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Idıopathıc granulomatous mastıtıs: Comparison of surgical and medical treatments

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Abstract

Objectives: Idiopathic granulomatous mastitis (IGM) is an uncommon benign disease with unclear optimal management. In our study, we aimed to compare different treatment methods and to evaluate the complete remission and recurrence rate of each group.

Methods: We searched for patients with the diagnosis of IGM between January 2013 and April 2021. Patients are classified according to treatment methods used for disease. The complete remission rate and recurrence rate between the groups are compared using the statistical software NCSS.

Results: 72 patients with IGM who had fulfilled the inclusion criteria of our study were analyzed for antibiotic treatment, oral steroids and surgical managements. 40(56%) patients had complete remission, 32(44%) patients had recurrences. Of these 40 patients who had complete remission, 28(70%) patients were treated with antibiotics, 6(15%) patients were treated with oral steroids, 6(15%) patients were treated with segmental mastectomy. 32 patients who had recurrences were treated with antibiotics (20 patients, 62%), oral steroids (7 patients, 22%), and with segmental mastectomy (5 patients, 16%). None of the patients treated with oral steroids had recurrence, 1 patient treated with segmental mastectomy had recurrence, and 9 patients treated with antibiotics had second recurrence. 5 of 9 patients who had second recurrence were treated with antibiotics, 3 of them were treated with oral steroids, and one of them was treated with segmental mastectomy. All patients achieved remission.

Conclusion: IGM is a benign inflammatory condition that gives good response to corticosteroid treatment. Segmental mastectomy also has low recurrence rate, but better remission rates are achieved with corticosteroids.

Keywords: Breast, granulomatous mastitis, corticosteroids, segmental mastectomy, antibiotic treatment

Introduction

Granulomatous mastitis (GM) is an uncommon disease of the breast that includes inflammatory mass development, and it is difficult to differentiate from breast cancer both clinically and radiologically [1, 2].

It is first described by Kessler and Wolloch in 1972 as a different well-defined mastitis entity, which is different from other types of mastitis and is characterized by granuloma and abscess formation [3]. Various etiological factors can induce GM, such as sarcoidosis, tuberculosis, fungal and parasitic infections, foreign material, and trauma [2, 4]. IGM is a diagnosis of exclusion, once other specific causes like tuberculosis and other infections, fat necrosis and systemic diseases like sarcoidosis have to be ruled out before making the diagnosis [2, 4]. IGM generally occurs in women of child-bearing age [5, 6, 7]. The clinical presentation can be mass, pain, erythema and inflammation [1, 5, 8]. Abscesses and fistulas are also common findings either at presentation or during the disease [8, 9]. Pathogenesis of IGM is still not clear. It seems to have an autoimmune base because it can be seen with other autoimmune diseases like erythema nodosum, wegener's granulomatosis and because it gives a good response to prednisolone therapy [2, 5, 6, 8]. Radiologic findings of breast cancer resemble breast cancer [5, 8, 9, 10]. The gold standard for the diagnosis of IGM is tissue biopsy. Core biopsy reveals non-caseating granulomas, microabscesses, chronic inflammation and necrosis [2, 7, 10]. The optimal treatment is still unclear [1, 11, 12, 13].

The main purpose of this study is to compare medical and surgical treatment methods. Clinical, radiologic, and pathologic findings of the disease are also discussed.

Materials and Methods

In this study, 83 patients with pathologically proven diagnosis of granulomatous mastitis between January 2013 and April 2021 are retrospectively analyzed. The information about age, gender, pathologic findings, radiologic findings, medications used during the treatment and phone numbers of our patients with GM are collected from our hospital's database and National health service database(e-nabız). Clinical findings, medications used, and any kind of complaints or recurrences are also confirmed by hospital recalls and/or control phone calls. Patients under 18 years old, patients who did not respond to hospital or phone recalls and patients who had a specific type of GM are excluded from the study. The ethics committee of our hospital has approved the study protocol.

Patients are divided into 3 study groups according to the type of treatment used: Antibiotic treatment, oral corticosteroid treatment, and segmental mastectomy. Antibiotics group consists of patients with limited IGM, i.e. with no mass lesion, with no draining sinus tracts, and whose complaints have weaned during the course of antibiotics treatment. They are observed and informed about high rates of recurrence. Patients who had complicated IGM and refused corticosteroid treatment and segmental mastectomy are also put into antibiotics group. Corticosteroid group consists of patients with limited IGM who do not respond to antibiotics treatment, patients with mass lesion, and/or draining sinus tracts, patients with large area of erythema. Segmental mastectomy group consists of patients who have been offered corticosteroid treatment and have refused, or patients who has wanted to get an immediate treatment and doesn't want to fallow the time period of corticosteroid treatment. Complete remission rate and recurrence rates are observed in each group. Complete remission is considered as loss of symptoms both clinically and radiologically. Patients are observed for at least 10 months to be accepted for complete remission.

Statistical Analysis

Statistical analyses were made by using NCSS (Number Cruncher Statistical System) Statistical Software 2007(Utah, USA). Data comparison is made by using Fisher -Freeman Halton test. $p<0.05$ is accepted as statistically meaningful.

Results

82 patients who had the pathological diagnosis of GM were retrospectively evaluated. Female patients over 18 years old were included in the study. 8 patients who did not respond to hospital recall and/or phone recall, and 1 patient who had the diagnosis of tuberculosis was excluded from the study, due to having the specific type of GM. 1 patient's treatment has not been completed yet and was excluded from the study. The youngest patient was 23 years old, and the oldest patient was 68 years old. Breast involved was unilateral in all cases. Tuberculosis, trauma and all other etiologic factors that cause specific GM are all excluded from the study. 8 patients were at menopause; others were at their reproductive age. The most common symptom was palpable mass which occurred in all our patients (100%). 11 of our patients had pain (15%), and 23 of them had erythema on the overlying skin (32%). 6 patients had spontaneous draining fistula (8%), 6 patients had ulcerative skin lesions on overlying skin (8%), and 16 patients had abscess (22%).

All of our patients had ultrasonographic examination of breast. Ultrasonographic findings were abscesses or microabscesses that tend to confluence, which was present in more than half of the patients. Other ultrasound findings were fistula tracts; large, isolated abscesses; irregular hypoechoic mass, skin thickening, axillary lymphadenopathy.

All patients had undergone tissue biopsy. 50(70%) of our patients had tru-cut biopsy, 10(13%) of them had incisional biopsy, and 12(17/%) of our patients had pathologic examination of segmental mastectomy material.

Patients were divided into 3 treatment groups: Patients treated with antibiotics were in one group, patients treated with corticosteroids were in another group, and patients treated with segmental mastectomy were the other. Among the 72 patients evaluated, 40 patients had complete remission, rest, 32 patients had recurrences. Of those patients who had complete remission, 28 were treated with antibiotics, 6 were treated with corticosteroids, and 6 were treated with segmental mastectomy. 32 patients, who had recurrences, were also treated with antibiotics, corticosteroids and segmental mastectomy. 20 of them were treated with antibiotics, 7 of them were treated with corticosteroids, and 5 of them were treated with segmental mastectomy. None of the patients treated with corticosteroids had recurrence, 1 of 5 patients treated with segmental mastectomy had recurrence, and 9 of 20 patients treated with antibiotics had their second recurrence. These 9 patients with second recurrence were also treated with antibiotics, corticosteroids and segmental mastectomy. 5 of them were treated with antibiotics, 3 of them were treated with corticosteroids and 1 of them was treated with segmental mastectomy. Finally, all patients had remission.

Discussion

In this study, different treatment methods for IGM have been compared, presenting symptoms, signs and ultrasonographic findings as well as diagnostic tools for IGM are also discussed.

Granulomatous mastitis is a rare disease of the breast, which is characterized by an inflammatory breast mass that is difficult to differentiate from breast cancer. Several agents can cause granulomatous mastitis like sarcoidosis, tuberculosis, foreign materials and infections. Idiopathic Granulomatous mastitis is a diagnosis of exclusion, i.e., other etiologic factors have to be ruled out to make the diagnosis of IGM. IGM especially occurs in women at their childbearing age. In our study, the youngest patient was 23 years old, and the oldest patient was 68 years old. 8 patients were at menopause; the remaining 64 patients were at their reproductive ages. The youngest patient in our series was 12 years old, which was excluded from the study because of not being suitable for the inclusion criteria of our study.

The presenting symptoms were palpable mass, ulcerative skin lesions, fistula, pain, and nipple retraction [7, 9]. It may be unilateral or bilateral. In our study, the most common symptom was mass lesion, which was present in all (100%) of our patients. The second most common symptom was erythema which was present in 23(32%) of our patients. 11(15%) patients had pain, 6(9%) patients had spontaneous draining fistulas, 6(9%) patients had ulcerative skin lesions. All of our patients were women, and all lesions were unilateral.

Table 1: Clinical Findings in IGM

Palpable mass	72(100%)
Pain	11(15%)
Erythema	23(32%)
Spontaneous draining fistula	6(8%)
Ulcerative skin lesion	6(8%)
Abscess	16(22%)

Gürleyik *et al* stated that the most common symptom was mass lesion which was seen in 79 % of patients in their study [1]. Montazer declared that the most common symptom was painful mass lesion [6]. Manogna stated that the most common complaint was breast mass(n=23) and 14 of them had accompanying pain [7]. Larsen stated that the most common symptom was mass lesion which was seen in 89% of their patients and pain, erythema, and inflammation were seen in 11% [5]. A study from Iran, Aghajanzadeh M. *et al*, observed 206 patients and the most common symptom was found to be breast mass which was found in 168 of 206 patients [14].

Etiology of IGM is unclear. It can be an autoimmune disease as it gives a good response to corticosteroid therapy. It has been associated with other autoimmune diseases like erythema nodosum, Wegener's granulomatosis, polyarteritis nodosa [2, 9, 15]. Although it is thought that there is an autoimmune relation, most of the patients do not have an autoimmune disease. Only two of our patients had autoimmune diseases. One of them had erythema nodosum, the other one had rheumatoid arthritis.

Ethnicity may play a role since nearly all studies are from Asia and Mediterranean region [6]. 206 patients were reported from Iran, 154 patients were reported from Turkey, 35 patients were reported from India, 93 patients were reported from Turkey [14, 12, 7, 8]. 30 patients were reported from Iran [6]. Studies from europe are review articles and meta-analysis [15].

The radiologic findings of IGM on mammography, ultrasound and MRI are similar to breast cancer and are not specific for IGM [5, 7, 15]. On mammography, an irregular mass lesion, or large focal asymmetric density, or diffusely increased density of the affected breast are seen [5]. On ultrasonography, the most common finding is a large irregular hypoechoic mass with tubular extensions [5, 7, 16]. Confluent lesions are also reported as common findings, and with advanced disease, abscesses may be found [9, 16]. In our study, all our patients had ultrasonographic examination. Pathologic ultrasonographic features were present in all women. The most common ultrasonographic finding was abscesses or microabscesses tending to confluence, which was present in more than half of the patients. Other ultrasound findings were fistula tracts, large, isolated abscesses; irregular hypoechoic mass, skin thickening, axillary lymphadenopathy. MRI findings are also not diagnostic, but in the literature, it is reported to be more specific than other radiologic examinations [7, 9, 16]. Although MRI is reported to be more specific, clinical examination of the patient and USG findings are enough to recall IGM to mind.

Definitive diagnosis is made on tissue biopsy. In the literature, on pathologic examination, lobulocentric non-necrotizing granulomas are seen [5, 10, 15]. There may be coalescence of granulomas and microabscesses [7]. In our study, 50 of our patients underwent tru-cut biopsy, 10 patients had abscess drainage together with incisional biopsy, and in 12 patient's segmental mastectomy material had been pathologically analyzed. On pathologic examination, non-caseating granulomas containing Langhans giant cells and histiocytes were detected. Neutrophilic microabscesses were also seen in many of our patients.

There is no accepted standard therapy for IGM. Treatment preferences have been more invasive in the previous 10 years, but more conservative treatments are tending to be used instead of surgical treatment which has included large excision of the infected parts of the breast. All of our patients were given broad spectrum antibiotics on their first hospital admission as the clinical presentation of the disease was similar to mastitis. Ultrasonographic examination was made to detect any abscess that might need drainage. In the presence of a large abscess, they were drained either with needle aspiration or surgically. In case of drainage of the abscess with needle aspiration, biopsy was made by tru-cut. If the abscess was too dense to be drained by needle aspiration, it was surgically drained, and incisional biopsy was the preferred method for pathologic examination. Regardless of which method had been used for abscess drainage, the material was sent for microbiological examination. Then, in case of pathological diagnosis of IGM, oral corticosteroid treatment with 30 mg prednisolone twice a day started. The dose was tapered gradually every two weeks according to the response to treatment on hospital recall. The duration of treatment ranged between a minimum of 8 weeks and a maximum of 6 months. Patients who refused corticosteroid treatment and had symptom relief following antibiotics were observed and had been informed about high rate of recurrence. Patients who refused corticosteroid treatment and had persistent symptoms were treated with segmental mastectomy.

This study aims to evaluate the effectiveness of treatment groups. In our study, 72 patients are retrospectively analyzed. They are divided into 3 groups according to the treatment modality that has been used: 1) Patients treated with antibiotics, 2) Patients treated with corticosteroids, 3) Patients treated with segmental mastectomy. Complete remission rate and recurrence rate of each group are evaluated. Complete remission criteria are loss of patient's symptoms, loss of signs of IGM on physical examination and on ultrasonography. Minimum observation time was 10 months, and maximum observation time was 8 years. 40 patients had complete remission, and 32 patients had recurrence. Of these 40 patients that had complete remission, 28 of them were treated with antibiotics, 6 of them were treated with corticosteroids, 6 of them were treated with segmental mastectomy. All of the patients that had recurrences (32), had had antibiotics treatment as initial therapy. After the recurrence, 20 of 32 patients were treated with antibiotics, 7 of them were treated with steroids, 5 of them were treated with segmental mastectomy. If we look at the whole and compare the first recurrence in all treatment groups. 60 patients were treated with antibiotics and 32 of them had recurrence, 6 patients in corticosteroid group and 6 patients in segmental mastectomy group did not have any recurrence. The recurrence rate in the antibiotics group was statistically significant($p<0, 001$).

Table 2: Recurrence rates of IGM according to treatment groups

			First Recurrence		p
			Recurrence (n=32)	**No recurrence (n=40)**	
Treatment Groups	Antibiotics (n=60)	n	32	28	0, 001**
		%	53, 2	46, 7	
	Corticosteroid (n=6)	n	0	6	
		%	0	100	
	Segmental Mastectomy(n=6)	n	0	6	
		%	0	100	

Fisher Freeman Halton test ***p<0, 01*

In the antibiotic group, 9 patients developed second recurrence, in corticosteroid group all of the patients had complete remission, in segmental mastectomy group, 1 of 5 patients developed second recurrence.

Table 3: Second recurrence rates in IGM treatment groups

			2nd Recurrence		p
			Yes(n=10)	**No (n=22)**	
Treatment Groups	Antibiotics (n=20)	n	9	11	0, 070
		%	45, 0%	55, 0%	
	Corticosteroids (n=7)	n	0	7	
		%	0	100%	
	Segmental Mastectomy (n=5)	n	1	4	
		%	20, 0%	80, 0%	

Fisher Freeman Halton test

5 of the 9 patients having a second recurrence in the antibiotics group were treated with antibiotics, 3 of the 9 patients in this group were treated with corticosteroids, and 1 of them was treated with segmental mastectomy. All of them had complete remission finally. 1 of the second recurrence in the segmental mastectomy group was treated with antibiotics and had complete remission. One of our patients had rheumatoid arthritis after 1, 5 months of oral corticosteroid treatment, her lesion regressed nearly totally, we referred her to our rheumatology clinic and corticosteroids are replaced by methotrexate and her breast lesion disappeared in two months, but methotrexate treatment lasted 1 year. She didn't have IGM relapse.

In 1980, DeHertogh *et al*. were the first to recommend corticosteroids as a treatment option and stated that skin ulcerations at the site of surgery and recurrency were frequent problems in cases of surgical management [17]. In 2011, Gurleyik *et al*. stated that they treated their patients with a combination of oral corticosteroids and surgery. First, they administered steroids that led the lesion to get smaller and they said that this gave the advantage ol more limited surgery [1]. In 2012, Kayahan *et al*. stated that both surgery and steroids were effective methods [18]. In 2015, Aghajanzadeh *et al*. from İran, studied a large patient population, 206 patients, which is a quite high number for such a rare disease, stated that corticosteroids were their first choice of treatment [14]. In 2016, Tahmasebi *et al*. stated that oral corticosteroids were a good treatment alternative that provide complete remission [13]. In 2017, Xin Lei *et al*. compared surgery, steroid and surgery+ steroid in his systematic review and meta-analysis and stated that all methods have success rate >70%. For patients who require rapid remission, surgery was suitable option, and for patients who had concerns about surgical scarring, oral steroids were an acceptable option [11]. In 2018, Wolfrum *et al*. stated that high dose steroid (30 mg twice a day) was highly effective, and surgery could be used in case of insufficient response [15]. In 2019, Montazer *et al*. compared low-dose and high-dose oral corticosteroid treatment and concluded that high- dose steroids resulted in high success rates and was a good alternative for surgery [6]. In 2020, Yüksekdağ *et al*.from Turkey, studied a large population also, which is 154 patients and stated that surgical resections were overtreatment, and antibiotics, abscess drainage and corticosteroids were successful in IGM treatment and in case of recurrent lesions, a second cycle could be tried, which gave good results[12] In 2020 Zhou *et al*. compared conservative methods with surgery and concluded that there was no significant difference in recurrence between the two groups[10]. In 2021, Kafadar *et al*. stated that low dose methotrexate in combination with steroids could be used in patients who were refractory to steroids, and this was an alternative to surgery in refractory cases [19]. In 2021, Toktaş *et al*. stated that pregnant women treated with intralesional corticosteroids together with topical steroids in cases with skin involvement achieved complete remission [20].

IGM is a benign disease that was treated only with surgery in the past. As the disease was found to have an autoimmune basis, alternative treatment methods gained currency, and oral corticosteroids gave good results. As steroids have many unwanted side effects, local steroid injections and other immune regulatory agents like methotrexate and colchicine have been tried and they also gave satisfactory results. Surgery is more likely to be totally replaced by immune regulatory agents in the near future.

Conclusion

In our center, a study which covered the period between 2008-2013 demonstrated that surgery and steroids had similar recurrence rates which was better than abscess drainage group [4]. In our recent study, the result is similar also, but steroids are found to be more effective. The difference may come from close patient follow-up and informing the patient about the side effects, decreasing the side effects with diet regulation and medications. We think that this increases the patient's compliance with treatment.

Conflict of Interest: Özlem Okur, Jülide Sağıroğlu, Mehmet Acar and Orhan Alimoğlu declares that they have no conflict of interest.

Ethics Committee: The manuscript studies have been approved by the appropriate ethics committee and have been performed in accordance with ethical standards laid down in Declaration of Helsinki and its later amendments.

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