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METAPLASTIC CARCINOMA OF BREAST: A CASE SERIES WITH REVIEW OF LITERATURE.

Pathology

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ABSTRACT

Background: Metaplastic carcinoma is a rare entity comprising of a group of neoplasms characterized by differentiation of the neoplastic epithelium into squamous cells and/or mesenchymal-looking elements. The aim of the study is to evaluate the clinicopathological features and to determine triple negative, basal like phenotype using immunohistochemistry. **Material and Methods:** The current study was conducted in a tertiary health care centre of western Odisha. A total of five cases of metaplastic breast carcinoma (MBC) were evaluated for clinico-pathological features. The cases were analysed immunohistochemically by ER, PR, HER - 2/neu, basal marker like CK5/6 and prognostic marker Ki-67 **Results:** All cases were females with unilateral breast swelling. The size varied from 3 – 6 cm. All the cases were negative for ER, PR and HER-2/neu except one case which was positive for PR. Immunoreaction for basal marker CK5/6 was positive in all cases suggesting it to be showing basal-like differentiation. Ki67 showed positivity in four cases. **Conclusion:** Four cases were considered as the triple negative breast cancer and majority of them exhibited basal-like phenotype. The findings were in consistent with literatures.

KEYWORDS

Breast, metaplastic carcinoma, squamous cell carcinoma, triple negative carcinoma.

INTRODUCTION

Metaplastic carcinoma encompasses a group of neoplasms characterized by differentiation of the neoplastic epithelium into squamous cells and/or mesenchymal-looking elements including but not restricted to spindle, chondroid, osseous, and rhabdomyoid cells. (1) It is a rare malignancy that accounts for 0.2 - 5% of all invasive breast cancers. (1) It was first recognised in 1973 by Huvos et al(2) but not defined as a unique histologic subtype by the World Health Organization until 2000. (3) Classification of MBC and its differential diagnosis is challenging due to the diversity of the histological patterns and rarity of the diagnosis. Sometimes small and focal areas of metaplastic elements are seen in invasive ductal carcinoma. These neoplasms may be either entirely composed of metaplastic elements, or a complex admixture of carcinoma or metaplastic areas. (1) The metaplastic component can be benign or malignant. Wargotz et al classified MBC into five subtypes: matrix-producing carcinoma, squamous cell carcinoma, spindle cell carcinoma, carcinosarcoma, and metaplastic carcinoma with osteoclastic giant cells. (4)

In infiltrating duct carcinoma (IDC), the presence of hormone receptor is associated with improved clinical outcomes while over expression of HER2 receptor negatively affects survival. Majority of MBCs do not express estrogen (ER), progesterone (PR), or Her-2/neu (HER2) receptors. (5) MBCs show a basal like phenotype, regardless of the type of metaplastic elements. (6) Basal or myoepithelial markers; CK5/6, p63, EGFR and SMA are often expressed. Due to its rare nature, it is difficult to assess the prognosis of metaplastic carcinomas, but various studies suggest it as a highly malignant tumour with early recurrence and poor survival. (1, 7, 8) Our aim is to study clinicopathological features and immunostaining to detect triple negative and basal like metaplastic carcinomas.

MATERIAL AND METHODS:

The current study consists of five cases of metaplastic breast carcinoma conducted at VSSIMSAR, Burla, Odisha from the year 2016 to 2019. The hematoxylin and eosin stained slides and paraffin blocks of the cases were retrieved and evaluated. All the cases were assessed for various clinicopathological features like age, clinical presentation, gross features like size, histological components, and lymph node status. The paraffin blocks were sectioned into 4 µm tissue sections following which sections were mounted on charged poly-L-lysine-coated slides and the immunohistochemical (IHC) procedure was done using monoclonal antibodies and by Dako envision FLEX/HRP detection reagent. Positive and negative controls were taken for each analysis. ER, PR, and Ki67 expression was considered as positive if strong nuclear staining was noted in at least 10% of the tumor cells. CK5/6 was interpreted as positive if there was moderate to strong cytoplasmic staining of more than 10% of tumor cells. HER2 was noted as positive if there was strong complete membranous staining (3+) in 30% or more of tumor cells according to latest ASCO-CAP 2018 guidelines. If the tumor shows triple negative (ER, PR & HER2) immunohistochemistry with positive for CK5/6 according to Gazinska criteria it is considered as basal-like phenotype. (9)

RESULTS:

All patients were female with a median age of 50 (40 – 65) years. Tumour size varied from 3 – 6 cm. All were presented with unilateral swelling in the breast and had undergone modified radical mastectomy. All the neoplasm had circumscribed lesion. Only two cases have sentinel lymph nodes. All the lymph nodes were free from malignant infiltrations. Four cases of metaplastic squamous carcinoma and one case of metaplastic carcinoma with osteoclastic giant cells were identified. Immunohistochemistry for ER, PR, HER - 2/neu showed negativity in all cases except one which showed PR positivity in metaplastic squamous carcinoma. Ki67 score was low in that case, rest of the cases showed high score. CK5/6 showed overexpression in metaplastic squamous cell carcinoma.

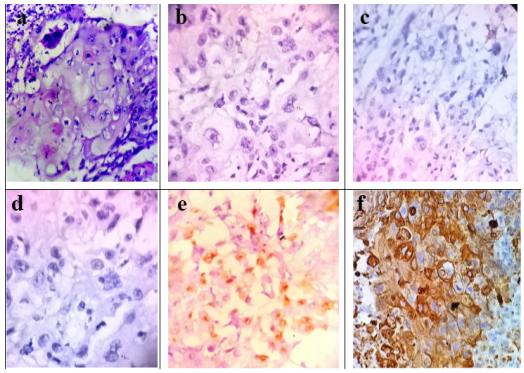

Figure 1: a. Microscopic findings of metaplastic squamous cell carcinoma (H&E x 400). Immunohistochemical findings: b – d: ER, PR and HER2/neu are negative. e: Ki67 index show 14% positivity. f: CK positivity.

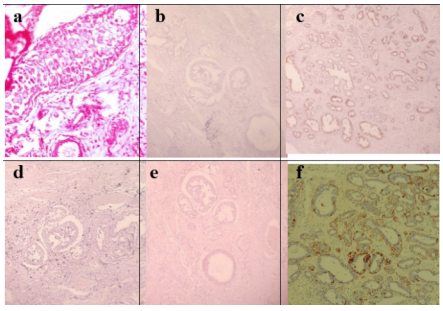

Figure 2: Microsection of metaplastic carcinoma showing nest of cells with metaplastic squamous cells and presence of few ducts. (H&E x 100). Immunohistochemistry: b: ER= Negative, c: PR = Positive in ducts, d: HER2/neu = Negative. e: Ki67 = Negative. f: CK5/6 = Positive in small groups of cells in stroma; also show basal cell positivity.

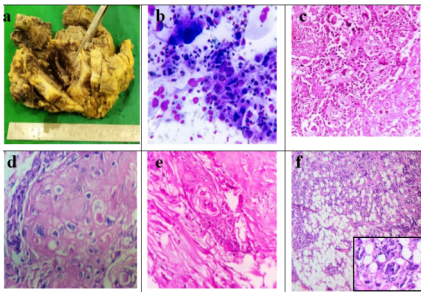

Figure 3: (a –c): (a) Gross picture of cut section of Metaplastic Squmous Cell Carcinoma showing gray – brown lesion. (b) FNAC smears shows pleomorphic polygonal to spindle cells along with few multinucleated giant cells (Diff - Quick x 400). (c). Microsection shows sheets of pleomorphic squamous cells along with tumour giant cells (H&E x 400) d. Microsection of metaplastic Squmous Cell Carcinoma showing polygonal cells and individual cell keratinization (H & E x 400). e. Another case with metaplastic squamous cells (H & E x 400). f. Microsection shows metaplastic carcinoma with pleomorphic spindle cells and osteoclastic multinucleated giant cells infiltrating the fat cells at the periphery. (H&E x 100); inset shows osteoclastic giant cells (H & E x 400).

DISCUSSION

Metaplastic breast cancer is an uncommon yet aggressive histologic type of breast cancer. Carcinoma showing extensive metaplastic change to squamous cells, spindle cells and heterologous mesenchymal elements are well recognized in breast. (10) The tumor may show variable proportion of carcinomatous and pseudocarcinomatous elements. (8) The sarcoma like component may resemble malignant fibrous histiocytoma, chondrosarcoma, osteosarcoma, rhabdomyosarcoma or a combination of these. (10) On needle core biopsy, metaplastic carcinoma should be considered in the differential diagnosis of virtually all spindle cell lesions. Search for a carcinomatous component and a large panel of immunohistochemical markers are required for the diagnosis.

The pathogenesis of MBC is unknown but there are some theories to clarify the morphological diversity of this tumor, including genetic and non-genetic mechanisms. (10)

Microscopically, all the neoplasm had predominantly circumscribed borders. One case appeared well circumscribed grossly, but microscopically showed pleomorphic spindle cells with fat infiltration at the periphery. According to Yamaguchi R et al, infiltration into adjoining breast tissue by the metaplastic component of MPC is a common feature. (5)

Yamaguchi R et al showed triple negativity (ER, PR and HER2/neu negative) in 80% of metaplastic carcinoma. (5) Our cases showed triple negativity in four cases. Only one case showed intermediate intensity of PR positivity. MBCs were also positive for basal CK 5/6, also shown by Yamaguchi R et al.(5)

The median age of metaplastic carcinoma in our study was 50 years. Alaoui M'hamdi et al. has reported a 53 year old female with spindle cell carcinoma of breast. (11) Two cases have sentinel lymph nodes. However, only reactive hyperplasia of lymph nodes were observed. Arora S et al, reported metaplastic Carcinoma with high grade spindle cell component with no local and distant metastasis. (8) The presence of multinucleated giant cells have been reported in many literatures. (12, 13) Wargotz ES et al (13) studied that osteoclastic giant cells were immunoreactive for vimentin and, to a lesser extent to actin, and not immunoreactive for keratins, thus confirming their mesenchymal nature. Metaplastic carcinomas are usually aggressive; however Wargotz and Norris described a "matrix-forming" pattern with a better prognosis than expected in metaplastic carcinoma. (14) Ki-67 index were high in all cases except one where it was low.

MBC rarely metastasize to axillary lymph nodes despite large size and are usually triple negative with high Ki-67 scores indicating aggressiveness and lack of response to hormonal therapy. Pezzi et al studied 892 patients and found MBCs as large sized tumor, with less lymph node involvement, higher tumor grade and higher proportion of triple-negative hormone receptor type. (15) Triple negative tumors in our studies of small series were consistent with the literature.

CONCLUSION

Metaplastic carcinoma is a relatively rare aggressive type of breast cancer. Majority were triple negative biologic type except one and therefore more likely high grade. The tumor cells immunoreactive for CK5/6 indicating basal like differentiation. In summary, metaplastic carcinomas should be included in the differential diagnosis of breast cancers.

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