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Imaging Findings in Idiopathic Granulomatous Mastitis (IGM) among Women in Sulaimani, The Kurdistan Region of Iraq

Alla Abdulrahman [1*], Kawa Abdulla Mahmood [2], Lana R. A. Pshtiwan [3], Mahabad Abdalaziz Salih [4]

[1] Breast Center and Department of Surgery, Shar Teaching Hospital, Sulaimani, Kurdistan Region, Iraq.

[2] Radiology, Department of Surgery,Shar Teaching Hospital & College of Medicine,University of Sulaimani, Sulaimani, Kurdistan Region-Iraq.

[3] Breast Imaging Specialist, Arab Board General Radiology, Shar Teaching Hospital-Breast center, Sulaimani, Kurdistan Region, Iraq.

[4] Lecturer at college of Medicine, University of Sulaimani, Sulaimani, Kurdistan Region, Iraq.

***Correspondence:** Alla Abdulrahman Ahmed, **E-Mail:** alla.ahmed@univsul.edu.iq,mobile:+9647717261048

ABSTRACT

Background: Idiopathic Granulomatous mastitis (IGM) is known as a rare condition, but it can mimic significant breast lesions like cancer. Variable nonspecific characteristics are present in IGM imaging. **Objectives**: The current study aimed to find the imaging characteristics of IGM among women of Sulaimani City in the Kurdistan Region of Iraq. **Patients and methods**: A retro prospective observational study was performed on 80 patients with IGM admitted to the Breast Center of Shar Hospital, from January 2014 to May 2022. The inclusion criterion was patients diagnosed histopathologically with IGM. Exclusion criteria were secondary granulomatous processes and incomplete patient data. We also reviewed ultrasonography (US), mammography, and magnetic resonance imaging (MRI) findings.

Results: Mean ages of patients was 35.8 (SD 5.7) years, and most of them (81.3%) were between 31 and 45 years of age. Most of participants were married and multiparous. Both breasts were nearly equally affected. Most patients (75%) presented with pain, followed by mass (70%). The commonest US finding was multiple hypoechoic masses and collections with tubular extension. Focal asymmetric increased density was the most frequent mammographic finding. MRI findings were asymmetric signal intensity change 10.0%, non-mass-like enhancement10.0%, type 1 enhancement 12.5%, and BI-RADS 3 in 10.0% of the patients. The BI-RADS score of most women who had MRI was upgraded.

Conclusions: Imaging characteristics of IGM are variable; the US and mammography are helpful as initial exams. MRI gives more details on the disease and can be used to assess the extent of the disease, especially in complicated cases, and monitor treatment.

Keywords: BIRADS, Idiopathic granulomatous mastitis, Secondary mastitis, Imaging findings, Radiological findings, Retrosepctive study, Sulaimani, Ira.

INTRODUCTION

Idiopathic granulomatous mastitis (IGM) is a rare benign chronic inflammatory disease of the breast. Kessler and Wolloch first reported the condition in 1972 [(1)]. The IGM primarily affects childbearing women, especially breastfeeding or postpartum women [(2)]. Although its etiology is unclear, studies suggested autoimmune disease or responses to hormonal, including oral contraceptive drugs, trauma, and metabolic processes [(2,3)]. By definition, the IGM is a diagnosis of exclusion from bacterial infections or histopathological biopsy findings of malignancies [(1,4)]. Further, IGM is histopathologically characterized by the nonnecrotizing granulomatous formation mainly confined to lobules of mammillary glands [(1-3)].

Besides, it is locally infiltrated by plasma cells, multinucleated giant cells, lymphocytes, neutrophils, and epithelioid histiocytes with organized micro abscess formations.

The IGM is usually aggressive and frequently shows properties of inflammatory breast tumors and infectious mastitis; thus, its diagnosis is usually delayed. Medical imaging of the breast shows varied features depending on the time the images were taken, prior interventions, and the extent of inflammation [(2)].

The strategy for breast imaging for diagnosing IGM is based on the patients' ages, risk factors, and clinical features. Further, ultrasonography (US), mammography, and magnetic resonance imaging (MRI) are helpful imaging modalities [(5)].

However, the core-needle biopsy, with or without the fine needle aspiration (FNA) for cytological examination and culture and sensitivity (C/S), is usually needed to exclude breast infections and malignant breast tumors [(6)].

The IGM can show up with variable nonspecific characteristics in imaging which usually looks like the appearance of breast malignancy or inflammatory diseases. Besides, these variabilities may be due to variable histopathological features like inflammatory processes, micro abscess formations, and fibrosis [(5)].

The imaging techniques required for the diagnosis of IGM include the US and mammography with other imaging techniques tailored to the imaging findings and patient characteristics. The US performs the usual initial imaging assessment, followed by mammography with mediolateral and craniocaudal views if required [(5)]. Usually, the patient presents with a palpable mass, focal pain, and focal skin changes; therefore, the US with a linear high-frequency probe is almost always performed [(5,6)]. The limitation of the US and mammography are usually due to pain which limits the patient tolerance to pressure or compression from these techniques, or

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edema, which limits assessment of the breast parenchyma [5].

Although the US and mammography are usually sufficient for diagnosing IGM and directing the histopathological examination, the MRI offers more evaluation of aggressive, advanced, refractory IGM or identifying biopsy targets [5,7]. Further, MRI is also beneficial for monitoring or assessing the residual disease after therapy [5].

The current study aimed to find the imaging characteristics of IGM among women of Sulaimani City in the Kurdistan Region of Iraq.

PATIENTS AND METHODS

A retro-prospective observational study was performed on 80 patients who visited the Shar Hospital's breast center; 65 were retrospective from January 2014 to December 2020, and 15 were taken prospectively from January 2021 to May 2022. The patients were randomly selected by using a simple random sampling method. Histopathological diagnosis of all patients was made by proper incisional or excisional biopsies.

The inclusion criteria included patients diagnosed histopathologically with IGM and patients before treatment. However, the exclusion criteria included patients diagnosed with secondary granulomatous processes associated with tuberculosis mastitis, duct ectasia, fat necrosis, postsurgical granulomatous reactions against foreign materials, fungal or bacterial infections, sarcoidosis & patients with IGM after treatment. Also, patients with limited quality imaging or incomplete patient data were excluded from the study.

Detailed clinical features such as age, occupation, residence, marital status, and obstetrical and gynecological history were recorded. Reviews of the US, mammography, and breast MRI were performed. The ultrasonography, the mammography, and the MRI were done using a linear probe with a frequency of using Samsung HS60 US system, GE mammography Senographe 2010, and dedicated breast coil from Siemens Symphony 2004 and Phillips Ingenia S 2019 1.5 Tesla MR systems, respectively. Also, US, mammography, and MRI were reported by using BIRADS [8]. Breast density on mammography was also determined by using ACR [9].

Sample size estimation was performed using the "GPower 3.1" program, which yielded 80 samples; thence, the sample size of 80 patients was obtained when the effect size of 0.5, a P-value of ≤0.05, and study power of >95% were selected.

Ethical approval:

The Ethical Committee of the College of Medicine, University of Sulaimani approved the study proposal, and a formal acceptance letter was obtained from the Shar Hospital before starting the study. Also, the patients have informed consent for their inclusion in the study.

Statistical analysis

The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (SPSS) version 25 for windows. Qualitative data were defined as numbers and percentages. Chi-Square test and Fisher's exact test were used for comparison between categorical variables as appropriate. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as means and SD, and independent sample t-test was used for comparison between groups. P value ≤0.05 was considered to be statistically significant.

RESULTS

The mean of the patients' ages was 35.8 (SD 5.7) years, ranging from 23 to 55 years. Further, the majority were married, multiparous, unemployed, and lived in the middle socioeconomic class, either in urban or semi-urban areas. The disease affected each breast side almost equally, with a slight predilection on the right side (**Table 1**).

Table (1): Sociodemographic characteristics of studied patients.

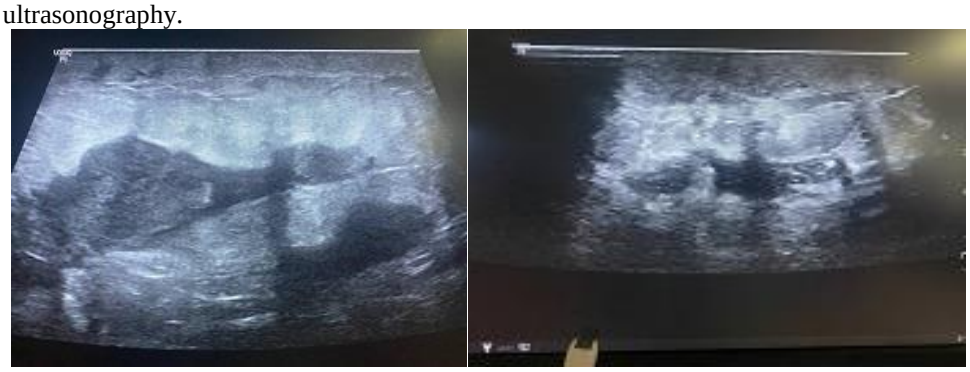
Patients' characteristics		Frequency	Percent
Age groups (year)	23-25	3	3.8
	26-30	10	12.5
	31-35	24	30
	36-40	28	35
	41-45	13	16.3
	46-50	1	1.3
	51-55	1	1.3
Resident	Urban	45	56.3
	Semi-urban	34	42.5
	Rural	1	1.3
Marital status	Married	78	97.5
	Unmarried	2	2.5
Occupation	Employed	13	16.3
	Unemployed	67	83.8
Socio-economic status	High	6	7.5
	Middle	64	80
	Low	10	12.5
Regularity of period	Regular	67	83.8
	Irregular	13	16.3
Parity	Nulliparous	3	3.8
	Uniparous	7	8.8
	Multiparous	70	87.5
Diseased side	Right	40	50
	Left	38	47.5
	Both	2	2.5
Total		80	100

The majority of women (75%) presented with pain, followed by mass (70%), signs of inflammation (13.8%), and nipple discharge (10%). The US findings vary, as stated in **Table 2**.

Table (2): US findings of the studied lesions.

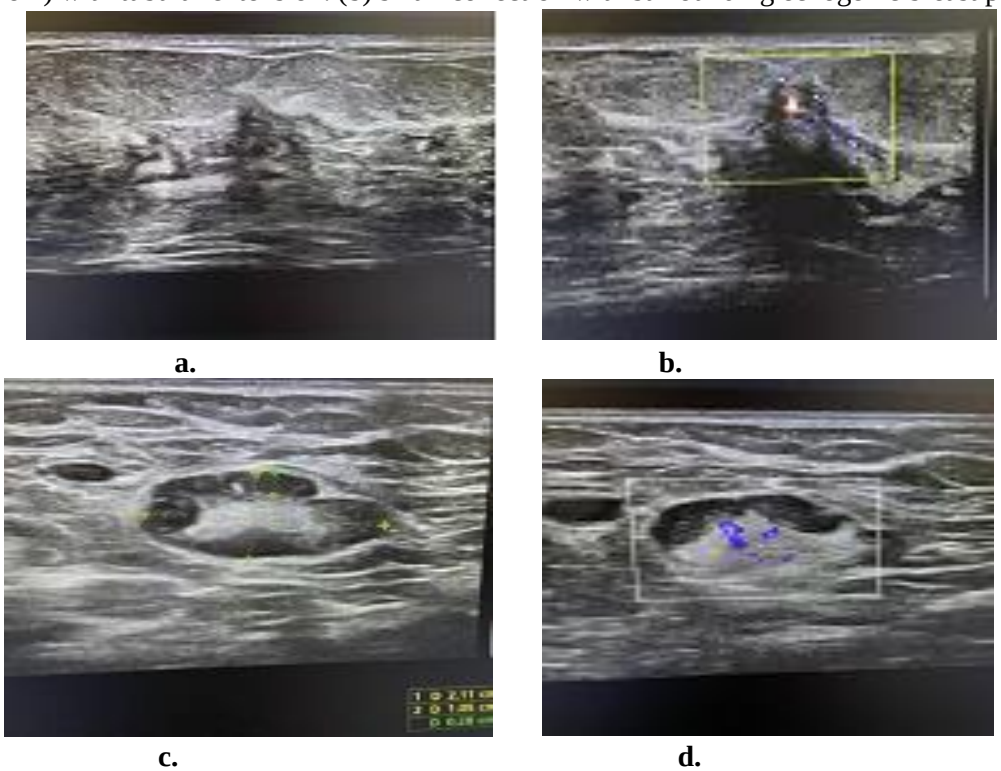
US findings	Frequency (%)	
Multiple hypoechoic masses and collections with a tubular extension*	40 (50)	
Irregular hypoechoic mass	15 (18.8)	
skin thickening	35 (43.8)	
Abscess**	15 (18.8)	
Fistula	2 (2.5)	
Lymph node involvement	Inflammatory***	60 (75)
	Suspicious	2 (2.5)
	No involvement	18 (22.5)
Color Doppler	Increased	20 (25)
	Not done	60 (75)
	Decreased	0 (0.0)
BIRADS on the US	1	8 (10)
	2	10 (12.5)
	3	49 (61.3)
	4	13 (16.3)

* as seen in Figure 1; ** as seen in Figures 2a and b; *** as seen in Figures 2 c and d; BIRADS = Breast Imaging Reporting and Data System; US = ultrasonography.



a. **b.**

Figure (1): IGM in a 37-year-old woman presented with right side breast pain and swelling (a) the US showed hypoechoic lesion (collection) with tubular extension. (b) small collection with surrounding echogenic breast parenchyma (edema).



a. **b.**

c. **d.**

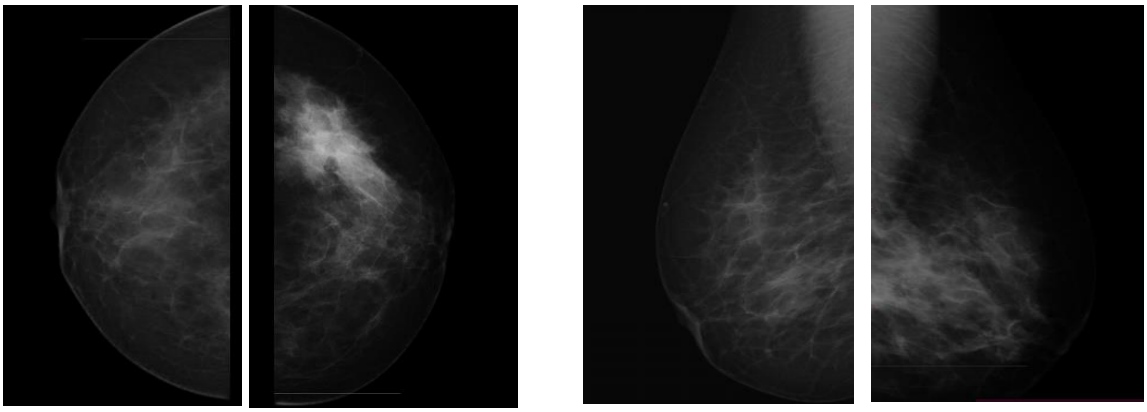
Figure (2): IGM in a 41-year-old patient who had a right side tender breast mass. (a) The US shows confluent micro abscess formation. (b) There is increased vascularity at the periphery of the lesion. (c) Ipsilateral enlarged lymph node oval in shape with preserved hilum, which is consistent with an inflammatory lymph node. (d) Positive hilar vascularity of lymph node.

The mammography was performed for 44 (55%) patients; the findings are listed in **Table 3**. The majority of women (61.3%) were afflicted with BIRADS 3; however, most (68.3%) had ACR C (**Table 3**).

Table (3): The frequencies of the mammography findings among the patients.

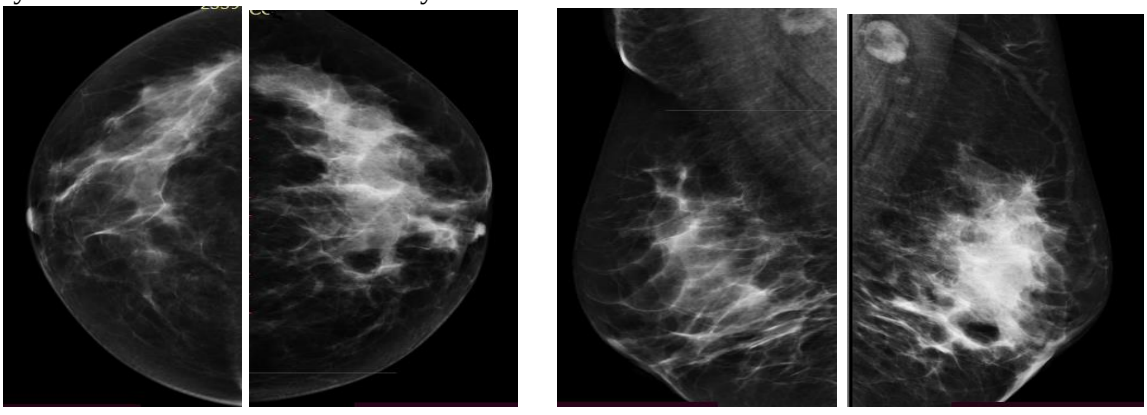
Mammography findings		Frequency (%)
Focal asymmetric increased density on mammography*		19 (43.1)
Normal finding		8 (18.1)
Irregular focal mass		8 (18.1)
Skin thickening		7 (15.9)
Diffuse asymmetric increased density**		5 (11.4)
Architectural distortion		4 (9.1)
Circumscribed mass		2 (4.5)
Calcification		2 (4.5)
BIRADS on mammography	1	7 (15.9)
	2	6 (13.6)
	3	27 (61.3)
	4	4 (9.1)
ACR on mammography	ACR A	1 (2.3)
	ACR B	11 (25.0)
	ACR C	30 (68.2)
	ACR D	2 (4.5)
Mammography was done for 44 (55%) of the patients		

ACR = the American College of Radiology; BIRAD = Breast Imaging Reporting and Data System,
*as seen in figure 3;** as seen in figure 4.



a. **b.**

Figure (3): IGM proved biopsy in a 39 years old patient presented with right left breast mass and pain. (a) mammographic craniocaudal (CC) view focal asymmetrical increased density in upper outer quadrant at 2-3 o'clock associated with distortion. (b) mammographic medial lateral oblique (MLO) view shows focal asymmetrical increased breast density.



a. **b.**

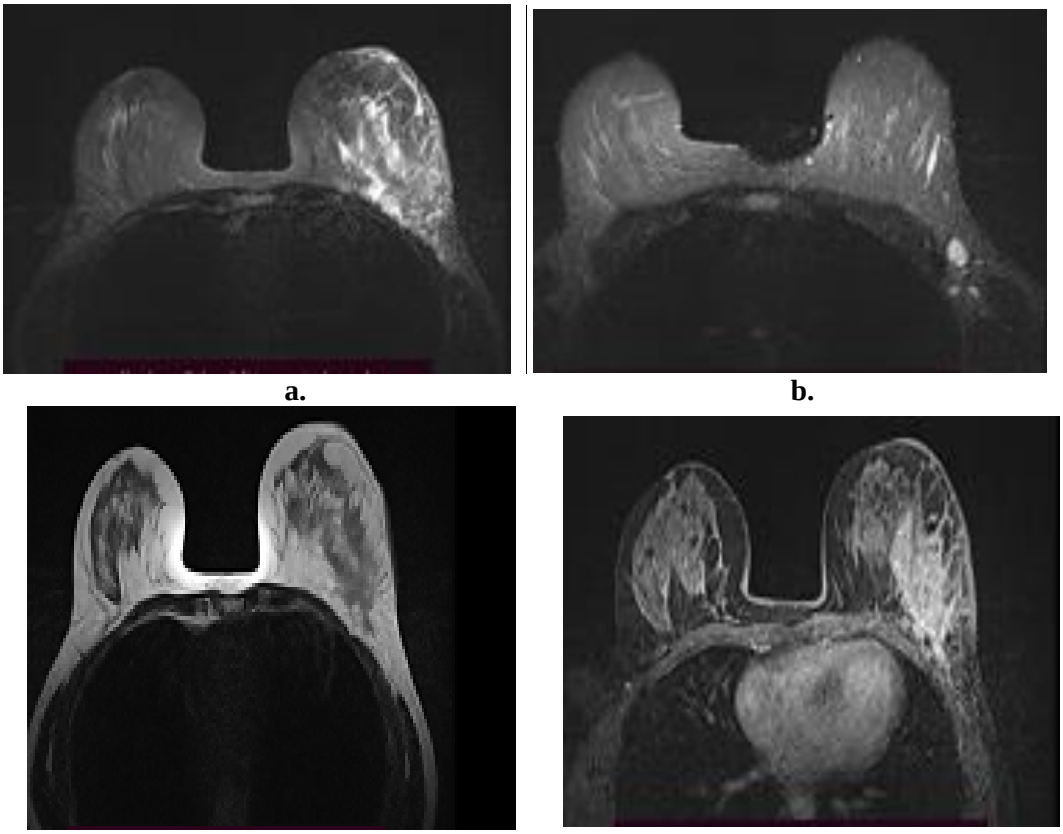
Figure (4): A 41-year-old patient presented with enlarging left side breast mass and tenderness. (a) mammographic CC view shows global increased asymmetrical breast density in the upper outer quadrant at 12-2 o'clock associated with distortion. (b) MLO view shows global asymmetrical increased density with bilateral single enlarged lymph node normal shape with the preserved fatty hilum.

Only 15 (18.8%) had an MRI examination; the results are listed in **Table 4**. Most of the MRI findings showed asymmetric signal intensity change, non-mass-like enhancement, type 1 enhancement, and BIRAD 3 in 53.3%, 53.3.0%, 86.6%, and 53.3% of the patients, respectively (**Table 4**).

Table (4): The frequencies of the MRI findings among the patients.

MRI findings		Frequency (%)
Lesion	Solitary lesion	5 (33.3)
	Multiple small lesions (<1 cm)	2 (13.3)
	Asymmetrical signal intensity changes	8 (53.3)
Enhancement	Peripheral ring enhancement	6 (40.0)
	Non-mass-like enhancement	8 (53.3)
	Heterogeneous enhancement	1 (6.6)
Enhancement curve	Type 1*	10 (66.6)
	Type 2**	2 (13.3)
	Type1 to type 2***	3 (20.0)
	Type 3****	0(0.0)
Lymph node involvement	Normal	6 (40.0)
	Unilaterally enlarged node*****	6 (40.0)
	Suspicious node******	3 (20.0)
BIRAD on MRI	2	4 (5.0)
	3	8 (10.0)
	4	3 (3.8)
MRI was done for 15 (18.8%) of the patients		

MRI = magnetic resonance imaging; * persistent enhancement pattern usually considered benign; ** initial uptake followed by plateau pattern considered concerning for malignancy; *** progression from type1to type 2; **** washout enhancement pattern initial increase and subsequent decrease in signal intensity considered strongly suggestive of malignancy; ***** length more than 1cm; ****** short axis diameter more than 1 cm and loss of central fatty hilum.



a. **b.** **c.** **d.**

Figure (5): A 35-year-old female presented with left side enlarging breast mass, pain, and skin inflammation. (a) MRI turbo inversion recovery magnitude (TIRM) sequence shows asymmetrical increased signal intensity (breast edema) with overlying skin thickening, trabecullation, and multiple dilated ducts toward the nipple. (b) TIRM sequence single left side enlarged lymph node with preserved fatty hilum. (c) T2 intermediate to high signal intensity changes confined to lateral quadrant (d) post-contrast, regional heterogeneous non mass like enhancement.

As shown in **Table 5**, the BIRAD score of most women who had MRIs was upgraded; however, three patients were downgraded when assessed by mammography, and five were downgraded when assessed by the US. Besides, three remained in the same score. The association between these changes was statistically insignificant.

Table (5): Association of BIRAD scores assessed by the US, mammography, and MRI.

BIRAD scores		BIRAD on MRI (%)			Total (%)	*P*-value
		2	3	4		
BIRAD on the US	**1**	2 (13.3)	0 (0)	0 (0)	2 (13.3)	0.198
	2	0 (0)	2 (13.3)	1 (6.7)	3 (20)	
	3	1 (6.7)	3 (20)	2 (13.3)	6 (40)	
	4	1 (6.7)	3 (20)	0 (0)	4 (26.7)	
BIRAD on mammography	**1**	2 (13.3)	0 (0)	0 (0)	2 (13.3)	0.216
	2	0 (0)	2 (13.3)	1 (6.7)	3 (20)	
	3	1 (6.7)	5 (33.3)	2 (13.3)	8 (53.3)	
	4	1 (6.7)	1 (6.7)	0 (0)	2 (13.3)	
Total		4 (26.7)	8 (53.3)	3 (20)	15 (100)	

BIRAD = Breast Imaging Reporting and Data System; MRI = magnetic resonance imaging; US = ultrasonography.

DISCUSSION

Idiopathic granulomatous mastitis (IGM) is a rare benign inflammatory breast disease with nonnecrotizing and noncaseating features on histopathological examination [10]. However, the precedent features do not prove the diagnosis of IGM unless excluding other differential diagnoses like foreign body granuloma, duct ectasia, secondary granulomatous mastitis, and malignancies histopathologically [1,4].

The current study found that most women were multiparous during childbearing. The current study finding agrees with other studies that suggested hypotheses for the causes of IGM because they are unknown, such as local inflammatory reaction to the extravasation of protein and lipid-rich secretions, oral contraceptive drugs, non-identifiable microorganisms, and autoimmune processes [2,3]. Further, during pregnancy and six years following pregnancy are associated with IGM [10].

Most of the women in the current study were presented with pain, mass, features of inflammation, and unilaterality. Similarly, the clinical features of IGM usually show up as a breast mass in one breast with association erythema, fever, lymphadenopathy, skin thickness, and fistula formation [10].

The current study's US findings are in agreement with the findings in the literature; the most common findings in the US were multiple hypoechoic masses and collections with a tubular extension and, to a lesser extent, an ill-defined irregular hypoechoic mass, abscess formations, and increased vascularity on Color Doppler if it has been performed. Further, the US findings are nonspecific for IGM; therefore, if the woman had a history of breastfeeding and multiple hypoechoic masses and collections with a tubular extension in the US, the plausible diagnosis is IGM. Moreover, only 25% of the women in the current study had a Color Doppler examination; however, all women who had Color Doppler (100%) had increased vascularity. Color Doppler US is not routinely performed, as only 40% of the patients in the study by ***Yildiz et al.*** had Color Doppler examination; however, if performed, it shows increased vascularity of as much as 100% [10]. This finding agrees with the current study in which.

The current study found that only 10.0% of women had a negative finding, although mammography was performed for 55% of the women. Further, IGM is usually a disease of reproductive age; thus, the sensitivity of the mammography is reduced because the breast tissue pattern is dense in this age group of women [11]. Contrary to the current study findings, mammography findings are nonspecific, and the result is negative for almost half of the patients [10].This can be explained by the fact that our patients are presented late and patients with doubtful diagnosis and complicated cases are refered for mammography. Nevertheless, other mammographic findings, such as Focal and diffuse asymmetric increased density, irregular focal mass, architecture distortion, calcification, and skin thickness in the current study, were similar to the literature [7,10,12–17].

Although MRI shows more details of the disease, it was performed only for 18.8% of the patients in the current study; all the women were already diagnosed with IGM histopathologically. The MRI findings in the current study were asymmetrical signal intensity changes, followed by solitary lesion and multiple small lesions. Also, most women who had breast MRI had a non-mass-like enhancement, followed by peripheral ring enhancement and heterogenous enhancement. The MRI findings of IGM are widely variable, including rim enhancement, strongly enhancing mass, or focal homogenous enhanced mass [7,10,12–17]. Although the sample size of the women who had an MRI was small, most of the BIRADS score was upgraded except for three downgraded in mammography and five downgraded in the US. However, the association

between these scores assessed by the imaging techniques was statistically insignificant. Therefore, we suppose that, as supported by literature [5,7], MRI is necessary to evaluate IGM in detail, guide biopsy targets, and monitor the disease during the treatment process. However, although the mentioned US, mammography, and MRI findings support the diagnosis of IGM, the definitive diagnosis is by taking excisional or incisional biopsies and histopathological examination [12-16].

IGM is a disease of middle-aged childbearing women who are married and multiparous. The majority have nonspecific clinical features like pain, mass, and features of inflammation. The imaging characteristics are also variable; US and mammography are helpful as initial exams. Color Doppler adds features of increased vascularity.The most common findings in US are multiple hypoechoic masses and collections with a tubular extension. Focal asymmetric increased density is the most frequent mammographic finding . The MRI findings are asymmetrical signal intensity changes, followed by solitary lesion and multiple small lesions, after giving contrast, most women have had a non-mass-like enhancement. MRI gives more details on the disease and can be used to assess the extent of the disease, monitor the treatment, and in complicated cases. However, the definitive diagnosis is by histopathological examination.

Limitations: Although the power of the current study was >95% for all 80 women, it has some limitations: 1) The first limitation is the retroprospective study design due to the time-consuming sample collection needed, and 2) The samples that had mammography and MRI were small.

RECOMMENDATIONS

1) Performing the same study prospectively; 2) Comparing all the radiological exams; and 3) Collecting equal sample sizes for all the radiological exams.

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