Ovarian tumors

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3 cell types in the normal ovary

• Surface (coelomic epithelium)
  ...the origin of the great majority of ovarian tumors
  ...90% of malignant ovarian tumors

• Totipotent germ cells

• Sex cord-stromal cells
Surface epithelial neoplasms

• Benign:
  …cystadenoma
  …cystadenofibroma

• Malignant:
  …cystadenocarcinoma
  …carcinoma...this term also includes “cystadenocarcinoma”

• Borderline ...better prognosis than overtly malignant tumors
Risk factors for malignant epithelial neoplasms

- Nulliparity
- Family history
- Germline mutations in certain tumor suppressor genes
- More in unmarried women and married women with low parity

*Note: prolonged use of oral contraceptives somewhat reduces the risk!

- 5% to 10% of ovarian cancers are familial, and most of these are associated with mutations in $BRCA1$ and $BRCA2$ tumor suppressor genes
- Average lifetime risk is 30% for carriers of $BRCA1$...less for $BRCA2$
- Mutations in $BRCA1$ and $BRCA2$ are found in only 8% to 10% of sporadic ovarian cancers
Surface epithelial tumors, serous neoplasms

- The most common of the ovarian epithelial tumors...and their malignancies are the most common ovarian malignancies

- 60% are benign, 15% are of low malignant potential, and 25% are malignant

- Benign...between 30 & 40 years of age

- Malignant...between 45 & 65 years of age
A brief note on pathogenesis of serous carcinoma

• There are 2 types:
  - **low-grade**
    ...arise on benign or borderline...slow progression
    ...*KRAS, BRAF or ERBB2* mutations
  - **high-grade**
    ...a good number arise from tubal intraepithelial carcinoma rather than ovarian coelomic epithelium!
    ...*TP53* mutations
Serous neoplasms, morphology

• 25% of the benign are bilateral, while 66% of the malignant are bilateral

• Grossly & imaging: malignant are more complex than benign

• Microscopically: the lining in benign is: single layer of tall columnar ciliated papillary formations and psammoma bodies are commonly seen especially in malignant
  ...the main differentiating feature between borderline and overtly malignant is: stromal invasion
Serous neoplasms, clinical notes

- Serous borderline tumors can seed the peritoneum but these implants are: noninvasive
- The survival rate of serous borderline tumors is 100%
- The prognosis of serous carcinoma is generally poor
Surface epithelial neoplasms, mucinous neoplasms

• Mucinous lining

• More likely to be benign than serous

• More likely to be larger than serous

• Much less likely to be bilateral than serous...important to differentiate from Krukenberg tumor

• Ruptured mucinous carcinoma with peritoneal seeding and production of copious amounts of mucin is called: pseudomyxoma peritonei

...in most cases, this clinical condition is caused by mucinous carcinoma of appendix
Surface epithelial neoplasms, endometrioid neoplasms

• Usually are malignant

• 15-30% have concomitant endometrial carcinoma

• Similar morphology to endometrial endometrioid carcinoma

• \textit{PTEN} mutations

• Sometimes associated with ovarian endometriosis
Surface epithelial neoplasms, Brenner tumors

- Most of them are benign
- Transitional epithelium
Germ cell tumors, teratomas

• 15-20% of all ovarian tumors

• More to occur in the first 2 decades of life

• The younger the person, the more likely to be malignant

  ...However, 90% are mature (benign) and the malignant ones (immature) form less than 10%

  minimally differentiated cartilage, bone, muscle, nerve, or other tissues
  ...immature neuroepithelial elements are the most important
Mature cystic teratoma

• Usually these tumors contain cysts lined by epidermis rich in adnexal appendages—hence the common designation *dermoid cysts*

• On imaging the calcification due to tooth-like structures may point to diagnosis

• 90% are unilateral

• For unknown reasons, these neoplasms sometimes produce infertility and are prone to undergo torsion (in 10% to 15% of cases)

• Rarely, limbic encephalitis (a paraneoplastic syndrome) may develop in women with teratomas containing mature neural tissue and often remits with tumor resection

• In about 1% of cases, malignant transformation, usually to a squamous cell carcinoma, is seen
Specialized Teratomas

• The most common example is struma ovarii, which is composed entirely of mature thyroid tissue that may actually cause hyperthyroidism

• Other specialized teratomas may take the form of ovarian carcinoid, which in rare instances produces carcinoid syndrome
Ovarian tumors of surface epithelial origin usually are asymptomatic until they become large enough to cause local pressure symptoms (e.g., pain, gastrointestinal complaints, urinary frequency). Indeed, about 30% of all ovarian neoplasms are discovered incidentally on routine gynecologic examination. Larger masses, particularly the common epithelial tumors, may cause an increase in abdominal girth. Smaller masses, particularly dermoid cysts, sometimes twist on their pedicles (torsion), producing severe abdominal pain that mimics an acute abdomen. Metastatic seeding of malignant serous tumors often causes ascites, whereas functioning ovarian tumors often come to attention because of the endocrinopathies they produce.

**CA-125** (a tumor marker):
- elevated in 75-90% of women with ovarian epithelial cancer
- However, CA-125 is undetectable in up to 50% of women with cancer limited to the ovary
- Also: it is often elevated in a variety of benign conditions and nonovarian cancers
- So it is more helpful to monitor response to therapy more than as screening
Other ovarian neoplasms

- **Other germ cell tumors:**
  - Dysgerminoma...gonadal dysgenesis (e.g., Turner) is a risk factor
  - Endodermal sinus (Yolk sac) tumor
  - Embryonal carcinoma
  - Choriocarcinoma
  - Mixed germ cell tumor

- **Sex cord-stromal tumors:**
  - Granulosa-theca cell tumors
  - Thecoma-fibroma
  - Sertoli-Leydig cell tumors
Non-neoplastic entities

- Physiological (functional) cysts

- Polycystic ovarian disease (Stein-Leventhal syndrome)