Methanol Intoxication: Differential Diagnosis from Anion Gap-increased Acidosis

Motoki Fujita, Ryosuke Tsuruta, Jun Wakatsuki, Hitoshi Takeuchi, Yasutaka Oda, Yoshikatsu Kawamura, Susumu Yamashita, Shunji Kasaoka, Kiyoshi Okabayashi and Tsuyoshi Maekawa

Abstract

We report a case of methanol intoxication, which was not distinguished from ethylene glycol intoxication during treatment. A 65-year-old man was transferred to our emergency department because of drowsiness and remarkable metabolic acidosis. He was intubated because his consciousness disturbance worsened. The diagnosis was suspected as methanol or ethylene glycol intoxication in addition to ethanol intoxication. Administration of ethanol and hemodialysis were chosen for his essential treatments. When he was extubated, he complained about visual loss. His brain computed tomography scans revealed putaminal lesions, which are rarely reported in methanol intoxication. Diagnosis of methanol intoxication was confirmed by the serum high methanol levels. (Internal Medicine 43: 750–754, 2004)

Key words: methanol, ethylene glycol, increased anion gap, metabolic acidosis, putaminal necrosis, visual loss

Introduction

Methanol is commonly used in canned heats, resolvents, vanishes, paint removers and antifreeze. Since methanol intoxication is uncommon, the definitive diagnosis of methanol intoxication is not easily obtained, while it is a life-threatening poisoning. When methanol intoxication is suspected, early treatments such as ethanol administration and hemodialysis are essential. We report a case of methanol intoxication, who was successfully treated before the definitive diagnosis.

Case Report

A 65-year-old man, a heavy drinker was transferred to our emergency department because of drowsiness and remarkable metabolic acidosis. On admission, he had consciousness disturbance (Glasgow Coma Scale 10). His vital signs were relatively stable, which were blood pressure 124/68 mmHg, pulse rate 68 beats/min, and core body temperature 36.4°C, except respiratory rate 26 breaths/min. There was an obvious odor of ethanol in his breath. His head was atraumatic, but his pupils were dilated to 6 mm each with absent light reflex. There was no abnormal finding of his neck, lungs, hearts, abdomen and all limbs. However, his entire body was cyanotic.

Laboratory examinations on admission showed the following results; serum sodium 137 mEq/l, potassium 5.5 mEq/l, chloride 104 mEq/l, bicarbonate less than 13.0 mEq/l, creatinine 1.0 mg/dl, blood urea nitrogen 11 mg/dl, C-reactive protein 0.05 mg/dl, glucose 358 mg/dl and anion gap more than 20 mEq/l. The white blood cell count was 13,100/µl and hemoglobin was 15.6 mg/dl. Amphetamines/methamphetamines, cocaine, opiates (heroin), phencyclidine (PCP), tetrahydrocannabinol (marijuana), barbiturates, benzodiazepines, tricyclic antidepressants and methadone were all negative by Triage DOA® (BIOSITE, San Diego, CA, U.S.A.). The arterial blood analysis under 10 l/min oxygen showed; PaO₂ 368 mmHg, PaCO₂ 74.5 mmHg, pH 6.62, base excess −26.2 mmol/l and lactate 8.3 mmol/l. Urinary ketone body was negative.

Because his consciousness level worsened, he was intubated and mechanically ventilated. Sodium bicarbonate was administrated to treat metabolic acidosis. His brain computed tomography (CT) scans on admission showed no abnormalities (Fig. 1A). Finally, his diagnosis was suspected as ethanol intoxication with methanol or ethylene glycol intoxication.

Administration of ethanol via nasogastric tube and con-
Continuous hemodialysis (CHD) for 11 hours were chosen. The clinical course of his acute phase is shown in Fig. 2. After the start of CHD, metabolic acidosis was improved. Arterial pH and base excess were normalized and his consciousness level was recovered 3 hours after the start of CHD. Therefore he was extubated. Following extubation, he complained about visual loss and explained that he had drunk about 40 ml methanol. His visual acuity was only perception in both eyes. Funduscopic examination revealed papilledema. On the sixth hospital day, his level of consciousness worsened again and hemiplegia on the right extremities occurred. The second brain CT scans showed low-density lesions on bilateral putamens and frontal lobes (Fig. 1B). He was diagnosed as multiple necrosis of brain including bilateral putaminal necrosis, which are typical findings in methanol intoxication. In spite of the treatments for methanol or ethylene glycol intoxication, neurological findings were not improved, and he was discharged from the ICU on the 12th hospital day. Three weeks later after admission it was noted that his serum methanol levels before and after CHD were 883 mg/l and 134 mg/l, respectively. The final diagnosis of methanol intoxication was confirmed.

Discussion

When the information of absorbed materials is insufficient, the diagnosis of poisoning is not easily obtained. However, some kinds of symptoms and laboratory data are specific in some kinds of poisoning. In this case, metabolic acidosis with increased anion gap was important to approach the diagnosis. Differential diagnoses of lactic acidosis, diabetic ketoacidosis, uremia, salicylates, alcohol, paraldehyde and ethylene glycol were necessary to consider. Weinberg et al (1) introduced the mnemonic ‘SEAL DUMP’ (salicylates, ethylene glycol, alcohol, lactic acidosis, diabetic ketoacidosis, uremia, methanol, paraldehyde) that indicates the differential diagnosis for anion gap-increased acidosis.

The differential diagnosis for anion gap-increased metabolic acidosis is shown in Fig. 3. Methanol or ethylene glycol intoxication often coincides with ethanol intoxication. Visual symptoms are seen in methanol intoxication. Calcium oxalate in the urine sediments may imply ethylene glycol intoxication, but it is revealed in only 50% of patients with ethylene glycol intoxication (2). The osmolar gap is also helpful to differentiate anion gap-increased metabolic acidosis, however the serum osmotic pressure was not measured in the present case.

In the present case, traces of three types of toxic alcohol existed because of alcohol odor. However, physical findings such as visual symptoms, were not obtained because of consciousness disturbance. Because it was not clear whether the intoxication was due to methanol or ethylene glycol,
Figure 2. Changes of arterial pH and base excess following treatments.

Figure 3. Differential diagnoses flow chart for anion gap-increased metabolic acidosis. (↑) indicates 'increase', and (+) means 'positive'.

Anion gap-increased metabolic acidosis

Lactic acidosis ± other metabolic acidosis

Further examination

Diabetic ketoacidosis

Blood glucose ↑ and Urine ketone body (+)

BUN ↑, Cre ↑ and History of hemodialysis

Uremia

Physical findings

Odor of alcohol (+)

Ethanol level in serum or expired gas ↓

Auditory symptoms (+)

Ethanol

Salicylate

Visual symptoms (+)

Calcium oxalate in urine sediments (+)

Methanol

Ethylene glycol

BUN: blood urea nitrogen
Cre: creatinine
treatments suitable to both were chosen. Retrospectively considering, the initial absence of light reflex might be considered related to the visual disturbance caused by methanol intoxication.

The therapy for ethylene glycol poisoning is basically effective for methanol intoxication, because the pathophysiological features of ethylene glycol intoxication are similar to those of methanol. Both methanol and ethylene glycol are absorbed rapidly from the gastrointestinal tract and mainly metabolized in the liver by alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (Fig. 4). In methanol intoxication, formic acid is toxic. On the other hand, glycoaldehyde, glycolic acid, glyoxylic acid and oxalic acid are toxic in ethylene glycol intoxication. In both intoxications, symptoms are caused by accumulations of these toxic acids. Therefore, the principle of the treatments is to suppress or eliminate these metabolites.

Ethanol infusion inhibits production of toxic acids via ADH pathway. Administration of sodium bicarbonate corrects metabolic acidosis and hemodialysis removes both toxic acids and methanol or ethylene glycol in blood. Administration of folate accelerates metabolism of formic acid to CO$_2$ and H$_2$O in methanol intoxication. Likewise, thiamine and pyridoxine accelerate metabolism of glyoxylic acid in ethylene glycol intoxication. Charcoal does not absorb methanol or ethylene glycol, and ipecac is contraindicated (1, 2). Recently, fomepizole, a potent and long-acting competitive inhibitor of ADH, has been introduced as a safe and effective reagent for methanol and ethylene glycol intoxication (3, 4). However, fomepizole is not available in Japan.

Methanol in serum reaches the peak level within 60 minutes after ingestion, although clinical symptoms appear 12–24 hours after ingestion (5). When methanol level is low or ethanol is absent, the half-life time of methanol is within 3 hours. But if ethanol is ingested with methanol, the half-life time is prolonged up to 52 hours (6). Early toxicity of methanol intoxication is due to methanol itself and appears as symptoms such as nausea, vomiting, headache and abdominal pain. Late toxicity is due to acidosis caused by formic acid and lactate. Visual symptoms including light flashes, blurring, and blindness are caused by accumulation of formic acid in the optic nerve.

Putaminal lesion after methanol intoxication is rare (7). The sign is extrapyramidal motor dysfunction including rigidity, tremors, masked face and monotonous speech. In the cases with putaminal necrosis, the concentration of formic acid in the putamen is higher than in other areas of brain (8). Fontenot et al (7) explain that putamen might be the most sensitive to an acidic environment in the brain. Though putaminal lesions of methanol intoxication are typical findings, methanol can also cause separate necrotic lesions in the cerebral white matter (9).

Definitive diagnosis of methanol intoxication requires a confirmed increase in the serum methanol level by gas chromatography. The qualitative analysis using chromotropic acid may be available (10). This procedure, in which formaldehyde in serum is reacted with chromotropic acid, changes the color to red-violet.

Indications of hemodialysis are as follows; amount of ingested methanol is greater than 30 ml, serum methanol level is greater than 500 mg/l, mental or visual symptoms are observed, acidosis can not be corrected by repeated bolus doses of bicarbonate (11, 12). Hemodialysis should be continued until the serum methanol level is less than 250 mg/l (1).

In the present case, CHD instead of hemodialysis was chosen. Because he was on a ventilator and CHD could be done by his bedside in our ICU. After the start of CHD, metabolic acidosis and consciousness disturbance were improved, and CHD was finished when the quantity of CHD was equal to that of daily hemodialysis (Fig. 2). Hemodialysis should be done with monitoring of the serum methanol level (1, 11, 12). But most institutions including ours are unable to measure it on time. In the present case, CHD was performed while observing the degree of acidosis and consciousness level. Comparing the initial serum methanol level (883 mg/l) to that after CHD (134 mg/l), CHD was considered effective to remove methanol in blood to an appropriate level of less than 250 mg/l (1).

In conclusion, the definitive diagnosis of methanol intoxication with consciousness disturbance is very difficult. If there are specific symptoms and abnormal laboratory data, which are common to both methanol and ethylene glycol intoxication, the principal treatment should be performed immediately.

References

1) Weinberg L, Stewart J, Wyatt JP, Mathew J. Unexplained drowsiness
