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Two Cases of Acute Retinal Necrosis Due to Varicella Zoster Despite Prior Shingles Vaccination

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Abstract

Purpose—To review 2 cases of acute retinal necrosis (ARN) in adults due to varicella zoster virus (VZV) despite prior shingles vaccination.

Methods—Retrospective chart review.

Patients—A 62-year-old male and a 64-year-old male with unilateral ARN who had shingles vaccinations 16 and 7 months prior to their ocular symptoms.

Results—Polymerase chain reaction (PCR) confirmation of VZV in the anterior chambers of both patients. Both patients had good responses to oral antiviral therapy and topical and/or oral steroids.

Discussion—These 2 cases demonstrate that shingles vaccination is not an absolute protection against VZV related ARN. However, such vaccination may reduce the severity of the ARN.

Keywords

Acute retinal necrosis; Varicella zoster virus; Prior shingles vaccination

Introduction

ARN was first described by Urayama and colleagues in 1971 as an acute necrotizing retinitis, retinal arteritis, vitritis and choroiditis followed by late-onset rhegmatogenous retinal detachment in otherwise non-immunocompromised adults in their report of 6 cases.¹ Young and Bird named the syndrome BARN (bilateral acute retinal necrosis) and described 4 additional cases in 1978.² Although initially thought to be a bilateral disorder, numerous cases of unilateral cases have since been reported and the syndrome is now simply referred to as ARN. This serious sight-threatening disease can now often be treated successfully with antivirals, anti-inflammatories and modern vitreoretinal surgery if caught early enough.³

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Herpes zoster (varicella zoster virus) is the most commonly identified viral etiology of acute retinal necrosis.^{4,5} Three cases of ARN following VZV vaccination have been previously reported.^{6,7} In these cases, ARN was severe and the patients became symptomatic within 6 weeks of vaccination.^{6,7} We report two cases of relatively mild ARN that developed 16 and 7 months following Zostavax® administration. VZV was confirmed with RT-PCR of aqueous samples, (reported to have sensitivity of 80.9% and specificity of 97.4% and calculated positive predictive value of 96.9%)⁸. To our knowledge, this is the first such report of VZV-related ARN that developed more than 6 weeks following VZV vaccination.

Case 1

A 64-year-old man with a history of metabolic syndrome and impaired glucose tolerance presented with six days of floaters and cloudy vision in his left eye that persisted despite topical prednisolone treatment. The patient was not otherwise immunocompromised. He had received Zostavax®, a live-attenuated VZV vaccine, 16 months earlier. Visual acuity was 20/200 and intraocular pressure was 10mmHg. Exam revealed significant anterior chamber and vitreous inflammation and superotemporal retinitis with a “headlight in the fog” appearance (Figure 1A). Empiric trimethoprim/sulfamethoxazole was started for presumed toxoplasmosis, a course of oral prednisone was initiated, and topical prednisolone was increased.

At one week follow-up, another region of retinitis was noted. Blood tests for infectious and inflammatory etiologies, including toxoplasma, were negative. PCR testing of his aqueous was positive for VZV. Antibiotics were discontinued and oral valgancyclovir was started at 2 grams 3times per day for three weeks, followed by 1 gram 3 times per day for three weeks with a steroid taper. Upon completion of therapy, retinitis had resolved and visual acuity was 20/30. At six months follow-up, visual acuity was 20/25 with a stable region of chorioretinal atrophy on exam(Figure 1B).

Case 2

A 62-year-old man with a history of end-stage liver disease and diabetes mellitus type 2 without retinopathy presented with two days of floaters and blurred vision in the left eye. The patient did not have other immune-related disorders or frequent infections. He had received Zostavax®7 months prior. Visual acuity was 20/60 and intraocular pressure was 16 mmHg. Exam showed inflammation in anterior chamber and vitreous, and multiple white retinal lesions (Figure 1C) that showed late fluorescein leakage and staining (Figure 1E). Oral valgancyclovir and topical difluprednate therapy was initiated for presumed CMV retinitis. Blood tests for infectious and inflammatory etiologies were negative apart from a borderline ANA. Subsequent PCR testing of his aqueous was positive for VZV. Valacyclovir 1 gram 3times per day was initiated in place of valgancyclovir. After 10 weeks, his visual acuity improved to 20/50, the vitritis resolved, and the retinal lesions became inactive (Figure 1D). Valacyclovir was decreased to 1 gram daily and topical steroids were tapered. The patient died from complications of his cirrhosis 6 months following his initial diagnosis of ARN.

Discussion

Unlike the previously reported cases of ARN following VZV vaccination, our patients experienced milder disease and longer latency periods; presenting at 16 months and 7 months post-Zostavax®, compared to symptoms beginning 6 days and 6 weeks in the two reported Zostavax® cases,^{6,7} and 1 week in the single reported Varivax® case.⁷ In children who experienced VZV disease after receiving Varivax®, vaccine-strain virus accounted for most cases occurring 15 to 42 days after vaccination, but wild-type virus accounted for most cases occurring after 42 days.⁹ In the Shingles Prevention Study, 315 of 19,270 patients who received the active VZV vaccine developed confirmed herpes zoster. Approximately 98% of these patients developed herpes zoster after 30 days, 93% of which was confirmed wild-type virus.¹⁰ The study did not report if patients developed ocular involvement.

In these studies of systemic VZV recurrence after vaccination, a longer latency period was associated with wild-type disease. Among the previously reported post-vaccination ARN cases, viral strain was reported only in the Varivax® case. Vaccine-strain virus was identified in this case of ARN that occurred after 1 week.⁷ Therefore, shorter latency periods may be associated with vaccine-strain virus, and longer latency periods (as in our patients) with wild-type virus in ARN due to VZV as well as systemic disease.

Immunocompetence may play a role in ARN after VZV vaccination. ARN severity has also been linked to the degree of immune dysfunction.¹¹ Two of the previously reported patients were on immunosuppressant medication, and the third had end-stage renal disease secondary to diabetes.^{6,7} Here, we report two patients who may have been relatively immunocompromised, one from end-stage liver disease and diabetes and the other from metabolic syndrome.

Although ARN following live-attenuated VZV vaccination is rare, physicians should be alerted to the risk of both breakthrough and vaccine-derived ARN after VZV vaccination. Patients who develop visual symptoms should undergo a prompt dilated ocular examination.

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Summary

Acute retinal necrosis (ARN) is a rare but potentially devastating ocular disorder that can occur in otherwise healthy individuals. We report 2 cases of ARN confirmed by polymerase chain reaction (PCR) to be positive for varicella zoster virus (VZV) despite having had live-attenuated VZV vaccine 16 and 7 months earlier.

Figure 1.

Acute retinal necrosis following live-attenuated VZV vaccine administration in two patients. Retina of a 64-year-old man (Case 1) with 20/200 vision, vitritis and a superotemporal area of active retinitis on presentation in the left eye 16 months following vaccination (A) with resolution of vitritis and stable area of inactive retinitis following treatment (B). Retina of a 62-year-old man (Case 2) with 20/60 vision and multiple areas of retinal whitening and necrosis on presentation in the left eye 7 months following vaccination (C), with resolution of vitritis and inactive lesions following treatment (D). Late phase fluorescein angiogram from Case 2 shows leakage and staining inferonasally corresponding to the area of CMV retinitis in the left eye (E) and a normal appearing angiogram of the right eye (F).