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Case Report

Pathology Section

Metaplastic Carcinoma of Breast with Extensive Chondroid Differentiation: A Case Report with Review of Literature

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ABSTRACT

Metaplastic carcinoma of breast (MBC) is a rare and aggressive type of invasive breast cancer. As it encompasses a variety of distinct histopathologic designations, diagnostic challenges abound. We present a case report of metaplastic carcinoma with extensive chondroid differentiation. This case merits presentation because of its rarity and difficulty to diagnose, especially if the tumour is composed mainly of sarcomatous elements. Standard chemotherapy regimes are ineffective against MBC. The prognosis of MBC is poor in comparison to classical invasive breast cancer. Data focusing on MBC is limited due to its rare incidence.

Keywords: Invasive breast cancer, Sarcomatous

CASE REPORT

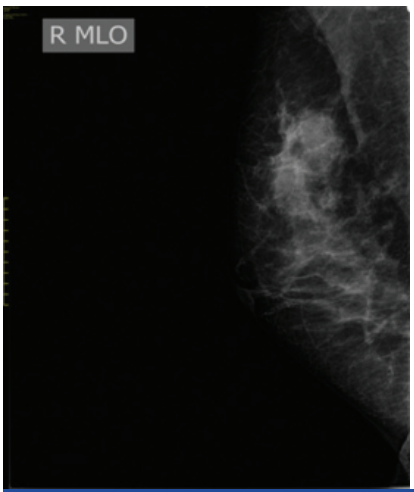
A 55-year -old female came to the surgical outpatient department with history of lump in right breast, since last 4 months, which rapidly grew in size over past 1 week. It was not associated with pain. Clinical examination revealed a firm to hard swelling in the right breast measuring 5 x 4 cm. The breast lump was fixed to the underlying muscle. The skin appeared normal with retraction of the nipple. There was no skin ulceration. Axillary lymph node was not palpable. Clinically the tumour was in Stage II-T2N0M0. Mammogram revealed a radiopaque lump with maximum diameter of 5.5cm, spiculated margins, and punctuate calcifications [Table/Fig-1]. It was categorized as BI-RADS4. The diagnosis offered on Fine needle aspiration cytology of breast lump was poorly differentiated adenocarcinoma, mostly of ductal origin, with poorly differentiated spindle cell component. Routine biochemical and haematological investigations were within normal limits.

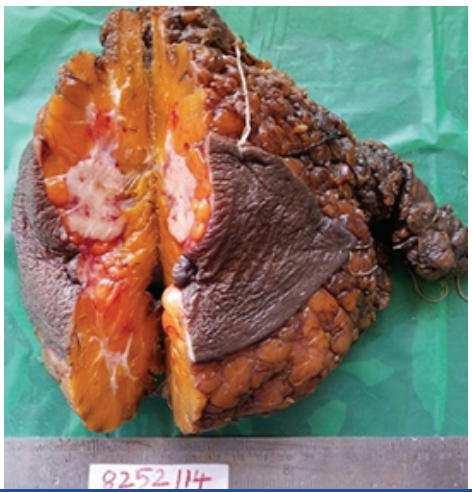
Radical mastectomy of right breast with axillary clearance was performed and sent for histopathological evaluation. The specimen revealed an infiltrating growth measuring 4 x 2.8 cm in upper quadrant of right breast. Nipple was retracted with no evidence of skin ulceration. Cut section of the tumour showed an irregular greyish to glistening white lesion, which was firm to hard in consistency and not adherent to the overlying skin [Table/Fig-2].

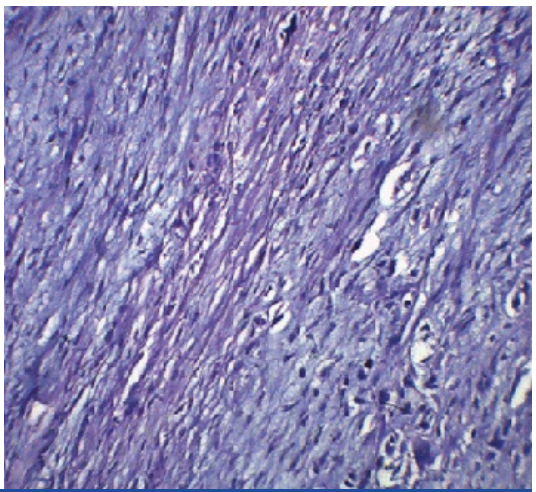
Histopathology showed tumour composed of interlacing bundles of pleomorphic, spindle shaped cells, with large pleomorphic hyperchromatic nucleus and abundant cytoplasm with frequent mitosis [Table/Fig-3]. Amidst these tumour cells, there were irregular clusters of large polygonal to pleomorphic tumour cells with cytoplasmic keratinisation along with anaplastic tumour giant cells [Table/Fig-4]. There were also round to polygonal cells arranged in irregular sheets and occasional ductal pattern. The stroma showed extensive areas of chondroid metaplasia with necrosis. There was no evidence of metastasis in axillary lymph nodes. Based on these features a histopathological diagnosis of Metaplastic Carcinoma (Adenosquamous carcinoma with spindle cell differentiation and extensive chondroid metaplasia), of histological grade 9-poorly differentiated tumour was made. Immunohistochemistry for ER, PR and Her-2/neu was negative. Cytokeratin and vimentin were positive [Table/Fig-5]. Patient was subjected to radiotherapy following surgery. There was no evidence of recurrence of tumour during the first 6 months of follow-up period.

DISCUSSION

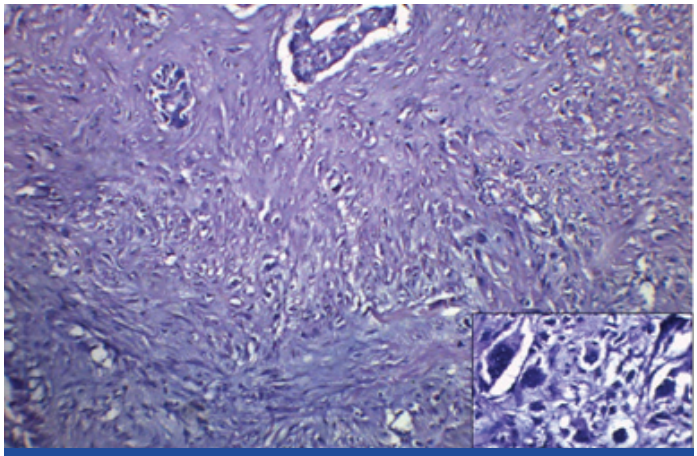
Metaplastic breast carcinoma (MBC) is a rare neoplasm and represents 0.25–1% of breast cancers [1,2]. A few cases have been reported in published literature which is compared with our study [Table/Fig-6]. These tumours are usually of larger size and are firm to hard in consistency on gross examination with a median size of 5 cm. Fixity to skin or deep fascia can be seen [3]. MBC less frequently involve axillary lymph nodes, as compared to classical breast adenocarcinoma [4]. Tseng and Martinez reported axillary lymph node involvement in 22% of MBC patients [2,5]. Purely spindled/sarcomatoid tumours have significant lower rate of nodal



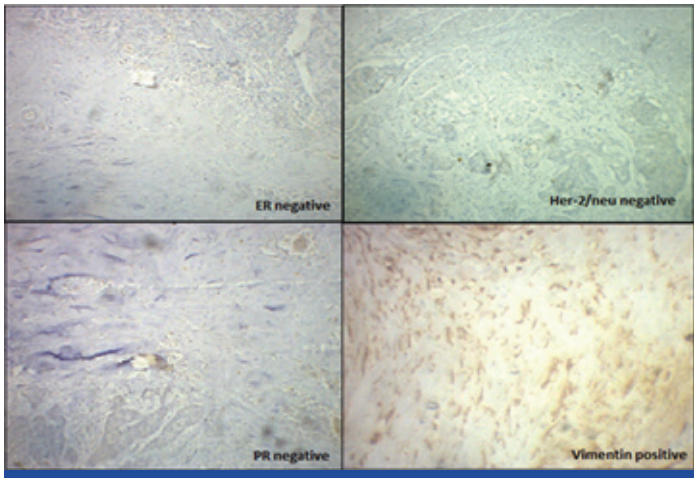




[Table/Fig-1]: Mammogram showing radiopaque lump with spiculated margins, punctuate calcification and diam. of 5.5cm. **[Table/Fig-2]:** Gross- cut section of the tumour showing irregular grey white infiltrating growth. **[Table/Fig-3]:** Malignant spindle cells with chondroid differentiation (H&E, X 100)



[Table/Fig-4]: Malignant spindle cells with chondroid differentiation and malignant ducts (H&E, X100). Inset: pleomorphic tumour giant cells (Inset: H&E, X400)



[Table/Fig-5]: IHC of tumour (X40)

metastasis than conventional ductal and lobular carcinomas [6]. There was no evidence of lymph node metastasis in our case.

Mammogram of MBC exhibits a high density lesion with circumscribed, irregular, obscured, and/or spiculated margins. Calcifications, if present, may be punctuate, amorphous, coarse or pleomorphic. Ultrasonogram usually demonstrates a hypoechoic solid mass or a mixed solid and cystic mass. The MRI exhibits, an irregular mass with spiculated margins, which is hypointense or isointense on T1 weighted imaging and shows intermediate to increased T2 signal intensity [1].

Histologically various classifications of MBC have been described by Tse et al., [7], Wargotz and Norris [8]. The World Health Organization histologically classifies MBC into (1) Epithelial type and (2) Mixed type. Epithelial-type MBC is classified into (i) Squamous cell carcinoma (ii) Adenocarcinoma with spindle cell differentiation (iii) Adenosquamous carcinoma. Mixed type MBC is further classified into (i) Carcinoma with chondroid metaplasia (ii) Carcinoma with osseous metaplasia (iii) Carcinosarcoma [1]. The tumour shows varying proportions of carcinomatous and pseudosarcomatous elements. The pseudo sarcomatous component may mimic malignant fibrous histiocytoma, rhabdomyosarcoma, osteosarcoma chondrosarcoma, or a combination of these [9]. The spindle cell component frequently resembles a reactive process viz. granulation tissue, or a low grade sarcoma which can pose diagnostic challenge. In the present case, sarcomatous component resembled malignant fibrous histocytoma with bizarre tumour giant cells.

Three major theories have been proposed to explain the co-existence of biphasic components. The collision theory for biclonal origin suggests synchronous growth of the carcinomatous component (CC) and heterogenous sarcomatous component (HSC) from separate progenitor cells which collide to form one tumour. The combination theory for monoclonal origin suggests a common multipotential progenitor cell. The conversion/metaplastic theory for monoclonal origin suggests that HSC are derived from the CC through metaplastic process. The co-expression of S-100, vimentin, and/or cytokeratin in both (CC and HSC) is evidence of metaplastic process. Definitive genetic evidence of monoclonal or biclonal origin is still limited [1].

The differential diagnosis of MBC depends on the degree of atypia observed in the tumour and includes nodular fasciitis, fibromatosis, exuberant scars, myofibroblastomas, pseudoangiomatous stromal hyperplasia, primary or metastatic sarcoma and malignant phyllodes tumour [3].

MBCs are mostly estrogen receptor (ER), progesterone receptor (PR) and Her2-neu negative and tend to have worse prognosis than other triple negative breast cancers [2]. Cytokeratin and vimentin positivity is the defining feature. Basal markers, which can be used as therapeutic targets, are commonly expressed, viz. CK14 & 17, EGFR, caveolin-1 and Vascular endothelial growth factor (VEGF) [3]. The spindle cells express myoepithelial markers (34 bE 12, smooth muscle cell actin) [7]. A higher percentage of AE1/AE3 expression, ranging from 63% to 100% is reported in recent studies [7,8].

There is no “standard” therapy for all patients with MBC, due to its rarity and intratumoural heterogeneity [2,11]. Most MBCs are managed by radical mastectomy followed by chemotherapy and radiotherapy. Traditional chemotherapy and hormonal therapies for IDC are ineffective against MBC and often associated with poorer survival [2]. Tseng et al., suggested that regardless of the type of surgery performed, adjuvant radiation improved both disease-specific and overall survival for all patients undergoing treatment for MBC [2,5]. The prognosis is similar to that of comparable stage of adenocarcinoma, and thus treatment should follow similar principles [10,12]. The mesenchymal element involved seems to be important in determining outcome [10].

	Sandhya arora et al..[6]	Sood et al., [3] 1st case	Sood et al.,[3] 2nd case	Corrine Wong et al.,[10]	Lorenzo rossi et al.,[11]	Present study
Age(yrs)	37	47	50	57	44	55
Chief complaint	Breast Lump- 4 months	Breast lump	Breast lump	Rapid swelling in right breast-4wks with pain and erythema	Breast lump	Breast lump- 4 months
Size at presentation	4x1.5 cm	4x2 cm	5.5x5 cm	16x11 cm	5.5x5 cm	5x4 cm
Histo-pathological diagnosis	MBC with high grade spindle cell component	IDC with areas of spindle and rhabdo-myoblastic differentiation	MBC with osteoclast- like giant cells	MBC with osteogenic sarcoma	MBC with squamous metaplasia, containing spindle-cell, chondroid and osteoclastic component	MBC with spindle cell differentiation and extensive chondroid metaplasia
Lymph node status	Negative for metastasis	1/12 LNs positive for metastasis	4 LNs, all positive for metastasis	16 LNs, all positive	Negative for metastasis	Negative for metastasis
Marker study	-	Triple negative(ER, PR, Her-2/neu)	Triple negative	ER and PR negative	CK and S-100 positive ER weakly positive PR & her2 negative	Triple negative

MBC- Metaplastic breast carcinoma, IDC- Infiltrating ductal carcinoma, LNs- Lymph Nodes, ER- Estrogen receptor, PR- progesterone receptor

[Table/Fig-6]: Comparison of Metaplastic breast carcinoma cases reported in literature with our case

CONCLUSION

MBC are very rare, aggressive and invasive breast cancers. These tumours are usually large at presentation with low rate of axillary node involvement. Rarely, these tumours may show extensive areas of chondroid differentiation. MBC are usually triple negative and need aggressive therapy as they are known for frequent recurrences. Early diagnosis and management provides complete cure. Further research studies are required to develop targeted treatments with goal of improving clinical outcomes.

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