



Posterior reversible encephalopathy syndrome in children: a case series

Serhat Emeksiz¹, Nurettin Onur Kutlu¹, Hüseyin Çaksen², Gülsüm Alkan³, Hülya Şeker Yıkmaz³, Hüseyin Tokgöz⁴

¹Department of Pediatric Intensive Care, Necmettin Erbakan University Meram School of Medicine, Konya, Turkey

²Division of Pediatric Neurology, Necmettin Erbakan University Meram School of Medicine, Konya, Turkey

³Department of Pediatrics, Konya, Necmettin Erbakan University Meram School of Medicine, Turkey

⁴Division of Pediatric Hematology, Necmettin Erbakan University Meram School of Medicine, Konya, Turkey

Abstract

Posterior reversible encephalopathy syndrome is characterized by hypertension, seizure, headache, clouding of consciousness, and visual disturbance, and is diagnosed in the presence of typical lesions on magnetic resonance imaging. We retrospectively evaluated five patients who were diagnosed as having posterior reversible encephalopathy syndrome and followed up in Meram Medical Faculty, Pediatric Intensive Care and Hematology wards, between January 2010 and January 2014. We reviewed the demographic and clinical data, and neuroimaging findings. The primary diseases of the subjects included acute lymphocytic leukemia (n=2), Henoch-Schönlein purpura (n=1), systemic lupus erythematosus (n=1), and acute poststreptococcal glomerulonephritis (n=1). The mean age was 10±4.58 years (range, 5-14 years). Acute elevation of blood pressure was found in all patients (n=5). Initial neurologic manifestations included seizure, clouding of consciousness, headache, and visual disturbance. After the diagnosis was made through clinical evaluations and magnetic resonance imaging, complete clinical recovery was obtained in all patients with the appropriate therapeutic approach. In conclusion, posterior reversible encephalopathy syndrome should be considered in the differential diagnosis of patients who present with encephalopathy and underlying diseases such as nephritis, vasculitis, malignancy accompanied by hypertension, and a history of use of medication. (Turk Pediatri Ars 2016; 51: 217-20)

Keywords: Hypertension, magnetic resonance imaging, pediatric intensive care, posterior reversible encephalopathy syndrome

Introduction

Posterior reversible encephalopathy syndrome (PRES) is usually a reversible condition characterized by a clinical picture of disturbance in mental state, headache, seizure, visual disturbances, and brain edema, which is more prominent in the parietal and occipital regions on brain imaging. The etiologic factors have a considerably wide spectrum and include mainly hypertensive encephalopathy, immunosuppressive and cytotoxic drugs, lupus nephritis, collagen vascular diseases, malignant disease, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, chronic renal failure, sepsis, and organ transplantation (1, 2)

Two main mechanisms in the pathophysiology of posterior reversible encephalopathy syndrome include vaso-

spasm and cytotoxic edema, accompanied by increased blood pressure and disruption in cerebral autoregulation, and development of vasogenic edema (2). If diagnosis and treatment is delayed, permanent effects and mortality in relation with PRES may be reported (3, 4).

In this article, the etiologic, clinical, and radiologic findings of five patients who presented with PRES findings are described and evaluated in light of the literature.

Cases

Five patients who were hospitalized in our pediatric intensive care unit and pediatric hematology ward between January 1st, 2010, and January 1st, 2014, and who were diagnosed as having PRES with clinical findings and brain imaging were included in the study.

Address for Correspondence: Serhat Emeksiz E-mail: serhatemeksiz@yahoo.com

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The patients' demographic properties, baseline clinical findings, the highest blood pressure values after PRES emerged, the time of clinical improvement, and brain magnetic resonance imaging (MRI) at the time of diagnosis and in the follow-up period were obtained. The age and sex among the demographic properties, the main diagnoses, triggering factors that could lead to changes in mental status, and baseline clinical states were evaluated. Increased blood pressure and increased intracranial pressure was treated carefully in all patients. The patients were treated by paying attention to keeping their heads at 30-45°C, keeping the partial oxygen pressure at normal values, avoiding hypercapnia, correcting electrolyte disturbances, keeping blood pressure values within normal limits, and seizure control.

Brain MRI was performed using SIEMENS AVANTO (1.5 Tesla). The T1- and T2-weighted axial, T1-weighted sagittal, fluid-attenuated inversion recovery (FLAIR) coronal images before injection of contrast material, and T1-weighted axial and coronal sequence images following intravenous (IV) injection of gadolinium were present in all patients. All MRIs were evaluated by a pediatric neurologist, radiologist, and intensive care physicians. The electroencephalogram (EEG) tests of the patients were performed using a Galileo NT – EB Neuro device.

The demographic and clinical properties of our patients are shown in Table 1. Three (60%) of five patients were girls and two (40%) were boys. The primary underlying diseases included vasculitis with renal involvement (systemic lupus erythematosus nephritis [patient 1], Henoch–Schönlein purpura nephritis [patient 5]), malig-

nancy (patients 3 and 4) and acute glomerulonephritis (patient 2). The highest blood pressure values measured after development of PRES were above the 99th percentile by age in all patients (mean systolic blood pressure values: 150±18.7 mm Hg, mean diastolic blood pressure values: 93.8±10.4 mm Hg). The most common neurologic symptom was seizure and this was present in all patients. Clouding of consciousness was observed in four patients, headache was observed in three patients, and visual disturbance was observed in two patients. The mean time for improvement of acute encephalopathy and the mean hospitalization period was 3.8 days (range, 3-4 days) and 36.4±11.41 days (range, 27-56 days), respectively. Neurologic sequelae were not present in any of the patients at the time of discharge.

The brain MRIs of our patients are shown in Table 1. Hyperintense areas were present in the parietal region in the T2 and FLAIR sequences in all patients (100%). In addition, hyperintense areas were observed in the T2 and FLAIR sequences in the occipital region in three patients and in the temporal region in two patients (Figure 1a). The findings were observed to have disappeared on the follow-up MRI performed one month after the diagnosis of PRES in three patients (Figure 1b). Follow-up MRI was not present in the other two patients. Written informed consent was obtained from the parents of the patients included in this study.

Discussion

Drugs including steroids, cyclophosphamide, cyclosporin, methotrexate, acyclovir, vincristine, and tacrolimus have been reported as causative agents in the etiology

Table 1. Demographic characteristics, clinical, and magnetic resonance imaging findings of the patients

Pt. No.	Age (years) / Sex	Primary disease	Triggering factor	Max blood pressure (mm Hg)	Clinical onset	LOS in ICU (days)	LOS on ward (days)	Anti-hypertensive drug	Neurologic sequela	MRI involvement
1	13/ Male	Lupus Nephritis	Corticosteroid	160/95	Clouding of consciousness, seizure, headache, sudden visual disturbance	4	27	Nifedipine, Losartan, Captopril	No	Parietal, Temporal
2	14/ Male	Acute Glomerulonephritis	Acute renal failure, HT	60/1107	Clouding of consciousness, seizure, headache	4	34	Nifedipine, Furosemide	No	Parietal, Occipital
3	5/ Female	Acute lymphoblastic leukemia	Corticosteroid Chemotherapeutic	130/85	Clouding of consciousness, seizure	3	56	Nifedipine	No	Parietal, Occipital
4	5/ Female	Acute lymphoblastic leukemia	Corticosteroid Chemotherapeutic	130/82	Clouding of consciousness, seizure	4	30	Nifedipine	No	Parietal, Temporal, Frontal
5	13/ Male	Henoch–Schönlein Purpura nephritis	Corticosteroid	170/100	Seizure, headache, sudden visual disturbance	4	35	Nifedipine, Captopril	No	Parietal, Occipital

ICU: intensive care unit; LOS: length of stay; MRI: magnetic resonance imaging; No: number; Pt: patient

of posterior reversible encephalopathy syndrome (5). Before the clinical picture of PRES developed, two patients were receiving cyclosporin and corticosteroid (patients 3 and 4), and two other patients (patients 1 and 5) were receiving corticosteroid treatment for the treatment of primary diseases. It has been reported in the literature that cyclosporin leads to potential hypertension by causing vascular endothelial damage and disrupting the blood-brain barrier (6). There are arguments presuming that the use of corticosteroids contributes to the occurrence of PRES by leading to hypertension and disrupting the autoregulatory mechanism of the brain (6). PRES should be considered in the differential diagnosis in cases of hypertension associated with suddenly-developing headache or seizure in patients receiving cyclosporin and/or corticosteroid.

The risk factors for PRES that develops in relation with systemic lupus erythematosus (SLE) or other vasculitis include endothelial damage related with vascular disease, disrupted blood-brain barrier, systemic inflammation, and cytotoxic and/or immunosuppressive therapies. In patients with lupus nephritis, hypertension is thought to lead to the clinical picture of PRES (7). In the literature, the association of sudden visual disturbance and headache has been reported frequently in vasculitis-related PRES (6, 7). In accordance with the literature, association of headache and visual disturbance was observed in both our patients who developed PRES following use of steroids with a background of vasculitis. It has been reported in the literature that occipital lobe involvement on MRI is more frequent in patients with visual disturbance. In one of our patients (patient 1), visual disturbance was present without occipital involvement.

The neurologic findings in PRES are frequently non-specific symptoms including clouding of consciousness, seizure, headache, and visual disturbance. In our case series, seizure was the most common neurologic finding and was present in all patients. Seizures may have very

different characteristics and status epilepticus may also be observed in PRES. Clouding of consciousness was observed in four of our patients. In the literature, it was reported that an episode of clouding of consciousness and seizure was observed in all patients in a pediatric case series of 14 patients with PRES (8). Hypertension has been reported in approximately 70-80% of patients with PRES in the literature. In these patients, vasogenic edema developing on a cytotoxic background in relation with different causes has been blamed (8). Hypertension was present in all of our patients. Nifedipine treatment was initiated for hypertension in our patients. Losartan (on the fourth day of hospitalization) was added and captopril was added (on the seventh day of hospitalization) to the treatment of patient 1; furosemide was added to treatment (on the second day of hospitalization) in patient 2; and captopril was added to treatment (on the fourth day of hospitalization) in patient 5, because hypertension continued. The mean time for normalization of blood pressure was found as 8.8 ± 4.5 days (range, 5-16 days) and the mean duration of antihypertensive drug use was 14.2 ± 7.6 days (range, 8-27 days). In pediatric intensive care, PRES should be considered in the presence of an associated neurologic problem and /or clouding of consciousness and hypertension.

Neuroradiologic evaluation plays an important role in terms of definite diagnosis. Although intracranial hypodensity is found on brain tomography, it rarely provides sufficient evidence. Diffusion-weighted MR imaging is more commonly preferred in the diagnosis of PRES, because it has a higher specificity and sensitivity (9). Vasogenic edema has been demonstrated in MRI, typically in the subcortical white matter, partially symmetrically in the parietal and occipital lobes and sometimes in the cortex (1). Involvement of the frontal region, basal ganglia, cerebellum, and thalamus has been reported in the literature (8). Typical involvements were generally observed in our patients. No atypical involvement was observed. In addition, MRI findings and distribution of hyperintense areas have not been found correlated with underlying disease, disease severity, and the level of hypertension (1). In our case series, there was no correlation between the distribution of MRI findings and the clinical pictures and blood pressure values of the patients.

In the differential diagnosis, cerebral venous thrombosis, bilateral posterior lobe infections, herpes virus and other viral encephalitis, and cerebral changes related with electrolyte disturbances should be considered (9). In our patients, venous or ischemic infarction was excluded by way of diffusion-weighted MRI and encephalopathy related with infections and electrolyte disturbances was excluded by way of history, physical examination, clinical status, and laboratory tests.

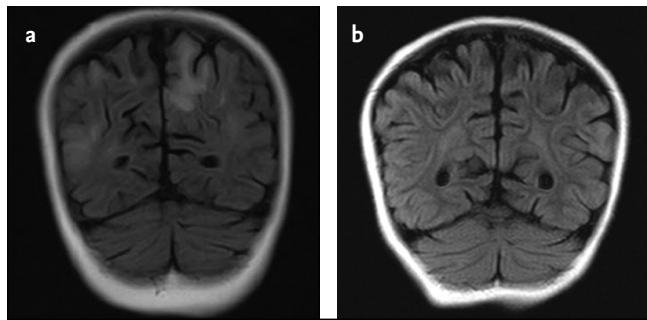


Figure 1. a, b. Areas with increased intensity are observed in the cortical and subcortical areas especially in the parieto-occipital region in both hemispheres on coronal FLAIR MRI in patient 4 (a) Normal follow-up FLAIR MRI of patient 4 (b)

There is no specific treatment for PRES. Supportive treatment directed to symptoms is the mainstay of treatment. Supportive treatment includes antihypertensives, antiepileptic drugs for seizure, discontinuation of drugs that may lead to the condition, and most importantly, controlling the underlying disease causing hypertension. Antiepileptic treatment is used in the emergency treatment of seizures related with PRES, but there is no need for long-term antiepileptic treatment (10). In our patients, the drugs that could cause PRES were immediately discontinued after the diagnosis was made and blood pressure values were controlled with antihypertensive drugs. The mean times for clinical recovery have been reported as 5.3 days in adult patients, and 4.8 days in pediatric case presentations (8, 10). In our patients, the mean time for clinical recovery was 3.8 days, which was in accordance with the literature. The mean time of hospitalization in our patients was 36.4 ± 11.41 days (range, 27-56 days). The time of hospitalization varied according to the underlying disease. Prior involvements were observed to have regressed on the follow-up MRIs in three patients.

Early diagnosis and treatment of PRES is essential. Otherwise, it may lead to permanent brain damage, neurologic sequelae including chronic epilepsy, and even mortality. In a series by Covarrubais et al. (3) who reported on 22 patients with PRES related with different etiologies, six patients had a fatal prognosis; recovery with permanent neurologic sequelae occurred in a significant portion of the patients. In another series, the rate of irreversible neurologic damage related with PRES was reported as 12% (4). Therefore, early diagnosis and treatment of the disease is paramount.

The limitations of our study included the retrospective design of the study and small number of patients. In addition, brain imaging and clinical follow-up were not performed within a specific protocol.

In conclusion, PRES should be considered in the differential diagnosis of acute encephalopathy in patients who present with new-onset seizures, systemic hypertension, and clouding of consciousness. The clinical findings, underlying disease, history of drug use, and brain imaging should be evaluated together, and it should be kept in mind that complete clinical recovery can be provided with early diagnosis and appropriate therapeutic approaches.

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