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INTRALESIONAL STEROID THERAPY IN PATIENTS WITH IDIOPATHIC GRANULOMATOUS MASTITIS

Mesude Seda Aydoğdu[1], Ahmet Karataş[1], Hakan Artaş[2], İbrahim Gündüz[1], Süleyman Serdar Koca[1]

[1]Fırat University Faculty of Medicine, Department of Rheumatology, Elazığ, Turkey
[2]Fırat University Faculty of Medicine, Department of Radiology, Elazığ, Turkey

Abstract

Aim: Idiopathic granulomatous mastitis (IGM) is a rare chronic inflammatory breast disease. Histopathology is characterized by non-caseating granulomas. Although oral contraceptive use, pregnancy, breastfeeding history, high prolactin levels, smoking, and chemical irritation have been blamed for its etiology, it has not been fully elucidated. We studied the responses obtained using intralesional (IL) steroid application in addition to conventional treatments in patients with IGM referred to the rheumatology and radiology departments of Fırat University Research Hospital.

Material and Methods: Seventy-six female patients diagnosed with IGM who were followed between January 2021 and May 2023 were included in the study. The pathologies of the patients, whose average age was 36.5±6.8 years, were compatible with IGM. In terms of differential diagnoses, other conditions that could cause granulomatous mastitis were excluded. The data obtained were analyzed with appropriate statistical methods using statistical package for social sciences (SPSS) for Windows 25.

Results: Remission was achieved in 55.3% of patients (42 patients). While remission was observed in 61.6% of the patients who received IL steroids, remission was achieved in only 23.1% of the patients who did not receive IL steroids, and this rate was found to be statistically significant (p=0.010). There was no statistically significant difference between the treatments received by patients who achieved remission and those received by patients whose treatment continued (p>0.05).

Conclusion: In our study, the treatments received by patients who were and were not administered IL steroids were similar, but a significant difference was observed in patients who were administered IL steroids in terms of achieving remission. This suggested that IL steroid administration would have a positive contribution to the treatment response.

Keywords: Idiopathic granulomatous mastitis, intralesional injection, steroid treatment

INTRODUCTION

Idiopathic granulomatous mastitis (IGM) is a benign chronic inflammatory breast condition, first described in 1972 by Kessler and Wooloch (1). IGM most often presents in women of childbearing age within a few years of pregnancy. It is most common in women of Asian, Hispanic, Middle Eastern, or African origin (2,3). Rarely, IGM has also been reported in nulliparous women and men (4,5).

It mimics breast cancer and abscesses. However, its etiology is still unknown. The pathogenesis of IGM remains unclear,

Address for Correspondence: Mesude Seda Aydoğdu, Fırat University Faculty of Medicine, Department of Rheumatology, Elazığ, Turkey
Phone: +90 506 486 78 59 **E-mail:** kinaci_seda@hotmail.com **ORCID ID:** orcid.org/0000-0001-7031-4716
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although evidence suggests that it is likely autoimmune in nature. Specific causes of infection with some *Corynebacterium* species, oral contraceptive pills, trauma, foreign body reactions, hyperprolactinemia, and diabetes mellitus should also be excluded (5). Environmental and genetic factors may also play an important role in the underlying etiology of the disease (6). Histopathologically, IGM is characterized by non-caseating granulomas around the lobules and ducts in the breast (5).

It usually causes symptoms such as a mass in the breast, pain, skin redness, abscess, fistula, nipple retraction, and discharge (7).

In diagnosis, it is first necessary to perform breast imaging with ultrasound, mammography, or magnetic resonance imaging. The main diagnosis is made histopathologically by core needle biopsy (8).

IGM treatment and management are not fully standardized yet. Treatment of IGM involved antibiotics, corticosteroids, immunosuppressants, methotrexate, colchicine, other anti-inflammatory agents, and surgical treatment modalities. Corticosteroids were first used by DeHertogh et al. (9) in 1980. Although steroid treatment is primarily used, methotrexate and azathioprine are also used as steroid dose reducers (10). Healing and cosmetic problems create disadvantages in surgical treatment methods. In recent studies, fluid aspiration and intralesional (IL) steroid injection approaches have been used as treatment methods (11,12). The use of local treatment has also been deemed valuable in terms of reducing the side effects of systemic treatment.

In our study, we studied the responses obtained from IL steroid application in addition to conventional treatments in patients with IGM.

MATERIAL AND METHODS

All female patients diagnosed with IGM who were followed up in the Fırat University Research Hospital Rheumatology and Radiology Clinics between January 2021 and May 2023 were included in the study. A total of 77 newly diagnosed patients were included. This was a prospective study. The diagnosis of IGM was confirmed histopathologically in all patients. For differential diagnosis, patients were examined and screened for tuberculosis, infectious causes, sarcoidosis, antineutrophilic cytoplasmic antibody-related vasculitis, and connective tissue diseases. Patients were divided into two groups depending on the treatment method: those who received IL steroid treatment and those who did not. The status of achieving remission and the treatments they received were compared between the two groups. The study protocol was approved by Fırat University Non-interventional Research Ethics Committee (approval number: 9613, date: 06/07/2022).

Statistical Analysis

All collected data were recorded in SPSS for Windows 25. Normal distribution analysis of variables was performed using Kolmogorov-Smirnov and Shapiro-Wilk tests. t-test for data complying with normal distribution; Mann-Whitney U test was used for non-parametric data that did not comply with normal distribution. For data complying with normal distribution, the results are mean ± standard deviation; for data that does not comply with normal distribution, the results are given as median and minimum-maximum. The chi-square test was used for categorical variables. Pearson's correlation test for parametric data for the existence of relationships between numerical values. For non-parametric data, Spearman's correlation test was used. Values with a p-value of 0.05 will be considered statistically significant. In the correlation analysis, r>0.3 and p-values below 0.05 were considered significant.

RESULTS

A total of 77 patients were included in the study. One of the 77 patients was excluded from the study because she discontinued treatment voluntarily during follow-up. All patients had given birth. The demographic and laboratory characteristics of the patients, whose average age was 36.5±6.8 years, are shown in Table 1. Remarkably, the average body mass index of the patients was 27.06±3.5 kg/m^2, which was above normal.

In our study, 42.1% of the patients received antibiotic treatment before or after diagnosis, and the most frequently used treatments were oral steroids (88.2%) and methotrexate (85.5%) (Table 2).

Remission was achieved in 55.3% of the patients (42 patients). While remission was observed in 61.6% of the patients who received IL steroids, remission was achieved in only 23.1% of the patients who did not receive IL steroids, and this rate was found to be statistically significant (p=0.010). There was no statistically significant difference between the treatments received by patients who achieved remission and those received by patients whose treatment continued (p>0.05) (Table 3). There was no statistically significant difference between the patients who received and those who did not receive IL steroid injection in terms of the treatment they received (p>0.05). The number of IL steroid injections (p=0.024) and total steroid dose (p=0.054) were found to be lower in patients with complete response (drug free remission).

A positive correlation was found between baseline C-reactive protein (CRP) levels and the number of IL injections (r=0.380, p=0.002) and total IL steroid dose (r=0.439, p=0.001). There was no difference in treatment response between those who had ≥3 births and those who had 2 births. However, it caught

Table 1. Demographical and laboratory characteristics

	All patients (n=76)	IL GC injections		p*
		Yes (n=63)	No (n=13)	
Mean age (years)	36.53±6.8	35.89±7.1	39.62±4.4	0.020
Mean BMI (kg/m²)	27.06±3.5	26.96±3.7	27.67±1.8	0.353
Mean pregnancy counts (n)	2.92±1.6	2.9±1.7	3.0±1.1	0.476
≥3 pregnancies (%)	51.6	50	60	0.562
Breastfeeding in the last 5 years (%)	88.7x	88.5	90	0.888
Smoking (active and history) (%)	8	7.7	10	0.593
ESR (mm/h)	39.95±22.6	39.7±22.9	41.1±21.7	0.706
CRP (mg/L)	18.48±27.5	18.6±28.5	17.9±22.9	0.971
WBC (10^3/µL)	8.87±2.4	8.96±8.9	8.4±1.6	0.591
HGB (g/dL)	12.61±1.4	12.7±1.3	12.1±1.3	0.069
PLT (10^3/µL)	388.9±387.9	396.4±423.1	352.7±118.7	0.777
ALB (g/dL)	4.5±0.3	4.5±0.3	4.4±0.3	0.072
GLOB (g/dL)	2.96±0.9	2.9±1.0	3.1±0.6	0.109

*p values for comparing IL GC injected and not injected patient, IL GC: Intralesional glucocorticoid, BMI: Body mass index, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, WBC: White blood count, HGB: Hemoglobin, PLT: Platelet, ALB: Albumin, GLOB: Globulin, n: Number

our attention that as the number of pregnancies increased, the number of injections also increased.

DISCUSSION

The clinical management of IGM patients is challenging. While some patients may present with a solitary mass that regresses spontaneously, others may experience marked erythema, fluid collection formation, and recurrent fistulization from the onset of the disease (13).

IGM is an orphan disease whose diagnosis and etiology have not been elucidated, and it has recently become a field of interest in rheumatology because of its response to immunosuppressive treatments. If it is not treated considering the risk of recurrence, it may very rarely go into remission without treatment. However, the use of immunosuppressive treatments such as steroids, methotrexate, and azathioprine is often required (3). In recent years, there has been an increasing interest in immunosuppressive treatments and IL steroid administration to reduce their side effects (14-19). It also provides advantages during breastfeeding and pregnancy. In our study, we examined the responses obtained with IL steroid application in addition to conventional immunosuppressive treatments in patients with IGM. Pregnancy and lactation are also included in the etiology of IGM. Because the number of IL injections increased as the number of pregnancies increased in our study (r=0.276, p=0.048), we thought that multiple pregnancy and/or multiple breastfeeding might be risk factors for severe disease. A correlation was observed between the CRP level measured at diagnosis and the number and dose of IL injections. This may suggest that higher doses of steroids or alternative therapy should be considered in patients with elevated CRP levels at baseline. We interpreted the fact that the number and dose of IL steroid applications were higher in patients who did not achieve remission and that the need for treatment in patients with an aggressive course increased, as expected. In our study, the treatments received by patients who were and were not administered IL steroids were similar, but a significant difference was observed in patients who were administered IL steroids in terms of achieving remission. This suggested that IL steroid administration would positively contribute to the treatment response (Figure 1). In addition, reducing the risk of systemic side effects and accelerating the

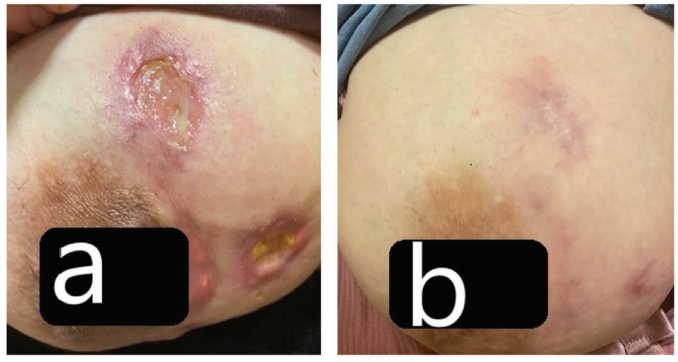

Figure 1. Glandulary lesions and wet wounds (a) healed after IL corticosteroid injections (b)
IL: Intralesional

Table 2. Clinical characteristics

	All patients (n=76)	IL GC injections		p*
		Yes (n=63)	No (n=13)	
Number of IL GC injections		2.29±1.8		
Total provincial GC dose (methylprednisolone mg)		57.41±47.3		
Localizations (%)				
-Left	63.2	60.3	20.8	0.521
-Right	26.3	28.6	15.4	
-Bilateral	10.5	11.1	7.7	
Antibioteraphy (%)	42.1	42.9	38.5	0.958
Systemic GC (%)	88.2	87.3	92.3	0.611
MTX (%)	85.5	84.1	93.2	0.445
AZA (%)	21.1	20.6	23.1	0.844
ADA (%)	2.6	3.2	0	0.515
Reached remission (%)	55.3	61.6	23.1	0.010

*p values for comparing IL GC injected and not injected patients, IL GC: Intralesional glucocorticoid, MTX: Methotrexate, AZA: Azathioprine, ADA: Adalimumab, GC: Glucocorticoid, n: Number

Table 3. Clues for remission of IGM

	Treatment discontinued* (n=42)	Treatment ongoing (n=34)	p
IL GC injection (%)	92.9	70.6	0.010
Number of IL GC injections	1.9±1.3	2.9±2.2	0.024
Total provincial GC dose (mg)	48.5±39.9	71.4±55.1	0.054
Localizations (%)			
-Left	56.3	43.8	0.947
-Right	55	45	
-Bilateral	50	50	
Antibioteraphy (%)	40.5	44.1	0.749
Systemic GC (%)	88.1	88.2	0.915
MTX (%)	88.1	82.4	0.479
AZA (%)	16.7	26.5	0.297
ADA (%)	0	5.9	0.111

*Treatment discontinued due to remission, IGM: Idiopathic granulomatous mastitis, IL GC: Intralesional glucocorticoid, GC: Glucocorticoid, MTX: Methotrexate, AZA: Azathioprine, ADA: Adalimumab, n: Number

treatment response were seen as important advantages. There are also other studies showing that local steroid application is beneficial (16,19).

Study Limitations

The limitations of this study are that the follow-up period of the patients continued for the last year and that the same dose of steroids was not administered because the progression of the patient clinics was not the same.

CONCLUSION

In conclusion, remission and discontinuation of treatment were nearly three times higher in IL steroid-injected IGM patients in our study. It can be suggested that IL steroid injection should be considered for treating IGM. However, this suggestion is a candidate to handle in randomized and placebo-controlled studies.

Ethics

Ethics Committee Approval: The study protocol was approved by Fırat University Non-interventional Research Ethics Committee (approval number: 9613, date: 06/07/2022).

Informed Consent: This was a prospective study.

Authorship Contributions

Surgical and Medical Practices: M.S.A., Concept: M.S.A., Design: M.S.A., A.K., H.A., Data Collection or Processing: M.S.A., A.K., H.A., İ.G., S.S.K., Analysis or Interpretation: M.S.A., A.K., H.A., İ.G., S.S.K., Literature Search: M.S.A., A.K., H.A., Writing: M.S.A.

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