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Increased choroidal thickness in a patient with acquired hyperopia and choroidal folds syndrome

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ABSTRACT

Purpose: syndrome of acquired hyperopia with choroidal folds is a rare syndrome characterized by flattening of the posterior pole with subsequent hyperopization of the eye and a creation of a space between the optic nerve and its sheath. Though uncommon and more often benign, it represents a diagnostic and therapeutic challenge. Correct diagnosis is helpful to exclude other possible causes of choroidal folds.
Observations: here we report a case of a 39-year-old woman who presented with sudden monolateral hyperopia and choroidal folds in the affected eye.
Conclusions and Importance: we performed a specific assessment of the thickness of choroid with the purpose to give further information for the understanding of the underlying condition. To date, the aspect and the thickness of the choroid in this condition, has not been evaluated yet.

1. Introduction

Acquired hyperopic shift syndrome is a benign syndrome. It is best known as syndrome of acquired hyperopia and choroidal folds (SAHCF). It is a well-defined syndrome characterized by unilateral or bilateral flattening of the posterior pole, variable enlargement of the optic nerve with a discernible space between the optic nerve and its sheath, distension of the perioptic subarachnoid space, scleral shortening and congestive choroidal thickening.[1,2] The ophthalmoscopic findings tend to remain stable over time.[2] No proptosis has been generally described.

This syndrome was first described by Kalina and Mills, who reported a group of patients which remained stable for up to over 20 years,[3] but other authors previously reported similar cases.[4] Usually, it is more an unilateral condition with a subacute onset. The patient may refer defocus due to hyperopia or metamorphopsia.[5] Choroidal folds (striae) are a salient feature of this condition and they are easily recognizable with a fundus evaluation. Causes of choroidal folds can be summarised in ocular and extraocular conditions which are extensively described in literature.[6] It is fundamental to know the features of this syndrome for early diagnosis and targeted diagnostic investigations and proper treatment. Fluorescence angiography and magnetic resonance are useful to exclude other causes in differential diagnosis. One thing that always needs to be considered is intracranial hypertension. Choroidal folds may in fact be related to idiopathic intracranial hypertension (IIH).[5] Lumbar puncture (LP) to exclude increased intracranial pressure is recommended even in the absence of papilledema. Though the name of choroidal folds, choroid shape and thickness is rarely investigated. To date in literature, choroidal thickness has not been evaluated yet. To the best of our knowledge, this is the first report about deep analysis of choroidal aspect in a case of choroidal folds.

2. Case report

We report a case of acquired monocular hyperopia and choroidal folds. A 39-year-old Caucasian female was referred to our Unit for gradual worsening of visual acuity in her left eye (LE) over the last 6 months. The patient was affected by thyroid hypoplasia in therapy with Eutirox 125 μg daily. She was a smoker with modest overweight. Blood laboratory testing showed only hypercholesterolemia (251 mg/dl, reference value < 200), CMV IgG positivity (100 U/ml, reference value < 12.0), while C-reactive protein, TSH, FT4, and FT3 were within normal limits. Three years ago the last documented refraction was right eye (RE) plano, and LE +0.25 sph + 0.25 cyl X 85°. At presentation the best corrected visual acuity (BCVA) was 20/20 in RE with +0.50 sph and

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20/25 + 2.50 sph in LE. Cycloplegic refraction confirmed the previous values. Anterior segment evaluation of both eyes was normal. Direct and consensual pupillary reactions, cover test, extraocular muscle movements, and intraocular pressure were normal in both eyes, and Hertel exophthalmometry was symmetric and within normal limits. Fundus examination in right eye was unremarkable, in the left eye there were prominent choroidal folds involving the macular and perioptic region, without evidence of papilledema (Fig. 1). Vitreous was clear. We first suspected a form of scleritis without pain and thus started dexamethasone 2 mg/ml eye drops five times daily and an oral therapy with Ibuprofen 400 mg two times daily. After 10 days, choroidal folds were confirmed by structural optical coherence tomography (OCT) and a bulbar echography excluded retro bulbar masses, and no T-sign was found. Visual acuity was stable after 10 days, but dropped to 20/32 after one month. Ocular biometry indicated that the axial length of the RE was 23.91 mm and 22.74 mm the LE. Keratometry was quite similar between two eyes (RE, K1 41.62D/K2 42.35 D; LE, K1 41.82 D/K2 42.45 D). Pupillary reflexes were normal, Ishihara® cards revealed only a mild dischromatopsia in the LE, with errors in plates 4 and 5. Visual field testing (30-2 Humphrey SITA™ Standard) showed a relative and modest reduction of peripapillary sensitivity in the LE. MR showed a posterior flattening of the left eye. The neurological evaluation was unremarkable ruling out intracranial hypertension, so LP was not performed. Coronal magnetic resonance imaging (MRI) scans evidenced a difference in the optic nerve diameter (LE vs RE of 0.67 vs 0.60 cm). Moreover, there is like a posterior invagination of the optic nerve which creates a “V” sign at the base of the posterior flat part of the eyeball with a straight optic nerve (Fig. 2). By means of structural OCT, we encountered some interesting findings: a quite similar subfoveal choroidal thickness (SFCT) between the two eyes (218 μm in the RE and 214 μm in the LE) but an enlargement of peripapillary choroidal vessels corresponding to the areas where the folds developed (Figs. 3 and 4). Mean value (G value) of the Peripapillary Choroidal Thickness (PCT) was 91 μm in the RE and 138 μm in the LE. Mean value (G value) of the RNFL was 103 μm in the RE and 108 μm in the LE. Volumetric map of the posterior pole for future follow up of the retinal thickness was collected.

Based on all these features, the diagnosis of syndrome of acquired hyperopia with choroidal folds was performed.

3. Discussion

Choroidal folds can develop as a result of any condition causing a reduction of the inner surface of the sclera like scleral thickening or shrinkage, determining a buckling force affecting the inner portion of the choroid, including Bruch’s membrane, the overlying retinal pigmented epithelium and the outer retinal layer. Simply indentation of the sclera without thickening or shrinkage does not produce chorioretinal folds.[6]

With the analysis of the previous literature (Table 1) we observed that SAHCF is more frequent in males (83%), the average age is 41 years old (SD 12.42), it is bilateral in 37% of the cases, and 23% of cases present papilledema. When the hypermetropic shift is bilateral, mono or bilateral papilledema is more frequent (58% of cases) and only in 38% presents bilaterally. In 70% of the previous reports in which LP was achieved, there are values above the norm. Moreover, depending on the timing of the evaluation, papilledema may or may not be present, and only choroidal folds may be seen as a reflection of increased intracranial pressure and therefore these patients should have an appropriate work-up before their findings are considered idiopathic.[5,7] The presence of horizontal choroidal folds without papilledema may be due to the presence of resolved papilledema or a retrolaminar optic nerve sheath enlargement with posterior wide globe indentation.[5] In these cases, the optic nerve sheath is distended, in response to increased intracranial pressure, without compressing the axons, but the pressure is transmitted through the nerve to the posterior posterior eye wall.[5,8] Probably the traslaminar pressure difference (TLPD) plays a role in the deformation circumferential to the optic nerve head.[9] Interestingly, this syndrome is more frequent in astronauts perhaps due to the intracranial cephalad fluid shifts that they are experiencing during prolonged microgravity exposure.[10] In our case, there was no clinical evident papilledema but this is not a reason to prevent our patient in future from developing it. Often, SAHCF or simply choroidal folds alone may precede papilledema by several years.[7,8] Rarely, after the resolution of the optic nerve swelling hypermetropia can recede.[11]

With intracranial hypertension, the elevated subarachnoid pressure is directly trasmitted from the intracranial compartment to the intra-orbital compartment through the perioptic space, resulting in distension

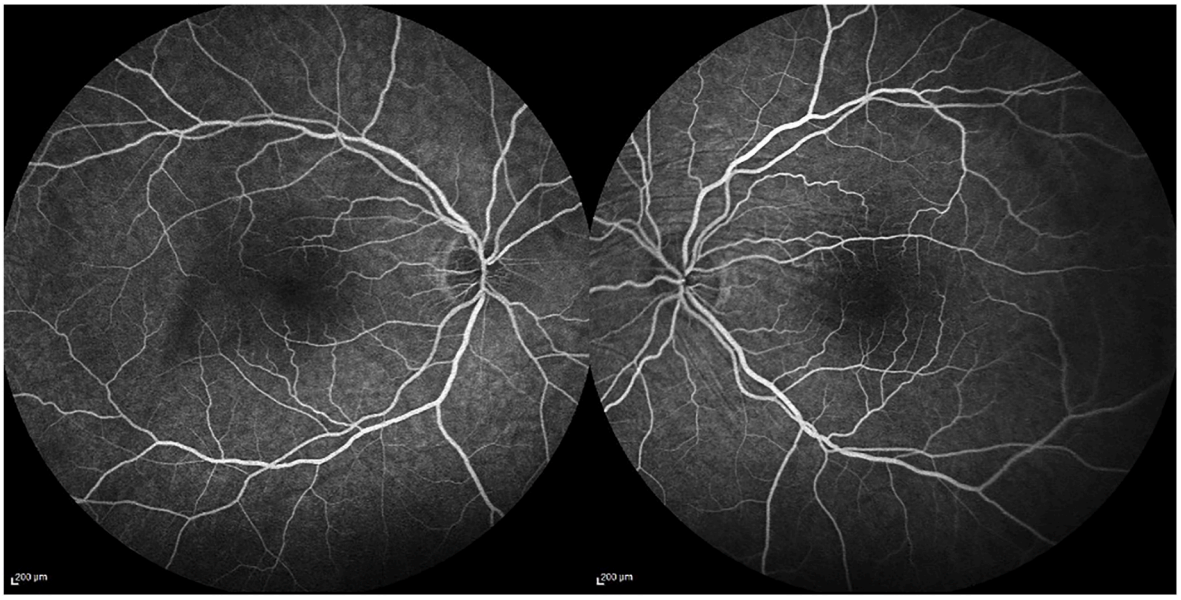

Fig. 1. Unremarkable right eye. In the left eye prominent choroidal folds involving the macular and perioptic region.

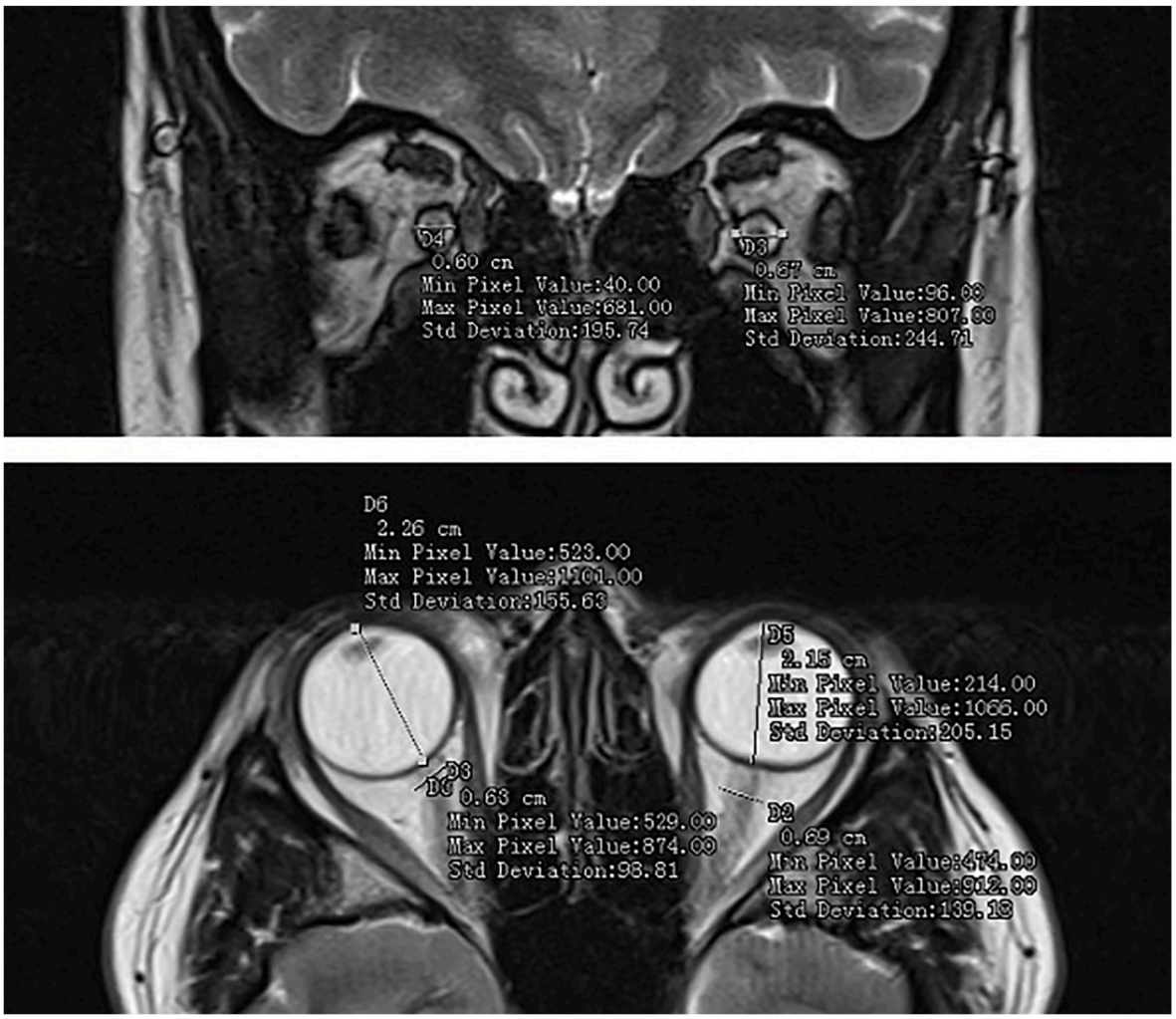

Fig. 2. Coronal MRI scan evidenced a difference in the optic nerve diameter (LE vs RE of 0.67 vs 0.60 cm). Transverse scan show a difference in axial length and optic nerve morphology: posterior invagination of the optic nerve which creates a "V" sign at the base of the posterior flat part of the eyeball with a straight optic nerve.

of the optic nerve sheaths. Elevation of optic perineural pressure has two consequences. First, it causes stasis of axoplasmatic flow through the optic nerve head, resulting in axonal swelling and ophthalmoscopically apparent disc edema. Second, the elevated intrasheath pressure can cause the subarachnoid compartment to act as a mass at the point of contact with the globe, resulting in axial length shortening and choroidal folds.[7] Variation of rigidity and insertion of the dural sheath may also explain choroidal folds associated or not with optic disc swelling.[5] It was suggested that a pliable distended optic nerve sheath may cause flattening of the posterior globe before axoplasmic flow is interrupted.[12] Choroidal folds and optic disk swelling may depend on the level of intracranial pressure.[8] If IIH is present, the first line therapy is oral acetazolamide and diet (if obese). Adesina reported in addition to pharmacologic therapy bilateral optic nerve sheath fenestration (ONSF), with subsequent slight reduction of papilledema and less frequent headaches, but unchanged other morphologic and clinical findings.[13]

Regarding refractive changes our case is in line with previous studies. In the series collected by Kalina, the refractive change was between 2 and 6 D (average 3.5 D).[3] Different authors confirm a strong association between chorioretinal folds not associated with any intra- or extra-ocular condition and hyperopic values between +1 and + 6 D.[6]

SAHCF may present clinically like the Space Flight-Associated Neuro-ocular Syndrome (SANS), the latter being a consequence of microgravity with cephalad fluid redistribution.

Given these anatomic findings, we propose that in individuals with SAHCF, there is a weakness or instability of the collagen structure of the sclera of the posterior globe and dural sheath of the retrobulbar optic nerve as they fuse. This causes an altered compliance, which, along with variations in the number and spacing of the subarachnoid trabeculae and septae, could promote local cerebrospinal fluid (CSF) entrapment in the bulbar segment of the SAS (subarachnoid space) through a 1-way valve effect. A local relative rise in CSF pressure, either transiently or chronically, could trigger optic nerve sheath dilatation, a posterior-anterior force resulting in globe flattening, redundancy and folding of the choroid, and axial shortening. Microgravity fluid shifts are well documented to cause jugular vein distension with cerebral venous congestion. The CSF drainage depends on the pressure difference between the CSF and the venous system and the impairment of CSF outflow leads to increased ICP maybe combined with decreased IOP. A second hypothesis suggests that CSF fluid dynamic in the unique cul de sac–like anatomic connection between the intracranial SAS and the SAS of the optic nerve may also create an environment that could be impacted by microgravity fluid changes.[10]

SAHCF may often be misdiagnosed, underestimated and labelled as idiopathic. In 3 large cases series, Olson, Leahey, Cangemi reported respectively n = 40, n = 54 and n = 53 patients with choroidal folds. Olson described six as idiophatic cases, 19 due to IIH and 18 with hypermetropia, while Leahey described in the unilateral cases 1 idiophatic, 2 with nerve edema and 1 with hypermetropia; in the bilateral cases 10 idiophatic, 0 with nerve edema and 12 with hypermetropia. Cangemi

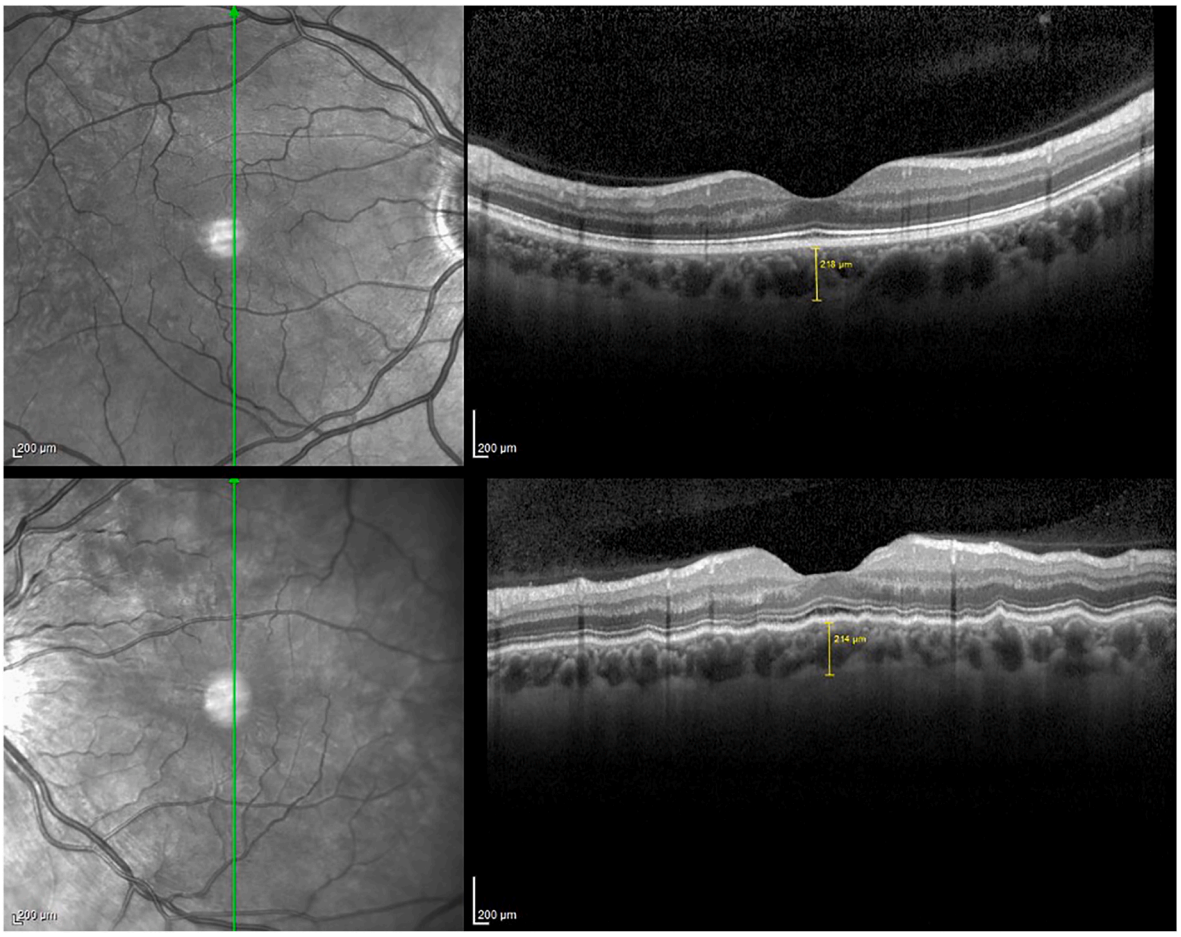

Fig. 3. Subfoveal choroidal thickness (SFCT).

described 10 eyes with idiophatic folds and 9 eyes with associated hypermetropia. Unfortunately, with the data provided in three studies is not possible to determine how many cases are attributable to SAHCF.[14–16]

Sound ultrasonography, another not invasive technique, is unable to detect choroidal folds but can demonstrate flattening and thickening of the posterior sclera and choroid, and therefore, provides characteristic images in cases of choroidal and retrobulbar masses, posterior scleritis and idiopathic orbital inflammation like orbital pseudotumor.[6] In posterior scleritis, the sclera is thickened.[2] More recently, OCT angiography (OCTA) characteristics of CRFs have been described in three affected eyes. Interestingly, the authors identified linear signal decreases in the choriocapillaris perfusion that were topographically associated with the folds. Based on these results, the authors hypothesized that choroidal swelling may cause a stretching of the choriocapillaris and a consequent reduction in perfusion.[17]

Sibony et al.[18] have shown that folds are structural instabilities of a surface layer that develop after exceeding a critical stress (force per unit area) and strain (percent deformation). The morphological pattern of folds depends on the structural geometry of the optic nerve head and the loading force conditions. For example, uniaxial compression of a laminar structure will cause sinusoidal folds orthogonal to the vector of compression, a property that can be illustrated by pinching loose skin on the back of the hand. Symmetrical indentation of a pressurized spherical shell produces a fixed number of radial folds that also depends on the bending stiffness. The wrinkles and folds in papilledema are the structural consequences of intracranial hypertension which distends the optic nerve sheath and increases retrolaminar tissue pressure, which may displace the lamina cribrosa and overlying soft tissue anteriorly.

In accordance with this, we hypothesize that the increased thickness of the peripapillary choroid is a consequence of the mechanical action produced by the posterior longitudinal thrust, with creation of more peripapillary space with adaptation of the choroidal vessels. In our opinion, the congestive hypothesis is less likely. We hypothesize that the biomechanical thrust from behind produces the radial folds (as in our case) and what we add is that the only layer that can extend (i.e., adapt by compensating) is the choroidal layer, resulting thicker in the peripapillary area.

This was the first case of SAHCF in which choroidal aspect was deeply evaluated. We therefore measured the SFCT and the PCT. For the former we used enhanced depth imaging optical coherence tomography (EDI-OCT), for the latter we measured choroidal thickness using the middle circular scan of the peripapillary choroidal thickness, in particular we used a 4.1 mm circular 360° peripapillary scan centered on the optic nerve head when measuring with the glaucoma BMO-RNFL mode. This scan was performed and choroidal thickness was delineated manually using the Heidelberg Software® as the area of visible choroidal vasculature between the outer pigment epithelial border and the inner scleral wall as described earlier.[19] The RNFL thickness sector algorithms computed automatically the PCT.

Analysing the G-Value (global value of the thickness of the layer of interest), we noticed that this was 91 µm in the healthy eye and 136 µm

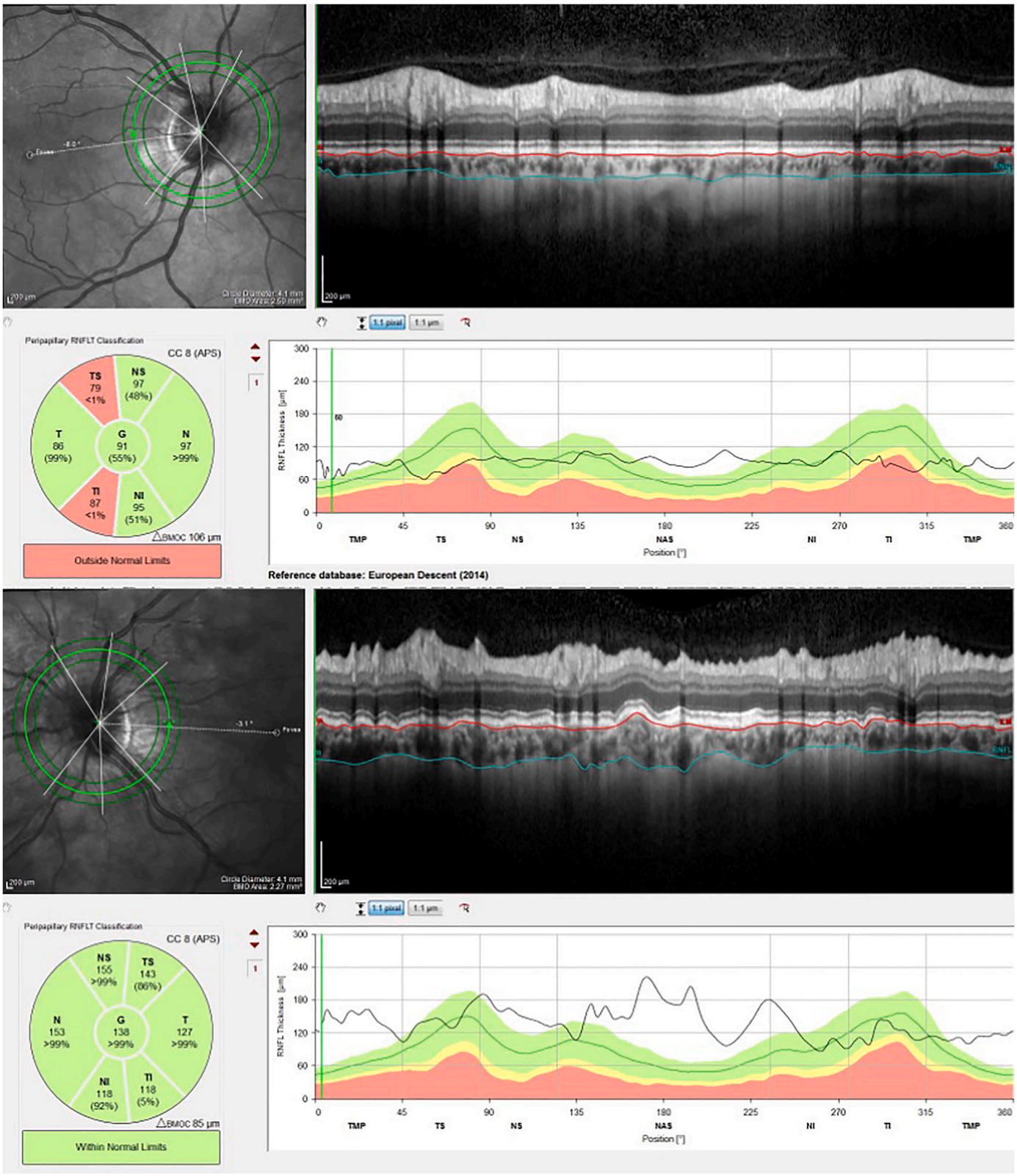

Fig. 4. Mean value (G value) of the Peripapillary Choroidal Thickness (PCT) was 91 microns in the RE and 138 microns in the LE.

in the eye with choroidal folds. To our knowledge, this is the first time that choroidal thickness is studied for this pathology, thus revealing an interesting marker of choroidal engorgement. Our hypothesis was that the eye with choroidal folds also had a higher peripapillary choroidal thickness explaining the pathogenesis of this condition.

We report a case of SAHCF, a rare and probably underestimated syndrome. This report highlights the importance of OCT in the diagnosis of this condition because it enables the physician to have a quick identification of the retinal folds and gives the possibility to evaluate the SFCT and PCT. These two markers could become OCT parameters to be

Table 1
Report of fully described cases related to the SAHCF.

Authors	Year	SAHCF (n)[a]	Mean age	Age Range	M	F	Hyperopic Bilateral Shift	PE	No PE	Bilateral PE	Lumbar puncture (n)	Mean ICP	ICP Range	Pathologic ICP[b]	Hyperopic shift with IH	ONS enlargement
Norton	1969	3	47	32–53	2	1	0	1	2	0	1	n.d	n.d	n.d.	n.d.	n.d.
Kalina	1980	6	33	25–47	5	1	2	0	6	1	1	320	320	1	1	n.d.
Dailey (Stimac)	1986	7	36	25–52	6	1	4	1	6	0	1	320	320	1	1	6
Atta	1988	2	42	36–48	2		0	0	2	0	n.d	n.d	n.d	n.d	n.d	1
Jacobson	1995	3	41	28–48	3		1	2	1	1	2	225	210–240	1	3	1
Sharma	1999	1	50	50	1		1	1	0	1	1	350	350	1	1	1
Griebel	2000	4	58	47–73	2	2	1	2	2	1	4	217,5	160–290	2	2	0
Murdoch	2002	1	46	46	1		0	0	1	0	0	n.d	n.d	0	0	1
Lavinsky	2007	2	51	47–54	2		2	0	2	0	2	280	260–300	2	2	2
Paz-Moreno	2010	2	39	29–50	2		0	0	2	0	0	n.d	n.d	n.d.	n.d.	2
Adesina	2016	1	32	32	1		1	1	0	1	1	270	270	1	1	1
Feinstein	2016	1	25	25	1		0	0	1	0	0	n.d	n.d	n.d.	n.d.	n.d.
Au	2017	1	26	26		1	0	0	1	0	n.d	n.d	n.d	n.d.	n.d.	0
Tuncay	2018	1	52	52	1		1	0	1	0	n.d	n.d	n.d	n.d.	n.d.	n.d.
Sum/ Average		35	41,00		29	6	13	8	27	5	13	261,67		9	11	15
SD			12,42									57,66				
Min				25									160			
Max				73									350			

PE = Papilledema; ICP = Intracranial pressure; IH = Intracranial Hypertension; ONS = Optic nerve sheath.
[a] Choroidal folds + Hyperopic Shift >0,75 sph.
[b] Pressure limits criteria from Corbett e Mehta (1983) (>200 mm H2O in non obese or 250 in obese).

considered in presumed case of SAHCF. This needs further evaluation.

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

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