The First Case of Human Herpesvirus 7-Related Epilepsy in the Republic of Belarus

Katerina Divakova, Elena Kishkurno, Tamara Amvrosieva, Oxana Romanova, Svetlana Belaya, Igor Zaitsau, and Yuliya Shilova

1. Pediatric Infectious Diseases Department, Belarusian State Medical University, Minsk 220116, Republic of Belarus
2. Republican Research and Practical Center for Epidemiology and Microbiology, Minsk 220114, Republic of Belarus
3. Infectious Diseases Department, Belarusian Medical Academy of Post-Graduate Education, Minsk 220013, Republic of Belarus
4. Republican Research and Clinical Center of Neurology and Neurosurgery, Minsk 220114, Republic of Belarus

Abstract: Background: Human herpesvirus (HHV)-7 is usually associated with febrile seizures. Later onset and higher frequency of seizures are characteristic of pediatric HHV-7, compared with HHV-6 infection. The HHV-7-related severe neurological disorders are predominantly observed in immunocompromised individuals. Reports of healthy individuals with HHV-7 infection and diverse neurological disorders are limited. Patient Description: We present a case of HHV-7-related epilepsy in an immunocompetent 11-year old boy and extensive infectious and autoimmune testing positive only for HHV-7 in the cerebrospinal fluid. The patient made a good recovery after treatment with intravenous immunoglobulin and methylprednisolone. Discussion: This is the first reported case of epilepsy associated with HHV-7 in a previously healthy individual. It also demonstrates that intravenous immunoglobulin and steroids may be used in the course of this disorder and may be beneficial for recovery.

Key words: HHV-7, epilepsy, child, case report, treatment.

1. Introduction

The role of human herpesvirus 7 in human disease has yet to be clearly defined. More than 95 percent of adults are HHV-7 seropositive. Infection with HHV-7 generally occurs during childhood, peaking around three years of age. HHV-7 infection is generally asymptomatic. Similar to other herpesviruses, HHV-7 causes latent infection that can become reactivated, particularly in immunodeficient patients.

Among children, HHV-7 is associated with acute febrile illness with or without rash, febrile seizure, exanthema subitum and neurologic disease (meningitis, encephalitis, and demyelinating conditions) [1, 2]. Attention to severe forms of neurologic disease caused by HHV-7 is increasing, with published reports of acute myelitis, myeloradiculoneuropathy, meningoradiculopathy, hemiconvulsion and hemiplegia syndrome and hemorrhagic brainstem encephalitis [3-7].

2. Case Report

An 11-year old male patient presented with first and sudden onset tonic-clonic seizures. He had a history of acute febrile illness with drowsiness and headache without nausea and vomiting a few days previously. Cerebrospinal fluid (CSF) examination revealed 1 white blood cell (WBC)/mmc, glucose 48 mg/dl and protein 10 mg/dl. All results, including immunological and virological tests by polymerase chain reaction (PCR) in blood and CSF, were negative. Cranial magnetic resonance imaging (MRI) and electroencephalogram (EEG) results were normal. Dehydration therapy and steroids (dexamethasone 0.5-1 mg/kg) were prescribed. The patient’s clinical condition improved temporarily – there were no seizures for 3 weeks. Unfortunately, convulsions...
resumed. As monotherapy with a first-line antiepileptic drug (carbamazepine) failed, combination therapy with lamotrigine and valproic acid (Depakine® chronosphere) was administered under plasma-valproate concentrations routine monitoring (Fig. 1).

Over six months the patient had polymorphic focal seizures with secondary generalization and bilateral tonic-clonic seizures 1-3 times per week. The development of motor seizures was often preceded by sensory and dizziness auras. The child became aggressive and irritable. Physical examination revealed only slight tremor of the distal extremities, more intense during movement. His WBC count and C-reactive protein were normal. Interictal EEG did not reveal any epileptic discharges during examination (Fig. 2a, b).

CSF testing showed 9 WBC/mmc (60% lymphocytes), an increased level of protein 40 mg/dl, glucose and lactate levels were normal. Parasitic diseases of the central nervous system neurocysticercosis, neurotoxocarosis, alveococcosis, cystic echinococcosis, ascariasis, and tick-borne encephalitis were excluded. Anti-NMDA-R, anti-CASPR2, anti-AMPA1-R, anti-AMPA2-R, anti-LGII, anti-GABAB-R in CSF and anti-NMDA-R, anti-CASPR2, anti-AMPA1-R, anti-AMPA2R, anti-LGII, anti-GABAR-B1/B2 in serum were negative. Real-time quantitative DNA PCR (qPCR) test of CSF assay performed with the commercial kit (AmpliSens EBV/CMV/HHV6) and a set of primers and probe [8] was positive only for HHV-7 ($10^2$ copies/ml). HHV-7 DNA was also detected in urine ($10^2$ copies/ml) and saliva. HHV-6 DNA was also detected in saliva (621 copies/ml). IgM, IgG HHV-7 antibody levels were not determined.

The patient received intravenous immunoglobulin (IVIG) (Octagam®) (total dose 2 g/kg at once) and methylprednisolone (initial dosage 10 mg/kg/d for 5 days intravenous, than per os for 3 months with gradual dose reduction), resulting in a disappearance of all types of seizures for 3 weeks.

At present, 1 year later, he still has only focal motor seizures (turning the head and eyes to the side) 1 time per month. These seizures stop on their own. Parents refused a control study of cerebrospinal fluid for HHV-7. At control examinations neurological symptoms, seizure frequency and EEG were evaluated.

![Fig. 1](image)  
**Fig. 1** Treatment regimen of patient.  
†† - no seizures  
*** - polymorphic focal seizures with secondary generalization and bilateral tonic-clonic seizures 1-3 times per week  
§§§ - focal motor seizures 1 time per month
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3. Discussion

Viral infections with neurotropic viruses such as Roseoloviruses have been linked to acute seizures and epilepsy in children [9, 10]. Although HHV-6A is thought to be more neurotropic, several studies and recent meta-analysis suggest a pathogenic role of HHV-6B infection in the development of epilepsy [11-13]. There are no reports about HHV-7-related epilepsy.

In our case, detection of HHV-7 DNA in CSF was the only DNA detected by real-time qPCR and no other alternative cause for the neurologic symptoms was identified.

Repeat MRI revealed cerebellopontine angle cyst (8 x 13 mm) (Fig. 3 a, b, c).

In vitro and clinical data suggest that HHV-7 is resistant to ganciclovir [14, 15]. Established HHV-7 disease can be treated with foscarinet or cidofovir [15], but they are not registered in Belarus. We used a treatment regimen for neurological diseases induced by HHV-7, which included IVIG and methylprednisolone [3, 4]. This had a clinical effect, allowed seizure control and did not require an increase
in anticonvulsant therapy (followed throughout the year). The child returned to his previous activities and studies in a regular school.

4. Conclusions

This case of an 11-year old boy with epilepsy associated with HHV-7 adds to the accumulating literature about the role of this virus in a broad range of neurological disorders, and is the first reported association of epilepsy with HHV-7 in a previously healthy individual. Despite a delay in diagnosis of several months due to the non-specific presenting symptoms, the patient showed improvement in neurological status following treatment with steroids and IVIG. He continued to recover well one year after discharge with ongoing rehabilitation.

The first occurrence of epilepsy after an episode of a rise in temperature or malaise requires the study of CSF, including a group of Roseoloviruses (HHV-7).

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