Breast
2013-2014

Structure of normal breast

- The breast is modified sweat gland covered by skin & subcutaneous tissue.
- It rests on fascia and muscle.
- Glandular tissue consists of 15 to 20 lobules that enter into branching and interconnected ducts.
- The lobules are comprised of acini that consist of layers of two types of cells (epithelial and myoepithelial)
- Lactiferous duct is a collecting duct that empties into the nipple
- Lactiferous sinus is a fusiform dilatation beneath the nipple
INFLAMMATION (MASTITIS)

I- Infective:  Breast abscess

II- Non Infective

A- Traumatic fat necrosis

B- Periductal plasma cell mastitis  (Mammary ductectasia)

**Breast Abscess**

**Predisposing factors**

It occurs during lactation especially in primipara due to:

1- Ignorance of nipple hygiene.

2- Nipple abrasion (tissue).

3- Retained milk.

**Pathology:**
* Single or multiple abscesses which may be:
  
  - Premammary - Intramammary - Retromammary.

* It may be acute or chronic.

Non Infective Mastitis

I- Traumatic fat necrosis

Posttraumatic fat necrosis and lipoatrophy can occur in the subcutaneous fat following falls, blunt injury, surgery, and minor procedures or injections. While these processes have no inherent serious medical consequences, they occasionally require treatment due to severe or concerning symptoms.

M/E:

- Partially necrotic adipose tissue with foamy macrophages, multinucleated giant cells and chronic inflammatory cells
- Often hemosiderin deposits, fibrosis and calcification
- Occasional metaplastic squamous epithelium

II- Periductal plasma cell mastitis (Mammary duct ectasia):

Uncommon inflammatory disease usually affects multipara, characterized by dilatation of mammary ducts, inspissation of breast secretions and marked periductal chronic inflammation rich in plasma cells.

Pathogenesis:

1- Narrowing of main excretory ducts due to post traumatic fibrosis (during lactation).
2- Retained milk causes ductal dilatation proximal to the narrowing and ruptures.
3- Milk escapes in surrounding breast tissue leading to inflammatory reaction and fibrosis.

N/E:

1- Lesion feels as a bag of worm in one or more segments of the breast.
2- C/S: dilated ducts containing cheesy material.
3- Later, the lesion forms a firm mass with nipple retraction and discharge from it.

M/E:
* Progressive dilatation of ducts with thinning of their lining epithelium which ruptures.

* Duct contents are debris; lipid laden fluid and foamy macrophages.

* Periductal tissue is infiltrated by chronic inflammatory cells (rich in plasma cells), foreign granuloma may be produced + fibrosis.

**DIFFERENTIAL DIAGNOSIS OF BREAST**

**LUMPs "MASS"**

**I- Traumatic**

1. Traumatic fat necrosis
2. Hematoma.

**II- Inflammatory:**

1. Breast abscess
2. Mammary ductectasia
3. Granuloma:TB, S., Actinomycosis

**III- Neoplastic:**

**Benign:**

1. Fibrocystic diseases
2. Fibroadenoma
3. Phyllloid tumours.
4. Others: - Duct papilloma.
   - Papillary cystadenoma.

**Malignant…. In situ or invasive**

**A- In situ**

**I- intraduct carcinoma:**

1. Papillary.
2. Cribriform.
5. intraduct carcinoma- Paget’s dis.

II- Lobular carcinoma in situ:

B- Invasive:

I- Invasive duct carcinoma:

1. NOS (65 -80%).
2. Medullary (1 -5%).
3. Mucinous (colloid).
4. Invasive carcinoma - Paget’s dis.

II- Invasive lobular carcinoma.

FIBROCYSTIC DISEASE OF BREAST

Cystic Mammary Hyperplasia

Incidence:
- The commonest breast lesion during the reproductive period (30-40 years). It usually occurs in multipara.

Cause: hyperestrogenemia.

Pathogenesis: Derangement of cyclic breast changes that occur normally during the menstrual cycle.

N/E:
- Bilateral or unilateral, multiple lumps or solitary mass.
- Uncapsulated, ill defined, rubbery in consistency,
- C/S: the lesion is ill defined, gray in a white background. It may show variable sized cysts which are thin walled and contain serous or hemorrhagic fluid.

M/E:
1. Adenosis: increase in the number of the ducts and acini with variation in size and shape.
2- **Cyst formation**: ducts and ductules undergo cystic dilatation; they are lined by a layer of cubical or flattened cells sometimes the lining epithelium change to large columnar cells with acidophilic cytoplasm and central nuclei (Apocrine metaplasia). The cells may form papillae.

3- **Epitheliosis**: hyperplasia of the epithelium lining the ducts and ductules. It may be typical or atypical (it is precancerous):

4- **Fibrosis**: periductal collagen.

5- **Lymphocytic** infiltration in the stroma.

**Prognosis of fibrocystic disease**

Epitheliosis increases the risk of breast cancer which is more evident with atypical hyperplasia.

**Prognosis:**

Epitheliosis increase incidence of breast cancer which is more evident with atypical hyperplasia

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**TUMOURS OF THE BREAST**

**I- Benign Tumors**

1- **Fibroadenoma**

- The commonest benign tumour of the breast.

- It is a true mixed tumour arising from the fibrous tissue and the epithelial element of the breast.

- It occurs during the reproductive period of life (peak incidence is in 3rd decade) especially in nullipara.
Cause: Estrogen stimulation.

N/E:

- Usually single mass, rounded or oval.
- Capsulated (true capsule), well defined, variable in size.
- Firm in consistency and freely mobile.
- C/S: capsulated mass, well circumscribed, greyish white in color, solid, (sometimes with slits).
- The pericanalicular fibroadenoma tends to be smaller in size, more firm and the cut surface is homogenous solid.
- The intracanalicular fibroadenoma is larger in size, less firm and its cut surface shows numerous small slits.

M/E:

a- True mixed tumour formed of neoplastic acini and ducts separated by fibrous tissue stroma which is neoplastic proliferation of fibroblasts.

b- Surrounded by true capsule. It may be:

1- Pericanalicular fibroadenoma.
2- Intracanalicular fibroadenoma.
3- Mixed.

(1) Pericanalicular fibroadenoma: there is equal proliferation of C.T. and epithelial element. It consists of:

a- proliferated ducts and acini (round or oval in cut section), with patent lumens. They are lined by 2 layers of cells, inner cubical and outer flattened.

b- They are separated by loose fibrous tissue stroma containing blood vessels.

(2) Intracanalicular fibroadenoma: there is more proliferation of connective tissue than epithelium. It consists of:

a- Proliferated ducts and acini which are compressed, elongated, curved and branched with reduced lumens to slits.

b- They are lined by two layers of cells (inner cubical and outer flattened) but they are so approximated that they appear as one layer.
- They are surrounded and invaginated by loose fibrous tissue stroma giving the false impression that epithelium surrounds fibrous tissue.

Effect: Malignancy is rare.

**Cystosarcoma phylloides = giant fibroadenoma.**

N/E:

Huge, rounded, well circumscribed mass.

**Consistency:** firm

**C/S:** greyish white and show cleft-like spaces or may be cysts.

**M/E:** intracanalicular fibroadenoma but stroma between acini is highly cellular and myxomatous. Cysts may be present.

**Prognosis:**

Most phylloides tumors are benign but few are malignant with hematogenous spread. Metastases consist of stroma cells only.

2- **Papillary cystadenoma.**
Rarely it can transform to papillary cystadenocarcinoma.

3- Duct papilloma

- Usually occurs in 4th or 5th decade.
- Usually manifests by nipple discharge (which may be clear, turbid, bloody) or may be presents as a small subareolar tumour (few mm. in diameter).

N/E:

Site: usually within a large duct (in a lactiferous duct) near the nipple.

Shape: papillary growth, sessile, pedunculated simple or compound.

Size: small (usually less than 1cm).

Consistency: friable.

C/s: solid.

M/E:

* Branching papillae within the duct formed of fibrovascular core covered by one or two layers of cuboidal or columnar epithelium.

Prognosis:

1- Involution leading to epithelial atrophy and hyalinization.
2- Rarely it changes to duct papillary carcinoma.

II- Malignant Tumors

Carcinoma of breast

Incidence:

- One of the commonest cancers in females.
- Incidence increases with old age.

Predisposing factors (risk factors) and precancerous lesions:

1- Age: old age (except familial).
2- Reproductive life:
   - More in nullipara.
- More when 1st pregnancy occurs above 30 years.
- More with prolonged reproductive life (early menarche and late menopause).

3- Genetic and familial predisposition:

- Occur at younger age. - Positive family history.
- Occur in 1st degree relatives. - Bilateral lesions are common.
- Familial association between cancer breast, ovarian tumour and endometrial carcinoma.
- Genetic mutation, e.g.: C-erb B$_2$, p$_{53}$, BRCA

4- Hyperestrinism:

a- Obesity (synthesis of estrogen in fat depot).

b- 50% of breast carcinomas are hormone dependent. They have estrogen receptors and progesterone receptors (N.B. they have better prognosis).

5- Mammary tumor virus (MTV= milk factor)

- Demonstrated in mice milk.
- Produce experimental breast cancer in mice.
- A similar mechanism may occur in man.

6- Ionizing radiation.

7- Breast lesions:

1- Fibrocystic disease especially with atypical hyperplasia.

2- Interference with breast drainage.

3- Carcinoma in situ: - In situ duct carcinoma (intraduct)

- In situ lobular carcinoma.

4- Carcinoma of other breast.

5- Benign tumors.

Site:

- Commonest site is outer upper quadrant.
- Left breast affected slightly more frequent than right.
- Bilateral in 4-10%.

**Classification:**

1. Carcinoma from the mammary ducts (90%).
   - In situ duct (intraduct) carcinoma.
   - Invasive (infiltrating) duct carcinoma.

2. Carcinoma from the mammary lobules. (10%)
   - In situ lobular carcinoma.
   - Invasive (infiltrating) lobular carcinoma.

**1- Carcinoma from mammary duct**

**1) In situ duct (intra duct) carcinoma.**

It is a preinvasive neoplasm which has not yet broken through walls of the ducts.

**N/E:**

1- Slowly growing small hard masses causing bloody or serous discharge from the nipple.

- C/S: shows dilated ducts filled with papillary structures (papillary intraduct carcinoma) or plugs of pasty-like yellowish necrotic tissue which can be extruded upon light pressure (comedocarcinoma).

2- Intraduct carcinoma with Paget's disease: a form of duct carcinoma that extends along the main mammary duct to infiltrate the epidermis covering the nipple and areola which shows eczema (the skin appears red, swollen, granular, fissured, eroded, ulcerating and oozing).
M/E:

1 - The ducts are dilated and distended by malignant cells without invasion of the basement membrane. The malignant cells are arranged within the ducts in the following patterns:

a- Papillary structure (intraduct papillary carcinoma).

b- Form anatomizing cords across the lumen of the ducts (cribriform pattern).

c- May occlude the duct completely.

d- Solid with central cells show necrosis - appears red and granular (Comedocarcinoma). Calcification of central necrosis may occur.

2- Paget's disease: The epidermis is thickened and show round, large pale vacuolated cells called Paget's cells.

Prognosis:

Good with complete removal.

(2) Invasive (infiltrating) duct carcinoma

a- Infiltrating duct carcinoma NOS (not otherwise specified).

- The commonest type (65%-80% of all mammary carcinoma).

N/E:

- Ill defined nodule of stony hard consistency about 1-4 cm in diameter, fixed with infiltrative borders.
- C/S: concave (retracted), hard in consistency (scirrhous carcinoma) with gritty sensation on cutting, greyish white with small foci of hemorrhage, necrosis and calcification.

- Skin changes: the skin covering the breast shows dimpling, retraction of the nipple, ulceration, and cancer en cuirasse or peau d’orange.

**M/E:**

Small groups or cords of malignant cells separated by abundant dense collagenous stroma (desmoplasia). The tumour cells are small, rounded or polygonal with darkly stained nuclei.

**B- Special variants**

1- **Medullary carcinoma:**

- 1 -5% of all mammary carcinomas.

**N/E:**

* Large fleshy mass.

* C/S: soft, fleshy with large numerous foci of hemorrhage and necrosis.

**M/P:**

-Solid sheets of malignant cells separated by scanty fibrous tissue stroma.

- The malignant cells are large with indistinct borders and vesicular pleomorphic nuclei with prominent nucleoli and frequent Mitoses. The stroma shows excess lymphocytes.

- The prognosis is relatively good.

**2- Mucinous (colloid) carcinoma.**

- occurs in older women.
N/E:
Slowly growing tumor forming soft, gelatinous large mass.

M/E:
- Lacks of mucin with scattered small islands of isolated malignant cells.
- The prognosis is good.

3- **Invasive duct carcinoma with Paget's disease:**
- The epidermis is thickened and shows Paget's cells.
- The dermis is infiltrated by masses of tumor cells.

**II- carcinoma from mammary lobule "lobular carcinoma"**

(1) **In situ lobular**
Usually discovered incidentally in biopsies of other lesions occur near the menopause.

M/E:
- One or more breast lobules are affected.
- All terminal ductules and acini of the affected lobule are filled and distended with malignant cells.
(2) Infiltrating lobular carcinoma

N/E:
- Ill defined mass, rubbery or may be hard.

M/E:
- Strands of malignant cells of Indian file pattern (i.e. one cell width), a separated by fibrous tissue stroma.
- The cells are small, uniform with little pleomorphism

Prognosis:
- Worse than infiltrating duct carcinoma.
- The tumour usually multicentric, bilateral.

Spread of infiltrating carcinoma of breast

* Direct Spread:
It involves:
- Deep fascia and pectoralis muscle, chest wall, pleura.
- Overlying skin: producing dimpling ulceration, nipple retraction. Occasionally the skin of the chest and arm is massively invaded by a scirrhous growth. The skin becomes thick, hard and fixed to the underlying structures. The picture is called cancer en cuirasse.

* Lymphatic spread:

- Common and early due to rich lymphatic of breast.

- It occurs by 2 ways:

1- Lymphatic emboli lead to metastasis in:
   a- Lymph nodes - Axillary either ipsilateral or contralateral
      - Internal mammary
      - Mediastinal.
      - Supraclavicular
   b- Opposite breast, liver peritoneum.

2- Lymphatic permeation (skin lymphatic) leads to:
   a- Formation of small malignant nodules under the skin.
   b- Cancer en cuirasse: due to wide spread affection of skin of chest, abdomen and arm by scirrhous growth.
   c- Peau d'orange: malignant obliteration of skin lymphatic oedema of skin except at sites of hair follicles attachment, the breast skin resembles orange peel (fine mammillated appearance).

III- Blood spread:

Occurs early or late → lung, liver, bone, brain and adrenal

Staging of cancer breast

TNM system

MALE BREAST

* Gynaecomastia:

Definition: enlargement of male breast.

Causes:
I - Physiological: at puberty and extreme old age.

2- Pathological: e.g.
   a- Liver cirrhosis: (liver unable to inactivate estrogen).
   b- Estrogen therapy for treatment of cancer prostate.
   c- Estrogen producing tumors of adrenal cortex and testis.
   d- Digitalis therapy "occasional"
   e- Klienfelter's syndrome (xxy).
      - Phenotypically (xxy)
      - Gynaecomastia.
      - Mental retardation.

N/E:

Button like subareolar swelling develops bilateral (occasionally unilateral).

M/E:

Breast lobules like normal breast

* Carcinoma of male breast:

   Occurs in old age more common with estrogen therapy. It is the same as cancer breast.

Prognosis:

   Bad as the tumor infiltrates the surrounding structures early due to the small size of breast.