Ovarian Neoplasms

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Pathologie
Ovarian neoplasms

- Epithelial
- MMMT
- Sex Cord
- Germ cell
- Metastases

- Mesothelial tumors
- Soft tissue tumors
- Other rare entities
Types of ovarian cancer

- **Type I Tumors**
  - Low-grade
  - Slow growing
  - Encompass all histologies, including:
    - low-grade serous carcinoma
    - low-grade endometrioid carcinoma
    - mucinous carcinoma
    - and some clear cell carcinomas
  - They likely evolve through a step-wise progress from borderline tumors
  - Usually chromosomally stable

- **Type II Tumors**
  - High-grade
  - Evolve rapidly
  - Include:
    - high-grade serous carcinoma
    - high-grade endometrioid carcinoma
    - carcinosarcoma
    - undifferentiated carcinoma
    - and some clear cell carcinomas
  - No recognizable precursors in the ovary
  - Widespread DNA copy number changes

Images:
- Endometrioid
- Mucinous
- Clear Cell
- Serous
- Endometrioid (Type II)
- Carcinosarcoma
- Clear Cell (Type II)
- Serous (Type II)
# Types of ovarian cancer

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Histology</strong></td>
<td>Low-grade serous</td>
<td>High-grade serous</td>
</tr>
<tr>
<td></td>
<td>Clear cell</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low-grade endometrioid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mucinous</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transitional</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Borderline</td>
<td></td>
</tr>
<tr>
<td><strong>Common genetic defects</strong></td>
<td>ARID1A</td>
<td>p53</td>
</tr>
<tr>
<td></td>
<td>BRAF</td>
<td>BRCA</td>
</tr>
<tr>
<td></td>
<td>B-Catenin</td>
<td>(mutation or promoter methylation)</td>
</tr>
<tr>
<td></td>
<td>KRAS</td>
<td>AKT</td>
</tr>
<tr>
<td></td>
<td>PTEN</td>
<td>NOTCH3</td>
</tr>
<tr>
<td></td>
<td>MAPK</td>
<td>FAT2</td>
</tr>
<tr>
<td></td>
<td>MLH1</td>
<td>FAT4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P532-CA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>WTI</td>
</tr>
<tr>
<td><strong>Proportion of cancers (%)</strong></td>
<td>20–25</td>
<td>75–80</td>
</tr>
<tr>
<td><strong>Primary tissue of origin</strong></td>
<td>Ovarian surface epithelium</td>
<td>Fallopian tube</td>
</tr>
<tr>
<td><strong>Pathway to cancer</strong></td>
<td>Cortical inclusion cyst</td>
<td>p53 Mutation</td>
</tr>
<tr>
<td></td>
<td>or tubo-ovarian neoplasms</td>
<td>in distal fallopian tube to ser to invasive carcinoma</td>
</tr>
<tr>
<td><strong>Clinical behavior</strong></td>
<td>Slower growing</td>
<td>Rapidly growing</td>
</tr>
<tr>
<td></td>
<td>Indolent to aggressive</td>
<td>Aggressive</td>
</tr>
</tbody>
</table>

- Sertoli-Leydig Intratubal carcinoma
Origin of ovarian serous carcinoma

- updated view
Diagnostic algorithm

Figure 1. Diagnostic algorithm for the diagnosis of STIC, atypical intermediate lesions (STIL), p53 signature and normal/reactive. Abn: abnormal expression pattern; STIC: serous tubal intra-epithelial carcinoma; STIL: serous tubal intra-epithelial lesion; WT: wild-type. See text for details regarding use of algorithm.
Epithelial

- Benign
- Borderline
- Malignant

- Serous
- Mucinous
- Seromucinous
- Endometrioid
- Clear cell
- Brenner
Serous epithelial tumors
Serous epithelial tumors
Serous epithelial tumors
Mucinous epithelial tumors
Mucinous carcinoma

- No defined grading system!
- Expansile vs. destructive invasion (prognosis!)
- Extensive sampling of all mucinous ovarian tumors (at least 1-2 sections per cm)
- Metastases!
- New entity: seromucinous tumors
Seromucinous tumors
Endometrioid epithelial tumors
Endometrioid epithelial tumors

- Differential between high-grade serous and endometrioid ovarian carcinoma

<table>
<thead>
<tr>
<th></th>
<th>endometrioid</th>
<th>serous</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT-1</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>p53</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>ER/PR</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>PAX8</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Clear cell and Brenner tumors
MMMT
Rare epithelial tumors

- Small cell carcinoma
- Tumors of the rete ovarii
- Wolffian tumors
- Solid pseudopapillary neoplasm
Germ cell tumors

- Teratoma
- Dysgerminoma
- Yolk sac tumor
- Embryonal carcinoma
- Chorioncarcinoma
Mature teratoma
Immature teratoma
Immature teratoma DD
Monodermal teratomas

- Struma ovarii
- Carcinoid
- Neuroectodermal-type Tumor
- Sebaceous Tumors
Dysgerminoma
Sex cord-stromal tumors

**Pure stroma tumors**
- Fibroma/Thecoma
- Sclerosing stromal tumor
- Signet-ring stromal tumor
- Microcystic stromal tumor
- Leydig cell tumor
- Steroid cell tumor

**Pure sex cord tumors**
- Granulosa cell tumor
  - adult/juvenile
- Sertoli cell tumor
- Sex cord tumor with annular tubules

**Mixed sex cord-stromal tumors**
- Sertoly-Leydig cell tumors
Fibroma/Thecoma
Adult granulosa cell tumor

- Proliferation of granulosa cells comprising at least **10%** of tumor
- Estrogenic manifestations in up to 2/3
- Association with endometrial neoplasia
- Stage is most important prognostic factor; late recurrences (low grade malignant)
- **Inhibin, calretinin, CD99, CD56 and WT-1** positive
Adult granulosa cell tumor
Juvenile granulosa cell tumor

• < 5% of all granulosa cell tumors
• median: 17 years
• 5-year survival rate > 90%
Juvenile granulosa cell tumor
Other sex-cord stromal tumors

- Sclerosing stromal tumor
- Signet-ring stromal tumor
- Microcystic stromal tumor
- Leydig cell tumor
- Steroid cell tumor

- Sertoli cell tumor
- Sex cord tumor with annular tubules
- Sertoly-Leydig cell tumors
Metastases

The preoperative CA-125 value was known in 46 patients (53%). Of these patients, the median serum CA-125 level was 85 U/mL (range, 5–9659 U/mL). In 33 of the 46 patients (72%), the serum CA-125 level was elevated (>35 U/mL).

Macroscopic Characteristics

The gross appearance of the ovarian metastases could be analyzed in 87 cases, with cysts present in 62 patients (71%) (Table 3). Tumors arising from the GI tract gave rise to cystic metastases in 83% of cases. Of the gynecologic malignancies, all 6 cases of cervical cancer gave rise to cystic lesions in the ovaries, whereas this was the case in 64% (9/14) of the endometrial malignancies.

Bilateral ovarian involvement was present in 69% of the patients (Table 3). Of the patients with a primary tumor of the GI tract, 71% had bilateral involvement of the ovaries, of which all the patients with a primary tumor of the stomach showed bilateral involvement. In patients with primary breast cancer, bilateralism was also seen in more than half the number (65%) of cases.

The size of the ovaries with metastatic disease was recorded in 126 ovaries of 79 patients (Fig. 1). Most ovaries with metastatic disease from primary breast and gynecologic tumors were 10 cm in diameter or less (95%). The ovarian metastasis of largest dimension mostly originated from the GI tract. Of 23 metastatic ovaries of 11 cm in diameter or more, 17 (74%) originated from the GI tract.

Histopathology

The histological types of the primary tumors of the GI tract that metastasized to the ovaries were most frequently adenocarcinomas (97%). Signet ring cells were found in 13 of all ovarian

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**TABLE 2. Origin of the primary tumor**

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>No. Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nongynecologic origin</td>
<td>86 (74)</td>
</tr>
<tr>
<td>Breast</td>
<td>32 (28)</td>
</tr>
<tr>
<td>Large intestine*†</td>
<td>23 (20)</td>
</tr>
<tr>
<td>Stomach†</td>
<td>7 (6)</td>
</tr>
<tr>
<td>Small intestine†</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Appendix†</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Sarcoma‡</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Pancreas†</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Others§</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Tumor of unknown origin†‖</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Gynecologic origin</td>
<td>30 (26)</td>
</tr>
<tr>
<td>Endometrium</td>
<td>23 (20)</td>
</tr>
<tr>
<td>Cervix</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Fallopian tube</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

*Tumors located in colon (n = 13), sigmoid (n = 6), cecum (n = 2), and rectum (n = 2).
†Tumors located in the GI tract (n = 45).
‡Sarcomas with unknown site of origin, of which one was malignant fibrous histiocytoma (n = 1).
§Tumors located in the kidney (n = 1) and extraovarian tumors (n = 3).
‖Tumors suggestive of primary tumors arising from the GI tract based on histological features (n = 8) and a carcinoid (n = 1) of unknown origin.
Colon

CDX-2 +
CK20 +
CK7-
PAX-8 -
ER/PR -
Breast

PAX-8-GATA-3+
Endometrium

Favor synchronous carcinoma if

- Unilateral ovarian involvement
- No L1 in uterus
- Endometriosis or adenofibroma in ovary
- No metastatic disease at other sites