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Are we overtreating intraductal papillomas?

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ABSTRACT

Background: The management of intraductal papillomas (IDPs) diagnosed on core needle biopsy (CNB) remains controversial regarding whether excision is required. We evaluated whether excision of IDPs might be overtreatment based on a consecutive patient population where all IDPs were routinely excised.

Materials and methods: We retrospectively reviewed the records of consecutive patients treated with excision of IDPs at our institution from 2009 to 2016. We evaluated the rate of upgrade of IDPs on CNB and factors predicting for malignant upgrade.

Results: Of 153 CNB specimens, 136 (88.9%) were IDPs without atypia and 14 (9.2%) showed atypia. The overall upgrade rate on final pathology was 7.3% with 1.3% for invasive cancer, 2.7% for ductal carcinoma *in situ*, and 3.3% for atypical ductal hyperplasia. Of the 14 patients with atypia on CNB, two of these patients (14.2%) were found to have ductal carcinoma *in situ*. In the absence of atypia on CNB, upgrade rates were 1.5% for invasive and 1.5% for *in situ* carcinoma. Personal history of breast cancer and magnetic resonance imaging–guided biopsy predicted for malignant upgrade.

Conclusions: IDPs on CNB have a low chance of harboring an occult malignancy. Given the low probability of upgrade to invasive breast cancer, it is reasonable to consider watchful surveillance in the absence of a prior personal history of breast cancer or atypia on CNB.

Introduction

Intraductal papillomas (IDPs) are tumors that form in the lactiferous ducts and are characterized as proliferative lesions of epithelium covering a fibrovascular core.[1] Depending on the location where tumors arise, IDPs may be solitary and centrally located or multifocal and peripherally located in the mammary ductal systems.[1] Multiple lesions occurring in the periphery of the breast are referred to as papillomatosis and are associated with a higher incidence of carcinoma.[1] Previous studies have shown that image-guided core needle biopsy (CNB) can correctly diagnose the majority of papillary lesions.[2]

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Although malignant papillary tumors are uncommon, some IDPs are susceptible to malignant change. Furthermore, there have been studies that classify papillomas with features more worrisome for malignant upgrade.[3,4] According to their pathologic features, papillomas can be potentially classified as benign or can be upgraded to atypical ductal hyperplasia, ductal carcinoma *in situ*, or invasive carcinoma.[4] CNBs yield small specimens that may not correctly characterize the entire lesion. Therefore, it is suggested to surgically excise the papilloma given a wide range of reported upgrade rates ranging from 2.3% to 39%.[5-10] Certain features such as atypical pathology on CNB, large size, palpability of the lesion, and symptomatic nature of IDPs are reasons to excise due to an increased risk of malignancy. However, Jaffer *et al.*[6] reported that incidental papillomas of a size less than 2 mm do not require excision. It has also been observed that benign IDPs without atypia may not require excision in the absence of a palpable mass or radiology/pathology discordance.[7]

Given that the patient population for this study was the Los Angeles County (LAC) + University of Southern California (USC) Medical Center, an urban safety-net institution, the routine management for IDPs was to excise all papillomas because of concerns regarding whether patients will have access to medical follow-up. The aim of our study was to evaluate whether excision of all IDPs might be overtreatment based on quantifying the rates of upgrade in a population where all IDPs diagnosed on CNB were consecutively excised. We sought to evaluate if routine excision of all IDPs is warranted based on the rate of upgrade to malignancy and to determine factors predicting for higher risk of malignant upgrade of IDPs.

Materials and methods

Medical records of patients treated for IDP at LAC + USC Medical Center from 2009 to 2016 were retrospectively reviewed. A total of 153 patients who had CNB proven IDPs and underwent surgical excision were included in this study. The patients' records were reviewed for demographic information, clinical presentation, radiographic features, type of biopsy performed, CNB histology, and final excisional pathology. Mammography and ultrasound were performed as routine imaging studies, and magnetic resonance imaging (MRI) was used for lesions with indeterminate radiologic findings or lesions that could not be seen on routine imaging. Palpability of the lesion was determined by the treating breast surgeons and documented in the medical record. The size of the tumor was determined by the single largest dimension given in the radiology report. The location of the lesion on ultrasound was defined as central if the lesion is located within 2 cm from the nipple and peripheral if it located at a distance greater than 2 cm from the nipple. The CNB procedures were performed in the Radiology Department of LAC + USC using a 14-gauge Tru-Cut automated core biopsy needle (Baxter Healthcare, Valencia, CA) or a spring-loaded biopsy gun (Magnum; Bard, Covington, GA) with a 14-gauge biopsy needle. MRI-guided core biopsies were performed using a 9-gauge vacuum-assisted device (Hologic, Marlborough, MA). Ethics approval for the study was obtained from the Health Sciences Institutional Review Board (IRB) at USC. The IRB granted a waiver of informed consent.

Statistical analyses were carried out using SPSS software, version 19.0, (SPSS, Inc. Chicago, IL, USA). We performed univariate analysis to evaluate the association between variables and IDPs without atypia versus IDPs with atypia or malignant upgrade. The association between variables was analyzed using the Chi-square test or the Fisher's exact test for categorical data and the Student's *t*-test for continuous data. Variables found to be significant on univariate analysis (P value < 0.05) were used for multivariate analysis. Unconditional logistic regression was used to assess odds ratios (ORs) and 95% confidence intervals (CIs). All tests were two-sided, and a P value < 0.05 was considered to indicate a statistically significant difference.

Results

Patient characteristics are presented in Table 1. The mean age of the patients was 54.8 ± 11.6 y. All patients in this study underwent mammography and ultrasound. Eight patients required MRI for diagnosis, and four out of eight required MRI-guided biopsy to confirm the diagnosis of papilloma. Among the four patients who underwent MRI-guided biopsy, two patients had bloody nipple discharge without abnormal findings on other diagnostic imaging. The other two patients had no clinical symptoms but were found to have architectural distortion on mammography. Common abnormal mammographic findings were mass, architectural distortion, and calcification (80.9%, 10.5%, and 8.6%, respectively). Among all 153 patients, 127 patients (83%) had their IDPs detected by mammographic imaging. We defined symptomatic patients as those with palpable lesions, nipple discharge, or both and therefore received diagnostic mammograms. Seventy-one patients were asymptomatic and identified by screening mammography. Fifty-four patients (35.3%) presented with a palpable mass. Thirty-seven patients (24.3%) presented with symptoms of nipple discharge. Of these, 16 patients (10.5%) presented with the "classic" bloody nipple discharge and 21 patients (13.8%) presented with clear nipple discharge (Table 1). One hundred thirty-eight lesions (93.9%) were centrally located in the breast. The remaining 15 peripherally located lesions were not associated with malignancy.

Of all 153 lesions, 136 (88.9%) had no atypia and 14 (9.2%) showed atypia on CNB pathology. On final pathology of all surgically excised specimens, 14 (9.2%) showed atypia, four (2.6%) showed ductal carcinoma *in situ* (DCIS), and two (1.3%) showed invasive carcinoma. Of the 14 patients (9.2%) found to have atypia on CNB, two of these patients (14.2%) were found to have DCIS, and six patients (42.9%) were found to have atypical ductal hyperplasia (ADH) on final excisional pathology. The overall upgrade rate on final pathology was 7.3% with 1.3% for invasive cancer, 2.7% for DCIS, and 3.3% for ADH. In patients with IDPs without atypia on CNB, only nine patients (6.7%) were upgraded to malignancy or atypia on final excisional pathology. In these patients, the upgrade rate to malignancy was 2.9% with 1.5% (2 patients) for invasive cancer and 1.5% (2 patients) for DCIS.

On univariate analysis, the patients with personal history of breast cancer, aged over 55 y, and MRI-guided biopsy were associated with overall upgrade of IDPs to either atypia or malignancy ($P = 0.005$, $P = 0.044$, and $P = 0.028$, respectively)