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Should we excise? Are there any clinical or histologic features that predict upgrade in papillomas, incidental or non-incidental?☆

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ABSTRACT

The clinical decision to excise intraductal papilloma (IDP) without atypia diagnosed on biopsy remains controversial. We sought to establish clinical and histologic predictors (if any) which may predict upgrade in IDP. 296 biopsies (in 278 women) with histologic diagnosis of IDP without atypia were retrospectively identified and placed into Incidental (no corresponding imaging correlate), or Non-incidental (positive imaging correlate) groups. 253/296 (85.5%) cases were non-incidental, and 43/296 (14.5%) were incidental. 73.1% (185/253) non-incidental and 48.8% (21/43) incidental cases underwent excision. 12.4% (23/185) non-incidental cases underwent an upgrade to cancer or high-risk lesion; namely 8-Ductal carcinoma in situ (DCIS), 8-atypical ductal hyperplasia (ADH), 6-lobular neoplasia, and 1-flat epithelial atypia. There was no histopathologic feature on the biopsy in the non-incidental group which predicted upgrade; however a past history of atypia was significantly associated with upgrade. 2 of the 21 incidental cases upgraded (1 to ADH and 1 to lobular neoplasia); the former had a past history of ADH. Both incidental upgrades were > 1 mm in size, and were not completely excised on the biopsy. None of the incidental cases which appeared completely excised on biopsy upgraded, irrespective of the size on biopsy. These findings suggest that all non-incidental IDPs should be considered candidates for surgical excision, given the 12.4% upgrade rate and no definitive histologic predictors of upgrade. Patients with incidental IDPs (if < 1 mm, completely excised on biopsy and with no history of high risk breast lesion) can be spared excision.

1. Introduction

The standard of care for the management of intraductal papillomas (IDPs) with atypia on biopsy is surgical excision, given the significant upgrade rate to carcinoma [1-5]. However, disagreement over the management of IDPs without atypia diagnosed on a breast biopsy persist [1,3,6,7]. On one hand, there is a body of literature that supports subsequent surgical excision in all IDPs (including IDP without atypia) because histopathology of the surgical excision may yield a more advanced lesion such as atypical ductal hyperplasia (ADH), carcinoma in situ, or invasive carcinoma [3,6-12]. In addition, this literature points to the unreliability of imaging features for accurately predicting upgrade [3,13]. On the other hand, there exists literature that supports observation alone for IDPs without atypia, provided that there is appropriate attention to radiologic-pathologic concordance and a close follow-up [2,3,5,14-17]. The upgrade rates for IDP without atypia in the literature are variable, from as low as 2.3% to as high as 35% [3,8-10,14,18].

The clinical decision to avoid or pursue a surgical excision is important because performing an unwarranted excision adds potential morbidity and increases healthcare costs. Proponents of surgical excision point to the risk of missing a more advanced lesion, including high risk lesions that may alter medical management. Therefore, in this study we sought to assess clinical and histologic predictors (if any) that could predict upgrade in IDP without atypia in an attempt to delineate a subset of patients with biopsy proven IDP without atypia who may be

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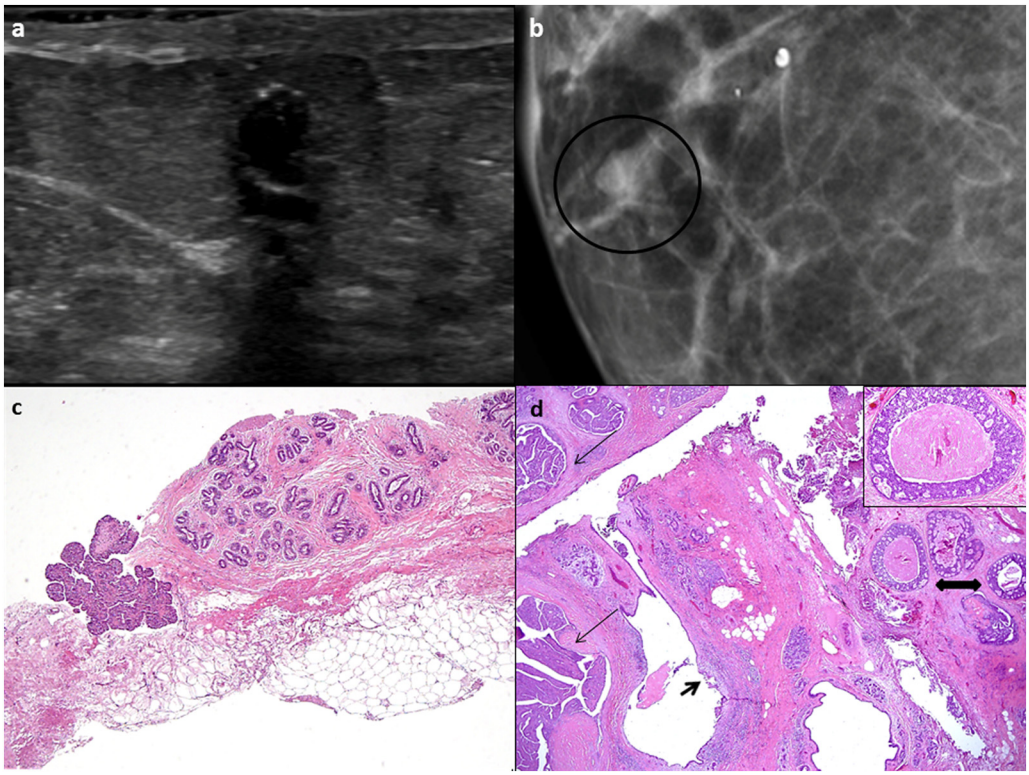

Fig. 1. Patient 170, non-incidental mass, right breast (a, b): Diagnostic ultrasound image and right cranio-caudal view screening mammography shows a suspicious mass, respectively; (c) Low power photomicrograph of biopsy shows an intraductal papilloma (IDP) without atypia (H&E ×40); (d) Excision (H&E ×20) illustrates the previous biopsy site changes (short arrow), residual IDP (thin arrow), and Ductal carcinoma in situ (DCIS) (double arrow). Inset shows DCIS (H&E ×100).

spared subsequent surgical excision.

2. Materials and methods

2.1. Case selection

The institutional review board approved this HIPAA compliant study (STUDY00006698). A retrospective search of our institution's pathology data base (Copath) was performed to identify 278 patients who underwent a breast biopsy (core or mammotome) at our institution performed from 01/01/2007 to 12/31/2016 with a histopathologic diagnosis of IDP without atypia. We excluded all biopsies where the IDP was associated with atypia, or carcinoma on core needle sampling. A careful review for radiologic-pathologic concordance was performed in all cases.

2.2. Clinical history

Clinical information, including age at diagnosis of the IDP, sex, and personal history of breast cancer were retrieved from the electronic medical record.

2.3. Radiologic examination

Two academic breast radiologists (AC and JM) reviewed all the imaging data. They divided the cases of biopsy proven IDP into two categories:

1. Incidental IDPs: defined as cases with no corresponding imaging correlate. A breast biopsy was performed for a suspicious imaging finding which had a concordant histologic result; the papilloma was considered a bystander, present histologically but without radiographic correlate.
2. Non-incidental IDPs: defined as cases with positive radiographic correlate. Positive radiographic correlate was defined as a papilloma described histologically which was considered consistent with the initial suspicious imaging finding and without any additional histologic findings that would explain the imaging abnormality.

We investigated the initial BI-RADS® Category 0 imaging exam and all subsequent breast imaging exams (including biopsy and post-biopsy imaging) when stratifying the IDPs into the two categories.

2.4. Histopathologic examination

2.4.1. Review of core needle and/or mammotome biopsies

One breast pathologist (DMK) and one pathology resident (MZ), blinded to the subsequent excision diagnosis reviewed the hematoxylin and eosin (H&E) slides (along with immunohistochemical stains if previously performed and available) of all biopsy cases included in this study. All slides were reviewed to confirm the diagnosis of IDP without atypia. An IDP on biopsy was defined as a papillary lesion composed of arborizing fibrovascular cores lined by epithelium and myoepithelium at the periphery of the lesion (if visualized) as well as around the fibrovascular cores. Cases of IDP showing usual ductal hyperplasia and apocrine metaplasia were included in the study. However, any cases showing any atypia and/or carcinoma associated with the papillary lesion were excluded.

Additionally, all the included biopsies were assessed for the following features:

1. Size of IDP: maximum cross sectional dimension of the IDP in a single core was measured and categorized into 1 of 3 groups: < 1 mm, 1–2 mm, and > 2 mm.
2. Assessment of fragmentation: whether the IDP was present as a single piece or was fragmented and present in multiple pieces.
3. Multiplicity: whether the IDP is present in a single intact core or in multiple biopsy cores
4. Likelihood of complete excision during biopsy: the IDP on core biopsy was considered to be completely excised when the entire IDP, including the periphery could be visualized circumferentially, and was surrounded by unremarkable breast parenchyma on all the