Breast cancer

By

Prof. Ahmed El-Samongy

professor of GI Surgery
objectives

- Aetiology
- Pathology
- Risk Factors
- Diagnosis
- Staging
- Treatment options
- The male breast
Breast cancer is the commonest cause of death in middle-aged women in the Western countries and will affect half million women worldwide each year.

**Aetiological factors:**

- **Geographical.** It occurs commonly in the Western world, accounting for 3-5 per cent of deaths. In developing countries it accounts for 1-3 per cent of deaths.
- **Age.** Carcinoma of the breast is extremely rare below the age of 20.
- **Gender.** Only 1 per cent of patients with breast cancer are males.
Genetic.

- It occurs more commonly in women with a +ve family history.
- Abnormality frequently exists in the short arm of chromosome (N.17).
- Also mutations in the "tumour suppressor" gene.
- At least two genes that predispose to breast cancer have been identified— BRCA 1 and BRCA 2.

Diet.

- Because breast cancer so commonly affects women in the “developed” world, dietary factors may play a part in its causation.
- There is increasing evidence that there is link between diets rich in saturated fatty acids and breast cancer and vitamin C may be protective.
- A high intake of alcohol may also be associated with an increased risk of developing breast cancer.
Endocrine.

- Breast cancer is commoner in nulliparous women, ↑ levels of estrogen ↑ risk.

- Breast feeding in particular appears to be protective. Also protective is having a first child at an early age.

- Breast cancer is more common in obese women. This is thought to be because of an increased conversion of steroid hormones to oestradiol in the body fat.
Pathology

Ca. breast represent 80% of all breast lesions.

- Site: mostly upper outer quadrant (50%).
- Cell of origin: - duct epithelium 95%.
  - acini 5%
Pathology.

- Breast cancer may arise from the epithelium of the duct system anywhere from the nipple end of major milk ducts to the terminal duct unit which is in the breast lobule.

- The degree of differentiation of the tumour is usually described by three grades. Well differentiated, moderately or poorly differentiated. *Ductal carcinoma* is the commonest variant, but *lobular carcinoma* occurs in up to 10 per cent of cases, although this may be *mixed.*
Rare histological variants, usually carrying a better prognosis, include colloid carcinoma whose cells produce abundant mucin, medullary carcinoma with solid sheets of large cells often associated with a marked lymphocytic reaction and tubular carcinoma.

Invasive lobular carcinoma is commonly multifocal and/or bilateral.
The spread of mammary carcinoma

**Local spread**
- The tumour increases in size and invades other portions of the breast.

**Lymphatic spread**
- Occurs primarily to the axillary LN and to Int. Mam. LN
- In advanced cases there is involvement of supraclavicular nodes and contralateral LN.

**Bloodstream spread**
- Skeletal metastases in the lumber vertebra, femurs, thoracic vertebra, ribs and skull; they are osteolytic tumour.
- Metastases may also occur in the liver, lung and brain, adrenal gland and ovaries.
Pathological types

Noninvasive Epithelial Cancers

- Lobular carcinoma in situ (LCIS)
- Ductal carcinoma in situ (DCIS) or intraductal carcinoma
**Invasive Epithelial Cancers (percentage of total)**

- Paget's disease of the nipple
- Invasive ductal carcinoma
  - Adenocarcinoma with productive fibrosis, scirrhous, (80)
  - Tubular carcinoma (2–3)
  - Mucinous or colloid carcinoma (2–3)
  - Medullary carcinoma (5)
  - Invasive papillary (1–2)
- Invasive lobular carcinoma (10)
- Rare cancers (adenoid cystic, squamous cell, apocrine)
# Carcinoma in situ

<table>
<thead>
<tr>
<th></th>
<th>LCIS</th>
<th>DCIS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>44-47</td>
<td>54-58</td>
</tr>
<tr>
<td><strong>CP</strong></td>
<td>None</td>
<td>Pain, mass, N. discharge</td>
</tr>
<tr>
<td><strong>Mammography</strong></td>
<td>None</td>
<td>Microcalcification</td>
</tr>
<tr>
<td><strong>Multicentricity</strong></td>
<td>60-90%</td>
<td>40-80%</td>
</tr>
<tr>
<td><strong>Bilaterality</strong></td>
<td>50-70%</td>
<td>10-20%</td>
</tr>
<tr>
<td><strong>Axillary LN metastasis</strong></td>
<td>1%</td>
<td>1-2%</td>
</tr>
<tr>
<td><strong>Subsequent BC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>Up to 35%</td>
<td>Up to 75%</td>
</tr>
<tr>
<td><strong>Laterality</strong></td>
<td>Bilateral</td>
<td>Unilateral</td>
</tr>
<tr>
<td><strong>Interval</strong></td>
<td>10-20 Ys</td>
<td>5-10 Ys</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>IDC</td>
<td>IDC</td>
</tr>
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</table>
Risk Factors for Breast Cancer

**Hormonal risk factors**
- Increased exposure to estrogen.
  - Female sex—women to men ratio is about 100:1
  - Early menarche, nulliparity, and late menopause.
  - Moderate levels of exercise and a longer lactation period.
  - Older age at first live birth.
- Obesity

**Nonhormonal risk factors**
- Radiation exposure.
  - Mantle radiation therapy for Hodgkin's lymphoma (75 times greater)
  - Survivors of the atomic bomb blasts in Japan during World War II
- Chronic consumption of foods with a high fat content
Familial breast cancer

Breast cancer may be:

- Sporadic breast cancer: 65–75%
- Familial breast cancer: 20–30%
- Hereditary breast cancer: 5–10%
Premalignant lesion

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Florid hyperplasia</td>
<td>1.5 -2-fold</td>
</tr>
<tr>
<td>Atypical lobular hyperplasia</td>
<td>4-fold</td>
</tr>
<tr>
<td>Atypical ductal hyperplasia</td>
<td>4-fold</td>
</tr>
<tr>
<td>Ductal involvement by cells of atypical ductal hyperplasia</td>
<td>7-fold</td>
</tr>
<tr>
<td>Lobular carcinoma in situ</td>
<td>10-fold</td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>10-fold</td>
</tr>
</tbody>
</table>
Diagnosis

Triple assessment:

1. Physical examination
2. Mammography and/or U/S
3. Biopsy
Clinical picture

Symptoms

- None
- Painless lump
- Pricking pain = Inflammatory cancer, infection, advanced cancer
- Bloody discharge per nipple
- Of metastasis.
Signs

- Mass which is:
  Hard, irregular, ill-defined
- LN enlargement
- Metastasis
Skin manifestations

- Dimpling
- Buckering
- Peau d’orange
- Nodule
- Ulcer
- Nipple retraction, ulceration, deviation
- Cancer en cuirasse
- Paget disease
Mastitis carcinomatosa (acute cancer) (2%):
- Occurs mostly during pregnancy and lactation.
- It is the result of an unbridled proliferation of cancer cells with very little fibrous reaction.
- Rapidly metastasizing tumour.
- Very bad prognosis. The patient dies within few months.
- Condition may resemble acute abscess. It differs:
  1. Oedema is more marked and extensive, (extends over more than 1/3 of breast. It is usually nonpitting. (Oedema indicates blockage of the subdermal lymphatics with malignant cells).
  2. Skin is dusky red with dilated veins.
  3. L.Ns. are hard & fixed.
  4. Fever and leucocytosis are absent.
  5. No response to antibiotics.
- The diagnosis is confirmed by aspiration biopsy or, better by axillary gland biopsy.
Paget's Disease of the breast (1%)

Clinical:

1) Eczema-like condition.

2) Mass behind the areola.

- Malignant eczema (Paget's) vs. Ordinary eczeme

1. Old female above 50y.
   - During childbearing period.

2. Unilateral.
   - Usually bilateral

3. Nipple & areola eroded
   - No erosion

4. Well defined margin with no vesicles.
   - Ill defined with vesicles.

5. Not oozing, not itching
   - Oozing & itching.

6. Followed by carcinoma
   - May be followed by abscess.

7. No response to treatment
   - Respond to treatment.
Biopsy

- FNAB
  1. Palpable lesions
  2. Mammographic abnormalities
- True cut biopsy
- Open biopsy
Staging of breast cancer

- There are two traditional systems of classification for breast carcinoma which predominantly rely on clinical staging of the disease.

- These are the Manchester system and the International Union Against Cancer TNM (tumour, nodes, metastases).
(A) International TNM staging

**Tumour T**

- Tis: In situ
- T1: <2cm
- T2: 2-5cm
- T3: >5cm
- T4: Fixed to skin or chest wall

**Nodes N**

- N0: Impalpable
- N1: Mobile
- N2: Fixed
- N3: Supraclavicular

**Metastasis M**

- M0: No mets
- M1: Distant mets
Staging

Primary tumor (T)

- TX  Primary tumor cannot be assessed
- T0  No evidence of primary tumor
- Tis  Carcinoma in situ
  - Tis (DCIS)  Ductal carcinoma in situ
  - Tis (LCIS)  Lobular carcinoma in situ
  - Tis (Paget's)  Paget's disease of the nipple
Staging

- **T1** Tumor 2 cm or less
  - **T1 mic** Microinvasion 0.1 cm or less
  - **T1a** Tumor 0.1- 0.5 cm
  - **T1b** Tumor 0.5 - 1 cm
  - **T1c** Tumor 1 - 2 cm

- **T2** Tumor 2 - 5 cm

- **T3** Tumor more than 5 cm
Staging

- **T4**  Tumor of any size with direct extension to (a) chest wall or (b) skin
  - T4a  Extension to chest wall
  - T4b  skin manifestations confined to the same breast
  - T4c  Both T4a and T4b
  - T4d  Inflammatory carcinoma
Regional lymph nodes—Clinical (N)

- **NX**  Regional lymph nodes cannot be assessed
- **N0**  No regional lymph node metastasis
- **N1**  Metastasis to movable ipsilateral axillary lymph node(s)
- **N2**
  - **N2a**  Metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures
  - **N2b**  Metastasis only in clinically apparent ipsilateral internal mammary nodes
Staging

$N_3$

$N_3a$ Metastasis in ipsilateral infraclavicular lymph node(s)

$N_3b$ Metastasis in ipsilateral internal mammary lymph nodes(s) and axillary lymph node(s)

$N_3c$ Metastasis in ipsilateral supraclavicular lymph node(s)

Distant metastasis (M)

$M_0$

$M_1$
TNM Stage Groupings

- **Stage 0**
  - Tis No Mo

- **Stage I**
  - T1 No Mo

- **Stage IIA**
  - T0 N1 Mo
  - T1 N1 Mo
  - T2 No Mo

- **Stage IIB**
  - T2 N1 Mo
  - T3 No Mo
TNM Stage Groupings

- **Stage IIIA**
  - $T_0 \ N_2 \ M_0$
  - $T_1 \ N_2 \ M_0$
  - $T_2 \ N_2 \ M_0$
  - $T_3 \ N_1 \ M_0$
  - $T_3 \ N_2 \ M_0$

- **Stage IIIB**
  - $T_4 \ N_0 \ M_0$
  - $T_4 \ N_1 \ M_0$
  - $T_4 \ N_2 \ M_0$

- **Stage IIIC**
  - Any $T \ N_3 \ M_0$

- **Stage IV**
  - Any $T \ Any \ N \ M_1$
Manchester staging

- **Stage I**
  A mobile mass in the breast. The tumour is not adherent to the pectoral muscles or chest wall. No palpable axillary lymph nodes.

- **Stage II**
  A mobile mass in the breast with or without skin tethering + Palpable mobile homolateral axillary nodes.

- **Stage III**
  Any of the following:
  - Skin involvement or Peau d'orange larger than the tumour but still limited to the breast.
  - Tumour fixed to pectoral muscle but not to the chest wall.
  - Homolateral axillary lymph nodes matted together or fixed to chest wall.
  - Homolateral supraclavicular lymph nodes.

- **Stage IV**
  - Oedema of the arm.
  - Skin involvement wide of the breast (cancer en cuirasse).
  - Fixation to the chest wall.
  - Distant metastases.
  - Involvement of the opposite breast or axilla.
Prognostic factors

- Age
- Low TNM
- Special types
- Vascular/lymph infiltration
TREATMENT OPTIONS

- Surgery
  - **Radical Halsted mastectomy** or Modified radical (Patey’s) mastectomy or simple Mastectomy. Pectorals minor divided at (their insertion) or removed to open the axilla.

- **Breast conservation**.
  - *Wide local excision or lumpectomy.* A quadrantectomy involves removing the entire segment of the breast which contains the tumour with axillary dissection and radiotherapy is known as **QUART**

- Radiation therapy (local control)
Adjuvant systemic therapy

1. **Chemotherapy** (systemic control)
   Cyclophosphamide, methotrexate and 5-fluourouracil for 6 cycle (CMF)

2. **Hormonal therapy** (systemic control)
   - Tamoxifen, the luteinizing hormone releasing hormone (LHRH) agonists. Zoladex=goserlin
   
   ➢ **Breast reconstruction**
   - Silicone gel implant under the pectoralis major M.
   - Musculocutaneous flap can be constructed either from the latissimus dorsi muscle (an LD flap) or contralateral transversus abdominis muscle (a TRAM flap)
Surgery

- Radical mastectomy
- Modified radical mastectomy

- Conservative breast surgery (BCS)
  1. Wide local resection with 2 cm safety margin
  2. Axillary sampling/ dissection
  3. Post-operative breast radiotherapy
Four structures are scarificed:

1- Medial pectoral nerve.
2- Lateral pectoral nerve.
3- Intercostobrachial nerve.
4- Acromiothoracic artery.

Four structures are preserved during Patey’s:

1- Nerve to *serratus anterior*. (injury leads to Winging of the scapula)
2- Nerve to latissimus.
3- Axillary vessels & nerves.
4- Cephalic vein. (If thromb.--- *Brawny oedema*)
Adjuvant Therapy

1. Radiation Therapy (local)
2. Chemotherapy (systemic)
3. Hormonal agents (systemic)
Radiation Therapy

- Radiation therapy is used for all stages of breast cancer.
- For women with limited stage 0, I & II treated by CBS, adjuvant radiation therapy is given to reduce the risk of local recurrence.
- Women with metastatic disease involving four or more axillary lymph nodes and premenopausal women with metastatic disease involving one to three lymph nodes also are at increased risk for recurrence and so are candidates for radiation therapy.
- In stage III, women are at high risk for recurrent disease following surgical therapy and adjuvant radiation therapy is employed to reduce the recurrence rate.
Chemotherapy

- **Chemotherapy Drugs**
  1. Adriamycin, Epirubicin
  2. Cytoxan
  3. Methotrexate, 5-fluorouracil
  4. Taxol, Taxotere

- Nausea, hair loss, low blood counts, cardiac toxicity, bladder toxicity, nerve damage
Hormonal agents

**Tamoxifen**

- Can be given to pre or post menopausal women
- Works by blocking estrogen receptors in breast cells, inhibiting their growth
- Side effects include hot flashes, depression, increased risk of uterine cancer and DVT
- Taken daily by mouth for 5 years
Hormonal agents

Aromatase Inhibitors

- Aromatase is the enzyme that converts androgens to estrogen
- AIs are only given to postmenopausal women
- “May” be more effective than Tamoxifen
- Examples:
  - Anastrozole
  - Letrozole
- Side effects include hot flashes, depression, osteoporosis, joint pains
- Taken daily by mouth for variable periods of time
Reconstruction following Mastectomy

- Exception locally advanced cancer requiring postmastectomy radiation
- Reconstruction should be delayed until treatment completed
- Multiple options:
  - Implants and tissue expanders
  - Autologous tissue transfers:
THE MALE BREAST

- **Gynecomastia**
  - Enlargement of the male breast due to hormonal imbalance (rel. ↑estrogens):
    - **Physiologic**; seen at puberty or old age
    - **Pathologic**; associated with cirrhosis, functional testicular tumours, certain drugs (alcohol, marijuana and anabolic steroids)
  - Can be unilateral/bilateral; present as diffuse enlargement /defined mass
  - Most important clinically as a marker of hyperestrinism
  - Neoplasia needs to be excluded in certain cases
Carcinoma

- Very rare occurrence; female cancer to male cancer ratio approx 100:1
- Pathology and behavior is similar to cancers seen in women although with less breast tissue, skin involvement is more frequent
THANK YOU