

Generalized Rash and Bilateral Retinal Necrosis in an Adult Healthcare Worker after Post-Exposure Herpes Zoster Vaccination: A Rare Case Report

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INTRODUCTION

Chickenpox is an acute and highly contagious infection caused by the varicella-zoster virus (VZV).¹ Varicella-zoster virus (VZV) is an exceptionally infectious virus. It presents as chickenpox when primary infection occurs and as herpes zoster (HZ) when it reactivates. The U.S. Centers for Disease Control and Prevention (CDC) recommend administering the VZV vaccine at baseline to every non-immune healthcare worker. In the event of exposure to VZV, CDC recommends immediate vaccination to prevent the dissemination of infection and furlough from the workplace for 10 - 21 days.²

Since 2006, the Advisory Committee on Immunization Practices (ACIP) recommends varicella vaccination (Varivax[®]) as a routine two-dose vaccine for children older than 12 months.³ Zoster vaccine (Zostavax[®]) was approved by the U.S. Food and Drug Administration (FDA) to prevent shingles among adults 60 years and older, with or without the prior history of reported infection.⁴ The FDA has expanded the vaccination administration for those who are 50 years and older. However, there were no studies present on the safety of this vaccine in those who had a history of zoster in the past. The implementation of universal immunization in children against varicella has led to a decrease in varicella incidence by 85%; however, about 30% of the adult population can still develop herpes zoster.³

In the healthcare settings, susceptible (non-immune) persons of all ages are at higher risk for severe varicella disease. Generalized rash from varicella vaccine is uncommon and described in 1 - 5% of the vaccinated persons, usually characterized by 5 - 50 lesions; however, it is enormously contagious. Herpes zoster involvement of the trigeminal nerve of the ophthalmic division can lead to distressing consequences. It is thought to be a result of cell-mediated immunity against the viral antigens in the eye.⁵ There are two types of vaccines available in the U.S. Varivax[®], a live attenuated varicella vaccine, has been reported to cause many ocular complications.⁶ On the other hand, Zostavax[®] has been linked to fewer ocular complications. Despite that fact, a case of interstitial keratitis in a 50-year-old woman, 35 days after receiving the Zostavax[®] vaccine, has been reported.⁷ She also had manifested multiple recurrences of her ocular disease expositions.

In this case report, a health worker case was described who developed generalized body rash and bilateral retinal necrosis 7 weeks and 14 weeks after the post-exposure vaccine, respectively.

CASE REPORT

A 42-year-old, male health worker was exposed to another health worker who had developed a typical chickenpox rash in a tertiary care hospital before being diagnosed. The patient was found non-immune, furloughed for days 10 - 21, and vaccinated with varicella vaccine three weeks after exposure. The patient's general past medical history was insignificant, with no varicella disease as a child. He also denied any immunodeficiency or other vaccine contraindications. The patient also had an unremarkable ophthalmological history in the past. However, at seven weeks after exposure (four weeks after vaccination), the patient presented at occupational health service (OHS) with generalized vesicular rash, characteristic for chickenpox. The health care worker also reported malaise, arthralgia, and body aches. The patient denied any fever. On physical examination, he had numerous widespread vesicles with erythematous bases all over the body. Molecular testing of a specimen from one of the rash lesions was positive for varicella-zoster virus (VZV). Subsequent analysis of markers that discriminate against the vaccine strain (Oka virus) from the wild type strain (open reading frame ORF 38 and ORF54) indicated that the patient VZV strain was consistent with the Oka virus vaccine and not wild type. Furthermore, vaccine strain-specific markers (ORF62) indicated that the patient VZV strain was consistent with the Oka virus vaccine. He was treated with oral acyclovir for 10 days. The OHS recommended further investigations and immune system evaluation in primary care settings.

At 14 weeks after exposure, the patient presented again with symptoms of blurred vision. Ophthalmologic examination showed bilateral retinal necrosis. The fundus examination of both eyes showed the progressive retinal opacification and outer retinal necrosis. The intraocular pressures in both eyes were within the normal range of 16 - 18 mm Hg. Intravitreal sample for polymerase chain reaction (PCR) was positive for VZV with the same vaccine strain that was detected previously from the rash lesion.

Furthermore, VZV was found in the cerebrospinal fluid as well. The immunologic evaluation identified the Human Immunodeficiency Virus (HIV) with CD4 counts of 98/ml and a viral load of 266,000 RNA copies/ml. The polymerase chain reaction (PCR) results for cytomegalovirus, herpes simplex, and *Toxoplasma gondii* were negative.

Therapy and Course. The patient was treated with intravitreal injections of gancyclovir and foscarnet. He also had received systemic treatment with intravenous acyclovir and foscarnet. Highly active anti-retroviral therapy (HAART) was started based on laboratory findings of positive human immunodeficiency virus (HIV) test and CD4 count. After the start of HAART therapy and treatment, his visual acuity improved within three weeks. This case represented the health damage of the healthcare worker beyond the customary level of vaccination side effects and response, so it was subjected to a notification to the public health authorities.

DISCUSSION

Varicella-zoster infection can rise as a result of natural exposure to the wild-type virus, or through the vaccination that contains a live attenuated virus.¹ This virus remains dormant in the dorsal root ganglia and can become reactivated in the later stage of life. Herpes zoster infection, also known as shingles, typically manifests as a

maculopapular rash along one or two dermatomes and usually does not cross the midline. However, disseminated infection can spread randomly across multiple dermatomes and have the potential to involve many internal body organs, such as lungs, liver, and central nervous system. Immunocompromised people are at a higher risk of developing a disseminated infection.⁸

Given the history of disseminated body rash and bilateral retinal necrosis, it is suggested that our patient had disseminated zoster due to the reactivation of the herpes zoster virus as a result of a live attenuated vaccine. Moreover, the Oka strain analysis test confirmed the cause of generalized body rash and ocular symptoms. The patient met the diagnostic criteria for acute retinal necrosis. According to the American Uveitis Society, acute retinal necrosis is defined as greater than 1 foci of retinal necrosis along with other criteria, such as retinal arterial involvement with occlusive vasculopathy, the progression of symptoms in the absence of active antiviral therapy, and finally a prominent inflammatory reaction in anterior and vitreous chambers.⁹ Immunocompetent patients also may develop this, but immunocompromised individuals are more prone to severe disease. Moreover, more cases of acute retinal necrosis due to herpes simplex 2 virus have been observed in young people. In contrast, cases due to herpes simplex 1 or herpes zoster occur in the elderly.¹⁰

Even though many hundreds of thousands of people get vaccinated, complications of the vaccine as a result of virus replication rarely have been highlighted and reported.¹¹ A clinical trial study involving more than 60,000 individuals reported a possible but unconfirmed case of Oka strain rash development within six weeks of immunization.^{11,12} Moreover, a case of Oka strain herpes zoster also has been reported after shingles vaccine administration, but there was no retinal involvement.¹³ Heath et al.¹⁴ reported a case of acute retinal necrosis caused by a zoster vaccine in an older patient with a confirmed Oka strain virus of the vaccine. There are two other cases of acute retinal necrosis after herpes zoster vaccination reported in the elderly, explaining the possible reactivation or infection by the Oka vaccine strain.¹⁵ However, to our knowledge, there was no case reported with a combination of clinical presentation of generalized body rash and acute bilateral retinal necrosis due to the Oka HZ vaccine virus strain.

Intravenous acyclovir has been regarded as a standard treatment for acute retinal necrosis. However, current guidelines recommended using oral valaciclovir or valganciclovir to treat acute retinal necrosis due to herpes simplex/zoster and cytomegalovirus, respectively.¹⁶ For those patients with valaciclovir resistance or with severe disease involving the optic nerve, intravitreal injection of foscarnet is recommended twice or thrice weekly. Oral corticosteroids are affected by patients with severe inflammation or sight-threatening disease with optic nerve involvement.¹⁶

In this case report, the patient was immunocompromised due to HIV and exhibited varicella-zoster infection seven weeks after the vaccination. His immune status put him at risk of disseminated varicella infection and acute retinal necrosis as it is one of the contraindications to the live attenuated vaccine.¹⁷ Additionally, despite the standard intravenous antiviral therapy for disseminated viral infection, the patient developed acute retinal necrosis several weeks after vaccination.

CONCLUSIONS

In summary, a case of disseminated varicella infection and acute retinal necrosis was reported following varicella-zoster vaccination as a post-exposure protocol. This case highlighted that immunocompromised persons are at high risk for disseminated rash and disseminated VZV disease following vaccination. Immune deficiency should be sought in atypical vaccine reaction, even in the setting of healthcare worker exposure investigation.

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