Original Article

JHSMR Journal of Health Science and Medical Research

Idiopathic Granulomatous Mastitis: A Retrospective Cohort Study of Treatment Modalities in 83 Patients From Southern Thailand

Puttiporn Puttawibul, M.D.[1], Siripen Kanchanasuwan, M.D.[2], Suphawat Laohawiriyakamol, M.D.[1]

[1]Department of Surgery, Faculty of Medicine, Prince of Songkla University, Songkhla 90110, Thailand.

[2]Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla 90110, Thailand.

Received 9 January 2023 ● Revised 8 March 2024 ● Accepted 9 March 2024 ● Published online 6 August 2024

Abstract:

Objective: Idiopathic granulomatous mastitis (IGM) is a rare condition that mimics breast cancer. Current treatment strategies include both surgical and medical therapy. This study aimed to report and describe the clinical signs, radiological findings, management, clinical course, and outcomes after treatment of IGM, from a major tertiary care institute in southern Thailand.

Material and Methods: The medical records of 83 patients with IGM treated at our institute between January 2001 and April 2022 were retrospectively studied. Patient characteristics, clinical presentations, radiological findings, microbiological workups, tissue pathologies, treatment modalities, outcomes and follow-up data were reviewed and analyzed. The success rate, recurrence rate, and time to heal were compared between the different treatment modalities.

Results: Overall, 83 patients were diagnosed with IGM. Due to insufficient follow-up periods, data from only 50 patients were used for the analysis. Initially, 34,3,8, and 5 were treated surgically, with steroids, anti-tuberculosis (TB) drugs, or other treatments, respectively; 32 (64%) achieved disease resolution. The median time to heal was 472 days, while the median time to heal after surgery, steroid therapy, anti-TB therapy, and others was 614.5, 333, 208.5, and 406 days, respectively. Surgery resulted in the longest time to heal; however, the difference was not statistically significant (p-value=0.23). Eighteen (36%) patients experienced recurrence.

Conclusion: There was no significant difference among the treatment modalities in terms of time to heal and recurrence. Surgery resulted in the longest healing time, the highest incidence of complications, and a recurrence rate of approximately 50%. Surgical treatment should be reserved for aggressive diseases.

Keywords: breast disease, granulomatous, idiopathic granulomatous mastitis, IGM, mastitis

Contact: Suphawat Laohawiriyakamol, M.D.
Department of Surgery, Faculty of Medicine, Prince of Songkla University, Songkhla 90110, Thailand.
E-mail: lsuphawa@medicine.psu.ac.th

J Health Sci Med Res 2025;43(1):e20241079
doi: 10.31584/jhsmr.20241079
www.jhsmr.org

Introduction

Idiopathic granulomatous mastitis (IGM) is a rare, benign, and chronic inflammatory disease first described by Kessler and Wolloch in 1972[1]. The clinical presentation of IGM may include masses, inflammatory manifestations, fistulae, and fluid collection, resulting in breast disfigurement[2,3]. Radiological findings have shown a varied appearance, based on the timing of radiographic evaluation and prior intervention. These typically demonstrate diffuse asymmetric dense masses with malignant features[4,5]. IGM can mimic breast cancer, with similar clinical presentation and radiological images. A definite diagnosis is achieved by histological examination that shows non-caseating chronic granuloma formation, with a localized infiltrate of multinucleated giant cells, plasma cells, epithelioid histiocytes and lymphocytes. Neutrophilic infiltration may also occur with the formation of microabscesses[6-8].

Many factors have been considered as causing IGM; including hormonal imbalance, autoimmune response, unknown infective etiology, or the result of direct trauma. However, the exact etiology remains unknown, and other causes of granulomatous mastitis; including tuberculosis, sarcoidosis, Wegener's granulomatosis, foreign body reaction as well as parasitic and fungal infections, should be excluded before making a diagnosis of IGM[9-11].

Because of the small number of case series and lack of prospective studies, there is still no consensus on the optimal treatment of IGM. The current treatment strategies include conservative approaches, medical therapy, and wide local excision in addition to incision and drainage. Due to the uncertainty of the diagnosis, most patients receive antibiotics before a definite diagnosis of IGM. However, as IGM is a sterile condition routine antibiotic use is not recommended[12-15].

Owing to high recurrence rates and delayed wound healing, surgical interventions are generally performed only for aggressive diseases or in cases that are refractory to medical treatment. Corticosteroids, which were first used by DeHertogh, have become the most commonly used agents today because of their non-invasiveness and reduced scarring[16]. Many studies have reported comparable outcomes between surgery and corticosteroid therapy, and systemic corticosteroid therapy resulted in faster recovery than expectant management. However, due to their various side effects, the use of systemic steroids should be limited, with local corticosteroids being better tolerated[13,17-20].

This study aimed to review and describe the clinical characteristics, radiographic findings, management, clinical course, and clinical outcomes after treatment of IGM, within a major tertiary care institute in southern Thailand.

Patients and methods

The medical records of patient at our institute; from January 2001 and April 2022, were retrospectively review. Overall, 83 patients (82 women and 1 man) diagnosed with granulomatous mastitis having evidence of histopathological confirmation were included in this study. Of these, 11 patients were excluded due to a positive microbiology of tuberculosis, and 22 were further excluded from the comparative analysis due to a very short follow-up period.

Patient characteristics, clinical presentations, radiological findings, microbiological workups, tissue histopathologies, treatment modalities, outcomes and follow-up data were also reviewed. All patients underwent histopathology to confirm the IGM diagnosis before medical treatment was begun. The criteria for the diagnosis of IGM included the presence of granulomatous inflammation on histopathology without an identifiable etiology. All specimens underwent microbiological analysis, staining, and culture for bacteria, fungi, and mycobacteria.

The patients were divided into four groups based on the initial treatment approach, which were surgery, steroid use, antituberculosis drugs, and other treatments. The main outcomes of this study were treatment results and time to heal. Disease cured was defined as absence of inflammatory processes and complete healing of all surgical wounds for

at least 1 year. Time to heal was defined as date of initial treatment to disease cured. Disease recurrence was defined as the re-appearance of symptoms, such as pain, fistulae, abscess, or mastitis, more than 3 months after the disease was cured. This study was approved by our institutional review board.

Results

Of the 83 patients, 72 were diagnosed with IGM, and 11 were classified as having TB granulomatous mastitis, all of whom had histopathological findings of granulomatous inflammation with tissue microbiology positive for tuberculosis. The baseline patient characteristics are shown in Table 1. The average age of the 83 patients was 39 years (range, 20–85 years). Most (68.7%) patients were aged between 21 and 40 years. Approximately one-third of the patients were overweight (28 patients, 33.33%). Forty-two patients had a history of pregnancy, and 7 had a recent breastfeeding history record; 14 had received oral contraceptive pills. Only 16 (22.22%) patients had comorbidities.

Clinical presentations of the 83 patients are presented in Table 2. In this study, most patients presented with only one mass, and only three patients presented with bilateral lesions. Most (86.1%) of the patients manifested a palpable mass located in the upper part of the breast. Radiological findings were usually suspicious and compatible with malignancy; masses in 48 patients were reported as being BI-RADS categories 4 and 5.

In the comparative analysis, the time to heal was 70–5,321 days. Overall, 49 (59%) patients underwent surgery as initial treatment, and 7, 18, and 9 patients were treated with systemic steroids, anti-tuberculosis drugs, and other treatments, respectively, as initial treatment. Twenty-three (27.7%) patients achieved disease resolution with the initial treatment modality. The surgical treatment consisted of excision, incision and drainage.

Table 1 Baseline characteristics of the 83 patients

Characteristics	Surgery (N=49)	Steroids (N=7)	Anti TB drugs (N=18)	Others (N=9)	p-value
Age (years)					0.294
20–40	36 (73.5)	6 (85.7)	11 (61.1)	4 (44.4)	
41–60	12 (24.5)	1 (14.3)	5 (27.8)	4 (44.4)	
>60	1 (2)	0	2 (11.1)	1 (4.8)	
BMI (kg/m^2)					0.849
<20	4 (8.2)	0	2 (11.1)	1 (11.1)	
20–24.9	20 (40.8)	4 (57.1)	9 (50)	5 (55.6)	
25–34.9	15 (31)	3 (42.9)	6 (33.3)	1 (11.1)	
>35	1 (2)	0	1 (5.6)	1 (11.1)	
Missing data	9 (18)	0	0	1 (11.1)	
Prior pregnancy	29 (59.2)	4 (57.1)	4 (22.2)	5 (55.6)	0.017
Recent lactation	5 (10.2)	1 (14.3)	0	1 (11.1)	
Contraception pills use	11 (22.4)	0	1 (5.6)	2 (22.2)	0.077
Co-morbidities					
Diabetes mellitus (DM)	4 (8.2)	0	2 (11.1)	0	0.818
Hypertension	0	0	2 (11.1)	1 (11.1)	0.076
Others	5 (10.2)	0	4 (22.2)	1 (11.1)	0.436

BMI=body mass index, kg=Kilogram, N=number, TB=Tuberculosis

Table 2 Clinical presentation of the 83 patients

Clinical presentation	N (%)
Signs and symptoms	
Mass	73 (88)
Ulcer	1 (1.2)
Mastitis/abscess	14 (16.9)
Pain	21 (25.3)
Number of mass lesions	
1	52 (62.7)
2	9 (10.8)
3	5 (6.0)
4	2 (2.4)
Missing data	15 (18.1)
Side (right:left:both)	41:39:03
Location of lesions	
Retro-areolar	7 (8.4)
Upper-inner quadrant	22 (26.5)
Upper-outer quadrant	18 (21.7)
Lower-inner quadrant	6 (7.2)
Lower-outer quadrant	6 (7.2)
Axillary/cervical lymph node	22 (26.5)
Missing data	2 (2.5)
BI-RADS	
2	9 (10.8)
3	12 (14.5)
4	45 (54.2)
5	3 (3.6)
Missing data	14 (16.9)

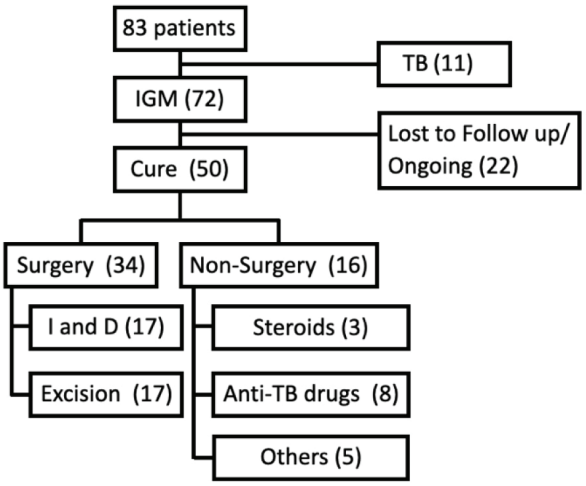
BI-RADS=breast imaging reporting and data system, N=number

One patient was treated with oral prednisolone 45 mg/day. However, the palpable mass persisted, prompting surgical treatment; she was lost to follow-up. One year later, she underwent evaluation, which revealed that the lesion had disappeared, and her mammogram result was BI-RADS 2.

One patient presented with a left breast mass underwent surgery and achieved disease resolution within 13 months. After 10 years, she developed a new lesion; however, at that time, the histopathological report of the new lesion revealed cancer.

A summary of the treatment modalities is shown in Figure 1.

The overall median time to heal was 472 days, while the median time to heal following surgery, steroids, anti-TB drugs, and others was 614.5, 333, 208.5, and 406 days, respectively. Surgical treatment resulted in the longest time to heal compared to non-surgical treatment; the difference was statistically significant (p-value=0.004) (Table 3). Of 18 (36%) patients that had recurrence of IGM, 14 (41.8%) patients had been treated with surgery, 1 (33.33%) had been treated with steroids, 5 (25%) had been treated with antituberculosis drugs, and 1 (20%) had been treated with other treatments. There was no association between patient characteristics, such as age group, body mass index, and co-morbidities, and treatment outcomes in our series. However, patients with co-morbidities tended to take a longer time to heal (Table 4). In this study, patients who had time to heal of ≥2 years had a recurrence rate 11 times higher than those who had a time to heal of <2 years; the difference was significant (p value<0.001).



IGM=Idiopathic granulomatous mastitis, TB=tuberculosis, I and D=incision and drainage

Figure 1 Flowchart of the 83 patients with granulomatous mastitis

Table 3 Comparison of time to heal among treatment modalities

Treatment	Time to heal (days)						p-value
	N	Median	IQR	Percentile 25	Percentile 75	Min:Max	
Surgery	34	614.5	572.7	389.5	962.2	123:5321	0.03
Steroids	3	333	31.5	306	337.5	279:342	
Anti TB drugs	8	208.5	194.7	177.5	372.2	70:2479	
Others	5	406	637	125	762	91:2368	

N=number, IQR=Interquartile range, TB=Tuberculosis

Table 4 Association between patient characteristics and treatment outcomes

Time to heal (days)	N	Median	IQR	p-value
Age (years)				
20–40	34	527.5	723	0.94
41–60	14	437	392.5	
>60	2	499	131	
BMI (kg/m^2)				
<20	3	357	198	0.69
20–24.9	23	534	516	
25–34.9	14	468	578.2	
>35	2	417.5	262.6	
Prior pregnancy				
Yes	25	559	640	0.62
No	2	559.5	202.6	
Missing data	23	468	557.5	
Contraceptive pills use				
Yes	11	599	465.5	0.65
No	12	426.5	323	
Missing data	27	521	728	
Co-morbidities				
Diabetic Mellitus	3	680	630.5	0.16
Hypertension	1	368		
Others	4	540	92.2	0.81

BMI=body mass index, kg=kilogram, IQR=interquartile range, N=number

Discussion

IGM is a rare disease, with only 83 patients having been treated in our institute in the past 22 years. Some studies have described an association between IGM and contraceptive pills, lactation, *Corynebacterium* infection, and trauma[6,19,21–23]. Greater severity and longer duration of the disease in the puerperal period were shown in one study[24]. In our series, >90% of the patients were of child-bearing age, and seven presented during the breastfeeding period. This study found no relationship between IGM and other factors, such as smoking or infection. The most important issue in diagnosing IGM is distinguishing it from cancer. In

our series, 88% of the patients presented with a palpable breast mass, with nearly half of these patients having radiological findings that were suspicious of malignancy. Other etiologies of IGM need to be excluded before diagnosing IGM, and it is suggested staining and culture for bacteria, fungi, and mycobacteria be performed, especially in areas with a high prevalence of tuberculosis. Treating IGM is still challenging, as there is currently no standard treatment and prospective studies are lacking. Uysal et al. reported that among 720 patients with IGM from 22 centers in Turkey, >50% of patients were treated with a multimodal approach, followed by corticosteroids in 39% of patients and surgery alone in 8%: the overall recurrence rate was 17%[25].

Wide, local excision with or without corticosteroid therapy was the treatment performed in several studies.[8,18,19] Local excision has the shortest healing time; however, delays in wound healing and high recurrence rates have been reported[15,26–28]. This study revealed that approximately 50% of patients who underwent surgery experienced complications, had a longer time to heal, and/or had a high recurrence rate. Although there was a high incidence of complications, some authors reported successful tissue reconstruction after surgery for IGM[29–31]. In this study, nine patients were conservatively treated initially, with four of them followed up. Of these, one patient experienced recurrence after conservative treatment. The natural history of IGM may be self-limiting; hence, treatment options should be discussed with the patient and medical team.

Owing to the rarity of the disease, there is a lack of prospective studies that compare each treatment modality. Surgery has been performed as the initial treatment, although this may not be suitable for all patients. Furthermore, one-third of patients required multimodal treatment in this study. Further studies are required to determine which treatment modalities are the most optimal for IGM.

Conclusion

There was no significant difference among the treatment modalities in terms of time to heal and recurrence. Surgery resulted in the longest healing time, the highest incidence of complications, and a recurrence rate of approximately 50%. Surgical treatment should be reserved for aggressive diseases. Multimodal treatment is recommended for IGM.

Ethic approval

The protocol was registered at the office of Human Research Ethics Committee (REC. 65-375-10-4). of the Faculty of Medicine, Prince of Songkla University

Acknowledgement

We wish to acknowledge the International Affairs Office Prince of Songkla University and Ms. Nannapat Pruphetkaew for their assistance with English language revision and statistical analysis, respectively.

Funding sources

There are no grants or financial support received by any authors in relation to this study or for the writing of this article.

Conflict of interest

None of the authors have any financial or personal relationships with other people or organizations that could inappropriately influence their works.

References

1. Kessler E, Wolloch Y. Granulomatous mastitis: a lesion clinically simulating carcinoma. Am J Clin Pathol 1972;58:642-6.
2. Khalaf A, El-Shemy GG. The myth of idiopathic granulomatous mastitis. Int Medical J 2020;1:116-23.
3. Chirappapha P, Thaweepworadej P, Supsamutchai C, Biadul N, Lertsithichai P. Idiopathic granulomatous mastitis: a retrospective

cohort study between 44 patients with different treatment modalities. Ann Med Surg (Lond) 2018;36:162–7.
4. Gautier N, Lalonde L, Tran-Thanh D, Khoury ME, David J, Labelle M, et al. Chronic granulomatous mastitis: Imaging, pathology and management. Eur J Radiol 2013;82:e165–e75.
5. Yilmaz E, Lebe B, Usal C, Balci P. Mammographic and sonographic findings in the diagnosis of idiopathic granulomatous mastitis. Eur Radiol 2001;11:2236–40.
6. Li SB, Xiong Y, Han XR, Liu ZY, Lv XL, Ning P. Pregnancy associated granulomatous mastitis: clinical characteristics, management, and outcome. Breastfeed Med 2021;16:759–64.
7. Yuan QQ, Xiao SX, Farouk O, Du YT, Sheybani F, Tan QT, et al. Management of granulomatous lobular mastitis: an international multidisciplinary consensus (2021 edition). Mil Med Res 2022;9:20.
8. Katz U, Molad Y, Ablin J, Ben-David D, Paran D, Gutman M, et al. Chronic idiopathic granulomatous mastitis. Ann N Y Acad Sci 2007;1108:603–8.
9. Altintoprak F, Kivilcim T, Ozkan OV. Aetiology of idiopathic granulomatous mastitis. World J Clin Cases 2014;2:852–8.
10. Gunduz Y, Altintoprak F, Tatli Ayhan L, Kivilcim T, Celebi F. Effect of topical steroid treatment on idiopathic granulomatous mastitis: clinical and radiologic evaluation. Breast J 2014;20:586–91.
11. Imoto S, Kitaya T, Kodama T, Hasebe T, Mukai K. Idiopathic granulomatous mastitis: case report and review of the literature Jpn J Clin Oncol 1997;27:274–7.
12. Bani-Hani KE, Yaghan RJ, Matalka II, Shatnawi NJ. Idiopathic granulomatous mastitis: time to avoid unnecessary mastectomies. Breast J 2004;10:318–22.
13. Toktas O, Konca C, Trabulus DC, Soyder A, Koksal H, Karanlik H, et al. A novel first-line treatment alternative for noncomplicated idiopathic granulomatous mastitis: combined intralesional steroid injection with topical steroid administration. Breast Care (Basel) 2021;16:181–7.
14. Williams MS, McClintock AH, Bourassa L, Laya MB. Treatment of granulomatous mastitis: is there a role for antibiotics? Eur J Breast Health 2021;17:239–46.
15. Sheybani F, Sarvghad M, Naderi H, Gharib M. Treatment for and clinical characteristics of granulomatous mastitis. Obstet Gynecol 2015;125:801–7.
16. DeHertogh DA, Rossof AH, Harris AA, Economou SG. Prednisone management of granulomatous mastitis. N Engl J Med 1980;303:799–800.
17. Lai ECH, Chan WC, Ma TKF, Tang APY, Poon CSP, Leong HT. The role of conservative treatment in idiopathic granulomatous mastitis. Breast J 2005;11:454–6.
18. Mahmodlou R, Dadkhah N, Abbasi F, Nasiri J, Valizadeh R. Idiopathic granulomatous mastitis: dilemmas in diagnosis and treatment. Electron Physician 2017;9:5375–9.
19. Kornfeld HW, Mitchell KB. Management of idiopathic granulomatous mastitis in lactation: case report and review of the literature. Int Breastfeed J 2021;16:1–6.
20. Çetin K, Sıkar HE, Göret NE, Rona G, Barışık NÖ, Küçük HF, et al. Comparison of topical, systemic, and combined therapy with steroids on idiopathic granulomatous mastitis: a prospective randomized study. World J Surg 2019;43:2865–73.
21. Dobinson HC, Anderson TP, Chambers ST, Doogue MP, Seaward L, Werno AM. Antimicrobial treatment options for granulomatous mastitis caused by corynebacterium species. J Clin Microbiol 2015;53:2895–9.
22. Yalcin Kehribar D, Izci Duran T, Kamali Polat A, Ozgen M. AB1053 Effectiveness of methotrexate in idiopathic granulomatous mastitis treatment. Ann Rheum Dis 2020;79(Suppl 1):1816.
23. Salehi M, Salehi M, Kalbasi N, Hakamifard A, Salehi H, Salehi MM, et al. Corticosteroid and Azithromycin in idiopathic granulomatous mastitis. Adv Biomed Res 2017;6:1–4.
24. Al-Khaffaf B, Knox F, Bundred NJ. Idiopathic granulomatous mastitis: a 25-year experience. J Am Coll Surg 2008;206:269–73.
25. Uysal E, Soran A, Sezgin E, Granulomatous mastitis study G. Factors related to recurrence of idiopathic granulomatous mastitis: what do we learn from a multicentre study? ANZ J Surg 2018;88:635–9.
26. Farrokh D, Alamdaran A, Feyzi Laeen A, Fallah Rastegar Y, Abbasi B. Tuberculous mastitis: a review of 32 cases. Int J Infect Dis 2019;87:135–42.
27. Going JJ, Anderson TJ, Wilkinson S, Chetty U. Granulomatous lobular mastitis. J Clin Pathol 1987;40:535–40.
28. Deng Y, Xiong Y, Ning P, Wang X, Han X-R, Tu G-F, et al. A case management model for patients with granulomatous mastitis: a prospective study. BMC Women's Health 2022;143:1–12.

29. Yau FM, Macadam SA, Kuusk U, Nimmo M, Van Laeken N. The surgical management of granulomatous mastitis. Ann Plast Surg 2010;64:9–16.
30. Hladik M, Schoeller T, Ensat F, Wechselberger G. Idiopathic granulomatous mastitis: successful treatment by mastectomy and immediate breast reconstruction. J Plast Reconstr Aesthet Surg 2011;64:1604–7.
31. Taghizadeh R, Shelley OP, Chew BK, WeilerMithoff EM. Idiopathic granulomatous mastitis: surgery, treatment, and reconstruction. Breast J 2007;13:509–13.