

Pregnancy Associated Breast Cancer with Preferential Lactation to the Affected Breast

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Abstract

Pregnancy associated breast cancer (PABC) is a challenging clinical and radiological diagnosis given the unique characteristics of the breast in this patient population. The prompt breast imaging work-up and possible biopsy of any palpable abnormality in pregnant and lactating patients is critical in reducing a delay in the diagnosis of breast cancer. Radiologists need to be familiarized with the sonographic, mammographic and magnetic resonance imaging (MRI) features of PABC. Understanding the differential diagnosis of the most common etiologies of palpable lesions in pregnant and lactating women is crucial in making an accurate assessment. This article presents the case of a lactating women who was initially treated for mastitis and months later diagnosed with breast cancer. She was preferentially breastfeeding from the affected breast, contrary to what some authors have proposed as the “milk rejection sign”, a possible early indication of breast cancer.

Keywords: Pregnancy Associated Breast Cancer; Breastfeeding; Breast Cancer; Lactation

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Introduction

Pregnancy-associated breast cancer (PABC) is defined as breast cancer diagnosed during pregnancy, throughout the first postpartum year or at any time while the patient is lactating [1]. Pregnancy-associated breast cancer is estimated to occur in 1 in 3,000 to 1 in 10,000 of all pregnancies and lactating women [2], and it represents 3% of all breast cancer diagnosis [3]. The median age of PABC is between 30 and 38 years of age [2]. The incidence of PABC is expected to increase as more women are delaying childbearing until their 30s or 40s. These cancers are associated with an advanced stage, exhibiting larger tumors and a higher likelihood of axillary nodal disease likely secondary to a delay in diagnosis [4]. Pregnant and lactating women with suspicious clinical and breast imaging findings should promptly be evaluated in order to avoid a delay in the diagnosis of PABC. We present the case of a lactating woman with preferential breastfeeding from the affected breast who initially was treated for mastitis and was later diagnosed with breast cancer.

Case Presentation

A 35-year-old female presented to the breast clinic in January 2021 reporting a palpable left breast mass, at that time she was 15 months post-partum and breastfeeding preferentially from the left breast. The patient reported a past medical history of mastitis in October 2020 that was treated with antibiotics, but was later referred by her gynecologist to the breast imaging service for work up of the left breast palpable mass. Bilateral diagnostic mammogram revealed an irregular, high

density palpable mass with spiculated margins in the upper outer quadrant of the left breast and morphologically abnormal left axillary adenopathy with diffuse cortical thickening and compressed fatty hilum (Figure 1). Breast ultrasound showed an irregular hypoechoic solid palpable mass with angulated margins, central cystic component, peripheral vascularity and posterior acoustic shadowing in the left breast 2:00 axis 4 cm from the nipple (Figure 2). Sonographic evaluation

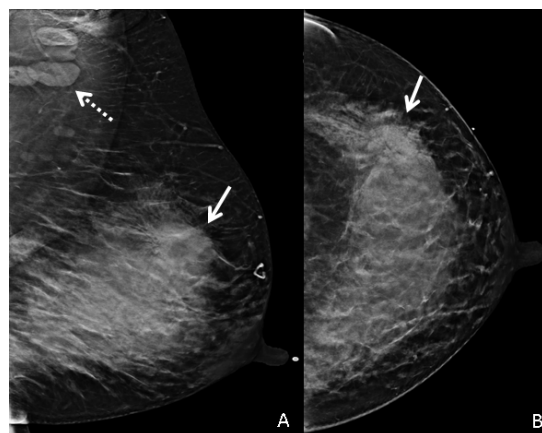


Figure 1: Mammogram left MLO (A) and CC (B) demonstrates an irregular high density palpable (triangle) mass with spiculated margins in the upper outer quadrant (solid arrows) subsequently biopsied and consistent with invasive ductal carcinoma. Left MLO (A) also shows morphologically abnormal axillary adenopathy with diffuse cortical thickening and compressed fatty hilum (dotted arrow). CC, craniocaudal; MLO, mediolateral oblique.

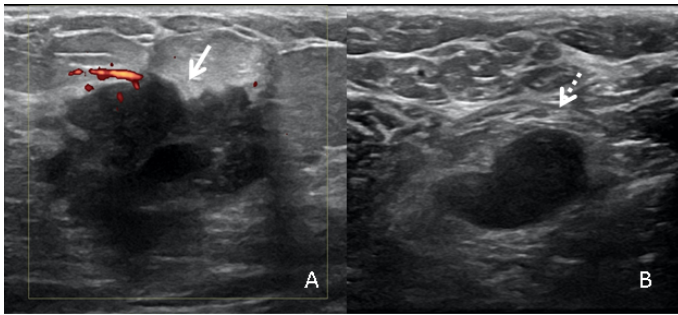


Figure 2: (A) Ultrasound power Doppler image shows an irregular hypoechoic solid palpable mass with angulated margins, central cystic component, peripheral vascularity and posterior acoustic shadowing in the left breast 2:00 axis 4 cm from the nipple (solid arrow). (B) Grey scale ultrasound image demonstrates a morphologically abnormal left axillary lymph node with diffuse cortical thickening and absence of the fatty hilum (dotted arrow).

confirmed morphologically abnormal left axillary lymph nodes (Figure 2). Ultrasound-guided core biopsies of the left breast 2:00 axis mass and left axillary lymph nodes were performed, yielding invasive ductal carcinoma, poorly differentiated, Nottingham grade 3, ER/PR >50% strong, HER-2 negative (1+) and metastatic carcinoma involving one lymph node, ER/PR positive >50% strong HER-2 negative (1+). Breast MRI demonstrated an irregular homogeneously enhancing mass with central cystic component and biopsy tract extending to the lateral skin and at least nine abnormal level I and II axillary lymph nodes (Figure 3). Breast MRI also showed asymmetric increased breast parenchyma in the left breast consistent with preferential breastfeeding from her affected breast. PET/CT showed a hypermetabolic mass in the upper outer quadrant of the left breast with SUV 9.2 and several enlarged FDG avid left axillary lymph nodes (Figure 4). The clinical stage of the

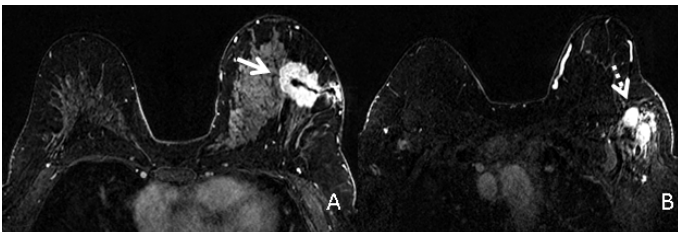


Figure 3: (A) Axial T1 postcontrast image at the level of the breast shows an irregular homogeneously enhancing mass with central cystic component and biopsy tract extending to the lateral skin. Also, note the asymmetric increased breast parenchyma in the left breast consistent with preferential left breastfeeding. (B) Axial T1 postcontrast image at the level of the axilla shows several abnormal levels I and II axillary lymph nodes with diffuse enhancement, cortical thickening and compressed fatty hilum (dotted arrow).

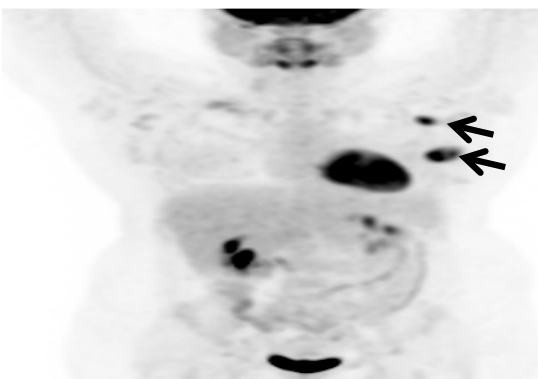


Figure 4: (A) Coronal PET MIP image shows a hypermetabolic mass in the upper outer quadrant of the left breast with SUV 9.2 (solid arrow), and several enlarged FDG avid left axillary lymph nodes (dotted arrow).

tumor was cT2 (3.6 cm) N2a (9 abnormal ALN by MRI) M0 left breast cancer ER/PR+>50%, HER2 negative (1+).

Outcome and Follow-up

The patient is currently undergoing neo-adjuvant chemotherapy prior to surgery which allows for in-vivo assessment of tumor response and potential down staging of the tumor rendering it more susceptible to complete surgical resection and potentially less extensive surgery. Upon completion of treatment and surgery, the patient will require adjuvant endocrine therapy given that the tumor is estrogen receptor positive, and she will require adjuvant radiation due to the locally advanced nature of her tumor.

Discussion

Even though the most common clinical and radiological presentation of PABC is a mass [3], more than 80% of the palpable masses biopsied in pregnant and lactating women are benign [5]. Other clinical manifestations of PABC include nipple discharge, focal pain, diffuse breast enlargement with skin thickening and/or infant refusing milk from the affected breast. Saber A, et al. (1996) [6], and Hadary A, et al. (1995) [7], have reported cases of infants refusing to breastfeed from the affected breast and have postulated that the recognition of the “milk rejection sign” can enable an early diagnosis of breast cancer [6,7]. However, this sign has not been accepted as such by the medical profession. In our case, the infant was preferentially breastfeeding from the affected breast.

Differential Diagnosis

The differential diagnosis of a palpable breast mass in a pregnant and lactating patient includes PABC, galactocele, abscess, lactating adenoma, fibroadenoma and phylloides tumor.

A galactocele is the most common breast mass in lactating patients and is defined as a retention cyst secondary to lactiferous duct occlusion during or after lactation [3]. Galactoceles can present clinically as a painless palpable mass in pregnant, lactating or early post-lactation patient. Sonographic features of galactoceles include a circumscribed round or oval mass with variable internal echogenicity [8]. Vascularity, if present, is peripheral in distribution and not inside the galactocele. Mammography is only necessary in cases with suspicious sonographic findings: the diagnosis of a galactocele is confirmed by a circumscribed fat containing mass with possible fat fluid levels. The majority of galactoceles resolve spontaneously after weeks or months. Ultrasound-guided fine needle aspiration is indicated for infected galactoceles and sonographic-guided core biopsy is advised in cases of atypical or suspicious imaging features.

It is estimated that approximately 4.8-11% of lactation-related mastitis can evolve into abscess, especially if treatment is delayed or inadequate [9]. The most common infectious agents include *Staphylococcus aureus* and *Streptococcus*. Signs and symptoms of breast abscess include a fluctuant mass in the affected breast, fever, breast tenderness, erythema, swelling and possible enlargement of axillary lymph nodes. Ultrasound is the breast imaging modality of choice for the diagnosis, treatment (ultrasound-guided needle aspiration) and follow up of a breast abscess. Sonographic features of breast abscess include a hypoechoic mass with heterogenous echotexture and posterior acoustic enhancement or a complex cystic and solid mass with thick wall and septations. Vascularity, if present, is peripheral in distribution and not inside the mass. The treatment of breast abscess includes ultrasound-guided fine needle aspiration and



antibiotic therapy. Clinical and sonographic follow up are indicated to ensure abscess resolution [10]. Mammography is only considered in atypical or refractory cases. Ultrasound-guided core biopsy is needed in the presence of suspicious findings.

Lactating adenomas are benign breast tumors in pregnant, lactating and postpartum woman [5]. They are often indistinguishable from fibroadenomas, presenting clinically as a soft, palpable and mobile mass. Lactating adenomas can outgrow their blood supply during pregnancy and undergo infarction which can manifest clinically as a firm, tender mass. Sonographically, they can appear as an oval, circumscribed homogenous hypoechoic to isoechoic mass with posterior acoustic enhancement. Although mammography is not usually indicated unless suspicious clinical or imaging findings are identified, these lesions present as low to equal density circumscribed oval masses. When encountered, short interval follow up is usually appropriate. Ultrasound-guided core biopsy can be obtained for tissue diagnosis when benignity cannot be confirmed or if the patient prefers. The majority of lactating adenomas regress spontaneously upon cessation of breastfeeding [11].

Fibroadenomas can be hormonally stimulated by estrogen and progesterone, enlarging during pregnancy and lactation and involuting at menopause [12]. Fibroadenomas can present clinically as a palpable, mobile, painless, firm mass. Similar to lactating adenomas, fibroadenomas can outgrow their blood supply during pregnancy and undergo infarction and manifest clinically as a painful mass. The breast imaging features of fibroadenomas are similar between lactating and nonlactating women. Sonographically, fibroadenomas are oval or round circumscribed, homogeneously hypoechoic or isoechoic solid mass, growing parallel to the chest wall. Mammographically, fibroadenomas appear as oval or round circumscribed equal density masses and with few gentle lobulations. When typically, benign features are present, short interval follow up is usually appropriate. During pregnancy and lactation, fibroadenomas can have atypical features including internal cystic changes and increased vascularity [13]. Ultrasound-guided core biopsy is indicated in the presence of atypical features such as irregular margins, heterogenous echotexture or microlobulations.

Phyllodes tumor typically occurs in middle-aged or older women and can manifest clinically as a rapidly growing palpable mass [12]. Sonographically, a phyllodes tumor can present as an oval or round circumscribed inhomogeneous mass, occasionally containing cystic spaces and producing posterior acoustic enhancement. Mammographically, phyllodes tumor can present as a rapidly growing large, dense, oval or round mass with circumscribed or indistinct margins. It is estimated that about 25% of phyllodes tumors are malignant, and 20% of the malignant type can metastasize hematogenously, most commonly to the lungs [14]. The most effective treatment for phylloides tumor is wide excision to avoid recurrence.

Imaging Findings of PABC

Ultrasound

Breast ultrasound should be the first imaging technique for pregnant and lactating patients with a breast mass due to the lack of ionizing radiation and a high sensitivity for the detection of PABC when compared to digital mammography [15]. The most common sonographic finding of PABC is a mass [16]. The sonographic features of PABC are similar to nonlactating women including a hypoechoic irregular mass with indistinct margins, and calcifications may or may not be present. Additional associated sonographic findings include

skin thickening and/or axillary adenopathy.

Mammography

The sensitivity of mammography in detecting breast cancer in pregnant and lactating women is lower than that of ultrasound due to the increased glandular tissue and water content which increases the parenchymal density [17]. Additional breast imaging with mammography or digital breast tomosynthesis (DBT) can be obtained if the initial sonographic evaluation is negative or demonstrates suspicious findings [18]. Mammography is generally safe during pregnancy and lactation and it may be useful to visualize microcalcifications, and the extent of disease including multifocality, multicentricity and contralateral breast cancer [17]. Lactating patients are encouraged to breastfeed or pump immediately before the mammographic examination in order to decrease the parenchymal density related to milk products. The mammographic features of PABC are similar to nonlactating women including masses, microcalcifications, focal asymmetry, architectural distortion, skin and trabecular thickening and axillary adenopathy.

MRI

Contrast-enhanced breast MRI is not recommended during pregnancy by the American College of Radiology (ACR) because the potential bioeffects of fetal gadolinium-based contrast agents (GBCA) exposure are not well understood [19]. Contrast-enhanced breast MRI can be safely performed in lactating patients with newly diagnosed breast cancer to evaluate the extent of disease. The sensitivity of breast MRI is limited in lactating patients by the physiologic hypervascularity and diffusely increased T2 signal from milk [20]. Lactating patients undergoing breast MRI are also encouraged to breastfeed or pump immediately before the examination. The MRI features of breast cancer in lactating patients are similar to nonlactating women and include irregular enhancing mass, mass with rim enhancement and central necrosis, segmental distributed nonmass enhancement, and diffuse unilateral enhancement [21]. The ACR recommends that it is safe for the lactating women to continue breastfeeding after receiving GBCA [19]. However, lactating patients may pump and discard the milk for 24 hours after the administration of GBCA, if desired.

Imaging-Guided Procedures

Biopsy should be recommended for any suspicious breast imaging findings. Ultrasound-guided core needle biopsy of any new solid mass during pregnancy or lactation is recommended to preclude a delay in diagnosis. If the suspicious finding is not identified sonographically, stereotactic or tomosynthesis-guided biopsies can be performed. MRI-guided biopsies can be obtained in lactating women with suspicious enhancing lesions. Patients should be informed of the slightly increased risks of milk fistula development or bleeding after percutaneous biopsy. Strategies to avoid fistulas include pre-procedure ice over the biopsy site, utilization of the smallest gauge needle, and avoidance of vacuum assisted devices whenever possible.

Prognosis

There is controversy and mixed results as whether PABC has a worse prognosis. Some studies have found no significant difference in the prognosis of PABC and non-PABC [22], while other studies suggest that PABC is associated with a poor prognosis [23].

Conclusion

Physicians should be familiarized with the most common benign



and malignant entities associated with palpable masses in pregnant and lactating women. While the majority of biopsied palpable masses during pregnancy and lactation are benign, palpable and suspicious masses in this patient population should be promptly evaluated sonographically by radiologists and subsequently biopsied. Reducing a delay in the diagnosis of PABC is critical in the prognosis of patients. Mammography is a supplementary breast imaging modality in pregnant and lactating women that can be obtained when suspicious sonographic findings are demonstrated or after the diagnosis of breast cancer. Breast MRI can be used in lactating patients with a diagnosis of breast cancer in order to evaluate the extent of disease.

Authors' Contributions

Yara Z Feliciano-Rivera: Conception and design, Radiology interpretation, literature review, drafting the article and critical revision.

Jose Net: Drafting the article and critical revision.

Monica M Yepes: Drafting the article and critical revision.

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Disclosures

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