Evaluation of optic disc blood flow of intraconal orbital tumors using laser speckle flowgraphy.

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Abstract

An orbital tumor can alter the blood hemodynamics and cause a change to optic disc blood flow. We evaluated the bilateral optic disc blood flow of patients with unilateral orbital tumors using laser speckle flow graphy. The optic disc blood flow of the tumor side significantly decreased or increased compared with the optic disc of the fellow eye, even in patients with subtle or absent clinical symptoms and signs. Laser speckle flowgraphy of the optic disc showed the alteration of orbital hemodynamics with tumors and could be useful to suggest the existence of the orbital tumors.

Keywords: Laser speckle flowgraphy, orbital tumors, optic disc blood flow.

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Introduction

Arterial supply to the orbit is complex and makes various anastomoses between the ophthalmic artery and external carotid artery branches [1]. An orbital tumor can alter the blood hemodynamics and cause changes to optic disc blood flow, which is supplied by the ophthalmic artery [2]. In fact, it has been reported that the blood flow of the central retinal artery ipsilateral to an orbital tumor is reduced, as measured by color Doppler imaging [3]. Laser speckle flowgraphy (LSFG) is a technology to measure the blood flow in the optic disc using the laser speckle phenomenon produced by laser refraction from red blood cells [4]. It measures the blood flow quantitatively, directly, noninvasively, and quickly. We have reported that optic disc blood flow is not significantly different between the right and left eye in a normal control group [5]. Therefore, comparing optic disc blood flow using LSFG could reflect the altering orbital hemodynamics induced by the orbital tumor.

The purpose of this study was to evaluate whether the optic disc blood flow with orbital tumors is different compared with the fellow eye using LSFG. If different, LSFG would be identified as a useful tool for detecting possible orbital tumors.

Patients and Methods

Participants: Six patients with unilateral intraconal orbital tumors were enrolled (2 lymphangiomas, 1 cavernous hemangioma, 1 neurogenic tumor, 1 optic nerve sheath meningioma, and 1 fibrous dysplasia). No patients had any other eye diseases such as glaucoma, optic neuritis, or ischemic optic neuropathy. All diagnoses were made using MRI findings by neuroradiologists. Informed consent was obtained from all patients. The University of Miyazaki Institutional Review Board/Ethics Committee approval has been obtained.

Measurements: Approximately 30 minutes after administering an eye drop mixture of 0.5% tropicamide and 0.5% phenylephrine hydrochloride (Mydrin®-P, Santen, Osaka, Japan), a minimum diameter of 5 mm of mydriasis was achieved, and both eyes were measured using LSFG-NAVI® (Softcare, Ltd., Fukuoka, Japan) in a dark room. The same examiner performed the measurements three times, and the mean value was calculated. We used the mean blur rate (MBR) as a marker for the amount of tissue blood flow. The MBR was originally established for measuring blood flow velocity, but the value now is considered to be strongly related to the amount of the tissue blood flow. The MBR is proportional to square blur rate (SBR), and the SBR is proportional to normal blur (NB). NB, which is an indicator of blood velocity, is closely related to the amount of tissue blood flow. The formula is as follows:

MBR=2 × SBR=2 × NB2 [6,7].

The area of measurement was within the optic disc circle. We compared the MBR of the optic disc between the right and left eyes in the patients. For the statistical analysis, the Mann-Whitney test was used to compare the ratio of the MBR of the right and left eyes between the tumor group and normal control group. (For the control group, we used previous data [5]. P values<0.05 indicated statistical significance.

Results

One patient (Table 1, Case 1) was a 73-year-old woman who presented with nausea at an internal medicine clinic in her neighborhood. The internist recommended that she go to a neurosurgery clinic. At the neurosurgery clinic, the patient underwent brain MRI, which showed an orbital tumor OS (Figure 4b) and she was refereed to us. She did not note any visual symptoms. Her medical history was unremarkable for malignancies. Her visual acuities were 20 /20 OD and 20 / 20 OS. An afferent pupillary defect was negative (Figure 1). Her intraocular pressure was 11 mmHg OU. Both optic discs appeared normal without swelling (Figure 2a). Her Optical Coherence Tomography (OCT) did not show a significant thinning of the Retinal Nerve Fiber Layer (RNFL) (Figure 2b). A Goldmann visual field test revealed an inferior nerve fiber bundle defect type visual field defect OS (Figure 3). The patient's left optic disc blood flow in the acute stage measured by LSFG was less than that of the right eye (MBR: 28.7 vs. 21.2 in the right vs. left

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Table 1. *Case characteristics.*

Case / tumor side	Age/Sex	Diagnosis	VA (Tumor side)	RAPD	Disc	NFLD[*1]	VF defect/pattern	Exophth-almos
1 / OS	71 / F	meningioma	20/20	(−)	n.l.	absent	(+) / NFLD[*2]	(−)
2 / OS	19 / F	Lymphan-gioma	20/20	(−)	n.l	absent	(−)	(−)
3 / OS	72 / F	Hemangioma	20/20	(−)	n.l	absent	(−)	(+)
4 / OD	83 / F	Fibrous tumor	10/200	(+)	pale	present	(+) / gene	(+)
5 / OS	43 / F	Lymphan-gioma	20/20	(−)	n.l	absent	(−)	(+)
6 / OS	56 / F	Neurogenic tumor	20/20	(−)	Partial swelling	absent	(+) / Mari	(+)

VA: Visual acuity
RAPD: relative afferent pupillary defect
NFLD[*1]*: nerve fiber layer defect detected by optical coherent tomography*
VF: Visual field
NFLD[*2]*: nerve fiber layer defect pattern*
Gene: generalized defect pattern
Mari: enlargement of blind spot

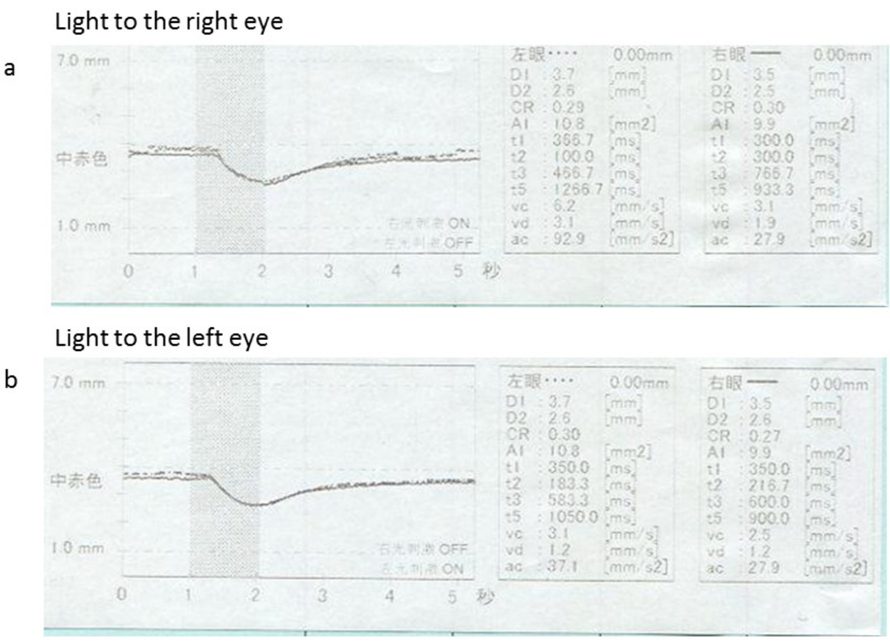

Figure 1. *Infrared pupillography of Case 1. (a) Red light stimulus to the right eye. (b) Red light stimulus to the left eye. Solid line: Reaction of the right eye. Dotted line: Reaction of the left eye. There was no difference of amplitude or latency between the eyes for the red light stimulus, which means there was no RAPD.*

eye (Figure 6a and 6b), MBR ratio was 73.9%. The case series and the results are shown in Table 1. Five of six cases showed a decreased MBR of the ipsilateral eye with the orbital tumor compared with the fellow eye (Table 1). The mean MBR of the involved eyes was 60.9%-78.1% lower than that of fellow eyes (Table 1). One patient showed an increased MBR in the eye with the orbital tumor compared with the fellow eye (Table 1, Case 3). The mean MBR of the eyes with orbital tumors was 120% higher than that of the fellow eyes. The MBR ratio of the patients' orbital tumor eyes and fellow eyes was significantly lower than that of the normal controls ($p=0.0135<0.05$, Mann-Whitney) (Figure 7). One case with positive APD showed a decrease in MBR in the orbital tumor eye (Table 1, Case 4). Three cases, which were incidentally discovered and had normal visual acuity, visual field, and negative APD, showed a decreased or increased MBR in the tumor side (Table 1, Cases 2, 3 and 5; Figure 5).

Discussion

We evaluated the bilateral optic disc blood flow of patients with unilateral intraconal orbital tumors using LSFG. LSFG allows for noninvasive quantification of blood flow in the optic disc and can be performed easily in a short time, as with a fundus camera. Therefore, both ophthalmologists and opticians can perform LSFG after a short training period. Another method of evaluating optic disc blood flow is color Doppler imaging. However, disadvantages of color Doppler imaging include the special training required to take appropriate vessel images, and

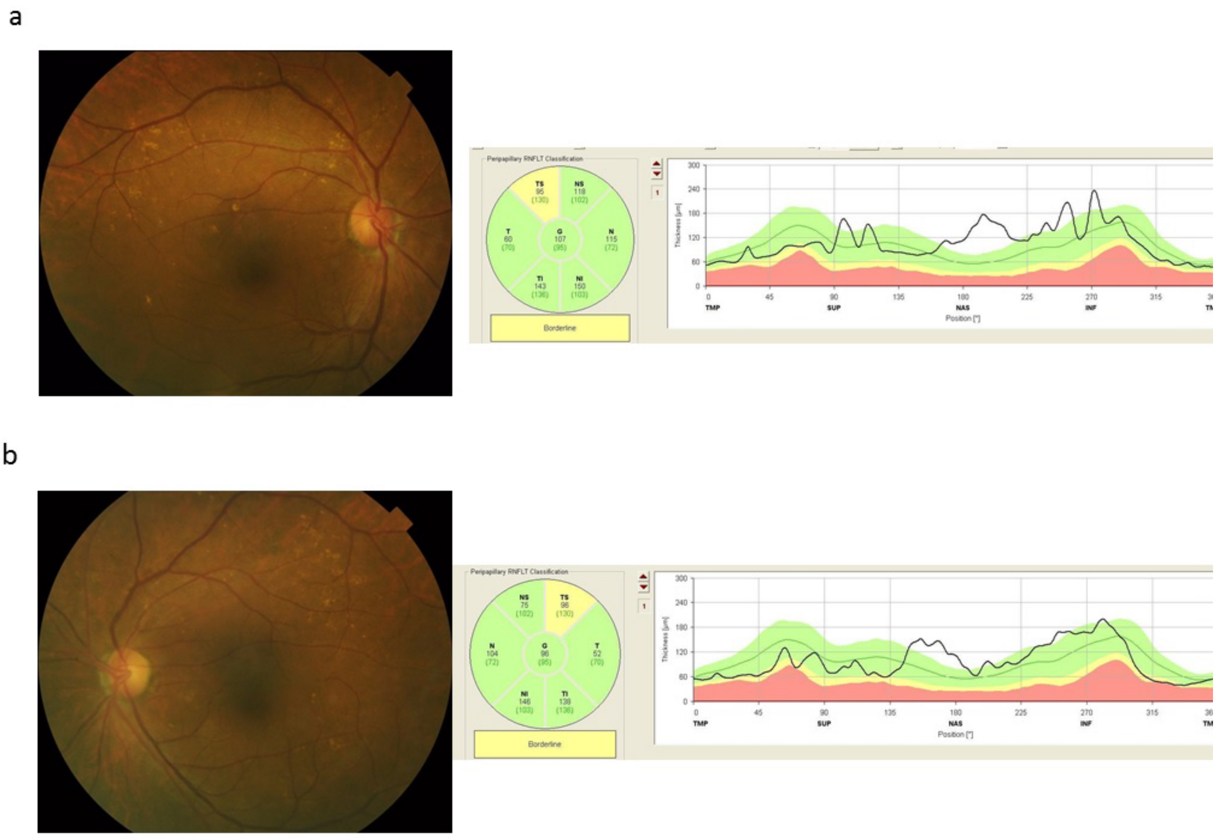

Figure 2. *Fundus photograph and optical coherence tomography (OCT) of the retinal nerve fiber layer (RNFL) a) thickness around the optic disc of Case 1. b) Both optic discs appeared normal without swelling. OCT did not show significant thinning of the RNFL.*

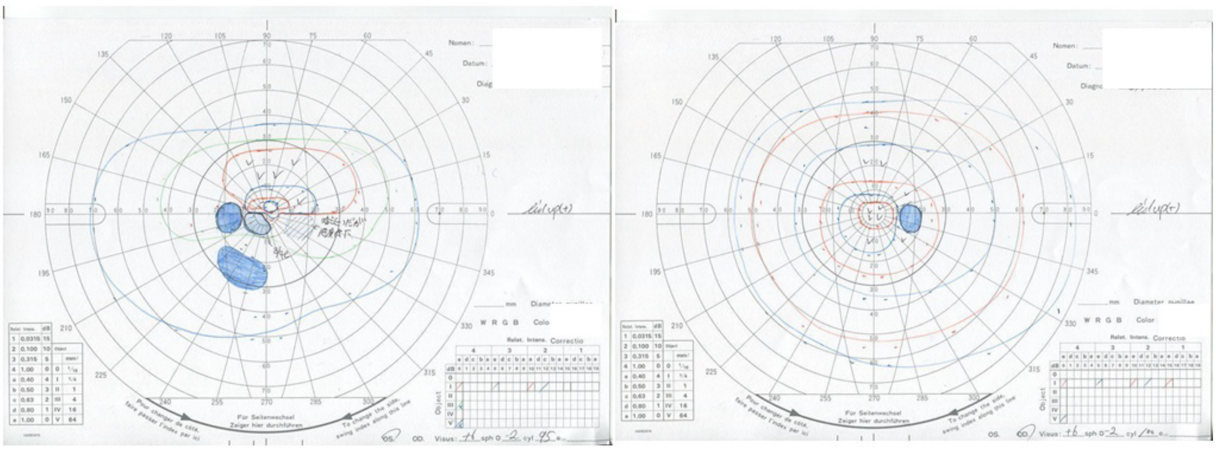

Figure 3. *Goldman visual field test of Case 1. The test results showed an inferior nerve fibre bundle defect type visual field defect in the left eye.*

its inability to show small vessels; it can only show medium to large vessels, such as the ophthalmic artery. LSFG-NAVI, a modified version of LSFG, has shown favorable reproducibility in evaluating optic disc blood flow [8]. It has been reported that the MBR in the optic nerve head is usable for inter individual and intergroup comparison by comparing it with hydrogen gas clearance measurements [9]. Therefore, LSFG-NAVI is useful for evaluating optic disc blood flow, which reinforces the reliability of our data. There have been no previously reported evaluations of optic disc blood flow of orbital tumors using LSFG as far as we know. Our data using LSFG-NAVI showed that MBR in the orbital tumor side decreased or increased compared with the fellow side. In addition, we have previously reported that MBR is not significantly different between the right and left eyes in a group with normal vision 5). Therefore, we hypothesized that the difference in MBR must reflect the altering orbital hemodynamics induced by an orbital tumor. Mendivil et al. have reported that optic nerve blood flow was impaired on the side of an intraoral mass [3]. Several reasons for decreased MBR have been considered. One is the reactive decreased blood flow followed by optic nerve atrophy due to compression by the tumor. The swept-source optical coherence tomography angiography of the optic disc in optic atrophy showed fewer micro vessels in the optic disc [10]. In normal

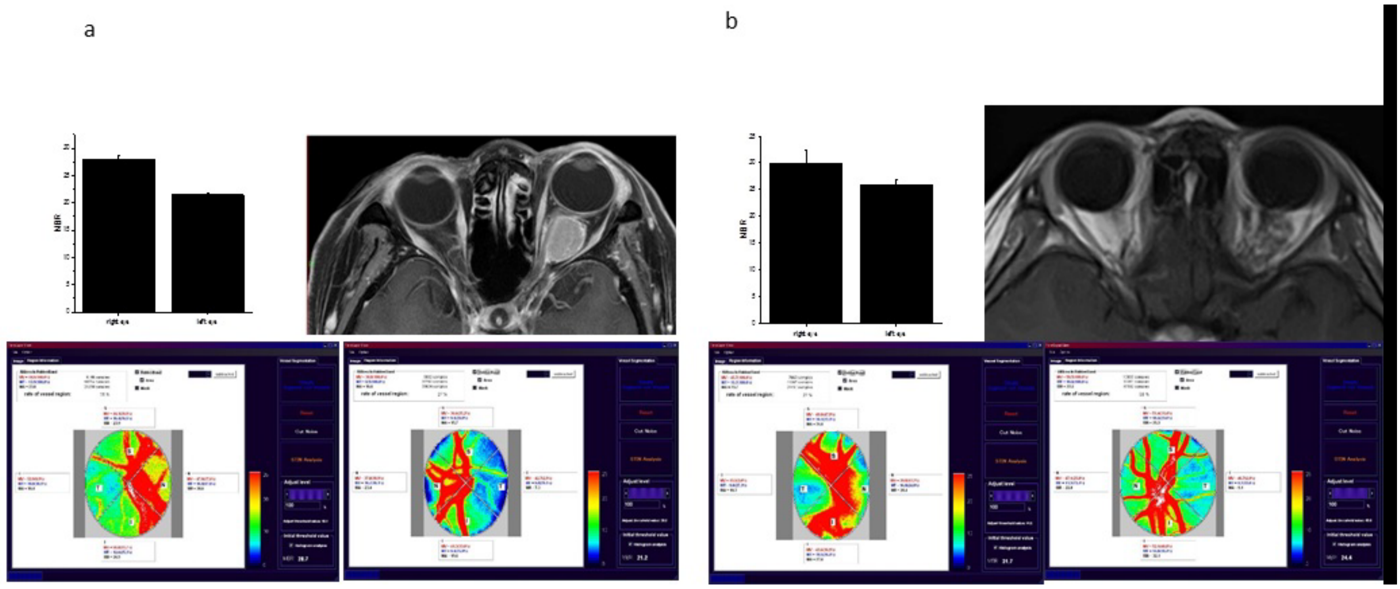

Figure 4. *a) Case 1: Mean MBR: right eye; 28.0 ± 0.59, left eye; 21.5 ± 0.38 (top left). Orbital MRI (top right). Representative LSFG of the right (bottom left), and left eye (bottom right). (b) Case 2: Mean MBR: right eye; 30.0 ± 0.21, left eye; 16.2 ± 1.17 (top left). Orbital MRI (top right). Representative LSFG of the right (bottom left), and left eye (bottom right).*

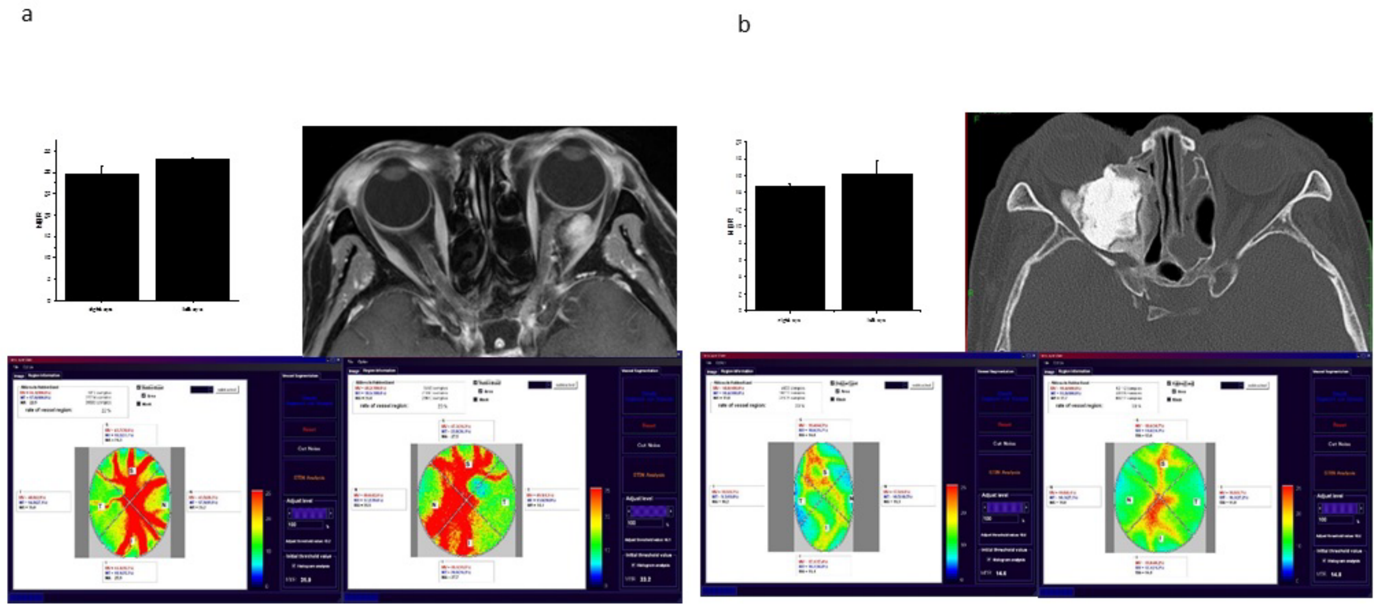

Figure 5. *(a) Case 3: Mean MBR: right eye; 29.5 ± 2.08, left eye; 33.1 ± 0.32 (top left). Orbital MRI (top right). Representative LSFG of the right (bottom left), and left eye (bottom right). (b) Case 4: Mean MBR: right eye; 14.8 ± 2.42, left eye; 25.7 ± 1.65 (top left). Orbital MRI (top right). Representative LSFG of the right (bottom left), and left eye (bottom right).*

tension glaucoma, it has been shown that as optic disc atrophy progresses, MBR in the optic discs decreases [11]. A second reason is the direct compression by the tumor of the central retinal artery or ophthalmic artery. In fact, Mendivil et al. have shown that, using color Doppler imaging, the time-velocity waveform demonstrated abnormally high vascular resistance in the central retinal artery of all affected eyes in the primary position compared with the normal waveform seen in the fellow eyes [3]. However, it is difficult to explain why one case in the present study showed increased blood flow in the tumor side. A third reason, we speculate, is that the change of the MBR observed with LSFG reflects the alteration of the orbital blood flow because of the tumor's presence. Vessels in the orbit form a complex anastomose between arteries from the external carotid artery and those from the internal carotid artery through the ophthalmic artery [1]. The hemodynamics in the orbit are not well known. It has been observed that the orbit can be supplied either by the ICA, with the blood within the OA regularly flowing anterogradely (ICA dominance); or by the ECA, with the flow within the OA backward directed toward the ICA (ECA dominance). Between these two extreme situations (ICA or ECA dominance), a variety of possible hemodynamically intermediate conditions (balanced hemodynamics) can be found. There are various channels between the ICA, ECA, and OA, and these channels form various anastomoses in relation to the various pathological states. The presence of a tumor

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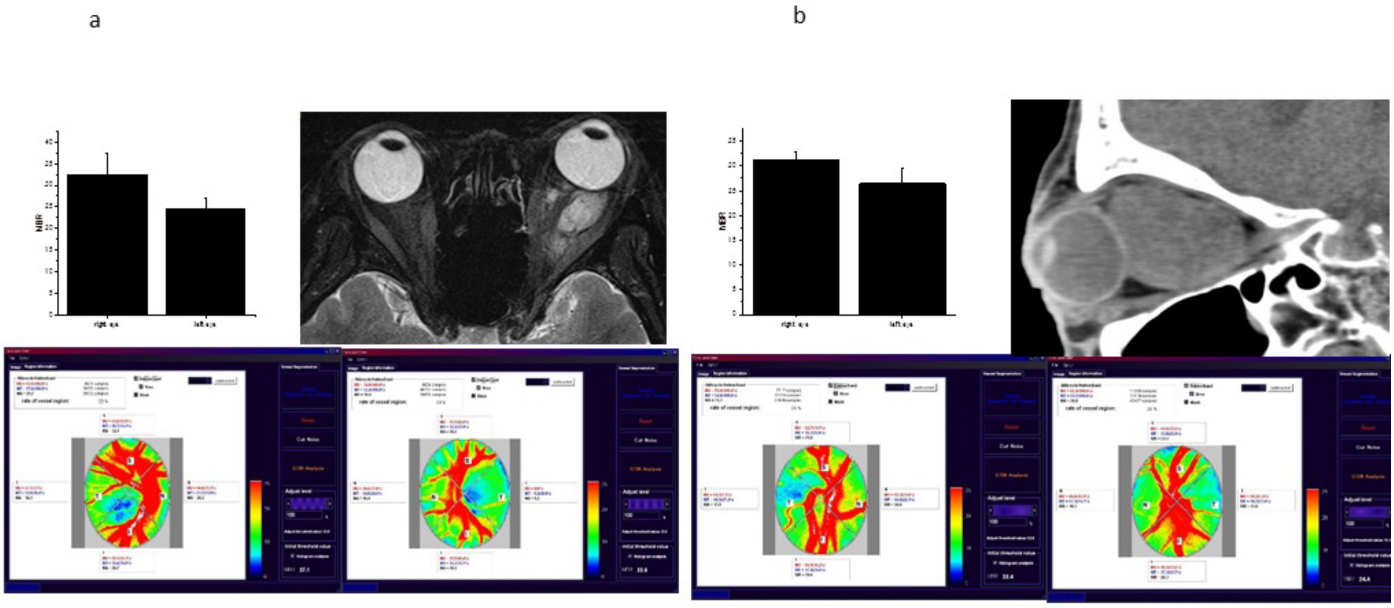

Figure 6. *(a) Case 5: Mean MBR: right eye; 32.4 ± 4.86, left eye; 24.63 ± 2.48 (top left). Orbital MRI (top right). Representative LSFG of the right (bottom left), and left eye (bottom right). (b) Case 6: Mean MBR: right eye; 31.3 ± 1.55, left eye; 26.4 ± 3.18 (top left). Orbital MRI (top right). Representative LSFG of the right (bottom left), and left eye (bottom right).*

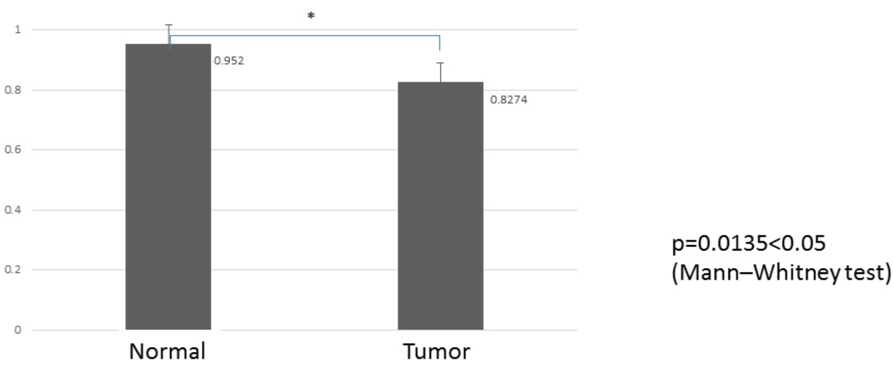

Figure 7. *The MBR ratio of the right eye and left eye of patients with orbital tumor and normal controls.*

could change the blood flow backward to the ECA, depriving the ophthalmic artery and thus decreasing the blood flow of the optic disc. Alternatively, a tumor could change the blood flow forward to the ICA and increase the blood flow of the ophthalmic artery, which would increase the blood flow of the optic disc. Our data showed that using LSFG, patients with positive clinical symptoms and signs, including decreased visual acuity, positive APD, and visual field defects, showed decreased MBR. Interestingly, other cases with subtle or absent clinical symptoms and signs showed either decreased or increased MBR using LSFG. Orbital tumors frequently are discovered incidentally by brain imaging for screening or during investigation for other brain diseases. This means that many patients with orbital tumors initially do not have clinical indications of visual disturbances. Although confirmation of the existence of an orbital tumor requires orbital imaging, including ultrasonography, CT or MRI, a difference in the MBR between both eyes, discoverable with LSFG, would suggest an alteration of the orbital blood flow, possibly caused by an orbital tumor. In conclusion, we evaluated the bilateral optic disc blood flow of patients with unilateral orbital tumors and found that the MBR of the optic disc of the tumor side decreased or increased compared with the optic disc of the fellow eye. Because we have previously shown that optic disc blood flow is not significantly different between the right and left eye in patients with normal vision, any difference warrants further investigation. Such a difference could indicate that the alteration of the orbital hemodynamics is being caused by the presence of a tumor. Therefore, LSFG could be useful to suggest the existence of an orbital tumor when patients present with no visual symptoms and signs.

Conflict of Interests

The authors declare that they have no conflicts of interest to disclose.

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