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● *Original Contribution*

DIAGNOSIS OF COLUMNAR CELL LESIONS AND ATYPICAL DUCTAL HYPERPLASIA BY ULTRASOUND-GUIDED CORE BIOPSY: FINDINGS ASSOCIATED WITH UNDERESTIMATION OF BREAST CARCINOMA

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Abstract—The aim of the study described here was to determine underestimation rates and identify radiologic predictors of underestimation for columnar cell lesions (CCLs) and atypical ductal hyperplasia (ADH) detected by ultrasound-guided core needle biopsy. A total of 103 CCLs and ADH lesions in 100 patients diagnosed by ultrasound-guided core needle biopsy were evaluated. Breast sonographic and mammographic findings were reviewed, and underestimation rates were determined by surgical excision, percutaneous vacuum-assisted excision or 2-y imaging follow-up. All underestimated lesions were ductal carcinoma *in situ*, and the underestimation rates of flat epithelial atypia (FEA), FEA + ADH and ADH were 5.9% (1/17), 44.4% (4/9) and 27.3% (12/44), respectively. There was no underestimation of CCLs without atypia. The presence of calcifications on ultrasound was significantly associated with underestimation ($p = 0.010$). Therefore, except for CCLs without atypia, all other lesions may require excision, especially when calcification is present on ultrasound or when FEA + ADH is found.
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Key Words: **Atypical ductal hyperplasia, Breast ultrasound, Columnar cell lesion, Core needle biopsy, Underestimation.**

INTRODUCTION

Columnar cell lesions (CCLs) are characterized by columnar epithelial cells lining the dilated terminal duct lobular units of the breast; these cells present as a single layer of columnar cells (columnar cell change [CCC]), multiple layers with apical tufting and stratification (columnar cell hyperplasia [CCH]) or monomorphic cells with cytologic atypia (flat epithelial atypia [FEA]) (Pandey et al. 2007; Schnitt and Vincent-Salomon 2003). Atypical ductal hyperplasia (ADH) is a type of proliferative intra-ductal breast lesion with some features of low-grade ductal carcinoma *in situ* (DCIS) (Tavassoli and Devilee 2003). FEA is distinguishable from ADH and DCIS by the absence of architectural atypia (Kunju and Kleer 2007; Pandey et al. 2007; Schnitt and Vincent-Salomon 2003), but some features of these lesions may overlap (Collins et al. 2007; Kunju and Kleer 2007; Ingegnoli et al. 2010; Lavoue et al. 2011; Lee et al. 2010; Piubello et al. 2009; Sudarshan et al. 2011; Tavassoli and Devilee 2003).

The rates of detection of CCLs and ADH have increased because of the widespread application of screening mammography and increased use of stereotactic or ultrasound (US)-guided percutaneous breast biopsy. CCC and ADH are indicated for follow-up imaging and excision, respectively (Ingegnoli et al. 2010; Kunju and Kleer 2007; Lee et al. 2010; Tavassoli and Devilee 2003). ADH diagnosed by US-guided core needle biopsy should be excised because of underestimation of breast cancer in the remaining portion of the lesion (Ingegnoli et al. 2010; Kunju and Kleer 2007; Mesurolle et al. 2014; Tavassoli and Devilee 2003; Youk et al. 2009). However, the rates of underestimation of CCC and ADH vary in much of the literature, and the

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management of these lesions remains controversial (Collins et al. 2007; Ingegnoli et al. 2010; Kunju and Kleer 2007; Lavoue et al. 2011; Lee et al. 2010; Piubello et al. 2009; Sudarshan et al. 2011; Tavassoli and Devilee 2003). Therefore, identification of radiologic findings that can distinguish between CCLs and ADH could improve management strategies for these conditions.

Many studies have reported mammographic findings for CCLs and ADH, including differences in the shape and distribution of microcalcifications. In 37%–74% of CCLs, microcalcifications appear round or amorphous instead of linear or branching (Fraser et al. 1998; Kim et al. 2006; Pandey et al. 2007; Senetta et al. 2009). Fine, rounded shape and clustered or regional microcalcifications are indicative of ADH rather than malignancy (Helvie et al. 1991; Hoang et al. 2008). Interestingly, only a few studies have thoroughly described breast US findings. Kim et al. (2006) found focal abnormalities in 58% (7/12) of the CCLs examined by breast US. Solorzano et al. (2011) described US findings for FEA diagnosed by core needle biopsy, and Youk et al. (2009) reported 21 cases of ADH diagnosed by US-guided core needle biopsy. However, these reports do not specify the US findings of atypia or predict underestimation.

Therefore, the purpose of this study was to determine underestimation rates and identify radiologic predictors of underestimation for CCLs and ADH detected by US-guided core needle biopsy.

METHODS

Patients

The institutional review board approved this retrospective study and waived informed consent. Between May 2003 and May 2013, 8184 US-guided core needle biopsies were performed at our institution after screening or diagnostic US revealed abnormal findings according to the Breast Imaging Reporting and Data Systems (BI-RADS), that is, category >4a (low suspicion of malignancy) (American College of Radiology 2003). Screening US was performed on young patients who did not want to undergo mammography or older patients who preferred US because of their breast features. Diagnostic US was performed on patients referred from other hospitals for further management after mammography or for breast-related symptoms. Histologic analysis revealed 2193 malignant (26.8%) and 5991 benign (73.2%) lesions, including 164 (2.0%) cases of CCL and 155 (1.9%) cases of ADH. We excluded 105 cases of ipsilateral breast cancer, 49 cases of lost to follow-up and 62 cases with a follow-up duration <2 y from the 319 histologically confirmed cases of CCL and ADH. Ipsilateral breast cancer was excluded because we aimed to determine isolated imaging findings associated with underestimation of these lesions and ensure that post-operative specimens were independent of other breast lesions. Thus, a total of 103 lesions from 100 patients were included in this study: 33 CCLs without atypia (including 30 lesions exhibiting CCC and 3 lesions exhibiting CCH), 17 lesions with FEA, 9 lesions with FEA + ADH and 44 lesions with ADH.

Imaging procedures

Breast US and US-guided core needle biopsy were performed by one of two breast radiologists who had 8–18 and 4–10 y of breast imaging experience, respectively, using high-resolution (12-MHz electronically focused linear-array transducer) US equipment (HDI 5000 or IU 22, Philips Healthcare, Bothell, WA, USA). Mammograms were routinely reviewed before performing US examination when available. US-guided core needle biopsy was then performed using a 14-gauge semi-automated gun with a coaxial needle (Stericut with coaxial, TSK Laboratory, Tochigi, Japan). A longitudinal freehand approach was applied to collect 4–10 specimens (mean = 5.4) in all cases. Specimen mammography was performed when the lesion included echogenic foci presumed to be calcification.

Mammography was performed with digital equipment (Senographe 2000 D from GE Healthcare, Buckinghamshire, UK; or Brestige from Medi-Future, Seongnamsi, Korea). Four views (bilateral, craniocaudal and mediolateral oblique) were obtained. Additional compression and magnification views were obtained to determine associations with calcification and US-detected lesions for further evaluation of calcifications. In general, mammography preceded breast US, except when the patient did not want mammography or had undergone imaging outside of our hospital.

Image analysis

Mammographic and breast US findings for each lesion were reviewed simultaneously and in consensus by two subspecialty-trained breast radiologists who had 2–4 and 4–10 y of experience, respectively. The reviewers were blinded to the clinical information and pathologic results, except for the location of the lesion. Lesion shape, margin, posterior acoustic features, orientation, lesion boundary, echogenicity and BI-RADS category were determined by US. When echogenic foci with or without acoustic shadowing were identified, calcifications were considered to be present. Mammographic findings were classified as negative, mass only, mass with calcification, calcification only and unknown (unavailable mammography). If calcification was present on mammography, the shape and distribution of the calcification were classified. Lesions and radiologic findings were described