How to Recognize Gynecologic Cancer Cells from Pelvic Washing and Ascetic Specimens

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Pelvic Washing and Ascetic Specimens

- Obtaining a pelvic washing sample is a common surgical procedure for gynecologic malignancies.
- The findings from those washing specimens have a significant impact for the decision of clinical management.
- They are mainly applied to gynecologic carcinomas, particularly for the carcinomas of ovary, fallopian tube, and/or peritoneum.
- Prior to initiating neoadjuvant chemotherapy, an accurate cytologic or pathologic diagnosis is typically required.
Perspectives of Cytopathologists

- Difficult to make definitive diagnosis on cytologic specimens
- The most common diagnosis is “Negative” vs “Positive for adenocarcinoma” or “Atypical”
- Within the positive category, most of the time without specifying cancer source.
- Part of the reasons are: these are cytologic specimens, not resection or biopsy specimens; lack of specific markers (previously).
Perspectives of Gynecologists or Oncologists

- Expect to be more specific for positive specimens: primary site (gyn vs non-gyn).
- “Atypical” is the most annoying diagnosis.
- They do not care much for washing diagnosis when the cancers are in the advanced stages or ovarian cancer with exophytic growth.
- But they do care in the following situations:
  - Lower stage (stage 1A vs 1C)
  - Presence of extensive adhesions (Positive vs reactive)
  - Presence of other cancers (breast cancer metastasis vs PSC)
- Significant attention to those patients for neoadjuvant chemotherapy from ascetic samples.
Neoadjuvant Chemotherapy

- Give chemotherapy prior to “debulking’ surgery.
- Started from two decades ago
- Almost exclusively for
  - Advanced stage ovarian cancer
  - Patients were medically too compromised to tolerate primary surgical cytoreduction.
- Diagnostic imaging criteria are developed to identify patients with advanced stage ovarian cancer who are unlikely to be optimally surgically cytoreduced at the initial surgery.
Neoadjuvant Chemotherapy:
Selective criteria and diagnostic accuracy (%)

The selection criteria:

- Physical examination consistent with advanced ovarian cancer (70)
- Diagnostic imaging studies consistent with an advanced stage ovarian cancer that is unlikely to be optimally cytoreduced (85-90)
- Cytologic or histologic specimens consistent with an ovarian epithelial cancer (>95)

Schwartz and Zheng, Gynecol Oncol, 2005
Pelvic Gynecologic Cancer Related Cytology

- Ovarian epithelial carcinoma (OEC): the most common. Among them, pelvic serous carcinoma (PSC) is the most prevalent:
  - Fallopian tube
  - Ovary
  - Peritoneum
- Metastatic cancers: GI, breast, mesothelioma, GU, etc
- Ovarian sex-cord stromal tumors: less common
- Endometrial cancer: less common
  - Mostly endometrial serous carcinoma
- Cervical cancer: rare
What are the cytologic features for OEC?
Cytologic features of OEC

Malignant cells with abundant cytoplasm not typical of mucinous carcinoma
Cytologic features of OEC

Malignant cells with abundant cytoplasm not typical of mucinous carcinoma
Cytologic features of OEC

Small papillary structures or minimal architectural features suggesting papillary formation, particularly when presence of psammoma bodies
Cytologic features of OEC

Micropapillary structures or minimal architectural features suggesting papillary formation, particularly when presence of psammoma bodies

Schwartz and Zheng, Gynecol Oncol, 2005
Micropapillary structures or minimal architectural features suggesting papillary formation, particularly when presence of psammoma bodies
Cytologic features of OEC

Malignant cells with vacuoles or a hint of clear cell differentiation suggests clear cell carcinoma or a serous or an endometrioid carcinoma with clear cell features.
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The presence of prominent nucleoli, commonly seen in high-grade serous and clear cell carcinomas.
Cytologic features of OEC

The presence of prominent nucleoli, commonly seen in high-grade serous and clear cell carcinomas
Cytologic features of OEC

Squaumous metaplasia is indicative of endometrioid carcinoma
Cytologic features of OEC

Endocervical type malignant cells are most compatible with a mullerian or ovarian primary.
Cytologic features of OEC

Adenocarcinoma with intestinal like mucin or signet ring appearance has a broader differential diagnosis.
Biomarkers useful to aid the diagnosis and differential diagnosis

- PAX8
- ER/PR
- p53
- WT1, CA125, BerEP4
- Inhibin, Calretinin
- Breast 2 (GCDFP15)
- CDX2
- CK7, CK20
PAX8

- PAX genes encode a family of nine well-characterized paired-box transcription factors (PAX1–PAX9), play roles in embryogenesis.
- A reasonably good “Mullerian” marker identifying epithelial cells of Mullerian origin.
- Nuclear location
- Can’t tell the difference between benign vs borderline or malignant.
- Also positive in kidney and thyroid tissues.
ER and PR

High-grade serous carcinoma (HGSC):
- ER is almost always positive: about 90% cases are positive ranging from 20 to 70% tumor cells.
- PR is almost always negative

Low-grade serous carcinoma
- Both ER and PR show various degree of positivity.
p53

- All or none phenomenon in high-grade serous carcinoma
  - Positive is defined by 75% or more cells stained or majority cancer cells stained in cytology
  - No cancer cell stained
- Various stainings in other cancers mainly depending on the degree of differentiation.
High-grade serous carcinoma

PAX8

p53
Borderline tumor or low-grade serous carcinoma

Xiang et al., Gynecol Oncol 2012

PAX8

p53
Common differential diagnoses from pelvic cytology specimens

- Breast cancer metastasis vs OEC
- Mesothelioma vs OEC
- GI vs GYN primary
- Reactive mesothelial cells vs positive cytology
- Endometrioid vs serous carcinoma
Breast metastasis vs OEC: PAX 8

Xiang et al., Gynecol Oncol 2012
Mesothelioma vs OEC: PAX8 and Calretinin

Laury et al., AJSP 2010
Colon metastasis vs OEC:
PAX8, WT1, ER, CD2, CK7, CK20

Mcknight et al., Cancer Cytolol 2010
Pancreatic metastasis vs ovarian mucinous carcinoma: PAX8, CDX2
# Reactive mesothelia vs Sex-cord stromal tumors

<table>
<thead>
<tr>
<th></th>
<th>Reactive mesothelia</th>
<th>Granulosa cell or Sertoli-Leydig cell tumors</th>
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<tbody>
<tr>
<td><strong>Inhibin</strong></td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td><strong>Calretinin</strong></td>
<td>Positive</td>
<td>Negative</td>
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### Endometrioid vs serous carcinoma

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<thead>
<tr>
<th></th>
<th>Endometrioid Carcinoma, G3</th>
<th>HGSC</th>
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<tr>
<td><strong>p53</strong></td>
<td>Focal (typically &lt; 25%)</td>
<td>Diffuse or null</td>
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<tr>
<td><strong>ER</strong></td>
<td>Negative or weak focal (less than 10%)</td>
<td>Apparent, ranging from 10 to 90%</td>
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<tr>
<td><strong>PR</strong></td>
<td>Focal or negative</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>WT1</strong></td>
<td>Negative</td>
<td>Positive</td>
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Thank You!