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Assessment of Surgical management of idiopathic granulomatous mastitis

Abdullah Hamed Ibrahim[1]; M.D and Ahmed Gamal El-Din Osman[2]; M.D.

[1] Lecturer of General Surgery, Faculty of Medicine, Ain Shams University, Egypt
[2]Assistant Professor of General Surgery, Faculty of Medicine, Ain Shams University, Egypt
drabdallah333@gmail.com

Abstract: Context: Idiopathic granulomatous mastitis (IGLM) is a uncommon chronic non-specific inflammation of the breast that similar to cancer both mammographically and clinically. IGLM; in spite of its frequency is low, but it represent a high concern owing to misdiagnosis as carcinoma of the mammary gland, yet confirming a suitable control is critical. Objective: The aim of this study is to assess the surgical management in patient with idiopathic granulomatous mastitis. Methodology: The work is a cohort prospective study performed on patients presenting to Ain-Shams University hospital's breast clinic diagnosed with idiopathic granulomatous mastitis and underwent surgical intervention (excisional biopsy) from 2015 to 2018. 40 patients identified with histopathological diagnosis of IGLM. Results: In our study, 26 patients out of 40 patients (65%) had a history of pregnancy in the last 5 years prior to diagnosis of IGLM with 24 patients (60%) having a history of previous lactation. Surgical management was employed after the control of the process using corticosteroids (Prednisolone). 24 patients presented with mass, 4 with pain and overlying skin changes (sinuses) and 12 patients with abscess. Conclusion: Surgical excision is a suitable option after the control of the inflammatory process using corticosteroids.
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Keywords: Surgical Management, Idiopathic granulomatous mastitis

1. Introduction:

Idiopathic granulomatous mastitis is called also idiopathic granulomatous lobular mastitis (IGLM)) is a scarce benign breast illness. Worldwide, the incidence of Granulomatous Mastitis is commonly lower than 1% between women suffering from breast difficulties though, records differ significantly according to the country and ethnic population, where in the United States the frequency of granulomatous mastitis (GM) was lower than1% between women who endured biopsy for diagnosis of breast diseases. The percent of prevalence was lower in the UK, it recorded 0.98% of patients admitted to the breast unit [(1)].

IGLM is a infrequent chronic non-specific inflammation of the breast that imitates tumor during clinical examination or during mammography of the breast [(2).]

IGLM; in spite of its frequency is minimal, is paying a great attention owing to difficulty in diagnosis and miss diagnosed with carcinoma of the breast yet confirming a suitable control is critical. IGLM is a scarce, benign chronic inflammatory disorder of the breast [(3)].

The causes of IGLM are remain unclear. Many postulations by authors which may be the etiology of disease such as a chemical reaction associated with oral contraceptive pills, an infection, the autoimmune disease, or even lactation. Macrophage and lymphocyte migration arises as a sequel of ductalepithelium deterioration, and a localized immune response is created [(4)].

The most common clinical symptoms is the presence of a unilateral, distinct breast swelling. Accurate diagnosis of IGLM can be performed by histopathological examination which considered a gold standard technique for diagnosis. Histologically, the lesion is characterized by the existence of multinucleated giant and epitheloid cells, granulomas restricted to the mammary lobules with micro-abscesses without clear causes [(5)].

Trials for treatment of IGLM is giving contradict results, but many investigators reported that complete surgical excision of the lesion with or without administration corticosteroids drugs has been proposed.

Aim of the Work:

The aim of this study is to assess the surgical management in patient with idiopathic granulomatous mastitis.

2. Patients and Methods:

Type of the study:

This is a prospective cohort study conducted on patients presenting to Ain- Shams University

hospital's breast clinic diagnosed with idiopathic granulomatous mastitis and underwent surgical intervention (excisional biopsy) from 2015 to2018.

Inclusion Criteria:

- Age >18y
- All female patient diagnosed with idiopathic granulomatousmastitis

Exclusion criteria:

1) Patient with specific infection granulomatous mastitis such as TB.
2) Patient with specific granulomatous mastitis such as sarcoidosis, Wegener's granulomatosis.
3) Patients who diagnosed finally with breast cancer.

Methods

All patients in the study were subjected to Triple assessment:

1- Clinical assessment:

- History: including age, history of pregnancy and lactation, history of TB or autoimmune disease, oral contraceptive use, smoking, and family history of breast cancer.
- Examination: General assessment of the possible clinical finding which include mass, abscess, sinus and skin changes including its onset and duration.

2- Radiological assessment:

Ultrasound was done for all patients, sonomamography was done for patient >30 years old. Dynamic breast MRI may be used in some cases, if the previous two were unconclusive.

3- Tissue biopsy:

True cut u/s guided biopsy was done for all patients with mass. Incisional biopsy was done for Patient underwent abscess drainage.

4- Culture and sensitivity:

It was used for patient with sinus or abscess without definite mass lesion. All patients were submitted to history taking including age, history of pregnancy and lactation, history of TB, oral contraceptive use and history of cancer breast.

5−PCR:

All our patients diagnosed with IGLM, confirmed by histopathology finding non caseating granulomatous mastitis, PCR was done for all patients to exclude TB.

Clinical picture including symptoms and duration. Sonomammography was done for all patients. (MRI) was used in 2 cases, either due to equivocal sonomammographic results or marked increase of breast density.

The general plan of management was to control the disease using corticosteroid, prior to surgical intervention.

Statistical Analysis:

The data were collected, tabulated and statistically analyzed. Description of quantitative variable will be done as mean and standard deviation, and qualitative data as frequency. Chi square test was used to compare the groups as regard qualitative variable. Student t-test was used to compare two groups as regard quantitative variable in parametric data. The results were considered significant (S) with $P < 0.05$ & highly significant (HS) with $P<0.01$. $P\geq0.05$willbe considered non-significant (NS). Analysis of data were done using IBM SPSS software (statistical program for social science version 21.

3. Results

Clinical characteristics:

40 patients identified with histopathological diagnosis of IGLM. Table 1 and 2 shows the clinical characteristics and presentation of those patients.

Table (1): Clinical characteristics of the study patients

		Total no. = 40
Age	Mean ± SD	36.75 ± 5.75
	Range	28 – 47
History of lactation		24 (60.0%)
History of TB		ZERO (0.0)
History of Breast cancer		4 (10.0%)
History of Pregnancy in last 5 years		26 (65.0%)
History of OCP		16 (40.0%)

Table (2): Clinical presentation of the study patients

Clinical presentation	**No. (%)**
Mass	24 (60.0%)
Abscess	12 (30.0%)
Skin changes (erythema, sinuses)	4 (10.0%)

The ages of participating affected women was ranged 28–47year with an average of 36 years, 24 patients (60%) has a history of previous lactation. None of the patients have a history of TB and four patients have a history of cancer breast on the contralateral side which was removed conservatively. 26 patients were pregnant during the last 5 years prior to diagnosis of IGL Mandonly 16 patients have a history of OCP use. 24 patients presented by a unilateral breast mass,12 patients presented by a unilateral breast abscess and 4 patients presented by skin changes including multiple sinuses and erythema.

Radiologic Assessment

Sonographic examination was done for all patients and showed ill-defined unilateral hypoechoic lesion associated with interstitial edema with

echogenic fat lobules in 28 patients, fluid collection in 12 patients. Mammographic examination was done for 4 patients revealed ill-defined mass with indistinct margins. MRI was performed in 2 patients either due to equivocal sonomammographic results or marked increase of breast density.

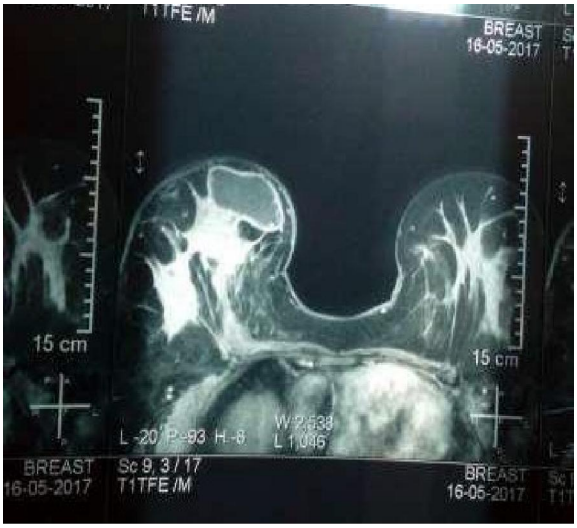

Figure (1): MRI showing Rt granulomatous breast mass

Suspicious of malignancy was noted in 18 patients. CXR was done for all patients to exclude pulmonary findings consistent with sarcoidosis.

Table (3): Radiological assessment of patients with IGLM

Radiological investigations	No. (%)
Ultrasound	40 (100.0%)
Mammogram	4 (10.0%)
MRI	2 (5.0%)

Histopathologic workup

Ultra-sonographic guided core biopsy was performed for 36 patients including all patients who presented with a breast mass (24), and for 12 patients who presented clinically with abscess.

Histopathologic findings included non caseating granulomatous inflammation characterized by scattered granulomas composed of epithelioid histiocytes and giant cells accompanied by lymphocytes, neutrophils, plasma cells, and eosinophil.

All slides or specimens were stained with Acid-fast bacilli (AFB) stain to exclude TB infection, all samples from all patients were negative for TB infection. Gram stain and cultures from pus in patients presented with abscess was negative.

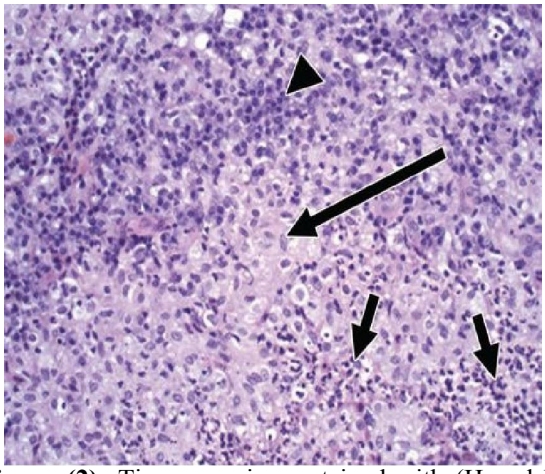

Figure (2): Tissue specimen stained with (H and E, ×200) of affected breast showing granulomatous inflammation (lymphocytes [*arrow head*] and epithelioid histiocytes [*long arrow*]) with a admixed neutrophils (*short arrows*).

Table (4): Workup

Workup		No. (%)
Core biopsy. (Histopathologic workup)		36 (=90.0%)
Culture and sensitivity	Negative Positive	12 (30.0%) 0 (0.0%)

Treatment modalities and recurrence rate

The general plan was to control the inflammatory disease process, prior to surgical intervention. Different treatment modalities were applied according to clinical presentation. 24 patients presented with mass, 4 with pain and overlying skin changes and 12 patients with abscess.

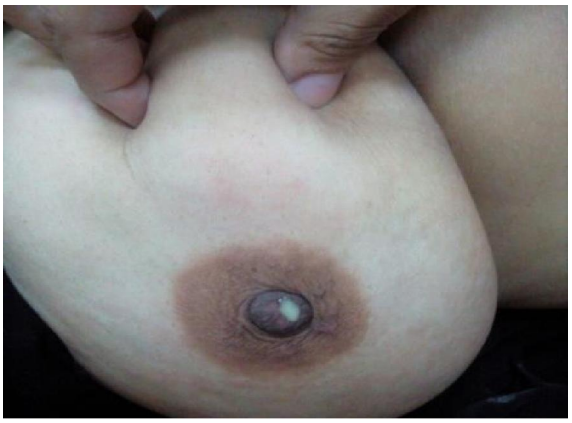

Figure (3): Pt. presented with mass.

For those patients who presented with a breast mass, and proved to be IGLM by histopathology, a course of corticosteroids was administered; as follows:

Prednisolone (Solupred®) 40-60 mg, given

for 3weeks.

Followed by 30-50 mg prednisolone for another 3weeks.

Then followed by 20-30 mg prednisolone for another 3weeks.

Then 10-20 mg prednisolone for another 3weeks.

And finally tapering over 10 days till stopping of the corticosteroid.

After this course we check for the improvement of the local inflammatory process clinically (shrinking of the mass and resolution of the inflammation). This resulted in the complete resolution of 6 patients, and shrinking of the mass in the other 18 patients, leaving a residual mass. here surgical intervention was used in the form of excisions biopsy for the residual mass. Post operatively healing was satisfactory and good cosmetic results were obtained in all of the 18 patients.

For 12 patients presented with abscess, drainage and tru-cut biopsy were done for all patients.

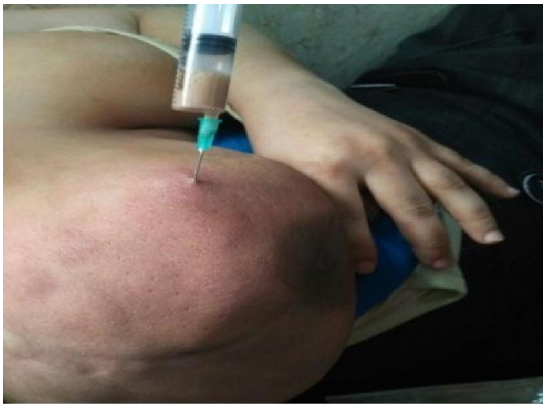

Figure (4): Pt. presented with abcess and its aspiration.

After that the same corticosteroid course (used for the mass) was used. This resulted in:

Complete resolution of 4cases.

Persistence of a remnant mass in 6patients.

Conversionoftheabscesstoadischargingsinusin 2patients, who repeated the corticosteroid course once again, giving risetoresolutionof1case and the persistence of aremnant mass in the other1.

Surgical intervention in the form of excisional biopsy was used for all cases with remnant mass.

Fourcasespresentedwithpainandskinchangesinthe formofmultiplesinusesanderythema, patients were treated short term antibiotics, which didn't lead to any improvement. Corticosteroid course was then started resulting in:

Complete resolution of 1case.

Persistence of a remnant mass in the other3.

Again surgical intervention as excisional biopsy was done for the patients with remnant mass.

So 28 patients were managed surgically after corticosteroid course, with good cosmetic outcome, and no encountered recurrences after 1 year of follow up.

4. Discussion

There is no ideal definitive treatment strategy for IGM. Oral contraceptives, surgery, antibiotics and immunosuppressive treatment are the preferred treatments for the IGM. The failure of the treatment is the recurrence of IGM and the excision of breast tissue ensures negative margins for IGM with low recurrence rates. However, the surgical treatment has unfavorable cosmetic results. On the other hand, some cases can be easily treated by oral corticosteroids [(7)].

In our study, we evaluated the outcome of the surgical management of IGLM and management of recurrent cases.

In our study, Mean age of our patients were of 36.75 ± 5.75 years, ranging between: 28 – 47 years which was Similar to **Donn *et al.*** [(2)] who reported that in women of reproductive age (25 to 36 years old) only 3 cases were diagnosed as idiopathic granulomatous mastitis and to Erkan Yilmaz et al., who reported 12 patients with IGLM and their average age was 37years (28 to 46 years) at onset of diagnosis.

Also **Mizrakli *et al.*** [(8)]**.** reported that 49 patients with IGLM their average age of the patients was 34.3 ± 4.37 years.

On the other side, **Lai *et al*** [(9)] carried out a study on nine patients, The age of women was ranged from 32–83 years (average 45.7 years) which is older than the fore mentioned studies and our study, most of studies including ours reflect a relation between age and occurrence of IGLM, as most of patients who presented with IGLM were of their reproductive ages.

In our study,26 patients out of 40 patients (65%) had a history of pregnancy in the last 5 years prior to diagnosis of IGLM with 24 patients (60%) having a history of previous lactation.

This was contrast to **Bani-Hani *et al.*** [(10)]**,** who done an investigation on 24 affected women, and showed that only 16%(4/24) of patients were pregnant, 4 women through 6 months had a history of birth and lactating and merely 2 women didn't pregnant**.**

Similar to our work, **Baslaim *et al.*** [(11)] reported that all diseased women had a history of breast-feeding and gestation, while, 2patients were breast-feeding, and only one women was pregnant. In addition, **Gurleyik *et al.*** [(7)] concluded in his study that 4/19 and 15/19 of IGLM women had a history of active breast-feeding, and breast-feeding, respectively. Also, **Oran *et al.*** [(12)] showed that 3/46 of IGLM patients were nulliparous. Moreover, some researchers found that all 11 cases had a history of birth and lactation within the past 5yearswith the exception of

one male case [13].

This reveals that Lactation is important in the etiology of IGLM as maximum of women suffering from IGLM are of age of child-bearing and had breast feeding during previous 5 years from appearance of lesion in the breast. The scientists analyzing the obtained huge data and postulated that IGLM may be returned to elevation in the concentration of prolactin in the circulation, leading to filling of the acini and distention of milk ducts related with clotting of milk and obstruction of acini and ducts which caused local inflammation and vasodilatation and may be subjected for infection with microorganisms leading to rupture of lobule and initiation of a granulomatous reaction with lymphocytic infiltration.

In our study, only 16 patients (16/40; 40%) had a history of OCP use. This was similar to **Gurleyik *et al***. (7) study, they reported that 42.1%(8/19) had a history of administration of oral contraceptive drugs (OCS), whereas, **Oran *et al.*** [12] recorded 21.7% (10/46;) of IGLM patients had history of oral contraceptive pills use, whereas, Al-Khaffaf et al, reported a low percentage of women had receiving OCP (27.7%).

In contrast, some researchers reported a lower rate of IGLM women had OCP use, 8.3% **(Bani-Hani *et al.*** [10]; 11.1% (**Asoglu *et al.*** [14]and 0% **Baslaim *et al.*** [11].

In our study, 12 patients (30%) presented by a unilateral breast abscess and 4 patients (10%) presented by skin changes including multiple sinuses and erythema.

Sonographic examination was done for all patients and showed ill-defined unilateral hypoechoic lesion associated with interstitial edema with echogenic fat lobules in 28 patients, fluid collection in 12 patients who presented by a breast abscess. Mammographic examination was done for 4 patients revealed ill-defined mass with indistinct margins. MRI was performed in 2 patients either due to equivocal sonomammographic results or marked increase of breast density. Suspicious of malignancy was noted in 18 patients.

US features of IGLM have been described relatively frequently. Some authors found that multiplefoci, frequently contiguous, by mammography image it seemed tubular hypoechoic lesions which may be found a large hypoechoic swelling mass, which may be diagnosed as granulomatous mastitis. Whereas, **Memis *et al.*** [15] added that one of the most sonographic features of IGLM is the presence of tubular hypoechoic areas or irregular hypoechoic mass lesions connecting to the mass lesion.

Idiopathic granulomatous mastitis appear by using mammography imaging if the form of poorly-distinct mass to an asymmetric compactness without remarkable boundaries. This mass lesion generally not showing a micro calcifications or architectural deformation. In young aged women, the accuracy of mammography for detection of IGLM lesion is poor, unspecific and can misdiagnose the case owing to the dense nature of the breast at young ages. In contrast, a dense, speculated lesion leading to asymmetry increases anxiety for tumors. In such condition, by using ultrasonography it is easy to distinguish the benign from malignant lesions. So, idiopathic granulomatous mastitis by ultrasound appear as a hypoechoic heterogeneous lesion with internal hypoechoic tubular structures (either the clustered are, separate or contiguous). The contiguous tubular structures is reliable with irritated ducts.

Memis *et al.* [15] stated that IGM by mammography appear as an asymmetric density, but by ultrasonography it appear as a heterogeneous echo pattern with tubular hypoechoic structures, while MRI is non-specific for IGM diagnosis, except in patients who have no significant pathology on MMG or US MRI. It was used in 2 patients in our study.

Due to deficient in pathognomonic imaging result linked with granulomatous mastitis, the histopathological technique plays the major role to confirming the diagnosis of disease. The lesion appears histologically as a non- caseating granulomas with multinucleated giant cells surrounded by lymphocytes and plasma cells. Absence of caseation used to differentiate IGM from.

Tuberculous mastitis which is the main differential diagnosis in developing countries.

The differentiation between granulomatous mastitis and tuberculous mastitis histologically, the latter have high quantities of fibrosis, caseation necrosis, localized tissue destruction and eosinophils, where in cases of granulomatous mastitis, there are a predominance of plasma cells and may be necrosis. The key to differentiate IGM from sarcoidos is depending mainly on the clinical case history, where by making chest x- ray in patients suffering from systemic sarcoidosis, other systems of the body are involved in addition to the breast like skin, musculoskeletal, pulmonary, eye, central nervous system and lymphatic.

In the current work, we established that clinical and radiological result are inadequate for accurate diagnosis of IGLM as they are can be conflicted by other diseases in the breast, therefore both clinical signs and radiological examination not sufficient for diagnosis of IGLM and misdiagnosed with carcinoma. Tissue sample either from WLE or abscess wall stained with H & E, Gramand Zeil Nelsen stain. So, histopathological examination as a golden standard for confirmation of lesions in the breast as well as in other parts of the body is highly significant in distinguishing

such lesions from other granulomatous condition.

IGM disease is discovered at least from four decades ago, yet, there is no compromise concerning the modality of first-line therapy. Many treatment protocols have been tried (antimicrobials with continual drainage, immunosuppresive drugs, oral steroids and extensive surgical removal or mastectomy, in addition to administration of methotrexate, and continuous follow-up), and successful outcomes have been obtained for each of the above regimen of therapy, but which is considered the more suitable therapy is still debating, although the most repeatedly applied treatment used are the surgical approach with administration of systemic steroids [16].

In our study, patients were managed by using a primary course of corticosteroid followed by surgical intervention after control of the inflammatory process. This led to a better post-operative outcome. 24 patients presented with mass, 4withpainandoverlying skin changes and 12 patients with abscess.

In our study, there was no encounter of recurrence, after the above mentioned procedures, after 1 year of follow-up.

Lai et al. [9] reported that after follow up for 14.5 months of GLM patients, 50% showed spontaneous complete recovery and 50% remaind unchanged in the disease condition. Also, they added in another work that treatment with antibiotics only for 6 weeks, all women were recovered from the disease without reappearance at least after 15 month follow-up period.

In many studies, corticosteroids were administered with surgical excision of the lesion or with drainage, and the data regarding using of corticosteroids alone not recorded widely. Sakura et al., treated GLM patients only with corticosteroids or in case of infection with antimicrobial drugs. All women recovered completely from the disease post administration of steroid treatment except one women, who underwent surgical excision for feeling with pain, for 4 -10 months.

Administration of steroid orally, in addition to topical steroids for treatment of skin diseases gave a favorable results other. Therefore, in absences of infection or presence of abscesses treatment with steroids alone is efficient. Some investigators found that the treatment with either steroids or surgical excision was nearly equal (20% vs.16.7%, respectively) in their efficiency for treatment of GLM disease [12]. Some authors found that the efficiency of steroids for treatment of GLM disease patients was more superior than surgical excision regarding recurrence incidence (0% vs. 100% recurrence, respectively). They recommended steroid treatment as first choice of therapy in GLM disease patients (**Akahane *et al.*** [17].

Conclusion:

IGLM is chronic nonspecific inflammatory breast disease, rare in occurrence, affecting mainly young women of reproductive age with obscure etiology. The general clinical symptoms are painful, irregular mass which mimics carcinoma.

The clinical examination or radiological investigation are enough for accurate diagnosis of IGLM, but the histopathological method plays the important role in differentiating IGM from other granulomatous diseases and breast carcinoma. Treatment is controversial. The disease has self-limiting nature allowing rule for expectant management. Managing using corticosteroids prior to surgical excision, gives the best results.

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