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Original Article

Iris Changes in Patients with Pediatric Behçet's Disease: A Cross-sectional Spectral Domain Optical Coherence Tomography Study

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ABSTRACT

Aim: The study aimed to assess whether pediatric Behçet's disease (PBD) eyes with a history of ocular inflammation in remission exhibit residual iris structural changes compared with BD eyes without ocular involvement and also healthy controls.

Materials and Methods: Twenty PBD patients without ocular involvement (Group 1), 6 PBD patients with inactive ocular involvement (Group 2), and 24 age-sex-matched healthy controls (Group 3) were included in this study. Their demographic characteristics and the patients' anterior and posterior segment examination findings were recorded. Iris thicknesses at 1 mm, 2 mm, and 3 mm from the pupillary margin in the nasal and temporal areas were measured using spectral domain optical coherence tomography (SD-OCT). Iris area measurements in the 3 mm area were evaluated using the ImageJ program.

Results: There was no statistical difference between the three groups in terms of their age or gender (p=0.920, p=0.482, respectively). There was no statistically significant difference between the three groups regarding their iris thicknesses at temporal and nasal 1 mm, 2 mm, and 3 mm (p>0.05). The three groups had no significant difference in their temporal and nasal 3 mm area measurements (p>0.05).

Conclusion: In PBD eyes with a history of uveitis which were in remission at the time of imaging, iris thickness and area did not differ from those of non-ocular BD eyes or healthy controls. These findings suggest that no persistent iris structural damage is detectable by SD-OCT after the resolution of inflammation, although longitudinal follow-up during both active and inactive phases is warranted.

Keywords: Behçet's uveitis, iris area, iris thickness, pediatric Behçet's disease, spectral domain optical coherence tomography

Introduction

Behçet's disease (BD) is a disease first described by a Turkish physician, Hulusi Behçet, in 1937, with a triad of oral ulcers, genital ulcers, and uveitis (1). Its prevalence is higher in the Silk Road Basin (2,3). It is stated that this disease occurs as a result of various unknown infectious or non-infectious agents activating a wide range of inflammatory conditions in genetically susceptible individuals and it can present with multisystem involvement (4,5).

Pediatric BD (PBD) is a sub-classification of BD used to define the age group in which the disease is diagnosed as a result of the clinical picture being established before the age of 16 years (6). Although there is no clear data in the literature regarding the prevalence in this age group, it has

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been stated that the prevalence of this disease is around 15% to 20% of all BD cases (7,8).

The eye is one of the most commonly affected organs in BD, and its presentation is often bilateral non-granulomatous panuveitis, similar in both adult and pediatric groups. However, in children under the age of 10 years, the presentation may differ, often manifesting as anterior uveitis (9,10). Although the ocular progression of BD can vary widely, it can affect all segments of the eye in patients who do not receive proper treatment and it can cause a wide range of complications ranging from decreased vision to blindness (9,11).

Although ocular involvement in BD can affect all uveal tissues, objective and non-invasive quantification of iris structural parameters in pediatric patients remains limited. Spectral domain optical coherence tomography (SD-OCT) enables reproducible and non-invasive assessment of iris morphology, including stromal thickness and area, providing an opportunity to investigate subtle anterior segment changes in this population. Therefore, this study aimed to determine whether the eyes of PBD patients in remission with inactive uveitis exhibit structural alterations in iris thickness and area, compared to the eyes of BD patients without ocular involvement, and with a healthy control group.

The present study, therefore, aimed to evaluate whether PBD eyes with a history of ocular inflammation but currently in remission (inactive uveitis) show residual or permanent structural changes in iris thickness and area compared with BD eyes without ocular involvement and healthy controls.

Materials and Methods

Our study was designed retrospectively between March 2024 and April 2024 and was approved by the Scientific Research Evaluation and Ethics Committee of University of Health Sciences Türkiye, Ankara Etlik City Hospital (approval no.: AEŞH-BADEK-2024-459, date: 22.05.2024). This study was conducted in accordance with the Declaration of Helsinki. Since this was a retrospective, non-interventional imaging study, written informed consent for the use of clinical and imaging data was obtained from the legal guardians of all participants. This study included 20 patients who were followed up with the diagnosis of PBD and had no ocular involvement, 6 PBD patients with inactive ocular involvement, and 24 age-sex-matched healthy controls. Twenty patients with PBD without ocular involvement were classified as Group 1, 6 pediatric patients with BD who were inactive in terms of ocular involvement were classified as Group 2 and the healthy control patients were classified as Group 3. Only the right eye of each subject was included to avoid inter-eye correlation.

All PBD patients with inactive ocular involvement were patients who had a single uveitis attack (3 eyes with anterior uveitis and 3 eyes with panuveitis) and had no history of uveitis activation within the prior 3 months. In addition, the inactivity of these cases was determined by fundus fluorescein angiography (FA) and flare measurements in the prior 3 months of follow-up; no leakage was detected in angiography and the flare value was measured as being less than 5 in repeated flare measurements. All PBD patients were not receiving any additional medication other than colchicine as systemic treatment.

The demographic characteristics such as age and gender, best-corrected visual acuity (BCVA), intraocular pressure (IOP), spherical equivalents (spherical power + cylindrical power/2), flare values, and detailed anterior and posterior segment examination findings were recorded from the patient files. Flare measurements were evaluated with a Kowa FM 700 laser flare meter (Kowa Company Ltd., Nagoya, Japan), and an average of at least 5 values was recorded. Anterior segment SD-OCT scans were obtained using the Sirius device with the SD-OCT module (CSO, Florence, Italy) in raster mode along the horizontal central pupil line by the same operator. All images were acquired without pharmacologic mydriasis, under standardized room illumination of 300-500 lux measured with a luxmeter, and between 09:00 and 12:00 a.m. in order to minimize diurnal variation. Pupillary diameter at the time of scanning was recorded, and for each eye, three consecutive scans were obtained with the mean value used for analysis. Image quality criteria included adequate signal strength and the absence of motion artefact; scans not meeting these criteria were excluded and reacquired. Iris area was measured via ImageJ (v1.54 g Bethesda, USA) after calibration to the device scale. A 3 mm radial sector from the pupillary margin was marked temporally and nasally, and the enclosed stromal area was recorded (Figure 1). All measurements were performed independently by two masked graders, and the average of their values was used for analysis; discrepancies greater than 10% were resolved by consensus before inclusion.

Patients with a BCVA worse than 0.0 logMAR, a spherical equivalent refractive error beyond ±2.0 D, IOP outside the range of 11-21 mmHg, or anterior chamber flare values ≥6 were excluded, as well as those with a history of intraocular surgery, significant anterior segment pathology (such as

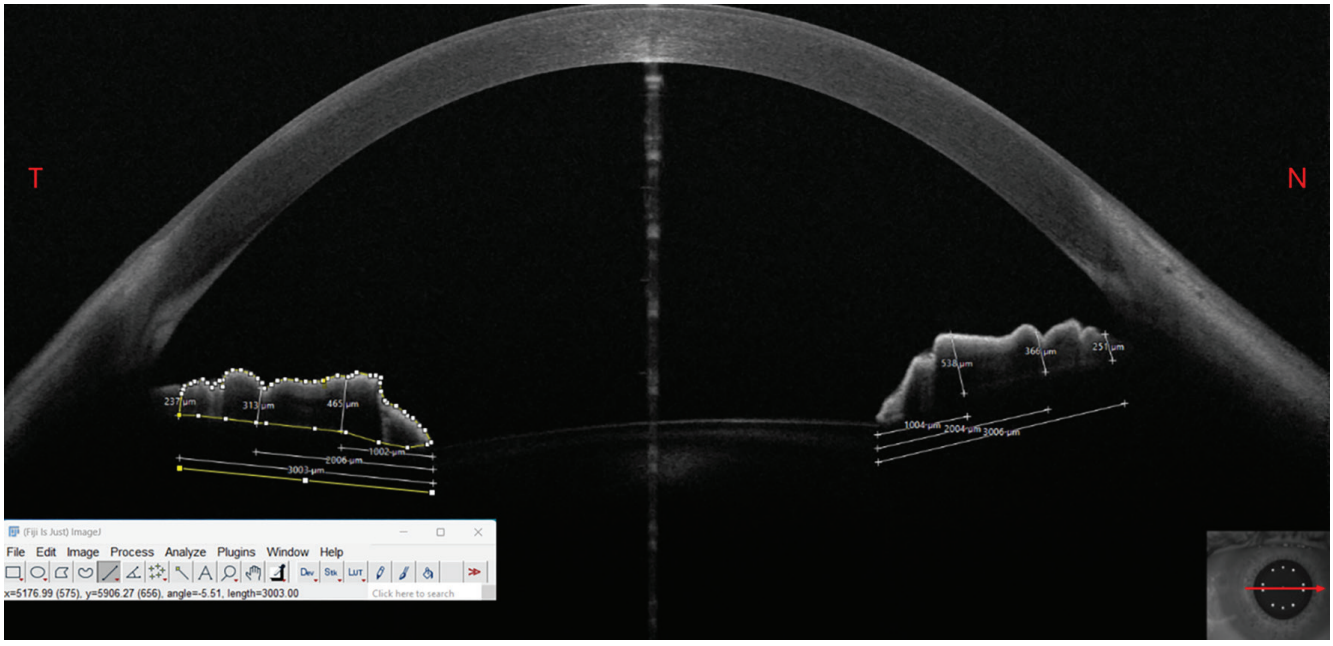

Figure 1. Evaluation of iris thickness using anterior segment optical coherence tomography and marking of the iris area using Image J program

corneal opacity or iris atrophy), active uveitis at the time of imaging, or the use of systemic medications known to affect pupillary function other than colchicine.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 23.0 (SPSS Inc., Chicago, IL, USA). For nominal (categorical) data, frequency and percentage values were calculated. For continuous variables, descriptive statistics including minimum, maximum, median, mean, and standard deviation were reported. The Kruskal-Wallis H test, a non-parametric test, was used to compare continuous variables among the three independent groups. When significant differences were detected, Dunn's post-hoc test with Bonferroni correction was performed for pairwise group comparisons. Effect sizes (η^2) with 95% confidence intervals (CIs) were calculated in order to quantify the magnitude of the observed differences. For comparisons between two independent groups, the Mann-Whitney U test was applied. Fisher's exact test was used for categorical variables. Additionally, post-hoc power analyses were performed based on observed effect sizes in order to evaluate the adequacy of the sample size. In order to check for potential confounding factors, covariate-adjusted analyses including age, spherical equivalent, and sex were conducted as sensitivity tests. A p-value <0.05 was considered statistically significant.

Results

Group 1 patients included 12 (60%) female and 8 (40%) male patients; Group 2 patients included 2 (33.3%) female and 4 (66.7%) male patients; Group 3 patients included 12 (50%) female and 12 (50%) male patients. There was no statistically significant difference between the groups in terms of gender (p=0.482). The mean age of Group 1 patients was 13.4±3.28 years, the mean age of Group 2 patients was 14.67±17.67 years, and the mean age of Group 3 patients was 13.67±3.13 years. No statistically significant difference was found between the mean ages of the patients (p=0.92). There was no statistically significant difference between the disease durations of Group 1 and Group 2 cases (p=0.234) (Table I).

The BCVA of all patients in Group 1, Group 2, and Group 3 was 0.0 logMAR. The biomicroscopic anterior segment and dilated fundus examination were normal in all eyes and Group 2 patients had no posterior synechiae. FA showed no vascular leakage in Group 2. All participants had brown irises.

The median (interquartile range) temporal iris thickness values at 1,000 µm, 2,000 µm, and 3,000 µm from the pupillary border were 446.5 (386-525) µm, 395 (318.75-465.75) µm, and 234.5 (208.5-290.75) µm in Group 1; 495.5 (464.25-518.25) µm, 386 (362.25-405.25) µm, and 269.5 (256-303.75) µm in Group 2; and 455 (412.25-502.5) µm, 365.5 (321.75-412.75) µm, and 269.5 (243-380) µm in Group

3, respectively. The median nasal iris thicknesses at 1,000 µm, 2,000 µm, and 3,000 µm were 483 (420.5-543.25) µm, 417.5 (338.75-471.75) µm, and 286 (255.75-324.5) µm in Group 1; 495 (450.25-550) µm, 375 (347.25-412.25) µm, and 249 (221.75-331.5) µm in Group 2; and 492.5 (448-548.5) µm, 394.5 (367-444) µm, and 289 (237.25-343.25) µm in Group 3, respectively. No statistically significant differences were found among the three groups for any of the temporal or nasal iris thickness parameters (p>0.05, Kruskal-Wallis test; η^2=0.01-0.05, 95% CI (0-0.15). The temporal and nasal iris areas measured up to 3,000 µm from the pupillary border were 1.52 (1.34-1.79) mm² and 1.57 (1.43-1.77) mm² in Group 1; 1.54 (1.48-1.72) mm² and 1.56 (1.09-1.72) mm² in Group 2; and 1.55 (1.47-1.65) mm² and 1.66 (1.52-1.72) mm² in Group 3, respectively. No significant intergroup differences were observed for the iris area measurements (p>0.05, Kruskal-Wallis test; η^2=0.01, 95% CI (0-0.06) (Table II).

Table I. Clinical and demographic characteristics of patients

	Group 1 (n=20)	Group 2 (n=6)	Group 3 (n=24)	p-value
Age (years)	13.4±3.28 Median: 13.5 Min-max: 6-17	14.67±3.20 Median: 16 Min-max: 9-17	13.67±3.13 Median: 14.5 Min-max: 6-17	0.920[K]
Gender				0.482[F]
Female	12 (60%)	2 (33.3%)	12 (50%)	
Male	8 (40%)	4 (66.7%)	12 (50%)	
Duration of pediatric BH (months)	24.75±24.9 Median: 12.5 Min-max: 2-84	14.17±17.7 Median: 6 Min-max: 2-48	-	0.234[M]

[K]: Kruskal-Wallis H-test, [F]: Fisher's exact test, [M]: Mann-Whitney U test, BH: Behçet's disease, Min: Minimum, Max: Maximum

Table II. Comparison of patients' iris thickness and iris areas

Iris thickness (µm)	Group 1 (n=20)	Group 2 (n=6)	Group 3 (n=24)	p-value	Effect size η^2 (95% CI)
Temporal 1000	446.5 (386-525), CI: 396.9-484.5	495.5 (464.25-518.25), CI: 444.6-529.0	455 (412.25-502.5), CI: 430.8-483.8	0.578[K]	0.02 (0-0.12)
Temporal 2000	395 (318.75-465.75), CI: 357.2-431.8	386 (362.25-405.25), CI: 355.7-422.3	365.5 (321.75-412.75), CI: 342.8-394.6	0.649[K]	0.01 (0-0.11)
Temporal 3000	234.5 (208.5-290.75), CI: 222.5-288.1	269.5 (256-303.75), CI: 250.4-303.6	269.5 (243-380), CI: 264.7-330.7	0.110[K]	0.05 (0-0.15)
Nasal 1000	483 (420.5-543.25), CI: 434.7-522.3	495 (450.25-550), CI: 441.1-552.5	492.5 (448-548.5), CI: 470.3-518.1	0.833[K]	0.01 (0-0.09)
Nasal 2000	417.5 (338.75-471.75), CI: 354.9-432.6	375 (347.25-412.25), CI: 333.6-426.4	394.5 (367-444), CI: 383.9-423.7	0.633[K]	0.01 (0-0.10)
Nasal 3000	286 (255.75-324.5), CI: 267.0-310.0	249 (221.75-331.5), CI: 208.8-334.2	289 (237.25-343.25), CI: 259.0-318.0	0.687[K]	0.01 (0-0.10)
Iris area (mm²)					
Temporal	1.52 (1.34-1.79), CI: 1.42-1.66	1.54 (1.48-1.72), CI: 1.45-1.73	1.55 (1.47-1.65), CI: 1.50-1.62	0.758[K]	0.01 (0-0.06)
Nasal	1.57 (1.43-1.77), CI: 1.49-1.68	1.56 (1.09-1.72), CI: 0.89-2.38	1.66 (1.52-1.72), CI: 1.57-1.71	0.711[K]	0.01 (0-0.05)

Data are presented as median (IQR), CI=95% confidence interval
[K]: Kruskal-Wallis H-test, η^2: Eta-squared effect size, IQR: Interquartile range, CI: Confidence interval

Discussion

PBD develops on average between the ages of 4.9 and 12.3 years and affects both sexes approximately equally (8). Ocular involvement can occur at very different frequencies in this group of patients, and it is stated that the frequency of ocular involvement can vary between approximately 9% and 76% of patients (9). These ocular inflammations which may develop can cause a wide variety of ocular complications, making close follow-up of these patients essential (9,11).

There are various data on the prevalence of uveitis in pediatric cases, and it has been stated that it is between 5% and 16%. In these cases, various segments of the eye can be affected depending on the type of uveitis and these cases can present with a wide variety of complications, from band keratopathy to posterior synechiae or optic atrophy to retinal detachment (12). The iris is the only part of the uvea which can be directly observed in biomicroscopic examination. The iris, which has a dynamic structure, consists of irregular superficial cells, sphincter and dilator pupil muscles, stromal cells, and iris pigment epithelium. The iris, which has a spongy structure, can cause changes in its thickness as a result of contractions and relaxations with a structure which allows fluid exchange between the stroma and aqueous. In eyes affected by uveitis, inflammation or iris vasculitis may lead to alterations in the iris tissue which are not easily detectable through biomicroscopic examination. Therefore, we investigated the measurement of iris thickness and area in PBD with and without ocular involvement and compared these results with age-matched healthy controls. In our study, we found no statistically significant differences between temporal and nasal iris thickness changes and iris areas in inactive ocular involvement BD, BD without ocular involvement, and the control group when compared to each other. In this study, we did not find any ocular complications on biomicroscopic examination in eyes with inactive ocular involvement.

In addition to obvious ocular complications, subclinical changes can be observed depending on the pathophysiology of the BD, and these changes may affect all segments of the eye with varying degrees of severity. Furthermore, eyes without ocular involvement have also been reported to be affected by the disease. In one study examining retinal vascular structures in BD without ocular involvement, a significant decrease was found in both superficial vascular density, deep vascular density, and choriocapillaris flow areas in patients when compared to a healthy group, and the results indicated that vascular changes can occur even in eyes without ocular involvement (13). In another study examining retinal vascular structures in PBD without ocular involvement, no difference was found in superficial vascular densities, but decreases in deep capillary plexus vascular densities were found (14). Considering the changes in these vascular structures, the need for close follow-up of these clinically asymptomatic patients emerges and it has been seen that a wide variety of retinal vascular changes occur in patients even in cases which appear to be asymptomatic.

Changes in the vascular system of the iris in patients with BD have been another research subject. In a study conducted by Yoshikawa et al. (15), the iris vascular system of patients with BD was examined in the remission phase and it was emphasized that the damage continued even in the inactive period. Based on these conditions, we wanted to investigate the usability of non-invasively measuring the iris thickness of patients in terms of follow-up, progression, and the detection of developing complications. In addition, retinal vascular involvement can be easily detected by OCT angiography in both eyes either with or without ocular involvement in BD, but iris vascular changes cannot be identified in more detail with the current technology.

In another study, corneal changes in BD which were active with ocular involvement, inactive with ocular involvement, and BD without ocular involvement were examined and the effectiveness of these data in determining the activity of the disease was evaluated. As a result, the researchers stated that endothelial dysfunction developed due to ocular inflammation and corneal thickness increased, but this was not observed in inactive patients and these parameters returned to normal. As a result, the authors stated that they could make an opinion about disease activity based on corneal thickness and that these data could be a guide in determining the best treatment method (16). In a further study examining corneal endothelial changes, the changes in the inactive period of BD patients with ocular involvement were examined. Although the researchers did not detect any difference in corneal thickness between a healthy group and the BD group, they stated that permanent changes in endothelial cell morphology could be observed, but these conditions did not cause decompensation of the cornea (17). Although it has been stated that these inflammation-related effects on corneal parameters do not result in decompensation after the inflammation ends, cellular effects occur and this shows the importance of long-term and close follow-up of the progression in these patients, even if they are asymptomatic. The results of the above studies suggest that inflammation may also have

an effect on iris tissue during acute attacks. In our study, we evaluated eyes with ocular involvement during the inactive phase of uveitis, and our findings suggest that after treatment of active uveitis attacks, inflammatory effects may not lead to measurable changes in the iris tissue of eyes with normal anterior segment findings.

It has also been reported that changes in iris thickness can occur in many ocular diseases. In a study examining the iris thickness in patients with neovascular glaucoma, it was stated that ischemia caused a decrease in iris thickness (18). Another place where iris thickness is examined is in cases with uveitis. Studies investigating changes in iris thickness and area in eyes with Fuchs' uveitis have reported reduced iris thickness and area compared to healthy eyes (19).

We found no statistically significant differences between temporal and nasal iris thicknesses and iris areas among inactive ocular involvement BD, BD without ocular involvement, and the healthy control group. These results should be interpreted with caution due to the limited sample size, right-eye-only analysis, and inclusion of only inactive cases. The small sample, particularly in the inactive ocular-involvement group, also limits the statistical power of this study. The absence of measurable differences may indicate that no permanent iris damage was demonstrated under inactive disease conditions. It is also possible that suppression of inflammation during the inactive phase may have prevented structural iris alterations. From a vascular perspective, ischemia associated with the vasculitis nature of BD might not have occurred because of systemic inactivation of the disease, or the changes may exist below the detection threshold of current imaging methods. Further longitudinal and active-phase studies with larger sample sizes are warranted in order to clarify the pathophysiological changes of the iris in PBD.

Study Limitations

The absence of active PBD with ocular involvement in our study, the fact that our study was a single-centre retrospective study, and the relatively small number of patients can be cited as the limitations of this study.

Conclusion

No permanent changes were demonstrated in iris parameters among PBD cases with inactive disease, and the values were comparable to those of the healthy controls. This study represents, to the best of our knowledge, the first evaluation of iris parameters in PBD using SD-OCT. Larger, longitudinal, and active-phase studies are needed in order to confirm these preliminary findings.

Ethics

Ethics Committee Approval: Approval was granted by the Scientific Research Evaluation and Ethics Committee of University of Health Sciences Türkiye, Ankara Etlik City Hospital (approval no.: AEŞH-BADEK-2024-459, date: 22.05.2024).

Informed Consent: Informed consent was obtained from all patients and or their legal guardians.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.Ş., Y.Ö.E., B.K., E.B., N.G.K., S.Ö., Concept: E.Ş., Y.Ö.E., B.K., Design: E.Ş., Data Collection or Processing: E.Ş., Y.Ö.E., B.K., E.B., N.G.K., S.Ö., Analysis or Interpretation: E.Ş., Y.Ö.E., Literature Search: E.Ş., Writing: E.Ş.

Conflict of Interest: No potential conflict of interest was reported by the author(s).

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