Original Article

Neutrophil-Lymphocyte Ratio in Branch Retinal Vein Occlusion

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Abstract:

Objective: Branch retinal vein occlusion (BRVO) is the most common retinal vascular disease following diabetic retinopathy. Pathogenesis of BRVO is multifactorial and could not be clarified enough yet. As BRVO is a disease that goes with thrombosis and inflammatory processes, inflammatory markers could help to predict the risk of BRVO. The aim of this study was to evaluate the association between neutrophil-lymphocyte ratio (NLR) and the BRVO.

Materials and Methods: Forty-three patients with BRVO were included to this retrospective study. Forty age and sex-matched healthy volunteers were recruited as the control group. Demographic characteristics, white blood cell (WBC), neutrophil, lymphocyte, monocyte, platelet counts and NLR were recorded and compared between the patients and the control group.

Results and Discussion: The mean WBC, neutrophil and NLR were significantly higher in the BRVO patients compared with control group (7.89±1.8fL vs 6.97±1.4fL, p=0.014, 4.85±1.4fL vs 4.01±0.9fL, p=0.002, 2.40±1.2 vs 1.87±0.5, p=0.026, respectively). There were no difference between two groups in terms of lymphocyte, monocyte and platelet counts (p=894, p=0.22, p=0.589, respevtively).

Conclusion: NLR was higher in patients with BRVO and higher NLR may contribute to development of BRVO associated with systemic and/or local inflammation.

Key Words: Biomarker; inflammation; branch retinal vein occlusion; NLR, neutrophil

Introduction

Branch retinal vein occlusion (BRVO) is recognized as the most common retinal vascular disease following diabetic retinopathy and may result in severe loss of vision (1). The pathogenesis of BRVO is multifactorial and underlying causes could not be clarified enough yet. Numerous systemic and ocular risk factors were considered to be involved in the etiology of BRVO (2). The most important systemic risk factors are hypertension and arteriolosclerosis (3,4).

The count of the white blood cell which is one of the basic cells for inflammation and sub-types are used as a classical marker for the inflammatory state especially in cardiovascular diseases (5). Beyond cardiac diseases, there are studies indicating that a low-grade inflammation exists in some conditions such as diabetes, hypertension, metabolic syndrome and obesity (6-9). Recently, neutrophil-lymphocyte ratio (NLR) is used as a well indicator of inflammation together with other inflammatory markers for cardiac and non-cardiac diseases and ocular pathologies (10-13). Suggestions about effectiveness of systemic and

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local inflammation on physiopathology of BRVO were made in the literature (2-4). To the best of our knowledge, there is few studies about NLR in patients with BRVO in the litareture (14,16). The aim of the present study is to review NLR levels in the patients with BRVO and to determine if any association exists between these.

Materials and Methods

Patients

Files of the patients who have referred our clinic due to the complaint of decreased visual acuity and been diagnosed with BRVO were reviewed retrospectively. Patients with signs of an acute stage of BRVO within a week and no history of previous treatment were included in the study. The study protocol was arranged in accordance with principles of the Helsinki Declaration and Ethics committee approval was received for this study from Local Ethics Committee. Informed consent was obtained from all subjects.

Exclution criteria

Age, gender, ocular findings, systemic diseases and drug usage history of the patients were recorded. Patients with hypertension were under control medication. Patients with diabetes, chronic heart or liver disease, acute or chronic kidney failure, acute infectious disease, inflammatory bowel diseases, chronic obstructive pulmonary disease or smoking, using anticoagulant agents or nonsteroidal anti-inflammatory drugs as well as the patients whose biochemical analyses have not been ordered at diagnosis were excluded.

Control group

Along with 43 patients meeting these criteria, 40 patients without any systemic disease except for hypertension whose routine preoperative laboratory tests were ordered because of cataract were included as the control group.

Procedures

Anterior and posterior segment examination, ocular blood pressure measurement, optic coherence tomography and fundus fluorescein angiography imaging were performed for all patients. BRVO was diagnosed by venous dilatation and folding increase on the arteriovenous crossing site, flame-shaped and spot-stain hemorrhages limited with distribution of the vein in the retina, retinal exudates and/or macular edema on the affected retinal site in the fundus examination performed by a split lamp.

Laboratory measurements

Blood samples were collected into the tubes (Vacuette) including ethylenediaminetetraacetic acid (EDTA); an automated blood count device (Beckman-Coulter LH 780 Analyzer, Miami, Florida, USA) was used for biochemical analysis. White blood cell (WBC), neutrophil, lymphocyte, monocyte and platelet levels which are automatically detected in complete blood count were recorded. NLR was obtained by diving the neutrophil count to the lymphocyte count. Reference values were determined as $4\text{-}10 \times 10^3/$ mm^3 for WBC, $1.5\text{-}7 \times 10^3/$ mm^3 for neutrophil, $1\text{-}3.7 \times 10^3/$ mm^3 for lymphocyte, $0\text{-}0.7 \times 10^3/$ mm^3 for monocyte and $160\text{-}450 \times 10^3/$ mm^3 for the platelet.

Statistical methods

A package program for statistics (SPSS for Windows, version 18.0, SPSS, Chicago, IL, USA) was used for statistical analysis. Distribution of the variables used in the study was analyzed by Kolmogrov-Smirnov test. Quantitative values were assessed by chi-square test; comparison of continuous variables was performed by parametric student t-test and non-parametric Mann-Whitney U test. Data were reported as mean±standart deviation (±SD). $p < 0.05$ values were accepted as significant.

Results

The mean age of 43 patients (23 females, 20 males) included into the study was 63.09±13.14 years and 40 control subjects (23 females, 17 males) group was 63.87±11.38 years. The patient group and the control group were similar in terms of age and gender (p=0.77, p=0.82, respectively). There was no statistical difference in the BRVO and control groups, according to presence of hypertension and intraocular pressure (Table 1).

Mean WBC and neutrophil were detected as 7.89±1.8fL and 4.85±1.4fL, respectively in the patients with BRVO whereas 6.97±1.4fL and 4.01±0.9fL, respectively in the control group; these values were significantly higher in the patient group than the control group (p=0.014, p=0.002, respectively). NLR was 2.40±1.2 in the patient

Table 1. Baseline characteristics of patients and the control group.

	BRVO n=43	Control n=40	p
Gender (F/M)	23/20	23/17	0.82
Age (years)	63.09±13.14	63.87±11.38	0.77
Hypertension	23/43	20/40	0.75
IOP (mm/Hg)	15.51±2.79	16.11±2.38	0.30

BRVO: Branch retinal vein occlusion; F: Female; M: Male; IOP: Intraocular pressure

Table 2. Laboratory data in the patient and the control group.

	BRVO n=43	Control n=40	p
WBC (fL)	7.89±1.8	6.97±1.4	0.014
Neutrophil (fL)	4.85±1.4	4.01±0.9	0.002
Lymphocyte (fL)	2.21±0.7	2.24±0.6	0.89
Monocyte (fL)	0.61±0.2	0.53±0.1	0.22
Platelet (x103 µL)	247.65±47.3	253.71±51.5	0.59
NLR	2.40±1.2	1.87±0.5	0.026

BRVO: Branch retinal vein occlusion; WBC: White blood cell count; NLR: Neutrophil-lymphocyte ratio

group and 1.87±0.5 in the control group; and the difference between both groups was significant (p=0.026). There was not any statistical difference between both groups in terms of lymphocyte, monocyte and platelet counts (p=0,89, p=0,22 and p=0.59, respectively). Numeric data of both groups were summarized in Table 2.

Discussion and Coclusion

The most important risk factors in development of BRVO are hypertension and arteriolosclerosis. The other risk factors include diabetes mellitus, hyperlipidemia, smoking, cardiovascular disease, pregnancy, oral contraceptive, age, increased body mass index, hyperviscosity, protein C or S failure and primary open angle glaucoma (1-3). However, to explain all these cases with these risk factors is difficult and exact pathophysiology of BRVO is not known completely (4).

Arteries and veins appear in a common glia sheath on crossing sites in the retina. Hypertension cause venous occlusion as a result of compression of the sclerotic artery onto the vein at arteriovenous crossing sites and lamina cribrosa level (17). Numerous similar studies showed that systemic atherosclerosis is a significant risk factor for development of BRVO (18,19). As the sclerotic changes and thickening occurred in the fibrous tissue by aging increase the arterial compression and cause stasis of the venous flow and hemodynamic changes. Compression of the vein causes increased retinal venous blood flow velocity, turbulence of blood flow, endothelial injury, secondary thrombosis and may lead occur inflammation (20).

Although inflammation plays a role in pathophysiology of many diseases, it also contributes to clinical outcomes of these diseases (21). White blood count and sub-types are used as a classical marker of the inflammatory state (5). Since NLR, in particular, is accepted as an independent prognostic factor in coronary artery diseases, it has attracted attention lately (21). Furthermore, inflammation has a important role in pathophysiology of the vascular diseases. Inflammation is important in hypertensive vascular changes and atherosclerotic process. White blood cells and sub-types are critical in arrangement of the inflammation which appears during atherosclerotic process (22). There are studies reporting that NLR values are significantly affected in atherosclerosis and systemic hypertension (21-24). The cause for detection of WBC, neutrophil count and NLR higher in the patients with BRVO than the control group may depend to underlying atherosclerotic and hypertensive vascular changes.

As is known, venous stasis, vascular wall injury and hypercoagubility are known as Virschow's Triad. Another mechanism of action involving inflammation in development of BRVO may be through increasing the hypercoagubility. Interleukin-1β, interleukin-6 and tumor necrosis factor-α are known as prothrombotic cytokines and cause changes in the blood flow (25). Similarly, increased plasma homocysteine levels cause chronic inflammation as well as hypercoagubility, injury on the vascular endothelium and blood flow deceleration (26).

There are studies indicating that systemic inflammatory risk factors along with local inflammation contribute to the etiology of BRVO (27-29). The aqueous flare level appeared as a result of the destruction of the blood-aqueous barrier were reported to be detected higher in the patients with BRVO than the patients in the control group (27). Moreover, detection of increased levels of VEGF and inflammatory cytokines were reported in vitreous fluids of the patients with BRVO (29).

To the best of our knowledge, there are few studies analyzing the NLR and mean platelet volume level in the patients with BRVO in the litareture and shown similar results with our results. (15,16). Unlike, in one study, the authors detected no difference in NLR values between BRVO patients and healty control group (14). Further investigations regarding its potentially use as a prognostic biomarker in patients with BRVO are needed.

One of the limitations of the current study is that it has a retrospective design and relatively low number of patients. Furthermore, since serum levels of other inflammatory factors such as C-reactive protein, interleukin-1β, interleukin-6

and tumor necrosis factor-α could not be known, the strength of the present study is reduced.

In conclusion, consequently, higher NLR levels detected in the patients with BRVO support the hypothesis that systemic and local inflammation may be effective in the etiology of BRVO. However, large-scaled, randomized controlled and prospective studies including more patients are required.

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