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## Case Report

# Posterior reversible encephalopathy syndrome (PRES) in a 6-year-old child with nephrotic syndrome

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## ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) is a variable etiology clinical syndrome with similar neuroimaging results and clinical symptoms. PRES can develop in both adults and children and is characterized by headaches, disorders of consciousness, seizures and especially focal visual disturbances, often associated with hypertensive state. In most cases, symptoms resolve without neurological consequences. The treatment strategy concerns early diagnosis and general measures to correct the underlying cause of PRES. Here, we report a case of PRES that occurs in a 6-year-old child with nephrotic syndrome.

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## Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinical syndrome which, although it may be due to various causes, occurs with similar neuroimaging results and clinical symptoms. It was first described by Hinchey in 1996 [1] and is characterized by a variable combination of consciousness deficit, convulsive activity, headache, vomiting, visual abnormalities (hemianopsia or cortical blindness) and focal neurological signs. Computed tomography (CT) and magnetic resonance imaging (MRI) images typically show symmetrically

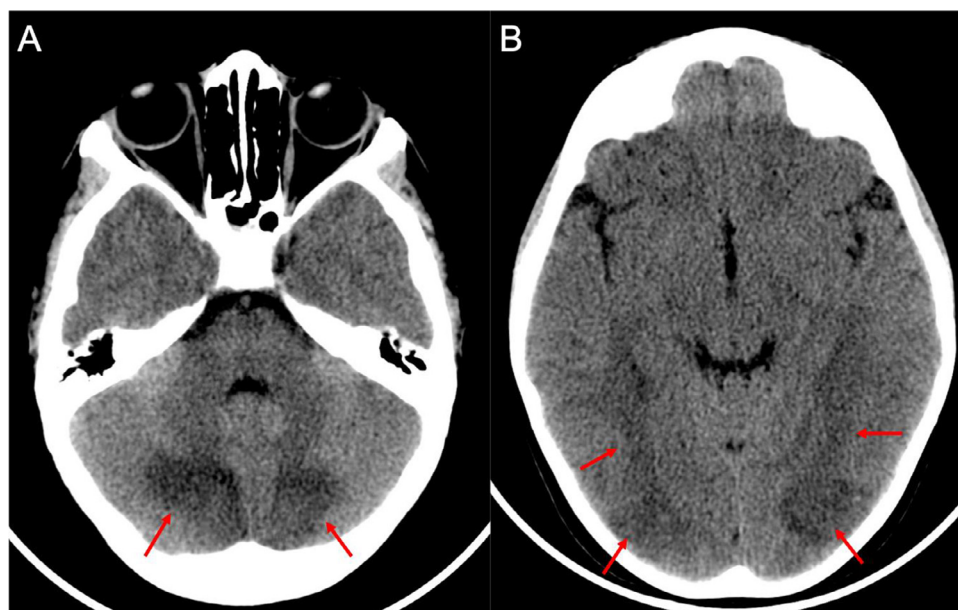
distributed areas of vasogenic edema, mainly within posterior circulation territories. PRES can develop in association with a wide range of clinical conditions including hypertension, systemic infections, organ transplants, autoimmune diseases (such as SLE or Wegener's granulomatosis), malignant tumors, chemotherapy and immunosuppression (especially with calcineurin inhibitors) [2–4]. The pediatric patient suffering from nephrological pathology, primary or secondary, acute or chronic, is a patient at high risk of developing acute neurological complications due to electrolyte imbalance, hemodynamic instability and the therapies used (dialysis and pharmacology). During the management of pediatric patients with

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**Fig. 1** – Brain CT scan documented a bilateral edema involving the cerebellum (A) and parieto-occipital lobes (B) (red arrows).

nephrotic syndrome, among the many medical complications that worsen the course of the disease, PRES is potentially serious if not recognized [5,6]. Here we present a case of PRES in a 6-year-old child with nephrotic syndrome.

### Case presentation

A 6-year-old Moroccan child, followed in his country for nephrotic syndrome, was admitted to our pediatrics unit for severe generalized body edema, proteinuria (18,600 mg/day), low serum albumin (0.9 g/L), high serum cholesterol (468 mg/dL). His blood pressure was 122/77 mmHg and heart rate was 86 beats/min. We treated him with intravenous steroids, albumin supplementation and continued cyclosporine. While his general condition was improving, on the seventh day of hospitalization he developed headache, vomiting, dizziness, temporal blindness. His blood pressure was 143/109 mmHg, heart rate was 80 beats/min and peripheral capillary oxygen saturation was 99%.

Laboratory tests were negative for infection. His venous blood gases, glucose level, as well as magnesium and calcium levels were normal. He had a low serum albumin of 2.56 g/L, normal serum urea of 23 mg/dL, normal serum creatinine of 0.15 mg/dL and normal serum electrolyte levels. A noncontrast CT scan was performed and showed symmetrical hypodensity in the cerebellum and parieto-occipital lobes (Fig. 1). After a few hours he developed 2 episodes of generalized tonic-clonic convulsion, followed by unconsciousness which were treated with rectal midazolam and required oxygen mask therapy and pediatric resuscitator intervention.

He was quickly transferred to the intensive care unit. MRI with fluid-attenuated inversion recovery showed cerebellar

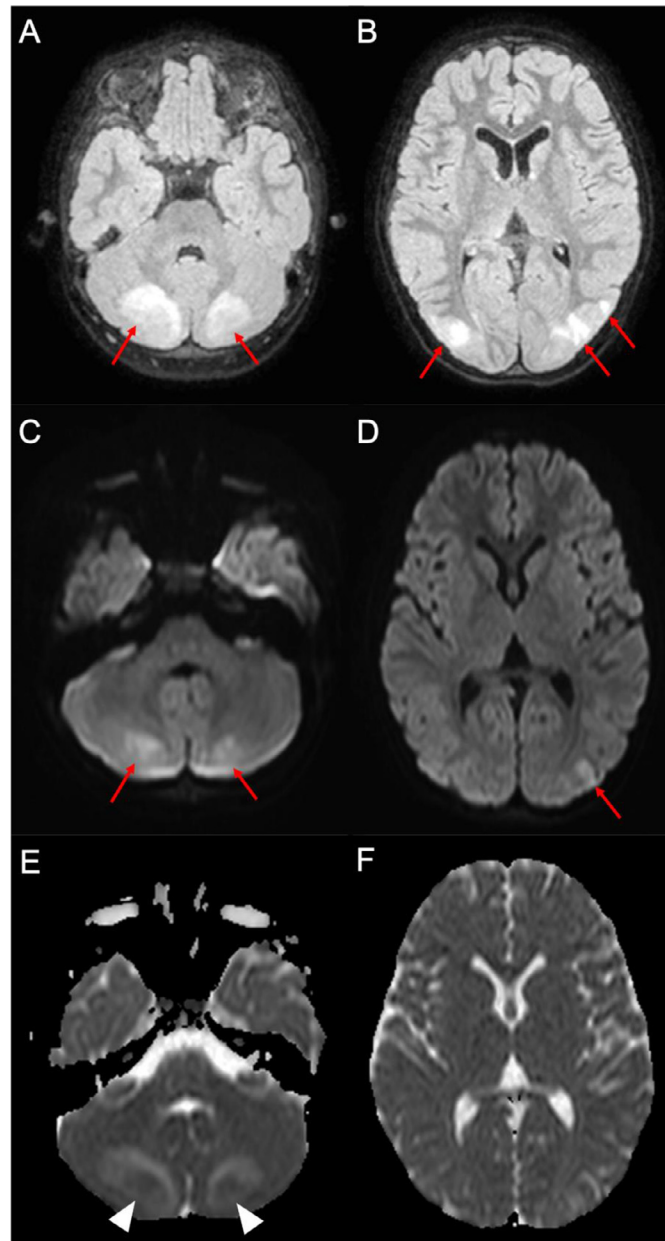
and cortico-subcortical parieto-occipital vasogenic edema with increased diffusion and slightly decreased ADC especially in the cerebellum (Fig. 2). The child was treated with antihypertensive drugs, diuretics, steroids and immunosuppressants (cyclosporine A), afterwards had no seizures and regained full consciousness and vision. His blood pressure was kept at normal values and the excretion of urinary proteins gradually decreased. The MRI performed 2 weeks later did not reveal any abnormality of the brain, which is usual in case of PRES.

### Discussion

The neurological changes seen in patients with renal disease and hypertension were first recognized in 1928 and defined hypertensive encephalopathy [7]. Only in 1984 the etiology was established to be cerebral edema due to the breaking of the blood-brain barrier [8].

The pathophysiological mechanism of PRES remains controversial. There are several hypotheses: one suggests that severe hypertension exceeds the ability to self-regulate blood pressure in the brain vessels, resulting in cerebral hyperperfusion, endothelial lesions, and vasogenic edema. The predilection for posterior brain regions could be due to relatively poor sympathetic innervations. Another hypothesis proposes that excessive cerebral vasoconstriction due to these self-regulatory mechanisms leads to hypoperfusion and cerebral ischemia, resulting in vasogenic edema. The mechanism by which immunosuppressive and antineoplastic agents cause PRES could act through a direct effect on cerebrovascular endothelium [9].

Acute leukemia, glomerulonephritis, hemolytic uremic syndrome, Henoch-Schonlein Purple, use of cytotoxic drugs



**Fig. 2 – MRI fluid-attenuated inversion recovery (FLAIR) axial images of the same patient showed cerebellar (A) and cortico-subcortical parieto-occipital (B) vasogenic edema (red arrows) with increased diffusion (C, D) and slightly decreased ADC (E, F) especially in the cerebellum (arrowheads).**

are closely associated with PRES in children. The clinical and radiological characteristics of PRES in children are similar to those of adults, according to few small case studies and case reports available [17]. From published studies it seems that the incidence is between 0.04% and 5.2% [10–12,17].

Nephrotic syndrome is one of the most common causes of chronic kidney disease in childhood with an incidence of 2–7 per 100,000 children. The most commonly reported neurological complication is cerebral thromboembolism, which remains one of the most serious and life-threatening events, but PRES is another neurological complication frequently reported in children with nephrotic syndrome [5,6,13,27].

In general, hypertension in children is commonly seen in association with systemic diseases, including parenchymal kidney disease, vascular kidney disease and endocrine abnormalities.

Although hypertension is common in pediatric patients, the mean blood pressure at onset of symptoms is lower than in adults [14]. Systemic hypertension has been found in 70%–80% of patients with PRES [15]. Tai Heng Chen et al. [16] in their systematic review indicate that 85% of pediatric cases are hypertensive, suggesting a critical and pathognomonic role of hypertension in childhood reversible posterior encephalopathy syndrome. Despite the nonspecific na-

ture of neurological symptoms, hypertension should be a red flag to alert the physician. Especially in the context of neurological emergencies, unlike adults, hypertension in children is often ignored or not recognized by their health care providers [18] because they think that hypertension is caused by agitation or hypersympathetic tone induced by seizures [19,20].

Seizures are the most common presentation symptom (60%-75%) followed by encephalopathy (50%-80%), visual disturbances (33%), headache (50%) and focal neurological deficits (10%-15%) [9,17,21].

Radiological investigations are essential for the diagnosis of PRES. The CT scan, which is usually easier to perform first, shows multiple hypodensities in the cortico-subcortical areas, which is different from acute infarct or bleeding. On MRI, T1-weighted hypointense, T2-weighted hyperintense and T2-weighted FLAIR hyperintense areas are revealed bilaterally in the occipital and parietal lobes, which can be partially or completely resolved with follow-up scans. Vasogenic edema is considered responsible for the pathophysiology of PRES and is in most cases reversible. On the other hand, the presence of cytotoxic edema is the main prognostic factor of the condition as it can mean an irreversible brain injury. The DWI sequence can be useful to distinguish between cytotoxic and vasogenic edema. Complications such as cerebral ischemia and cerebral hemorrhage can also be detected radiologically [22].

The treatment strategy focuses on early diagnosis and general measures to correct the underlying cause of PRES. Patients may need immediate correction of blood pressure or seizures, discontinuation of offending drugs or agents, dialysis or other interventions.

PRES symptoms and lesions may resolve completely if the diagnosis and treatment is as rapid as it was for our patient.

PRES is known to have a favorable outcome, as most patients fully recover within a week, although some may take longer [13,17,23,26]. Recurrent PRES was observed in 4% of patients in retrospective studies [12,25,27].

## Conclusion

Through our case report and a review of the literature, we wish to emphasize that the development of PRES occurred at the time of the moderate to severe nephrotic condition in most pediatric patients with nephrotic syndrome. In addition to cyclosporine administration and hypertension, there seem to be several additional factors that predispose the development of PRES in these patients, namely low serum albumin levels, generalized edema, increased vascular permeability, unstable fluid state and renal failure [5,12]. In our case, hypertension was undoubtedly an important cause, but we were not sure that cyclosporine A also had a pathogenic role.

In conclusion, PRES should always be considered in pediatric patients with nephrotic syndrome who develop an unexpected episode of neurological signs [13,24,26], especially if they have systemic hypertension and are on prolonged immunosuppressive therapy.

Early diagnosis through clinical suspicion is essential to achieve a good prognosis.

Further research is needed to develop guidelines for the diagnosis and treatment of PRES.

## Declaration of Competing Interest

The authors declare that no competing interests exist.

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