

Metaplastic Breast Carcinoma: A Case Series with Three Different Presentations

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ABSTRACT

Metaplastic Breast Carcinoma (MBC) is one among the rare types of breast carcinoma. MBC was recognised as a separate entity by World Health Organisation (WHO) in 2020. According to WHO, metaplastic carcinoma is classified into six types based on the histology which includes: low grade adenosquamous carcinoma; fibromatosis like metaplastic carcinoma; squamous cell carcinoma; spindle cell carcinoma; carcinoma with heterologous mesenchymal differentiation; and mixed metaplastic carcinomas. This rare type of tumour shows both epithelial and/or mesenchymal elements within the same lesion. The management of these patients remains an enigma due to the rarity of the tumour and the treatment responses between patients following therapy. In the present case series, five cases of MBC and their follow-up have been described. All patients were females within the age group of 50-65 years. All five patients underwent modified radical mastectomy. Lymph node involvement was noted in one case. Among the five cases, two patients had adenosquamous carcinoma, two patients had metaplastic carcinoma with heterologous mesenchymal differentiation and one patient had mixed metaplastic carcinoma.

Keywords: Adenosquamous carcinoma, Prognosis, Triple negative breast carcinoma

INTRODUCTION

The MBC, which accounts for approximately 0.2-1% of breast carcinoma, is a subtype of triple negative breast tumours [1]. Metaplastic carcinoma belongs to a heterogenous group of invasive breast carcinomas which is characterised by differentiation of neoplastic epithelium to squamous/mesenchymal elements. Different variants of metaplastic carcinoma include: low grade adenosquamous carcinoma; fibromatosis like metaplastic carcinoma; squamous cell carcinoma; spindle cell carcinoma; carcinoma with heterologous mesenchymal differentiation; and mixed metaplastic carcinomas. Being a rare and heterogenic entity, treatment of these patients becomes a challenging one. Files of the patients who were operated between January 2016 and June 2021 were retrieved from the hospital database. From the available information, five cases of MBC were identified. The patient's age, gender, presenting complaints, surgical procedure done, tumour size and histologic grading were noted down from the pathology reports.

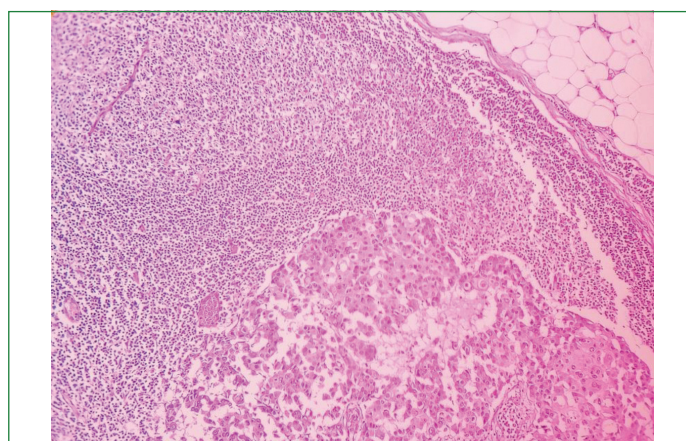
CASE SERIES

Case 1

A 56-year-old female presented to the General Surgery Department with complaints of lump in the right breast for the past two years which was progressively enlarging. The patient also presented with history of weight loss. Clinical diagnosis was given as breast carcinoma. On examination mass measuring 4×3 cm was noted. Gross examination of the specimen revealed a grey white mass measuring 3×2.5 cm. Microscopy revealed a tumour composed of nests and sheets of squamoid cells with areas showing tumour cells arranged in glandular pattern. Clusters of lymphocytes were noted surrounding the tumour cells. Final diagnosis was MBC- Low grade Adenosquamous carcinoma. Metastases to axillary lymph node were noted [Table/Fig-1].

Case 2

A 50-year-old female presented to the General Surgery Department with complaints of lump in the left breast for the past six months which was progressively enlarging. On examination mass measuring 2×1 cm was noted. The mass was painless and slightly mobile. Mammography revealed a low-density soft tissue mass; clinically,



[Table/Fig-1]: Adenosquamous carcinoma with nodal metastasis (H&E, 40x).

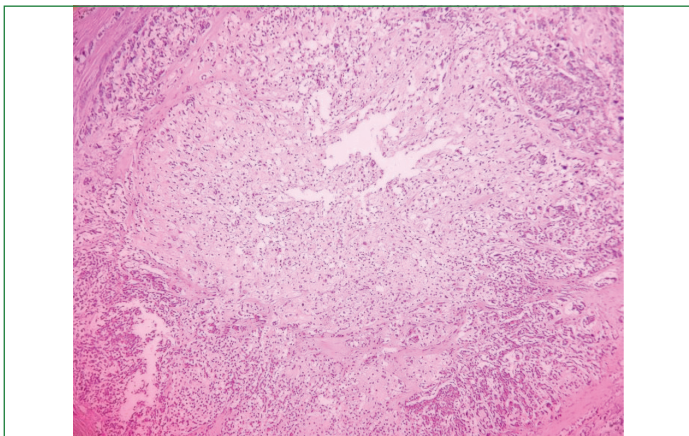
diagnosed as breast carcinoma. Gross examination of the specimen revealed a grey white mass measuring 4×4×1.5 cm [Table/Fig-2,3]. Microscopy revealed an infiltrative tumour composed of neoplastic cells arranged in tubules along with mesenchymal components (cartilage). The tubules were composed of round cells having hyperchromatic nuclei. Extensive areas showing cartilage and areas of myxoid changes was noted [Table/Fig-4]. Final diagnosis was MBC with heterologous mesenchymal differentiation.



[Table/Fig-2]: Modified Radical Mastectomy (MRM) specimen with tumour.



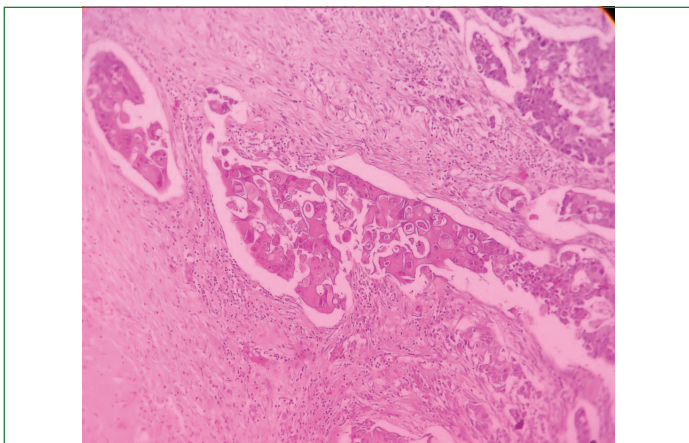
[Table/Fig-3]: Cut surface showing grey white well-defined mass.



[Table/Fig-4]: Tumour showing chondroid matrix (H&E, 10x).

Case 3

A 52-year-old female presented to the General Surgery Department with complaints of lump in the right breast for the past one year. Patient had nipple discharge for the past one week. On examination, a mass measuring 3x3 cm was noted. Ultrasonogram revealed a lobulated heterogenous solid mass beneath the nipple areola complex. Gross examination of the specimen revealed a grey white mass measuring 3x2x2 cm. Clinical diagnosis of breast carcinoma was established. Microscopy revealed a tumour composed of nests and sheets of squamous cells with focal areas showing tumour cells arranged in glandular pattern [Table/Fig-5]. Cystic cavities lined by squamoid cells were noted. Extensive necrosis was seen. Also, neoplastic component arranged in ducts were noted. The neoplastic cells were moderately pleomorphic columnar cells confined within the duct. Final diagnosis was MBC- low grade adenosquamous carcinoma with foci of ductal carcinoma in-situ.



[Table/Fig-5]: Squamoid areas in adenosquamous carcinoma (H&E, 40x).

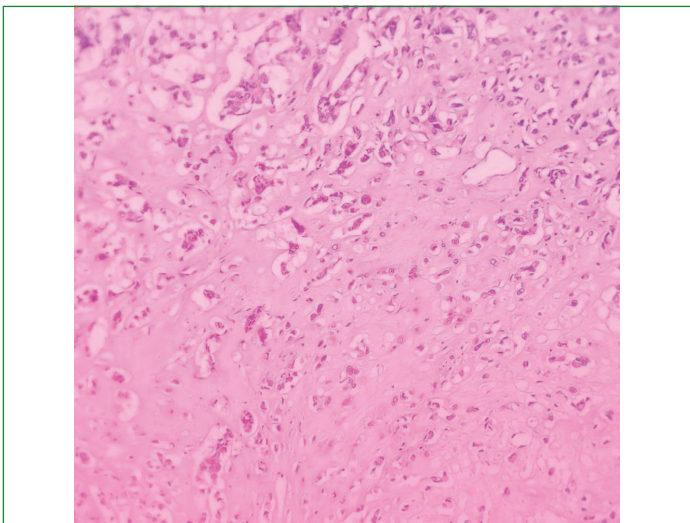
Case 4

A 58-year-old female presented to the General Surgery Department with complaints of lump in the right breast for the past nine months

which was progressively enlarging. Diffuse redness of the skin was noted over the swelling. On examination, a mass measuring 2x1 cm was noted. Fine needle aspiration cytology had been performed earlier in an outside centre and was reported as ‘few atypical cells seen’. No conclusive diagnosis was given. Based on the clinical evaluation, breast carcinoma was suspected. Gross examination of the specimen revealed a grey white mass measuring 2x2x1.5 cm [Table/Fig-6]. Microscopy revealed a tumour composed of neoplastic cells arranged in tubules along with mesenchymal components (cartilage). Intervening stroma showing myxoid changes and dense chronic inflammation was also noted [Table/Fig-7]. Desmoplastic stroma was seen. Final diagnosis was MBC with heterologous mesenchymal differentiation.



[Table/Fig-6]: MRM- cut surface showing an ill-defined grey white lesion with adjacent areas of fibrosis.



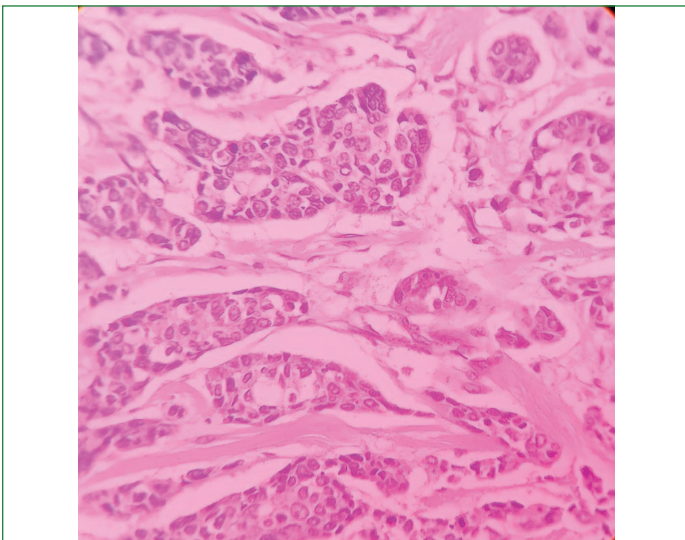
[Table/Fig-7]: Tumour showing chondroid matrix (H&E, 40x).

Case 5

A 64-year-old female presented to the General Surgery Department with complaints of lump in the left breast for the past one and a half years. Increase in size was noted for the past two months along with pain. On examination mass measuring 4.5x4 cm was noted. Ultrasonogram revealed a heterogeneous lesion with both cystic and solid areas. Clinical diagnosis was given as breast carcinoma. Ulceration of skin and a protruding mass was noted. Gross examination of the specimen revealed the nipple area complex being replaced by the mass, overlying skin showed ulceration and a protruding grey white mass measuring 5.5x4.5x4 cm [Table/Fig-8]. Microscopy revealed a tumour composed of chondroid matrix, nests of squamous cells and spindle cells. The squamous cells were seen in nests. Focal cystic cavities lined by squamoid epithelium were noted. Few foci showing elongated, spindle shaped cells were noted. Focal area showed tumour cells arranged in tubules representing infiltrating ductal elements were also seen [Table/Fig-9]. Final diagnosis was MBC- mixed metaplastic carcinoma.



[Table/Fig-8]: MRM-mass lesion on the skin surface replacing nipple areola complex.



[Table/Fig-9]: Tumour cells arranged in tubules (H&E, 40x).

DISCUSSION

The MBC was recognised as a distinct pathologic entity by WHO in 2000. Even after the recognition of MBC as a specific entity, the incidence of these tumours remains under 1% in comparison to other breast malignancies [2]. The WHO recognises different variants of metaplastic carcinoma based on the histology which includes low grade adenosquamous carcinoma, fibromatosis like metaplastic carcinoma, squamous cell carcinoma, spindle cell carcinoma, carcinoma with heterologous mesenchymal differentiation and mixed metaplastic carcinomas [3]. All the metaplastic variants except low grade adenosquamous carcinoma and fibromatosis like carcinoma have high propensity for metastasis [4]. The actual pathogenesis of MBC remains unknown. Three hypothesis, collision theory, combination theory of monoclonal origin and conversion/metaplastic theory gives explanation for the origin of MBC having both mesenchymal and epithelial components [5].

In the present case series, two low grade adenosquamous carcinoma, two cases of metaplastic carcinoma with heterologous mesenchymal differentiation and one case showing mixed metaplastic carcinoma features were presented.

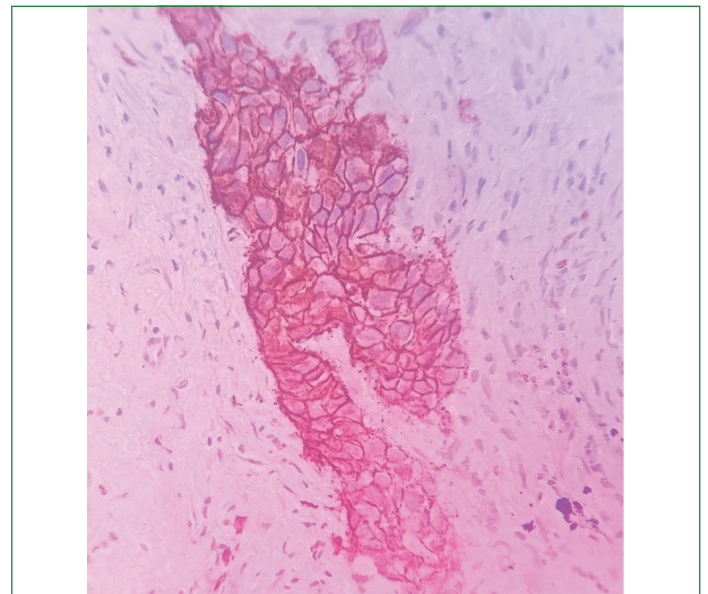
Among the two patients who were diagnosed as having low grade adenocarcinoma, one patient presented with breast lump and weight loss and the other patient presented with history of nipple discharge along with complaints of breast lump. Histology of both breast lumps revealed a tumour composed of predominantly nests and sheets of squamoid cells. Few foci show glandular arrangement of tumour cells. Lymphocytic aggregates were noted surrounding the tumour cells. One patient with low grade adenosquamous carcinoma had lymph node metastasis. In all other cases, no evidence of lymphovascular emboli was noted.

In metaplastic carcinoma with heterologous mesenchymal differentiation, mesenchymal components and carcinomatous

areas were present. Histology of both cases showed chondroid matrix which is a mesenchymal component along with tumour cells arranged in tubular configuration which represented the carcinomatous component.

The case which was diagnosed as mixed metaplastic carcinoma presented with history of breast lump and pain over the breast. Histology of the lesion showed tumour arranged in glandular and tubular pattern. Nests and sheets of squamoid cells along with foci showing spindle cells were seen. Mixed metaplastic carcinoma showed both metaplastic and conventional adenocarcinomatous elements.

The MBC being a triple negative carcinoma do not express Estrogen Receptor (ER), Progesterone Receptor (PR) and Her2neu receptors and vast majority of tumours show negative immunohistochemistry. The prognosis of MBC was worse when compared to other types of triple negative breast carcinoma [6]. When compared to Triple Negative Breast Carcinoma (TNBC), MBC presents with large tumour size and high histological grade along with overexpression of p53 and Ki-67 [1]. This is consistent with the present study since all five cases showed overexpression of p53. In present series, one case of adenosquamous carcinoma showed a mild positivity for Her2neu [Table/Fig-10]. This is attributed to the EGFR gene mutations in a subset of metaplastic tumours [7]. All the tumours exhibited positivity for CK5/6, a high molecular weight cytokeratin.



[Table/Fig-10]: Tumour showing Her2neu positivity (H&E, 40x).

Metaplastic carcinoma is commonly seen in women above 50 years of age. In present series, all patients were above 50 years which is consistent with the literature [2]. All patients underwent modified radical mastectomy. Three patients had previous trucut biopsy which showed features of metaplastic carcinoma. One patient had a previous biopsy reported as Invasive breast carcinoma Not Otherwise Specified (NOS), the patient underwent chemotherapy after which MRM was done which was concluded as low grade adenosquamous carcinoma. Based on the trucut biopsy diagnosis for this patient, there was no response to chemotherapy after which MRM was done. Three patients received adjuvant radiation and chemotherapy and follow-up was uneventful. Records regarding postsurgical treatment and follow-up were not available for other two cases. Even though MBC is highly aggressive, because of the rarity of the lesion and poorly understood natural history, MBC does not have a clear-cut management guidelines [8]. The attempt to predict the prognostic markers of MBC has not provided any solid conclusions till now. However, high Ki67 scores and lymphovascular invasion are considered to be associated with poor prognosis of MBC [2]. Demographic and clinical details of all cases has been mentioned in [Table/Fig-11].

Age in years/Gender	Clinical presentation	Clinical diagnosis	Histopathology findings	Follow-up details
56/female	Lump in right breast x 2 years weight loss	Breast carcinoma- Bi-RADS 4	Tumour composed of nests and sheets of squamoid cells with areas showing tumour cells arranged in glandular pattern. Clusters of lymphocytes were noted surrounding the tumour cells. Final diagnosis was MBC-Low grade Adenosquamous carcinoma. Metastases to axillary lymph node were noted.	Not known
50/female	Lump in left breast x 6 months painless, progressive enlargement.	Breast carcinoma Bi-RADS 5	Tumour cells arranged in tubules along with mesenchymal components (cartilage). The tubules were composed of round cells having hyperchromatic nuclei. Extensive areas showing cartilage and areas of myxoid changes noted. Final diagnosis was MBC with heterologous mesenchymal differentiation	Not Known
52/female	Lump in right breast x 1 year nipple discharge	Breast carcinoma Bi-RADS 5	Tumour composed of nests and sheets of squamous cells with focal areas showing tumour cells arranged in glandular pattern. Cystic cavities lined by squamoid cells were noted. Extensive necrosis was seen. Also, noted neoplastic component arranged in ducts. The neoplastic cells were moderately pleomorphic columnar cells confined within the duct. Final diagnosis was MBC-Low grade Adenosquamous carcinoma with foci of Ductal carcinoma in-situ.	Uneventful-1 year
58/female	Lump in right breast x 9 months progressively enlarging redness over the skin	Breast carcinoma Bi-RADS 5	Tumour composed of neoplastic cells arranged in tubules along with mesenchymal components (cartilage). Intervening stroma showing myxoid changes and dense chronic inflammation noted. Desmoplastic stroma seen. Final diagnosis was MBC with heterologous mesenchymal differentiation.	Uneventful-1 year
64/female	Lump in left breast x 1 and a half years. Progressively enlarging. Pain over the left breast.	Breast carcinoma Bi-RADS 4	Tumour was composed of nests and sheets of squamous cells with focal areas showing tumour cells arranged in glandular pattern. Cystic cavities lined by squamoid cells were noted. Extensive necrosis was seen. Also, noted neoplastic component arranged in ducts. Few foci showing elongated, spindle shaped cells noted. Focal area showing tumour cells arranged in tubules representing infiltrating ductal elements also seen. Final diagnosis was MBC-mixed metaplastic carcinoma.	Uneventful-5 months

[Table/Fig-11]: Clinical presentation and case details.

CONCLUSION(S)

Though MBC is an aggressive disease, due to the rarity of the tumour there is no satisfying details regarding the pathogenesis, risk factors, prognostic factors and treatment protocols. The current knowledge on MBC disease progression and treatment efficiency is limited. Studies and clinical trials on large number of patients can provide a good insight about the disease and targeted therapies.

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