Egyptian Journal of Radiology and Nuclear Medicine

CASE REPORT Open Access

Radiographic–histopathologic correlation case report of a benign intraductal papilloma upstaged to invasive lobular carcinoma

Mariam Hanna[1,5*], Peter Vonu[2], Ruth Asirvatham[3], Lisa Spiguel[4] and Irina Gruzinova[1]

Abstract

Background: Intraductal papilloma is a common breast lesion that may be associated with malignancy. While there is general agreement regarding surgical excision of intraductal papilloma with atypia, the management of benign intraductal papilloma is variable, involving either excision or observation. Of the small number of benign intraductal papillomas that upstage to malignancy on subsequent surgical excision, a significant number of these demonstrate malignancy in peripheral tissues adjacent to the biopsy site.

Case presentation: This report serves to illustrate two cases of benign intraductal papilloma upstaging to invasive lobular carcinoma and ductal carcinoma in situ.

Conclusion: Given the low rate of malignancy in benign intraductal papillomas, close surveillance may be recommended over surgical excision, however, generous sampling of the adjacent tissue about the target lesion should be considered.

Keywords: Intraductal papilloma, High risk breast lesion, Malignancy, Pathologic upstaging, Excision, Management

Introduction and background

Benign breast disease includes a diverse spectrum of proliferative and non-proliferative pathologies, which correspond to different risks for manifestation of clinical breast cancer [1]. One example is the intraductal papilloma (IDP), a benign intraductal proliferation characterized by a fibrovascular core lined by luminal epithelial cells with intervening myoepithelium [2]. Papillomas can be classified into solitary or multiple papillomas [3]. They are subdivided into central papillomas, mostly found in the subareolar region, and peripheral papillomas arising in the terminal duct lobular unit [3]. Previous reports have suggested that the peripheral location is associated with the presence of multiple papillomas, atypia and an increased risk of malignant potential [3, 4]. It is generally recommended that papillary lesions with atypia or malignancy diagnosed on core needle biopsy (CNB) should undergo surgical excision [2, 5–7]. Other published data have suggested that surgical excision is also warranted when a benign papillary lesion is diagnosed by CNB [8, 9] as a small but significant percentage ranging from 1 to 4% of benign IDPs upstage to malignancy [2, 5, 10]. Roughly half of these initially benign IDPs have been shown to upstage to malignancy in the tissues adjacent to the previous biopsy site [10]. This presentation serves to describe 2 examples of IDPs which were upstaged to malignancy in peripheral tissues with concordance upon re-review by a radiologist and a pathologist.

Case presentation: imaging/pathologic findings

A 72-year-old woman was found to have suspicious microcalcifications on bilateral screening mammogram (Fig. 1A). Diagnostic mammogram with CC magnification/spot compression was performed (Fig. 1B)

*Correspondence: hannmw@radiology.ufl.edu
[5] Program Director of Medical Student Education, Division Chief Breast Imaging, Department of Radiology, University of Florida College of Medicine, 1600 SW Archer Rd, Gainesville, FL 32610, USA
Full list of author information is available at the end of the article

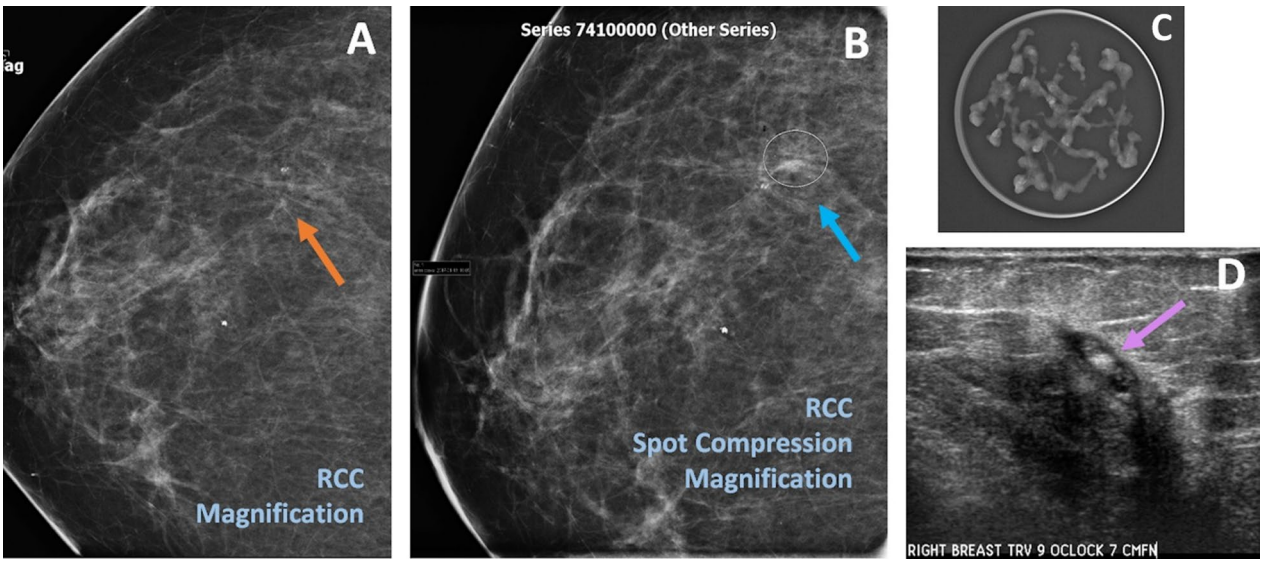

Fig. 1 A 72-year-old woman was found to have suspicious microcalcifications on bilateral screening mammogram (**A**). Diagnostic mammogram with CC magnification/spot compression at image **B** demonstrates grouped amorphous calcifications in the posterior right breast at the 7:00 position, 9 cm from the nipple (blue circle). The number of calcifications in this group has increased compared to the prior mammogram at image **A** (orange circle). BIRADS category of 4 was assigned. Stereotactic core needle biopsy was performed (radiographic imaging of biopsied tissue on image **D**) with pathology showing IDP with benign features. Sonographic evaluation demonstrated appropriate location of the biopsy clip in the biopsy site (purple arrow, **C**)

demonstrating grouped amorphous calcifications in the posterior right breast at the 7:00 position, 9 cm from the nipple (circled). The number of calcifications in this group had increased compared to the prior mammogram at image A. BIRADS category of 4 was assigned. The patient's only significant past medical history was hormone replacement therapy since her hysterectomy in the 1980's until 2 years prior to presentation. She was asymptomatic with no palpable lesions. Stereotactic CNB was performed with pathology that showing fibroadenoma/fibroadenomatoid change with associated microcalcifications adjacent to a small, 1-mm-IDP (Fig. 2). Sonographic evaluation demonstrated appropriate location of the biopsy clip in the biopsy site (Fig. 1D). Ultrasound guidance was utilized for surgical excision with subsequent histologic evaluation positive for cytokeratin AE1/AE3 that demonstrating attenuated staining with e-cadherin consistent with invasive lobular carcinoma (ILC)

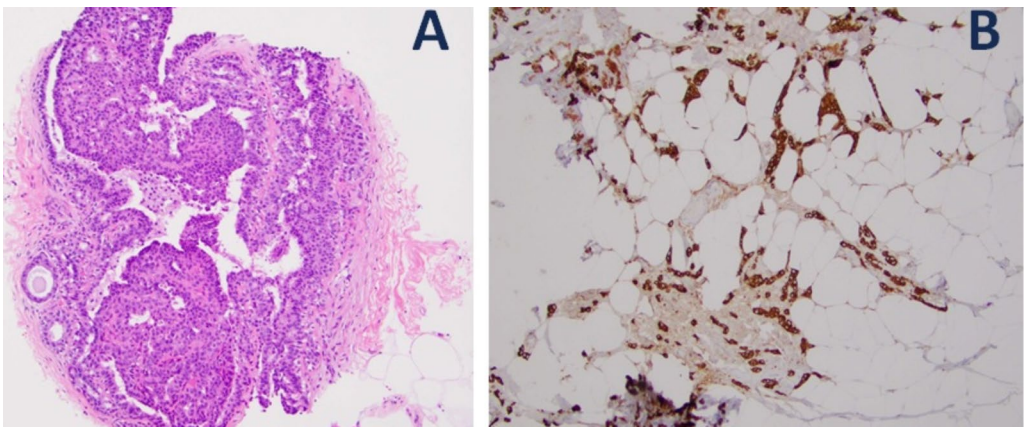

Fig. 2 Core biopsy with a small intraductal papilloma, H&E stain, 100× magnification (**A**). Cytokeratin AE1/AE3 Immunostain highlights invasive lobular carcinoma infiltrating adipose tissue, 100× magnification (**B**)

infiltrating adipose tissue (B). This tissue was distant from the biopsy site and not involving the papilloma. Following re-review by a radiologist and a pathologist, the BIRADS and pathologic-radiology correlation of the significantly upstaged case described above demonstrated concordance.

A 65-year-old female presented with clear nipple discharge from a single duct in the left breast. Sonographic evaluation demonstrated debris within one of these ducts at the 6:00 position of the retroareolar left breast. Subsequent biopsy was scheduled but no intraductal mass was identified via ultrasound at that time. On a 3-month follow-up, a hypoechoic lesion in the left retroareolar region at the 5:00 to 6:00 position was identified (Fig. 3A, blue arrow), and BIRADS 4 was assigned. Ultrasound-guided automated tissue excision and collection (ATEC) vacuum assisted core biopsy yielded IDP with benign features. Image B shows radiograph of the excised specimen.

Figure 4 demonstrates photomicrograph fragments of a sclerosing intraductal papilloma with no overt atypical features (A). Excisional biopsy demonstrated residual intraductal papilloma (B). Cribriform ductal carcinoma in situ (DCIS), low nuclear grade was identified in the breast tissue adjacent to, but not involving the papilloma, spanning 10 mm in longest dimension (C).

Conclusion

Given the low upstaging rate of IDP lesions identified as benign on CNB to excisable malignant lesions such as DCIS and ILC, close surveillance rather than surgical excision of IDPs without atypical features on CNB may be considered. This management strategy would spare patients the emotional and painful toll of potentially unnecessary procedures. However, it is notable that perhaps as many as half of malignant upgrades occur in the tissues adjacent to the intraductal papilloma, as occurred

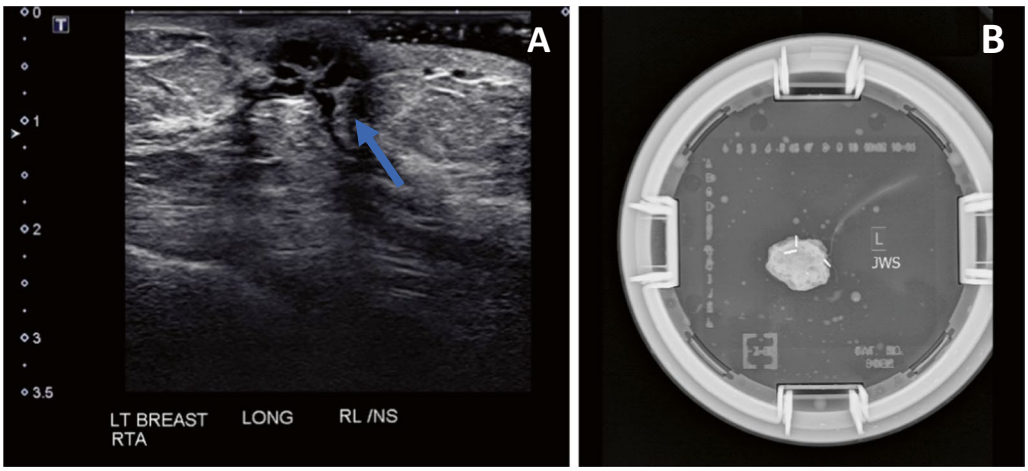

Fig. 3 65-year-old female with clear nipple discharge, sonographic evaluation showing hypoechoic lesion in the left retroareolar region at the 5:00 to 6:00 (**A**, blue arrow), BIRADS 4 was assigned. Ultrasound-guided ATEC vacuum assisted core biopsy yielded IDP with benign features. Image **B** shows radiograph of the excised specimen

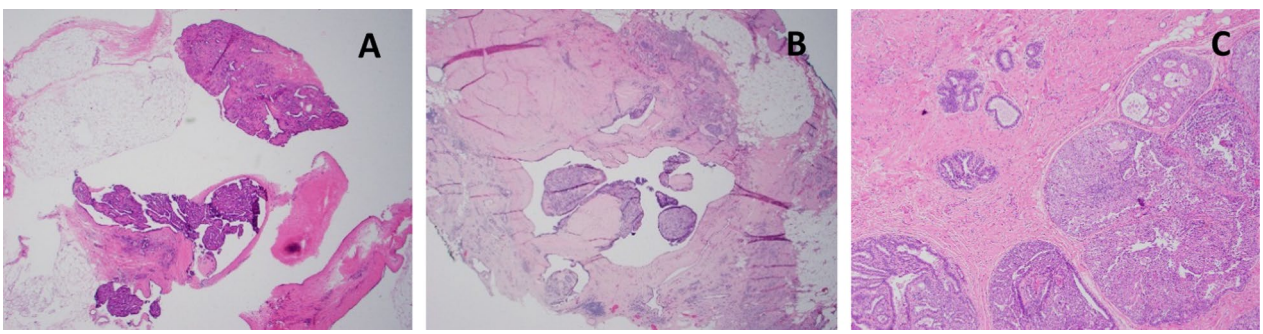

Fig. 4 Photomicrograph shows fragments of a sclerosing intraductal papilloma, hematoxylin and eosin, total magnification 20× (**A**). Excisional biopsy demonstrated residual intraductal papilloma, total magnification 20× (**B**). Cribriform ductal carcinoma in situ, low nuclear grade was identified in the breast tissue adjacent to, but not involving the papilloma, spanning 10 mm (**C**)

in the patients described above. This trend underscores the risk of under-sampling and how perhaps more generous sampling of the adjacent tissue about the target lesion should be considered. Among the explored clinical, radiologic and pathologic features of IDPs at our institution, multiplicity was the only factor that significantly correlated with pathologic upstaging within the benign core biopsy group.

Abbreviations
IDP: Intraductal papilloma; CNB: Core needle biopsy; DCIS: Cribriform ductal carcinoma in situ; ILC: Invasive lobular carcinoma; ATEC: Automated tissue excision and collection.

Acknowledgements
Not applicable.

Authors' contributions
PV analyzed and interpreted the data and was a major contributor in writing the manuscript. MH analyzed and interpreted the data and was a major contributor in writing the manuscript. IG analyzed and interpreted the data and was a contributor in writing the manuscript.All authors PV, MH, IG, RA, LS read and approved the final manuscript.All authors read and approved the final manuscript.

Funding
Not applicable.

Availability of data and materials
The datasets used and/or analyzed data during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study is IRB approved by the University of Florida Institutional Review Boards (IRBs) study # 201702101.

Consent for publication
No identifiable information is used in the study, and study is IRB approved. Not applicable under the University of Florida IRB approval.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of Radiology, University of Florida Health, Gainesville, FL, USA. [2]University of Florida College of Medicine, Gainesville, USA. [3]Department of Anatomic Pathology, University of Florida Health, Gainesville, FL, USA. [4]Department of Surgical Oncology, University of Florida Health, Gainesville, FL, USA. [5]Program Director of Medical Student Education, Division Chief Breast Imaging, Department of Radiology, University of Florida College of Medicine, 1600 SW Archer Rd, Gainesville, FL 32610, USA.

Received: 20 October 2021 Accepted: 30 December 2021
Published online: 19 January 2022

References
1. Hartmann LC, Sellers TA, Frost MH et al (2005) Benign breast disease and the risk of breast cancer. N Engl J Med 353:229–237
2. Han SH, Kim M, Chung YR et al (2018) Benign intraductal papilloma without atypia on core needle biopsy has a low rate of upgrading to malignancy after excision. J Breast Cancer 21:80–86
3. Ohuchi N, Abe R, Kasai M (1984) Possible cancerous change of intraductal papillomas of the breast. A 3-D reconstruction study of 25 cases. Cancer 54:605–611
4. Boufelli G, Giannotti MA, Ruiz CA et al (2018) Papillomas of the breast: factors associated with underestimation. Eur J Cancer Prev 27:310–314
5. Khan S, Diaz A, Archer KJ et al (2018) Papillary lesions of the breast: to excise or observe? Breast J 24:350–355
6. McGhan LJ, Pockaj BA, Wasif N, Giurescu ME, McCullough AE, Gray RJ (2012) Atypical ductal hyperplasia on core biopsy: an automatic trigger for excisional biopsy? Ann Surg Oncol 19:3264–3269
7. Rizzo M, Lund MJ, Oprea G, Schniederjan M, Wood WC, Mosunjac M (2008) Surgical follow-up and clinical presentation of 142 breast papillary lesions diagnosed by ultrasound-guided core-needle biopsy. Ann Surg Oncol 15:1040–1047
8. Shiino S, Tsuda H, Yoshida M et al (2015) Intraductal papillomas on core biopsy can be upgraded to malignancy on subsequent excisional biopsy regardless of the presence of atypical features. Pathol Int 65:293–300
9. Holley SO, Appleton CM, Farria DM et al (2012) Pathologic outcomes of nonmalignant papillary breast lesions diagnosed at imaging-guided core needle biopsy. Radiology 265:379–384
10. Tartarian T, Sokas C, Rufail M et al (2016) Intradu ctal papilloma with benign pathology on breast core biopsy: to excise or not? Ann Surg Oncol 23(8):2501–2507

Publisher's Note