West Nile Virus Chorioretinitis With Foveal Involvement: Evolution of Lesions on Optical Coherence Tomography

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Abstract
Purpose: To describe the clinical course of foveal West Nile virus (WNV) chorioretinitis with longitudinal spectral domain optical coherence tomography (SD-OCT) imaging. Methods: Case report. Results: A 41-year-old man with diabetes mellitus presented with flashes and floaters of both eyes (OU) and decreased vision of the right eye (OD) 2 weeks after being discharged from a local hospital. He had been treated for WNV meningoencephalitis, and he recovered systemically with supportive therapy. Ophthalmic examination revealed WNV chorioretinitis bilaterally, with predominantly foveal involvement OD. His best-corrected visual acuity (BCVA) was 8/200 OD and 20/20 of the left eye (OS). Spectral domain optical coherence tomography revealed 2 distinct lesion types—the “classic” outer retinal lesion and an intraretinal lesion. Both lesions had associated disruption of the normal outer hyperreflective retinal layers on SD-OCT. Longitudinal SD-OCT over the ensuing 6 weeks revealed a gradual reconstitution of these layers, with BCVA concurrently improving to 20/40 OD. Conclusion: We describe the consecutive findings seen on SD-OCT of retinal lesions in WNV chorioretinitis. The tomographic natural history of these lesions involved reconstitution of OCT deficits, with corresponding improvement in functional visual status.

Keywords
OCT, systemic conditions and the eye, uveitis

Introduction
West Nile virus (WNV) chorioretinitis is caused by a mosquito-borne single-stranded RNA arbovirus infection. It is typically discovered shortly after symptoms of systemic WNV and characteristically presents bilaterally with multifocal chorioiditis. We describe an antibody-confirmed case that involved the fovea. We present the consecutive evolution of retinal WNV lesions by longitudinal spectral domain optical coherence tomography (SD-OCT) imaging. We demonstrate the natural history of tomographic findings for this uncommon entity, which have not been previously reported.

Case Report
A 41-year-old man with noninsulin-dependent diabetes mellitus presented to the emergency department at Hennepin County Medical Center, Minneapolis, Minnesota, with a diffuse maculopapular rash over the trunk and proximal extremities. He had headache, fatigue, and a low-grade fever. He denied any recent travel, camping, or known tick or mosquito bites. Serum investigations confirmed the presence of WNV antibody immunoglobulin M. Due to the self-limited course, he was given supportive treatment; however, the following day, he deteriorated with worsening headache and intractable nausea and vomiting. A lumbar puncture was positive for WNV IgM, and he was admitted for supportive treatment of WNV meningoencephalitis. He was discharged 2 days later in stable condition.

Two weeks after discharge, he noticed gradually decreased vision of the right eye (OD) associated with mild photophobia and intermittent flashes and floaters of both eyes (OU). On examination, his best-corrected visual acuity (BCVA) was 8/200 OD and 20/20 of the left eye (OS). There was 1+- anterior cell OU and 3+ vitritis OU. Posteriorly, there was no optic nerve edema or hemorrhage nor any vasculitis. The macula revealed multiple, nummular yellow-white lesions of various sizes including the fovea OD and similar lesions in the extrafoveal area OS (Figure 1A). Peripheral examination in both eyes revealed similarly active lesions.

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Based on his clinical history and classic fundus lesions, he was diagnosed with WNV chorioretinitis. Given the anterior segment inflammation, he was prescribed topical prednisolone acetate drops 4 times daily OU.

Spectral domain optical coherence tomography OU was performed at baseline, 2 weeks, and 6 weeks. This revealed lesions with 2 distinct phenotypes, based on their tomographic appearance and location within the retina. Both eyes contained the classic lesion, best demonstrated by the extrafoveal lesion of the left eye (Figure 2D). Spectral domain optical coherence tomography revealed a deep hyperreflective lesion extending from the retinal pigment epithelium (RPE) to the outer nuclear layer (ONL), with associated loss of the overlying external limiting membrane (ELM), ellipsoid zone (EZ), and cone outer segment tips (COST) lines. There were no discernable disruptions to the overlying inner retina. Fluorescein angiography of some of these lesions revealed a hypofluorescent center surrounded by a hyperfluorescent rim (Figure 1C). Subsequent SD-OCT images of these classic lesions at 2 weeks revealed gradual reconstitution of ELM and EZ, while the COST line remained indistinct (Figure 2E). At 6 weeks, the COST line was fully reconstituted (Figure 2F).

Figure 1. Imaging of bilateral West Nile virus chorioretinitis. Color fundus photography (A), red-free photography (B), and arterial–venous phase of fluorescein angiography (C) of both eyes.
The second lesion type was present in the right fovea (Figure 2A). Spectral domain optical coherence tomography revealed a thickened fovea with a disrupted contour. There was a distinct intraretinal hyperreflective foci spanning the ONL to the outer plexiform layer, with adjacent disruption of retinal architecture, but no frank intraretinal or subretinal hyporeflective areas resembling fluid. External limiting membrane band was visible, but EZ and COST lines were indistinct. The inner retinal layers were discernible, but with its normally smooth contour disrupted. Early and late fluorescein angiography of this lesion did not reveal any associated hyperfluorescence. After 2 weeks, the intraretinal hyperreflective lesion had resolved, with an improvement of the foveal contour. The EZ line was reconstituted, while the COST line remained indistinct (Figure 2B). The BCVA OD improved to 20/60. At 6 weeks, the COST line continued to reconstitute but remained disrupted (Figure 2C). The posterior vitreous opacities of the SD-OCT scans, consistent with vitritis, gradually improved as well, which corresponded with his clinical examination. The BCVA OD at 6 weeks was 20/40.

Discussion

Approximately 80% of infected patients with WNV are symptomatic and 20% develop fever. Less than 1% of patients develop encephalitis, and chorioretinitis is similarly rare. West Nile virus chorioretinitis is characterized by deep, nummular, yellow-white lesions of various sizes with overlying vitritis. The lesions are predominantly in the posterior pole, but there are also characteristic radially oriented contiguous lesions in a curvilinear pattern in the midperipheral retina.1 There may also be concurrent optic nerve swelling, occlusive vasculitis, and retinal hemorrhaging.2 The main risk factors for ocular involvement are diabetes and older age.1,2

Multimodal imaging has been used to describe 3 cases of WNV chorioretinitis.3 The authors focused on the imaging characteristics of the classic deep retinal lesion originating from the RPE layer, with no discernable inner retinal disruption. They argued that the primary location of disease activity was the outer retina and RPE, with a hematogenous spread of the virus via the choriocapillaris. The SD-OCT of the classic deep lesion in the left eye of our patient supports this (Figure 2D). With longitudinal SD-OCT, we are able to show that the initial disruption of the outer hyperreflective bands associated with this outer retinal lesion eventually reconstitute, as early as 2 weeks after presentation, with the EZ line returning earlier than the COST line.

The local loss of the ELM, EZ, and COST lines represent photoreceptor damage. The sequence of recovery, which started with the ELM and EZ and ended with the COST line, is consistent with the process and direction by which photoreceptors regenerate.4 External limiting membrane recovery is thought to be necessary prior to subsequent distal regenerative processes due to its supportive role in enabling the correct alignment and orientation of photoreceptor regeneration.5,6 Optical coherence tomography studies of photoreceptor regeneration after retinal detachment and macular hole repair demonstrate a similar sequence, with the presence or early
reconstitution of the ELM line as a positive prognostic indicator for photoreceptor regeneration and ultimate visual status.\textsuperscript{5,7}

Additionally, our patient exhibited another WNV lesion that was distinct from the classic lesion and yet to be described in detail in the literature by SD-OCT. It appears to have its focus in the intraretinal space with associated loss of the EZ and COST lines in addition to inner retina disruption. Compared to the classic lesion, there was a slower reconstitution of the outer hyperreflective bands. The actual intraretinal lesion resolved at 2 weeks, and similar to the classic lesion, the EZ line returned earlier than the COST line.

It is not clear whether these intraretinal lesions represent a different pathophysiology compared to the classic lesion. Of note, for the reported 3 cases by Learned et al, only seropositivity was present without neuroinvasive disease.\textsuperscript{3} In contrast, a neuronal route of spread has been postulated for those with concurrent WNV meningoencephalitis. The result is predominant inner retinal layer insults via ganglion cell axons, which is also hypothesized to more likely lead to foveal involvement.\textsuperscript{8,9}

Histopathologic analysis of infected retinal tissue would further our understanding of this virus’ route of spread.

Vision in the right eye improved as the outer layers reconstituted. Although the clearing of vitritis may also have contributed to the visual improvement in the right eye, the left eye had the same level of vitritis but had a baseline BCVA of 20/20. Thus, the intraretinal foveal lesion and associated retinal disruption contributed largely to a significant visual decline. This lesion is distinct from macular thickening associated with hemorrhage and vasculitis, which can lead to macular edema.\textsuperscript{10}

As the classic lesions were extrafoveal, we were not able to determine its effect on visual function. Microperimetry or electrophysiology studies would have provided insights into the functional deficits and subsequent improvements resulting from these lesions.

Indocyanine green angiography (ICGA) was not performed but may have contributed to our understanding of the pathophysiology of the intraretinal lesion. The classic outer retinal lesion of SD-OCT shows an exactly corresponding hypocystic lesion on ICGA, thought to be due to blockage from inflammatory material in the RPE, microscopic granuloma in the choriocapillaris, or less likely, choroidal hypoperfusion.\textsuperscript{3,11}

Given the intraretinal location of the foci, a normal underlying ICGA would have further supported that this lesion did not originate from the choroid.

With longitudinal SD-OCT, we are able to demonstrate the natural history of tomographic findings for this uncommon entity, which has not been previously reported. There is a reconstitution of the outer layers, which continue to support the clinical correlate of its self-limited effect on visual function. Furthermore, we describe the SD-OCT characteristics of an intraretinal WNV lesion, which can have a significant effect on visual function. Reassuringly, as with the classic lesion, the initial disruptions of the retinal architecture appear to improve, with a corresponding response in visual function. Although initial visual loss may be severe, this case continues to support close observation as the initial step in management for similar lesions.

Authors’ Note
Almeida had full access to all the patient information and clinic reports and takes full responsibility for the integrity of the information. Almeida contributed to study concept and design; administrative, technical, or material support; and study supervision. All authors contributed to acquisition of data, analysis and interpretation of data, drafting of the manuscript, and critical revision of the manuscript. Full adherence to the Declaration of Helsinki and all Federal and State laws. This report has not been previously presented in a professional meeting.

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