

# Posterior reversible encephalopathy syndrome following rapid correction of anemia

<sup>1</sup>Soonwoong Hong MD, <sup>1</sup>Jin Man Jung MD, <sup>2</sup>Hwa Jung Ryu MD PhD, <sup>1</sup>Do-Young Kwon MD PhD, Moon-Ho Park MD PhD

<sup>1</sup>Department of Neurology & <sup>2</sup>Dermatology, Korea University College of Medicine, Republic of Korea

## Abstract

A 49-year-old woman with anemia who developed headache and seizure after blood transfusion was diagnosed with posterior reversible encephalopathy syndrome (PRES). Magnetic resonance imaging showed typical PRES findings including lesions in bilateral parieto-occipital subcortical white matter and overlying cortex. Only a few cases of PRES after transfusion have been reported and this case is unique in that there was a latent period between infusion and development of PRES. We postulate that rapid change of hemoglobin level may disrupt cerebral autoregulation and result in delayed PRES. We suggest that neurological symptoms after blood transfusion should be appropriately investigated.

## INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is characterized by headache, altered mental status, loss of vision, and seizures. PRES has a distinctive pattern on brain imaging studies of symmetric distribution with vasogenic edema. The lesions predominate in the posterior cerebral regions, but the temporal frontal, and brainstem regions may also be involved.<sup>1</sup> Although various etiologies of PRES have been reported, the exact pathophysiology of PRES is still controversial. Herein we report a patient with PRES following blood transfusion. Only a few cases of PRES after transfusion have been reported and this case is unique, due to the development of clinical symptoms several days after transfusion.

## CASE REPORT

A 49-year-old woman had recently undergone subtotal hysterectomy at a local gynecologic hospital for a uterine myoma with symptomatic anemia. She was referred via emergency department with altered mental status and seizures. Nine days before her surgery, she received 1.6 liter of packed red blood cells (RBC) due to a hemoglobin level of 4.6 g/dl (normal 13.8-17.7g/dl). She tolerated the transfusion well. Her hemoglobin level increased to 11.4 g/dl without other associated symptoms, aside from a new-onset headache immediately after the transfusion and right before surgery, but her vital signs remained unremarkable. During and

after the hysterectomy, all vital signs were stable and the operation was completed without any surgical complications. Immediately after surgery, however, she complained of a severe headache and binocular blurred vision. She experienced a generalized tonic-clonic seizure five hours later. She was subsequently transferred to our hospital. On admission, her vital signs were stable (blood pressure: 115/53mmHg, body temperature: 36.8°C, heart rate: 96/minute, and respiratory rate: 22/minute), and she was mildly drowsy on mental status examination. Laboratory studies revealed findings compatible with iron deficiency anemia (Hb: 8.6 g/dl, MCV: 80.2 fL, MCHC: 30.0 g/dl, Fe 27 µg/dl). Other serology studies including liver function, kidney function, electrolytes and thyroid function were unremarkable. We performed a cerebrospinal fluid (CSF) study to exclude possible infection or inflammatory causes of seizure without remarkable abnormalities. Brain magnetic resonance image (MRI) demonstrated symmetric gyral swelling and effacement of bilateral parieto-occipital subcortical white matter and overlying cortex with patterns of mixed cytotoxic and vasogenic edema on diffusion-weighted MRI (DWI) (Figure 1A-C). MR angiography (MRA) showed vasoconstriction in bilateral posterior cerebral arteries (Figure 1D). Electroencephalogram (EEG) showed diffuse background theta slowing and frequent bilateral independent occipital rhythmic delta activity (Figure 2). Single photon emission computed tomography (SPECT) to check for a hypoperfusion

Address correspondence to: Do-Young Kwon, MD, PhD, Department of Neurology, Korea University Ansan Hospital, 516 Gojan-1-dong, Danwon-gu, Ansan-city, Gyeonggi-do [425-707], South Korea. Tel: 82-31-412-5150, Fax: 82-31-412-5154, E-mail: kwondoya@hanmail.net

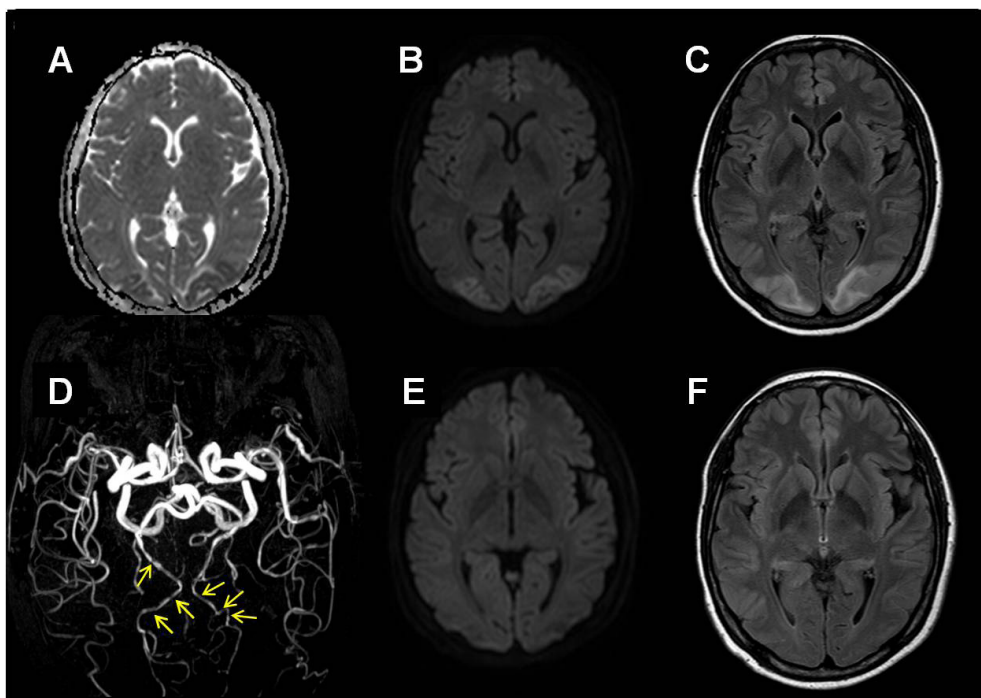


Figure 1. Initial diffusion-weighted MR images taken on the first day of admission demonstrate symmetrical diffusion restricted areas at bilateral parieto-occipital subcortical white matter and overlying cortex, which consistent patterns with mixed cytotoxic and vasogenic edema (ADC map, A and b-1000, B). Initial fluid attenuated inversion recovery (FLAIR) MR image showed high signal intensities at same area with DWI and mild swelling (C). MR angiography demonstrates multiple vasoconstrictions of bilateral posterior cerebral artery (arrows, D). These lesions were completely resolved on follow-up brain DWI (b-1000) and MRI, respectively (E, F).

state demonstrated symmetric normal perfusion pattern in the brain. Further laboratory data including serum IgG, IgA, IgM, C3, C4, RA factor, anti-microsomal antibody, FANA, ANCA, lupus anticoagulant, anti-phospholipid antibody, and anti-cardiolipin antibody were all unremarkable.

We diagnosed PRES based on brain image findings and symptoms. As there were no obvious causes for her condition aside from blood transfusion, we surmised that transfusion played an important role in the development of PRES. Her mental status and headache completely resolved. Follow-up MRI (including DWI) of the brain performed one month later revealed complete resolution of the abnormal high signal (Figure 1E-F) and her EEG also returned to normal.

## DISCUSSION

Various causes of PRES have been reported, but the exact pathomechanism of PRES is still debatable. PRES following blood transfusion is rare when considering how common RBC

transfusion is in clinical practice.<sup>2-6</sup> Most of the previously described PRES patients had associated extremely high blood pressure or renal insufficiency. While our patient had normal blood pressure throughout the disease course, she did have an iron deficiency anemia and a history of receiving large volumes of packed RBC during a short period of time. Similar to other reports, she complained of a headache immediately after transfusion, but there were no other neurologic deficits or compatible symptoms of PRES. What is unique about this case is the nine-day latent period before presentation of typical PRES symptoms. Although the pathophysiology of PRES is still controversial, there is some evidence to support that impaired cerebral autoregulation associated with disordered cerebral vasculature and a disrupted blood-brain barrier are important factors in the development of PRES.<sup>8</sup> Also, it is suggested that large volumes of preserved RBC transfusion could damage the vasculoendothelial system, increase endothelial vascular permeability, and cause vasoconstriction as a sign of disrupted cerebral autoregulation.<sup>9</sup> Her initial hemoglobin

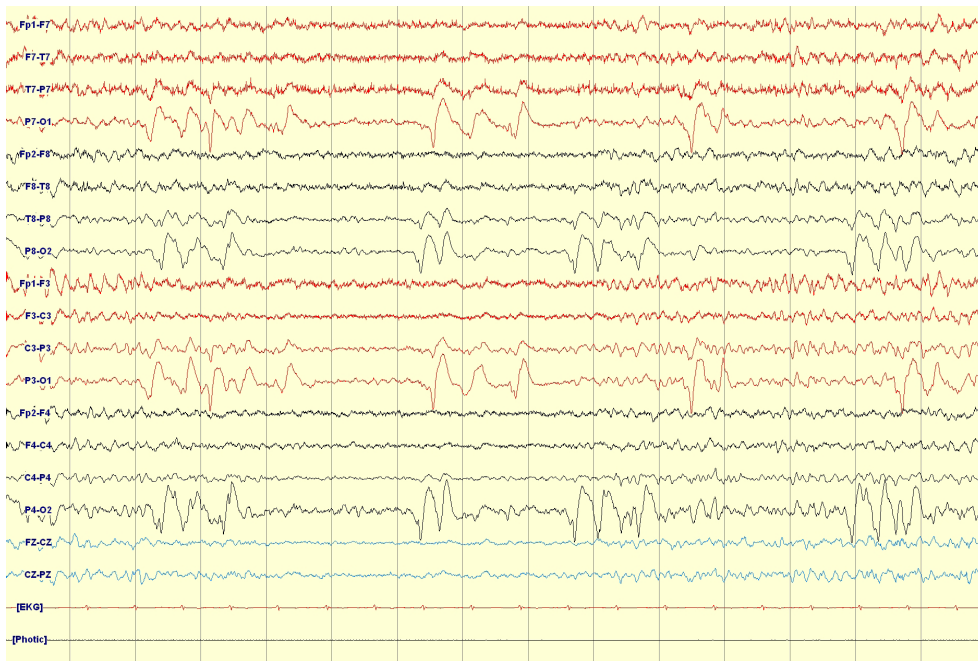


Figure 2. Electroencephalography (EEG) showed diffuse background theta slow and frequent bilateral independent occipital rhythmic delta activities

level after operation was 4.6 g/dl and increased to 11.4 g/dl after the blood transfusion, but her hemoglobin level at our hospital was 8.6 g/dl, meaning that her blood volume status fluctuated considerably over a nine-day period. Headache following rapid correction of the anemia was likely the first manifestation of PRES, but a fluctuation in hemoglobin level during surgery may have aggravated the disruption of her cerebrovascular system autoregulation, which exacerbated her typical symptoms of PRES. In our opinion, the probable etiology of PRES in this patient was a rapid change of blood volume causing dysfunction of normal vascular permeability and secondary vasoconstriction, while her rapidly fluctuating hemoglobin level may have exacerbated the clinical presentation over time. After she was admitted to our hospital and received supportive care, her symptoms improved and she was discharged without neurological deficit.

In summary, we report a case of PRES following blood transfusion after a nine day latency period. We suggest that a rapid change of hemoglobin level may cause disruption of cerebral autoregulation and result in delayed exacerbation of PRES. When considering blood transfusion for anemia patients, careful observation is recommended and mild neurological complaints should not be overlooked. Further investigation is needed to elucidate the association between blood volume change and the development of PRES.

## REFERENCES

1. Bartynski WS. Posterior reversible encephalopathy syndrome, part 1: fundamental imaging and clinical features. *AJNR Am J Neuroradiol*.2008; 29:1036-42.
2. Boughammoura A, Touze E, Oppenheim C, Trystram D, Mas JL. Reversible angiopathy and encephalopathy after blood transfusion. *J Neurol* 2003; 250:116-8.
3. Heo K, Park SA, Lee JY, Lee BI, Lee SK. Post-transfusion posterior leukoencephalopathy with cytotoxic and vasogenic edema precipitated by vasospasm. *Cerebrov Dis* 2003; 15:230-3.
4. Huang Y, Tsai P, Yeh J, Chen WH. Reversible posterior leukoencephalopathy syndrome caused by blood transfusion: a case report. *Acta Neurol Taiwan* 2008; 17:258.
5. Ito Y, Niwa H, Iida T, *et al*. Post-transfusion reversible posterior leukoencephalopathy syndrome with cerebral vasoconstriction. *Neurology* 1997; 49:1174-5.
6. Sato Y, Hirose M, Inoue Y, *et al*. Reversible posterior leukoencephalopathy syndrome after blood transfusion in a patient with end-stage renal disease. *Clinical Experimental Nephrology* 2011; 15:942-7.
7. Ahn KJ, You WJ, Jeong SL, *et al*. Atypical manifestations of reversible posterior leukoencephalopathy syndrome: findings on diffusion imaging and ADC mapping. *Neuroradiology* 2004; 46:978-83.
8. Bartynski WS. Posterior reversible encephalopathy syndrome, part 2: controversies surrounding pathophysiology of vasogenic edema. *AJNR Am J Neuroradiol* 2008; 29:1043-9.
9. Tinmouth A, Fergusson D, Yee IC, Hébert PC. Clinical consequences of red cell storage in the critically ill. *Transfusion* 2006; 46:2014-27.