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Personalized Treatment Outcomes in Idiopathic Granulomatous Mastitis: A Retrospective Study of Ninety-Two Patients

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ABSTRACT

Objective: Idiopathic granulomatous mastitis (IGM) is a rare benign inflammatory breast disease with a high risk of relapse. The study objective was to evaluate relapse predictors and treatment outcomes in a large cohort of IGM patients.

Materials and Methods: We retrospectively analyzed female patients diagnosed with IGM (2018–2024) at the Central Military Hospital, Baku. Diagnosis was confirmed by core needle biopsy. Patients were managed with systemic therapy (corticosteroids and/or immunosuppressants) when clinically indicated; local measures (e.g., aspiration/drainage, intralesional steroid) were used selectively in localized disease. Relapse was defined as reappearance of clinical or radiological findings after remission. Univariable and multivariable logistic regression models were applied to identify independent predictors.

Results: The cohort consisted of 92 patients. Relapse occurred in 22/85 methotrexate-treated patients (25.9%), with most relapses occurring between the third and fifth months. No relapse events were observed in the azathioprine subgroup (n = 7). However, this finding should be considered observational only due to the small numbers and zero-event data. In multivariable analysis, erythrocyte sedimentation rate (ESR) >20 mm/h (and angiotensin converting enzyme >52 U/L, where applicable) were associated with relapse, whereas apparent associations with tumor necrosis factor alpha inhibitors and cyclosporine likely reflect confounding by indication because these agents were used as rescue therapy in refractory/relapsing disease. Elevated ESR was also associated with prolonged treatment duration (p = 0.006).

Conclusion: A structured and individualized treatment approach may contribute to favorable clinical outcomes in patients with IGM. Observed relapse patterns support the importance of risk-adapted management rather than a uniform therapeutic strategy. Given the retrospective design and limited subgroup sizes, these findings should be interpreted cautiously and considered hypothesis-generating. Prospective, multicenter studies are required to validate relapse-associated factors and optimize treatment strategies.

Keywords: Idiopathic granulomatous mastitis; relapse; immunosuppressive therapy; methotrexate; azathioprine; risk-adapted treatment

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KEY POINTS

- Idiopathic granulomatous mastitis.
- Relapse.
- Immunosuppressive therapy.
- Methotrexate.
- Azathioprine.

Introduction

Idiopathic granulomatous mastitis (IGM) is a rare, chronic, and benign inflammatory breast disease, first described in 1972 (1). It predominantly affects women of reproductive age, most commonly occurring within the first five years postpartum, typically between the ages of 30 and 45 years (2). Rarely, IGM occurs in men and postmenopausal women (3). The exact etiology of the disease remains unclear; however, several factors, such as autoimmune processes, hormonal influences, pregnancy, lactation, use of oral contraceptives, and hyperprolactinemia are believed to play a role in its pathogenesis (4).

The involvement of autoimmune mechanisms is supported by the favorable response of IGM to corticosteroids and immunosuppressive agents (5). Furthermore, the common presence of extra-mammary inflammatory manifestations, such as erythema nodosum and arthritis, further supports the hypothesis of immune-mediated pathology (6). Histologically, IGM is characterized by non-caseating granulomas predominantly affecting the breast lobules, often accompanied by microabscesses (7). Given its granulomatous nature, infectious etiologies, such as tuberculosis, fungal infections, sarcoidosis, and granulomatosis with polyangiitis must be considered in the differential diagnosis. Biopsy confirmation is mandatory (8).

Clinically, IGM typically presents as a palpable breast mass, often accompanied by pain, erythema, nipple retraction, and occasionally the formation of fistulous tracts (9). Axillary lymphadenopathy may also be observed, which can complicate differentiation from malignant tumors (10). The disease course is variable, with recurrence rates ranging from 5% to 50% (11). Due to its chronic and recurrent nature, long-term follow-up is necessary (12).

Management strategies for IGM remain controversial, and no consensus exists regarding the optimal treatment approach (13). Therapeutic options include corticosteroids, immunosuppressive agents, including methotrexate and azathioprine, antibiotics, and surgical intervention (14). While some studies suggest that surgical excision may be associated with higher recurrence rates, others advocate for a multimodal approach that incorporates systemic therapy (15). The aim of this study was to identify clinical and laboratory predictors of relapse in IGM and evaluate the effectiveness of a structured, individualized treatment strategy.

Materials and Methods

This retrospective study was conducted at the Rheumatology Department Outpatient Clinic of the Central Military Hospital of the Ministry of Defence between 2018 and 2024. Female patients who were either referred with a diagnosis of IGM or were newly diagnosed in our clinic were included. The mean follow-up duration was more than one year, allowing assessment of treatment response and early recurrence but late relapses may have been missed due to the chronic course of IGM. The diagnosis of IGM was histopathologically confirmed by findings of granulomatous inflammation consistent with mastitis, including epithelioid histiocytes, Langhans-type giant cells, and lymphocytic infiltration.

Ethical approval was obtained from the Ethics Committee of Liv Bona Dea, Baku Hospital (approval no: BDP-2023/174, date: 02.11.2024).

Inclusion criteria comprised patients with IGM confirmed by a tru-cut biopsy performed due to a breast mass. Serological profiles including anti-nuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (ANCA), rheumatoid factor (RF), angiotensin converting enzyme (ACE), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were analyzed to exclude other granulomatous diseases such as sarcoidosis, autoimmune, and vasculitic conditions. ANA positivity was defined as titers ≥1:160, and ACE levels >52 U/L were considered elevated. All data were retrospectively extracted from the hospital's electronic medical records system. To assess relapse predictors, univariate and multivariate binary logistic regression models were constructed using clinical and treatment variables, including ESR, CRP, immunosuppressant use, and age. Statistical significance was defined as $p<0.05$.

Demographic data included patient age, age at diagnosis, the interval (in months) between symptom onset and diagnosis, and time since last childbirth. Comorbidities were also recorded and included type 2 diabetes mellitus, coronary artery disease, other organ-specific or systemic conditions and heart failure.

Clinical evaluation included characteristics of the breast masses, including painful/painless, erythema, discharge, abscess, appearance, recurrent abscesses, unilateral/bilateral lesions, lesions ≥5 cm in diameter, and laterality of breast involvement. Laboratory and imaging data included ESR >20 mm/h, CRP ≥5 mg/L, and ACE >52 U/L. Baseline ultrasound was used to document mass size ≥5 cm. ANA, ANCA, and RF tests were performed for all patients.

All patients initially presented to the general surgery outpatient clinic and were then referred to rheumatology. Initial treatments, including surgical interventions (abscess drainage or mass excision, without distinction), were recorded.

Recurrence was defined as the reappearance of clinical or radiological signs of disease following a period of complete remission lasting at least 4 weeks. Number of recurrences, time to first and second recurrence (in months), and treatment modalities during recurrence (antibiotics, steroids, methotrexate, azathioprine) were documented.

Treatment Strategy

Treatment was individualized based on clinical disease activity. Treatment decisions were individualized based on disease extent, inflammatory activity (ESR/CRP), symptom severity, and patient factors (including lactation). Because non-severe IGM can be managed with a de-escalation approach, observation, and/or local therapies (e.g., ultrasound-guided aspiration/drainage and intralesional corticosteroid injection) were considered as initial management for mild, well-localised disease, before resorting to systemic immunosuppression. Systemic therapy was reserved for clinically active, extensive, progressive, or refractory disease, or when symptoms significantly affected quality of life. When systemic therapy was used, oral prednisolone (0.5–1 mg/kg/day) was initiated during the active inflammatory phase and tapered according to clinical response and tolerability. Once clinical stability was achieved, steroids were tapered over approximately 4 weeks. Dose selection was individualized and adjusted according to clinical response and tolerability.

Patients were pragmatically stratified into mild, moderate, and severe categories based on lesion size, inflammatory markers (ESR/CRP), and symptom severity to guide treatment intensity.

- Mild: Localized disease with normal or minimally elevated ESR/CRP and minimal clinical inflammation.
- Moderate: Symptomatic inflammatory disease and/or moderate elevations in ESR/CRP.
- Severe: Marked inflammatory activity (elevated ESR/CRP), extensive disease and/or lesion diameter ≥5 cm, or complicated disease (e.g., abscess/fistula).

This stratification was used as a center-specific practical tool and does not represent a validated consensus classification.

Stratification into mild, moderate, and severe forms was based on a combination of lesion size, CRP/ESR levels, and severity of clinical symptoms. This stratification enabled a personalized treatment approach. To reduce cumulative corticosteroid exposure, a steroid-sparing immunosuppressant (most commonly methotrexate in this cohort) was introduced in patients requiring prolonged steroids, those with extensive disease, or those with relapse. In refractory or relapsing cases, tumor necrosis factor aplha (TNF-α) inhibitors (adalimumab) and cyclosporine were used. Patients were monitored monthly with clinical and laboratory assessments, and treatment doses were adjusted based on response. The pragmatic stepwise, risk-adapted treatment pathway used in our centre is summarized in Figure 1.

Treatment Modalities

1. Corticosteroid Therapy: Prednisolone was used as systemic therapy for patients with clinically active inflammatory disease and tapered in parallel with clinical improvement. In relapse, a previously effective dose could be reintroduced temporarily while steroid-sparing therapy was optimized.

2. Immunosuppressive Therapy: Methotrexate (85 patients) and azathioprine (7 patients) were used. Azathioprine was used in selected postpartum/breastfeeding patients when methotrexate was not preferred. Azathioprine was used in selected postpartum/breastfeeding patients when methotrexate was not preferred. Refractory and relapsing cases were managed with TNF-α inhibitors (adalimumab) and cyclosporine.

3. Antibiotic Therapy: Administered when an infectious component was confirmed.

4. Combination Therapy: Two main combinations were used. In patients treated with biological agents (adalimumab, cyclosporine), infection markers, liver function, and complete blood counts were closely monitored. Screening for hepatitis and latent tuberculosis (purified protein derivative or Quantiferon) was performed. No serious infections requiring hospitalization were documented in the available records; however, adverse events were not systematically captured in this retrospective dataset, so toxicity may be underestimated. Routine monitoring during systemic immunosuppression included clinical assessment and periodic laboratory testing (complete blood count and liver function tests), with infection screening prior to biologic therapy as described.

- Methotrexate + Cyclosporine (200 mg/day for 4–6 months)
- Methotrexate + Adalimumab (40 mg every other week)

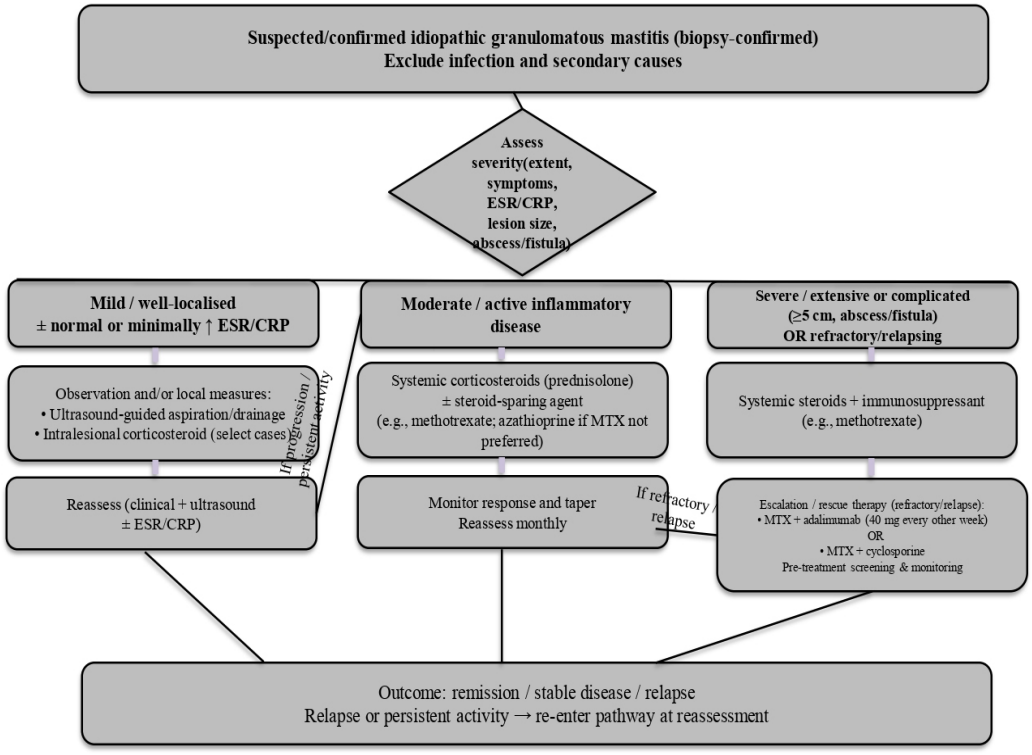

Figure 1. Treatment algorithm (pragmatic, stepwise, risk-adapted). Pragmatic stepwise, risk-adapted treatment pathway used in our centre. Mild, well-localised disease may be managed initially with observation and/or local therapies, whereas systemic immunosuppression is reserved for clinically active, extensive, progressive, or refractory disease. Escalation (e.g., adalimumab or cyclosporine) was used as rescue therapy in relapsing/refractory cases

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; OR: Odds ratio; MTX: Methotrexate

Corticosteroid duration varied according to disease activity and response. In patients with persistent or relapsing disease, tapering was slowed and/or a steroid-sparing immunosuppressant was optimized. The primary outcome was defined as disease recurrence, determined by the reappearance of clinical or radiological findings after achieving complete or partial remission. Secondary outcomes included time to recurrence and treatment response (remission, stable disease, or progression). In cases where clinical improvement was not satisfactory, the steroid dose was increased again to regain disease control.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 29 (SPSS Inc., Chicago, Illinois). Descriptive statistics for continuous variables are presented as mean ± standard deviation or median (minimum-maximum), and categorical variables as frequencies (n) and percentages (%). The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess normality of continuous variables. Depending on distribution, independent t-test or Mann-Whitney U test was applied for group comparisons. For categorical variables, Pearson's chi-square or Fisher's exact test (when expected cell values were <5) was used.

To evaluate associations with recurrence and treatment duration, univariable and multivariable logistic regression models were applied. Variables entered into the regression model included age, ESR, CRP, lesion size, laterality, and immunosuppressant use (methotrexate, azathioprine, TNF-α inhibitors, cyclosporine, corticosteroids, surgical intervention). Odds ratios with 95% confidence intervals were calculated. Linear regression was used for continuous outcome variables. Correlation analyses employed Pearson or Spearman tests, depending on data type. A two-tailed p-value <0.05 was considered statistically significant. In subgroups with limited event counts (e.g., azathioprine), multivariate regression was restricted.

Results

Data from 92 patients were analyzed. The mean age of patients was 36.10±9.63 years. The average treatment duration was 9.84±4.70 months, reflecting the typical course of therapy. In

terms of comorbitities, five patients had thyroid dysfunction, five had hypertension, and two had diabetes mellitus. However, these comorbidities did not show any significant effect on treatment duration or relapse rates, likely due to the younger age distribution of the cohort. ANA positivity was detected in 4 (4.35%) patients and RF in 1 (1.1%) patient. Of the 85/92 (92.4%) patients treated with methotrexate, 22 experienced a relapse (25.9%), primarily occurring between the third and fifth month of treatment. A comparison of clinical, laboratory, and treatment characteristics between recurrent and non-recurrent IGM patients is summarized in Table 1. All relapses were observed in the methotrexate group. None of the 7 patients treated with

Table 1. Comparison of clinical, laboratory, and treatment characteristics between recurrent and non-recurrent IGM patients

Variable	IGM recurrence - no (n/%)	IGM recurrence - yes (n/%)	*p*-value
Total patients	70 (76.1%)	22 (23.9%)	-
Baseline characteristics			
Age (mean ± SD)	36.10±9.63	36.10±9.63	>0.05
Time from symptom onset to diagnosis (months)	Not specified	Not specified	-
Clinical features			
Presence of mass	70 (100%)	22 (100%)	-
Painful mass	50 (71.4%)	18 (81.8%)	-
Redness	32 (45.7%)	10 (45.4%)	-
Discharge	27 (38.5%)	9 (40.9%)	-
Fistula	5 (7.1%)	3 (13.6%)	-
Nipple retraction	10 (14.3%)	5 (22.7%)	-
Cellulitis	4 (5.7%)	2 (9.1%)	-
Erythema nodosum	6 (8.5%)	2 (9.1%)	-
Recurrent abscess	Not specified	Not specified	-
Unilateral lesion	61 (87.1%)	18 (81.8%)	-
Mass ≥5 cm on initial ultrasound	18 (26%)	8 (36%)	-
Laboratory findings			
ESR >20 mm/h	21 (30%)	10 (45%)	0.023
CRP ≥5 mg/L	26 (37%)	8 (36%)	0.056
ACE >52 U/L	10 (14%)	4 (18%)	-
Prolactin (mean)	Not specified	Not specified	>0.05
Risk factors			
Comorbidities	10 (14%)	5 (23%)	-
Stress factor	30 (43%)	9 (41%)	-
Oral contraceptive use	7 (10%)	2 (9%)	-
Menopause	3 (4.3%)	1 (4.5%)	-
Breast trauma	Not specified	Not specified	-
Treatment & follow-up			
Initial steroid use	70 (100%)	22 (100%)	-
Initial methotrexate use	63 (90%)	22 (100%)	0.473
Initial azathioprine use	7 (10%)	0 (0%)	0.494
TNF-α inhibitor use	0 (0%)	17 (77.3%)	-
Methotrexate + cyclosporine	0 (0%)	5 (22.7%)	-
Combination therapy (any)	0 (0%)	22 (100%)	-
Follow-up status	Not specified	Not specified	-

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; IGM: Idiopathic granulomatous mastitis; ACE: Angiotensin converting enzyme; TNF-α: Tumor necrosis factor alpha; SD: Standard deviation

azathioprine experienced a relapse but this was not different from the relapse rate in the methotrexate group ($p = 0.494$). Among the 22 relapsing patients, 5 received methotrexate + cyclosporine (200 mg/day, for 4–6 months), and 17 received methotrexate + adalimumab (40 mg every other week).

Correlation analyses identified the following associations. No statistically significant correlation was found between relapse and use of methotrexate ($r = 0.076$, $p = 0.473$) or azathioprine ($r = 0.072$, $p = 0.494$). A significant positive correlation was found between relapse and treatment duration ($r = 0.422$, $p<0.001$), suggesting that relapses are associated with prolonged therapy, possibly due to repeated clinical and radiologic recurrence. No correlation was found between patient age and treatment duration. A significant weak positive correlation was identified between ESR and treatment duration ($r = 0.246$, $p = 0.023$), suggesting that elevated ESR is associated with longer treatment periods. However, there was no correlation between CRP and treatment duration ($F = 1.638$, $p = 0.056$), showing a trend without significance. No significant correlation was found between treatment duration and other immunosuppressive (methotrexate, azathioprine, TNF-α inhibitors, cyclosporine) or antibiotic therapies.

To further explore the effect of laboratory variables on treatment duration, one-way ANOVA analyses were performed This indicated a statistically significant difference in treatment duration across ESR groups ($F = 2.172$, $p = 0.006$), suggesting that higher ESR levels are associated with longer treatment periods. However, CRP showed ($F = 1.638$, $p = 0.056$), a trend toward association with treatment duration, but this did not reach statistical significance.

Overall, the findings suggest that clinical or radiologic relapse after achieving remission is significantly associated with extended treatment durations. Elevated ESR was associated with longer treatment duration and relapse status. In contrast, factors such as age, surgical intervention, and various immunosuppressive or antibiotic regimens did not show a statistically significant effect on treatment duration. These findings provide important insights for optimizing relapse risk assessment and patient monitoring strategies in clinical practice.

In the multivariable logistic regression model, ESR >20 mm/h, TNF-α inhibitor use, and cyclosporine treatment showed statistical associations with relapse status (Table 2). These treatment-related associations should be interpreted cautiously because TNF-α inhibitors and cyclosporine were used as rescue therapy in refractory/relapsing disease (confounding by indication). No relapse events were observed in the azathioprine subgroup but the small sample size was very small and there were zero-event data. Table 3 illustrates the distribution of relapse onset over time, showing a peak between the third and fifth months after treatment initiation.

Table 2. Logistic regression model showing variables associated with relapse status

Variable	OR	95% CI	*p*-value
ESR >20 mm/h	2.45	1.10–5.46	0.023
CRP ≥5 mg/L	1.95	0.98–4.22	0.056
TNF-α inhibitor	4.87	1.70–13.90	<0.001
Cyclosporine	3.85	1.48–10.03	0.006
Azathioprine	-	-	0.494 (no relapses observed)
Age	0.98	0.93–1.03	0.398
Surgical intervention	1.55	0.82–2.91	0.184
ACE >52 U/L	2.26	1.12–4.53	0.010

TNF-α inhibitors and cyclosporine were used as rescue therapy in relapsing/refractory cases; therefore, their statistical associations with relapse should be interpreted cautiously due to confounding by indication, TNF-α: Tumor necrosis factor alpha; OR: Odds ratio; CI: Confidence interval; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein

Table 3. Time distribution of relapse occurrence following initiation of treatment, with clustering between 3rd and 5th months

Variable	Association (OR)	95% CI	*p*-value
ESR >20 mm/h	2.32	1.01–5.34	0.048
TNF-α inhibitor	4.12	1.38–12.30	0.011
Cyclosporine	3.44	1.22–9.76	0.019
ACE >52 U/L	2.05	0.98–4.29	0.060 (borderline significance)

TNF-α: Tumor necrosis factor alpha; OR: Odds ratio; CI: Confidence interval; ACE: Angiotensin converting enzyme; ESR: Erythrocyte sedimentation rate

Discussion and Conclusion

Our findings indicate that the personalized and phased treatment protocol we implemented resulted in a relapse rate of only 25.9% in patients with IGM. This relapse rate falls within the lower range of rates reported in the international literature, which range from 20% to 47.5% (16). Several retrospective studies have reported even higher relapse rates, between 35% and 50%, highlighting the tendency of IGM to relapse frequently during its natural course (17). These differences support the effectiveness of our individualized approach in routine clinical practice.

The low relapse rate likely reflects the structured, multi-phase treatment protocol. Common challenges frequently reported include premature tapering of corticosteroids, delayed initiation of biological therapies, and inadequate follow-up (18). In contrast, our center applied a pragmatic, stepwise approach in which systemic therapy was generally reserved for clinically active or extensive disease, and steroid-sparing agents were used to reduce cumulative corticosteroid exposure when prolonged treatment was required, followed by gradual tapering and long-term immunosuppressive support using methotrexate or azathioprine (19). Despite the small sample size the azathioprine subgroup exhibited zero relapse events. Therefore, this observation should be considered exploratory and not interpreted as evidence of superior efficacy. In steroid-refractory or relapsing cases, biologic agents (e.g., adalimumab) and cyclosporine were used only as rescue therapy in refractory/relapsing disease, and observed outcomes should be interpreted in the context of the presence of confounding by indication (20).

In the methotrexate group (n = 85), the relapse rate was 25.9% (n = 22) and tended to occur between three and five months of therapy. This highlights the importance of careful steroid dose adjustment and sustained immunosuppressive therapy (21). Recent efforts have aimed to standardize clinical classification and improve comparability across IGM cohorts. A consensus study has proposed a practical clinical classification framework, and a Pittsburgh classification-based treatment algorithm has also been presented, emphasizing stepwise escalation from observation/local measures to systemic immunosuppression for severe or refractory disease. Our mild/moderate/severe stratification overlaps conceptually with these emerging frameworks but was applied retrospectively and should be regarded as a center-specific pragmatic approach rather than a validated consensus classification (22, 23).

Prospective studies comparing methotrexate- and azathioprine-based regimens are warranted to clarify relative efficacy and safety (24).

Despite the favorable relapse outcomes observed in this cohort, systemic immunosuppressive therapy carries an inherent risk of overtreatment, particularly in patients with mild disease or limited inflammatory activity. Therefore, treatment intensity should be carefully individualized, balancing potential benefits against systemic adverse effects. Risk-adapted decision-making remains essential in the management of IGM.

Local treatment modalities, including intralesional corticosteroid injections and surgical drainage, represent valid therapeutic options in selected patients with localized disease. The limited use of these approaches in the present cohort reflects institutional practice patterns rather than a recommendation against local therapies. Treatment selection should remain individualized, incorporating both systemic and local strategies when clinically appropriate.

Combination therapies applied in refractory and relapsing cases also yielded meaningful clinical outcomes. The regimens of methotrexate + cyclosporine (200 mg/day for 4–6 months) and methotrexate + adalimumab (40 mg every other week) resulted in early positive clinical and laboratory responses from the first month of treatment, although these observations should again be interpreted cautiously due to the retrospective design (25). These results align with a recent report supporting the promising role of TNF-α inhibitors in granulomatous inflammatory diseases, including IGM (26).

Moreover, our study adopted a stringent definition of relapse, considering only those recurrences that occurred after complete clinical and radiological remission. The therapeutic strategy was guided by a structured and stepwise protocol: For non-severe localized disease, observation and/or local measures may be appropriate as initial management, with systemic immunosuppression reserved for clinically active, extensive, progressive, or refractory disease, and the introduction of combination therapy (methotrexate + cyclosporine or adalimumab) only in cases of relapse (27). Monthly monitoring and individualized steroid tapering were central to relapse prevention. In contrast, many studies classify any clinical fluctuation as relapse, potentially inflating relapse rates and limiting comparability (28). Unlike many previous reports limited to univariate or descriptive analyses, our study employed multivariate regression, which allowed us to explore variables statistically associated with relapse in this retrospective cohort. This methodological strength enhances the reliability of our conclusions. The relatively low relapse rate in our cohort compared with previous reports further highlights the potential value of our structured treatment strategy. The relapse clustering between months 3 and 5 may relate to steroid tapering dynamics, reinforcing the need for immunosuppressive maintenance.

We also observed a statistically significant association between ESR and treatment duration. The observed associations between relapse status and the use of TNF-α inhibitors or cyclosporine

should be interpreted with caution. These agents were not initiated as first-line therapies but were introduced after relapse as rescue treatments for refractory disease. Therefore, their statistical association with relapse reflects confounding by indication rather than a causal or predictive effect. This highlights the inherent limitations of retrospective analyses when interpreting treatment-related regression outcomes. There may be benefit in measuring ESR when monitoring treatment response and relapse risk. This finding reinforces the established role of systemic inflammation in the clinical course of IGM but may also indicate poor control of the inflammatory response or may simply indicate continued non-specific inflammation from some unidentified cause or confounder (29).

Although prolactin has been hypothesized as a contributing factor in IGM, our study did not find a significant association between prolactin levels and recurrence, consistent with findings from previous research (30). Surgical intervention, while sometimes necessary, was associated with a tendency toward higher relapse rates in our small subset of surgically treated patients, aligning with other studies emphasizing the risks of surgery without concurrent immunosuppression (31).

Ultimately, our study illustrated the complexity of IGM management. There is no universally superior treatment approach. Rather, individualized, multimodal strategies tailored to each patient's clinical presentation and disease severity appear to yield optimal results. Future research should prioritize randomized controlled trials and long-term follow-up studies to refine therapeutic algorithms and improve patient outcomes (32).

Study Limitations

This study is limited by its retrospective design and relatively small subgroup sizes, which restricted some multivariate comparisons. Larger, prospective studies are required to validate these predictors.

The retrospective design of this study also prevents causal inference and is subject to incomplete data capture and indication bias. In addition, the median follow-up duration of only 14.3 months may be insufficient to detect late relapses, given the chronic and recurrent nature of IGM. Additionally, this was a single-center cohort with a postpartum/breastfeeding-enriched population, which may limit generalizability to broader or non-endemic settings. Therefore, long-term disease control and durability of remission could not be fully assessed. Adverse events related to corticosteroids, methotrexate, azathioprine, and biologic agents were not systematically graded or quantified due to the retrospective nature of the study. Consequently, the true incidence of treatment-related toxicity may be underestimated. Future prospective studies with standardized safety reporting are needed to better define the risk-benefit profile of systemic immunosuppressive therapies in IGM.

This study demonstrated that a structured and individualized treatment approach may contribute to favorable clinical outcomes in patients with IGM. The observed relapse patterns highlight the importance of risk-adapted management strategies rather than a uniform therapeutic algorithm. However, given the retrospective design, limited subgroup sizes, and follow-up duration, the present findings should be interpreted cautiously and require further validation. Prospective, multicenter studies are warranted to validate relapse-associated factors and to define the optimal balance between systemic and local treatment modalities.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of Liv Bona Dea, Baku Hospital (approval no: BDP-2023/174, date: 02.11.2024).

Informed Consent: Retrospective study.

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Footnotes

Authorship Contributions

Concept: R.J., A.A., I.B., R.A., K.S., N.A., E.S.; Design: R.J., A.A., I.B., R.A., K.S., N.A., E.S.; Data Collection or Processing: R.J., A.A., I.B., R.A., K.S., N.A., E.S.; Analysis or Interpretation: R.J., A.A., I.B., R.A., K.S., N.A., E.S.; Literature Search: R.J., A.A., I.B., R.A., K.S., N.A., E.S.; Writing: R.J., A.A., I.B., R.A., K.S., N.A., E.S.

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