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Clinical and ophthalmological findings in patients with Behçet's uveitis at first presentation

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ABSTRACT

Aims: The present study attempted to demonstrate the clinical, demographic, and ophthalmological findings of patients with Behçet's disease (BD) at first admission and relevant treatment modalities.

Methods: We considered 161 eyes of 103 patients applying to the Uvea Unit of Ulucanlar Eye Training and Research Hospital between 2000-2012 and already suffering from BD or diagnosed with BD at their follow-ups. Then, we retrospectively investigated their clinical, demographic, and ophthalmological findings at first admission and the treatment modalities with the help of their medical records.

Results: There were 70 (68%) male and 33 (32%) female patients, and 17 patients (16.5%) initially presented with ocular symptoms. While the patients' mean diagnosis age was 26.79±9.24 years (4-61 years), it was 29.52±9.49 years (6-62 years) at the first eye attack. Eye involvement was bilateral in 58 patients (56.3%) and unilateral in 45 (43.7%). About half of the eyes (55.9%) were presented as panuveitis, 22.4% as posterior uveitis, 15.5% as anterior uveitis, and 6.2% as intermediate uveitis. While there were anterior chamber reaction + vitritis + retinitis and/or vasculitis (panuveitis) in 90 (55.9%) eyes, the others were characterized by isolated retinitis (12.4%) and isolated iridocyclitis (8.7%). Only two eyes (0.1%) had hypopyon at admission. We discovered at least one complication in 111 eyes (68.9%) at first admission. In particular, the most prevalent complication was found to be isolated macular edema in 45 eyes (28%) and isolated cataracts in 17 eyes (10.6%). On the other hand, topical steroid + systemic steroid + immunosuppressive (23.6%), topical + systemic steroid (16.8%), and systemic steroid + immunosuppressive (11.8%) became the most prevalently adopted medical treatments (with additions/alterations) at first admission, respectively.

Conclusion: In a nutshell, BD is considered a multisystemic condition with frequent ocular manifestations. BD-associated uveitis often presents as panuveitis. Thus, early and efficient treatment of ocular complications seems to be critical for better visual prognosis.

Keywords: Behçet's disease, first presentation, uveitis

INTRODUCTION

Affecting multiple organ systems, Behçet's Disease (BD) is a chronic condition first described in 1937, particularly seen in Mediterranean, Middle East, and Far East countries, the etiology of which has not been fully elucidated yet.[1] The previous research reported its prevalence to be 20-420/100,000 in Türkiye, 0.12-0.33/100,000 in the United States, and 0.64/100,000 in the United Kingdom.[2,3] As it can be diagnosed in the pediatric age group and older adults, it prevalently occurs among those aged 25-30 years. Moreover, males are predisposed to this disorder.[2]

The most apparent underlying pathology in BD may be the development of a vasculitis that affects the arterial and vein systems of all sizes (particularly veins) and causes occlusion and necrosis in these vessels, which, in turn, harms an entire organ system.[4,5] Despite affecting all organ systems, BD presents especially with oral and genital ulcerations, ocular inflammation, and skin lesions.[2]

A wide variety of ocular findings (e.g., episcleritis, scleritis, and extraocular muscle paralysis) are likely to be present in about 70% of BD patients, but its major presentation is uveitis with recurrent attacks.[4,6-9] It may be unilateral or bilateral and may harm the anterior and posterior segments of the eye (anterior uveitis, intermediate uveitis, posterior uveitis, panuveitis).[10-12]

The present research was to reveal the clinical and demographic characteristics and complications of patients with known BD or diagnosed with BD after an attack of uveitis, the treatment modalities, and their accompanying systemic characteristics and to explore the interactions between these variables.

METHODS

This study was produced from the thesis, ethics committee approval is not required at that tim. Institutional approval has been obtained. We retrospectively investigated the medical records of 103 patients applying to the Uvea Unit of Ulucanlar Eye Training and Research Hospital between 2000-2012 and already suffering from BD or diagnosed with BD at their follow-ups. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

We retrospectively investigated the medical records of 103 patients applying to the Uvea Unit of Ulucanlar Eye Training and Research Hospital between 2000-2012 and already suffering from BD or diagnosed with BD at their follow-ups. In this regard, we included and classified 161 eyes of these patients based on the criteria proposed by the Standardization of Uveitis Nomenclature (SUN) working group.[13] The study was carried out in accordance with the Helsinki declaration. Due to the retrospective nature of the study, we did not obtain patient consent. The patients were diagnosed with Ocular BD based on the criteria offered by the International Study Group for Behçet's Disease and the findings consistent with the disease (e.g., diffuse vitritis, non-granulomatous pattern, retinal vasculitis, retinal vascular occlusion).[14] When necessary, a multidisciplinary approach was adopted with rheumatology, dermatology, and other relevant departments.

The patients' demographic characteristics (age, sex), anterior and dilated posterior segment examinations, first best corrected visual acuity (BCVA), intraocular pressure (with applanation tonometry), advanced complications, pre- and post-admission treatments, family history, extraocular findings, age at the first eye attack and pathergy results were recorded at their first admission. Visual acuity was measured with the Snellen chart and corrected according to LogMAR (logarithm of the minimum angle of resolution). High intraocular pressure was evaluated as a measurement over 21 mmHg by applanation tonometry. Besides, azathioprine, cyclosporine, and mycophenolate mofetil were grouped as immunosuppressive drugs. Finally, Optical Coherence Tomography (OCT) and Fundus Fluorescein Angiography (FFA) were performed on all patients.

This article was produced from the specialty thesis titled Clinical and Ophthalmological Findings at First Admission in Patients with Behçet's Uveitis in 2012.

Statistical Analysis

We tested the normality of the data distribution with the Kolmogorov-Smirnov test. While normally-distributed continıus data are shown as means and standard deviations, categorical data are presented as numbers and percentages. We compared the categorical data using the chi-square test (Yates continuity corrected chi-square test and Fisher's exact test). Besides, we utilized Welch's ANOVA to make comparisons of continuous data due to the heterogeneous variances. All statistical analyses were performed on the SPSS 16.0 (Statistical Package for Social Sciences) program, and a p-value of < 0.05 was accepted as statistically significant.

RESULTS

There were 70 (68%) male and 33 (32%) female patients, and 17 patients (16.5%) initially presented with ocular symptoms. While the patients' mean age at the diagnosis of BD was 26.79±9.24 years (4-61 years), it was 29.52±9.49 years (6-62 years) at the first attack. While the mean age at diagnosis and the first eye attack were found to be 27.36±12.43 years (4-61 years) and 30.63±12.20 years (6-62 years) for females, these values became 26.51±7.35 years (10-42 years) and 29.0±7.95 years (13-50 years) for males, respectively. The patients had their first eye attack an average of 2.74±9.36 years after the diagnosis. In this regard, the mean time from diagnosis to the first eye attack was found to be 2.49±7.65 years for males and 3.27±12.30 for females. However, we could not conclude a significant difference between the age at diagnosis and the age of the first attack for both males and females (p=0.718 and 0.486, respectively). Besides, eye involvement was discovered to be bilateral in 58 patients (56.3%) and unilateral in 45 patients (43.7%). Behçet's uveitis was observed bilaterally in 51.5% of the females and 58.5% of the male patients. Yet, there was no statistically significant difference in laterality by sex (p=0.563) (**Table 1**). Thrity-six eyes (22.4%) had a LogMAR of > 1, 48 (29.8%) had a LogMAR of 0.4-1, and 77 (47.8%) had a LogMAR of < 0.4.

Table 1: Patients' Demographic and Clinical Characteristics

	Female	Male
Number (n)	33 (32%)	70 (68%)
Age of diagnosis	27.36±12.43 years (4-61)	26.51±7.35 years (10-42)
Age of the first eye attack	30.63±12.20 years (6-62)	29.0±7.95 (13-50 years)
Time between the diagnosis and the first attack	3.27±12.30 years	2.49±7.65 years
Laterality		
Unilateral	48.5%	41.5%
Bilateral	51.5%	58.5%

About half of the eyes (55.9%) presented as panuveitis, 22.4% as posterior uveitis, 15.5% as anterior uveitis, and 6.2% as intermediate uveitis. Panuveitis was the significantly most prevalent presentation in both males and females (p=0.001). The exact rates were found to be 36% among females and 64.9% among males (**Table 2**).

Table 2: Uveitic Presentation by Sex

Anatomical Location	Females (50 eyes)	Males (111 eyes)
Anterior	15 (30%)	10 (9%)
Intermediate	4 (8%)	6 (5.4%)
Posterior	13 (26%)	23 (20.7%)
Panuveitis	18 (36%)	72 (64.9%)

Among the patients, the mean age of the first eye attack was 26.88±10.70 years (6-44 years) for those with anterior uveitis, 38.5±12.57 years (25-53 years) for those with intermediate uveitis, 28.17±7.11 years (13-42 years) for those with posterior uveitis, and 29.66±9.18 years (6-62 years) for those with panuveitis. However, we could conclude no significant difference between the mentioned ages by anatomical localization of BD (p=0.082).

While most of the uveitis in all localizations (72% of intermediate uveitis, 60% of intermediate uveitis, 55.6% of posterior uveitis, and 80% of panuveitis) were bilateral, 62.1% of bilateral and 40% of unilateral cases were panuveitis. In this sense, panuveitis had a statistically significant bilateral course (p=0.038).

While there were anterior chamber reaction + vitritis + retinitis and/or vasculitis (panuveitis) in 90 (55.9%) eyes, the others were characterized by isolated retinitis (12.4%) and isolated iridocyclitis (8.7%). Only two eyes (0.1%) had hypopyon at admission (**Table 3**).

We discovered at least one complication in 111 eyes (68.9%) at first admission. In particular, the most prevalent complication was found to be isolated macular edema in 45 eyes (28%) and isolated cataracts in 17 eyes (10.6%) (**Table 4**). There was panuveitis in 65.8% of the eyes with complications, posterior uveitis in 26.1%, anterior uveitis in 7.2%, and intermediate uveitis in 0.9%. The probability of developing complications at first admission was significantly higher in the eyes with panuveitis compared to those with other anatomical involvements (p<0.001).

Table 3: Ocular Findings at First Presentation

Clinical Findings	Eyes (n)
Anterior chamber reaction + Vitritis + Retinitis and/or Vasculitis (Panuveitis)	90 (55.9%)
Retinitis	20 (12.4%)
Iridocyclitis	14 (8.7%)
Iridocyclitis + Vitritis	11 (6.8%)
Vitritis	10 (6.2%)
Vitritis + Retinitis	9 (5.6%)
Vasculitis	7 (4.3%)

Table 4: Complications at First Presentation

Complications	Eyes (n)
N/A	50 (31.1%)
Macular Edema	45 (28%)
Cataract	17 (10.6%)
Posterior synechiae	12 (7.5%)
Macular Edema + Papilledema	8 (5%)
Retinal Vein Occlusion	8 (5%)
Papilledema	5 (3.1%)
Retinal Hemorrhage	5 (3.1%)
Vitreous Hemorrhage	4 (2.5%)
Papillitis	2 (1.2%)
Cataract + Macular Edema	2 (1.2%)
Glaucoma + Macular Edema	1 (0.6%)
Papilledema + Vitreous Hemorrhage	1 (0.6%)
Optic Atrophy	1 (0.6%)

Before admission to our hospital, 72 of 161 eyes had received or were receiving one or more medical treatments. The following treatment modalities had been or were being applied for them: colchicine (20.5%), topical steroid (6.8%), and colchicine plus topical and systemic steroid treatment (4.3%). On the other hand, topical steroid + systemic steroid + immunosuppressive (23.6%), topical + systemic steroid (16.8%), and systemic steroid + immunosuppressive (11.8%) became the most prevalently adopted medical treatments (with additions/alterations) at first admission, respectively. (**Table 5**). However, no patient was taken for surgery at first admission. Before admission, phacoemulsification + intraocular lens implantation was performed in 7 eyes (4.3%), while one patient (0.6%) underwent phacoemulsification + intraocular lens implantation + vitreoretinal surgery due to vitreous hemorrhage.

Among 63 patients with a known pathergy test result, 28 (44.4%) were pathergy positive. We discovered panuveitis in 67.9% of them, anterior uveitis in 21.4%, and posterior uveitis in 10.4%. Thus, pathergy positivity was found to be significantly higher in patients with panuveitis (p=0.036). Besides, as the initial sign of BD, 76.7% of the patients suffered from oral aphthae, 16.5% from ocular involvement, and 5.8% from genital ulcer (**Table 6**). Almost all patients (94.2%) had a history of at least one oral aphthae. In addition, 8 patients (7.8%) had a family history of BD; interestingly, all these patients were males (11.4%). Nevertheless, the family history of BD did not significantly differ by sex (p=0.052). While there was a family history of BD in 2 patients with anterior uveitis (12.5%), 4 patients with panuveitis (7.5%), and 2 patients with posterior uveitis (7.4%), it was not the case for the patients with intermediate uveitis. The findings yielded no difference in the anatomical localization of the uveitis by family history of BD (p=0.875).

Table 5: Treatment Modalities Used in Behçet's Disease Associated Uveitis

Treatment Modality	Medical Treatments at Preadmission	Medical Treatments at First Admission
N/A	55.3%	3.1%
Colchicine	20.5%	
Topical Steroid	6.8%	7.5%
Colchicine + Topical Steroid + Systemic Steroid	4.3%	-
Topical Steroid + Retrobulbar Steroid + Systemic Steroid + Immunosuppressive	3.1%	-
Colchicine + Immunosuppressive	2.5%	3.1%
Immunosuppressive	2.5%	8.1%
Topical Steroid + Systemic Steroid	1.9%	16.8%
Topical Steroid + Intravitreal Steroid + Systemic Steroid	1.9%	-
Colchicine + Topical Steroid	1.2%	-
Topical Steroid + Systemic Steroid + Immunosuppressive	-	23.6%
Systemic Steroid + Immunosuppressive	-	11.8%
Retrobulbar Steroid	-	6.8%
Topical Steroid + Retrobulbar Steroid + Systemic Steroid	-	6.8%
Retrobulbar Steroid + Immunosuppressive	-	3.7%
Systemic Steroid	-	2.5%
Colchicine + Topical Steroid	-	2.5%
Topical Steroid + Immunosuppressive	-	2.5%
Colchicine + Systemic Steroid + Immunosuppressive	-	0.6%
Retrobulbar Steroid + Systemic Steroid + Immunosuppressive	-	0.6%

Table 6: Behçet's Disease First Symptom

Symptom	n
Oral Aphthae	79 (76.7%)
Eye Finding	17 (16.5%)
Genital Aphthae	6 (5.8%)
Skin Finding	1 (1%)

DISCUSSION

BD is a systemic condition that affects the eyes rather prevalently and may result in permanent vision loss.[15] The emergence of systemic symptoms of the disease is often followed by uveitis within a few years in 10% to 20% of the patients and an average of four years in 60% to 80%.[2,4,16] BD-related uveitis often appears in the late 20s and early 30s.[2,10,17,18] Despite research reporting males' predisposition to BD, the literature also hosts a study indicating no significant sex-associated difference in the condition. Yet, the mentioned research also noted that the sex-related insignificance might depend on the sample size.[2,10,18] In this study, we found that

the mean age of the first diagnosis was 26.79±9.24 years and that the first eye attack occurred 2.74±9.36 years after diagnosis. Our findings overlap with the previous results in the literature. In general, 20% of BD patients first present with ocular inflammation.[19,20] We found that 16.5% of the patients first applied to our clinic with ocular findings and were diagnosed with BD.

While BD-associated uveitis often presents as bilateral and panuveitis, there are also presentations as unilateral and as anterior and intermediate uveitis.[10,15,21,22] In our study, 56.3% of the patients had bilateral uveitis. Despite the predominance of panuveitis, we discovered the presence of all uveitis presentations in our research. Moreover, we found that panuveitis was significantly bilateral (p=0.038) and was significantly higher in both males and females (p=0.001).

Typical ocular manifestations of BD are non-granulomatous panuveitis and retinal vasculitis.[23] Krause et al.[24] reported the most prevalent first ocular finding to be panuveitis (67.8%), followed by retinal vasculitis (16.0%) and iridocyclitis (13.9) and found hypopyon (0.7%) to be rare as a manifestation. Similarly, we discovered that the most prevalent finding at first admission was panuveitis (55.9%) and that iridocyclitis with hypopyon was present in only two eyes (0.1%) as an initial finding.

Macular edema, cataract, posterior synechia, and glaucoma are known to be the leading complications in BD-related uveitis that may cause reversible or permanent vision loss.[10,17,24] In this study, 111 eyes (68.9%) had at least one complication, and the most prevalent complication was found to be isolated macular edema in 45 eyes (28%), isolated cataract in 17 eyes (10.6%), and posterior synechia in 12 eyes (7.5%), overlapping with the literature. In addition, we found that the probability of complication development at first admission was significantly higher in eyes with panuveitis than those with other anatomical involvements, which may be because panuveitis affects all uveal regions, increasing the possibility of complications in all segments of the eye. On the other hand, we discovered glaucoma in only one patient, possibly because we considered the data at the time of admission but excluded follow-up data. We estimate that glaucoma may be more prevalent during follow-ups, depending on the nature of the disease and the steroid treatments used.

Steroid preparations (topical, periocular, and systemic), immunosuppressive agents, and biological agents are adopted in the treatment of BD-associated uveitis. Despite the robust efficacy of colchicine in skin lesions and joint inflammation, it has no significant effect in patients with uveitis. Thus, steroid preparations may be adopted as a primary treatment modality to suppress immediate inflammation. While steroid preparations can be applied topically in isolated anterior uveitis, periocular therapy can be preferred to systemic treatment in cases affecting the unilateral posterior segment. In addition, intravitreal steroid treatment in patients with treatment-resistant macular edema assists systemic treatment in suppressing inflammation and inhibiting macular edema. Immunosuppressive agents can be utilized in cases where the condition cannot be suppressed by steroid therapy due to their properties, such as reducing steroid-related side effects and helping early systemic immunosuppression. Biological agents are switched as a second step in refractory cases.[15] In our study, we uncovered that only retrobulbar steroid was administered to 11 eyes (6.8%) at first admission, but none of the patients received intravitreal steroid therapy at admission. Topical steroid + systemic steroid + immunosuppressive (23.6%), topical + systemic steroid (16.8%), and systemic steroid + immunosuppressive (11.8%) became the most prevalently adopted medical treatments (with additions/alterations) at first admission, respectively.

Some previous studies indicated that the history of oral aphthous ulcerations may reach 100% in patients with BD-associated uveitis.[10,22] We found this rate to be 94.2% in our study, which may be due to the inability of the patients to understand or remember the lesions described or the absence of ulcerations.

Limitations

Since the present study was performed retrospectively in a branch hospital and did not include follow-up data, it cannot offer information about visual prognosis, follow-up complications, and alterations in treatment modalities.

CONCLUSION

In a nutshell, BD is considered a multisystemic condition with frequent ocular manifestations. Although it is often presented as panuveitis, it can appear with a wide variety of ocular presentations, even with ocular findings at first admission. Thus, early and efficient treatment of ocular complications seems critical for better visual prognosis. A timely transition to immunosuppressive therapy - when needed - may be an effective method to alleviate steroid-related side effects and control inflammation.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was produced from the thesis, ethics committee approval is not required.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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