

Case report**Bilateral Pleomorphic Ductal Carcinoma Of Breast- A Rare Presentation With Its Diagnostic Dilemma***Meghadipa Mandal¹, Anadi Roy Chowdhury²***Abstract**

Pleomorphic carcinoma of breast is a rare morphological subtype of Invasive Breast Carcinoma No Special Type (IBC NST), which has histomorphological overlap with other entities. Here we present such a case with bilateral breast involvement in 45 years old nulliparous woman with family history of breast carcinoma. Typical numerous multinucleated cells (>50%) with marked pleomorphism and wide areas of necrosis were histopathological presentation. AE1/AE3 and Vimentin were positive. Ki-67 labelling index was high along with HER2 amplification. Important differentials were IBC NST with Osteoclast-like giant cells, Choriocarcinomatous pattern, metaplastic carcinoma & metastatic disease all of which was ruled out with proper clinical, histological & immunohistochemical approach. Despite the aggressive nature of the neoplasm and presence of adverse prognostic factors, this case responded well with adjuvant chemotherapeutic regimen.

Keywords: Pleomorphic carcinoma, giant cells, bilateral involvement, HER2 amplification Vimentin.

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Introduction

Pleomorphic carcinoma of breast is an uncommon variant of Invasive Breast Carcinoma of No Special Type (IBC NST). Its rare occurrence and paucity of available literature poses a challenge for the oncopathologists. This is not a well-recognized entity within the histomorphologic spectrum of breast neoplasms¹. As per previous reports, it is aggressive in nature with poorer clinical outcome². The diagnostic dilemma posed by this entity is further compounded by the histomorphologic overlap with other high grade malignant neoplasms of breast. Hence, timely and appropriate diagnosis with use of suitable ancillary investigations is essential in this case for directing the therapeutic protocol. Here, one such rare entity has been discussed.

Case Report

A 45 years old female patient attended surgery

OPD with lump in both breasts for last 4-5 months with rapid increase in size for last 2 months. Her mother died of breast carcinoma 6 years back. She was nulliparous, with no history of intake of Oral Contraceptive Pills for a long duration or any Hormone Replacement Therapy. Palpation revealed bilateral firm to hard masses measuring around 8 cm each in maximum dimension. The nipple was puckered on both the sides with peau d'orange like change on the overlying skin. Axillary lymph nodes were non-palpable.

Ultrasound of bilateral breast masses showed an average dimension of 8 cm and 7 cm of right and left breast respectively. They were hypoechoic lesions with irregular shape, angulated & spiculated margins, areas of microcalcifications, with final impression of BI-RADS (Breast Imaging Reporting and Data System) 5, i.e., highly suggestive of malignancy. Serum tumor marker study for CEA (Carcinoembryonic Antigen)

1. Dept. of Pathology, R. G. Kar Medical College & Hospital, Kolkata, India.
2. Dept. of Pathology, Murshidabad Medical College, West Bengal, India.

Correspondence to: Meghadipa Mandal, Senior Resident, Dept. of Pathology, R. G. Kar Medical College & Hospital, Kolkata, West Bengal, India. E-mail: meghadipa.mandal41@gmail.com

showed a high level of 10 ng/mL (Normal Range is <3 ng/mL).

Initial tru-cut biopsy gave a diagnosis of Invasive Breast Carcinoma No Special Type, BR grade 3, with negative ER/PR status but a positive HER2/neu expression in both the breasts. Suitable chemotherapeutic regimens were given followed by Modified Radical Mastectomy (MRM) of right breast and repeat tru-cut biopsy of opposite breast. Mastectomy of second breast was planned at a later date.

Histopathological study:

Gross examination revealed a mass measuring 5 cm in maximum dimension in upper-outer quadrant of right breast with unremarkable skin and slightly retracted nipple areola complex (NAC). Tumor was away from all the resection margins. Cut section of the growth was solid, greyish brown with areas of necrosis. There were also patchy fibrotic areas possibly as an effect of neoadjuvant chemotherapy. No lymph nodes were found grossly. The tru-cut biopsy from opposite breast was also submitted.

Hematoxylin & Eosin stained sections from both the breasts showed markedly pleomorphic tumor cells, with >50% giant cells (*Figure 1*). Individual cells had vesicular chromatin, prominent nucleoli, increased and atypical mitosis and wide areas of geographic necrosis (*Figure 2*). There was a very small foci of Ductal Carcinoma In Situ (DCIS) along with metaplastic spindle cells. The tumor mostly had infiltrative margin with surrounding breast tissue with areas of inflammation, fibrosis and sheets of foamy macrophages indicating probable response to neoadjuvant therapy. The above observation indicated an aggressive epithelial neoplasm of breast with high grade nuclear features and predominant component of tumor giant cells. Pleomorphic Ductal Carcinoma of breast, IBC NST with Osteoclast-like giant cell pattern, Choriocarcinomatous pattern, Metaplastic Carcinoma of Breast and metastatic breast disease were considered in the differential diagnosis.

Immunohistochemical (IHC) study was performed which revealed strong Vimentin positivity for spindle cell component & AE1/AE3 (Pan cytokeratin) for the tumor giant cells (*Figure 3 & 4*). They were negative for CD68 & β -hCG. The tumor cells were Hormone receptor (ER/PR)

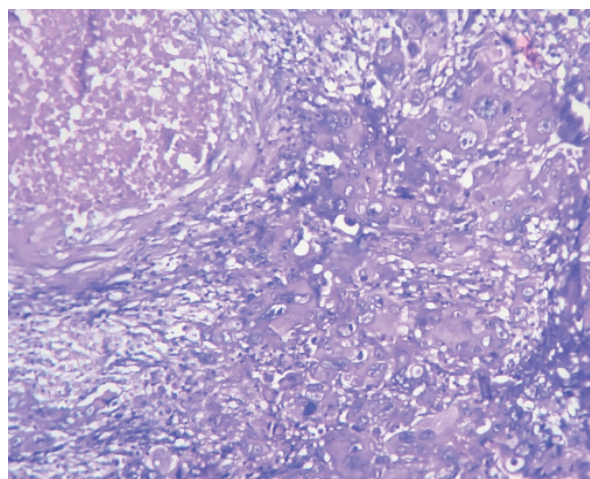


Figure 1: Pleomorphic tumor cells

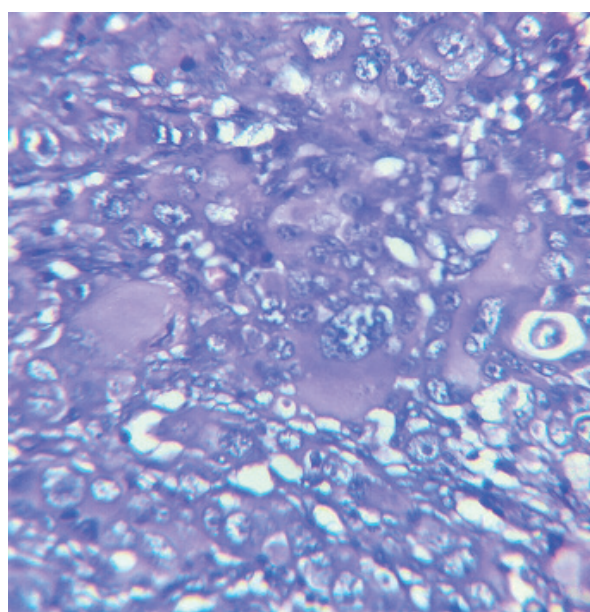


Figure 2: Necrosis with plenty of tumor giant cells (400x magnification) (100x magnification)

negative but HER2 positive (*Figure 5*). Ki-67 proliferation index was very high (50%) (*Figure 6*). Similar histomorphological spectrum with similar immunohistochemical findings were seen in the tru-cut biopsy specimen of opposite breast.

After ruling out the various differentials, a diagnosis of **Bilateral Pleomorphic Ductal Carcinoma of Breast** was offered. pTNM staging for the right breast was ypT2NxMx.

The patient was put on adjuvant chemotherapy and the mastectomy of the opposite breast was performed after 6 months. The patient since then has been kept on chemotherapeutic regimen with no signs of recurrence or metastasis within 2 years of follow up, till the publication of this case.

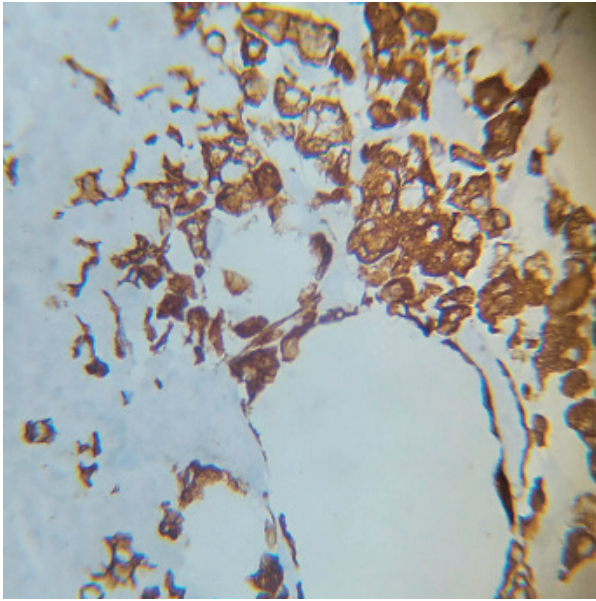


Figure 3: AE1/AE3 positivity

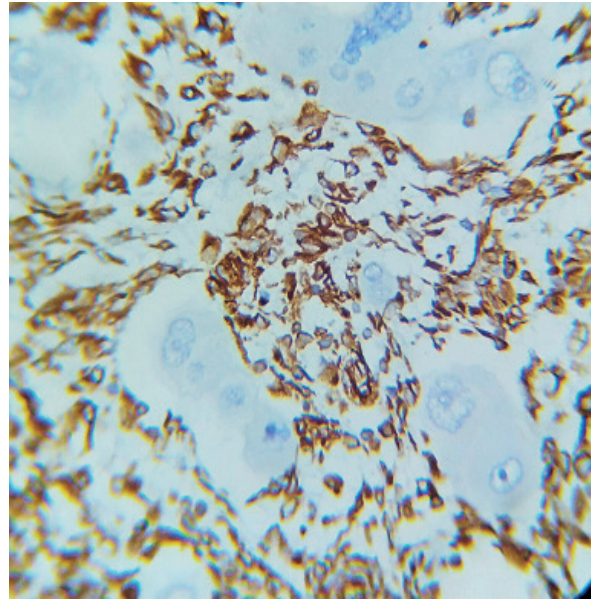


Figure 4: Vimentin positivity in spindle cells

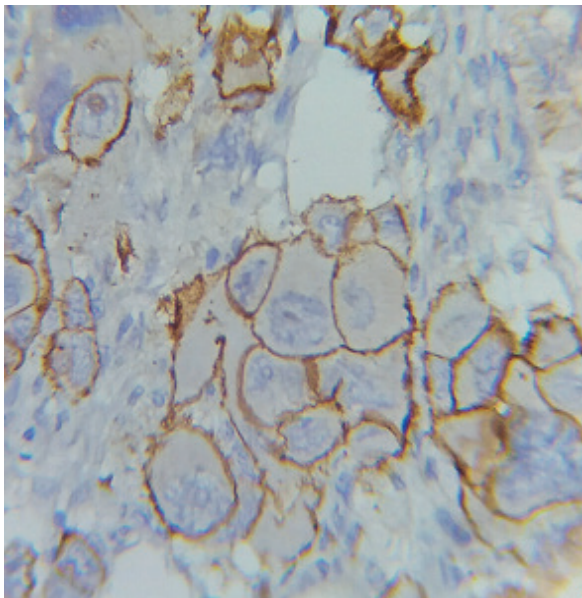


Figure 5: HER2/neu positivity

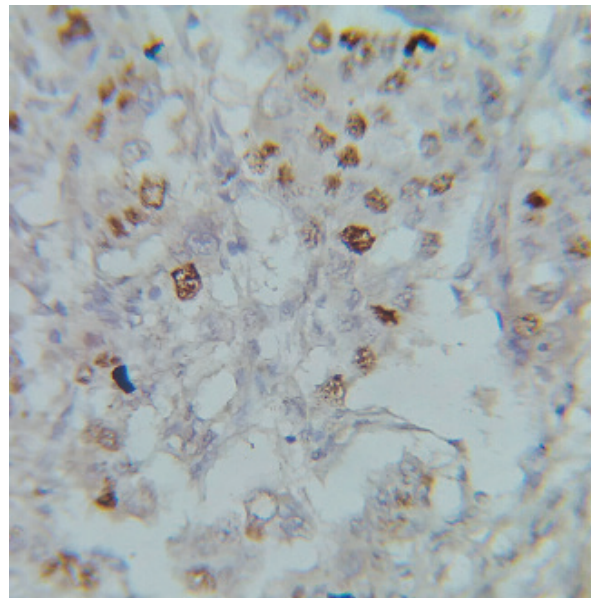


Figure 6: High Ki-67 expression

Discussion

Pleomorphic carcinoma of breast is a fairly rare entity with unique morphological features, predominantly (>50%) composed of multinucleated tumor giant cells with marked nuclear pleomorphism ranging from six-to-ten folds the nuclear size³. Silver SA and Tavassoli FA were the first to report a case of Pleomorphic Carcinoma, which falls at the extreme end of the Grade 3 IBC NST spectrum⁴. Although it is a variant morphological subtype of IBC NST, its identification is essential for differentiating it from other breast neoplasms with overlapping histomorphology.

In bilateral breast masses, presence of foci of DCIS indicated a primary epithelial neoplasm of breast, thereby ruling out the possibility of metastasis or any primary pleomorphic sarcomas of breast. CD68 negativity & CK positivity goes against IBC with osteoclast-like giant cells. Absence of β -hCG expression excludes IBC NST with Choriocarcinomatous pattern. Metaplastic carcinoma of breast was also ruled out as they are typically Triple Negative phenotypes, whereas HER2 is positive for this case. However, this case had a focal area of metaplastic spindle cell component which was positive for Vimentin.

Presence of metaplastic spindle cell component is again a predictor of poorer outcome amongst a subset of Pleomorphic carcinoma cases, as has been established in a multivariate analysis⁵. Typical histomorphology of giant cells and definitive DCIS component with supportive IHC concluded the final diagnosis of **Pleomorphic Carcinoma of bilateral breasts**. Pleomorphic carcinomas are occasionally HER2 amplified, which was the scenario for this case⁶.

A similar histological picture of multinucleated cells will be diagnosed as Undifferentiated Carcinoma in organs like bladder, prostate or pancreas and is associated with overall unfavourable prognosis⁷. Similarly, a diagnosis of this entity in breast carries poor outcome with decreased overall survival. Additionally, high Ki-67 positivity, wide areas of necrosis & spindle metaplastic components were the bad prognostic indicators for this case, as was demonstrated by Nguyen *et al*⁸.

Despite the presence of poor predictors, this particular case has responded well with the chemotherapeutic regimen with no sign of metastasis or recurrence till date.

Conclusion

What makes this case unique is presence of bilateral Pleomorphic carcinomas in a patient with family history of breast carcinogenesis. The high grade histological features directed towards a large number of differentials, which were excluded with suitable ancillary studies. The neoadjuvant protocol for this patient was tailored in the backdrop of hormone receptor status, HER2 expression & adverse prognostic indicators.

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