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ORIGINAL ARTICLE

Does Behcet's disease associate with neuropathic pain syndrome and impaired well-being?

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Abstract Previously peripheral neuropathy signs have been reported in inflammatory chronic diseases but the presence of neuropathic pain syndrome (NPS) in Behcet's disease (BD) is unclear. The aim of this study was to investigate the association of BD with NPS and impaired quality of life and sleep quality. A total of 111 patients diagnosed as BD and 52 healthy controls were included. Pain severity was assessed by visual analogue scale (VAS) in rest and during activity. The NPS was diagnosed according to the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) index. The well-being and sleep disturbances of the groups were evaluated with Psychological General Well-Being (PGWB) Scale and Pittsburg Sleep Quality Index (PSQI). Although there were no one with NPS in healthy controls, the proportion of NPS in patients with BD was 19.8 % (p= 0.001). The VAS scores both in activity and at rest were higher in BD (p<0.001). There was statistically significant decrease in total PGWB score in BD patients compared to healthy controls (p<0.001). And significant increase in LANSS score was observed in patients with BD compared to healthy controls (p=0.000). The total LANSS scores showed significant positive correlation with PSQI scores (r=0.322) and negative correlation with total PGWB scores (r=-0.672) in patients with BD. We observed a positive correlation between LANSS and VAS (rest and activity) scores (r=0.44, r=0.42 respectively). The NPS seems to be associated with BD which should be taken into consideration in patients with neuropathic signs. The quality of life (QoL) and quality of sleep of the patients with BD were found to be impaired and this may be due to the presence of NPS.

Keywords Behcet's disease · Neuropathic pain syndrome · Quality of life · Sleep quality

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Introduction

Behcet's disease (BD) is a chronic and multisystemic disorder with characteristic triad with aphthous ulcers of the mouth and genital and relapsing uveitis [1]. Multisystemic involvement of BD also includes the nervous system. Neurologic involvement includes both the central nerve system (CNS) and peripheral nerve system (PNS). Primary neurologic involvement related to vascular inflammation mostly comprise cerebral venous thrombosis, headache, neuropsycho-Behçet's, and peripheral nerve system. PNS involvement is directly related to BD or indirectly related to complications to the treatment [2].

The peripheral nerve involvement consist of peripheral neuropathy, polyradiculoneuritis, and mononeuritis multiplex [2, 3]. Although peripheral neuropathy seems rare in BD, there is an increase electrodiagnostic studies showing peripheral involvement [4]. Peripheral neuropathy is a common reason of neuropathic pain syndrome (NPS). Additionally, subclinical sympathetic and parasympathetic autonomic dysfunctions were recorded in patients with BD which may also a reason of NPS [5]. NPS is characterized by unpleasant sensation with burning, stabbing, or aching and mostly associated with comorbid diseases such as diabetes, arthritis, infections, and other [6, 7]. Peripheral neuropathy signs have been reported in inflammatory chronic diseases but the presence of neuropathic pain syndrome in BD is unclear. The aim of this study was to investigate (1) does NPS associates with BD? and (2) BD associates with impaired well-being?

Material and methods

A total of 111 patients diagnosed as BD (62 females, 49 males) and 52 healthy controls (19 females, 33 males) were included in the study. The diagnosis of BD is based on the International Study Group Classification Criteria for BD [8]. The exclusion criteria included the presence of other systemic autoinflammatory diseases, acute flare of BD, diabetes mellitus, vitamin B deficiency, or other diseases that may affect the neurological system.

After detailed physical and neurologic examination, patients were evaluated by means of pain, neuropathic pain, quality of life, and sleep. The diagnosis of neuropathic pain syndrome was based on the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) index [9]. LANSS consists of five questions about the characterization of pain in the preceding week and additional sensorial testing for the presence of allodynia. A score of 12 or more was defined as neuropathic pain. The Turkish version of the scale was found to be valid [10].

Pain severity was assessed by visual analogue scale (VAS) in rest and during activity where 0 indicated no pain and 10 indicated worst pain. Quality of life consisted both general well-being and sleep quality. General well-being was assessed by Psychological General Well-Being (PGWB) Index. The PGWBI is a widely used generic health-related quality of life questionnaire. It consists of six subareas: anxiety (five items), depressed mood (three items), positive well-being (four items), self-control (three items), general health (three items), and vitality (four items) with a total of 22 items. The results were assessed by a six-point likert scale (0–5; 0, reflecting the most distress; 5, reflecting the highest level of well-being). The scores range between 0 and 110, and the higher the scores, the better the well-being. Also, the Turkish version of PGWBI was found to be reliable and valid [11, 12].

Sleep quality was measured by using the Pittsburg Sleep Quality Index (PSQI). Turkish version of this scale was found valid and reliable. PSQI has seven subgroups and measures subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The scoring system was based on a likert scale (0–3). The cut off value was "5" and the scores over it indicates poor sleep [13].

This study, was approved by the University of Ufuk Human Research Ethics Committee. At the beginning of this study, all participants were informed of the study and signed written informed consent.

Statistical analysis

The means and standard deviations were given as descriptive statistics. The differences between two groups were analyzed with t test. In order to find out the correlation between variables, Spearman correlation test was obtained. A level of significance of $p<0.05$ was accepted for this study. All analyses were performed by using the SPSS for Windows 15.0 software program.

Results

Demographic properties and baseline clinical evaluation of Behçet's disease patients and healthy controls were shown in Table 1. The mean age of the BD and control group were 38.49±11.01 and 35.19±11.24 years. The disease duration was 9.98±7.63 years. We observed that neuropathic pain is associated with BD. The NPS was found in a ratio of 19.8 % in BD (13 females and 9 males) and none in healthy controls. Also, significant increase in LANSS scores was observed in patients with BD compared to healthy controls ($p=0.000$). There were statistically significant differences in pain severity between groups. VAS scores both in activity and at rest were higher in BD ($p=0.000$) (Table 2).

There was statistically significant decrease in total PGWB score in BD patients compared to healthy controls ($p=0.000$) (Table 2). Also, most of the patients with BD had poor sleep quality (69.4 %) compared to healthy controls (55.8 %). However, this was not statistically significant ($p=0.097$).

The total LANSS score showed significant positive correlation with PSQI score ($r=0.32$) and negative correlation with total PGWB score ($r=-0.67$) in patients with BD. Also, we observed positive correlations between LANSS and VAS (rest and activity) scores ($r=0.44$, $r=0.42$, respectively). The results were shown in Table 3.

Table 1 Demographic properties and baseline clinical evaluation of Behçet's disease patients and healthy controls

	Behcet's disease (n=111, %)	Healthy controls (n=52, %)	p value
Age (year)	38.49±11.01	35.19±11.24	0.078
Gender			
Female	62 (55.9 %)	19 (36.5 %)	0.021*
Male	49 (44.1 %)	33 (63.5 %)	
Education			
Primary school	37 (33.3 %)	3 (5.8 %)	0.001**
Secondary school	9 (8.1 %)	3 (5.8 %)	
High school	40 (36 %)	27 (51.9 %)	
University	25 (22.5 %)	19 (36.5 %)	
NPS	22 (19.8 %)	0 (0 %)	0.001**
Sleep quality			
Good	34 (30.6 %)	23 (44.2 %)	0.097
Poor	77 (69.4 %)	29 (55.8 %)	

NPS neuropathic pain syndrome

*p<0.05; **p<0.01

Discussion

Neurological involvement of BD mostly affects the small veins in parenchyma due to the inflammation and known as intra-axial neuro-Behçet's syndrome. The extra-axial neuro-Behçet's syndrome is caused by cerebral venous sinus thrombosis. Both of these represent the CNS pathologies [14]. Peripheral nerve system involvement (PNS) was rarely reported in BD. In small series, the electrodiagnostic studies showed that the involvement of PNS consist of sensorimotor axonal neuropathy, mononeuritis multiplex, and polyradiculoneuritis [3, 4, 15]. Multiple etiological factors including peripheral and central neuropathies cause NPS. Akbulut et al. studied the PNS involvement electrophysiologically in BD and compared it with healthy controls [4]. Peripheral neuropathy was found in a ratio of 14.2 % and predominantly sensory nerves were affected more than motor nerves in BD. Another study investigated 69 BD patients electrophysiologically and 13 of them (18.8 %) showed PNS involvement with no related signs and symptoms [16]. All of the studies preferred an electroneuromyographic investigation in concerning PNS involvement. It should be taken into consideration that subclinic neuropathy may not be detected by electrophysiological studies in early stages. In this study, we used LANSS to detect NPS which can easily distinguish the nociceptive and neuropathic pain from each other. In BD, vascular involvement of vasa vasorums may be another factor in existing NPS.

Table 2 The results of pain, neuropathic pain, general well-being, and sleep quality of patients with Behçet's disease and healthy controls

	Behcet's disease group	Healthy controls	p value
VAS			
Rest	3.45±3.49	0	0.000*
Activity	4.34±3.77	0	0.000*
LANSS	7.49±6.80	0	0.000*
$PGWB_{total}$	66.22±19.61	79.65±16.25	0.000*
$PGWB_{anxiety}$	13.57±6.32	17.82±4.97	0.000*
$PGWB_{depression}$	10.81±3.28	12.05±2.75	0.020**
$PGWB_{positive\ well\text{-}being}$	9.16±3.05	11.46±3.15	0.000*
$PGWB_{vitality}$	11.47±4.38	14.23±3.52	0.000*
$PGWB_{self\text{-}control}$	11.32±3.51	12.25±2.55	0.093
$PGWB_{general\ health}$	9.98±2.99	11.82±2.66	0.000*
PSQI	7.07±4.13	5.32±2.77	0.006*

VAS visual analogue scale, *LANSS* Leeds assessment of neuropathic symptoms and signs index, *PGWB* psychological general well-being scale, *PSQI* Pittsburg sleep quality index

*p<0.05; **p<0.01

Table 3 Correlation between LANSS and pain severity, quality of life, and sleep quality

Behcet's disease group		
	LANSS	
VAS		
Rest	r=0.44	p=0.000
Activity	r=0.42	p=0.000
$PGWB_{total}$	r=−0.67	p=0.010
PSQI	r=0.32	p=0.025

VAS visual analogue scale, *LANSS* Leeds assessment of neuropathic symptoms and signs index, *PGWB* psychological general well-being scale, *PSQI* Pittsburg sleep quality index

The importance of quality of life (QoL) in chronic rheumatologic conditions were studied before [17–19]. There are several QoL assessment instruments, and in this study, PGWB index was used for measuring both psychological health and general well-being. Studies assessing QoL and life satisfaction as an outcome measurement in BD are increasing in recent years. BD patients particularly associated with arthritis have impaired quality of life and functional disability similar to rheumatoid arthritis patients [20]. Ertam et al. investigated the QoL and its relation with disease severity and reported that BD patients had impaired QoL compared to the control group [21]. Furthermore, the subgroups of measurement parameters such as general health, role-physical, and level of independence had significant negative correlations with disease severity. Similarly, Gur et al. noted that pain intensity, QoL, anxiety, and depression scores were significantly higher in BD patients than healthy controls. They used Nottingham Health Profile (NHP) and Health Assessment Questionnaire and concluded that mostly the existence of arthritis affects the QoL and

pain severity [22]. In another study, Bodur et al. investigated the QoL and life satisfaction in BD. They used NHP and life satisfaction index as outcome parameters. They reported that arthritis and genital ulcers were the main reasons for impaired QoL and life satisfaction in BD [23]. Moreover to clinical involvement, NPS itself has a negative correlation with QoL [24]. Similarly, various studies showed that both anxiety and depression play negative role in QoL [25–27]. This may lead to poor sleep quality as in this study the majority of the BD patients had sleep disturbance. We think all these factors may alter the sleep patterns which may result with impaired sleep quality.

One of the limitations of our study is that we did not study electrophysiological procedures. It would be better to investigate the presence of peripheral neuropathy or autonomic nervous system dysfunction by using electrophysiological tests. The second limitation is that we did not investigate the relationship between manifestations of BD with assessment parameters including QoL and pain severity.

Conclusion

The NPS seems to be associated with BD which should be taken into consideration in patients with subclinic neuropathy. The patients with BD should be evaluated with simple questionnaires in order to diagnose NPS. The QoL and quality of sleep of the patients with BD were found to be impaired and this may be due to the presence of NPS.

Disclosures None.

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