MANAGEMENT OF IDIOPATHIC GRANULOMATOUS MASTITIS: DILEMMAS IN DIAGNOSE AND TREATMENT

Running Title: Dilemmas in granulomatous mastitis
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ABSTRACT

Background: Idiopathic granulomatous mastitis (IGM) is a rare inflammatory disease. Because it’s uncommon etiology and rareness, diagnose and treatment is still a challenge. Owing to wide spectrum of IGM it is difficult to standardize and optimize the treatment. The aim of this study was to report and describe the clinical signs, radiological findings, management, clinical course and the recurrence ratio of the patients which were treated due to IGM.

Material and Methods: With this retrospective review of 24 patients diagnosed IGM histopathologically between January 2006 and December 2011. Medical reports, ultrasonography (US) and mammography (MMG) findings, follow-up information and recurrence were obtained from records.

Results: Painful, firm and ill defined mass was the symptom of all patients. While parenchymal heterogeneity, abscess and mass were the findings of US, increased asymmetric density was the main finding of MMG. Total excision was performed in 15 (62.5 %) patients, incisional biopsy with abscess drainage was performed in 9 (37.5 %) patients. Median follow-up was 34.8 (range 10-66) months.

Conclusions: While the physical examination give rise to thought breast carcinoma, the appearance of parenchymal heterogeneity and abscess formation on US especially with enlarged axillary lymph nodes support the presence of an inflammatory process.

Keywords: breast, granulomatous, mastitis, diagnose, treatment
INTRODUCTION

IGM was first described by Kessler and Wolloch in 1972 (1). IGM is a rare inflammatory disease of the breast, but it is important because of two reasons. First clinical and radiological findings of IGM mimicks breast carcinoma and the differential diagnosis can only be confirmed histopathologically. Second, it is difficult to treat IGM especially if presented with fistula and abscess formation. Because of it’s unclear etiology and rareness, diagnosis and treatment is still a challenge (2). An optimal treatment has not been yet established, while medical therapy, total excision and abscess drainage are currently the favored treatment options for IGM (3). The aim of this study was to report and describe the clinical signs, radiological findings, management, clinical course and the recurrence ratio of the patients which were treated due to IGM.

MATERIAL AND METHODS

We reviewed records of 24 patients diagnosed IGM histopathologically between January 2006 and December 2011 with this retrospective study. The design of the study has been approved by local ethics committee thus meets the standards of the Declaration of Helsinki. Due to retrospective nature of the study, the ethics committee did not require a written consent from the participants.

Medical reports about the patient’s complaints, presence of pregnancy, number of pregnancies, use of contraceptives, follow-up informations and recurrence were obtained from clinical records. All of the patients underwent a clinical breast examination. An US was performed on all patients. A MMG was obtained from patients older than 40 years. An magnetic resonance imaging (MRI) was performed in one patient. Histopathological diagnosis was obtained from incisional or total excisional biopsy. Periductal mastitis and mastitis during lactation were excluded from the study. All aspirates and tissue samples were examined with hematoxylin-eosin staining procedure as well as special stains for tuberculosis and fungal infection. Microbial cultures were performed for the patients with abscess formation. US and physical examination were performed every month until resolution of lesions was confirmed.
RESULTS

24 patients diagnosed IGM histopathologically and had complete follow-up data has been evaluated and included in the study. The mean age was 38.4 years ranged from 28 to 60 years. 87.5 % of patients (n=21) were at reproductive ages. All patients had got children. None of the patients had a history of oral contraceptive use and lactation in a last one year. Painful, firm and ill defined mass was the symptom of all patients. Painful mass lesions were accompanied with skin changes such as erythema and edema in 16 (66.6 %) patients. The left breast was affected in 13 (54.1%) patients, right breast in 9 (37.5%) patients and bilateral in 2 (8.3%) patients. The lesions were located in upper external quadrant in 5 (20.8 %) patients, in upper internal quadrant in 1 patient (4.2 %), in inferior external quadrant in 3 (12.5%) patients, in periareolar region in 7 patients (29.2 %) and diffuse involvement was seen in 7 patients (29.2%). (Table 1).

Parenchymal heterogeneity with no discrete mass had been established in 7 patients (29.1 %), irregular mass in 7 patients (29.1 %), abscess formation in 4 patients (16.6 %), irregular mass with heterogeneity in 1 patients (4.2 %), heterogeneity with abscess formation in 4 patients (16.6 %), heterogeneity, abscess formation and mass in 1 patient (4.2 %) on US (Table 2) (Figure 1). Associated enlarged axillary lymph nodes were present in 14 (41.7 %) patients.

MMG was obtained from 7 patients. MMG detected increased asymmetric density in 3 patients, asymmetric density with skin thickening in 2 patients and asymmetric density with skin thickening and nipple inversion in 2 patients.

MRI was performed in one patient which involvement was diffuse and bilateral and resistant to the treatment (Figure 2). MRI was needed for this patient to obtain additional information.

Total excision was performed in 15 (62.5 %) patients, incisional biopsy with abscess drainage was performed in 9 (37.5 %) patients. Each case demonstrated the presence of epithelioid histiocytes, lymphocytes, plasma cells, polymorphonuclear leukocytes and multinucleated Langhas-type giant cells without caseous necrosis (Figure 3). Serologic and bacterial tests were negative in all patients.

Median follow-up was 34.8 (range 10-66) months. Treatment with surgical excision could be successfully performed in 15 patients. There was recurrence after 24 months in one patient in the another quadrant of the breast and treated with reexcision. The mean
interval of resolution in patients with abscess formation was 5.1 months (range 3-10 months). In one patient which involvement was diffuse and bilateral relapsed the disease repeatedly with an abscess formation. At first she was reluctant for use of corticosteroid but obliged to receive because her quality of life was very affected. We administrated corticosteroid with a dose of 16 mg prednisone twice a day but could not be continued because of glucose intolerance.

**DISCUSSION**

IGM, is a rare benign inflammatory breast disease mostly seen in females at a reproductive age (3). In our study, all but three of patients were at retroductive age and all patients were parous. Many agents, such as local irritants, oral contraceptive pill, viruses, mycotic and parasitic infections, hyperprolactinemia, diabetes mellitus, smoking, alfa 1 antitrypsin deficiency, otoimmunity have been proposed to explain the etiology of IGM but never proven (3,4,5). Although many reports has been emphasized on oral contraceptive pill (3,4,6,7,8), none of the patients had a history of use of oral contraceptive pill in our study.

IGM presents most commonly with a painful, firm, tender, ill defined mass in the breast and unilateral (1,8). The lesions may be located in any quadrant of the breast (8). In consequence of granulomatous inflammation, IGM can cause skin thickness, sinus and abscess formation, axillary lymphadenopathy and nipple retraction which may be clinically mistaken for breast carcinoma (1,3,8). All patients requested with painful mass to our institution, 66.6 % of these accompanied with skin changes. The lesions were located in any location but there were the tendency the subareolar and diffuse involvement with percentage of 41.7 %. Thus bilateral involvement is reported very rare (6,8), there were two patients in our series with bilateral and diffuse involvement. The all masses were firm and ill defined and enlarged axillary lymph nodes were present in 14 (41.7 %) patients, but all of these enlarged nodes were established reactive and not suspicious for malignancy on US.

US and MMG identify an irregular and ill defined mass in the majority of patients. The information, obtained from US and MMG is non-spesific and lack of specificity to diagnose IGM or to exclude breast carcinoma. Memiş et al. reported the appearance of irregular hypoechoic mass lesions and tubular hypoechoic areas connecting to the mass
as frequent sonographic features (10). In other studies, parenchimal heterogeneity and areas of mixed echo pattern have been reported (7). Distinct from these lesions enlarged axillary lymph nodes give rise to thought a locally advanced breast carcinoma (7). In our study, the most common US findings were parenchimal heterogeneity, irregular hypoechoic mass and abscess collection. 41.7% of patients presented enlarged axillary lymph nodes, but these nodes did not show malignant criteria such as cortical thickness (cut-off 2.5mm) and the absence of the fatty hilum (11) on US. To our opinion, while physical examination give rise to thought a locally advanced breast carcinoma, the appearance of parenchimal heterogeneity and abscess formation on US especially with enlarged reactive axillary lymph nodes support the presence of an inflammatory granulomatous process.

An ill defined mass, aсимmetrically increased diffuse or focal density without parenchimal distortion or microcalcification are the most common findings on MMG (7,12). Concordant with previous report asymmetric density was detected in our all patients.

According to some studies, MRI does not provide adjunct information for the differentiation of IGM from carcinoma (7). But Dursun et al. reported that the kinetic features are usually nonsuspicious and can be helpful in the differential diagnosis from carcinoma (12). But MRI does not play a role in the differential diagnosis between the other inflammatory and granulomatous disease and IGM (1,8,12).

These above mentioned imaging modalities are not specific enough, faithful to diagnose IGM and cannot differentiate IGM from carcinoma and other causes of granulomatous and inflammatory lesions such as bacterial mastitis, tuberculous mastitis, foreign body granulomas, sarcoidosis and Wegener’s granulomatosis (8). Since physical examination and imaging modalities fail to diagnose and differential diagnose, histopathologic evaluation must be performed. Histopathologic diagnose can be achieved with fine needle aspiration cytology (FNAC), core, incisional or excisional biopsy (7). But the usefulness and reliability of FNAC has been debated, because some authors informed the useful role of FNAC and the others expressed that the various causes of granulomatous inflammation cannot be differentiated with FNAC (6,13,14). In our patients, the histopathologic diagnosis was obtained from excisional and incisional biopsy, we have not preferred FNAC.
A total excision can be appropriate treatment also provide exact diagnosis. After total excision, if possible, further therapy is not needed. Different recurrence rates (range 5.5%-50%) are reported after surgical excision (1,8). There was one (6.6%) recurrence of 15 patients performed total excision in our patients.

According to our opinion, there is no problem if can be performed total excision. As a matter of fact, complicated IGM with abscess, fistula or diffuse involvement poses the problem. There is not ideal treatment for complicated IGM. In these patients, surgical excision cannot be achieved. Lai et al. reported that spontaneous resolution occurred in 50% of cases of IGM without any treatment with a mean interval of 14.5 months (15). Also, we had 9 patients which could not be performed total excision because of abscess formation and/or diffuse involvement. The lesions of the patients all but one resolved with a mean interval of 5.1 months (range 3-10 months). In one patient which involvement was diffuse and bilateral relapsed the disease repeatedly with an abscess formation. There was not recurrence in the other patients with abscess formation.

Corticosteroid treatment should be administered for complicated and resistant cases or diffuse lesions before excision to reduce the size (1). But there has been reluctance for side effects. We suggested steroid to our complicated patients after abscess drainage and antibiotics, but any patient accepted by reason of side effects, they preferred conservative treatment with close follow-up.

Though some studies have suggested that the recurrence rate with complete excision is higher than corticosteroid treatment (8), we consider that complete excision is the better treatment of choice of IGM if possible. We hesitate to recommend corticosteroids already if complicated cases for several reasons. Because, there is not consensus about timing, duration and dose of corticosteroid administration. According to the study of Sakurai et al, complete resolution of mass lesions with corticosteroid was achieved from 4 to 10 months (2). Moreover spontaneous resolution occurred with a mean interval of 3.3 months in the patients with abscess drainage in our study. But clinical presentation of patient population was different in abovementioned study and in our series. Accordingly it is necessary to know if corticosteroid may be proved rapidly resolution of lesions than conservative approach. According to us it is important to keep in mind that spontaneous resolution may occur rapidly contrary to expectations. At least, we
consider that corticosteroid administration may be suspended after a short follow-up period to see if spontaneous resolution is present or not.

There is still not any commonly accepted optimal treatment for IGM. A total excision and corticosteroid administration has been reported for the first line treatment of IGM. The wide spectrum of clinical signs, symptoms and course of IGM make difficult to choose a favorable treatment. Which one of the treatment modalities should be favorable? When should total excision or corticosteroid be preferred? Is it true to administrate the same dose or duration of corticosteroids for any patient? What should it be done if patient is reluctant to corticosteroid?

It is clear there is a need of prospective randomized trials compared conservative approach, total excision and corticosteroid administration to optimize and standardize the diagnose and treatment of IGM. Nevertheless, it may be possible to compose an algorithm which is mandatory for treatment of IGM.

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None
REFERENCES:


Figure 1. Transvers US scan shows cystic lesion with thickened wall consistent with abscess formation.

Figure 2. T2 weighted fat saturated image demonstrate an irregular non-mass lesion in lower inner quadrant in left breast showing high signal intensity. After administration of Gadolinium based contrast agent (L kont T1) the lesion enhanced partly in type I and in type II pattern heterogenously.

Figure 3. Microscopic finding of incisional biopsy. It shows multiple noncaseating granulomas composed of giant cells and neutrophilic infiltrates (H/E: magnification ×100)

Table 1: Location of lesions in the breast

Table 2: US findings of patients with IGM
Additional files provided with this submission:

Additional file 1: Table 1.docx, 11K
http://www.biomedcentral.com/imedia/8881619421155795/supp1.docx
Additional file 2: Table 2.docx, 11K
http://www.biomedcentral.com/imedia/1152564321155795/supp2.docx