Predicting Invasion in the Excision Specimen From Breast Core Needle Biopsy Specimens With Only Ductal Carcinoma In Situ

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**Objective.**—Some patients with ductal carcinoma in situ on breast core needle biopsy will have invasion at excision. The aim of this study was to determine if patients at increased risk for invasion could be identified.

**Methods.**—The results of all breast core needle biopsies with a diagnosis of ductal carcinoma in situ during a 50-month period were reviewed. A variety of histologic features were identified and correlated with the presence of invasion at excision.

**Results.**—Of 3026 cases, 152 (5%) were diagnosed as ductal carcinoma in situ; excisional biopsies were available for 91 (60%) of these 152 cases, and 17 (19%) showed invasive tumor. Neither the radiographic findings, presence of comedonecrosis, comedo histology, lobular extension, size of the largest focus, nor aggregate size was significantly associated with an increased incidence of invasion (all \( P > .05 \)). However, comedo histology with a cribriform/papillary architecture was significantly associated with an increased risk of invasion (5/7 [72%] cases with invasion, \( P = .002 \)), as were tumors greater than 4 mm with lobular extension (6/15 [40%], \( P = .03 \)).

**Conclusion.**—Patients with comedo ductal carcinoma in situ with a cribriform/papillary pattern or tumor involving more than 4 mm with lobular extension in breast core needle specimens are at increased risk for invasion at excision. (Arch Pathol Lab Med. 2002;126:39±41)

**METHODS**

The results of breast core needle biopsy specimens interpreted from August 20, 1996 to October 31, 2000 at Baptist Hospital of Miami (Miami, Fla) were reviewed. All cases with a diagnosis of ductal carcinoma in situ (DCIS) alone on core needle biopsy will have invasion in the subsequent excision. This rate may be reduced by extensive sampling at the time of biopsy. \(^2\) Nevertheless, since at least some of these patients will require lymph node sampling as a result of this finding, it would be of value if patients at risk for invasion could be identified. To assess this issue, a large number of breast core needle biopsy specimens with the diagnosis of DCIS were reviewed and the findings were correlated with the results of excision.

**RESULTS**

**Patient Population**

During the study period, biopsies of a total of 3026 lesions from 2507 women were performed. The ages of these women ranged from 18 to 89 years (mean 53 years). Of the total number of samples, 1476 were from the left breast, 1361 from the right, and 68 represented bilateral biopsies (189 total biopsies). Reasons for performing the biopsies included calcifications (\( n = 1411 \)), asymmetry (\( n = 106 \)), and a mass (\( n = 1509 \)). Three hundred forty cases (11%) were diagnosed as invasive carcinoma (317 ductal, 13 lobular), 152 (5%) as DCIS, 18 as lobular carcinoma in situ (LCIS) or atypical lobular hyperplasia, 1 as papillary carcinoma, 7 as possible phyllodes tumors, 1 as lymphoma, 216 (7.1%) as atypical, and the remaining 2291 (76%) as benign (967 fibrocystic changes, 1138 fibroadenomas, 23 papillomas, 9 lymph nodes, 52 fat necrosis/abscess, 2 granulomas, and 100 normal breast tissue).
Comedo ductal carcinoma in situ with papillary/cribriform architecture. All 3 images are from the same tumor and demonstrate high-grade nuclei with abundant necrosis. In contrast to the cells of more typical comedocarcinoma, there is less abundant granular (apocrine) cytoplasm, and in some areas the cytoplasm appears clear. Interestingly, detached fragments of tumor (a) in which the papillary architecture can be appreciated (hematoxylin-eosin, original magnification ×200).

Table: Correlation of Histologic Features in Breast Core Needle Biopsies With Ductal Carcinoma In Situ With Invasion in the Excision

<table>
<thead>
<tr>
<th>Feature</th>
<th>No. of Cases or Mean ± SD With Invasion</th>
<th>No. of Cases or Mean ± SD Without Invasion</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases</td>
<td>17</td>
<td>74</td>
<td>NA</td>
</tr>
<tr>
<td>Grade 3 tumor</td>
<td>11</td>
<td>26</td>
<td>.32</td>
</tr>
<tr>
<td>Necrosis</td>
<td>11</td>
<td>44</td>
<td>.79</td>
</tr>
<tr>
<td>Comedo histology</td>
<td>8</td>
<td>25</td>
<td>.28</td>
</tr>
<tr>
<td>Lobular extension</td>
<td>6</td>
<td>11</td>
<td>.08</td>
</tr>
<tr>
<td>Grade</td>
<td>2.5 ± 0.7</td>
<td>2.3 ± 0.8</td>
<td>.15</td>
</tr>
<tr>
<td>Size of largest focus, mm</td>
<td>3.9 ± 1.6</td>
<td>3.8 ± 1.5</td>
<td>.84</td>
</tr>
<tr>
<td>Aggregate size, mm</td>
<td>5.6 ± 2.3</td>
<td>5.2 ± 2.5</td>
<td>.48</td>
</tr>
<tr>
<td>Comedo histology with papillary/cribriform features</td>
<td>5</td>
<td>2</td>
<td>.002</td>
</tr>
<tr>
<td>Aggregate size &gt;4 mm with lobular extension</td>
<td>6</td>
<td>9</td>
<td>.03</td>
</tr>
</tbody>
</table>

* NA indicates not applicable.

Slide Review and Follow-up Biopsy

Of the 152 cases of DCIS, 91 (60%) had subsequent excisional biopsies. On review, the diagnosis of DCIS in the original core biopsy was confirmed in every case. Biopsies were performed in 82 cases for calcifications, in 8 for a mass, and in 1 for asymmetry.

Every excision had a corresponding biopsy site. The excision showed only fibrocystic changes in 5 cases, atypical ductal hyperplasia in 3 cases, DCIS alone in 66 cases, and invasive carcinoma in 17 (19%) cases. In the cases with invasion, the in situ carcinoma resembled that seen in the biopsy. The invasive focus measured less than 2 mm in 6 cases, 2 to 5 mm in 4 cases, and greater than 5 mm in the remaining 7 cases. Axillary lymph nodes with metastatic carcinoma were present in 2 of 29 cases in which lymph nodes were sampled; invasion was present in both cases.

There was no correlation between the radiographic findings (mass, calcifications, or asymmetry) and invasion in the subsequent excision (P = .32).

The results of histologic analysis of the core needle biopsy specimens are shown in the Table. Neither high-grade cytology, comedonecrosis, comedo histology, lobular extension, size of the largest individual focus, nor aggregate size correlated with an increased risk of invasion. There was no correlation between any of these features and invasion when invasive carcinomas were separated by the size of the invasive focus (<2 mm, 2–5 mm, >5 mm, all P > .05). However, 5 of 7 cases with DCIS showing comedo histology and a cribriform/papillary architecture showed invasive carcinoma at excision (P = .002) (Figure). In contrast to more typical cases of comedocarcinoma, these tumor cells lacked apocrine features, specifically abundant granular cytoplasm, but instead had scant cytoplasm that was focally clear. Interestingly, detached fragments of carcinoma were present in the core of 3 of the invasive cases. In addition, the presence of lobular extension in a tumor greater than 4 mm was also associated with an increased risk of invasion (P = .03). All 15 cases with these findings also had comedonecrosis and grade 2 or 3 nuclei. There was no correlation between either of these findings and the size of the invasive focus at excision.

COMMENT

The goal of this study was simple: to identify histologic features in core needle biopsies with DCIS that might be...
able to predict an increased risk of invasion in the subsequent excision. In this and previous series, a relatively large number of patients with only DCIS on biopsy turn out to have invasion at the time of excision.\textsuperscript{9–11} If reliable features could be identified, then axillary node sampling at the time of excision may be warranted.

Unfortunately, it is clear that it is not always possible to predict invasion. Most likely, this inability is related to sampling.\textsuperscript{9} Many of the invasive foci found were quite small, and it may not be possible to always sample this exact focus with a core biopsy. Nevertheless, in this study, the largest such study to date, there were 2 histologic features that did show a significantly increased risk of invasion; these were tumors larger than 4 mm with lobular extension and tumors with comedo histology and a papillary/cribriform architecture.

The increased risk for relatively large DCIS tumors with lobular extension is not surprising. All of these lesions were large and had comedonecrosis and grade 2 or 3 nuclei as well. However, the association of invasion with a cribriform/papillary architecture was surprising. Indeed, when these cases were originally reviewed, this pattern was not one of the original histologic criteria identified. However, when all of the invasive tumors were subsequently examined together, the architectural pattern was noted to be quite common. The frequent presence of detached tumor cells was also quite striking. It is important to note that although these tumors were papillary, they all had high-grade nuclei and were different than the more common low-grade papillary carcinoma. The results did not identify an increased incidence of invasive carcinoma with low-grade papillary carcinoma. In addition, the architecture of these lesions, as well as the lack of apocrine features (as illustrated in the Figure), is different from the more common solid type of comedocarcinoma. Nevertheless, while the finding was significant in this study, the number of cases with this pattern was small, and the true significance of this pattern, as well as that of large foci of DCIS with lobular extension, needs to be confirmed in other studies.

Strategies have been devised by others to deal with discrepancies between diagnoses in core needle biopsies and subsequent open excisions.\textsuperscript{12} These strategies are focused on further characterizing borderline cases with qualifiers, such as favor benign and favor malignant. These strategies are more difficult to apply if sampling alone is the cause of the discrepancy. Nevertheless, judging from the data in this series, it might be worthwhile to consider qualifying cases with large areas of DCIS with lobular extension or comedo histology with a papillary/cribriform architecture with a note such as “invasion cannot be ruled out.”

In conclusion, this study found that it is not always possible to predict the presence of invasion at excision in a core needle biopsy of the breast with only DCIS. Nevertheless, patients with large foci of DCIS and lobular extension and patients with comedo histology with a papillary/cribriform architecture appear to be at a relatively increased risk, and lymph node sampling at the time of excision may be warranted.

\textbf{References}