CASE REPORT
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Triple negative breast cancer originating from a cystic lesion

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ABSTRACT

Malignant neoplasm diagnosed after radiological evaluation of a simple breast cyst is rare. This report described the case of a young patient with an initial simple cystic lesion, whom, in 18-month follow-up examinations, showed a change in the imaging pattern of the cyst, and underwent biopsy, where a triple negative carcinoma was identified. In addition, the diagnosis occurred during pregnancy, which makes the present report even rarer.

KEYWORDS: breast neoplasms; fibrocystic breast disease; pregnancy; triple negative breast neoplasms.

INTRODUCTION

According to the World Health Organization, 2.3 million women worldwide were diagnosed with breast cancer in the year 2020[1]. Triple negative breast cancer, which lacks the expression of hormone receptors and HER-2, accounted for 12% of breast tumors diagnosed in the United States of America between 2012 and 2016[2]. In addition to the known risk factors for the development of breast cancer, specifically in this type of neoplasm, there are other risk factors, such as age below 40 years, mutation in BRCA1/2 genes and African American ethnicity[2,3].

The diagnosis of invasive breast carcinoma is made through associated clinical and radiological characteristics and confirmation by cytopathological or histopathological biopsy[4]. Considering the classification of the American College of Radiology (BI-RADS®), simple cysts are classified, in general, as a benign finding, that is BI-RADS 2. However, they can be evaluated as suspicious or highly suspicious (BI-RADS 4 or 5) when presenting hemorrhagic content, signs of wall thickening, irregular septa, associated solid lesion, irregular vascularization, among other radiological findings related to malignancy[4-6]. Semiology is important to identify a change in the biological behavior of a simple cyst. Cystic lesions characterized as benign, but showing alterations, such as increased size and suspicious radiological characteristics, should be investigated[5,6].

The objective of this work was to document the case of a young pregnant patient with triple negative breast cancer, diagnosed in the wall of a lesion, previously characterized as a simple cyst.

CASE REPORT

Female patient, 35 years old, seeks assistance complaining of a lump in the left breast for one year. She underwent breast ultrasonography (USG) examination, in which a simple cyst was described in the union of the lateral quadrants of the left breast. This injury had already been documented in two other previous USGs, performed within an interval of six months. In the first exam, dated June 2020, the cystic lesion was characterized as anechoic, with defined limits, round shape, with dimensions of 1 cm x 0.9 cm, BI-RADS 2 (Figure 1a). In a new radiological evaluation, carried out in December 2020, the dimensions of the lesion became 1.6 cm x 1.9 cm, but it maintained the other ultrasound characteristics of the previous examination and was classified as BI-RADS 3 (Figure 1b).

In March 2021, by the same time she underwent the diagnosis of the second pregnancy, the lesion increased in size, at which time it was palpable. In a new USG, it was possible to identify a solid component close to the cyst wall, in addition to an overall enlargement of the lesion (3.5 cm x 2.1 cm) (Figure 1c). On physical examination, it was possible to characterize an oval, well-defined, fibroelastic nodule with the same measurements documented in the most recent USG report, located at the junction of the lateral quadrants of the left breast. No palpable lymph node was found in the axillary and ipsilateral supraclavicular regions. The patient was then submitted to a USG-guided core biopsy, in which fragments of the solid area were removed and fine needle aspiration of the liquid content was carried out (output of 7 ml of serohemorrhagic content). On the day of the procedure, the

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lesion already measured 5.25 cm x 3.34 cm (Figure 1d). Both the histological and cytological examination identified atypical cell proliferation. The consultation initially described took place in May 2021, when the patient was in the 19th week of pregnancy.

As it was a lesion characterized by cellular atypia and due to the patient's gestational stage, in addition to the radiological data considered, an excisional biopsy of the lesion under local anesthesia was the elected maneuver. The palpable area, including 2 to 3 mm of adjacent healthy breast tissue, was completely removed. On macroscopic examination, a lesion with a solid vegetative component on the wall projecting into the cystic area was observed, measuring together 5.5 cm x 4.2 cm x 3.0 cm (Figure 2). In the histological examination, features of grade 3 Nottingham invasive ductal carcinoma were identified, associated with necrosis (pT2), with one of the margins close to the resection line. According to the anatomopathological analysis, the neoplasm was classified as pT2, as there was invasion of the breast parenchyma in an extension between 2 and 5 cm. In an

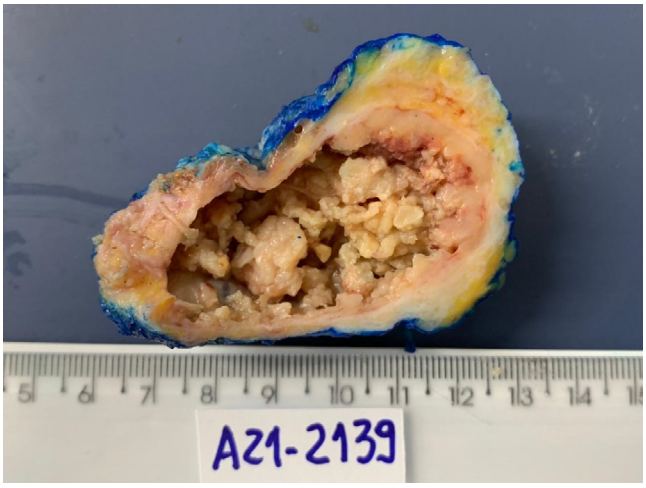

Figure 2. Macroscopic aspect of the neoplastic lesion after surgical excision (longitudinal section), where it is possible to observe an area of granularity throughout the inner wall of the cyst, forming vegetations.

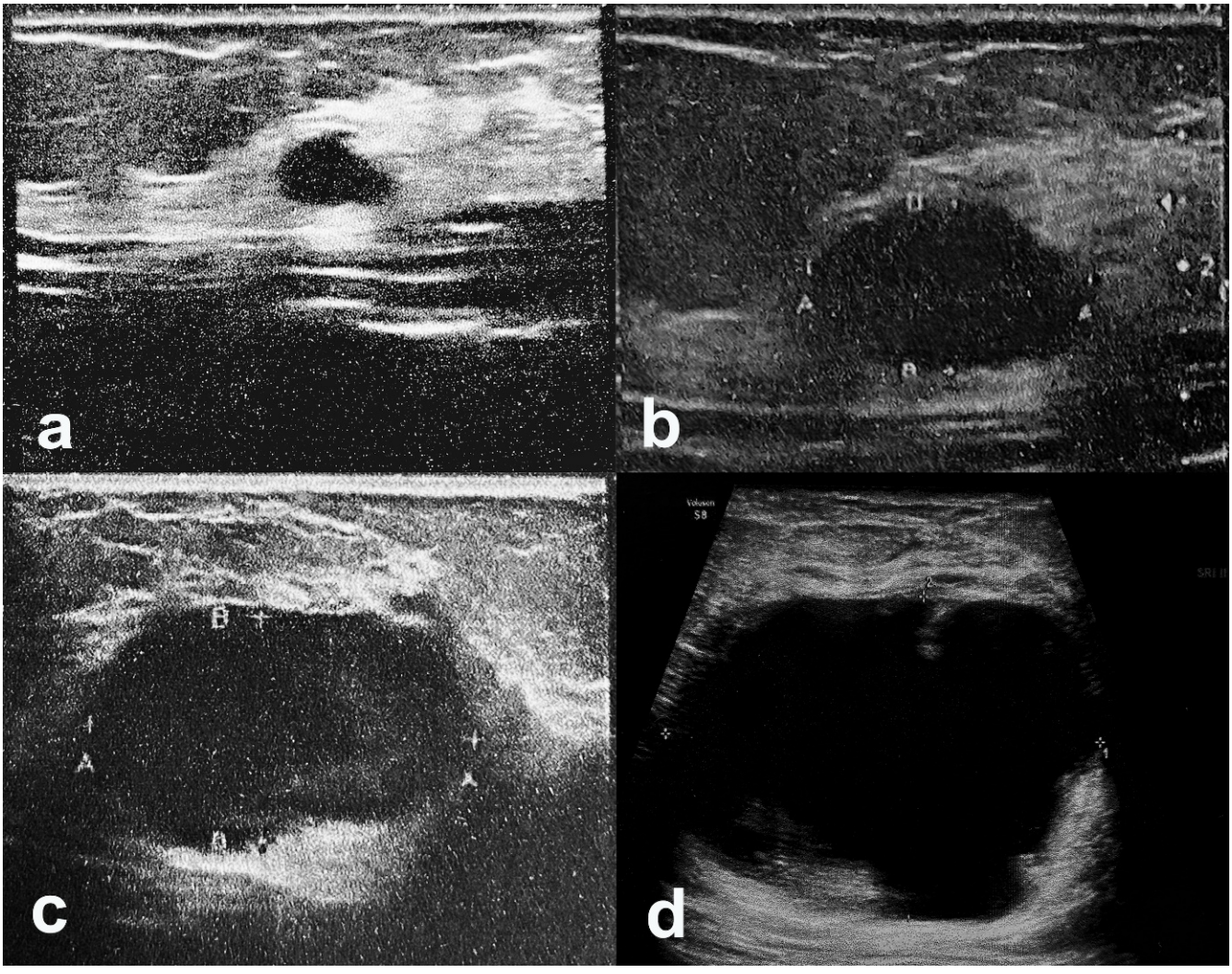

Figure 1. Ultrasound aspect of the lesion over the months of follow-up. (A) image documented in June 2020, (B) December 2020; (C) March 2021, and (D) May 2021 (time of collection of material for cytology and histology).

immunohistochemical examination, the neoplasm was characterized as a triple negative carcinoma with a Ki-67 cell proliferation index greater than 90%. Due to the patient's gestational period (21 weeks, at this stage of diagnosis), it was decided to perform adjuvant chemotherapy with 4 cycles of doxorubicin and cyclophosphamide; and 12 cycles of paclitaxel (AC-T). The patient continued the pregnancy and underwent a cesarean section at 38 weeks, without intercurrences. After 15 days, enlargement of the breast margin and biopsy of the sentinel lymph node were performed, in which no residual lesion was identified either in the breast parenchyma or in the axillary lymph node. At the moment, the patient is in clinical follow-up, and adjuvant radiotherapy was completed 11 months after the initial diagnosis (dose of 2/46 Gy on the breast, as well as lymphatic drainage, associated with 2/10 Gy on the surgical site of the breast, totaling a dose of 56 Gy). Although the patient did not have a family history of breast cancer, but because the triple negative subtype was diagnosed, a genetic test was performed with a panel of genes related to the hereditary disease. However, no germline pathogenic or probably pathogenic variants were identified.

DISCUSSION

The clinical manifestation of breast cancer that develops in the wall of a cyst has already been documented in reports such as that by Mehta et al., but it is usually a papillary carcinoma[6]. In the case described, the histological morphology of a papillary carcinoma was not characterized, although the macroscopic findings were similar to this subtype of breast cancer.

The identification of an oval nodule with a well-defined contour on a mammogram may correspond to malignancy in 10% to 20% of cases. The rapid growth capacity of a neoplasm may result in a rounded shape and considerably precise limits in imaging exams and clinical perception. When invasive carcinomas are diagnosed in lesions with these characteristics, they often represent poorly differentiated neoplasms (grade III) and are associated with triple negative subtypes or subtypes that overexpress the HER2 receptor. Grade I neoplasms, generally related to the luminal immunohistochemical subtype, have a slow biological behavior, which would allow the formation of a more irregular tumor lesion, including spicules[4,7,8].

The case report described constitutes a diagnostic and therapeutic challenge. Triple negative breast cancer has a greater biological capacity for dissemination compared to other types of breast cancer, in addition to presenting a lower response to systemic therapies due to the absence of target receptors[9]. The diagnosis of invasive carcinoma was based on the investigation of a possible previously documented simple cyst that presented clinical and radiological changes during the follow-up period, which became more pronounced during the patient's gestational period.

Simple cystic lesions or those with thick content and without additional findings are, in most cases, classified at USG as BI-RADS 2 and 3, respectively. When classified as BI-RADS 3, it is important that the attending physician reinforces the importance of performing a new exam in six months. In these cases, performing a cytological or histological biopsy will be indicated if there is a change in the previously described ultrasonographic findings, which include wall thickening, appearance of septa, solid area, among other characteristics related to the suspicion of malignancy[7,8]. The diagnosis of malignant neoplasm in complex cystic lesions ranges from 23% to 31%[8].

Just as the diagnosis of breast cancer in cystic lesions is a rare event, when this combination occurs in pregnant patients, it becomes a clinical situation documented only in case reports/series[10,11]. In addition, due to the physiological and morphological changes of the breast during the gestational period, the diagnosis of breast diseases, both radiological and pathological, is challenging[12].

Breast cancer diagnosed during pregnancy or within one year after delivery is characterized by an unfavorable scenario, that is, with a greater chance of increased tumor extension and low expression of hormone receptors. In these cases, as in the case reported, the therapeutic options must be adequate to maintain the health of both mother and fetus. Chemotherapy is contraindicated during the first trimester of pregnancy, while radiotherapy should not be performed, regardless of the stage of pregnancy[13]. In the case described, complete staging was subsequently established, based on a sentinel lymph node study, which was negative (considering clinical and radiological findings before chemotherapy and the anatomopathological description), defining stage IIA, according to NCCN[14], and the complementary treatment with radiotherapy was started three months after the cesarean section.

The diagnosis of a triple negative breast cancer in a young patient in which the clinical and radiological manifestation occurred in an unusual way requires the investigation of the presence of germline mutation of genes such as BRCA1 and BRCA2, ATM, CHEK2, PALB2, TP53, among others[15]; however, there was no identification of pathogenic variants described in the genetic panel performed in the patient. This does not completely rule out the presence of germline mutation, as new variants are constantly being described, reinforcing the importance of the patient maintaining clinical follow-up with a geneticist.

Considering the immunohistochemical subtype and disease stage, the patient would benefit from neoadjuvant chemotherapy[13,14]. However, the present report presented peculiar conditions, justifying the conduct employed, due to the radiological change of the initial well-delimited simple cystic lesion, during the gestational period, which turned out to be a triple negative breast cancer.

CONCLUSIONS

The clinical and/or radiological manifestation of breast cancer is most often associated with a solid lesion. However, in rare cases, it may evolve in a lesion characterized as cystic. The data from the reported case reinforce the importance of monitoring breast lesions that show changes in dimensions and radiological characteristics, regardless of whether they were previously classified as benign or probably benign.

AUTHORS' CONTRIBUTION

MM: Conceptualization, Formal Analysis, Methodology, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. MLMF: Data curation, Visualization, Writing – original draft, Writing – review & editing. JBA: Data curation, Visualization, Writing – original draft, Writing – review & editing.

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