Ohsawa et al., J Nephrol Ther 2013, 3:1
DOI: 10.4172/2161-0959.1000130

Journal of Nephrology & Therapeutics

Research Article Open Access

Occurrence of Reversible Posterior Leukoencephalopathy Syndrome in a Continuous Ambulatory Peritoneal Dialysis Patient

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Abstract

A 25 year-old man presented with reversible posterior leukoencephalopathy syndrome manifesting as seizure, loss of consciousness and severe hypertension. He had contracted end stage kidney disease due to Alport syndrome and was treated with continuous ambulatory peritoneal dialysis for one year. Because his residual renal function was declining, he had refractory hypertension for several months before admission. On the admission, brain T-2 intensified magnetic resonance imaging revealed hyperintensive changes that were restricted to the cortex and the subcortical white matter of the parietal lobe, temporal lobe and posterior lobe. His clinical symptoms were improved by appropriate control of blood pressure using antihypertensive drugs and fluid depletion by continuous hemodiafiltration. Previous hyperintensive lesions disappeared in brain magnetic resonance imaging. He was transferred to maintenance hemodialysis three times weekly and discharged. One month later, he had a seizure attack again because of refractory hypertension which may be derived from low compliance with sodium and water restriction. We report here a reversible posterior leukoencephalopathy syndrome patient on peritoneal dialysis with severe hypertension and volume overload.

Keywords: Reversible posterior leukoencephalopathy syndrome; Continuous ambulatory peritoneal dialysis; Hypertensive encephalopathy; Hemodialysis; Alport syndrome

Abbreviations: RPLS: Reversible Posterior Leukoencephalopathy Syndrome; CAPD: Continuous Ambulatory Peritoneal Dialysis; HE: Hypertensive Encephalopathy; HD: Hemodialysis; SUN: Serum Urea Nitrogen; ANP: Atrial Natriuremic Peptide; RRF: Residual Renal Function; MRI: Magnetic Resonance Imaging

Introduction

Reversible posterior leukoencephalopathy syndrome (RPLS) is a clinico-radiological syndrome that includes symptoms such as headache, confusion, seizures, and visual disturbances, and radiological findings of edema involving the white matter in the posterior regions of the cerebral hemispheres, and in particular bilaterally in the parietooccipital regions of the brain [1]. The pathophysiology of RPLS remains poorly understood, but it is theorized to be a result of vasospasms or loss of cerebrovascular autoregulation leading to arteriole leakage and vasogenic edema [2]. Many types of clinical settings, including hypertensive encephalopathy, eclampsia, general anesthesia interaction with cytotoxic drugs, thrombotic thrombocytopenic purpura, hemolytic-uremic syndrome and immunosuppressive drugs are regarded as causes of RPLS. RPLS is often reversible with treatment of concurrent hypertension or removal of the causative agent. However, delayed diagnosis may result in profound and permanent central nervous system dysfunction or death. Although reports of RPLS with different backgrounds have increased, the pathogenesis of RPLS in patients with end stage kidney disease is yet to be defined [3,4]. Here, we report a patient with onset of RPLS resulting from severe hypertension and volume overload under continuous ambulatory peritoneal dialysis (CAPD).

Case Presentation

A 27 year-old man was diagnosed Alport syndrome. The definite diagnosis was based on renal biopsy and his family history of bilateral sensorineural hearing loss. He started CAPD therapy when he was twenty-four years old {serum urea nitrogen (SUN) 56 mg/dL, serum creatinine (s-Cr) of 12.5 mg/dL, atrial natriuremic peptide (ANP; normal range <43) of 30.7 pg/mL}. His residual renal function (RRF) gradually deteriorated. One year later, his systolic blood pressure increased above 200 mmHg and excess fluid was uncontrollable. He received high dose CAPD and was administered several antihypertensive drugs including diuretics, but the symptoms were not improved. Although a blood examination performed in November 2006 also indicated decrease of RRF (SUN of 61 mg/dL, s-Cr of 14.0 mg/dL, ANP of 70.5 pg/mL) and low efficacy of dialysis (kt/v=1.1), he had refused to switch renal replacement therapy from CAPD to hemodialysis (HD). In December 2006 (at 25 years of age), he had been transferred to our emergency room because of a seizure, loss of consciousness and high-grade fever. Visual deterioration and headache had developed from the previous day. On physical examination, his blood pressure was 180/98 mmHg, heart rate was 114 beats per minute, respiratory rate was 16 times per minute and body temperature was 39.1°C. The breath sounds were clear. No hepatomegaly or splenomegaly was found. There was mild neck stiffness. The chest and abdominal X-rays showed no abnormalities. His electrocardiogram showed a solitary premature ventricular contraction. Initial SUN and s-Cr levels were 62 mg/dL and 18.67 mg/dL, respectively. ANP was 101 pg/mL. Peripheral white blood cells count was 18,700 /mm^3 (neutrophils: 89.5%, lymphoid cells: 5.5%, monocytes: 4%). Hemoglobin was 10.5 g/dL and the platelet count was 274,000/mm^3. Other biochemistry data and hormonal data showed no gross abnormalities {total protein of 6.9 g/dL, albumin of 4.2 g/dL, sodium of 143 mmol/L, potassium of 4.9 mmol/L, chloride of 93 mmol/L, cortisol of 12.2 μg/dL (normal range 4.0-18.3), adrenalin of 15 pg/mL (normal range <100), nor-adrenalin

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Received March 20, 2013; **Accepted** June 17, 2013; **Published** June 21, 2013

Citation: Ohsawa I, Nishitani T, Fukuda H, Takeda Y, Matsuzaki K, et al. (2013) Occurrence of Reversible Posterior Leukoencephalopathy Syndrome in a Continuous Ambulatory Peritoneal Dialysis Patient. J Nephrol Ther 3: 130. doi:10.4172/2161-0959.1000130

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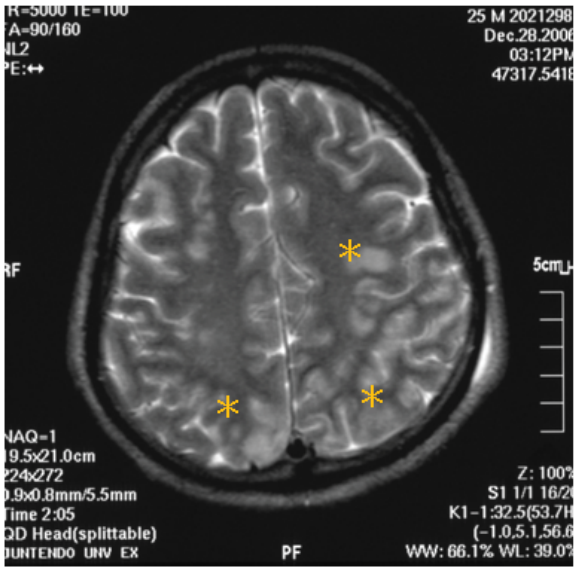
of 467 pg/mL (normal range 100-450), dopamine of 24 pg/mL (normal range <20), plasma-renin activity of 2.1 ng/mL/hr (normal range 0.3-2.9), plasma aldosterone concentration of 46.2 pg/mL (normal range 29.9-159), TSH of 2.09 μIU/mL (normal range 0.5-5.0), free T3 of 3.4 pg/mL (normal range 2.3-4.3), free T4 of 1.3 ng/mL (normal range 0.9-1.7)}. The patient's cerebrospinal fluid was clear with glucose of 84 mg/dL concentration (serum glucose of 106 mg/dL on examination), a protein level of 37 mg/dL, cell count of 1/fields and no bacteria or fungus. He was given an intravenous antihypertensive (nicardipine), anticonvulsants (diazepam, phenytoin), and underwent mechanical ventilation. At this point, there were possibilities that he suffered viral or bacterial encephalitis, prophylactic antiviral and antibacterial agents (aciclovir, ceftriaxone) were administered. The electroencephalogram showed a burst suppression pattern suggesting local brain damage or deep anesthesia with several intravenous or volatile anesthetics. Neither hemorrhage nor space-occupying mass was found in brain CT. The brain T-2 intensified MRI image revealed hyperintense signals that were restricted to the cortex and the subcortical white matter in the parietal lobe, temporal lobe and posterior lobe (Figure 1, left). Although we could not determine the focus of the infection, we used continuous veno-venous hemodiafiltration to deplete excess fluid (Figure 2).

On the second day, the blood pressure was lowered to 150/90 mmHg because of 5000 mL fluid removal. On the 8th day, abnormal findings in MRI images completely disappeared (Figure 1, right). On the 11th day, he underwent an arterio-venous fistula operation. He completely shifted from CAPD to HD and he underwent maintenance HD at a local outpatient clinic.

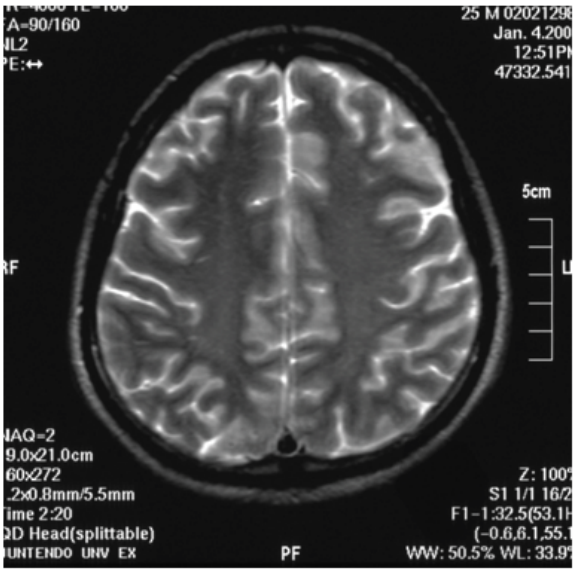
One month later, his blood pressure rose gradually because of volume overload (more than 5kg of increase between HD intervals) which may be derived from low compliance with sodium and water restriction. Since the medical staff barely managed to adjust the dry weight, his hypertension became uncontrollable. Four months after the previous admission, he was transferred to our emergency room again because of severe headache, vomiting, nausea, recurrent seizures and loss of consciousness. On physical examination, blood pressure was 210/114 mmHg, heart rate was 60 beats per minutes, and body temperature was 36.8°C. There was no sign of neck stiffness. SUN and s-Cr levels were 64 mg/dL and 16 mg/dL, and ANP was not determined. Since no remarkable findings were found in brain MRI, he was diagnosed with hypertensive encephalopathy and not RPLS. He was administered intravenous antihypertensive (nicardipine) and anticonvulsants (diazepam, phenytoin) in combination, and also underwent fluid depletion by HD immediately. Then blood pressure was controlled at a level of 130/70 mmHg. Three days later, his neurological findings returned to normal (total of 3000 mL of fluid depleted), and he was discharged.

Discussion

RPLS is a clinicoradiological syndrome, first described by Hinchey et al in 1996, that can be associated with several clinical conditions, including hypertensive encephalopathy, chronic renal insufficiency, blood transfusion and eclampsia [1]. Principal differential diagnostic parameters include cerebral vein thrombosis and acute cerebral ischemia, which are ruled out by MRI examinations. The main finding is hyperintense T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences, located in the posterior white matter edema, often with a strikingly symmetrical involvement of the parietal and occipital lobes [1]. Exact pathogenesis of RPLS remains unclear but is probably related to failure of cerebral autoregulation and vascular endothelial damage. Excessive elevation of systemic blood pressure overwhelms cerebrovascular autoregulation and causes extravasation of fluid into the brain parenchyma. RPLS often develops in the parieto-occipital region, because posterior cerebral circulation shows less sympathetic adrenergic innervation, and therefore is potentially more susceptible to hypertension [5]. It is interesting to note that abnormal structure



1st hospital day



8th hospital day

Figure 1: Reversible of brain MRI. On the first hospital day, a T-2 intensified MRI image revealed hyperintense signals (*) that were restricted to the cortex and the subcortical white matter of the parietal lobe, temporal lobe and posterior lobe (left side image). On the eighth hospital day, these findings disappeared along with improvement of the clinical symptoms (right side).

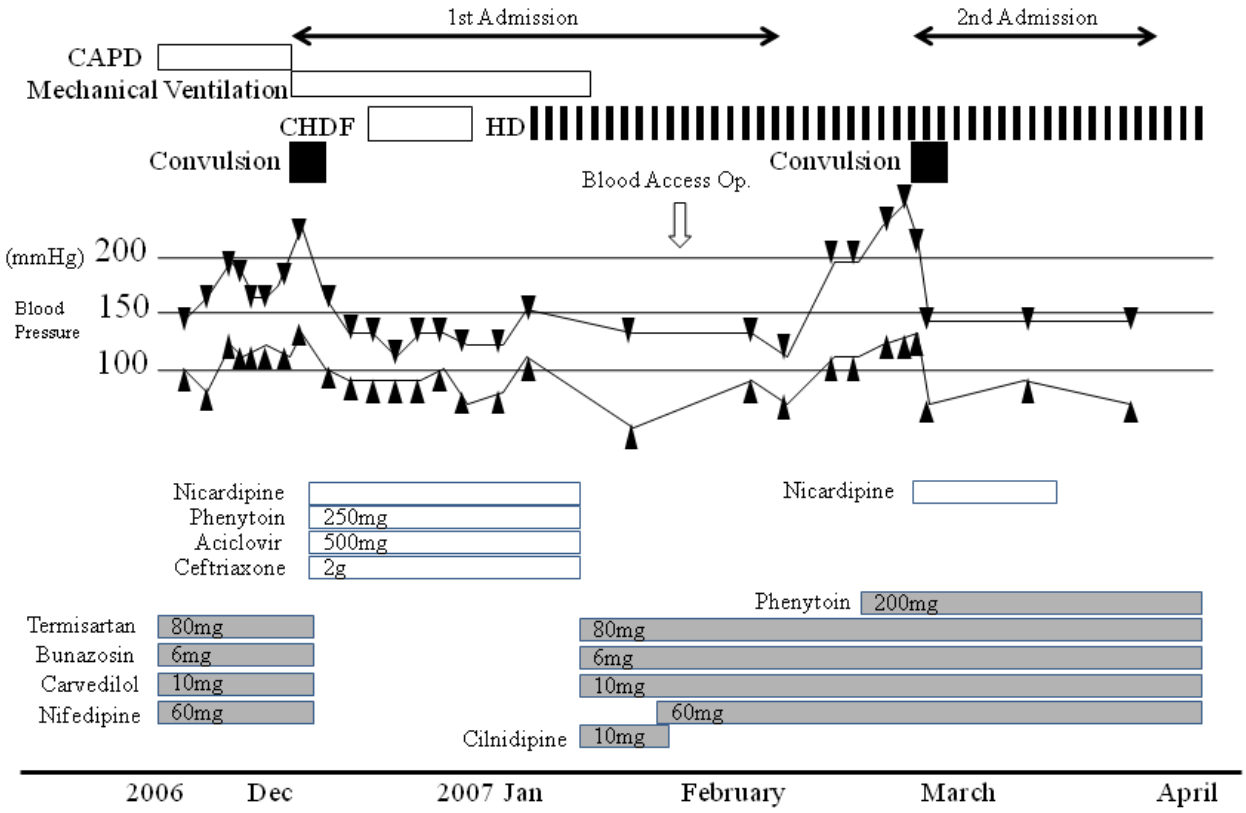


Figure 2: Clinical course of this case. Recurrent convulsions appeared with worsening of blood pressure control. Along with improvement of blood pressure control by anti-hypertensive agents and removal of excess body fluid by blood purification (CHDF and HD), the clinical symptoms disappeared.

of capillary walls is a hallmark of the Alport syndrome [6], and there is possibility that there might be abnormal permeability which intertwined in the pathogenesis of angioedema in our case.

RRF also plays a role in removal of middle molecules and control of water and sodium removal [7,8]. The relationship among RRF, morbidity and survival in CAPD patients is well known. In our case, excess body fluid and uremic toxins may have induced refractory hypertension. Many authors have pointed that RPLS is caused by an acute elevation of blood pressure [9]. We hypothesize that uncontrolled hypertension resulting from elimination of RRF might lead to onset of RPLS. There is a supportive case report of RPLS in a patient on CAPD with poor compliance and their suggestion is same as ours [10].

His second episode of hypertensive encephalopathy was also due to over hydration derived from his excessive dietary sodium intake, which is the major cause of extracellular volume expansion in renal insufficiency. Patients with renal insufficiency often combined low serum albumin and hypertension. These factors organize low colloid osmotic pressure and high hydrostatic pressure which enhance vascular permeability. These complications predispose to the development of RPLS [11]. His first brain MRI findings were recognized as typical findings of RPLS, but there were no remarkable images in the second attack. This difference might be derived from the levels of uremic toxins. In PD patients with uncontrollable hypertension, we have to notice that the occurrence of RPLS and change the dialysis prescription. Reports of recurrence of RPLS in different patient populations have increased recently in the literature (ex. sickle cell disease, antibody-positive autoimmune disease, bone-marrow transplantation), but there is little information on recurrence of this syndrome in patients with previous renal replacement therapy.

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