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Flux and Flip-Flop-Metaplastic Carcinoma Breast

Bajaj A*

Consultant Histopathologist, AB Diagnostics, India

***Corresponding author:** Anubha Bajaj, Consultant Histopathologist, AB Diagnostics, A-1 Ring Road Rajouri Garden, New Delhi 110027, India, Tel: 00911141446785; Email: anubha.bajaj@gmail.com

Editorial

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Keywords: Breast Carcinoma; Tumour; Metaplastic Carcinoma; Sarcomatoid Carcinomas; Lymph Nodes

Abbreviations: NOS: Not Otherwise Specified; NST: No Special Type; AJCC: American Joint Committee on Cancer; SMA: Smooth Muscle Actin; ER: Oestrogen Receptor; PR: Progesterone Receptor.

Editorial

Metaplastic carcinoma breast emerges as a heterogeneous group of invasive breast carcinomas. Characteristically, tumefaction exhibits differentiation of neoplastic epithelium towards squamous cells or elements simulating mesenchyme as spindle shaped cells, osseous or chondroid tissue or diverse mesenchymal components.

Preponderantly emerging as a variant invasive breast carcinoma, tumefaction is constituted of atypical squamous epithelial cells, spindle shaped cells or may demonstrate mesenchymal and matrix producing differentiation.

Lesions devoid of ductal carcinoma in situ or conventional mammary carcinoma component may be challenging to ascertain and require cogent immunohistochemistry with high molecular weight cytokeratin or p63 in order to detect focal epithelial differentiation.

Additionally designated as metaplastic carcinoma not otherwise specified (NOS), alternative terminologies as carcinosarcoma, sarcomatoid carcinoma, carcinoma with pseudosarcomatous metaplasia or carcinoma with pseudosarcomatous stroma are not recommended. The infrequently discerned neoplasm demonstrates average age of disease occurrence at 55 years [1,2].

Neoplasm may emerge from diverse anatomical segments of the breast of multifactorial aetiology and obscure pathogenesis, heterogeneous tumour components are posited to demonstrate a monoclonal genesis. Factors contributing to disease emergence recapitulate the elements concordant with invasive carcinoma breast of no special type (NST), especially triple negative breast carcinoma [1,2].

Metaplastic carcinoma breast demonstrate a basal-like or claudin low molecular subtype. Nevertheless, a consistent molecular profile is absent. Tumefaction may implicate TP53, RB1, TERT promoter genes, chromatin remodelling genes as ARID1A, KMT2C, genes related to PI3K pathway as PIK3CA, PIK3R1, PTEN, MAPK pathway with NF1, KRAS, NRAS genes or WNT pathway comprised of FAT1, APC, CCN6 genes [2,3].

Metaplastic carcinoma breast manifests with clinical symptoms resembling invasive breast carcinoma of no special type (NST). Biological behaviour pertains to neoplastic countenance and simulates the behaviour as encountered with low grade neoplasms to high grade tumefaction [2,3].

Tumour represents with enlarged lesions, minimal implication of regional lymph nodes and advanced tumour stage as per staging obtained with American Joint Committee on Cancer (AJCC). Neoadjuvant systemic therapy is associated with inferior therapeutic response and demonstrates proportionate pathology complete response (pCR) at ~10% to 17% [2,3].

Cytological examination smears composed of tumour cells demonstrating moderate to significant cytological atypia. Neoplasm is constituted of singularly dispersed or aggregates of enlarged, pleomorphic cells, spindle shaped cells or malignant appearing squamous epithelial cells. Exceptionally,

foci of malignant cartilage or bone are observed. Osteoclast-like giant cells are intermingled within the cellular component. However, dual components appear unidentified [3,4].

Grossly, a firm, well circumscribed and solid tumefaction is encountered. Cut surface expounds a pearly, glistening, whitish to greyish tumefaction with squamous epithelial and chondroid differentiation. Mean tumour magnitude appears at 3.9 centimetres whereas neoplasm ranges from 2 centimetres to > 10 centimetres in diameter [3,4].

Upon microscopy, a morphologically heterogeneous neoplasm is expounded. Tumefaction may singularly arise from epithelial cells and configure carcinomas, pure or monophasic sarcomatoid carcinomas or delineate biphasic epithelial and sarcomatoid carcinomas. Singularly epithelial only carcinomas are comprised of low grade adeno-squamous carcinoma, high grade adeno-squamous carcinoma and squamous cell carcinoma [3,4].

Pure or monophasic sarcomatoid carcinomas are comprised of fibromatosis-like metaplastic carcinoma and spindle cell carcinoma. Tumefaction is constituted of heterologous mesenchymal components as chondroid, osseous, rhabdomyosarcomatous, angiosarcomatous, liposarcomatous and focal neuroglial differentiation or an amalgamation of aforesaid components [3,4].

Mesenchymal component expounds significant cellular and nuclear atypia with occurrence of minimal atypia to focal malignant metamorphosis. Neoplastic evaluation may be challenging and extensive tissue sampling or cogent immunohistochemistry may be necessitated for discerning the epithelial component [3,4] (Figures 1 & 2).

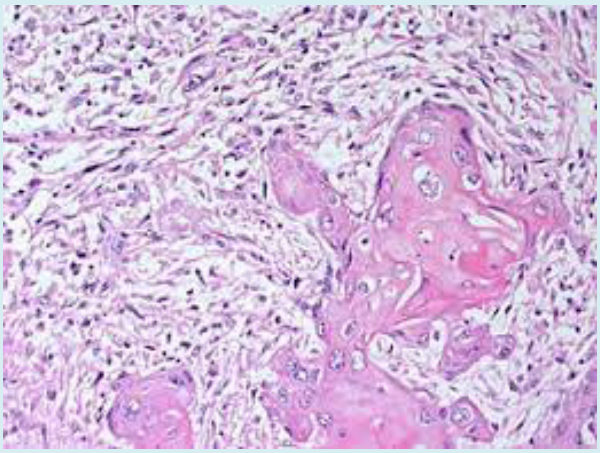

Figure 1: Metaplastic carcinoma breast demonstrating aggregates of squamous epithelial cells admixed with mesenchymal elements as chondroid tissue and spindle shaped cells [5].

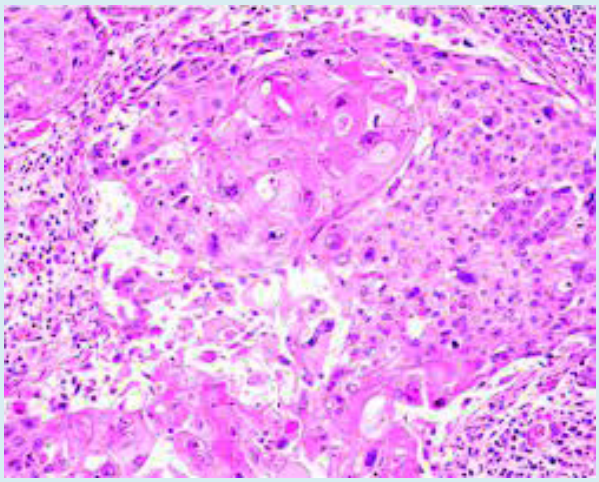

Figure 2: Metaplastic carcinoma breast delineating aggregates of squamous epithelial cells commingled with mesenchymal elements as spindle shaped cells and cartilaginous foci [6].

Staging of Carcinoma Breast as Per American Joint Committee on Cancer (AJCC) 8th Edition

Stage 0: Constituted of non-invasive or in situ carcinoma wherein disease is confined to breast tissue ducts. Invasion into surrounding breast tissue is absent (Tis, N0, M0).
Stage IA: Wherein tumour is miniature, invasive and devoid of regional lymph node metastasis (T1, N0, M0).
Stage IB: Is comprised of tumour dissemination into regional lymph nodes > 0.2 millimetre and < 2 millimetre magnitude. Tumour confined to breast tissue is absent or tumour within breast tissue is ≤20 millimetres diameter (T0 or T1, N1mi, M0).
Stage IIA: Describes lesions demonstrating ~absence of tumour within the breast although tumour disseminates into one to three axillary lymph nodes. Distant metastasis is absent (T0, N1, M0). ~tumour is ≤ 20 millimetre diameter and disseminates into one to three axillary lymph nodes (T1, N1, M0). ~tumour >20 millimetres and <50 millimetres and devoid of metastasis into axillary lymph nodes (T2, N0, M0).
Stage IIB: Is constituted of ~tumour > 20 millimetres and < 50 millimetres and disseminates into one to three axillary lymph nodes (T2, N1, M0). ~tumour is > 50 millimetres and devoid of axillary lymph node metastasis (T3, N0, M0).
Stage IIIA: Is comprised of tumour of variable magnitude with dissemination into 4 to 9 axillary lymph nodes or into internal mammary lymph nodes. Distant metastasis is absent. (T0, T1, T2, or T3, N2, M0) OR tumour > 50 millimetres with dissemination into one to three axillary lymph nodes (T3, N1, M0).
Stage IIIB: Is comprised of tumour demonstrating swelling

or ulceration of breast or tumour dissemination into chest wall OR tumour may configure as an inflammatory breast cancer. Tumour dissemination into up to 9 axillary or internal mammary lymph nodes may or may not occur. Distant metastasis is absent (T4, N0, N1 or N2, M0).

Stage IIIC: Is comprised of tumour of variable magnitude with dissemination into ≥10 axillary lymph nodes, internal mammary lymph nodes and/or supraclavicular lymph nodes. Distant metastasis is absent (any T, N3, M0).

Stage IV (Metastatic): Is constituted of tumour of variable magnitude with distant metastasis into diverse organs as bones, pulmonary parenchyma, brain, hepatic parenchyma, distant lymph nodes or chest wall (any T, any N, M1). De novo metastatic breast cancer upon initial representation occurs in ~6% instances within preceding lesions or upon therapeutic intervention of preliminary stages of breast carcinoma.

Recurrent Carcinoma Breast

Is constituted of breast carcinoma which relapses following therapy. Tumour is denominated as local, regional, and/or with distant lesions and mandates additional evaluation.

Metaplastic carcinoma breast appears immune reactive to various cytokeratin as AE1/AE3, CAM5.2, OSCAR, 34βE12, MNF116, high molecular weight keratin as CK5/6, CK14, p63, low molecular weight keratin CK8/18, CK7 or CK19 and myoepithelial cell markers as smooth muscle actin (SMA) or CD10. Tumour cells appear immune non reactive to oestrogen receptor(ER), progesterone receptor (PR), HER2, CD34, desmin and heavy chain of smooth muscle myosin [7,8].

Metaplastic carcinoma breast requires segregation from neoplasms as phyllodes tumour, primary breast carcinoma, metastatic sarcoma, adenomyoepithelioma, myoepithelial carcinoma or pleomorphic adenoma [7,8]. Imaging features simulate the features expounded by invasive carcinoma breast (NST). Upon mammography, majority of neoplasms represent as a tumour mass with mean magnitude of 32 millimetres. Infrequently, micro-calcification may be discerned, especially within carcinoma in situ component. Cogent histopathological evaluation of surgical tissue samples is optimal for categorizing the neoplasm [8,9].

Metaplastic carcinoma breast may be appropriately subjected to mastectomy or localized surgical excision. Additionally, radiation therapy or chemotherapy may or may not be employed. However, conventional chemotherapy is associated with minimal therapeutic response [8,9]. Variants such as fibromatosis-like carcinoma and low grade adeno-squamous carcinoma are associated with indolent biological behaviour. Matrix producing metaplastic carcinoma is accompanied by superior prognostic outcomes [8,9]. High grade spindle cell carcinoma, squamous cell carcinoma, high grade adeno-squamous carcinoma and quantifiably significant lesions within mixed metaplastic carcinomas are associated with inferior prognostic outcomes [8,9].

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5. Image 1 Courtesy: Libre pathology.

6. Image 2 Courtesy: Europe PMC.

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