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In vivo visualization of variable photoreceptor alteration in a case of peripapillary congenital hypertrophy of the retinal pigment epithelium using spectralis ® high magnification module

Sina Elahi, Alexandra Miere *, Ala El Ameen, Eric H. Souied

Department of Ophthalmology, Centre Hospitalier Intercommunal de Créteil, 40 avenue de Verdun, 94000, Créteil, France

A R T I C L E I N F O

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A B S T R A C T

Purpose: To analyze using the high magnification module (HMM) a case of peripapillary congenital hypertrophy of retinal pigment epithelium (CHRPE) and to correlate the findings to multimodal imaging and swept-source optical coherence tomography angiography (SS-OCTA, PLEX® Elite 9000, Carl Zeiss Meditec, Dublin, California, USA) imaging.

Observations: A 57-year-old Caucasian woman presenting a peripapillary CHRPE of the left eye (LE) was examined using HMM and SS-OCTA, in addition to multimodal imaging. SS-OCTA disclosed the gradual changes, with four distinguishable zones: Zone 1 with complete outer retinal and retinal pigment epithelium (RPE) atrophy, Zones 2 and 3, corresponding to incomplete outer retinal (and RPE) atrophy presenting increased flow deficits, and normal choriocapillaris outside the lesion (Zone 4). High Magnification Module (HMM, Spectralis ®, Heidelberg Engineering) showed small polygonal hyperreflective outlines over the pigmented parts of the lesion (Zone 2), and partly over the narrow halo surrounding the lesion (Zone 3), with an absence of these outlines over the lacunae (Zone 1).

Conclusions and importance: HMM is a non-invasive imaging modality, allowing the in vivo visualization of a mosaic pattern, corresponding to the hyperreflective polygonal outlines, or absence thereof, in different zones of CHRPE.

1. Introduction

Described by Reese in 1960[1] as a "flat, jet-black area sometimes mistaken for a malignant melanoma", Congenital Hypertrophy of the Retinal Pigment Epithelium (CHRPE) is characterized by a single, well-demarcated, flat, slowly growing lesion on the retina with variable degrees of dark pigmentation, often located peripherally, and which may be associated with lacunae, and a depigmented halo.[2] The lesion is quite common and its reported prevalence is up to 4.4% of the normal population.[3–5] It must be differentiated from other pigmented lesions such as melanoma, and Grouped Pigmentation of the Retina (GPR) which consists of smaller, multiple lesions, arranged in a typical "bear track" pattern.[4] The latter has been associated with Familial Adenomatous Polyposis, Gardner Syndrome, and colon cancer, while classic CHRPE is a benign lesion, although rare malignant transformation of intralesional nodules has been described.[6]

CHRPE classically starts dark and pigmented and evolves into a heterogeneous, less pigmented lesion with lacunae. About 85% of lesions enlarge slowly over time, growth seemingly being linked to the area of lacunae coverage.[7] In case of homogeneous dark lesions, involved RPE appears hyperreflective, thickened and irregular, with posterior shadowing.[3] With time, the lesion becomes more disorganized, demonstrating photoreceptor loss, and at lacunae sites, the complete absence of RPE. Histological studies have shown that the pigmented areas corresponded to hypertrophic RPE cells with melanosomes and absence of lipofuscin, while depigmented areas were characterized by atrophic and thinned RPE cells with rare melanosomes.[4] Clinicopathologically, there are gradual changes from the pigmented areas to the non-pigmented areas in both photoreceptors and RPE-Bruch membrane complex.[4,5] As a benign lesion, the management of CHRPE is largely observational, especially for growth, atrophy development, and rare malignant transformation, but care must be taken to rule out the aforementioned associated systemic diseases.

In 2018, Heidelberg Engineering introduced the new High

* Corresponding author.
E-mail address: alexandra.miere@chicreteil.fr (A. Miere).

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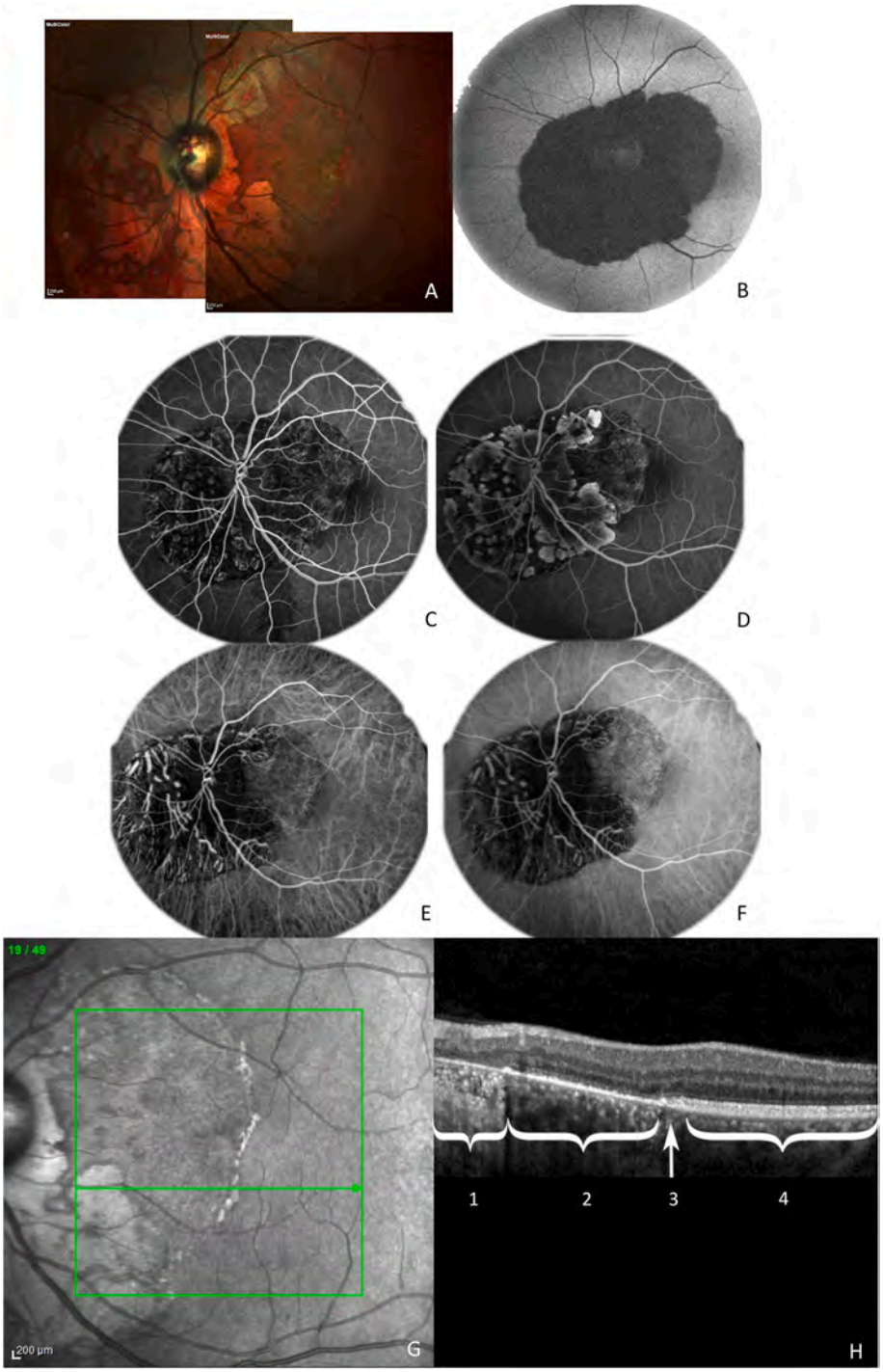

Fig. 1. Multimodal imaging of CHRPE. A. Well-demarcated peripapillary lesion with lacunae, areas of varied pigmentation and a slightly pigmented halo surrounding the lesion were seen on multicolor imaging. B. Fundus Autofluorescence (FAF) imaging showed a homogeneously peripapillary hypoautofluorescent lesion. C, D. Fluorescein angiography at early (C) and late (D) frames of the examination, revealed a hypofluorescent lesion, with areas of window defect. E, F. Indocyanine green Angiography (ICGA) at early (E) and late (F) frames of the examination, was non-specific and showed hyperfluorescent choroid in the areas of lacunae and retinal atrophy. G. Infrared imaging and corresponding optical coherence tomography (H) displayed four distinctive areas, labeled as zones 1–4. At lacunae' sites, areas of complete RPE and outer retinal atrophy with absence of IS/OS junction (cRORA- Zone 1) were observed, and in more pigmented areas of the lesion, incomplete RPE and outer retinal atrophy with altered but preserved IS/OS junction (iRORA – Zone 2). The halo surrounding the lesion corresponded to outer retinal atrophy with thickened IS/OS junction (iORA - Zone 3), and finally, preserved retina was seen outside the lesion (Zone 4). . (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Magnification Module (HMM), a high definition confocal scanning laser ophthalmoscopy (cSLO) presumably capable of identifying microstructures otherwise invisible on fundoscopy or fundus photography, supposedly at the cellular level, enabling photoreceptors' (cones and rods) visualization. HMM, by means of an objective lens, magnifies the fundus to provide a field of view of 8°, thereby improving the visualization of microscopic fundus details. CHRPE being associated with variable photoreceptor loss, the purpose of this case report was to use HMM to analyze a case of peripapillary CHRPE as well as describing it for the first time using swept-source optical coherence tomography angiography (SS-OCTA) imaging.

2. Clinical presentation

A 57-year-old Caucasian woman with no past medical history or family history (including the lack of bowel changes) was referred to our tertiary center for a second opinion. A slowly expanding, peripapillary CHRPE of the left eye (LE) was detected 10 years ago and she was now complaining of progressive vision loss in this eye. Best-corrected visual acuity (BCVA) of the right eye (RE) was 20/20 and 20/40 on the LE. Intraocular pressure was normal on both eyes. Anterior segment slit-lamp examination was unremarkable. The rest of the examination and investigations on the RE were unremarkable.

LE fundus examination and Multicolor imaging revealed an oval-

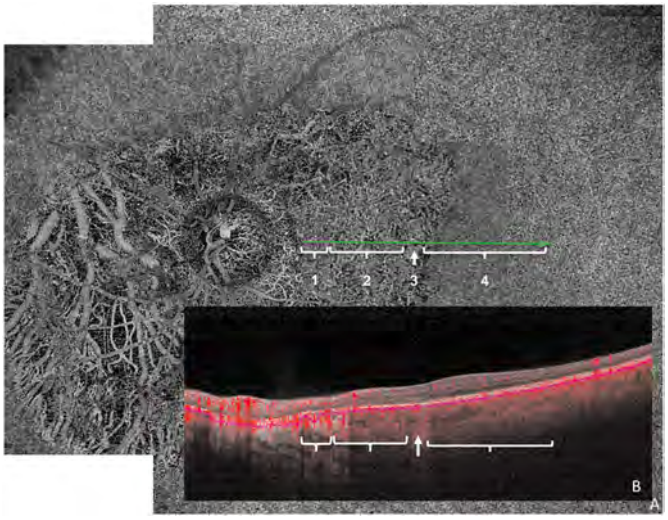

Fig. 2. Swept-source widefield optical coherence tomography angiography montage (SS-OCTA) en-face flow image of the choriocapillaris automatic segmentation (A) disclosed the same gradual changes seen on SD-OCT and the corresponding B-scan with flow overlay (B): iRORA areas (Zone 2) showed increased flow deficits, and so did areas of iORA (Zone 3). Choriocapillaris was normal outside the lesion (Zone 4).

shaped well-defined peripapillary lesion, with alternating internal areas of depigmented lacunae and pigmentation, accompanied by a surrounding halo. (Fig. 1, Panel A).

On infrared imaging, the lesion was isoreflective with hyperreflective lacunae and a hyperreflective band. On fundus autofluorescence (FAF), it was uniformly hypoautofluorescent. (Fig. 1, Panel B).

Fluorescein angiography (FA) revealed a hypofluorescent lesion in the early frames, with areas of window defect at lacunae' sites at the later ones (Fig. 1, Panel C&E). Indocyanine green angiography (ICGA) allowed the visualization of Haller's layer in areas of atrophy and showed moderate hypofluorescence temporally to the optic disc. (Fig. 1, Panel D&F).

On spectral domain optical coherence tomography (SD-OCT, Spectralis ®, Heidelberg Engineering), the lesion was characterized by four distinctive areas, labeled as zones 1–4. At lacunae' sites, areas of complete RPE and outer retinal atrophy with absence of IS/OS junction (cRORA- Zone 1), and in more pigmented areas of the lesion, incomplete RPE and outer retinal atrophy with altered but preserved IS/OS junction (iRORA – Zone 2). The halo surrounding the lesion corresponded to outer retinal atrophy with thickened IS/OS junction (iORA - Zone 3), and finally, preserved retina was seen outside the lesion (Zone 4). (Fig. 1, Panels G and H). SS-OCTA (PLEX® Elite 9000, Carl Zeiss Meditec, Dublin, California, USA) disclosed the same gradual changes seen on SD-OCT. iRORA areas (Zone 2) showed increased flow deficits, and so did areas of iORA (Zone 3). Choriocapilaris was normal outside the lesion (Zone 4). (Fig. 2).

High Magnification Module (HMM, Spectralis ®, Heidelberg Engineering) showed small polygonal hyperreflective outlines over the pigmented parts of the lesion (Fig. 3, Zone 2), and partly over the narrow halo surrounding it (Fig. 3, Zone 3), with an absence over the lacunae (Fig. 3, Zone 1).

3. Discussion

This case confirms the previous literature on the multimodal imaging findings of CHRPE on fundus photographs, infrared (IR), FAF, FA, ICGA, or OCT. Although CHRPE has been recently described using OCTA,[8] the authors of the previous paper noted the poor quality of their images and difficulty in segmenting the layers as the lesion was very peripheral. In our case, the peripapillary location allowed an easier acquisition and a more precise analysis.

The main goal of this multimodal description was therefore to use the established knowledge to better assess the findings of the HMM, a device presumably able to visualize photoreceptors as a mosaic hyperreflective polygonal outlines (HPO). Careful superposition of IR, OCT, and OCTA images, allowed the identification of 4 zones: cRORA (Zone 1), iRORA (Zone 2), a delimitating halo (Zone 3), and normal retina (Zone 4). By correlating HMM imaging to multimodal imaging, we were able to document in vivo that Zone 1 (deprived of photoreceptors in histology) was indeed deprived of such hyperreflective polygonal outlines on HMM. Areas with preserved photoreceptors (Zone 2–4), however, displayed the fore-mentioned hyperreflective polygonal pattern on HMM (Fig. 3). Although more studies would be needed to confirm such finding, with other pathologies, since the sole known difference between the zones displaying the hyperreflective polygonal outlines and those that do not is the involvement of the photoreceptor layer, it seems indeed likely that these outlines are, as presumed, an in vivo visualization of photoreceptors.

This would represent an important breakthrough in retinal imaging, and perhaps lead to a better understanding of retinal diseases' pathophysiology. HMM is a non-invasive imaging modality that could be added to the multimodal array available to retina specialists. HMM's focus must be, however, well adjusted, in order to see effectively this mosaic pattern corresponding to the hyperreflective polygonal outlines or absence thereof.

In conclusion, the in-vivo visualization of individual photoreceptors seems to be a new possibility thanks to HMM imaging, which may help improve the understanding and diagnosis of photoreceptor alteration in CHRPE.

Patient consent

The patient consented to publication of the case.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

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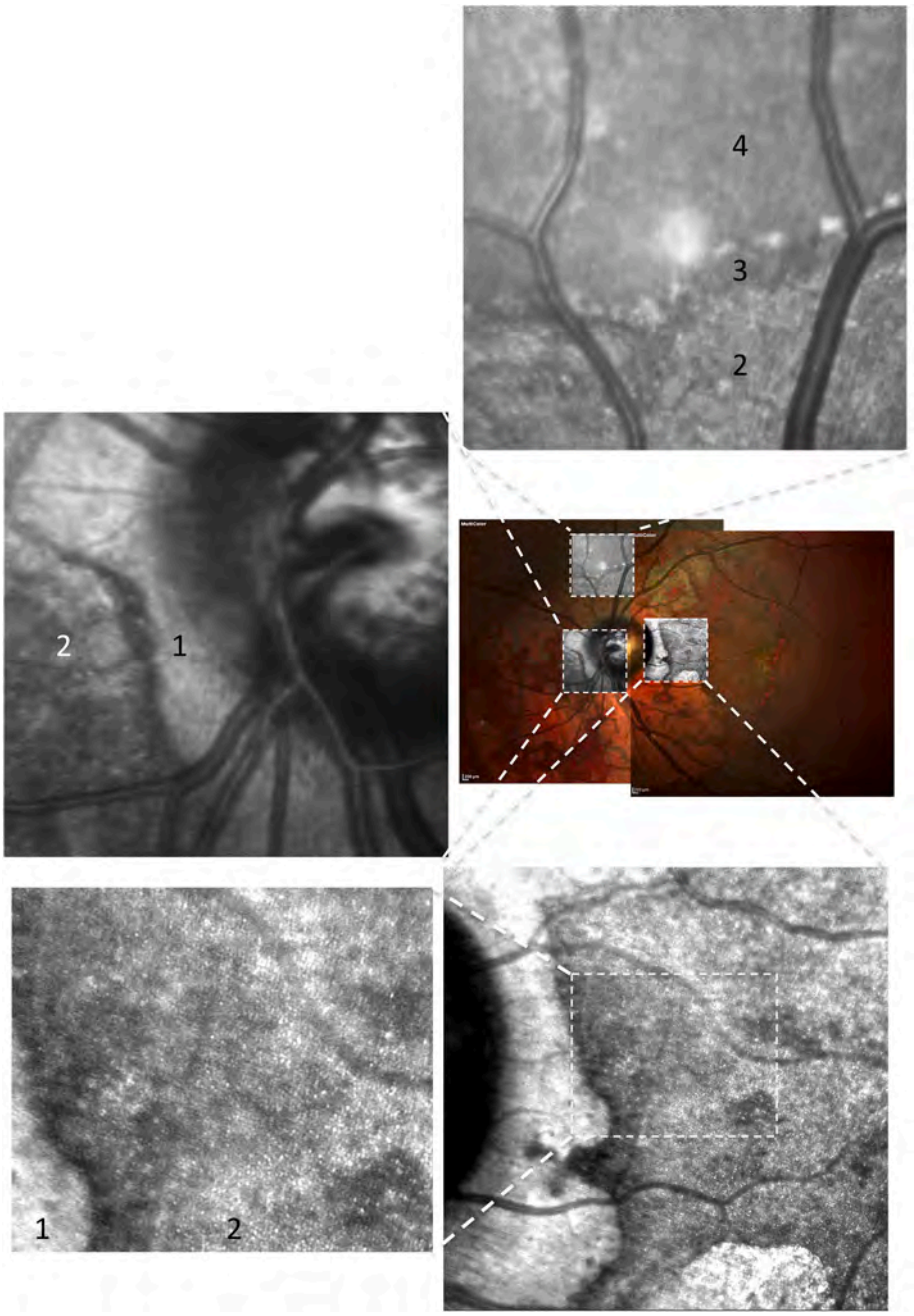

Fig. 3. High Magnification Module (HMM) imaging of the CHRPE lesion. High Magnification Module overlayed on the Multicolor Imaging, disclosed small polygonal hyperreflective outlines over the pigmented parts of the lesion (Zone 2), and partly over the narrow halo surrounding it (Zone 3), with an absence over the lacunae (Zone 1). The aspect of normal retina corresponded to Zone 4.

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