Is the Incidence of Fibromyalgia Syndrome Higher in the Patients with Behcet Disease and is Related to Disease Activity of Behcet Disease?

Fibromyalji Sendromu İnsidansı Behçet Hastalığı Olanlarda Yüksek midir ve Hastalık Aktivitesi ile İlişkili midir?

Feray Soyupek, Ali Murat Ceyhan*, Sedat Yıldız, Mehmet Yıldırım*

From Department of Physical Medicine and Rehabilitation, Süleyman Demirel University Medical Faculty, Isparta
**From Department of Dermatology, Süleyman Demirel University Medical Faculty, Isparta, Turkey*

ABSTRACT

Objective: We aimed to investigate the frequency of fibromyalgia syndrome (FS) in the patients with Behcet disease (BD) and aimed to investigate if there was an associated with Behcet Disease (BD) and the disease activity score of BD or not.

Methods: Patients were divided into 3 groups: 1. subjects with BD (BD group), 2. subjects with rheumatologic disorders including ankylosing spondylitis (AS) and rheumatoid arthritis (RA) (rheumatology group) and 3. The healthy normal controls (HNC). The rheumatology group divided into two RA and AS subgroups. All the patients were examined for FS. The disease duration, score of disease activity, laboratory parameters of the BD patients were recorded.

Results: The frequency of FS was 14.5% in the BD group. The presence of FS in BD group was not significantly higher than HNC. There was no correlation between the presence of FS, BD disease activity score and laboratory parameters of BD (p>0.05).

Conclusion: FS should be seen together with BD but the presence of FS was not related with BH disease activity. *(JPMRS 2009;12:113-6)*

Keywords: Fibromyalgia, Behcet syndrome, disease activity

ÖZET

Giriş: Behçet hastalığında (BH) fibromyalji sendromunun (FS) sıklığını ve BH hastalık aktivite skoru ile FS arasında ilişki olup olmadığını araştırmaktır.

Gereç ve Yöntem: Çalışmada; 1. BS olan hasta grubu (BS grubu), 2. Ankilozan spondilit (AS) ve romatoid artrit(RA) olan hasta grubu (romatoloji grubu) ve 3. Sağlıklı normal hasta grubu (kontrol grubu) olmak üzere üç grup vardı. Romatoloji grubu AS ve RA olmak üzere iki alt gruba ayrıldı. Tüm hastalar FS varlığı açısından değerlendirildi. BS hastalarının hastalık süresi, hastalık aktivite skorlaması ve laboratuvar parametreleri kaydedildi.

Bulgular: BS grubunda FS görülme sıklığı %14,5 idi. BS grubunda FS görülme sıklığı kontrol, RA ve AS alt grubundan istatistiksel olarak farklı bulunmadı (p>0,05). FS varlığı ile BS hastalık aktivite skoru ve laboratuvar parametreleri arasında korelasyon bulunmadı (p>0,05)

Sonuç: FS, BS ile beraber görünsede bu beraberliğin frekansı çok yüksek değildir. *(FTR Bil Der 2009;12:113-6)*

Anahtar kelimeler: Fibromyalji, Behçet hastalığı, hastalık aktivitesi

Corresponding Author
Yazışma Adresi
Dr. Feray Soyupek
From Department of Physical Medicine and Rehabilitation Süleyman Demirel University Medical Faculty, Isparta, Turkey
Phone: +90 312 211 25 18
E-mail: feraysoyupek@yahoo.com

Received/Geliş Tarihi: *17.02.2009*
Accepted/Kabul Tarihi: *16.09.2009*

3. Ulusal Romatizmal Hastalıklar Kongresi, Mayıs, 2008, Antalya

Introduction

Behcet Disease is a protean multisystem polysymptomatic disease with unpredictable exacerbations and remissions (1). All organs and musculoskeletal components of the body can be affected concomitantly or consecutively so all subspecialties can be involved in the care of these patients (1,2).

Fibromyalgia syndrome (FS) has been defined as a constellation of complaints including diffuse chronic pain and the presence of tender points (3). The prevalance of FS ranges from 1% to 10% in the general population (4). The condition is more common among females than males (5). Trauma, emotional stress and various rheumatologic disorders may trigger FS (6). Additionally, 25% of the patients with rheumatologic disorders meet the criteria of FS (7). In this study, we investigated whether FS was associated with BD and compared the prevalance of FS with the other rheumatologic diseases while evaluating the existence of FS with disease activity.

Material and Method

It is a prospective study. We studied three groups: 1. subjects with BD (the BD group) and 2. Subjects with rheumatologic disorders (rheumatology group) including ankylosing spondylitis and rheumatoid arthritis. Rheumatology groups divided into two subgroups; RA subgroup and AS subgroup. 3. the healthy normal controls (HNC) recruited from the hospital staff and other volunteers (the HNC group).

The records of BD patients who were diagnosed and followed at Süleyman Demirel University, Department of Dermatology were examined. Patients were invited to the hospital by phone. After giving informed consent, fifty-five patients with BD who met the criteria of International Study Group criteria participated to this study. Fifty-two patients with rheumatoid arthritis (RA), twenty-eight patients with ankylosing spondylitis (AS) which were diagnosed and followed-up in the department of Physical Medicine and Rehabilitation were included in rheumatology group and fifty-four healthy normal controls were chosen to HNC group. Differential diagnosis was made to exclude any other disease causing widespread pain such as hypothyroidism, chronic fatigue syndrome.

All the patients were examined for FS by the same physiatrist. The diagnosis of FMS was based on the 1990 criteria of ACR (3). Tender points examination involved a uniform manual finger pressure (4 kg) until the fingernail bed blanched, at each of 9 paired anatomically locations. Definite tenderness at any point was considered to be present if some involuntary verbal or facial expression of pain was noted or if a wince or withdrawal was observed. The tenderness was calculated by summing the number of tender points.

All participants completed self administered questionnaire that included age and sex. The age at diagnosis and disease duration were recorded. We collected the clinical data including clinical manifestation to score the disease activity of BD. The disease activity score was calculated by summing the points for all the disease manifestations as follows: 1 point for each mild symptom (oral or genital ulcer, skin lesions, monoarticular arthritis and superficial thrombophlebitis); 2 points for each moderate symptom (arthritis, small or medium-sized vessel involvement, anterior uveitis and gastrointestinal ulceration); and 3 points for each severe disease manifestation (posterior/pan uveitis or retinal vasculitis, gastrointestinal ulceration with bleeding or perforation, major vessel involvement and major organ involvement) (8). Sedimentation rate (SR) and C-reactive protein (CRP) level of patients with BD were measured. Patients with BD completed fibromyalgia related symptoms questionnaire that included headaches, sleep disturbance. The answers were expressed as 'yes' and 'no'.

Serum concentrations of thyroid stimulating hormone (TSH) were measured by radioimmunoassay to exclude thyroid disease.

The Statistical Package for the Social Sciences 15.0 for Windows was used for data analysis. In nominal variables, the chi-square and fisher exact test were used. For numerical variables showing normal distribution, we used the independent sample t-test. To analyze the differences between more than two groups, we used the one way analysis variance and Tukey's honestly significant difference posthoc tests for numerical variables that showed normal distribution and the chi-square test for nominal variables. Pearson and Spearman correlation tests were used for correlation tests. $P<0.05$ was considered statistically significant. Sample size calculation was done by Epi Info Stat-Calc Version 6 programme.

Results

The mean age of BD, rheumatology and HNC groups were 39.30±11.40, 40.87±10.05, 38.5±16.1 years, respectively (p=0.501). The mean ages of BD group, RA and AS subgroups, HNC were demonstrated in Table 1. Fifty-eight percentage of the BD group, 73% of RA subgroup, 57% of the AS subgroup and 59% of the HNC group were women (p=0.338).

The frequency of FS were 14.5%, 5.6%, 28.8% and 25% in the BD, HNC group, RA and AS subgroups, respectively (p=0.011). The frequency of FS in RA subgroup was significantly higher than HNC group (p=0.002) but there was no significant difference between the BD and HNC groups (p>0.05). The prevalences of FS in the patients with RA and AS were higher than that of patients with BD but this differences were not significant (p>0.05). Ninety-two percent and 85 % of the patients with FS in RA and AS subgroups were women, respectively. The mean number of tender points and frequency of FS were demonstrated in Table 1.

The mean disease activity scores of the patients with BD were 1.54±1.25 (minimum 0, maximum 5). The mean duration time of BD group was 11.27±9.08 years. SR and CRP levels of the BD group were 17.76±13.86 mm/h (minimum 1- maximum 80), 10.14±5.10, respectively. The mean haemoglobin level was 13.79±1.69 g/dL, blood platelet number was $302.14x10^3$±$78.67x10^3$/μL. The TSH levels of the patients were in normal ranges.

The BD group was divided into two subgroups according to coexistence of FS and named as BD with FS and BD without FS. The demographic features, disease activity scores, presence of headache, sleep disturbance, and laboratory parameters were demonstrated in Table 2.

Presence of headache and sleep disturbance were more common in the BD with FS subgroup ($p<0.05$). Additionally, the number of mean tender point was higher in BD with FS subgroup ($p<0.001$). In correlation analysis, we could not find any correlation between the presence of FS and the disease duration, age at diagnosis, disease activity score and laboratory parameters of BD ($p>0.05$). The tender point counts were not correlated with CRP, SR and disease activity score ($p>0.05$).

Discussion

In this study, we analyzed the coexistence of FS and BD and association of concomitant FS with disease activity score in the patients with BD. Our analysis have shown that FS was found in 14.5% of BD patients and also shown that FS was not significantly associated with disease activity in the patients with BD.

The prevalence of the FS in the general population in Turkey has not been not studied but there was a study about the prevalence of FS in a city of Turkey (9). Topbaş et al. assessed 1930 women to diagnose FS and found that the prevalence of FS was 3.6%. However, we studied a small sample of the healthy controls and the result was close to the result reported by Topbaş et al. (9). The frequency of FS was increased if there was concomitant disease. FS may occur when a person who is genetically predisposed is exposed to a certain environment, such as physical trauma, infection, emotional stress, endocrine disorders and various autoimmune disorders (7). Clauw et al. reported that 25% of the patients with rheumatologic disorders such as systemic lupus erythematosis, rheumatoid arthritis and anklosing spondylitis meet the ACR criteria for FS (7). Ranzolin et al. reported that the overall prevalence of FS in the patients with RA was 13.4% (10). They also investigated the association of concomitant FS with disease activity score (DAS) and suggested that FS was related to worse scores on the DAS in patients with RA. Aloush et al. investigated the frequency of FS in women with AS and found that 50 % of them met the ACR criteria for FS (11). In this study, the frequency of FS in the patients with RA and AS were approximately 29%, 25% respectively. There are limited studies regarding the frequency of FS in BD. Yavuz et al. demonstrated the coexistence of BD and FS in only 9.2% of the patients with BD (12). Al-İzzi et al. found that 8.9% of BD patients met the

Table 2. The demographic features, disease activity scores, presence of headache, sleep disturbance, laboratory parameters of the patients wth and without FS

	BD without FS n=47	BD with FS n=8	P value
Age	39.4±11.9	39.0±8.8	0.935
Sex (female/male)	25/22	7/1	0.072
Age at diagnosis (years)	27.70±10.26	29.00±11.58	0.747
Disease duration (years)	11.48±9.19	10.00±8.89	0.672
Disease activity score	1.7±0.9	0.9±0.8	0.087
Headache	57.4%	100%	0.019
Sleep disturbance	57.4%	100%	0.019
Tender point number	2.2±2.4	12.5±1.1	0.000
SR	18.9±14.5	11.1±6.7	0.085
CRP	11.2±10.1	4.0±1.2	0.449
Hb	13.9±1.8	13.2±1.2	0.288
Plt	$30.36x10^4$	$29.35x10^4$	0.740

Table 1. The mean number of tender points and frequency of FS

	BD group	Rheumatology group		HNC group
	n=55	RA (n=52)	AS (n=28)	n=54
Age (year)	39.3±11.4	48.3±11.0[1]	37.4±11.0	38.5±16.1
FS frequency (%)	14.5%	28.8%[2]	25.0%	5.6%
	(n=8)	(n=15)	(n=7)	(n=3)
Tender point number	3.7±2.3	6.7±4.8[4,5]	6.2±4.5[3]	3.3±3.4
(mean±SD) (min-max)	(0-15)	(0-14)	(0-14)	(0-12)

[1] p<0.001, RA subgroup vs BD group, AS subgroup and HNC group
[2] p<0.05, RA subgroup vs HNC group
[3] p<0.05, BD group vs AS subgroup
[4] p<0.001, RA subgroup vs HNC group
[5] p=0.001, RA subgroup vs BD group

ACR criteria for FS but the frequency of FS in the controls was 2.5% (13). In the other study by Lee SS et al., 37.1% BD patient had FS concomitantly (14). In the present study, 14.5% of the BD patients had FS. The differences in the FS prevalence among the BD patients can be explained the gender difference. Population studies of FS using the ACR criteria have shown that females has FS more often than males, estimates ranging from 1.0-4.9% in females as compared to 0.0-1.6% in males. The FS is predominantly found in women (15). A clear female predominance in the prevalence of FMS should prompt the search for a sex hormones-related aetiology. The ratio of female to male ratio in BD was different in all studies. Al-İzzi et al. (13) had the lowest ratio, Lee et al. (14) had highest ratio. Consequently, Lee et al. reported the highest FS prevalence in the BD patients.

Lee et al. (14) evaluated the manifestation of BD according to presence of clinical features. In the study of Lee et al., the presence of one or more of the following clinical features was regarded as a severe manifestation: posterior uveitis or retinal vasculitis, gastrointestinal ulcerations with bleeding or perforation, major organ involvement and major vessel involvement. The presence of FS did not differ significantly between BD patients with and without severe manifestation. There were no difference between BD patients with FS or without FS in disease activity and CRP. Additionally they could not find any correlation tender point counts and CRP, disease activity as our study. Yavuz et al. (12) reported that 10% and 39% of the BD patient with and without FS respectively had severe manifestation. In our study, we found that the score of disease activity was lower in patient without BS. Furthermore, there was not any relation between FS and disease activity of BS.

As a conclusion, there was a trend for an increased frequency of FS in BS patients. The possibility of the coexistence of these two systemic diseases must always be considered in suspicious clinical settings. The treatment of FS provides pain relief and increases the quality of life of BD patients. Lastly, the presence of FS does not seem to correlate with disease activity.

References

1. Sakane T, Takeno M, Suzuki N, Inaba G. Behcet's disease. N Engl J Med 1999;341:1284-91.
2. Yurdakul S, Yazici H, Tüzün Y, Pazarli H, Yalçin B, Altaç M, Ozyazgan Y, Tüzüner N, Müftüoğlu A. The arthritis of Behcet's disease: a prospective study. Ann Rheum Dis. 1983;42:505-15.
3. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell, P, Campbell SM, Abeles M, Clark P, Fam AG, Farber SJ, Fiechtner JJ, Franklin CM, Gatter RA, Hamaty D, Lessard J, Lichtbroun AS, Masi AT, McCain GA, Reynolds WJ, Romano TJ, Russell IJ, Sheon RP: The American College of Rheumatology 1990 criteria for the classification of fibromyalgia: Report of the multicenter criteria committee. Arthritis Rheum 1990;33:160-72.
4. Bliddal H, Danneskiold-Samsøe B. Chronic widespread pain in the spectrum of rheumatologic diseases. Best Pract Res Clin Rheumatol. 2007;21:391-402.
5. Yunus MB. Gender differences in fibromyalgia and other related syndromes. J Gend Specif Med 2002;5:42-7.
6. Clauw DJ, Crofford LJ. Chronic widespread pain and fibromyalgia: what we know and what we need to know. Best Pract Res Clin Rheumatol 2003;17:685-701.
7. Clauw DJ, Katz P. The overlap between fibromyalgia and inflammatory rheumatic disease: when and why does it occur?. J Clin Rheumatol 1995;1:335-42.
8. Hong SN, Park JC, Yoon NS, Lee SR, Kim KH, Hong YJ, Park HW, Kim JH, Ahn Y, Jeong MH, Cho JG, Kang JC. Carotid artery intima-media thickness in Behcet's disease patients without significant cardiovascular involvement. Korean J Intern Med 2008;23:87-93.
9. Topbas M, Cakirbay H, Gulec H, Akgol E, Ak I, Can G. The prevalence of fibromyalgia in women aged 20-64 in Turkey. Scand J Rheumatol. 2005;34:140-4.
10. Ranzolin A, Brenol JC, Bredemeier M, Guarienti J, Rizzatti M, Feldman D, Xavier RM. Association of concomitant fibromyalgia with worse disease activity score in 28 joints, health assessment questionnaire, and short form 36 scores in patients with rheumatoid arthritis. Arthritis Rheum. 2009;61:794-800.
11. Aloush V, Ablin JN, Reitblat T, Caspi D, Elkayam O. Fibromyalgia in women with ankylosing spondylitis. Rheumatol Int. 2007;27:865-8.
12. Yavuz S, Fresko I, Hamuryudan V, Yurdakul S, Yazici H. Fibromyalgia in Behcet's syndrome. J Rheumatol 1998;25: 2219-20.
13. Al-Izzi MK, Jabber AS. Fibromyalgia in Iraqi patients with Behcet's disease. J Med Liban 2004;52:86-90.
14. Lee SS, Yoon HJ, Chang HK, Park KS. Fibromyalgia in Behcet's disease is associated with anxiety and depression, and not with disease activity. Clin Exp Rheumatol 2005;23:15-9.
15. Grant JT. The epidemiology of chronic generalized musculoskeletal pain. Best Pract Res Clin Rheumatol 2003;17:547-61.