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CASE REPORT

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Uremic encephalopathy manifesting with a unique MRI finding (the lentiform fork sign) in an adult male: A case report

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Key Clinical Message

A novel radiologic sign in patients with renal failure and uremic encephalopathy (UE) with metabolic acidosis has recently been identified as the lentiform fork sign. On magnetic resonance imaging (MRI), the "lentiform fork sign" has been described as bilateral symmetrical hyperintensities in the basal ganglia encircled by a hyperintese rim delineating the lentiform nucleus. Changes in uremic solute retention, aberrant blood–brain barrier transport, disordered vascular reactivity, altered electrolyte and acid–base balance, and altered hormone metabolism are the most likely causes of the condition. A 56-year-old male with end-stage renal disease was brought to the emergency room for a progressive change in mental status and involuntary arm movements over the previous 5 days, which were accompanied by mild dyspnea. A brain MRI was performed, and it revealed hyperintensity on T2/FLAIR in the white matter surrounding the basal ganglia. the patient was treated with dialysis and improved greatly. Intensified hemodialysis and glycemic control are the cornerstones of treating diabetic uremic syndrome (DUS) with likely reversible clinical symptoms and remission of imaging abnormalities.

KEYWORDS

diabetic uremic syndrome, lentiform fork, uremia, uremic encephalopathy

1 | INTRODUCTION

Uremic Encephalopathy (UE) is common in patients with either acute or chronic renal failure. Patients with severe renal failure may develop toxic-metabolic encephalopathy as a consequence of endogenous uremic toxins.[1] The disorder is most likely caused by changes in uremic solute retention, abnormal blood–brain barrier transport, disturbed vascular reactivity, altered electrolyte and acid–base balance, and changed hormonal metabolism. The pathogenesis is uncertain and complicated.[2]

The diagnosis is frequently confirmed after the improvement of the patient's symptoms following dialysis or transplantation.[2]

The "Lentiform fork sign" has been reported on magnetic resonance imaging (MRI), and is shown as bilateral

symmetrical hyperintesities in the basal ganglia surrounded by a hyperintense rim delineating the lentiform nucleus. It has been postulated to result from cases of severe metabolic acidosis, such as metformin-associated encephalopathy, pyruvate dehydrogenase deficiencies, uremic encephalopathy, propionic acidemia, mitochondrial diseases, and methanol/ethylene glycol intoxication.[3]

Here we report a case of a 56-year-old patient with uremic encephalopathy in the setting of renal failure; presented with a unique MRI finding "Lentiform fork sign."

2 | CASE PRESENTATION

2.1 | Case history

A 56-year-old male with end-stage renal disease is brought to the emergency department for a progressive altered mental status and involuntary arm movements associated with mild dyspnea over the last 5 days. The patient was diagnosed 4 months ago with end-stage renal disease due to long-standing uncontrolled type 2 diabetes mellitus and hypertension and he was programmed on hemodialysis three times a week. The patient was put on Liraglutide for glycemic control, and losartan for his blood pressure control without clear adherence. The past medical history was unremarkable.

In the emergency department, his vital signs were as follows: temperature 37.2°C, blood pressure 140/90 mmHg, heart rate 95 bpm, O2 saturation 95, the patient was tachypneic (RR = 28) with mild distress. The patient was lethargic, disoriented, and aroused by vocal stimuli (Glasgow coma scale was 13/15) on physical examination. Pupils were sluggishly reactive to light. Tremor and asterisk were noted without nuchal rigidity or any other focal neurological signs. He had bilateral diminished breath sounds at lung bases and pitting edema in the lower extremities.

2.2 | Differential diagnosis, investigations, and treatment

The initial laboratory tests were WBCs 11×10^3 cells/mL, RBCs 3.3×10^6 cell/ml, Hb 10.5 mg/dL, platelets 170×10^3/mL, Urea 205 mg/dL, Creatinine 12.1 mg/dL, Glucose 99 mg/dL, Sodium 139 mg/dL, Potassium 5.9 mg/dL, the Arterial blood gases (ABGs): PH = 6.9, HCO3 = 2.2 mEq/L, and PO2 = 100 mmHg, PCO2 = 11.4 mmHg, which are consistent with severe metabolic acidosis. Sodium bicarbonate was infused to correct the acidosis, and an emergent hemodialysis session was conducted. After that, the patient was admitted to the ICU, until he was stabilized. The ABGs were re-evaluated after 12 h and showed: PH = 7.19, HCO3 = 11 mEq/L, PCO_2 = 22 mmHg, PO_2 = 98 mmHg. The patient then regained his consciousness and was alert and oriented. However, the tremor and asterixis remained.

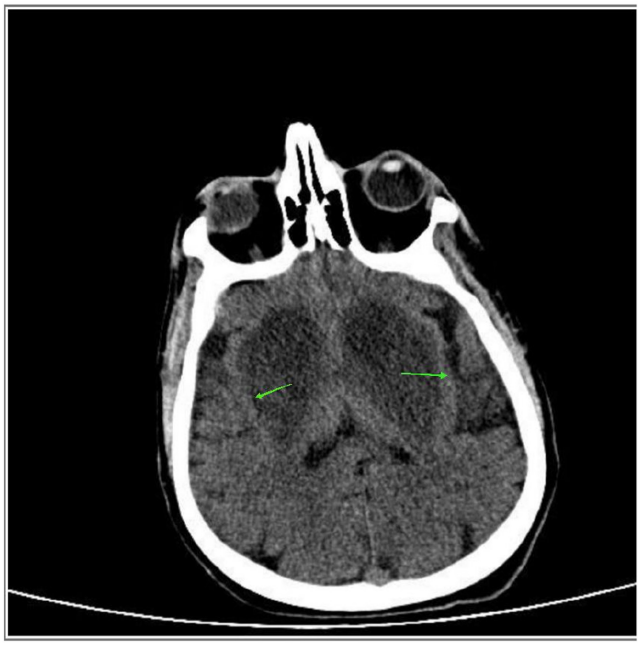

FIGURE 1 A hypodensity in the basal ganglia on brain CT.

A brain MS CT showed areas of hypodensity at the level of the basal nuclei on both sides of the midline, which may be in the context of hypoxia or metabolic damage, senile changes, calcifications on the midline in the frontal area (Figure 1). A brain MRI was performed and it showed a hyperintensity on T2/FLAIR in the white matter surrounding the basal ganglia (the internal and external capsule) (Figure 2A,B). These features are characteristic of lentiform fork sign (LFS) which is pathognomic for uremic encephalopathy.

Based on his clinical presentation, laboratory results, and imaging finding, the patient was diagnosed with uremic encephalopathy associated with extrapyramidal syndrome associated with chronic kidney disease and dialysis.

Further questioning revealed that the patient had missed his last couple of dialysis sessions, and he was put on Haloperidol by his primary care physician to treat his confusion.

2.3 | Outcome and follow-up

The haloperidol was stopped and three more dialysis sessions were performed afterward, and after 10 days all of his symptoms and laboratory results improved immensely.

The laboratory results before discharge are demonstrated in Table 1.

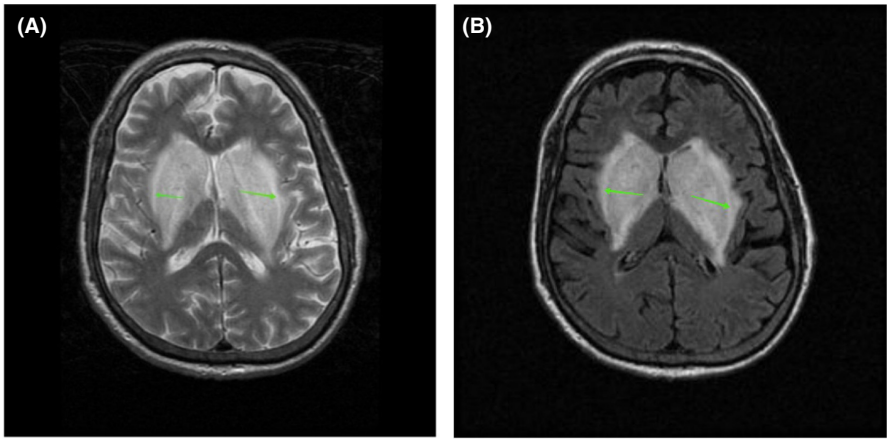

FIGURE 2 (A) A hyperintensity on the T2 sequence in the basal ganglia. (B) A hyperintensity on T2/FLAIR in the basal ganglia.

TABLE 1 Laboratory results upon discharge.

WBC	**5.4×10^3**	**RBC**	**3.7×10^6**	**Hb**	**10.3**	**MCV**	**96**	**Plt**	**170×10^3**
Urea	61	Cr	3.4	Glu	95	Na	138	K	4
Cl	101	PH	7.4	Hco_3	20	Pco_2	36	Po_2	88

3 | DISCUSSION

We describe a case of a patient with diabetes, chronic kidney disease, severe metabolic acidosis, and uremic encephalopathy who demonstrated a rare imaging finding called the lentiform fork sign.

Wang et al. were the first to propose a condition called "Diabetic uremic syndrome" in diabetic patients who have end-stage renal disease, complaining of neurological symptoms, and bilateral basal ganglia lesions.[4,5]

Manickavasagar et al.[6] suggested the term "extrapyramidal syndromes of chronic kidney disease and dialysis (EPS-CKDD)" in a retrospective case series review of 20 patients receiving dialysis. The diagnostic criteria were based on the presentation of an acute extrapyramidal movement disorder manifesting either as hypokinetic acute parkinsonism or a hyperkinetic form with acute chorea/athetosis associated with bilateral basal ganglia injury.

The key risk factors for EPS-CKDD were type 2 diabetes, metformin use, dialysis, female sex, and potentially thiamine deficiency. Metabolic acidosis, elevated lactate, and thiamine deficiency were the related laboratory abnormalities. The study also indicated that early recognition and treatment of the condition may improve outcomes.[6]

Our case presentation supports the suggested diagnostic criteria of EPS-CKDD as the patient was on hemodialysis for end-stage renal disease, diabetic, complained of extrapyramidal symptoms, demonstrated lentiform fork sign on imaging, and his laboratory analysis disclosed severe metabolic acidosis (PH = 6.9).

Uremic encephalopathy (UE) is a neurologic complication associated with acute or chronic renal failure that causes acute or subacute onset of reversible neurologic symptoms.[7] The symptoms of UE are most likely caused by the harmful effects of neurotoxic compounds. The accumulation of uremic toxins, such as guanidine compounds, can increase the neurotoxic effects of excitatory N-methyl-D-aspartate receptors. Additionally, the inhibition of inhibitory γ-aminobutyric acid receptors may also contribute significantly to the development of UE.[8] Signs of UE may include altered mental status, movement disorder (asterixis, myoclonus, tremor), and cognitive impairment.[9]

The basal ganglia are susceptible to damage from various toxins and metabolic disturbances.[10]

Lentiform fork sign was recently described as a unique radiologic sign in patients with renal failure and UE with metabolic acidosis. A similar lesion has also been described in patients with normal renal function who had metabolic acidosis secondary to various other causes, suggesting that metabolic acidosis is an essential element in pathogenesis.[11]

Vasogenic edema of the lentiform nuclei is the underlying cause of this condition. It has been documented in cases of uremic encephalopathy, as well as in patients affected by methanol and ethylene glycol toxicity, propionic acidemia, pyruvate dehydrogenase deficiency, and mitochondrial disorders.[12]

It also can be observed in metformin-associated encephalopathy (ME).[13] However, despite the strong association that has been reported in many cases between diabetic uremic syndrome with lentiform fork sign and

metformin use, our patient was not using metformin in his medication regimen.

The elements of the lentiform fork sign are (1) the lateral arm, formed by the edematous external capsule and extending from the anterior end of the putamen to the stem; (2) the stem, created by merging of the edematous external and internal capsules at the inferoposterior end of the putamen; and (3) the medial arm, which extends from the stem anteriorly up to one-third of the medial edge, where it splits into two slightly less T2/FLAIR-hyperintense branches engulfing the globus pallidus.[12]

In this case, considering the rapid onset of movement and consciousness disturbance immediately before admission. the diabetic uremic syndrome with lentiform fork sign may have occurred with haloperidol-induced extrapyramidal symptoms which exacerbated the movement manifestations. In addition, another possible contributing factor is haloperidol-induced lactate elevation,[14] which may have played a role in inducing this rare MRI finding. It has been hinted in some studies that lactate elevation in haloperidol and other antipsychotics may be an important biomarker in extrapyramidal symptoms development.[15]

Correction of metabolic acidosis with intensive hemodialysis and glycemic control is the cornerstone of treatment of DUS with potential reversible clinical manifestations and resolution of imaging findings. Withdrawal of metformin and thiamine supplementation may also be considered in the management.[6,13] It is important to be aware of the potential increase in blood lactate levels and extrapyramidal side effects when using haloperidol. Therefore, prescribing antipsychotics with a lower risk of adverse effects is recommended.[14,15]

4 | CONCLUSION

The lentiform fork sign is a pathognomonic MRI finding for uremic encephalopathy, especially when it is associated with extrapyramidal movements. It is of great importance to recognize and treat movement disorders in patients with ESRD and dialysis, and physicians should keep in mind the effect of metabolic disturbances on the neurotransmitters of the brain, and must always consider the adverse reaction of the prescribed drugs (such as haloperidol) and their impact on their patients.

AUTHOR CONTRIBUTIONS

Ayham Alhusseini: Writing – review and editing. **Suaad Hamsho:** Writing – review and editing. **Hadi Alabdullah:** Writing – original draft. **Mohammed Alaswad:** Writing – review and editing. **Mouhammed Sleiay:** Writing – original draft. **Omar Alsamarrai:** Writing – review and editing.

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DATA AVAILABILITY STATEMENT

Not applicable.

ETHICS STATEMENT

Not applicable because all data belong to the authors of this article.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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