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Original Article

An evaluation of mean platelet volume, sedimentation, and crp in brucellosis patients

Brucelloz hastalarında ortalama platelet volumu, sedimentasyon ve crp değerlendirilmesi

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Abstract

Aim: Brucellosis is an important infectious disease in Turkey and our region. Mean platelet volume(MPV) is a marker of platelet function, production, and activation. The purpose of this study was to evaluate the relation between epidemiological characteristics of brucellosis patients and MPV and other inflammatory markers.

Material and Methods: Brucellosis patients hospitalized for monitoring at the Infectious Diseases Clinic in 2007-2015 were included in the study. One hundred patients with positive tube agglutination tests and/or with bone marrow culture growth, and 100 controls group without diagnosis of brucellosis were enrolled. Patients' MPV, sedimentation, and CRP values were compared with those of the controls.

Results: Men constituted 64% of the patients were men, and the mean age of the patient group was 37.33±16.88 years. The control group consisted of 62% men, with a mean age of 40.35±15.46. There was no statistically significant difference between patients and controls in terms of age or sex. CRP, MPV, and sedimentation were significantly higher in patients with brucellosis than in the controls.

Conclusion: MPV is novel, low cost, easily applied marker. It may be of greater value when assessed together with other inflammatory markers. Our findings suggest that MPV values may be a useful inflammation marker and prognostic factor in brucellosis patients.

Key words: Brucellosis; epidemiology; mean platelet volume; platelet count; platelet activation

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Öz

Amaç: Bruselloz, Türkiye'de ve bölgemizde önemli bir enfeksiyöz hastalıktır. Ortalama trombosit hacmi (MPV) trombosit fonksiyonunun, üretiminin ve aktivasyonunun bir belirtecidir. Bu çalışmanın amacı, bruselloz hastalarının epidemiyolojik özelliklerinin MPV ve diğer inflamatuvar belirteçlerle arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntemler: 2007-2015 yıllarında Enfeksiyon Hastalıkları Kliniği'nde izlenmesi için yatırılan Bruselloz hastaları çalışmaya dahil edildi. Pozitif tüp aglütinasyon testi ve / veya kemik iliği kültürü üremesi olan 100 hasta ve bruselloz tanısı olmayan 100 kontrol grubu alındı. Hastaların MPV, sedimantasyon ve CRP değerleri kontrol grubu ile karşılaştırıldı.

Bulgular: Hastalrın % 64'ü erkek ve yaş ortalamaları 37.33 ± 16.88 yıl idi. Kontrol grubu yaş ortalaması 40.35 ± 15.46 ve % 62'si erkek idi. Hasta ve kontrol grubu arasında yaş ve cinsiyet açısından istatistiksel olarak anlamlı fark yoktu. CRP, MPV ve sedimantasyon değerleri brusellozlu hastalarda kontrol grubuna göre anlamlı derecede yüksekti.

Sonuç: MPV yeni, düşük maliyetli ve kolay uygulanabilir bir belirteçdir. Diğer inflamatuvar belirteçlerle birlikte değerlendirildiğinde daha değerli olabilir. Bulgularımız, brusellozlu hastalarda MPV değerlerinin yararlı bir inflamasyon belirteci ve prognostik faktör olabileceğini düşündürmektedir.

Anahtar kelimeler: Bruselloz; epidemiyoloji; ortalama platelet hacmi; platelet sayısı, platelet aktivasyonu

Introduction

Brucellosis is a zoonotic, inflammatory, systemic infectious disease [1]. It remains an important public health problem in Turkey and developing societies. In Turkey, it is most common in the eastern, southeastern, and central Anatolian regions [2, 3]. The incubation period is 2-3 weeks. Transmission is frequently via the gastrointestinal system, conjunctiva, skin, and inhalation [1, 3, 4, 5]. The most common symptoms are elevated body temperature, listlessness, lack of appetite, sweating, and muscle and joint pains. The bacterium has a high affinity for the organs of the reticuloendothelial system (liver, spleen, bone marrow, and lymph nodes) [1,4]. Hematological complications such as anemia, thrombocytopenia, and leukopenia are therefore frequently reported in acute brucellosis [5, 6, 7]. Severe thrombocytopenia is rare. Hypersplenism, reactive hemophagocytosis, and immune system breakdown have been implicated as probable causes of thrombocytopenia [8]. Platelets play a major role in thrombus formation [9]. In addition to hemostasis, they also play an active role in antimicrobial host reponse, such as inflammation and tissue repair [8, 10].

Despite numerous recent scientific advances, it is still difficult to diagnose, treat, and monitor brucellosis in endemic areas [11]. Diagnosis is based on clinical manifestation, culture results, and serological investigation [1, 119. Laboratory findings may also be normal in some cases [7]. The inflammatory process in brucellosis occurs with an increase in acute phase reactants [11]. Easily studied, inexpensive markers are needed in brucellosis. MPV is a marker of platelet function and activation that can be investigated in routine blood tests, involves no additional costs, and is easy to apply [7, 9]. It is also the most studied platelet activation marker [11]. MPV is a good indicator of platelet activation, production, and function [5, 8, 9, 11, 129. It can be affected by cardiovascular risk factors such as smoking, diabetes, obesity, dyslipidemia, and hypertension [8, 9].

The role of MPV has been examined in various infectious and non-infectious diseases, including Familial Mediterranean fever, Crimean-Congo hemorrhagic fever, chronic hepatitis B, chronic hepatitis C, pulmonary hydatid cyst, pulmonary tuberculosis, Behçet's disease, ankylosing spondylitis, rheumatoid arthritis, systemic lupus erythematosus, myocardial infarction, ulcerative colitis, cellulitis, acute appendicitis, and acute pancreatitis [2, 5, 9, 10, 13, 14, 15, 16, 17, 18, 19].

The purpose of this study was to evaluate risk factors, and clinical and laboratory findings of brucellosis patients hospitalized in our clinic for treatment, and to determine the relations between patient and control group MPV and other acute phase reactants.

Materials and Methods

One hundred patients with brucellosis admitted for treatment to the Atatürk University Medical Faculty Infectious Diseases and Clinical Microbiology Clinic, Turkey, were evaluated retrospectively. Patients with positive tube agglutination tests and/or with bone marrow culture growth were enrolled. One hundred healthy individuals were recruited as the control group. Individuals with infection other than brucellosis, a history of chronic inflammatory disease, systemic disease, or long-term medication use were excluded. Age, sex,

complete blood count, platelet and MPV values, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and serum tube agglutination and culture results were recorded. Serum AST, ALT, creatine phosphokinase (CK), and lactate dehydrogenase (LDH) levels were measured using original kits (Roche Diagnostics, Mannheim, Germany). Biochemical measurements were determined by standard laboratory methods. Blood count parameters were determined with the Beckman Coulter LH 780 (Beckman Coulter Ireland Inc. Mervue, Galway, Ireland) device in the laboratory. Blood count parameters using standard biochemical techniques were studied in kits (LH 780, USA). ESR and CRP were measured using automatic equipment. Threshold values for ESR and CRP measurement were 20 mm/h and 0-5 mg/dL, respectively. Definite diagnosis in patients with clinical manifestations was made with Rose Bengal test positivity and tube agglutination test positivity (≥1/160), and with Brucella spp. growth in urine specimens. Patients were classified as acute (0-2 months), subacute (2-12 months) and chronic (›12 months) depending on duration of symptoms.

Ethics Approval

The study was approved by Ataturk University Faculty of Medicine.

Statistical Analysis

Statistical analysis was performed on SPSS 20 software (Chicago, IL, USA) and using descriptive statistics. Categorical variables were expressed as percentages and frequencies, and continuous variables as mean plus standard deviation. Since these variables were not normally distributed, comparison of patient and control group MPV, platelet, ESR and CRP values was performed using the Mann Whitney u test and the chi-square test. p values <0.05 were regarded as statistically significant.

Results

Sixty-four patients (64%) were men and 36 (35%) were women, with a mean age of 37.33±16.88 years (min 16- max 80). In terms of occupation, 35 (35%) were housewives, 27 (27%) worked in animal husbandry, 24 (24%) were self-employed, and 12 (12%) worked in agriculture. Sixty-two percent of the control group were men, and the group's mean age was 40.35±15.46. Acute brucellosis was present in 64 (64%) of the patients, subacute brucellosis in 32 (32%), and chronic brucellosis in 4 (4%). The principal risk factors were consumption of unpasteurized milk and milk products (81%), and working in animal husbandry (27%). Articular pain was present in 80 (80%) patients, fever in 75 (75%), listlessness in 73 (73%), sweating in 72 (72%), lack of appetite in 57 (57%), myalgia in 54 (54%), and headache in 34 (34%). Patients' symptoms and laboratory values are shown in tables 1 and 2.

Although clouded consciousness was present in six patients, neurobrucellosis was detected in 10. The most common physical examination findings were hepatomegaly in 71 patients (71%) and splenomegaly in 68 (68%). Lymphadenopathy was present in 7 (7%) patients. Brucella spp. grew in blood or bone marrow culture in 33 (33%) patients. Accompanying spondylodiscitis was present in 11 (11%) patients. At antibody analysis using ELISA, IgG was positive and IgM negative in 25 patients, both were negative in 19, IgM was positive and IgG negative in 24 patients, and both antibodies were positive in 31 patients. Rose Bengal was positive in 76 (76%) patients. The Wright test was positive at 1/160 or above in 94 patients.

MPV values were significantly higher in the patient group than in the control group (p=0.008). Significant elevation was also observed in sedimentation and CRP in the patient group (p< 0.001) (Table 3).

Table 1. Distribution of Symptoms in Brucellosis Patients

Symptoms	Number	(%)
Articular pain	80	80
Fever	75	75
Listlessness	73	73
Sweating	72	72
Lack of appetite	57	57
Headache	34	34
Backache	30	30
Nausea	22	22
Hip pain	20	20
Weight loss	18	18
Spondylodiscitis	11	11
Neurobrucellozis	10	10
Testicular swelling	9	9
Dysuria	7	7
Diarrhea	5	5
Rash	2	2

Table 2. Cases' Laboratory Values

Mean ±SD	Min -Max
Age 37,33±16,88	16-80
ALT 61,32±73,37	5,00-426,00
AST 70,56±103,65	14,00-669,00
GGT 70,88±67,83	4,00-369,00
ALP 134,79±90,23	42,00-590,00
TBİL 0,59±0,42	0,10-3,20
Sedimentation 33,45±22,39	2,00-125,00
CRP 40,14±70,95	0,30-514,00

Table 3. Patient and control group MPV, ESR and CRP Values

	Brusellosis	Control	P
MPV(fL)	7.9±1.2	7.7±1.3	p=0.008
Sedimentation (mm/h)	33.4±22.4	13.8±11.2	p<0.001
CRP (mg/dL)	40.1±70.9	1.8±1.6	p<0.001

Doxycycline and streptomycin therapy was given to 49 patients, doxycycline and rifampicin to 19, and doxycycline, rifampicin and third-generation cephalosporin to eight. Medical treatment was unsuccessful in nine patients.

Discussion

Brucellosis is the most widespread zoonosis in the world and can affect all organs and systems. It can mimic various diseases with various clinical spectra [1,4]. Hematological abnormalities can be seen in brucellosis [79. Anemia has been reported at a level of 36% in hematological involvement, leukopenia at 11%, and thrombocytopenia at 10% [4, 7]. Thrombocytopenia has been reported as a hematological complication of brucellosis at a level of 2.4-33% [4, 69. MPV reflects platelet activation, and can be used to assess hematological abnormalities in patients with brucellosis.

MPV is a simple parameter routinely measured at complete blood count [7, 8, 11, 12] and is the most studied indicator of platelet activation. In addition to endothelial adhesion and aggregation, platelet activation also plays a role in the upregulation of the inflammatory process [20]. MPV serves as a negative or positive acute phase reactant in diseases progressing with inflammation. It may increase or decrease, depending on the intensity of systemic inflammation [5, 9, 21]. We determined higher MPV values in the patients than in the controls.

MPV has been used as a risk marker in diseases associated with atherosclerosis. It is also reported to be capable of reflecting chronic inflammation in diseases such as malignities, cardiac diseases, and liver cirrhosis [18].

Low MPV values have been determined in association with high-degree inflammation in ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, pancreatitis, acute appendicitis, and Familial Mediterranean Fever attacks. High MPV has been linked to low-degree inflammation risk factors causing cardiovascular, cerebrovascular, arterial and venous thrombosis. These diseases include chronic hepatitis B and C, pulmonary hydatid cyst, CCHF, and myocardial infarction [2, 9]. MPV increase is explained in terms of release of large platelets into the circulation, and decreased MPV in terms of depletion of platelets in circulation [21]. Some studies have shown that MPV increases with treatment [8, 16]. The high MPV values in our patients may be due to the large number of acute cases, greater numbers of large platelets, and an increase in systemic inflammation. One of the limitations of our study is that MPV values were not investigated post-treatment.

Gasparyan et al. [9] reported negative correlation between MPV level and platelet count. They attributed this to an endeavor to keep platelet number at specific levels to maintain equilibrium.

MPV has been widely used in the evaluation of platelet functions in several diseases. Large platelets have a denser granule content than small ones. Large platelets are more active and produce more prothrombotic factor. They contain more prothrombotic substances, such as thromboxane A2. Glycoprotein Ib, IIb and IIIa receptor expression is also greater. In other words, large platelets have a greater thrombotic potential [5, 22, 23].

MPV is a direct marker of increased platelet synthesis. Platelet numbers are disposed to fall in conditions in which MPV increases. This may be due to enhanced production of platelets with greater aggregability or to increased destruction [9, 23]. A fall in platelet numbers may be linked to increased platelet activity and aggregated platelets. Information can be obtained concerning platelet activation by examining MPV and platelet count, easily and inexpensively, from complete blood count.

The release of non-mature platelets from bone marrow due to rapid platelet depletion, and the earlier depletion of small platelets has been implicated as the cause of increased MPV in acute coronary syndrome [24]. High MPV has been associated with mortality in ischemic stroke patients [9, 22]. We think that elevation in MPV values can be used in acute phase reactant and disease progression evaluation in brucellosis.

The retrospective, cross-sectional and a case controlled nature of the study is its principal limitation. Prospective data comparing pre- and post-treatment values are now needed. The limiting aspect of this study is its retrospective nature and that blood count values after treatment could not be obtained for all patients.

Conclusion

Brucellosis is an important infectious disease due to its high morbidity rate, the economic burden it imposes, and its ability to affect large numbers of people. Detailed history, family history, and occupational and dietary factors must be investigated. It may assume various different clinical

manifestations. Brucellosis must be considered at differential diagnosis in cases of high temperature, articular pains, hematological findings, and various system involvements in endemic regions. MPV is a marker of platelet functions and can be used as an acute phase reactant in determining the activity of the disease and in follow-up in this patient group. More extensive prospective studies are now needed.

Declaration of conflict of interest

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