Indian Journal of Pathology and Oncology 2020;7(4):661–664

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Indian Journal of Pathology and Oncology

Journal homepage: www.ijpo.co.in

Case Report

Metaplastic carcinoma of breast: A rare histological entity

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ARTICLE INFO

Article history:
Received 29-01-2020
Accepted 29-06-2020
Available online 19-11-2020

Keywords:
Metaplastic carcinoma
Breast
Adenosquamous carcinoma

ABSTRACT

Metaplastic breast carcinomas constitutes <1% of all the invasive breast carcinomas, characterized by areas of metaplasia, typically with squamous, spindle, osseous, or chondroid differentiation in the background of adenocarcinoma. We report a case of a 50 year old female who presented with a large, non tender, hard lump since 1 month diagnosed as low grade adenosquamous carcinoma on histopathological examination along with triple negativity on immunohistochemistry. The case is presented to highlight its rarity, histomorphological characteristics, undefined treatment and poor prognosis.

1. Introduction

Metaplastic Carcinoma is a rare form of cancer and accounts for 0.3% of all the breast cancers.[1] It is characterized by areas of metaplasia, typically with squamous, spindle, osseous, or chondroid differentiation in the background of adenocarcinoma. These tumors are aggressive, refractory to treatment having poor prognosis.[2] They are triple negative tumors with variable positivity for myoepithelial and cytokeratin markers.[1] We present a case of a 50 year old female with a triple negative low grade adenosquamous variant of metaplastic carcinoma of breast.

2. Case Report

A 50-year-old female presented with history of lump in the left breast since one month. Palpation revealed a diffuse non tender, hard lump, measuring approximately 12x10cms involving the upper and lower inner quadrant with absence of nipple retraction and nipple discharge. Axillary lymphadenopathy was not noted. There was no significant past or family history.

Ultrasonography performed was suggestive of Phyllodes Tumour. A clinical diagnosis of Phyllodes tumour was made based on general examination and ultrasonography findings. Mammogram performed, revealed a BIRADS 6 category. Trucut biopsy performed showed histological features positive for malignancy.

A Modified radical mastectomy procedure was performed. On gross examination we received a specimen of Left Breast measuring 20x13x4cms with an overlying ellipse of skin bearing nipple and areola measuring 20x13cms. On cut surface a large grey white firm mass measuring 12x7.5x3.5cms was noted in the left upper and inner quadrant (Figure 1 a). The tumor mass was grayish white, cauliflower like growth, soft to firm in consistency (Figure 1 b). Six axillary lymph nodes were detected, the largest measuring 1.5x1cms.

Microscopically the sections showed well-developed glandular and tubular formations lined by pleomorphic ductal epithelial cells (Figure 1 c). The glands were intermingled with solid nests of squamous epithelial cells. They were polygonal having large hyperchromatic nuclei with prominent nucleoli at places and moderate eosinophilic cytoplasm (Figure 1 d). The intervening stroma showed lymphoplasmocytic infiltrate. Mitotic activity was noted along with areas of hemorrhage and necrosis. The margins

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https://doi.org/10.18231/j.ijpo.2020.130

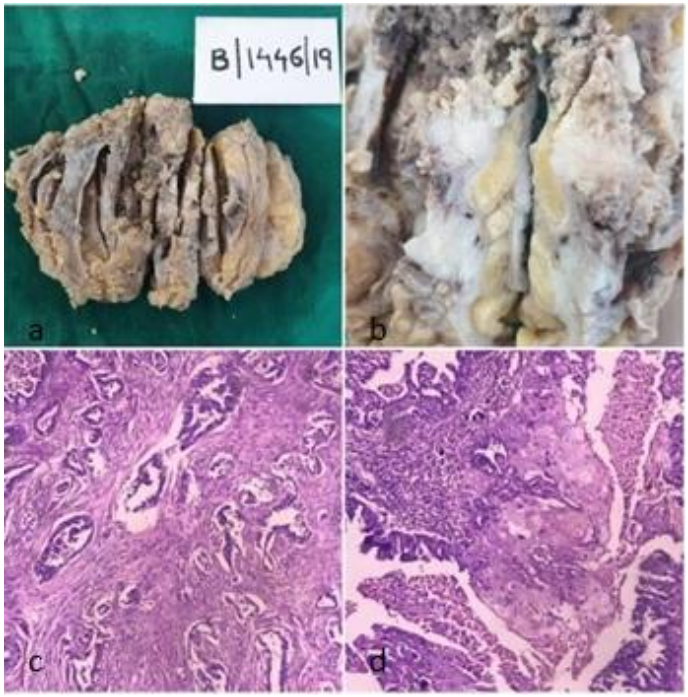

Fig. 1: Gross specimen of Modified Radical mastectomy showing **(a):** Growth involving upper and inner quadrant of breast; **(b):** Cut surface of the lesion showing grayish white cauliflower like growth. Photomicrograph showing; **(c):** Malignant ductal epithelial cells arranged in glandular pattern (H and E x 100); **(d):** Glandular component along with solid nests of squamous epithelial cells showing prominent nucleoli and eosinophilic cytoplasm. (H and E x 400).

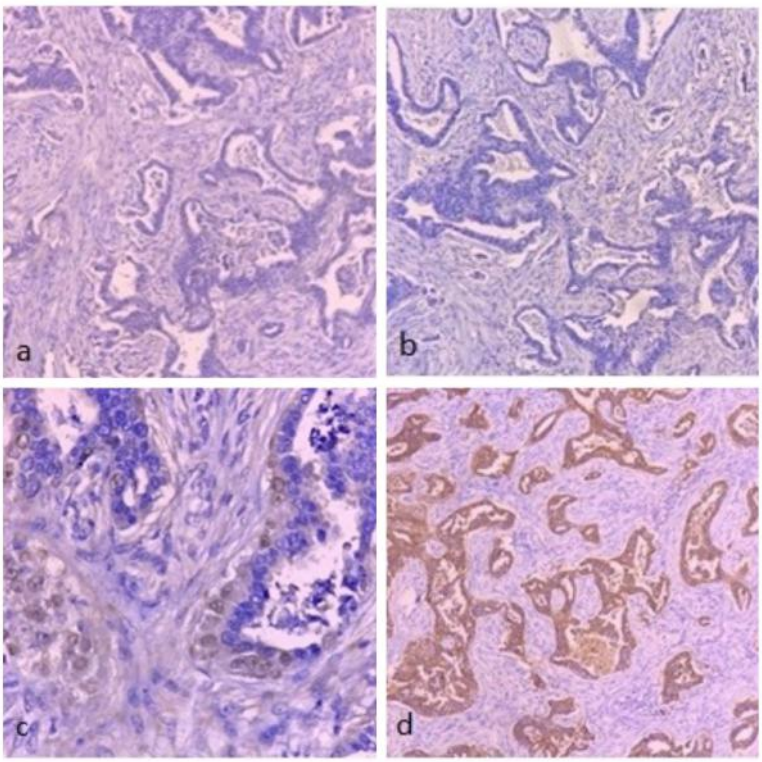

Fig. 2: Photomicrograph showing **(a):** ER and PR nuclear negativity; **(b):** HER-2 membranous negativity; **(c):** p63 nuclear positivity; **(d):** CK-PAN diffuse cytoplasmic positivity (3+)

and base were free from tumor. All the lymph nodes were free from metastatic deposits. Lymphovascular invasion was not identified. Immunohistochemistry studies were performed which showed triple negativity(ER, PR, Her-2) (Figure 2 a,b) and p63 and CK-PAN positivity (Figure 2 c,d).

The diagnosis of Metaplastic Carcinoma of breast Grade 1(Nottingham's score-2+2+1=5), TNM staging- pT3N0M0, Low Grade Adenosquamous variant was made based on Histopathology.

3. Discussion

Metaplastic breast carcinomas belong to heterogenous group of malignant lesions and they constitute <1% of all invasive breast carcinomas. They consist of an intimate admixture of adenocarcinoma component along with dominant areas of spindle cell, squamous cell and/or mesenchymal differentiation.[3] WHO has classified them into; Low grade adenosquamous carcinoma, Squamous cell carcinoma, Fibromatosis-like metaplastic carcinoma, Spindle cell carcinoma and Carcinoma with Mesenchymal differentiation (Chondroid,Osseus and other types).

The histological origin of this Metaplastic breast carcinomas still remains unclear. There are different theories explaining this phenomenon like, malignant growth of intrinsic epidermal elements or metaplasia from breast parenchyma (e.g., cystosarcoma phyllodes, fibroadenomas, or breast malignancies, e.g., intraductal carcinoma) or from chronic abscess.[2]

Rosen and Ernsberger in the year 1987, were the first to describe Adenosquamous carcinomas of the breast. It is a rare tumour which is included as a subtype of metaplastic carcinoma of breast in the World Health Organization (WHO) classification.[3] They described 11 cases of this tumor describing its characteristic histological features.[1] These tumors account for 0.2-5% of all invasive breast cancers and are usually present in women more than 50 years of age.[4] Adenosquamous carcinomas has two variants:- low grade and high grade. Although highly aggressive, low grade adenosquamous carcinomas are relatively indolent with no metastasis and a good prognosis.[1] In contrast, High grade adenosquamous are also aggressive and result in poor prognosis due to lymph node metastasis at the time of diagnosis.[3] It is difficult to distinguish them from other benign and low-grade lesions based on preliminary investigations like mammography, ultrasonography, fine needle aspiration cytology, trucut biopsy, and on frozen sections. Definitive diagnosis can therefore be derived upon by an excision biopsy.[5]

In comparison to intraductal carcinomas, metaplastic carcinomas of breast present with a relatively larger breast mass and lower rate of lymph node involvement.[6] Apart from a lower rate of lymph node metastases, metaplastic carcinomas display poorer prognostic features relative to intraductal carcinoma.[7]

On histopathological examination, well developed glandular and tubular formations are intimately admixed with solid nests of squamous epithelial cells. The carcinomatous component shows small glandular structures, which have rounded rather than angulated contours, along with solid cords of epithelial cells, containing either squamous cells, squamous pearls or squamous cyst formation. The invasive neoplastic component characteristically shows infiltrate and long, slender extensions at the periphery invading the normal breast structures.

Immunohistochemistry profile of these tumors have been described by Kawaguchi and Shin.[8] Low grade adenosquamous carcinoma show triple negative IHC profile for ER, PR and Her-2 neu. They also show variable degree of positivity for cytokeratin and myoepithelial markers. Our case also showed triple negativity for ER, PR, Her-2 neu along with positivity for CK-PAN and p63.

Low grade adenosquamous carcinoma may arise in association with adenomyoepithelioma and benign sclerosing lesions. The differential diagnoses of other variants especially spindle cell variant includes phyllodes tumor, primary sarcomas and fibromatoses. In our case, the clinical and radiological diagnosis was suggestive of phyllodes tumour. Immunohistochemistry studies with cytokeratin panel and myoepithelial marker p63 helps in distinguishing phyllodes from metaplastic carcinoma of breast. P63 is expressed in >90% of metaplastic breast carcinomas and is negative in case of phyllodes tumour. In our case also p63 was expressed which gave a confirmatory diagnosis of metaplastic carcinoma.

Large size and no axillary Lymph Node metastasis in our case suggested the diagnosis of Low Grade Adenosquamous Metaplastic Carcinoma. However there is high hematogenous metastatic potential to lung and bone leading to poor prognosis.[4]

The definitive management of Metaplastic Carcinoma of Breast is Modified Radical Mastectomy.[2] Single institution retrospective studies and genomic profiling has suggested these tumors to be largely chemoresistant. Hormonal therapy has no role in the management of metaplastic carcinomas and has been proven to be as ineffective as chemotherapy. Chemotherapy and hormonal therapy that is traditionally used for Intra ductal carcinoma are of no use in metaplastic carcinoma. Targeted therapies based on individualized gene profiling are the new histology specific chemotherapeutic strategies that offer a survival advantage. Adjuvant radiation has a limited role however maybe considered in case of patients with four or more large metastatic axillary nodes, large (≥5cms) primary tumour and chest wall invasion.[7]

Prognosis depends most importantly on tumor size and tumor stage amongst several other factors.[2] Tumour size

>5 cms and lymph node involvement are poor prognostic factors for Metaplastic Carcinoma of breast.[6] Rayson et al., using systemic treatment, reported the median survival from detection of metastasic disease as 8 months.[9]

4. Conclusion

This case is presented to highlight its rarity, morphological features undefined treatment and poor prognosis.

5. Source of Funding

None.

6. Conflict of Interest

None.

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Cite this article: Buch A, Khandekar P, Kambale T, Jain K. Metaplastic carcinoma of breast: A rare histological entity. *Indian J Pathol Oncol* 2020;7(4):661-664.