

Posterior Reversible Encephalopathy Syndrome (PRES) in 5-year-old girl with nephrotic syndrome

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Abstract

OBJECTIVE: Posterior Reversible Encephalopathy Syndrome (PRES) is a rare complication of nephrotic syndrome in children. This clinical condition is caused by localized brain angioedema mostly in parieto-occipital region and results in dramatic and acute features as sudden loss of consciousness, epileptic paroxysms, strong headache or visual disturbances. Uncontrolled hypertension often participates in PRES development.

CASE: We present the case of a 5-year-old girl treated for relapse of nephrotic syndrome.

RESULTS: At the time of edema regression and weight reduction, a sudden loss of consciousness and worsening of hypertension occurred. Brain MRI demonstrated extended multifocal changes strongly suspicious of encephalitis. After exclusion of herpetic encephalitis, the clinical picture was classified as PRES. Successful antihypertensive treatment led to general improvement of the girl's health within 48 hours and resolution of MRI brain hyperintensities occurred within the next three months.

CONCLUSIONS: The aim of our case report is to us remind of possible development of PRES at the time of edema regression in nephrotic syndrome.

Abbreviations:

ADC	- apparent diffusion coefficient
CRP	- C-reactive protein
DWI	- diffusion weighted image
FLAIR	- fluid attenuated inversion recovery
ICU	- intensive care unit
MRI	- magnetic resonance imaging
NS	- nephrotic syndrome
PRES	- Posterior Reversible Encephalopathy Syndrome

INTRODUCTION

Posterior Reversible Encephalopathy Syndrome (PRES) is a rare complication of nephrotic syndrome (NS) in children. PRES was firstly described by Hinchey *et al.* (1996). Only three other articles were published about PRES in pediatric population with renal disease (Ishikura *et al.* 2008; Onder *et al.* 2007; Wirrell *et al.* 2007) and to our knowledge, ours is the first description of PRES development in nephrotic syndrome at the time of significant edema regression. Multifocal brain lesions on MRI of the brain represent a morphologic correlate with PRES. Pathophysiology is not clear, there is a focal cerebral angioedema, systemic hypertension is mostly important pathogenetic factor. Lowering the blood pressure significantly improves the clinical picture and eventually leads to reversal of the changes in MRI appearance.

CASE

A 5 year-old girl was admitted to our hospital with the 1st relapse NS during pharyngitis. She had the first attack of NS two years ago. After the initial corticosteroid therapy, complete remission was maintained for 18 months. At the admission she was fatigued, subfebrile and with firm edema of lower extremities up to inguinal regions. She had bilateral eyelid edema and signs of pharyngitis with bilateral reactive submandibular lymphadenitis. Her weight was 24.7 kg, height 118 cm and blood pressure 110/65 mm Hg.

Initial laboratory findings confirmed the relapse of NS, S-albumine was 13 g/l, selective proteinuria was 5.47 g/24 hours, S-cholesterol 7.4 mmol/l, inflammatory markers were slightly elevated, CRP was 21 mg/l. Albumine infusion and combined diuretic therapy were administered for marked oliguria and signs of secondary hyperaldosteronism within the first 24 hours of admis-

sion. Enalapril 5 mg pro die for moderate hypertension and corticosteroid therapy was started. After this treatment, diuresis increased to 1.5 ml/kg/hour with well-balanced fluid turnover. Furthermore, diuresis increased to 3.5 ml/kg/hour within the next three days, the edema resolved and weight dropped by 1 kg. However, during the 4th and 5th day, her hypertension progressed in spite of treatment from values of 85/60 to 120/100.

She started vomiting repeatedly and complained of headache and abdominal pain during the night of the 5th day. The next morning, sudden loss of consciousness occurred. On examination, she had trismus and horizontal nystagmus. After administration of 5 mg of diazepam she was transported to the emergency care unit.

Her Glasgow comma scale was 8, pulse frequency 100/min, breath frequency 29/min, blood pressure 118/67, temperature 36 grades and weight was 23 kg at the time of admission to ICU. To painful stimuli she reacted with flexion response, pupil photoreaction was symmetric, there was isocoria, moderate hypertension and slight tachycardia. Some swelling was noted around the ankles. She was ameningeal. MRI of the CNS for differential diagnosis of unconsciousness of unknown origin was immediately performed, with the finding of multifocal brain lesions especially in the parieto-occipital region (Figure 1). Herpetic encephalitis was considered. Examination of cerebrospinal fluid however showed normal findings.

Within the first 12 hours in ICU her systemic hypertension reached as high as 155/105 mm Hg, and was treated with nitroprusside, verapamil and enalapril. Nitroprusside was administered for 48 hours. Consciousness disturbances continued 48 hours, after that gradually normalized.

Three months later MRI of the brain was performed and complete regression of multifocal finding was documented (Figure 2). The patient continues corticotherapy for NS, is asymptomatic and doing well.

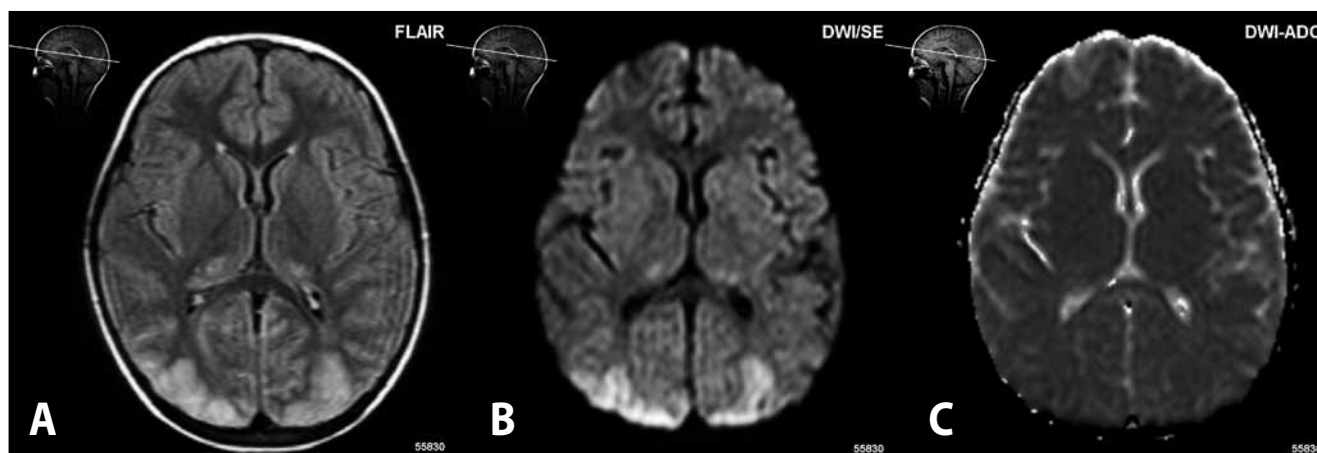


Fig. 1. A: Axial FLAIR (fluid attenuated inversion recovery), bioccipital foci of high signal intensity involving the cortex and subcortical white matter. **B, C:** DWI (diffusion weighted image) (**B**), ADC map (apparent diffusion coefficient) (**C**). The same slice as on Figure 1A, high signal on DWI (restriction diffusion), normal ADC map.

DISCUSSION

PRES is a reversible disturbance of the cerebrovascular autoregulation, resulting in encephalopathy due to focal brain edema. Edema is localized mostly in the posterior skull fossa, predominately in occipital or parietal region (Bartynski & Boardman 2007). Focal character of the brain changes evokes the suspicion of encephalitis in immunosuppressed patients or of metastases in oncologic patients.

Clinical presentation is dramatic, with unconsciousness, epileptic paroxysms, strong headaches, visual disturbances and other CNS symptoms (Kozak *et al.* 2007). Unconsciousness can continue for several days, but the prognosis with the adequate therapy is generally good.

Hypertension is often present, but PRES could also develop in disorders and situations without marked hypertension as in immunosuppressive and cytostatic treatment, significant hypercalcaemia, thrombocytopenic syndromes, anaphylactoid purpura or systemic lupus erythematoses. Cyclosporine, tacrolimus, L-asparaginase and corticosteroids are suspected of cytotoxic action. Drugs as cocaine, methamphetamine and rarely lysergamide could precipitate PRES development (Legriel *et al.* 2008).

Mechanisms of the brain angioedema development are not completely clarified. Probably, there is a hyperperfusion leading to the failure of vessel autoregulation, disturbances in blood/brain barrier, leading to extravasation and progression of cortical and subcortical edema (Bartynski 2008). However, some authors suspect hypoperfusion due to vasoconstriction as a main cause of PRES development (Brubaker *et al.* 2005).

Magnetic resonance is the main imaging method for PRES diagnosis. Typical findings are hyperintensities in FLAIR (fluid attenuated inversion recovery), less marked in T2W images, mainly in the parieto-occipital and posterior frontal cortex and subcortical white matter. In T1W images there are hypointense cortical, subcortical lesions, and after contrast administration no enhancement or variable patchy enhancement is observed. FLAIR is the most important for the diagnosis, but it fails to distinguish between vasogenic and cytotoxic edema (both have hyperintense lesions in FLAIR). The typical imaging appearance is: no restriction of diffusion in diffusion weighted image (DWI) (vasogenic edema) and ADC (apparent diffusion coefficient) is markedly elevated (bright areas). Sometimes restriction in DWI is observed, mostly with pseudo-normalized ADC maps and changes in DWI are of a smaller extent compared to the lesions on FLAIR; this may indicate irreversible infarction (cytotoxic edema) (McKinney *et al.* 2007). Logically, these findings were detectable from the beginning of MRI usage, but only conventional MRI in connection with DWI and ADC maps are capable of distinguishing PRES from irreversible conditions, such as in metabolic diseases, viral encephalitis and acute ischemic stroke in adults.

The hyperintensities are mostly localized in parieto-occipital region; less commonly in basal ganglia, in cerebellum and in brainstem. Rarely, other brain regions can be involved (McKinney *et al.* 2007). The posterior prevalence of typical PRES finding could be explained by the difference in autonomic innervation of anterior and posterior regions of the brain (Karoui *et al.* 2008).

PRES is described in the nephrotic syndrome, glomerulonephritis and in end-stage renal failure in the population of pediatric and adolescent patients (Onder *et al.* 2007). Hypertension and cyclosporine treatment are the most common precipitators.

Hypertension is an uncommon sign in the idiopathic nephrotic syndrome. When it occurs, careful blood pressure monitoring is necessary even after edema regression and diuresis normalization, to prevent PRES.



Fig. 2. Control MRI after 2 months, axial FLAIR (A), DWI (B), ADC map (C) normalization of signal intensity on FLAIR, no restriction diffusion, normal ADC map.

CONCLUSION

Although many cases of PRES were published in recent literature, this case report highlights the possibility of PRES development even after successful treatment of NS relapse, and also contributes to the differential diagnosis of herpetic encephalitis. Aggressive treatment of hypertension resulted in rapid clinical improvement. Within 3 months, MRI findings resolved as well.

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REFERENCES

- 1 Bartynski WS, Boardman JF (2007). Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. *Am J Neuroradiol.* **28**: 1320–1327.
- 2 Bartynski WS (2008). Posterior Reversible Encephalopathy Syndrome, Conversies surrounding pathophysiology of Vasogenic Edema. *Am J Neuroradiol.* **29**: 1043–1049.
- 3 Brubaker LM, Smith JK, Lee YZ *et al.* (2005). Hemodynamic and Permeability Changes in Posterior reversible Encephalopathy Syndrome Measured by Dynamic Susceptibility Perfusion-weighted MR Imaging. *Am J Neuroradiol.* **26**: 825–830
- 4 Hinchey J, Chaves C, Appignani B *et al* (1996). A reversible posterior leukoencephalopathy syndrome *Lancet.* **334**: 494–500.
- 5 Ishikura K, Ikeda M, Hamasaki Y *et al.* (2008). Nephrotic state as a risk for developing posterior reversible encephalopathy syndrome in paediatric patients with nephrotic syndrome. *Nephrol Dial Transplant.* **23**: 2531–6. Epub Feb 7.
- 6 Karoui KE, Le Quintrec M, Dekeyser E *et al.* (2008). Posterior reversible encephalopathy syndrome in systemic lupus erythematosus. *Nephrol Dial Transplant.* **23**: 757–763.
- 7 Kozak OS, Wijdicks EF, Manno EM *et al* (2007). Status epilepticus as initial manifestation of posterior reversible encephalopathy syndrome. *Neurology.* **69**: 894–897.
- 8 Legriél S, Bruneel F, Spreux-Varoquaux O *et al.* (2008). Lysergamid acid amid- induced posterior reversible encephalopathy syndrome with status epilepticus. *Neurocrit care.* **9**: 247–252.
- 9 Mc Kinney AM, Short J, Truwit ChL *et al.* (2007). Posterior reversible Encephalopathy Syndrome: Incidence of Atypical Regions of Involvement and Imaging Findings. *Am J Radiol.* **189**: 904–912.
- 10 Onder AM, Lopez R, Teomete U *et al.* (2007). Posterior reversible encephalopathy syndrome in the pediatric renal population. *Pediatr Nephrol.* **22**: 1921–9. Epub 2007 Aug 11.
- 11 Wirrell EC, Hamiwka LD, Hamiwka LA, Grisaru S, Wei X (2007). Acute glomerulonephritis presenting with PRES: a report of 4 cases. *Can J Neurol Sci.* **34**: 316–21.