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All pure flat atypical atypia lesions of the breast diagnosed using percutaneous vacuum-assisted breast biopsy do not need surgical excision

Lobna Ouldamer [a, b, c, *], Elodie Poisson [a, c], Flavie Arbion [d], Carole Bonneau [e], Anne Vildé [f], Gilles Body [a, c], Patrick Michenet [e]

[a] Department of Gynecology, CHRU de Tours, Hôpital Bretonneau, 2 Boulevard Tonnellé, 37044 Tours, France
[b] INSERM Unit 1069, Tours, France
[c] François Rabelais University, Tours, France
[d] Department of Pathology, CHRU de Tours, Hôpital Bretonneau, 2 Boulevard Tonnellé, 37044 Tours, France
[e] Department of Pathology, CHR D'Orléans, Hôpital La Source, Orléans, France
[f] Department of Radiology, CHRU de Tours, Hôpital Bretonneau, 2 Boulevard Tonnellé, 37044 Tours, France

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ABSTRACT

Background: The purposes of this study were to evaluate the outcome of women with pure flat atypical atypia (FEA) diagnosed at vacuum-assisted breast biopsy (VABB) targeting microcalcifications and to determine whether clinical, radiological and pathologic parameters are able to predict which lesions will be upgraded to malignancy.

Materials: 2414 cases of consecutive VABB for microcalcifications using VA 8-, 10- or 11-Gauge stereotactically guided core biopsy performed between January 2005 and December 2011 from two french breast cancer centers were evaluated. Data of women with VABB-diagnosed pure FEA who underwent either excisional surgery or mammographic follow-up were analyzed. Cases with mass lesions or ipsilateral cancers were excluded. Two pathologists (FA,PM) reviewed the results of procedures performed. Clinical, radiological, as well as histological criteria have been studied in order to determine the correlation between these factors and carcinoma underestimation.

Results and conclusion: This study included 70 cases of pure FEA. Twenty women underwent surgical excision and 50 had clinical and mammographic surveillance only. In three women FEA was upgraded to breast cancer on excision. Clinical and mammographic follow-up for a mean of 56 months ± 27 in the group without excision showed two cancers in the same breast (Intermediate grade DCIS, and invasive ductal carcinoma 84 and 48 months respectively after VABB). Three factors were significantly predictive of underestimation or occurence of cancer for pure FEA when the radiologic lesions are calcifications: age≥ 57 years, radiologic size >10 mm and number of FEA foci ≥4.

1. Introduction

A variety of terms has been proposed in the literature for Flat Atypical Atypia (FEA): atypical cystic lobules [1,2], columnar cell hyperplasia with atypia [3,4], columnar cell change with atypia, columnar alteration with apical snouts and secretions [5–7], clinging carcinoma in situ [8], ductal intraepithelial neoplasia grade 1a (DIN1a) is also used [6,9–14]. The term "Flat Epithelial Atypia" has been proposed by the World Health Organization (WHO) working group on pathology and genetics of tumors of the breast [15]. Other epithelial atypia are divided into atypical ductal hyperplasia (ADH or DIN 1b) and lobular neoplasia (LN).

FEA is an intraductal alteration of mammary terminal duct lobular units characterized by replacement of the native epithelium by a population of monotonous, mildly atypical cuboidal to columnar epithelial cells, one to several layers in thickness, with a flat architectural pattern with the complete absence of intraluminal proliferation with architectural atypia. The involved ducts appear variably distended and often contain intraluminal calcifications and

* Corresponding author. Department of gynecology, CHU Bretonneau, 2 Boulevard Tonnellé, 37000 TOURS , France
E-mail address: l.ouldamer@chu-tours.fr (L. Ouldamer).

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secretory material, which can be the only manifestation on mammography [6,15].

Although the biological and clinical significance of FEA is still far from completely understood, recent literature suggests that FEA may represent a precursor of low-grade breast cancer [16–18].

The diagnosis of FEA on biopsy specimens is becoming more frequent and because of potential undersampling of ductal carcinoma in situ (DCIS) or invasive cancers associated with neighboring FEA, excisional biopsy is currently recommended when FEA is identified after core needle biopsy or vacuum assisted breast biopsy (VABB). Upgrade occurs when DCIS or invasive cancer is found at excisional biopsy or when carcinoma occurs in the site of biopsy after FEA has been diagnosed as the highest-risk lesion at VABB or core needle biopsy. Because of the heterogeneity of study populations in literature (type of biopsy, type of radiological lesions targeted) there is conflicting evidence in literature as to whether subgroups of patients with FEA at biopsy can safely avoid surgical excision.

The aim of this study was to determine the upgrades rates of pure FEA diagnosed as the highest risk lesions at VABB who underwent either subsequent surgery or clinical follow-up and to identify predictive factors of underestimation on the basis of clinical, radiological and pathologic features to define a subgroup of patients with pure FEA who may be spared surgery.

2. Materials and methods

For this study, we included patients who received a diagnosis of pure FEA by means of VABB targeting calcifications between January 2005 and December 2011 at the university hospital center of Tours as well as at the regional hospital of Orléans. Patients for this study were identified through our pathology databases.

All patients underwent mammographic examination. Images sent to our referent centers for VABB were reviewed and reclassified. Radiological lesions were classified according to the breast imaging Reporting and Data System (BiRADS) [19].

Lesions were biopsed under stereotactic guidance using a digital prone table and a directional vacuum-assisted biopsy device. Two types of VABB devices were used: in Tours lesions had been sampled with stereotactic guidance using 10-gauge, vacuum-assisted biopsy (Vacora® breast biopsy system, Bard). In Orléans, lesions had been sampled with stereotactic guidance using 8-, 10- or 11-gauge, vacuum-assisted biopsy (Mammotome, Ethicon EndoSurgery). The stereotactic biopsies were performed with patients prone on a dedicated table. For target lesions, removal was confirmed by specimen radiography of the cores: Adequacy of sampling of microcalcifications was confirmed by visualizing calcifications on specimen radiographs. Cores containing calcifications had been considered “positive”. Post-biopsy mammogram was performed to determine how much of lesional area was removed by VABB sampling.

VABB were also performed on patients with BI-RADS category 3 calcifications with familial or personal history of breast cancer and when the repeated re-evaluation of the lesions at 4-month intervals caused them anxiety.

The radiology records were reviewed [1]: Mammographic and/or ultrasound findings (calcifications vs mass) [2], Classification of the lesion using the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) [3]. Number of tissue core obtained, number of positive tissue core and presence of residual microcalcifications on post-stereotactic VABB radiograms. A clip was left to mark the biopsy site.

If no microcalcifications were found, the biopsies were considered unrepresentative and the cases were excluded from the study. (No patient was excluded for this reason in our departments).

The clinical records of the cases included were reviewed: the relevant clinical data (age, parity, menopausal status and treatment, personal or family history of breast cancer) and the radiological signs that led to the core VABB were also noted.

Each local pathologist (FA,PM) with experience in breast pathology and breast screening pathology reviewed histology reports and slides of her/his VABB biopsies and the surgical excision specimens. Pathologists were blinded to the follow-up information.

We included patients with pure FEA where FEA was the most advanced atypical lesion in the breast core biopsy. All biopsies showing any associated atypical intraductal hyperplasia (atypical ductal hyperplasia, radial scar or lobular neoplasia), DCIS or invasive breast cancer in the same breast were excluded.

Histologically, FEA was diagnosed when an intraductal alteration of mammary terminal duct lobular units was found, characterized by replacement of the native epithelium by a population of monotonous, mildly atypical cuboidal to columnar epithelial cells, one to several layers in thickness, with a flat architectural pattern with the complete absence of intraluminal proliferation with architectural atypia [6,15].

When the diagnosis of FEA was considered, at least three additional levels of sectioning of VABB were routinely performed in view of the possibility of coexisting of more advanced breast lesions [20].

Management of all VABB was routinely discussed at the weekly breast multidisciplinary meetings between radiologist, pathologist and surgeon and further treatment was determined. Patients were recommended for surgery or clinical and radiological follow-up within 12 months depending mostly on the presence or absence of residual calcifications on post-VABB radiograms and histological features (number of foci, location on biopsies with/without microcalcifications).

The vast majority of patients who underwent VABB in our institutions irrespective of subsequent surgical excision are being clinically and mammographically monitored at regular 6–12 months intervals.

The upgrade rate was defined as the total number of patients who received the diagnosis of ipsilateral breast cancer after surgical excision or in the follow-up period divided by the number of patients [21,22].

Statistical analyses were performed by R 2.13.1 (http://www.cran.r-project.org/). For numeric data, results are reported as mean and median values ± standard deviation (SD). Numeric data were analyzed with Student's t-test if normally distributed, and the Mann-Whitney test if not. Categorical data were analyzed with the chi-squared test or with Fisher's exact test.

Comparisons of the clinical, radiological and pathological from VABB according to the development or not of cancer were performed with logistic regression. Odds Ratio (OR) were reported with 95% confident intervals [95%CI]. Multivariate analysis was performed using a logistic regression model. We considered $p \leq 0.05$ to be statistically significant.

3. Results

The pathologic review of the 101 cases selected from the database of 2414 lesions sampled for calcifications with VABB during the study period confirmed FEA without DCIS or invasive carcinoma in 91 cases.

Pure FEA was diagnosed in 70 cases. We excluded biopsies with FEA associated with radial scar n = 3, with lobular neoplasia n = 6, and with atypical ductal hyperplasia n = 12. Table 1 summarize the clinical, radiologic and pathological characteristics of the patients.

Excision was performed in 20 patients (28.6%) and the remaining 50 patients (71.4%) had clinical and radiological