Unilateral Posterior Reversible Encephalopathy Syndrome Secondary to Renal Artery Obstruction: A Case Report

Posterior reversible encephalopathy syndrome (PRES, or posterior leukoencephalopathy syndrome) is a neurological condition caused by reversible cortical/subcortical vasogenic brain edema secondary to hypertension, cytotoxic drugs, immunosuppressants, autoimmune diseases, renal disease, eclampsia or pre-eclampsia. It is characterized by acute neurological symptoms such as headache, seizures, visual disturbances, and impaired levels of consciousness. Brain imaging usually reveals bilateral, cortical/subcortical vasogenic edema. Completely unilateral PRES constituted only 2.6% of the cases in a previous study. Here we report the case of a pediatric patient with completely unilateral PRES. A 13-year-old boy was admitted with acute gastroenteritis. On the fourth day of hospitalization, he started to complain of headache and vomiting. He then developed generalized tonic-clonic seizure 3 times. His blood pressure was 180/121 mmHg during the first seizure, 188/112 mmHg during the second seizure and 152/92 mmHg during the third seizure. T2-weighted imaging with fluid attenuation by inversion recovery (T2 FLAIR) demonstrated high-signal intensity in the cortical gyri of the left frontal, parietal, and occipital lobes. Follow-up magnetic resonance imaging (MRI) was performed 2 weeks after the seizure onset, which indicated a significant improvement in the patient’s condition. Abdominal pelvic computed tomography (CT) and renal CT angiography showed abnormal narrowing of the left renal artery. In summary, we present a case report of unilateral PRES secondary to renovascular hypertension due to left renal arterial obstruction.

Key Words: Unilateral posterior leukoencephalopathy syndrome, Seizure, Hypertension, Renal artery obstruction

Introduction

The neurologic symptoms that characterize posterior reversible encephalopathy syndrome (PRES) include headaches, visual disturbances, seizures, and impaired levels of consciousness. Hypertension, immunosuppressants, eclampsia, pre-eclampsia, cytotoxic drugs, autoimmune diseases, or renal diseases can lead to reversible vasogenic edema in the cortical and/or subcortical region of the brain; this edema, in turn, can cause PRES\(^4\). In PRES, neuroimaging usually reveals a bilateral cortical/subcortical edema of vasogenic origin. Most commonly this involves the parietal-occipital region, but it may also involve the frontal, in-
A previous study found that completely unilateral PRES comprised only 2.6% of all PRES cases. However, it is important that healthcare professionals be aware of unilateral PRES, because if the correct diagnosis and treatment is delayed, permanent sequelae may ensue. We report a 13-year-old male patient presenting with PRES involving the left frontal, parietal, and occipital lobes unilaterally due to renal artery stenosis.

**Case Report**

A 13-year-old boy was admitted to our hospital with acute gastroenteritis. During the first four days of hospitalization, he complained of fever and multiple bouts of diarrhea daily. On the day he was admitted to the hospital, his blood pressure was 128/96 mmHg. On the fourth day of hospitalization, he started to complain of headache and vomiting. Shortly thereafter, he developed generalized tonic-clonic seizures with upward eyeball deviation which lasted for 5 min. During the seizure, his blood pressure, pulse and respiratory rate were 180/121 mmHg, 102 beats per min (bpm), and 28 breaths per minute (bpm), respectively. Body temperature remained normal. Thirty minutes later, he complained of right arm weakness and developed another generalized tonic-clonic seizure. Lorazepam was administered and the seizure stopped a minute later. His blood pressure, pulse, respiratory rate and body temperature were 188/112 mmHg, 122 bpm, 30 bpm, and 37.3℃, respectively. Immediately after the second seizure, hydralazine was administered and nicardipine infusion was started. Five hours later, he developed a third generalized tonic-clonic seizure, which was treated with lorazepam. His blood pressure and pulse were 152/92 mmHg and 115 bpm, respectively, after the seizure.

At this point, the physical examination results, including lung and heart auscultation findings, were unremarkable. The patient’s abdomen was soft and flat, without organomegaly. He was lethargic but responsive (Glasgow coma scale: eye response 3, verbal response 5, motor response 6). There was no neck stiffness. Nicardipine infusion normalized his diastolic blood pressure, and his systolic blood pressure remained within the range of 100 to 140 mmHg.

T2-weighted imaging with fluid attenuation by inversion recovery (T2 FLAIR) demonstrated elevated signal intensity in the cortical gyri of the left frontal, parietal, and occipital lobes (Fig. 1A). In addition, diffusion-weighted (DW) imaging revealed mild edema in the cortex and subcortical white matter. There was no ischemic injury (Fig. 1B).

After the third seizure, a cerebrospinal fluid (CSF) exam was performed to rule out encephalitis. The CSF exam results showed a red blood cell (RBC) count 910/μL, white blood cell (WBC) count 0/μL, protein 27.3 mg/dL, glucose 64 mg/dL, and negative CSF culture. In addition, all of the following were negative: CSF enteroviruses PCR, stool enteroviruses PCR, CSF group B streptococcus (GBS) PCR, CSF H. influenzae type B PCR, CSF L. monocytogenes PCR, CSF N. menigitidis PCR, CSF S. pneumonia PCR, CSF Epstein-Barr Virus (EBV) PCR, CSF cytomegalovirus (CMV) PCR.
PCR, serum CMV antibody IgM, serum rubella virus antibody IgM, CSF varicella zoster virus (VZV) PCR, serum VZV antibody IgM, CSF herpes simplex virus (HSV) type 1 PCR, CSF HSV type 2 PCR, and serum HSV IgM. Electroencephalography (EEG) revealed a generalized background slowing, indicating diffuse central nervous system dysfunction in this patient. At this point, his Glasgow coma scale score was 12 (eye response 2, verbal response 5, motor response 5). Echocardiography showed a normal image.

His blood pressure was still high after these seizures ended. To determine the cause of hypertension, a contrast medium was administered and an abdominal and pelvic computed tomographic scan (CT scan) was performed. CT revealed a poorly delineated left renal artery and low shadows inside the blood vessel, suggesting left renal artery stenosis. Renal artery CT angiography (Fig. 2) showed near-occlusive stenosis at the proximal portion of the renal artery and abnormally small and poorly perfused left kidney.

Laboratory tests showed elevated renin, at 110.39 ng/mL/hr (normal range: supine 0.15–2.33, standing 1.31–3.95), and elevated aldosterone, at 188.5 ng/dL (normal range: 1.2–34). Vasculitis-related laboratory parameters were all negative as follows: antinuclear antibodies, antiphospholipid antibodies (IgM and IgG), anti-cardiolipin antibodies (IgG and IgM), anti-β2 glycoprotein I antibodies (IgG and IgM), lupus anticoagulants, anti-SS-A/Ro, anti-SS-B/La, myeloperoxidase antibodies, proteinase 3 antibodies and rheumatoid factor.

The patient was finally diagnosed with PRES and renovascular hypertension due to left renal arterial stenosis.

A dimercaptosuccinic acid (DMSA) scan and Tc-99m diethylene-triamine-pentaacetate diuretic renography were performed. These tests showed normal uptake and blood flow to the right kidney, while the left renal blood flow and uptake were considerably reduced. Split renal function was 88% on the right and 12% on the left. Peripheral angiography with 5F pigtail catheter showed complete occlusion of the left renal artery. After the diagnosis of near-total occlusion, balloon angioplasty was performed in the left renal artery using a Coyote 2×20 mm percutaneous transluminal angioplasty (PTA) balloon for 180 s. Adjuvant balloon inflation was performed with an Advance Micro® 14 3×20 mm PTA balloon for 120 s. Follow-up angiography revealed 30% residual stenosis without arterial dissection.

Intravenous nicardipine was tapered and switched to oral enalapril (15 mg twice daily) and amlodipine (10 mg in the morning and 5 mg in the evening). After intravenous medication was thus changed to oral medication, the blood pressure remained in the normal range. Follow-up magnetic resonance imaging (MRI) (Fig. 3) was performed 2 weeks after the onset of seizure. The lesion in the left hemisphere almost disappeared, and the punctate lesion with high-signal intensity remained in the superior frontal lobe in T2-weighted images and FLAIR images. No new lesions were observed in the remaining brain parenchyma, suggesting recovery from PRES. The patient was seizure-free and was discharged without any neurological sequelae.

Discussion

PRES is suspected when a patient who is experiencing renal failure, blood pressure fluctuation, autoimmune diseases, eclampsia, or preeclampsia presents with additional acute neurological symptoms, which may include seizures, headaches, visual disturbances, and altered consciousness. Studies suggest that PRES can also follow immunosuppressant therapy after organ transplantation, chemotherapy, and sepsis. In a tertiary care center in India, the most common cause of PRES during a 5-year period was renal disease (20 [62.5%] out of the 32 reported PRES cases during the 5-year period).

While the pathophysiology of PRES is not completely understood, several hypotheses related to the etiology of PRES have been proposed, and four of these hypotheses are discussed below. The first hypothesis suggests that cerebral perfusion pres-
sure exceeding the upper limit of the cerebral blood flow range may result in hyperperfusion, which in turn may damage the blood–brain barrier and induce endothelial wall injury. Endothelial dysfunction may result in extravasation of plasma and macromolecules, which may lead to cerebral vasogenic edema. The posterior portion of the brain is more vulnerable because autoregulation and sympathetic activity are relatively weak in the posterior area. The range of cerebral perfusion pressure in which the autoregulation of cerebral blood flow functions normally differs individually. Furthermore, the range of cerebral perfusion pressure in which the autoregulation of cerebral blood flow is normal is narrower in pediatric patients than in adult patients. A previous study found that the threshold of cerebral autoregulation was 50–60 mmHg in adults compared with 40 mmHg in children. Systolic blood pressure at the onset of PRES is higher in adults than in children. Siebert et al, suggested that the median systolic BP at the onset of PRES was 140 mmHg (124–160 mmHg) in children compared with 170 mmHg (150–180 mmHg) in adults. However, other studies reported 15–20% PRES in normotensive or hypotensive patients. The second hypothesis suggests that cytokines may directly induce endothelial dysfunction. In inflammation, the activation of monocytes and lymphocytes triggers the release of various cytokines including interleukin-1, interferon gamma, and tumor necrosis factor alpha. Activation by these cytokines leads to the release of vasoactive factors by endothelial cells, resulting in increased vascular permeability and interstitial brain edema. Cytokine activation explains PRES secondary to sepsis. During infection, polymorphonuclear leukocytes are activated, move to the vascular wall, and adhere to the vascular endothelium. Additional mediators are released, increasing vascular permeability resulting in interstitial edema, and PRES. The third hypothesis suggests that immunosuppressants used after organ transplantation or chemotherapy may provoke endothelial injury or dysfunction, leading to extravasation of fluid. The fourth hypothesis relates to hypoperfusion in the brain. According to this hypothesis, vasocorstriction may lead to hypoperfusion, resulting in endothelial cell damage (ischemia). The consequent disruption in the blood–brain barrier may lead to vasogenic edema.

The symptoms of PRES include seizure, visual disturbances, altered consciousness, headache, nausea, vomiting, and focal neurologic deficits. Seizure is the most common symptom. Approximately 60–75% of PRES patients suffer generalized tonic–clonic seizures. Furthermore, the seizure frequency is higher in pediatric PRES patients compared with adults. Siebert et al, reported on 19 pediatric and 91 adult cases of PRES. In their study, 18 (94.7%) pediatric patients developed seizures, compared with only 60 (65.9%) adults. Patients may develop any type of seizures, although they usually develop focal seizures that subsequently progress to generalized seizures. The second most common symptom in pediatric PRES involves altered consciousness. The third, fourth and fifth most common symptoms include visual disturbances, headache, and focal neurological symptoms, respectively. Previous study suggested that pediatric PRES was less likely to involve visual disturbances than adult PRES, Siebert et al, reported that 2 (10.5%) of 19 pediatric patients developed visual disturbances, compared with 32 (35%) of 91 adult patients.

Fig. 3. The left figure is Fig 1A and the right image is second T2-weighted axial FLAIR imaging.
Brain MRI is the most effective modality for the differential diagnosis of PRES\textsuperscript{2,7}. Cortical and subcortical edema in the posterior occipital and parietal lobes are usually detected in brain imaging\textsuperscript{2,7}. Cerebral edema is apparent as increased T2 and FLAIR signals\textsuperscript{2,7}. The imaging findings are classified into two categories: "typical" and "atypical." Edema in the parieto-occipital region is classified as "typical," while edema in the frontal lobes, thalamus, brainstem, or cerebellum is classified as "atypical." In pediatric cases of PRES, edema is frequently found in the frontal lobe\textsuperscript{11}. In a previous study by Siebert et al., the parieto-occipital lobe was involved in 8 (42.1%) out of 19 pediatric patients and 51 (56%) out of 91 adult patients, while the superior frontal sulcus was involved in 7 (36.8%) out of the 19 pediatric patients and 11 (12.1%) out of 91 adult patients\textsuperscript{11,16}. Siebert et al. and Fugate et al. both reported cytotoxic edema, infarctions, hemorrhages, laminar necrosis, and gliosis in patients with PRES\textsuperscript{2,10}. Cytotoxic edema showed reduced signal in the apparent diffusion coefficient map\textsuperscript{10}. In PRES, the cerebral edema is usually bilateral, but a few published studies have reported unilateral cerebral edema\textsuperscript{2,11}. In a previous study by McKinney et al., completely unilateral PRES accounted for 2.6% of the PRES cases\textsuperscript{2}. Unilateral PRES is very rare and includes the following reports: 1 case reported by Schambra et al. in 2006\textsuperscript{11,12}, 2 cases reported by Dhar et al. in 2011\textsuperscript{2,11}, 1 case reported by Voetsch et al. in 2011\textsuperscript{11,16}, 1 case reported by Huijgen et al. in 2014\textsuperscript{11}, and 1 unilateral PRES case reported by Çamlıdag et al. in 2015\textsuperscript{11}. Pathophysiology of unilateral PRES is not completely understood, although it was explained on the basis of hyperperfusion theory\textsuperscript{12}. The authors hypothesized that arterial stenosis in an artery supplying one cerebral hemisphere can redirect the arterial blood flow to the contralateral hemisphere, inducing hypertension in the contralateral hemisphere\textsuperscript{12}. If the cerebral perfusion pressure in the contralateral hemisphere exceeds the upper limit of the cerebral blood flow autoregulation range, it may result in hyperperfusion, which in turn may damage the BBB and trigger endothelial wall injury\textsuperscript{2}. Endothelial dysfunction may result in extravasation of plasma and macromolecules, which may lead to cerebral vasogenic edema, resulting in PRES. However, another study hypothesized that blood vessels distal to a stenotic portion may be chronically dilated by a compensatory mechanism\textsuperscript{15}. An abrupt increase in the systolic blood pressure may elevate the cerebral perfusion pressure above the autoregulation range, resulting in failure\textsuperscript{15}. The consequence damage to the BBB may induce vasogenic edema, leading to PRES\textsuperscript{11}. We concluded that the most probable cause of unilateral cerebral edema in our patient was endothelial wall injury resulting from hypertension caused by renal artery stenosis. The patient’s left hemisphere may have been more sensitive to hypertension because of a possible though unobserved transient unilateral vascular occlusion of the cerebral vessels\textsuperscript{8,14}. Such transient unilateral vascular occlusion of the cerebral vessels could be related to the observed renal artery stenosis, or have another unknown cause.

Treatment of PRES requires elimination of all the precipitating factors (e.g., the use of immunosuppressants or cytotoxic drugs) and treatment of the underlying disease (e.g., sepsis, pre-eclampsia, eclampsia, autoimmune disease)\textsuperscript{2,15}. One of the most important precipitating factors is hypertension\textsuperscript{2,11,12}. Treatment of hypertension should include initial reduction to 20–25% of the blood pressure within the first few hours\textsuperscript{2,15}. However, rapid blood pressure reduction can lead to cerebral ischemia\textsuperscript{2}. The primary cause of PRES in our patient was hypertension. While essential hypertension is the most common type of hypertension in adults, secondary hypertension is the most common in pediatric patients. Secondary hypertension in pediatric patients usually has a renovascular origin\textsuperscript{9,16}. Etiologies of renovascular hypertension in pediatric patients include fibromuscular dysplasia and extrinsic compression; vasculitis such as Kawasaki disease, polyarteritis nodosa, Takayasu's disease, and moyamoya disease; and other causes such as neurofibromatosis, tuberous sclerosis, Marfan syndrome, trauma, radiation, and congenital rubella\textsuperscript{16}. Treatment of PRES secondary to renovascular hypertension requires control of hypertension and the management of underlying causes such as renovascular disease. Antihypertensive drugs are indicated, and revascularization via percutaneous transluminal renal angioplasty (PTRA) or surgical intervention is needed in most patients. PTRA revealed complete occlusion of the left renal artery. Following balloon angioplasty, an angiographic follow-up study revealed 30% residual stenosis without arterial dissection. The patient also needed several additional balloon angioplasty procedures. While treating PRES, it is also important to control the risk of seizure. Antiepileptic drugs such as benzodiazepine, phenobarbital, and phenytoin are needed to treat the seizures\textsuperscript{15}.

PRES usually has a favorable prognosis, without any sequelae if promptly treated\textsuperscript{2,15}. Fugate et al. found that complete recovery occurred in 2 to 8 days\textsuperscript{2}. However, delayed treatment of PRES may leave sequelae\textsuperscript{2,17}. Permanent neurological sequelae ensue in 10–20% of PRES patients\textsuperscript{2}. Fugate et al. reported hemorrhage and infarction during PRES lead to neurologic sequelae\textsuperscript{2}. In conclusion, we report a case of unilateral PRES caused by renovascular hypertension. PRES is usually reversible after the elimination of precipitating factors\textsuperscript{2}. However, irreversible neurological sequelae may ensue in the absence of prompt diagnosis and treatment. Therefore, it is important for healthcare professionals to
요약
가역성 후두부 백질 증후군(이하 ‘PRES’라 한다)은, 고혈압, 면역 억제치료, 신장질환, 자가 면역질환, 전자간증, 자간증 등 다양한 원인에 의하여, 경련, 두통, 시력장애, 의식장애 등의 증상이 발생되는 신경학적 증후군이다. PRES는 대뇌피질 및 피질 하백질의 부종에 의해 발생하며, 뇌기능기증양상에서 뇌MRI 검사로 보통 대칭적으로 나타난다. 대칭이 아닌 한쪽 방향으로만 PRES가 생긴 경우는 전체의 2.6% 비율에 불과하다. PRES의 진단이 늦어졌을 때, 해당 환자들에게 영구적이고 치명적인 후유증을 남길 수 있다. 본 증례보고는 한쪽 방향으로 발생한 PRES을 보고하고자 한다. 13세 난�이 입원한 4일째 두통과 구토를 호소하고 터어 3번 전신성 긴장을 겪었다. 첫번째 경기시에는 혈압이 180/121 mmHg이었다. 두번째 경기시에는 혈압이 188/112 mmHg 그리고 3번째 경기시에는 152/92 mmHg였다. 뇌 자기공명영상에서 왼쪽 전두엽, 두정엽, 후두엽에 피질의 신호강도가 증가하였다. 2주 후에 시행한 뇌 자기공명영상에서는 증가하였던 신호강도가 호전되었다. 복부 컴퓨터단층촬영 및 신장혈관 촬영에서 왼쪽 신장혈관이 좁아져 있었다. 본 증례보고는 한쪽 방향으로만 PRES가 생긴 경우는 전체의 2.6% 비율에 불과하다. PRES의 진단이 늦어졌을 때, 해당 환자들에게 영구적이고 치명적인 후유증을 남길 수 있어 한쪽에서만 PRES가 발생한 경우에 대해 강조하고자 증례보고 하는 바이다.

References