Research Article

Gynecology & Reproductive Health

Electron Microscopy of Encapsulated and Solid Papillary Carcinomas, Is This an In-Situ or an Invasive Entity?

Silverman S*, M.D

Department of Laboratory Medicine and Pathology, Misericordia Hospital, Edmonton, Canada.

***Correspondence:**
Silverman S, Department of Laboratory Medicine and Pathology, Misericordia Hospital, Edmonton, Canada, Tel: 780-735-2472, E-mail: sveta@ualberta.ca.

Received: 12 September 2017; **Accepted:** 17 October 2017

Citation: Sliverman S. Electron Microscopy of Encapsulated and Solid Papillary Carcinomas, Is This an In-Situ or an Invasive Entity?. Gynecol Reprod Health. 2017; 1(3): 1-4.

ABSTRACT

Background: *for long time encapsulated and solid papillary carcinomas have been debated either an in-situ or an invasive entity. The goal of our study was to examine the presence or absence and the quality of myoepithelial cells, the presence or absence and thickness of basement membrane in all the selected cases.*

Methods: *8 cases of encapsulated and solid papillary carcinomas, 3 cases of low to intermediate grade DCIS in association with low grade IDC NOS and 2 cases of combined IG DCIS and encapsulated papillary carcinomas as well as 2 cases of normal breast were selected from your database. The morphology was reviewed, immunohistochemical stains to highlight myoepithelial cells were performed and all cases were subjected for digital electron microscopy.*

Results: *All 5 cases of encapsulated papillary carcinoma show the presence of continuous or discontinuous attenuated basement membrane and absence of myoepithelial cells, 3 solid papillary carcinomas show possible small myoepithelial cells.*

Conclusions: *We think that encapsulated papillary carcinomas represent a category of neoplasms in transition from an in-situ to invasive carcinomas, and at this stage should be interpreted as low grade invasive ductal carcinomas with favorable behavior. Solid papillary carcinomas should be divided into 2 categories: an invasive solid papillary carcinoma and in-situ solid papillary carcinomas.*

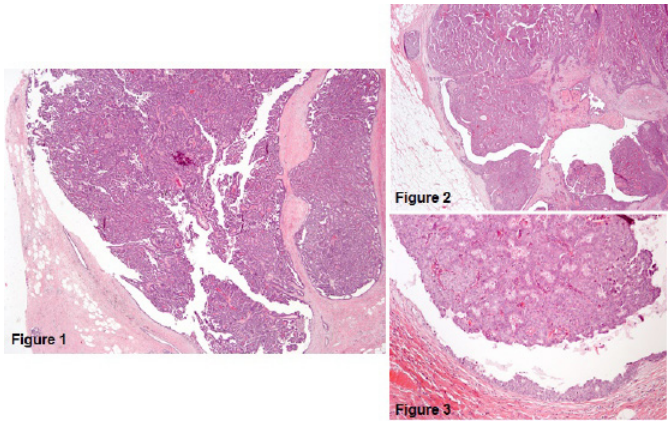
Introduction

As defined in WHO "Blue Book" 2012 edition [1], an encapsulated/intracystic/encysted papillary carcinoma is a papillary lesion of low to intermediate nuclear grade with no myoepithelial cell layer with in papillae or at the periphery of the lesion. These carcinomas represent approximately 0.5% to 2% of all breast cancers and typically occur in postmenopausal women [2]. Encapsulated papillary carcinoma is a neoplastic papillary neoplasm, identified in the dilated pseudoencapsulated and fibrotic duct. Solid papillary carcinoma is a form of papillary carcinoma with a solid growth and delicate and inconspicuous fibrovascular cores at low magnification. Neuroendocrine differentiation is frequent. Both entities frequently lack a peripheral myoepithelial cell layer. Immunostaining analyses have failed to demonstrate the presence of a myoepithelial cell layer in the most of papillary carcinomas of those types [3]. The precise distinction between in situ and invasive disease in solid papillary carcinomas is difficult as We have performed an electron microscopy on selected cases of encapsulated and solid papillary carcinomas of the breast in an attempt to categorize these lesions as either in situ or invasive carcinomas via presence or absence of myoepithelial cells and basement membrane.

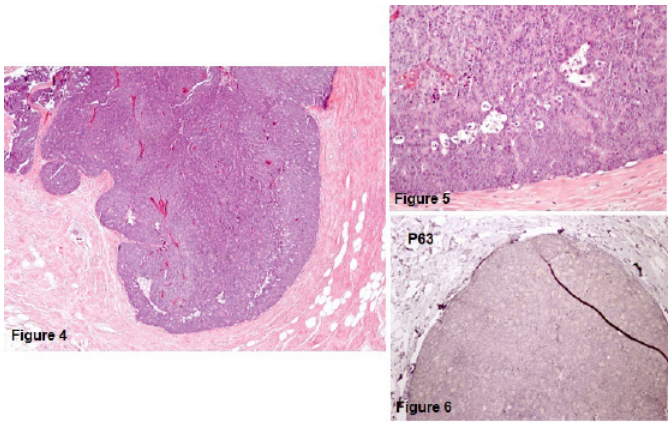
Methods

We have selected 5 cases of encapsulated papillary carcinomas (Figures 1-3), 3 cases of solid papillary carcinomas (Figures

4-6) from patients ranging from 44 to 75 years of age, 3 cases of low to intermediated grade DCIS in association with low grade IDC (Figures 7 and 8) and 2 cases of normal breast from one of pathologist's practice, since choosing 2010 to 2011 cases.



Figures 1-3: Encapsulated papillary carcinoma, H&E, x 2.0.



Figures 4 and 5: Solid papillary carcinoma, H&E, X 4.
Figure 6: Solid papillary carcinoma, X 10, P63 with absence of myoepithelial cells.

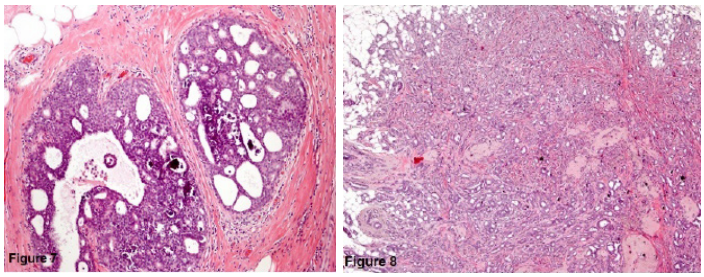


Figure 8: Low grade invasive ductal carcinoma.

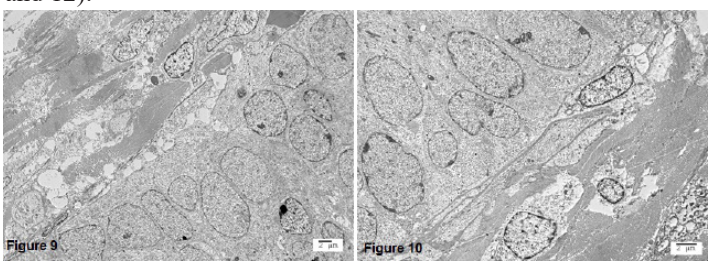
The cases were selected upon morphology, supported by the myoepithelial cell immunohistochemical markers and CK5/6 stain. The following antibodies have been used: P63: Mouse monoclonal BC4A4 (Biocare) Stained on the Ventana, Mild CC1 retrieval, Iview (avidin-biotin) detection with A/B block and amplification 28 min primary, Antibody comes predilut, CK5/6: Mouse monoclonal D5/16B4 (Dako) Stained on the Dako, High pH in the PT Link, Flex+30 polymer detection 30min primary with a 1/100 dilution, SMMHC: Mouse monoclonal SMMS-1 (Dako) Stained on the Dako, Low pH in the PT Link, Flex+20 polymer detection 20 min primary with a 1/200 dilution. Electron microscopy was performed on all 13 cases. Biopsy material for electron microscopy was salvaged from paraffin blocks initially prepared for light microscopic slide preparation. A small representative focus (less than 2 mm squared) was circled on an H & E stained light microscopic slide section (selected by one of pathologists, SS). The section was correlated with the tissue remaining in the corresponding paraffin block, and tissue of interest was removed from the block. This material was de-paraffinized using xylene, brought to alcohol and re-hydrated through a graded series of aqueous solutions. The rehydrated tissue was placed in 2% glutaraldehyde, and then processed for electron microscopy using conventional methodology. This involved post-fixation in 1% Osmium tetroxide, dehydration in a graded series of ethanol solutions, and infiltrating tissue with the embedding media, Epon 812. The embedded tissue was cured at 80 C for 12 hours to produce Epon blocks. These blocks were trimmed and sectioned for light microscopy, and the resultant Toluidine Blue stained slide sections were examined by light microscopy and related to the original H & E Light microscopic slide, to ensure the area of interest was maintained and captured. Upon selection of an appropriate area on an Epon block, the block was sectioned at 100 nm using an ultramicrotome. The sections were placed on copper mesh grids, and then contrasted using Lead Citrate and Uranyl Acetate. The ultrathin sections were examined using a Hitachi H-7650 Electron Microscope for presence or absence of myoepithelial cells and basement membrane. Areas of interest were photographed and documented using an AMT 16000-B bottom mount digital camera.

Results

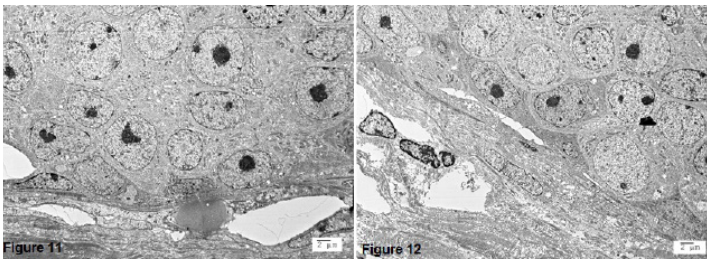
The normal breast elements display thick, continuous basement membrane and prominent large myoepithelial cells (Figure 16).

Images of low to intermediate grade DCIS reveal thick to thin continuous basement membrane and prominent, but smaller, myoepithelial cells (Figures 13 and 14).

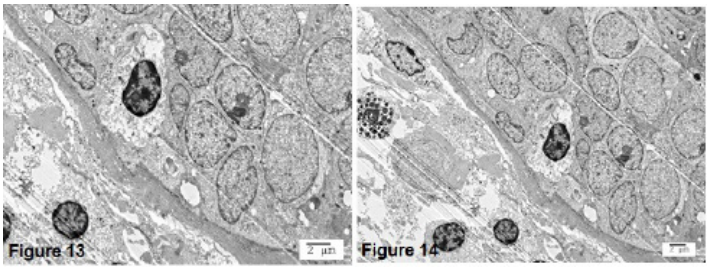
Images of low grade invasive ductal carcinoma show no evidence of neither basement membrane nor myoepithelial cells (Figure 15). All of 8 cases of encapsulated and solid papillary carcinomas reveal presence of basement membrane. It was identified in either continuous or discontinuous, and attenuated/thinned fashion (Figures 9 and 10). None of 5 cases of encapsulated papillary carcinomas show the presence of myoepithelial cell layer. 3 solid papillary carcinomas display small and flat nuclei, possibly representing nuclei of attenuated myoepithelial cells (Figures 11 and 12).



Figures 9 and 10: Encapsulated papillary carcinoma. Electron micrography demonstrating. discontinuous and attenuated basement membrane and no myoepithelial cells.



Figures 11 and 12: Solid papillary carcinoma, electron microscopy demonstrating discontinuous thin basement membrane and attenuated small rare myoepithelial cells (pointed by arrow).



Figures 13 and 14: Low to Intermediate grade DCIS, electron microscopy demonstrating continuous thick basement membrane and small but prominent myoepithelial cells (pointed by arrow).

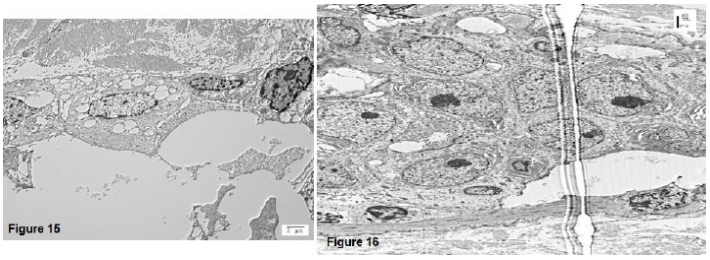


Figure 15: Low grade invasive ductal carcinoma, electron microscopy demonstrating no basement membrane and no myoepithelial cells.

Figure 16: Normal breast tissue. Electron microscopy demonstrating thick continuous basement membrane with large myoepithelial cell. Arrow indicates myosin densities.

Discussion

Encapsulated and solid papillary carcinomas usually present as well defined lesions with pushing type borders mostly in postmenopausal women [2]. Encapsulated papillary carcinoma contains papillary fronds of low to intermediate nuclear grade cells bound by fine fibrovascular cores and surrounded by bands of connective tissue in dilated ducts. Solid papillary carcinomas are compacted masses of low to intermediate nuclear grade cells with very faint or negligible fibrovascular cores. The obvious question is whether encapsulated papillary carcinomas and solid papillary carcinomas represent invasive or in-situ entities. Since the initial description of the inconsistent presence of myoepithelial cell in the encapsulated or intracystic papillary carcinomas [4], there has been controversy over the classification of these lesions as in-situ or invasive [4,5]. The recent review article by Rakha et al. has suggested the "EPC lacking myoepithelial cells are a special type of invasive breast carcinoma with favorable prognosis, whereas EPC showing an intact peripheral layer of myoepithelial cells should be regarded as in situ carcinomas" [6]. F. O'Malley et al. have reported micrometastases in lymph nodes in cases of EPC [5]. This contrasts with work by Esposito et al. [2], who has demonstrated a "continuous, intense collagen type IV immunoreactivity entirely circumscribing the majority of these lesions, favoring an in situ carcinoma designation.

Upon our limited series, we combine myoepithelial cell markers and ultrastructural examination for the presence of basal lamina in cases of low grade EPC and solid papillary carcinoma in comparison to normal breast tissue, conventional not otherwise specified low grade DCIS and low grade invasive ductal carcinoma. We have established that both encapsulated and solid papillary carcinomas are still encompassed by basement membrane, thin, attenuated, discontinuous, but still present basement membrane. All encapsulated papillary carcinomas show no evidence of myoepithelial cell presence and some solid papillary carcinomas show the presence of small, attenuated and rare myoepithelial cells. We think that encapsulated and solid papillary carcinomas, which lack myoepithelial cells, do not represent in situ carcinomas; however, they do not fall into the category of frank invasive carcinomas either. We think that encapsulated and solid papillary carcinomas represent an intermediate link between DCIS and frank invasive ductal carcinoma and certainly should not be over treated [7-18].

References

1. WHO classification of Tumors of the Breast: Encapsulated Papillary Carcinoma, Solid Papillary Carcinoma. 4th edn. 2012.
2. Esposito NN, Dabbs DJ, Bhargava R. Are Encapsulated Papillary Carcinomas of the Breast in Situ of Invasive? Am J Clin Pathol. 2009; 131: 228-242.
3. Nassar H, Qureshi H, VolkanAdsay N, et al. Cliniopapthologic Analysis of Solid Papillary Carcinoma of the Breast and Associated Invasive Carcinomas. Am J Surg Pathol. 2006; 30.
4. Collins LC, Carlo VP, Hwang H, et al. Intracystic Papillary Carcinomas of the Breast: A Reevaluation using a Panel of Myoepithelial Cell Markers. Am J Sur Pathol. 2006; 30.
5. Mulligan AM, O'Malley FP. Metastatic Potential of Encapsulated (Intracystic) Papillary Carcinoma of the Breast: A Report of 2 Cases with Axillary Lymph Node Micrometastases. International Journal of Surgical Pathology. 2007; 15: 143-147.
6. Rakha EA, Gandhi N, Climent F, et al. Encapsulated Papillary Carcinoma of the Breast: an Invasive Tumor with Excellent Prognosis. Am J Surg Pathol. 2011; 35.
7. Hardisson D, Gonzalez-Peramato P, Perna C, et al. Fine Needle Aspiration Cytology of Solid Papillary Carcinoma of the Breast. Acta Cytologica. 2003; 47: 259-264.
8. Maluf HM, Koerner FC. Solid Papillary Carcinoma of Breast: An Ultrastructural Study. Ultrastructural Pathology. 1997; 21: 153-161.

9. Jaffer S, Chen X, Lee, L, et al. Pleomorphic Solid and cystic Papillary Carcinoma of the Breast: Two cases occurring in Young Women. Annals of Diagnostic Pathology. 2004; 8: 126-129.
10. Laforga JB, Gasent JM, Sanchez I. Encapsulated Apocrine Papillary Carcinoma of the Breast: Case Report with Clinicopathologic and Immunohistochemical Study. Diagnostic Cytopathology. 39: 288-292.
11. Kuroda N, Fujishima N, Inoue K, et al. Solid papillary carcinoma of the breast: imprint cytological and histological findings. Med Mol Morphol. 2010; 43: 48-52.
12. Devouassoux-Shishe Boran, Jousselin de Saint Hilaire P, Leveugle-Pin J, et al. Fine Needle Aspiration Cytology of a Solid Papillary Carcinoma of the Breast. Acta Cytologica.1998; 42: 725-728.
13. Seal M, Wilson C, Naus G J, et al. Encapsulated apocrine papillary carcinoma of the breast- a tumour of uncertain malignant potential: report of five cases. 2009; 455: 477-483.
14. Maluf H M, Koerner F C. solid Papillary Carcinoma of the Breast, A Form of Intraductal Carcinoma with Endocrine differentiation Frequently Associated with Mucinous Carcinoma. the American Journal of Surgical Pathology. 1995; 19: 1237-1244.
15. Dragoumis D M, Assimaki A S, Tsiftsoglou A P. Solid variant of pure intracystic papillary carcinoma of the breast: case report. Eur. J. Gynaec. Oncol. 2008; 29: 545-547.
16. Imoto S, Hasebe T. Intracystic Papillary Carcinoma of the Breast in Male: Case Report and Review of Japanese Literature. Jpn J Clin Oncol. 1998; 28: 517-520.
17. Nicolas MM, Middleton LP, Gilcrease MZ. Loss of myoepithelium is variable in solid papillary carcinoma of the breast. Histopathology. 2007; 51: 657-665.
18. Otsuki Y, Yamada M, Shimizy S, et al. Solid-Papillary carcinoma of the breast: Clinicopathological study of 20 cases. Pathology International. 2007; 57: 421-429.