

A rare lentiform fork sign in a patient with methanol intoxication with neurological sequelae of parkinsonism and cognitive dysfunction: A case report and literature review

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Abstract

Methanol intoxication is rare in developed countries. Early identification and elimination of the methanol metabolites are vital to an optimal prognosis. A characteristic brain imaging finding is bilateral basal ganglia necrosis and subcortical white matter changes. Here, we report a rare neuroradiological feature called the lentiform fork sign in a patient with methanol intoxication who survived the acute poisoning stage. We report a 31-year-old woman who presented to the emergency department with acute-onset incoherent speech, consciousness disturbance, and a high-anion-gap metabolic acidosis caused by methanol intoxication. She was treated with antidote administration of fomepizole and enhanced methanol elimination through hemodialysis. Neurological sequelae of cognitive decline and parkinsonism developed, with preserved vision. Brain MRI showed bilateral putaminal necrosis and subcortical white matter changes. The apparent diffusion coefficient map showed low signal intensities in the putamen and globus pallidus bilaterally, with brightly hyperintense rims surrounding both putamina that resembled a fork, indicating a lentiform fork sign. She then had sequelae of cognitive decline and delayed parkinsonism feature, which are compatible with the brain lesions on neuroimage studies. Methanol poisoning is an uncommon life-threatening event, and neurological sequelae result from the accumulation of formic acid, a methanol metabolite that inhibits cytochrome c oxidase in mitochondria, leading to neuronal injury. Methanol intoxication should be considered in patients with imaging findings of bilateral basal ganglia necrosis with lentiform fork sign and a metabolic acidosis of unknown origin.

Keywords: Methanol intoxication, basal Ganglia, parkinsonism.

INTRODUCTION

Methanol intoxication has been a global public health issue because it occurs in a variety of household and industrial products, including antifreeze, carburetor fluid, windshield washer fluid, copy machine fluid, perfumes, cleaning agents, and gasoline mixtures.¹ Occasionally, poisoning results from ingesting alcoholic beverages adulterated with methanol. Accidental or suicidal oral ingestion of products containing methanol is the main cause of intoxication, but inhalation or dermal exposure also can cause toxicity.¹ Acute intoxication triggers severe metabolic acidosis that can lead to multi-organ injury, including central nervous system (CNS)

depression, visual disturbances, severe epigastric pain, agitation, stupor, coma, and can be fatal.²

Methanol is inebriating like other alcohols, but not directly toxic. The toxic effects result from its metabolites, formaldehyde and formic acid. These metabolites inhibit oxidative phosphorylation in mitochondria, causing adenosine triphosphate depletion, lactate accumulation, and severe metabolic acidosis with a high anion gap.^{3,4} In the CNS, the basal ganglia are particularly vulnerable to a wide range of neurotoxins, including methanol, and metabolic disturbances.⁵ Early identification of this disorder and elimination of the methanol metabolites by reversing metabolic acidosis are vital to an optimal prognosis.⁶ Various

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neurologic sequelae are observed in patients who survive the acute stages of poisoning, such as permanent visual impairment, parkinsonism features, polyneuropathy, seizures, and cognitive decline.⁷ A characteristic brain imaging finding is bilateral basal ganglia necrosis, although subcortical white matter also can be affected.⁸

Here, we report a rare neuroradiological finding called the lentiform fork sign in a patient with methanol intoxication who survived the acute poisoning. She presented with sequelae of cognitive decline, abulia, and parkinsonism features but with preserved vision.

CASE REPORT

A 31-year-old woman with a history of bipolar disorder was taken to the emergency department for agitation with disorganized speech lasting 2 days. At the triage stage, her Glasgow coma scale (GCS) score was E3V4M6, and her vital signs were stable without fever. Blood values were unremarkable except that venous blood gas analysis showed mild respiratory acidosis (pH 7.287, pCO₂ 54.2, pO₂ 56.9, HCO₃ 25.3). Non-contrast brain CT at 1 hour after admission was unremarkable (Figure 1A). About 17 hours after admission, she became comatose, with a GCS score of E1V1M2. Dilated pupils, roving eyes, absent brainstem reflex, and generalized flaccid muscle tone were noted. Babinski sign was negative. A follow-up brain CT showed diffuse brain swelling with hypodensity changes in the bilateral caudate, putamen, globus pallidus, and white matter and hemorrhage in the left putamen (Figure 1B). Subsequent blood tests

showed a high-anion-gap metabolic acidosis (pH < 6.9, pCO₂ 54.5, pO₂ 43.6, HCO₃ 5.6, anion gap 29.2) with elevated lactate (9.57 mmol/L; normal range, <1.5 mmol/L). The serum osmolal gap was 93.41 mOsmol/kg (normal range, <10 mOsmol/kg), indicating the presence of organic acid. Further analysis revealed a high serum concentration of methanol (417 mg/dL; normal range, undetectable) with ethanol <5 mg/dL, suggesting methanol intoxication. She was intubated and transferred to the intensive care unit.

The antidote of methanol intoxication, fomepizole, was administered, along with folic acid.⁹ The patient also underwent continuous venovenous hemodiafiltration for 21 hours until serum methanol returned to the normal range. Brain CT on day 4 after admission showed progressive diffuse brain swelling and symmetric confluent hypodense lesions with mass effect at the bilateral basal ganglia and periventricular white matter, with bilateral putaminal hemorrhage (Figure 1C). On day 5, her consciousness improved to E4M6VT. She was extubated smoothly and transferred to the general ward. Neurological examination showed she was awake and could follow simple orders. There was no focal limb weakness, but generalized hyperreflexia was noted, and poor attention and some perseveration and disinhibition behaviors were observed. Fundus examination revealed no retinal lesions, and her visual acuity was preserved at 20/100, although a visual evoked potential examination showed a prolonged latency of her right eye. Brain MRI on day 23 after admission revealed fluid-attenuated inversion recovery (FLAIR) hyperintensities with

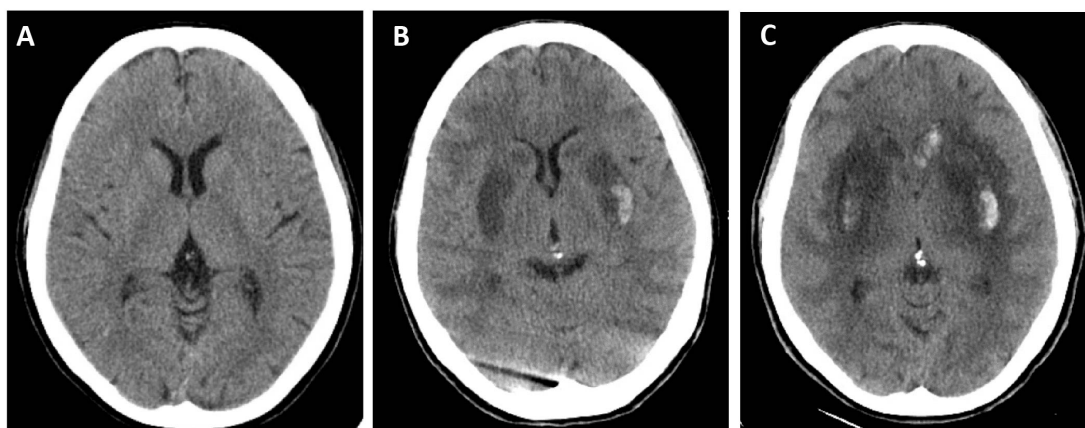


Figure 1. Brain CT images of the index patient. (A) Unremarkable within 1 hour of admission, (B) diffuse brain swelling and bilateral symmetrical hypodensities in basal ganglia with left putaminal hemorrhage 18 hours after admission, and (C) progressive diffuse brain swelling and confluent hypodense lesions in bilateral periventricular white matter and bilateral basal ganglia with hemorrhages.

mild mass effect involving the bilateral substantia nigra, caudate head, lentiform nuclei, and periventricular white matter, especially the frontal lobe (Figure 2A). Diffusion-weighted imaging (DWI) showed slightly increased intensities in the corresponding areas and hypodensity changes in the bilateral basal ganglia centered with brightly hyperintensity in the putamen (Figure 2B). Of note, the apparent diffusion coefficient (ADC) map showed low signal intensities in the putamen and globus pallidus bilaterally, with brightly hyperintense rims surrounding both putamina that resembled a fork, indicating a lentiform fork sign (arrows, Figure 2C).

One month after the initial presentation, extrapyramidal signs developed, manifesting as

bilateral striatal hands, bradykinesia, and rigidity, which was worse in the right limbs. Her Mini-Mental State Examination score was 11/30, and she scored 61/100 on the Cognitive Abilities Screening Instrument, indicating impaired cognitive function. She was then discharged with partially dependent functions of daily activity.

DISCUSSION

We describe a case of acute methanol intoxication with neurological sequelae of parkinsonism that showed bilateral basal ganglia and substantia nigra involvement and diffuse white matter changes focused in the frontal lobes on brain MRI. Of note, DWI and ADC sequences reflected

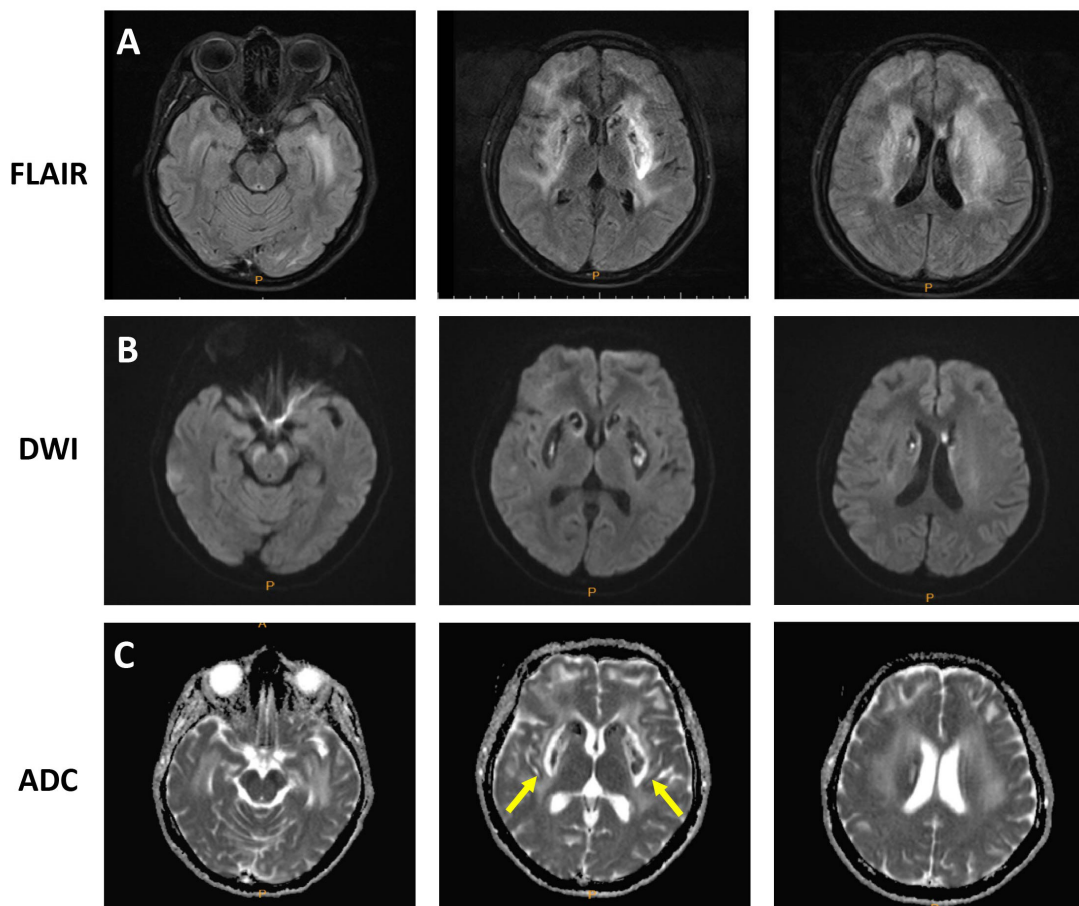


Figure 2. Brain MRI images of the index patient. (A) FLAIR images showed hyperintensities with mild mass effect involving the bilateral caudate head, basal ganglia, and periventricular white matter, especially in the frontal lobe. (B) DWI images showed slightly increased intensities in the bilateral substantia nigra and hypodense changes in the bilateral basal ganglia, centered with bright hyperintensity in the putamen. (C) ADC map showing low signal intensities in the putamen and globus pallidus bilaterally and brightly hyperintense rims surrounding both putamina that resembled a fork (arrows), suggesting the lentiform fork sign, along with hyperintensity changes in the bilateral periventricular areas and cortical regions of the frontal lobes.

Table 1: Clinical characteristics of patients with methanol intoxication having neurological sequelae of parkinsonism

Reference	Age (years)	Sex	Route of ethanol intoxication	Exposure time	Presentations in acute stage	Onset of parkinsonism after exposure to methanol	Other neurological sequelae	Brain MRI findings
Finkelstein <i>et al.</i> , 2002 ¹⁵	40	F	Inhalation with chemicals mixed with methanol	6 years	N.A.	Progressive onset, 6 years after exposure to methanol	Dystonia	Bilateral bright T2 signals in subcortical white matters
Franquet <i>et al.</i> , 2012 ¹⁷	18	F	N.A.	N.A.	N.A.	Progressive onset, 3 months	Dystonia, Hypophonia	Bilateral necro-hemorrhagic lesions in the putamen
Mohammed <i>et al.</i> , 2022 ¹⁶	30	F	Inhalation with perfume mixed with methanol	Chronic exposure and then produce a large batch of perfume using adulterated alcohol	Consciousness change, vision loss	Progressive onset, several months	Poly-minimyoelonus	Bilateral bright T2 signals involving diffuse white matters and basal ganglia with surrounding oedema
Current study	31	F	Oral ingestion of adulterated alcohol	1 day	Consciousness change	Progressive, 1 month	Cognitive decline, hypophonia, dystonia	Bilateral bright T2 signals involving diffuse white matters, basal ganglia necrosis with lentiform fork sign

N.A. not available; F, female.

a rare lentiform fork sign demonstrating bilateral putaminal hypointensities with restricted water diffusion and development of vasogenic edema in the external capsule, resembling a fork.

Neurotoxicity is a distinctive feature of methanol poisoning.¹⁰⁻¹³ In our patient, visual acuity was not severely impaired, although the latency of the visual evoked potential was prolonged. The most characteristic neuropathological findings of patients with methanol intoxication are putaminal necrosis, with or without hemorrhage, and extensive subcortical white matter necrosis.¹⁴ Our patient had sequelae involving cognitive decline and delayed parkinsonism features, which are compatible with the brain regions identified as showing methanol-related neuropathology. Disorders of extrapyramidal symptoms, including parkinsonism and dystonia, have been reported before with methanol poisoning¹⁵⁻¹⁷, all involving delayed-onset parkinsonism features after methanol intoxication, and some patients also having other movement disorders, including dystonia and myoclonus (summarized in Table 1).¹⁵ The mechanism of selective vulnerability of the basal ganglia remains unclear, but the high metabolic demand of the putamen and its location in the boundary zones of vascular perfusion may expose this region in an unstable hemodynamic state. Another possibility is that decreased blood flow through the basal veins of Rosenthal, secondary to hypotension, leads to formic acid accumulation in the putamen rather than in other brain areas, strengthening the direct toxic effect in the basal ganglia.^{14,18-20}

In consistent with the neuropathologic observations¹⁴, the most distinctive MRI findings are bilateral hemorrhagic putaminal necrosis with variable degrees of subcortical and deep white matter and optic nerve lesions.^{8,18} However, the findings are not specific to methanol intoxication and can be seen in patients with Wilson's disease, Leigh disease, and uremic encephalopathy.²¹ Of note, our patient's imaging also showed the lentiform fork sign, a rare MRI finding. This imaging finding is not specific to methanol intoxication and it has been reported in patients with various conditions including metabolic acidosis, alcoholic intoxication, Wilson's disease, Leigh disease, Kearns-Sayre syndrome, uremic encephalopathy, hypoxic-ischemic injury, systemic lupus erythematosus and metformin-associated encephalopathy.²²⁻²⁴

The constitutive elements of the lentiform fork include the lateral arm, which is formed by the edematous external capsule and extends from the

anterior end of the putamen to the stem.²³ The ADC map in this case showed low signal intensities in the putamen and globus pallidus, surrounded by high signal intensities of the forks bilaterally. These findings suggested that the lentiform fork demonstrated increased water mobility caused by vasogenic edema. Vasogenic edema may be attributed to differences in metabolic vulnerability between neurons of the basal ganglia and astrocytes in the surrounding white matter.²⁵ We postulate that metabolic acidosis may disrupt the blood-brain barrier, leading to vasogenic edema, which could have an important role in generating this sign.

In summary, we present a rare neuroradiological finding of the lentiform fork sign in a patient with methanol intoxication and neurological sequelae of cognitive decline and parkinsonism. Methanol poisoning should be considered in patients with imaging findings of bilateral basal ganglia necrosis with lentiform fork sign and a metabolic acidosis of unknown origin.

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DISCLOSURES

Financial support: None

Conflict of interest: None

Ethics: This study was approved by the Institutional Review Board of the National Taiwan University Hospital and all study participants provided informed consent before inclusion in the study. This study has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). The study participant provided informed consent for publication of the brain images.

Date availability: The data supporting the findings of this study are available upon request.

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