Significance of Myoepithelial Cell Layer Absence Around Ducts with Papillary Ductal Intraepithelial Neoplasia 1-3/Papillary Ductal Carcinoma *In Situ* 1-3

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ABSTRACT

Introduction: While persistence with adjacent conventional invasive carcinoma (IDC), the size and stage of the carcinoma could vary substantially depending on whether the papillary component is interpreted as invasive or intraepithelial.

Design: In a retrospective search of the pathology database at our institution for all PDIN 1-3 (Papillary DCIS) with excisional biopsy between 2001 to 2011, a total of 50 (PDIN, solid), 2 (PDIN, intracystic), 12 PDIN with associated IDC were identified and reviewed. 27 low grade PDIN of solid and intracystic types with or without associated IDC were further evaluated with 3 ME (p63, calponin and CD10) and 2 basement membrane markers (collagen IV & laminin).

Results: All low grade PDIN (22) showed absence of ME (>90%) within the intra-luminal papillary fronds and focal or discontinuous ME cell around the duct; BM markers showed retention of BM around distended ducts with PDIN. PDIN with associated IDC (n = 5) showed complete absence of ME cells around the distended ducts with PDIN. BM was present around PDIN, but absent around foci of IDC. The size of the PDIN varied from 3 mm to 6.0 cm, while the adjacent IDC varied from <0.1 to 1.3 cm. Only one of the 22 cases had nodal metastases, this case had IDC.

Conclusions: The majority of papillary DIN 1-3 is non-invasive with an expansile growth in distended ducts. The IDC associated with PDIN (5) was a conventional IDC (n = 4) or mucinous (n=1). The absence of ME cells around ducts in the absence of typical IC architecture is not an indication of an invasive carcinoma. Ultimately, the prudent use of both histologic criteria and IHC in papillary DIN 1-3 with or without associated IDC is critical to avoid overstaging and overtreatment. Papillary DIN 1-3 lesions devoid of any ME cells have excellent prognosis similar to DIN 1-3 (DCIS, grades 1-3).

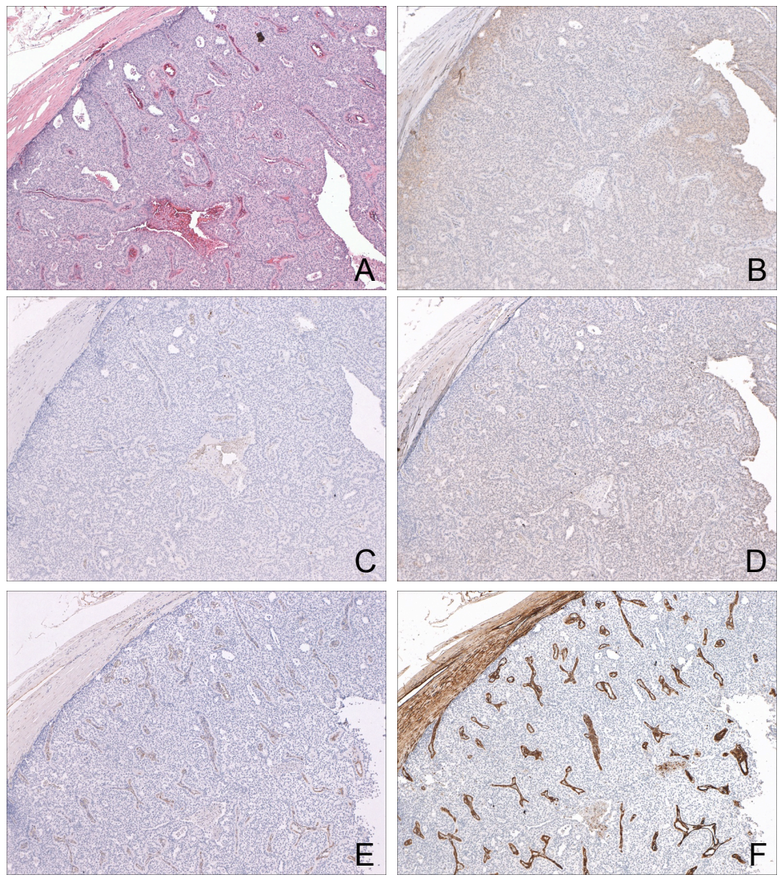
INTRODUCTION and METHODS

- Papillary proliferations of the breast distend the duct within which they develop.
- This distension stretches the myoepithelial cell layer so that it is very difficult to identify individual myoepithelial cells by standard hemotoxylin and eosin (H&E) stains.
- In the typical papilloma, this is not significant as it is does not affect management.
- What constitutes invasion in a solid papillary proliferation lacking myoepithelial cells within the papillae and around the ducts remains controversial. As such neoplasms are not infrequently quite large, this could significantly impact the stage.

INTRODUCTION

- The pathology database at our institution was searched for atypical and more advanced papillary lesions.
- The slides of all atypical papillary lesions (central and peripheral types) were reviewed. The size of the papillary lesion, any adjacent non-papillary DIN/DCIS, or IDC and the degree of atypia were recorded.
- Immunostains were performed for p63, CD10, Calponin, Laminin, and Collagen IV on a representative section of each atypical papillary proliferation.

Figure 1

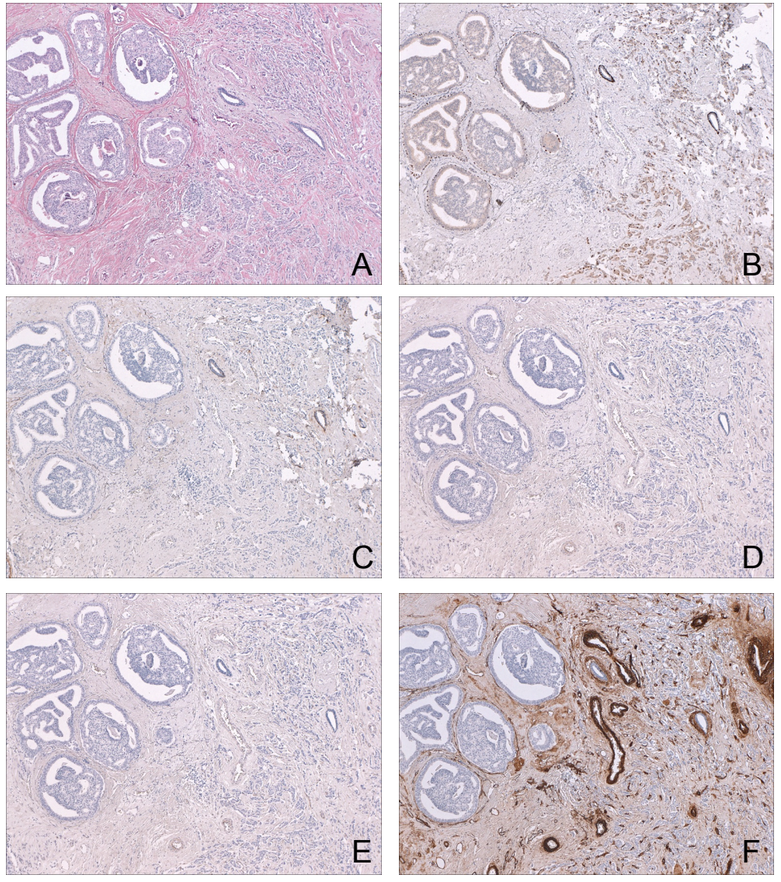


A. This solid papillary ductal intra-epithelial neoplasia/ Ductal Carcinoma *In Situ* (DCIS) was 6cm with only a 0.6cm accompanying infiltrating ductal carcinoma (IDC). **B-E.** The expansile growth pattern led to attenuation of the myoepithelial cell layer and a loss of expression of p63 **(B)**, CD10 **(C)**, and Calponin **(D)**. **E-F.** The basement membrane proteins Laminin **(E)** and Collagen IV **(F)** were still apparent both around the periphery of the lesion as well as within the papillary fronds.

RESULTS

- ME cells are frequently lost within the papillary fronds and around the periphery of the expansile lesions.
- Basement membrane is generally retained around these papillary lesions, but not the associated IDC.

Figure 2



A. An admixture of a papiilary lesion involved by intra-epithelial neoplasia with adjacent infiltrating ductal carcinoma (IDC). **B.** p63 is retained around the papillary lesion but not the IDC. **C-D.** CD10 **(C)** and Calponin **(D)** are absent from both the papillary lesion as well as the IDC. **E-F.** Basement membrane proteins, Laminin (E) and Collagen IV **(F)**, are seen around the periphery of the papillary lesion but not the islands of IDC.

CONCLUSIONS

- A high proportion (>90%) of papillary DIN/DCIS lesions show a loss of ME cells but retention of basement membrane.
- Therefore, only typical invasive carcinomas adjacent to such lesions should be considered invasive and measured as such.