Journal of Medical Case Reports and Reviews
Received 26 Feb 2022 | Revised 29 Feb 2022 | Accepted 30 Apr 2022 | Published Online 06 May 2022

DOI: https://doi.org/10.52845/JMCRR/2022/5-5-1
JMCRR 05 (05), 1119−1122 (2022)
ISSN (O) 2589-8655 | (P) 2589-8647 IF:2.964

Case Report

Metaplastic carcinoma with mesenchymal differentiation: Case series

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Abstract
Metaplastic carcinoma with mesenchymal differentiation of breast is an extremely rare and aggressive type of carcinoma with a direct transition of carcinoma to the cartilaginous or osseous matrix without an intervening spindle cell component. In our study post menopause women with no significant medical and family history complained of painless lump in the left breast. Fine needle aspiration cytology (FNAC) of one case showed malignant cells and tru-cut biopsy of other case showed infiltrating ductal carcinoma. Further, both underwent mastectomy and histological examination revealed matrix producing metaplastic carcinoma and were staged as pT2N0. Tumor showed admixture of mesenchymal component along with carcinomatous areas.
Keywords: Metaplastic carcinoma, chondromyxoid stroma, Breast, Invasive Ductal Carcinoma

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Implication for health policy/practice/ research/medical education:

Two rare cases of metaplastic carcinoma mixed with mesenchymal cancer cells are also seen in the breast staging pT2N0 according to WHO. Tumor is confirmed histopathlogically, cytologically and immunohistochemically in these

Supplementary information The online version of this article (https://doi.org/xx.xxx/xxx.xx) contains supplementary material, which is available to authorized users.

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INTRODUCTION

Metaplastic Carcinoma with mesenchymal differentiation of the breast is an extremely rare and aggressive subtype of metaplastic carcinoma. It is defined as invasive breast carcinoma, with a direct transition of carcinoma to the cartilaginous or osseous matrix without an intervening spindle cell component. [1] Matrix-producing carcinoma (MPC) of the breast was first described by Wargotz and Norris in 1989 [1, 2]. Metaplastic carcinomas are morphologically heterogeneous and comprise of low- and high-grade tumors. According to WHO classification, MBC was classified into squamous cell carcinoma, low-grade adenosquamous carcinoma, fibromatosis-like Metaplastic carcinoma, spindle cell carcinoma, carcinoma with mesenchymal differentiation (including chondroid, osseous, or other types) mixed metaplastic and myoepithelial carcinomas [3,4,5,6]. Metaplastic carcinoma of the breast with mesenchymal differentiation is accounting for less than 1% of all breast carcinoma [5,6,7].

Immunohistochemistry is an integral part of the diagnosis of metaplastic carcinoma; a combination of several stains (eg, cytokeratin cocktail, p63 and high-molecular-weight cytokeratins) is usually needed and is extremely helpful to make an accurate diagnosis. Immunohistochemical analysis of Metaplastic carcinoma has revealed that >90% of these cancers are negative for ER, PR and HER2 [7]. In present cases, we describe metaplastic carcinoma with mesenchymal differentiation, and observed clinical features, histological examination and immuno-histochemical profile in matrix-producing carcinoma of the breast.

CASE SERIES

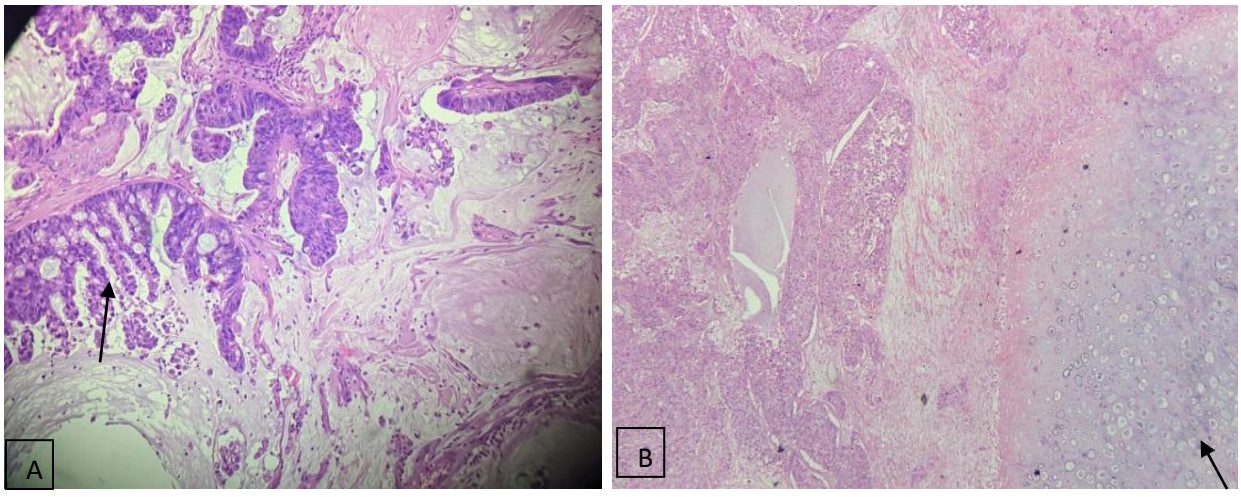
Case 1

The case of a 61yr old women with no significant past medical and family history presented with complaints of painless lump in her left breast for the last 4 months. Sono - mammography, revealed nodular swelling with round margins and BIRADS grade III. FNAC (fine needle aspiration cytology) showed singly scattered atypical ductal cells having pleomorphic and hyperchromatic nuclei and positive for malignant cells Invasive Ductal carcinoma.

After a thorough preoperative evaluation, the patient underwent modified radical mastectomy of the left breast with axillary node dissection. The breast measured 16× 11× 5.5cm**.** Nipple and areola were unremarkable. On serial sectioning, whitish firm and shiny well-defined tumor measuring 4.5×4×3.8 cm was identified, situated in upper outer quadrant from 2-3' clock position in left breast. Histological examination evaluated metaplastic carcinoma with mesenchymal differentiation (matrix producing carcinoma) and was staged as pT2N0. Microscopic examination showed tumor had two distinct patterns; epithelial elements showing invasive ductal carcinoma in the form of glandular tubules (Fig. A) and solid clusters and focal areas showing chrondroid and osseous differentiation (Fig. B). Matrix was of low grade with small bland nuclei and smooth nuclear contours. Distribution of matrix was focal, comprising of 30% of entire tumor components. It had well-delineated pushing margin. This Histological grade was "3". Microcalcification was present. Lymphovascular invasion was not present. Dermolymphovascular invasion were not identified. All surgical margin and skin free of tumor. The adjacent breast showed no significant finding. Right breast and axillary lymph node were not affected. There 18 lymph nodes all were negative for tumor metastasis. Immunohistochemical profiling showed the tumor cells negative for hormone receptor (estrogen and progesterone) and HER 2/Neu (human epidermal growth factor receptor) as showed in fig. D and positive for CK5/6 and S100. The patient received adjuvant chemotherapy consisting of four cycles of adriamycin and cytoxan followed by four cycles of taxanes.

Case 2

A 48yr old female presented with history of lump in her left breast. Sono-mammography showed lump in upper outer quadrant and BIRADS grade IV. Tru-cut biopsy of left breast lump showed Infiltrating Ductal carcinoma. There was no past medical and family history of cancer. Thereafter, the patient underwent modified radical mastectomy of the left breast with axillary node dissection. The breast measured 19× 10× 7cm**.** Nipple and areola were unremarkable. On serial sectioning, glistening whitish tumor measuring 4.5×4.5×4 cm was identified. Histological examination evaluated metaplastic carcinoma with mesenchymal differentiation (matrix producing carcinoma) and was staged pT2N0 as in case 1. Histological grade was "3" which represented poorly differentiated highly grade of carcinoma. Mesenchymal component was chondrosarcoma and Carcinoma component was infiltrating duct carcinoma with mucinous and papillary differentiation was seen. Focal squamous differentiation was also seen (fig. C). Lymphovascular and Dermolymphovascular invasion was not present. Ductal carcinoma In Situ component was 2% in cribriform pattern of nuclear grade 2 was also seen. Immunohistochemical profiling showed the tumor cells were negative for hormone receptor (estrogen and progesterone) and HER 2/Neu (human epidermal growth factor receptor) (fig. D). Squamous cell carcinoma component was positive for CK5/6 (fig. E). The patient received adjuvant chemotherapy consisting of four cycles of adriamycin and cytoxan followed by four cycles of taxanes.



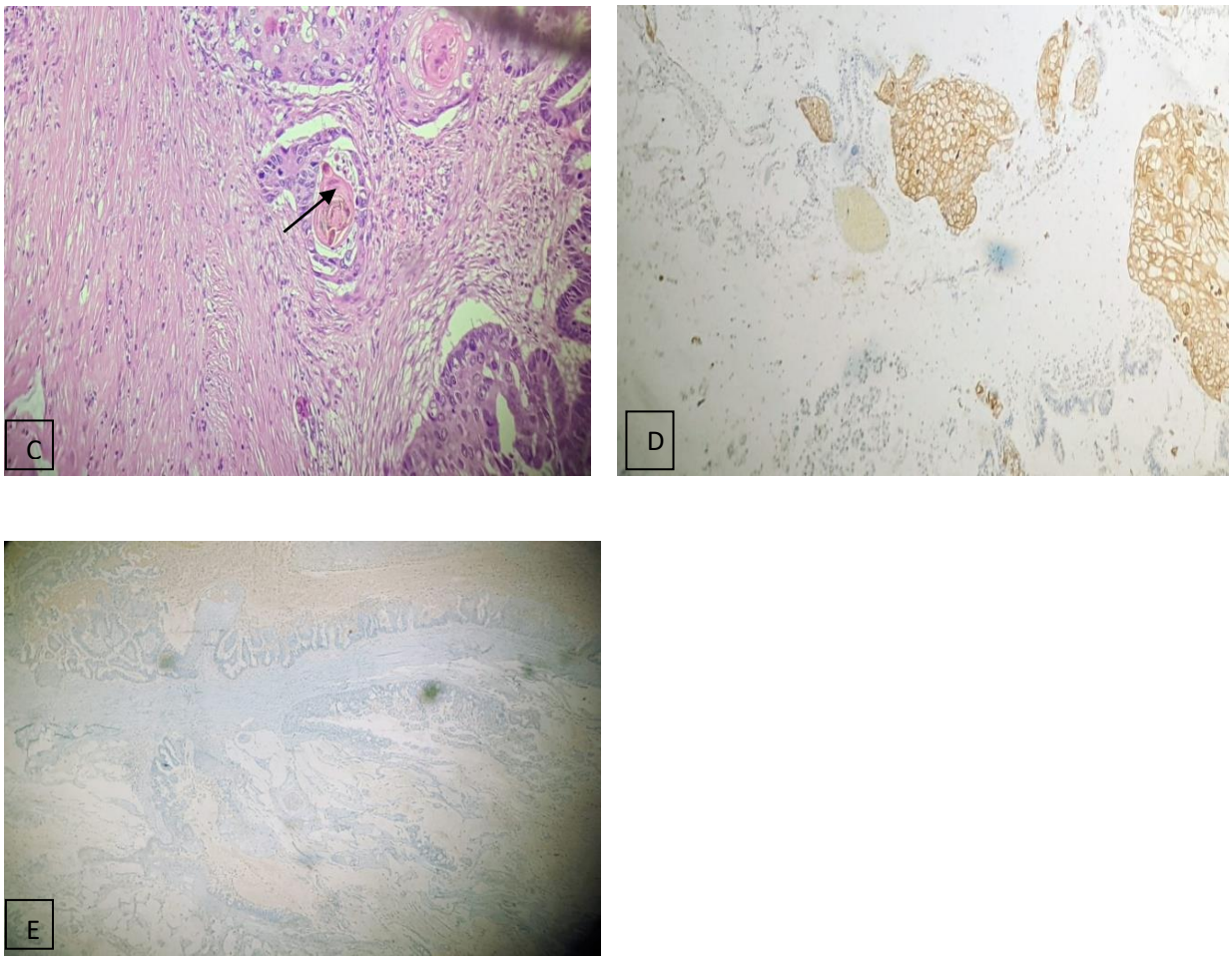


Figure**: - A.** Invasive Ductal Carcinoma component (➔) 40X. Fig. B Chondromyxoid stroma (40X). Fig. C Squamous cell carcinoma component (➔) 40X. Fig.D CK 5/6 Positive(➔) 40X. Fig. E Negative Hormone Receptor (➔) 40X

DISCUSSION

Metaplastic carcinoma with mesenchymal differentiation of the breast, previously known as carcinosarcoma, is a rare, aggressive and highly heterogeneous group of tumors that are characterized by an admixture of epithelial and mesenchymal components [8]. Histologically, carcinoma with mesenchymal differentiation may exhibit varying patterns and combinations of mesenchymal elements including chondroid, osseous, rhabdomyoid, and rarely neuroglial elements. The cell of origin for MBC is not clear but many studies suggest that myoepithelial cells will differentiate along mesenchymal lines and produce matrix elements. The heterologous components can show a wide spectrum of atypia, ranging from bland to overtly malignant, although some tumors may demonstrate osteoclast-type giant cells [3,8,9]. The nature of matrix was variable, ranging from bland cartilage to a typical chondroid to osteoid to overt bone formation [10]. MBCs usually are high-grade neoplasm that present with a large size mass, as in our cases the tumor was large, well circumscribed, whitish firm. Most of them arising de-novo, but there are reported cases that arose from pre-existing lesions as complex sclerosing lesions, papillomas and nipple adenomas [11]. MPC is an aggressive variant of metaplastic breast carcinoma with increased loco regional and distant tumor recurrence [1]. To further identification of an atypical epithelial or carcinomatous component immunohistochemical evidence of carcinomatous differentiation are extremely helpful in the differential diagnosis. In our study immunohistochemical examination showed tumor cell expressed CK5/6 and S100 and triple negative immuno phenotype in both cases. Surgery is the main curative treatment modality since MBC has shown a suboptimal response to the standard chemotherapy. Conservative surgery with radiotherapy is followed for tumors <5 cm in size and total mastectomy followed by chemotherapy and radiotherapy is followed for tumors >5 cm in size with skin or chest wall involvement or >4 axillary lymph node metastasis [12]. The prognosis of patients with metaplastic breast carcinoma depends on the stage of disease, Tumor size larger than 5 cm, histological type, degree of differentiation, histological type and degree

of mesenchymal component, presence of axillary lymph node and distant metastasis [10, 12]. Large tumor size is suggested to be a result of rapid growth rate due to poorly differentiated or undifferentiated tumors [7]. As tumor cell expressed triple hormone receptor negative and CK5/6 positive which represent poor prognosis of MPC. Findings reported by other researchers suggest that the size of the neoplasm at the time of initial treatment best correlated with the prognosis [13]. Further genomic analysis can be done to know the involvement of the gene mutation such as TP53, PIK3CA, PTEN and for further investigation of Metaplastic carcinoma [9].

CONCLUSION

These study revealed metaplastic carcinoma with mesenchymal differentiation which is rare. The prognosis of Metaplastic breast carcinoma is worse than Infiltrating Ductal Carcinoma, the same stage of no special type (NST) breast carcinoma and lower response rate to conventional adjuvant chemotherapy.

ACKNOWLEDGEMENT

Authors are thankful to all staff of Neuberg Supratech References Laboratory, Ahmedabad for their assistance.

DECLARATION OF INTEREST

The authors have declared that no competing interests exist.

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