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CASE SERIES

Chorea in Hemodialysis Patients: Report of Two Cases

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Video abstract

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Background: Chorea is rare in maintenance dialysis patients but seriously affects the quality of life, and there are few previous reports of this condition. We report two patients undergoing regular hemodialysis for end-stage renal disease, both of whom presented with progressively intensified involuntary limb movements, but originating from different etiologies.

Case Presentation: We report two patients undergoing regular hemodialysis for end-stage renal disease who presented with progressively intensified involuntary limb movements. Treatment with sedatives alone proved ineffective in both cases. Through differential diagnosis, one patient was diagnosed with diabetic striatopathy and managed with intensive glycemic control, while the other was found to have uremic metabolic encephalopathy and treated with a combination of hemodialysis and hemoperfusion. Subsequently the patients' symptoms improved significantly.

Conclusion: Choreiform movements in hemodialysis patients arise from a variety of etiologies. These two cases suggested the susceptibility to the onset of chorea in the early stage of maintenance hemodialysis.

Keywords: hemodialysis, chorea, case report, end-stage renal disease

Background

Chorea encompasses a spectrum of nervous system disorders stemming from dysfunctions in voluntary motor regulation, characterized primarily by involuntary, rapid, and sudden limb movements. While infrequent among maintenance hemodialysis (MHD) patients, it exerts a notable impact on their quality of life.[1] Despite the similarity in presenting symptoms, patients may have distinct underlying causes. Understanding the underlying mechanisms and promptly identifying the causative factors are crucial for effective management and optimal patient outcomes.

In this context, we present two compelling cases of MHD patients who developed choreiform movements, highlighting the diagnostic challenges and therapeutic strategies employed in each case. The first case demonstrates a patient diagnosed with diabetic striatopathy, emphasizing the significance of intensive glycemic control in managing chorea associated with this condition. Conversely, the second case illustrates the successful treatment of uremic metabolic encephalopathy-induced chorea through a combination of hemodialysis and hemoperfusion, underscoring the importance of improving dialysis adequacy in MHD patients.

Case Presentation

Case 1

A 67-year-old man with end-stage diabetic nephropathy had been undergoing regular hemodialysis for four months when he presented to our hospital with a two-week history of progressively worsening involuntary movements in his right

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limbs, along with muscle soreness and difficulty falling asleep. He had been prescribed oral "sulpiride" at another medical facility, but the symptoms persisted unabated.

The patient's medical history revealed hypertension for over 10 years and diabetes mellitus for approximately 20 years (with no use of hypoglycemic drugs or insulin since initiating dialysis), and no previous neurological conditions. He did not experience any fever, sore throat, or arthralgia over the past year. On physical examination, his blood pressure was measured at 150/90 mmHg, and he exhibited continuous extension and flexion movements in the right upper and lower extremities. Despite these involuntary movements, he maintained clear consciousness and speech, showing no signs of disorientation or pathological symptoms.

Laboratory tests indicated elevated muscle enzymes and glycated hemoglobin, hypoproteinemia, hypot3-emia, and mild hypocalcemia, with no significant anemia or hyperparathyroidism (Table 1). Despite intensive hemodialysis, correction of uremia-related complications, and nutritional support therapy, the involuntary limb movements persisted. Throughout the hospitalization, terminal blood glucose levels fluctuated between 14–25 mmol/L, with negative urine ketone levels.

A T1-weighted magnetic resonance imaging (MRI) conducted five days post-admission revealed high signal intensity in the right basal ganglia with clear boundaries and no surrounding tissue edema (Figure 1). The patient was diagnosed with diabetic striatopathy and initiated insulin therapy. Following one week of hypoglycemic treatment, the involuntary limb movements significantly improved, and muscle enzyme levels returned to the normal range. The patient was discharged 14 days after admission, but was lost to follow-up.

Case 2

A 50-year-old man was diagnosed with end-stage renal disease and had been receiving regular hemodialysis at another hospital since 11 months prior. The patient suffered from gradually intensified involuntary movements in both lower

Table 1 Laboratory Data of the Two Cases After Admission

Parameter	Case 1	Case 2	Normal Range
Urea nitrogen (mmol/L)	17.30↑	27.27↑	2.86–8.20
Creatinine (μmol/L)	919.00↑	1132.60↑	53.00–123.00
β_2-microglobulin (mg/L)	16.80↑	48.70↑	0.8–2.8
Hemoglobin (g/L)	122	98↓	110–130 for CKD patients[2]
Thyroid stimulating hormone (mIU/L)	0.9277	3.7572	0.3500–4.9400
Free triiodothyronine (pmol/L)	<2.30	3.40	2.43–6.01
Free thyroxine (pmol/L)	10.34	10.92	9.00–19.00
Parathyroid hormone (pg/mL)	187.10	74.60	15.00–68.30 (2 to 9 times the upper normal limit for dialysis patients[3])
Creatine phosphate kinase (U/L)	7737.00↑	356.00↑	50–310
Potassium (mmol/L)	5.01	3.88	3.50–5.30
Sodium (mmol/L)	137.80	143.80	137.00–147.00
Calcium (mmol/L)	2.08↓	1.87↓	2.11–2.52
Albumin (g/L)	30.80↓	42.00	40–55
Vitamin B1 (ng/mL)	2.43	1.39	1.00–10.00
Glycosylated hemoglobin(%)	11.00	5.10	4.0–6.0
Rheumatoid factor (IU/mL)	<20.00	<20.00	0–20
Antistreptolysin-O (IU/mL)	<20.00	<25.00	0–100
C-reactive protein (mg/L)	25.90↑	13.40↑	0–8
Hepatitis B surface antigen (IU/mL)	0.000	0.000	<0.050
Hepatitis B core antibody (S/CO)	0.950	0.050	<1.00
Hepatitis C antibody (S/CO)	0.008	0.011	<1.00
Treponema pallidum antibody (S/CO)	0.008	0.024	<1.00
Human immunodeficiency virus antibody (S/CO)	0.14	0.18	<1.00
Antinuclear antibody	Negative	Negative	Negative
Anti-double stranded DNA	Negative	Negative	Negative
Antineutrophil cytoplasmic antibody	Negative	Negative	Negative

Notes: "↑" indicates values above the normal range, while "↓" indicates values below the normal range.

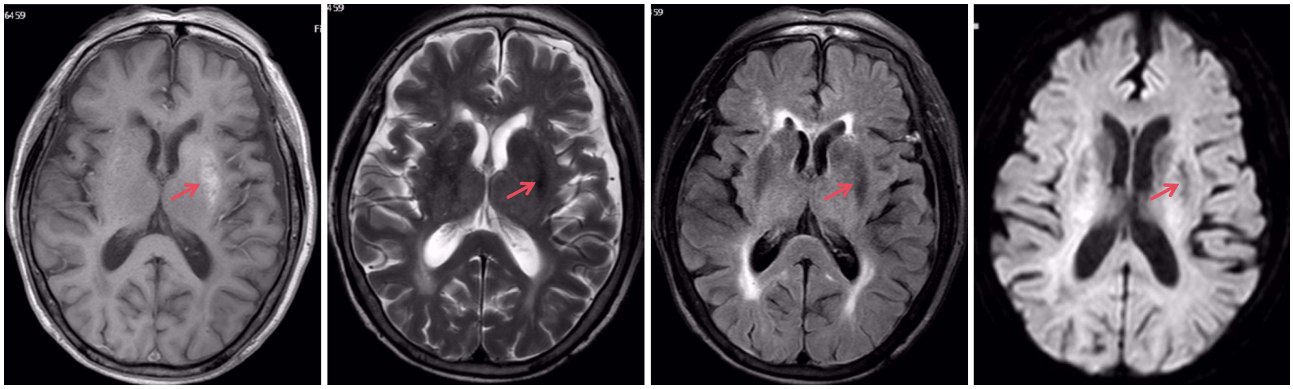

Figure 1 Case 1. An abnormal signal shadow in the left basal ganglia, characterized by a distinct lesion boundary, absence of occupying effects or surrounding tissue edema, and no involvement of the internal capsule. The red arrows point to the lesions. The shadow manifests high signals in T1-weighted images (T1WI), iso-low signals in T2-weighted images (T2WI) and flair sequences, and low signals in diffusion-weighted imaging (DWI).

limbs without apparent triggers for two weeks, resulting in an inability to walk. He had previously received intravenous haloperidol treatment which induced rapid onset of sleep at another hospital, but the symptoms recurred upon waking.

The patient had a five-year history of type 2 diabetes and had been on long-term "metformin" therapy (discontinued at the onset of the current illness, noting subsequent self-testing of fingertip blood sugar levels did not indicate high readings). No fever or joint pain occurred since the initiation of maintenance hemodialysis. He underwent parathyroidectomy at another hospital one month ago for severe secondary hyperparathyroidism, followed by regular oral "calcium carbonate" treatment. Additionary, there was no reported family history of neurological diseases.

Physical examination revealed alternating uncontrollable extension and flexion, as well as internal and external rotation, of both lower limbs, accompanied by lumbar twisting. Tendon reflexes and body depth sensation were within normal limits. No impairment of consciousness or speech was found, and trousseau's sign was negative. Laboratory tests showed mild anemia, a slight decrease in blood calcium and parathyroid hormone levels, and a mild increase in muscle enzymes. Thyroid function indicators and glycated hemoglobin levels were predominantly normal, and there was no evidence of vitamin B1 deficiency (refer to Table 1). Post-admission blood glucose levels fluctuated between 6–12 mmol/L, within an acceptable range for patients undergoing hemodialysis.[4] Due to the onset of involuntary movements, the patient was unable to cooperate with lumbar puncture for cerebrospinal fluid examination. The cranial MRI displayed speckled abnormal signal shadows in the bilateral frontal subcortex and adjacent to the ventricles bilaterally, as well as symmetric abnormal signal shadows in the bilateral basal ganglia. These areas exhibited iso-low signals in T1-weighted images (T1WI) and diffusion-weighted imaging (DWI), iso-high signals in T2-weighted images (T2WI), and high signals in Flair sequences (Figure 2).

Initially, the patient received an escalated dose of calcium supplementation (to mitigate limb twitching associated with hypocalcemia), daily intramuscular injection of vitamin B1 at a dosage of 100 mg (to prevent and manage Wernicke's encephalopathy stemming from vitamin B1 deficiency), and a conservative regimen of clonazepam (0.5 mg thrice daily) for sedation. However, despite three days of adherence to these interventions, the involuntary limb movements exhibited no amelioration. Subsequent to a comprehensive multidisciplinary consultation and deliberation, the patient received a diagnosis of uremic metabolic encephalopathy and underwent treatment involving hemodialysis coupled with hemoperfusion (HDP). We found that the effectiveness of uremic toxin clearance in HDP is superior to that in hemodialysis (Table 2 presents the levels of uremic toxin indicators both before and after hemodialysis, as well as for HDP). Following two HDP sessions, a gradual reduction in lower limb twisting was observed, with substantial alleviation noted after four sessions. Subsequently, the patient was discharged to an alternate medical facility for maintenance dialysis, demonstrating no recurrence of involuntary limb movements during a three-month follow-up period.

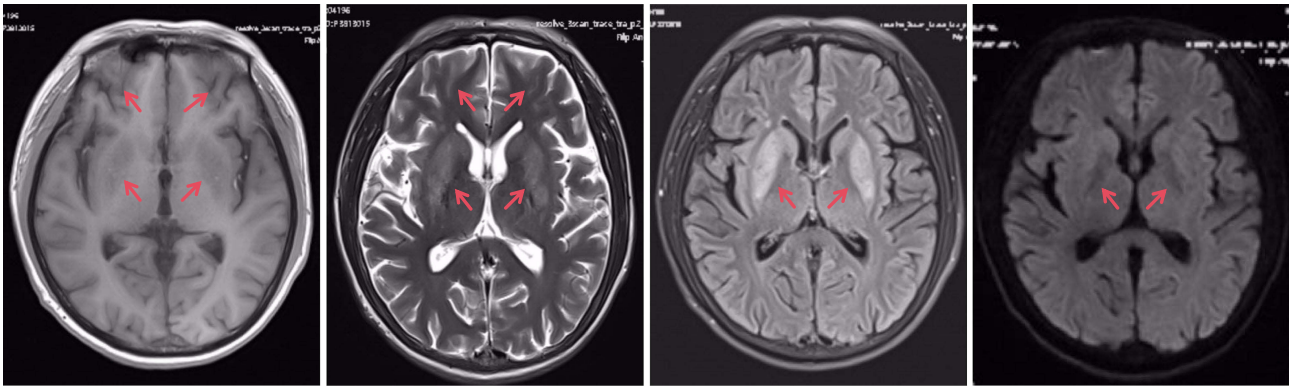

Figure 2 Case 2. Speckled abnormal signal shadows in the bilateral frontal subcortex and adjacent to the ventricles bilaterally, as well as symmetric abnormal signal shadows in the bilateral basal ganglia. The red arrows point to the lesions. These areas exhibited iso-low signals in T1-weighted images (T1WI) and diffusion-weighted imaging (DWI), iso-high signals in T2-weighted images (T2WI), and high signals in flair sequences.

Discussion

Case 1 presented with typical symptoms of diabetic striatopathy, including hemichorea, non-ketotic hyperglycemia, and a striatal high signal on T1-weighted MRI.[5] Diabetic striatopathy, also known as hemichorea associated with non-ketotic hyperglycemia, needs to be distinguished from striatal infarction and rheumatic microchorea. In our findings, the diffusion-weighted imaging of case 1 did not reveal diffusion restriction, ruling out striatal infarction. Additionally, the patient was elderly, had no recent history of fever or joint pain before symptom onset, and tested negative for anti-"O" antibody, excluding rheumatic chorea (ie, chorea minor).

The incidence of diabetic striatopathy has been reported to be approximately 1/100,000, with the majority of reported cases involving Asian patients. This incidence might be underestimated due to misdiagnosis as cerebral hemorrhage.[6] The pathophysiological basis of diabetic striatopathy has not been fully elucidated. It is currently believed to be associated with inadequate striatal perfusion caused by diabetic cerebrovascular lesions, as well as gamma-aminobutyric acid depletion and motor neuron disinhibition due to anaerobic metabolism of brain tissue during hyperglycemia.[7] Hypoglycemic therapy and sedatives have been reported to lead to short-term improvement in chorea symptoms, but with a subsequent risk of recurrence.[8] Recognition of sudden chorea symptoms and MRI imaging findings (such as T1-weighted high signal shadow in the striatum) can aid in early diagnosis and treatment of diabetic striatopathy.

It has been observed that diabetic patients undergoing hemodialysis experience greater fluctuations in blood glucose levels, and those who are on insulin therapy may encounter hypoglycemic episodes during the hemodialysis process.[9] Some patients have chosen to discontinue hypoglycemic measures to avoid hypoglycemia during dialysis, but this

Table 2 Uremic Toxin Levels Pre and Post Hemodialysis and HDP of Case 2

Parameter	Hemodialysis		HDP	
	Pre	Post	Pre	Post
Urea nitrogen (mmol/L)	27.27	10.47	26.49	7.82
Creatinine (μmol/L)	1132.60	477.20	1053.10	372.90
β_2-microglobulin (mg/L)	48.70	29.30	44.60	18.60
spKt/V	1.12		1.41	
URR	0.616		0.705	

Abbreviations: HDP, hemodialysis combined with hemoperfusion; spKt/V, single-pool urea removal index; URR, urea reduction rate.

decision can increase the risk of hyperglycemia and its associated complications. Therefore, it is crucial to enhance glycemic management in MHD patients.

In Case 2, stable blood glucose levels and the absence of obvious striatal lesions on cranial MRI did not meet the criteria for a diagnosis of diabetic striatopathy. Furthermore, there was no evidence of rheumatic chorea, as indicated by the absence of fever, joint pain, or elevated anti-"O" antibodies. Additionally, the absence of vitamin B1 deficiency coupled with the lack of response to supplementation ruled out Wernicke's encephalopathy. The ineffectiveness of sedatives and the absence of medical or family history of Huntington's chorea-related illness did not support the diagnosis of Huntington's chorea. Instead, a treatment protocol for uremic metabolic encephalopathy was implemented by increasing dialysis adequacy, which resulted in positive outcomes.

Patients with end-stage renal disease are susceptible to neurological complications as a result of uremic toxin retention, electrolyte disturbances, anemia, and malnutrition.[10] The risk of uremic encephalopathy, although reduced after dialysis, can be heightened by factors such as inadequate dialysis, significant changes in the internal environment, infections, or inflammation.[11] Uremic metabolic encephalopathy commonly presents with psychiatric abnormalities, hallucinations, coma, muscle tremors, seizures, and other symptoms,[10] while choreoathetoid symptoms are seldom reported.[12] A limited number of previous cases indicated that the presence of chorea in chronic kidney disease was associated with reduced serum vitamin B1 levels (also known as Wernicke encephalopathy), and all patients improved after Vitamin B1 supplementation.[13] However, this finding is inconsistent with the current cases. Therefore, the identification of uremic metabolic encephalopathy should be based on the specific clinical conditions observed in each patient.

Hemodialysis is the predominant renal replacement therapy for patients with end-stage renal disease in China,[14] which excels in removing excess water and micromolecule toxins, but may not be as effective in macro-middle molecule toxins.[15] In contrast, hemoperfusion eliminates endogenous or exogenous macro-middle molecule toxins, as well as a certain protein-bound toxins, through non-specific physical adsorption. Studies have reported that its combination with hemodialysis effectively attenuates the inflammatory response, mitigates peripheral nerve injury, and reduces the incidence of cardiovascular events.[16] Therefore, the combined utilization of hemoperfusion in MHD patients is recommended to enhance dialysis adequacy.

Moreover, both patients underwent hemodialysis for a duration not exceeding one year (4 months and 11 months, respectively), suggesting that inadequate dialysis therapy and swift alterations in the internal milieu could precipitate neurological complications in the initial phase of hemodialysis. Nephrologists have recommended intensified supervision of patients in the early stages of dialysis, encompassing evaluations of dialysis adequacy and proactive management of complications to improve long-term outcomes.[17]

Conclusion

In summary, chorea rarely manifests in uremic patients undergoing maintenance hemodialysis; however, it can stem from diverse etiologies and necessitates individualized analysis based on the patient's specific condition. Patients with diabetes mellitus should be carefully managed to maintain optimal blood glucose levels, while dialysis adequacy should be a focal point throughout the course of maintenance dialysis, particularly in the initial stages. The integration of hemodialysis with hemoperfusion has shown promise in enhancing dialysis adequacy, improving quality of life, and augmenting survival rates.

Data Sharing Statement

Data are available from the corresponding author upon reasonable request and with permission of Science and Technology Department of Nanjing First Hospital.

Ethics Approval and Consent to Participate

This case study was conducted ethically in accordance with the Declaration of Helsinki. This study was approved by the ethical committee of Nanjing First Hospital (KY20220425-02).

Consent for Publication

The authors have obtained consent for the publication of information and images from the patients discussed in the report.

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Disclosure

The authors have no conflicts of interest to declare.

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