Idiopathic Granulomatous Mastitis – A Clinical Study of Multiple Cases

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Abstract

Background: Idiopathic granulomatous mastitis (GM) is a chronic inflammatory disease of the breast, which is difficult to differentiate both clinically and radiologically from infectious etiologies such as tuberculosis, fungal infection, and also from malignancy.

Materials and Methods: We have operated 79 patients with clinical diagnosis of mastitis/breast abscess in the Department of Surgery, Sree Gokulam Medical College and Research Foundation, Venjaramoodu, Trivandrum, during the period of January 2013–December 2016. In this group, seven patients were identified histopathologically as GM, of this seven, two were found to be histopathologically non-suppurative mastitis, considered with idiopathic GM.

Results: Age of presentation ranged from 27 to 67 years with the mean age being 50.86 years. Among 79 patients presented with mastitis/breast abscess and operated, 7 (8.86%) were GM, 4 (5%) were acute inflammatory lesion with granulation tissue and abscess, 5 (6.3%) patients were lactational or puerperal mastitis, and 6 (7.5%) were having breast abscess with fibrocystic changes in the breast. The incidence of non-suppurative GM (idiopathic GM) and suppurative GM was 2 (28.5%) and 5 (72.5%), respectively. Incidence of idiopathic lobular mastitis is 1/79 (1.26%). Recurrence of the disease is noted in 4/7 patient. Two patients (2/7) are on psychotropic drugs such as prothinden (antidepressant), amisulpride, and aripiprazole (atypical antipsychotic). Even with angry breast lesion, only two patients are having leukocytosis. There was the elevation of erythrocyte sedimentation rate with a range of 25–80 mm/hr. Of seven cases after surgery, 2 (28.5%) patients had a lump alone and 5 (71.5%) patients had an abscess. Recurrence history is noted for 4/7 (57.1%) cases. 4/7 patients attain full remission were as 3/7 had a partial remission.

Conclusion: More studies are needed to be done, retrospectively as well as prospectively, to identify the environmental, clinical, as well as biological factors that play a role in the pathogenesis of GM, to formulate reasonable treatment algorithms.

Key words: Granulomatous lobular mastitis, Granulomatous mastitis, Non-suppurative mastitis

INTRODUCTION

Granulomatous mastitis (GM) is a rare chronic inflammatory disease that has clinical and radiological findings similar to those of carcinoma breast. The problems are the varied clinical presentations, the low index of suspicion among clinicians, lack of awareness of this clinical entity among surgeons, and the patient going from surgeons to surgeons at the time of recurrence.

Mastitis (also called mammitis) is inflammation of breast usually due to infection. *Staphylococcus aureus* is the most common pathogen responsible, but *Staphylococcus epidermidis* and streptococci are occasionally isolated as well. It is called puerperal mastitis (lactation mastitis) when it occurs in pregnancy, breastfeeding, or weaning. Other inflammatory conditions not associated with the above are called non-puerperal mastitis. Mastitis can, in
rare cases, occur in men. Inflammatory breast cancer has symptoms very similar to mastitis and must be ruled out.

Puerperal mastitis can be classified as (1) milk stasis, (2) non-infectious or infectious inflammation, and (3) abscess. Milk stasis, non-infectious and infectious inflammation can be distinguished only by leukocyte count and bacteria culturing. Symptoms such as pyrexia, the intensity of pain, redness, or rapid onset of symptoms cannot be used to distinguish these. The symptoms are similar for puerperal and non-puerperal mastitis, but predisposing factors and treatment can be very different. It is relatively common, the estimated is between 5 and 33% depending on the methodology. However, only about 0.4–0.5% of puerperal mastitis patients develop an abscess and may need drainage.\[1\]

Non-puerperal mastitis is the inflammatory lesions occurring at the breast, unrelated to pregnancy and breastfeeding. Skin-related conditions such as dermatitis and folliculitis are a separate entity. In general, non-puerperal mastitis includes mastitis, subareolar abscess, duct ectasia, periductal inflammation, Zuska’s disease (subareolar abscess), and others.

GM is a benign C/c inflammatory condition of the breast which is diagnosed histologically by the presence of “granulomas.” GM is divided into two main groups of specific and non-specific.

Specific GM may be due to tuberculosis (TB) and other infections and inflammatory conditions (fungi – Blastomyces, Cryptococcus, Histoplasmosis, and Actinomycosis, filarial infection, bacterial - Bartonella henselae and Corynebacterium, and autoimmune causes such as sarcoidosis, vasculitis (granulomatosis with polyangiitis – Wegner’s granulomatosis and giant cell arteritis). Special forms of GM occur as a complication of diabetes (lipoideca). Some cases are due to silicone injection (silicone-induced granulomatous inflammation) or other foreign body reactions. The polarizing foreign material was found in the case of GM associated with foreign bodies.

TB of the breast is an uncommon disease that is often difficult to differentiate from carcinoma of the breast when it presents as a lump. It should be considered in diagnosis in women with clinically suspicious breast lump who are from high-risk populations and from endemic areas. The single most important differential diagnosis of idiopathic GM (IGM) in the Asian subcontinent is TB. The predominance of neutrophils in the background and relative absence of caseous necrosis favors a diagnosis of GM. Then, these granulomas join together and lead to suppuration and liquefactive necrosis. Biopsy should be performed to establish the diagnosis before deciding further treatment options. Granulomatous lesions in tuberculous mastitis are associated with the duct, then with lobules. Fibrosis may be prominent in chronic cases. It may not always be possible to detect acid-fast bacilli (AFB) in histological sections taken from patients with mastitis. Polymerase chain reaction (PCR) test results for Mycobacterium tuberculosis DNA can be done if stains for microorganism are negative. Numerous non-caseating granulomas may be seen in biopsy specimens.\[3\]

GM may be associated with sarcoidosis. Such patients may present as mastitis with elevated erythrocyte sedimentation rate (ESR) and serum angiotensin-converting enzyme (ACE) rise more than 2 times usually (if the patient is not on any ACE inhibitors drugs). ACE increases in 60% of the sarcoidosis patient and in 20% of chronic sarcoidosis patient. Computed tomography chest will show hilar lymph node of size more than 2 cm in short axis. Diagnostic investigations like KVIEM SCIHS procedure, in which intradermal injections of splenic aspirate from a known sarcoidosis patient done. Bronchoalveolar lavage for of CD receptor can also be done. Biopsy will show naked granuloma (without lymphocyte cuffing).

Non-specific GM is also known as IGM or granulomatous lobular mastitis, which refers to conditions that can lead to a granulomatous reaction in the breast or conditions for which the etiological factors cannot be determined. Primary presentation of any of these conditions as mastitis

Figures 1: (a-h)Photograph of patient 2 showing pre-operative, post-operative delirium (POD) 5, POD 14, POD 21, POD 28
Table 1: A brief profile of our patients is given

<table>
<thead>
<tr>
<th>C</th>
<th>Age (years)</th>
<th>Clinical features</th>
<th>Months</th>
<th>Size (cm)</th>
<th>TC</th>
<th>ESR (mm/h)</th>
<th>Recurrence</th>
<th>MRF</th>
<th>USG/MMG</th>
<th>FNAC</th>
<th>C and S/ Staining</th>
<th>SX</th>
<th>HPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60</td>
<td>Painful, firm, tender lump Left breast, with skin dimpling, axilla neg., no fever. Opposite breast n equally N</td>
<td>2</td>
<td>3×3</td>
<td>10,100</td>
<td>24</td>
<td>Major depressive disorder – On antidepressant (Prothinden 50), hypothyroid, HTN</td>
<td>Suppurative inflammation</td>
<td>No growth/ AFB and GMS neg.</td>
<td>Lumpectomy</td>
<td>Non-suppurative GM</td>
<td>Granulomatous mastitis</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>27</td>
<td>Left breast abscess with multiple discharging sinuses, nipple retraction, axilla neg., no fever</td>
<td>2</td>
<td>6×5</td>
<td>13,800</td>
<td>60</td>
<td>Once</td>
<td>Subclinical hyperthyroid disorder</td>
<td>USG – irregular abscess, diffuse inflammatory changes</td>
<td>-do-</td>
<td>I and D with local excision of wall for BX</td>
<td>GLM with suppuration and sinus formation</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>33</td>
<td>Progressively increasing painful lump left breast, no fever, axilla neg., LCB 4 years back</td>
<td>6</td>
<td>8×7</td>
<td>9500</td>
<td>80</td>
<td>Trice</td>
<td>USG – hypoechoic focal lesion, subareolar with regular borders</td>
<td>GM with suppuration</td>
<td>-do-</td>
<td>WLE</td>
<td>Granulomatous mastitis</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>36</td>
<td>Right breast painful lump, Outer lower quadrant, axilla neg., no fever</td>
<td>6</td>
<td>3×1</td>
<td>9800</td>
<td>48</td>
<td>Once</td>
<td>-</td>
<td>-do-</td>
<td>I and D wall bx</td>
<td>Suppurative GM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>29</td>
<td>Right breast abscess, no fever, axilla neg., LCB 5 year. BF-2, 1/2 years back</td>
<td>3</td>
<td>5×4</td>
<td>8000</td>
<td>50</td>
<td>-</td>
<td>-</td>
<td>-do-</td>
<td>I and D with wall bx</td>
<td>Suppurative GM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>67</td>
<td>Painful lump, lower medial Q, under the NAC, axilla 2×2 cm LN+</td>
<td>1</td>
<td>5×4</td>
<td>7800</td>
<td>42</td>
<td>-</td>
<td>Fiberadenoma/ fibroadenosis/ mammo-BIRAD2</td>
<td>Inflammatory lesion/GM/ resolving abscess?</td>
<td>-do-</td>
<td>Lump excision</td>
<td>Non-suppurative GM</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>52</td>
<td>Painful lump left breast, with irregular surface, with well-defined margin, axilla neg.</td>
<td>4 days</td>
<td>12×9</td>
<td>10,700</td>
<td>40</td>
<td>Once-old HPR-GM</td>
<td>On antipsychotics- (Aripiprazole, Amisulpride), DM, hypothyroid.</td>
<td>Suppurative inflammatory lesion</td>
<td>-do-</td>
<td>WLE</td>
<td>Suppurative GM</td>
<td></td>
</tr>
</tbody>
</table>
is very rare and in many cases probably predisposed by other breast or systemic conditions. Although GM is easily confused with cancer, it is a completely benign (non-cancerous) condition. Treatment is radically different for IGM and other granulomatous lesions of the breast, the precise diagnosis is, therefore, very important. Chronic granulomatous inflammation constitutes about 24% of all inflammatory events of the breast that is histopathologically defined.\(^4\)

**MATERIALS AND METHODS**

A total of 79 cases with clinical diagnosis of mastitis and/or breast abscess were operated in the Surgery Department, Sree Gokulam Medical College and Research Foundation, Trivandrum, Kerala, between January 2013 and December 2016. Seven cases were diagnosed as GM histopathologically. Clinical profile of seven cases was checked carefully after retrieving the case sheet from medical records. The surgical procedures were incision and drainage with cavity wall biopsy (2 cases), wide local excision (WLE) (2 cases), and lump excisions (3 cases). Biochemical, radiological, microbiological, and pathological results were also analyzed. The variables considered were the age distribution, incidence, probable etiological factors, image, and histopathological features.

**RESULTS**

Age of presentation ranged from 27 to 67 years with the mean age being 50.86 years. Both premenopausal (4/7) and postmenopausal (3/7) age groups are involved. The majority of them are premenopausal. The most common presentation was a painful hard breast lump (5 cases) with features of inflammation and node negative axilla. Two cases presented as breast abscess. Constitutional symptoms such as fever, chills, and rigor were absent in all cases. The mean duration of symptoms varied from 4 days to 6 months. Routine hemogram of 2 cases, there was a borderline elevation of the total count. ESR was raised in all cases with a range from 24 to 80 with a mean of 49.14 mm/h. Routine chest radiograph revealed no abnormalities. Three had endocrine abnormalities such as hypothyroidism (2 cases of hypothyroidism) and hyperthyroidism (subclinical). Two patients were having psychiatric problems such as depression and psychosis and were on treatment with an antidepressant (prothinden 5) and antipsychotics (aripiprazole and amisulpride – atypical antipsychotic), respectively. Clinically, the size of the lesion varies from 8 mm to 12 cm in the longest dimension of the lesion. Sonomammogram reports of five patients were retrieved. Among postmenopausal three patients, carcinoma breast is suspected (Breast Imaging, Reporting and Data System 4) (case no 6 and 7). Fine-needle aspiration cytology (FNAC) in majority of cases was suppurative lesions and two were GM. Mycobacterium, fungi, and Gram staining were negative for the aspirate.

Incidence of GM was 8.8% (7/79). The incidence of non-suppurative GM and suppurative GM was 2 (28.5%) and 5 (72.5%), respectively. The clinical features and imaging characters of GM overlap with those of breast malignancy. Four patients had a hard lump with focal asymmetric density on mammography (MMG) and an irregular hypoechoic mass on ultrasound. History of prior surgery and recurrence of the disease is noted in four patients. All patients were managed with therapeutic antibiotics. Lesion was located in subareolar region (3 cases) and periphery of the breast (4 cases). Follow-up periods range from 1 to 6 months. One patient (case no-2) with non-suppurative GM (idiopathic GM) had a recurrence on follow-up and was treated with steroids and she improved drastically on oral prednisolone. ATT for a period of 6 months was given for a patient (case no3) with suppurative GM. All others were asymptomatic during follow-up [Figures 1-3 and Tables 1 and 2].

### Table 2: Granulomatous mastitis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Incision and drainage</th>
<th>Excision</th>
<th>Prednisone</th>
<th>ATT</th>
<th>Treatment outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Full remission</td>
</tr>
<tr>
<td>2</td>
<td>Yes</td>
<td>No</td>
<td>Started</td>
<td>No</td>
<td>Partial remission</td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Full remission</td>
</tr>
<tr>
<td>4</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Partial remission</td>
</tr>
<tr>
<td>5</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Full remission</td>
</tr>
<tr>
<td>6</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Full remission</td>
</tr>
<tr>
<td>7</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

**Treatments and Outcomes of Treatment**

![Graph showing age distribution of patients](image-url)
GM was defined for the 1st time in 1972 by Kessler and Wolloch and was described in detail in 1977 with a five-
case series by Cohen.[5] IGM was defined as a distinct clinical entity among benign breast diseases since 1972. Its clinical presentation is very vague, mimicking breast abscesses, breast mass, and inflammatory carcinoma of the breast. It has a chronic course with frequent recurrences. Rare inflammatory breast disease of Unknown etiology. IGM mostly emerges in young-middle age women (3rd and 4th decades), the age range that has been reported in literature is considerably wider (11–83 years). In one relatively large series of 25 patients published recently, the mean age at presentation was 36.5 years. Perimenopausal women may also be affected. In a study by Baslaim et al., histopathologically proven cases of IGM were found in 1.8% of 1106 women with benign breast disease. In our observation, we were found in 1.26% of 79 women with mastitis and/or abscess, for which surgery was performed. Although it is seen globally, a higher racial predilection in Latin and Asian women is known.

**Ethnicity**

Google search of GM in the PubMed database (since 1995), with terms “IGM or granulomatous lobular mastitis” and “GM,” we found hardly 67 and 442 articles, respectively. Until 1999, there were only 120 cases described in the world literature. Most of these studies were case presentations. Larger case series from the Mediterranean region and the developing countries in Asia. France had the highest number of cases (55 cases) among European countries, and no other country exceeded 50 cases.

The distribution of IGM cases that were reported in PubMed since 1995 according to the country.[6]

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turkey: &gt;200</td>
<td></td>
</tr>
<tr>
<td>China: 129</td>
<td></td>
</tr>
<tr>
<td>South Korea: 128</td>
<td></td>
</tr>
<tr>
<td>United States: 126</td>
<td></td>
</tr>
<tr>
<td>Saudi Arabia: 96</td>
<td></td>
</tr>
<tr>
<td>France: 55</td>
<td></td>
</tr>
<tr>
<td>United Kingdom: 48</td>
<td></td>
</tr>
<tr>
<td>Iran: 46</td>
<td></td>
</tr>
<tr>
<td>Brunei: 43</td>
<td></td>
</tr>
<tr>
<td>Malaysia: 42</td>
<td></td>
</tr>
<tr>
<td>India: 36</td>
<td></td>
</tr>
<tr>
<td>Japan: 33</td>
<td></td>
</tr>
<tr>
<td>Morocco: 30</td>
<td></td>
</tr>
<tr>
<td>Jordan: 25</td>
<td></td>
</tr>
</tbody>
</table>

IGM is usually seen within a couple of years after delivery, and most of the patients have a history of at least one live birth and breastfeeding. In contrast, specific GM is frequently seen in Asian and African countries and can be detected at any age.[7]

**IGM – Presentation**

Patients mostly present with a hard lump in one breast (89%) without any sign of a systemic disease. Other possible symptoms include nipple retraction, pain, inflammation of the overlying skin, nipple discharge, fistula, enlarged lymph nodes (15%), and in rare case peau d’ orange like changes. The presentation is unilateral, but a significant number of cases reported were even bilateral, and in many cases, contralateral or bilateral recurrences were also documented. Several cases occurring together with fever, polyarthralgia, and erythema nodosum were documented. The periphery of the breast was usually involved. It can also present as an abscess. Systemic symptoms such as fever are generally not present. The incidence is the same in both breasts, the lesion is usually unilateral.

**Pathogenesis**

The pathogenesis of IGM is not exactly known, but different steps occur in the disease pathogenesis. One of these steps is non-specific lobulitis, which involves multiple lobules, and causes reactive lymphoplasmacytic infiltration. A granulomatous formation with central suppurative necrosis occasionally occurs due to lobule deformation. Abscesses develop due to an increase in the number of these foci. A process starting with non-puerperal secretion has been proposed as the most rational theory for the pathogenesis of IGM. A hormonal imbalance in the estrogen-progesterone ratio or hyperprolactinemia is believed to cause this secretion and subsequent inflammation. Ductal ectasia can occur due

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**Figure 2:** Case no. 2 – photomicrograph of tissue specimen shows granulomatous inflammation (epithelioid histiocytes [long arrow] and lymphocytes [arrowhead]) with admixed neutrophils (short arrows) (hematoxylin and eosin, ×200)
to the accumulation of intraductal protein-rich secretion. Permanent inflammation occurs following perforation of the duct and contact between the secretion and stromal cells. The accumulation of secretion, ductal ectasia, intraductal inflammation, and chronic GM are steps in the pathophysiological process.\[8\]

Autoimmunity against the extravasated secretion that from the lobules is also consider to cause this event. There is a similarity between IGM and granulomatous inflammation of the testicles or the thyroid gland. Considering that, mechanical factors are responsible for the formation of granulomas. The possibility that trauma represents another stage in IGM pathogenesis should not be disregarded.\[9\]

Current Arguments for Etiology of this Idiopathic Disease Includes
(1) Hormonal imbalance, (2) autoimmunity, (3) infections (unknown microbiological agents), (4) immune response to extravasated secretions from lobules, (5) smoking, and (6) α1-antitrypsin (AAT) deficiency have been suggested to play a role in disease etiology.\[6\]

AAT Deficiency
AAT is a glycoprotein synthesized by hepatic cells. Similar to anti-thrombin 3, ovalbumin, and thyroid-binding globulin, AAT is a member of the serine protease inhibitor family. Primary function is to prevent the destructive effects of proteases secreted from activated neutrophils (proteinase 3, elastin, and cathepsin G). AAT level is elevated during inflammation. Deficiency in AAT leads primarily to lung and liver pathologies. In 2001, Schelfout et al. demonstrated AAT deficiency in patients with IGM.

Smoking
A definitive association between smoking and IGM has not yet been established. According to the results of various case series, Baslaim et al. reported no association,\[10\] Asoglu et al., suggest a strong association of smoking with IGM (77.8%), whereas 34.8% association in Oran et al. study, 16.7% in Al-Khaffaf et al., and 50% in Ozel et al., respectively.

Oral Contraceptives (OCs)
OCs have been considered a potential etiological factor, as they increase breast secretion (the secretion theory). However, a significant association between OCs and IGM has not been determined. Oran et al. found that 21.7% of patient had a history of OCs use, Gurleyik et al. – 42.1%, Al-Khaffaf et al. – 27.7%, Bani-Hani et al. – 8.3%, and Asoglu et al. 11.1%, respectively. Contradicting above observation, Baslaim et al. reported that none of 20 patients had a history of OCs use. In conclusion, the association between IGM and OCs use has been reported to range between 0% and 42%

Gestation, Birth, and Breastfeeding
IGM is usually detected in women <50 years of age and frequently involves a recent history of birth or breastfeeding; these factors have beαal alterations in these processes, secretion, and inflammation have an effect on disease pathophysiology. While almost all studies reported a history of parity but failed to explain the timing of the parity. IGM is a reproductive age disorder, with a history of gestation and breastfeeding. The incidence among wide age range (11–83 years) in the literature make it difficult to say only gestation,
birth, and breastfeeding responsible for the etiology of IGM.[4]

**Hyperprolactinemia**
Considering the secretion theory, hyperprolactinemia has also been considered responsible for the pathogenesis of IGM, similar to other hormonal disorders. In 1984, Rowen determined comorbid prolactinoma in an IGM case. However, future studies did not provide prolactin levels in details.[11]

**Autoimmunity**
Good response to steroid and immunosuppressive treatment. Patients with extramammary involvement such as erythema nodosum, arthritis, and the demonstration of T-lymphocyte predominance in immunohistochemical studies support the autoimmunity hypothesis. The patient was positive for rheumatoid factor (RF), antinuclear antibody (ANA), and anti-double-stranded DNA (anti-dsDNA). Classical serological tests, which are used for autoimmune disorders such as ANA and RF, reveal different results in patients with IGM. It’s an autoimmune pathophysiological outcome that progressed with reactive T-cell-mediated inflammation and centrilobular granulomas against ductal damage. Comorbid autoimmunity disorder constitutes only a minor fraction of all cases.

**Microbiological Agents**
The normal endogenous bacteria flora of the breast is similar to the skin flora. Dominant organisms include coagulase negative streptococci, Propionibacterium sp., and Corynebacterium sp. Corynebacteria cause mastitis in livestock. However, these bacteria are not expected pathogens in humans. These bacteria became the center of attention since 2003, with detection of corynebacteria in IGM cases by Taylor et al. (54.4%).[12] It is hard to distinguish whether these organisms cause infection, colonization, or contamination. These bacteria could be a possible factor if (1) a Gram-positive bacillus accompanying polymorphonuclear leukocytes is present or (2) Corynebacterium sp. is detected in a tissue that is expected to be sterile under normal conditions. Four different Corynebacterium species have been detected in IGM cases. Corynebacterium kroppenstedtii is the most frequently observed species and is different from others due to its lipophilic nature and positive esculin test. Corynebacterium accolens, Corynebacterium amycolatum, and Corynebacterium tuberculosis are other identified species. The role of antibiotics – after 3-week intravenous penicillin treatment, the expected benefit was not observed in reported cases.

**IGM – Investigations**
Manage as a breast mass. MMG, ultrasound (ultrasound sonography [USG]) – 10–12-MHz transducer, magnetic resonance imaging (MRI), NAC – using an 18-gauge needle, core biopsy – percutaneous ultrasound-guided core biopsy (14-gauge) or surgical WLE. The slides were analyzed with hematoxylin and eosin stain, special stains such as (1) Kinyoun AFB, (2) Gomori methenamine silver (GMS) for fungi, and (3) Gram cultures for bacteria. Immunohistochemistry, polarization, etc., help in assessment of patients. PCR for M. tuberculosis DNA can also be performed to confirm the diagnosis of TB if stains for microorganisms are negative.

**MMG and IGM**
Small, multiple, ill-defined masses without microcalcification. Most commonly reported that the finding of IGM is an asymmetrically increased density without a distinct margin or pressure effect. Though this is not specific low sensitivity caused by dense breast tissue limits the value of MMG in this age group.

**Mammogram Findings Include**
- Large focal asymmetric density.
- Lobulated or irregular mass.
- Diffusely increased density.
- Axillary adenopathy.
- Skin thickening.

Granulomatous lobular mastitis has clinical and imaging characteristics similar to breast carcinoma. However, the mammographic finding of a focal asymmetric density and presence of an irregular hypoechoic mass with multiple tubular extensions on sonography suggests granulomatous lobular mastitis.[13]

**MRI and IGM**
MRI shows the presence of segmental heterogeneity and hypointense on pre-contrast T1-weighted images and hyperintense on T2-weighted sequences. Post-contrast dynamic T1-weighted scans showed heterogeneously enhancing ring-like abscesses. Abscess walls had a benign type time-signal intensity curve (gradual and progressive enhancement without washout). IGM is rare and the number of patients in the studies conducted so far is less, so the image characterization cannot be generalized. Rieber et al. found that MRI did not provide any additional information in differentiating IGM from inflammatory carcinoma since both exhibit signs of inflammation. MRI may play a complementary role to increase the conspicuity of lesions that are not visualized by mammograms and ultrasound adequately.[14]

**Histopathology and IGM**
Biopsy still remains the golden method of definite diagnosis of IGM. Even after aspiration cytology, diagnosis is difficult and often does not deliver any diagnostic information. Only <30% of cases can be diagnosed by FNAC. The absence of necrosis.
and a predominantly neutrophils infiltrate in the background favor the diagnosis. These signs overlap with other etiologies like TB. The characteristic histopathologic features for IGM are multinucleated giant cells and epithelioid histiocytes forming non-caseating granulomas around lobules. Often, minor ductal and periductal inflammation is present. The lesion is in some cases very difficult to distinguish from breast cancer and other causes such as infections (TB, syphilis, corynebacteria infection, and mycotic infection), autoimmune diseases (sarcoidosis and granulomatosis with polyangiitis), foreign body reaction, and granulomatous reaction in a carcinoma must be excluded. IGM is characterized pathologically by chronic granulomatous inflammation of the lobules without necrosis. TB mastitis was associated with ducts more than with lobules. Fibrosis may be prominent in a chronic case.

### Table: Differential Diagnosis

<table>
<thead>
<tr>
<th>Granulomatous lobular mastitis</th>
<th>Mammary duct ectasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centered on lobules</td>
<td>Centered on ducts</td>
</tr>
<tr>
<td>Granulomatous inflammation</td>
<td>May have giant cells but usually lacks</td>
</tr>
<tr>
<td>Nearly all cases postpartum</td>
<td>May occur without associated pregnancy</td>
</tr>
<tr>
<td>Granulomatous lobular mastitis</td>
<td>Sarcoïdosis</td>
</tr>
<tr>
<td>Centered on lobules</td>
<td>Widespread distribution</td>
</tr>
<tr>
<td>Granulomas may not be well formed</td>
<td>Frequently lacks extensive accompanying inflammation (naked granulomas)</td>
</tr>
<tr>
<td>Associated inflammation may be extensive</td>
<td></td>
</tr>
<tr>
<td>May have associated fat necrosis and abscess</td>
<td>Necrosis and abscess rare</td>
</tr>
</tbody>
</table>

**Histological Features Include**

(1) Granulomas (100%), (2) background of inflammatory infiltration (88%), (3) foamy macrophages, epithelioid histiocytes, and multinucleated giant cells (65%), (4) microabscesses, (5) the ducts appear normal without evidence of malignancy or caseation, (6) stains for fungi and AFB are negative, (7) occasional features – fat necrosis, abscesses, sinus tract, eosinophils, and (8) Schaumann and asteroid bodies absent to rare.

**The Differential Diagnosis Includes**

(1) Infectious organisms: Bacteria (culture), (2) mycobacteria (Kinyoun AFB stain and necrotizing necrosis), and (3) fungus (GMS stain), (4) sarcoidosis ("naked" granulomas, i.e. lacking lymphocytic inflammation), (5) traumatic fat necrosis (foamy macrophages and non-lobular), (6) ruptured cyst (non-lobular), (7) duct ectasia (periductal fibrosis), (8) plasma cell mastitis (non-granulomatous), (9) Wegener’s granulomatosis (vasculitis), (10) carcinoma (keratin immunohistochemistry), and (11) foreign body reaction (polarizable material) (Ramachandran et al. Pathology. 2004).

**Treatment of IGM**

Few articles have described treatment protocols for IGM. Effective diagnostic protocols and treatment plans for granulomatous lobular mastitis have not yet been established. Before starting treatment, other causes such as TB, fungal infection, and sarcoidosis must be excluded. The treatment of IGM remains controversial, ranging from conservative management with antibiotics to WLE and corticosteroid therapy. Treatment must be tailored to the patient’s clinical presentation. Lai et al. found that spontaneous resolution occurs in 50% of cases in a mean time interval of 14.5 months without any treatment. Kiyak et al. reported that WLE was not the ideal treatment in GM with complications such as abscess formation, fistulas, and in the diffuse involvement of breast. A short interval follow-up should be done before deciding on steroid treatment. Before 1980, surgical excision (WLE) of the entire lesion was performed. Current arguments for management include surgical excision – WLE +/- reconstruction (wide surgical excision is more beneficial than limited excision in patients with localized disease). The role of I and D is controversial because it may lead to increased scarring and non-healing of incision tracks, which subsequently leads to the formation of sinus tracts. Judicial use of systemic steroid/immunosuppressant considering amount of immune suppression and after excluding underlying infective cause. Current literature recommends the use of steroid treatment after excision. A course of Prednisone 60 mg/day for 2 weeks; this course is tapered over weeks 3, 4, 5, and 6. If prednisone therapy fails, the second course of steroids is repeated. If minimal or no improvement is seen after the second steroid course, consider adding Methotrexate 10 mg/week. Patients those who had recurrence may need long-term low-dose steroids with or without Methotrexate and local excision.

**Follow-up of Patients By**

(1) With high-dose steroids, close surveillance is needed due to the potential side effects, which include glucose intolerance and Cushing’s syndrome. (2) Patients are examined by the breast surgeon at least once each month until symptoms have resolved. (3) In addition, ultrasound should be performed at 1- and 3-month intervals after the start of treatment and earlier if there is no improvement or if symptoms worsen.
(4) Once symptoms have resolved, 6-month follow-up ultrasound is performed. (5) The patient returns to annual screening when she is asymptomatic and imaging is negative.

Diagnostic and therapeutic algorithm for women of child-bearing age who present with abscess, mass, inflammation, or pain in whom GM is suspected (institutional protocol).

**CONCLUSION**

More studies are needed to be done, retrospectively as well as prospectively, to identify the environmental, clinical, as well as biological factors that play a role in the pathogenesis of GM, to formulate reasonable treatment algorithms.

There is a need to spread awareness of this disease among the surgeons so that these patients who present with recurrent breast abscesses with failure to respond to antibiotics and multiple incision and drainage.

A biopsy should be taken from the abscess wall during operation, particularly in women in perimenopausal age group presenting as abscess, without much constitutional symptoms, history of psychotropic medications, usage of OCP, without much leukocytosis, with a raised ESR, clinically inflamed breast with or without lump, and a negative axilla and FNAC s/o a suppurative lesion.

IGM is a benign entity which has varied and nonspecific appearance on USG and MMG and often mimics malignancy.

MMG commonly shows focal asymmetric density and skin thickening while parenchymal heterogeneity, irregular mass, and hypoechoic mass with tubular extension are seen on USG.

It often mimics breast carcinoma clinically and radiologically; hence, histopathological evaluation is necessary to establish the diagnosis before deciding on treatment options.

Results of randomized controlled trials are not available at present due to its rarity of this disease entity.

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**REFERENCES**


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