OBJECTIVES

• Review breast anatomy localize different lesions
• Discuss acute mastitis
• Distinguish fat necrosis from cancer
• Define the components of fibrocystic changes

Objectives (cont’d)

• Compare/contrast fibroadenoma and phyllodes tumor
• Recognize intraductal papilloma as the most common cause of bloody nipple discharge in younger women
• Describe the mechanism of Paget’s disease
• Rank fibroadenoma, ADH, DCIS, and LCIS in terms of developing invasive carcinoma after diagnosis

Objectives for Breast Cancer

• Common breast cancer histologic type(s)
• Breast cancers with better prognosis
• Compare and contrast BRCA1/BRCA2 mutations
• Recognize 4 molecular types of breast cancers
TERMINAL DUCT LOBULAR UNIT

From histology for pathologists
Young women
Fibrous

Pregnancy: Numerous & larger lobules

Older women
Less lobules; Stroma replaced by Adipose tissue

Inflammatory Conditions
Acute Mastitis

- Occurs during lactation
  - Staphylococcal and streptococcal infections
  - First month of breast feeding
  - Cracks/fissures in nipple → bacterial entry
  - Erythema, pain, fever

FAT NECROSIS

- Generally associated with trauma
  - Occasionally prior surgery or radiation therapy
  - 50% may not report trauma
- Clinical significance:
  - Confusion with cancer due to palpable mass or calcification on mammogram
- Histology:
  - Necrotic fat cells surrounded by macrophages and neutrophils, then fibroblasts, lymphocytes and histiocytes
FAT NECROSIS

CHRONIC INFLAMMATION

NECROTIC FAT CELLS

FIBROCYSTIC CHANGES

- Two types: Non-Proliferative and Proliferative.
- Single most common breast disorder
  - Non-proliferative
- Clinically relevant:
  - Mass, mammographic calcification or nipple discharge occurs
- Accounts for >50% of all breast surgical procedures
- Age at diagnosis: 20 - 40 y.o.

CANCER
FIBROCYSTIC CHANGES

Non-proliferative Breast Changes

<table>
<thead>
<tr>
<th>Pathologic Lesion</th>
<th>Relative Risk of Developing Invasive Carcinoma</th>
<th>Breast at Risk</th>
<th>Modifiers of Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duct Ectasia</td>
<td>1.0</td>
<td>Neither</td>
<td></td>
</tr>
<tr>
<td>Cysts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apocrine Change</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild Hyperplasia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibroadenoma (without complex features)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3 Main Features

- Cystic change with apocrine metaplasia
- Fibrosis
- Adenosis
Fibrocystic Change - Adenosis

- Increase in the number of acini per lobule
- In pregnancy – normal physiologic adenosis
- Non-pregnant women – adenosis; focal change

FIBROADENOMA

- Most common benign tumor, usually small
- Occur during reproductive life (more common <30 years old)
- Young women: palpable mass
- Hormone (estrogen) driven
- Gross: Sharply circumscribed nodule
- Microscopically
  - Delicate stroma around compressed, distorted slit-like glandular spaces (stroma proliferates and compresses the ducts)
Increase in fibrous stroma
Compressed glands
Calcifications

• Most common in older patients (6th decade)
• Larger compared to fibroadenomas
• Overgrowth of fibrous component
• Benign, borderline and malignant types (mostly benign)
• Phyllodes = leaf like
• Distinguished from fibroadenomas on the basis of cellularity, mitotic rate, nuclear pleomorphism, stromal overgrowth and infiltrative borders.
PHYLLODES TUMOR

- Leaf-like
- Increased stromal cellularity

Fibroadenoma  Phyllodes tumor

Pathologic Lesion | Relative Risk of Developing Invasive Carcinoma | Breast at Risk | Modifiers of Risk
--- | --- | --- | ---
Proliferative Disease Without Hypothesis | 1.2-2.0 | Both breasts | Increased risk if there is a family history of breast carcinoma
Decreased risk 10 years after biopsy

- Moderate or Florid Hyperplasia
- Sclerosing Adenosis
- Papilloma
- Complex Sclerosing Lesion (radial scar)
- Fibroadenoma (with complex features)
INTRA DUCTAL PAPILLOMA

- Most common cause of bloody nipple discharge in younger women
- Multiple branching fibrovascular cores, each having a connective tissue axis lined by luminal and myoepithelial cells
- Must distinguish from papillary carcinoma

### Pathologic Lesion

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Proliferative Disease With Atypia</td>
<td>4.0 - 5.0</td>
<td>Both Breasts</td>
<td>Increased risk if there is a family history of breast carcinoma</td>
</tr>
<tr>
<td>Atypical ductal hyperplasia</td>
<td></td>
<td>Both Breasts</td>
<td>Increased risk if premenopausal</td>
</tr>
<tr>
<td>Atypical lobular hyperplasia</td>
<td></td>
<td>Both Breasts</td>
<td>Decreased risk 10 years after biopsy</td>
</tr>
</tbody>
</table>

- Atypical ductal hyperplasia
- Atypical lobular hyperplasia
Atypical ductal hyperplasia

TDLU expansion

Atypical lobular hyperplasia

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Carcinoma in-Situ</td>
<td>8.0 – 10.0</td>
<td>Both breasts</td>
<td>Treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ipsilateral</td>
<td></td>
</tr>
<tr>
<td>DCIS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCIS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ATYPICAL Hyperplasia: Associated with an increased risk of breast cancer development in either breast. Marker of breast cancer risk.
Ductal carcinoma in situ (Cribriform type)

Lobular carcinoma in situ

Atypical lobular hyperplasia

PAGET DISEASE

- Rare manifestation of breast cancer (1-4%)
- DCIS arising within ductal system of the breast can extend up the lactiferous ducts into nipple skin without crossing the BM
- Underlying invasive carcinoma or DCIS (almost always)
- Prognosis depends on extent of the underlying carcinoma
PAGET DISEASE OF THE NIPPLE

Invasive Breast Carcinoma
To be discussed by Dr. Lo

- Incidence
- Mortality
- Risk Factors

DISTRIBUTION OF HISTOLOGIC TYPES OF BREAST CANCER

<table>
<thead>
<tr>
<th>In Situ Carcinoma</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ductal carcinoma in situ</td>
<td>80%</td>
</tr>
<tr>
<td>Lobular carcinoma in situ</td>
<td>20%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Invasive Carcinoma</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ductal carcinoma (no special type)</td>
<td>79%–MC</td>
</tr>
<tr>
<td>Lobular carcinoma</td>
<td>10%</td>
</tr>
<tr>
<td>Tubular/cribriform carcinoma</td>
<td>6%</td>
</tr>
<tr>
<td>Mucinous (colloid) carcinoma</td>
<td>2%</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>2%</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>1%</td>
</tr>
</tbody>
</table>
INVASIVE LOBULAR CARCINOMA

BREAST CANCER - Prognostic Factors

- Histologic subtype
- Tumor grade: Nottingham histologic score
- Lymph node invasion
- Size of tumor
- Metastasis
- Estrogen and progesterone receptors
- Proliferative rate (Ki-67)
- Expression of oncogenes (e.g., HER-2/neu)
- Gene expression profiling

Features That Indicate Increased Likelihood of Having BRCA Mutations

- Multiple cases of early onset breast cancer (<50 years)
- Ovarian cancer (with family history of breast or ovarian cancer)
- Breast and ovarian cancer in the same woman
- Bilateral breast cancer
- Ashkenazi Jewish heritage
- Male breast cancer
- BRCA1 and BRCA2 gene carriers (25%)
- Other genetic syndromes (e.g. Li-Fraumeni (p53 mutation), Cowden’s disease (PTEN mutation), Peutz-Jeghers syndrome (LKB1/STK1), ATM)
BRCA1 and BRCA2

<table>
<thead>
<tr>
<th></th>
<th>BRCA1</th>
<th>BRCA2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosome</td>
<td>17q21</td>
<td>13q12.3</td>
</tr>
<tr>
<td>Function</td>
<td>Tm suppressor</td>
<td>Tm suppressor</td>
</tr>
<tr>
<td>Mutations</td>
<td>&gt;500</td>
<td>&gt;300</td>
</tr>
<tr>
<td>Risk of breast cancer (70%)</td>
<td>40-80%</td>
<td>30-40%</td>
</tr>
<tr>
<td>Age at onset</td>
<td>40s to 50s</td>
<td>50 years</td>
</tr>
<tr>
<td>Ovarian cancer (%)</td>
<td>20-40%</td>
<td>10-20%</td>
</tr>
<tr>
<td>Male breast cancer</td>
<td>Lower than BRCA2</td>
<td>More frequently seen</td>
</tr>
<tr>
<td>Pathology</td>
<td>Triple negative (basal-like cancers)</td>
<td>Similar to sporadic breast cancers</td>
</tr>
</tbody>
</table>

Identification of carriers is important, since increased surveillance, prophylactic mastectomy, and oophorectomy can reduce cancer-related morbidity and mortality.
The Male Breast

THE MALE BREAST

GYNECOMASTIA
- Unilateral or bilateral
- Indicator of hyperestrinism
  - Cirrhosis or functioning testicular tumor
  - Marked micropapillary hyperplasia of ductal lining occurs
  - Periductal lymphocytic infiltrate
  - Fibrosis
Gynecomastia

THE MALE BREAST
CARCINOMA
• Rare (lifetime risk: 0.11%)
• Risk factors: First-degree relatives with breast ca, decreased testicular function, age, infertility, obesity, radiation, residency in western countries.
• Gynecomastia is not a risk factor
• BRCA2 mutation (4-14%)
• The same histologic subtypes of invasive cancer are present

Question 1
• The most common infectious agent found in acute mastitis is:
  – S. Aureus.
  – M. tuberculosis.
  – S. Bovis.
  – C. Albicans
Question 2
• The most common type of breast cancer is:
  – Invasive lobular carcinoma
  – Metaplastic carcinoma
  – Invasive ductal carcinoma
  – Papillary carcinoma
  – Tubular carcinoma

Question 3
• What is the most common breast pathology in men:
  – Invasive lobular carcinoma
  – Invasive ductal carcinoma
  – Gynecomastia
  – Chronic mastitis
  – Granulomatous mastitis
  – Infectious mastitis

Question 4
• What is the most common cause of bloody nipple discharge:
  – Intraductal papilloma
  – Paget’s disease
  – Fibroadenoma
  – Invasive ductal carcinoma
Question 5

• Of the following breast carcinomas which is the one with the best prognosis
  – Fibroadenoma
  – Phyllodes tumor
  – Tubular carcinoma
  – Metaplastic carcinoma
  – Invasive ductal carcinoma

Question 6

• What are the 2 most important prognostic factors in breast cancer:
  – Laterality and histologic grade
  – Size and histologic grade
  – Histologic grade and lymph node metastasis
  – Lymph node metastasis and size
  – Size and resistance

Question 9

• A 35 year old female discovers a 2 cm mass in her breast, imaging reveals a mass and suspicious calcifications, a core biopsy diagnosis is: Fibroadenoma, non proliferative fibrocystic changes, atypical lobular hyperplasia and ductal carcinoma in situ. What is her risk of developing invasive breast cancer in the future:
  • 1
  • 1.5-2
  • 4-5
  • 8-10