

## Unveiling Granulomatous Mastitis: Cytological Insights and Diagnostic Dilemmas of a Rare Breast Condition- A Five-Year Study

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### ABSTRACT

**Introduction:** Granulomatous Mastitis (Gm) Is A Rare Benign Inflammatory Disorder Of The Breast, Characterized By The Presence Of Painful Lumps. It Primarily Affects Young Women, Who Often Report A History Of Antibiotic Use That Does Not Provide Significant Relief. Gm Can Be Classified Into Two Categories: Idiopathic And Specific. Due To Its Clinical And Radiological Presentation, Which Closely Resembles That Of Breast Malignancy, Gm Should Be Included In The Differential Diagnosis Of Chronic Mastitis.

**Aim And Objectives:** This Study Aims To Thoroughly Evaluate The Cytomorphological Characteristics Of Gm, Highlight Its Key Clinical Features, And Effectively Differentiate It From Conditions That Mimic Breast Carcinoma, Thereby Preventing Unnecessary Mastectomies.

**Materials And Methods:** A Retrospective Observational Study Was Conducted Over Five Years At Smsr, Sharda University, Involving 15 Confirmed Cases Of Gm. Aspirates Were Stained Using Giemsa Stain, And Special Stains, Including Ziehl-Neelsen And Pas, Were Employed To Exclude Mycobacterial Or Fungal Etiologies.

**Results:** The Study Reviewed 15 Cases Of Gm, With A Mean Age Of 29.2 Years. Notably, Left Breast Involvement Was Found In 53% Of The Cases, While Overlying Skin Inflammation Was Observed In 60%. Histopathological Examination Consistently Revealed Non-Caseating Granulomas Along With A Significant Presence Of Polymorphs In The Background, Indicating Gm. Importantly, Tuberculosis Was Confirmed In 40% Of The Cases, And Additional Ancillary Tests Further Supported The Diagnosis.

**Conclusion:** Gm Poses A Complex Challenge For Diagnosis And Treatment Due To Its Rarity And The Necessity To Differentiate It From Other Causes Of Mastitis And Breast Malignancies. Timely And Accurate Diagnosis Is Essential To Prevent Unnecessary Mastectomies And Ensure Appropriate Management.

**Keywords:** *Granulomatous mastitis, granuloma, tuberculosis, breast carcinoma, chronic mastitis.*

### 1. INTRODUCTION

Granulomatous Mastitis (GM) is a rare but significant inflammatory disorder of the breast, first described in 1972 by Kessler E and Wolloch Y<sup>[1]</sup>. This condition often mimics breast cancer in both clinical and radiological presentations. It is characterized by lobulo-centric granulomatous inflammation while sparing the interlobular stroma. Symptoms may include nipple discharge, an "orange peel" appearance of the skin, and irregular masses. Due to these similarities with breast cancer, diagnosing GM can be quite challenging.

GM is categorized into two main types: Idiopathic Granulomatous Mastitis (IGM) and Specific Granulomatous Mastitis (SGM). IGM typically occurs in women of reproductive age, particularly between the ages of 17 and 42, and is most common 2 to 6 years postpartum. The exact cause of IGM remains unknown, but several risk factors have been associated with the condition, including pregnancy, use of oral contraceptives, diabetes, smoking, and autoimmune disorders.

SGM, in contrast, is more commonly linked to infections such as tuberculosis, sarcoidosis, as well as fungal or parasitic infections, and autoimmune diseases, including reactions to foreign bodies<sup>[2]</sup>. An increase in SGM cases, especially in regions like Asia and Africa, has been partially attributed to undiagnosed tuberculosis infections<sup>[3]</sup>.

The diagnosis of GM primarily relies on histopathological examination, where the presence of non-caseating granulomas within the breast tissue and lobulitis with or without neutrophilic micro-abscesses are key indicators<sup>[4]</sup>. Though less commonly explored, cytological features can also assist in diagnosis.

Treating GM can be challenging, particularly for IGM, as the approach depends on various factors such as the extent of lesions, the presence of associated skin changes like fistulas or abscesses, and underlying causes. While GM is benign, misdiagnosis or delayed diagnosis can result in unnecessary treatments and complications. Given its rarity, a high level of suspicion is essential in cases where standard treatments for breast infections or abscesses fail to alleviate symptoms. There is a need for standardized treatment protocols and further research into the cytological and histological features of GM to improve patient outcomes<sup>[1,5]</sup>.

## 2. MATERIAL AND METHOD:

A retrospective study conducted at Sharda Hospital, Greater Noida, between 2019 and 2024, reviewed 15 cases of granulomatous and tubercular breast diseases. Fine Needle Aspiration Cytology (FNAC) was performed using a 22G needle, and the slides were stained with Giemsa to examine the cytological features. To rule out tuberculosis and fungal infections, special stains like Ziehl-Neelsen (ZN) and Periodic Acid-Schiff (PAS) were applied. The study focused on analyzing the cytological features of all granulomatous mastitis cases, specifically assessing cellular composition and granuloma formation. Thus, thorough diagnostic approach enabled accurate identification of granulomatous mastitis and helped differentiate it from other possible causes of breast inflammation.

## 3. RESULTS

In this series of 15 cases of granulomatous mastitis (GM), all the patients were female and presented with a breast lump, discharging sinuses (see **Figure 1**), and mastalgia. The patient's age ranged from 19 to 60 years with mean age of 29.2 years. Maximum patients (n=11) were in the age group of 21-30 years. **Table 1** shows detailed age and sex distribution of 15 patients.

Unilateral breast involvement was observed in all cases, with a predominant occurrence in the left breast (n=9/15). **Table 2** shows detailed age group and sex distribution in different types of mastitis.

**Table 1. Age and sex distribution of 15 patients**

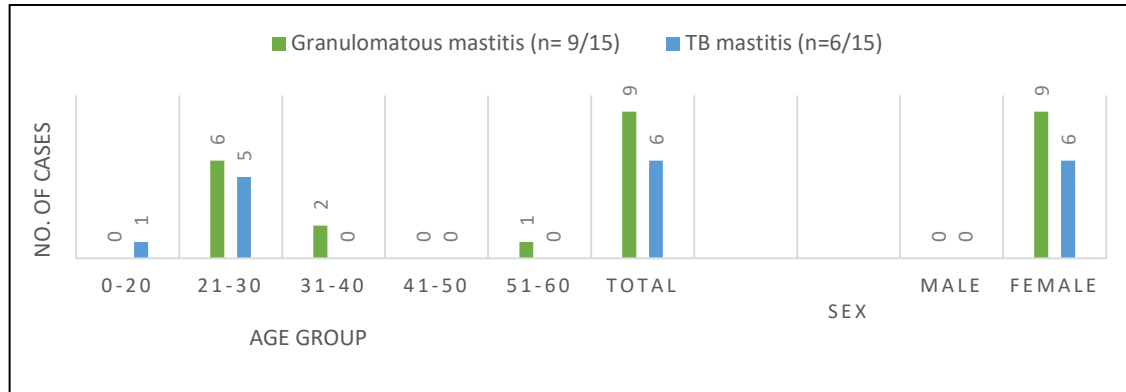
<i>Age (Years)</i>	Female	Male	Total
0-20	1	0	1
21-30	11	0	11
31-40	2	0	2
41-50	0	0	0
51-60	1	0	1
<b>Total</b>	15	0	15



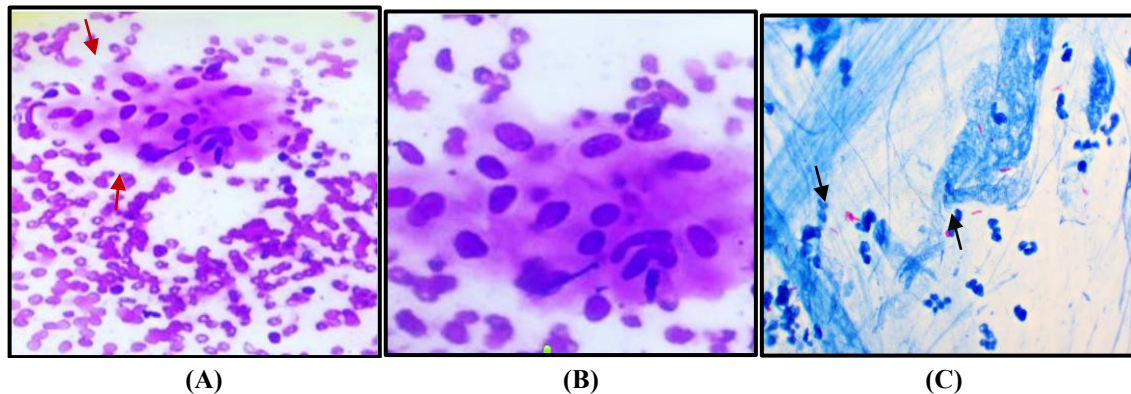
**Figure 1: Discharging sinus**

Based on clinical findings and morphology of granuloma with other inflammatory cells, giant cells and presence or absence of AFB in FNA smears, etiology of GM was specified. Out of 15 cases, maximum i.e. 9 cases (60%) were diagnosed as granulomatous mastitis followed by 6 cases (40%) of tuberculous mastitis (TM).

**Table 2. Bar chart showing age group and sex distribution in different types of mastitis**



Ultrasonography was done in all cases. Commonest finding (n=15) was hypoechoic lesion with 2 cases showing additional finding as collection of fluid. 9 cases had a history of lactation. Cytomorphological features were studied in detail and GM diagnosis was made by the presence of epithelioid granulomas or scattered epithelioid cells along with other inflammatory cells with or without giant cells in FNA smears (see Figure 2).



**Figure 2: (A) Epithelioid Granuloma- Giemsa stained smear (100X); (B) (400X);**

**(C) AFB positive (ZN stain)**

ZN stain was performed on all FNA smears, revealing AFB in 6 cases. Fungal stain (PAS) was done in all cases and none of the cases showed fungi (Table 3).

**Table 3: Clinicopathological parameters of all 15 patients.**

S. no.	Age (in Yrs)	Clinical Features	Diagnosis (H&E)	ZN stain	USG Imaging	Size (in cm)	Site	Lactation
1	23	Breast lump, tenderness, discharge	Tubercular Mastitis	Positive	Hypoechoic lesion	3x2	LUOQ	Present
2	28	Breast lump, tenderness	Granulomatous Mastitis	Negative	Hypoechoic lesion	3x1	RUOQ	Absent
3	26	Breast lump, mastitis	Granulomatous Mastitis	Negative	Hypoechoic lesion	2x2	LLIQ	Present
4	19	Breast lump,	Tubercular	Positive	Hypoechoic	3x3	LUOQ	Absent

		discharge	Mastitis		lesion			
5	60	Breast lump, mastitis	<b>Granulomatous Mastitis</b>	Negative	Hypoechoic lesion	2x2	RLIQ	Absent
6	30	Breast lump, mastitis	<b>Granulomatous Mastitis</b>	Negative	Hypoechoic lesion	1x1	RUOQ	Present
7	26	Breast lump, tenderness	<b>Granulomatous Mastitis</b>	Negative	Hypoechoic lesion	3x2	LUOQ	Present
8	22	Breast lump, Discharge	Tubercular Mastitis	<b>Positive</b>	Hypoechoic lesion, collection of fluid	2x1	LLIQ	Present
9	30	Breast lump, mastitis, tenderness	<b>Granulomatous Mastitis</b>	Negative	Hypoechoic lesion	3x3	LUOQ	Present
10	37	Breast lump, tenderness, Discharge	<b>Granulomatous Mastitis</b>	Negative	Hypoechoic lesion	2x1	RUOQ	Present
11	22	Breast lump, mastitis	Tubercular Mastitis	<b>Positive</b>	Hypoechoic lesion, Collection of fluid	2x2	LUOQ	Absent
12	39	Breast lump, mastitis, tenderness	<b>Granulomatous Mastitis</b>	Negative	Hypoechoic lesion	3x2	RUOQ	Present
13	30	Breast lump, Discharge	<b>Granulomatous Mastitis</b>	Negative	Hypoechoic lesion	3x1	LUOQ	Absent
14	23	Breast lump, tenderness+, fever	Tubercular Mastitis	<b>Positive</b>	Hypoechoic lesion	2x2	RLOQ	Absent
15	23	Breast lump, tenderness, discharge	Tubercular Mastitis	<b>Positive</b>	Hypoechoic lesion	3x3	LUOQ	Absent

(LUOQ: Left upper outer quadrant; RUOQ: Right upper outer quadrant; LLIQ: Left lower inner quadrant; RLIQ: Right lower inner quadrant)

Granulomatous mastitis (GM) was the final diagnosis, characterized microscopically by non-necrotizing granulomas, consisting of clusters of epithelioid histiocytes, with no detectable microorganisms or features of other pathological entities and the definitive diagnosis of tuberculous mastitis was established based on FNA findings, which revealed epithelioid cells or granulomas with caseous necrosis and AFB positivity.

All patients with TM received anti-tuberculous therapy while patients with GM received antibiotics and steroids. Wide surgical excision is often therapeutic.

#### 4. DISCUSSION

Granulomatous mastitis (GM) is a rare, benign, chronic inflammatory condition of the breast first described by Kessler and Wolloch Y in 1972. Despite decades of research, its exact etiology remains unclear<sup>[1]</sup>. Though granulomatous mastitis can occur at any age, it is more common in parous women of childbearing age with a history of breast feeding<sup>[6,7,8]</sup> and commonly occur in 3rd and 4th decade. Males are rarely affected<sup>[6]</sup>.

The majority of patients in our study presented with a unilateral breast lump accompanied by pain, with a higher prevalence in the left breast. On the whole, unilateral involvement of the breasts is typical, although bilateral disease has been described<sup>[9]</sup>.

Due to its clinical and radiological resemblance to breast malignancies, it is often misdiagnosed. This study aims to analyze the clinical and cytological characteristics of GM while comparing our findings with previously published literature.

GM predominantly affects women of reproductive age. In our study, the median age was 29.2 years, which is consistent with findings from Ayush et al. (2022) (24.7 years) and Bhalla S et al (2018) (34.5 years)<sup>[3,10]</sup>.

Intake of oral contraceptive pills (OCPs) has been believed as a potential contributing factor in the development of GM. In our study, 60% of cases had a history of OCP use, which is comparable to the findings of Ayush et al. (2022) (78.1%) and Shirish et al (2024) (36.3%), further reinforcing the role of hormonal influences in the pathogenesis of the disease<sup>[3,6]</sup>.

Other notable symptoms observed included nipple retraction (6.7%), axillary lymphadenopathy (13.3%), and inflammation (46.7%)<sup>[8]</sup> (**Table 4**). These clinical manifestations closely resemble infective mastitis and breast malignancies, making an accurate diagnosis particularly challenging.

Classical cytological features suggestive of tubercular etiology on FNA include epithelioid cells, small lymphocytes, plasma cells, and Langhans-type giant cells within a caseous necrotic background. In contrast, numerous neutrophils with scattered epithelioid histiocytes but without caseous necrosis indicate idiopathic granulomatous mastitis (IGM).

Cytological analysis revealed epithelioid cells, non-caseating granulomas, and lymphocytic infiltrates, characteristic of granulomatous mastitis (GM). In our study, Ziehl-Neelsen (ZN) staining confirmed tuberculous mastitis (TM) in six cases with AFB positivity. This underscores the need to rule out tuberculosis before steroid therapy to prevent worsening of undiagnosed TB infection<sup>[10]</sup>.

Radiological findings remain non-specific. Ultrasound imaging typically reveal ill-defined hypoechoic masses.

Granulomatous mastitis (GM) is a diagnosis of exclusion, requiring the elimination of other granulomatous conditions such as tuberculosis, syphilis, histoplasmosis, vasculitis, and foreign body reactions. Its etiology includes infectious (bacterial, fungal, protozoal), autoimmune (Crohn's, sarcoidosis, vasculitis), and foreign body-related causes (silicone, beryllium)<sup>[12,13]</sup>.

**Table 4: Comparison of our study with previous literature**

<i>Factors</i>	<b>Our study</b> <b>(2024)</b> <b>[15 cases]</b>	<b>Shirish et al (2024)</b> <b>[33 cases]</b>	<b>Ayush et al (2022)</b> <b>[32 cases]</b>	<b>Bhalla S et al</b> <b>(2018)</b> <b>[1670 cases]</b>
<i>Total cases [n]</i>	15	33	32	1670
<i>Total cases of granulomatous mastitis</i>	9 (60%)	4 (12.12%)	32 (100%)	51 (3.05%)
<i>Period of study</i>	5 years	5 years	3 years	2 years
<i>Median Age group (in yrs)</i>	29.2	34.9	24.7	34.5
<i>Lactation history</i>	9/15	5/33	27/32	26/1670
<i>Axillary lymph nodes</i>	2/15	3/33	8/32	5/1670
<i>Nipple retraction</i>	1/15	6/33	26/32	2/1670
<i>Inflammation</i>	7/15	20/33	20/32	5/1670
<i>OCP intake</i>	9/15	12/33	25/32	-
<i>Laterality</i>	All unilateral (Left predominance)	All unilateral	All unilateral (Left predominance)	All unilateral (Left predominance)

Tuberculosis is the major differential diagnosis. In the literature, most diagnosis of granulomatous mastitis are based on ruling out tuberculosis by histochemical staining and clinical evaluation.<sup>[14-18]</sup>

## 5. CONCLUSION



Granulomatous mastitis remains a challenging condition due to its uncertain etiology, overlapping clinical features with malignancies, and diagnostic difficulties. The association with lactation, hormonal changes, and immune responses suggests a multifactorial pathogenesis. Our findings emphasize that accurate diagnosis requires a multidisciplinary approach, integrating clinical, cytological, and microbiological evaluations.

Differentiating GM from tuberculosis is critical to avoid inappropriate steroid therapy, which could worsen an underlying TB infection.

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