CASE REPORT

Dilemma in the management of methanol poisoning at a district hospital in Malaysia

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SUMMARY

There are increasing reports of methanol poisoning (MP) incidence worldwide. In Malaysia, the largest first methanol poisoning was reported in Selangor in 2013 with a total of 41 patients and cluster of cases been reported from the country since then. Often MP involved adulterated alcohol containing more than the legal permissible concentration of methanol. Methanol is rapidly absorbed and metabolised into formic acid which causes variable symptoms of the central nervous system such as blindness, seizure, coma and gastrointestinal disturbances. Mortality could reach up to 83% as reported using the coma state, pH and pCO_2 level in the worst-case scenario.

INTRODUCTION

The occurrence of methanol poisoning (MP) is usually accidental (unintentional) and much smaller percentage of cases being intentional. Clusters or outbreaks occur when it is mistakenly substituted for ethanol or when methanol contaminants are used to ferment (e.g., wine) or illicitly distilled (moonshine whisky) alcoholic beverages. In such circumstances, hundreds of victims of MP have been reported. In recent years in the developing countries, both medical journals and the news media have identified MP as a frequent problem. Such reports have resulted in the involvement of a large non-governmental organisations and the World Health Organization had identified this as a global problem.[1] In Malaysia, a total of 86 cases of MP had been notified up till September 2018 with 29 deaths. Clusters of cases continue to re-emerge especially among foreign labourers who sought-after cheaper alcohol and they often present to hospital late due to unrecognised symptoms. To make matters worse, the presentations of MP fit into many differential diagnoses which could result in late or wrong treatment administered. In our three cases, two patients died due to their severity of illness. We report the first outbreak of methanol poisoning in the District of Batu Pahat, Johor, Malaysia involving foreign labourers who presented along with the challenges and limitations we faced.

CASE DESCRIPTION

Case 1

A 26-year-old male Nepalese worker presented with severe epigastric pain and visual disturbances after consuming[11] cans of 'Milu deer' beer. He was hemodynamically unstable with severe high anionic gap metabolic acidosis (Table I), hence was promptly ventilated. He made an uneventful recovery the next day after dialysis with complete resolution of the anionic gap and acidosis.

Case 2

A 34-year-old male Nepalese worker presented with abdominal pain, vomiting and blurring of vision. At presentation, his Glasgow Coma Scale (GCS) was 9 (E4 V2 M3), pupils were dilated and unequal. His vital signs were 141/90mmHg, pulse rate 86 beats per minute, respiratory rate of 14 breaths per minute, and temperature of 36.4°C. The working diagnosis was a case of suspected methanol poisoning as he had consumed 5 cans of tainted "Milu deer" beer prior to development of his symptoms. Computed tomography of the brain was not done as he became unstable. Unfortunately, he went into cardiorespiratory arrest due to severe metabolic acidosis (Table I).

Case 3

A 35–year-old aboriginal Malaysian male presented with sudden painless bilateral vision loss associated nausea and abdominal pain. His condition deteriorated quickly, and he required mechanical ventilation because of the respiratory distress but went into cardiorespiratory arrest due to severe metabolic acidosis (Table I). He returned to spontaneous circulation after 5 minutes of resuscitation. The severe metabolic acidosis with a wide anionic gap (31mmol/L) was due to consumption of 5 cans of "Bieremark' beer one day before presentation. There were persistent neurological deficits despite improvement in the other laboratory parameters. A computed tomography of the brain showed putaminal necrosis (Figure 1 and 2). He eventually succumbed to pneumonia 12 days after his initial presentation.

In case 1 and 2, fomepizole was not administered as it was unavailable in our centre. In the three cases discussed above, treatments were given promptly with a loading dose of oral ethanol 20% along with maintenance until the resolution of the wide anion gap acidosis. Intravenous fomepizole was obtained from nearby tertiary centre for case 3 and a loading dose of 15mg per kilogram was administered followed by 600mg 4 hourly (during dialysis) and subsequently 12 hourly (upon completion of dialysis). All three

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Table I: Laboratory results

	Case 1			Case 2			Case 3		
	Day 1	Post SLED	Day 2	Day 1	Post SLED	Day 2	Day 1	Post SLED	Day 2
Hb (g/L)	19.2		13.9	16.1		15	17.9		15.3
TWC (10^9/L)	25		11.3	24.33		20	26.4		16.8
Platelet (10^9/L)	374		171	501		490	339		391
Urea (mmol/L)	11.6	7	5.3	5.6	5	6	8.2	8	7
Creatinine (umol/L)	151	105	54	174	150	160	117	105	61
Sodium (mmol/L)	135	135	140	134	145	142	138	146	130
Potassium(mmol/L)	5.1	3.1	3	3.5	2.8	3.5	3.4	3.0	4.7
Chloride (mmol/L)	94	103	100	102	101	104	95	105	101
Anionic gap	43.4	13.1	22	31.9	30.9	20.2	45	19.7	8.7
Osmolar gap									
pH	7.054	7.33	7.361	6.712	7.041	6.899	6.71	7.35	7.42
pCO2 (mmHg)	10	41.6	36.8	30.2	58.7	109.1	12.0	43.6	39.4
pO2 (mmHg)	153	241	51.8	160.9	58.3	66.3	225.4	187	135
HCO3 (mmol/L)	2.7	22	21	3.6	15.9	21.3	1.4	24.3	25
Base Excess	-25.5	-3.5	-3.4		-16.7	-17.1	-26	-3.0	-1.9
ALT	109	24	26	36	34	32	57	49	26
ALP	55			176			20		
Blood Methanol (mg/dL)	30			31			36		
Blood Ethanol	Absent			Absent			Absent		
Urine Methanol (mg/dL)	50			51			52		
Urine Ethanol	Absent			Absent			Absent		

SLED: Sustained low efficiency dialysis.

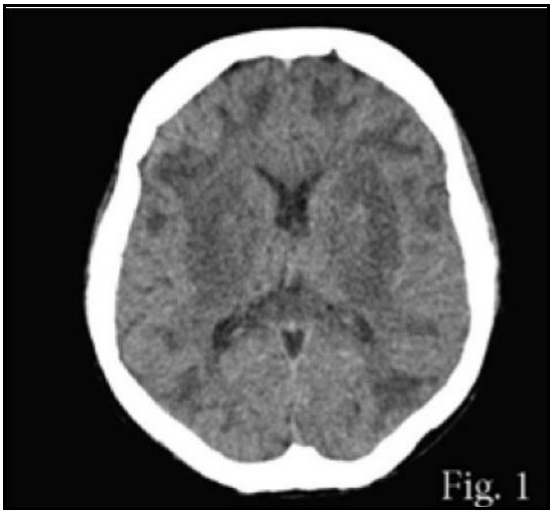

Fig. 1: Plain CT brain showing bilateral symmetrical low attenuation at both putamen selective of putaminal necrosis with high attenuation at bilateral putaminal foci (attenuation ranging from 50 to 55 HU) due to putaminal haemorrhage.

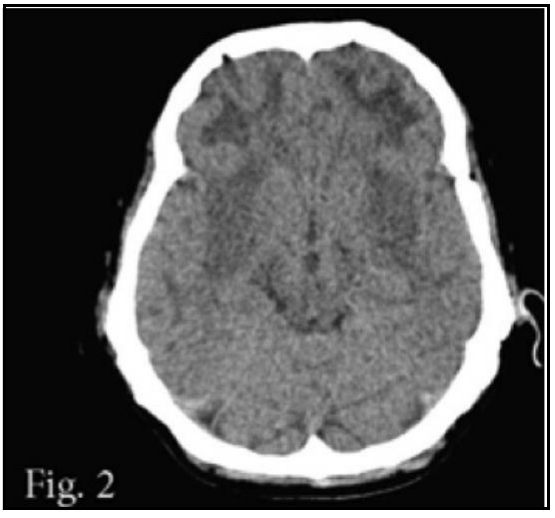

Fig. 2: There is diffuse bilateral subcortical white matter hypo-densities in bilateral frontal and parietal regions.

patients were started on free heparin, sustained low efficiency dialysis (SLED) with a high flux membrane. Other treatments included folinic acid, thiamine, pyridoxine and sodium bicarbonate.

DISCUSSION

Methanol is metabolised by alcohol dehydrogenase to formaldehyde and later to formic acid which leads to metabolic acidosis.[1] Formic acid is responsible for the effects of MP. Folates, including folic acid and leucovorin acts at the final step of methanol elimination by accelerating conversion of formic acid to carbon dioxide and water.[2-3] Often the first dose is usually administered before haemodialysis, and the second dose should be administered at the completion of haemodialysis because this highly water-soluble vitamin would have been eliminated.[2-3]

The treatment of MP includes inhibition of ADH, enhancing elimination of formate and early haemodialysis.[1] The competitive substrate ethanol is commonly administered to prevent methanol metabolism in the body.[2-3] Although fomepizole is costlier than ethanol, it is safer and easier to be delivered especially outside the intensive care unit setting. Ethanol may be preferred in a mass casualty situation or until fomepizole stock is procured. The need for haemodialysis is based on the presence of toxic metabolites which is inferred by the presence of metabolic acidosis.[3]

J. Md Noor et. al (2020) reported suboptimal laboratory support in a local tertiary centre in providing timely serum methanol, ethanol and formic acid results.[4] Serum methanol and ethanol tests are currently conducted at the National Toxicology Laboratory Center in Hospital Sungai Buloh, Selangor, Malaysia and results are made available after 24 to 48 hours. Due to the delay in obtaining the results from the laboratory, most of the cases reported to smaller hospitals are diagnosed clinically.[4]

Often the availability of fomepizole pose a problem due to a higher cost. Fomepizole appears safer and although being more costly than ethanol, has the advantage of easier delivery especially outside the ICU.[4-5] Jeffrey Brent et al., reported in a multicentre prospective trial that fomepizole is a safer and more effective treatment for MP.[5] There was a significant reduction in plasma formic acid concentrations in all patients after the administration of fomepizole. In general, the management of MP includes assessing and securing the airway, breathing and circulation monitoring and mechanical ventilation if required in severe intoxicated cases.[5] A consultation with a medical toxicologist would be beneficial given that such poisoning occurs infrequently. A comprehensive urine toxicology screening should be performed.[5] More vigilant public health education on MP should be conducted. Notification forms on MP should be introduced to speed up the control of outbreaks.

CONCLUSION

Based on our three case vignettes described above, the authors encountered difficulties in acquiring urgent toxicology results. This is a common limitation faced by many hospitals especially in the district settings. A clinical history of adulterated alcohol ingestion along with metabolic acidosis should alert the clinician on possible MP. In dire situations, fomepizole therapy should be initiated immediately without waiting for the toxicology results.[5]

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INFORMED CONSENT

Written informed consent (including images, case history and data) was obtained from the patient/guardian for publication of this paper, including accompanying figures.

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