

Lecture 4

Ovarian Cysts and Tumors



432 Pathology Team

Done By: Abdulmohsen Al-Meshari

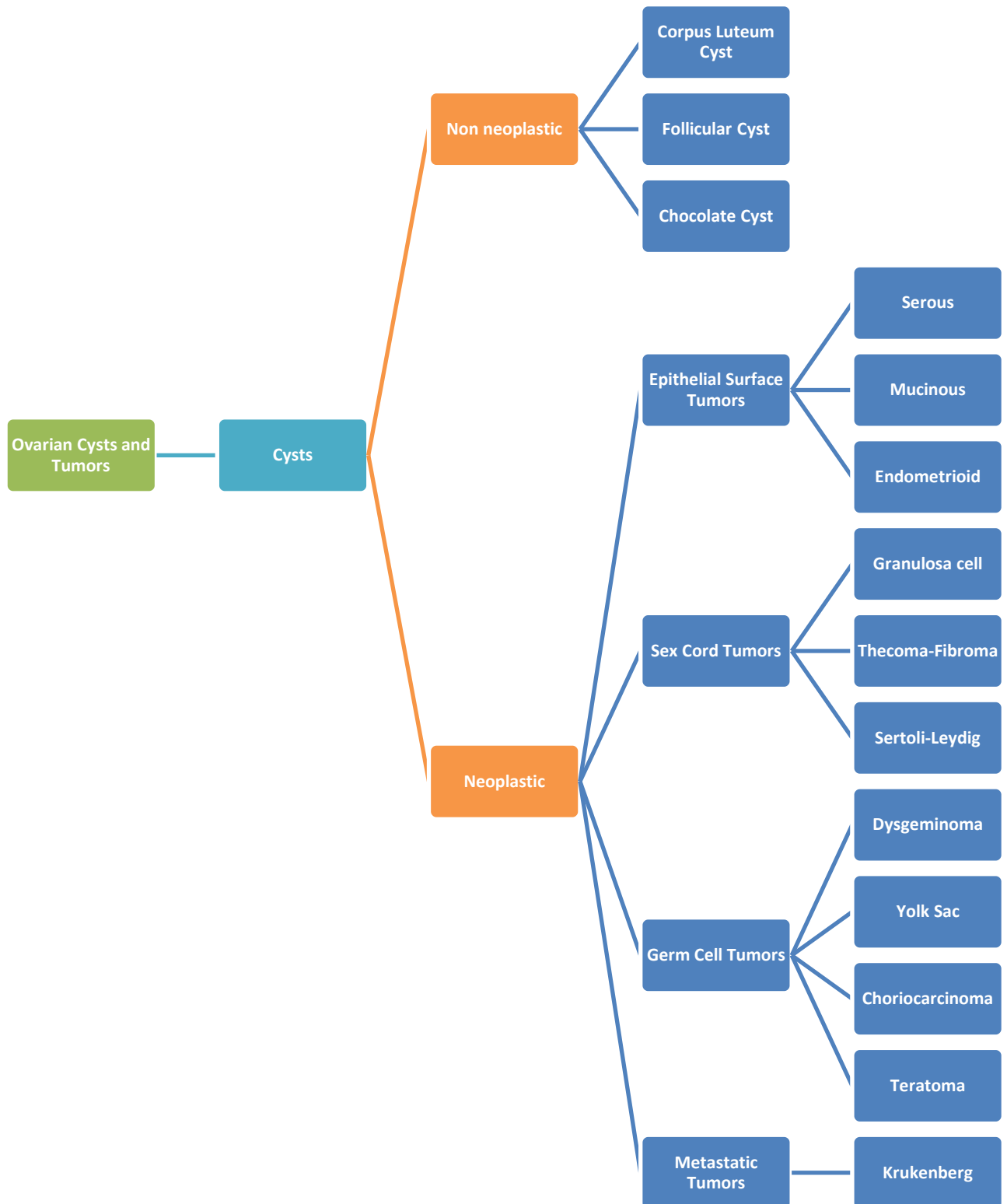
Reviewed By: Eman Al-Bedia

Reproductive Block



Ovarian Cysts and Tumors

Mind Map:



Introduction:

The ovaries are affected by physiologic changes involving the menstrual cycle, changes associated with aging, as well as a variety of tumors from its component tissues. Ovarian masses can be either Physiological or Neoplastic (Benign or Malignant). In the U.S., carcinomas of the ovaries account for more deaths than do cancers of the cervix and uterine corpus combined. Their silent growth makes them one of the **most dangerous tumors** known to the human body. Ovarian cysts are commonplace and can be broadly divided into those arising from the ovarian follicle and those with an epithelial lining. The most important medical problem in ovaries are the neoplasms. Non Neoplastic cysts are common but they are not serious problems. Primary inflammation of ovaries is rare. Salpingitis of the fallopian tubes frequently causes periovarian reaction. (Salpingo-Oophoritis).

I/ Non Neoplastic and Functional Cysts of the Ovary

- Non Neoplastic Cyst are more common than the neoplastic.
- Corpus Luteum and Follicular cysts → **physiological** cysts.

A. Corpus Luteum Cyst

- A corpus luteum cyst results from **delayed resolution** of a corpus luteum's central cavity and **hemorrhage** into this persistent mature corpus luteum.
- This condition is self-limited.

B. Follicular Cysts

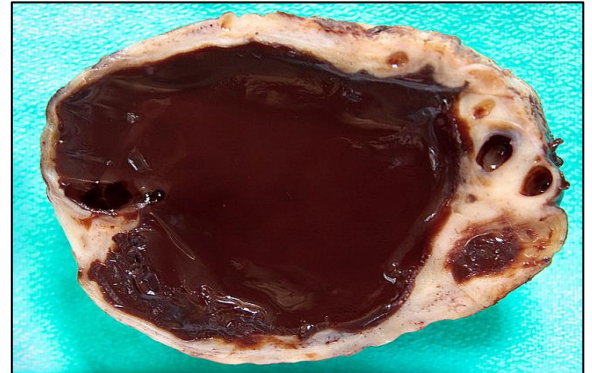
- Are thin walled fluid filled structures lined **internally by granulosa cells and externally by theca interna cells**.
- They arise from the ovarian follicles and are less than 5 cm.
- Are due to distension of **un-ruptured graafian follicle**.



Occasionally such cysts may reach several centimeters in size and, if they rupture, can cause abdominal pain.

C. Chocolate/Endometriotic Cyst

- Chocolate cyst is a blood containing cyst resulting from **endometriosis** with hemorrhage.
- Under the microscope you'll find:
 1. Endometrial epithelium (Gland)
 2. Stroma (Beneath it)
 3. Macrophages (Hemosiderin laden macrophages)You don't need all 3 to diagnose. 2 of 3 are enough.



NOTE: Endometriosis: The presence of endometrium elsewhere than in the lining of the uterus; causes premenstrual pain and dysmenorrhea.

NOTE: The doctor focused on the microscopic findings.

II/ Ovarian Neoplasms

- The fifth most common cancer in US women.
- 80% are benign – young (20-45).
- 20% are Malignant - older (>40).
- 6% of all cancers in women.
- **50% deaths** due to **late detection**. (As we mentioned earlier, SILENT tumors).

Risk Factors:

- Null parity(**Parity: the number of liveborn children a woman has delivered**).
- Gonadal Dysgenesis.
- Family History.
- Ovarian cancer genes.
- BRCA1 (17q12) & BRCA2(13q12) (Cancer suppressor, Breast & ovary).

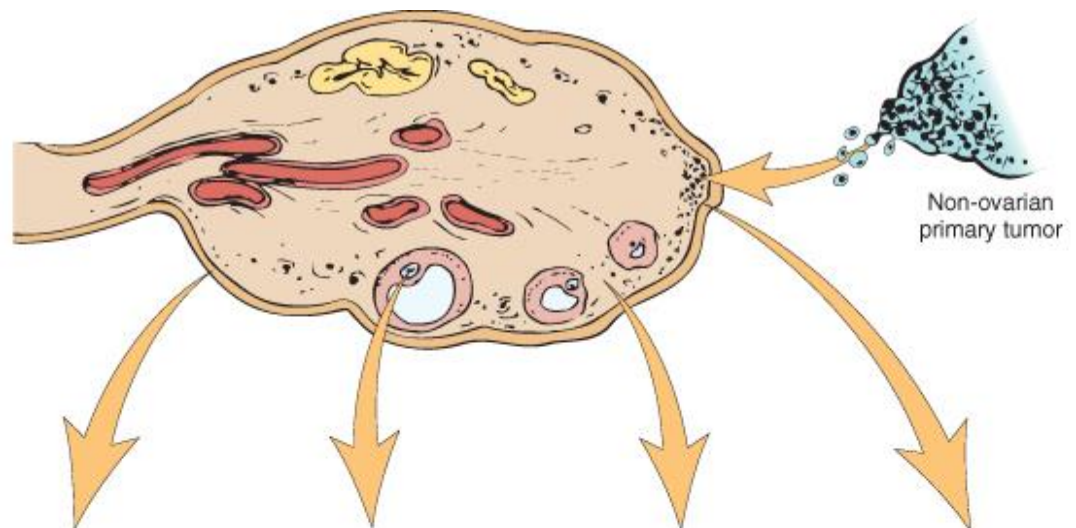
Classification:

There are THREE main types of primary ovarian tumors:

1. **Epithelial Surface Tm:** are derived from the **cells on the surface** of the ovary. This is the **most common** form of ovarian cancer and occurs primarily in adults.
2. **Germ Cell Tm:** ovarian tumors are derived from the egg producing cells within the body of the ovary. This occurs primarily in **children and teens** and is rare by comparison to epithelial ovarian tumors.
3. **Sex Cord Tm:** ovarian tumors are also rare in comparison to epithelial tumors and this class of tumors often **produces steroid hormones**.

In addition cancers derived from other organs can also spread to the ovaries Secondary /**Metastatic** Tumors.

NOTE: Because the 3 major cell types make up the normal ovary, there are >25 types of ovarian tumors each with many variants.



ORIGIN	SURFACE EPITHELIAL CELLS (Surface epithelial–stromal cell tumors)	GERM CELL	SEX CORD–STROMA	METASTASIS TO OVARIES
Overall frequency	65%-70%	15%-20%	5%-10%	5%
Proportion of malignant ovarian tumors	90%	3%-5%	2%-3%	5%
Age group affected	20+ years	0-25+ years	All ages	Variable
Types	<ul style="list-style-type: none"> • Serous tumor • Mucinous tumor • Endometrioid tumor • Clear cell tumor • Brenner tumor • Cystadenofibroma 	<ul style="list-style-type: none"> • Teratoma • Dysgerminoma • Endodermal sinus tumor • Choriocarcinoma 	<ul style="list-style-type: none"> • Fibroma • Granulosa–theca cell tumor • Sertoli–Leydig cell tumor 	

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II/ 1. Surface Epithelial Tumors

- Most common primary neoplasms
- 90% of malignant tumors of ovary

Examples:

- Serous** (tubal = Fallopian tube epithelium).
- Mucinous** (endocervical & intestinal (**goblet cells**) mucin secreting type cells).
- Endometrioid**.
- Transitional cell (Brenners tumor)** .

Morphologically:

- Cystic** – eg: Cystadenomas
- Solid/cystic** – eg: Cystadenofibromas
- Solid** – eg: Adenofibromas

All types can be benign, borderline , or malignant:

- **Benign** : -**Gross**: mostly cystic. **Microscopic**: fine papillae, single layer covering (no stratification), no nuclear atypia, no stromal invasion.
- **Borderline**: **Gross**: cystic / solid foci. **Microscopic**; papillary complexity, stratification, nuclear atypia, no stromal invasion.
- **Malignant** : **Gross**: mostly solid & hemorrhage / necrosis. **Microscopic**: papillary complexity, stratification, nuclear atypia, **stromal invasion**.

NOTE: Borderline is a level between benign and malignant, without stromal invasion.

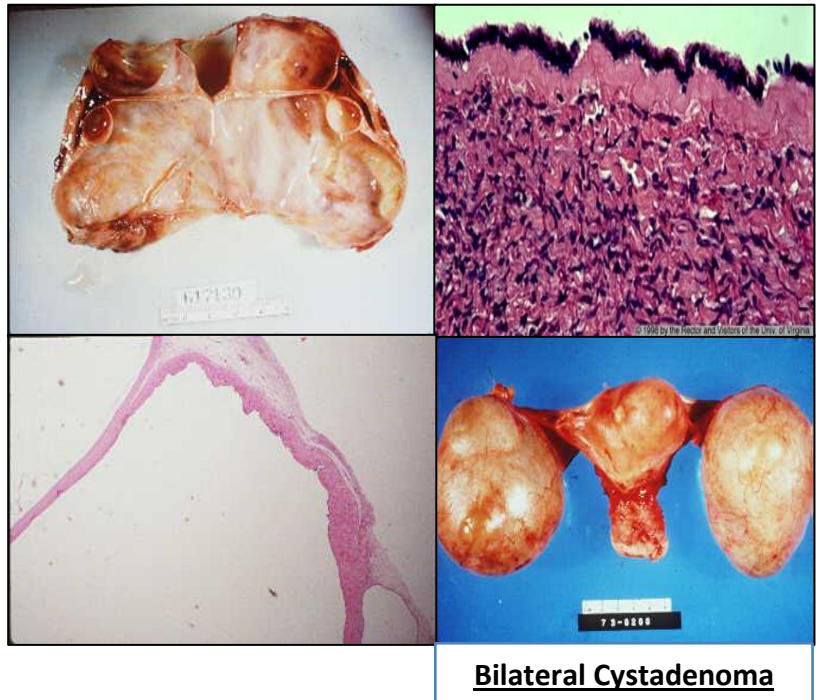
A. Serous Tumors

- Frequently bilateral (30-66%).
- 75% benign/borderline, 25% malignant.
- One unilocular cysts, papillary/less solid → **benign/borderline**
- Tall columnar ciliated epithelium.
- Papillary, solid, hemorrhage, necrosis or adhesions → **malignancy**
- Extension to peritoneum – bad prognosis.

Serous Cystadenoma: (Benign):

Microscopically:

- Single layer of columnar ciliated
- Fine papillae

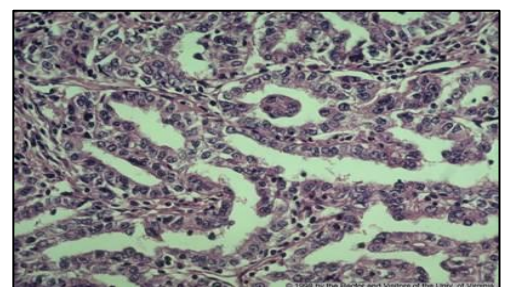


Serous Cystadenocarcinoma: (Malignant):

- Malignant serous tumor (**serous cystadenocarcinoma**) is the commonest malignant ovarian tumor, forming about a third of all cancers of the ovary.
- The tumors are **partly cystic and partly solid** with exuberant excrescences, often with **necrosis and hemorrhage**.
- Ovarian surface involvement may be present.
- These tumors usually present with **ascites** due to abdominal metastases

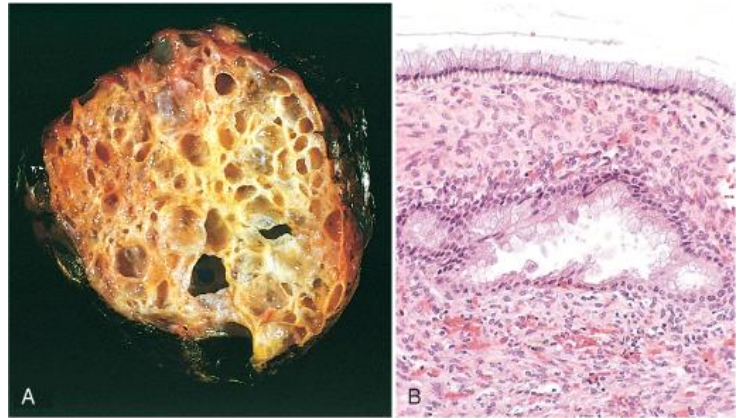
Microscopically:

- Papillary complexity
- **Nuclear stratification & atypia**
- Stromal invasion
- **Psammoma bodies** (Concentric Calcifications)



B. Mucinous Tumors

- Less common 25%, very large.
- Rarely malignant - 15%.
- Multiloculated, many small cysts.
- Rarely bilateral – 5-20%.
- Tall columnar, apical mucin.
- Pseudomyxoma peritonei.

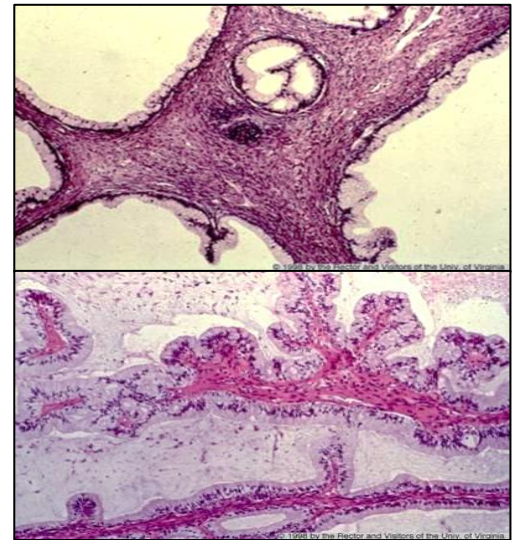


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Mucinous Cystadenoma:

Microscopically:

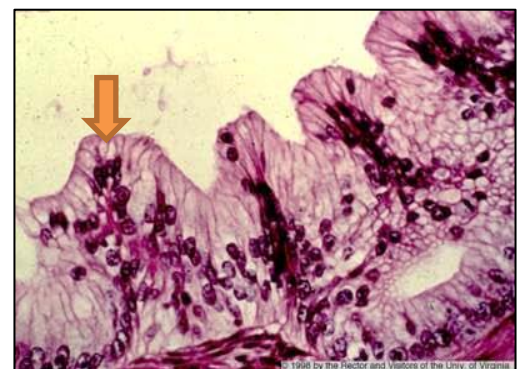
Multilocular cyst lined by **single layer** of columnar cells with basally placed nuclei and apical mucin.



Mucinous Cystadenoma-Borderline:

Microscopically:

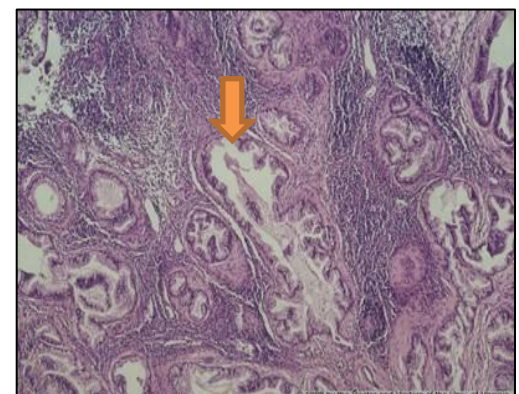
- Papillary complexity
- Nuclear stratification & atypia
- **No stromal invasion**



Mucinous Cystadenocarcinoma:

Microscopically:

- Papillary complexity
- Nuclear stratification & atypia
- **stromal invasion**



C. Endometrioid Tumors

- Most are **unilateral** (40% are bilateral)
- Cells look **like endometrium** even though they are coming from the ovary.
- Most of them are malignant
- About 20% of all ovarian tumors
- **Many are associated with endometrial cancer (30%)** in patient who has chocolate cyst.
- Patient may have concurrent endometriosis

Endometrioid Adenocarcinoma:

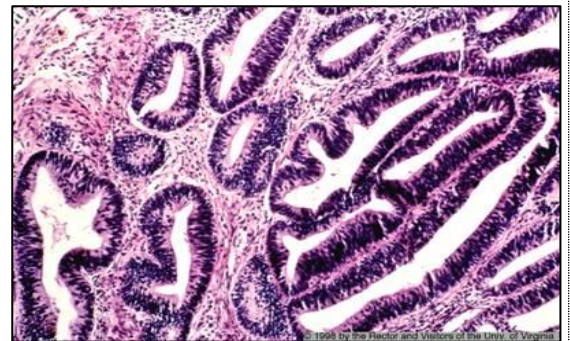
Gross:

Solid/Cystfilled by hemorrhage and Necrosis.



Histo:

Stromal invasion by irregular malignant endometrial glands.



REMEMBER:

In Surface Epithelial tumors:

All types can be benign, borderline , or malignant:

- **Benign** : -**Gross**: mostly cystic. **Microscopic**: fine papillae, single layer covering (no stratification), no nuclear atypia, no stromal invasion
- **Borderline** : **Gross**: cystic / solid foci. **Microscopic**; papillary complexity, stratification, nuclear atypia, no stromal invasion
- **Malignant** : **Gross**: mostly solid & hemorrhage / necrosis. **Microscopic**: papillary complexity, stratification, nuclear atypia, stromal invasion

II/ 2. Sex Cord-Stromal Tumors

A. Granulosa Cell Tumor

- Unilateral, solid and cystic.
- Hormonally active tumor.
- The most common **estrogenic ovarian neoplasm**.
- Can be associated with endometrial hyperplasia and carcinoma.
- The **adult form** occurs mainly in **postmenopausal women**, associated with endometrial hyperplasia and carcinoma .
- The **juvenile type** occurs in the first two decades, cause **precocious (Early) sexual development**.

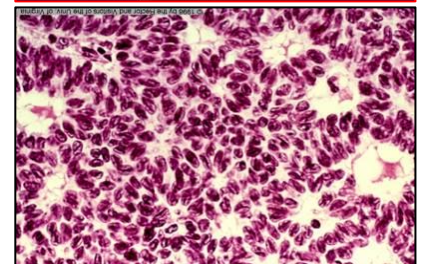
Gross:

Solid with hemorrhage.



Histo:

Sheets of granulosa cells containing spaces lined by the cells to give a follicle-like appearance (Call-Exner bodies). The nuclei have a coffee bean like appearance. (Grooved nuclei)



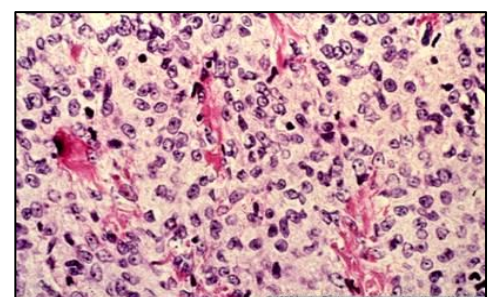
B. Thecoma-Fibroma

- Functional tumors producing **estrogen**.
- It occur in postmenopausal women.
- Endometrial hyperplasia or carcinoma may develop.

Gross: Solid tumor with variegated **yellow - orange appearance**. (Color depends on amount of lipid)



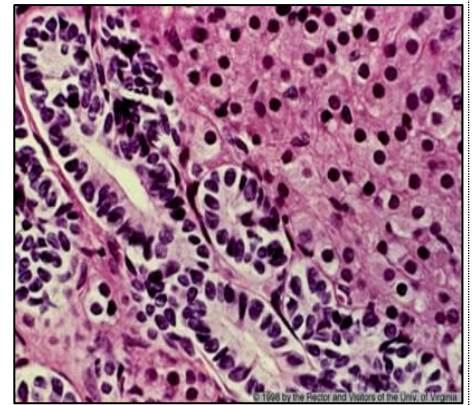
Histo: sheets of round to oval cells with pale cytoplasm containing lipid



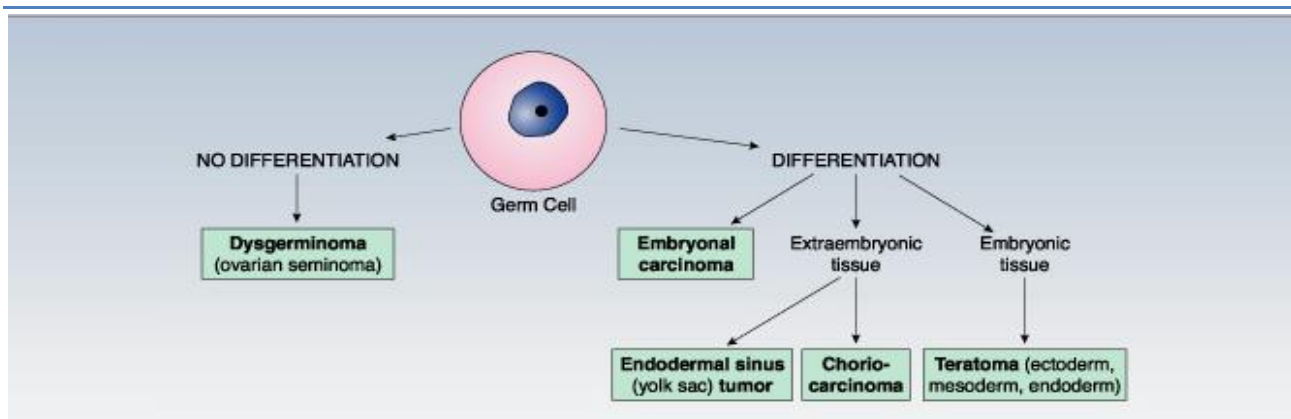
C. Sertoli-Leydig Cell Tumors

- 1% of ovarian neoplasms
- It occur predominantly in young women.
- Commonly **androgenic**, cause defeminization of women manifested as breast atrophy, amenorrhea, and loss of hair and hip fat , to virilization with hirsutism.

Histo: Tubules lined by Sertoli cells and sheet of Leydig cells.

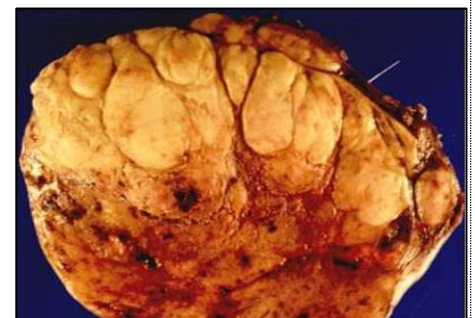


II/ 3. Germ Cell Tumors

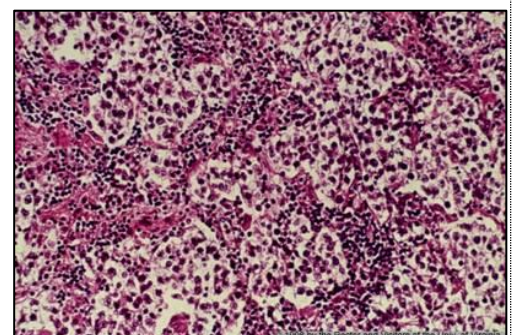


A. Dysgerminoma

- The ovarian counterpart of the **testicular seminoma**
- 2% of all ovarian malignancies
- **Most common malignant germ cell tumor**
- Affects primarily younger females with the majority in the second and third decades.
- It is the **most frequently encountered ovarian malignancy in pregnancy**
- An excellent prognosis. Highly radiosensitive .
- **Composed of malignant germ cells, admixed with nonneoplastic chronic inflammatory cells (lymphocytic infiltration) and occasionally granulomatous inflammation.**



Solid/ lobulated mass with foci of hemorrhage



Sheets of monotonous rounded cells with pale cytoplasm and central nuclei

B. Embryonal Carcinoma

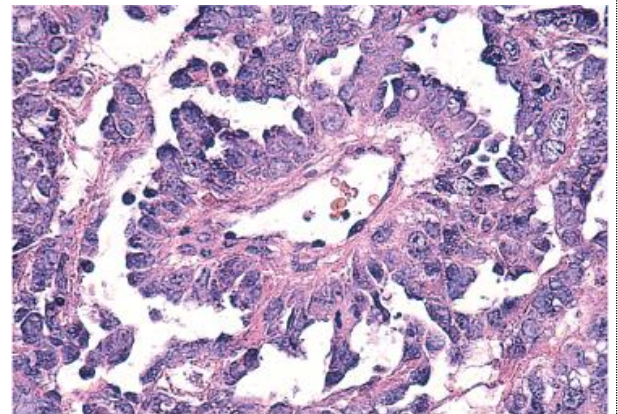
- Uncommon ovarian germ cell neoplasm.
- Usually occurs in combination with yolk sac tumor.
- Occurs in children and young adults.
- Typically unilateral, solid tumor **with hemorrhage and necrosis**.
- Aggressive, highly malignant neoplasm that is radio-resistant but responds to combination chemotherapy.

C. Endodermal Sinus Tumor (Yolk Sac Carcinoma)

- Tumor is a highly malignant and clinically aggressive neoplasm.
- Most frequently in children and young females.
- Can be pure or a component of a mixed germ cell tumor.
- Almost always a unilateral solid or solid cystic.
- Highly malignant neoplasm that is radio resistant but responds to combination chemotherapy.
- **Fatal within 2 years of diagnosis.**
- Associated with elevated serum **AFP (Alpha Feto Protein) levels.**

Histo: Its characteristic histologic feature is a glomerulus-like structure composed of a **central blood vessel** enveloped by **germ cells within a space lined by germ cells** (Schiller-Duval body)

Classic pattern shows perivascular formations (Schiller-Duval bodies) and **eosinophilic globules** that contain AFP



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NOTE: The doctor focused on the Schiller-Duval bodies feature.

D. Choriocarcinoma

- Rare. Occurs as a pure ovarian neoplasm or as a component of a mixed germ cell tumor.
- Occurs in children and young adults.
- Associated with elevated serum **HCG levels** (Human Chorionic Gonadotropin).
- Typically a unilateral, solid, **hemorrhagic tumor**.
- Composed of malignant **cytotrophoblast** and **syncytiotrophoblast**.
- Generally have metastasized widely through the bloodstream to the **lungs**, liver, bone, and other viscera by the time of diagnosis.

E. Teratoma

- 15-20 % of Ovarian tumors.
- Majority in the first 2 decades.
- The younger the patient ,the greater the likelihood of malignancy.
- Tumors are subdivided into **mature, immature and monodermal**.
- Unlike those in the testis, the vast majority of ovarian germ cell tumors are benign mature cystic teratomas.
- **Immature** teratomas are **malignant** and rare.

Mature Cystic Teratoma

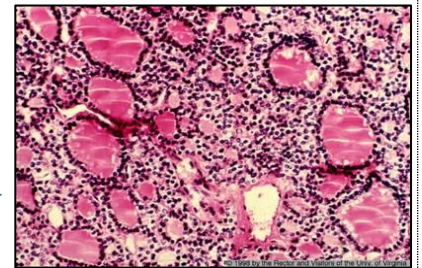
- Most common ovarian teratoma and most common ovarian germ cell tumor
- Benign neoplasm that typically occurs during reproductive years.
- Cystic tumor with firm capsule, filled with sebaceous material and hair (occasionally teeth can be found), thickened area from which hair and teeth arise is called "**Rokitansky's protuberance**".
- Composed of mature elements derived from all three germ layers (ectodermal elements such as skin, hair, sebaceous glands, and mature neural tissue predominate; cartilage, bone, respiratory and intestinal epithelium are common).
- Complications include torsion, rupture, infection, struma ovarii & immature teratoma.

NOTE: Struma Ovarii: A rare ovarian tumor defined by the presence of thyroid tissue comprising more than 50% of the overall mass.

Monodermal Teratoma

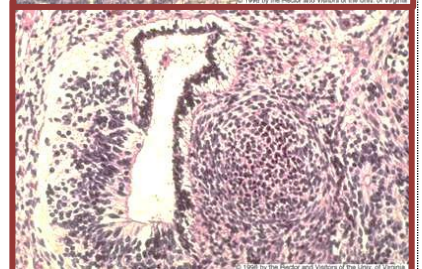
A teratoma composed predominantly of one tissue element.

Most common type is "Struma Ovarii".



Immature Teratoma

- Usually a unilateral, solid tumor.
- Similar to mature teratoma but contains immature or embryonal tissues ,mainly neuroepithelium, with multiple neural tubes



II/ 4. Metastasis to Ovaries

Krukenberg Tumor

- One of the most classic forms of metastatic carcinoma involving the ovaries is the Krukenberg tumor.
- This tumor is a metastatic carcinoma.
- Composed of **signet ring cells** embedded within a hypercellular ovarian stroma that mimics sarcoma.
- The most common sites of origin include stomach, colon and appendix.



NOTE: Signet Ring cell: A malignant cell type seen predominantly in carcinomas that are associated with the stomach. They contain a large amount of mucin which pushes the nucleus to the periphery.

Summary from Robbins

Ovarian Tumors

- Tumors may arise from any of the major components of the ovary: surface epithelium, ovarian stromal and follicle lining granulosa cells, or germ cells.
- Epithelial tumors are the most common malignant ovarian tumors and are more common in women older than 40 years of age.
- The major types of epithelial tumors are serous, endometrioid, and mucinous. Each has a benign, malignant, and a low malignant potential (border-line) counterpart.
- Germ-cell tumors (mostly cystic teratomas) are the most common ovarian tumor in young women; the majority is benign.
- Germ cell tumors may differentiate toward oogonia (dysgerminoma), primitive embryonal tissue (embryonal), yolk sac (endodermal sinus tumor), placental tissue (choriocarcinoma) or multiple fetal tissues (teratoma).
- Sex cord stromal tumors may display differentiation toward granulosa, Sertoli, Leydig or ovarian stromal cell. Depending on differentiation, they may produce estrogens or androgens.

Summary

1/ Non Neoplastic

Tumor	Notes	Microscopic
A. Corpus Luteum Cyst	1-Results from delayed resolution of the corpus luteum. 2- Hemorrhage. 3- Physiological cyst.	_____
B. Follicular Cysts	1- Due to distension of un-ruptured graafian follicle. 2- Lined internally by granulosa cells and externally by theca interna cells.	_____
C. Chocolate/ Endometriotic Cyst	Resulting from endometriosis	1-Gland 2- Stroma 3- Macrophages

II/ Ovarian Neoplasms

Tumor	Notes	Grossly	Microscopically
1. Epithelial Surface Tm	1-From the cells on the surface. 2- Most common	1-Benign: mostly cystic 2- Borderline : solid foci / cystic 3-Malignant: solid & hemorrhage / necrosis	1-Benign: -No nuclear atypia, no stromal invasion. -No stratification 2- Borderline: Nuclear atypia, no stromal invasion, stratification 3- Malignant: Stratification, nuclear atypia, stromal invasion.
Types:			
<ul style="list-style-type: none"> • Serous Tumors a- Serous Cystadenoma: (Benign) 			-Single layer of columnar ciliated -Fine papillae
Serous Cystadenocarcinoma: (Malignant)		1-Partly cystic and partly solid. 2-Necrosis and hemorrhage	1-Nuclear stratification& atypia. 2- Psammoma bodies
<ul style="list-style-type: none"> • Mucinous Tumors: a- Mucinous Cystadenoma-Borderline: 		Pseudomyxoma peritonei	Single layer of columnar cells with basally placed nuclei and apical mucin. - Nuclear stratification& atypia - No stromal invasion
b- Mucinous Cystadenocarcinoma :			- Nuclear stratification& atypia - Stromal invasion
<ul style="list-style-type: none"> • Endometrioid Tumors: a- Endometrioid Adenocarcinoma 		1-Unilateral. 2-Cells look like endometrium Solid/Cystfilled by hemorrhage and Necrosis	Stromal invasion by irregular malignant endometrial glands
2.Germ Cell Tm		Primarily in children and teens	
3.Sex Cord Tm			
a- Granulosa Cell Tumor:	Produces steroid hormones: - Adult form: in postmenopausal women. - Juvenile type: cause precocious (Early) sexual development.		(Call-Exner bodies). The nuclei have a coffee bean like appearance
b- Thecoma-Fibroma :	- Producing estrogen - It occurs in postmenopausal women.	Yellow - orange appearance.	Round to oval cells with pale cytoplasm containing lipid
c- Sertoli-Leydig Cell Tm	-Commonly androgenic. cause defeminization of women		Tubules lined by Sertoli cells and sheet of Leydig cells.

Questions

1/ A 15-year-old girl presents with left lower abdominal pain. She has noted recent enlargement of her breasts. Her last menstrual period was 10 weeks ago. She denies having had sexual intercourse. Serum levels of hCG are markedly elevated. Which of the following is the most likely diagnosis?

- (A) Choriocarcinoma
- (B) Hydatidiform mole
- (C) Mature cystic teratoma
- (D) Serous cyst adenocarcinoma

2/ A 40-year-old woman presents with 6 months of increasing abdominal girth. Gynecologic examination reveals large bilateral ovarian masses. The patient undergoes bilateral oophorectomy. The pathology report reads "Krukenberg tumor," and the histopathologic findings are done. Which of the following tests would likely provide the highest diagnostic yield?

- (A) Serum AFP level
- (B) Biopsy of the cervix and endometrial curettage
- (C) Gastric endoscopy
- (D) Serum hCG level

3/ A 50-year-old woman presents with a 1-month history of intermittent vaginal bleeding. A Pap smear is normal. Pelvic examination reveals a left adnexal mass. A uterine curettage shows complex endometrial hyperplasia without atypia. A CT scan of the abdomen reveals a 5-cm mass replacing the left ovary. The patient undergoes hysterectomy and bilateral salpingo-oophorectomy. Histologic examination of the ovarian mass is done. Which of the following is the appropriate pathologic diagnosis?

- (A) Dysgerminoma
- (B) Endometrioid carcinoma
- (C) Granulosa cell tumor
- (D) Mucinous cyst adenocarcinoma

For more questions please refer to Revision Team files

Answers:

- 1- A
- 2- C
- 3- C

اللهم إني استودعك ما قرأت و ما حفظت و ما تعلمت فرده علي عند حاجتي إليه انك على كل شيء قدير

If there is any mistake or feedback please contact us on: 432PathologyTeam@gmail.com

