The brain is greatly susceptible to damage from products of altered metabolism and various toxins. MRI can often show the damage at both early and delayed phases of the disease. In the early phase, MRI detects acutely injured brain areas responsible for the sudden onset of neurologic dysfunction, whereas in the chronic phase, when the clinical dysfunction has become permanent, MRI allows identification of neurologic sequelae. However, the severity and extent of the brain lesions may not necessarily match the clinical status in either setting. Knowledge of the imaging appearances of various toxic injuries to the brain may help narrow the differential diagnosis in a case of acute encephalopathy. Also, in a patient with known exposure to a toxic agent, topographic distribution of the lesions can help exclude other causes of neurologic impairment. This article describes the more classic MRI features of the several toxic and acquired metabolic encephalopathies. Inborn errors of metabolism are not discussed, although they may have similar imaging features.

In general, toxic and acquired metabolic disorders produce a widespread, symmetric pattern of injury that often involves the deep gray nuclei and cerebral cortex. Myelin, with its high lipid content, is particularly vulnerable to lipophilic toxic substances [1].

Hepatic Encephalopathy

Hepatic encephalopathy (HE) can occur in the setting of acute fulminant hepatic failure, or as a more chronic process in patients with hepatocellular dysfunction that leads to portosystemic shunting. Acute HE can be rapidly fatal, whereas chronic HE is usually a more indolent process causing neuropsychiatric symptoms [2]. Cerebral edema caused by increased intracellular osmolytes is postulated as the pathophysiologic basis underlying both the acute and chronic forms of HE [3]. The clinical features are variable, and the diagnosis may not be readily apparent in some patients. Conventional MRI may reveal hyperintense signal on T1-weighted images in the globus pallidus, subthalamic region, and midbrain, and may also show diffuse cortical edema and hyperintensity on T2-weighted images, with sparing of the perirolandic and occipital regions. Similar imaging findings may be seen in cases of sporadic Creutzfeldt-Jacob disease, which can present with a rapid progressive dementia. MR spectroscopy can detect intracellular metabolic shifts in HE. The increased intracellular osmolality caused by hyperammonemia results in a reduction of choline and myoinositol peaks and a rise in the glutamine and glutamate peaks (Fig. 1). The metabolic abnormalities correlate with the clinical severity, and reverse after treatment [4].

Hypoglycemic Encephalopathy

Hypoglycemic coma can be fatal if prolonged and severe. Lesions are described that involve the temporal, occipital, and insular cortex; the hippocampus; and the basal ganglia [5], with sparing of the thalamus (Fig. 2).
These findings can be similar to sporadic Creutzfeldt-Jacob disease, although the clinical setting should exclude the neurodegenerative disorder. Additionally, the deep white matter may be involved, with hypoglycemic injury in the form of symmetric hyperintensity involving the internal capsule, corona radiata, and splenium on T2-weighted images. The lesions may show restricted diffusion [6].

Osmotic Pontine Myelinolysis

Osmotic or central pontine myelinolysis is classically described in alcoholics after rapid correction of hyponatremia. Clinical manifestations vary from minimal symptoms to a complete locked-in syndrome, coma, or death. MRI usually shows a centrally located lesion in the pons with sparing of its peripher al rim. Extrapontine structures such as the cerebral white matter, thalamus, and basal ganglia may be involved [1]. The lesions appear hyperintense on T2-weighted and FLAIR imaging and may show increased signal on diffusion-weighted imaging that is presumably due to cytotoxic edema [7] (Fig. 3).

Carbon Monoxide Poisoning

Carbon monoxide is a colorless and odorless gas that is the most common cause of accidental poisoning in Europe and North America, as well as being a major cause of suicidal deaths. The exposure may be acute or chronic at a low level. Necrosis of the globus pallidus is the most common brain injury occurring in carbon monoxide poisoning and is usually bilateral and symmetric. These lesions appear hypointense on T1-weighted and hyperintense on T2-weighted images (Fig. 4). The caudate and putamen may also be affected [8], as well as the frequently involved cerebral white matter. Patients with a good outcome have normal MRI or minimal involvement in the form of signal abnormalities in the globus pallidus. Patients with a poor outcome generally show more widespread involvement [8].

Methanol Toxicity

Methanol may be ingested accidentally or intentionally and can be fatal unless treatment is instituted early. Bilateral necrosis of the putamen is the most characteristic finding [9]; the presence of hemorrhage correlates with a poor prognosis. The lesions show increased signal intensity on T2-weighted images and variable T1-weighted signal, depending on the presence and stage of hemorrhage (Fig. 5). Enhancement is also variable, ranging from none to intense (Fig. 6). In the chronic setting, cystic cavities may develop in the putamen. Additional involvement of other basal ganglia nuclei, subcortical white matter, brainstem tegumentum, and cerebellum are described [9].

Ethylene Glycol Toxicity

Ethylene glycol is usually ingested intentionally for suicide. Literature on the MRI features of ethylene glycol toxicity is sparse. A few case reports have described bilateral and symmetric involvement of the basal ganglia, thalamus, amygdala, hippocampus, and brainstem [10] (Fig. 7). Involvement of the white matter tracts with restricted diffusion may also be present [10].

Metronidazole Toxicity

Metronidazole can produce neurologic symptoms at doses exceeding 2 g/d [11]. The symptoms commonly described are dysarthria, gait disturbance, weakness of the extremities, and mental confusion [12]. On MRI, the dentate nuclei in the cerebellum are most commonly involved (Fig. 8), followed by the tectum, red nucleus, periaqueductal gray matter, and dorsal pons [12]. The dorsal medulla (Fig. 8) and the corpus callosum are less often affected. The splenium is affected in all cases in which the corpus callosum is involved (Fig. 8). Lesions involving the dentate nuclei, red nuclei, dorsal pons, and medulla are often bilateral and symmetric. The lesions show increased signal intensity on T2-weighted images, do not show contrast enhancement, and are reversible after discontinuation of the drug [12] (Fig. 8).

Cyclosporine Toxicity

Solid organ transplant patients receiving cyclosporine may present with headache, altered sensorium, visual disturbance, and seizures. MRI often shows areas of hyperintensity on T2-weighted and FLAIR images in the subcortical white matter of the posterior temporal, parietal, and occipital lobes (Fig. 9). Overlying cortical gray matter may occasionally be involved. The frontal lobes may also be involved. The lesions characteristically show vasogenic edema on apparent diffusion coefficient maps [13] and are usually reversible after withdrawal of the drug (Fig. 9). This condition is termed “posterior reversible encephalopathy syndrome.” Other causes of posterior reversible encephalopathy syndrome include tacrolimus toxicity, eclampsia, severe hypertension, and glomerulonephritis.

Cocaine Encephalopathy

Cocaine can cause vasospasm and vasculitis leading to ischemic and hemorrhagic infarction. Cocaine can also produce a toxic encephalopathy from direct toxic effects after IV or inhalational use. On MRI, lesions with increased signal intensity on T2-weighted images are reported in the globus pallidi, splenium, and cerebral white matter, with affected regions often showing restricted diffusion [14] (Fig. 10).

Conclusion

MRI plays an important role in the management of acutely encephalopathic patients. It can rule out surgically correctable causes of a decreased level of consciousness. The basal ganglia, thalamus, cerebral cortex, and hemispheric white matter are common targets of various toxic and acquired metabolic causes of encephalopathy, making a definite diagnosis difficult for the radiologist. However, understanding the characteristic imaging features, in combination with detailed clinical history, can often aid in quickly establishing the correct diagnosis. This may in turn reduce the cost of unnecessary metabolic or toxic screening tests. In some toxic and metabolic encephalopathies, the extent of brain involvement on imaging may predict the prognosis and clinical outcome.

References

MRI of Metabolic Encephalopathies


Fig. 1—66-year-old man with hepatic cirrhosis, ascites, and decreased level of consciousness due to hepatic encephalopathy after acute upper gastrointestinal hemorrhage.
A and B, Axial FLAIR images show widespread cortical hyperintensity and sparing of occipital lobes and perirolandic regions.
C, Diffusion-weighted image shows restricted diffusion in affected cortex.
D, Short-echo MR spectroscopy (TE, 35) with voxel placed over bilateral parietooccipital cortex reveals diminished choline and elevated glutamine–glutamate peak (arrow).
Fig. 2—43-year-old man with hypoglycemic coma who was found to have serum glucose level of 1.2 mmol/L (normal reference range, 4–6 mmol/L). A and B, Axial FLAIR images show cortical and striatal hyperintensity. Note sparing of thalami. C and D, Corresponding diffusion-weighted images show restricted diffusion in affected areas.

Fig. 3—48-year-old man, chronic alcohol abuser, with decreased level of consciousness due to osmotic demyelination from rapid correction of serum sodium. Serum sodium on admission was 110 mEq/L, which was corrected to 126 mEq/L over 12 hours. A and B, Axial T2-weighted images show hyperintensity in pons (A) and basal ganglia (B). Pontine lesion is central in location with sparing of periphery. Basal ganglia involvement suggests extrapontine myelolysis. (Fig. 3 continues on next page)
Fig. 3 (continued)—48-year-old man, chronic alcohol abuser, with decreased level of consciousness due to osmotic demyelination from rapid correction of serum sodium. Serum sodium on admission was 110 mEq/L, which was corrected to 126 mEq/L over 12 hours. C and D, Corresponding diffusion-weighted images show restricted diffusion in pons and basal ganglia.

Fig. 4—51-year-old woman with drowsiness and instability that was diagnosed as accidental carbon monoxide poisoning caused by faulty domestic heating. A, Axial T2-weighted image shows increased signal intensity of bilateral globus pallidi. B, Corresponding diffusion-weighted image shows restricted diffusion in bilateral globus pallidi.

Fig. 5—31-year-old man who was admitted to hospital with acute methanol intoxication and decreased level of consciousness. A, Axial T2-weighted image shows marked hyperintensity of bilateral putamina and caudate. B, Axial gradient-echo image shows punctate area of signal loss due to susceptibility artifacts and suggests microhemorrhage. Susceptibility artifacts are present in A and B bilaterally at level of coronal and lambdoid sutures.
Fig. 6—33-year-old man with methanol intoxication, blindness, and stupor. Imaging was performed 2 weeks after ingestion. 

A. Axial T2-weighted image shows markedly increased signal intensity of putamina that is suggestive of necrosis.

B. Contrast-enhanced T1-weighted axial image shows marked enhancement of putamina. Punctate areas of enhancement in bilateral frontal opercula are probably infarcts.

Fig. 7—25-year-old man with decreased level of consciousness after suicide attempt by ingesting ethylene glycol.

A–C, Axial FLAIR images show increased signal intensity in bilateral basal ganglia, thalami (A), midbrain (B), hippocampi, amygdala (B and C), and upper pons (C).

D, Diffusion-weighted image shows restriction of diffusion in cortex, suggesting cytotoxic edema due to infarctions. Basal ganglia and thalami do not show any restriction of diffusion.
Fig. 8—54-year-old man who was taking metronidazole prophylactically and presented with acute onset gait ataxia and dysarthria. 
A and B, Axial FLAIR images show increased signal intensity in bilateral dentate nuclei (arrowheads, A) and dorsal medulla (arrows, A) and subtle hyperintensity in splenium (arrow, B). 
C and D, Axial FLAIR images 3 months after cessation of metronidazole show complete resolution of abnormalities.

Fig. 9—51-year-old woman who developed headaches, tremors, and visual changes 4 weeks after liver transplantation and initiation of cyclosporine therapy. 
A, Axial FLAIR image shows symmetric hyperintensities in subcortical white matter of posterior temporal and occipital lobes. 
B, Follow-up axial FLAIR image obtained after 1 week of cessation of drug shows complete resolution of abnormalities.
Fig. 10—32-year-old male drug abuser with loss of consciousness after cocaine overdose. Metabolites of cocaine were found in blood and urine samples. 

A and B, Axial T2-weighted images show hyperintensity of globus pallidi (A) and white matter with sparing of subcortical U-fibers (B). 

C and D, Corresponding diffusion-weighted images show restricted diffusion in bilateral globus pallidi and white matter.