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Case Report

Rare Case of Human Herpes Virus-6 Meningitis in Immunocompetent Adult Patient Presented as Decrease Level of Consciousness

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Abstract

Background: Human herpesvirus 6 (HHV-6) is typically known for causing roseola in children, but its role in encephalitis among immunocompetent adults is less documented.

Case Presentation: We report a case of a 35-year-old Indonesian male with no significant medical history, who was admitted in August 2024 with high fever and altered consciousness. Symptoms began 10 days prior, escalating from fever to severe headache and neck stiffness. Initial treatment with paracetamol and levofloxacin was ineffective. Neurological examination revealed reduced consciousness (GCS 9/15) and behavioral abnormalities. Investigations included a CT scan, blood tests, and CSF analysis.

Investigations: Initial CSF analysis showed elevated protein and lymphocyte predominance. The CSF FilmArray Meningitis Panel confirmed HHV-6 infection. EEG indicated cerebral dysfunction, and MRI revealed non-specific white matter changes.

Treatment and Follow-Up: The patient received empirical treatment with vancomycin, ceftriaxone, and acyclovir, later switched to ganciclovir, leading to significant recovery. Follow-up indicated resolution of fever and neurological symptoms.

Discussion: This case underscores HHV-6 as a potential cause of severe encephalitis in immunocompetent adults. The effectiveness of the FilmArray Meningitis Panel in diagnosing HHV-6 emphasizes the need for awareness of this virus in encephalitis cases. Further research is needed to refine treatment and diagnostic protocols for HHV-6 infections.

Conclusion: HHV-6 should be considered in the differential diagnosis of encephalitis in adults, especially when common pathogens are excluded. Improved understanding and treatment strategies are essential for better patient outcomes.

***Keywords:** Viral Infection, Ganciclovir, Filmarray Meningitis Panel, Cerebrospinal Fluid, Immunocompetent Adults, Encephalitis, Hhv-6, Human Herpesvirus 6*

Introduction

Human herpesvirus 6 (HHV-6) is a widely encountered virus, primarily recognized for causing exanthema subitum (roseola) in young children. While HHV-6 is well-established as a causative agent of encephalitis in infants and immunocompromised individuals, its involvement in encephalitis among immunocompetent adults is less frequently documented. (1,2)

Case Presentation

Patient History

We present a case of a 35-year-old Indonesian male with a previously unremarkable medical history, admitted in August 2024 with high fever and diminished level of consciousness, characterized by drowsiness, eye-opening in response to voice, incomprehensible vocalizations, and lack of responsiveness to surroundings or commands. The patient's symptoms commenced 10 days prior to admission, initially presenting as persistent high-grade fever (38-40°C). Five days into the illness, he developed severe headache, neck pain, and stiffness. Despite receiving two doses of IV paracetamol at other facilities and starting oral levofloxacin (500 mg once) two days before admission, there was no improvement. On admission, the patient displayed a reduced level of consciousness, necessitating further diagnostic

Investigation

The patient has no history of chronic illnesses or seizures. Employed in IT at an airline head office, he reported camping in Jabal Qarnayt, Taif, Saudi Arabia, in June and performing Umrah in Makkah in early August. Additionally, he attended a large event involving many children two days prior to the onset of his symptoms. He denies recent medication use beyond paracetamol and levofloxacin, recent international travel, exposure to mosquitoes, ticks, animals (e.g., bats, dogs), sick contacts, and no fresh/salt water exposures. His immunization history includes all required childhood vaccinations, COVID-19 (three doses of Moderna), and the influenza vaccine administered in 2021. He is married, with a sexual history confined to his spouse, no evidence of engagement in illicit sexual activities, and no history of illicit drug use."

Examination on Admission

Upon admission, the patient was noted to be drowsy with a Glasgow Coma Scale (GCS) score of 9/15. He demonstrated eye-opening in response to verbal stimuli, produced incomprehensible sounds, and exhibited withdrawal from painful stimuli. Vital signs were as follows: blood pressure 137/84 mmHg, heart rate 83 bpm, respiratory rate 24 breaths per minute, temperature 38.3°C, and oxygen saturation ranged from 94% to 96%.

Neurological Findings

The patient presented with aphasia and was unable to follow simple commands. Behavioral abnormalities included unintentional wandering and agitation. There was no evidence of facial weakness; pupils were reactive, extraocular movements were intact, and the gag reflex was present. Due to the patient's decreased level of consciousness, a dysphagia assessment was not conducted. Motor power was estimated at 3/5 overall, though this was limited by the patient’s lack of cooperation, with no clear signs of lateralization.

There were no observed myoclonus, tremor, or flaccid paralysis.

Meningeal Signs

Neck stiffness was noted; however, other meningeal signs could not be thoroughly assessed due to the patient's reduced level of consciousness. There were no skin rashes, palpable lymphadenopathy, or skin ulcerations present.

Investigations

On Presentation

- CT Scan: Brain CT was unremarkable.
- CBC: WBC 4.14 x 10^9/L, Hb 14.4 g/dL, Plt 179 x 10^9/L. Electrolytes were within normal limits. CRP: 12.2 mg/dL, D-Dimer: 3.02 µg/mL, INR: 1.89, HbA1c: 5.65%, TSH: 1.56 µIU/mL, Urinalysis: Positive for glucose, ketones, pus cells (8-10 per high power field), and bacteria, Urine and Blood Cultures: No growth.

Table 1. Virology Investigation Schedule.

Virus	Result
Influenza B	Negative
COVID-19 Rapid Antigen Test	Negative
HIV Ag/Ab Combo	Non-reactive
Dengue IgM	Negative
Influenza A	Negative

Lumbar Puncture: Initial lumbar puncture was deferred due to an elevated INR, which was corrected with fresh frozen plasma. Opening pressure was not done.

Table 2. The subsequent lumbar puncture yielded the following results.

CSF (CHEMISTRY CELL COUNT)	Result
Color	Reddish
Appearance	Turbid
Glucose	64 mg/dl
Total Protein	166.9 mg/dl
Chloride	120.5 mmol/l
RBC	102,000/mm^3
Total Nucleated Cells	61/mm^3
Neutrophils	21.3%
Lymphocytes	75.4%
Monocytes/Macrophages	3.3%

Microbiological Analysis

- Gram Stain, Ziehl-Neelsen Stain, and Cultures: Negative
- Meningitis Panel (BioFire MicroArray Meningitis/Encephalitis multiplex PCR): Positive for HHV-6 PCR; negative for other pathogens.

Table 3. CSF Film Array Meningitis.

Test Name	Result
ME Panel Escherichia coli K1	Not Detected
Haemophilus influenzae	Not Detected
Neisseria meningitidis	Not Detected
Streptococcus agalactiae	Not Detected
Listeria monocytogenes	Not Detected
Streptococcus pneumoniae	Not Detected
Cytomegalovirus	Not Detected
Enterovirus	Not Detected
Herpes simplex virus 1	Not Detected
Herpes simplex virus 2	Not Detected
Human herpesvirus 6	Detected
Varicella zoster virus	Not Detected
Cryptococcus neoformans/gattii	Not Detected
Human parechovirus	Not Detected

Additional Investigations:

- EEG: Demonstrated neurophysiological evidence of mild focal right fronto-parieto-central as well a generalized cerebral dysfunction.
- MRI Brain: Revealed bilateral periventricular and subcortical non-specific white matter changes, with no abnormal signal intensity in the temporal lobes.

Treatment and Follow-Up

Empirical therapy with vancomycin, ceftriaxone, and acyclovir was commenced, alongside dexamethasone at a dosage of 10 mg every 6 hours. Significant improvement in the patient's level of consciousness was observed within 24 hours, although headache and fever persisted. Subsequent evaluations showed full recovery of consciousness, intact language function, and normal neurological findings. Vancomycin, ceftriaxone, and dexamethasone were discontinued after 3 days, while acyclovir was continued for an additional 7 days. Given the persistence of elevated temperatures and recurring headaches, a switch from acyclovir to ganciclovir was considered, as ganciclovir is the preferred treatment for HHV-6.(3) Furthermore, a repeat lumbar puncture was recommended, in line with current guidelines, to assess CSF leucocyte counts, glucose concentration levels, and protein levels, particularly in cases where clinical improvement is not evident within 48 hours of appropriate.

Table. The repeat CSF.

CSF (CHEMISTRY CELL COUNT)	Result
Color	Pale yellow
Appearance	Slightly turbid to clear
Glucose	75.1 mg/dl
Total Protein	168.1 mg/dl
Chloride	111.9 mmol/l
RBC	4,000/mm^3
Total Nucleated Cells	164/mm^3
Neutrophils	0.6%
Lymphocytes	98.2%
Monocytes/Macrophages	1.2%

Gram Stain: Polymorphonuclear leukocytes present (+2), no bacteria observed.

Ziehl-Neelsen Stain: Absence of acid-fast bacilli.

Table 5: CSF Film Array Meningitis Panel Results sent again and showed.

Test Name	Result
ME Panel Escherichia coli K1	Not Detected
Haemophilus influenzae	Not Detected
Neisseria meningitidis	Not Detected
Streptococcus agalactiae	Not Detected
Listeria monocytogenes	Not Detected
Streptococcus pneumoniae	Not Detected
Cytomegalovirus	Not Detected
Enterovirus	Not Detected
Herpes simplex virus 1	Not Detected
Herpes simplex virus 2	Not Detected
Human herpesvirus 6	Not Detected
Varicella zoster virus	Not Detected
Cryptococcus neoformans/gattii	Not Detected
Human parechovirus	Not Detected

Discussion

Human Herpesvirus 6 (HHV-6), traditionally linked to childhood exanthema subitum, has increasingly been recognized as a significant cause of encephalitis in immunocompetent adults. This case illustrates that HHV-6 can lead to severe encephalitis in otherwise healthy individuals, characterized by symptoms such as high fever, headache, neck stiffness, and altered mental status. The diagnosis was confirmed through the detection of HHV-6 DNA in cerebrospinal fluid (CSF) using the CSF FilmArray Meningitis Panel. (5)

The CSF FilmArray Meningitis Panel is a rapid multiplex polymerase chain reaction (PCR) diagnostic tool designed to detect a wide array of bacterial, viral, and fungal pathogens directly from CSF samples. This panel provides a significant advantage in clinical settings by enabling simultaneous detection of multiple pathogens, which is crucial for prompt and accurate diagnosis of central nervous system infections. Results are typically available within an hour, allowing for timely initiation of appropriate treatment. (6).

Reliability of the Test

The reliability of the FilmArray Meningitis Panel is high, with both sensitivity and specificity making it effective for detecting pathogens, including HHV-6. The sensitivity of the test ensures that true positive cases are identified, although it may vary depending on the stage of the infection and the viral load in the CSF. High specificity reduces the likelihood of false positives, which, while rare, can occur due to factors such as contamination or cross-reactivity with similar viral sequences. (6).

False Positives and Negatives

1. False Positives: Although the specificity of the FilmArray ME Panel is generally high, false positives can occur. These instances may arise from sample contamination during collection or handling, as well as cross-reactivity with other viral DNA present in the sample. Such occurrences, while infrequent, highlight the importance of interpreting results in conjunction with clinical findings and patient history.

2. False Negatives: False negatives are also a consideration, particularly if the viral load in the CSF is low or if the sample is obtained too early in the course of the illness. This emphasizes the necessity of clinical correlation; if there is strong suspicion of HHV-6 infection despite a negative result, repeat testing or additional diagnostic methods may be warranted. (6)

Given these factors, the FilmArray Meningitis Panel stands out as a highly effective diagnostic tool for identifying pathogens in cases of suspected meningitis or encephalitis, but clinicians must remain vigilant in interpreting results and considering the broader clinical context.

Regarding antiviral therapy, acyclovir has been noted to exhibit partial effectiveness against HHV-6; however, it is not typically recommended as a first-line treatment for this virus. Evidence suggests that while acyclovir may provide some clinical benefit, particularly in the early stages of infection, it does not consistently achieve the desired therapeutic outcomes. In contrast, ganciclovir has emerged as the preferred antiviral agent for HHV-6 infections. The significant clinical improvement observed in this patient following the administration of ganciclovir underscores its efficacy and supports its use as the treatment of choice. (7)

This case highlights the importance of considering HHV-6 in the differential diagnosis of encephalitis, particularly when other etiologies have been excluded. The variability in clinical presentations associated with HHV-6 infections necessitates a high degree of clinical suspicion and awareness among healthcare providers.

Further research is warranted to optimize treatment protocols and enhance our understanding of the mechanisms by which HHV-6 induces neurological disease in adults. This could ultimately lead to improved diagnostic and therapeutic strategies for managing HHV-6-related encephalitis in immunocompetent patients.

Conclusions

This case report highlights the role of Human Herpesvirus 6 (HHV-6) as a potential cause of encephalitis in immunocompetent adults. The patient's severe neurological symptoms prompted thorough testing, leading to the identification of HHV-6 via the CSF Film Array Meningitis Panel. The successful transition from acyclovir to ganciclovir treatment underscores the importance of effective antiviral selection.

This case emphasizes the need for heightened awareness of HHV-6 in the differential diagnosis of encephalitis, particularly when other common pathogens are ruled out (8). Ongoing research is essential to refine treatment strategies and improve diagnostic methods, ultimately enhancing patient outcomes for HHV-6-related encephalitis.

Disclosures

Human subjects

Consent was obtained or waived by all participants in this study.

Conflicts of Interest

In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work.

Financial Relationships

All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

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