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Massachusetts General Hospital & Harvard Medical School

PAPILLOMA
Uncomplicated
Superimposed UDH
Sclerosing papilloma

Look papillary because they are growing on the scaffolding of a papilloma

Intrinsic papillary growth

PAPILLOMA involved by AH
Superimposed ADH
Superimposed ALH

PAPILLOMA involved by CIS
Superimposed DCIS
Superimposed LCIS

PAPILLARY CARCINOMAS

Papillary
• Papillary DCIS
• Encapsulated papillary CA
• Invasive papillary CA

Solid Papillary
• Solid papillary DCIS
• Invasive solid papillary CA

Invasive papillary growth

Papillary
• Papillary CIS
• Encapsulated papillary CA
• Invasive papillary CA
**PAPILLOMA**

- **Central Large Duct Solitary**
  - No Atypia: 2X
  - + Atypia: 5X

- **Peripheral Small Duct Multiple**
  - No Atypia: 3X
  - + Atypia: 7X

**RR for Breast Cancer**

- PDWA only: 1.9X
- AH only: 4.2X

Lewis JT et al. AJSP 2006;30:665-672

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**Slide Image with Annotations**

1. [Annotation](#)
2. [Annotation](#)
Complex glandular pattern in stalk

PAPILLOMA can have superimposed: UDH
### Myoepithelial Cells in Papillary Lesions

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<td>+ / Rarely in proliferative areas</td>
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Sclerosing Papilloma

“Pseudoinvasion”

PAPILLOMA

can have superimposed:
- UDH
- ADH or DCIS
Look outside of papilloma!

Look along the duct wall!

- Diagnosis
- Prognosis

Look outside of papilloma!
Low-Grade Atypical Ductal Proliferations Involving Papillomas: ADH or DCIS?

**METHOD 1**
Size of Atypical Proliferation
- ≤ 3mm: ADH involving papilloma
- > 3mm: DCIS involving papilloma

**METHOD 2**
Proportion of Papilloma Involved by Atypical Proliferation
- <33%: ADH involving papilloma
- 33-<90%: DCIS involving papilloma

**METHOD 3**
Evaluate as for Non-Papillary Breast Tissue
- Diagnose DCIS if combined cytological and architectural features fulfill the usual criteria
Along Stalks

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Myoepithelial Cells in Papillary Lesions

PAPILLOMA
can have superimposed:

UDH

ADH or DCIS

ALH or LCIS

PAPILLOMA

can have superimposed:
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PAPILLARY CARCINOMA

Papillary DCIS
<table>
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<tr>
<th></th>
<th>PAPILLOMA</th>
<th>PAPILLARY CARCINOMA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of fronds</strong></td>
<td>Few</td>
<td>Many</td>
</tr>
<tr>
<td><strong>Shape of fronds</strong></td>
<td>Broad and blunt</td>
<td>Long and slender</td>
</tr>
<tr>
<td><strong>Amount of stroma</strong></td>
<td>Moderate to abundant</td>
<td>Scant</td>
</tr>
<tr>
<td><strong>Main Cell Type(s)</strong></td>
<td>Luminal and myoepithelial</td>
<td>Luminal</td>
</tr>
<tr>
<td><strong>Cytologic features</strong></td>
<td>Benign</td>
<td>Atypical</td>
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Look along the duct wall for help.
Myoepithelial Cells in Papillary Lesions

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<td>~ / 1 / Occasionally +</td>
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PAPILLARY CARCINOMA

- Papillary DCIS
- Encapsulated Papillary Carcinoma
- Invasive Papillary Carcinoma
“Encapsulated” Papillary CA

Collins L et al. AJSP 2006;30:1002-7
- 22/22 IPCs negative for MECs
- Conclusion → Most are indolent invasive carcinomas

Wynveen C et al. AJSP 2011;35:1-14
- 33/40 IPCs negative for MECs
- 7/40 Focally positive for MEC markers
- Conclusion → Spectrum of in-situ to invasive, predominately invasive

Rakha E et al. AJSP 2011;35:1093-103
- Studied 208 IPC with IHC on subset
- Conclusion → Most are indolent invasive carcinomas

Stage as In-situ or Invasive Carcinoma?

WHO 4th edition:
Encapsulated Papillary Carcinoma
- Only rare cases of axillary or distant metastases
- Stage as Tis
- Diagnose IDC only if conventional invasive carcinoma is present and stage the “frankly invasive component” without including encapsulated component

Lakhani SR et al., WHO Classification of Tumors of the Breast, 4th ed. 2012
Tan PH et al., Papillary and neuroendocrine breast lesions: The WHO stance Histopathology 2013; 66:761-70
“High-Grade Encapsulated Papillary CA”

- Rare: 3% of pure EPC
- Median age: 58 y
- Median size: 2.7 cm
- High nuclear grade & high mitotic rate
- 68% triple-negative
- More aggressive than non-high grade EPC
- Manage and stage the same as conventional IDC


PAPILLARY CARCINOMA

- Papillary DCIS
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Invasive Papillary CA

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<tr>
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Solid Papillary CA

- Expansile cellular nodules punctuated by delicate fibrovascular cores
- Cytologic features can superficially resemble UDH
- Neuroendocrine differentiation, spindle cell morphology, and mucin production are common
- Can be either in-situ or invasive
  - Can invade in the form of rounded, expansile nests that may mimic an in-situ process.
Solid Papillary CA
Clues to Invasion
• Jigsaw-like pattern
• Irregular anastomosing islands
• Confluent growth
• Angulated or irregular contours
• Desmoplastic stroma
• Engulfment of normal elements
• Lack of myoepithelial cells
Solid Papillary Carcinoma

Fused Cribriform Growth in Encapsulated Papillary CA

Solid Papillary Carcinoma

Stage as In-situ or Invasive Carcinoma?

WHO 4th edition:

Solid Papillary Carcinoma

- Myoepithelial cells (MEC) present = In-situ CA
- Irregularly-shaped nests with jigsaw pattern and no MEC = Invasive CA
- Rounded nodular masses without MEC = Possible non-conventional form of invasive CA but due to indolent behavior stage as Tis

Lakhani SR et al., WHO Classification of Tumors of the Breast, 4th ed. 2012
Tam PH et al., Papillary and neuroendocrine breast lesions: the WHO stance. Histopathology 2015; 66:761-70

No myoepithelial cells: In-situ or invasive?
No myoepithelial cells: In-situ or invasive?

Myoepithelial Cells in Papillary Lesions

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<td>–</td>
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<tr>
<td>Solid Papillary DCIS</td>
<td>+ / i / –</td>
<td>+ or –</td>
</tr>
<tr>
<td>Invasive Solid Papillary CA</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Papilloma</td>
<td>Variable +</td>
<td>Variable +</td>
</tr>
<tr>
<td>Papilloma with UDH*</td>
<td>+ in UDH</td>
<td>Heterogeneous + in UDH</td>
</tr>
<tr>
<td>Papilloma with ADH/LG-DCIS*</td>
<td>– in ADH/LG-DCIS</td>
<td>Diffuse + in ADH/LG-DCIS</td>
</tr>
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<td>Papillary DCIS</td>
<td>–</td>
<td>Diffuse +</td>
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<td>–</td>
<td>Diffuse +</td>
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*IHC most informative in areas of expansile epithelial proliferation rather than in papillary areas.

### Issues Regarding Core Biopsies

- Exclusion generally recommended after core biopsy diagnosis of papilloma
  - Upgrade to ADH/ALH/LCIS: ~10%
  - Upgrade to DCIS/Inv CA: ~10%
  - Sampling error due to eccentric distribution of CA
  - Difficult diagnostic area
- Exclusion recommended if atypia or higher is diagnosed
- Can be difficult to distinguish in situ from invasive papillary carcinomas due to limited view of border and overall architecture
  - Peripheral MEC: In situ
  - Peripheral MEC: ? In situ with attenuated MECs vs Invasive

### GROUP 1
**PAPILLOMA +/- superimposed proliferation (UDH, AH, CIS)**
- Identify any areas of solid/expansile epithelial proliferation
- Evaluate using same cytologic and architectural criteria used for non-papillary intraductal proliferations
- Characteristics of epithelium more important than amount of myoepithelium
- Threshold for ADH: DCIS: similar or higher

### GROUP 2
**PAPILLARY & SOLID PAPILLARY CA:** Papillae intrinsic part of tumor growth
- Papillary carcinoma characterized by complex architecture with numerous ramifying papillae lined by atypical epithelium
- Solid papillary carcinoma has distinctive histologic features beyond just solid growth with fibrovascular cores
- Encapsulated papillary carcinoma and certain nested solid papillary carcinomas are consistent with indolent forms of invasive carcinoma