EXTENDED REPORT

Topographic optic disc analysis by Heidelberg retinal tomography in ocular Behçet's disease

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Aim: To compare the topographic characteristics of the optic discs in patients with severe and mild ocular Behçet's disease by using Heidelberg retinal tomography (HRT).

Methods: This prospective study included 47 eyes of 47 patients with ocular BD who were being followed-up at the Uveitis Clinic of the Ankara Ulucanlar Eye Research Hospital, Ankara, Turkey. The patients were divided into two groups. Group 1 consisted of 21 eyes with mild uveitis, and group 2 consisted of 26 eyes with severe uveitis. All patients underwent topographic optic disc analysis by HRT II, and the quantitative optic disc parameters of both groups were compared by non-parametric Mann-Whitney U test.

Results: The mean cup volume, rim volume, cup area, disc area and cup depth in group 1 were found to be statistically significantly greater than those in group 2 ($p < 0.0001$, $p = 0.03$, $p = 0.021$, $p = 0.01$ and $p = 0.017$, respectively), while the difference between the mean cup-to-disc ratios in group 1 and group 2 were found to be statistically insignificant ($p = 0.148$).

Conclusion: A relationship was found between the severity of ocular BD and optic disc topography determined by HRT. In eyes with smaller optic discs, uveitis was observed to have a more severe course with more frequent relapses than those with larger discs.

Behçet's disease (BD) is a multisystemic disease characterised by chronic recurrent uveitis, arthritis, oral and genital aphthous ulcerations and skin lesions. It is commonly seen in the Mediterranean and Far Eastern countries. Aetiopathogenetic studies have shown phenotype HLA B51 to be four times greater in cases of BD than in the normal population.^{1–3} Histopathologically, the disease is characterised by leukocytoclastic vasculitis that result in the obliteration of the vascular endothelial lumen.⁴

Ocular involvement has been reported in 70% to 75% of patients with BD. The most common ocular findings with BD include recurrent iridocyclitis, vitritis, retinitis, retinal vasculitis and retinal vascular occlusion.^{1–8} Progressive visual deterioration develops as a result of chronic recurrent inflammation, ischemic vasoocclusion and microvasculitis of arterioles of the optic nerve that lead to axonal necrosis of the optic nerve, ischemic optic neuropathy and progressive optic atrophy.⁹

The topographic characteristics of the optic disc are well known to predispose a number of ocular diseases. Confocal scanning laser tomography (Heidelberg retinal tomograph (HRT), software V.2.1; Heidelberg Engineering, Germany) enables quantitative measurements of the optic disc in various ocular pathologies.^{9–13}

In this study, we compared the optic disc topography in patients with severe and mild ocular BD, and we observed the association between the topographic changes of the optic disc and the frequency of the relapses of uveitis.

METHODS

This study prospectively enrolled 47 patients with ocular BD who were being followed-up at the Uveitis Clinic of the Ankara Ulucanlar Eye Research Hospital, Ankara, Turkey. All patients fulfilled the international criteria for BD. The patients were divided into two groups. Group 1 consisted of 21 eyes from 21 patients with mild ocular involvement and Group 2 consisted of 26 eyes from 26 patients with severe ocular involvement. Mild ocular involvement was defined as iridocyclitis $\pm$ vitritis with <4 relapses per year, in which complete anatomic and visual recovery

was obtained after treatment, whereas severe ocular involvement was defined as posterior uveitis $\pm$ iridocyclitis with ≥ 4 relapses per year, poorly responsive to treatment. Posterior uveitis included retinitis, macular and/or perivascular exudation, retinal haemorrhages and oedema in the presence of the clinical and fluorescein angiographic findings of retinal occlusive vasculitis.

Inclusion criteria of the study were the presence of ocular BD for at least 1 year prior to the study, absence of other systemic diseases, ocular surgery, ocular trauma, glaucoma and family history of glaucoma. The patients who had intraocular pressure >21 mmHg, glaucomatous optic nerve changes, unreliable optic disc image, cataract, best corrected visual acuity worse than 20/30, high spherical (>-5 dioptri or $>+3$ dioptri) or cylindrical ($>+1$ dioptri) refractive errors and active posterior uveitis at the time of HRT were excluded from the study.

Following the detailed ophthalmologic examinations, confocal scanning laser ophthalmoscopy with HRT II (Heidelberg Retinal Tomograph, software version 2.1; Heidelberg Engineering, Germany) was performed by the same experienced physician (UE). The procedure was achieved without pupillary dilatation and with a $15 \times 15^\circ$ field of view, under the same intensity of dim room lighting. Three topographic images were obtained for each eye and a composite image created from these images was used for data analysis. The disc margin contour line was drawn manually at the inner edge of the scleral ring by determining 8 to 10 points. The software calculated various parameters relative to a reference plane 50 μm posterior to the retinal surface at the papillomacular bundle. HRT assessment of disc area, cup area, cup-to-disc ratio, rim volume, cup volume and cup depth were evaluated. Statistical analysis of the study was performed by using the non-parametric Mann-Whitney U test and statistical significance was set as $p < 0.05$.

This study followed the tenets of the declaration of Helsinki, and was approved by the institutional ethics committee. All patients gave written informed consents prior to the study.

Abbreviations: BD, Behçet's disease; HRT, Heidelberg retinal tomography

RESULTS

Group 1 consisted of 21 patients (21 eyes), of which 14 were male (66.7%) and 7 were female (33.3%) with a mean age of 34.6 ± 9.6 (range, 19–52 years). Group 2 consisted of 26 patients (26 eyes), of which 18 were male (69.2%) and 8 were female (30.8%) with a mean age of 34.4 ± 6.8 (range, 20–45 years). The mean duration of ocular BD, defined as the time passed from diagnosis of ocular BD until the initiation of the present study was 8.8 ± 7.2 years (range, 1–20 years) in group 1, and 9.6 ± 5.01 years (range, 1–21 years) in group 2. The difference between the demographic characteristics of the two groups was not statistically significant ($p > 0.05$) (table 1).

Biomicroscopic anterior chamber examination revealed iridocyclitis with two positive inflammatory cells in 4 eyes (19.1%) in group 1, and in 12 eyes (46.2%) in group 2. Posterior synechiae and pigmentary cells on the lens surface were recorded in all of the eyes. Fundoscopy showed normal retinal findings in all but eight eyes in group 1, which had vitreous condensation due to previous episodes of vitritis. In group 2, five eyes (19.2%) had the sequela of previous retinal vasculitis and branch retinal vein occlusion with empty vessels and all eyes had vitreous condensation to some degree.

Iridocyclitis was treated with topical corticosteroids (hourly instillation for 2 weeks, and gradual taper thereafter), and cycloplegic agents (3 times per day). According to the medical charts of the patients, single usage or combinations of oral corticosteroids (1 mg/kg/day), cyclosporine A (5 mg/kg/day) and azathioprine (2 mg/kg/day) were used during the active posterior uveitis. At the time of the study none of the patients were receiving corticosteroids, while five patients with severe ocular involvement were receiving prophylactic doses of cyclosporine A and azathioprine.

The mean cup volume, rim volume, cup area, disc area, and cup depth of group 1 were measured as 0.097 mm^3 , 0.403 mm^3 , 0.417 mm^2 , 1.912 mm^2 and 0.172 mm , respectively, and those of group 2 were measured as 0.05 mm^3 , 0.38 mm^3 , 0.39 mm^2 , 1.871 mm^2 and 0.129 mm , respectively. The parameters in group 1 were statistically significantly smaller than the ones in group 2 ($p < 0.0001$, $p = 0.03$, $p = 0.021$, $p = 0.01$, $p = 0.017$, respectively). However, no statistically significant difference was found between the mean cup-to-disc ratio of group 1 (0.218) and that of group 2 (0.208), ($p = 0.148$) (table 2).

DISCUSSION

The evaluation of topographic characteristics of the optic disc and the peripapillary retinal nerve fibre layer (RNFL) provide important clues during the diagnosis and follow-up of various diseases involving the optic nerve.^{9–16} Until several years ago, the evaluation of the optic disc was performed either clinically or by stereoscopic fundus photography. Although informative, these procedures were not quantitative, were prone to measurement errors, and produced anatomical data in only two dimensions.¹¹ In recent years, the development of confocal scanning laser tomography enabled quantitative measurements and three-dimensional images of the optic nerve head, optic

disc, cup, neuroretinal rim and RNFL.^{9–13} Although several confocal scanning systems have been available, HRT (the original HRT-I, and the newer HRT-II) has become the most widely used system.¹⁰ HRT provides three-dimensional topographic images of the optic disc and adjacent nerve fibre layer. It uses diode laser with a wavelength of 670 nm that rapidly scans the retina point by point, collects confocal images at x-, y- and z-axes, and produces a three-dimensional representation of the surface topography. The software automatically calculates a series of stereometric values, including disc area, cup area, cup depth, cup volume, rim area, rim volume, and cup-to-disc ratio. The results are reproducible and are considered accurate for following topographic changes.¹⁰

The development of HRT was mainly initiated by the need for quantitative evaluations of the optic disc in early diagnosis of glaucoma, as well as the monitorisation of its progression.¹⁰ Although the most widespread use has been in patients with glaucoma and suspected glaucoma, the clinical use of HRT became much extensive in recent years. It is now being used in the evaluation of non-glaucomatous optic neuropathies, as well as various retinal disorders such as macular oedema, macular holes and epiretinal membranes, where topographic changes are required to be quantified. In the study of Saito *et al*, optic disc topography of the patients with non-arteritic anterior ischemic optic neuropathy (AION) was compared with those of open-angle glaucoma. They found that, disc topography of the eyes with non-arteritic AION was quantitatively characterised by small and shallow cupping and a larger rim area compared to eyes with open angle glaucoma.¹⁴ Trip *et al* applied HRT to patients with optic neuritis and they concluded that HRT-II could have a role in detecting axonal loss, and consequently in monitoring the efficacy of neuroprotective therapies in optic neuritis.¹¹ Despite these studies, the reports of HRT usage in non-glaucomatous optic nerve diseases are still quite limited.

Posterior uveitis caused by ocular BD tends to involve all structures of the retina. However, its most common retinal pathology is known as retinal vasculitis leading to retinal vascular occlusion, and subsequent retinal ischemia, optic atrophy and retinal and disc neovascularisations.^{8, 17, 18} Although less common, papillitis can also occur as a result of the chronic ischemic vasoocclusive attacks leading to demyelination or axonal necrosis of the optic nerve.^{19, 20} Depending on these vascular pathologies of BD, we thought that there might be an association between the topographic optic disc characteristics and the severity of uveitis. Moreover, similar to the early detection and monitorisation in patients with glaucoma, BD might also be monitored by investigation of changes in topographic characteristics of optic discs using HRT. To the best of our knowledge, the study of Tekeli *et al* is the only one in which HRT was used in order to analyse the topographic characteristics of optic disc in ocular BD. In their study, they compared optic nerve topographic changes of normal subjects with those of the ones with ocular and non-ocular BD. They reported that, the mean disc area, cup area, cup volume and cup depth in ocular and non-ocular cases with BD were significantly smaller than those of normal subjects.⁹ In our study, we evaluated and compared the topographic parameters of the optic discs of the patients with severe and frequent relapses of uveitis, with those of the patients with mild and rare relapses. We found that the parameters including the mean disc area, cup area, cup volume, rim volume and cup depth were significantly smaller in eyes with severe uveitis and frequent relapses. However, the difference in mean disc area between the two groups was quite small (1.912 in group 1, and 1.871 in group 2). Even though a statistical significance was found, a clinical significance might be debatable because of this relatively small difference between the two groups. The mean cup-to-disc ratio was also numerically smaller in eyes with severe uveitis, but the difference was not

Table 1 Demographic characteristics of the cases in groups 1 and 2

	Group 1	Group 2
Patient, n (%)	21 (44.7)	26 (55.3)
Age, median years (range)	34.6 (19–52)	34.4 (20–45)
Male, n (%)	14 (66.7)	18 (69.2)
Female, n (%)	7 (33.4)	8 (30.8)
Presence of ocular BD, median years (range)	8.8 (1–20)	9.6 (1–21)

Table 2 Optic disc topographic changes of group 1 and group 2

	Group 1	Group 2	p Value:
Mean cup volume (SD)	0.097±0.11 mm ³	0.05±0.021 mm ³	p<0.0001
Mean rim volume (SD)	0.403±0.21 mm ³	0.38±0.1 mm ³	p=0.03
Mean cup area (SD)	0.417±0.31 mm ²	0.39±0.19 mm ²	p=0.021
Mean disc area (SD)	1.912±0.47 mm ²	1.871±0.48 mm ²	p=0.01
Mean cup depth (SD)	0.172±0.08 mm	0.129±0.05 mm	p=0.017
Mean cup/disc (SD)	0.218±0.08	0.208±0.06	p=0.148

statistically significant between the two groups. According to Tekeli *et al*, small and crowded optic nerve head was a risk factor for retinal vascular complications. Furthermore, vasculitis caused thrombotic occlusion of retinal vessels in BD.⁹ The results of our study support their opinion. We observed that more severe episodes of uveitis and vasculitis were found in the eyes with smaller optic discs. This might be a result of ischaemia due to chronic vasooclusive attacks in vasculitis, however, there might also be unknown pathophysiological mechanisms triggering the relapses of uveitis in eyes with smaller optic discs, which should be further evaluated.

Our study might be an indicator of the relationship between optic disc topographic changes and ocular inflammatory diseases involving the retinal vessels. This study demonstrates that HRT might be useful in monitoring the patients with BD. The quantitative measurements obtained by HRT could provide early determination of the course of uveitis in BD, which might be useful to prevent the impending ocular complications to a great extent. However our results still need to be supported by further studies. As similar associations might also be found in other entities of vasculitis and uveitis, further investigation of changes in topographic characteristics of optic discs in patients with uveitis should be encouraged.

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