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Editorial

Sifter and Mesh-Cribriform Carcinoma Breast

Anubha Bajaj*

Department of Histopathology, Panjab University/A.B. Diagnostics, India

***Corresponding Author:** Anubha Bajaj, Department of Histopathology, Panjab University/A.B. Diagnostics, India.

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Abstract

Invasive cribriform carcinoma breast emerges as a low grade subtype of invasive carcinoma breast. Neoplasm preponderantly (>90%) delineates a pure cribriform architecture or may represent as a mixed tumour composed of 10% to 90% of variant morphological subtype. Tumefaction is constituted of islands or nests of malignant epithelial cells demonstrating spherical or angulated contours or configure well defined cribriform spaces articulated by arches of epithelial cells, thereby delineating a sieve-like appearance with intercellular lumens impregnated with secretions. Miniature tumour cells display mild to moderate pleomorphism with absent nuclear atypia. Cribriform carcinoma breast is immune reactive to oestrogen receptors (ER) or progesterone receptors (PR) and immune non reactive to HER2 or diverse myoepithelial markers. Cribriform carcinoma breast requires segregation from neoplasms as adenoid cystic carcinoma, cribriform variant of ductal carcinoma in situ, collagenous spherulosis, well differentiated neuroendocrine tumour or well differentiated invasive breast cancer of no special type (NST). Neoplasm may be appropriately ascertained by mammography or ultrasonography of the breast. Cribriform carcinoma breast may be appropriately alleviated by primary surgical eradication of the lesion.

Keywords: Low Grade; Sieve-Like; Oestrogen/ Progesterone+

Abbreviations

Invasive cribriform carcinoma breast emerges as a low grade, invasive carcinoma of mammary tissue. World Health Organization (WHO) classifies the tumefaction as a specific subtype of invasive carcinoma breast.

Upon morphological assessment, tumefaction expounds a predominant, characteristic cribriform pattern wherein >90% of tumour cells demonstrate islands, nests and a definitive cribriform pattern of malignant epithelial cells. Tumour cells are impregnated with low grade or grade I nuclei. Mitotic figures are sparsely disseminated. Tumour cells appear immune reactive to oestrogen receptors and immune non reactive to HER2.

Invasive cribriform carcinoma breast may depict distinct variants as

- Neoplasms preponderantly (>90%) delineating pure cribriform architecture
- Mixed tumour composed of 10% to 90% of a variant morphological subtype, apart from tubular carcinoma [1,2].

Mean age of disease emergence is 63 years. Commonly, tumefaction arises within postmenopausal female subjects and is infrequently observed < 50 years. However, nearly 2% of elderly male subjects may be implicated [1,2].

The exceptionally discerned invasive cribriform carcinoma commonly implicates the breast, axillary region or accessory breast tissue.

Of obscure aetiology, tumefaction is posited to activate luminal A molecular pathway. The specific subtype of carcinoma breast expounds hormone receptors and appears devoid of overexpression of HER2. Invasive cribriform carcinoma may be asymptomatic or represent as a miniature lump within the breast tissue [1,2].

The clinically occult tumefaction appears multifocal in ~10% to 20% instances. Regional lymph node metastases may occur within pure invasive cribriform carcinoma. In contrast, ~25% of mixed invasive cribriform carcinoma are associated with regional lymph node metastasis [2,3].

Cytological smears exhibit three dimensional cellular clusters, sheets and cohesive aggregates of bland ductal epithelial cells articulating a distinctive cribriform pattern. Generally, smears are devoid of naked nuclei, bipolar nuclei or myoepithelial cells. Appropriate neoplastic ascertainment upon cytological evaluation is exceptionally achieved. Tissue samples obtained with core needle biopsy are preferentially examined [2,3].

Grossly, neoplasm recapitulates the features enunciated with invasive ductal carcinoma breast. Tumefaction appears as a miniature lesion with magnitude < 2 centimetres. Few lesions appear between 2 centimetres to 5 centimetres diameter. Neoplasm appears as firm to hard mass with spiculation. Focal calcification expounds a gritty texture [3,4].

Upon microscopy, neoplasm predominantly (>90%) exemplifies an irregular, cribriform pattern of tumour evolution. Majority (>90%) of cells configure a distinct cribriform pattern wherein cells constituting pure invasive cribriform carcinoma expound nuclear grade I.

Mixed tumours are constituted of 10% to 90% component of diverse morphological subtypes, in the absence of tubular carcinoma component [3,4].

Low grade neoplasms are categorized as Nottingham grade 1 tumours.

The invasive neoplasm is constituted of islands or nests of malignant epithelial cells demonstrating spherical or angulated contours.

Tumour cells configure well defined cribriform spaces articulated by arches of epithelial cells, thereby delineating a sieve-like appearance. Tumour cells appear miniature and display mild to moderate pleomorphism. Nuclear atypia is absent [3,4].

Intercellular lumens configured by the cribriform pattern may be impregnated with secretions which can be highlighted by mucin stain. Additionally, lumen may be incarcerated with micro-calcification. Myoepithelial cell component is absent. Nevertheless, osteoclastic giant cells may be encountered. Mitotic activity is minimal to absent.

Tumour cell component is circumscribed by desmoplastic stroma. Invasive cribriform carcinoma may be associated with cribriform ductal carcinoma *in situ* (DCIS).

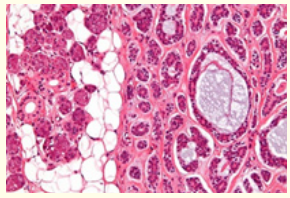

Figure 1: Invasive cribriform carcinoma delineating a distinct cribriform pattern with islands and nests of miniature, mildly pleomorphic epithelial cells surrounded by a desmoplastic stroma [7].

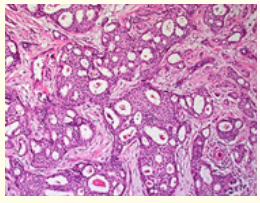

Figure 2: Invasive cribriform carcinoma expounding a distinct cribriform pattern composed of islands and nests of miniature, mildly pleomorphic epithelial cells circumscribed by a desmoplastic stroma [8].

Upon ultrastructural examination, tumour cells are permeated with innumerable mitochondria. Luminal surface of tumour cells are pervaded with abundant microvilli [3,4].

Staging of carcinoma breast as per American Joint Committee on Cancer (AJCC) 8th edition [2,3]

- 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 < 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)
    - Ttumour 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.

Cribriform carcinoma breast is immune reactive to oestrogen receptors (ER) or progesterone receptors (PR).

Tumour cells appear immune non reactive to HER2. Besides, immune non reactive myoepithelial markers assist in segregating invasive cribriform carcinoma from cribriform variant of ductal carcinoma in situ [5,6].

Cribriform carcinoma breast requires segregation from neoplasms as adenoid cystic carcinoma, cribriform variant of ductal carcinoma *in situ*, collagenous spherulosis, well differentiated neuroendocrine tumour or well differentiated invasive breast cancer of no special type (NST) [5,6]. Cribriform carcinoma breast may be appropriately ascertained by diverse imaging techniques as mammogram or ultrasonography of the breast.

Upon mammography, breast tissue depicts asymmetry, enhanced density and micro-calcification. Neoplasm may represent as a spiculated lesion.

Upon ultrasonography, a distinctive tumour mass may be observed. Upon magnetic resonance imaging (MRI), tumour mass expounds a distinct focus of image enhancement.

Besides, cytological or histological evaluation of implicated breast tissue may be beneficially adopted [5,6].

Cribriform carcinoma breast may be appropriately alleviated by primary surgical eradication of the lesion. Characteristic therapeutic strategies of breast conservation pertain to aforementioned special subtype of carcinoma breast and may be employed with curative intent.

Following surgical intervention, localized radiation therapy may be beneficial.

Additionally, cogent endocrine therapy may be optimally adopted.

Pure invasive cribriform carcinoma is associated with superlative prognostic outcomes. Generally, neoplasm demonstrates a decimated tumour stage and is associated with minimal regional lymph node metastasis [5,6].

Mixed subtype of invasive cribriform carcinoma is accompanied by inferior prognostic outcomes, although outcomes are superior to invasive ductal carcinoma of no special type (IDC-NST).

Invasive cribriform carcinoma is associated with superior prognosis, in contrast to invasive carcinoma breast with minimalistic cribriform pattern or low grade invasive ductal carcinoma.

Regional lymph node metastasis or distant metastasis are exceptionally encountered [5,6].

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7. Image 1 Courtesy: Medical news today.

8. Image 2 Courtesy: Libre pathology.