Fundus Autofluorescence in Cystoid Macular Edema: Can it Be an Ancillary Test?*

Kistoid Makula Ödeminde Fundus Otofloresansı: Tanısal Yöntem Olabilir mi?

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ABSTRACT

Purpose: To evaluate the findings of fundus autofluorescence (FAF) in cystoid macular edema (CME).

Materials and Methods: Sixty-seven eyes of 55 patients having CME secondary to diabetic retinopathy, retinal vein occlusion, uveitis, cataract extraction, epiretinal membrane and age-related macular degeneration were recruited. All cases were evaluated by FAF, fundus fluorescein angiography (FFA) and optical coherence tomography (OCT).

Results: Mean central macular thickness was detected as 419.3±131.1μm by OCT. FAF images revealed increased autofluorescence signal in a round or oval fashion at the fovea corresponding to the flower petaloid pattern on FFA. Dark septa within the petaloid leakage on FFA were seen as decreased autofluorescent areas on FAF imaging. Sixty-four eyes had CME on both FFA and FAF. In one eye of a patient having macular edema after cataract extraction, FAF revealed no CME when CME was observed on FFA. In 2 eyes, although there was no typical leakage pattern on FFA, CME was apperant on FAF imaging.

Conclusions: In addition to FFA and OCT findings, FAF data may reveal noteworthy information in CME. FAF imaging may be used as a non-invasive and rapid ancillary test for the diagnosis of eyes having CME.

Key Words: Cystoid macular edema, fundus autofluorescence.

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ÖZ

Amaç: Kistoid makula ödemi (KMÖ) varlığında fundus otofloresans (FOF) bulgularını değerlendirmek.

Gereç ve Yöntem: Diyabetik retinopati, retina ven oklüzyonu, üveit, katarakt cerrahisi, epiretinal membran ve yaşa bağlı makula dejenerasyonu nedeniyle KMÖ saptanan 55 hastanın 67 gözü çalışmaya dahil edildi. Bütün olgular FOF, fundus floresein anjiografisi (FFA) ve optik koherens tomografi (OKT) ile incelendiler.

Bulgular: OKT ile ortalama merkezi makula kalınlığı 419.3±131.1 μm olarak tespit edildi. FOF görüntülemesinde, foveada FFA'daki petaloid görünüme uyan şekilde yuvarlak veya oval şekilli artmış otofloresans sinyali kaydedildi. FFA'daki petaloid sızıntı içerisindeki koyu septaların FOF görüntülemesinde azalmış otofloresans alanları şeklinde olduğu görüldü. 64 gözde hem FFA hem de FOF incelemesinde KMÖ tespit edildi. Katarakt cerrahisi sonrasında KMÖ gelişen 1 gözde, FOF görüntülemede KMÖ tespit edilemezken FFA'da KMÖ'ye ait sızıntı izlendi. FFA'da tipik sızıntı gözlenmemesine rağmen 2 gözde FOF incelemede KMÖ'ye ait belirgin sinyal değişikliği olduğu görüldü.

Sonuç: KMÖ varlığında FOF görüntüleme ile FFA ve OKT bulgularına ilave olarak önemli bilgiler elde edilebilinir. FOF görüntülemenin, KMÖ olgularında kullanılabilecek non-invazif ve hızlı bir tanısal yöntem olduğu düşünülmektedir.

Anahtar Kelimeler: Kistoid makula ödemi, fundus otofloresansı.

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INTRODUCTION

Cystoid macular edema (CME) is a consequence of disruption of the blood-retinal barrier secondary to numerous etiology. Retinal vasculopathies like diabetic retinopathy, hypertensive retinopathy, retinal vein occlusion, choroidal neovascularization; intraocular inflammation related to uveitis and cataract surgery; vitreoretinal interface abnormalities causing traction on macular vessels mainly cause the development of CME. Intraretinal cysts may be visualized by biomicroscopic examination with a +60D or +90D contact lens and particulary with retro-illumination using a narrow slit. Fundus fluorescein angiography (FFA) and more recently optical coherence tomography (OCT) has been the most frequently used methods for the diagnosis of CME in the daily ophthalmology practice.[1-3] Retinal thickness analyzer, scanning laser retinal tomograph may also detect the increase in retinal thickness in cases of CME.[4,5] Recently, the changes of fundus autofluorescence (FAF) has attracted attention in eyes having CME.[6,7]

FAF imaging has been progressively more used for the diagnosis and follow-up of various retinal pathologies. FAF is derived from the natural fluorophores within RPE layer, mainly lipofuscin.[8] Lipofuscin is generated as a by-product of retinoid cycle after the phagocytosis of photoreceptor outer segments and demonstrates fluorescence between 500 and 750 nm with a peak emission of 630 nm.[9] This relatively novel method of retinal imaging demonstrates the state of lipofuscin in RPE in vivo, and therefore allows to evaluate the alterations in RPE in numerous retinal diseases.[9,10] The aim of this particular study is to evaluate the findings of FAF imaging in cases with CME.

MATERIAL AND METHODS

Patients diagnosed to have CME were selected from the FAF database between January 2008 and June 2009. Patients having CME secondary to diabetic retinopathy, retinal vein occlusions, uveitis, cataract surgery, epiretinal membrane and age-related macular degeneration were included in the study. An informed consent was obtained from all of the patients, and all tenets of the Declaration of Helsinki were followed. Complete ophthalmic examination followed by FFA and OCT were performed. The ophthalmic examination involved best-corrected visual acuity determination, anterior segment evaluation, intraocular pressure measurement by applanation tonometer, and a detailed fundus examination. FAF imaging was obtained prior to FFA. Eyes with significant media opacity, cataract and poor FAF images were excluded. In the late phase of FFA, pathognomonic leakeage of fluorescein at the fovea in a petaloid configuration with feathery margins was considered as CME. The data of FFA and FAF images were evaluated by a single clinican (UAD).

Fundus Autofluorescence (FAF) Imaging

FAF imaging was performed with a confocal scanning laser ophthalmoscope (Heidelberg Retinal Angiograph 2, Heidelberg Engineering, Germany) using a view mode of 30°. The pupil was dilated using phenylephrine 2.5% and tropicamide 1% eyedrops to a diameter of at least 6 mm. Autofluorescence was excited by the argon blue wavelength (488 nm). A barrier filter with a wavelength of 500 nm was used for the detection of the emitted light. First, the camera was aligned using the infrared illumination. Once a sharp well-focused image was obtained, the illumination was changed to FAF mode. Mean of 9 frames was obtained for a high quality image

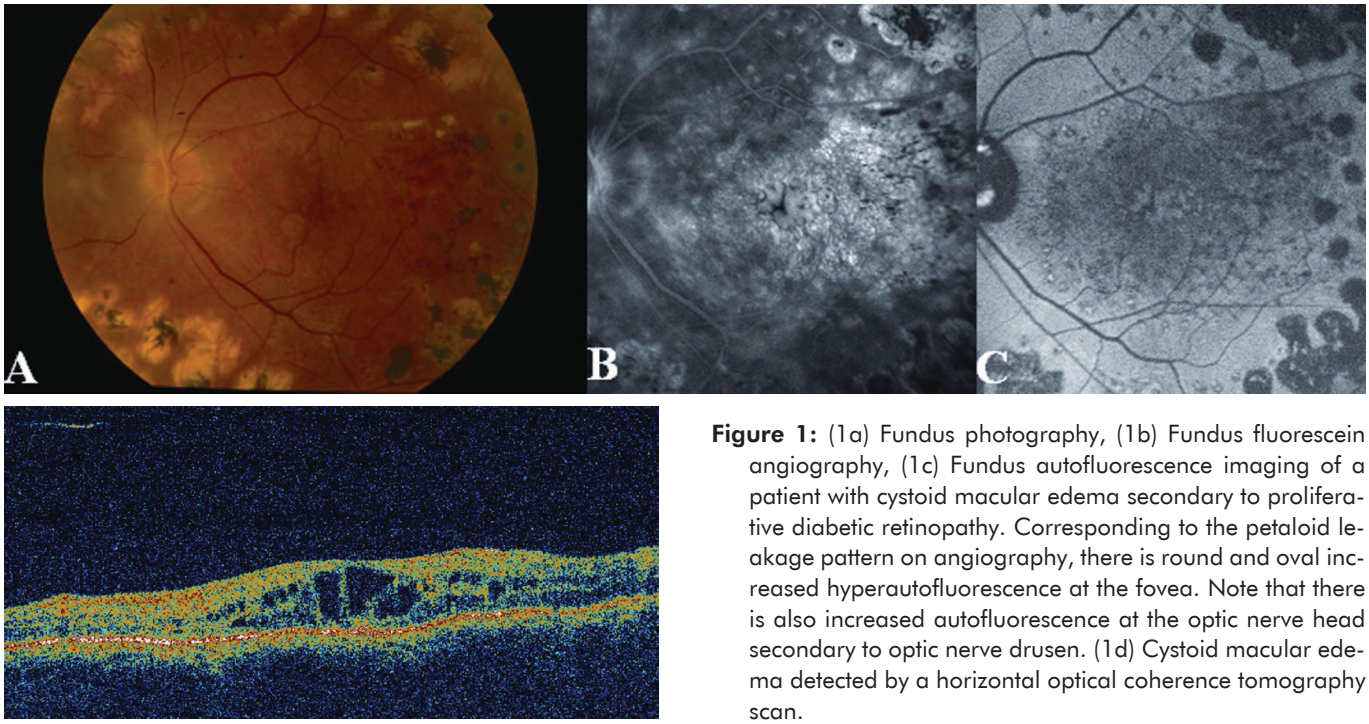

Figure 1: (1a) Fundus photography, (1b) Fundus fluorescein angiography, (1c) Fundus autofluorescence imaging of a patient with cystoid macular edema secondary to proliferative diabetic retinopathy. Corresponding to the petaloid leakage pattern on angiography, there is round and oval increased hyperautofluorescence at the fovea. Note that there is also increased autofluorescence at the optic nerve head secondary to optic nerve drusen. (1d) Cystoid macular edema detected by a horizontal optical coherence tomography scan.

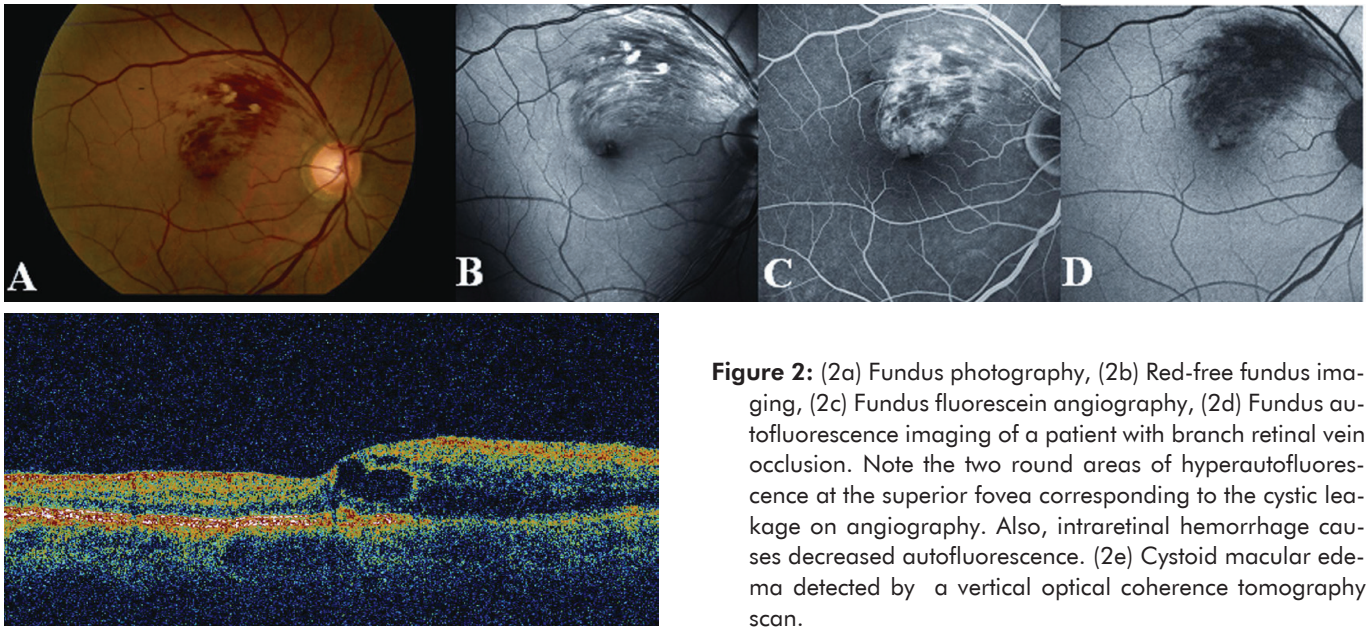

Figure 2: (2a) Fundus photography, (2b) Red-free fundus imaging, (2c) Fundus fluorescein angiography, (2d) Fundus autofluorescence imaging of a patient with branch retinal vein occlusion. Note the two round areas of hyperautofluorescence at the superior fovea corresponding to the cystic leakage on angiography. Also, intraretinal hemorrhage causes decreased autofluorescence. (2e) Cystoid macular edema detected by a vertical optical coherence tomography scan.

during FAF acquisitions. FAF images that were not in focus were eliminated.

Optical Coherence Tomography

OCT was performed using the Humphrey model 3000 (Stratus-OCT, Zeiss-Humphrey Instruments, San Leandro, CA). After a pupillary dilation, six consecutive 6 mm long scans containing 512 axial profiles (A-scans) at equally spaced angular orientations in a radial spoke pattern centered on the fovea (known as Macular Thickness Protocol) were obtained for each eye. Using Retinal Thickness Mapping Software, mean retinal thickness value which was measured in the central disc with a diameter of 1000 μm in the center of the macula was used as central foveal thickness. Intraretinal fluid accumulation as cystic cavities mainly in the outer plexiform and inner nuclear layer with loss of foveal contour and increase in macular thickness was considered as CME on OCT evaluation. Eyes having subfoveal serous retinal detachment on OCT accompanying CME were excluded.

RESULTS

Sixty-seven eyes of 55 patients (27 female, 28 male) with a mean age of 62.1±14.4 years were enrolled in the study. CME was evident secondary to diabetic retinopathy in 36 eyes, central retinal vein occlusion in 1 eye, branch retinal vein occlusion in 13 eyes, uveitis in 4 eyes, cataract extraction in 3 eyes, macular epiretinal membrane in 5 eyes and age-related macular degeneration in 5 eyes.

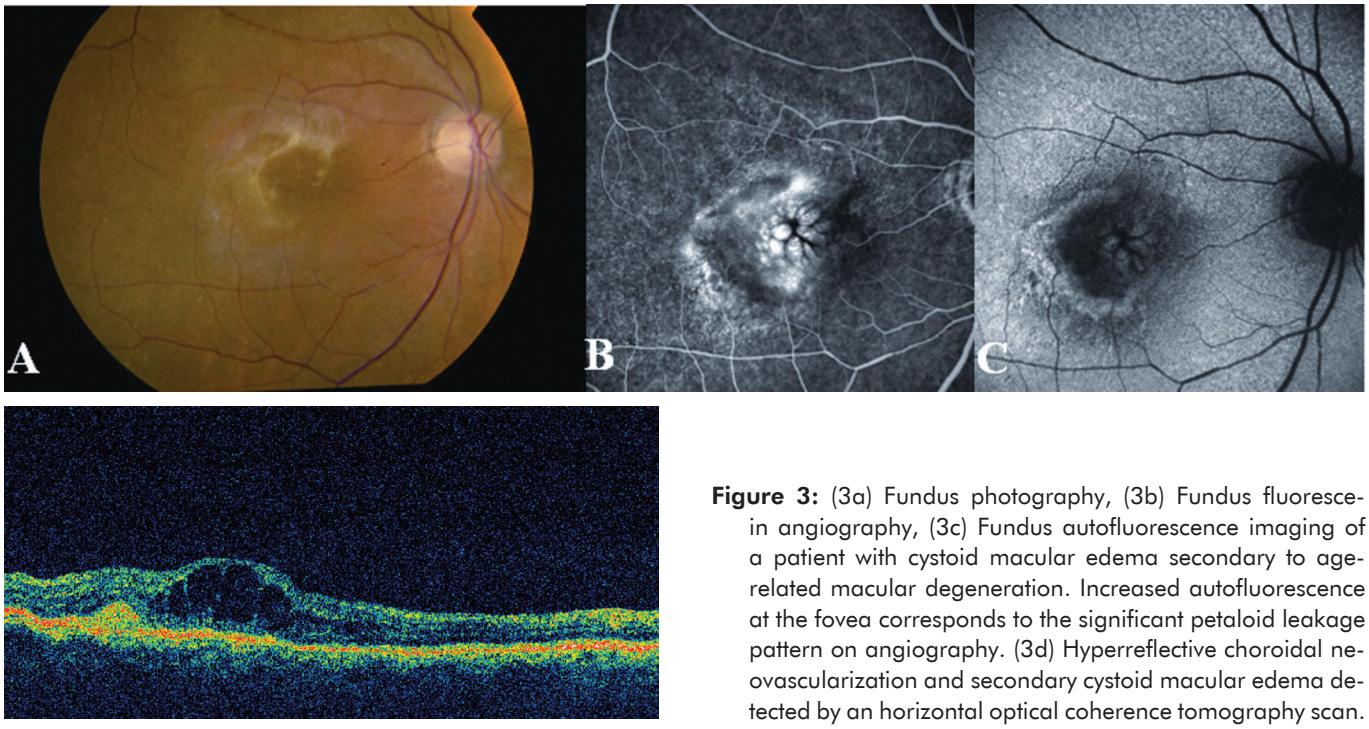

Figure 3: (3a) Fundus photography, (3b) Fundus fluorescein angiography, (3c) Fundus autofluorescence imaging of a patient with cystoid macular edema secondary to age-related macular degeneration. Increased autofluorescence at the fovea corresponds to the significant petaloid leakage pattern on angiography. (3d) Hyperreflective choroidal neovascularization and secondary cystoid macular edema detected by an horizontal optical coherence tomography scan.

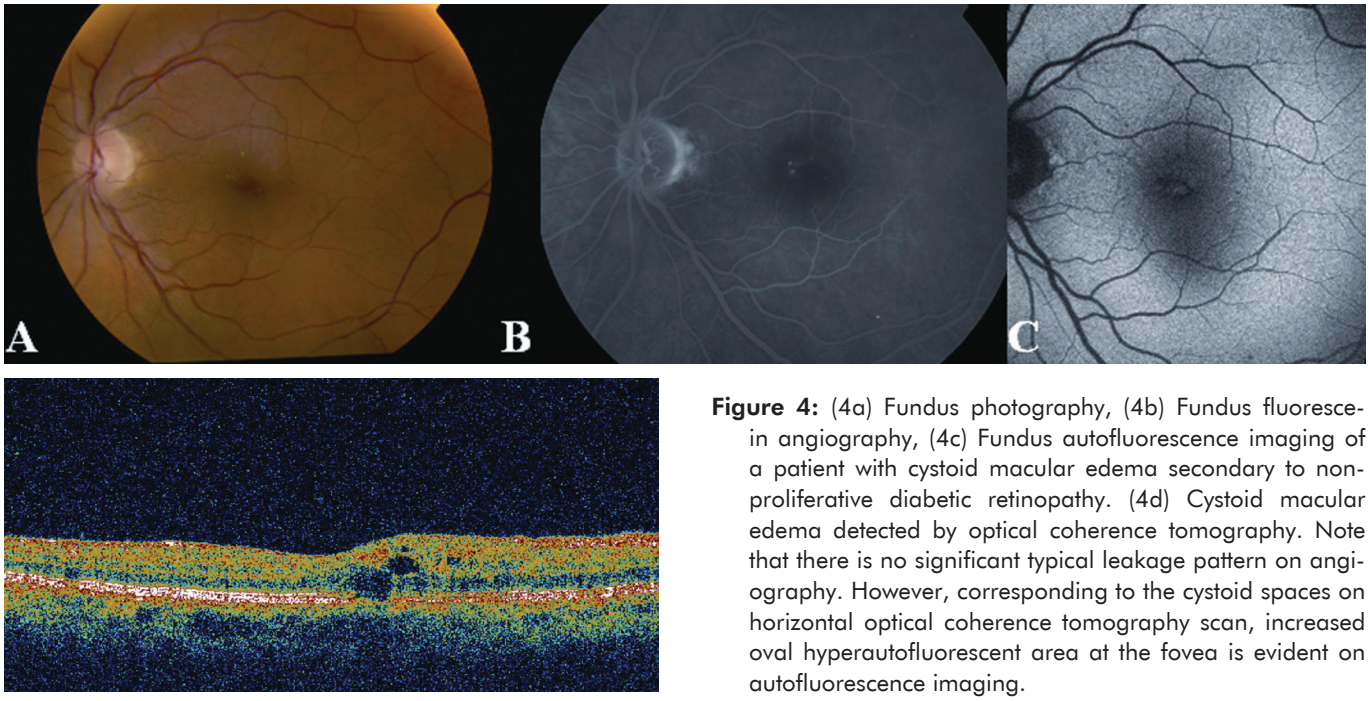

Figure 4: (4a) Fundus photography, (4b) Fundus fluorescein angiography, (4c) Fundus autofluorescence imaging of a patient with cystoid macular edema secondary to non-proliferative diabetic retinopathy. (4d) Cystoid macular edema detected by optical coherence tomography. Note that there is no significant typical leakage pattern on angiography. However, corresponding to the cystoid spaces on horizontal optical coherence tomography scan, increased oval hyperautofluorescent area at the fovea is evident on autofluorescence imaging.

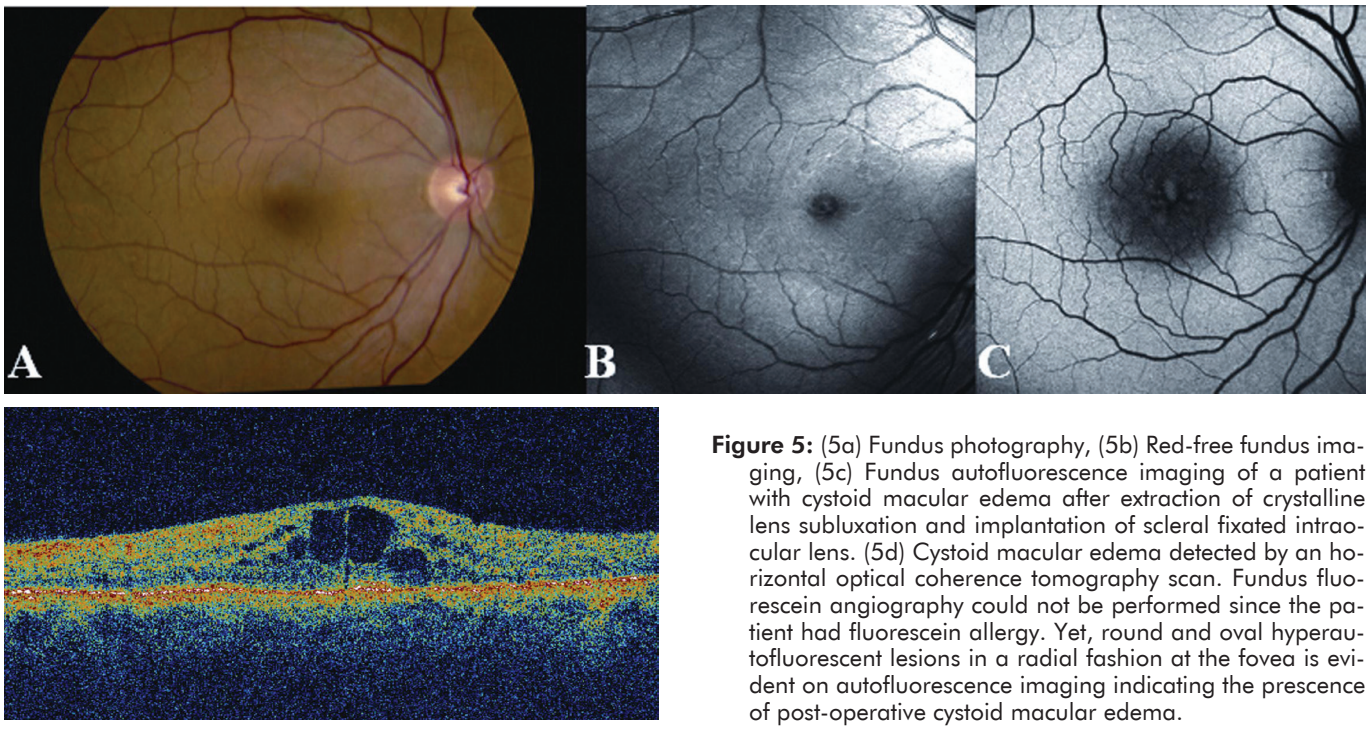

Figure 5: (5a) Fundus photography, (5b) Red-free fundus imaging, (5c) Fundus autofluorescence imaging of a patient with cystoid macular edema after extraction of crystalline lens subluxation and implantation of scleral fixated intraocular lens. (5d) Cystoid macular edema detected by an horizontal optical coherence tomography scan. Fundus fluorescein angiography could not be performed since the patient had fluorescein allergy. Yet, round and oval hyperautofluorescent lesions in a radial fashion at the fovea is evident on autofluorescence imaging indicating the prescence of post-operative cystoid macular edema.

Findings of CME during FFA and OCT were common in all retinal pathologies. During the early phases of the FFA, hypofluorescence was evident secondary to fluid within cystoid spaces. In the late phase, there was slowly accumulating hyperfluorescence within cystoid spaces and increasing leakage of petaloid pattern. Mean central macular thickness detected by OCT was 419.3±131.1 μm. All eyes demonstrated multiple, round, optically clear cystic cavities having low reflectivity on OCT evaluation of the central macula.

FAF images revealed increased autofluorescence signal in a round or oval fashion at the fovea corresponding to the flower petaloid pattern on FFA (Figure 1). Dark septa within the petaloid leakage on FFA were seen as decreased autofluorescent areas on FAF imaging (Figure.[1-3]

Sixty-four eyes had CME on both FFA and FAF. In one eye of a patient having macular edema after cataract extraction, FAF revealed no CME when CME was observed on FFA. In 2 eyes, although there was no typical leakage pattern on FFA, CME was apperant on FAF imaging (Figure 4).

DISCUSSION

FAF imaging reveals functional and/or morphological abnormalities of the retina which may not be discovered during biomicrosopic examination and conventional methods such as fundus photography and angiography. In a normal fundus, optic disc and retinal vascular structures reveals hypoautofluorescence secondary to the lack of fluorophores, whereas the macula, especially the fovea displays a relative hypoautofluorescence due to the absorbtion of the exciting blue light by the luteal pigments.

Hypoautoofluorescence (decreased FAF) occurs secondary to the atrophy of RPE layer; increased melanin content in RPE layer; blockage of FAF due to retinal hemorrhage, edema, media opacities. Hyperautofluorescence (increased FAF) originates from increased accumulation of lipofuscin in the RPE layer like hereditary macular dystrophies and age-related macular degeneration; increased visibility of RPE layer such as macular holes.

Multiple cystoid spaces exist within the outer plexiform layer of Henle in the classic pathology of CME. However, those cystoid cavities can be seen in various layers of the neurosensory retina depending in part on the underlying etiology.[11,12]

The petaloid leakage pattern with dark septa on FFA is characteristic for CME. The dark septa which compartmentalize the petaloid leakage at the foveal region are caused by the fibers of Müller cells. This septa configuration of the Müller's fibers can also be clearly visualized by OCT evaluation.

McBain and colleagues studied FAF in the diagnosis of 96 consecutive patiens with CME secondary to cataract extraction, inherited retinopathies, inflammatory eye disease and idiopathic cases.6 Only 34 eyes were included to their study. The authors reported that FAF imaging had 81% sensitivity and 69% specitivity in the diagnosis of CME when compared with standard FFA. They also noticed that CME could be detected 100% in eyes having florid edema based on FFA. Bessho et al examined 3 eyes with diabetic macular edema and 11 eyes with central retinal vein occlusion.[7] They detected macular autofluorescence of a similar shape to that of CME in FFA in all participants.

In the current study, we observed oval and round stellate areas of increased autofluorescence in a radial fashion, representing the intraretinal cystic cavities which corresponded to the parafoveal petaloid leakage pattern on FFA and cystoid spaces on OCT.

The radiating striae detected as decreased autofluorecence between the stellate areas presumably corresponded to the walls of intraretinal cysts constructed by the Müller's fibers in the outer plexiform layer.

Macular luteal pigment was shown to localize in the outer nuclear and outer plexiform layers of the retina.6 The detection of increased FAF signal in CME is possibly secondary to the displacement of luteal pigments and subsequent reduction of foveal pigment density which allows the visualization of an increased FAF signal, as the blockage of the exciting blue light is decreased by the lateralization of luteal pigments.[6,7]

Bessho and colleagues defined the increased FAF in CME as a "pesudo" or "relative" hyperautofluorescence.[7] Increased FAF in CME is not secondary to lipofuscin accumulation at the level of RPE, rather caused by increased visibility of the autofluorescence of RPE layer.

FFA is still widely used for the confirmation of the diagnosis of CME. However, FFA is an invasive procedure with possible complications. Although the dynamic process of fluorescein leakage and macular perfusion is demonstrated by FFA, detailed information about morphologic changes can not always be detected by FFA as detected by OCT.

In addition, interpretation of FFA can be subjective, qualitative and time-consuming.[13,14] OCT evaluation is a non-invasive method that may reveal the increase in retinal thickness and the presence of typical intraretinal cysts which are not evident on FFA. Good correlations between FFA and OCT findings were previously reported.[15,16] In a study, CME secondary to uveitis was detected with a sensitivity of 96% and specitivity of 100% by OCT.[3]

FAF imaging is a non-invasive, safe and rapid method. Morphologic changes at the macula secondary to CME can be easily noticed especially when the optical media is clear.

The studied surface must be in focus for an optimal FAF image. Therefore, FAF data that are out of focus should be excluded.17 In addition, FAF data obtained by different imaging devices should not be compared during clinical practice. FAF imaging can be easily applied when FFA is contarindicated such as in patients having hypersensitivity to fluorescein dye or in case of pregnancy (Figure 5).

In the present study, distinctive patterns of FAF in CME were documentated. The diagnosis of CME is fortified by the demonstration of characteristic leakage pattterns on FFA and typical changes at the macular anatomy on OCT.

In addition to FFA and OCT findings, FAF data may reveal noteworthy information in CME, especially in clear optical media. In conclusion; FAF imaging may be used as a non-invasive and rapid ancillary test for the both diagnosis and follow-up of eyes having CME.

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