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Sociodemographic and Clinical Characteristics of Patients with Behçet's Disease Followed Up in the Physical Therapy and Rehabilitation Department of a Tertiary Hospital

Üçüncü Basamak Bir Hastanenin Fizik Tedavi ve Rehabilitasyon Kliniği Tarafından Takip Edilen Behçet Hastalarının Sosyodemografik ve Klinik Özellikleri

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Abstract

Objective: Behçet's disease (BD) is a multisystemic inflammatory disease that causes significant morbidity worldwide. In this study, we aimed to evaluate the clinical and demographic characteristics of the patients with BD.
Materials and Methods: Patients admitted to our physical medicine and rehabilitation clinic between January 2015 and December 2018 were evaluated retrospectively. One hundred sixty patients who met the diagnostic criteria of the International Study Group for BD were included in the study. In addition to the patients' demographic characteristics, their clinical features, including age at onset, symptoms on initial admission, disease duration, systemic/organ involvement and medical treatments used, were recorded.
Results: The mean age of the 160 patients included in the study was 40.48±10.0 [minimum (min): 19, maximum (max): 72]. The mean age at disease onset was 30.54±8.46 (min: 14, max: 62). The most common involvement type in BD was mucocutaneous manifestations, and oral aphthae were the most common mucocutaneous symptom, with an occurrence rate of 100%. Regarding clinical manifestations, 36.3% (n=58) of patients showed ocular involvement, 16.9% (n=27) had vascular involvement and 15% (n=24) had musculoskeletal involvement. The rarest involvement was that of the genitourinary system, with a rate of 0.6% (n=1). Colchicine was the most commonly used therapeutic agent, whereas steroids, azathioprine, cyclosporine and various biologicals could also be used, depending on clinical status.
Conclusion: The results of our study suggest that, although the most common manifestation of BD is mucocutaneous involvement, the involvements of various systems, such as the ocular, musculoskeletal and neurological systems, are not rare and are associated with severe morbidity and mortality. Treatment modalities vary according to the systems and organs involved. Therefore, it is very important to systematically evaluate patients with BD and to arrange appropriate and effective treatment.
Keywords: Behçet's disease, ocular involvement, uveitis, oral aphthae, musculoskeletal involvement, epidemiology

Öz

Amaç: Behçet hastalığı (BH) dünyada önemli morbiditelere neden olan, multisistemik enflamatuvar bir hastalıktır. Bu çalışmada BH tanılı hastalarımızın klinik ve demografik özelliklerini incelemeyi amaçladık.
Gereç ve Yöntem: Ocak 2015-Aralık 2018 tarihleri arasında fiziksel tıp ve rehabilitasyon kliniğine başvuran hastaların kayıtları retrospektif olarak incelendi. Uluslararası Behçet Hastalığı Çalışma Grubu'nun tanı kriterlerini karşılayan 160 hasta çalışmaya dahil edildi. Hastaların demografik özelliklerine ek olarak hastalığın başlangıç yaşı, ilk başvuru yakınması, hastalık süresi, sistemik bulgular ve kullanılan medikal tedaviler de dahil olmak üzere klinik özellikler kayıt altına alındı.
Bulgular: Çalışmaya alınan 160 hastanın yaş ortalaması 40,48±10,0 [minimum (min): 19, maksimum (maks): 72] idi. Hastalığın ortalama başlangıç yaşı 30,54±8,46 (min: 14, maks: 62) olarak hesaplandı. Hastalığın en sık tuttuğu sistemlerin başında deri yer alırken; en sık deri bulgusu %100 ile oral aftlardı. Sırasıyla diğer en sık tutulum bölgeleri %36,3 (n=58) ile göz, %16,9 (n=27) ile vasküler yapılar ve %15 (n=24) ile eklemlerdi. En nadir tutulum %0,6 (n=1) ile genitoüriner sistemdi. Tedavide en sık kullanılan ajan kolşisin olup hastanın klinik durumuna göre steroidler, azatiopürin, siklosporin ve çeşitli biyolojik ilaçlar tedavide kullanılan farklı gruplardan ajanlardır.
Sonuç: Çalışmamızın sonuçları BH'nin en sık görülen tutulum şekli mukokütanöz tutulum olsa da; oküler, kas-iskelet sistemi ve nörolojik sistem tutulumu gibi ciddi morbidite ve mortalite ile ilişkili farklı tutulumların da nadir olmadığını göstermektedir. Tedavi, tutulan sistem ve organlara göre değişir. Bu nedenle, BH hastalarını sistematik olarak değerlendirmek ve uygun ve yeterli tedaviyi düzenlemek çok önemlidir.
Anahtar kelimeler: Behçet hastalığı, göz tutulumu, üveit, oral aft, kas iskelet sistemi tutulumu, epidemiyoloji

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Introduction

Behçet's disease (BD) is a multisystemic inflammatory disease characterized by recurrent oral aphthae (OAs), genital ulcers (GU), skin lesions, uveitis, joint involvement and vascular lesions. It was first described by a Turkish dermatologist, Hulusi Behçet, in 1937, with recurrent OAs, GU and hypopionic iridocyclitis triple symptom (1). The underlying pathology in BD is known to be vasculitis. However, the etiopathogenesis of the BD is still unclear. Central nervous system, genitourinary system (GUS), gastrointestinal system (GIS) and respiratory system involvements can also be seen in BD. Myocardial infarction, pericarditis and glomerulonephritis due to BD are rare. Therefore, BD is not only a serious cause of morbidity but also a serious cause of mortality. BD diagnosis is based on the diagnostic criteria of the International Study group for Behçet's Disease (ISGBD). According to ISGBD criteria; in addition to recurrent OAs that cannot be explained with any other clinical situation; at least two of the four findings (GU, ocular lesions, skin lesions and pathergy test positivity) are diagnosed as BD (2). Although BD is reported from different parts of the world, it is more common in the Mediterranean, the Middle East and the Far East regions. In epidemiological studies, Turkey is the most prevalent country for BD with 370-420/100,000 (3,4). Although BD starts more often at the age of 20-40 years, it can be seen in all ages, including childhood and old ages (5,6). Involvement types may vary in different societies and geographical regions. For example, gastrointestinal involvement was more frequent in Japanese and Americans (7); on the other hand pathergy positivity rather high in Turkey and Japan, it is low in western countries such as America and England (8). Neurological, ophthalmologic and pulmonary involvements of BD may cause severe complications that may result in complete loss of vision or even death. Therefore, the aim of this study is to determine the prototypic features of BD in our country retrospectively by evaluating the demographic and clinical characteristics of the patients with BD admitted to our clinic and to draw attention to possible morbidity and mortality risks of BD.

Materials and Methods

One hundred sixty patients diagnosed with BD according to ISGBD criteria (9) admitted to our outpatient clinic between January 2015 and December 2018 were included to this study. In accordance with the Declaration of Helsinki, ethics committee approval was obtained from the Clinical Studies Ethics Committee of Tokat Gaziosmanpaşa University Faculty of Medicine with protocol number 19.02.2019/19-KAEK-034.

The data of the patients were analyzed retrospectively from the electronic media files in the hospital automation system. Informed consent could not be obtained from the patients due to the retrospective design of the study. In addition to the demographic characteristics of the patients, clinical features including age at onset, initial admission symptom, disease duration, systemic findings and medical treatments used were recorded. Systemic involvement findings were evaluated as follows:

Mucocutaneous involvement: OAs, GU, papulopustular lesions, erythema nodosum, pathergy response.

Ocular involvement: Anterior uveitis, posterior uveitis, panuveitis, total loss of vision.

Musculoskeletal system involvement: Foot, knee, hip, elbow, shoulder, sacroiliac joint.

Vascular involvement: Systemic arterial, pulmonary vascular, venous occlusion, varices.

Neurological involvement: Seizure, paresthesia, hemiplegia/ hemiparesis, diplopia.

GIS involvement: Fistula/ulcer, portal venous thrombosis.

GUS involvement: Epididymitis, orchitis.

Cardiac involvement: Myocarditis, pericarditis, endocarditis.

Pulmonary involvement: Pleuritis, pulmonary parenchymal involvement, pulmonary vascular involvement.

Medical treatments: Colchicine, steroids, azothiopurine, cyclosporine, anti-tumor necrosis factor-alfa (anti TNF-α) agents were recorded.

Systemic examinations of the patients were performed by specialists of the related clinics (dermatology, ophthalmology, cardiovascular surgery, neurology, gastroenterology, cardiology). Iridocyclitis was evaluated as anterior uveitis; vitritis, retinitis and vasculitis were evaluated as posterior uveitis. Findings not related to BD were not recorded. The patients who were examined for musculoskeletal involvement were found to have arthritis with direct radiography, scintigraphy or magnetic resonance imaging (MRI). Doppler ultrasonography (USG), computed tomography (CT) or conventional angiography findings of the patients examined for vascular system involvement were accepted as involvement. Only the findings of CT, MRI, venography/ angiography and electroencephalography examinations of the patients who were examined for neurological involvement were considered to be related with BD. Echocardiography was used for the evaluation of cardiac involvement and direct X-ray and CT results were taken into consideration while pulmonary involvement was evaluated. Subjective complaints such as headache and dizziness were not evaluated. Only one patient with a complaint of GUS was evaluated in the relevant clinic diagnosed as epididymitis. USG, endoscopy and colonoscopy findings were taken into consideration while evaluating GIS involvement. The Pathergy skin test was performed under sterile conditions by a 20 gauge needle and evaluated by a dermatologist 48 hours later. The test was not administered to systemic drug users and the presence of papules or pustules was considered positive.

Statistical Analysis

Descriptive analyzes were used to give information about the general characteristics of the study groups. Data of continuous variables are in the form of mean ± standard deviation; data on categorical variables are given as n (%). When comparing the means of the quantitative variables between the groups,

the significance of the difference between two means test was used. Cross-tables and chi-square tests were used to evaluate whether there is a relationship between qualitative variables. P values less than 0.05 is considered to be statistically significant. In analyzes, computerized statistical software program "IBM SPSS Statistics 19" was used (IBM SPSS Statistics 19, SPSS inc., an IBM Co., Somers, NY).

Results

One hundred and sixty patients participated in our study and 59.4% (n=95) of the cases were female; 40.6% (n=65) were male. The mean age of the females was 40.54±10.57 [minimum (min): 19, maximum (max): 72], while the mean age of the males was 40.38±9.18 (min: 23, max: 60) (p=0.925). The distribution of ages at onset and at the time of admission; and the duration of the disease are shown in Table 1.

The most common involvement type was mucocutaneous manifestations in BD and OA was the most common mucocutaneous symptom with 100% of the patients. This is a normal result of the diagnostic criteria used in our study. Regarding clinical manifestations, 36.3% (n=58) of the patients showed ocular involvement, 16.9% (n=27) vascular involvement and 15% (n=24) musculoskeletal involvement.

The most rarely seen involvement is GUS with 0.6% (n=1). OA was present in 76.9% (n=123) of the patients. The second most common involvement type at admission was ocular involvement with 19.4% (n=31). The onset admission symptoms and age characteristics by gender are shown in Table 2. The characteristics of the patients by clinical involvements and used medical treatments are as follows:

Mucocutaneous involvement: Recurrent OAs was observed in all of the patients according to ISGBD criteria. Eighty-seven patients (54.4%) had recurrent GUs. Papulopustular lesions were seen in 67 patients (41.9%) and erythema nodosum was seen in 32 patients (20%). Pathergy test was positive in 24 (15%) patients.

Ocular involvement: Ocular involvement was detected in 58 patients (36.3%). Nineteen (11.8%) patients had isolated anterior uveitis and 39 (24.3%) had panuveitis. However, 9 (5.6%) patients had total loss of vision due to panuveitis.

Musculoskeletal system involvement: Joint involvement was detected in 24 patients (15%). The most commonly involved joints were ankle joint (15 patients, 9.37%), sacroiliac joint (12 patients, 7.5%), wrist joint (5 patients, 3.1%), knee joint (4 patients, 2.5%), elbow joint (3 patients, 1.9%) and hip joint (1 patient, 0.6%). In 16 (10%) patients with joint involvement, more than one joint was involved.

Vascular involvement: Twenty-seven patients (22.5%) had vascular involvement. Five patients (3.1%) had systemic arterial vasculitis. Two patients (1.3%) had pulmonary artery aneurysm, 12 patients had venous occlusion and 14 patients had varicose veins. The distribution of the cases with venous occlusion was in the form of deep vein thrombosis in 7 patients, superficial venous thrombosis in 2 patients and portal vein thrombosis in 3 patients. In addition, 6 patients with varicose veins also had a history of venous thrombosis. Vascular involvement was significantly higher in males (p=0.031).

Neurological involvement: There were 10 (6.3%) patients who were followed up as neuro-Behçet disease (NBD). Paresthesia was present in 7 patients (4.4%), hemiparesis in 2 patients (1.3%) and diplopia in 1 patient (0.6%). Headache was not evaluated as neurological involvement unless it was accompanied by other neurological examination findings and pathological imaging tests, but all patients followed up as NBD had headache.

GIS involvement: Three patients (1.9%) had Budd-Chiarri

Table 1. The distribution of ages at onset and at the time of admission; and the duration of the disease

	Mean ± standard deviation	Median [Min-Max]
Age at admission	40.48±10	39 [19-72]
Age at onset	30.54±8.46	29 [14-62]
Duration of the disease	9.78±5.65	8 [1-31]

Min: Minimum, Max: Maximum

Table 2. The onset admission symptoms and age characteristics by gender

	Gender		p
	Female	Male	
Onset admission symptoms			
Oral aphthae	79 (83.2)	44 (67.7)	0.145
Genital ulcers	1 (1.1)	0 (0)	
Ocular involvement	12 (12.6)	19 (29.2)	
Musculoskeletal involvement	1 (1.1)	1 (1.5)	
Neurological involvement	1 (1.1)	1 (1.5)	
Gastrointestinal system involvement	1 (1.1)	0 (0)	
Age at admission	40.54±10.57	40.38±9.18	0.925
Age at onset	31.27±8.82	29.46±7.84	0.184

For qualitative variables chi-square test and for quantitative variables the significance of the difference between two means test were used

syndrome due to portal venous thrombosis. Two patients (1.3%) had ileocecal ulcers.

GUS involvement: One patient (0.6%) was referred to the urology outpatient clinic because of scrotal pain. He was diagnosed as epididymitis by detailed examination and scrotal USG.

Cardiopulmonary involvement: Three patients (1.9%) had pericardial effusion and 2 (1.3%) patients had pleural effusion (see vascular involvement). All 3 patients with cardiac involvement were male.

Except vascular and cardiac involvement, there was no statistically significant difference in organ and system involvement by gender ($p>0.05$).

Medical treatments: Colchicine was the most commonly used treatment with 98.1%. Seventeen patients (10.6%) were taking steroids with colchicine treatment. There were 37 patients (23.1%) receiving azothiopurine (28 patients for ocular involvement, 4 patients for vascular involvement, 3 patients for neurological involvement, 1 patients for musculoskeletal system involvement, 1 patients for GIS involvement), 7 patients (4.4%) using cyclosporine A (all for ocular involvement), and 8 patients (5%) using anti-TNF agents. Of these 8 patients; 5 were using infliximab (3 for ocular involvement, 2 for neurological involvement), 2 were using adalimumab (for ocular involvement) and 1 were using etanercept (for musculoskeletal system involvement).

Discussion

This study presents the demographic and clinical characteristics of 160 patients diagnosed with BD over a 3-year period. Mucocutaneous manifestations are the most common symptoms in BD. As in our study, the only symptom seen in all patients was painful OAs with recurrent character. There are studies reporting that ethnicity and environmental factors change the prevalence and clinical manifestations of BD. BD may begin especially in the third decade and rarely in childhood (10).

The mean age at onset of the disease was 27.6±7.2 in males and 29.0±9.3 in females in the study of Soylu et al. (11). The mean age at onset of the disease was found to be 28.03±7.57 in Brazil, 35.52±9.25 in Greece and 33.2±10.2 in Korea (12-14). The mean age at onset of the patients included in our study was found to be 30.54±8.46 and was consistent with the literature. In the literature, there are some studies reporting that the disease starts at an earlier age in individuals with BD in their family (15). However, there was no regular information about family histories in the retrospective scanned files of the patients in our study group. Therefore, the relationship between family history and early onset of the BD could not be evaluated.

Mucocutaneous findings in BD are the most common onset admission symptom in many studies (10,16,17) and even the diagnostic criteria of ISGBD have identified OAs, one of the mucocutaneous findings, as a prerequisite for diagnosis (9). In our study, OAs were observed in all of our patients because patients were included in the study according to the diagnostic criteria of ISGBD.

In a study by Soylu et al. (11), GUs were detected in 82.8% of the patients, whereas 54.4% of the patients had GUs in our study. Pathergy test positivity has been reported by various researchers at different rates (16,17). In the study of Tursen et al. (16), Patergy positivity was 56.1%. In our study, Pathergy test was positive in 24 (15%) patients. Whether this is caused by test standardization or other factors, such as drug use, is unclear and requires further investigation.

Ocular involvement is one of the most important causes of morbidity in BD. In addition, ocular involvement is the second most common onset admission symptom after mucocutaneous manifestations (18). In general evaluation, the frequency of ocular involvement is around 50-68% in BD (18,19). When ocular controls are not performed regularly, some cases carry a risk of poor prognosis that may go up to total vision loss. In 31 (19.4%) of our cases, the onset admission symptom was ocular involvement, whereas the second most common involvement after mucocutaneous manifestations was ocular involvement in general, and 58 (36.3%) of the patients had ocular involvement. Nine (5.6%) of the patients had total loss of vision. Therefore, ocular involvement should be considered carefully and it is important to evaluate asymptomatic Behçet's patients for ocular involvement.

Vascular involvement is one of the poor prognostic factors in BD. The risk for other vascular complications increases after the first vascular manifestation. The prevalence varies between 5-40% in the literature. This difference may be due to different reasons such as the clinic in which the study was conducted or the ethnic origin of the patients participating in the study (20-24). In our study, vascular involvement was observed in twenty-seven patients (22.5%). It is also known that the prevalence of vascular involvement, which is the cause of serious morbidity and even mortality, is increased in the follow-up periods (20). For this reason, careful monitoring of vascular complications in patients with BD is necessary; provided that one who has experienced a vascular event once, more closely.

Although musculoskeletal problems in the form of arthritis or arthralgia are not included in the ISGBD criteria, it is a major finding in approximately half of the patients with BD (25). Articular involvement has been reported from 16% to 93% from different countries (26-28). Although BD tends to involve the large joints of the lower extremity, it may also involve the large joints of the upper extremity, the small joints of the hand and foot, and the sacroiliac joint (29,30). In our study, articular involvement was detected in 24 patients (15%) and our results are consistent with the literature. Although Behçet's arthritis is usually self-limiting, intermitant and non-erosive; it may rarely cause erosion in the joint (31). Articular involvement has been shown to have a negative effect on the quality of life (QoL) of the patient (32). In order to improve the QoL and to prevent the complications that may occur due to arthritis/arthralgia, it would

be appropriate to use different techniques such as scintigraphy and MRI in case of clinical suspicion.

NBD is a rare manifestation of BD associated with severe morbidity and mortality. One of the most serious organ involvement is NBD and the frequency was reported as 3-10% in large BD cohorts (33,34). In our study, there were 10 patients (6.3%) followed with NBD. Our results were consistent with the literature. Patients with NBD may present with different clinical findings such as venous thrombosis, intracranial vasculitic involvement and brain stem involvement. Bolek et al. (32) found that ocular involvement is also common in patients with NBD. In our study, 40% (n=4) of the patients with NBD also had ocular involvement. Therefore, to evaulate patients with ocular involvement in terms of presence of NBD and patients with NBD in terms of ocular involvement is important both for the regulation of appropriate treatment and for the prevention of possible comorbidities.

Epididymitis is common in BD. It is even considered one of the minor criteria of BD (35). In a study, epididymitis was detected in 17% of the patients with routine scrotal USG performed independently of complaints in BD (36). It is known that pain due to GUs and epididymitis can be confused with each other. In our study, urogenital examination was performed in only one patient due to pain and epididymitis was detected. In order to prevent urogenital comorbidity, routine urogenital examinations of the patients especially with GU may be useful.

GIS involvement is important because it is associated with serious morbidity and mortality in BD patients, and its prevalence has been reported in the literature at rates ranging from 2.8% to 60% (31,37-41). In our study, three patients (1.9%) had Budd-Chiari syndrome as a result of portal venous thrombosis and two patients (1.3%) had ileocecal ulcers. Our results are consistent with the literature showing gastrointestinal involvement rate in Turkey (16). Routine gastroenterological examination and endoscopic evaluations will contribute to the detection of subclinical involvement and accuracy of the data.

Cardiac involvement is a rare manifestation of BD but there are variable involvement types. Endocarditis, myocarditis, pericarditis, coronary arteritis and coronary artery aneurysms are some of the cardiac manifestations of BD (42). Also, pulmonary manifestations of BD are rare and can be summarized as follows: Pleuritis, pulmonary vasculitis, pulmonary fibrosis, pulmonary embolism and pulmonary infections (43). In our study, 3 patients (1.9%) had pericardial and 2 patients had pleural effusion (1.3%). Pulmonary artery aneurysm was also detected in two patients (1.3%).

The main goal of the treatment in BD is to achieve remission and improve the QoL of the patient. The clinical presentation and involved systems determine the basis of the treatment in BD. Comorbid conditions, involved organs, disease severity, age and sex of the patients are the main parameters to make a decision for treatment. Colchicine, steroidal and nonsteroidal anti-inflammatory agents, azathioprine, cyclosporine A, cyclophosphamide, biological agents and monoclonal therapies are among the main agents used in treatment (44). In our study, colchicine was the most commonly used agent in our patients with 98.1% while the number of the patients using anti TNF-α agents was 8 (5%). The frequency of organ involvement in BD may vary depending on the diagnostic criteria used in the study and the clinic in which the study was conducted (45). Therefore, the involvement rates of the systems show significant differences in different studies. In addition, it is clear that in prospective studies, different system involvements may be included to the patients' clinic during the follow-up periods.

Study Limitations

The main limitations of our study were that the retrospective design of the study did not allow us to evaluate the family history of the patients and the initial symptoms until the diagnosis. New multicentred and multidisciplinary researches will provide a better definition of the clinic of BD and will also contribute to the standardization of the parameters used in BD follow-ups.

Conclusion

The results of our study suggest that, although the most common manifestation of BD is mucocutaneous involvement, different involvements which are associated with severe morbidity and mortality, such as ocular, musculoskeletal and neurological systems are not rare. Treatment varies according to the involved systems and organs. Therefore, it is very important to systematically evaluate patients with BD and to arrange appropriate and adequate treatment.

New studies evaluating the immunopathogenesis, clinical characteristics and epidemiology of BD will contribute to many different subjects such as developing new laboratory tests, new diagnostic criteria, measuring disease activity and determining the best treatment methods.

Ethics

Ethics Committee Approval: In accordance with the Declaration of Helsinki, ethics committee approval was obtained from the Clinical Studies Ethics Committee of Tokat Gaziosmanpaşa University Faculty of Medicine with protocol number 19.02.2019/19-KAEK-034.

Informed Consent: Informed consent could not be obtained from the patients due to the retrospective design of the study.

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Authorship Contributions

Surgical and Medical Practices: N.Y., Concept: N.Y., O.D., Design: N.Y., O.D., Data Collection or Processing: N.Y., O.D., Analysis or Interpretation: N.Y., O.D., Literature Search: N.Y., O.D., Writing: N.Y., O.D.

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References

1. Behcet H. Uber rezidiverende, aphtose durch ein Virus verursachte Geschwure am Mund, am Auge, und den Genitalien. Dermat Wochensch 1937;105:1152-7.
2. Criteria for diagnosis of Behçet's disease. International Study Group for Behçet's Disease. Lancet 1990;335:1078-80.
3. Yurdakul S, Günaydin I, Tüzün Y, Tankurt N, Pazarli H, Ozyazgan Y, et al. The prevalence of Behçet's syndrome in a rural area in northern Turkey. J Rheumatol 1988;15:820-2.
4. Azizlerli G, Köse AA, Sarica R, Gül A, Tutkun IT, Kulaç M, et al. Prevalence of Behçet's disease in Istanbul, Turkey. Int J Dermatol 2003;42:803-6.
5. Yazici H, Fresko I, Yurdakul S. Behçet's syndrome: disease manifestations, management, and advances in treatment. Nat Clin Pract Rheumatol 2007;3:148-55.
6. Tsuyoshi S, Mitsuhiro T, Noboru S, Goro I. Behçet's disease. Journal Rheumatology 2002;12:134-6.
7. O'Neil TW, Rigby AS, McHugh S, Silman AJ, Barnes C. On behalf of the international study group for behçet's disease. Regional differences in clinical manifestations of Behçet's disease. Amsterdam: Elsevier; 1993. p. 159-63.
8. Kaklamani VG, Vaiopoulos G, Kaklamanis PG. Behçet's Disease. Semin Arthritis Rheum 1998;27:197-217.
9. 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.
10. Çirkinoğlu MS, Demir S, Bilginer Y, Özen S. Behçet's disease in children: single-center experience. Turk Pediatri Ars 2019;54:179-84.
11. Soylu M, Şekeroglu HT, Erdem E, Demircan N. Behçet's Disease: The Clinical and Demographic Characteristics of 406 Patients. Turk J Rheumatol 2012;27:115-20.
12. Sachetto Z, Mahayri N, Ferraz RH, Costallat LT, Bertolo MB. Behçet's disease in Brazilian patients: demographic and clinical features. Rheumatol Int 2012;32:2063-7.
13. Zouboulis CC, Vaiopoulos G, Marcomichelakis N, Palimeris G, Markidou I, Thouas B, et al. Onset signs, clinical course, prognosis, treatment and outcome of adult patients with Adamantiades-Behçet's disease in Greece. Clin Exp Rheumatol 2003;21(4 Suppl 30):19-26.
14. Bang DS, Oh SH, Lee KH, Lee ES, Lee SN. Influence of sex on patients with Behçet's disease in Korea. J Korean Med Sci 2003;18:231-5.
15. Karincaoglu Y, Borlu M, Toker SC, Akman A, Onder M, Gunasti S, et al. Demographic and clinical properties of juvenile-onset Behçet's disease: A controlled multicenter study. J Am Acad Dermatol 2008;58:579-84.
16. Tursen U, Gurler A, Boyvat A. Evaluation of clinical findings according to sex in 2313 Turkish patients with Behçet's disease. Int J Dermatol 2003;42:346-51.
17. Dogan B, Taskapan O, Harmanyeri Y. Prevalance of pathergy test positivity in Behçet's disease in Turkey. J Eur Acad Dermatol Venereol 2003;17:228-9.
18. Ozyazgan Y, Ucar D, Hatemi G, Yazici Y. Ocular Involvement of Behçet's Syndrome: a Comprehensive Review. Clin Rev Allergy Immunol 2015;49:298-306.
19. Özyazgan Y. Behçet Hastalığında Göz Tutulumu. Turkderm 2009;43(Özel Sayı 2):48-53.
20. Kural-Seyahi E, Fresko I, Seyahi N, Ozyazgan Y, Mat C, Hamuryudan V, et al. The long-term mortality and morbidity of Behçet syndrome: a 2-decade outcome survey of 387 patients followed at a dedicated center. Medicine (Baltimore) 2003;82:60-76.
21. Wu X, Li G, Huang X, Wang L, Liu W, Zhao Y, et al. Behçet's disease complicated with thrombosis: a report of 93 Chinese cases. Medicine (Baltimore) 2014;93:263.
22. Alibaz-Oner F, Karadeniz A, Ylmaz S, Balkarl A, Kimyon G, Yazc A, et al. Behçet disease with vascular involvement: effects of different therapeutic regimens on the incidence of new relapses. Medicine (Baltimore) 2015;94:494.
23. Saadoun D, Asli B, Wechsler B, Houman H, Geri G, Desseaux K, et al. Long-term outcome of arterial lesions in Behçet disease: a series of 101 patients. Medicine (Baltimore) 2012;91:18-24.
24. Sarica-Kucukoglu R, Akdag-Kose A, Kayaball M, Yazganoglu KD, Disci R, Erzengin D, et al. Vascular involvement in Behçet's disease: a retrospective analysis of 2319 cases. Int J Dermatol 2006;45:919-21.
25. Can M, Direskeneli H. Behçet hastalığında kas, iskelet sistemi ve damar tutulumu. Turkderm 2009;43:54-60.
26. Cheng YK, Thong BY, Chng HH. Behcet's disease: experience in a tertiary rheumatology centre in Singapore and a review of the literature. Ann Acad Med Singap 2004;33:510-4.
27. Gürler A, Boyvat A, Türsen U. Clinical manifestations of Behçet's disease: an analysis of 2147 patients. Yonsei Med J 1997;38:423-7.
28. Seaman G, Pearce RA. Behcet's Disease manifestation in a population drawn from the UK Behcet's Syndrome Society. In: Hamza M, editor. Behcet's Disease. 1st ed. Tunisia, CN: Pub Adhoua; 1997. p. 196-9.
29. Gur A, Sarac AJ, Burkan YK, Nas K, Cevik R. Arthropathy, quality of life, depression, and anxiety in Behcet's disease: relationship between arthritis and these factors. Clin Rheumatol 2006;25:524-31.
30. Cho SB, Lee JH, Ahn KJ, Bae BG, Kim T, Park YB, et al. Anti-cyclic citrullinated peptide antibodies and joint involvement in Behçet's disease. Yonsei Med J 2012;53:759-64.
31. Davatchi F, Shahram F, Chams-Davatchi C, Shams H, Nadji A, Akhlaghi M, et al. Behcet's disease: from East to West. Clin Rheumatol 2010;29:823-33.
32. Bolek EC, Sari A, Kilic L, Kalyoncu U, Kurne A, Oguz KK, et al. Clinical features and disease course of neurological involvement in Behcet's disease: HUVAC experience. Mult Scler Relat Disord 2020;38:101512.
33. Akman-Demir G, Ayranci O, Kurtuncu M, Vanli EN, Mutlu M, Tugal-Tutkun I. Cyclosporine for Behçet's uveitis: is it associated with an increased risk of neurological involvement? Clin Exp Rheumatol 2008;26(4 Suppl 50):84-90.
34. Davatchi F, Shahram F, Chams-Davatchi C, Shams H, Nadji A, Akhlaghi M, et al. Behcet's disease in Iran: analysis of 6500 cases. Int J Rheum Dis 2010;13:367-73.
35. Cho SB, Cho S, Bang D. New insights in the clinical understanding of Behçet's disease. Yonsei Med J 2012;53:35-42.
36. Yilmaz O, Yilmaz S, Kisacik B, Aydogdu M, Bozkurt Y, Erdem H, et al. Varicocele and epididymitis in Behcet disease. J Ultrasound Med 2011;30:909-13.
37. Ebert EC. Gastrointestinal manifestations of Behçet's disease. Dig Dis Sci 2009;54:201-7.
38. al-Dalaan AN, al Balaa SR, el Ramahi K, al-Kawi Z, Bohlega S, Bahabri S, et al. Behçet's disease in Saudi Arabia. J Rheumatol 1994;21:658-61.
39. Chen YC, Chang HW. Clinical characteristics of Behçet's disease in southern Taiwan. J Microbiol Immunol Infect 2001;34:207-10.
40. Wang LY, Zhao DB, Gu J, Dai SM. Clinical characteristics of Behçet's disease in China. Rheumatol Int 2010;30:1191-6.
41. Singal A, Chhabra N, Pandhi D, Rohatgi J. Behçet's disease in India: a dermatological perspective. Indian J Dermatol Venereol Leprol 2013;79:199-204.
42. Geri G, Wechsler B, Thi Huong DL, Isnard R, Piette JC, Amoura Z, et al. Spectrum of cardiac lesions in Behçet disease: a series of 52 patients and review of the literature. Medicine (Baltimore) 2012;91:25-34.
43. Davatchi F, Chams-Davatchi C, Shams H, Shahram F, Nadji A, Akhlaghi M, et al. Behcet's disease: epidemiology, clinical manifestations, and diagnosis. Expert Rev Clin Immunol 2017;13:57-65.
44. Saleh Z, Arayssi T. Update on the therapy of Behçet disease. Ther Adv Chronic Dis 2014;5:112-34.
45. Yücel A, Sönmezoğlu Marakli S, Aksungur VL, Uzun S, Sertdemir Y, Alpsoy E. Clinical evaluation of Behçet's disease: a five year follow-up study. J Dermatol 2005;32:365-70.