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Sixth nerve palsy and keratouveitis in patient with varicella zoster virus reactivation posterior to COVID-19 vaccine

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ABSTRACT

BACKGROUND: We present a case of herpes zoster-induced by the COVID-19 vaccine, with present sixth nerve palsy and keratouveitis.

CASE PRESENTATION: A 77-year-old patient presented to the hospital with a right-sided headache, dysesthesias in the trigeminal territory, diplopia, and restricted abduction in the right eye. She had been vaccinated with the Pfizer/BioNTech vaccine three weeks prior. Examination revealed the weakness of abduction and elevated intraocular pressure of the right eye. Brain imaging tests were normal. At follow-up, a pseudo-dendritic corneal ulcer and iridocyclitis were noted. The polymerase chain reaction of aqueous humor confirmed the diagnosis of herpes zoster ophthalmicus. Treatment with oral valacyclovir and topical prednisolone was started, with gradual improvement of the symptoms.

CONCLUSION: Herpes zoster is an uncommon cause of sixth nerve palsy. The association between the COVID-19 vaccine and increased incidence of herpes zoster has recently been described. Awareness must be created for prompt diagnosis and treatment.

KEY WORDS: herpes zoster ophthalmicus; herpes zoster sine herpete; sixth cranial nerve palsy; COVID-19 vaccine

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INTRODUCTION

Herpes zoster ophthalmicus (HZO) is the definition of the varicella-zoster virus (VZV) reactivation along the ophthalmic division of the fifth cranial nerve (CN V1). The most frequent ophthalmic manifestations in HZO are uveitis, keratitis, and conjunctivitis. Reactivation of HZO represents 10–20% of VZV cases [1], and it is generally due to a decrease in the cellular immune response mediated by T lymphocytes, secondary to numerous factors such as: aging, chemotherapy, malignancy, immunological disorders, and human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS). We report a case of HZO, which manifested as a unilateral sixth cranial nerve (CN VI) palsy and keratouveitis three weeks after receiving her third dose of a COVID-19 vaccination.

CASE PRESENTATION

A 77-year-old woman with a medical history of hypertension and dyslipidemia presented to

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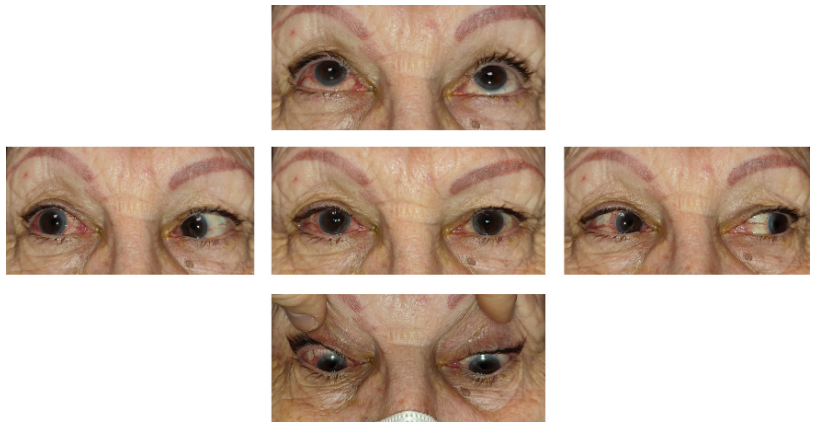

FIGURE 1. Motility examination revealed mild right esotropia in primary gaze and restricted right eye abduction

the ophthalmology department for the evaluation of intense right-sided cephalalgia, horizontal diplopia, and restricted abduction of her right eye (RE). She had been evaluated by her primary physician two weeks prior with a diagnosis of right-eye keratitis, treated with topical erythromycin ointment.

She had received the third dose of the Pfizer/BioNTech vaccine 20 days before her consultation with her primary care physician, after which she experienced generalized weakness for two days.

Upon examination, the patient referred severe dysesthesias in the V1 and V2 distribution. Best-corrected visual acuity (BCVA) was 20/200 in RE, and 20/32 in the left eye (LE). Both pupils were equal sizes and reactive to light. There was no apparent lid ptosis or exophthalmos. The RE had a subtle esotropia of 6 prism diopters at primary gaze. Extraocular motility manifested a limited abduction of RE, consistent with an isolated right CN VI palsy (Fig. 1). Slit-lamp examination showed severe conjunctival injection in the right eye and moderate stromal edema with inferior keratic precipitates. Visibility of the anterior chamber was comprised due to corneal edema. Intraocular pressure (IOP) was 35 mm Hg in RE and 18 mm Hg in the LE (Goldmann tonometry). Slit-lamp examination of LE was normal. Fundoscopy was normal in both eyes.

An emergency computed brain and orbital tomography scan with contrast showed no orbital pathology, and there was no evidence of a carotid-cavernous fistula. She was medically discharged with topical hypotensive medication (timolol/bimatoprost and brinzolamide/brimonidine).

The patient was evaluated at 48 h. Severe dysesthesias in the V1 and V2 persisted. Visual acuity had not improved. However, right-eye slit-lamp examination revealed, aside from the conjunctival injection, an epithelial pseudo-dendritic corneal ulcer visualized with fluorescein staining (Fig. 2) and anterior stromal infiltrates and the presence of 3+ anterior chamber cells. IOP was 14 mm Hg in the RE (with hypotensive medication) and 16mmHg in the LE. This finding raised the suspicion of HZO. A positive quantitative polymerase chain reaction (PCR) result was found for VZV DNA in the aqueous humor confirming the diagnosis of HZO complicated with keratouveitis and CN VI palsy after COVID-19 vaccine.

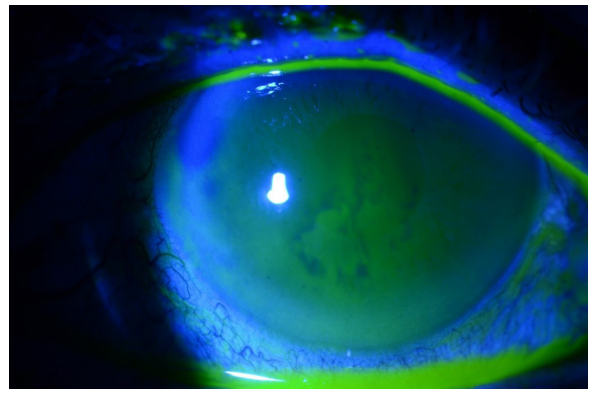

FIGURE 2. Pseudodendritic epithelial ulcer stained with fluorescein using a cobalt blue filter

The patient started treatment with oral valaciclovir (3 × 1000 mg/24 h) for 10 days combined with topical acyclovir ointment 5 times a day and topical prednisolone 1%. Progressive amelioration in ocular motility was perceived over the following weeks. Keratouveitis completely resolved after 2 weeks of treatment. Antiglaucomatous medications were also discontinued in the follow-up period

DISCUSSION

VZV is a DNA virus from the herpes simplex virus group, which establishes latent infection in peripheral sensory ganglia. VZV infection typically presents with numerous painful and pruritic unilateral vesicles, generally circumscribed to a single dermatome [2]. Reactivation of herpes zoster along CN V1 causes HZO, which accounts for 10–20% of VZV infections [1]. About 50% of all HZO will have ocular involvement, especially affecting the anterior segment (keratitis, uveitis and conjunctivitis) [3]. Although the cutaneous eruption is a distinct trait of herpes zoster, an atypical form known as "zoster sine herpete" has been described in patients with intense unilateral neuropathic pain or who present with features of HZ in the absence of an apparent cutaneous involvement [4].

Involvement of the extraocular muscles has been reported in 10–30% of all HZO cases [5]. Various hypotheses have been postulated, including contiguous intracavernous radiculomeningitis, muscle ischemia, vasculitis, or cranial motor neuropathy6. The most frequent palsy in HZO concerns CN III. This is succeeded by CN VI and CN IV palsies, respectively [7].

In our case report, due to the absence of a zosteriform rash and the combination of CN VI palsy and ocular hypertension, organic and vascular compressive syndromes (carotid-cavernous fistula) had to be ruled out. Emergency computed brain, and orbital tomography scan with contrast showed no orbital pathology. The presence of an epithelial pseudodendritic ulcer and uveal involvement, including keratitic precipitates together with sensory involvement of the first and second branches of the trigeminal, raised the suspicion of HZO, complicated with isolated abducens nerve palsy secondary to VZV. The option of an HZO "sine herpete" was considered since there was no clinical evidence of skin lesions apparent to the physician or patient. It has also been recognized as a probable cause of severe, anterior granulomatous iridocyclitis [11]. Aqueous humor PCR confirmed the diagnosis.

Although HZO is usually diagnosed clinically, detection of viral DNA in aqueous humor remains the gold standard for establishing a definitive diagnosis of VZV13. Treatment of HZO when there is the involvement of the extraocular muscles is highly debated. Systemic antiviral medication appears to decrease the risk of viral shedding, with some benefit in diminishing the clinical manifestations of HZO [6, 7, 14]. In our case, the patient was treated with oral valacyclovir (3 x 1000 mg/24 h), and topical prednisolone for the anti-inflammatory effect. The prognosis for recovery of extraocular muscle function has been reported to be favorable [6, 7].

VZV appears to occur when there is a decrease in the class 1 histocompatibility complex levels. This variation would produce inhibition of the response mediated by interferon, whose action is predominantly antiviral, therefore facilitating the viral replication. Risk factors classically associated with this immunologic comprise include: stress, trauma, HIV, malignancy, chemotherapy, and advanced age. Herpes zoster can also be reactivated by vaccines, as has been observed in cases described secondary to hepatitis A, rabies, influenza, or Japanese encephalitis vaccine. The COVID-19 vaccination has recently been associated with the increased incidence of herpes zoster [9]. The exact mechanism by which our patients' immune systems are depressed after vaccination remains challenging to understand. As with COVID-19 infection, the phase I/II trial with BNT162b1 (Pfizer/BioNTech vaccine) demonstrated a dose-dependent reduction in lymphocytes in the first days subsequent to the inoculation of the vaccine [10]. The mean onset of symptoms between COVID-19 vaccine and herpes infection is variable according to the different publications. Many of them are descriptions of isolated cases. Tejeda Cifuentes et al. reported 29 cases of herpes virus infection in patients recently vaccinated with COVID-19 vaccine, noting that the average onset of symptoms after vaccination was 24 days [12]. In our case report patient presented with symptoms compatible with HZO approximately 20 days after her third dose of the Pfizer/BioNTech vaccine, behaving as a trigger.

A wide range of dermatological and ophthalmic herpetic clinical manifestations have been described post COVID-19 vaccination [9]. However, to our knowledge, this is the first case reporting an association between COVID-19 vaccination and reactivation of HZO complicated with CN VI palsy. Ophthalmologists should be alert about the herpetic reactivation after COVID-19 vaccine, which can present with ocular and neurological complications.

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