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Research Article

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CLINICAL SIGNIFICANCE OF PLATELET PARAMETERS IN THE DIFFERENTIAL DIAGNOSIS OF THROMBOCYTOPENIA

TROMBOSİTOPENİNİN AYIRICI TANISINDA TROMBOSİT PARAMETRELERİNİN KLİNİK ÖNEMİ

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Öz

Amaç: Hipoprodüktif (örn: AA, AML, ALL, MDS) ve hiperdestrüktif trombositopeninin (örn: ITP) ayrımında en geçerli tanı yöntemi kemik iliği incelemesidir. Ancak kemik iliği incelemesi oldukça invaziv bir yöntem olup ITP gibi hiperdestrüktif trombositopeninin tanısında yapılması bazı çalışmalarda önerilmemektedir. Son yıllarda yapılan bazı çalışmalarda MPV, PCT ve PDW gibi platelet parametrelerin trombositopeninin ayırıcı tanısında kullanılabileceği ileri sürülmüştür. Bu çalışmada amacımız, bu parametrelerin trombositopeninin ayırıcı tanısındaki etkinliğini araştırmaktır.

Materyal ve Metot: Çalışmaya trombositopenisi olan 164 hasta dahil edildi. Hastalar tanısına göre hiperdestrüktif (75 ITP) ve hipodestrüktif(25 AA, 25 MDS, 24AML, 15 ALL) trombositopeni olarak iki gruba ayrıldı. Hastaların tanısı güncel hematoloji, patoloji rehberleri ve kromozom analizleri kullanıldı. K3EDTA'lı tüplere alınan kan örnekleri Beckman-Coulter otomatik cihazlarda çalışıldı.

Bulgular: Trombosit sayısı açısından iki grup arasında herhangi bir farklılık yoktu. Cinsiyet, yaş ve PDW açısından iki grup arasında herhangi bir farklılık izlenmedi. Bununla birlikte MPV, hiperdestrüktif grupta hipodestrüktif gruptakilere göre belirgin olarak daha yüksekti. Bunun aksine PCT değeri hiperdestrüktif grupta hipodestrüktif gruba göre önemli ölçüde daha düşüktü.

Sonuç: Bu çalışmada; trombosit parametrelerinin kullanımının, ITP hastalarının tanısını güçlendirebileceği, diğer klinik ve laboratuvar testleri ile birlikte faydalı olabileceği saptandı.

Anahtar Kelimeler: MPV, trombosit parametreleri, trombositopeni.

Abstract

Objectives: Bone Marrow (BM) examination is the gold-standard test in discriminating between hyperdestructive thrombocytopenia and hypoproductive thrombocytopenia. However, BM examination is an invasive, time-consuming, and expensive approach. Therefore, BM study is not recommended as the first-line method. Recent studies showed that platelet parameters such as mean platelet volume (MPV), plateletcrit (PCT), platelet size deviation width (PDW) could be used for differential diagnosis of thrombocytopenia. In the present study, accordingly, we aimed to investigate the significance of these parameters in the differential diagnosis of thrombocytopenia.

Materials and Methods: One hundred sixty-four (164) patients with thrombocytopenia were included in the present study. The patients were divided into two groups according to the time of the diagnosis of thrombocytopenia: hyperdestructive (75 ITP) and hypoproductive (25 AA, 25 MDS, 24 AML, 15 ALL). The diagnosis was made based on hematological, pathological, and chromosomal analyses and guidelines. Samples for complete blood counts were collected in K3EDTA tubes and analyzed with an automated hematology analyzer, Beckman-Coulter.

Results: The platelet count was similar in both groups. The present results showed that there were no statistically significant differences between the groups in terms of age, gender and PDW. However, MPV was significantly higher in the hyperdestructive group than the hypoproductive group. By contrast, PCT was considerably lower in the hyperdestructive group than the hypoproductive group.

Conclusion: The results of the present study indicated that these platelet parameters might provide additional contributions to strengthen the diagnosis in patients diagnosed with ITP and would be beneficial to consider the thrombocyte parameters as well as the clinical and other laboratory tests of the patient.

Keywords: MPV, platelet parameters, thrombocytopenia.

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Introduction

Platelets are blood cells that play a fundamental role in primary hemostasis. The normal number of platelets in the circulating blood is about 150-450x 10^9. Thrombocytopenia is shown to be the most common cause of abnormal bleeding in daily health practices.[1] It is critically important to determine whether the thrombocytopenia is primarily owing to the increase in hyperdestruction of platelets or hypoproduction of them after excluding splenic sequestration in defining the etiology of thrombocytopenia or not.[2] Decrease in platelets outside the bone marrow due to platelet destruction and normal or increased platelet-derived megakaryocytes are monitored in bone marrow examinations in the hyperdestructive thrombocytopenia. The best examples that can be cited in this group might be immune thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP) and disseminated intravascular coagulation syndrome (DIC). On the other hand, reduced or no megakaryocytes are observed in bone marrow examinations in hypoproductive thrombocytopenia. The best examples that can be mentioned in this group might be bone marrow damages leading to acute and chronic leukemia, aplastic anemia (AA), and myelodysplastic syndrome (MDS), chemotherapy and drug use.[2] Examination of bone marrow aspirations and various biochemical tests are used to differentiate the type of thrombocytopenia. Although invasive bone marrow aspiration is the gold standard and technically not difficult in the discrimination of the thrombocytopenia, but it is a painful, uncomfortable, time-consuming, and expensive approach. Therefore this method is not recommended in the diagnosis of hyperdestructive thrombocytopenia such as ITP.[3,-6] Overall, these studies do not suggest the use of bone marrow aspiration as first-step approach in the management of the thrombocytopenic patients.[5,6] Nonetheless, bone marrow examination is mandatory and necessary for diagnosis in other patient groups, except for ITP and several clinics continue to use the examination of it in the differential diagnoses of thrombocytopenia type.

Rapid advances in automated hematology analyzers have allowed easy and rapid measurements of several blood parameters. Among these, platelet parameters such as MPV, PDW, and PCT can provide important information regarding the kinetics of platelets.[7-13] These tests are inexpensive, non-invasive, requiring no additional blood samples and they can be performed using an automated hematology analyzer in each health center. In addition, some studies suggest that these platelet parameters can be used in the differential diagnosis of thrombocytopenia.[14-24] Nonetheless, these parameters are not currently used in the differential diagnosis of thrombocytopenia. In the present study, we aimed to investigate the usefulness of the platelet parameters in the differential diagnosis of thrombocytopenia based on the hyperdestructive or hypoproductive nature of thrombocytopenia.

Materials and Methods

Study design and participants

The patients at ages between 18-85 years old with platelet counts <100x10^9 were enrolled in the present study, but those patients diagnosed with splenic sequestration, disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura (TTP), chronic systemic diseases, thrombocytopenia due to use of drug or chemotherapy were excluded from the current study.

Data screening process

The data pertaining to the patients were evaluated prospectively. The distribution of the patients enrolled in the present study based on their diagnosis was as follow 75 patients with idiopathic thrombocytopenic purpura (ITP), 24 with acute myeloid leukemia (AML), 15 with acute lymphoblastic leukemia (ALL), 25 aplastic anemia (AA) and 25 myelodysplastic syndrome (MDS) patients (Figure 1). Diagnoses of the impairment of the patients were determined using hematological, pathological, chromosomal analyses and other guiding tests. The bone marrow aspiration and biopsy examination were carried out for all of the patients enrolled in the present study. Of the entire patients, 75 patients were classified in the hyperdestructive group and 89 patients were classified in the hypoproductive group. The samples for complete blood counts were collected in K3EDTA tubes and analyzed with an automated hematology analyzer, Beckman-Coulter.

Statistical Analysis

IBM SPSS 20 was used for statistical analyses of the data obtained from the present study. Continuous variables were expressed as mean ± SD and they were compared using Shapiro Wilk normality test. Mann-Whitney U test was used to compare non-normally distributed continuous variables. Median (Quartiles) values were provided for descriptive statistics. Finally, categorical variables were defined as percentages and they were analyzed via Fisher's Exact Chi-Square and Continuity Correction.

Results

No differences were noted regarding the effectiveness of the platelet parameters in the differential diagnosis of thrombocytopenia between the groups in terms of age (p=0.974). Serum hemoglobin and white blood cell levels were found to be lower in the hypoproductive group than in the hyperdestructive group (p <0.001). The platelet counts were similar between the groups (p=0.444). Moreover, while MPV was 7.4 fl in the hypoproductive group, it was 10.7 fl in the hyperdestructive group. The difference in the level of the MPV

between the groups was statistically significant (p<0.001). In addition, the PCT level was lower in the hyperdestructive group than in the hypoproductive group (p=0.039). There was also no difference in PDW between the groups (p=0.907) (Table 1). Furthermore, levels of leukocytes and hemoglobin were markedly reduced in the hypoproductive group with respect to the hyperdestructive group (p<0.001).

Table 1. Features pertaining to the groups

	Hyperdestructive Group (n=75)	**Hypoproductive Group (n=89)**	**p**
Hemoglobin (gr/dl)	13.5(13.025-14.10)*	7.9(6.42-9.25)*	<0.001
Leucocyte (10^3 /□l)	6800 (5900-8475)*	2200 (1400-4225)*	<0.001
Platelet (10^3 /□l)	24 (9.25-49.75)*	18 (9.0-39.25)*	0.444
MPV (fl)	10.7 (10.0-11.75)*	7.4 (7.1-7.9)*	<0.001
PCT (%)	0.02 (0.0052-0.05)*	0.024 (0.011-0.0462)*	<0.039
PDW	16.99±1.08 #	16.97±1.19 #	0.907

#: Values expressed as mean ± Standard Deviation
*: Values expressed as median (25-75%)

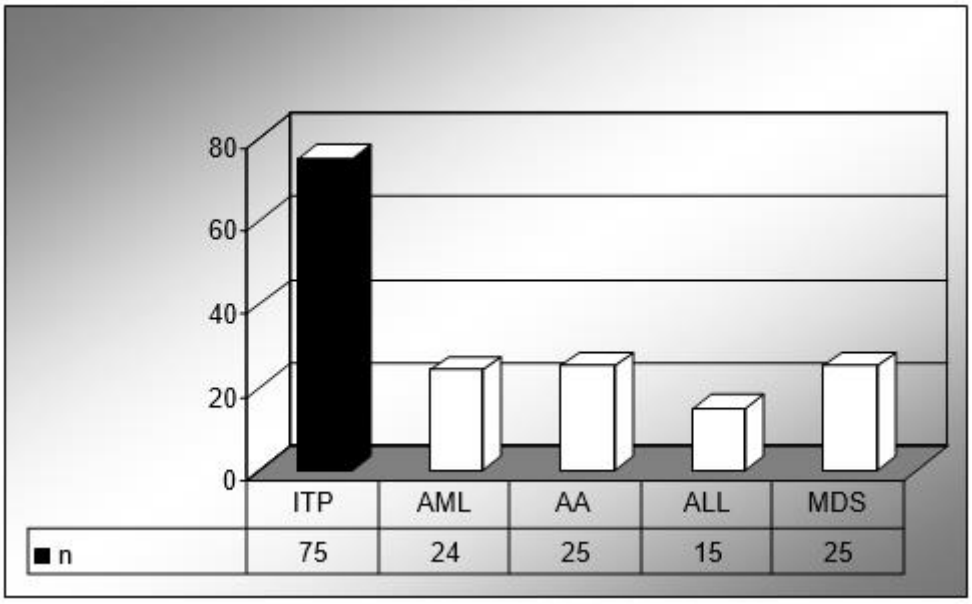

Figure 1: Causes of thrombocytopenia

Discussion

Differential diagnosis of thrombocytopenia is intricate since there are many factors playing a role in the platelet etiology. It is crucially vital to determine whether thrombocytopenia is developed owing to platelet shortage or surplus for the proper differential diagnosis of thrombocytopenia. Inspection of bone marrow aspiration and various biochemical tests are used for differential diagnosis. Even though bone marrow aspiration is the gold standard in the discrimination of thrombocytopenia, it is invasive, time-consuming, expensive, demanding an experienced hematologist and detailed examination. In addition, this method is not recommended in the diagnosis of hyperdestructive thrombocytopenia (e.g., ITP).[3-6] Studies indicate that bone marrow aspiration should not be performed on thrombocytopenic patients as the first-line method[5,6]; therefore, a novel, easy and non-invasive method is required for the diagnosis of thrombocytopenic patients. Several studies assert that particular platelet parameters such as MPV, PDW, and PCT can be useful as the first-line method for managing thrombocytopenic patients.[10-28] Besides, previous studies indicate that while levels of MPV and PDW are higher in the hyperdestructive group but lower in the hypoproductive group.[12,13,29,30] Present results concerning the levels of MPV are consistent with the literature. Accordingly, current results showed that the levels of MPV were 10.7 fl in the hyperdestructive group and 7.4 fl in the hypoproductive group ($p<0.001$).

The results of the current study suggest that the platelet parameters such as MPV and PCT can be used in the differential diagnosis of thrombocytopenia as first-line methods. They are cheaper, easily available, reliable, require no additional blood sample, and can be performed in health centers in addition to the clinical and other laboratory tests of the patient. We think that although the platelet parameters alone are not considered to be thoroughly effective in uncovering the etiology of thrombocytopenia, they are useful as a first-line approach and can play a critical role in determining the direction of the etiological investigation for the diagnosis of thrombocytopenia.

Ethical considerations

Our study was designed in accordance with the principles of the Helsinki Declaration and regulation of patient rights and approved by the clinical research ethics committee of Eskişehir Osmangazi University with the date of 28.07.2020 and the number of 08.

Conflict of İnterest

The author declares no conflict of interest.

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