

Granulomatous Mastitis: Incidence and Experience in a Mexican Institute

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How to cite this paper: Topete, A., Carrasco, O., Barrera, G., Garzón, J., Gutierrez, E., Márquez, C., Dávila, R., Cuervo, M. and Rivera, M.I. (2019) Granulomatous Mastitis: Incidence and Experience in a Mexican Institute. *Journal of Biosciences and Medicines*, 7, 24-32.

<https://doi.org/10.4236/jbm.2019.76003>

Received: April 25, 2019

Accepted: June 1, 2019

Published: June 4, 2019

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Abstract

The significance of this work is that chronic granulomatous disease can mimic two common breast diseases; breast cancer and breast abscess; so it is mandatory that the diagnosis is made in order to avoid mistaken carcinoma diagnosis. On the other hand, the current treatment of this particular disease still remains controversial. **Objectives:** The aim of this study is to expose and describe the chronicity and the impact in a patient's quality of life with Granulomatous Mastitis diagnosis. We describe the evolution of the disease and the treatment of the disease in a Mexican Institution. **Material and methods:** In a descriptive retrospective study we identified 9 patients with idiopathic granulomatous mastitis (IMG), all of them were diagnosed with histopathological findings. **Results:** In a period of time between January 2005 and December 2017, we included a total of 9 female patients. All of them have had histopathological findings consistent with granulomatous mastitis. The age range was 25 - 83 years old (mean 50.8 yrs). In 4 patients (44.4%) had the right side affected, three patients (33.3%) had the left side affected and 2 patients (22.2%) had a bilateral presentation. In 3 patients (33.3%) we observed more than one affected quadrant and 4 patients (44.4%) had a diffuse presentation on image. The most common symptom was breast pain in 9 patients (100%) and the most common sign was the presence of a nodule, 8 patients (88.8%). We observed erythema in 7 cases (77.7%) followed by abscess, edema and pus secretion in 6 patients (66.6%). The most frequent treatment was the use of a combination of NAIDs and antibiotic in 8 patients (88.8%). Six patients were incised with scalp and drained. Six patients underwent mastectomy.

Keywords

Idiopathic Granulomatous Mastitis, Incidence and Experience, Descriptive

Retrospective Study

1. Introduction

Idiopathic granulomatous mastitis (MGI) is a chronic inflammatory disease of the breast, benign, noninfectious, uncommon and difficult to diagnose. It was described in 1972 by Kessler and Wolloch [1]. It is characterized by chronic granulomatous inflammation of the lobes without necrosis and its clinical signs and symptoms can be so variable ranging from pain, fistula and secretion to the presence of a mass or tumor of the breast.

1.1. Mechanisms and Pathophysiology

Granulomatous mastitis is an idiopathic condition for which it has been proposed several mechanisms including autoimmune [2], infectious [3] processes and local reactions to chemical secretions [4]. However, the favorable responses to steroids in studies such as that of Ogura *et al.* [5] and Kazuhisa *et al.* [6] where MGI is classified as related and not related to Immunoglobulin 4 (IgG4), the consistent finding of negative cultures [7], as well as their association with other rheumatic diseases support an autoimmune etiology.

1.2. Clinical Presentation

MGI can mimic two very common breast diseases, breast cancer and breast abscess [8]. Most of the patients are of reproductive age, have a recent history of pregnancy and breastfeeding in the last 5 years [8]. However, cases have been reported in patients as young as 11 years [9] [10] to 80 years of age [11] [12].

It presents as a palpable unilateral mass, accompanied by abscesses that after culturing them in media for bacteria, mycobacteria and fungi are negative (aseptic cultures), although it constitutes a chronic inflammation of the gland, it can present local or systemic erythema (**Figure 1**, **Figure 2**), changes in the skin with retraction of the nipple or fixed to the pectoral muscle. MGI can occur in any quadrant of the breast, except in the subareolar region [8].

1.3. Diagnosis

The diagnosis of this disease is reached after ruling out other diseases. Multiple biopsy techniques are used in the diagnosis of MGI. Fine needle aspiration biopsy is the least invasive method [13] [14], but it can lead to confusing results that often require confirmation by open biopsy. Open excisional biopsy is used with a good success rate, considering it the safest method to rule out malignancy [13]. The histological characteristic of the disease describes the presence of granulomas surrounded by stroma with giant cells, lymphocytes, plasma cells and neutrophils (**Figure 3**). However, histological features are also a challenge. In a study published by Lacambra *et al.* [7] comparing the histological differences

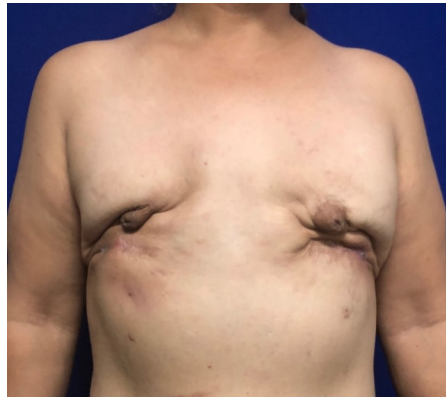


Figure 1. Severe bilateral case of recurrent Idiopathic Granulomatous Mastitis in a 33 years old female unsuccessfully treated with multiple pharmacological therapies and surgical resections along 10 years of evolution.



Figure 2. Image taken from: Binesh F. Idiopathic Granulomatous Mastitis, a Clinicopathological Review of 22 Cases. *Journal of Clinical & Experimental Pathology*. 2014; 04(02).

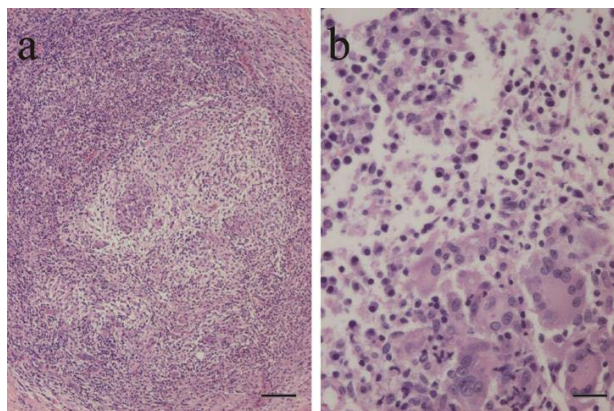


Figure 3. Histological findings showing granulomatous inflammation of the lobes without caseous necrosis and the presence of multinucleated giant cells and plasma cells. (Image taken from Kazuhisa Akahane *et al.* (2013). Therapeutic strategy for granulomatous lobular mastitis: a clinicopathological study of 12 patients. *Nagoya J. Med. Sci.* 75:193-200.)

between Idiopathic Granulomatous Mastitis (33 cases) and Tuberculous Mastitis (29 cases), the group with tuberculous mastitis showed significantly more fibrosis, eosinophils and necrosis, while the MGI group showed significantly more plasma cells, so the diagnosis, although confirmed histologically, required other studies that rule out infectious etiology or foreign body reaction.

1.4. Treatment

There is no unification of criteria regarding treatment. Extensive surgical resections have been proposed, including total or partial mastectomy, curettage, surgical drainage, punctures, mechanical washes, as well as conservative treatments such as the use of anti-inflammatories, antibiotics and steroids combined with immunosuppressants.

Treatment with steroids was first proposed by Dehetrogh *et al.* [8] [15] and its efficacy in the treatment of MGI has been reported in several studies [5] [6] [8]. The steroid dose should start at 1 mg/kg/day and decrease gradually according to the clinical response [16]. Some patients may present hyperglycemia as an effect of high doses of prednisone [8], so the use of steroid-sparing agents such as methotrexate or azathioprine provides options that may facilitate the decrease of steroids [8] [17] [18]. Patients with a mass or pseudotumor equivalent to 20% - 50% of the size of the breast that shows failure in medical treatment or intolerance to steroids are candidates for treatment with therapeutic mastectomy techniques [19]. Frequently, surgical management of MGI leads to disfigurement of the breast. However, the reconstruction of this must be a secondary objective, since the recurrence of the disease has occurred up to 24 months after the remission of symptoms. In a study conducted by Binesh *et al.*, the findings demonstrated that surgical treatment is not always effective and is associated with a high recurrence rate [13] ranging from 5% to 50% [8] [12] [20].

2. Materials and Methods

We performed a descriptive retrospective study of the records from a Pemex Hospital in Mexico city for patients diagnosed with Idiopathic Granulomatous Mastitis histopathologically over a twelve year period between January 2005 and December 2017. During this period 9 women were diagnosed with IGM and treated. All of the women underwent a clinical breast examination to identify palpable lumps, skin thickening or axillary lymphadenopathy and breast pain. Definitive diagnosis was obtained by biopsy or surgical excision. The parameters assessed included age of patient, systemic and local symptoms and histological findings of inflammatory cells, granulomas, necrosis, multinucleated giant cells, fibrosis and calcifications. We included data and correlations in clinical presentation, comorbidities and treatment of patients with IGM in this hospital. We performed a descriptive analysis using central tendency measures.

3. Results

In a period of time between January 2005 and December 2017 (12 years), we in-

cluded a total of 9 female patients. All of them have had histopathological findings consistent with granulomatous mastitis.

These patients were studied in a retrospective way after we analyzed their clinical presentation, evolution, histology and management of their disease. The age range was 25 - 83 years old (mean 50.8 yrs). Just one patient (11.1%) has had a baby and recent lactation history. And another patient (11.1%) had taken oral contraceptives. In 4 patients (44.4%) had the right side affected, three patients (33.3%) had the left side affected and 2 patients (22.2%) have had a bilateral presentation. In 3 patients (33.3%) we observed more than one affected quadrant and 4 patients (44.4%) had a diffuse presentation on image, **Table 1**.

The most common symptom was breast pain in 9 patients (100%) and the most common sign was the presence of a nodule, 8 patients (88.8%). We observed erythema in 7 cases (77.7%) followed by abscess, edema and pus secretion in 6 patients (66.6%). The less frequent sign was nipple retraction in 2 patients (22.2%) and axillary adenopathies in 3 patients (33.3%).

The most frequent treatment was the use of a combination of NAIDs and antibiotic in 8 patients (88.8%). We only treated one patient combining NSAIS and immunosuppressant. And another one was treated using antituberculosis drugs without confirming mycobacteria in culture. Regarding the surgical management of this disease, 6 patients were incised with scalp and drained. 6 patients underwent mastectomy, 2 of them had bilateral mastectomy and another 2 were treated by quadrantectomy.

In the follow-up the mean of office consultations were 51.3 with mean of 6.2 surgical interventions in between. The mean of hospitalizations was 5.3 and the mean of hospital stay was 42.3 days. One particular patient accumulated a total of 270 days of stay, which was the longest period of time reported in all cases. Five patients had no signs and symptoms after a 5 year period of treatment.

4. Discussion

Idiopathic Granulomatous Mastitis (IGM) is characterized by the presence of granulomatous necrotizing lobulitis of unknown etiology [21] [22]. We can find

Table 1. Characteristics of patients with idiopathic granulomatous mastitis.

PatientsNo.	1	2	3	4	5	6	7	8	9
Age	43	83	74	65	33	70	25	36	29
Parity	-	-	-	-	-	-	-	+	-
Breast fed	-	-	-	-	-	-	-	+	-
Contraceptives	-	-	-	-	-	-	+	-	-
Affected breast	R	L	R	L	B	R	Di	L	B
Affected quadrant	1	1	1	1	>1	1	>1	1	>1
Distribution	Lo	Lo	Lo	Lo	Di	Di	Di	Lo	Di

-: Negative; +: Positive; R: Right; L: Left; Lo: Local; Di: Difuse.

this entity in 24% of all the breast inflammatory pathologies [23]. Until 1999 we can identify 120 reported cases [24] in international literature since the complete description of the illness performed by Kessler y Wollock in 1972 [1]. Recently a study performed in 22 breast center in Turkey was published [25], that included 720 patients diagnosed with IGM treated between January 2011 and March 2016 and supports greatest knowledge and suspicion of this disease.

The mean age of the patients studied in our work presented a mean age of presentation, of 50.8 years old. whilst international literature report a mean age of presentation under 50 years [21], with a mean age of 36.5 years old [22] [26]. It's also reported that up to 11.1% of the patients with this disease have an association with contraceptive use and breastfeeding, a different study reported that one third of the patients with this disease presented a history of oral contraceptives use [21], however, the greatest series of cases [25] reported no association between the disease and the use of contraceptives or breastfeeding.

In our study we observed breast pain (mastalgia) in 100% and unilateral nodule present in 88.8% of the patients as the most frequent symptoms of the disease, similar to international literature that reports the presence of unilateral mass in 57% and mastalgia in 33% [22] [25] [26]. Axillary lymphadenopathies and nipple retraction were the less frequent signs observed as many other studies has reported [22] [26], however, some of the complications that may be developed include abscesses, fistula and chronic discharge of pus or other secretion [21] [27].

We found bilateral affection in 22% of this group of patients, 44% had right breast presentation and 33% in left side. We performed a comparison with international reports where they describe a 3% - 5% bilateral affection and 38% and 58% right and left affection respectively [25] [26].

During the patients files review we observed the clinical approach of the disease including a number of lab and cabinet studies such as FNA-biopsies ultrasound guided, ultrasound images, mammography, CT scan and MRI. These last two had reported malignancy findings most frequently. Some authors suggest to perform sequenced studies using FNA-biopsy or excisional biopsy in a prior way until undergoing mastectomy in order to avoid mistaken diagnosis and rule out carcinoma [21]. Negative cultures using different types of stains, Polymerase Chain Reaction (PCR), anti rheumatoid antibodies also were made to supports idiopathic nature of granulomatous mastitis.

We suspected IGM ruling out differential diagnosis and the presence of histopathological findings in every specimen analyzed. These findings included granulomatous inflammation with diffuse obliteration of lobar architecture, likewise inflammatory infiltrate with leucocytes, polymorphonuclear cells, plasmatic cells, epithelioid cells and Langhans giant cells in the granulomas. We observed that the term granulomatous mastitis is overused by pathological findings compatible with inflammatory response [22]. In fact 31 patients have been diagnosed with granulomatous mastitis; however, only 9 patients were compatible with this disease over the clinical presentation and following, clinical criteria suggesting that

we need to overlook the whole presentation of the disease in order to make an accurate diagnosis.

Antibiotics are the most commonly used agents in the treatment of IMG as well as systemic steroids [25]. Authors recommend to suspend the use of antibiotics once the diagnosis is confirmed since is not about an infectious disease. Prednisone 0.8 mg/kg/day divided in two doses is the initial dose recommended [28].

Other authors reported oral steroids as treatment of choice (39%) followed by antibiotics in 37%, a combination of these two in 13% and methotrexate intake in 1% of the patients [25]. In our institution we used the combined form of treatment consisting in oral NSAIDs and antibiotics in 88.8%, steroid and immunosuppressant agents in 11.1% and anti-tuberculous agents in 11.1% of the patients.

The results involving surgical treatment shows better outcomes when compared versus steroid therapy with decrease recovery time and lower recurrence rates. This is the reason why some authors recommend the steroid treatment option for recurrent disease only. Performing drainage in the presence of abscess has the highest recurrence reported by 50% of the patients [28], so they suggest performing initial extended excision rather than drainage.

Carrying out this study we realized that we have had higher rates of surgical management of the disease in our Institution than the rates reported by international literature. We observed that 66% of the patients underwent mastectomy, 22% extended excision and only 12% were treated by drainage. None of our patients received only medical management for their disease. In recent studies medical treatment is used in 36% as a single therapy. The surgical intervention was reported only by 8%. The combination of these two in 56% being the extended excision the most commonly surgical treatment used in 69%, followed by drainage in 29% and mastectomy in 1.3% [21].

The recurrence rate is described to be up to 38% of the patients. So they recommend follow up after surgical treatment or indicate corticosteroids therapy [21].

5. Conclusion

Granulomatous Mastitis is a chronic benign disease with high recurrence rate and it is mandatory that the diagnosis is made in order to avoid mistaken carcinoma diagnosis. We need to correlate clinical evolution and histopathological findings in order to obtain an accurate diagnosis. The current treatment of this particular disease still remains controversial. We observed a different patient response in the current treatment options. However, we believe that the use of a combination of immunosuppressant and NSAIDs represents an open-door in our institution because of the strong information with sustaining evidence that supports efficacy and effectiveness of this treatment option. We also analyzed the days the patients were hospitalized and the number of surgical interventions

performed in every case.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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