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Original Research Article

An observational study on the efficacy of intralesional steroids in patients with idiopathic granulomatous lobular mastitis in a tertiary care centre

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ABSTRACT

Background: Granulomatous lobular mastitis (GLM) is a rare benign disease of the breast which usually affects young women of childbearing age. The patients usually present with a painful breast mass or with multiple discharging sinuses of breast. Diagnosis is usually established by means of clinical examination followed by radiological, microbiological and histopathological evaluation. The ideal management of patients with GLM is still a matter of debate and treatment modalities such as surgery, systemic and intra-lesional steroids, as well as immunosuppressive agents are being used in clinical practice. In our study, we assessed the clinical response of patients with GLM, treated with intra-lesional steroid injection.
Methods: In this prospective observational study, from December 2021 to December 2023, a total of 29 patients who were diagnosed as having GLM and who opted for intra-lesional steroid therapy as the solo treatment, were enrolled. After obtaining informed consent, intra-lesional steroid injection was administered in all the 29 patients. The treatment response was assessed after a period of 3 months from the date of injection.
Results: A complete resolution of symptoms and signs was found in majority of the patients (75.9%), 4 (13.8%) had a partial resolution and 2 (6.9%) had persistence of symptoms. One patient (3.4%) was lost to follow up. None had any worsening of symptoms.
Conclusions: Intra-lesional steroid can be effectively used in the treatment of GLM and this modality can be completed in a few minutes in an Outpatient setting and is extremely cost effective.

Keywords: GLM, Chronic inflammation, Systemic steroids, Intra-lesional steroids, Treatment efficacy, Complete response

INTRODUCTION

Granulomatous lobular mastitis (GLM) is a rare chronic benign inflammatory condition of the breast with an unclear Aetiology that proposes an association with immune dysfunction, such as autoimmunity.[1] GLM usually presents in women of childbearing age within a few years of pregnancy and breast feeding, and is most common in women of Hispanic, Asian, Middle Eastern or African origin.[2] The overall incidence of the disease is 2.4 per 100,000 women.[3]

Miller and Smith in 1971, proposed the concept of GLM as breast lobules infiltrated with acute and chronic inflammatory exudates with a mass of foreign body giant

cells.[4] The clinical characteristics of the disease were first described by Kessler and Wolloch in 1972.[5]

The most widely adopted theory for the pathogenesis of GLM considers it as an immune reaction that involves both humoral and cell mediated immunity stimulated by stasis of the patient's secretions such as retained milk. This is postulated as resulting in local inflammation within the breast tissue leading to activation of delayed-type hypersensitivity and finally to the formation of localized granulomas.[6]

Patients with GLM present with breast masses, abscesses, sinuses, pain and nipple changes. Diagnosis of GLM requires the efforts of a multidisciplinary team that includes a clinician, radiologist and a pathologist. Due to the similarity in the clinical presentations of GLM to that of breast cancer or other inflammatory breast diseases, the evaluation should include history, clinical examination, imaging, bacteriological and or immunological and pathological examination.

Even though GLM has been widely studied, currently no international unified guidelines are available for the therapeutic management of IGM. In 1980, De Hertogh et al proposed oral corticosteroids in the management of GLM.[7] There have been many studies done on the efficacy of corticosteroids since then and have been shown to provide a faster recovery than expectant management. However, their use is limited owing to the fact that they have a wide range of side effects.

Recent evolution in the management of GLM include minimally invasive approaches such as aspiration of pus/fluid under ultrasound guidance and intra-lesional injection of steroids.[8,9] In this study, our objective was to assess the treatment response to intra-lesional steroid in patients with GLM.

METHODS

This prospective mono-centric observational study was conducted at Apollo main hospitals, Chennai, Tamil Nadu, from December 2021 to December 2023. IRB approval was obtained from the institutional ethical committee-biomedical research-Apollo hospitals. Patients who presented as outpatients to the department of breast surgery in Apollo main hospital during this time period, with signs and symptoms suggestive of GLM, were enrolled in the study after obtaining informed consent.

The primary objective of our study was to assess the efficacy of intra-lesional steroid injection in the management of patients with GLM. Patients with cystic neutrophilic granulomatous mastitis were excluded from our study.

The patients enrolled were clinically examined and the findings were recorded digitally. A comprehensive history with respect to complaints, prior medical and surgical treatment was noted. The use of anti-tubercular drugs, oral or injectable contraceptive or other female sex hormones and drugs with the potential to raise serum prolactin levels was obtained in particular. The patients were then evaluated by means of an ultrasound of the breast followed by microbiological evaluation (routine culture and sensitivity, AFB stain and culture and GeneXpert TB test). Histopathological examination of an image guided core biopsy sample, from the index area was done to clinch the diagnosis of GLM.

The patients who were diagnosed with GLM during this study period were counselled regarding the nature of the disease and the different modalities of treatment available along with the benefits and side effects of each of them. 29 patients who opted for Intra-lesional steroid injection as the sole treatment modality were included as the final study population. Patients who were found to have breast abscess, were managed initially by aspirating pus under ultrasound guidance following which they were treated with intra-lesional steroids.

After obtaining Informed consent from the patients, injection triamcinolone acetonide suspension was used. Each mL of the sterile aqueous suspension provided 40 mg triamcinolone acetonide, with 0.9% (w/v) benzyl alcohol IP as a preservative and water for injections I.P (qs). 20 mg of triamcinolone acetonide (0.5 mL) was administered by intra-lesional injection for all the 29 patients as a minor outpatient procedure. They were re-evaluated 3 months after injection. They were assessed for resolution of symptoms and signs (pain, mass, recurrent abscess, sinus etc.). This was followed by an ultrasound scan of the affected breast for mass resolution, scarring (post operative or in response to treatment), sinus healing, residual pocketing of pus etc.

The response to treatment was quantified into complete response-when they had complete absence of signs and symptoms, partial response-when there was 50-75% reduction of signs and symptoms and no response-when there was no reduction of signs and symptoms.

Data was first entered in MS-excel (Microsoft corporation, Microsoft excel. 2018) and the clean data was analyzed in SPSS Software. (IBM Corp. released 2017. IBM SPSS statistics for Windows, version 25.0. NY: IBM corp.)

Descriptive statistics were represented with percentages for qualitative data. Fisher exact test was applied for comparison of proportions. $P \leq 0.05$ was considered as statistically significant.

RESULTS

Out of the 29 patients studied, 14 (48.3%) belonged to the age group between 31-40 years, 10 (34.5%) were between 21-30 years, 4 (13.8) patients between 41-50 years and 1(3.4%) patient were above the age 50 years.

The youngest patient was 21 and the oldest was 53 years old. The mean age was 33.8 (Table 1).

Table 1: Table showing demographic details and clinical presentation.

Variables	N
Age (in years)	
Range	21-53
Mean±SD	33.8±7.76
Parity	
Nulliparous	Nil
Parous	29 (100%)
Co-morbid conditions	
Present	Nil
Absent	29 (100%)
Tobacco usage (Chewing/smoking)	
Yes	Nil
No	29 (100%)
Actively breast feeding	
Yes	Nil
No	29 (100%)
Medication history (hormone containing pills, anti-psychotics or antidepressants)	
Yes	Nil
No	29 (100%)
Clinical symptoms	
Mass	24 (82.8%)
Sinus with pus discharge	16 (55.2%)
Pain	14 (48.3%)
Elicited nipple discharge	4 (13.8%)
Nipple changes	3 (10.3%)
Recurrent abscesses	1 (3.4%)

All the patients enrolled were parous, having at least one child and all of them had completed breast feeding 12-36 months earlier. None of them had any co-morbidities such as diabetes mellitus, hypertension, dyslipidemia, obesity or cardiac diseases. Regarding medication history, out of the study population, 2 (6.9%) patients gave a history of having been empirically treated by anti TB drugs with no resolution of symptoms. Also, all the 29 patients had been treated with multiple courses of Antibiotics previously. But none of them had a history of intake of hormone containing pills, anti-psychotic or anti-depressant drugs (Table 1). Serum prolactin levels were also found to be within normal limits for all the patients studied.

All patients had unilateral disease. The most common clinical presentation was a breast mass which was present in 24 (82.8%) patients, followed by a non-healing breast sinus with pus discharge in 16 (55.2%) and breast pain in 14 patients (48.3%). Other symptoms present were elicited nipple discharge in 4 (13.8%), nipple changes in 3 (10.3%) and recurrent abscesses in 1 (3.4%) patient (Table 1).

Out of the 29 patients, 11 (38%) patients gave a history of previous surgery to the breast in the form of either a breast lump excision or incision and drainage of breast abscess, following which they had recurrence of symptoms and gross distortion of the breast (Figure 1).

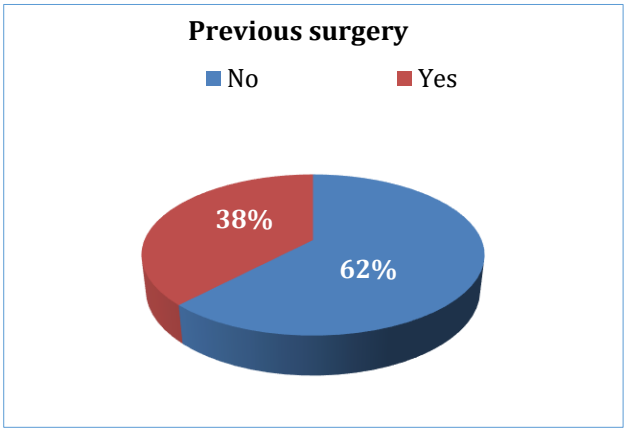

Figure 1: Distribution of patients according to history of previous surgery to breast.

All 29 patients were diagnosed as having GLM after triple assessment of the breast (clinical examination, ultrasound imaging and ultrasound guided core needle histopathology) and bacteriology. They were treated with a single intra-lesional injection of 20 mg of triamcinolone acetonide, in the centre of the involved area as an outpatient procedure after extensive counselling and specific consent. The 28 (96.6%) patients were reviewed after 3 months and assessed for resolution of symptoms. Only 1 (3.4%) patient was lost to follow up.

Out of the 29 patients who were treated with intra-lesional steroid injection, 22 (75.9%) had a complete resolution of their symptoms, 4 (13.8%) had a partial resolution and 2 (6.9%) had persistence of symptoms. One patient (3.4%) was lost to follow up (Figure 2).

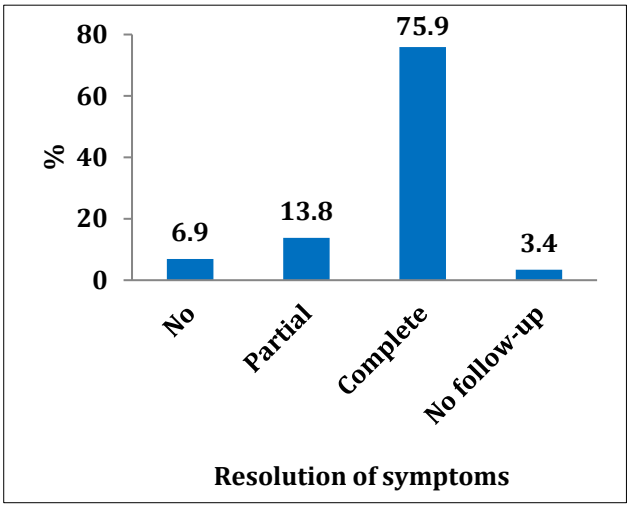

Figure 2: Distribution of patients according to treatment response.

Out of the 11 patients with a previous history of surgery for the breast, a complete resolution was seen in 7 (63.6%) patients, following intra-lesional steroid injection. Four (36.4%) had either no response or partial response to the injection. In contrast, among the 17 patients who had not had previous surgery to the breast, 15 (88.2%) had complete resolution of their symptoms after intra-lesional steroid injection. But the difference was not statistically significant, p=0.17 (Table 2).

Table 2: Comparison of treatment response with respect to previous surgery.

Previous surgery	Recovery			
	No / partial		Complete	
	N	%	N	%
No	2	11.8	15	88.2
Yes	4	36.4	7	63.6
Total	6	21.4	22	78.6
*P=0.17				

*Fisher's exact test.

DISCUSSION

GLM is a chronic inflammatory condition of a largely unknown aetiology and pathogenesis and usually affects women of child bearing age group.[10] GLM is rarely reported in nulliparous women, very young girls and males.[11,12] In such instances, the problem is attributed to high levels of serum prolactin, and in the male population due to increased endogenous oestrogen to androgen ratio.

Auto immunity has been accepted as the possible primary aetiology in GLM.[13] Lactational disorders which result in milk stasis, hyperprolactinemia and blunt trauma to the breast are thought to be additional factors.[14]

The common clinical presentations of GLM include breast masses with or without pain, pus discharging sinuses, nipple abnormalities and recurrent abscesses. There have been many studies conducted regarding the various treatment modalities for GLM. However, there is no report of a single treatment modality where a complete response ensued without disease recurrence.

Yuan et al introduced a consensus document on a multidisciplinary approach (Surgeon, radiologist, pathologist etc.) towards the management of GLM.[6] This included a clinical staging system based on clinical features and disease progression. They classified self-limiting disease as stage I, congestive swelling stage as stage-II, abscess formation as stage-III and a complex refractory stage as stage IV.

Literature suggests expectant management for GLM with stage-I disease and intervention only when there is disease progression. The use of antibiotics is limited to patients who test positive for the presence of pathogenic bacteria. Systemic steroid therapy (oral) remains the mainstay of medical treatment, at present.[15] But treatment with oral steroids requires dose adjustment and duration of treatment according to disease progression.

There are other treatment modalities for GLM, such as the use of immunosuppressant drugs (e.g. Methotrexate), as well as surgical approaches involving wide local excision, drainage of abscesses, excision of sinuses and fistulas etc.[16-18] These may be indicated while dealing with extensive disease which is resistant to Steroid therapy or when the patient develops serious side effects to treatment with Steroids. However, there are no clear-cut indications for these in the literature.

Moreover, the effectiveness of these treatments remains a matter of debate. Each treatment modality is associated with its own disadvantages. A study conducted by Shin et al concluded that the recurrence rates associated with surgery was higher when compared to steroid therapy and that it leaves the patient with extensive scarring and distortion of the breast, which is cosmetically unacceptable.[19]

The main disadvantage of systemic steroids is the all too numerous side effects. Thus, the latest recommendation in literature for the treatment of GLM suggests the use of Intra-lesional and topical Steroids as an alternative to systemic steroids. This has the advantage of a lower side effect profile, lower recurrence rates and a clinical response equal to or superior to systemic steroids.[20]

In this study, our aim was to assess the efficacy of intra-lesional steroids as the sole treatment in patients with GLM. The mean age of our patients was 33.8±7.76 (Range: 21-53 years). The most frequent symptom of presentation was a breast mass (82.8%) followed by discharging breast sinus and pain. A study done by Soltany et al the clinicopathological features of patients with GLM, had findings similar to our study.[21] The most frequent symptom they encountered was a palpable lump (41%) followed by axillary lymphadenopathy (35%) and breast pain (29%). In a similar study done by Yildirim et al the frequency of symptoms was once again similar with a painful breast lump being the most common symptom.[22]

Literature suggests ultrasound breast as the first line modality for the evaluation of patients with GLM.[23] MRI is an useful tool when a suspected GLM must be differentiated from breast cancer.[24] Before proceeding with the treatment, the possibilities of other conditions of breast which forms the differential diagnosis for GLM, such as periductal mastitis, tuberculosis, Zuska disease as well as carcinoma of breast, must be ruled out.[25]

After confirming the diagnosis of GLM, all the 29 patients were treated with local injection of steroid. While assessing treatment response after 3 months, complete resolution of symptoms and signs was found in majority of the patients (75.9%) and only a small subset

(6.9%) had no response to the treatment. None had worsening of symptoms.

A variety of minor side effects of intra-lesional steroid injection has been reported in literature. These include thinning of skin, fat atrophy, infection or abscess formation.[26] No such side effects were seen in our patients.

Toktas et al while comparing the efficacy of Intralesional Steroids with concomitant topical steroids to systemic Steroid therapy found that the overall response rate to be 93.5% in the steroid-injected group and only 71.9% in the systemic steroid group (p=0.012).[27]

They also found that the response to treatment was more prominent by the end of second month and by third the month most of their patients had complete remission. From their study, they concluded that local therapy with Steroids in the form of intra-lesional Injection was more effective in the treatment of GLM when compared to systemic steroids. This can be attributed to the increased bio availability of the drug to the target region as well as the dose administered per unit area with local administration of steroids. Moreover, there were lower side effects and recurrence rates. Similar results are seen in other studies also.[28,29] The absence of potential side effects with local steroids makes it a superior treatment option.

An interesting finding in our study was the difference in treatment response among the patients with previous surgical treatment and those who did not have surgery earlier. Among the group which had recurrence following previous surgery, the complete resolution rates were less when compared to the group who had no previous surgery. This might be attributed to the distortion of the breast tissue following surgery and the excessive scarring that occurred subsequently.[30] This perhaps prevents the Intralesional steroid from diffusing through affected area.

Limitations

The main limitation of our study was the small study population as this was a pilot-study. With a larger sample size, the extrapolation of data would have been more valid. The follow-up period was also short, hence long-term recurrence could not be assessed effectively. Another limitation was the heterogenous study population, as our study included patients who had no prior treatment for GLM as well as patients who had undergone prior medical and surgical treatment for GLM. This aspect had a significant impact on the overall clinical response to the treatment modality studied.

CONCLUSION

Intra-lesional steroids can be effectively used in the treatment of GLM in all the stages of the disease. In our study, most patients had a complete clinical response after administration of a single dose of intra-lesional steroid injection and none developed side effects. Moreover, this treatment modality is rapid, completed in a few minutes in an outpatient setting and is extremely cost effective, coupled with the absence of side effects.

Recommendations

Even though local injection of steroids for patients with GLM is now being used in clinical practice, long term data on its efficacy is lacking. Most of the studies to date are based on short term results. Prospective randomized control studies involving a larger study group with a longer study period is required.

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