Author Affiliations: Ophthalmology Department, Edouard Herriot Hospital, Hospices Civils de Lyon, Lyon, France (Chirpaz, Bricout, Elbany, Rocher, Burillon, Dot); LEO Ophthalmologic Center, Private Hospital of Eastern Lyon, Saint-Priest, France (Loria); Claude Bernard Lyon 1 University, Lyon, France (Burillon); Military Health Service Academy, Val-de-Grâce, Paris, France (Dot).

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Corresponding Author: Nicolas Chirpaz, Burillon's Ophthalmology Department, Edouard Herriot Hospital, Five Place d'Arsonval, Lyon 69003, France (nicolas.chirpaz@chu-lyon.fr).

Conflict of Interest Disclosures: Dr Dot reported personal fees from Bayer, AbbVie, Novartis, Roche, and Horus Pharma. No other disclosures were reported.

Additional Contributions: We thank the patient for granting permission to publish this information.

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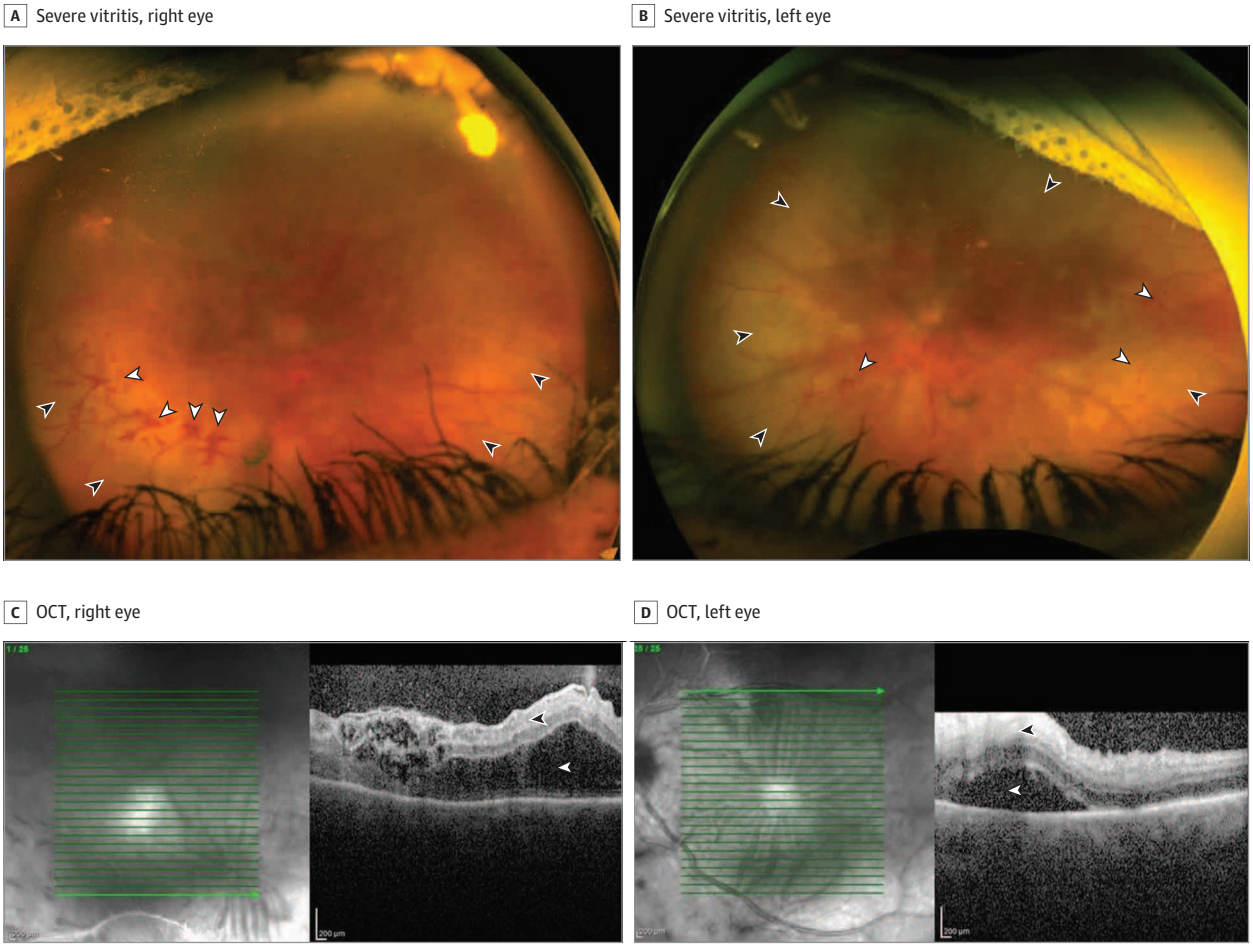
Bilateral Acute Retinal Necrosis After Oncolytic HSV-1 Treatment of Glioblastoma

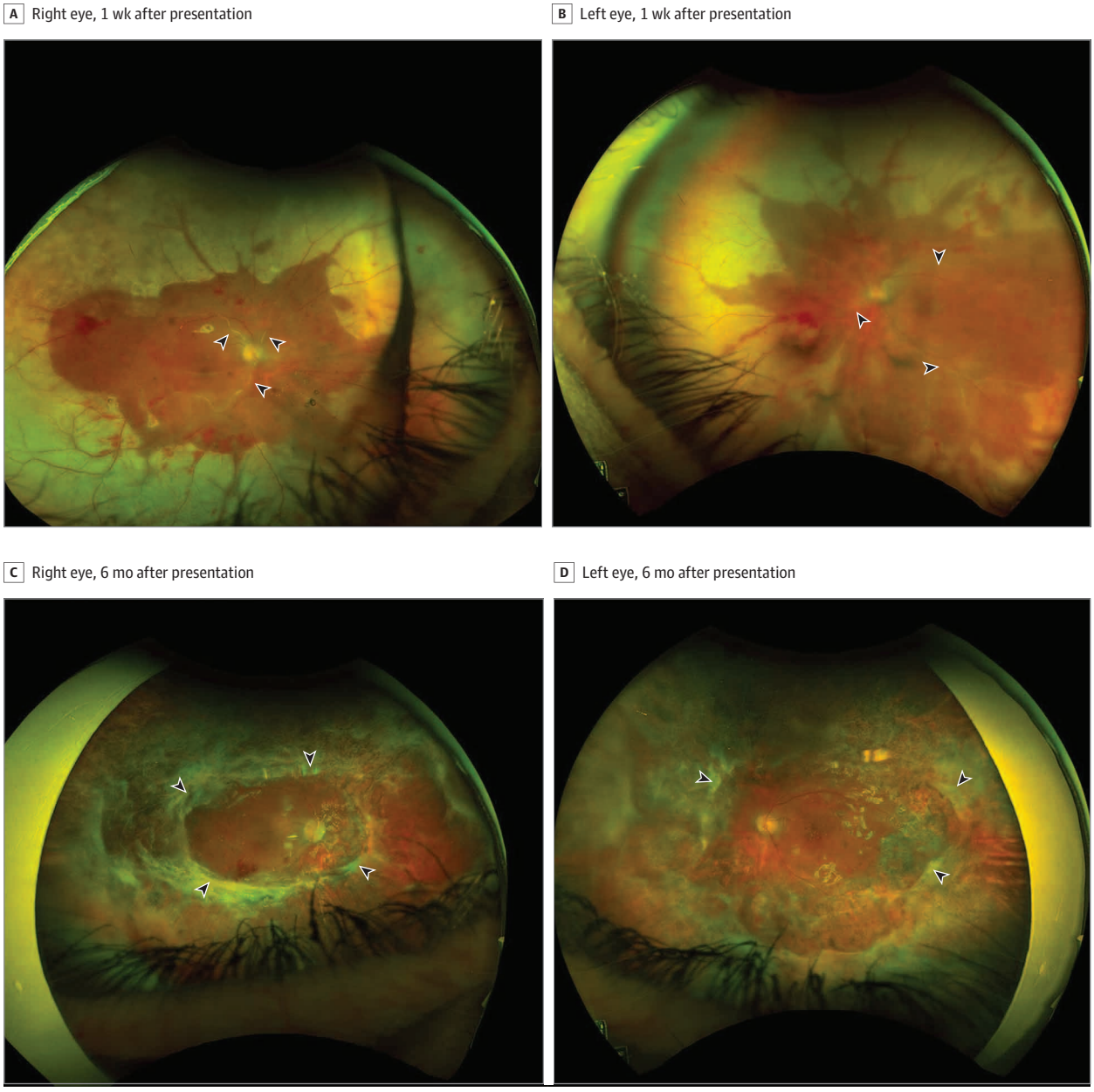
Report of a Case | A 55-year-old female with a known right parieto-occipital World Health Organization grade IV glioblastoma presented to the eye emergency department for 2 weeks of bilateral floaters followed by eye pain, photophobia, and blurry vision. She had previously undergone partial tumor re-

Figure 1. Bilateral Vitritis and Retinal Necrosis



A, Severe vitritis in the right eye and moderate vitritis in the left eye (B) obscuring 360° of peripheral retinal whitening (black arrowheads) with scattered perivascular hemorrhages (white arrowheads). C, Optical coherence tomography (OCT) of the right eye inferotemporal macula displaying inner retinal hyperreflectivity (black arrowhead), retinal thickening, and areas of intraretinal fluid and disorganization (white arrowhead). D, OCT of the left eye superior macula showing an area of inner retinal hyperreflectivity (black arrowhead) overlying subretinal fluid (white arrowhead).

Figure 2. Bilateral Acute Retinal Necrosis at 1 Week and 6 Months After Presentation



A, Right eye 1 week after presentation and 5 days after initial pars plana vitrectomy with retinal detachment repair and silicone oil insertion. There is a clearly demarcated line of peripheral retinal whitening and persistent perivascular hemorrhages. With the vitreous removed, vascular whitening indicative of severe ischemia can be appreciated (arrowheads). B, Left eye moderate vitritis, peripheral retinal whitening, and perivascular hemorrhages remain 1 week after presentation. Posterior and peripheral vascular whitening is present (arrowheads). C, Right eye 6 months after presentation, after a total of 3 retinal detachment repairs. Proliferative vitreoretinopathy with traction has recurred along the vascular arcades (arrowheads). D, Left eye 6 months after initial presentation, after a total of 2 retinal detachment repairs. Proliferative vitreoretinopathy is present peripherally (arrowheads).

section and 1 round of chemotherapy. A direct infusion of herpes simplex virus type 1 (HSV-1), C134 oncolytic virus was injected into her glioblastoma as part of a clinical trial 3 weeks before presentation.

Her presenting visual acuity was 20/400 OD and 20/40 OS. Corneal edema and 3+ anterior chamber cell were present in both eyes. Vitritis obscured details of the fundi, but peripheral retinal whitening and perivascular hemorrhages were appreciable bilaterally. Optical coherence tomography of the maculae showed intraretinal and subretinal fluid (**Figure 1**).

The patient was admitted for intravenous acyclovir. A diagnostic anterior chamber tap and bilateral intravitreal foscarnet injections were performed. Serological infectious and autoimmune testing was negative.

One day after admission, a rhegmatogenous retinal detachment developed in the right eye and a pars plana vitrec-

tomy with retinal detachment repair and silicone oil insertion was performed. Intraoperative pure vitreous samples revealed more than 1 million copies/mL of HSV. Subsequent specialized polymerase chain reaction (PCR) of these samples confirmed the presence of HSV-1, C134.

Biweekly intravitreal antiviral injections were administered for 3 weeks (alternating ganciclovir and foscarnet). Prednisone, 60 mg, by mouth was initiated after 2 days of antiviral therapy. The patient was monitored in the intensive care unit for 6 days before discharge and given valacyclovir, 2 g, by mouth three times daily.

Over a 3-month period, she underwent 3 vitrectomies in the right eye and 2 in the left eye, repairing rhegmatogenous retinal detachments with proliferative vitreoretinopathy.

Discussion | PCR detection of HSV-1, C134 in bilateral vitreous samples confirmed that the retinal necrosis was iatrogenic. To our knowledge, this represents the first reported case of bilateral acute retinal necrosis secondary to a recombinant oncolytic virus.

The phase 1 clinical trial in which the patient is enrolled uses the genetically engineered oncolytic virus HSV-1, C134. The C134 strain was engineered to safely replicate inside of and kill glioma tumor cells, while sparing healthy cells.[1,2]

Acute retinal necrosis occurs when virally infected cells undergo cytolysis triggering an immune response that causes progressive retinal damage. Necrotic retinal holes and contractile membranes progress to retinal detachment in approximately 50% of infected eyes.[3]

After the virus was injected into the occipital lobe tumor, it presumably infected the retinas by retrograde transneuronal spread along the optic pathway. Neurosurgical procedures have been associated with the development of HSV encephalitis and bilateral acute retinal necrosis[4]; however, the absence of adjacent encephalitis and the confirmation of HSV-1, C134 in the vitreous bilaterally make this etiology unlikely. Hematogenous spread was also considered, however, serological PCR testing was negative for HSV-1, C134. This evidence, along with the well-described transsynaptic spread of HSV viruses,[5] strongly suggests a transneuronal mechanism.

Despite advancements in glioblastoma treatment, average survival remains under 18 months from the time of diagnosis, highlighting the need for ongoing research and clinical trials.[6]

Since this adverse event in the HSV-1, C134 trial, several safeguards have been implemented. The viral infusion dose has been reduced. Patients undergo a mandatory baseline ophthalmic examination before treatment and are closely monitored while in the trial. Participants are informed of the risk of ophthalmic infection and are educated on the signs and symptoms of acute retinal necrosis. The US Food and Drug Administration and the data safety monitoring board have approved continuation of the trial with these revisions in place.

Patient Outcome | The patient's current visual acuity is 20/200 OD and 20/40 OS. Both retinas remain attached 18 months after her last ocular surgery (**Figure 2**).

Jonathan S. Fuerst, MD
Veena Danthuluri, MD
Jason N. Crosson, MD
Richard M. Martindale, MD

Author Affiliations: University of Alabama at Birmingham, Birmingham (Fuerst, Danthuluri, Crosson, Martindale); Retina Consultants of Alabama, Birmingham (Fuerst, Crosson, Martindale); Southeastern Retina Associates, Knoxville, Tennessee (Fuerst).

Corresponding Author: Jonathan S. Fuerst, MD, Southeastern Retina Associates, 140 Capital Dr, Ste 2A, Knoxville, TN 37922 (jfuerst@seretina.com).

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CORRECTION

Error in Figures: The Observation titled "Retinopathy Associated With Hair Dye,"[1] published on September 12, 2024, was corrected to fix errors in the labels for Figure 1 and replace the images in Figure 2C and D with the correct images. This article was corrected online.

1. Chirpaz N, Bricout M, Elbany S, et al. Retinopathy associated with hair dye. *JAMA Ophthalmol*. Published online September 12, 2024. doi:10.1001/jamaophthalmol.2024.3453