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Analysis of optic disc tilt angle in intrapapillary hemorrhage adjacent to peripapillary subretinal hemorrhage using swept-source optical coherence tomography

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A R T I C L E I N F O

Keywords:
Intrapapillary hemorrhage with adjacent peripapillary subretinal hemorrhage (IHAPSH)
Tilted disc
Tilt angle
Disc hemorrhage
Myopia
Optical coherence tomography (OCT)

A B S T R A C T

Purpose: To report findings on the tilt angle of optic nerve heads (ONHs) that developed intrapapillary hemorrhage with adjacent peripapillary subretinal hemorrhage (IHAPSH) using swept-source optical coherence tomography (SS-OCT).

Observations: Five consecutive patients who presented with IHAPSH were reviewed retrospectively. We reviewed five consecutive eyes from the five patients, analyzed the optic tilt angle obtained from SS-OCT B-scans, and compared the results and other clinical characteristics. All patients had larger optic disc tilt angles in the eyes with IHAPSH than in the contralateral, unaffected eye. The mean ratio of the tilt angle in the eyes with IHAPSH to that in the contralateral eye was 1.37 (95% confidence interval 1.15–1.58).

Conclusions and Importance: The ONH of IHAPSH was evaluated quantitatively with SS-OCT for the first time in this study. Larger angle tilted discs in IHAPSH-affected eyes are anatomically and histologically more vulnerable and may explain why IHAPSH develops monocularly.

1. Introduction

Intrapapillary hemorrhage with adjacent peripapillary subretinal hemorrhage (IHAPSH) is a clinical syndrome most commonly affecting young Asians with mild myopia, who experience the condition abruptly and monocularly.[1–5] IHAPSH has been described since 1975 [6]; however, it is a relatively rare syndrome, and the cause of this condition is still uncertain. Because hemorrhage resolves spontaneously without sequelae,[1–5] there are only a few cases that lead to an ophthalmic consultation, and the reported cases are limited to those with subjective symptoms due to vitreous hemorrhage. Therefore, the etiology of this condition is still unknown. One of the risk factors is a tilted disc. Kokame et al. reported that 8 eyes out of 10 eyes had a tilted disc.[2] Zou et al. observed IHAPSH that met our criteria in 34 eyes out of 38 eyes and reported that all of them had a tilted disc.[4] The definition of a tilted disc, however, is subjective and has not yet been quantitatively evaluated in eyes with IHAPSH. In this study, we measured the tilt angle using swept-source optical coherence tomography (SS-OCT) and revealed that eyes with larger tilt angles developed IHAPSH compared with contralateral eyes.

2. Methods

2.1. Study design

The current study is an observational case series in which we retrospectively reviewed the records of patients who had been diagnosed with IHAPSH at Osaka University Hospital from June 2015 through June

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Table 1
Subject demographics and clinical characteristics.

Case	Case 1	Case 2	Case 3	Case 4	Case 5
Age	13	20	13	19	12
Sex	F	M	F	F	M
Affected Eye	R	R	R	L	R
Spherical Equivalent [D]	−4.25; −4.50	−7.25; −6.875	−3.75; −3.75	−5.75; −5.50	−2.625; −2.75
BCVA [SNELLEN]	20/12.5; 20/12.5	20/63; 20/12.5	20/16; 20/16	20/12.5; 20/12.5	20/12.5; 20/12.5
Axial Length [mm]	–	27.36/27.14	–	–	25.54/25.55
Vitreous Hemorrhage	+	+	+	+	+
[A] Tilt Angle [degrees] in Eyes with IHAPSH	9.44	12.01	23.29	8.63	8.80
[B] Tilt Angle [degrees] in Eyes without IHAPSH	7.01	9.88	14.65	6.45	6.41
Tilt Angle Ratio ([A]/[B])	1.35	1.22	1.59	1.34	1.37
Recurrence	none	none	none	none	none
Sequelae	none	Permanent visual field impairment	none	none	none
Family History of Ocular Diseases	–	Father: glaucoma suspected	Mother: keratoconus	–	–

BCVA, best-corrected visual acuity.

2021. The research adhered to the tenets of the Declaration of Helsinki. The institutional review board of Osaka University approved the study.

2.2. Diagnosis

The diagnosis of IHAPSH was based on the characteristic findings on color fundus photography and SS-OCT in all cases. All patients showed both intrapapillary hemorrhage and continuous subretinal hemorrhage. Exclusion criteria included disc hemorrhage only without adjacent peripapillary subretinal hemorrhage, subretinal hemorrhage only without associated intrapapillary hemorrhage, optic disc drusen, peripapillary subretinal neovascularization, ischemic optic neuropathy, Terson's syndrome, polypoidal choroidal vasculopathy, optic neuritis and Leber's idiopathic stellate neuroretinitis. All patients were followed up until the bleeding was completely resolved, and in cases 2 and 3, visual field tests were performed regularly every 6 months until the writing of this report to confirm the lack of progress.

2.3. Imaging and examination

Medical records were reviewed for the following data: refraction test results, best-corrected visual acuity (BCVA), axial length (with an IOLMaster 700; Carl Zeiss Meditec, Dublin, CA), and Goldmann perimetry, slit-lamp biomicroscopy, standard automated perimetry (with a Humphrey Field Analyzer II; Swedish interactive threshold algorithm; Carl Zeiss, Meditec, Dublin, CA), dilated fundus stereoscopic examination, fundus color stereophotography (with a TRC-50DX; Topcon, Tokyo, Japan) and SS-OCT (with a DRI OCT-1; Atlantis, Topcon Corporation, Tokyo, Japan) results.

2.4. SS-OCT analysis

We (R.K., an experienced glaucoma specialist, and S.T., a retina specialist) measured the optic disc tilt angle using SS-OCT B-scan and ImageJ software (version 1.53, http://imagej.nih.gov/ij/;provided in the public domain by the National Institutes of Health, Bethesda, MD, USA) in accordance with previously described methods.[7–9] SS-OCT B-scan images were acquired in radial scans centered on the optic disc to select the direction indicating the maximum tilting around the optic disc. As described in previous studies, the optic disc tilt angle was defined as the angle between the reference plane, which connects the inner edge of the nasal and temporal Bruch membrane (BM), and the optic disc canal plane, which connects the inner edge of the nasal BM and temporal margin of the optic disc canal, which was defined as the end of the externally oblique border tissue.[8–11] The tilt angle in the eye with IHAPSH divided by that in the eye without IHAPSH is defined as the tilt angle ratio.

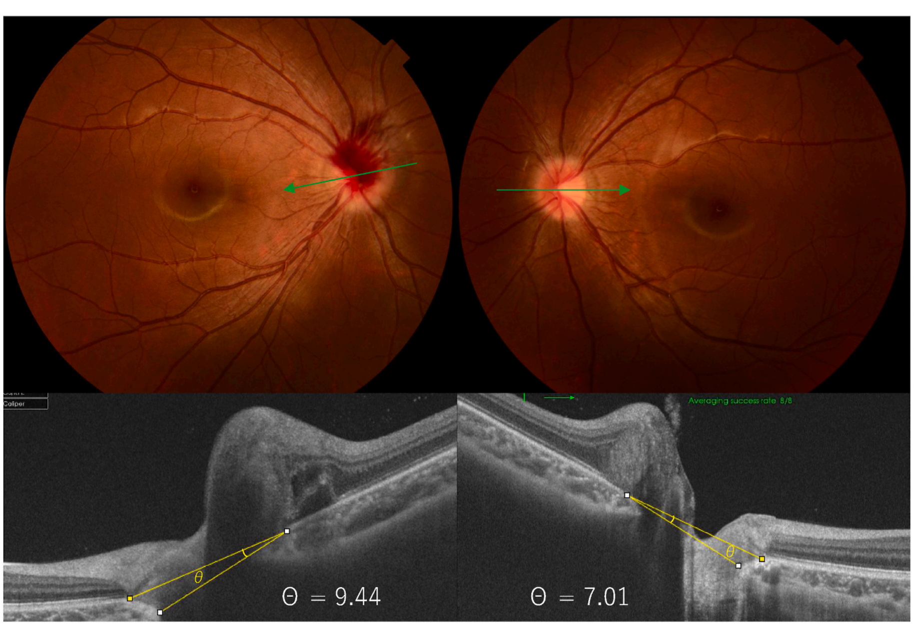

Fig. 1. Case 1. While watching TV, a 13-year-old female suddenly recognized floaters in her right eye. Top row: Fundus photographs. Intrapapillary bleeding can be seen on the nasal side of the optic nerve head (ONH) of the right eye, and subretinal hemorrhage spreads to the upper nasal side.
Bottom row: Swept-source optical coherence tomography (SS-OCT) B-scan images. The tilt angle is 9.44° in the right eye and 7.01° in the left eye (tilt-angle ratio: 1.35 (9.44/7.01)).

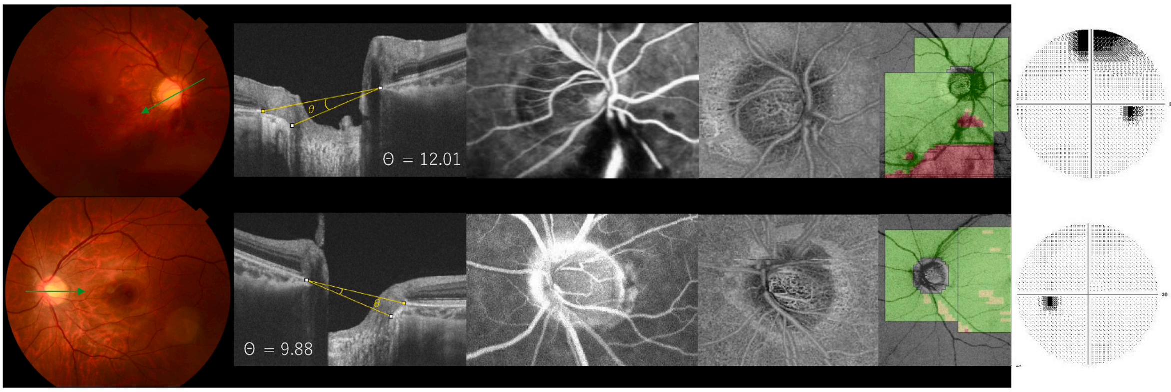

Fig. 2. Case 2. After a 20-year-old male underwent surgery for a tongue tumor, he complained of blurred vision in his right eye.
First column: Fundus photographs one week after onset showed IHAPSH extending to the inferior SRH, vitreous hemorrhage and subinternal limiting membrane hemorrhage.
Second column: SS-OCT B-scan images. The tilt angle is 12.01° in the right eye and 9.88° in the left eye (tilt-angle ratio: 1.22 (12.01/9.88)).
Third column: Fluorescein angiography demonstrating a blocking defect resulting from intrapapillary hemorrhage but unremarkable focal disc staining, which suggests possible inflammation of the nerve with stimulation of the hemorrhage. The arcade vein at the bleeding site is dilated, and mild leakage is observed, indicating increased permeability by inflammation.
Fourth column: Optical coherence tomography (OCT) angiography of the ONH 4 months after onset shows normal density of the intrapapillary vessel network.
Fifth column: OCT retinal nerve fiber layer (RNFL). The red color indicates a thinned RNFL, which is consistent with the lesion of the visual field defect on Humphrey 30-2 examination (sixth column).Sixth column: Humphrey 30-2 examination one year after onset shows a visual field defect along the inferior arcade in the right eye, likely due to retinal atrophy caused by SRH. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

3. Statistics

To analyze the effect of refraction on the tilt angle of the ONH, we calculated Spearman's correlation coefficients (alpha = 0.05) between the spherical equivalent and tilt angle. Differences in variables between paired eyes were assessed using the Wilcoxon signed-rank test (alpha = 0.05) for parameters without a normal distribution. Statistical analyses were performed using R software version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria; https://www.r-project.org/).

4. Results

Table 1 shows the clinical features of 5 eyes of 5 patients (2 men, 3 women; mean age, 15 ± 3.8 years). All patients had not only an acute onset of visual symptoms at presentation, including blurred vision, floaters, and decreased visual acuity, but also vitreous hemorrhage. In case 2, the patient had a preceding history of Valsalva maneuvers. Of the 5 cases, 4 cases progressed without sequelae as the bleeding was absorbed as previously reported,[1–5] but only 1 case (case 2) had extensive subretinal hemorrhage (SRH)-induced visual field impairment. All eyes were myopic, including 1 mildly myopic (≦3 diopters (D)), 3 moderately myopic (-3D to −6 D), and 1 severely myopic (≧6 D). The best-corrected Snellen visual acuities were 20/16 or better in 4 eyes and 20/63 in case 2, which improved to 20/16 one week later.

In all cases, the tilt angle of the affected eye was larger than that of the contralateral eye. The mean value of the tilt angle ratio of the 5 cases was 1.37. The spherical equivalents in the affected and contralateral eyes were practically uncorrelated with the optic disc tilt angle according to Spearman's correlation coefficients.

4.1. Case 1

While watching TV, a 13-year-old female suddenly recognized floaters in her right eye, and as there was no improvement, she visited a local ophthalmologist. The patient was referred to our clinic for the treatment of optic disc hemorrhage and vitreous hemorrhage in the right eye. There was no personal or family history of ophthalmological or systemic disease. Her BCVA was 20/12.5 in both eyes, and the intraocular pressure (IOP) was 16 mmHg in the right eye and 18 mmHg in the left eye. She underwent follow-up without treatment of IHAPSH in the right eye, and the hemorrhage resolved spontaneously. We diagnosed the patient with congenitally anomalous because the optic disc margin was unclear bilaterally from the initial visit and it persisted after absorption of bleeding in the involved eye. The tilt angle measured by SS-OCT was 9.44° in the right eye and 7.01° in the left eye (tilt angle ratio: 1.35) (Fig. 1).

4.2. Case 2

A 22-year-old man presented with low visual acuity in the right eye. He had a previous history of tumor resection and left forearm flap grafting under general anesthesia for tongue cancer. On regaining consciousness from general anesthesia, he complained of severe left arm pain and had to be restrained to avoid falling from the bed. A Valsalva maneuver was then performed. Immediately after regaining consciousness, he reported decreased vision in his right eye and was referred to our hospital. The BCVA in his right eye was 20/63, and he had high myopia. Examination of the fundus showed IHAPSH extending to an inferior SRH, as well as a vitreous hemorrhage and subinternal limiting membrane hemorrhage. The tilt angle of the ONH on the SS-OCT image was larger in the affected eye than in the contralateral eye (12.01° versus 9.88°, respectively; tilt angle ratio: 1.22). Fluorescein angiography revealed no thrombosis, a normal arm-to-retinal circulation time and a blocking defect resulting from intrapapillary hemorrhage but unremarkable focal disc staining, which suggested possible inflammation of the nerve with stimulation of the hemorrhage. Blood laboratory work-up and brain computed tomographic scans showed no remarkable abnormalities. At the 1-week follow-up, the vitreous hemorrhage was prominently resolved, the BCVA had improved to 20/16, and OCT angiography showed no vascular abnormalities at the ONH. One year after onset, however, a visual field defect was noted along the inferior arcade, likely due to retinal atrophy caused by SRH (Fig. 2).

4.3. Case 3

A 13-year-old female who often experienced headaches suddenly noticed a black shadow that appeared in the right eye before going to bed. The patient visited a nearby ophthalmologist. The patient was referred to our department because of a right vitreous hemorrhage. She had moderate myopia but had no history of ophthalmological disease.

Fig. 3. Case 3. A 13-year-old female who often experienced headaches suddenly noticed a black shadow in the right eye before going to bed.
Top row: Fundus photographs. IHAPSH can be observed at the nasal superior quadrant of the ONH in the right eye, but it does not correspond with the site of the visual field defect (see Goldmann perimetry (GP) in the third row).
Second row: The tilt angle measured is 23.29° in the right eye and 14.65° in the left eye (the tilt-angle ratio: 1.59)
Third row: GP at presentation reveals bilateral temporal hemianopsia due to optic disc hypoplasia.
Bottom row: There was no significant change in the visual field defects according to GP 6 years later.

The mother had a keratoconus. The BCVA was 20/16 in both eyes, and the IOP was 12 mmHg in the right eye and 13 mmHg in the left eye. Fundus color photography revealed binocular blurred optic disc margins, but we concluded them to be congenitally anomalous because they had not changed without any inflammation. Goldmann perimetry revealed bilateral temporal hemianopsia, and head magnetic resonance imaging showed no intracranial tumor or other abnormal findings. IHAPSH was found at the nasal superior quadrant of the ONH in the right eye, but it did not correspond with the site of the visual field defect. Since it has not changed at the time of writing, it is presumed to be a congenital defect due to optic nerve hypoplasia. All the bleeding was absorbed in 3 months. The tilt angle measured was 23.29° in the right eye and 14.65° in the left eye (tilt angle ratio: 1.59) (Fig. 3).

4.4. Case 4

The patient was a 19-year-old female who suddenly developed floaters in the left eye and visited a nearby ophthalmologist. A left optic disc hemorrhage and vitreous hemorrhage were observed. The patient was referred to our department after resolution of the vitreous hemorrhage. There was no family history. She had myopia of −5.50 diopters in the right eye and −5.25 diopters in the left eye. The BCVA was 20/16 and the IOP was 16 mmHg in both eyes. The unclear optic disc margin was observed in both eyes over the course of treatment, even after

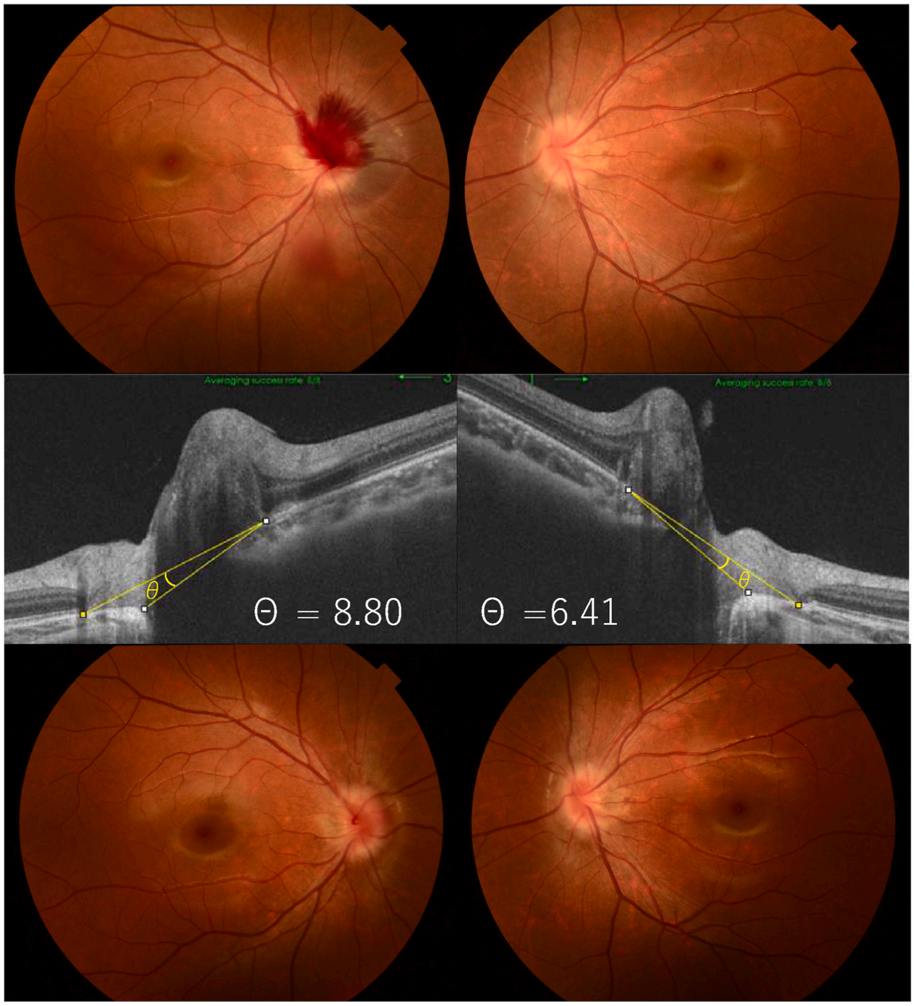

Fig. 4. Case 5: A case of IHAPSH in a 12-year-old boy
Top row: Color fundus photograph at onset shows bleeding on the upper nose of the optic disc in the right eye. The unclear optic disc margin is observed in both eyes, but it has remained unchanged 4 months later (bottom row). We diagnosed the patient with congenitally anomalous.
Middle row: SS-OCT shows a tilt angle of 8.80° in the right eye and 6.41° in the left eye (tilt-angle ratio: 1.37). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

bleeding resolution. Head MRI and blood tests were performed to exclude optic neuritis, but no findings of inflammation were observed. The tilt angle was 6.45° in the right eye and 8.63° in the left eye. Five and a half months later, the papillary hemorrhage was also absorbed, and the patient's course was good, so a final follow-up was performed (Table 1).

4.5. Case 5

A 12-year-old boy suddenly noticed blurry vision and floaters in the right eye one night without any inciting event, and the next day, he visited a local ophthalmologist. He was referred to our department on the same day because the slit-lamp examination revealed IHAPSH in the right eye. The BCVA was 20/12.5 in both eyes. He had mild myopia (S −2.625 diopters OD and −2.75 diopters OS) and an axial length of 25.54 mm in the right eye and 25.5 mm in the left eye. Fundus color photography showed IHAPSH in the right eye. He had no history of ophthalmic disease or family history. The tilt angle was 8.80° in the right eye and 6.41° in the left eye (tilt angle ratio: 1.37) (Table 1). The optic disc margin in both eyes persisted unclear even after absorption of the bleeding in the right eye (Fig. 4).

5. Discussion

In this study, the patient in case 2 did not seem to have tilted discs from the fundus photographs at first glance; however, SS-OCT revealed that the optic discs were tilted, with a clearly larger angle than that of the normal eyes without myopia ($2.3 \pm 1.7°$).[8] As a result, discs defined as nontilted in previous literature[1–5,12] could be redefined as tilted with the measurement method in this study. Quantifying the tilt angle might allow us to clarify the disease concept of IHAPSH. On the other hand, moderate to high myopia (-1.50 to −7.00 spheres) is one of the characteristics of IHAPSH,[1–6,12] and it is presumed intuitively that the diopters of myopia are correlated with the eyes with IHAPSH, but that was not the case here. Therefore, it is not possible to predict which eye is its onset from the severity of myopia.

IHAPSH largely occurs monocularly.[1–5,12] This might be explained by the results of this study, which showed that there was a difference in the optic disc tilt angle between the eyes; the tilt angle of the affected eye was larger than that of the other eye in all cases. The tilt angle ratio of the affected eye to the contralateral eye ranged between 1.22 and 1.59; the mean value across the 5 cases was 1.37, and its 95% confidence interval ranged between 1.15 and 1.58. This supports the hypothesis that when changes in blood flow pressure occur in the ONH for some reason, such as during Valsalva maneuvers[13] and sneezing,[14] bleeding occurs in discs that have a greater tilt angle, i.e., are anatomically and histologically more vulnerable to changes in blood pressure. The IOP and cerebrospinal and intravascular pressure increase, which can lead to bleeding from vulnerable blood vessels.[15] In fact, over 60% of young healthy eyes during Valsalva maneuvers can show significant anterior displacement of the lamina cribrosa,[16] causing mechanical damage to the ONH. The prelaminar region is supplied by peripapillary choroidal arteries and posterior short ciliary arteries.[17] Choroidal vessels without barriers are likely to become congested with increased pressure.

Peripheral vessels derived from the short posterior ciliary artery around the prelaminar region, which is not supported by the lamina cribrosa, may have ruptured and bleed.[17]

There are several limitations to this study. First, the sample size was too small to analyze the data in detail and the study had a retrospective design. Second, there were no data allowing a comparison of normal right and left eyes. Therefore, the cutoff value for the tilt angle ratio could not be determined because the normal tilt angles were not available. In future research, we plan to conduct case-control studies to proceed with the analysis. Finally, the axial length was measured in only two cases. The axial length is correlated with the tilt angle,[9] but this could not be confirmed in this case series. Since we had no perspective on the correlation between the tilt angle and the axial length and measurement of the axial length for retinal hemorrhage is not performed in daily practice, the axial length was not measured in many cases.

6. Conclusions

In conclusion, to the best of our knowledge, the ONH of IHAPSH was evaluated quantitatively with SS-OCT for the first time in this study. Furthermore, in all cases, the eye affected by IHAPSH had a larger tilt angle than the contralateral eye. A larger tilt angle may be correlated with the development of IHAPSH. This might explain the mechanism by which IHAPSH develops monocularly.

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.

Declaration of competing interest

The following authors have no financial disclosures: (S.T., R.K., T.M., S.S., D.S., K.N., R.K., H.S., K.N.)

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