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.\(^8\)
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 beneficial 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 cases or 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.

The control 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].
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, $5.6 \pm 1.8$ versus $7.9 \pm 3.1$ 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, $7.8 \pm 3.4$ versus $7.2 \pm 2.8$ 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. 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.
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 pigmentation 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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