

Gynecologic Pathology III Pathology of the Ovary and Fallopian Tube

Carey Z. August, M.D.

*Attending Pathologist, Advocate Illinois Masonic Medical
Center*

Clinical Assistant Professor of Pathology, UIC

Phone: 773-296-7900

e-mail: carey.august-MD@advocatehealth.com

UIC College of Medicine

M2 Pathology Course

Lecture #55

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10:30-11:20

Reading: Robbins Pathologic Basis of Disease, 1999, 6th edition, pp.1065-1079

Summary: This lecture will review the causes of the adnexal mass, not only on the basis of biologic behavior and cell of origin, but also with respect to the likely possibilities given the clinical presentation of the individual patient. The concept of borderline malignancy in ovarian epithelial neoplasms and general concepts of spread and staging of ovarian carcinoma will be reviewed. The major diseases of the fallopian tube will be presented.

Keywords: Ovary, Fallopian tube, serous, endometrioid, mucinous, borderline, germ cell, sex cord-stromal tumor, Krukenberg.

Goals and objectives:

The student should know the information in the reading and the hand-out. In particular:

1. Given a clinical history, determine the most likely cause of an adnexal mass in a female patient.
2. Understand the distinction between the 3 major categories of ovarian neoplasm in terms of cell of origin.
3. Understand the morphologic and biologic differences between ovarian epithelial tumors which are classified as benign, borderline, and malignant.
4. Know the distinction between a Krukenberg tumor and other secondary ovarian tumors.
5. Describe the sequelae of salpingitis.

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Ovary

I. General comments

- A. Most ovarian pathology will present with an adnexal mass.

- B. Important clinical questions and findings:
 - Age? Hormonal abnormalities (hirsutism, anovulation, abnormal uterine bleeding)?
 - Unilateral vs. bilateral? Pleural effusion or ascites? Functional? Cystic vs. solid?
 - Complex vs. simple (imaging studies)?

- C. Classifications;
 - Neoplastic vs. non-neoplastic
 - Functional vs. non-functional
 - Neoplasms: epithelial, germ cell, sex cord-stromal, metastatic, other.

II. Non-neoplastic and functional cystic lesions

- A. May present with pain and/or mass.

- B. May change with menstrual cycles and/or hormone therapy.

- C. Follicle cyst-unruptured Graafian follicle, lined by granulosa cells.

- D. Corpus luteum cysts-cystic change in a corpus luteum.

- E. Theca lutein cysts- proliferation of the theca interna layer; cysts associated with high levels of HCG.

- F. Polycystic ovarian disease-follicle cysts with hyperplastic theca interna and cortical fibrosis
 - Stein-Leventhal Syndrome: PCOD with oligomenorrhea; may also have persistent anovulation, obesity, hirsutism, infertility. Unopposed estrogen stimulation of the anovulation may lead to endometrial hyperplasia and adenocarcinoma.

III. Epithelial tumors

- Two basic ways of classifying these:
 - Epithelial cell type giving rise to the tumor: serous, endometrioid, mucinous, other
 - Biologic behavior: benign (“cystadenoma”, “cystadenofibroma”, adenofibroma”), borderline (“low malignant potential”), malignant (“cystadenocarcinoma”)

- A. Serous-tall columnar cells resembling those of the fallopian tube
 - frequently contain psammoma bodies (laminated calcifications)
 - Most common of the epithelial tumors
 - Most common of the epithelial tumors to be bilateral.
 - Most common malignant epithelial tumor.

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1. Benign-may be simple cyst lined by serous epithelium or may be mixture of fibrous tissue and simple papillary structures. No cytologic atypia, no stratification of cells or tufting, and no invasion of underlying stroma.
2. Borderline-predominantly cystic with areas of papillary excrescences showing cytologic atypia, stratification of cells and tufting and increased mitotic rate; no invasion of underlying stroma.
3. Malignant-papillary adenocarcinoma with destructive invasion of stroma and complex glandular pattern.

B. Mucinous-columnar cells containing mucin vacuoles-may resemble mucinous cells of either the intestines or the endocervix

- least frequent of the 3 main epithelial tumor types to be bilateral.
- least frequent of the 3 main epithelial tumor types to be malignant.

1. Benign-multiloculated cystic masses filled with viscous fluid-monolayer mucinous epithelial lining.
2. Borderline-have areas of papillary excrescences and stratification of cells, tufting, cytologic atypia, increased mitotic rate; no invasion of underlying stroma.
3. Malignant-mucin-producing adenocarcinoma with destructive invasion of stroma and complex glandular pattern.

C. Endometrioid-most endometrioid tumors are malignant (carcinoma).

-epithelium is columnar, looks like normal proliferative endometrial epithelium.

1. Benign-nonneoplastic endometrioma –cyst with degenerating hemorrhagic material lined by simple endometrial-type epithelium and stroma.
2. Borderline-have areas of papillary excrescences and stratification of cells, tufting, cytologic atypia, increased mitotic rate; no invasion of underlying stroma.
3. Malignant-adenocarcinoma with destructive invasion of stroma and complex glandular pattern; looks like endometrioid adenocarcinoma of the endometrium.
 - 15% of endometrioid adenocarcinomas of the ovary appear to arise from endometriosis.
 - 15-30% of endometrioid adenocarcinomas of the ovary patients have a concomitant endometrioid adenocarcinoma of the endometrium

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D. Other types of epithelial tumors

1. Clear cell adenocarcinoma-malignant; may also be associated with endometrioid differentiation and endometriosis.

2. Brenner tumor-adenofibroma (i.e., solid with epithelial structures that generally resemble urothelial cells set in a fibrous background); most are benign, but rare borderline and malignant forms exist

3. Small cell carcinoma-highly aggressive malignant tumor composed of small cells; associated with hypercalcemia in 30% of cases; patients are generally younger than patients with other types of ovarian carcinoma.

E. Other important information about ovarian carcinoma (epithelial malignancies)

1. Generally occur in patients 40-70 (borderline tumors present in a slightly younger age group).

2. Besides a palpable mass, ovarian carcinoma may cause vague GI and urinary symptoms, ascites, and pain. Because many of the symptoms are vague, there may be delay in diagnosis, so many patients are diagnosed at an advanced stage.

3. Ovarian carcinoma spreads not only to lymph nodes and hematogenously, but very commonly on peritoneal surfaces leading to ascites and adhesions. Thus, surgery includes TAH, BSO, omentectomy, pelvic washes, lymph node biopsy and removal of as much of this peritoneal "seeding" as possible.

4. Staging of ALL ovarian malignancies (germ cell and sex-cord stromal, too):
 - I. Confined to ovaries
 - II. Tumor involves peritoneal tissue in the pelvis
 - III. Tumor involves peritoneal tissue outside the pelvis and/or regional lymph nodes
 - IV. Distant parenchymal metastases.

5. Risk of ovarian cancer increased in nulliparous patients and women with family history of ovarian cancer (mutations in the BRCA 1 and BRCA 2 genes associated with increased risk).

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IV. Germ cell tumors-

A. Benign-most are Mature cystic teratoma (“Dermoid”); rarely solid.

1. Common tumors of children and young women. Bilateral in 10-15%.
2. Contain mature tissues from all 3 germ layers. Hair, cheesy material, even teeth!
You don’t want to rupture it in the patient during surgery—chemical peritonitis.
3. If it is predominantly thyroid tissue-“struma ovarii”.
4. May contain a carcinoid, which will vary rarely be malignant.
5. Very, very rarely, a carcinoma arises in one of the tissue elements.

B. Malignant

1. Immature teratoma-solid tumor in adolescents and young women
 - Contains tissues from all 3 germ layers, but they are immature (like fetal tissue).
 - The more immature neuroepithelium they have, the more aggressive the tumor.
2. Dysgerminoma-unilateral solid tumor, generally of 2nd and 3rd decades
 - ovarian counterpart of testicular seminoma (large, “fried-egg” tumor cells in nests separated by lymphocytes and plasma cells).
 - some arise in patients with gonadal dysgenesis
 - may contain rare syncytiotrophoblast cells, yielding elevated serum betaHCG
 - sensitive to radiation and chemotherapy
3. Endodermal sinus tumor (Yolk sac tumor)
 - unilateral, highly aggressive tumor of children and young women
 - characteristic histologic findings: Schiller-Duval body (blood vessel enveloped by the tumor cells, surrounded by a space lined by tumor cells), hyaline droplets.
 - produce alpha fetoprotein (AFP) and alpha 1-antitrypsin—use AFP as serum tumor marker.
4. Choriocarcinoma
 - highly aggressive tumor generally seen in association with other germ cell malignancies.
 - hemorrhage, necrosis, highly atypical cytotrophoblast and syncytiotrophoblast.
 - elevated serum levels of beta HCG

5. Mixed germ cell tumors

V. Sex-cord-stromal tumors-granulosa, theca, fibromatous, Leydig, Sertoli, combinations

A. Fibroma/Thecoma/Fibrothecoma (they are frequently mixed).

1. Solid, unilateral tumors of women usually >40 yo; virtually all benign.
2. Spindle cell tumors with collagenous background. Theca cells plumper.
3. Large fibroma with ascites and right-sided pleural effusion=Meig’s syndrome.

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4. Thecoma may have estrogenic effects.

5. Basal cell-nevus syndrome patients may have multinodular, bilateral fibromas, at a younger age than typical fibroma patients.

B. Granulosa cell tumor

1. 2/3 in postmenopausal patients-estrogenic effects may lead to abnormal uterine bleeding, endometrial hyperplasia, and rarely endometrial adenocarcinoma.

About 1/3 in prepubertal patients-estrogenic effects lead to precocious puberty
Some have androgenic effects-lead to virilization.

2. Virtually all unilateral. May be solid, cystic, combination.

3. Macrocystic, microcystic, trabecular, solid-patterns of granulosa cells, which are and shaped like coffee beans with longitudinal nuclear grooves. Form Call-Exner bodies when the cells surround eosinophilic material in an attempt to recapitulate follicles.

4. Most are benign, but rare cases may recur or metastasize even years later. We don't always know how to predict which ones will behave in a malignant fashion, so they are all considered "potentially" malignant.

C. Others-Sertoli-Leydig Cell, Hilus cell, Gonadoblastoma, Pregnancy luteoma

VI. Metastatic tumors

A. Most common metastases are from other parts of the female genital tract ("Mullerian").

B. Most common extraMullerian metastases are from breast and GI tract.

C. Krukenberg tumor=metastatic signet ring cell carcinoma; usually bilateral, usually of gastric origin.

FALLOPIAN TUBE

I. Ectopic pregnancy

II. Endometriosis

III. Salpingitis-acute suppurative (mostly gonococcal)

Chronic salpingitis-results in changes of fallopian tube structure leading to infertility.

IV. Paratubal cysts and Hydatids of Morgagni-simple serous cysts; benign

V. Adenocarcinoma-rare; looks like ovarian serous adenocarcinoma.