

[ CASE REPORT ]

## Wernicke-Korsakoff Syndrome in a Young Adult on Dialysis Who Showed Bilateral Ganglia Lesions

Masaoki Hidaka<sup>1</sup>, Masaya Kumamoto<sup>1</sup>, Tatsuya Suenaga<sup>2</sup>, Ayaka Itsuji<sup>1</sup>, Yuka Kanazawa<sup>1</sup>,  
Seiji Goto<sup>1</sup>, Hitonori Takaba<sup>1</sup> and Takanari Kitazono<sup>3</sup>

### Abstract:

A 30-year-old man admitted with renal dysfunction (serum creatinine, 8.19 mg/dL) was diagnosed with immunoglobulin A nephritis through a renal biopsy. He was treated with intravenous methylprednisolone pulse therapy and urgent hemodialysis, and eventually, he underwent maintenance hemodialysis. On day 108, he developed amnesia. Magnetic resonance imaging revealed bilateral basal ganglia lesions. Wernicke encephalopathy (WE) was diagnosed based on decreased serum thiamine concentration (12.8 µg/dL; reference range, 24-66 µg/dL). Thiamine replacement therapy was initiated, but the Wernicke-Korsakoff syndrome persisted. Careful monitoring of thiamine is required in patients undergoing dialysis. In addition, patients with WE may exhibit bilateral basal ganglia lesions.

**Key words:** Wernicke encephalopathy, hemodialysis, bilateral ganglia lesions, case report

(Intern Med 62: 113-118, 2023)

(DOI: 10.2169/internalmedicine.8910-21)

### Introduction

Wernicke encephalopathy (WE) is an acute neurologic disorder caused by thiamine deficiency. Chronic alcoholism is the most common cause of WE (1). If left untreated, WE may cause severe neurologic deficits, such as Korsakoff syndrome and even death. Therefore, an early diagnosis and immediate treatment are essential. WE is characterized by a triad of oculomotor abnormalities, mental status changes, and ataxia (2). However, a definitive diagnosis is difficult, as previous studies have revealed that this triad occurs in only 16-33% of patients with WE (3). Magnetic resonance imaging (MRI) can assist in determining an early diagnosis (4).

We herein describe a non-alcoholic patient with WE complication after the introduction of hemodialysis who showed bilateral basal ganglia lesions on MRI.

### Case Report

A 30-year-old man presented to the nephrology depart-

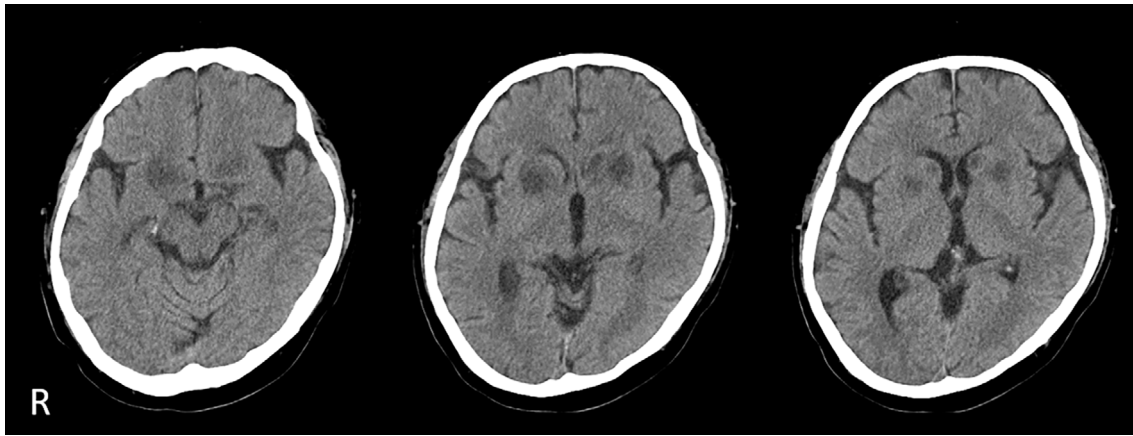
ment of our hospital with dyspnea and leg edema. He had a four-year history of hypertension and proteinuria; however, he had not received any medical treatment. Laboratory tests on admission revealed renal dysfunction (serum creatinine, 8.19 mg/dL; blood urea nitrogen, 82.6 mg/dL). He underwent urgent hemodialysis three times a week. A renal biopsy was performed on day 24, and immunoglobulin A (IgA) nephritis was diagnosed. Intravenous methylprednisolone pulse (1 g/day) was initiated for 3 days, followed by oral prednisone. His renal function improved slightly, and intermittent hemodialysis was discontinued on day 43. However, the renal function gradually deteriorated, and he underwent maintenance hemodialysis from day 86 onward.

On day 80, the patient exhibited appetite loss. On day 108, he presented with amnesia and could not remember whether he had taken his daily medication. Head computed tomography showed bilateral decreased intensity lesions in the basal ganglia (Fig. 1), and the patient was referred to our department. At the initial examination, the blood pressure and heart rate were 150/90 mmHg and 105 bpm, respectively. The patient was afebrile and showed no respira-

<sup>1</sup>Department of Cerebrovascular Medicine and Neurology, Kyushu Central Hospital of the Mutual Aid Association of Public School Teachers, Japan, <sup>2</sup>Department of Nephrology, Kyushu Central Hospital of the Mutual Aid Association of Public School Teachers, Japan and <sup>3</sup>Department of Medicine and Clinical Science, Graduate School of Medical Sciences, Kyushu University, Japan

Received: October 26, 2021; Accepted: April 1, 2022; Advance Publication by J-STAGE: May 21, 2022

Correspondence to Dr. Masaoki Hidaka, hidaka.masaoki.590@s.kyushu-u.ac.jp



**Figure 1.** Head computed tomography conducted on day 108. Computed tomography revealed areas with decreased density, especially in the bilateral basal ganglia.

tory failure. A physical examination revealed no distinct findings, except for pitting edema on his legs. On a neurologic examination, he was well oriented to his person and place but exhibited disorientation regarding the date and current events. A cranial nerve examination revealed horizontal gaze nystagmus on both sides. He showed no other cranial nerve abnormalities such as extra-ocular movement restriction or dysarthria. A muscular examination revealed a normal tone and full strength. His perception of touch and pinprick over the limbs was normal; he also exhibited a normal vibratory sense on the fingers, knees, and toes. The Romberg sign was absent. Deep tendon reflexes were within the normal range, and Babinski reflexes were absent. He showed left-dominant cogwheel rigidity in his limbs. He also exhibited position tremor in his upper limbs. His gait was ataxic and therefore unstable over a wide distance. He denied any family history of movement disorders. He also denied drug or alcohol abuse.

A laboratory evaluation on the same day revealed normal blood counts, serum electrolytes, and glucose levels. The patient had normal liver and thyroid functions. Tests for anti-nuclear antibodies, perinuclear anti-neutrophil cytoplasmic antibodies, cytoplasmic anti-neutrophil cytoplasmic antibodies, antibodies to SSA, SSB, ds-DNA, and U1RNP antigens were all negative. Tests for tumor markers CEA and CA19-9 and a paraneoplastic antibody panel showed negative results. A lumbar puncture showed an increased (26 cm H<sub>2</sub>O) cerebrospinal fluid pressure (CSF) and a slightly increased protein level (84 mg/dL). No visible white blood cells were observed in the CSF.

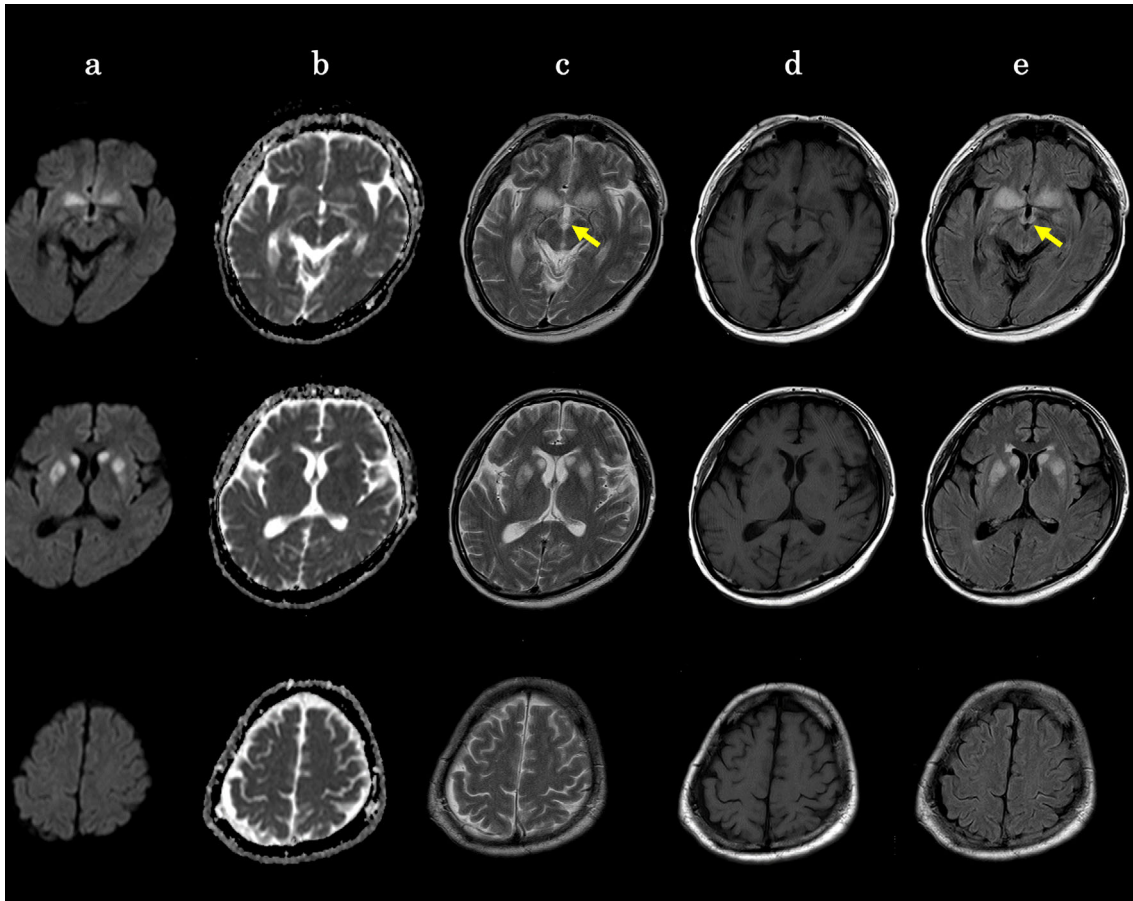
Diffusion-weighted imaging (DWI) revealed high signal intensities in the bilateral striatum on MRI. These DWI lesions showed a slightly decreased apparent diffusion coefficient (ADC), suggesting cytotoxic edema. On fluid-attenuated inversion recovery (FLAIR) images and T2-weighted imaging (T2WI), hyperintensities were seen in the bilateral striatum and mamillary bodies (Fig. 2). Magnetic resonance angiography and magnetic resonance venography revealed no abnormalities (data not shown).

We suspected a type of metabolic encephalopathy and administered intravenous multivitamins (vitamin B1, 108 mg; vitamin B6, 100 mg; vitamin B12, 1 mg) on day 111, but no remarkable improvement was observed. Follow-up MRI conducted on day 112 showed an additional DWI-hyperintense lesion in the left frontal cortex with FLAIR hyperintensity. Furthermore, FLAIR imaging and T2WI showed swelling of the caudate head. These lesions were depicted as having an increased signal intensity on DWI and iso-intensity on ADC-suspected vasogenic edema (Fig. 3). Because we could not rule out the possibility that IgA vasculitis was causing the brain damage, additional methylprednisolone pulse therapy was administered from days 112 to 114. However, his clinical symptoms did not change.

On day 121, laboratory test results indicated that he was in a state of thiamine deficiency (serum thiamine concentration, 12.8 µg/dL; reference range, 24-66 µg/dL). The other laboratory test results are summarized in Table 1. He was diagnosed with WE, and 1,500 mg/day of thiamine was immediately administered intravenously. The dose was gradually tapered, and his blood thiamine levels normalized (53.5 µg/dL) on day 130. Most of his symptoms, including appetite loss, gaze nystagmus, and extrapyramidal symptoms, gradually improved, but the memory disturbance persisted. Specifically, he could not remember the name of the hospital where he was hospitalized or the details of conversations with the people around him. The Mini-Mental State Examination score was 26/30. However, he did not present any indication of confabulation. It seemed that his condition was complicated with Wernicke-Korsakoff syndrome. Follow-up MRI conducted on day 151 revealed faintly hyperintense lesions in the basal ganglia on FLAIR, T2WI, and T1WI (Fig. 4). He was transferred to another hospital for rehabilitation on day 156 (Fig. 5).

## Discussion

We encountered a case of a non-alcoholic patient complicated with WE during hemodialysis. A number of non-



**Figure 2.** Initial magnetic resonance imaging conducted on day 108. Diffusion-weighted imaging revealed high signal intensities in the bilateral striatum, which showed a decreased apparent diffusion coefficient, suggesting cytotoxic edema. Fluid-attenuated inversion recovery images and T2-weighted imaging revealed hyperintensities in the bilateral striatum and mamillary bodies (arrow).

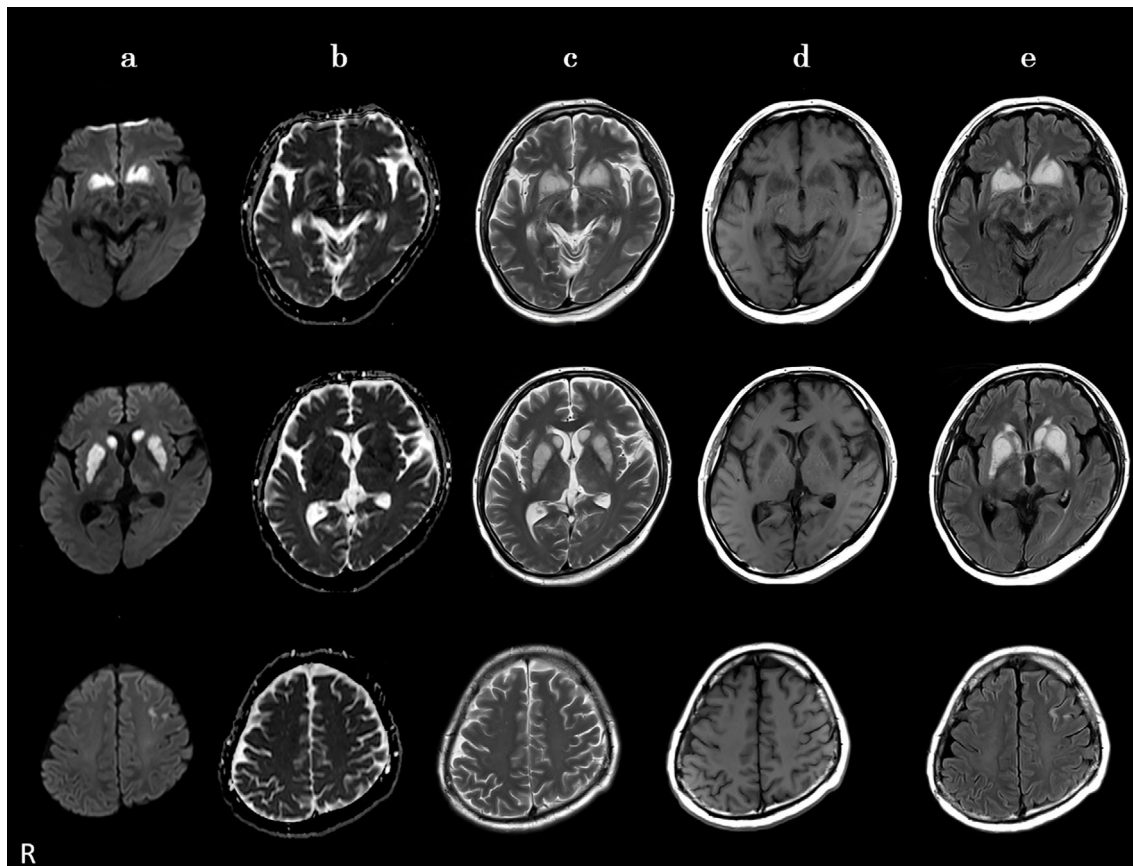
alcoholic conditions, such as hemodialysis, gastrointestinal surgery, chemotherapy, and dietary imbalance, can cause WE (5, 6); however, clinicians may be less likely to recognize these conditions as risk factors than alcohol-associated ones.

In our patient, WE might have been induced by two possible causes: hemodialysis or dietary imbalance. First, thiamine can be lost during dialysis. A previous study showed that thiamine diphosphate, the bioactive compound of vitamin B1, is substantially decreased during hemodialysis (7). Ueda et al. reported a patient on hemodialysis who had WE complication (8). Peritoneal dialysis can also induce WE (9). Second, dietary imbalance reduced the thiamine intake in our patient. Approximately four weeks before the onset of WE, our patient exhibited appetite loss due to emotional shock, which might have been due to undergoing maintenance hemodialysis despite his relatively young age. Thus, clinicians should bear in mind that patients on dialysis or with a reduced dietary intake can develop WE, so careful monitoring of thiamine is required in such patients.

Bilateral basal ganglia lesions on MRI were key in identifying the state of metabolic encephalopathy in our patient. Differential diagnoses of bilateral basal ganglia lesions include those associated with vascular disorder (i.e., cerebral

infarction), metabolic disorders (i.e., hypoxic ischemic brain injury, carbon monoxide poisoning, hypoglycemia, Wilson disease, manganese intoxication, central pontine myelinolysis, and post-irradiation), inherited disorders (i.e., biotin-responsive basal ganglia diseases, Canavan disease, and Krabbe disease), degenerative disorders (i.e., Huntington disease and multiple systemic atrophy), and infectious diseases (i.e., herpes simplex virus encephalitis and Creutzfeldt-Jakob disease) (10). However, these disorders were unlikely in our patient.

A summary of the clinical features of previous cases is presented in Table 2. Although rare, patients with WE can develop basal ganglia lesions. These patients exhibit at least one of the triad of WE but do not necessarily show signal intensity alterations in the mamillary bodies, medial thalami, periaqueductal gray matter, or tectal plate on MRI (6), which are typical findings in patients with WE. Thiamine supplementation did not completely improve our patient's neurologic manifestations, and the patient had Wernicke-Korsakoff syndrome as a complication, but other previous cases responded well to the therapy. This might be because we did not consider WE as a differential diagnosis and took a longer time to initiate treatment than with other cases. Thus, we should be alert for typical neurologic manifesta-



**Figure 3.** Follow-up magnetic resonance imaging conducted on day 112. Diffusion-weighted imaging revealed a hyperintense lesion in the left frontal cortex, and fluid-attenuated inversion recovery imaging also revealed hyperintensity. Fluid-attenuated inversion recovery and T2-weighted imaging showed swelling of the caudate head. These lesions are depicted as areas of increased signal intensity on diffusion-weighted imaging and iso-intensity on apparent diffusion coefficient-suspected vasogenic edema.

**Table 1.** Other Laboratory Tests Performed in Our Department.

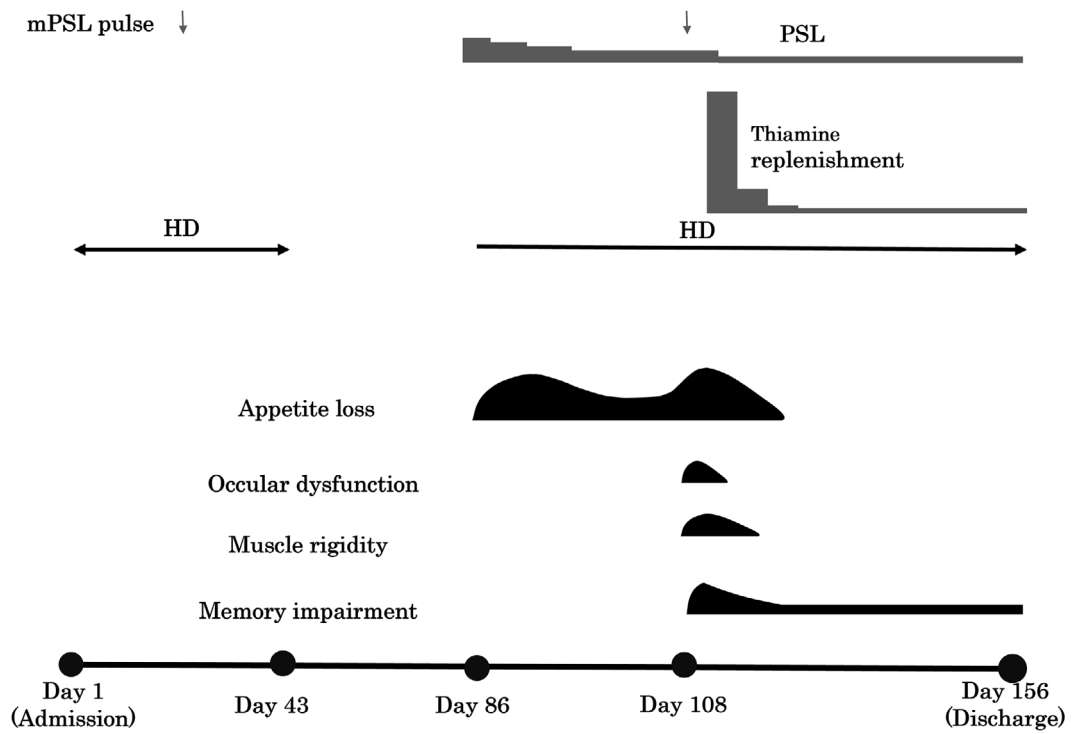
Test	Result	Reference range
Ceruloplasmin	10.7 mg/dL	21-37 mg/dL
Copper	36 µg/dL	66-130 µg/dL
Thiamine	12.8 µg/dL	24-66 µg/dL
Vitamin B12	338 pg/mL	233-914 pg/mL
Homocysteine	244.5 µmol/L	3.7-13.5 µmol/L

tions of WE in patients with bilateral basal ganglia lesions, particularly if there is a danger of WE as a complication. Furthermore, thiamine supplementation should be immediately started if WE is suspected.

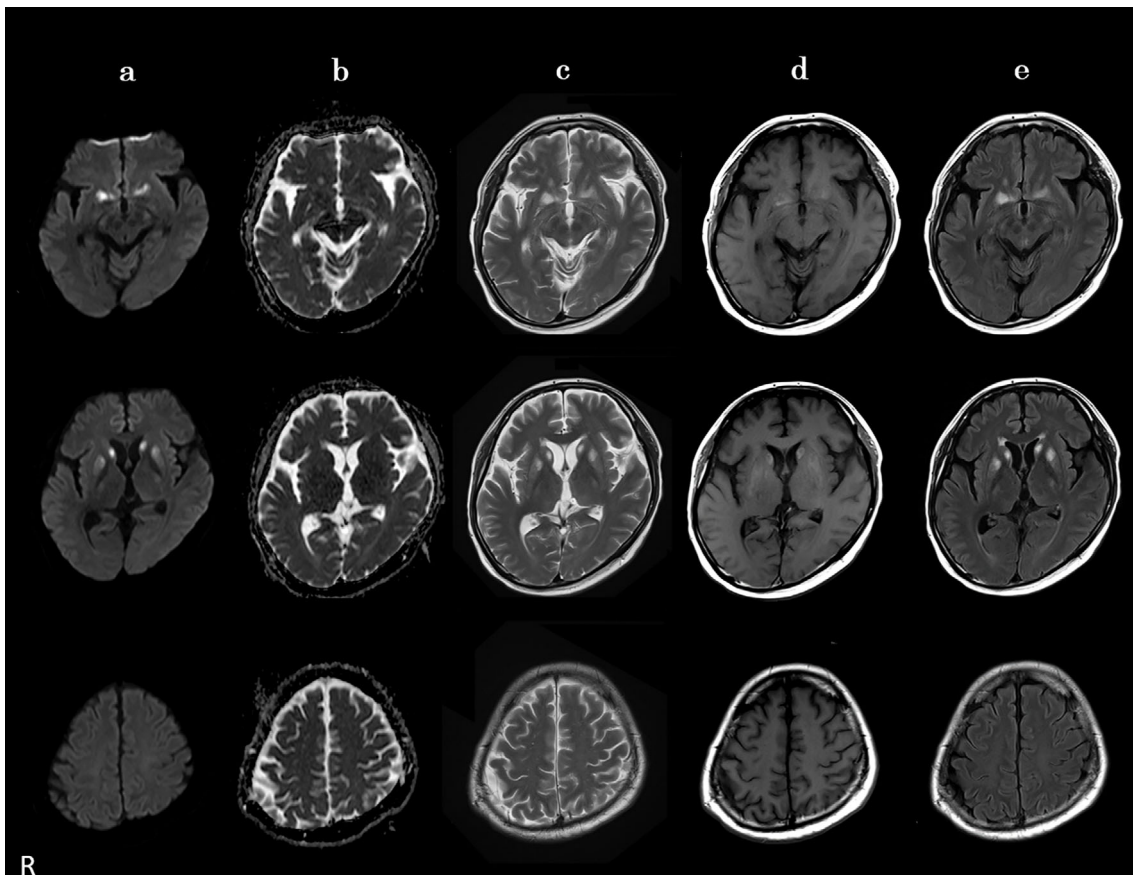
Regarding the patient's atypical basal ganglia lesions, we believe that the neurons in the basal ganglia rely more on mitochondrial energy production than those in other regions of the central nervous system (CNS). Neurons are the most energy-consuming cells in the CNS (11). Glucose, which is an essential energy substrate for the brain, is first processed into pyruvate by glycolysis. Pyruvate then enters the mitochondria and is metabolized by the tricarboxylic (TCA) cycle and oxidative phosphorylation. Glycometabolism in the

mitochondria produces approximately 15-18 times more energy than glycolysis. It is believed that neurons have an active TCA cycle and oxidative phosphorylation but have a limited ability to upregulate glycolysis (11). Pyruvate dehydrogenase (PDH), which is a thiamine-dependent enzyme, converts pyruvate into acetyl-CoA in order to enter the metabolic cascade in the mitochondria (12). In our case, thiamine deficiency induced decreased PDH activity and impaired mitochondrial energy production. Interestingly, Cirillo et al. reported that mitochondrial toxin 3-nitropropionic acid induced selective bilateral striatal necrotic lesions in rat brain (13). This result may support our idea that mitochondrial energy production is essential for neurons in the basal ganglia. In addition, our patient had copper deficiency. Copper is essential for enzymes involved in mitochondrial oxidative phosphorylation (14). Therefore, copper deficiency might somewhat affect the mitochondrial function in neurons. However, most patients with WE complication do not exhibit basal ganglia lesions. Thus, such lesions might be induced by other causes. Further studies and the accumulation of similar cases are required.

Finally, while our case was complicated by copper deficiency and hyperhomocysteinemia, we believe that these two



**Figure 4.** Follow-up magnetic resonance imaging conducted on day 151. Faintly hyperintense lesions remained in the basal ganglia on fluid-attenuated inversion recovery imaging and T2- and T1-weighted imaging. HD: hemodialysis, mPSL: methylprednisolone, PSL: prednisolone



**Figure 5.** Clinical course of the patient, a 30-year-old man with Wernicke encephalopathy. Most of his symptoms gradually improved with thiamine supplementation, but memory disturbance remained.

**Table 2. Summary of Clinical Features of Patients with WE Presented Bilateral Basal Ganglia Lesions**

	This case	Patient 1 (1) <sup>a</sup>	Patient 2 (5) <sup>a</sup>	Patient 3 (5) <sup>a</sup>
Age, sex	30, M	40, F	65, F	39, F
Possible cause of thiamine deficiency	Hemodialysis, Dietary imbalance	Alcoholism	Gastrectomy	Enterectomy
Triad of WE				
Oculomotor abnormality	+	+	+	+
Mental status change	+	+	+	-
Ataxia	-	+	+	-
Other neurological symptoms	Extrapyramidal signs		None	Seizure
Typical brain lesions	Mamillary bodies	None	None	Mamillary bodies Medial thalami Periaqueductal grey matters
Atypical brain lesions	Basal ganglia Cerebral cortices	Basal ganglia	Basal ganglia Cerebellar hemispheres	Basal ganglia Cerebral cortices
Time to initial treatment	4 days	1 day	2 days	1 day
Response to thiamine supplementation	PR	CR	CR	NM
Wernicke-Korsakoff syndrome	+	-	-	NM

CR: complete response, F: female, M: male, NM: not mentioned, PR: partial response, WE: Wernicke encephalopathy

complications had little effect on his neurologic symptoms. First, patients with copper deficiency typically manifest symptoms of myelopathy and peripheral neuropathy (15). However, our case had no signs of myelopathy or peripheral neuropathy. Second, patients with hyperhomocysteinemia may present with microvascular stroke, but our case did not have microvascular thrombosis complications (16). Therefore, hyperhomocysteinemia had little effect on his neurologic symptoms. Finally, thiamine replacement therapy improved most of his neurologic manifestations. Based on the aforementioned information, we believe neither copper deficiency nor hyperhomocysteinemia caused the neurologic symptoms; instead, we believe that thiamine deficiency was the main underlying cause of his neurologic symptoms.

### Conclusion

Patients undergoing dialysis require careful monitoring of thiamine levels. Furthermore, patients with WE may exhibit bilateral basal ganglia lesions on MRI.

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

### References

- Eren OE, Schöberl F, Campana M, Habs M, Conrad J. A unique MRI-pattern in alcohol-associated Wernicke encephalopathy. *Acta Neurol Belg* **120**: 1439-1441, 2020.
- Zuccoli G, Pipitone N. Neuroimaging findings in acute Wernicke's encephalopathy: review of the literature. *Am J Roentgenol* **192**: 501-508, 2009.
- Ota Y, Capizzano AA, Moritani T, Naganawa S, Kurokawa R, Srinivasan A. Comprehensive review of Wernicke encephalopathy: pathophysiology, clinical symptoms and imaging findings. *Jpn J Radiol* **38**: 809-820, 2020.
- Zuccoli G, Siddiqui N, Bailey A, Bartoletti SC. Neuroimaging findings in pediatric Wernicke encephalopathy: a review. *Neuroradiology* **52**: 523-529, 2010.
- Zuccoli G, Cravo I, Bailey A, Venturi A, Nardone R. Basal ganglia involvement in Wernicke encephalopathy: report of 2 cases. *Am J Neuroradiol* **32**: E129-E131, 2011.
- Zuccoli G, Santa Cruz D, Bertolini M, et al. MR imaging findings in 56 patients with Wernicke encephalopathy: nonalcoholics may differ from alcoholics. *Am J Neuroradiol* **30**: 171-176, 2009.
- Jankowska M, Rudnicki-Velasquez P, Storoniak H, et al. Thiamine diphosphate status and dialysis-related losses in end-stage kidney disease patients treated with hemodialysis. *Blood Purif* **44**: 294-300, 2017.
- Ueda K, Takada D, Mii A, et al. Severe thiamine deficiency resulted in Wernicke's encephalopathy in a chronic dialysis patient. *Clin Exp Nephrol* **10**: 290-293, 2006.
- Nakashima Y, Ito K, Nakashima H, et al. Wernicke's encephalopathy that developed during the introduction period of peritoneal dialysis. *Intern Med* **52**: 2093-2097, 2013.
- Bekiesinska-Figatowska M, Mierzewska H, Jurkiewicz E. Basal ganglia lesions in children and adults. *Eur J Radiol* **82**: 837-849, 2013.
- Magistretti PJ, Allaman I. A cellular perspective on brain energy metabolism and functional imaging. *Neuron* **86**: 883-901, 2015.
- Martin PR, Singleton CK, Hiller-Sturmhöfel S. The role of thiamine deficiency in alcoholic brain disease. *Alcohol Res Health* **27**: 134-142, 2003.
- Cirillo G, Cirillo M, Panetsos F, Virtuoso A, Papa M. Selective vulnerability of basal ganglia: insights into the mechanisms of bilateral striatal necrosis. *J Neuropathol Exp Neurol* **78**: 123-129, 2019.
- Horn D, Barrientos A. Mitochondrial copper metabolism and delivery to cytochrome c oxidase. *IUBMB Life* **60**: 421-429, 2008.
- Kumar N, Crum B, Petersen RC, Vernino SA, Ahlskog JE. Copper deficiency myelopathy. *Arch Neurol* **61**: 762-766, 2004.
- Ansari R, Mahta A, Mallack E, Luo JJ. Hyperhomocysteinemia and neurologic disorders: a review. *J Clin Neurol* **10**: 281-288, 2014.

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).