

## Case Report

# Infection-provoked Reversible Posterior Leukoencephalopathy Syndrome in Children Experiencing Nephrotic Syndrome: A Case Report



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## ABSTRACT

**Background and Aim:** Reversible posterior leukoencephalopathy syndrome (RPLS), also known as posterior reversible encephalopathy syndrome (PRES), is an uncommon and varied cliniconeurological condition that can manifest with a range of clinical symptoms, such as visual disturbances, altered consciousness, headaches, and seizures. Hypertension and immunosuppression are two primary factors that increase the likelihood of developing RPLS. Nevertheless, RPLS can also occur in the presence of other risk factors.

**Case Presentation:** A 10-year-old Asian boy diagnosed with nephrotic syndrome exhibited symptoms of seizures and fever. His blood pressure (BP) was within the normal range, and he received treatment with immunosuppressive medications.

**Conclusion:** In cases where patients with nephrotic syndrome develop an infection, it is important to assess for symptoms of RPLS. Timely diagnosis and proper management of RPLS can help prevent mortality and morbidity.

**Keywords:** posterior reversible encephalopathy syndrome (PRES), Nephrotic syndrome, Infection, Immunosuppressive



## Introduction

**R**eversible posterior leukoencephalopathy syndrome (RPLS), also referred to as posterior reversible encephalopathy syndrome (PRES), is characterized by a range of clinical and neuroradiological manifestations stemming from diverse causes. It is typically marked by a rapid onset of symptoms such as headaches, altered consciousness, seizures, vomiting, visual disturbances (including hemianopia or cortical dysfunction), and changes in white matter that suggest cerebral edema [1-3].

Computed tomography (CT) and magnetic resonance imaging (MRI) typically reveal symmetrically divided areas of vasogenic brain edema, primarily located in the posterior regions of the cerebral hemispheres. RPLS can be treated within a few days to a week; therefore, it must be identified and addressed quickly [4, 5].

PRES can arise from a variety of medical conditions, including hypertension, preeclampsia or eclampsia, kidney diseases (like nephrotic syndrome, which may cause hypovolemia and secondary hypertension due to the activation of the renin-angiotensin system), renal failure, liver disease, exposure to various or cytotoxic immunosuppressive medications, autoimmune diseases, sepsis, or chemotherapeutic agents [6-8].

The majority of patients with RPLS are pediatric nephrotic patients, and it is rare in adults [9]. Hypertension and many immunosuppressant drugs are two of the primary causes associated with the development of PRLS [2, 10]. Blood pressure (BP) is the main factor contributing to RPLS, an unusual condition that is considered a close differential diagnosis of hypertensive encephalopathy. Patients treated with long-term steroids or calcineurin inhibitors are particularly susceptible to developing RPLS [11].

Case reports in pediatrics indicate that nephrological patients are more susceptible to developing acute neurological complications because of electrolyte disturbances, hemodynamic instability, and the treatments administered [12, 13].

There is a lack of evidence regarding pediatric PRLS in the literature. This case report aimed to emphasize the possible existence of PRLS in children and to identify causes that complicate the diagnostic process. Here, we present an unusual case of PRLS associated with nephrotic syndrome due to an infection in a child who

had normal BP. Infections can produce cytokines, which are small proteins typically composed of a few hundred amino acids, secreted by immune system cells and other cell types. Their role is to transmit signals from one cell to another, but they can sometimes have undesirable effects on the patient's organs.

## Case Presentation

A 10-year-old boy was admitted to our hospital after experiencing a generalized tonic-clonic seizure. He reported headache, nausea, and vomiting two hours before the seizure.

According to the renal biopsy, he had a medical history of nephrotic syndrome caused by membranoproliferative glomerulonephritis (MPGN). He did not have any family history of kidney problems. Clinical suspicion of RPLS is initially established based on the patient's symptoms and is then confirmed by MRI. The brain MRI revealed bilateral parieto-occipito-temporal white matter hyperintensities. He received prednisolone, MMF, sirolimus, and tacrolimus as immunosuppressants, along with amlodipine as an antihypertensive medication.

Upon admission, the physical examination showed that the patient was afebrile (temperature: 37.2 °C), with a BP of 120/80 mm Hg and a heart rate of 100 beats per minute. No neurological deficits were observed during the neurological assessment. Laboratory tests indicated leukocytosis with a left shift (WBC: 19,000; neutrophil count: 85%), an elevated C-reactive protein level (50 mg/dL), and a serum albumin level of 2.5. Urinalysis showed the presence of proteinuria (spot urine: 3+).

In the present case, we described an unusual and rare case of RPLS resulting from infection and immunosuppressive drugs. We conclude that in cases of new-onset seizures in children with nephrotic syndrome, it is essential to investigate infection and immunosuppressive treatment, as these two factors can alter or disrupt the auto-regulation of the blood-brain barrier.

In this patient, two risk factors as triggers of PRESS are present: Infection and a high dose of immunosuppressants. The immunosuppressants were initiated two weeks prior. After seven days of antibiotic and antiepileptic treatment and the discontinuation of immunosuppressants, his symptoms improved. PRES can occur as a result of immunosuppressive agents, and it is crucial for clinicians to diagnose it quickly; otherwise, there is a risk of serious and irreversible clinical complications. A follow-up MRI conducted one month later revealed

that the previously observed hyperintensities in the brain lobes had resolved. A definitive diagnosis of RPLS was established. Another study similar to ours was conducted in 2018, which focused on immunosuppression-associated PRES in a case of acute leukemia.

## Discussion

RPLS is a clinico-radiographic diagnosis with several causes, first reported in a small case series of patients in 1996. The clinical manifestations typically include headache, confusion, visual disturbances, disorders of consciousness, and seizures [2, 14]. The incidence of PRES has not yet been clearly defined. PRES is encountered more frequently in females and appears to be associated with impaired cerebral autoregulation and endothelial dysfunction.

The main finding in neuroimaging is posterior cerebral white matter edema [15]. The underlying mechanism is not yet well understood; however, it has been documented in various case series [16, 17].

The present case involving nephrotic syndrome indicates that RPLS can arise in pediatric patients due to infection and immunosuppressants rather than solely from acute hypertension. Although RPLS may be associated with kidney disorders in different contexts, it primarily increases BP [18, 19].

The causes of RPLS vary and include hypertension, immunosuppressive treatment, eclampsia or pre-eclampsia, vasculitis, and kidney disease. Previously, hypertension was identified as one of the important risk factors for RPLS in children, often caused by kidney scarring due to frequent urinary tract infections and hemolytic uremic syndrome (HUS) [20, 21].

Nephrotic syndrome-induced RPLS may share a similar pathogenesis associated with endothelial dysfunction, which is characteristic of both hypertension and immunosuppression-related RPLS [8]. In this case, infection and immunosuppressants served as triggers for RPLS.

However, immunosuppressants and infection, the two primary causes in the present case, are rarely reported as causal factors for the occurrence of RPLS [3, 8]. Based on previous studies, RPLS induced by infection may have similar developmental mechanisms involving endothelial dysfunction, which is typical of both hypertension and immunosuppressant-related RPLS.

Both nephrotic syndrome and infection are linked to a heightened risk of endothelial dysfunction, which in turn disrupts cerebral autoregulation and ultimately leads to leakage in brain capillaries [12, 20]. Additionally, these factors can occur together, increasing the likelihood of RPLS episodes. This may explain why RPLS can be triggered by infection, as demonstrated in our case involving nephrotic syndrome without the presence of hypertension.

## Conclusion

In cases with nephrotic syndrome and secondary infection, it is important to assess for symptoms of RPLS. Timely diagnosis and proper management of RPLS can help prevent mortality and morbidity.

## Ethical Considerations

### Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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### Authors' contributions

All authors contributed equally to the conception and design of the study, data collection and analysis, interpretation of the results, and drafting of the manuscript. Each author approved the final version of the manuscript for submission.

### Conflict of interest

The authors declared no conflicts of interest.

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