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CASE REPORT

Unintentional diethylene glycol poisoning following the consumption of a shared alcoholic beverage

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ABSTRACT

Diethylene glycol (DEG) is an uncommon cause of toxic alcohol poisoning. In the past, its ingestion in contaminated pharmaceutical products has resulted in mass outbreaks. We describe two isolated cases of unintentional DEG poisoning following the consumption of a shared alcoholic beverage and highlight the challenges that were confronted during the diagnostic work-up and management. Despite appropriate therapy, both cases had fatal outcomes, which emphasises the importance of early recognition of the condition and of instituting specific treatment.

Keywords: Diethylene glycol; poisoning; alcoholic beverage.

INTRODUCTION

Diethylene glycol (DEG) is an uncommon cause of toxic alcohol poisoning that is characterised by a fulminant and often fatal course [1-4]. Numerous epidemics have occurred throughout the world with children frequently affected due to the ingestion of pharmaceutical products in the syrup formulation [1,3-5]. We report on two isolated cases of ingestion of an unknown quantity of a contaminated, locally bottled, alcoholic beverage with characteristic clinical, laboratory and pathological features of DEG poisoning.

CASE 1

A 34-year-old male presented with a 3-day history of feeling unwell, nausea, vomiting and confusion. At the peripheral hospital, he was found to have severe acute kidney injury (AKI) and was transferred to our centre for dialysis support. Due to his obtundation, no history could be obtained, and no collateral history was available at the time. Other than his cognitive impairment, the rest of the clinical examination was unremarkable.

Initial laboratory results revealed a high anion gap (AG) metabolic acidosis without a raised osmolal gap (OG) and severe renal impairment (see Table 1). A lumbar puncture was performed and the cerebrospinal fluid (CSF) was blood-stained but analysis revealed a very high protein concentration of 11.3 g/L.

A diagnosis of severe, unexplained AKI was made and haemodialysis was initiated due to clinical deterioration. A collateral history was eventually obtained from a relative who reported that he was well prior to attending a party 4 days prior to presentation. He had shared an alcoholic beverage with a female friend (case 2), who was also currently admitted to a peripheral hospital with similar findings.

He continued to deteriorate despite dialysis support and died two days later. An autopsy was performed that revealed centrilobular hepatic necrosis and renal cortical necrosis without any calcium oxalate crystals, excluding a diagnosis of ethylene glycol poisoning (EGP).

CASE 2

A 41-year-old female was referred from the same peripheral hospital with complaints of generalised abdo-

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minal pain and diarrhoea. The patient reported that the symptoms had started one week prior to presentation, after sharing an alcoholic beverage with her partner (case 1). She noted that the beverage had tasted sweeter than usual. The gastrointestinal symptoms persisted with a progressive decline in urine volume.

She had HIV and was taking anti-retroviral therapy. There was no history of any pre-existing neurological or kidney disease, nor a history of alcohol dependence or abuse.

Examination revealed that she was afebrile with a heart rate of 102 beats per minute, a blood pressure of 120/90 mmHg and a respiratory rate of 20 breaths per minute. She

Table 1. Serum chemistry, blood gas and cerebrospinal fluid analysis.

Serum chemistry	Reference range	Case 1	Case 2
Sodium	135–147 mmol/L	138	126
Potassium	3.5–5.1 mmol/L	4.2	5.1
Chloride	101–109 mmol/L	60	95
Urea	2.6–7.0 mmol/L	51	38
Creatinine	49–90 µmol/L	1602	1430
Total bilirubin	5–21 µmol/L	9	–
Alanine transaminase	7–35 U/L	666	78
Lipase	13–60 U/L	–	99
Glucose	4.1–5.9 mmol/L	6.4	5.5
Osmolality	275–295 mOsm/kgH_2O	348	324
Osmolal gap	<10 mOsm/kgH_2O	<10	17
Anion gap	7–16 mmol/L	62.4	32.0
Blood gas analysis			
pH	7.36–7.44	7.40	7.30
PaO_2	10.3–13.3 kPa	12.1	17.0
$PaCO_2$	4.7–6.0 kPa	3.2	2.0
Bicarbonate	23–27 mmol/L	15.6	12.0
Lactate	0.5–1.0 mmol/L	2.7	1.4
CSF analysis			
Protein	0.1–0.45 g/L	11.3	15.0
Glucose	2.2–3.9 mmol/L	6.6	4.7
RBC	0 per mm^3	Blood-stained	1408
PMN leucocytes	0 per mm^3	Blood-stained	12
Lymphocytes	0–10 per mm^3	Blood-stained	37
India ink stain	–	Negative	Negative
CLAT	–	Negative	Negative

Abbreviations: CSF, cerebrospinal fluid; RBC, red blood cells; PMN, polymorphonuclear leukocytes; CLAT, cryptococcal latex agglutination test.

was fully orientated with no focal neurological deficits. The remainder of the clinical examination was normal.

Laboratory results revealed a high OG and a high AG metabolic acidosis, AKI and raised hepatic transaminases (see Table 1). Due to her anuria, no specimen was available for urinalysis.

A diagnosis of an unidentified toxic alcohol ingestion was suspected, possibly EGP. She was immediately started on haemodialysis.

Three weeks following her presentation she developed new-onset bulbar palsy together with facial diplegia. She was also noted to have anisocoria, paralysis with reduced reflexes and autonomic dysfunction as evidenced by orthostatic hypotension, tachycardia and urinary retention. A non-contrasted computed tomography scan of the head was normal; however, the lumbar puncture revealed a very high CSF protein concentration of 15 g/L with a pleocytosis. Nerve conduction studies revealed absent motor responses in the lower limbs but with normal responses in the upper limbs.

With the evolution of her neurological deficits a diagnosis of DEG poisoning was made. Six weeks following her initial presentation, she died despite treatment for nosocomial sepsis and continued dialysis support. An autopsy was performed that revealed similar findings to case 1.

DISCUSSION

DEG is an uncommon cause of toxic alcohol poisoning. It is a colourless, odourless liquid with a sweet taste and is used as a solvent for water-insoluble chemicals. It is metabolised, in a similar fashion to other toxic alcohols, by the liver into its end-product of 2-hydroxyethoxyacetic acid (2-HEAA) with eventual renal elimination. This end-product is thought to be responsible for the renal and nervous system toxicity [6,7].

The last documented outbreak in South Africa was reported in 1972 involving 7 children treated with over-the-counter medications, Pronap and Plaxim [1]. During contemporary times, it tends to occur in developing countries with poor quality control measures, where DEG is used during the drug manufacturing process instead of more expensive, less toxic glycols such as propylene glycol [4,7].

Three distinct clinical phases of DEG poisoning have been reported, namely: phase 1 – early neurological and gastrointestinal symptoms; phase 2 – severe kidney failure and liver toxicity; and finally, phase 3 – neurological sequelae may evolve if the patient survives the phase 2 [4,8]. Case 2 demonstrated all three phases. Gastrointestinal symptoms include abdominal pain, nausea, vomiting and diarrhoea. These symptoms may have a delayed onset if the liquid is co-ingested with a significant quantity of ethanol. This may explain the late presentation of both our cases.

Phase 2 usually follows 1–3 days after ingestion and its inception is marked by the onset of AKI with eventual anuria due to renal cortical necrosis. Moderate elevations of hepatic transaminases usually accompany the renal injury. Severe AKI and a mild hepatitis were present in case 2. Of note was the normal venous lactate concentration on a point-of-care blood gas analysis. While ethylene glycol poisoning (EGP) may produce similar features, the normal serum lactate, which is falsely elevated in EGP when measured using the enzymatic method [9,10], as well as the mild hepatitis, were initial clues of an alternative toxic alcohol ingestion [8,11]. Also, autopsy findings were identical to the cases described previously in South Africa [1] with the absence of calcium oxalate deposits in parenchymal tissue, normally seen in EGP, excluding this latter diagnosis.

The development of neurological deficits marks the onset of the final phase. This phase occurs 5–10 days after ingestion. The peripheral nervous system is predominantly affected with involvement of cranial nerves that presents with symptoms and signs of diplopia, facial diplegia and bulbar palsy. Peripheral neuropathies of the upper and/or lower limbs may result in quadri- and paraparesis. Case 2 demonstrated most of these neurological features. These findings are rare in other toxic alcohol poisonings [4,5,11].

The offending alcoholic beverage was never recovered to confirm DEG contamination. Although alcoholic beverages have been reported to be contaminated with DEG, cough mixtures, acetaminophen syrup and sedatives are most frequently seen with mass outbreaks [4,5]. Contamination of these pharmaceutical products resulted in epidemics of DEG poisoning. As it usually does not occur in isolation, a high clinical index of suspicion should be maintained when multiple cases present with inebriation together with gastrointestinal upset, followed by the rapid development of AKI.

Direct measurements of blood toxic alcohol levels are frequently not available; however, a raised serum OG (difference between the measured and calculated serum osmolality) is the first step to early diagnosis. As was seen in our second case, a mild OG was still present a few days following ingestion. However, compared to other toxic alcohols, DEG poisoning is least likely to increase the serum OG and can frequently be normal at first presentation [4,8]. The median OG in one outbreak was reported to be only 7.6 mOsm/kg [5]. When freezing-point depression is used to measure serum osmolality, high molecular

weight substances will have a lower serum osmolality per unit concentration. As DEG consists of two ethylene glycol molecules linked together by an ether bond, it has a higher molecular weight relative to other toxic alcohols and therefore the OG may be normal or only modestly raised as in our second case. Another diagnostic clue to DEG poisoning is a severely elevated CSF protein concentration as was found in both of our cases. The Panama epidemic of 2006 reported that the CSF protein concentration ranged from 0.39–5.17 g/L without any pleocytosis [5].

Other than supportive care such as the administration of sodium bicarbonate for severe metabolic acidosis, benzodiazepines for seizures and intravenous fluids with or without vasopressor support, the aim of therapy is directed at reducing the conversion of DEG into its toxic metabolite, 2-HEAA. This is achieved by the administration of either fomepizole or ethanol, which acts as an inhibitor or competitive substrate for the enzyme, alcohol dehydrogenase, respectively [4]. The presence of an OG implies that the toxic alcohol is still present and therefore the administration of the latter drugs may still be of benefit in preventing its conversion to 2-HEAA. Since fomepizole is not available in SA, ethanol should be used. Elimination of DEG and 2-HEAA can be achieved with haemodialysis or haemodiafiltration. As with our cases, this is the only option available when patients present late with established renal failure and anuria.

Even with the best supportive care, the overall prognosis of DEG poisoning is poor. Until 2008, a total of 5/13 documented outbreaks reported 100% mortality [5]. A lethal dose of DEG is ~1 ml/kg [4]. We suspect that the delayed presentation to hospital contributed largely to the eventual death of our cases. Those that require dialysis and survive inevitably become dialysis dependent and may have permanent neurological complications.

CONCLUSIONS

DEG is an uncommon cause of toxic alcohol poisoning and is usually associated with mass outbreaks. Hallmark clinical features include severe, oligo-anuric acute kidney injury together with a mild hepatitis and eventually severe peripheral neuropathies. Early diagnosis and initiation of therapy may improve survival; however, mortality remains high. A continued search for the root cause of contaminated products is mandatory to prevent larger outbreaks.

Ethics approval

This case report was approved by the Human Research Ethics Committee (HREC) of Stellenbosch University (HREC reference number C17/12/019).

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REFERENCES

1. Bowie MD, McKenzie D. Diethylene glycol poisoning in children. S Afr Med J. 1972; 46(27):931-934.
2. Cantarell M, Fort J, Camps J, Sans M, Piera L, Rodamilans M. Acute intoxication due to topical application of diethylene glycol. Ann Intern Med. 1987; 106(3):478-479.
3. Singh J, Dutta A, Khare S, Dubey N, Harit A, Jain N, Wadhwa T, Gupta S, Dhariwal A, Jain D. Diethylene glycol poisoning in Gurgaon, India, 1998. Bull World Health Organ. 2001; 79(2):88-95.
4. Schep LJ, Slaughter RJ, Temple WA, Beasley DMG. Diethylene glycol poisoning. Clin Toxicol. 2009; 47(6):525-535.
5. Sosa NR, Rodriguez GM, Schier JG, Sejvar JJ. Clinical, laboratory, diagnostic, and histopathologic features of diethylene glycol poisoning – Panama, 2006. Ann Emerg Med. 2014; 64(1):38-47.
6. Heilmair R, Lenk W, Löhr D. Toxicokinetics of diethylene glycol (DEG) in the rat. Arch Toxicol. 1993; 67(10):655-666.
7. Schier J, Hunt D, Perala A, McMartin K, Bartels M, Lewis L, McGeehin M, Flanders W. Characterizing concentrations of diethylene glycol and suspected metabolites in human serum, urine, and cerebrospinal fluid samples from the Panama DEG mass poisoning. Clin Toxicol. 2013; 51(10):923-929.
8. Kraut JA, Kurtz I. Toxic alcohol ingestions: clinical features, diagnosis, and management. Clin J Am Soc Nephrol. 2008; 3(1):208-225.
9. Morgan TJ, Clark C, Clague A. Artifactual elevation of measured plasma L-lactate concentration in the presence of glycolate. Crit Care Med. 1999; 27(10):2177-2179.
10. Verelst S, Vermeersch P, Desmet K. Ethylene glycol poisoning presenting with a falsely elevated lactate level. Clin Toxicol. 2009; 47(3):236-238.
11. Morelle J, Kanaan N, Hantson P. Cranial nerve palsy and acute renal failure after a 'special drink'. Kidney Int. 2010; 77(6):559-560.