·Clinical Research·

Infrared autofluorescence, short-wave autofluorescence and spectral-domain optical coherence tomography of optic disk melanocytomas

Peng Zhang, Yan-Nian Hui, Wen-Qin Xu, Zi-Feng Zhang, Hai-Yan Wang, Dong-Jie Sun, Yu-Sheng Wang

Department of Ophthalmology, Eye Institute of Chinese PLA, Xijing Hospital, the Fourth Military Medical University, Xi'an 710032, Shaanxi Province, China

Correspondence to: Yu-Sheng Wang. Department of Ophthalmology, Eye Institute of Chinese PLA, Xijing Hospital, the Fourth Military Medical University, Xi'an 710032, Shaanxi Province, China. wangys003@126.com

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Abstract

• **AIM: To investigate the findings of infrared fundus autofluorescence (IR-AF) and spectral-domain optical coherence tomography (SD-OCT) in eyes with optic disc melanocytoma (ODM).**

• **METHODS: IR-AF findings and those of other ophthalmologic imaging examinations, including short-wave autofluorescence (SW-AF), fluorescein angiography (FA), fundus color photography, and SD-OCT of 8 eyes of 8 consecutive cases with ODM were assessed.**

• **RESULTS: The ODMs in all cases (100%) presented similar IR-AF, SW-AF, and FA findings. On IR-AF images, ODMs showed outstanding hyper-AF with well-defined outline. On SW-AF images, the area of ODMs presented as hypo-AF. FA images revealed the leaking retinal telangiectasia on the surface of the ODMs. On SD-OCT images in 8 cases (100%), the ODMs were sloped with highly reflective surface, which were disorganized retina and optic nerve layers. In 7 cases (87.5%), peripapillary choroids were involved. The melanocytomas of 8 cases (100%) presented as optically empty spaces. Vitreous seeds were found in one case (12.5%).**

• **CONCLUSION: IR-AF imaging may provide a new modality to evaluate the pathologic features of ODMs, and together with SW-AF imaging, offers a new tool to study biological characteristics associated with ODMs. SD-OCT is a valuable tool in delimitating the tumor extension and providing morphological information about the adjacent retinal tissue.**

• **KEYWORDS:** melanocytoma; angiography; autofluorescence; optical coherence tomography

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INTRODUCTION

Optic disc melanocytoma (ODM) is a stationary tumor that classically occurs in the optic disk, sometimes with contiguous involvement of the adjacent retina or choroid. Ophthalmoscopically, melanocytoma has a characteristic appearance of intensely pigmented mass that occupies the optic disk and extends for a variable distance into the optic disk. Histopathologically, ODM is composed of intensely pigmented round to oval nevus cells containing giant round cytoplasmic melanosomes with relative sparsity of other cytoplasmic organelles with benign features[1].

In most cases, ODMs are seemed to be a stable lesion with no tendency to grow [2]. However, 10%-15% of them show subtle enlargement over several years. The larger, growing tumor can cause compressive optic neuropathy, visual field defect, vascular occlusion, and loss of vision [2-4]. Moreover, malignant change is estimated to occur in about 5% of cases[5].

ODM is usually diagnosed by ophthalmoscopic examination due to the characteristic appearance of the tumor. Ancillary imaging procedures, such as fundus photography, fluorescein angiography (FA), and optical coherence tomography (OCT), are useful for diagnosis and follow-up evaluations of ODM.

In addition, short-wave autofluorescence (SW-AF), a non-invisive examination based on the endogenous lipofuscin in retinal pigment epithelium (RPE) excited by an external blue light, is described to be helpful for diagnosing ODM[6].

In our view, another type of AF, infrared fundus autofluorescence (IR-AF) should be more valuable in diagnosing ODM. IR-AF could be derived from melanin excited by infrared light [7]. The melanosome is melanin-containing organelle in melanocyte. Melanocytoma is mainly composed of melanocytes, theoretically, which should be responsible for the exogenous exciting light to originate IR-AF. Recent years, IR-AF has been used in the assessment of RPE related diseases, such as central serous chorioretinopathy, macular dystrophy and macular choroidal neovascularization[8-10], but not yet in melanocytoma.

Table 1 Patient demographic and optic disk melanocytomas data

Case No.	Gender	Age (a)	Eye	BCVA	Site and extent of tumor	Optic disc involvement (clock hours)
1	M	42	Right	0.8	Optic disk and subretina	8
2	F	60	Left	1.0	Optic disk	6
3	F	38	Left	1.0	Optic disk and subretina	3
4	F	46	Right	0.8	Optic disk and subretina	6
5	F	55	Right	0.6	Optic disk and subretina	5
6	F	62	Right	0.4	Optic disk and subretina	10
7	F	49	Left	0.6	Optic disk and subretina	5
8	M	57	Right	0.5	Optic disk and subretina	8

F: Female; M: Male; BCVA: Best-corrected visual acuity (LogMAR).

OCT is the optical analog of ultrasound imaging and is emerging as a powerful imaging technique that enables non-invasive, *in vivo*, high resolution and speed, achieving the visualization of tissue architectural morphology *in situ* and in real time *in vivo* [11].

Our purpose in the present study was to compare abnormal AF images, including IR-AF and SW-AF images, with spectral-domain OCT (SD-OCT) and FA images to investigate the utility of IR-AF, SW-AF and SD-OCT at diagnosis and detection of ODMs.

SUBJECTS AND METHODS

The study was a retrospective review of 8 consecutive cases with ODM (Table 1) imaged with fundus color photography, IR-AF, SW-AF, FA, and SD-OCT in the Department of Ophthalmology of Xijing Hospital. The Ethics Committee of the Xijing Hospital approved this study. The written informed consents related to use data, and publish images were obtained from all cases. This study, data collection, analysis, and presentation conformed to the tenets of the Declaration of Helsinki.

IR-AF, SW-AF and FA were performed using the Heidelberg spectralis HRA (Heidelberg Retina Angiograph; Heidelberg Engineering, Heidelberg, Germany). AF images were obtained after maximum pupillary dilation was achieved with instillation of 0.5% tropicamide and 0.5% phenylephrine. After the acquisition of AF, FA was performed after fluorescein sodium injection.

SD-OCT (3D-OCT™ system, Topcon, Tokyo, Japan) with single scan through the center of the optic disc, routinely.

RESULTS

This series consists of 8 cases (6 females and 2 males) with a mean age of 51.13y (range: 38 to 62y). All the cases were Chinese.

Dilated funduscopic examination revealed the pigmented ODMs appearing as dark brown or black elevated masses covering the optic disk and adjacent retina (Figure 1A) in 8 cases (100%). ODMs in all cases (100%) presented similar IR-AF, SW-AF, and FA features. On IR-AF images, ODMs showed outstanding hyper-AF with well-defined outline (Figure 1B) corresponding to the area of pigmented masses in images of fundus color photography. On SW-AF images, hypo-AF corrsponding to the pigmented masses combined with uninvolved optic discs (Figure 1C). FFA images of all cases (100%) revealed the leaking retinal telangiectasia on the surface of the tumors, and melanocytomas themselves demonstrated hypofluorescence throughout the angiogram due to the absence of blood vessels (Figure 1D, 1E). On SD-OCT images of 8 cases (100%), nerve fiber layers and retinas above the ODMs presented as disorgnized hyperreflectivity. All the melanocytomas presented as optically empty cavities due to anterior aspects of the melanocytomas with abrupt and complete shadowing (Figure 1F, 1G). Choroidal involvements were found in 7 cases (87.5%), on SD-OCT images, the peripapillary choroidal tumor invasion defined as thickening, hyperreflectivity or hyporeflectivity of the choroid (Figure 1F). No patients had OCT evidence of subretinal fluid or cystoid macular edema in this series. Hi-reflective spots in the vitreous cavity near by the tumor and corresponding to vitreous seeding were found in one case (12.5%) (Figure 1G).

DISCUSSION

ODMs are slow growing, relatively common and benign tumors that generally do not affect visual acuity. This tumor appears to have a slight predominance for females, and have an equal incidence in all races [3]. In the past, these tumors were often confused with melanomas and the patients were treated by enucleation[3,12].

However, ODMs may cause a various degrees of visual field defects, including enlargement of the blind spot or major visual field defects. Moreover, some of the tumors can produce several complications, such as retinal vein occlusion, papilledema or optic nerve atrophy inducing visual loss due to local compression [1,13-14]. Some ODMs can induce ischemic optic neuropathy associated with tumor necrosison, rare occasions, can undergo malignant transformation into melanomas [15-17]. Hence, patients with ODM should be emphasized the need for experiencing carefully periodic ocular examination[18].

The diagnosis of a ODM usually can be made by its characteristic features of dark brown or black mass in the optic disk ophthalmoscopically. Because the melanocytes are deeply pigmented and closely compact with relatively little

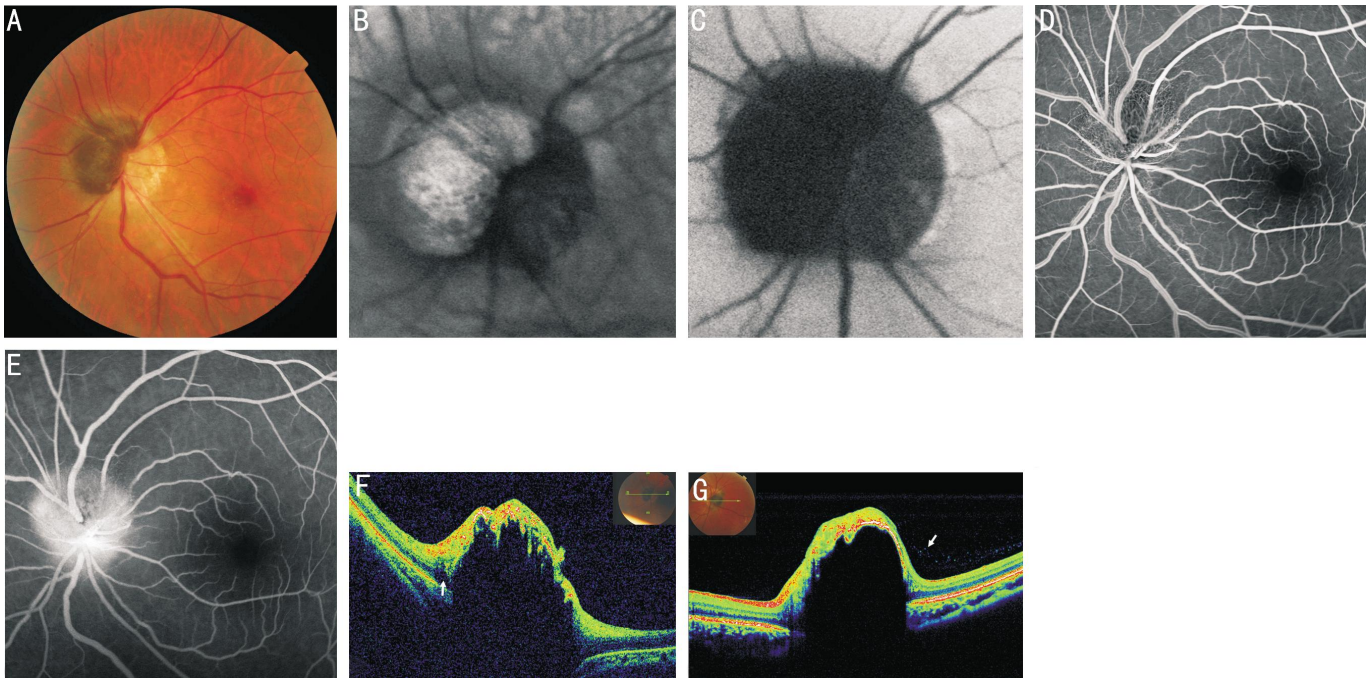

Figure 1 Images of optic disc melanocytomas A: Color fundus photograph shows optic disc melanocytoma presenting as a pigmented mass, involving part of optic disc and retina in left eye; B: IR-AF image, the optic disc melanocytoma shows hyper-AF with well-defined outline; C: SW-AF image, the optic disc melanocytoma and adjacent tissues including optic disc appear as hypo-AF; D: Early phase of FFA demonstrates the retinal telangiectasia on the surface of optic disc melanocytoma in left eye; E: Late phase of FFA shows the leaking retinal telangiectasia on the surface of optic disc melanocytoma; F: SD-OCT image reveals the hyperreflective retina and optic nerve fiber layers, followed by optically empty mass. Involved choroid presents as local thickening and hyporeflection in left eye (see arrow); G: SD-OCT image reveals the hyperreflective retina and optic nerve fiber layers, followed by optically empty mass. Some hyperreflective vitreous seeds can be found within the posterior vitreous in right eye (see arrow).

vascularity, FA and indocyanine green angiography (ICGA) are helpful ancillary examinations to diagnosis and follow-up evaluation of ODM for the reason of hypofluorescence inside of the tumor throughout the angiogram. In addition, trichangiectasia on the tumor can be verified by FFA [12]. To perform FFA or ICGA, fluorescein sodium or indocyanine green must be used intravenously, therefore, adverse reactions including nausea, vomiting, hives, acute hypotension, even cardiac arrest or anaphylactic shock may happen[19-20].

SW-AF and IR-AF are two types of non-invasive, dye-free endogenous fluorescence examinations. Guerra *et al*[6] reported that ODM appeared as an outstanding hypo-SW-AF lesion and the remaining retina was isoautofluorescent. SW-AF is useful in differential diagnoses of choroidal nevus and choroidal melanoma. Suspicious choroidal nevi appears as very bright hyper-SW-AF areas[21-22]. Choroidal melanoma shows discrete and bright hyper-SW-AF for the existence of overlying intracellular lipofuscin[23].

In this clinical study, we found the presence of hypo-SW-AF in ODMs, secondary to the absence of lipofuscin over or inside the tumor, and the association with the highly pigmented mass blocking the posterior RPE. Except for the melanocytomas, optic disc and retinal vascular structures are hypo-SW-AF. On the image of SW-AF, it is difficult to distinguish ODM from neighbouring tissues with hypo-SW-AF. In contrast, IR-AF is more sensitive in evaluating ODM. IR-AF is derived from melanin in the RPE and choroid physiologically. Melanin in the RPE plays an important role in the protection of eyes against phototoxicity that may be involved in age-related dysfunction of the fovea [24]. In a normal fundus, optic disc and retinal vascular structures are hypo-IR-AF secondary to the lack of melanin,whereas the macula, especially the fovea has the increased IR-AF than that in other location, it is the reason that distribution of melanin is more dense in fovea [25-26]. Since the melanocytomas composed by multiple intensely melanocytes, we confirmed that melanocytomas emit outstanding hyper-IR-AF with well-defined outline. Owing to this unique feature of melanocytes, the technique of IR-AF appears to be useful in diagnosis, and investigating pathological changes of ODMs.

To evaluate the extension of the tumor into the retrolaminar portion of the optic nerve and surrounding retina, choroid. ODM with diameter greater than 0.5 mm could be demonstrated with ultrasonography, computed tomography (CT) or magnetic resonance imaging (MRI). But these imaging examination techniques cannot easily differentiate melanocytoma from other elevated lesions of the optic disk. Furthermore, microscopic extension of the tumor is unlikely to be determined by above mentioned examinations[3,5].

SD-OCT is another valuable tool for correlating directly with

morphological changes on and around ODM. Specific features of OCT findings with ODMs include the overlying retinal and peripapillary nerve fiber layer are disorganized, and relatively hyperreflective, followed by a abrupt posterior optical shadowing. Moreover, this study revealed that tumor invasion, namely the choroidal involvement could be verified by SD-OCT[27].

Choroidal involvement is suggested by upward displacement of the normal RPE architecture or hyperreflectivity of the choroid, because the normal choroid is hyporeflective. Besides, SD-OCT can be used to document some complications secondary to ODMs, such as cystoid retinal edema, subretinal fluid, hemorrhage and disk edema [28]. Vitreous seeds are evident in one patient in this study, this phenomena supposed to be due to disruption of the internal limit membrane, melanocyte cells disseminated into the vitreous cavity[29].

In conclusion, ODMs are benign, slow growing tumors that generally do not affect visual acuity. Based on our personal experience and on review of the literatures, serious complications, such as retinal vascular obstruction, malignant transformation are very possibility. It is very important to emphasize the need for long-term surveillance of these tumors. ODMs have unique imaging characteristics of SW-AF, IR-AF and SD-OCT, except for traditional ophthalmoscopic examination, this new generation of ancillary imaging procedures may be helpful for confirming suspicious melanocytic lesions.

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