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Case Report

Excitotoxicity in encephalopathy associated with STEC O-157 infection

Shigenobu Ishida [a], Kumi Yasukawa [a], Mai Koizumi [a], Katsuhiro Abe [a], Nozomi Hirai [a], Takafumi Honda [a], Hiroshi Sakuma [b], Hiroko Tada [b], Jun-ichi Takanashi [a,*]

[a] Department of Pediatrics, Tokyo Women's Medical University Yachiyo Medical Center, Yachiyo, Japan
[b] Department of Brain Development and Neural Regeneration, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

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Abstract

Cytokines play an important role in the pathogenesis of the severe complications of Shiga toxin-producing *Escherichia coli* (STEC) infection, such as hemolytic uremic syndrome (HUS) and acute encephalopathy. A 3-year-old boy with acute encephalopathy associated with STEC O-157 HUS showed increased levels of IL-6 and IL-10, which normalized after methylprednisolone pulse therapy, and additionally exhibited a transient increase of glutamine on MR spectroscopy. This finding suggests that excitotoxicity, in addition to hypercytokinemia, may play an important role in the pathogenesis of HUS encephalopathy.

Keywords: Acute encephalopathy; *Escherichia coli*; Hemolytic uremic syndrome; MR spectroscopy; Excitotoxicity

1. Introduction

Diarrhea-associated hemolytic uremic syndrome (HUS) is a complication in 6–9% of patients with Shiga toxin (Stx)-producing *Escherichia coli* (STEC) infection. Also, CNS involvement is observed in about 10% of patients with HUS. Renal lesions in HUS are characterized by thrombotic microangiopathy, however, the pathogenesis of the CNS lesions has been reported to be mainly due to a cytokine storm [1,2]. We firstly report a patient with HUS encephalopathy in whom MR spectroscopy revealed a transient increase of glutamine (Gln) in the subacute stage, suggesting excitotoxicity is an additional pathomechanism.

2. Case report

A 3-year-old boy ate meat with his family on day 1, and presented with diarrhea and abdominal pain on day 3. On day 4, fosfomycin was prescribed with a probable diagnosis of bacterial enterocolitis by his family doctor after examining a stool culture. He was admitted to our hospital due to prolonged abdominal pain and watery bloody diarrhea on day 5. On admission, he had severe abdominal pain and a fresh bloody stool, but he was completely alert and his vital signs were almost normal, except his blood pressure was high (128/94 mmHg). The results of blood and urine analysis were almost normal, except for a stool culture revealing STEC O-157. On day 9, a diagnosis of HUS was made based on the following laboratory data: hemoglobin 8.3 g/dl with evidence of erythrocyte destruction, platelet count 1.8×10^4/μl, and creatinine 0.93 mg/dl. On

* Corresponding author at: Department of Pediatrics, Tokyo Women's Medical University Yachiyo Medical Center, 477-96 Owadashinden, Yachiyo-shi 276-8524, Japan.
E-mail address: jtaka@twmu.ac.jp (J.-i. Takanashi).

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day 9, he also became lethargic with a Glasgow Coma Scale score of 4, and presented tonic seizures lasting about five minutes, which were stopped by administration of midazolam. Brain CT showed symmetric low density lesions in the bilateral putamen and ventrolateral thalamus, and EEG showed high-amplitude slow waves, leading to a diagnosis of acute encephalopathy associated with O-157 HUS. He was treated by continuous hemodiafiltration, and methylprednisolone (mPSL) pulse therapy on days 9–11. His consciousness level gradually improved and EEG normalized after these therapies. On days 15 and 16, he presented with tonic seizures again. MRI on day 16 showed T1 and T2 high signal lesions in the bilateral putamen suggesting hemorrhagic components, T2 high signal lesions with increased diffusion in the internal and external capsules suggesting vasogenic edema, and T2 high signal lesions with reduced diffusion in the ventral thalamus suggesting cytotoxic edema. DWI also showed high signal lesions in the cerebral white matter suggesting lacunar infarctions (Fig. 1). The second mPSL pulse therapy was performed on days 16–18. The patient was discharged on day 137, moderate neurological sequelae remaining; he can walk with assistance, but presents moderate intellectual disability and spastic quadriplegia.

3. MR spectroscopy

MR spectroscopy (PRESS, TR/TE = 5000 ms/30 ms) of the left white matter was performed on days 16 and 54, and quantitatively analyzed with LCModel (Fig. 2) [3]. MR spectroscopy on day 16 revealed decreased N-acetyl acetate (NAA) with increased Gln and lactate (Lac). Follow-up MR spectroscopy on day 54 showed decrease of NAA and glutamate (Glu) with normal Gln.

4. Cytokines

Interleukin (IL)-6 and 10 in serum were measured on days 8 (before encephalopathy), 9 (onset of encephalopathy), 11 (just after first mPSL pulse therapy), 15 (day of second seizures), 19 (after second mPSL pulse therapy), and 55 (stable period) (Fig. 3). IL-6 and 10 were significantly elevated on day 9, but decreased to almost within the normal ranges after the first mPSL pulse therapy.

5. Discussion

The most important finding for this patient is that MR spectroscopy revealed a transient increase of Gln, suggesting excitotoxicity, as well as hypercytokinemia,

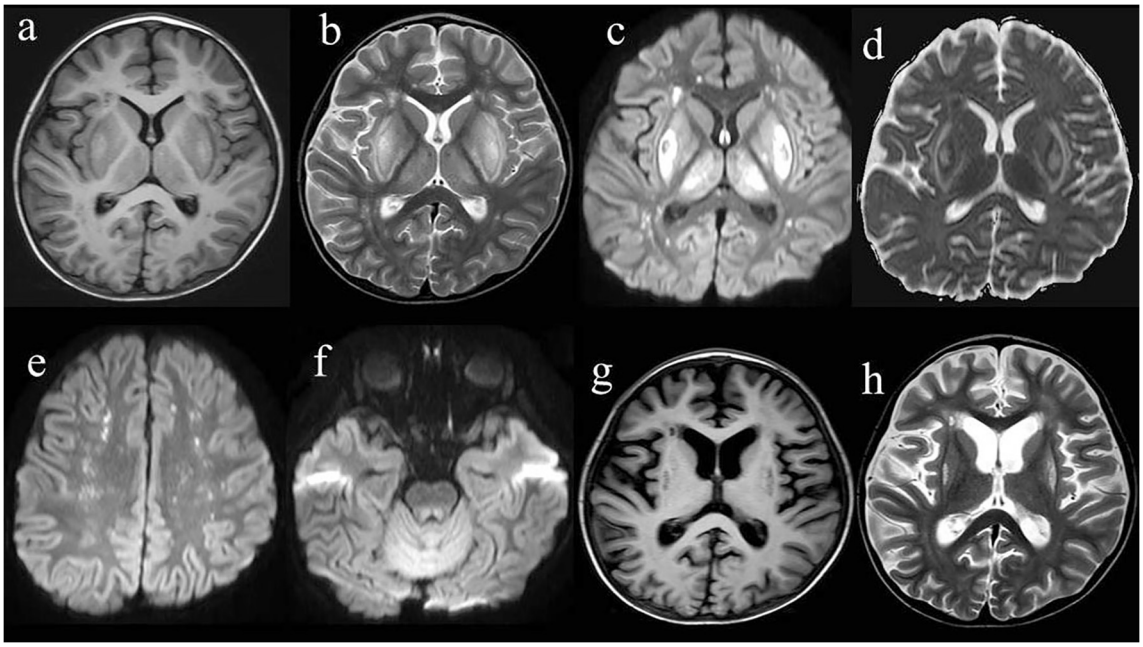

Fig. 1. MRI on day 16 (a-f), and day 54 (g and h). T1- weighted image (a) showed T1 high signal lesions in the bilateral putamen, and low signal lesions in the internal and external capsules. T2-weighted image (b) showed T2 high signal lesions in the bilateral putamen, internal and external capsules, and dorsolateral thalamus. DWI showed high signal lesions in the bilateral putamen, thalamus and dorsal pons, and multiple spotty lesions in the cerebral white matter (c, e and f). ADC showed increased diffusion in the bilateral putamen, and internal and external capsules (d). On day 54, T1 (g) and T2 (h)-weighted images showed low and high signal lesions in the bilateral putamen, respectively.

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