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Sonographic Features of Flat Epithelial Atypia Manifesting as a Non-Mass-Like Lesion: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 47
Final Diagnosis: Flat epithelial atypia of the breast
Symptoms: —
Medication: —
Clinical Procedure: —
Specialty: Radiology

Objective: Rare disease
Background:

The incidence of flat epithelial atypia of the breast has been increasing owing to the increasing use of ultrasonography (US) and US-guided core needle biopsy. However, reports describing the sonographic features of flat epithelial atypia are fewer than those on its mammographic features.

Case Report: A 47-year-old female had a regular 6 month-interval follow-up US for multiple bilateral breast masses detected on US. A new focal non-mass-like lesion measuring 2 cm in maximum diameter was noted in the 10 o'clock direction of the right breast on the follow-up US. Mammography was not performed during the follow-up period. The patient had no breast symptoms and no family history of breast cancer or other pertinent medical history. US-guided 14-gauge core needle biopsy yielded a pathological diagnosis of flat epithelial atypia without up-grade to malignancy, and this was further confirmed after complete excision of the non-mass-like lesion.

Conclusions: Flat epithelial atypia can present as a focal non-mass-like lesion on US, which has not been reported previously.

MeSH Keywords: Breast • Breast Diseases • Ultrasonography, Mammary

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Background

Flat epithelial lesions are the most advanced subgroup of in columnar cell lesion spectrum. They are characterized by columnar epithelial cells lining the dilated terminal duct lobular units of the breast and comprise columnar cell change, columnar cell hyperplasia, and flat epithelial atypia [1,2]. Columnar cell change is composed of a single layer of columnar cells, while columnar cell hyperplasia is composed of multiple layers of columnar cells with apical tufting and stratification [1]. By contrast, flat epithelial atypia is composed of one to several layers of a single epithelial cell (monomorphic) showing low-grade cytological atypia [3]. Flat epithelial atypia differs from atypical ductal hyperplasia and ductal carcinoma *in situ* in that architectural atypia is absent [1]. The collective term “flat epithelial atypia” was first established by the World Health Organization Working Group in 2003; before that, several terms had been used synonymously with flat epithelial atypia including columnar cell change with atypia, columnar cell hyperplasia with atypia, atypical cystic duct and lobules, columnar alteration with prominent apical snout, ductal

intraepithelial neoplasia 1- flat type, and clinging carcinoma (monomorphic type) [4,5].

With the increased use of breast sonography for both screening and diagnostic purposes, columnar cell lesions, including flat epithelial atypia, have become a frequent diagnosis on sonography-guided core needle biopsy for breast lesions with suspicious sonographic findings [6,7]. The incidences of flat epithelial atypia on core needle biopsy range from 0.7% to 3.7% [3]. However, sonographic findings of flat epithelial atypia are rarely reported. This paper reports on a focal non-mass-like lesion as an unusual sonographic presentation of flat epithelial atypia of the breast.

Case Report

A 47-year-old female had undergone regular follow-up US for sonographically detected multiple bilateral breast masses with 6-month intervals, for 3 years. During the follow-up period, the breast masses partly fluctuated in size and number and

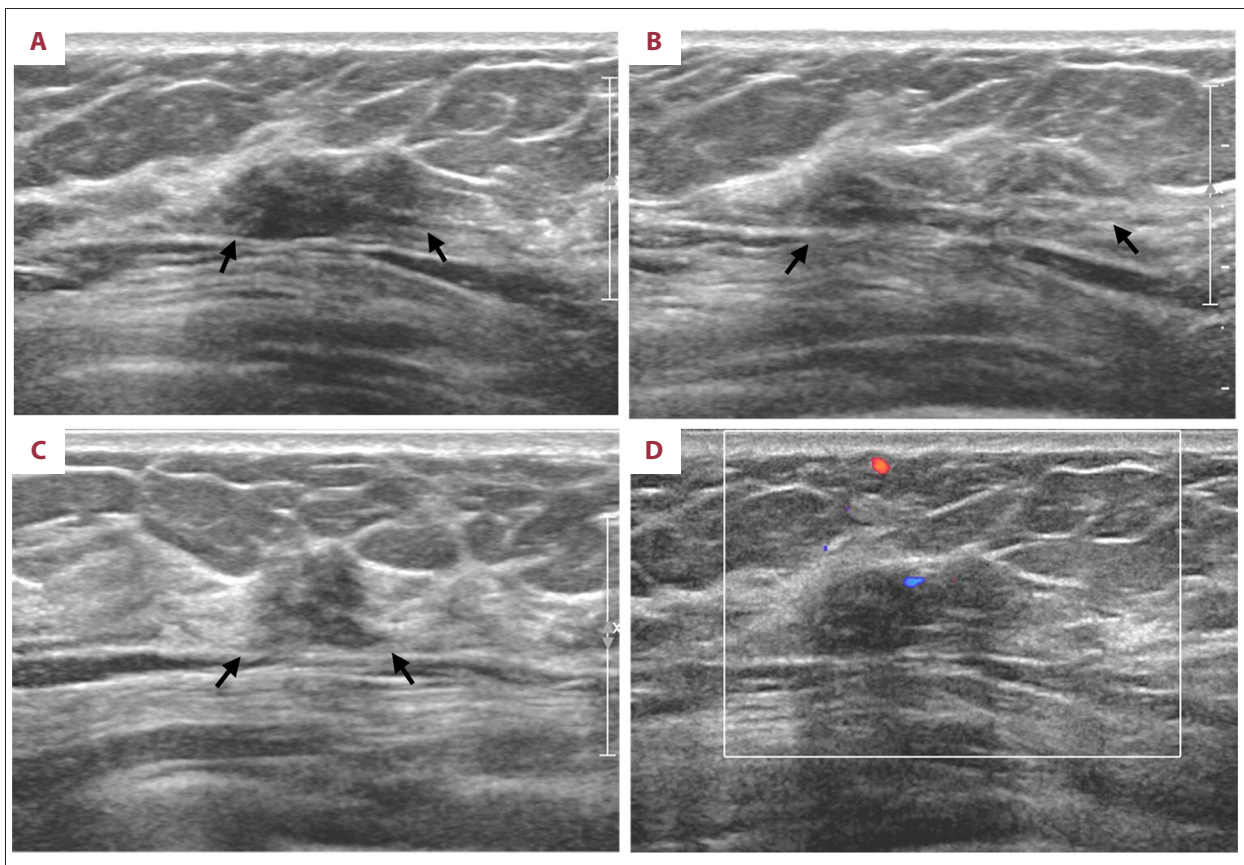


Figure 1. (A) Transverse, (B) radial, and (C) longitudinal gray-scale sonograms show focal indistinct hypoechoic area (arrows) in the right breast, which is discernable from the surrounding fibroglandular tissue, but does not conform to the definition of a mass. There are intervening normal fibroglandular tissues within the hypoechoic area. (D) Color Doppler sonogram shows a few spotted increased vascularity within the non-mass-like lesion.

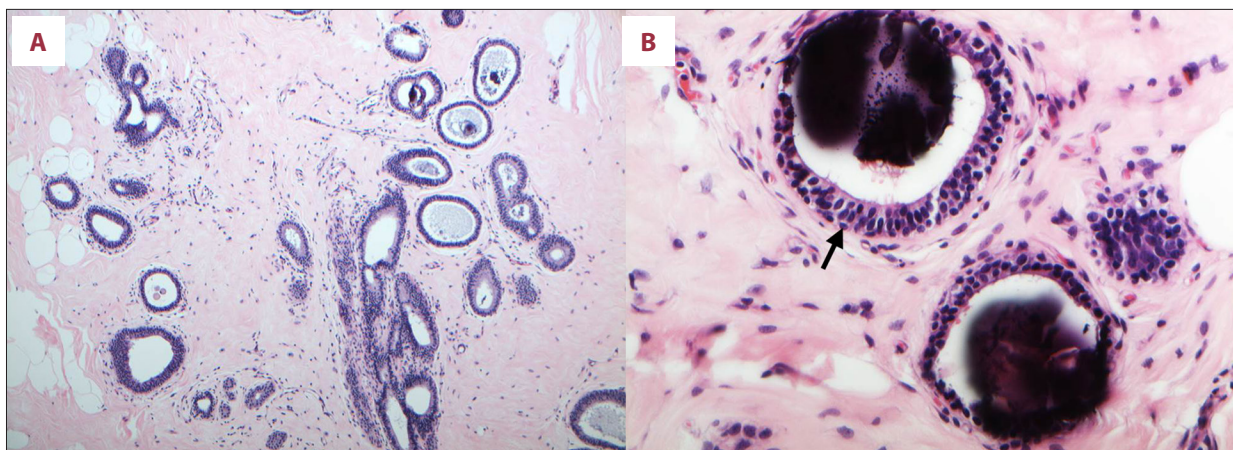


Figure 2. (A) This terminal duct lobular unit shows dilated acini, with microcalcifications and intraluminal secretions. Most acini are lined by 2 layers of columnar epithelial cells with prominent apical cytoplasmic snouts (hematoxylin & eosin, 100 \times). (B) Multifocal areas of the acini lined by columnar epithelial cells showed mild cytologic atypia, characterized by plump, monotonous nuclei and increased nuclear/cytoplasmic ratio (hematoxylin & eosin, 400 \times).

were assessed as benign (category 3) according to the Breast Imaging Reporting and Data System (BI-RADS) classification. At the patient's last US in the 3-year follow-up, a new focal non-mass-like lesion measuring 2 cm in maximum diameter was noted in the 10 o'clock direction of the right breast. It was an indistinct hypoechoic area with intervening normal fibroglandular tissue, which was discernable from background fibroglandular tissue, but did not conform to the characteristic of a mass (Figure 1). The non-mass lesion was assessed as low suspicion for malignancy (category 4a) according to the BI-RADS classification. At that time, she had no accompanying breast symptoms, no family history of breast cancer, and no pertinent medical history. Mammography was not performed during the follow-up period.

US-guided 14-gauge core needle biopsy led to a pathological diagnosis of flat epithelial atypia without upgrade to malignancy. This was further confirmed after complete surgical excision of the lesion. Microscopic findings of the excised non-mass-like lesion showed dilated acini lined by 2 layers of columnar epithelial cells with prominent apical cytoplasmic snouts and mild cytologic atypia (Figure 2).

Discussion

Previously, flat epithelial atypia was mainly discussed in association with mammographic surveillance, and the main imaging feature of flat epithelial atypia was described as microcalcifications [7,8]. Solorzano et al. [8] reported that the most common mammographic finding of flat epithelial atypia was clustered (70%), amorphous (65%), or microcalcifications (61%), while less common findings were masses (12%) with or without microcalcifications, and architectural distortions (6%).

Khoumais et al. reported that microcalcifications seen on core-needle biopsy of flat epithelial atypia encompasses diverse morphology, including amorphous (19%), fine pleomorphic (28%), coarse heterogeneous (26%), and punctate (27%); however, fine pleomorphic and amorphous morphology are more significantly associated with malignant surgical outcome than round and coarse heterogeneous morphology [7]. Sonographic features of flat epithelial atypia are rarely reported, and they have been only briefly described as mass, hypoechoic nodule, cystic lesions [3,4] or presented in combination with atypical ductal hyperplasia [1]. Only 1 study has described the sonographic findings of flat epithelial atypia in detail. In that study, 22 cases of flat epithelial atypia showed no abnormality in 11 cases (50%), a mass in 9 cases (41%), and an architectural distortion in 2 cases (9%) [8]. Sonographically, the flat epithelial atypia commonly presented as an irregular, microlobulated, hypoechoic, or complex-echoic mass [8]. In the aforementioned study, a high percentage of flat epithelial atypia that manifested as masses at sonogram was upgraded to malignancy (2 of 9 masses); therefore, surgical excision was recommended for all flat epithelial atypia that present as a mass at sonogram [8].

Our case report demonstrated a unique sonographic presentation of flat epithelial atypia in which a focal non-mass-like lesion corresponded to the pathology of flat epithelial atypia. Advanced image quality with high-resolution US and increased use of bilateral whole breast US enables the detection of a hypoechoic area (non-mass lesion) that do not conform to the criteria of a mass defined by the BI-RADS as a space-occupying lesion seen in 2 different planes [9]. The current BI-RADS classification does not provide a lexicon for these non-mass-like lesions detected in US [9]. There is no standardized guideline for the interpretation and management of non-mass-like lesions, and thus it is currently dependent on operator

experience and judgement in individual clinical setting [9]. Recently, attempts to discriminate between benign or malignant non-mass-like lesions based on a combined analysis of B-mode, color Doppler US, strain, or shear wave elastography have consistently demonstrated improved diagnostic performances [10–13]. Non-mass-like lesions are known to reflect a broad spectrum of breast pathologies including benign, high-risk, and malignant lesions [14]. In a recent analysis of ultrasonographic features of ductal carcinoma *in situ*, the most frequent findings were hypoechoic areas (48.6%), followed by mass (28.0%) [15]. High-risk lesions manifesting as non-mass-like lesions included atypical ductal hyperplasia, lobular carcinoma *in situ*, papillary neoplasm, and flat epithelial atypia [14,16]. The frequency of flat epithelial atypia among non-mass-like lesions ranges from 2.1% to 0.7% (3 of 145 and 1 of 152 non-mass-like lesions, respectively) [14,16], and imaging findings of flat epithelial atypia presenting as a non-mass-like lesion are yet to be reported.

There are 2 important concerns related to flat epithelial atypia that remain unresolved; one is regarding the risk of developing breast cancer in the future and the other is regarding management after diagnosis on core needle biopsy (i.e., whether to excise or not) [17]. Flat epithelial atypia is known to be frequently associated with lobular neoplasia, low-grade ductal carcinoma *in situ*, and tubular carcinoma (Rosen triad) [18] and is often proposed as a precursor lesion in the low-grade breast cancer pathway [2]. However, the risk of developing breast carcinoma and the expected time course for its development are still not clearly defined for flat epithelial atypia [18]. A long-term follow-up study has shown that columnar cell lesions are associated with minimally increased relative risk for later cancer development in either breast (relative risk of 1.47 when compared with the risk of no proliferative disease) [19]. Meanwhile, there were no significant differences in the relative risk of breast cancer according to subtypes of columnar cell lesions (columnar cell change, columnar cell hyperplasia, and flat epithelial atypia) [19]. Recently, a study reported evidence against the precursor role of columnar cell lesion in the development of breast cancer after reviewing the clinicopathologic features of carcinoma subsequent to columnar cell lesion (i.e., the occurrence of carcinoma in either breast and similar grade and type distribution as sporadic breast cancer) [17]. Moreover, columnar cell lesions or flat epithelial atypia appeared to have no independent impact on breast cancer, i.e.,

the coexistence of columnar cell lesion or flat epithelial atypia did not increase the risk of breast cancer in the subgroup of patients with atypical hyperplasia or proliferative disease without atypia [2,20]. The reported upgrade rate of flat epithelial atypia diagnosed at core needle biopsy to invasive or *in situ* carcinoma widely varied from 0% to 42% [21]. Although there is no current consensus regarding the management of flat epithelial atypia diagnosed on core needle biopsy, surgical excision is generally favored [21,22].

The reported upgrade rate of flat epithelial atypia diagnosed on core needle biopsy to malignancy ranged from 0% to 15%. The optimal management strategy for columnar cell lesion following imaging-guided core needle biopsy is yet to be determined [6]. Flat epithelial atypia is usually recommended to be excised when radiologic findings are suspicious for malignancy. However, for a subgroup of patients, imaging follow-up is recommended instead of surgical excision when the lesion size is ≤ 10 mm on US [3], columnar cell lesion without atypia [6] or focal involvement is observed on pathology (flat epithelial atypia involving fewer than 3 adjacent acinar spaces within a lobule or adjacent lobules), and there is no personal history of breast cancer [23]. Flat epithelial atypia without residual microcalcifications after stereotactic vacuum-assisted breast biopsy could be managed with mammographic follow-up [18]. By contrast, surgical excision is further recommended when calcifications are present on sonogram or in cases of co-occurring flat epithelial atypia and atypical ductal hyperplasia [1]. Meanwhile, changes in radiographic images or lesion size warrant further pathological evaluation through surgical excision among patients recommended only for imaging follow-up [3].

Conclusions

This report demonstrated a unique sonographic presentation of flat epithelial atypia as a focal non-mass-like lesion. With increasing diagnosis of flat epithelial atypia on US-guided core needle biopsy, awareness of its various sonographic presentation can be useful when assessing imaging-pathology concordance.

Conflict of interest

None.

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