

## Research Article

# Granulomatous Mastitis: A Single Center Experience from Azerbaijan

 Altay Aliyev,<sup>1</sup>  Arturan Ibrahimli,<sup>1</sup>  Tarana Huseynli,<sup>1</sup>  Gunel Rahimova,<sup>2</sup>  Elgun Samadov,<sup>3</sup>  
 Ceyhun Isayev<sup>3</sup>

<sup>1</sup>Department of Oncology, Liv Bona Dea Hospital, Baku, Azerbaijan

<sup>2</sup>Department of Radiology, Liv Bona Dea Hospital, Baku, Azerbaijan

<sup>3</sup>Department of Surgery, Liv Bona Dea Hospital, Baku, Azerbaijan

### Abstract

**Objectives:** Granulomatous mastitis is a rare benign inflammatory disease of the breast commonly seen in women at childbearing age. The aim of this study is to describe clinical and paraclinical characteristics of GM patients, to demonstrate the management and follow-up experience of our center, and review the literature on the topic.

**Methods:** 30 GM cases were identified among the 3248 patients who applied to the breast health center of the Liv Bona Dea hospital between January 2018 and August 2023. Cases were identified as granulomatous mastitis histopathologically from the biopsy specimens. Patient data was evaluated from the database, and missing information was retrieved by calling the patients.

**Results:** Among the 3248 patients who were admitted to our breast health center, 30 patients (0.9%) had a diagnosis of GM and were identified as applicable to our study. All the patients were female, with a median age of 33, ranging from 27 to 66. Of the 30 patients, 11 were overweight and 7 were obese at the time of diagnosis (mean BMI: 26.7).

While the majority (n=23, 76%) of the patients presented with a breast lump, only 1 (3%) of the patient's only symptom was breast lump. 8 (27%) of the cases had comorbidities, including Hashimoto Thyroiditis (n=1), Hypertension (n=6), Diabetes Mellitus type 1 (n=1), Diabetes Mellitus type 2 (n=4), Major Depression (n=1). Of the lesions, 16 (53%) showed high suspicion with a Bi-Rads score  $\geq 4$ , and 14 (47%) showed low suspicion with a Bi-Rads score  $\leq 4$ . 18 (60%) of patients received only medical treatment, 11 (37%) patients received both surgery (excision) and medical treatment, and only 1 (3%) received surgery (excision) alone.

**Conclusion:** Even though idiopathic GM is the most common GM type, results from the paper of Ercan Kokrut et al. suggest that Tuberculosis should not be skipped, especially in developing countries, with reported 20% as a cause of GM. A multidisciplinary team is crucial in the diagnosis and treatment of GM to be able to distinguish it from breast cancer.

To conclude, Granulomatous mastitis is a tricky condition that can cause high anxiety in physicians as high as in patients. Idiopathic GM is the most common type, but evaluation of other reasons, such as tuberculosis mastitis, must be on the checklist. More research regarding the outcome of different treatment modalities will give a straightforward approach for physicians.

**Keywords:** Breast, granulomatous mastitis, mastitis

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**Address for correspondence:** Altay Aliyev, MD. Department of Oncology, Liv Bona Dea Hospital, Baku, Azerbaijan

**Phone:** +994502519931 / +994125290900 **E-mail:** draltayaliyev@gmail.com

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Granulomatous mastitis is a rare benign inflammatory disease of the breast commonly seen in women at childbearing age. First described in 1972 by Kessler and Wolloch, GM can cause high anxiety and misdiagnose due to its symptom and imaging resemblance with inflammatory breast cancer.<sup>[1]</sup> It is characterized histopathologically by caseous necrosis, granuloma with epithelioid histiocytes, and sometimes micro-abscess formation.<sup>[2,3]</sup> GM is defined as two types according to its etiology: idiopathic and secondary to other granulomatous diseases. Although the etiopathogenesis of idiopathic granulomatous mastitis is still mysterious, some potential causes are discussed nowadays by scientists, such as reaction to trauma, metabolic or hormonal processes, autoimmunity, infection with *corynebacterium kropfenstedtii*, even seasonal changes.<sup>[4-6]</sup> Secondary GM can be caused by several conditions, and all of them should be excluded before idiopathic GM diagnosis is made. Some examples of secondary GM are infections (tuberculosis, histoplasmosis, actinomycosis, and corynebacterium infection), foreign body reactions, and vasculitis.<sup>[7]</sup> Before making the idiopathic GM diagnosis, the mentioned causes should be excluded to prevent misdiagnoses and wrong medication use. There are three commonly used treatment methods: medical treatment, surgery, and both. There is not enough evidence of the superiority of the methods over one another.<sup>[8-11]</sup> The aim of this study is to describe clinical and paraclinical characteristics of GM patients, to demonstrate the management and follow-up experience of our center, and review the literature on the topic.

## Methods

30 GM cases were identified among the 3248 patients who applied to our breast health center between January 2018 and August 2023. Cases were identified as granulomatous mastitis histopathologically from the biopsy specimens. Patient data was evaluated from the database, and missing information was retrieved by calling the patients. The following data was analyzed retrospectively: Age, Gender, Body Mass Index, symptoms at admission, comorbidities, smoking history, history of breast trauma, family history, aesthetic breast surgery history, presence of fistula, time from first symptom until diagnosis, time from first diagnosis until now, etiology, lactation history, medication history, first used imaging method, ultrasound findings, mammography findings, magnetic resonance findings, malignancy suspicion according to bi-rads score ( $\geq 4$  considered as high suspicious), menopausal status, menstrual cycle regularity, number of pregnancies, age at first pregnancy, time between the last resulted pregnancy and diagnosis, type of biopsy, type of treatment for GM (Medical or Surgical), type and duration of medical treatment, type of surgical treatment, dimensions of

the mass, presence of recurrence, presence of axillary lymphadenopathy, BCG (bacille calmette guerin) vaccine history, localization of mass, oral contraceptive use.

## Results

Among the 3248 patients who were admitted to our breast health center, 30 patients (0.9%) had a diagnosis of GM and were identified as applicable to our study.

All the patients were female, with a median age of 33, ranging from 27 to 66. Of the 30 patients, 11 were overweight and 7 were obese at the time of diagnosis (mean BMI: 26.7). 27 (90%) of the patients were premenopausal, while 3 (10%) of them were menopausal. 5 (17%) of the patients had irregular menses at the time of diagnosis. All of the patients had pregnancy history (completed and incompleting pregnancies in total) and 27 (90%) of them were multipar when the GM diagnosis was made. 3 (10%) of them had only 1 pregnancy, 11 (37%) of them had 2 pregnancies, 7 (23%) of them had 3, 2 (7%) of them had 5, and 2 (7%) of them had 6 pregnancies. Age at first pregnancy ranged from 18 to 35, and the average time from the last pregnancy until the GM diagnosis was 8 years (ranging from 6 months to 38 years). While only 1 of the patients had a lactation history during the last year, all our patients had a lactation history during their life. 8 (27%) of the cases had comorbidities, including Hashimoto Thyroiditis (n=1), Hypertension (n=6), Diabetes Mellitus type 1 (=1), Diabetes Mellitus type 2 (n=4), Major Depression (n=1). Only 15 of the patients had prior BCG vaccination history, 9 of the cases did not know their vaccination status, and 6 of them stated they did not have BCG vaccination. Just 2 (7%) of the cases reported significant family history; one of the patient's mother had Breast cancer at age 46, and one of them had an aunt with GM diagnosis at age 34. Another remarkable result was that 3 (10%) of the patients had a prior trauma history to the breast, and one had it recently (8 months before the GM diagnosis). None of our patients had a smoking history. One of the patients had aesthetic breast surgery 3 years ago. Our patients' time from the first symptom to diagnosis was very long; the earliest was 3 days, but the latest was 3 years (mean time: 5 months).

While the majority (n=23, 76%) of the patients presented with a breast lump, only 1 (3%) of the patient's only symptom was breast lump. 11 (37%) of the patients presented with pain, 3 (10%) patients had nipple discharge, 11 (37%) of the patients had hyperemia on the lesion site, and 2 (7%) of the patients had nipple retraction. Only 1 (3%) of our patients had a high body temperature. 21 (30%) of the lesions were in the left breast, and only 6 (20%) of them were in the right, while 3 (10%) of the patients had bilateral multiple lesions (Fig. 1). None of our patients were using oral contra-



ceptives at the time of diagnosis.

6 (20%) of the lesions were localized centrally/retro-areolar, 6 (20%) of them were localized in the upper-inner quadrant, 7 (23%) of the lesions were localized in the upper-outer quadrant, 6 (20%) of them were in the lower-outer quadrant, 1 (3%) of the lesions were in the lower-inner quadrant. In comparison, 3 (10%) of the lesions were diffusely distributed in multiple quadrants.

The first imaging method was ultrasound in 24 (80%) patients and mammography in 6 (20%). Ultrasound imaging showed heterogenic lesions in 14 of the patients and hypoechoic mass in 10 of the patients. Mammography findings showed an irregular lesion in 5 (17%) cases and a solid mass in 1 (3%) of the patients. In addition to ultrasound and mammography, 5 (17%) patients underwent magnetic resonance imaging for high malignancy suspicion (3 – USM, 2- Mammography) because of indetermination, and all 5 cases illustrated irregular lesions. Of the lesions, 16 (53%) showed high suspicion with a Bi-Rads score  $\geq 4$ , and 14 (47%) showed low suspicion with a Bi-Rads score  $\leq 4$ . Axillary lymphadenopathy was detected in 16 (53%) of the lesions. The average size of the masses was 5 cm, ranging from 0.6cm to 15 cm.

All patients accepted the biopsy except one who declined it because of fear. Of the 29 patients, 22 (76%) had undergone a core biopsy, while 6 (20%) of them had undergone Fine Needle Aspiration (FNA) biopsy, and in only 1 case excision biopsy was needed for definitive diagnosis. Pathology reported granulomatous mastitis in 26 (87%) patients,

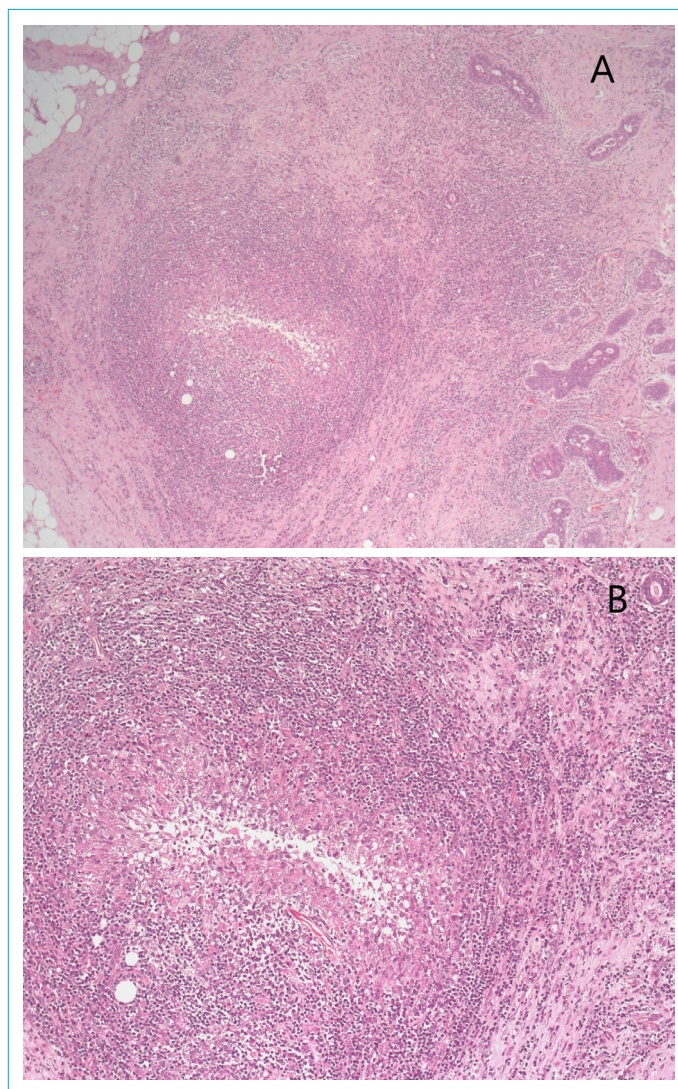


**Figure 1.** Granulomatous Mastitis in right breast upper medial quadrant.

Tuberculosis in 2, and malignancy in 1 case (Fig. 2).

18 (60%) of patients received only medical treatment, 11 (37%) patients received both surgery (excision) and medical treatment, and only 1 (3%) received surgery (excision) alone. 22 (83%) patients received only a prednisone regimen, 2 (7%) of them received prednisone + methotrexate, 3 (10%) of the patients received antibiotic therapy, and 2 (7%) of the cases received anti-tuberculosis treatment. In 6 of the cases, drainage of the lesion is required by the surgeon because of abscess formation. 5 of the cases underwent surgical excision of the lesion.

Recurrence occurred in 7 (23%) cases, with a mean period of 20 months ranging from 3 months to 5 years. None of the recurrences occurred in patients who underwent surgical excision.



**Figure 2 .** Sections show a lobulocentric mastitis with histiocytes, granulomas, neutrophils and lymphocytes. (a) 10x magnitude (b) 20x magnitude.

## Discussion

Granulomatous mastitis is an unusual disease of the breast. While there are several case reports and case series in the literature, it is the first paper from the Azerbaijan with a broad history of information.

Although it is commonly seen in women in reproductive ages, there are examples of male patients or women in menopausal ages.<sup>[12]</sup> The median of the ages of our patients was 33, ranging from 27 to 66, and 3 (10%) of them were menopausal, which is quite unusual for GM. Although the relationship of GM with parity and lactation is well-known, there are still reported cases in nulliparous women.<sup>[12]</sup> Our series supports this information as all of the cases had pregnancy history, with 90 percent of them being multiparous.

Even though idiopathic GM is the most common GM type, results from the paper of Ercan Kokrut et al. suggest that Tuberculosis should not be skipped, especially in developing countries, with reported 20% as a cause of GM.<sup>[5]</sup> 2 (7%) of our cases had tuberculosis mastitis and received anti-tuberculosis treatment for 9 months, but interestingly only half of the patients reported prior BCG vaccination and 9 cases did not remember their vaccination status. The etiology of Idiopathic GM is still unknown, but there are several usual suspects, and some of them are high prolactin levels, oral contraceptives, and prior blunt trauma history.<sup>[12]</sup> Neither of any patients had hyperprolactinemia, nor any of them were using oral contraceptives. However, 3 of our patients reported prior blunt trauma to the breast. Another interesting finding that needs to be mentioned is that none of our patients had a smoking history. Altintoprak et al. suggest that genetics can be predisposing to idiopathic GM.<sup>[13]</sup> Of the patients, 2 of them reported idiopathic GM diagnosis in their family.

The most common presentation was breast lump, as most studies also report the same result, 3 of our patients had nipple discharge, and one of them reported bloody discharge, which was very concerning for the patient.<sup>[5,14,15]</sup>

Axillary lymphadenopathy is another concerning finding in GM, which may arouse high anxiety and suspicion in patients and physicians. Axillary lymphadenopathy was detected in 53% percent of our patients. GM can also present extramammary symptoms such as arthritis, episcleritis, and erythema nodosum, resembling systematic diseases.<sup>[16-19]</sup>

Since it is a rare condition with high similarity with inflammatory breast cancer, sometimes diagnosing the cases can be tricky for physicians.<sup>[1,12]</sup> Reported cases show that nearly 50% of the patients were misdiagnosed with breast cancer.<sup>[19-21]</sup> In our series, 12 (40%) patients were misdiagnosed with breast cancer.

A valuable paper by Yaghan RJ et al. emphasizes that a multidisciplinary team is crucial in the diagnosis and treatment of GM to be able to distinguish it from breast cancer.<sup>[22]</sup>

In the absence of pathognomonic definitive imaging signs, the US is the most commonly used imaging method to detect GM as it illustrates heterogeneous, hypoechogenic lesions that are difficult to distinguish from cancer.<sup>[14]</sup> In 3 of our cases, MRI was used in addition to the US for high suspicion of breast cancer. Mammography findings are usually normal or show an irregular mass in GM. 2 of 6 patients whose first imaging was mammography had undergone MRI because of high suspicion of physicians.

The biopsy is done for almost every patient except one who rejected the biopsy because of fear. Core Biopsy was the most selected method generally and in our series. Although FNA is not recommended by some authors, all of our cases that underwent FNA were diagnosed with GM without needing another sample.<sup>[5,23]</sup>

There has been a lack of consensus on the management of GM until 2021, when Yuan QQ et al. developed a precious and essential international consensus regarding the management of GM.<sup>[12]</sup> Antibiotics can be required based on bacterial and drug susceptibility tests. Corticosteroids are remaining as the first-line treatment in cases without bacterial cause. In addition to the curative effect, they can be used prior to surgery to decrease the extent of excision. Since oral contraceptives have a broad range of side effects, several papers emphasize the feasibility and effectiveness of intralesional and topical use of corticosteroids, especially in patients with skin lesions such as fistula or ulcers.<sup>[24-28]</sup>

Methotrexate can be used if the disease is not responding to corticosteroids or the patient is not tolerant to long-term corticosteroid treatment.<sup>[12]</sup>

Surgery remains as the most effective method in complex lesions. Indications for surgery are reported as intolerance to medical treatment, recurrence despite the medical treatment, extensively distributed lesions, lesions complicated with abscess, sinus or fistula formation, and extramammary symptoms such as erythema nodosum.<sup>[12]</sup> In our patients, glucocorticoid use alone was the most commonly used method. At the same time, 11 of the patients who used glucocorticoids required surgical intervention, including abscess drainage. Interestingly, no recurrence occurred in the patients after surgical excision. This finding supports the finding by Lei X et al., which shows a 94.5% cure rate after surgery.<sup>[24]</sup>

To conclude, Granulomatous mastitis is a tricky condition that can cause high anxiety in physicians as high as in patients. Idiopathic GM is the most common type, but evaluation of other reasons, such as tuberculosis mastitis, must



be on the checklist. With the latest consensus regarding its management, outcomes are expected to get better. More research regarding the outcome of different treatment modalities will give a straightforward approach for physicians.

### Disclosures

**Ethics Committee Approval:** The protocol of the study accepted by the ethics committee of the Liv Bona Dea Hospital on 12.07.2023.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Altay Aliyev, Arturan Ibrahimli, Gunel Rahimova, Tarana Huseynli, Elgun Samadov, Ceyhun Isayev confirm equal sole responsibility for the study conception and design, data collection, analysis and interpretation of results, and manuscript preparation.

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