Overview of Breast Pathology and Correlation with Radiologic Findings

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Objectives

- Overview of breast pathology and basic breast disease
- Correlate breast biopsies and excisions with imaging findings
- Tour through the pathology lab
- The importance of tissue handling in regards to patient care
Anatomy of the Breast

- Epithelial component: ducts and lobules
- Stromal component: adipose tissue, fibrous stroma, blood vessels, nerves, lymphatics
- Multiple duct systems (~10), each with associated lobular units, which drain through the lactiferous ducts to the nipple
- Most malignant tumors arise from the epithelial component

Normal Benign Breast

- Epithelial component: acini (ductules), lobules and ducts

Normal Benign Breast

- Fibrous component: adipose tissue (fat), fibrous tissue (stroma), blood vessels, nerves, lymphatics

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Benign Breast

Young female | Older female

Overview of Benign Breast Lesions

- Fibroepithelial tumors
- Fibrocystic changes
- Mesenchymal tumors (stromal lesions)
- Myoepithelial lesions and nipple tumors

Fibroepithelial lesions

- Composed of both fibrous component and epithelial component.
- Includes:
  - Fibroadenoma
  - Phyllodes tumor
**Fibroadenoma**

- Most common benign breast tumor
- Age range: teens – 70 years
- Painless, often found by patient
- 15% of patients have multiple fibroadenomas
- Up to 4 cm in size

**Phyllodes tumors (3 main types)**

- Benign phyllodes
- Borderline phyllodes (low grade malignant)
- High grade malignant phyllodes
  - Phyllodes tumors may recur;
  - Malignant phyllodes tumors may metastasize

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**Phyllodes tumors**

- Benign
- Borderline (low grade malignant)
- Malignant
Phyllodes tumor – mitotic figures

Overview of Benign Breast Lesions

- Fibroepithelial tumors (fibroadenoma is most common)
- Fibrocystic changes
- Mesenchymal tumors (stromal lesions)
- Myoepithelial lesions and nipple tumors

Fibrocystic Changes (FCC)

- Most common disorder of breast; accounts for majority of breast biopsies.
- Usually affects premenopausal patients.
- A wide range of microscopic changes.
- FCC includes cysts, calcifications, fibrosis, hyperplasia, apocrine change, radial scars, papillomas, etc.
- Changes range from innocuous to those associated with increased risk of cancer (ADH, ALH, LCIS).
**FCC: Cysts**

- Cysts = expanded ducts.
- Can present as a palpable mass
- Can contain calcifications
- Can rupture leading to pain and inflammation

**FCC: Calcifications**

- Secretory products within cysts calcify, leading to microcalcifications on patients' mammograms

**Calcifications**

- Breast calcifications are very common.
- 80% of breast calcifications are benign.
- Two types of calcifications:
  1. **Macroccalcifications**: degenerative changes in the breast resulting from old injuries, inflammations, or aging of the breast arteries and are usually not related to cancer. Most often they do not require a biopsy.
  2. **Microcalcifications**: specks of calcium that may be found in an area of rapidly dividing cells. The residue left by rapidly dividing cells.
Calcium Oxalate calcifications

Calcifications: Typically Benign

- Benign calcifications
- Suture calcifications
- Large rod-like calcifications
- Coarse calcifications
- Degenerating fibroadenoma
- Dystrophic calcifications
- Fibrocystic change
- Milk of calcium

Calcifications: in Fibroadenoma

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Calcifications: Intermediate Concern/Suspicious

- Coarse calcifications
- Low grade DCIS
- Amorphous calcifications
- ADH
- Coarse calcifications
- Low grade DCIS
- Amorphous calcifications
- LCIS

Calcifications: in FCC

Calcifications: in Pregnancy-like change

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Calcifications: in Pregnancy-like change

- Can occur in patients who are neither pregnant or lactating, and in nulliparous patients
- Etiology is unknown
- No risk of developing cancer
Calcifications:
in ADH

ADH (atypical ductal hyperplasia)
FCC: Radial Scar

US – vertically oriented irregular mass with angular margins

Overview of Benign Breast Lesions

- Fibroepithelial tumors (fibroadenoma is most common)
- Fibrocystic changes
- **Mesenchymal tumors (stromal lesions)**
- Myoepithelial lesions and nipple tumors
**Mesenchymal/stromal lesion**

40 y/o woman presents with a breast lump.

She is 6 weeks post partum.

Negative mammogram

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**Pseudoangiomatous stromal hyperplasia (PASH)**

Proliferation of breast stromal cells (myofibroblasts).

Can present as a clinically palpable/radiographically visualized mass.

Results from a physiologic response to hormones.

Typically seen in premenopausal women or in postmenopausal women undergoing HRT.

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Other stromal lesions:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>• Fibromatosis*</td>
<td>* Excision for some of these lesions required for treatment to decrease risk of recurrence, or for definitive diagnosis</td>
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<tr>
<td>• Myofibroblastoma*</td>
<td></td>
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<tr>
<td>• Fibrous mastopathy</td>
<td></td>
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<tr>
<td>• Granular cell tumors*</td>
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<tr>
<td>• Nodular fasciitis*</td>
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<tr>
<td>• Lipoma</td>
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Malignant Breast Tumors

- Ductal carcinoma in situ (DCIS)
- Invasive breast carcinoma
- Malignant mesenchymal tumors
- Malignant lymphoma
- Metastatic tumors

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Breast Cancer

- **Ductal Carcinoma in situ (DCIS)**
- Non-invasive breast cancer (cannot spread/metastasize)
- Precursor lesion for development of invasive breast cancer
- **Invasive (infiltrating) breast cancer**
- Can spread or metastasize

DCIS (ductal carcinoma in situ)

- Precursor to invasive breast cancer
- Arises in TDLU of breast
- Often associated with calcifications (occas. forms a mass, or presents with nipple discharge)

DCIS (cont.)

- Striking increase in detection with screening mammography
- Completely curable type of breast cancer
Calcifications: Higher probability of malignancy

- Pleomorphic calcifications
  - High grade DCIS
  - Pleomorphic calcifications
  - Intermediate grade DCIS
  - Pleomorphic, linear calcifications
  - Low grade DCIS

Calcifications: Distribution modifiers

- Segmental distribution of pleomorphic calcifications
  - High grade DCIS

Classification of DCIS:

- Architectural patterns:
  - solid
  - cribriform
  - apocrine
  - micropapillary
  - Comedo

- Nuclear grades:
  - nuclear grade 1
  - nuclear grade 2
  - nuclear grade 3
Case
Asymptomatic 62 y/o woman.

Comedo DCIS
- High nuclear grade (3) with central necrosis
- Highest risk of developing into invasive breast cancer
- Invasive carcinoma in patient with DCIS

Cribriform DCIS
Micropapillary DCIS

• DCIS typically follows contiguously along ducts.
• Micropapillary type can be multifocal/multicentric and with skip areas of involvement along ducts.

Invasive (infiltrating) breast cancer

• Malignant tumors that have invaded through duct walls, into breast stroma.
• Capable of spreading to lymph nodes &/or distant sites.
• 40-50% occur in UOQ.
• Present as mass, palpable or seen on mammogram/ultra-sound.
• Incidence increases with age.

Invasive breast cancer: Classification:

- Architectural patterns:
  - Ductal
  - Lobular
  - Mucinous
  - Micropapillary
  - Metaplastic
  (over 20 types as defined by WHO)

- Nottingham grades (I, II, III), based on:
  - Tubule formation
  - Nuclear grade
  - Mitotic count
Types of invasive breast cancer: Invasive ductal carcinoma (IDC)

- IDC is most common type (52-75%).
- IDC is typically seen in familial (BRCA1 and BRCA2) cases.

Types of invasive breast cancer: Invasive lobular carcinoma (ILC)

- ILC represents 5-15% of breast cancers.
- May be multicentric or bilateral.
- Harder to see by mammography and to detect clinically.
- May present as asymmetry or architectural distortion, seen only on one (CC) view.

Types of invasive breast cancer: Mucinous carcinoma

- Typically low grade cancer that is well circumscribed
- Usually presents in older women; has a good prognosis
Suspicious imaging findings that lead to biopsy of breast masses

- **Margins**: microlobulated, indistinct, spiculated, irregular (mammography, US, MRI)
- **Developing asymmetry** (mammography)
- **Mass orientation**: taller-than-wide (US)
- **Acoustic features**: posterior acoustic shadowing (US)
- **Washout enhancement** (MRI)

What happens in the pathology lab?
Path-Rad Correlation

- Pathologist reviews imaging report on every case.
- Specimen radiographs on cores with calcifications are reviewed by pathologist and compared to histologic slides.
1. Intraoperative evaluation of lumpectomies for targeted lesion/radioactive seed/localization wire
2. Intraoperative assessment of DCIS margins
3. Identification of prior core biopsy clips (particularly to identify tumor bed in neoadjuvant therapy cases)
4. Identification of calcifications in tissue blocks or specimens
**Imaging in the Pathology Lab**

1. Intraoperative evaluation of lumpectomies for targeted lesion/radioactive seed/localization wire
2. **Intraoperative assessment of DCIS margins**
3. Identification of prior core biopsy clips (particularly to identify tumor bed in neoadjuvant therapy cases)
4. Identification of calcifications in tissue blocks or specimens

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**Specimen radiograph**

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**Lumpectomy radiograph of slices**

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Lumpectomy; DCIS at deep margin in slice 3

Large calcification near margin

DCIS transected at the margin
1. Intraoperative evaluation of lumpectomies for targeted lesion/radioactive seed/localization wire
2. Intraoperative assessment of DCIS margins
3. Identification of prior core biopsy clips (particularly to identify tumor bed in neoadjuvant therapy cases)
4. Identification of calcifications in tissue blocks or specimens

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Mastectomy s/p neoadjuvant chemo

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Mastectomy s/p neoadjuvant chemo
Mastectomy specimen: pCR

5 Sentinel Lymph Nodes

SLN with Prior Core Biopsy Clip
Determining Optimal Treatment of Breast Cancer

- Accurate diagnosis (categorizing in specific types)
- Nodal status (if tumor spread to lymph nodes)
- Size of tumor
- Stage of tumor (if it is confined to breast, or spread to other tissues)
- Assessment of tumor in relation to margins (adequate surgical removal)
- However......

Determining Optimal Treatment of Breast Cancer (continued)

Prognostic markers, proliferation rates, and gene expression are emerging as the most important factors leading to “Targeted Therapies” for breast cancer

One patient’s sample: importance of fixation times

Estrogen receptor IHC


Molecular testing: Oncotype DX

- Paraffin block is sent to companies to do gene profiling.
- These studies help predict which patients may benefit from chemotherapy.

In Summary...

- Breast cancer is a spectrum of diseases.
- Careful radiologic evaluation combined with pathologic evaluation helps accurately identify and classify the lesion.
- A multidisciplinary approach to handling breast specimens is crucial.
- Genetic profiling of the tissue to determine optimal targeted therapy will account for increased survival.

Thank you for your attention!