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Bilateral multicentric encapsulated papillary carcinoma of the breast: A rare case report

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Abstract
Intraductal papillary carcinomas of the breast account for 2% of all breast cancers. Most occur during the fifth and sixth decades of life. Although they are considered in situ carcinomas, debate and uncertainty still exist regarding their true nature, because immunohistochemistry for myoepithelial cells has shown absence of myoepithelial cell layer along the epithelial-stromal interface of the tumor in many cases. Clinically, these tumors present as a palpable, centrally located mass or can be multifocal or present as bloody nipple discharge. Here is reported a rare case of bilateral multicentric encapsulated papillary carcinoma of the breast in a 45 year old female who presented with a two year history of lumps in both the breasts.

Keywords: Intraductal, encapsulated, papillary carcinoma, immunohistochemistry, bloody nipple discharge, myoepithelial cell, epithelial-stromal interface

Introduction
Papillary lesions of the breast have been evaluated in a wide spectrum ranging from benign intra ductal papilloma (with or without atypia) to papillary carcinoma in situ and invasive papillary carcinoma [1]. It represents 0.5% of invasive breast cancers, typically presenting with bloody nipple discharge, an abnormal mass, or radiographic abnormalities [2].
It is more frequently seen in the elderly, median age being 69.5 yrs, more frequent in women (upto 96.5%) than in men (upto 3.5%) [3].
The classification of intracystic papillary carcinoma as a form of invasive ductal carcinoma or ductal carcinoma *in situ* is controversial. Although the absence of myoepithelial cell layer would suggest intracystic papillary carcinoma as a form of invasive ductal carcinoma, the presence of collagen IV would suggest that it is a form of ductal carcinoma *in situ*. The WHO Working Group reached a consensus that intracystic papillary carcinoma should be staged and managed like ductal carcinoma *in situ* [4].
Macroscopically, the papillary carcinomas are well-defined and they usually contain haemorrhagic and cystic components. They may be solitary or multiple [5].
Histopathologically it is characterized by four cellular patterns: cribriform, compact columnar epithelial, stratified spindle cell or a transitional cell resembling urothelium and unlike papillary DCIS these tumours lack myoepithelial cells at the periphery [6].
There is an excellent prognosis for patients diagnosed with IPC regardless of whether the tumor is diagnosed as in situ or invasive [7].
Because of its rarity, there is paucity of literature about the tumour. Bilateral papillary carcinomas are extremely rare. Only a limited number of large clinical studies safely assess its appropriate treatment and expected outcome [3].

Case Report
A 45 year old female presented to the Surgery department with complaints of bloody discharge from right nipple for 3 months and lump in both the breasts since 2 years. Physical examination revealed multiple, tender nodules involving the periareolar region and lower inner quadrant of right breast each measuring about 0.5 x 0.5 cms. Nipple retraction was seen. No lymph nodes were palpable.

Examination of Left breast revealed a palpable mass of size 3x2 cm with irregular margins in the retroareolar region.

The patient underwent a mammogram which was reported as multiple nodular lesions in bilateral breasts, BIRADS GRADE III-IV, with mild dilatation of bilateral lactiferous ducts. A few bilaterally enlarged benign appearing axillary lymph nodes noted.

USG guided FNAC was done from both the breasts. Smears from left breast showed a sparsely cellular aspirate with irregular cohesive clusters of ductal epithelial cells in a background of cyst macrophages and blood. (Figure 1) Smears from the right breast (from both periareolar and lower inner quadrant) showed monolayered/multilayered/papillaroid clusters of ductal epithelial cells in a background of cyst macrophages, rare spindly stromal fragments and blood. (Figure 2) Some of the clusters showed nuclear enlargement and hyperchromasia. Hence a possibility of Multicentric papillary carcinoma of breast was suggested.

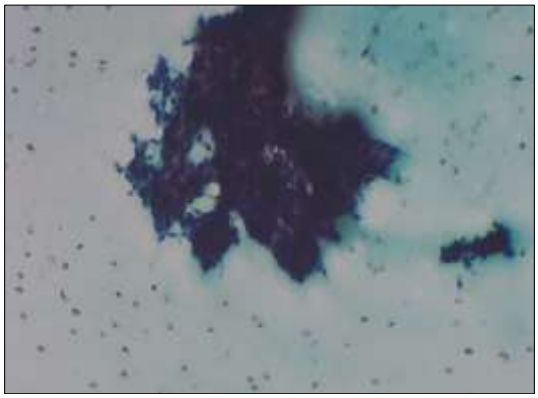

Fig 1: Clusters of atypical epithelial cells

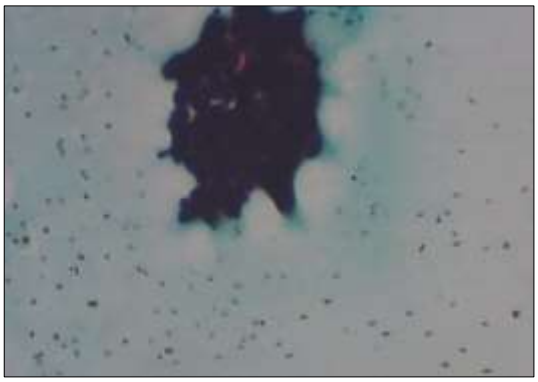

Fig 2: Irregular clusters of atypical epithelial cells

Modified radical mastectomy of the right breast was done along with lumpectomy of the left breast and axillary lymph node dissection. The gross examination of the specimen showed entire breast tissue with nipple and areola. Cutsection through the nipple showed a well circumscribed, solid, grey white growth measuring 2x1.5x1.5 cm; located 2.5 cm below the nipple and 1.5 cm from the base and 4 cm from nearer resection margin. (Figure 3).

A second nodule measuring 0.6x0.5 cm situated 1.5 cm away from primary growth. (Figure 4) Serial sections showed 5 more nodules each measuring 0.6x0.6 cm. (Figure 5). The nodules were located 0.3 cm to 6 cm away from nearest surgical margin. The left breast lumpectomy specimen was a single, irregular grey white fibrofatty tissue mass measuring 7.5x5x2 cm. Cutsection showed 7 whitish nodules each measuring 0.5x0.5 cm, except one measuring 1x1 cm which was situated 0.2 cm from the nearest resection margin. The specimen marked as axillary lymph node was a single grey brown tissue bit, cut section of which revealed a single lymph node measuring 0.5x0.5 cm.

Following previous surgery, patient was posted for left modified radical mastectomy along with left axillary lymph node clearance after a month. The specimen weighed 250 gm and measured 13x10x2.5 cm; Nipple appeared retracted. Remaining skin showed a linear scar measuring 2x0.4 cm above areola. Cutsection through the nipple showed 2 nodules, larger measuring 0.6x0.5 cm located 0.5 cm below the nipple, and smaller measuring 0.3x0.2 cm. serial section showed 7 more nodules each measuring 0.3x0.3 cm. The nodule location ranged from 0.1 to 0.5 cm away from posterior resection margin. Examination of the axillary lymph node specimen revealed 12 lymph nodes largest measuring 1.5x1.5cms, smallest measuring 0.2x0.1 cms. C/S of the nodes showed grayish white solid areas.

Fig 3, 4, 5: Cut section showing multiple nodules of varying sizes

Histopathological examination of the tumour from right breast showed a proliferative neoplasm within cystically dilated and tortuous duct formed of columnar or cuboidal cells in tubules, branching thin core papillae, cribriform pattern and focally as broad core papillae. (Figure 6, 7) Tumor cells showed vesicular nuclei and tiny nucleoli. (Figure 8) Nearby breast tissue showed a total of six more discrete similar tumors. Adjacent breast tissue showed fibrosis, periductal inflammatory cell infiltration, adenosis with multiple cystically dilated ducts. (Figure 9) Nipple region showed involvement of the lactiferous duct by similar tumor, with prominent cystic dilatation. Lymph node showed sinus histiocytosis. (Figure 10)

Sections from Left lumpectomy showed 7 discrete papillary neoplasms within dilated ducts with focal areas of high grade atypia and insitu changes. Two of them showing atypia, branching papillae and tubules and two more showing papilloma with mild atypia. (Figure 11)

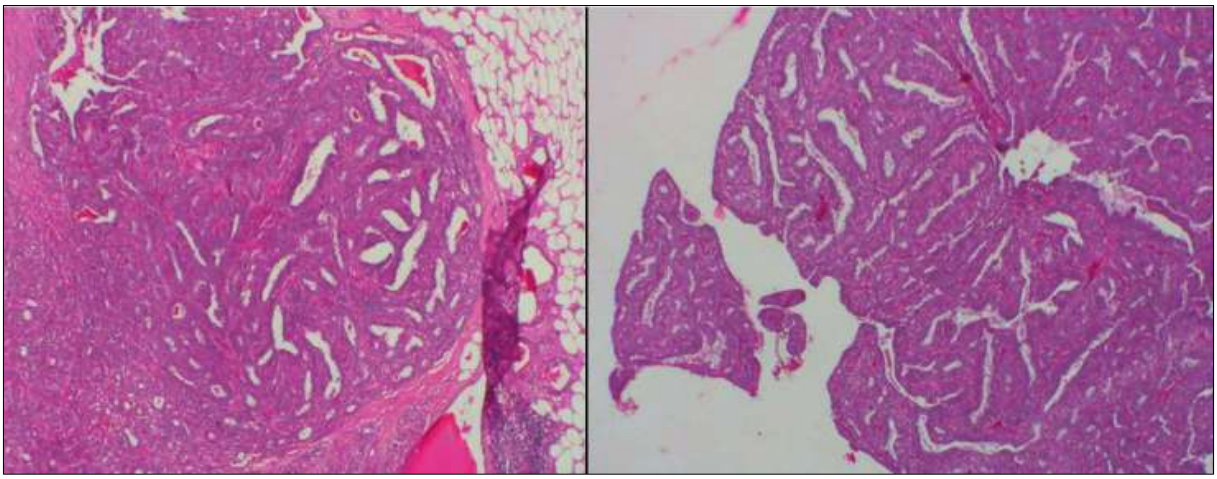

Fig 6, 7: Histopathological examination showing thin core papillae, cribriform pattern.

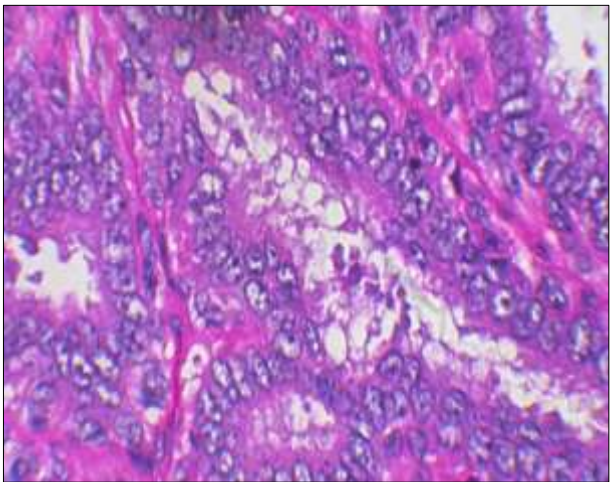

Fig 8: Tumor cells showed vesicular nuclei and tiny nucleoli

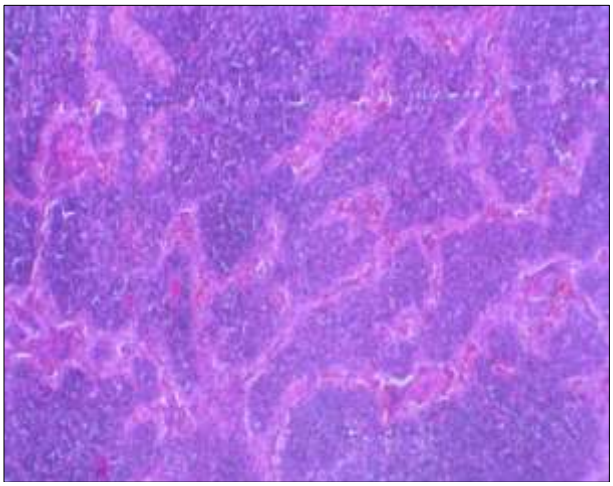

Fig 10: H&E of lymph node showing sinus histiocytosis

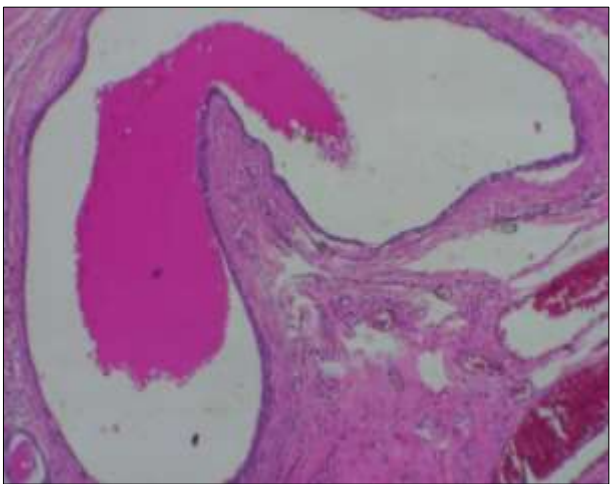

Fig 9: H&E section showing multiple cystically dilated ducts

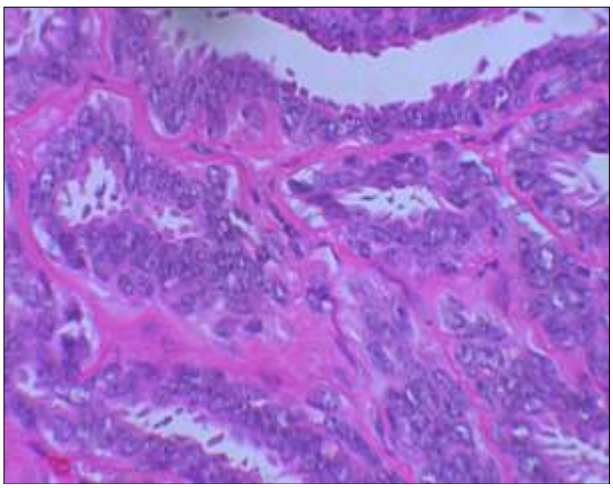

Fig 11: atypical branching papillae with mild atypia

Sections from left breast showed multiple intraductal papillary carcinomas located in lactiferous duct. Random breast tissue also showed intraductal papilloma with atypia. Intervening breast tissue showed fibrosis, foci of adenomatoid hyperplasia, periductal round cell infiltration and few dilated ducts. Examination of 11 lymph nodes showed reactive changes.
TNM stage Tis (DCIS, Multicentric, bilateral) N0Mx. ER PR status not known.

Discussion

Intraductal papillary carcinomas account for 2% of all breast cancers. Most occur during the fifth and sixth decades of life [8].
All malignant papillary proliferations of the breast lack an intact myoepithelial cell layer within the papillae, an important feature which allows distinction from benign intraductal papillomas [2, 8].
Depending on their location in the mammary duct system, papillary lesions may be solitary, centrally (subareolar) located or multifocal, and peripherally located within terminal duct-lobular units. These are associated with different risks for associated carcinoma or subsequent carcinoma [8].
Approximately half of the papillary carcinomas arise in the retro areolar region of the breast and the usual clinical manifestation is a palpable mass, nipple retraction, nipple bleeding or nipple discharge [9].
Variants of intraductal papillary carcinoma includes Intracystic papillary carcinoma and solid papillary carcinoma [8].
Precise classification of papillary lesions of the breast on fine-needle aspiration remains a challenging area in cytology. The aspirates are commonly hypocellular and admixed with haemosiderophages due to the highly vascular nature of IPCs. If adequate material is obtained then it is highly cellular with complex papillae, nuclear hyperchromasia, stratification and foamy macrophages [6].
Radiological findings may show on a mammogram as an oval or lobulated, circumscribed lesion and on the ultrasound as a complex cystic mass with a solid component demonstrating vascular flow within the solid component of the cystic mass on a colour Doppler scan [10].
Most cases of papillary carcinoma are low-grade, slow-growing cancers, with good recovery. In 2010, Bhosale *et al* did a study on gradually increasing painless subareolar mass for 4 months in the left breast of a 55 year old postmenopausal female which was diagnosed histopathologically as invasive papillary carcinoma on left-sided modified radical mastectomy. Patient was followed up with postoperative chemotherapy for 6 months with no evidence of local or distant recurrence of tumor metastases [11].
The incidence of bilateral papillary carcinomas is very low, with only one case reported in the literature [12].
In 2013, Yoshimura *et al* did a study on a case of synchronous bilateral solid papillary carcinomas of the breast. However the association between bilaterality and solid papillary carcinomas has not been discussed so far [13].
In 2015, Testori *et al* presented a study on a unusual case of encapsulated papillary carcinoma of right breast with axillary tumor spread and a contralateral invasive ductal carcinoma. He also concluded that these papillary tumors may be multifocal and can be a “pure” form or associated with in situ neoplasms or invasive carcinomas [14].
Lymph node exploration is currently debated. Although rare and despite being a large and bulky tumor, invasive papillary cancer has an excellent prognosis due to a high-grade hormonal response and uncommon axillary node metastases. The prognosis is favorable also for women presenting with axillary metastases [14].
Depending on the extent of invasion or presence of lymph node or distant metastases, patients are treated with trimodality therapy (surgery, radiation and chemotherapy). Endocrine therapy was more common in patients with invasive papillary carcinoma and *in situ* papillary carcinoma associated with DCIS [2]. Association with invasive carcinoma and the difficulty in evaluating the focus of the invasive lesion may indicate sentinel axillary lymph node biopsy for IPC [3].

Conclusion

Intraductal Papillary Carcinoma is a rare breast carcinoma with an excellent prognosis. Bilateral Papillary carcinomas of the breast is rarely seen. Awareness, early and prompt diagnosis of this clinicopathological entity is important especially because of the good prognosis it carries

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