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CASE REPORT

Reversible Posterior Leukoencephalopathy Syndrome in Children with Nephrotic Syndrome: a Case Report

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REVERSIBLE posterior leukoencephalopathy syndrome (RPLS) is a rare neurological syndrome characterized by headache, altered mental status, seizures, and visual disturbance, associated with reversible white matter changes.¹ It has been commonly reported in patients with severe hypertension and pre-eclampsia. Here we report a case with nephrotic syndrome complicated by RPLS.

CASE DESCRIPTION

The patient in this case is a 6-year-old girl without a previous history of neurological manifestations. Four months before, the patient suddenly demonstrated severe edema in face and lower extremity, and oliguria without any obvious inducing factors, with no fever or respiratory symptoms. She was admitted to a local hospital. The urine routine test displayed significantly increased urine protein. Biochemical test showed hypoproteinemia and hypercholesterolemia. Based on the symptoms and laboratory examination, the girl was diagnosed as having nephrotic syndrome. She received intravenous administration of methylprednisolone at a dose of 1000 mg first, followed by oral prednisone acetate 35 mg per day half a month later,

the urine protein decrease. Just before decreasing the dose of prednisone acetate to 30 mg, the patient had a upper respiratory tract infection and fever, the dose was increased to 32.5 mg per day, and anti-infection and symptomatic treatments were applied. However, the urine protein was not turned to negative. Two days before, the edema in this patient aggravated all over the body while urine volume decreased gradually, so the girl was transferred to our hospital for further examination and treatment.

Upon admission to our hospital, physical examination recorded moon face, severe lower extremity edema, and blood pressure being 130/70 mmHg. Laboratory tests revealed a blood urea nitrogen of 8.0 mmol/L, serum creatinine of 41 μ mol/L, serum cholesterol of 8.40 mmol/L, serum triglycerides of 4.80 mmol/L, serum albumin of 22.4 g/L, serum calcium of 1.9 mmol/L, serum sodium of 131 mmol/L, serum total protein of 35.5 g/L, blood serum antithrombin III at 0.47, and fibrinogen of 475 mg/dl; blood routine test revealed hemoglobin at 153 g/L, lymphocyte count at 6.05×10^9 /L, neutrophilic granulocytes at 13.63×10^9 /L, blood platelets count at 471×10^9 /L, erythrocyte count at 5.05×10^{12} /L, leucocyte count at 21.1×10^9 /L, urine protein at 3.0 g/L, epithelial cell at 50/ μ l. Blood glucose, electrolytes, and bicarbonate were in the normal range. Chest X-ray showed bilateral hydrothorax, abdominal ultrasonography revealed ascites. The diagnosis of nephrotic syndrome is confirmed. We treated her with

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steroid hormone, anti-inflammatory therapy, and oral administration of tacrolimus. On the 5th day during hospitalization, she developed a severe headache and her blood pressure rose to 178/98 mmHg. The following day she experienced sudden generalized tonic-clonic seizures twice and became lethargic. The seizures were treated successfully with intravenous diazepam and the hypertension was controlled by using nifedipine. Emergency brain computed tomography (CT) scan revealed cerebral atrophy, brain CT recheck 2 days later disclosed bilateral low-density areas in the parieto-occipital lobes. Magnetic resonance imaging (MRI) showed a high-signal intensity area on T2-weighted fluid-attenuated inversion-recovery images and a low-signal intensity area on T1-weighted images in the same lesions in the parieto-occipital region and thalamus, and diffusion-weighted imaging (DWI) demonstrated isointense signals in the lesions (Fig. 1). Electroencephalography conducted 2 days later showed diffuse slow activity without any sharp wave. Cerebrospinal fluid examination demonstrated no abnormality, with negative result for myelin basic protein test. Follow-up MRI in 2 weeks showed that the lesions in the parieto-occipital lobes disappeared (Fig. 2A). The head magnetic resonance angiograph (Fig. 2B) and magnetic resonance venography (Fig. 2C) appeared normal. These manifestations were compatible with the diagnosis of RPLS. Considering the possible role of tacrolimus in the syndrome, we stopped this medication. She gradually recovered consciousness and had no further episodes of convulsions. No neurological abnormality remained. Her blood pressure and urine protein were well controlled when she was discharged from our hospital.

DISCUSSION

RPLS, first characterized by Hinchey et al,¹ is a clinical

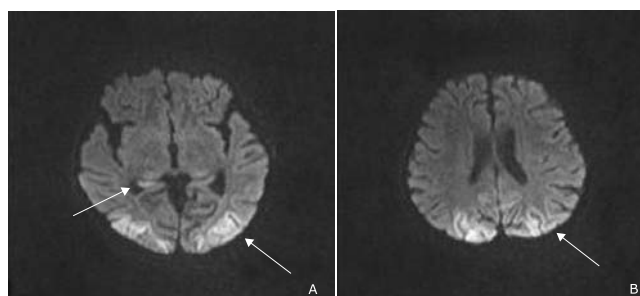


Figure 1. Brain magnetic resonance imaging (MRI) 2 days after seizures episode. There is a high-signal intensity area on T2-weighted fluid-attenuated inversion-recovery images and a low-signal intensity area on T1-weighted images in the parieto-occipital region and thalamus, diffusion-weighted imaging showing isointensity in the lesions.

A. The lesions in the parieto-occipital region and thalamus (arrows);

B. The lesion in the occipital region (arrow).

and radiological syndrome that is characterized by sudden onset of headache, altered mental function, seizures, and cortical blindness. Radiological findings of bilateral white matter abnormalities suggest edema in the posterior regions of the cerebral hemispheres on brain CT scan or MRI.

The underlying mechanisms of RPLS are still not fully understood. However, the rapid resolution of clinical and neuroradiological abnormalities suggests that cerebral edema, caused by impaired cerebrovascular autoregulation and endothelial injury, is the main pathophysiological mechanism.² It is believed that there is a failure of the autoregulatory abilities of the cerebral vessels in RPLS, resulting in brain hyperperfusion and blood-brain barrier injury, and subsequent vasogenic edema. The preferential involvement of the parietal and occipital lobes can be attributed to the less extensive sympathetic innervation of

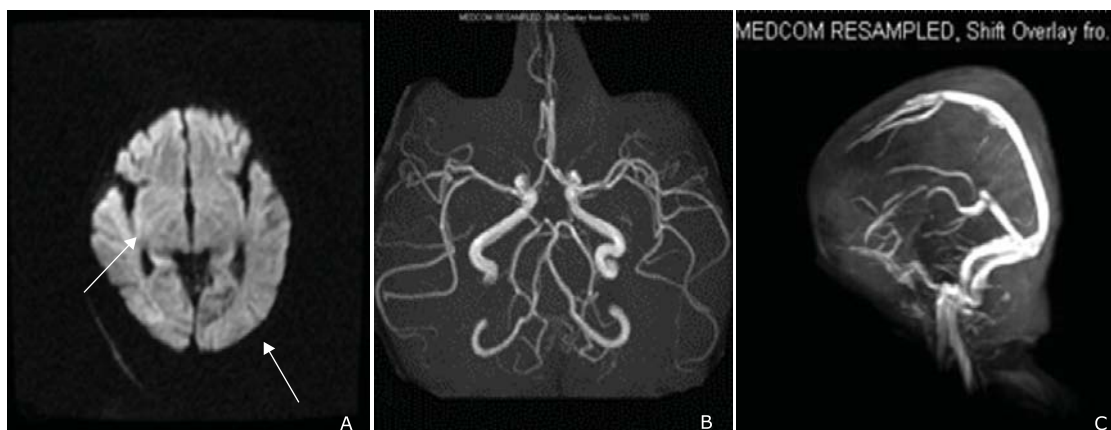


Figure 2. As shown in brain MRI 2 weeks after seizures episode, the lesions in the parieto-occipital lobes and thalamus disappeared (A). Magnetic resonance angiography (B) and magnetic resonance venography (C) reveal no abnormalities as well.

the posterior circulation compared with the rest of intracranial arteries. The theory was confirmed by single photon emission computed tomography, MRI, diffusion weighted imaging, and apparent diffusion coefficient that the edema is vasogenic, such as in hypertension encephalopathy.³ Hypertension is considered to be the most common cause of RPLS, although there are a number of cases without severe hypertension.² Other explanation^{4,5} of RPLS is that some drugs can induce blood-brain-barrier injury such as chemical and cytotoxic drugs, water and macromolecule substance, even erythrocyte exosome to intercellular substance, which aggravates the brain edema. Furthermore, multiple mechanisms including water-sodium retention, enhancement of ferritin-angiotensin system activity, accumulation of metabolic products are also the causes of RPLS.

Nephrotic syndrome is a nonspecific kidney disorder characterized by a number of signs: proteinuria, hypoalbuminemia, and edema. It is characterized by an increase in permeability of the capillary walls of the glomeruli leading to high levels of protein in urine [proteinuria ≥ 3.5 g/(day $\cdot$ 1.73 m² body surface area)], low levels of protein in the blood (hypoproteinemia or hypoalbuminemia), ascites, in some cases edema, hyperlipemia, and a predisposition for coagulation. Patients with renal disease have disturbance of vasopressor homeostasis and endothelial function related to elevated lipoproteins, high blood pressure, azotemia, and medication, all of which can result in RPLS.

The administration of cytotoxic agents, such as tacrolimus, may have a direct toxic effect on the cerebral vasculature, which can also lead to RPLS. Ishikura et al⁶ investigated 7 patients with idiopathic nephrotic syndrome, aged 1.5-15.1 years. The re-administration of cyclosporine after the episodes of PRLS was carried out in 4 of the 7 patients. During the 17-51 months after the re-administration, the recurrence of PRLS was not observed in these patients. Yamada et al⁷ reported a 13-year-old female nephrotic patient with recurrent PRLS during and after cessation of cyclosporine A. She had headache, visual disturbance, and acute hypertension, followed by seizures. Cessation of cyclosporine A brought clinical improvement. Six months later, she had similar symptoms, edema, severe hypoalbuminemia, and renal insufficiency before seizures. Youssef et al⁸ reported a case of a 9-year-old girl who presented with nephrotic syndrome and moderate hypertension. Nine days after the initiation of steroid therapy, she developed disturbed consciousness and generalized tonic-clonic seizures. Her blood pressure was 145/90 mmHg. She was treated with furosemide, and convulsions were controlled.

After regaining consciousness, she complained of loss of vision. MRI, axial fluid attenuated inversion recovery images, and diffusion-weighted imaging showed hyper-intensity signal in the parieto-occipital areas. She regained full consciousness and normal vision 4 days later. RPLS was diagnosed based on the typical pattern of brain imaging and the reversibility of symptoms. They concluded that nephrotic syndrome in children should be considered a risk factor of PRLS even without the use of immunosuppressive agents or high doses of steroid.

The patient in this case is a definite nephritic syndrome patient. During her course of disease, she took steroids (methylprednisolone and prednisone acetate), anti-inflammatory and immunosuppressive agents (tacrolimus). In hospitalization, she developed a severe headache, elevated blood pressure, and generalized tonic-clonic seizures. Emergency brain CT scan and MRI confirmed the diagnosis of RPLS. This patient presented several known risk factors of RPLS, including azotemia, increased blood pressure, recent cytotoxic agents use, and sodium-water retention.

REFERENCES

1. Hinchey J, Chaves C, Appignani BA, et al. A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 1996; 234:494-500.
2. Ay H, Buonanno FS, Schaefer PW, et al. Posterior leukoencephalopathy without severe hypertension: utility of diffusion-weighted MRI. *Neurology* 1998; 51:1369-76.
3. Schwartz RB, Mulkern RV, Gudbjartsson H, et al. Diffusion-weighted MR imaging and hypertensive encephalopathy: clues to pathogenesis. *AJNR Am J Neuroradiol* 1998; 19: 859-62.
4. Singh N, Bonham A, Fukui M. Immunosuppressive-associated leukoencephalopathy in organ transplant recipients. *Transplantation* 2000; 69 :467-71.
5. Gijtenbeek JM, van den Bent MJ, Vecht CJ. Cyclosporine neurotoxicity: a review. *J Neurol* 1999; 246:339-46.
6. Ishikura K, Ikeda M, Hamasaki Y, et al. Nephrotic state as a risk factor for developing posterior reversible encephalopathy syndrome in paediatric patients with nephrotic syndrome. *Nephrol Dial Transplant* 2008; 23:2531-6.
7. Yamada A, Atsumi M, Tashiro A, et al. Recurrent posterior reversible encephalopathy syndrome in nephrotic syndrome: case report and review of the literature. *Clin Nephrol* 2012; 78:406-11.
8. Youssef D, Fawzy F. Posterior reversible encephalopathy syndrome in a child with steroid sensitive nephrotic syndrome. *Arab J Nephrol Transplant* 2012; 5:163-6.