Musculoskeletal Involvement in Pediatric Behçet's Disease: A Single Center Experience

Pediatrik Behçet Hastalığında Kas İskelet Sistemi Tutulumu: Tek Merkez Deneyimi

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ABSTRACT

Objective: Behçet's disease (BD) is an inflammatory disease characterized by recurrent oral ulcers, genital ulcers, ocular manifestations, and vascular involvement. Musculoskeletal symptoms are common both at the time of presentation and throughout the course of BD. This study aims to report the frequency and characteristics of musculoskeletal involvement in pediatric Behçet's disease (PEDBD) followed by our clinic.

Material and Methods: This retrospective medical record review included patients diagnosed with PEDBD before the age of 16 between January 2010 and December 2022.

Results: Of the 90 patients included in the study, 48 (53.3%) were female. Their mean age at diagnosis was 12.4 ± 3 years. All patients (100%) had recurrent oral ulcers, while 55 (61.1%) had genital ulcers, 44 (48.9%) had musculoskeletal involvement, 37 (41.1%) had skin manifestations, 19 (21.1%) had ocular involvement, 17 (18.9%) had neurological involvement, and 17 (18.9%) had vascular involvement. Among the patients with joint involvement, 27 (65.9%) had arthritis, 41 (100%) had arthralgia, 37 (90.1%) had oligoarticular joint involvement, and 29 (70.7%) had asymmetrical involvement. The most frequently affected joints in patients were knee (63.4%), ankle (31.7%), wrist (19.5%), sacroiliac joints (14.6%), hands (12.2%) (Involvement of the metacarpophalangeal joint in one patient and the proximal interphalangeal joint in four patients), elbow (9.8%) and feet (4.9%) (One of the patients had metatarsophalangeal joint involvement and the other had proximal interphalangeal joint involvement).

Conclusion: Musculoskeletal symptoms are common in PEDBD and can be observed as an early sign of the disease at the time of diagnosis. Therefore, it is important to thoroughly inquire about possible BD in children with musculoskeletal symptoms.

Key Words: Arthralgia, Arthritis, Pediatric Behçet's disease, Musculoskeletal system

ÖZ

Amaç: Amaç: Behçet hastalığı (BH) tekrarlayan oral ülserler, genital ülserler, oküler bulgular ve vasküler tutulum ile karakterize inflamatuvar bir hastalıktır. Kas-iskelet sistemi semptomları hem başvuru sırasında hem de Behçet hastalığının seyri boyunca yaygındır. Bu çalışmanın amacı, kliniğimiz tarafından pediatrik Behçet hastalığı (PEDBH) tanısı ile takip edilen hastalarda kas-iskelet sistemi tutulumunun sıklığını ve özelliklerini bildirmektir.

Gereç ve Yöntemler: Bu retrospektif tıbbi kayıt incelemesi, Ocak 2010 ile Aralık 2022 tarihleri arasında 16 yaşından önce PEDBH tanısı alan hastaları kapsamaktadır.

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Conflict of Interest / *Çıkar Çatışması*: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethics Committee Approval / *Etik Kurul Onayı*: Ethics Committee of Ankara Bilkent City Hospital (Ethics Committee Approval No/Date: E2-23-3123/04.01.2023)

Contribution of the Authors / Yazarların katkısı*:** All authors made substantial contributions to the conception or design of the work, have approved the final manuscript, and takes full responsibility for the manuscript. ***COŞKUN S, ÇELİKEL ACAR B: reviewed and revised the manuscript, ***COŞKUN S, EKEİCİ TEKİN Z, ÇELİKEL E, GÜNGÖRER V and ÇELİKEL ACAR B:*** contributed to the writing of the manuscript, ***COŞKUN S, TEKGÖZ N, SEZER M, KARAGÖL C, ÖNER N, KAPLAN MM and POLAT MC*** were responsible for data collection and analysis.

How to cite / *Atıf yazım şekli* : Coşkun S, Ekici Tekin Z, Çelikel E, Güngörerer V, Tekgöz V, Karagöl C, et al. Musculoskeletal Involvement in Pediatric Behçet's Disease: A Single Center Experience. Turkish J Pediatr Dis 2023;17:483-487.

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Received / Geliş tarihi : 09.06.2023
Accepted / Kabul tarihi : 03.08.2023
Online published : 25.08.2023
Elektronik yayın tarihi
DOI: 10.12956/tchd.1312002

Bulgular: Çalışmaya dahil edilen 90 hastanın 48'i (%53.3) kadındı. Ortalama tanı yaşı 12.4±3 yıldı. Tüm hastalarda (%100) tekrarlayan oral ülserler, 55'inde (%61.1) genital ülserler, 44'ünde (%48.9) kas-iskelet sistemi tutulumu, 37'sinde (%41.1) deri bulguları, 19'unda (%21.1) göz tutulumu, 17'sinde (%18.9) nörolojik tutulum ve 17'sinde (%18.9) vasküler tutulum vardı. Eklem tutulumu olan hastaların 27'sinde (%65.9) artrit, 41'inde (%100) artralji, 37'sinde (%90.1) oligoartiküler eklem tutulumu ve 29'unda (%70.7) asimetrik tutulum vardı. Hastalarda en sık etkilenen eklem diz (%63.4) olurken, bunu ayak bileği (%31.7), el bileği (%19.5), sakroiliak eklemler (%14.6), eller (%12.2) (Bir hastada metakarpofalangeal eklem ve dört hastada proksimal interfalangeal eklem tutulumu vardı), dirsek (%9.8) ve ayaklar (%4.9) (Hastalardan birinde metatarsofalangeal eklem tutulumu ve diğerinde proksimal interfalangeal eklem tutulumu vardı) takip etti.

Sonuç: Kas-iskelet sistemi semptomları PEDBH'de yaygındır ve tanı anında hastalığın erken bir belirtisi olarak gözlemlenebilir. Bu nedenle, kas-iskelet sistemi semptomları olan çocuklarda olası BH'nin ayrıntılı bir şekilde araştırılması önemlidir.

Anahtar Sözcükler: Artralji, Artrit, Pediatrik Behçet hastalığı, Kas iskelet sistemi

INTRODUCTION

Behçet's disease (BD) is an etiology unknown inflammatory disease characterized by recurrent oral ulcers, genital ulcers, ocular manifestations, skin lesions, gastrointestinal, neurological, musculoskeletal, and vascular involvement, which can affect all organs and systems (1,2). BD often occurs between the second and fourth decades of life. BD can also be observed in children. In fact, studies show that 4-26% of BD patients appear in childhood (3). There is increasing awareness about pediatric Behçet's disease (PEDBD), but information of PEDBD is still limited in the literature. Musculoskeletal symptoms are common both at the time of presentation and throughout the course of BD (4). The most common musculoskeletal symptoms in BD are arthritis and arthralgia, followed by enthesopathy, avascular necrosis, myalgia, and myositis (5). Arthritis occurs in 20-40% of PEDBD cases, is usually oligoarticular and non-erosive, but erosive arthritis is rarely seen in BD (6-9). BD commonly affects the knees, ankles, wrists, and elbows, and rarely causes sacroiliitis (8). Localized myositis is not common in BD and has only been reported in a few children (8).

This study aims to report the frequency and characteristics of musculoskeletal involvement in PEDBD followed by our clinic.

MATERIAL and METHODS

This retrospective medical record review included patients diagnosed with PEDBD before the age of 16 between January 2010 and December 2022. Patients diagnosed with PEDBD before 2016 were evaluated according to the International Study Group for Behçet's Disease (ISG) and International Criteria for Behçet's Disease (ICBD) criteria, while those diagnosed with PEDBD after 2016 were evaluated according to Pediatric Criteria (PedBD) (10-12). Before conducting the study, the diagnoses of all patients were confirmed by experts (BÇA, EÇ, ZET) according to the PedBD criteria. Table I shows the diagnostic criteria for BD. Patients with incomplete medical data, those who did not attend regular follow-up visits, and those diagnosed with BD after the age of 16 years were not included in the study.

The patients' demographic, clinical, laboratory (complete blood count, C-reactive protein, erythrocyte sedimentation rate), and treatment-related data were recorded from their electronic files. Their musculoskeletal symptoms including arthritis, arthralgia, enthesopathy, myalgia, and myositis were noted in the study.

Joint involvement was defined as the presence of joint pain [None of the patients had metabolic (such as electrolyte imbalance) or structural (such as hypermobility, deformity) reasons to explain joint pain], swelling, and/or limited joint mobility, while muscle system involvement was defined as the presence of muscle pain and/or signs of inflammation in the muscle (13).

Laboratory data were examined for the presence of antinuclear antibodies (ANA) and human leukocyte antigen-B51 (HLA-B51).

This study was approved by the Ethics Committee of Ankara Bilkent City Hospital (Ethics Committee Approval No/Date: E2-23-3123/04.01.2023) and conducted in accordance with the Helsinki principles.

Table I. Diagnostic criteria for Behçet's disease

ISG (Adult)*
ROA (mandatory) at least 3 pieces/year
GU
Skin lesions
Ocular involvement
Pathergy test positivity
ICBD (Adult)†
ROA (2 points) at least 3 pieces/year
GU (2 points)
Skin lesions (1 point)
Ocular involvement (2 points)
Vascular involvement (1 point)
Neurological involvement (1 point)
PEDBD (Pediatric)‡
ROA (1 point) at least 3 pieces/year
GU (1 point)
Skin lesions (1 point)
Ocular involvement (1 point)
Vascular involvement (1 point)
Neurological involvement (1 point)

GU:** Genital ulcer, **ICBD:** International Criteria for Behçet's disease, **ISG:** International Study Group, **PEDBD:** Pediatric Behçet's Disease, **ROA:** Recurrent oral aphthosis ** Mandatory criteria and at least 2 of the others, **†:** 4 and over points, **‡:** 3 and over points*

Statistical analysis

The data were evaluated using the SPSS version 22. Descriptive statistics were used to present quantitative variables as mean± standard deviation (SD) if they had normal distribution, or as median (minimum-maximum) if they did not. Categorical variables were presented as numbers and percentages. When comparing quantitative data, the Student-t test was used for parametric data and the Mann-Whitney U test for non-parametric data. The chi-square test was used to compare categorical variables. The correlation between variables was examined using Pearson's correlation analysis. A p value less than 0.05 was considered statistically significant.

RESULTS

Demographic, clinical, and laboratory parameters

A total of 90 patients, 48 (53.3%) of whom were female, were included in the study. Their mean age at diagnosis was 12.4 ± 3 years. Their median time to diagnosis was 1 year (0-12), and their median follow-up duration was 3 years (1-13). All patients had recurrent oral ulcers, while 55 (61.1%) had genital ulcers, 44 (48.9%) had musculoskeletal involvement, 37 (41.1%) had skin manifestations, 19(21.1%) had ocular involvement, 17 (18.9%) had neurological involvement, 17(18.9%) had vascular involvement, and 6(6.7%) had epididymitis. In addition, HLA-B51 positivity was present in 48(53.3%) patients, and ANA positivity was present in 6 (6.7%) patients. A family history of BD was found in 38(42.2%) patients. Table II summarizes the patients' demographic, clinical, and laboratory parameters.

Musculoskeletal involvement

Musculoskeletal involvement was present in 44(48.9%) patients. Among these patients, 32(72.7%) had musculoskeletal symptoms at the time of diagnosis, and 18 (40.9%) had recurrent musculoskeletal involvement. Regarding the distribution of musculoskeletal symptoms in PEDBD patients, 41(45.6%) had joint involvement, 20(20.2%) had myalgia, and 11(12.2%) had enthesitis.

Among the patients with joint involvement, 27(65.9%) had arthritis, all (n=41, 100%) had arthralgia, 37(90.1%) had oligoarticular joint involvement, and 29(70.7%) had asymmetrical involvement. The most commonly affected joints the patients are the knees (26 patients, 63.4%), followed by the ankle (13 patients, 31.7%), the wrist (8 patients, 19.5%), sacroiliac joints (6 patients, 14.6%), hands (5 patients,12.2%) (Involvement of the metacarpophalangeal joint in one patient and the proximal

Table II: Demographic, clinical and laboratory characteristics of paediatric patients with Behcet's disease

	All patients	Musculoskeletal involvement	Non-musculoskeletal involvement	p
Age at diagnosis years*	12.4 (2-16)	13.5 (5-16)	14 (2-16)	0.620
Age at onset of symptoms years median (min-max)	10.3 (2-15)	10.5 (2-15)	11 (2-15)	0.780
Time to diagnosis years median (min-max)	1 (0-12)	1 (0-12)	1 (0-10)	0.747
Gender†				
Male	42 (46.7)	19 (21.1)	23 (25.6)	0.534
Female	48 (53.3)	25 (27.7)	23 (25.6)	
ROA†	90 (100)	48 (53.3)	42 (46.7)	
GU†	55 (61.1)	24 (26.7)	31 (34.4)	0.280
Skin lesions†	37 (41.1)	16 (17.8)	21 (23.3)	0.284
Ocular involvement†	19 (21.1)	11 (12.2)	8 (8.9)	0.444
Vascular involvement†	17 (18.9)	5 (5.6)	12 (13.3)	0.175
Neurological involvement†	17 (18.9)	10 (11.1)	7 (7.8)	0.593
Epididymitis†	6 (6.6)	2 (2.2)	4 (4.4)	0.429
Pathergy test positivity†	29 (32.2)	15 (16.7)	14 (15.5)	0.822
WBC ($x10^9$ /L)*	7.8 (3.6-25.4)	7.6 (4.6-12.9)	8.1 (3.6-25.4)	0.064
Neutrophils ($x10^9$ /L)*	4.5 (1.4-21.4)	4.3 (2.1-10.3)	4.8 (1.4-21.4)	0.153
Lymphocytes ($x10^9$/L)*	2.3 (0.9-6.3)	2.3 (0.9-3.5)	2.2 (1.1-6.3)	0.551
Thrombocytes, ($x10^9$ /L)*	278 (124-583)	289 (177-583)	264 (124-563)	0.061
CRP (mg/dL)*	4.8 (0-43)	4.6 (0-13.2)	4.9 (0-43)	0.888
ESR (mm/saat)*	10 (2-113)	10 (3-54)	10.5 (2-113)	0.642
HLA B-51†	48 (53.3)	24 (26.7)	24 (26.7)	0.673
Family history†	38 (42.2)	20 (22.2)	18 (20)	0.670

*****median(min-max)*, †*n(%)*, **CRP:** C-reactive protein, **ESR:** erythrocyte sedimentation rate, **GU:** Genital ulcer, **HLA:** Human leukocyte antigen, **ROA:** Recurrent oral aphthosis, **WBC:** White blood cells*

interphalangeal joint in four patients), the elbow (4 patients, 9.8%), and the feet (2 patients, 4.9%) (One of the patients had metatarsophalangeal joint involvement and the other had proximal interphalangeal joint involvement).

All patients with musculoskeletal involvement received colchicine treatment, and additional non-steroidal anti-inflammatory drugs (NSAIDs) were given to 36.6% of patients. Four patients who did not respond to colchicine and NSAID treatment required additional therapy. One patient with sacroiliitis was started on sulfasalazine and achieved clinical and radiological remission in the third year of treatment, leading to discontinuation of therapy. One patient with polyarticular joint involvement was started on azathioprine, but joint restrictions persisted in the first year. The patient with no evidence of active arthritis received a physiotherapy programme for restriction. Methotrexate treatment was initiated for one patient with involvement in the knee joint, and treatment was discontinued in the second year when complete remission was achieved. Another patient with bilateral knee involvement received two intra-articular steroid treatments at one-year intervals, and adalimumab was started during follow-up. Although the patient did not show active arthritis symptoms in the first year of treatment, there was still restriction in both knees. The patient with no evidence of active arthritis in the knees was entered into a physiotherapy programme for restriction.

Out of the 44 patients with musculoskeletal involvement, 42 (95.5%) were in complete remission regarding musculoskeletal symptoms, while 2 (5.5%) patients with while 2 patients with arthritis had restriction in the joints.

There were no significant differences between the patients with musculoskeletal involvement and those without musculoskeletal involvement in terms of demographic, clinical, and laboratory data (Table II).

DISCUSSION

Musculoskeletal symptoms can be observed as an early manifestation of BD in 20-40% of children with BD (14). This study focused on musculoskeletal involvement in PEDBD, and found that musculoskeletal symptoms were present in approximately one-third of the patients at the time of diagnosis. Arthritis and arthralgia were the most common musculoskeletal symptoms among the patients with BD. Some of the patients had oligoarticular and asymmetrical joint involvement. Complete remission of musculoskeletal symptoms was achieved with treatment in 95.5% of patients.

Joint involvement is common in patients with BD. Although it may not be included in the diagnostic criteria, joint involvement is an important component of BD and can sometimes be the sole presenting symptom (15). The frequency of joint involvement in BD patients varies between 5.2% and 60.1% in Türkiye (16). This may be because some studies do not consider arthralgia as joint involvement but only consider arthritis as joint involvement (16). Davachi et al. (17) reported an incidence of joint involvement of 39.4% in the study of 6.075 BD patients . Sarıcaoğlu et al. (18) evaluated 30 PEDBD patients and reported that arthritis and/or arthralgia were present in 50% of them. Peripheral arthritis was detected in 47.4% of patients in a PEDBD cohort (14). Studies have reported that arthritis in BD generally shows a recurrent, acute, self-limiting course without deformity or erosion, and follows a mild and transient course, primarily affecting large joints such as knees and ankles (8,19). In this study, similar to those in the literature, joint involvement was present in 45.6% of PEDBD patients, and joint involvement was predominantly oligoarticular, with knees and ankles being the most commonly affected joints (7,8).

There are several studies suggesting a higher presence of acneiform skin lesions in BD patients with arthritis (20,21). Although the mechanism of arthritis in BD is not fully understood, the coexistence of acne and arthritis raises the possibility of a pathogenic connection (5,8). Many researchers have emphasized the clustering of cutaneous manifestations with arthritis (21,22). Gaggiano et al. (22) reported a higher prevalence of mucocutaneous clustering in children with BD who initially presented with musculoskeletal symptoms. Our study found no relationship between acneiform skin lesions and arthritis symptoms. Yurtkuran et al. (23) evaluated 57 adult BD patients and reported that hand joint involvement correlated with disease duration. Permanent arthropathies are rare in BD patients (8). Destructive arthropathies have been reported in case reports or limited case series for BD. Frikha et al. (24) evaluated a total of 553 adult BD patients and reported that 1.4% of them had destructive arthritis. In our study, sequela lesions were present in 2.2% of the patients. Early onset of joint involvement may increase the frequency of sequela lesions. However, definitive conclusions can be reached through studies comparing large patient groups of adults and children.

Sacroiliac joint involvement and enthesopathy can also be observed in BD patients (14). Although the prevalence of enthesopathy has been reported to be as high as 38% in some clinical studies, low rates such as 3.4% have also been reported in some other studies (5). The wide variation in reported frequency of enthesopathy in BD patients can be attributed to the lack of sensitive methods for detecting enthesopathy through radiography and physical examination, as well as differences in the selected study populations (5). Özelçi et al. (25) found a frequency of 21.1% for sacroiliitis in BD patients. In the present study, sacroiliitis was present in 14.6% of the patients, while enthesopathy was not detected among them. This may be because the rate of enthesopathy is also found to be very low in the literature.

In BD, arthritis is self-limiting and usually resolves within 2-3 weeks, so drug treatment may not be necessary in most cases (26). Colchicine and NSAIDs are the preferred medications

for the treatment of non-erosive arthritis in BD (27-30). However, various therapeutic alternatives are available for destructive arthritis, including local corticosteroid injections and low-dose systemic corticosteroids. Azathioprine and tumor necrosis factor-alpha (TNF-α) blockers may be effective in rare cases resistant to treatment (5). In this study, four patients resistant to colchicine and NSAID treatment received sulfasalazine, azathioprine, methotrexate, adalimumab, and intra-articular steroid treatments. Complete remission in terms of musculoskeletal involvement was achieved in 97.8% of the patients. Similar to other studies in the literature, persistent arthritis in BD was rare in our study.

The main limitations of the study are that it is a single-center study with a retrospective design, and that BD is less common in childhood than in adults. However, considering the limited number of studies on musculoskeletal involvement in PEDBD, this study will contribute to the literature.

In conclusion, musculoskeletal symptoms are a self-limiting, benign, and common finding in children with BD, which can be considered an early manifestation of the disease. Therefore, it is important to thoroughly inquire and evaluate children with musculoskeletal complaints for possible BD.

REFERENCES

1. Batu E. D. Diagnostic/classification criteria in pediatric Behçet's disease. Rheumatol Int 2019; 39: 37–46.
2. Bettiol A, Prisco D, Emmi G. Behçet: the syndrome. Rheumatology (Oxford, England) 2020; 59: 101–7.
3. Koné-Paut I. Behçet's disease in children, an overview. Pediatr Rheumatol Online J 2016; 14:10.
4. Vaiopoulos A. G, Kapsimali V, Kanakis M. A, Vaiopoulos G, Samarkos M, Zouboulis C. et al. The frequency of arthritis in Adamantiades-Behçet's disease in Greek patients. J Eur Acad Dermatol Venereol 2019; 33: 416–20.
5. Bicer A. Musculoskeletal Findings in Behcet's Disease. Pathology res Int 2012; 653806.
6. Yıldız M, Köker O, Adrovic A, Şahin S, Barut K, Kasapçopur Ö. Pediatric Behçet's disease- clinical aspects and current concepts. Eur J Rheumatol 2019; 5;7:1-10.
7. Mülkoğlu C, Ayhan FF. A case with Behçet's disease involving erosive Metacarpophalangeal joint arthritis: the value of ultrasonography in the diagnosis of an Erosion. BMC Med Imaging 2020; 20: 60.
8. Kötter I, Lötscher, F. Behçet's Syndrome Apart From the Triple Symptom Complex: Vascular, Neurologic, Gastrointestinal, and Musculoskeletal Manifestations. A Mini Review. Front Med (Lausanne) 2021; 8: 639758.
9. Shahram F, Nadji A, Akhlaghi, M, Faezi S. T, Chams-Davatchi C, Shams H, et al. Paediatric Behçet's disease in Iran: report of 204 cases. Clin Exp Rheumatol 2018; 36: 135–40.
10. Alibaz-Oner F, Direskeneli H. Update on the Diagnosis of Behçet's Disease. Diagnostics (Basel) 2022; 23;13:41.
11. International Team for the Revision of the International Criteria for Behçet's Disease (ITR-ICBD). The International Criteria for Behçet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. J Eur Acad Dermatol Venereol 2014; 28:338-47.
12. Koné-Paut I, Shahram F, Darce-Bello M, Cantarini L, Cimaz R, Gattorno M. et al. PEDBD group. Consensus classification criteria for paediatric Behçet's disease from a prospective observational cohort: PEDBD. Ann Rheum Dis 2016;75:958-64.
13. Tse S, Colbert R. Textbook of Pediatric Rheumatology. Eighth Edition. Philadelphia: Elsevier 2021:253-54.
14. Yildiz M, Haslak F, Adrovic A, Sahin S, Koker O, Barut K, et al. Pediatric Behçet's Disease Front Med (Lausanne) 2021;8:627192.
15. Köseoğlu H, Yücetürk T, Bayraktar N, Tufan M, Gencer M, Yücel A. Anti-CCP Antibodies in Behcet's Disease with or without articular Involvement. Yeni Tıp Dergisi 2011; 28: 92- 4.
16. Rota D. D, Tanacan E, İbis O, Gündüz Ö, Erdoğan F. G, Gürler A. Clinical and Demographic Characteristics of 197 Behçet Patients. J Ankara Univ Fac Med 2021;74:60-7.
17. Davatchi F, Chams-Davatchi C, Shams H, Nadji A, Faezi T, Akhlaghi M, et al. Adult Behcet's disease in Iran: analysis of 6075 patients. Int J Rheum Dis 2016;19: 95–103.
18. Sarıcaoğlu H, Erdem H, Toker ÇS, Başkan EE, Yücel A, Tunalı Ş. The Clinical and Demographic Characteristics of Pediatric Behçet's Patients. Güncel Pediatri 2008;6: 89-93.
19. Davatchi F. Behçet's disease. Int J Rheum Dis 2018;21:2057-8.
20. Zou J, Luo JF, Shen Y, Cai JF, Guan JL. Cluster analysis of phenotypes of patients with Behçet's syndrome: a large cohort study from a referral center in China. Arthritis Res Ther 2021;23:45.
21. İlgen U. Clusters in Behçet's syndrome. Arthritis Res Ther 2022;24:242.
22. Gaggiano C, Maselli A, Sfikakis PP, Laskari K, Ragab G, Hegazy MT, et al. Musculoskeletal manifestations in children with Behçet's syndrome: data from the AIDA Network Behçet's Syndrome Registry. Intern Emerg Med 2023;18:743-54.
23. Yurtkuran, M, Yurtkuran M, Alp A, Sivriogl, K, Dilek K, Tamgaç F, et al. Hand involvement in Behçet's disease. Joint bone spine 2006;73:679–83.
24. Frikha F, Marzouk S, Kaddour N, Frigui M, Bahloul Z. Destructive arthritis in Behçet's disease: a report of eight cases and literature review. Int J Rheum Dis 2009;12: 250–5.
25. Özelçi R, Şahin Ö, Öztoprak İ, Hayta E, Kaptanoğlu E, Elden H. Determining the prevalence of sacroiliitis in Behçet's disease by magnetic resonance imaging. Cumhuriyet Med J 2010; 32: 298-302.
26. Hatemi G, Christensen R, Bang D, Bodaghi B, Celik A. F, Fortune F, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis 2018;77:808–18.
27. Hatemi G, Seyahi E, Fresko I, Talarico R, Uçar D, Hamuryudan V. Behçet's syndrome: one year in review. Clin Exp Rheumatol 2022;40:1461-71.
28. Alibaz-Oner F, Direskeneli H. Advances in the Treatment of Behcet's Disease. Curr Rheumatol Rep 2021; 20;23:47.
29. Esatoglu SN, Hatemi G. Update on the treatment of Behçet's syndrome. Intern Emerg Med 2019; 14:661-75.
30. Vitale A, Rigante D, Lopalco G, Emmi G, Bianco MT, Galeazzi M, et al. New therapeutic solutions for Behçet's syndrome. Expert Opin Investig Drugs 2016; 25:827-40.