



Unveiling the enigma: understanding the complex disease course of granulomatous mastitis and seeking ways to shorten it

Jia Liu^{1,2#}, Wei-Yi Lin^{1,2#}, Qiu-Zhou Wang^{1,2}, Xiao-Qin Yang^{1,2}, Qing Lv^{1,2}, Qiu-Wen Tan^{1,2}

¹Division of Breast Surgery, Department of General Surgery, West China Hospital, Sichuan University, Chengdu, China; ²Breast Center, West China Hospital, Sichuan University, Chengdu, China

Contributions: (I) Conception and design: J Liu, QW Tan; (II) Administrative support: Q Lv, XQ Yang, QW Tan; (III) Provision of study materials or patients: QZ Wang, Q Lv, QW Tan; (IV) Collection and assembly of data: J Liu, WY Lin, QZ Wang; (V) Data analysis and interpretation: J Liu, QW Tan; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Qiu-Wen Tan, MD. Division of Breast Surgery, Department of General Surgery, West China Hospital, Sichuan University, 37 Guoxue Alley, Chengdu 610044, China; Breast Center, West China Hospital, Sichuan University, Chengdu, China. Email: hxtanqiuwen@163.com.

Background: Granulomatous mastitis is an infrequent and intricate ailment. Limited knowledge exists regarding how granulomatous mastitis progresses and its impact on disease management. We aim to prospectively capture symptoms in the general population to accurately ascertain the duration of illness and the prevalence of long-lasting symptoms.

Methods: This study reports data from 169 prospectively enrolled real-world patients with pathologically confirmed granulomatous mastitis. Patients were enrolled after screening according to the inclusion and exclusion criteria. Patients were followed-up every 2–4 weeks during treatment, then every 3–6 months (Year 1) and 6–12 months (Year 2). Outcomes included symptom resolution, disease course, and relapse. Associations between clinical variables and outcomes were assessed using appropriate statistical models, with significance defined as $P < 0.05$.

Results: The median disease course of granulomatous mastitis was 257 days (range, 55–1,500 days), with the majority of disease regression occurring within a span of 6 months subsequent to diagnosis; 72.78% of patients preferred steroids as the initial treatment. The use of steroids was associated with a shorter disease course after adjusting for age, lump size, abscess, and sinus formation ($P = 0.02$). Abscess formation was observed in 58.57% of patients. Notably, abscess formation during disease progression contributed to a prolonged disease course (358.67 *vs.* 278.24 days, $P = 0.03$).

Conclusions: Our findings highlighted the heterogeneity of granulomatous mastitis disease course and emphasized the importance of steroid usage in shortening disease course. Avoiding abscess and sinus formation, early steroid usage during granulomatous mastitis treatment might be beneficial. These evidences provide novel insights and supports the use of steroids in patients with granulomatous mastitis for modulating their immune response. Studies are urgently needed to further elucidate the role of steroid in granulomatous mastitis management.

Keywords: Granulomatous mastitis (GM); corticosteroids; abscess; immune response; autoimmune disorders

Submitted Dec 21, 2024. Accepted for publication Mar 07, 2025. Published online Apr 25, 2025.

doi: 10.21037/gs-2024-557

View this article at: <https://dx.doi.org/10.21037/gs-2024-557>

Introduction

Granulomatous mastitis (GM), also referred to as granulomatous lobular mastitis (GLM) and idiopathic granulomatous mastitis (IGM), represents a predominant form of non-puerperal mastitis (1,2). Characterized by frequent recurrences and significant breast changes, it presents significant challenges to both patients and clinicians, requiring tailored treatment approaches to address disparities in care (1,3-5).

The etiology and disease progression pattern remain unclear due to the low incidence and limited research. Extra-breast symptoms (i.e., arthritis and erythematous nodules), immune cell infiltrating lesion and response to immunosuppressive treatment are the main evidence that has supported the autoimmune reaction as the primary etiology for GM (6-8). In addition, the use of oral steroids shows a high complete response rate according to a recent

meta-analysis (2). In our previous study, an overall response rate of 80.7% was observed in GM patients treated with methylprednisolone, and a relapse rate of 33.33% was reported with an average follow-up of 283 days (1). Corticosteroids and other immunosuppressive agents serve as an immunomodulator therapy and may be a useful therapeutic adjunct by modifying the initial immune response to slow the host immune response. However, whether steroids could alter the disease course is unclear.

Based on the limited study available, the clinical course of GM exhibits significant heterogeneity, ranging from asymptomatic to aggressive and destructive forms. Patients may develop abscesses and fistulas shortly after clinical symptoms onset, while some cases show spontaneous regression over 1–2 months (4,5,8). However, studies are predominantly retrospective studies with a small sample size, lacking factors predicting treatment sensitivity and long disease course. Furthermore, GM patients usually receive treatment in the outpatient setting, and symptoms are not well recognized. Few studies prospectively capture symptoms in the general population to accurately ascertain the duration of illness and the prevalence of long-lasting symptoms.

Since August 2019, we have established a prospective dataset of patients with non-puerperal mastitis. Disease progression and treatments are documented using standardized case report form (CRF). In the present study, we report the clinical features and disease course of pathologically confirmed GM. We also explore possible factors predicting worse disease prognosis, providing new clues for guiding clinical treatment for GM. We present this article in accordance with the STROBE reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gs-2024-557/rc>).

Methods

Establishment of prospective patient datasets

This study included pathologically proven GM seeking treatment at the breast disease center, West China Hospital since August 2019. Demographic, diagnostic, treatment, and follow-up information were prospectively collected using CRF.

Patients were included in the study if they had a pathologically confirmed diagnosis of GM via fine needle aspiration biopsy, agreed to participate in the study. Briefly, the location of the lesion was determined

Highlight box

Key findings

- Granulomatous mastitis (GM) has a highly variable course, with 28.4% of patients experiencing a disease duration of over a year. The median disease course is 257 days, typically ranging between 161 and 376.5 days. Abscess and sinus formation are key factors contributing to a longer disease course.
- Corticosteroids are the most commonly used treatment (72.8%) and are associated with a shorter disease course, especially for cases with large masses or abscesses.
- Abscesses develop in 58.57% of patients, which prolong the disease course but do not affect relapse rates. Antibiotics are rarely needed unless a bacterial infection was present.

What is known and what is new?

- GM is a rare, poorly understood disease with a variable course. Previous studies suggested that it could be self-limiting, with some cases resolving spontaneously.
- This study provides new prospective data, showing that abscess and sinus formation predict a longer disease course. It also suggests that corticosteroids may shorten the disease duration.

What is the implication, and what should change now?

- Treatment should be tailored to disease severity. For aggressive GM with large masses or abscesses, corticosteroids are recommended as first-line treatment to shorten disease duration. Long-term effects of steroids on disease progression require further investigation.
- Larger, more robust studies are needed to clarify the role of corticosteroids and other treatments. Further research on the etiology, especially in relation to abscess formation, is essential. The role of surgery in GM management remains unclear and warrants more investigation.

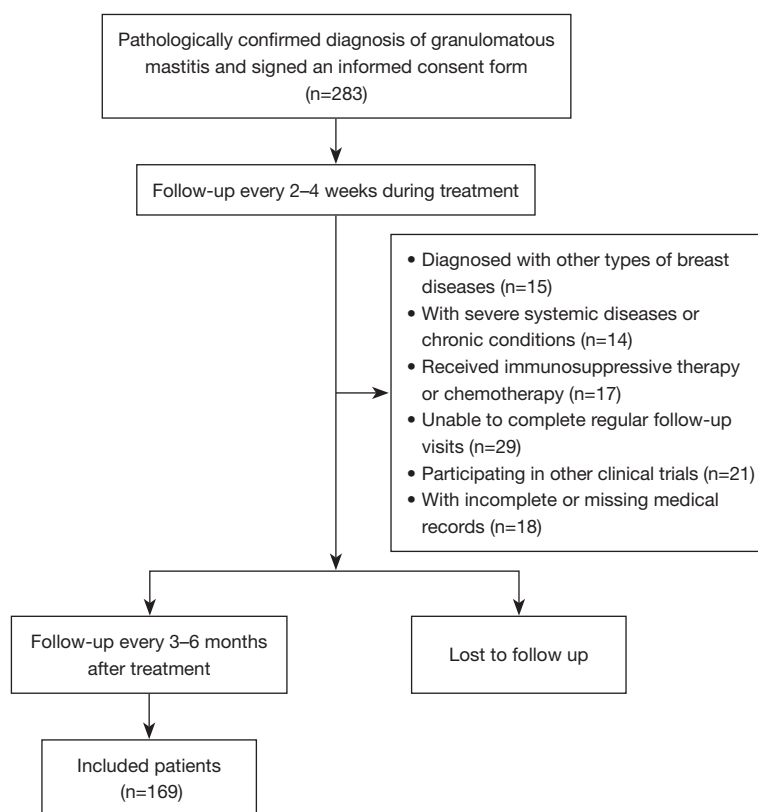


Figure 1 Inclusion and exclusion criteria of patients in this study.

by ultrasound, 3 mL of 2% lidocaine was used for local anesthesia, a puncture needle (16G) was placed in front of the lesion under ultrasound guidance, and the lesion tissue was removed under ultrasound guidance and sent for pathological examination. Only patients with complete clinical data, including demographic information, diagnosis, treatment, and follow-up details, were enrolled.

Patients were excluded if they had other types of breast diseases (e.g., breast cancer, plasma mastitis, tuberculous mastitis and other forms of mastitis), severe systemic diseases or chronic conditions (e.g., uncontrolled diabetes, severe cardiovascular diseases, chronic liver or kidney diseases) that could affect GM treatment and follow-up. Patients who had received systemic immuno-suppressive therapy or chemotherapy (excluding drugs used to treat GM) were also excluded. Additionally, those who were unable to complete regular follow-up visits or participated in other clinical trials that might affect study outcomes, were not included. Patients with incomplete or missing medical records were also excluded from the study (*Figure 1*).

Patients were routinely followed up in the outpatient

clinic every 2–4 weeks during treatment. When treatments were finished, follow-up was usually performed every 3–6 months for the first year, then every 6–12 months for the second year. Telephone follow-up was performed each year. For patients with prolonged treatment duration who achieve partial remission (PR) of the breast mass but remain stable, we considered either surgical intervention or observation based on the patient's preference. For those who fail to respond to multiple courses of steroid therapy or experience significant adverse effects from such treatment, referral to traditional Chinese medicine therapy or surgical excision was recommended.

From August 2019 to July 2023, 283 patients diagnosed with GM received treatment at Breast Center, West China Hospital, Sichuan University. Out of the total 283 patients, 169 patients (59.72%) completed at least 1-year follow-up via regular outpatient clinic or telephone.

Statistical analysis

Symptoms relating to GM mainly included breast mass,

pain, skin inflammation, abscess, arthritis, fatigue, and fever. Pain was evaluated using visual analogue scale (VAS). Pain was categorized into levels of mild, moderate, and severe pain. Disease onset was defined as the first day of symptoms occurred. Disease end was defined as the day of clinical symptom disappeared. Inactive symptoms, including stable mass and stable small abscess for consecutive 14 days, were also defined as the disease end. Disease course was defined as the period from disease onset to disease end. For statistical analysis, a disease course that longer than 342 days (12 months \times 28 days/month) was defined as long disease course.

Descriptive analysis was performed to reveal the data distribution for continuous variables and reported as median (inter quartile range). Statistical differences were analyzed using the independent Student's *t*-test or Wilcoxon-Mann-Whitney *U* test, as appropriate. Categorical variables were reported as frequencies and percentages, and statistical differences were analyzed using the Pearson's Chi-squared test.

Multivariable logistic regression using the backward-forward stepwise method (with $P < 0.05$ for entrance and $P < 0.10$ for removing variables) was employed to identify the variables independently associated with a long disease course and the developing abscess. Relapse was defined as symptoms reoccurring after the disease end at the primary lesion site or a new site in the same breast.

A *P* value < 0.05 was considered statistically significant. Statistical analysis was performed using the statistical software SPSS (version 20.0, SPSS Inc., Chicago, IL, USA).

Ethics statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study received approval from the ethics board of the West China Hospital (No. 2021020A). Signed informed consent form was obtained from all participants prior to their inclusion in the study.

Results

Clinical features of granulomatous mastitis at diagnosis

A total of 169 pathologically confirmed GM were identified with a follow-up of at least one year (Table 1). The median age at diagnosis was 32 years old, with a range from 16 to 53 years old. The age-distribution analysis indicated that the age at diagnosis is concentrated between 29 and 35 years old (Figure 2).

GM occurrence is closely correlated with parity and

Table 1 Baseline characteristics and clinical management for the whole cases (n=169)

| Variations | N | % |
|-----------------------------|-----|-------|
| Age (years) | | |
| <20 | 1 | 0.6 |
| 20–29 | 42 | 24.9 |
| 30–40 | 107 | 63.3 |
| >40 | 19 | 11.2 |
| BMI (kg/m ²) | | |
| <18.5 | 11 | 6.5 |
| 18.5–23.9 | 104 | 61.5 |
| >23.9 | 54 | 32.0 |
| Gravidity | | |
| G0 | 14 | 8.28 |
| \geq G1 | 155 | 91.72 |
| Parity | | |
| P0 | 20 | 11.83 |
| \geq P1 | 149 | 88.17 |
| Abortion | | |
| A0 | 92 | 54.44 |
| \geq A1 | 75 | 44.37 |
| Missing | 2 | 1.18 |
| Lactation duration (years) | | |
| None | 30 | 17.8 |
| 0–1 | 95 | 56.21 |
| >1 to \leq 2 | 41 | 24.3 |
| Missing | 3 | 1.78 |
| Time since delivery (years) | | |
| None | 31 | 18.4 |
| >0 to <1 | 8 | 4.7 |
| \geq 1 to \leq 2 | 35 | 20.7 |
| \geq 2 to <3 | 28 | 16.6 |
| \geq 3 to <4 | 26 | 15.38 |
| \geq 4 | 36 | 21.3 |
| Missing | 5 | 2.96 |
| Affected breast | | |
| Left | 93 | 55.0 |
| Right | 72 | 42.6 |
| Bilateral | 4 | 2.4 |

Table 1 (continued)

Table 1 (continued)

| Variations | N | % |
|---|-----|-------|
| Mass size at the first visit (cm) | | |
| <3 | 19 | 11.2 |
| 3–5 | 109 | 64.5 |
| >5 | 41 | 24.3 |
| Affected quadrant | | |
| Central region | 72 | 42.6 |
| Upper inner quadrant | 51 | 30.2 |
| Lower inner quadrant | 20 | 11.8 |
| Upper outer quadrant | 79 | 46.7 |
| Lower outer quadrant | 29 | 17.2 |
| Presence of abscess at the first visit | | |
| Yes | 55 | 32.5 |
| No | 114 | 67.5 |
| Presence of sinus at the first visit | | |
| Yes | 29 | 17.2 |
| No | 140 | 82.8 |
| Presence of skin redness at the first visit | | |
| Yes | 77 | 45.56 |
| No | 92 | 54.44 |

BMI, body mass index.

lactation. In the present study, the majority of women were multigravida (88.17%), with a history of lactation (139 patients, 82.25%). The median duration of breast-feeding was 8 months. In women with a history of lactation, 69.78% (97/139 patients) of patients experienced disease onset within 4 years after delivery. Among all included patients, comorbidity conditions were reported, including hyperprolactinemia (n=4, 2.4%) and psychiatric disorders (n=6, 3.5%).

Breast lumps (n=165, 97.6%) and pain (n=103, 60.9%) are the primary symptoms of GM, as well as the primary reason for outpatient visits; 26.0% (n=44) patients experienced moderate to severe pain at the initial disease onset, and reported quickly relief in weeks. As high as 45.56% (n=73) patients reported skin involvement at the first clinical visit; 32.5% patients reported abscess formation at the first visit. Erythema nodosum (n=4, 2.4%) and joint pain (n=3, 1.8%) were also reported as noticeable symptoms. Disease lesions were mostly observed at the upper quadrant and central zone of the breast.

Disease managements

Mastitis at different stage usually requires different therapeutic strategies. Concerning the management of GM, the primary treatment in the present cohort consisted of oral steroids (n=123, 72.78%) and topical Chinese herbs (n=117, 69.05%) as the initial treatment (Figure 3). Steroids were the primary choice for lesions with a large size, abscess and sinus. Among all patients, 146 patients received steroids as the initial treatment. They received methylprednisolone tablets 20 mg once a day for 14 days (9) and then went to the outpatient clinic to evaluate whether they needed further treatment. The median course for steroid usage was 130.86 days (range, 7–420 days). Antibiotics were the primary treatment options for 21.43% of patients at the initial diagnosis. Only 0.59% patients chose antibiotics during disease progression. The primary antibiotic choices were levofloxacin and cephalosporins, with a treatment duration of 1–2 weeks.

In our study, the topical Chinese herbs referred to Lihuedan, a well-established topical traditional Chinese medicine formula widely used for cellulitis and acute pancreatitis (10,11). Apply 50 g of this ointment to the affected area daily, once a day for 2 days per course of treatment, and the next course of treatment will be carried out after evaluation at the outpatient clinic every 14 days. Lihuedan is usually chosen in combination with steroids or alone for mastitis without skin involvement and superficial abscess.

Clinical course and disease outcomes

Although a noticeable proportion of GM is refractory, the disease progression and regression showed some regularity (Figure 4). The disease course of GM was concentrated between 161 (25 percentile) and 376.5 days (75 percentile), with a median disease course of 257 days (range, 55–1,500 days). Less than 10% of cases regressed in 3 months, and that for 6 months was 39.52% (66 in 169 cases).

Refractory disease, characterized by a long disease course, is of particular interest for disease management. We performed univariate and multivariate logistic regression analyses for long-term disease course. In our datasets, 28.40% of patients (48/169) exhibited a long disease course, which was defined as a disease course of more than 1 years. Abscess and sinus formation during disease progression appear to be factors contributing to a longer disease course (Table 2).

The role of steroid in GM is unclear and under debate for years. In the present cohort, 146/169 of patients

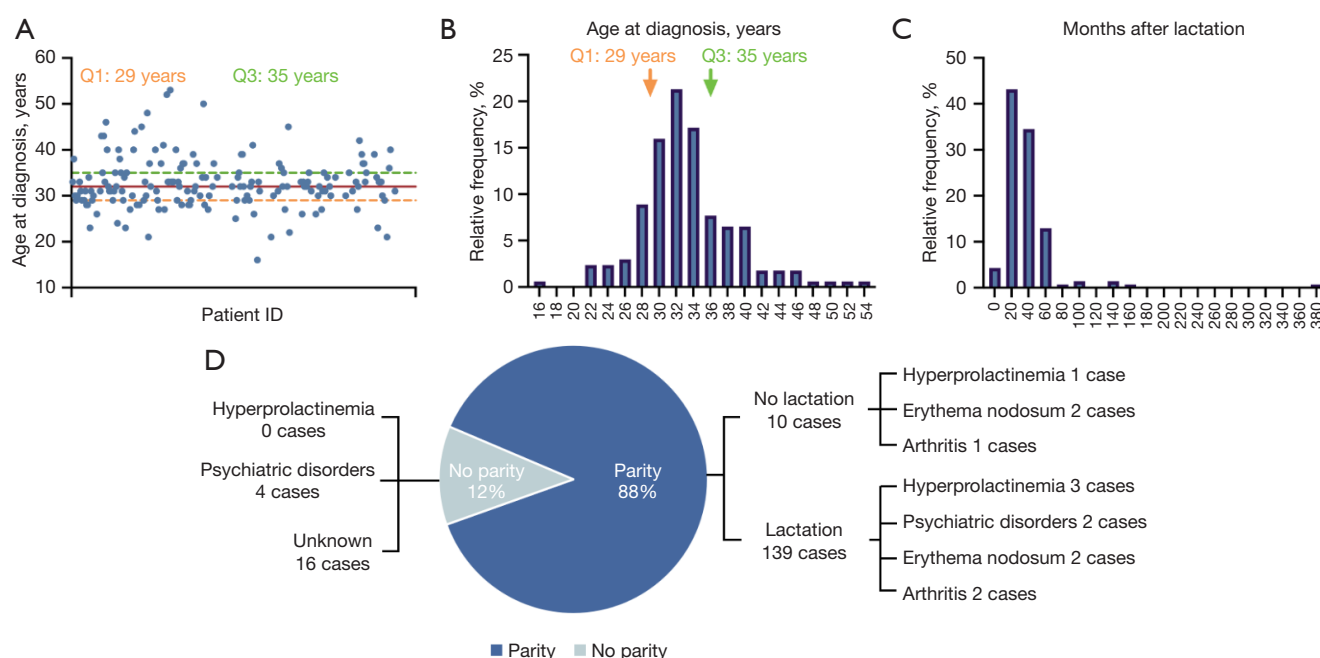


Figure 2 Characteristics of study population at diagnosis. (A,B) Age distribution of GM at diagnosis. Age distribution of women at GM diagnosis. Orange line and arrow represents 25 percentiles, while green line and arrow represent 75 percentiles. Lactation statuses and parity for patient at diagnosis. (C) Time to disease occurs after lactation. (D) Fertility and comorbidity statuses of GM patients at diagnosis. GM, granulomatous mastitis.

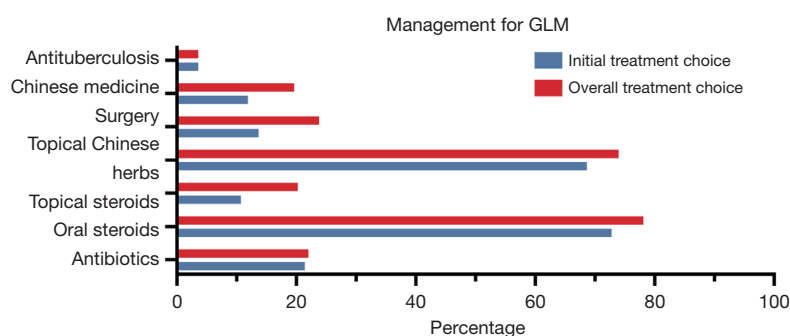


Figure 3 Initial and overall treatments for granulomatous mastitis. Oral steroids mainly include methylprednisolone and prednisolone. Topical steroids mainly contain halometasone and betamethasone cream. Topical Chinese herbs mainly indicate Liuheadan. GLM, granulomatous lobular mastitis.

received steroids as the initial choice. The rate for steroid usage as the initial treatment was significantly higher in short-course groups (75% *vs.* 90.9%, $P=0.007$). After adjusting for age, lump size, abscess, and sinus formation, steroid usage was associated with a shorter disease course ($P=0.02$) (Table 2). The usage of steroids appears to decrease the disease course. However, as patients received treatment with a combination of multiple drugs, it is challenging to

disentangle the separate effects of each medicine.

Abscess formation and its clinical implication

Abscess formation was observed in 58.57% (99/169) of all participants. Unlike conventional bacterial associated abscess, symptoms accompanied with GM related abscess formation were mild, with only 3 cases of low-grade fever

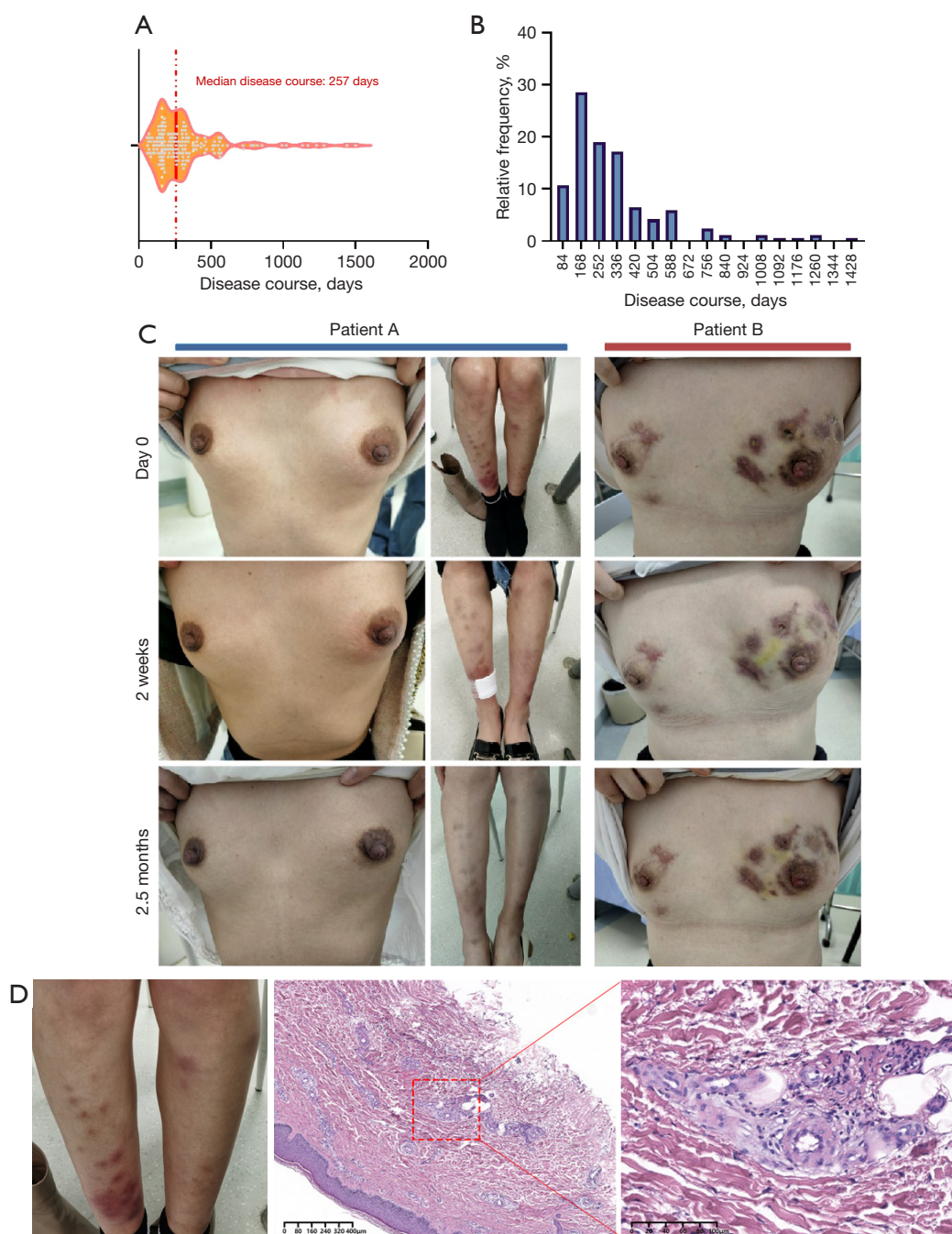


Figure 4 Distribution of disease course. Violin plot (A) and histograms (B) illustrating the distribution of the disease course. (C) Representative cases with diverse disease courses of GM are presented. Patient A is a 35-year-old woman who complained of a firm lump in the entire left breast (diameter of 7.5 cm), resulting in breast asymmetry. She also reported erythema nodosum on both lower limbs. After 2.5 months of oral methylprednisolone, lesions on the breast and limbs completely disappeared. No recurrence was observed during the 13 months of follow-up. Patient B is a 32-year-old woman who complained of a 5-cm lump in the right breast, with abscess formation at the initial clinical visit. She received anti-tuberculosis and Chinese herbs as the initial treatment but failed in the disease control. Mastitis finally healed with 6 months of oral methylprednisolone, leaving scars in her right breast. However, two months after treatment was finished, GM in the left breast occurred. Disease progressed rapidly and abscess formation occurred within 1 months of disease onset in the left breast. Due to Cushing's syndrome, oral methylprednisolone was changed into local injection of triamcinolone. Until now, the patient is still under

treatment with a disease course of 21 months. (D) Histopathological features of erythema nodosum. Hematoxylin and eosin staining of skin tissue specimens under light microscope revealed perivascular inflammation in the dermis. Homogeneous red-stained protein and suspicious microthrombosis were observed in vascular lumens. Infiltration of neutrophils and chronic inflammatory cells were also observed. GM, granulomatous mastitis.

Table 2 Univariable and multivariable logistic regression analysis for long disease course

| Variables | Long course (n=48) | Short course (n=121) | Univariable analysis | Multivariable logistic regression | | |
|--------------------------------|-----------------------|-------------------------|----------------------|-----------------------------------|--------------|-------|
| | | | P | OR | 95% CI | P |
| Age (years), mean | 32.83 | 32.38 | 0.52 | 1.006 | 0.9424–1.072 | 0.85 |
| Lump size (cm), mean | 5.12 | 4.34 | 0.02 | 1.171 | 0.9828–1.409 | 0.08 |
| Abscess, n (%) | | | 0.006 | 2.459 | 1.164–5.466 | 0.02 |
| Yes | 36 (75.0) | 63 (52.1) | | | | |
| No | 12 (25.0) | 58 (47.9) | | | | |
| Sinus formation, n (%) | | | 0.005 | 0.35 | 0.165–0.741 | 0.006 |
| Yes | 18 (37.5) | 21 (17.4) | | | | |
| No | 30 (62.5) | 100 (82.6) | | | | |
| Steroid as first choice, n (%) | | | 0.007 | 3.028 | 1.181–7.763 | 0.02 |
| Yes | 36 (75.0) | 110 (90.9) | | | | |
| No | 12 (25.0) | 11 (9.1) | | | | |
| Steroid usage, n (%) | | | 0.005 | 3.685 | 1.369–9.789 | 0.01 |
| Yes | 37 (77.1) | 112 (92.6) | | | | |
| No | 11 (22.9) | 9 (7.4) | | | | |

CI, confidence interval; OR, odds ratio.

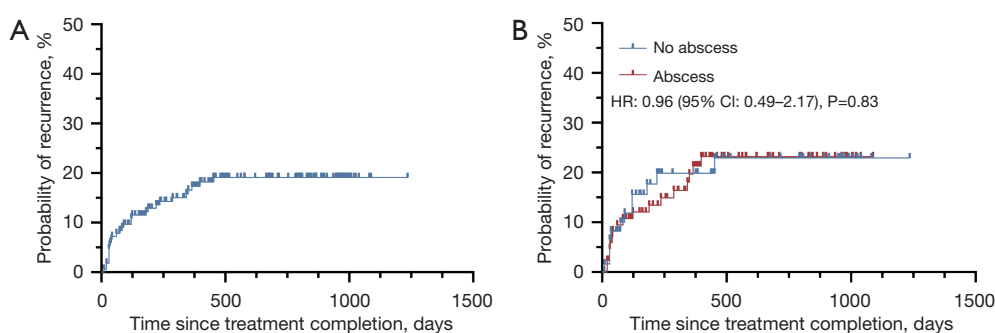


Figure 5 Disease relapse for GM after treatment finished. (A) Disease relapse for whole cases of GM. (B) Disease relapse according to abscess formation. CI, confidence interval; GM, granulomatous mastitis; HR, hazard ratio.

and tiredness was recorded. Among the 100 cases developing breast abscesses, only 65 underwent blood tests, and 7 underwent pus culture. 58.5% (38/65) of patients showed elevated inflammatory indicators (elevated white blood cells).

1 patient showed positive pus culture (1/7), with *Kroppenstedt Corynebacterium* was identified. Women with abscess formation during disease progression exhibited a significantly longer disease course (358.67 vs. 278.24 days, $P=0.03$) (Table 3).

Table 3 Factors relating to abscess formation

| Factors | Abscess formation | | P |
|---|-------------------|-----------|------|
| | Yes (n=99) | No (n=70) | |
| Lump size at diagnosis (cm), mean | 4.93 | 4.04 | 0.29 |
| Disease course (days), mean | 358.67 | 278.24 | 0.03 |
| Steroid as primary choice, n (%) | | | 0.39 |
| Yes | 69 (69.7) | 53 (75.7) | |
| No | 30 (30.3) | 17 (24.3) | |
| Overall steroid usage, n (%) | | | 0.62 |
| Yes | 76 (76.8) | 56 (80.0) | |
| No | 23 (23.2) | 14 (20.0) | |
| Overall course for steroid usage (days), mean | 109.81 | 91.47 | 0.42 |
| Antibiotic usage, n (%) | | | 0.79 |
| Levofloxacin | 34 (34.34) | 7 (10.00) | |
| Anti-tuberculosis drugs | 7 (7.07) | 2 (2.86) | |
| Cephalosporin | 8 (8.08) | 1 (1.43) | |
| Surgical managements after abscess formation, n (%) | | | 0.08 |
| Needle aspiration | 23 (13.6) | – | |
| Incision | 15 (8.9) | – | |

Relapse and disease outcomes

With a median follow-up of 412 days (range, 0–1,235 days), 29 relapses were observed after completed treatment. Relapse occurred mostly in the first 2 years after treatment (Figure 5). Although abscess significantly prolonged the disease course, it did not increase the disease relapse rate after treatment [hazard ratio (HR) =0.96; 95% confidence interval (CI): 0.49–2.17; P=0.83].

Discussion

GM is a rare but troublesome disease affecting women of child-bearing age. The pathology and natural course of GM are insufficiently understood. Describing the disease course and factors associated with longer disease course might facilitate the understanding of disease occurrence and further clarify the treatment procedure.

The natural course of GM has been under debate for years. Some studies have suggested that GM is a self-limited process that can resolve spontaneously over 5–20 months (4,7,11). A retrospective study included 120 GM patients

from 2006 to 2019, and 112 of them achieved complete remission on average in 5 months (0–20 months) (4). Apart from the sparse data and small sample size, interpreting studies relating to the disease course of GM has been very difficult due to their retrospective design, lack of standardization, and non-accuracy of chart documentation. In order to better describe the disease, we defined the long course of disease as 342 days based on the average course of disease of 325.35 days.

The present study reported a significant heterogeneity in the disease course for women with GM. Predicting patients with a prolonged and recurrent disease course is important for disease management. Abscess and sinus formation were identified as independent predictors for a prolonged disease course, consistent with previous findings. This finding is consistent with previous studies which found the mass size, skin ulcer and sinus was positively related with long disease course (12,13). In fact, as a common outcome for mastitis, breast abscesses could cause a wide range of morbidity. One cross sectional analysis of 89 patients with breast abscesses requiring surgical intervention found that 14% were lactational and 86% were non-lactational (14). In this study,

the median disease course was approximately 9 months, with 28.40% of patients experiencing a disease course longer than 1 year. Differentiating the natural course from the impact of unstandardized treatment remains difficult.

The role of GM related abscess is under-recognized. With disease progression, skin ulceration and sinus formation occur in 19–39% of abscess cases (2). Current knowledge on the best management for GM related abscess is scarce. Although studies have indicated that corynebacteria support the pathogenesis of GM, it is still difficult to associate specific species with the etiology of GM to confirm the precise cause (15,16). Based on our current clinical practice experience, we tentatively accept the aseptic inflammatory theory. Antibiotics are not typically recommended in Breast Center, West China Hospital, Sichuan University unless a concurrent bacterial infection is identified, such as through symptoms like fever, weakness, abnormal blood test results, or culture-positive pus. For large size abscess, needle aspiration is preferred to reduce the need for tube or surgical drainage. More studies are needed to explore the characteristics and management for GM related abscess and sinus.

There is no single treatment strategy that can solve every case or stage of GM due to its undefined etiology and heterogeneous disease course. The general treatment principle is choosing suitable treatment plan based on disease etiology and disease severity. As recommended in our previous study and others (17), treatment options for GM include steroids, Chinese herbs, antibiotics, and surgery, as well as regular follow-up. In the present studies, Chinese herbs and steroids are the most frequently used in our real clinical practice. In China, the use of Chinese herbal medicine for non-puerperal mastitis is favored by multiple guideline and expert consensus (9,18–20), without definite indication. In our practice, Chinese herbal medicine is recommended for masses with small in size or localized refractory mastitis.

Corticosteroids were primarily suggested as first-line treatment for moderate or severe cases. However, whether steroid provides short term symptomatic relief or have a positive long-term effect on the disease course is a matter of debate. In the present study, most of our patients chose steroids as the first treatment and we found an association of steroid usage with a shorter disease course. The result favors corticosteroids usage for masses with a large-size or abscess formation. However, the study has inherent selection bias and potential residual confounding, as do most small sample observational studies. More studies are required

to clarify the role of corticosteroids in GM managements. Treatment time of corticosteroid needs to be adjusted according to the progression of disease. To our practice, the median time of oral corticosteroid usage was about two months (17). Topical steroid cream or intralesional steroid injections may be considered as alternatives to oral steroids. For more severe or refractory cases, non-corticosteroid immunosuppressive agents such as methotrexate or azathioprine may be used in addition to or instead of oral steroids. Besides, emerging new immunological approaches may be a potential alternative (21).

The role of surgery on disease control remains unclear. In our experience, surgery was not recommended as an initial treatment due to a recurrence rate comparable to that of nonsurgical therapy, as reported up to 15–23% (7,22). In a recent meta-analysis, surgical treatment (with or without corticosteroids) was associated with a high cure rate and a relatively low recurrence rate. The cure rates of oral corticosteroids and surgeries were 90.6%, 94.5%, respectively, and the recurrence rates were 6.8%, 4.0%, respectively (23). The destructive scar and post-operative pain during dressing change are also our primary concerns for surgery. Furthermore, most patients come to the clinic with a median size of larger than 3 cm, making it challenging to achieve acceptable post-operative cosmetic outcomes. Surgery might be effective in localized mass, sinus tract. Indications for surgery remain controversy.

This study aims to summarize the disease course and explore the clinical implications of GM. Limitations include the prospective observational design, potential selection bias, and a small sample size. Despite these limitations, in our opinion, this study provides novel and interesting data about the heterogeneous disease course of GM and factors associated with a long disease course. The general treatment principle for GM is choosing suitable treatment plan based on disease etiology and severity. Our study supports corticosteroids as the initial treatment for both mild and severe disease, as well as those with abscess formation.

Conclusions

GM is a complex and heterogeneous disease with a highly variable clinical course. This study provides valuable insights into the natural progression of GM and identifies important factors that influence disease duration and outcome. In this study, the median disease duration was 257 days, with 28.4% of patients experiencing disease duration of more than one year. Abscess and sinus formation were

identified as significant predictors of a longer disease course, highlighting the need for targeted management strategies in these cases. Corticosteroids were used as initial treatment in 86.39% of patients. Our findings suggest that the use of steroids is associated with a shorter disease course in patients with GM, and that steroid use does not pose a risk of abscess formation. This supports the use of corticosteroids as first-line therapy in the treatment of GM cases, with potential benefits in terms of disease modulation and symptom control. The treatment principle for GM involves choosing a suitable treatment plan based on disease severity and disease progression rate. Treatment options include but are not limited to steroid therapy, surgical treatment, Chinese medicine treatment, antibiotics, etc. For complex situations such as invasive lesions, abscess formation, and large masses, the choice should be made based on the specific situation.

Acknowledgments

None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/gs-2024-557/rc>

Data Sharing Statement: Available at <https://gs.amegroups.com/article/view/10.21037/gs-2024-557/dss>

Peer Review File: Available at <https://gs.amegroups.com/article/view/10.21037/gs-2024-557/prf>

Funding: None.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gs-2024-557/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study received approval from the ethics board of the West China Hospital (No. 2021020A).

Signed informed consent form was obtained from all participants prior to their inclusion in the study.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

1. Steuer AB, Stern MJ, Cobos G, et al. Clinical Characteristics and Medical Management of Idiopathic Granulomatous Mastitis. *JAMA Dermatol* 2020;156:460-4.
2. Scott DM. Inflammatory diseases of the breast. *Best Pract Res Clin Obstet Gynaecol* 2022;83:72-87.
3. Zou J, Nelson N, Botnar K, et al. Clinical Trends in Granulomatous Mastitis Incidence, Prevalence, and Treatment: A Retrospective Study Highlighting Ethnic Differences in Care. *J Surg Res* 2024;302:732-8.
4. Goulabchand R, Hafidi A, Van de Perre P, et al. Mastitis in Autoimmune Diseases: Review of the Literature, Diagnostic Pathway, and Pathophysiological Key Players. *J Clin Med* 2020;9:958.
5. Martinez-Ramos D, Simon-Monterde L, Suelves-Piqueres C, et al. Idiopathic granulomatous mastitis: A systematic review of 3060 patients. *Breast J* 2019;25:1245-50.
6. Zhou Y, Wu J, Ma L, et al. Differences and significance of peripheral blood interleukin-6 expression between patients with granulomatous lobular mastitis and those with benign breast tumors. *Front Med (Lausanne)* 2023;10:1273406.
7. Coombe RE, Hamed H. An update on granulomatous mastitis: a rare and complex condition. *Br J Hosp Med (Lond)* 2021;82:1-7.
8. Wolfrum A, Kümmel S, Theuerkauf I, et al. Granulomatous Mastitis: A Therapeutic and Diagnostic Challenge. *Breast Care (Basel)* 2018;13:413-8.
9. Zhang C, Hu J, Zhao X. Hunan expert consensus on diagnosis and treatment of granulomatous lobular mastitis (2021 edition). *Chinese Journal of General Surgery* 2021;30:1257-73.
10. Zhou J, Fang L, Xie H, et al. A pilot study using the Chinese herbal paste Liu-He-Dan to manage radiodermatitis associated with breast cancer radiotherapy.

- Curr Oncol 2015;22:e453-6.
11. Wan MH, Zhao XL, Chen WW, et al. Therapeutic Effect of Chinese Herbal Ointment Liu-He-Dan in Patients with Acute Pancreatitis. *Chin Med J (Engl)* 2016;129:1128-30.
 12. Yılmaz TU, Gürel B, Güler SA, et al. Scoring Idiopathic Granulomatous Mastitis: An Effective System for Predicting Recurrence? *Eur J Breast Health* 2018;14:112-6.
 13. Basim P, Argun D, Argun F. Risk Factors for Idiopathic Granulomatous Mastitis Recurrence after Patient-Tailored Treatment: Do We Need an Escalating Treatment Algorithm? *Breast Care (Basel)* 2022;17:172-9.
 14. Bharat A, Gao F, Aft RL, et al. Predictors of primary breast abscesses and recurrence. *World J Surg* 2009;33:2582-6.
 15. Ong SS, Xu J, Sim CK, et al. Profiling Microbial Communities in Idiopathic Granulomatous Mastitis. *Int J Mol Sci* 2023;24:1042.
 16. Chen W, Zhang D, Zeng Y, et al. Clinical characteristics and microbiota analysis of 44 patients with granulomatous mastitis. *Front Microbiol* 2023;14:1175206.
 17. Tan QW, Zhang YN, Jia YP, et al. Methylprednisolone for idiopathic granulomatous mastitis: a prospective observational cohort study. *Gland Surg* 2022;11:1538-45.
 18. Zhou F, Liu L, Yu Z. Expert consensus on diagnosis and treatment of non-lactating mastitis. *Chinese Journal of Practical Surgery* 2016;36:755-8.
 19. Liu X, Chen Q. Traditional Chinese medicine expert consensus on diagnosis and treatment of granulomatous lobular mastitis (2021 edition). *Chinese Journal of Surgery of Integrated Traditional and Western Medicine* 2022;28:597-602.
 20. Zhou F, Shang XC, Tian XS, et al. Clinical practice guidelines for diagnosis and treatment of patients with non-puerperal mastitis: Chinese Society of Breast Surgery (CSBrS) practice guideline 2021. *Chin Med J (Engl)* 2021;134:1765-7.
 21. Wang X, He X, Liu J, et al. Immune pathogenesis of idiopathic granulomatous mastitis: from etiology toward therapeutic approaches. *Front Immunol* 2024;15:1295759.
 22. Zhou F, Liu L, Liu L, et al. Comparison of Conservative versus Surgical Treatment Protocols in Treating Idiopathic Granulomatous Mastitis: A Meta-Analysis. *Breast Care (Basel)* 2020;15:415-20.
 23. Lei X, Chen K, Zhu L, et al. Treatments for Idiopathic Granulomatous Mastitis: Systematic Review and Meta-Analysis. *Breastfeed Med* 2017;12:415-21.

Cite this article as: Liu J, Lin WY, Wang QZ, Yang XQ, Lv Q, Tan QW. Unveiling the enigma: understanding the complex disease course of granulomatous mastitis and seeking ways to shorten it. *Gland Surg* 2025;14(4):646-657. doi: 10.21037/gs-2024-557