Vision Loss After Intravitreal Ocriplasmin: Correlation of Spectral-Domain Optical Coherence Tomography and Electroretinography

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Ocriplasmin (Jetrea; Thrombogenics) is a recombinant protease with activity against components of the vitreo-retinal interface, including fibronectin and laminin. Ocriplasmin was recently approved for the treatment of symptomatic vitreomacular adhesion (VMA). A previous report has described transient vision loss associated with disruption of the photoreceptor inner segment-outter segment (ellipsoid) layer on SD-OCT and reduced ERG amplitudes in the patient's symptom of darkened vision. The ERG demonstrated a greater reduction in scotopic function compared with photopic function.

**IMPORTANCE** Clinical trials indicate that visual impairment is significantly greater in patients receiving ocriplasmin than placebo. The mechanism of this symptom has not been explained. We report a patient with persistent darkening of vision after intravitreal ocriplasmin and describe ancillary testing findings that may yield insights into the effects of ocriplasmin and the cause of this symptom.

**OBSERVATIONS** We describe a 71-year-old woman with symptomatic vitreomacular traction who received intravitreal ocriplasmin and experienced darkening of vision in dim illumination for 4 months, despite improvement in visual acuity and release of symptomatic vitreomacular traction. We demonstrate that disruption of photoreceptor inner segment-outter segment (ellipsoid) layer on SD-OCT and reduced ERG amplitudes correspond to the patient's symptom of darkened vision. The ERG demonstrated a greater reduction in scotopic function compared with photopic function.

**CONCLUSIONS AND RELEVANCE** On the basis of these findings, it is possible that ocriplasmin may have a diffuse enzymatic effect on photoreceptors or the retinal pigment epithelium that is not limited to areas of vitreomacular adhesion. The rod photoreceptors may be more susceptible than cone photoreceptors to the effects of ocriplasmin. Further work is needed to understand mechanisms of visual impairment after ocriplasmin.

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creased implicit time in the treated left eye (Figure 2D). Notably, the retinal pigment epithelial layer remained intact on SD-OCT throughout the postinjection course, and no pigmen-
tary abnormalities were apparent on examination. Fluores-
ccein angiography and autofluorescence were not performed.

Discussion

Phase 3 clinical trials of ocriplasmin indicated that blurred
vision, visual impairment, and photopsias are significantly
greater in patients receiving ocriplasmin than those receiving
placebo (drug vehicle diluted with saline). Notably, 5.4% of
patients who received ocriplasmin compared with 1.6% who
received placebo reported visual impairment. In addition, 2%
of patients receiving ocriplasmin noted dyschromatopsia (de-
scribed as a yellowing of their vision) with a corresponding
decrease of a- and b-wave amplitudes on ERG in half of these af-
fected patients. In this case report, there was an immediate
release of VMT and a subsequent improvement in visual acu-
ity and distortion. However, the symptom of dark vision per-
sisted and was associated with alteration of the IS/OS (ellip-
soid) layer on SD-OCT and a significant decrease in ERG
amplitudes. It is possible that this effect of the medication may
be due to a diffuse enzymatic effect of the protease on the pho-
toreceptors or the retinal pigment epithelium throughout the
retina. In this case, there is a greater reduction in scotopic func-
tion compared with photopic function, suggesting that rod pho-
Figure 2. Electroretinography (ERG) 4 Months After Intravitreal Injection With Ocriplasmin

A, Multifocal ERG (central 20°) comparing the left and right eyes shows a marked reduction in the foveal peak amplitudes and surrounding 3 rings in the treated left eye compared with the untreated right eye. B, Dim flash (scotopic) ERG demonstrates markedly reduced amplitude (arrows) in the left eye compared with the right eye, indicating rod dysfunction. C, Bright flash ERG demonstrates reduced a- and b-wave amplitudes (arrows) in the left eye compared with the right eye, indicating both rod and cone dysfunction. D, Photopic 30-Hz flicker demonstrates an approximate 30% reduction in cone function (vertical arrows) with an increased implicit time (33.5 vs 30.5 milliseconds) in the left eye compared with the right eye (horizontal arrows).
toreceptors may be more susceptible than cone photoreceptors to the effects of ocriplasmin, but both classes of photoreceptors are affected. Further work is needed to understand the effects of ocriplasmin on photoreceptors and determine which patients may be more susceptible to a prolonged reduction in photoreceptor activity.

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REFERENCES