Asian Biomedicine Vol. 5 No. 2 April 2011; 243 - 248 **DOI: 10.5372/1905-7415.0502.031**

Original article

Atypical papillary lesions after core needle biopsy and subsequent breast carcinoma

Tuenchit Khamapirad[a], Caitlin Andrews[a], Jenjeera Prueksadee[b], Morton Leonard Jr[a], Louisea Bonoan-Deomampo[a], Qing Ahao[c], Natalia Golardi[c], Mahmoud A. Eltorky[c]

[a]*Department of Radiology, University of Texas Medical Branch at Galveston, Texas 77555, USA,* [b]*Department of Radiology, King Chulalonkorn Memorial Hospital and Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand,* [c]*Department of Pathology, University of Texas Medical Branch at Galveston, Texas 77555, USA*

Background: Papillary lesions of the breast cause diagnostic problem because papillary structures are found in benign and malignant processes. Core needle biopsy is important to make an initial diagnosis, but it still has potential pitfalls. Comparison between core needle biopsy and excisional biopsy can predict the possibility of malignant change in atypical papillary lesions.

Objective: Evaluate the concordance between core needle biopsy and excisional results in atypical papillary lesions of the breast.

Materials and methods: The pathology database of University of Texas Medical Branch at Galveston, USA was searched for patients with atypical papillary lesions at core needle biopsy who subsequently underwent surgical excision. Pathology reports from the excisional biopsies was also examined to assign each case to one of three categories, downgrade to benign papilloma, no change (remained atypical papillary lesion), and upgrade to carcinoma. The mammograms and ultrasounds were reviewed for each case. They characterized the lesions according to multiple imaging criteria.

Results: Twenty-four patients with atypical papillomas at core biopsy subsequently underwent surgical excision. The lesions were downgraded to benign papilloma in 25%, remained atypical papillary lesion in 33%, and upgraded to carcinoma in 42%. On mammographic presentations (n = 23), masses were in 61%, architectural distortion in 4.3%, mass with calcifications in 9%, mass with architectural distortion and calcifications in 4.3%, calcifications alone in 17.4%, and architectural distortion and calcifications in 4.3%. On ultrasound findings (n = 21), solid masses were in 90%, intracystic masses in 10%, peripheral in locations in 81%, and subareolar in location in 19%.

Conclusion: Due to the high upgrade rate of atypical papillary lesions to carcinoma (42%), excision of all atypical papillary lesions with wide excision margin is recommended for cases with pathologic diagnosis of atypical papillary lesion on core-needle biopsy.

Keywords: Atypical papillary lesions, breast carcinoma, core-needle biopsy, mammography

Papillary lesions of the breast have a wide spectrum of lesions that includes benign papilloma, papilloma with atypical ductal hyperplasia (ADH), papillary carcinoma in situ, and invasive papillary carcinoma [1]. By definition, papillary lesions are characterized by epithelium with a fibrovascular core that arborizes into branching papillae and protrudes into the duct lumen [1-3]. The presence or absence of a myoepithelial cell layer in the papillary component of the lesion is the most important feature that helps differentiate a benign papilloma from a papillary carcinoma [1].

However, these lesions are less frequently encountered, and there are limited data upon which to base management recommendations. In addition, the histological evaluation of lesions by core needle biopsy (CNB) may not always accurate due to sampling error, and CNB only samples a portion of

Correspondence to: Jenjeera Prueksadee, MD, Department of Radiology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand. E-mail: jenjeera@hotmail.com

the lesion, cancerous parts of the lesion can be missed [4]. In this study, we retrospectively reviewed the concordance between CNB and excisional biopsy (EB) and imaging findings in atypical papillary lesions of the breast on the pathology database of University of Texas Medical Branch (UTMB) at Galveston, USA.

Materials and methods

We retrospectively searched the pathology and radiology databases at the UTMB at Galveston, USA. In the patients in whom an atypical papillary lesion was diagnosed, both CNB and EB were available for evaluation. We examined the excisional biopsy reports in all the patients to determine the concordance between core needle biopsy and excision. We noted whether the lesion/lesions in each patient downgraded to benign papilloma without atypia, remained the same (atypical papillary lesion) or upgraded to carcinoma. The image evaluations were reviewed by experienced radiologists. These included mammographic and sonographic findings. On mammograms, we characterized the lesion by the presence of mass/masses alone, mass/masses with architectural distortion, mass/masses with calcifications, mass with architectural distortion and calcifications, calcifications alone and architectural distortion and calcifications. On ultrasonography (US), we also characterized masses according to location (periphery or subareolar), composition (intracystic or solid) and color flow study (increased or none). All the patients with radiographically detected calcifications and lesions not identified at US underwent stereotactic biopsy.

Results

The data of 24 women diagnosed with an atypical papillary lesion at core biopsy within a seven-year period between 2000 and 2007 were collected. The mean patient age was 60.5 years (range: 36-81 years). The patients had different clinical presentations, 12 cases with asymptomatic, 10 cases with palpable mass, three cases with breast pain, and one case with nipple discharge (**Table 1**).

Concordance between core biopsy and excision showed that six patients (25%) downgraded to benign papilloma. Eight patients (33%) stayed atypical papillary lesion, and ten patients (42%) upgraded to carcinoma at excision. **Figure 1** shows radiographic, ultrasonic, and histologic images of atypical papillary lesion.

In the group of carcinoma, these lesions had carcinoma arising in a papilloma in six (25%), intracystic papillary carcinoma in three (13%), and invasive ductal carcinoma in one (4%). These images are shown in **Figure 2**.

One patient with excisional pathology reported of benign papilloma was excluded from imaging evaluation due to loss of imaging data record. At mammography (n = 23) these lesions manifested as mass/masses in 14 (61%), mass and architectural distortion in one (4.3%), mass with calcifications in two (9%), mass with architectural distortion and calcifications in one (4.3%), calcifications alone in four (17%), and architectural distortion and calcifications in one (4.3%). **Figure 3** shows radiographic images of atypical papillary lesion.

Various mammographic observations are summarized shown in **Table 2.**

Twenty-three lesions were evaluated with ultrasound. Ultrasound scans were available for 21 lesions. Two lesions with atypical papillary lesions were not visualized with US. **Table 3** shows various ultrasound findings. Interestingly, there was no case of benign papilloma where flow increased.

Table 1. Clinical presentations.

Symptoms	Papilloma (n = 6)	Atypical papillary lesion (n = 8)	Carcinoma (n = 10)	Total (n = 24)
Asymptomatic	3	5	4	12
Palpable mass	3	1	6	10
Breast pain	1	0	2	3
Nipple discharge	0	0	1	1

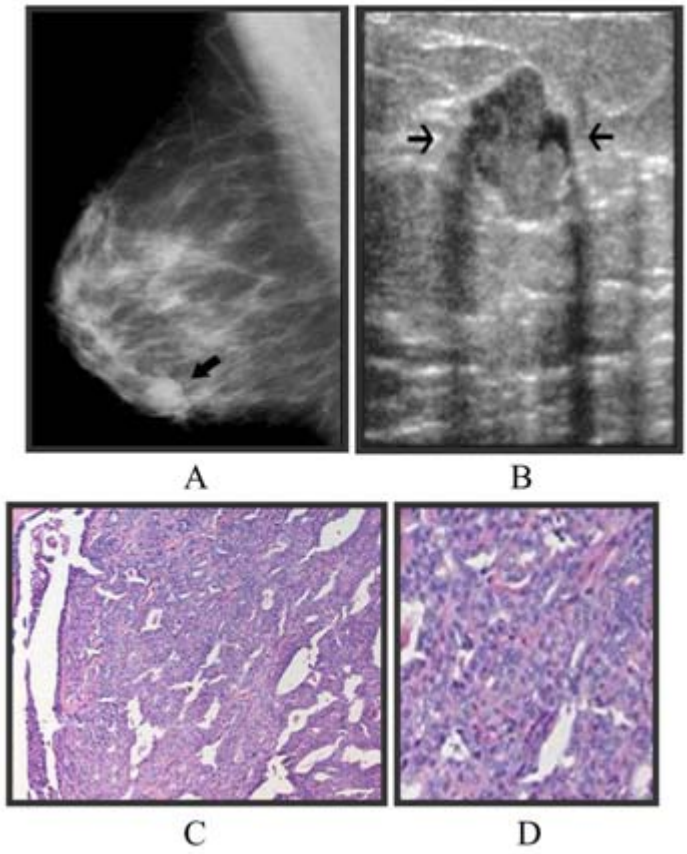

Figure 1. Atypical papillary lesion. **A**: Mediolateral oblique view of the right breast showing a slightly hyperdense mass with partially circumscribed, obscured margins (indicated by an arrow). **B**: Ultrasound image demonstrating a lobulated mixed solid cystic mass (indicated by arrows). **C**: High power field of pathology image indicating less than 30% of the lesion contains cytologic atypia (larger nucleus, basophilic cytoplasm, prominent nucleoli) and rare myoepithelial cells. **D:** Magnification image of the pathology.

Discussion

Intraductal papillary lesions are relatively uncommon lesions in most breast biopsy specimens. These were previously reported in 1% to 3% of breast biopsies [5-7]. Breast papillomas may be either solitary or multiple. Solitary papillomas are usually found in a subareolar location within the larger ducts, and more than half of patients present with spontaneous nipple discharge. In contrast, multiple papillomas usually arise within the terminal duct lobular units, and are most frequently peripheral in location. Multiple papillomas are defined by the presence of multiple (at least five) papillomas in at least two consecutive surgical pathology tissue blocks. These patients rarely present with nipple discharge [3, 8]. It has been suggested that there is an **in**creased risk for the development of breast carcinoma in women with multiple papillomas [1, 3]. The relative and/or absolute risk for the development of invasive breast carcinoma in patients with a history of ADH or dual carcinoma in situ (DCIS) at breast biopsy has been well documented [9, 10]. However, the risk of these lesions within a papillary lesion has not been fully established [11]. One study showed that the presence of atypia in a papilloma is associated with a significantly increased risk of the development of breast cancer about eight times higher than in benign papillomas [10]. Other studies [11-13] showed that atypical papillary lesions, consisting of papillomas with atypia or atypical ductal hyperplasia, have an increased risk of subsequently developing invasive carcinoma compared with papillomas in general. Therefore, these lesions should be surgically excised.

A diagnosis of carcinoma or atypical papillary lesion by CNB should warrant an EB. On the other hand, benign papillomas may be followed if imaging findings are concordant and do not need to be excised. These were also shown by Ivan et al. [14] and

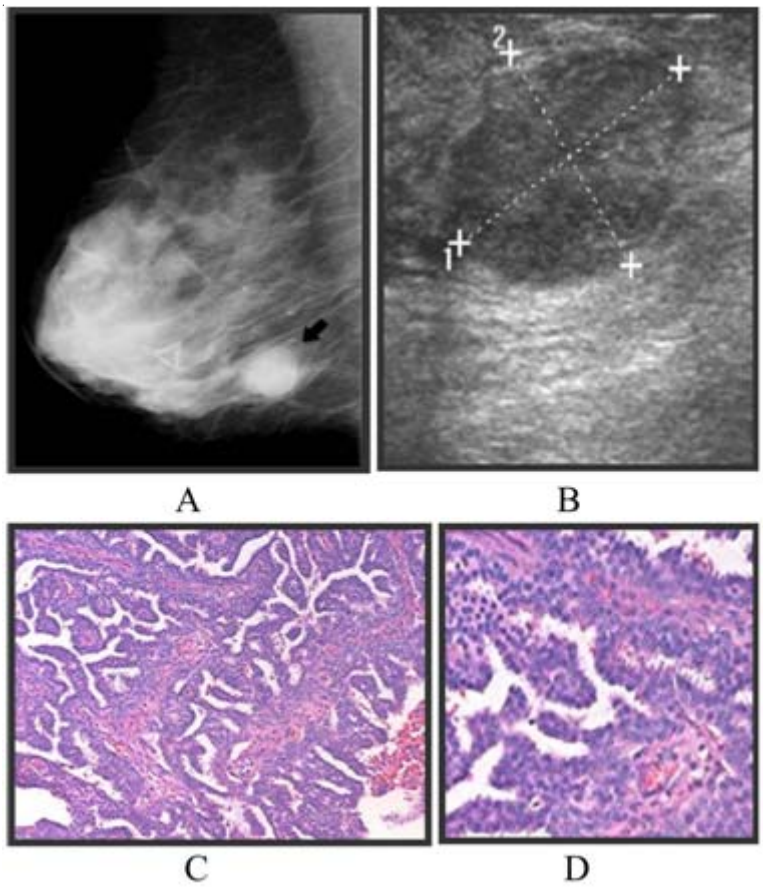

Figure 2. Intracystic papillary carcinoma. **A**: Mediolateral oblique view revealing a high density round mass with irregular margin (indicated by an arrow). **B**: Ultrasound image recognizing solid mass with irregular margin and posterior enhancement (indicated by cross lines). **C**: High power field pathology image showing intracystic papillary carcinoma. Fibrovascular cores lined by malignant epithelial cells. Myoepithelial cells are absent in more than 90% of the lesion. **D**: Magnification images of the pathology.

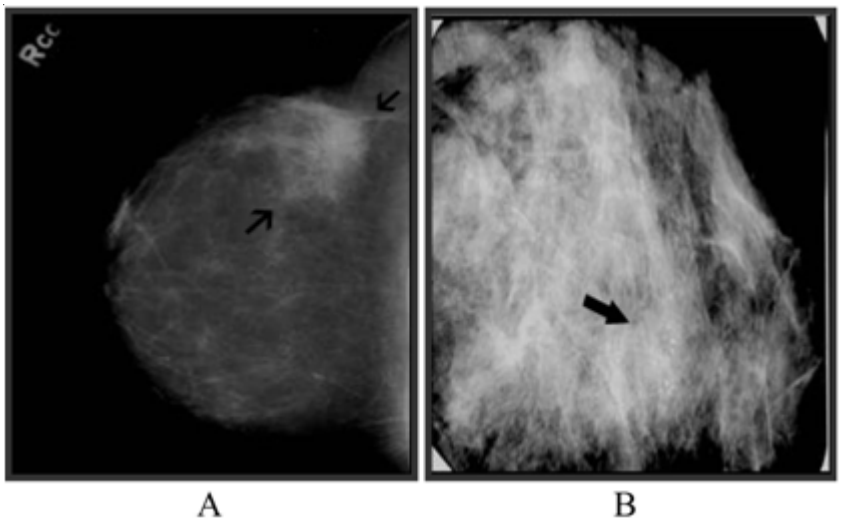

Figure 3. Atypical papillary lesion. **A**: Craniocaudal view showing a focal area of architectural distortion (indicated by an arrow). **B:** Another case with magnification view demonstrating group of amorphous, pleomorphic, punctate calcifications.

Table 2. Mammographic findings.

Mammographic finding	Papilloma (n = 5)	Atypical Papillary lesion (n = 8)	Carcinoma (n = 10)	Total (n = 23 (%)
Mass/masses alone	3	3	8	14 (61)
Mass with architectural distortion	1	0	0	1 (4.3)
Mass/masses with calcifications	0	2	0	2 (9)
Mass with architectural distortion and calcifications	0	0	1	1 (4.3)
Calcifications alone	1	2	1	4 (17)
Calcifications and architectural distortion	0	1	0	1 (4.3)

Table 3. Ultrasound findings.

Sonographic finding	Papilloma (n = 5)	Atypical Papillary lesion (n = 6)	Carcinoma (n = 10)	Total n=21 (%)
Mass/masses	5	6	10	21 (100)
Peripheral	4	4	9	17 (81)
Subareolar	1	2	1	4 (19)
Solid	4	6	9	19 (90)
Intracystic	1	0	1	2 (10)
Increased color flow	0	2	6	8 (38)

Renshaw et al. [15]. One study revealed that diagnosis by percutaneous core biopsy of benign papillary lesions proved to be accurate when concordant with imaging findings. Surgical excision was indicated when diagnosis by percutaneous biopsy revealed atypical papillary lesions or papillary DCIS [6]. According to Mercado et al. [4], the considerable rate of upgrade to either ADH or DCIS was 26% for all patients with excised benign papillary lesions, which recommended excision of all benign papillary lesions of the breast diagnosed with core-needle biopsy [4]. The most recent study by Sydnor et al. [16] revealed that benign papilloma diagnosed at core biopsy infrequently (3%) was associated with malignancy, and mammographic follow-up was reasonable. Because of the high association with malignancy (67%), the diagnosis of atypical papilloma at core biopsy should prompt excision for definitive diagnosis [16]. Similar to previous studies, our study revealed a considerable upgrade rate to carcinoma (42%) in atypical papillary lesions diagnosed at core biopsy. This may be due to inadequate sampling by CNB of the lesion or adjacent tissue, which may contain foci of carcinoma. One study demonstrated the risk factors for malignancy, palpability, size, or Breast Imaging Reporting and Data System (American College of Radiology, Reston, USA) did not help to differentiate benign from malignant disease [17].

In our study, most mammographic presentation of atypical papillary lesions manifested as mass/masses in 14 patients (61%) similar to one study [4], which most mammographic findings were mass (23 in 43). Other mammographic findings include calcifications, architectural distortion, and combinations of several of these features are variable ranging from 4.3% to 17%. Most of carcinoma manifested on ultrasound as solid masses (9 in 19 cases) in peripheral locations (9 in 17 cases). Our results suggested that atypical papillary lesions were more likely to present as solid than intracystic masses, with 19 out of 21 masses being solid. However, our sample sizes were too small to ascertain any significant differences between papilloma, atypical papillary lesion, and carcinoma with respect to these imaging features.

In conclusion, due to the high upgrade rate in atypical papillomas diagnosed at core biopsy (42%), the surgical excision with wide margin of all atypical papillary lesions diagnosed at core needle biopsy is

recommended. Although CNB is still recommended as a first line diagnostic tool for suspicious lesions, decisions about management should not be based on the CNB alone for atypical papillary lesions. The final diagnosis must be made from the excisional biopsy.

Acknowledgment

We express special thanks to Ms. Terry Taylor (UTMB, Galveston) for obtaining patient jackets, and Ms. Laura Lemley (UTMB, Galveston) for obtaining pathology reports and slides.

The authors have no conflict of interest to report.

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