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Effect of anterior uveitis in Behçet's disease on neutrophil to lymphocyte ratio

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中性粒细胞与淋巴细胞比值对伴随前葡萄膜炎的 Behçet 病的影响

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摘要

目的:调查中性粒细胞与淋巴细胞比值(NLR)对伴随前葡萄膜炎的 Behçet 病(BD)的影响。

方法:回顾性研究。研究 2004~2013 年间我院接收的符合 BD 诊断的患者。经过筛选 735 例 BD 患者,选取 135 例患者纳入本研究。其中 68 例患有前葡萄膜炎,其余患者(n=67)没有任何眼部疾患。同时记录前葡萄膜炎患者的全血计数,计算 NLR。

结果:前葡萄膜炎组的 NLR 为 2.55±0.96。眼部正常组的 NLR 为 1.67±0.50。前葡萄膜炎组的 NLR 远高于眼部正常组(P<0.05)。

结论:伴随前葡萄膜炎的 BD 患者的 NLR 高于眼部正常 BD 患者。

关键词:Behçet 病;前葡萄膜炎;中性粒细胞与淋巴细胞比值

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Abstract

• AIM: To investigate the effect of anterior uveitis in Behçet's disease (BD) on neutrophil to lymphocyte ratio (NLR).

• METHODS: Retrospective research. The patients who were admitted to Kayseri Training and Research Hospital between 2004 - 2013 and fulfilled the BD criteria are accepted in the study. The records of 735 patients with BD were screened and 135 of them were taken to the study. Sixty-eight of them had anterior uveitis, the rest (n=67) did not have any ophthalmological pathology. The patients' total blood counts were taken at the same visit that anterior uveitis was noted. Then the neutrophil to lymphocyte ratio were calculated.

• RESULTS: In the anterior uveitis group the mean NLR was 2.55±0.96. In the ophthalmologically normal group it was 1.67±0.50. NLR was determined higher in the anterior uveitis group (P<0.05).

• CONCLUSION: The NLR is found higher in the Behçet's disease with anterior uveitis patients when compared with the ophthalmologically normal patients.

• KEYWORDS: Behçet's disease; anterior uveitis; neutrophil lymphocyte ratio
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INTRODUCTION

Behçet's disease (BD) is a multi-systemic disease with an unknown etiology in which oral aphthae, genital ulcers, skin lesions, ophthalmological and central nervous system involvements can be observed. It was first described by Hulusi Behçet in 1937[1-2]. Diagnosis is made according to the clinical findings. It's diagnosed when, in addition to recurring oral aphthae at least two of genital ulcer, typical ophthalmological findings, typical cutaneous lesions and positive pathergy test are seen. This diagnostic criteria was accepted in 1990 by the international study group. Although it is still accepted by many international researchers, the criteria have limitations and should be developed this subject was well discussed in the review of Yazici *et al*[3] since there is no specific laboratory test, researchers aimed to investigate some relations between BD and laboratory parameters that could be predictive for or it's complications[4-7]. Etiologically many

factors were blamed but still it's an obscure.

The most common ophthalmological finding in BD is anterior uveitis (bilateral, recurrent and non-granulomatous), but the characteristic finding in BD is occlusive and necrotizing retinal vasculitis and affects both arteries and veins. The other possible presentations are periphlebitis and/or obliterating. Some posterior segment findings such as optical disc edema, retinal hemorrhage, exudates, dilated veins and capillaries macular edema, macular hole, choroiditis, tapered vessels, optical atrophy, edema, papilledema, retinal neovascularization can also be seen[8].

Anterior uveitis is one of the mostly seen ophthalmological finding and can easily diagnosed by the ophthalmologists. Neutrophil to lymphocyte ratio (NLR) is elevated in diseases which have higher inflammatory processes and in many courses this change can give an idea about the activation of the disease. Since BD is an inflammatory disease and the amount of inflammation in anterior uveitis is even higher, we compared the NLR between the ophthalmologically affected and non-affected groups. According to our review of the literature no such study was created before.

SUBJECTS AND METHODS

We investigated retrospectively 735 patients who were admitted to Kayseri Training and Research Hospital between the dates of 2004-2013 and fulfilled the BD criteria. Medical history (age, sex, previous diseases and drugs) was recorded from each patient's chart. The patients who were ophthalmologically examined and had anterior uveitis were compared with the patients who did not have any ophthalmological pathology. The patients with any disease that can change NLR like cardiovascular diseases, renal failure (we used the highest value of 1.0 mg/dL for serum creatinine and patients have creatinine higher than 1.0 mg/dL was excluded) and any infections were ruled out of the study. Some other patients did not have ophthalmological examination then excluded. After all this exclusion criteria 68 patients with anterior uveitis and 67 ophthalmologically normal patients remained. The important point was it was a retrospective research and the entire reported laboratory values were taken during the period of patients examination and anterior uveitis were active, but most of them were not the first uveitis attack. The patients' total blood counts were taken at the same visit that anterior uveitis was noted. Then the neutrophil to lymphocyte ratio were calculated.

We got the ethics committee approval due to the WMA Declaration of Helsinki.

For statistical analysis, the statistical package for the social sciences (SPSS version 16, Inc., Chicago, Illinois, USA) was used. Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov Test. We reported continuous data as mean and standard deviation. Categorical variables were summarized as percentages and compared with the Chi-square test. $P<0.05$ were considered significant. We performed Mann-Whitney test for the relation between inhomogeneous groups.

Table 1 Laboratory findings correspondence of laboratory into groups $\bar{x}\pm s$

Variables	Intact eyes ($n=68$)	Anterior uveitis ($n=67$)	P
Age (a)	38.70±11.25	36.56±10.55	$P<0.05$
NLR (ratio)	1.67±0.50	2.55±0.96	$P<0.05$
WBC ($10^3/\mu L$)	6.943±1.391	8.081±2.024	$P<0.05$
NEU ($10^3/uL$)	3.889±0.962	5.094±1.538	$P<0.05$
LYM ($10^3/uL$)	2.427±0.591	2.123±0.630	$P<0.05$
PLT (/μL)	278221±79068	279343±61472	$P>0.05$
CRP (mg/L)	3.79±1.45	5.49±5.10	$P>0.05$

NLR: Neutrophil to lymphocyte ratio; WBC: White Blood cell; NEU: Neutrophil; LYM: Lymphocyte; PLT: Platelet; CRP: C-reactive protein.

RESULTS

In this retrospective research, 135 patients, 68 of whom had anterior uveitis were examined. The mean age was 38.70±11.25 in the ophthalmologically unaffected group. It was 36.56±10.55 in the group with anterior uveitis. Difference between the ages was not statistically significant ($P>0.05$). Among males, 50 (73.5%) had anterior uveitis and 18 (26.5%) were ophthalmologically normal. Among females 23 (31.1%) had anterior uveitis and 51 (68.9%) had no eye involvement. It the group 68.5% ($n=50$) of the subjects with anterior uveitis were male and 32.5% ($n=23$) of them were female. Among males, anterior uveitis ratio was statistically high ($P<0.05$).

The mean NLR in the control group was1.67±0.50 and this ratio was 2.55±0.96 in the patients who had anterior uveitis. NLR was higher in the patients who had anterior uveitis and this difference was statistically significant ($P<0.01$). Some laboratory findings were briefed in Table 1.

DISCUSSION

The primary finding of this study was demonstrating the elevation of NLR in BD with anterior uveitis. Since there is no specific laboratory feature in BD, finding such relationship is important.

Neutrophil to lymphocyte ratio is accepted as an indicator of worsening or recurrence of chronic diseases. When the literature is reviewed, elevated NLR is mostly used as a bad prognostic factor in cardiovascular diseases and cancers[9-11]. Lafçi *et al*[12] suggested the admission NLR value as a potential predictive parameter for determining the in-hospital mortality of acute type I aortic dissection. It is also investigated in respiratory system diseases, pulmonary tuberculosis and serious infections, colonic polyps, and likewise found higher[13-15]. Similarly, systemic inflammation has also been reported as a significant factor for metabolic syndrome including obesity and diabetes mellitus[16-17]. Cananzi *et al*[18] reviewed recent evidence that immunological phenomena may explain the unexpectedly good response rate in patients with advanced disease. The simple estimation of the NLR has been advocated as a prognostic marker for several cancers and they show that it is likewise useful in metastatic

melanoma Ataseven *et al*[19] researched NLR as an inflammatory marker with a relation of disease severity in psoriasis.

In our study, in BD with anterior uveitis this rate was higher in males (Table 1). According to this research, anterior uveitis was more common in males. Also our study showed the relation between NLR and BD with anterior uveitis.

Nitric oxide levels in aqueous humor of patients with BD were found elevated when compared to the controls[20]. Mechanisms of these associations between systemic inflammation and prevalent conditions remain unclear. One hypothesis is that, cellular response of blood components might be mediated through the endothelial dysfunction. Inflammation modifies endothelial function and an inability of the endothelium to produce nitric oxide and prostacyclin can result in the depletion of vasodilator, antithrombotic and antiatherogenic properties of the vascular endothelium[21]. Furthermore, stimulated leukocytes alter rheological properties with an increased capacity to adhere to vascular endothelium and may result in capillary leukocytosis and subsequent increased vascular resistance. The tissue damage in BD is thought to be due to release of the neutrophil lysosomal enzymes into the extracellular environment and production of excessive free radicals by stimulated neutrophils[22].

To our knowledge this is the first study that investigated the role of NLR as a measure of systemic inflammation in relation to BD's anterior uveitis. Systemic inflammation measured by NLR has a significant association with prevalent chronic inflammatory conditions including BD with anterior uveitis. As a result we observed that in BD with anterior uveitis, NLR had a tendency to increase as in many of the other inflammatory diseases. Also we observed that males are more likely to have anterior uveitis.

The major benefit of this study is creating awareness for clinical suspicion to anterior uveitis during the course of BD. Any clinician in any clinic may easily have the total blood count and if the NLR is higher compared to previous one, he/she can suspect that something is going wrong. It can be a sign of an extra inflammation. Then the patient should send to an ophthalmologist. The diagnose of anterior uveitis is easy for an ophthalmologist. On the other hand, NLR may reflect the course of anterior uveitis. In our opinion, the next research should be designed for correlating NLR and the course of anterior uveitis.

Yet the topic is so fresh, that's why further research is needed to investigate this relationship with longitudinal data to establish the temporal association between these variables.

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