Pathology of the Female Genital Tract III
Ovary & Fallopian Tube

Kamran M. Mirza, MD PhD

Modifed from original lecture by Theresa M. Kristopaitis, MD

Topics

• Ovary
  – Cysts, polycystic ovary disease
  – Neoplasms

• Fallopian Tube
Each follicle houses a primary oocyte arrested in the prophase of the first meiotic division. The most developed Graafian follicle releases its ovum during ovulation, i.e., when primary oocyte is being released. If fertilized by the male gamete, resulting in a secondary follicle, and a ovum in the mature ovum, becoming a secondary follicle, and a ovum in the mature ovum. If not fertilized, the Graafian follicle degenerates into the corpus luteum, which eventually degenerates into the corpus albicans.

Follicles

Mesothelium (also called germinal epithelium)
Ovarian follicle

- **Primordial follicle:** Prior to puberty
- **Primary follicle:** (after puberty)
  - Primary oocyte surrounded by single layer of squamous cells (granulosa cells) embedded in ovarian stroma
- **Secondary follicle:**
  - Increased thickness of granulosa cells and formation of the theca folliculi (stroma cells around the follicle)
  - **Graafian (pre-ovulatory) follicle:** final stage

Mature Graafian Follicle

- **Graafian (pre-ovulatory) follicle:** final stage
  - Large antrum filled with fluid (liquor folliculi)
  - Ready to release oocyte in response to LH surge

Corpus Luteum

- After ovulation, remaining wall of graafian follicle transforms into corpus luteum
- Wall of corpus luteum is folded and contains granulosa lutein cells derived from granulosa cells which secrete progesterone
LH acts on Theca cells – induces androgen production
FSH stimulates Granulosa cells – convert androgen to estradiol
Estradiol induces LH surge - leads to ovulation

Ovarian Follicle and Luteal Cysts

- Unruptured Graafian follicle or ruptured follicle that immediately seals
- Multiple, small (~1cm), filled with clear serous fluid
  - Sometimes large (4-5cm)

Polycystic Ovarian Syndrome (PCOS)

- Characterized by
  - Excess secretion of androgenic hormones
  - Persistent anovulation
  - Many subcapsular ovarian cysts -> enlarged ovaries
PCOS Pathogenesis

- Initiating event is not clear
- Increased secretion of LH

PCOS

- 5-10% women
- Multiple clinical sequela

PCOS Pathogenesis

- Initiating event is not clear
- Increased secretion of LH
Androgen is converted in adipose tissue to estrone resulting in what long-term potential complication of PCOS?
A. Cervical squamous cell cancer
B. Uterine endometrioid endometrial cancer
B. Uterine serous papillary endometrial cancer
C. Leiomyosarcoma of uterus

PCOS
- Histology – follicles lined by granulosa cells with hyperplastic theca (interna)
- Theca cells produce androgens
  - Hirsutism
  - Sometimes virilism
  - Acne

PCOS Clinical Sequela
- Reproductive, metabolic, cardiovascular
  - Hirsutism
  - Chronic anovulation, oligomenorrhea, infertility
  - Insulin resistance
  - Obesity
  - Endometrial hyperplasia, endometrioid cancer
PCOS Treatment

- Weight reduction
- Hormonal therapy to interrupt constant excess of androgens
- Metformin
  - DM, metabolic syndrome
  - Increased insulin sensitivity, decreased testosterone, enables LH surging

Ovarian Neoplasms

- Ovarian cancer – 5th leading cause of death in women
- No universally accepted screening modality
Surface Epithelial Tumors

Often cystic

Serous

Mucinous

Benign

Borderline

Malignant

Surface Epithelial Tumors

<table>
<thead>
<tr>
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<th>Serous (%)</th>
<th>Mucinous (%)</th>
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</thead>
</table>
| Benign
  Cystadenomas   | 60         | 80           |
| Age              | 30-40      | 30-40        |
| Gross            | Single     | Multilocular |
| Histology        | Single layer of tall columnar cells | Mucin-producing epithelial cells |
| Malignant
  Cystadenocarcinomas | 30         | 10           |
| Age              | 45-60      | 45-60        |
| Gross            | Bulky      | Bulky        |
| Histology        | Complex papillary formations, invasion of stroma | Complex architecture, cytologic atypia, stroma invasion |

Bilateral tumors: More common than Less common

Benign serous cystadenoma

Cyst with thin and smooth surface

Single layer of lining cells similar to that of fallopian tube mucosa

No cytologic atypia

No invasion
Serous Cystadenocarcinoma

Bulky, solid tumor replacing ovary

Papillary Formations

Stromal invasion

“Psammoma Bodies”

• Concentrally laminated concretions
• Seen with papillae

Benign Mucinous Cystadenoma

Uniform mucin containing epithelial cells
Mucinous cystadenocarcinoma

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Solid and cystic cut surface
Stromal invasion, confluent growth pattern
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“Borderline Tumors”

- Morphology and behavior “in between” benign and malignant
- Limited invasive potential
- Better prognosis than overtly malignant carcinomas
- May seed the peritoneum

Cystadenocarcinomas

- Risk factors: nulliparity, family hx, germline mutations of tumor suppressor genes
  - Prolonged use of OCP may reduce risk
- 5-10% familial
  - BRCA1, BRCA2 mutations
- Overall poor prognosis
  - Stage is major determinant of outcome
    - Mucinous little better than serous
- Tumor marker CA-125 – monitor response to tx and recurrence
Why “nulliparity” increases risk?

- Development of epithelial neoplasms from repeated disruption and repair of epithelial surface
  - MORE with repeat ovulation (nulliparity)
  - LESS with pregnancy, OCPS

Other Surface Epithelial Tumors

<table>
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<tr>
<th>Endometrioid</th>
<th>Brenner</th>
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Ovarian Neoplasms
Germ Cell Tumors

- 15% - 20% of all ovarian tumors
- Children and young adults

Histogenesis of Tumors of: Germ Cell Origin

Teratomas

*slide revisit from Neoplasia I lecture*

<table>
<thead>
<tr>
<th>Tissue of Origin</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derived from 1 germ cell layer</td>
<td>Pleomorphic Adenoma</td>
<td>Malignant mixed tumor of salivary gland</td>
</tr>
<tr>
<td>Salivary Glands (epithelium + myxoid stroma)</td>
<td></td>
<td></td>
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<tr>
<td>Derived from more than one germ layer</td>
<td>Mature teratoma</td>
<td>Immature teratoma, teratocarcinoma</td>
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<tr>
<td>Gonads (arises from totipotential germ cells)</td>
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</tbody>
</table>
Benign Mature (Cystic) Teratoma

- Comprise 90% of all teratomas
- Derive from all germ layers
  - Ectoderm, Endoderm, Mesoderm
    - Hair, bone, cartilage, skin, bronchial/GI epithelium
    - Neural, thyroid
Malignant Teratoma

• ~1% mature teratomas undergo malignant transformation
  – Squamous cell carcinoma
  – Thyroid carcinoma
  – Melanoma

Immature Teratoma

• Presence of immature tissue (usually neural)
• Bulky, necrotic tumors
• Prognostication
  – Grade and Stage
Histogenesis of Tumors of Germ Cell Origin

GERM CELL

Neoplastic transformation

No differentiation

Dysgerminoma

Differentiation

Primordial Embryonal Carcinoma

Endodermal Sinus Tumor (yolk sac tumor)

Choriocarcinoma

Embryonic Tissue

Teratoma

Differentiation

Early metastasis

Often fatal

Dysgerminoma

Endodermal Sinus Tumor (Yolk Sac Tumor)

Choriocarcinoma

Embryonal Carcinoma

Behavior

Malignant

Radiosensitive

Malignant

Malignant

Gross

Solid mass

Friable mass

Small, hemorrhagic

Unilateral mass

Histology

Large cells, clear cytoplasm

Stroma with lymphocytes

Schiller-Duvall Bodies (glomerulus like structure)

Like placental tissue with Trophoblasts and syncytiotrophoblast

NO villi

Large primitive cells

Tumor marker

LDH, AFP, hCG

Other

Male counterpart = testis

Seminoma; Associated with Gondal Dysgenesis

Pure choriocarcinoma rare; usually component of other germ cell tumor

Dysgerminoma

Large cells with clear cytoplasm

Stroma with lymphocytes
Endodermal Sinus Tumor

Schiller-Duval Body
Central vessel surrounded by tumor cells

Sex-Cord Stromal Tumors

- Originate from undifferentiated gonadal mesenchyme
- Any age
- Most benign, low malignant potential
- Hormonally active
Granulosa Cell Tumor

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<tr>
<th>Histology</th>
<th>Sertoli–Leydig cell tumor</th>
<th>Thecoma–Fibroma</th>
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<tr>
<td>Neoplastic granulosa cells; “Call-exner bodies”</td>
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Endocrine

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<th>Estrogen Production</th>
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Clinical

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<th>Reproductive Age – bleeding</th>
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<td>Postmenopause– endometrial hyperplasia</td>
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Granulosa Cell Tumor

Call-Exner bodies: gland like structures filled with eosinophilic material Recapitulate ovarian follicle

Fibroma-Thecoma

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<th>Well circumscribed firm mass</th>
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<td>Bland spindle-shaped cells (fibroma)</td>
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Plump, lipid-laden cells (thecoma)
Ovarian Neoplasms

Krukenberg tumor

• Metastatic mucinous tumor to the ovaries
  — Gastric most common

Fallopian Tube

• Salpingitis
  — Inflammation as component of PID
• Paratubal Cysts
  — Common
• Adenocarcinomas
  — Serous or endometrioid type
  — BRCA association
  — Usually present at advanced stage
FIN

kamran.mirza@lumc.edu

@kmirza