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Original Article

Evaluation of mean platelet volume and distribution width in childhood infectious mononucleosis

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Abstract

Aim: Epstein-Barr virus (EBV) is an infectious agent that affects more than 95% of the world's population and is usually diagnosed through characteristic clinical findings, hematologic changes in complete blood counts, and atypical lymphocytes in peripheral smears. A definitive diagnosis requires serological confirmation of the EBV infection. This study intends to investigate the relationship between the mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT) values, which are platelet indices that can be used as markers of inflammation in different inflammatory diseases, and the EBV-associated infectious mononucleosis (IM) disease.

Material and Methods: A total of 54 patients (30 males, 24 females) with EBV-associated infectious mononucleosis diagnosed at the Department of Pediatrics, University of Gaziantep University between January 2015 and June 2017 were retrospectively analyzed. Meanwhile, 68 age and gender-matched children were involved as the control group. White blood cell (WBC), hemoglobin (Hb), MPV, PDW and PCT values were compared across the patient and control group.

Results: While the MPV values of the EBV-associated IM patient group were significantly high, the PDW values were significantly low ($p<0.001$). The mean (WBC) counts of the IM patients were higher than those of the control group ($p<0.001$). There was no significant difference between the groups in terms of PCT, platelet and Hb values.

Conclusion: According to our findings, PDW and particularly MPV may be useful markers of inflammation during EBV-associated IM.

Keywords: Infectious mononucleosis; mean platelet volume; platelet distribution width

INTRODUCTION

Epstein-Barr virus is an infectious agent that affects more than 95% of the world's population and is primarily transmitted via oral secretions and sexual intercourse. Infectious mononucleosis, on the other hand, is a clinical syndrome often caused by EBV and its typical trio of symptoms are fever, pharyngitis, and generalized lymphadenopathy (1). While the epidemiology of the disease depends on the age, geographical region and ethnicity of the patient, its prevalence ranges from 10-90% (2). Infectious mononucleosis usually affects infants and those in early childhood from developing countries. However, in more industrialized societies, the average age of diagnosis is shifting from 6-8 years to younger adolescents. It is usually diagnosed through characteristic clinical findings, hematologic changes in complete blood counts, and atypical lymphocytes in peripheral smears. Differential diagnosis is important because other infections such as cytomegalovirus (CMV), Toxoplasma gondii, adenovirus, hepatitis virus, HIV, or possibly rubella virus may cause infectious mononucleosis-like illnesses. Especially CMV is particularly the common cause of IM with clinic and laboratory signs after EBV. So a definitive diagnosis is needed and requires serological confirmation of EBV infection (heterophile antibody tests or EBV-specific antibodies). A moderate increase in liver function tests without leukocytosis (mainly lymphocytes), mild thrombocytopenia or jaundice is a laboratory finding that can be seen in more than 50% of IM patients (1,3).

Many recent studies have shown that platelets have a complex role in acute and chronic inflammatory responses, microbial host defense and the healing of wounds (4). The

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mean platelet volume, PDW and PCT values have been found to be associated with platelet morphology and proliferation kinetics along with the number of platelets, and platelet markers have been reported to be used as markers of inflammation for different inflammatory diseases. There are different studies in the literature reporting that MPV correlates positively or negatively with inflammatory activity (5). As another platelet marker, PDW is also a determinant parameter, especially in cases of platelet width variability and thrombocytosis (6). In addition, both parameters are widely used in clinical practice. This study examines the relationship between the MPV, PDW and PCT values of EBV-associated IM patients and those of the control group.

MATERIAL and METHODS

A total of 54 patients (30 males, 24 females) with EBV-associated IM diagnosed at the Department of Pediatrics, Gaziantep University between January 2015 and June 2017 were retrospectively analyzed. The patients with the presence of typical clinical symptoms with atypical lymphocytosis in the peripheral blood and whose diagnosis was confirmed with a serologically positive EBV VCA Ig M test were enrolled in the study. For differential diagnosis, each patient was evaluated especially for CMV by serological tests (CMV IgM) and throat cultures were taken from the patients with high fever for group A Streptococcus. EBV VCA IgM levels were measured with Architect Macro ELISA (Abbott) Machine in the Microbiology Laboratory of our hospital. The values higher than 1 S/CO were accepted positive. The patient's demographic data and some complete blood count parameters, checked during the diagnosis, including white blood cell, hemoglobin (Hb), platelet (PLT), MPV, PDW, and PCT counts were reached from the archive. Meanwhile, 68 age and gender-matched healthy children's white blood cell, Hb, platelet, MPV, PDW, and PCT counts were measured and these parameters were compared between the patients and control group. The control group consisted of healthy children who applied Social Pediatrics outpatient clinic of our hospital. Voluntary consent forms obtained from the control group were presented to the ethics committee. Gaziantep University Ethics Committee's approval was obtained for the study.

Statistics

All values obtained from the groups were recorded in the SPSS 20 (Statistical Package for Social Sciences) program for statistical analysis. The mean and standard deviation values of the laboratory data were calculated. The student's t-test was used for continuous variables and the chi-square test for categorical variables was used in the analysis of the data. $p<0.05$ was considered statistically significant.

RESULTS

The presence of disease symptoms in the patient group were given in Table 1. The demographic characteristics and laboratory results of the 54 patients and 68 healthy children were given in Table 2. The mean diagnosis age of the patients and the control group were 6.48±2.91 and 7.69±5.08, respectively. There was no significant difference between the groups in terms of age and gender distribution. When parameters of patients were compared those of controls, the MPV values of patients were significantly higher, while the PDW values were significantly lower in patients ($p<0.001$). The white blood cell values of the IM patients were higher than those of the control group ($p<0.001$). There was no significant difference between the groups in terms of PCT, platelet and Hg values.

Table 1. Presence of disease symptoms in the patient group

Disease Symptoms	N	%
Fever	46	85.1
Sore Throat	41	75.9
Malaise, Fatigue	29	53.7
Myalgia	17	22.2
Abdominal Pain	12	31.4

Table 2. Demographic characteristics and laboratory findings of patients and control group

	Patient (N=54)	Control (N=68)	P Value
Age (Years)	6.48±2.91	7.69±5.08	0.102
Sex (F/M)	24/30	34/34	0.587
Hg (Gr/Dl)	12.22±1.21	12.84±1.39	0.010
Leukocytes (X10/L)	12.20±5.32	9.30±2.87	**<0.001**
Platelets (X10/L)	404.20±756.65	314.11±67.46	0.387
Mpv (Fl)	9.36±1.20	8.03±0.89	**<0.001**
Pdw (%)	12.05±2.98	15.21±2.48	**<0.001**
Pct (%)	0.28±0.12	0.24±0.51	0.096

DISCUSSION

Epstein-Barr virus – one of the most common viruses to which more than 95% of the world's population is exposed – is the most common cause of IM. Specific EBV antibodies are used for definitive diagnosis, while changes in complete blood count values also help with the diagnosis. Mild thrombocytopenia is observed in more than 50% of patients, while leukocytosis with lymphocytosis is observed in more than 90% of patients (4). This study intended to review the changes of some platelet indices including MPV, PDW and PCT as markers of acute inflammation during EBV-associated IM. Many studies have been conducted in recent years to better understand the role of platelet indices during inflammation, there has

been more academic interest in MPV as a determinant of platelet activation (7, 8). MPV is a measure of platelet size and shows the rate of platelet production and activation (8). Given that thrombopoiesis is regulated by certain inflammatory cytokines and thrombopoietin, systemic inflammation is expected to affect the platelet production and volume. In this context, MPV can be used as a marker in pro-inflammatory and prothrombotic conditions.

Higher systemic inflammation was found to be associated with smaller platelet volume. This inverse relationship reflects the tendency to maintain homeostasis by keeping the circulating platelet mass constant (5, 9).

Looking at studies on autoinflammatory diseases, Yazıcı et al. showed that MPV increased in direct proportion to disease activity in patients with ankylosing spondylitis and decreased through anti-inflammatory therapy (10). On the other hand, in a different study with FMF patients in the pediatric age group, MPV was found to be lower during attacks (11). Another research on Behçet's disease revealed that no significant relationship was found between MPV and the disease activity (12, 13). Alternatively, in a retrospective study of adult patients with acute myocardial infarction, Coşkun et al. showed that MPV might provide information about the severity of coronary artery disease (14). Similarly, Tümtürk et al. found MPV to be predictive for the diagnosis of central nervous system tumors in children with non-specific symptoms (15). In studies on viral infectious diseases such as HIV and RSV, MPV was found to be low whereas, in a study on tuberculosis patients, MPV was found to be high (16). In our study, the MPV values of EBV-associated IM patients were significantly higher than those of the control group. Different results between inflammation and MPV in different studies may be due to the consumption of large volume platelets on the inflammation area that increase with inflammation, or the lack of standardization of MPV measurement (17).

The hypothesis proposing a "constant platelet mass" provided by changing the volumes of platelets in order to maintain blood homeostasis seems to be more suitable for auto-inflammatory diseases (5). According to a meta-analysis reported by Beyan and Beyan of 181 MPV-related studies using healthy control group data, the time between drawing blood and the measurement, as well as the techniques used, may affect the results (18).

PDW, another platelet marker, reflects platelet activation similar to MPV, has also attracted quite a lot of scholarly attention; it reflects the platelet volume variability, in other words, the platelet heterogeneity, and rises in cases of platelet anisocytosis (19). In addition, it may exhibit variations during inflammation. In this regard, Dinç et al. found increased PDW values in acute appendicitis patients compared to healthy controls (20). According to them it might be more important than complete blood count and neutrophil percentages in the diagnosis of acute appendicitis. Similarly, some other studies revealed that that PDW has been found increased in cholecystitis, pulmonary tuberculosis, and coronary artery diseases (21-23). However, in our study, PDW was found significantly low in the patient group. Similar to the findings of our study, Liang et al. found lower PDW values in patients with Alzheimer's and dementia (24). On the other hand, Yılmaz et al. found no relationship between PDW and prognostic factors such as overall survival and sequel development in pediatric acute ischemic stroke patients (25). Similarly, PDW levels were found to show no changes either in intensive care patients or in children with urinary tract infection or in patients who have leukocytosis. To be mentioned that, to our knowledge, literature regarding PDW values during viral infections is scarce.

PCT which is a parameter showing amount occupied by platelets in the blood demonstrated no difference between patients and controls. However, some studies reported various results. For instance, high PCT percentages were found to be associated with autoimmune gastritis and PCT was reported to be correlated with either the severity or activation of inflammatory bowel diseases (26,27). When we look at the infectious conditions, there have been a limited number of studies on PCT, an example of these is tuberculosis in which increased PCT percentages were reported (21).

As a limitation, we were not able to monitor the patients during the all course of their diseases or at their recovery. Therefore, it was not possible to present a change pattern of MPV and PDW during all phases of disease in this study.

CONCLUSION

In conclusion, we found that MPV was increased and PDW was decreased in EBV associated IM patients. These parameters showed a pattern of change possibly due to inflammation at EBV infection. Although the mechanism of these changes is not clear yet, PDW and MPV seem to be capable of reflecting inflammation during this infection. However, further studies are required to support our findings.

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