Case 1

- 68 year old woman
- Bilateral adnexal masses
- Elevated CA125 (793)
- Hysterectomy in 2008
- Underwent BSO and tumor debulking in 2011; 6-8 L of ascites
- Extensive metastases noted, with carcinoma involving the diaphragm, peritoneum, and bowel (stage III C)

Case 1 Gross Pathology

- The ovaries were small
- Right ovary: Pale tan multinodular solid mass 4 cm in maximum dimension; tumor involved the surface
- Left ovary: Cystic and solid, 5 cm in maximum dimension, papillary excrescences from cyst linings
- Fallopian tubes: Unremarkable
- Omentum, mesentery, bowel: Riddled with mostly small nodules, largest 4.5 cm

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Professor
Department of Pathology
UCSF

Ovarian Epithelial Tumors
Right ovary 4 cm maximum dimension
Left ovary 5 cm maximum dimension
CASE 1 Diagnosis

**High Grade Serous Carcinoma**
Discussion Points for Case 1

• Classification and general features of epithelial tumors
• Histologic features of high grade serous carcinoma
• Immunophenotype
• Molecular pathology – p53
• BRCA
• The fallopian tube connection and histogenesis of pelvic high grade serous carcinoma

Epithelial Tumors

Clinical Presentation

• Rare in patients < 20 years
• Carcinoma occurs mainly > 40 years
• Presenting symptoms are nonspecific:
  – Pelvic or abdominal pain or discomfort
  – Gastrointestinal symptoms
  – Disturbances of menstruation
  – Abdominal distention
• Standard treatment is surgery and, often, platinum + taxane chemotherapy

Epithelial Ovarian Cancer

• High grade serous
• Low grade serous
• Endometrioid
• Clear cell
• Mucinous
• Carcinosarcoma (MMT)
• Transitional Cell / Malignant Brenner
• Rare tumor types
• Mixed types
• Undifferentiated
• Unclassified
Distribution of Ovarian Tumor Types

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>High grade serous</td>
<td>68.1</td>
</tr>
<tr>
<td>Low grade serous</td>
<td>3.4</td>
</tr>
<tr>
<td>Clear cell</td>
<td>12.2</td>
</tr>
<tr>
<td>Endometrioid</td>
<td>11.3</td>
</tr>
<tr>
<td>Mucinous</td>
<td>3.4</td>
</tr>
<tr>
<td>Other</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Ovarian Cancer FIGO Stages

- **Stage I** - Limited to the ovaries
  - IA - One ovary, intracystic
  - IB - Both ovaries, intracystic
  - IC - Rupture; tumor on surface; + cytology
- **Stage II** - Spread to pelvis
- **Stage III** - Spread to abdomen or LN
- **Stage IV** - Distant spread

Survival With Serous Carcinoma

Int J Gynecol Pathol 2010; 29:203-211

High Grade Serous Carcinoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>% of all tumors in this stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I or II (localized)</td>
<td>35.5</td>
</tr>
<tr>
<td>III or IV (widespread)</td>
<td>87.7</td>
</tr>
</tbody>
</table>

High Grade Serous Carcinoma Standard Histologic Features

- Cystic
- Papillae, tufts of cells, micropapillae
- Glands, labyrinthine glands, slit like glands
- Solid areas
- Cribriform glands, microcystic pattern
- High grade nuclei (grade 2 or 3)
- High mitotic rate (> 12/10 hpf)
High Grade Serous Carcinoma
New Criteria

- Standard patterns of high grade serous differentiation: papillary, micropapillary, slit like glands, etc.
- Predominantly undifferentiated carcinoma with any serous features
- High grade glandular tumor without squamous differentiation
- Transitional cell tumor with any serous features
- High grade carcinoma with mixed serous and clear cell features

Justification for Grouping With High Grade Serous

- Similar gene expression patterns
- Similar immunophenotypes (p53+, p16+, WT1+)
- Similar mutation patterns
- Areas of typical serous carcinoma tend to be intermixed
- Metastases often have typical morphology of serous carcinoma
- Similar clinical behavior (survival, chemotherapy response)
Immunohistochemistry in the Diagnosis of High Grade Serous Carcinoma

Is This an Ovarian Tumor?

<table>
<thead>
<tr>
<th>Stain</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK7</td>
<td>+</td>
</tr>
<tr>
<td>CK20</td>
<td>-</td>
</tr>
<tr>
<td>CDX2</td>
<td>-</td>
</tr>
<tr>
<td>PAX8</td>
<td>+</td>
</tr>
<tr>
<td>CA125</td>
<td>+</td>
</tr>
<tr>
<td>ER</td>
<td>+</td>
</tr>
</tbody>
</table>

Stains for Tissue of Origin

PAX8

CK7

CA125

Immunohistochemistry

Is This High Grade Serous Carcinoma?

<table>
<thead>
<tr>
<th>Stain</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>P53</td>
<td>Positive test result: Strong positive staining throughout; &gt; 50%, usually &gt;80-90%</td>
</tr>
<tr>
<td>P53</td>
<td>Positive test result: Completely negative; no staining in any tumor cells</td>
</tr>
<tr>
<td>P16</td>
<td>Positive test result: Strong staining in every or nearly every tumor cell; 95-100%</td>
</tr>
<tr>
<td>WT1</td>
<td>Positive</td>
</tr>
<tr>
<td>HMGA2</td>
<td>Positive</td>
</tr>
<tr>
<td>PAX2</td>
<td>Negative; positive suggests low grade serous or borderline</td>
</tr>
</tbody>
</table>