Radiology Case Reports 16 (2021) 3104–3108

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journal homepage: www.elsevier.com/locate/radcr

Case Report

Breast imaging screening in a BRCA1-mutated lactating patient: A potential pitfall mimicking malignancy ☆,☆☆,★

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ARTICLE INFO

Article history:
Received 31 May 2021
Accepted 10 July 2021

Keywords:
Background parenchymal enhancement
Breast cancer
Breastfeeding
Magnetic resonance imaging
Ultrasound

ABSTRACT

Breast imaging screening during lactation poses a real clinical challenge, especially in high-risk patients. We presented the case of a 34-year-old BRCA1-mutated woman showing marked, asymmetric background parenchymal enhancement on the right breast suspicious for malignancy in the context of annual screening magnetic resonance imaging. The patient revealed that she was still occasionally breastfeeding her two-year-old child only from right side. Ultrasound evaluation reported typical benign lactational findings on the right enhancing breast. An in-depth understanding of expected/ physiologic breast changes during lactation and an accurate clinical-radiological correlation are required to appropriately guide patient management and avoid misdiagnosis.

Introduction

Histological and imaging changes of the breasts during pregnancy and lactation are not well-understood and still represent a diagnostic challenge for radiologists worldwide. The peculiar physiologic breast modifications secondary to the hormonal changes of pregnancy and lactation result in increased breast volume with associated palpable nodularity, firmness, and parenchymal hyperdensity [1]. These changes may affect clinical and radiologic evaluations of the breasts and potentially lead to diagnostic errors. In particular, atypical background parenchymal enhancement (BPE) can be easily misdiagnosed at first glance, especially in case of high-risk screening imaging (e.g., BRCA-mutated patients).

The purpose of this report is to underline the importance of an accurate radiological-clinical correlation when interpret-

☆ Acknowledgements: The authors have not received any grants.
☆☆ Competing Interest: None.
★ Patient Consent: Written informed consent for publication was obtained from the patient. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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https://doi.org/10.1016/j.radcr.2021.07.019

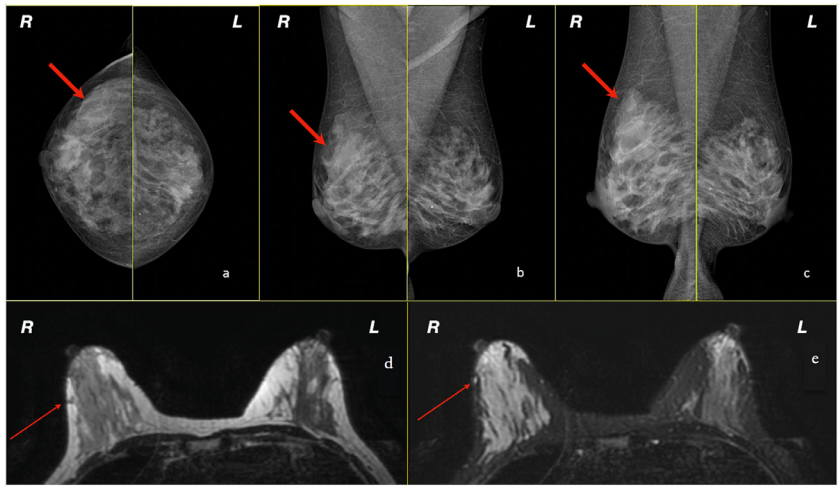

Fig. 1 – Mammography in all 3 projections (A. craniocaudal; B. mediolateral oblique; C. laterolateral) showing mild, diffuse, asymmetric increased density of the right breast. Axial T1 weighted (D) and axial T2 weighted (E) fat-suppressed images showing asymmetric increased density of the right breast compared to the left and showing high free water content.

ing breast imaging features of lactating patients, especially in case of high-risk factors (e.g., BRCA mutations).

Case presentation

A 34-year-old woman with a mutation in BRCA1 gene was admitted to our Breast Imaging Department for annual screening mammography. The patient skipped her scheduled checkups in the last two years after she had given birth. Her past medical history was otherwise unremarkable. No signs and symptoms were reported.

Mammography was performed in three standard projections and revealed a mild, diffuse increased density of the right breast compared to the left, without architectural distortions or microcalcifications (Fig. 1 **A-C**). Breast MRI (magnetic resonance imaging) examination was then performed in the prone position using a dedicated breast coil with a 3T system. Axial fat-saturated T2-weighted, axial T2-weighted, DWI (diffusion-weighted imaging) sequences were obtained. The initial examination proved a diffuse increased density and a high free water content of the right breast (Fig. 1 **D-E**), without diffusion restriction in DWI and ADC (apparent diffusion coefficient) mapping (Fig. 2). Dynamic contrast-enhanced images were obtained using axial and sagittal fat-saturated T1-weighted sequences once before and five times after the administration of contrast material at 40-second intervals and evaluated on standard subtraction images. The dynamic study demonstrated an early, marked and diffuse contrast-enhancement of the right breast (Fig. 3). For analysis of enhancement kinetics, time-intensity curves were plotted based on the signal intensity values in a region of interest (ROI) in the central region of the right breast on serial dynamic images (Fig. 4) and a type 2 curve ("plateau pattern") was obtained. Given mammographic and MRI findings, the patient was also evaluated with US (ultrasound) examination. US images revealed diffuse enlargement of the right glandular component with diffuse hyperechogenicity and unilateral prominent ductal system as per lactating breast, whereas no significant findings were observed in the left breast (Fig. 5).

Upon further medical investigation, the patient revealed that she had been occasionally breastfeeding her two-year-old child only from right breast for the past two years; therefore, radiological images were interpreted as benign physiological changes of lactational breast.

Discussion

We presented an illustrative case of lactational breast radiological changes mimicking malignancy in a BRCA-1 mutated patient during annual imaging screening. A thorough understanding of both the anatomy and physiology of the normal lactating breast is necessary to properly recognize any potential abnormality while avoiding misdiagnosis.

Hormonal changes during pregnancy and lactation are primarily responsible for the major physiologic breast structural changes. During pregnancy, estrogen and progesterone act synergistically to stimulate glandular proliferation and differentiation, ductal distension and stromal involution, while inhibiting prolactin and milk production. As estrogen and progesterone levels drop off after delivery, the lactogenic effect of prolactin becomes un-opposed and results in increased milk production. Generally, there is a bilateral increased size and density and the mammary vascular flow doubles in volume. Involution occurs three months after the suspension of breastfeeding [1].

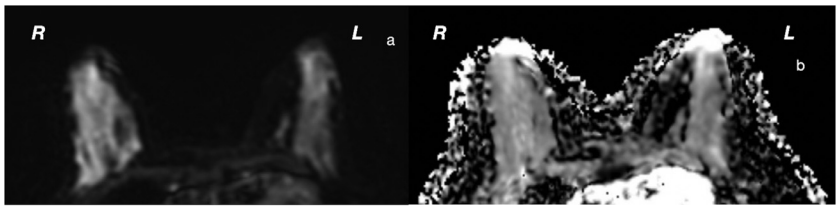

Fig. 2 – Axial DWI weighted images (A) and ADC map (B) showing no restriction of diffusion bilaterally and in particular on the right breast.

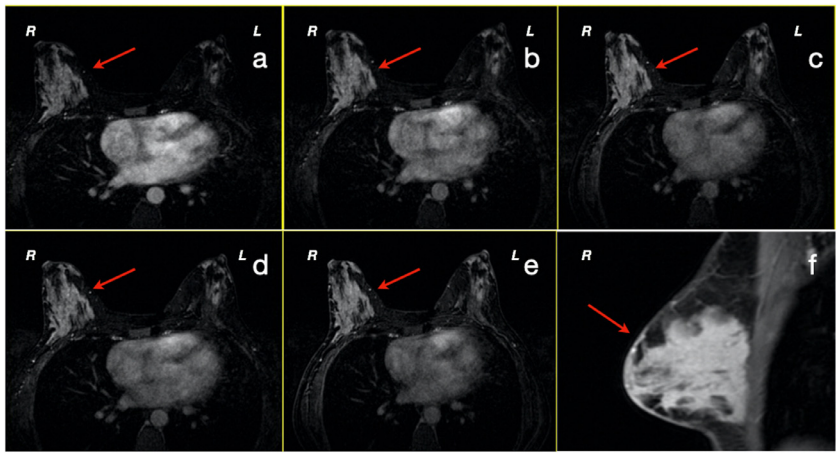

Fig. 3 – Marked, asymmetric BPE at screening MRI imaging. (A-E) Serial dynamic axial contrast-enhanced T1-weighted fat-suppressed images; (F) Sagittal contrast-enhanced T1-weighted fat-suppressed image of the right breast showing unilateral, diffuse rapid contrast enhancement.

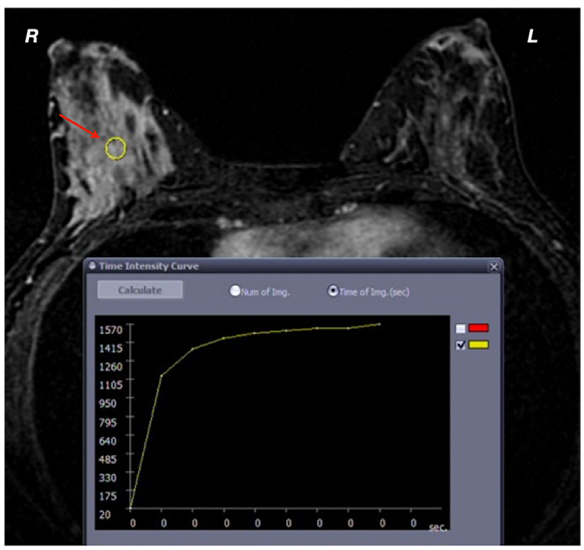

Fig. 4 – The curve of enhancement "plateau-shaped" (type 2) obtained by kinetics analysis on a ROI put in the retroareolar deep region of the right breast.

Breast imaging findings during lactation reflect these physiologic changes and could mimic breast malignancies, making radiological evaluations quite challenging. As in our case, breast MRI findings in lactating patients include the following: (a) increased breast size and density; (b) incremented and rapid BPE due to increased vascularity; (c) diffusely increased T2 signal secondary to the water content of breast milk. On ultrasound examination, most breast parenchyma appears hyperechoic and hypervascularized as a result of combined glandular enlargement and milk engorgement [2,3].

Breast cancer occurring during gestation, lactation or within 1 year from delivery is called pregnancy-associated breast cancer (PABC); it accounts for 1%-2 % of all newly diagnosed breast cancers each year. PABC is generally biologically aggressive, being estrogen and progesterone receptor negative and Her2-neu receptor positive. It is common to overlook, underestimate or misdiagnose PABC because of the difficulties in the clinical evaluation and imaging interpretation of breast disorders in this period, so it has a poor prognosis and is often advanced at diagnosis [3].

MRI assessment of PABC during lactation is controversial and limited by a high number of false positives. Lactating parenchyma shows rapid and marked gadolinium uptake similar to that seen in malignancies, attributed to increased vascularity and vascular permeability [4]. BP is the normal contrast enhancement of fibroglandular breast tissue. The level of global BPE is assessed in four BI-RADS categories: minimal (<25% of glandular tissue enhanced), mild (25%-50% of glandular tissue enhanced), moderate (50%-75% of glandular tissue enhanced) and marked (>75% of glandular tissue

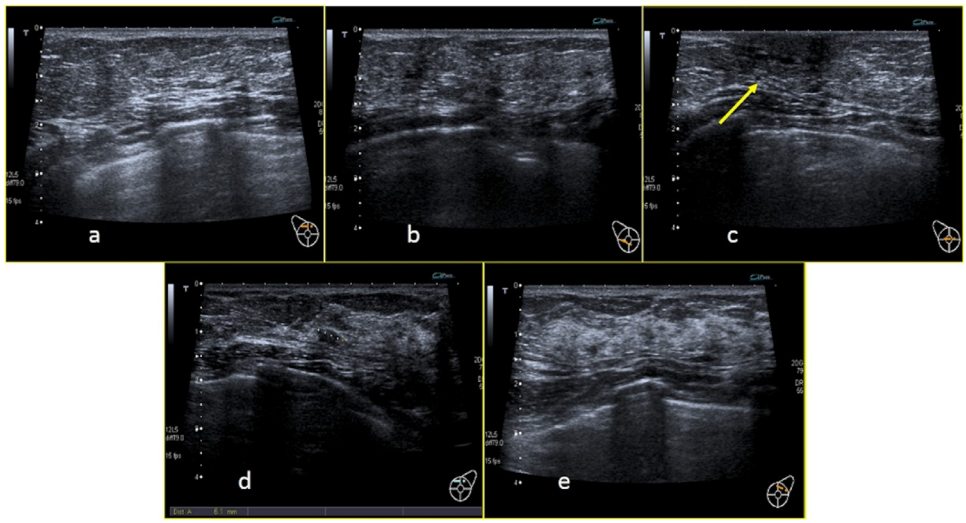

Fig. 5 – (A-C) US images of the right breast showing diffuse hyperechogenicity of parenchyma related to the production of milk, which is rich in fat; (C) retroareolar region US image showing a mild prominent ductal system (arrow) due to milk secretion; (D-E) US images of the left breast proving the normal echogenicity of a fibroglandular breast, without pathologic appearances (in the upper internal quadrant there is a benign lesion of 6 mm in size).

enhanced) [4]. It is generally mild, bilateral, symmetric, with diffuse distribution; however, it may be marked, unilateral, asymmetric and these atypical patterns of BPE cause diagnostic difficulties because these morphology and temporal degree can be seen with non-mass enhancement (NME) malignancies [5]. Just as high density decreases the sensitivity of mammography, so moderate to marked BPE can affect the accuracy of MRI interpretation [6]. However, Oh et al. [4] suggested confounders such as increased BPE and T2 signal: in these patients, if cancer does not appear as a lump – i.e., low-signal-intensity mass on T2 weighted images – it can be difficult to recognize a malignancy. As reported by Sabate et al. [6], US is an appropriate radiologic tool for evaluating breast disorders in pregnancy and lactation because the sonographic semiology of breast does not change significantly in these women [7-10]. In particular, US has a great sensitivity (nearly 100%) in detection and characterization of palpable breast masses in pregnant and lactating women [9].

In our case, breast imaging screening was even more demanding since the lactating patient was also BRCA1-mutated. The current breast cancer screening guidelines of the American College of Radiology (ACR) states that an annual screening MRI is appropriate and effective for patients at high risk for breast cancer including BRCA mutation carriers at the age of 25 years, in addition to an annual mammogram at the age of 30 years; many of these young women are pregnant or breastfeeding during the time of screening [8,10].

ACR guidelines recommend that contrast-enhanced MRI can be safely performed in lactating women and it is safe for the mother to continue breastfeeding after receiving gadolinium [3,7,10].

In conclusion, while joining the scant evidences on lactational breast radiological changes, we argue that an understanding of expected physiologic breast changes during lactation and a careful radiological-clinical correlation are required to successfully guide patient management and avoid misdiagnosis.

Ethical statement

Written informed consent was obtained from the patient. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2021.07.019.

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