Benign Papillary Lesions of the Breast: Multimodality assessment with histological correlation

Poster No.: C-2000
Congress: ECR 2014
Type: Educational Exhibit
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Keywords: Breast, Oncology, Mammography, MR, Ultrasound, Education, Galactography, Education and training
DOI: 10.1594/ecr2014/C-2000

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Learning objectives

• To characterize and illustrate the clinical and imaging features of benign papillary lesions (BPL)
• To identify the utility and benefit of each modality in the diagnosis of BPL
• To correlate the imaging findings with histopathologic features.
Background

Benign Papillary Lesions of the breast are common lesions with varied morphologic features found mainly in middle-aged women that are challenging to diagnose as benign or malignant.

Not only from an imaging perspective where there is an overlap in the characteristics of benign and malignant papillary lesions that contributes to this challenge but also from a histological view where the need to examine the entire lesion for accurate grading is necessary due to the fact that small foci of carcinoma in situ or an area of abruption of the myoepithelial layer might not be targeted in fine needle aspiration or even core biopsy.¹

The differentiation in benign or malignant papillary lesions poses a problem for even the most experienced pathologists thus leading to a continuous topic of debate that is the correct management of patients with benign papillary lesions diagnosed on needle biopsy or stereotactic directional vacuum-assisted biopsy.

In this group are included solitary intraductal papillomas, multiple papillomas and juvenile papillomatosis(JP).²

Solitary Intraductal Papillomas

- Solitary Intraductal Papillomas usually arise from the large subareolar ducts and are generally grossly apparent, solitary, and centrally located in the breast, thus justifying being also called "Central Papilloma".

- Clinically these lesions usually present themselves as a nipple discharge that can be bloody, serous or clear, or they can appear as a palpable retroareolar mass. They were more associated with perimenopausal women but with the advent of ultrasonography and the greater availability of these exams, benign papillary lesions are being found more and more commonly in younger patients without symptoms.

Multiple Intraductal Papillomas

- Multiple Intraductal Papillomas or Peripheral Papillomas are mostly found, as the name implies, in the terminal ductal lobular units thus justifying their peripheral location in the breast.

- Usually their clinical appearances are as palpable masses in the outer areas of the breasts without nipple discharge associated.
In comparison with solitary intraductal papillomas, multiple intraductal papillomas are less common and are more associated with atypia, ductal carcinoma in situ or malignancy. It is believed that their increased risk of carcinoma is connected to the presence of proliferative epithelial change.

**Juvenile Papillomatosis**

- **Juvenile Papillomatosis is a localized proliferative condition** encountered mainly in young women between the ages of 12 and 48.\(^3\) Clinically patients usually present with a painless mass that, on physical examination, is circumscribed, easily mobile and most often thought to be a fibroadenoma.

- Although being a benign lesion, follow up studies have suggested that about 10% of the patients with juvenile papillomatosis are thought to develop breast cancer later in life, especially if the lesion is bilateral and the patient has a family history of breast cancer. It is also believed that these patient’s female relatives have an increased risk of breast cancer.

**Histopathology**

Intraductal papillomas are characterized by papillary fronds attached to the inner mammary duct wall by a fibrovascular core that is covered with ductal epithelial and myoepithelial cells.\(^4\) (Fig. 1) They are divided into central or peripheral types being the central ones usually solitary and the peripheral are often multiple.

The absence of a myoepithelial cell layer in the fibrovascular fronds of a papillary lesion indicates a carcinoma, however, the presence of myoepithelial cells does not invariably exclude the diagnosis of intraductal papillary carcinoma.

Despite being histologically similar to papillomas, juvenile papillomatosis has to be histologically differentiated from them since the main characteristics of JP consist of papillomatosis and extensive cyst formation (Fig.2)

**Differential diagnosis**

- Ductal carcinoma in situ
- Invasive ductal carcinoma with an in situ component.
- Papillary carcinoma of the breast
Treatment of Benign Papillary Lesions of the Breast.

The correct strategy for benign papillary lesions of the breast continues to be a controversial subject.

Analyzing the earlier studies on the subject we find some authors arguing that, when the histological results of a core biopsy or stereotactic directional vacuum-assisted biopsy are overlapping with imaging findings, excision can be dismissed as these techniques may be enough to distinguish malignant from benign papillary lesions.

However, in more recent studies, the authors defend that due to sampling error, to the scarce material obtained at core biopsy and to the inherent heterogeneity of papillomas, areas of atypia or carcinoma can be missed if excision is not executed. In their study, Chang J. et al., presented that 3.1% of the papillomas detected in ultrasound-guided 14-gauge core needle biopsy had associated ductal carcinoma in situ (DCIS) at surgical excision, representing a higher rate than the accepted probability of malignancy for BI-RADS category 3 lesions (i.e., probably benign) of 2% or lower for which conservative management is recommended. Due to these results they recommend surgical excision for the accurate diagnosis of ultrasound-detected benign papillomas.

Recently, Brennan S. et al. also presented a 6% rate of papillomas with DCIS associated at surgical excision in patients that underwent MRI-guided 9-gauge vacuum assisted biopsy (VAB). Meaning that even for lesions yielding a benign concordant diagnosis of papilloma at MRI-guided VAB, surgical excision may be warranted.

Given these results we must remember that the rates, although significant, are not very high and whether surgical excision is needed for a benign papilloma found on core biopsy or VAB, remains controversial.
Fig. 1: A and B) Photomicrograph of excised specimen shows a lesion with papillary structure that is covered with ductal epithelial and myoepithelial cells, compatible with benign intraductal papilloma.

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Fig. 2: A and B) Photomicrograph of excised specimen shows a benign lesion with multiple cystic and hyperplasia areas, compatible with juvenile papillomatosis.

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Findings and procedure details

Solitary Intraductal Papillomas

Mammography:
- Round to oval-shaped mass with well-circumscribed margins in larger lesions and ductal ectasia in some cases. (Fig.3) Smaller papillomas can be occult on mammography if they have a retroareolar location because of the higher breast density in this area. In about 25% of the cases, benign appearing calcifications can be associated. (Fig.4)

Galactography:
- Sharply-defined mural-based filling defects with smooth or lobulated contours (Fig.5). In some cases ductal dilatation is the only finding usually due to partial or complete ductal obstruction.
- Be aware of potential pitfalls produce by inadvertently injected bubbles of air into the ductal system during galactography.

Ultrasonography:
- Well-defined intraductal mass in a dilated duct or as solid nodules with precise borders (Fig.6). The presence of fluid-filled dilated ducts without an intraductal mass can also be found. On color Doppler imaging, flow may be detected within the papilloma arising from a vascular feeding pedicle. (Fig.7)

Magnetic resonance imaging:
- This imaging modality has a limited role in the evaluation of these lesions because they can present a kinetic curve indistinguishable from invasive cancer.
- Intraductal papillomas can show three types of patterns, one is a small well-defined mass at the end of a dilated duct, corresponding to the filling defect found on the galactography. On a second pattern, the MRI can be negative, despite the confirmed presence of a papilloma, thus not being detected on both contrast-enhanced and fat-suppressed T1-weighted images. Finally, the most difficult pattern to analyze in which the papilloma appears as a round enhancing mass with rapid initial early enhancement and a late plateau or washout on kinetic curves, mimicking an invasive cancer. (Fig.8)

Multiple Intraductal Papillomas
Mammography:

- They can have diverse appearances that include:
  - Round, oval or lobulated well-defined or spiculated masses with or without calcifications,
  - Group of microcalcifications,
  - Asymmetric densities.

Ultrasonography:

- Multiple intraductal papillomas are usually described as round, oval or microlobulated hypoechoic solid masses with well-circumscribed walls. In more unusual cases multiple papillomas can appear as complex masses.

Magnetic resonance imaging:

- This exam poses the same inconvenience as in the solitary intraductal papillomas because multiple intraductal papillomas can appear as enhancing nodules with either washout or plateau kinetics, making differentiation from invasive malignancies a difficult task.

**Juvenile Papillomatosis**

Mammography:

- These lesions usually appear as an asymmetric dense breast tissue with no detectable lesion. Occasionally mammograms may show microcalcifications or a prominent intraductal pattern.

Ultrasonography:

- These lesions usually appear as ill-defined heterogeneous mass with multiple peripheral small cystic (up to 4mm) \(^{11}\) (Fig.9). Occasionally microcalcifications can be seen.

Magnetic resonance imaging:

- One of the most specific feature is the presence of multiple small internal cysts, best shown on the T2 weighted images.

- On T1 they usually appear as hypointense lobulated masses which enhance markedly in the post-contrast images. In the dynamic sequence the lesion showed a benign enhancement profile.\(^ {12}\)
Fig. 3: A and B) Craniocaudal and mediolateral views from a mammography that show a oval well-defined retroareolar mass that after excision histology showed a intraductal papilloma.

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**Fig. 4:** Solitary intraductal papilloma - Right craniocaudal breast tomosynthesis showing a retroareolar round-shaped mass with well-circumscribed margins and a microcalcification inside.

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Fig. 5: A and B) Left breast galactography that shows mildly dilated ducts with a small filling defect on the first branches proximal to the nipple area.

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Fig. 6: A) Images from US that show a quistic lesion with solid component protruding from one of the walls; B) A fine needle core-biopsy was preformed and showed: "Breast tissue fragment on which a papillary frond was identified showing benign characteristics on that fragment". The patient underwent surgery to remove the lesion.

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Fig. 7: Doppler Ultrasound showing flow within the papilloma possibly arising from a vascular feeding pedicle.

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Fig. 8: A) Axial T1 gadolinium-enhanced MR image that shows heterogeneous enhancement of a nodule with well-circumscribed margins. B) On axial T2 MR image the lesion appears heterogeneously hipointense. The histological result was intraductal papilloma.

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**Fig. 9:** A and B) Ultrasonograms of left breast showing an oval and circumscribed isoechoic mass measuring 11x6mm with some quistic areas inside (B). The patient underwent US-guided VAB that removed almost completely the lesion and the histological result showed Juvenile Papillomatosis

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Conclusion

Papillary lesions consist of an heterogeneous group that pose a trouble when it comes to its classification in benign or malignant and while further study is still needed, becoming familiarized with their imaging features can be helpful in achieving diagnosis and proper management.
References