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Case Report

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Third cranial nerve palsy with confirmed HHV-6 positivity

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ABSTRACT

We present a rare case of a 38-year-old man diagnosed with third cranial nerve paralysis, where no abnormalities were detected on magnetic resonance imaging (MRI). Human herpes virus-6 (HHV-6) infection affecting the central nervous system and associated with cranial nerve paralysis is an unusual occurrence. This report underscores the importance of considering HHV-6 as a differential diagnosis in patients presenting with cranial nerve palsy and suggests the use of cerebrospinal fluid (CSF) HHV-6 polymerase chain reaction (PCR) testing for confirmation.

Keywords: HHV-6, cranial nerve palsy, human herpes virus, oculomotor nerve palsy

INTRODUCTION

The third cranial nerve is responsible for innervating several extraocular muscles, including the superior, inferior, and medial rectus, the inferior oblique, and the levator palpebrae superioris muscles. Oculomotor paralysis can arise due to a variety of causes, extending from lesions in the mesencephalon to pathology in the orbital segment.[1]

Human herpes virus-6 (HHV-6) is primarily recognized for causing roseola infantum, also known as exanthema subitum, predominantly affecting children under two years of age. This virus is commonly associated with symptoms like febrile seizures and encephalitis, though asymptomatic infection is present in 90-95% of healthy adults.[2]

Here, we examine a case of third nerve palsy in an immunocompetent 38-year-old male, where HHV-6 DNA was detected in the cerebrospinal fluid.

CASE

A 38-year-old male presented with sudden onset of diplopia, which had persisted for a week, and right-sided eyelid drooping, which had developed over the past three days. He reported a throbbing headache on the right side, ongoing for three months, without associated nausea or vomiting. Neurological examination showed right eyelid ptosis and restricted movement in all directions except lateral gaze (Figure 1). Bilateral light reflexes were intact. Also, hypoesthesia was detected in the right V1, V2, and V3 sensory branches of the trigeminal nerve.

Extensive imaging, including brain magnetic resonance imaging (MRI), computed tomography (CT) angiography, orbital MRI, and venography, showed no abnormalities. However, cerebrospinal fluid (CSF) analysis revealed the presence of HHV-6 DNA, detected through PCR. CSF pressure, cell count, and protein levels were within normal limits, and no growth was observed in the CSF culture (CSF pressure: 15 mmHg, glucose: 68 mg/dl, simultaneous blood glucose: 100 mg/dl, protein: 40 mg/dl). Following the detection of HHV-6 positivity, the patient was started on 2x350 mg ganciclovir by the department of ınfectious diseases and clinical microbiology.

Additionally, petechial rashes were noted on the patient's limbs, which were diagnosed as cutaneous candidiasis. A comprehensive immunological workup revealed normal CD4, CD2, CD3, and CD8 lymphocyte counts, as well as adequate immunoglobulin levels and immune function. Tests for other infectious agents, including HIV, HBV, HCV, EBV, Treponema pallidum, and Leishmania, were all negative.

The patient's neurological examination remained stable on the 8th day of treatment. He was referred back to the infectious disease specialists for a review of the treatment plan, and it was recommended to extend the antiviral therapy for another 14 days. On the 14th day, with no significant change in symptoms, oral steroids at a dose of 1 mg/kg were initiated, and a follow-up visit was scheduled for ten days later. At this follow-up, the right eyelid ptosis had improved, though restrictions in inward and upward gaze persisted (Figure 2). Continued oral methylprednisolone treatment was recommended, with another clinic review planned in two weeks.

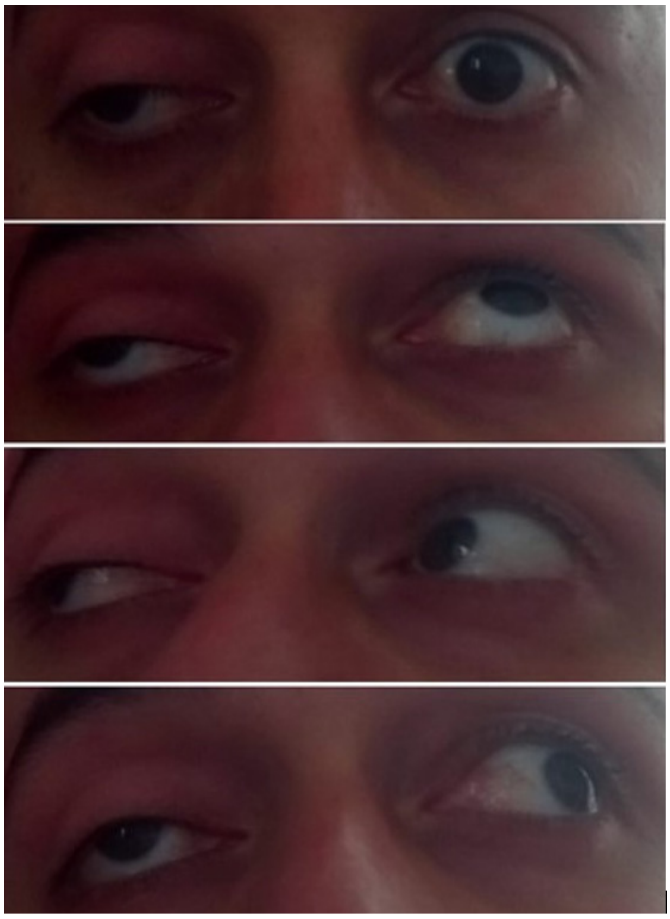

Figure 1. A. Exotropia and ptosis in the right eye in the primary position **B**. Limitation of upward gaze in the right eye **C**. Introspection limitation in the right eye **D**. Lateral gaze is preserved in the right eye

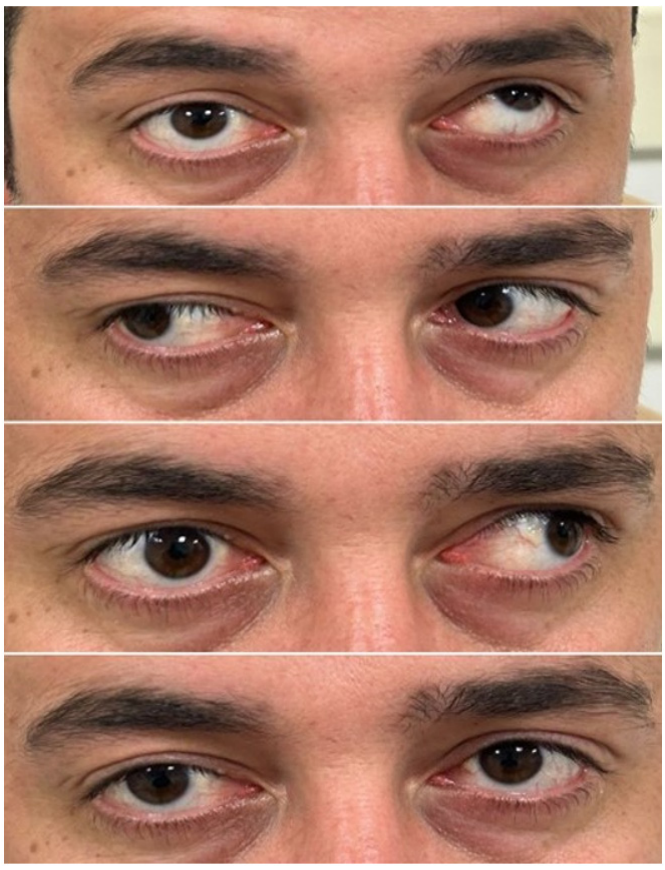

Figure 2. Eye movements of the patient after treatment **A**. A regression was observed in the limitation of upward gaze. **B**. Lateral gaze is preserved in the right eye. **C**. A regression in introspection limitation was observed in the right eye. **D**. In the primary position, regression of exotropia and ptosis was observed in the right eye.

DISCUSSION

Though HHV-6 is primarily known for causing febrile illness in children, it has also been implicated in neurological disorders such as multiple sclerosis, encephalitis, and epilepsy.[1] The mechanism through which the virus invades the central nervous system is not fully understood. However, though it has been hypothesized that viral reactivation within brainstem nuclei could contribute to cranial nerve palsies.[10]

In this case, although MRI showed no inflammatory changes, the presence of HHV-6 DNA in the CSF suggests a viral involvement in the patient's third nerve paralysis. Previous studies report on the molecular mechanisms of inoculation, dissemination, persistence, latency and reactivation of HHV-6 in inflammatory processes in the ocular tissue. After inoculation of the cornea, viral antigen was found in ocular nerves.[12] Although our patient's MRI did not show an inflammation in the orbital and brainstem MRI, 3rd. cranial nerve paralyses may be caused by due to a molecular mechanism.

A post-mortem study showed that herpesviruses can establish latency in cranial ganglia, with HHV-6 being the most commonly detected virus in autopsy studies of trigeminal and facial ganglia in latently infecting 64% of cases.[11] Cranial nerves are not only the pathways along which viruses are transported from one tissue to another, but are also sites of pathological changes resulting in their dysfunction.[3,5,10] The patient also exhibited hypoesthesia in the V1, V2, and V3 branches of the trigeminal nerve. It has been previously demonstrated that herpesviruses, including HHV-6, can randomly infect cranial nerve nuclei.[8-10] A case report presented fourth cranial nerve palsy following HHV 6 infection of the central nervous system.[6]

Though typically benign, HHV-6 has been associated with more severe central nerve system (CNS)-manifestations, even in immunocompetent individuals.[1,13] It can rarely occur as a complication of roseola or as a primary manifestation of HHV-6 infection in immunocompetent individuals. In our case, the patient demonstrated normal immune function.

As suggested in case reports, possible treatment options include ganciclovir, foscarnet, cidofovir, and brincidofovir.[7] The department of ınfectious diseases initiated a 14-day course of ganciclovir therapy for the patient, who exhibited a mild clinical response to the antiviral treatment. Corticosteroids are commonly used to address inflammation, and pulse steroid therapy within the first 24 hours of symptom onset has been linked to reduced rates of complications in HHV-6/HHV-7-related neurological manifestations.[4] After reviewing the immunologic panel, we initiated oral steroid treatment. Although the exact mechanisms of viral damage to cranial nerve cells are not fully understood, several case reports support the link between cranial nerve injury and herpetic infections, with appropriate antiviral therapy often leading to improvement or full complet recovery of cranial nerve function

CONCLUSION

To the best of our knowledge, 3rd cranial nerve palsy is association with HHV6 infection has been reportedly very rare. This report highlights that HHV-6 should be taken into consideration as a possible cause and might be included in the panel of diagnostic analyses even in immunocompetent adults.

ETHICAL DECLARATIONS

Informed Consent

All patients signed the free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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