437 Team: Obstetrics and Gynecology

Benign & Mal Ovarian Tumors

Objectives:

- Compare Describe the initial management of a patient with an adnexal mass
- the characteristic of functional cyst,benign ovarian neoplasm and ovarian cancer
- List the risk factors and protective factors for ovarian cancer
- Describe the symptoms and physical findings associated with ovarian cancer
- Describe the three histological categories of ovarian neoplasms

References:

- Kaplan USMLE step 2 CK - Obstetrics and Gynecology
- Online Meded videos
- Team 435

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Color index: Important | Notes | Meded | Video-Case

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Definition

Adnexal Mass: in gynecology, it is anything next to the uterus, usually involving the **fallopian tubes and ovaries**. The term adnexal mass is often used interchangeably with the term pelvic mass.

Classification of Ovarian Masses

1- Functional Cyst:

- **Physiologic,** formed with normal ovulatory function.
- Composed of **Follicular cell** and **Corpus Luteum cells**.
- Resolve **spontaneously**.
- Functional cysts should not form if the patient has been **on oral contraception for at least 2 months,** because gonadotropins should have been suppressed.
- Can require surgical intervention **only if symptomatic**:
    - Size becomes larger
    - There is a torsion
    - There is uncontrolled bleeding within the cyst (hemorrhagic 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. Either of these structures, the follicle or corpus luteum, can **become fluid-filled and enlarged, producing a functional cyst.**

2- Benign and Malignant Ovarian Neoplasms:

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

A. Epithelial Cell Type (80%);

- Most common type of histologic ovarian carcinoma
- Occur predominantly in postmenopausal women
- **These include:**
    - Serous (Most Common Type)
    - Mucinous
    - Brenner
    - Endometrioid
    - Clear cell tumors

Serous Carcinoma Triad:

- Postmenopausal
- Pelvic mass
- ↑ CEA or CA125 level

B. Germ Cell Type (15%):

- Derived from the **primary germ cell**.
- May contain relatively differentiated structures such as: hair and bone.
- **Most common malignant germ cell type is:**

  Dysgerminoma (uniquely x-ray sensitive).
- **Most common histology seen is:**

  Ectodermal skin appendages (hair, sebaceous glands), thus the name "dermoid".

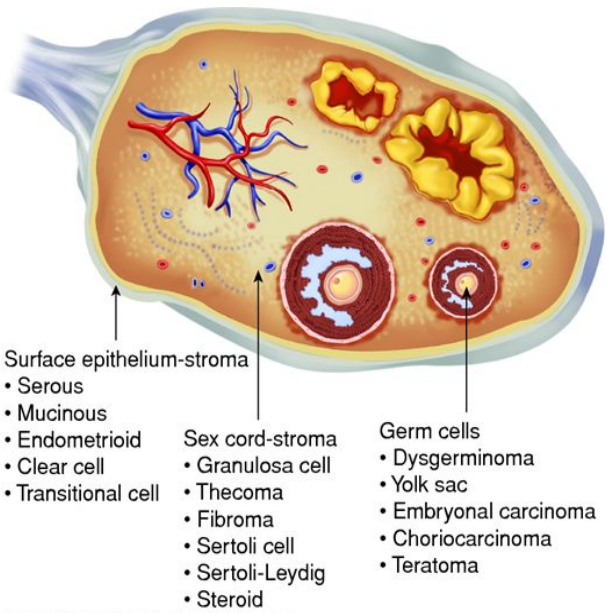
Benign: Mature Cystic Teratoma (Dermoid Cyst)

- Most common tumor of women of all ages
- Often in pre-menopausal women
- Demonstrates tissues of all three embryological cell types:
  - Ectodermal
  - Mesodermal
  - Endodermal

MCQ: What is the origin of Dermoid?

Malignant:

- Most common ovarian cancer
- In women <20 years old
- May become functional producing β-hCG or α-fetoprotein
  - Dysgerminoma (Most Common) - Associated with ↑ LDH
  - Endodermal sinus tumor - Yolk Sac
  - Immature teratoma
  - Choriocarcinoma



Benign Cystic Teratoma Triad:

- Pelvic mass in reproductive years
- β-hCG negative
- Sonogram complex mass (calcifications)

Dysgerminoma Triad:

- Solid pelvic mass in reproductive years
- β-hCG negative
- ↑ LDH level

Choriocarcinoma triad:

- Postmenopausal woman
- Pelvic mass
- ↑ hCG level

C. Stromal cell type (5%):

- Derived from specialized **sex-cord stroma** of the developing gonads.
- They are functionally active.
- They metastasize infrequently, and then require chemotherapy, (Vincristine, Actinomycin, and Cytoxan).

Benign: Thecoma and Fibroma

MEIG's Syndrome: Benign ovarian fibroma + Ascites + pleural effusion.

Tricky question: differentiate between MEIG's (benign) and cancer.

Malignant:

Rare tumor that produces hormones:

1. **Granulosa Cell Tumor (most common)**:
    - Secrets large amount of **estrogen**
    - Can cause bleeding from endometrial hyperplasia.
2. **Sertoli Leydig tumor:**
    - Secrets large amount of **androgens**
    - Can produce masculinization syndromes

Sertoli-Leydig Tumor Triad:

- Postmenopausal pelvic mass
- Masculinization
- ↑ testosterone level

Endometrial Carcinoma Metastatic to Ovaries triad:

- Postmenopausal woman with bilateral pelvic masses
- Postmenopausal bleeding
- Enlarged uterus

Metastatic tumors

The most common sources are the:

- Endometrium
- GI tract
- Breast.

Krukenberg tumors: Mucin-Producing tumors from the stomach or breast metastatic to the ovary.

Borderline Cancers:

Another entity of ovarian cancer is the borderline tumors also known as tumors of **low malignant potential**. These are characterized by **no invasion of the basement** membrane and can also be treated conservatively.

Signs & Symptoms

The most common symptoms are GastroIntestinal NOT Gynecological symptoms.

- Abdominal distension (mass effect)
- Lower abdominal or pelvic pain or discomfort
- Urinary urgency (mass effect)
- Decreased energy
- Constipation (mass effect)

Limited to the ovaries, it would not cause symptoms **(Stage I & II - Good Prognosis).** Higher stages invade, causing symptoms **(Stage III & IV - Poor Prognosis & High Mortality)** 85% of ovarian cancers are unfortunately diagnosed at Stage III **(late diagnosis).**

Cancer grows from the ovary into the pelvis **(Urinary Symptoms)** and abdomen **(GI Symptoms).** Spreading everywhere, it causes **adhesions.** With adhesions, bowel movements get restricted, causing **obstruction.** The peritoneum is responsible for the reabsorption of peritoneal fluid; in the presence of cancer cells within the peritoneum, reabsorption is limited, and **ascites** develops.

Risk Factors	Protective Factors
Personal or family history of breast/ovarian Cancer	↓ **period of ovulation:** OCP use (≥ 5 years) High Parity Breast Feeding Hysterectomy Bilateral tubal ligation Salpingectomy
BRCA1-2 and HNPCC genetic mutation	
↑ **period of ovulation:** Late menopause, Nulliparity, and Infertility	
Endometriosis	
Increased age	
White Race	

MCQ: Where does ovarian cancer arise from? Fimbria. Therefore, If hysterectomy is indicated (for whatever reason), the tubes must be removed as well in order to prevent ovarian cancer.

1 in every 5 BRCA positive patients will develop ovarian cancer. Positive family history, or personal history of ovarian/breast cancer indicates screening for BRCA. BRCA-positive patients, **unlike the general population (even BRCA-negative with personal history),** require screening and counseling.

Options are limited to breast/ovaries removal. If the patient looks forward to children, follow her up annually, or twice annually, to check the **ovaries** and **CA125.** At 35-40 years of age, the surgery is a must.

HNPCC: associated with increased risk of colon, renal, uterine, and ovarian cancer.

Diagnosis & Evaluation

1. Detailed History and a thorough Pelvic Exam.

2. Laboratory Investigation:

A. Qualitative Beta-Human Chorionic Gonadotropin (β-hCG) Test:

Rule out pregnancy

B. Tumor Markers:

Epithelial Cell	Non-Epithelial Cell
CA125 Cancer Antigen 125 (Most Common)	**CEA -** Mucinous (colorectal) • Carcinoembryonic antigen • For possibility of ovarian epithelial cancer
	∝-Fetoprotein (AFP) - Yolk Sac • Endodermal Sinus tumor • For possibility of germ cell tumors
	LDH - Dysgerminoma
	β-HCG - Choriocarcinoma, Mixed Germ Cell Tumors
Estrogen & Testosterone	For possibility of stromal tumors

Non-specific CA125 elevations:

Seen in pregnancy, endometriosis, PID, cirrhosis, and any abdominal infection/inflammation, hence, screening is limited to BRCA-positive patients. Ovarian Cancer is of multiple types, Epithelial Cell being the most common. **MCQ: Which marker goes with what tumor? MCQ: DDx of high CA125?**

3. Radiological Imaging:

A. Pelvic Ultrasound (best first line test)

B. Transvaginal Ultrasound (most accurate)

Aim: To evaluate the characteristics of the adnexal mass.

Categorization as to whether this is a **simple (cystic)** or **complex** adnexal mass.

A simple cyst is fluid filled. Any solid component represents a Complex cyst. (not necessarily cancer, but is not a good sign). **Other Bad Signs:** increased vascularity and papillary projections **Questions to answer with Pelvic Transvaginal Ultrasound:** Is it coming from the ovary? What is the Size? Is it Simple? Is there a solid component? Is it cancerous?

C. Chest Radiograph and Abdominal Pelvic CT:

Rule out metastasis.

4. Others:

A. Fecal Occult Blood, Barium Enamea, and Colonoscopy:

Rule out colon cancer metastasizing to ovary.

B. Upper GI Endoscopy:

For those with significant GI symptoms (krukenberg tumor in stomach).

C. Mammograms:

Breast cancer can metastasize to ovary.

5. Surgical exploration

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.

Absolute indication:

If the cyst is >7 cm or if patient had been on prior steroid contraception.

It is a definitive next step in evaluation if there is a high suspicion. Even if the cyst is simple in appearance surgical evaluation should be performed.

Stage I: Spread limited to the ovaries	**IA**. Limited to **one** ovary, capsule **intact, negative** cytology **IB**. Limited to **both** ovaries, capsules **intact, negative** cytology **IC**. One or **both** ovaries but **ruptured** capsule, **positive** cytology
Stage II: Extension to the pelvis	**IIA**. Extension to uterus or tubes **IIB**. Extension to other pelvic structures **IIC**. Extension to pelvis with positive cytology
Stage III: Peritoneal metastases or positive nodes. This is the most common stage at diagnosis.	**IIIA**. Microscopic peritoneal metastases **IIIB**. Macroscopic peritoneal metastases ≤2 cm **IIIC**. Macroscopic peritoneal metastases >2 cm
Stage IV: Distant metastases	**IVA**. Involves bladder or rectum **IVB**. Distant metastasis

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 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 and BSO, omentectomy, and bowel resection, if necessary.

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

Follow-Up

If it was a Benign mass: followed up in the office on a **yearly** basis for regular examination.

If it was a Malignant cancer: 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.

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

Simple cysts	Complex cyst
By using the transvaginal ultrasound you will see: 1-unilocular cyst 2-anechoic cysts 3-homogeneous cyst 4-small cyst	By using the transvaginal ultrasound you will see: 1-multilocular cyst 2-multi-echoic cyst 3-heterogeneous cyst 4-Large 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.	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 (video case)

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.

Questions

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

1. **History and Examination** (Already done, what is your next step?)

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.

   <u>If Cystic, mobile, and less than 10 cm</u> - Good Ultrasound Signs

   A simple cyst (functional) is natural with every menstrual cycle, and fades away.

   - 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

   <u>If Solid or complex, fixed (unmobile), size >10 cm, or bilateral</u> - Bad Ultrasound Signs

   Surgical exploration/removal

   Bilateral: because a functional cyst associated with ovulation is unilateral

   Other Bad Signs: increased vascularity and papillary projections

   Questions to answer with Pelvic Transvaginal Ultrasound: Is it coming from the ovary? What is the Size? Is it Simple? Is there a solid component? Is it cancerous?

Q1. Continued:

3. **Tumor Markers:**

Epithelial Cell	Non-Epithelial Cell
CA125 (Most Common)	**CEA -** Mucinous (colorectal) tumors
	∝-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,

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

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?

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)	

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	Protective Factors
Personal or family history of breast/ovarian Cancer	↓ **period of ovulation:** OCP use (≥ 5 years) High Parity Breast Feeding Hysterectomy Bilateral tubal ligation Salpingectomy
BRCA1-2 and HNPCC genetic mutation	
↑ **period of ovulation:** Late menopause, Nulliparity, and Infertility	
Endometriosis	
Increased age	
White Race	

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.	