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Changes in choroidal circulation and pulse waveform in a case of pregnancy-induced hypertension with serous retinal detachment

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ABSTRACT

Purpose: We aimed to examine the changes in choroidal blood flow (CBF), choroidal pulse waveform, and central choroidal thickness (CCT) in a case of pregnancy-induced hypertension (PIH) using laser speckle flowgraphy (LSFG) and enhanced depth imaging optical coherence tomography (EDI-OCT) before and after treatment with antihypertensive drugs.

Observations: A 24-year-old Japanese woman diagnosed with PIH presented with complaints of worsening and blurred vision in the right eye. Funduscopic findings at the initial visit showed serous retinal detachment (SRD), retinal hemorrhage, and arterial tortuosity. The LSFG color map showed a warm color. Macular mean blur rate (MBR), which is an index of relative blood flow velocity, in both eyes was high, along with choroidal thickening. Blowout time (BOT), which indicates the rate of time in which the MBR is greater than half the amplitude during one heartbeat, was low and acceleration time index (ATI), which represents the time-to-peak of MBR, was high. Several weeks after treatment with antihypertensive drugs, the CBF and ATI gradually decreased with regression of the SRD and thinning of the CCT. On the other hand, BOT gradually increased after treatment, showing a significant decrease in vascular resistance. Ocular perfusion pressure decreased after treatment because of the reduction in blood pressure.

Conclusions and Importance: LSFG might reveal choroidal overperfusion and increased vascular resistance, along with SRD and choroidal thickening, in a patient with PIH with reversal after treatment with antihypertensive drugs. These findings demonstrate the importance of evaluation of ocular blood flow and vascular resistance in women with PIH in order to routinely assess the clinical and systemic condition.

1. Introduction

Pregnancy-induced hypertension (PIH) complicates 6–10% of pregnancies, and is a complication resulting in maternal, fetal, and newborn mortality due to central nervous system dysfunction, thrombocytopenia, and disseminated intravascular coagulation.[1] PIH-related complications have been reported to occur in early-onset (<32 gestational weeks) compared to late-onset PIH.[2] PIH is also associated with ocular physiologic changes, and previous reports demonstrated that bilateral serous retinal detachment (SRD) is one of the causes of impaired vision in PIH, with a prevalence varying from 0.1% to 32.4%.[3,4] Additionally, vascular resistance is increased in cases of PIH due to an increase in resting sympathetic activity.[5]

In order to evaluate the retinal circulation, fluorescein angiography (FA) is a common and extraordinarily valuable procedure for the diagnosis of ocular disease. However, severe complications of FA such as spontaneous abortion, babies with low birth weights, and birth defects have been reported in pregnant women, in addition to vomiting or nausea.[6] Therefore, evaluations of the ocular circulation and vascular resistance are important in women with normal pregnancies as well as those with PIH using non-invasive method.

Laser speckle flowgraphy (LSFG-NAVI®, Softcare Co. Ltd., Fukuoka, Japan) is a non-invasive quantitative method that is very useful for measuring and assessing choroidal blood flow (CBF)[7,8] and pulse waveforms[9] based on the changes in the speckle pattern of the reflection of laser light from the fundus photo.[10] The mean blur rate (MBR) is a parameter of blood flow speed. A previous report has demonstrated the change in CBF in patients with acute hypertensive chorioretinopathy treated with antihypertensive agents.[11] However, to the best of our knowledge, changes in pulse waveforms in cases of PIH using LSFG before and after treatment has not yet been investigated. In the current case, we demonstrate the changes in pulse waveform and CBF in a case

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of PIH with SRD by using LSFG.

2. Case presentation

A 24-year-old woman presented with sudden worsening of visual acuity 1 week after an emergency cesarean section, which was indicated due to acute elevation of blood pressure caused by PIH at 32 weeks of gestation. She was referred to Toho University Sakura Medical Center in Sakura, Japan for a detailed eye examination.

Her blood pressure was 150/90 mmHg, and visual acuities of the right and left eyes were 20/25 and 20/20, respectively. The funduscopic examination showed SRD, involving macula, and tortuosity of the retinal arteries in both eyes, and retinal hemorrhage and tiny Elschnig's spots in the left eye (Fig. 1A and B). An enhanced-depth imaging optical coherence tomography (EDI-OCT) (Spectralis OCT, Heidelberg Engineering Inc., Heidelberg, Germany) scan revealed macular SRD, pachyvessels, thinning of the choroidal inner layers, and choroid thickening exceeding 800 and 524 μm in the right and left eyes, respectively (Fig. 1C and D).

We measured the CBF in both eyes using LSFG. LSFG panorama composite color images of both eyes are shown in Fig. 2A and B. The LSFG image of both eyes showed a warm color in the macular region, and the significant warm color in the right eye was observed at the choroidal area around the optic nerve head (ONH).

Subsequently, we performed FA and indocyanine green angiography (ICGA). FA also revealed massive multiple fluorescein leakage points around the optic nerve head of the right eye (Fig. 2C), and there were also mild leakage points in the left eye around the ONH (Fig. 2D). ICGA findings of both eyes also showed slight delayed filling of the choroid, dilated choroidal vessels, and clear multiple leakage points corresponding to the FA findings (Fig. 2E and F).

We diagnosed the patient with SRD associated with PIH, and initiated treatment with intravenous hydralazine and a calcium blocker. Two weeks after the initial visit, her blood pressure decreased to 128/98 mm, and the visual acuities of both eyes improved to 20/20. The panorama and macular LSFG color maps of the right and left eyes indicated that the amount of cool colors was higher (Fig. 3A–D) compared with that at the initial visit. EDI-OCT showed that CCT of the right and left eyes (346 and 343 μm, respectively) was decreased compared to baseline along with an improvement in SRD (Fig. 4A and B).

At the 6-week follow-up (the last visit), fundoscopic findings showed resolution of the SRD and retinal hemorrhage (Fig. 3E and F). LSFG color maps of the right and left eyes showed a cooler color at the 6-week follow-up (Fig. 3E and F). CCTs of the right and the left eye were 372 and 333 μm, respectively (Fig. 4C and D). By the end of the follow-up period, there was neither recurrence of SRD nor an increase in blood pressure.

3. Methods

3.1. Choroidal thickness

The central choroidal thickness (CCT) was assessed via EDI-OCT[12] (Fig. 1, bottom). The CCT were measured by two independent examiners (K.Y. and M.O.). CCT was determined via EDI-OCT by manually measuring the distance from the outer border of the hyper-reflective line corresponding to the retinal pigment epithelium (RPE) to the outer border of the choroid beneath the fovea, using a horizontal scan through the fovea. All examinations were performed between 12:00 noon and 3:00 p.m. in order to avoid circadian variations in choroidal thickness.[13]

3.2. Choroidal blood flow and pulse waveforms

LSFG was used to demonstrate the CBF and measure MBR, which is an indicator of blood flow, in patients with PIH.[10] In order to investigate the CBF at the subfovea using LSFG Analyzer software (Ver. 3.5.0.0, Softcare Co., Ltd), we set the measurement circle at the center of the macula in both eyes. We manually determined the circle's position by comparing infrared reflectance fundus images obtained by OCT.

Pulse waveform parameters were calculated by the LSFG Analyzer software. Blowout time (BOT) indicates the rate of time in which the MBR is greater than half the amplitude during one heartbeat. BOT is calculated according to the following formula[10]:

BOT = (duration of upper half amplitude/duration of a heartbeat) × 100.

Acceleration time index (ATI) represents the time taken to reach the peak of MBR. It is the ratio of the time taken to reach the peak to the duration of a complete heartbeat.[10]

ATI = (duration of peak/duration of a heat beat) × 100.

3.3. Hemodynamics

We measured IOP using a non-contact tonometer (Canon TX-F; Canon Inc., Tokyo, Japan). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using an automated sphygmomanometer (HBP-9020; OMRON Healthcare, Kyoto, Japan), in the sitting position, at the same time as measuring CBF, because there is a linear relationship between CBF and ocular perfusion pressure (OPP).[14] OPP was calculated from measurements of the patient's IOP and blood pressure, as described earlier.[7,8]

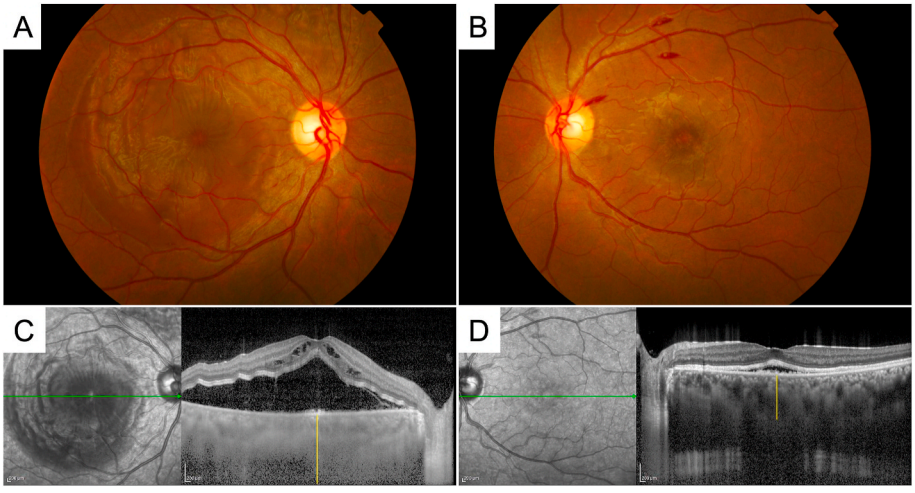

Fig. 1. Color fundus photography and enhanced-depth imaging optical coherence tomography findings at the initial visit. A color fundus photography in the right eye (A) and the left eye (C) shows serous retinal detachment involving the macular region. There was intraretinal hemorrhage in the left eye. Enhanced depth image optical coherence tomography (EDI-OCT) findings in the right (C) and the left eyes (D) revealed macular serous retinal detachment and choroid thickening over 800 μm and 524 μm at the initial visit. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

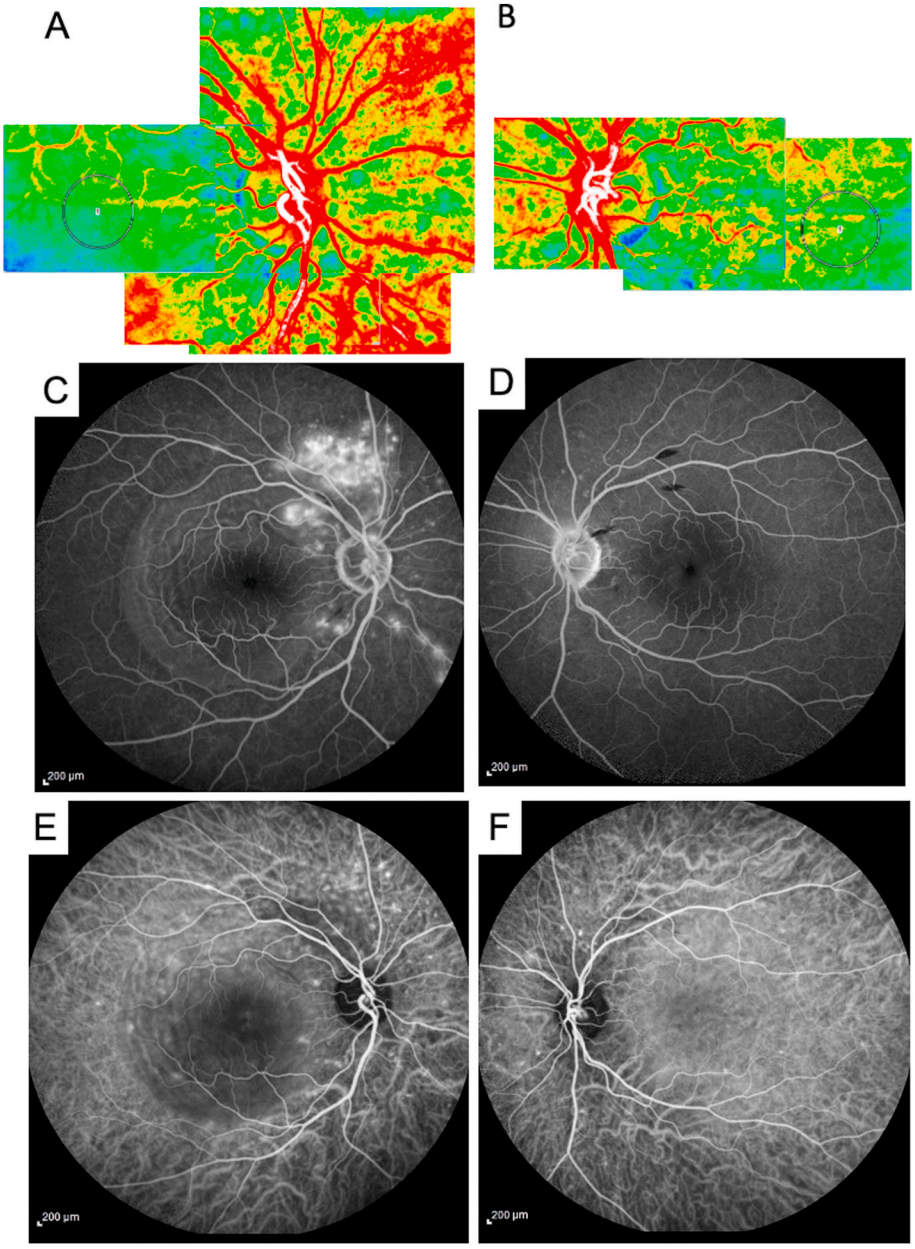

Fig. 2. Laser speckle flowgraphy as well as fluorescein and indocyanine green angiography findings at the initial visit. (A, B) Panorama laser speckle flowgraphy (LSFG) composite color images of both eyes. The LSFG image of both eyes showed warm colors in the macular region, and significant warm colors in the right eye were observed at the choroidal area around the ONH. (C, D) Fluorescein angiography (FA) findings at the late phase. Multiple massive and mild leakage points in the right and left eyes were observed. (E, F) The indocyanine green angiography findings of both eyes also revealed multiple leakage point corresponding to the FA findings. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

4. Results

4.1. Choroidal thickness

The CCT of the right and left eyes were 800 and 524 μm at the initial visit, 346 and 343 μm at the 2-week follow-up, and 372 and 333 μm at the 6-week follow-up, respectively.

4.2. Choroidal blood flow and pulse waveforms

The time course in MBR, BOT, and ATI in the right and left eyes are shown in Table 1. Fig. 5A and B shows changes in pulse waveforms between the initial visit and 2-week follow-up in the right and left eyes. MBR decreased and the ratio of the half width to the duration of one complete cardiac cycle increased at the 2-week follow-up.

MBR, mean blur rate; AU, arbitrary units; BOT, blowout time; ATI, acceleration time index.

4.3. Ocular perfusion pressure

The OPP was 62.3 mmHg in each eye at the initial visit; at the 2-week and 6-week follow-up visits, the OPP in the right and left eyes were 59 and 57 mmHg, and 41.7 and 44.7 mmHg, respectively. There was no correlation between the OPP and CBF.

5. Discussion

This study was the first to report changes in choroidal circulation and vascular resistance in a patient with PIH and SRD before and after treatment with antihypertensive medications using non-invasive LSFG and BOT, which has been reported to be significantly and negatively correlated with systemic vascular resistance.[5]

At the initial visit, the CBF of both eyes was significantly increased along with CCT. During the pregnancy, nitric oxide (NO), which has an important role in controlling CBF (i.e., autoregulation),[15] is a key factor in both maternal and fetal homeostasis. The dysfunction of the NO system during pregnancy has been reported to be involved in placental

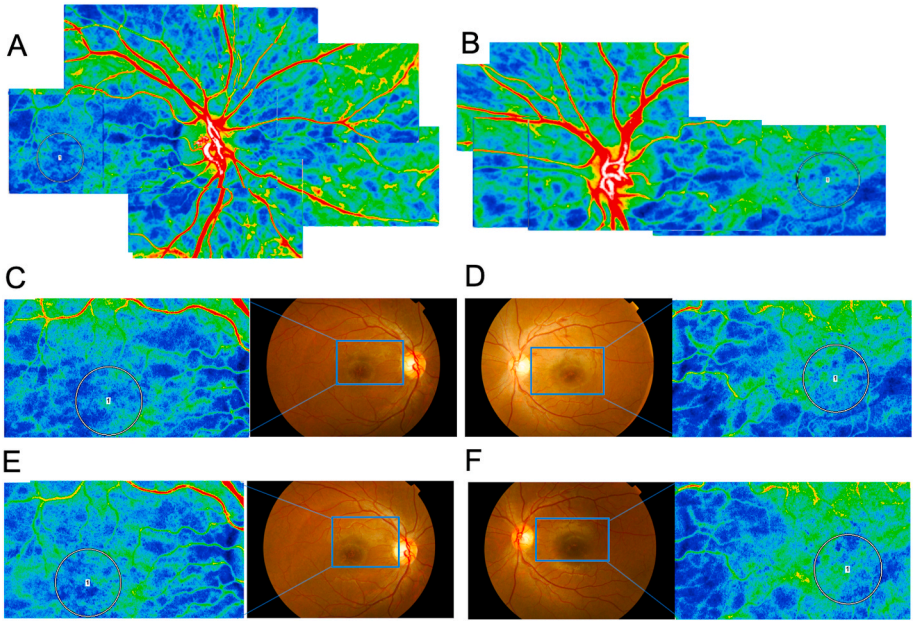

Fig. 3. Change in laser speckle flowgraphy (LSFG) color image before and after treatment with antihypertensive drugs. (A, B) Panorama LSFG findings of the right and left eye 2 weeks after the initial visit. A significant increase in the cooler colors was observed. (C, D) Color composite map of the choroid and fundus 2 weeks after the initial visit. (E, F) Color composite map of the choroid and fundus 6 weeks after the initial visit. LSFG images show that cool colors increased over time. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

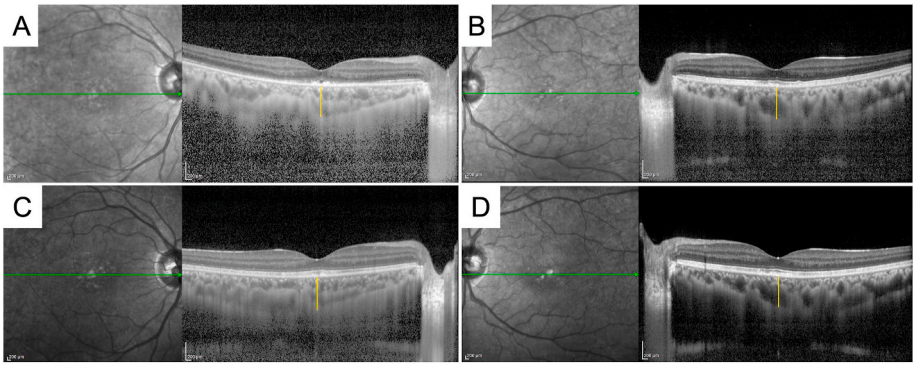

Fig. 4. Change in central choroidal thickness before and three months after the treatment. Enhanced depth imaging optical coherence tomography (EDI-OCT) findings of both eyes at two and six weeks after the treatment are shown. (A, B) The central choroidal thickness in the right eye (346 μm) and the left eye (343 μm) 2 weeks after the treatment. (C, D) The central choroidal thickness in the right eye (372 μm) and the left eye (333 μm) 6 weeks later the treatment.

Table 1
Changes in choroidal blood flow and pulse waveforms.

	Right eye			Left eye		
	MBR (AU)	BOT	ATI	MBR (AU)	BOT	ATI
Initial visit	10.7	47.5	36.2	14.1	42.6	37.6
2 weeks	5.4	58.4	25.5	6.2	54	31.1
6 weeks	5.6	56.7	21.3	6.6	52.9	23.1

and vascular-related diseases such as PIH.[16] In the current case, OPP was increased due to the elevated blood pressure at the initial visit.

The choroidal circulation is very well known to have a very weak autoregulatory system. Akahori et al. reported a linear relationship between CBF and OPP in healthy young subjects, within a certain range.[17] Regarding the relationship between CCT and OPP, a significant positive correlation has been reported in patients with central serous chorioretinopathy (CSC) with SRD.[18] From the above findings and the fact that there is a greater volume of circulating blood in pregnant women,[19] the mechanism for the increases in CBF and CCT in patients with PIH might result from the acutely elevated OPP and impaired choroidal vascular autoregulation via dysfunction of the NO system.

However, a previous study in an uncomplicated pregnancy showed no change in the retinal blood flow throughout.[20] On the other hand, the retinal blowout score tended to increase, and resistivity index significantly decreased between 28 and 30 weeks of pregnancy. The contradictory findings in the current case might be related to differences in the elevation of blood pressure and the differences in the autoregulatory capacity of the retina and choroid.

In contrast to an increase in CBF, the BOT in the choroid at the initial visit was decreased compared to that at other time points. The BOT was significantly and negatively correlated with systemic vascular resistance.[21] Additionally, an increase in BOT was observed along with the regression of SRD in the patient with acute CSC.[9] The previous report demonstrated that PIH might be associated with a greater resting sympathetic output compared with normal pregnancies.[5] Besides, the levels of peripheral vascular resistance were higher in women who developed PIH than those who had a normal pregnancy.[22] In light of these findings, lower BOT in the macular region might demonstrate higher vascular resistance of the choroidal vasculature due to elevated sympathetic activity in PIH.

As well as an increase in CBF, the ATI in the choroid at the initial visit was higher than at other time-points. Considering that ATI represents the time to reach the peak of MBR,[10] it is understandable that an increase in ATI might indicate higher vascular resistance.

In this case, acute central serous chorioretinopathy (CSC) should be

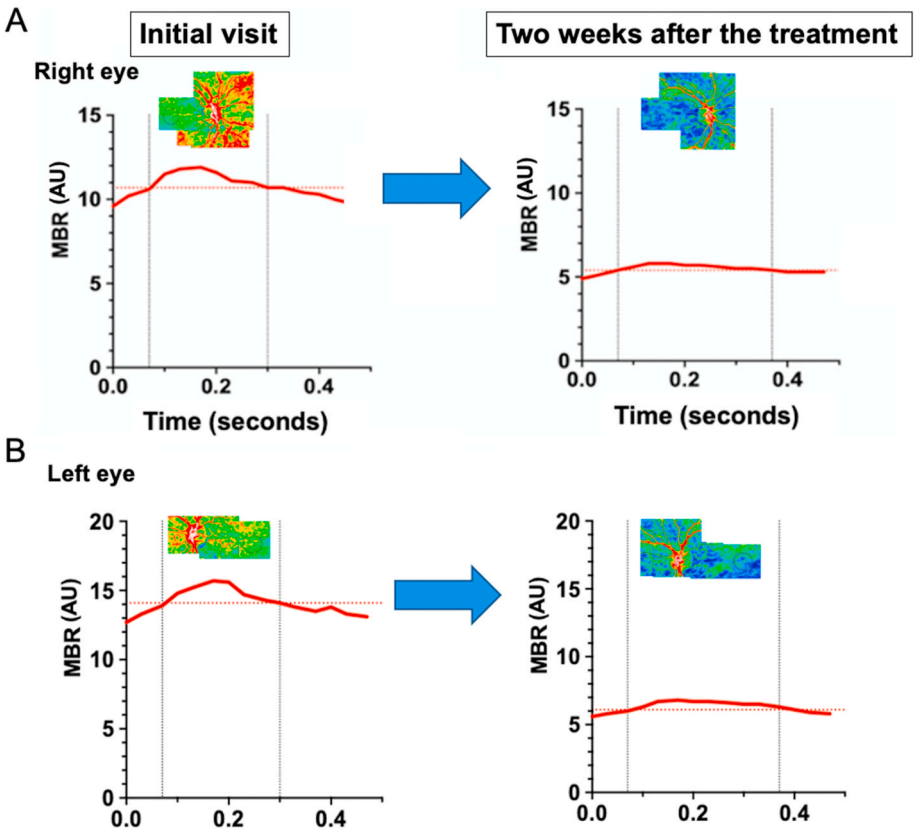

Fig. 5. Change in the pulse wave forms before and after treatment with antihypertensive drugs. (A, B) The pulse wave forms of the right and left eyes were shown. A decreased in mean blur rate and an increased ratio of the half width to the duration of one complete cardiac cycle 2 weeks after the initial visit were observed.

considered as a differential diagnosis. Pregnancy is thought to be a predisposing factor for CSC.[23] However, the patient presented with sudden worsening of visual acuity after an emergency cesarean section, and her blood pressure was high, despite presenting with no history of hypertension. Considering the history and funduscopic findings of retinal hemorrhage and vessel tortuosity, we diagnosed SRD associated with PIH.

Saito et al. reported that the etiology of elevated macular blood flow in acute CSC eyes might lie in local vasoconstriction of choroidal arteries due to sympathetic overactivity.[9]

They also speculated that disturbed perfusion in the choriocapillaris leads to a secondary passive overflow into the surrounding large choroidal veins via adjacent branches of the lobule's circulatory unit in acute CSC eyes.[9] The current case showed higher CBF, along with the higher vascular resistance (low BOT and high ATI), before the treatment. Taken together, the pathogenesis of SRD associated with PIH might be very similar to that of acute CSC.

After the treatment of antihypertensive agents, OPP was reduced due to the improvement in systemic blood pressure, and LSFG findings revealed a decrease in MBR and ATI and an increase in BOT, along with the resolution of SRD.

In this case, the patient was treated with hydralazine and a calcium channel blocker at the initial visit. Hydralazine and calcium channel blockers have been reported to play an essential role in direct vasodilation of the arterioles.[24,25]

The findings of this case suggest that the mechanism for the decreased CBF and vascular resistance might be associated with treatment modalities aimed at reducing the peripheral vascular resistance.

6. Conclusions

In conclusion, LSFG might reveal choroidal overperfusion and increased vascular resistance, along with SRD, and choroidal thickening in a patient with PIH, with changes after treatment with antihypertensive drugs. The pulse waveform and MBR parameters using LSFG might be useful to assess and quantitively follow cases of PIH.

6.1. Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

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Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

Authors' contributions

All authors contributed significantly to the creation of this manuscript; each fulfilled the criteria established by the ICMJE.

Declaration of competing interest

None.

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