Reversible Posterior Leukoencephalopathy Syndrome: A Case Report and Review of the Literature

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Abstract- A 23-year-old man with minimal-changed nephrotic syndrome presented reversible posterior leukoencephalopathy syndrome (RPLS) which manifested as visual disturbance, renal hypertension, headache, generalized seizure and altered mental status. T2-weighted images and fluid-attenuated inversion recovery images magnetic resonance imaging (MRI) showed high signal intensity lesions in the right posterior temporo-parieto-occipital region and left posterior temporal area. Diffusion-weighted brain MRI did not show hyperintense signal in these lesions. After control of his hypertension, these lesions disappeared with improvement of clinical symptoms. We report this case and review the literature and suggest that RPLS in brain MRI may be the results of hypertensive encephalopathy due to vasogenic edema.

Key Words: Reversible posterior leukoencephalopathy syndrome, Nephrotic syndrome, Magnetic resonance image, Hypertensive encephalopathy

INTRODUCTION

Reversible posterior leukoencephalopathy syndrome (RPLS) is a recently recognized brain disorder, mostly associated with a variety of conditions in which blood pressure rises acutely or with the use of immunosuppressive and cytotoxic agents. It is clinically characterized by rapidly evolving neurological symptoms and signs, including headache, nausea, vomiting, visual disturbance, altered mental status and occasionally focal neurological deficits. In neuroimaging studies of RPLS, computed tomography (CT) and magnetic resonance imaging (MRI) show bilateral edematous changes in the posterior regions of cerebral hemispheres and posterior fossa structures. Early recognition of this urgent neurological condition is very important because that prompt control of blood pressure or withdrawal of immunosuppressive drugs will cause reversal of neurological symptoms and neuroimaging abnormality. Delay in diagnosis and treatment can result in permanent injury of affected brain tissues. Clinicians often overlook this disorder. Therefore, we report a case of RPLS caused by hypertensive encephalopathy (HE) and review the relevant literature.

CASE REPORT

A 23-year-old man, who had been a chronic case of hepatitis B virus infection for 6 years, began experiencing progressive generalized anasacca in July 2002.
During that period, he visited our nephrologic clinic and serial examinations showed blood urea nitrogen (BUN) 10 mg/dL, serum creatinine (Cr) 1.4 mg/dL, total serum cholesterol 797 mg/dL, triglyceride 331 mg/dL, albumin 1.8 mg/dL, daily urinary protein 8 mg/dL, and creatinine clearance (Ccr) 71 mL/min. Nephrotic syndrome was diagnosed and sonography-guided kidney biopsy showed minimal change nephropathy. He received diuretics and prednisolone for two weeks and then he discontinued the medications and started taking herbal drugs.

During the following two months, he gained weight of 30-kilograms and began to suffer from acute onset of headache, dizziness, nausea and visual disturbance on September 27, 2002. Two days later, he experienced a generalized seizure and was sent to our emergency room. At our ER, his blood pressure was 205/115 mmHg. Neurologic examinations showed altered mental status, and bilateral mild papilledema. Brain computed tomography (CT) on September 29 showed low-density lesions in bilateral posterior temporal and parietal regions with cortical and subcortical area involvement, and no obvious enhancement after contrast study (Fig. 1).

On October 2, brain MRI showed high signal intensity mainly in the subcortical white matter of right posterior temporal area on T2-weighted (Figs. 2A-B) and fluid-attenuated inversion recovery (FLAIR) (Figs. 2C-D) MRI imaging studies. Diffusion-weighted MRI did not show the increased intensity in these lesions (Figs. 2E-F). After treatment with antihypertensive drugs, his mentality returned to normal and no other seizures occurred. On October 24, a follow-up brain MRI showed that the hyperintense lesions disappeared, and no residual abnormal signal intensity (Fig. 3). On October 26, he was discharged without neurological sequelae and nephrotic syndrome was under control.

**DISCUSSION**

RPLS, the term first coined by Hinchey et al[1], is a newly recognized neurologic disorder characterized predominantly by white matter edema affecting the occipital and posterior parietal lobes of the brain. Many terms have been used referring to this disorder including HE, extensive brain stem hyperintensity, pontine reversible edema, posterior reversible edema syndrome, and reversible occipito-parietal encephalopathy syndrome[2-7]. RPLS is often associated with an abrupt increase of blood pressure and is usually seen in patients with eclampsia, renal disease, HE and in patients treated with cytotoxic and immunosuppressive drugs including cyclosporine A, tacrolimus, and interferon alpha[8-10]. From the literature, only three reports have described this syndrome (RPLS) with the nephrotic syndrome[11-13]. In this study we present the second case of nephrotic syndrome and RPLS but he did not have cyclosporine A treatment.

Although the exact cellular mechanisms leading to loss of endothelial function in RPLS are still poorly understood, two divergent theories have been invoked. Initially, investigators argued that RPLS patients would develop vasospasm secondary to sudden and marked rise of blood pressure and ischemia of the brain tissues[14,16]. However, the imaging studies showed no signs of cytotoxic edema or subsequent infarction and the reversibility of imaging abnormalities after an appropriate immediate treatment were not consistent with the
The hypothesis of vasospasm and cerebral ischemia\(^4\)\(^1\)\(^4\) has been supported by recent investigations suggesting that RPLS resulted from a rapid rise of blood pressure which might overcome the normal autoregulation of cerebral blood flow. This disturbance in autoregulation produces dilation of the cerebral arterioles with opening up of endothelial tight junctions and leakage of plasma and red cells into the extracellular space, leading to cerebral edema (vasogenic edema)\(^4\)\(^1\)\(^0\)\(^4\).

The most common neuroimaging abnormality in RPLS is brain edema, mainly in the white matter of the parieto-occipital regions\(^1\). The edema sometimes extends to the adjoining gray matter\(^7\)\(^1\)\(^5\). The edematous lesions are also frequently recognized in brain stem, cerebellum, and basal ganglia\(^1\)\(^\)\(^1\)\(^6\)\(^1\)\(^7\). These abnormal findings are most recognized as hyperintense areas on T2-weighted and FLAIR MRI imaging studies. Recent diffusion-weighted and perfusion MR imaging studies have provided more etiological information on this syndrome. The apparent diffusion coefficient of the hyperintense areas on T2-weighted images was increased, and these areas appeared as iso- or hypointense on the diffusion-weighted images\(^2\)\(^1\)\(^8\)\(^1\)\(^9\)\(^2\)\(^0\). These findings indicate that while the RPLS lesions increased water diffusibility associated with vasogenic edema, there was no evidence of cytotoxic edema or infarction\(^2\)\(^1\)\(^8\)\(^1\)\(^9\)\(^2\)\(^0\). Such findings may help to differentiate RPLS from the ischemic events such as “top of basilar syndrome” which may produce bilateral occipital infarctions. Proton MR spectroscopic imaging allows the in vivo measurement of various neurochemicals, which can provide information regarding the metabolism, cellular composition, and pathophysiology of brain lesions. In cases of RPLS, proton MR spectroscopic imaging shows diffusely

**Figure 2.** Brain MRI (10/02) showed high signal intensity mainly in the subcortical white matter (arrow) of bilateral posterior temporo-parietal regions (A) and the right occipital region (B) on T2-weighted images; high signal intensity mainly in the subcortical white matter (arrow) of bilateral posterior temporo-parietal regions (C) and the right occipital region (D) on FLARE images but no increased signal intensity in the subcortical white matter of bilateral posterior temporo-parietal regions (E) and right occipital region (F) on diffusion-weighted images.
reversible metabolic abnormalities (with increases both choline and creatinine and mild reductions in N-acetylaspartate) in both white and gray matter throughout the brain. These findings can help to distinguish RPLS from acute infarction or demyelination\(^9\). An important characteristic of RPLS is the reversibility of imaging abnormalities. If appropriate management is delayed, permanent neurological damages, including persistent visual system abnormalities, hemiparesis or even death may occur, especially in patients who have a delayed diagnosis or cyclosporin A treatment with poor control of hypertension\(^5,8,19\). Hyperintense diffusion-weighted imaging signal lesions and leukomalacia of the white matter on follow-up MRI were also reported in some cases\(^5,8,19\).

The management of RPLS includes (1) early recognition and withdrawal of the immunosuppressive and cytotoxic drugs, (2) antihypertensive drug treatment, and (3) appropriate parenteral anticonvulsant treatment with phenytoin or fosphenytoin, benzodiazepines, or barbiturates, or a combination\(^21\). In patients with RPLS due to HE, the mean arterial pressure should be reduced by about 20\% or to a diastolic blood pressure of 100 mm Hg, within the first hour\(^21\). Caution is necessary particularly in elderly patients and in those with pre-existing hypertension in whom aggressive reduction of blood pressure may be accompanied with a worsening of the neurological status and even stroke. Common suitable antihypertensive agents in the management of RPLS include sodium nitroprusside, labetalol, enalapril, and hydralazine\(^21\). Alternatively, in patients with RPLS due to immunosuppressive and cytotoxic drugs, the medications should be discontinued and antihypertensive therapy should be added if coexisting with high blood pressure\(^3,8,10,22\).

Although RPLS is a new clinical entity, its incidence can be expected to increase with the increased use of immunosuppressive and cytotoxic therapies after transplantation surgery and cancer treatment\(^8,19\). The diagnosis is suggested by posterior cerebral white matter abnormalities seen on T2-weighted MR imaging, and by the presence of headache, altered mental status, seizures, and disturbance of vision. Diffusion-weighted MRI is useful in differentiating RPLS from other central ner-
vous system abnormalities such as infarction, pontine glioma, multiple sclerosis, and central pontine myelinolysis. The clinicians should be aware of the characteristics of RPLS, because these striking clinical and neuro-radiological findings can be reversed by prompt lowering of raised blood pressure, and by stopping the administration of offending immunosuppressive and cytotoxic agents.

REFERENCES