Papillary Lesions of the Breast: Part 1 of 2

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• Photo and content credits:
  – Dr. Pedram Argani, Professor of Pathology and Oncology, The Johns Hopkins Hospital

Outline

• Papilloma Size and Terminology
• Papilloma Variants
• Atypical Hyperplasia and DCIS involving Papilloma
• Papillary DCIS
• Papillary Carcinoma
• True Invasion in Papillary Carcinoma
• Metaplastic Carcinoma arising in Papilloma
• Pseudopapillary Carcinoma
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Benign Papillary Lesions:
Terminology

• Papilloma (Central)-involves lactiferous ducts
• Micropapilloma (Peripheral)-involves TDLUs and intermediate-sized ducts

Intraductal papilloma: Locations

- Peripheral papilloma (micropapilloma)
- Terminal duct lobular unit (TDLU)
- Often multiple
- Central Papilloma
- Large peri-areolar ducts or lactiferous sinuses
- Often solitary
Intraductal Papilloma: Central

- Clinical
  - Mass below the nipple
  - Bloody nipple discharge
- Pathology
  - Involves large (excretory) ducts
  - Fibrovascular stalks lined by both myoepithelial cells and benign secretory cells

Myoepithelial cells in papillary lesions

Papilloma

Myoepithelial cells within papillary cores
Myoepithelial cells around periphery

Central papilloma: Gross pathology

Macroscopic features:
Papillary lesion visible in dilated duct/cyst
Central papilloma: Microscopic

**Microscopic Features:**
Epithelial and myoepithelial cell layer supported by fibrovascular cores
Intraductal Papilloma: Peripheral

- Peripheral papilloma often = micropapilloma
  - Originate in terminal duct lobular unit (TDLU) and extend into intermediate to medium sized ducts
  - Often multiple
Clinical Features of Intraductal Papillomas

<table>
<thead>
<tr>
<th>Classification</th>
<th>Demographic characteristics</th>
<th>Nipple discharge</th>
<th>Other Clinical presentation</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>Women at their 60&lt;sup&gt;th&lt;/sup&gt;, may occur in males</td>
<td>-87% of cases -Serous or serosanguineous</td>
<td>Palpable mass</td>
<td>2X</td>
</tr>
<tr>
<td>Peripheral</td>
<td>Women ~10 years younger (40-50s) than central papilloma</td>
<td>-33% of cases -Serous or serosanguineous</td>
<td>Calcification, nodules, masses, or various opacities in mammogram</td>
<td>3.4X</td>
</tr>
</tbody>
</table>

Intraductal Papillomas are benign neoplasms

- **Significance**
  - Minimal risk of cancer (less than 2 fold)
- **Treatment**
  - Somewhat controversial
  - Previously, all recommended for surgical excision and usual follow-up
  ...That being said...

Intraductal Papillomas: Is excision necessary?

- Excision has been recommended due to “unacceptably high” upgrade rate to cancer
- However, studies on upgrade rate don’t always have rad-path correlation
Intraductal Papillomas: Is excision necessary?

- Excision has been recommended due to "unacceptably high" upgrade rate to cancer
- However, studies on upgrade rate don’t always have rad-path correlation
- Lack of follow-up data on un-excised papillomas
- Potential lesional heterogeneity
- Variability and conflicting results in studies

**Breast Intraductal Papillomas without Atypia in Radiologic-Pathologic Concordant Core Needle Biopsies: Predictors of Upgrade to Carcinoma at Excision**

Fresia Pareja [...] Edi Brogi; Cancer 2016; 122:2819-2827

- Methods: Women with CNB diagnosis of intraductal papilloma without atypia or carcinoma. Radiologic-pathologic concordance was assessed for all cases, and discordant cases were excluded.

- Results: 189 women with 196 IDPs; 166 women (171 IDPs) underwent excision. The upgrade rate was 2.3% (4/171). The upgrade lesions were 2 invasive lobular carcinomas and 2 cases of ductal carcinoma in situ (DCIS). One case of DCIS involved the residual IDP, whereas the other 3 carcinomas were ≥8 mm away. Twenty-four women (25 IDPs) did not undergo excision, and had stable imaging at follow-up (median of 23.5 months).

- Conclusion: "Our findings suggest that observation is appropriate for patients with radiologic-pathologic concordant CNB yielding IDP, regardless of its size."

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Papilloma Variants and Pitfalls

- Florid UDH→Solid Papilloma  
  DDX: Papillary carcinoma

- Adenosis (aka, ductal adenoma)  
  DDX: Cribriform DCIS

- Collagenous Spherulosis  
  DDX: Cribriform DCIS

- Adenomyoepithelioma  
  DDX: ALH in papilloma

- Myxoid stroma (Benign mixed tumor)  
  DDX: Metaplastic ca

- Needle tract displacement  
  DDX: IDC

- Sclerosis with entrapped glands  
  DDX: IDC

- Infarction  
  DDX: IDC

- Complex Sclerosing Lesion  
  DDX: IDC

- Nipple Duct Adenoma  
  DDX: Paget’s Disease (Clinically)
Immunohistochemistry of epithelium and hyperplasia in papillary lesions

<table>
<thead>
<tr>
<th>Lesion</th>
<th>CK5/6</th>
<th>ER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papilloma (like UDH)</td>
<td>Mosaic pattern (patchy)</td>
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</tr>
<tr>
<td>Papillary Carcinoma (or ADH/DCIS)</td>
<td>Absent</td>
<td>Diffusely positive</td>
</tr>
</tbody>
</table>
Note: there are some ER and CK5/6 IHC Pitfalls

- Myoepithelial cells: CK5/6+
- Columnar cell change: ER+, CK5/6-
- Basal-like DCIS: CK5/6+
Note: there are some ER and CK5/6 IHC Pitfalls

<table>
<thead>
<tr>
<th>Area</th>
<th>Staining</th>
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</thead>
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<tr>
<td>Myoepithelial cells</td>
<td>CK5/6+</td>
</tr>
<tr>
<td>Columnar cell change</td>
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</tr>
<tr>
<td>Apocrine metaplasia</td>
<td>CK5/6-</td>
</tr>
<tr>
<td>Apocrine ADH/DCIS</td>
<td>ER+/</td>
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Papilloma with Inverted Adenosis
(aka Ductal Adenoma, Complex Glandular Pattern, Pseudo-cribriform Adenosis)

DDX: Cribriform DCIS

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  (Clinically)
ADENOMYOEPITHELIOMA =

PAPILLOMA WITH PROMINENT MYOEPITHELIAL CELLS/
PROLIFERATING MYOEPITHELIAL CELLS
DDX: ALH involving a papilloma
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BENIGN MIXED TUMOR =

PLEOMORPHIC ADENOMA
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Case example:

Papilloma with Sclerosis Overcalled IDC
Intraductal papilloma

"DESMOPLASIA" (actually, sclerosis)
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(actually, sclerosis)
Contrast: Invasive Carcinoma with sclerosis

Often, immunostains for myoepithelial cells are needed to definitively exclude invasive carcinoma.
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Some complex sclerosing lesions are the end stage of a completely sclerotic intraductal papilloma (where you might not appreciate any underlying papillary architecture)
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