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Original Article

Comparison of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in patients diagnosed with trigeminal neuralgia and healthy controls

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Abstract

Aim: Trigeminal neuralgia (TN) is a common cranial nerve disease, but its pathogenesis has not yet been fully elucidated. The neutrophil-lymphocyte ratio (NLR) and the platelet-lymphocyte ratio (PLR) have been investigated in recent years as markers of systemic inflammation, and their determination presents as a lower-cost, more practical, and simpler method compared to other inflammation markers. This study aimed to evaluate the possible role of systemic inflammation in TN etiopathogenesis based on NLR and PLR values.

Materials and Methods: The study included 55 male and female patients aged 18 to 60 years, who were diagnosed with TN at the Neurology Clinic of our university according to the criteria of Headache Classification Committee of the International Headache Society 2018 (Cephalalgia2018), and 48 healthy controls. Demographic and clinical variables, such as age and gender were retrospectively obtained from medical records.

Results: In terms of sociodemographic data, both groups had similar characteristics. The NLR values were 1.84±0.81 for the patient group and 1.92±0.79 for the control group. There was no statistically significant difference in NLR between the two groups (p = 0.447). The PLR values were 101.91±30.24 and 97.84±30.24 for the patient and control groups, respectively, indicating no statistically significant difference (p = 0.439).

Conclusions: The role of systemic inflammation in TN pathophysiology remains controversial. It is considered that an inflammatory process may occur in the pathophysiology of TN, but this is characterized by local neurogenic inflammation rather than the effect of a systemic inflammatory response.

Keywords: Cranial nerve; headache; inflammation; neutrophil-lymphocyte ratio; platelet-lymphocyte ratio; trigeminal neuralgia

INTRODUCTION

Trigeminal neuralgia (TN) is a chronic pain syndrome and frequent disorder characterized by hemifacial sporadic, shock-like, prickling, stabbing type of pain and repetitive attacks localized to the small areas of the face innervated by the trigeminal nerve branches (1,2). The pathogenesis of TN has not yet been fully elucidated (2). Typically, a TN attack lasts a few seconds, but duration of over two minutes has also been reported in some cases. Pain attacks can continue for weeks or months, and then there may be periods of spontaneous remission of months or years. There are also painless periods between pain attacks. Attacks are triggered, albeit not always, by mild sensory stimulation of the trigger regions that can be found anywhere within the region of the affected trigeminal nerve. Typical early stimuli include a light touch, wind, eating, drinking, washing, talking, shaving, and applying makeup (1,3). Although the age of onset is generally middle and advanced ages, young adults and children can also be affected (4). The annual incidence has been reported as 27 per 100,000 (5).

Most TN cases are idiopathic, which is known as the classic form of TN (6). The leading hypothesis in TN pathophysiology is demyelination, which occurs in the root entry zone of the nerves compressed by blood vessels (1). Among the few cases in which the causes can be detected, inflammatory factors, such as tumors that compress the nerve externally, vascular malformations, pontine infarct, and multiple sclerosis (MS) have been implicated (7). The detection of vascular

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compression in normal trigeminal nerves and the absence of vascular compression in all patients with TN have led to the idea that additional factors may play a role in the development of this condition in many cases (8). Experimental research in recent years has shown a close relationship between neuropathic pain and inflammation (2). Some studies have suggested that a number of local inflammatory neuropeptides also play an important role in the trigeminovascular system (9). However, there is not sufficient research to determine the direct relationship between TN and inflammatory markers obtained from the peripheral blood of TN cases (2).

The neutrophil-lymphocyte ratio (NLR) and the platelet-lymphocyte ratio (PLR) have been investigated in recent years as markers of systemic inflammation, and their determination can be applied as a lower-cost, more practical and simpler method compared to other inflammation markers (10,11). There are also studies showing that the results are more significant when the two parameters are evaluated together (12). The levels of neutrophils and platelets are elevated during inflammation. In a number of systemic inflammatory diseases like rheumatoid arthritis, Sjögren's syndrome and psoriasis, the NLR and PLR values are used as indicators of inflammation and disease activation (13). In this study, we aimed to evaluate the possible role of systemic inflammation in TN etiopathogenesis based on NLR and PLR values.

MATERIALS and METHODS

This is a retrospective case control study comparing a patient group diagnosed with TN and a control group. The data were obtained from the medical records of the patients who applied between 01.01.2018 and 01.01.2020. The study included 55 male and female patients aged 18 to 60 years, who were diagnosed with TN at the Neurology Clinic of our university according to the criteria of Headache Classification Committee of the International Headache Society 2018 (14) and 48 healthy controls. Demographic and clinical variables, such as age and gender were retrospectively obtained from medical records. Patients with hematological diseases, active infection, endocrine abnormalities, hypertension, cardiac failure, pulmonary pathologies, malignancies, chronic kidney failure, chronic liver failure, or autoimmune or rheumatological diseases, those receiving treatment that might affect the inflammatory response, and pregnant or lactating women were excluded from the study. The cranial magnetic resonance imaging (MRI) findings of all TN patients included in the study were within completely normal limits. Antecubital venous blood samples were taken after 12-hour fasting from the patient and control groups to evaluate the parameters. NLR, PLR also hemoglobin (HBG), total white blood cell (WBC), platelet (PLT), neutrophil (NEU), lymphocyte (LYM), monocyte (mono), basophil (baso), eosinophil (eos), mean platelet volume (MPV) values obtained from hemotological examinations. NLR was calculated by dividing the neutrophil count by the lymphocyte count, and PLR by dividing the platelet count by the lymphocyte count. Approval for the study was obtained from the ethics committee of our university. Ethics committee approval date: 14.01.2020 and number: 2020/1-28.

Statistical Analysis

Statistical analyses were carried out using SPSS software version 17.0. The suitability of the variables to normal distribution was examined with histogram graphics and the Kolmogorov-Smirnov test. When presenting descriptive analyses, the mean, standard deviation and median values were used. The inter-group comparisons were undertaken using the independent samples t-test for the variables with normal distribution (parametric) and the Mann-Whitney U test for those without normal distribution (non-parametric). The results with a p value below 0.05 were evaluated as statistically significant.

RESULTS

A total of 103 individuals, comprising 55 TN patients and 48 controls, were included in the study. In terms of sociodemographic data, both groups had similar characteristics. In the TN group, 39 females (70.90%), and the mean age was 44.38±9.84 years. The control group consisted of 34 women female (70.83%), with a mean age of 40.70±10.58 years. The sociodemographic data are shown in Table 1.

Table 1. Demographic characteristics of the participants (n=103)

	Patients (n = 55)	Control (n = 48)	p[1]
Gender			
Male	16	14	
Female	39	34	
Age (year)	44.38±9.84	40.70±10.58	0.439

[1] Mann Whitney U Testi

The NLR values were 1.84 ± 0.81 for the patient group and 1.92 ± 0.79 for the control group. There was no statistically significant difference in NLR between the two groups (p = 0.447). The PLR values were 101.91 ± 30.24 and 97.84 ± 30.24 for the patient and control groups, respectively, revealing no statistically significant difference (p = 0.439). Concerning the remaining parameters measured, there was no statistically significant difference between the two groups in terms of the HBG, WBC, PLT, NEU, LYM, MONO, BASO, EOS and MPV. All hemogram findings are shown in Table 2.

Table 2. Comparison of the patient and control groups in terms of the measured parameters

	Patient		Control		
	Mean± SD	Median	Mean± SD	Median	p
WBC (x10³ /mm³)	7.55 ± 1.72	7.36	7.84± 2.00	7.39	0.427²
HBG (mg/dL)	13.53 ± 1.84	13.30	13.84 ± 1.56	13.62	0.366²
PLT (x10³ /mm³)	240.03 ± 60.36	232.40	230.20 ± 44.76	221.75	0.618¹
NEU (x10³ /mm³)	4.29 ± 1.35	3.81	4.60 ± 1.73	4.30	0.496¹
LYM (x10³ /mm³)	2.46 ± 0.58	2.53	2.50 ± .63	2.41	0.775²
MONO (x10³ /mm³)	0.52 ± 0.17	0.50	0.52 ± 0.16	0.49	0.908¹
BASO (x10³ /mm³)	0.08 ± 0.03	0.07	0.07 ± 0.03	0.07	0.430²
EOS (x10³ /mm³)	0.19 ± 0.13	0.14	0.16 ± 0.09	0.15	0.386¹
MPV (fL)	8.16 ± 1.61	7.92	8.82 ± 2.00	8.81	0.058¹
NLR	1.84 ± .81	1.69	1.92 ± .79	1.68	0.447¹
PLR	101.91 ± 30.24	94.54	97.84 ± 29.73	90.76	0.439¹

¹Mann-Whitney U test; ²Independent samples t-test
WBC: White blood cell, HBG: Hemoglobin, PLT: Platelet NEU: Neutrophil, LYM: Lymphocyte, Mono: Monocyte, Baso: Basophil, EOS: Eosinophil, MPV: Mean Platelet Volume, RDW: Red Cell Distribution Width, NLR: Neutrophil-Lymphocyte ratio, PLR: Platelet-Lymphocyte ratio

DISCUSSION

TN is a common cranial nerve disease. Although inflammation has been associated with neuropathic pain in many recent studies, its role in TN remains uncertain, and there is only limited research on this subject. However, inflammatory factors, such as tumor necrosis factor (TNF), chemokine ligand 2, interleukin 6 (IL-6) and transient receptor potential ankyrin 1 have been reported to induce the progression of TN (2). Thus, this study aimed to demonstrate the relationship between TN and systemic inflammation.

Studies have attempted to elucidate the underlying mechanisms of neuropathic pain symptoms, such as allodynia, hyperalgesia and spontaneous pain, especially in animal subjects and revealed the effects of immune and inflammatory cells and neuroinflammatory mediators secreted from these cellson the pathophysiology of neuropathic pain and activation of nociception (15). It has been reported that inflammatory mediators, including prostoglandins and proinflammatory cytokines can cause pain with direct nociceptor activation in primary sensorial neurons (16). In our study, we investigated the role of systemic inflammation in TN pathophysiology using inflammatory markers, namely NLR and PLR, as well as peripheral blood cell measurements of WBC, PLT, NEU, LYM, MONO, BASO, EOS and MPV. When the NLR and PLR values were compared between the patients with TN and the control group, no significant difference was observed.

In a similar study conducted with 141 patients with TN, the NLR and PLR values were compared to the control group, and the NLR value was found to be higher in the patient population, but no statistical difference was detected in the PLR values (2), which is consistent with our results. The underlying reason for the different results in this study may be that the number of patients is different from our study. Also it is considered that hematological parameters, such as NEU, LYM and PLT countsbeing easily affected by a wide range of conditions, including age, gender, ethnicity, nutritional habits, and environmental factors may have contributed to this result.

In another study, inflammatory proteins were preoperatively measured in the cerebrospinal fluid (CSF) of TN patients, and it some of the measured proteins were reported to be decreased in the postoperative re-examination (8). Another group of researchers determined that the substance p values, a neuroinflammatory mediator in CSF, were significantly higher in patients with TN compared to the control group (17). Calcitonin gene-related peptide (CGRP) is an important neuropeptide in trigeminal sensorial pathways, considered to significantly contribute to the underlying neurogenic inflammation of a number of diseases originating from craniofacial structures (18). In an animal study, high rates of CGRP, IL-1β, IL-6 and TNF were found in the trigeminal ganglia of rats with trigeminovascular disorder (19). These results suggest that an inflammatory process may be involved in the pathophysiology of TN, but this is due to a local neurogenic inflammation rather than the effect of a systemic inflammatory response. This idea is supported by the coexistence of MS and TN. In patients with MS, the prevalence of TN is 20 times higher compared to the normal population (20). In MS, another common condition is local subarachnoid meningeal inflammation (21), which has been considered as a source of proinflammatory cytokines aggregating TN (22). This also suggests that local inflammatory factors play a role in the pathophysiology of TN.

During surgery, thickened and opaque arachnoid membranes surrounding the trigeminal nerve root are frequently observed in TN patients (23). This may be considered in favor of inflammation, but performing intraoperative biopsy of the trigeminal nerve does not comply with ethical values (2). There are also some radiodiagnostic studies performed to reveal structural changes. Using modern MRI techniques based on diffusion tensor imaging, some microstructural changes have been detected in the trigeminal root entrance zone (24). Demyelination has also been shown in the same localization (1). These studies confirm the idea that local factors should be considered more prominently in the pathophysiology of TN.

LIMITATIONS

The limitations of this study are the absence of an evaluation of other biomarkers that indicate inflammation, such as C-reactive protein, procalcitonin, sedimentation, IL 1, and IL-6, and the results not being confirmed by disease duration or severity. We believe that multi-center randomized prospective studies with a larger number of patients are needed to further elucidate this subject.

CONCLUSION

The results obtained from this study suggest that systemic inflammation does not contribute to the pathophysiology of TN. The changes in a number of microstructures and demyelination detected in the trigeminal root entrance zone, as well as increased neuroinflammatory mediators and proteins in both trigeminal ganglia and CSF in patients with TN support the idea that additional factors playing a role in the TN pathophysiology are as a result of a predominant local neuroinflammatory condition.

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