Clinicopathologic Spectrum of Granulomatous Mastitis

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Abstract: Background: Granulomatous mastitis (GM) is a rare and often confusing chronic inflammatory breast condition with unknown etiopathogenesis and vivid clinical presentation. It was first described by Kessler and Wolloch in 1972. Generally it is of two types, Idiopathic GM and specific GM. It is almost impossible to make its diagnosis or even suspicious diagnosis of granulomatous mastitis clinically and radiologically. Diagnosis is made purely on FNAC (Fine Needle Aspiration Cytology) and histology.

Methodology: We had planned a two year retrospective study of granulomatous mastitis which initially presented with chief complaints of lump breast in surgery OPD.

Results: Review of cytological archives revealed 12 cases of granulomatous mastitis. Two cases were tubercular mastitis and 10 cases were diagnosed as idiopathic granulomastitis.

Conclusion: GM is still a diagnostic challenge for surgeons and pathologist even after 45 years of its first documentation because of its unknown etiopathogenesis. More proactive research studies are required to establish its etiopathogenesis. Secondary causes should be ruled out to establish diagnosis of IGM. Patients should be followed up regularly so that no case of developing/underlying malignancy is missed.

Keywords: Granulomatous Mastitis, Clinicopathologic, Etiopathogenesis.

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Introduction

Granulomatous mastitis (GM) is a rare benign disease of the breast, first described by Kessler and Wolloch in 1972 [1]. It is a rare and often confusing chronic inflammatory breast condition with unknown etiopathogenesis and vivid clinical presentation. Generally it is of two types, Idiopathic GM and specific GM. Idiopathic GM is defined as GM without any other attributable causes and specific GM can be a rare secondary complication of tuberculosis, syphilis, corynebacterial infection, sarcoidosis, Wegener's granulomatosis, foreign body reaction, vasculitis, fungal and parasitic infections, etc.[2-4].

It is almost impossible to make its diagnosis or even suspicious diagnosis of granulomatous mastitis clinically. Imaging studies also do not provide pathognomonic signs of GM and are by no means reliable in distinguishing tubercular mastitis (TM) from that of a breast malignancy [5].

Diagnosis is made purely on FNAC and histopathologic examination.

The importance of this condition lies in the fact that it is seldom possible to differentiate it from carcinoma of breast clinically or radiologically. Patients present to physicians with varied symptoms like lump breast, abscesses (acute or chronic), discharging sinuses, mastitis and even some time with axillary lymph node mass, making it difficult to differentiate from carcinoma breast.

However, pain and palpable tenderness is associated more frequently with a tuberculous mass than with a malignant breast mass and involvement of the nipple and areola complex is less commonly seen in mammary tuberculosis [6-9]. But due to limited literature and rarity of this condition, no specific protocol has been prepared for treatment purposes. Patient often undergoes a wide variety of treatment options ranging from incision and drainage, corticosteroid
administration, Anti tubercular medication to even mastectomy.

We had planned a two year retrospective study of granulomatous mastitis which initially presented with chief complaints of lump breast in surgery OPD. All of them had either hard irregular lump with retraction of nipple or had pus discharging mass. History of onset of lesion in all cases ranged from 1 month to 4 months. Initial suspicion of malignancy was kept in most of these cases and they were investigated accordingly. Ultrasound of the breast suggested irregular hypoechoic lesion with BIRAD 3-4. FNAC was necessary in all of these cases to reach a conclusive diagnosis.

**Materials and Method**

Data was collected retrospectively over a period of two years (2015-2017) in Dr. RPGMC Kangra at Tanda (H.P). These patients initially presented in surgery OPD with chief complaints of lump breast which were either hard irregular or an inflammatory appearance with discharging sinuses. Initial suspicions of malignancy were kept and were sent for radiological and cytological investigation. USG revealed irregular hypoechoic lesion with BIRAD 3-4.

Informed consent and relevant history was obtained and FNA procedure was performed on above patients. Giemsa and PAP staining was done on the smears. In addition ZN staining, AFB Culture and CBNAAT and fungal profile studies were conducted for evidence of tubercular or fungal infection. Patients were categorised in to idiopathic granulomatous mastitis and tubercular granulomatous mastitis owing to presence of epithelioid cell granulomas, lymphocytes, plasma cells, macrophages, multinucleated giant cells and presence or absence of tubercular bacilli. In idiopathic granulomatous mastitis no etiologic agent could be identified.

**Observation and Results**

Review of cytological archives revealed 12 cases of granulomatous mastitis. Two cases which were diagnosed as tubercular granulomatous mastitis had positive CBNAAT report in both cases while ZN stain showed AF bacilli in only one case. Rest 10 was diagnosed as idiopathic granulomatous mastitis. Stained cytosmears showed non-caseating epithelioid cell granulomas, lymphocytes, multinucleated giant cell and macrophages (Figure 1 and 2).

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**Fig. 1:** Showing non caseating epithelioid cell granuloma

**Fig. 2:** Depicting multinucleated giant cell and neutrophils
In addition interestingly neutrophilic infiltrate was noticed in eight out of ten cases of idiopathic granulomatous mastitis (Figure 3).

Two of the cases showed mild to moderate reactive cytological atypia in duct epithelial cells [Figure 4].

Age and Sex Distribution

All patients were married females in the age group of 26 to 60 years. Figure 5.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>26-35</td>
<td>50%</td>
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<tr>
<td>36-40</td>
<td>0%</td>
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<tr>
<td>40-48</td>
<td>33%</td>
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<td>49-60</td>
<td>17%</td>
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All patients were parous females except one nulliparous female who was on infertility treatment for past 4 months. History of ongoing lactation was present in only one patient, while duration of last child birth ranged from 5-25 years. No history of intake of oral contraceptive/ hormonal pills was present in 11 patients except the nulliparous female, who was on treatment for infertility. Out of 12 patients, seven patients (58.3%) presented with left breast involvement while right breast was involved in five patients (41.7%).None of the patient gave history of breast implant, autoimmune diseases, thyroiditis or trauma. One patient of tubercular mastitis gave previous history of antitubercular therapy. History of recurrence of idiopathic granulomatous mastitis was observed in one patient.

Outcome

These patients were followed up after 6 months. Seven patients of idiopathic granulomatous mastitis were treated conservatively with 2-3 weeks of broad spectrum antibiotic treatment. After 6 months 70% of idiopathic cases showed spontaneous resolution of lesion. One patient was treated with wide local excision of lesion. No follow up details were available for two patients. Two cases of tubercular granulomatous mastitis showed response on antitubercular therapy.

Discussion

Idiopathic granulomatous mastitis is a rare chronic inflammatory disorder of unknown etiology. It was first described by Kessler and Wollach in 1972 [1] with its etiology still vague. Although the aetiology of Idiopathic granulomatous mastitis (IGM) remains unclear, some factors are claimed to cause the disease including autoimmune diseases such as granulomatous thyroiditis, granulomatous prostitutes, granulomatous orchitis, immune response to local trauma, local irritants, undetected organisms such as viruses, mycotic, and parasitic infections, hyperprolactinemia, diabetes mellitus, alpha-1 antitrypsin and the use of oral contraceptives[10,11].

Affected women are nearly always parous and usually present in their early thirties [12]. In our study also; all were parous women except one who was nulliparous and on infertility treatment. Many believed autoimmunity to be the major etiologic factor for IGM owing to quick response to steroids. Leyla ozel conducted serologic tests in eight IGM patients and found RF positivity in six patients and ANA and anti dsDNA positivity in rest of two patients, thus postulating autoimmune basis for the disease [13]. Although in stark contrast Fatih Altintoprak failed to support the eventual existence of an autoimmune basis for IGM in his study [14].

Breast tuberculosis accounts for less than 0.1% of all known breast diseases globally but it comprises up to 3% of treatable breast lesions in developing countries [15]. It is very important to differentiate between IGM mastitis and tubercular mastitis because treatment modalities of both lesions are altogether different. On one hand wide local excision and ATT are unnecessary in IGM, on the other side steroid treatment given in IGM, may aggravate tubercular GM.

Clinically breast mass with an associated sinus tract is most common presentation in tubercular GM. Many patients present with associated axillary lymphadenopathy. Cytologically it is difficult to differentiate between IGM from tubercular GM. However some authors have suggested absence of necrosis and presence of neutrophils in the background as the factors favouring idiopathicGM [16]. In our study 80% of IGM mastitis showed absence of necrosis and presence of neutrophilic infiltrate in the background.

Granulomatous mastitis as a pathological condition is more worrisome because it mimics carcinoma clinically and has tendency to recur. Mazlanluqman reported a case of 34yr old female who had recurrent episodes of right breast swelling and abscess for 8 years. These were proven to be chronic granulomatous mastitis histologically on 3 different occasions. A trucut biopsy of the right breast was then done and showed features consistent with an infiltrating ductal carcinoma [17]. We also had two cases in our study which showed moderate atypia and were advised biopsy and regular follow up.

Diagnosis of this condition requires histopathological confirmation with presence of granuloma formation. Once this histological picture is present then a wide spectrum of investigations are needed to find the cause of granulomatous reaction.
Tuberculosis, Sarcoidosis, Wegner’s granulomatosis, fungal infections, syphilis, giant cell arteritis, PAN all need to be considered with detailed history suggestive of any association with these granulomatous diseases. Even after doing extensive search many a times it is not possible to reach a conclusive diagnosis and a possibility of idiopathic granulomatous mastitis is to be kept.

The treatment modalities for this disease are also varied and non specific. They range from medical treatment (Anti tubercular drugs, corticosteroids, antibiotics to antifungal drugs), surgical treatment (drainage to excision to even mastectomy) and to a close regular clinical surveillance.

**Conclusion**

- GM is still a diagnostic challenge for surgeons and pathologist even after 45 years of its first documentation because of its unknown etiopathogenesis. More proactive research studies are required to establish its etiopathogenesis.
- Secondary causes should be ruled out to establish diagnosis of IGM.
- Patients should be followed up regularly so that no case of developing/underlying malignancy is missed.

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