The Ductal Carcinomas: Classic Presentations on Mammography

Jennifer Broder, HMS IV
Advanced Radiology Rotation
Beth Israel Deaconness Medical Center
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Where in the breast does cancer develop?

Most breast cancer develops in the “terminal ductal lobular unit” (TDLU)

The epithelium inside the lobules is histologically distinct from the epithelium in the extralobular ducts.

Healthy TDLU Histology

Terminal ductal lobular unit (TDLU)

Several TDLU at low magnification (10x)

A TDLU at high magnification (63x)

A single ductule transverse section (250x)

Jensen, H. Anatomy and Histology of the Normal Human Breast. UC Davis, Dept. of Pathology. 1999
Breast cancer can be divided into two major groups.

**IN SITU**
Tumor cells have not invaded the basement membrane.

**INVASIVE**
Tumor cells invade the breast stroma. They have the potential to metastasize and result in death of the patient.
Breast cancer can be divided into two major groups.

IN SITU

1. Lobular Carcinoma In Situ
   Controversial! Many consider this a marker of increased risk for malignancy in the future rather than true cancer.

2. Ductal Carcinoma In Situ

INVASIVE

1. Invasive Lobular Carcinoma
2. Invasive Ductal Carcinoma

This presentation will focus on the DUCTAL carcinomas.
Ductal cancer evolves over time.

Clinical and molecular research have demonstrated that there is likely often a linear progression of sequential stages of epithelial proliferation.

- Normal Terminal Ductal Lobular Unit
- Atypical Ductal Hyperplasia (ADH)
- Ductal Carcinoma In Situ (DCIS)
- Invasive Ductal Carcinoma (IDC)
But it is also possible that atypia/malignancy develop directly from normal epithelium.

Sometimes the distinction between ADH and low-grade DCIS isn’t clear.

- Epithelium involved in ADH proliferates at rates 2-3 times higher than normal terminal ductal epithelium.

- In ADH, this neoplastic proliferation is associated with clonal cytologic atypia.

- ADH is distinguished from low-grade DCIS by
  - the extent of duct involvement with atypia
  - how uniform the atypia is

- Thus, it is at times pathologists can disagree on the diagnosis.
ADH Histology

Duct with hyperplastic monoclonal atypia

Right: http://www-medlib.med.utah.edu/WebPath/TUTORIAL/BREAST/BRCA003.html
As DCIS develops, it can distinguish itself.

- The epithelium proliferates at a rate up to 10x greater than normal.
- The cells have greater genetic instability and mutations.
- In low-grade DCIS, punctate, round/oval, irregular calcifications can develop in associated secretions.
- In high-grade DCIS, debris from tumor necrosis can lead to a characteristic pattern of pleomorphic calcifications (varying in size, shape, density) with a linear branching pattern recognizable on mammogram.
- Sometimes, there are other less easily recognizable patterns of calcification deposition.
DCIS Histology

5 Subtypes:
1. Comedo
2. Cribiform
3. Micropapillary
4. Papillary
5. Solid

For example:

Comedo pattern (High-grade DCIS): The cells in the center are often necrotic and calcify.

Cribiform pattern (Low-grade DCIS): Neoplastic cells within the duct have holes with sharp margins.

http://www-medlib.med.utah.edu/WebPath/TUTORIAL/BREAST/
DCIS Patient 1 (49 y.o.):
Screening mammography shows 1 small lesion

Heterogenously dense breast with small cluster of pleomorphic microcalcifications in upper mid breast.
DCIS Patient 1: Follow-Up

- Mammographic needle localization prior to surgical excision of lesion

- Pathology demonstrated micropapillary and cribiform DCIS with positive margins

- Re-excision with wider margins => Pathology showed 1mm margins

- No information available yet about treatment plan
DCIS Patient 2 (58 y.o.): Screening mammography shows multiple lesions

In this case, three distinct clusters of pleomorphic microcalcifications were all part of a more extensive lesion in a single duct network.
DCIS Patient 2: Follow-Up

• Mammographic needle localization of lesions prior to surgical excision

• Pathology demonstrated comedo and solid DCIS with positive margins

• No information available yet on treatment plan
DCIS Patient 3 (41 y.o.): Screening mammography shows extensive lesions

Heterogenously dense breast with extensive clustered pleomorphic microcalcifications in left medial lower breast extending 9 cm from posterior-most breast to 3 cm from the nipple.
DCIS Patient 3: Follow-Up

- Mammographic needle localization prior to surgical excision
- Pathology demonstrated comedo and cribiform DCIS with positive margins
- Patient has had consultation for radiation treatment and will have reconstructive surgery
A caveat about calcs...

- Calcifications are very common.

- However, most calcifications are not indicative of cancer. Mammography has limited specificity regarding calcifications, because there is overlap in appearance of benign vs. malignant.

- It is hard to know when to biopsy; many of the biopsies we do turn out to be benign.
Invasive Ductal Carcinoma (IDC)

• IDC accounts for 85-90% of invasive breast cancers.

• When the malignant cells infiltrate the breast tissue outside the duct, they induce a fibrous response.

• Combined with the neoplastic cells, this fibrous response contributes to the formation of a mass, which sometimes can be detected on physical exam, mammography, and/or ultrasound.
IDC Histology

Infiltration of ill-defined epithelial cells into the surrounding stroma. Note the associated calcification in lower right corner.

IDC at low magnification demonstrates atypical cells radiating out from a central area of fibrosis.

http://medlib.med.utah.edu/WebPath/TUTORIAL/BREAST
What does IDC look like on mammography?

- IDC can have a wide range of appearances.

- In some women, IDC might show only slight architectural distortion of the breast tissue.

- The masses representing IDC classically have
  - any size
  - irregular shapes
  - micro-lobulated, ill-defined, and/or spiculated borders
  - +/- pleomorphic microcalcifications
IDC Patient 1: 72 y.o. with family h/o breast cancer presents to screening mammography

Left breast with new (within 1 year) 8 mm slightly rounded mass with partially ill-defined borders. On US hypoechoic solid mass with shadowing.
IDC Patient 1: After resection, the specimen radiograph demonstrates spiculated borders.
IDC Patient 1: Follow-up

- Lesion demonstrated here found in 2000 and removed after mammographic needle location
- Pathology demonstrated IDC with negative lymph nodes
- Resection was followed by treatment with radiation and tamoxifen and an aromatase inhibitor
- Yearly mammography has not revealed new suspicious microcalcifications or masses
IDC Patient 2: 72 y.o. presents to screening mammography

New 12 mm irregularly shaped poorly-defined mass in lower inner right breast
IDC Patient 2: Follow-up

- Lymphoscintigraphy prior to surgical excision
- Wide-excision of 1.5 cm tumor. 1 of 7 lymph nodes with carcinoma
- Patient has declined chemotherapy and has opted for radiation with adjuvant aromatase inhibitor
IDC Patient 3: 90 y.o. presents from a nursing home with palpable breast mass

Right CC view

Dense 40 mm mass with poorly defined margins and irregular microcalcifications demonstrating associated DCIS
IDC Patient 3: Follow-up

- Surgery deferred due to advanced age and dementia
- Pt to be seen by medical oncology to determine
  - if treatment plan will require imaging for staging,
  - if she will benefit from treatment with tamoxifen or an aromatase inhibitor
IDC Patient 4: 44 y.o. presents with palpable right breast mass

No masses seen on CC or MLO view

US: 10 mm irregularly shaped poorly-defined hypoechoic mass with shadowing
IDC Patient 4: Follow-up

- Lymphoscintigraphy follow by surgical excision
- Lymph nodes (to level II) were positive on frozen section
- Next step: When path results back, she will meet with medical oncology to determine treatment plan, which will probably include radiation and chemotherapy, with adjuvant endocrine therapy.
Summary

- **Ductal Carcinomas**
  - Likely develop through a stepwise cellular changes in the terminal ducts
  - But are also postulated to develop directly from normal epithelium

- **Ductal Carcinoma In-situ**
  - Classically present with pleomorphic calcifications in a linear branching distribution
  - But predicting whether calcifications represent cancer can be very difficult

- **Invasive Ductal Carcinoma**
  - Classically appears as a mass of any size with an irregular shape
  - Borders can be micro-lobulated, ill-defined, and/or spiculated
  - Can be occult on mammogram, and require ultrasound to make the diagnosis
References

- Beth Israel Deaconess Medical Center PACS, Boston, MA.
- http://medlib.med.utah.edu/WebPath/TUTORIAL/BREAST
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To the memory of Elizabeth Anne Prostic 1973-2005
A phenomenal woman whose life was cut short by breast cancer