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Concordant, non-atypical breast papillomas do not require surgical excision: A 10-year multi-institution study and review of the literature

Lars J. Grimm[a,*], Christine E. Bookhout[b], Rex C. Bentley[c], Sheryl G. Jordan[d], Thomas J. Lawton[e]

[a] Department of Radiology, Duke University, DUMC Box 3808, Durham, NC 27710, USA
[b] Department of Pathology and Laboratory Medicine, The University of North Carolina at Chapel Hill, 101 Manning Dr, Cb #7525, Chapel Hill, NC 27514, USA
[c] Department of Pathology, Duke University, DUMC Box 3712, Durham, NC 27710, USA
[d] Department of Radiology, University of North Carolina at Chapel Hill, 430 Waterstone Drive, First Floor, Hillsborough, NC 27278, USA
[e] Department of Pathology and Laboratory Medicine, University of California Los Angeles, 10833 Le Conte Ave, Los Angeles, CA 90095, USA

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ABSTRACT

Purpose: Non-atypical papillomas (NAPs) diagnosed on core needle biopsy (CNB) frequently undergo surgical excision due to highly variable upstaging rates. The purpose of this study is to document our dual-institution upgrade rates of NAPs diagnosed on core needle biopsy and review the upgrade rates reported in the literature.
Materials and methods: Following IRB approval, CNB results from Duke University (7/1/2004–6/30/2014) and the University of North Carolina Chapel Hill (1/1/04–6/30/2013) were reviewed to identify non-atypical papillomas. All cases with surgical excision or 2 years of imaging follow up were included. In addition, a literature review identified 60 published studies on upgrades of NAPs diagnosed at CNB. Cases in our cohort and the published literature were reviewed for confounding factors: [1] missing radiologic-pathologic concordance and/or discordance, [2] papillomas included with high-risk lesions, [3] high risk lesions counted as upgrades, [4] review by a nonspecialized breast pathologist, and [5] cancer incidentally detected.
Results: Of the 388 CNBs in our dual-institution cohort, 136 (35%) patients underwent surgical excision and 252 (65%) patients had imaging follow up. After controlling for confounders, no cancers (0/388) were found at surgical excision or during follow up imaging. The literature review upstaging rate was 4.0% (166/4157) but 1.8% (4/227) after excluding studies with confounders. The combined upstaging rate from the literature and this study was 0.6% (4/615).
Conclusion: The upstaging rate for CNB diagnosed NAPs was 0% in our cohort and 0.6% overall after adjusting for confounders. This low rate does not warrant reflexive surgical excision and diagnostic imaging follow up should be discretionary.

1. Introduction

Non-atypical papillomas (NAPs) have often been included in the group of high risk breast lesions due to reported surgical upgrade rates to ductal carcinoma in situ (DCIS) or invasive carcinoma at as high as 33% [1–60]. However, the studies published in the literature have highly variable methodologies with inconsistent inclusion and exclusion criteria. In particular, there are five primary reasons why reported upstaging rates may be artificially elevated: [1] missing radiologic-pathologic concordance and/or discordance (e.g., fine linear branching calcifications seen on mammography but core needle biopsy [CNB] reveals only a benign papilloma), [2] papillomas included with high-risk lesions (e.g., papilloma and atypical ductal hyperplasia both identified at initial CNB), [3] high risk lesions counted as upgrades (e.g., benign papilloma at CNB and atypical papilloma at surgical excision counted as an upgrade), [4] review by a non-specialized breast pathologist, and [5] cancer incidentally detected (e.g., DCIS found in an adjacent duct).

Artificially elevated NAP upstaging rates can have multiple negative implications for patients. First, patients may undergo unnecessary surgical excision with the associated morbidity and cosmetic changes. Second, patients with a core needle biopsy proven NAP may suffer from increased anxiety if they are led to believe that they are now at increased risk of cancer. Third, older research suggests that patient follow up compliance after surgical excision may be worse than with vacuum-assisted biopsy [61]. As a result, it is important that the risk associated with a core needle biopsy of a NAP is accurately quantified.

The purpose of this study was twofold. First, a dual-institution

* Corresponding author.
E-mail address: lars.grimm@duke.edu (L.J. Grimm).

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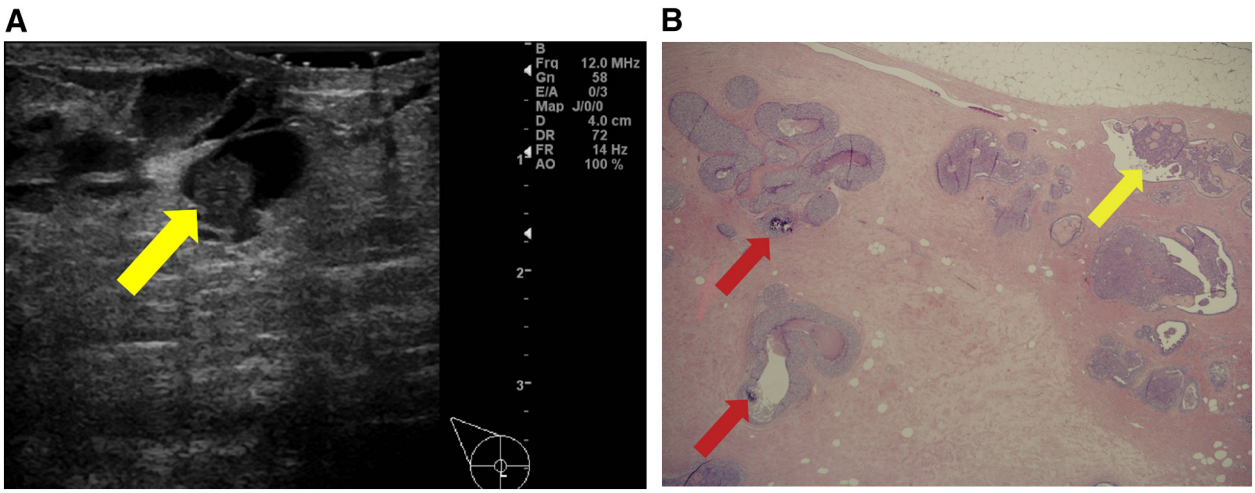

Fig. 1. A 63-year-old woman with spontaneous nipple discharge presents for diagnostic imaging. (A) A subareolar ultrasound revealed an intraductal mass (arrow). This mass was biopsied under ultrasound guidance and pathology identified a sclerosing intraductal papilloma. The findings were deemed concordant and a 6 month follow up was recommended, but the patient elected to undergo surgical excision. (B) At surgical excision, the benign papilloma (yellow arrow) was identified as well as incidental grade 2 ductal carcinoma in situ (red arrows) in a separate unrelated duct to the papilloma. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

review of upstaging rates to cancer following a core needle biopsy diagnosis of NAP was performed while controlling for the confounding factors. Second, these confounding factors were applied to previously published series in the literature to quantify adjusted upstaging rates. Collectively, this analysis allowed for the most accurate assessment of upstaging rates for core needle biopsy diagnosed NAPs to date which may have direct implications on clinical care.

2. Materials and methods

2.1. 10-year dual-institution review

Institutional Review Board approval and a waiver of consent was obtained at Duke University and the University of North Carolina Chapel Hill. Both institutions are large tertiary care academic medical centers servicing similar demographic groups in near proximity to one another. At each institution, fellowship trained breast radiologists and pathologists utilize state of the art imaging and pathology equipment/techniques to diagnose a large volume of breast cancers yearly. At each institution, the surgical pathology database was searched for the following terms: "breast," "core biopsy", "papilloma", and "papillary lesion" for the approved time period from July 1, 2004 to June 30, 2014 (Duke University) and January 1, 2004 to June 30, 2013 (the University of North Carolina Chapel Hill) (n = 1159). Any case containing a coexistent high-risk lesion (atypical ductal hyperplasia, atypical lobular hyperplasia, lobular carcinoma in situ, or flat epithelial atypia) identified at CNB was excluded from the study set (n = 575). Any case not surgically excised or with < 2 years of imaging follow-up was excluded from the study set (n = 176). Finally, discordant cases on radiologic-pathologic review (n = 19) were excluded, based on review by the radiologists at their respective institutions (names withheld). A total of 389 NAPs in 371 patients met criteria and represent the study set. All cases were initially interpreted by a specialized breast pathologist at their respective institution as part of the routine clinical workflow. A specialized breast pathologist was defined as a pathologist with fellowship training in breast pathology. Cases of DCIS or invasive cancer identified at surgical excision or subsequent biopsy within the two-year period were considered upgrades. If DCIS or invasive cancer was found at surgical excision, the relationship between the NAP diagnosed at CNB to the cancer was determined to decide if the upgrade was incidental or related to the NAP. If this information was not apparent from a retrospective review of the pathology report (e.g., incidental note was made of DCIS 1 cm from the papilloma) then the case was rereviewed by a specialized breast pathologist to confirm the relationship between the cancer and the papilloma.

2.2. Literature review

PubMed/National Library of Medicine was searched for English language articles using combinations of the terms "papilloma", "papillary lesion", "core biopsy" and "breast" from 1999 through 2016. This search yielded 173 articles. Articles were then reviewed individually and only those that contained information on upgrade rates for papillomas were included (i.e., studies related to imaging techniques were not eligible). Articles were excluded if they did not include at least 5 cases, so as to remove case reports. The pool included 60 published articles representing 4157 cases that specifically addressed the upgrade rates following a core biopsy diagnosis of NAPs.

Each study was then reviewed for potential confounding factors: [1] missing radiologic-pathologic concordance and/or discordance (n = 11), [2] papillomas included with high-risk lesions (n = 3), [3] high risk lesions counted as upgrades (n = 6), [4] review by a non-specialized breast pathologist (n = 17), and [5] cancer incidentally detected (n = 26). Several studies had multiple potential confounding factors. If a confounding factor was not addressed then the study was counted as having the confounding factor (e.g., a study which did not mention who reviewed the pathology slides would be counted as not having a specialized breast pathologist review). There were 3 studies without any potential confounding factors. An overall upstaging rate was calculated for the initial pool of 60 published studies and then a revised upstaging rate was calculated for the final pool of 3 studies which did not have any confounding factors.

3. Results

3.1. 10-year dual-institution review

Of the 389 patients with NAPs from the two institutions, 136 (35%) patients underwent surgical excision and 252 (65%) patients underwent imaging follow up for at least two years. At surgical excision, one case of DCIS was incidentally found but was unrelated to the benign sclerotic intraductal papilloma and was thus not considered an upgrade (Fig. 1). The remaining 135 surgical excisions did not reveal any cancer. Among patients who underwent imaging follow up, no patients