

Original Article

Ratio of neutrophil/lymphocyte and platelet/lymphocyte in patient with ankylosing spondylitis that are treating with anti-TNF

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Received July 4, 2014; Accepted July 19, 2014; Epub September 15, 2014; Published September 30, 2014

Abstract: Ankylosing spondylitis (AS) is a type of chronic inflammatory arthritis resulting in ankylosis of the spine and inflammation in the tendons. After NSAIDs, the use of anti-TNF medications has provided a significant contribution to the treatment of patients with AS. The present study was a retrospective, controlled and multicenter study. A total of 105 patients followed in the outpatient clinics of the Department of Physical Therapy in Abant İzzet Baysal University and Harran University and 50 healthy controls were included in the study. The patients had been receiving anti-TNF therapy at least for 6 months. Hemogram results of the patient and control groups examined retrospectively. There was no significant difference between the groups in terms of N/L ratio; however, the P/L ratio was significantly different between the two groups. The present study found a significantly different P/L ratio in patients with AS when compared to the control group. However, the N/L ratio was not significantly different between the groups. The P/L ratio can be used as a marker to monitor disease progression and indicate subclinical inflammation in patients with AS.

Keywords: Ankylosing spondylitis, inflammation, neutrophil, marker

Introduction

Ankylosing spondylitis (AS) is a type of chronic inflammatory arthritis resulting in ankylosis of the spine and inflammation in the tendons. The prevalence of AS ranges from 0.1 to 1.1%, and the prevalence is higher in individuals who are HLA B27 positive. AS can result in serious mobility problems. Although AS is slow-progressing disorder, spine involvement is progressive and associated with pain, stiffness, fatigue, and dysfunction, and the inflammation could persist even years after the diagnosis [1, 2]. Patients with AS may have decreased the quality of life and a restricted social life [2-4].

After NSAIDs, the use of anti-TNF medications has provided a significant contribution to the treatment of patients with AS. TNF-alpha is an important mediator of inflammation in patients with rheumatic disorders such as AS, rheumatoid arthritis (RA), and psoriatic arthritis. The studies have reported increased expression of

TNF-alpha in the serum, synovial fluid, and sacroiliac joints of the affected patients [5]. The inhibition of TNF-alpha reduces joint damage and the symptoms of arthritis [6].

Previous studies have shown higher values in patients with inflammatory rheumatic disorder when compared to healthy individuals. The inflammation may continue in the silent phases of rheumatic disorders [7, 8]. The intention in the present study was to evaluate N/L and P/L ratios in order to indicate subclinical inflammation in the inactive phase of disease in patients with AS.

Methods

The present study was a retrospective, controlled and multicenter study. A total of 105 patients followed in the outpatient clinics of The Department of Physical Therapy in Abant İzzet Baysal University and Harran University and 50 healthy controls were included in the study. The

Table 1. Hemogram test results in the patient and the control group

Parameters	AS Group	Control Group
Neutrophil	4.63 ± 1.43	3.92 ± 1.34
Lymphocyte	2.53 ± 0.75	2.13 ± 0.62
Platelet	262.950 ± 63.990	256.620 ± 55.350

Table 2. N/L, neutrophil to lymphocyte ratio; P/L, platelet to lymphocyte ratio

Parameters	AS Group	Control Group
N/L	1.98 ± 0.89	1.91 ± 0.71
P/L	113.19 ± 48.43	128.03 ± 40.8

study was approved by The Ethics Committee of Abant Izzet Baysal University.

The patients diagnosed with AS and in whom disease control was achieved by anti-TNF therapy were included in the study. The patients in the active phase of the disease and those with any disorder affecting the hematological parameters were excluded from the study. The study included 50 healthy subjects in the control group. The subjects with hypertension (HT), diabetes mellitus (DM), metabolic syndrome, coronary heart disease, impairment in thyroid functions, renal and hepatic dysfunction, malignancy, local or systemic infection, and patients with the history of surgery in the last 3 months, smokers, and those with inflammatory disorder, anemia, chronic obstructive pulmonary disease (COPD), and patients who underwent medical therapy for inflammation were not included in the control group.

The study group consisted of patients who were on follow-up at our clinic and who did not sustain exacerbation of the disease in the last 3 months. The patients had been receiving anti-TNF therapy at least for 6 months. The patients receiving anti-TNF therapy were those who remained unresponsive to disease-modifying antirheumatic drugs (DMARD) therapy and with poor prognosis.

Statistical analysis

The statistical analyses were carried out using SPSS 18.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Distributions of parametric variables were evaluated with one-sample Kolmogorov-Smirnov test. For the comparison of independent samples, analysis of independent

samples *T* test was used if the data were normally distributed, whereas the Mann-Whitney *U* test was used if the data were not normally distributed. The chi-square test was used in the comparison of categorical data between the groups. All demographic and quantitative data were expressed as mean ± SD. Differences with *P*-values < 0.05 were considered to be statistically significant and all results were expressed with a 95% confidence interval.

Results

Hemogram results were showed in **Table 1** and N/L and P/L ratios were showed in **Table 2**. The AS group consisted of 27 females and 78 males. The mean age was 46.83 ± 14.94 years. The control group consisted of 22 females and 28 males, and the mean age was 41.02 ± 17.37 years. There was no difference between the patient and the control groups in terms of gender (*p* = 0.022). There was a significant difference between the patient and the control groups in terms of lymphocyte and neutrophil ratio (*p* = 0.001 and *p* = 0.04), but platelet ratio was not different between the groups (*p* = 0.549). There was no significant difference between the groups in terms of N/L ratio; however, the P/L ratio was significantly different between the two groups (*p* = 0.003).

Discussion

The present study found a significantly different P/L ratio in patients with AS when compared to the control group. However, the N/L ratio was not significantly different between the groups. The disease activity was monitored with CRP levels in patients with AS. The presence of sub-clinical inflammation can be detected by P/L ratio in patients who achieved remission with anti-TNF therapy. The inflammation can be progressive in AS patients with axial involvement.

The white blood cell count (WBC) is considered to be a biological marker of inflammation that can be used in the clinical practice. The N/L ratio and P/L ratio are among the laboratory markers that have been introduced into the clinical practice to evaluate systemic inflammation [9]. Demir et al. found a positive correlation between N/L ratio and blood pressure [10]. Cardiovascular mortality could be predicted by the sub-parameters such as N/L ratio despite normal WBC levels. The N/L ratio is affected by

the presence of HT, DM, metabolic syndrome, left ventricular dysfunction, acute coronary syndrome, valvular heart disease, impaired thyroid functions, renal and hepatic dysfunction, malignancy, local or systemic infection, past infections within the last 3 months, inflammatory disorders, and medical therapies administered for inflammatory conditions. Furthermore, mean platelet volume, and platelet and erythrocyte distribution weight can also be considered to be a marker that can be used to predict prognosis in patients with colon cancer [9].

Recent studies suggested that activated platelets could be important in increased atherogenesis [11]. It has been suggested that the interaction of platelets with other cell types could initiate inflammation in the arterial wall [12]. Chronic inflammation helps to understand the development of atherosclerosis [13]. In the study by Kultigin et al., the P/L ratio showed better performance than the N/L ratio in the prediction of inflammation in patients with end-stage renal disease [14].

An inflammatory process has been suggested to play a role in the etiopathogenesis of osteoporosis. Bone healing is delayed in the absence of lymphocytes [15]. In the study by Zeynel et al., the N/L ratio was found to be higher in osteoporotic patients compared to osteopenic patients and those with normal BMD, and an independent variable in the prediction of osteoporosis, and there was correlation between the N/L ratio and the score of osteoporosis [16].

The studies have shown that the N/L ratio was an important marker in determining subclinical inflammation and the risk of developing amyloidosis in patients with FMF [17]. Another study found a higher N/L ratio in patients with familial Mediterranean fever (FMF) compared to the control group, and the N/L ratio was even higher in patients harboring the M694V gene mutation that is associated with an increased risk of amyloidosis compared to patients who do not harbor this gene mutation [7, 8].

Subclinical inflammation can continue and various complications can occur despite achieving remission in some rheumatic disorders [7, 8, 17, 18]. Extra-articular complications can be observed in patients with AS, and these complications may show progressive involvement. The prevention of this process requires close

follow-up and evaluation. If these ratios prove beneficial in other studies, these parameters will provide a cheaper and easy-to-perform marker in the follow-up of AS. Other inflammatory cytokines and serum amyloid A levels can be studied to further indicate subclinical inflammation. The studies with a larger number of patients and more comprehensive analyses will provide further data on these ratios. The present study may have been considered to have small number of patients. Further studies can be conducted comparing the data of patients in the active phase of AS with those in the inactive disease phase.

In the current study, the researchers found significant differences between the patient and control groups in terms of neutrophil and lymphocyte counts; however, there was no significant difference between the two groups in terms of N/L ratio. The P/L ratio was significantly different between the two groups. The P/L ratio can be used as a marker to monitor disease progression and indicate subclinical inflammation in patients with AS.

Disclosure of conflict of interest

None.

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