An Illustrated Forensic Pathology Case: Bilateral Putaminal Hemorrhages After Methanol Ingestion

Blumenthal, Ryan MBChB (Pret), MMed (Med Forens)(Pret), Dip For Med (SA), FC For Path(SA), PhD(Wits)*Barbara Roth, Lisa MD†

*Department of Forensic Medicine, University of Pretoria, Pretoria, South Africa

†Ludwig-Maximilians-Universität Munich, Munich, Germany.

The authors report no conflict of interest.

Correspondence to: Ryan Blumenthal, Department of Forensic Medicine, University of Pretoria, Rm 4-44, Pathology Bldg, 5 Bophelo Rd, Prinshof South Campus, 0084, Corner of Steve Biko and dr Savage Rd, Pretoria, Gauteng, South Africa.
E-mail: ryan.blumenthal@up.ac.za.

CASE HISTORY

A 45-year-old African man presented himself to the regional hospital's emergency department with complaints of acute onset of vomiting and confusion. According to the available history, he had ingested methylated spirits (Fig. 1). A formal meeting with his sister presented us with information that he had a history of chronic ethanol use. Because of COVID-19 restrictions at the time, in which there was a statutory ban on the sale of ethanol, many people took to brewing and procuring their own ethanol, and it was in this context that he drank the methylated spirits.

FIGURE 1. The warning label on the back of the 750 ml bottle of Methylated Spirits.

He had arrived in an encephalopathic state, and his condition deteriorated. It was decided to turn off the ventilator the following day. This was deemed an unnatural death, and a medicolegal autopsy was arranged in accordance with the national regulations. The medicolegal autopsy took place the day after his death.

AUTOPSY FINDINGS

An adult Black man had no fatal external injuries to the body. The brain was pale and weighed 1386 g. Serial sections of the brain showed bilateral globus pallidus lesions (Fig. 2). These acute hemorrhages were confirmed on histology (Fig. 3). No other significant findings were identified at autopsy.

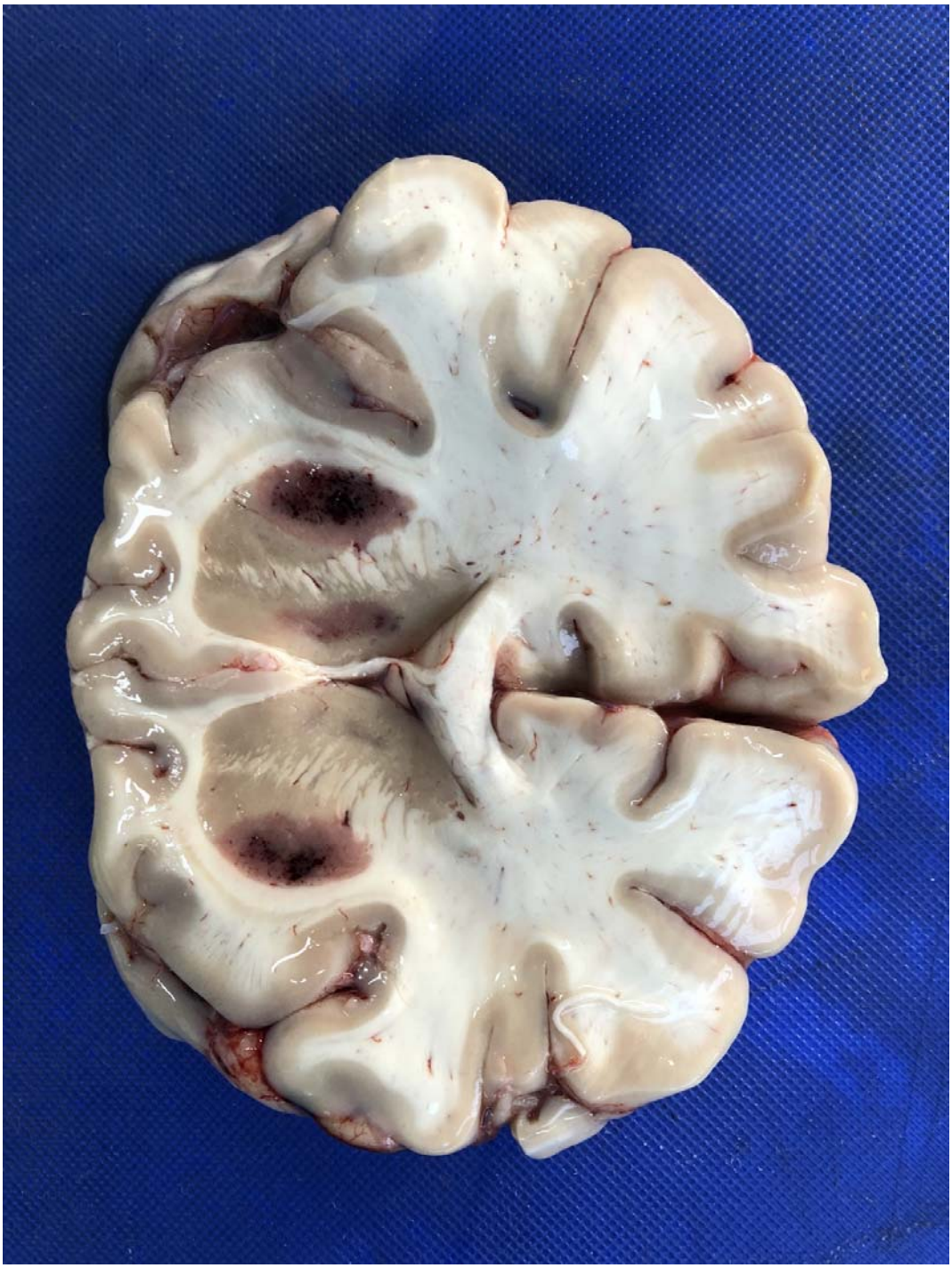

FIGURE 2. Fresh bilateral putaminal hemorrhages.

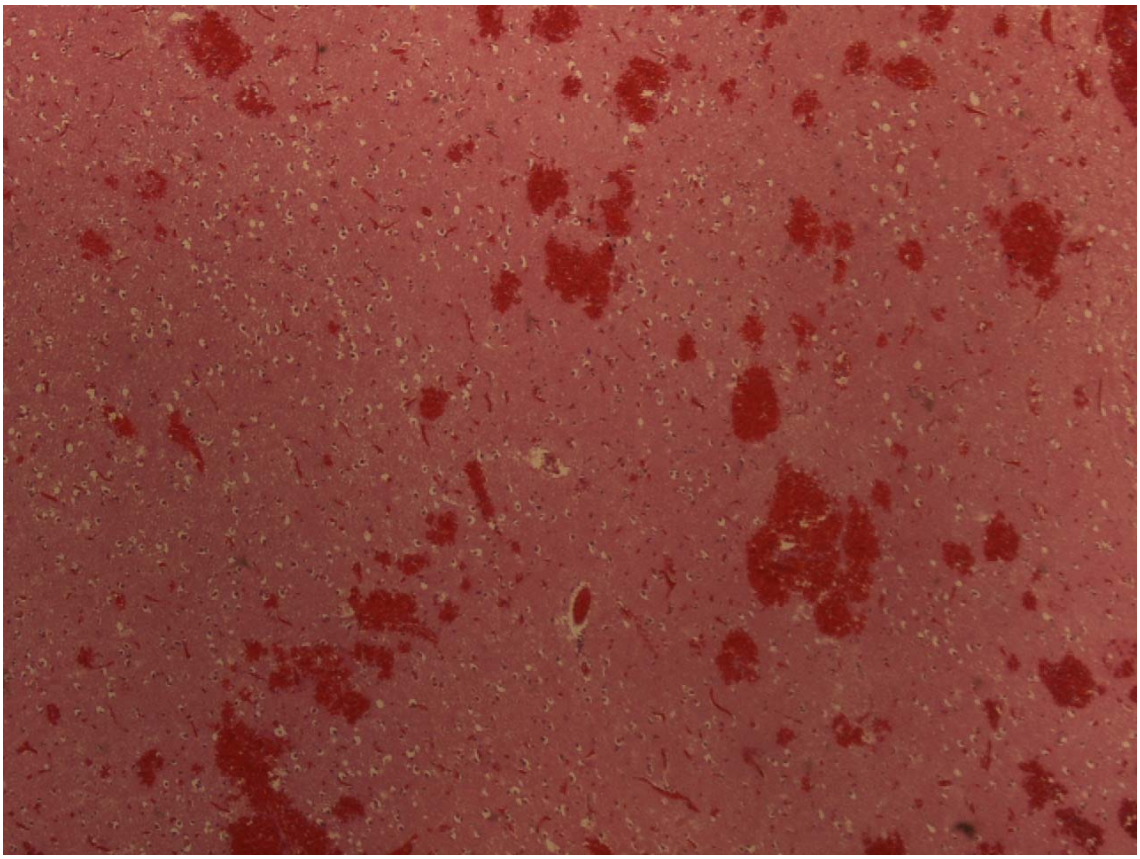

FIGURE 3. Histological demonstration of the fresh putaminal haemorrhages. Peri-cellular and peri-vascular open spaces in the background are suggestive of associated oedema.

DISCUSSION

Methylated spirits is a denatured alcohol, also known as "wood alcohol" or "Columbian spirits." It is a multifunctional cleaning agent typically used for household purposes.[1,2] It mainly contains pure ethanol, although it may be made unpalatable by mixing it with other, often toxic chemicals, to prevent recreational abuse. Traditionally, methanol was used to make the violet-colored fluid bitter. Nowadays, other additives, including Bitrex, isopropyl alcohol, acetone, methyl ethyl ketone, and methyl isobutyl ketone, are typically used.[1–4] Multiple reports of methanol poisoning have been published.[3,5–7] Although initial symptoms are typically caused by methanol itself, the long-term effects are mainly caused by its metabolites.[2] Once methanol is consumed and has reached the organs, it is converted into formaldehyde via the enzyme alcohol dehydrogenase. Formaldehyde dehydrogenase quickly metabolizes formaldehyde into formic acid. Eventually, formic acid will be transformed into carbon dioxide and water. This last reaction is rather slow, which leads to an accumulation of formic acid.[7,8] Formic acid is toxic to humans, and it blocks mitochondrial oxidase systems, for example, cytochrome C, which leads to tissue hypoxia. This explains the symptom of metabolic acidosis, caused by high lactic acid levels due to anaerobic glycolysis.[1] Metabolic acidosis, combined with an elevated anion gap, is a strong sign of methanol poisoning (Fig. 4).[7]

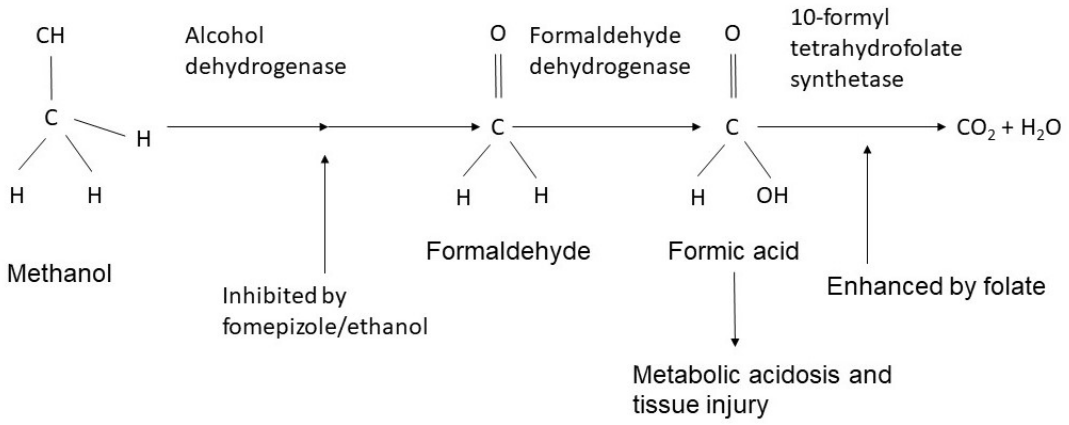

FIGURE 4. Metabolism of methanol to formic acid. Oxidation of methanol to formaldehyde by alcohol dehydrogenase is the rate limiting step in the metabolism of methanol that is inhibited by fomepizole. Administration of folic acid enhances catabolism of formic acid to carbon dioxide and water by 10-tetrahydrofolate synthetase. (Courtesy of Nazir S, et al. BMJ Case Rep 2016. doi:10.1136/bcr-2015-214272).

The electrocardiogram may show sinus tachycardia or nonspecific T-wave changes.[9] A computed tomography scan, possibly normal at the onset of symptoms, may later show characteristic bilateral putaminal necrosis, associated with hemorrhage, and signs of brain edema.[2,10]The combination of visual damage and bilateral putaminal necrosis is pathognomonic of methanol intoxication. Bilateral putaminal lesions combined with visual symptoms are unique to methanol.[5] Because of the lesions in the basal ganglia, survivors may show signs of Parkinson syndrome.[2] The symptoms and survival time are determined by the amount of methanol in the serum.[3,10,11] Methanol causes destruction of myelin in the optic nerve leading to permanent visual sequelae.[1] Interestingly, our patient did not report any visual disturbances.There are multiple hypotheses as to why specifically the putamen is affected by methanol poisoning whereas other structures of the basal ganglia stay intact. One hypothesis suggests that phylogenetically older neurons, for example, in the globus pallidus, are more resistant than the newer brain areas such as the putamen. Another hypothesis states that putaminal neurons may show a higher sensitivity to acidic environments; therefore, these are more affected by formic acid than other structures of gray matter.[12,13]Bilateral basal ganglia lesions may also be seen in carbon monoxide poisoning, ethylene glycol poisoning, hepatic encephalopathy, viral encephalitis, cocaine abuse, amphetamine abuse, Wilson disease, or Hallervorden Spatz disease (http://links.lww.com/FMP/A38).[2,5,14–16]

ACKNOWLEDGMENT

The authors thank the next-of-kin for providing their consent. The authors also thank the South African Police Services and the Director of Public Prosecutions for their assistance and the Research Ethics Committee, Faculty of Health Sciences, University of Pretoria (Ethics Reference No. 376/2020).

REFERENCES

1 Ran M. Clinical features, treatment, and prognosis of acute methanol poisoning: experiences in an outbreak. **Int J Clin Exp Med**. 2019;12(5):5938–5950

2 Comoğlu S, Özen B, Ozbakir S. Methanol intoxication with bilateral basal ganglia infarct. **Australas Radiol**. 2001;45:357–358.

3 Suit PF, Estes ML. Methanol intoxication: clinical features and differential diagnosis. **Cleve Clin J Med**. 1997;57(5):464–471.

4 Schwär TG, Loubser JD, Olivier JA. The Forensic ABC in Medical Practice. A Practical Guide. **Haum Educational Publishers**. Pretoria, South Africa; 1988;349.

5 Singh P, Paliwal VK, Neyaz Z, et al. Methanol toxicity presenting as haemorrhagic putaminal necrosis and optic atrophy. **Pract Neurol**. 2013;13:204–205.

6 AbdulRahim F, Shiekh A. Substance abuse and homelessness: mass methanol poisoning in Khartoum. **Sudan Med J**. 2012;48(1):1–6.

7 Nazir S, Melnick S, Ansari S, et al. Mind the gap: a case of severe methanol intoxication. **BMJ Case Rep**. 2016;2016:bcr2015214272.

8 Finkelstein Y, Vardi J. Progressive parkinsonism in a young experimental physicist following long-term exposure to methanol. **Neurotoxicology**. 2002;23(4–5):521–525

9 Jaff Z, McIntyre WF, Yazdan-Ashoori P, et al. Impact of methanol intoxication on the human electrocardiogram. **Cardiol J**. 2014;21(2):170–175.

10 Coulter CV, Farquhar SE, McSherry CM, et al. Methanol and ethylene glycol acute poisonings - predictors of mortality. **Clin Toxicol (Phila)**. 2011;49(10):900–906.

11 Karayel F, Turan AA, Sav A, et al. Methanol intoxication: pathological changes of central nervous system (17 cases). **Am J Forensic Med Pathol**. 2010;31(1).

12 Hawker K, Lang AE. Hypoxic-ischemic damage of the basal ganglia. **Mov Disord**. 1990;5(3):219–224

13 Gutierrez LG, Rovira A, Portela LA, et al. CT and MR in non-neonatal hypoxic-ischemic encephalopathy: radiological findings with pathophysiological correlations. **Neuroradiology**. 2010;52:949–976.

14 Yarid NA, Harruff RC. Globus pallidus necrosis unrelated to carbon monoxide poisoning: retrospective analysis of 27 cases of basal ganglia necrosis. **J Forensic Sci**. 2015;60(6):1484–1487.

15 Kim HJ, Na JY, Lee YJ, et al. An autopsy case of methanol induced intracranial hemorrhage. **Int J Clin Exp Pathol**. 2015;8(10):13643–13646.

16 Penndorf-Wehner F, Grunert JH, Hendrickx P. Methanolvergiftung mit doppelseitiger Nekrose des Putamens und zusätzlicher Beteiligung des Globus pallidus. **Rofo**. 1997;167(1):99–100.