Original Article

Fundus Autofluorescence in Chronic Essential Hypertension

Alireza Ramezani[1,2], MD; Peyman Saberian[1], MD; Masoud Soheilian[1,2], MD; Saeed Alipour Parsa[2,3], MD Homayoun Koohi Kamali[2,3], MD; Morteza Entezari[1,2], MD; Mohammad-Mehdi Shahbazi[1], MD; Mehdi Yaseri[1,4], PhD

[1]Ophthalmic Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Department of Cardiology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Department of Biostatistics and Epidemiology, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Purpose: To evaluate fundus autofluorescence (FAF) changes in patients with chronic essential hypertension (HTN).

Methods: In this case-control study, 35 eyes of 35 patients with chronic essential HTN (lasting >5 years) and 31 eyes of 31 volunteers without history of HTN were included. FAF pictures were taken from right eyes of all cases with the Heidelberg retina angiography and then were assessed by two masked retinal specialists.

Results: In total, FAF images including 35 images of hypertensive patients and 31 pictures of volunteers, three apparently abnormal patterns were detected. A ring of hyper-autofluorescence in the central macula (doughnut-shaped) was observed in 9 (25.7%) eyes of the hypertensive group but only in 2 (6.5%) eyes of the control group. This difference was statistically significant (P = 0.036) between two groups. Hypo- and/or hyper-autofluorescence patches outside the fovea were the other sign found more in the hypertensive group (22.9%) than in the control group (6.5%); however, the difference was not statistically significant (P = 0.089). The third feature was hypo-autofluorescence around the disk noticed in 11 (31.4%) eyes of hypertensive patients compared to 8 (25.8%) eyes of the controls (P = 0.615).

Conclusion: A ring of hyper-autofluorescence in the central macula forming a doughnut-shaped feature may be a FAF sign in patients with chronic essential HTN.

Keywords: Autofluorescence; Chronic Essential Hypertension; Hyper-autofluorescence; Hypo-autofluorescence

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INTRODUCTION

Hypertension (HTN) is defined as persistently high blood pressure with currently accepted thresholds at 140/90 mmHg[1] which may be classified as either essential (the most common) or secondary. Essential HTN has no specific medical cause.[1] Although HTN is often asymptomatic, the disease is related to different types of target organ damage and associated clinical conditions.[2] It has been shown that in the eye, three distinct and independent manifestations occur due to HTN including hypertensive retinopathy, hypertensive optic neuropathy and hypertensive choroidopathy.[3]

The underlying mechanism for hypertensive choroidopathy relates to choroidal ischemia and its effects on the retinal pigment epithelium (RPE) and retina.[4] The more commonly described features of hypertensive choroidopathy are choroidal vascular sclerosis, focal areas of degenerative RPE (Elschnig spots), diffuse patchy atrophic RPE degeneration (in chronic HTN),[5,6] linear RPE changes (Siegrist's streaks),[7] and serous retinal detachment.[8]

Correspondence to:
Alireza Ramezani, MD. Department of Ophthalmology, Imam Hossein Medical Center, Madani St., Imam Hossein Ave., Tehran 16177, Iran.
E-mail: arramezani@gmail.com

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Fundus autofluorescence (FAF) is an imaging method that allows topographic mapping of lipofuscin distribution in the RPE cell monolayer.[9] Excessive accumulation of lipofuscin granules in the RPE cells represents a common downstream pathogenetic pathway in various retinal diseases. FAF imaging has been shown to be benefitial to understand the pathophysiologic mechanisms, diagnostics, and to identify the predictive markers of disease progression. This imaging technique gives information beyond that obtained by conventional imaging methods and its clinical value coupled with its simple, efficient, and noninvasive nature is increasingly appreciated.

Considering the RPE changes accompanying hypertensive choroidopathy and the ability of FAF imaging to demonstrate functional or structural changes of the RPE cells, it is anticipated that some abnormal findings would be observed on the FAF images of patients with long standing HTN. To determine such findings, we conducted the present study comparing FAF images of patients with chronic essential HTN with FAF images of individuals without HTN.

METHODS

This prospective case-control study was approved by the Review Board/Ethics Committee of the Ophthalmic Research Center at Shahid Behshti University of medical sciences, Tehran, Iran. The study protocol and the safety of taking FAF images were explained to all subjects before recruitment. The authors obliged themselves to notify the patients or the healthy subjects in case of finding any incidental pathology on the images that demanded management. Informed consent was obtained from both patient and control individuals.

All cases aged 30-50 years being followed in the cardiology clinic with a diagnosis of chronic essential HTN were included sequentially. Chronic essential HTN was defined as systolic and/or diastolic HTN higher than 140 and 90 mmHg, respectively, lasting >5 years and necessitating antihypertensive medication. The control group was selected from healthy patients' accompanying persons within the same age range. They did not have any history of HTN nor had a high blood pressure during the examination. Cases with diabetes, congestive heart failure, chronic renal failure, cigarette smoking, pregnancy, prior intraocular surgery, and any retinal disease that might alter FAF images were not included. We also did not include subjects with history of taking drugs which may lead to pigmentary changes in the fundus.

All cases, hypertensive or control, underwent systolic and diastolic blood pressure measurement and their age, sex, and history of ischemic heart disease were recorded. Then an ophthalmic examination consisted of checking anterior chamber angle and red reflex was performed. The subjects with an occludable angle or a poor red reflex precluding mydriasis and good-quality retinal images were excluded.

Mydriasis was achieved by three times installation of tropicamide 1% eye drop in the right eye. Then a foveal-centered FAF picture was recorded from the right eye of all cases with a SLO (model HRA/HRA 2; Heidelberg Engineering, Dossenheim, Germany). This instrument uses blue laser light at 488 nm for illumination and a barrier filter at 500 nm. The time for acquisition was approximately 30 s. The FAF images consisted of bit-mapped laser scans, 512 × 512 pixels in size. The setting was the same for each scan. Each image was the average of 6-9 raw scans automatically composed by the SLO software. We used the normalized FAF images for evaluation. All the FAF images were assessed by two retinal specialists at the same time and not independently. They were masked to the cases and recorded any probable abnormal findings.

Statistical Analysis

Assuming 5% abnormal FAF images in the control group, a sample size of 33 in each group could detect a 25% difference (5% vs. 30%) with a power of 80%. As some dropout were expected, we added two samples in each group.

Kolmogorov-Smirnov test was performed on data not showing any deviation from normality. To describe data, we utilized mean ± standard (SD) deviation, frequency (percent) and odds ratio (OR) with its related 95% confidence interval (95% CI). To investigate relations between qualitative data, we used Chi-square (or Fisher's Exact) tests. *T*-test was performed to compare quantitative data between two groups. $P < 0.05$ was considered to be statistically significant. All statistical analysis was performed using SPSS software (version 15; SPSS, Inc., Chicago, IL, USA).

RESULTS

A total of 35 FAF images of 35 patients in the hypertensive group were compared with 31 FAF images of 31 non-hypertensive individuals as controls [Table 1]. The groups were matched regarding age and gender. Mean systolic and diastolic pressure as well as history of ischemic heart disease were significantly more common in hypertensive patients.

In total, three apparently abnormal findings in all pictures were detected:

1. A ring of hyper-autofluorescence in the central fovea (doughnut-shaped) [Figure 1]
2. Hypo- and/or hyper-autofluorescence patches outside the fovea [Figure 2]
3. Hypo-autofluorescence around the disk [Figures 1-3].

Table 1. Comparison of the initial characteristics of the groups

	Hypertensive group (*n*=35) (%)	Normotensive group (*n*=31) (%)	*P* value
Mean age (years)	46.9±5.2	45.7±6.8	0.631*
Female/male	23/12	19/12	0.709**
Mean systolic pressure (mmHg)	146±21	117±5	<0.001*
Mean diastolic pressure (mmHg)	90±10	76±6	<0.001*
Ischemic heart disease	20 (57.1)	2 (6.5)	<0.001**

*Based on *t*-test, **Based on Chi-square test

A doughnut–shaped ring of hyper-autofluorescence in the central macula was noticed in 9 (25.7%) eyes of the hypertensive patients [Figure 1]. Such appearance was detected only in 2 (6.5%) eyes of the control group. The difference between the groups was statistically significant (P = 0.036) with an OR of 5.0 (95% CI: 1.05-25.39).

Hypo- and/or hyper-autofluorescence patches outside the fovea were observed more commonly in the hypertensive eyes as compared to the control eyes [Figure 2], 8 (22.9%) versus 2 (6.5%) eyes with an OR of 4.3 (95% CI: 0.8–22.1). However, the difference did not reach a significant level (P = 0.089). Mean time for history of HTN did not differ significantly between the subgroups with and without patches, 5.6 ± 1.8 versus 7.9 ± 3.1 years, respectively (P = 0.057).

In 4 out of 9 eyes in the hypertensive group and in 1 out of 2 eyes in the control group the rings were not complete [Figure 3]. Mean duration of HTN did not differ among hypertensive patients with and hypertensive patients without the doughnut–shaped ring of hyper-autofluorescence, 7.8 ± 3.4 versus 7.2 ± 2.8 years, respectively (P = 0.602).

Hypo-autofluorescence around the disk was found in 11 (31.4%) and 8 (25.8%) eyes of the HTN and control groups, respectively [Figures 1-3]. The difference was not statistically significant between the groups (P = 0.615). The OR was 1.3 (95% CI: 0.1-18.6).

DISCUSSION

FAF imaging gives information beyond conventional fundus photography and fluorescence angiography and represents a valuable means in the evaluation of RPE function in some ocular diseases.[10] In the present study, we intended to find some pathologic changes, discoverable by FAF imaging technique, mostly at the RPE level, and it was demonstrated that a doughnut–shaped feature in the central fovea on FAF images was seen significantly more in patients with chronic essential HTN as compared to normotensive cases,

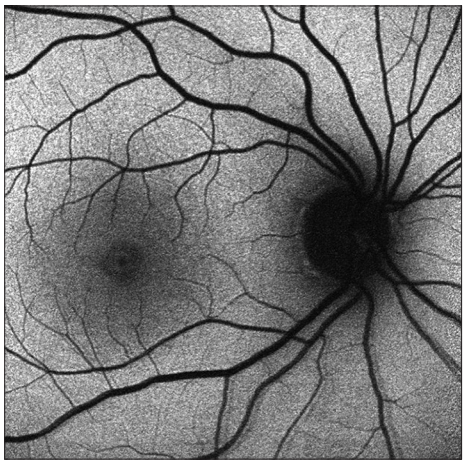

Figure 1. Fundus autofluorescence image of a hypertensive patient demonstrating a doughnut-shaped ring of hyper-autofluorescence in the central macula and accompanying hypo-autofluorescence around the disk.

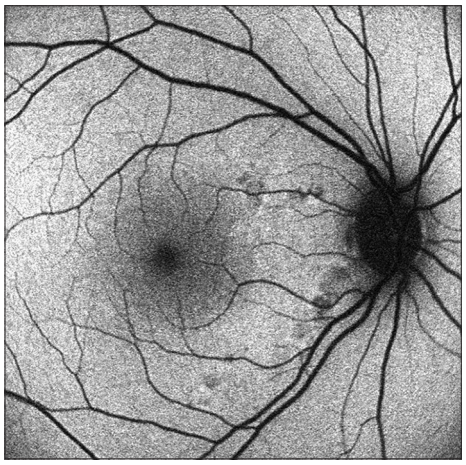

Figure 2. Fundus autofluorescence image of a hypertensive patient with multiple hypo- and/or hyper-autofluorescence patches outside the fovea and accompanying hypo-autofluorescence around the disk.

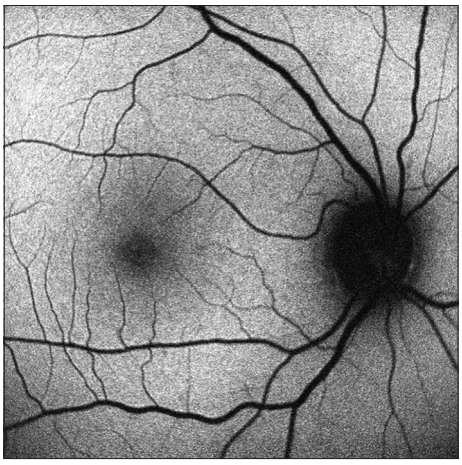

Figure 3. Fundus autofluorescence image of a hypertensive patient showing an incomplete ring of hyper-autofluorescence in the central macula and accompanying hypo-autofluorescence around the disk.

25.7% versus 6.5%. This feature consisted of an abnormal ring-shaped hyper-autofluorescence surrounding a small hypo-autofluorescence area centered on the fovea. In addition, the possibility of finding hypo- and/or hyper-autofluorescence patches outside the fovea was more on FAF images of cases with chronic HTN, but not to a significant level.

Evaluating 400 FAF images of cases (with or without early age-related macular degeneration) between 41 and 90 years of age, Trieschmann et al[11] identified four various types of macular pigment distribution based on size, distribution and intensity of hypo-and hyper-autofluorescence. All of these four types had a common feature, which was hypo-autofluorescence of the central fovea. The authors believed that this local hypo-autofluorescence may be due to a high level of blue light-absorbing macular pigment (i.e., lutein and zeaxanthin) and/or it may be a consequence of decreased emission by locally reduced levels of lipofuscin. The presence of a doughnut-shaped ring of hyper-autofluorescence in the macula of some hypertensive patients in our study might be due to higher accumulation of lipofuscin in RPE cells and/or reduction of macular pigment; either could be as a result of a chronic damage caused by high blood pressure.

Choroidopathy secondary to acute high blood pressure is a well-known phenomenon. Transmission of acute rises in blood pressure leads to choroidal ischemia and RPE necrosis and then formation of hypo-and hyper-pigmented patches in the central (Elschnig spots) or peripheral retina (Siegrist's streaks).[12,13] It may be hypothesized that long standing HTN (at least 5 years in our study) through chronic ischemia can cause stress on RPE cells and affects their function or may change macular pigmentations thus forming a ring of hyper-autofluorescence observed in our study. Nonetheless, it should be noted that RPE cells harboring a long-lasting stress, such as in chronic HTN might eventually die and result in hypo-autofluorescence. The absence of such finding, however, may be explained by the fact that HTN was nearly under control in most of our cases. Some other unknown mechanisms may be assumed for the formation of such rings, since this sign was also noted in two of our normotensive cases.

In a study, evaluating eyes with age-related macular degeneration, seven different types of autofluorescence changes named minimal change pattern, focal increased pattern, patchy pattern, linear pattern, lacelike pattern, reticular pattern, and speckled pattern were described.[10] None of them was noticed in our hypertensive patients. Furthermore, to the best of our knowledge, the doughnut-shaped hyper-autofluorescence of the macula has not been reported in association with any other diseases.

Another abnormal feature was hypo- and/or hyper-autofluorescence patches outside the fovea detected more frequently among hypertensive cases. This finding might represent previous attacks of acute high blood pressure. In other words, it might be correlated with the earlier mentioned pigmentary changes following accelerated blood HTN.[12,13] Since the difference between the groups regarding this finding did not reach a significant level, we could not draw any conclusion and this findings could be a coincidence. Should we evaluate more cases; however, this sign might also be recognized as another autofluorescence finding in hypertensive cases.

Hypo-autofluorescence around the disc was another abnormal finding in the present study noted in both case and control groups. However, this feature seemed to be a normal variant of autofluorescence pattern images considering its high occurrence (about 30%). Opposite to this finding is parapapillary hyper-autofluorescence which has been reported in patients with ocular HTN.[14]

In this study, we did not correlate visual acuity to the detected abnormal findings. There was a possibility that the eyes showing such findings may suffer from changes in visual acuity, visual field, color vision, or contrast sensitivity. Not-performing quantitative analysis on FAF images was another limitation of this study. Such evaluations could able us to detect more subtle changes in hypertensive patients.

To our knowledge, the current study was the first evaluation regarding changes in FAF images in patients with chronic HTN. It showed that a ring of hyper-autofluorescence in the central macula forming a doughnut–shaped feature might be an FAF sign in cases suffering from chronic essential HTN lasting >5 years. We may conclude that hypertensive patients may have some retinal problems which cannot be recognized by the other routine images and FAF imaging can be used for early detection of hypertensive retinopathy or choroidopathy. In addition, these changes may explain some visual complaints in hypertensive patients with no apparent cause. These findings, however, should be confirmed through future studies with larger sample.

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