Management of B3 lesions

Pathological view

Abeer Shaaban

Queen Elizabeth Hospital Birmingham
B3 lesions

- FEA
- AIDP
- In situ Lobular neoplasia
- Papilloma
- Radial scar
- Fibroaepithelial lesion
- Mucocoele like lesion
- Other: spindle cell lesions, apocrine atypia...
B3 category

• Includes lesions of variable significance.

• Includes lesions with and without atypia.

• Risk of upgrade increases in the presence of atypia.

• Requires further sampling: surgery/other.
Factors affecting frequency & upgrade

- Patient population: screening vs symptomatic
- Method of biopsy: NCB vs VAB (gauge of needle)
- Type of B3 lesion
- Presentation: calcs/mass
- Presence of atypia
Screen detected vs symptomatic

Is Mode of Presentation of B3 Breast Core Biopsies (Screen-Detected or Symptomatic) a Distinguishing Factor in the Final Histopathologic Result or Risk of Diagnosis of Malignancy?

Cael M. MacLean · Stephen P. Courtney · Hilary Umeh · Sriathan Sanjeev · Colin McCormick · Brendan M. Smith

- No difference in distribution of lesions
- Upgrade 17% (screen detected) and 20% (symptomatic)
Atypia vs no atypia
- **Papillary lesions**
  - Without atypia: 3.8%  
    - Noyak et al 2013
  - With atypia: 33% (vs 3%)  
    - McGhan et al 2013

- **Mucocoele-like lesion**
  - Without atypia: 4%  
  - With atypia: 21%  
    - Rakha et al, Histopathology 2013
Radial scar without associated atypical epithelial proliferation on image-guided 14-gauge needle core biopsy: Analysis of 49 cases from a single-centre and review of the literature

S. Bianchi\textsuperscript{a,*}, E. Giannotti\textsuperscript{b}, E. Vanzi\textsuperscript{b}, M. Marziali\textsuperscript{b}, D. Abdulcadir\textsuperscript{b}, C. Boeri\textsuperscript{b}, L. Liv\textsuperscript{c}, L. Orzalesi\textsuperscript{d}, L.J. Sanchez\textsuperscript{e}, T. Susini\textsuperscript{f}, V. Vezzosi\textsuperscript{g}, J. Non\textsuperscript{b}

\textsuperscript{a}Pathological Anatomy Unit, Department of Critical Care Medicine and Surgery, AOU Careggi, Largo C.A. Brambilla 2, 50134 Florence, Italy
\textsuperscript{b}Diagnostic Senology Unit, AOU Careggi, Florence, Italy
\textsuperscript{c}Radiotherapy Unit, Department of Clinical Physiopathology, AOU Careggi, Florence, Italy
\textsuperscript{d}Breast Unit, Department of Critical Care Medicine and Surgery, AOU Careggi, Florence, Italy
\textsuperscript{e}General Surgery Unit, AOU Careggi, Florence, Italy
\textsuperscript{f}Gynecology Unit, Department of Gynecology, Perinatology and Human Reproduction, AOU Careggi, Florence, Italy

- 49 cases of radial scar without atypia
- In 9 cases (18.3%): atypia on surgical excision.

Conclusion: diagnosis of RS without atypia does not exclude malignancy. Further sampling by VAB or surgical excision is required.
<table>
<thead>
<tr>
<th>Reason for B3 diagnosis on NCB</th>
<th>No (% of the total)</th>
<th>Benign</th>
<th>Malignant in-situ</th>
<th>Malignant invasive</th>
<th>PPV%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial Atypia present³</td>
<td>511 (50)</td>
<td>304</td>
<td>144</td>
<td>63</td>
<td>40.5</td>
</tr>
<tr>
<td>Pure ADH</td>
<td>248</td>
<td>123</td>
<td>92</td>
<td>33</td>
<td>50.4</td>
</tr>
<tr>
<td>Pure FEA</td>
<td>24</td>
<td>19</td>
<td>4</td>
<td>1³</td>
<td>20.8</td>
</tr>
<tr>
<td>Atypia unspecified</td>
<td>189</td>
<td>119</td>
<td>46</td>
<td>24</td>
<td>37.0</td>
</tr>
<tr>
<td>All LN</td>
<td>79</td>
<td>56</td>
<td>8</td>
<td>15</td>
<td>29.1</td>
</tr>
<tr>
<td>Pure ALH</td>
<td>33</td>
<td>25³</td>
<td>3</td>
<td>5</td>
<td>24.2</td>
</tr>
<tr>
<td>Pure LCIS</td>
<td>20</td>
<td>17³</td>
<td>1</td>
<td>2</td>
<td>15.0</td>
</tr>
<tr>
<td>LN unspecified</td>
<td>8</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>LN and ADH</td>
<td>13</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>61.5</td>
</tr>
<tr>
<td>LN and RS/CSL</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>60.0</td>
</tr>
<tr>
<td>No Epithelial Atypia (other B3 lesions)</td>
<td>514 (50%)</td>
<td>459</td>
<td>33</td>
<td>22</td>
<td>10.7</td>
</tr>
<tr>
<td>Papillary lesion</td>
<td>185 (18)</td>
<td>154</td>
<td>24</td>
<td>7</td>
<td>16.7</td>
</tr>
<tr>
<td>With atypia</td>
<td>30</td>
<td>19</td>
<td>10</td>
<td>1</td>
<td>16.7</td>
</tr>
<tr>
<td>Without atypia</td>
<td>155</td>
<td>135</td>
<td>14</td>
<td>6</td>
<td>12.9</td>
</tr>
<tr>
<td>RS/CSL</td>
<td>329 (32)</td>
<td>284</td>
<td>26</td>
<td>19</td>
<td>13.6</td>
</tr>
<tr>
<td>With atypia</td>
<td>51</td>
<td>31</td>
<td>12</td>
<td>8</td>
<td>39.2</td>
</tr>
<tr>
<td>Without atypia</td>
<td>278</td>
<td>253</td>
<td>14</td>
<td>11</td>
<td>8.9</td>
</tr>
<tr>
<td>FE lesions</td>
<td>52 (5)</td>
<td>51³</td>
<td>0</td>
<td>1</td>
<td>1.9</td>
</tr>
<tr>
<td>B3 miscellaneous</td>
<td>52 (5)</td>
<td>44</td>
<td>4</td>
<td>4</td>
<td>15.4</td>
</tr>
<tr>
<td>Total</td>
<td>1,025</td>
<td>763</td>
<td>177</td>
<td>85</td>
<td>25.6</td>
</tr>
</tbody>
</table>

Rakha et al 2014
Type of B3 lesion/combination of lesions
Columnar Cell Lesions on Breast Needle Biopsies: Is Surgical Excision Necessary?

A Systematic Review

Anoek H. J. Verschuuren-Maes, MD,* Carolien H. M. van Deursen, MD, PhD;† Evelyn M. Monninkhof, PhD, ‡ and Paul J. van Diest, MD, PhD§

Upgrade rate

- Columnar cell change: 1.5%
- CCC with atypia: 9%
- ADH with CCC: 20%
Flat epithelial atypia with and without atypical ductal hyperplasia: to re-excise or not. Results of a 5-year prospective study

- N=3948 core biopsies
- 145 FEA and 58 FEA +ADH
- Upgrade rate: 3.2 and 18.6%
- Conclusion: pure FEA has a very low association with carcinoma and these patients may benefit from close clinical and mammographic follow up, while combined FEA/ADH may be excised

Uzoaru et al Virchows Archives 2012
Characterization and outcome of breast needle core biopsy diagnoses of lesions of uncertain malignant potential (B3) in abnormalities detected by mammographic screening

Emad A. Rakha¹,², Andrew H.S. Lee², Jacquie A. Jenkins³, Alison E. Murphy³, Lisa J. Hamilton⁴ and Ian O. Ellis²

- Two UK regions: West Midlands and South Central region
- Final histology: 25% malignant
<table>
<thead>
<tr>
<th>Lesion</th>
<th>PPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure ADH</td>
<td>50.4</td>
</tr>
<tr>
<td>LCIS</td>
<td>15</td>
</tr>
<tr>
<td>ALH</td>
<td>24.2</td>
</tr>
<tr>
<td>LN (unspecified)</td>
<td>25</td>
</tr>
<tr>
<td>LN+ADH</td>
<td>61.5</td>
</tr>
<tr>
<td>LN+CSL/RS</td>
<td>60</td>
</tr>
<tr>
<td>Papilloma with atypia</td>
<td>36.7</td>
</tr>
<tr>
<td>Papilloma without atypia</td>
<td>12.9</td>
</tr>
<tr>
<td>RS with atypia</td>
<td>39.2</td>
</tr>
<tr>
<td>RS without atypia</td>
<td>8.9</td>
</tr>
<tr>
<td>Authors</td>
<td>FEA</td>
</tr>
<tr>
<td>------------------------</td>
<td>----------</td>
</tr>
<tr>
<td>Rakha et al</td>
<td>14% (1/7)</td>
</tr>
<tr>
<td>Lee et al</td>
<td>14% (1/7)</td>
</tr>
<tr>
<td>Chivukula et al</td>
<td>14% (5/35)</td>
</tr>
<tr>
<td>Kunju &amp; Kleer et al</td>
<td>21% (3/14)</td>
</tr>
<tr>
<td>Kumaroswamy et al</td>
<td>22% (2/9)</td>
</tr>
<tr>
<td>Rajan et al</td>
<td>19% (7/37)</td>
</tr>
</tbody>
</table>
Conventional core vs 1st line VAB
Positive predictive value for malignancy on surgical excision of breast lesions of uncertain malignant potential (B3) diagnosed by stereotactic vacuum-assisted needle core biopsy (VANCB): A large multi-institutional study in Italy

- 22 Italian centres
- 3107 B3 VAB diagnoses
- 1644 (54.2%) underwent surgical excision
- Overall PPV: 21.2%
<table>
<thead>
<tr>
<th>Lesion</th>
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<tr>
<td>Pure ADH</td>
<td>27.3</td>
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<td>FEA</td>
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<tr>
<td>ALH</td>
<td>24.2</td>
</tr>
<tr>
<td>LIN</td>
<td>22</td>
</tr>
<tr>
<td>RS</td>
<td>10.6</td>
</tr>
<tr>
<td>All B3</td>
<td>21.2</td>
</tr>
</tbody>
</table>
Are B3 patients being over treated?
The majority of patients with B3 diagnosis (75%) will have a benign histology on further sampling.

Is surgical excision necessary?
Aim to adequately sample to rule out coexistent cancer

Follow up
Addressing Over-diagnosis / Over-treatment

LORIS: The Low Risk DCIS Trial

<table>
<thead>
<tr>
<th>Main Eligibility Criteria:</th>
<th></th>
</tr>
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<tbody>
<tr>
<td><strong>Inclusion</strong></td>
<td></td>
</tr>
<tr>
<td>• Female, age ≥ 46 years</td>
<td></td>
</tr>
<tr>
<td>• Screen-detected or incidental microcalcification</td>
<td></td>
</tr>
<tr>
<td>• Low risk DCIS on large volume VAB, confirmed by central pathology review</td>
<td></td>
</tr>
<tr>
<td>• Patient fit to undergo surgery</td>
<td></td>
</tr>
<tr>
<td>• No previous breast cancer or DCIS diagnosis</td>
<td></td>
</tr>
</tbody>
</table>
Current state

- Management is inconsistent across screening units.
- Increasing use of VAB
- Over-treatment is a recognised issue
- Local guidelines: Leeds pathway, London QARC
Advantages of $2^{nd}$ line VAB

For patients

- Targeted sampling: less tissue removed.
- Outpatient procedure, well tolerated by patients.
- Avoid complication of anaesthesia and surgery
- No scarring, easier further imaging and assessment.
- Rapid turnaround of results.
Advantages of 2\textsuperscript{nd} line VAB

For MDT

\begin{itemize}
\item Improved pre-operative diagnosis rate.
\item Reduced benign surgical biopsy rate.
\item Planning therapeutic surgery for cancer patients.
\item Reducing the risk of over-diagnosis/over-treatment
\end{itemize}
Reduction in benign diagnostic surgery

From Dr S Rajan
B3 Guidelines Group

Remit

- To undertake review of the literature on lesions categorised as B3
- To come up with guideline document for a practical approach to management of these for the NHS BSP.
Proposed plan

- Review the literature on the upgrade rate of each of lesions categorised as B3, of uncertain malignant potential.

- Consider if these upgrade rates are influenced by presentation (screen-detected vs symptomatic vs incidental)
Explore how radiological and histological diagnostic features may influence management approach.

Consider any present guideline/publications.

Propose safe and nationally applicable approaches to the different lesions.

Write a document for publication through NHS BSP and circulate to ‘Big 18s’ for feedback/ratification.
Composition of the B3 group

- **Chair**: Prof Sarah Pinder
- **Radiologists**: Nisha Sharma, Louise Wilkinson
- **Surgeons**: Simon pain, Desai Anil, Ashu Gandhi
- **Pathologists**: Sarah Pinder, Andrew Lee, Abeer Shaaban
Approach

- Management recommendations lesion by lesion.
- Use of diagrams/flow charts
- General principles: radiological/pathological concordance
- 14g core/first line VAB : diagnostic sampling
- Guidance on second line VAB adequate sampling
- Advice on follow up
Pathological issues

- Complete excision of lesion by VAB biopsy (false positive)
Comment on:
Marker clip reaction
Evidence of previous biopsy
Calcification/type of lesion in current biopsy

Review original core/mammotome
- **Sizing of lesion:** e.g. AIDP
  - Pragmatic approach
  - Largest size on any biopsy provided
Difficult interpretation of some lesions if piecemeal: Papilloma with atypia, fibroepithelial lesions, spindle cell lesions
Consistency in pathological diagnosis

- Low reproducibility in diagnosing some B3 lesions as FEA, AIDP.
- Discussion with colleagues, courses
Extensive calcification

- Sampling two ends of the lesion by 1\textsuperscript{st} line VAB
- Follow by 2\textsuperscript{nd} line VAB
Incidental small RS/Papilloma

- Lee et al 2011 examined incidental microscopic papillomas (n=18) and radial scars (n=17).

- If no atypia and the lesion is fully represented on core/VAB, categorise as B2.

- If not sure is completely excised, code as B3 and discuss at MDT meeting. If confirmed wholly excised, no further action is needed.
Summary

- Current management of B3 lesions is not uniform and likely to represent over-treatment.

- The majority of lesions are benign on excision.

- Radiological-pathological correlation is essential for planning management.
There is increasing use of VAB for further sampling as alternative to diagnostic surgery.

Guidelines for B3 management are being developed.
THANK YOU

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