

## Surgery or Medical Treatment In Idiopathic Granulomatous Mastitis?

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**Abstract:** There is no consensus on the treatment of the IGM. It is a chronic and self limiting benign disease and the management of the disease is based on the clinical symptoms of the patients. Treatment modalities differs among patients from follow-up to surgical resection of the tissue. In this study, we compared azathioprine treatment to surgical treatment. In this study, between January 2008 and April 2016 at Uludağ University Medicine Faculty Department of General Surgery, Unit of Breast Surgery; 99 patients who show signs of granulomatous mastitis and proved histopathological methods were enrolled. They were allocated in two groups. First group contains 26 patients treated with azathioprine and undergone no surgery while second group contains 73 patients are surgically treated. All the patients were female and 96 people were married while 3 people were unmarried. In our study, relapses are seen at %23.80 (n=19) of 80 patients with no surgery, %58.30 (n=7) of 12 patients with abscess drainage for once, %14.1 (n=1) of 7 patients with abscess drainage for more than once. According to relapse rate, statistical difference were found between groups. Relapse rate were higher at the group with drainage of abscess for once than the group with no surgery. In our study, we conclude that medical therapy is effective for disease treatment but long term therapy is necessary.

### INTRODUCTION

The term granulomatous mastitis is used for all granulomatous lesions of the breast. It was first described as a non-malignant chronic inflammatory breast disease by Kessler and Wolloch in 1972<sup>1</sup>. It can be seen all over the world and in all races and the incidence of the disease has been reported as 2.4 per 100,000<sup>2</sup>. It is mostly seen in the reproductive age, often in the 2nd-4th decades, and in the first 6 years after birth<sup>3-5</sup>. Causes such as sarcoidosis, histoplasmosis, Wegener's granulomatosis, tuberculosis, actinomyces, brucellosis, fungus, and parasites can be factors of granulomatous mastitis<sup>6</sup>. However, the most common cause is idiopathic granulomatous mastitis (IGM). Although its etiopathogenesis is not known exactly, it has been thought that an autoimmune response develops to secretions that are extravasated from lobules or it may be a cell-mediated reaction against lobular epithelial cells<sup>7</sup>. The most common symptom of the disease is palpation of a mass in a single breast without systemic symptoms. In addition, patients may present with findings such as orange peel appearance on the breast skin, retraction in the nipple, pain, redness, ulceration, abscess, fistula, enlarged lymph nodes in the breast and axilla<sup>8,9</sup>. In this study, treatment options of IGM are discussed.

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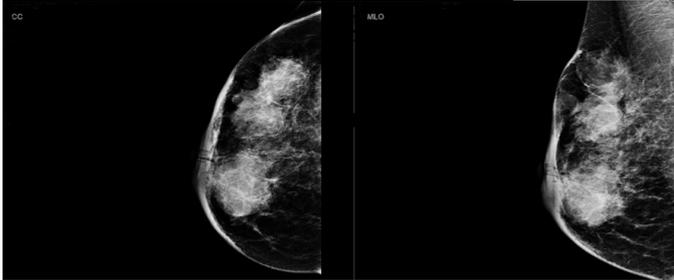
**Table 1.** Granulomatous mastitis classification.

A- Infection	B- Autoimmun	C- Idiopathic Granulomatous Mastitis
Mycobacterium tuberculosis	Sarcoidosis	
Actinomyces	Wegener granulomatosis	
Corynebacterium	Systemic lupus erythematosus	
Lepae	Vaccine	
Blastomycosis		
Cryptococcosis		
Histoplasmosis		
Echinococcus alveolaris		
Philarial infections		





**Fig. I:** 26-year-old patient with left breast swelling, redness, nipple discharge and fistulized lesion on the skin.



**Fig. II.** Mammographic image of the fistulized lesion in the breast.

## MATERIALS and METHODS

### Ethics committee approval

The study was initiated with the approval of the Ethics Committee of Bursa Uludağ University Faculty of Medicine, dated 27.12.2016 and numbered 2016-21/23.

### Patients and Study Design

Records of 99 patients who received granulomatous mastitis treatment between January 2008 and April 2016 in Bursa Uludağ University Faculty of Medicine, Department of General Surgery, Breast Surgery Unit were retrospectively reviewed.

The patients were divided into two main groups. The first group (n = 26) consisted of patients who were treated with Azathioprine without surgery. After histopathological diagnosis, Azathioprine tablet 1x25 mg was started orally in these patients. Hemogram was studied every 15 days. If leukopenia was not detected, the dose was gradually increased (2x25 mg, then 3x25 mg). When clinical and radiological response was obtained, the current treatment was continued for 1 month without dose increase. If the lesion disappeared radiologically and clinically or when significant regression was observed, the dose was gradually reduced and discontinued. In patients with no clinical or radiological response, the dose of Azathioprine was increased to 2x50 mg, followed by 3x50 mg. The second group included patients who underwent surgery (n = 73). These patients were divided into 3 subgroups; those who underwent surgery after failure with medical therapy (azathioprine) (patients incompatible with medical treatment, patients who did not respond to medical treatment, and patients who started with medical treatment and changed their decision and preferred surgery) (n = 24), those who received maintenance medical therapy after surgery (azathioprine), specific antibiotherapy) (n = 26) and patients who underwent surgery only (n = 23), and these groups were compared in terms of duration of treatment and recurrence. The duration of treatment of patients who underwent only surgery was accepted as 1 month.

### Statistical Analysis

In the statistical analysis of the study, the compatibility of continuous variables to normal distribution was examined using the Shapiro

Wilk test. Continuous variables are expressed as median (minimum-maximum) values as descriptive statistics. Kruskal Wallis and Mann Whitney U tests were used for comparisons between groups according to the results of the normality test. Categorical variables were compared between groups using chi-square test, Fisher's exact chi-square test or Fisher-Freeman-Halton tests. SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) program was used for analysis and the significance level was determined as  $p = 0.05$  in statistical comparisons.

## FINDINGS

All of our patients were women. It was found that 92 patients had idiopathic, 3 patients had tuberculosis, 2 patients had actinomyces, and 2 patients had granulomatous mastitis due to foreign body reaction. Considering the mean age, the median age in the non-operated group was 34.50 (25:56), while the median age in the operated group was 34 (20:64). There was no statistically significant difference in both groups ( $p = 0.503$ ).

**Table II.** Demographic data of patients.

	n	%
Married patients	96	97
Pregnant patients	2	2
Having a child	92	92,9
Breastfed diseased breast	86	86,9
Oral Contraseptive	16	16,2
Smoker	21	21,2
Using psychiatric medication	19	19,2
Premenopausal	92	92,9

When the demographic data of the patients were examined, it was observed that 96 patients (97%) were married and 2 patients (2%) were pregnant when diagnosed. It was found that 92 (92.9%) of the patients had a pregnancy history and 86 of them (93.4%) were breastfeeding the diseased breast. In addition, 92 patients (92.9%) were premenopausal, 21 patients (21.2%) smoked, and 16 patients had OCS use anamnesis. While 3.6% (n = 1) of these 16 patients with a history of OCS use had recurrence after the treatments performed in our center, recurrence was observed in 27 patients (32.50%) after the treatments performed in our center for 83 patients without a history of OCS use. Recurrence rate was found to be lower in the group using OCS ( $p = 0.036$ ).

Considering the blood group distribution, blood group data of 74 patients could be reached. Among these patients, the group most common with 30 patients was A Rh (+), while A Rh (-) 2, B Rh (+) 10, A B Rh (+) 5, 0 Rh (+) 23 and 0 Rh (-) 4 patients (Table III).

**Table III.** Distribution of patients according to their blood groups.



The complaints of the patients were palpable mass, skin rash and nipple discharge. The treatment duration of 34 patients with fistula was 5.50 (1:46) months, while the treatment duration of 65 patients without fistula was 13 (1:72) months. There was a statistically significant difference between the two groups according to the duration of treatment ( $p = 0.022$ ).

**Table IV.** Symptoms of Patients

	n	%
Breast Mass	85	85,8
Cellulite	63	63,6
Fistula	34	34,3
Pain	64	64,6

The first 1 month after surgery was evaluated as the treatment period of the patients who underwent surgery, and the time until the end of the medical treatment of the patients who underwent surgery and/or medical treatment was evaluated as the treatment period. Recurrence of the disease after this period was accepted as recurrence. Based on this period, 13 of 99 patients (13.1%) were on the ipsilateral side within the first 6 months, 5 patients (5.1%) on the ipsilateral side after 6 months, 4 patients (4%) within the first 6 months on the opposite side, 6 In the patient (6.1%), the disease recurred after 6 months on the opposite side. In the post-treatment follow-up of the patients;

It was seen that the disease recurred in 5 (20.8%) of 24 patients (24.2%) who received only medical treatment. The disease recurred in 6 (26.08%) of 23 patients (23.2%) who received only surgical treatment, and in 7 (29.1%) of 24 patients (24.2%) who underwent surgery after medical treatment was attempted and failed. 9 (33.3%) of the 27 patients (27.3%) who underwent medical treatment following surgery saw a recurrence of the disease. Statistical analysis of these groups showed no significant differences in the incidence of recurrence ( $p=0.512$ ).

When the treatment durations of the patients were compared, the median duration of treatment was found to be 14.50 (5:41) months in the non-operated group, and 6 (1:72) months in the operated group. The duration of treatment was longer in the non-operated group, and a statistically significant difference was found between the treatment durations ( $p < 0.001$ ).

## DISCUSSION

IGM is defined as simple mastitis considering the inflammation findings by physicians who are inexperienced in breast diseases and it is tried to be treated with antibiotic treatments. However, recurrence is inevitable even if partial response is obtained in these patients. It is a benign but difficult to manage breast disease in which differential diagnosis from breast cancer is essential. Fine needle aspiration biopsy performed in the early period for the diagnosis of the disease is a rapid diagnosis method to rule out malignancy, and tissue biopsy is required for a definitive diagnosis

When the time elapsed between the onset of the complaints of the patients and their application to our center is examined recurrence was observed in 25% ( $n = 8$ ) of 32 patients who applied within the first 3 weeks, 30.8% ( $n = 8$ ) of 26 patients who presented after 4-6 weeks, and in 29.3% ( $n = 12$ ) of 41 patients who presented 6 weeks and after their complaints after the treatments applied in our center. As it can be understood from here, we think that early diagnosis has an important place in effective treatment.

When the complaints of the patients were questioned, 85 patients

(86.7%) had localized or diffuse stiffness that could not be differentiated from the mass, 63 patients (63.6%) had erythema-cellulitis and nipple discharge in 34 patients (34.3%). The treatment duration of 34 patients with fistula was 5.50 (1:46) months, while the treatment duration of 65 patients without fistula was 13 (1:72) months. There was a statistically significant difference between the two groups according to the duration of treatment ( $p = 0.022$ ). The longer duration of treatment in patients without fistula can be explained by the tendency for surgical treatment in patients with fistula and/or the compliance of patients with fistula to treatment.

When the history of using OCS of the patients was examined, it was found that 16 patients used OCS. 3.6% ( $n=1$ ) of these 16 patients using OCS had a relapse after treatment in our center, while 83 patients without OCS had a relapse in 27 patients (32.50%) after treatment in our center. Recurrence rate was found to be lower in the group using OCS ( $p = 0.036$ ). Considering the use of OCA as a predisposing factor in this situation, it may be considered to eliminate the factor by discontinuing OCS after the disease. However, it is possible to interpret the granulomatous mastitis secondary to OCS as a better response to treatment compared to other granulomatous mastitis.

In the surgical treatment of IGM, abscess drainage, wide excision or mastectomy can be applied. Apart from this, successful results can be obtained with only medical treatment. Corticosteroids, nonsteroidal anti-inflammatory agents, colchicine, methotrexate or azathioprine are the main agents used. If cortisone is to be used, 0.8 mg/kg day/oral prednisolone is preferred. Duration of treatment is 6 months. However, 50% recurrence rates have been reported after discontinuation of treatment<sup>10,11</sup>. In the study conducted by Erozgen *et al.*, 24 of 25 patients who were diagnosed with IGM developing after birth were administered steroid treatment, it was reported that one patient had recurrence after steroid treatment among the patients followed for 11 months, and the complaints of other patients completely disappeared<sup>12</sup>. After steroid treatment, the recurrence rate has been reported to be 50%<sup>13</sup>. In our study, 21 patients were given steroids. Recurrence was observed in 8 patients (42.1%) who received steroid therapy during their follow-up. Besides, only azathioprine treatment was used in 26 patients. While recurrence was observed in 6 patients (23.07%), recurrence was observed in 15 (36.5%) of these patients who were given azathioprine combined with surgery in 41 patients. In 1 patient, methotrexate was initiated due to steroid and azathioprine resistance and response was obtained.

Although azathioprine treatment is effective in selected patients with histopathologically diagnosed IGM, surgical treatment should be considered as the first choice in abscess, skin fistula and persistent wound infections. In the study conducted by Aksoy *et al.*, Only wide excision was applied to 15 of 19 patients and they stated that there was no recurrence in the 12-month follow-up of these patients<sup>14</sup>. In our study, 19 of 73 patients who underwent surgical wide excision did not receive additional treatment to surgery, while 2 (10.5%) of these patients had recurrence during their follow-up. In 41 patients, azathioprine was used with surgery, while 12 (29.6%) patients had recurrence in their follow-up, while 13 patients had recurrence in 5 (38.4%) of these patients who were combined with surgery.

As a result, we concluded in our study that the disease can be treated both surgically and medically. Although abscess drainage is not sufficient in surgical treatment, recurrence is more common in these patients. We concluded that the recurrence rates can be reduced by surgically wide excision of the lesion with safe margins. In patients who do not prefer surgery, it should be known that the disease can be treated medically, but a long-term treatment process awaits the patients. In addition, although steroid was first recommended in medical treatment in the literature, azathioprine was found to have positive results as well as steroid in our study.

### ***Conflict of interest***

Authors declare that they have no financial interests or personal conflicts that may affect the study in this article.

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