

This is an Open Access article licensed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 License (www.karger.com/OA-license), applicable to the online version of the article only. Distribution for non-commercial purposes only.

Posterior Reversible Encephalopathy Syndrome during Recovery from Acute Kidney Injury after Hepatitis A Infection

Soo Min Kim Heejung Choi Yoonjung Kim Junam Shin
Hye Ryoung Jang Jung Eun Lee Wooseong Huh
Dae Joong Kim Ha Young Oh Yoon-Goo Kim

Division of Nephrology, Department of Medicine, Samsung Medical Center,
Sungkyunkwan University School of Medicine, Seoul, Korea

Key Words

Posterior reversible encephalopathy syndrome · Acute kidney injury · Hepatitis A

Abstract

The patient was a 25-year-old healthy male who experienced fever, chills, and abdominal pain for 5 days prior to the hospital visit. He was diagnosed with acute hepatitis A, and at admission he presented with anuric acute kidney injury and hepatic encephalopathy. He received continuous renal replacement therapy followed by intermittent regular hemodialysis. His urine output increased to 1,610 ml/day after 31 days. On day 32, he suddenly developed a headache and visual disturbance and experienced three short convulsions, which were followed by postictal confusion and high fever. T₂ and FLAIR MRI images of the brain revealed hyperintense signal alterations in bilateral subcortical regions of the temporoparietal and occipital lobes, consistent with posterior reversible encephalopathy syndrome. His mental status was fully recovered after 7 h of conservative treatment, including antihypertensive therapy. On hospital day 56, the renal function of the patient had recovered, and he was discharged without neurologic sequelae.

Introduction

Posterior reversible encephalopathy syndrome (PRES) is characterized by visual disturbances, seizures, headache, confusion, and loss of consciousness [1]. Although the pathogenesis of PRES remains unclear, autoregulatory failure and endothelial

dysfunction have been suggested as possible mechanisms [2]. Many medical conditions, including acute nephritis and nephrotic syndrome, have been associated with PRES [1, 3]. However, PRES has rarely been reported in patients with acute kidney injury after viral hepatitis.

There is an increase in the incidence of hepatitis A infection among the adult population of Korea. In patients with hepatitis A, a variety of extrahepatic manifestations such as hemolytic anemia, arthritis, acute pancreatitis, acalculous cholecystitis, mononeuritis, and Guillain-Barré syndrome have been observed [4]. Acute kidney injury with or without fulminant hepatitis A is also common [4, 5].

Here, we report a case of PRES during the recovery phase of acute kidney injury after fulminant hepatitis A infection.

Case Report

A 25-year-old male presented at the emergency room of our hospital. He had experienced fever, chills, and abdominal pain for 5 days prior to the hospital visit and was diagnosed with acute hepatitis A. He had no history of hepatic or renal disease but was anuric at the time of admission.

His blood pressure was 115/65 mm Hg, his pulse rate 85 beats per minute, and his body temperature 37.3°C. Initial physical examination showed icteric sclera and a dehydrated tongue. Peripheral edema and crackle were absent. Blood chemistry revealed BUN 37.3 mg/dl; creatinine 5.19 mg/dl; albumin 3.7 mg/dl; AST 19,964 U/l; ALT 6,434 U/l; ALP 164 U/l; total bilirubin 7.5 mg/dl; direct bilirubin 4.9 mg/dl; PT 3.5 (INR); glucose 82 mg/dl; white blood cell count 7,520/μl; hemoglobin 13.3 g/dl, and C-reactive protein 6.42 mg/dl. The patient was positive for hepatitis A IgM antibodies. The serum levels of C3 and C4 were 45.5 and 15.5 mg/dl, respectively. Urinalysis showed many red blood cells and a 3+ index for albumin. Chest radiography excluded pulmonary edema.

After 3 days, the patient developed disorientation and confusion. His total bilirubin was 15.9 mg/dl, his ammonia level 149 μmol/l, and his body temperature reached 39°C. There were no microorganisms in a blood culture and no neck stiffness was observed. Brain CT and EEG were performed to exclude brain lesions. No brain edema or hemorrhage was evident on the CT image, and the EEG showed changes reflecting diffuse cerebral dysfunction but no specific epileptic waves. Therefore, the patient was diagnosed with grade 2 hepatic encephalopathy.

On hospital day 8, the patient's hemoglobin level had decreased to 8.5 g/l, his haptoglobin level was 4.2 mg/dl, his reticulocyte count had increased to 9.7%, his LDH level was 955 IU/l, and he tested positive for direct Coomb's IgG. This suggested hemolytic anemia; however, his glucose-6-phosphate dehydrogenase activity was normal. In addition, bilateral proximal intermuscular thigh hematomas, pseudoaneurysms in both radial arteries, and a bleeding gastric ulcer were detected.

The patient's liver function, confusion status, and anemia gradually improved. As his renal function had not returned to normal by day 20, he underwent intermittent hemodialysis. His urine output had increased to 1,610 ml/day by hospital day 31. His blood pressure was controlled using a calcium channel blocker. On hospital day 32, he suddenly developed headache and visual disturbance and experienced three generalized tonic-clonic convulsions followed by postictal confusion and high fever. At that time, his blood pressure was 180/90 mm Hg, whereas his blood pressure had previously been stable (120–140/50–80 mm Hg). Therefore, spinal tapping was performed immediately.

The opening pressure was 25 cm H₂O, and cerebrospinal fluid analysis showed white blood cells 0/HPF; red blood cells 0/HPF; protein 22.7 mg/dl, and glucose 49 mg/dl (serum glucose level 108 mg/dl). T₂ and FLAIR MRI images of the brain revealed hyperintense signal alterations in bilateral subcortical regions of the temporoparietal and occipital lobes that were consistent with PRES. His mental status was fully recovered after 7 h of conservative treatment with continuous renal replacement therapy and intravenous infusion of an antihypertensive drug. The headache, visual disturbance, and fever gradually improved. Continuous renal replacement therapy was stopped after

12 h because urine volume increased to more than 150 ml/h, and the azotemia improved. Hemodialysis was not required thereafter. MRI conducted 14 days after the convulsions revealed that the previous abnormal findings had resolved completely ([fig. 1](#)).

The patient was discharged on hospital day 56 and experienced no liver dysfunction or neurologic sequelae. The patient's renal function recovered to 68.7 ml/min/1.73 m² of eGFR after discharge.

Discussion

The precise pathogenic mechanism responsible for PRES has not been elucidated completely. The most commonly suggested pathophysiological explanation is that severe hypertension that exceeds the limits of autoregulation may promote brain hyperperfusion, breakdown of the blood-brain barrier, and fluid extravasation into the intercellular space [1]. Even though the patient's mean blood pressure was well controlled by antihypertensive medication, his blood pressure and intravascular volume fluctuated between intermittent bouts of hemodialysis because of long-standing severe oliguric acute kidney injury. This may have disrupted autoregulation of the brain.

However, PRES also develops in normotensive patients and in patients with mild blood pressure elevation [2, 3, 6]. This has been mentioned in many reports, including those concerning patients with eclampsia, cyclosporine toxicity, and sepsis [6]. As a secondary theory, some researchers have focused on the immune response and direct endothelial dysfunction in patients with PRES. Endotoxins cause diffuse endothelial activation, which induces the release of thromboxane A₂ and endothelin, resulting in systemic vasoconstriction, labile blood pressure, microembolism, hemolysis, systemic toxicity, and tissue hypoperfusion. Hypoxia stimulates angiogenesis and increases endothelial permeability [2, 7], which may alter adhesion between endothelial cell tight junctions. These changes in the blood-brain barrier could explain the presence of vasogenic edema in PRES.

Acute hepatitis A is clinically characterized by high fever at the onset and is often accompanied by extrahepatic manifestations such as renal injury. Several mechanisms have been proposed for the renal effect of acute hepatitis A, including dehydration, vasoconstriction due to hyperbilirubinemia, immune-mediated nephritis, and endotoxemia [5, 8]. High circulating levels of immune complexes are more frequently detected with acute hepatitis A than with other types of viral hepatitis. A high level of immune complexes in the circulation is associated with dysfunction of the Kupffer cells in acute hepatitis A and associated endotoxemia [9]. Tamika et al. [10] questioned whether a common target exists in the brain and kidneys. Some transport proteins are present in the blood-brain barrier and in the kidneys. For instance, p-glycoprotein, an adenosine triphosphate export pump, is present on the luminal side of the brain capillary endothelium and in proximal renal tubules [11]. Thus, a common target for endothelial damage could explain the occurrence of PRES in acute kidney injury after hepatitis A. The patient suffered from high fever, hemolytic anemia, pseudoaneurysms in arteries, and acute kidney injury. Even though we did not test for endotoxemia directly, we assume these complications after acute hepatitis A infection were caused by endotoxin-associated acute viral hepatitis A. However, we are uncertain why PRES developed in the renal function recovery phase.

When a patient with acute hepatitis A and acute kidney injury presents with sudden neurological changes such as altered mental status or a seizure but there is no definite evidence of infection, PRES should be considered in the differential diagnosis, and adequate supportive management should be started promptly.

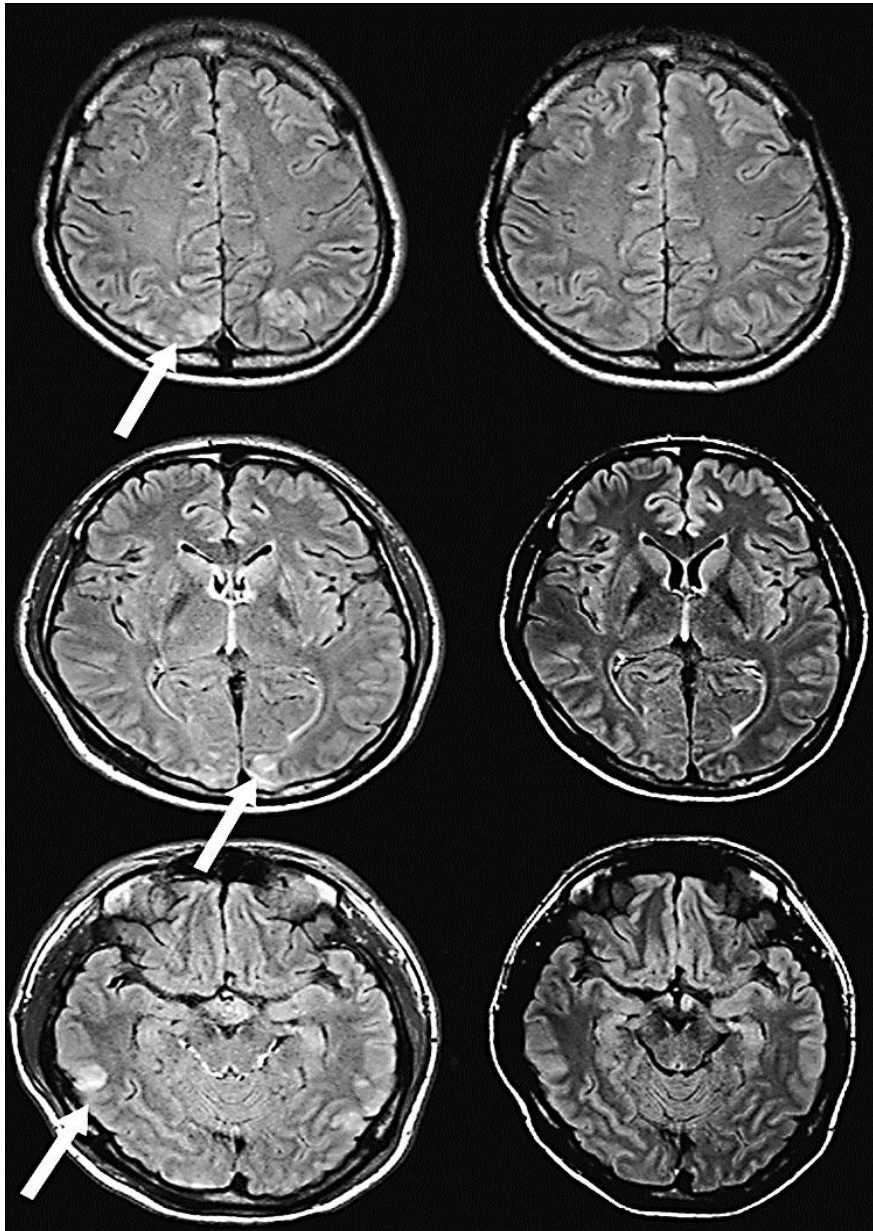


Fig. 1. Brain MRI (T₂-weighted). Bilateral symmetric high-intensity areas (arrows) were apparent in the temporoparietal occipital regions (left), and the abnormalities resolved on the follow-up (right).

References

- 1 Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al: A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 1996;334:494–500.
- 2 Bartynski WS: Posterior reversible encephalopathy syndrome, part 2: controversies surrounding pathophysiology of vasogenic edema. *AJNR Am J Neuroradiol* 2008;29:1043–1049.
- 3 Ishikura K, Ikeda M, Hamasaki Y, Hataya H, Nishimura G, Hiramoto R, et al: Nephrotic state as a risk factor for developing posterior reversible encephalopathy syndrome in paediatric patients with nephrotic syndrome. *Nephrol Dial Transplant* 2008;23:2531–2536.
- 4 Cuthbert JA: Hepatitis A: old and new. *Clin Microbiol Rev* 2001;14:38–58.
- 5 McCann UG 2nd, Rabito F, Shah M, Nolan CR 3rd, Lee M: Acute renal failure complicating nonfulminant hepatitis A. *West J Med* 1996;165:308–310.
- 6 Fabbian F, Pala M, Fallica E, Capone J, Monetti VC, Fratti D, et al: Posterior reversible encephalopathy syndrome in an 87-year-old woman with *Escherichia coli* bloodstream infection. *Clin Exp Nephrol* 2010;14:176–179.
- 7 Mueller-Mang C, Mang T, Pirker A, Klein K, Prchla C, Prayer D: Posterior reversible encephalopathy syndrome: do predisposing risk factors make a difference in MRI appearance? *Neuroradiology* 2009;51:373–383.
- 8 Lee DK, Do JK, Kim YJ: Guillain-Barre like syndrome associated with acute renal failure and thrombocytopenia following acute viral hepatitis A. *J Korean Med Sci* 1997;12:151–156.
- 9 Tanikawa K, Sata M: Endotoxin and Kupffer cells in liver disease. *Adv Exp Med Biol* 1990;25:481–495.
- 10 Tamika B, Mandrekar J, Wijdicks EF, Rabinstein AA: Renal failure and posterior reversible encephalopathy syndrome in patients with thrombotic thrombocytopenic purpura. *Arch Neurol* 2010;67:831–4.
- 11 Bauer B, Hartz AM, Fricker G, Miller DS: Modulation of p-glycoprotein transport function at the blood-brain barrier. *Exp Biol Med (Maywood)* 2005;230:118–127.