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CONVENTIONAL AND DIFFUSION-WEIGHTED MRI IN THE EVALUATION OF METHANOL POISONING

A case report

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Abstract

Cerebral lesions were studied in 2 methanol-poisoned patients using conventional magnetic resonance imaging (MRI). In 1 patient, diffusion-weighted MRI (DWI) was also performed. In this patient, conventional MRI showed symmetrical, bilateral increased signal in the lentiform nuclei, involving predominantly putamina, but also extending into the corona radiata, centrum semiovale and subcortical white matter. DWI showed decreased diffusion, which most probably reflects cytotoxic edema. In the other patient, fluid attenuated-inversion recovery (FLAIR) and T2-weighted images showed hyperintensity in the putamina, characteristic of post-necrotic changes.

Key words: Methanol poisoning; magnetic resonance imaging; diffusion-weighted imaging; brain, necrosis; toxic encephalopathy.

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Methanol is available as a component of many commercial products including various solvents and cleaners (7, 9). Most poisonings are, however, a result of intake of illicit spirits or "moonshine". Methanol ingestion can cause severe metabolic acidosis, visual defects ranging from blurring to total loss of vision, permanent neurologic dysfunction and death (10). Methanol poisoning is effectively treated with alkali to combat acidosis, antidotes (ethanol or fomepizole) to block production of the toxic metabolite formic acid, and hemodialysis to remove methanol and formate (10). Despite effective treatment, the morbidity and mortality in methanol poisoning remains high because of delayed diagnosis. Because few hospitals run methanol analyzes, simple laboratory findings such as increased anion and osmol gaps are important diagnostic clues (10, 11).

The diagnostic problems in methanol poisoning and the fact that many patients are admitted late in a comatose stage may sometimes result in diagnostic computed tomography (CT) or magnetic resonance imaging (MRI) findings because the basal ganglia, especially the putamina, are one of the target areas in this medical emergency. We present the conventional MRI findings in two cases of methanol poisoning. Diffusion-weighted MRI (DWI) was also obtained in one of the patients. To our knowledge, despite an extensive literature search, there is only one previous report of using DWI in the evaluation of cerebral toxicity of methanol poisoning (6).

Case Reports

Case 1: A 54-year-old woman was admitted because of severe dyspnoea and "almost blindness" several days after ingestion of a methanol/ethanol mixture. Upon admission, her S-methanol was 15.6 mM (50 mg dl^{-1}), S-formate 20 mM, pH 6.91, pCO_2 1.9 kPa, HCO_3 2.8 mM, and base deficit 39 mM. S-ethanol and S-ethylene glycol was zero. Fundoscopy revealed the typical "pseudopapilitis" seen in severe methanol-poisoned subjects. She was immediately treated with bicarbonate (750 mmol) and fomepizole twice [total dose 25 mg kg^{-1} intravenously (i.v.)]. Hemodialysis was initiated 2 h after admission and continued for 5 h. Acid-base status normalized within 3 h and visual disturbances also regressed completely. Conventional MRI performed on day 2 showed hyperintensity on the T2-weighted and fluid attenuated-inversion recovery (FLAIR) images in the putamina, particularly affecting the lateral portions of the nuclei (Fig. 1).

She was discharged in good condition on day 3 after a complete normal ophthalmologic exam, including perimetry.

Case 2: A 42-year-old man was admitted because of dyspnoea and blurred vision days after ingestion of a similar methanol/ethanol mixture. Upon admission, his S-methanol level was 32.5 mM (104 mg dl^{-1}) and S-formate 21 mM. Arterial pH was 6.87, pCO_2 2.9 kPa, HCO_3 3.8 mM, and base deficit 29 mM. Fundoscopy revealed typical "pseudopapilitis". He was immediately treated with bicarbonate (750 mmol) and fomepizole four times (total dose 45 mg kg^{-1}). Hemodialysis was initiated 2 h after the admission and continued for 8 h. Because of respiratory arrest 30 min after admission, he was intubated and treated with mechanical ventilation for 25 days, also due to pneumonia and sepsis. An initial non-enhanced CT scan showed low attenuation lesions involving the basal ganglia bilaterally and cerebral white matter (not shown). Conventional MRI on day 3 showed extensive, symmetrical, bilateral increased signal in FLAIR and T2-weighted images in the lentiform nuclei, extending to the corona radiata, centrum semiovale and subcortical white matter. In addition, the T2-weighted and FLAIR images showed increased signal in the right hippocampus (Fig. 2a, b). Axial diffusion-weighted (DW) images with corresponding apparent diffusion coefficient (ADC) maps demonstrated hyperintensity and hypointensity, respectively, in corresponding areas, consistent with cytotoxic edema (Fig. 2c–f). DWI was acquired using single-shot echo-planar sequences with *b*-values of 0 and 1000 s/mm^2 in three orthogonal gradient directions (x, y and z). From these data, ADC maps were computed. None of the lesions enhanced with gadolinium (not shown). Conventional MRI performed 3 weeks after admission, showed lesions that were hyperintense on T2-weighted images of the basal ganglia as well as in the subcortical white matter. Axial T2-weighted gradient-echo images showed small areas of low signal in the putamina and subcortical white matter, predominantly within occipital lobes, consistent with hemorrhagic transformation (Fig. 2g, h). Post-contrast T1-weighted images demonstrated linear and nodular enhancement within the bifrontal subcortical white matter (not shown).

He was transferred to a nursing home 49 days after admission. He then suffered from permanent brain damage and reduced vision which could not be further evaluated.

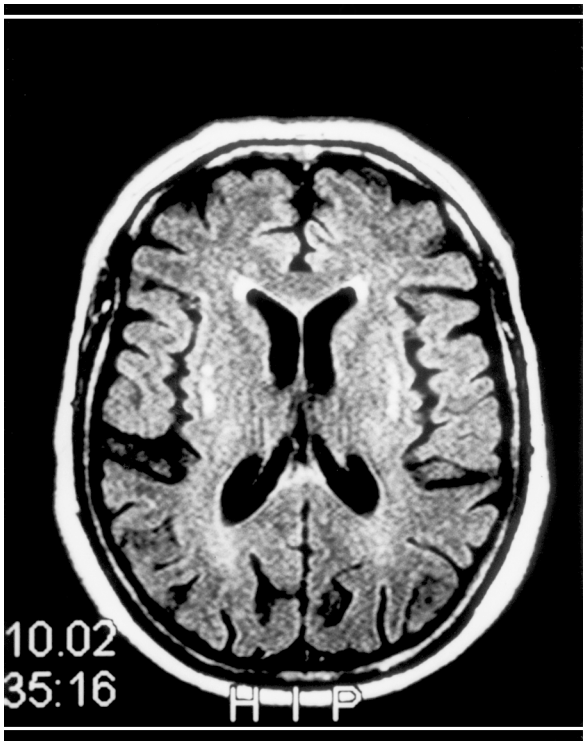

Fig. 1. Case 1. Axial fluid attenuated-inversion recovery (FLAIR) MR imaging demonstrates bilateral symmetric increased signal intensity within the putamina.

Discussion

Methanol ingestion is an uncommon form of poisoning that can cause severe metabolic acidosis, visual disturbance, permanent neurologic dysfunction and sometimes death (10–12). After ingestion, methanol is metabolized by hepatic alcohol dehydrogenase into formaldehyde and then to formic acid (9–11), which accumulates in primates and is responsible for the metabolic acidosis and toxicity

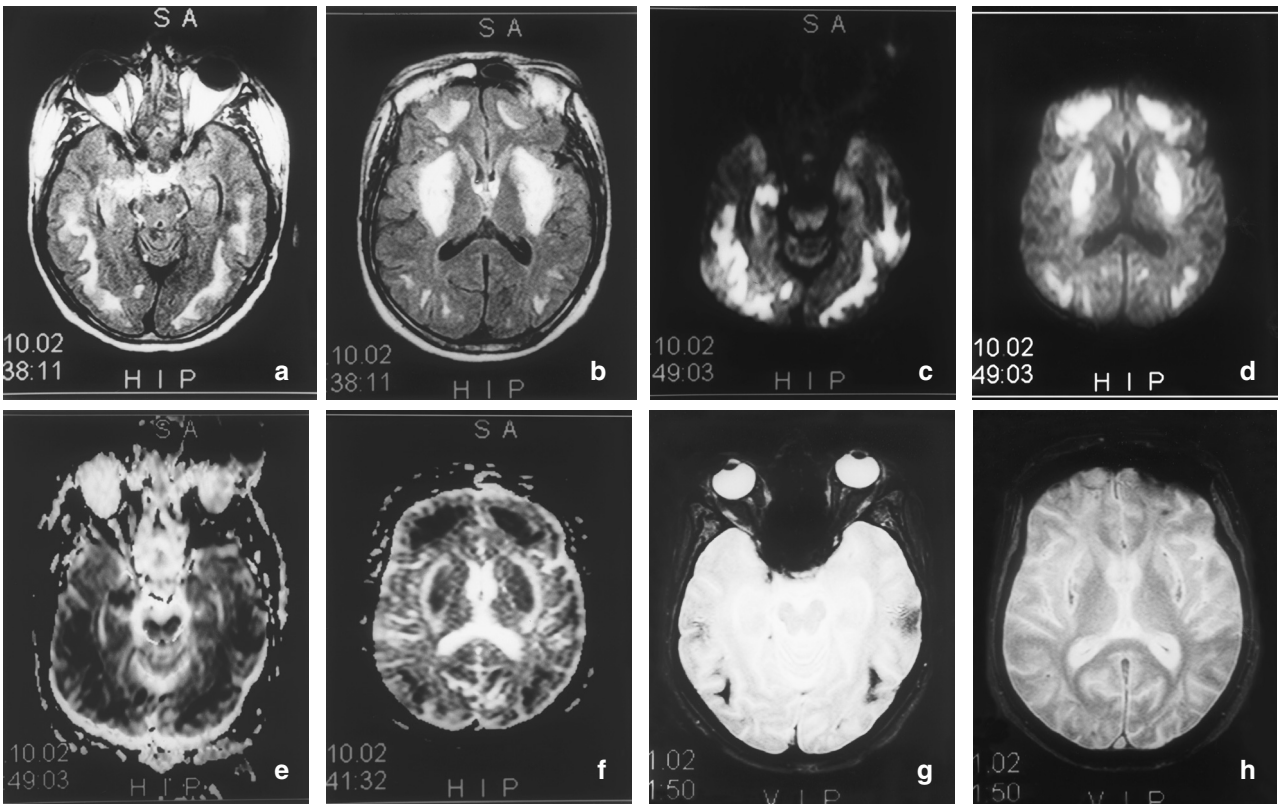

Fig. 2. a–h). Case 2. a, b) Initial axial FLAIR MRI shows bilateral symmetric high signal intensity areas involving the posterior temporal, occipital, frontal and parietal subcortical white matter. Note abnormal signal intensity within the basal ganglia and also the right hyppocampus. c, d) Axial DW images (*b*-value 1000 s/mm^2), c) at a lower level and d) at a higher level, demonstrate high signal intensity and e, f) low ADC in the subcortical white matter, basal ganglia, and right hyppocampus, as can be seen in cytotoxic edema. g, h) Axial T2-weighted gradient-echo images at 3 weeks show low signal foci in the putamina and subcortical white matter, predominantly within occipital lobes, representing focal hemorrhage.

by inhibition of cytochrome oxidase in the respiratory chain of the mitochondria (10). The diagnosis is sometimes elusive and requires a high index of suspicion. Intoxication with methanol should be suspected in cases of combined increase of osmolal and anion gaps (11).

Methanol intoxication produces classic neuropathological changes (15). Optic atrophy related to loss of myelin in the optic nerves is perhaps the best known neuropathological change after methanol poisoning (1, 13). Post-mortem studies of poisoned patients who survive for a period of days or weeks have shown a distinctive pattern of brain injury characterized by bilateral putamen necrosis (7, 14), white matter hemorrhagic necrosis, especially affecting subcortical regions (7). These lesions spare the most peripheral white matter, the subcortical association fibers (1, 19).

Neuroradiological findings in methanol poisoning have occasionally been described in the literature. These include bilateral putaminal hemorrhagic necrosis, cerebral and intraventricular hemorrhage, diffuse cerebral edema, and cerebellar necrosis, sparing subcortical association fibers (5, 8, 12, 19).

Patient 1 shows injury characterized by bilateral putaminal hyperintensity, particularly affecting the lateral portions of the nuclei (Fig. 1), consistent with necrosis. These changes have been well documented in previous studies (5, 8, 9). Putaminal changes on conventional MRI are not specific to methanol intoxication and have been described in Wilson's disease, Kearns–Sayre syndrome, Leigh disease, and various other neurodegenerative disorders (5, 8, 9, 19). Furthermore, there are pathologic similarities between methanol poisoning and carbon monoxide inhalation (5, 21), hypoxic-ischemic injury (3–5, 8), and acute cyanide intoxication (17).

In our case 2, the initial MRI scan at 3 days revealed symmetrical, bilateral hyperintensity in the lentiform nuclei, corona radiata, centrum semiovale, right hippocampus and subcortical white matter (Fig. 2a, b). These MR changes have also been shown in the few cases described to date in the literature (8, 12). To the best of our knowledge, there is only one previous study that used DWI in methanol poisoning (6). Deniz (6) reported that bilateral putaminal hyperintensity was seen on DW images with decreased ADC values. However,

bilateral hyperintensity areas on DW images with low signal on the ADC maps (restricted diffusion) involving the subcortical white matter have never been reported (Fig. 2c–f). This most probably reflects cytotoxic edema. Lesions with restricted diffusion or cytotoxic edema are less likely reversible and indicate non-viable tissue (20). These findings might also explain the very serious clinical status in our case. Cytotoxic edema is usually observed in acute ischemic stroke. Ischemia causes disruption of energy metabolism, leading to failure of the Na^+/K^+ adenosine triphosphatase (ATPase) pump which transports Na^+ and K^+ ions across the membrane. This leads to loss of ionic gradients and a flux of water from the extracellular to the intracellular space (18, 20). A possible factor contributing to the diffusion abnormalities is that the accumulation of formic acid has been shown to be responsible for the production of metabolic acidosis and inhibition of cytochrome oxidase, which causes anoxia (10) and the subsequent most possible failure of the Na^+/K^+ ATPase pump. Because formic acid also produces a failure of the Na^+/K^+ ATPase pump, a reduction in ADC values is also to be expected (6). Another additional possible cause of the findings is hypoxic insult secondary to respiratory arrest. However, a period of prolonged profound hypoxic insult was not documented in this patient, and rapid resuscitation was performed. We could not identify the presence of blood products or contrast enhancement of brain lesions in this initial MRI.

The second follow-up MRI examination, performed 3 weeks after the admission, showed small areas of hemorrhage in the putamina and subcortical white matter (Fig. 2g, h). The appearance of hemorrhage has been reported in up to 14% of patients who have methanol poisoning (9, 16) and has been suggested to indicate poor prognosis (2, 8). Glazer (9) and Kuteifan (12) described one case in which the MR images showed hemorrhage only in the putamina. In our case, we demonstrated hemorrhagic necrosis both in the putamina and similar signal intensity changes along the subcortical white matter. These findings have been demonstrated in previous neuropathologic examinations (7). It has been suggested that heparinization during hemodialysis may contribute to the hemorrhage or hemorrhagic transformation of necrosis (8, 9, 16). On the other hand, the dialyzed patients are those most severely poisoned and therefore those most likely to suffer from such complications. Anderson (1) reported one patient with enhancing lesions in the caudate nuclei, putamina, hypothalamus, and subcortical white matter by MRI, 12 days after ingestion. In our case, tiny foci of enhancement were found in frontal regions. Metabolic dysfunction and cellular injury involving endothelial cells of the central nervous system are a potential mechanism explaining the disruption of the blood–brain barrier represented by contrast enhancement (1).

The basis for the selective vulnerability of methanol intoxication is unknown (7, 8). The observed lesions most probably represent direct toxic effects of the metabolite formate (10), as well as injury secondary to hypoxia and acidosis (7).

In conclusion, methanol poisonings are rare, but do still occur. It is therefore important for radiologists to be aware of the appearance of these radiological findings in the proper clinical setting. The present study adds further evidence that the predominant involvement of bilateral hemorrhagic necrosis of the putamen and subcortical white matter correlates well with the neuropathologic findings. Abnormalities on DWI correlated with restricted diffusion (cytotoxic edema) in the early stage, and may provide useful information about the prognosis.

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