Journal of Clinical Virology 78 (2016) 66–70

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Case report

Acute encephalopathy in an immunocompromised boy with astrovirus-MLB1 infection detected by next generation sequencing

Masanori Sato[a,*], Makoto Kuroda[b], Masashi Kasai[a], Hikoro Matsui[a], Tetsuhiro Fukuyama[c], Harutaka Katano[d], Keiko Tanaka-Taya[e]

[a] Department of Pediatric Intensive Care, Nagano Children's Hospital, 3100 Toyoshina, Azumino City, Nagano 399-8288, Japan
[b] Pathogen Genomics Center, National Institute of Infectious Diseases, 1-23-1 Toyama, Shinjuku-ku, Tokyo 162-8640, Japan
[c] Division of Pediatric Neurology, Nagano Children's Hospital, 3100 Toyoshina, Azumino City, Nagano 399-8288, Japan
[d] Department of Pathology, National Institute of Infectious Diseases, 1-23-1 Toyama, Shinjuku-ku, Tokyo 162-8640, Japan
[e] Infectious Disease Surveillance Center, National Institute of Infectious Diseases, 1-23-1 Toyama, Shinjuku-ku, Tokyo 162-8640, Japan

ARTICLE INFO

Article history:
Received 3 January 2016
Received in revised form 3 March 2016
Accepted 7 March 2016

Keywords:
Astrovirus MLB1
Encephalopathy
Next generation sequencing
Immunodeficiency

ABSTRACT

We report a case of an immunodeficient 4-year-old boy with acute encephalopathy possibly related to human astrovirus-MLB1 infection. The astrovirus-MLB1 genome was identified in his stool, serum, cerebrospinal fluid, urine, and throat swabs by next generation sequencing. We present additional evidence showing human astroviruses are important infectious agents, regardless of their clades, involving the central nervous system in immunocompromised hosts.

1. Why this case is important?

Astroviruses (AstVs) are small, non-enveloped, single-stranded RNA viruses and are described in humans and many types of other mammalian animals. Species belonging to the family *Astroviridae* are finely classified, and human AstVs (HAstVs) are known to cause gastroenteritis in infected individuals. In addition to the eight classical HAstV genotypes (HAstV-1 to HAstV-8), new HAstV strains have been reported [1,2]. Now there are at least three major clades of AstVs affecting humans, which include classic, MLB- and VA-clades. Past surveys on classic HAstVs in children show that HAstV-1 is the most common serotype [3,4], and antibodies to HAstV-1 are found in >90% of the human population [5]. However, much of the pathogenic role of MLB- and VA-clades in humans still remains unclear. To date, many enteric infections caused by HAstV are reported mainly in children and immunocompromised hosts. Although there are a few reports of extra-intestinal localization of HAstVs, the pathogen has recently been identified as a potential causative agent of central nervous system infections in immunocompromised patients [6–10]. Here, we report the case of encephalopathy potentially caused by the HAstV-MLB clade.

2. Case description

A 4-year-old Japanese boy, diagnosed with congenital aplastic anemia at birth, presented with recurrent right-sided clonic convulsions. He underwent cord blood cell transplantation at the age of 20 months. The graft was mismatched at two human leukocyte antigen alleles (B and DR). After the transplantation, chronic pulmonary graft-versus-host disease was diagnosed, and he was administered some immunosuppressants.

Following recurrent right-sided clonic convulsions on the morning after 2 days of fever and recurrent diarrhea at home, he was ambulanced to a nearby hospital. His convulsion persisted, and he received intravenous midazolam and fosphenytoin. He was given an intravenous bolus of glucose because his blood sugar concentration was below detectable levels. Despite the administration of these drugs, his convulsions continued episodically in clusters. The patient was persistently drowsy and was transferred to Nagano Children's Hospital (NCH) for further intensive care. At that time, he was being given mycophenolate mofetil at 50 mg/kg/day as an immunosuppressive agent.

Abbreviations: AstV, astrovirus; HAstV, human astrovirus; PICU, pediatric intensive care unit; GCS, Glasgow Coma Scale; CSF, cerebrospinal fluid; MRI, magnetic resonance imaging; PCR, polymerase chain reaction; HBoV, human bocavirus.

* Corresponding author.
E-mail address: watasihasatoanataha@yahoo.co.jp (M. Sato).

http://dx.doi.org/10.1016/j.jcv.2016.03.010
1386-6532/

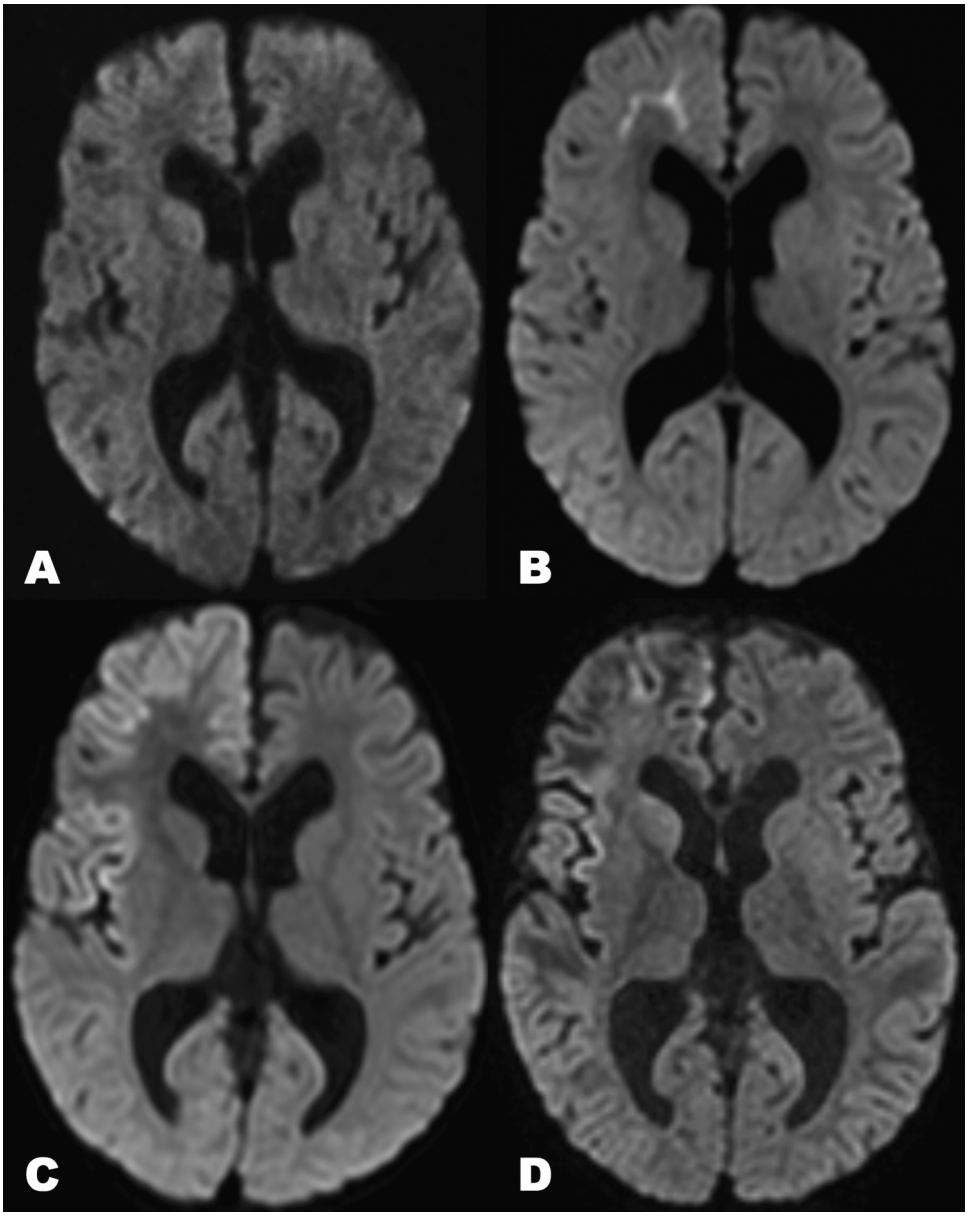

Fig. 1. Magnetic resonance imaging (MRI) finding of the patient. Compared with 1-year old images (A), diffusion-weighted MRI showed a new high-intensity lesion at the right frontal white matter on his admission (B). The MRI findings worsened on the third hospital day (C), however, improved on the 14th hospital day (D).

Upon admission in the pediatric intensive care unit (PICU) of NCH, his convulsions had already subsided. He had a fever but was well perfused. His Glasgow Coma Scale (GCS) was E1V2M4, which means no eye opening, moaning but no words, and withdrawing to pain. Laboratory data were as follows: leukocytes, 12.9×10^9/L; C-reactive protein, 9.0 mg/L; and blood sugar, 14.6 mmol/L. Although liver deviation enzymes were slightly elevated (AST, 119 U/L; ALT, 70 U/L), other values were almost normal including values of serum electrolytes. Blood gas analysis showed mild metabolic acidosis. Rapid antigen tests for rotavirus and adenovirus of stool were negative. In addition, cerebrospinal fluid (CSF) analysis showed no abnormalities.

Although a computed tomography scan without contrast showed no abnormalities, his diffusion-weighted magnetic resonance imaging (MRI) on admission showed a new high-intensity lesion at the right frontal white matter, when compared with one year-old images, which was diagnosed as encephalopathy. An electroencephalogram showed right-sided slowing without paroxysmal discharges. A 3-day course of hypothermia therapy was then initiated. He was treated with acyclovir, cyclosporine, immune globulin, and edaravone. Acyclovir was discontinued on his second hospital day after polymerase chain reaction (PCR) results showed CSF to be negative for human herpes simplex virus. Bacterial cultures of blood, CSF, and urine were negative. Although MRI findings worsened on his third hospital day, his gastrointestinal symptoms were almost resolved and the electroencephalogram showed gradual normalization. On his fifth hospital day, he was extubated. After extubation, the patient continued to show decreased mental status for a few days, but his level of consciousness gradually improved. He left PICU on his ninth hospital day, with the MRI findings markedly improved on his 14th hospital day (Fig. 1). He was discharged on hospital day 19, being almost fully recovered.

To elucidate the pathogen causing his neurologic symptoms, the clinical samples of his serum, CSF, stool, urine and throat swab were analyzed. DNA and RNA were extracted from the samples using QIAamp MinElute Virus Spin Kit (Qiagen; Valencia, CA, USA). These