Human Herpesvirus 7 encephalitis manifests with epileptic seizures in an immunocompetent adult and review of the literature

Yi Li
First Affiliated Hospital of Dalian Medical University

Qiu Ming Deng (✉️ 1252091260@qq.com)
First Affiliated Hospital of Dalian Medical University

Case Report

Keywords: HHV-7, Encephalitis, immunocompetent adult, epileptic seizures

Posted Date: October 24th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2172031/v1

License: ☝️ This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Introduction: Human Herpesvirus 7 (HHV-7) is a widespread double-strand DNA virus in human population that belongs to β-herpesvirinae subfamily and it replicates in CD4 + T lymphocytes. The virus has the ability of lifelong latency and easy to reactivate in immunocompromised patients (1,2). Primary HHV-7 infection regularly occurs during childhood and may manifest several clinical symptoms, mainly fever and exanthem subitum. Furthermore, HHV-7 Encephalitis is the severely type of the infection, epileptic seizures belongs to its clinical manifestation, however there exist uncertain aspects about infection route except the past history of the infectious agent in patients. In particular, as a lymphotropic virus, it has obvious tropism for the central nervous system (CNS), but its neuropathogenesis are underestimated (3), one the other hand, the case of encephalitis associated with human herpesvirus-7 infection in an immunocompetent patient has been rarely reported.

Thus, we mainfest an immunocompetent 26-year-old woman with encephalitis that the infection reason is not clear and review current literature. With the treatment of acyclovir and ganciclovir. The clinical outcome in our patient was recovered.

Case Presentation

A 26-year-old female undergraduate presented to critical care medicine with a 29-day history of fever accompanied with mental and behavior disorder. With the body temperature rising, thus leading to a state of coma and intermittent convulsions during the last 28 days. Also There was no significant personal history.

Before admission, She had received treatment in two hospital. Her cerebrospinal fluid (CSF) sample was colorless and routine analysis indicated total cells is 2/mm³ with 50% leukocytes total protein and glucose levels were 0.341g/L and 2.8mmol/L, CSF cultures were negative for bacterial and fungal organisms. Normal findings was obtained from the autoimmune encephalitis examination and cranial CT. Electroencephalography (EEG) expressed irregular activity with epileptiform discharge in the anterior temporal and bilateral frontal areas. HHV-7 DNA was detected in the metagenomics next generation sequencing (mNGS) of CSF, she was dignosed as meningitis and/or encephalitis in other hospital and then the acyclovir was added. Sputum cultures was Acinetobacter baumannii , Burkholderia cepacia. After active medical intervention, the body temperature is lower than the initial state, but progressive deterioration of the level of the consciousness was uncontrolled, and then led to a requirement for mechanical ventialtion.

On admission Physical examination revealed that she was in a comatose state, underwent mechanical ventilation via tracheostomy. She had a fever lung crackles neck stiffness and unconscious limb convulsions. Lumbar puncture was performed and CSF pressure was 252mmH₂O The patient was empirically treated with ganciclovir, meropenem, tigecycline, micafungin, corticoids, glycerolfructose, midazolam, Levetiracetam, topiramate, Perampanel, Clonazepam, phenobarbital. On the third evolution
day, her respiratory function improved along with nasal catheter oxygen inhalation via tracheostomy. Furthermore anti-ANA-IgG in serum was mild positive. But a wide spectrum of antibodies (anti-nRNP, anti-Sm, anti-SS-A, anti-Ro-52, anti-SS-B, anti-Scl-70, anti-Jo-1, anti-ACA, anti-AnuA, anti-AHA, anti-ARPA, anti-AMA-M2, anti-PCNA, anti-PM-Scl100, anti-HHV-1-IgG, anti-HHV-2-IgG, anti-Toxo-IgM, anti-CMV-IgM, anti-Rubella-IgM) in serum were normal. In order to check the brain function, unfortunately the cranial CT was negative, MRI was not performed because she has been wearing dental appliance. The second mNGS of CSF indicated Enterococcus faecium and anti-Aspergillus-IgG in blood was positive, thus we added the contezolid and voriconazole to ameliorate previous treatment. On the 18th day of admission, the body temperature was up again combine with epilepsia gravior. Also lumbar puncture was performed and CSF pressure was 210mmH₂O, but the CSF cultures and CSF mNGS were negative, then the blood antibodies(anti-HHV-1-IgG, anti-HHV-2-IgG, anti-Toxo-IgG, anti-CMV-IgG, anti-Rubella-IgG) was positive. With the adjustment of treatment combined with personal immune system recovered, the body temperature returned to normal and the Glasgow Coma Score (GCS) was 15 points(E4 V5 M6). However her memory ability was damaged, for the sake of better rehabilitation therapy and was subsequently discharged. Suddenly, Her body temperature rose again accompanied by generalized epileptic, then returned back our hospital after one day. The 4th CSF mNGS indicated HHV-1 and EEG expressed irregular activity with slow wave in the temporal and bilateral frontal areas. Urine cultures was Klebsiella pneumoniae. The patient was treated with cincontezolid, corticoids, levetiracetam, topiramate, Perampanel, Clonazepam, amika, ganciclovir. As time went by, Her memory ability improved quickly and could eat by herself. Whereas she often felt choking when she ate chewy food. The result of gastroscopy indicated normal, To some extent implied she had psychological disorder. So with the help of humanistic concern and antiepileptic drugs, nally the patient had recovered after two months.

The diagnostic evaluation of the HHV-7 encephalitis needs to be guided by epidemiologic, laboratory tests, imaging examination and clinical proof, these information are as follows. First line investigation, HHV-7 DNA was detected in CSF, but there was no abnormal personal history(information provided by her relatives). Second line investigation, On day 1, the respiratory pathogen spectrum(Legionella, Mycoplasma pneumonia, Chlamydia pneumonia, Respiratory syncytial virus, Adenovirus, Influenza virus A, Parainfluenza virus, Coronavirus) was negative. But Influenza-virus-B-IgM in serum was positive. Hepatitis virus hepatitis A, hepatitis B, hepatitis C, hepatitis E, Treponema pallidumand, Human immunodeficiency virus were negative, Sputum cultures was Acinetobacter baumannii, Burkholderia cepacia, we added antibiotics. On day 3, tubercle bacillus in blood was negative, bacterial culture in the blood and CSF was negative. On day 7, a wide spectrum of blood antibodies (anti-nRNP, anti-Sm, anti-SS-A, anti-Ro-52, anti-SS-B, anti-Scl-70, anti-Jo-1, anti-ACA, anti-AnuA, anti-AHA, anti-ARPA, anti-AMA-M2, anti-PCNA, anti-PM-Scl100) were negative, anti-ANA-IgG was mild positive, its titers was more than 1:100. However these indications had no high specicity for the diagnostic of disease. On day 8, Neisseria meningitidi, Cryptococcal neoformans(serum and CSF) was also negative. Then a wide spectrum of CSF antibodies (anti-HHV-1-IgG, anti-HHV-2-IgG, anti-Toxo-IgM, anti-CMV-IgM, anti-Rubella-IgM) were negative. Third line invsetigation, the cranial CT was negative, the MRI was not performed due to the dental appliance affect the MRI result. Finally, on day 8, Enterococcus faecium was detected in the mNGS of CSF,
we added cefazolin. The CSF mNGS indicated HHV-1 on day 33, the patient was treated with ganciclovir intermittently about 4 weeks.

**Discussion**

Viral encephalitis is defined as acute brain parenchyma inflammatory induced by viral infection. The clinical symptoms of it includes fever and/or seizure. However the causes of the clinical presentation may due to infection or not. So the differential diagnosis of this patient that excluded bacterial and fungal meningitis, malaria, brain structural lesions, toxic and metabolic encephalopathies, and other noninfectious causes of encephalopathy. The mNGS of CSF indicated HHV-7 DNA that supported HHV-7 as the most likely cause of the encephalitis. After we added ganciclovir, the HHV-7 DNA was not detected. Due to the HHV-7 infection characterizations, and due to lack of the HHV-7 avidity testing, we can not distinguish between the past infection and primary infection. Among the viral encephalitides, HHV-7encephatitis is associated with epilepsy, the type of the epileptic seizures has been described as late unprovoked or acute symptomatic, the current case represent the later one, and it may has better outcome than the former. However refer to individual treatment. A huge gap between the antiviral therapy and the outcome of patients(2).
These cases presented on the table elucidate the similar clinical manifestation and the evolution of the cases in the literature. The patients’ ages ranged from 26 to 52 year old, median 35 years, only one female. The mortality is 14.2%(4-10). Ganciclovir was given in 6 of the patients, ganciclovir and foscarnet was recommended in immunocompromised patients with HHV-6 infection(10), the treatment of Encephalitis associated with human herpesvirus-7 infection still limited and unclear. It is common to see ganciclovir, acyclovir, foscarnet and intravenous immunoglobulin therapy was used, also there were some cases that was reported improvement without antiviral agent. In a retrospective analysis, we added ganciclovir empirically, and foscarnet has high vitro activity than ganciclovir. The foscarnet was highly regarded(6.7). Maybe foscarnet would be a great choice of reducing the length of stay in ICU and severity of disease for the HHV-7 encephatitis.

### Conclusion

As for unknown cause encephalitis cases present with seizures, the mNGS and PCR are alternative option for indentifying the potential causes, HHV-7 infection could result in serious CNS disease that should be kept in mind. HHV-7 DNA has enough high specificity to guide the next treatment and early clinical
intervention is crucial, yet the individual therapy need a big step forward to apply to the HHV-7 encephatitis.

**Declarations**

**Ethical Approval**

The study was approved by the Ethics Committee of the The First Affiliated Hospital of Dalian Medical University.

**Competing interests**

The authors declare that they have no competing interests.

**Consent for publication**

Written informed consent was obtained from the patient for publication of this report.

**Authors' contributions**

Li carried out the collection of the patient's microbiological data and drafted the manuscript. Deng carried out the collection of the patient's clinical data and drafted the manuscript. Li and Deng reviewed the literature and interpreted the data. Wan coordinate the management of the case and wrote the manuscript. All authors read and approved the final manuscript.

**Funding**

Not applicable

**Availability of data and materials**

Not applicable

**References**


