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Metaplastic Carcinoma of Breast.

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Abstract: *Metaplastic carcinoma of breast (MBC) is a rare type of invasive breast carcinoma. It poses diagnostic challenge due to its varied histology and diverse differentiation. These are heterogenous group of tumors in which part or whole of the carcinomatous component is transformed into a metaplastic mesenchymal component and runs an aggressive clinical course. We present two cases of metaplastic carcinoma of breast with monophasic and biphasic patterns with its cytology mimicking other neoplasms. We present these cases due to its rarity with difficulty in diagnosis and subtyping.*

Keywords: *Breast, Metaplastic carcinoma, spindle cell carcinoma.*

I. Introduction

Metaplastic carcinoma of breast (MBC) is a rare and aggressive tumor, accounting for 0.2 to 5% of the symptomatic invasive breast tumors[1]. The pathogenesis of these tumors has been the subject of much controversy. The clinical presentation is varied, forming well circumscribed to irregular spiculated masses[2]. These uncommon tumors show other cellular components besides carcinomatous elements. The biphasic pattern comprising both carcinomatous and mesenchymal elements are common. Monophasic pattern with spindle cell component is rare, and is included under spindle cell carcinoma- Metaplastic carcinoma[1]. Although these tumors rarely show axillary nodal involvement like sarcomatous tumors, metastasis to the lung has been commonly described[3].

II. Case History

Case 1:

A 58 year old P3L3 postmenopausal female, presented to the breast clinic with a history of right breast lump for four months and mastectomy month back, now with breathlessness. There was no other significant past history. Reviewed slides from the breast showed a malignant tumor consisting of islands, nests and tubules of cuboidal cells with pleomorphic nuclei. Interspersed amidst glandular cells were clusters of malignant squamoid cells and sheets of plump spindle cells with pleomorphic nuclei. Bizarre nuclei with multinucleation, necrosis and increased mitosis including atypical mitosis were seen. There were ducts with high grade insitu carcinoma of comedo type at the tumor periphery (Fig 1a, 1b, 1c). The tumor cells were positive to Vimentin (Fig 1d), Pan CK (Fig 2a) and CK 5/6 and negative to ER, PR and Her2neu (Fig 2b, 2c, 2d). Two lymphnodes were involved by tumor. A diagnosis of metaplastic carcinoma with sarcomatous stroma was made.

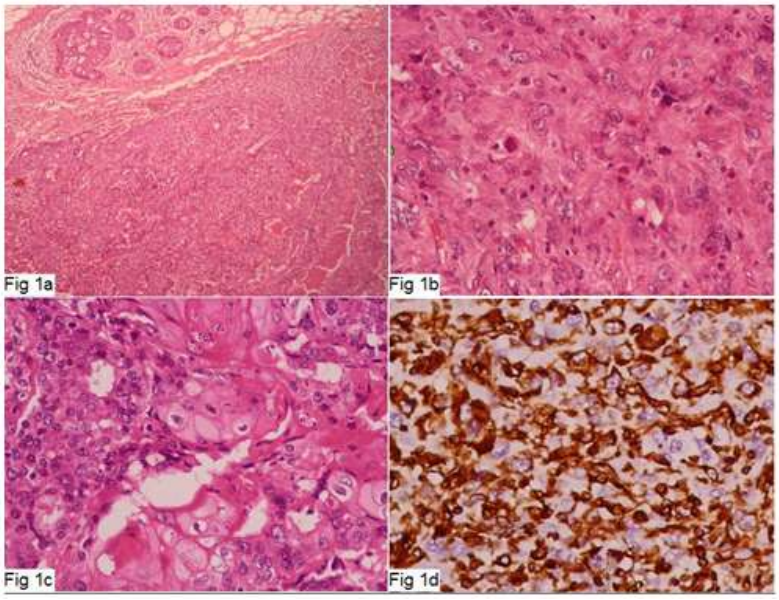

Fig 1. Metaplastic carcinoma with sarcomatous stroma and a duct with DCIS at the periphery (1a), High power view of sarcomatoid stroma with pleomorphic nuclei (1b), High power view showing invasive carcinoma no special type and squamoid component (1c), Vimentin positivity in tumor cells (1d).

PET scan done for staging, revealed a left upper lobe lung nodule. CT guided aspirate from the lung lesion showed clusters of atypical cells with pleomorphic nuclei, suggestive of malignancy. She was given palliative chemotherapy with paclitaxel and carboplatin, but failed to respond and developed local recurrence and additional lung nodules.

Case 2:

A 70 year old P2L2 postmenopausal female presented to the breast clinic with symptoms of painful lump in the left breast for past three months. There was no significant past medical or surgical history. On examination, she was found to have a firm mobile lump in the lower outer quadrant. There were no skin changes or nipple retraction. Mammogram revealed a BIRAD 4 hypo echoic lesion in the left breast with angular margins and pleomorphic micro calcification. Fine needle aspiration revealed cellular fragments and dispersed spindly cells with mild to moderate atypia (Fig 3a, 3b). A diagnosis in favour of Phyllodes tumor was made. Chest X ray and other blood investigations were normal.

Modified radical mastectomy with axillary clearance was done. Gross examination revealed a circumscribed and lobulated firm tumor measuring 3.7x3x3 cm. Skin, nipple and areola were free.

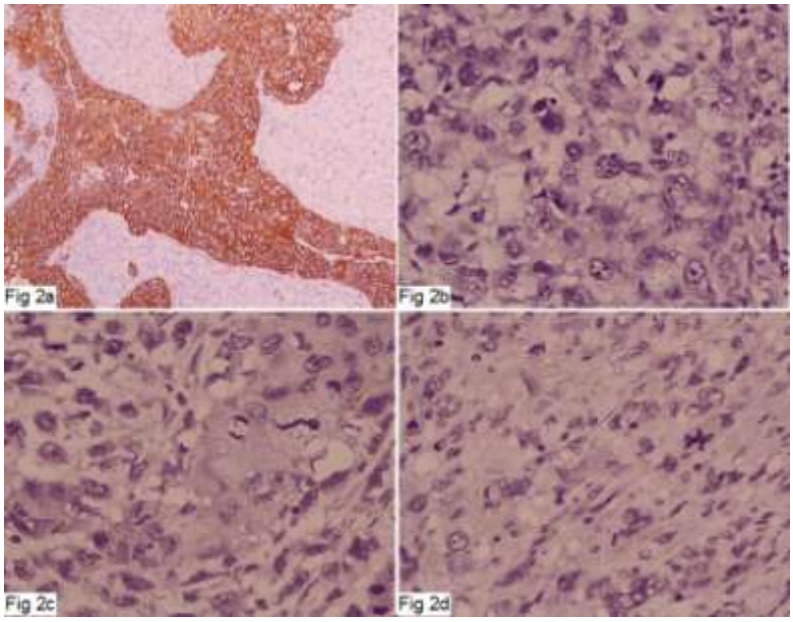

Fig 2: Epithelial component positive to cytokeratin (2a), tumor cells negative to hormone recptors ER (2b), PR (2c), and Her2neu (2d).

Microscopy showed spindle cells in anastomosing trabeculae with pleomorphic nuclei and increased mitosis, There was lympho vascular invasion and a duct with solid insitu ductal carcinoma at the tumor periphery (Fig 3c, 3d). Lymph nodes were negative for metastasis, but most of them had necrotising granulomas with occasional acid fast bacilli. With the differentials of spindle cell carcinoma and Phyllodes tumor, IHC was done. The tumor cells were positive to Pan CK, EMA, Vime
ntin, ER, PR and Her2neu (Fig 4a, 4b, 4c, 4d). CD34 and BCL2 were negative. Hence a diagnosis of spindle cell carcinoma with coexisting tuberculous lymphadenitis was made.

III. Discussion

Metaplastic breast carcinoma is a heterogenous tumor of uncertain histogenesis and difficult to subtype. The rarity of this tumor is exemplified by the fact that it accounts for 0.2-5% of all invasive breast cancers containing a mixture of epithelial and mesenchymal elements[1]. Although there may be foci of invasive carcinoma of no special type, the predominant component may be mesenchymal with apparent histological features on light microscopy and Immunohistochemistry. The carcinomatous component may be

The metaplastic carcinoma has been broadly classified as pure epithelial (Squamous cell carcinoma, Invasive carcinoma no special type with spindle cell differentiation and adenosquamous carcinoma) and mixed

epithelial and mesenchymal (invasive carcinoma with mesenchymal matrix ranging from chondroid/ osseous matrix to frank sarcoma) tumors[1].

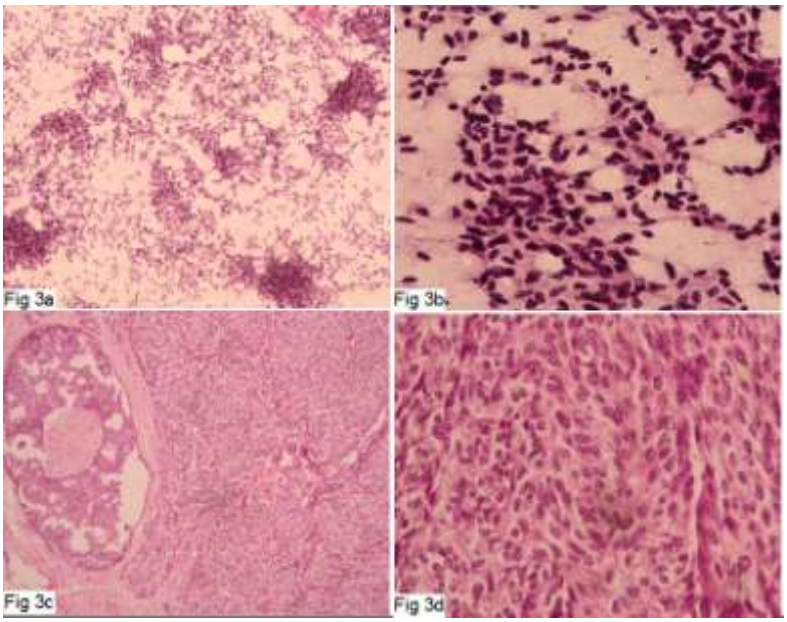

Fig 3: FNAC showing spindle cells in clusters and dispersed with mild atypia (3a, 3b), Histology showing spindle cells in trabeculae with mild atypia and a duct with DCIS at the tumor periphery (3c, 3d).

The tumor can be monophasic or biphasic. The monophasic variant is characterised by predominant spindle cell pattern with either bland appearing cells or with high grade sarcomatoid appearance. Though ductal and squamous cell patterns may be present, there can be pure spindle cell pattern[5] as seen in our case 2 mimicking Phyllodes tumor. The diagnosis of such cases by cytology and routine histology becomes difficult. Other differential diagnosis include myofibroblastic lesions, and inflammatory pseudotumor[6]. The presence of DCIS at the tumor periphery or admixed with the lesion is a clue to the diagnosis of spindle cell metaplastic carcinoma[1]. Similar problems were encountered in our case with spindle cell pattern (case 2). IHC can be helpful to confirm the diagnosis as the spindle cells are positive to Vimentin and Pan CK, while phyllodes tumor show CD34 and BCL2 positivity[1,3].

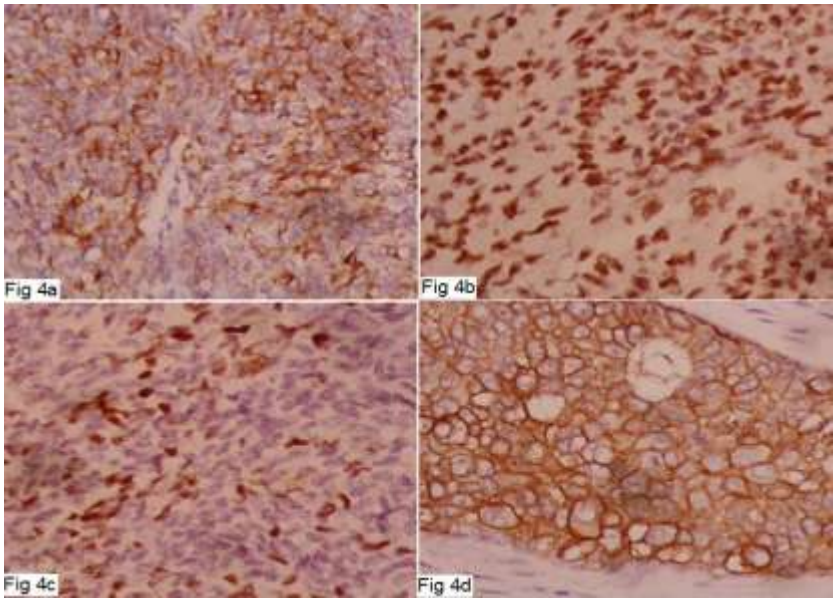

Fig 4: Spindle cell carcinoma. The tumor cells are positive to Cytokeratin (4a), ER (4b), PR (4c) and Her2neu (4d).

Carcinoma with glandular and mesenchymal elements (biphasic) is well recognised, and the proportion of these elements may vary. Diagnosis of such tumors becomes difficult unless extensive sampling is done to recognise the small focal area of classic invasive carcinoma of no special type, contiguous or subtly merging with the sarcomatous stroma[1,4]. Ours had a significant proportion of invasive carcinoma in addition to malignant squamous component and sarcomatous stroma resembling pleomorphic sarcoma with bizarre cells, increased mitosis and atypical mitosis. The cells show variable positivity to Vimentin, Pan CK and CK 5/6. ER, PR and Her2neu are usually negative[3]. The Triple negative feature correlates with its aggressive behaviour as in case 1 with lung metastasis and poor response to chemotherapy.

The exact histogenesis of the tumor is unknown. Few theories were proposed like Collision theory, Combination theory, and Conversion/ Metaplastic theory. The most popular theory is through transformation of myoepithelial cells or a multipotent progenitor cells after p53 mutation, to differentiate into epithelial as well as mesenchymal elements[7]. The tumor size and the mesenchymal component involved determines the outcome[3,8]. Our study also demonstrated lymph node and lung metastasis in the patient with sarcomatoid stroma with histology of pleomorphic sarcoma and had poor outcome.

These tumors metastasize more commonly to lungs. The incidence of lymph node metastasis in metaplastic carcinoma is lower compared to invasive carcinoma, in keeping with its sarcomatous phenotype[9]. However our first case, metaplastic carcinoma with sarcomatoid phenotype had lymph node and lung metastasis at the time of presentation. The sarcoma like elements of these tumors has acquired Vimentin positivity (phenotypical switch) with focal demonstrable Cytokeratin positivity[10].

IV. Conclusion

Metaplastic carcinoma of the breast is an extremely rare malignancy with divergent differentiation and controversial histogenesis. The prognosis is predicted to be worse similar to other triple negative breast carcinomas. Meticulous extensive sampling of tumor, DCIS at the tumor periphery, and co expression of Vimentin and Cytokeratin would help to conclude the diagnosis in difficult situations.

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