Premalignant Lesions

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Premalignant lesions
- Atypical ductal hyperplasia
- Atypical lobular hyperplasia
- Lobular carcinoma in situ

Diagnosis made on biopsy to rule out cancer or to remove a benign lesion

Epidemiology (incidence) unknown

Not all agree that these lesions are "premalignant", may be just risk markers

Unknown how many such abnormalities will progress to cancer

Case of Breast atypia
- JW 39 yr old healthy Asian woman
- Pain and 2 solid nodules L breast
- Previous open biopsy same area benign
- Mammogram neg. U/S 1.8 solid mass
- Needle biopsy- fibroadenoma
- Open biopsy- fibroadenoma with atypical ductal hyperplasia in adjacent fibrocystic breast
Atypia

Mild or Moderate Hyperplasia

- Mild hyperplasia is defined by having at least 3 cells above the basement membrane—no real significance
- Moderate and florid hyperplasia (proliferative) similar but with more cells, often filling the ductal space and with snouts of cells or slitlike spaces between groups and myoepithelial cells

Ductal Hyperplasia

Relative risk for invasive ca

- No increased risk in non-proliferative disease as cysts, duct ectasia
- Slight (1.5-2X) increased risk in hyperplasia of usual type, sclerosing adenosis, papilloma
- Moderate risk (4-5X) in atypical hyperplasia
- High risk (8-10X) in LCIS
Definition of ADH or ALH

- Lesion defined by changes similar to DCIS or LCIS but lack the complete criteria for the diagnosis or are less than the fully developed form.
- Could be DCIS but only one microscopic duct involved
- Absence of defined architectural and cytologic features of DCIS
- Diagnostic reproducibility of ADH is poor
- Hence there are inter-pathologist variations in interpretation

Atypical Ductal Hyperplasia

DCIS Low Grade

DCIS Intermediate Grade
Clinical presentation

- Mammographic abnormality (usually cluster of calcifications)- diagnosis made on stereotactic core biopsy or fine wire localization biopsy
- Palpable lesion- atypia in association with a benign lesion

Diagnosis on core biopsy

- Ms K age 63
- Obese, diabetic woman of East Indian decent
- Screening mammogram shows calcifications
- Core biopsy atypical ductal hyperplasia

Ms K mammogram

Ms. K fine wire biopsy
Atypia on core biopsy
- Most of the data comes from the radiological literature
- Long term follow up not easily found
- A core is only a 14 gauge needle and thus only represents a portion of the lesion

Core biopsy AH-risk of cancer
- Zhao NC 2003    1036 pts
- 5.1% (53) core biopsy shows AH
- 39 pt open bx – 7 (24%) DCIS
- 1 invasive
- 14 pt observed – 6 DCIS or invasive ca within few years
- 50% overall have breast ca
Core biopsy AH-risk of cancer

- Winchester 2003, Ill
- 1750 patients
- 77 ADH (4.4%)
- 65 have open biopsy
- 17% cancer

Lobular hyperplasia or ALH at core and risk of cancer

- Foster 2004, Michigan 6081 pts
- 15 LCIS - 27% DCIS or invasive ca on open biopsy
- 1.5% have atypia
- 20 ALH – 10 % DCIS on open biopsy
- 75 ADH – 17% Cancer (insitu or invasive)

ALH on core and ca risk

- Dymtrasz 2003 NY
- 766 pt. 1.7% (13) ALH
- 6 open biopsies - 3 DCIS
- 1 invasive ca

ALH ,ADH or LCIS on core bx

- If atypia of any type is found on core biopsy, then
- 17 to 50% will have cancer (insitu or invasive) found on excision of the area
- All authors recommend fine wire localized excision
Clinical case of atypia

- CY dob 1955 Chinese extraction
- Feb 2000 first screening mammo shows calcification R breast
- No symptoms, no family history
- Slim woman with small breasts. No masses
- Films obtained and has bilat calcifications
- Considered too small for stereotactic core bx
- Bilateral fine wire localization biopsies done showing bilat sclerosing adenosis and a solitary focus of ADH on the L (not near a margin)

Clinical CY continued (2)

- Aug 2000 path reviewed by BCCA screening program shows 3mm DCIS (close to margin)
- Nov 2000 negative mammogram
- Feb 2001 seen in office discussion of options – no further surgery
- April 2003 mass L breast - seen by GP and sent for mammo and US showing mass read as fibroadenoma - no bx recommended
- Dec 2003 patient seen at her request No change in mass or in US and mammo
- 1cm mass in LOQ- open biopsy done

Clinical CY continued (3)

- Jan 2004 biopsy shows infiltrating ductal cancer 1 cm and DCIS to margins.
- Metastatic workup neg
- Very small breasts.
- Bilateral mastectomies L axillary dissection and bilat tissue expander reconstruction
- Clear margins, 1 of 4 nodes involved
- R breast negative
- Chemo and radiation

Atypia and risk of invasive ca

- Dupont and Page 1985 NEJM
- Previous open biopsy followed for 17 yrs
- 3303 women-1925 with proliferative disease
- cysts 1.3
- Proliferative disease 1.9
- ADH 5.3
- AH with Family history 11
Atypia and risk of invasive ca

- London et al 1992
- 8 yr follow up

<table>
<thead>
<tr>
<th>Condition</th>
<th>Relative Risk</th>
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<tbody>
<tr>
<td>No proliferation</td>
<td>1</td>
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<tr>
<td>Proliferative disease</td>
<td>1.6</td>
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<tr>
<td>AH</td>
<td>3.7</td>
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Atypical Hyperplasia

- Does the entire lesion need to be excised?
- Yes, if you believe this is a progressive lesion
- No, if you believe it is simply a risk marker

Atypical Lobular Hyperplasia
Atypical Lobular Hyperplasia
- Page et al 2003 (lancet)
- Retrospective analysis of 252pt (261) biopsies 1952-1985
- 50 (20%) developed invasive ca
- 68% in same breast
- 24% in contralateral breast
- ALH risk intermediate between local process and overall risk

LCIS and cancer risk
- LCIS is considered a marker for increased risk of ca in both breasts
- Risk assessed at increasing at 1% per year for a lifetime risk of up to 30%
- Higher risk if associated family history (up to 50%)

LCIS History

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1941</td>
<td>LCIS is designated as &quot;carcinoma&quot; and mastectomy is recommended</td>
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<tr>
<td>1941–1970</td>
<td>Mastectomy with contralateral biopsy is favored over observation</td>
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<tr>
<td>1970</td>
<td>Introduction of mammographic screening and increased public awareness of breast cancer</td>
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<tr>
<td>1978</td>
<td>Rosen and colleagues reported that invasive carcinoma subsequent to LCIS was exceptional</td>
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<tr>
<td>1985</td>
<td>NSABP legitimated breast preservation as alternative to mastectomy</td>
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<tr>
<td>1986</td>
<td>Haggensen reports that the majority of patients with LCIS develop invasive carcinoma</td>
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<tr>
<td>1990</td>
<td>Observation is favored over mastectomy with contralateral biopsy</td>
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LCIS and risk of breast ca

- NSABP data 2004
- 180 pt with 12 year follow up
- 26 (14%) ca in same breast, 9 were invasive (8 lobular invasive)
- 96% in the same quadrant
- 14 (8%) ca in contralateral breast, 8 were invasive (6 were lobular inv.)

Treatment options for ADH, ALH or LCIS

- Excise entire lesion
- Close follow up with yearly mammograms and 6 mo clinical exam
- Tamoxifen for 5 years - 49% risk reduction in prevention trials
- Raloxifene (STAR study) and aromatase inhibitors under study in post menopausal women only
- Bilateral mastectomies (consider with family history)

BCPT Results: Cumulative Rate of Invasive Breast Cancer

- Placebo
  - Events: 175
  - Rate per 1000: 43.4
- Tamoxifen
  - Events: 89
  - Rate per 1000: 22.0

BCPT Results: Invasive Breast Cancer Cases in All Age Groups

- Total: 175
- 35-49: 89
- 50-59: 58
- 60+: 57

LCIS with Family History
- 42 yr old woman with abnormal L mammogram
- Fine wire biopsy shows extensive LCIS
- Mother, grandmother and sister have had premenopausal breast ca
- Does not want to wait for genetic testing
- Bilateral mastectomies with reconstruction

Conclusions
- ADH, LDH and LCIS are lesions that the surgeon will frequently encounter
- If detected on core biopsy, surgical excision biopsy is appropriate
- There is a significant increased risk of developing insitu or invasive cancer in the future with the risk increasing over time
- Patients need to be counselled on the long term risk and on the options of treatment

Prophylactic mastectomies