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Relationship Between Idiopathic Granulomatous Mastitis and ABO Blood Groups

İdiyopatik Granülomatöz Mastitis ve ABO Kan Grupları Arasındaki İlişki

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ABSTRACT

Objective: This study aimed to evaluate whether the A, B and O blood groups (ABO) subgroup distribution of patients with idiopathic granulomatous mastitis (IGM) is different or not differs from that of the general population.

Methods: The patients with IGM who were followed up in the breast unit and applied for routine control between July 2021 and October 2021 were included in the study.

Results: During this period, 101 IGM patients were enrolled. The patients' age ranged between 21 and 61 years (median, 33 years). The most common ABO blood subgroup in both the patient and control groups was Group A (48.5% and 44.7%, respectively). Between the groups, the difference in ABO subgroups was not statistically significant ($p=0.122$). Eight patients had erythema nodosum. In 75% of patients with erythema nodosum, the most common ABO subgroup was Group A. Eight patients developed relapses. The ABO subgroup was A in five of the patients who had a relapse. However, the comparison of ABO subgroups according to both erythema nodosum and relapse status could not be performed because there were few such cases, and the data did not satisfy the necessary assumptions for the chi-square test.

Conclusion: In our study, the ABO blood group distributions in both patient and control groups were similar, and our data did not support a relationship between IGM and ABO blood groups.

Keywords: Idiopathic granulomatous mastitis, ABO subgroups, etiology

Öz

Amaç: Bu çalışmada, idiyopatik granülomatöz mastit (İGM) hastalarının A, B ve O kan grupları (ABO) kan alt grup dağılımının genel popülasyondan farklı olup olmadığının değerlendirilmesi amaçlanmıştır.

Yöntemler: Temmuz 2021-Ekim 2021 tarihleri arasında meme ünitesinde takip edilen ve rutin kontrollere başvuran İGM hastaları çalışmaya dahil edildi.

Bulgular: Bu dönemde 101 İGM hastası çalışmaya dahil edildi. Hastaların yaşları 21 ile 61 arasında değişiyordu (ortanca, 33 yıl). Hem hasta hem de kontrol grubunda en sık görülen ABO kan alt grubu Grup A idi (sırasıyla %48,5 ve %44,7). Gruplar arasında, ABO alt grupları arasındaki fark istatistiksel olarak anlamlı değildi ($p=0,122$). Sekiz hastada eritema nodozum vardı. Eritema nodozumlu hastaların %75'inde en sık görülen ABO alt grubu Grup A idi. Sekiz hastada nöks gelişti. Nüks gelişen beş hastanın ABO alt grubu A idi. Ancak, hem eritema nodozum hem de nöks durumuna göre ABO alt gruplarının karşılaştırılması, bu tür vakaların az olması ve verilerin ki-kare testi için gerekli varsayımları karşılamaması nedeniyle yapılamadı.

Sonuç: Çalışmamızda, hem hasta hem de kontrol gruplarında ABO kan grubu dağılımları benzerdi ve verilerimiz IGM ile ABO kan grupları arasında bir ilişki olduğunu desteklemedi.

Anahtar Sözcükler: İdiyopatik granülomatöz mastit, ABO alt grupları, etiyoloji

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INTRODUCTION

Idiopathic granulomatous mastitis (IGM) still has mysterious aspects since its first description in 1972 by Kessler and Wolloch (1). These mysterious issues are ethnicity, etiopathogenesis that cannot be exactly explained, and the fact that an appropriate treatment approach has not yet been fully established (2-4). Why is IGM more common in some countries, such as Türkiye, China, and Iran, although ethnicity is a significant factor? There is limited information on this subject. The possible relationship between human leukocyte antigens (HLA) classes I and II, and IGM was revealed in a study conducted in Türkiye (5). We believe that the distribution of HLA antigens is associated with IGM and should be investigated in other countries where IGM is common. Another important subject is the etiopathogenesis of IGM. Although some issues about autoimmunity and dysregulation in the immune system have been emphasized recently in IGM, the etiopathogenesis has not been exactly explained until now. Recent studies on the coincidence of extramammary manifestations, like erythema nodosum and arthritis with rheumatological diseases, such as Sjögren's syndrome, support the role of autoimmunity and immune dysregulation in the etiopathogenesis of IGM (2-4, 6-15).

The relationship between blood group antigens and certain diseases has been an interesting topic of research for more than a century. The associations between blood group antigen profiles and hematologic, cognitive, infectious, malignant, and metabolic diseases are known (16,17). A, B and O blood groups (ABO) antigens are found as membrane antigens on the erythrocytes' surfaces, platelets, vascular epithelial cells, intestinal, cervical, and mammary gland epithelial cells, as well as in plasma, milk, urine, and feces (16,17). The possible association of ABO blood groups with the etiopathogenesis of IGM may be of interest since ABO antigens are also found on mammary gland epithelial cells.

In this study, our aim was to evaluate whether the ABO subgroup distribution of patients with IGM was different from the general population without IGM.

MATERIALS AND METHODS

Patients

The newly diagnosed IGM patients and the patients histopathologically diagnosed with IGM, were treated and under follow-up between July 2021 and October 2021, were included in this cross-sectional study. Another inclusion criterion was that the patients gave consent to participate in the study. In addition to routine microscopic examination with hematoxylin and eosin stain, the Ehrlich-Ziehl-Neelsen stain was used to exclude tuberculosis in IGM patients. Refusal to participate in the study was the only exclusion criterion. The patients' age, parity status, history of breastfeeding, smoking, use of oral contraceptive pills, period since their last delivery, diagnosed chronic diseases, and medications were recorded. Furthermore, the patients' complaints at the time of diagnosis, the duration of complaints, physical examination findings, treatment approaches, and outcomes of treatment were noted.

The IGM patients were classified as patterns A (mass without inflammation), B (mass with inflammation), C (abscess-like), or

D (mass with ulcer, sinus, or fistula), clinically according to the classification by Yaghan et al. (18).

During this period, blood groups determined at the Selçuk University Medical Faculty Hospital Blood Bank were taken as the control group. These blood groups belonged to patients, excluding IGM, donors, or people who wanted to know their blood group.

Assessment of ABO/Rh Blood Groups

The blood samples were taken from newly diagnosed IGM patients at the time of diagnosis, and from patients who were either in remission or still under treatment at the control visit. The DG Gel ABO/Rh card (Diagnostic Grifols®, Barcelona, Spain) was used for the determination of. The test was conducted according to catalogue information and the manufacturer's recommendations.

This study was approved by Selçuk University Local Ethical Committee (approval number: 2021/345, date: 23.06.2021). The principles outlined in the Declaration of Helsinki were followed. Written consent was obtained from all participants.

Statistical Analysis

The GraphPad Prism 9 Software (La Jolla, CA, USA) was used for the statistical analysis in this study. The frequency and percentage values were used for the categorical data. There was no numerical data other than age. The minimum and maximum ages were reported alongside the median age. The chi-square test and Fisher's exact test were used for the comparison of categorical data, depending on whether they met the necessary assumptions. The p-value <0.05 was considered statistically significant.

RESULTS

A total of 101 of the 185 IGM patients followed up in the Breast Unit between July 2021 and October 2021 were included in the study. The patients' age ranged between 21 and 61 years (median, 33 years). Most of the patients were premenopausal (n=96, 95%).

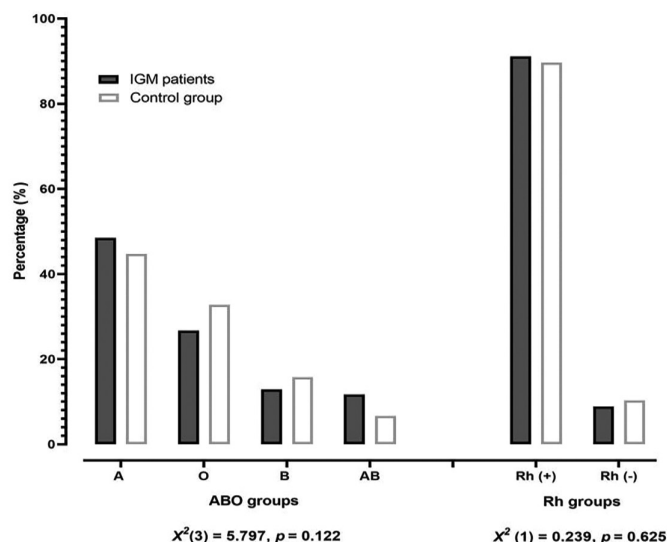


Figure 1. The blood subgroups of patients with idiopathic granulomatous mastitis and control groups.

IGM: Idiopathic granulomatous mastitis, ABO: A, B and O blood groups

There were 97 parous (96%) and 4 nulliparous (4%) patients. Ninety-seven of the patients had a history of breastfeeding. Twenty-five patients (24.8%) were using oral contraceptive pills. Furthermore, seven patients (6.9%) had a history of smoking.

The most common ABO blood subgroup both in the patient and control groups was Group A (48.5% and 44.7%, respectively). The chi-square test showed no statistically significant difference between the patient and control groups from the point of ABO subgroups [χ^2 (3)=5.797, $p=0.122$] (Figure 1; Table 1). Thus, the null hypothesis was accepted. Eight patients had erythema nodosum (8%). The distribution of ABO blood subgroups in patients without erythema nodosum is given in Table 2.

In 75% of patients with erythema nodosum, the most common ABO subgroup was A, while the most common ABO subgroup in patients without erythema nodosum was also A (46.2%). However, the ABO subgroup comparison of patients with and without erythema nodosum could not be performed statistically, since the necessary assumptions for the chi-square test were not met.

Eight patients developed relapse. The ABO subgroup distribution of these patients is in Table 2. The ABO subgroup was A in five of the patients who had a relapse. Similarly, the ABO subgroup comparison of patients with and without relapse could not be calculated because the necessary assumptions for the chi-square test were not met.

DISCUSSION

IGM has remained a mystery since it was first described. The etiology of IGM has not been exactly explained, and no ideal treatment approach has been established. However, studies about the role of the immune system in etiology have been increasing in recent years (2-4,6-8,10,11). Another important point is ethnicity. Why is IGM more common in some countries like Türkiye, China, Iran, South America, and so forth? However, the importance of immune dysregulation and autoimmunity remains a mystery.

ABO antigens are found on the surface of many cells in the human body, such as erythrocytes, platelets, vascular epithelial cells, and intestinal, cervical, and mammary cells. These antigens are also found in plasma, milk, urine, and feces (16,17). Blood group antigens have been used to predict the inheritance of diseases that are coded by genes closely located to the blood group genes on the same chromosome. Also, the discussions on the relationships of blood group antigens and antibodies with some diseases are ongoing. Given all this information, our study aimed to evaluate whether ABO subgroup distribution of patients with IGM is different from the general population.

Almost all of the studies showing the relationship between breast diseases and the ABO subgroup associate these diseases with breast

Table 1. The comparisons of the blood subgroups of patients with idiopathic granulomatous mastitis and control groups

	Patient Group		Control Groups		Statistics		
	n	%	n	%	χ^2	df	p-value
ABO subgroups					5.797	3	0.122
A	49	48.5	1119	44.7			
O	27	26.7	821	32.8			
B	13	12.9	397	15.9			
AB	12	11.9	167	6.7			
Rh subgroups					0.239	1	0.625
Positive	92	91.1	2243	89.6			
Negative	9	8.9	261	10.4			

ABO: A, B and O blood groups, df: Degrees of freedom

Table 2. ABO and Rh subgroups according to pattern, erythema nodosum and relapse status

	ABO subgroups				p-value	Rh groups		p-value
	A n, (%)	O n, (%)	B n, (%)	AB n, (%)		Positive	Negative	
Pattern					0.860			0.476
Non-complicated A + B, (n=39)	18, (46.2)	10, (25.6)	5, (12.8)	6, (15.4)		37, (94.9)	2, (5.1)	
Complicated C + D, (n=62)	31, (50)	17, (27.4)	8, (12.9)	6, (9.7)		55, (88.7)	7, (11.3)	
Erythema nodosum					*			<0.9999
Positive, (n=8)	6, (75)	1, (12.5)	0, (0)	1, (12.5)		8, (8.7)	0, (0)	
Negative, (n=93)	43, (46.2)	26, (28)	13, (14)	12, (11.8)		84, (91.3)	9, (100)	
Relapse					*			0.149
Developed, (n=93)	5, (62.5)	3, (37.5)	0 (0)	0, (0)		86, (93.5)	7, (7.5)	
Undeveloped, (n=8)	44, (47.3)	24, (37.5)	13, (100)	12, (100)		6, (6.5)	2, (22.2)	

*Statistical analysis could not be performed because the necessary assumptions for chi-square tests could not be satisfied

cancer (19-22). In their prospective cohort study, Gates et al. (19) investigated whether there were any relationships between the ABO subgroups and the known risk factors of breast cancer and survival. The authors found no association between the ABO subgroups and risk factors for breast cancer nor between the ABO subgroups and survival. Another study on this subject was a case-control study of Flavarjani et al. (20). The authors investigated the relationship between the ABO subgroups and breast cancer. The distribution of blood groups of both breast cancer patients and the control group was similar. Likewise, they found no difference between different breast cancer types, including invasive ductal carcinoma, medullary carcinoma, invasive lobular carcinoma, and Paget's disease. In their case-control study, Bothou et al. (21) found a relationship between breast cancer and blood group A, marking it as the first study in the literature to demonstrate this relationship. The most important limitation of this study, as emphasized by the authors, was the low number of both patients and subjects in the control groups. In another case-control study by Bezek et al. (22), the ABO subgroups of breast cancer patients and the control group were compared both genotypically and phenotypically. The authors found no difference. Similarly, no relationship could be demonstrated between tumor grade and tumor receptor status and the ABO subgroups.

In our study, we aimed to investigate whether there is a relationship between IGM and ABO subgroups in the context of the presence of ABO antigens in mammary epithelial cells. The most common ABO subgroup in the patients and the controls was subgroup A. There was no statistical difference between the distribution of ABO blood groups the patient group and the control group in our study.

Study Limitations

The most important limitation of our study is the small number of IGM patients with erythema nodosum or relapses, which limits the ability to perform precise statistical analysis.

CONCLUSION

A biochemical understanding of blood subgroups has enabled us to comment on their associations with some diseases. To shed light on the underlying responsible mechanisms, a large series of patients is needed to clarify the possible relationships between certain blood subgroup antigens and diseases thought to be associated.

Ethics

Ethics Committee Approval: This study was approved by Selçuk University Local Ethical Committee (approval number: 2021/345, date: 23.06.2021). The principles outlined in the Declaration of Helsinki were followed.

Informed Consent: Written consent was obtained from all participants.

Footnotes

Authorship Contributions

Surgical and Medical Practices: F.T., H.K., E.B., K.G., M.Ç., Concept: F.T., U.A., K.G., Design: H.K., U.A., E.B., Data Collection or Processing: F.T., U.A., K.G., M.Ç., Analysis or Interpretation: H.K., E.B., Literature Search: H.K., K.G., M.Ç., Writing: F.T., U.A., E.B., M.Ç.

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