Management of granulomatous mastitis

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ABSTRACT
Granulomatous mastitis (GM) is an uncommon mild inflammatory breast disorder that primarily affects the people who had the breastfeeding experience. However, the inflammation related to wound response, metabolic or hormonal mechanisms, autoimmunity and a Corynebacterium kroppenstedtii infection are concerned. Etiopathogenesis is an unknown issue carrying the symptoms of pain, weight, hyperemia and inflammation. Etiopathogenesis is also prolonged and the clinical appearance is capable of imitating bacterial mastitis or inflammatory carcinoma. Histopathology is used for its diagnosis. The biopsy reveals granulomatous development coupled with scattered invasion of giant multi-nucleated cells, plasma cells and histiocytic epithelium cells. Mammography, ultrasound and “Magnetic Resonance Imaging” are not specific methods, however, can be performed to exclude other pathologies through the ultrasound and mammography. GM management is problematic due to lack of evidence even randomized controlled trials. Majority of clinicians used a therapy plan beginning with antibiotics and corticosteroids in Western developed world accompanied by constant steroid care and procedure of patients with chronic symptoms requiring accurate cares. Up to now, there is no proof over the immunotherapy function that needs further knowledge about the rare disorder.

Key word: granulomatous mastitis (GM), Idiopathic granulomatous mastitis (IGM)


INTRODUCTION
When GM was initially identified by Kessler and Wolloch in 1972, many cases have been recorded as a benign disease entity in the world. In this case, GM with about 2.4 prevalence in 100,000 women and 0.37% in United States is counted as an unusual differential diagnosis [2]. That the...
most cases have been seen in non-white patients in US proves its low occurrence in Europe, especially in Germany [3]. The lack of valid evidences backs to lack of condition. The etiology of genetically engineered substances is hypothetical and there is no agreement on disease management [4]. However, the diagnoses of a GM patient could be a problem for a clinician and patient who suffer from a weird disease path with an immense effect on his/her life satisfaction. Different mastitis triggers and malignancy must typically be eliminated prior the GM diagnosing [5]. This study has focused on the etiology, clinical appearance and diagnosis of GM and modern therapeutic methods to summarize the existing evidences.

**Promotion and Etiology**

GM is a benign inflammatory breast disease [1] and the statistics of GM in Europe or Germany are not reliable in terms of incidence or prevalence. However, majority of reports in literature show that the disease appears mainly in infants often with breastfeeding records. Typically, disease develops at the middle of 30 years around 2 years after breastfeeding [6], reporting just 2 male GM [7, 8]. Women with grown GM across the pregnancy or lactation have been nominated [9, 10]. Majority of publications belong to Mediterranean nations, Middle East, Asia and US. A higher prevalence of GM has been reported for Asian, Arabs and Spanish females” [11, 12]. 7 GM diagnoses were detected in Indiana in 2008 on the Spanish females. Despite the monitoring of the case by the Centre for Disease Control in Atlanta Analysis to classify the potential risk factors of disease, there was no particular factor [2]. Though there are some theories, the etiology of GM is uncertain. Hence, GM could be defined as an allergic inflammatory reaction to epithelial injury, but it highly could be associated to delivery and breastfeeding. In other words, inflammatory reactions could appear when there is a response to the extravagant secretions from the lobules [12]. Sometimes, the lesions of GM are cultivated that might play great role in causing *Corynebacterium (C) kroppenstedtii*. GM was also called 'cystic neutrophilic granular mastitis' by some scholars owing to the high proportion of data for this lipophilic gram-positive rod [6]. Recently, non-lactation-related risk factor hyper-prolactinemia induced by antipsychotic drugs has been addressed. Prolactin has a proinflammatory impact and defined as a help for ductal ectasia and milk stagnation. 37% of patients with GM were reported by Wong et al. [13]. The medical history of kroppenstedtii related to mastitis requiring medical drug poses the concern, whether this form of treatment could contribute to an elevated risk for GM or not. Adding that the exact amount of C infections is underestimated. Due to the slow-growing *C Kroppenstedtii* could not show routine culture.
mechanisms utilizing PAS staining or Ziehl-Neelsen. Up to now, corynebacteria has not been highly researched; also the level of serum prolactin has not been tested in GM patients [13]. GM levels are still measured. Inflammation is helped by finding the nodosum or arthritis concomitant erythema [14, 15] in GM etiology. Antitrypsin is found out as a relative risk factor for GM induction [14], also Alpha-1 is an autosomal codominant disease of Caucasian originated from US and European and highly associated with antitrypsin. Sometimes the symptoms of panniculitis are related. Panniculitis has been mainly reported by histopathological studies. Whether this rivalry with GM is actually due to the imprecise histopathology or whether it is an unusual observation in GM patients is still unknown.

![Image of a woman with granulomatous mastitis](image)

Fig. 1. Shows a woman (29 years) with a mass in the left breast (upper quadrant) plus fistula signs and inflammation for 2 years. Ultrasound and Mammography was conducted (ACR B, BIRADS 4, Core needle biopsy). GM was diagnosed.

**Presenting Symptoms**

A sore mass is the main sign of GM. Due to the breast inflammation; up to 50 percentages of patients have experienced swelling and erythema. Additionally, Hyperemia, isolar recurrence, fistula and ulceration are the other symptoms plus abscess seen in 37% of patients [16]. The loss occurs in breast quadrant, but primarily seen in the retroareolar area from which radially spreads. Most samples are arises on one-side. The mass is similar to a bacterial abscess or clinically breast cancer by causing the retraction of skin or nipple. Up to 15% of patients suffer from lymphadenopathy [17]. Considering many phases from the start of indications to a precise diagnose; unidentified signs are sometimes confusing during the diagnosing [18]. Figure 1 shows a woman (29 years) before the corticosteroid therapy. There are the symptoms of mass, inflammation and fistula in the outer upper quadrant of left breast for nearly 2 years.
**Diagnosis**

**Histopathology**

GM could be defined just by histopathology. Combined with the epithelium histiocyte, plasma cells, lymphocyte and localized infiltrate of multi-nucleated giant, GM is defined by the development of non-necrotizing granuloma (Fig. 2). Generally, organized sterile micronutrition occurs with neutrophilic infiltrates. The severity of disease is observed by the inflammation spread to the surrounding lobules. Parenchyma also means that the acinum functions are lost and ducts are weakened \([18, 19]\). GM is obviously a non-infectious disease, though the corynebacteria’s role is highly regarded in GM generation. Taylor et al (2003) \([20]\) has separated corynebacteria from the lipid filled vacuoles inside the granuloma, resulting that the life of corynebacterium species is significant in the properties of GM. Align with Taylor et al. (2003), other studies provided few corynebacterial species \((C.\ freneyi, C.\ tuberculostearicum and C.\ kroppenstedii)\) \([21, 22]\). Isolated C is in the sequence of one case in Japan. \(C.\ Kroppenstedii\) was seen in 6 cases out of 19 GM cases \([23]\). Discovering of Corynebacteria is highly important i.e. an under group kroppenstedi in GM lesions due to its histopathological presence of cystic spaces or vacuoles \([7]\), granulomate and neutrophilic inflammation, called 'cystic neutrophilic granulomateous mastitis. Corynebacteria are also regarded as a contaminant of natural skin flora in GM lesions \([17]\). “Core needle lesion biopsy” is the main technique for GM diagnosing (96%), however, 4 out of 19 patients have been diagnosed by “fine needle aspiration” (FNA) (likely inadequate material and undefined susceptibility of 21.1% i.e. fat necrosis and abscess) \([24]\). Pathology separates the GM of granulomatosis, Wegener's TB and sarcoidosis from other granulomatotic and autoimmune diseases. External body reaction, histoplasmosis, IgG4 RD mastitis, fat necrosis, actinomycosis and particularly inflammatory breast cancer are various diagnoses \([22]\). Comparing the biopsy of issue taken from the “core needle
biopsy” to FNA, the former shows better results. The histological pathology methods consist of using gram and rapid stains, Grocott's methenamine silver and hematoxylin and eosin to differentiate of tuberculosis or sarcoidosis. Lacambra et al.[25] has reported that tuber lesions are defined by more necrosis, eosinophils and fibrosis including more plasma cells compared to the genetic modifier population. The clinician must consider a different diagnosis of tuberculosis in those with the symptoms of compromised immune system or lung disease. In younger patients with more diagnostic clinical mass, the disease is probably growing. For the syndrome of Lofgren, nodosis commonly shows sarcoidosis.

**Laboratory Findings**

It was assumed that autoimmunity underlines the etiology of GM, however, no reliable blood-related values have been provided to support this hypothesis. Serum complement titers and typical rheumatoid factor(s) (RF) were recognized [26], while others have positive RF and Lupus erythematosus-associated (in some cases) “anti-neutrophil cytoplasmic autoantibody” (ANCA) and anti-dsDNA antibodies [19]. A link among ANCA, c-ANCA, interleukin 2 receptor or angiotensin-converting enzyme are not specific, however, the specifics of these variables might aid if other autoimmune diseases are excluded [27]. Normally, the C-reactive protein levels are stable or slightly raised to 1.1-1.5 mg / dl (typical: < 0.5 mg / dl) as an unspecific index of infection and the levels of “carcinoembryonic antigen and cancer antigen” (CA) 15-3 are confined [20].

<table>
<thead>
<tr>
<th>Table 1. Symptoms, treatment and the results of patients with granulomatous mastitis</th>
</tr>
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<tbody>
<tr>
<td><strong>Imaging</strong></td>
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<table>
<thead>
<tr>
<th>Aghajanzadeh et al., 2015</th>
<th>Elzahaby et al., 2016</th>
<th>Freeman et al., 2017</th>
<th>Calis et al., 2017</th>
<th>Bashir et al., 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n (%)</td>
<td>206 (100)</td>
<td>30 (100)</td>
<td>14 (100)</td>
<td>19 (100)</td>
</tr>
<tr>
<td>Breast mass, n (%)</td>
<td>169 (82)</td>
<td>27 (90)</td>
<td>14 (100)</td>
<td>5 (26)</td>
</tr>
<tr>
<td>Erythema, n (%)</td>
<td>24 (12)</td>
<td>7 (50)</td>
<td>3 (16)</td>
<td>5 (26)</td>
</tr>
<tr>
<td>Pain, n (%)</td>
<td>24 (12)</td>
<td>5 (26)</td>
<td>4 (44)</td>
<td></td>
</tr>
<tr>
<td>Ulceration, n (%)</td>
<td>37 (18)</td>
<td>8 (57)</td>
<td>13 (68)</td>
<td>15 (83)</td>
</tr>
<tr>
<td>Received antibiotics, n (%)</td>
<td>206 (100)</td>
<td>8 (57)</td>
<td>13 (68)</td>
<td>15 (83)</td>
</tr>
<tr>
<td>Improved on antibiotics, n (%)</td>
<td>6 (12)</td>
<td>3 (21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Received steroids, n (%)</td>
<td>200 (97)</td>
<td>0 (0)</td>
<td>8 (33)</td>
<td></td>
</tr>
<tr>
<td>Corticoid regimen</td>
<td>2-3× 10-20 mg prednisolone daily for 2-6 months with tapering</td>
<td>2× 16 mg prednisolone daily for 2 weeks, slow tapering over 2 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved on steroids, n (%)</td>
<td>11 (5.3)</td>
<td>30 (100)</td>
<td>9 (64)</td>
<td>5 (26)</td>
</tr>
<tr>
<td>Wide surgical excision, n (%)</td>
<td>144 (72)</td>
<td>9 (64)</td>
<td>5 (26)</td>
<td>9 (38)</td>
</tr>
<tr>
<td>Improved after surgical excision, n (%)</td>
<td>1 (7)</td>
<td>1 (7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete mastectomy, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
There is a correlation between malignant lesions and GM imagery outcomes. Accordingly, mammography, ultrasound and MRIs could be found unspecific in GM [28]. Many hypoechoic masses with subsequent acoustic changes or subsequent acoustic shadowing are routine ultrasound results. Fluid collections and cavities related to skin fistulas are advanced. "Doppler Imaging" can be found in some cases of hypervascularity [15]. In all cases, 15% to 55% show reactive ipsilaterally swollen axillary lymph nodes [20, 29]. Despite the 24% failure of Mammography in detecting abnormality, it has the most common pattern of unilateral focal or regional asymmetry. In 15 of 45 women, lesions were mammographically due probably to a thick excessively widespread trend in most people (36 in 45) [20]. MRI outcome is always complex and depends on the degree of inflammation that mightily display heterogeneous undefined masses and non-mass increase. Fazzio etal [28] has established T2 hyperintensity that increases masses peripherally in core non-enhancement areas that reflect the growth of abscesses (a frequent occurrence in advanced cases).

**Treatment**

Despite the common treatment processes for mastitis, majority of patients received blind antibiotic therapy at the beginning of treatment, in which there is no bacterial infection. Since GM is a sterile inflammatory disorder, antibiotic therapy typically fails [30, 31] (Table 1). Up to a third of GM patients show abscess signs as bulk, discomfort and erythema while being observed by ultrasound fluid buildup and reactive lymphadenopathy. Table 1 shows the results and achievements ratio in patients with GM. Based on the lesion degree, abscess puncture, drain or incision is seen in GM patients. Aspiration might fail because there is often necrotic tissue in the center of abscess, which makes the aspirates dense and hard to remove. Normally, microbiological cultures are negative. Cultures positive for Corynebacterium spp. are of no consequence for the actual therapeutic strategy as so far there is no effective treatment against corynebacteria; also, the agent would have to be active in lipid environment while many antimicrobials are hydrophilic with less dissemination to lipid environments. According to previous studies, when GM is detected, two methods are used as corticosteroid medicine instead of surgical solution. De-Herthogh et al. (1980) [32] has initially prescribed high-dose of prednisolone corticosteroid (30 mg / day) for at least 2 months. Despite the reduction of lesion diameter, few negative influences as Cushing’s syndrome risk, obesity and hyperglycemia (routine side effects) are seen. Freeman et al. have prescribed a lower dose of prednisolone (16 mg / 2 per day) for 2 weeks and gradual tapering over 2 months [16]. In the
following, 2 out of 3 patients has rejected this treatment that negatively affected by corticosteroids. The effectiveness of high dose prednisolone therapy up to (1 mg/ kg weigh of patient/ per day) was presented in a German poster presentation [26] demonstrated the success of a high-dose therapy with prednisolone up to 1 mg/kg/day [26]. There was no surgery treatment for 13 GM patients treated already by steroids for 2 - 6 months (15% recurrence was reported). In this case, there is a dramatic decline in the toxicity of patient's corticosteroid. The impact of topical hydrocortisone butyrate cream (0.1%, 2/ day) on alternate days toward the large local excision has been studied. Methotrexate is another treatment, particularly for the patients with failure experience in corticosteroid therapy. However, except some case studies [17], there is a doubt toward the appropriateness of methotrexate in treating of childbearing age women [13]. Another solution is the total excision of lesion. The stage and level of surgery has been precisely analyzed because the level of operation varies from broad excision to mastectomy [17, 18, 31]. The option of medical treating or surgery is based on various regional parameters as the surveillance opportunities or the patient preferences. Some clinicians prefer surgery, while for some the medical treatment is the first priority. Many apply a broad screening of grain injury (Table 1). In neither USA nor Germany, there is consensus or clarification on the surgical and medical policy. There has not been any guideline for treating GM, in particular by AWMF (German Workshop of Scientific Medical Societies) and AGO, so a wide range of studies relating to the risk of recurrences due to a variety of treatment methods have been developed[33]. It is noted that antibiotics are the lowest efficient in a bacterial mastitis treatment with the effectiveness ratio of 6%- 21% (Table 1), however, the effectiveness ratio of corticosteroid therapy is 66% - 72%. Meta-analysis brings a pooled recurrence risk of 20% for oral steroid therapy Lei et al[5]. Surgery alone or in combination with corticosteroids seems to have the lowest recurrence rates of 6.8 and 4%, respectively [5]. Considering the relative low frequency of recurrence, Yilmaz et al tried to make a recurrence system estimation while evaluating 8 out of 63 patients [33]. Figure 3 shows the possible GM-control algorithm changed by Freeman et al. [16] to conform to local breast unit 'Kliniken Essen-Mitte’ requirements. This algorithm shows the comparatively effective result of the conventional corticosteroid therapy for avoiding the painful treating that might bring the risks of unsatisfactory aesthetic outcomes, asymmetry, wounds and breastfeeding concerns as mastectomy or large excision.
The authors agree that surgery should be reserved for particular situations only in circumstances when the reaction to corticosteroid treatment is inadequate.

**PATIENTS AND METHODS**

There were 14 patients diagnosed as IGM between 2014–2019 in Azadi Teaching Hospital followed up with eleven. Their clinical files were retrospectively reviewed. Until the end of 2014, 3 patients were left behind for follow-up. Similar to the guidelines for rendering the diagnosis, 3 classes of patients were individualized and 10 patients with a particular histopathology were in the first class (IHP). There were two patients with giant cells in the second class (CP) obtained by “fine-needle aspiration” from cytopathology. Two patients were not included in last category (TC), also histopathology was non-specific for them, but the clinical presentation and experience were common. Other conditions were omitted. Both patients were exposed to the clinical exams and breast ultrasound, while clinical details were compiled in clinical reports and performed by telephone questionnaire or during consultation. On a biopsy, (non necrotizing granulomas).

**RESULTS**

**Clinical features**

According to the results, 125 cases were described in 14 patients with IGM. Table 1. Shows Symptoms, treatment and the results of patients with granulomatous mastitis imaging talks about the clinical features of patients with the mean age of 33 ± 17 (SD) (18-50 years). All were
Premenopausal and no one of them was breastfeeding or lactating while being diagnosed. Except the 3 patients with type 2 diabetes (IHP1, IHP7 and IHP10), none has infectious disorders or other chronic diseases. Initially, either as a mass presenting breast quadrant or as an inflammatory region, all patients were consulted for a painful unilateral lesion. Generally, the lesion was consistent with axillary lymphadenopathy.

Table 2. Clinical features of patients

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>BMI (kg/m²)</th>
<th>Smoking</th>
<th>OC use</th>
<th>Parity</th>
<th>Time since last childbirth (years)</th>
<th>Breast feeding</th>
<th>Type 2 diabetes</th>
<th>Ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHP1</td>
<td>45</td>
<td>25</td>
<td>No</td>
<td>?</td>
<td>1</td>
<td>12</td>
<td>Yes</td>
<td>Yes</td>
<td>Caucasian</td>
</tr>
<tr>
<td>IHP2</td>
<td>30</td>
<td>20</td>
<td>No</td>
<td>No</td>
<td>1</td>
<td>3</td>
<td>No</td>
<td>No</td>
<td>Caucasian</td>
</tr>
<tr>
<td>IHP3</td>
<td>42</td>
<td>31</td>
<td>No</td>
<td>No</td>
<td>5</td>
<td>6</td>
<td>Yes</td>
<td>No</td>
<td>African</td>
</tr>
<tr>
<td>IHP4</td>
<td>18</td>
<td>18</td>
<td>No</td>
<td>No</td>
<td>0</td>
<td>/</td>
<td>No</td>
<td>No</td>
<td>Caucasian</td>
</tr>
<tr>
<td>IHP9</td>
<td>46</td>
<td>22</td>
<td>Yes</td>
<td>Yes</td>
<td>1</td>
<td>8</td>
<td>No</td>
<td>No</td>
<td>Caucasian</td>
</tr>
<tr>
<td>IHP9</td>
<td>21</td>
<td>19</td>
<td>Yes</td>
<td>Yes</td>
<td>0</td>
<td>/</td>
<td>No</td>
<td>No</td>
<td>Asian</td>
</tr>
<tr>
<td>IHP7</td>
<td>50</td>
<td>32</td>
<td>No</td>
<td>?</td>
<td>2</td>
<td>17</td>
<td>Yes</td>
<td>Yes</td>
<td>Caucasian</td>
</tr>
<tr>
<td>IHP8</td>
<td>16</td>
<td>17</td>
<td>No</td>
<td>No</td>
<td>0</td>
<td>/</td>
<td>No</td>
<td>No</td>
<td>Asian</td>
</tr>
<tr>
<td>IHP9</td>
<td>43</td>
<td>17</td>
<td>Yes</td>
<td>No</td>
<td>0</td>
<td>/</td>
<td>No</td>
<td>No</td>
<td>Caucasian</td>
</tr>
<tr>
<td>IHP18</td>
<td>18</td>
<td>35</td>
<td>Yes</td>
<td>Yes</td>
<td>2</td>
<td>Diagnosis 6 years before</td>
<td>No</td>
<td>Yes</td>
<td>Caucasian</td>
</tr>
<tr>
<td>CP1</td>
<td>41</td>
<td>32</td>
<td>No</td>
<td>No</td>
<td>5</td>
<td>1</td>
<td>No</td>
<td>No</td>
<td>Maghribi</td>
</tr>
<tr>
<td>CP2</td>
<td>37</td>
<td>26</td>
<td>Yes</td>
<td>Yes</td>
<td>0</td>
<td>/</td>
<td>No</td>
<td>No</td>
<td>Maghribi</td>
</tr>
<tr>
<td>TC1</td>
<td>41</td>
<td>24</td>
<td>No</td>
<td>No</td>
<td>2</td>
<td>7</td>
<td>Yes</td>
<td>No</td>
<td>Maghribi</td>
</tr>
<tr>
<td>TC2</td>
<td>21</td>
<td>24</td>
<td>No</td>
<td>No</td>
<td>0</td>
<td>/</td>
<td>No</td>
<td>No</td>
<td>Maghribi</td>
</tr>
<tr>
<td>Mean</td>
<td>33</td>
<td>24.43</td>
<td>0.5</td>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
<td>0.4</td>
</tr>
</tbody>
</table>

*OC, oral contraception; IHP, initial specific histopathology; CP, cytopathology; TC, typical clinical presentation; ? unknown; SD, standard deviation.

*p = 0.0371

The lesions were different from periareolar to the arenola. Fluid accumulation and fistula developing with aseptic flow was generally accompanied by an inflammation in acute episodes. Just one cell displayed an "orange skin" lesion.

![Figure 4. Surgical management](image)

DISCUSSION

Idiopathic granulomatous mastitis (IGM) is a rare disease and there is no standard treatment IGM [11]. Specifically, these results advocate the surgical implementation and management of
conservative steroid therapy in special cases as intercurrent bacterial abscesses. The aforementioned reports of the IGM clinical features [2, 12] are affirmed in this series. A therapeutic method has been proposed and either the recent reviewed cytology [6,13] or microbiopsies were conducted only in complex differential diagnosis of malignant lesions. The diagnosis was supported by especial IGM episodes of prior experience(s). Steroid positions and Surgical were controversial. Though surgery is the first priority of treatment for many years, it is also regarded as symptomatic treatment. In other word, iterative surgeries could bring mastectomy as it couldn’t not prevent recurrences. Yau et al has performed the surgical treatment of granulomatous mastitis for 11 patients [7] while only 8 of them (72.7 %) needed iterative surgery. On the whole, 32 operations including 5 partial mastectomies and one full mastectomy were performed. In this study, relapses were occurred less frequently after prednisone therapy than after surgery. In series of12 patients, Azlina et al [2] has proposed a complete resection followed by the steroid therapy as an adjuvant treatment for more than 6 weeks. In the following, 6 patients relapsed after the initial injection while requiring extra doses and achieving 50%more efficacy. At the end of treatment,3 patients had chronic disease. If any additional value was given by surgery, it was not apparent. Few studies have proposed steroids as the first priority in treatment, while surgery could be done in the absence of reactions or complications as fistulas or abscesses [4,6]. Regarding fistula, surgery is not the usual care technique; however, corticosteroids could be effective and simple method for treating of fistulas. In another study including 54 women [6], antibiotics treatment was not effective for 2/38 individuals, while 77% of the 13 women treated with corticosteroids indicated relief in 77% of the cases. Steroids or excision and observation are proposed for the cases with mild symptoms, steroid therapy for severe symptoms and wide-excision surgery when the reaction was partial or unsuccessful. There is no published data on steroid treatment opposed to steroid therapy and antibiotics. Steroids with antibiotics were used in this study, and then it is not possible to judge the need and efficiency of antibiotic. Also, clarythromycin [14,15] was used in this research due to the immunomodulatory and anti-inflammatory properties accompanying its antimicrobial action. In terms of recurrences, it is not clear that many long-term variables were applied in it. Thus, it should be examined in a study testing the corticosteroid treatment alone or combined with clarythromycin. Steroids could be seen with serious side effects and low efficient while its dosage is too low. On the other hand, there is inadequate evidence for the use of nonsteroidal anti-inflammatory drug in IGM [16,17]. The benefit of methotrexate in IGM 8 and 9 was shown in few episodes. However, methotrexate was commonly used as a chronic drug lacking efficacy. Another choice is abstention.
In Hovanessian Larsen et al. [6] test, patients were treated with mild complaints. Accordingly, Lai et al [13] tracked an average of 18.7 months for 8 women with IGM, and then no medication or surgery was prescribed. No recorded recurrences were in 50% of cases and 50% were in stable condition. Surgical treatment or steroid was recommended in the case of chronic pathology or refractory. There was highly care toward this group and any attacks could be highly unpleasant needing caution. This retrospective framework is the limitation of our sequence. Other retrospective studies include small follow-up features and not qualified for effective management evaluation. Despite the low prevalence of disease, randomizing different treatment services was not feasible. Our research strengths its thorough follow-up that provide the accurate assessment of recurrences. Since the course of the disease is unpredictable, only long-term follow-ups could delineate the patient care for the periods of flare and inactive conditions.

CONCLUSION

It is significant to consider the likelihood of GM as the underlying condition in a patient with recurrent mastitis symptoms. The clinical reports of GM and imaging correlate with that of malignancy. Conducting a core needle or excisional biopsy is essential for receiving a histopathologic diagnosis. Considering the recent studies on GM, there is no new research over this unusual benign breast condition, and then the appropriate treatment is under doubt. Based on the clinical evidences and surgery, the most common treatment is the administration of high-dose corticosteroids for around 3-6 months in cases of inadequate reaction to conservative therapy. Then, 30 mg prednisolone corticosteroid was prescribed (2 /day) for 2 weeks, tapering progressively, based on the clinical results. Later, for assessing the medication response and potential negative effects, regular visiting was performed (every 2 weeks). To mitigate potential adverse effects, corticosteroids should be used for a minimum 8 weeks for 6 months [34]. A topical injection of 0.5% hydrocortisone acetate could be an alternative therapeutic option once a day for the patients with declined oral corticosteroid medication and moderate symptoms. Based on figure 1, there was 50% decrement in breast mass after 3 weeks of topical hydrocortisone acetate medication No side effects occurred [35]. In patients with relapsed or who can’t stand high-dose corticosteroid medication, methotrexate is a proper choice. Similar to the prescription of patients of persistent rheumatoid disorders, a low-dose regimen was provided: methotrexate as a monthly dose (7.5-25 mg) beside folate (every day or once a week) [36].Leukopenia, nausea, undue weakness, dizziness,
ulcerative stomatitis, gastrointestinal pain, reduced infection tolerance, chills and fever are the most commonly recorded adverse reactions. Due to lack of evidence, all indications should be highly accurate and all patients should be evaluated every 2-4 weeks. Initiating many trials and assessing the feasibility of potential treatments that contribute to universal surgery prevention is impossible due to the rarity of condition. As a result, there is a huge need to new methods to understand the underlying causes of disease considering geographic aggregation that might gather extra data by introducing a register or multicenter analysis.

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