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SHORT COMMUNICATION

MR imaging characteristics of breast cancer diagnosed during lactation

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Objectives: To describe the MR imaging characteristics of breast cancer diagnosed during lactation and evaluate the usefulness of MR imaging.

Methods: The MR images of nine patients (age range, 29–37 years) with pathologically confirmed breast carcinoma during lactation were evaluated retrospectively. Background parenchymal enhancement of the lactating mammary tissue was determined. The images were reviewed for evaluation of lesion detection, enhancement type (mass/non-mass), shape, margin, contrast enhancement and time-intensity curve pattern in the dynamic study. The breast MR images after neoadjuvant chemotherapy were also reviewed.

Results: Although the breasts showed marked ($n = 7$) or moderate ($n = 2$) background parenchymal enhancement, MR imaging depicted breast cancer in all patients. All nine tumours were visible as masses. The most common shape

and margin of the masses were an irregular mass ($n = 5$) with an irregular margin ($n = 9$). Contrast enhancement was heterogeneous or rim enhancement. The predominant kinetic pattern was rapid increase ($n = 9$) in the initial phase and washout ($n = 5$) in the delayed phase. Additional sites of cancer other than the index lesion were detected with MR imaging in three patients (33.3%). MR imaging demonstrated partial response in five of six patients who were evaluated for response to chemotherapy.

Conclusion: All breast cancers in lactating females in this study were observed on breast MR imaging despite the moderate-to-marked background parenchymal enhancement of lactating mammary tissue.

Advances in knowledge: MR imaging can be used in the evaluation of disease extent and assessment of therapeutic response after neoadjuvant chemotherapy of breast cancer diagnosed during lactation.

INTRODUCTION

Breast cancer occurring during gestation, lactation or within 1 year from delivery is called pregnancy-associated breast cancer.^{1,2} The increased hormone levels associated with pregnancy and lactation cause an increase in the volume and firmness of the breast, which makes clinical and radiologic detection and evaluation of breast masses difficult. Additionally, a lack of awareness regarding breast masses may preclude well-timed imaging or biopsy and delay diagnosis of pregnancy-associated breast cancer into more advanced stages compared with age-matched non-pregnancy-associated breast cancer cases.³

While contrast-enhanced MR imaging is not recommended during pregnancy because of insufficient data regarding the safety of gadolinium, it can be safely performed

in females who are breastfeeding. According to the American College of Radiology guidelines, it is safe for the mother and infant to continue breastfeeding after receiving gadolinium-based contrast media. Gadolinium-based contrast media is excreted into the breast milk in the first 24 h, and the expected systemic dose absorbed by the infant from the breast milk is less than 0.0004% of the intravascular dose given to the mother. The likelihood of an adverse effect from such a minute fraction of gadolinium chelate absorbed from breast milk is very low.⁴ Even though contrast-enhanced MR imaging has been used in patients with newly diagnosed breast cancer and it can be safely performed during lactation, the reported MR imaging findings of breast carcinoma during lactation are limited and the number of patients is small. Few studies on the usability or accuracy of MR imaging in breast cancer

during lactation exist. One study suggested limited accuracy of MR imaging in the diagnosis of breast cancer in lactating females because of the high enhancement of normal lactating mammary tissue.⁵ Another study reported that MR imaging depicted breast carcinoma in each of five patients during lactation, even though the surrounding background lactating mammary tissue showed rapid moderate contrast enhancement.⁶

The purpose of this study is to describe MR imaging characteristics of breast cancer diagnosed during lactation and evaluate the usefulness of MR imaging in this clinical setting.

METHODS AND MATERIALS

Patients

The Institutional Review Board approved this retrospective study, and requirement for informed patient consent for review of images and records was waived. We surveyed electronic medical records for patients with breast carcinoma examined at our institution from October 2008 to July 2016. In total, 12 cases of breast cancer during lactation were found. We excluded three patients who had not undergone pre-treatment MR imaging ($n = 2$) and underwent excision biopsy after core needle biopsy ($n = 1$). Nine patients who underwent MR imaging for evaluation of tumour extent after diagnosis of breast cancer by ultrasound-guided core needle biopsy were included in this study. The mean age of the patients was 32.1 years (range, 29–37 years). At the time of breast cancer diagnosis, the females had been breastfeeding for a period ranging from 1 to 40 weeks (mean, 19 weeks). All patients presented with a palpable breast mass. One patient presented with breast pain and one with a palpable mass in the axilla in addition to a palpable breast mass. All patients were currently breastfeeding or had stopped breastfeeding within 7 days before their MR imaging examination. Six patients underwent breast MR imaging both before and after neoadjuvant chemotherapy.

Sonographic results of all patients were available for review. Each sonographic lesion was reviewed for mass characteristics (shape, margin and echo pattern) using the Breast Imaging Reporting and Data System (BI-RADS) criteria from the American College of Radiology.⁷ Mammography was available for review in four patients. Each mammographic lesion was reviewed and characterized according to lesion type (mass only, mass with microcalcifications, microcalcifications only, focal asymmetry or architectural distortion) and mass characteristics (shape and margin) using the BI-RADS criteria.⁷

MR Imaging technique

The MR imaging was performed in the prone position using a dedicated breast coil with a 3.0 T system (Tim Trio, Siemens Healthcare, Erlangen, Germany). Bilateral whole-breast MR imaging was performed using the following sequences and parameters: axial fat-saturated T_2 weighted spin echo (TR/TE, 5200/79; echo-train length, 21; section thickness, 4 mm; FOV, 320 × 320 mm; matrix size, 384 × 288; gap, 4.8 mm; acquisition, 1) and sagittal fat-saturated T_1 weighted (TR/TE, 500/12; echo-train length, 3; section thickness, 4 mm; FOV, 180 × 180 mm; matrix size, 320 × 224; gap, 1 mm; acquisition, 1). After the initial examination, dynamic contrast-enhanced images were obtained

using an axial fat-saturated T_1 weighted spoiled gradient echo sequence (TR/TE, 4.3/1.6; echo-train length, 1; flip angle, 10°; section thickness, 2 mm; FOV, 320 × 320 mm; matrix size, 448 × 246; gap, 1 mm; acquisition, 1). For dynamic contrast-enhanced images, a bolus of 0.1 mmol kg⁻¹ of gadodiamide (Omniscan, GE Healthcare) or gadoterate meglumine (Dotarem, Guerbet) was injected into the antecubital vein within 7–10 s, followed by a 16 ml saline flush. Dynamic axial MR images were obtained once before and five times after the administration of contrast material at 40 s intervals.

For analysis of enhancement kinetics, time–intensity curves were plotted based on the signal intensity values obtained in the regions of interest on serial dynamic images. To assess the increase in signal intensity during the early phase, we evaluated the enhancement of the first contrast-enhanced image at 60 s after injection of contrast material. Standard subtraction images (*i.e.* unenhanced images subtracted from early contrast-enhanced images) and reverse subtraction images (*i.e.* last contrast-enhanced images subtracted from early contrast-enhanced images) were obtained on a pixel-by-pixel basis. Subsequently, reformatted images with a maximum intensity projection were created from the standard and reverse subtraction images.

Interpretation of MRI findings

The breast MR images were reviewed retrospectively by one radiologist with 12 years of experience. Interpretation of the breast MR images was based on the BI-RADS MR lexicon.⁷ The amount of fibroglandular tissue (FGT) was determined in accordance with BI-RADS criteria as follows: almost entirely fat, scattered FGT, heterogeneous FGT or extreme FGT. Background parenchymal enhancement (BPE) of the contralateral breast was determined. The level of global BPE, rather than the highest BPE in a single quadrant, was assessed using a combination of unenhanced and initial contrast-enhanced T_1 weighted fat-saturated and subtracted images and maximum intensity projection images with BI-RADS categories: minimal, mild, moderate or marked.

Areas of abnormal enhancement were described as mass or non-mass enhancement. For the masses, MR images were reviewed to evaluate size, shape (round, oval or irregular) and margin (circumscribed, irregular or spiculated), contrast enhancement within the mass (homogeneous, heterogeneous, rim or dark internal septation) and signal intensity. The signal intensity of the mass was compared with that of the surrounding glandular tissue. Morphologic analysis was performed on the first post-contrast image. For non-mass enhancements, MR images were reviewed to evaluate distribution (focal, linear, segmental, regional, multiple regions or diffuse) and internal enhancement pattern (homogeneous, heterogeneous, clumped or clustered ring). The time–signal intensity curve was generated. The initial phase (slow, medium or rapid) and the delayed phase of enhancement (persistent, plateau or washout) were evaluated. The presence of additional site of malignancy was also assessed. Additional site was defined as a lesion in the same breast quadrant but was separated from the index cancer by at least 1.0 cm of intervening normal breast tissue, a lesion contiguous with the index cancer but extended at least 4.0 cm beyond the site of the

Table 1. Patient data

Patient no.	Age	No. of weeks breastfeeding	Symptoms	Histologic type	Molecular subtype
1	31	16	Palpable mass Breast pain	NOS	Triple negative
2	33	40	Palpable mass	NOS	Triple negative
3	33	28	Palpable mass	NOS	Luminal B
4	32	8	Palpable mass	NOS	Triple negative
5	37	1	Palpable mass Mass in axilla	NOS	Luminal A
6	29	4	Palpable mass	Metaplastic carcinoma	Triple negative
7	33	40	Palpable mass	NOS	Her2
8	32	36	Palpable mass	NOS	Triple negative
9	29	4	Palpable mass	NOS	Triple negative

NOS, nvasive ductal carcinoma, not otherwise specified.

index cancer, or a lesion located in a different breast quadrant from the index cancer.⁸

Associated features, such as nipple change, skin change, pectoralis muscle or chest wall invasion and axillary adenopathy, were also noted. Axillary lymph nodes with irregular margins, absent fatty hilum and inhomogeneous cortex were considered to be abnormal lymph nodes.

The breast MR images after neoadjuvant chemotherapy were also reviewed to monitor response in six patients. Tumour response to the chemotherapy was categorized as complete response, partial response, stable disease or progressive disease based on the Response Evaluation Criteria in Solid Tumors (RECIST) guideline.⁹

RESULTS

Histopathologic analysis revealed invasive ductal carcinoma (not otherwise specified) in eight patients and metaplastic carcinoma in one patient. The clinical data with histopathology and molecular subtype are shown in Table 1.

Four patients who underwent mammography had positive mammographic findings. The mammographic findings consisted of irregular mass in three patients and mass with microcalcifications in one patient.

Sonography was performed in all patients including ultrasound-guided percutaneous 14-gauge core needle biopsy. On sonography, all cases showed masses. The most common sonographic features of the masses were irregular shapes ($n = 6$, 66.7%), not circumscribed margins ($n = 8$, 88.9%) and complex cystic and solid ($n = 3$, 33.3%) or hypoechoic ($n = 4$, 44.4%) echo patterns. In one patient, additional irregular hypoechoic masses that were clinically and mammographically occult were detected on sonography.

Nine patients underwent MR imaging for evaluation of the extent of tumour after diagnosis. All patients had extreme ($n = 6$) or heterogeneous ($n = 3$) FGT and showed marked ($n = 7$) or moderate ($n = 2$) BPE. Although the breasts showed marked or moderate

BPE, MR imaging depicted breast cancer in all patients. Nine tumours were observed as masses on MR imaging. The median size of the masses on MRI was 4.2 cm (range, 2.0–8.5 cm). The MR imaging findings are shown in Table 2. Five of the tumours were hypointense on T_2 weighted images compared with the surrounding glandular tissue. The most common shape and margin of the masses were an irregular mass with an irregular margin. The tumours showed heterogeneous or rim enhancement, and three tumours showed large cystic portions within the mass. The molecular subtype of the tumours that showed rim enhancement was triple negative. Additional sites of cancer other than the index lesion were detected in three patients (3 of 9, 33.3%). Associated non-mass enhancement with segmental distribution extending more than 4.0 cm was observed in two patients, which was pathologically confirmed as ductal carcinoma *in situ* (Figure 1). An additional mass separated from the index cancer by 1.3 cm of intervening normal tissue was observed in one patient, which was pathologically confirmed as invasive ductal carcinoma after surgery. Enlarged axillary lymph nodes were present in eight patients. Fine needle aspiration cytology was performed in seven patients, and axillary lymph node metastases were found in three patients. One patient underwent sentinel lymph node biopsy during surgery and no metastasis was found.

Of the nine patients, six patients underwent pre-operative neoadjuvant chemotherapy. Breast MR imaging both before and after neoadjuvant chemotherapy was performed in six patients. After neoadjuvant chemotherapy, a decrease in BPE to minimal ($n = 3$) or mild ($n = 3$) was seen in all six patients found to have marked BPE before treatment. Breast MR imaging demonstrated partial responses in five patients (Figure 2) and stable findings in one patient. Breast conservation surgery after neoadjuvant chemotherapy was performed in five patients (four patients showed partial response and one patient showed stable finding); residual breast cancer was found in five patients on pathologic examination. One patient was transferred to another hospital due to patient's preference.

Table 2. MR imaging findings of breast cancer in lactating females

Patient no.	Breast tissue		Signal intensity		Characteristics of the lesion				Additional sites
	FGT	BPE	T1 weighted imaging	T2 weighted imaging	Shape	Margin	Enhancement	Delayed phase	
1	Extreme	Marked	Low	Mixed ^a	Round	Irregular	Rim	Plateau	No
2	Extreme	Marked	Iso	Low	Oval	Irregular	Rim	Plateau	No
3	Extreme	Marked	Low	Low	Irregular	Irregular	Heterogeneous	Washout	Segmental non-mass enhancement
4	Heterogeneous	Moderate	Iso	Iso	Irregular	Irregular	Heterogeneous	Washout	Irregular mass
5	Heterogeneous	Marked	Iso	Low	Irregular	Irregular	Heterogeneous	Washout	No
6	Extreme	Marked	Iso	Mixed ^a	Irregular	Irregular	Rim	Washout	No
7	Extreme	Marked	Iso	Mixed ^a	Irregular	Irregular	Heterogeneous	Washout	Segmental non-mass enhancement
8	Extreme	Moderate	Iso	Low	Oval	Irregular	Rim	Plateau	No
9	Heterogeneous	Marked	Iso	Low	Oval	Irregular	Rim	Plateau	No

BPE, Background parenchymal enhancement; FGT, Fibroglandular tissue.

^aThe mass with iso-signal intensity and focal hyperintense portion on T₂ weighted images.

DISCUSSION

Sonography is the first diagnostic imaging modality used for evaluation of the breast during lactation. Ultrasound is more sensitive than mammography in the evaluation of patients with carcinoma. The sensitivity of mammography is reduced due to the diffusely increased parenchymal density, glandularity and additional water content of the lactating breast.^{10,11} However, mammography may demonstrate suspicious microcalcifications not detected on ultrasound and may be useful in the evaluation of the extent of disease. Bilateral mammography is therefore recommended in any patient with highly suspicious sonographic or clinical findings and in any patient with pregnancy-associated breast cancer.¹²

In a first case report, it was thought that MR imaging of lactating females would be limited because of dense breast tissue and a high number of false positives caused by high enhancement of normal lactating mammary tissue. The authors suggested that it would be difficult to distinguish breast cancer from lactating breast tissue because normal lactating breast showed rapid gadolinium uptake similar to that seen in malignancy.⁵ However, in a study evaluating the MR imaging features of five lactating patients who had biopsy-proven breast cancer, Espinosa et al found that despite confounders of increased BPE and T₂ signal, all of the cancers were readily identified on both unenhanced T₂ weighted sequences and contrast-enhanced T₁ weighted sequences. Normal lactating glands showed rapid contrast enhancement followed by an early plateau of enhancement, a feature attributed to increased vascular permeability; the cancer was conspicuous as low-signal-intensity mass against high signal intensity of the surrounding lactating breast tissue on T₂ weighted images. All tumours were visible by strong rapid initial contrast enhancement with early washout compared with normal lactating breast tissue, irregular margins and occasional rim enhancement on contrast-enhanced T₁-weighted images.⁶ Taylor et al in a series of six patients with breast cancer during pregnancy and lactation, reported that MR imaging showed unsuspected disease in one patient and overestimation of lesion size occurred in one patient because of a compressed zone of adenosis.¹³

To our knowledge, our study is the largest reported series of breast MR imaging in patients with breast cancer diagnosed during lactation. In our study, BPE did not impair lesion detection even though all of the lactating mammary tissue showed moderate-to-marked BPE. An increased likelihood of identifying the cancer was attributed to greater conspicuity of the enhancement of the cancer relative to BPE. Unlike the study published by Espinosa et al⁶ in which all five cancers had lower signal intensity on T₂ weighted images, masses with iso-signal intensity and hyperintense portions on T₂ weighted images were seen in three patients and a mass with iso-signal intensity on T₂ weighted images was seen in one patient in our study. MR imaging found additional lesions in three of nine patients (33.3%) and defined the tumour extent more accurately than mammography or sonography, thus facilitating the appropriate treatment plan. This result does not differ from that of Liberman et al in which MR imaging identified additional

Figure 1. A 33-year-old lactating female with invasive ductal carcinoma, not otherwise specified, in the right breast. (a) Medio-lateral oblique view of mammogram shows extremely dense breast tissue and an irregular mass (arrow). (b) Ultrasound image shows an irregular, complex cystic and solid mass in the area corresponding to the palpable mass. Ultrasound-guided core needle biopsy showed invasive ductal carcinoma, not otherwise specified. (c–e) Axial contrast-enhanced fat-suppressed subtraction T_1 weighted MR images (c and d) and a maximum intensity projection MR image (e) show an irregular heterogeneously enhancing mass (arrows) in the upper outer right breast. In addition, segmental clumped non-mass enhancement is observed in the upper outer right breast (arrowheads) that extends more than 4.0 cm, which was confirmed as ductal carcinoma *in situ* on pathologic diagnosis.

sites of ipsilateral cancer in 27% of non-pregnancy-associated breast cancer patients.⁸

Neoadjuvant chemotherapy has been increasingly used for treatment of breast cancer and breast MR imaging can also be useful to assess disease response during and after neoadjuvant chemotherapy. Since many of the pregnancy-associated breast cancer patients present with advanced stages at diagnosis, neoadjuvant chemotherapy serves an important role. Yang et al demonstrated that ultrasonography was a useful modality in the assessment of response of pregnant females to neoadjuvant chemotherapy by measurements of tumour shrinkage.¹² Breast MR imaging can aid in the assessment of response of lactating females to neoadjuvant chemotherapy. In our study,

six patients underwent breast MR imaging both before and after neoadjuvant chemotherapy to monitor response; residual disease was confirmed at surgery in five patients who showed partial response in four patients and stable finding in one patient. After neoadjuvant chemotherapy, decrease in BPE to minimal or mild was observed in all six patients in this study. Chen JH et al reported that younger females tended to have higher BPE than did older females. Further, BPE was significantly decreased in follow-up MR imaging after neoadjuvant chemotherapy in younger females. They suggested that reduction in BPE was most likely due to ovarian ablation induced by chemotherapeutic agents.¹⁴ The decreases in BPE seen in our study might be due to the cessation of lactation or the ovarian ablation induced by chemotherapy, or both.

Figure 2. A 37-year-old lactating woman with invasive ductal carcinoma, not otherwise specified, in the right breast. (a) Axial contrast-enhanced fat-suppressed subtraction T_1 weighted MR image shows an irregular heterogeneously enhancing mass (arrows) in the right breast. (b) Evaluation of response to neoadjuvant chemotherapy by using follow-up breast MR imaging shows reduction in size of tumor (arrow) in the right breast.

In conclusion, all breast cancers in lactating females were visualized on breast MR imaging, and detection of the lesion was not impaired even though lactating mammary tissue showed

moderate-to-marked BPE. MR imaging can be useful in assessment of therapeutic response after neoadjuvant chemotherapy in lactating females.

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