### Papillary lesions of the breast - Imaging findings and diagnostic challenges

<table>
<thead>
<tr>
<th>Poster No.:</th>
<th>R-0146</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congress:</td>
<td>RANZCR-AOCR 2012</td>
</tr>
<tr>
<td>Type:</td>
<td>Educational Exhibit</td>
</tr>
<tr>
<td>Authors:</td>
<td>P. Jagmohan, F. J. Pool</td>
</tr>
<tr>
<td>Keywords:</td>
<td>Breast, Mammography, Ultrasound, MR, Biopsy, Pathology, Cancer, Neoplasia</td>
</tr>
<tr>
<td>DOI:</td>
<td>10.1594/ranzcraocr2012/R-0146</td>
</tr>
</tbody>
</table>

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply RANZCR's endorsement, sponsorship or recommendation of the third party, information, product or service. RANZCR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold RANZCR harmless from and against any and all claims, damages, costs, and expenses, including attorneys’ fees, arising from or related to your use of these pages.

Please note: Links to movies, .ppt slideshows, .doc documents and any other multimedia files are not available in the pdf version of presentations.

www.ranzcr.edu.au
Learning Objectives

Learning objectives:

1. Describe the various benign, atypical and malignant papillary lesions of the breast
2. Recognise the spectrum of imaging findings on mammography, ultrasound and MRI
3. Discuss the radiologist's role and diagnostic challenges in evaluation of these lesions

Background

Background:

Papillary breast lesions are uncommon, accounting for less than 10% of benign breast lesions and 1-4% of breast carcinomas. They encompass a wide spectrum of pathologies ranging from benign lesions such as solitary intraductal papilloma to the rare invasive papillary carcinoma. Overlapping features make differentiation of benign and malignant papillary lesions difficult on imaging and tissue diagnosis is essential. Categorisation on histopathology however may also be a diagnostic challenge. Additionally even percutaneous biopsy benign papillomas have been associated with an increased risk of high risk lesions and neoplasia. Due to overlapping findings on imaging and histopathology and to varying malignant potential, papillary lesions constitute significant diagnostic and management challenges for the radiologist, pathologist and surgeon alike.

This exhibit looks at papillary lesions from a radiologist's standpoint. We briefly review the types of papillary lesions and discuss the multimodality imaging findings as well as the radiologist's role.

Brief overview of the types and clinical features of papillary lesions:

A key feature of a papillary lesion is a fibrovascular stromal core with a lining of epithelial and myoepithelial cells that is attached to the duct wall and projects into the lumen [6].
Papillary lesions can be broadly divided into benign and malignant [6].

Benign papillary lesions include:

1. solitary intraductal papilloma
2. multiple intraductal papillomas
3. atypical hyperplasia within a papilloma

Malignant papillary lesions include:

1. Ductal carcinoma in situ (DCIS) arising in a papilloma
2. Papillary DCIS
3. Intracystic papillary carcinoma
4. Solid papillary carcinoma
5. Invasive papillary carcinoma arising in an intracystic papillary carcinoma
6. Invasive papillary carcinoma

Intraductal papillomas (IPD):

Solitary papillomas arise from a large central duct and are more common in the perimenopausal age group. The usual presentation is bloody or clear nipple discharge. Multiple papillomas arise from the terminal duct lobular unit and are thus peripheral lesions. They are more commonly seen in a younger age group and present as a palpable mass.

Both solitary and intraductal papillomas can be associated with proliferative and high risk lesions such as radial scars and are also associated with an increased risk of cancer. This risk is more in multiple papillomas. A study by the Mayo clinic estimated that patients with a solitary papilloma without atypia have a 2 fold increase risk of cancer while those with multiple papillomas have a relative risk of 3 [6].
Atypical Ductal Hyperplasia and DCIS within an IPD :

This term describes a neoplastic population of cells within an IPD, however the atypical component is defined in a variety of ways. Some authors define atypical ductal hyperplasia (ADH) when the population of such cells is ≤ 3 mm and DCIS when it is > 3 mm, but others recommend that these lesions should be considered as in situ papillary carcinoma. The terms "atypical papilloma" and "carcinoma arising within a papilloma" have also been used by some authors when these features involve less than one third of the papilloma and between one third and 90% of the papilloma respectively.

Atypia is more common in multiple papillomas and most studies suggest that it is a generalised risk factor rather than a precursor lesion. According to the Mayo clinic series, patients with solitary and multiple papillomas with atypia have a 5 and 7 fold increase risk of cancer respectively [6].

Papillary DCIS :

A variant of DCIS, this lesion is characterised by neoplastic cells that grow around the internal lining of a duct with papillary projections. Extensive ramification within the ductal system and underestimation of the non-calcified part of the DCIS may make it difficult to obtain clear margins on excision. These lesions are also associated with a higher rate of multicentricity and micro-invasion than other DCIS variants.

Papillary carcinoma :

Papillary carcinomas are uncommon neoplasms and are seen in 1-4% of breast malignancies. They are most common in the postmenopausal age group. Common clinical presentations are a palpable central mass and nipple discharge. The absence of an intact myoepithelial cell layer within the papillae is an important feature for differentiating malignant lesions from benign papillomas.

Intracystic or encapsulated papillary carcinoma refers to the presence of papillary carcinoma within a cystically dilated duct. The tumor rarely metastasizes and prognosis is usually excellent with reported 10 year survival rates of 100%. A minority of intracystic papillary carcinomas may be associated with an invasive component and are staged according to the size of the invasive component [6].
A solid papillary carcinoma is an indolent tumor composed of circumscribed nodules of ovoid or spindle shaped epithelial cells with low nuclear grade. Axillary lymph nodal or distant metastases are rare.

Invasive papillary carcinoma is described as an infiltrating breast carcinoma exhibiting an exclusively papillary morphology. It is associated with a better prognosis compared to other forms of invasive carcinomas.

**Imaging Findings OR Procedure Details**

**Imaging findings:**

Like their pathology, the imaging features of papillary lesions are diverse.

**Papillomas:**

A solitary intraductal papilloma is usually seen on mammography as a rounded or ovoid well circumscribed retroareolar mass which may be associated with ductal dilatation. Smaller lesions may be occult on mammography. Multiple papillomas are usually seen in a peripheral location and can be bilateral. Calcifications are an uncommon feature of papillomas and include both coarse dense calcifications as well as microcalcifications. [2,3]

The characteristic US finding of a papilloma is a solid mural nodule within a dilated duct (fig 1). Other features include an intracystic mass or a well circumscribed hypoechoic solid mass [2,3]. Ductal dilatation may be the only US finding in a small papilloma. Color Doppler can depict a vascular pedicle within the mural nodule. (Fig 2,3,4,5) Ductography may show an intraluminal filling defect, ductal dilatation, ductal wall irregularity and/or distortion. Atypical papillomas may have similar imaging features to benign papillomas and the diagnosis is usually made on histopathology (fig. 6,7)

The current role of MRI for evaluation of papillomas is unclear and most papillomas are seen as incidental masses. The MRI features are similar to mammography and ultrasound; and include a round or ovoid well-circumscribed mass and ductal dilatation. Variable enhancement patterns may make differentiation from malignancies difficult [2,3]. In atypical papillomas with DCIS, MRI may have a role in evaluating the extent of DCIS.
MRI ductography using a microcoil has been also proposed as a non-invasive alternative to conventional ductography for the detection of intraductal lesions.

**Papillary DCIS:**

Papillary DCIS can be occult on mammography, US and MRI. Findings also include pleomorphic calcifications and architectural distortion on mammography; an ill defined hypoechoic mass or calcifications on US and non mass like enhancement in the involved region on MRI [3]. (Fig. 8)

**Papillary carcinomas:**

Mammography findings of papillary carcinomas include a round or oval circumscribed solitary or cluster of mass, which may be associated with microcalcifications. Spiculations are less common, probably due to the lack of fibrosis. On US, the lesion may be seen as an intraductal mass with or without ductal dilatation, a complex solid cystic mass or as a single or multiple solid nodules. These lesions are usually vascular and have a tendency to bleed spontaneously resulting in intracystic fluid-debris levels. (Fig 9,10,11,12) [2,3]

On MRI, papillary carcinomas may appear as enhancing nodular lesions or enhancing complex cysts with variable enhancement patterns. Imaging findings may be indistinguishable from papillomas and as such there is limited data about the imaging features and role of MRI for these lesions.

**Differentiating benign and malignant papillary lesions on imaging:**

Papillary carcinomas and papillomas often have overlapping imaging findings. A larger solid component and a higher frequency of intracystic haemorrhage resulting in fluid levels has been described in papillary carcinomas compared with benign papillomas. A nonparallel orientation, an echogenic halo, posterior acoustic enhancement and associated microcalcification is also more frequent in malignant lesions. However imaging findings are neither sensitive nor specific for differentiating benign and malignant lesions, necessitating tissue diagnosis [1].

**Imaging differentials of papillary lesions:**
Segmental ductal dilatation with no demonstrable ductal mass may also be seen in ductal ectasia. Intraductal contents such as blood products, inspissated secretions in ductal ectasia and neoplastic cells in DCIS can mimic a papillary lesion. Differentials for a complex cystic lesion include hematomas, abscesses and fat necrosis. A papillary lesion appearing as a well defined solid nodule may be indistinguishable from a fibroadenoma. Additionally malignant non papillary carcinomas and papillary carcinomas can have similar appearances. (fig 13)

**The radiologist's role and challenges:**

The role of imaging is crucial in:

a) lesion identification and assessing extent,

b) tissue sampling by fine needle aspiration, trucut and vacuum assisted biopsy

c) follow up

A multimodality approach is used for lesion identification with mammography and ultrasound forming the mainstay. However some lesions such as small papillomas or papillary DCIS may be occult or have equivocal findings such as non specific sectorial ductal dilatation. Ductography can help detect small papillary lesions with a possible role for MRI. Assessing the extent of the lesion is also critical especially in multiple papillomas, DCIS and carcinomas and here again MRI may have a role to play especially in cases of papillary DCIS.

Tissue sampling of papillary lesions can be done by fine needle aspiration, core biopsy and vacuum assisted biopsy. Ultrasound guided percutaneous core biopsy is used most frequently as this allows for real time visualisation which is essential for sampling the solid component of the lesion.

Providing an adequate sample for the pathologist is important. Even so, histopathological categorisation of papillary lesions on percutaneous biopsy samples may be difficult due to numerous reasons such as tissue fragmentation and undersampling. Studies have evaluated the reliability of core biopsy for evaluation of papillary lesions. While results have been variable, a number of studies indicate that there is a significant upgrade rate to atypia or malignancy for benign papillomas diagnosed on percutaneous core biopsy. This has resulted in some authors recommending a surgical excision even for imaging concordant benign papillomas. [5]
Other studies suggest observation and close follow up for benign papillary lesions without atypia diagnosed by core biopsy. They argue that the risk of malignancy is low and wider lesion sampling with increased number of cores or the use of 8 - 11 G vacuum assisted probe can obviate the need for a surgical excision for imaging concordant benign papillomas. Vacuum assistance has also been used for the removal of select papillary lesions such as small, solitary and screen detected papillomas and has the potential to reduce the number of open surgeries [4]. Here again the potential for recurrence suggests the need for a close follow up.

Images for this section:

**Fig. 1:** Benign intraductal papilloma without atypia: Mammogram and ultrasound done for a patient with bloody discharge from the left nipple. Mammogram shows a partially circumscribed partially obscured opacity in the left periareolar region. A dilated duct with an intraluminal mildly vascular hypoechoic lesion was seen in the left periareolar region on the US. 14 G core biopsy was done and confirmed a benign intraductal papilloma without atypia.
Fig. 2: A patient with a palpable left breast lump. Mammogram MLO and CC views show a well circumscribed ovoid left retroareolar opacity. US shows the palpable lesion as a well defined hypoechoic solid nodule at 10:00 next to the nipple with prominent internal vascularity. Histopathological examination (HPE) showed a benign intraductal papilloma.
Fig. 3: A patient with a palpable central right breast lump. MLO and CC views show a well circumscribed density in the right retroareolar region with few scattered coarse and punctate calcifications. On US this density corresponds to a complex cystic lesion at 06:00 in the retroareolar region with diffuse low level internal echoes. A solid component is seen along the posterior wall of this lesion which shows vascularity on the color flow images. A benign papilloma without atypia within a dilated duct was confirmed on HPE.
Fig. 4: A patient with persistent left nipple bloody discharge. Mammogram was unremarkable. US shows a dilated central duct with hypoechoic mildly vascular intraductal contents. Presence of vascularity confirms the solid nature of the lesion and differentiates it from inspissated secretions in ductal ectasia. A benign papilloma was seen on HPE.
**Fig. 5:** Multiple papillomas: A patient who had a previous excision biopsy for a left breast nodule which was lobular in situ carcinoma (LCIS) and ductal papilloma on HPE. Follow up US showed three new hypoechoic irregular nodules in both breasts (right 11:00, left 9:00 and 11:00). All three were benign papillomas on HPE. Note the peripheral location of the lesions compared to the solitary papillomas.
**Fig. 6:** Papilloma with atypia: Left bloody nipple discharge in a patient with a normal mammogram. US shows a distended duct in the left 4 o'clock position with some low level internal echoes within. At the 10 o'clock position, there is a small ovoid hypoechoic intraductal structure near the nipple. The lesions underwent excision biopsy following hook wire localisation. Both were intraductal papillomas and the 10:00 lesion showed a 1.3 mm focus of ductal carcinoma in situ.
Fig. 7: Papilloma with atypia: Patient with a palpable left breast lump. US shows an irregular hypoechoic mass at the left 1:00 position 2cm from the nipple. This was mammographically occult. Excision biopsy following hook wire localisation was done. HPE showed ductal papillomas with atypical ductal hyperplasia and atypical apocrine hyperplasia.
Fig. 8: Papillary DCIS: A patient with a large biopsy proven invasive ductal carcinoma right breast for contralateral breast imaging. Incidental pleomorphic microcalcifications seen in the left breast mammogram MLO, CC and spot magnification views at the 12:00 position. A marker was placed for an overlying mole. The ultrasound was unremarkable. Low nuclear grade papillary ductal carcinoma in situ was seen on HPE.
Fig. 9: Intracystic papillary carcinoma: A patient with a palpable left breast lump. Mammomogram shows a large well circumscribed lobulated opacity with rim calcifications in the left retroareolar region. Note the associated rim calcifications and slight retraction of the left nipple. Ultrasound shows a complex well defined cystic mass with low level internal echoes. A small solid component with prominent vascularity is seen at the anterosuperior aspect. An intracystic papillary carcinoma was confirmed on histopathology. Note the overlapping features of this lesion and the benign intraductal papilloma shown in Fig 3. Both benign and malignant papillary lesions can have similar imaging features.
**Fig. 10:** A patient with left breast pain and bloody nipple discharge. US shows a slightly tall hypoechoic mildly lobulated lesion at 6:00 position, 3cm from the nipple. On elastography, it appears solid with a distance ratio of approximately 1. HPE showed an encapsulated papillary carcinoma.

**Fig. 11:** A patient with a palpable right breast lump. Mammogram MLO and CC views show a well circumscribed lobulated opacity in the right upper central breast. US shows an irregular mass at the 12:00 position 3 cm from nipple. Right mastectomy specimen showed an encysted papillary carcinoma with 0.5 cm focus of invasive ductal carcinoma, NOS, Grade 1.
Fig. 12: A patient with a palpable right breast lump. Mammogram MLO and CC views show overlapping ovoid opacities in the right upper outer quadrant. US shows a few solid nodules, some with cystic components at the 11:00 position 3 cm from nipple. HPE of the right mastectomy specimen showed invasive ductal carcinoma, solid papillary type.

Fig. 13: Mimics of papillary lesions. (a) Complicated cyst - US shows a cystic lesion with intracystic contents, the cyst collapsed completely on FNA. Differentiating debris/clots and solid components within a cyst may be difficult and demonstration of vascularity on Doppler aids in establishing solid nature. (b) Biopsy proven fibroadenoma seen on US as a well defined ovoid hypoechoic retroareolar nodule which mimics a papillary lesion.
Conclusion

Conclusion:

Papillary lesions are an uncommon group of breast diseases which present unique diagnostic and management challenges due to a wide spectrum of imaging appearances, pathologies and malignant potential. This exhibit describes the imaging spectrum of various papillary lesions and discusses the role of imaging in their evaluation.

Acknowledgement: This review includes studies done at the National University and KK Women's and Children's Hospitals, Singapore. The authors would like to thank the Breast Imaging Unit teams for their assistance. We are also very grateful to A/Prof Ong Chiou Li, Dr Teo Sze Yiun and Dr Thida Win from the Department of Diagnostic and Interventional Imaging, KK Women's and Children's Hospitals for their help and guidance.

Personal Information

References

References: