

Original research article

A Study on Granulomatous Mastitis in Males and Role of Cytology in Evaluation of Granulomatous Mastitis.

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Abstract

Introduction: Granulomatous mastitis (GM) is a rare inflammatory condition of the breast in males that clinically mimics Gynecomastia and carcinoma that creating a diagnostic dilemma . It was first described in 1972 by Kessler and Walloch. Breast tuberculosis is rare form of tuberculosis was reported by Sir Astley Cooper 1n 1829 who called it scrofulous swelling of the bosom.

Methods: The current study was performed at the ESI medical college & hospital, Kalaburagi, Karnataka over a period of 2 years from March 2016-2018. The cases were retrieved from the archives of cytopathology and histopathology laboratories. All cases reported as granulomatous mastitis on cytology were included in the study.

Results: A total of 10 cases of granulomatous mastitis were diagnosed on cytology during 2 years' period. All the patients were male with a mean of 50 years range (40-50). In 07 out of 10 cases the lesion was in the right breast and three were on the left side, while the size of the lump varied from 2-5 cm in diameter. The duration of the lump ranges from 2 months to 3 years.

Conclusion: Cytology plays a significant role in the diagnosis of GM. Breast TB in men is a rarely reported entity even in high TB burden countries. Since the clinical features are not well defined. TB of Breast can be difficult to diagnose and the diagnostic delays can be long.

Keywords: Granulomatous ,Breast ,Gynacomastia

Introduction

Granulomatous mastitis (GM) is a rare inflammatory condition of the breast in males that clinically mimics Gynecomastia and carcinoma that creating a diagnostic dilemma (1). It was first described in 1972 by Kessler and Walloch (2). Breast tuberculosis is rare form of tuberculosis was reported by Sir Astley Cooper 1n 1829 who called it scrofulous swelling of the bosom (3). Breast tuberculosis is rare in western countries, but cases are encountered frequently in our set up due to high prevalence of tuberculosis (3). TB of the breast is an uncommon disease particularly in men (4). The first case of breast tuberculosis was reported in women in 1829, was only made by the end of 19th century. The first case of breast tuberculosis in men was reported about a century later 1927, and by 1945, there were only 21 known cases of breast TB in men (4). It is generally believed that infection of breast is usually secondary to tuberculosis foci elsewhere in the body which may or may not be clinically apparent. There are no well-defined clinical features of male breast TB, which may be confirmed with the clinical conditions, such as gynecomastia and breast carcinoma. Therefore, TB of the breast can be difficult to diagnose and the diagnostic delay lead to several months (4). The majority of breast lesions in men are benign. Gynecomastia and breast cancer are the two most important diseases of male breast. Most of the other diseases found in the male breast arises from the skin and subcutaneous tissues, e.g.- fat necrosis,

lipoma and epidermal inclusion cyst. Tuberculosis mastitis is an uncommon form of extra pulmonary tuberculosis. It is predominant in young women, the common age concerned between 20-40 years of the period of reproductive age. Breast tuberculosis is extremely rare in males (5). Tuberculous mastitis is a rare clinical entity accounting for approximately 3% of all mammary lesions, many affecting Indian and African females. It may occur as a part of systemic tuberculosis or as an isolated lesion (1). Although histopathology remains the gold standard for establishing the correct diagnosis, Fnac plays a pivotal role in the early diagnosis of Granulomatous mastitis as a minimally invasive, simple and cost effective outpatient technique. Here we are presenting a series of 10 cases of Granulomatous mastitis diagnosed cytologically over a period of 2 years. Through this study we wish to reemphasize that all granulomatous mastitis cases can suspect tuberculosis in endemic countries like India, more over it highlights the role of cytology in accurate and early diagnosis of these lesions particularly in males, so that unnecessary surgery can be avoided.

Materials and Methods:

The current study was performed at the ESI medical college & hospital ,Kalaburagi, Karnataka over a period of 2 years over a period of 2 years, march 2016-2018. The cases were retrieved from the archives of cytopathology and histopathology laboratories. All cases reported as granulomatous mastitis on cytology were included in the study. The patients presented to surgical outpatient department with a breast lump and were referred to cytopathology laboratory. Fine needle aspiration cytology (fnac) of the lump was performed and smears were evaluated. In all the cases cytological parameters were evaluated including the presence of epithelioid cell granulomas, histiocytes, multinucleated giant cells, necrosis and neutrophils. The Ziehl Nielsen (ZN) stain for Acid fast bacilli (AFB) and Periodic Schiff (PAS) stain for fungi were performed on all cytological cases. The clinical details including gender, age, history of trauma, family history of TB along with radiological findings (if available) of all the patients were recorded. Routine hematological findings with the erythrocyte sedimentation rate (ESR) and Mantoux test along with tuberculous polymerase chain reaction (TB-PCR) were correlated. Where ever histopathology was available the diagnosis was confirmed on hematoxylin & eosin stained smear sand ZN stain was applied.

Results:

A total of 10 cases of granulomatous mastitis was diagnosed on cytology during 2 years' period. All the patients were male with a mean of 50 years range (40-50). In 07 out of 10 cases the lesion was in the right breast and three were on the left side, while the size of the lump varied from 2-5 cm in diameter. The duration of the lump ranges from 2 months to 3 years. All the cases had varied clinical presentations with few showing irregular hard lump, and were given provisional clinical diagnosis of gynecomastia and malignancy. Ultrasonography was done in 5 cases and was reported variably as Gynecomastia, irregular hypoechoic mass and suspicious of malignancy. The clinicopathological details of all the cases shown in table 1.

Table 1: Clinicopathological details of all cases.

Cases	Age (yrs)	Site	Mantoux	Esr	Usg	Clinical	Cyto	TB-PCR	Histo
Case 1	42	Right	Positive	44	Irregular mass	Malignancy	GM	Negative	GM
Case 2	44	Right	Positive	56	S/o Malignancy	Malignancy	GM	Negative	GM
Case 3	41	Left	Negative	33	----	Gynecomastia	GM	Negative	---
Case 4	46	Right	Positive	44	Irregular mass	Gynecomastia	GM	----	-----
Case 5	54	Right	Positive	60	S/o	Malignancy	GM	Negative	-----

					Malignancy				
Case 6	47	Left	Positive	84	-----	Gynecomastia	GM	Positive	TBM
Case 7	48	Right	Positive	34	Gynecomastia	Malignancy	GM	-----	GM
Case 8	50	Right	Negative	32	-----	Malignancy	GM	Negative	GM
Case 9	44	Right	Positive	54	-----	Gynecomastia	GM	-----	GM
Case 10	45	Left	Positive	64	-----	Gynecomastia	GM	Negative	GM

ESR: Erythrocyte sedimentation rate, **USG:** Ultrasonography, **CYTO:** Cytology, **TB-PCR:** Tuberculosis polymerase chain reaction, **HISTO:** Histopathology, **GM:** Granulomatous mastitis, **TBM:** Tuberculous mastitis

On fine needle aspiration blood mixed aspirate was found (Fig-1&Fig-2). Seven cases showed presence of ill-defined granulomas. One case has scattered epithelioid histiocytes. Out of ten cases 09 cases showed no caseous necrosis but only 01 case showing patchy caseous necrosis, multinucleated giant cells containing nuclei ranging from 5 to 18 were present. These eight cases also had predominance of lymphocytes among other inflammatory cells. 02 cases showed the presence of benign ductal cells of the breast – Fig-1. The cytological features of all the cases were depicted in table – 2.

Table 2: Spectrum of cytological features of all the cases of GM.

Cases	Granuloma	Necrosis	Chronic inflammation	Giant cells	Ductal cells	AFB	TB-PCR	Cytology
Case 1	Present	Absent	Present	Present	Absent	Negative	Negative	GM
Case 2	Present	Absent	Present	Occasional	Absent	Negative	-----	GM
Case 3	Present	Absent	Present	Present	Absent	Present	Positive	TBM
Case 4	Present	Patchy	Present	Present	Occasional	Present	Positive	TBM
Case 5	Epithelioid histiocytes	Absent	Present	Absent	Occasional	Negative	-----	GM
Case 6	Present	Absent	Present	Absent	Absent	Negative	Negative	GM
Case 7	Present	Absent	Present	Absent	Absent	Negative	-----	GM
Case 8	Present	Absent	Present	Occasional	Absent	Negative	-----	GM
Case 9	Present	Absent	Present	Absent	Absent	Negative	-----	GM
Case 10	Present	Absent	Present	Occasional	Absent	Negative	-----	GM

Case 3 & 4 was TB-PCR positive, so was finally labelled as TBM.

AFB: Acid fast bacilli, **GM:** Granulomatous mastitis, **TBM:** Tuberculous mastitis, **TB-PCR:** Tuberculosis polymerase chain reaction

On application of Z N Stain two cases showed presence of AFB, thereby confirming the diagnosis of TB mastitis, which was further reaffirmed on histopathology. The PAS stain for fungus was negative for all cases. TB-PCR was sent for 4 cases that turned to be out granulomatous mastitis on cytology, 02 came positive. Two case underwent surgery and tissue was sent for histopathological examination. On histopathology one case showed presence of well-defined granulomas other showed ill-defined granulomas. There were

multinucleated giant cells and necrosis seen in one case and designated as tuberculous mastitis and other suggestive of granulomatous mastitis. Both were negative for Z N staining.

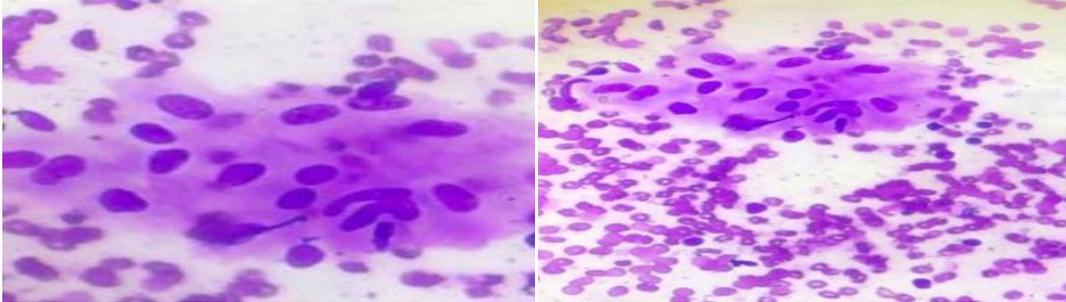


Fig. 1 & 2: Showing ill defined granulomas comprised of aggregated epithelioid cells.

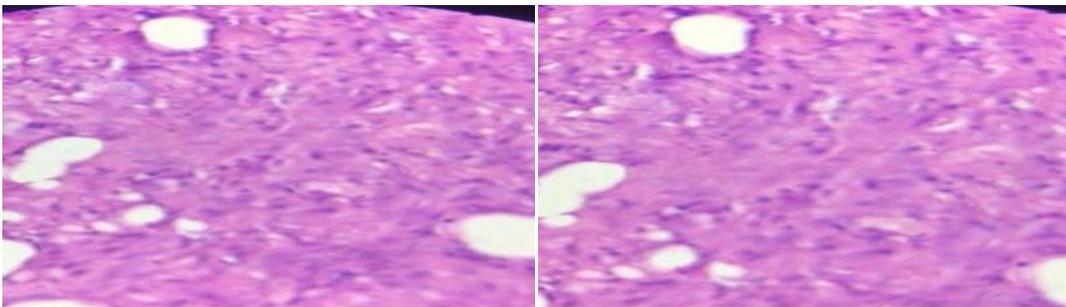


Fig:3 & 4: Showing ill defined granulomas.

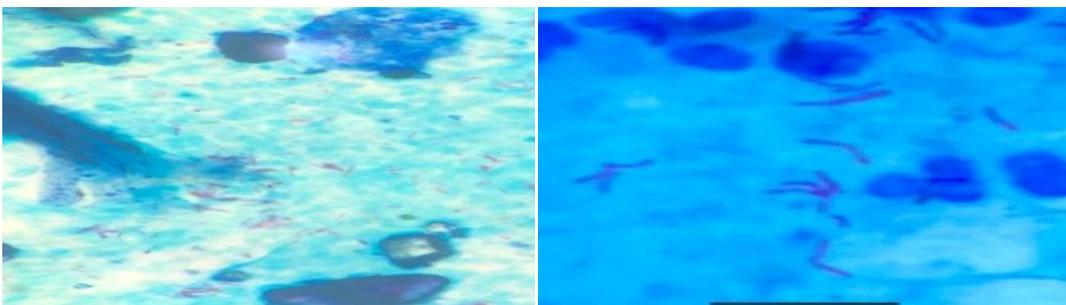


Fig 5 & 6: Showing acid fast bacilli (AFB)

Discussion:

Granulomatous mastitis (GM) is an uncommon breast lesion that was first described in 1972 and representing approximately 0.02-3% of all surgically treated breast diseases. (1). The clinical presentation of breast TB in men is poorly described in the literature and important elements are not uniformly reported at all. The combination of specific signs and symptoms, the challenges of diagnosing breast TB especially in resource constrained settings, and lack of awareness of the condition, both by the patient and health provider leads to significant delay. The main differential diagnosis to be considered are gynecomastia and breast cancer. Breast TB is often difficult to diagnose in both genders, computer tomography scan, magnetic resonance, mammography and ultrasound can provide useful information particularly on the extent of the disease. However, none of these image findings are specific for breast. The yield of FNAC which detects the presence of epithelioid granulomas and necrosis is variable. In the present and the past reviews, it was the most common diagnostic modality for breast TB. Here it proved highly sensitive as all the specimens tested for FNAC were positive. The review suggests that diagnosing breast TB requires a combination of clinical history and radiological findings complemented with when possible with two

diagnostic techniques, including fnac with AFB staining. PCR – whenever possible. (4). The breast and skin are considered to be the rarest sites of extra pulmonary tuberculosis constituting only approximately 0.1-0.5% of all TB cases. Tuberculosis of the breast is an uncommon disease that is often difficult to differentiate from cancer of the breast when it presents as a lump. Fnac is the primary investigation for breast lesions so awareness about granulomatous mastitis is most among cytopathologists. The cytological features that have been evaluated includes epithelioid histiocytes, granulomas, giant cells, necrosis and lymphocytes in the background. (1). Breast tuberculosis is commonly affects women in reproductive age group. It is uncommon in prepubescent females and elderly women. (5), and it is extremely rare in males, accounts for only 4% of all cases. (5). Breast tuberculosis overall appears to have a good prognosis, though no specific guidelines are available for the treatment of breast TB, whether in men or women. The optimum duration of therapy is unclear and objective criteria for assessing response are lacking. A standard Anti TB regimen four drugs 2 months' intensive phase followed by 2 drugs four months' continuation phase often accompanied or preceded by incision and drainage or lump excision appears to achieve satisfactory responses. (4). During our extensive search of literature on GM, we came across several studies across the globe. Seo et al. in 2012 retrospectively reviewed the records of 68 patients with GM. FNAC was performed in 30 cases with histopathology in all 68 cases, out of which 10 cases were TBM. While IGM was the final diagnosis in the rest of them. Helal et al studied 65 cases of IGM over a period of 6 years they have explained cytomorphological and histomorphological features of IGM. They emphasized the efficacy of cytology in diagnosis of such lesions. Ail et al obtained 21 cases of granulomatous mastitis diagnosed on cytology over 8 years out of which 16 cases were of nonspecific granulomatous mastitis and 5 were TBM. (1). Fnac establishes the diagnosis in most of cases. Khanna reported a success rate of 100% in his series. While Kakkar et al. reported a success rate of 73%. Tse has emphasized the presence of epithelioid histiocytes as the single most common indicator of granulomatous inflammation in the absence of granulomas which were absent in half of the cases reviewed by them. (6). Hemlata et al. revealed cytological features of non caseating granulomas along with plenty of polymorphs in the background is suggestive of granulomatous mastitis. (7). Srinivas et al. yielded 24 cases of male tubercular mastitis, most presented with an isolated breast lump. Constitutional symptoms were rare (21.4%) and associated tuberculosis foci, mostly inactive were seen in 43.8%. Fine needle aspiration was the commonest diagnostic modality, and acid fast bacilli were demonstrable in a minority (33%). (8). In the present study we evaluated 10 cases of granulomatous mastitis in males over a period of 2 years. Cytological parameters were evaluated in all the cases with applications of special tests like Z N and PAS stain. Histopathological evaluation was done wherever possible 2 out of 10 cases were labelled as Tuberculous mastitis based on ZN Stain / TB PCR and the remaining 8 cases were IGM. The comparative analysis of various studies by cytopathological evaluation of GM is depicted in table – 3.

Table 3: Comparative analysis of various studies based on cytopathological evaluation.

S no.	Year	Authors	Location of study	Duration (years)	No of cases	No of TB mastitis (AFB/PCR) POSITIVE	Histological correlation	Comments
1	2012	Seo et al.	Korea	10	68	10	68	Fnac performed in 30 cases
2	2016	Helal et al.	Egypt	6	65	-	65	All cases of IGM
3	2017	Ail et	India	8	21	5	4	--

		al.						
4	2020	Present study	India	2	10	2	1	8 cases of IGM

AFB/TB-PCR: Acid fast bacilli/ Tuberculosis polymerase chain reaction, **IGM:** Idiopathic granulomatous mastitis, **FNAC:** Fine needle aspiration cytology

Conclusion:

In conclusion cytology plays a significant role in the diagnosis of GM. Breast TB in men is a rarely reported entity even in high TB burden countries. Since the clinical features are not well defined. TB of Breast can be difficult to diagnose and the diagnostic delays can be long. A combination of granulomatous mastitis, necrosis and clinical response to antitubercular therapy was the commonest mode of establishing the diagnosis, and all the 10 cases responded to antitubercular therapy alone. This study reemphasizes the role of the cytopathologists in accurate and early diagnosis of these lesions, so that unnecessary surgery can be avoided.

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