Serous Tumors
LOW-GRADE SEROUS CARCINOMA (LGSCA)

Serous carcinomas are classified as high-grade and low-grade serous carcinoma. LGSCA has been recognized as a type of serous carcinoma based on 2-tier grading system. LGSCAs most commonly arise from serous borderline tumors or adenofibroma through step-wise progression and have mutations of KRAS, BRAF or ERBB2 genes and lack TP53 mutations. In contrast to LGSCA high-grade serous carcinomas (HGSCA) arise de novo from the surface epithelium or its inclusion cysts and are characterized by TP53 mutations. Some of high-grade serous carcinomas arise from benign or borderline serous tumors.

Diagnostic criteria of LGSCA:
1) Destructive stromal invasion (>5mm).
2) Mild to moderate cytologic atypia.
3) Infrequent mitotic figures.

Clinical significance of distinction between LGSCA and HGSCA:
1) Much better prognosis of LGSCA.
2) Chemoresistance of LGSCA to platinum-based chemotherapy.

Differential diagnosis from invasive implant:
Quantitative difference: LGSCA > invasive implant.

NEW CONCEPTS ON ORIGIN OF OVARIAN HIGH-GRADE SEROUS CARCINOMA

Traditional view on origin of HGSCA:
De novo, ovarian surface epithelium or inclusion cyst.
Proposed theory of tubal origin:
Presence of serous tubal intraepithelial carcinoma in 70% of sporadic ovarian and peritoneal HGSCA suggests that primary ovarian HGSCA originate in other pelvic organs, fallopian tube.

The current truth:
Fundamental questions remain to be addressed in this model.

MUCINOUS TUMORS
Mucinous tumors are the largest of all ovarian tumors. Mucinous tumors are divided into benign, borderline tumors and mucinous carcinoma according to degree of malignancy.

Mucinous cystadenoma vs mucinous borderline tumors:
In mucinous borderline tumors there is abnormal proliferation of epithelium of mucinous type greater than mucinous cystadenoma, with stratification, papillae, filiform or branching, at least 10% of inner surface of cysts. But there is no destructive stromal invasion.

Endocervical-like(Mullerian-type) mucinous borderline tumors:
15% of mucinous borderline tumors.
Complex papillae with columnar mucin-containing cells that resemble endocervical cells as well as indifferent polygonal cells with abundant eosinophilic cytoplasm.
Acute inflammatory infiltrate in stroma and epithelial lining.
No intestinal differentiation.
No association with pseudomyxoma peritonei.

Intestinal-type mucinous borderline tumors(IMBTs):
Intestinal type epithelium with goblet cells.
Stratified lining to 2-3 layers, nuclear atypia, usually mild or moderate.
No microinvasion >10mm².
Almost always stage I
Intestinal –type mucinous borderline mucinous tumor associated with pseudomyxoma ovarii and pseudomyxoma peritonei:
Almost always metastatic, usually from the appendix.

IMBTs in association with a dermoid cyst:
Association with pseudomyxoma ovarii and pseudomyxoma peritonei.

Grade 3 nuclear atypia in IMBTs:
Intraepithelial carcinoma.

Mucinous cystadenocarcinoma
Primary vs metastatic mucinous tumors:
Exclude metastatic mucinous tumors by applying features common among primary ovarian mucinous tumors including unilaterality, size> 15 cm, smooth capsule, and lack of extraovarian spread and features common among metastatic mucinous tumors of the ovary including bilaterality, small size, surface involvement, nodular involvement and destructive stromal invasion and immunostains(CK7, CK20, ER and CDX).

Expansile invasion vs infiltrative invasion in mucinous cystadenocarcinoma:
It is important to differentiate between mucinous cystadenocarcinoma with expansile invasion and infiltrative invasion since mucinous cystadenocarcinoma with expansile invasion are almost invariably stage I and recur in only about 5 % of cases.

Expansile invasion: Confluent growth(>10 mm2) of back-to-back or almost back-to-back glands or cysts lined by malignant epithelium.

Infiltrative invasion: Irregular infiltration of stroma by clusters, cords, nests or irregularly shaped glands. Usually fatal, stage II or higher in one half of cases.

Mucinous tumors with mural nodules:
Sarcoma-like mural nodules vs anaplastic carcinoma nodules vs sarcomas.
CLEAR-CELL TUMORS
5% of all ovarian tumors and more frequently associated with endometriosis (truncating mutations in ARIDIA).

Clear-cell carcinoma with typical morphology:

**Immunophenotypic features:**
- Hepatocyte nuclear factor (HNF) +
- Estrogen receptor (ER) –
- Progesterone receptor (PR) –
- Wilms tumor 1 (WT1) –
- P53 –

Clear-cell carcinoma vs serous borderline tumor:
Differential diagnostic problem not well recognized.
Unilaterality, nonhierarchical branching, a monomorphic cell population, luminal hobnail cell, at least focally marked cytologic atypia, presence of endometriosis, immunoprofile of WT1-/ER-, and more typical clear-cell carcinoma patterns elsewhere in the tumor are helpful in distinguishing clear-cell carcinoma from serous borderline tumor.

Reference