Neutrophil to lymphocyte and platelet to lymphocyte ratios as an indicator of inflammation in patients with recurrent aphthous stomatitis

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Abstract

Objective: Recently, the ratios of neutrophil to lymphocyte (NL) and platelet to lymphocyte (PL) have been used as an indicator of inflammation. We aimed to investigate the relation of recurrent aphthous stomatitis (RAS) to inflammation by analyzing the ratios of NL and PL.

Methods: We conducted a case-control study on 143 patients with RAS and 134 healthy control cases between February 2015 and March 2016. Age, sex, neutrophil count, platelet count, lymphocyte count, and the ratios of NL and PL of the participants were recorded.

Results: One hundred and forty-three RAS patients and 134 control cases were included in the study. The ratios of NL and PL of RAS group were significantly higher than in the control group (p=0.004 and p=0.010, respectively). The NL ratio was the only independent predictor of RAS in multivariate logistic regression analysis (p=0.014). The cut-off value of NL ratio for predicting RAS was 3.49 with 13.3% sensitivity and 99.9% specificity (p=0.010).

Conclusion: We have found that the ratios of NL and PL were higher in RAS group than the control group. The results of our study support that inflammation has an important role in the pathogenesis of RAS.

Keywords: Lymphocyte, neutrophil, platelet, recurrent aphthous stomatitis.

Özet: Rekürren aftöz stomatitli hastalarda enflamasyon göstergeleri: Nötrofil/lenfosit ve trombosit/lenfosit oranları

Amaç: Son zamanlarda, nötrofil/lenfosit (NL) ve trombosit/lenfosit (TL) oranları enflamasyonun bir göstergesi olarak kullanılmaktadır. Bu çalışmada NL ve TL oranlarını değerlendirerek rekürren aftöz stomatitin (RAS) enflamasyon ile ilişkisini incelemeyi amaçladık.

Yöntem: Şubat 2015 ile Mart 2016 tarihleri arasında 143 RAS hastası ve 134 sağlıklı kontrol üzerinde bir olgu-kontrol çalışması yürüttük. Çalışmada katılımcıların yaş, cinsiyet, nötrofil, trombosit ve lenfosit değerleri ve NL ve TL oranları kaydedildi.

Bulgular: Yüz kırk üç RAS hastası ve 134 kontrol çalışmamıza dahil edildi. RAS grubunun NL ve TL oranları kontrol grubundakinden anlamlı olarak yüksekti (sırasıyla p=0.004 ve p=0.01). Çok değişkenli lojistik regresyon analizinde, NL oranı RAS için tek bağımsız prediktör olarak bulundu (p=0.014). RAS'ı tahmin etmede NL oranının kesme değeri %13.3 duyarlılık ve %99.9 spesifite ile 3.49 olarak tespit edildi (p=0.01).

Sonuç: NL ve TL oranları RAS grubunda kontrol grubundan yüksek bulundu. Çalışmamızın sonuçları RAS patogenezinde enflamasyonun önemli bir role sahip olduğunu desteklemektedir.

Anahtar sözcükler: Lenfosit, nötrofil, platelet, rekürren aftöz stomatit.

The most common cause of oral ulcers is recurrent aphthous stomatitis (RAS) in adults and children.[1] The prevalence of RAS varies from 5% to 60%.[2] Pathogenesis of RAS is multifactorial that trauma, stress, hormonal status, family history, food hypersensitivity, infectious factors, and immunological factors have a role in the development of RAS.[1] RAS can appear in three forms: minor aphthous ulcers, major aphthous ulcers, and herpetiform ulcers.[2] It has been considered that there are some changes in cellular immunity of RAS patients. It has been found that the rate of

CD8+/CD4+ of peripheral blood increased in RAS patients.[3] In oral ulcers, whereas the levels of interleukin (IL)-2, IL-6, IL-8, the tumor necrosis factor-α (TNF-α), which are pro-inflammatory cytokines, are increased, the level of IL-10, which is an anti-inflammatory cytokine, is decreased.[3-6]

Recently, the ratios of neutrophil to lymphocyte (NL) and platelet to lymphocyte (PL) have been noticed to be an indicator of inflammation for some cardiovascular or non-cardiovascular diseases.[7] Moreover, these ratios have been used as an indicator of poor prognosis in various cancers.[8,9]

To our knowledge, there are a few studies reporting the NL and PL ratios as inflammation predictors in RAS patients. In this study, we aimed to investigate the relation of RAS to inflammation by analyzing the ratios of NL and PL.

Materials and Methods

We conducted a case-control study on 143 patients with RAS and 134 healthy control cases between February 2015 and March 2016 in the Dermatology and Otorhinolaryngology Outpatient Clinics. The approval of Ethics Committee was obtained for this study from the Ethics Committee of Muğla Sıtkı Koçman University. We had age- and sex-matched subjects in RAS and the control groups. Diagnosis of RAS was based on the typical clinical findings and only the patients with minor aphthous stomatitis were included in the study.

The patients with diabetes mellitus, hypertension, coronary artery disease, connective tissue disease, vasculitis, inflammatory bowel disease, chronic renal insufficiency, chronic liver failure, malignancy, Bell's palsy, vertigo, tinnitus, and obesity were excluded from the study.

Complete blood count was analyzed in the RAS patients with active ulcers. Age, sex, neutrophil count, platelet count, lymphocyte count, and the ratios of NL and PL of the participants were recorded.

The statistical software "SPSS for windows 20.0" (SPSS Inc., Chicago, IL, USA) was employed for the data analysis. The chi-square test was used for the qualitative data. The distribution of quantitative variables was checked with Kolmogorov-Smirnov test. Independent samples T test for normal distributed variables and Mann-Whitney U test for abnormal distributed variables were used. Logistic regression analysis was performed to identify independent risk factors for RAS. The factors with the p<0.10 significance level in the univariate analysis were entered into multivariate regression analysis. A p-value <0.05 was considered significant.

Results

One hundred and forty-three RAS patients (46 male, 97 female; mean age 41.54 years) and 134 control cases (47 male, 87 female; mean age 38.36 years) were included in the study.

The ratios of NL and PL of the RAS group were significantly higher than those of the control group (p=0.004 and p=0.010, respectively). Lymphocyte count of the control group was significantly higher than those of the RAS group (p<0.05) (**Table 1**). The neutrophil count, lymphocyte count, NL ratio, and PL ratio levels were correlated with each other (p<0.001).

The NL ratio was the only independent predictor of RAS in multivariate logistic regression analysis (p=0.014) (**Table 2**). The cut-off value of NL ratio was 3.49 for predicting RAS with 13.3% and 99.9% specificity (p=0.010) (**Fig. 1**).

Table 1. Comparison of the demographic and hematologic parameters in RAS and the control groups.

	RAS group n (%) or mean ±SD	Control group n (%) or mean ±SD	p-value
Female	97 (67.8)	87 (64.9)	0.609
Male	46 (32.2)	47 (35.1)	
Age	41.54±15.88	38.36±13.65	0.076*
Neutrophil count (K/mL)	3.96±1.33	3.76±1.33	0.271†
Lymphocyte count (K/mL)	1.91±0.56	2.10±0.56	**0.004†**
Platelet count (K/mL)	260.22±58.61	262.04±63.11	0.804*
NL ratio	2.25±1.07	1.85±0.64	**0.004†**
PL ratio	145.89±48.33	131.56±41.65	**0.010†**

Chi-square test, Independent T test (*), and Mann-Whitney U test (†). **NL:** neutrophil/lymphocyte; **PL:** platelet/lymphocyte; **RAS:** recurrent aphthous stomatitis; **SD:** standard deviation.

Table 2. Predicting the presence of RAS in the participants with multiple regression analysis.

Independent variables	p-value	Odds ratio (95% CI)
Lymphocyte count	0.370	1.305 (0.729–2.337)
NL ratio	0.014	0.632 (0.438–0.912)
PL ratio	0.898	0.999 (0.992–1.007)

CI: confidence interval; **NL:** neutrophil/lymphocyte; **PL:** platelet/lymphocyte; **RAS:** recurrent aphthous stomatitis.

Discussion

RAS is a disease characterized by recurrent round/oval ulcers with erythematous halo and yellow/gray base.[10] Etiopathogenesis of RAS is still unclear while trauma, stress, family history, and immunological factors have been attribute to be responsible for oral ulcers.[1,11] In the differential diagnosis, there are traumatic lesions, malign lesions, drug reactions, vesiculobullous diseases, hematological disorders, gastrointestinal system diseases, vasculitidis, and infections.[3]

It has been demonstrated that levels of some pro-inflammatory cytokines (IL-2 and TNF-α) are high and level of IL-10, an anti-inflammatory cytokine, is low in the oral ulcers of RAS patients. In recent years, the NL ratio is gaining importance as an easy and cost-effective method to identify systemic inflammation.[7] The increased NL ratio levels have been demonstrated to be related to cytokines involving TNF-α, IL-6, IL-7, IL-8, IL-12, and IL-17. [12] Calculation of NL ratio is an easier and cheaper method than the measurement of these inflammatory cytokines.[12,13]

In various studies, the NL ratio levels have been reported increased in the patients with cardiovascular or non-cardiovascular diseases. However, studies investigating hematological ratios in RAS are scarce. Firstly, Soylu Özler et al. have demonstrated a relationship between the NL ratio and RAS.[14] Seçkin et al. have investigated the effect of colchicine treatment on hematologic inflammatory parame-

ters in the patients with RAS and showed significant decrease in the levels of NL ratio, leukocyte count, and red cell distribution width after the colchicine treatment.[15] In another study, Terzi et al. have reported an increased NL ratio in 80 patients with RAS compared to 80 healthy control cases and supported the role of inflammation in the pathogenesis of RAS.[16] Hypertension and diabetes mellitus have been found associated with high NLR levels.[7] Moreover, the NL ratio has been demonstrated as an predictor of morbidity and mortality in the patients with acute coronary syndrome.[12] Among cutaneous diseases, the NL ratio has been noticed significantly increased in the psoriasis patients.[17] Torun et al. have reported that the NL ratio may be a promising marker to indicate disease severity in ulcerative colitis.[18] Ozbay et al. have reported that mean NL ratio levels were significantly increased in the patients with tinnitus and peripheral vertigo.[19,20] In another study, the NL ratio has been found higher in the patients with a sudden hearing loss than healthy control cases.[21] Atan et al. have reported that both NL and PL rates were significantly higher in the patients with Bell's palsy than the control group.[22]

In conclusion, we found that increased NL and PL ratio levels are the inflammation predictors in the patients with RAS. To our knowledge, there are a few studies demonstrating the relation of RAS to inflammation by using the NL and PL ratios. Since the current study was conducted on the patients with minor aphthous stomatitis, further studies are needed involving patients with major and herpetiform aphthous ulcers to show differences in the pathogenesis.

Conflict of Interest: No conflicts declared.

Fig. 1. Receiver operating characteristics curve of NL ratio for predicting recurrent aphthous stomatitis in the participants.

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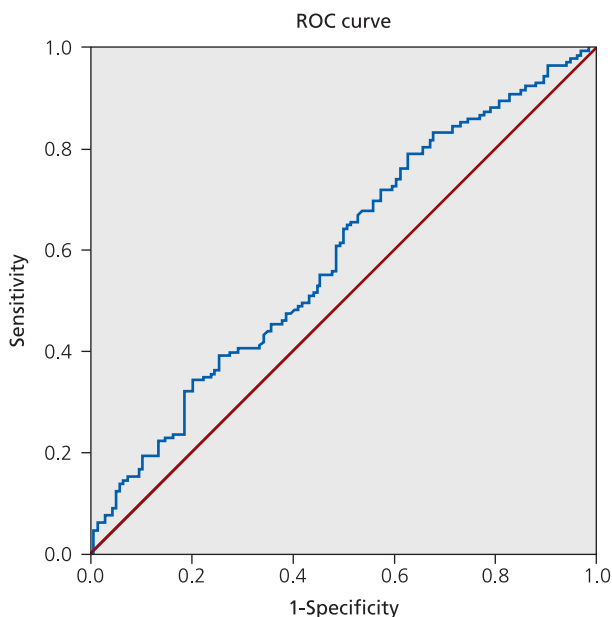
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