Mixed Tumors of the Uterine Corpus and Cervix

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UCSF Current Issues in Anatomic Pathology 2014
Disclosure

- I have nothing to disclose
Case

43 year old had a hysterectomy for fibroids; sections are from a sub-mucosal mass
Diagnosis?

Endometrioid Adenomyoma

vs

Atypical Polypoid Adenomyoma

vs

Mullerian Adenosarcoma
Outline

• Endocervical adenomyoma
• Endometrioid-type adenomyoma
• Atypical polypoid adenomyoma
• Mullerian adenosarcoma, uterine cervix and corpus
• Carcinosarcoma, uterine cervix and corpus
Endocervical Adenomyoma

Clinical Features

• Rare
• Typically premenopausal women (range 21-56 years)
• Asymptomatic, abnormal uterine bleeding, mucoid discharge
• May prolapse through os
Endocervical Adenomyoma

Gross Features

- Frequently polypoid (may be multiple)
- Occasionally centered in outer cervix
- Wide size range (up to 23 cm)
- Well demarcated, firm cut surface
Endocervical Adenomyoma

Usually grey to white on cut section
Endocervical Adenomyoma
Endocervical Adenomyoma
Endocervical Adenomyoma

Differential Diagnosis

- Minimal deviation adenocarcinoma
- Mullerian adenosarcoma
- Endocervicosis
Minimal Deviation Adenocarcinoma

Poorly defined mass or thickening
Minimal Deviation Adenocarcinoma

Irregular, haphazard growth

Lacks lobular architecture
Minimal Deviation Adenocarcinoma

- Stromal reaction
- Malignant cytologic features
- HIK1083 diffusely positive*

Endocervicosis

- Centered in outer cervical wall/paracervical soft tissue
- Lacks circumscription, lobulation, smooth muscle component
Mullerian Adenosarcoma

- Little to no smooth muscle
- Intracystic papillary projections
- Periglandular stromal condensation
Endometrioid-type Adenomyoma

Clinical Features

- Wide age range (usually > 30 yrs)
- Corpus > cervix
- Typically present with abnormal bleeding
Endometrioid-type Adenomyoma

**Gross Features**

- **Corpus**
  - Intra-myometrial > endometrial, subserosal (rarely polypoid, pedunculated)

- White, whorled firm cut surface + cystic spaces filled with blood (mean 4 cm)
Endometrioid-type Adenomyoma
Endometrioid-type Adenomyoma
Endometrioid-type Adenomyoma
Endometrioid-type Adenomyoma
Endometrioid-type Adenomyoma

*Unusual Histologic Features*

- Smooth muscle component
  - Hypercellular
  - Bizarre nuclei
  - Hydropic change
  - Hyalinization
Endometrioid-type Adenomyoma
Endometrioid-type Adenomyoma

Differential Diagnosis

- Leiomyoma with entrapped glands
- Glands located at periphery
- Myomatous endometrial polyp
- Smooth muscle in core (near vessels)
Myomatous Endometrial Polyp
Endometrioid-type Adenomyoma

Differential Diagnosis

- Adenomyosis
- Atypical polypoid adenomyoma
- Mullerian adenosarcoma
Adenomyosis
Adenomyosis
Atypical Polypoid Adenomyoma

Clinical Features

• Uncommon

• Pre/perimenopausal (mean 40 years); occasionally postmenopausal women

• Abnormal uterine bleeding; occasionally prolapsing mass through os
Atypical Polypoid Adenomyoma

Gross Features

• Typically located in lower uterine segment
• Usually solitary and well circumscribed
• Often pedunculated, but can be sessile
• Range 0.7 – 6.0 (mean 2.0) cm
Atypical Polypoid Adenomyoma
Polypoid Fragments
Endometrioid type glands
Squamous morules
Atypical Polypoid Adenomyoma

Differential Diagnosis

- Myoinvasive endometrial adenocarcinoma
- Endometrioid-type adenomyoma
- Mullerian adenosarcoma
Atypical Polypoid Adenomyoma

• Distinguish from myoinvasive adenocarcinoma by:
  – Well circumscribed (in hysterectomy)
  – Typiically less architecturally complex
  – Lack of separate fragments of typical adenocarcinoma
Endometrioid-type Adenomyoma

- Typically uterine corpus (not LUS)
- Less abundant glandular component (less complex)
- No morules
- Variable amount of endometrial stroma
Atypical Polypoid Adenomyoma

- Persistent, recurrent disease (45-60%); rare progression to carcinoma

- Local excision, hormonal therapy and close clinical follow-up vs. hysterectomy
Müllerian Adenosarcoma

• Low grade müllerian tumor with a biphasic growth of benign or atypical epithelium and malignant stroma (usually low grade sarcoma)
• Uterus > Ovary > Extragenital sites
• Extragenital tumors particularly associated with endometriosis
• Outcome depends on site and whether sarcomatous overgrowth is present
Uterine Adenosarcoma

• Age distribution
  – Typically postmenopausal women (mean 58 yrs)
  – 30% arise in premenopausal women
  – Younger age (mean 38 yrs) if arise in cervix

• Clinical features
  – Abnormal vaginal bleeding, pelvic pain
  – History of recurring polyps
  – Enlarged uterus
  – Hyperestrinism (including tamoxifen) and prior XRT are risk factors
Müllerian Adenosarcoma

• Diagnostic features
  – Phyllodes-like architecture
  – Intraglandular papillary projections
  – Marked stromal cellularity (with condensation)
  – Significant cytologic atypia
  – Mitoses $> 2$ per 10 high power fields
  – Altered epithelial differentiation
Phyllodes-Like Architecture
Stromal hypercellularity with condensation
Endometrial stromal appearance
Significant cytologic atypia
Mitotic Activity
Altered differentiation
Müllerian Adenosarcoma

• Useful diagnostic criteria
  – Well developed phyllodes-like architecture
  – Intraglandular papillary projections
  – Marked stromal cellularity (with condensation)
  – Significant cytologic atypia
  – Mitoses ≥ 2 per 10 high power fields
Müllerian Adenosarcoma

• What is the diagnostic threshold?

Atypical Uterine Polyps Sub-Diagnostic Of Müllerian Adenosarcoma: A Clinicopathologic Analysis Of 29 Cases With Long-Term Followup
Follow-up data was available on 28 of 29 patients (97%).

Overall followup time:
- Range 4.9-247 months (0.4-20.6 years)
- Mean 96.3 months (8 years)
- Median 83 months (7 years)
• Reasons why polyps with atypical architecture, stromal cuffing around glands, and stromal mitoses were NOT called adenosarcoma:
  – Character of cuff
    • Rarified or vague, ill-defined cuffing
  – Poorly developed phyllodes-like architecture
  – Partial involvement
Partial involvement of polyp
Rarified/loose periglandular cuff
Non-Diagnostic Cases

- Endometrial polyp with atypical features, see COMMENT.

COMMENT: The polyp is remarkable for X (cellular stroma, stromal atypia, unusual architectural feature); however, the findings are not diagnostic of an adenosarcoma. Clinical followup and consideration of followup sampling in 6 months is recommended to exclude the possibility of regrowth.
Sarcomatous Overgrowth

• Definition
  – Area of sarcoma must account for 25% of tumor volume OR should occupy 1 low power field in one slide

• Appearance
  – May have appearance of low grade sarcoma (ESS, fibrosarcoma) but usually high grade
  – Heterologous elements may be present (~25%)
  – Sex cord-like elements may be seen
Sharp demarcation
Sarcomatous Overgrowth – Low grade
Sarcomatous Overgrowth - Heterologous
Rhabdomyosarcoma
Müllerian Adenosarcoma

Ovarian and peritoneal adenosarcoma appear to behave more aggressively (with greater risk of recurrence and death due to disease) than uterine counterpart (without sarcomatous overgrowth)

- Uterine corpus recurrence: 15-25%
- Uterine corpus +SO recurrence: 45-70%
- Ovary recurrence: 77%
- Peritoneum recurrence: 60%
Müllerian Adenosarcoma

– Uterine corpus DOD: 10-25%
– Uterine corpus +SO DOD: ~55%
– Ovary DOD: ~65%
– Peritoneum DOD: 40%
Uterine Adenosarcoma

- Histologic features associated with risk of recurrence
  - Presence of sarcomatous overgrowth
  - Deep myometrial invasion
  - 60% with SO have deep myometrial invasion
  - Presence of heterologous elements (controversial)
Müllerian Adenosarcoma

- Differential Diagnosis – Uterine Corpus
  - *Cellular endometrial polyp* – homogeneously cellular, no architectural changes, no cuffing, no cytologic atypia
Endometrial Polyp with Cellular Stroma
Müllerian Adenosarcoma

➢ Differential Diagnosis – Uterine Corpus

➢ *Endometrial polyp with stromal atypia* – focal atypia, no mitotic activity, no cuffing
EMP with Stromal Atypia
Müllerian Adenosarcoma

- Differential Diagnosis – Uterine Corpus
  - Endometrial polyp with adenomyomatous stroma – Smooth muscle component, no architectural changes, no cuffing
Adenomyomatous Polyp
Adenomyomatous Polyp
Müllerian Adenosarcoma

- Differential Diagnosis – Uterine Corpus

- *Atypical polypoid adenomyoma* – smooth muscle is predominant component, squamous morules common, no periglandular cuffing, no intraluminal polypoid projections, no heterologous components
Müllerian Adenosarcoma

- Differential Diagnosis – Uterine Corpus
  - Carcinosarcoma (Malignant mixed müllerian tumor) – carcinomatous component, lack of phyllodes architecture, no stromal condensation
Müllerian Adenosarcoma

- Differential Diagnosis – Cervix
  - *Embryonal rhabdomyosarcoma* – Can be polypoid, have stromal condensation, contain heterologous elements (cartilage in 50%) BUT is more edematous/myxoid, has a sparse glandular component (entrapped) and lacks leaf-like or cystic glands
Embryonal Rhabdomyosarcoma

- Typically younger age
- Characteristic exophytic, ‘grape-like’ growth (so-called sarcoma botryoides) occurs at mucosal sites
Embryonal Rhabdomyosarcoma - Cervix
Embryonal Rhabdomyosarcoma
Carcinosarcoma

Clinical Features

• Most common type of mixed mullerian tumor of uterus
• < 5% of malignant uterine tumors (corpus >> cervix)
• Higher incidence in black women
• Usually postmenopausal women (mean 65 years)
  – <5% in women <50 years
Carcinosarcoma

**Clinical Features**

- Vaginal bleeding
- Enlarged uterus/pelvic pain
- 2/3 present at advanced stage
- Shares similar risk factors with endometrioid adenocarcinoma (obesity, exogenous estrogen, tamoxifen therapy, nulliparity)
- 40% have history of prior XRT (develop tumors at younger age)
- High risk HPV associated (cervical)
MMMT – sarcomatous component (ESS)
MMMT/Carcinosarcoma

Differential Diagnosis

- Dedifferentiated endometrioid carcinoma
  - Non-cohesive undifferentiated component juxtaposed to well differentiated component
  - No sarcomatous component
  - EMA only focally positive in undifferentiated component
MMMT/Carcinosarcoma

Differential Diagnosis

- Endometrioid carcinoma with corded/hyalinized foci
  - Low-grade cytologic features
  - Abrupt transition to squamous differentiation
MMMT/Carcinosarcoma

Differential Diagnosis

- Spindled endometrioid carcinoma
  - Merging of spindled and epithelioid components
  - Low-grade cytologic features
  - Keratins diffusely positive
  - No heterologous component
MMMT/Carcinosarcoma

Differential Diagnosis

- Mullerian adenosarcoma with sarcomatous overgrowth
  - Areas of typical adenosarcoma (phyllodes architecture, periglandular cuffing, etc)
Returning to the Case
Diagnosis:

Atypical polypoid adenomyoma associated with myoinvasive well differentiated adenocarcinoma (Invasive APA)
Take Home Points

- Prior to making the diagnosis of adenoma malignum, consider endocervical adenomyoma
  - Helpful features include circumscription, lobular arrangement of glands, fascicular arrangement of smooth muscle, lack of cytologic atypia and mitoses
Take Home Points

• Atypical polypoid adenomyoma should be considered in any complex endometrial glandular proliferation; search for precancerous change in other fragments of tissue

• Müllerian adenosarcoma should be rigorously separated from mimics and the threshold for diagnosis should be reconsidered, particularly in young patients
Take Home Points

- Both embryonal rhabdomyosarcoma and mullerian adenosarcoma of the cervix can be polypoid, have stromal condensation, and contain cartilage; however, the former is more edematous/myxoid, has a sparse glandular component (entrapped) and lacks leaf-like or cystic glands.