ISSN 2564-0127 (Print)
ISSN 2564-0135 (Online)

Canadian Journal of Medicine 3(2021) 195-201

Canadian Journal of Medicine

WWW.CIKD.CA

journal homepage: https://www.cjm.cikd.ca

Case Report

Cerebral Methanol Intoxication: A Case Report with Literature Review

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Keywords:
Methanol, Brain, Hemorrhage, Imaging, Emergency

Received
01 December 2021
Received in revised form
22 December 2021
Accepted
24 December 2021

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ABSTRACT

We report the case of a 24-year-old man admitted to the emergency room with a history of headache exacerbated. At the emergency room, he was unresponsive to drug or alcohol consumption. At this time, computed tomography (CT) did not detect the brain and abdomen lesions. At the intensive care unit (ICU), 6h later, he suddenly developed shallow respirations, followed by loss of consciousness, hypotension, and blurred vision. He was intubated immediately and underwent mechanical ventilation. Arterial blood gases and biochemical analyses indicated intense metabolic acidosis (Day1: pH 7.25, PCO2 49 mmHg, PO2 65 mmHg, HCO3 15 mmol/L and day 2, pH 7.32, PCO2 45 mmHg, PO2 60 mmHg, and HCO3=19 mmol/L) and elevated liver enzymes. The clinical diagnosis of toxic alcohol ingestion was based on the history, arterial blood gases results, and significant biochemical changes. In ICU, the patient underwent ethanol infusion and hemodialysis and the impression of methanol intoxication. He underwent redialysis with a minimal dose of heparin (5000 IU/mL). A second CT scan revealed basal ganglia ischemia, and an MRI scan exhibited clear abrasion and basal ganglia necrosis. Finally, he died due to severe methanol intoxication, but the probability of cerebral hemorrhage may be the cause of the patient death associated with heparin

Background

Methanol (MeOH, CH3OH) intoxication causes serious toxicological concerns. Its adverse effects are associated with its metabolites (e.g., formic and lactic acid), which are responsible for toxic due to cellular hypoxia and may cause a public health problem, metabolic damage, neurological dysfunction, cardiovascular disease, visual impairment, and even death [1-3]. In

addition, it is involved in the agglomeration of formic acid inhibits cytochrome c oxidase activation in the mitochondria, resulting in damage of the basal ganglia, causing metabolic acidosis and visual disturbance [4,5].

In addition to symptoms containing headache, abdominal pain, nausea, vomiting, and loss of vision may appear several hours to days after exposure, elevated serum osmolal gap and anion gap metabolic acidosis can be evidence of its toxic presence [6,7].

On the other hand, the production of toxic metabolites by the enzymes alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) can lead to bilateral necrosis of the central nervous system (CNS), which can be identified on computed tomography (CT) and magnetic resonance imaging (MRI) [8,9].

Case Presentation

A 24-year-old man presented to our emergency department because of a headache exacerbated at 3 am in June 2019. The emergency room physician eventually demands a CT scan for the patient (Figure 1). He did not exhibit any lesions on the CT scan of the head and abdomen. Initially, the patient showed no indication of medication and or alcohol consumption. Furthermore, the patient was admitted to the intensive care unit (ICU) at 9-11 am, and the possibility of alcohol intoxication was raised with a new history of blurred vision. Then, the patient rapidly deteriorates about 2 hours after admission to the ICU and develops respiratory distress (with quick, shallow respirations) and reduction of consciousness level. In parallel, regarding the shallow respiration, the patient was intubated immediately and underwent mechanical ventilation in the ICU. Subsequently, the advice of a nephrology and poisoning consultant were requested.

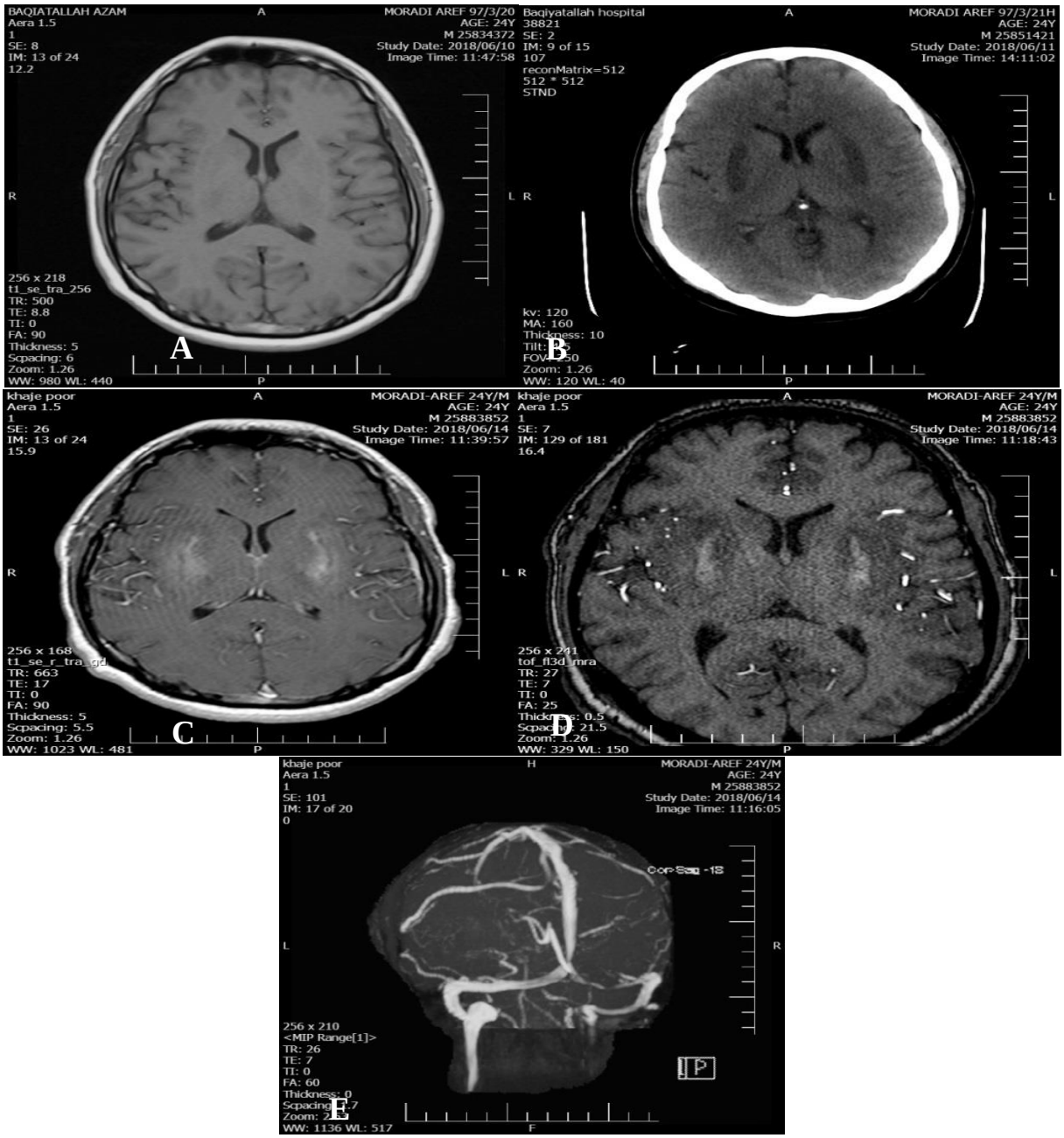

Figure 1. **A:** Brain MRI showed a normal pattern without any specific lesion on the 1st day. **B:** Brain CT Scan of the patient revealed bilateral putamenal ischemia at day 2. **C and D:** Brian MRI with contrast revealed significant Putamenal necrosis at day 4. **E:** Brain angiography did not show any vascular abnormality at day 4.

The possibility of methanol poisoning was given by Toxicological analysis service due to the history of headache, hypotension and arterial blood gas (ABG) changes, and respiratory disorder, and he swiftly underwent emergency Shaldon catheter and then underwent dialysis for 4 hours. In the ward, the patient was hospitalized and other supportive actions were done for the patient. The serum ethanol and methanol levels were subsequently measured. Regarding the primary status of methanol level (9 mg/dl. The presence of metabolic acidosis and the status of bicarbonate therapy can be stated due to the patient's physiological situation at the sampling time. The Osmolol and Anion Gap gauges were unavailable, and the formula calculation did not help much.

On the first day, initial ABG laboratory findings included pH 7.25, PCO_2 49 mmHg, PO_2 65 mmHg, and HCO_3 15 mmol/L. On the second day, ABG was also determined (pH 7.32, PCO_2 45 mmHg, PO_2 60 mmHg, and HCO_3=19 mmol/L). Again the advice of the nephrology consultant recommended that the patient undergo redialysis with the minimal dose of heparin (5000 IU/mL) (Table 1). From day 3, his consciousness and respiratory status gradually recovered, he became alert, and his blurred vision extremely improved.

Table 1

The Biochemical Parameters of the Patient with Methanol Poisoning

Variables	Day 1	Day 2	Day 3	Day 4
pH	7.25	7.32	-	7.46
PCO_2(mmHg)	49	45	-	37
PO_2(mmHg)	65	60	-	29
HCO_3 (mEq/L)	15	19	-	27.6
WBC x 10^3/µL	9.0	24.4	13.5	12.4
RBC x 10^6/µL	5.42	5.53	4.66	3.81
Hemoglobin (g/dL)	16.3	17.1	14.5	11. 7
Hematocrit %	45.6	44.7	37.4	33
MCV fl	84.13	80.83	80.26	86.61
MCH Pg	30.07	30.92	31.12	30.71
MCHC g/dL	35.75	38.26	88.77	35.45
Platelet (/uL)	221	232	127	76
Sodium (mEq/L)	135	133	138	135
Potassium (mEq/L)	5.5	3.2	2.9	3.6
Calcium-Ca (mg/dL)	7.5	-	8.3	0.8
Phosphorus-P (mg/dL)	6.0	-	-	3.5
Magnesium (Mg) (mg/dL)	2.9	-	-	-
Methanol mg/dL	9	-	-	181
Prothrombin time (s)	17.5	15.2	-	-
PTT.Patient time (s)	50	127	-	-
Blood sugar (mg/dL)	443	172	154	107
Blood Urea Nitrogen mg/dL	21	34	33	10
Creatinine mg/dL	2.1	2.2	1.6	0.8
AST UI/L	25	-	140	92
ALT UI/L	28	-	71	60
CK-MB (ng/mL)	8.29	-	-	-
Troponin I (ng/mL)	0.016	-	-	-
CRP-quantitative (mg/L)	5.3	-	-	-
creatine phosphokinase (CPK) U/L	157	-	-	2821
Lactate dehydrogenase (LDH) U/L	351	-	-	
Serum Amylase U/L	-	-	236	49
Total Bilirubin (mg/dL)	-	-	1.0	0.6
Direct Bilirubin(mg/dL)	-	-	0.4	0.3

On the third day, ABG status was not measured, and ABG measurement was then requested by the poisoning service, in addition to redialysis orders by one of the physicians. After the third dialysis, the status of consciousness gradually became confused. Finally, at the end of day 3, CT scans were impaired, and basal ganglia ischemia was reported. And the final MRI showed clearly abrasion and basal ganglia necrosis.

This point should be noticed that the hemodynamic status was well within three or four days of hospitalization. Only on the first day, he had severe acidosis, respiratory disorder, loss of consciousness, and hypotension, which elevated by improving ventilation and giving two vials of sodium bicarbonate 2 to 44 mEq/kg IV of blood pressure remained.

In the time of consciousness, the patient received 600 mg of N-acetylcysteine (NAC) (IV, 3 times daily) for 3 days, but NAC (2 g per 12 h) and folic acid (50 mg of folic acid per 12 h for 3 days) was injected on the second day. Despite the continued intensive care of the patient and his treatment, unfortunately, he eventually died in ICU due to severe methanol intoxication.

In the patient's clinical record, the cause of death was respiratory failure related to methanol intoxication. Regarding ischemic necrosis, the probability of cerebral hemorrhage may cause

the patient death. The therapeutic intervention was delayed; he was treated only with hemodialysis and a single dose of ethanol.

Discussion and Conclusion

The patients with MeOH intoxication presented to the emergency ward with multifarious complaints. Typical signs of MeOH intoxication included metabolic acidosis, central nervous system depression or sequelae, vision disturbances, or ocular changes caused by formic acid, a toxic metabolite of MeOH [8, 10]. Symptoms can typically include dizziness, headache, dyspnea, nausea, vomiting, abdominal pain, impaired sensorium, weakness, hardness of movement, and blurring vision [1, 2], as well as respiratory arrest [11], coma, and death in severe poisoning [6]. In parallel, we observed the symptoms such as headache, hypotension, respiratory disorder, and even blurred vision in the present case. The majority of the clinical abnormalities are the intensity of intoxication. The clinical outcomes correlate more with the acidosis level than the MeOH levels, and metabolic acidosis is likely due to formic acid and lactic acid agglomeration. All in all, these observations possibly could reflect the accumulation of the above metabolites [12, 13]. Systemic effects are mostly due to metabolic acidosis resulting from formic acid reposition [14] as well as the ocular impairment is associated with the acidosis degree [11].

Based on pathogenesis mechanisms, methanol is metabolized to formaldehyde by alcohol dehydrogenase and then to formic acid with high toxicity (responsible for the systemic metabolic acidosis[the toxic effects and cause the increase of lactic acid]) by formaldehyde dehydrogenase in the hepatic using metabolic pathways. This conversion happens extremely fast, with a half-life of 1-2 minutes in humans [7, 10, 11, 15]. In addition, the CNS is very sensitive to formic acid toxicity, which inhibits some oxidase systems like cytochrome oxidase, and blocks adenosine triphosphate production (ATP) in mitochondria, resulting in axonal cell death and cellular hypoxia, lactic acid reposition or lactate formation, and elevated academia [3, 6, 16]. Regarding mechanisms mentioned, Zakharov et al. and Nurieva and Kotikova et al. reported that methanol poisoning could be associated with violent visual disturbance and basal ganglia damage [4, 17]. Our patient revealed blurred vision and basal ganglion necrosis in agreement with the above findings. Of course, the mechanism responsible for necrosis is unknown. Nevertheless, the above outcomes make methanol metabolites (such as formic acid and metabolic acidosis) better indicators of methanol toxicity when measured 48 h after MeOH ingestion and remedial intervention [3, 9, 18].

Hemorrhage is one of the usual side effects of any anticoagulant, and heparin is the most common anticoagulation factor utilized for dialysis [19]. Many studies reported that heparinization in MeOH poisoned patients during hemodialysis may contribute to cerebral hemorrhagic complications in the necrotic areas of the brain and recommended a deleterious role of systemic anticoagulation during hemodialysis [19-23]. In contrast, Taheri et al . and Vyas et al. defined an unknown mechanism as main indicator of putaminal hemorrhage and brain necrosis in patients with MeOH toxicity [24, 25]. Furthermore, Aisa and Ballut and Zakharov et al. indicated no relationship of cerebral hemorrhage with systemic anticoagulation such as heparin during dialysis [26, 27]. Furthermore, McLean et al. and Ganguly et al. demonstrated that hemorrhagic brain lesions in the basal ganglia are due to the direct poisonous effect of formic acid in patients with MeOH poisoning [28, 29].

In summary, heparin could be associated with converting from basal ganglia necrosis to cerebral hemorrhage in ICU. It seems that heparin (ICU 5000 daily from day 2) may cause a brain hemorrhage. Nevertheless, there is a definite association between systemic

anticoagulation (such as heparin) and cerebral hemorrhage in patients with MeOH intoxication as the cause of death in these patients?

On the other hand, optimal treatment of MeOH intoxication is historically difficult, but it requires primary accurate and fast diagnosis, and rapid initiation of effective therapy guarantees a better prognosis.

Abbreviations

MeOH= Methanol, CT =computed tomography, ICU =intensive care unit, IVH= intraventricular hemorrhage, ATP= adenosine triphosphate production, NAC= N-acetylcysteine, NAC= N-acetylcysteine, ADH= alcohol dehydrogenase, ALDH= aldehyde dehydrogenase, CNS= central nervous system , MRI= magnetic resonance imaging

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Ethics approval and consent to participate

This case report was described in accordance with the ethical standards laid down in the "Declaration of Helsinki 1964".

Consent for publication

Written informed consent for publication of the case report was obtained from the patient's parents.

Availability of data and materials

All data supporting our findings are contained within the manuscript

Competing interests

The authors declare that they have no competing interests

Funding

The authors have not declared a specific grant for this research from any funding agency in public, commercial or not-for-profit sectors.

Authors' contributions

All authors participated in the literature review, designed the manuscript, revised the manuscript, and completed this case report. All authors read and approved the final manuscript

Acknowledgements

Not applicable.