

Original article

Analysis of breast MRI performed on patients with axillary nodal metastasis and negative mammogram and ultrasound

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Abstract

Background: Occult breast cancer is a rare type of breast cancer which magnetic resonance imaging (MRI) has an immense role to confirm diagnosis and disclose non-demonstrable finding on initial modality.

Objectives: To analyze breast MRI findings in patients with axillary nodal metastasis and negative mammogram and ultrasound and retrospectively review the initial mammography and second-look ultrasound.

Methods: From January 2010 to January 2023, women who diagnosed occult breast cancer by presenting metastatic axillary lymph node on pathological report with negative mammography and ultrasonography, underwent breast MRI to identify occult breast carcinoma. Their breast MRI were retrospectively reviewed. The imaging findings on breast MRI were collected and confirmed associated findings on second-look ultrasound and initial mammograms.

Results: There were 12 patients diagnosed with occult breast cancer. Breast MRI detected primary cancer in 4 of 12 (33.0%) patients. In two out of four patients, the MR-correlated second-look ultrasound localized lesions that were not detected on the initial exam. One case demonstrated MR-correlated finding on retrospective mammography and the other case was detected as suspicious lesions on both second-look ultrasound and retrospective mammography.

Conclusion: Breast MRI is an important modality for investigation of occult breast cancer. MR-correlated second-look ultrasound and retrospective mammography localized lesions from the prior negative reports are valuable learning points to improve detection and interpretation skills.

Keywords: Axillary metastasis, breast MRI, occult breast cancer, negative mammography, second-look ultrasound.

Breast cancer is the most common cancer in woman both in the developed and developing country. ⁽¹⁾ It is a second-leading cause of cancer-related deaths among women in worldwide. ⁽²⁾ Occult breast cancer is a rare type of breast cancer which the incidence is reported about 0.1% - 1.0% of all breast cancer patients. ^(3, 4) This condition is presented by isolated metastatic axillary lymph node, which is confirmed by tissue pathology, with no lesion of primary breast cancer detectable on physical examination, mammography, and ultrasound.⁽⁴⁾

Many studies show that early detection of breast cancer with screening mammography can reduce death from breast cancer by earlier start in the course

of the disease, possibly before it spreads. ^(5, 6) Therefore, mammography and supplemental breast ultrasound are utilized in screening cases in clinical practice. Whereas mammography is the important tool for screening breast cancer, occult breast cancer is an exceptional condition. As a result of negative mammography and ultrasound findings in this breast cancer type, more advanced diagnostic modality as breast magnetic resonance imaging (MRI) is applied to be a further investigation.

Nowadays, technique and quality of images of breast MRI have improved significantly better than in the past, and dynamic contrast enhancement MRI has improved the sensitivity to diagnosis and evaluate breast cancer, so breast MRI is an important modality for this condition. ⁽⁷⁾ This leads us to study MRI findings in diagnosed occult breast cancer patients and determine association between MRI findings and second-look ultrasound, and retrospective review of the initial mammography.

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Materials and methods

Population

This was a descriptive design and retrospective review of breast MRI of diagnosed occult breast cancer patients by presenting metastatic axillary lymph node on pathological report with no clinical and radiologic evidence (mammography and ultrasound) of primary breast cancer at King Chulalongkorn Memorial Hospital, the Thai Red Cross Society from January 2010 to January 2023.

Imaging technique and interpretation

All the patients performed at least two standard views on screening mammography: craniocaudal (CC) and mediolateral oblique (MLO) views. The supplemental breast ultrasound was also done.

The breast MRI was performed on one of the 1.5 Tesla (Magnetom Espree, Siemens), 3 Tesla (Ingenia, Philips) or 3 Tesla (Discovery MR750w, GE imaging system). All patients were in the prone position and using bilateral breast surface coils. The slice thickness was ≤ 2 mm (1 or 1.5 mm in post contrast study) with routine breast pulse sequences as follows; Pre-contrast: Axial- TSE T2WI without FS, STIR, T1WI 3D; Coronal -T1WI without FS Post-contrast dynamic study: Axial -T1WI 3D FS with and without subtraction, T1WI 3D high resolution, DWI and ADC; Sagittal- T2WI FS.

The MRI were reviewed using a medical grade diagnostic workstation with optimal window display via the picture archiving and community system (PACS, Synape version 4.3.2).

Blinded to the patient's information, an experienced breast imaging radiologist and researcher reviewed the breast MRI, second-look ultrasound, and retrospective review the initial mammography with a consensus imaging interpretation.

After completing imaging investigation, any suspicious findings from retrospective review mammography or second-look ultrasound in the area corresponding to suspicious enhancements on the breast MRI were confirmed by ultrasound-guided biopsy, mammography-guided biopsy or surgery.

Data collection

Hospital electronic medical records and synapses were searched for diagnosed occult breast cancer patients.

All breast MRI, second-look ultrasound and initial mammograms were retrospectively reviewed and

described findings according to ACR BI-RADS 5th edition and find correlation to the area of interest on breast MRI.

All protected health information (PHI) was encrypted and stored in password protected computer without traceable patient's data.

Statistical analysis

The data were analyzed by using statistical descriptive analysis. The results were presented by frequency and percentage.

Results

From January 2010 to January 2023, we identified sixteen patients who were diagnosed occult breast cancer by presenting metastatic axillary lymph node on pathological report with no clinical and initially negative mammography and ultrasound of primary breast cancer. Three patients were excluded from the study due to non-available breast MRI in PACS and one patient was excluded due to non-available initial mammography. Finally, twelve patients fulfilled the criteria and were enrolled in our study. All cases were pathologically proven to have axillary lymph node metastases before undergoing breast MRI. The information about all cases are presented in **Table 1**.

The MRI findings were categorized into foci, non-mass enhancement (NME), and mass. The NME was described distribution and internal enhancement pattern, and the mass was described shape, margin, and internal enhancement characteristics according to ACR BI-RADS 5th edition. The kinetic curve enhancement (KCE) of both NME and mass on MRI findings were also analyzed.

The breast MRI studies of all twelve diagnosed occult breast cancer patients showed eight cases (67.0%) with negative primary breast cancer on MRI study and no suspicious malignant finding on retrospective mammography.

The Neuromuscular electrical stimulation (NMEs) were detected in 3 of 12 cases (25.0%) with focal distribution, heterogeneous internal enhancement, and type II KCE in all cases. The only one case (8.0%) was found mass with irregular shape, irregular margin, heterogeneous enhancement, and type II KCE on MRI study. Second-look ultrasounds were performed in all abnormal MRI cases.

Table 1. Summary of the twelve patients with axillary nodal metastasis and negative mammogram and ultrasound (diagnosed occult breast cancer).

	MRI				Retrospective review mammography	Location	Treatment
	Foci	Non-mass enhancement	Mass	Second-look ultrasound			
1	(-)	(-)	(-)	(-)	(-)	(-)	ALND + CMT + RT
2	(-)	(-)	(-)	(-)	(-)	(-)	ALND + CMT + RT
3	(-)	(-)	(-)	N/A	(-)	(-)	ALND + CMT + RT
4	(-)	(-)	(-)	N/A	(-)	(-)	ALND + CMT + RT
5	(-)	(-)	(-)	N/A	(-)	(-)	ALND + CMT + RT
6	(-)	(-)	(-)	N/A	(-)	(-)	Mastectomy + ALND + CMT + RT
7	(-)	(-)	(-)	N/A	(-)	(-)	Mastectomy + ALND + CMT + RT
8	(-)	(-)	(-)	N/A	(-)	(-)	N/A
9	(-)	(+) Focal, Heterogeneous, Type II KCE	(-)	(+) Irregular indistinct hypoechoic mass	(+) Focal asymmetry with a group of amorphous calcifications	RUOQ	Mastectomy + ALND + CMT + RT
10	(-)	(+) Focal, Heterogeneous, type II KCE	(-)	(-)	(+) Focal asymmetry	LUOQ	Mastectomy + ALND + CMT + RT
11	(-)	(+) Focal, Heterogeneous, Type II KCE	(-)	(+) Irregular indistinct hypoechoic mass	(-)	LUOQ	BCS + ALND + CMT + RT
12	(-)	(-)	(+) Irregular, Heterogeneous, Type II KCE	(+) Irregular indistinct hypoechoic mass	(-)	LUOQ	BCS + ALND + CMT + RT

KCE, kinetic curve enhancement; RUOQ, right upper outer quadrant; LUOQ, left upper outer quadrant; N/A, not available
BCS, breast conserving surgery; ALND, axillary lymph node dissection; CMT, chemotherapy; RT, radiation therapy.

One of three NMEs cases on MRI studies showed an irregular indistinct hypoechoic mass at left upper outer quadrant on second-look ultrasound with no suspicious finding on retrospective review mammography (**Figure 1**). The second case showed negative finding on second-look ultrasound, but focal asymmetry on retrospective mammography was detected (**Figure 2**). The last case showed both irregular indistinct hypoechoic mass at right upper mid part on second-look ultrasound and focal asymmetry with a group of amorphous calcifications on retrospective mammography (**Figure 3**).

The only one case with irregular shape, irregular margin, heterogeneous enhancing mass, and type II KCE on MRI study, demonstrated an irregular indistinct hypoechoic mass on second-look ultrasound (**Figure 4**). There is no suspicious finding on retrospective review mammography in this case.

The most cases of diagnosed occult breast cancer had no suspicious finding on breast MRI, second-look ultrasound, and retrospective mammography (8 of 12 cases, 67.0%), followed by non-mass enhancement (3 of 12 cases, 25.0%) and mass (1 of 12 cases, 8.0%).

The common abnormal finding on second-look ultrasound was irregular hypoechoic masse which was

found in 3 cases (3 of 12 cases, 25.0%), while this finding was not detected on screening ultrasound.

The abnormal finding on retrospective mammography was found only focal asymmetry (2 of 12 cases, 17.0%).

After completing imaging investigation, most case studies with negative MRI and other imaging were treated by axillary lymph node dissection (ALND) + chemotherapy + radiation (5 out of 8 cases, 63.0%) followed by mastectomy + ALND + chemotherapy + radiation (2 out of 8 cases, 25.0%) which pathological reports showed no malignancy in one case and another case showed metastatic carcinoma, and loss follow up in one case (12.0%). Two cases with focal asymmetry on retrospective mammography were treated by mastectomy + ALND + chemotherapy + radiation (2 of 2 cases, 100.0%) which pathological reports showed invasive ductal carcinoma and invasive lobular carcinoma. Two cases with irregular hypoechoic mass on second-look ultrasound were treated by breast conservative surgery + ALND + chemotherapy + radiation (100.0%) which pathological reports showed invasive ductal carcinoma and invasive mammary carcinoma.

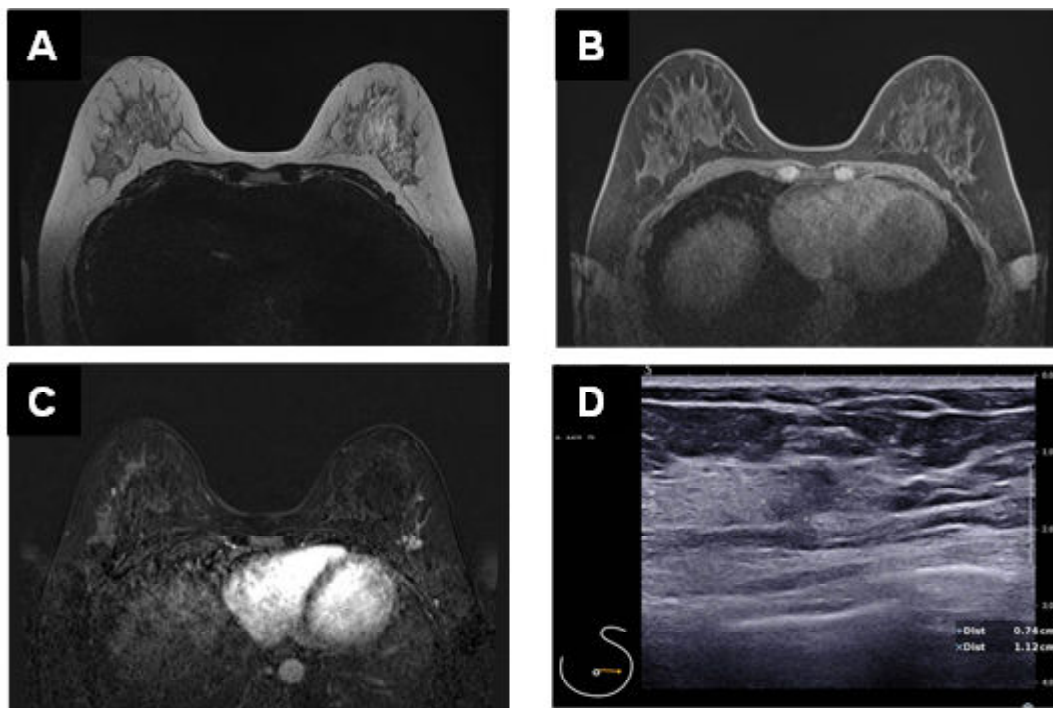


Figure 1. A 43-year-old female with diagnosed occult breast cancer. Breast MRI, axial T2WI (A), T1WI fat-suppressed (B), T1WI fat-suppressed post-contrast with subtraction (C) showed a focal heterogeneous non-mass enhancement at left upper outer quadrant. The second-look ultrasound (D) showed corresponding irregular indistinct hypoechoic mass at left upper outer quadrant. The pathological result was invasive ductal carcinoma.



Figure 2. A 66-year-old female with diagnosed occult breast cancer. Breast MRI, axial T2WI (A); T1WI fat-suppressed (B); post-contrast with subtraction (C); and axial MIP (D) showed a focal heterogeneous non-mass enhancement at left upper outer quadrant. The retrospective mammogram (E, F) showed corresponding focal asymmetry at left upper outer quadrant (arrow). The pathological result was invasive lobular carcinoma.

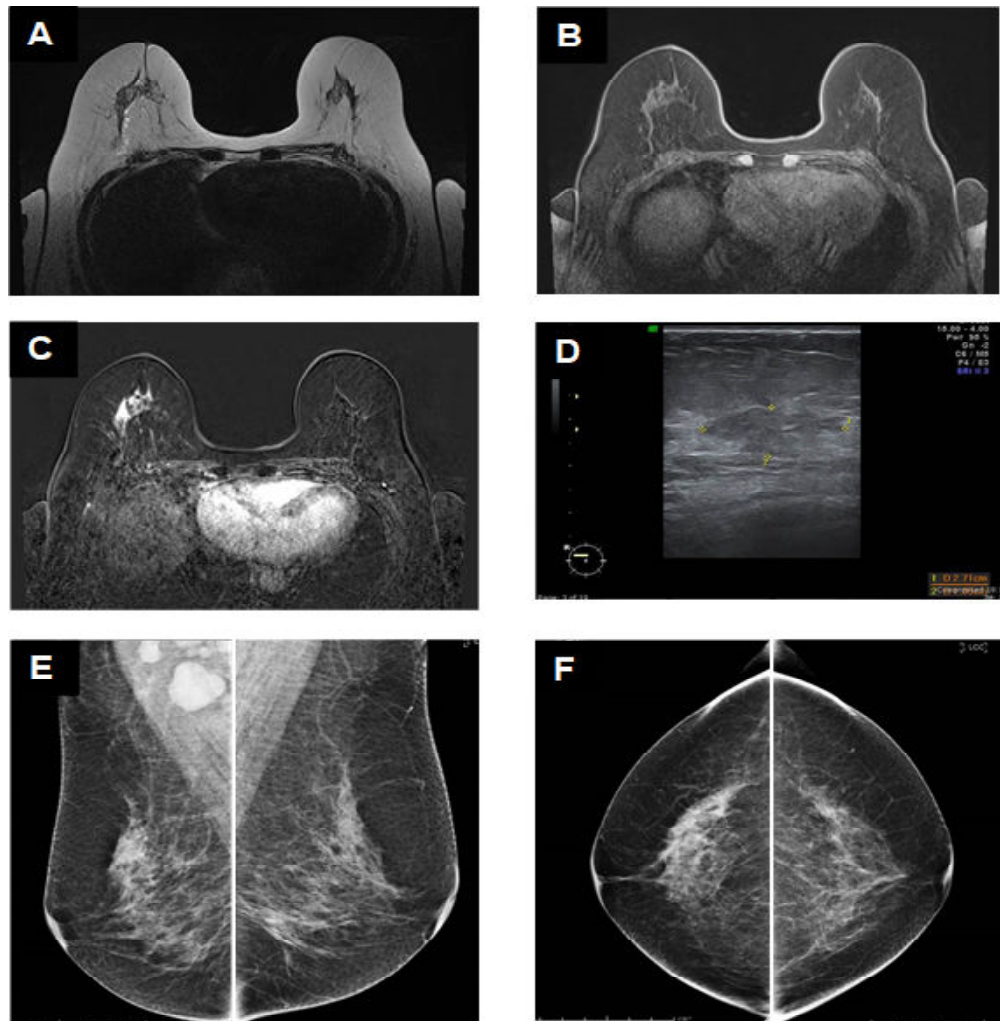


Figure 3. A 74-year-old female with diagnosed occult breast cancer. Breast MRI, axial T2WI (A); T1WI fat-suppressed (B); and post-contrast with subtraction (C) showed focal heterogeneous non-mass enhancement at right upper outer quadrant (RUOQ). Second-look ultrasound (D) demonstrated an irregular indistinct hypoechoic mass at RUOQ. The retrospective mammogram (E, F) showed corresponding focal asymmetry with a group of amorphous calcifications at RUOQ (arrow). The pathological result was invasive ductal carcinoma.

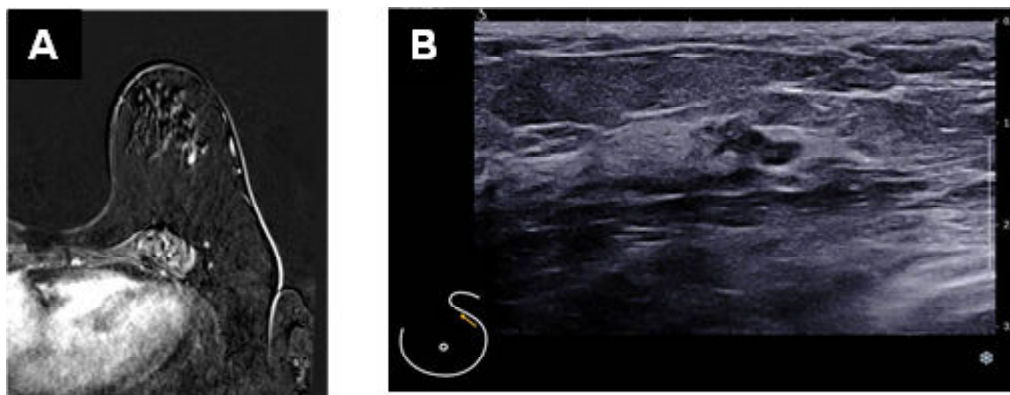


Figure 4. A 66-year-old female with diagnosed occult breast cancer. The initial ultrasound showed negative finding in both breasts (not shown). Breast MRI, axial T1WI fat-suppressed post-contrast with subtraction (A) showed a heterogeneous enhancing mass corresponding to an irregular indistinct hypoechoic mass at left upper outer quadrant on second-look ultrasound. The pathological result showed invasive mammary carcinoma (B).

Discussion

Occult breast cancer is defined as axillary lymph node metastasis with no primary tumor identified in the breast on physical examination, mammography, or ultrasound.⁽⁸⁾ In clinical practice, mammography is the recommended modality for screening and early detection of breast cancer, but it is a crucial perceptual task and error prone.⁽⁹⁾ The previous studies had reported about 20.0% - 30.0% of false negative rates^(10, 11) and low sensitivity of mammography about 45.0%.⁽¹²⁾

Recently, the advanced diagnostic modality as contrast-enhanced breast MRI was developed to be a high sensitivity tool and applied to identify primary breast cancer, especially in patients with negative mammography and ultrasound study.⁽⁷⁾

Previous studies reported that detection rate of breast MRI in occult breast cancer patients is wide range about 37.0% - 86.0%.^(7, 13) In our study, breast MRI demonstrated suspicious findings in 33.0% of all diagnosed occult breast cancer patients. The most common suspicious finding on breast MRI in our study is focal heterogeneous non-mass enhancement with type II KCE (75.0%) followed by irregular heterogeneous mass with type II KCE (25.0%) of all positive suspicious finding on breast MRI which is different from prior studies. In prior studies demonstrated enhancing mass to be the most common suspicious finding followed by regional enhancement.^(14, 15)

Of all occult breast cancer cases with focal heterogeneous NME (3 cases), 33.0% showed

irregular hypoechoic mass on second-look ultrasound, 33.0% showed focal asymmetry on retrospective review mammography, and 33.0% showed suspicious lesion on both second-look ultrasound and retrospective review mammography. Only one case with irregular heterogeneous mass with type II KCE on breast MRI demonstrated irregular hypoechoic mass on second-look ultrasound. All these cases were not found suspicious finding on screening ultrasound.

The false-negative cancer or missed cancer was defined as retrospectively review on the recent imaging showed suspicious finding but negative interpretation. The missed cancer was reported about 10.0% - 30.0% of breast cancer.⁽¹⁶⁾

Based on prior study review, we found that the most common mammographic finding associated with a false negative cancer is a mass without calcification (about 54.0% of all missed cancers), followed by calcifications (with or without associated mass), asymmetry, and architectural distortion.⁽¹⁷⁾ According to our study, the common missed findings were focal asymmetry and focal asymmetry with suspicious calcifications.

Many factors impacted the interpretation of mammography such as technical problems with poor compression or positioning may lead to inability to see and characterize lesions, patient-related factor with dense breast parenchyma causing lesion obscuration, location of lesion near edge of tissue or edge of image, large breast, perceptual error, and interpretive error by radiologists can cause missed finding.^(18 - 20) The quality of mammography should be first considered before diagnostic interpretation.

During imaging interpretations, up to 60.0% - 80.0% error by radiologist is error in perception (not detect abnormality when it is present). The factors of perceptual errors are associated with obscured by dense breast tissue, one-view findings, small lesions, low-density lesions, developing asymmetries, and subtle calcifications.

In our study, we found one case of false negative cancer which showed focal heterogeneous enhancement of NME and initial mammography reported no suspicious finding in the breast. The associated focal asymmetry was found on retrospective mammography, and it was proved as malignancy. Two cases of focal heterogeneous NME on MRI with negative finding on initial ultrasound, were found irregular heterogeneous mass on second-look ultrasound. They were proved as malignancy.

The false negative is not only found in detection but also in misinterpretation to assess the lesion as benign. ⁽²¹⁾ One case in our study reported focal asymmetry with amorphous calcification as BI-RADS 3. MRI showed focal heterogeneous enhancement of NME in area associated with that lesion and proven malignancy.

Limitations of the study include its retrospective nature, limited sample size and the dependence of ultrasound operator skill and experience. The information of the ultrasound was retrospectively reviewed per images available obtained by an attending radiologist at that time. Additionally, the time interval between initial mammogram, ultrasound and MRI may change the tumor conspicuity because malignant tumor usually shows rapid growing. However, in this study all patients performed MRI within 1 month after initial images.

Conclusion

Contrast-enhanced breast MRI is a powerful tool for evaluating occult breast cancer in patients with axillary nodal metastasis and negative mammography and ultrasound. MRI improves localization of the lesion in case of interpretation error on mammogram and ultrasound. Thus, radiologists play an important role in detection and interpretation the suspicious lesions. Occult breast cancer can be truly occult, or we missed. Some mistakes or errors make a more valuable lesson to learn.

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Conflict of interest statement

Each of the authors has completed an ICMJE disclosure form. None of the authors declare any potential or actual relationship, activity, or interest related to the content of this article.

Data sharing statement

The data sets generated or analyzed during the present study are available from the corresponding author on reasonable request.

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