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Results of 78 Patients with Idiopathic Granulomatous Mastitis Who Received Peroral Steroid Therapy: Our Clinical Experience

Fatih Dal, Hasan Ökmen

University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of General Surgery, İstanbul, Turkey

ABSTRACT

Introduction: For approximately half a century, synthetic steroids have been the most commonly used medical treatment for idiopathic granulomatous mastitis (IGM). We present the outcomes of patients who experienced relapse after systemic peroral steroid treatment (SPST) and achieved remission.

Methods: This study included a total of 78 patients who were diagnosed with IGM and started on SPST from 2010 to 2020.

Results: The mean age of the patients included in the study was 33.4±6.8 years (minimum-maximum: 19.0-53.0 years) and 94.9% of all patients were premenopausal. After the clinicalopathological diagnosis, while complete remission was achieved in 46.2% of the patients receiving SPST at the first session, 53.8% showed resistance to therapy and/or had a relapse. In the group of patients who experienced relapse, the rate of bilateral disease, abscess drainage, and secondary side effects of SPST were significantly higher ($p<0.05$). Of the patients who showed resistance to treatment and/or experienced relapse, 39.7% (31 of 78) achieved remission after a combination of medical treatments and 14.1% (11 of 78) achieved remission after a combination of medical and surgical treatments.

Conclusion: In patients with clinical-radiological presentation of abscess and/or bilateral disease before treatment, the disease tends to have an aggressive course and the frequency of secondary side effects of SPST is higher. These patients should be informed about the risk of relapse, side effects, and combined treatments, and they should be followed up more closely.

Keywords: Breast, idiopathic granulomatous mastitis, steroid, recurrence, risk factor

Introduction

Idiopathic granulomatous mastitis (IGM) is a rare benign disease of the breast. IGM was first defined by Kessler Wolloch in 1972 (1-4). Although the annual prevalence of IGM in the literature is reported to be 2.4 per 100,000 women aged between 20 and 40 years of age, there are large case series reported worldwide, mostly from Eurasian countries (1,3,5).

IGM is diagnosed by ruling out a specific etiology through clinical and pathological means. In terms of differential diagnosis, it can be confused with breast cancers, as well as pyogenic and specific granulomatous mastitis of the breast [infectious specific granulomatous mastitis (such as breast tuberculosis and bacterial, fungal, and parasitic granulomatous mastitis) and non-infectious specific granulomatous mastitis (such as breast sarcoidosis, Wegener's granulomatosis, giant cell arteritis, foreign body, ductal ectasia, fat necrosis, and sclerosing lymphogranulomatous mastitis)] (1-4,6-8).

There are many hypotheses regarding the pathophysiology of the disease. These are the secretion theory, the autoimmune theory, and the geographic or ethnic hypothesis, respectively. Therefore, although a definitive relationship cannot be established, autoimmune diseases, hyperprolactinemia, hormonal imbalances, oral contraceptive (OCP) use, trauma, local irritants, lactation, parity, type 2 diabetes mellitus, smoking, ductal ectasia, and antipsychotic drug use are suggested as predisposing risk factors in etiopathogenesis (2,3,6-12).

Patients diagnosed with IGM based on clinical and pathological findings can be managed with various treatment options, including the watch-and-wait approach and the use of steroids, methotrexate (MTX), azathioprine, bromocriptine, colchicine, non-steroidal anti-inflammatory drugs (NSAIDs), surgical approaches (partial or total mastectomy), and/or combination therapies (2,3,6-10,13-16). Despite the availability of different treatment methods, steroids are currently the most commonly used treatment method for IGM (13-15). In clinical practice, the most commonly used steroid preparations are prednisone, prednisolone, and methylprednisolone, each with varying levels of potency. According to the literature, the equivalent doses of these medications are 20 mg of hydrocortisone, 5 mg of prednisone, 5 mg of prednisolone, and 4mg of methylprednisolone. The daily doses of prednisone are classified into low dose (<7.5 mg/day), medium dose (7.5-30 mg/day), high dose (30-

Address for Correspondence: Fatih Dal MD, University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of General Surgery, İstanbul, Turkey
Phone: +90 507 816 90 65 **E-mail:** fatihdal07@gmail.com **ORCID ID:** orcid.org/0000-0002-9768-8125

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100 mg/day), very high dose (>100 mg/day) and pulse therapy (≥250 mg/day) in clinical practice (17,18).

According to the literature, recurrence rates of the disease vary between 0% and 100%, depending on different clinical manifestations and treatment methods reported in various studies (3,6-10,13,19,20). Our aim is to present the outcomes of patients who experienced relapse after SPST between 2010 and 2020 and achieved remission.

Methods

This study was conducted in line with the ethical standards defined by the Institutional Research Committee and the 1964 Helsinki Declaration. Ethics committee approval for the study was obtained from the University of Health Sciences Turkey, İstanbul Training and Research Hospital Local Ethics Committee (approval number: 116, date: 12.05.2023).

Patient selection: We retrospectively reviewed the data of patients aged 18 years and older (n=84) whose IGM diagnosis was confirmed based on histopathological and microbiological findings and who gave consent to SPST in our clinic between 2010 and 2020. The study included patients (n=78) who received at least one course of SPST and had at least one follow-up visit after completion of treatment. Patients (n=6) who were non-compliant with treatment were excluded from the study.

Diagnosis, treatment, follow-up, and data collection: Before treatment, we reviewed the medical records of the patients to collect information on their coexisting systemic diseases, demographic data, physical examination findings, viral hepatitis, brucellosis (Rose Bengal plaque agglutination test), antinuclear antibodies, anti-ds DNA, hyperprolactinemia, rheumatoid factor, non-specific acute phase reactants, hemogram index parameters (HIP), and basic biochemical tests. Radiological assessments were performed to evaluate sarcoidosis and exposure to *Mycobacterium tuberculosis*, including chest X-rays. Breast ultrasound and/or magnetic resonance imaging (MRI) were used to assess the extent of the disease, and mammography results were reviewed for patients over the age of 40 (1-3,6,11,12,21).

The patients' tissue biopsies (tru-cut or abscess wall); were examined for the presence of non-caseating granulomas, along with lymphocytes, plasma cells, and epithelioid histiocytes that were rarely accompanied by eosinophils in and around the lobules, as well as Langhans giant cells. The presence of microorganisms (by gram staining for bacteria, periodic acid-Schiff staining for fungi, Erlich-Ziehl-Neelsen staining/polymerase chain reaction for tuberculosis) and the absence of a specific etiology were also checked. Additionally, microbial negativity was recorded by culturing and microscopically examining tissue biopsies for fungal, parasitic, and bacterial infections (1-4,6,14).

Patients with acute mastitis symptoms were treated with empirical antibiotic therapy and NSAIDs for 10-15 days until laboratory results were obtained. Those with abscesses received drainage either percutaneously or through an incision. Patients who were confirmed to have IGM after histopathological and microbiological evaluations and gave consent for SPST were started on medium-/high-dose prednisolone (0.5-1 mg/kg/day). The drug dose was gradually reduced after treatment. To prevent the side effects of steroids during treatment, patients were advised to take calcium and vitamin D supplements, proton pump inhibitors, and restrict their intake of salt and carbohydrates (2,3,6,15,17,18). After treatment, the complete disappearance of the mass, inflammation, fistula, and skin lesions in the breast and the absence of disease recurrence were defined as remission. During treatment, the persistence of the disease or its recurrence after treatment was considered a relapse. In addition, the development of IGM in the contralateral breast after treatment was considered a relapse.

The patients who experienced relapse were offered treatment options including a second round of SPST, SPST + MTX, watch and wait, and surgical treatment. Once they gave their consent, the treatment of choice was initiated. MTX treatment was initiated after a short course (3 weeks) of SPST. The patients received a divided dose of 15 mg/week for 6 months. During the treatment, patients were advised to follow a low-carbohydrate and low-salt diet to minimize the side effects of steroids and MTX. Additionally, they were started on calcium, vitamin D, PP, and folic acid to protect against adverse effects. Furthermore, due to the toxic side effects of MTX, hemogram and biochemistry tests were performed every two months to check patients' well-being. In the watch-and-wait method, the patients were followed up using empirical antibiotherapy, NSAIDs, and drainage (percutaneous or incisional) in case of mastitis and/or breast abscess. Our surgical treatment recommendation was either partial or total mastectomy with sound surgical margins based on the extent of the disease (2,3,6-10,13-18).

Study design: The patients' HIP, demographic characteristics, and pre-and post-treatment options were recorded. The examination findings were recorded according to the initial presentation side, and the measurement of lesion sizes was performed based on the largest inflamed tumor after clinical and radiological evaluation. After the first session of SPST, patients were grouped based on those who achieved remission and those who were resistant to treatment and/or experienced relapse and were then compared.

Statistical Analysis

We used descriptive statistics of the mean, standard deviation, median, minimum, maximum, frequency, and ratio. The Kolmogorov-Smirnov test was used to measure the distribution of the variables. The independent sample t-test and the Mann-Whitney U test were employed in the analysis of quantitative independent data. Quantitative independent data were analyzed using the chi-square test, but when the conditions for the chi-square test were not met, we used the Fisher's exact test. The SPSS 28.0 program was used for the analyses.

Results

The mean age of the patients included in the study was 33.4±6.8 years (minimum-maximum: 19.0-53.0 years) and 94.9% of all patients were in premenopause. In patients' medical history, 17.9% reported smoking, 14.1% had a history of OCP use, and 92.3% had at least one pregnancy and lactation history. The prevalence of accompanying chronic diseases was 15.4%, with a distribution of 7.7% autoimmune diseases [Hashimoto's thyroiditis (n=4), rheumatoid arthritis (n=2)], 3.8% hypertension (n=3), and 3.8% other disorders [chronic obstructive pulmonary disease (n=1), migraine (n=1), and anemia (n=1)]. In our study group, 55.1% of the cases had IGM originating from the left breast.

The most common symptom and finding was a breast mass with an average size of 5.9±2.6 cm. The distribution of other symptoms and findings was as follows: 98.7% inflammation, 79.5% abscess, 70.5% fistula, and 16.7% nipple retraction. Physical examination findings were evaluated radiologically using US in 100% of cases, MRI in 69.2%, and MG in 11.5% of patients over the age of 40 (Table 1).

Tissue biopsies for histopathological and microbiological diagnosis were obtained from the abscess wall through a mini-incision in 16.7% of cases

Table 1. Distribution of patients receiving peroral systemic steroid therapy after histopathological and microbiological diagnosis

		Min.-Max.	Median	Mean ± SD -%(n)/%(n)
Age		19.0-53.0	32.5	33.4±6.8
Menopause status	Premenopause/ postmenopause			94.9 (74)/5.1 (4)
History of giving birth and breastfeeding	+/-			92.3 (72)/6.4 (5)
Smoking	+/-			17.9 (14)/80.8 (63)
Oral contraceptive	+/-			14.1 (11)/85.9 (67)
Chronic disease	+/-			15.4 (12)/84.6 (74)
	Autoimmune disease			7.7 (6)
	Hypertension			3.8 (3)
	Other diseases			3.8 (3)
Side	Right/left/bilateral			37.2 (29)/55.1 (43)/7.7 (6)
Mass size (cm)		1.5-15.0	5.9	5.9±2.6
Mass	+/-			100 (100)/0 (0)
İnflammation	+/-			98.7 (77)/1.3 (1)
Fistula	+/-			70.5 (55)/29.5 (23)
Nipple retraction	+/-			16.7 (13)/83.3 (65)
Abscess drainage	+/-			79.5 (62)/20.5 (16)
Tissue diagnosis	Abscess wall/tru-cut			16.7 (13)/83.3 (65)
Radiological imaging	US/MRI/MG			100 (78)/69.2 (54)/11.5 (9)
WBC ($x10^9$/L)		4.0-20.0	8.8	8.9±2.8
Neutrophil ($x10^9$/L)		2.2-18.1	5.8	6.1±2.7
Lymphocyte ($x10^9$/L)		0.8-3.5	2.0	2.1±0.7
Monocyte ($x10^9$/L)		0.04-1.08	0.53	0.55±0.21
Basophil ($x10^9$/L)		0.01-0.4	0.03	0.04±0.07
Platelets ($x10^9$/L)		168.0-595.0	302.5	313.0±80.0
NLR		1.19-17.85	2.79	3.48±2.74
PLR		67.6-461.9	146.9	169.1±75.7
LMR		1.3-21.0	3.8	4.3±2.6
LBR		3.9-314.8	82.2	91.7±55.6
CRP (mg/dL)		0.0-78.9	0.8	4.6±12.3
Sedimentation (mm/h)		7.0-106.0	33.0	41.3±25.2
Prednisolone dosage (mg/day)		20.0-90.0	60.0	55.9±17.8
Initial prednisolone time (month)		0.7-2.0	1.0	1.1±0.3
Prednisolone discontinuation time (month)		0.7-4.3	1.4	1.5±0.8
Total prednisolone treatment time (month)		1.4-5.3	2.5	2.6±0.9
Follow-up time (month)		0.5-124.3	60.6	60.5±29.0
Prednisolone side effects	+/-			60.3 (47)/39.7 (31)
	Edema			42.3 (33)
	Hirsutism			6.4 (5)
	Buffalo humb			1.3 (1)
	Arthralgia			7.7 (6)
	Menstrual irregularity			2.6 (2)
Remission/recurrence				46.2 (36)/53.8 (42)

WBC: White blood cells ($x10^9$/L), NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, LMR: Lymphocyte to monocyte ratio, LBR: Lymphocyte to basophil ratio, CRP (mg/dL): C-reactive protein, US: Ultrasonography, MRI: Magnetic resonance imaging, MG: Mammography, Min.: Minimum, Max.: Maximum, SD: Standard deviation

and by tru-cut biopsy in 83.3% of cases. Seventy-seven patients (98.7%) with symptoms of acute mastitis were started on empiric antibiotic therapy and NSAIDs for 10-15 days until their sterility was confirmed by culture and microbiological tests. Sixty-two patients (79.5%) requiring drainage underwent abscess drainage [percutaneous (n=49), mini-incision (n=13)] (Table 1).

For patients in whom no descriptive etiology was found in the tissue samples obtained, oral prednisolone was started at an average dose of 55.9±17.8 mg/day for 1.1±0.3 months in the first session. SPST was gradually discontinued over an average of 1.5±0.8 months. During the treatment, 60.3% of the patients experienced side effects related to the use of steroids. The distribution of side effects was as follows: 42.3% edema, 7.7% arthralgia, 6.4% hirsutism, 2.6% menstrual irregularity, and 1.3% buffalo hump (Table 1).

After clinical and pathological diagnosis, remission was achieved in 46.2% of patients after the first session of treatment, 83.3% after the second session, and 100% after the third session. Partial mastectomy was performed in 14.1% of patients. After the first session of SPST treatment, the rate of bilateral disease, abscess, and secondary side effects due to steroid treatment were significantly higher ($p<0.05$) in the group (53.8%) who were resistant to treatment and/or had a relapse following treatment. There was no significant difference ($p>0.05$) between the patients regarding non-specific acute phase reactants and HIP. Of the patients who showed resistance to treatment and/or experienced relapse, 39.7% (31 of 78) achieved remission after a combination of medical treatments and 14.1% (11 of 78) achieved remission after a combination of medical and surgical treatments (Table 2-4).

Discussion

Although it has been reported in the literature that IGM can occur in all age groups, including children and the elderly (from 11 to 83 years of age), it most commonly presents with a unilateral or bilateral mass in women of reproductive age. In addition to the mass, inflammation,

Table 2. Comparison of clinical data and blood tests between groups before the first session peroral steroid treatments

		Remission		Recurrence		p
		Median	Mean ± SD -%(n)/%(n)	Median	Mean ± SD -%(n)/%(n)	
Age		32.5	33.0±6.5	32.5	33.7±7.1	0.623[t]
Menopause status	Premenopause/ postmenopause		94.4 (34)/5.6 (2)		95.2 (40)/4.8 (2)	1.000[x2]
Birth history and breastfeeding	+/-		97.2 (35)/2.8 (1)		88.1 (37)/9.5% (4)	0.215[x2]
Smoking	+/-		19.4 (7)/80.6 (29)		16.7 (7)/81.0 (34)	0.788[x2]
Oral contraceptive	+/-		19.4 (7)/80.6 (29)		9.5 (4)/90.5 (38)	0.209[x2]
Chronic disease	+/-		16.7 (6)/83.3 (30)		14.3 (6)/85.7 (36)	0.771[x2]
Side	Right/left/bilateral*		47.2 (17)/52.8 (19)/0 (0)		28.6 (12)/57.1 (24)/14.3 (6)	0.030[x2]
Mass size (cm)		5.8	5.7±2.5	5.9	6.1±2.7	0.588[m]
Mass	+/-		100 (36)/0 (0)		100 (42)/0 (0)	1.000[x2]
İnflammation	+/-		97.2 (35)/2.8 (1)		100 (42)/0 (0)	0.462[x2]
Fistula	+/-		66.7 (24)/33.3 (12)		73.8 (31)/26.2 (11)	0.490[x2]
Nipple retraction	+/-		19.4 (7)/80.6 (29)		14.3 (6)/85.7 (36)	0.542[x2]
Abscess drainage	+/-		61.1 (22)/38.9 (14)		95.2 (40)/4.8 (2)	0.000[x2]
Tissue diagnosis	Abscess wall/tru-cut		11.1 (4)/88.9 (32)		21.4 (9)/78.6 (33)	
Radiological imaging	US/MRI/MG		100 (36)/72.2 (26)/13.9 (5)		100 (42)/66.7 (28)/9.5 (4)	
WBC ($x10^9$/L)		8.2	8.9±2.7	9.1	8.9±2.9	0.819[m]
Neutrophil ($x10^9$/L)		5.3	6.0±2.6	6.3	6.2±2.8	0.772[m]
Lymphocyte ($x10^9$/L)		2.1	2.2±0.7	1.9	2.0±0.6	0.190[t]
Monocyte ($x10^9$/L)		0.53	0.54±0.22	0.53	0.56±0.2	0.612[t]
Basophil ($x10^9$/L)		0.03	0.04±0.07	0.02	0.04±0.07	0.238[m]
Platelets ($x10^9$/L)		319.5	3192±72.4	282.5	308.2±85.9	0.259[m]
NLR		2.7	3.3±3.0	2.8	3.6±2.6	0.383[m]
PLR		146.9	163.4±77.9	150.0	173.4±74.7	0.527[m]
LMR		4.2	4.9±3.4	3.6	3.9±1.7	0.099[m]
LBR		77.3	96.0±69.5	85.0	88.5±42.8	0.694[m]
CRP (mg/dL)		1.0	7.3±17.9	0.8	2.4±3.5	0.805[m]
Sedimentation (mm/h)		27.0	34.3±22.1	39.8	46.3±26.5	0.083[t]

[t]: T-test, m: Mann-Whitney U test, [x2]: Chi-square (Fisher's test), WBC: White blood cells ($x10^9$/L), NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, LMR: Lymphocyte to monocyte ratio, LBR: Lymphocyte to basophil ratio, CRP (mg/dL): C-reactive protein, US: Ultrasonography, MRI: Magnetic resonance imaging, MG: Mammography

abscess, ulceration, fistula, nipple retraction, and erythema nodosum can accompany IGM (1-3,6,8,13,14,19,20). These symptoms can also present in breast cancers, pyogenic, and specific granulomatous mastitis (1-4,6-8). The initial radiological evaluation was performed using breast US. With US, the size of the mass, area of inflammation, abscess, sinus formation, and axillary lymphadenopathy can be evaluated in the breast. Additionally, US is a good guide for biopsy and a useful method for follow-up after percutaneous abscess drainage and treatment. In MG requested for screening malignancies in patients over the age of 40, there may be findings of thickening of the skin, distortion, asymmetry (focal/diffuse), and calcification. When the extent of the disease is not adequately assessed by MG and/or US, MRI can be used. However, although radiological methods are useful in the diagnosis of the disease, they cannot clearly distinguish malignancy. The diagnosis of the disease is made by excluding a descriptive etiology after a histopathological, microbiological, and clinical evaluation (1-4,6-10,13-16,19-21).

Our study is consistent with the literature, as the average age of the patients was 33.4±6.8 years years and 94.9% were premenopausal. The most common physical examination finding was a breast mass, and all patients were evaluated with breast US. Tissue biopsies for histopathological and microbiological examination were obtained using a tru-cut needle in 83.3% and from the abscess wall in 16.7% of the patients.

Although 60 years have passed since its first description, the pathophysiology of the disease remains unclear. While IGM is generally regarded as a self-limiting, slowly resolving, benign inflammatory disease in the literature, the management of recurrent and persistent symptoms is still controversial. There is no consensus on the treatment of IGM, where the aim is to achieve the fastest recovery and the lowest recurrence rate after clinical and pathological diagnosis (2,6,7,13,14,16). Prior to 1980, aggressive surgical treatment methods were dominant. However, during this period, the problem was the risk of recurrence due to inadequate partial mastectomy, and the problem was cosmetic dissatisfaction with extensive partial mastectomy. After 1980, with the introduction of immunosuppressive agents, surgical treatment was replaced by medical treatments, the watch-and-wait method, and/or their combinations. Among medical treatments, steroids are the most commonly used anti-inflammatory and immunosuppressive agents (3,6,7,13-16,21,22). In addition to their immunosuppressive effects, steroids also have effects on the hematopoietic, urinary, cardiovascular, and central nervous systems as well as on endocrinological and calcium, lipid, glucose, and protein metabolism (17,18). As a result of using moderate to high doses of systemic glucocorticoids orally, patients may experience side effects such as edema (weight gain), Cushing syndrome, hirsutism, diabetes, and osteoporosis at rates ranging from 0 to 81.3% (9,11,14,21-23). In our study, 60.3% of patients experienced side effects, with edema being the most common affecting 42.3% of patients.

Table 3. Comparison of the first session peroral steroid treatments and side effects between groups

		Remission		Recurrence		p
		Median	Mean ± SD -%(n)/%(n)	Median	Mean ± SD -%(n)/%(n)	
Prednisolone dosage (mg/day)		50.0	52.8±16.1	60.0	58.6±18.9	0.150[m]
Initial prednisolone time (month)		1.0	1.1±0.3	1.0	1.1±0.4	0.875[m]
Prednisolone discontinuation time (month)		1.4	1.5±0.7	1.3	1.6±0.8	0.417[m]
Total prednisolone treatment time (month)		2.3	2.5±0.9	2.7	2.6±0.9	0.640[m]
Follow-up time (month)		59.7	58.2±32.2	61.5	62.4±26.0	0.523[t]
Prednisolone side effects	+/-		47.2 (17)/52.8 (19)		71.4 (30)/28.6 (12)	0.029[x2]

[t]: T-test, [m]: Mann-Whitney U test, [x2]: Chi-square (Fisher's test).

Table 4. After histopathological and microbiological diagnosis, 1st session, 2nd session, 3rd session treatment distribution

	Treatment		Medical/surgical	Recurrence	Remission	Total remission
			% (n)/% (n)	% (n)	%(n)	% (n)
After clinicalopathological diagnosis	1st	P	100 (78)/0 (0)	53.8 (42)	46.2 (36)	46.2 (36)
	2nd	P/P	93.6 (73)/6.4 (5)	9.2 (8)	7.7 (6)	83.3 (65)
		P/SO		1.3 (1)	6.4 (5)	
		P/W-W		1.3 (1)	17.9 (14)	
		P/P + MTX		3.8 (3)	5.1 (4)	
	3rd	P/P/SO	85.9 (67)/14.1 (11)	0.0 (0)	3.8 (3)	100 (78)
		P/P/W-W		0.0 (0)	5.1 (4)	
		P/P + MTX/SO		0.0 (0)	1.3 (1)	
		P/SO/W-W		0.0 (0)	1.3 (1)	
		P/W-W/SO		0.0 (0)	1.3 (1)	
		P/P + MTX/W-W		0.0 (0)	3.8 (3)	

P: Systemic peroral prednisolone therapy or systemic peroral steroid therapy, MTX: Methotrexate, SO: Surgical operation, W-W: Watch and wait

There is no standard treatment approach for IGM, which is a sterile disease, and antibiotics play no role in managing this condition. However, until a definite diagnosis of the disease is made based on clinical and pathological findings, EA may be recommended for patients with clinical signs of mastitis, and drainage (percutaneous or incisional) may be recommended in the presence of an abscess. In addition, antibiotherapy and drainage may also be effective in case of clinical aggravation secondary to contamination from fistulas and ulcerative lesions or in the management of recurrent abscesses following medical treatment after clinical-pathological diagnosis (2,3,6,7,13,16,19,22). In this study, inflammation was present in 98.7% of patients and abscess drainage [percutaneous (n=49), mini-incision (n=13)] was performed in 79.5% of patients before clinical-pathological diagnosis. Due to the 2-week period needed for clinicalopathologic diagnosis in our clinic, short-term empirical antibiotic therapy and NSAIDs were initiated for 98.7% (n=77) of these patients presenting with acute mastitis symptoms. However, after confirming the sterility status, antibiotic and NSAID treatments were discontinued and SPSTs were rearranged.

The disease may present as a non-complicated inflammatory solitary mass or with complicated mastitis symptoms such as an abscess or fistula accompanying the mass in the breast. In 2021, Toktas et al. (14) reported that local steroid treatment is an effective treatment method in patients with non-complicated IGM. It was reported in the study by Ertürk et al. (24) that local steroid therapy was effective for non-complicated lesions smaller than 3 cm, but less effective for complicated lesions presenting with fistulas (39.5%) and abscesses (63.2%) and with a size of 3 cm or larger. According to the authors, this was due to the inability to provide sufficient steroid dosage in patients with fistulas and the re-formation of abscesses after injection in patients with abscesses (24). According to Velidedeoglu et al. (6), in cases of non-omplicated IGM with non-mass or small lesions (lesion size <2 cm), it was enough to follow up with patients via the watch-and-wait approach or with NSAIDs. In a study conducted by Yaghan et al. (25) in 2019, patients were divided into groups based on their presentations as follows: mass (13.23%), inflamed mass (52.94%), abscess (26.47%), and skin lesions (ulcer, sinus, fistula) (7.35%) in the breast. No recurrence was observed in patients who only had a mass and underwent surgery. However, they observed recurrence in 50% of patients who presented with inflammation, abscess, or skin lesions and received both surgical and medical treatment (25). In the study by Tan et al. (20), before treatment, 100% of patients presented with a mass, 71.6% with inflammation, 54.5% with abscess, and 19.38% with fistula. The size of the masses was distributed as follows: <2 cm in 4.5% of patients, ≥2 to <5 cm in 67.0%, and ≥5 cm in 28.4%. The study reported a response rate of 80.7% and clinical-radiological complete remission in 47.6% of patients after SPST. The authors reported that the masses that became smaller (lesion size <3 cm) were suitable for the watch-and-wait method or partial mastectomy (20). In our study, lesion size (average mass size 5.9±2.6 cm) and the incidence of acute mastitis (98.7%), breast abscess (79.5%), and breast skin symptoms (70.5%) were higher compared to the literature studies. However, our study was similar to the literature in that complete remission was achieved in 46.2% of the patients who received systemic treatment with peroral prednisolone in the first session after clinical and pathological diagnosis. After the additional second session (83.3%) and third session (100%) for patients who showed resistance to treatment and/or had recurrence, all patients achieved complete remission, and 14.1% of the patients underwent partial mastectomy.

IGM is a disease with a heterogeneous structure and determining the risk profile for recurrence in patients before treatment is important in the management of the disease. In the literature, clinical parameters associated with recurrence include undiagnosed breast infections, smoking, low vitamin B12 levels, accompanying rheumatic diseases, erythema nodosum, OCP, history of childbirth and breastfeeding, obesity, fistula, abscess, and luminal inflammation degree (7,26-28). Velidedeoglu et al. (19) observed at least one recurrence in all patients with bilateral IGM in 2016. Following additional combined treatments, complete remission was achieved in 90% (9/10) of these patients, while the disease remained static in one patient (19). In another study conducted by the same authors in 2022, there was no relationship between disease recurrence and factors such as breastfeeding, trauma, OCP use, and smoking (6). Similarly, Çetinkaya et al. (29) did not observe a relationship between age, body mass index (BMI), OCP use, tobacco use, and preoperative platelet to lymphocyte ratio (PLR) in patients who experienced recurrence after surgical treatment. However, the pre-operative neutrophil to lymphocyte ratio (NLR) was significantly associated with recurrence in that study (29). Similarly, in Kargın et al. (30), NLR before surgical and medical treatment was significantly higher in patients with recurrence. In 2022, Ciftci et al. (16) analyzed data from 85 patients they treated using different treatment modalities. It was revealed in the study that treatment methods, BMI, parity, HIP [white blood cells, neutrophil, lymphocyte, thrombocyte, NLR, PLR), C-reactive protein (CRP)], and sedimentation values were not associated with recurrence. According to the multivariate analysis, smoking and the albumin/globulin ratio were independent risk factors for recurrence. The authors reported that CRP, sedimentation and HIP was dynamic parameters that could change daily and be influenced by body fluid balance (15). As it is seen, there are different results regarding the identification of the risk profile of the patients in the literature due to the use of various treatment modalities, different study designs, patients' hemodynamics, which are subject to daily changes, and heterogenous clinical properties of the disease. In our study, the incidence rate of abscess and side effects secondary to treatment was significantly higher ($p<0.05$) in the group of patients who showed resistance to treatment and/or experienced recurrence (53.8%) in the first session of SPST and the side effects were the limitations of SPST. Of the patients who showed resistance to treatment and/or experienced relapse, 39.7% (31 of 78) achieved remission after a combination of medical treatments and 14.1% (11 of 78) achieved remission after a combination of medical and surgical treatments.

Study Limitations

This study has some limitations. First, the study data were retrospectively collected. Second, the sample size was small due to the rarity of IGM. Third, we could not evaluate erythema nodosum, albumin, globulin, albumin/globulin ratio, and BMI because of insufficient data in patients' medical records.

Conclusion

IGM is a benign chronic disease of the breast that is characterized by heterogeneous clinical findings and may have an aggressive course

from time to time. In patients with clinical-radiological presentation of abscess and/or bilateral disease before treatment, the disease tends to have an aggressive course and the frequency of secondary side effects of systemic peroral steroid therapy is higher. Combined medical and/or surgical treatments may be required for the management of the disease in these patients. For this reason, these patients should be informed about the risk of relapse, side effects, and combined treatments, and they should be followed up more closely.

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