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Fatal Methanol Intoxication – Two Exceptional Cases

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1. Introduction

Poisonings from toxic alcohols, such as methanol (MeOH) are a serious toxicological concern worldwide. In an endemic methanol poisoning in 2012 in the Czech Republic 121 subjects had consumed adulterated beverages and 41 died from the poisoning. An additional 20 subjects still suffer from visual/CNS sequelae [1]. In addition to mass poisonings single cases of methanol poisoning had been published recently [2-4]. Toxicity of methanol is related to the production of toxic metabolites by the enzymes alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH), which can lead to metabolic acidosis, blindness and death. Therapy usually consists of general supportive care, hemodialysis and use of antidotes. While hemodialysis is still considered a key element in the treatment of methanol intoxication there are two antidotes available which allow to block ADH-mediated metabolism of methanol: ethanol and fomepizole [5-9]. In the following, two exceptional cases of methanol poisoning from routine work in the ZIFM (Zurich Institute of Forensic Medicine) are presented.

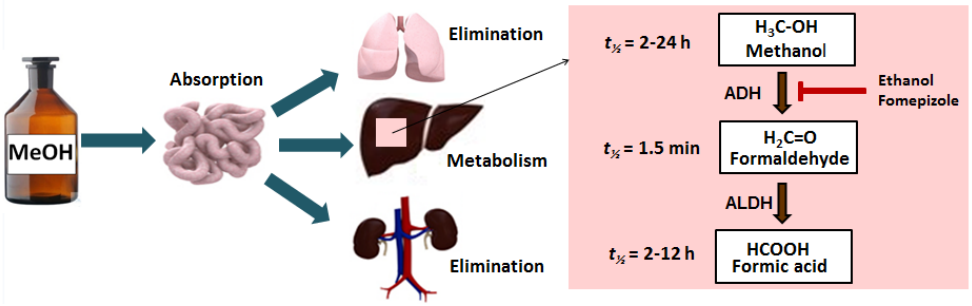

Fig. 1. Major metabolic pathway of methanol.

2. Case History

Two independent cases of methanol ingestion are presented. In case I, a 53-year-old female laboratory assistant was hospitalized with symptoms such as dizziness, nausea, impaired vision and a systolic blood pressure over 250 mm Hg. The woman fell into a coma despite a correct diagnosis and immediate therapy (hemodialysis, ethanol 1g/L). One month after hospitalization, the woman died due to irreversible central nervous system lesions. In case II, a middle-aged male was found dead in a public toilet.

3. Materials and Methods

Methanol levels were determined in postmortem samples (blood, urine, gastric content) from the male decedent. All available clinical and postmortem samples from the hospitalized woman were analyzed for methanol. In addition, the methanol metabolite formic acid, ethanol

from antidote therapy and a marker for ketosis (β-hydroxybutyric acid) were determined using gas chromatography electron capture detection (GC-ECD) or headspace gas chromatography mass spectrometry (HS-GC-MS). Ethyl glucuronide (EtG) was determined in hair in both cases using GC-negative chemical ionization (NCI)-MS. Systematic toxicological analysis was performed using GC-MS after enzymatic hydrolysis, liquid-liquid extraction and acetylation.

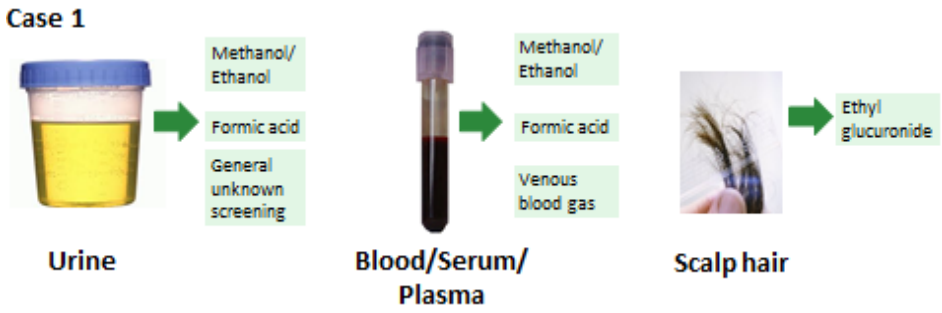

Fig. 2. Case I: Samples and analytes tested for.

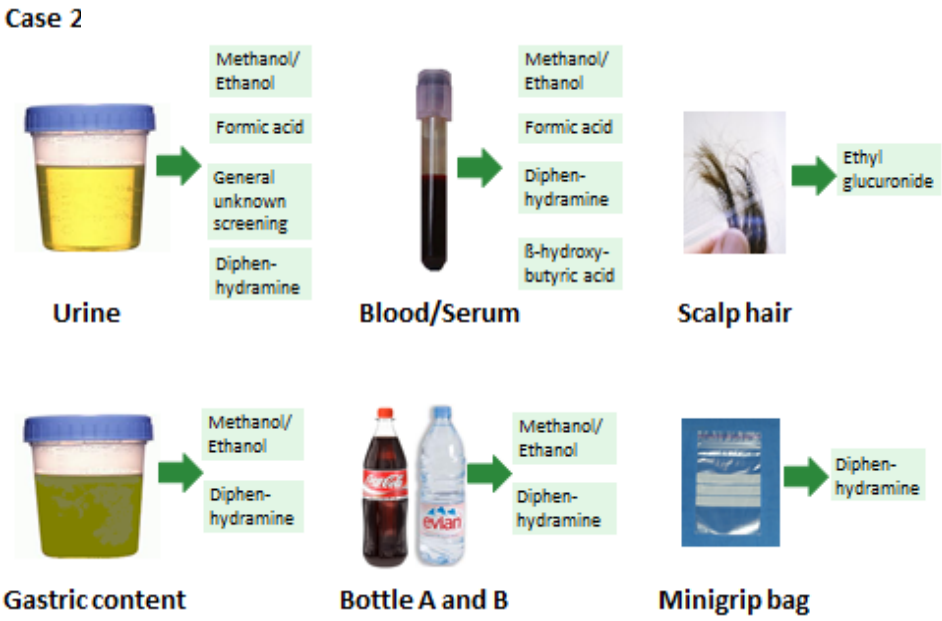

Fig. 3. Case II: Samples and analytes tested for.

4. Results

Methanol concentrations were 1.5 g/L of plasma for the first clinical sample of case I and 3.7 g/L of blood for case II. Ethanol was not detected in these blood samples. Methanol could no longer be detected 18 h after admission. Ethanol concentration in blood from ethanol therapy was 1.1 g/L. To check for ethanol abuse, hair was analyzed for ethyl glucuronide (EtG). In both cases, EtG concentrations were under 7 pg/mg, indicating ethanol abstinence. In case I, general unknown screening was negative and an acidosis (pH 6.76) with a base excess of -30.8 mval/L was determined in clinical chemistry.

In case II, diphenhydramine in addition to methanol was detected in gastric content, blood and urine and quantified in the latter two matrices (4.5 mg/L and 6.7 mg/L, respectively). Beta-

hydroxybutyric acid as a marker for ketosis was in the physiological range (126 µmol/L). One of the seized bottles contained pure methanol and the minigrip bag contained diphenhydramine.

Central failure of regulatory functions was claimed as the cause of death in both cases. Hemorrhagic necrosis was observed in case I because of the longer survival time.

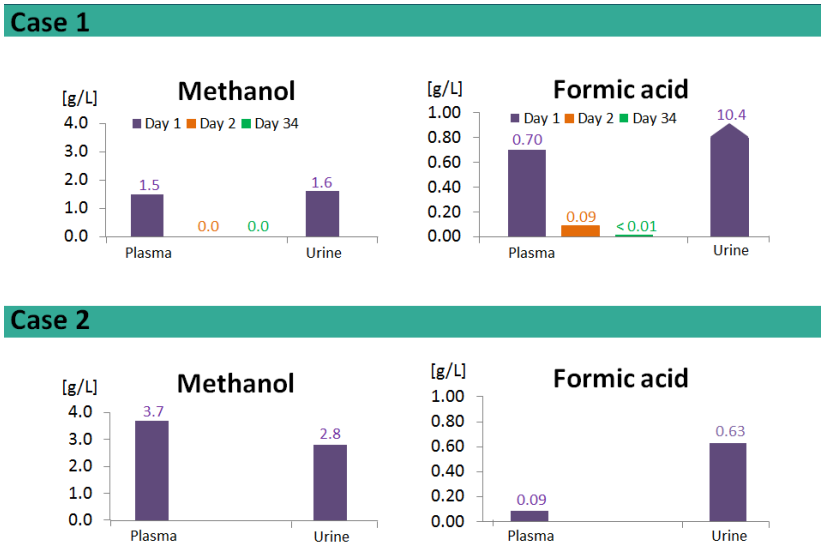

Fig. 4. Methanol and formic acid concentrations in blood and urine.

5. Discussion

Methanol is a commonly used organic solvent which can cause metabolic acidosis, neurologic sequelae, and even death, when ingested. It is well-absorbed through the gastrointestinal tract and is also absorbed through the skin and by inhalation. Its toxic effects arise from its metabolism to formaldehyde and formic acid. The toxic dose of methanol varies depending on the individual and on the possibilities of treatment. Blood methanol concentrations above 0.5 g/L are associated with severe toxicity, and concentrations above 1.5-2.0 g/L may lead to death in untreated patients [10]. The main principles of treatment are to prevent further metabolism of methanol, correct metabolic abnormalities and provide other supportive care. Metabolism can be blocked by the administration of ethanol or fomepizole [5]. Supportive measures may include the correction of acidosis with sodium bicarbonate, intubation and mechanical ventilation and the use of extracorporeal elimination such as hemodialysis.

In both cases presented here, concentrations of methanol and formic acid were in the toxic range. Death was caused by a central failure of regulatory functions. Although the subject in Case I survived the initial methanol intoxication, metabolic acidosis lead to brain lesions despite immediate therapy (ethanol, hemodialysis). Brain lesions could be observed using MRI (Fig. 5).

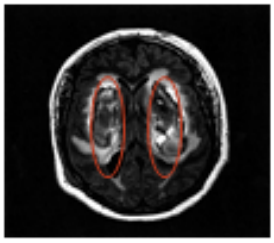

Fig. 5. Case I: MRI of brain at day 10. Hemorrhagic necrosis areas are marked with red circles.

The subject in Case II died of acute intoxication. In this case, diphenhydramine might have prevented nausea, which might have contributed to the high methanol concentration found in this case. Combination of methanol and diphenhydramine increased central nervous depression. As in case I, a brain edema was diagnosed (MRI not available).

In methanol poisonings, neither kind of hemodialysis (continuous vs. intermittent) nor choice of antidote (ethanol vs. fomepizole) seem to have an influence on the mortality. Severity of metabolic acidosis, state of consciousness, and serum ethanol on admission were the only significant parameters associated with mortality in the Czech mass poisoning event [1].

6. Conclusion

Even after an initial survival of methanol intoxication, disturbances of the acid-base balance can lead to brain lesions and failure of regulatory functions. Moreover, the risk of acute respiratory depression is increased by additional intake of central nervous depressants (e.g. diphenhydramine). Therefore, an additional screening for CNS depressing substances in cases of methanol intoxication is recommended.

7. Acknowledgements

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8. References

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