

Premalignant Lesions

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Premalignant lesions

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

Premalignant Lesions

- Diagnosis made on biopsy to rule out cancer or to remove a benign lesion
- Epidemiology (incidence) unknown
- Not all agree that these lesions are “pre malignant”, 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

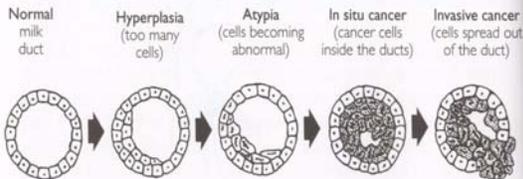


Figure 6: Breast cancer does not develop overnight. Gradually the cells become more abnormal-looking or atypical (see text). Eventually, the cells are recognized as being sufficiently abnormal to be called cancer cells that are initially inside the milk ducts (in situ cancer), and later become invasive breast cancer cells.

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

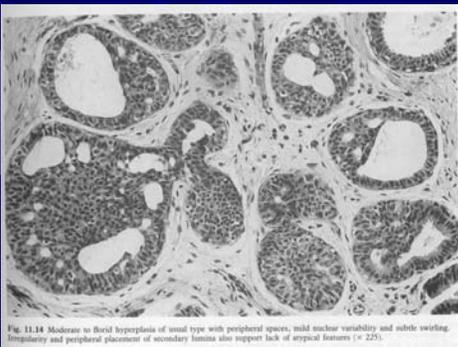


Fig. 11.14 Moderate to florid hyperplasia of usual type with peripheral spaces, mild nuclear variability and subtle swirling. Irregularity and peripheral placement of secondary lumina also support lack of atypical features ($\times 225$).

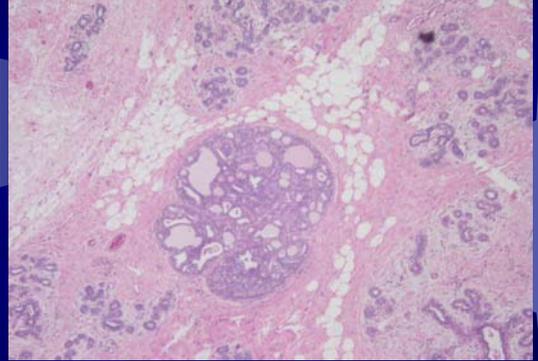
Relative risk for invasive ca

- 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

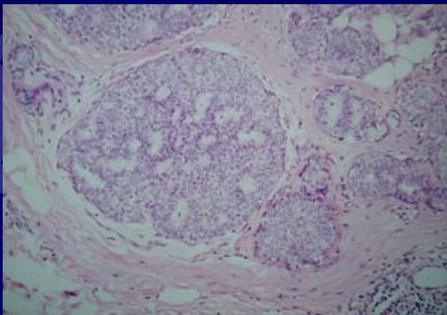
Definition of ADH or ALH

- 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

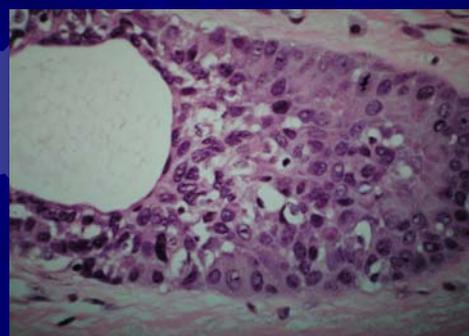
Atypical Ductal Hyperplasia



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

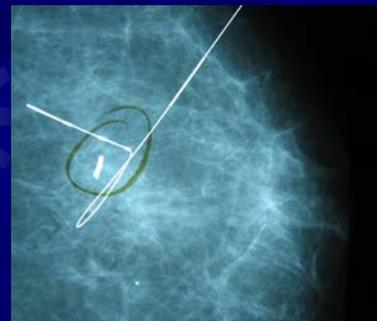
Diagnosis on core biopsy

- 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



Ms K specimen radiograph



Ms K final pathology

PATHOLOGY REVIEW

SLIDES FROM ST. PAUL'S HOSPITAL
W04-3994 (9) Sep. 9

7 X 3 X 1 CM FINE WIRE LOCALIZATION BIOPSY OF LEFT BREAST

- Low grade cribriform ductal carcinoma in situ extending within less than 1 mm of multiple biopsy margins.
- Overall size of ductal carcinoma in situ indeterminate, at least 1 cm.
- Additional microscopic foci of atypical duct hyperplasia, including atypical ductal hyperplasia within small intraductal papillomas.

Comment: Microcalcifications are seen within scattered small areas of low grade cribriform ductal carcinoma in situ and within atypical duct hyperplasia. There are also scattered small intraductal papillomas with varying degrees of ductal atypia. There are scattered small foci of low grade ductal carcinoma in situ extending within less than 1 mm of margins in a few foci within different sections, as designated in the outside hospital pathology report.

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, III
- 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 tx 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
- relative risk
- cysts 1.3
- Proliferative disease 1.9
- ADH 5.3
- AH with Family history 11

Atypia and risk of invasive ca

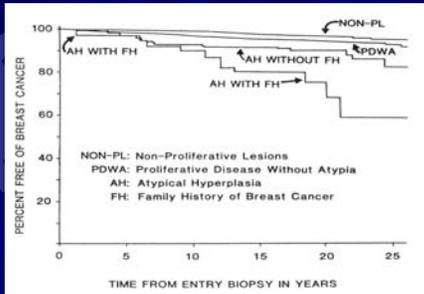


Figure 1. Proportion of Patients Free of Invasive Breast Cancer, as a Function of the Time since the Entry Biopsy.

Atypia and risk of invasive ca

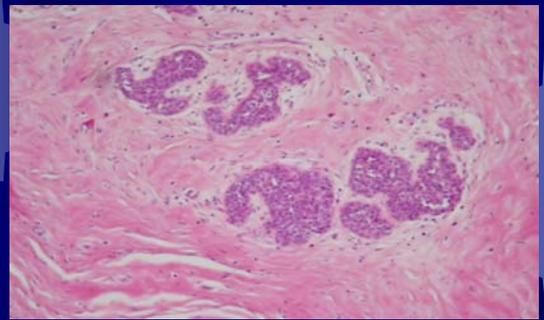
- London et al 1992
- 8 yr follow up

	relative risk
No proliferation	1
Proliferative disease	1.6
AH	3.7

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

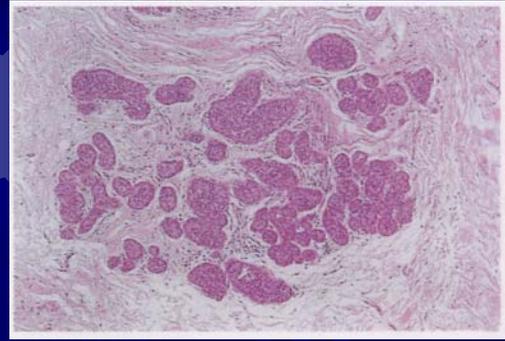
Atypical Lobular Hyperplasia



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



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

Clinical Management of ALH and LCIS

1941	LCIS is designated as "carcinoma" and mastectomy is recommended
1941-1970	Mastectomy with contralateral biopsy is favored over observation
1970	Introduction of mammographic screening and increased public awareness of breast cancer
1978	Rosen and colleagues reported that invasive carcinoma subsequent to LCIS was exceptional
1985	NSABP legitimized breast preservation as alternative to mastectomy
1986	Haagensen reports that the majority of patients with LCIS never develop invasive carcinoma
1996	Observation is favored over mastectomy with contralateral biopsy

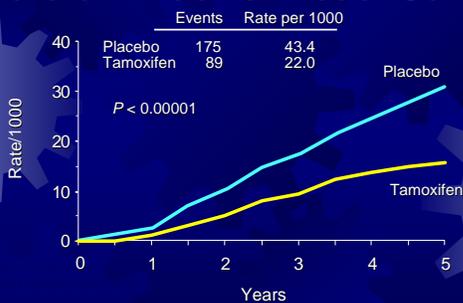
LCIS and risk of breast ca

- 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

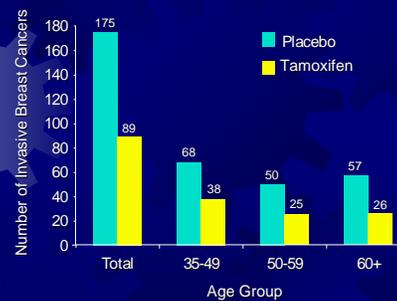
- Excise entire lesion
- Close follow up with yearly mammograms and 6 mo clinical exam
- Tamoxifen for 5 years- 49% risk reduction in prevention trials
- Raloxifene (STAR study) and aromatase inhibitors under study in post menopausal women only
- Bilateral mastectomies (consider with family history)

BCPT Results: Cumulative Rate of Invasive Breast Cancer



Adapted from Fisher et al. *J Natl Cancer Inst* 1998;90:1371-1388.

BCPT Results: Invasive Breast Cancer Cases in All Age Groups



Adapted from Fisher et al. *J Natl Cancer Inst* 1998;90:1371-1388.

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

Prophylactic mastectomies



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