Clinical Imaging 58 (2019) 182–186

Contents lists available at ScienceDirect

Clinical Imaging

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

Breast Imaging

Pregnancy-associated breast cancer: A review of 47 women

Füsun Taşkın[a,*], Yasemin Polat[b], İbrahim H. Erdoğdu[c], Aykut Soyder[d]

[a] Acibadem University School of Medicine, Department of Radiology, 34303 Istanbul, Turkey
[b] Adnan Menderes University School of Medicine, Department of Radiology, 09010 Aydin, Turkey
[c] Adnan Menderes University School of Medicine, Department of Pathology, 09010 Aydin, Turkey
[d] Adnan Menderes University School of Medicine, Department of General Surgery, 09010 Aydin, Turkey

ARTICLE INFO

Keywords:
Pregnancy
Breast cancer
Pregnancy-associated breast cancer
Mammography
Ultrasonography
Magnetic Resonance Imaging

ABSTRACT

Purpose: Pregnancy-associated breast cancer (PABC) is a rare disease. However, its expected incidence tends to be increased because of delayed maternal age. The purpose of this study was to describe the clinical, radiological, and histopathological characteristics of PABC cases diagnosed in our center.
Methods: The clinical-radiological findings and histopathological characteristics of patients diagnosed and treated with PABC at our institution between January 2011 and January 2017 were retrospectively evaluated.
Results: Mammography and ultrasonography were performed in all patients. MRI examination was performed in 18 patients. Nine (19.1%) out of 47 patients were diagnosed with breast cancer during pregnancy, and 38 (80.9%) were in their first year after delivery. The most frequent finding (95.7%) during imaging was one or more masses. Mammography-detected pure or accompanying microcalcifications were found in 12 (25.5%) patients. MRI detected additional multifocal and multicentric disease in 14 (29.8%) patients and contralateral cancer in one (2.1%) patient.
Conclusions: Pregnancy-related breast cancer tends to be diagnosed in an advanced stage with poor prognosis. Any breast abnormalities observed in this period should alert clinicians, and a meticulous radiological evaluation is mandatory. The early diagnosis of this disease would increase the chances of successful treatment.

1. Introduction

Breast cancer is the second leading cause of mortality in women. However, pregnancy-associated breast cancer (PABC) is less well known because it is not commonly clinically encountered. Recent publications note that the incidence of PABC has increased because of delayed childbearing [1,2].

Pregnancy-associated breast cancer is defined as all breast cancers diagnosed in pregnancy and within one year after delivery [3,4]. The delayed diagnosis of PABC is a major contributing factor to its lower survival rate than that in age-matched patients with non-PABC [5–10]. The most significant reason for late stage diagnosis is the differentiation of breast tissue due to hormonal changes specific to this period. The increased levels of estrogen, progesterone, and prolactin cause early breast changes in the first trimester of pregnancy. The development of new ductus, lobular growth, spontaneous involution in the stroma, and an increase in glandular tissue vascularization are primarily detected secondary to the effect of estrogen. Progesterone is dominant in the second and third trimesters, causing lobular growth with a relative decrease in stroma and an increase in cellular proliferation [11,12]. These microenvironment changes can potentially affect the growth and aggressiveness of PABC. These changes detected in the breast are also a challenge during physical examination and can cause a delay in diagnosis [6,7].

Radiological imaging methods play an important role in the diagnosis of PABC, and ultrasonography, with a sensitivity close to 100%, is the most frequently used and most appropriate imaging method. Mammography and biopsy must also be performed when suspicious lesions are detected in the initial ultrasonographic examination [6–8,13].

To date, most publications have focused on ultrasonography and mammography; in contrast, there are only a few publications reporting the MRI findings in PABC [14].

Late presentation, delayed diagnosis and delayed treatment of PABC lead to increasing social and economic consequences like termination of pregnancy, risk of fetal damages, psychological trauma of parents, ethical problems, increased cost of treatment. For this reason, awareness and early diagnosis play an important role in the accurate management of PABC. In this study, we identified the clinical, radiological, and histopathological characteristics of PABCs detected over a 7-year

* Corresponding author.
E-mail address: fusuntaskin@yahoo.com (F. Taşkın).

https://doi.org/10.1016/j.clinimag.2019.07.012
Received 28 February 2019; Received in revised form 25 July 2019; Accepted 30 July 2019

period and emphasize the reasons for the difficulty in imaging and diagnosing of PABC.

2. Material and methods

Institutional ethics committee approval was obtained. This study was conducted as a case series. A retrospective review of the clinical, radiological, and histopathological findings of 47 women who were diagnosed with PABC between January 2011 and January 2017 was performed. Two radiologists with 15 years and 5 years of experience in breast radiology, respectively, retrospectively reviewed the mammography and sonography findings of all patients and the MRI findings of 18 patients.

The Breast Imaging Reporting and Data System (BIRADS) classification was used in the evaluation. The inclusion criteria for this study were: the diagnosis of PABC with imaging and the availability of complete clinical and histopathological data. The characteristics of the patients and their symptoms, the findings of physical examination, the imaging findings and the histopathological results were obtained from the digital hospital archive.

The obtained data were analyzed using the Statistical Package for the Social Sciences (SPSS for Windows, v. 20.0, Chicago, USA) program, and the descriptive statistics were demonstrated as the mean (minimum-maximum) with the frequency percentage distribution.

3. Results

Forty-seven lesions (index lesion if there was more than one tumor) were evaluated in 47 women with PABC. Nine (19.1%) women were in the pregnancy period, and 38 (80.9%) were within the first year after delivery. The mean age of the patients was 32 (25–44) years. No patient had a family history of breast cancer. Pregnancy was not terminated in patients whose cancer was diagnosed during pregnancy. A palpable mass was detected in the breast or axilla of 40 (86%) patients in the physical examination. Other symptoms in the patients were nipple retraction and/or bloody nipple discharge (8%) and diffuse breast swelling and pain (6%). All patients presented for diagnostic examination. None were screening detected. Description of study group summarized in Table 1.

All patients were first evaluated with ultrasonography, and then mammography was performed. Ultrasonography was used to detect all of the lesions. The mean lesion size was 47 (12 − 130) mm. Forty-five (95.7%) of the 47 lesions were masses (Fig. 1a, b), and the remaining 2 (4.3%) lesions were nonmass lesions by sonography. Sonographic nonmass lesions were architectural distortions and microcalcifications. Ultrasonography detected 8 cases of multifocal and 4 cases of multicentric disease. Nineteen (42.2%) of the 45 masses were round (5/19) or oval (14/19) shaped (including lobulated lesions), and 26 (57.8%) were irregularly shaped. In 16 (35.6%) of the 45 mass lesions, the margins were circumscribed, and 29 (64.4%) mass lesions had noncircumscribed margins. The internal echo pattern was heterogeneous in 34 masses (75.5%), homogenous in 2 (4.5%) masses and mixed solid and cystic in 9 (20%) of 45 masses.

Table 1
Description of the study group.

Characteristics	All patients (n = 47)
Mean age	32 (25–44)
Pregnancy status	9 (19.1)
Pregnant	38 (80.9)
First year after delivery	
Histological tumor type	45 (95.8)
Invasive ductal cancer	2 (4.2)
Invasive lobular cancer	
Axillary metastasis	25 (53.2)
Distant metastasis	2 (4.2)
Receptor status	31 (68.8)
ER positive	25 (53.2)
PR positive	9 (19.1)
HER-2 positive	

Note: Unless otherwise noted, values are the number of patients, with percentages in parentheses. ER: Estrogen receptor, PR: Progesterone receptor, HER-2: Human epidermal growth factor receptor.

Mammography detected 41 (87.2) of the 47 cancers. Mammography showed microcalcifications in 12 (25.5%) patients (pure segmental microcalcifications in two patients and microcalcifications accompanying masses in 10 patients). The sonographic and mammographic lesion characteristics are summarized in Table 2.

Breast MRI was performed in 18 (38.3%) of the 38 patients whose cancers were diagnosed in the first year of delivery. The indications of the MRI were to evaluate disease extension, sonographic and mammographic size discrepancy, and indeterminate findings of multicentric disease. In all patients, MRI was performed immediately after nursing.

Background parenchymal enhancement was found in all patients. BPE was mild in 2 (11.1%) patients, and moderate or marked in 16 (88.9%) patients. Background parenchymal enhancement did not affect the detection of the lesions (Fig. 2). MRI detected 11 (61.1%) masses, 5 (27.8%) mass and accompanying nonmass enhancements (NME) and two (11.1%) NMEs of all index tumors. MRI showed multifocal (in same quadrant of breast, 6/18) and multicentric (in different quadrants of breast, 9/18) disease in 15 (83.3%) of 18 patients. Additional one contralateral cancer was detected by MRI (Fig. 3). The contrast kinetics of the index lesions were type 1 (persistent) in one NME, type 2 (plateau) in 12 masses and/or NMEs and type 3 (washout) in 6 masses. The MRI findings are summarized in Table 3.

Metastatic axillary lymph nodes were detected in 25 (53%) patients. There was distant metastasis in 2 (4.3%) of 47 patients.

The histological tumor grade was grade 3 in 39 (83%) patients and grade 2 in the remaining 8 (17%) patients. Forty-five (95.7%) patients were diagnosed with invasive ductal cancer, and 2 (4.3%) patients were diagnosed with invasive lobular cancer. Estrogen and/or progesterone receptors were positive in 31 (66%) patients. Twenty-two tumors (46.8%) were luminal A, 9 (19.1%) were luminal B, 7 (15%) were triple-negative, and 9 (19.1%) were HER-2 positive breast cancer. Ki-67 levels in all tumors except two were higher than 20% (range 23%–70%). Ki-67 was detected at 13% and 14% in two patients diagnosed with invasive ductal cancer.

4. Discussion

Although PABC has rarely been described, recent publications highlight an increase in its incidence. In previous studies, it was reported that 6–15% of patients who were diagnosed with breast cancer at 40 years of age or younger were in the pregnancy period [10,15–17]. Appropriate planning and the evaluation of imaging results are crucial to prevent a delay in diagnosis.

In the last 7-year period, 4.3% of the breast cancers detected in our center were pregnancy-associated. In this study, none of the patients had a family history of breast cancer. Therefore, even if there is no risk factor, the clinician and the radiologist should maintain a high index of suspicion and careful when evaluating patients during this period. In the present study, the mean age of the women diagnosed with PABC was 32 years. Most of the cancers (81%) were diagnosed in the postpartum period. All cancers were detected by diagnostic exams, and a palpable mass found in the physical examination and single or multiple masses observed in imaging. Our results were consistent with the literature [6–8].

In PABC, physical evaluation and imaging may be difficult due to the physiological changes in the breast during pregnancy and the breast feeding period. The intensive proliferative changes in this period lead to an increase in the breast density which makes the diagnosis difficult [1,11,12]. Diagnostic delays may also occur if the clinician or

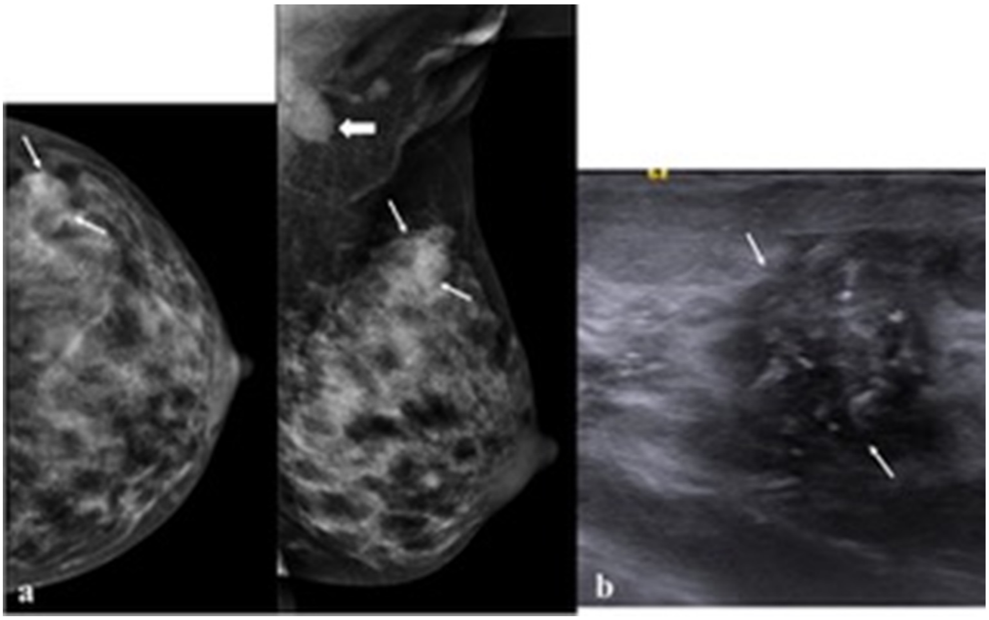

Fig. 1. a, b, c: A 29-year-old lactating woman (postpartum third month) presented with a palpable mass on her right breast. The transverse sonogram showed an oval, partially irregular mass with partially indistinct margins (a). Craniocaudal and mediolateral oblique mammograms detected a mass partially obscured by dense breast tissue in the lower inner quadrant of the right breast (arrows) (b). The mass was clearly detectable on axial pre-contrast non-fatsat T1W and axial subtracted post-contrast T1W images on MRI (arrows). There is a high background parenchymal enhancement on axial T1W subtracted post-contrast images (c). Ultrasonography-guided biopsy revealed a high-grade, triple-negative invasive ductal cancer.

Table 2
Lesion characteristics according to imaging methods.

Lesion characteristics	Mammography	Ultrasonography
Lesion type		
Mass	26 (63.4)	45 (95.7)
AD or asymmetry	13 (31.7)	2 (4.3)
Microcalcifications	12	4 (8.5)
Pure	2 (4.9)	
Accompanying	10	4
Lesion distribution		
Solitary	37 (78.7)	35 (74.5)
MF	4 (8.5)	8 (17)
MC	6 (12.8)	4 (8.5)
Mass/Shape		
Round	3 (11.5)	5 (11.1)
Oval	11 (42.3)	14 (31.1)
Irregular	12 (46.2)	26 (57.8)
Mass/Margin		
Circumscribed	7 (26.9)	16 (35.6)
Not circumscribed	19 (73.1)	29 (64.4)
Indistinct	10	14
Angular		1
Microlobulated		2
Spiculated	9	12
Mass/Sonographic		
Internal echo pattern		
Homogenous		2 (4.3)
Heterogeneous		34 (75.7)
Complex cystic and solid		9 (20)

Note: Unless otherwise noted, values are the number of patients, with percentages in parentheses.
AD: Architectural distortion, MF: Multifocal, MC: Multicentric.

radiologist does not suspect PABC. The mean tumor size in pregnancy-associated cancers is larger, the axillary lymph node involvement rates are higher, and the tumors are generally of a higher grade than other cancers detected in the screening age group [1,6,8–10]. Similarly, the mean tumor size was larger in the present study (47 mm), axillary lymph node metastasis was detected in 53% of the patients, and 83% of the patients had grade 3 tumors. Diagnostic delay causes an increased estimated risk of axillary metastasis. According to Nettleton and colleagues, risk of axillary metastasis can estimate by using delay time and tumor doubling time in a few mathematical equations. If a tumor has a 130-day doubling time, a one-month delay causes a 0.9% increased risk, and a 6-month delay causes a 5.1% increased risk of axillary metastasis. If the tumor has a 65-day doubling time, a one-month delay causes a 1.8% increased risk, and a six-month delay causes a 10.2% increased risk of axillary metastasis [17]. These findings highlight the importance of early diagnosis, which would increase the chance of receiving effective treatment.

Ultrasonography detected all lesions in this study. The most frequent sonographic finding was a solid mass. Almost half of the masses (42%) were round/oval shaped and well circumscribed. The rate of spiculated masses was 27%, which was lower than that for the screening age group. Nine (20%) masses were well-circumscribed complex cystic and solid masses. It should be noted that, typical malignant characteristics such as spiculated margins, may not be detected in pregnancy-associated cancers; however, benign morphological characteristics, such as parallel orientation, increased sound transmission, and circumscribed margins may be observed. In addition, complex cyst morphology, which may be confused with galactocele or abscess, could be detected in this period [6–8]. When a suspicious mass detected by imaging, biopsy must be performed rather than follow up for masses detected during pregnancy and the breast feeding period, due to characteristics that may overlap with those in benign lesions. Patients should be informed regarding the possibility of milk fistula and increased risk of bleeding [18].

The increased breast density in the pre- and postpartum period is known to decrease mammographic sensitivity. In this study, 87% of the cancers were detected with mammography in women with PABC. Mammography facilitates the diagnosis and staging of breast cancer and the detection of accompanying findings such as microcalcifications or secondary lesions. Mammography can be performed safely during pregnancy and must be performed for all clinically suspicious lesions which is especially important to evaluate extent of disease given that MRI is contraindicated [6–8,13,21,22].

Dynamic contrast-enhanced breast MRI (DC-MRI) should not be performed during pregnancy due to the potential harm of the contrast agent to the fetus. However, contrast-enhanced MRI can be performed safely during the lactation period [18]. Increased background parenchymal enhancement (BPE) is expected in the breast feeding period. Since tumor enhancement is more intense and rapid than that of the parenchyma, tumors can be detected and characterized using dynamic contrast-enhanced MRI. In this study, BPE did not affect lesion detection or characterization. MRI contributes to the differentiation of multifocal-multicentric lesions and to the evaluation of accurate tumor size and involvement [23,24]. In our study, additional multicentric

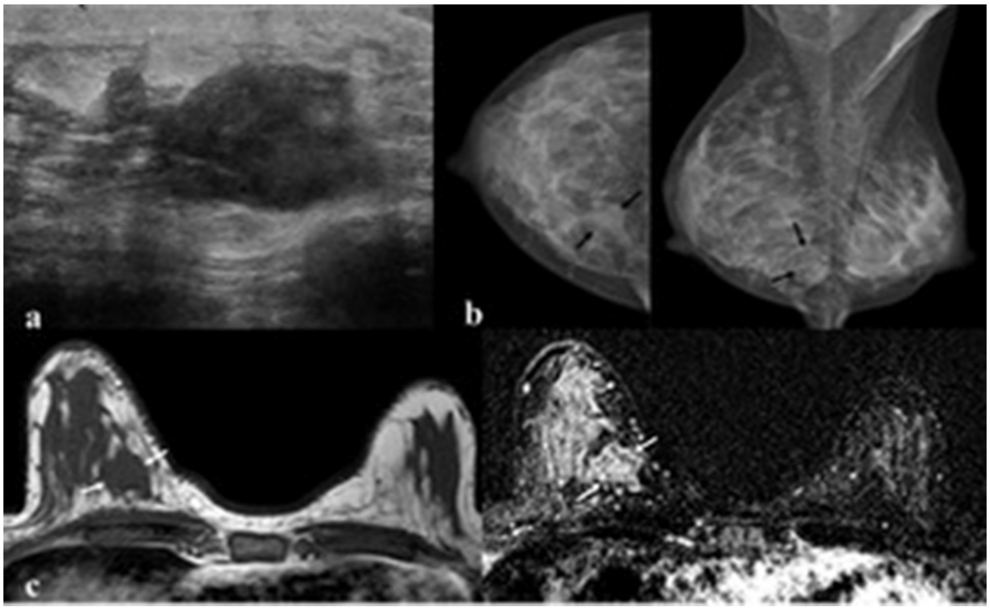

Fig. 2. a, b, c: A 28-year-old lactating woman (postpartum sixth month) presented with diffuse enlargement of her left breast with skin thickening. A transverse sonogram showed a large, heterogeneous, hypoechoic mass with indistinct margins. Mammography showed diffuse increased density and skin thickening on the left breast. Axial subtracted postcontrast T1W MRI images showed mild background parenchymal enhancement. MRI demonstrated diffuse tumor extension on the left breast and additional small nonmass enhancement of the right breast (arrows). Ultrasonography-guided biopsy revealed receptor-positive, high-grade, invasive ductal cancer on the left breast and right breast.

cancers (47.3%) and one contralateral cancer (5.3%) were detected with MRI in 18 patients. MRI detected additional five lesions that cannot be detected by ultrasonography.

In the literature, the most frequently detected histopathological type of PABC is invasive ductal cancer (range, 71%–100%). The incidence of invasive lobular cancer was reported to be low, and in situ ductal cancer was rarely reported [24]. In our study, 95.7% of cancers were invasive ductal carcinoma, and 4.3% were invasive lobular carcinoma. There are a small number of publications investigating the association between molecular subtypes of PABC in the literature. Some studies reported 28%–50% hormone receptor positivity [25–28]. However, some studies reported 50% or more in their studies [5,10,17]. In our study, no association was detected between the molecular subtype and PABC in accordance with the data in the literature to date. Collins and colleagues reported higher rates of luminal A in 707 women with PABC younger than 40 years of age; however, they reported no association between the molecular subtype and PABC [29]. Similarly, 65.9% of cancers were hormone receptor positive in this study. The most important limitations of our study are its retrospective design and the small number of patients. MRI was not performed in all patients diagnosed after delivery because we were not sure about the efficiency of MRI in the lactation period during the first years of our MRI experience. However, we believe that the results of this study will contribute to the current information on this topic because of the limited

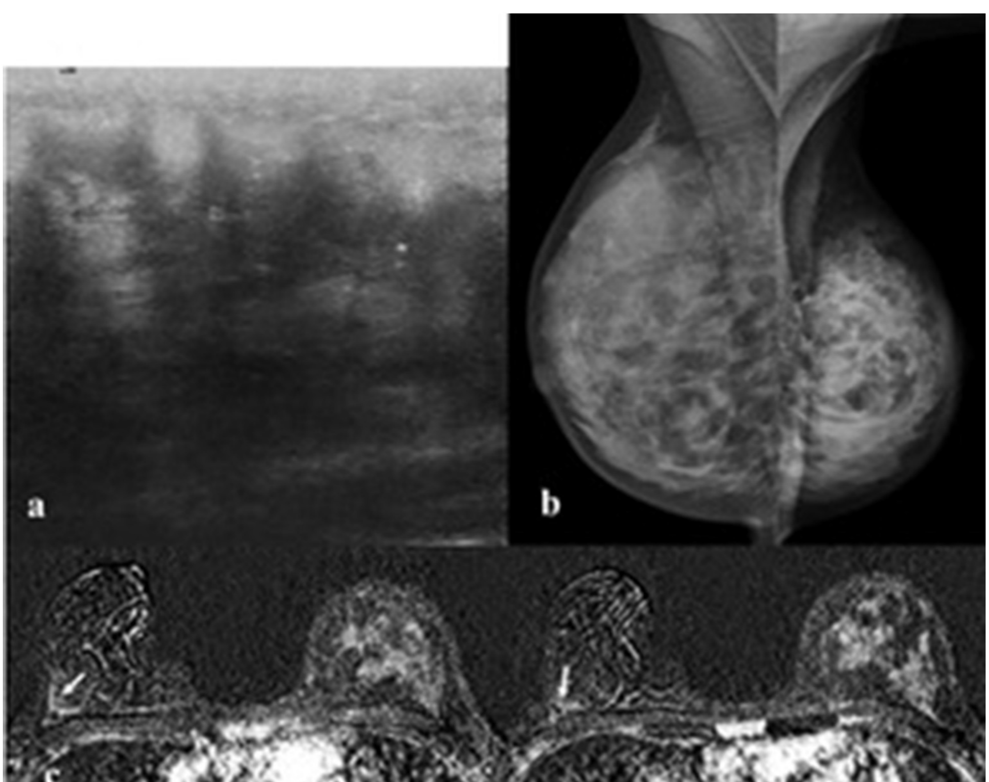

Fig. 3. a, b: A 41 year-old pregnant woman (29 weeks) presented with palpable mass on her left breast. Craniocaudal and mediolateral oblique mammograms showed the mass with microcalcifications on upper outer quadrant of her left breast (arrows) and enlarged axillary lymph node (thick arrow) (a). Heterogeneous hypoechoic mass with indistinct margins and accompanying microcalcifications were seen on transvers sonography image (b). Ultrasonography-guided biopsy revealed high grade, receptor-positive invasive ductal cancer.

Table 3
MRI findings according to tumor types.

MRI findings of 18 patients	Invasive ductal cancer	Invasive lobular cancer
Background parenchymal		
enhancement	2 (11.1)	
Mild	10 (55.5)	1 (5.6)
Moderate	4 (22.2)	1 (5.6)
Marked		
Lesion type		
Mass	11 (61.1)	
Mass and NME	3 (16.7)	2 (11.1)
NME	2 (11.1)	
Lesion distribution[a]		
Solitary	2 (10.5)	1 (5.3)
Multifocal	5 (26.3)	1 (5.3)
Multicentric	9 (47.3)	
Contralateral	1 (5.3)	
Mass/Internal enhancement		
Homogenous	3 (21.4)	
Heterogenous	5 (35.7)	
Rim	4 (28.6)	2 (14.3)
NME/Type		
Heterogenous	3 (42.8)	1 (14.3)
Clumped		1 (14.3)
Clustered ring	2 (28.6)	
NME/Distribution		
Linear	1 (14.3)	
Regional	1 (14.3)	2 (28.6)
Segmental	3 (42.8)	
Contrast kinetic		
Persistent	1 (5.6)	
Plateau	10 (55.5)	1 (5.6)
Wash-out	5 (27.7)	1 (5.6)

Note: Unless otherwise noted, values are the number of patients, with percentages in parentheses.
NME: Nonmass enhancement.
[a] One contralateral cancer included.

number of studies in the literature.

PABC is a serious disease because of its increasing incidence and socioeconomic consequences. Delayed diagnosis and treatment significantly reduces overall survival [1]. Imaging studies revealed characteristics that overlap with those of benign lesions in this patient group. Radiological evaluation should be performed carefully, and if there is any suspicious finding, biopsy should be performed. MRI is a useful tool for evaluating disease extension and contralateral breast in post-pregnancy and lactation period.

5. Conclusions

In conclusion, although PABC is rarely encountered, women presenting breast symptoms should be carefully evaluated in this time period. All patients must be attentively evaluated with a multidisciplinary approach including mammography and biopsy when indicated. The benefit of the high sensitivity of MRI may be used to plan treatment for women presenting with breast symptoms within 1 year after pregnancy should be carefully evaluated.

Ethical approval

The authors provided a statement that the work has been approved.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

References

[1] Polivka Jr. J, Altun I, Golubnitschaja O. Pregnancy-associated breast cancer: the risky status quo and new concepts of predictive medicine. EPMA J 2018;9:1–13. https://doi.org/10.1007/s13167-018-0129-7.

[2] Azim Jr. HA, Santoro L, Russell-Edu W, Pentheroudakis G, Pavlidis N, Peccatori FA. Prognosis of pregnancy-associated breast cancer: a meta-analysis of 30 studies. Cancer Treatment Rev 2012;38:834–42. https://doi.org/10.1016/j.ctrv.2012.06.004.

[3] Viswanathan S, Ramaswamy B. Pregnancy-associated breast cancer. Clin Obstet Gynecol 2011;54(4):546–55. https://doi.org/10.1097/GRF.0b013e318236e436. Dec.

[4] Hogge JP, De Paredes ES, Magnant CM, Lage J. Imaging and management of breast masses during pregnancy and lactation. Breast J 1999;5(4):272–83. https://doi.org/10.1046/j.1524-4741.1999.98077.x.

[5] Michieletto S, Saibene T, Evangelista L, Barbazza F, Grigoletto R, Rossi G, et al. Preliminary monocentric results of biological characteristics of pregnancy associated breast cancer. Breast 2014;23(1):19–25. https://doi.org/10.1016/j.breast.2013.10.001. Feb.

[6] Sabate JM, Clotet M, Torrubia S, Gomez A, Guerrero R, de las Heras P, et al. Radiologic evaluation of breast disorders related to pregnancy and lactation. Radiographics 2007;27(Suppl. 1):S101–24. https://doi.org/10.1148/rg.27si075505. Oct.

[7] Ayyappan AP, Kulkarnı S, Crystal P. Pregnancy-associated breast cancer: spectrum of imaging appearances. Br J Radiol 2010;83(990):529–34. https://doi.org/10.1259/bjr/17982822. Jun.

[8] Vashi R, Hooley R, Butler R, Geisel J, Philpotts L. Breast imaging of the pregnant and lactating patient: imaging modalities and pregnancy-associated breast cancer. AJR 2013;200:321–8. https://doi.org/10.2214/AJR.12.9814.

[9] Ishida T, Yokoe T, Kasumi F, Sakamoto G, Makita M, Tominaga T, et al. Clinicopathologic characteristics and prognosis of breast cancer patients associated with pregnancy and lactation: analysis of case-control study in Japan. Jpn J Cancer Res 1992;83(11):1143–9. https://doi.org/10.1111/j.1349-7006.1992.tb02737.x. Nov.

[10] Langer A, Mohallem M, Stevens D, Rouzier R, Lerebours F, Chérel PA. Singleinstitution study of 117 pregnancy-associated breast cancers (PABC): presentation, imaging, clinicopathological data and outcome. Diagn Interv Imaging 2014;95(4):435–41. https://doi.org/10.1016/j.diii.2013.12.021. Apr.

[11] Salazar H, Tobon H, Josimovich JB. Developmental gestational and postgestational modifications of the human breast. Clin Obstet Gyecol 1975;18:113–37.

[12] Yu JH, Kim MJ, Cho H, Liu HJ, Han S, Ahn T. Breast diseases during pregnancy and lactation. Obstet Gynecol Sci 2013;56(3):143–59. https://doi.org/10.5468/ogs.2013.56.3.143. May.

[13] Committee opinion no. 723: guidelines for diagnostic imaging during pregnancy and lactation. https://www.ncbi.nlm.nih.gov/pubmed/28937575;; 2017.

[14] Myers KS, Green LA, Lebron L, Morris EA. Imaging appearance and clinical impact of preoperative breast MRI in pregnancy-associated breast cancer. AJR Am J Roentgenol 2017;209(3):W177–83. https://doi.org/10.2214/AJR.16.17124. Sep.

[15] Nugent P, O'Connell TX. Breast cancer and pregnancy. Arch Surg 1985;120:1221–4. https://doi.org/10.1001/archsurg.1985.01390350007001.

[16] Beadle BM, Woodward WA, Middleton LP, Tereffe W, Strom EA, Litton JK, et al. The impact of pregnancy on breast cancer outcomes in women ≤35 years. Cancer 2009;115:1174–84. https://doi.org/10.1002/cncr.24165.

[17] Nettleton J, Long J, Kuban D, Wu R, Shaeffer J, El-Mahdi A. Breast cancer during pregnancy: quantifying the risk of treatment delay. Obstet Gynecol 1996;87:414–8. https://doi.org/10.1016/0029-7844(95)00470-X.

[18] Breast imaging of pregnant and lactating women. ACR appropriateness criteria Available at: ACRhttps://acsearch.acr.org/docs/3102382/Narrative; 2018.

[21] Wang PI, Chong ST, Kielar AZ. Imaging of pregnant and lactating patients: part 1, evidence-based review and recommendations. AJR Am J Roentgenol 2012;198(4):778–84. https://doi.org/10.2214/AJR.11.7405. Apr.

[22] Wang PI, Chong ST, Kielar AZ, Kelly AM, Knoepp UD, Mazza MB, et al. Imaging of pregnant and lactating patients: part 2, evidence-based review and recommendations. AJR Am J Roentgenol 2012;198(4):785–92. https://doi.org/10.2214/AJR.11.8223. Apr.

[23] Expert Panel on MR Safety, Kanal E, Barkovich AJ, Bell C, Borgstede JP, Bradley Jr. WG, et al. ACR guidance document on MR safe practices: 2013. J Magn Reson Imaging 2013;37(3):501–30. https://doi.org/10.1002/jmri.24011. Mar.

[24] De Santis M, Straface G, Cavaliere AF, Carducci B, Caruso A. Gadolinium periconceptional exposure: pregnancy and neonatal outcome. Acta Obstet Gynecol Scand 2007;86(1):99–101. https://doi.org/10.1080/00016340600804639.

[25] Murphy CG, Mallam D, Stein S, Patil S, Howard J, Sklarin N, et al. Current or recent pregnancy is associated with adverse pathologic features but not impaired survival in early breast cancer. Cancer 2012;118(13):3254–9. https://doi.org/10.1002/cncr.26654. Jul (1).

[26] Elledge RM, Ciocca DR, Langone G, McGuire WL. Estrogen receptor, progesterone receptor, and HER-2/neu protein in breast cancers from pregnant patients. Cancer 1993;71(8):2499–506. https://doi.org/10.1002/1097-0142(19930415)71:8<2499::AIDCNCR2820710812>3.0.CO;2-S. Apr 15.

[27] Middleton LP, Amin M, Gwyn K, Theriault R, Sahin A. Breast carcinoma in pregnant women: assessment of clinicopathologic and immunohistochemical features. Cancer 2003;98(5):1055–60. https://doi.org/10.1002/cncr.11614. Sep 1.

[28] Aziz S, Pervez S, Khan S, Siddiqui T, Kayani N, Israr M, et al. Case control study of novel prognostic markers and disease outcome in pregnancy/lactation associated breast carcinoma. Pathol Res Pract 2003;199(1):15–21. https://doi.org/10.1078/0344-0338-00347.

[29] Collins LC, Gelber S, Marotti JD, White S, Ruddy K, Brachtel EF, et al. Molecular phenotype of breast cancer according to time since last pregnancy in a large cohort of young women. Oncologist 2015;20(7):713–8. https://doi.org/10.1634/theoncologist.2014-0412. Jul.