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THE ROLE OF DIFFUSION-WEIGHTED MR IMAGING IN EVALUATING THE RESPONSE TO STEROID THERAPY IN IDIOPATHIC GRANULOMATOUS MASTITIS LESIONS

İDİYOPATİK GRANÜLOMATÖZ MASTİT LEZYONLARINDA STEROİD TEDAVİSİNE YANITIN DEĞERLENDİRİLMESİNDE DİFÜZYON AĞIRLIKLI MR GÖRÜNTÜLEMENİN ROLÜ

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ABSTRACT

Objective: The aim of this study was to investigate the role of diffusion-weighted magnetic resonance imaging (DW MRI) with an apparent diffusion coefficient (ADC) map in evaluating the response to treatment of steroid-treated idiopathic granulomatous mastitis (IGM) lesions.

Materials and Methods: This retrospective study included 99 lesions of 58 female patients (average age: 32.91 years; range: 22–55 years) with biopsy-proven IGM. Patients were treated with oral and topical steroids. All pre-treatment and post-treatment MR examinations were evaluated. The maximal size of the masses and non-mass enhancement (NME) lesions were measured. Patients were classified as complete response (CR), partial response (PR), and non-response (NR) according to the dynamic contrast-enhanced (DCE) MR findings after treatment.

Results: ADC values of areas occupied by IGM (0.933±0.317x10^{-3} mm^2/sec) were lower than contralateral normal parenchyma (1.259±0.423x10^{-3} mm^2/sec). Twenty-two (22.22%) of the lesions were in the NR group, 30 (30.30%) in the PR group, and 47 (47.47%) in the CR group. There was no significant difference between the pre-treatment ADC values in NR, PR, and CR groups (p=0.228). There was a significant difference between the pre-treatment and post-treatment ADC values in the PR groups (p=0.001).

Conclusion: DW MR imaging in IGM is a useful method to monitor the response to treatment. However, it is not successful in predicting response to treatment.

Keywords: Granulomatous Mastitis, Magnetic Resonance Imaging, Diffusion-Weighted MRI, Treatment Response, Steroid Therapy

ÖZET

Amaç: Bu çalışmanın amacı, idiyopatik granülomatöz mastit (İGM) lezyonlarının steroit tedavisine yanıtını değerlendirmede, görünür bir difüzyon katsayısı (ADC) haritası ile difüzyon ağırlıklı manyetik rezonans görüntülemenin (DW MRG) rolünü araştırmaktı.

Gereç ve Yöntem: Bu retrospektif çalışma, biyopsi ile kanıtlanmış İGM'li 58 kadın (ortalama yaş 32,91 yıl, aralık=22-55 yıl) hastanın 99 lezyonunu içeriyordu. Hastalar oral ve topikal steroidlerle tedavi edildi. Tüm tedavi öncesi ve tedavi sonrası MR incelemeleri değerlendirildi. Kitlelerin ve kitlesel olmayan kontrastlanmaların maksimum boyutu ölçüldü. Tedavi sonrası dinamik kontrastlı (DK) MR bulgularına göre hastalar tam yanıt, kısmi yanıt ve yanıtsız olarak sınıflandırıldı.

Bulgular: İGM (0,933±0,317x10^{-3} mm^2/sn) tarafından işgal edilen alanların ADC değerleri, kontralateral normal parankimden (1,259±0,423x10^{-3} mm^2/sn) daha düşüktü. Lezyonların 22'si (%22,22) yanıtsız, 30'u (%30,30) kısmi yanıt ve 47'si tam yanıt (%47,47) grubundaydı. Üç tedavi grubunda tedavi öncesi ADC değerleri arasında anlamlı bir fark yoktu (p=0,228). Kısmi yanıt grubunda tedavi öncesi ve tedavi sonrası ADC değerleri arasında anlamlı fark vardı (p=0,001).

Sonuç: İGM'de DW MR görüntüleme, tedaviye yanıtı izlemek için yararlı bir yöntemdir. Ancak tedaviye yanıtı tahmin etmede başarılı değildir.

Anahtar Kelimeler: Granülomatöz mastitis, Manyetik rezonans görüntüleme, Difüzyon ağırlıklı MRG, Tedavi yanıtı, Steroid tedavisi

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INTRODUCTION

Idiopathic granulomatous mastitis (IGM) is a benign, recurrent, and rare inflammatory disease of the breast. It is most often diagnosed in women of childbearing age with a breastfeeding history. The most common clinical finding is a painful, unilateral palpable mass (1,2). Among imaging methods, mammography and ultrasound (US) are the preferred modalities. Imaging findings are nonspecific and vary according to the stage of the disease, as well as the degree of inflammation (3,4). Focal asymmetry is the most common finding in mammography. On US, IGM most often presents as a large, irregularly shaped, hypoechoic mass that is parallel to the skin (5,6). The sensitivity of magnetic resonance imaging (MRI) is high, and the most frequently reported findings are heterogeneous or a rim-enhancing mass and non-mass enhancement (NME) (3-8). IGM is an exclusion diagnosis and is histologically confirmed to distinguish it from malignancies and other inflammatory diseases of the breast. Histological examination reveals lobulocentric noncaseating granulomas with inflammatory cell infiltration. While abscess formations are frequently detected, necrosis and fibrosis are less noticeable features (9,10). Recently, medical treatment has been preferred in the first stage, with surgical treatment reserved for resistant cases. Steroids, methotrexate, and bromocriptine are medical treatment options and have been found useful (11-14). More than one treatment protocol may be required for complete regression (15). Spontaneous resolution can be seen after 6-12 months without any treatment (4,16). Recurrence occurs in both conservative and surgical treatment (15). Imaging is crucial in evaluating the response to treatment and detecting recurrence. Defining the extent of the disease, the response of lesions to treatment, and the presence of new lesions are important in evaluating the success of treatment (3,4). DW MRI is an examination technique based on measuring the mobility of water molecules in vivo to provide numerical data with ADC values without using contrast material. It analyzes the microscopic structure of tissues such as cellularity, membrane integrity, viscosity, organelles, and macromolecules (17).

The aim of this study is to investigate the role of DW MR imaging in evaluating treatment response in IGM lesions.

MATERIALS AND METHODS

This study is retrospective and was approved by Kartal Doktor Lutfi Kırdar Training and Research Hospital Ethics Committee (Date: 25.11.2020, No: 514/190/3). The requirement to obtain informed consent from patients was waived.

Patient population

Between June 2015 and November 2021, the results of MR examinations performed both before and after treatment on 65 patients with a diagnosis of IGM were evaluated. IGM diagnosis was proven by core biopsy in all patients. Microbiological testing (Gram, periodic acid-Schiff and Ziehl-Neelsen staining, mycobacterial cultures, fungal analysis with Grocott–Gomori methenamine silver staining) was performed to exclude other types of mastitis. Purified protein derivative skin test (PPD) and QuantiFERON test were also done to rule out tuberculous mastitis. Five patients were excluded from the study because new lesions developed in the breast after the treatment, and two patients' scans were not of optimal quality due to artifacts in the MR examinations. The remaining 58 patients and 99 lesions of these patients were included in the study. Patients were treated randomly with two methods. Thirty-one (53.44%) patients were treated with 0.4 mg/kg methylprednisolone once a day and 0.125% prednisolone pomad on weekdays. Twenty-seven (46.55%) patients were treated with 0.8 mg/kg of oral methylprednisolone once a day. Superficial abscesses with fluctuation were drained either on admittance or during the treatment.

MR imaging technique

MR examinations of all patients before and after treatment were performed on a 1.5 T system (Philips Ingenia, Philips Healthcare, Best, The Netherlands). Three-dimensional fat-saturated ultrafast spoiled gradient echo DCE sequences (FOV:342x342, matrix:342x340, FA:10, TR:5 TE:3, section thickness:2, section gap:1) were acquired. DCE sequences consisted of a total of five series, one of which was pre-contrast (90, 142, 194, 246, and 298 seconds after injection). Image parameters were FOV:342x342, matrix:342x340, FA:10, TR:5, TE:3, section thickness:2, section gap:1. Diffusion-weighted images were obtained with b-values of 0 and 1000 s/mm^2 (FOV:364x364, matrix:151x146, FA:90, TR:9400, TE:71, section thickness:3, section gap:3).

Examinations were performed with a dedicated phase array 16 channel breast coil in the prone position, and 0.1 mmol per kilogram of body weight gadoteric acid was used with an automated injector.

MR image analysis

MR evaluations were performed with consensus by two radiologists with six and nine years of experience in breast imaging (G.R, M.A.). All MR images were reviewed on the picture archiving and communication system of an EIZO GS520 workstation. Pre- and post-treatment MR examinations were evaluated.

Rim-enhancing lesions and mass lesions were considered masses. Masses and non-mass enhancements (NME) were noted. The characteristic features, maximal sizes, and average ADC values of the lesions detected in pre-treatment MR examinations were noted. These measurements were repeated by finding the corresponding

target lesions on MRI after treatment. Maximal lesion size was measured on the first DCE images, which were obtained after 90 seconds.

For ADC value measurements, the section with the longest diameter of the lesion was selected from the DCE MR images of the lesions. It was made manually by drawing the entire lesion by finding its equivalent from the ADC map. (Figure 1). The ADC measurement was not performed for lesions less than 1 cm in diameter in the MR examination before or after treatment. The ADC value was measured from the contralateral normal breast parenchyma using a 100 mm^2 ROI. Pre-treatment and post-treatment MR examinations were correlated, and ADC measurements of lesions showing complete regression with an ROI of 100 mm^2 from the area corresponding to the localization of the lesions were performed. The areas occupied by these lesions were found with the help of the residual architectural distortion. The localization of lesions that do not cause structural distortion was found by referring to the distance to the nipple, adjacent fat lobules, and vascular structures.

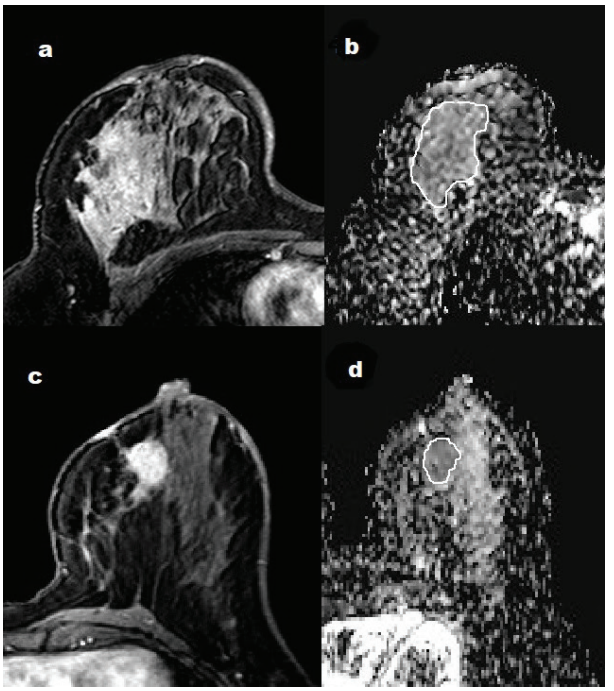

Figure 1: A 27-year-old female patient with IGM diagnosis has NME in the middle outer quadrant of the right breast in fat-suppressed T1W MR images (a). ADC values were calculated manually by drawing around the entire lesion in the section where the lesion was best seen (b). Contrast-enhanced fat-suppressed T1W MR images of a 28-year-old female patient with a diagnosis of IGM with a mass in the middle inner quadrant of the left breast (c). The ADC value was measured manually by drawing the entire lesion from the ADC map value (d).

Treatment response

Patients were divided into three groups according to the DCE MRI findings after treatment: complete response (CR), partial response (PR), and non-response (NR). The disappearance of all lesions in post-treatment MR imaging was accepted as CR. A ≥30% reduction in the maximal size of the targeted lesions was accepted as PR.

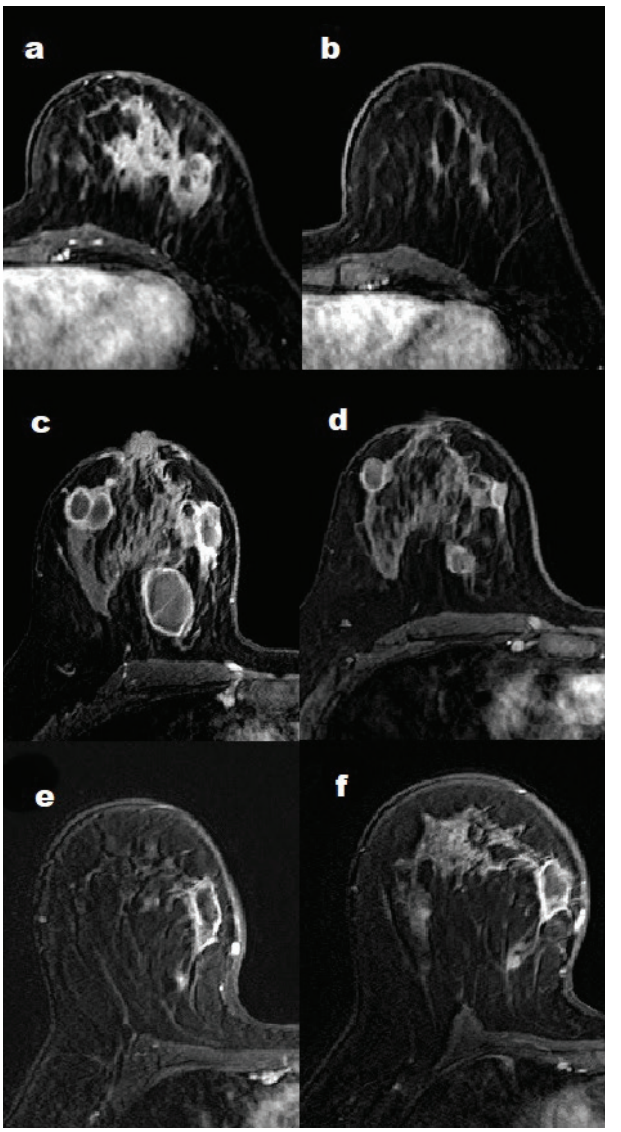

Figure 2: DCE MR images of patients in groups CR, PR, and NR according to treatment response. In the NR group, the heterogeneously enhanced mass in the left breast in a 30-year-old patient disappeared on MRI after 83 days (a,b) In the PR group, the size of 3 abscesses in the right breast of a 41-year-old female patient significantly regressed on MRI 54 days later (c,d). In the NR group, there was no significant change in the size of the abscess in the right breast of the 38-year-old female patient on MRI performed 146 days later (e,f).

Masses that showed resolution after treatment but had NME in the space they occupied were also included in the PR group. Targeted lesions that showed a <30% reduction, stability, and increased maximal size were evaluated as NR (18) (Figure 2). Since there was no lesion for comparison on MRI before treatment, patients who developed new lesions after treatment were excluded from the study.

Statistical analysis

Percentage, mean, and standard deviation were the statistics used to evaluate the descriptive findings. The one-sample Kolmogorov–Smirnov test was performed to determine whether the groups conformed to a normal distribution. Normally distributed results were evaluated using a paired t-test. Results not conforming to a normal distribution were evaluated using the Mann-Whitney U test to compare groups that did not show normal distribution. Wilcoxon signed-rank test was used to compare dependent groups and Kruskal Wallis test was used to compare three independent groups. One-way ANOVA was used to evaluate independent triple groups. Pearson's correlation test was used to evaluate within-group agreement. P-values <0.05 were considered statistically significant.

RESULTS

This study included 58 patients (mean age: 32.91 years; range: 22–55 years) with a total of 99 lesions. Post-treatment MR examinations of these patients were made after an average of 128 days (range: 27–233). In pre-treatment MR examinations, 72 (72.72%) of the lesions were masses, while 27 (27.27%) were NME.

Of the 58 patients, 25 (43.10%) were in the CR, 20 (34.48%) were in the PR, and 13 (22.41%) were in the NR group.

After treatment, 47 (47.47%) of the lesions were in the CR group, 30 (30.30%) in the PR group, and 22 (22.22%) in the NR group (Table 1). Nine (12.5 %) mass lesions included in the PR group disappeared in post-treatment MR imaging with residual NME in the same location. The mean maximal size of the lesions was 35.65±18.27 mm before treatment and 14.20±17.09 mm after treatment, and it decreased significantly after treatment (p=0.000).

Pre-treatment ADC values of areas occupied by IGM (0.933±0.317x10^{-3} mm^2/sec) were lower than those of contralateral normal parenchyma (1.259±0.423x10^{-3} mm^2/sec). There was a significant increase in ADC values of the PR group after treatment (p=0.001) (Table 2).

There was no significant difference between the pre-treatment ADC values in the CR, PR, and NR groups (p = 0.228). There was a significant difference in ADC values between PR and CR (p=0.017), PR and NR (p=0.041), and CR and NR (p=0.000) groups after treatment. There was no significant difference between the post-treatment ADC values of the CR group and the ADC values of the contralateral normal parenchyma (p=0.60).

Table 1: Mean size and response groups of lesions

Groups	Pretreatment mean size (mm±SD)	Posttreatment mean size (mm±SD)	CR	PR	NR
All lesions (n=99)	35.65±18.27	14.20±17.09*	47 (47.47%)	30 (30.30%)	22 (22.22%)
Mass (n=72)	33.00±16.52	13.08±15.51*	34 (47.20%)	22 (30.55%)	16 (22.22%)
NME (n=27)	42.74±20.99	16.22±20.30*	13 (48.14%)	7 (25.92%)	7 (25.92%)

*: p=0.000, NR: Non-response, PR: Partial response, CR: Complete response, NME: Non-mass enhancement

Table 2: Mean ADC and p values of groups

Lesion groups	Pre-treatment ADC (x10^{-3} mm^2/sec)	Post-treatment ADC (x10^{-3} mm^2/sec)	p value
Contralateral normal parenchyma (n=58)	1.259±0.423	1.367±0.567	0.18
All lesions (n=99)	823.85±299.51	1028.3±559.55	0.000
NR (n=22)	0.882±0.228	0.852±0.406	0.277
PR (n=30)	0.861±0.178	1.140±505	0.001
CR (n=47)	1.002±0.401	1.305±0.446	0.000
Mass (n=38)	0.918±0.357	1.102±0.443	0.001
NME (n=14)	0.973±0.169	1.294±0.571	0.008

NR: Non-response, PR: Partial response, CR: Complete response

DISCUSSION

IGM is a persistent, recurrent inflammatory disease often seen in women of childbearing age.

Response time to treatment is long and problematic, and recurrence is common (1,2). The duration of the complete disappearance of the lesions with conservative treatment ranges from 2 to 24 months (4). MR examination has a very high sensitivity in IGM imaging and can successfully show the extent of the disease. It is also successful in evaluating response to treatment and detecting recurrence (3,4,8).

In our study, there was a similar response to treatment in both NME and mass. This shows that with steroid therapy, mass and NME respond similarly to treatment; thus, characteristic features of lesions have no prognostic benefit in determining response to treatment. A study conducted by Altunkeser et al. showed that the characteristic features of IGM lesions, including MR imaging findings, do not provide any benefit for predicting treatment success (19).

We found that the ADC values of IGM lesions were lower than normal parenchyma and consistent with previous studies (3,20,21). Intense inflammatory cell infiltration without necrosis and abscess formation in areas occupied by IGM may be the cause of diffusion restriction.

According to the results of our study, the lack of significant difference between the pre-treatment ADC values in the CR, PR, and NR groups shows that the ADC values are not useful in predicting the response to treatment.

According to our results, DW-MR examination appears to be a good biomarker as a method of detecting changes in the microenvironment of lesions in the response of IGM to steroid treatment. The advantage of this method is that it does not require contrast material and does not contain radiation.

The limitations of our study are the small number of patients and the lack of agreement between observers. In addition, lesion responses after treatment were not evaluated histopathologically.

In conclusion, based on the findings of our study, ADC values are useful in monitoring response to treatment. ADC values and characteristic features of the lesions are also not useful in predicting treatment success. However, the findings in our study need to be supported by further studies.

Ethics Committee Approval: This study was approved by Kartal Doktor Lütfi Kırdar Training and Research Hospital Ethics Committee (Date: 25.11.2020, No: 514/190/3).

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