Acute retinal necrosis following recombinant subunit varicella-zoster virus vaccine

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ABSTRACT

Purpose: Previously, secondary prevention of herpes zoster required live-attenuated vaccination, which is contraindicated in immunocompromised populations. More recently, a recombinant subunit vaccine (Shingrix, GlaxoSmithKline, Research Triangle Park, North Carolina) was approved by the Food and Drug Administration. Iatrogenic varicella-zoster virus (VZV) infection is theoretically impossible as it does not contain a live virus. We present a case of acute retinal necrosis (ARN) and disseminated zoster after receiving the recombinant subunit vaccine. Observations: A 65-year-old woman with past medical history of multiple myeloma treated with a previous autologous hematopoietic stem cell transplant and now with daratumumab and pomalidomide developed disseminated zoster and subsequently acute retinal necrosis weeks after receiving the zoster subunit vaccine. Molecular testing confirmed the presence of VZV, and the absence of herpes simplex virus, cytomegalovirus, and toxoplasmosis. The VZV was found to be genotypically wildtype and not related to the Oka strain used in the live-attenuated zoster vaccine. She was treated with systemic valacyclovir and intravitreal foscarnet. Conclusions and importance: This is the first report of VZV infection following the zoster subunit vaccine. The Advisory Committee on Immunization Practices (ACIP) has recommended the recombinant subunit vaccine over the live-attenuated vaccine due to its superior efficacy. The off-label use of the subunit vaccine in immunocompromised populations has been supported up to this point by studies demonstrating its relative safety. Though post-vaccination VZV infection or reactivation appears to be rare, clinicians should be aware of this potential complication to the recombinant subunit vaccine.

1. Introduction

Herpes zoster is the result of reactivation of the varicella-zoster virus (VZV) from its latent state in nerve ganglion. Reactivation of VZV is associated with a decline in cell mediated immunity that occurs with natural aging or an acquired immunocompromised state. Herpes zoster most commonly presents as a painful localized rash confined to a single dermatome. However, a myriad of neurologic, ophthalmic, and severe systemic manifestations have been reported and can be associated with significant mortality and morbidity. In 2017, the Food and Drug Administration (FDA) approved a recombinant subunit vaccine for herpes zoster (Shingrix, GlaxoSmithKline, Research Triangle Park, North Carolina). We present a case of acute retinal necrosis (ARN) and disseminated varicella zoster infection after receiving the recombinant subunit vaccine.

1.1. Case report

A 65-year-old woman presented with 2-week history of worsening floaters and blurred vision in her left eye (OS) for 5 days. She had a past medical history of multiple myeloma treated with a previous autologous hematopoietic stem cell transplant and now with daratumumab and pomalidomide. Notably, she received the first dose of the recombinant zoster subunit vaccine (Shingrix) 2 months prior to presentation. Six weeks after receiving the vaccine, she was hospitalized after developing a systemic vesicular rash and hypoxic respiratory failure, during which she was treated for disseminated varicella and viral pneumonia. She was treated with intravenous acyclovir 10 mg/kg every 8 hours and discharged on oral acyclovir 400 mg twice daily.

Two weeks after discharge from the hospital, she developed floaters, followed by progressive blurry vision (OS). On exam, her best corrected visual acuity was 20/25 in the unaffected right eye (OD) and 20/70–1 in...
the left eye. She had a left afferent pupillary defect and intraocular pressures of 14 and 21 mmHg in her right and left eyes, respectively. Full oculard examination of the right eye was unremarkable. Slit lamp examination of the left eye revealed 2+ anterior chamber cells and 2+ anterior vitreous cells. Funduscopic exam OS demonstrated 2+ vitreous haze and peripheral multifocal areas of retinal whitening with associated artery sheathing (Fig. 1).

An anterior chamber paracentesis was performed on the left eye due to the high suspicion of viral retinitis based on her presentation. Her aqueous was sent for polymerase chain reaction (PCR) detection of VZV, herpes simplex virus (HSV), cytomegalovirus (CMV), and toxoplasmosis. The patient was given an intravitreal injection of foscarnet (2.4 mg/0.1 ml) and started on valacyclovir 2 g three times per day. The patient was asked to stop her immunotherapy. Five days after presentation, PCR testing for HSV, CMV, and toxoplasmosis DNA resulted as undetectable. VZV DNA was detected. Genotyping performed by the Centers for Disease Control (CDC) identified the virus as wild-type and not associated with the Oka strain used to manufacture the live attenuated vaccine.

The patient was continued on therapeutic dose valacyclovir and treated with biweekly intravitreal injections of foscarnet for a total of 11 weeks. At week 8, there was consistent regression of retinitis, and the patient was asked to restart her immunotherapy. Five days after presentation, PCR testing for HSV, CMV, and toxoplasmosis DNA resulted as undetectable. VZV DNA was detected. Genotyping performed by the Centers for Disease Control (CDC) identified the virus as wild-type and not associated with the Oka strain used to manufacture the live attenuated vaccine.

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recombination or mutation. The temporal relationship of this patient’s disseminated zoster and ARN shortly following receipt of the recombinant subunit vaccine raises the possibility of an immunomodulatory phenomenon contributing to dormant VZV reactivation. It is also possible that the disseminated zoster and ARN are not related to the Shingrix vaccine.

Varicella activation or reactivation after any form of VZV vaccination is rare. In the Shingles Prevention Study, only 17 of the 19,270 patients who received the live attenuated Oka vaccine reported a varicella-like rash, with only 5 testing positive for wild-type VZV by PCR and none for Oka strain. In comparison, the efficacy study that prompted FDA approval of the VZV recombinant subunit vaccine reported a high rate of injection-site reaction (81.5% with pain and myalgia, but no patient developed a varicella-like rash). Post-licensure safety monitoring through the Vaccine Adverse Event Reporting System (VAERS) reported rates of post-immunization herpes zoster of 6.1 cases per 100,000 compared to 12.7 cases per 100,000 patients following Shingrix (October 2017–June 2018) compared to 12.7 cases per 100,000 (2781/21,846, 030) patients following Zostavax (May 2006–February 2015).

Among those who had received Shingrix, VAERS also reported a rate of post-immunization inflammatory eye disease at 0.4 per 100,000 patients. Of the 13 patients reported with post-vaccination inflammatory eye disease, 9 developed herpes zoster near the eye with subsequent ocular involvement, 2 developed primary herpes zoster iridocyclitis, and 1 report each of ocular herpes zoster and herpes zoster keratoconjunctivitis. Our patient is the first reported case of disseminated zoster and ARN occurring shortly after Shingrix administration amongst 11 million patients who received at least one dose in the United States.

3. Conclusions

In conclusion, our case of disseminated zoster and acute retinal necrosis following vaccination with the recombinant subunit has important clinical implications. The Advisory Committee on Immunization Practices (ACIP) has recommended the use of the recombinant gE vaccine over the live-attenuated Zostavax vaccine for secondary prevention of herpes zoster due to its wider range of efficacy. Additionally, there is significant interest in the recombinant vaccine’s potential to benefit immunosuppressed patients in whom Zostavax is contraindicated, and the off-label use of Shingrix in these populations has been supported up to this point by studies demonstrating its relative safety in hematopoietic stem cell or solid organ transplant recipients. Though post-vaccination VZV infection or reactivation appears to be rare, clinicians should be aware of this potential complication to the recombinant subunit vaccine.

3.1. Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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