Case Report

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Two cases of methanol poisoning: CT and MRI features

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SUMMARY

Methanol poisoning in Australia is now very rare as methanol has been removed from methylated spirits. In acute intoxication methanol may result in a wide range of damage to the central nervous system. Few cases have been imaged with MRI. We present two cases and their striking neuroimaging findings with a discussion of the published work on methanol poisoning.

computed tomography; magnetic resonance imaging; methanol; poisoning; putamen.

CASE REPORT

Two male sailors aged 43 and 44 years were imaged in our department following their consumption of a quantity of liquid containing 58% methanol, which they mistakenly believed to be ethanol. Both sailors were inebriated when they arrived in the emergency department. Neither had any significant medical history.

Patient 1

This patient presented with nausea, vomiting and impaired vision. He complained of general darkening of his vision with black spots in his visual field. His clinical state rapidly deteriorated into a coma and he had a generalized seizure before being intubated. Initial biochemistry showed profound acidosis with a pH of 6.82 and lactate of 7.4 mmol/L. Blood ethanol was undetectable, but 0.17 g/L of methanol was detected producing an increased anion gap.

Emergency treatment consisted of oral and i.v. ethanol to compete with the metabolism of methanol. I.v. bicarbonate was also given. In the intensive care unit (ICU), haemodialysis followed by continuous veno-venous haemodialysis was undertaken. These interventions resulted in the prompt correction of the acidosis and elimination of the methanol.

The patient was extubated the next day. Examination findings at this stage included a mildly unsteady gait, poor short-term memory and motor dyspraxia for simple tasks such as eating. His vision was reduced to counting fingers. There was some improvement over the subsequent days. Brain CT and MRI were carried out on day 4.

His CT showed bilateral putaminal and cerebral deep white matter low attenuation (Fig. 1a). There was a predominant frontal and occipital distribution to the white matter involvement. Bilateral foci of cerebellar white matter low attenuation were also present (Fig. 2). No putaminal or other focal haemorrhage was present. The MRI was slightly degraded by movement artefact, but mirrored the CT findings (Figs 1a,2b).

Patient 2

This patient presented with nausea, vomiting and rapidly deteriorated in the emergency department. He had a generalized seizure, which was complicated by pulmonary aspiration before intubation. His biochemical derangement was slightly worse than patient 1 with a pH of 6.7 and lactate of 10.6 mmol/L. His methanol level was 0.21 g/L.

Emergency treatment was identical to that received by patient 1, although he also required a prolonged, supportive ICU admission. He never regained consciousness and died 20 days post-methanol ingestion. Brain CT was carried out on day 10 and MRI on day 15.

More striking generalized cerebral deep white matter low attenuation is seen on the second patient's CT. The cerebellum

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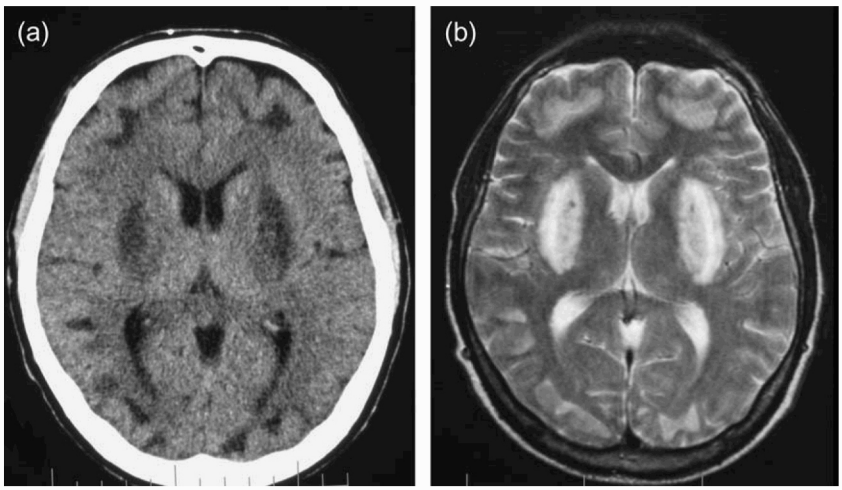

Fig. 1. (a) Non-contrast CT head at the level of the lentiform nuclei shows low attenuation in the putamina and subcortical white matter consistent with infarction and oedema. (b) Long echo time, long repetition time MRI at the level of the lentiform nuclei shows extensive putaminal and predominant frontal and occipital lobe white matter high signal abnormalities due to oedema and necrosis from toxic brain injury.

is unaffected. No haemorrhage is present on the CT, but 5 days later the MRI shows multiple scattered foci of haemorrhage at the grey–white interface of the cerebral hemispheres. The largest focus measures 2 cm in diameter located in the left frontal lobe. Putaminal necrosis is present but there is no haemorrhage. There is extensive deep white matter signal alteration consistent with oedema/necrosis and this extends to involve the subcortical U fibres but not the overlying cortex (Fig. 3a–c). The temporal lobes are relatively spared.

DISCUSSION

Methanol toxicity is related to its metabolites. Formic acid is the main metabolite of methanol causing damage to susceptible areas of the brain through histotoxic ischaemia.[1,2] Formic acid inhibits the mitochondrial enzyme cytochrome *c* oxidase, which is involved in oxidative metabolism leading to the synthesis of adenosine triphosphate (ATP).[2,3] *In vitro* and *in vivo* studies of rodent cerebral cortex and retina have shown formate-induced cytotoxicity to cerebral neurones, optic nerve cells and retinal cells with corresponding decreases in cellular ATP concentrations consistent with impairment of mitochondrial oxidative metabolism.[4,5]

The importance of formaldehyde, the precursor of formate, in toxicity is uncertain. Formaldehyde is believed to be too rapidly metabolized to formate to reach toxic levels, yet it can be detected in involved putamina.[2,6,7] Acidosis, which can be profound, also contributes to toxicity and is due to formate and lactate accumulation.[8] Lactate accumulates as a result of the formate-induced block to mitochondrial oxidation.

Methyl alcohol is found as a constituent of many commercial products such as photocopier fluid, fuel antifreeze and in many countries (not Australia) in methylated spirits. After initial inebriation there is a latent period of 6–48 h between ingestion and the development of toxic effects. This is the time required for metabolism of methanol in the liver to its more toxic metabolites and the concurrent development of acidosis.[2,8–11] Greater than 95% of ingested methanol is converted to formaldehyde by alcohol dehydrogenase and catalase. Formaldehyde is metabolized to formic acid by aldehyde dehydrogenase.[1,2,11] Formate is in turn metabolized by the hepatic enzyme 10-formyl-tetrahydrofolate dehydrogenase, which in humans is present in low

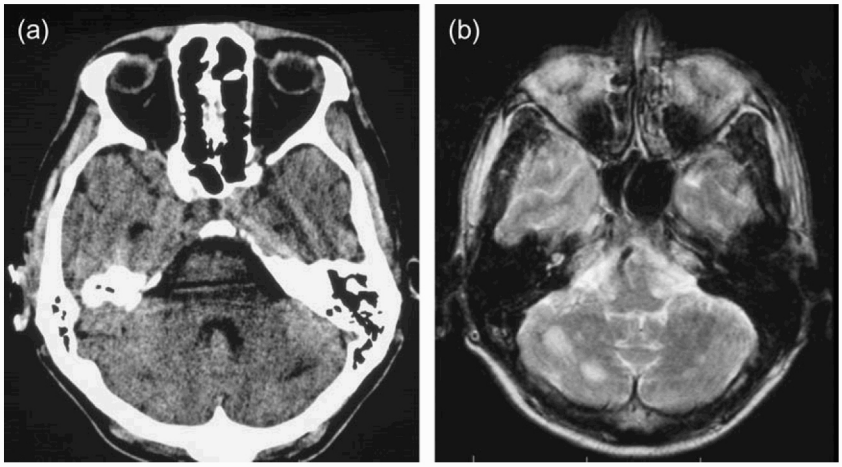

Fig. 2. (a) CT through the posterior fossa shows small areas of cerebellar low attenuation. (b) Long TE and long TR MR image at the same level as the CT shows multiple hyperintense foci within the cerebellar white matter.

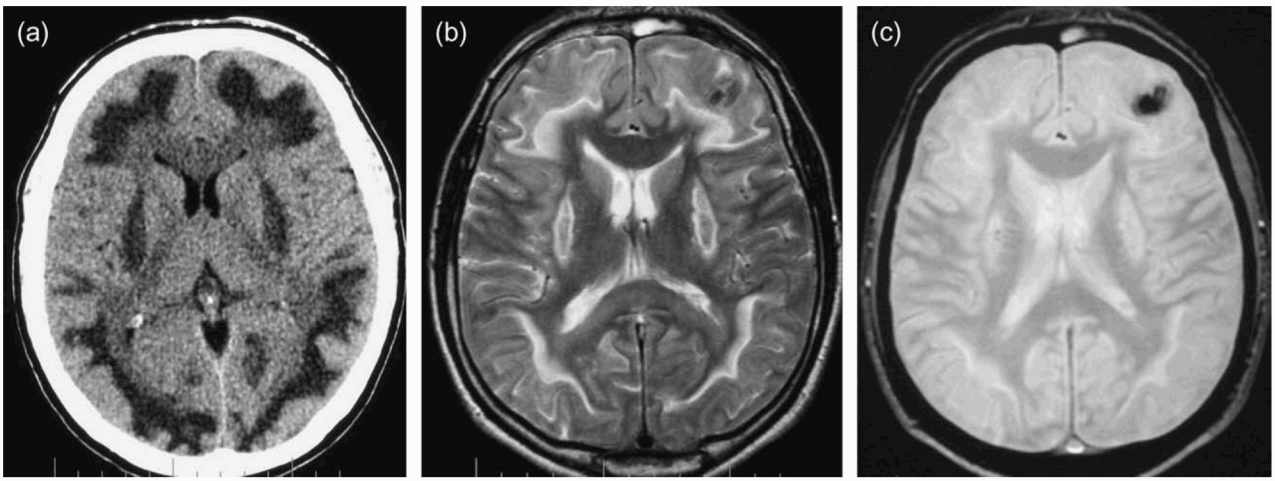

Fig. 3. (a) Computed tomography through the level of the lentiform nuclei with marked low attenuation in the putamina and cerebral white matter. No haemorrhage is visible. (b) Long echo time (TE), long repetition time (TR) MRI at the level of the lentiform nuclei shows marked putaminal and white matter high signal. The MRI, which was carried out 5 days after the CT also shows development of a focal area of low signal in the left frontal lobe consistent with a subacute haematoma containing intracellular methaemoglobin (on short TE, short TR sequence, not shown; the haematoma showed intermediate signal with a bright rim). (c) T2* FLASH sequence with susceptibility artefact at the site of haemorhage from field inhomogeneity induced by the methaemoglobin.

quantities, and as a result formate accumulates.[12] The lungs and kidneys eliminate 2.5 and 1% of methanol, respectively.[11]

There is marked inter-individual variation between the blood methanol level and toxic effects so the need for treatment should be based on the degree of acidosis and the presence of adverse clinical signs such as seizures.[11] Interestingly, chronic methanol drinkers are resistant to toxicity and frequently require no treatment when presenting with inebriation.[13] Common early symptoms of intoxication are nausea, vomiting, abdominal pain and diminution of vision. Inebriation may progress to obtundation, seizures and coma, with death in 5–12% of the individuals.[10,14,15] Pancreatitis is also reported.[11]

These two cases show extensive cerebral changes at the severe end of the range associated with methanol toxicity. A wide variety of lesions occurring with variable incidence can be found in the published work.

Patients who survive for more than 24 h show characteristic CT findings of bilateral low attenuation lesions in the putamina and cerebral deep white matter.[6,9,16–24] The occipital and frontal lobes are more commonly involved.[20] Putaminal haemorrhage is not uncommon and very rarely this may extend into the ventricular system.[24] Dialysis may increase the risk of haemorrhage.[24]

Cerebral cortex involvement is rare. Cerebellar involvement is occasionally seen and may involve the cortex, white matter and cerebellar nuclei.[6,21] There is a single reported case of subarachnoid haemorrhage.[25]

The severity of the imaging findings may aid in assessing prognosis although there is marked individual variation and patients with severe haemorrhagic putaminal necrosis have made full symptomatic recoveries.[9,20]

Magnetic resonance imaging acutely shows the areas of necrosis as high signal on long echo time (TE), long repetition time (TR) images (T2-weighted) and low signal on short TE, short TR images (T1 weighted). Subcortical U fibres are usually spared, although it was not so in the second patient's case.[19] Low signal areas in the putamen on long TE, long TR sequences suggest haemorrhage. Enhancement of these lesions post-contrast may be observed due to disruption of the blood–brain barrier.[16] Histotoxic ischaemia to the endothelial cells is also proposed as the mechanism for blood–brain barrier breakdown.[16]

Other conditions to consider in the setting of bilateral putaminal necrosis are Wilson disease, Leigh disease, rarer neurodegenerative states and anoxic and hypoxic insults.[20,21] Carbon monoxide poisoning also results in histotoxic ischaemia, but tends to more frequently involve the globus pallidus.[6]

Pathological specimens have confirmed the presence of necrosis, which may be haemorrhagic in cortical, subcortical and striatal neurones. Within the optic nerves demyelination is the usual pathology with non-haemorrhagic axonal necrosis observed uncommonly.[1,2] Although not always well shown radiologically the neuronal damage may be widely distributed with neuronal injury and loss also observed in the brainstem, thalamus and cord at autopsy.[1]

Whereas the mechanism of cytotoxicity of methanol is well understood the predilection for damage to deep white matter, retrolaminar optic nerves and the putamina is uncertain. In part this distribution of injury appears to relate to the blood supply with these being watershed areas.[2] As a result these areas are subjected to greater tissue hypoxia and an increased likelihood of infarction. Poor venous drainage of the putamen has also been proposed.[1]

Treatment, as was given to these two patients, is aimed at correcting the acidosis and preventing metabolization of methanol. Ethanol has 20 times greater affinity for alcohol dehydrogenase and so it effectively competes with methanol at this enzyme. Dialysis is carried out to eliminate the methanol.[7,10,11,13,26]

The most common neurological sequela is visual impairment due to optic nerve damage from retrolaminar demyelination and probably also axonal damage. Parkinsonism may develop because of basal ganglia damage and can be treated with standard dopamine replacement drugs.[18] Higher functions, as in the first case, may also be impaired presumably as a result of the widespread deep white matter and cerebral cortex involvement.

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