

Assessment of relation between neutrophil lymphocyte, platelet lymphocyte ratios and epicardial fat thickness in patients with ankylosing spondylitis

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ABSTRACT

Aim To investigate whether there is a relation between neutrophil-lymphocyte (N/L) and platelet-lymphocyte (P/L) ratios and epicardial adipose tissue (EAT) thickness in patients with ankylosing spondylitis (AS).

Methods Thirty patients diagnosed with ankylosing spondylitis and 25 healthy people (controls) were included in the study. Age, gender, body mass index (BMI), height, hemogram, sedimentation, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, CRP, hepatic and renal function tests, lipid profile of the all patients were recorded. Data related to duration of the disease, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) values of the cases in the patient group were obtained. A cardiologist measured EAT thickness by ECHO in both patient and control groups.

Results In the patient group, mean BASDAI and BASFI scores were 2.48 ± 2.21 and 1.5 ± 2.07 , respectively. Age, gender, BMI values did not show statistically significant difference between the patient and the control groups. N/L and P/L ratios did not change significantly in the patient group having higher EAT, BASFI values and taking anti-TNF compared to the control group.

Conclusion In patients with AS, EAT measurements, which are related to inflammatory response increase, can be used for monitoring of the risk of development of cardiac disease. We could not find the relation between EAT and N/L, P/L ratios in terms of evaluation of inflammatory response.

Keywords: ankylosing spondylitis, inflammation, clinical markers

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INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease, which more frequently affects young adults. Extra-articular involvement can be seen in various rates with uvea, bowels, skin, lungs, kidneys affected most frequently and heart is affected less frequently (1). In patients with AS, cardiac involvement is seen in 10-30% of the patients. Its incidence is higher in HLA-B27 positive patients (2). In the most frequently seen cardiac involvement, aortic root and aortic valves are affected. As the inflammation becomes chronic, the inflammatory process extends into ventricular septum, atrio-ventricular node, its bundles and fascicles (3). As a consequence, myocarditis, high-velocity conduction disorders, excessive myocardial fibrosis and involvement of ascending aorta can occur (3). Mortality rates related to cardiovascular diseases are higher than in normal population (4). In patients with AS, mediators as IL1, IL6, TNF-alpha, adhesion molecules have been considered as etiological agents of increased mortality (4,5). Inflammatory biomarkers are good predictors of cardiovascular risk (6). Ectopic fat accumulation is a more important predictor of metabolic and cardiovascular diseases than overall bodily distribution of fat (7). Epicardial adipose tissue (EAT) is natural visceral adipose tissue, which is localized on the left ventricular apex and surrounds subepicardial coronary arteries. It is a complex endocrine organ with systemic effects. It has been associated with the development of coronary atherosclerosis (8). It releases many cytokines related to atherosclerosis and genes encoding proteins. In biopsy studies, it has been demonstrated that EAT contains excess amounts of IL1, IL6, TNF and MicroRNA and also a correlation has been shown between thickness of EAT and severity of coronary artery disease (8). The EAT is a new cardiometabolic risk factor and a strong correlation exists between EAT and accumulation of abdominal fat. Recently, EAT has been used as an indicator of atherosclerosis and cardiovascular risk factor in patients with AS and rheumatoid arthritis (9). It can be also used in the determination of the correlation between clinical parameters, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) parameters, as well as inflammatory

markers, neutrophil-lymphocyte (N/L) and platelet-lymphocyte (P/L), N/L ratios etc. (9,10).

The neutrophil, lymphocyte, and platelet counts can be simply obtained by a hemogram. The neutrophils are the major fraction of the circulating immune cells and rapidly accumulate in areas of infection and inflammation. There are studies demonstrating that N/L and P/L ratios can be used as a marker of systemic inflammation (11).

In the present study, we aimed to investigate whether there is a relation between neutrophil-lymphocyte (N/L), platelet-lymphocyte (P/L) ratios and epicardial adipose tissue in the patients with ankylosing spondylitis.

PATIENTS AND METHODS

Patients and design of the study

Patients and volunteers who participated in the study were informed about the study and their written informed consents were obtained. Thirty patients who were followed up with the diagnosis of AS in the Department of Physical Rehabilitation and Therapy at Abant İzzet Baysal University Physical Therapy and Rehabilitation Hospital were included in the study. Patient group (n=30) was subgrouped into two, either using biological drugs (n=18) or disease modifying antirheumatic drugs (DMARDs) (n=12). Twenty-five healthy people without any disease were included in the study as a control group. The patients in the control group were selected among the people coming to outpatient clinics. Patients with systemic inflammatory diseases, history of known cardiac diseases, patients whose first degree relatives had heart attack at an earlier age, those with diabetes mellitus, hypertension, hepatic and renal dysfunction, systemic or local malignancies were not included in the study.

Methods

Age, gender, body weight, height of the study participants were recorded. Data related to duration of the disease, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) values of the cases in the patient group were obtained (10). Biochemical parameters such as hemogram, sedimentation, CRP, hepatic and renal function tests, lipid profile were measured. The N/L, P/L ratios were calculated by dividing the number of lym-

phocytes, neutrophils and platelets. (There are no standard values for these ratios). A cardiologist measured EAT thickness on echocardiograms in both patient and control groups.

Statistical analysis

Parametric tests were applied to data of normal distribution and non-parametric tests were applied to data of questionably normal distribution. Data are expressed as mean±SD or median (interquartile range), as appropriate. Statistical significance was assumed for $p < 0.05$.

RESULTS

Thirty patients with AS (19 males and 11 females) and 25 healthy individuals (16 males and 9 females) as a control group were enrolled in our study. Mean age of the patients and the control groups was 38.6 ± 8.3 and 37.1 ± 9.4 years, respectively. Mean duration of the disease was 8.8 ± 8 years. Median body mass index (BMI) values in the patient and the control groups were 25.18 and 25.27 kg/m^2 , respectively.

In the patient group, mean BASDAI and BASFI scores were 2.48 ± 2.21 and 1.5 ± 2.07 , respectively. Mean BASDAI and BASFAI scores of biological drug and DMARD users were 2.1 ± 2.1 and 2.9 ± 2.2 vs 1.4 ± 1.7 and 1.8 ± 2.4 , respectively. Hemogram, sedimentation, CRP, glucose, hepatic and renal enzyme levels of both patient and control groups were within normal limits.

In the patient group, lipid profile was analyzed and LDL (99.76 ± 31.61 mg/dL), HDL (47.8 ± 11.8 mg/dL), triglyceride (127.76 ± 62.95 mg/dL) and cholesterol (174.8 ± 38.03 mg/dL) values were obtained as indicated.

Other measured parameters in the patient and the control groups were as follows: N/L 1.98 ± 1.24 vs 1.71 ± 0.67 ; P/L 164660 ± 135130 vs 152757 ± 111059 .

Age, gender, BMI, N/L, P/L ratios did not differ significantly between the patient and the control groups.

The BASDAI score of 8 patients was higher than 4. The BASFI score of the patients were divided higher than 2 (10 patients) and less than 2 (20 patients). In the patients (17 patients) receiving anti-TNF, N/L and P/L ratios were 1.97 ± 0.53 and 147413 ± 73600 respectively. Maximum EAT thickness was roughly 7 mm in the control group and 16 patients had higher EAT thickness than 7

mm. The N/L, P/L ratios did not differ significantly between the control group and the patient group having higher EAT thickness, receiving anti-TNF therapy, higher BASDAI and BASFI scores.

DISCUSSION

The N/L, P/L ratios obtained in this study, which are shown to be useful as the inflammation marker were not correlated EAT thickness which could be associated with inflammation (6,11). The results of this study have shown higher EAT values in the patient group compared with the control group; there was no significant difference in the patients receiving anti-TNF therapy, having higher BASDAI and BASFI scores in terms of N/L and P/L ratios.

In a study by Resorlu et al., the authors found higher carotid artery intimal-medial thickness (CIMT) and EAT values in patients with AS. When they were correlated EAT and CIMT with disease duration and increased TG values could not detect any correlation between BASDAI, BASFI on one hand and EAT, CIMT on the other hand (12). In a study, higher EAT values were detected in female patients. Besides, in patients treated with biological drugs lower EAT values were detected when compared with those treated with DMARDs (13). In a study by Mazurek et al. the authors compared epicardial and subcutaneous adipose tissues and detected that EAT induced relatively greater amounts of inflammatory cytokines (14). In our study, N/L, P/L ratios did not differ significantly between the control group and the patient group having higher EAT thickness.

In some studies higher N/L ratio in patients with familial Mediterranean fever (FMF) compared to the control group were found, 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 (15,16). 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 familial Mediterranean fever (FMF) (17). The authors maintain that high platelet/lymphocyte ratio reflects inflammation, atherosclerosis and platelet activation (18).

Subclinical inflammation can continue and various complications can occur despite achieving remission in some rheumatic disorders. Extra-articular complications can be observed in patients

with AS, and these complications may show progressive involvement (16,17). 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 (16-19). Inal et al. found that there was no significant difference between patients having ankylosing spondylitis and control groups in terms of N/L and P/L ratios. They found weakly positive correlation between BASDAI scores and N/L and P/L ratios (10). We could not find a correlation between disease activity, patient's functional situation, EAT thickness and N/L, P/L ratios.

In the present study, scarce number of patients can be considered as a limitation. Studies encompassing higher number of patients which will take

inflammatory cytokines into consideration can be realized. Thus, correlations between the severity of inflammation and cardiovascular involvement can be more clearly established.

In conclusion, in patients with AS, EAT thickness related to inflammatory response can increase. We could not find a relation between EAT and N/L, P/L ratios in terms of inflammatory response evaluation. Further studies with larger patient populations can be designed to find out the relationships more openly.

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TRANSPARENCY DECLARATION

Competing interests: none to declare.

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