

# Granulomatous mastitis mimicking Tuberculous mastitis: A series of cases in a Tertiary Care Hospital

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**Abstract:** Granulomatous mastitis is rare chronic inflammatory breast disease. The most common causative organism is Mycobacterium tuberculosis though there have been cases reported of atypical mycobacterium causing tubercular mastitis. It is a diagnostic challenge because of its similarity with carcinoma, bacterial abscess and idiopathic granulomatous mastitis. The main objective of this study was to examine the histomorphology of Granulomatous mastitis.

**Materials and Methods:** Over a period of 2 years (2019-2021), out of 112 breast biopsies, 15 patients were diagnosed with Granulomatous mastitis. Data were collected regarding age, gender, patient's complain, site and, any swelling in opposite breast and axilla. Histomorphological features were studied on the breast biopsies received.

**Results:** Of the 15 patients, all were female with mean age of 34 years (25–50 years). The clinical presentation is as breast lump with or without sinus, associated lymphadenopathy. On microscopy caseating and non-caseating granuloma formation, epithelioid cells, Langhan's giant cells and caseous necrosis were noted. 3 specimens were positive for acid fast bacilli.

**Discussion:** Granulomatous mastitis mimics a breast abscess, tuberculous mastitis or carcinoma hence final diagnosis is a diagnosis of exclusion of other causes of granuloma and typical histomorphological findings on biopsy.

**Keywords:** Granulomatous mastitis, FNAC, Necrosis.

## INTRODUCTION

Granulomatous mastitis is an uncommon benign chronic inflammatory breast disease, which affects mostly young women of age between 17 and 42 years.<sup>1</sup> It was first described by Kessler and Wolloch in 1972. Granulomatous mastitis is an extremely rare disease with estimated incidence of <0.1% in the western countries whereas in developing countries like India it still occurs at a rate of 1-4%.<sup>2</sup>

Breast tissue is resistant to tuberculosis as is skeletal muscle and spleen and is unsuitable for the survival and multiplication of Mycobacterium tuberculosis. The cause is still not known hence the diagnosis is made by exclusion; however, inflammation as a result of a reaction to trauma, hormonal process, infections, autoimmunity are considered the most probable causes.<sup>3</sup> The most common causative organism is Mycobacterium tuberculosis though there have been cases reported of atypical mycobacterium causing tubercular mastitis. It is a diagnostic challenge because of its similarity with carcinoma, bacterial abscess and idiopathic granulomatous mastitis.<sup>4</sup>

The clinical presentation of the Granulomatous mastitis is variable. The early diagnosis is challenging and mimic other breast diseases. The leading symptom is a painful lump. Most common location of lump is retro-areolar from where it extends to upper outer quadrant of the breast. It is probably due to extension of tuberculosis from axillary nodes to the breast.<sup>5</sup> Other symptoms include tenderness, pain, swelling or fluctuation in abscess formation in the breast, with or without discharging sinuses.

Radiological imaging and mammographic findings are all nonspecific; hence are not diagnostic.<sup>6</sup> Fine needle aspiration and core biopsy are useful for diagnosis.<sup>7</sup> Diagnosis is based on the identification of typical histological features or the tubercle bacilli under microscopy or culture. However, smear positivity for acid-fast bacilli by Ziehl-Neelsen staining is low, and in the majority of cases, the diagnosis can only be accurately diagnosed by histological identification of the typical granulomatous lesion and microbiological work-up.<sup>8</sup>

The optimal management of GM remains controversial. The main concern is the risk of recurrence observed for the different therapeutic approaches.<sup>9</sup> Antibiotics present the lowest efficacy in the treatment of mastitis in the absence of bacterial infection. By comparison, corticosteroid therapy has a success rate of between 66 and 72%. Surgery alone or in combination with corticosteroids seems to have the lowest recurrence.

## OBJECTIVE

The main objective of this study was to examine the histomorphology of Granulomatous mastitis. Also, to study clinical presentation of Granulomatous mastitis.

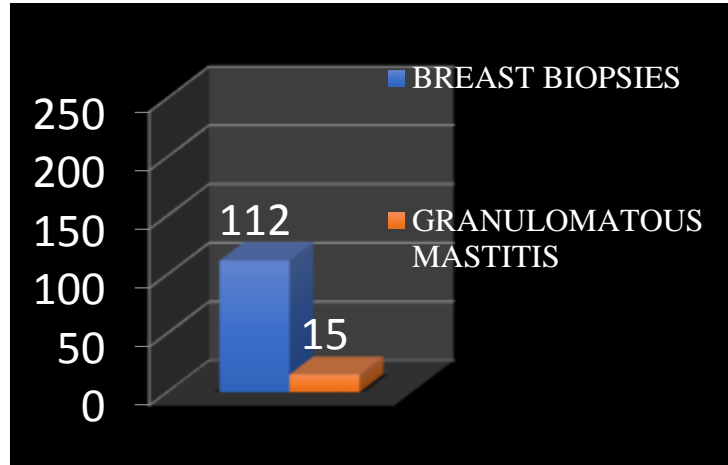
## MATERIALS AND METHODS

Over a period of 2 years from 2019 to 2021, total of breast biopsies were received, out of which 15 patients are diagnosed with Granulomatous mastitis. Breast lesions diagnosed as Breast Malignancy on FNAC. Mammography was not performed in any of these patients as this is an expensive investigation and was considered necessary for patient management. Data were collected regarding age, gender, patient's complain, site and size of the lesion, any swelling in opposite breast and axilla. Biopsy was taken as tru-cut biopsy or excisional biopsy or lumpectomy. Slides were made from the block and were stained with both Haematoxylin

and Eosin and Ziehl Neelsen stain. On microscopic examination, histological findings of inflammatory cells, granulomas, necrosis, multinucleated giant cells, fibrosis and calcifications were noted.

**Results**

Total of 112 breast biopsies, 15 patients were reported as Granulomatous mastitis. Of the 15 patients, all were female. The mean age of the patients was 34 years (25–50 years) and the mean duration of symptoms was 8.5 months. Among the female patients, 6 were lactating at the time of diagnosis. The right and left sides of the breast were equally involved and the disease was bilateral in two patients.

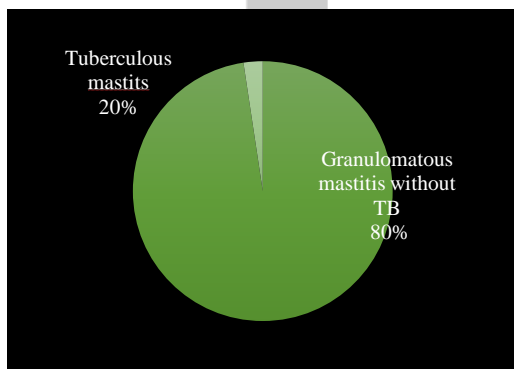


**GRAPH 1**

Constitutional symptoms of tuberculosis in the form of fever, weight loss, night sweats, or failing general health were present in only 4 patients (26%). The clinical presentation of the breast lesion is depicted in table 1.

**Table 1** Symptoms of 15 patients with Granulomatous mastitis

Symptoms	No of cases(%)
Breast lump	11 (73%)
Breast lump with sinus	3 (20%)
Sinus without lump	1 (6%)
Tender nodularity	10 (66%)
Associated axillary lymphadenopathy	4 (26%)
Previously drained abscess	3 (20%)



Out of total **15** cases diagnosed with granulomatous mastitis; **03** cases were diagnosed as Tuberculous mastitis incidence being **20%**.

**GRAPH 2**

The leading symptom is painful lump with cosmetic disfigurement. Most common location of lump is retro areolar from where it extends to upper outer quadrant of the breast. It is probably due to extension of tuberculosis from axillary nodes to the breast. Other symptoms include tenderness, pain, swelling or fluctuation in abscess formation in the breast, with or without discharging sinuses.

**Table 2:** Spectrum of clinical, radiological and FNAC findings in 15 cases.

Patient	Age (years)	Complaints	Complaint duration	Size of lesion in cms.	Site of lesion	Any other swelling	Radiological Diagnosis	FNAC
1	30	Painless, hard lump	2 months	3x2 cm	Right breast; retroareolar	No	Benign lesion	Not done
2	36	Painless, firm lump	4.5 months	2x2 cm	Left breast; upper inner quadrant	No	Benign lesion	Not done
3	35	Painful soft lump, fever, draining sinus	15 days	4x2 cm	left breast, upper inner quadrant	No	Breast Abscess	Acute suppurative lesion
4	29	Painless, firm lump	25 days	4x4 cm	right breast, lower outer quadrant	No	Benign lesion	Not done
5	47	Painful, Soft, well-defined nodule	15 days	2x1 cm	right breast, retroareolar	No	Breast abscess	Granulomatous mastitis
6	38	Ill-defined thickening, tenderness, nipple retraction	10 days	5x4 cm	left breast, upper inner quadrant	Yes, axillary lymph node	Complex Mass	Granulomatous mastitis
7	50	painful, draining sinus	20 days	1.5x1.5 cm	Right breast, upper quadrant	No	Benign lesion	Not done
8	31	firm, hard, painful lump	5 months	5x3 cm	Right breast	No	well defined lesion	Not done
9	39	Soft lump, painful, fever	10 days	4x2cm	Right breast, upper outer quadrant	Yes, right axillary lymph node	Breast abscess	Granulomatous mastitis
10	21	painless, hard	1 month	3x2 cm	Right breast, retroareolar	No	benign lesion	Not done
11	21	soft, painful, nodule	2.5 months	4x2 cm	Right breast, upper outer quadrant	No	Well defined lesion	Not done
12	29	soft, painful, lump	15 days	2x2 cm	right breast, lower outer quadrant	No	Breast abscess	Acute suppurative lesion
13	32	Soft, painful node, draining sinus	2 years	7x8 cm	Left breast, retroareolar	Left axillary lymph node	Inflammatory changes s/o mastitis	Breast abscess
14	32	Soft, painful lump	20 days	3x2 cm	Left upper outer quadrant	No	benign lesion	Granulomatous mastitis
15	33	hard, painless lump	25 days	2x2 cm	left breast, upper inner quadrant	No	Well defined lesion	Not done

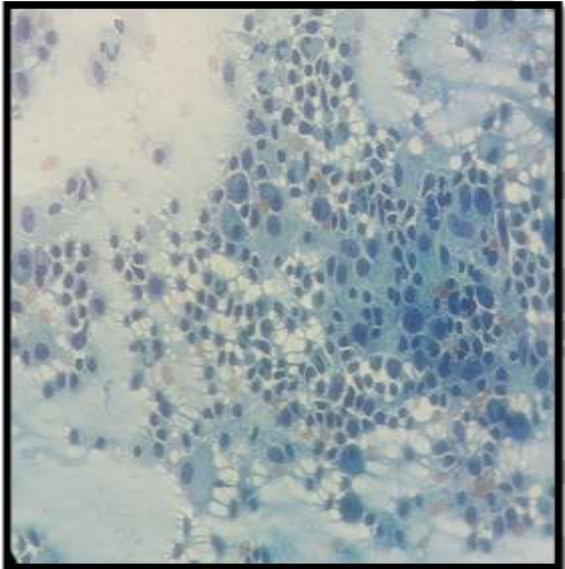
Eleven patients had a lump in the breast, most commonly in the central subareolar region (7 patients), and 3 of these patients had a discharging sinus in association with the lump. Another one patient had multiple sinuses without an underlying lump. Ten patients had symptoms of mastalgia and tender modularity without a cyclical pattern, and four had associated axillary lymphadenopathy. Ultrasonography was done for all the breast biopsies. Mammography was not performed in any of these patients as this is an expensive investigation and was not considered necessary for patient management.



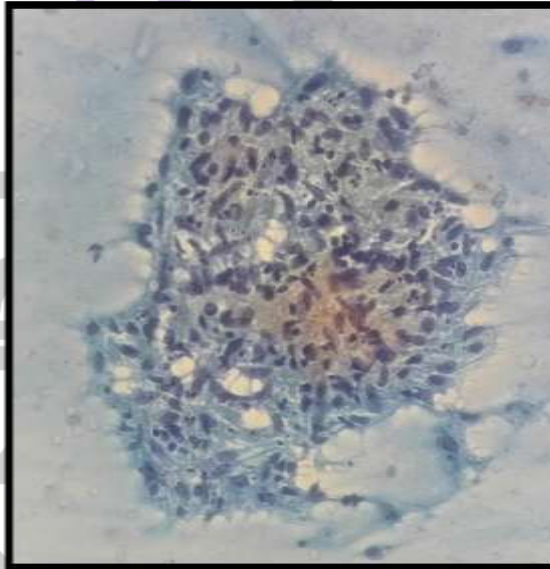
**Figure 1:** Ill-defined thickening in upper outer quadrant: note the nipple retraction.



**Figure 2:** Well defined granuloma formation on PAP smear (4x)



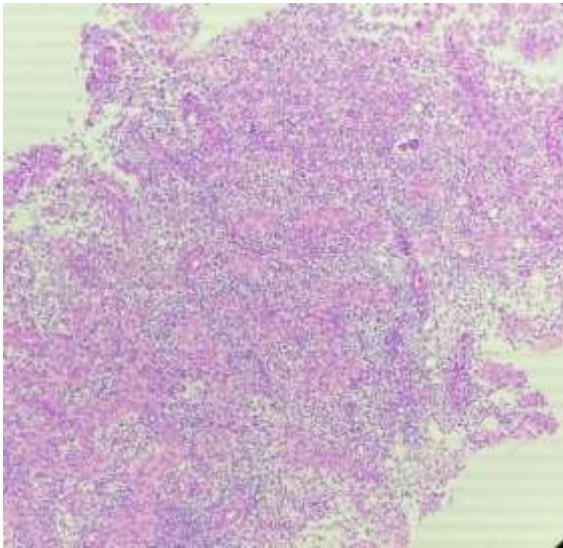
**Figure 3:** PAP smear showing cyst macrophages with inflammatory infiltrate along with Adipocytes



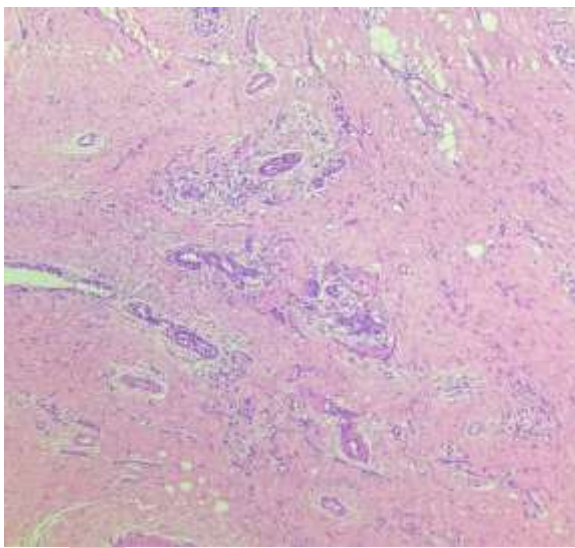
**Figure 4:** PAP smear showing well-formed granuloma along with Adipocytes

Histopathological examination, FNAC, trucut biopsy or open biopsy are also important for diagnosis, with FNAC being the most widely used initial invasive diagnostic method. 7 patients with a breast lump or nodularity were subjected to fine needle aspiration cytology (FNAC). On FNAC, the cytological findings of 4 aspirates were suggestive of Granulomatous mastitis, and 2 with Acute suppurative lesion and one suggestive of Breast Abscess. The cytological findings of epithelioid cell granulomas, Langhans' giant cells, and lymphohistiocytic aggregates confirmed the diagnosis of granulomatous mastitis. The lymph node FNAC (3) showed reactive lymphadenitis.

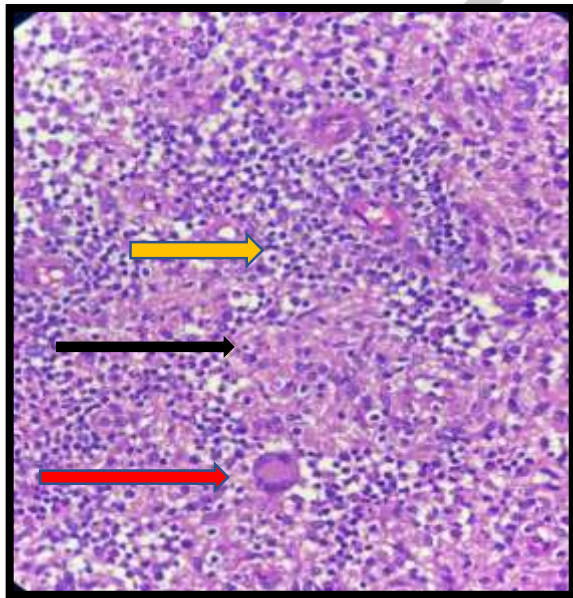
Histopathological specimen was received as tru-cut biopsy (9) and lumpectomy (6). Upon histopathological examination of 15 tissue samples, the granulomatous inflammation was observed in all cases; granulomatous inflammation with caseous necrosis was detected in 8 cases; non-caseous necrosis inflammation was detected in 6 cases. Also noted were well to ill formed granulomas, epithelioid cells, Langhan's type and foreign body type multinucleated giant cells along with aggregates of lymphocytes. One case was diagnosed as Idiopathic granulomatous mastitis. 3 specimens proved positive for acid fast bacilli on staining Ziehl-Neelsen stain. GeneXpert was traced for these 15 cases and out of which 3 cases with AFB positive.



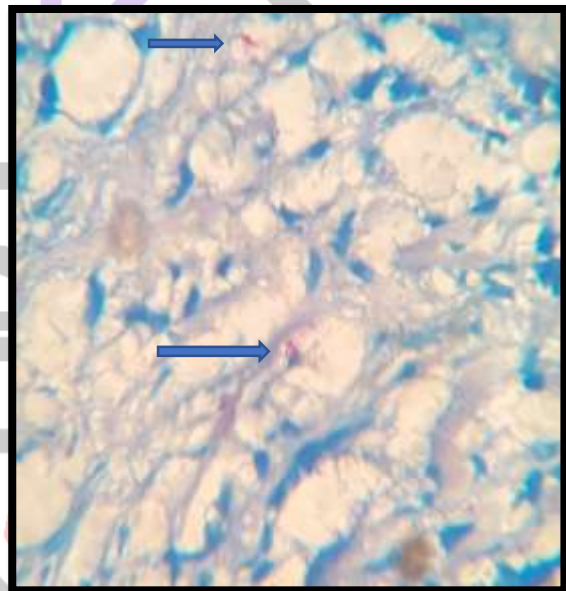
**Figure 5:** Epithelioid granuloma and Langhan's giant cells admixed with lymphocytic inflammatory infiltrate



**Figure 6:** Epithelioid granuloma and adjacent lobular acini surrounded by a lymphocytic inflammatory infiltrate



**Figure 7:** Granulomatous inflammation epithelioid histiocytes forming granulomas [black arrows] and lymphocytes [yellow arrows] and Langhans giant cells (red arrows).



**Figure 8:** Ziehl Neelsen stain showing rod shaped bacilli (blue arrows).

**DISCUSSION**

In 1972, Kessler and Wolloch emphasized in their study that granulomatous mastitis is a rare condition and its aetiology is not known. Subsequently, Jayram G from India reported cases of granulomatous mastitis of tubercular aetiology.<sup>10</sup> Breast is an uncommon site for tuberculosis even in countries like India, where tuberculosis is rampant. It affects commonly women in the reproductive age group of 21 to 40 years.<sup>11</sup> In our study mean age 34 years(25-50years). In our study duration of symptoms were from 1 week to 2 years. Dubey et al and Shukla et al also noted that symptoms vary from weeks to several years.<sup>12,13</sup> Bilateral breast involvement is uncommon.<sup>14</sup> In our study, no patient had bilateral involvement. Histopathological examination, FNAC, trucut biopsy or open biopsy are all important for diagnosis, with FNAC being the most widely used initial minimally invasive diagnostic method.<sup>15</sup> In our study, 4/7 FNAC samples were of granulomatous mastitis with caseous necrosis. Similar findings were noted in other studies like Kakkar et al, where 74% cases of FNAC had granulomas with caseous necrosis.<sup>16</sup> Failure to demonstrate tuberculosis on FNAC does not rule out the cause as sample is too less to be examined. Although preoperative FNAC helps the surgeon to avoid unnecessary surgical interventions as one of our cases which was clinically suspected as malignancy and

radiologically reported as complex mass, turned out to be granulomatous mastitis on FNAC. The gold standard for diagnosis of Granulomatous mastitis is core needle biopsy of the lesion with a sensitivity of 96%.<sup>17</sup> The differential diagnosis of granulomatous inflammation in the breast includes: Other infections- Mycobacterium Tuberculosis, Blastomycosis, Corynebacterium, Sarcoidosis, Granulomatous reaction to tumour, foreign body reaction, Mammary duct ectasia, Wegener's granulomatosis. So the challenge for both pathologist and clinician is to differentiate among various causes of granulomatous inflammation of breast. In developing countries like India, where prevalence of tuberculosis is high, detection of AFB on ZN stain is not mandatory as extrapulmonary tuberculosis is likely to be paucibacillary with number of bacilli less than 10,000/ml of material.<sup>18</sup> In tuberculous mastitis, granulomas are centred around ducts rather than lobules, but in the more destructive granulomas it was difficult to identify any structures. TB is associated with ducts more than lobules.

## CONCLUSION

As per this study the experience say one should not only depend on FNAC and smear which concludes AFB negative. As matter of fact, follow up needle core biopsy can be of more use and can throw light on aetiology which can be missed on FNAC. New diagnostic test like PCR can be used in atypical cases with smear, culture and even HPE negativity. The treatment of granulomatous mastitis is way different from tuberculous mastitis, so definitive diagnosis of granulomatous mastitis is important.

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