
FUNDUS AUTOFLUORESCENCE IN A CASE OF OCCULT MACULAR DYSTROPHY

RASQUIN F., VAN NECHEL C.,
CORDONNIER M.*

ABSTRACT

Purpose: To document for the first time intrinsic retinal pigment epithelium (RPE) fluorescence in occult macular dystrophy (OMD). This entity is characterized by a central cone dysfunction leading to a decline of visual acuity without visible fundus and fluorescein angiography abnormalities. A great variability in clinical findings and in the pattern of inheritance have been reported suggesting probably several etiologies of which some are well known but seen too early to detect significant changes.

Methods: Fundus autofluorescence imaging is a recent method to detect early retinal pigment epithelial alterations. It may visualise disease specific abnormalities in the retinal pigment epithelium often not yet visible on ophthalmoscopy such as Stargardt disease, rod-cone dystrophy. This method was applied in a member of a family with OMD.

Results: The normal fundus autofluorescence observed in our patient allowed the distinction between well-known maculopathies not yet visible on ophthalmoscopy but showing abnormal autofluorescence, and genuine occult macular dystrophy.

Conclusion: Fundus autofluorescence imaging in our case of dominant autosomal OMD suggests a healthy and functional RPE. This examination of RPE should therefore be added to the work-up of suspected OMD.

KEY WORDS

Autofluorescence, multifocal electroretinogram, occult macular dystrophy

.....

* *Department of Ophthalmology, Erasme University Hospital, Université Libre de Bruxelles, Belgium*

Submitted: 01-08-09

Accepted: 05-10-09

INTRODUCTION

Occult macular dystrophy (OMD) described in 1989 by Miyake is characterized by a central cone dysfunction leading to a loss of vision with a normal fundus and normal fluorescein angiography findings (1,2). The key to its diagnosis is the normal full-field electroretinogram (ERG) with an abnormal multifocal electroretinogram (mfERG) in the macular area. However, other well-known maculopathies can in the early stage share the same characteristics, such as Stargardt disease.

We therefore performed fundus autofluorescence in a member of a family with OMD to define other parameters allowing the distinction between already known macular dystrophies not yet visible on ophthalmoscopy and genuine OMD.

MATERIALS AND METHODS

Two members (mother and daughter) of a family were referred with an unexplained decrease of visual acuity in both eyes.

In addition to routine examination, the two patients underwent fundus photography, fluorescein angiography, color-vision testing, visual field studies, ERG and mfERG following International Society for Clinical Electrophysiology of Vision standards (3,4). MfERG responses from 61 hexagonal elements within the central 30 degrees were recorded and the first order component was extracted using Retiscan (Roland Instruments, Germany).

Foveal thickness measured by optical coherence tomography (OCT) (Carl Zeiss Meditec Model 3000, OCT₃ system) and fundus autofluorescence (FAF) images recorded by confocal scanning laser ophthalmoscope (Heidelberg Retina Angiograph 2, Heidelberg Engineering, Heidelberg, Germany) were performed on the younger patient. The confocal scanning laser ophthalmoscope uses an argon laser for generation of excitation light at 488nm and a barrier filter > 500 nm for the detection of the emitted signals. The image resolution for FAF was 768 × 768 pixels. Six images per second were recorded and 9 single images were averaged to generate a mean image.

RESULTS

CASE 1

In 1996, a 74 year old woman complained of progressive decline in visual acuity of 16 years duration. The best corrected visual acuity was 20/100 at the right eye and 20/200 at the left eye with slight myopia. There was no pupillary defect.

Visual field testing showed high foveal threshold on both sides and numerous scotomas in the 30° areas. Color vision was evaluated using Ishihara, AO H-R-R pseudoisochromatic plates, Farnsworth Panel D-15 and revealed dyschromatopsia in the red-green axis.

Funduscopy demonstrated unremarkable optic nerves, peripapillary chorioretinal depigmentation, normal vessels and retinal periphery. There were no abnormalities at the macular region of either eye.

Fluorescein angiograms were normal.

The amplitudes of full field ERG were in the normal range for rod and cone components. Electrooculogram (EOG) was normal. The mf-ERG exhibited reduced amplitude in all concentric hexagon rings within the 30° of central visual fields. The differences in the amplitudes in comparison with normal subjects were predominant for rings 1 and 2 (within 10° of the fovea). Implicit times across the whole testing field were slightly delayed. Seven years later, the vision had not changed and the patient died a few months later.

CASE 2

Her daughter aged 50 presented from 1997 to 2007 a progressive vision loss in both eyes. The best corrected visual acuity decreased from 20/35 in 1997 to 20/60 in 2007 at the right eye and from 20/20 to 20/25 at the left eye. No pupillary defect was present. There were central scotomas in the visual field bilaterally. Color vision was also altered on Ishihara and Boström-Kugelberg plates. Fundus examination and fluorescein angiography were unremarkable (Fig A).

The full-field ERG results showed normal scotopic, mixed component and photopic responses in both eyes. The mf-ERG revealed severely reduced amplitude responses in the central area

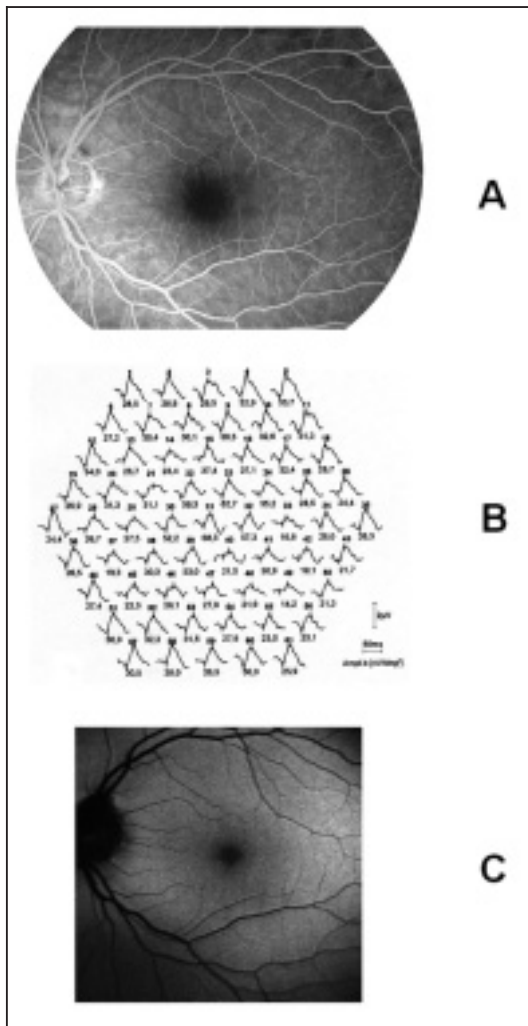


Fig A: Fluorescein angiography from the left eye of case 2 showing essentially normal findings.

Fig B: Multifocal electroretinograms responses of the left eye of case 2 demonstrating depressed signals from the macular area.

FIG C: Normal fundus autofluorescence in case 2

(ring 1 and 2). At the most peripheral areas, the amplitudes were nearly normal (Fig B). The mean implicit times were slightly delayed. The foveal thickness measured by OCT was within the normal range (RE: 174 μm , LE: 160 μm). FAF images showed homogeneous background fluorescence and a gradual decrease in the inner macula towards the foveola due to the masking effect of macular pigment. These results can be considered as normal (Fig C).

DISCUSSION

Occult macular dystrophy described by Miyake is characterized by a progressive decline of visual acuity with an essentially normal fundus and normal fluorescein angiography. Localized severe macular dysfunction detected only by focal macular electroretinograms or mfERG was found in this disease suggesting an abnormality in the central retina distal to the ganglion cells (1,2). There is a great variability in clinical findings and in the pattern of inheritance of reported cases. OMD was initially described as an inherited progressive condition based on familial occurrence in half of reported cases (2). On the other hand, recently, a series of nine patients with OMD has been reported without clear evidence of progression or inheritance pattern (5). These last results should be viewed cautiously because the absence of inheritance pattern could only have been concluded if mfERG had been performed in all family members, since visual acuity of 20/20 can be associated with an abnormal mfERG. However, should these results be found to be accurate, this might suggest several etiologies of which some are well known but seen too early to detect significant changes or might represent genetic heterogeneity with a specific clinical phenotype (OMD) determined by mutation of different genes.

In our cases, the pattern of inheritance is autosomal dominant. Case 1 was followed up for 23 years from the beginning of complaints. No fundus changes were noted during this period. No evolution of the fundus in the daughter was observed after 10 years of follow up.

Electrophysiological recordings and particularly mfERG remain the gold standard to detect the level of the pathological process and to make the diagnosis of OMD. These tools are very helpful in the differential diagnosis of other conditions of vision loss with normal fundus such as amblyopia, optic nerve disease or psychological vision problems.

So far, there has been no histopathologic report on this condition. The only significant anatomic changes demonstrated by OCT and spectral domain OCT are a reduced foveal thickness associated with thinning of the outer nuclear layer (6) and a defect in the junction between the inner and outer segments of the foveal

photoreceptors (7). The choroidal circulation evaluated by indocyanine green video-angiography has been described as normal in two patients with this pathology (8).

FAF imaging is a recent method to detect early retinal pigment epithelial alterations. The accumulation with age of lipofuscin in the lysosomal compartment of the retinal pigment epithelium is responsible for intrinsic fluorescence. This exam may visualise disease-specific distributions of lipofuscin in the retinal pigment epithelium (RPE) often not yet visible on ophthalmoscopy such as Stargardt disease, rod-cone dystrophy (9). The normal fundus autofluorescence in our case suggests a healthy and functional RPE. This finding is in correlation with the pathophysiology of OMD since the disease is distal of ganglion cells.

In conclusion, FAF imaging in our case of dominant autosomal OMD suggests a healthy and functional RPE. In our opinion, this examination of RPE by fundus autofluorescence should be added to the work-up of suspected OMD in order to exclude well known maculopathies not yet visible on ophthalmoscopy and to better define OMD.

REFERENCES

- (1) MIYAKE Y., ICHIKAWA K., SHIOSE Y., KAWASE Y. – Hereditary macular dystrophy without visible fundus abnormality. *Am J Ophthalmol* 1989; 108: 292-9.
- (2) MIYAKE Y., Horiguchi M., TOMITA N., et al. – Occult macular dystrophy. *Am J Ophthalmol* 1996; 122: 644- 53.
- (3) MARMOR M.F., HOOD D.C., KEATING D., KONDO M., SEELIGER M.W., MIYAKE Y. – Guide-

- lines for basic multifocal electroretinography (mfERG). *Doc Ophthalmol* 2003; 106:105-15.
- (4) MARMOR M.F., HOLDER G.E., SEELIGER M.W., YAMAMOTO S. – Standard for clinical electroretinography (2004 update). *Doc Ophthalmol* 2004; 108:107-14.
- (5) LYONS JS (2005) – Non-familial occult macular dystrophy. *Doc. Ophthalmol* 111: 49-56.
- (6) BROCKHURST R.J., SANDBERG MA. – Optical coherence tomography findings in occult macular dystrophy. *Am J Ophthalmol* 2007; 143: 516-8.
- (7) KOIZUMI H., MAGUIRE J.I., SPAIDE RF. – Spectral domain optical coherence tomographic findings of occult macular dystrophy. *Ophthalmic Surg Lasers Imaging*. 2009; 40: 174-6.
- (8) Fujii S., Escano M.F.T., Ishibashi K., Matsuo H., Yamamoto M. – Multifocal electroretinography in patients with occult macular dystrophy. *Br J Ophthalmol* 1999; 83: 879-80.
- (9) WABBELS B., DEMMLER A., PAUNESCU K., WEIGSCHEIDER E., PREISING M.N., LORENZ B. – Fundus autofluorescence in children and teenagers with hereditary retinal diseases. *Graefes Arch Clin Exp Ophthalmol* 2006; 244: 36-45.

.....

Adress for correspondence:
RASQUIN Florence
Erasmus University Hospital
Department of Ophthalmology
808, Route de Lennik
1070 Brussels
Belgium
E-mail: frasquin@ulb.ac.be
Phone: 003225554514
Fax: 003225556737