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Original Research Article

Utility of fine needle aspiration cytology (FNAC) in granulomatous mastitis with clinical, radiological and cytological findings association

[1]Dr. Jaymala Solanki, [2]Dr. Hiren Mundiya

[1]Assistant Professor, NAMO Medical College, Silvassa, Dadra and Nagar Haveli and Daman and Diu, India
[2]Assistant Professor, Department of Pathology, GMERS Medical College, Morbi, Gujarat, India
Corresponding Author:
Dr. Hiren Mundiya

Abstract
Objective: Granulomatous Mastitis is chronic inflammatory disease of breast which almost always mimics cancer in young individuals. Although Histopathology remains gold standard for the correct diagnosis, FNAC plays a pivotal role in the early diagnosis of GM as a minimally invasive, simple and cost effective outpatient treatment.
Material and Method: In present study cases reported as GM during period of 2018-2019 (2 year period) were retrospectively searched. In all cases, FNAC of the breast were performed by the pathologist using 22 or 23 gauge needle. Smears stained with H and E stain, Pap stain, giemsa stain and ZN stain. In cases of Pus material TB PCR run on CBNEET machine.
Result: In the present study 19 cases of GM were obtained over period of 2 years. Out of 19 cases 4 cases were diagnosed as TBM (21.05) bases on positive AFB staining and positive Gene Expert for tuberculosis (CBNAAT). Remaining 15 cases were labelled as IGM (78.94%) because of negative culture from pus discharge, negative PAS and AFB staining. In all patients there were no history of other causes of GM like sarcoidosis, fungal infection, previous trauma or surgery, autoimmune disease. So our study consists of TBM and IGM patients. All patients of TBM and IGM were female and presented with breast lump.
Conclusion: Granulomatous Mastitis including NGM and TBM are an uncommon chronic inflammatory disease of breast which almost always mimics cancer in young individuals and have overlapping clinical and cytological finding. FNAC along with proper clinical history help in differentiating these two entities.

Keywords: Granulomatous mastitis, Fine needle aspiration cytology (FNAC)

Introduction

The Granulomatous mastitis (GM) is uncommon breast lesion that was first described by Kessler and Woolloch [1]. Granulomatous Mastitis is chronic inflammatory disease of breast which almost always mimics cancer in young individuals [2]. GM commonly found in young parous female. They present as breast lump within 5 years of childbirth [3]. Aetiology of GM is divided into specific and non-specific type. The term "specific GM" is used when aetiological factor can be identified [2]. These can be categorisied as infectious causes like mycobacterium Tuberculosis, blastomycosis, Cryptococcosis, histoplasmosis, actinomycosis. Autoimmune process such as Wegener granulomatosis and Giant cell arteritis. Foreign body granuloma, ductectasia, diabetes Mallitus, sarcoidosis and fat necrosis are other rare causes [4]. Nonspecific granulomatous mastitis (NGM) is also known as idiopathic granulomatous mastitis or granulomatous lobular mastitis, for which aetiological factor can not be

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determined [2, 4]. NGM is a self-limiting disease which is characterized by slow disease progression and abscess and discharging sinuses [5].

The GM, NGM, TBM have overlapping clinical, radiological and cytological features and their treatment differs considerably. So they are important to distinguished from each other. They are often misinterpreted as carcinoma clinically and radiologcally [1, 7, 8]. Cytologically GM is characterized by epitheliod cells forming granulomas, multinucleated giant cells with or without necrosis, inflammatory cells and benign ductal epithelial cells [9]. NGM in addition to the above features has neutrophils and abscent caseous necrosis [5, 8].

The Tuberculous mastitis is rare clinical entity accounting for approximately 3% of all mammary lesions mainly affecting Indian and African Females and is often clinically misdiagnosed as other benign or malignant lesions of the breast. It may occur as an isolated lesion or part of systemic tuberculosis [7]. Bacteriological culture and positive AFB by ZN stain is gold standard for the diagnosis of tuberculosis but they are less sensitive in cases of TBM. This may necessitate the use of TB PCR. Demonstration of the acid fast bacilli (AFB) makes definitive diagnosis [10, 8]. Most cases of IGM respond well to steroid therapy. Wide surgical excision is advised in complicated cases, while TBM requires anti tubercular therapy for six months like pulmonary tuberculosis [11].

Although Histopathology remains gold standard for the correct diagnosis, FNAC plays a pivotal role in the early diagnosis of GM as a minimally invasive, simple and cost effective outpatient treatment [7]. In current study our attempt was to study and compare clinical and cytological profile of various granulomatous condition of breast and promote definite diagnosis at FNAC level, to ensure early and effective treatment. So that unnecessary surgery can be avoided.

Material and Methods

In present study cases reported as GM during period of 2018-2019 (2 year period) were retrospectively searched in the department of cytopathology, NAMO medical Education and research institute at Silvassa, Dadra and Nagar Haveli. In all cases, FNAC of the breast were performed by the pathologist using 22 or 23 gauge needle. An average of six to eight stained slides were obtained in all cases, out of which 2 smears stained with H and E stain,2 with Pap stain, 1 stain with giemsa stain and one smear stained with ZN stain. In cases of Pus material TB PCR run on CBNEET machine. Detailed history of patient including age, sex, presenting symptoms, past history and treatment history collected. The cytology slides of all the cases were examined by pathologist for the following findings: epithelioid cell granulomas, multinucleated giant cells, necrosis-caseous or non caseous and presence of other inflammatory cells like polymorphs, macrophages etc.

Result

In the present study 19 cases of GM were obtained over period of 2 years. Out of 19 cases 4 cases were diagnosed as TBM (21.05) bases on positive AFB staining and positive Gene Expert for tuberculosis (CBNAAT). Remaining 15 cases were labelled as IGM (78.94%) because of negative culture from pus discharge, negative PAS and AFB staining. In all patients there were no history of other causes of GM like sarcoidosis, fungal infection, previous trauma or surgery, autoimmune disease. So our study consists of TBM and IGM patients. All patients of TBM and IGM were female and presented with breast lump.

In TBM out of 4 patients, pus aspirated in one patient and blood mixed caseous cheesy material aspirated in rest of three patients. Gene expert was done in aspirated pus in which Mycobacterium Tuberculosis (MTB) detected.

IN IGM out of 15 patients, pus aspirated in 4 patients which came negative for MTB in gene expert.

In TBM Group, Oldest patient was 55 years of age and youngest was 22 years of age. The mean age was 38.5.The most patients belong to 20-30 years of age. An average size of lump was 2-3 cm. The duration of symptoms ranges from 15 days to 2 months. One patient out of four patients was known to have tuberculosis (25%) and was having treatment for the same.

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None of the patients complained of tenderness (0%). None had history of discharging sinuses from the breast lump (0%). None women had history of active breast feeding. Two patient had axillary lymph nodes (50%). Two patient had clinical suspicious of breast carcinoma (50%).One patient had radiological suspicious of malignancy (25%).

In IGM, Oldest patient was 65 years of age and youngest was 25 years of age. The mean age was 45 year. The most patients belong to 25-35 years of age. On examination majority of patients presented with firm to hard, ill-defined breast lump with an average size of lump was 3-5 cm. The duration of symptoms ranges from 15 days to 6 months. Out of 15 NGM patients, 10 patients complained of tenderness (66.67) with associated signs of inflammation like raised temperature and redness in 8 patients (53.33%). 1 patient had history of active breast feeding (6.67%). 4 patients had associated axillary lymph nodes (including palpable and non-palpable but radiologicaly confirmed) (26.67%). 3 patients had multiple discharging sinuses and had history of incision and drainage (20%). 2 patients had clinical suspicious of malignancy. (13.33%) In 3 patients radiology was suspicious of malignancy. (20%) (Figure/table-1)

Cytological smears of NGM consist of abundant epithelioid histiocytes, variable granulomas, neutrophils, no caesous necrosis, occasionally foreign body type giant cells and ductal epithelial cells with reactive nuclear atypia.

In the present study, cytological smears of NGM, 14(93.33%) smears showed ductal epithelial cells and many showed reactive nuclear atypia. All smears had epithelioid cells chiefly singly scattered and intermixed with polymorphs (100%). Necrotic material consisting of degenerated inflammatory cells chiefly poymophs and apoptotic body seen in 8 cases (53.33%). Foreign body type multinucleated giant cells seen in 11 cases (73.33%). Caseous necrosis was not seen any of the cases. Epithelioid cell granulomas were seen in 7 cases (46.67%). Histiocytes were found in all 14 cases (93.33%). Background inflammation consisting of polymorphs seen in 13(86.67%) cases and mixed polymorphs and lymphocytes seen in 2(13.33%) cases. Out of 4 patient of axillary lymphadenopathy, pathologist able to perform FNAC in 2 patients and in rest of 2 cases, lymph nodes were not palpable and detected on radiology. Out of 2 patients aspirated only in one patient satisfactory material aspirated. Which shows changes of reactive nonspecific lymphadenitis. (Figure/Table-2)

Cytological smears of TBM consistent of Caseous necrosis, epithelioid cells singly or forming granulomas, langhans type multinucleated giant cells and background inflammatory cells consisting of chiefly lymphocytes and histiocytes (Figure/Table-3).

In the present study 2 out of 4 cases (50%) of TBM showed ductal epithelial cells with mild nuclear atypia. Caseous necrosis found in all 4 cases (100%). One case did not show well formedepithelioid cell granuloma, multinucleated giant cells or ductal cells and showed chiefly caseous necrosis with scattered epithelioid cell and histiocytes (Figure 1). Epithelioid cell scattered singly were seen in all 4 cases (100%). Langhans type giant cells found in 2 cases (50%). Well-formed epithelioid cell granuloma were seen in 3 cases (75%). All cases showed plump histiocytes (100%). Background inflammation chiefly consist of lymphocytes in 3 cases (75%). Smears from two case of axillary lymphadenopathy showed foci of caseous necrosis and scattered epithelioid cell granuloma. All four cases showed Acid Fast Bacilli on ZN stain and from one case aspirated pus was positive for TB PCR (CBNAAT).

Table 1: Clinical and radiological Findings summarized

Sr. No.	Clinical and radiological Findings (total 19 cases)	TGM (4 cases)	NGM (15 cases)
		No and percentage (%)	No and percentage (%)
1.	Mean Age in years	38.5 years (22-55)	45 years (25-65)
2.	Mean Size of breast swelling (lump)	2 to 3 cm	3 to 5 cm
3.	Average duration of symptoms	15 days to 2 months	15 days to 6 months
4.	Presence of tenderness	0(0%)	10(66.67%)
5.	Axillary lymphadenopathy	2(50%)	4(26.67%)

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6.	Sings of inflammation and discharging sinuses	0(0%)	3(20%)
7.	History of pregnancy and active breastfeeding	0(0%)	1(6.67%)
8.	Clinical suspicious of malignancy	2(50%)	2(13.33%)
9.	Radiological suspicious of malignancy	1(25%)	3(20%)

Table 2: Cytological findings Summurized

Sr. No.	Cytological Findings (total 19 cases)	TGM(4 cases)	NGM(15 cases)
		No and percentage (%)	No and percentage (%)
1.	Ductal epithelial cells	2(50%)	14(93.33%)
2.	Epithelioid cells	4(100%)	15(100%)
3.	Histiocytes	4(100%)	14(93.33%)
4.	Caseous necrosis	4(100%)	0(0%)
5.	Inflammatory necrosis	0(0%)	8(53.33%)
6.	Epithelioid cell granuloma	3(75%)	7(46.67%)
7.	Foreign body type giant cells	0(0%)	11(73.33%)
8.	Langhangs giant cells	2(50%)	0(0%)
9.	Polymorphs	1(25%)	13(86.67%)
10.	Lymphocytes	3(75%)	2(13.33%)

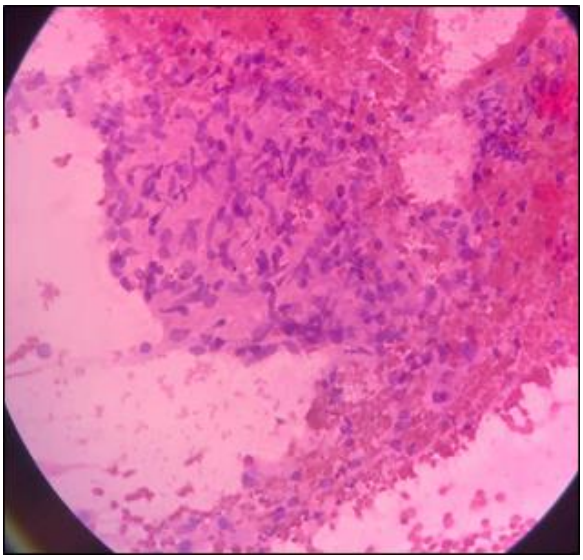

Fig 3.1: Showing well formed epithelioid cell granuloma

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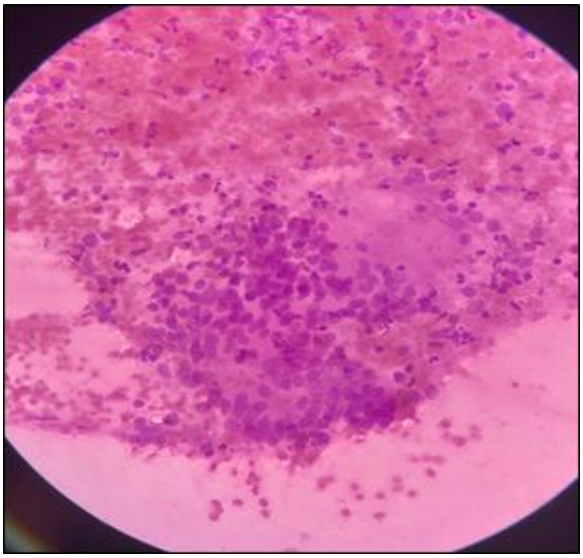

Fig 3.2: Showing multinucleated giant cells with acute inflammatory cells in the background

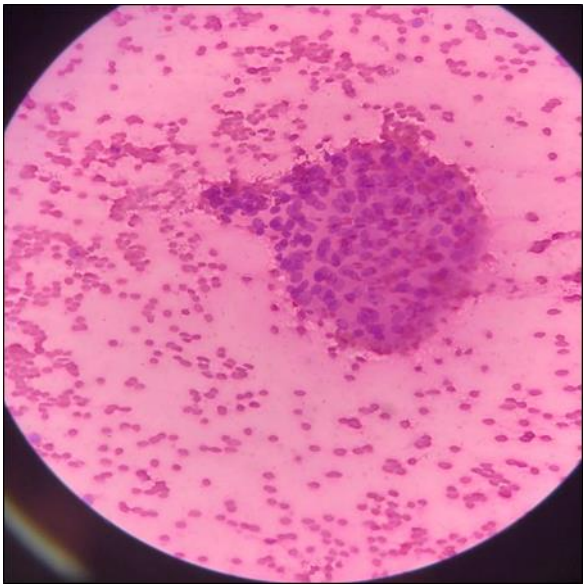

Fig 3.3: Showing multinucleated giant cells

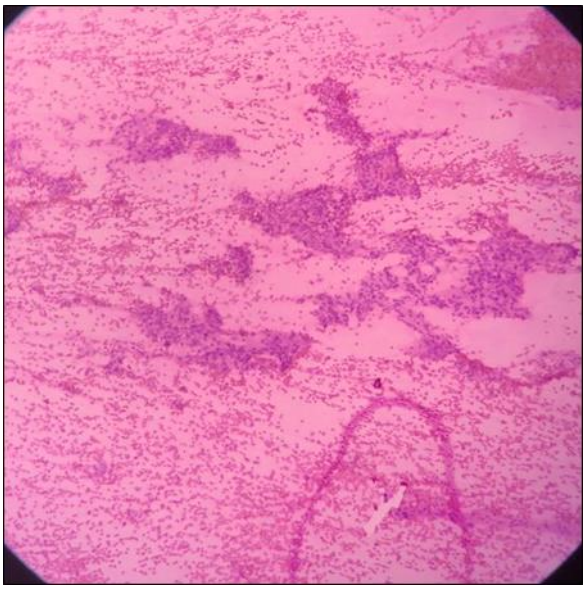

Fig 3.4: Showing multiple epithelioid cell granuloma

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Discussion

The Granulomatous mastitis is uncommon breast lesion that was first described by Kessler and Woolloch [1]. Granulomatous Mastitis is an uncommon chronic inflammatory disease of breast which almost always mimics cancer in young individuals [2]. GM commonly found in young parous female. They present as breast lump whithin 5 years of childbirth [3]. NGM and TBM are two rare cause of granulomatous disease of breast. They interest many physician due to their overlapping features and resemblance to malignancy clinical and radiologically [5]. Although Histopathology remains gold standard for the correct diagnosis, FNAC plays a pivotal role in the early diagnosis of GM as a minimally invasive, simple and cost effective outpatient treatment [7]. Diagnosis of TBM requires demonstration of AFB for which bacterial load of 10,000 to 1,00,000/ml material is required and culture isolates organism only in 25% of cases [9, 10]. Conclusive diagnosis by FNAC will reduces the unnecessary investigation and allow early and definite therapy [9]. Though both the entities have an overlapping cytological features our study highlights some of clinical and cytological differences which will help in definite diagnosis.

In NGM patients, age can ranges from 11 to 83 years. Althogh it is disease of young to middle aged women [8]. NGM is a self-limiting disease which is characterized by slow disease progression and abscess and discharging sinuses following the incision and drainage [5]. It is said to develop within couple of years after giving birth and recent history of breastfeeding is often obtained [5, 8]. In our study maximum number of patient of NGM were in age group of 25-35 years of age with mean age was 45 years. Recent history of pregnancy and breastfeeding were obtained in 6.67% patients. Similarly study by HeeRiNa seo [8], also revealed recent history of breastfeeding in 10.3% of patients. While TBM can occur at any age, varies from 6 months to 73 years [13]. Women of reproductive age are mainly affected due to frequent changes occurs in the breast during childbearing age and susceptibility of trauma and infection [10]. In our study the maximum number of patients of TBM were in age group of 20-30 years of age. None of the our patients were had history of recent pregnancy or lactation. Similar study done by Divya Achutha Ali *et al.* [16] did not reveal recent history of breastfeeding. Thus, both NGM and TBM affect women of younger age group in their reproductive age. Our study also revealed that TBM affects younger women as compared to NGM which is comparable to study done by Divya Achutha Ali *et al*., Kishore B *et al.* [16, 9]. Similar to literature, the duration was shorted in TBM patients than NGM [9, 10].

NGM presents commonly as hard unilateral discrete mass [8]. Mass can vary from 0.5 cm to 9 cm. some can show nipple retraction and sinus formation raising possibility of malignancy [4]. Similarly In our study majority of patients of NGM had unilateral firm, hard and ill-defined mass with average size of 3 to 5 cm. Two of them had clinical suspicion of malignancy. TBM usually present with solitary unilateral mass. Lump may be illdefined or well defined and mobile or fixed lump [10]. Size of lump can ranges from 1 cm to 8 cm with skin ulceration or sinus [8]. In our study majority of patient of TBM also had unilateral mass which were mobile with average size of 2-3cm.The average size was small in TBM patients compare to NGM patient, probably because early diagnosis in our cases. NGM is characterized by formation of microabscess around the granulomatous response and hence present with tenderness [5, 8]. In our study 10 patients of NGM (66.67%) complained of tenderness in breast lump, whereas none of TBM patients had tenderness. In study by divya Achutha Ali *et al*. 62.5% NGM and 0% TBM and Seo HR *et al*., 58% NGM and 5% IGM were associated with tenderness [16, 8]. So, by eliciting history of tenderness in the breast lump, right diagnosis can be made. Microabscess in NGM common for which patient comes to hospital [5, 8]. In our study 20% patients gave prior history of treatment in the form of Incision and drainage and following that developed discharging sinuses. This is also observed in study done bydivya Achutha Ali *et al*., Tse GMK *et al*., Seo HR *et al*., [16, 5, 4]. Involvement of breast in the tuberculosis may occur via lymphatics, hematogenous or continuous seeding and rarely by direct inoculation of bacilli via abraded nipple. Out of all lymphatic route is most likely route of breast involvement which occur from axillary lymph nodes. This is supported by involvement of

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axillary lymph nodes in 50 to 75% of cases of TBM [6]. In our study 50 % of TBM patients had axillary lymphadenopathy. Axillary lymphadenopathy can be seen in up to 15% of cases of NGM [4]. In our study 26.67% of patients NGM presented with axillary lymphadenopathy. In study done by divya Achutha Ali *et al*., the presence of axillary lymphnode among NGM and TBM were 6.25% and 40% and in study by Seo HR *et al*., Axillary lymphadenopathy seen in 12% and 5% patients of NGM and TBM respectively [16, 8].

Cytological smears of TBM consistent of caseous necrosis, epithelioid cells singly or forming granulomas, langhans type multinucleated giant cells and background inflammatory cells consisting of chiefly lymphocytes and histiocytes [8, 14]. Cytological smears of NGM consist of abundant epitheioidhistiocytes, variable granulomas, neutrophils, no caesous necrosis, occasionally foreign body type giant cells and ductal epithelial cells with reactive nuclear atypia [15]. Both findings of TBM and NGM considerably overlap. Our study reflect the same findings. In our study NGM and TBM both demonstrated epitheloid cells in 100% of smears. Epithelioid cell granuloma were demonstrated in 46.67% and 75% of NGM and TBM smears respectively. The Plump histiocytes were seen in 100% and 93.33% of TBM and NGM smears respectively which is comparable to study done by divya Achutha Ali *et al*., [16]. The multinucleated giant cells are common in granulomatous mastitis [14, 15]. Foreign body type giant cells are seen in NGM (73.33%) smears and laghans type of giant cells seen in (50%) smears of TBM. Study done by divya Achutha Ali *et al.* Foreign body type giant cells are seen in 75% of NGM smears and langhans type of giant cells seen in (60%) smears of TBM [16]. The caseous necrosis was seen only in patient of TBM and abscent in NGM. This findings is consistent with study done by Bakasi S *et al*., Seo HR *et al*., Singh S *et al*., [4, 8, 13]. In our study NGM showed inflammatory necrosis consisting of degenerated polymophs in 53.33% cases. Majority of NGM had polypmophs (86.67%) in the background and TBM had lymphocytes (75%) in the background. Our findings are supported by Tse GMK *et al*. and divya Achutha Ali *et al*. who also found the polymophs in NGM and lymphocytes in TBM [5, 16].

Conclusion

Granulomatous Mastitis including NGM and TBM are an uncommon chronic inflammatory disease of breast which almost always mimics cancer in young individuals and have overlapping clinical and cytological findings. FNAC along with proper clinical history help in differentiating this two entities. Clinically young reproductive aged female, with short duration of history, unilateral, solitary and firm breast lump, with absence of tenderness point toward the TBM. Presence of tenderness and history of incision and drainage followed by multiple discharging sinus support the diagnosis of NGM. Prence of axillary lymphadenopathy support the diagnosis of TBM. It can be seen in small no of cases of NGM which is reactive in nature.

Cytologically presence of caseousnecrosis, well formed epitheloid cell granuloma and langhans type of multinucleated giant cells over background of lymphocytes and histiocytessupport the diagnosis of TBM. While NGM shows predominance of polymophs, plump histiocytes, foreign body type multinucleated giant cells and inflammatory necrosis consisting of degenerated neutrophils and apoptotic bodies. In addition to this ZN stain and PAS stain along with TB PCR help in reaching to definite diagnosis.

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