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Case Series

Pathology Section

Uncommon Papillary Lesions in Human Breast-Rare Pathology

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ABSTRACT

Breast cancer is a lesion that usually affects female but the male community is not spared from being affected. The cause of male breast cancer is not clear but predisposing factors found are increased age over 50's, family history of breast cancer, Klinefelter's syndrome, obesity with BMI 30 or more. Hyperoestrogenism resulting from gonadal dysfunction, obesity, even excess alcohol consumption causes increased risk of breast cancer in males. we report three cases; two cases of invasive papillary carcinoma of breast in one male patient aged 45 years and one female patient aged 72 years. These two cases presented breast masses which were diagnosed by FNAC and confirmed by histopathological examination. The third case is of a 50 year male reported as Intraductal papilloma on histopathology.

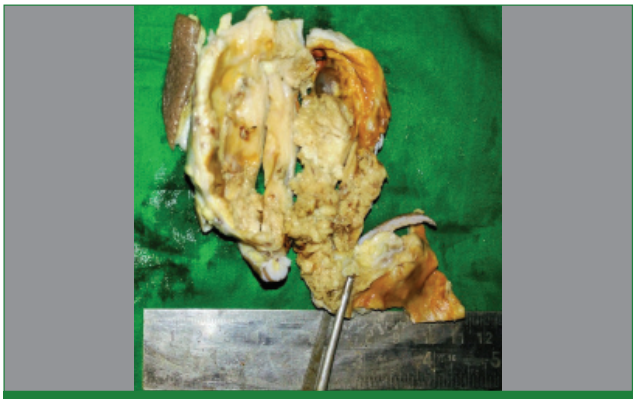
Keywords: Intracystic, Immunohistochemistry, Myopepithelial, Papillary carcinoma, Papilloma

In males, breast carcinoma is rare accounting for 0.6% of all malignancy and less than 1% of all malignancies in men [1]. Papillary carcinoma is one subtype of breast carcinoma which may be intracystic or intraductal and may be invasive or non-invasive. Intracystic Papillary Carcinoma (IPC) is extremely rare in males constituting 5-7.5% of all breast carcinoma in male population [2].

CASE REPORT

Case-1

A 45-years-old, non-diabetic, hypertensive male patient presented with a swelling in the right breast. The swelling was pea sized 9 months ago. Then the swelling gradually increased in size and it was about 7 x 5 x 2.5 cm. It presented as a painless lump with no associated discharge or nipple retraction. This was associated with mild weight loss and associated weakness as said by the patient.There was no positive family history. Ultrasonography revealed a cystic lesion with presence of a frond like mass within a dilated duct, a complex intracystic lesion. Mammography showed a circumscribed area in the sub-areolar region of the breast with partially obscured margins Fine Needle Aspiration (FNA) of the lesion yielded blood mixed material. Few atypical cells were seen which raised suspicion of ductal carcinoma of breast. Mastectomy was performed. Right sided mastectomy specimen which was partially skin covered was received, measuring 7.5x7.0x2.5 cm [Table/Fig-1] overlying skin eclipse measured 6.5x5.5 cm. Nipple areola complex was intact. On cut there was a growth measuring 6x3x2 cm. The growth was friable showing cystic areas as well as pale white papillary structures projecting into the cavity. It was 0.3 cm from the first margin, 0.5 cm from second margin, 0.3 cm from the base. It was extending upto the mediolateral margin and 1.2 cm from the other mediolateral margin. Post operative period was uneventful. As no lymph nodes were found positive and also the resected margins were negative, chemotherapy was not done.

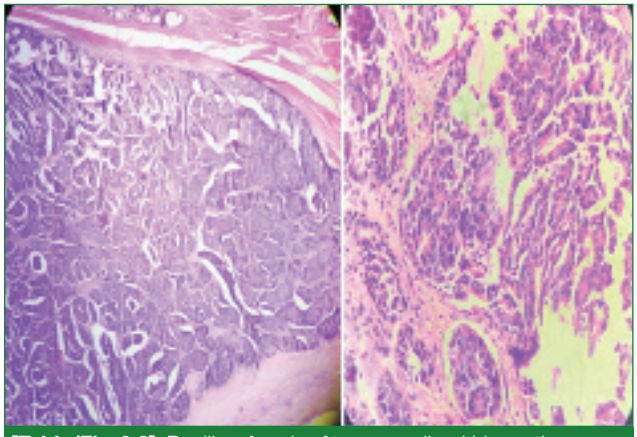


[Table/Fig-1]: Mastectomy specimen with greyish-white friable mass and small papillary projections.

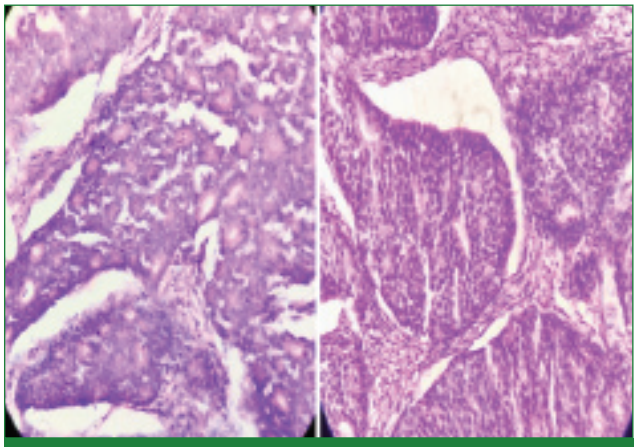
On histopathology, cystic spaces having papillary fronds were seen [Table/Fig-2,3]. These papillary fronds are lined by atypical columnar cells. These papillary fronds are supported by fibrovascular core. Fibrovascular cores covered by a single layer of epithelium without an intervening myoepithelial layer were evident [Table/Fig-4,5]. On immunohistochemistry, ER-PR was found positive and HER2/neu was negative [Table/Fig-6,7]. Ki-67 not done as papillary lesion was not very actively

proliferative lesion and shows good prognosis. Disease respond well to surgical management and radiotherapy.

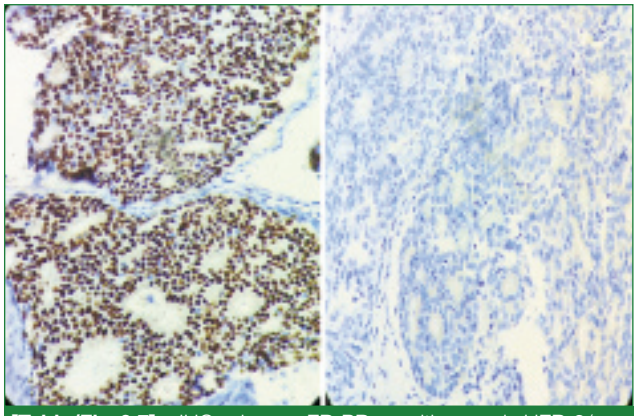
This case is presented with the consent of patient.



[Table/Fig-2,3]: Papillary fronds of tumour cells within cystic spaces (H&E, 100X).



[Table/Fig-4,5]: Papillae lined by atypical columnar cells with stratification and fibrovascular core (H&E, 400X, 100X).

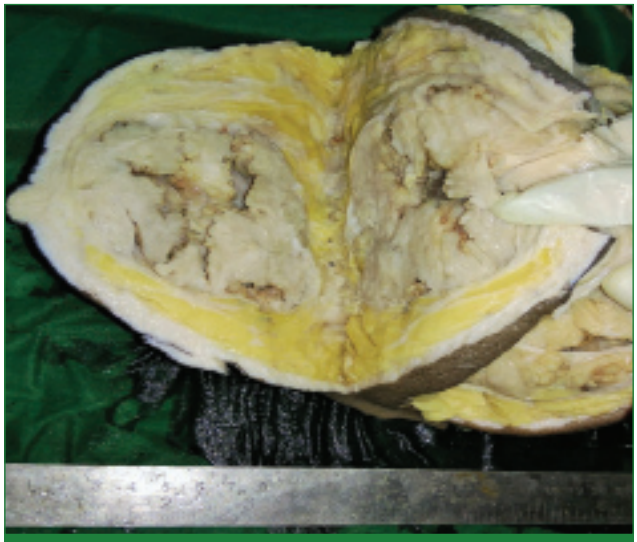


[Table/Fig-6,7]: IHC shows ER-PR positive and HER-2/neu negative.

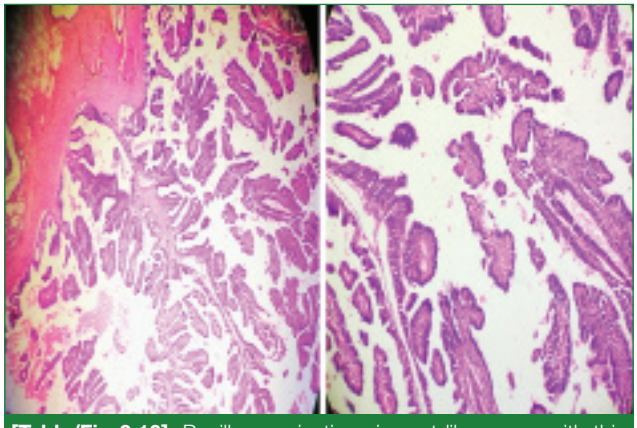
Case-2

A 72-year-old female who presented with complaints of breast lump which gradually increased in size. On FNA, blood mixed material obtained showing occasional atypical ductal cells and extensive necrosis. She underwent modified radical mastectomy for the mass in the left breast. On gross examination, specimen measured 15x8x1.5 cm [Table/Fig-8]. Skin with nipple and areola measured 8x6 cm. Serial sections of the mass in the sub-areolar region revealed a tumour measuring 5x3 cm. Tumour was situated 0.5 cm below the resected margin. Nipple areola complex was intact. Cut section was greyish white in colour and showed small papillary projections. Small haemorrhagic areas were also seen. Five lymph nodes identified but no lymph node was found positive. Patient is passing unremarkable post-op life. Ki-67 not done as papillary lesion are not very actively proliferative and show good prognosis. Disease responded well to surgical management and radiotherapy.

On histopathological examination, atypical epithelial cells was found arranged in papillary, cribriform as well as in solid



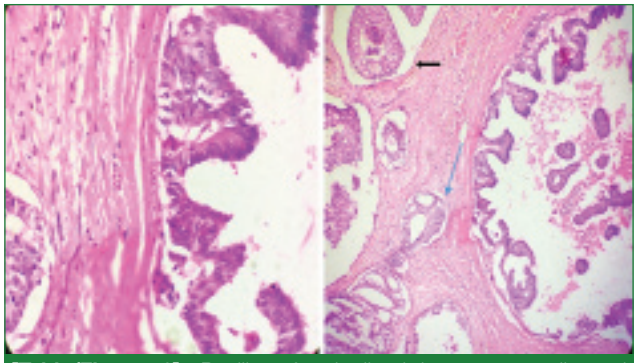
[Table/Fig-8]: Mastectomy specimen show greyish white friable growth with papillary projection in cystic areas.



[Table/Fig-9,10]: Papillary projections in cyst like space with thin fibrovascular core (H&E, 100X).

patterns within a cyst [Table/Fig-9,10]. Atypical epithelial cells lining the fronds show increased nuclear cytoplasmic ratio with hyperchromatic nucleus and prominent nucleoli. These cells are showing uneven stratification and loss of polarity also. The tumour cells invaded the stroma and deeper muscles and there were occasional mitoses [Table/Fig-11,12]. Micropapillary fronds are also seen. Numerous areas of necrosis were seen. It was reported as invasive papillary carcinoma breast. On immunohistochemical study the tumour cells were ER and PR positive and HER-2/neu negative.

This case is presented with the consent of patient.

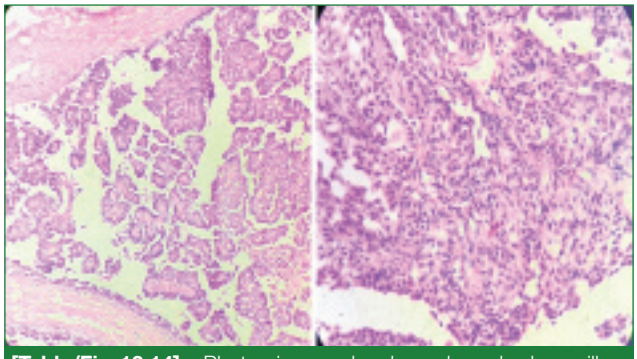


[Table/Fig-11,12]: Papillary fronds lined by tumour cells and necrosis (black arrow) and stromal invasion (blue arrow) respectively (H&E, 400X and 100X).

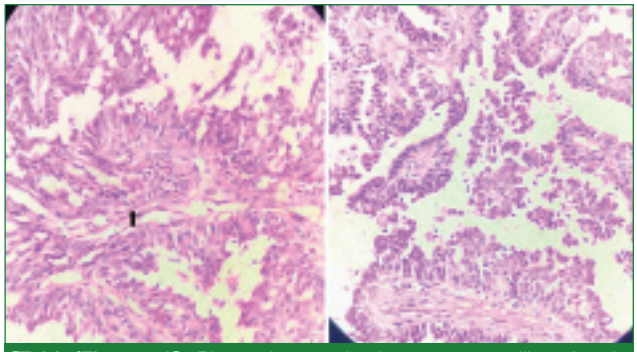
Case-3

A 50-year-old male presented with small breast lump since five months. FNAC was attempted, no material was obtained. He underwent quadrantectomy. On gross specimen it was a friable nodule measuring 3x2x1 cm. Cut section shows heterogenous greyish white areas admixed with cystic and hemorrhagic areas. On histological examination prominent sclerotic fibrous cores were seen. Stromal cores were slender and poorly formed, containing fibrous tissue and vessels [Table/Fig-13,14]. The papillary processes was covered by a two cell types-myoepithelial layer and luminal epithelial layer [Table/Fig-15,16]. Myoepithelial cell layer was interposed between the stroma and luminal cell layer. Finally, it was reported as intraductal papilloma breast. Patient is passing unremarkable post operative life. Ki-67 not done as it was a benign lesion having less significance of proliferative marker.

This case is presented with the consent of patient.



[Table/Fig-13,14]: Photomicrograph show branched papillary structures lined by benign columnar cells and fibrovascular core. (H&E Stain, 100X, 400X).



[Table/Fig-15,16]: Photomicrograph shows true papillary fronds lined by benign cells having fibrovascular core (solid dark arrow) (H&E, 400X).

DISCUSSION

Malignant Papillary Lesion

Incidence of papillary lesions of the breast is less than 10% of benign breast lesions; while these papillary lesions form 0.5-2% of all malignant breast tumours [1,2]. Intracystic papillary breast carcinoma is uncommon in females and exceedingly rare in males [3]. The IPC are more commonly found among older woman with an average age between 55 to 67 years and in man is usually seen more in older age group usually 7th and 8th decades [4]. However, in our patient, IPC developed in earlier decades which were unusual. Nearly 95% cases are unilateral and majority arising in central quadrant of breast. Grossly, tumours are usually bulky in size ranging from less than 1 cm to 15 cm in size [5]. Papillary carcinoma can be divided into invasive and non invasive form. Non invasive papillary carcinoma can be further subdivided into-a diffuse form, the papillary variant of Ductal Carcinoma In Situ (DCIS), and a localized form, IPC [6]. FNA in papillary lesion is not much advantageous as FNA may reveal only areas of DCIS and cyst macrophages. Papillary lesion being peripheral lesion will be left under diagnosed. Macroscopically, papillary carcinoma can present with haemorrhagic as well as cystic areas. Our first case presented with cystic areas whereas second case presented with haemorrhagic solid areas. Haemorrhage in papillary carcinoma is usually due to torsion and infarction of the intracystic nodule. Axillary metastasis is seen very rarely. In this case as well, no axillary metastasis and no recurrence was seen post operative after six months. Historically, IPC was treated with radical mastectomy. However, recurrence rates following treatment with only wide local excision appear to be low. Wide local excision of the breast lesion with or without sentinel node biopsy can be done for pure IPC. Axillary dissection is not required since nodal metastasis is rare. Mastectomy is done for large tumours, for tumours with associated intraductal component and those with frank invasion. Further management for these groups of patients is

radiation therapy and hormone therapy. These lesions show good response to hormone therapy as lesions are usually ER-PR positive [7,8].

Benign Papillary Lesion

Papilloma can be classified as solitary papilloma, multiple papilloma and juvenile papillomatosis [9]. Intraductal papilloma is rare benign lesion of breasts which are of two types. In perimenopausal age group usually central solitary large duct papilloma are seen which are located in sub areolar region near the nipple and peripheral papilloma often are found in terminal duct lobular unit [10]. Papillomas and duct ectasia are associated with nipple discharge [11]. However in our case no nipple discharge was seen. Bloody nipple discharge can occur due to duct obstruction and hemorrhage.

CONCLUSION

Women and men with IPC may have no symptoms, but may present as palpable mass, or may present with bloody discharge. FNA may reveal cellular smear with complex papillae, foamy macrophages, and nuclear hyperchromasia and stratification. However, cytological features being unreliable and inconsistent it is difficult to distinguish between benign and malignant papillary diseases. In papillary lesion, invasion is seen at periphery. FNAC and core needle biopsy samples are obtained from centre of lesion and may miss the lesion, especially if only Ductal Carcinoma in Situ (DCIS) is seen. So again it becomes difficult to differentiate between in situ and invasive lesion. Cytological examination can yield false negative result due to necrotic, degenerative changes in diagnostic cells also. But in above reported cases of papillary carcinoma only blood was obtained with few or occasional atypical cell. Triple assessment including FNAC, radiological examination and clinical examination is mainstay for diagnosis of IPC. IPC is a slow growing tumour showing excellent prognosis. Intraductal papillomas are most controversial lesions to be diagnosed on clinical and radiological examination. Very small portion of papilloma are known to undergo malignant transformation. Differential diagnosis and management of papillary breast lesions can be extremely complex. Therefore, pathological confirmation is always needed.Treatment of choice for papilloma of single duct is microdochectomy. Tissue sampling with radiologic and clinical correlation is usually mandatory for diagnosis of papillary lesion.

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