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MICROSTRUCTURAL ABNORMALITIES IN MEWDS DEMONSTRATED BY ULTRAHIGH RESOLUTION OPTICAL COHERENCE TOMOGRAPHY

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Abstract

Background— Histopathological studies of acute multiple evanescent white dot syndrome (MEWDS) have not been reported because of the transient and benign nature of the disease. Ultrahigh resolution optical coherence tomography (UHR-OCT), capable of high resolution in vivo imaging, offers a unique opportunity to visualize retinal microstructure in the disease.

Methods— UHR-OCT images of the maculae of five patients with MEWDS were obtained and analyzed. Diagnosis was based on clinical presentation, examination, visual field testing, and angiography.

Results— UHR-OCT revealed disturbances in the photoreceptor inner/outer segment junction (IS/OS) in each of the five patients (six eyes) with MEWDS. In addition, thinning of the outer nuclear layer was seen in the case of recurrent MEWDS, suggesting that repeated episodes of MEWDS may result in photoreceptor atrophy.

Conclusions— Subtle disruptions of the photoreceptor IS/OS are demonstrated in all eyes affected by MEWDS. UHR-OCT may be a useful adjunct to diagnosis and monitoring of MEWDS.

Multiple evanescent white dot syndrome (MEWDS) is a disease of unknown etiology that characteristically occurs in women in the second to fifth decades.¹ Ophthalmoscopic examination typically reveals multiple, 100- to 200- μ m yellow-white dots deep to the retina as well as a unique foveal granularity. Fluorescein angiography (FA) and electrophysiologic studies suggest that the location of the disease process is in the outer retina and/or the retinal pigment epithelium (RPE).² On indocyanine green angiography (ICG), lesions of MEWDS are hypofluorescent and disappear with clinical recovery, suggesting pathologic choroidal nonperfusion or RPE inflammation. Visual field alterations correlate well with ICG findings.^{3,4}

Ultrahigh resolution optical coherence tomography (UHR-OCT) offers a new technique for imaging in vivo retinal microstructure in details approaching that of histology.⁵ Capable of 3

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μm axial resolution in the retina, UHR-OCT offers a significant improvement over the 10 μm resolution available with StratusOCT (Carl Zeiss Meditec, Inc., Dublin, CA). In particular, UHR-OCT allows enhanced visualization of outer retinal layers, including the junction between photoreceptor inner and outer segments.

We present UHR-OCT images of the maculae of five patients with MEWDS. Diagnosis was based on clinical presentation, examination, visual field testing, and angiography. Using UHR-OCT, unique micro-structural retinal abnormalities were visualized in these patients.

Case 1

A 42-year-old woman presented with a 3-week history of photopsias in both eyes. Best-corrected visual acuity (BCVA) was 20/200 in the right eye and 20/15 in the left. Examination revealed foveal granularity and multiple, yellow-white 100- to 200- μm lesions deep to the retina in both eyes (Figure 1A). FA demonstrated typical early hyperfluorescence and late staining of these lesions as well as disk leakage bilaterally. ICG showed hypofluorescence of the spots bilaterally.

StratusOCT of the right eye was unremarkable. UHR-OCT imaging, however, demonstrated attenuation of OCT signal from the photoreceptor inner/outer segment junction (IS/OS). In the left eye, StratusOCT showed subtle attenuation of the IS/OS junction inferiorly (Figure 1B). Attenuation of both the IS/OS junction and the RPE was visualized in the inferior macula with UHR-OCT (Figure 1, C and D).

Case 2

A 46-year-old woman presented with a 1-month history of paracentral scotoma in the left eye. BCVA was 20/15 bilaterally. Examination of the left eye was remarkable for mild macular RPE changes and a few scattered yellow-white lesions deep to the retina. Visual fields testing showed an enlarged blind spot in the left eye.

Both StratusOCT and UHR-OCT images were normal in the right eye. In the left eye, StratusOCT showed small interruptions of the normally linear OCT signal from the photoreceptor IS/OS junction. UHR-OCT more clearly demonstrated these small disruptions in the IS/OS junction.

Case 3

A 52-year-old woman had photopsias in the right eye for the past 2 weeks. She also reported having similar symptoms in her left eye 4 years ago. BCVA was 20/20 bilaterally. Examination of her right eye revealed mild subfoveal RPE changes and several parafoveal yellow-white lesions (Figure 2A). The left eye was unremarkable. Visual fields testing demonstrated enlarged blind spots bilaterally.

StratusOCT of the symptomatic right eye was normal (Figure 2B). The corresponding image on UHR-OCT, however, showed several small interruptions of the photoreceptor IS/OS junction band across the subfoveal area (Figure 2, C and D). In the supero-temporal macula, signal from the RPE was also attenuated. Both StratusOCT and UHR-OCT of the patient's left eye were normal.

Case 4

A 49-year-old man presented with a 1-month history of floaters, flashes, and a central scotoma in the left eye. BCVA was 20/20 in the right eye and 20/40 in the left. Examination of the left eye was remarkable for multiple, widely scattered, 100- to 200- μm spots deep to the retina and

foveal granularity (Figure 3A). FA demonstrated early hyperfluorescence and late staining of the spots. Visual field testing revealed an enlarged blind spot in the left eye.

StratusOCT of left eye showed areas of missing signal from the photoreceptor IS/OS junction (Figure 3B). UHR-OCT more clearly showed these large areas of missing signal from the photoreceptor IS/OS junction (Figure 3, C and D).

Case 5

A 20-year-old woman presented with a pericentral blind spot in the right eye of 3 days' duration. History was significant for documented MEWDS in the right eye 10 years ago and in the left eye 7 years ago. BCVA was 20/50 in the right eye and 20/20 in the left. Examination of the right eye revealed multiple 100- to 200- μ m yellow spots and orange foveal granularity. FA showed typical early hyperfluorescence of the lesions with late staining, as well as disk edema.

OCT images of the affected eye were obtained 1 month after presentation. At this time, the patient was still symptomatic. Ophthalmoscopic examination showed a decreased number of white dots and persistent, prominent foveal granularity (Figure 4A). StratusOCT showed several areas of interruption of the IS/OS junction, as well as thinning of the outer nuclear layer (Figure 4B). UHR-OCT more clearly demonstrated these photoreceptor disturbances (Figure 4C, arrows) and outer nuclear layer thinning (Figure 4, C and D, asterisks).

Discussion

UHR-OCT, capable of 3 μ m axial resolution, revealed disturbances in the photoreceptor IS/OS junction in each of the five patients (six eyes) with MEWDS. Thinning of the outer nuclear layer was seen in Case 5, in whom the disease was recurrent, suggesting that repeated episodes of MEWDS may result in permanent photoreceptor atrophy. StratusOCT, capable of 10 μ m resolution, detected photoreceptor disruptions in four of the six eyes with MEWDS.

In all four figures, many areas of interruption or signal attenuation of the IS/OS junction are present across the macula. Interruptions of the IS/OS junction secondary to overlying retinal vessels appear as vertical lines of signal attenuation extending posteriorly from each vessel. In some of the cases of MEWDS presented here, small regions of photoreceptor outer segment disturbance appeared similar; however, the lack of an overlying vertical line of signal attenuation distinguishes these disturbances from OCT signal attenuation secondary to an overlying vessel. Signal attenuations of the IS/OS junction without association with an overlying retinal vessel is typically absent on OCT images of patients with normal retinas, suggesting these interruptions of the IS/OS band represent true anatomic disturbance of photoreceptor outer segments.

The areas of photoreceptor disruption seen on StratusOCT and UHR-OCT correlated well with clinical findings. In Case 1, the patient was seen clinically to have multiple, yellow-white 100- to 200- μ m lesions deep to the retina, mostly inferiorly (Figure 1A). Attenuation of the IS/OS junction was visualized in the inferior macula with StratusOCT (Figure 1B) and more clearly with UHR-OCT (Figure 1, C and D). In Case 3, the patient clinically showed mild subfoveal RPE changes (Figure 2A). UHR-OCT showed disruptions of the subfoveal photoreceptor IS/OS junction (Figure 2, C and D). The patient in Case 4 had multiple, widely scattered, 100- to 200- μ m spots deep to the retina and foveal granularity (Figure 3A). StratusOCT revealed multiple areas of interruption of the photoreceptor IS/OS junction band (Figure 3B). UHR-OCT more clearly showed these pathologic disruptions in the photoreceptor IS/OS junction (Figure 3, C and D). In Case 5, clinical examination at the time of OCT imaging demonstrated several white lesions inferior-temporally and prominent, orange foveal granularity (Figure 4A). Both StratusOCT and UHR-OCT illustrated subfoveal photoreceptor disturbances. The

additional parafoveal involvement seen on OCT imaging can be explained by subclinical lesions or persistent damage from previous disease in this patient. The clinically visible lesions inferior-temporally are not captured in the OCT scanning fields.

FA and ICG reviews suggest that the photoreceptor abnormalities of MEWDS are due to either choroidal ischemia or RPE inflammation.^{3–5} RPE disturbances are normally visualized as an increase in OCT signal penetration into the choroid. RPE disturbance was not prominent in UHR-OCT of MEWDS, which would be expected during acute choroidal ischemia. It is possible that the RPE regenerated following episodes of choroidal ischemia, while photoreceptors do not have this capability. It is also possible that because of the high pigment concentration, small RPE disturbances are not visible as a disruption on UHR-OCT. However, UHR-OCT findings suggest that MEWDS is more likely associated with RPE inflammation. Swollen but intact RPE cells would likely appear normal on OCT imaging. Inflammation of the RPE cells could interrupt the orientation of photoreceptor outer segments acutely, causing attenuation of OCT signal from the IS/OS junction as the outer segments become misaligned.

We did not examine the optic disk or nerve fiber layer (NFL) with OCT. Future studies may be performed to correlate OCT images of the optic disk and NFL to clinical examination, FA, and visual field findings. Furthermore, we did not perform serial UHR-OCT imaging of these patients with MEWDS. It would be interesting to elucidate whether OCT abnormalities are evanescent as suggested by clinical findings. The literature reports no reference to other conditions causing similar changes in the outer retina. This would be an interesting area for future studies, with particular attention to other white dot syndromes.

Due to the transient and benign nature of the disease, histopathologic studies of acute MEWDS are not practical. OCT, capable of high resolution in vivo imaging, offers a unique opportunity to visualize retinal microstructure in the disease. The increased axial resolution offered by UHR-OCT allows highly detailed images approaching histopathology. The UHR-OCT images presented show subtle disruptions of the photoreceptor IS/OS junction in all eyes with MEWDS. UHR-OCT may be a useful adjunct to diagnosis and monitoring of MEWDS.

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Fig 1. Case 1, left eye. (A) Color photograph revealing foveal granularity and multiple, yellow-white 100- to 200- μ m lesions deep to the retina. Arrow demonstrates direction of optical coherence tomography scans. (B) StratusOCT showing subtle disruptions in the photoreceptor inner/outer segment junction (IS/OS) (red arrow). (C) Ultrahigh resolution optical coherence tomography (UHR-OCT) more clearly demonstrating photoreceptor disruptions in patient with multiple evanescent white dot syndrome (red arrow). Outer retinal layers are indicated: outer nuclear layer (ONL), external limiting membrane (ELM), retinal pigment epithelium (RPE). (D) Higher magnification (2x) of boxed area of UHR-OCT image.

Fig 2.

Case 3, right eye. (A) Color photograph revealing mild retinal pigment epithelium changes near the macula. (B) StratusOCT of the symptomatic right eye appeared normal. (C) The corresponding image on ultrahigh resolution optical coherence tomography (UHR-OCT), however, showed several disruptions of the photoreceptor inner/outer segment (IS/OS) junction across the macula. (D) Higher magnification (2x) of boxed area of UHR-OCT image, showing small foveal disruptions in the IS/OS junction (red arrows).

Fig 3. Case 4, left eye. **(A)** Color photograph capturing multiple, 100- to 200- μ m spots deep to the retina and foveal granularity. **(B)** Stratus OCT revealing subtle areas of disruption of the photoreceptor inner/outer segment junction (red arrows). **(C)** Ultrahigh resolution optical coherence tomography (UHR-OCT) showing diffuse disturbances of the photoreceptor outer segments (red arrows). **(D)** Higher magnification (2x) of boxed area of UHR-OCT image.

Fig 4.

Case 5, right eye. (A) Color photograph 1 month after presentation revealing decreased number of lesions and persistent foveal granularity. (B) StratusOCT showing disruption of the photoreceptor inner/outer segment junction (red arrows). (C) Ultrahigh resolution optical coherence tomography (UHR-OCT) more clearly demonstrated these disruptions (red arrows). In addition, there was thinning of the outer nuclear layer (red asterisks), representing atrophy of the photoreceptor cell bodies. (D) Higher magnification (2x) of boxed area of UHR-OCT image. Areas of photoreceptor atrophy are shown (red asterisks).