

Cytological Features of Granulomatous Mastitis- A study of ten cases

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Abstract

Introduction: Granulomatous mastitis is a rare benign disease, the exact cause of which is still unknown. It usually presents as a mass which may simulate carcinoma. Many patients are put on long term antibiotics because of breast abscess suspicion, but are not cured. This disease usually affects women of child-bearing age with a history of oral contraceptive use. Most cases have been reported in third decade. In previous studies most of cases of idiopathic granulomatous mastitis were within six years of pregnancy. There are two types of granulomatous mastitis, specific and idiopathic.

Aim: To study cytological features of granulomatous mastitis, the age group involved and how to differentiate it from malignancy to prevent unnecessary mastectomies.

Method: FNAC was performed with 22G needle. Slides prepared were stained with leishman stain. Special stains like Zeihl Nelson stain and Periodic Acid Schiffs were done to rule out mycobacterium and fungal etiology.

Result: Cytological features of noncaseating granuloma along with plenty of polymorphs in the background is suggestive of granulomatous mastitis. History of lactation and oral contraceptives along with special tests further aids in its diagnosis.

Conclusion: In this study of ten cases we describe the importance of cytology in diagnosis of granulomatous mastitis which helps us to prevent unnecessary mastectomies. GM is essentially a diagnosis of exclusion that is by excluding other causes of chronic inflammation. Infective causes such as tuberculosis should always be ruled out before stating treatment with steroid.

Keywords: Breast, Mastitis, Granuloma, Polymorphs

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Introduction

Kessler and Wolloch were the first to describe granulomatous mastitis as a specific entity.[1] Cohen further elaborated it in 1977.[2] It has also been called granular lobular mastitis by Going et al (1987) [3], based on histological samples that had a lobule-centered distribution from patients with the disease. The disease is seen mostly in parous women, presents as a firm tender lump and simulates carcinoma clinically. It can be divided into idiopathic type and granulomatous mastitis secondary to tuberculosis and other infections, sarcoidosis and granulomatosis with polyangiitis, diabetes, silicone injection or other foreign body reactions. It has been found to be associated with the use of oral contraceptive pills, autoimmune disorders, hyperprolactinaemia, alpha-lantitrypsin deficiency and Corynebacterium spp. Uptil 2011, 541 cases have been reported since 1972.[4] Few cases have been reported in males[5] Though it is frequently reported from

western countries, very few cases have been described from India.[6] The aim is to study the cytological features of granulomatous mastitis ,the age group involved and how to differentiate it from malignancy to prevent unnecessary mastectomies .

Materials and Methods

A retrospective study was conducted between January 2012 to September 2015. In all the cases, patients detailed history along with whether lactating or non lactating, whether on oral contraceptives, their age and site of lump were taken. Fine needle aspiration was done from breast lump by commercially available 22-G needle attached to 10ml disposable syringe. Specimens were immediately smeared on glass slides and air dried for Leishman stain. In all the cases special stain that is ZN stain for tuberculosis and PAS stain to rule out any fungal etiology was applied. All the ten cases reported as granulomatous mastitis were reviewed for their cytological features.

Results

The present study consisted of 10 cases.(Table 1) The age ranged from 16yrs to 49yrs. Mean age group was 31.5 yrs. Seven patients were between age group 30-38yrs and had pregnancy within last six years and had history of taking oral contraceptives Out of seven, four patients were lactating. Three patient had inverted

nipple Clinically all the patients presented with lump in breast. One patient had erythema of skin just above the lump. One had associated small lymphnode measuring 0.5cm and the disease mimicked carcinoma breast. Two patients were girls of age 16yrs and 19years. One was premenopausal of 49years. Patient with inverted nipple and those who were lactating gave the history that the baby didn't took breast feeding properly from that side of breast. Out of ten in six patient(60%) left breast was involved and in four patient (40%) right breast was involved.

Table 1: Age, Sex and Site of breast lump in patients

S. No.	Age/Sex	Breast Lump
1	35yrs/F	Right
2	32yrs/F	Right
3	32yrs/F	Left
4	35 yrs/F	Left
5	37yrs/F	Left
6	30yrs/F	Left
7	16yrs/F	Right
8	30yrs/F	Right
9	19yrs/F	Left
10	49yrs/F	Left

Smears prepared showed noncaseating granulomas, multinucleated giant cells in the background of plenty of polymorphs and few lymphocytes.(Figure 1,2,3) ZN stain for AFB and PAS stain was done in each case. If frank pus was aspirated it was sent for culture sensitivity. Three cases(Figure 4,5) were positive for mycobacterium tuberculi, one case who had associated axillary lymphadenopathy was positive for atypical mycobacteria on PCR. All other cases were negative on ZN and PAS stain. One of the patient in whom no organism was identified was given different treatments but she finally responded to antitubercular treatment. Two cases underwent surgery and biopsy was sent to histopathology department. Rest cases were treated conservatively

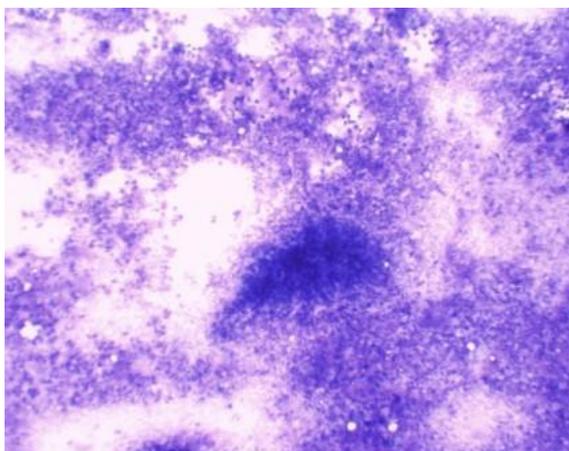


Fig. 1: Leishman stain. Shows plenty of polymorphs and histiocytes and a granuloma in centre.(4x)

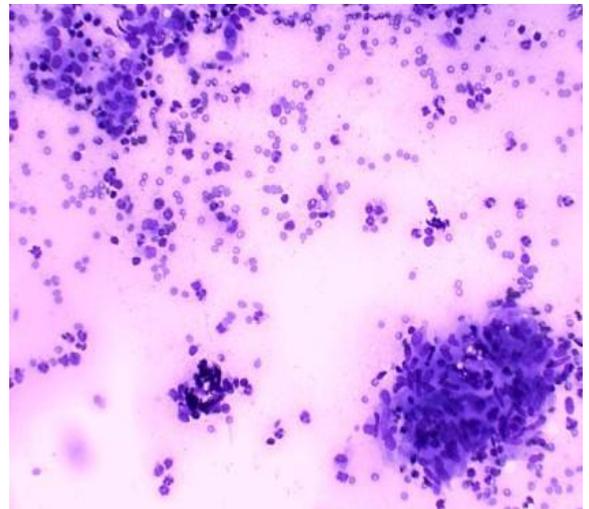


Fig. 2: Leishman stain. Shows epithelioid granuloma(10x)

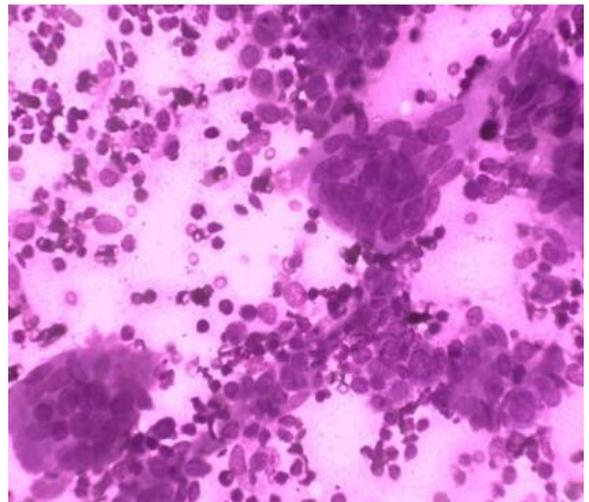


Fig. 3: Leishman stain shows multinucleated giant cells(40x)

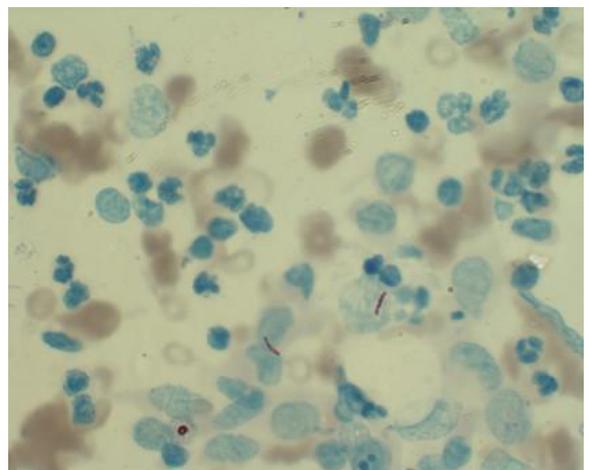


Fig. 4: ZN stain shows AFB in background of polymorphs and epithelioid histiocytes.(100x)

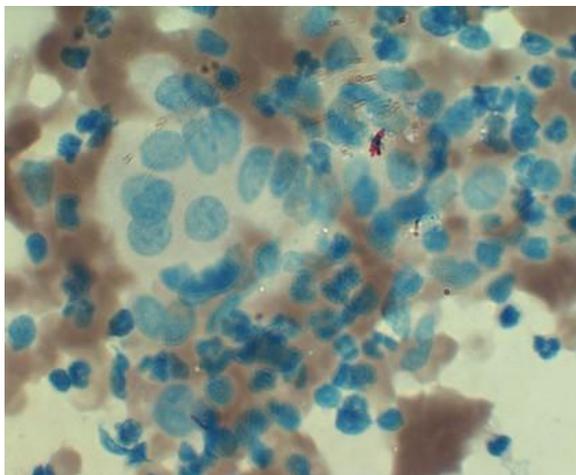


Fig. 5: ZN stain shows AFB in background of polymorphs and epithelioid histiocytes(100x)

Discussion

Granulomatous mastitis is a rare benign noncaseating chronic inflammatory disease of unknown etiology. The disease is rare because it also presents as breast carcinoma or infections both clinically and radiologically. Reported pretreatment diagnosis of malignancy is 51% in IGM.[7] Patients with IGM have been reported from national cancer centres. [8] The patient usually presents with breast lump in one of the quadrant but the lump can occur in any of four quadrants, firm to hard in consistency, local pain and may or may not be associated with skin ulcerations, abscesses and fistula. Clinically, it may mimic breast abscess, infective mastitis and breast cancer. Similarly, in our study also there was unilateral involvement of breast. One patient of age 35years presented clinically as carcinoma breast and had a single axillary lymph node and one patient presented as infectious mastitis. Seven of ten patients were in age group 30-38years and had pregnancy within last six years. Only Yip et al [9] have reported idiopathic granulomatous mastitis in bilateral breasts. Davies JD et al [10] in their study had most patients childbearing age with a recent history of pregnancy and lactation. Cytological findings include non caseating granulomas, multinucleated giant cells in the background of polymorphs and lymphocytes. But the cytological diagnosis of granulomatous mastitis (GM) is difficult. The features overlap with other aetiologies, including tuberculosis. But still if infective cause is ascertained unnecessary mastectomies can be prevented. The absence of necrosis and a predominantly neutrophilic infiltrate in the background favour a diagnosis of GM. Diagnosis should be considered if large number of epithelioid histiocytes are seen even if the granulomas are absent. The definitive diagnosis depends on histopathology. But if we aspirate pus or fluid, special stains and culture can find out micro-organism in many cases and it can prevent invasive procedures in such patient. No exact cause for the

patient who were of 16 yrs, 19yrs and 49yrs could be found. So they were treated as idiopathic granulomatous mastitis.

However in few cases, atypical cells and nuclear hyperchromasia can be seen and possibility for carcinoma breast can be reported. Such cases should definitely undergo sonography and biopsy. The absence of necrosis, predominant neutrophilic infiltrate, history and age of patient favour a diagnosis of GM. In our institute most patients were treated conservatively. Only two patients underwent open biopsy. The histological diagnosis of granulomatous mastitis was made when noncaseating, nonvasculitic granulomatous inflammatory reaction, composed of epithelioid cells, lymphocytes, and foreign body type of giant cells, centered mainly on breast lobules. In addition there can be squamous metaplasia of ductular or lobular epithelium and microabscesses. In such cases, immunohistochemical stains for cytokeratin or smooth muscle actin is necessary to identify a carcinoma against this background. Besides mimicking breast carcinoma, other diseases must be excluded that might cause a granuloma in the breast, such as tuberculosis, syphilis, histoplasmosis infections, as well as a foreign-body granuloma, vaccination granuloma, mammary duct ectasia, sarcoidosis, Wegener's granulomatosis, giant cell arteritis, and polyarteritis nodosa. In our study we have labeled the patient as granulomatous mastitis only after finding noncaseating granulomas apart from other inflammatory cells(polymorphs) or necrosis. We applied Z N stain on all the smears. In three cases reported as tuberculous mastitis there was no caseous necrosis, but their smears were positive for acid fast bacilli on Zeihl Nelson stain. Detection of mycobacteria is important because treating tuberculosis with steroids would aggravate the infection, whereas giving unnecessary antituberculosis drugs may cause numerous side effects. Other differential diagnoses are rare specific causes of granulomatous inflammation, including fungal infection or non-infectious causes, such as sarcoidosis or Wegener's granulomatosis. Because GM is essentially a diagnosis of exclusion, we must try to exclude as many causes as we can.

Exact etiology of granulomatous mastitis is unknown but it has been hypothesized that elevated prolactin levels or overt hyperprolactinemia stimulates immune system which prevents involution of breast gland after weaning. Prolactin signaling can also be triggered by other hormones like insulin and growth hormone[11]. Other hypothesis include autoimmune reaction to extravasated fat and protein rich luminal fluid (denaturated milk) is triggered in lactation. Farhan Abbas and Anwal in their study, found that fat necrosis was the most predominant feature.[6] In the recently reported cases, immunostaining showed that the lesions contained predominantly stromal T lymphocytes which favoured the possibility of a local immune response[6]. Today, widely accepted mechanism states that

autoimmune response to secretions originating from damaged ducts may have a role in IGM. Secretions in the mammary ducts get collected which lead to duct ectasia. As a result the duct rupture, the secretions spread to the stromal tissue resulting in a chronic inflammation(12). Few authors have found association with oral contraceptives. Oral contraceptives induce hyperplasia in the lobular ductule, thus leading to the obstructive desquamation of the ductules, distention of the ductules and perilobular inflammatory reactions but this has a conflicting data.(13) Apart from infective causes we found that retention of milk in breast is important cause of granulomatous mastitis.

Mammography and sonography aid in diagnosis but they do not give a definitive diagnosis. Focal asymmetry without a mass on mammography and heterogeneous echo pattern on sonography is the most common imaging finding in IGM.[14] MRI is not conclusive; it usually shows a heterogeneous enhancing area with ring-like enhancing abscesses [15]. Some authors have suggested that IGM is a self-limiting condition, with a range of two to 24 months but a chronic presentation could last for several years. Complications encountered during the treatment of IGM are recurrent infections, abscess and/or sinus formation, and delayed wound healing. In recurrent cases without any findings suggesting an infectious process, oral steroid therapy (prednisolone) can be administered until a remission is obtained Dose of the steroids is tapered off when a clinical response is observed. In case of recurrence, patients should be evaluated for tuberculous mastitis before initiating steroid treatment, especially in countries where tuberculosis is a widespread health problem. Recurrences after steroid treatment may be managed by administering methotrexate 10-15 mg/week in addition to low dose steroids for 12 to 24 months (16).

Conclusion

Fine needle aspiration cytology is a simple, cost effective and non invasive technique. To diagnose it is a challenge because the features overlap with other etiologies like tuberculosis (TB), fungal infections, fat necrosis, sarcoidosis etc. So even if we find scattered single epithelioid cells in the absence of granuloma we should rule out the possibility of granulomatous mastitis. Though the cause of granulomatous mastitis is unknown we in our study have found that in most cases the cause is either of improper breast feeding or inverted nipple because of which the patient is unable to feed as a result of which there is retention of milk which may lead to rupture of duct or collected secretions with time lead to chronic granulomatous inflammation. Though we found mycobacterium in few cases, idiopathic granulomatous mastitis is more common and diagnosis on cytological features can reduce the need of open biopsies and unnecessary mastectomies.

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