

INTERNATIONAL SOCIETY OF  
GYNECOLOGICAL PATHOLOGISTS  
PATHOLOGY OF THE UTERINE CORPUS,  
PART 2: MESENCHYMAL TUMORS –  
CURRENT STATE OF THE ART

# Mesenchymal Uterine Tumors

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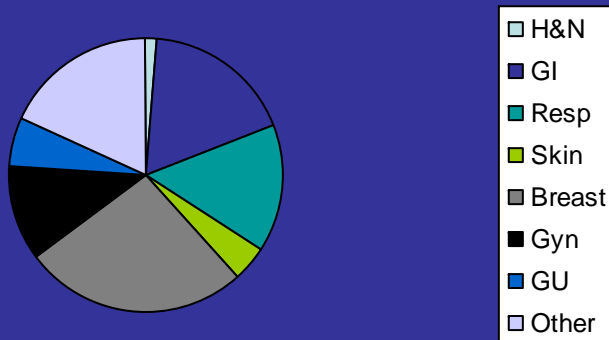
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# The charge!

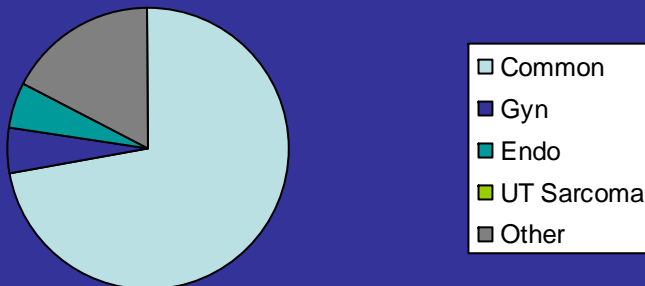
- What do you expect from the pathologists and what are the most common problems/limitations in your practice

# The rare of the rare...

**Distribution of New Cancers**



**Distribution of Uterine Cancers**



- Uncommon tumors arising from mesenchymal elements
- Most common: CS → LMS → ESS → AS
- Vs. Endometrial cancer → look, spread, and are Rx'd differently
- Heterogeneous group → separate out groups clinically

# Leiomyosarcoma

- Median age of diagnosis- 55 years
- Vaginal bleeding most common symptom (56%), followed by a palpable pelvic mass (54%), and pelvic pain (22%)
- Difficult to establish a pre-operative diagnosis
  - →pt/surgeon “surprised”, limited surgery more common
- Considerable complexity of histologic criteria necessary for the diagnosis of LMS, with a variety of smooth ms tumors from which LMS must be distinguished

# Clinico-path characteristics

- Clinico-path study of uterine sarcomas → TAH/BSO/ LND
- 530 pts enrolled → 59 uterine LMS
- Extra-uterine spread was infrequent
  - LN (+) 4%, Adnexa 3%, Cytology 5%
- Pathologic characteristics
  - 50% tumors 6-10 cm, LVSI (+) 34%
  - Mitoses/ 10 HPF: 15% (10-15), 20%(16-20), 60% (>20)

# Behavior

- Aggressive tumor- 5yr survival: 25-75%, risk recurrence 45-73%
- GOG series (N=59)
  - 3 yr PFS 31%
  - 1<sup>st</sup> site failure: lung 41%, pelvis 14%
  - mitotic rate independent predictor PFS
- Mayo series (N=208)
  - Median DSS =5 yrs- survival assoc lower stage, lower grade, < 51yr, tumor < 5 cm
  - ovarian preservation assoc with better survival

# Treatment

- No demonstrated value of any adjuvant therapy
  - Observation vs pelvic radiation vs chemotherapy
- Doxorubicin
- Docetaxel/Gemcitabine
  - GOG 131G- 1 prior → RR 27%, med OS 6+ mo
  - GOG 87L- no prior → RR 36%, med OS 16+ mo
  - Adjuvant use stage I-IV → stage I-II (N=18), 2 yr PFS 59%

# Where we struggle...

- With evolving data that the combination docetaxel/gemcitabine regimen may be (for the first time) a effective strategy:
  - are there characteristics of uterine LMS which speak to aggressiveness and poor prognosis (pathologic prognostic factors)
  - are there any pathologic factors that may be predictive of response to (any) therapies.

# Endometrial Stromal Sarcoma

- Symptoms- irregular vaginal bleeding. pelvic pain, palpable mass, asymptomatic uterine enlargement
  - Pre-operative diagnosis challenging
- Soft, fleshy, smooth, polypoid masses
- Local invasiveness, (+) LVSI
  - infiltrate and separate the muscle fibers of the uterus.
- Low grade tumors- disease confined to the uterus with Stage I-II disease ~ 70% of series.
  - Patients with HGESS had Stage I-II disease in 40-50% of cases.
- PR (+) common- progestins as adjuvant or for recurrence
- Observation vs pelvic XRT vs progestins

# Adenosarcoma

- Unusual tumor with low malignant potential
- Present with abnormal vaginal bleeding
- On gross evaluation → usually polypoid mass can fill the endometrial cavity.
  - Involvement of the cervix and myometrium less common-  
Myometrial invasion 15%- deeply invasive 4%
- Benign or atypical neoplastic glands with a sarcomatous stroma
- Recurrence in ~25% (mostly local), in one third appeared 5 years after diagnosis
- Sarcomatous overgrowth assoc with increased risk

# Where we struggle...

- **Endometrial Stromal Tumors:** Clinically we often think of these tumors as more indolent with favorable biologic behavior. What pathologic characteristics may describe tumors with poorer prognosis.
- **Adenosarcoma:** As these are such rare tumors, what is the differential diagnosis that should be considered in these tumors, and what are distinctive diagnostic criteria that need to be assessed. What are the relevant prognostic features that should be assessed.

# Carcinosarcoma

- Post-menopausal bleeding
- Prolapsing polypoid or intracavitary masses
- Masked by high grade epithelial components
- Extrauterine spread frequently → intraperitoneal, distant mets @ presentation

# Clinico-path characteristics

- GOG study uterine sarcoma N=301 (62%) pts CS
- Extra-uterine spread common
  - LN (+) 17%, Adnexa 12%, Cytology (+) 21%
- Pathologic Characteristics
  - Homologous/Heterologous (55%/45%)
  - LVSI 41%, DOI Outer ½ 36%,

# Behavior

- Aggressive behavior
  - 53% of all pts recurred, 43% stage I recurred
  - Pelvic and distant sites of failure common
    - 17% pelvic failure rate after XRT
- Radiation therapy “standard” for many
- EORTC 55874 Stage I-II- RCT  
observation vs XRT → local recurrences  
24% → 14% with XRT, but no impact on  
PFS/OS

# Treatment

- Limited value of adjuvant therapy disease
  - observation vs pelvic XRT vs chemotherapy
- GOG 150- stage I-IV IFX/CDDP vs WART
  - Rec @ 5 yr 51% chemo vs 58% WART
  - Recurrence risk 21% lower for chemo [RH 0.78], death rate 29% lower [RH 0.71]-NS
- GOG 161- adv/rec pts IFX vs IFX/paclitaxel
  - RR 29% vs 45%, Med OS 5.8 mo vs 13.5 mo with paclitaxel
- Future...
  - Combine XRT + chemo
  - IFX/paclitaxel vs paclitaxel/carboplatin

Wolfson. Gynecol Oncol. 2007;107:177-185. Homesley. J Clin Oncol. 2007;25:526-531.

# Treatment → Directions

- CS are poorly differentiated endometrial adenocarcinomas (EAC) (! vs ?)
  - Molecular markers support common origin of epithelial/sarcomatous components of CS
  - Disease spread/distribution similar Gr3 or PS EAC
  - Outcomes similar to high-risk EAC
  - Treatment moving to the same as EAC → paclitaxel/carboplatin

# Where we struggle...

- What pathologic evidence exists to support or refute that uterine carcinosarcomas are really a manifestation of high grade endometrial cancers.
- There is much debate currently ongoing in developing clinical trials to study uterine carcinosarcomas- should we include them with high grade endometrial cancers or should we treat them as a different entity

# Conclusions

- Rare tumors, limited (strong) data → more religion than science
- Pathologists play key role in identifying the “needles in the haystack”

*All great truths begin as  
blasphemies*

George Bernard Shaw