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ACUTE RETINAL NECROSIS IN MULTIPLE SCLEROSIS: A NEUROIMMUNOLOGIC CHALLENGE!

We report a case of a 32-year-old woman with a 2-year history of multiple sclerosis (MS) who presented to the ophthalmology clinic 1 week after the completion of pulse steroids with complaints of blurred vision associated with pain in the left eye. She was treated with 3 courses of high-dose methylprednisolone (1,000 mg a day for 3 days) for recurrent relapses in the 5 months before presentation (brain MRI, figure, A). Her symptoms during these relapses were left hemiparesis, right hemiparesis, and worsening right hemiparesis, in that order. She was started on glatiramer acetate 1 month before presentation. Given the frequent relapses, changing her disease-modifying therapy to natalizumab was being considered.

Ophthalmologic examination on presentation (2 weeks after symptom onset) showed no light perception and presence of granulomatous keratic precipitates, and cells in the aqueous and vitreous, suggesting vitritis with infiltrated optic nerve necessitating a vitrectomy (figure, B and C). Pathologic examination revealed retinitis, arteritis, areas of retinal hemorrhage, and sloughing, consistent with acute retinal necrosis (ARN) of viral etiology. IV acyclovir was started. Serology and PCR for cytomegalovirus, Epstein-Barr virus, varicella zoster virus (VZV), and toxoplasma were negative. She was seronegative for HIV with a CD4 count of 1,107. Herpes simplex virus 2 (HSV-2) immunoglobulin G was positive and PCR was positive in the vitreal biopsy (figure, D). Her final diagnosis was ARN caused by HSV-2, precipitated by repeated pulses of high-dose steroids for management of MS relapses. She completed treatment with IV acyclovir for 1 week and was switched to oral valacyclovir. At a 3-month follow-up, her visual acuity was limited to perception of hand motion in the left eye.

Discussion. ARN is a rare but devastating condition characterized by inflammatory cells in the anterior chamber and vitreous as well as foci of retinal necrosis with vasculitis. The term ARN was introduced in 1978 in a case series reporting bilateral retinal necrosis of obscure etiology in 4 patients.¹ Recent literature suggests viral infections as the underlying etiology, with VZV being most common, followed by HSV, although other herpes viruses such as cytomegalovirus and Epstein-Barr virus

have been reported as well.² ARN usually occurs in immunocompetent individuals, but there have been reports of occurrence in immunosuppressed patients with HIV.² A few cases of ARN after systemic,³ vitreal, and epidural steroids have been reported.

The occurrence of (sub)acute eye pathology poses a special challenge in patients with demyelinating diseases, whose symptoms may be attributed to optic neuritis. Not only can this lead to a delay in diagnosis, but the administration of high-dose steroids may lead to unintentional worsening of their infection. Poor visual outcome was reported in 2 patients with neuromyelitis optica who developed ocular infections (toxoplasmosis and cytomegalovirus retinitis) while they were on immunosuppressants and the dose was increased because they were thought to have a relapse of their optic neuritis.⁴ Another case series reported 2 patients with no history of demyelinating disease who were diagnosed with ARN due to VZV after they were initially thought to have inflammatory optic neuritis and treated with steroids.⁵ One of these patients experienced permanent vision loss. There is one previously reported case of ARN due to VZV in MS that occurred after the administration of steroids.³ The visual symptoms were initially attributed to optic neuritis and the visual outcome was poor. Hence, patients should be evaluated carefully and treated empirically with antivirals if any suspicion of viral retinitis exists; however, diagnosis must be confirmed by serum and vitreous testing with PCR.⁶

We report a rare case of ARN due to HSV in a patient with MS treated with pulse steroids, resulting in poor visual outcome. Both a serious herpetic infection and unilateral near-blindness complicated future management of her MS. She has had an aggressive MS disease course with frequent relapses, warranting highly effective disease-modifying treatment (DMT). Although natalizumab is not associated with an increased incidence of herpes, it is associated with serious herpetic infections.⁷ Fingolimod and alemtuzumab are associated with high risk of herpetic infections. The choice of DMT is challenging in this patient, and antiviral prophylaxis should be considered if the above-mentioned DMTs are chosen. Given the patient's monocular status, any future eye symptoms need to be managed carefully to exclude recurrent herpes and treated aggressively to save

(A) Brain MRI, fluid-attenuated inversion recovery, and postcontrast sequences showing confluent white matter lesions with contrast enhancement. (B) MRI orbit T2 fat suppressed and postcontrast sequences showing thickening of the left optic nerve with contrast enhancement. (C) Funduscopy showing areas of microhemorrhages (indicated by arrows), diffuse retinitis, and periarteritis. Shown within the dotted circle is a flattened edematous optic nerve due to elevated intraocular pressure caused by inflammation. (D) PCR melting curves and melting peaks noted at the same temperature as the HSV-2 control sample. A large melting curve is seen, which is due to a greater amount of viral material compared to control, suggesting high viral load. HSV = herpes simplex virus; NC = negative control; PC = positive control.

the functional eye. If thought to be due to MS relapse, plasmapheresis and/or IV immunoglobulin without a trial of steroids might be appropriate.

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Author contributions: Dr. Sheikh has designed, drafted, revised, and edited the manuscript and contributed to neuroimages. Dr. Jain has revised and edited the manuscript, contributed to the funduscopy image and PCR curves, and created the final image. Dr. Hillen has revised and edited the manuscript for intellectual content and approved all final changes.

Study funding: No targeted funding reported.

Disclosure: The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

Received July 15, 2015. Accepted in final form November 3, 2015.

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