2019

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American Journal of Ophthalmology Case Reports 15 (2019) 100465

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.elsevier.com/locate/ajoc

Case report

Utility of *en-face* imaging in diagnosis of occult macular dystrophy with RP1L1 mutation: A case series

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ARTICLE INFO

Keywords:
En-face imaging
Ellipsoid zone
Occult macular dystrophy
RP1L1

ABSTRACT

Purpose: To report *en-face* imaging findings at the level of ellipsoid zone (EZ) in two cases of occult macular dystrophy (OMD) with retinitis pigmentosa 1-like 1 (RP1L1) p.Arg45Trp mutation.
Observations: In both patients who presented with decreased vision, pupillary examination, intraocular pressure, and anterior examination were normal. Ophthalmoscopic examination showed prominent choroidal marking whereas fundus autofluorescence was unremarkable. Spectral domain optical coherence tomography (SD-OCT) showed subtle gaps between EZ and retinal pigment epithelium (RPE). The photoreceptor disruption became more evident with *en-face* imaging at the EZ plane.
Conclusions and importance: This is a report of two patients with EZ *en-face* imaging that aided in the diagnosis of OMD where other structural imaging was largely unremarkable. The *en-face* imaging modality can also be used to monitor OMD progression.

1. Introduction

Occult macular dystrophy (OMD) is a retinal disease characterized by progressive decline in central visual acuity in the presence of normal fundus, autofluorescence, and angiographic findings.[1] The current gold standard for diagnosis is multi-focal ERG (mfERG) followed by genetic confirmation of hereditary cases. Patients have a reduction of multi-focal ERG (mfERG) amplitude in central areas.[2] Genetics analyses from patients with family history revealed that dominant mutation in Retinitis Pigmentosa 1 Like 1 (RP1L1) gene p.Arg45Trp as the cause.[3] However, sporadic patients usually do not have the same mutations, suggesting other genes may also cause similar symptoms and signs. Even within patients with RP1L1 p.Arg45Trp mutation, the age at which patients report subjective decrease of vision varies widely from 6 to 60 years old.[1]

Here, we report *en-face* imaging of retinitis pigmentosa 1-like 1 (RP1L1) associated OMD that accentuates photoreceptor disruption in OMD and can aid in its diagnosis at initial presentation, thus avoiding unnecessary testing and procedures.

2. Findings

Two patients with adult-onset occult macular dystrophy were included.

2.1. Case 1

A 56-year-old woman with psoriatic arthritis presented with ongoing blurry vision for 4 years. She had undergone bilateral cataract surgery with minimal improvement in her vision at the age of 52. A year after cataract surgery, she was diagnosed with central serous retinopathy (CSR). Given her continued visual symptoms, she underwent an MRI at 54 years old and was found to have a right ophthalmic artery aneurysm that was stented without improvement in vision. On presentation, her best-corrected vision acuity (BCVA) was 20/100 in each eye with normal pupillary exam, intraocular pressures, and color plates in both eyes. Ophthalmoscopic exam showed tilted nerves with prominent choroidal markings (Fig. 1A and B) and fundus autofluorescence was unremarkable (Fig. 1C).

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https://doi.org/10.1016/j.ajoc.2019.100465
Received 5 October 2018; Received in revised form 9 December 2018; Accepted 7 May 2019
Available online 09 May 2019

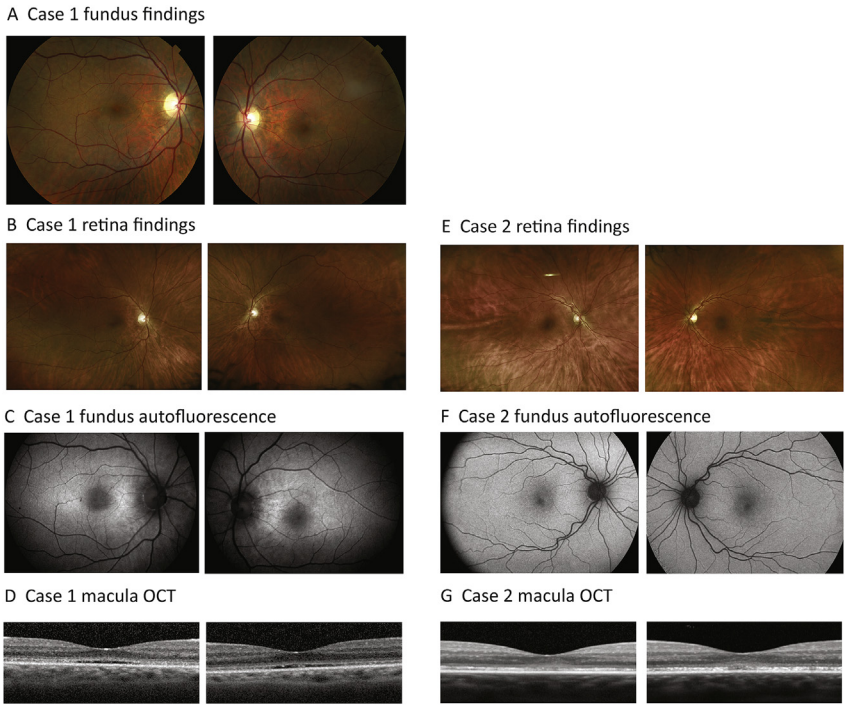

Fig. 1. Multimodal Imaging of RP1L1 associated Occult Macular Dystrophy. A: Case 1 fundus photos show tilted nerves and prominent choroidal markings, B: Case 1 wide angle retina photo, C: Case 1 fundus autofluorescence is unremarkable, D: Case 1 SD-OCT of the macula shows a gap between EZ and RPE. E: Case 2 fundus photos show prominent choroidal markings, F: Case 2 fundus autofluorescence shows normal findings, G: Case 2 macula SD-OCT shows a gap between EZ and RPE.

2.2. Case 2

A 46-year-old man was referred to the retina clinic for suspected cone dystrophy. Past ocular history was significant for decreased vision for the last 20 years. His parents were second cousins. Family history was significant for cone dystrophy in a cousin. On exam, his BCVA was 20/50 OD and 20/60 OS. Pupillary exam, intraocular pressure, and anterior examination were unremarkable. Full field ERG was also within normal limits. Funduscopic exam showed prominent choroidal markings (Fig. 1E) and autofluorescence (Fig. 1F) were normal.

In both cases, spectral domain optical coherence tomography (SD-OCT) through the fovea showed gaps between the ellipsoid zone (EZ) and retinal pigment epithelium (RPE) bilaterally (Fig. 1D, G). Although subtle and almost undetectable in certain areas on structural OCT, the photoreceptor disruption in both cases was starkly evident with *en-face* imaging of the ellipsoid zone (Fig. 2).

Given these findings, OMD was suspected. Whole exome sequencing (WES) revealed heterozygous mutations in RP1L1 (p.Arg45Trp) both cases, which was confirmed by Sanger sequencing.

3. Discussion

Occult macular dystrophy only affects the macula and is difficult to diagnose with the commonly used imaging methods in ophthalmologic clinic. Multi-focal ERG (mfERG), which is time-consuming and labor intensive, is usually performed after high clinical suspicion for OMD. Typically, OMD patients show central loss of response density and normal periphery in mfERG.[4] Whole exome sequencing is cost-prohibiting and time consuming. Moreover, sporadic OMD patients usually do not have the predictable mutations due to genetic heterogeneity. Even with RP1L1 p.Arg45Trp mutation that is common in familial OMD, the age of onset varies,[3] further increasing the difficulty of diagnosis. SD-OCT is the most sensitive imaging modality to diagnose OMD as central loss of outer segment (OS)-RPE interdigitation zone and low reflectivity of EZ are detected in more than 85% of the OMD patients.[5] Even in asymptomatic patients with RP1L1 mutations, one study showed parafoveal loss and foveal preservation of photoreceptors through SD-OCT.[6] However, these changes can easily be missed by those not experienced at closely studying structural SD-OCTs. Moreover, it is difficult to estimate the area of affected photoreceptors on structural SD-OCT. The ellipsoid zone *en face* findings of these two patients corresponded to the loss EZ and low reflectivity in SD-OCT. Compared to the SD-OCT B-scans, ellipsoid *en face* images more distinctively illustrated photoreceptor loss in these two patients. The diagnosis can be confirmed by single gene sequencing of RP1L1. In addition, since ellipsoid zone *en face* is time-efficient and non-invasive, it can be a useful modality to monitor OMD longitudinally.

4. Conclusions

This is a report of ellipsoid zone *en-face* imaging in aiding diagnosis of OMD. This imaging modality can help raise clinical suspicion of OMD, which can be confirmed with genetic testing or mfERG. *En-face* imaging can also be valuable to monitor OMD progression.

Patient consent

The patient consented to the submission and publication of this case report with documentation on file.

Funding

No funding or grant support.

Conflicts of interest

None of the authors have financial disclosures related to this article.

Authorship

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

Acknowledgements

We thank the photographers in Columbia University Medical Center and Vitreous Retina Macula Consultants of New York for their help in obtaining imaging. We also thank Macula Foundation. for support.

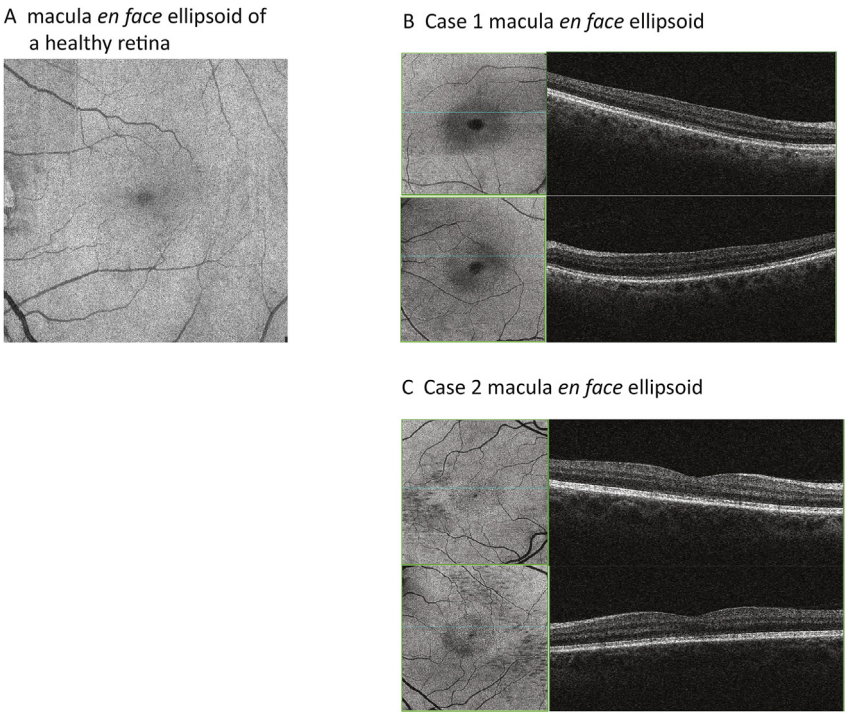

Fig. 2. *En-face* Imaging of RP1L1 associated Occult Macular Dystrophy. Case 1 and 2 *en face* ellipsoid analysis shows photoreceptor disruption with limited SD-OCT findings. Aqua line indicates position of the SD-OCT B-scan.

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