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Original article

Surgical excision of pure flat epithelial atypia identified on core needle breast biopsy

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ABSTRACT

The biology of flat epithelial atypia (FEA) is still being investigated as its presence becomes more frequent on biopsy specimens. FEA is more commonly associated with malignancy when found in association with ADH, ALH or LCIS. Pure FEA is only upgraded to cancer in 3.2% of patients. Surgical excision of pure FEA found on core needle biopsy results in overtreatment in the vast majority of breast patients and may not be necessary.

Introduction

Flat epithelial atypia (FEA) of the breast is a relatively new descriptive term of unknown significance in breast pathology. It is characterized by native epithelia replaced by atypical enlarged terminal duct units lined by columnar cells. The definition was established by the World Health Organization Working Group on the Pathology and Genetics of Tumors of the Breast and Female Genital Organs in 2003 [1]. The pathologic entity currently described as flat epithelia atypia has had numerous other labels such as clinging carcinoma, monomorphous type; atypical cystic lobules; atypical cystic duct; atypical columnar alteration with prominent apical spouts and secretions; ecstatic ducts lined by atypical cells with apocrine secretions; ductal intraepithelial neoplasia 1A, flat type; and columnar cell change with atypia [2]. Pure FEA falls on the spectrum of benign breast lesions, categorized as proliferative lesions with atypia (Fig. 1). Other proliferative lesions with atypia include atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS).

The biology of flat epithelial atypia is still being investigated as its presence becomes more frequent on biopsy specimens. FEA is seen in 3.8–10% of core needle biopsy samples and is rarely upgraded to malignancy when found in isolation [3]. Instead, FEA is more commonly associated with malignancy when found in association with ADH, ALH or LCIS. Rates of upstaging to breast cancer on surgical excision have been estimated at 5–20% with ADH [4], 14–25% with ALH [5], and 25–40% with LCIS [5,6] respectively. Due to the assumed incidence of associated malignancy, surgical excision is the standard clinical recommendation when FEA is discovered on biopsy. There are no established guidelines for excision of FEA likely due to paucity of data.

Percutaneous core needle biopsy (CNB) is the current recommendation for evaluation of breast abnormalities, both palpable and nonpalpable. The overall sensitivity of CNB is 92–94%, specificity 88–94.8%, accuracy 93.4%, positive predictive value (PPV) 85–100%, and negative predictive value (NPV) 95–100% [7,8]. CNB may be performed using ultrasound, stereotactic, or magnetic resonance imaging (MRI) guidance, with or without vacuum assistance. A core biopsy retrieves a small core of tissue, obtained with multiple passes (generally three to six, four are recommended). The accuracy of ultrasound guided CNB is reported as 98%, sensitivity 96%, and false negative rate 0–12% [9,10]. Stereotactic CNB is often used for microcalcifications, using a 9- or 10-gage spring loaded biopsy needle, with a sensitivity of 98%, specificity 93%, PPV 86% and NPV

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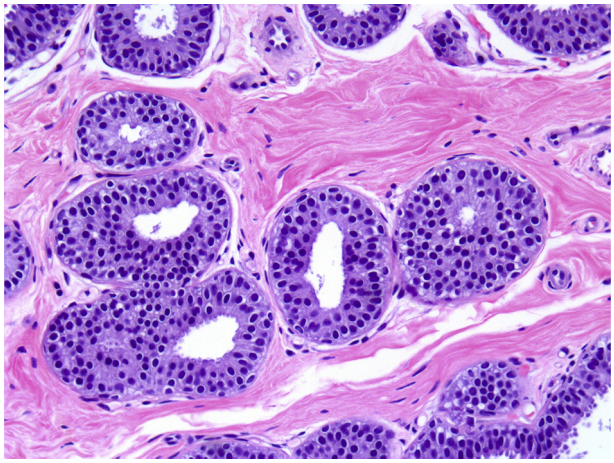

Fig. 1. Flat epithelial atypia characterized by a proliferation of uniform epithelial cells with low grade atypia and loss of orientation to the basement membrane. Note the absence of architectural atypia.

99% [11]. The sensitivity of MRI for breast cancer detection is 71–100%, with specificity of 65–75%, PPV of 15–40% and NPV of 95% [12]. MRI with vacuum assistance is utilized over MRI-guided core needle biopsy so that tissues do not shift in situ.

The histology of the lesion obtained via percutaneous biopsy is generally followed by either excisional biopsy or observation with appropriate imaging. With more widespread use of mammography and image-guided core biopsies, clinicians are seeing increasing numbers of lesions that are not definitively malignant [13]. Due to concerns regarding the specificity and sensitivity of percutaneous biopsy, surgical excision is frequently recommended for these indeterminate lesions.

This study was conducted to evaluate our institutional experience with FEA in an effort to improve management decisions. We specifically examined the detection of FEA diagnosed on core needle biopsy, rates of breast cancer in individuals undergoing surgical excision for a primary diagnosis of FEA, and clinicopathologic features associated with the upstaging of these lesions.

Materials and methods

An institutional review board-approved single institution database of patients undergoing diagnostic breast imaging, percutaneous core needle biopsy, and surgical excision from 2005 to 2010 was used to identify women diagnosed with FEA. Cases with associated ADH or ALH were included. All patients were seen at either a diagnostic breast clinic or were in follow-up for a previously treated breast cancer. All patients had diagnostic imaging and biopsy by a breast-specific radiologist at our institution, followed by surgical excision at our institution by one of four fellowship-trained breast surgical oncologists. Core needle biopsies were obtained by either stereotactic, ultrasound or MRI-guidance, with or without vacuum assistance. Biopsy specimens were routinely subjected to specimen radiography to confirm the presence of calcifications in the sample when indicated. All core biopsy and excision specimens were examined in at least three sections by a breast pathologist. Cases ultimately upgraded on excision were re-reviewed by a single breast pathologist for the purpose of this study.

Out of the initial 300 patients examined, fifty-two were identified as having FEA on core needle biopsy. Clinical, radiologic, and pathologic data were collected from the electronic medical record. Data included patient characteristics, mammogram and other imaging results, reason for and biopsy details, and final surgical histology. Individuals with concurrent FEA and cancer on core biopsy of the same breast, or patients who did not have an excisional biopsy, were excluded from the study. Malignancy was defined as ductal carcinoma in situ (DCIS) or invasive carcinoma. Cases ultimately upgraded on excision were re-reviewed by a single breast pathologist for the purpose of this study. Due to the relatively small number of cases, the analysis was limited to descriptive statistics.

Results

Of 300 patients, fifty-two were identified as having FEA on core needle biopsy (17.3%) (Table 1). The mean age was 52 years (range 35–74) at diagnosis, median age was 52, and all were female. There were 23 (44%) premenopausal and 29 (56%) postmenopausal women. Three (6%) patients had a personal history of breast cancer, and 14 (27%) had a family history of breast cancer in a first degree relative.

Core needle biopsy was recommended in 40 (77%) patients due to suspicious calcifications on mammography; five (10%) for a palpable mass; two (4%) for both calcifications and a mass; and five (10%) due to a cyst, architectural distortion or irregular enhancement on MRI. Multiple cores (range 3–12) were obtained on all lesions using a large bore needle (9–14 gage) with ultrasound, stereotactic or MRI-guidance. Forty-two patients underwent stereotactic CNB, 39 of which were obtained with vacuum assistance; eight had ultrasound guided biopsies in which two used vacuum assistance; two had MRI CNB with vacuum assistance. Of patients with pure FEA, 20 out of 24 core biopsies were obtained with vacuum assistance. The two patients with MRI-guided biopsies were lesions seen only on MRI. Overall, 43 (83%) biopsies were obtained with vacuum assistance. Mammographic calcifications were associated directly with FEA in 30 (58%) cases, and with other diagnoses in 32 (62%) specimens. The mean time between CNB and excisional biopsy was 12.7 weeks.

The 24 patients (46%) who had pure flat epithelial atypia on core needle biopsy had no associated malignancy on excisional biopsy (Table 3). Twenty-two patients (42%) had residual FEA on final surgical pathology; 2 had no residual lesions on excision, these were presumably excised at the time of percutaneous core biopsy.

Table 1
Patient characteristics.

Age at diagnosis (Years)	52.5 (range 35–72)
Menopausal status	
Premenopausal	23 (44%)
Peri- or Postmenopausal	29 (56%)
Breast history	
History of prior breast biopsy	16 (31%)
Family history of breast cancer (1st degree relative)	14 (27%)
Personal history of breast cancer	3 (6%)
Reason for biopsy	
Microcalcifications	40 (77%)
Mass	5 (10%)
Mass and microcalcifications	2 (4%)
Other	5 (10%)
BIRADS category	
3	1 (2%)
4	47 (90%)
5	3 (6%)
Unknown	1 (2%)
Biopsy imaging modality	
Stereotactic	41 (79%)
Ultrasound	9 (47%)
MRI	2 (4%)
Calcification characteristics	
Pure FEA	24 (46%)
Associated with ADH	17 (33%)
Associated with ALH	6 (12%)

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