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# Metplastic Breast Carcinoma-Histological Spectrum A Review of Literature

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**Abstract**
*Metaplastic breast carcinomas areheterogenous group of neoplasms with predominant component other than epithelial or glandular. It is due to transformation of epithelial component into non glandular component such as spindle cells, squamous cells or heterologous elements. It is a rare subtype of invasive breast carcinoma that has a clinically aggressive behavior and poor response to standard chemotherapy which results in over all worst prognosis. Here we are reporting 6 cases of metaplastic breast carcinoma presented at our hospital during the year 2018-19.*

## Introduction

Metaplastic carcinomas are rare forms of invasive breast carcinoma representing 0.3% of invasive carcinoma of breast. Histologically it is a poorly differentiated heterogenous tumor composed of ductal carcinoma admixed with areas of spindle, squamous, choroid or osseous elements. Metaplastic components are of following categories:

Spindle cell carcinoma
Squamous cell carcinoma
Carcinomas with osteoclast like gaint cells
Carcinosarcomas and matrix producing carcinoma
Melanocytic differentiation
Pleomorphic carcinoma
Choriocarcinomatous features[1]

It has gained importance due to its aggressive behaviour and poor prognosis. Its triple negative nature limits treatment options. It expresses higher P53, CK5/6 and EGFR receptors hence are treated with EGFR receptor inhibitors such as geftinib and cetuximab. They have high rate of local recurrence and metastasis. Disease free survival rate is 78.1% when compared to invasive breast carcinoma it is 91%.[2]

Genetically oncogenes such as SNAIL and TWIST encode transcription factors whose primary functions is to promote epithelial to mesenchymal transition (EMT). In EMT carcinoma cells down regulate certain epithelial markers (E-cadherin) and upregulate mesenchymal markers (vimentin and smooth muscle actin).[3]

## Case Report

### Patient-1

51 yr old female patient presented with lump in right breast, FNAC was done which differential diagnosis was given as poorly differentiated carcinoma with multinucleated gaint cells and high grade sarcoma with multinucleated gaint cells. The patient underwent right MRM. On gross cut section revealed a tumor measuring 3.3□3□3 cm with variegated appearance, another hard white nodule noted 3.5cm away from main tumor

measuring 1.5□1□0.8cm. Histomorphological features favor metaplastic carcinoma; metaplastic component is high grade malignant fibrous histocytoma like. Sarcomatous component is 80%, smaller nodule showed infiterating duct carcinoma, grade 3 is about 20%. Axillary nodes were free of tumor. On IHC, ER and PR were weakly positive [30%] and C-erb B2 negative [0%]. Further CK is negative in sarcomatous component and positive in ductal component.

**Patient -2**

A 57 year old female presented with lump in left breast. core biopsy was done which revealed infiltrating duct carcinoma high nuclear grade. Patient underwent left MRM. On gross a solid firm white tumor measuring 4 X 3 X 3cm in central quadrant. On histopathological examination it revealed adenosquamous carcinoma, metaplastic carcinoma. Axillary lymph nodes were free of tumor. On IHC, ER and PR were negative [0%] and C-erb B2 positive [70%]. squamous areas are also similar positivity with additional positivity with ck5/6.

**Patient -3**

A 26 year old female was known case of carcinoma left breast in 2016, presented to us with secondary's at brain and lung. Patient was planned for lung lobectomy, which on gross revealed a solitary tumor measuring 5 X 4.6 X 3.5 cm. on histopathological examination revealed poorly differentiated carcinoma with focal cartilaginous differentiation, in view of history of carcinoma breast it can be considered as metastatic carcinoma. On IHC, ER, HER2Neu were negative. AR and GATA3 were also done which showed positive result.

**Patient-4**

A 45 year old female presented with breast lump. She was evaluated and planned for MRM. On histology the tumor showed high grade pleomorphic spindle cell tumor with pleomorphic spindle cells and multinucleated gaint cells. Osteoid differentiation was visible. On IHC the tumor demonstrated ER, PR, HER2Neu and cytokeratin negative. Multinucleated gaint cells were also CK negative, differentiated duct carcinoma component not seen but also features of phyllodes tumor not seen.

**Patient-5**

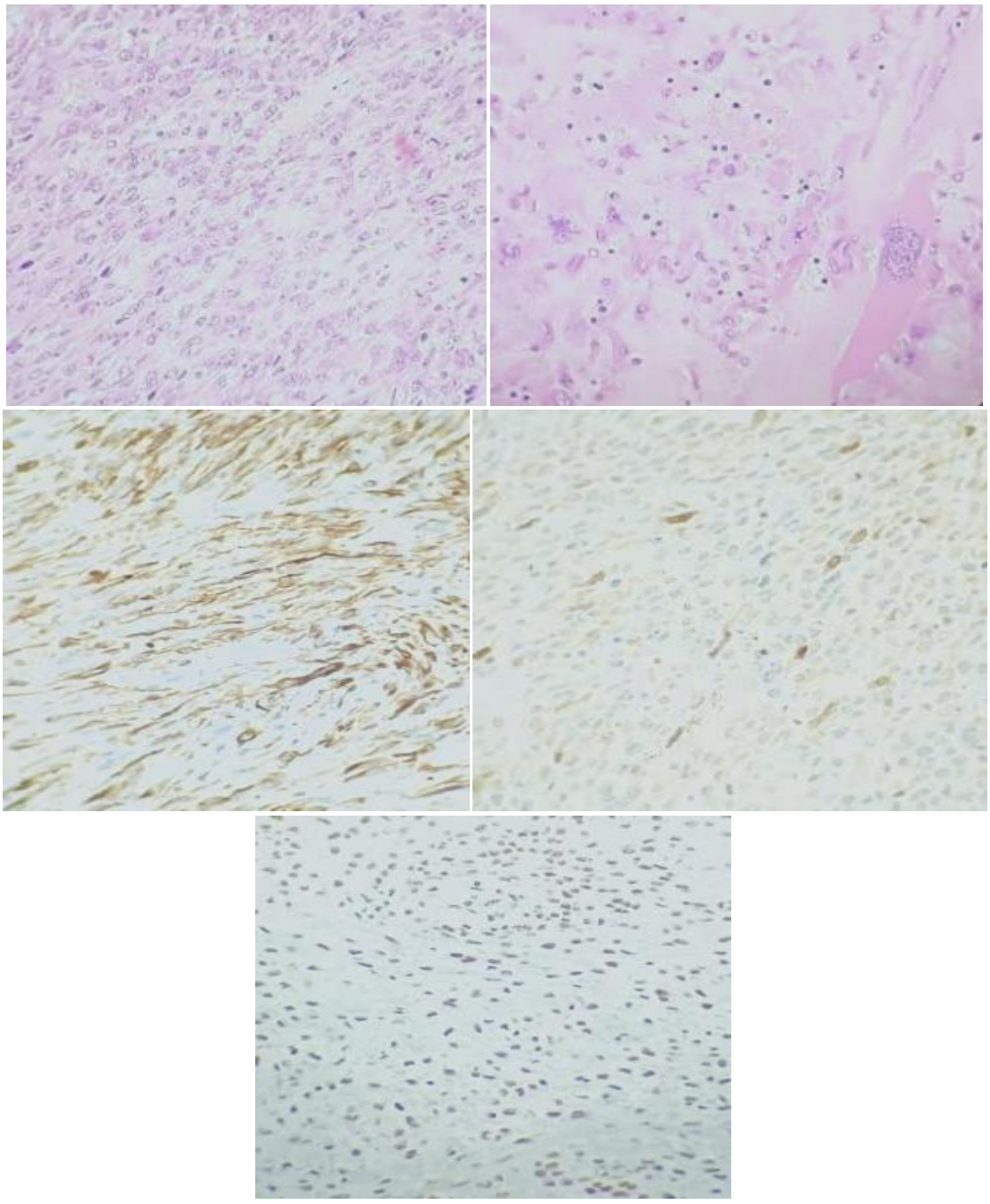
A 51 year old female patient presented with lump in breast. MRM was done. On gross cut section revealed a tumor measuring 2.2x1x1cm. on histopathology the lesion showed biphasic tumor pattern with differentiated component composed of high grade IDC (30%) and pleomorphic spindle cell component with multinucleated gaint cells (70%). Axillary lymph nodes do not show any metastasis. On IHC, ER, PR and HER2NEU were negative. CK was positive in pleomorphic large cells and MIB was high.

**Patient-6**

33 years female patient presented with right breast lump. The patient was evaluated, PET CT scan showed hypermetabolic right breast soft tissue lesion suggesting primary. No other evidence of metabolically active disease in rest of the scanned segment of the body. The patient underwent right modified radicle mastectomy. On gross cutsection revealed an ill defined tumor measuring 7.5x5.5x4.5cm. Histopathology revealed high grade spindle cell sarcoma with heterologous elements, favour rhabdomyosarcoma, spindle cell variant. Definite carcinomatous, DCIS or phylloides elements not seen.20 lymph nodes dissected all were free of tumor. On IHC the tumor cells were positive for desmin and focally positive for myogenin, CD34 and FLI-1. Tumor cells were negative for CK, CD31, SMA, ER and PR.

| S.No | Age | TNM Status | ER, PR, HER2NEU | Other IHC | Metaplastic component |
|---|---|---|---|---|---|
| 1 | 51yrs | pT2N0 | ER,PR-30% +ve<br>Her2neu –score 0 | CK negative | Sarcomatous |
| 2 | 57yrs | pT2N0 | Her2neu-score-3, ER and PR-negative | CK5/6 positive | Keratinization |
| 3 | 26yrs | M1 | ER,PR,Her2neu-negative | AR-+ve<br>GATA3-+ve | Cartilage |
| 4 | 45yrs | pT2N0 | ER,PR,Her2neu-negative | CK- negative | Osteoid |
| 5 | 51yrs | pT2N0 | ER,PR,Her2neu-negative | CK +VE<br>MIB%high | Sarcomatous |
| 6 | 33yrs | pT3N0 | ER,PR negative | Desmin,myogenin,CD34 and FLI-1 positive.CK,CD31 and SMA negative | Sarcomatous |

**Histology**



H/E-high grade spindle cellsarcoma.IHC- desminpositive, myogenin & FLI-1 focally positive.

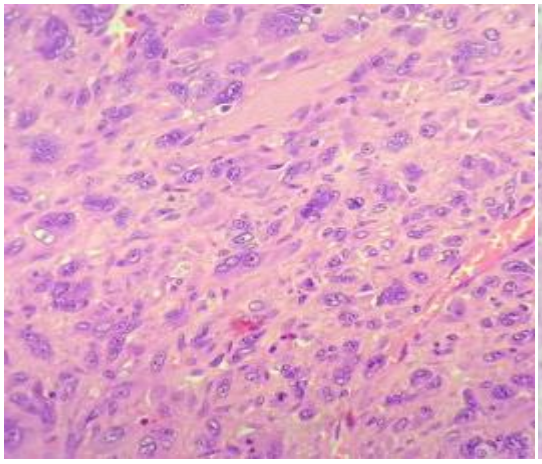


**Figure-1** Sarcoma

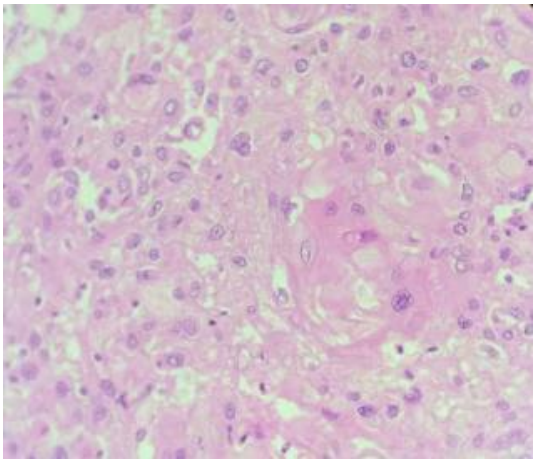


**Figure-2** Keratinization

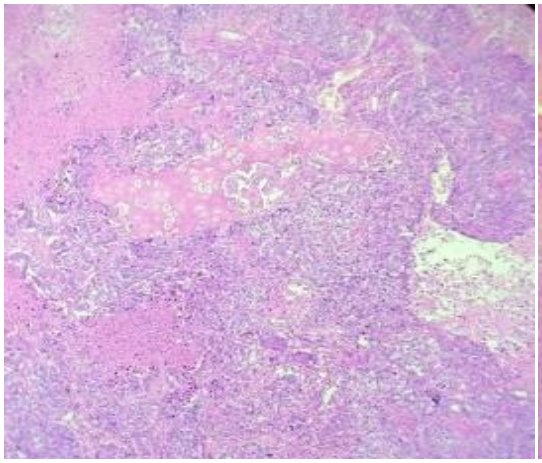


**Figure-3** Cartilage

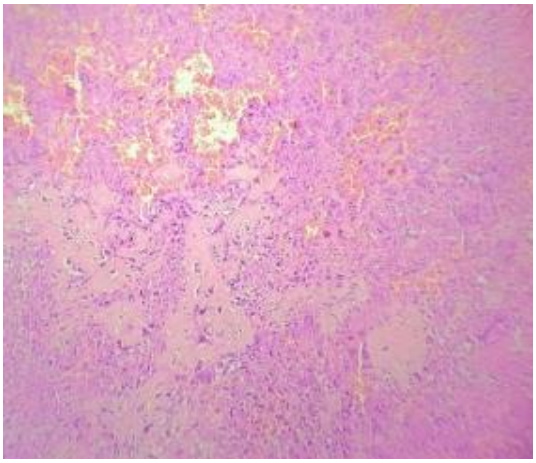


**Figure-4** Osteoid

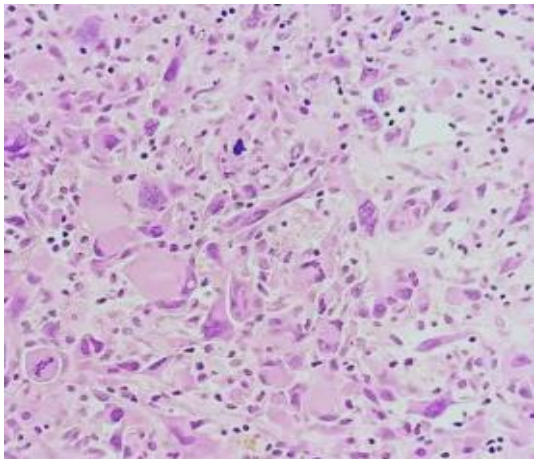


**Figure-5** Multinucleated Gaint Cells

**Discussion**

Metaplastic breast carcinomas are diverse group with biological heterogeneity. There diagnosis largely depends on histomorphology and IHC. The mean age of presentation was around 50 years, and mean size of tumor was around 5cm. lymph node involvement was uncommon. On IHC they demonstrated triple negative status. According to WHO they are classified as:

1] Epithelial type

2] Mixed type

Epithelial type are further classified into a] SCC b] adenocarcinoma with spindle cell differentiation c] adenosquamous.

Mixed type were classified as a] carcinoma with chondroid metaplasia b] carcinoma with osseous metaplasia c] carcinosarcoma.[4]

Histologically metaplastic carcinomas tend to be cellular, mitotically active, cause necrosis and appear high grade. Metaplasia is a reversible conversion of one differentiated cell type to another differentiated cell type. So in these carcinomas breast glandular epithelial cells are differentiated into non glandular mesenchymal tissue. Our above mentioned cases show varied spectrum of metaplasia, showing spindle cells, squamoidcells, cartilaginous and osseous differentiation. On histopathologically it is difficult to diagnose the sarcomatous metaplasia and must be considered in the differential diagnosis of other spindle cell lesions such as fibromatosis, primary low grade sarcoma, inflammatory myofibroblastic tumor and malignant phyllodes tumor.

However due to IHC it has become possible to identify the histological type. Cytokeratin [CK] is negative in sarcomatous component indicating absence of epithelial elements. GATA3 positivity indicates cells are derived from breast. These tumors are generally triple negative breast carcinoma in 90% of cases because they are associated with poorly differentiated carcinomas. This shows there aggressive nature and poor prognosis. MBS have been reported to overexpress EGFR receptors.

Although axillary lymph node do not show any invovment but tendency of metastasis to lung, liver, brain and bone has been reported.

IHC plays a key role in the diagnosis of metaplastic breast carcinoma. Specific markers like myogenin, desmin, GATA-3, AR, FLI-1 and cytokeratins were useful for the diagnosis[5].

MRM is the treatment of choice, as partial mastectomy is associated with high local recurrence. Role of chemotherapy and radiotherapy is unclear. However EGFR inhibitors are used in the treatment.

**Conclusion**

We described a series of cases which are rare with limited treatment options and associated with poor prognosis. Since they are triple negative with basal like features makes it aggressive neoplasm. It requires a rigorous histopathological and IHC examination to confirm the diagnosis.

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