**Case Report**

# Status epilepticus due to posterior reversible encephalopathy syndrome in a Sri Lankan child with nephrotic syndrome.

K.H.D. Madhusankha[1*], L. Kumarasiri[2], D. Jayasekara[2], T. Bandara[2]
[1]Postgraduate Institute of Medicine, University of Colombo, Sri Lanka
[2]National Hospital, Kandy, Sri Lanka

**Abstract**

The Posterior Reversible Encephalopathy Syndrome (PRES) is an acute clinical condition that is characterized by multiple neurological symptoms such as seizures, impairment of consciousness, headaches, visual abnormalities, nausea, and vomiting. The characteristic imaging finding is vasogenic oedema predominantly in the parieto-occipital white matter of the brain. Delaying seizure control, refractory status epilepticus, and malignant PRES carry high morbidity and mortality. We report a case of Sri Lankan girl with nephrotic syndrome developing status epilepticus due to PRES.

**Keywords:** status epileptics, posterior reversible encephalopathy syndrome, nephrotic syndrome



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*✉ **Correspondence:** dammika.edu@gmail.com, https://orcid.org/0000-0001-9005-6398

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## Introduction

Status epilepticus is a pediatric neurological emergency, and currently, it is defined as clinical or electrographic seizure activity lasting for more than 5 minutes or recurrent seizures without recovery between seizures [1]. This seizure activity can be convulsive, non-convulsive, focal or myoclonic. Early provision of appropriate treatment prevents morbidity and motility, including permanent brain damage. Refractory status epilepticus is status epilepticus that does not respond to appropriate antiepileptic drugs and carries a bad prognosis. There are multiple etiologies for status epilepticus, either known epilepsy disorder or other seizure disorders secondary to systemic illness. Common etiologies are central nervous system infection, metabolic abnormities, head injury, toxins, hypoxia and hypertensive emergency.

Here we discuss status epilepticus due to Posterior Reversible Encephalopathy Syndrome in a 9 years old girl diagnosed with Nephrotic Syndrome. Posterior Reversible Encephalopathy Syndrome (PRES) is an acute clinical condition characterized by multiple neurological symptoms such as seizures, impaired consciousness, headaches, visual abnormalities, nausea, and vomiting. Characteristic imaging changes due to vasogenic oedema are predominantly seen in the parieto-occipital white matter of the brain. In the majority of cases, it is reversible if detected and treated early [2].

Although the pathophysiology of PRES is not fully understood, certain theories are suggested for understanding it. The most popular theory is that; acute hypertension may be associated with dysfunction of cerebral autoregulation, causing the breakdown of the blood-brain barrier and leading to extravasation from vessels into the brain parenchyma. Poor sympathetic

innervation in the posterior circulation predisposes predilection for brain oedema in this region [2].

The occurrence of a PRES has been described in all decades of life, with a peak in young to middle adulthood, but this can occur in small children as well as in elderly people. Systemic hypertension is the most common cause, but there are other etiologies, including immunosuppressant drug use, organ transplant, nephrotic state, and sepsis.

Children who receive prolonged steroid therapy or calcineurin inhibitor therapy for nephrotic syndrome are at risk of developing PRES [3].

**Case Report**

A 9-year-old Asian girl was diagnosed with nephrotic syndrome at the age of 5 years. She has been a frequent relapser showing poor response to prednisolone. Her last relapse was eight months before the current admission. She had been marked by frequent relapse and high-dose steroid dependence. Her renal biopsy was done at the age of eight, compatible with minimally changed nephrotic syndrome. She was started on tacrolimus 1mg twice daily. There was good compliance for the first three months and deflated treatment afterwards. She was off treatment and follow-up for six months duration.

She was brought to our Emergency Department (ED) with a one-day history of headache and two episodes of vomiting followed by three episodes of generalized tonic-clonic seizures lasting 30 minutes without regaining consciousness. The patient's history did not reveal head injury, febrile illness or drug overdose.

On examination, it was observed that she was drowsy. Her pulse rate was at 125 beats/min, her blood pressure was at 120 / 84 mm of Hg (below 99th percentile for age and sex), and her oxygen saturation was at 70% in the ambient air, which was corrected with face mask oxygen. Her pupils were bilaterally equal and reacting to light. The rest of the neurological examination was unremarkable. Her status epilepticus was managed according to the Advanced Pediatric Life Support protocol (APLS), and seizures were resolved after administering IV midazolam two boluses and IV phenobarbital loading dose. IV levetiracetam was given to prevent seizures from recurring.

Urine analysis showed trace proteinuria without hematuria. The urine protein to creatinine ratio was 0.53 g/day, which suggests non-nephrotic range proteinuria (>3.5g/day). Serum creatinine was 2.7 mmol/L (2.5-8.2), and BUN was 12 mg/dL. Serum $Na^+$ was 138 mEq/L, $K^+$ was 3.8 mEq/L. There was a high serum total cholesterol level of 608mg/dL (<200mg/dL). Serum-corrected calcium was 1.95mmol/l (2.25-2.625), which was corrected with IV calcium gluconate infusion. Her vitamin D levels and parathyroid hormone levels were 35ng/mL (20-40) and 38pg/mL (10-55), respectively.

A Non-Contrast Computed Tomography (NCCT) scan of the brain conducted after stabilizing the patient showed no abnormality, which also ruled out some differential diagnoses like cerebral haemorrhage, subarachnoid haemorrhage, head trauma, tumour or malformation. According to the electroencephalogram, evidence of moderate encephalopathy with focal seizure tendency in the occipital regions was observed, and the features were consistent with PRES.

A Magnetic Resonance Imaging (MRI) of the brain was done (see figure-1), and it demonstrated T2W and FLAIR high signal intensities in the B/L posterior parietal regions and right side temporo-parietal region, involving mainly the grey matter with restricted diffusion on DWI. The affected areas are edematous, and the MRI findings confirmed the diagnosis of PRES.

The seizures were controlled by administering IV levetiracetam twice daily with standard supportive care, and the patient was discharged on oral levetiracetam. Reassessment after one month showed normal neurological function without subsequent seizure episodes.

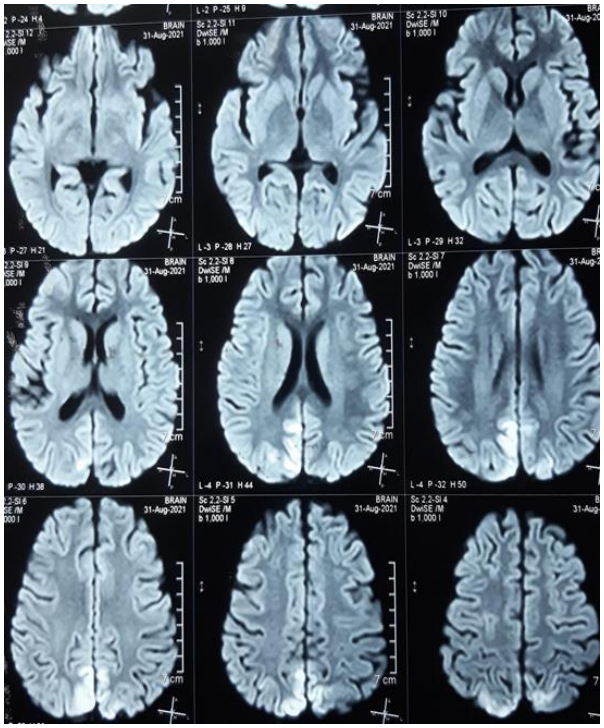

**Figure 1:** MRI of the brain showing T2W and FLAIR high signal intensities in bilateral posterior parietal regions and right sidedtempro-parietal region, involving mainly grey matter.

**Discussion**

Managing a patient with nephrotic syndrome is challenging because multiple medical complications can deteriorate the disease course. Among them, PRES is potentially serious unless the disease progression is controlled soon. PRES was initially described as reversible posterior leukoencephalopathy syndrome in 1996, and the main risk factors identified as hypertension, renal insufficiency and immunosuppressive drugs [4]. However, the same report also mentions many other risk factors, including abnormal vascular endothelial autoregulation, electrolyte disturbance and co-existing multiple risk factors. Nephrotic syndrome patients are identified as having a high risk of developing PRES as they pose multiple co-existing risk factors [4,5].

Patients with nephrotic syndrome are exposed to PRES because kidney disease and hypertension are correlated, and systemic hypertension is considered one of the most common causes associated with PRES. A study conducted to find blood pressure fluctuations in PRES found that only 52% of the cases are directly correlated with hypertension [6]. This case study showed upper normal blood pressure for the age and sex with other risk factors such as electrolyte disturbances, perturbation in volume, renal dysfunction along with the immunosuppressive drugs and their degree of toxicity are all risk factors for the development of PRES [5,6].

The nephrotic condition poses a particular risk for PRES because of multiple risk factors. These patients are often hypertensive, receive steroids, have severe hypoproteinemia or tissue oedema with fluid retention, changes in vascular permeability, immunosuppressive drugs and electrolyte imbalance. Unlike adults, pediatric patients' cerebral blood flow autoregulation is not well developed, making them more susceptible to PRES [6,7].

The clinico-radiological picture in children and adults is the same, and the gold standard for diagnosing PRES is MRI brain. Hyperintensities are seen in T2-weighted or FLAIR sequences showing oedema, usually in the parietal and occipital region (see figure1). The involvement of regions such as the frontal lobe, cerebellar hemisphere, basal ganglia, and deep white matter can also be seen. Lesions are often subcortical, bilateral and symmetrical in the parieto-occipital regions [2,8]. Computed Tomography (CT) is frequently abnormal, with diffuse posterior hypodensities not taking up the contrast. In these cases, imaging is important in eliminating urgent and fatal diagnoses, including cerebral thromboembolism, a known complication frequently reported in patients with nephrotic syndrome and other serious acute cerebral insults, which may mimic a clinical picture of PRES.

The therapeutic strategy for PRES depends on its aetiology and severity. Recognizing and stopping the triggering factor is one of the first and easy and saving steps. There is no specific consensus for prescription antiepileptic or antihypertensive drugs in treating PRES, but the cornerstone of treatment is treating high blood pressure and controlling seizures [2,5]. So, in this case, we used advanced pediatric life support guidelines to control status epilepticus and institutional protocol for post-seizure supportive care. The Advanced Pediatric Life Support (APLS) status epilepticus initial management protocol gives clear, time-sensitive management steps.

The prognosis of PRES is generally good, and the majority of patients return to their normal baseline, as indicated by the name of the pathology. Total recovery has been reported in cases by a percentage of 75-90%, and recovery occurs within a week, while for some patients, it may take a longer time interval with the presence of sequelae of 10-20 %. The mortality rate has been estimated at 3-6% of cases [3,5]. Recurrent PRES has been observed in 4% of cases [7]. Malignant PRES is a persistent low Glasgow coma scale below eight despite medical management and radiological findings such as intracranial haemorrhage, mass effect, infarction or cerebral herniation [5].

As PRES can be the origin of brain insult, it can lead to serious neurological complications and cause life-threatening conditions such as oedema in the posterior cerebral fossa, which can compress the brainstem, hydrocephalus or increased intracranial pressure. The prognosis also depends on the underlying cause of PRES, the time to treatment, and the imaging results. However, our patient showed improvement in visual acuity, blood pressure control, and seizure control one month after the initial presentation.

**Conclusion**

Posterior reversible encephalopathy syndrome is a potentially life-threatening condition that should be considered during the seizure activity of a nephrotic syndrome patient. Early control of seizure activity according to APLS protocol followed by risk factor modification is one aspect of the initial management. Delaying seizure control, refractory status epilepticus, and malignant PRES carry high morbidity and mortality. However, the prognosis remains favourable if the treatment is commenced early, as evidenced by our case study.

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