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Original Research Article

Papillary Neoplasms of Breast- Experience at a Cancer Centre in South India

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Abstract: Papillary neoplasms of breast are a rare entity which poses diagnostic challenge to pathologists. There is limited data regarding this entity in Indian population, majority being case reports. Our objective is to evaluate the demographic, clinicopathologic, survival characteristics and management protocols of this rare entity. This is a retrospective audit of cases reported as papillary neoplasms of breast over a period of 4 years (2013-2016). Data of these patients is retrieved from the Institutional Cancer Registry. A total of 20 cases of papillary neoplasms are diagnosed during this period of which there are16 cases of invasive carcinomas, three cases of carcinoma in situ and a single benign lesion. Mean age of presentation is 57 years, 70% being postmenopausal. There was a single case of male papillary carcinoma. FNAC was done in 55% of cases, with a definite diagnosis of carcinoma in 27% of cases. 60% of cases showed a cystic appearance grossly. Most common histologic type among carcinomas was encapsulated papillary carcinoma with invasion (36%). IHC was performed for myoepithelial markers in all cases and for hormonal status in carcinomas. ER positivity noted in74%, PR positivity in 68% and HER2 positivity in 10% cases. Most carcinomas are of clinical stage IIA and MRM was the most common surgical treatment. In case of carcinomas , mean follow up is 24 months with 94% cases showing disease free survival. There was no incidence of mortality till the last follow up.
Keywords: papillary neoplasm, breast, FNAC.

INTRODUCTION:

Papillary neoplasms of the breast include a broad spectrum of lesions, ranging from benign papilloma, papilloma with atypical ductal hyperplasia (ADH), papillary ductal carcinoma in situ (DCIS) to invasive carcinoma. Distinction between benign, premalignant, and malignant (invasive and non-invasive) components of papillary lesions, especially in core biopsies, is a challenge for pathologists, owing to the overlapping features among these lesions. It is equally challenging to the clinician as the mammary papillary lesions pose dilemma in patient management. Literature review reveals few data regarding this entity in Indian population, most being single case reports. Moreover data regarding treatment of papillary neoplasm is limited and patterns noted in available series suggest a highly variable approach to this disease. The scarcity of information emphasises the need for further diagnostic, treatment and outcome-related studies in papillary neoplasms of the breast.

MATERIALS AND METHODS:

A retrospective single centre study of 4 years duration from January 2013 to December 2016. Data of patients with final diagnosis of papillary neoplasm of breast were retrieved from Institutional Cancer Registry. IHC was done in FFPE tissue using antibodies against p63 for myoepithelial cells and for ER-PR & HER2 receptor status.

OBSERVATIONS AND RESULTS:

A total of 20 cases of papillary neoplasms were studied of which there were16 cases of papillary carcinomas, 3 cases of carcinoma in situ and a single benign lesion- intraductal papilloma. Mean age of presentation was 57 years, 70% being postmenopausal. There was a single case of male papillary carcinoma. No definite side preponderance was noted in our study. 95% of cases presented with breast lump while nipple discharge was the presenting complaint in 5%. Nipple retraction was seen in 3 cases (15%). Mammography was done in 8 cases (40%) with a histo radiological concordance of 87%. FNAC was done in 11 cases (55%) all with a clinicioradiological diagnosis of carcinoma, but a definite diagnosis of carcinoma was made only in 3 cases (27%). Rest was reported as epithelial proliferative lesion with moderate atypia.

60% of cases appeared grossly cystic. Most common histologic type among carcinomas was encapsulated papillary carcinoma with invasion (36%). Papillary pattern predominated. In most cases nuclei exhibited mild pleomorphism (50%) and nucleoli was seen in 7 cases (35%). Necrosis was noted in 20% and calcification in 10% of cases. Most invasive carcinomas belonged to Nottingham Grade II (54%) while 40% belonged to Grade I and 6% to Grade III. Lymphovascular emboli were seen in 25% of invasive carcinomas while perineural invasion was seen in none. Most patients with carcinomas presented at tumour stage –T2 (42%) and nodal status N0 (63%). Metastasis was not seen in any of the cases.

IHC was done for myoepithelial markers in all cases and for hormonal status in carcinomas. ER positivity noted in74%, PR positivity in 68% and HER2 positivity in 10%. Most invasive carcinomas were of stage IIA (50%). MRM was the most commonly performed surgical treatment (80%). 68% also received hormonal treatment. In case of carcinomas, mean follow up is 24 months with 94% cases alive without disease and 6% alive with disease at the time of last follow up. 2 cases of invasive carcinomas and 1 case of intraductal papilloma were lost to follow up.

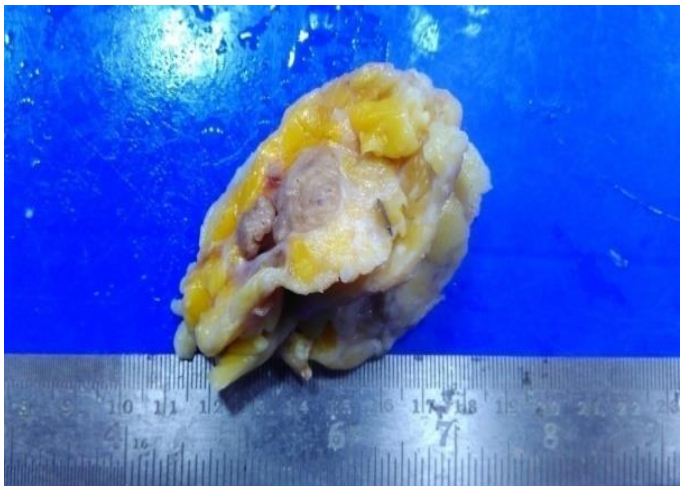


Fig-1: Gross, solid papillary carcinoma

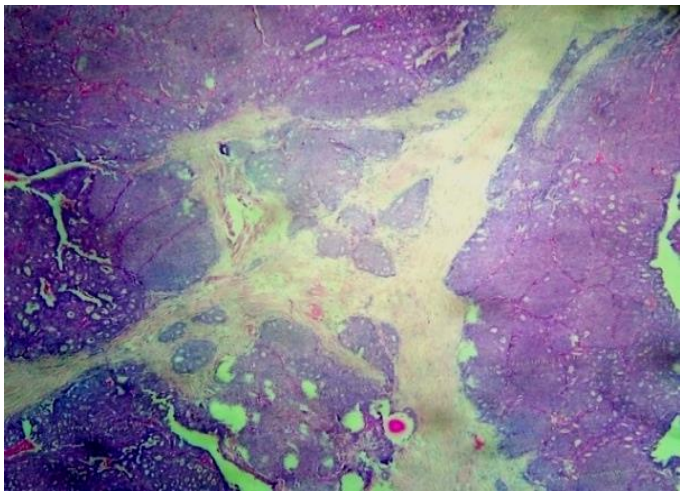


Fig-2: Solid papillary carcinoma

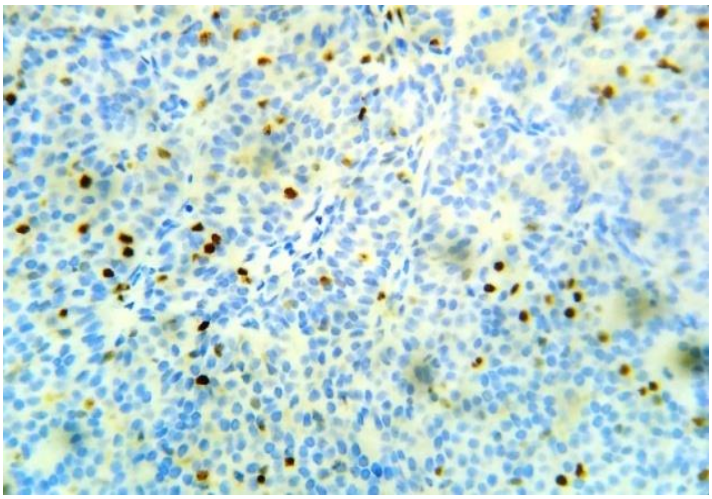


Fig-3: ki67 20-30% invasive papillary carcinoma

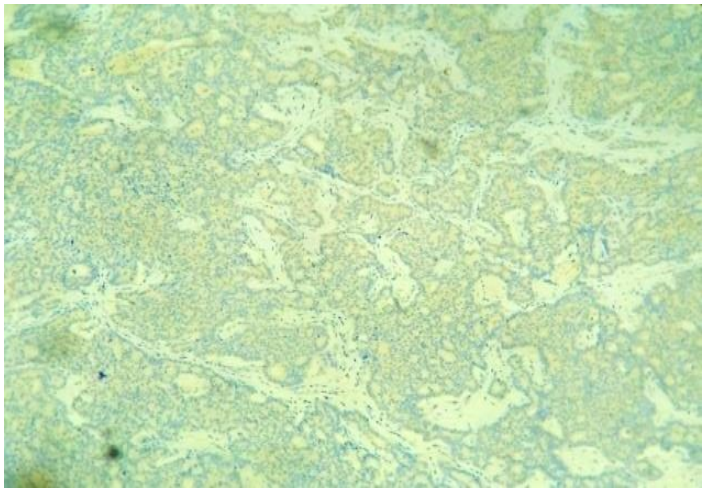
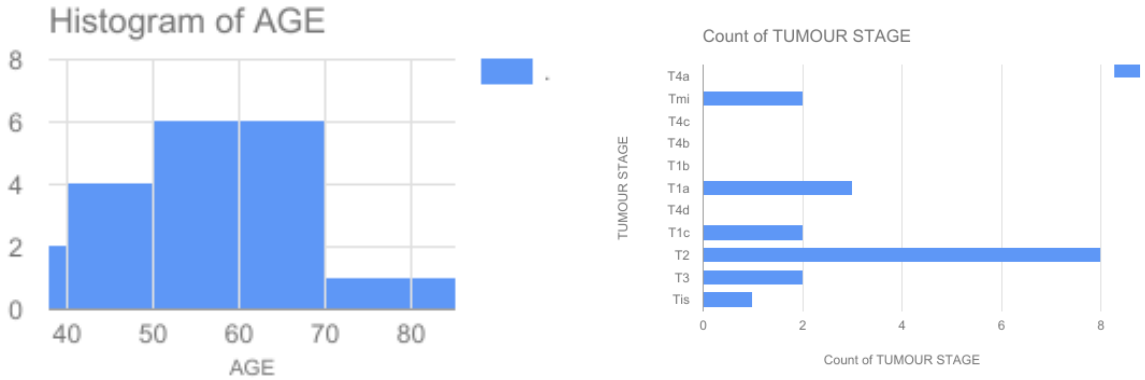


Fig-4: P63 negative (Solid papillary carcinoma)



Papillary carcinoma (invasive and non-invasive):

Type of papillary neoplasm	**Number of cases**
Encapsulated papillary carcinoma with invasion	7
Encapsulated papillary carcinoma without invasion	2
Solid papillary carcinoma with invasion	1
Solid papillary carcinoma without invasion	1
Invasive papillary carcinoma	5
Invasive micro papillary carcinoma	1
Intraductal papilloma with DCIS	2

Papillary carcinoma (invasive and non-invasive):

Feature	**Percentage**
Breast lump as presenting complaint	95%
Mammogram done	40%
Mammogram-histology concordance	87%
FNAC done	55% (n=11)
Definite FNAC diagnosis	27% (n=3)
Predominant histologic type Encapsulated Papillary Carcinoma with invasion	35%
Predominant histologic grade Nottingham grade II	54%
Predominant histologic pattern Papillary pattern	100%
Histologic features: Necrosis Calcification Lymphovascular emboli Perineural invasion Mild nuclear pleomorphism Nucleolus	 20% 10% 25% (inv.ca) 0% (inv.ca) 50% 35%
Predominant tumour stage (inv.ca) T2	42%
Predominant nodal stage (inv.ca) N0	63%%
Immunohistochemistry(IHC) ER +ve PR+ve HER2+ve	 74% 68% 10%
Predominant surgical modality: MRM(surgical) Hormonal therapy	 80% 68%

DISCUSSION:

Papillary carcinoma of the breast is a rare variant of breast cancer representing approximately 0.5% of all newly diagnosed cases of breast cancer [9]. Papillary carcinoma is more often seen in older women, with a mean age in the seventh decade, as compared with other breast cancer subtypes [1]. Though 70% of cases in our study are post-menopausal women, the mean age is 57 years, which is slightly lower than in the published literature. According to Lakhani *et al.;* 50% cases present as a central breast lump and 30% of patients report with bloody nipple discharge [2]. In our study, 95% cases presented with breast lump and 5% with nipple discharge. Papillary lesions of breast have diverse radiological features. Differentiating benign and malignant papillary lesions based on imaging features may often be difficult. A lesion radiologically benign may be malignant in histopathology [3]. In our centre, mammography was done in all cases clinically suspicious of malignancy, and we had an excellent radio histopathological correlation of 87%.

Papillary carcinomas are mostly low grade carcinomas and often have bland nuclei and scanty mitosis. These features make a definite diagnosis of malignancy difficult in FNAC [4, 5]. Most pathologists tend to give a report of epithelial proliferative lesion with atypia. In our study, FNAC was performed in all cases with a clinical suspicion of carcinoma, but a definite diagnosis of carcinoma could be made in only 3 cases. The term papillary neoplasm encompasses a morphologically heterogeneous group of lesions, all of which share a growth pattern characterized by the presence of arborescent fibro vascular stalks lined by epithelial cells [9]. Though pathologic characterization of papillary lesions of the breast is based primarily on morphologic considerations, the use of IHC staining is mandatory in evaluation and accurate classification. The most frequently used groups of markers include myoepithelial and hormone markers.

According to Pal SK *et al.;* loss of myoepithelial cells within the fibro vascular papillae is the most important feature for the identification of malignant papillary proliferations and their separation from benign intraductal papillomas. Myoepithelial cells are difficult to discern on routine hematoxylin and eosin stain preparations and so the help of myoepithelial markers has to be sought. P63 is the usually used myoepithelial marker. This is because unlike other

myoepithelial markers, p63 shows nuclear staining and minimal cross-reactivity with stromal cells or myofibroblasts, and is thus considered to be a superior myoepithelial marker for diagnosis [6]. We have used p63 as myoepithelial marker in all cases.

IHC for hormone receptors ER and PR was done in all carcinomas and HER2 in all invasive carcinomas. ER positivity noted in74%, PR positivity in 68% and HER2 positivity in 10%. Genetic features may also aid in distinguishing papillary carcinoma from benign papillary lesions. Cristofano CD *et al.;* suggested that loss of heterozygosity (LOH) of 16q23 was specific to malignant lesions [11]. Literature review shows that patients with papillary carcinomas were diagnosed with early stage disease, usually stage I. This contrasts with our study where majority of cases were of Stage II [9].

The Netherlands Cancer Registry offers a perspective on different therapeutic modalities. Rendered in practice for patients with papillary carcinoma [10]. In reporting treatment strategy, they stratified patients by age (less than 70, 70 or more than 70). In patients less than 70 years of age, 31% received surgery alone, while 45% received surgery with radiation therapy. Systemic therapy was offered with surgery in 10% and triple modality of therapy namely surgery, radiotherapy and chemotherapy was rendered in an additional 10% patients. In patients aged 70years or greater, 29% received surgery alone and 42% received surgery and radiation therapy. MRM was the most commonly performed surgical treatment (80%) in our institution. 68% also received hormonal treatment.

CONCLUSION:

Papillary lesions include a broad spectrum of lesions, ranging from benign to malignant. Pathologists, clinicians and radiologists should be aware of the emerging studies that have defined specific histologic, molecular, radiographic and prognostic features of papillary neoplasms of the breast. Papillary carcinomas are usually low grade tumours with good prognosis, except for invasive variants, the prognosis of which depends on grade and stage of tumours [8]. We had similar experience - 90% cases are alive without disease and 5% alive with disease in a mean follow up period of 24 months. Future researches on the topic should be based on morphological and molecular diversity of papillary neoplasms with emphasis on treatment- and outcome-related analyses of this heterogenous group of lesions.

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