Examination of inflammation markers in patients with idiopathic macular telangiectasia type 2

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ABSTRACT

Purpose: In this study, we aimed to compare blood inflammation markers, namely the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) between patients with IMT and healthy individuals.

Material and Methods: Forty-two patients with IMT and 50 healthy controls of similar age and gender without comorbidities were included in the study. Inflammation markers in the blood values of patients and controls were examined.

Results: The mean age of the patients with IMT was 60.27 ± 8.47 years, and that of the control group was 60.70 ± 10.38 years. The mean NLR, PLR, LMR, and red cell distribution width (RDW) values were 2.68 ± 0.98, 137 ± 30.30, 4.17 ± 0.98, and 13.85 ± 1.01% respectively, in the IMT group and 1.57 ± 0.32, 100.72 ± 16.78, 4.52 ± 1.29, and 12.93 ± 0.95% respectively, in the control group. In the IMT group, the NLR, PLR and RDW values were statistically significantly higher, and the LMR value statistically significantly lower compared to the control group ($p < 0.001$, $p < 0.001$, $p = 0.01$, $p < 0.001$, respectively).

Conclusion: This study is the first to compare inflammation markers in the blood values of patients with IMT and healthy controls. In this study, the patients with IMT presented with statistically significantly higher NLR, PLR, and RDW values and a statistically significantly lower LMR compared to the control group. We consider that the damage caused by inflammation and oxidative stress to Müller cells is effective in the pathogenesis of IMT.

Keywords: Idiopathic macular telangiectasia type 2, Inflammation, Lymphocyte-to-monocyte ratio, Neutrophil-to-lymphocyte ratio, Platelet-to-lymphocyte ratio.

INTRODUCTION

Idiopathic macular telangiectasia type 2 (IMT) is a condition that involves bilateral telangiectasia and aneurysmal dilatations of retinal capillaries in the juxtafoveolar region. IMT is more common among individuals in their fifth and sixth decades of life.[1] The findings of IMT include telangiectatic vessels, right-angle venules, retinal exudation, retinal pigment hyperplasia, foveal atrophy, and subretinal neovascularization. Biomicroscopic examination, fundus fluorescein angiography (FFA), and optical coherence tomography (OCT) are used in the diagnosis of the disease.[2]

Although the pathogenesis of the disease is not yet clearly known, neurodegeneration and Müller cell dysfunction are held responsible.[3] Prior research has demonstrated increased inflammation markers in various conditions such as glaucoma, cataract, retinal vein occlusion, retinitis pigmentosa, and senile macular degeneration and suggested that inflammation is effective in the etiopathogenesis of these conditions.[4,5]

IMT presents with changes in the vascular densities of the posterior segment of the eye. We consider that inflammation and oxidative stress may be effective in inducing these changes. In this study, we aimed to compare the blood levels of inflammation markers, namely the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) between patients with IMT and healthy individuals.

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MATERIALS AND METHODS

The study included 42 patients with IMT followed up in our clinic and 50 healthy controls of similar age and gender who presented to our clinic for routine check-ups without any comorbidities.

The exclusion criteria were as follows: any eye pathology other than IMT (e.g., glaucoma, uveitis, diabetic retinopathy, amblyopia, and epiretinal membrane), myopia higher than -6 diopters, axial length greater than 26 mm, a history of eye surgery other than uncomplicated cataract surgery, the presence of systemic disease, and smoking. At the time of the examination and assessment, there were no signs of active systemic infection in any of the patients.

Demographic characteristics (age, gender, medications used, etc.) and examination findings of the patients and controls were available in their files. The findings of a full ophthalmological examination, FFA, optical coherence tomography (OCT), biomicroscopy, and fundus examination of the patients and controls were also evaluated. While a slight intraretinal staining was observed on FFA among the patients with IMT who were in the early stages of the disease, filling in superficial telangiectatic capillaries and leakage in deep capillaries were detected in those with significant telangiectatic changes. In OCT, there wasan increase in foveal thickness and intraretinal cystoid changes in the IMT group.

The total neutrophil count (TNC), total lymphocyte count (TLYC), total leukocyte count (TLEC), total monocyte count (TMC), NLR, PLR, LMR, monocyte-to-high-density lipoprotein ratio (MHR), erythrocyte distribution width (RDW), and mean platelet volume (MPV) values were compared between 42 patients with IMT and 50 healthy individuals of similar age and gender.

Statistical Analysis

All the data obtained from the study were analyzed using the Statistical Package for the Social Sciences version 24.0 (SPSS Inc., Chicago, IL) package program. Descriptive statistics are given as percentages for categorical variables and mean, standard deviation, median, minimum, and maximum values for numerical variables. The suitability of numerical variables for the normal distribution was evaluated with the Kolmogorov-Smirnov and Shapiro-Wilk tests. The independent-samples t-test was used for pairwise comparisons that conformed to the normal distribution, while the Mann-Whitney U test was employed for pairwise comparisons that did not conform to the normal distribution. The correlations between the numerical values were assessed with the non-parametric Spearman correlation test. The results were evaluated within the 95% confidence interval, and p values of <0.05 were considered statistically significant.

RESULTS

Forty-two patients with IMT and 50 healthy controls of similar age and gender participated in the study. The mean age of the patients with IMT was 60.27 ± 8.47 years, and that of the control group was 60.70 ± 10.38 years. The demographic characteristics of the participants are given in Table 1.

Table 2 shows the comparison of the TNC, TLYC, TLES, and TMC values of the patients with IMT and controls. The mean TNC was found to be 5.62 ± 1.68 10^3/µl in the IMT group and 3.65 ± 0.90 10^3/µl in the control group. The mean TLEC was 8.53 ± 1.79 10^3/µl in the IMT group and 6.85 ± 1.34 10^3/µl in the control group. The TNC and TLEC values of the IMT group were statistically significantly higher than those of the control group ($p < 0.001$ and $p = 0.03$, respectively). However, no statistically significant difference was found in the comparison of the TLYC and TMC values between the two groups.

Table 3 shows the comparison of the NLR, PLR, LMR, MHR, RDW, and MPV values between the study groups. The mean NLR, PLR, and LMR values were determined to be 2.68 ± 0.98, 137 ± 30.30, and 4.17 ± 0.98 in the IMT group and 1.57 ± 0.32, 100.72 ± 16.78, and 4.52 ± 1.29 in the control group. The patient with IMT had statistically

Table 1: *Demographic characteristics of the study groups*

Variable	IMT group	Control group
Mean age (years)	60.27 ± 8.47	60.70 ± 10.38
Female patients (n)	22	26
Male patients (n)	20	24
Total number of patients	42	50

IMT: Idiopathic macular telangiectasia type 2

Table 2: *Comparison of white blood cell counts between the study groups*

Variables	Group	n	Mean	SD	Min	Max	P
Total neutrophil count (10^3/µl)	IMT Control	4250	5.62 3.65	1.68 0.90	3.99 2.30	59.21 5.57	<0.001*
Total lymphocyte count (10^3/µl)	IMT Control	42 50	2.21 2.36	0.55 0.49	1.72 1.61	3.58 3.69	0.063*
Total leukocyte count (10^3/µl)	IMT Control	42 50	8.53 6.85	1.79 1.34	6.40 4.80	12.80 9.80	0.03*
Total monocyte count (10^3/µl)	IMT Control	42 50	0.53 0.55	0.09 0.17	0.36 0.27	0.72 1	0.35*

Bold values represent statistical significance IMT: Idiopathic macular telangiectasia type 2, SD: Standard deviation, Min: Minimum, Max: Maximum, *Mann-Whitney U test.

Table 3: *Comparison of the values of various inflammation markers between the study groups*

Variables	Group	n	Mean	SD	Min	Max	P
Neutrophil-to-lymphocyte ratio	IMT Control	42 50	2.68 1.57	0.98 0.32	1.14 0.72	4.25 1.97	<0.001*
Platelet-to-lymphocyte ratio	IMT Control	42 50	137 100.72	30.30 16.78	87.54 75.86	173.25 140	<0.001*
Monocyte-to-lymphocyte ratio	IMT Control	42 50	4.17 4.52	0.98 1.29	3.12 2.33	6.02 8.40	0.01*
Monocyte/high-density protein ratio	IMT Control	42 50	0.008 0.009	0.002 0.005	0.006 0.001	0.013 0.021	0.80*
Mean platelet volume (fl)	IMT Control	42 50	10.64 10.34	1.10 1.26	12 7.10	15.50 12.50	0.92*
Red cell distribution width (%)	IMT Control	42 50	13.85 12.93	1.01 0.95	15.50 10.90	0.72 15.90	<0.001**

Bold values represent statistical significance. IMT: Idiopathic macular telangiectasia type 2, SD: Standard deviation, Min: Minimum, Max: Maximum, *Mann-Whitney U test, **Student's t-test

significantly higher NLR and PLR values and a statistically significantly lower LMR value compared to the controls ($p < 0.001$, $p < 0.001$, and $p = 0.01$, respectively). The mean RDW values of the IMT and control groups were 13.85 ± 1.01% and 12.93 ± 0.95%, respectively, indicating a statistically significantly higher value among the patients with IMT($p<0.001$). However, no statistically significant difference was found in the comparison of the MHR or MPV values between the two groups. Lastly, there was a statistically significant, positive correlation between NLR and PLR ($r=0.52$, $p=0.01$).

DISCUSSION

IMT is a vascular disease that causes telangiectasia and aneurysmal dilatations in the eye vessels. Although the pathogenesis of IMT is not yet fully known, Müller cell degeneration and vascular restructuring are held responsible. Ongoing research aims to elucidate the etiology of this disease.[6,7]

IMT is a disease in which vascular atrophy, vascular proliferation, and fibrosis affect the retinal vessels. It has been suggested that Müller cell damage may be effective in inducing this change in patients with IMT. Müller cells are responsible for intercellular connections and neuronal support in the retina. These cells are involved in retinal blood flow regulation, cytokine production, and fluid-electrolyte exchange. Through these properties, Müller cells promote angiogenesis. Inflammation and oxidative stress can lead to the damage of Müller cells, which in turn can result in telangiectatic vessel formation and neovascularization. In other words, the pathogenesis of IMT is considered to be associated with inflammation and oxidative stress, as well as the consecutive damage to Müller cells.[6-8]

In a study comparing 28 patients with glaucoma and 27 healthy individuals, Atalay et al. found the mean NLR value to be 1.82 ± 0.68 in the glaucoma group and 2.24 ± 0.84 in the control group. The NLR value was determined to be statistically significantly higher in patients with glaucoma compared to the controls (p = 0.07).[9] In another study, Meng et al. compared 104 patients with dry eye disease with 97 healthy individuals and reported their mean NLR values to be 2.59 ± 1.25 and 2.20 ± 1.24, respectively. The NLR value was statistically significantly higher in patients with dry eye disease compared to the control group (p=0.027).[10] Atum et al., comparing 46 patients with retinal artery occlusion and 51 healthy individuals, determined the mean NLR value as 2.85 ± 1.70 in the former and 1.63 ± 0.59 in the latter, indicating a statistically significantly higher value in the patient group compared to the control group (p < 0.001).[11] In the literature, the NLR has been found to be higher in various conditions, such as cataract, retinal vein occlusion, senile macular degeneration, and retinitis pigmentosa, compared to controls.[4,5,12,13] In addition, there are researchers indicating a higher NLR value in the presence of conditions where inflammation is effective, including cardiovascular diseases, renal diseases, and Behçet's disease.[14-16] In the current study, the mean NLR was 2.68 ± 0.98 in the IMT group and 1.57 ± 0.32 in the control group.

NLR has recently been used as an inflammatory marker in many studies. Neutrophils are one of the main cells involved in inflammation. Proteases secreted by neutrophils destroy proteins and cell membranes and cause the proteolytic activation of the complement system. In addition, substances released from neutrophils increase vascular permeability and cause chemotaxis, leading to the deepening of inflammation. The neutrophil count increases in the presence of systemic inflammation. Mediators secreted from neutrophils can also cause tissue and vascular damage. Lymphocytes are responsible for preventing cell proliferation and migration. In addition, the lymphocyte count generally decreases in cases of systemic inflammation.[10,11,14] Furthermore, while inflammation in the vessels causes the number of neutrophils to increase, it also accelerates lymphocyte apoptosis.[17] The inflammation and increased oxidative stress in the vessels in patients with IMT cause Müller cell damage, which leads to telangiectatic vessel formation. Therefore, we consider that the NLR value can be used as an inflammation marker in IMT.

In a study comparing 42 keratoconus patients and 42 healthy individuals, Elbeyli et al. found the mean PLR value to be 143 ± 36 in keratoconus patients and 106 ± 23 in controls. The PLR value was statistically significantly higher in the patient group compared to the control group (p < 0.001).[18] Icel et al., who compared 50 patients with high myopia and 29 emmetropes, reported the mean PLR values of these groups to be 114.62 ± 23.21 and 91.42 ± 18.73, respectively. Accordingly, the PLR value was statistically significantly higher in patients with high myopia compared to the controls (p < 0.001).[19] Celik et al. performed a comparison of 78 patients with dry eye disease and 60 healthy individuals. The authors found the mean PLR values of the dry eye and control groups to be 138.4 ± 62.6 and 118.5 ± 64.7, respectively, indicating a statistically significantly higher value in the former (p = 0.026).[20] In our study, the mean PLR was 137 ± 30.30 in the IMT group and 100.72 ± 16.78 in the control group.

Recently, PLR has been utilized as an indicator of inflammation in several studies. Platelets are basically responsible for facilitating clotting. However, some mediators released from platelets are also effective in inflammation. α-granules, lysosomes, and thrombin released from platelets are important in the inflammation cascade, chemotaxis, and stimulation of endothelial cells. In addition, mediators released from platelets are effective in the activation of leukocytes and promote the role of leukocytes in inflammation.[19-22] We consider that inflammation is effective in promoting new vessel formation in IMT. Therefore, it can be suggested that PLR can also be used as an inflammation marker in this disease.

Gokce et al. followed up 210 patients with pseudoexfoliation syndrome and compared patients with and without complications after cataract surgery. The authors determined the mean TNC value to be 5.19 ± 0.64 10^3/µl in patients with complications and 4.43 ± 0.86 10^3/µl in those without complications. The TNC value was statistically significantly higher in the complicated group compared to the non-complicated group (p < 0.001).[4] Szydelko et al. determined the mean TNC value as 3.78 ± 1.42 10^3 /µl in patients with Graves' orbitopathy and 3.11 ± 0.46 10^3/µl in controls. Accordingly, the TNC value was statistically significantly higher in patients with Graves' orbitopathy compared to the control group (p < 0.001).[23] In the same study, the mean TLEC value was found to be 6.64 ± 2.09 10^3/µl in the group with Graves's disease who had Graves' orbitopathy and 5.96 ± 1.56 10^3/µl in those with Graves's disease without Graves' orbitopathy. The TLEC value was statistically significantly higher in patients with Graves' orbitopathy compared to the other group (p = 0.022).[23] In our study, the mean TNC and TLEC values were 5.62 ± 1.68 10^3/µl and 8.53 ± 1.79 10^3/µl, respectively, in the

IMT group and 3.65 ± 0.90 10^3/µl and 6.85 ± 1.34 10^3/µl, respectively, in the control group.

Neutrophils and other leukocytes play an active role in inflammation in the body. Mediators released from these cells direct inflammation and assume roles in various processes, such as chemotaxis, increased vascular permeability, apoptosis, and necrosis. As a result, neutrophil and leukocyte counts increase in the presence of inflammation.[14,17] Therefore, we consider that TNC and TLEC can be used as inflammation markers in diseases such as IMT, where inflammation is effective.

Elbeyli et al. reported the mean RDW value to be 14.3 ± 1.60% in keratoconus patients and 12.9 ± 0.54% in controls, revealing a statistically significantly higher value in the former ($p < 0.001$).[18] In another study, Tang et al. found that the mean LMR value was statistically significantly higher in glaucoma patients (4.57 ± 1.78) than in controls (5.35 ± 1.99) ($p < 0.001$).[24] In the current study, the mean RDW and LMR values of the patients with IMT were 13.85 ± 1.01% and 4.17 ± 0.98, respectively, while those of the control group were 12.93 ± 0.95% and 4.52 ± 1.29, respectively.

In recent studies, the RDW and LMR values have begun to be employed as markers in various diseases caused by inflammation. In our study, similar to previous research, the RDW value was higher and the LMR value was lower among the patients with IMT compared to the control group.

Concerning the limitations of the study, the major shortcoming was the small number of patients. However, we consider that this study is important since it has the potential to pave the way for future multicenter investigations aimed at elucidating the inflammatory etiology of IMT.

CONCLUSION

This study is the first to compare the blood values of inflammation markers between patients with IMT and healthy controls. In this study, the patients with IMT were found to have statistically significantly higher NLR, PLR, and RDW values and a statistically significantly lower LMR value compared to the controls. We consider that the damage caused by inflammation and oxidative stress to Müller cells is effective in the pathogenesis of IMT. Therefore, it can be suggested that the NLR, PLR, LMR, and RDW values can be used as inflammation markers in this disease.

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