Brief Report

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

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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 her 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–outer 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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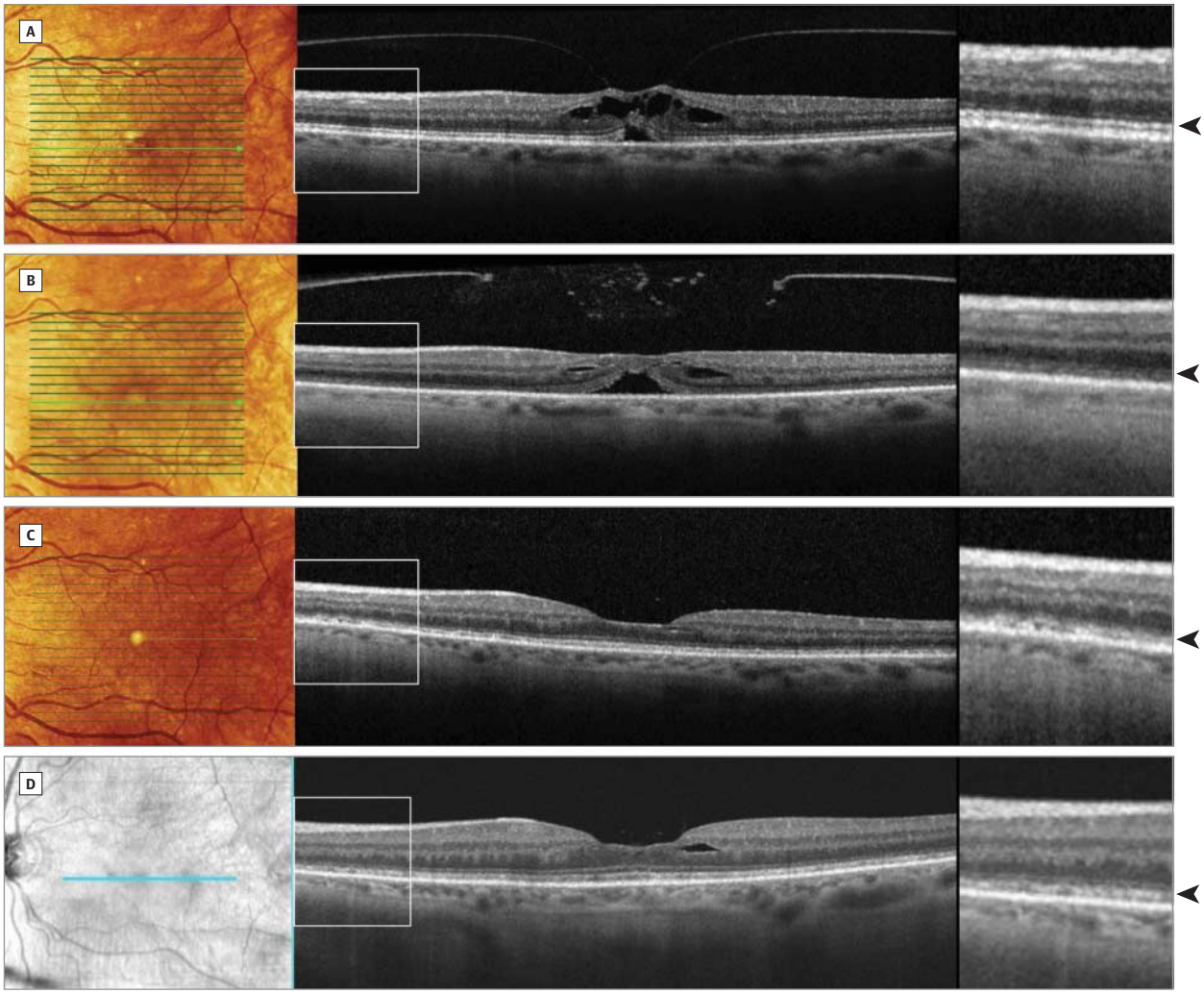
Ocriplasmin (Jetrea; Thrombogenics) is a recombinant protease with activity against components of the vitreoretinal interface, including fibronectin and laminin. Ocriplasmin was recently approved for the treatment of symptomatic vitreomacular adhesion (VMA).[1] A previous report[2] has described transient vision loss associated with disruption of the photoreceptor outer segments after ocriplasmin injection. We describe a 71-year-old woman with symptomatic vitreomacular traction (VMT) who received intravitreal ocriplasmin and experienced persistent darkening of vision in her left eye for 4 months after treatment, despite improvement in visual acuity and release of VMT. Using both spectral-domain optical coherence tomography (SD-OCT) and electroretinography (ERG), we demonstrate that the disruption of the photoreceptor inner segment–outer segment (IS/OS) (ellipsoid) layer and reduced a- and b-wave ERG amplitudes correspond to the patient's symptom of darkened vision.

Report of a Case

A 71-year-old woman presented with metamorphopsia and decreased vision in her left eye. On initial examination, visual acuity was 20/20 OD and 20/60 OS. Fundus examination and SD-OCT of the left eye revealed VMT with distortion of the foveal contour and cystoid changes within the retina (**Figure 1**A). One day after intravitreal injection of ocriplasmin (0.125 mg/0.1 mL), her vision decreased to 20/200. Spectral-domain optical coherence tomography demonstrated release of VMT with near disappearance of the IS/OS (ellipsoid) layer (Figure 1B). Two months later her vision improved to 20/50 and visual distortion also improved, but she continued to report darkening of her vision in the left eye in dim illumination. Spectral-domain optical coherence tomography revealed resolution of the cystoid changes in the retina and the integrity of the IS/OS layer was improved, although still irregular (Figure 1C). Approximately 4 months after injection, her visual acuity improved to 20/40, but she reported persistent darkening of vision; there was no evidence of an afferent pupillary defect on examination. The SD-OCT image was nearly identical to that taken 2 months after injection (Figure 1D). Multifocal ERG revealed a significant decrease in the foveal peak and surrounding 3 rings of the treated eye (**Figure 2**A). Full-field ERG revealed decreased a- and b-wave amplitudes most prominently on the scotopic ERG (Figure 2B). The photopic ERG also revealed an approximate 30% reduction in amplitude and an in-

Figure 1. Spectral-Domain Optical Coherence Tomography (SD-OCT) Images Before and After Treatment With Ocriplasmin



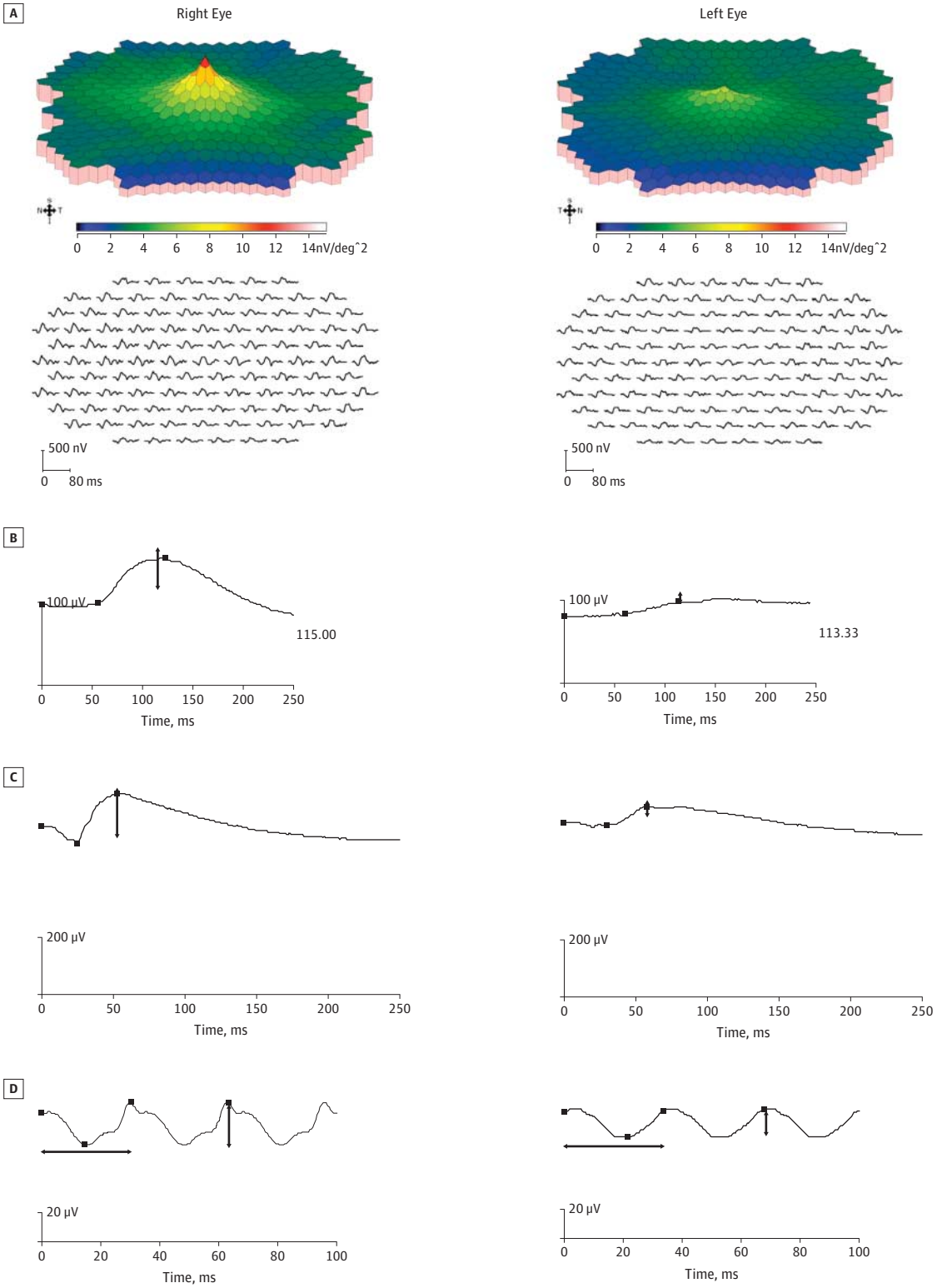
A, On presentation, vitreomacular traction (VMT) with distortion of the foveal contour with cystoid changes in the inner and outer retina is apparent. A ×2 magnified area of the nasal macula shows an intact inner segment–outer segment (IS/OS) (ellipsoid) layer (arrowhead). B, The day after treatment, the VMT had released and there was a decrease in the cystoid changes in the inner retina. A ×2 magnified area in the nasal macula shows a near disappearance of the IS/OS (ellipsoid) layer (arrowhead). C, Two months after treatment, VMT and cystoid changes in the retina had resolved, with an improvement in the continuity of the IS/OS layer. A ×2 magnified area of the nasal macula shows improvement in the IS/OS (ellipsoid) layer; however, it remains irregular (arrowhead). D, Four months after treatment, there is persistent discontinuity of the IS/OS (ellipsoid) layer. A ×2 magnified area of the nasal macula shows this more clearly (arrowhead). Images A through C were acquired by Heidelberg Spectralis SD-OCT (Heidelberg Engineering), and image D was acquired by Cirrus SD-OCT (Carl Zeiss Meditec Inc).

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 pigmentary abnormalities were apparent on examination. Fluorescein 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).[1] Notably, 5.4% of patients who received ocriplasmin compared with 1.6% who received placebo reported visual impairment.[1] In addition, 2% of patients receiving ocriplasmin noted dyschromatopsia (described as a yellowing of their vision) with a corresponding decrease of a- and b-wave amplitudes on ERG in half of these affected patients.[3] In this case report, there was an immediate release of VMT and a subsequent improvement in visual acuity and distortion. However, the symptom of dark vision persisted and was associated with alteration of the IS/OS (ellipsoid) 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 photoreceptors or the retinal pigment epithelium throughout the retina. In this case, there is a greater reduction in scotopic function 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, indicative of 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 30.50 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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Study concept and design: Tibbetts, Witkin.
Acquisition of data: All authors.
Analysis and interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: All authors.
Administrative, technical, or material support: All authors.
Study supervision: Reichel, Witkin.

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