Uremic Encephalopathy Presenting with Unilateral Destructive Leukoencephalopathy Successfully Treated with Hemodialysis

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Abstract:
An 81-year-old woman was hospitalized with progressive consciousness disturbance. Blood tests showed acidemia with severe renal dysfunction, and a cerebral spinal fluid (CSF) test showed pleocytosis with myelin basic protein (MBP) elevation. Brain magnetic resonance imaging showed unilaterally dominant subcortical white matter lesions with lentiform fork sign on T2-weighted imaging. After initiating hemodialysis, her consciousness disturbance and white matter lesions improved, suggesting uremic encephalopathy (UE). Unilaterally dominant leukoencephalopathy and high pleocytosis with MBP elevation in CSF are less common than previously identified characteristics of UE. When unilateral leukoencephalopathy occurs in patients with renal failure, UE should be considered.

Key words: Leukoencephalopathy, uremic encephalopathy, myelin basic protein, hemodialysis

Introduction
Neurological complications associated with uremia have severe effects on the outcome of patients with advanced renal failure. Uremic encephalopathy (UE) is a metabolic disorder that can occur in patients with advanced renal failure and can be resolved with hemodialysis (1, 2). However, its pathophysiology remains to be fully elucidated (1, 2).

We herein report a patient with atypical UE who presented with unilateral leukoencephalopathy with cerebrospinal fluid (CSF) pleocytosis and myelin basic protein (MBP) elevation and was successfully treated with hemodialysis.

Case Presentation
An 81-year-old woman was transferred to our emergency department because of acute progressive consciousness disturbance and left hemiparesis. She had a history of hypertension and progressive renal sclerosis, and she had undergone arteriovenous shunt surgery to start chronic hemodialysis as scheduled 3 days before admission to our hospital. Although she had no complications following her shunt surgery, her consciousness gradually worsened after surgery. On her arrival, she only had moderate hypertension (systolic blood pressure 173 mmHg and diastolic blood pressure 74 mmHg) and no other vital sign abnormalities (heart rate 80 bpm, respiratory rate 16 bpm, and body temperature 37.3°C). She was able to open her eyes in response to our call but could not speak, and a neurological examination revealed complete left hemiparesis and left hemi-spatial neglect. She did not have meningeal sign.

On a physical examination, there were no eye or cutaneous abnormalities. Brain magnetic resonance imaging (MRI) with diffusion-weighted imaging showed hyperintense lesions with mixed apparent diffusion coefficient decline and elevation in the right hemisphere (Fig. 1A-1, A-2). T2-weighted imaging showed severe subcortical white matter lesions with lentiform fork sign (LFS) in the basal ganglia (Fig. 1A-3). Magnetic resonance angiography (MRA) showed no occlusion or stenosis in the major cerebral arteries (Fig. 2A, 2B). Laboratory tests showed a slightly ele-
Figure 1. Imaging findings of the present case. A-1, A-2: Axial diffusion-weighted imaging showed hyperintense lesions with mixed apparent diffusion coefficient decline and elevation in the right hemisphere (arrowheads). A-3: T2-weighted imaging showed severe subcortical white matter lesions with brain edema accompanied by lentiform fork sign in the basal ganglia (arrows). B: Follow-up magnetic resonance imaging (MRI) at one week showed white matter expansion to the left hemisphere. C: Follow-up MRI at one month showed improvement in brain edematous changes. D: Follow-up MRI at six months after symptom recovery showed resolution of the edematous changes, but the bilateral white matter lesions remained.

Figure 2. Angiographical findings of the present case. A, B: Magnetic resonance angiography showed no occlusion or stenosis in the major cerebral arteries.

Elevated white blood cell count (10,600/μL) with neutrophilia (87%) and slightly elevated C-reactive protein level (2.55 mg/dl). The CSF showed marked neutrophilic pleocytosis (1,061 cells/μL, with polymorphonuclear leukocyte 92%), elevated protein levels (313 mg/dL), and markedly elevated MBP levels (17,000 pg/mL, standard value <102 pg/mL) with negative findings for oligoclonal bands. We did not detect any bacteria in her CSF culture. An arterial blood gas analysis revealed acidemia (pH 7.241), metabolic acidosis (HCO₃⁻ 8.7 mEq/L) without anion gap, and hyperkalemia (K 5.8 mEq/L). We started emergent hemodialysis immediately, and her neutrophilia rapidly improved three days after admission. For several days after hemodialysis initiation, her symptoms temporarily deteriorated to quadriplegia, and follow-up MRI performed one week after initiation showed white matter expansion to the left hemisphere (Fig. 1B). However, her consciousness and quadriplegia improved with continuing hemodialysis, and the edematous changes resolved after one month (Fig. 1C). Because her symptoms improved with only hemodialysis, we diagnosed her with UE, and she was transferred to another hospital for rehabilitation two months after...
admission. Six months later, her symptoms had fully resolved, and follow-up brain MRI revealed resolution of the edematous changes, but bilateral white matter lesions remained (Fig. 1D).

Discussion

We experienced a case of UE presenting as unilaterally dominant and bilaterally progressive leukoencephalopathy with brain edema and pleocytosis with MBP elevation. The new findings of our case were atypical findings of unilaterally dominant leukoencephalopathy and pleocytosis with MBP elevation as UE.

UE is a metabolic disorder that occurs due to the accumulation of uremic toxins in patients with end-stage renal disease (1, 2). The pathophysiology of UE is considered to involve disruption of the blood-brain barrier due to the cytotoxic and vasogenic effects of uremic toxins (2, 3). UE is characterized by non-specific symptoms, such as consciousness disturbance, headache, myoclonus, and seizures. A diagnosis is made when symptoms improve with hemodialysis. Abnormal MRI findings typically demonstrate mixed cytotoxic and vasogenic edema in the subcortical white matter or basal ganglia (3). One specific MRI finding observed in UE is LFS, which is characterized by hyperintensity in the basal ganglia surrounded by a more hyperintense rim delineating the lentiform nucleus on T2-weighted imaging; these imaging findings reflect edema of these regions (3).

In the present case, MRI findings initially showed unilaterally dominant leukoencephalopathy. Therefore, we considered other types of unilateral leukoencephalopathy, such as progressive multifocal leukoencephalopathy, Hashimoto encephalopathy, gliomatosis cerebri, and medication-induced leukoencephalopathy. However, we did not find any signs that suggested these syndromes, and she was not taking any medications that could cause encephalopathy. Another differentiative diagnosis was neuro-Sweet diseases. However, this patient did not have cutaneous abnormalities. Her neutrophilia at admission was rapidly improved after dialysis initiation. In addition, the symptoms and imaging findings of this patient improved with dialysis alone. Although we did not determine the HLA typing or CSF IL-6 level, these findings could support the low possibility of neuro-neutrophilic diseases.

Posterior reversible encephalopathy syndrome (PRES) was another major differential diagnosis. PRES is characterized by vasogenic edema, occurs in the setting of renal failure (4), and is sometimes accompanied by UE (1). In the present case, however, the patient did not show extremely high systolic blood pressure. In addition, cytotoxic edema with apparent diffusion coefficient decline was observed within the vasogenic edema, which is usually seen in UE but rarely seen in PRES (3). Furthermore, the marked pleocytosis and elevated CSF protein levels were not typical finding of PRES (5). Therefore, PRES was not strongly suspected in the present case. Since metabolic encephalopathy can present as unilaterally dominant encephalopathy (6), unilateral encephalopathy may not be a rare finding of metabolic encephalopathy. We comprehensively diagnosed the patient with UE, considering the dialysis effectiveness and positivity for LFS.

The CSF findings of UE are not yet fully understood (1, 2). The neutrophilic CSF pleocytosis with elevated protein and MBP values, as observed in the present study, have not been previously reported. UE causes the disruption of the BBB, resulting in inflammation and cytotoxic brain edema (2). In addition, in a pathological study of UE in a goat, spongiform encephalopathy with myelin vacuolation was observed (7). These findings may suggest that UE can cause destructive and demyelinating brain lesions (3, 7). Therefore, neutrophilic CSF pleocytosis with MBP elevation in the present case may reflect the inflammatory response due to destructive brain lesions. In the present case, good symptom recovery despite remaining white matter lesions may also be associated with demyelination. Our findings suggest that destructive leukoencephalopathy may be another aspect of UE.

In conclusion, UE can present as unilateral and destructive leukoencephalopathy. When unilateral leukoencephalopathy occurs in patients with renal failure, UE should be considered as a differential diagnosis, and treatment with hemodialysis may be required.

The authors state that they have no Conflict of Interest (COI).

References


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