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Short Communication

Heteroclite and Preternatural - Atypical Ductal Hyperplasia Breast

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Atypical ductal hyperplasia is an intra-ductal, proliferative mammary lesion which emerges as a precursor and demonstrates enhanced probability with frequent metamorphosis into invasive carcinoma breast.

Atypical ductal hyperplasia enunciates intra-ductal proliferation of neoplastic epithelial cells incriminating terminal duct-lobular units.

The pre-neoplastic ductal lesion of mammary gland denominated by atypical ductal hyperplasia enhances possible emergence of invasive carcinoma breast by up to ~5 times.

Intra-ductal, clonal epithelial cell proliferation is observed which morphologically resembles low grade ductal carcinoma in situ (DCIS) although mammary gland involvement or volume of lesion is insufficient. In contrast to low grade ductal carcinoma in situ, the confined atypical ductal hyperplasia exhibits homogeneous incrimination of mammary parenchyma ≤ 2 membrane bound spaces or magnitude ≤ 2 millimetres.

Singular or dual expression of aforesaid criterion is an appropriate methodology adopted by World Health Organization (WHO) for classifying the lesion [1,2].

Atypical ductal hyperplasia is additionally designated as B3 lesion of uncertain malignant potential, atypical intra-ductal hyperplasia (AIDH), ductal intraepithelial neoplasia (DIN)1B or mammary intraepithelial neoplasia (MIN) [1,2].

Core needle biopsy can be adopted to detect an 'atypical intra-ductal proliferative lesion' with subsequent surgical excision and precise evaluation of surgical specimen with pertinent classification of lesion. Intra-ductal clonal epithelial cell proliferation exhibits rigid intra-luminal bridges, nuclear polarization surrounding glandular lumen and an intense, diffuse immune reactivity to oestrogen receptor (ER).

A female preponderance is observed. Disease emergence is common within fourth decade. Lesion is incidentally discovered and infrequently associated with gynecomastia [1,2].

Declining postmenopausal hormonal therapy is associated with decimated emergence of atypical ductal hyperplasia. Besides, an estimated ~ 5 times proportionate emergence of ductal carcinoma in situ is observed within 5 years. Alternatively, a mean latency period of 8 years to 12 years following initial disease discernment is encountered.

Atypical ductal hyperplasia (ADH) discerned within surgical tissue samples obtained from mammary glands may demonstrate evolution into ductal carcinoma in situ or invasive carcinoma breast in an estimated 20% lesions [1,2].

In contrast to contralateral breast, disease is predominant within ipsilateral breast with a proportion of 2:1 [1,2].

Commonly, low grade progression from normal breast parenchyma into benign proliferative breast disease and atypical ductal hyperplasia is observed.

Overexpression of enhancer of zeste homolog 2 (EZH2) is significantly involved with mammary gland oncogenesis [1,2].

Perpetual exposure to oestrogens induces continual accumulation of genomic alterations with deficient regulation of growth and epithelial proliferation. Atypical ductal hyperplasia demonstrates chromosomal gains within 1q and loss of 16q-17p, akin to low grade ductal carcinoma in situ [1,2].

Upon gross examination, atypical ductal hyperplasia is challenging to discern. Cut surface appears gritty on account of associated micro-calcifications.

Morphologically, atypical ductal hyperplasia simulates low grade ductal carcinoma in situ [1,2].

Upon microscopy, lesion is well defined and composed of monomorphic neoplastic cells with a well defined perimeter and uniform, miniature, spherical, evenly spaced nuclei [1,2].

Tumour cells configure complex, atypical articulations such as solid, cribriform or micro-papillary. Neoplastic architectural pattern is variable and denominated as

- Solid variant
- Cribriform variant with nuclear polarization circumscribing glandular lumens.
- Micro-papillary variant articulating club-shaped structures with tips of micro-papillae broader than the base. Segments of incriminated ducts demonstrate usual ductal hyperplasia [1,2].

Lesion can be uni-centric or multi-centric and enunciates uniform thickness of rigid bridges or arcades traversing ductal lumens. Intraluminal micro-calcification is frequently discerned [1,2].

Exceptionally, atypical ductal hyperplasia is intermingled with foci of usual ductal hyperplasia or various ductal proliferations within a singular mammary lobule [1,2].

Segregation from low grade ductal carcinoma in situ is challenging. Generally, atypical ductal hyperplasia is distinguished contingent to

- Lesion magnitude ≤ 2 millimetres.
- Space between incriminated foci ≤ 2 spaces or a segment of space occupied by clonal cells [1,2].

Categorization of atypical ductal hyperplasia singularly upon assessment of nuclear magnitude is to be circumvented. However, irrespective of nuclear magnitude or extent of lesion, nuclear atypia may warrant tumour categorization as intermediate grade or high grade ductal carcinoma in situ [1,2].

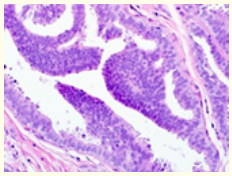

Figure 1: Atypical ductal hyperplasia with rigid, intra-luminal bars, epithelial multi-layering and minimal nuclear pleomorphism or mitotic activity [5].

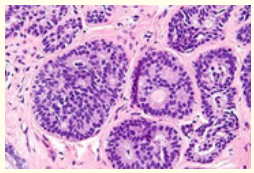

Figure 2: Atypical ductal hyperplasia delineating rigid epithelial bars confined to the lumen with occasional cribriform pattern, minimal epithelial pleomorphism and negligible mitosis [6].

The Nottingham Histologic Score system, additionally designated as 'Elston-Ellis modification of Scarff-Bloom-Richardson grading system' employs specific morphological features for evaluating neoplastic grade of carcinoma breast designated as

- Cellular differentiation with configuration of glands or tubules simulating normal breast architecture.

- Nuclear features with proportionate pleomorhism of neoplastic nuclei.
- Mitotic activity to assess proliferative activity of the neoplasm. Aforesaid features are scored from 1 to 3 and final score is ascertained which appropriately grades the neoplasm from low grade to tumours of advanced grade [2,3].

Table 1: Tumour grading with Nottingham's histologic score system [2,3].

Parameter	Grade I	Grade II	Grade III
Glandular/tubular differentiation	>75% neoplastic glandular component	10% to 75% neoplastic glandular component	<10% neoplastic glandular component
Nuclear pleomorphism	Uniform cells with miniature nuclei akin to normal breast epithelium	Mildly enlarged, pleomorphic cells with vesicular nuclear chromatin and visible nucleoli	Markedly pleomorphic cells with vesicular nuclear chromatin and prominent nucleoli
Mitotic count	<7mitosis/10hpf	8-15mitosis/10hpf	>16mitosis/10hpf

Grade I neoplasms are well differentiated, minimally aggressive, depict a score of 3-5 and are immune reactive to oestrogen receptors (ER+).

Grade II neoplasms are moderately differentiated and delineate a score of 6-7.

Grade III neoplasms are poorly differentiated, aggressive, display a score of 8-9 and are commonly 'triple-negative' or immune non reactive to oestrogen receptors, progesterone receptors and HER2 receptors [2,3].

Nottingham score and histologic tumour grading is adopted to assess requirement of postoperative radiation therapy following surgical manoeuvers as lumpectomy or mastectomy [2,3].

Grade III or lesions of advanced grade are associated with enhanced possible tumour reoccurrence.

Histologic tumour grade is beneficial in assessing requirement of additional dose of radiation subsequent to a course of radiotherapy in order to determine eligibility for accelerated partial breast radiation (APBI) and radiotherapy for regional lymph node metastasis [2,3].

Besides, young subjects with grade III, triple-negative carcinoma breast devoid of regional lymph node metastasis can be assessed for employment of chemotherapy or hormonal therapy [2,3].

Atypical ductal hyperplasia is immune reactive to low molecular weight cytokeratin as CK8, CK18, CK19 and intensely immune reactive to oestrogen receptor. Tumefaction is immune non reactive to CK5/6 [3,4].

Atypical ductal hyperplasia requires segregation from conditions such as usual ductal hyperplasia or low grade ductal carcinoma in situ.

Atypical ductal hyperplasia is devoid of pertinent diagnostic features upon imaging and segregation of epithelial atypia from malignant neoplasms can be challenging [3,4].

Tumefaction is incidentally discovered, exhibits microcalcifications and is discernible upon screening mammography. Surgical tissue samples obtained for eradicating calcification discerned upon imaging may enunciate atypical ductal hyperplasia [3,4].

Surgical tissue sampling followed by conservative therapeutic approach is recommended. Surgical extermination of lesion is necessitated for appropriate disease discernment, especially with lesions borderline between atypical ductal hyperplasia and low grade ductal carcinoma in situ [3,4].

Magnetic resonance imaging (MRI) exemplifies non mass enhancement of mammary gland [3,4].

Lesions confirmed upon surgical tissue sampling can be subjected to cogent and variable surgical excision contingent to imaging features as miniature versus significant calcification, category and magnitude of surgical sampling and individual preference. Vacuum assisted surgical sampling is associated with significant proportion of surgical excision of lesion [3,4].

Tamoxifen ingestion decimates possible emergence of subsequent invasive carcinoma breast [3,4].

Atypical ductal hyperplasia can be optimally treated with localized surgical extermination of neoplasm with a wide perimeter of uninvolved tissue [3,4].

Factors associated with adverse prognostic outcomes are lesion emergence in young subjects, occurrence of BRCA1 or BRCA2 genetic mutations, family history of atypical ductal hyperplasia, several, diverse disease foci and extent of lobular involution as partial or complete, concurrent to age of incriminated subject [3,4].

Bibliography

1. Tomlinson-Hansen S., *et al*. "Atypical Ductal Hyperplasia". Stat Pearls International 2022, Treasure Island, Florida (2022).

2. Bong TSH., *et al*. "Atypical Ductal Hyperplasia of the Breast on Core Needle Biopsy: Risk of Malignant Upgrade on Surgical Excision". *Journal of Breast Cancer* 25.1 (2022): 37-48.

3. Khoury T. "Pre-neoplastic Low-Risk Mammary Ductal Lesions (Atypical Ductal Hyperplasia and Ductal Carcinoma *In Situ* Spectrum): Current Status and Future Directions". *Cancers (Basel)* 14.3 (2022): 507.

4. Sanders ME and Podoll MB. "Atypical Ductal Hyperplasia-Ductal Carcinoma *In Situ* Spectrum: Diagnostic Considerations and Treatment Impact in the Era of De-escalation". *Surgical Pathology Clinics* 15.1 (2022): 95-103.

5. Image 1 Courtesy: Pathology outlines.

6. Image 2 Courtesy: Libre pathology.