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THE CLINICAL FEATURES OF ARTHRITIS IN BEHÇET'S DISEASE

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Abstract

Aim: This study aims to explore the clinical, laboratory, and systemic differences between Behçet's disease (BD) patients with arthritis and those without, focusing on how arthritis influences disease progression and treatment strategies.

Material and Methods: A retrospective, observational study was conducted on 881 patients diagnosed with BD according to the International Study Group criteria. Patients were categorized into two groups: those with arthritis (n=233) and those without (n=648). Clinical findings, laboratory markers [C-reactive protein (CRP), erythrocyte sedimentation rate (ESR)], and systemic manifestations, including neurological and vascular complications, were compared between the groups. Statistical analyses were performed to identify significant differences.

Results: Patients with arthritis exhibited higher systemic inflammation, as evidenced by elevated ESR (37.6±23.9 vs. 31.1±23.9, p=0.000) and CRP (25.9±32.2 vs. 18.6±34.6, p=0.006) at baseline. Family history of BD was more prevalent in the arthritis group (15% vs. 10%, p=0.041). Neurological involvement was significantly higher in the non-arthritis group (11% vs. 4%, p=0.002), as were vascular complications, including: pulmonary artery aneurysms (2%, p=0.043) in the non-arthritis group and arterial thrombosis (5% vs. 1%, p=0.025). Patients with arthritis were more likely to receive corticosteroid therapy (36% vs. 21%, p=0.019), while pulse corticosteroid use was higher in the non-arthritis group (9% vs. 4%, p=0.008).

Conclusion: BD patients with arthritis demonstrate heightened systemic inflammation, a stronger genetic predisposition, and greater reliance on corticosteroids. In contrast, those without arthritis have higher rates of severe systemic complications, including neurological and vascular involvement. These findings emphasize the importance of individualized management strategies tailored to the presence or absence of arthritis, addressing the diverse clinical spectrum of BD.

Keywords: Behçet's disease, arthritis, systemic inflammation, vascular complications, neurological involvement, individualized management

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INTRODUCTION

Behçet's disease (BD) is a chronic, multisystem inflammatory disorder that typically presents with recurrent oral and genital ulcers, uveitis, and various systemic manifestations such as arthritis, neurological, vascular, and gastrointestinal involvement (1). First described by the Turkish dermatologist Hulusi Behçet in 1937, BD predominantly affects individuals from countries along the "Silk Road," such as Türkiye, Japan, and Iran. Despite extensive research, the exact pathogenesis of BD remains poorly understood, although both genetic predisposition and environmental factors are believed to play key roles in its development (2). The disease's heterogeneous nature, coupled with its multi-organ involvement, makes it a challenging condition to diagnose and treat. In the absence of a definitive diagnostic test, diagnosis is primarily clinical, and management involves a multidisciplinary approach to control inflammation and manage symptoms (3).

Arthritis is one of the most common manifestations of BD, affecting approximately 40% to 60% of patients (4). It is typically a non-deforming, inflammatory condition that can affect various joints, with the knee joint being the most frequently involved (5). However, not all BD patients experience arthritis, and its presence or absence may influence the disease's clinical course and treatment strategies. Several studies have shown that BD patients with arthritis tend to have higher levels of systemic inflammation, as measured by elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) (6). In addition, arthritis may be associated with other systemic complications, including vascular and neurological involvement, which may affect prognosis. Untreated ocular, vascular, nervous system, and gastrointestinal tract involvement may lead to serious damage and even death (7,8).

BD also presents with a range of other systemic manifestations, such as vascular complications, including arterial thrombosis and pulmonary artery aneurysms, which contribute significantly to morbidity and mortality in BD patients (9). Vascular involvement can be seen in 50% of patients with BD, mostly as superficial and deep vein thrombosis (10). Neurological involvement can occur in 5.3% to 59% of cases of BD and can cause serious complications such as central nervous system vasculitis and meningoencephalitis, which are associated with poor outcomes (11). Given the broad spectrum of organ involvement in BD, it is essential to understand how the presence or absence of arthritis impacts the severity and progression of these complications.

This study aims to compare the clinical features, laboratory findings, and systemic manifestations between BD patients with and without arthritis. By identifying potential differences between these two groups, the study seeks to enhance our understanding of how arthritis influences the course of BD, contributing to more personalized and effective management strategies. Understanding these differences could also improve early diagnosis and prognostic prediction for patients with BD.

MATERIAL AND METHODS

This retrospective, observational study was conducted at our Rheumatology Clinic between February 1, 2013, and December 31, 2023, and included 881 patients diagnosed with BD. The approval was obtained from the Ondokuz Mayıs University Local Ethics Committee (approval number: B30.2.OMD.0.20.08/488-536, dated: 14.11.2023) and was conducted in accordance with the tenets set forth in the Helsinki Declaration. Signed informed consent forms were obtained from the patients participating in the study. The study aimed to compare the clinical features, laboratory findings, and systemic manifestations between BD patients with arthritis and those without arthritis.

The inclusion criteria were patients aged 18 years and older who had a confirmed diagnosis of BD, as defined by the ISG criteria (12). Patients with other chronic inflammatory diseases or those with incomplete medical records were excluded from the study. A detailed review of patient medical records was performed, gathering demographic information, clinical findings, and laboratory results, including CRP, ESR, and other relevant markers. The presence of arthritis was determined by clinical examination and radiographic imaging. Patients were categorized into two groups: those with arthritis and those without arthritis.

Data on additional systemic manifestations, including neurological, vascular, and gastrointestinal involvement, were also collected. Family history of BD, corticosteroid use history, and current medications were recorded. The laboratory values of ESR and CRP were measured at baseline and after treatment, and comparisons were made between the two groups.

Statistical Analysis

Statistical analyses were performed using IBM Statistical Package for the Social Sciences for Windows Version 25.0. Descriptive statistics, such as means, standard deviations, and frequencies, were calculated for demographic and clinical characteristics. Comparisons between groups were made using independent t-tests for continuous variables and chi-square tests for categorical variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 881 BD patients were included in the study, consisting of 434 females (49%) and 447 males (51%). Of these, 233 (26.4%) patients had arthritis, while 648 (73.6%) did not. The mean age of

patients with arthritis was 41.7±11.5 years, while the mean age of patients without arthritis was 39.3±11.6 years. The average age at diagnosis was 31.3±9.7 years in the arthritis group and 30.3±9.9 years in the non-arthritis group (Table 1).

Significant differences were found between the two groups in terms of laboratory markers. The ESR was significantly higher in the arthritis group (37.6±23.9) compared to the non-arthritis group (31.1±23.9) (p<0.001). Similarly, the mean CRP level was higher in the arthritis group (25.9±32.2) than in the non-arthritis group (18.6±34.6) (p=0.006). However, after treatment, there were no significant differences in ESR or CRP levels between the groups.

Family history of BD was more prevalent in the arthritis group (15%) than in the non-arthritis group (10%) (p=0.041). Neurological involvement was significantly more common in the non-arthritis group, with 11% of patients in this group showing neurological manifestations, compared to only 4% in the arthritis group (p=0.002).

Vascular complications also showed significant differences between the groups. Pulmonary artery aneurysm was found only in the non-arthritis group (2%, p=0.043); and arterial thrombosis was more common in the non-arthritis group (5%) compared to the arthritis group (1%) (p=0.025).

Regarding medication use, corticosteroid therapy was more commonly used in the arthritis group, with 36% of patients currently using corticosteroids compared to 21% in the non-arthritis group (p=0.019). Pulse corticosteroid therapy, however, was more frequently used in the non-arthritis group (9% vs. 4%, p=0.008). There were no significant differences between the groups regarding the use of other immunosuppressive medications, such as colchicine, azathioprine, and methotrexate.

The most commonly affected joint in patients with arthritis was the knee, with 124 patients (53%) exhibiting knee involvement. Among these, 71 patients (30%) had unilateral knee involvement, and 53 patients (23%) had bilateral knee involvement. The least affected joint was the elbow, with only 14 patients (6%) reporting involvement (Table 2).

Table 1. Comparison of demographic characteristics, laboratory values and clinical features of cases with and without arthritis

	Arthritis present (n=233)	No arthritis (n=648)	p-value
Age (years)	41.7±11.5	39.3±11.6	0.007
Gender (female/male)	105/128 (45/55%)	329/319 (51/49%)	0.078
Age at diagnosis	31.3±9.7	30.3±9.9	0.167
ESR before treatment (mm/h)	37.6±23.9	31.1±23.9	0.000
ESR after treatment (mm/h)	23.5±18.4	23.4±18.0	0.960
CRP before treatment (mg/L)	25.9±32.2	18.6±34.6	0.006
CRP after treatment (mg/L)	7.7±12.3	7.2±13.6	0.646
Family history	34 (15%)	65 (10%)	0.041
Neurological involvement	9 (4%)	68 (11%)	0.002
Pulmonary artery aneurysm	0 (0%)	12 (2%)	0.043
Arterial thrombosis	3 (1%)	30 (5%)	0.025

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

Table 2. Locations of joints affected in cases of arthritis

Joint	No involvement	Unilateral involvement	Bilateral involvement
Knee	109 (47%)	71 (30%)	53 (23%)
Ankle	139 (60%)	43 (18%)	51 (22%)
Wrist	169 (72%)	32 (14%)	32 (14%)
Elbow	219 (94%)	7 (3%)	7 (3%)
Hip	211 (91%)	12 (5%)	10 (4%)
Sacroiliac	211 (91%)	22 (9%)	0
Hand joints	198 (85%)	35 15(%)	0

DISCUSSION

This study aimed to investigate the clinical and demographic differences between patients diagnosed with BD who presented with arthritis and those who did not. The results highlighted significant differences in several clinical aspects, such as age at diagnosis, laboratory values, family history, and the occurrence of specific complications, which are consistent with findings from previous studies on BD. These differences provide valuable insights into the disease's systemic manifestations and may guide clinical management.

One of the notable findings of this study was the slight difference in age between patients with arthritis and those without. The mean age of onset for arthritis was 31.3 years, which is consistent with earlier reports that suggest a delayed onset of arthritis in BD compared to other symptoms, such as, oral ulcers or ocular involvement (6). Previous studies have suggested that BD-associated arthritis tends to present later in the disease course, which may reflect a more advanced or aggressive disease state (12). This observation may prompt clinicians to monitor for arthritis as the disease progresses, particularly in those with early BD manifestations. In the study conducted in Greece, oligoarthritis was found in 20.0% and 41.6% of male and female patients, respectively, and a significant difference was found between the sexes (13). In our study, arthritis findings were detected in 27% of the patients, and no significant difference was found between male and female genders.

Regarding laboratory markers, sedimentation rate and CRP levels were higher in patients with arthritis, indicating a more pronounced inflammatory response, similar to the findings of Alibaz-Oner et al. (8). The significantly elevated sedimentation rate (37.6±23.9) and CRP levels (25.9±32.2) in patients with arthritis suggest that these individuals experience greater systemic inflammation, which aligns with previous reports that describe elevated inflammatory markers in BD patients with joint involvement (14).

However, the lack of significant difference in these markers after treatment highlights the effectiveness of current therapies in controlling systemic inflammation across both groups, as previously observed in studies on BD management (15).

The family history of BD was more prevalent in patients with arthritis (15%) than in those without (10%), a finding that is consistent with earlier research suggesting a genetic predisposition to more severe forms of BD, including the development of arthritis (16,17).

A family history has been linked to an increased risk of systemic manifestations in BD, such as arthritis, which may reflect the underlying genetic factors that contribute to both disease severity and the tendency to develop multisystem involvement (8). This suggests that family history could be a useful marker for predicting the risk of arthritis in BD patients, though further genetic studies are needed to better understand this relationship.

The study found that neurological complications were more common in patients without arthritis (11%) compared to those with arthritis (4%). This is in line with earlier studies that reported a higher prevalence of neurological involvement in BD patients without joint symptoms (18). Neurological manifestations, including central nervous system involvement, are considered to be one of the most severe complications of BD, and their higher frequency in patients without arthritis may reflect different disease mechanisms at play in those without joint involvement. Therefore, careful monitoring for neurological complications is crucial in all BD patients, particularly those with milder joint symptoms or those in the early stages of the disease.

The study also identified a significant difference in vascular complications between the two groups. Pulmonary artery aneurysm was found exclusively in the non-arthritis group, while arterial thrombosis was more common in the non-arthritis group. These findings corroborate previous studies, such as those by Baskar et al. (9), which suggested that vascular involvement, particularly arterial thrombosis and aneurysms, tends to be more prevalent in patients without arthritis. The underlying pathophysiological mechanisms of BD-related vascular complications are complex and multifactorial, but they might be more pronounced in patients with fewer joint involvement, suggesting different disease phenotypes. This highlights the need for careful vascular screening in BD patients, especially in those without arthritis.

In terms of corticosteroid use, the results demonstrated that patients with arthritis were more likely to be treated with corticosteroids (36%) compared to those without arthritis (21%). This finding is consistent with the clinical experience that arthritis in BD often requires more intensive treatment, potentially due to its impact on larger joints or its role in causing significant disability (19).

Conversely, pulse corticosteroid use was higher in the non-arthritis group (9% compared to 4%), which may reflect the acute flare of BD or involvement of other organ systems, as pulse steroids are often employed in cases of severe systemic involvement or vascular complications. The higher frequency of corticosteroid therapy in the arthritis group may indicate that joint involvement is a key determinant in treatment decisions, aligning with previous research on the therapeutic approach for BD patients with arthritis (20).

Finally, the use of other immunosuppressive medications, such as colchicine, azathioprine, and methotrexate, did not show

significant differences between the two groups. This suggests that the decision to initiate these therapies is likely driven by disease severity and multisystem involvement rather than the presence or absence of arthritis, as noted also in studies by Gül et al. (4). It is interesting to note that despite the lack of significant differences in drug use, the choice of therapy in BD often involves a multidisciplinary approach, tailored to the patient's individual needs, and clinical manifestations, including the presence of systemic involvement such as gastrointestinal or neurological issues.

Study Limitations

Limitations of this study include its retrospective design, which may introduce selection bias and limit causal inferences. The reliance on medical records may result in incomplete data, particularly for systemic manifestations. Additionally, the study was conducted at a single center, which may limit the generalizability of the findings. Future prospective, multicenter studies are needed to validate these results and explore the mechanisms underlying the observed differences.

CONCLUSION

In conclusion, this study provides important insights into the clinical differences between BD patients with and without arthritis. Patients with arthritis tended to exhibit higher systemic inflammation, a stronger family history, and more intensive corticosteroid use. In contrast, those without arthritis experienced more neurological and vascular complications, highlighting the diverse clinical spectrum of BD. These findings underscore the importance of individualized treatment strategies that consider both the systemic nature of BD and the presence or absence of specific manifestations such as arthritis.

Ethics

Ethics Committee Approval: The approval was obtained from the Ondokuz Mayıs University Local Ethics Committee (approval number: B30.2.OMD.0.20.08/488- 536, dated: 14.11.2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: C.K.K., M.Ö., D.Y.K., Ö.K., Concept: C.K.K., M.Ö., D.Y.K., Ö.K., Design: C.K.K., M.Ö., D.Y.K., Ö.K., Data Collection or Processing: C.K.K., M.Ö., D.Y.K., Ö.K., Analysis or Interpretation: C.K.K., M.Ö., D.Y.K., Ö.K., Writing: C.K.K., M.Ö., D.Y.K., Ö.K.

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