Acute Retinal Necrosis After Herpes Zoster Vaccination

Acute retinal necrosis (ARN) is a severe viral infection of the retina that can lead to significant vision loss. Varicella-zoster virus (VZV) and herpes simplex virus are thought to cause ARN. Recent studies suggest that VZV is implicated in most cases.1

Report of Cases. The varicella vaccine is available as 2 formulations, both given as subcutaneous injections: the Varivax (Merck, Whitehouse Station, New Jersey) live attenuated varicella vaccine, intended as primary vaccination for infants, and the Zostavax (Merck) live attenuated varicella vaccine, approved for secondary prevention of reactivation (herpes zoster). The primary difference between these vaccines is that Varivax is given as a series of 2 lower-dose injections ($\geq 1350$ plaque-forming units per injection), whereas Zostavax is given as a single higher-dose injection ($\geq 19,400$ plaque-forming units).2

To our knowledge, viral retinitis attributed to the varicella vaccine has not been reported. Herein, we describe 2 patients who developed polymerase chain reaction (PCR)–positive ARN following live attenuated varicella vaccination.

Case 1. A 77-year-old woman with a medical history significant for diabetes mellitus with secondary end-stage renal disease manifested severe vision loss in her left eye. She had a positive history of chickenpox as a child. She received the Zostavax vaccine 6 days prior to a rapid loss of vision in her left eye. On examination, visual acuity was bare light perception OS. Slitlamp examination revealed moderate conjunctival injection, diffuse mutton-fat keratic precipitates, an intraocular pressure of 14 mm Hg, and moderate vitritis. Fundus photographs are shown in Figure 1 and Figure 2. Retinal hemorrhages were absent. The right eye was unremarkable.

The patient was diagnosed as having ARN, began treatment with valacyclovir hydrochloride (1 g orally 3 times daily), and received an intravitreous ganciclovir sodium injection. Vitrectomy with vitreous biopsy and silicone oil tamponade was performed 5 days after the initial visit owing to a lack of clinical improvement.

Varicella-zoster virus DNA was positively detected by PCR on the vitreous sample. The PCR results for DNA from Toxoplasma gondii.
dii, cytomegalovirus, and herpes simplex virus were negative.

Case 2. An 80-year-old man with a medical history of hypertension and renal transplantation had bilateral severe vision loss for 2 weeks. His medications included mycophenolate mofetil, tacrolimus, and prednisone (5 mg/d). Two months prior to loss of vision, he had received the Zostavax vaccine. Within days of vaccination, he developed a varicellalike illness including rash and fever. The systemic illness resolved after local hospital admission for intravenous treatment with acyclovir sodium. He was not taking antiviral medication at the time of his initial visit for ocular symptoms.

On examination, visual acuity was hand motions OD and 20/150 OS. Slitlamp examination revealed moderate inflammation in both eyes. Fundus photographs (Figure 3 and Figure 4) show peripheral retinal detachment with hemorrhage in the right eye and retinal necrosis in the left eye. The patient received intravitreous foscarnet sodium in both eyes and was again admitted to the local hospital for a short course of intravenous acyclovir treatment. He was discharged and prescribed valacyclovir, 1 g orally 3 times daily. Shortly thereafter, he underwent bilateral vitrectomy with silicone oil tamponade for progression of retinitis and bilateral retinal detachments. An anterior chamber paracentesis specimen at the time of foscarnet injection was positive for VZV DNA and negative for herpes simplex virus DNA.

Comment. To our knowledge, viral retinitis following live attenuated varicella vaccination has not been reported. In addition, ocular adverse events following vaccination are rarely described. A review of the literature reveals a single case of uveitis following vaccination in a healthy 16-year-old girl who developed anterior chamber inflammation 7 days after receiving Varivax.3 This patient additionally exhibited a generalized vesicular rash. She was successfully treated with topical medication and oral acyclovir without residual sequelae. Cases of interstitial keratitis after the vaccine have been reported as well, suggesting that vaccination may indeed promote a pathologic and hyperacute immune response even to attenuated virii.4 Evidence of varicella activation in any form after vaccination is uncommon but does occur.2 Of the 19 270 participants in the Shingles Prevention Study who received the vaccine, only 17 participants reported a varicellalike rash during the 42-day surveillance period, and just 5 of these had positive PCR results for wild-type VZV.5 None of these 5 had positive PCR results for the attenuated Merck strain. Other clinical trials in support of vaccine licensure have shown only 2 postinjection rashes with PCR results positive for the Merck strain, with manifestation on days 8 and 17 after vaccina-
In the childhood Varivax vaccine, by contrast, a varicellalike rash occurred in approximately 4%, with a peak incidence 5 to 26 days after vaccination. The fact that varicellalike rashes are observed after vaccination with the live attenuated virus suggests that reactivation of varicella in any organ, including the eye, is physiologically possible.

Herein, we describe 2 cases of VZV-positive ARN in short temporal relation to the VZV vaccine. In the first instance, the retinitis was noted 6 days after vaccination, fitting with the time noted in the Shingles Prevention Study. This patient certainly could have developed ARN prior to vaccination, but the temporal relationship between vaccination and the rapid development of vision loss is suspicious.

In case 2, the patient was immunosuppressed from medications and exhibited disseminated varicella shortly after vaccination. His immunosuppression may have predisposed him to a systemic varicella infection and ARN (immunodeficiency and immunosuppression are contraindications to the vaccine). Despite intravenous antiviral therapy, the patient developed symptomatic ARN several weeks after vaccination.

In both cases, it is unclear whether the viral retinitis represents reactivation of varicella or a primary infection from the vaccine strain virus. As detection of the vaccine strain virus is rare in patients who develop a varicella rash after vaccination, it is more likely that these represent reactivation of varicella. In the second case, however, infection from the vaccine strain virus is possible given the presence of immunosuppression.

In conclusion, we report 2 cases of ARN following varicella vaccination. While postimmunization infections are rare, clinicians should be aware of this potential complication of vaccination.

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