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Ophthalmic findings in Behcet's disease: Cases without apparent ocular signs

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Abstract

Purpose: To evaluate the fluorescein angiography and infrared autofluorescence finding in patients with confirmed Behcet's disease (BD) but without clinical ocular signs.
Methods: In this prospective, non-interventional case series, montage fluorescein angiography (MFA) and infrared autofluorescence imaging were performed for all patients with confirmed BD but without ocular signs in clinical examination.
Results: Fifty BD patients (100 eyes) without clinical ocular manifestations were investigated. In MFA, we found fluorescein angiography (FA) leakage in 22 cases (44%) in both eyes, mostly at the periphery of retina. In infrared autofluorescence, profound changes were found in 43 patients, 86 eyes (86%). Twenty-five patients, 50 eyes (50%), presented retinal vascular branching modifications, straightening, tortuosity, and shunt.
Conclusion: MFA of retina may be useful in patients with presumed BD for early diagnosis, early treatment, and follow-up of patients.

Keywords: Behcet's disease; Montage fluorescein angiography; Infrared autofluorescence; Branching pattern of retinal vasculature

Introduction

Behcet's disease (BD) is a multisystemic inflammatory vasculitis with periodic recurrences causing obliteration, necrosis, and fibrosis of vascular system where it extends.[1] Oral and genital mucosa, skin, and eyes are the most vulnerable sites for its manifestations.[2] When the eyes get involved, it may have very severe consequences ending with blindness.[3] Therefore, the prompt diagnosis of the disease and prompt treatment could alter its course or at least reduce its severe consequences.[4]

For diagnosis of BD, the involvement of the eye has been considered to be one of the major elements along with mucosal aphthosis and skin lesions.[5,6]

The prevalence of ocular involvement in BD is highly variable in the world. In Iran, it is reported to be 59%.[7] In many cases, the eyes remain indemned, at least when examined by routine examinations such as biomicroscopy and fundoscopy. However, by more sophisticated technology, such as montage fluorescein angiography (MFA) to detect particularly peripheral retinal vascular leakage. Infrared autofluorescence of pigmented cells of choroid, indicating changes in structural architecture of choroid. Indocyanine green angiography (ICG) clearly shows us the vascular and anatomical changes in the choroid. Retinal vascular fractals (D_f)[8] quantify the changes in the branching pattern of the retinal vessels.[8] We may detect some pathological points to confirm the involvement of the eyes.

The significance of such sophisticated methods of investigation is not only to detect the ocular disease, but to obtain an additional element for the diagnosis of BD and to confirm the disease and treat it promptly and severely to overcome the undesired consequences.

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Herein, we investigated 50 patients (100 eyes) with confirmed BD (according to Japanese criteria)[6] and without any apparent clinical ocular involvement. We particularly investigated the peripheral retinal vascular leakage on MFA and secondly, we looked for changes of infrared autofluorescence of choroid and branching pattern of retinal vessels.

Methods

In this prospective, non-interventional case-series investigation from April 2014 to January 2015, 50 patients with clinically diagnosed BD (Japanese criteria)[6] but without any apparent clinical ocular involvement (incomplete Behcet) were included. The patients were selected from Behcet's Unit of Shariati Hospital of Tehran University of Medical Sciences (TUMS). They were all under treatment of Colchicine 1 mg/daily (Modava, Iran). The initial examinations were performed at Shariati Hospital, Behcet's Unit. Visual acuity was taken by Snellen chart, the eyes were examined by Haag-Streit slit lamp biomicroscopy, and funduscopy was performed using three mirror of Goldmann. None of the patients had any apparent ocular sign of vasculitis, uveitis, or macular edema and had no treatment for uveitis, retinal vasculitis, or any ocular disease. Best corrected visual acuity was 20/20 in all eyes. Patients with diabetic retinopathy, congenital vitreoretinal disease, previous ocular surgery, and treatment for uveitis were excluded. The patients were referred to Farabi Eye Hospital, for fluorescein angiography (HRA II Heidelberg, Heidelberg, Germany). Angiography was taken from central retina and four peripheral quadrants (superior, temporal, nasal, and inferior) of retina to obtain a complete view of retina. MFA and fundus infrared autofluorescence was obtained at the same time. The angiographies were evaluated by two retinal experts independently (ZAH, HC). Abnormal fundus infrared autofluorescence and angiography imaging changes were compared with normal appearing images of the same group of patients. All patients were informed of our project. The study was approved by the Ethical Board of TUMS.

Results

Twenty-four men and 26 women were included. The mean age of men was 32.7 $\pm$ 9.05 years (range, 16–52), and the mean age of women was 36.92 $\pm$ 10.05 years (range, 21–53). The duration of BD in men was 10.04 $\pm$ 8.01 years (range, 2–31 yrs), and in women, it was 12.08 $\pm$ 10.56 (range, 1–41 yrs). On the FA, 22 patients, 44 eyes (44%), had leakage of fluorescein at the periphery of retina in both eyes and mostly from the final branches (Figs. 1–3). In addition to peripheral leakage, four patients presented minimal leakage from the optic disc and one from the posterior pole (Fig. 4). In fundus infrared autofluorescence, the eyes were categorized in two groups. Forty-three patients, 86 eyes (86%), presented profound modifications and hyper and hypo autoreflectivity of the fundus infrared autofluorescence compared to the remaining 14 normal eyes (Fig. 5). Twenty-five patients, 50 eyes (50%), presented retinal vascular branching modifications, tortuosities,

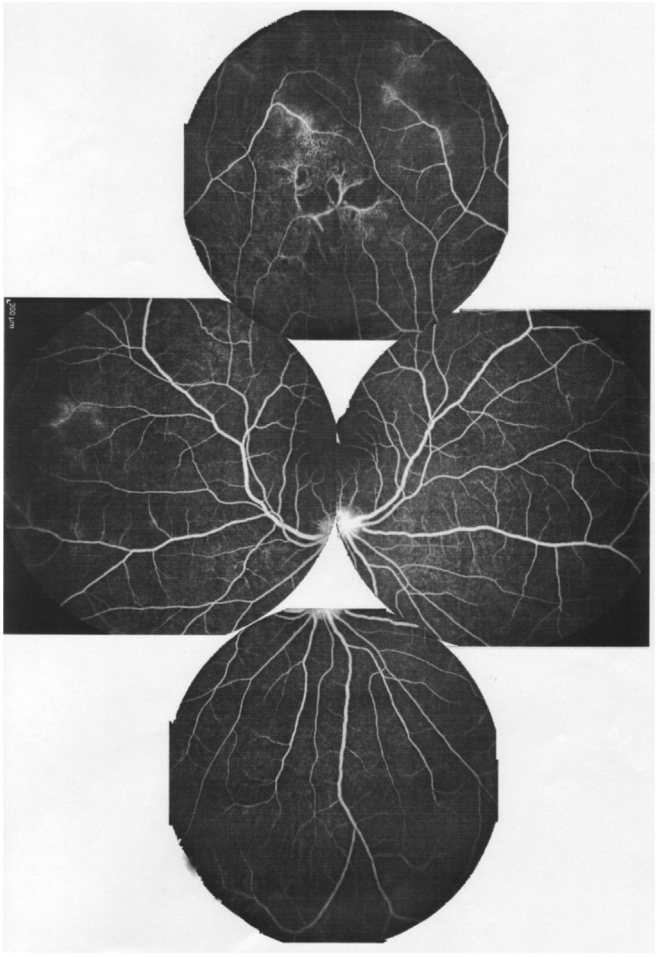

Fig. 1. Montage fluorescein angiography showing fluorescein leakage of the peripheral vessels.

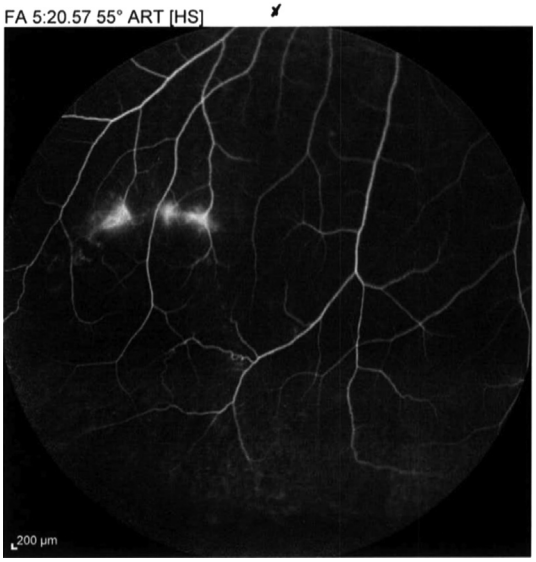

Fig. 2. Leakage on FA at the inferior area of retina of the right eye with retinal ischemia and vascular irregularity at 5:20 min of FA.

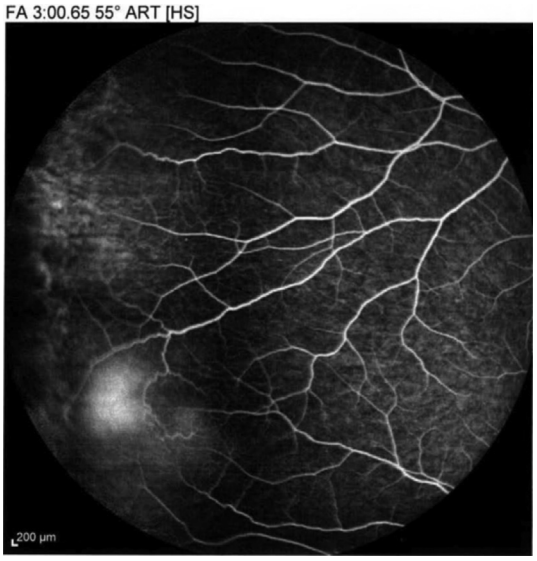

Fig. 3. Fluorescein leakage on FA at the periphery of the infero-temporal retina of the right eye with retinal pigment epithelium changes and vascular modification at 3:00 min of FA.

and straightening (Fig. 6), and one patient had vascular shunt at the periphery of retina (Fig. 7).

Discussion

Ocular involvement in the diagnosis of BD has a major role. In fact, ocular involvement (uveitis, retinal vasculitis) is considered one of the major criteria for diagnosis of BD as well as mucosal and skin lesions.[5,6] In many cases with lack of sufficient evidence for the confirmation of the disease, the treatment is delayed for years. It is presumed that the sooner we treat the patients, the better the outcome will be.[4]

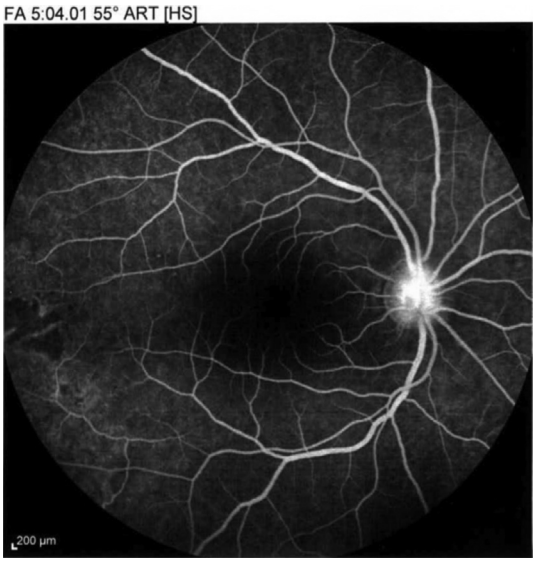

Fig. 4. Leakage of fluorescein from the disc of the right eye at 5:04 min of angiography.

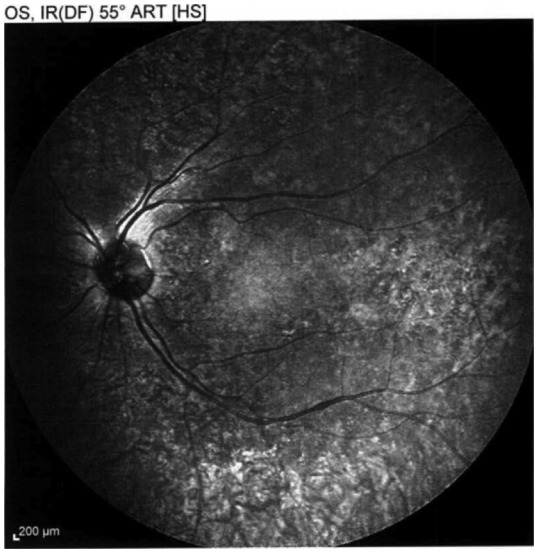

Fig. 5. Deep changes on infrared autofluorescence of choroid of the left eye with hyper and hypo reflectivity.

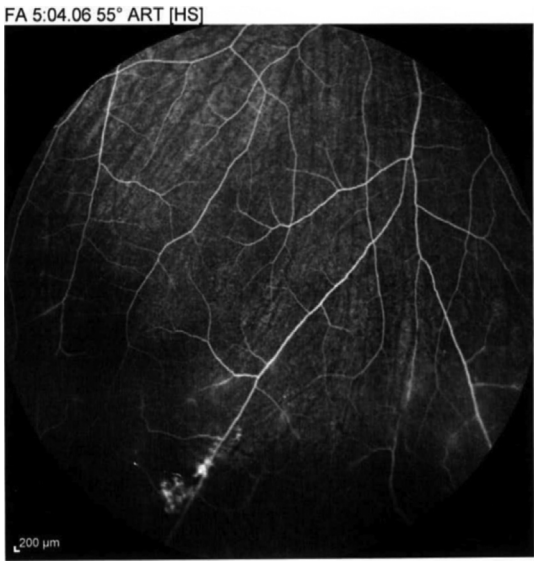

Fig. 6. Fluorescein angiography of the right eye showing changes in the architecture of retinal vessels straightening and tortuosity and peripheral leakage at 5:04 min of angiography.

Retinal vasculitis and its progression are the most threatening elements in the blinding outcome of ocular BD.

In their report of posterior segment involvement of ocular BD, Ozdal PC et al. studied 257 eyes and declared that the most frequent finding was vascular sheathing, observed in 23.7% of their cases, and they found diffuse FA leakage at the fundus on FA in 38% of their patients.[9] In our report on the causes of blindness in ocular BD, investigating 374 eyes of 187 patients retinal vasculitis (periphlebitis, periarteritis, vascular necrosis, or fibrosis) was observed in 77.5% of the eyes, significantly higher than our control group (non-blind cases), $p = 0.000$, and the most important cause of blindness was end-

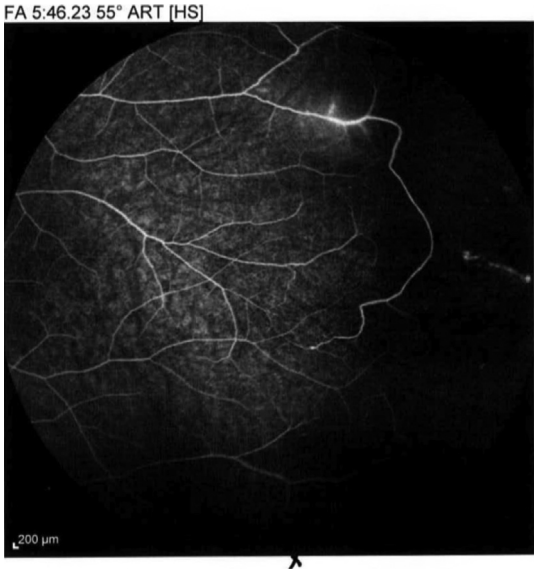

Fig. 7. Peripheral vascular shunt of the retinal vessels of the left eye with fluorescein leakage at 5:46 min of FA.

stage disease (58.5% of cases), which was the consequence of progression of chorioretinal vasculitis (vascular obliteration, necrosis, and fibrosis) causing chorioretinal and optic atrophy.[10]

It is well-established that retinal vasculitis of BD at its early appearance can regress and disappear under treatment, but if untreated, remains constant and progressive, causing obliteration, necrosis, and fibrosis of vessels.[4]

In this prospective, case-series study we investigated 50 BD patients (100 eyes) with apparently no ocular signs by routine clinical ophthalmic examination such as slit-lamp and 3-mirror of Goldmann; however, on FA of peripheral retina, we found fluorescein leakage in 44% of our cases.

Some investigations have emphasized the importance of widefield FA in the diagnosis of peripheral retinal lesions, which are not detectable otherwise.[11–13]

In our cases, we also observed profound changes (84% of eyes) on infrared autofluorescence of choroid hypo and hyper reflectivity, indicating deep changes of pigmentary cells and presumably vascular modifications of choroid. Atmaca et al. studied 112 eyes of ocular BD patients by ICG and reported hyper fluorescent lesions in 35.7% of the eyes, hypo fluorescent lesions in 15.2%, hypo and hyper fluorescent lesions 10.7%, and leakage from choroidal vessels in 9.8% on ICGA.[14]

In our cases, we also found modification of branching of vascular trees of retina in 25 patients (50% of cases), including straightening, tortuosity, and vascular shunt, which were essentially seen at the periphery of retina. Norouzpour et al. reported that retinal vascular fractal (D_f), which is used to quantify the changes in the branching pattern of the retinal vessels, was significantly lower in patients with ocular BD than the normal population.[15]

Peripheral retinal vascular leakage on FA, infrared modifications, and changes in retinal vascular branching could be seen in other diseases such as diabetes mellitus, trauma, or other vitreoretinal diseases, but our patients were free from all of these pathologies. Peripheral retinal abnormalities have even been reported in normal eyes.[11]

Ultra-widefield imaging is an evolving technology allowing better evaluation of the various vitreoretinal diseases including uveitis.[12,13] This technology offers a unique opportunity for quantitative analysis of peripheral vasculitis, ischemia, and vascular leakage. Although montage images do not reach the widefield of view of ultra-widefield imaging instruments, it offers a more peripheral view of fundus compared with conventional fundus FA.

Since our main interest was to study FA in these patients to detect retinal vasculitis by use of FA, we did not proceed more deeply to investigate the pattern of infrared hyper reflectivity of choroid, nor did we do D_f, which could be considered shortcomings of our work.

However, the major limitation of our study was the low number of patients and absence of a control group from the normal population to compare MFA, infrared autofluorescence, and branching tree of retinal vessels in those cases. We also included both eyes of patients, which may pose a bias from correlations between fellow eyes.

We recommend future studies to further evaluate the role of widefield imaging in BD as well as profound investigations of IR autofluorescence, ICG, and retinal vascular fractals, particularly for early diagnosis and the follow-up of these patients.

MFA of retina may be useful as an adjustment tool for early diagnosis of BD, early treatment, and follow-up of patients.

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