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Case report

Herpes zoster ophthalmicus following recombinant zoster vaccine: A case report and brief literature review

Joshua M. Garcia, Ramez I. Haddadin *

Department of Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

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ABSTRACT

Purpose: Immunizations have long been pivotal in preventing diseases like HZ (herpes zoster), caused by VZV (varicella zoster virus). This study aims to evaluate the efficacy and safety of the RZV (recombinant zoster vaccine) compared to the ZVL (zoster vaccine live) and to report rare adverse events following RZV administration.

Observation: Herein, we report an unusual case of a 59-year-old man who developed a V1-limited rash with a positive HZ PCR (polymerase chain reaction) test following administration of RZV in the United States.

Conclusion: The development of RZV has significantly improved the prevention of HZ compared to ZVL. Nevertheless, rare adverse events, such as dermatomal reactions, underscore the importance of ongoing monitoring and research into the immunomodulatory effects of RZV. Physicians should continue to administer the RZV to patients but be cognizant that reactivation may rarely subsequently occur.

Case Presentation: The patient with a history of benign prostatic hyperplasia was treated at an outside hospital two days after receiving the RZV complaining of paresthesia and a rash on his nasolacrimal area and forehead. The patient presented to the ED (emergency department), 9 days post-vaccination due to persistence of his symptoms despite use of amoxicillin, valacyclovir, and an unidentified eye drop. The dose of valacyclovir was increased, and he completed 1 g TID (three times a day) PO (per orally) for 10 days with subsequent resolution of symptoms. A positive PCR test confirmed the diagnosis of HZ. Topical mupirocin ointment was initiated and the patient was referred for ophthalmologic evaluation.

Introduction

Immunizations have been an integral part of medicine in order to prevent disease and reduce complications. HZ, caused by the VZV, is an infection known for its propensity to develop painful, blistering rashes in a dermatomal distribution [1]. The reactivation of VZV commonly causes constitutional symptoms including headache, fever, malaise, rash, and fatigue [2]. HZ may be complicated by post-herpetic neuralgia, encephalitis, and various forms of ocular manifestations, which may result in vision loss [3]. The elderly are more commonly affected, with 1 in 3 Americans getting HZ in their lifetime [4]. In order to combat this frequent, debilitating viral reactivation, the development of VZV vaccines began.

Two vaccines were developed: a live attenuated virus and a recombinant, adjuvanted subunit. The ZVL was approved by the FDA (Food and Drug Administration) in 2006 and its widespread use began soon after [5]. Due to the risk of ZVL causing the dissemination of VZV in immunocompromised patients, the development of a new vaccine was imperative. The RZV was approved by the FDA and came into the market in 2017 [5]. The RZV is given as two intramuscular doses, with each dose 2 to 6 months apart [5]. During clinical trials, the RZV demonstrated superior efficacy and safety compared to the ZVL, as evidenced by a RR (risk ratio) of 0.15 for HZ and 0.38 for post-herpetic neuralgia [6]. The RVZ displayed a vaccine efficacy of over 90 % against HZ across all age groups, whereas the ZVL had lower efficacy [7]. Unlike the ZVL, the RZV clinical trials of ZOE-50 and ZOE-70 did not show any dissemination of HZ in immunocompromised patients and is recommended by the Center for Disease Control for all immunocompromised individuals aged 19 and above [8]. Consequently, the Advisory Committee on Immunization Practices recommends the RZV as the preferred vaccine over the ZVL in the United States [9]. Even with its superior efficacy, it should be noted that the RZV still has some adverse side effects.

Rarely, a dermatome reaction following the RZV has been reported.

* Correspondence to: Department of Ophthalmology, Northwestern University Feinberg School of Medicine, 259 E Erie St Ste, Suite 1520, Chicago, IL 60611, USA.
E-mail address: ramez.haddadin@nm.org (R.I. Haddadin).

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HZ occurs when the VZV reactivates after the initial infection; VZV can remain dormant for many years [10]. Reactivated VZV travels along sensory nerve fibers, leading to the characteristic herpetiform vesicles in a specific dermatome region observed in HZ. The ophthalmic division of the trigeminal nerve is a commonly affected pathway, resulting in ophthalmic zoster [10]. Here, we present the case of a 59-year-old Caucasian male who experienced paresthesia on his left eyelid and a limited rash in the V1 dermatome two days after receiving the RZV.

Case presentation

A 59-year-old-man with a history of benign prostatic hyperplasia controlled with 0.4 g of tamsulosin daily, presented to the ED. The patient was treated at an outside hospital, two days after receiving the RZV, complaining of a rash on his nasolacrimal area and forehead, limited to V1 dermatome (as seen in Fig. 1). At the outside hospital, he was prescribed amoxicillin, valacyclovir 1 g BID (twice a day) PO, and unidentified eyedrops. The vesicles fully developed around day 9, at which point he presented to the ED since his medications were not alleviating any symptoms. The patient described pain and "tingling" on the left side of his face; however, he denied any vision changes. In the ED, he was prescribed mupirocin 2 % TID for 10 days to prevent secondary infection. Systemic evaluation of the patient did not reveal any other signs or symptoms consistent with vaccine-related adverse events or manifestations of HZ. He was then referred for an ophthalmology consult.

On day 10, he was seen by an ophthalmologist, and his valacyclovir dose was increased to full treatment of 1 g TID, which he completed within the next 10 days. During this consult, corneal haze was noted in the peripheral cornea. This did not look particularly active.

20-day follow-up: The slit lamp examination showed the corneal haze remained unchanged. The patient had finished his full dose of valacyclovir and his V1 dermatome rash had resolved.

33-day follow-up: Another slit lamp examination revealed no new intraocular inflammation and stable corneal haze. The patient's corneal haze was felt to be chronic and inactive finding, and most likely unrelated to HZ.

Investigation

During the ED visit, a sample was taken from the vesicles. PCR testing from this was negative for herpes simplex virus (HSV) 1 and HSV 2 but positive for VZV. In addition, HIV (Human immunodeficiency virus) antigen/antibody tests were negative.

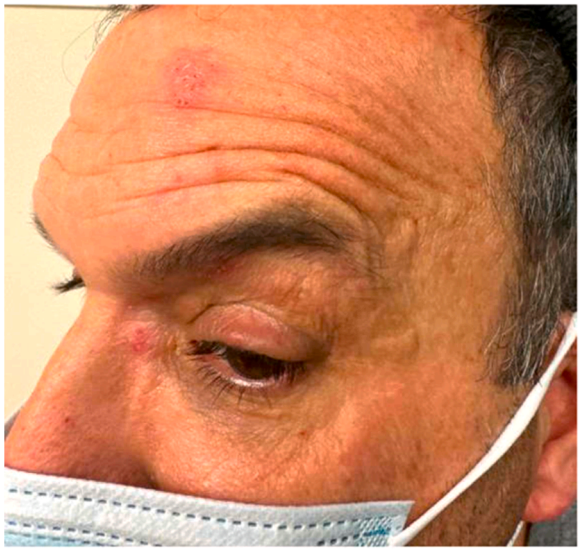

Fig. 1. Vesicles limited to V1 dermatome in emergency department on day 9.

Differential

Differentials for the patient included HSV 1, HSV 2, and VZV. The positive VZV PCR test with a recent RZV confirmed the diagnosis of VZV.

Discussion

The ZVL, once the standard of care for combating HZ, had several side effects, notably the dissemination of VZV in immunocompromised patients [2]. To address these issues, the recombinant vaccine was developed. The RZV uses a surface protein called gE (glycoprotein E). It is combined with ASO1B, which is composed of two different lipids, MPL (monophosphoryl lipid A) and QS-21 (saponin) [7,11]. This combination of ASO1B and gE generates a long-lasting immunological response, which has been shown to be more effective in reducing HZ in older patients than ZVL [7,11]. In addition, it had no reports of dissemination of VZV infections throughout both clinical trials ZOE-50 and ZOE-70 [8]. While clinical trials showed no dissemination of HZ, one global analysis documented adverse events, which included dermatomal reactions that resembled HZ.

This analysis was conducted on reported data spanning 2.5 years, focusing on vesicular and bullous cutaneous eruptions following RZV administration. Among the global distribution of 32,597,779 RZV doses, a total of 2423 adverse events were reported [12]. These adverse events included 120 cases of blisters, 80 cases of vesicular rashes, and 8 cases of ophthalmicus herpes unrelated to the injection site [12]. While the prevalence of these events is generally low in immunocompetent patients, the presence of certain risk factors can significantly increase an individual's likelihood of developing HZ. Notable risk factors include HIV/acquired immune deficiency (RR: 3.22), family history (RR: 2.48), malignancy (RR: 2.17), physical trauma (RR: 2.01), and older age (RR: 1.65) [13]. These risks are well known to healthcare providers; however, less known is the dissemination of HZ from the RZV.

There have been multiple reported cases of patients experiencing dermatomal reactions after receiving the RZV. This phenomenon is well-known from the previous ZVL, but such reactions were not observed during clinical trials of RZV [8]. It is worth noting that the majority of these cases lacked laboratory testing, or had negative PCR results. This case study exhibits a rare instance of the RZV having caused a V1-limited rash with a positive HZ PCR test in the United States. Other notable cases include a case study involving a 74-year-old female patient with ulcerative proctosigmoiditis who developed a blistering autoimmune skin reaction after receiving both doses of the RZV [14]. In both instances, the skin reaction resolved with systemic steroid treatment. Another case study described a 51-year-old woman with Crohn's disease who developed a bullous rash on her left arm and axilla two days after receiving the second dose of the RZV [15]. Mittal et al. showcased a 73-year-old woman with hypertension, hypothyroidism, and stage IIA infiltrating ductal breast cancer, who had undergone bilateral mastectomy, reported a mild, itchy rash on her L3-L4 dermatome region three days after receiving the first dose of the RZV [16]. Another case documented a 60 year old immunocompetent female who developed a dermatomal pruritic and vesicular rash in her L4–L5 area one week after administration of the RZV [17].

There have been many documented incidences of HZO following the administration of VZV; however, instances following the RZV are rare. One case report described a 63-year-old man who developed varicella skin eruptions two months after receiving the VZV vaccine, followed by progressive vision deterioration one month later [18]. Another study highlighted a 67-year-old woman who developed herpes zoster keratouveitis two weeks after receiving the VZV vaccine [19]. A notable case following the RZV involved a 78-year-old woman with a history of HZO who experienced progressive corneal thinning one week after her second dose [20]. While rare, instances of HZO are documented in the literature

with both vaccinations.

In conclusion, the ZVL was once the standard of care but caused the dissemination of VZV in immunocompromised patients and had low efficacy in reducing HZ. Thus, the development of the RZV ensued, demonstrating improved efficacy and safety. The case reports discussed in this paper demonstrate instances of dermatomal reactions and HZO following RZV administration. This underscores the need for constant monitoring and assessment of the RZV. Further studies are necessary to better understand how the immunomodulatory effects of RVZ may provoke reactivation of HZ. Physicians should continue to administer the RZV to patients but be cognizant that reactivation may rarely subsequently occur.

Patient consent

Informed consent to publish this case was obtained from the patient. A copy of the written consent is available for review upon request by the Editor-in-Chief of this journal.

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Declaration of Competing Interest

Dr. Haddadin is an advisor for Pandorum International Inc., a company with a product for treatment of neurotrophic keratitis.

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