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Original Research Article

Papillary Carcinoma of the Breast: Cytohistopathological and Immunohistochemical Study

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Abstract

Introduction: Papillary carcinoma of the breast is very rare, constituting 1–2% of breast cancers with favourable prognosis. However cytohistopathologic features of these have not been studied in great detail.

Aim and Objective: To analyze the clinical presentation, cytomorphological aspects, histopathological features and immuno histochemical study of papillary carcinoma.

Material and Methods: The present study included 06 retrospective cases of papillary carcinoma of breast in a regional cancer centre in north eastern part of India during a period of 5 years. FNAC was carried out on all of them. Cytomorphological features were studied and correlated with clinico-histopathological features. In all cases Immunostaining for ER, PR and HER2neu was done.

Results: This was a retrospective study of 06 cases of papillary carcinoma out of total 1250 cases of breast cancer over a period of 5 years. On cytological examination, 2 cases were reported as papillary neoplasm suspicious of malignancy. Rest 4 cases reported as papillary carcinoma. Histopathological examination was done in all 6 cases and reported as intracystic papillary carcinoma in 2 cases and invasive carcinoma in 4 cases. 5 cases had strong staining for estrogen and progesterone receptors. One case was triple negative. Only one case was positive for HER2neu.

Conclusion: Papillary carcinoma of the breast is very rare. The utility of FNAC is limited by the overlapping morphological features of benign and malignant neoplasm. Thus for papillary lesions diagnosed using FNAC, excision is required to facilitate accurate diagnosis.

Keywords: Intracystic; Invasive papillary carcinoma breast.

Introduction

In 2018, an estimated 2,088,849 (11.6% of all sites) cases of breast cancer in both sexes were diagnosed worldwide and leading to 626,679 (6.6%) deaths.[1] Papillary breast carcinoma is very rare, constituting 1–2% of breast cancers.[2] Papillary carcinoma are categorized into solid, intracystic without invasion, intracystic with a focus of invasion and invasive carcinomas.[3] Preoperative cytology sometimes pose a diagnostic challenge due to overlapping morphologic features of benign and malignant neoplasms. Histopathology helps in confirmatory diagnosis. Hormone receptor testing enables application of more targeted therapy.

In literature, studies on papillary carcinoma encompass a very small number, mostly case studies.[3] We present a study of detailed

cytohistological and immunohistochemical study of 06 cases with their clinical correlation.

Material and Methods

This is a retrospective study of 06 cases of papillary carcinoma of breast in a regional cancer centre in north eastern part of India during a period of 5 years.

Inclusion criteria: Patients with diagnosed papillary carcinoma.

Out of total of 1250 cases of breast cancer cases, 06 cases of histologicaly proven papillary breast cancer were studied. In all cases cytology slides, H&E and IHC slides were retrieved and reviewed if availabale. Relevant clinical and pathological information like age, tumor size, grade, nodal status were recorded.

For sake of uniformity, all immunostained slides were reviewed using the following criteria.

Assessment of ER and PR-ER and PR were considered positive if >1% tumor cell nuclei are immunoreactive and negative if less than 1% immunoreactive.[4]

Assessement of HER2/neu – HER2/neu immunohistochemical staining was scored from 0 to 3+ using FDA approved Hercept guideline into following categories : 0– No immunostain; 1– Weak incomplete membrane positivity in any proportion of tumor cells; 2– complete membranous stain,either non-uniform or weak in at least 10% tumor cells ; 3– intense uniform staining in at least30% tumor cells.0 and 1+ is negative ,2+ equivocal or borderline and 3+ is considered as positive.[5]

Result

In the present study total number of patients comprised of 06 cases who were diagnosed as papillary carcinoma out of total 1250 cases of carcinoma breast diagnosed during a period of 5 years. The age of the patients ranged from 44 to 79 years with a mean being 58.5 years (Table 1). Size of the swelling ranged from 1.8 cm to 4.0 cm. On cytological examination (Table 2), 2 cases were reported as papillary neoplasm suspicious of malignancy. Rest 4 cases reported as papillary carcinoma. Histopathological examination was done in all 6 cases and reported as Intracystic carcinoma in 2 cases and invasive papillary carcinoma in 4 cases (Table 3). In all cases IHC was done and reported as follows (Table 4).

Table 1: Clinical features of 6 cases.

S.No.	Age/Sex	Presenting Symptom	Tumor Size	Axillary Lymphadenopathy
1	61Y/F	Painless mass right breast	3x2 cm	–
2	50Y/F	Painless lump left breast	4x3 cm	–
3	55Y/F	Painless mass right breast+Nipple retraction	3x3 cm	+
4	44Y/F	Painless mass right breast+Bloody discharge	3cm in diameter	–
5	62Y/F	Gradually increasing lump right breast+bloody discharge	2x2 cm	–
6	79Y/F	Painless subareolar mass left breast	1.8 cm	–

Table 2: Cytological Features of 6 cases.

Cytological Features	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Cellularity	High	High	High	Moderate	High	High
Papillary Fragment	Many	Occasional	Many	Few	Many	Few
Cystic Macrophages	+	–	–	+	–	–
Apocrine cells	–	–	–	+	–	–
Atypia	Mild	Mild	Moderate	Mild	Moderate	Mild
Diagnosis on FNAC	Papillary carcinoma	Suspicious for Papillary carcinoma	Papillary carcinoma	Suspicious for Papillary carcinoma	Papillary carcinoma	Papillary carcinoma

Table 3: Histological features.

Histological Features	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Fibrovascular Septa	+	+	+	+	+	+
Palisading	+	+	+	+	+	+
Nuclear Atypia	1	1	2	1	1	2
Mitotic Count (per 10 hpf)	2	3	8	0	4	1
DCIS Component	_	_	+	_	+	_
Invasive Tumor	+	_	+	_	+	+

Table 4: IHC Findings.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
ER	+	+	–	+	+	+
PR	+	+	–	+	+	+
HER2neu	+	–	–	–	–	–

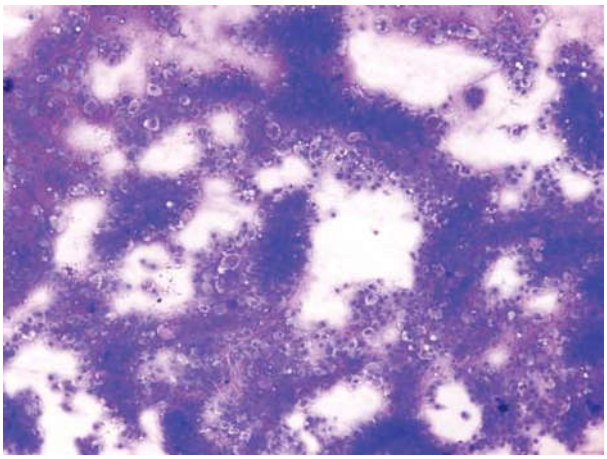

Fig. 1: Papillary fragments of cells with nuclear atypia, FNA (MGG stain 100X).

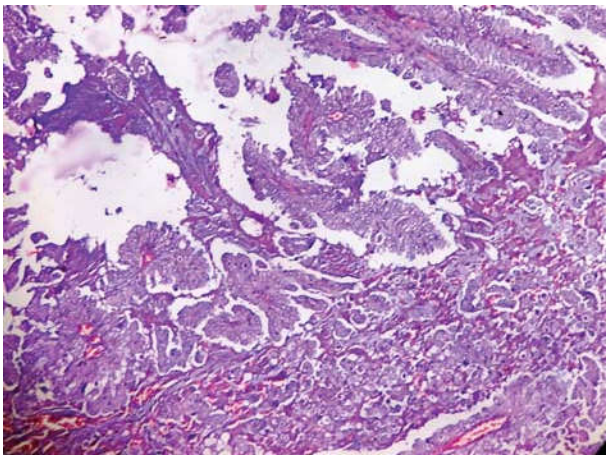

Fig. 2: Intracystic Papillary Carcinoma of breast (H&E stain 100X).

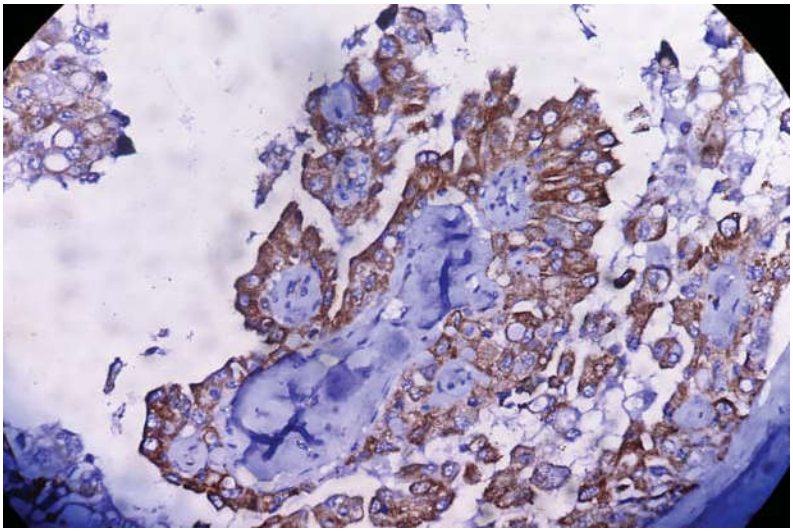

Fig. 3: Immunohistochemistry for Her-2/neu 3+, Positive.

Discussion

A 5 year study was done to study cytolohistogical and immunohistochemical features of papillary carcinoma.

Papillary lesions of the breast encompass a complete spectrum including benign lesions (papilloma) to intraductal/intracystic papillary carcinoma to invasive papillary carcinoma. Papillary carcinomas are characterized by fibrovascular core covered by neoplastic epithelial cells with absence of myoepithelial cell layer within fibrovascular core and periphery of lesion, differentiating it from benign papillary lesions.[6]

Age of patient varied from 44–79 years (mean 58.5 years). Otsuki et al reported mean age 66 years (ages 31–80 years).[7] The commonest presenting symptom was painless lump in breast seen in 4 cases followed by bloody discharge (2 cases) and nipple retraction. Similar observations were made by Leena J.B. et al.[8] However, bloody discharge is the most common presenting symptom in literature.[9] In literature, tumor size varies from less than 1 cm to 15 cm.[10,11,12] In our study size of swelling ranged from 1.8 to 4 cm.

In this study out of 6 cases, 2 cases were diagnosed as suspicious for papillary carcinoma and 4 as papillary carcinoma on FNAC. Diagnosis

was based on presence of cells in clusters and papillary fragments with mild to moderate atypia. Macrophages and apocrine metaplasia was seen in few cases. Cellular changes such as high cellularity, variable nuclear enlargement, pleomorphism, papillary fragments, single cell type, hemosiderin laden macrophages, apocrine metaplasia, mitosis and absence of bipolar nuclei are suggestive of papillary carcinoma.[13,14] However the distinction between papillary carcinoma, papilloma and other lesions with papillary component like fibroadenoma and fibrocystic change cannot be reliably made on FNAC.[13] Thus for papillary lesions diagnosed using FNAC, excision is required to facilitate accurate diagnosis.[15]

In our study, on histology 2 cases which were labelled as suspicious for papillary carcinoma on FNAC were diagnosed as intracystic papillary carcinoma. Intracystic papillary carcinoma is characterized by malignant papillary proliferation involving a cystic duct with absence of myoepithelial cells at periphery. Some studies propose that intracystic papillary carcinoma may be form of carcinoma in transition between insitu and invasive carcinoma.[16] According to WHO Working group intracystic papillary carcinoma without invasion should be staged and treated as Tis.[16] Remaining four cases were diagnosed as invasive carcinoma based on presence of malignant epithelial cells beyond the fibrous capsule and stromal reaction. Frank invasion should be differentiated from entrapped malignant epithelial cells in the fibrous capsule and from their displacement into the needle entry site. The invasive component can be mucinous or neuroendocrine type carcinoma, ductal carcinoma (NOS) type and rarely micropapillary variant.[10,12] The staging should be based on the size of invasive carcinoma for management, for preventing overtreatment of such cases.[3,17]

Papillary breast cancers are usually positive for the estrogen and/or progesterone receptors and negative for the Her2/neu receptor.[11] In this study, 5 cases had strong staining for estrogen and progesterone receptors. One case was triple negative. Only one case was positive for HER2neu. In the literature only two cases of invasive papillary carcinoma have been reported as triple negative.[18,19] Axillary lymphadenopathy was present in only one case.

Tumor resection with negative margins is the mainstay of treatment for intracystic papillary carcinoma. However, the role of radiotherapy and endocrine therapy in such cases remains unclear.[20] The consensus of National Comprehensive Cancer Network was that receptor-positive diseases in postmenopausal patients with stage IIA to IIIA may be considered for neoadjuvant hormone therapy.[21] Sentinal node biopsy instead of full axillary dissection could be done in patients of intracystic papillary carcinoma with DCIS or invasive carcinoma.[20]

Intracystic papillary carcinoma have a favourable prognosis. In cases with invasive elements, outcome depends on the type of invasive carcinoma.[12]

Conclusion

In conclusion, papillary lesions diagnosed on cytology should undergo excision to facilitate accurate diagnosis. Our study emphasizes that further research should focus on search of new molecular markers and targeted therapy.

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