

Non-Bacterial Post-Traumatic Meningitis due to Human Herpesvirus-6 in an Immunocompetent Patient

by Jana Publication & Research

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Abstract

Background: Human herpesvirus 6 (HHV-6) is a ubiquitous β -herpesvirus with seroprevalence up to 90% in adults. While recognised in immunocompromised patients and children, symptomatic neuro-meningeal infection in immunocompetent adults is exceptional. Post-traumatic central nervous system (CNS) infections are usually bacterial, and viral meningitis in this setting is extremely rare.

Objectives: To describe a rare case of post-traumatic HHV-6 meningitis in an immunocompetent adult, and highlight diagnostic and therapeutic implications in a resource-limited setting.

Methods: We report the case of an 80-year-old man admitted to intensive care after severe traumatic brain injury with multiple skull base fractures and probable cerebrospinal fluid (CSF) leakage. Clinical course, imaging, CSF analysis, and management were reviewed.

Results: After initial neurological improvement, the patient developed fever and somnolence on day ten. Cerebral CT showed no new lesions. Lumbar puncture revealed haemorrhagic CSF with pleocytosis and hyperproteinorrachia. Multiplex PCR identified HHV-6 DNA exclusively in CSF, while bacterial cultures and other viral tests were negative. In the absence of ganciclovir or foscarnet, intravenous acyclovir was initiated, resulting in rapid clinical improvement and defervescence within 48 hours.

Conclusion: HHV-6 meningitis in an immunocompetent adult following traumatic brain injury is exceptionally rare. Clinicians should consider viral etiologies in secondary neurological deterioration. Early lumbar puncture, multiplex PCR, and pragmatic antiviral therapy may aid diagnosis and improve outcomes, even in resource-limited settings.

Keywords: Human herpesvirus 6, Post-traumatic meningitis, Viral meningoencephalitis, Critical care

Introduction

Human herpesvirus 6 (HHV-6) is a β -herpesvirus, highly prevalent in the general population, with adult seroprevalence approaching 90% [1]. Primary infection usually occurs in childhood as exanthema subitum and is followed by latency within various tissues, including the central nervous system (CNS) [2]. Under conditions of immunosuppression or physiological stress, viral reactivation may occur, occasionally causing severe neuro-meningeal disease [3].

Neurological manifestations of HHV-6 are most often encephalitis, particularly in immunocompromised hosts such as transplant recipients or patients with HIV infection [4]. Isolated meningitis is rare, especially in immunocompetent adults [5].

In the post-traumatic context, CNS infections are almost exclusively bacterial, favoured by skull base fractures and dural breaches [6]. Viral meningitis in this setting is exceptionally reported, and to our knowledge, HHV-6 has not been previously documented.

We report the case of an elderly immunocompetent patient who developed HHV-6 meningitis after severe traumatic brain injury. This case illustrates the importance of considering rare viral causes in post-traumatic neurological deterioration and highlights the diagnostic value of multiplex PCR.

Case Presentation

An 80-year-old man was admitted to our unit after severe cranial trauma. His medical history included type 2 diabetes managed with oral agents, without known immunosuppression. Lymphocyte count was normal.

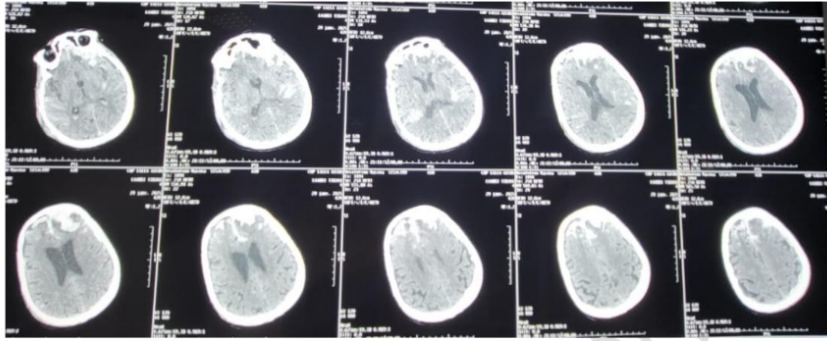
On admission, his Glasgow Coma Scale (GCS) was 12 (E3 V4 M5). Examination revealed a parieto-occipital scalp laceration and right-sided otorrhagia.

Initial cerebral and whole-body CT showed bilateral frontal contusions with subarachnoid haemorrhage, minimal bilateral subdural haematomas, and a right parietotemporal skull fracture extending into mastoid air cells and posterior tympanic wall. A right occipital fracture involving the sigmoid sinus was also noted with associated pneumocephalus. No intrathoracic, abdominal, or spinal injuries were seen (Figure 1).

Neurosurgical evaluation did not indicate urgent surgery. The patient was admitted to the ICU, where secondary brain injury prevention was implemented. Serial transcranial Doppler monitoring guided haemodynamic management. He gradually improved, with recovery of GCS to 15.

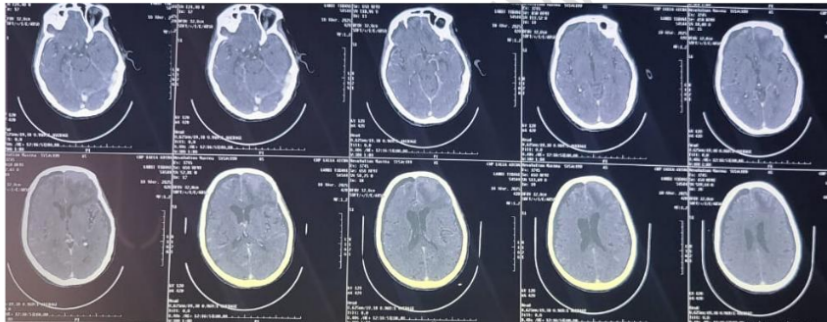
On day ten, he developed fever (39 °C) and somnolence. Control CT scanner demonstrated regression of contusions without new lesions (Figure 2). Lumbar puncture yielded haemorrhagic cerebrospinal fluid (CSF). Analysis showed 384,000 RBC/mm³, 560 WBC/mm³ (90% lymphocytes), protein 5.8 g/L, glucose 1.4 g/L (capillary glycaemia 2.19 g/L), and a cellularity index of 5. Multiplex PCR detected HHV-6 exclusively, while HSV-1/2, VZV, EBV, and enteroviruses were negative. Bacterial cultures were sterile (Figure 3).

Broad-spectrum antibiotics were initiated but discontinued after bacterial exclusion. Intravenous acyclovir was started empirically and maintained after PCR confirmation. The patient received a 21-day course, with favourable outcome. Fever resolved within 48 h, and neurological status improved progressively.



69

70 *Figure 1 : Initial cerebral CT showing bilateral contusions, subarachnoid haemorrhage and skull base*
 71 *fractures with pneumocephalus*



72

73 *Figure 2 : Follow-up cerebral CT scan showing regression of frontal contusions without evidence of*
 74 *expanding haematoma or newly developed lesions*

PCR MULTIPLEX MENINGITES / MENINGO-ENCEPHALITES

Nature de prélèvement

LCR

Détection du génome d'agents infectieux responsables de Méningites / Méningo-encéphalites

Escherichia coli K1	Recherche négative
Haemophilus influenzae	Recherche négative
Listeria monocytogenes	Recherche négative
Neisseria meningitidis	Recherche négative
Streptococcus agalactiae	Recherche négative
Streptococcus pneumoniae	Recherche négative
Cytomegalovirus (CMV)	Recherche négative
Enterovirus	Recherche négative
Herpes simplex virus 1 (HSV1)	Recherche négative
Herpes simplex virus 2 (HSV2)	Recherche négative
Human herpesvirus 6 (HHV6)	RECHERCHE POSITIVE
Paréchovirus humains (Human parechovirus)	Recherche négative
Virus varicelle-zona (VZV)	Recherche négative

Figure 3 : **Détection of HHV-6 DNA in CSF Multiplex PCR Results**

Discussion

HHV-6 is a highly prevalent virus, yet its clinical significance in adults remains debated. In immunocompetent patients, viral detection in CSF may represent asymptomatic reactivation or chromosomal integration, making interpretation challenging [7]. Distinguishing between incidental viral presence and true infection is particularly important in critical care, where multiple factors may contribute to neurological decline. In our case, the correlation between clinical deterioration, CSF pleocytosis, marked hyperproteinorrachia, and exclusive PCR positivity for HHV-6 strongly supports a causal role.

Secondary neurological deterioration after traumatic brain injury is a common and feared complication in ICU practice. The usual causes include expanding haematomas, cerebral oedema, ischaemia, post-traumatic seizures, metabolic disturbances such as hyponatraemia, or bacterial meningitis [9]. Viral aetiologies are rarely investigated in this context. This case illustrates that when structural and metabolic causes are excluded, viral meningitis should be considered, especially if CSF shows lymphocytic pleocytosis.

92 Previous reports of HHV-6 CNS disease in immunocompetent adults are scarce. Most describe
93 encephalitis rather than meningitis [4,5,13]. Clinical presentation is variable, ranging from mild
94 headache and fever to seizures, altered consciousness, and focal deficits. Our patient presented
95 with somnolence and fever, overlapping with bacterial meningitis or secondary traumatic
96 complications, which emphasises the importance of broad diagnostic consideration.

97 The post-traumatic context may have facilitated viral invasion through several mechanisms.
98 First, the skull base fractures extending into the mastoid and tympanic structures represented a
99 direct communication between ENT cavities and the subarachnoid space, traditionally associated
100 with bacterial meningitis [6,8]. It is plausible that this anatomical breach also provided an entry
101 route for latent or localised viral agents. Second, the systemic inflammatory and neuroendocrine
102 stress responses following severe trauma are known to impair immune function [9,10].
103 Herpesviruses, including HHV-6, are particularly prone to reactivation under such stress. Finally,
104 diabetes mellitus is recognised as a state of chronic functional immunosuppression, altering
105 lymphocyte and macrophage activity [11]. The convergence of these factors likely explains viral
106 reactivation in an otherwise immunocompetent elderly patient.

107 The diagnostic process in this case underscores ¹the importance of early lumbar puncture. In
108 many ICUs, LP is delayed or avoided in post-traumatic patients due to concerns about raised
109 intracranial pressure. However, our case demonstrates that when neurological deterioration is
110 unexplained by imaging, LP provides critical information. The haemorrhagic appearance of CSF
111 could initially suggest traumatic tap or residual haemorrhage, but the associated pleocytosis,
112 hyperproteinorrhachia, and normal glycorrachia were consistent with viral infection. Multiplex
113 PCR then provided definitive evidence of HHV-6.

114 Molecular diagnostic tools have transformed the evaluation of CNS infections. Multiplex PCR
115 allows simultaneous testing for common neurotropic viruses, improving speed and accuracy
116 [22]. However, most diagnostic protocols focus on bacterial pathogens, particularly in post-
117 traumatic meningitis. Our case supports expanding viral panels in selected patients, especially
118 when CSF findings are not typical of bacterial infection. The role of HHV-6 remains
119 controversial, as its detection may reflect reactivation without disease [7]. Nevertheless, in the
120 appropriate clinical context, PCR can provide crucial diagnostic guidance.

121 Therapeutic management of HHV-6 CNS infection remains challenging. Ganciclovir and
122 foscarnet are the recommended first-line antivirals [4,12]. Their absence in our setting highlights
123 disparities in access to essential treatments [15]. Despite limited activity against HHV-6,
124 acyclovir was administered empirically and maintained after virological confirmation. The
125 patient improved rapidly, with fever resolution within 48 hours. Although this cannot definitively
126 establish causality, it suggests either partial antiviral efficacy or spontaneous resolution aided by
127 supportive care. Similar outcomes have been reported in other case reports [13]. This raises an
128 important clinical question: should acyclovir be considered as a pragmatic option when
129 ganciclovir is unavailable? While not ideal, our experience suggests it may provide benefit and
130 should not be dismissed in resource-limited environments.

131 This case also raises broader implications for neurocritical care. First, clinicians should maintain
132 diagnostic vigilance when facing unexplained deterioration, especially in elderly patients with

comorbidities. Second, viral pathogens may be under-recognised contributors to post-traumatic CNS infections. Third, therapeutic decisions often need to be adapted to local realities, balancing scientific evidence with drug availability.

Finally, reporting such rare cases is essential to build cumulative knowledge. The literature currently contains very few reports of HHV-6 meningitis in immunocompetent adults, and none in a post-traumatic context [5,6,8]. By documenting and publishing these observations, clinicians contribute to refining diagnostic algorithms, guiding future research, and informing consensus recommendations.

Conclusion

This case exemplifies the exceptional occurrence of HHV-6 meningitis in an immunocompetent adult after traumatic brain injury. Clinicians should consider viral etiologies when facing unexplained post-traumatic neurological deterioration. Early CSF analysis and multiplex PCR are essential for diagnosis, and pragmatic antiviral therapy can achieve favourable outcomes even in resource-limited settings. Further case reporting will help clarify the spectrum and management of HHV-6 CNS infections in neurotrauma.

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