Turk J Med Sci
34 (2004) 141-145

SHORT REPORT

Reversible Posterior Leukoencephalopathy Syndrome Secondary to Acute Hepatic Failure

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Received: August 12, 2003

Key Words: Posterior leukoencephalopathy, hepatic failure

The term reversible posterior leukoencephalopathy syndrome (RPLS) describes a syndrome of headaches, confusion, seizures, and visual disturbances associated with transient, predominantly posterior cerebral lesions revealed by neuroimaging (1). RPLS usually occurs in association with hypertension (2) or the use of immunosuppressive drugs such as cyclosporine (3). May the list of causes of RPLS is growing, and more information is needed regarding the underlying pathophysiology of this transient disorder (4). In the literature 92 children were reported as having RPLS or a RPLS-like syndrome, of these the youngest was 2 years old (5). As far as we know, RPLS secondary to acute hepatic failure has not been reported before.

Case Report

A 6-month-old boy had developed fever, vomiting, and diarrhea, and suffered generalized tonic-clonic seizures 6 times. He had been examined at the district hospital and referred to our hospital with intravenous fluid administration.

He had not been given any medication recently. Until presentation, he had been alert, demanding and feeding normally. His physical examination on admission revealed an axillary temperature of 38.4 °C, blood pressure of 90/60 mmHg, pulse of 120 beats per minute, height of 62 cm (3-10%), and weight of 6300 g (10-25%). He was sleepy, but responded to verbal stimuli, his pupils were equal and reactive, and his reflex eye movements were intact. He was moderately dehydrated. The chest was clear on auscultation. There was no heart murmur, and the liver edge was palpable 2 cm below the costal margin. Other systemic examinations were normal. Initial investigations revealed the following findings: white cell count 19.6 x 10^9/l (90% neutrophils), platelets 155 x 10^9/l, hemoglobin 14.6 g/dl, ammonia 195 µmol/l, hepatitis A, B, C, D and E markers negative, reducing substance in urine negative, antinuclear antibody negative, acyl-carnitine normal, erythrocyte sedimentation rate 75 mm/h, blood glucose 24 mg/dl, blood urea nitrogen 63 mg/dl, creatinine 1 mg/dl, sodium 154 mEq/l, potassium 4.3 mEq/l, total bilirubin 0.6 mEq/l, aspartate aminotransferase 1192 U/l, alanine aminotransferase 978 U/l, lactate dehydrogenase 7349 U/l, creatine kinase 4008 U/l, C-reactive protein 3.5 mg/l, activated partial thromboplastin time 120 s, and prothrombin time 70 s. Urinalysis, thyroid function tests, immunoglobulins, urine and blood amino acid levels, arterial blood gases and the spinal fluid were within

normal limits. N-acetyl tyrosine and 3-OH isovaleric acid were mildly elevated in urine organic acid screening. EEG was consistent with encephalopathy.

Cranial CT showed brain edema and diffusion MRI revealed signal changes consistent with vasogenic edema in the bilateral parasagittal area with corticomedullary involvement, having hyperintense signal characteristic in b:1000 images, and hypointense signal characteristics in apparent diffusion coefficient map images (Figure 1A, B).

Control MRI showed a remarkable improvement 1 week later and complete resolution of the lesions 4 weeks later (Figure 2A, B). All these findings appear consistent with reversible posterior leukoencephalopathy.

In spite of the phenytoin treatment, convulsions were not controlled. After using vigabatrin and carbamazepine subsequently, seizures were controlled completely on day 15.

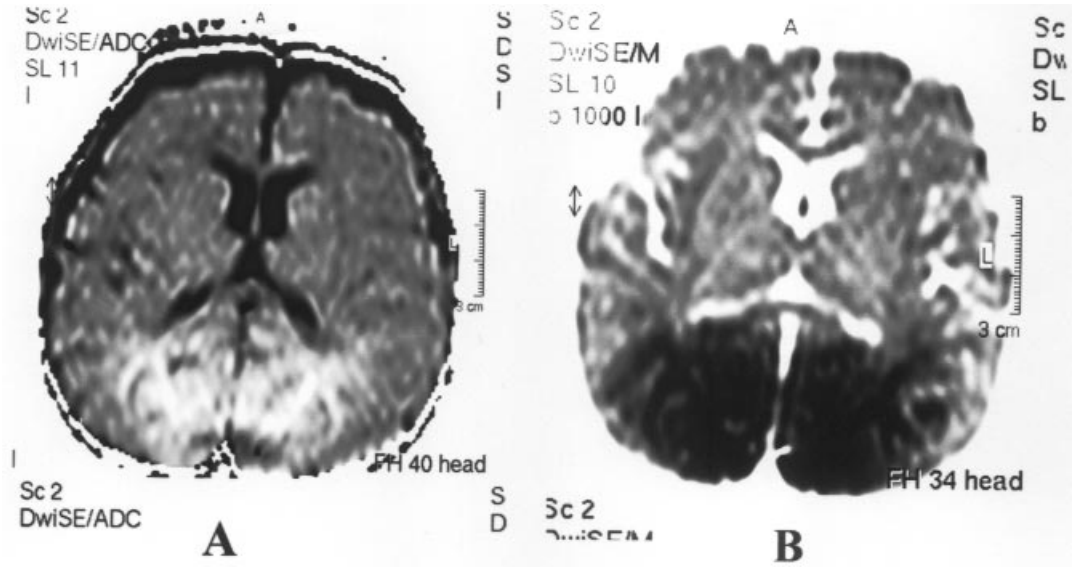

Figure 1. Diffusion MRI shows signal changes in the bilateral parasagittal area with corticomedullary involvement, having A) hypointense signal characteristics in ADC map image, B) hyperintense signal characteristics in b:1000 image.

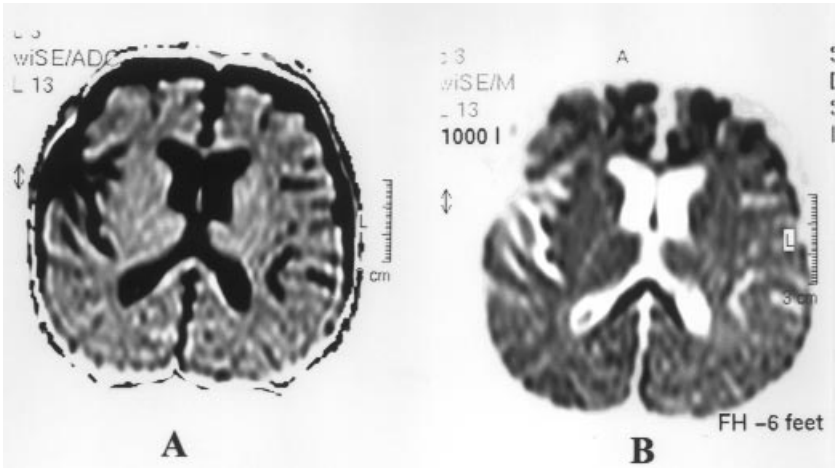

Figure 2. Complete resolution of the lesions are seen in A) ADC map image and B) b:1000 image, 4 weeks later.

Diffusion MRI performed 4 weeks later revealed complete resolution and the patient was discharged without any neurological sequelae.

Hinchey et al. in 1996 described RPLS as a syndrome of headaches, confusion, seizures, and visual disturbances associated with transient, predominantly posterior cerebral lesions revealed by neuroimaging (1). In a retrospective study, they reported white matter edema on neuroimaging in the posterior temporo-parieto-occipital region in a variety of conditions including severe hypertension. They proposed the name reversible posterior leukoencephalopathy syndrome, emphasizing its location and relatively reversible nature. Fifteen patients (1 was under 18 years of age) were reported to elucidate this clinical syndrome by Hinchey et al. (1). Only a few cases of RPLS have been reported since then.

The cases in the literature are commonly reported to be associated with hypertension secondary to renal failure (4), glomerulonephritis (6,7), eclampsia (8), or various immunosuppressive therapies (3,4). Our case differs from the literature in that MRI detected neurological deterioration developed after acute hepatic failure. Follow up did not show the development of hypertension, and neurological and radiological findings improved periodically. On the other hand, the present case has the distinct features of being the youngest case ever reported, not having hypertension and not having a history of immunosuppressive therapy.

Descriptions of RPLS have emphasized characteristic clinical and radiological presentations. Radiological abnormalities are most commonly seen within the white matter of the occipital lobes, as a low-density change on CT and as a high signal change on T2 weighted and FLAIR MRI sequences (3). In MR spectroscopy, increased choline and creatine, and mildly decreased N-acetylaspartate were found (9).

We performed diffusion MRI to show the radiological abnormalities. Diffusion MRI has the advantages of an earlier diagnosis in perfusion disorders than the other imaging modalities and very short performance time (half a minute).

The underlying pathophysiology of RPLS is not well understood, but 2 main mechanisms have been suggested. One hypothesis is that cerebral vasospasm results in ischemia. Alternatively, it has been suggested that there is a temporary failure of the autoregulatory

Table. Etiologic causes in children with RPLS reported in the literature.

Reference	No. of Patients	Age	Etiologic causes
Hinchey et al.[1]	1	15 years	Puerperal eclampsia
Singhi et al. [2]	2	-	Hypertension
Kwon et al.[5]	12	2-20 (mean 9.8) years	Intrabdominal neurogenic tumors, hypertension
Soylu et al.[6]	1	7 years	Glomerulonephritis
Froehlich et al.[7]	2	-	Glomerulonephritis
Arora et al.[8]	1	18 years	Hypertension
Pavlakis et al.[11]	45*	<18 (mean 11.1) years	Hypertension
Pavlakis et al.[12]	1	14 years	Hypertension
Henderson et al.[13]	3	3-9 years	Sickle cell disease, respiratory failure and erythrocytapheresis
Garg et al.[14]	1	13 years	Post-infectious hemorrhagic leukoencephalitis
Tomita et al.[15]	4	-	Hypertension
Kim et al.[16]	1	16 years	A Down syndrome patient with nephrotic syndrome
Ikeda et al.[17]	1	9 years	Nephrotic syndrome
Shin et al.[18]	3	-	Acute lymphoblastic leukemia
Antunes et al.[19]	1	2 years	Down syndrome and allogeneic bone marrow transplantation
Lanzino et al.[20]	1	13 years	Organ transplantation
Woolfenden et al.[21]	1	10 years	Henoch-Schönlein purpura
Total	92		

* These cases were reported prior to the description of RPLS and presented with RPLS-like clinical features.

capabilities of the cerebral vessels, leading to hyperperfusion, breakdown of the blood-brain barrier, and consequent vasogenic edema (4,9). Based on clinical and radiological findings, the posterior brain region vasculature seems the most vulnerable (1,10).

We think that a failure to detoxify toxic substances and the increase in the amount of organic acids in acute hepatic failure can lead to RPLS by impaired cerebral flow.

Pavlakis et al. (11) reported a case of occipito-parietal encephalopathy syndrome with occipital magnetic resonance spectroscopy showing a decrease in N-acetyl-aspartate/creatinine and they concluded that there were neuronal, axonal or synaptic abnormalities. In their study evaluating 52 children with similar clinical pictures reported in the literature since 1985, Pavlakis et al. stated that this syndrome is not new and all children develop leukoencephalopathy secondary to hypertension (11,12).

We searched Medline using the key words "posterior leukoencephalopathy syndrome" and "children" and found 22 articles. Of these, 4 articles did not concern RPLS cases. The articles found and the etiological features and number of cases are listed in the Table.

As these data show, our knowledge of this clinical syndrome, revealed with the routine use of MRI, is limited. To clarify the etiopathogenesis of this syndrome, which includes acute hepatic failure, we need more comprehensive studies.

We presented this case to show the association between RPLS and acute hepatic failure and we think that diffusion MRI with a short performance time is helpful for an early diagnosis.

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