

## Posterior Reversible Encephalopathy Syndrome (PRES) Presenting with Status Epilepticus in the Context of Post-Streptococcal Glomerulonephritis

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### Abstract

**Background:** PRES is an increasingly recognized cliniconeuroradiological disorder, presenting with headache, nausea, vomiting, seizures, altered consciousness and visual disturbances. It is mainly associated with kidney disease, organ transplantation, immunosuppressives, autoimmune diseases and eclampsia. Typical MRI findings include white matter vasogenic edema predominantly affecting the posterior parietaloccipital lobes of the brain. The symptoms may persist for several days and the radiological findings resolve within few weeks.

**Case-diagnosis/treatment:** We report a previously healthy 7-year old patient, who presented with status epilepticus, following a 2-day history of nausea, vomiting and headache. The patient was afebrile and had no history of epilepsy or recent history of head trauma or ingestion of toxic substances. During the seizures, raised systolic blood pressure was recorded. Periorbital edema and proteinuria were noted for 24 hours post-seizure. Persistent microscopic hematuria and hypertension were also recognized. Based on a positive personal history of tonsillitis 2 weeks before the onset of the seizures, persistent microscopic hematuria, raised blood pressure for one week, low C3 and C4 levels, raised Antistreptolysin O titer and typical MRI findings that resolved 4 weeks later, PRES was diagnosed in the context of post-streptococcal glomerulonephritis.

**Conclusions:** PRES should always be considered in patients with glomerulonephritis presenting with acute hypertension and rapidly progressive neurological manifestations. Since it is often unsuspected, prompt recognition and treatment is important for the resolution of the symptoms and radiological features, as well as for preventing unnecessary investigations and therapies.

**Keywords:** Hematuria; Hypertension; Post-streptococcal glomerulonephritis; PRES; Proteinuria; Status epilepticus

### Introduction

Posterior Reversible Encephalopathy Syndrome (PRES), previously known as Reversible Posterior Leukoencephalopathy Syndrome, represents a distinctive clinical entity characterized by neurological symptoms and specific radiological findings. The syndrome was initially described in adults with kidney insufficiency, eclampsia, Systemic Lupus Erythematosus and immunosuppression.

The clinical presentation of PRES is variable and includes altered consciousness, seizures, headache, nausea, vomiting, and visual disturbance [1]. The syndrome is associated with eclampsia or preeclampsia, chronic kidney disease, acute kidney injury, nephrotic syndrome, hemolytic uremic syndrome, acute glomerulonephritis, immunosuppressive drugs (cyclosporine, tacrolimus, monoclonal antibodies, high-dose corticosteroids, and chemotherapy), thrombotic thrombocytopenic purpura, autoimmune diseases, solid organ transplantation, leukemia. In the majority of the cases, severe hypertension is present and possibly represents the trigger for the evolution of the syndrome.

Vasogenic edema is the proposed pathophysiological mechanism. Two controversial theories have been suggested as the predisposing

factors for the edema. The most popular theory is interruption of brain auto-regulation, resulting in hyper-perfusion and cerebral vessel damage. An alternative theory suggests the presence of endothelial dysfunction and hypo-perfusion secondary to systemic inflammation [2].

Typical MRI head findings involve bilateral abnormalities in the white matter of the posterior regions of, most commonly, the occipital and parietal lobes of the cerebral hemispheres. The MRI findings are not always confined to the white matter or the posterior cerebral areas and they are potentially reversible [3].

Blood pressure control, withdrawal of the responsible drug and the elimination of any other possible cause are of critical importance for enhancing recovery and avoiding complications.

The prognosis of the syndrome is accepted as benign, albeit rare complications, such as intracranial hemorrhage or cerebral infarction, have been reported, particularly in the context of prolonged seizures or persistent hypertension [4].

There have been reports of PRES in children with predisposing factors, but the prevalence of the syndrome in the pediatric population is unknown [5]. Because PRES remains poorly understood and it has mainly been described in the adult population, it is often unsuspected and remains undiagnosed in children, especially out of the setting of chronic kidney disease, chemotherapy or immunosuppression. Since

children share the same predisposing factors with adults, they are probably at similar risk for developing the syndrome; therefore the prevalence of this condition in the pediatric population is probably higher than estimated.

### Case Presentation

We report a 7-year old boy who presented with status epilepticus in the form of 2 episodes of seizures, 20 minutes apart. The first episode occurred while the patient was in sitting position and involved loss of consciousness, loss of muscle tone, urine loss and perioral cyanosis. The episode lasted 15 minutes and was followed by a 10-minute postictal phase. 20 minutes later, and whilst the patient had reached the hospital, a second episode of generalized tonic-clonic seizure followed. He received two doses of diazepam and a loading dose of Phenytoin before the seizures were controlled.

The history started 2 days before the seizures occurred, with occasional nausea and vomiting, as well as headache that woke the patient up the two previous nights. Fever was not reported.

From the recent medical history, the patient was previously fit and well, with normal development and no history of seizures, recent head trauma or ingestion of medications/toxic substances. The patient had autoimmune neutrophilia for 2 years, until the age of 4 years, and was treated for hypothyroidism for 2 years from the age of 2 years.

There was no family history of epilepsy or other chronic medical conditions.

On examination, the patient was drowsy. His vital signs were: Blood pressure: 170/84 mmHg, heart rate: 69/min, SatO<sub>2</sub>: 96% and he was apyrexial. There were no signs of meningism, his pupils were equal and reactive and bilateral peri-orbital edema was noted. The rest of the physical examination was unremarkable.

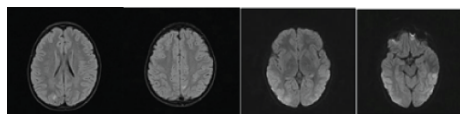
Laboratory tests, including renal function and electrolytes, were within normal range and the inflammatory/infection markers were -ve. Urinalysis revealed microscopic haematuria and a 24 hour urine collection exhibited significant proteinuria. The results of the blood and urine investigations are shown in Table 1.

<b>Hct (%): 37.0</b>	
<b>Hb (g/dl): 12.7</b>	K (mmol/l): 4.6
<b>WBC (/mm<sup>3</sup>): 8920</b>	
<b>(P:72.9%, L: 19.1%, M: 5.9%)</b>	Na (mmol/l): 137
	Ca (mg/dl): 9.6
	Cl (mmol/l): 108
<b>PLT (/mm<sup>3</sup>): 285000</b>	Mg (mg/dl): 2.2
<b>CRP (U/l): 0.2</b>	SGOT (U/l): 25, SGPT (U/l): 15, $\gamma$ GT (U/l): 11
<b>Glu (mg/dl): 113</b>	LDH (U/l): 323, ALP (U/l): 82, CPK (U/l): 102
<b>BUN (mg/dl): 31</b>	Creat (mg/dl): 0.6
	Urinalysis (Day 1): Hb:+2, WBC: 2-4, RBC: 15-20, protein: +1
	24 h urine protein: 178 mg
<b>Venous blood gas: pH:7.337, pCO<sub>2</sub>:41.9mmHg, HCO<sub>3</sub>:22.5 mmol/L</b>	Urinalysis (Day 11): Hb: +3, WBC: 1-2, RBC: >100, protein.
<b>Renin (pg/ml): 20, 2</b>	
<b>Aldosterone (pg/ml): 41, 4</b>	Ena/Ro/La/RNP/SCL70/CENP/Histones/Jo1: -
<b>C-ANCA</b>	
<b>P-ANCA</b>	IgG (mg/dl): 2170, IgA (mg/dl): 257, IgM (mg/dl): 62, IgE (IU/ml): 17 (within normal range)
<b>Anti-dsDNA</b>	C3 (mg%): 7
<b>ANA</b>	C4 (mg%): 12
<b>ASTO (mg/dl): 2360</b>	

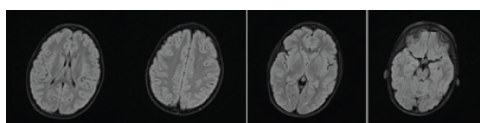
**Table 1:** Blood and urine results during hospitalization.

A fundoscopy showed no abnormal findings, whereas an urgent CT head scan excluded intra- and extracerebral haemorrhage, but revealed abnormal architecture of the right parietal cerebral cortex. Subsequently, a MRI head scan was performed that revealed regions of hyperintense signal in Axial T2 Weighted/T2 FLAIR sequences,

suggestive of vasogenic oedema, within the occipital and parietal regions, as shown in Figures 1 and 2. Most lesions were symmetrical, with right lobe predominance. An EEG showed no abnormalities.



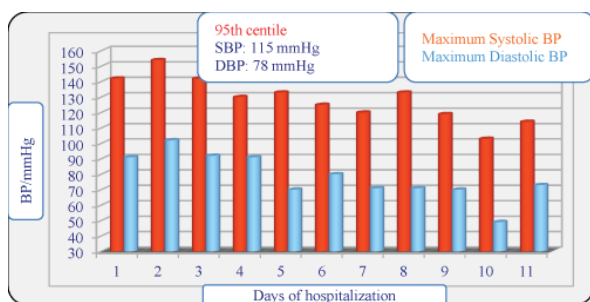
**Figure 1:** MRI images on diagnosis: regions of hypointense signal, suggestive of vasogenic oedema, within the occipital and parietal regions. Most lesions were symmetrical, with right lobe predominance.



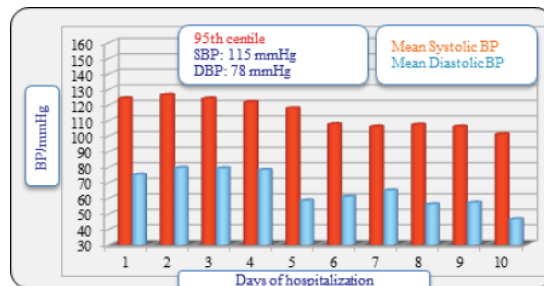
**Figure 2:** MRI images 4 weeks after diagnosis-normalized.

### Clinical Course

The patient recovered completely from the post-ictal phase within hours from admission and remained afebrile and in very good mental state and clinical condition for the 11 days of his hospitalization. The periorbital edema and proteinuria persisted for the first 24 hours, whereas microscopic haematuria remained until the day of discharge. Persistent systolic and diastolic hypertension (SBP and DBP > 95th centile) was noted with gradual improvement. The maximum blood pressure readings reached normal levels after day 8 of hospitalization, whereas mean blood pressure levels normalized after day 5. The progress of the blood pressure levels during hospitalization are shown in Figures 3 and 4. Renal function was closely monitored and was not impaired at any time. Maximum concentrations of creatinine were 0.7 mg/dl. A cardiology assessment, including an ECG and a cardiac echocardiogram, showed no pathology. A renal ultrasound was also normal.



**Figure 3:** Maximum blood pressure measurements during hospitalization.



**Figure 4:** Mean blood pressure measurements during hospitalization.

Because of the persistent hypertension and microscopic hematuria, a more detailed history was obtained, which revealed an episode of tonsillitis 2 weeks before the episodes of seizures. Antistreptolysin titers were tested and were found significantly elevated (2360 mg/dl), whereas C3 and C4 concentrations were low (C3: 7 mg%, C4: 12 mg%) (Table 1).

The combination of the 2 episodes of seizures, the antecedent symptoms of nausea, vomiting and headaches, the recent history of tonsillitis, the elevated ASTO titers, the evidence of nephritis and the typical findings in the MRI head scan, confirmed the diagnosis of PRES syndrome secondary to post-streptococcal glomerulonephritis.

The patient received Phenytoin for 7 days, following the recommendation of a Paediatric Neurologist, and presented with no more episodes of seizures or neurological symptoms. He also received antibiotic treatment for 10 days. He was discharged 11 days after the episodes of seizures and was followed up by a Paediatric Nephrologist thereafter. On a 24-hour blood pressure monitoring post discharge, 30% of the systolic BP measurements and 34% of the diastolic BP measurements were above the 95th centile for height. The following days, the BP measurements normalized further and remained normal. Because of the restoration of the BP levels soon after the diagnosis of PRES was established, treatment with anti-hypertensives was not initiated.

The patient was followed up once weekly and random urine protein and urinalysis were monitored. BP measurements were assessed on a daily, subsequently weekly and then monthly basis. Microscopic haematuria is still on-going 4 months post-diagnosis, with no other remaining signs of nephritis. C3 and C4 concentrations normalized 6 weeks later.

A repeat MRI scans 4 weeks post-seizures showed resolution of all the abnormal findings (Figure 2).

### Discussion

PRES is a rare clinicoradiological disorder that is considered to be a variant of hypertensive encephalopathy, with hypertension being the most commonly associated feature. Although it has mainly been described in the adult population, increasing experience regarding the paediatric population is evolving. Several studies have described children with PRES in the setting of acute renal failure, chronic nephritis, vasculitis, malignancy, nephrotic syndrome and a history of use of medication [6-8]. However, the syndrome is extremely rare in previously healthy children with not known renal disease and, to our

knowledge; just a few cases of PRES have been described in children secondary to streptococcal glomerulonephritis.

Our case demonstrates that PRES should be suspected and searched for in children with previously unremarkable medical history, when hypertension or renal disease and neurological symptoms are present. Acute glomerulonephritis is a clinical scenario that the general Pediatrician quite often encounters, therefore PRES should be considered as a possibility when neurological manifestations become evident in such a setting. Because of the low index of suspicion, prompt identification and treatment of the syndrome is of critical value for the resolution of the symptoms and radiological features and in order not only to avoid unnecessary investigations and treatments, but also complications, such as permanent neurological deficit.

### Disclosures

None.

### Conflict of Interest

The authors declare that they have no conflict of interest.

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