



DOI: 10.32768/abc.202310157-65



Review of Mammographic and Sonographic Features of an Uncommon Inflammatory Breast Disease: Granulomatous Lobular Mastitis

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ARTICLE INFO

Received:
25 November 2022
Revised:
10 January 2023
Accepted:
12 January 2023

Keywords:

Granulomatous lobular mastitis, Interconnecting tracts, Peripheral hyperechogenicity, increased vascularity

ABSTRACT

Background: Granulomatous lobular mastitis (GLM) is a rare inflammatory disease of the breast. Its clinical features and imaging findings often mimic malignancy. The aim of this study is to review the mammographic and ultrasound features of granulomatous lobular mastitis to help differentiate it from other diagnoses.

Methods: In our study, imaging data of 51 patients were reviewed retrospectively, who were diagnosed with granulomatous lobular mastitis by core needle biopsy and culture analysis.

Results: The mammographic findings of granulomatous lobular mastitis observed in our study group were focal or global asymmetry (52.6%), oval or round lesions with obscured margins (15.7%), irregular mass with indistinct margins (15.7%) and associated skin thickening (26.3%) with no specific pointers to differentiate from malignancy. The most common morphological abnormality on ultrasound was single or multiple collections with or without tracts (72.5%). Other morphological abnormalities were non-mass areas with tracts (25.5%), dilated ducts with debris (13.7%) and mass (3.9%). The common associated abnormalities were perilesional increased echogenicity (86.3%), increased peripheral vascularity (88.2%), intercommunicating tracts (76.5%) and axillary adenopathy (68.6%) and these ultrasound features were pointers to differentiate granulomatous mastitis from malignancy.

Conclusion: Granulomatous lobular mastitis has non-specific clinical and imaging features. Imaging, especially ultrasound as in our study, is found to be indispensable in diagnosing GLM and excluding other causes such as infective mastitis and malignancy.

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INTRODUCTION

Granulomatous lobular mastitis (GLM) is a rare inflammatory disease of the breast that was first described in 1972 by Kessler and Wolloch. It most commonly affects women in the childbearing age

group.¹ The etiology of GLM is still unknown. GLM has two forms: non-specific granulomatous lobular mastitis and specific granulomatous lobular mastitis. Specific GLM can be associated with chronic infections like tuberculosis, fungal infections, parasitic infections, corynebacterial infections, or complications of systemic inflammatory diseases like sarcoidosis, Wegener's granulomatosis, syphilis and foreign body reaction due to an implant.² It may mimic infective mastitis and malignancy based on clinical presentation and imaging findings, but

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diagnosis is usually made by histopathological examination.³

To the best of our knowledge, there is a lack of extensive work on the imaging findings of GLM to characteristically differentiate it from other diagnoses.

The aim of this study is to review the imaging findings particularly mammographic and ultrasound features of granulomatous lobular mastitis and to identify specific imaging features to differentiate it from malignancy.

METHODS

The present research is a single institute retrospective study approved by the institutional ethical and scientific committee. It was done between January 2019 and November 2022 in the Department of Radiology, Kovai Medical Center and Hospital, Coimbatore (Tertiary care hospital). Overall, 54 patients who were diagnosed with GLM by core needle biopsy in histopathology were included.

Out of the 54 patients, three patients were excluded from the study due to either association with tuberculosis or other infective organisms in the final culture analysis and hence were categorized as specific GLM. A total of 51 patients with the diagnosis of idiopathic or non-specific GLM were included. Imaging data of all 51 patients were reviewed retrospectively.

Equipment and protocols

Mammograms (MG) with supplementary ultrasound were performed in all patients above the age of 40 years and in patients between 30-40 years of age, with a clinical suspicion of malignancy. Standard craniocaudal and mediolateral-oblique projections were performed with a Siemens (Mammomat Inspiration) or Hologic 3 Dimensions equipment. Additional views had been performed as per the patient's study requirements.

Ultrasound was performed in all patients who were less than 30 years of age and when there was no clinical suspicion of malignancy in patients between 30 and 40 years of age. Ultrasound examinations of both breasts were performed using a high-frequency transducer (5 -18 MHz) in a Supersonic Aixplorer Ultimate or Supersonic Mach 30 ultrasound equipment. A conclusive diagnosis was obtained by ultrasound guided core needle biopsy using 14G Bard core biopsy needle and a minimum of 3 cores per biopsy.

Statistical analysis

All the data were entered in excel and analyzed using SPSS version 22. Categorical variables are presented as frequency and percentages.

RESULTS

In this study, 51 patients who were diagnosed with GLM in biopsy with negative culture analysis belonged to the age group between 20-64 years. Overall, 10/51 (19.6%) patients belonged to < 30 years age group, 32/51 (62.7%) patients belonged to 31-40 (17.6%) years age group and 9 patients belonged to >40 years age group. Out of 51 patients, 32 patients underwent only ultrasound and 19 underwent digital mammograms with ultrasound.

Mammographic Findings

The most common mammographic finding was focal or global asymmetry which was seen in 10/19 (52.6%) patients (Figures 1 & 2). Focal asymmetry with associated architectural distortion was found in 3 patients.

Other findings including irregular mass with indistinct margins, oval or round lesions with obscured margins, and associated skin thickening were also noted. None of the lesions showed calcifications. Table 1 shows the common and uncommon mammographic findings of idiopathic granulomatous mastitis.

Table 1. Mammographic findings in idiopathic granulomatous mastitis

Mammography (N= 19)	Number of patients (%)
Focal or global asymmetry	10 (52.6%)
Oval/round lesion with obscured margins	3 (15.7%)
Irregular mass with indistinct margins	3 (15.7%)
Associated skin thickening	5 (26.3%)
Calcifications	0

Ultrasound Findings

Single or multiple collections with or without tracts were the most common morphological abnormality in ultrasound that was seen in 37 patients (72.5%). Other morphological abnormalities were irregular hypoechoic non-mass area, irregular hypoechoic mass and dilated ducts. The common associated abnormalities were, perilesional hyperechogenicity, increased peripheral vascularity, skin thickening and axillary adenopathy. Table 2 and Figures 1 to 3 show the common and uncommon sonographic findings in GLM.

Sinus tracts extending to the skin surface were seen in 8/51 (15.7%) patients.

DISCUSSION

Granulomatous lobular mastitis is characterized by granuloma and abscess formation.⁴ Women commonly present with a unilateral breast mass that that may or may not be associated with pain, skin thickening and sinus formation.⁵

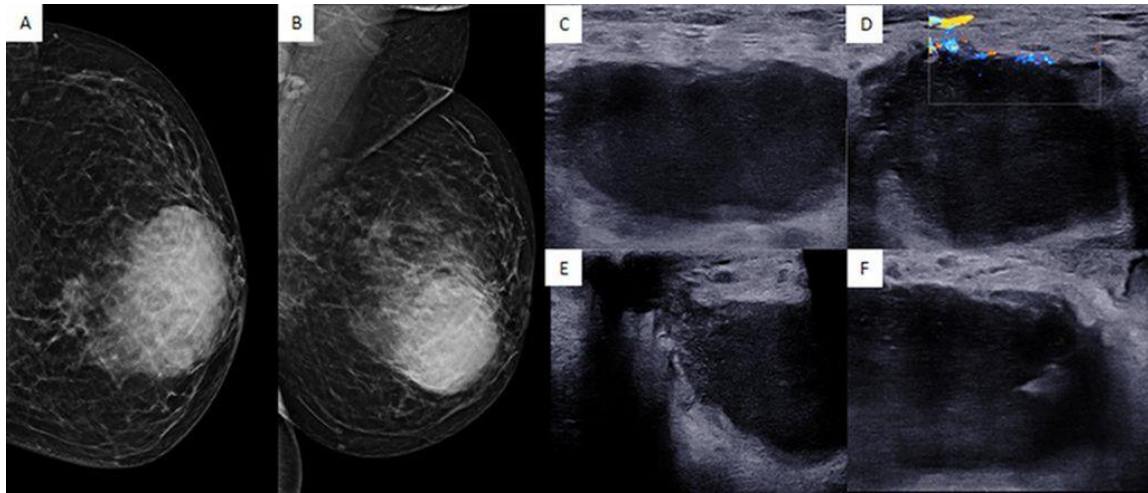


Figure 1. A 40-year-old patient, presented with a palpable lump in left breast with spontaneous left white nipple discharge for 1 month. A&B: Left craniocaudal and mediolateral-oblique mammogram showed an oval high-density lesion with obscured margins. C to E: On ultrasound, a large hypoechoic collection with moving internal echoes within. Few ducts appear to be communicating with the collections. F: USG guided aspiration of the collection was done and biopsy was taken from the wall of the collection. Histopathology was suggestive of granulomatous lobular mastitis.

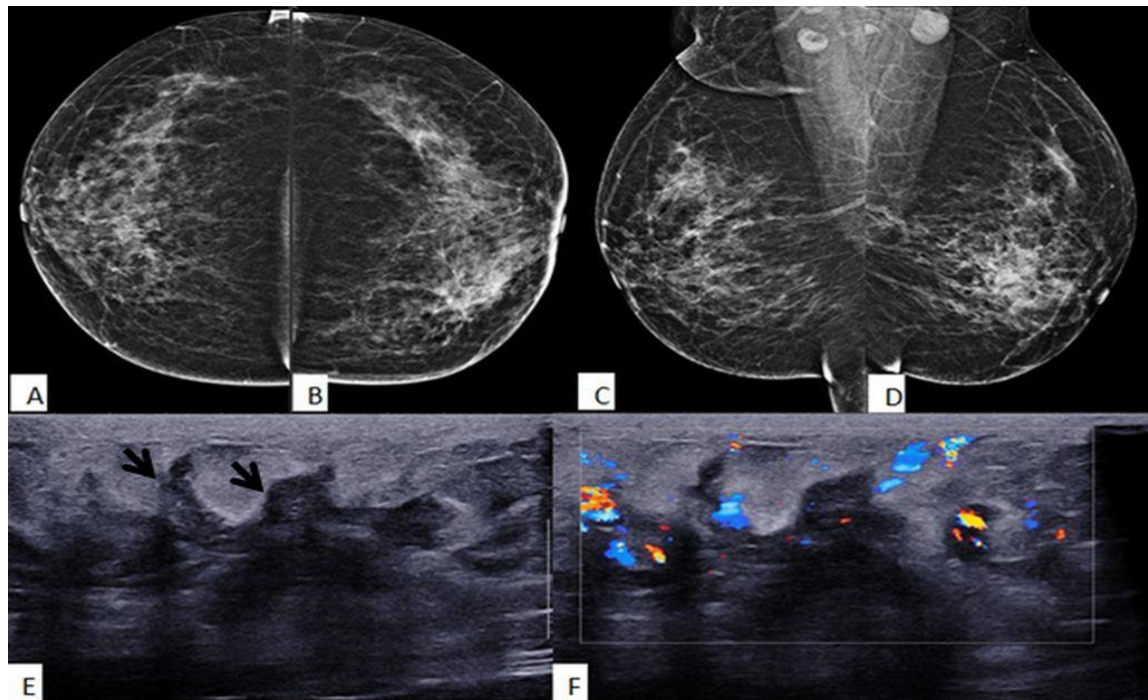


Figure 2. A 34-year-old patient, presented with a palpable lump in left breast. A to D: Bilateral craniocaudal and mediolateral-oblique mammogram showed a focal asymmetry in the inner central quadrant of left breast. E&F: On ultrasound irregular heterogeneous hypoechoic area with tubular extensions into the subcutaneous plane (black arrows) with surrounding inflammation and peripheral vascularity is noted. Biopsy was suggestive of granulomatous lobular mastitis.

Table 2. Sonographic findings in granulomatous lobular mastitis

Sonographic	Number of patients (%)
Morphological abnormalities:	
Single or multiple collections with or without tracts	37 (72.5%)
Irregular hypoechoic non-mass area	13 (25.5%)
Dilated	7 (13.7%)
Mass	2 (3.9%)
Associated features:	
Perilesional parenchymal hyperechogenicity	44 (86.3%)
Peripheral vascularity	45 (88.2%)
Skin thickening	24 (47.1%)
Axillary lymphadenopathy	35 (68.6%)



The etiology has been uncertain, and it had been suggested that GLM results from a local autoimmune response to an initial insult to the ductal epithelial cells, which causes extravasation of luminal secretions into the lobular stroma, leading to inflammatory processes in stromal tissue with accumulation of lymphocytes, macrophages, and subsequent granuloma formation.⁶

GLM is commonly associated with hyperprolactinemia and shows increased incidence in non-white women.^{7,8} Several studies have found a strong association between IGM and a history of pregnancy and lactation, with most patients reporting having a pregnancy within 5 years before the diagnosis.^{1,4,8,9} All our patients who were < 40 years of age had a history of lactation within 10 years. Five of our patients were on antidepressants resulting in hyperprolactinemia.

Our study shows GLM is usually unilateral and predominantly involves peripheral location, with few of the cases showing bilateral as well as retroareolar and subareolar involvement. Similar findings were described by Oztekin PS *et al.*¹⁰, Memis *et al.*¹¹, and Aghajanzadeh *et al.*¹²

The most common findings in our study on mammography were focal or global asymmetry with or without architectural distortions. Oztekin PS *et al.*¹⁰, Memis *et al.*¹¹, Yilmaz *et al.*¹³, and Fazio *et al.*¹⁴ also described ‘focal asymmetric density’ as the most frequent mammographic pattern. Han *et al.*¹⁵ reported ‘multiple small masses’ or a ‘large focal asymmetric density’ as the most common finding.

Three of our patients showed oval lesions with obscured margins and three of the patients showed irregular masses with indistinct margins. Lee *et al.*¹⁶ described an irregular ill-defined/obscured mass as the most common finding in their study.

Though mammographic findings are non-specific, they are helpful in differentiating malignancies that mimic GLM by ruling out suspicious microcalcifications or masses and all our patients who underwent mammography did not show any suspicious microcalcifications.

Single or multiple collections with or without tracts were the most common morphological abnormality in ultrasound, similar to the studies by Memis *et al.*¹¹ and Gautier *et al.*⁷ The second most common morphological abnormality was irregular hypoechoic non-mass area with tubular extensions and tracts. These findings were concordant with other studies reported by Han *et al.*¹⁵, Yilmaz *et al.*¹³, Lee *et al.*¹⁶, and Manogna *et al.*¹⁷. The tracts/tentacles explain the insinuating nature of IGM around the breast lobules. Seven patients had dilated ducts.

The common associated abnormality on ultrasound irrespective of morphological abnormality was perilesional hyperechogenicity and increased peripheral vascularity which were seen in 86.3% and 88.2% of patients, respectively.

Associated inflammatory changes such as skin thickening, sinus tracts and axillary lymphadenopathy were also observed. Whenever there was an abnormal axillary lymph-node, the nodes showed only diffuse cortical thickening with increased vascularity.

Additional findings such as heterogeneous breast parenchyma, a circumscribed hypoechoic mass and parenchymal distortion with acoustic shadowing but without a discrete mass were described by Hovanesian Larsen *et al.*¹⁸ and Dursun *et al.*¹⁹ Table 3 shows differentiating clinical and imaging features between infective mastitis and granulomatous lobular mastitis.

Table 3. Differentiating features of infective mastitis and granulomatous lobular mastitis.

Features	Granulomatous lobular mastitis	Infective mastitis
Clinical background	Develops after cessation of lactation commonly within 5 years of childbirth	Commonly seen during lactation
Constitutional symptoms	Disproportionately less compared to the extent of the disease	Prominent feature at presentation
Clinical examination	Local inflammatory changes are absent/less	Local inflammatory changes like erythema, tenderness and skin edema are more pronounced
Imaging	Interconnecting tracts, sinuses in between collections/ non mass area are more specific	Seen as focal mastitis or inflammatory mass representing evolving abscess/ frank abscess. Interconnecting tracts are uncommon
Course	Does not resolve with antibiotics	Generally, resolves with a course of sensitive antibiotics



The differentiation of IGM from aggressive malignancy such as inflammatory breast cancer is necessary, since these malignancies can have similar clinical profiles and imaging findings such as focal

asymmetry, skin edema or thickening, and axillary lymphadenopathy.²⁰

Table 4 shows the differentiating features between granulomatous lobular mastitis and malignancy.

Table 4. Differentiating features between granulomatous lobular mastitis and malignancy.

Feature	Granulomatous mastitis	Malignancy
Age group	Younger age more common	Middle and older age
Morphological abnormalities	Collections, non-mass abnormality and ductal abnormalities more common Presence of collections – specific finding that rules out malignancy When seen as non-mass areas or ductal abnormality, interconnecting tracts peripheral hyper-echogenicity and increased vascularity – specific for granulomatous mastitis	Non-circumscribed mass with or without calcifications is more common No collections. May present as necrotic mass When seen as non-mass areas or ductal abnormality, central vascularity and absence of surrounding inflammation – pointer for malignancy
Lymph-nodes	When enlarged, will have diffuse cortical thickening and increased vascularity	Asymmetrical cortical thickening, non-hilar blood flow, loss of fatty hilum – more specific for malignancy
Diagnosis	Biopsy from the wall or the periphery of the abnormality yields the diagnosis	Biopsy from the abnormality yields the diagnosis

In diagnostic evaluation, ultrasound is always performed either as an only modality or as a supplementary examination with mammogram and the characteristic ultrasound findings in GLM include

hypoechoic tracts connecting the irregular collections and extending to the subcutaneous plane. On color Doppler, there is peripheral vascularity with surrounding inflammation (Figure 3).

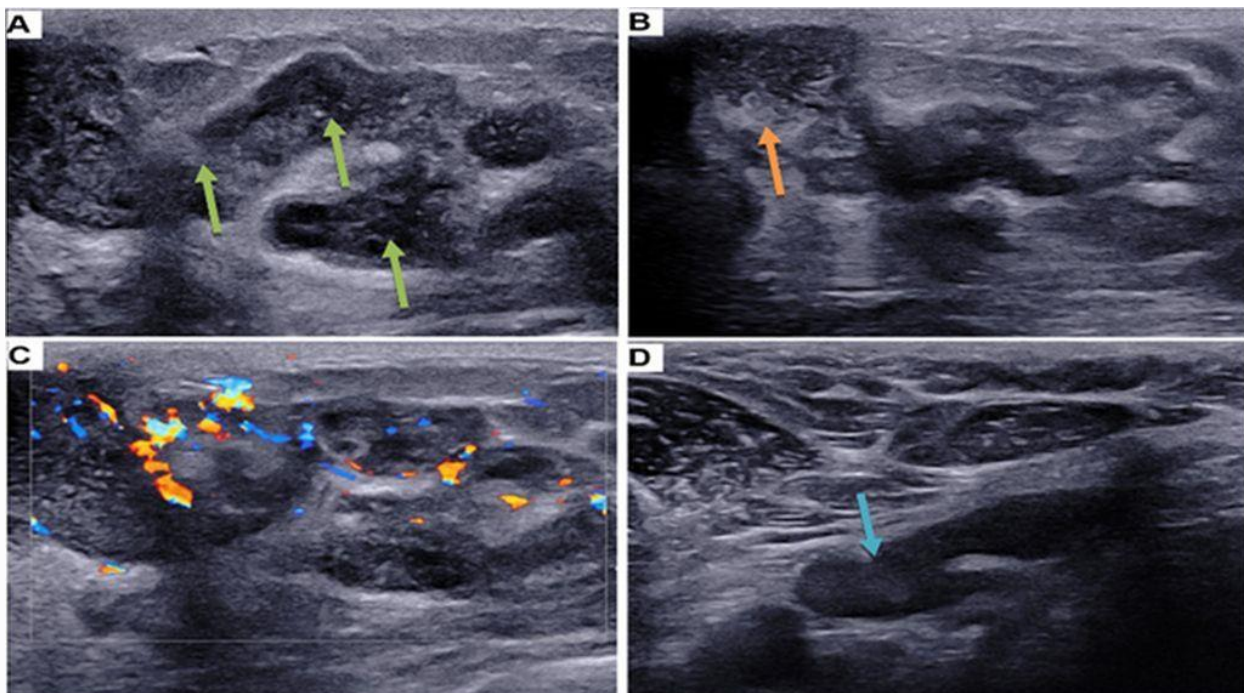


Figure 3. A 33-year-old patient, presented with pain in the right breast. A to C: Ultrasound revealed multiple dilated ducts with mobile internal echoes, thickened walls traceable up to the nipple and increased periductal vascularity. The surrounding parenchyma shows inflammatory changes. D: Right axilla shows enlarged lymph nodes with diffuse cortical thickening. Biopsy was suggestive of granulomatous lobular mastitis.



Thus, ultrasound remains the cornerstone modality to suspect granulomatous mastitis and guide further investigations and treatment.

In our study, we found ultrasound as the most useful imaging modality to diagnose GLM and to

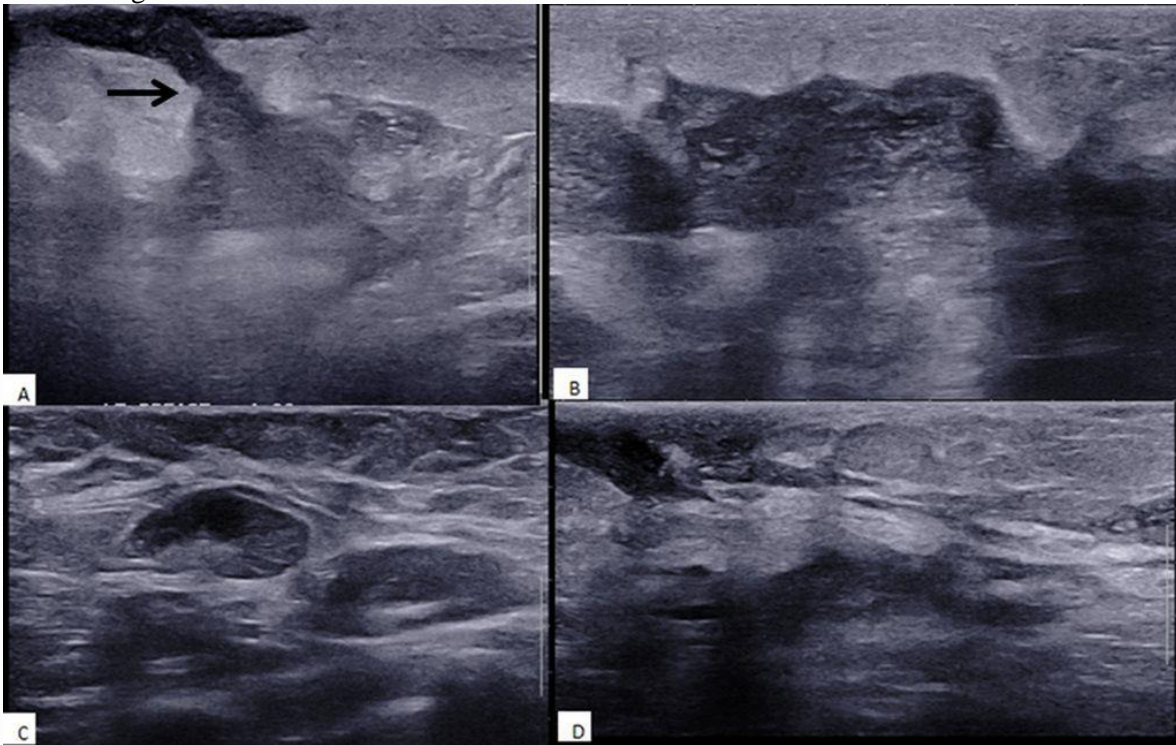


Figure 4. A to C: Ultrasound images of a 24-year-old female patient who presented with left breast lump and pain for 2 weeks shows irregular hypoechoic collections with moving internal echoes with sinus tracts extending to subcutaneous tissue (black arrow) and skin with reactive left axillary lymph-nodes. D: Biopsy from the wall of the collection was suggestive of granulomatous lobular mastitis and the patient was treated with wide excision of the involved area because of the extensive nature of the disease with discharging sinuses followed by oral steroid. D: Follow-up ultrasound shows resolution of the abnormalities.

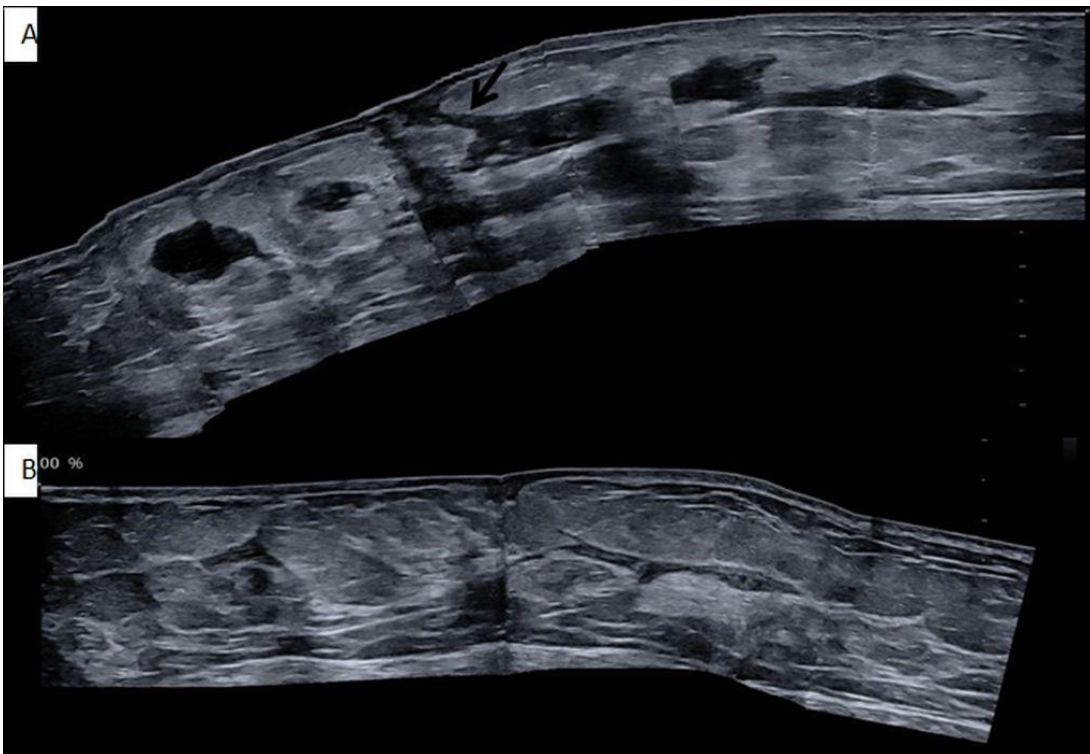


Figure 5. A 25-year-old patient, presented with a palpable lump in the right breast. A: Panoramic ultrasound view showing irregular hypoechoic collections with interconnecting hypoechoic tracts extending to the subcutaneous plane (black arrow) in the right breast. B: Significant interval reduction in right breast collections and tracts after oral steroid treatment for 3 months.



The treatment of GLM remains controversial and includes surveillance, medical management with oral, intralesional and topical steroids and surgery²¹⁻²⁶. The natural course of the disease is a relapsing and remitting course with eventual burn-out in 1 to 2 years. For incidentally detected lesions and patients with mild symptoms, we suggested conservative management with imaging surveillance. Patients who

had significant symptoms were started on oral steroids for at least 3 months with monthly follow-up (Figure 4 and 5). Patients who had extensive disease, progressive disease on medical management were treated surgically.

Figure 6 shows the approach to diagnosing granulomatous lobular mastitis.

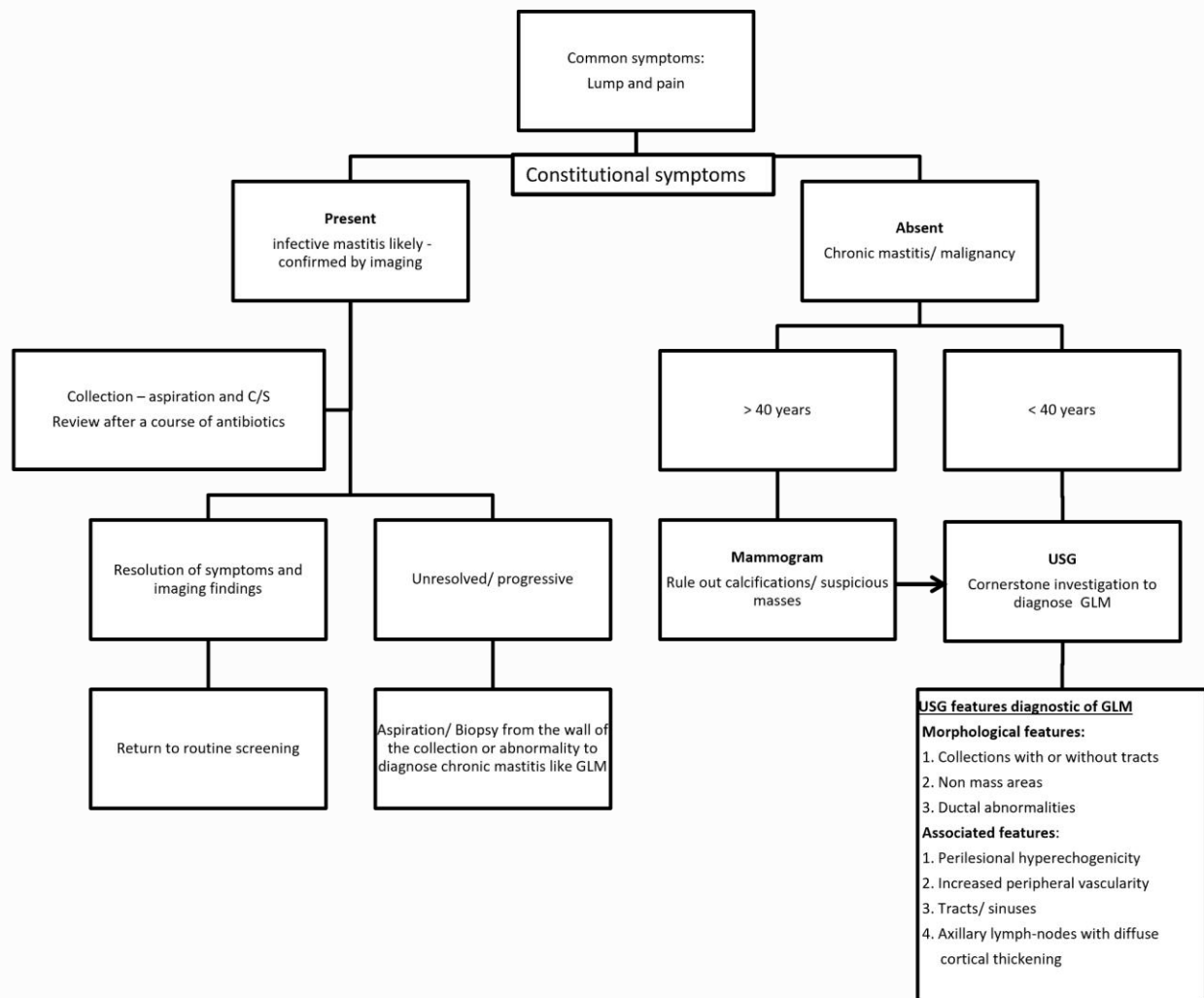


Figure 6. Algorithmic approach to the diagnosis of granulomatous lobular mastitis. C/S - culture and sensitivity, GLM - Granulomatous Lobular Mastitis.

Our study has several limitations, including retrospective and descriptive parameters. The role of magnetic resonance imaging to characterize the GLM was not evaluated.

CONCLUSION

Though imaging cannot differentiate GLM from malignancy on all occasions, our study revealed certain specific ultrasound features of GLM. Mammography was not informative for the diagnosis of GLM except for ruling out microcalcifications which would point towards malignancy. When GLM presents as non-mass areas or ductal abnormalities,

presence of perilesional hyperechogenicity, peripheral rather than central vascularity, absence of suspicious calcifications, presence of interconnecting tracts and benign enlargement of lymph-nodes help to differentiate it from malignancy.

ACKNOWLEDGEMENTS

None.

CONFLICTS OF INTERESTS

Nothing to declare.

FUNDING

None.



ETHICAL CONSIDERATIONS

This study was approved by institutional scientific and ethical committee. Approval number: EC/AP/867/11/2021

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How to Cite This Article

Thakur V, Renganathan R, Subramaniam P, Rajalakshmi PP. Review of Mammographic and Sonographic Features of an Uncommon Inflammatory Breast Disease: Granulomatous Lobular Mastitis. Arch Breast Cancer. 2023; 10(1):57-65.

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