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● *Original Contribution*

CLINICAL AND IMAGING CHARACTERISTICS OF PAPILLARY NEOPLASMS OF THE BREAST ASSOCIATED WITH MALIGNANCY: A RETROSPECTIVE COHORT STUDY

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Abstract—Papillary neoplasms of the breast comprise a broad range of pathologies ranging from papillomas to papillary carcinomas and have been associated with breast cancers. In this study, we evaluated the clinical, mammographic and sonographic features of papillary breast neoplasms from benign papillary breast lesions to malignancy-associated papillary lesions. A total of 194 lesions in 179 patients were analyzed, including 117 benign papillomas, 24 atypical papillomas, 41 benign papillomas with malignancies and 12 papillary carcinomas found between January 2003 and August 2011 in our institution. Statistically significant clinical factors included patient age ($p = 0.001$), lesion multiplicity ($p = 0.009$) and peripheral location ($p = 0.003$). Among these factors, the odds ratio for malignancy was 8.9 for bilateral multiple lesions. Visibility ($p = 0.001$) and density ($p = 0.039$) were significant factors for malignancy in mammograms, and echo patterns ($p = 0.006$), boundary ($p = 0.001$) and vascularity ($p = 0.005$) were significant features on ultrasound that differentiated malignancies from benign lesions. Overall, when papillary breast lesions are located bilaterally and peripherally in older patients, they are correlated with breast cancers. Additionally, for papillary breast lesions that appear highly dense on mammograms and/or exhibit positive vascularity on ultrasound, the probability of malignancy is relatively high. (E-mail: dr_philic@naver.com or seonhyeong.choi@samsung.com) **© 2014 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Breast, Malignancy, Papillary neoplasm, Papillary lesion, Mammography, Ultrasound.**

INTRODUCTION

Papillary lesions of the breast comprise a broad range of pathologies and can be further classified into a number of categories, including benign papillomas, atypical papillomas, papillomas with atypical ductal hyperplasia, ductal carcinomas *in situ*, invasive ductal carcinomas and papillary carcinomas (Cheng et al. 2009; Ibarra 2006). The overlap of clinical presentations, radiologic appearances and histopathologic features among papillary lesions makes definitive diagnosis a challenge (Bode et al. 2009; Brookes and Bourke 2008; Chang et al. 2007; Ganesan et al. 2006; Ibarra 2006; Renshaw et al. 2004; Rizzo et al. 2008). There is also a high risk of sampling error and a high frequency of upgrade to carcinoma after core biopsy (Kim et al. 2008; Youk et al. 2011). Thus, for patients who have papillary breast lesions confirmed by percutaneous needle biopsy, the decision to undergo surgical excision or vacuum-assisted biopsy or simply to be followed up clinically can be debatable with no definite protocol. For this reason, a rational analysis of cancer risk, based on clinical and radiologic features of benign and malignant neoplasms, can improve patient management. Our study compared a wide range of benign and malignancy-associated papillary lesions of the breast, using clinical examination, mammography and ultrasound (US) to identify characteristics.

METHODS

This retrospective study was approved by the institutional review board in our institution, and informed consent was waived.

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Patient selection

From January 1, 2003, to August 31, 2011, 2075 patients underwent breast surgery or US-guided vacuum-assisted excision at our institution. During this period, 238 cases of papillary breast lesions in 223 patients were diagnosed by open surgery (excision or mastectomy), US-guided 14-gauge core needle biopsy (CNB), US-guided vacuum-assisted biopsy or vacuum-assisted excision (VAE) using an 8- or 11-gauge needle. The pathology report on each case was reviewed, and the size and location of the papillary lesions noted in these reports were compared with the radiologic images at diagnosis. All cases were reviewed by two radiologists and a pathologist together in one setting to confirm the location and size of the lesions. Tissue pathology slides were re-evaluated by a pathologist in cases where there were no remarks about the initial diagnosis by CNB in the final pathology reports or where there were size discrepancies between the pathology reports and imaging features. Cases were excluded if (1) the papillary lesions were diagnosed by fine-needle aspiration biopsy or CNB with no subsequent surgical excision or VAE (n = 24); (2) no imaging records were available (n = 6); (3) histologic findings did not correspond to imaging findings with the histologic sizes of lesions not corresponding to imaging sizes on mammography or US because of the small size of the lesions themselves (n = 5); and (4) there was no pathologic information regarding the lesion (n = 9), for instance, when lesions were found only through 14-gauge CNB without being confirmed or found on surgical specimens. The included cases were categorized based on pathology reports: group A = benign papilloma; group B = atypical papilloma or papilloma with atypical ductal hyperplasia; group C = papilloma with invasive ductal carcinoma or ductal carcinoma *in situ* (DCIS); and group D = papillary carcinoma.

Clinical features

Medical records were reviewed for patient age, lesion location, single or multiple lesions and associated symptoms, such as palpability, nipple discharge and breast pain. Lesions < 3 cm from the nipple were categorized as central, and those ≥ 3 cm from the nipple were considered peripheral. The distance was measured on mammography or US or on the pathologic specimen by two radiologists and a pathologist.

Imaging analysis

Mammography was performed using with one of the following units: Senographe DMR or DS (GE Healthcare, Waukesha, WI, USA); Brestige (Medi-Future, Sungnam-si, Gyeonggi-do, ROK); Selenia (Hologic, Bedford, MA, USA). Sonographic exams and US-guided CNBs were performed by one of three dedicated breast radiologists with 5–20 y of clinical experience. US exams were performed using one of the following high-resolution US systems with a 12-5 or 15-4 MHz linear-array transducer: HDI 5000 (Philips/ATL, Bothell, WA, USA); iU22 (Philips Healthcare, Bothell, WA, USA); LOGIQ7 (GE Healthcare); AiExplore (SuperSonic Imagine, Aix-en-Provence, Provence-Alpes-Cote d'Azur, France). The period from US exam and/or US-guided biopsy to surgery was less than 6 wk.

Initially two radiologists and one pathologist sat down together and reviewed the radiologic images and pathology reports to confirm the location and size of the lesions. Then, all mammographic and US images were retrospectively re-evaluated for consensus by two radiologists with 3–10 y of experience in breast imaging interpretation. Images were assessed according to the Breast Imaging Reporting and Data System (BI-RADS) lexicon for mammography and US (American College of Radiology 2003).

On mammography, lesion detectability was assessed, and lesion type (mass, asymmetry, calcification only); shape (oval, round, lobular, irregular); density (low, equal, high); margins (circumscribed, microlobulated, indistinct, speculated); calcifications (absent, macrocalcification, microcalcification); and associated features (architectural distortion, nipple areolar retraction) were evaluated. On US, lesion type (mass, non-mass); shape (oval, round, irregular); margins (circumscribed, not-circumscribed); orientation (parallel, nonparallel); echo pattern (anechoic, hyper-echoic, hypo-echoic, iso-echoic); boundary (abrupt, echogenic halo); calcifications (absent, microcalcification, macrocalcification); and vascularity (absent, present) were evaluated. As a mass is a subject that occupies space, it was observed in two different projections (Fig. 1), and the non-mass designation was used for lesions that did not have mass. For echo patterns, the lesions were initially divided into solid masses and mixed echoic lesions (Fig. 1a), and then the echogenicity from the solid portion was used to designate an echo pattern. For vascularity, if there was no color signal suggesting a vascular structure or blood flow within the lesion, it was defined as negative on color Doppler images. Ductal dilation (>3 mm) was also recorded (Fig. 2b).

Statistical analyses

A bio-statistician in our institution was consulted for statistical analyses and interpretations. Student's *t*-test or the Mann–Whitney *U*-test was used to compare continuous variables, patient age, and lesion diameter among the four papillary lesion groups (A–D). The χ^2-test or Fisher's exact test was used to assess the statistical significance of categorical variables, including clinical symptoms and the BI-RADS lexicons of each modality. Analysis of variance was used to compare clinical and