CASE REPORT

Mind the gap: a case of severe methanol intoxication

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SUMMARY

We report a case of a 37-year-old woman with non-insulin-dependent diabetes on sitagliptin, an alcohol abuser who was brought unresponsive to the emergency department of our hospital. On arrival, the patient was intubated and mechanically ventilated due to a low Glasgow Coma score of 3/15. Initial laboratory testing identified profound high anion gap metabolic acidosis. Owing to the dubious circumstances and the depth of acidosis, methanol and ethylene glycol intoxication was suspected. Further evaluation revealed a significantly increased serum osmolal gap. Pending volatile compound screen, fomepizole was started and urgent haemodialysis undertaken. Subsequent brain MRI identified changes in putamen of bilateral basal ganglia, suggestive of methanol intoxication. The patient was later found to have an initial methanol level of 237 mg/dL. She was successfully extubated on day 2 of hospitalisation, with residual cognitive and visual deficits.

BACKGROUND

Methanol intoxication is associated with significant morbidity and mortality in the USA.¹ Although methanol itself is not very toxic, it is metabolised by alcohol dehydrogenase into formaldehyde and subsequently into formic acid, as shown in [figure 1](#). These metabolites cause anion gap metabolic acidosis, blindness, irreversible brain damage and death attributed to methanol toxicity.² Diagnosis can be difficult in cases where history is not readily available and requires a high degree of suspicion. Prompt recognition and early treatment with inhibitors of alcohol dehydrogenase are crucial, as the degree and irreversibility of damage caused by formic acid is time-sensitive.

CASE PRESENTATION

A 37-year-old woman with a history of non-insulin-dependent diabetes on sitagliptin and of alcohol abuse was brought unresponsive to the emergency department of our hospital. According to family members, the patient reported blurred vision shortly before becoming unresponsive. On initial vitals, she was normotensive and afebrile with agonal breathing and oxygen saturation of 88% on room air. Examination revealed a Glasgow Coma score of 3, and fixed dilated and non-reactive pupils. The rest of the examination was unremarkable. The patient was intubated and mechanically ventilated. CT scan of the brain without contrast was unremarkable and the ECG was at baseline. The patient was transferred to the medical intensive care unit for further management.

INVESTIGATIONS

Relevant initial laboratory testing identified arterial pH of 6.724, serum bicarbonate 4.8 mEq/L, serum glucose 361 mg/dL, anion gap 29 mEq/L, β -hydroxybutyrate 0.28 mmol/L and lactic acid of 9.2 mEq/L. The rest of the laboratory studies were unremarkable including negative blood ethanol, salicylate and acetaminophen level. The presence of high anion gap metabolic acidosis was initially thought to be secondary to diabetic ketoacidosis and hyperlactaemia. However, the degree of lactic acidosis and ketonaemia was not high enough to explain the depth of the acidosis and severity of presentation.

Owing to the extent of acidosis, severity of disease, profound anion gap along with history of alcohol abuse and blurred vision reported by the family, ingestion of toxic alcohol such as methanol was suspected. On further evaluation, the patient was found to have high measured serum osmolality of 416 mOsm/kg, calculated osmolality of 300 mOsm/kg and a significantly increased osmolal gap of 115 mOsm/kg. Following this, a volatile compound screen was sent to a reference laboratory as testing for toxic alcohols was not available at our hospital. These findings were remarkable enough to warrant treatment for intoxication by toxic alcohol such as methanol or ethylene glycol. A brain MRI carried out later on the day of admission after initiating treatment showed restricted diffusion and a hyperintense signal within the putamen of bilateral basal ganglia, suggestive of non-haemorrhagic necrosis, as shown in [figure 2](#).

TREATMENT

Pending definite drug levels, fomepizole was started to block the metabolism of methanol/ethylene glycol, and cofactor therapy with folic acid intravenously was started to enhance the metabolism of formic acid. Sodium bicarbonate intravenously was given to correct the acidosis. A decision to undertake haemodialysis was taken because of the severity of disease and pH refractory to initial bicarbonate treatment. The patient underwent a total of 6 h of haemodialysis resulting in normalisation of blood pH and resolution of the anion as well as osmolal gaps. She was eventually found to have initial methanol level of 237 mg/dL.

DIFFERENTIAL DIAGNOSIS

Disorders that can present with high anion gap metabolic acidosis and increased osmolal gap include:

- Methanol intoxication
- Ethylene glycol intoxication

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Figure 1 Metabolism of methanol to formic acid. Oxidation of methanol to formaldehyde by alcohol dehydrogenase is the rate limiting step in the metabolism of methanol that is inhibited by fomepizole. Administration of folic acid enhances catabolism of formic acid to carbon dioxide and water by 10-tetrahydrofolate synthetase.

- ▶ Diethylene intoxication
- ▶ Propylene glycol intoxication
- ▶ Diabetic ketoacidosis
- ▶ Lactic acidosis
- ▶ Alcohol ketoacidosis
- ▶ Advanced chronic kidney disease

OUTCOME AND FOLLOW-UP

The patient was successfully extubated on day 2 of hospitalisation. On recovery, she admitted to taking large amounts of windshield wiper fluid as an ethanol substitute. Throughout her hospitalisation, she continued to show signs of residual neurological deficits such as tremor and hypokinesia. She also continued to have a fluctuating level of consciousness with agitation and restlessness at times. She was able to count fingers at a distance of 2 feet. However, an accurate visual assessment was difficult to determine because of the patient's lack of cooperation for a complete eye examination. She was finally transferred to a rehabilitation facility on day 5 of hospitalisation. A follow-up with ophthalmology and neurology was recommended on improvement of her mental status.

DISCUSSION

Methanol (wood alcohol) is a colourless, flammable and poisonous liquid that is commonly used as an industrial solvent. Methanol poisoning most often occurs from ingestion of windshield-washer fluid.³ It is also used in copy machines, embalming fluids and canned-heating products. Following oral ingestion, methanol is rapidly and completely absorbed with peak serum concentrations reached within 1–2 h. In the absence

of treatment, elimination follows zero-order kinetics and has been estimated at 8.5 mg/dL/h following overdose.⁴ Diagnosis of methanol intoxication requires a high index of suspicion, as testing for definite drug levels is not widely available and frequently must be performed at a reference laboratory. Such laboratory testing rarely, if ever, gives results in time to assist clinical decision-making. In cases where history is not readily available or the patient is severely obtunded, the presence of laboratory abnormalities such as high anion gap metabolic acidosis and increased serum osmolal gap serve as an important diagnostic clue. However, either can be absent depending on time after exposure when blood is sampled as well as concomitant presence of ethanol.^{5–6} In our patient, the aetiology of high anion gap acidosis with concomitant high serum osmolar gap could have been attributed to the presence of hyperlactataemia or diabetic ketoacidosis.^{7–8} Nevertheless, a very high osmolal gap as seen in our patient is almost always due to ingestion of toxic alcohol such as methanol and has a specificity of 85% at a cut-off value of ≥ 20 mOsm/kg of H₂O.⁹ In unconscious patients such as ours, neuroimaging can be helpful in distinguishing methanol intoxication from other conditions causing altered sensorium. Bilateral putaminal necrosis with or without haemorrhage is a classic hallmark finding seen with MR brain imaging.^{10–12} Management involves correction of the acidosis, with intravenous sodium bicarbonate, in patients presenting with significant acidosis, as patients with methanol intoxication fare worse when systemic acidemia is present.¹³ It also involves administration of fomepizole or ethanol to inhibit alcohol dehydrogenase, a critical enzyme in the metabolism of methanol, and administration of intravenous folic acid to enhance the

Figure 2 Methanol intoxication. MR brain imaging showing bilateral putamen lesions. (A) Axial diffusion-weighted image with restricted diffusion. (B) Axial fluid attenuated inversion recovery sequence with hyperintense signal. (C) Axial T2 fat suppression, fast spine echo with hyperintense signal. These findings are suggestive of non-haemorrhagic necrosis.

metabolism of formic acid.¹⁴ Haemodialysis is the best method to rapidly remove both the parent alcohol and toxic metabolites, and plays a fundamental role in treating severely poisoned patients such as those with seizures, coma, new vision deficits, metabolic acidosis with blood pH $\leq$ 7.15 and a serum anion gap higher than 24 mmol/L.¹⁵ The presence of residual neurological deficits such as tremor, as seen in our patient, correlates strongly with putamen necrosis.¹³ However, the presence of such deficits can be seen in the absence of neuroimaging findings. Visual disturbance due to toxic optic neuropathy has been shown to recover partially and in some cases fully in survivors of methanol intoxication.^{16 17} Unfortunately, accurate assessment of visual recovery was difficult to determine in our patient due to obtundation with no baseline visual assessment.

Learning points

- ▶ An increased osmolal gap with otherwise unexplained high anion gap metabolic acidosis is an important clue to the presence of toxic alcohol ingestion such as of methanol.
- ▶ Prompt recognition and early treatment is essential in the management of methanol intoxication and is associated with decreased morbidity and mortality.
- ▶ Neuroimaging such as MRI of the brain can help in supporting the diagnosis of methanol intoxication due to its characteristic findings. However, treatment should not be delayed for imaging when intoxication is highly suspected.

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REFERENCES

- 1 Mowry JB, Spyker DA, Cantilena LR, *et al.* 2013 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 31st Annual Report. *Clin Toxicol (Phila)* 2014;52:1032–283.
- 2 Manuchehri AA, Alijanpour E, Daghmehi M, *et al.* A case of methanol poisoning leading to prolonged respirator dependency with consequent blindness and irreversible brain damage. *Caspian J Intern Med* 2015;6:180–3.
- 3 Brent J. Fomepizole for ethylene glycol and methanol poisoning. *N Engl J Med* 2009;360:2216–23.
- 4 Höjer J. Severe metabolic acidosis in the alcoholic: differential diagnosis and management. *Hum Exp Toxicol* 1996;15:482–8.
- 5 Haviv YS, Rubinger D, Zamir E, *et al.* Pseudo-normal osmolal and anion gaps following simultaneous ethanol and methanol ingestion. *Am J Nephrol* 1998;18:436–8.
- 6 Glaser DS. Utility of the serum osmol gap in the diagnosis of methanol or ethylene glycol ingestion. *Ann Emerg Med* 1996;27:343–6.
- 7 Schelling JR, Howard RL, Winter SD, *et al.* Increased osmolal gap in alcoholic ketoacidosis and lactic acidosis. *Ann Intern Med* 1990;113:580–2.
- 8 Davidson DF. Excess osmolal gap in diabetic ketoacidosis explained. *Clin Chem* 1992;38:755–7.
- 9 Krasowski MD, Wilcoxon RM, Miron J. A retrospective analysis of glycol and toxic alcohol ingestion: utility of anion and osmolal gaps. *BMC Clin Pathol* 2012;12:1.
- 10 Jain N, Himanshu D, Verma SP, *et al.* Methanol poisoning: characteristic MRI findings. *Ann Saudi Med* 2013;33:68–9.
- 11 Azeemuddin M, Naqi R. MRI findings in methanol intoxication: a report of three cases. *J Pak Med Assoc* 2012;62:1099–101.
- 12 Thirunavukkarasu S, Nair PP, Wadwekar V. Acute bilateral putaminal haemorrhagic necrosis in methanol poisoning. *BMJ Case Rep* 2013;2013:pil: bcr2013201026. <http://dx.doi.org/10.1136/bcr-2013-201026>
- 13 Galvez-Ruiz A, Elkhamary SM, Asghar N, *et al.* Visual and neurologic sequelae of methanol poisoning in Saudi Arabia. *Saudi Med J* 2015;36:568–74.
- 14 Barceloux DG, Bond GR, Krenzelok EP, *et al.* American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. *J Toxicol Clin Toxicol* 2002;40:415–46.
- 15 Roberts DM, Yates C, Megarbane B, *et al.* Recommendations for the role of extracorporeal treatments in the management of acute methanol poisoning: a systematic review and consensus statement. *Crit Care Med* 2015;43:461–72.
- 16 Sanaei-Zadeh H, Zamani N, Shadnia S. Outcomes of visual disturbances after methanol poisoning. *Clin Toxicol (Phila)* 2011;49:102–7.
- 17 Sivilotti ML, Burns MJ, Aaron CK, *et al.* Reversal of severe methanol-induced visual impairment: no evidence of retinal toxicity due to fomepizole. *J Toxicol Clin Toxicol* 2001;39:627–31.

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