A Comparative Study of Conservative versus Surgical Treatment Protocols for 77 Patients with Idiopathic Granulomatous Mastitis

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Abstract: The purpose of this study was to analyze the clinical features and demographic data of patients with idiopathic granulomatous mastitis (IGM) and to compare the results of conservative versus surgical treatment protocols. The demographic data, clinical findings, microbiological and pathologic features, scanning and treatment methods, recurrence, and recovery rates of 77 patients were analyzed retrospectively. The patients were divided into two groups based on the type of treatment received. Core biopsies were used to diagnose 37 patients: 26 using incisional biopsies and 14 using excisional biopsies. Of the patient population with IGM, 31 were treated with surgical excision, one with a simple mastectomy, and one with a subcutaneous mastectomy combined with a breast implant, whereas 44 were treated with steroids. The recovery rates of the 44 patients who were treated conservatively were 6 (1–15) months while for the 33 patients who were treated surgically, it was 1 (1–5) month (p = 0.001). Nine patients from the conservative treatment group experienced a recurrence while there were no recurrences in the surgically treated group (p = 0.009). Among all patients, the recurrence rate was 11.7% (9/77) while the average follow-up period was 16.57 ± 18.57 months. As a comparative study between conservative treatment protocols and surgical ones for patients with idiopathic granulomatous mastitis (IGM), this study is the largest to date. A wide surgical excision is the preferred approach for treating patients with IGM because of the low recurrence rate.

Key Words: conservative treatment, corticosteroid, idiopathic granulomatous mastitis, recovery rate, recurrence, surgical treatment

idiopathic granulomatous mastitis (IGM) is a rare benign breast disease of unknown etiology (1). Patients frequently present with a tender, erythematous breast mass suggestive of an abscess; a chronic draining sinus is also common (2,3). Although it is a benign medical condition, it mimics breast cancer, so there is a need for recurrent core or incisional biopsies to rule out this risk (4,5). A definitive diagnosis can be made only by histopathological means. While the appropriate treatment method for IGM is not yet clear, surgical removal of the diseased section is the most commonly recommended approach (6,7). More conservative alternatives include single or combined methods; however, varying rates of recurrence are reported (6,8–10). Some studies report recovery rates as high as 77% in patients treated with nonsurgical alternatives and 100% in patients treated with a wide surgical excision (11,12). Many studies demonstrate the advantages and disadvantages of both treatment protocols, but they are limited in that the group sizes are small. There are no studies to date comparing the results of these two treatment methods in the same patient population.

The purpose of this study was to determine the most effective treatment approach for patients with IGM.
MATERIALS AND METHODS

This study was carried out on 77 patients diagnosed with IGM and treated at our center between 1999 and 2013. The patients’ medical records were retrieved from the archives and data were analyzed, retrospectively. This study was approved by Baskent University Institutional Review Board and supported by Baskent University Research Fund (KA13/187). Diagnostic and therapeutic management of all identified patients was undertaken by the same medical team. All IGM cases were diagnosed histopathologically. Etiologic factors such as use of oral contraceptives, time between the last delivery or breast-feeding and presentation, smoking, family history of breast cancer, comorbid diseases, number of pregnancies, previous surgeries, mastitis, and history of autoimmune disease were recorded. In addition; demographic characteristics of the patients, clinical findings, radiological examinations, biopsy methods, microbiological and histopathological features, treatment methods, and recovery times were included. Patients were divided into two groups based on their treatment protocol. This decision was made taking into account the size of the mass, ratio of the mass to breast tissue, previous mastitis treatment, and change in mass size following treatment with antibiotics, patient’s esthetic concerns, and the rate of inflammation in the breast tissue. Group 1 was treated surgically and Group 2 was treated using a conservative protocol and steroids. Patients who presented with hyperemia and an abscess were treated with antibiotics before deciding which treatment protocol to use. Diseased tissue was removed with clean surgical margins among those in Group 1, and in cases with diffuse inflammation, recurrence, or resistance to conservative treatment, a wider excision and/or reconstruction was implemented. Group 2 was treated using methylprednisolone at 0.8 mg/kg/day during the first week and at 0.1 mg/kg/day thereafter.

In our clinical practice, patients without serious abscesses or severe infections received steroid treatment. However, patients with evident abscesses and severe infections were treated with antibiotics followed by surgical treatment to correct the abscess. Almost all the patients in Group 1 were clinically severe and steroid treatment was not given. Six patients initially in Group 2 did not respond to steroid treatment or exhibited adverse effects, and thus were transferred to Group 1.

Microbiological Assessment

Pus and tissue samples were taken from the patients and antibiotics administered based on lab results. Tuberculosis was assessed by taking acid-resistant bacteria and Lowenstein-Jensen cultures and assessing the polymerase chain reaction in the tissues samples. The IGM diagnosis was established by using a core needle biopsy and surgically administered open biopsies. All pathologic preparations were treated with Hematoxylin and Eosin stain for histopathologic evaluation, gram staining for detection of microorganisms, Ziehl–Neelsen staining for tuberculosis factor, and periodic acid-Schiff staining to evaluate fungal infection.

Statistical Analysis

The SPSS 16.0 software package was used for statistical analysis (SPSS, Chicago, IL). Categorical measurements were summarized using numerics and percentages while continuous measurements were summarized using averages and standard deviations (as medians and minimum–maximums when necessary). To compare categorical variables, a Chi-squared or Fisher’s exact test was used. To compare continuous measurements between groups, the Mann–Whitney test was used because the data were not normally distributed. For all tests, p < 0.05 was statistically significant.

RESULTS

All the patients in our study group were female. The clinical and demographical characteristics of the patients in both groups are shown in Tables 1 and 2. Analysis of patients’ medical history showed that 13 were postmenopausal, six had histories of mastitis, four had histories of breast cancer, had lumpectomies, five had hypertension (HT), two had diabetes mellitus (DM), one had chronic obstructive lung disease, and one had DM, HT, and chronic kidney dysfunction. There were eight patients with rheumatic diseases, four with rheumatoid arthritis, two with Sjogren syndrome, one with familial Mediterranean fever, and one with ankylosing spondylitis. Only two were single. In each of the two groups, there were four patients with rheumatic diseases, and these patients had previously received steroids. The recovery rate in this subgroup was not different than that in the entire group. Patients’ complaints and physical examination findings are shown in Table 2. During the physical
examination, IGM was most frequently observed on the upper-outer quadrant of the right breast (45% of Group 1 and 59% of Group 2). Radiological assessments were carried out on all patients using ultrasonography (USG), on 27 using magnetic resonance imaging (MRI), and on 18 using mammography (MMG). Images can be seen in Figure 1.

Microbiological cultures obtained from 57 patients were studied, and reproduction was observed in eight of them. Of those, reproduction of methicillin-sensitive coagulase-negative staphylococci was found in six, of acinetobacter baumanni in one, and of diphtheria bacilli in the final culture. Eight of the 57 patients were treated with antibiotics, and three underwent a wide surgical excision, whereas the remaining was treated with the conservative protocol. The recovery rate for patients in the subgroup who were treated surgically was 1.53 ± 0.67 months, while that for patients who were treated with the conservative approach was 5.21 ± 2.01 months (p = 0.10). Diagnosis was made using core biopsies in 37, incisional biopsies in 26, and excisional biopsies in 14 patients. Thirty one patients underwent a wide surgical excision (lumpectomy), one underwent a simple mastectomy, and one underwent a subcutaneous mastectomy with a breast implant. In 25 (75.7%) of these 33 patients, the diseased tissue was observed to have invaded the main mammary duct, and surgical excision was performed to include the main mammary duct. There were no statistically significant differences between the groups with regard to demographic and etiological factors.

In patients who underwent a wide surgical excision, surgical margins were determined to be pathologically negative and no recurrence was observed during follow-up. Average length of recovery for the 33 surgically treated patients was 1 (1–5) month, whereas it was 6 (1–15) months for the 44 who received steroids (p = 0.001; Table 2). In Group 1, no recurrences were observed; however, in Group 2, there were nine (p = 0.009). The overall recurrence rate was 11.7% (9/77), and the average follow-up period was 16.57 ± 18.57 months.

**DISCUSSION**

A benign disease of the breast, IGM usually presents in women during the postnatal period (1). Most articles published are case reports and small group studies (12–17). Our study group of 77 patients is the largest reported to date.

Idiopathic granulomatous mastitis commonly presents as a rapidly growing breast mass with inflammation, abscesses, nipple retraction, and chronic draining sinus formation can also occur (1,18). The lump may mimic clinical presentation of a breast carcinoma by invading the underlying pectoralis muscle with nipple retraction, involving the overlying skin and auxiliary lymphadenopathy (5,19,20). In this study, the most common reason for patient referral to a surgeon was a palpable mass and pain. The most frequently observed site for the mass was the right upper-outer quadrant. Auxiliary lymphadenopathy was reported in 26% of IGM patients in a study conducted by Konan et al. (8). Likewise, it was observed in 25.9% of our patients. While IGM is generally observed with the same frequency in each breast, it has also been
reported to be bilateral (21,22). However, all the patients in our study group had only unilateral involvement. The rates of involvement of the right and left breast were 53.2% and 46.8%, respectively. Approximately, 27% of the patients presented with a mass in the upper-outer right quadrant.

A physical examination can result in a misdiagnosis, so advanced assessments are necessary to rule out breast cancer. Similarities between IGM and breast cancer are observed not only during the physical exam but also the radiological exam. Since a preoperative definitive diagnosis of IGM is an important step in the treatment plan, radiological assessments were carried out on all our patients. The most frequently used radiological assessment in our study was USG, because it is a better choice than MMG, with which it is difficult to detect IGM. However, even when using MMG together with USG, IGM can easily be confused with breast cancer. For breast scanning, MRI is used as a complementary assessment tool and for following up on size changes of IGM lesions (16,20,23). In 27 of our patients, MRI was used to confirm IGM diagnosis.

Histopathological assessments are crucial in patients with IGM to avoid misdiagnosis. In several studies based on clinical and radiological assessments alone, nearly 50% of patients had suspected malignancy (15,24). Preoperative histopathologic confirmation

Figure 1. Radiological imaging from ultrasonography, MRI and mammography of patients with IGM. (a) IGM of the right breast is seen as large heterogeneous hypoecho genicity containing internal hypoechoic tubular lesions giving no posterior enhancement or shadowing with indistinct borders (open arrows). (b and c) Mammography MLO projection images demonstrate ill-defined densities without mass formation and skin thickening of the right breast (open arrows). (d) Axial T2. Asymmetrical tissues of high signal intensity on the lateral aspect of the left breast is seen on axial T2 weighted image. (e) Axial fat supressed T2. On axial T2 weighted fat supressed images the lesion is seen as heterogeneously hyperintense (open arrows). (f) Axial postcontrast subtracted image. Heterogeneously enhancing areas and ring-like enhancement of abscess are seen on postcontrast MRI (open arrows).
using core biopsy is a crucial step in creating a treatment plan for IGM patients. A definitive diagnosis can be made using fine-needle aspiration biopsy (FNAB), a core biopsy, or an open surgical biopsy. While studies on the use of FNAB in pathologic diagnoses are limited, accuracy rates in a study conducted by Tse et al. were reported at 50% (25). Some reported cases that were initially assessed to be malignant unnecessarily underwent mastectomies (5,21). In a study conducted by Oran et al., 100% accuracy was achieved using core biopsy for diagnosis (6). We had the same result.

Because using both MRI and core biopsy improved the accuracy of diagnosis in our study, we recommend using routine MRI on patients with suspected IGM during prediagnosis followed by confirmation by pathologic diagnosis via core biopsy.

Rheumatologic disease was present in eight patients in our study. Steroid therapy can be useful in diseases such as IGM, which theoretically occurs in this group of patients. However, according to our data, in spite of a limited number of patients, no significant difference was observed in recovery rates.

Among the patients with positive microbiological cultures, three were treated surgically and five with steroids. Recovery rates of the patients in Group 1 were better than those in Group 2, leading us to believe that surgical treatment is a better choice, especially for those patients with abscess formation and positive microbiological cultures. However, positive microbiological cultures are rarely seen in patients with IGM, therefore, to suggest the most effective curative treatment, more studies using larger numbers of patients are needed.

Treatment methods include mastectomy, excision, drainage, drug therapies, and observation; however, the optimal treatment method has yet to be determined (3,5,16,24–28). Conservative treatment alternatives are generally preferred in patient groups with mild symptoms and for small-mass lesions, but in patients with larger masses and severe symptoms, surgical treatment alternatives are usually preferred. In a study conducted by Al-Jarrah et al., all patients were treated exclusively with antibiotics and no recurrences were observed during a 15-month follow-up period (10). In recent years, a trend has developed using immunosuppressive drugs concurrently with steroids (8). There are also studies that combine conservative and surgical protocols depending on the course of the disease (29). Following excision, steroid therapy may also be used in unresponsive cases (3,23,30). In patients with steroidal side effects or who have a resistance to steroids, hydroxychloroquine, methotrexate, azathioprine, and/or colchicines can be used (9,31). In a study where steroid and azathioprine treatments were administered concurrently, a success rate of 73% was achieved (8).

Using wide surgical excision to treat IGM has gained acceptance in recent years, because limited excisions tend to result in recurrences (1,16,19,32). Recurrence rates ranging from 8% to 50% are reported in patients following excision (12,15,18). Surgical excision showed particularly fast recovery, high success rate (90.3%) and low recurrence rate (8.7%) according to Hur et al. (33).

Among our patients, Group 1 experienced no recurrences during an average follow-up period of 23.18 ± 24.8 months. Here, the main point is limiting the possibility of recurrence and minimizing complications complete excision of the breast or wide excision of the involved inflamed tissue provides a more satisfactory result than limited excision (16,34). We performed surgery after the inflammation collapsed with antibiotic therapy and in cases with abscess formation or inflammation, the surgical resection should be kept wide to ensure clean margins.

Mastectomy or wide surgical excision to obtain clean surgical margins is a difficult decision both for the surgeon and the patient when considering cosmetics. However, insufficient conservative and surgical interventions both prolong the time required for treatment and increase the need for secondary treatments.

Wide surgical resections used to treat increasing numbers of IGM patients also increase the need for reconstructive surgery as part of the treatment plan (3,26,35,36). For 1 patient in our series, a prosthetic breast implant was placed after removing the affected tissue during a subcutaneous mastectomy. There are limited numbers of studies regarding implant and reconstruction practices during IGM treatment (35). This is an area that needs further study to properly evaluate recovery rates and results for these patients.

Initially, the majority of our patients were treated using conservative methods (steroids or steroids and antibiotics). Because of a lack of response, high recurrence rates, and adverse side effects, the treatment protocol was revised. As a result, patients were treated with surgical excision more frequently. When patient groups were compared in terms of recurrence and recovery rates, statistics showed that the surgically
treated group had a significantly faster recovery rate and no recurrences, while those undergoing conservative treatments had a recurrence rate of 20.4%. But, to reach the conclusion that surgical approaches have better recurrence rates and outcomes, randomized controlled studies with longer follow-up periods should be performed.

In 25 of the 33 patients who underwent surgical intervention, the disease was linked to the main mammary duct, making excision of the main mammary duct in all of these patients a must. This is most likely one of the main reasons behind the observation that none of the patients in this group had recurrences.

Most studies promote their own treatment approaches, arguing that theirs has greater advantages and low recurrence rates. As a result of this trend in reporting, merely comparing a new study group with the existing ones is not expedient in arguing that one treatment modality results in a more significant outcome.

LIMITATIONS OF THE STUDY

As our study is retrospective, lacking of common evaluation algorithm for patients. Treatment strategy have been performed according to clinical preference of surgeon. Thus, individual preferences may have interfered with proper treatment strategy.

CONCLUSION

All treatment outcomes are influenced not only by the equipment used by the treatment center, but most importantly by the experience of the pathologist, radiologist, and surgeon. To determine the most effective treatment approaches, studies that compare conservative and surgical treatment approaches in the same patient study group at the same medical facility are crucial.

In this paper, we analyzed the largest study group in published literature where conservative treatment therapies and surgical excision methods are compared in detail in the same patient population. Because no recurrence was observed in the group that underwent surgical excision, this treatment approach can be considered a preferred treatment protocol for patients with IGM. Nevertheless, to reach such a conclusion, randomized controlled studies with longer follow-up periods should be performed.

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CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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