Atypical breast lesions

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• Why do surgeons still operate on patients who do not have cancer or pre-cancer (DCIS)?
  – Management of atypical core biopsy
  – Management where definitive pathology is an atypical lesion
Atypical lesions

- Definitions
- Management of atypical core biopsy
- Management where definitive pathology is an atypical lesion

Percutaneous biopsy

- Evolved along with mammographic screening
- Radically reduced “unnecessary surgery”
  - Clearly benign lesions – leave
  - Clearly malignant lesions – remove
  - Invasive cancer – assess/manage nodes
- What about the atypical core biopsy?
Atypical biopsy

- Proliferative lesions
  - ADH
  - ALH, LCIS
- Radial scars
- Papillomas

Columnar Cell change with atypia
Standard management

• Incidence of more serious pathology in vicinity
  – Diagnostic excisional biopsy

Low grade DCIS
Indication for surgery is risk of upstaging

- What is the rate of upstaging?
  - Can lesions with minimal risk of upstaging be defined?

- Series of 4035 core biopsies
  - 372 borderline (B3)
- Outcomes of surgical excision defined


Incidence of upstaging

<table>
<thead>
<tr>
<th>Subcategory of B3 core needle biopsy (number with excision cases)</th>
<th>Number with concordant histology (number with excision cases)</th>
<th>Incidence of upstaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADH (34) (141)</td>
<td>78 (51.2)</td>
<td>invasive cancer</td>
</tr>
<tr>
<td>HPV (57)</td>
<td>9 (29.3)</td>
<td>invasive cancer</td>
</tr>
<tr>
<td>Phyllodes tumor (44)</td>
<td>24 (54.5)</td>
<td>invasive cancer</td>
</tr>
<tr>
<td>Neoplastic (147)</td>
<td>25 (81.3)</td>
<td>invasive cancer</td>
</tr>
<tr>
<td>Phyllodes tumor (34)</td>
<td>21 (61.8)</td>
<td>invasive cancer</td>
</tr>
<tr>
<td>B3 not otherwise specified (5)</td>
<td>4 (80.0)</td>
<td>invasive cancer</td>
</tr>
</tbody>
</table>

Table 1: Lesion excision malignant potential B3 on CNB excision histology outcomes for different B3 lesions and associated PPV for breast malignancy.

ADH = atypical ductal hyperplasia; DCIS = ductal carcinoma in situ; HPV = high risk epithelial neoplasia; NA = not applicable; PPV = positive predictive value. *Where excision histology confirms ADH, or high risk epithelial neoplasia, DCIS is the dominant lesion. PPV based on all cases verified with excision histology and cases shown to have remained stable on follow-up (N = 1038). PPV based on all cases verified with excision histology (N = 279). ADH on CNB is more appropriately described as atypical intraductal epithelial proliferation.

Incidence of upstaging

<table>
<thead>
<tr>
<th>Core needle histology</th>
<th>Underestimate category</th>
<th>No. of underestimates</th>
<th>Underestimate rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BI underestimate (upgraded to invasive cancer)</td>
<td>108/128</td>
<td>29.7 (28.5 - 31.0)</td>
<td></td>
</tr>
<tr>
<td>BI underestimate excluding ADH or atypical lobular hyperplasia</td>
<td>72/128</td>
<td>28.8 (27.5 - 30.0)</td>
<td></td>
</tr>
<tr>
<td>Upgraded to DCIS</td>
<td>48/138</td>
<td>23.0 (22.0 - 24.0)</td>
<td></td>
</tr>
<tr>
<td>Upgraded to DCIS or invasive cancer</td>
<td>63/138</td>
<td>44.2 (41.0 - 47.5)</td>
<td></td>
</tr>
<tr>
<td>LN underestimate (upgraded to invasive cancer)</td>
<td>108/128</td>
<td>22.0 (21.0 - 23.0)</td>
<td></td>
</tr>
<tr>
<td>Overall underestimate</td>
<td>210/756</td>
<td>27.7 (26.5 - 28.9)</td>
<td></td>
</tr>
</tbody>
</table>

95% CI indicates 95% confidence interval. BI, benign lesion; DCIS, ductal carcinoma in situ; ADH, atypical ductal hyperplasia.

Based on individuals who had core-needle biopsy results that potentially may have represented an underestimate from a series of 255 consecutive core-needle biopsies (Carter et al., 2007).


Lobular neoplasia

- 106 cases – 73 ALH, 33 LCIS
  - 76 had LN alone (no ADH)
- Upgrade rate
  - 16% (4/25) for LN + ADH
  - 4.4% (3/68) for LN alone – all w extensive foci


- 285 cases – 201 underwent surgical excision
  - Upgrade rate – 8% for ALH, 19% for LCIS

Model to predict upstaging

- 204 patients with ADH, ALH, LCIS on core
- 49 cancers on excision

- Factors associated with upstaging on MVA
  - Older age
  - Size of mammographic lesion >15mm
  - Persistence of lesion after biopsy

- Model found that 50% of patients could be spared surgery, with a 10% risk of DCIS or cancer diagnosis being delayed

Can the pathologist help?

- Intraductal proliferative lesions
  - UDH
  - ADH
  - DCIS

- Florid UDH vs ADH/low grade DCIS is key
  - ADH and DCIS are excised
To excise or not?

Immunohistochemistry

UDH is a polymorphic proliferation
• Patchy staining (no diffuse ER)
• Mosaic pattern CK5/6

ADH/ low grade DCIS is a monomorphic proliferation
• Diffuse ER staining
• CK5/6 negative
• IHC not helpful to distinguish
ADH/DCIS

ADH/low grade DCIS

ER diffuse

CK5/6 negative

UDH

Florid UDH

ER not diffuse

CK5/6 positive
Summary

• If the pathologist is sure it there is atypia, excision is generally required

Standard management

• Incidence of more serious pathology in vicinity
  - Diagnostic excisional biopsy

• Increased risk of subsequent breast cancer
  - Modified surveillance
  - ?Chemoprevention
Breast cancer risk

- Natural history of atypical lesions in Boston
- 76,333 path reports, 1987-2010

- 2938 women with atypical lesions
  - 40% ADH, 28% ALH, 19% LCIS, 12% severe ADH
- 1658 without chemoprevention

- Risk of breast cancer assessed
- Impact of chemoprevention assessed


Increased risk

- Different types of atypia had similar risk
- ALH/LCIS patients had more inv ca (70%)
- ADH had 50% DCIS
- Ipsilateral ca more common

Fig. 1: Estimated 5- and 10-year breast cancer risks based on atypia type for the no chemoprevention group. *Significantly fewer predicted breast cancers at 5 years with ADH (p = 0.036)

Atypia + family history

• Synergistic impact on future breast cancer risk

• Atypia in a gene carrier?

Impact of chemoprevention

Fig. 2 Unadjusted Kaplan–Meier curves for onset of breast cancer after atypia diagnosis with and without chemoprevention

Conclusions

• ADH, ALH, LCIS, severe ADH markedly increase risk of breast cancer
• Chemoprevention should be considered in these patients


Papilloma
Do papillomas require excision?

RMH experience

• Aim:
  – To assess the incidence of malignant lesions discovered on the final histopathology from patients with benign core biopsies who have concordant radiology


Papillomas

• Retrospective review: Feb 1995-Sept 2007

• All core biopsies with benign papillary lesions with surgical follow-up
  – All atypia, ADH, DCIS, IDC excluded
  – All mammographically suspicious lesions excluded

• 5783 core biopsies in 633 163 screens
  – 80 (0.01%) benign papillary core biopsies

### Final pathology

<table>
<thead>
<tr>
<th></th>
<th>Benign core</th>
<th>Benign excision</th>
<th>ADH</th>
<th>DCIS</th>
<th>IDC/ILC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>80</td>
<td>54 (66%)</td>
<td>11 (13%)</td>
<td>8 (10%)</td>
<td>7 (9%)</td>
</tr>
</tbody>
</table>


### Example of final surgical specimen

![Image of surgical specimen]

Followup after papilloma excision

• Solitary papilloma
  – no increased breast cancer risk
  – no indication for enhanced surveillance*

• Multiple papillomata
  – modest increased cancer risk
  – annual mammography indicated

* Cancer Care UK guideline (BreastScreen Australia silent on issue)

Radial Scar
Radial scar

• Significant risk of associated DCIS or Invasive cancer - ~7-10%
  – Excision required

• ?Moderate increased risk of cancer
  – ?Annual mammography

Atypical FA/phyllodes

• Fibroepithelial lesions are a spectrum
  - Most are clearly benign fibroadenomas
    – No need for excision, unless
      • ?new lesion in women >40
      • ?enlarging lesion

• Some are clearly malignant
• Some are uncertain
  – cellular stroma with possible atypia
  – diagnostic excisional biopsy
Summary/conclusions

• Standard management of atypical lesions is excision due to risk of upstaging
  – Selective management a research objective
• Atypical proliferative lesion a significant future cancer risk
  – Possible group for chemoprevention
• Papillomas generally require excision
• Radial scars requires excision and surveillance