Feasibility of Surgical Management in Patients with Granulomatous Mastitis

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Abstract: Granulomatous mastitis (GM) is a rare inflammatory breast disease of unknown etiology. Although it usually presents with sinus formation and abscesses, it may mimic the clinical characteristics of breast cancer. The aim of this study was to identify the clinical, radiologic, and pathologic characteristics of patients with GM and to show the results of surgical treatment in these patients. A chart review was performed for patients that were treated with a diagnosis of GM at the Breast Unit, Department of Surgery, Istanbul Medical Faculty, University of Istanbul, between September 1998 and January 2003. Eighteen patients were eligible for this study. The median age was 41.5 years (range 16–80 years). Seventeen patients were evaluated by both ultrasonography and mammography; whereas one young patient only had ultrasonography. Three patients were further examined with color Doppler ultrasonography and magnetic resonance imaging (MRI). Fourteen patients (78%) presented with a mass as the chief symptom, with a median size of 3.9 cm (range 1–8 cm), whereas four patients presented with fistula in their breasts. None of the radiologic techniques distinguished benign disease from cancer in any of the 14 patients that presented with a mass except one patient with normal mammography findings. Ultrasonography was only helpful to localize the abscess associated with a fistula tract in one patient. Therefore fine-needle aspiration biopsy (FNAB) was performed in six patients, followed by surgical excisional biopsy. The remaining eight patients with a clinical suspicion of malignancy underwent wide surgical excision with frozen section analysis under general anesthesia. All of the FNAB and frozen section evaluations revealed benign findings. All of the 18 patients underwent a wide excisional biopsy and had a definitive histopathologic diagnosis of GM. The median follow-up was 36 months (range 6–60 months). Only one patient had a recurrent disease, which was diagnosed at 12 months. GM is a rare breast disease that mimics cancer in terms of clinical findings. Preoperative radiologic diagnosis might be difficult. Complete surgical excision is the treatment of choice.

Key Words: granulomatous mastitis, surgery, treatment

Granulomatous mastitis (GM) is a rare inflammatory breast disease of unknown etiology. Although it usually presents with sinus formation and abscesses, it may simulate the clinical characteristics of breast cancer (1). Most patients are of child-bearing age (1,2). The treatment of GM is controversial. Use of antibiotics or corticosteroids and wide excision of the affected tissue have been reported as treatment options (3–5). However, there is no consensus about the most appropriate therapy in these patients.

In our series we performed wide local excision in these patients after systemic antibiotic treatment. To address the question of whether GM requires surgical intervention, we reviewed our patients diagnosed with GM and also all relevant cases published in the literature.

MATERIALS AND METHODS

Between September 1998 and January 2003, 18 patients were diagnosed with GM and underwent surgery for diagnosis and/or therapy at the Breast Unit, Department of Surgery, Istanbul University, Istanbul Medical Faculty, Istanbul, Turkey. These patients represented 3.4% of all patients who underwent surgery for benign breast diseases in our clinic during the study period. A careful history (including data about the patients’ complaints, presence of pregnancy, number of pregnancies, last delivery time, nicotine abuse, use of oral contraceptives, family history of breast disease, and presence of autoimmune disease) was taken and a thorough physical examination was performed.

Diagnostic Evaluation

Serologic tests were performed for rheumatoid factor (RF) and antinuclear antibody (ANA). The slides, which were obtained from all biopsy specimens and special
stains (Gram, Ziehl-Neelsen, periodic acid-Schiff), were examined for organisms. Seventeen patients were examined with both ultrasonography and mammography, whereas one patient had ultrasonography alone.

Fine-needle aspiration biopsy (FNAB) was performed in six patients that were not distinguished from cancer by radiologic examination. GM was defined as a granulomatous inflammatory reaction that was detected on lobules in the absence of a caseous necrosis or any specific organism, such as acid-fast bacilli. All patients underwent a wide excisional biopsy and had a definitive histopathologic diagnosis of GM.

Treatment

All patients underwent antibiotic therapy of 2–6 weeks before surgery. All patients were treated with wide surgical excision with negative margins for inflammatory granulomatous tissue. In cases with fistula formation, a wide surgical excision was performed with methylene blue dye injection from a fistula. Steroid therapy was used in one patient who had a recurrence following a wide excisional biopsy.

RESULTS

Clinical Characteristics

The clinical characteristics of all patients with GM are shown in Table 1. The median age of the patients was 41.5 years (range 16–80 years). The median duration between admission and the beginning of symptoms was 6 months (3–12 months). Fourteen patients had a history of nicotine addiction. The left breast was affected in 12 cases and the right breast was involved in the remaining 6 cases. Furthermore, 14 patients (78%) had unilateral, extra-areolar breast masses, and 6 of them also had palpable axillary lymph nodes. The median size of the mass lesions was 3.9 cm (range 1–8 cm). Furthermore, four patients (22%) had fistula formation as the chief presenting symptom (Fig. 1). One of these four patients also revealed acute inflammatory findings such as local temperature increase, hyperemia, and edema in her breast.

Radiologic Evaluation

All of the radiologic findings are shown in Table 2. Ultrasonography and mammography were performed in 17 cases, and 3 of them were further examined with magnetic resonance imaging (MRI) and color Doppler ultrasonography. The mammography revealed normal findings in 1 patient, focally or diffusely increased asymmetric density in 10 patients, ill-defined masses in 2 patients, architectural distortions in 2 patients, and solitary or multiple circumscribed masses in 2 patients. The ultrasonography findings were as following: solitary or multiple clustered heterogeneous hypoechoic lesions with a tubular configuration \((n = 8)\), multiple hypoechoic masses with contiguous, long tubular hypoechoic lesions \((n = 6)\), massive parenchymal heterogeneity and hypoechogenicity \((n = 3)\), and abscesses with sinus tracts to the skin \((n = 1)\).

### Table 1. The Clinical Characteristics of Patients with GM

| Age (years) | Recent pregnancy history | No. of pregnancies | Side | OC use | FNAB | Type of surgery | Cosmesis of the breast | Local recurrence |
|-------------|--------------------------|--------------------|------|--------|------|-----------------|-----------------------|-----------------|
| 50          | No                       | 3                  | Right | No     | No   | Wide excision\(^b\) | Good                 | No              |
| 68          | No                       | 4                  | Left  | No     | No   | Wide excision\(^b\) | Good                 | No              |
| 60          | No                       | 3                  | Left  | No     | Yes  | Wide excision\(^c\) | Good                 | No              |
| 16          | No                       | —                  | Left  | No     | Yes  | Quadrantectomy\(^c\) | Good                 | No              |
| 30          | No                       | 2                  | Left  | Past   | No   | Wide excision\(^c\) | Average              | No              |
| 37          | No                       | 2                  | Left  | Past   | No   | Wide excision\(^c\) | Good                 | No              |
| 31          | No                       | —                  | Left  | No     | Yes  | Quadrantectomy\(^c\) | Good                 | No              |
| 38          | No                       | 2                  | Left  | No     | Yes  | Wide excision\(^c\) | Good                 | No              |
| 43          | No                       | 4                  | Right | No     | No   | Wide excision\(^c\) | Good                 | No              |
| 32          | No                       | 1                  | Left  | Yes    | Yes  | Wide excision\(^c\) | Average              | No              |
| 32          | No                       | 2                  | Right | Yes    | No   | Wide excision\(^c\) | Average              | No              |
| 51          | No                       | 3                  | Right | Past   | No   | Quadrantectomy\(^c\) | Good                 | No              |
| 36          | No                       | 1                  | Left  | No     | No   | Wide excision\(^c\) | Good                 | No              |
| 29          | No                       | 1                  | Right | No     | Yes  | Wide excision\(^c\) | Good                 | No              |
| 80          | No                       | 4                  | Left  | No     | No   | Wide excision\(^c\) | Good                 | No              |
| 28          | No                       | —                  | Left  | No     | Yes  | Wide excision\(^c\) | Good                 | Yes             |
| 53          | No                       | 5                  | Left  | Past   | No   | Wide excision\(^b\) | Good                 | No              |
| 34          | No                       | 2                  | Right | No     | No   | Wide excision\(^c\) | Good                 | No              |

\(^{a}\)OC, oral contraceptive.

\(^{b}\)Cosmesis of the breast was evaluated according to the presence of scar tissue on the operation side and any asymmetry in both of the breasts.

\(^{c}\)Under local anesthesia.

\(^{d}\)Under general anesthesia.
Enlarged axillary lymph nodes were detected in three patients by mammography and in four patients by ultrasonography (Figs 2 and 3). Doppler examination \((n = 3)\) showed increased arterial and venous vascularization within and around the lesion, but the spectral analysis findings were not specific for GM (Fig. 4).

Magnetic resonance imaging was performed in three patients. Findings according to their architectural features included solitary mass with parenchymal asymmetry \((n = 1)\), parenchymal distortion \((n = 1)\), and parenchymal asymmetry \((n = 1)\). The lesions showed different contrast enhancement patterns, such as diffuse parenchymal enhancement \((n = 1)\), heterogeneous parenchymal enhancement \((n = 1)\), and ring-shaped enhancement \((n = 1)\). Two

**Table 2. Comparison of Radiologic Findings with Physical Examination in Patients with GM**

| Patient no. | Physical examination | Clinical impression         | US                | MMG                  | Doppler US          | MRI                  |
|-------------|---------------------|-----------------------------|-------------------|----------------------|---------------------|----------------------|
| 1           | Mass                | Malignant                   | Hypoechoic lesions| —                    | —                   | —                    |
| 2           | Mass                | Malignant                   | Parenchymal heterogeneity | Asymmetric density | Increased vascularization | Parenchymal asymmetry |
| 3           | Mass                | Malignant                   | Parenchymal heterogeneity | Asymmetric density | —                   | —                    |
| 4           | Mass                | Malignant                   | Parenchymal heterogeneity | Asymmetric density | —                   | —                    |
| 5           | Mass                | Malignant                   | Hypoechoic masses  | Asymmetric density   | —                   | —                    |
| 6           | Mass                | Malignant                   | Hypoechoic masses  | Asymmetric density   | —                   | —                    |
| 7           | Mass                | Malignant                   | Hypoechoic masses  | Asymmetric density   | —                   | —                    |
| 8           | Mass                | Malignant                   | Hypoechoic masses  | Asymmetric density   | —                   | —                    |
| 9           | Mass                | Malignant                   | Hypoechoic masses  | Asymmetric density   | —                   | —                    |
| 10          | Mass                | Malignant                   | Hypoechoic lesions | Ill-defined mass     | —                   | —                    |
| 11          | Mass                | Malignant                   | Hypoechoic lesions | Ill-defined mass     | —                   | —                    |
| 12          | Mass                | Benign                      | Hypoechoic masses  | Asymmetric density   | Increased vascularization | Solitary mass |
| 13          | Mass                | Benign                      | Hypoechoic lesions | Normal               | —                   | —                    |
| 14          | Mass                | Benign                      | Hypoechoic lesions | Architectural distortion | —                   | —                    |
| 15          | Fistula             | Benign                      | Hypoechoic lesions | Architectural distortion | Increased vascularization | Parenchymal distortion |
| 16          | Fistula             | Benign                      | Hypoechoic lesions | Circumscribed mass   | —                   | —                    |
| 17          | Fistula             | Benign                      | Hypoechoic lesions | Asymmetric density   | —                   | —                    |
| 18          | Fistula and abscess | Benign                      | Abscess           | Circumscribed mass   | —                   | —                    |

US, ultrasound; MMG, mammogram; MRI, magnetic resonance imaging.
of the lesions revealed gradual and progressive enhancement in enhancement profiles (Fig. 5). However, these findings were not found as a specific pattern for GM that distinguishes this benign disease from cancer.

None of the radiologic techniques distinguished benign disease from cancer in any of the 14 patients that presented with a mass, except one patient with normal mammography findings. Ultrasonography was only helpful to localize the abscess or the fistula tract in one patient.

**Diagnostic and Histopathologic Evaluation**

Serologic tests for RF and ANA were found to be negative in all patients. Radiologic examination could not distinguish benign disease from cancer in all cases that presented with a mass. Therefore FNAB was performed in six patients, followed by surgical excision under general anesthesia. All FNAB findings were consistent with the definitive histopathologic finding of mastitis, and revealed many epithelioid cells with multinucleated Langhans-type giant cells, neutrophils, lymphocytes, and stromal cells, which are characteristics of GM (Fig. 6). The remaining eight patients with a clinical suspicion of malignancy underwent wide surgical excision with frozen section analysis under general anesthesia (Table 1). Frozen section results revealed benign findings. Final histopathologic diagnosis of the

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**Figure 3.** Ultrasonography of the breast reveals a hypoechoic and irregular-shaped mass with ill-defined margins.

**Figure 4.** Doppler examination shows increased arterial and venous vascularization within and around the lesion. The enhancement curve shows an initial increase in the intensity of more than 90% within the first 2 minutes, followed by a washout of contrast material.

**Figure 5.** A subtraction image shows enhancement in a diffuse zone with focal regular mass.

**Figure 6.** Fine-needle aspiration cytology of the breast mass shows many epithelioid cells admixed with multinucleated Langhans-type giant cells, neutrophils, lymphocytes, and stromal cells (Papanicolaou; magnification ×310).
specimens was exclusively granulomatous inflammatory reaction, whereas neither caseous necrosis nor any specific organism, such as acid-fast bacilli, were detected (Fig. 7).

**Treatment and Outcome**

All patients had a history of antibiotic therapy of 2–6 weeks before the definitive diagnosis. They further received 7 days of intravenous ampicillin-sulbactam therapy before surgery and underwent a surgical excision of the lesion with negative margins for inflammatory granulomatous tissue. They were also administered 7 days of oral ampicillin-sulbactam therapy in the postoperative period. Four patients that presented with a fistula in their breast underwent a surgical excision following methylene blue injection through the sinus tract.

The median follow-up was 36 months (range 6–60 months). Only one patient (6%) developed local recurrence as a discrete mass, which appeared in the same quadrant of the breast 1 year after surgery. This patient was treated by reexcision, with oral prednisone following surgery (16 mg/day for 2 months, then slowly tapered based on the findings of ultrasonography and physical examination). No further recurrence was observed in this patient during a 1 year follow-up period.

**DISCUSSION**

Granulomatous mastitis is a rare chronic inflammatory breast disease (4,5). The microscopic features of GM were first described by Kessler and Wolloch in 1972 (6). The etiology of GM is unknown. Some authors have speculated that the cause may be an autoimmune process, undetected organisms, use of oral contraceptives, or a reaction to childbirth (7–11). There have been approximately 120 reported cases in the literature in the last 3 decades (1–20). Studies have shown that GM is seen in young parous women, frequently in association with recent pregnancy (5,7,8) and lactation (14,15). However, GM has also been reported to occur in some patients who did not receive oral contraceptives (4,14,15). In our series, only two patients had a current history of oral contraceptive use, whereas none of them had a recent pregnancy.

Autoimmunity is often claimed as an etiology. It is possible that damage to the ductal epithelium produced by local trauma, local chemical irritation, or infection may allow luminal secretions to escape into the lobular connective tissue, thereby causing a granulomatous response with lymphocyte and macrophage migration. However, serologic tests for ANA and RF autoimmune antibodies, which are evidence of an autoimmune phenomenon, are usually found to be negative. We also did not observe any ANA and RF positivity in our patients. In addition, no microorganisms have been isolated from the tissue, and histologic staining for pathogens has routinely revealed negative findings in agreement with previous studies (11–14).

On the other hand, most of our patients with GM had nicotine addiction, pointing to a relationship between smoking and GM. However, more clear evidence is needed, since there have been no reports regarding any relationship between nicotine addiction and GM in literature.

The clinical findings of GM often suggest carcinoma. The involvement is usually unilateral, whereas bilateral involvement has rarely been reported in the literature (4). Regional lymphadenopathy may be present. In our series, the majority of the patients had unilateral, extra-areolar breast masses, and almost half of these patients also had palpable axillary lymph nodes.

The mammographic appearance of GM has been previously described as normal or as a suspicious mass or a mass suspicious of cancer (4,7,8). The sonographic appearance of GM is described as a nonhomogeneous, irregular hypoechoic lesion with focal posterior shadowing and tubular configuration (4,16,17). MRI has been used in some studies and detected focal homogeneous enhancing masses with irregular borders (18,19). Doppler examination also has been used and revealed increased vascularization within or around the lesion (16). Even though MRI and color Doppler sonography could not differentiate GM from malignancy in three patients, our patient number is too small to make a conclusion about the use of these techniques in diagnosis. In our series, ultrasonography was used in all patients with GM. Our results suggest that the sonographic appearance might be
useful in detecting abscess formation in patients. Furthermore, only one patient with a mass had normal mammographic findings. Therefore it appears that the role of radiologic imaging is limited in distinguishing GM from malignancy.

Histopathologic diagnosis plays a very important role in patients that were admitted with a palpable mass and possible GM. Diagnosis of GM can be made by FNAB or excisional biopsy (15,20). In our series, all FNAB findings were consistent with a definitive diagnosis of GM. However, cytology may not always differentiate between GM and the other granulomatous diseases of the breast, as reported in the published literature. Demonstration of granulomatous inflammation of the lobular units is required for a definitive diagnosis of GM (4,20). Furthermore, a false-positive FNAB result may lead surgeons to a more aggressive surgery (22). Considering the small number of FNAB samples in this study, other studies with larger numbers of patients are required to make a more definite conclusion about the accuracy of FNAB in the diagnosis of GM. Therefore adequate tissue examination may be needed for differential diagnosis of GM from other pathologies, including malignancy and other infectious pathologies resulting in granulomatous inflammation.

Awareness of this rare entity is important for the pathologist because the definitive diagnosis is made microscopically by evaluation of a wide breast tissue sample. The histologic feature of GM is a predominantly lobular distribution of inflammatory infiltrate (4,14,15). The inflammation is consistent with a granulomatous process. The infiltrate is composed of histiocytes, a few polymorphonuclear leukocytes, and multinucleated giant cells of the foreign body and Langhans type. Abscess formation can occur, and although these are usually small, involvement of the whole lobule can occasionally occur (11,12,14,15). The possibilities of breast tuberculosis and sarcoidosis must be considered in differential diagnosis (4,15). Tuberculous mastitis presents with caseating granulomas and acid-fast bacilli, whereas GM has discrete noncaseating granulomas. However, it might be more difficult to distinguish sarcoidosis from GM because it also presents with noncaseating, epithelioid granulomas, and the granulomas are scattered throughout the breast tissue with no relation to the lobules, in contrast to GM where inflammation is generally confined to the breast lobules (Fig. 7). Furthermore, other granulomatous infections such as blastomycosis, cryptococcosis, histoplasmosis, actinomycosis, and filarial infection should also be considered in the differential diagnosis (4,15,17).

Management of GM remains controversial (4,14,15). DeHertogh et al. (21) first advocated the use of corticosteroids for the treatment of GM after an observation that a granulomatous mass disappeared within 3 weeks with administration of high-dose prednisone. Some reports also suggest that it may be necessary to continue high doses of corticosteroids until complete resolution following a diagnosis of GM by FNAB (8,15,21). The patients receiving steroid therapy should be closely observed for side effects, including glucose intolerance and cushingoid features. Furthermore, the concern about possible involvement of an infectious agent often challenges the use of steroids.

Wide excision of the mass was performed traditionally, but the recurrence rate in surgical treatment is reported to be higher than steroid treatment in some studies (8,15,18). However, GM can mimic breast carcinoma, and an accurate preoperative diagnosis may be difficult. Seventy-eight percent of the our patients with GM presented with breast masses that could not be distinguished from cancer. Therefore our management is based on surgical excision in patients with a suspicion of GM. In cases with fistula formation, methylene blue dye is injected from the fistula and surgical excision was performed with negative surgical margins. There was only one patient with recurrent disease. The low recurrence rate might be due to negative surgical margins in terms of inflammatory tissue.

Recurrences and fistula formation are known complications of GM. In some cases, excision of the recurrence alone may not be an adequate treatment and additional steroid therapy may be necessary (4). The patient with recurrence in our series was successfully treated by reexcision followed by oral steroid therapy.

In conclusion, GM is a rare benign breast disease that is difficult to distinguish from other inflammatory breast diseases or cancer using radiologic tools or FNAB. Side effects of steroid treatment may be challenging in such a benign disease, which is curable by surgery in a shorter time and with fewer complications. Therefore surgical excision of the mass remains the treatment modality of choice.

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