

PLEOMORPHIC DUCTAL CARCINOMA OF BREAST - A RARE VARIANT

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ABSTRACT

Back ground: A 57 year old women presented with left breast mass of one month duration with recent rapid increase in size and pain. On local examination, a hard, firm and painless mass of size 6×4cm was palpable in the upper outer quadrant of the left breast. Ultrasonography indicated an infiltrative, ill defined heterogenous mass measuring 5.6×2.5 cm in size. Fine Needle Aspiration Cytology suggestive of Ductal carcinoma - Not Otherwise Specified. The patient then underwent a modified radical mastectomy. The final diagnosis of pleomorphic carcinoma has been made based on histology and further confirmed by immunohistochemistry.

Key Words: Breast carcinoma, Immunohistochemistry, Pleomorphic Carcinoma

INTRODUCTION

Pleomorphic carcinoma of the breast is a rare high grade breast carcinoma .It is characterised by distinctive pleomorphic giant tumor cells with bizarre nuclei and atypical mitosis. In 2012 World Health Organization (WHO) classification, pleomorphic carcinoma is an uncommon variant of high-grade invasive carcinoma of no special type (NST) of breast characterized by proliferation of pleomorphic and bizarre tumor giant cells comprising >50% of the tumor cells in a background of adenocarcinoma or adenocarcinoma with spindle or squamous differentiation(Ellis et al., 2012). There is marked nuclear pleomorphism and characteristically contains multinucleated giant tumor cells. It has an aggressive behavior and poorer clinical outcome. One original paper described that less than 0.1% breast tumors were classified as Pleomorphic carcinomas among a large series of surgically resected cases (Zhao, 2010). Herein, we report a rare case of pleomorphic carcinoma of the breast displaying pleomorphic and bizarre tumor giant cells, and a component of invasive ductal carcinoma in a 57 year old woman.

CASE REPORT

A 57-year-old woman noted a mass in her left breast of one month duration and visited surgical outpatient department. She had no past history of malignancy and no family history of breast carcinoma. On physical examination, a hard, firm and painless mass about 4×3cm was palpable in the upper outer quadrant of the left breast and no lymphnodes were palpable. There were no abnormalities in the right breast. Ultrasonography of abdomen and other routine blood tests were normal. Ultrasonography of breast indicated an infiltrative, ill defined heterogenous mass measuring 2.6×2.5 cm in size and areas of cystic change noted around the nipple region. The Fine needle aspiration cytology specimens contained many individual bizarre cells, multi-nucleated giant cells having hyperchromatic pleomorphic nuclei, prominent nucleoli, and relatively abundant cytoplasm, admixed inflammatory cells in the background (Fig.1 & 2). Based on these features, a diagnosis of ductal carcinoma, not otherwise specified was made. The patient then underwent a modified radical mastectomy with left axillary lymph nodes clearance.

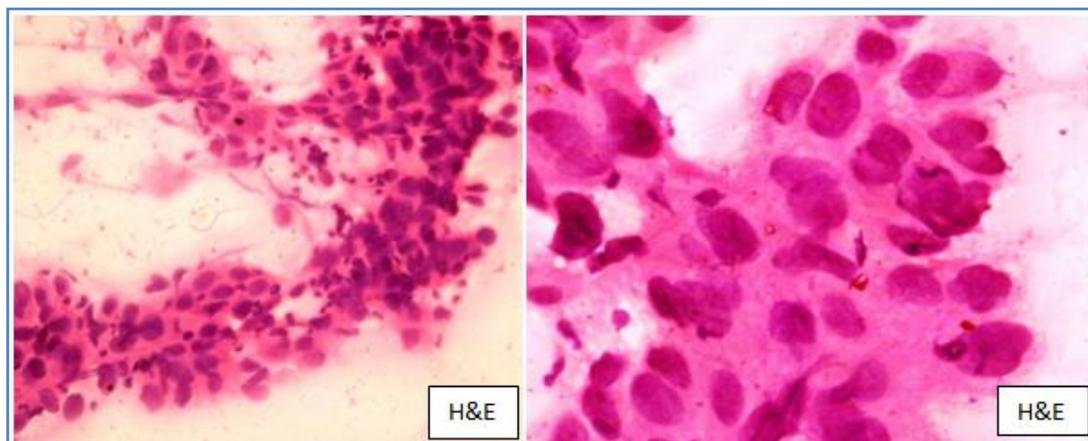


Figure 1&2: Cytospin smears (40x & 100x) showing cells with abundant eosinophilic cytoplasm, pleomorphic and hyperchromatic nuclei

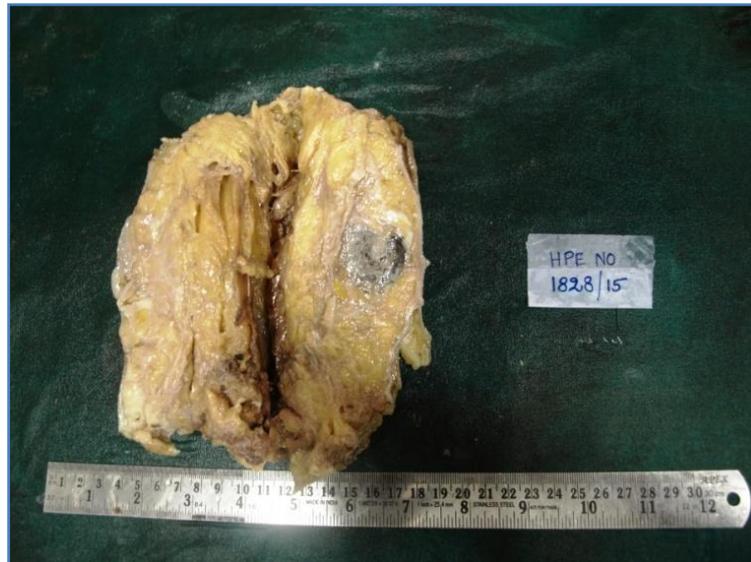


Figure 3: Macroscopic picture of mastectomy specimen showing nipple and areola with cut surface showing grey brown tumor

On gross examination, the mastectomy specimen measured 18×12×5cm with tumor 1 cm from nipple and areola. On cut surface, the tumor was hard measuring 3×2.5 cm in size and gray white to gray brown (Fig. 3). Four lymphnodes were dissected. Representative tissue samples were processed and stained with hematoxylin and eosin.

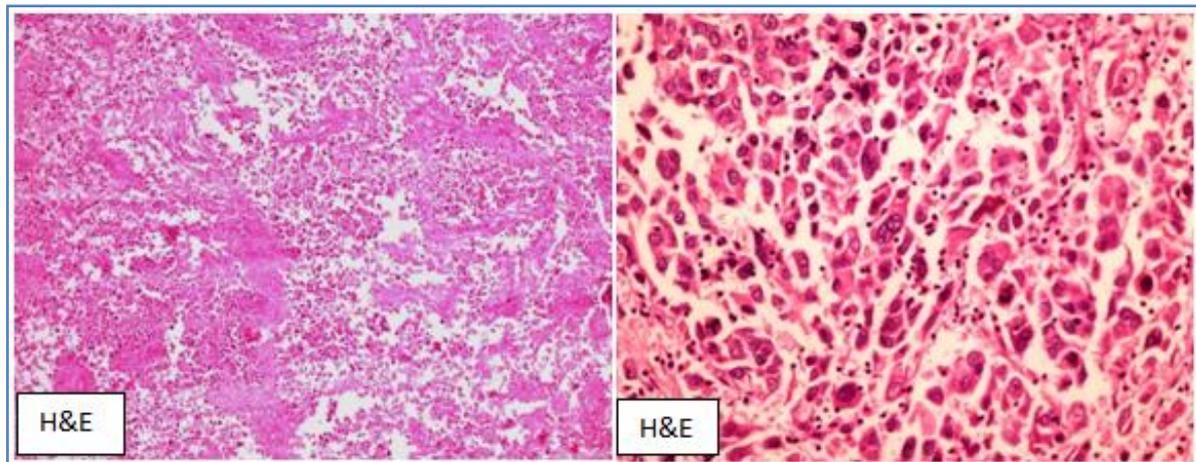


Figure 4&5: 10x & 40x view showing tumor with pleomorphic epithelial cells and giant cells

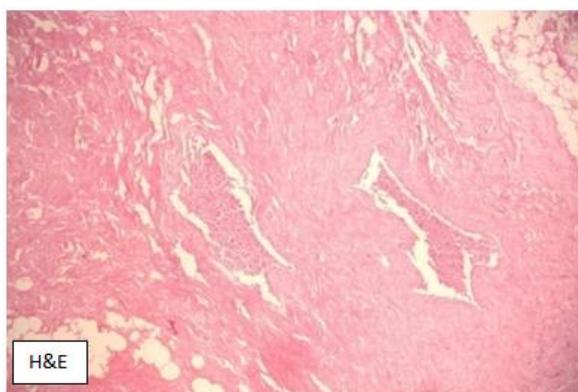


Figure 6: 4x view showing lymphovascular tumor emboli

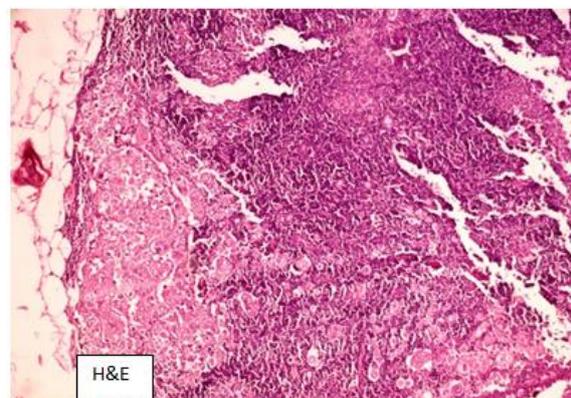


Figure 7: 10x view showing Metastatic deposits of tumor cells in the axillary lymphnode

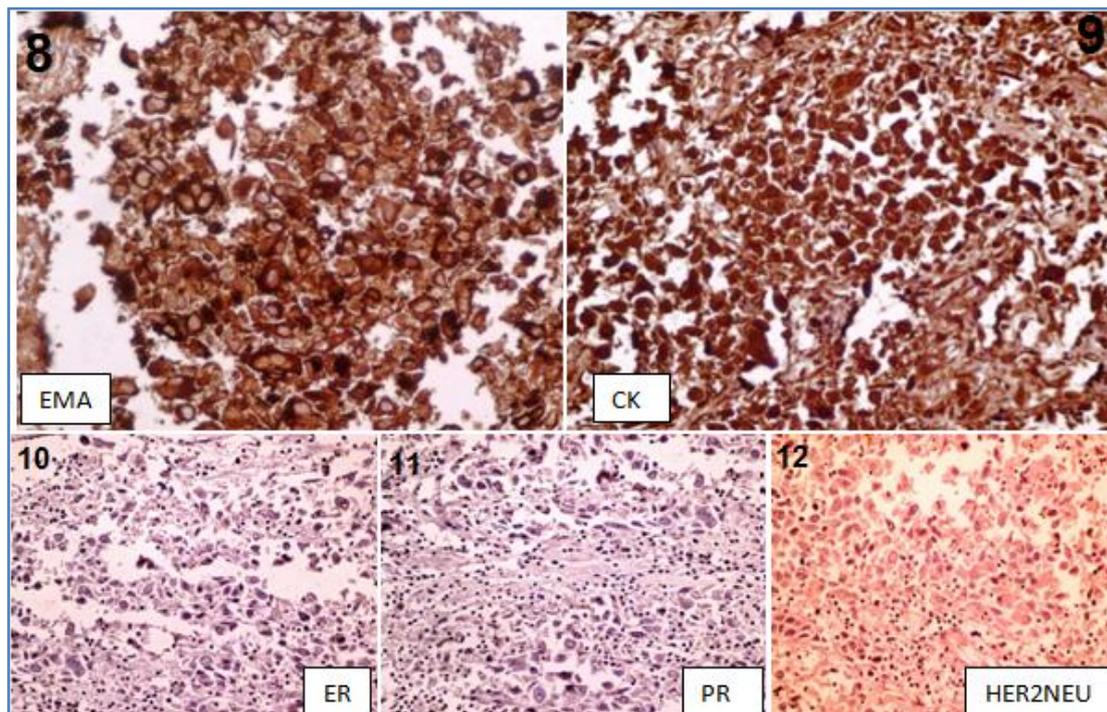


Figure 8, 9, 10, 11&12: Immunohistochemistry showing tumor cells- EMA with strong membrane positivity.CK -showing cytoplasm positivity, Triple negative (ER, PR, HER2NEU)

Microscopic examination demonstrated tumor tissue in sheets and nests having bizarre discohesive cells showing highly pleomorphic nuclei with abundant eosinophilic cytoplasm, binucleate, multinucleate cells, areas of necrosis and classical invasive ductal carcinoma component, mitotic activity 3 to 4/HPF (Fig. 4 & 5). Background showed inflammatory cells. Tumor emboli are seen focally (Fig. 6). One of the four dissected lymphnodes showed tumor deposits (Fig. 7). Based on the above findings, a diagnosis of pleomorphic carcinoma has been made. Immunohistochemical studies were performed using antibodies to ER (1D5), PR(PR88), HER2NEU(EP1045Y), CK,EMA(E29). The pleomorphic tumor cells were positive for CK and EMA (Fig.8 & 9), Triple negative(ER, PR, HER2NEU) (Fig. 10, 11 & 12).

DISCUSSION

Pleomorphic carcinomas have distinct characteristic morphological features. Pleomorphic carcinoma has been previously described in many organs, most frequently in the lung, rarely in the breast, pancreas, intestine, kidney, liver, urinary bladder, gall bladder, thyroid, stomach and prostate(Al-Nafussi, 2005). Silver SA and Tavassoli FA firstly reported pleomorphic carcinoma and indicated that it represents the extreme end of the morphological spectrum of grade III invasive ductal carcinoma of breast (Silver SA et al, 2000). But in recent WHO classification (Ellis et al., 2012), this tumor has been considered as a variant of invasive carcinoma, No specific type.

Pleomorphic tumor cells can be present in other breast neoplasms such as invasive pleomorphic lobular carcinoma, invasive carcinoma with osteoclast-like giant cells, invasive carcinoma with chorioepithelioma features, mammary sarcoma and metastatic tumors (Al-Nafussi, 2005). Gross, microscopic examination and a panel of immunohistochemistry for epithelial and mesenchymal markers can lead to a correct diagnosis. Pleomorphic lobular carcinoma is a variant subtype of invasive lobular carcinomas. It also exhibits enlarged nuclei with hyperchromasia, irregularities and marked pleomorphism. However, pleomorphic lobular carcinoma often tends to grow in linear arrays and lack of E-Cadherin expression. The E-Cadherin positivity and presence of conventional ductal carcinoma component can help to distinguish these two different types of breast cancer (Monhollen et al., 2012 ; Wahed et al., 2002). CD68 and CK helps to differentiate invasive ductal carcinoma with osteoclast like giant cells (CD68 positive, CK negative) from pleomorphic ductal carcinoma(CD68 negative, CK positive) (Córdoba et al., 2012; Kurokawa et al., 2009). β -HCG positivity is used to make diagnosis of invasive carcinoma with chorioepithelioma features. Pleomorphic carcinoma can be differentiated from mammary sarcomas by the expression of antibodies to CK and EMA, which confirms the epithelial nature of the giant cells. Metastatic carcinoma to breast is a rare event and intends to be multicentric, and the patient has a history of other primary tumor.

Case Report

Pleomorphic carcinoma is usually associated with rapid tumor dissemination and unfavourable outcome as in other organs like bladder, ovary, prostate (Silva et al., 1991; Komatsu et al., 1985; Lopez-Beltran et al., 2010). Cases of pleomorphic carcinoma of breast in most previous reports have been associated with aggressive behavior (Caruso et al., 2011; Yamaguchi et al., 2010). In one study, Nguyen et al indicated that not all these tumors behave badly and the presence of the spindle cell metaplastic component, higher mitotic rate and bigger tumor size are associated with the poor prognosis (Nguyen et al., 2010).

CONCLUSION

It is important to recognize pleomorphic ductal carcinoma of breast as this variant of ductal carcinoma has aggressive behaviour, triple negative expression and poor outcome. Histomorphology and immunochemical markers- CK and EMA will aid in accurate diagnosis ruling out other differential diagnoses.

REFERENCES

- Al-Nafussi AI (2005).** Tumour Diagnosis: Practical Approach and Pattern Analysis. Al-Nafussi (ed.). Hodder Arnold Publication, London 1193-1213.
- Caruso R, Palmeri R, Racchiusa S, Bonanno A, Lucianò R, Scardigno M, Branca G & Fedele F (2011).** Pleomorphic ductal carcinoma of the male breast: report of a rare case and review of literature. *Anticancer Research*, **31** 3069-3071.
- Córdoba A, Del Rosario Mercado M, Vicente F, Ederra M, Torrea N & Guerrero-Setas D (2012).** Pleomorphic carcinoma of the breast with expression of macrophage markers: report of two cases. *Pathology International*, **62** 491-495.
- Ellis IO, Collins L, Ichihara S & MacGrogan G (2012).** Invasive carcinoma of no special type. In: Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, van de Vijver MJ, editors. WHO Classification of Tumors of the Breast. 4th edition. IARC Press, Lyon 34-38.
- Komatsu H, Kinoshita K, Mikata N & Honma Y (1985).** Spindle and giant cell carcinoma of the bladder. Report of 3 cases. *European Urology*, **11** 141-144.
- Kurokawa K, Mouri Y, Asano A, Kamei K, Iwata Y, Isogai M, Saga S & Ichihara S (2009).** Pleomorphic carcinoma with osteoclastic giant cells of the breast: immunohistochemical differentiation between coexisting neoplastic and reactive giant cells. *Pathology International*, **59** 91-97.
- Lopez-Beltran A, Cheng L, Comperat E, Rouprêt M, Blanca A, Menendez CL & Montironi R (2010).** Large cell undifferentiated carcinoma of the urinary bladder. *Pathology*, **42** 364-368.
- Monhollen L, Morrison C, Ademuyiwa FO, Chandrasekhar R & Houry T (2012).** Pleomorphic lobular carcinoma: a distinctive clinical and molecular breast cancer type. *Histopathology*, **61** 365-377.
- Nguyen CV, Falcón-Escobedo R, Hunt KK, Nayeemuddin KM, Lester TR, Harrell RK, Bassett RL Jr & Gilcrease MZ (2010).** Pleomorphic ductal carcinoma of the breast: predictors of decreased overall survival. *American Journal of Surgical Pathology*, **34** 486-493.
- Silva EG, Tornos C, Bailey MA & Morris M (1991).** Undifferentiated carcinoma of the ovary. *Archives of Pathology & Laboratory Medicine*, **115** 377-381.
- Silver SA & Tavassoli FA (2000).** Pleomorphic carcinoma of the breast: clinicopathological analysis of 26 cases of an unusual high-grade phenotype of ductal carcinoma. *Histopathology*, **36** 505-514.
- Wahed A, Connelly J & Reese T (2002).** E-cadherin expression in pleomorphic lobular carcinoma: an aid to differentiation from ductal carcinoma. *Annals of Diagnostic Pathology*, **6** 349-351.
- Yamaguchi R, Tanaka M, Yamaguchi M, Fukushima T, Kaneko Y, Otsuka H, Isobe S, Terasaki H, Nakashima O, Kage M & Yano H (2010).** Pleomorphic carcinoma of the breast in a 17-year-old woman. *Medical Molecular Morphology*, **43** 43-47.
- Zhao J, Lang R, Guo X, Chen L, Gu F, Fan Y, Fu X & Fu L (2010).** Clinicopathologic characteristics of pleomorphic carcinoma of the breast. *Virchows Archiv*, **456** 31-37.