IMAGES IN RADIOLOGY
Robert G. Stern, MD, Section Editor

THE AMERICAN JOURNAL of MEDICINE®

Portrait of a Methanol-intoxicated Brain

Amita Singh, MD, Rohan Samson, MD, Ankur Girdhar, MD
Department of Internal Medicine, University of Florida and Shands College of Medicine, Jacksonville.

PRESENTATION

Whether accidental or intentional, the ingestion of methanol (methyl alcohol) can have serious adverse effects. These effects can include brain damage associated with the specific radiologic pattern seen in the following case.

A 33-year-old man with a history of depression and multiple suicide attempts presented with sudden-onset altered mental status after ingesting methanol at home. He had been brought in to the Emergency Department by emergency medical services after his neighbors found him collapsed at home. When he arrived his vital signs were: temperature 32.39°C (90.3°F), pulse 89 beats per minute, respiration 20 breaths per minute, and blood pressure 130/60 mm Hg.

On general examination, the patient was confused, with decreased mentation, and could not follow commands. His pupils were bilaterally dilated and sluggishly reactive to light. His lungs were clear to auscultation, and his heart sounds were normal, without any murmur, rubs, or gallops. Abdominal examination revealed hypoactive bowel sounds. His extremities exhibited no edema, clubbing, or cyanosis. The neurological examination revealed withdrawal from painful stimuli, and 2+ deep tendon reflexes with downgoing (normal) Babinski signs bilaterally.

ASSESSMENT

Blood tests revealed a leukocyte count of 11.5×10^3 cells/mm^3, hemoglobin 13.3 g/dL, sodium 136 mEq/dL, bicarbonate 3 mEq/dL, blood urea nitrogen 12 mg/dL, and creatinine 0.89 mg/dL. The calculated anion gap was 34 mmol/L, and the osmolar gap was 89 mOsm/kg. A toxicology screen done at presentation revealed a serum methanol level of 80 mg/dL and no detectable ethyl alcohol, ethylene glycol, acetaminophen, or salicylate. An arterial blood gas analysis revealed an arterial pH of 6.87. A chest radiograph showed no infiltrates, and an electrocardiogram showed normal sinus rhythm. The patient was intubated for airway protection.

Computed tomography (CT) scan of the head demonstrated high-density lesions along the basal ganglia bilaterally (Figure 1). Magnetic resonance imaging (MRI) scan of the brain performed 24 h after presentation corroborated the CT findings (Figures 2–4).

DIAGNOSIS

The CT, MRI, and toxicology findings indicated a diagnosis of bilateral putaminal necrosis secondary to methanol intoxication, which usually results from the accidental or suicidal ingestion of commercially available methanol or of methanol-contaminated whiskey.[1] Methanol is obtained from wood distillation and is used as a solvent in a variety of materials, including enamels, plastics, film, textiles, dyes, and windshield cleaners. When pure, it is colorless and has a light scent similar to that of ethanol. The crude form of methanol is unpalatable due to the presence of pungent impurities.

Ingestion of methanol causes nausea, vomiting, abdominal pain, blurred (snowstorm) vision, and mental status changes after a 12- to 24-hour latent period. Metabolic derangements including severe anion-gap metabolic acidosis are commonly present. Severe methanol poisoning characteristically induces permanent neurologic sequelae such as optic neuropathy, leading to blindness, seizure and coma, and putaminal necrosis.[2]

Methanol is rapidly absorbed from the gastrointestinal tract and metabolized in the liver, where it is converted to formaldehyde by alcohol dehydrogenase and then to formic acid by aldehyde dehydrogenase. The majority of methanol's effects are attributable to the accumulation of formic acid, which is toxic in the body. The delay in the generation of toxic metabolites is the cause of the latent period that occurs before the onset of symptoms, signs of intoxication, and eventual profound metabolic acidosis.[2] These eventual effects result from the inhibition of cytochrome oxidase, a

Funding: No funding was received for the writing of this manuscript.
Conflict of interest: All authors claim no conflicts of interest.
Authorship: All authors had access to the data and played a role in writing the manuscript.

Requests for reprints should be addressed to Amita Singh, MD, Department of Internal Medicine, University of Florida and Shands College of Medicine, 655 8th Street West, Jacksonville, FL 32209
E-mail address: amita.singh@jax.ufl.edu

0002-9343/$ -see front matter Published by Elsevier Inc.
doi:10.1016/j.amjmed.2010.09.001

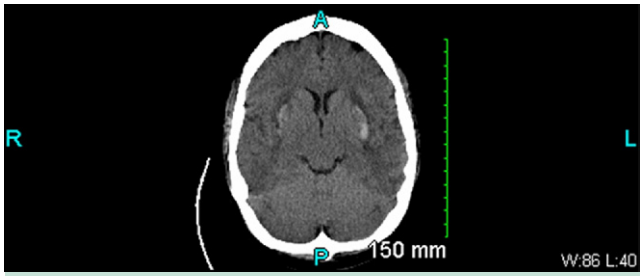

Figure 1 Contrast computed tomography scan of the head demonstrating evolving hypoattenuation within the bilateral putaminal regions. No midline shift is visible.

mitochondrial enzyme that is essential for oxidative phosphorylation; its inhibition leads to anoxia, cellular edema, and cell death (histotoxic anoxia/hypoxia).[3]

Bilateral putaminal necrosis is a rarely reported but characteristic finding of methanol intoxication.[2] Although the mechanism responsible for putaminal necrosis remains unknown, metabolic demands on the putamen are higher than those on other regions of the brain; this increased demand might cause increased accumulation of toxic formic acid in the putamen. Another suggested mechanism is decreased blood flow through the basal veins of Rosenthal.[2] Although linked to methanol intoxication, putaminal necrosis can also be seen in Wilson disease, Leigh disease,[4] Kearns-Sayre syndrome, striatal degeneration associated with Leber optic atrophy,[5] carbon monoxide inhalation, hypoxic-ischemic injury, and acute cyanide intoxication.[6]

The characteristic distribution of pathologic findings in methanol toxicity comprises involvement of the subcortical white matter and central gray matter with sparing of the peripheral gray matter. This distribution is probably multifactorial,[7] resulting from the cerebral microvascular anatomy and the direct toxic effects of methanol metabolites. The characteristic CT findings of bilateral, low-attenuation lesions in the putaminal and cerebral deep white matter are believed to be visible only in patients who survive for more

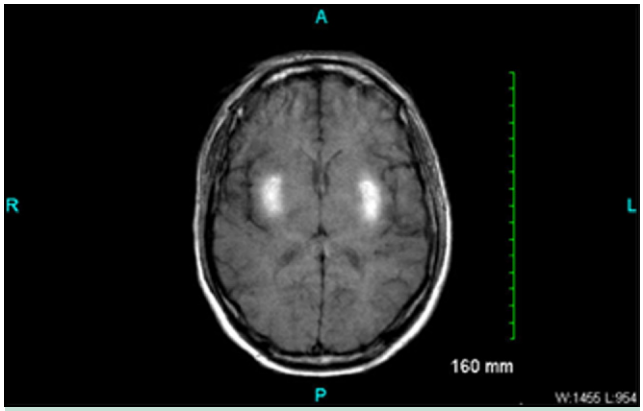

Figure 2 T1-weighted magnetic resonance image showing increased signal in the bilateral putaminal areas of the brain.

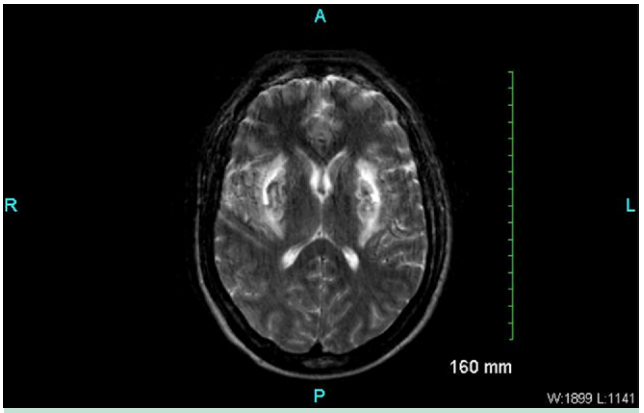

Figure 3 Fluid-attenuated inversion recovery (FLAIR) magnetic resonance image showing decreased intensity in the bilateral putaminal areas in the brain, consistent with hemorrhage.

than 24 hours; in the acute period of methanol intoxication, the CT findings can be normal.[6] Individuals who survive the acute phase of methanol intoxication may develop extrapyramidal symptoms and signs including rigidity, tremors, masked facies, and monotonous speech.[2] Because abnormal findings of methanol poisoning are demonstrated earlier in a diffusion-weighted MRI scan than in a head CT scan, some authors have proposed that a brain MRI scan should be performed as soon as possible in patients who exhibit altered mental status and unclear clinical symptoms or are suspected of methanol intoxication.[6]

MANAGEMENT

Fomepizole is a safe and effective antidote for methanol poisoning,[8] although the presence of putaminal hemorrhage and insular subcortex white matter necrosis are associated with a poor clinical outcome.[6] The plasma concentration of fomepizole that is necessary to inhibit alcohol dehydrogenase is approximately 0.8 μg/mL. Patients with acidosis

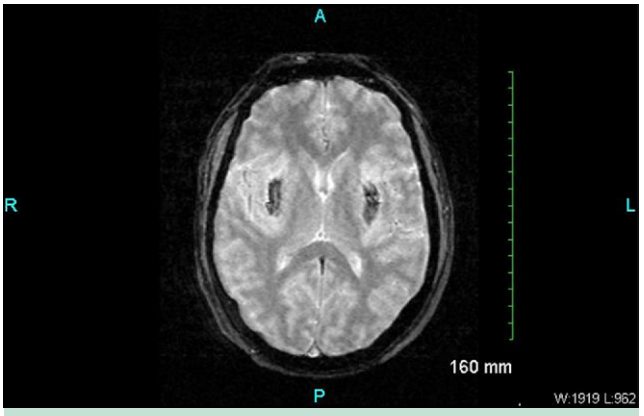

Figure 4 T2-weighted magnetic resonance image showing a margin of increased signal around the hemorrhage in the bilateral putaminal areas.

usually require hemodialysis. Because methanol has a long plasma half-life (54 hours), treatment with hemodialysis may be warranted to prevent prolonged hospitalization of patients with very high plasma methanol concentrations, even in the absence of acidosis.[8]

Our patient was treated with hemodialysis and fomepizole infusion, and the acidosis and anion gap subsequently resolved. Although his mentation improved progressively, he developed short-term amnesia, attention deficit, and tremors of the lower extremities.

References

1. Ahsan H, Akbar M, Hameed A. Diffusion weighted image (DWI) findings in methanol intoxication. *J Pak Med Assoc*. 2009;59:321-323.
2. Fontenot AP, Pelak VS. Development of neurologic symptoms in a 26-year-old woman following recovery from methanol intoxication. *Chest.* 2002;122:1436-1439.
3. Albrecht G. MRI of the brain in methanol intoxication. *Clin Neuroradiol*. 2008;18:122-126.
4. Blanco M, Casado R, Vázquez F, Pumar JM. CT and MR imaging findings in methanol intoxication. *AJNR Am J Neuroradiol*. 2006;27:452-454.
5. Glazer M, Dross P. Necrosis of the putamen caused by methanol intoxication: MR findings. *AJR Am J Roentgenol.* 1993;160:1105-1106.
6. Taheri MS, Moghaddam HH, Moharamzad Y, et al. The value of brain CT findings in acute methanol toxicity. *Eur J Radiol.* 2010;73:211-214.
7. Sefidbakht S, Rasekhi AR, Kamali K, et al. Methanol poisoning: acute MR and CT findings in nine patients. *Neuroradiology*. 2007;49:427-435.
8. Rent JB, McMartin K, Phillips S, et al. Fomepizole for the treatment of methanol poisoning. *N Engl J Med*. 2001;344:424-429.