Clinical Case Report

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Spontaneous remission of West syndrome following a human herpesvirus 7 infection in a Chinese infant

A case report

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Abstract

Rationale: West syndrome (WS) is an age-dependent epileptic encephalopathy that is characterized by intractable epileptic seizures, hypsarrhythmia, and observed through electroencephalogram (EEG) and significant neurodevelopmental regression. The spontaneous remission of epileptic seizure is clinically rare and has not previously been reported in a Chinese infant. Herein, we reported a Chinese infant with WS whose seizures disappeared following a human herpesvirus 7 (HHV-7) infection.

Patient concerns: The male Chinese infant was born at the gestational age of 36 weeks with a birth weight of 1.65 kg and an Apgar score of 7 at the first minute. At the age of 6 months, the infant developed seizures that manifested as flexor spasms with trunk involvement and mental regression.

Diagnosis: Brain magnetic resonance imaging revealed leukomalacia of the posterior horn and a reduction in the size of the periventricular of the bilateral ventricle and the corpus callosum. An EEG revealed hypsarrhythmia and typical spasm seizures. Therefore, the infant was diagnosed with symptomatic WS.

Interventions: The infant was treated with adequate vitamin B6 intravenous drip and oral treatment with topiramate and levetiracetam.

Outcomes: The observed seizures disappeared spontaneously 40 days after onset, without any changes in the anti-epileptic drug treatment, following a febrile rash due to a HHV-7 infection.

Lessons: Spontaneous remission of epileptic seizures can occur following viral infection of HHV-7 in children with WS. The mechanism behind this spontaneous remission warrants further research.

Abbreviations: DQ = developmental quotient, EEG = electroencephalogram, HHV-6 = human herpesvirus 6, HHV-7 = human herpesvirus 7, IFAT = immunofluorescence antibody test, Ig = immunoglobulin, IL-2 = interleukin-2, PBMC = peripheral blood mononuclear cells, TNF = tumor necrosis factor, WS = West syndrome.

Keywords: epileptic seizure, human herpesvirus 7, spontaneous remission, West syndrome

1. Introduction

West syndrome (WS) is an intractable epileptic syndrome that is observed in infancy. The prognosis in patients with WS is poor.[1] In addition to structural, metabolic, and genetic causes, immunological dysfunction and inflammatory factors are also involved in the pathogenesis of WS.[2] Previous studies have shown that immunomodulatory dysfunction in humoral immunology and cytokine levels in patients with WS.[3] Patients with the clinical feature of epileptic spasms have higher levels of antibodies against the N-methyl-d-aspartate-type glutamate receptor in the cerebrospinal fluid.[4] The levels of serum immunoglobulins (Igs) and complement proteins of IgA, IgM, IgG, C3, and C4 have been found to be lower in patients with WS than in control patients.[5] In the cell-mediated immune system, higher levels of interleukin-2 (IL-2), tumor necrosis factor (TNF)-α, and interferon-α are found in patients with WS.[6] These factors might be involved in the inflammatory mechanisms of WS. Generally, epileptic seizures might be provoked and/or exacerbated by fever or infectious diseases in children with epilepsy. We, herein, report spontaneous seizure cessation following viral infection of human herpesvirus 7 (HHV-7) in a Chinese infant with WS and discuss the possible significance of this phenomenon.

2. Case presentation

The patient was born by vaginal delivery at 36 gestational weeks, due to a premature rupture of the fetal membrane. The birth

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weight of the infant was 1.65 kg and the Apgar score at the first minute was 7. The family history of the patient was unremarkable. His psychomotor development was slightly delayed. He acquired head control at 4 months old and the ability to roll his body over inflexibly at the age of 6 months. At 6 months of age, the patient developed seizures that manifested as flexor spasms with trunk involvement. The seizure frequency varied between 10 and 30 series per day, and each series included between 10 and 20 episodes with intervals of between 5 and 10 seconds. After the onset of the spasms, motor regression was observed. The child was unable to hold his head steadily. The findings of the physical examination were unremarkable. Brain magnetic resonance imaging revealed leukomalacia of the posterior horn and a reduction in the size of the periventricular of the bilateral ventricle and the corpus callosum (Fig. 1). A video electroencephalogram (EEG) revealed hypsarrhythmia and typical spasm seizures (Fig. 2). Therefore, a diagnosis of symptomatic WS was made. Vitamin B6 was administrated intravenously, with an initial dose of 100 mg per day for 7 days. Instead of the expected improvement, we observed an increase in the seizure frequency to 20 to 30 series per day during the waking period. The vitamin B6 medication was substituted for a gradual titration of both topiramate, at an initial dose of 1 mg/kg.d increasing to 50 mg/kg.d, and levetiracetam, at an initial dose of 10 mg/kg.d increasing to 50 mg/kg.d. No significant improvement in the seizure frequency was observed after reaching the target doses of topiramate and levetiracetam. Forty days after the onset of WS, the patient developed a fever, reaching a peak body temperature of 40°C. The fever persisted for 4 days, following which the body temperature decreased to within the normal range. Concurrently, red skin rashes appeared on the patient's neck and spread through the trunk. This leads to a diagnosis of exanthema

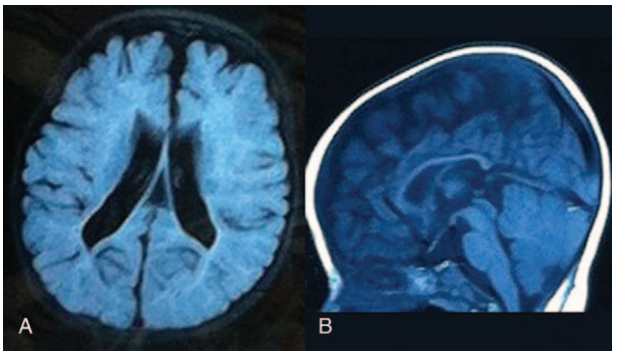

Figure 1. Brain magnetic resonance imaging. (A) Leukomalacia of the posterior horn and periventricular of the bilateral ventricle can be observed. (B) The corpus callosum is slightly smaller than average.

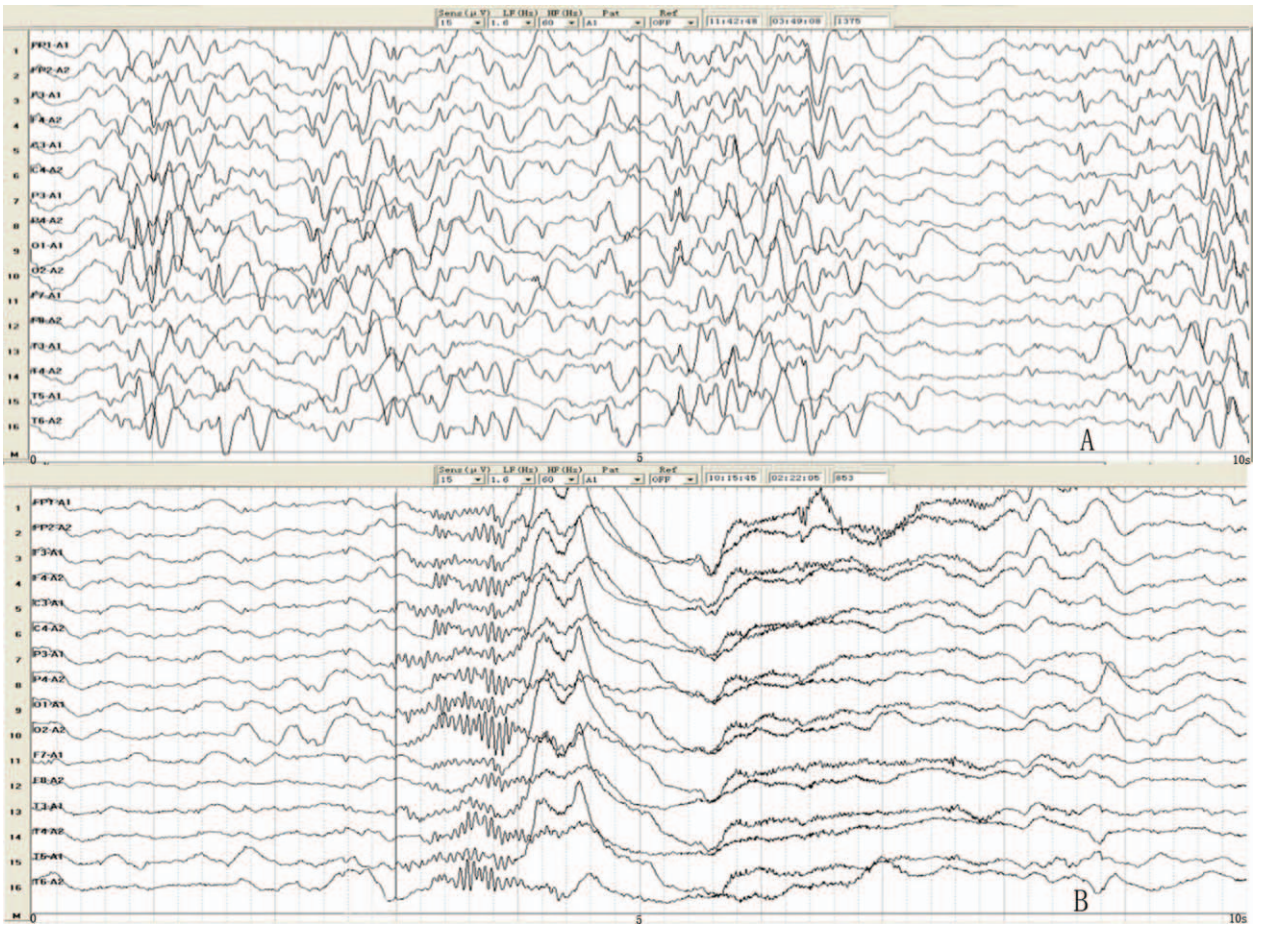

Figure 2. Video electroencephalogram at the onset of the infantile spasms. (A) Recording displaying hypsarrhythmia. (B) Recording displaying typical spasm seizures.

subitum. At the same time, as the body temperature decreased to within the normal range, the epileptic spasms disappeared spontaneously. Two weeks after spasm cessation, the oral antiepileptic drugs were stopped by his parents. The EEG results revealed a remarkable improvement, with no manifestations of hypsarrhythmia and only a spike and sharp wave at the right occipital area observed after a 3-month remission period (Fig. 3). Antibody titers to human herpesvirus 6 (HHV-6) IgM and IgG were measured using an indirect immunofluorescence antibody test (IFAT). Three days after the onset of the febrile rash illness, the titers to HHV-6 IgM and IgG were 1:10 and 1:80. In contrast, both the titers of HHV-7 IgM and IgG were 1:10. Two weeks after the onset of the rash, no changes were found in the HHV-6 IgM and IgG levels, while the titers of HHV-7 IgG rose from 1:10 to 1:160, and the titers to HHV-7 IgM rose to 1:40. The assay was not a routine examination and the test kit of IFAT was obtained from the EUROIMMUN medical diagnosis company limited (China). A follow-up was performed after 2 years of remission. The patient remained seizure free, was able to walk independently and could communicate with others using simple words and phrases. According to the Gesell Developmental Scales, the developmental quotient (DQ) of all areas were as follows: 80 in gross motor, 86 in final motor, 77 in adaptive, 82 in language, and 79 in social area (a DQ >85 indicates normality).

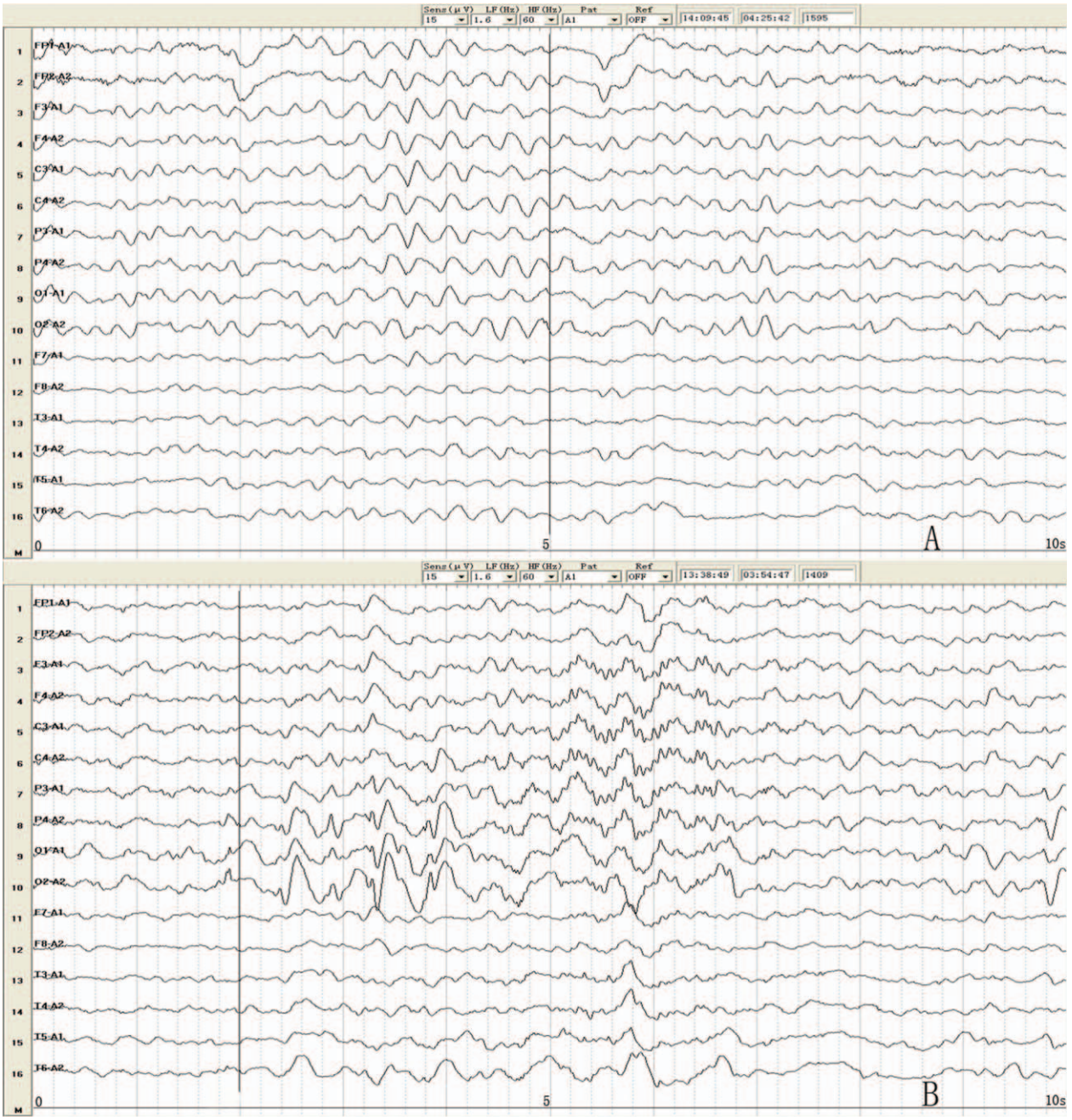

Figure 3. Video electroencephalogram 3 months after seizure remission following HHV-7 infection. (A) Recording displaying background activity. (B) Spike and ware wave at the right occipital area. HHV-7 = human herpesvirus 7.

3. Discussion

WS is characterized by intractable epileptic seizures, hypsarrhythmia on EEG, and neurodevelopmental regression. This condition is an age-dependent epileptic encephalopathy that occurs in infancy, with a peak onset age of between 4 and 7 months.[7] The observance of spontaneous remission of epileptic seizure is clinically rare. To the best of our knowledge, this is the first report demonstrating the spontaneous remission of seizures in a Chinese infant with WS following an HHV-7 infection.

The specific mechanisms of the spontaneous remission in this case remain unclear. Exanthema subitum is a common disorder that occurs during infancy. This disorder has the characteristics of fever and rash. Two kinds of human herpesviruses, HHV-6 and HHV-7, have been isolated as causal agents of exanthema subitum.[8,9] In this patient, the HHV-7 IgG titers increased from 1:10 to 1:160 during the convalescent phase, and HHV-7 IgM positivity was also detected. These features suggest that this was a case of a primary HHV-7 infection. Although the HHV-6 IgG titers were positive during the acute phase, there was no change in the titers during the convalescent phase, and the HHV-6 IgM titer was always negative. Thus, it is possible that the patient had a secondary infection of HHV-6 or acquired the antibodies from his mother. Recent evidence has suggested that WS might be T cell-mediated immune related epilepsy that involves cytokines, and that patients with WS have excessive T cell activation and proliferation.[2,10] IL-2 and TNF-α are the main cytokines that are involved in inflammation and have recently been associated with infantile spasm.[3] Liu et al[6] revealed that the expression levels of IL-2 are higher in patients with WS than in controls. IL-2 is secreted by activated CD4 + T cells and CD8 + T cells. IL-2 receptor signaling is important for effector T cells and plays a critical role in T cell differentiation, survival, and proliferation.[11] The daily seizure frequency was found to positively correlate with the levels of IL-2R. Furthermore, after prednisone treatment, the serum levels of IL-2R, IL-8, and TNF-α were reduced in children with WS.[12] In addition, IL-2 had been shown to induce seizures and produce recurrent seizure activity in animal models.[13] Interestingly, the levels of IL-2 is significantly decreased in HHV-7-infected cells of human peripheral blood mononuclear cells (PBMC), and HHV-7 infection can also inhibit the lymphocyte proliferation induced by various stimuli.[14] Thus, an HHV-7 infection can cause significant immunomodulatory effects regarding the cytokine synthesis in PBMCs, which might be 1 factor to the spontaneous remission of WS following HHV-7 infection. The other proposed mechanism for the observed remission in this case might be the increased levels of antibodies,[10] such as IgG, after HHV-7 infection, as this is similar to immunoglobulin therapy. Concerning this point, adrenocorticotrophic hormone (ACTH) is recommended as the first-line therapy for patients with WS.[15] Furthermore, clinical application of high-doses of immunoglobulin or corticosteroids have been shown to be effective in the treatment of spasms in WS.[10,16] The limitation in the approach used in this case was that the currently preferred first-line antiepileptic drug options, such as ACTH and vigabatrin, were not initially selected as they were not available. Therefore, the infant's condition did not improve significantly within 40 days of onset.

Overall, we report that the spasms in a case with WS in a Chinese infant spontaneously disappeared following an HHV-7 infection. The mechanism behind this spontaneous remission warrants for further research.

Author contributions

Conceptualization: Honghua Li.
Data curation: Bing Wang, Ling Shan, Lin Du.
Formal analysis: Feiyong Jia.
Writing – original draft: Honghua Li.
Writing – review & editing: Bing Wang, Ling Shan, Lin Du, Feiyong Jia.

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