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Risk-Associated Breast Lesions Diagnosed on Core Needle Biopsy

By Hongxiu Ji, MD, PhD

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A palpable or imaging-detected breast lesion is often first evaluated by core needle biopsy (CNB) under ultrasound, stereotactic or MRI guidance. The pathology can be divided into three categories: benign, malignant and risk-associated breast lesions. Benign lesions usually show proliferative disease without atypia, such as usual ductal hyperplasia (UDH), fibroadenoma, apocrine metaplasia, pseudoangiomatous stromal hyperplasia (PASH) or columnar cell change/hyperplasia. For those lesions, routine surveillance is sufficient. On the other hand, frankly malignant lesions, including all forms of invasive breast carcinoma, malignant stromal tumors and ductal carcinoma in situ (DCIS), are typically managed with well-defined clinical guidelines. The third category - risk-associated breast lesions, remains unsettled. Although a large body of observational data has been accumulated, our understanding and ability in the appropriate handling of those cases are still limited and evolving.

The risk-associated breast lesions comprise several uniquely defined histologic entities, including atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), classic and non-classic variants of lobular carcinoma in situ (LCIS), flat epithelial atypia (FEA), complex sclerosing lesion and radial scar (SCL/RS), intraductal papilloma (IP), and mucocele-like lesion (MLL). The typical imaging findings, corresponding histologic features and upgrade rate of those lesions on subsequent resections are summarized in Table 1. The immediate concern regarding those lesions is from the observations of variable, sometimes considerable, upgrade rate on subsequent resections. The upgrade rate was reported as high as 30% for ADH. As for long term implications of those lesions, available literature, albeit conflicting, points to a mild to moderate increase of risk (up to 20%) in developing breast cancer in those women in follow-up studies. A diagnosis of atypical hyperplasia (ADH/ALH) and LCIS carries 4-5 times the risk increase compared to the general population. However, more recent studies on women with other risk-associated lesions, such as FEA, IP, CSL/RS and MLL, have demonstrated a similar long term risk of developing breast cancer to those with proliferative disease without atypia, a 1.5-2-time risk increase compared to the general population.

TABLE 1. THE COMMON IMAGING FINDINGS, TYPICAL HISTOLOGY AND UPGRADE RATE OF RISK-ASSOCIATED BREAST LESIONS

Diagnosis on CNB	Common Imaging Findings	Typical Histology	Upgrade rate on subsequent surgical resection
ADH	Amorphous calcification, architectural distortion, incidental finding within a mass lesion	Atypical monomorphic intraductal epithelial proliferation, distinct cell borders, round nuclei, even chromatin Architecturally may be cribriform or micropapillary with rigid bars and arches Quantitatively not enough for low grade DCIS negative for CK5/6, diffusely positive for ER	18-30% Upgrade to DCIS: 3-5 times more than invasive carcinoma

FEA	Calcification, architectural distortion, mass, incidental without imaging correlate	Variably enlarged acini of TDLU lined by low grade monotonous cells with rounded and enlarged nuclei, distinct nucleoli and loss of polarity	0-7%
ALH	Usually incidental without imaging correlate	Monomorphic epithelial cell population lacks nuclear atypia and cellular cohesion with intracytoplasmic vacuoles <50% filling of TDLU Negative for E-cadherin	0-9%
LCIS, Classic	Usually incidental without imaging correlate, amorphous calcification	Cytomorphology similar to ALH Significant expansion of TDLU Negative for E-cadherin	With imaging correlation: <10% Incidental finding: <4%
Non-Classic LCIS Variants	Mass, calcifications	Intermediate to high nuclear grade Discohesive epithelial cells expand ducts or lobules with or without necrosis Negative for E-cadherin	Up to 40%
CSL/RS	Architectural distortion	Stellate dense stromal fibrosis with adenotic epithelial elements radiating outwards	0-5%
IP	Mass, architectural distortion	Intraductal papillary epithelial growth with fibrovascular cores	Benign and imaging concordant: 0-5% Incidental, <2 mm: 0%
MLL	Incidental or mass	Mucin-filled dilated ducts and extravasated mucin in stroma, epithelium completely benign or lacking	Unselected: up to 30% Benign MLL: <=1%

When encountering a risk-associated breast lesion, the following three steps should be taken:

First, before accurately assessing the risk of upgrading on resection and long term breast cancer risk, the pathologist should render an accurate diagnosis based on systematic review and adherence to standard diagnostic criteria, i.e., to properly recognize the histologic features of the lesion and place the lesion into an appropriate diagnostic category. This can be achieved by reading multiple tissue levels, performing appropriate immunohistochemical stains and applying quality assurance measures, such as having more than one pathologist examine every breast biopsy. This effort will help to avoid over-diagnosis and subsequently reduce financial and emotional burden relating to over-treatment and excessive monitoring.

Secondly, it is essential to ask and answer the following question on every breast CNB case: does the CNB pathology reflect sampling of the imaging-detected target lesion or represent incidental finding? For example, a histologic complex sclerosing lesion (CSL) correlates with an MRI finding of architectural distortion, while minute focus of ALH is not representative for an ultrasound-detected mass lesion. Likewise, classic LCIS may be an incidental finding, but pleomorphic LCIS is often biopsied for a lesion with suspicious microcalcifications. Good imaging-pathology correlation is therefore crucial (Figure 1). Whenever an imaging-pathology correlation cannot be reliably established, close surveillance, additional imaging, repeat CNB, or surgical excision may be warranted.

Finally, after a definitive pathology diagnosis is rendered on a CNB sample that represents imaging-detected target lesion, the probability of upgrading on resection and the long term risk of developing breast cancer are discussed with the patient. This is followed by the selection of an individualized management plan by the breast radiologist, breast surgeon or a multidisciplinary team, taking consideration of the recently published recommendations by the American Society of Breast Surgeons (Table. 2).

TABLE 2. MANAGEMENT RECOMMENDATIONS ON PATIENTS WITH RISK-ASSOCIATED BREAST LESIONS BY AMERICAN SOCIETY OF BREAST SURGEONS (ASBS)

Diagnosis on CNB	ASBS Recommends	Alternative Management
ADH	Surgical excision	Clinical follow-up only for very small amount of ADH in certain patients.
FEA	Clinical follow-up	Re-biopsy or surgical excision for patients with discordant imaging finding.
ALH and classic LCIS	Clinical follow-up if concordance with imaging finding	Excision if enhancing lesion, discordance with imaging finding, limited sampling or presence of another higher risk lesion.
Pleomorphic LCIS or LCIS with necrosis	Complete surgical excision, similar to DCIS	
CSL/RS	Surgical excision	Clinical follow-up if small RS (<5 mm) well-sampled or completely removed by CNB.
LP	Surgical excision for palpable lesion and those with atypia	Clinical follow-up if incidental and without atypia.
MLL	Surgical excision	Clinical follow up if imaging finding concordant, completely benign and without atypia.

Taken together, risk-associated breast lesions diagnosed on core needle biopsy pose unique challenges in individualized risk assessment and management planning. It is important to achieve imaging and pathology concordance. In addition, timely and effective communication among the members of a multidisciplinary team, including surgeons, radiologists and pathologists, is essential to ensure appropriate management of those risk-associated breast lesions.

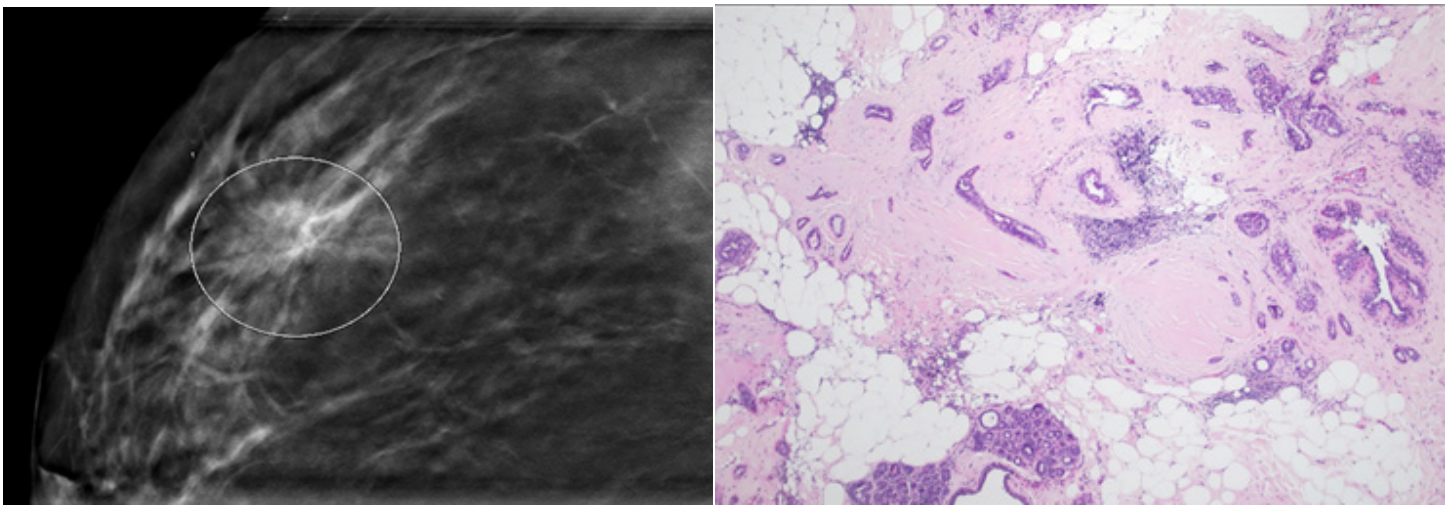

FIGURE 1. A good example of imaging-pathology correlation. A 52-year-old woman with screening mammogram-detected architectural distortion of the right breast (A, Tomosynthesis mammogram), who underwent stereotactic-guided core biopsy. A complex sclerosing lesion/radial scar was found on histologic examination (B).

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