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Video Case

Benign and Malignant Ovarian tumors

Objectives:

- → List the differential diagnosis of an ovarian mass
- → Mention the classification of ovarian neoplasms
- → Compare between functional ovarian cysts, benign ovarian tumours, and ovarian cancers in terms of:
  - ○ Etiology & risk factors
  - ○ Cell type of origin
  - ○ Characteristic clinical features
  - ○ Findings in diagnostic investigations
  - ○ Management options
  - ○ Describe staging of primary carcinoma of the ovary

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Female presentation

Video Case | Editing File

Ovarian Masses

In gynecology, **Adnexal / pelvic mass** it is anything next to the uterus, usually involving the fallopian tubes and ovaries.

- As indicated in Table 20-1, Adrenal mass / ovarian masses may be :
  - **Ovarian cyst :** fluid-filled sacs on or in the ovaries.
    - **Functional**
    - **Neoplastic** (benign and malignant)
  - **Inflammatory**
  - **Metaplastic**

TABLE 20-1
DIFFERENTIAL DIAGNOSIS OF OVARIAN MASSES

Pathogenesis	Specific Type
Functional	Follicular cysts Lutein cysts Polycystic ovaries
Inflammatory	Salpingo-oophoritis Pyogenic oophoritis—puerperal, abortal, or related to an intrauterine device Granulomatous oophoritis
Metaplastic	Endometriomas
Neoplastic	Premenarchal years—10% are malignant Menstruating years—15% are malignant Postmenopausal years—50% are malignant

01 Functional Cyst

During the reproductive years the ovaries are functionally active, producing a dominant follicle in the first half of the cycle and a corpus luteum after ovulation in the second half of the menstrual cycle (they develop ≤ 2cm). **Either of these structures, the follicle or corpus luteum, can become fluid-filled and enlarged** (reach a diameter of at least 3 cm) **, producing a functional cyst.**

- Which mean functional cysts result when the normal, cyclic development of the ovarian follicles is disrupted.
- It may appear from time to time as part of the normal function (physiologic) of the ovary and **it is confirmed when the lesion regresses** on Transvaginal US over the course of the next several cycles.

Type	Definition
Follicular cyst (most common ovarian mass in young individual)	Develops when an **ovarian follicle fails to rupture** (LH doesn't happen during a given menstrual cycle)
• **Polycystic ovarian syndrome / PCOS**	Develops when pt have multiple follicular cysts.
Corpus Luteal cyst	develop when **corpus luteum** fails to regress and continues to grow after 14 days
• **> Hemorrhagic corpus luteal cysts**	As it grows, the arteries nourishing it can rupture and hemorrhage.
Theca-lutein cysts (cyst usually bilateral)	Develop when there is more hCG than usual (it's hormone that's produced by the placenta so they're only seen in pregnancy and it is bilateral cyst) (like when there are multiple fetuses or gestational trophoblastic disease, where tumours made up of placental cells causes higher than normal hCG levels)

- **Management :**
  - Can require surgical intervention **only if symptomatic:** Size becomes **larger , Torsion, or** There is **uncontrolled bleeding within the cyst,** (hemorrhagic cyst)

02 Benign and Malignant Ovarian Neoplasms

- Ovarian cancer is the 5th most common cause of cancer death in women in the United States.
- It has the highest mortality rate among gynecological approximately 55% of patients will die within five years of diagnosis

The 3 histological cell types that give arise of benign and malignant ovarian neoplasm:

You need to know each ovarian cancer originate from which cell type

Histological cell types	Classification	Types	
Epithelial ovarian neoplasm (Taken as a group, **the epithelial tumors are by far the most common**)	Benign	**Transitional cell tumor / Brenner tumor**	
		Cystadenoma	**Serous** (most common epithelial ovarian tumors)
			Mucinous
		Endometriomas	
	Borderline	**Serous** or **Mucinous** tumors : Mix of characteristic from benign and malignant	
	malignant	**Endometrioid carcinoma**	
		Cystadenocarcinoma	**Serous** (most common MALIGNANT ovarian and fallopian tubes neoplasm)
			Mucinous
		Clear cell tumors	
Sex cord / stromal ovarian neoplasm	benign	**Ovarian fibroma**	
		Theca cell tumor / thecoma	
		Sertoli-Leydig cell tumor "usually benign"	
	malignant	**Granulosa cell tumor** (most common malignant stromal tumors)	
Germ cell tumors	Benign	Teratoma	**Dermoid cysts / mature cystic teratoma** (most common ovarian neoplasm in all age women / "often in" premenopausal woman)
			• Struma ovarii
	Malignant (the germ cell type is the most common ovarian cancer in women less than 20 years old)		**Immature teratoma**
		Dysgerminoma (most common malignant germ cell tumors)	
		Yolk sac tumor of the ovary / endodermal sinus tumor	
		Non Gestational **choriocarcinoma**	
		Embryonal carcinoma of the ovary	

1 Epithelial Cell Type :

- **It derived from the epithelium (mesothelial) cells lining the surface of the ovary** and also lining the peritoneal cavity.

Epithelial Cell Type cont.

- Cytology and Histology :
  - **A Brenner tumor** resemble transitional cells of the bladder + the cell nuclei are "coffee bean shaped".
  - A **serous tumors** resemble the lining of the fallopian tubes + contain psammoma bodies.
  - A **mucinous ovarian neoplasm** resembles the endocervical epithelium,
  - **Endometriomas** and **endometrioid neoplasm** resembles the endometrium cell
    - Because **endometriomas** functionally the same as the endometrial tissue inside the uterus, it respond to hormones just like the uterus would. And because of this, endometriomas tend to bleed within the cyst cavity during menstruation, and over time, they fill up with old blood that turns a dark brown color **"chocolate cysts"**
  - Clear cell carcinoma: they occur in association with endometriosis.
- CA-125 is tumor marker and monitoring the response treatment for epithelial cell types, it is more useful in postmenopausal women because false-positive measurements occur commonly in premenopausal women in association with endometriosis, pelvic inflammatory disease, or uterine fibroids.

2 Stromal / sex cord cell type :

- Derived from **sex-cord and** specialized **stroma** (granulosa cell and theca cell) of the developing gonads.
- Cytology, Histology and some information :
  - Benign :
    - **Fibroma** : Bundles of fibroblast, associated with **MEIGS' SYNDROME** (fibroma + Ascites + right pleural effusion)
    - **thecoma** : Composed of theca cell.
    - **Sertoli-Leydig cell tumor** : Seminiferous-like tubules lined by Sertoli cells and leydig cell that contain reinke crystals.
  - Malignant :
    - **Granulosa cell tumor** : Granulosa like cells (so there is increase in inhibin " hormone that produce by granulosa cell" < tumor marker)
- They are Hormonally active **EXCEPT** Fibroma because fibroblasts produce the structural and supportive tissues of the ovary and are not associated with hormonal function
- If the ultimate differentiation of cell types is **feminine,** the neoplasm becomes a **granulosa cell tumor**, a **theca cell tumor**, or mixed granulosa-theca cell tumor
  - Because they secrete excessive **estrogen,** They promote feminizing signs and symptoms, such as :

Stromal / sex cord cell type cont.

- Premenarchal: precocious menarche or premenarchal uterine bleeding during infancy and childhood, or precocious thelarche.
- Reproductive : menorrhagia (with alternating amenorrhea), endometrial hyperplasia
- Postmenopausal: Postmenopausal bleeding may occur.

- **Masculine** differentiation become **Sertoli-Leydig cell tumors.**
  - Because they secrete excessive **androgen** (testosterone)**,** They promote virilizing signs and symptoms, such as : hirsutism, Acne, temporal baldness, deepening of the voice, clitoromegaly ,breast atrophy and a defeminizing change in body habitus to a muscular build.

3 Germ Cell Type :

- Derived from the **primary germ cell.**
- Cytology, Histology and some information :
  - Benign :
    - Dermoid cysts / mature cystic teratoma : develop from 1-3 embryological / germinal cell layers : Ectodermal, Mesodermal and Endodermal. it is **defferiated/fully develop** tissue like bone, hair, skin, nails .... Inside.
      - **Most common histology seen is:** Ectodermal skin appendages (hair, sebaceous glands), thus the name "**dermoid"**
  - Malignant : these may be functional producing beta-hCG or α-fetoprotein
    - Immature teratoma : develop from 1-3 embryological / germinal cell layers : Ectodermal, Mesodermal and Endodermal. It is **undifferentiated** fetal tissue.
    - Dysgerminoma : Tumor arise from oocyte, **Associated with ↑ LDH**.
    - Endodermal sinus tumor - Yolk Sac : resembles the **yolk sac**, Associated with↑ α-fetoprotein

Granulosa or theca cell Tumors Triad:
- pelvic mass
- β-hCG negative
- feminine
- ↑estrogen level

Sertoli-Leydig Tumor Triad:
- pelvic mass
- β-hCG negative
- Masculinization
- ↑ testosterone level

Benign Cystic Teratoma Triad:
- Pelvic mass
- β-hCG negative
- Sonogram complex mass (**calcifications**)

Dysgerminoma Triad:
- pelvic mass
- β-hCG negative
- **↑ LDH level** >11

Yolk sac tumor Triad:
- pelvic mass
- β-hCG negative
- ↑ AFP

Metastatic tumors / secondary cancer

The most common sources are the:

1. Breast
2. GI: colon
3. GI: gastric
4. Endometriums.

Krukenberg tumors: a metastatic malignancy of the ovary (bilateral ovarian mass) characterized by mucin-rich signet-ring adenocarcinoma that primarily arises from a gastrointestinal site (stomach) in most cases and less commonly from other site

Risk factor of ovarian cancer

The cause of ovarian cancer is unknown. The patient characteristics found to be associated with an increased risk for ovarian cancer include :

- Family history of cancer of the ovary, breast, or bowel
  - The breast-ovarian cancer syndrome is caused by germline mutations in BRCA1 or BRCA2,
  - Lynch II syndrome / **H**ereditery **N**on**P**olyposis **C**olorectal **C**ancer syndrome (HNPCC), is associated with mutations in the mismatch repair genes
- ↑ number of ovulatory cycle (↑ cell division thus mean more likely to mutate) :
  - Nulliparous women
  - Prolonged intervals of ovulation uninterrupted by pregnancy.
  - Infertility
  - Early menarche
  - Late age at menopause
- Endometriosis

Having children, breastfeeding, oral contraceptive use (≥ 5 years) , bilateral **tubal ligation,** Salpingectomy, **and hysterectomy** are associated with a decreased risk of the disease.

Osmosis - ovarian cyst : clinical

Adnexal masses can develop in females of all ages, and can be discovered **incidentally during a pelvic US (asymptomatic)**, or when they **cause symptoms** like **pain or pressure on the affected side.**

when a patient presents with pelvic mass is important to perform a thorough :

1- pelvic examination

- for Pre-menarche the ovary **should not be palpable**
- for reproductive age group women a normal ovaries palpable about half of the time
- for post menopausal women The ovaries are usually not palpable

2- Pelvic US, it is the primary component of an evaluation of adnexal mass.

When encountering an adnexal mass :

- **the 1st step is to assess whether or not it's a medical emergency** (adnexal masses that cause **severe and abrupt pain,** along with other symptoms like nausea, vomiting, fever, or vaginal bleeding)
  - **Do pregnancy test** ,if +ve ? think about ectopic pregnancy. **if it -ve ?**
    - **Ovarian torsion**
      - Risk factor : ovarian mass , and an ovary greater than 5 centimeters in diameter.
      - **In US**, (not diagnosed using US, NEVER rule out because of negative US, 50% wouldn't appear) may show :
        - One ovary is larger than the other one, because of edema and blood pooling up in the ovarian veins, and the affected ovary might look like a twisted mass.
        - it shows decreased or absent blood flow within the ovary,and the "whirlpool sign" may be present, which is when blood flow inside the ovarian vessels seems to flow in a spiral around a central axis.]
      - Urgent surgical detorsion of the ovary is required to avoid ischemic injury and loss of the ovary and fallopian tube. (NEVER do oophorectomy for ovarian torsion, untwist it, it could revascularize within to week)

- **Ruptured ovarian cyst**
  - If there's minor bleeding + not affect the hemodynamic status or hematocrit : NSAIDs are given to help with the pain, and symptoms resolve in a few days.
  - if there's major bleeding + peritoneal irritation (muscle guarding and abdominal tenderness) + US show blood in the peritoneal cavity / hemoperitoneum :
    - Stable vital signs : hospitalized and given IV fluids, and get closely monitored for vital sign changes and drops in their hematocrit.
    - If there is hemodynamic instability / uncontrolled, or if the hematocrit continues to fall, then surgery is recommended to stop the bleeding and remove the cyst.
- **Tubo-ovarian abscess.** Usually associated with Hx of PID,

- if it's not, **whether the mass is benign or malignant**?
  - Do US to help you

Simple cysts : They are often either a functional cyst or a noncancerous tumor	**Complex cysts:**
HOW cyst appear in US	
Unilateral	Bilateral
Mobile	Fixed
Less than 10 centimeters	Larger than 10 centimeters
Have thin, regular walls	Have irregular borders,
Unilocular : meaning they have a single cavity,	Have internal septations creating a multilocular appearance.
Filled with an anechoic fluid - so they look like a balloon filled with black fluid. That fluid is also homogenous, meaning nothing is floating around.	The fluid inside these cysts is usually heterogeneous, meaning there's something other than fluid inside it (it is solid)
NOTE : A US will confirm the cystic nature of the mass, but it cannot differentiate with **certainty** between a functional and a neoplastic tumor. Table 20-3 contains a risk assessment tool that can be **useful for evaluating adnexal masses** in pre- and postmenopausal women. It is **called the Risk of Malignancy Index** or RMI.	

MANAGEMENT
Wait and reexamine the patient after her next menses 6-8 weeks. • However, If the cyst **grows** during this time, or causes **significant discomfort,** it may need to be surgically removed..

TABLE 20-3

CALCULATION OF THE RISK OF MALIGNANCY INDEX FOR AN OVARIAN MASS

Criteria	Scoring System
A. Menopausal Status	
Premenopausal	1
Postmenopausal	3
B. Ultrasonic Features	
Multiloculated	1 feature = 1
Solid areas Bilaterality Ascites	2 or more features = 3
C. Serum CA-125 titer	Absolute value (normal = <35 U/mL)

Pt presentation for malignant ovarian neoplasm :

- 5th decade of life
- Lower abdominal or pelvic pain or discomfort with/without pelvic mass
- Mass effect : Abdominal distension - Constipation - Urinary urgency
- Ascites or an upper abdominal mass **(** unless the patient has hyperstimulation syndrome, **Any adnexal mass found in the presence of ascites or an upper abdominal mass should be considered malignant until proven otherwise,** bc Extensive blockage of the diaphragmatic lymphatics is at least partially responsible for the development of ascites)
- Decreased energy

It is important to know that the most common symptoms are gastrointestinal NOT gynecological symptoms

Surgical exploration is definitive next step in the evaluation when there's a high suspicion

- Routine preoperative hematologic and biochemical studies should be obtained, as should a chest radiograph. A pelvic and abdominal CT scan will exclude liver metastases and may demonstrate retroperitoneal lymphadenopath**y.**

Staging

The 2013 FIGO staging system for ovarian, fallopian tube, and peritoneal cancer is presented in Table 39-1. Even though all macroscopic (visible) disease may appear to be confined to the ovaries and/or fallopian tubes at the time of laparotomy, microscopic spread may have already occurred; thus, patients must undergo a thorough "surgical staging" . Definitive diagnosis requires an intraoperative frozen section.

- Unlike endometrial and cervical cancers, ovarian cancer is difficult to obtain an in-office biopsy from (due to increased risk of spreading). Rather, we perform a complete hysterectomy and send to Pathology for staging.

TABLE 39-1

INTERNATIONAL FEDERATION OF GYNECOLOGY AND OBSTETRICS STAGING FOR CANCER OF THE OVARY, FALLOPIAN TUBE, AND PERITONEUM (2014)

International Federation of Gynecology and Obstetrics (FIGO)		Tumor, Node, Metastasis (TNM)
Ov	**Primary tumor, ovary**	Tov
FT	**Primary tumor, fallopian tube**	Tft
P	**Primary tumor, peritoneum**	Tp
X	**Primary tumor cannot be assessed**	Tx
Designate histologic type: **High-Grade Serous (HGS), Endometrioid (E), Clear Cell (CC), Mucinous (M), Low-Grade Serous (LG), Other or cannot be classified (O), Germ Cell (GC), Sex-Cord Stromal Cell Tumor (SC)**		
Stage I	**Tumor confined to ovaries or fallopian tube(s)**	**T1**
IA	Tumor limited to one ovary (capsule intact) or fallopian tube No tumor on ovarian or fallopian tube surface No malignant cells in the ascites or peritoneal washings	T1a
IB	Tumor limited to both ovaries (capsules intact) or fallopian tubes No tumor on ovarian or fallopian tube surface No malignant cells in the ascites or peritoneal washings	T1b
IC	Tumor limited to one or both ovaries or fallopian tubes, with any of the following:	T1c
IC1	Surgical spill intraoperatively	
IC2	Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface	
IC3	Malignant cells in the ascites or peritoneal washings	
Stage II	**Tumor involves one or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or peritoneal cancer (Tp)**	**T2**
IIA	Extension and/or implants on the uterus and/or fallopian tubes/and/or ovaries	T2a
IIB	Extension to other pelvic intraperitoneal tissues	T2b
Stage III	**Tumor involves one or both ovaries, fallopian tubes, or peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes**	**T3**
IIIA	Metastasis to the retroperitoneal lymph nodes with or without microscopic peritoneal involvement beyond the pelvis	T1, T2, T3aN1
IIIA1	Positive retroperitoneal lymph nodes only (cytologically or histologically proven)	
IIIA1(i)	Metastasis ≤10 mm in greatest dimension	
IIIA1(ii)	Metastasis >10 mm in greatest dimension	
IIIA2	Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes	T3a/T3aN1
IIIB	Macroscopic peritoneal metastases beyond the pelvic brim ≤2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes	T3b/T3bN1
IIIC	Macroscopic peritoneal metastases beyond the pelvic brim >2 cm in greatest dimension, with or without metastases to the retroperitoneal nodes (Note 1)	T3c/T3cN1
Stage IV	**Distant metastasis excluding peritoneal metastases**	**Any T, Any N, M1**
IVA	Pleural effusion with positive cytology	
IVB	Metastases to extraabdominal organs (including inguinal lymph nodes and lymph nodes outside of abdominal cavity)	

Note 1: Includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ

Note 2: Parenchymal metastases are stage IVB

Additional notes:
1. The primary site—that is, ovary, fallopian tube, or peritoneum—should be designated where possible. In some cases, it may not be possible to clearly delineate the primary site, and these should be listed as "undesignated."
2. The histologic type should be recorded.
3. The staging includes a revision of the stage III patients, and allotment to stage IIIA1 is based on spread to the retroperitoneal lymph nodes without intraperitoneal dissemination, because an analysis of these patients indicates that their survival is significantly better than the survival of those who have intraperitoneal dissemination.
4. Involvement of retroperitoneal lymph nodes must be proven cytologically or histologically.
5. Extension of tumor from omentum to spleen or liver (stage IIIC) should be differentiated from isolated parenchymal splenic or liver metastases (stage IVB).

From FIGO Committee on Gynecologic Oncology: Pratt J, on behalf of FIGO committee: Staging classification for cancer of the ovary, fallopian tube, and peritoneum. *Internat J Gynaecol Obstet* 124(1):1-5, 2014.

To Make it easy :

- **Stage I: Spread limited to the ovaries or fallopian tube**
- **Stage II:** Tumor involves one or both ovaries or fallopian tubes **with pelvic extension below pelvic brim or peritoneal cancer**

^ it would not cause symptoms (Stage I & II - Good Prognosis).

- **Stage III:** Tumor involves one or both ovaries, fallopian tubes, or peritoneal cancer, **with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes** (Lymphatic dissemination to the pelvic and para-aortic nodes is common) **.** This is the most common stage at diagnosis.
- **Stage IV: Distant metastasis excluding peritoneal metastases**

^ It causing symptoms (Stage III & IV - Poor Prognosis & High Mortality), Unfortunately most ovarian tumors are diagnosed in late stages (3 and 4) since there is still no screening test

Management

Management

Conservative surgery:

- A patient who desires further fertility with a **unilateral benign** or **borderline** cancer of the ovary can be treated with a USO (unilateral salpingo-oophorectomy) surgical removal of one ovary and one fallopian tube with preservation of the uterus and the opposite adnexa.

Aggressive surgery:

- If the patient has completed her family and have **benign** or **borderline** ovarian cancer then the most acceptable treatment would be a TAH and BSO.
- In **Malignant histology** a debulking procedure (cytoreduction) should be performed. This procedure consists of a TAH (total abdominal hysterectomy) and BSO (bilateral salpingo-oophorectomy) both ovaries and Fallopian tubes , omentectomy, and bowel resection, if necessary.

Chemotherapy:

- Postoperative chemotherapy (carboplatin and Taxol) should be administered in malignant histology of the ovary.

Follow-Up

Benign { Followed up in the office on a **yearly** basis for regular examination

Malignant { Followed up every three months for the first two years and then every six months for the next two years with follow-up of the **CA125 tumor marker**

Kaplan

Differential Diagnosis of polycystic cysts:

- **Pregnancy**: most common cause of a pelvic mass in the reproductive years
- **Complex mass:** most common complex adnexal mass in young women is a dermoid cyst or benign cystic teratoma;
- **Other diagnoses** include endometrioma, tubo- ovarian abscess, and ovarian cancer

THECA LUTEIN CYSTS

- These are benign neoplasms stimulated by high levels of FSH and β-hCG. They are associated with twins and molar pregnancies but they are only rarely associated with a normal singleton pregnancy. The natural course of these tumors is postpartum spontaneous regression and require only conservative management.

Metastatic ovarian cancer

- Ovarian Carcinoma with Peritoneal Metastasis triad :Postmenopausal bilateral pelvic masses Weight gain, anorexia Abdominal "shifting dullness"
- Meigs syndrome is the triad of ascites, pleural effusion, and benign ovarian fibroma.
- Diagnosis: Lab abnormalities/diagnostic criteria. In a patient with an adnexal mass and ascites, an abdominal pelvic CT scan should be ordered for evaluation of the upper abdomen. The most common method of ovarian carcinoma spread is by peritoneal dissemination (exfoliation) and is commonly seen metastatic to the omentum and to the
- GI tract. The cause of death of patients with advanced ovarian carcinoma is bowel obstruction.

Prepubertal Pelvic Mass:

- functional ovarian cysts are not possible because ovarian follicles are not functioning. Therefore any ovarian enlargement is suspicious for neoplasm.
- Sudden onset of acute abdominal pain is a typical presentation of germ cell tumors of the ovary. These tumors characteristically grow rapidly and give early symptomatology, as opposed to the epithelial cancers of the ovary that are diagnosed in advanced stages. Germ cell tumors of the ovary are most common in young women and present in early stage disease.
- Diagnosis :Table II-5-1.

Surgical diagnosis	Simple cyst	Laparoscopy
	Complex mass	Laparotomy
Management	Benign	Cystectomy Annual follow-up
	Malignant	Unilateral S&O Staging, chemotherapy
Prognosis	95% survival with chemotherapy	

Definition of abbreviations: S&O, Salpingo-oophorectomy.

Table II-5-1. Prepubertal Pelvic Mass

- ovarian cysts can only be physiological in the reproductive years and they can be simple or complex.
- ovarian cysts in the perimenstrual period are cancerous (originate from germ cells)
- ovarian cysts in the postmenopausal period are cancerous (originate from epithelial cells) .
- we can differentiate between simple cyst and complex cyst by using the transvaginal ultrasound.

Simple cysts

- Complex cyst By using the transvaginal ultrasound
- By using the transvaginal ultrasound you will see:
  - unilocular cyst
  - anechoic cysts
  - homogeneous cyst
  - small cyst
- The management of simple cysts:
  1. if the cyst <3 cm leave it.
  2. if the cyst <10 cm usually it will resolve by itself,but if it grows then you have to remove by using laparotomy or laparoscopy (laparoscopy is the best) .
  3. if the cyst >10 cm you have to remove it by using laparotomy or laparoscopy (laparoscopy is the best)
  4. you can't do aspiration and you can't give the patient OCP.

Complex cysts

- By using the transvaginal ultrasound you will see: you will see:
  - multilocular cyst
  - multi-echoic cyst
  - heterogeneous cyst
  - Large cyst
- The management of complex cysts:
  1. Teratoma: it's benign and it can be seen in young women,it can be diagnosed by using TVUS ,and you can treat it by cystectomy.
  2. Torsion the suspensory ligament of the ovary get twisted,the patient will present with abdominal pain and sometimes toxemia,it can be diagnosed by using TVUS,and it can be treated by untwist the ovary.

Teaching case

A 48 year-old G3P3 woman comes to the office for a health maintenance exam. She is in good health and has no concerns. She had three normal vaginal deliveries and underwent a tubal ligation after the birth of her third child 15 years ago. She has no history of abnormal Pap smears or sexually transmitted infections. Her cycles are regular and her last menstrual period was 18 days ago. She is not taking any medications. Her family history is significant for a maternal aunt who was diagnosed with ovarian cancer at age 60. On examination, she has normal vital signs. Her heart, lung and abdominal exams are normal. On pelvic examination, she has normal external genitalia, vagina and cervix. On bimanual exam, she has a slightly enlarged uterus and a palpable 6 cm mobile, non-tender right adnexal mass which is confirmed on the rectovaginal exam.

Q1: What is the next step in the management of this patient?

1. **History and Examination**
2. **Pelvic Transvaginal Ultrasound**
   Aim: To evaluate the characteristics of the adnexal mass. Categorization as to whether this is a simple (cystic) or complex adnexal mass is crucial to the management.

   If Cystic, mobile, and less than 10 cm - Good Ultrasound Signs →
   - Observation is reasonable for a premenopausal patient who is asymptomatic, and with no family history of ovarian cancer.
   - A **repeat** ultrasound in 6-12 weeks to determine if the cystic ovary is:
     - **Persistent** or increasing in size → surgical exploration/removal
     - **Resolves**, or becomes smaller → representing a functional cyst

   If Solid or complex, fixed (unmobile), size >10 cm, or bilateral - Bad Ultrasound Signs →
   - Surgical exploration/removal

3. **Tumor Markers**

Epithelial Cell	Non-Epithelial Cell
CA125 (Most Common)	**CEA -** Mucinous (colorectal) tumors
	α-Fetoprotein (AFP) - Yolk Sac Germ Cell Tumors
	LDH - Dysgerminoma
	β-HCG - Choriocarcinoma, Mixed Germ Cell Tumors

Non-specific CA125 elevations:
Seen in pregnancy, endometriosis, PID, cirrhosis, and any abdominal infection/inflammation,

Teaching case

Q2: How different is your approach if the patient was postmenopausal at 62 years of age?

437 notes:
Do not reassure the patient. We have to consider their age even if a cyst is simple. These patients are not ovulating, hence, no functional cyst is supposed to be found. Surgical exploration/removal if the cyst persists or increases in size after observation.

Q3: You obtain an ultrasound which shows a 6 cm right complex ovarian cyst. What is your differential diagnosis?

437 notes:
A small sized cyst is not necessarily benign. Always enlist your DDx as Benign & Malignant.

Benign	
Functional (follicular, corpus luteum, theca lutein)	**Endometrioma** (chocolate cyst, bloody)
Gonadal stromal tumors (fibroma/thecoma)	**Tubo-ovarian abscess**
Germ cell tumors (teratoma dermoid cyst) - **Common**	**Cystadenoma**
Malignant	
Epithelial tumors (serous, mucinous, clear cell, endometrioid, Brenner)	
Germ cell tumors (dysgerminoma, endodermal sinus tumor, immature teratoma)	
Sex cord stromal tumors (Sertoli-Leydig, Granulosa)	

Teaching case

Q4: What risk factors does this patient have for ovarian cancer?

- This patient's risk factors include a **family history of ovarian cancer.**

Risk Factors

- Personal or family history of breast/ovarian Cancer
- BRCA1-2 and HNPCC genetic mutation
- ↑ **period of ovulation:** Late menopause, Nulliparity, and Infertility.
- Endometriosis
- Increased age
- White Race

Protective factors

↓ **period of ovulation:**

- OCP use (≥ 5 years)
- High Parity
- Breast Feeding
- Hysterectomy
- Bilateral tubal ligation
- Salpingectomy

Q5: List elements of the history and physical examination, which would help support the diagnosis of ovarian cancer.

	Epithelial Ovarian Cancer	Germ Cell/Stromal Tumor
History	Abdominal discomfort/bloating (50%)	Acute Pain Due to ovarian torsion
	Gastrointestinal disturbances (20%)	
	Urinary symptoms (15%)	Precocious pseudopuberty Due to tumor Estrogen and Testosterone production
	Vaginal bleeding/menstrual irregularities (15%)	
	Weight loss (15%) B Symptoms	Virilization
Exam	Typically include the presence of an adnexal/pelvic mass. In advanced stages, abdominal distension with ascites and/or an abdominal mass may be noted.	

441 Drs notes

functional cyst:

- follow up and repeat US, if it persists we counsel the patient about the options:
  - Observation by serial US
  - Surgical intervention (but if the patient has high risk for surgery then we just follow up and educate the patient about rupture risk)
- Oral contraceptives has no role in treating / managing of ovarian cyst, its to prevent the recurrence

Epithelial cell types:

- Serous types:
  - High grade: 70% advanced ovarian cancer , origin: fallopian tubes
  - Low grade: less common, borderline histology , origin: ovary itself as a borderline
- Mucinous:
  - First thing to check is colon cancer, it's bowel until proven otherwise (usually GI source > metastases, only 20% ovarian source) , do upper GI endoscopy.
- Endometrioid:
  - Precursor is endometriosis.

Germ cell types:

- all should receive chemotherapy except dysgerminoma stage 1A grade 1 and immature teratoma stage 1 grade 1 (DON'T GIVE CHEMO!)
- dysgerminoma Has the BEST prognosis because it responds to chemotherapy and radiotherapy (we don't give radiotherapy anymore due to high complications with similar results to chemotherapy)
- Yolk sac has the WORST prognosis

Stromal cell types:

- We only give chemotherapy if advanced (stage 1C and above)
- Stage 1C is controversial but the majority would give chemotherapy
- If a patient presented with granulosa cell tumor stage 1A or 1B dont give chemotherapy
- What kind of chemotherapy? BEC (curative & aggressive)
  - Bleomycin
    - question: What's the most common complication? Pulmonary fibrosis
  - Etoposide
    - question: What's the most common side effect? Systemic effects
  - Cisplatin
    - question: What's the most common complication? nephro problem

441 Drs notes

Management of ovarian tumors:

- Age of the patient:
  - Pediatric and post menopausal are at higher risk of malignancy
- Postmenopausal with Adnexal mass is cancer until proven otherwise
- After investigation categorise (based on symptoms of: ascites, GI symptoms, distention, CT scan showing evidence of extra-ovarian disease) into:
  - Advanced stage ovarian cancer
    - Most common type is high grade serous.
    - bad prognosis, goal of treatment isn't for curative but prolongs survival
  - Apparently early stage ovarian tumor
    - We don't go for chemotherapy, go for surgery directly for **surgical staging** to rule out risk of occult metastases (explore the abdomen and at least one salpingo oophorectomy > send to pathology to identify > if metastasis do aggressive resection, if still persist > its aggressive do Chemotherapy)
- we have two options of the management:
  - Surgery
  - Neoadjuvant chemotherapy followed by interval debulking surgery can be considered in patients with advanced-stage disease and high perioperative risk.
  - Hyperthermic intraperitoneal chemotherapy (HIPEC)
- In young patients do surgery with 6 rounds of chemotherapy

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Approach to ovarian tumors

1- full detailed history

Ask about:

- GI symptoms (constipation)
- urinary symptoms: urgency, stress incompetence, retention if it's pressing on the bladder, flank pain in case of hydronephrosis
- B symptoms (fever, night sweats and unintentional loss of more than 10 percent of body weight over 6 months)
- Family history of breast and ovarian cancers
- Genetic testing (BRCA1 and 2)
- History of STDs
- Previous abnormal Pap smear

Check for risk factors for ovarian cancer

- family history of breast and ovarian cancers
- BRCA1 and 2 (a positive"defective" BRCA 1 and 2 is a good thing, patients with positive BRCA 1 and 2 are more responsive to chemotherapy (chemo-sensitive))

2- physical examination

3- Laboratory Investigation:

- CBC : Hb to check for bleeding
- Tumor markers: CA125 (sensitive but not specific)

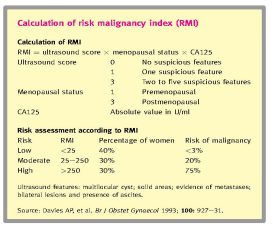
CA125 can be elevated by many causes, remember them as the 3P's:
1- plural: Any cause that lead to pleuritis
2- pericardium: any thing that can cause pericarditis
3- peritoneum: any cause that cause peritonitis like PID, endometriosis, cirrhosis

- Transvaginal US

US features of benign tumors: mobile, cystic, size less than 10, unilocular and no calcification
US features of malignant tumors: unmobile, solid mass, size more than 10, irregular borders, hypervascularity, presence of ascites and metastases

4- calculate the RMI score (risk of malignancy index)

- used to triage patients and predicts risk for an adnexal mass to be malignant


Calculation of risk malignancy index (RMI)

Calculation of RMI

RMI = ultrasound score × menopausal status × CA125

Ultrasound score	0	No suspicious features
	1	One suspicious feature
	3	Two to five suspicious features
Menopausal status	1	Premenopausal
	3	Postmenopausal
CA125	Absolute value in U/ml	

Risk assessment according to RMI

Risk	RMI	Percentage of women	Risk of malignancy
Low	<25	40%	<3%
Moderate	25–250	30%	20%
High	>250	30%	75%

Ultrasound features: multilocular cyst; solid areas; evidence of metastases; bilateral lesions and presence of ascites.

Source: Davies AP, et al. *Br J Obstet Gynaecol* 1993; **100**: 927–31.

three features:
1- age (pre of postmenopausal)
2- US features
3- CA125

- A score of 200 or more indicates a high malignancy risk.

5- Management:

- Depends on RMI score and stage of cancer

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Cases:

1. A 40yo woman , her CA125 is 600 and her US showed solid component with vascularity, moderate amount of ascites, next step?

surgical excision (high RMI score) with no suspension of metastasis

2. A premenopausal woman with a CA125 of 23, US showed bilateral simple cysts, one is 2cm on the right and one is 4.5cm on the left, next step?

Observe and repeat US after 6 months
If after 6 months it still looks the same, tumor markers are still normal with no symptoms then follow her again after 6 months

3. A 60yo woman with uncontrolled DM and HTN, her CA125 is 12, her US showed 3cm solid mass with no symptoms and no family history of cancer, next step?

follow her up after 6 months. She is still a low risk patient

4. A 60 yo woman came complaining of nausea, vomiting, night sweats, chills, early satiety and an abdominal distention that started two months ago, positive shifting dullness test on PE, her CA125 is 1200, on US large amount of ascites and bilateral multicystic ovarian masses with some solid components and irregular borders, you asked for abdominal CT and it showed omental caking with multiple peritoneal deposits (signs of metastasis) , next step?

Take a biopsy, we don't take her to the OR right away since she has signs of metastasis surgical excision will not work (we can't do optimal debulking " surgical removal of uterus uterus (hysterectomy), along with both ovaries and fallopian tubes (bilateral salpingo-oophorectomy or BSO), as well as the omentum (an omentectomy) and lymph node dissection")

After taking the biopsy, start few cycles of neoadjuvant chemotherapy then we repeat CT, if she responds to the chemotherapy then we can do an interval debulking surgery then give postoperative chemotherapy.

5. A 20 yo woman came to the ER with severe pain, US showed 4cm mass, next step?

pregnancy test to rule out ectopic pregnancy.

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Good Luck!

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