CASE REPORT
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Low-grade carcinoma *in situ* in fibroadenoma: a case report

Carolina Queiroz Feijó[1*], Rafael Everton Assunção Ribeiro da Costa[1], Danilo Rafael da Silva Fontinele[1], Augusto Cesar Maia Rio Lima Silveira[1], Raimundo Gerônimo da Silva Júnior[1], Ana Lúcia Nascimento Araújo[2], Sabas Carlos Vieira[2]

ABSTRACT

Fibroadenomas are the most common benign breast neoplasms. In rare cases, a carcinoma may develop within a fibroadenoma. The aim of this study was to report a case of low-grade carcinoma *in situ* in a fibroadenoma. A 31-year-old female, G0P0A0 and without family history of cancer, arrives at the service with an expressive breast lump growth along the year year. Core biopsy, histopathological and immunohistochemical studies showed an in-situ carcinoma in a fibroadenoma. Surgical resection was performed with a safety margin, and anatomopathological study and immunohistochemistry of the surgical specimen confirmed the core biopsy diagnosis. Currently, the patient is under annual clinical follow-up with mammography and breast ultrasound and no evidence of neoplastic disease. Although this is a rare event and few cases are described in the literature, carcinomas *in situ* can occur in a fibroadenoma.

KEYWORDS: breast neoplasms; breast carcinoma in situ; fibroadenoma; case reports.

INTRODUCTION

Fibroadenomas (AF) are the most common benign tumors of the breast and usually occur between the second and the third decades of life. They are mixed neoplasms with epithelial and stromal components. Breast carcinomas rarely develop within an AF. The frequency of malignancy of the epithelial component of AF is low (0.3%), usually with good prognosis. Whether the presence of an AF is a risk factor for breast cancer remains unclear. Cases of malignancy within an AF are more common in carcinomas ***in situ*** than in invasive breast cancers[1]. The conduct in these cases depends on whether the cancer is invasive or *in situ*[2].

The aim of this study is to report the case of a low-grade carcinoma *in situ* in an AF.

CASE REPORT

A female patient, 31-year-old, G0P0A0 and no family history of cancer, had noticed four years ago a lump in her left breast that had grown from 1.7 to 3.5 cm in the last year. Upon clinical examination, she had a palpable nodule in the upper lateral quadrant of the left breast measuring approximately 3.0 cm in diameter, and no lymph nodes suspected of neoplastic involvement in the ipsilateral axilla. Ultrasonography showed a solid, hypoechoic nodule, larger in the horizontal axis, with defined contours, without flow on Doppler and no calcifications (BI-RADS® 3).

Core biopsy and histopathological study were indicated due to the recent growth in the nodule, and showed atypical intraductal epithelial proliferation, apocrine metaplasia and stromal fibrosis. Immunohistochemistry showed positive cytokeratin 5/6 in myoepithelial cells, positive p64 in myoepithelial cells, negative CD34, Ki67 10%, negative protein s-100, positive vimentin in the stromal component — results consistent with carcinoma *in situ* in an AF. Resection was performed with a safety margin of 1.0 cm and reconstruction with local flap and intraoperative freezing of margins, which were negative. Histopathological examination of the surgical specimen showed a low-grade ductal carcinoma *in situ* (DCIS) developing within an AF (Figure 1). The anatomopathological examination showed atypical intraductal proliferation in AF, 3.8 cm tumor. Immunohistochemistry results: estrogen receptors (ER)+(90%), progesterone receptors (RP)+(90%), negative human epidermal growth factor (HER2) type 2 receptors (0-1), Ki-67 of 20%, positive cytokeratin in few isolated cells and absent in some ducts, and positive E-cadherin. The patient evolved well postoperatively.

[1]Universidade Estadual do Piauí, Medical Student, Health Sciences Center – Teresina (PI), Brazil.
[2]Oncocenter – Teresina (PI), Brazil.
***Corresponding author:** rafaelearcosta@gmail.com
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The possibility of a genetic panel to detect high penetrance germline mutations was discussed, but the patient chose not to perform it due to the low risk of *de novo* mutation and no history of cancer in her family. Annual clinical follow-up or adjuvant treatment with tamoxifen and radiotherapy was proposed. The patient opted for annual follow-up with mammography and breast ultrasound. Currently, the patient has no complaints and no evidence of recurrence on mammography and breast ultrasounds, being followed-up for approximately four years.

This study is part of a project conducted with cancer patients approved by the Research Ethics Committee of Universidade Estadual do Piauí (UESPI) — opinion number 4,311,835 (Certificate of Presentation of Ethical Appreciation: 30154720.0.0000.5209). The patient signed an informed consent form.

DISCUSSION

A breast carcinoma rarely develops within an AF. In the literature, there are about 250 cases described[3], being <15% invasive cancers (about 11% are invasive carcinomas of no special type (NST) and 3.4% are lobular invasive carcinomas), and the remainder intracellular carcinomas[1]. This case presented itself as a breast nodule with benign characteristics that increased in size, so a diagnostic investigation was indicated. Ultrasound and clinical examination results were compatible with an AF or a benign phyllodes tumor. After anatomopathological study by biopsy, the hypothesis of a carcinoma *in situ* was raised (unusual presentation at this age and with a palpable nodule — carcinomas *in situ* usually present initially with clustered microcalcifications or segmental distribution).

DCIS, also called intraductal carcinoma, is a neoplasm that does not invade the basement membrane. The breast carcinoma *in situ* develops within the ductal system, often in the terminal lobular duct unit[4]. It lacks the ability to spread through the body and is non-lethal. But its presence indicates a higher risk of invasive cancer if left untreated.

While AF occur more frequently in women aged 20 to 30 years old, carcinomas that develop within an AF occur mostly in women in the fourth decade of life[1,5], which is at odds with the patient reported in this case, as she was 31 years old at diagnosis.

In fact, it is not known for sure whether an AF is a risk factor for breast cancer. Dupont et al. reported a risk of developing invasive breast cancer 2.17 times higher in patients with AF and 3.10 times higher in patients with AF with complex changes[5]. However, other studies have attributed the increased incidence of breast cancer within an AF to selection bias[6]. It is known, however, that the rates of malignancy of the epithelial component of an AF are very low, between 0.002% and 0.3%.

In addition, during diagnosis, radiological findings are often non-specific for malignancy and may appear to be benign. New ultrasound techniques can show more characteristics of malignant lesions, such as shear wave elastography. This technique provides information on the elasticity of soft tissue components and can better characterize the risk of malignancy of breast nodules, especially those classified as BI-RADS® 3, avoiding unnecessary biopsies[7]. Shear waves propagate laterally, creating an elasticity map by measuring the parameters of lateral wave propagation. In the present case, elastography was not performed.

In this case, immunohistochemistry revealed epithelial malignancy, such as positive cytokeratin 5/6 and the presence of vimentin in the stromal component. Biomarkers RE/RP were positive and HER2 receptors were negative.

Therapeutic options for this type of carcinoma include conservative surgery with safety margins (at least 2 mm) or mastectomy — depending on the extent of the tumor and the relation between tumor size and breast size —, and adjuvant treatment with radiotherapy and hormone therapy in cases of RE/PR+[8], as discussed with the patient.

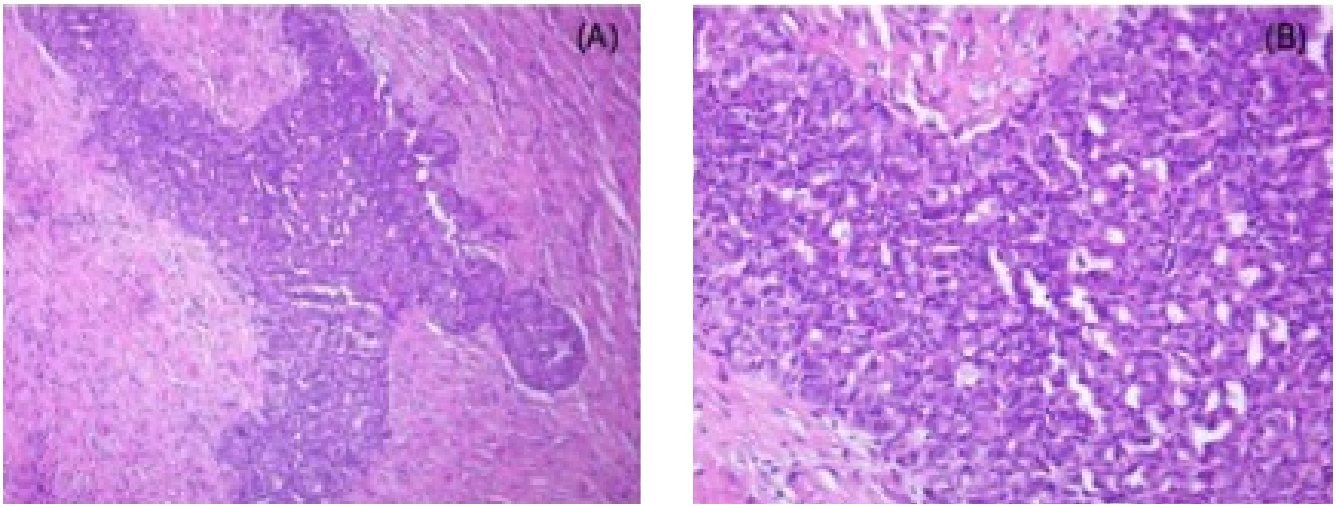


Figure 1. Low-grade carcinoma *in situ* in fibroadenoma – Hematoxylin-eosin. (A): 100x magnification. (B): 400x magnification.

CONCLUSIONS

Carcinomas *in situ* can occur in AFs, although they are a rare event and few cases are reported in the world literature.

AUTHORS' CONTRIBUTION

CQF: Conceptualization, Data curation, Formal analysis, Project administration, Writing – original draft, Writing – review & editing. REARC: Conceptualization, Data curation, Formal analysis, Project administration, Writing – original draft, Writing – review & editing. DRSF: Conceptualization, Data curation, Formal analysis, Project administration, Writing – original draft, Writing – review & editing. ACMRLS: Conceptualization, Data curation, Formal analysis, Project administration, Writing – original draft, Writing – review & editing. RGSJ: Conceptualization, Data curation, Formal analysis, Project administration, Writing – review & editing. ALNA: Conceptualization, Data curation, Formal analysis, Project administration, Writing – review & editing. SCV: Conceptualization, Data curation, Formal analysis, Project administration, Writing – review & editing.

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