Interesting Cases in Gynecologic Pathology

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Case 1

History:

- 50 year old woman with a uterine mass
- Hysterectomy and BSO
- 11 cm yellow-white, gelatinous tumor
Case 1 – Uterine Mass
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Case 1 – Uterine Mass
Case 1- Differential Diagnosis

- Myxoid leiomyosarcoma
- Inflammatory myofibroblastic tumor
- Leiomyoma with degeneration or hydropic change
- Myxoid endometrial stromal sarcoma
Case 1- Immunohistochemistry

- Smooth Muscle Actin (+)
- ALK (-)
Case 1- Final Diagnosis

- MYXOID LEIOMYOSARCOMA

Dr. Esther Oliva, MGH, Boston, MA
Case 1- Myxoid Leiomyosarcoma

A rare and distinct malignant tumor
Case 1 - Myxoid Leiomyosarcoma

A rare and distinct malignant tumor:

- Doesn’t conform to the conventional leiomyosarcoma diagnostic features
- Worse prognosis
- Good recent paper:
Case 1- Myxoid Leiomyosarcoma

Gross Features:
- Large (average size 11 cm)
- Gelatinous, mucoid or myxoid
- Infiltrative growth pattern

Case 1- Myxoid Leiomyosarcoma

Histology:
- Spindle cell tumor arranged in a myxoid matrix
- Variable mitotic activity (may be as low as 2/10hpf)
- Variable necrosis
- Variable atypia

- What’s Not Variable?
  - Infiltrative border
  - Retained positivity for at least 1 smooth muscle marker
Case 1- Myxoid Leiomyosarcoma

Case 1- Myxoid Leiomyosarcoma

Case 1- Myxoid Leiomyosarcoma

Immunohistochemistry:
- SMA, Desmin are most sensitive
- CD10 (+) in 66%
- KI-67 of little utility
- Alcian Blue stains myxoid LMS (negative in edema/hydropic change)
Case 1 - Myxoid Leiomyosarcoma

Treatment:
- Surgery
- Chemo/radiation have little effect

Prognosis:
- Poor prognosis
- Worse than conventional LMS
Practical Classification of Smooth Muscle Tumors with Typical Spindle Cell Differentiation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Geographic Tumor Necrosis</th>
<th>Mitotic Rate (per 10 HPF)</th>
<th>Atypia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leiomyosarcoma</td>
<td>Present</td>
<td>Any</td>
<td>Present or absent</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>Absent</td>
<td>&gt;10</td>
<td>Moderate to severe</td>
</tr>
<tr>
<td>STUMP</td>
<td>Absent</td>
<td>&gt;15</td>
<td>Absent</td>
</tr>
<tr>
<td>Atypical Leiomyoma</td>
<td>Absent</td>
<td>&lt;10</td>
<td>Moderate to severe</td>
</tr>
<tr>
<td>Leiomyoma with increased mites</td>
<td>Absent</td>
<td>&lt;15</td>
<td>Absent</td>
</tr>
</tbody>
</table>

Table adapted from textbook: Crum et Al, Diagnostic Gynecologic and Obstetric Path, 2011
Case 1- Myxoid Leiomyosarcoma

Diagnostic Features:

1. >50% myxoid matrix
2. Infiltrative border, plus any one of the following:
   - 2 or more mites /10 hpf
   - Unequivocal coagulative tumor necrosis
   - Moderate to severe nuclear atypia
Strange things growing on walls…
Case 2

History:
- 74 year old woman, cystic intra abdominal mass
- Hysterectomy and BSO
  - 35 cm cystic ovarian mass
  - 12.0 cm mass involving the fallopian tube
Case 2 – Ovarian Cyst with Nodule
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Case 2 – Ovarian Cyst with Nodule
Case 2 - Differential Diagnosis

- Sarcoma
- Carcinoma
  - Metastasis
  - Focus of anaplastic carcinoma
- Lymphoma
- Sarcoma-like mural nodule
CD 3
Case 2 - Immunohistochemistry

- CD68 (+)
- CK7 (+ patchy)
- AE1/3 (+ patchy)
- ER (-)
- CD10 (-)
- CD3 (+ small scattered lymphocytes)
- CD20 (-)
Case 2 - Final Diagnosis

- MUCINOUS CYSTADENOMA WITH A SARCOMA-LIKE MURAL NODULE

Dr. Robert Young, MGH, Boston
Case 2- Mural Nodules

Strange things can be found growing in the wall of cystic ovarian neoplasms…

Which ones are benign? Which ones are more problematic?
Case 2- Mural Nodules

General Features:
- Well demarcated nodule or plaque in the wall of an ovarian cyst
- Variable appearance:
  - Yellow, pink, red, hemorrhagic, necrotic
  - Single or multiple
- 1 to 20 cm
- Benign or malignant
Types of mural nodules:

- Benign:
  - “Sarcoma-like mural nodule”
- Malignant:
  - Sarcomatous mural nodule
  - Mural nodule with anaplastic carcinoma
Benign:
- Younger
- Smaller (<6cm)
- Sharply demarcated
- Heterogeneous cell population (giant cells, spindle cells and inflammation)

Malignant:
- Older
- Larger
- Infiltrative/vascular invasion
- Uniform cell population (spindled or carcinoma)
Case 2- Sarcoma-Like Mural Nodule

Histology:

- Shows mix of MNGCs, spindle cells and inflammation
- WITH significant pleomorphism, mites, atypical mites
Case 2 – Sarcoma-Like Mural Nodule
Case 2- Sarcoma-Like Mural Nodule

Immunohistochemistry:

- Cytokeratin
  - Negative or patchy in sarcoma-like mural nodules
  - Strong and diffuse in anaplastic carcinoma
Case 2 - Sarcoma-Like Mural Nodule
Case 2- Sarcoma-Like Mural Nodules

Prithwijit et al, (2014)
Sarcomatous nodule

Hitoshi et al, (2013)
Anaplastic Mucinous Carcinoma

Prat: www.bdiap.org/Belf02/Prat/8-MucinAnapl-Ca.jpg
Cueva do los cristales, Chihuaua, Mexico
Case 3

History:
- 62 year old woman with pain and vaginal bleeding
- Anemic
- Ultrasound showed fibroid uterus
- Hysterectomy
  - Simple ovarian cyst
  - Endometriosis
Case 3 – Ovarian Cyst
Case 3 – Endometriosis
Case 3
Case 3
Case 3
Case 3
Case 3
Case 3 - Differential Diagnosis

- Carcinoma
- Metastasis
- Sex cord stromal tumor
- Mesonephric remnants
- Adenomatoid tumor
- Monodermal teratoma
  - Struma ovarii
  - Carcinoid
CK7 (+)
Calretinin
Inhibin (Focally +)
Other Stains:

- PAX 8 (weak focal +)
- CD10 (-)
- ER (-)
- Chromogranin (-)
- Synaptophysin (-)
- TTF-1 (-)
Case 3 - Final Diagnosis

“In my opinion, the diagnosis here is endometrioid adenocarcinoma, grade 1 of 3, arising out of the background of a mucinous cystadenoma. The mucinous cystadenoma is of mullerian mucinous type, and of course that cell type is very closely related to endometriosis. As is so typical, there is a background of endometriosis. That a carcinoma arising on the background of a mucinous cystadenoma should be endometrioid is no surprise. I think one has to call it endometrioid because there is simply no mucinous nature to the low-grade carcinoma…”

Dr. Robert Young, MGH, Boston
Case 3 - Mucinous Ovarian Tumors

General Features:
- Second most common epithelial-stromal neoplasm of the ovary
- 80% benign
- 10% borderline
- 10% malignant
Case 3 - Mucinous Ovarian Tumors

Clinical Features:

• Age at presentation
  • Benign tumors - younger women
  • Borderline and malignant tumors - average 50’s
• Commonly accompanied by hormone manifestations (androgen or estrogen)
• CA-125 is less sensitive for mucinous tumors
Case 3 - Mucinous Ovarian Tumors

Other common cyst wall findings:
- 5% have a mature teratoma component
- Not uncommonly associated with Brenner tumor
Case 3 – Ovarian Cyst with Brenner Tumor
Case 3 – Ovarian Cyst with Brenner Tumor
Case 3 - Endometrioid Ovarian Tumors

General Features:
- Benign endometrioid tumors of the ovary are rare
- Second most common ovarian malignancy after serous
Case 3 - Endometrioid Ovarian Tumors

Clinical Features:

- Postmenopausal
- Mid 50’s
- Discovered at earlier stage than serous
  - (stage for stage, same prognosis)
- Frequently associated with endometriosis
- Often bilateral
Case 3 - Endometrioid Ovarian Tumors

Classic Histology:
- Back to back glands, fibrotic stroma
- Stratified epithelial cells
- Squamous morules
- May be villous or papillary
- Grading in ovary same as for uterine tumors
Case 3 - Endometrioid Ovarian Tumors

Classic Endometrioid Histology

FIGO grade I  FIGO grade II  FIGO grade III

Malpica A et al. Modern Pathol 2016
Case 3 - Endometrioid Ovarian Tumors

Endometrioid carcinoma with villoglandular pattern

Malpica A et al. Modern Pathol 2016
Case 3 - Endometrioid Ovarian Tumors

Variant Histology:
- Secretory
- Oxyphilic
- Ciliated
- Balloon Like
- Spindle Cell

* In each, finding a focus of typical endometrioid carcinoma facilitates a correct interpretation
Case 3 - Endometrioid Ovarian Tumors

Endometrioid carcinoma with secretory changes

Malpica A et al. Modern Pathol 2016
Case 3 - Endometrioid Ovarian Tumors

Endometrioid carcinoma with spindle cells

Malpica A et al. Modern Pathol 2016
Case 3 - Endometrioid Ovarian Tumors

Endometrioid carcinoma with clear cell changes

Malpica A et al. Modern Pathol 2016
Case 3 - Endometrioid Ovarian Tumors
Endometrioid carcinoma with sex cord stromal pattern

Malpica A et al. Modern Pathol 2016
Case 3 - Endometrioid Ovarian Tumors

Endometrioid carcinoma with microglandular pattern

Malpica A et al. Modern Pathol 2016
Case 4

History:

- 30 year old woman
- 10 month history of heavy vaginal bleeding
- Endometrial biopsy at outside hospital
Case 4 - CT Scan
Case 4 – Uterine Mass
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Case 4 – Uterine Mass
Case 4 - Differential Diagnosis

- Endometrioid Adenocarcinoma
- Carcinosarcoma
- Metastasis
- Sex Cord Stromal Tumor
- Ewing's/PNET
- Small Cell
- Rhabdomyosarcoma
- Germ Cell Tumor
Stains:

- CAM5.2 Patchy (+)
- Vimentin (+)
- AE1/3 (-)
- CK7 (-)
- PAX8 (-)
- ER (-)
- Chromogranin (-)
- Synaptophysin (-)
- Desmin (-)
- Myf4 (-)
- Inhibin (-)
- AFP (-)
- CD99 (-)
- FLI1 (-)
- EWSR1 FISH (-)
Case 4 - Diagnosis

- HIGH GRADE ADENOCARCINOMA
Case 4 - History Cont.

- One month later, increasing abdominal pain
- Rapid recurrence and peritoneal carcinomatosis
- Urgently started on carboplatin/paclitaxel
- Showed little response
Case 4 - History cont.

- Pathology sent for consultation:

- Dr. Robert Young offered another diagnosis and 2 weeks later her chemo was changed to VIP (etoposide/ifosfamide/cisplatin)

- 6 Cycles, near complete response
“I feel this is a primitive neuroectodermal tumor (PNET)… of course we use the term primitive neuroectodermal tumor for the central-type morphology one sees in the ovary and uterus more commonly than one sees in the peripheral (Ewing’s) variant.”

Dr. Robert Young, MGH, Boston, MA
Case 4 - Uterine PNET

General Features:

- Small round blue cell tumors
  - Ewing family of tumors (a spectrum)
    - Characteristic translocations $t(11:22) EWSR1/FLI1$

Ewing $\langle$-----------------------------$\rangle$ PNET

- Small round cell morphology
- Neural differentiation

- PNET further Divided into:
  - Central-type PNET
  - Peripheral-type PNET
Case 4 - Uterine PNET

• Peripheral-type PNET / Ewing Sarcoma
  • Usually have EWSR1 translocations
  • Neural crest derived
  • Occur outside the CNS

• Central-type PNET / Neuroblastoma
  • Usually don’t have EWSR1 translocations
  • Develop from / Involve CNS
  • Most uterine and ovarian tumors are cPNET
Case 4 – Uterine PNET

Clinical Features:

- Rare in the Gyn tract
  - Ovary most common, then uterus
- Postmenopausal or adolescent women, abnormal vaginal bleeding and uterine mass
- Presents in advanced stage, rapidly progressive
- Associated with VHL disease
Histology:

- EWING and PNET have similar morphology
  - Uniform, small round cells, powdery chromatin, small nucleoli
  - May have rosettes, fibrillary background
  - Numerous mites, necrosis
  - Pure form or admixed with other uterine tumors

Case 4 – PNET
Case 4 – Uterine PNET

IHC:
- CD99 (usually +) (7/9 + in case series)
- FLI-1 (usually +)
- Vimentin (+)
- May express keratins, chromogranin, synaptophysin, NSE and S100

FISH:
- Usually negative for EWSR1 rearrangements
Case 4 – Uterine PNET

Prognosis:
• Very few case reports of uterine PNET
• Poor prognostic factors
  • Older age
  • Higher stage
  • Tumor >8 cm
  • Poor chemo response
  • Absence of EWSR1 translocation
Case 4 – Uterine PNET

Treatment:

• Patients without mets at presentation respond well to intense multi-modal treatment
• Case reports of long disease free survival with platinum based chemo and etoposide
Case 4 – Uterine PNET

Take Home:

- Rapid diagnosis important
- Keep in mind that Ovarian and Uterine PNET tends to be of the central type
  - No EWSR1 translocation
  - May not express CD99 or FLI1

Follow up on our patient:
- Currently, no evidence of disease
Thank You

Witches Finger, Carsbad Caverns, NM
References:


IMAGES:


Anaplastic Mucinous Carcinoma: http://www.bdiap.org/Belf02/Prat/8-MucinAnapl-Ca.jpg
Prof. Jaime Prat, Hospital de la Santa Creu i Sant Pau, Autonomous University of Barcelona, Spain