



Case Report

Rotavirus meningitis in an adult with transient aphasia

Nived Collercandy^{1,2}, Marion Miguères^{2,3}, Benjamin Hallak¹, Camille Garnier¹,
Stella Rousset¹, Adrien Delourme⁴, Pierre Delobel^{1,2}, Guillaume Martin-Blondel^{1,2,*}

¹CHU de Toulouse, Service des Maladies Infectieuses et Tropicales, Toulouse, France

²Institut Toulousain des Maladies Infectieuses et Inflammatoires (Infinity) INSERM UMR1291 - CNRS UMR5051 - Université Toulouse III, Toulouse, France

³CHU de Toulouse, Laboratoire de Virologie, Toulouse, France

⁴CHU de Toulouse, Service de Neurologie, Toulouse, France



ARTICLE INFO

Article history:

Received 20 May 2022

Revised 26 June 2022

Accepted 2 July 2022

Keywords:

Rotavirus

Viral meningitis

Central nervous system infection

HaNDL syndrome

ABSTRACT

We identified an additional case of documented Rotavirus meningitis in an adult with full medical history. A previously healthy 37-year-old patient presented herself for transient aphasia associated with fever and headaches at the end of a one-week history of gastroenteritis. Cerebrospinal fluid (CSF) analysis revealed lymphocytic meningitis, and treatment with aciclovir was initiated. Rotavirus A reverse transcription-polymerase chain reaction (RT-PCR) was positive in CSF and the patient's stools in favor of Rotavirus meningitis. Testing for other viruses was negative. Magnetic resonance imaging (MRI) showed no signs of encephalitis. Aphasia was resolutive in less than 12 hours, and no neurological symptoms relapsed. All symptoms evolved favorably despite aciclovir discontinuation.

Viral sequencing methods have recently identified unexpected viruses as potential causative agents in meningitis, including Rotavirus. We confirm the detectability of Rotavirus in the analysis of CSF in the context of Rotavirus gastroenteritis in an adult. This case suggests postviral headache and neurological deficits with cerebrospinal fluid lymphocytosis (HaNDL) syndrome may be linked to previously undetected direct viral infection of the central nervous system.

Therefore, clinicians should consider Rotavirus meningitis in diagnosing meningitis associated with gastroenteritis in adults.

© 2022 Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Case Report

Etiological diagnosis of meningitis may be challenging. The absence of microbial identification can lead to unnecessary probabilistic treatment. McGill et al., 2022 have recently shown that clinically relevant and unexpected viruses could be detected in the CSF using viral capture sequencing in cerebrospinal fluid (CSF) from 73 adults with suspected viral meningitis. They notably identified Rotavirus A as a potential causative agent in two adults, which had never been described in adults before.

In February 2022, we were directed to the case of a 37-year-old female patient who presented to our hospital for acute aphasia. She only had a medical history of visual migraine aura. She reported acute gastroenteritis starting seven days before admission, with abundant watery diarrhea and nonbilious vomiting for

five days. Her household, including her husband and two children, displayed the same symptoms for a shorter period. She also reported headaches, daily fever with a temperature of 39°C, moderate shivers, and sweating. At hospital admission, she presented severe speech aphasia with paraphasia and jargon aphasia, associated with persistent headaches and neck stiffness. Blood analysis found a C-reactive protein level of 7.2 mg/l, a blood cell count in a normal range, and an alanine aminotransferase level of twice the normal. CSF analysis revealed pleocytosis of 40 white cells/μL with 98% lymphocytes, an elevated protein level (1.04 g/l), and a CSF/serum glucose ratio of >0.6. Intravenous aciclovir at 10 mg/kg three times per day was started under the suspicion of acute herpetic encephalitis. Electroencephalography revealed frontal intermittent rhythmic delta activity, which was aspecific and may not be pathological. Brain MRI did not show any signs of herpetic encephalitis and only revealed bilateral posterior occipito-parietal sulcus hypersignals in contrast-enhanced FLAIR (FLuid Attenuated Inversion Recovery) sequence, which were nonsignificant. Herpes simplex virus-1 (HSV-1), HSV-2, varicella-zona virus, enterovirus, and hepatitis E virus were undetected by polymerase chain reaction

* Corresponding author at: Guillaume Martin-Blondel, CHU de Toulouse, Service des Maladies Infectieuses et Tropicales, 31000 Toulouse, France

E-mail address: martin-blondel.g@chu-toulouse.fr (G. Martin-Blondel).

(PCR) in CSF. Serologies for Epstein-Barr virus and cytomegalovirus showed no evidence of acute infection, and serologies showed no sign of HIV or syphilis infection. Speech fully recovered in 12 hours after symptoms onset. A second lumbar puncture was performed on day three of admission, showing a normalized level of proteins and a white cell count of 78/ μ L (100% lymphocytes). Aciclovir was discontinued as HSV remained undetectable by PCR in CSF. A multiplex reverse transcription (RT)-PCR was performed on both CSF samples and the stool to detect enteric viruses (Amplidiag® Viral GE, Mobidiag). Both the first sample of CSF and stool were positive for Rotavirus A, within 40 cycle threshold (Ct) in CSF, which was confirmed with a second test on a different tube of the same CSF in favor of Rotavirus meningitis. Rotavirus was undetected in the second CSF. The patient was discharged on day six after admission, with a favorable outcome and the absence of neurological symptoms relapse.

We hereby report the third case to our knowledge of documented Rotavirus meningitis in an adult. The full clinical story supports the suggestion of Rotavirus as a previously undiagnosed etiological agent. Rotavirus neurological disease has previously only been reported in children in which it could cause encephalitis or meningitis in the context of Rotavirus gastroenteritis (Dickey et al., 2009; Wong et al., 1984). The high Ct value for Rotavirus detection in our case suggests the virus is difficult to detect in CSF in case of meningitis and could have been missed in meningitis cases associated with Rotavirus gastroenteritis. The pathophysiological mechanisms enabling the presence of viral RNA in patients' CSF have yet to be determined. Its clinical presentation, however, supports a potential pathogeny of Rotavirus in the central nervous system (CNS). Rotavirus viremia has notably been reported in immunocompetent children, and a blood-brain barrier crossing is thus possible (Chiappini et al., 2005). Although contamination may have led to the positive PCR result, we ruled out contamination of the sample by repeating all the processes on a different CSF tube. Each PCR run included a negative control to detect contamination. The CSF was tested separately from the stool sample. The only possibility for a contaminated PCR would be at the time of CSF collection, which is not likely.

Our patient's aphasia was initially imputed to a syndrome of transient headache and neurological deficits with CSF lymphocytosis (HaNDL) (Gómez-Aranda et al., 1997; Guillan et al., 2016). The hypothesis of an aura with the atypical presentation was rejected because of the absence of those symptoms' occurrence in the past and their duration. Concordantly, aphasia was spontaneously resolute, and the absence of MRI anomalies did not seem in favor of direct viral encephalitis. However, the HaNDL definition excludes cases with etiological findings. Therefore, although it may be possible that our patient presented mild Rotavirus encephalitis in addition to meningitis, this cannot be asserted with certainty.

Interestingly, HaNDL is often described as a postviral syndrome, and we have shown that Rotavirus detection in CSF is difficult. We

hypothesize that at least a similar mechanism may be implied, and it may be possible that viral infection has been undetected in the CSF of patients with HaNDL. The development of metagenomic in CSF is likely to provide new insights into microbial involvement in previously undiagnosed CNS inflammatory processes (Ramachandran and Wilson, 2020; Wilson et al., 2019).

Our case confirms the possibility of Rotavirus A involvement in undocumented adult meningitis suggested by McGill et al., especially in the context of concomitant gastroenteritis. In addition, new sequencing techniques could help identify new pathogens in previously considered aseptic CSF.

Conflicts of interest

The authors have no competing interests to declare.

Funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval statement

Ethical approval was not required.

Author contributions

Original draft preparation: NC, MM, GMB; Review and Editing: all authors

References

- Chiappini E, Azzari C, Moriando M, Galli L, de Martino M. Viraemia is a common finding in immunocompetent children with rotavirus infection. *J Med Virol* 2005;76:265–7.
- Dickey M, Jamison L, Michaud L, Care M, Bernstein DI, Staat MA. Rotavirus meningoencephalitis in a previously healthy child and a review of the literature. *Pediatr Infect Dis J* 2009;28:318–21.
- Gómez-Aranda F, Cañadillas F, Martí-Massó JF, Díez-Tejedor E, Serrano PJ, Leira R, et al. Pseudomigraine with temporary neurological symptoms and lymphocytic pleocytosis. A report of 50 cases. *Brain* 1997;120:1105–13.
- Guillan M, DeFelipe-Mimbrera A, Alonso-Canovas A, Matute MC, Vera R, Cruz-Culebras A, et al. The syndrome of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis mimicking an acute stroke. *Eur J Neurol* 2016;23:1235–40.
- McGill F, Tokarz R, Thomson EC, Filipe A, Sameroff S, Jain K, et al. Viral capture sequencing detects unexpected viruses in the cerebrospinal fluid of adults with meningitis. *J Infect* 2022;84:499–510.
- Ramachandran PS, Wilson MR. Metagenomics for neurological infections – expanding our imagination. *Nat Rev Neurol* 2020;16:547–56.
- Wilson MR, Sample HA, Zorn KC, Arevalo S, Yu G, Neuhaus J, et al. Clinical metagenomic sequencing for diagnosis of meningitis and encephalitis. *N Engl J Med* 2019;380:2327–40.
- Wong CJ, Price Z, Bruckner DA. Aseptic meningitis in an infant with rotavirus gastroenteritis. *Pediatr Infect Dis* 1984;3:244–6.