Papillary Lesions of the Breast With and Without Atypical Ductal Hyperplasia

Can We Accurately Predict Benign Behavior From Core Needle Biopsy?

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Key Words: Papillary lesions; Breast; Core needle biopsy

Abstract

Evaluation of papillary lesions of the breast can be difficult, and in core needle biopsy specimens, accurate diagnosis is challenging. Initial studies suggested that all papillary lesions revealed by core biopsy required surgical excision. Recent data suggest that only papillary lesions with atypical ductal hyperplasia (ADH) revealed by core biopsy need surgical excision. We evaluated our experience at the University of Washington Medical Center, Seattle, with papillary lesions with and without ADH on core biopsy to determine whether diagnostic accuracy can be achieved. In 51 core biopsy specimens, we evaluated the presence or absence of ADH: 25 were benign papillomas; 26 were papillomas with ADH. Surgical follow-up was available for 36 cases (11 papillomas and 25 papillomas with ADH). Clinical (radiologic) follow-up was available in 5 papilloma cases (average follow-up, 35.6 months). Follow-up revealed that all papillomas on core biopsy were benign. Excisional biopsy revealed ductal carcinoma in situ or invasive carcinoma in 12 (48%) of 25 papillary lesions with ADH. Benign papillomas can be adequately diagnosed with core biopsy. All papillary lesions with ADH require surgical excision owing to the high rate of associated neoplasia.

The spectrum of papillary lesions of the breast includes benign papilloma, papilloma with atypical ductal hyperplasia (ADH), papillary carcinoma in situ, and invasive papillary carcinoma. The evaluation of papillary lesions of the breast can be difficult on surgical excision specimens, with the distinction between a papilloma with ADH and papillary carcinoma in situ frequently being problematic. With the advent of core needle biopsy, accurate diagnosis of benign papillary lesions vs papillary lesions with ADH or worse has been challenging. Some initial data suggested that all papillary lesions seen on core biopsy required follow-up surgical excision to exclude in situ or invasive carcinoma. This idea is supported by the fact that radiologic imaging, while helpful, cannot reliably distinguish between benign and potentially malignant papillary lesions revealed by core biopsy. More recent data have suggested that benign papillary lesions can be diagnosed comfortably by using core biopsy (particularly on larger core samples), and only papillary lesions with ADH revealed by core biopsy need surgical excision.

Because this area remains controversial, the purpose of the present study was to evaluate our experience at the University of Washington Medical Center (UWMC), Seattle, with papillary lesions revealed by core biopsy to determine whether diagnostic accuracy can be achieved by using core biopsy alone.

Materials and Methods

The Department of Pathology files were searched for papillary lesions of the breast diagnosed at UWMC by using
core needle biopsy from January 1995 to January 2003. The core biopsy devices used ranged from 14-gauge (non–vacuum-assisted) to 11- and, more recently, 9-gauge vacuum-assisted devices.

During the study period 2,090 breast needle core biopsy specimens were received, and from those, 51 benign papillary lesions and papillary lesions with ADH were retrieved. Six of the biopsy specimens were from outside consultations (5 papillomas with ADH and 1 benign papilloma) with clinical or pathologic follow-up performed at UWMC. All specimens were fixed in buffered neutral formalin and embedded in paraffin, from which 4- to 5-µm-thick sections were cut and stained with H&E. Approximately 3 to 6 levels were cut on each case, with, at most, 3 blocks per biopsy.

The presence or absence of ADH was evaluated in each case based on review of all slides by S.N.A. and T.J.L. The core specimens were reviewed and evaluated for ADH before review of the excision specimens. Follow-up data were obtained from the clinical record, the pathology database, or both. The criteria used for assessing ADH in a papilloma were similar to those set forth by Kraus and Neubecker (ie, the presence of hyperchromatic nuclei or marked nuclear atypia, cribriform pattern, absent supporting stroma, and a monotonous cell population without admixed myoepithelial cells). Clinical (radiographic) follow-up was considered significant only if the follow-up period was at least 2 years; otherwise, it was not included in the analysis. Pathologic follow-up consisted of surgical excision.

The Fisher exact test with a 2-tailed $P$ value was used to test for associations between variables. This research was conducted with approval of the Human Subjects Division at the University of Washington.

**Results**

Of the 51 papillary lesions on core biopsy, 25 were benign papillomas and 26 were papillomas with ADH. The initial diagnosis was the same as the review diagnosis in each case. The data are summarized in **Table 1** (note that cases without significant follow-up were not included in Table 1).

Of the benign papillomas **Image 1**, 16 had significant follow-up, and all were revealed as benign on excision

**Table 1**

Clinical and Pathologic Characteristics of Benign Papillomas and Papillary Lesions With ADH Shown on Core Needle Biopsy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Papilloma (n = 16)</th>
<th>Papilloma With ADH (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age (y)</td>
<td>54.5</td>
<td>53.0</td>
</tr>
<tr>
<td>Clinical manifestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mass</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Clear fluid</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Bloody fluid</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Mammographic findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mass</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Calcifications</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>FAD</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>FAD with calcifications</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Follow-up findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>ADH</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>DCIS</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Invasive carcinoma</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

ADH, atypical ductal hyperplasia; DCIS, ductal carcinoma in situ; FAD, focal architectural distortion.

* Cases without significant follow-up were excluded from the analysis.

**Image 1** Benign papilloma revealed by core needle biopsy (H&E, A, ×40; B, ×400). Note the prominent stoma, single layer of epithelial cells, and presence of myoepithelial cells.
(11 cases) or stable clinically or radiographically (5 cases). The average time for follow-up in the clinical follow-up cases was 35.6 months (median, 41 months; range, 24-51 months).

Of the papillary lesions with ADH [Image 2I, 25 had significant follow-up (all excisions). Of those, 6 (24%) were benign, 7 (28%) were papillary lesions with ADH, and 12 (48%) were shown to be ductal carcinoma in situ (10 cases) or invasive carcinoma (2 cases) on excision. The presence of ADH on core biopsy was associated significantly with DCIS or invasive carcinoma on follow-up biopsy ($P = .001$).

The average age of the patients overall was 53.6 years (range, 30-83 years). The average age of patients with a benign papilloma was 54.5 years (range, 31-83 years) and for patients with a papilloma with ADH, 53.0 years (range, 30-79 years).

Twelve lesions were detected clinically (by the patient or the physician) as the presence of a palpable mass (7 cases), clear fluid expressed from the nipple (4 cases), or bloody fluid expressed from the nipple (1 case). Mammography findings were normal in 3 of the clinically detected cases.

Mammography detected 47 of the lesions, which were seen as a mass (25 cases), calcifications (11), a mass with calcifications (1), a focal architectural distortion (1), or a focal architectural distortion with calcifications (1). All lesions detected by mammography were labeled “suspicious” for malignancy.

There were no statistically significant associations between lesions manifesting as a mass, calcifications, or expressed fluid and subsequent DCIS or invasive carcinoma revealed by the excisional biopsy.

### Discussion

Papillary lesions of the breast remain a challenging subject in diagnostic breast pathology, and controversy remains about whether needle core biopsy is sufficiently accurate in the diagnosis of benign pathology to avoid surgical biopsy. Our study indicates that needle core biopsy is accurate in the diagnosis of benign papillary lesions and that any ADH in a papillary lesion shown on core needle biopsy necessitates surgical excision.

The criteria we used in this study were developed in 1962 by Kraus and Neubecker, and those criteria remain valid in the diagnosis of ADH in papillary lesions. The presence of ADH in our study was correlated significantly with the presence of invasive or preinvasive carcinoma of the breast. These findings are similar to those of Ivan and colleagues, who found that for 63% (5/8) of their papillary lesions with ADH diagnosed on core biopsy, excisional biopsy revealed carcinoma in situ.

Our study also confirms previous reports that mammography is not reliable for the distinction between benign and atypical papillary lesions. All of the radiologically detected lesions in our study were designated as suspicious for malignancy on mammography. This is similar to studies by Soo et al. and Woods and colleagues, who found that papillary carcinoma and solitary breast papillomas can have overlapping features and are difficult to distinguish radiologically.

However, close radiologic follow-up is essential for benign papillomas because an interval change in the lesion could predict malignancy. The average clinical follow-up time in our study for benign papillary lesions shown on core biopsy was 35.6 months, which compares well with the established literature but cannot be considered long-term.

![Image](https://academic.oup.com/ajcp/article-abstract/122/3/440/1759445) Papilloma with atypical ductal hyperplasia (H&E, A, ×40; B, ×400). The epithelial cell population focally appears more monomorphic with increased nuclear atypia and a suggestion of cribriform architecture.
follow-up. In the study by Lee and colleagues of 355 lesions with benign core biopsy diagnoses followed by mammography, mammographic change occurred in 7% of cases, and malignancy was diagnosed in only 2 cases that showed change at 6 and 24 months. This study did not specifically address papillary lesions, however, and additional studies with longer-term follow-up are needed to assess the clinical course of benign papillary lesions that are not excised after core biopsy.

At UWMC, core needle biopsies are performed using a variety of sizes of biopsy devices depending on whether the core biopsy is performed by a surgeon on a palpable mass or whether the lesion is localized by ultrasound vs stereotactic techniques. There is some controversy in the literature about whether the size of the core biopsy device correlates with complete evaluation of the lesion and the need for excision. Our study was designed to look at papillary lesions shown on core biopsy and does not specifically address this issue.

Our experience at UWMC with core needle biopsy shows it to be accurate in the distinction between benign papillomas of the breast and those with malignant potential. Core needle biopsy is an effective and accurate way to evaluate papillary lesions of the breast. However, benign papillomas shown on core needle biopsy still should be followed up closely clinically and radiologically, and more studies with long-term follow-up are warranted. Any ADH in papillary lesions shown on core needle biopsy warrants surgical excision, as a significant proportion of these lesions contain in situ or invasive carcinoma.

References