CASE REPORT

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Movement Disorder Due to Involvement of Bilateral Basal Ganglia in Diabetic Uremic Patient

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ABSTRACT Basal ganglia, which are one of the most active and permeable regions of the brain, can be reversibly or irreversibly damaged due to metabolic diseases, carbon monoxide intoxication, hypoxia, infectious and vasculitic causes. This may lead to various manifestations, especially movement disorders, but also epilepsy, encephalopathy and gait abnormalities. We present a 64-year-old female patient who had involuntary movements of the limbs. Her diffusion brain magnetic resonance imaging (MRI) showed bilateral basal ganglia hyperintense lesions in T2 weighted flair sequences. The involvement of the basal ganglia is explained by lactic acidosis, caused by metformin usage despite chronic renal failure. In this study, we present a case of generalized choreatethosis and involvement of basal ganglia due to lactic acidosis in end stage renal failure.

Keywords: Basal ganglia; chorea; movement disorders; uremia; acidosis, lactic; metformin

Involvement of basal ganglia in uremia is a syndrome and was first described in 1998 by Wang et al.[1] Central involvement due to uremic encephalopathy is observed as white matter, corticosubcortical and rarely basal gaglionic involvement. Symmetric involvement of bilateral basal ganglia can cause movement disorders such as parkinsonism and chorea as well as speech disorders, epilepsy, gait abnormalities and altered mental status disorders.[2]

CASE REPORT

A 64-year-old female patient presented with involuntary movements of the limbs, difficulty in walking and inability to perform daily functions for two days. In patient past history she had chronic renal failure, coronary artery disease, type 2 diabetes mellitus (for 14 years), and hypertension. Her drugs were metformin 1000 mg/day, amlodipine 10 mg/day and acetylsalicylic acid 100 mg/day. She had been on hemodialysis twice a week for three months due to chronic renal failure.

On neurological examination, the patient was conscious, her orientation and cooperation were complete. Cranial nerve examinations were normal. On motor examination, extremities were on full muscle strength. Deep tendon reflexes were hypoactive. Cerebellar examination could not be evaluated due to involuntary movements. There were no signs of bradykinesia and rigidity, but choreic movements were observed in proximal and distal muscle groups in four extremities.

Laboratory tests performed at the emergency department revealed that blood glucose level was 62 mg/dl, urea 142 mg/dl, creatinine 10.4 mg/dl, sodium 141 mEq/l, potassium 5.8 mEq/l. Lactate level 69 mg/dl, ph 7.38, pCO_2 20.4 mmHg, HCO_3 15.2 mEq/l were detected in arterial blood suggesting compensated lactic acidosis.

Diffusion magnetic resonance imaging (MRI) sequences showed hyperintense lesions in T2 weighted flair sequences and diffusion sequences and

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a hypodensity on cranial computed tomography imaging (CTI) in basal ganglia bilaterally (Figure 1).

Hemodialysis was performed after the nephrology consultation. Metformin, which was blamed to cause the lactic acidosis, was discontinued. During follow-up, lactic acid level gradually decreased from 69 mg/dl to 12 mg/dl and choreic movements disappeared.

At the tenth day before the discharge of the patient, on control CT and MR imagings bilateral basal ganglia lesions were disappeared (Figure 2).

Informed consent was taken from the patient.

DISCUSSION

Central nervous system involvement in uremia occurs mostly at the cerebral cortex level and may manifest with encephalopathy, loss of cognitive abilities, asterixis, multifocal myoclonus and epileptic seizures.[3] Involvement of basal ganglia in uremia is rare and may cause movement disorders such as parkinsonism, gait anomalies, dysarthria, dysphagia, chorea, hemiballismus and atetosis.[4]

Mechanisms that are thought to cause uremic encephalopathy include coexistence with diabetic complication microangiopathy, increase in uremic toxins, occurrence of metabolic acidosis, and hypo or hyperglycemia. These mechanisms lead to the imbalance in excitatory and inhibitory amino acids causing the disruption of related postsynaptic pathways and blood brain barrier that ultimately cause edema.[5] While vasogenic edema plays a major role in cerebral cortical damage, both vasogenic and cytotoxic edema are thought to play a role in basal ganglia involvement.[6] Basal ganglia involvement commonly accompanies with diabetic uremia althought accumulation of uremia on cerebral cortex can occur on the absence of diabetes.

The involvement of basal ganglia is explained by the high energy requirement of the globus pallidus

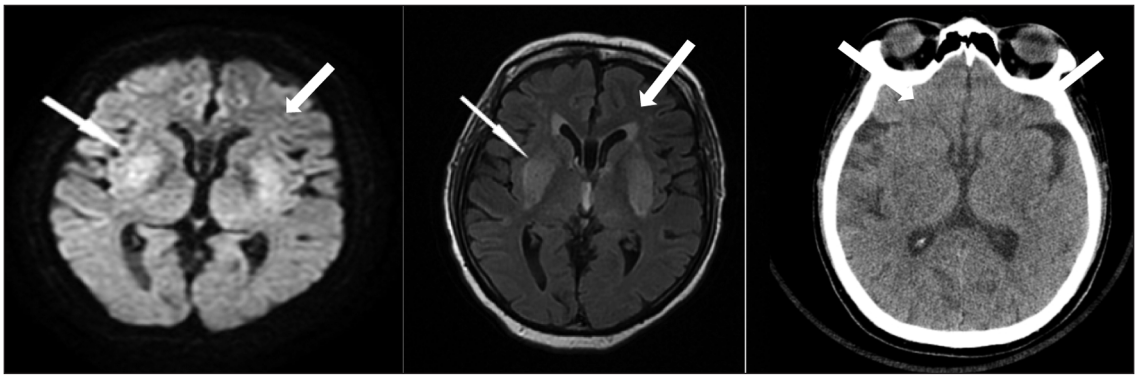

FIGURE 1: On the first day basal ganglia were seen hypodense on CT image; hyperintense on T2 weighted flair and diffusion sequences in MRI. Also the patient has cavum septi pellucidi and cavum Vergae variation.

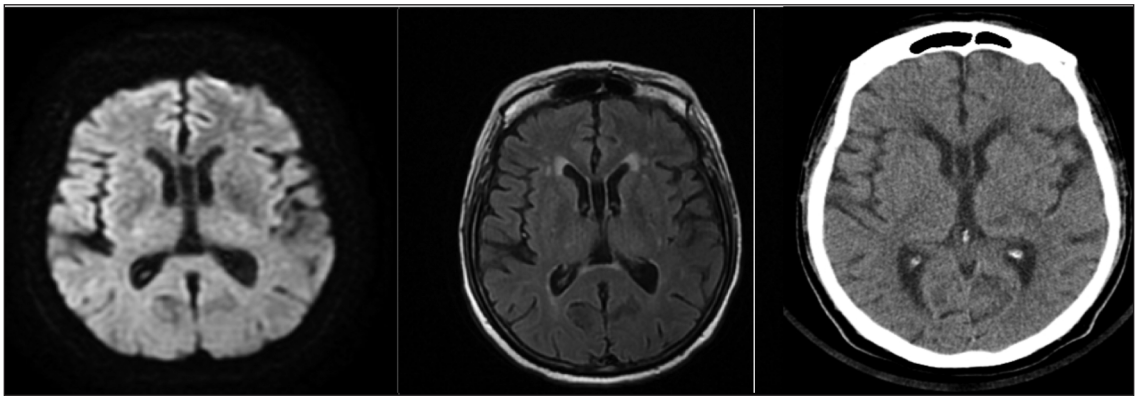

FIGURE 2: Basal ganglia hypodense/hyperintensity disappered on diffusion MRI and CTI on the tenth day.

and by the vulnerability of the mitochondrial and nuclear structures in this region.[7] Cytotoxic and vasogenic edema may cause a decreased intensity in T1-weighted imaging and increased intensity in T2-weighted imaging sequences of basal ganglia bilaterally.[8,9] Metabolic diseases, Wilson's disease, carbon monoxide intoxication, hypoxia, ischemia, infectious and vasculitic, toxic causes such as methylguanidine, aluminium, parathyroid hormone should be considered in the differential diagnosis of the symmetrical involvement of basal ganglia.[10]

Metformin is a small molecule of 165 da that can be easily filtered through the kidney, with little binding to proteins. It shows its anti-diabetic effect by decreasing the intestinal absorption of glucose and increasing anaerobic metabolism, while secondarily lactic acid production may increase. The accumulation of lactic acid can be tolerated in healthy individuals, but in patients that are over 80 years of age or have heart and/or renal failure, this increase cannot be tolerated and may cause acidosis that affect basal ganglia.[11,12]

The common side effects of metformin are abdominal discomfort, gastrointestinal disturbance, nausea, vomiting, diarrhoea. But also we must know that infrequent adverse events are hemolytic anemia, acute hepatitis and lactic acidosis. Metformin-induced lactic acid elevation leads to metabolic acidosis especially in chronic renal failure and creates various neurological symptoms including dysarthria, encephalopathy, movement disorders, epilepsy, gait abnormalites and rarely visual impairment.[12-14] But some rare reports exist reporting metformin-associated encephalopathy with normal renal function.[15,16] There are several reasons for this condition, one of which is diabetes mellitus alone for hyperlactaxia, and others have different predisposition such as having septic focus, being elderly, liver disease, alcoholism, cardiopulmonary diseases.[16,17]

In the use of metformin, bicarbonate substitute fluid and hemodialysis have been used successfully in the treatment of lactic acidosis. Hemodialysis not only corrects acidosis, but also effectively removes metformin from plasma, prevents further lactate overproduction and removes lactate.[18] Hemodynamically imbalanced patients, continuous renal replacement therapy does the same things more gradually than traditional hemodialysis and is therefore preferable. A disadvantage compared to traditional hemodialysis may be the slower cleaning rate.[19] With the use of activated charcoal in the acute phase of metformin overdose, metformin can be absorbed and absorption by the intestines can be prevented. Rapid diagnosis and treatment is expected to improve without sequelae in many cases.

In our case, as the lactic acid level decreased after hemodialysis and drug regulation, both the clinical and brain images of the patient improved.

In conclusion, we want to emphasize that metabolic diseases should be taken into consideration in patients presented with an acute movement disorder. The symptoms can be treated by regulating the metabolic parameters and drugs used.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Hülya Özkan;* ***Design:*** *Merve Melodi Çakar;* ***Control/Supervision:*** *Hülya Özkan;* ***Data Collection and/or Processing:*** *Merve Melodi Çakar;* ***Analysis and/or Interpretation:*** *Merve Melodi Çakar;* ***Literature Review:*** *Hülya Özkan;* ***Writing the Article:*** *Merve Melodi Çakar;* ***Critical Review:*** *Merve Melodi Çakar;* ***Materials:*** *Hülya Özkan.*

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