Encapsulated papillary carcinoma (EPC) of breast: A clinical, pathological and immunohistochemical analysis of eight cases

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Abstract

Encapsulated papillary carcinoma (EPC) is a rare low grade carcinoma of the breast with excellent prognosis. This case series focuses on its histopathological and clinical characteristics in our material. Cases of papillary lesions of breast from 1st January 2012 to 30th December 2014 were retrieved from the hospital database. A total of 8 cases were categorized as EPC. Mean age of patients was 66 years. Breast lump with tumour size ranged from 1.5 to 5.0cm, and was the presentation in 75% of cases. Histopathology showed a well circumscribed lesion within a dilated duct comprising of fibro vascular cores lined by neoplastic cells, surrounded by thick fibrous capsule. Immunohistochemistry, for antibody panel p63, ASMA and CK 5/6 were negative for myoepithelial cells. Invasive carcinoma was seen in 3 (37.5%) with associated DCIS in 4 (50%) cases. Meticulous gross, attention to morphology and correct interpretation of immunohistochemistry are imperative for accurate diagnosis.

Keywords: Encapsulated papillary carcinoma, Myoepithelial cells, Prognosis, Immunohistochemistry.

Introduction

Papillary lesions of the breast are a distinct histopathological entity with varying clinical features, histology, radiology and malignant potential. They represent a diagnostic dilemma in terms of their histopathological identity. The recent WHO classification of tumours of the breast (2012) subdivides intraductal papillary lesions into 4 categories; Intraductal papilloma, intraductal papillary carcinoma, encapsulated papillary carcinoma and solid-papillary carcinoma.[1]

Encapsulated papillary carcinoma (EPC) synonymous with intracystic papillary carcinoma is used to describe malignant papillary proliferation involving a cystically dilated duct.[2]

Although it was previously thought of as an insitu lesion but the demonstration of lack of myoepithelial layer at the lesion's periphery and the report of lung metastasis in patient with EPC[3] have led to the presumption that these tumours may represent a low grade or indolent form of invasive carcinoma. These tumours have an excellent prognosis in the absence of associated ductal carcinoma in situ or frank invasive carcinoma. The relative survival rate is 100% at 10 years with a disease free survival rate of 91%.[4]

Since EPC is a recently described entity in "WHO Classification of Tumours of the Breast" and is not routinely encountered, the purpose of this case series is to analyze the histopathological and clinical characteristics of these tumours in our patients for better understanding and ease of diagnosis.

Case Series

A retrospective study was carried out at histopathology department, Shifa International Hospital. Cases diagnosed as EPC from 1st January 2012 to 30th December 2014 were retrieved from hospital's computerized records. There were 33 cases of papillary lesions, out of which 08 (24.2%) were diagnosed as EPC. There were 04 lumpectomy specimens, 02 mastectomy specimens whereas 02 were received as blocks for second opinion. No further clinical data could be obtained in these 02 cases.

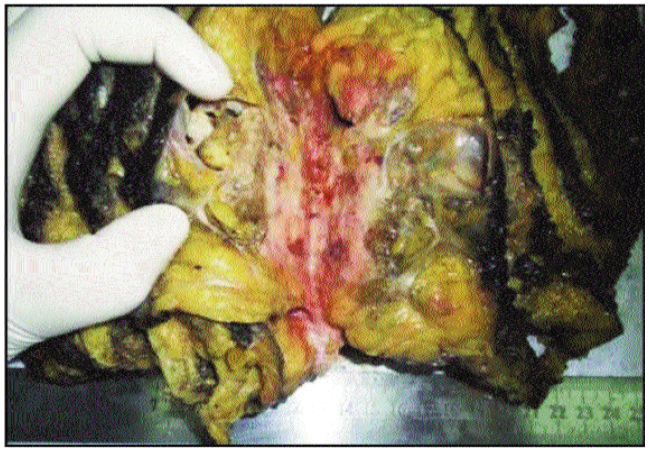

Figure-1: Gross examination showing a solid growth within a cystically dilated duct.

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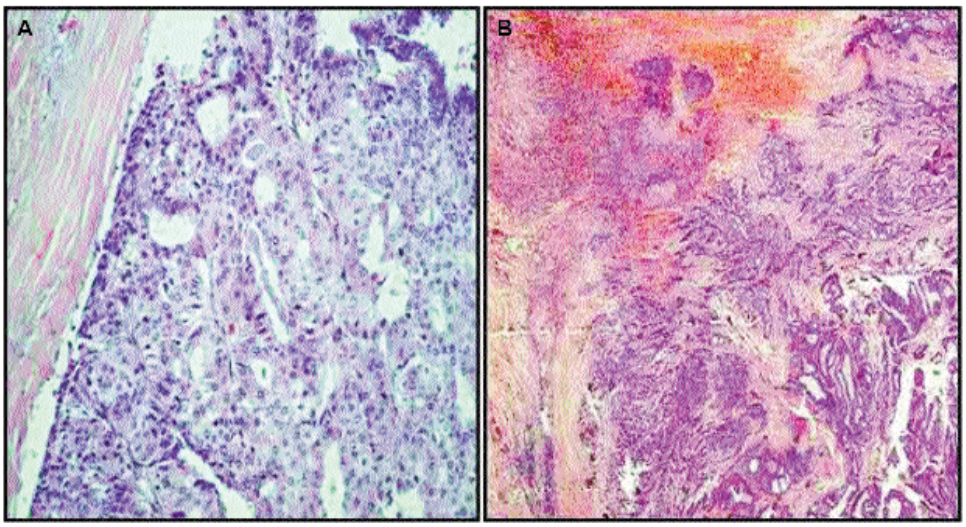

Figure-2: A) Papillary fronds lined by monotonous malignant epithelial cells with surrounding thick fibrous capsule (original magnification 200x). B) Encapsulated papillary carcinoma with associated invasive carcinoma (original magnification 100x).

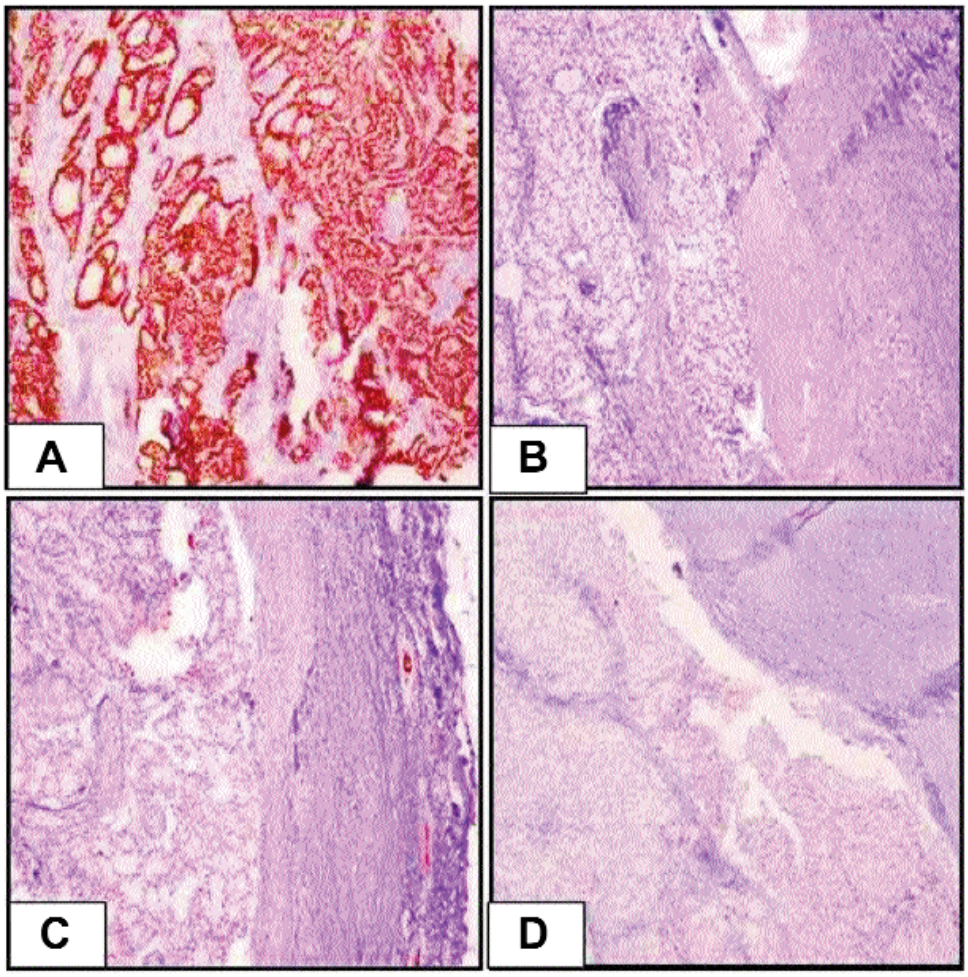

Figure-3: On immunohistochemistry tumour showing (A) nuclear positivity for ER whereas (B) p63 (C) ASMA (D) CK5/6 fail to highlight myoepithelial cells both within and outside the lesion. (Original magnification 100x[A.B.C.D]).

Cases included had patient's age between 55-84 years with a mean of 66±9.4 years. Six patients (75%) presented with lump breast, whereas 02 (25%) of them also had associated bloody nipple discharge. Five (62.5%) patients had tumours in breast, whereas in 01(12.5%) case axillary breast tissue was the primary site of tumour.

FNAC was performed in 04 (50%) cases. Three of them were non diagnostic, whereas 01 was categorized as C4 (suspicious for malignancy).

On gross examination tumour size ranged from 1.5 to 5.0 cm with a mean size of 2.7±1.3cm. 3 out of 6 (50%) cases showed a solid growth within a cystic cavity (Figure-1), whereas the remaining cases showed a well circumscribed tan white, firm tumour.

Histolopathology, showed a well circumscribed lesion with a thick fibrous capsule in all 8 cases. The cystically dilated duct showed papillary fronds lined by neoplastic, monotonous population of epithelial cells (Figure-2A). Myoepithelial cell layer was lacking both within these cores and at the periphery of the lesion. Extensive sampling was done in all cases which showed associated DCIS in 4(50%) cases. DCIS was of intermediate grade in 3 cases and of high grade in 1 case. Three of these cases (n=37.5%) also had associated invasive carcinoma, NOS (Figure-2B). Immunohistochemistry was performed in 05 (62%) cases which showed the tumour to be strongly positive for ER, whereas 34betaE12, p63, ASMA and CK5/6 showed lack

of myoepithelial cells (Figure-3).

Lymph node dissection was performed in 4 out of 8 cases (n=50%) and all recovered lymph nodes were free of tumour. Two patients (n=25%) had previous history of carcinoma in contra lateral breast, whereas one patient (12.5%) had past history of ovarian carcinoma.

These patients were followed after a period of 1 year. Informed consent was taken from these patients. Four patients took hormonal therapy. In 1 patient after hormonal therapy for 3 months, mastectomy was performed. They were all doing fine. The others lost to follow up.

Discussion

EPC is a rare malignant tumour, described in postmenopausal women.[4] In a study by Thaer et al of 22 cases of EPC collected over a period of eight years, the mean age of patients was found to be 73 years[5] which is in accordance with our study having a mean age of 66 years. It is known to present commonly as a palpable mass,[6] with bloody nipple discharge reported as the second frequent complaint.[7] Six of our patients presented with lump, of which two also had bloody nipple discharge.

A peculiar finding in our study was previous history of carcinoma in contra lateral breast in two patients while one had history of ovarian cancer. Whether this is an incidental finding or has clinical significance needs further study.

Cytology remains partially unreliable in papillary lesions of breast and is unable to differentiate accurately between benign and malignant lesions. Most studies have shown a low concordance between diagnosis of papillary lesions on FNAC and on histopathology.[1] Our results also show mixed results.

Previously, EPC was thought be a form of DCIS but in DCIS myo epithelial layer at the periphery of the duct remains intact. Recent studies have shown that EPC lacks myoepithelial cells both within and outside of the lesion, thus proving it to be a separate entity. Collins et al, stained 22 cases of EPC with a panel of 5 antibodies used to highlight myoepithelial cells. These included smooth muscle myosin, calponin, p63, CD10 and CK5/6 however, all of them failed to demonstrate MEC at the periphery of the lesion.[6] In another study 25 out of 27 cases of EPC showed complete absence of p63 staining whereas remaining 02 showed focal positivity.[8] In our study we utilized p63, CK5/6, 34betaE12and ASMA to highlight MEC singly or in combination, and all 08 cases showed lack of MECs within and at periphery of lesion.

Although patients with pure EPC have an excellent prognosis; disease free survival in case of associated DCIS and/or invasive carcinoma remains controversial. Some studies report no statistical difference in disease free survival or risk of recurrence in patients of EPC with and without invasive component.[9,10] Others believe that associated DCIS or invasive component calls for a worse prognosis and increased risk of local recurrence.[2] Therefore many published data to date recommend adjuvant radio and endocrine therapy in patients with associated DCIS or invasive component.[11]

In our study 4 out of 8 cases (n=50%) had an associated DCIS component and 3 of them also showed an invasive component. In other studies, synchronous invasive carcinoma NOS was seen in variable proportion of cases. In a study by Nicole et al 6 out of 27(22%) cases had associated invasive carcinoma.[8] However a study by Thaer et al showed associated DCIS and invasive carcinoma in a greater number of cases, that is; 54.5% and 41% of cases. A study was carried out by Grabowski et al with the largest number of EPC cases, which is 917. He found 427 (47%) cases of EPC in situ and 490 (53%) cases with associated invasion. The authors concluded that at 05 years the mean survival of patients with pure EPC was better as compared to those with associated invasion(85.0% vs 75.0%, P=0.05). At 10 years, however, patients with pure EPC and those with associated invasion IPC had almost identical cumulative survival (61.7% and 60.6%, p=0.08).[12] In our study 4 of the patients could be followed, 2 of them had pure EPC where as other 2 had associated invasive carcinoma. All of them were performing well after 1 year.

Conclusion

EPC is a rare entity and its diagnosis on histopathology mandates confirmation by immunohistochemistry to rule out other papillary lesions. Gross specimen in such cases should be meticulously sampled to rule out associated DCIS and invasive component since it effects both prognosis and treatment outcome.

Disclaimer: This manuscript has not been published and is not under consideration for publication elsewhere.

Conflicts of Interest: We have no conflicts of interest to disclose.

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