International Journal of Contemporary Pediatrics
Alkazak MA et al. Int J Contemp Pediatr. 2025 Aug;12(8):1461-1464
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20252175

Case Report

A rare case of neonatal viral meningitis caused by co-infection HHV6 and HPeV

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Received: 26 June 2025
Revised: 09 July 2025
Accepted: 10 July 2025

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ABSTRACT

Neonatal meningitis is considered a serious, life-threatening condition. Human parechovirus (HPeV) and herpesvirus 6 (HHV-6) are well-known neurotropic viruses with the ability to affect the central nervous system (CNS) of children, even in the neonatal period. However, isolated viral meningitis with single infections caused by both pathogens were previously reported, but co-infection in the neonatal period remains very uncommon. We are reporting a case of a 14-day-old term neonate admitted with history of low-grade fever for one day with no other significant symptoms. A full septic workup was conducted, including cerebrospinal fluid (CSF) analysis, and started on antibiotic therapy CSF analysis came with white blood cell count of 8 - (considering normal range for this age) - with a predominance of lymphocytes (95%), and normal levels of glucose and protein. Others inflammatory markers such as CRP and procalcitonin and all bacterial cultures (blood, urine and CSF) were reported also within normal limits. PCR testing of the CSF confirmed the presence of both Human Parechovirus (HPeV) and Human Herpesvirus 6 (HHV-6), leading to a diagnosis of dual viral meningitis. The neonate continued on conservative care with close monitoring. The patient gradually recovered and discharged home with no immediate neurological deficits. Despite an initial presentation, inflammatory markers were within normal, the case supported consideration multiple viral etiologies in the workup of neonatal meningitis and highlights the utility of multiplex PCR testing in the diagnosis of co-infections. Identification of such atypical presentations is crucial in early diagnosis, appropriate management, and counseling of the prognosis.

Keywords: Neonate, Co-infection, Viral meningitis, CSF, Multiplex PCR testing

INTRODUCTION

Central nervous system (CNS) infection in neonates and young infants, causing by viral meningitis is most commonly associated with enteroviruses, herpes simplex virus (HSV), and human herpesvirus 6 (HHV-6).[1] In recent years, human parechoviruses (HPeVs)-particularly HPeV type 3-surfaced as important neurotropic pathogens in neonates, with the ability to cause sepsis-like illness, meningitis, and encephalitis, often in the absence of significant inflammatory markers or cerebrospinal fluid (CSF) pleocytosis.[2,3] HHV-6 is a DNA virus that typically causes roseola infantum, but it has also been found in CNS infections, including meningitis and encephalitis, especially in young children and immunocompromised patients.[4,5] Congenital HHV-6 infection, either by transplacental transmission or chromosomally integrated HHV-6 (ciHHV-6), adds to the complexity of its diagnostic and clinical implications in neonates.[6,7]

The clinical presentations of HPeV and HHV-6 infections often overlap, with symptoms such as fever, with or without irritability, and seizures, making it difficult to distinguish between the two, using routine laboratory methods.[2,5] The use of multiplex polymerase chain reaction (PCR) assays (meningoencephalitis) has significantly improved the sensitivity and specificity of

viral detection in CSF, enabling clinicians to identify simultaneous infections that might otherwise be missed.[1,8]

While infections with either HPeV or HHV-6 alone are well documented, co-infection involving both viruses are exceedingly rare. Here, we present a unique case of neonatal viral meningitis due to dual infection with HPeV and HHV-6, highlighting the diagnostic utility of molecular testing and the importance of considering unusual co-infections in neonate presenting with fever as the dominant symptom.

CASE REPORT

We report a 14-days-old female neonate who brought in our pediatric emergency with complaints of two spike of fever, she presented in emergency room with temperature of 38.1℃. Parents deny any history of cough, breathing difficulty, vomiting or diarrhea. One family member was suffering from flu symptoms. Baby admitted in pediatric ward for further work up to ascertain the cause of fever.

There was no significant antenatal and birth history, maternal serologies negative, GBS status negative, baby born by normal vaginal delivery, birth weight: 2.8 kg, stayed with mother in post-natal ward for 48 hours and discharge home in good condition. Physical examination at admission time revealed febrile infant with mild irritability, vitals sign HR -180/min, RR- 52/ min, well perfused, capillary refilling time less than 2 seconds, good volume peripheral pulse, anterior fontanel at level, normal muscle tone, no abnormal eye movement, no rashes, clear chest, no heart murmur. Rest physical examination normal.

Laboratory work up

Initial work up was normal. White cells count 8400 /mm^3, platelets-458000/ mm3, hemoglobin-13 g/l, CRP -0 mg/l, Procalcitonin-0.33ug/l. Respiratory panel negative. Due to recurrent spike of fever and normal initial work up, a full septic workup done and lumber puncture performed. CSF analysis result shown normal glucose, normal protein, WBC in CSF 8 (95% lymphocytes). CSF PCR detected human par echovirus and HHV6 virus. Although the bacteriological examination of blood, urine and CSF were negative, Laboratory findings are summarized in Table 1.

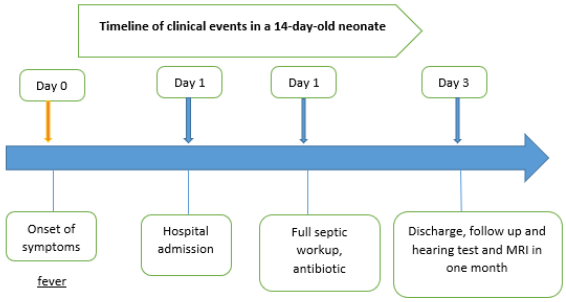

Figure 1: Timeline of clinical events for a 14-day-old neonate.

Case discussed with pediatric neurologist and pediatric infectious disease, no additional treatment advocated. Baby improved within 24 hours, fever subsided after 1 day of admission, and baby discharged home on 3rd day. MRI brain and Hearing test considered in follow up. The clinical timeline is summarized in Figure 1.

Table 1: Summary of laboratory findings in a 14-day-old neonate with fever.

Test	Result	Reference range
White blood cells	8,400 /mm^3	4,500-13,500 /mm^3
Platelets	458,000 /mm3	150,000-450,000 /mm^3
Haemoglobin	13 g/dl	13.5-17.5 g/dl (newborn)
C-reactive protein	0 mg/l	<5 mg/l
Procalcitonin	0.33 µg/l	<0.5 µg/l
CSF biochemistry	8 WBC cells/mm^3	0-15 cells/mm (newborn)
CSF MN	95%	N/A
CSF PMN	5%	N/A
CSF Glucose	Normal	4070 mg/dl
CSF Protein	Normal	15–45 mg/dl
CSF, urine, blood cultures at 72 hours	Negative	Negative
CSF PCR	Parechovirus and HHV6 positive	N/A
Respiratory panel	Negative	negative
Chest x-ray	Normal / clear	Normal / clear

DISCUSSION

Neonatal meningitis as a result of human parechovirus (HPeV) or human herpesvirus 6 (HHV-6) is rare and under-appreciated pathology. Both viruses can involve the central nervous system in young infants, but we believe this to be the first reported of co-infection in neonates, as it is exceedingly uncommon. HPeV, a member of the Enterovirus genus, has emerged as an important cause of sepsis-like illness in neonates,

particularly type 3. It typically presents with high fever and irritability, often without localized symptoms, which makes it clinically similar to bacterial sepsis in early infancy.[9,10] One of the challenges in diagnosing HPeV meningitis is that routine investigations may appear relatively normal. CSF often shows no pleocytosis, and protein and glucose levels remain within normal ranges, which can delay diagnosis or lead to misdiagnosis.[11,12] Have clear diagnosis very important because according to others reviews on the outcomes after parechovirus infection suggested that neonates and young children (<3 months old) with parechovirus infection of the CNS might have normal short-term outcomes, but develop long-term neurological sequelae and neurodevelopmental delay.[13]

Similarly, HHV-6 is a common virus in early childhood, best known for causing roseola, but it can also involve the CNS, leading to meningitis or encephalitis. In neonates, HHV-6 can be transmitted congenitally-either trans placentally or through chromosomal integration (ciHHV-6)-or as acquired postnatal infection. This makes interpretation of HHV-6 PCR results challenging, as chromosomal integration may result in persistently high viral DNA levels in the blood or CSF without active infection.[14,15] Nevertheless, HHV-6 should not be overlooked as a potential neuroinvasive pathogen in neonates, especially since its presentation can also occur without significant inflammation or CSF abnormalities.[16]

In this case, the neonate was presented with only a low-grade fever and no other significant symptoms. Despite normal inflammatory markers and CSF findings, multiplex PCR testing (meningoencephalitis panel) revealed dual infection with HPeV and HHV-6. This emphasizes the importance of using broad molecular diagnostic panels when evaluating neonates with unexplained fever, even in the absence of laboratory evidence of CNS infection. Identifying such viral infections early can help avoid unnecessary antibiotic treatment and prolonged hospitalization, aid in family counseling and also follow up any future neurological abnormality. Although the infant in this case recovered well without complications, both HPeV and HHV-6 are neurotropic viruses and therefore long-term develop-mental follow-up is advisable. This case serves as a reminder that clinicians should consider multiple viral etiologies in neonates with fever and that molecular tools are invaluable in uncovering atypical or co-infections that might otherwise be missed

CONCLUSION

The case supports that serious infections -including viral meningitis- can occur even with usually harmless symptoms like a low-grade fever in a well-appearing newborn. Human parechovirus and HHV-6 can both involve the central nervous system in infants, sometimes with minimal signs of infection and no significant laboratory anomalies. This is why it is incredibly valuable to have fast-acting advanced diagnostic tools like meningoencephalitis panel. In this case, we uncovered a rare co-infection acute meningitis and we were able to treat the baby with supportive care alone therefore avoiding unnecessary treatment and over treatment with long-term prophylactic antibiotics. As paediatricians, we should keep viral infections - including meningitis-in our mind specially when assessing neonate who presenting with febrile illness, even when their initial assessment and laboratory results look normal. Early diagnosis can offer appropriate care of the patient, reassuring to families, and provide prompt follow-up if necessary to monitor for any long-term sequences.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Alkazak MM, Alkaysi SN. A rare case of neonatal viral meningitis caused by co-infection HHV6 and HPeV. Int J Contemp Pediatr 2025;12:1461-4.