

Granulomatous Mastitis: A Masquerading Entity

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Abstract

Introduction: Granulomatous mastitis (GM) is a rare chronic inflammatory lesion of breast of unknown etiology. This entity clinically and radiologically may simulate carcinoma and presents as palpable breast lump with history of associated pregnancy, lactation or history of oral contraceptive intake. Cytological diagnosis is difficult as microscopic features are non specific and overlaps with other etiologies. *Aims/Objectives:* To study clinical presentation and cytological features of granulomatous mastitis with histopathological correlation. *Methods:* Prospective study of 24 cases was done over a period of three years and diagnosed as granulomatous mastitis on FNAC. Clinical data were collected and histopathological correlation was done among 18 cases. *Results:* Study comprised of 24 cases of granulomatous mastitis with age group ranging from 18 to 48 years (mean age - 33 years). Out of 24 cases, 16 cases had history of taking oral contraceptive pills and 14 were lactating. All the patients presented with breast lump, with abscess in four cases and axillary lymphadenopathy in three cases. Diagnosis of granulomatous mastitis was done on cytology based on the presence of epithelioid cells either in granulomas or scattered along with multinucleated giant cells against background comprising predominantly of neutrophils. Histopathological correlation was done among 18 cases with 100% correlation. *Conclusion:* Granulomatous mastitis is essentially a diagnosis of exclusion, which can be established by fine needle cytology in majority of cases thereby preventing unnecessary surgeries. Herein, we describe 24 cases of granulomatous mastitis diagnosed on cytology with 100% histopathological correlation.

Keywords: Granulomatous; Mastitis; Cytology; Histopathology; Granulomas.

Introduction

Granulomatous mastitis (GM) is an uncommon but a specific type of chronic inflammatory breast lesion that clinically and radiologically mimics carcinoma [1]. This entity was first described by Kessler and Wolloch and was further elaborated by Cohen [2,3].

Granulomatous mastitis can be divided into idiopathic type and granulomatous mastitis secondary to tuberculosis, fungi, actinomyces, cat-scratch disease, foreign bodies (including sutures, silicon

injections or leaking breast implants), subareolar abscess and duct ectasia [4].

Several etiologies have been postulated including an immune reaction to extravasated milk secretion, trauma, infection, use of oral contraceptive pills and prolactinemia. Granulomatous mastitis is commonly found in young parous females and presents as a firm tender lump within five years of child birth. Idiopathic granulomatous mastitis remains a diagnosis of exclusion [5].

Fine needle aspiration is a routinely used non invasive OPD procedure done on all palpable breast lesions. Diagnosis of granulomatous mastitis was done on the presence of epithelioid cells either in granulomas or scattered along with multinucleated giant cells against neutrophilic background. However,

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cytological features are non specific and may overlap with other etiologies. The histological features of granulomatous mastitis have been well described as consisting of non caseating granuloma formation within the breast parenchyma and lymphocytic lobulitis with or without neutrophilic microabscesses⁶.

Hence this study was undertaken with an aim to study the cytological features, the age group involved along with histopathological correlation wherever possible to avoid overdiagnosis of malignancy thereby preventing unnecessary mastectomies.

Materials and Methods

This prospective study comprised of 24 cases, diagnosed as granulomatous mastitis on fine needle aspiration cytology (FNAC) done at our tertiary care hospital from June 2013 to June 2016. Patients diagnosed as non- granulomatous inflammatory lesion and neoplastic breast lesions were excluded from the study.

Clinical details of all the patients were collected in a Proforma designed for the study and patients were studied in terms of age group, site involved, lactating or non lactating, history of oral contraceptive pill use, clinical presentation, ultrasound and mammogram

findings.

FNAC was done from breast lump using 22 gauge needle and smears were prepared and stained with Leishman, Pap and H&E stains. In all the cases, special stains such as Zeihl-Neelsen stain for tuberculosis and PAS stain to rule out any fungal etiology were applied.

Among all the patients, six cases were treated conservatively. In others, definitive histopathological correlation was done on material obtained either by core, wide excision or excision biopsy.

Statistical analysis was done using SPSS (Statistical package for social sciences), to obtain descriptive statistics in the form of mean \pm SD or as a percentage.

Results

In the present study of 24 patients diagnosed as granulomatous mastitis, age ranged from 18 - 48 years with mean age group of 31-40 years. Among these, 22 patients were married and had children. History of pregnancy within last 5 years was present in 18 patients among which 16 cases had history of taking oral contraceptive pills and 14 patients were lactating. Unmarried females were of 18 and 23 years of age respectively.

Table 1: Depicting clinical features, FNAC findings and histopathological correlation.

| Variable | Frequency | Percentage |
|--|-----------|------------|
| Clinical features | | |
| Age group: | | |
| 10-20 | 01 | 4.1% |
| 21-30 | 03 | 12.5% |
| 31-40 | 18 | 75% |
| 41-50 | 02 | 8.3% |
| Site: | | |
| Right side | 08 | 33.3% |
| Left side | 16 | 66.6% |
| Lactational status: | | |
| Lactating | 14 | 58.3% |
| Non lactating | 10 | 41.6% |
| History of intake of contraceptive pills | 16 | 66.6% |
| FNAC (24 cases) | | |
| Well defined granulomas | 18 | 75% |
| Scattered epithelioid cells | 06 | 25% |
| ZN stain for AFB | 04 | 16% |
| PAS for fungal elements | 00 | 00% |
| Histopathology (18 cases) | | |
| Epithelioid cell Granulomas | 18 | 100% |
| Lymphocytic lobulitis | 12 | 66.6% |
| Caseating necrosis | 02 | 11.1% |
| Neutrophilic abscess | 04 | 22.2% |
| Cyto-Histopathological correlation (18 cases) | 18 | 100% |

Clinically all patients presented with lump in the breast, with 16 involving left breast and 8 involving right side. Two patients had erythema of skin just above the lump, five patients had inverted nipples, one patient had history of nipple discharge and one had discharging sinus. Axillary lymphadenopathy was seen among three patients. The duration of symptoms ranged from one month to ten months with history of long duration cough in 18 year old patient.

Ultrasound examination done among all patients showed hypoechoic nodular mass in 12 cases, irregular hypoechoic lesion in seven cases and mixed hypoechoic and hyperechoic lesion in rest of the five cases. Mammography showed an ill defined mass in ten cases, asymmetrical density in six cases and normal study in two cases.

On FNAC, smears prepared showed non caseating epithelioid cell granulomas with multinucleated giant cells in 18 cases. Rest of the six cases showed scattered epithelioid cells with background of neutrophils and lymphocytes.

Out of 24 cases, four cases showed tubercle bacilli on ZN stain for AFB done on cytology. All other cases were negative for ZN and PAS stain. Six cases were treated conservatively while in others (18 cases), biopsy was done for histopathological confirmation.

On histopathological examination, 16 cases showed well defined granulomas with multinucleated giant cells and two cases showed scattered epithelioid cells. Inflammatory cell infiltrate was predominantly of lymphocytes in ten cases and polymorphs in eight cases. Caseating necrosis was seen in two cases, which were positive for ZN stain for AFB on cytology. Significant lymphocytic lobulitis was seen in 12 cases, ductal hyperplasias in two cases and four cases showed neutrophilic abscess.

Table 1 shows the varied clinical presentations along with cytological and histopathological findings among all cases diagnosed as granulomatous mastitis.

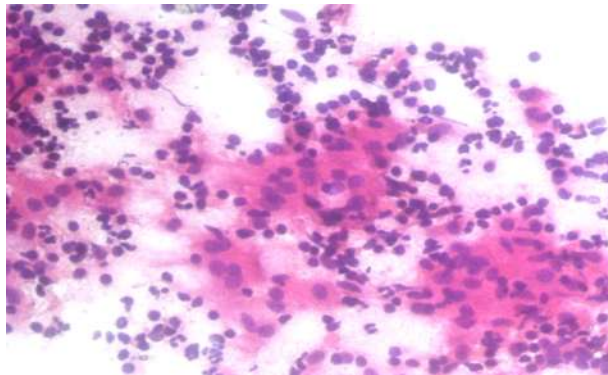


Fig. 1: Photomicrograph showing granuloma composed of epithelioid histiocytes in an inflammatory background (H and E stain; x200)

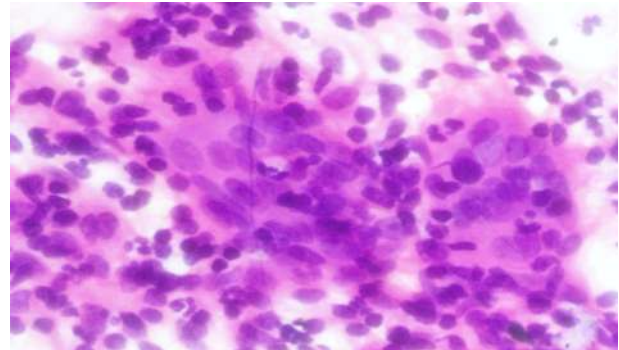


Fig. 2: Photomicrograph showing epithelioid cell granuloma surrounded by mixed inflammatory cells (H and E stain; x400).

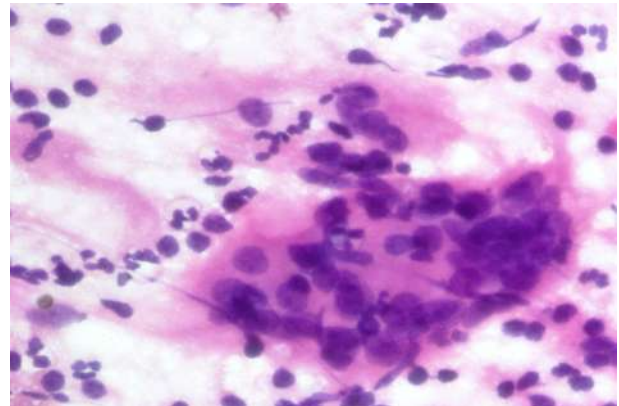


Fig. 3: Photomicrograph showing multinucleated giant cell surrounded by mixed inflammatory cells (H and E stain; x400).

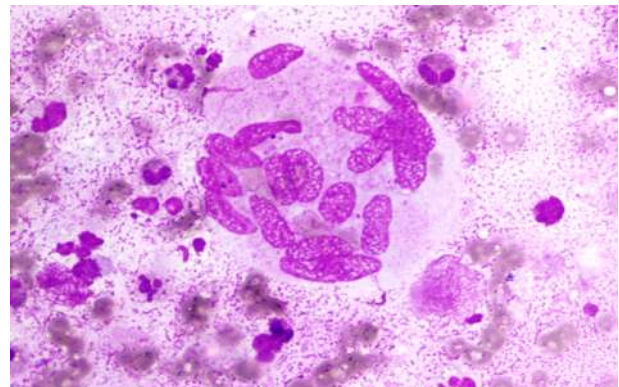


Fig. 4: Photomicrograph showing multinucleated giant cell surrounded by neutrophils. (Leishman's stain; x400).



Fig. 5: Photomicrograph showing acid fast bacilli - mycobacterium tubercle (Ziehl-Neelsen stain; x1000).

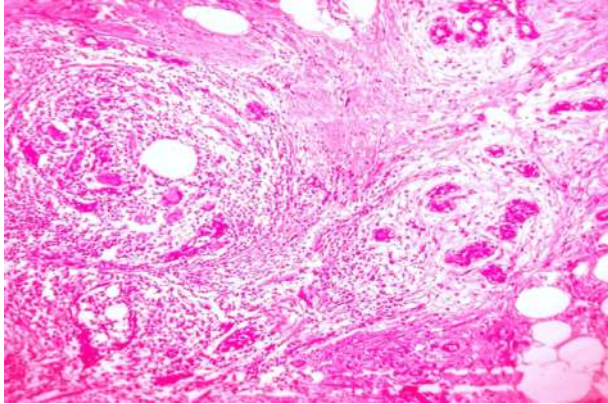


Fig. 6: Photomicrograph showing lymphocytic lobulitis with granuloma and multinucleated giant cells on histopathology (H and E stain, x100)

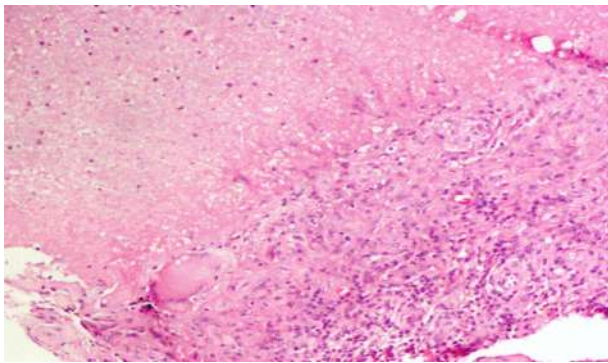


Fig. 7: Photomicrograph showing histopathological features of caseating necrosis surrounded by epithelioid cell granulomas and Langhans type of multinucleated giant cell (H and E stain; x100)

Recurrence was noticed only in two cases, both of them responded to corticosteroid therapy. The cases which showed positivity on ZN stain for AFB were treated with anti-tubercular drugs.

Discussion

Granulomatous mastitis, because of its worrisome clinical presentation as a hard breast lump particularly in younger women is considered as rare entity and diagnosis of exclusion. In most of the cases, it is considered as having idiopathic etiology and has to be distinguished from rare specific granulomatous conditions including tuberculosis, sarcoidosis and Wegener's granulomatosis. The disease usually affects women of reproductive age especially in postpartum period and may be associated with lactation. Clinically and radiologically, granulomatous mastitis is difficult to distinguish from carcinoma [6].

According to Hemalata et al, pretreatment diagnosis of malignancy was given in 51% of patients of Idiopathic granulomatous mastitis and same has been

reported from National Cancer Centre [7].

Study done by Kuba S et al showed that the patient usually presents with breast lump in one of the four quadrants but lump can occur in any of the four quadrants, firm to hard in consistency with local pain and may or may not be associated with skin ulceration, abscess and fistula, which correlated with our study wherein all the cases presented with unilateral involvement of breast whereas study conducted by Yip et al showed bilateral involvement of breasts in idiopathic granulomatous mastitis [8,9].

Hemlata T et al, who studied 10 cases of granulomatous mastitis showed that maximum number of cases were between age group of 30-38 years with history pregnancy within last six years and had history of taking oral contraceptives which correlated with our study, as maximum number of cases belonged to age group of 31-40 years [7].

In our study, 14 cases (58.3%) were lactating and 16 cases (66.6%) had history of intake of oral contraceptive pills. Exact etiology of granulomatous mastitis is unknown, but varied hypothesis such as hyperprolactinemia, autoimmune reactions to extravasated fat and protein rich luminal fluid and autoimmune response to secretions originating from damaged ducts suggests a role in idiopathic granulomatous mastitis [10]. Few authors have found association with oral contraceptive pills use which causes obstructive distension of ductules followed by rupture and perilobular inflammation [11].

With increasing use of FNAC as the initial, non-invasive diagnostic procedure for breast lesions, more cases of granulomatous mastitis will probably be encountered by the cytopathologist, necessitating an increased awareness of this disease entity [6].

Among the few large series describing the FNAC features of Granulomatous mastitis in the literature, the usefulness of FNAC in Granulomatous mastitis has been debated. Authors have confirmed the usefulness of FNAC in diagnosing granulomatous mastitis while few others concluded that the various causes of GM cannot be confidently differentiated by FNAC [9,12].

The diagnostic cytological criteria for GM remain poorly defined and include epithelioid histiocytes, granulomas and giant cells in the background of polymorphs and lymphocytes. The cytological features overlap with other etiologies including tuberculosis. The absence of necrosis and a predominantly neutrophilic infiltrate and large no of epithelioid histiocytes seen in the absence of granuloma favours a diagnosis of GM [6,7].

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.

Besides mimicking breast carcinoma, other diseases that might cause granulomas must be excluded. Though bacterial culture remains gold standard for diagnosing tuberculosis, but 6-8 weeks time is required for AFB culture which is an important limitation [13]. In our study, four cases showed positivity for acid fast bacilli on Ziehl Neelsen Stain. Detection of mycobacteria is important because treating tuberculosis with steroids would aggravate the infection, whereas antitubercular drugs may cause numerous side effects [13].

According to Morgan (1931), incidence of tubercular mastitis is between 0.5 to 1.04% [14]. In Indian scenario, where there is high prevalence of pulmonary tuberculosis and rapid spread of AIDS, tubercular mastitis is no longer considered uncommon. Breast tissue is markedly resistant to tuberculosis because it provides infertile environment for survival and multiplication of tubercular bacilli. Breast may become infected in a variety of ways which may be hematogenous, lymphatic, direct inoculation or ductal infection [13].

In tubercular mastitis, the common cytological features include epithelioid histiocytes, Langhans giant cells, granulomas and caseating necrosis. The presence of predominantly neutrophils in the background and lack of caseous necrosis may favor diagnosis of granulomatous mastitis rather than tuberculosis [6].

Histopathological correlation was obtained in 18 cases, of which two cases showed caseating necrosis. There was 100% correlation with all cases showing features of granulomatous mastitis. According to author Tse GM et al, who studied 26 cases of granulomatous mastitis showed 100% cytohistopathological correlation, with all the cases showing granulomas, lymphocytic lobulitis in 13 out of 19 cases (68%) and necrosis in three cases (11%) which correlated almost with findings of our study [15].

Idiopathic Granulomatous Mastitis (IGM) considered as self limiting condition ranges from 2-24 months but can last for several years. Complications include recurrent infections, abscesses, sinus formation and delayed wound healing [7].

The treatment of choice for GM is oral steroid therapy until remission is obtained. In case of recurrence, patients should be evaluated for tuberculosis and may be managed by methotrexate

and low dose of steroids for 12-24 months [16].

Conclusion

FNAC of palpable breast lumps is a useful, non invasive, cost effective and simple OPD procedure. Granulomatous inflammation of breast is an uncommon entity but should be considered in the differential diagnosis of a lump in the breast. To diagnose granulomatous mastitis is challenging because clinically it mimics carcinoma and microscopically features overlap with other etiologies like tuberculosis, fungal infections, fat necrosis, sarcoidosis etc. Although histopathological examination is confirmatory, granulomatous mastitis can be diagnosed accurately based on cytological features thereby reducing open biopsies and extensive mutilating mastectomies.

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