Imaging appearances of toxic and acquired metabolic encephalopathic disorders

ABSTRACT

Most imaging findings relating to toxic and acquired metabolic disorders follow a certain pattern with affinity to a specific topographic area, which can help narrow the differential diagnosis. This is especially useful when the clinical presentation can be variable and there is diagnostic uncertainty. Usually, there is bilateral symmetrical abnormality within the deep grey matter structures and the cerebral cortex because of the high metabolic activity and raised oxygen requirements in these areas. Magnetic resonance imaging, particularly diffusion weighted imaging and fluid-attenuated inversion recovery sequences, is very important in differentiating between various aetiologies in this group. Magnetic resonance imaging can be useful in demonstrating both acute and chronic damage, in evaluating treatment response and in disease prognostication. This pictorial review discusses the computed tomography and magnetic resonance imaging appearances of a spectrum of toxic and metabolic disorders observed in a district general hospital with reference to clinical presentation and imaging features that may allow diagnosis. This includes carbon monoxide poisoning, hypoglycaemia, non-ketotic hyperglycaemia, osmotic demyelination syndrome, posterior reversible encephalopathy syndrome, hypoxic ischaemic encephalopathy, the syndrome of delayed post-hypoxic leukoencephalopathy, hepatic encephalopathy and cocaine toxicity.

This pictorial review highlights the imaging features associated with toxic and metabolic encephalopathies that may be encountered in a district general hospital, to facilitate an early diagnosis especially when there is clinical uncertainty (Bathla and Hegde, 2013).

Carbon monoxide poisoning

Extreme hypoxic-anoxic encephalopathy results when carbon monoxide binds with haemoglobin to form carboxyhaemoglobin following inhalation of carbon monoxide gas, resulting in both acute and chronic neurological sequelae (Sener, 2003). Delayed effects are caused by carbon monoxide interfering with mitochondrial oxidative phosphorylation resulting in lipid peroxidation and oxidative injury. Patients can present acutely with headache, nausea, vomiting, seizure or altered conscious state. Delayed neuropsychological sequelae, occurring weeks after recovery from the acute episode, include dementia, memory deficits, parkinsonian-like symptoms and gait disturbances. Histology includes demyelination, oedema and necrosis.

Computed tomography demonstrates bilateral symmetrical hypodensities within the globus pallidi (*Figure 1a*) and/or diffuse hypodensity in the cerebral white matter. Features seen on magnetic resonance imaging include bilateral symmetrical hypointensities (necrosis) or hyperintensities (haemorrhage) within the globus pallidi on T1-weighted images. Ischaemia or infarction is demonstrated on T2-weighted images as hyperintensity in the bilateral globus pallidus which restricts acutely on diffusion-weighted imaging (*Figures 1b* and *c*). Other affected areas include the cerebral white matter, corpus striatum, insular lobe, temporal lobe cortex and less commonly the hippocampus (Sener, 2003). Hyperbaric oxygen therapy within 6 hours gives the best outcome.

Dr Tharunniya Vamadevan, ST4 Radiology Registrar, Department of Clinical Radiology, Brighton and Sussex University Hospitals NHS Trust, Brighton BN2 1ES

Professor David Howlett, Consultant Radiologist, Department of Clinical Radiology, Eastbourne District General Hospital, Eastbourne

Dr Maria Filyridou, Consultant Radiologist, Department of Clinical Radiology, Eastbourne District General Hospital, Eastbourne

Correspondence to: Dr T Vamadevan (tharunniyav@hotmail.com)

Osmotic demyelination syndrome

Osmotic stress occurs in relation to rapid electrolyte correction, particularly in alcoholics and chronically debilitated patients, and can cause osmotic demyelination syndrome (Alleman, 2014).

Oligodendrocytes are most affected and histologically there is extensive demyelination with subsequent abundant foamy lipid-laden macrophages. Clinical symptoms emerge within a week following correction of hyponatraemia and include seizures, altered mental status, dysphagia, dysarthria, pseudobulbar palsy (Landais, 2014) if the central pons is involved, and movement disorder if there is extrapontine involvement (basal ganglia, thalamus and subcortical white matter). Computed tomography demonstrates hypoattenuation in the affected areas. Magnetic resonance imaging demonstrates trident or batwing-shaped T2/fluid-attenuated inversion recovery central pontine hyperintensity (as a result of sparing of the peripheral and descending corticospinal tracts) (*Figure 2a*) which returns restricted diffusion in the acute phase (*Figure 2b*)(Alleman, 2014). Usually there is no enhancement. Treatment is supportive.

Posterior reversible encephalopathy syndrome

Posterior reversible encephalopathy syndrome is a neurotoxic syndrome. Failure of autoregulation in response to an acute change in blood pressure, particularly

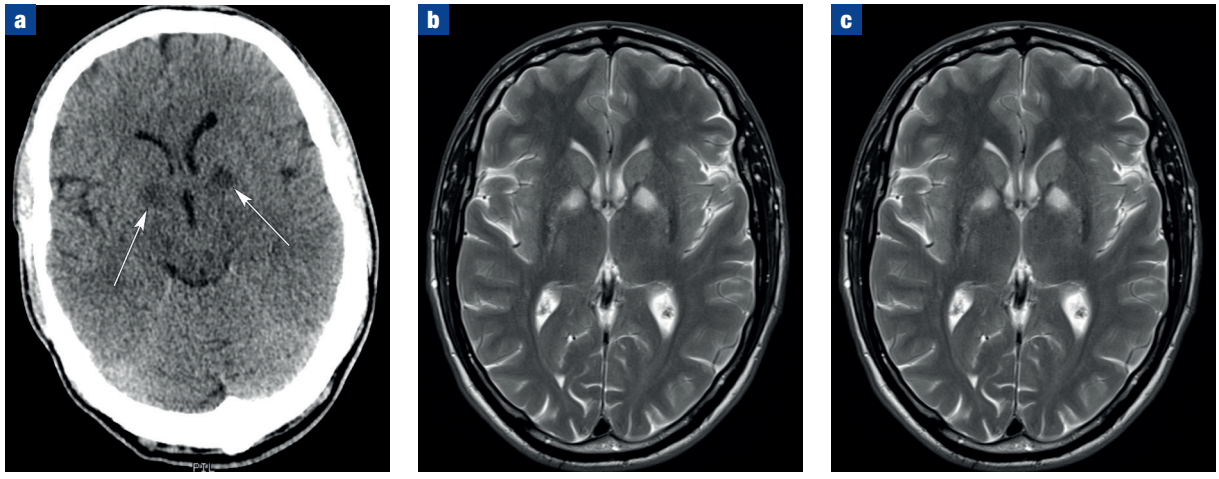

Figure 1. **a.** Axial computed tomography image at the level of the third ventricle demonstrates bilateral symmetrical hypodensities in the globus pallidi (arrows). **b.** Axial T2-weighted image demonstrates bilateral symmetrical hyperintensity in the globus pallidi. **c.** Diffusion-weighted imaging demonstrates diffusion restriction as high signal in the globus pallidi.

involving the posterior circulation, leads to disruption of the blood–brain barrier with resultant vasogenic oedema. It is associated with hypertension, pre-eclampsia or eclampsia, sepsis, drugs and uraemia. Clinical features include headache, seizure, reduced mental status and visual symptoms.

Usually cortical and subcortical areas are affected with a predilection for the parieto-occipital areas (Bartynski and Boardman, 2007). Less commonly affected areas include the frontal and temporal lobes at the junction of the vascular watershed zones and rarely the basal ganglia, the splenium, the pons or the cerebellum (Bartynski and Boardman, 2007).

Computed tomography may demonstrate subcortical hypodensities or vasogenic oedema.

In typical cases magnetic resonance imaging demonstrates symmetrical cortical and subcortical T2 or fluid-attenuated inversion recovery hyperintensities in the parieto-occipital lobes of both hemispheres. In more severe cases, vasogenic oedema may involve more parts of the cerebral hemispheres (*Figures 3a* and *b*) and the cerebellum. Haemorrhage can occur, including focal parenchymal haemorrhage, microhaemorrhages or convexity subarachnoid haemorrhage (Stevens and Heran, 2012). Restricted diffusion can be seen as an associated finding and has been shown to be potentially reversible. There is evidence of variable patchy enhancement. Following successful treatment of the precipitating factor, there can be a lag between radiological and clinical improvement; the imaging features usually completely resolve, but this can take up to a few weeks.

Hypoglycaemia-induced encephalopathy

Imbalance in glucose supply and use either as a result of an intentional or accidental overdose of hypoglycaemic medication or an insulin-secreting tumour may result in brain injury. Patients present with seizures, coma or a reduced level of consciousness.

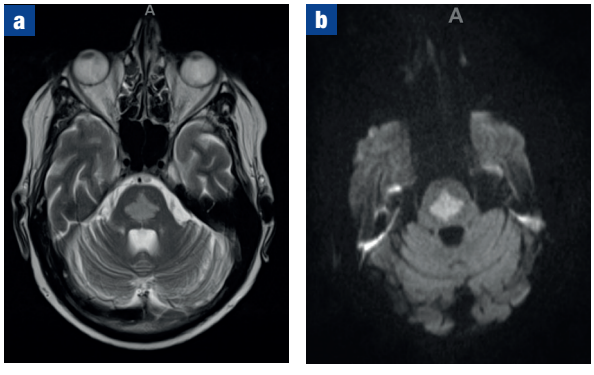

Figure 2. **a.** Axial T2-weighted image demonstrating classic trident central pontine hyperintensity. **b.** Diffusion-weighted imaging demonstrates high signal during the acute phase.

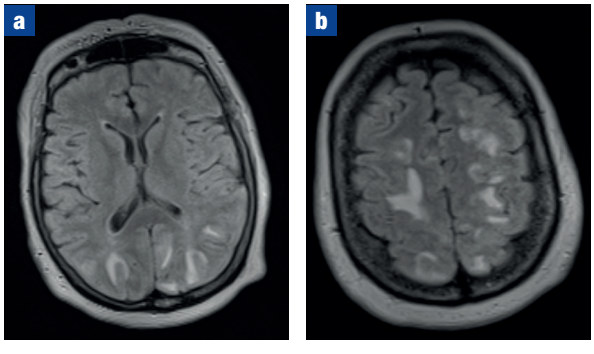

Figure 3. Uraemia-associated posterior reversible encephalopathy syndrome. Fluid-attenuated inversion recovery images demonstrate vasogenic oedema **(a)** in the subcortical white matter of the occipital lobes and **(b)** in the centrum semiovale. Following improvement of the renal function 10 days later, magnetic resonance imaging (not shown) demonstrated complete resolution of these findings.

Magnetic resonance imaging demonstrates bilateral T2 hyperintensities in the posterior limb of the internal capsule, cerebral cortex, hippocampus and basal ganglia (Bathla and Hegde, 2013). In adults, the cerebellum,

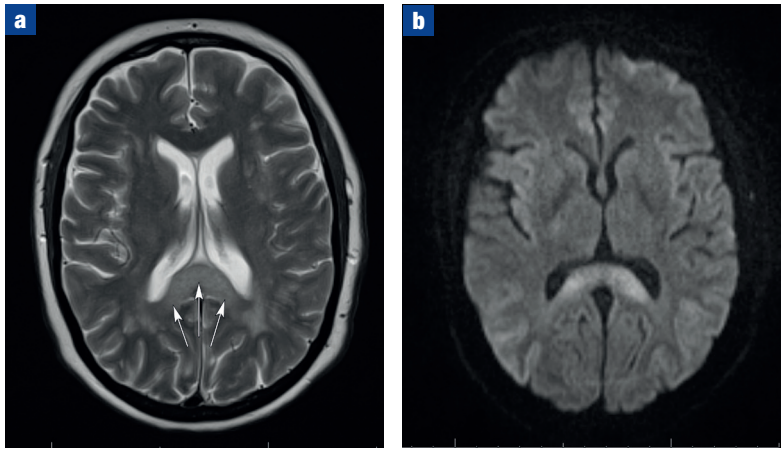

Figure 4. **a.** Diffuse hyperintensity in T2-weighted images within the splenium (arrows) in a hypoglycaemic patient. **b.** Corresponding diffusion-weighted imaging demonstrates high signal restricted diffusion in the acute phase in the splenium and parts of the cortex.

thalami, subcortical and deep white matter are usually spared. The splenium of the corpus callosum can be affected producing the so-called 'boomerang' appearance (*Figure 4a*). Restricted diffusion is demonstrated in the acute stage (*Figure 4b*) which may be reversible.

Clinical outcome depends on the severity, the duration of the hypoglycaemic episode and the extent of brain damage.

Non-ketotic hyperglycaemic hemichorea

This is a rare neurological complication of non-ketotic hyperglycaemia, most frequently seen in elderly type 2 diabetic patients, who may present with choreatic movements (Wintermark et al, 2004). The underlying pathophysiology in patients with non-ketotic hyperglycaemic hemichorea is not fully understood, hypotheses include hyperglycaemia causing hyperviscosity resulting in disruption of the blood–brain barrier or a non-ketotic state resulting in decreased GABA (gamma aminobutyric acid) availability in the corpus striatum (Narayanan, 2012).

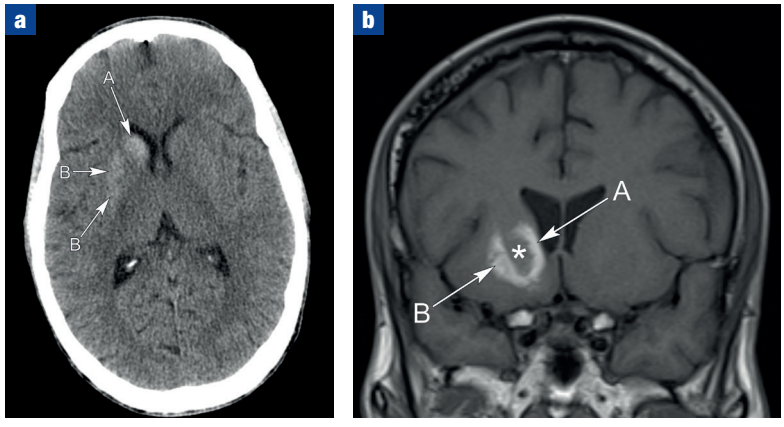

Figure 5. **a.** Axial computed tomography image demonstrates hyperdensity within (A) the caudate and (B) the putamen. **b.** Coronal T1-weighted image demonstrates hyperintensity within (A) the caudate and (B) the putamen, sparing the anterior limb of the internal capsule (*).

Computed tomography demonstrates hyperdensity in the corpus striatum (*Figure 5a*) and corresponding hyperintensity on the T1-weighted images (*Figure 5b*) (Wintermark et al, 2004). If unilateral, these changes are contralateral to the symptomatic side (Wintermark et al, 2004). Theories proposed to explain these imaging findings include transient ischaemia and protein desiccation related to Wallerian degeneration (Wintermark et al, 2004). Treatment includes intravenous fluids to rehydrate and insulin to normalise glucose levels. The symptoms tend to resolve spontaneously with normalisation of hyperglycaemia within hours, days or weeks.

Hepatic encephalopathy

Hyperammonaemia results from liver dysfunction and portal hypertension which can be acutely rapidly fatal or present with neuropsychiatric symptoms in the more indolent chronic phase. Magnetic resonance imaging demonstrates T2 or fluid-attenuated inversion recovery hyperintensity within the insula, posterior limb of the internal capsule, thalamus and cingulate gyrus in mild cases (Rovira et al, 2008). In more severe cases there is diffuse cortical oedema, with sparing of the perirolandic and occipital regions. These areas can demonstrate restricted diffusion on diffusion-weighted imaging. In chronic cases there can be T1 hyperintensity in the basal ganglia bilaterally, possibly secondary to manganese deposition (*Figure 6*). Gradient echo or susceptibility weighted imaging sequences may demonstrate micro-haemorrhages. Treatment mainly involves identifying the precipitating cause, treating the conducive conditions

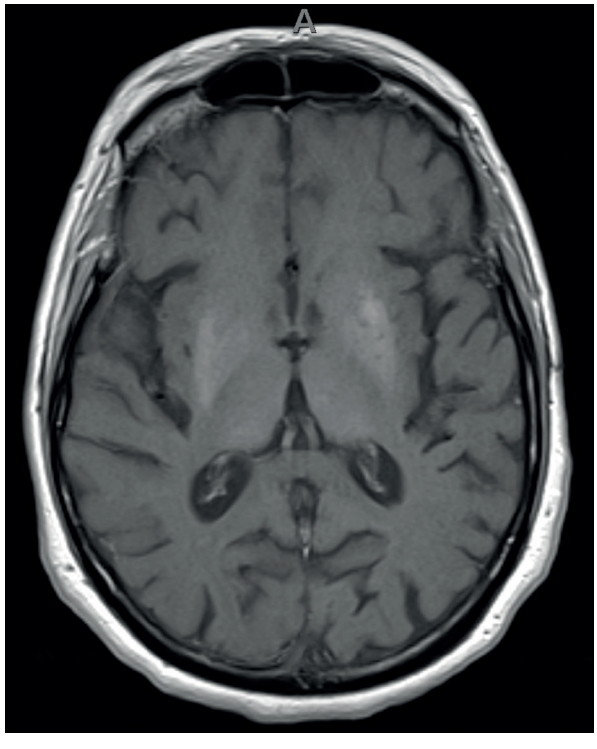

Figure 6. Bilateral T1 hyperintensity in the basal ganglia of a patient with liver failure.

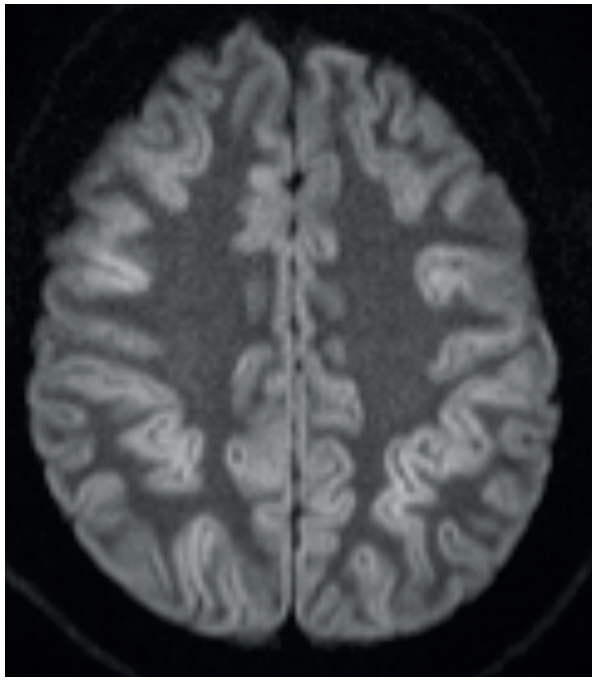

Figure 7. Axial diffusion-weighted imaging demonstrates diffuse high signal (restricted diffusion) in the cortex of both cerebral hemispheres in a case of acute cerebral hypoxic injury.

and removal of excess ammonia via haemofiltration (Bleibel and Al-Osaimi, 2012).

Hypoxic ischaemic encephalopathy

Hypoxia or hypoperfusion as a result of cardiac arrest or cerebrovascular disease can result in hypoxic brain injury. Grey matter structures including the cerebral cortex, basal ganglia and hippocampi are more susceptible to hypoxia or ischaemia. Computed tomography acutely may demonstrate diffuse cerebral oedema with bilateral effacement of the CSF spaces, loss of grey-white matter differentiation and reduced attenuation in the basal ganglia. A feature of severity on computed tomography is the 'white cerebellum sign', which is encountered when there is diffuse low attenuation of the cerebrum with relatively increased attenuation of the cerebellum, indicative of very poor prognosis (Han et al, 1989). Diffusion-weighted imaging is positive within hours of insult (*Figure 7*). The basal ganglia may appear hypointense or hyperintense (haemorrhagic) on T1-weighted images and hyperintense on T2-weighted images (Beltz and Mullins, 2010).

The white matter can be affected in mild hypoxia, or injury may be more evident in severe cases of hypoxia in the subacute phase. Post-hypoxic leukoencephalopathy (Huang et al, 2008) is a rare syndrome of delayed white matter injury characterized by acute onset of neuropsychiatric symptoms days to weeks after a hypoxic-ischaemic event. Magnetic resonance imaging demonstrates diffuse confluent areas of restricted diffusion throughout the cerebral white matter (*Figures 8a* and *b*)(Huang and Castillo, 2008).

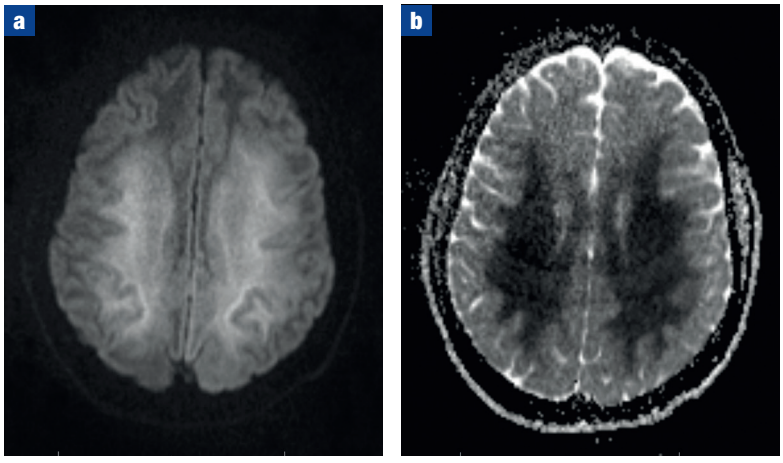

Figure 8. **a.** Axial diffusion-weighted imaging demonstrates bilateral extensive white matter restricted diffusion 14 days after an acute hypoxic episode. **b.** The corresponding apparent diffusion coefficient map for the same patient.

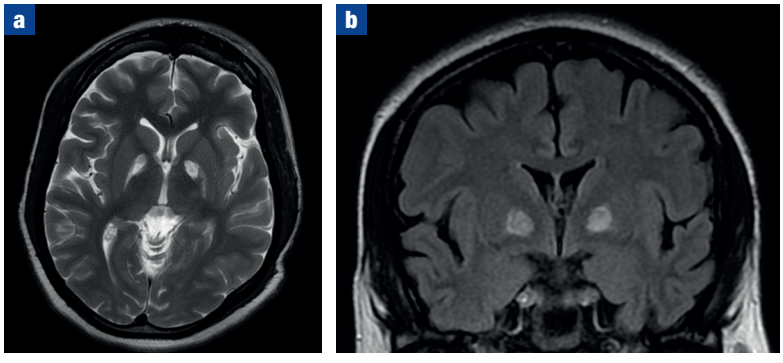

Figure 9. **a.** Axial T2-weighted image demonstrates bilateral globus pallidi infarcts in a case of cocaine misuse. **b.** Coronal fluid-attenuated inversion recovery demonstrates bilateral hyperintensities in the globus pallidi.

Cocaine toxicity

The route of administration of cocaine (either intranasal or inhalation) determines the onset of action, with the inhaled route leading to more rapid CNS accumulation (Tamrazi and Almast, 2012). The drug causes hypertension, tachycardia, vasoconstriction and increased cardiac output. The hydrochloride form of the drug has more haemorrhagic potential whereas the alkaloid counterpart has equal haemorrhagic and ischaemic potential (Tamrazi and Almast, 2012). Cocaine can cause multiple neuropathologies including ischaemia, either involving the watershed areas, the basal ganglia (*Figures 9a* and *b*) or the mesencephalon (Tamrazi and Almast, 2012). There is also increased incidence of reperfusion haemorrhagic infarcts as a result of direct vasospasm. Cocaine can also cause intraparenchymal or subarachnoid haemorrhages, the latter may be secondary to underlying aneurysm or arteriovenous malformation. Vasculitis can also occur (Sharma et al, 2009).

Conclusions

Toxic and acquired metabolic entities may have variable clinical presentation and may create diagnostic uncertainty. Computed tomography and magnetic resonance imaging

KEY POINTS

- Early recognition of characteristic imaging appearances of toxic and acquired metabolic entities will aid in prompt diagnosis and initiation of treatment, especially when there is clinical uncertainty.
- Toxic and acquired metabolic disorders follow a certain radiological pattern with affinity to a specific topographic area, which can help narrow the differential diagnosis.
- Computed tomography and magnetic resonance imaging (particularly diffusion-weighted imaging and fluid-attenuated inversion recovery sequences) are very important in differentiating between various aetiologies in this group.

play an important role in the assessment and early recognition of characteristic imaging features which will allow prompt diagnosis and initiation of treatment. **BJHM**

Conflict of interest: none.

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