Childs Nerv Syst (2014) 30:535–540
DOI 10.1007/s00381-013-2342-y

CASE REPORT

Posterior reversible encephalopathy syndrome in children: report of three cases

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Received: 30 October 2013 / Accepted: 9 December 2013 / Published online: 20 December 2013

Abstract
Purpose Posterior reversible encephalopathy syndrome (PRES) is a condition characterized by varying degrees of headache, nausea, vomiting, visual disturbances, focal neurologic deficit, and seizures due to severe systemic hypertension. The knowledge of secondary hypertension in children is most commonly due to renal abnormalities, suggesting that the leading cause of PRES in childhood is renal diseases.
Methods Three pediatric patients who developed PRES due to various underlying renal diseases were reviewed.
Results The etiology of hypertension of our patients was all renal problems including atrophic kidney, hydronephrosis secondary to reflux nephropathia, nephrotic syndrome, and acute poststreptococcal glomerulonephritis. While two of them had typical of the parieto-occipital and frontoparietal involvement, the other had brain stem involvement. All of the patients were recovered by the control of high blood pressure.
Conclusion Primary involvement of the brain stem is rare in children. PRES should be taken into account, especially in children with renal disease in the appropriate clinical settings.

Keywords Posterior reversible encephalopathy syndrome · Renal disease · Brain stem involvement · Hypertension · Pediatric

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Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinical and radiological syndrome, first described by Hinchey et al. in 1996 [5]. Common clinical features of PRES are seizure, headache, nausea, vomiting, altered mental status, cortical blindness, and transient motor deficits. The main finding in neuroimaging is posterior white matter edema which principally affects the occipital and parietal lobes and posterior fossa structure [5].

Typically, PRES involves the parieto-occipital lobes; however, it can involve atypical localizations such as frontal lobe, basal ganglia, thalamus, and gray matter [4, 10]. Brain stem involvement is quite rare in children with PRES.

PRES has been reported in various conditions including eclampsia, Wegener granulomatosis, systemic lupus erythematosus, postchemotherapy, nonspecific renal inflammatory conditions, and after transplantation [2]. Here, we report three cases that developed PRES in the course of renal diseases.

Materials and methods

The files of three pediatric patients who developed PRES due to various underlying renal diseases were reviewed.

Results

Case 1

A 9-year-old girl was admitted to our hospital with the complaints of headache, vomiting, visual disturbances, and change in consciousness. She had a history of headache at irregular intervals for 5 months. The past medical history was unremarkable.

Her physical examination revealed the following: pulse rate, 122/min; respiratory rate, 28/min; blood pressure, 210/160 mm/Hg; and temperature, 36.8 °C. On neurological examination, there was bilateral nystagmus, weakness of left upper and lower extremities, and positive Babinski sign on left. The fundus examination revealed bilateral papilledema with grade 4 hypertensive changes. There was no evidence of infection. Other physical examination was normal.

Laboratory examinations including complete blood count, serum electrolytes, and liver function tests were all within normal limits. Noncontrast cranial CT images showed nothing except hardly noticed hypodensity in the brain stem. Cranial magnetic resonance imaging (CMRI) revealed an extensive increased signal in the brain stem caudal to pons on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images (Fig. 1a–c). The brain stem was mildly hypointense on T1-weighted images (Fig. 1d). Small hyperintense focuses in the lateral parts of the cerebellum and cortical regions of occipital and parietal lobs were noted. Mild periventricular elevated signals were also present. There was no diffusion restriction on diffusion-weighted images (Fig. 2a). Apparent diffusion coefficient (ADC) images showed hyperintensity in the brain stem (Fig. 2b). Ultrasonography and MR urography showed atrophy of the right kidney and bilateral markedly hydronephrosis secondary to reflux nephropathia possibly as an etiologic factor for arterial hypertension.

In view of the clinical and typical imaging features, the diagnosis of atypical PRES was obtained. The patient rapidly recovered with antihypertensive treatment. CMRI 2 weeks

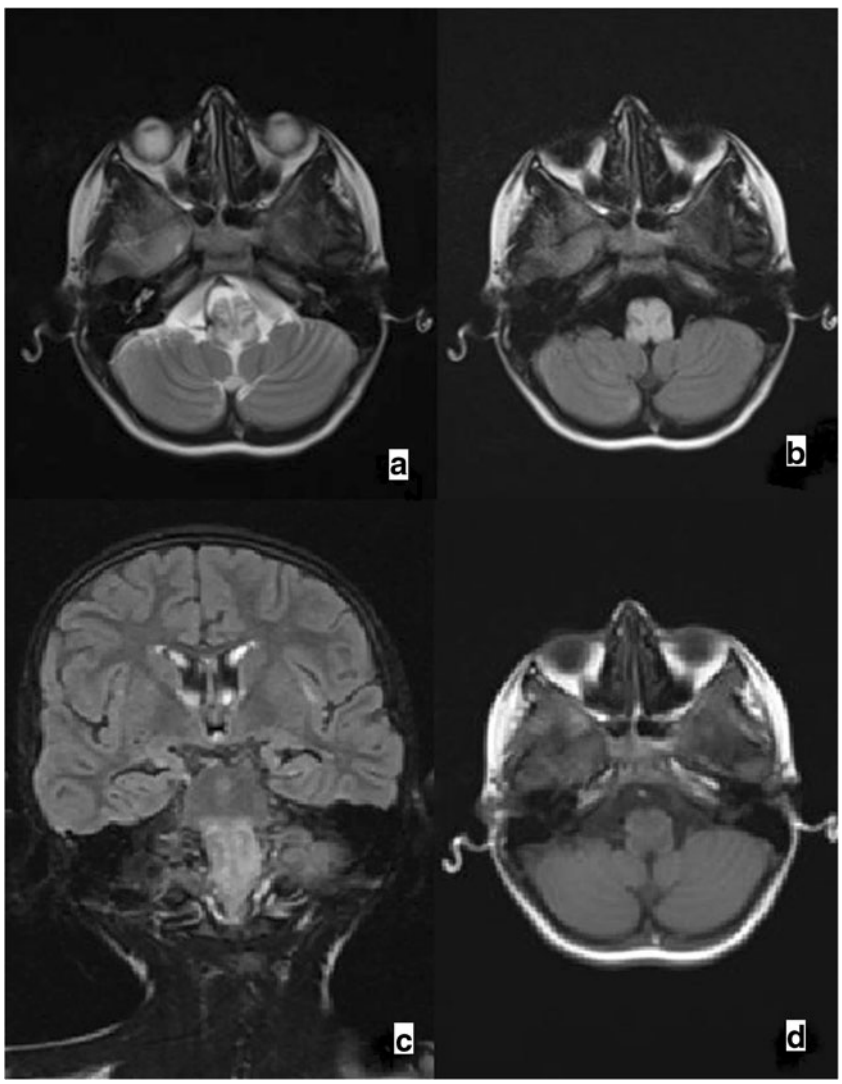

Fig. 1 CMRI of case 1. Axial plane T2-weighted image showed hyperintensity on bulbus (**a**). There were linear hypointensities on coronal plane which correlates with unaffected spinal neuronal pathways. Axial and coronal plane FLAIR images showed a hyperintense brain stem lesion with peripheral cerebellar lesions and periventricular hyperintensity (**b**, **c**). Axial plane T1-weighted image showed hypointense brain stem (**d**)

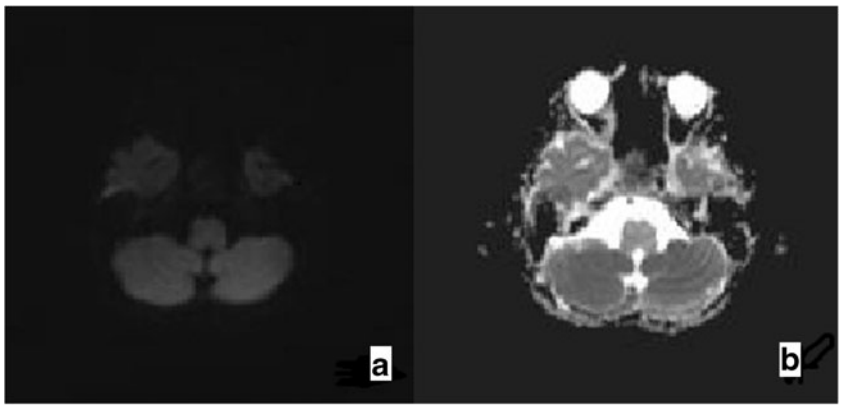

Fig. 2 CMRI of case 1. There was no diffusion restriction on diffusion-weighted images (**a**). ADC image showed hyperintensity that correlates with vasogenic edema (**b**)

later (Fig. 3a, b) indicated a resolution of hyperintensity confirming a variant of PRES secondary to hypertension with involvement of the brain stem.

Case 2

A 13-year-old boy admitted to our clinic with the complaints of fatigue and periorbital swelling for 10 days. His past medical and family history revealed nothing remarkable.

On physical examination, the body temperature was 36.7 °C, blood pressure was 120/70 mmHg, and pulse rate was 107/min. He had bilateral periorbital swelling with a normal fundus examination.

Laboratory studies showed the following data: hemoglobin, 13.2 g/dl; platelets, 310,000/mm^3; and white blood cell count, 11,900/mm^3. His serum blood urea nitrogen (BUN) was 67 mg/dl, creatinine 0.69 mg/dl, total protein 5.1 g/dl, albumin 2.9 g/dl, complements component 3 (C3) 1.02 g/l (0.9–1.8) and C4 0.09 g/l (0.1–0.4), sedimentation rate 67 mm/h, and C-reactive protein 132 mg/l (0–10). The antistreptolysin O (ASO) titer was highly elevated at 1,270 IU/ml. Hepatitis profile was negative, and cholesterol and triglyceride levels were within normal levels. Urinalysis revealed +3 proteinuria. Twenty-four-hour urinary protein excretion was 77 mg/m^2/h. Percutaneous renal biopsy showed findings consistent with acute poststreptococcal glomerulonephritis (APSGN).

Furosemide and methyl prednisolone 60 mg/m^2/day treatment was started. While his arterial blood pressure began to rise, furosemide was replaced with doxazosin. On the 7th day of hospitalization, his arterial blood pressure reached up to 150/100 mmHg, and he experienced a generalized tonicoclonic seizure for two times which were managed with diazepam and phenytoin treatment. CMRI revealed high signal intensities in frontoparietal lobes on T2-weighted images. There was no diffusion restriction on diffusion-weighted images. ADC images showed iso-hyperintensity in associated lobes (Fig. 4). These findings were consistent with PRES. No more seizure was observed during hospitalization. While his blood pressure was normal and proteinuria was recovered, he was discharged with phenytoin and methyl prednisolone treatment. Because the patient was lost to follow-up, a control CMRI could not be performed.

Case 3

A 4-year-old girl who was followed up with the diagnosis of nephrotic syndrome for 1 year admitted with generalized

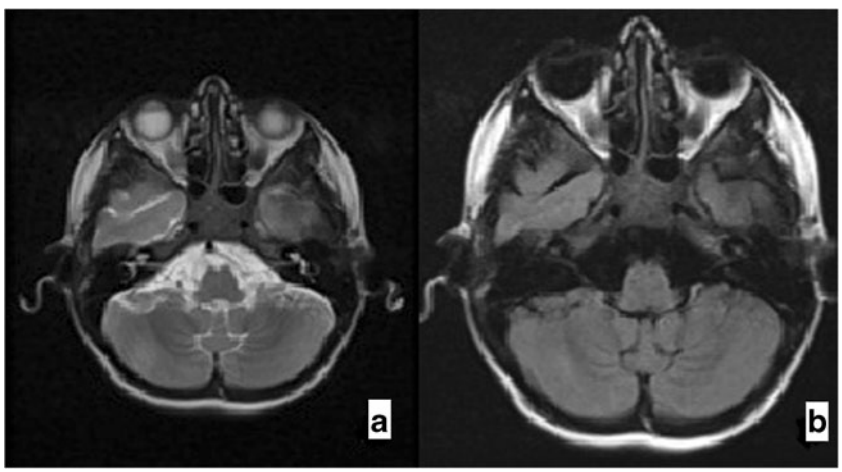

Fig. 3 Control CMRI of case 1 after 2 weeks. Axial plane T2-weighted (**a**) and FLAIR (**b**) images showed complete recovery

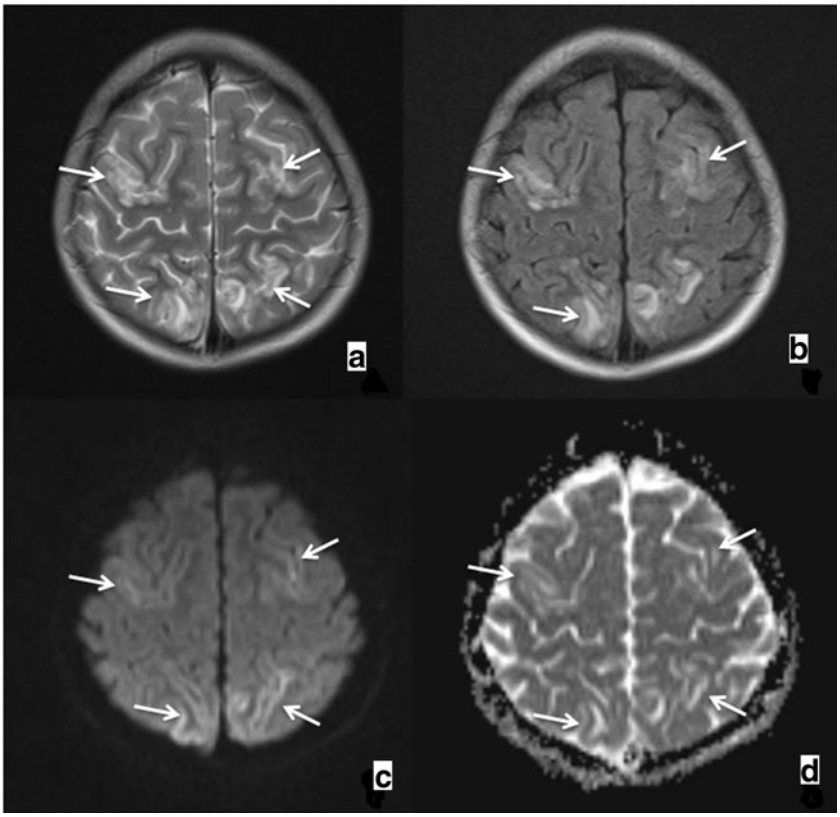

Fig. 4 CMRI of case 2. Axial plane T2-weighted (**a**) and FLAIR (**b**) images revealed hyperintense signal changes on bilateral frontal and parietal lobs at the level of vertex. Diffusion-weighted image (**c**) and ADC map (**d**) showed an increased intensity, excluding ischemia. Findings were well correlated with PRES

tonicoclonic seizure. She had been receiving cyclophosphamide, enalapril, and prednisolone for nephrotic syndrome.

Seizure was still continuing on admission. On physical examination, the body temperature was 36.6 °C, blood pressure was 170/110 mmHg, and pulse rate was 107/min. Other findings were normal. Seizure was stopped after diazepam and phenytoin administration.

CMRI images revealed a hyperintense signal on the cortical and subcortical white matter of the bilateral parietal and left occipital lobes. There was no diffusion restriction on diffusion-weighted images. No significant changes were seen on ADC images (Fig. 5).

The diagnosis of PRES was obtained. Hypertension was managed with sodium nitroprusside and nifedipine. The fundus examination was normal. During the follow-up, no more seizure was seen, and hypertension was controlled. She was discharged with phenytoin and doxazosin. A control CMRI after 1 month revealed a resolution of abnormal findings.

Discussion

PRES arises from failure of cerebrovascular autoregulation at high blood pressures, which results in cerebral hyperperfusion, interruption of the blood–brain barrier, and vasogenic edema. Autoregulation maintains a constant blood flow to the brain despite systemic BP alterations [1]. In animal models, an upper limit of BP at which cerebral autoregulation deteriorates has been reported. When this limit is exceeded, constricted arterioles dilate because of increased BP, and the increased perfusion overcomes the blood–brain barrier, allowing extravasation of fluid, macromolecules, and red blood cells into the brain parenchyma [6].

The knowledge of secondary hypertension in children is most commonly due to renal abnormalities, suggesting that the leading cause of PRES in childhood is renal diseases [7]. The etiology of HT of our patients was all renal problems including atrophic kidney, hydronephrosis secondary to reflux nephropathia, nephrotic syndrome, and APSGN.

PRES typically affects the parieto-occipital lobes. Subcortical white matter and cortex of the posterior circulation are the most frequently involved regions. Regions other than the parieto-occipital lobes, including frontal lobe, basal ganglia, thalamus, brain stem, and subcortical white matter, are rarely involved. High signal intensities on T2-weighted images are examined in these patients' MRIs [4, 10]. Brain stem involvement seen in our case 1 is extremely rare in children. There have been a few case reports with involvement of the brain stem in PRES, especially in adults [2, 3]. Diffuse hyperintensity in the brain stem predominantly affecting the pons in a patient with hypertensive crisis should alert one to the possibility of reversible brain stem edema, a variant of PRES because of hypertension. Moosa et al. reported a case of PRES in an 8-year-old girl with primary involvement of the

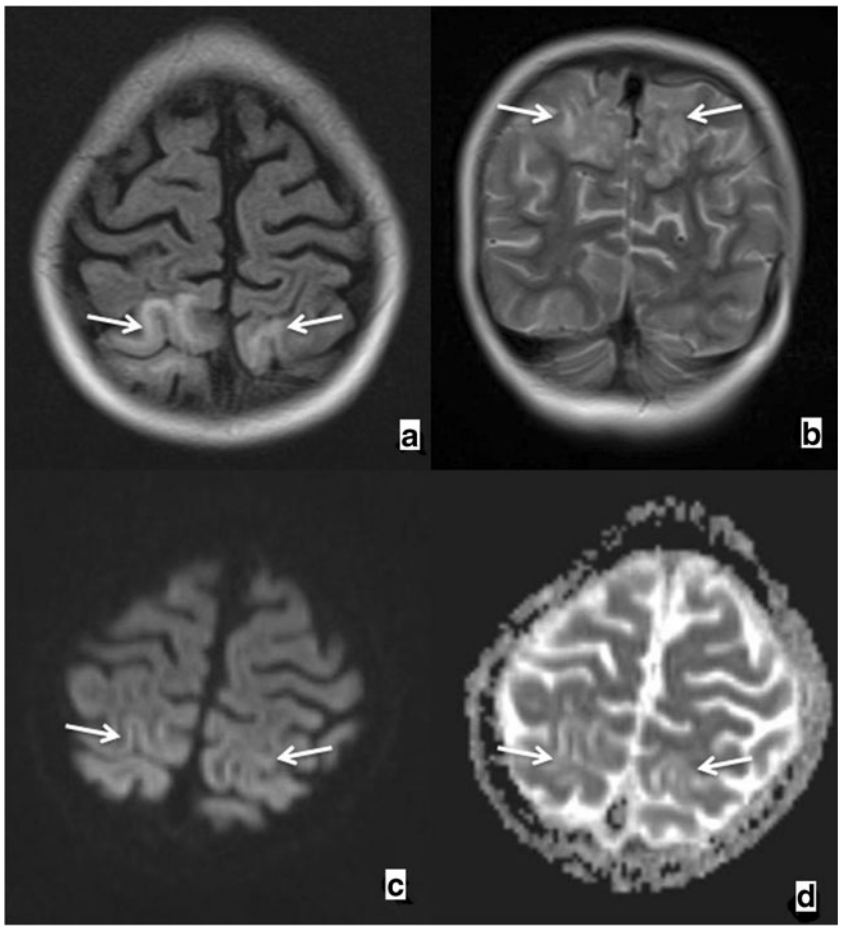

Fig. 5 CMRI of case 3. Axial plane FLAIR image (**a**) and coronal plane T2-weighted image (**b**) revealed an increased intensity on bilateral posterior parietal cortical and subcortical regions, symmetrically. These areas showed an increased intensity on diffusion-weighted image(**c**) and ADC map (**d**) that confirms vasogenic edema. Increased intensity on ADC map excludes cytotoxic edema

brain stem and thalamus [8]. It is unclear why children are less predisposed to this presentation which may be due to decreased incidence of hypertension in children than adults.

Cases with predominantly brain stem involvement should be differentiated from brain stem infarction, pontine glioma, central pontine myelinolysis, and infective encephalitis because the neurologic symptoms are reversible with precise treatment. In cases of PRES, areas of increased signal intensities on T2WIs show increased ADC values, representing vasogenic edema. This may be useful in differentiating PRES from infarction, and other metabolic brain disorders with cytotoxic edema in which ADC mapping values are decreased, and signal intensities are higher than those of surrounding brain tissue on DWI [9]. Our patient showed isointensity on diffusion-weighted images and hyperintensity on ADC. The MRI features of our patient were unusual in that they predominantly involved the brain stem.

In conclusion, PRES is a condition characterized by headache, nausea, vomiting, visual disturbances, focal neurologic deficit, and seizures in the setting of severe systemic hypertension. While secondary hypertension in children is most commonly due to renal abnormalities, PRES should be taken into account, especially in children with renal disease in the appropriate clinical settings. Clinical and radiological improvement is achieved by the control of high blood pressure. Primary involvement of the brain stem is rare in children. As there are a few reports of PRES with brain stem involvement, we think that this form of PRES is likely underdiagnosed.

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