

## Case Report

# Posterior Reversible Encephalopathy Syndrome (PRES); in a 5-year-old, dialysis dependent child with chronic kidney disease

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**Keywords:** posterior reversible encephalopathy syndrome (PRES), vasogenic cerebral edema, severe uncontrolled hypertension, haemodialysis.

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Received: July 2017, Accepted revised version August 2017, Published: October 2017

Competing Interests: Authors have declared that no competing interests exist

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## Introduction

Posterior reversible encephalopathy syndrome (PRES) is a reversible neurological condition characterized by vasogenic oedema of the brain due to a wide variety of causes. Headache, nausea, vomiting, blurring of vision and seizures are the commonest modes of presentation. Characteristic radiological findings in the CT and MRI confirm the diagnosis. Management includes the correction of reversible causes and supportive measures.

We present the timely diagnosis and management of PRES in a child with severe uncontrolled hypertension who was dialysis dependent.

## Case report

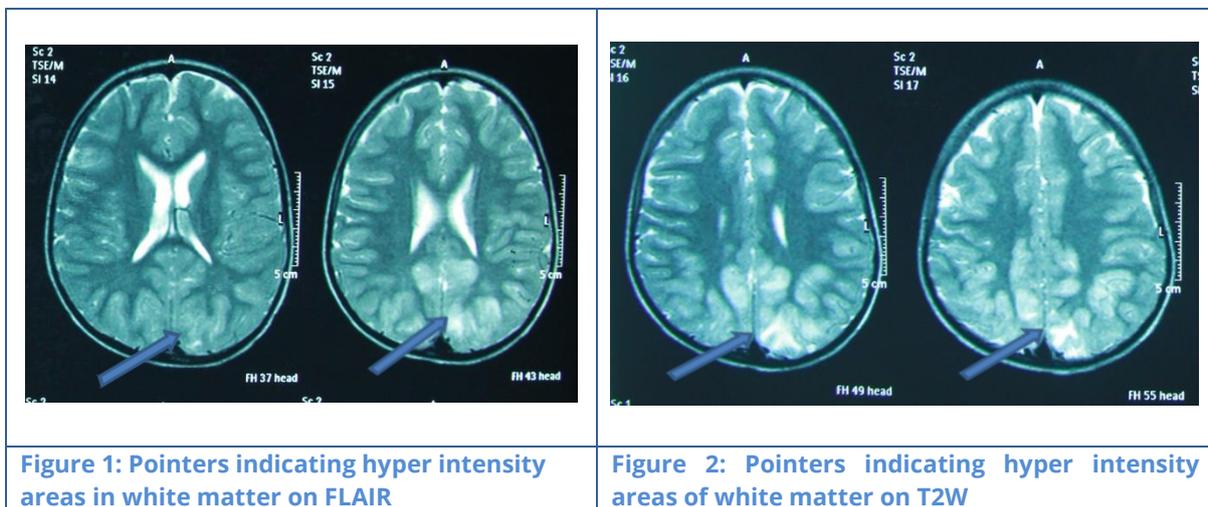
A 5-year-old boy, diagnosed to have chronic renal failure for two years, presented with a history of severe headache, blurring of vision and vomiting. On admission to the ward he was drowsy and febrile with no neck stiffness and had a pulse rate of 104beats/min, blood pressure of 190/110mmHg and a respiratory rate 20 breaths/min. On auscultation, his lungs were clear and he had an oxygen saturation of 99% on air. No focal neurological signs were detected.

Further inquiry revealed that he was on regular haemodialysis (HD) every other day and had undergone HD earlier that day. There had an alteration in the HD settings of the last HD, where the ultra-filtrate was reduced from 1litre to 500ml. He was on nifedipine 5mg twice a day for the last 6 months with reasonable blood pressure control. However, after admission his blood pressure did not respond to a combination of three oral antihypertensive agents (nifedipine, prazosin, losartan) and remained as high as 200/120 mmHg. A Few hours after admission, he developed recurrent generalized tonic-clonic seizures, not responding to anti-epileptics (midazolam, phenobarbitone) and progressed into status epilepticus. He was intubated and transferred to intensive care unit. Soon after

admission to the ICU, he developed frequent episodes of ventricular tachycardia but with stable haemodynamics.

Significant laboratory findings were significant for an elevated potassium level of 7.1 mmol/L (3.6-5.2 mmol/L) with normal sodium 136 mmol/L (135-145 mmol/L) and calcium 2.34 mmol/L (2.2-2.7 mmol/L). White cell count was in the normal range. He was anaemic with a haemoglobin 8.6 g/dL, PCV of 22.2% and platelet count of  $230 \times 10^9/L$ . His blood urea nitrogen level was 171.4 mg/dL (7-17 mg/dL), and serum creatinine was 15.01 mg/dL (17.7-70 mg/dL). PT, PTT, INR and liver profile were within normal limits. An arterial blood gas analysis on  $F_i O_2$  of 60% showed pH, 7.23;  $P_a CO_2$ - 35.0 mmHg;  $P_a O_2$ -230.0 mmHg;  $HCO_3^-$ , 16.5 mmol/L; lactate 2.5 mg/dL and oxygen saturation of 98.4%. His C-reactive protein level was 0.8 mg/dL

The differential diagnoses included, central nervous system infection, disequilibrium syndrome, hypertensive encephalopathy and PRES. Once the initial stabilization was done, the child was sent for imaging. MRI brain showed swelling of the cortex with increased T2W and fluid attenuated inversion recovery (FLAIR) signal intensity in bilaterally in the parietal and occipital lobes. Marked high intensity was noted in the deep aspects of the affected cortices/sub cortical white matter. The lesions showed low signal on T1W sequence. There was no contrast enhancement. Deep aspects of the lesions showed high signal on diffusion weighted imaging (DWI) and low signals on ADC map, consistent with restricted perfusion/cytotoxic oedema. There were T2W and FLAIR high signal intensities in the posterior aspect of the pons, parietally extending into the superior cerebellar peduncles. There were no space occupying lesions (SOL) and the ventricular system appeared normal. Findings were compatible with PRES.



He was paralyzed and ventilated for the initial few hours. Reasonable control of blood pressure was achieved with IV hydralazine and IV labetalol infusions. Elevated potassium levels were initially controlled with insulin dextrose and IV calcium gluconate. Continuous monitoring and other systemic support systems were established. After initial stabilization, he was sent for urgent hemodialysis.

Following dialysis, his blood pressure became well controlled and the ventricular tachy-arrhythmia completely settled following the dialysis. His level of consciousness improved and there were no further convulsions or development of focal neurological signs. He was extubated on the third day and sent to the ward on oral anti-hypertensive agents.

Outreach care was given during his ward stay. Renal function and other laboratory parameters returned to normal with haemodialysis given every other day. Repeat MRI on day 14 revealed complete resolution of the abnormalities. His overall condition was completely restored and the child is awaiting renal transplantation.

## Discussion

The human brain possesses the ability to maintain a constant blood flow within a wide range of mean arterial pressures (MAP) from 60 – 140 mmHg, which is described as cerebral autoregulation [1]. Sudden elevation of blood pressure and accumulation of vasoactive chemicals can disturb this autoregulation and result in disruption of the blood brain barrier causing brain damage [1].

PRES is a reversible neurological condition characterized by vasogenic oedema of the occipital and parietal lobes often associated with severe hypertension. Apart from elevated blood pressure, PRES has been described with; chronic renal failure [2], Chemotherapy [3], adrenocortical disease, organ transplantation, immunosuppressive drugs [4] and pre-eclampsia or eclampsia.

Several theories are proposed to explain the pathophysiology of PRES. The exact mechanism of the vasogenic oedema is uncertain. Two theories have been reviewed and suggested by Bartynski [5]. According to the first theory, severe uncontrolled hypertension disrupts cerebral autoregulation causing hyper-perfusion, arteriolar dilatation, endothelial damage and vasogenic oedema. This hypothesis is supported by the fact that sympathetic stimulation can right shift the upper threshold of the autoregulatory curve. Since the vascular beds of the posterior cerebral circulation are sparsely innervated by sympathetic nerves the damage is more prominent in these vascular territories [6]. However, there is some conflicting evidence, such as blood pressure being either normal or minimally elevated in some cases [7, 8] and the severity of vasogenic oedema not always correlating with the degree of hypertension [9]. The second theory states that cerebral vasoconstriction due to various factors results in hypo-perfusion of the brain leading to ischaemia, capillary leak and vasogenic oedema. This theory explains the association of PRES with systemic diseases such as chronic kidney disease, and pre-eclampsia [10]. Many cases have been reported due to elevated blood urea in patients with CKD in the presence of normal or slightly elevated blood pressure. In summary, PRES is the cumulative effect of cerebral hypo-perfusion, endothelial dysfunction and ischaemia in the presence of systemic conditions.

The prevalence of PRES among children is not established; however, hypertension, renal disease, immunosuppression, and chemotherapy of malignancies are triggers for PRES irrespective of age group. Seizures, headache, visual disturbances and altered level of consciousness are the commonest presentations of PRES in children [5]. Pallor, fever,

malaise and flushing have also been reported in the context of PRES. Our patient presented with a history of headache and blurred vision, and was found to have very high blood pressure which was resistant to antihypertensive medications. A reduced level of consciousness was noted soon after admission and then he developed repeated convulsions which required elective intubation and ventilation. A few differential diagnoses were considered including disequilibrium syndrome, CNS infection, hypertensive encephalopathy and PRES.

The diagnosis of PRES can be made either with CT or MRI using DWI. Focal regions of asymmetrical abnormalities in the watershed areas of the brain are seen in the posterior and parieto-occipital lobes bilaterally. These abnormalities demonstrate the areas of vasogenic oedema. The spared medial occipital structures help to distinguish PRES from posterior cerebral artery infarcts [11]. Abnormalities are also seen in the temporal lobes, cerebellum, basal ganglia and brain stem showing high signal on T2-weighted attenuated FLAIR sequences. Complete resolution of the radiological abnormalities are observed in repeat MRI once the causative factor is reversed. Permanent structural damage can occur in the presence of haemorrhages [6]. In our case, there were increased T2 weighted FLAIR signals in the occipito-frontal lobes, pons and cerebellar peduncles bilaterally, with high signals on DWI and low signals on ADC map, resembling restricted diffusion or cytotoxic oedema. The overall MRI radiological appearance was compatible with PRES.

In our patient, the possibility of CNS infection was clinically excluded by the absence of clinical features such as a contact history, fever, neck stiffness, elevated WBC count or CRP. Since the blood urea levels were within the normal range and not significantly reduced with the previous dialysis, the possibility of dialysis disequilibrium syndrome was also excluded. The cardiac instability was attributed to the high serum potassium level which was temporarily controlled with insulin dextrose and calcium infusion followed by urgent hemodialysis.

Hypertensive encephalopathy giving rise to PRES was the leading differential diagnosis and was confirmed with the radiological evidence. Further investigations such as lumbar puncture and CSF culture were abandoned since there was no strong clinical evidence to suspect a diagnosis other than PRES. Initial blood pressure control required intravenous antihypertensives. His condition improved with gradual control of blood pressure and electrolyte optimization after haemodialysis. There was complete clinical recovery of and disappearance of radiological abnormalities was seen in the repeat MRI after 2 weeks.

## Conclusion

PRES is a rare condition among children. Aetiology and presentation can vary. Clinical suspicion and early radiological investigation is the key to diagnosis. Early administration of effective therapy will reduce unnecessary interventions and shorten the length of hospital stay.

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