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Case Report

Delayed Death Due to Methanol Poisoning: An Autopsy Case Report

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ABSTRACT

Methanol is a non-drinking type of alcohol used for industrial and automotive purposes. Methanol itself is not dangerous, but its harmful metabolites may cause the accumulation of acid in the blood, leading to metabolic acidosis, permanent blindness, and death. In this case report study, the case was a 28-year-old Nepalese man who was admitted in a semi-unconscious state to the emergency department. A working diagnosis of methanol poisoning was made. After more than two weeks, he succumbed to death due to a worsening cerebral infarction. At autopsy, extensive hemorrhagic infarction was observed, involving bilateral cerebral hemispheres. Well-defined subcortical hemorrhages leading to laminar necrosis were seen at the frontoparietal lobes. Cystic or lacunar necrosis was present at the basal ganglia. The brainstem showed the presence of duret hemorrhage. The man died approximately three weeks after the methanol ingestion. This case highlights the important pathological changes and accumulating effects of methanol in the brain.

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1. Introduction

Methanol or methyl alcohol is a volatile, colourless and flammable liquid with a distinctive odour that is slightly sweeter than ethanol [1]. It is used widely as a solvent in many industries [2, 3]. Methanol poisoning is rare and usually associated with accidental ingestion or suicidal intention [4, 5]. The lethal concentration in blood is 0.04 g/dL, and 15 mL of 40% methanol has been reported as the smallest amount to cause death [3]. Methanol is rapidly metabolised into formaldehyde and subsequently formic acid, which is highly toxic, causing central nervous system depression, metabolic acidosis, loss of vision, and involvement of other organs [1, 2, 4]. Methanol poisoning is characteristic based on the findings of magnetic resonance imaging (MRI), which include hemorrhagic putaminal necrosis, subcortical, and deep white matter lesions [1]. In this case report, we aimed to demonstrate the accumulative toxic effects of methanol in the brain which ultimately caused death.

2. Case Presentation

The case was a 28-year-old Nepalese man who had alcoholic drinking at a party in mid-September 2018. Two days later, he started to have abdominal pain and frequent vomiting, associated with lethargy and general feeling of being unwell. The following day, he visited a clinic, where he was prescribed with painkillers. Later, his friends noticed that he was drowsy and very ill; hence, they brought him to a hospital immediately. At the Emergency Department (ED), it was reported that his pupils were dilated and had Kussmaul breathing. He was sedated and intubated immediately. Subsequent blood assessment showed a full blood count, hemoglobin=18.6 g/dL (reference range: 12.5-18.5 g/dL), white blood cell=19.4×10^9 ($4\text{-}10\times10^9$), platelet=339×10^9 (reference range: $150\text{-}410\times10^9$), hematocrit=56.6% (reference range: 40-50 %), and random blood glucose=7.8 mmol/L (reference range: 7.8-11.1 mmol/L). Based on the vital signs chart, body temperature was 37°C, pulse rate was 112/minute, respiration rate was 19/minute, and blood pressure was 127/80 mmHg. Blood parameters obtained from arterial blood gases were as following: pH=6.734 (reference range: 7.35-7.45), PO_2=341 mmHg (reference range: 72-103 mmHg), PCO_2=48.8 mmHg (reference range: 35-48 mm/Hg), HCO_3=6.1 mmol/L (reference range: 21–29 mmol/L), base excess=-25.7 (reference range: -7 to 2). The provisional diagnosis was high anion gap metabolic acidosis secondary to methanol poisoning. He was transferred to the intensive care unit (ICU) and treated with an ethanol infusion. One day after the hospital admission, a computed tomography (CT) scan of the brain was done. It was reported that he had normal CT scan. Three days later, MRI was performed, revealing bilateral symmetrical diffuse leukoencephalopathy, necrosis of deep gray matter with relative preservation of cortical gray matter. Subsequent brain CT scan showed worsening cerebral edema and necrosis, with bilateral optic neuropathy. His condition deteriorated, and he finally succumbed to the cerebral hemorrhage 16 days after admission to the ED. The body was sent to the Forensic Department for a medicolegal autopsy examination. Prior to autopsy, further medical history was obtained. The deceased was a healthy, young immigrant with no history of illness or hospital admission.

3. Results

Autopsy findings

The deceased was a well-nourished, muscular adult male with 162-cm height and 76-kg weight. Upon internal examination, the brain showed marked cerebral edema. The liver was enlarged, weighing 1360 g, with generalized fatty changes of the parenchyma. The heart was normal. The right and left lungs weighed 440 and 385 g, respectively. Cut surfaces of the lungs, spleen, and kidneys showed congested blood vessels. Cut surfaces of the fixed brain specimen revealed extensive hemorrhage infarction involving bilateral cerebral hemispheres, from frontal to the occipital lobes. Well-defined, subcortical hemorrhages leading to laminar necrosis was seen at the parietal lobes, bilaterally. Cystic or lacunar necrosis were also present at the basal ganglia, bilaterally (Figure 1a). The white mater showed softening of the parenchyma along with infarction (Figure 1b). Duret hemorrhage was present in the brainstem, mostly prominent in pons (Figure 1c). The cerebellum showed tonsillar herniation.

Histopathology findings

Representative tissue samples from the brain, heart, lungs, liver, kidneys, and spleen were obtained for microscopy examination. Sections of the brain showed extensive areas of hemorrhage and necrosis of the parenchyma. In the areas with necrosis, the parenchyma was completely replaced by numerous reactive microglial cells (Figure 2a). Within and adjacent to these necrotic areas, the blood vessels were mostly congested and some were thickened with mild to moderate degenerative changes. There was also infiltration, mainly by microglia, within the blood vessels layers. The areas of necrosis had very minimal lymphocytes or neutrophilic infiltrates. The surrounding area had edema, extensive gliosis with fibrosis, and microglial cell infiltration. Further immunohistochemical staining using glial fibrillary acidic protein (GFAP) showed discernible amount of neurofilament protein loss and degeneration (Figure 2b). The viable neuronal tis-

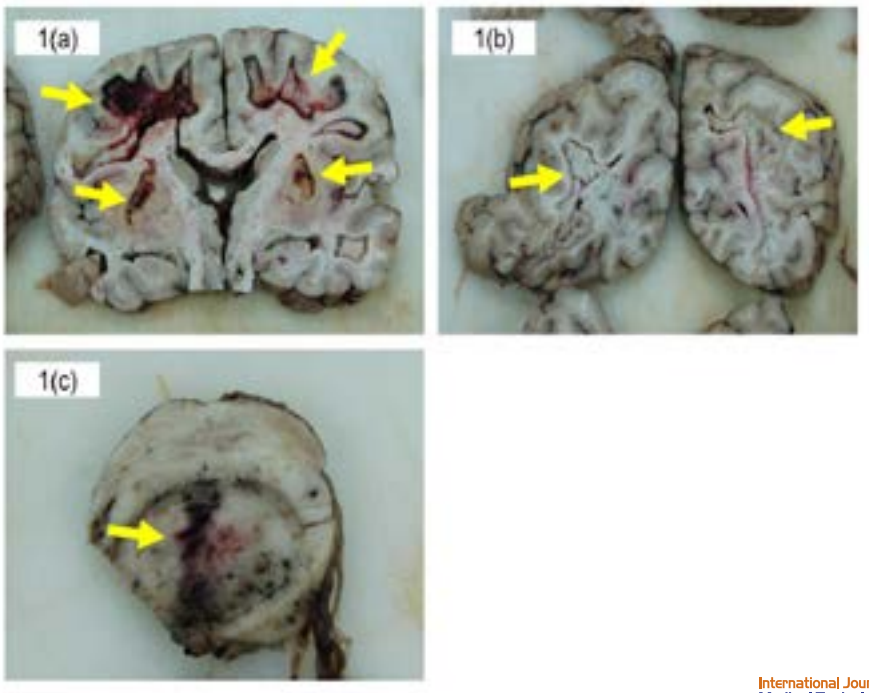

Figure 1. Autopsy findings

a) The frontoparietal lobes showing subcortical bilateral hemorrhage infarction and lacunar infarction in the basal ganglia (yellow arrows), b) Deep white matter infarction of bilateral occipital lobes (yellow arrows), c) Duret hemorrhage of the brainstem (yellow arrow)

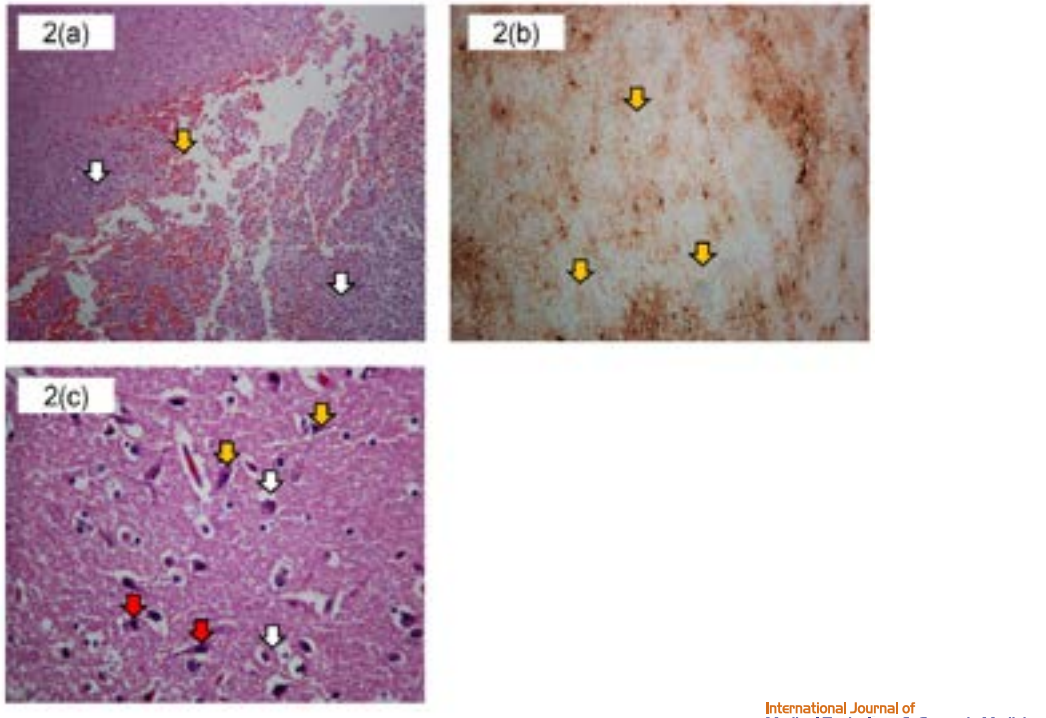

Figure 2. Histopathology findings

a) Reactive microglial cells (white arrows) at the necrotic and hemorrhagic parenchymal area (yellow arrows), b) Lack of neurofilaments fibre at the central area, with glial cell loss that is supposed to be stained by GFAP (yellow arrows), c) Neuronal degeneration changes in vacuolar (white arrows) and eosinophilic cytoplasm (yellow arrows) with many pyknotic nuclei (red arrows)

sue had abundant red cell necrosis with pyknotic nuclei and eosinophilic cytoplasm (Figure 2c). There was also pallor and swelling of the cell bodies. Proliferation of the astrocytes were also observed, and some appeared to be gemistocytic. Sections of the lungs, heart, kidney, spleen and liver showed vascular congestion.

Laboratory findings

Serial blood samples were collected during the ICU admission and were sent for alcohol analysis. Unfortunately, the first blood sample was obtained five days after the admission. Methanol was not detected in the first or subsequent samples. At autopsy, we obtained blood, vitreous humor, urine, gastric content, and bile for toxicology analyses in the forensic laboratory and a reference laboratory. Methanol was also absent from all five post-mortem samples. According to history records, autopsy findings, and microscopy examination, the cause of death was concluded to be hemorrhagic cerebral infarction secondary to methanol poisoning.

4. Discussion

Methanol is not protein-bound and is absorbed rapidly via the gastrointestinal tract in less than 10 minutes. Methanol itself is relatively nontoxic; however, its metabolite and formic acid is much more toxic, because it easily invades cells, inhibits cytochrome c oxidase, and affects aerobic metabolism, inducing acidosis [6]. Clinical manifestations including abdominal pain, nausea, vomiting, and drowsiness may begin several hours after the ingestion; however, when adulterated alcohol is the culprit, a latent period of 12-24 hours may take place. Manifestations of decompensated metabolic acidosis with accompanying worsening cardinal symptoms occur after the latency period [5]. In our case, the authors suggest that the late onset of symptoms could be attributed to the latency period, as the victim had unknowingly ingested the contaminated alcoholic drink at the party.

In the central nervous system, acute methanol poisoning leads to global cerebral hypoxic injury and edema. In severe cases, it may cause widespread necrosis and hemorrhage [7-9]. Anderson et al. postulated that the brain is the most susceptible organ to injury due to the lipophilic properties of methanol [2]. Accumulation of formic acid can directly damage the cellular proteins of the neurons as well as the glial tissue, leading to cytoplasmic edema, and nuclear pyknosis. The hallmark of the accumulated toxicity is the variable stages of neuronal injury [2].

A person with methanol poisoning may die because of cerebral edema, multi-organ failure, extensive cerebral infarction, or intracerebral hemorrhages [1, 10, 11]. In our case, the deceased survived for approximately 20 days after the methanol ingestion. The accumulating toxic effects of methanol caused an extensive and irreversible damage to the brain, leading to his demise. The absence of methanol from the blood analysis can be explained by the late sampling. The first blood sample for methanol detection was obtained five days after the hospital admission, approximately eight to nine days after the liquor's ingestion. Unmetabolized methanol can be detected if it is not sufficiently cleared through the kidneys and lungs. Its effective half-life is about 30-85 hours [12].

The deceased was one of the fatal victims of an methanol poisoning outbreak in the country in 2018. The victims succumbed to the toxic effects of methanol after an accidental ingestion of methanol-contaminated alcoholic beverages of a few brands which were popularly known among the immigrant community. Police investigation led to a series of arrests and confiscation of the contraband items, which revealed the source of it was bootleg alcohol, home-made using the recycled bottles of popular brands, deceiving the unsuspected victims.

5. Conclusion

The toxic effects of methanol on the brain are unmistakably outstanding. The extensiveness of the lesion and the involvement of bilateral cerebral hemispheres should serve as a good indication of the accumulating toxic effects of methanol.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors' contributions

Conceptualization, supervision, review and editing: Razuin Rahimi; Methodology: Razuin Rahimi, Norizal Mohd Noor and Noor Alicezah Bt Mohd Kasim; Data collection, analysis and original draft writing: All authors.

Conflict of interest

The authors declared no conflict of interest.

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