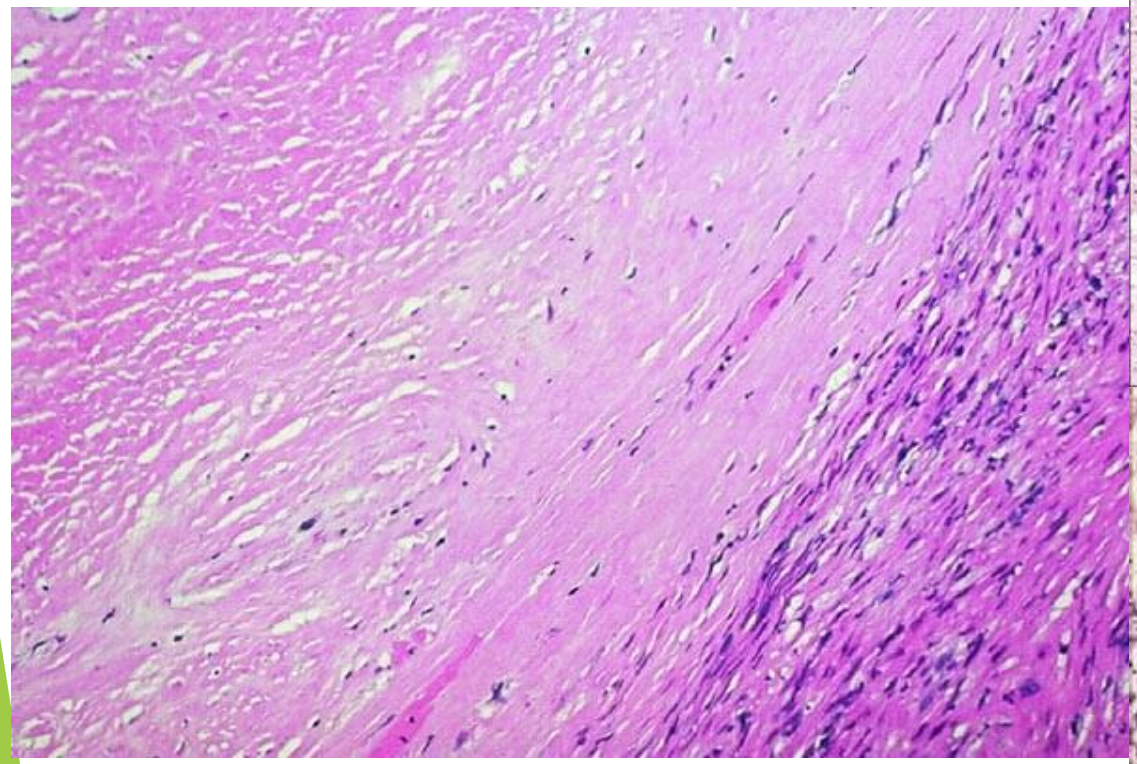
- The most accepted situations in which STUMP can be considered include
- (1) tumors indeterminate for coagulative necrosis,
- (2) tumors with significant atypia and mitotic index near the threshold for malignancy,
- (3) epithelioid and myxoid variants of USMT with mitotic activity or atypia intermediate between the benign and malignant counterparts,
- (4) tumors with histologic features worrisome for an epithelioid or myxoid variant of USMT

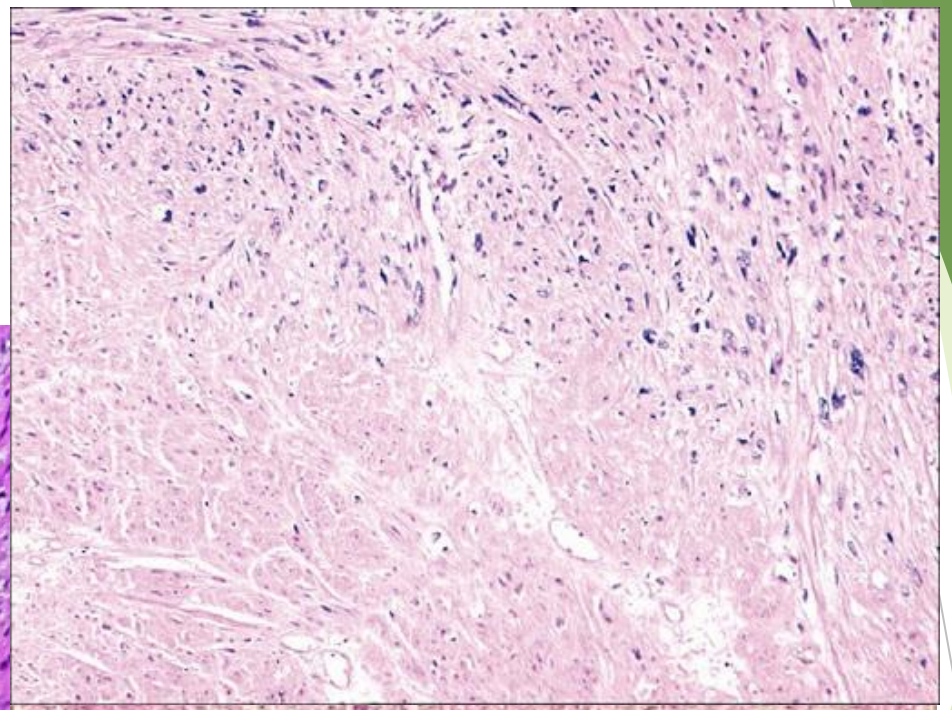
Coagulative (Tumor) Necrosis: Is It or Is It Not?

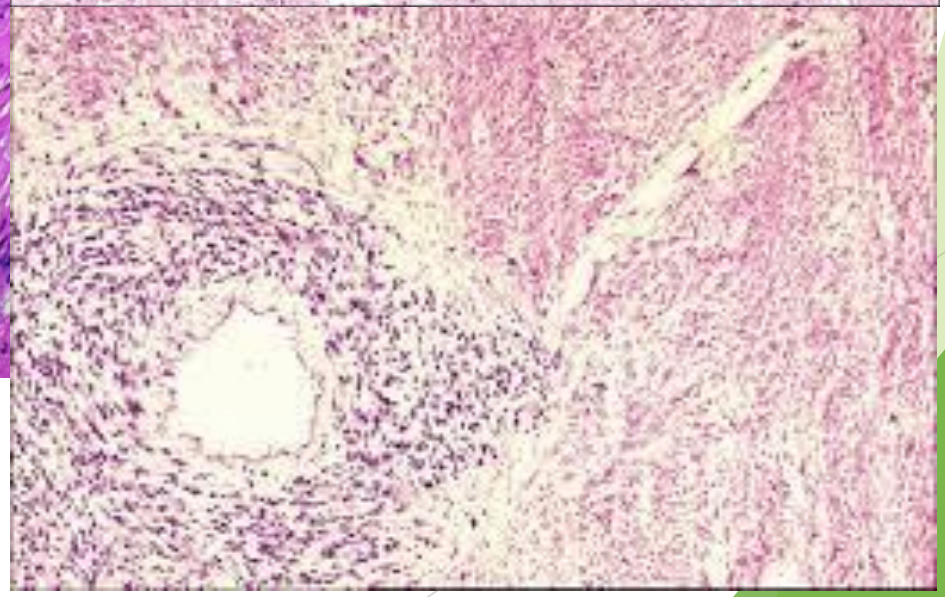
The characteristic histologic features of coagulative tumor cell necrosis include

- **abrupt transition** from viable to necrotic areas,
- **ghost outline of cytologically atypical tumor cells** in the necrotic foci,
- preservation of a rim of **viable tumor cells around vessels** within the necrotic areas

Coagulative (Tumor) Necrosis







GYN Pathologists agreement

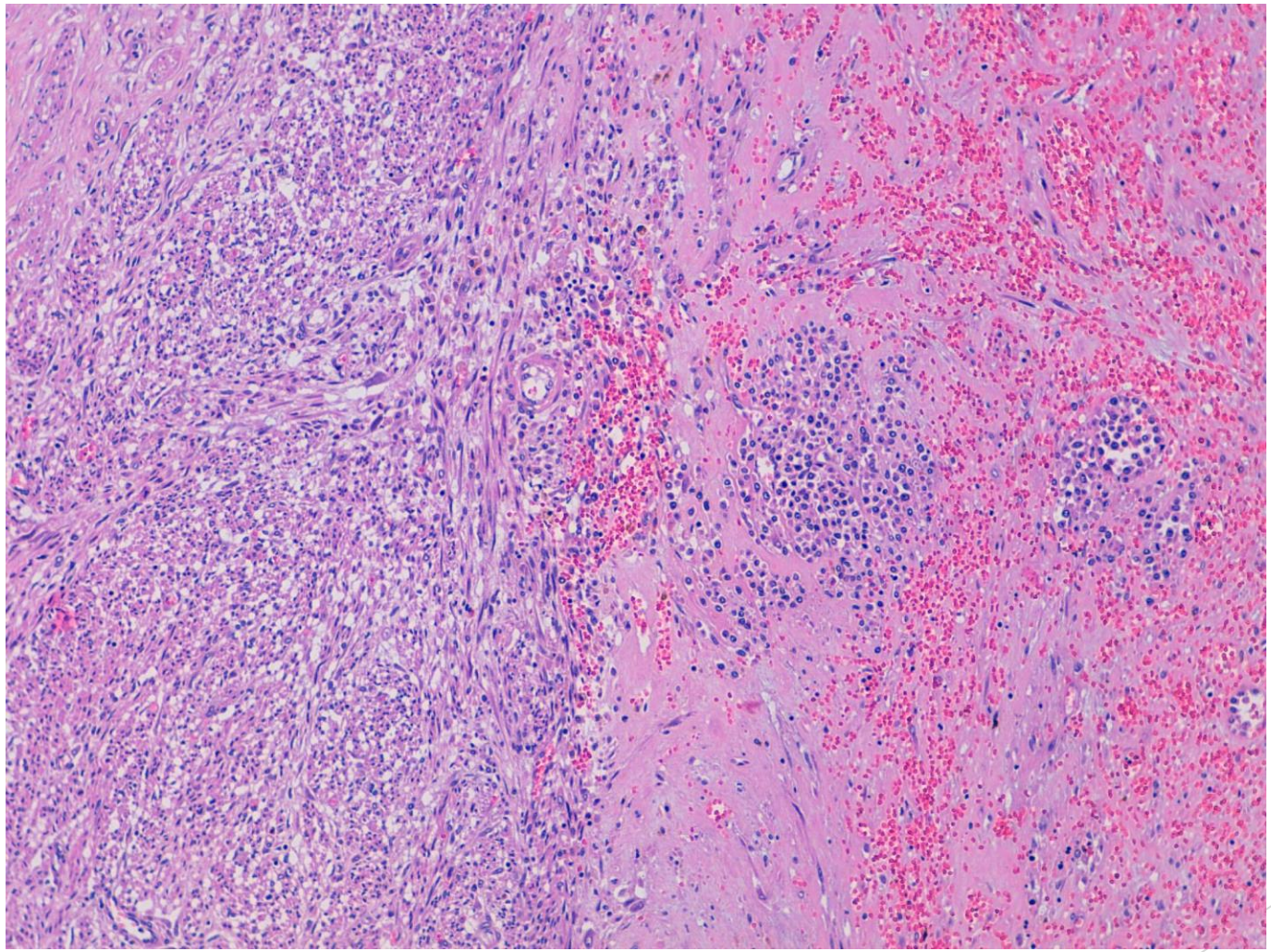
- Evaluated the interpretation of coagulative tumor cell necrosis in leiomyosarcoma by 6 experienced gynecologic pathologists. The agreement even among experienced subspecialized gynecologic pathologists was moderate ($\kappa = 0.436$) in determining the presence or absence of coagulative tumor cell necrosis. Thus, for the diagnosis of leiomyosarcoma, it is always important to take the mitotic index and cytologic atypia into account, especially when the type of necrosis is difficult to classify.

Hyaline or ischemic necrosis

- **Rim of granulation tissue, with inflammatory cells or hyalinization** at the interface of viable and necrotic areas.

- The distinction between these 2 types of necrosis can be challenging in **early stages**, when granulation tissue, inflammation, or fibrocollagenous tissue are not developed

Hyaline or ischemic necrosis



Counting Mitoses

- Average number of mitotic figures on high-power magnification **(×40 objective) in at least 10 fields**.
- If mitotic **"hot spots"** are identified, those areas should be included in the count. Of note, mitotic index will be higher near necrotic areas or in ulcerated areas of leiomyomas, there Atypical mitoses can be very helpful, as they reflect genomic instability and are a reliable indicator of the biologic potential of the tumor.
- recognized in metaphase and anaphase.
- R/O Mast cells

Utility of **Ancillary Studies** in Classifying Uterine Smooth Muscle Tumors

IHC

Expression of p16, p53, and MIB-1

- Demonstrated that p16 overexpression in leiomyosarcoma is strong and diffuse (>66% of tumor cells with nuclear and cytoplasmic positivity) and it can aid in further classification of USMTs with ambiguous necrosis
- MIB-1 index of 30% or more was only seen in leiomyosarcoma, but there was no difference in MIB-1 staining between leiomyoma, its variants, and STUMP.
- ER, PR

Stains

- A **trichrome stain** was used to highlight hyalinization and fibrosis, which were more common in nonviable areas of **leiomyoma.**

- A **reticulin stain**, on the other hand, was useful in identifying the retained **honeycomb reticulin network in the necrotic areas of leiomyosarcoma**, since it is usually lost in leiomyoma.

Therapy-Related Changes in Uterine Smooth Muscle Tumors and Potential Impact on Diagnosis

Hormonal therapy

- It is important for surgical pathologists to be aware of the histologic changes in leiomyoma associated with hormonal treatment because a history of medication usage is not always provided by the clinician.
- pregnancy,

During which they can often enlarge and may exhibit edema, bizarre cytologic atypia, infarction, hemorrhage, and hyalinization.

synthetic progesterone (progestin)

- Alter the histologic findings of leiomyoma, Similarly, oral contraceptives
- necrosis in leiomyomas.
- increased mitotic activity , mitotic count of up to 10 mitoses/10 HPFs,
- myxoid change
- stellate hemorrhage (apoplectic change), and “red degeneration.
- common finding early infarct-type necrosis, often multifocal without a reparative rim of granulation tissue (which could be mistaken for coagulative tumor cell necrosis).
- The most characteristic progestin-associated change is the appearance of myocytes with pyknotic nuclei and abundant deeply eosinophilic cytoplasm adjacent to the necrotic areas. This change can be confused with an epithelioid variant of USMTs.
  - These histologic findings may persist for months after cessation of hormonal treatment.

(GnRH) agonist

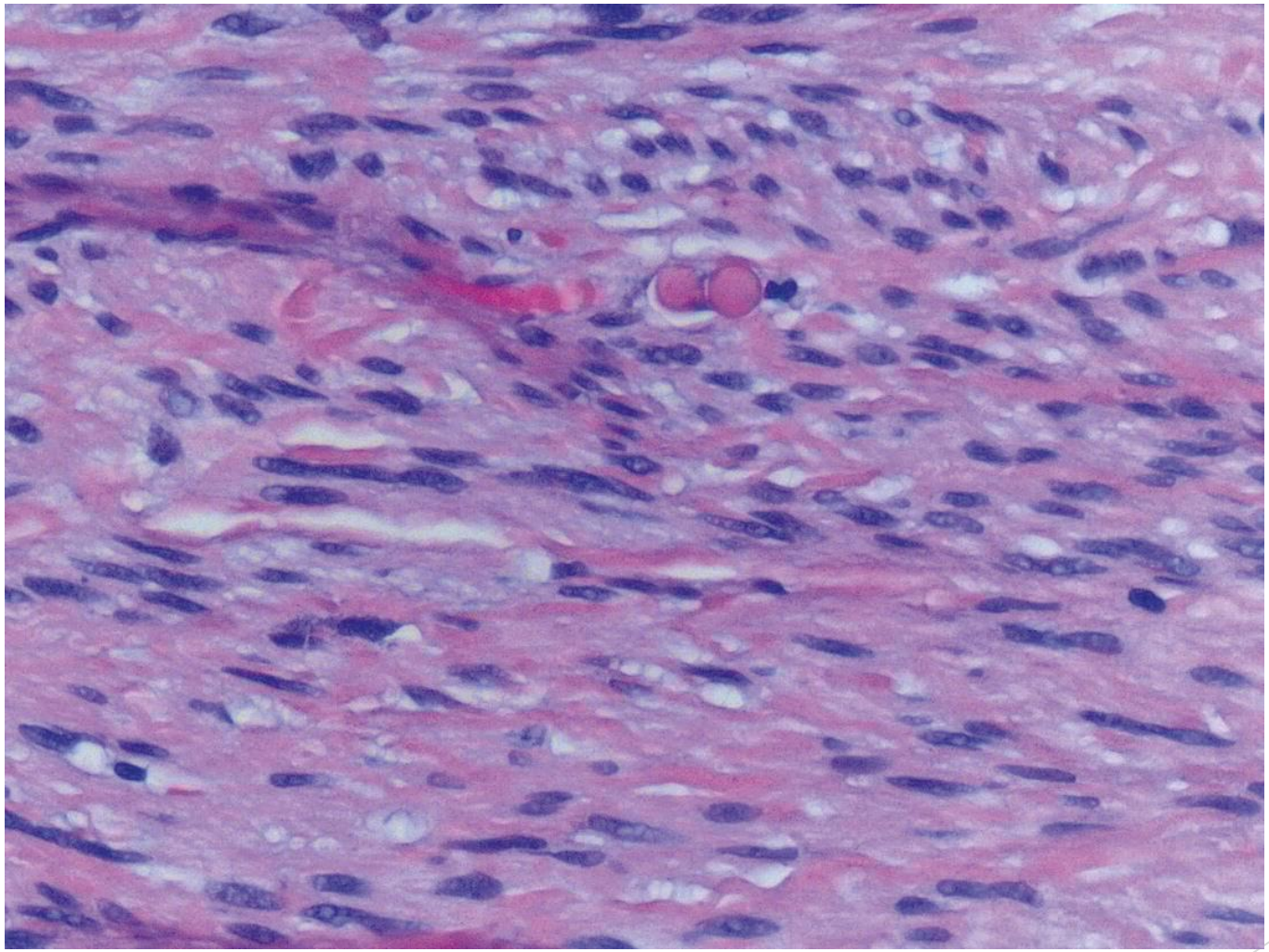
- Hypoestrogenic state
- Hypercellularity
- coagulative necrosis
- Hyaline necrosis
- lymphoid infiltrates
- vasculitis

Non Hormonal therapy

uterine artery embolization

- polyvinyl alcohol emboli in vessels
- foreign body–type giant cell reaction or thrombosis.
- **Early hyaline (ischemic)-type necrosis**, often associated with vacuolar change secondary to myocytolysis.
- It should be pointed out that if coagulative tumor cell necrosis is present in a leiomyoma post therapy, other histologic features of malignancy should be evaluated carefully.
- Other rare complications : necrotizing endomyometritis, myometritis, or cervical necrosis.

uterine artery embolization



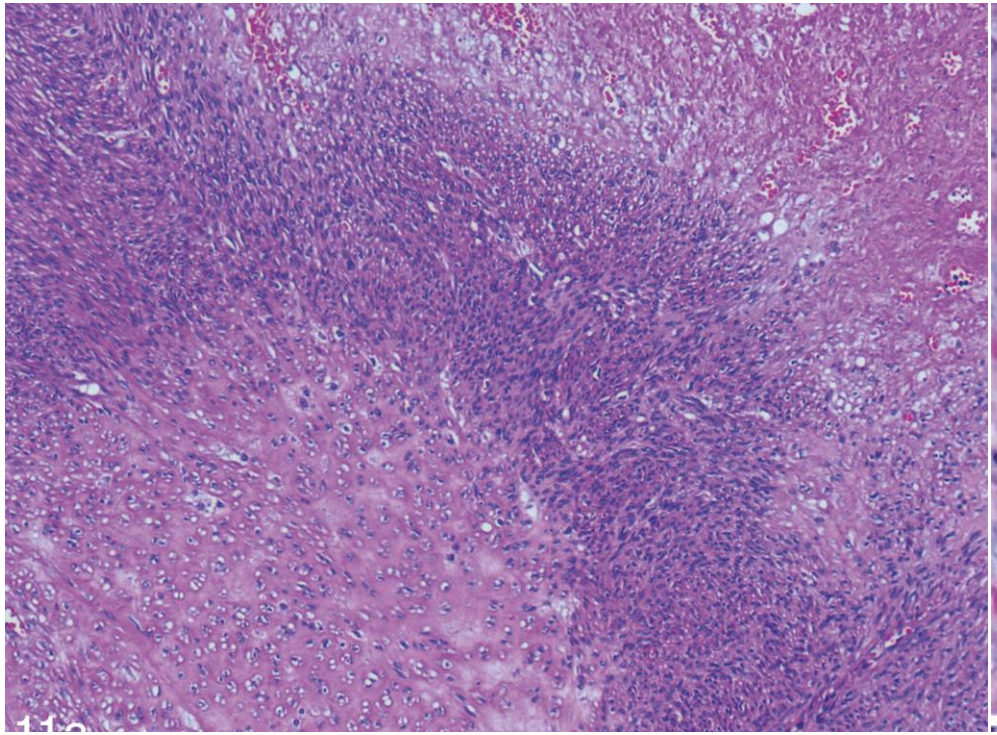
Tranexamic acid

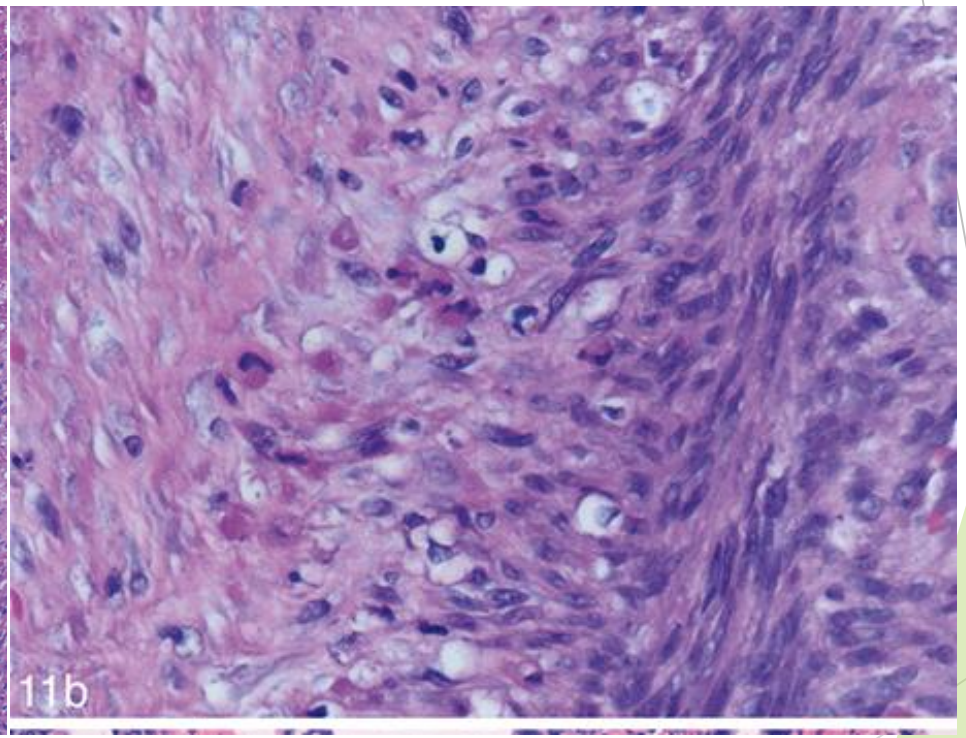
- Menorrhagia ,antifibrinolytic agent,
- Early infarct-type necrosis and thrombosis in leiomyoma were more common
- leading to the misdiagnosis of STUMP.

- **In the case of tranexamic acid**

(appearing after 7-11 days in their study)

Tranexamic acid





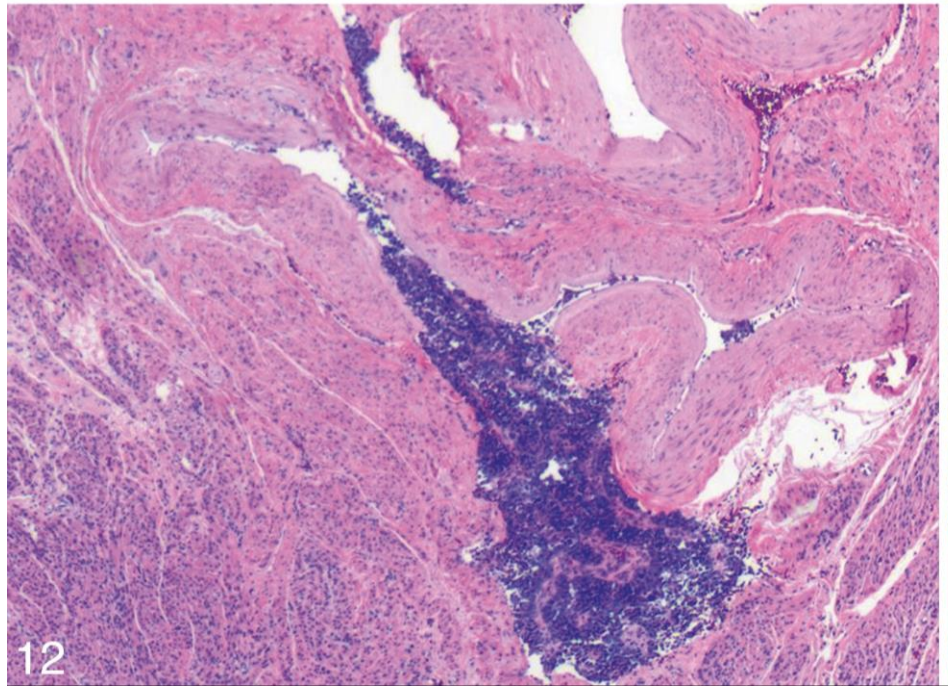
MINIMALLY INVASIVE HYSTERECTOMY PROCEDURES

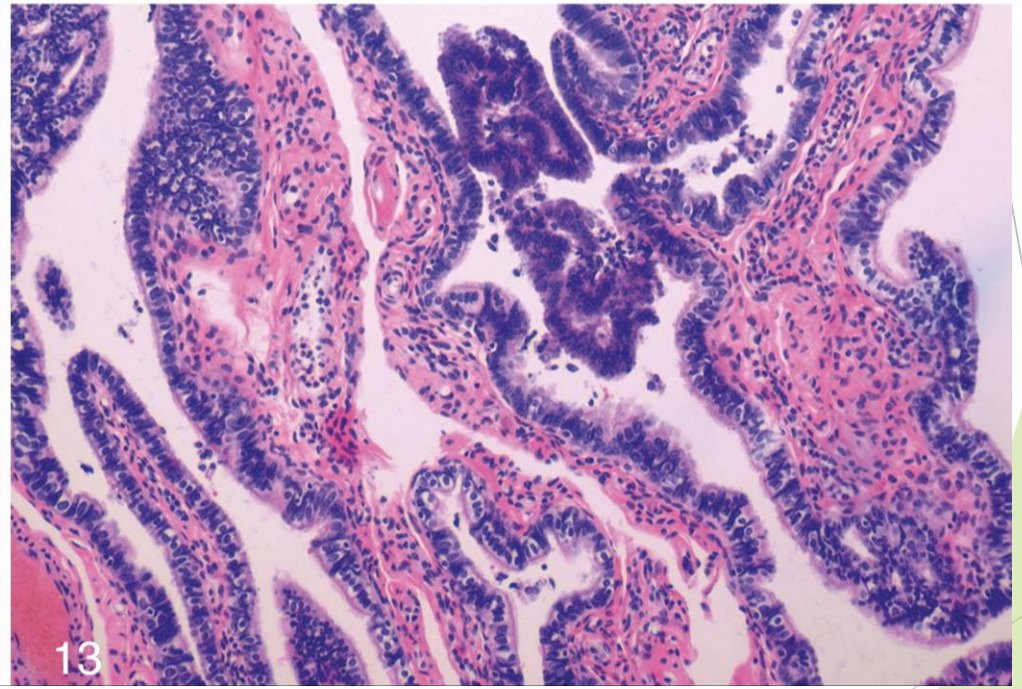
- total laparoscopic hysterectomy, laparoscopy-assisted vaginal hysterectomy, and robotic hysterectomies,
- During the procedure, the intrauterine balloon creates positive pressure inside the uterine cavity.
- various histologic artifacts due to “displacement” of tissue fragments, such as pushing epithelium into vascular channels and, in the setting of endometrial cancer.

laparoscopic hysterectomy

- Lymphovascular “Pseudo invasion”
- Positive Peritoneal Washing
- (tumor fragments found in nonvascular spaces within the myometrium), intratubal tumor Misinterpretate these myoinvasion or fallopian tube involvement can lead to overstaging and unnecessary adjuvant therapy.

laparoscopic hysterectomy





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Thank you