Diagnostic Approach to "Ductal" Lesions

Jean F. Simpson, M.D.
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Pre-malignant Breast Disease

- 1950-1980 - confusing
  "The female breast is a precancerous organ" .......... Fred Steward, AFIP fascicle
- 1980-1990 - risk defining
- 2000’s - refining
  - Impact of breast imaging
  - Mimics
  - Molecular aspects

Risk Factors for Breast Cancer in Women with Proliferative Breast Disease

Dupont and Page, NEJM 1985

10,542 benign breast biopsies
1950-1968
85% follow up at 20 years
Nashville Breast Cohort Studies

• Specific histologically-defined terms linked to levels of later malignancy risk

• Regionality of risk, i.e. local vs. diffuse

Stratification of Breast Cancer Risk

• No proliferative disease = NO ↑ RISK

• Proliferative disease, no atypia = SLIGHT RISK

• Atypical hyperplasia = MODERATE RISK

Distribution of Breast Lesions
Nashville series (1950-1968)

Distribution of Mammographically Detected Lesions

Rubin et al, Cancer 1988
Stratification of Breast Cancer Risk

- No proliferative disease = NO ↑ RISK
- Proliferative disease, no atypia = SLIGHT RISK
- Atypical hyperplasia = MODERATE RISK

Relative Risk

- Used to compare groups (not individuals), one group has characteristic, one group does not
- Slight increase risk = amount detectable in population
- Statistically significant, but not significant for patients

Relative Risk

\[
RR = \frac{\text{Women with PD who develop breast cancer}}{\text{Women with PD, no cancer development}} \times \frac{\text{Women in the general public who develop breast cancer}}{\text{Women in the general public, no cancer development}}
\]
Relative Risk

Women with PD who develop breast cancer

Women in the general public who develop breast cancer

Relative Risk

Women with PD, no cancer development

Women in the general public, no cancer development

Relative Risk Varies with Time Since Diagnosis

Atypical Hyperplasia

Proliferative Disease without Atypia

No Proliferative Disease

Relative Risk

1st 10 years

After 10 years

Denominator

Relative Risk for Developing Cancer After Benign Biopsy

• No increased risk
  – cysts
  – duct ectasia
  – adenosis
  – hyperplasia, mild

• Slightly increased risk
  • Early menarche
  • Late menopause
  • Nulliparity

• Moderately increased risk
  – Atypical ductal hyperplasia
  – Atypical lobular hyperplasia
DCIS vs ADH vs FHWA: cytology and histology

Cribiform DCIS

FHWA

ADH

Normal

Three individual spaces are presented with each of the three diagnoses illustrated. Each space is bounded by a basement membrane and contains epithelial cells.
Relative Risk for Developing Cancer After Benign Biopsy

- No increased risk
  - cysts
  - duct ectasia
  - adenosis
  - hyperplasia, mild

- Slightly increased risk
  - hyperplasia, moderate or florid, no atypia
  - sclerosing adenosis
  - solitary papilloma

- Moderately increased risk
  - Atypical ductal hyperplasia
  - Atypical lobular hyperplasia

DCIS vs ADH vs FHWA: cytology and histology

Three individual spaces are presented with each of the three diagnoses illustrated. Each space is bounded by a basement membrane and contains epithelial cells.
Minimum Criteria for DCIS

- Uniform population of cells, maintaining rounded, geometric configurations
- Even cell placement, without swirling or streaming
- Fully populating two adjacent spaces (3 mm)

Atypical Ductal Hyperplasia

- Uniform cytology
- Architecture
  - cribriform, micropapillary, solid
- Extent
Confirmatory Studies

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<th></th>
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<tbody>
<tr>
<td>Proliferative disease without atypia</td>
<td>1.5-2X</td>
<td>1.6X</td>
<td>1.3X</td>
<td>1.9X</td>
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<tr>
<td>Atypical hyperplasia</td>
<td>4-5X</td>
<td>3.7X</td>
<td>4.3X</td>
<td>4.24X</td>
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</table>
Confounders

• Mammography
• Minimally invasive biopsy procedures
• Hyperplasia in unusual settings

Underdiagnosis of ADH

• Core needle biopsy 41%
• Mammothome 15%

• Core needle biopsy (14 g) 44%
• Mammothome (14 g) 39%
• Mammothome (11g) 19%


When to excise after core biopsy?

• Diagnostic difficulty
• Sampling issues

Atypical Ductal Hyperplasia

• Uniform cytology
• Architecture
• Extent
### Extent of ADH on Core Biopsy (n=47)

<table>
<thead>
<tr>
<th>Findings in Excised Specimen</th>
<th>benign</th>
<th>ADH</th>
<th>DCIS</th>
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<tr>
<td># ADH foci</td>
<td></td>
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<tr>
<td>&lt;2</td>
<td>14</td>
<td>7</td>
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<td>4</td>
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<tr>
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### Extent of ADH on Core Biopsy (n=42)

<table>
<thead>
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<th># ADH foci</th>
<th>benign</th>
<th>ADH</th>
<th>DCIS</th>
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<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>7</td>
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<tr>
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<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>≥4</td>
<td>5</td>
<td>2</td>
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</tr>
</tbody>
</table>


### Factors Influencing Underdiagnosis of ADH

- Device used
- Extent of removal of mammographic lesion
- Microcalcifications vs mass

Jacobs et al, AM J Surg Pathol, 2002

### ADH vs low grade DCIS

“At least atypical ductal hyperplasia, excision necessary to evaluate extent of the lesion”
Diagnosis

1. Usual hyperplasia without atypia
2. Atypical ductal hyperplasia
3. Ductal carcinoma in situ, low grade

Choose best diagnosis:

Best diagnosis

1. Usual hyperplasia without atypia
2. Atypical ductal hyperplasia
3. Ductal carcinoma in situ, intermediate grade
Choose the best diagnosis:

Best diagnosis:

1. Usual hyperplasia without atypia
2. Atypical ductal hyperplasia
3. Ductal carcinoma in situ, low grade
ADH vs DCIS

• Differential diagnosis is LOW GRADE DCIS

• Extent of involvement is key

• Be conservative on core biopsy