IJCMBS

Original Article

doi.org/ 10.5281/zenodo.17686124 JCMBS 2025; 5(3):136-141

Ocular Findings and Fundus Fluorescein Angiography Characteristics in Ocular Behçet's Disease

Oküler Behçet Hastalığında Oküler Bulgular ve Fundus Florescein Anjiyografi Özellikleri

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Abstract

Background: To evaluate ocular findings and the characteristics of fundus fluorescein angiography (FFA) in ocular Behçet's disease (OBD).

Material and Methods: A retrospective study was conducted on 104 patients (208 eyes) with OBD who were seen in our ophthalmology clinic between 1996 and 2006. The diagnosis of all patients was made according to the criteria of the International Study Group for Behçet's Disease. All patients underwent FFA. Information on the patients' gender, age, disease duration, ocular findings, FFA findings, ocular complications, and visual acuity were collected.

Results: The mean age of the patients included in the study was 32.54±9.45 (19-48) years. Of the total cases, 57 (54.8%) were male and 47 (45.2%) were female. Ocular involvement was bilateral in 73.1% and unilateral in 26.9% of the cases. The most common ocular finding was panuveitis, observed in 54.4% of the cases. The most frequent FFA finding was optic disc leakage, observed in 81.1% of the cases. The rate of anterior uveitis was 12.7%, while the rate of posterior uveitis was 32%. The proportion of eyes with a visual acuity of 0.5 or higher was 67.2%, those with a visual acuity between 0.5 and 0.1 were 21.1%, and those with a visual acuity of 0.1 or lower were 11.6%.

Conclusions: In OBD, the most frequent ocular finding is panuveitis, and the most common FFA finding is leakage from the optic disc. FFA plays a significant role in the diagnosis and follow-up of retinal complications in OBD.

Keywords: Fundus fluorescein angiography, Ocular Behçet's Disease, Uveitis.

ÖZ

Amaç: Oküler Behçet Hastalığında (OBH) göz bulgularını ve fundus floresein anjiyografinin (FFA) özelliklerini değerlendirmek.

Gereç ve Yöntem: 1996-2006 yılları arasında göz kliniğimizde OBD tanısıyla izlenen 104 hasta (208 göz) üzerinde retrospektif bir çalışma yürütüldü. Tüm hastaların tanısı Uluslararası Behçet Hastalığı Çalışma Grubu kriterlerine göre konuldu. Tüm hastalara FFA uygulandı. Hastaların cinsiyeti, yaşı, hastalık süresi, oküler bulgular, FFA bulguları, oküler komplikasyonlar ve görme keskinliği bilgileri toplandı.

Bulgular: Çalışmaya dahil edilen hastaların ortalama yaşı 32.54 ± 9.45 (19-48) yıldı. Toplam olguların 57'si (%5.8) erkek, 47'si (%4.2) kadındı. Oküler tutulum olguların %73,1'inde bilateral, %26,9'unda ise unilateraldi. En sık görülen oküler bulgu %54,4 ile panüveitti. En sık görülen FFA bulgusu ise %81.1 ile optik disk kaçağıydı. Ön üveit oranı %12,7 iken, arka üveit oranı %32 idi. Görme keskinliği 0.5 veya daha yüksek olan gözlerin oranı %67.2, görme keskinliği 0.5 ile 0.1 arasında olanların oranı %21.1 ve görme keskinliği 0.1 veya daha düşük olanların oranı %11.6 idi.

Sonuç: OBH'nda en sık görülen oküler bulgu panüveit, en sık görülen FFA bulgusu ise optik disk kaçağıdır. FFA, OBH'ndaki retinal komplikasyonların tanı ve takibinde önemli rol oynar.

Anahtar kelimeler: Fundus fluorescein anjiyografisi, Oküler Behçet Hastalığı, Üveit.

Highlights

- Detection of ocular findings in ocular Behçet's disease is important in the follow-up and treatment of the disease.
- Fundus fluorescein angiography has an important role in the evaluation of retinal findings in ocular Behçet's disease.

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Received: 27 March 2025 **Accepted:** 29 September 2025

***Cite as*:** Atalay Ozmen. O et al. Ocular Findings and Fundus Fluorescein Angiography Characteristics in Ocular Behçet's Disease JCMBS 2025; 5(3):136-141 doi.org/ 10.5281/zenodo.17686124

Introduction

Behçet's disease (BD) is a chronic, multisystemic inflammatory disorder characterized by oral and genital ulcers, intraocular inflammation, and specific skin lesions. Less commonly, it can also involve the joints, gastrointestinal system, and nervous system. The disease follows a geographical distribution along the ancient Silk Road, extending from Japan to the Mediterranean region, with the highest incidence observed in Türkiye (1). BD typically begins in the second and third decades of life and, with decreasing disease activity in later years, follows a pattern of remission and relapse (2). The course and severity of the disease vary from person to person (2). While the exact etiology of BD remains unclear, it is generally accepted that in genetically predisposed individuals, environmental factors trigger an irregular immune response that leads to vascular damage in most organ systems (3).

The common histopathological lesion in all organ systems affected by BD is occlusive vasculitis. The primary pathological findings of the disease include the accumulation of lymphomononuclear cells around blood vessels, swelling or proliferation of endothelial cells, partial occlusion of small vessels, and fibrinoid degeneration (4). Due to the wide clinical spectrum of the disease, the lack of a laboratory method that can definitively establish the diagnosis, and sometimes the absence of typical clinical features or the involvement of multiple organ systems, diagnosing BD can be challenging. Studies conducted in countries along the Silk Road have shown a marked association with HLA-B51 positivity in Behçet's patients, while no such association is observed in Western countries (5). Fluorescein angiography (FFA) in BD with posterior segment involvement can reveal dye leakage from retinal arteries, veins, and capillaries, providing valuable information about the retinal vascular system. FFA is essential for identifying primary retinal inflammation and for detecting abnormalities such as dye leakage from retinal vessels secondary to uveitis, retinal vein branch occlusion (RVO), retinal ischemia, neovascularization, macular edema, and macular ischemia (6).

Ocular Behçet's disease (OBD) is typically characterized by bilateral non-granulomatous panuveitis and retinal vasculitis, with isolated anterior uveitis and unilateral involvement being rare (7). Recurrent posterior uveitis attacks can lead to irreversible damage in the posterior segment and permanent vision loss (8). Retinal vasculitis is a major cause of vision loss in OBD (9). Recurrent retinal vasculitis attacks can lead to permanent sequelae. Secondary to occlusive vasculitis, RVO and, rarely, central retinal artery and vein occlusions can occur (9). In males and young adults, involvement is more frequent, and the disease course is more severe, whereas in females and older individuals, involvement is less frequent, and the disease course is milder (5). In the advanced stages of the disease, there may be increased tortuosity of retinal vessels, retinal ischemia, and consequently optic disc neovascularization (NVD), retinal neovascularization (NVE), macular edema, and diffuse retinal edema (4).

In our study, we aimed to identify ocular findings associated with OBD, their frequency, and the characteristics of FFA.

Material and Methods

Study design

The data of 104 patients diagnosed with OBD and followed up at our clinic between January 1996 and December 2006 were retrospectively reviewed. Patients with systemic diseases such as diabetes mellitus, hypertension, coronary heart disease, other rheumatologic diseases, and pregnancy, as well as those with ocular conditions such as corneal scarring, corneal dystrophy, glaucoma, diabetic retinopathy, and age-related macular degeneration, were excluded from the study. Patients with unknown follow-up durations and incomplete data were also excluded. A detailed medical history was taken from each patient. Best-corrected visual acuity was measured using the Snellen chart, and intraocular pressures were measured with a Goldman applanation tonometer. Anterior segment examinations were performed using slit-lamp biomicroscopy, and fundus examinations were conducted with a 90 diopter lens. The patients' ages and genders were recorded. Cases with iridocyclitis were classified as anterior uveitis, while cases with vitritis, retinal vasculitis, and retinitis without iridocyclitis were classified as posterior uveitis. Cases with involvement of both anterior and posterior segments were classified as panuveitis. The follow-up durations were recorded in months. The diagnostic criteria for ocular Behçet’s disease were evaluated according to the 2014 International Criteria for Behçet’s Disease (ICBD). The diagnostic criteria and scoring system included: ocular

involvement (2 points), anterior/posterior uveitis, retinal vasculitis, chorioretinitis, papilledema (presence of any of these findings), oral aphthous lesions (2 points), recurrent oral aphthous ulcers at least three times per year, genital ulcers (2 points), recurrent genital aphthous lesions, cutaneous findings (1 point), papulopustular lesions, erythema nodosum-like eruptions, neurological involvement (1 point), parenchymal central nervous system involvement, venous sinus thrombosis, vascular manifestations (1 point), venous thromboembolism, superficial thrombophlebitis, arterial thrombosis, aortic and pulmonary aneurysms, and a positive pathergy test (1 point). Diagnosis is confirmed for cases with a total score of 4 or more (ocular involvement was a prerequisite). This scoring system is based on the results of a multicenter study involving 27 countries, which demonstrates high sensitivity and specificity (10). During each follow-up visit, FFA (Zeiss FF 450 / Visupac) was performed on all patients. In FFA, increased hyperfluorescence in the late phase at the optic disc (OD) was defined as OD leakage. Retinal vasculitis was defined by leakage, staining, and occlusion in retinal vessels. Retinitis was defined as inflammation in the retina. OD edema was identified by hyperfluorescent appearance at the OD in FFA. Macular edema was defined by increased hyperfluorescence in the macula on FFA. New vessel formation at the optic disc was described as NVD, and new vessel formation in the retina was described as NVE. RVO was defined by localized hemorrhage in the retina. Central retinal artery occlusion (CRAO) was defined by the typical "Japanese flag" appearance in the macula and non-perfusion.

Statistical analysis

Statistical evaluations of the study were performed using SPSS 22.0 software. The normality of distribution was assessed using the Kolmogorov-Smirnov test. Categorical variables were presented as frequencies and percentages. Measurable data that met the parametric conditions were expressed as mean ± standard deviation.

Ethical Approval

This study approval was obtained from the Uludag University Faculty of Medicine, Ethics Committee (number: session: 17/2007 decision no: 12 date: 23.10.2007). This study was conducted retrospectively. Therefore, no consent form was obtained. All procedures were carried out in accordance with the Declaration of Helsinki.

Results

A total of 104 patients (208 eyes) diagnosed with OBD were included in the study. Of these patients, 57 (54.8%) were male and 47 (45.2%) were female. The mean age was 32.54±9.45 years (ranging from 15 to 64 years). Ocular involvement was detected in 180 eyes (86.53%) of the 104 patients (208 eyes) diagnosed with OBD. Demographic characteristics and baseline characteristics are presented in Table 1.

Table 1. Demographic Characteristics and Key Features

Variables		Values
Age, years		32.54 ± 9.45
Gender, (%) **Male**		57 (54.82)
Female		47 (45.19)
OBD Number of case		104 (208)
Follow-up period, months		46.4 ± 26.3

Abbreviations: OBD: Ocular Behçet Disease, SD: standard Deviation

Of all cases, 28 (26.9%) had unilateral involvement, and 76 (73.1%) had bilateral involvement. The distribution of involvement types, including anterior, posterior, and panuveitis, is shown in Table 2.

Table 2. Distribution of Involvement Types in Ocular Behçet's Disease According to Uveitis

Types of Involvement	Anterior uveitis, n (%)	Posterior uveitis, n (%)	Panuveitis, n (%)

Unilateral (n:28; 26.9%)	5 (17.8)	9 (32.1)	14 (50)
Bilateral (n: 76; 73.1%)	9 (11.8)	25 (32.8)	42 (55.2)

The most common ocular finding was panuveitis, observed in 98 eyes (54.4%). The most common FFA finding was optic disc (OD) leakage, detected in 146 eyes (81.1%). Anterior uveitis was present in 23 eyes (12.7%), while posterior uveitis was observed in 59 eyes (32%). Panuveitis was present in 98 eyes (54.4%). The frequencies of retinal vasculitis, macular edema, retinitis, optic disc edema, RVO, optic disc hyperemia, increased tortuosity of retinal vessels, diffuse retinal edema, CRAO, dye leakage from retinal vessels, new vessel formation in the retina (NVE), and new vessel formation at the optic disc (NVD) were as follows: 28.8%, 17.7%, 13.3%, 6.62%, 1.12%, 10.5%, 7.75%, 4.45%, 0.55%, 26.2%, 6.72%, and 2.23%, respectively (Table 3).

Visual acuity results showed that 121 eyes (67.2%) had a visual acuity of 0.5 decimal or higher, 38 eyes (21.1%) had a visual acuity between 0.5 decimal and 0.1 decimal, and 21 eyes (11.6%) had a visual acuity of 0.1 decimal or lower **(Table 4)**.

Table 3. Ocular and Fundus Fluorescein Angiography Findings in Ocular Behçet's Disease

Ocular Findings	Number of affected eyes	%
Anterior uveitis	23	12.7
Posterior uveitis	59	32.7
Panuveitis	98	54.4
Retinal Vasculitis	52	28.8
Macular edema	32	17.7
Retinitis	24	13.3
Optic disc edema	12	6,62
Retinal vein branch occlusion	2	1,12
Optic disc hyperemia	19	10,5
Increased tortuosity of retinal vessels	14	7,75
Diffuse retinal edema	8	4,45
Central retinal artery occlusion	1	0,55
Leakage from the optic disc	146	81.1
Dye leakage from retinal vessels	47	26.2
Peripheral retinal neovascularization	12	6.72
Optic disc neovascularization	4	2.23

Table 4. Distribution of Ocular Behçet Disease Cases According to Visual Acuity

Visual Acuities (Decimal)	Number of Affected Eyes (n:180)	%	Visual Acuities (Decimal)
≥ 0.5	121	67.2	≥ 0.5
0.1-0.5	38	21.1	0.1-0.5

Discussion

BD is a chronic, systemic inflammatory disorder with multi-organ involvement. The disease typically presents in the second and third decades of life, and its severity tends to decrease with age (11). Ophthalmic findings of Behçet's disease can be listed as follows: 1- Anterior uveitis 2- Posterior uveitis 3- Panuveitis 4- Retinal vasculitis 5- Retinal vein occlusion 6- Optic disc edema 7- Retinitis 8- NVD, NVE

In our study, we found the rate of anterior uveitis to be 12.7%, posterior uveitis to be 32.7%, and panuveitis to be 54.4%. Similarly, in the study by Tutkun et al. involving 880 cases of ocular BD, the rates of anterior uveitis, posterior uveitis, and panuveitis were reported as 11%, 28.8%, and 60.2%, respectively (12). In the study by Khairallah et al. conducted in Tunisia, the rates of anterior uveitis, posterior uveitis, and panuveitis were reported as 4.5%, 34.2%, and 61.3%, respectively (13). In contrast to our study, Khairallah et al. reported a lower rate of anterior uveitis. This difference could be attributed to geographical variations and differences in sample size. Mohammad et al. reported anterior uveitis in 17% of cases and posterior uveitis in 25% (14). Similarly, Accorinti et

al. conducted a study with 2211 OBD cases in Italy and reported anterior uveitis in 11.4%, posterior uveitis in 20.8%, and panuveitis in 66.8% (15).

FFA is considered the gold standard imaging technique in the diagnosis and monitoring of uveitis in ocular BD. It is crucial for monitoring retinal inflammatory processes associated with posterior uveitis (16). In our study, the most common FFA finding was OD leakage (81.1%). Gedik et al. reported the rate of OD leakage in FFA in OBD cases as 89.8%, while Keorochana et al. reported it as 74% (17,18). Similarly, in our study, the OD leakage rate was 81.1%.

Khairallah et al. reported retinal vasculitis in 80.2% of OBD cases (13). Tutkun et al. reported the rate of retinal vasculitis as 89% (12). Keorochana et al. reported a rate of 42.5% (18). In our study, however, the rate of retinal vasculitis in OBD was 28.8%. This difference is likely due to the smaller sample size in our study. Gedik et al. reported the rate of leakage from retinal vessels as 73.5%, and Yu et al. reported it as 73.4% (17,19). In our study, the rate of leakage from retinal vessels was 26.2%. Leakage from retinal vessels is common, particularly during active attacks in patients with OBD. We believe that this difference may stem from the fact that our study did not focus on active phase of the disease.

In our study, the rate of macular edema in OBD cases was 17.7%. Similarly, Khairallah et al. reported a rate of 19.8%, and Keorochana et al. found 11% (13,18). However, Tutkun et al. reported a much higher rate of macular edema (44.5%) (12). We believe this difference could be due to the lack of optical coherence tomography (OCT) in our study, leading to some cases of macular edema being overlooked.

New vessel formation (NVD) is an indicator of poor visual prognosis in OBD. Visual outcomes associated with NVD remain poor, even with vitrectomy and immunosuppressive agents (20). Tutkun et al. reported the rates of NVD and NVE as 4.3%, while Khairallah et al. reported them as 5.4% (12,13). In line with these findings, we found the rate of NVD in our study to be 2.23%. We also found the rate of retinal vein branch occlusion (RVDT) in OBD cases to be 1.12%, which is consistent with the literature (12,13,18).

Central retinal artery occlusion (CRAO) is very rare in OBD. Özdal et al. reported only one case of CRAO (0.4%) in their study (21). CRAO in Behçet's disease has been reported in the literature as isolated case reports. In our study, one eye (0.55%) had CRAO. Khairallah et al. reported that 57.7% of Behçet's uveitis patients had visual acuity of 20/40 or better, 21.1% had visual acuity between 20/200 and 20/40, and 21.1% had visual acuity of less than 20/200 (13). In our study, the percentage of eyes with visual acuity of 0.5 or better was 67.2%, while 21.1% had visual acuity between 0.1 and 0.5, and 11.6% had visual acuity of 0.1 or worse.

Study limitations

Limitations of our study include its retrospective design, which may have led to missing or incomplete data; the small sample size; the lack of optical coherence tomography for diagnosing and classifying macular edema; the absence of records on systemic medication use; and the inclusion of only those patients with ocular manifestations of Behçet's disease who visited the ophthalmology department.

Conclusions

In conclusion, the most common ocular finding in OBD is panuveitis, and the most frequent FFA finding is OD leakage. FFA plays an important role in diagnosing and monitoring posterior uveitis and secondary complications in OBD. It is an essential imaging technique for monitoring inflammatory processes in the posterior segment and preventing irreversible visual function loss due to complications in ocular Behçet's disease.

Acknowledgements: *None.*

Ethical Approval: *This study approval was obtained from the Uludag University Faculty of Medicine, Ethics Committee (session: 17/2007 decision no: 12 date: 23.10.2007. This study was conducted retrospectively. Therefore, no consent form was obtained.*

Author Contributions: Concept: ACE, HHE. Literature Review: ACE, MG. Design: ACE, ME. Data acquisition: ACE, MG, ME. Analysis and interpretation: MKK, HB. Writing manuscript: ACE. Critical revision of manuscript: MG, ME, HHE.

Conflict of Interest: *The author(s) do not have any potential conflict of interest regarding the research. Authorship and/or publication of this article.*

Data Availability: *The data used to support the findings of this study are available from the corresponding author upon request*

Financial Disclosure: *No financial support was received for this study.*

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