Is excisional biopsy warranted after a diagnosis of flat epitelial atypia (FEA) at vacuum-assisted biopsy?

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Aims and objectives

The development of mammographic screening programs has led to a considerable increase in the number of biopsies performed for subclinical mammographic abnormalities, mainly microcalcifications. As a consequence, a diagnosis of " flat epithelial atypia" (FEA) is increasingly frequent.

FEA is not a new entity. It was described in 1979 as a distinctive intraepithelial neoplastic lesion breast lesion, which was named "clinging carcinoma in situ" (1). Since then, it has received a wide variety of appellations such as "atypical ductal cells with apocrine snouts", "atypical cystic lobules" and "well-differentiated DCIS with a clinging architecture", to name a few. Given the lack of a unified nomenclature, in 2003, the World Health Organization Working Group on the Pathology and Genetics of Tumors of the Breast, introduced the term FEA (2).

As defined by the WHO, FEA is an "intraductal alteration characterized by replacement of the native epithelial cells by a single or 3-5 layers of monotonous atypical cuboidal to columnar cells with apical snouts. The ducts involved are variably distended and often contain intraluminal microcalcifications or secretory material" (1-4).

FEA is distinguished from columnar cell change and columnar cell hyperplasia by the presence of mild cytologic atypia and from atypical ducal hyperplasia and ductal carcinoma in situ by the absence of architectural atypia (1,5,6).

The management of FEA after a percutaneous biopsy is discussed, ranging from imaging follow-up to open surgical biopsy. However, the use of vacuum-assisted biopsy (VAB) systems instead of 14G automatic gun, especially for performing stereotactic biopsies in case of microcalcifications, supposes a lower frequency of histologic underestimation (7) and a lower false-negative results, with an overall improvement in lesion characterization.

The aim of this study was to determine the frequency of malignancy after surgical excision of vacuum-assisted biopsy-proven FEA, and to evaluate the outcome of lesions that were followed up instead of surgically excised.

Methods and materials

Study population

We reviewed our database of all stereotactically (n=724) and sonographically (n=521) vacuum assisted biopsy procedures performed in our hospital between January 2007 and December 2010. We included in the study 45 lesions (45 patients) biopsied under stereotactic (n=34) and sonographic (n=11) VAB guidance in which FEA was the most advanced lesion at pathologic examination.

All 45 patients underwent surgical excision (n=27) or a minimum of 2 years´ imaging follow-up (n=18).

The patient´s age, personal history of breast cancer, clinical presentation (if the lesion was palpable), mammographic breast composition, type of VAB probe, type of lesion (microcalcifications, mass, distortion, asymmetry), lesion size, BIRADS classification, percentage of lesion removal in case of calcifications, histopathology results if the patient underwent surgery or imaging follow-up if not were recorded.

FEA underestimation were defined as lesions yielding FEA at VAB and carcinoma at excisional surgery (performed immediately after VAB or during the follow-up period due to changes at site of VAB).

Imaging techniques

Bilateral mammography was performed with a dedicated FFDM unit (Senographe 2000D, GE Healthcare, Milwaukee, USA), with magnification views obtained in all cases of microcalcifications.

Ultrasonography was performed using a high -frequency linear-array 7 -12 Mhz transducer (MyLab 70XV, Esaote, Biomedica, Genoa, Italy).

Biopsy

All VAB were obtained under stereotactic guidance (Fischer stereotactic table) using the 11G Mammotome® Vacuum Biopsy System (Ethicon Endosurgery, Johnson & Johnson). Specimen radiographs were routinely obtained in case of calcifications and a clip marker

was deployed at the site of biopsy in cases of complete or almost complete removal of the lesion. Regular mammogram after each stereotactically guided biopsy was also performed (Fig.1).

VAB performed under sonographic guidance were performed using either 12G (n=4), 11G (n=4), 8G (n=2) and 9G (n=1) probes (Mammotome® system and ATEC® and Suros Surgical Systems) (Fig.2).

Images for this section:

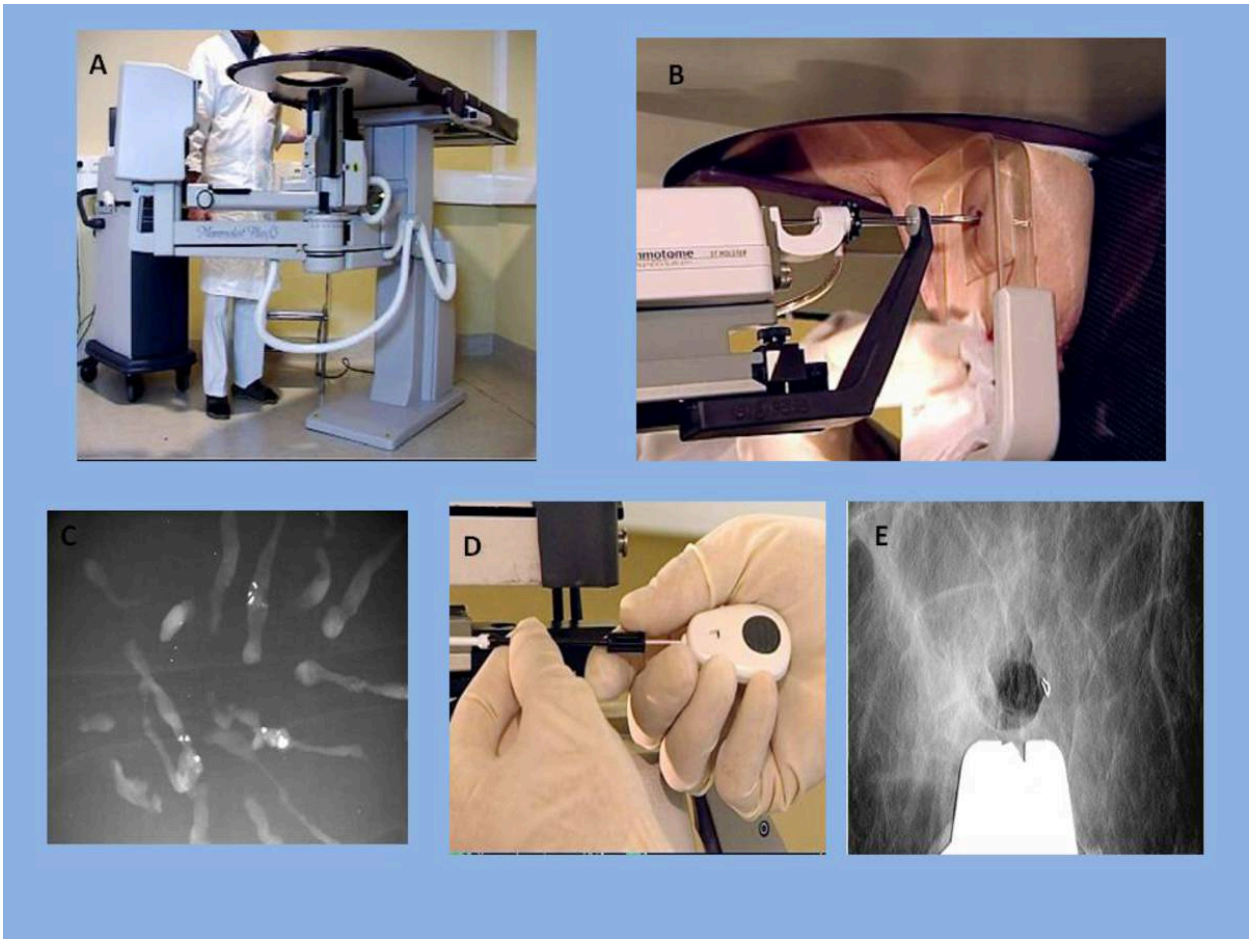

Fig. 1: Stereotactically vacuum-assisted biopsy. (A,B) Prone biopsy table. (C) Specimen radiographs showing microcalcifications. (D,E) Clip marker introduced at the site of biopsy.

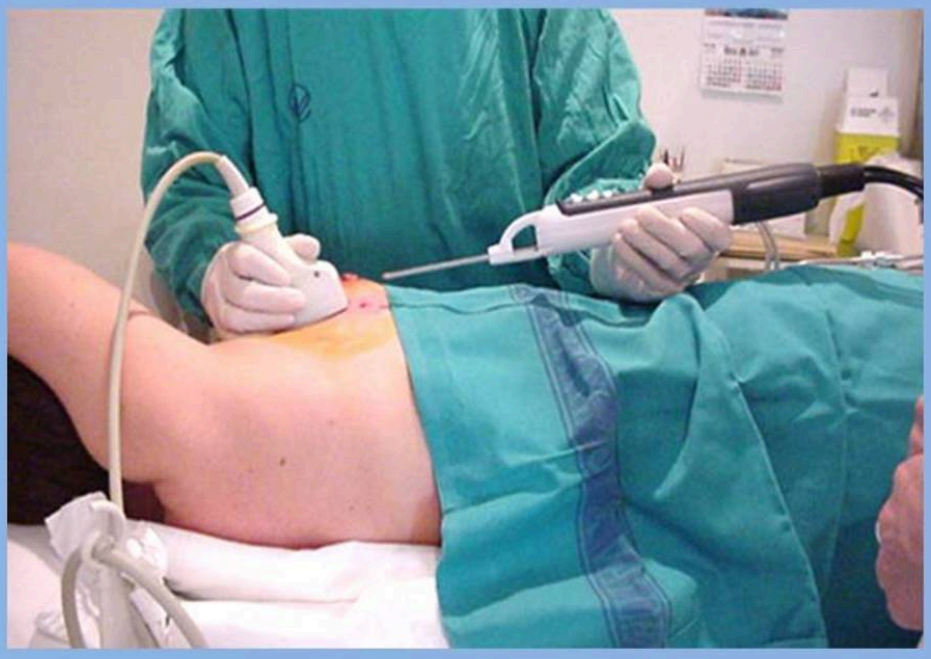

Fig. 2: VAB performed under sonographic guidance

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Results

RESULTS

Of the 1245 vacuum-assisted biopsies, 45 yielded FEA (3.6 %). Thirty-four of 45 FEA were obtained under stereotactic guidance (75 %) and 11 under sonographic guidance (25 %).

Clinical Findings

The average patient age was 49 years (range, 37-67 years). FEA was found during the staging of a synchronous cancer in the same breast in two patients. One patient had a history of previous cancer in the contralateral breast. Six patients had familial history of breast cancer. Six of the 45 lesions were palpable.

Imaging Findings

All 45 patients underwent a mammogram and 13 patients an ultrasound as well.

Mammography

Mammographic breast composition displayed a type 4 pattern (extremely dense) in two of 45 patients (4.4%), a type 3 pattern (heterogeneously dense) in 22 patients (51%), a type 2 pattern (scattered fibroglandular densities) in 18 patients (40%), and a type 1pattern (fatty) in two patients (4.4%). In one patient mammogram could not be reviewed because it was performed at another institution.

On mammography, 42 flat epithelial atypia lesions were visible, and 3 were occult. Flat epithelial atypia appeared as microcalcifications in 31 of the 45 lesions (69 %), as a mass without calcifications in 5 lesions (11%), as a mass with calcifications in one lesion (2%), as a distortion without calcifications in two lesions (4.5%), as a distortion with calcifications in one lesion (2%), as an asymmetry with calcifications in one lesion (2%) and as a asymmetry without calcifications in one lesion (2%).

Thirty of the 31 cases of microcalcifications were BIRADS 4 (6 BIRADS a, 11 BIRADS b and 12 BIRADS c), and one was catalogued as BIRADS 5. In one patient BIRADS

classification could not be assigned because mammogram was performed at another institution.

The distribution according BIRADS for the rest of 11 also lesions visible on mammography was as follows: one case of BIRADS 2 (a hialinized fibroadenoma), four BIRADS 3 and six BIRADS 4 (1 BIRADS a, 2 BIRADS b and 3 BIRADS c).

The mean lesion size of the 42 lesions seen mammographically was 1.3 cm (range, 0.3-4.0 cm).

Sonography

Sonography was performed in 13 lesions: nine masses, three distortions and one asymmetry. Among these, all lesions except three masses had a mammographic correlation. Most masses displayed and oval shape (9/13 [69%]), with circumscribed margins (7/13 [54%]) and hypoechoic echotexture (7/13 [54%]).

For the three lesions only visible on sonography, one was classified as BIRADS 3 and two as BIRADS 4a.

The mean lesion size of the 13 lesions was 1.7 cm (range, 0.8-3.5 cm).

Imaging-guided Needle Biopsy

Of the 45 lesions biopsied, 32 (71%) were visible on mammogram only (all cases of microcalcifications and one case of asymmetry with microcalcifications) and were biopsied under stereotactic guidance, eight (6 masses and two distortions: 18%) were seen on mammogram and ultrasound and biopsied under ultrasound guidance, two (one distortion and one asymmetry: 4%) were seen on mammogram and ultrasound and biopsied under stereotactic guidance and three (three masses: 7%) were seen only on ultrasound and biopsied under ultrasound guidance.

With respect to stereotactically VAB of microcalcifications, complete removal was achived in 35% (11/31). In another 16% (5/31),the percentage of microcalcifications removed was more than 75%.

Assesment After Imaging-Guided Biopsy

Surgical Excision

Twenty-six of 45 patients (58%) underwent surgical excision without a follow-up interval. Surgical pathology confirmed the diagnosis of FEA in eight cases (31%)(Fig.3). Atypical ductal hyperplasia (ADH) was found in six lesions (23%), lobular neoplasia in four lesions (15%) and five cases proved to be benign at excision (19%). Surgery revealed two cases of DCIS (8%) and one case of infiltrating ductal carcinoma (IDC) (4%)(Fig.4,5 y 6).

The three cases of carcinoma were large groups (2.7, 3.5 and 4 cm) of microcalcifications BIRADS 4c biopsied under stereotactic guidance. One patient had history of previous cancer in the contralateral breast. In all cases the percentage of microcalcifications removed was less than 75%.

Follow-up

In nineteen lesions (42%), an imaging follow-up was decided. One of them, a mass of 1.3 cm biopsied under sonographic guidance, underwent surgical excision ten months later because after a complete excision, a sonographic evaluation revealed a new 0.5 cm mass at site of biopsy. Surgery yielded FEA.

The other eighteen patients underwent a minimum 2 years´ imaging follow-up (27 -76 months), with no significant change documented.

Images for this section:

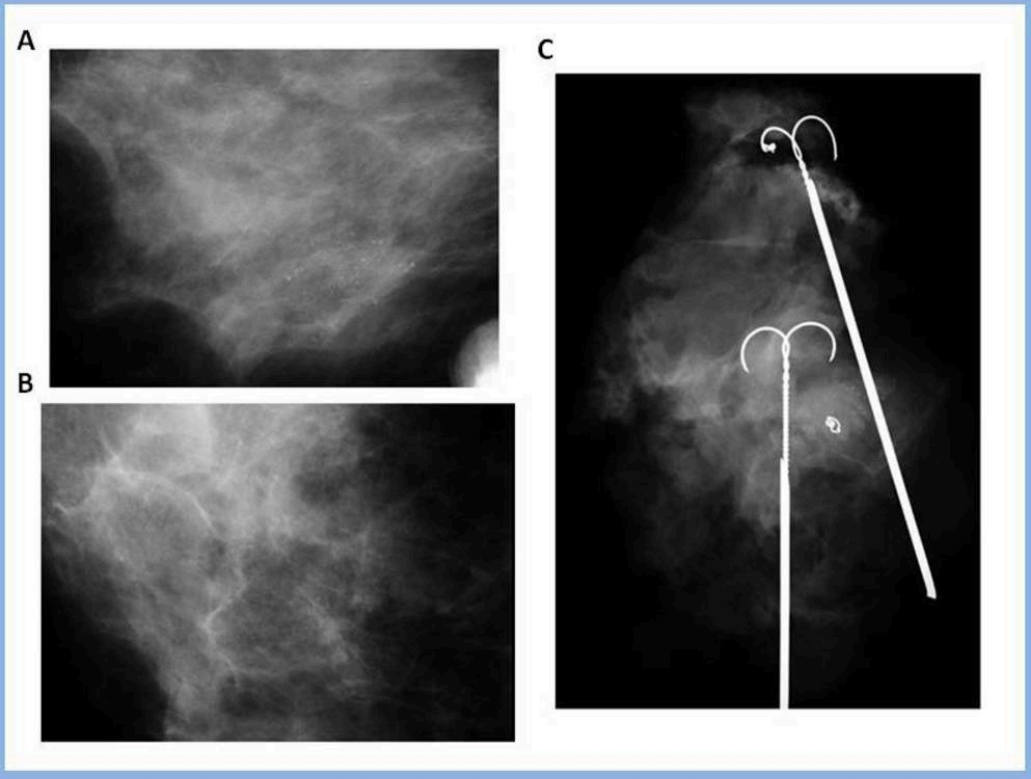

Fig. 3: 45-year-old asymptomatic woman familial history of breast cancer. (A,B) Screening mammogram detected a 1.6 cm cluster of BIRADS 4b microcalcifications. Stereotactically guided biopsy was performed with 11-gauge vacuum-assisted device and yielded flat epithelial atypia (percentage of microcalcifications removed < 75%). A clip marker was deployed at the site of biopsy. (C) Surgical excision pathology confirmed the diagnosis of flat epithelial atypia.

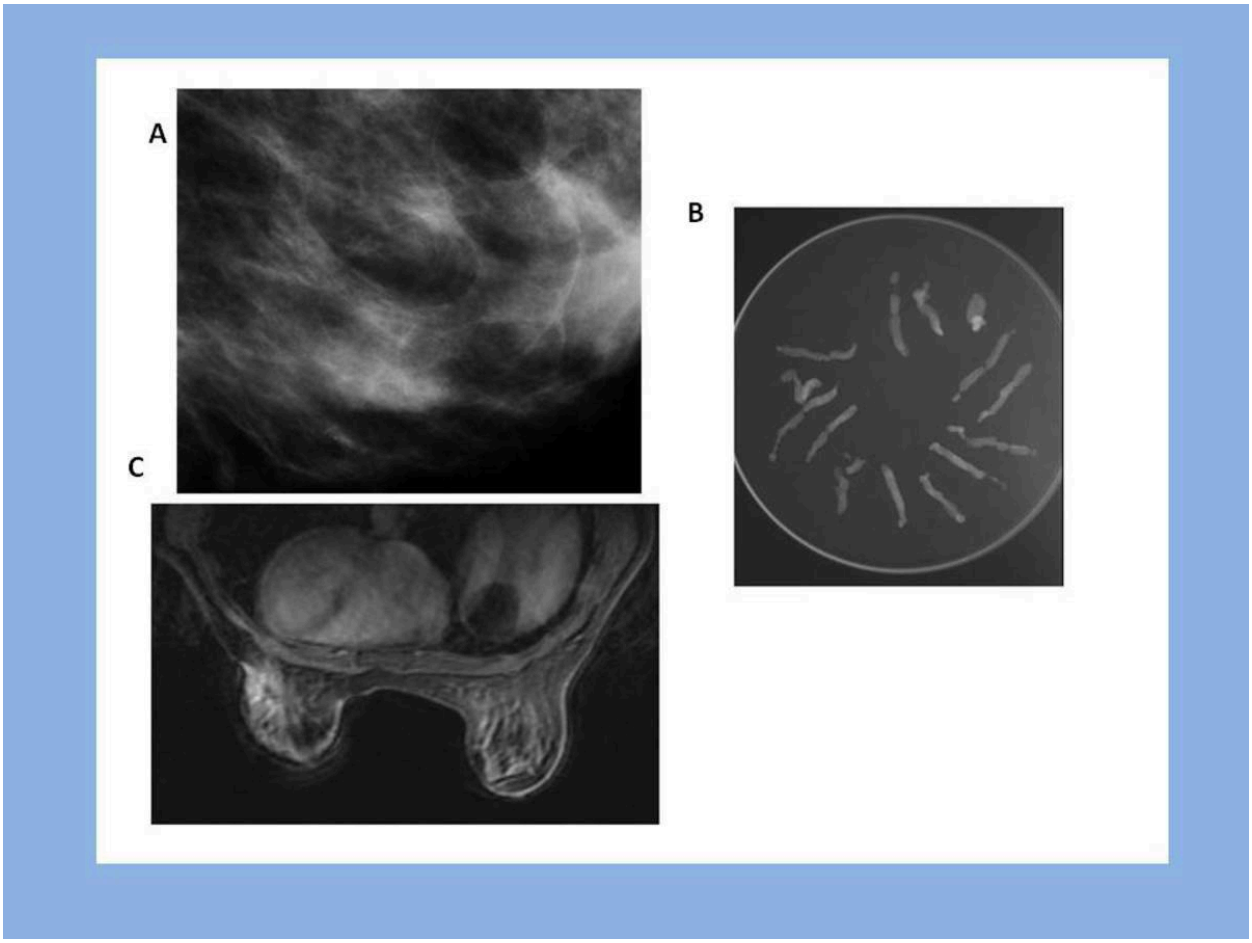

Fig. 4: 44-year-old asymptomatic woman with a history of previous cancer in the lower outer quadrant of the left breast (conserving surgery). (A) Screening mammogram detected a 4.0 cm group of BIRADS 4c microcalcifications in the same breast and quadrant. (B) Stereotactically guided biopsy was performed with 11-gauge vacuum-assisted device and yielded flat epithelial atypia (percentage of microcalcifications removed < 25%). (C) A contrast-enhanced MR was also performed and demonstrated a "non-mass" enhancement in the area of the microcalcifications. Surgical excision pathology found infiltrating ductal carcinoma.

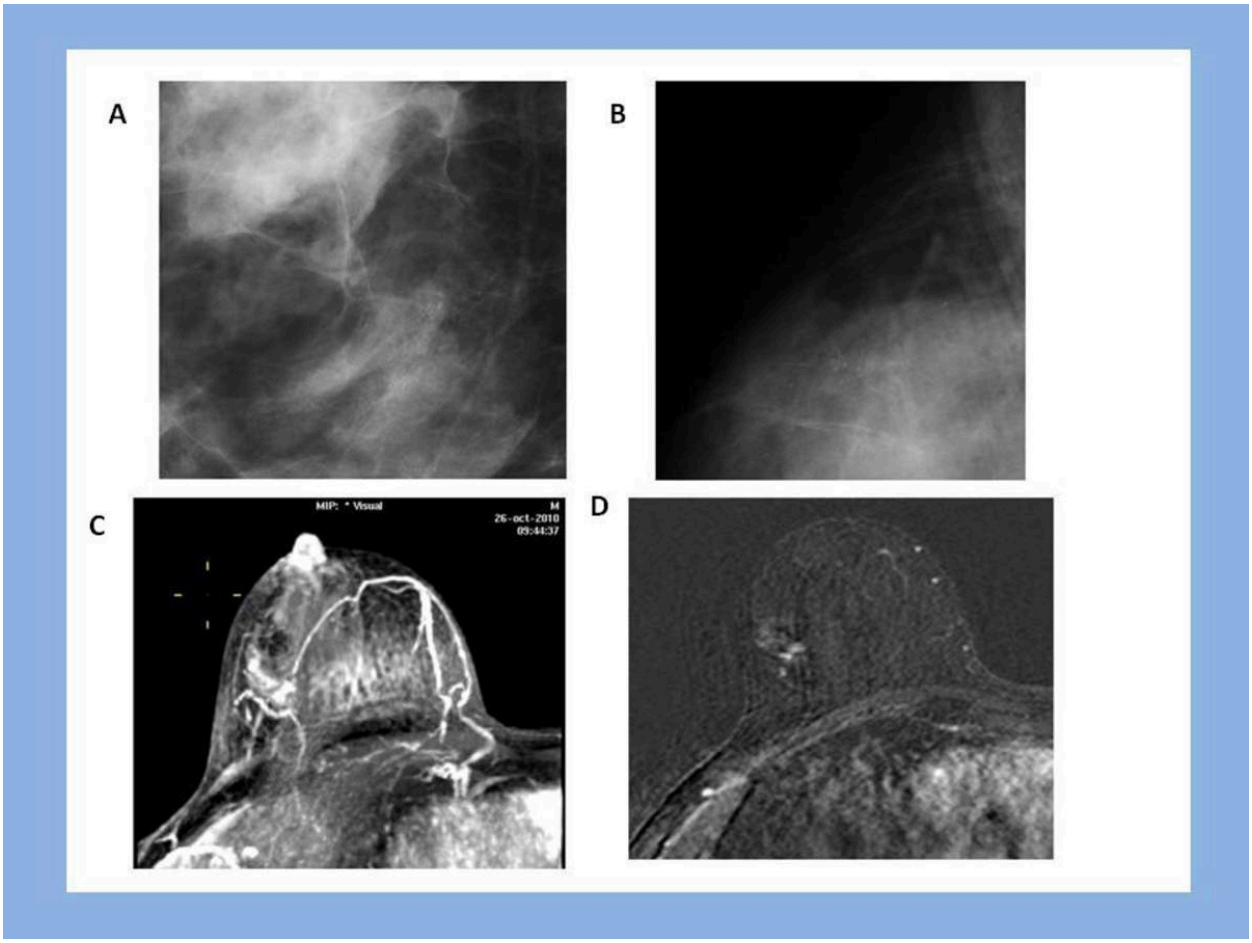

Fig. 5: 53-year-old asymptomatic woman. (A,B) Screening mammogram detected a 2.7 cm group of BIRADS 4c microcalcifications. Stereotactically guided biopsy was performed with 11-gauge vacuum-assisted device and yielded flat epithelial atypia (percentage of microcalcifications removed < 75%). (C,D) A contrast-enhanced MR was also performed and demonstrated a "non-mass" enhancement in the area of the microcalcifications. Surgical excision pathology found ductal carcinoma in situ.

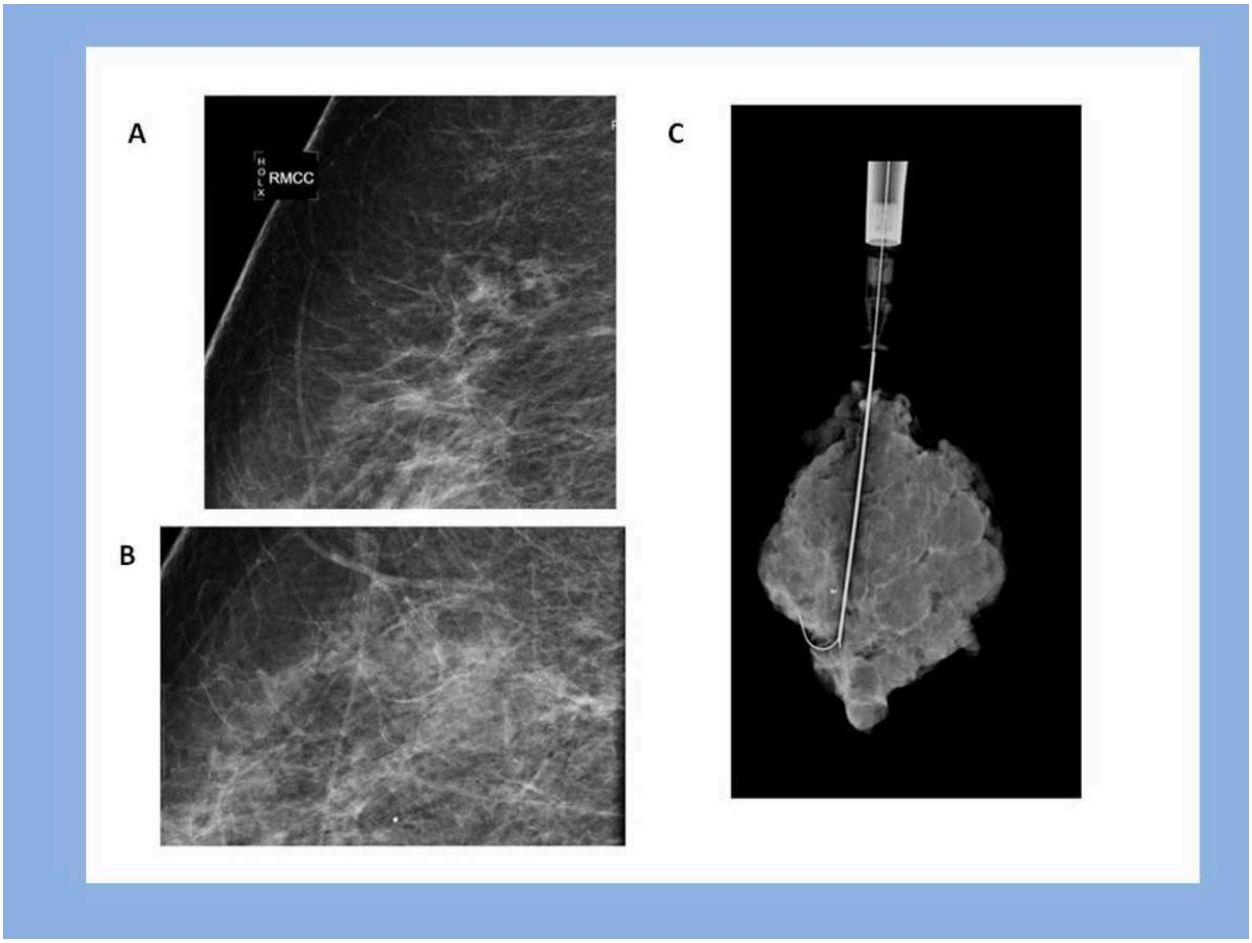

Fig. 6: 52-year-old asymptomatic woman. (A,B) Screening mammogram detected a 3.5 cm cluster of BIRADS 4c microcalcifications. Stereotactically guided biopsy was performed with 11-gauge vacuum-assisted device and yielded flat epithelial atypia (percentage of microcalcifications removed < 75%). (C) Surgical excision pathology found ductal carcinoma in situ.

Conclusion

In this study of 45 vacuum-biopsied FEA, the underestimation rate was 6.7 % (3/45).

We conclude that a diagnosis of FEA with vacuum-assisted biopsy requires surgical excision, but the size of the lesion and the percentage of microcalcifications removed may be helpful in predicting the possibility of upgrade to malignancy.

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