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Papillary carcinoma breast: A tertiary care institute experience

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Abstract
Introduction: Breast cancer is the most common cancer in women globally and in India. Papillary lesions of the breast constitute around 5% of all the breast lesions. They encompasses a morphologically heterogeneous group of lesions, all of which share a growth pattern characterised by the presence of arborescent fibrovascular stalks lined by epithelial cells with or without a layer of myoepithelial cells. Invasive papillary carcinoma is an invasive adenocarcinoma which has predominant papillary morphology >90% in the invasive component. Invasive micropapillary carcinoma is a rare type accounting for only 0.9 to 2.0% of all invasive breast tumours. Encapsulated papillary carcinoma consists of fibrous capsule surrounding a nodule composed of delicate fibrovascular stalks, covered by monomorphic population of neoplastic epithelial cells. Micropapillary carcinoma is characterized by higher incidence of lymph node metastasis and lymphovascular invasion resulting in poor prognosis. The purpose of this study is to share the last 13 years experience regarding papillary lesions of breast in the department of pathology in our institute.
Material and Methods: A 13-year (2006-2019) retrospective review of database of patients diagnosed with breast cancer was performed. The medical records of 8 patients with papillary breast cancer who underwent surgery were retrieved and their clinical data, surgical treatment and pathological findings were reviewed.
Results: A total of 884 patients underwent mastectomy for invasive breast cancer during the 13 year period. Out of 884 patients, eight were diagnosed with papillary carcinoma breast (0.90%). Amongst the eight, three were diagnosed as invasive papillary carcinoma, two as encapsulated papillary carcinoma and rest three as invasive micropapillary carcinoma. The mean age of presentation was 63.3 (range 45-80) years. The tumour size ranged between 3.5 to 6cm in its greatest dimension. Two out of eight patients had lymph node metastasis with no distant metastasis.
Conclusion: Papillary carcinoma of the breast is a rare entity, the reported incidence of pure micropapillary carcinomas is 0.9 to 2% of all breast cancers. It is associated commonly with lymph node metastasis at the time of presentation and have relatively poor prognosis. Much lower prevalence of papillary carcinoma breast was seen in our institutional study.

Keywords: breast, carcinoma, papillary, micropapillary

Introduction

Invasive breast cancer is the most common carcinoma in women, accounting for 23% of all cancers in women globally and now the most common cancer in Indian women , having recently overtaken cervical cancer in this respect.[1]Papillary breast cancer represents approximately 0.5% of these invasive breast cancers.[2]They encompasses a morphologically heterogeneous group of lesions, all of which share a growth pattern characterised by the presence of arborescent fibrovascular stalks lined by epithelial cells without a layer of myoepithelial cells.[3] Encapsulated papillary carcinoma also known as intracystic or encysted papillary carcinoma is composed of delicate fibrovascular stalks, covered by a monomorphic population of neoplastic epithelial cells, surrounded by thick fibrous capsule.[4] Invasive papillary carcinoma is an invasive adenocarcinoma which has predominant papillary morphology in >90% in the invasive component. Invasive micropapillary carcinomas are rare accounting for approximately 0.9-2.0% of invasive breast cancers. [5] Micropapillary carcinoma is characterised by higher incidence of lymph node metastasis and lymphovascular invasion resulting in poor prognosis. [6]
The purpose of this study is to share the last 13 years experience regarding papillary breast carcinomas, of the Department of Pathology of our institute which is a tertiary care centre of

North India.

Material and Methods: This study was done in Pathology department of our institute, a tertiary care centre of North India. A 13-year (July 2006 – June 2019) retrospective review of database of patients diagnosed with breast cancer was performed. The prevalence of various pathological types of breast cancer based on database of our institution was determined. The medical records of 8 patients with papillary breast carcinomas who underwent surgery were retrieved and their clinical data, surgical treatment and histopathology reports along with the histopathology slides were reviewed in detail. The patients in whom the diagnosis of papillary carcinoma of breast (including encapsulated papillary, invasive papillary and micropapillary breast carcinoma) was given on histopathology was only included in the study. Patients of breast cancer of other pathological types were excluded from the detailed study. All procedures done and methods used in this study were in accordance with the ethical standards of institutional research committee.

Results

A total of 884 patients underwent mastectomy for invasive breast cancer during the 13 year period. Amongst which six (0.68%) were male patients and rest were females (99.32%). Most common histopathological diagnosis was Invasive carcinoma of no special type (91.18%) followed by lobular (3.17%), mucinous carcinoma (1.58%) and other rare varieties. Out of 884 patients, eight were diagnosed with papillary carcinoma breast (0.90%). Amongst the eight, two were diagnosed as encapsulated papillary carcinoma, three as invasive papillary carcinoma and rest three as invasive micropapillary carcinoma. The mean age of presentation was 63.3 (range 45-80) years. All (100%) patients had a palpable mass in their breast. The laterality of the lesions was left-sided in 02 (25%) patients and right-sided in 06 (75%) patients. All patients underwent modified radical mastectomy. All the cases in this study presented with a hard grey white area ranging from 3.5 to 6cm in cross section on mastectomy specimen. Two out of eight patients had lymph node metastasis with no distant metastasis.

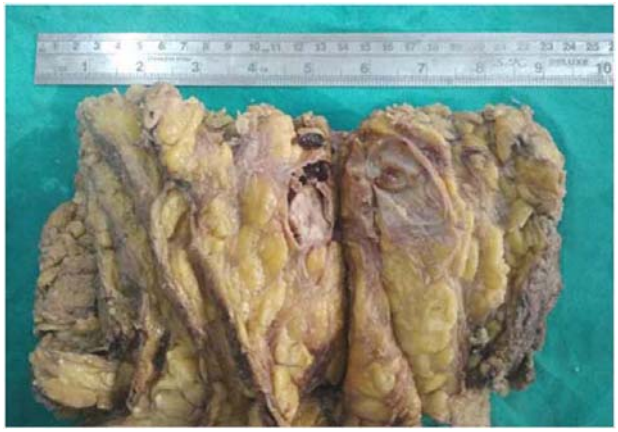

Fig 1: Mastectomy specimen showing a grey white hard growth enclosed with in an encapsulated cystic space. (Encapsulated Papillary Carcinoma)

On microscopic examination encapsulated papillary cacinoma showed a fibrous capsule surrounding a nodule composed of delicate fibrovascular stalks, covered by monomorphic population of neoplastic epithelial cells. This carcinoma typically lacked myoepithelial cells both within the fibrovascular cores and at the periphery of the lesion.

Invasive papillary carcinoma showed invasive elements harbouring a papillary architecture with papillae formed by malignant epithelial cells intimately related to fine fibrovascular cores >90% of the invasive component.

Invasive micropapillary carcinoma showed presence of hollow or morula like aggregates of cuboidal to columnar neoplastic cells devoid of fibrovascular cores, surrounded by empty stromal spaces. Cells displayed a reverse polarity (i.e.inside-out pattern), whereby the apical pole of neoplastic cells faced the empty stromal spaces rather than the hollowed central aspects of the tumour cell aggregates.

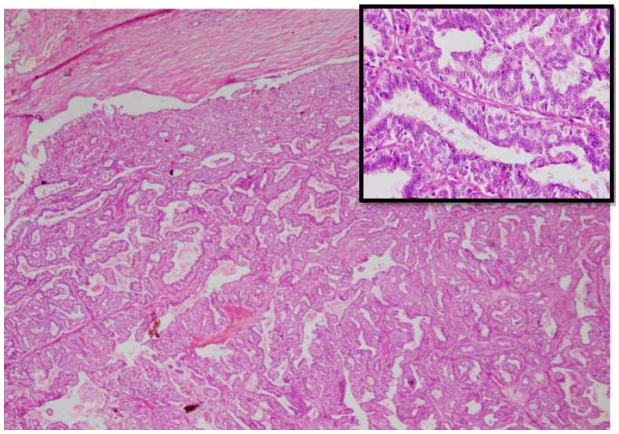

Fig 2: Photomicrograph of encapsulated papillary carcinoma showing papillae covered by neoplastic cells surrounded by a thick fibrous capsule. (H&E; 10X), inset shows that papillae are lined by neoplastic epithelial cells and lack myoepithelial cells at higher power. (H&E; 40X)

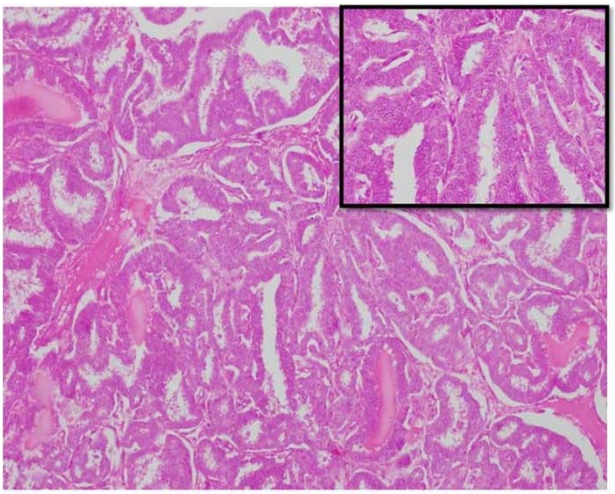

Fig 3: Photomicrograph of invasive papillary carcinoma showing tumour cells >90% of which have frankly papillary configuration. (H&E; 10X), inset shows fibrovascular cores covered by cytologically atypical tumour cells at higher power. (H&E; 40)

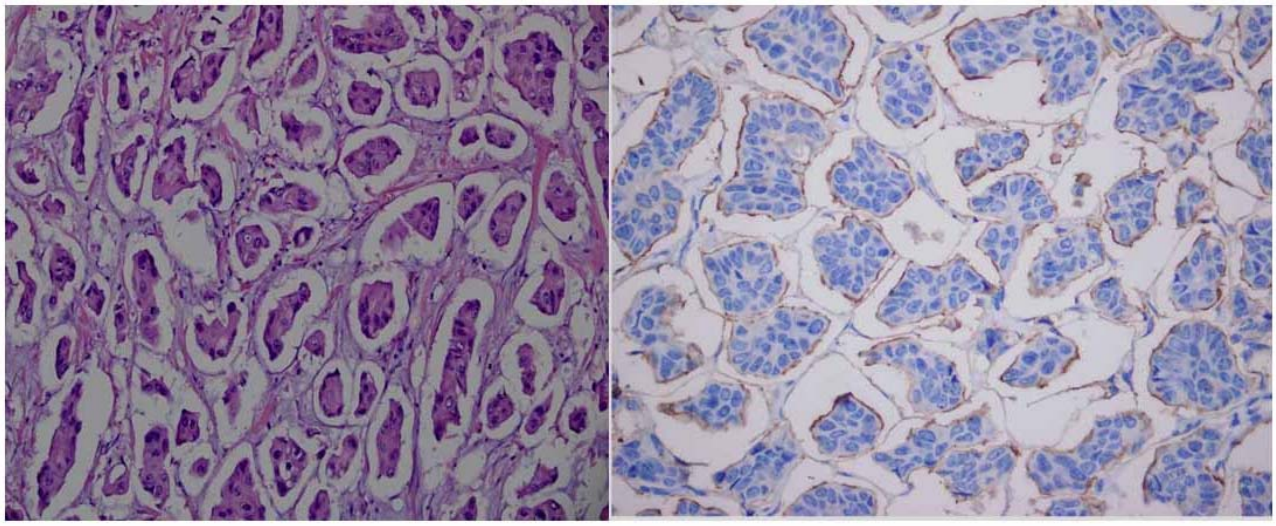

Fig 4(a): Microphotograph showing cells displaying a reverse polarity (i.e. "inside-out" pattern) in micropapillary carcinoma.(H&E ;40X) and 4(b) Intense EMA immunoreactivity is seen around the outside of the glands, emphasizing the "inside-out" pattern or reverse polarity in 76-100% of the neoplastic cells depicting score 4+.

Discussion

Papillary breast cancer represents approximately 0.5% of all breast cancers. In our study the reported incidence of papillary breast carcinoma is 0.90%. Any papillary growth of the breast presents both a diagnostic and a therapeutic challenge. For each one of them a diagnosis of whether they are malignant or benign in nature as well as appropriate staging and suitable treatment is required. Histological characterisation of papillary carcinoma breast suggests proliferation of cells arranged around fibrovascular cores, grossly forming a circumscribed mass. Some papillary carcinomas may create a lump large enough to feel with the fingers, and that may cause breast tenderness. Discharge is also possible. Often, papillary carcinomas don't cause any symptoms and are not caught with breast self-examination. [7] In our study all the cases of papillary breast carcinoma presented with clinically palpable breast lump. Papillary carcinoma breast is more frequent in the elderly women (median age of 69.5 years, range (22 to 99) and much more frequent in women than in men. Also in our study all the cases of papillary carcinoma breast was seen in elder women. The mean age of presentation was 63.3 (range 45-80) years. In the large study using data from the database of the National Cancer Institute, Surveillance, Epidemiology and End Results 1973-1998, Giordano *et al*, reported 385,683 cases of breast cancer of which 2,537 (0.65%) involved men. Of these men, only 63 (2.6%) had papillary histology. [8] In our study out of 884 patients underwent mastectomy for invasive breast cancer during the 13 year period only six (0.68%) were male patients and rest were females (99.32%). Out of eight patients diagnosed with papillary breast carcinoma all were female, none of the male patients had papillary histology. Various papillary lesions of the breast includes – intraductal papilloma, intraductal papilloma with ADH, encapsulated papillary carcinoma, intraductal papillary carcinoma, solid papillary carcinoma, invasive papillary carcinoma and micropapillary carcinoma. Intraductal papilloma and papilloma with ADH are considered as benign papillary lesions of breast whereas malignant papillary lesions of breast includes encapsulated papillary carcinoma, intraductal papillary carcinoma, solid papillary carcinoma, invasive papillary carcinoma and micropapillary carcinoma. Encapsulated Papillary Carcinoma of the breast (EPC) is a rare malignancy accounting for <0.5% of all breast cancers. [9] In our study encapsulated papillary carcinoma breast accounts for (0.23%) of cases. In encapsulated papillary carcinoma breast , cells can be arranged in solid or cribriform patterns and exhibit low- or intermediate-grade nuclei.[4] Myoepithelial cells are not present, neither at the periphery of the lesion nor within the fibrovascular cores and their absence can be verified by immunohistochemical stains. These lesions have been traditionally regarded as a variant of DCIS by most authorities given their discrete nodular growth, lack of stromal reaction.[10] The carcinomatous epithelium in encapsulated papillary carcinoma is negative for high molecular weight cytokeratins -CK5/6, CK -14 and shows strong diffuse positivity with ER and PR, although high-grade tumors with less-consistent ER staining are occasionally encountered.[11] Its matter of debate as some other studies shows that this tumor represents an indolent form of invasive carcinoma, as the absence of peripheral myoepithelium argues against the concept of an in situ carcinoma. As a consequence, staging of pure EPC is controversial. However, according to the WHO Working Group, these lesions, in the absence of conventional invasive carcinoma, should be considered and treated as Tis disease. In our case also papillae are lined by neoplastic epithelial cells with the absence of peripheral myoepithelial cells .The latter proposal has been further supported by the finding of occasional lymph node and distant metastasis associated with these lesions.[12] In our study also both the cases of encapsulated papillary carcinoma had no lymph nodes metastasis. A minority of encapsulated papillary carcinomas may be associated with a component of invasive carcinoma (invasive carcinoma arising in an encapsulated papillary carcinoma). The invasive component is characterized by an infiltrative appearance with extension beyond the fibrous capsule of the lesion and an associated stromal reaction. Invasive areas in general do not display

papillary features, but rather exhibit the morphology of an invasive ductal carcinoma, not otherwise specified. In cases of encapsulated papillary carcinomas with associated invasion, it is currently recommended that staging be determined based on the size of the invasive component only, without consideration of the encapsulated component of the tumor, in order to prevent over treatment.[13] Papillary carcinomas of the breast (EPCs included) present some architectural histological similarities to papillary thyroid carcinoma, but without any evidence of rearranged during transfection (RET) oncogene rearrangements. [14] The term invasive papillary carcinoma is reserved for infiltrating breast carcinomas exhibiting a exclusive papillary morphology >90% of the invasive component and should be distinguished from another malignant papillary lesions. [15] Encapsulated and solid papillary carcinomas are not currently classified as invasive papillary carcinomas, though a subset of these tumors may represent low grade carcinomas exhibiting an expansile type of invasion. [16] True invasive papillary carcinomas are very rare. In our study invasive papillary carcinoma constitutes only (0.34%) of cases. Invasive papillary carcinoma should not be confused with invasive micropapillary carcinoma, which is a clinically and pathologically separate entity. The distinction of invasive papillary from micropapillary carcinoma has relevant clinical implications as the latter is considered an aggressive form of mammary carcinoma frequently associated with lympho-vascular invasion and axillary lymph node metastases. The IMPC is a relatively rare tumor, first described in the breast by Fisher *et al*. [17] in 1980, where this configuration was referred as having an "exfoliative appearance." After 13 years, the term invasive micropapillary carcinoma of the breast was proposed by Siriaunkgul and Tavassoli. [18] It is a rare variant of breast carcinoma accounting for 0.9 to 2.0% of invasive breast cancers associated with a poor prognosis. The reported incidence of micropapillary carcinoma breast in our study is (0.34%). However, the incidence of IMPC has been increasing since 2008 mostly due to better recognition of its histological features. [17] We also have reported these three cases in the duration of last two years. IMPC shows a highly distinctive architecture, characterized by tufts of cells arranged in pseudopapillary structures devoid of fibrovascular cores and surrounded by empty, clear spaces lined by delicate strands of fibrocollagenous stroma. The cells often display an inside-out arrangement, with the luminal aspect of the cell present on the outer surface of the cluster. Correct diagnosis of micropapillary carcinoma is important because of its aggressive nature. The aggressiveness of invasive micropapillary carcinoma is presumed to be related to lymphotropism and inverse polarity of tumour cell clusters. Micropapillary carcinoma has higher frequency of axillary lymph node metastasis present in upto 100% of the cases in some studies.[18] Guo *et al* found that 55% (28 of 51) of the IMPCs had dense lymphocytic infiltrates, and 96% (27 of 28) of them developed LNM, significantly more than the 61% (14 of 23) in the group without lymphocytic infiltrates.[6] Zekioglu *et al* suggested that extranodal tumor invasion was responsible for the frequent local tumor recurrence in chest walls and supraclavicular nodes. In our study two out of three cases (66% of cases) of micropapillary carcinoma showed lymph node metastasis. Nassar *et al*. reported that the nodal status and skin involvement were the only parameters that predicted a poor prognosis in IMPC [5]. The prognosis of IMPC is significantly worse than that of invasive ductal carcinoma of the scirrhous type and the 5-year overall survival rate of IMPC is 50.5%, compared to 85.6% in scirrhous type cases. The 5-year recurrence rate was 62.6% for IMPC and 24.0% for scirrhous type tumors. [19] However, another study showed that the disease-specific survival rate in IMPC was similar to that of invasive ductal carcinoma (91.9% versus 88%).[20] Micropapillary carcinoma breast can be confused with invasive ductal carcinoma of NST in which artifactual retraction of stroma around nests of tumour cells can produce similar appearance. IMPC which is positive for hormone receptors and negative for HER2, tend to have a higher incidence of nodal metastasis compared with their counterparts in all invasive carcinomas. In contrast, lesions containing an IMPC component and classified as hormone receptor negative and HER2 positive have a lower incidence of nodal metastasis.[21] Tumour cells of micropapillary carcinoma shows typical (inside out pattern) reverse polarity which can be confirmed immunohistochemically. In other words, lineal deposits of EMA substances can be seen rimming externally clusters and pseudo-tubules of cancer cells, indicating the inversion of the cellular polarity. [22] In our study all the three cases of micropapillary carcinoma breast showed Intense EMA immunoreactivity around the outside of the glands, emphasizing the "inside-out" pattern or reverse polarity in 76-100% of the neoplastic cells depicting score 4+.

Conclusion

Papillary carcinoma of the breast is a rare entity, the reported incidence of papillary carcinomas is 0.5% of all breast cancers. The reported incidence in our study is 0.82%. Familiarity with morphological features of malignant papillary proliferations and their separation from benign intraductal papilloma is important. Hence it is important to make a correct and early diagnosis especially in case of micropapillary carcinoma as it is associated commonly with lymph node metastasis at the time of presentation and have relatively poor prognosis. This can be recognised fairly, accurately on the basis of histopathological features and further confirmed on immunohistochemistry.

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