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Case report

A case study of choroideremia carrier – Use of multi-spectral imaging in highlighting clinical features

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ABSTRACT

Purpose: To report the use of non-invasive multi-spectral imaging of a female choroideremia (CHM) carrier with mild visual symptoms and extensive fundus mottling.

Observation: This was an observational case report study. A symptomatic 42-year-old female with a history of binocular CHM presented for routine ocular examination and underwent review of her clinical and photographic records, optical coherence tomography (OCT), intravenous fluorescein angiography (IVFA) and multi-spectral imaging (MSI). Dilated fundus examination and photography revealed similar outcomes of diffuse mottling with normal looking vessels. IVFA showed large irregular and confluent patches of RPE atrophy in the peripapillary and parapapillary areas as well as the midperiphery, corresponding to the OCT findings. The entire range of MSI imaging (520–940 nm) clearly illustrated the anomalies of the fundus including retinal pigment epithelium (RPE) mottling with melanin clumping not readily seen with the other imaging modalities. MSI fundus autofluorescence (MSI-FAF) showed a spotty hypo and hyperautofluorescent appearance of the fundus, consistent with the observations seen on IVFA and OCT images.

Conclusion and Importance: MSI significantly improves visualization of the retinal pigment epithelium in choroideremia. The non-invasive nature of MSI technique is a valuable tool in monitoring the effect of retinal and choroidal presentation in patients with CHM.

1. Introduction

Choroideremia (CHM) is a recessive X-linked chorioretinal dystrophy caused by mutation in the CHM Xq21 gene which encodes the protein REP-1 [1]. The condition is a progressive, diffuse degeneration of the choroid, retina, retinal pigment epithelium (RPE) and photoreceptors. Symptoms include bilateral nyctolopia in childhood followed by annular scotomas leading to concentric visual field loss and impairment of visual acuity, color vision and stereopsis by mid-adulthood, specifically in males. Fundus changes are observed as non-specific pigmentary stippling and focal areas of choroidal atrophy in the mid-periphery. With degenerative changes of the RPE, window defects showing remnants of the choroidal vasculature become apparent in peripapillary areas and macula. As the disease advances, the sclera becomes visible on fundus examination in the areas of complete choroidal and retinal atrophy.

Differential diagnosis includes retinitis pigmentosa and gyrate atrophy. In the former there is a greater amount of pigment migration and in the later there is elevated plasma concentration of orinithine. Non-invasive visualization of the RPE can assist in the differential diagnosis.

Female carriers of CHM may also show varying degrees of chorioretinopathy, RPE atrophy and granular pigmentary atrophy in the periphery. Severe visual impairment rarely occurs and is typically attributed to skewed X-inactivation [2]. Visual function remains fairly good, with either no symptoms or mild to moderate nyctalopia. Full-field electroretinograms (ERG) vary in female carriers and there is no definitive expected outcome. Most cases are normal or only slightly reduced [3].

Theories on the pathophysiology of CHM include degeneration of rod photoreceptors followed by degeneration of the choroid or primary RPE degeneration [2,4,5]. Advances in ocular imaging have

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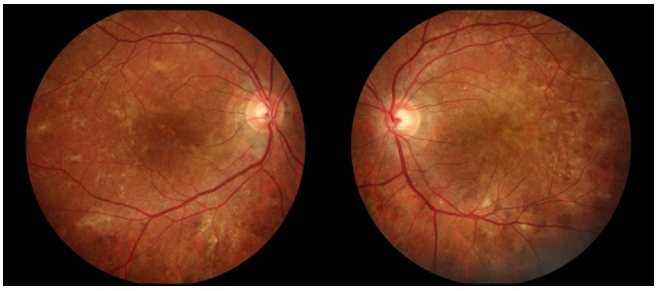

Fig. 1. 50° fundus images of the patient showing discoloration of the retina central and mid-peripherally (right eye < left eye).

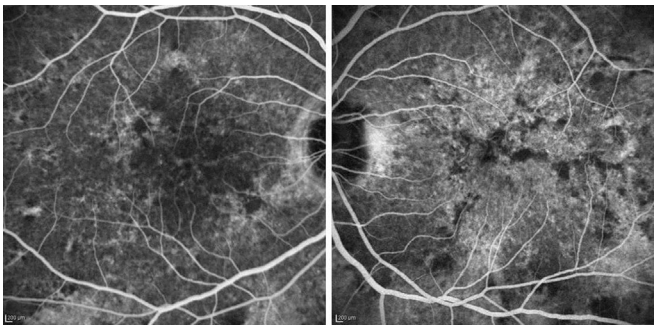

Fig. 2. Intravenous fluorescein angiography (IVFA).

led to better understanding of CHM morphological patterns. Optical coherence tomography (OCT) is used to detect chorocapillaris loss and choroidal neovascularization associated with CHM [6]. An important diagnostic criterion in female carriers is the mottled RPE changes which cause patchy fundus autofluorescence (FAF) irregularities with areas of hypo and hyperautofluorescence [7].

In this case report, a female carrier of CHM was imaged with traditional technologies as well as with multi-spectral imaging (MSI). MSI has the capability of highlighting the detailed structure of RPE, particularly melanin for early morphologic changes that are not generally visible clinically or with traditional fundus imaging modalities in routine practice [8]. Given the important role of the RPE in the pathogenesis of CHM and other retinal pathologies, examination of this layer with MSI may prove highly valuable for noninvasive differential diagnosis from RP and for monitoring progression.

2. Case report

A 42-year old female presented to the retinal clinic for her annual eye examination, as directed by her physician. She was a known carrier of choroideremia having been diagnosed in her teens and had a positive family history of CHM, with a brother exhibiting the disease. Best-corrected visual acuities (BCVA) were 20/20 in each eye with a refraction of +3.00−0.50 × 090 OD and +2.50−0.75 × 115 OS. The patient had full confrontational visual fields in each eye and refused to have an automated visual field test. Her past medical history was unremarkable with no history of smoking. Her family history of systemic and ocular conditions included heart diseases, arthritis, glaucoma and cataracts. The patient was not on any medications and was allergic to Codeine and Omeprazole. She complained of blurry vision at distance initially, due to under-corrected refractive error, but had no symptoms of CHM including nyctalopia. She refused an electroretinogram (ERG) or specific genetic testing for further assessment of her condition.

Her ocular anterior segment examination was unremarkable. Dilated fundus examination revealed diffuse mottling with normal vasculature. There was some peripapillary atrophy OU. Fundus photography images (Canon CF-1 OIS version 11.4.0) revealed diffuse mottling and scattered changes in fundus coloration centrally and in the mid-periphery (Fig. 1). The intravenous fluorescein angiography (IVFA) images showed large irregular and confluent patches of RPE atrophy (Fig. 2). The patient was further imaged with the spectral domain optical coherence tomography (SD-OCT; Spectralis, Heidelberg Engineering, Germany) where shortening of the photoreceptor inner and outer segments in areas corresponding to RPE atrophy were observed. Additionally, changes in the RPE thickness were seen corresponding to the hypo-reflective regions on the scanning laser ophthalmoscope (SLO) scans. The remaining laminations, however, appeared to be normal in both eyes (Fig. 3).

The patient was imaged on the FDA approved, RHA™ Multi-Spectral Imaging Device (Annidis Corporation, Ottawa, Canada). The system uses twelve specific individual, non-overlapping, narrow-band LED light sources in a range from 520 nm to 940 nm to create en-face spectral images throughout the posterior segment from internal limiting membrane (ILM) to the choroid. The short-wavelength images (MSI-580 nm and MSI-590 nm), which increase the visibility of the anterior retinal layers, showed healthy looking vasculature OU but hyper-reflective white anomalies were seen in the mid-periphery of both eyes (Fig. 4A and B). With the use of longer-wavelength images (MSI-620 nm – MSI-850 nm)

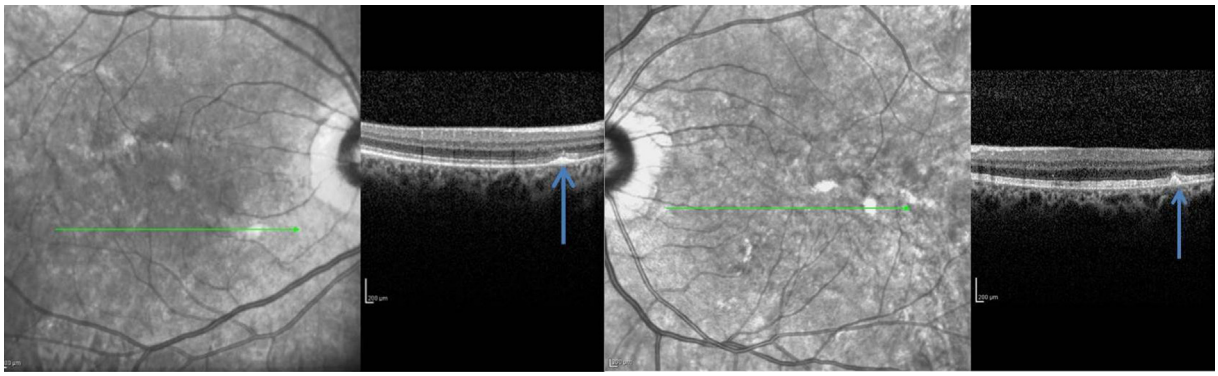

Fig. 3. Optical coherence tomography (OCT) scans of patients eyes. The blue arrows indicate areas of irregularities of the retinal pigment epithelium in both eyes in the OCT en-face thickness scan corresponding to hypo-reflective spots in the per-macular area (see green lines through the area of irregularity).