

*433 Teams*

# **OBSTETRICS & GYNECOLOGY**

## **Ovarian Neoplasms**

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## 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

# 1. List the differential diagnosis of an ovarian mass :

First , what is adnexal mass ?

in gynecology it is anything next to the uterus usually involving the fallopian tubes and ovaries .

Second , Any ovarian mass it could be :

## ✓ Gynecologic :

- Ovarian cyst
- Malignant neoplasms
- Benign neoplasms
- Ectopic pregnancy
- Leiomyoma
- Tubo-ovarian abscess

## ✓ Nongynecologic :

- Appendicitis
- Diverticular abscess
- Gastrointestinal carcinoma
- Peritoneal cyst

when the patient presents with adnexal mass :

- You have to take a detailed history and do pregnancy test to exclude ectopic pregnancy
- You must do a pelvic exam .

- **Premenarche girls** the ovaries should not be palpable
- **Reproductive age women** normally the ovary is palpable about half of the time .
- **Menopausal women** the ovaries usually not palpable.
- **25% of ovarian tumors in postmenopausal women are malignant .**
- **10% of ovarian tumors in reproductive age women are malignant**
- **Pelvic ultrasound is the primary component of evaluation of an adnexal mass**

## 2. Mention the classification of ovarian neoplasms :

### The main classification of ovarian masses :

- Functional cysts
- Benign ovarian neoplasm
- Malignant ovarian neoplasm

- Ovarian cancer is the 5th most common cause of cancer death in USA .
- The highest mortality rate among gynecological malignancies, 55% of patients will die with in 5 years of diagnosis .

# 3. Compare between functional ovarian cysts, benign ovarian tumors and ovarian cancers:

## 3.1 functional ovarian cysts

The most common cause of a simple cystic mass in the reproductive age years is a physiologic cyst (**luteal or follicular 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 follicular OR corpus luteum, can become **fluid-filled and enlarged, producing a functional cyst.**

### ❖ Clinical Features :

#### • Follicular cyst :

- Asymptomatic
- Simple
- Can reach 15 cm in diameter
- Regress during the sub-sequent menstrual cycle

#### • Corpus luteum cyst :

- Cause pain
- Cause delayed menses
- Smaller than the follicular cyst

**In general , a functional cyst is mobile, unilateral and not associated with ascites**

## 3.1 functional ovarian cysts

### ❖ Diagnosis :

- **Qualitative  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) test:** If negative, this will rule out pregnancy.
- **Sonogram:** A complex mass on ultrasound appearance is incompatible with a functional cyst ( if the cyst < 10 cm , mobile and unilateral )
- **Surgical exploration :** If the adnexal cystic mass is solid or complex, fixed, size >10 cm and bilateral

### ❖ Management :

#### Observation :

- If the sonogram shows a simple cyst it is probably benign but careful follow-up is needed. Follow-up examination should be in 8-12 weeks, at which time the functional cyst should have spontaneously resolved.
- If the CA-125 titer normal and Risk for malignancy index (RMI ) is low .

#### Surgical exploration :

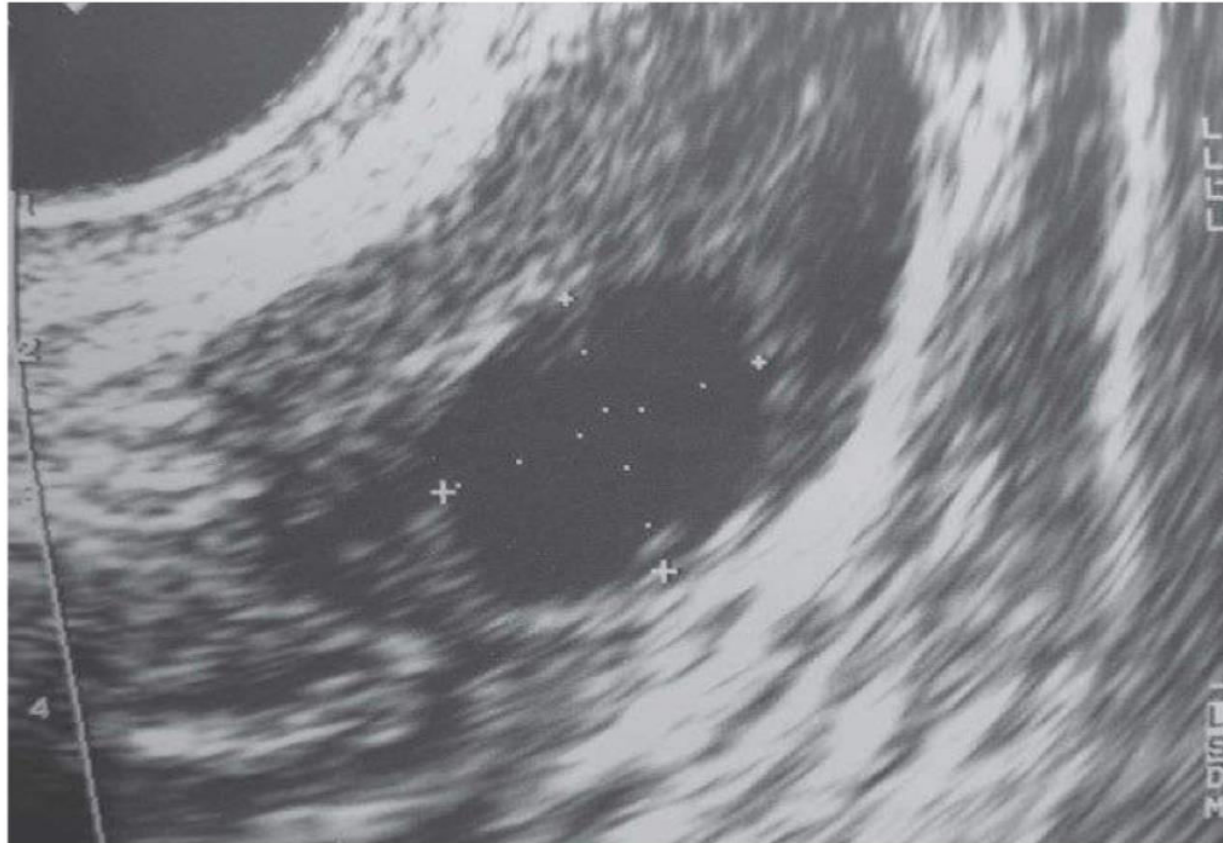
- If the cyst solid, fixed, painful and has high RMI
- In case of torsion
- Hemorrhagic cyst

### ❖ Protective factors :

Oral contraceptive medication can be used to help prevent further functional cysts from forming



## 3.1 functional ovarian cysts



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**Figure II-5-1.** Ultrasonographic Appearance of a Functional Cyst

Criteria	Scoring System
<b>A. MENOPAUSAL STATUS</b>	
Premenopausal	1
Postmenopausal	3
<b>B. ULTRASONIC FEATURES</b>	
Multiloculated	1 feature = 1
Solid areas	≥2 features = 3
Bilaterality	
Ascites	
<b>C. SERUM CA-125 TITER</b>	Absolute value

### CALCULATION OF THE RISK FOR MALIGNANCY INDEX FOR AN OVARIAN MASS

## 3.2 Benign ovarian neoplasms

25% of adnexal masses in the reproductive age women are benign

❖ There are three histological cell types they give arise to benign ovarian neoplasms :

**Epithelial cell types** the largest class of neoplasms

- ❖ **Serous (the most common benign neoplasms )** resembles fallopian tube epithelium
- ❖ **Mutinous** resembles endocervical epithelium
- ❖ **Endometriod** resembles carcinomas of the endometrium.

**Germ cell types** are derived from the primary germ cells and that is may contain relatively deferent structures like hair and bone

- ❖ **mature cystic teratoma ( Dermoid ) :**
  - **most common tumor of women of all ages**
  - **often in pre-menopausal women**
  - **demonstrate tissues of all three embryologic cell types ( ectodermal , mesodermal and endodermal )**

**Stromal cells types** benign ovarian neoplasm is derived from specialized sex-cord stroma of the developing gonads

- ❖ **Fibroma**
- ❖ **Thecoma**

**MEIGS' Syndrome : Benign ovarian fibroma + Ascites + Right pleural effusion**



## 3.2 Benign ovarian neoplasms

### ❖ Clinical features :

- The clinical features of benign ovarian tumors are often nonspecific. Except for the functioning ovarian neoplasms (stromal cell types), **most benign ovarian tumors are asymptomatic unless they undergo torsion or rupture.**
- They usually enlarge very slowly, so that an increase in abdominal girth or pressure on surrounding organs is not perceived **until the later stages of growth.**
- Any pelvic pain is generally mild and intermittent, unless the tumor twists on its pedicle (torsion), when infarction may induce severe pain and tenderness.

### ❖ Diagnosis :

- **transvaginal ultrasonography**
- **serum CA 125**, as part of the RMI (**distinguish between benign and malignant masses, particularly in a postmenopausal patient**)
- **Laparoscopy** (**distinguishing between a uterine myoma, a quiescent hydrosalpinx, and an ovarian tumor, but it will not distinguish between a functional cyst, a benign neoplasm, and an encapsulated malignant ovarian neoplasm**)

### ❖ Management :

- **Benign epithelial ovarian neoplasms are generally treated by :**
  - unilateral salpingo-oophorectomy **if the patient is young and nulliparous**
  - total abdominal hysterectomy and bilateral salpingo-oophorectomy **if the patient is old and there is suspicion of malignancy**
- **Stromal cell neoplasms of the ovary are generally treated by unilateral salpingo-oophorectomy**
- **Cystic teratomas (“dermoids”) can be treated by ovarian cystectomy**

### 3.3 Malignant ovarian neoplasms

- ❖ There are three histological cell types they give rise to malignant ovarian neoplasms :

**Epithelial cell types** constant of 90% of all ovarian malignancies

- ❖ Serous
- ❖ Mucinous
- ❖ Clear cell
- ❖ endometrioid

**Germ cell types** most common ovarian cancer in women < 20

- ❖ Dysgerminoma
- ❖ Endodermal sinus tumor
- ❖ Immature teratoma

**Sex-cord stromal types** ( rare ) :

- ❖ granulosa cell tumor **secretes large amount of estrogen**
- ❖ sertolileydig tumor **secretes large amount of androgens**

### 3.3 Malignant ovarian neoplasms

#### ❖ Clinical features :

-Age : 5th decade of life

Sx :

-abdominal bloating

-abdominal distension

-abdominal or pelvic pain

-early satiety

-the most common symptoms are GI not gynecological symptoms

#### ❖ Diagnosis :

-It is important to be aware of early warning signs of ovarian cancer

-Radiological imaging : **pelvic ultrasound is the best first line test**

-CA-125 Levels : **most helpful in post-menopausal women with a pelvic mass** ( this is because there are many cases of elevated CA 125 levels in pre-menopausal women for reasons such as : fibroid, PID and endometriosis which make it less useful )

-CEA (carcinoembryonic antigen) should also be drawn for the possibility of ovarian epithelial cancer.

- LDH, hCG, and cx-fetoprotein should be drawn for the possibility of germ cell tumors.

- Estrogen and testosterone should be drawn for the possibility of stromal tumors.

- **Surgical exploration is definitive next step in the evaluation if there is high suspicion**

### 3.3 Malignant ovarian neoplasms

#### ❖ Management 432 team work :

- a) Staging: No macroscopic disease suggestive of metastasis.
- b) Cytoreduction (debulking): removal of all gross disease to reach a residual disease less than 1cm.
  - Primary
  - Interval

**Example:** If the patient underwent U.S. for gallstones and they found an ovarian mass as an incidental finding you would go for staging. However, if the patient presented with severe disease, abdominal mass and ascites you would go for cyto-reduction and the use of neo-adjuvant chemotherapy maybe indicated.

- c) Chemotherapy: Can be given either as adjuvant therapy (post surgery) or neo-adjuvant (before surgery to reduce the size). Also it can be given as multiple agents or single agent if the patient can't tolerate multiple agents. Chemotherapy can be administered intra-peritoneal with minimal residual disease.

- Adjuvant and Neo-adjuvant
- Multiple agents
  - Platinum base
  - Paclitaxel.
- Single agent
- Intra-peritoneal

Special regimen: Germ cell tumor

**B** leomycin

**E** toposide

**P** <sup>10</sup>latinum or Cisplatin

5 yrs. survival 90 – 95% and good prognosis

### 3.3 Malignant ovarian neoplasms

#### ❖ Staging :

- 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  $\leq 2$  cm
  - IIIC. Macroscopic peritoneal metastases  $> 2$  cm
- Stage IV: **Distant** metastases
- IVA. Involves bladder or rectum
  - IVB. Distant metastasis



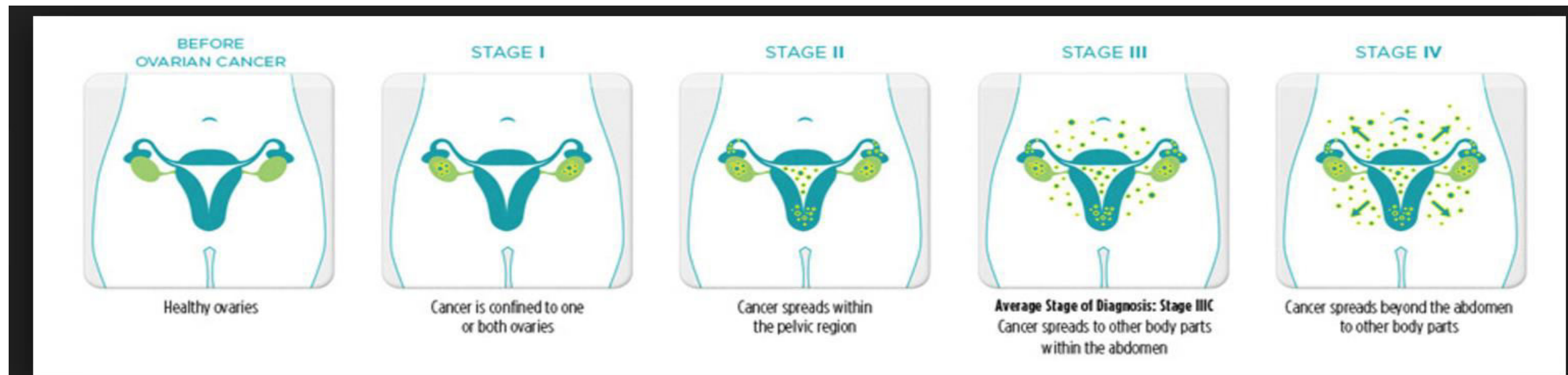
### 3.3 Malignant ovarian neoplasms

#### Risk factors :

- Nulliparity
- Primary infertility
- Endometriosis
- Inherited mutations ( BRCA and HNPCC )

#### Protective factors :

- OCP for at least 5 years
- Tubal ligation
- Hysterectomy



Helpful link

<https://youtu.be/Ugm3Fh5VKFc>



## TEACHING 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.**

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

- Pelvic transvaginal ultrasound is essential 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, observation is reasonable in the pre-menopausal patient who is asymptomatic (and with no family history of ovarian cancer).** A repeat ultrasound in 8-12 weeks will assist in determining if this is persistent or increasing, at which point surgical exploration would be advisable. In this case, this is most likely a neoplasm. If the cystic ovary resolves or is smaller, then this likely represents a functional cyst.
- If the adnexal cystic mass is solid or complex, fixed, size >10 cm, or bilateral, then surgical exploration is recommended.
- CA125: tumor marker often elevated in women with advanced epithelial ovarian cancer. CA 125 was developed originally to follow response to chemotherapy treatment (as surrogate marker for response), but now used to assess for relapsed disease and to triage women with a pelvic mass (to gyn oncologist or gynecologist for further investigations). Non-specific elevations seen among premenopausal women with gynecologic and non-gynecologic conditions (endometriosis, fibroids, benign cystic neoplasms, infection/inflammation, cirrhosis). More likely to be discriminating among postmenopausal women with adnexal masses.
- Other tumor markers to consider: CEA (mucinous tumors), AFP (yolk sac germ cell tumors), LDH (dysgerminoma), beta-HCG (choriocarcinoma, mixed germ cell tumors)

## 2. How would your approach be different if the patient was postmenopausal at 62 years of age?

Any postmenopausal patient with a complex cystic/solid mass requires surgical exploration and removal. If the cyst is simple in nature, then observation is reasonable provided the patient is asymptomatic, there is no significant family history of ovarian cancer, and CA125 is normal.

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

### Benign:

- Functional cyst (follicular, corpus luteum, theca lutein)
- Endometrioma
- Tubo-ovarian abscess
- Serous/mucinous cystadenoma
- Gonadal stromal tumors (fibroma/thecoma)
- Germ cell tumors (teratomas)

### 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)

#### 4. What risk factors does this patient have for ovarian cancer?

- This patient's risk factors include a **family history of ovarian cancer**.
- Other risk factors include: family history breast cancer, personal history of breast cancer, **BRCA 1/2 genetic mutation, increasing age**, nulliparity, infertility
- Protective factors include: oral contraceptive use, tubal ligation, increasing parity

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

##### ❖ Presenting symptoms for epithelial ovarian cancer include:

- Abdominal discomfort/bloating (50%)
- Gastrointestinal disturbances (20%)
- Urinary symptoms (15%)
- Vaginal bleeding/menstrual irregularities (15%)
- Weight loss (15%)
- Germ cell tumors may present with acute pain. Precocious pseudopuberty and virilization may be seen with some germ cell and sex cord/stromal tumors.

##### ❖ Physical exam findings typically include the presence of an adnexal/pelvic mass. In advanced stages, abdominal distension with ascites and/or an abdominal mass may be noted.

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