

MECHANISMS OF HUMAN DISEASE: LABORATORY SESSIONS
PATHOLOGY OF THE FEMALE GENITAL TRACT II
March 26, 2013

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GOALS:

- 1. Describe the basic morphologic and pathophysiologic changes in various conditions of the breast, uterus and ovary.**
- 2. Correlate the structural changes in the organs with clinical manifestations of the diseases.**

OBJECTIVES:

- 1. Describe the basic morphologic and clinical features associated with ovarian neoplasia.**
- 2. Describe the basic morphologic and clinical features associated with placental moles.**
- 3. Describe the basic morphologic and clinical features associated with various neoplastic and non-neoplastic conditions of the breast.**

CASE 1

CHIEF COMPLAINT:

“I feel a lump in my breast.”

HISTORY:

A 23-year-old woman presents with a palpable mass in her right breast. She felt the mass while bathing. The mass is not painful. There is no nipple discharge. She is an active, athletic woman who participates in many sports. Three days ago, during a volleyball game, the ball was spiked into her right upper chest. “It stung for a minute, but it was no big deal.” Her medical history is unremarkable; however, her mother died of breast cancer at age 46 years.

The patient’s obstetric/gynecologic history includes the following information: menarche age 11, menses were irregular until she began taking oral contraceptives at age 19 years, menses occur every 27 days and last for 4 days. She is gravida 0.

PHYSICAL EXAMINATION:

Inspection of the thorax reveals a small mole-like lesion of the skin. The brown lesion is circumscribed, flat with a central elevated region, 0.6 cm in diameter and located in the “milk line” just caudal to the left breast. The breasts are examined with the patient in sitting and supine positions. The breasts are small and slightly asymmetrical (left > right). The contour of each breast is smooth; there is no evidence of dimpling, retraction, or edema.

The nipples and areolae are pink-tan and non-eczematous. Although the nipples are not inverted, the left nipple points somewhat higher than the right. Palpation reveals a well delineated firm mass in the lower-inner quadrant of the right breast. The lesion is non-tender, movable (not fixed to the chest wall) and smooth. Estimated diameter of the mass is 1-1.5 cm. Bilateral compression of the nipples reveals no discharge. The remainder of the breast tissue is without abnormality.

1. What is the primary clinical problem?

Palpable breast mass

2. Develop a differential diagnosis for this problem:

- A. **Fibrocystic change**
- B. **Cancer**
- C. **Fibroadenoma**
- D. **Traumatic fat necrosis/abscess**
- E. **Acute mastitis**
- F. **Intraductal papilloma**
- G. **Galactocele/Lactating adenoma (pregnant or postpartum)**
- H. **Phyllodes tumor**
- I. **Lesion of fat or skin, e.g., lipoma or benign tumor of skin**

*** All lesions are described in Robbins except those associated with pregnancy**

3. Determine the diagnosis of Cases 1, 2 and 3 by using only the history and physical findings. What questions do you have to ask?

Where is the mass?

How long has the patient noticed the mass?

Is the mass painful? Is the breast painful?

Has the mass changed in size, shape, or consistency?

Does the mass change cyclically? What is the relationship of this change to menses?

Has there been a mass or lesion before this event?

Are there other changes in the breast, areola-nipple, overlying skin, or axilla?

Has there been a change in bra size?

Has there been trauma to the breast or radiation or procedures performed on the breast?

What the patient's reproductive/menstrual history?

What is the family history?

4. Summarize Case 1

Young woman with a unilateral, solitary, non-painful breast mass.

Mass is firm, discrete, non-tender, and movable.

No other changes are noted in the breasts, including nodularity.

Lesion is non-tender, despite recent modest trauma to breast during sports

Menstrual history is normal

Positive family hx - mother died from breast cancer

– **Patient is very young to have cancer.**

Breast asymmetry is normal (slight asymmetry is not uncommon)

Brown lesion in the milk line represents polythelia

– **An incidental finding.**

5. What is your clinical diagnosis?

Fibroadenoma

(fibroadenoma is favored over traumatic fat necrosis. Fat necrosis, though it may be movable and nontender, usually presents as a firm, tender, indurated, ill-defined mass)

6. Describe the gross and histologic characteristics.

Gross: Well circumscribed mass freely movable from surroundings breast tissue.

Histologic: Delicate stroma around compressed, distorted glandular spaces.

7. What is your final diagnosis?

Fibroadenoma

Most common benign tumor of female breast

Peak incidence is in third decade

CASE 2

CHIEF COMPLAINT:

“I feel a lump in my breast.”

HISTORY:

A 34-year-old woman presents with a palpable mass in the upper outer quadrant of her left breast. She first noticed the mass two months ago during a self-examination. The mass gradually enlarged, but there are no changes in the overlying skin, nipple, or areola. There is no liquid discharge from the nipple. Although the mass is not painful now, she experiences pain and tenderness every month prior to her menses. She states, “Both breasts get swollen and they’re sore as hell just before my period. You know, doc, as soon as my period is over, the pain goes away. This has been going on for years.” She does not remember injuring her breasts.

Her past medical history is unremarkable other than having an appendectomy at age 13. She is a homemaker and mother of three children. She smokes one pack of cigarettes per day (since age 17) and does not drink alcohol or coffee.

Her obstetric/gynecologic history reveals menarche at age 11. Her menses have been regular since age 17. Her menses occur every 27-30 days, lasting 5 days. Menstrual flow is moderate and consistent with each period. She is gravida 4, para 3 with one spontaneous abortion at age 31. She breast fed all of her children. She does not take oral contraceptives.

PHYSICAL EXAMINATION:

The breasts are examined with the patient in sitting and supine positions. The breasts are large, round, and symmetrical. The contour of each is smooth with no evidence of dimpling, retraction, or edema. The nipples and areolae are symmetrical, brown, and show no eczema or inversion. Palpation reveals a distinct, round, non-tender mass in the upper outer quadrant of the left breast. The lesion is firm, smooth, and movable (not fixed to the chest wall). The adjacent breast tissue is firm or rubbery and contains multiple small nodules of varying size. Both breasts contain firm, nodular tissue. Bilateral nipple compression produces no discharge. Palpation of the axillae, infraclavicular spaces, and the supraclavicular fossae reveal no lymphadenopathy.

1. What is the primary clinical problem?

Palpable breast mass

2. Develop a differential diagnosis for this problem:

- A. **Fibrocystic change**
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3. Case 2 Summary:

**Young woman with a palpable mass x 2 months
Associated with pain/tenderness**

– cyclical, occurring prior to each menstruation
Mass is firm, discrete, smooth and movable
No history of recent injury or pregnancy
Menstrual history is normal
Examination (as well as history) reveals changes in both breasts described as nodularity
No other changes in the breast, skin, and axilla
Previous episodes of bilateral breast changes during menstrual cycle
History/examination are consistent with a cyst.
The association of alcohol and coffee is questionable

4. What is your clinical diagnosis?

Fibrocystic change

5. Describe the histologic characteristics of this entity.

The patterns of fibrocystic breast disease are cysts, apocrine metaplasia, dense fibrosis and adenosis.

6. What, if any, is the relationship between this entity and breast carcinoma?

Minimal or no increased risk of cancer with nonproliferative fibrocystic changes

– Fibrosis, cysts, apocrine metaplasia

Increased risk with proliferative changes and epithelial hyperplasia

– Slightly increased risk (1.5-2x) with hyperplasia without atypia, ductal papillomatosis, sclerosing adenosis

– Significantly increased risk (5x) with atypical hyperplasia of ductal or lobular epithelium

CASE 3

CHIEF COMPLAINT:

“I have a lump in my left breast.”

HISTORY:

A 62-year-old woman presents with a “lump” in the upper, outer part of her left breast. She admits that she first noticed the lump about two months ago while bathing. She did not seek medical attention at the time because “I thought it was a cyst. When I was having my babies, I had lumpy breasts and the doctor told me not to worry because they were cysts.” She is worried now because “the lump is hard, and it’s bigger.” She felt the lump two months ago but it was not visible. Since that time, however, the lump “has grown” and is visible as “swelling near my armpit.” Although the breast lump is not painful now, “sometimes it is sore when I touch it.” She denies nipple discharge and changes of the areolae and nipples. She has not had mammogram for 8 years.

PHYSICAL EXAMINATION:

With the patient in a sitting position, her breasts are large, pendulous, and asymmetric. The left breast is larger than the right breast, showing a fullness in the upper outer quadrant that extends into the left axilla. The skin of the upper outer quadrant is dimpled. The dimpling is exaggerated and an underlying mass is visible when the patient presses the palmar surfaces of her hands against her hips or raises her arms above her head. The skin of the left breast, nipple, and areola is not thickened or inflamed. While in a sitting position, the patient leans forward; palpation of the left breast reveals a large (4-5 cm), stony hard mass in the upper outer quadrant.

The left axilla contains 3 or 4 enlarged, firm, non-tender lymph nodes. The largest node is one centimeter in diameter. Examination of the right breast and axilla reveal no pathologic findings. In a supine position, palpation of the left breast reveals a non-tender, stony hard mass that is fixed to the anterior chest wall. Careful inspection/palpation of the remainder of the left breast reveals no additional masses. There is no lymphadenopathy of the right axilla or the right and left infraclavicular regions of the chest wall. Compression of the nipples reveals no bloody discharge. The nipples are not retracted.

1. What is the primary clinical problem?

Palpable breast mass

2. Develop a differential diagnosis for this problem:

- A. **Fibrocystic change**
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3. Case 3 Summary

Post-menopausal woman with a solitary, hard non-painful mass in the upper outer breast fixed to the chest wall

Skin overlying the mass is dimpled.

Axilla with non-tender, enlarged lymph nodes

History of fibrocystic changes of the breast

4. What is your clinical diagnosis?

Breast Cancer

5. Describe the histologic findings.

The tumor is composed of malignant cells arranged in cords, nests, and tubules invading the stroma.

6. What is your final diagnosis?

Invasive (infiltrating) ductal carcinoma

7. Determine the stage of the lesion in Case 3 based on the data given.

Stage III (refer to page 1147 in Robbins) Tumor greater than 2 cm diameter, positive axillary lymph nodes, FIXATION TO CHEST WALL.

CASE 4

CHIEF COMPLAINT:

“My abdomen seems to be getting bigger.”

HISTORY:

A 49-year-old woman without a significant past medical history presents to her doctor with increasing abdominal girth.

PHYSICAL EXAMINATION:

Thin woman is in no acute distress. Heart and lung exams are normal. Her abdomen is protuberant. Shifting dullness during abdominal percussion and a fluid wave are appreciated. There is no hepatosplenomegaly, though the exam is limited.

1. What is the main clinical problem?

Abdominal swelling - Ascites

2. Develop a differential diagnosis

Cirrhosis

Congestive heart failure

Nephrotic syndrome

Disseminated carcinomatosis

Diagnostic Imaging:

Computed tomographic scan of the abdomen demonstrates ascites as well as a large adnexal mass.

3. Describe the characteristic pathologic changes in the virtual microscopy slide:

Section of ovarian neoplasm reveals large and small cystic spaces filled with papillary tumor. The papillary structures are composed of connective tissue cores covered by neoplastic epithelium which appears to form cilia.

4. Diagnosis:

Cystadenocarcinoma

(papillary serous cystadenocarcinoma)

Most common malignant ovarian tumor

5. What are risk factors for the development of this disease?

Family history

Increased risk in unmarried women and married women with low parity

BRCA1 and BRCA2 mutations portend an increased risk

Gonadal dysgenesis

6. What is the pathogenesis of the ascites?

Epithelial ovarian cancers can spread intraperitoneally

The most common and earliest mode of spread is by exfoliation of cells that implant along the surfaces of the peritoneal cavity

Results in alterations in the permeability of the peritoneum or obstruction of peritoneal lymphatics and development of ascites

CASE 5

CHIEF COMPLAINT:

“I’m passing blood clots and clumps of white stuff from my vagina.”

HISTORY:

A 39-year-old woman presents with vaginal bleeding, and passage of clots and “clumps of white stuff” per vagina. She had missed her last period, had a positive home urine pregnancy test result and was arranging her first visit with an obstetrician/gynecologist.

PHYSICAL EXAMINATION:

The uterus is enlarged but fetal activity is not detected.

Laboratory Data

Serum hCG >100,000 mIU/mL

Transvaginal Ultrasound:

Enlarged uterus with a central heterogeneous mass with numerous discrete anechoic spaces. No embryo or fetus detected. No amniotic fluid.

1. Identify the organ:

placenta

2. Describe the characteristic pathologic changes:

Fragments of tissue containing markedly swollen chorionic villi covered by neoplastic trophoblast. The villi are edematous and avascular. The trophoblastic cells are atypical.

3. Diagnosis:

Hydatidiform mole

- Complete and partial moles are usually benign forms of gestational trophoblastic disease
- The tumors develop as a result of an aberrant fertilization event leading to proliferation of trophoblastic tissue
 - Sperm meets egg...however
 - In complete mole there is fertilization of an empty ovum that lacks functional maternal DNA
 - In partial mole, normal ovum is fertilized by two normal spermatazoa

Review of main features distinguishing complete from partial hydatiform moles.

Features	Complete Mole	Partial Mole
Karyotype	46, XX (46, XY)	Triploid
Villous Edema	All villi	Some villi
Trophoblast Proliferation	Diffuse, circumferential	Focal, slight
Atypia	Often present	Absent
Serum HCG	Elevated	Less elevated
Behavior	2% choriocarcinoma	Rare choriocarcinoma