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Metaplastic Breast Cancer with Chondroid Differentiation

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ABSTRACT

Background: Metaplastic breast cancer (MBC) cancer is a rare subtype of breast carcinoma and carries a worse prognosis. Chondroid differentiation is the rarest among all its histologic subtypes. We report a case of MBC with chondroid differentiation and review its clinicopathological details, genetic basis, and management.

Case presentation: A 56-year female presented with right-sided large breast lump. She noticed this lump 4 months before presenting. Trucut biopsy was suggestive of invasive ductal carcinoma. She underwent breast conservation surgery and histology was consistent with MBC with chondroid differentiation, pT2N3aM0. Tumour was triple-negative for ER, PR, and Her-2- neu receptors. Adjuvant treatment with chemotherapy followed by radiotherapy was given and she has been doing fine during 11 months of follow-up.

Conclusion: The MBC is an uncommon subtype with heterogeneity in biological and morphological features and its knowledge is paramount while evaluating a breast lump. Understanding the pathologic and molecular basis is imperative in developing the targeted therapy to improve outcomes.

Introduction

Metaplastic breast cancer (MBC) is an extremely rare subtype identified in 2000. It represents 0.2-1% of breast cancer and is typically composed histologically of poorly differentiated invasive ductal carcinoma coexisting with areas of squamous or mesenchymal differentiation.¹ The pathologic diagnosis of MBC is difficult due to heterogeneity. Aggressive biological parameters like high histological grade are more frequently found in MBC compared to invasive ductal carcinoma which drives a more aggressive treatment. Mastectomy rates are higher due to larger tumour size at the time of presentation despite lower incidence of axillary lymph node involvement.² They typically do not express estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor

receptor-2 (HER2), which is suggested to be a reflection of absence of extensive glandular component. This cancer is considered as a subgroup of basal like breast cancers when classified by gene expression and carry a poor prognosis due to lack of response to hormonal therapy. MBC with chondroid differentiation is the rarest among all histologic subtypes of breast cancer.³ It has worse prognosis compared to infiltrating ductal carcinoma, even when adjusted for stage, with a 3-year overall survival rate of 48-71% and 3-year disease-free survival rate of 15-60%.⁴ We report a case of metaplastic carcinoma with chondroid differentiation.

Case Presentation

A 56-year-old woman presented with a lump in right breast in upper outer quadrant. There was no history suggestive of nipple discharge. Family history was non-contributory. On examination, a hard non-tender mass measuring approximately 4 x 5 cm was noted in upper outer quadrant of right breast extending into axillary tail. Mass was not fixed to overlying and underlying structures. There were no obvious skin changes. A lymph node was

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palpable in the right axilla. Mammography was suggestive of a single lesion in the upper outer quadrant with few nodes in the axilla. The PET-MRI Fusion study was done revealing a well-defined rim enhancing hypermetabolic altered signal intensity lesion in upper outer quadrant at 9 -11 o' clock in anterior depth measuring 4.3 x 4.2 x 4.5 cm. It showed nodularity along the periphery and internally with washout pattern of enhancement. Lesion was 2.2 cm, 1.5 cm and 7 cm away from nipple, skin and chest wall, respectively. A few enlarged hypermetabolic axillary lymph nodes, the largest measuring 2.1 x 1.7 cm, were noted. There was no evidence of disease elsewhere. Fine needle aspiration cytology revealed a poorly differentiated carcinoma consistent with mammary duct origin. Biopsy of mass revealed invasive ductal carcinoma in a background of dense stromal fibrosis. The patient underwent right-sided breast conserving surgery with latissimus dorsi flap reconstruction.

Histology revealed a tumour measuring 3.8 x 2.9 x 1.2 cm solid cystic lesion containing haemorrhage and papillary excrescences. Skin and nipple were negative for tumour. Histological type was a metaplastic carcinoma with chondroid differentiation, as shown in Figure 1 a, b. The tumour was triple negative on immunohistochemistry as oestrogen receptor (ER), progesterone receptor (PR), and HER-2 neu were negative, as shown in Figure 2 a,

b. Tumour cells showed some degree of anisocytosis with a nuclear pleomorphism score of 3, and mitotic figures in tumour cells were frequent with an average of 8 mitoses or more per square mm. Overall Nottingham score was 9 (Tubule formation (3) + Mitotic Count (3) + Nuclear Pleomorphism (3) = 9), with the grade being 3. Lymphovascular emboli were present along with nodal involvement with extracapsular extension. Totally, 14 lymph nodes were involved out of 28 (pT2N3aM0).

Adjuvant chemotherapy with AC-T (Adriamycin, Cytoxan, and Taxol) was initiated. She developed taxol-induced sensory neuropathy leading to early discontinuation of Taxol. She also received radiotherapy and has been under surveillance with no evidence of recurrence for 11 months.

Discussion

The MBC is a rarely encountered tumour and constitutes less than 1% of all malignant breast tumours. World Health Organization (WHO) classifies MBC into (1) epithelial type and (2) mixed type. Epithelial type of MBC is further classified into squamous cell carcinoma, adenocarcinoma with spindle cell differentiation and adenosquamous carcinoma. Mixed type is further classified into carcinoma with chondroid metaplasia, carcinoma with osseous metaplasia, and carcinosarcoma. Prognosis of

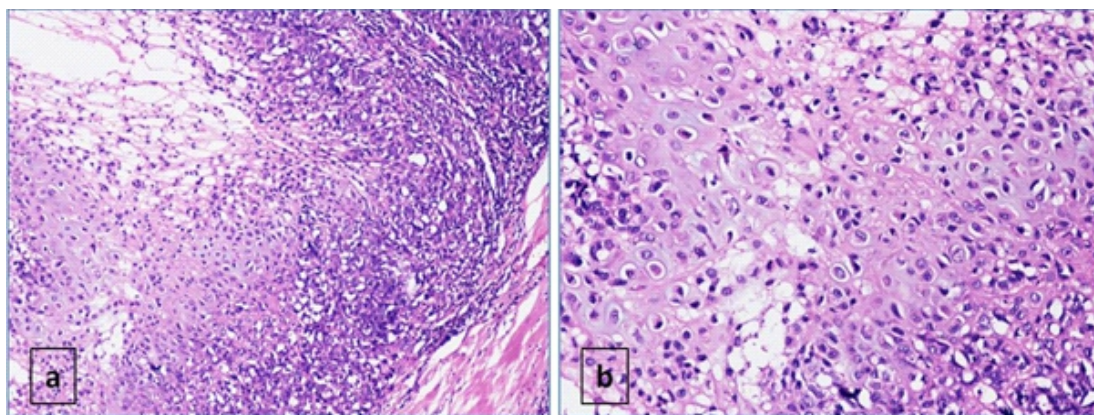


Figure 1. Hematoxylin and Eosin stained slide showing metaplastic breast carcinoma with chondroid differentiation, a. 20x, b. 40x.

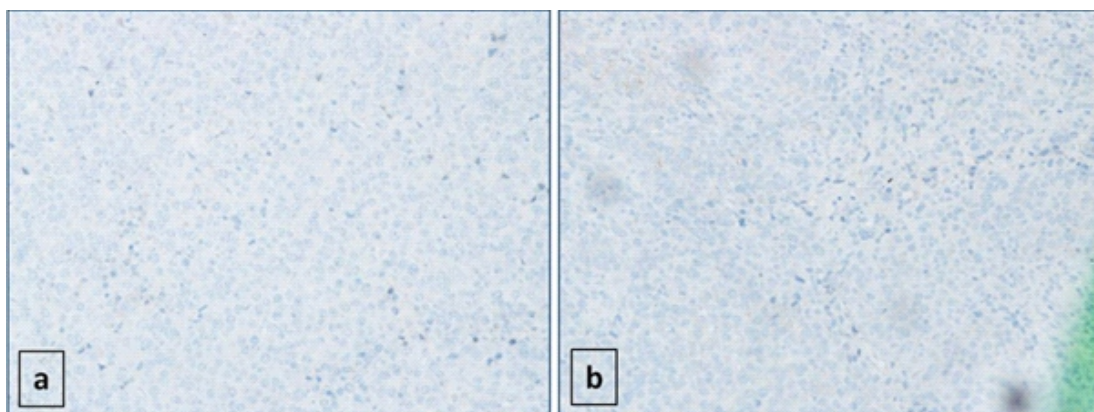


Figure 2. Immunohistochemistry negative for Estrogen, a and HER2 Neu, b.



each of these varies widely. Typical histologic picture is comprised of poorly differentiated infiltrating ductal carcinoma coexisting with areas of squamous or mesenchymal differentiation. Chondroid differentiation is the rarest among all above varieties and carries the worst prognosis.⁵

MBC usually affects the females over 50 years old. The common clinical presentation is a palpable and firm large breast mass usually greater than 3 cm. The history is usually of short duration and around 20% cases present with skin tethering. Our patient presented with a right sided large breast lump. No skin changes were observed. Large tumour size and hence higher T stage is explained by rapid growth kinetics in poorly differentiated tumours.⁶

Diagnosis is usually inconclusive on fine needle aspiration biopsy due to large size and tumour heterogeneity and is established mainly after excisional biopsy or resection. Trucut biopsy in our case was suggestive of infiltrating ductal carcinoma but final histology showed MBC with chondroid differentiation.

Spread to axillary lymph node is less common despite large tumour size and high histologic grade. The paucity of lymph nodal involvement was attributed to the presence of mesenchymal elements. Higher incidence of axillary lymph node metastasis has been reported in squamous subtype by Huvos et al.⁷ Even with rarity of lymph nodal involvement, axillary dissection cannot be avoided as diagnosis is sometimes not clear. In our case, axillary clearance was done and 14 out of 28 lymph nodes were positive. Despite low rates of axillary involvement, MBC has high potential for distant metastases via hematogenous route, mostly to lung and bone.⁸

Treatment is largely on lines of invasive ductal carcinoma. Large tumour size is responsible for high rates of mastectomy but rates of breast conservation surgery and mastectomy are similar to other tumours if corrected for tumour size. Breast conservation therapy with adjuvant radiation can be considered if the tumour size is less than 5 cm. If tumour size exceeds 5 cm, total mastectomy is suitable.⁹

Response to conventional chemotherapy is limited but as per current guidelines, adjuvant treatment is the same as invasive ductal carcinoma.¹⁰⁻¹² This cancer is associated with poor prognosis and common poor prognostic factors are younger age, skin involvement, lymphovascular invasion, high Ki67 scores, nodal involvement and squamous cell carcinoma in lymph nodes. Positive basal marker and cancer stem cell expression in tumor cells are independent indicators for poor prognosis. Some immunohistochemical characteristics like EGFR overexpression, EGFR gene amplification, and focal staining of CK14 have been reported to be associated with decreased disease free survival.¹³

In molecular terms, MBCs usually cluster with triple-negative breast cancers (TNBCs) preferentially

with basal-like or claudin-low molecular subtypes and frequently harbour mutations in TP53 gene. MBC has markers of epithelial-mesenchymal transition and cancer stem cells responsible for production of chemotherapy resistant cells capable of dedifferentiation and propensity for invasion. Overexpression of epithelial-mesenchymal transition inducers like vimentin and SPARC has been found to be associated with higher grade and triple negative status in MBC.¹⁴ The recent literature is also suggestive of this. Studies investigating genetic basis of MBC which explore potential therapeutic targets are the way forward. Gene expression profiling of tumor holds great promise in developing targeted therapy for MBC in future.¹⁵

In conclusion, the limited knowledge of MBC is due to its rarity and heterogeneity in biological and morphological features as well as various classifications and different treatment strategies. It is imperative to keep MBC in differential diagnosis while evaluating any breast lump and giving due treatment. In a small and selected group of patients treated according to cancer stem cell characteristics, the results are encouraging; hence, more efforts are needed to explore potential molecular targets and improve outcomes.

Ethical consideration

The informed consent was obtained.

Conflict of Interest

The authors declared no conflict of interests.

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Figure 2. Immunohistochemistry negative for Estrogen, a and HER2 Neu, b.