Radiological imaging in the diagnosis of granulomatous mastitis: the role of MRI

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Aims and objectives

Granulomatous mastitis (GM) is an uncommon benign inflammatory condition of the breast. Idiopathic granulomatous mastitis, originally described by Kessler and Wolloch in 1972 (1), represents a sub-group of GM with unknown etiology. The remaining cases of GM are associated with infectious conditions such as fungal infections, actinomycosis, histoplasmosis, brucellosis, and tuberculosis in particular, as well as with other conditions such as Wegener's granulomatosis and sarcoidosis (2). The real incidence of GM is unknown, with only a few hundred cases reported in the literature (3). Clinically, radiologically, and even cytologically it can be confused with malignancy, requiring histopathological examination for a definitive diagnosis (4, 5). Conventional radiological findings are non-specific and exhibit a wide variation. In this regard, MRI emerges as an important diagnostic tool providing certain advantages over other imaging modalities in the differential diagnosis of breast conditions. In this study, conventional radiological vs. MRI findings are presented in patients with GM, with an emphasis on the contribution of MRI to the differential diagnosis of GM.
Methods and materials

This retrospective study involved a total of 29 GM patients between 20 and 69 years of age (mean age: 35.14) who were diagnosed between 2009 and 2014 in our clinic. The study protocol was approved by the Institutional Ethics Committee. Majority of the patients (90%) was in the reproductive age and none had a history of autoimmune disease, sarcoidosis, or systemic tuberculosis. Two patients had a family history of breast cancer.

The symptoms had been present for 15 days to 4 months before a diagnosis was made and they included breast pain (26/29), palpable mass in the breast (23/29), erythema and inflammation (9/29). Three patients had sinus tract and one had nipple retraction. The condition was unilateral in all cases, with 20 being on the right side.

For 14 patients over 35 years of age, mammography (MG) was chosen as the initial diagnostic modality (Lorad M-IV, Hologic). In the remaining 15 patients less than 35 years of age, MG was not performed. All patients underwent an ultrasound (US) and a MRI examination, and their results were documented. High resolution US images (Xario SSA-660A, Toshiba) were obtained by a linear-array transducer with a center frequency of 7.5 MHz. MRI indications included exclusion of inflammatory cancer in treatment-resistant cases, further assessment in patients with inconclusive mammography and/or sonography results, and determination of the extent of the disease. MRI was performed after conventional examinations in all patients in a manner that would not result in any treatment delay. MRI examinations were performed with a 1.5-T whole-body imaging system (Signa Excite, GE Healthcare, Milwaukee, WI, USA). The patients were scanned in the prone position with the breast suspended in a four-channel breast coil. MR images were obtained in the transverse and sagittal planes with fat suppression. Pre-contrast transverse acquisitions were performed using a T1-weighted fast spin-echo sequence and transverse T2-weighted fast spin echo short-tau inversion recovery (STIR) imaging; and pre-contrast sagittal acquisitions were performed using a T2-weighted fast spin echo sequence imaging with fat suppression. Sagittal pre- and post-contrast dynamic imaging were performed using a 3D multi-phase Fast Gradient Echo pulse sequence called VIBRANT (flip angle 10º; minimum echo time 2.4; maximum echo time 14.0 msec; section thickness 3 mm with no intersection gap; field of view 20 cm; matrix size, 256x256; NEX 1; one signal acquired; imaging time, 1 minute for each phase). Additionally, transverse post-contrast T1-weighted images were acquired using the fast spoiled gradient-recalled-echo sequence in the same manner as it was used to acquire the pre-contrast images, without a change in the position of the patient. Subtraction images were done. The patients were given a bolus intravenous injection of gadolinium contrast (0.2 mmol per kilogram of body weight) with a power injector. Both morphological features and kinetic characteristics of the lesions were examined. All MR examinations were reviewed on high-resolution PACS monitors (General Electric Medical Systems).
Results

Mammography findings: Nine of the 14 patients who underwent MG had dense and heterogeneous dense parenchymal breast pattern. Nine patients had focal asymmetric densities, two had ill-defined nodular densities, 1 had diffuse increase in density, and two had no pathological findings with dense pattern. No pathological calcifications were observed.

Ultrasonography findings: Sixteen patients had ill-defined lesions with tubular extensions, 8 had well-demarcated lesions with posterior acoustic enhancement, three had parenchymal edema-heterogeneity, one had a mass lesion with irregular borders, and one had normal findings. All lesions exhibited heterogeneous hypoechochogenicity. Three had fistula tracts. Twelve patients had axillary lymph nodes with mild to moderate enlargement, echogenic hilus, and symmetric or asymmetric thick cortex. One patient had markedly enlarged lymph nodes with fatty hilus, which could not be clearly visualized. On Doppler examination, increased arterial and venous vascularization was evident at lesion level in 16 cases.

MRI findings: In 25 of the 29 participants, there were one or more separate or confluent lesions consistent with abscess formation with regular or irregular borders and marked circumferential contrast enhancement following IV Gad injection that were hyperintense in T2-weighted images (T2WI) and hypointense in T1WI with variable signal intensities depending on the protein content of the fluid (16/24 hyperintense at T2WI, and hypointense at T1WI; 5/24 intermediate at T1WI, and heterogeneous hyperintense at T2WI; 4/24 hypointense at T1WI, and heterogeneous hyperintense at T2WI, 1/24 heterogeneous hypointense at T1WI, and heterogeneous hyperintense at T2WI). On the same level with these lesions or their adjacency, areas with heterogeneous signal changes without well-defined borders or mass effect, and contrast enhancing segmental/regional heterogeneous non-mass like lesions were observed. The size of MRI lesions ranged from 5-6 mm to 5 cm. In four patients, no lesions were observed other than parenchymal heterogeneity and non-mass like segmental contrast enhancement. Kinetic analyses at non-mass like contrast enhancing areas, lesions and lesion walls showed Type 1 kinetic curves in 24 patients at all levels, Type 2 kinetic curves at lesion walls in four patients, and Type 3 kinetic curves at lesion walls and non-mass like contrast enhancing areas in one patient. The patient with Type 3 kinetic curves had a positive family history. MRI showed the presence of lesions in only one quadrant in 13 patients, while multiple quadrants were involved in 16. Twenty had peripheral, two had retroareolar, and seven had both peripheral and retroareolar involvement. Fistula tract was present in three patients. Sixteen patients had mildly or moderately enlarged axillary lymph nodes with symmetric or asymmetric thick cortex structure in MRI. A single patient had enlarged lymph nodes without echogenic fatty hilum.

Figure 1-4 shows some examples of imaging findings from study participants.
Twenty-six patients underwent a core biopsy, while three had excisional biopsy. Due to inconsistent radiological and core-biopsy findings in four patients, an additional excisional biopsy was performed. In those patients undergoing excisional biopsy, sampling from axillary lymph nodes was also performed. A diagnosis of tuberculosis associated GM was made in 10 patients and a diagnosis of cat-scratch disease associated GM was made in another patient, while no causative factors could be determined for the remaining 18 patients (Figure 5).

Conventional methods (US/US plus MG) could identify 16 out of 29 cases with lesions of benign and inflammatory origin. However, these methods could not distinguish the remaining 13 cases from malignancy (11 suspicious of malignancy, 2 highly suspicious of malignancy). In the MRI examination of these 29 cases, 24 were deemed benign and inflammatory in nature, 4 were considered suspicious for malignancy, and one was considered highly suspicious for malignancy.

Specificity of conventional methods and MRI in predicting granulomatous mastitis was 55.17% and 82.75%, respectively. Negative predictive value for MRI was 100%.
Fig. 1: Figure 1.a,c. Bilateral MLO mammography in a 35-year old patient presenting with palpable mass in the breast: (a) a nodular density surrounded by the peripheral fibroglandular tissue in the right breast; (b) US shows a heterogeneous hypoechoic lesion with tubular extensions; (c) axillary examination showing moderately enlarged lymph node with thickened cortex.
Fig. 2: Figure 1 d-h: Also in the same patient STIR axial (d), T1-weighed fat suppressed axial (e), T2-weighed fat suppressed sagittal (f), and T1-weighed fat suppressed postcontrast substruction sagittal (g) MR images showing a mass lesion with peripherally ring enhancement and irregular borders consistent with abscess formation. Type 1 kinetic curve from the kinetic analysis of the lesion wall (h).

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**Fig. 3:** Figure 2.a,d. A 42-year old patient presenting with breast pain. Bilateral CC graphy (a) showing asymmetric density increase, which is more prominent in the inner quadrant of the left breast. Ultrasound (b) showing a hypoechoic heterogeneous ill-defined lesion, and with tubular extensions. Postcontrast fat suppressed MIP reformatted axial (c) and T1 weighed fat suppressed postcontrast subtraction sagittal (d) MR images showing non-mass like segmental contrast enhancement. Type 1 kinetic curves obtained at the level of contrast enhancement (d).

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Fig. 4: Figure 3.a,e. A 40-year old patient presenting with palpable breast lesion. (a) Bilateral CC radiography showing asymmetric increase in density, which is more prominent in the right lateral quadrant of the right breast. Ultrasound showing (b) heterogeneous hypoechoic ill-defined lesions with tubular extensions. STIR axial (c), T2-weighted fat suppressed sagittal (d), and T1-weighted fat suppressed postcontrast subtraction sagittal (e) MR images showing parenchymal heterogeneous intensity changes, non-mass like regional contrast enhancement, and lesions less than 1 cm in diameter with peripheral contrast enhancement consistent with microabscess formation. Type 3 kinetic curves obtained from the adjacency of the lesions (e).

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Fig. 5: Figure 4.a,f. A 33-year old patient presenting with pain, erythema, discharge and nipple retraction in the breast. Bilateral CC radiography (a) showing thickening of the skin and asymmetric density increase more prominent in the inner quadrant of the right breast. US showing (b, c) heterogeneous hypoechoic ill-defined lesions with tubular extensions opening up in the skin. T2-weighed fat suppressed sagittal (d) T1-weighed fat suppressed postcontrast dynamic sagittal (e), postcontrast MIP reformatted sagittal (f) MR images showing parenchymal heterogeneous intensity changes, non-mass like regional contrast enhancement, and multiple lesions with peripheral contrast enhancement consistent with abscess formation. Moderately enlarged axillary lymph nodes (e).

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Fig. 6: Figure 5.a,b. Granulomatous structures characterized by granulomatous reaction (H&E x100), histiocytes, and giant cells (H&E x200)

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Conclusion

GM is an uncommon inflammatory condition of the breast characterized by granuloma and abscess formation (2) generally affecting young women in the reproductive age and occurring mostly in the first five years following labor (2-7). Until now, the largest reported patient series is that of Buefettal et al., which included 20 patients with a diagnosis of idiopathic granulomatous mastitis (7). Thus, to our knowledge, our study represents the largest patient series with GM in the literature.

Absence of complaints or clinical signs suggestive of inflammation despite the presence of palpable mass in the majority of the patients with GM and enlarged axillary lymph nodes in a certain proportion of the same subjects may lead to a suspicion of breast cancer. In addition, GM may not be readily differentiated from the breast cancer radiologically (1-17). It generally involves one breast, although bilateral involvement has also been reported (2, 5, 7, 9). In our study, all of our cases had unilateral granulomatous mastitis where peripheral involvement was predominating; and the proportion of patients with retroareolar involvement was higher than that reported previously (6, 10, 11).

Several studies have reported on MG and US findings in GM patients and a general consensus exists as to the conventional radiological signs in GM. MG generally shows non-specific signs, the most common of which is the focal asymmetric increased density with ill-defined borders and mass-effect or irregular masses with ill-demarcated borders (3,8,10-14). Mammography has a low sensitivity in this condition, particularly when one considers the younger women population affected. The abovementioned findings may not be detected in women with dense breast pattern (3, 6, 12, 15). Mammographic findings in our study are in line with previous reports, and the lesion could not be detected in two of our patients who had dense breast pattern.

Since US is commonly used for the initial assessment of young females with palpable breast lesions, most of the patients with GM undergo a US examination prior to diagnosis. The most common US findings in these patients is heterogeneous hypoechoic ill-defined lesions with tubular extensions, as in our study (3, 6, 10, 12, 14). However, other findings such as hypoechoic lesions with regular or irregular contours and posterior acoustic enhancement or shadowing, parenchymal heterogeneity, and distortions may also be seen, in addition to thickening of the skin and diffuse parenchymal edema (12). One specific advantage of US is its ability to facilitate aspiration in case of suspected fluid collection. However, it should be borne in mind that cytology alone may not be adequate to exclude an underlying malignancy or to diagnose granulomatous mastitis, necessitating a histopathological confirmatory diagnosis (3). In addition, a normal US examination cannot exclude a diagnosis of GM, as exemplified by one of our cases with asymmetric densities in mammography that were not detected by US.

MRI is an imaging modality with a high sensitivity and specificity for breast lesions allowing the detection and assessment of the extension of inflammatory breast
conditions. Literature data on the use of MRI in GM is scarce with a variety of different definitions used for the description of MRI findings (2, 3, 5, 7, 13, 15). In suspected cases of GM, MRI examination should not lead to a delay in biopsy and may be used as a complementary diagnostic method in addition to US and mammography, in order to exclude a diagnosis of inflammatory breast cancer in cases with symptoms of treatment-resistant mastitis (17). However, MRI can help in detecting lesions that cannot be visualized by US and mammography due to parenchymal edema. In addition, since GM generally affects younger females, MRI may also be useful in cases where mammography or US is inconclusive due to the character of the breast parenchyma. The most common MRI finding in our study was multiple non-mass like heterogeneous abscesses of different sizes with peripheral ring contrast enhancement in post-contrast dynamic series and without marked borders or mass effect with heterogeneous signal changes in the pre-contrast series (25/29 patients). These observations are similar to those reported by Kocaoglu et al. and Gautier et al. Previous studies have reported variable kinetic curve analysis results across different patients and different lesions (2, 5, 15). In the study by Gautier et al., non-mass like contrast-enhanced areas were generally associated with Type 1 kinetic curves, while Type 3 was the dominant kinetic curve in areas with annular contrast enhancement. In the present study, circumferential contrast enhancement was mostly associated with Type 1 kinetic curves, while our findings were consistent with previous reports of non-mass like contrast enhancement. In this study, MRI could accurately and clearly identify the typical findings of the inflammatory process in most of the patients and specificity of MRI was 82.75% for the diagnosis of granulomatous mastitis.

Finally, several limitations of our study should be mentioned including its retrospective design. In addition, examination of all MRI studies by the same experienced radiologist precludes assessment of the inter-observer variability.

In conclusion, MRI, as a complementary diagnostic tool to clinical and conventional radiological findings, assist in diagnosis and differentiation from malignant processes in patients with GM. However, histopathology remains essential for definitive diagnosis and appropriate management plan.
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