CASE REPORT

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The Spectrum of Imaging Findings of Hypoxic-Ischemic Encephalopathy: A Must Know for the Critical Care Specialist

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Abstract

Hypoxic-ischemic injury (HII) is a worldwide cause of mortality and critical neurological disability. Patients may present with acute onset neurological deficit or acute, chronic neurological events. Imaging investigations are essential to make the diagnosis and proper treatment. There are many factors influencing findings on imaging, such as the patient's age that defines brain maturity, duration and severity of injury/insult, type of injury, and timing of imaging investigation. In HII, term and preterm preferentially affects the deep grey matter, with perirolandic involvement seen in later age group. There are less profound injury characteristics such as periventricular white matter injury in preterm neonates, intraventricular haemorrhage and parasagittal watershed territory infarct in term neonates. In the postnatal period, severe HII results in diffuse grey matter insult with associate the sparing of the perirolandic cortex and posterior circulation supplied structures. Profound hypoxic ischaemia insult is characterised in children and adults, injury seen in the deep grey-white matter nuclei, cortices, hippocampi and cerebellum. Imaging modality provides valuable information about the disease and helps in management in acute onset. In critical care settings, it is of utmost importance to have a basic idea about the imaging features of HII to start the appropriate treatment. In most cases, there is a long time gap between the imaging and its reporting by a radiologist, and the time is what a critical care physician often does not have.

Introduction

Hypoxic-ischemic injury (HII) is an encompassing mechanism, which starts during the insult/injury and extends into the recovery stage after resuscitation. Hypoxic-ischemic encephalopathy (HIE) in infants, children, and adults, also known as global HIE, is seen in many instances and often has a death or grievous neurological sequelae. Neuro-imaging with magnetic resonance imaging (MRI) plays an essential role in diagnosis, early interventions workup, evaluation of the severity of the disease, injury extension and follow-ups[1,2,3]. Treatment of HII includes long-term supportive care to prevent the current injury that occurs immediately after the causative insult/injury. Making early diagnosis and mapping out the extension of injury is essential for a better disease prognosis. Many treatments options are available, including administration of excitatory amino acid antagonists and hypothermia. These treatments have a limited time of effectiveness (in a few cases, six hours), so early imaging investigation is critically important for better prognosis and proper treatment[4]. Imaging findings in HII are fluctuating, which depends on brain maturity, duration of insult, the severity of the disease, timing of the investigation, and type of imaging modality used for investigation. On imaging, acute or early insult findings can be subtle and are often ignored. So, for detecting the subtle findings, it is of utmost necessity to know about the pattern of injury in the suspected case of the HII.

Most commonly, HII is caused by low cerebral blood flow (known as ischaemia) and reduced blood oxygenation (known as hypoxaemia). Infants and children commonly have asphyxial events, (i.e., drowning, chocking, or nonaccidental trauma) that causes hypoxic brain ischemic injury, while adults have secondary hypoxia during a cerebrovascular disease or cardiac arrest[5].

Severe asphyxial injury in postnatal infants and young children between 1 - 2 years of age results in injuries to hippocampi, lateral geniculate nuclei, the corpora striata and cerebral cortex (particularly the anterior frontal and parietooccipital cortex), with relative sparing of the thalami and perirolandic cortex[6].

Mild-to-moderate asphyxia in postnatal infants and young children result in watershed zone injury involving the subcortical white matter and cortex.

In adults, mild-to-moderate injury lead to watershed zone infarcts, while the severe insult primarily affects the grey matter structures; cerebellum, hippocampi, cerebral cortex (in particular the sensorimotor and visual cortices, although involvement is often diffuse), the basal ganglia and thalami[7].

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Case series

Case 1

A 13-month-old boy with a history of birth asphyxia and delayed milestones underwent an MRI scan. Diffusion-weighted image (Fig. 1A) demonstrated abnormal high signal intensities with loss of grey-white matter differentiation in bilateral parietal and occipital lobes; FLAIR (Fig. 1B) and T2WI (Fig. 1C) showed subtle hyperintense signal in periventricular white matter in peritrigonal area and hypointense signal in corresponding areas on T1WI (Fig. 1D). The diagnosis was made as mild-to-moderate HII.

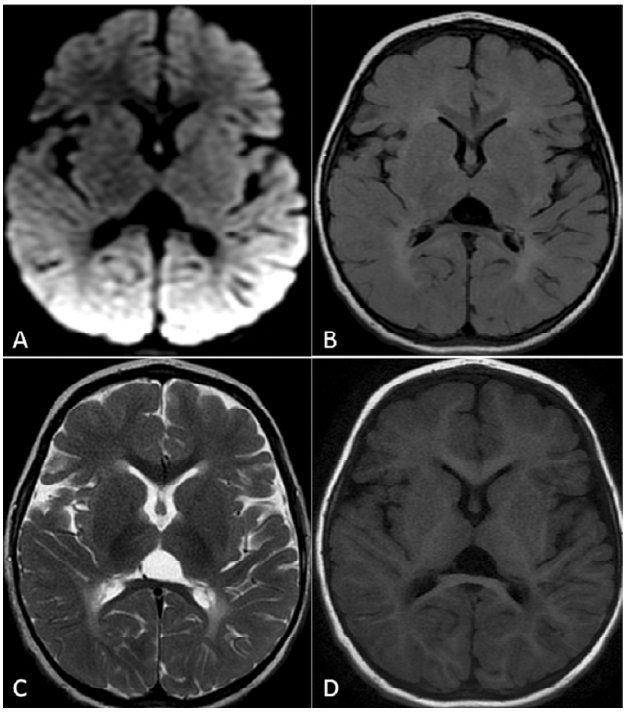


Fig. 1: *A 13-month old boy with a history of birth asphyxia and delayed milestones underwent a magnetic resonance imaging (MRI) scan. (A) Diffusion-weighted image (WI) demonstrates abnormal high signal intensities with loss of grey-white matter differentiation bilaterally in parietal and occipital lobes, (B) Fluid-attenuated inversion recovery and (C) T2WI are showing subtle hyperintense signal in periventricular white matter in peritrigonal area and hypointense signal in corresponding areas on T1WI (D).*

Case 2

Non-contrast computed tomography head in a two-year-old boy who presented with status epilepticus revealed features of chronic mild-to-moderate hypoxic-ischemic injury in the form of areas of cystic encephalomalacia/gliosis, focal loss of white matter and colpocephaly (dilated occipital horns) (Fig. 2).

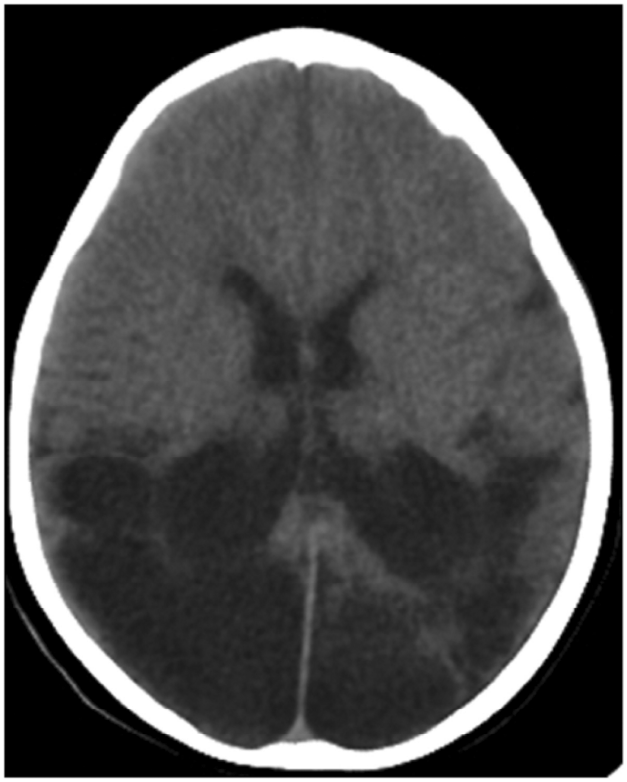
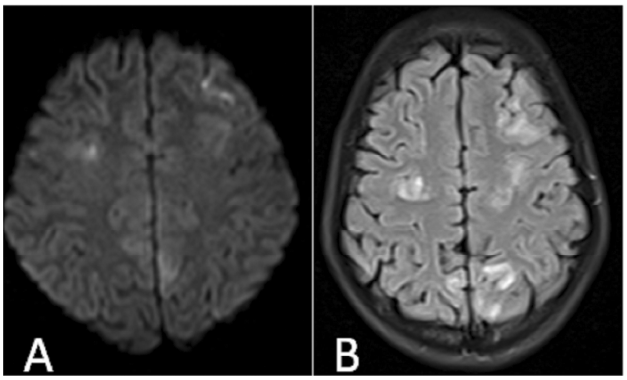


Fig. 2: *Non-contrast computed tomography head (axial) in A 2-year-old term boy showing features of chronic mild moderate hypoxic ischemic injury in the form of areas of cystic encephalomalacia/gliosis, focal loss of white matter and colpocephaly (dilated occipital horns).*

Case 3

A 15-year-old female came to the hospital with complaints of generalised tonic-clonic seizure for the last five hours. The patient underwent an MRI scan in which diffusion-weighted images showed diffuse restriction in subcortical regions of bilateral parietal lobes (watershed territory infarcts) (Fig. 3A). FLAIR (Fig. 3B) and T2 (Fig. 3C) weighted images demonstrated high signal intensities in the corresponding areas suggestive of cytotoxic oedema. A diagnosis of mild-to-moderate global HII was made based on these MRI findings.



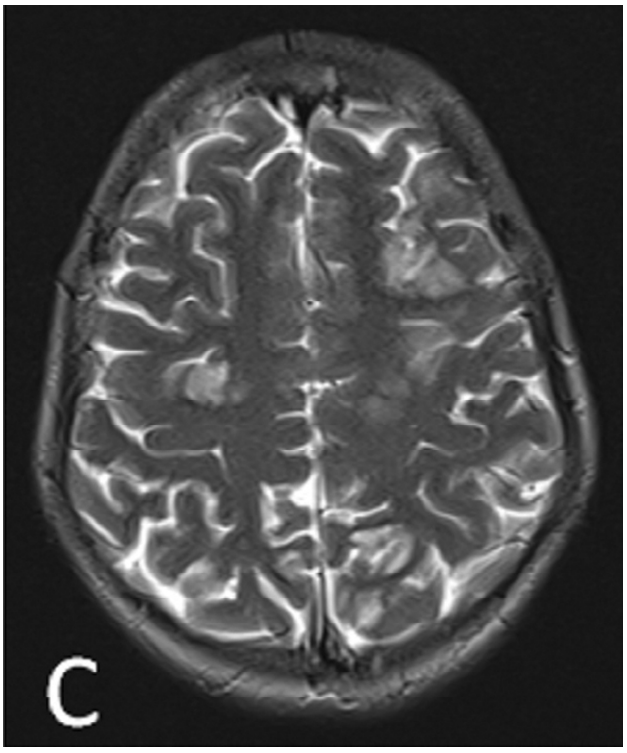
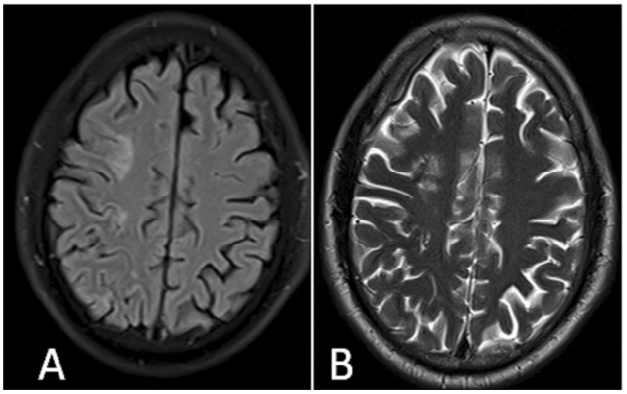


Fig. 3: *A 15-year-old female came to the hospital with complaints of generalised tonic–clonic seizure since five hours. The patient underwent MRI scan (A) Diffusion-weighted image showing diffuse restriction in subcortical regions of bilateral parietal lobes (watershed territory infracts). (B) Axial FLAIR and (C) axial T2 weighted images demonstrate high signal intensities in the corresponding areas suggestive of cytotoxic oedema.*

Case 4

A 32-year-old male presented with seizures and unconsciousness one day and underwent an MRI scan. FLAIR (Fig. 4A) and T2 (Fig. 4B) weighted images demonstrated a high signal area in the right high frontal lobe with restriction on the diffusion-weighted image in the corresponding areas (Fig. 4C). The diagnosis was made as mild-to-moderate HII. In mild-to-moderate global HII in adults result in watershed infarcts which are better evaluated on the diffusion-weighted images.



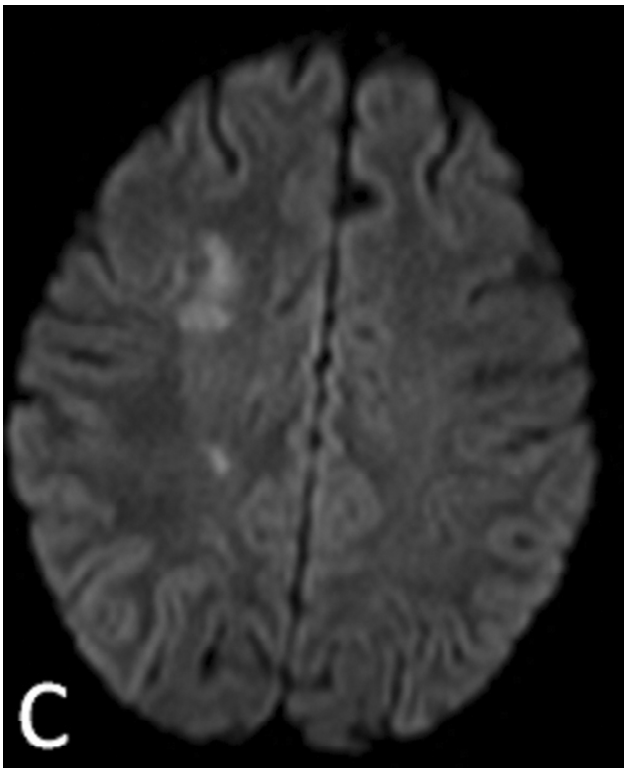


Fig. 4: *A 32-year-old male presented with seizures and unconsciousness since one day and underwent MRI scan (A) axial FLAIR and (B) axial T2 weighted images demonstrate high signal area in the right high frontal lobe with restriction on the diffusion-weighted image in the corresponding areas (C).*

Case 5

A 5-month-old preterm male infant underwent an MRI scan for the complaints of seizures. The FLAIR weighted images (Fig. 5 A and B) revealed extensive bilateral areas of cystic encephalomalacia with moderate dilatation of ventricles. Findings were in favour of typical prolonged and severe grade of HII.

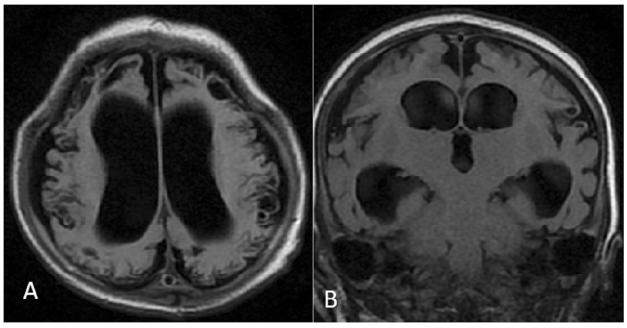


Fig. 5: *A 5-month-old preterm male infant underwent MRI scan for the complaints of seizures (A) axial and (B) coronal FLAIR images reveals extensive bilateral areas of cystic encephalomalacia with moderate dilatation of ventricles.*

Case 6

A seven-month-old boy with a preterm low birth weight birth history presented to the hospital with a cardiac arrest. The patient was admitted under the cardiac department for the treatment of cardiac arrest, and for further workup of his neurological symptoms, the patient underwent a CT scan. Axial unenhanced CT brain showed diffuse cerebral swelling. There was a reversal of the typical grey-white matter attenuation pattern within the cerebral hemispheres (reversal sign) with relative sparing of the cerebellum (white cerebellum sign) (Fig. 6). The diagnosis of severe grade HII was made.

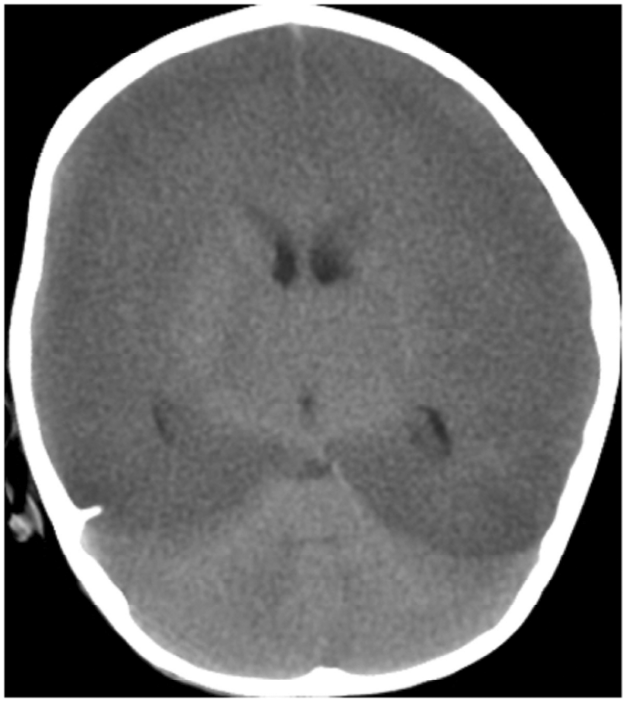


Fig. 6: *A 13-month-old boy with a history of birth asphyxia and delayed milestones underwent a magnetic resonance imaging (MRI) scan. (A) Diffusion-weighted image (WI) demonstrates abnormal high signal intensities with loss of grey-white matter differentiation bilaterally in parietal and occipital lobes, (B) Fluid-attenuated inversion recovery and (C) T2WI are showing subtle hyperintense signal in periventricular white matter in peritrigonal area and hypointense signal in corresponding areas on T1WI (D).*

Case 7

A two-year-old female child bought to the hospital with a history of foreign body inhalation that caused asphyxia, followed by an episode of seizure. In the emergency ward, the foreign body was removed. For further work-up, the patient underwent an MRI scan. Diffusion-weighted image (Fig. 7A) showed symmetrical areas of restricted diffusion in bilateral globus pallid; FLAIR and (Fig. 7B) T2 (Fig. 7C) weighted images demonstrated markedly increased signal intensities in bilateral globus pallidi with low signal intensities on the corresponding T1 (Fig. 7D) Weighted image. These findings suggested the diagnosis of a severe grade HII. MR imaging is the first choice of imaging modality for evaluating children with HII. Diffusion-weighted images demonstrate high signal intensities in the ventrolateral thalamic and basal ganglia (particularly the posterior putamina).

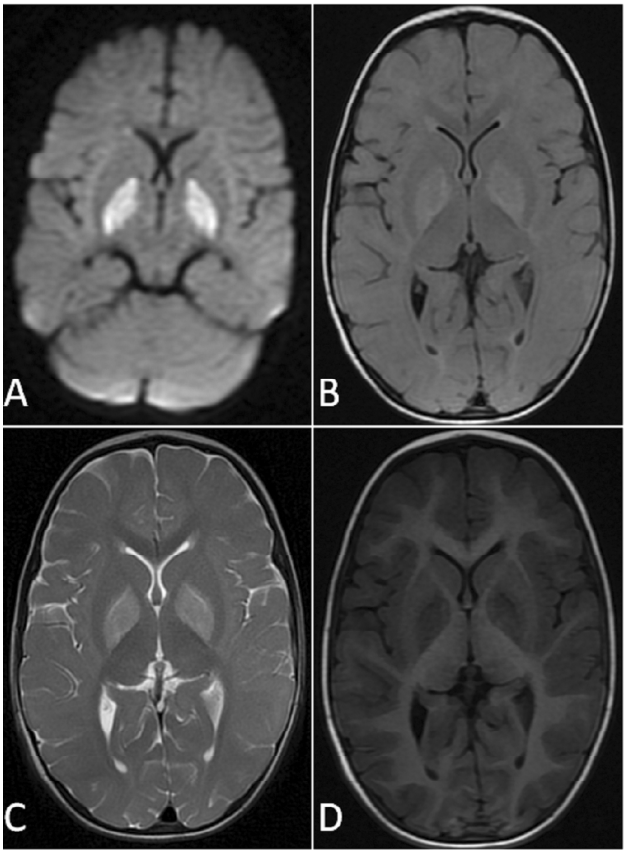


Fig. 7: *A Two-year-old term female child bought to the hospital with seizures and a history of foreign body inhalation that caused asphyxia. The patient underwent MRI scan (A) Diffusion-weighted image shows symmetrical areas of restricted diffusion in bilateral globus pallidi (B) Axial FLAIR and (C) Axial T2-weighted images demonstrating markedly increased signal intensities in bilateral globus pallidi with low signal intensities on corresponding T1-Weighted image.*

Case 8

A 12-year-old female patient who presented with cerebral palsy, presented with seizures. For further work-up for her condition, the patient underwent an MRI scan, where T2W (Fig. 8A), FLAIR (Fig. 8B), and coronal FLAIR (Fig. 8C) images revealed bilateral symmetrical areas of cystic encephalomalacia predominantly involving the occipital lobes, which showed high signal on T2 and suppression on FLAIR weighted images. Bilateral symmetrical areas of gliosis were also observed in the occipital and temporal lobes. DWI (Fig. 8D) images showed no diffusion restriction. There was generalised cortical atrophy with ex-vacuo dilatation

of the ventricular system. The diagnosis was made as sequel to severe grade HII.

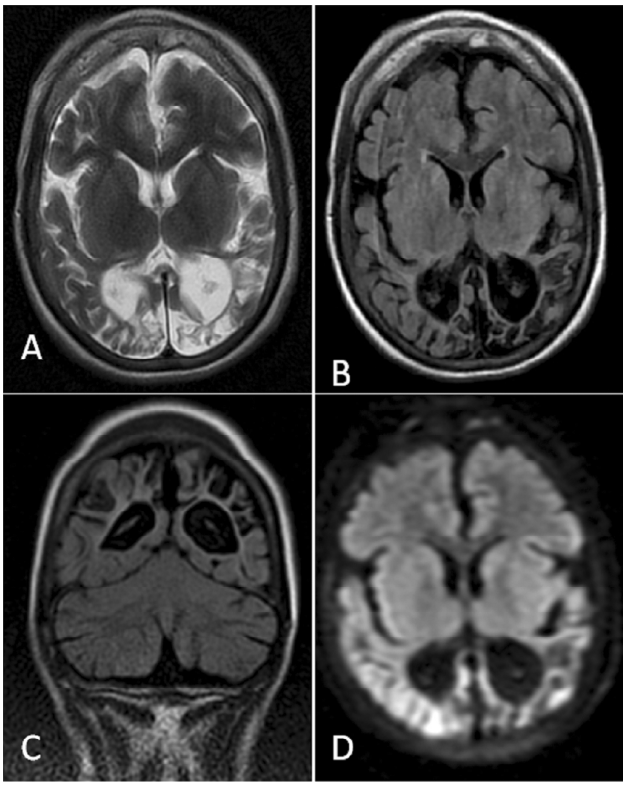


Fig. 8: *MR images of the 12-year-old female patient with cerebral palsy. Axial T2W (A), axial FLAIR (B), and coronal FLAIR (C) images show bilateral symmetrical areas of cystic encephalomalacia predominantly involving the occipital lobes, which show high signal on T2 and suppression on FLAIR weighted images. Bilateral symmetrical areas of gliosis are also seen in occipital and temporal. DWI (C) image shows no diffusion restriction. There is generalized cortical atrophy with ex-vacuo dilatation of the ventricular system.*

Case 9

A 15-year-old male experienced sudden cardiac arrest in which his blood pressure decreased to a non-palpable pulse level for 10 minutes. The patient was admitted to the cardiac department for further work-up, and after stabilisation, he underwent an MRI scan for further evaluation. A diffusion-weighted image (Fig. 9A) revealed restricted diffusion along the cortical and subcortical regions of bilateral cerebral hemispheres. FLAIR (Fig. 9B) and T2W (Fig. 9C) images showed no obvious signal abnormality in the corresponding areas. The diagnosis of acute severe grade HII was made. Acute HII findings are more conspicuous on the diffusion-weighted images than on the FLAIR and T2W images.

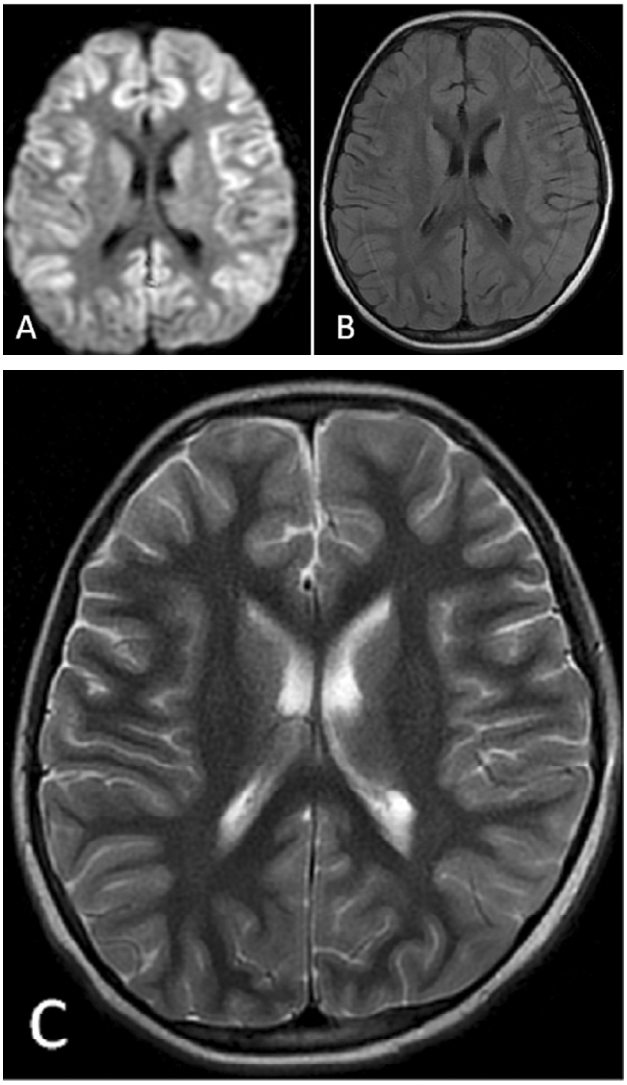


Fig. 9: *A 15-year-old male experienced sudden cardiac arrest in which her blood pressure decreased to non-palpable for 10 min. Diffusion-weighted image (A) shows restricted diffusion along the cortical and sub cortical regions of bilateral cerebral hemispheres. Axial FLAIR (B) and axial T2W (C) images show no obvious signal abnormality in the corresponding areas. Acute HIE findings are more conspicuous on the diffusion-weighted images than on the FLAIR and T2W images.*

Case 10

An 18-year-old female presented with a status epilepticus. The MRI scan demonstrated mild diffusion restriction along the cortical and subcortical regions of bilateral cerebral hemispheres on the diffusion-weighted image (Fig. 10A) and subtle hyperintense signal in periventricular white matter in peritrigonal areas corresponding to FLAIR image (Fig. 10B). Patient admitted in female intensive care unit under neurology department, treated with anticonvulsants and therapeutic hypothermia. A follow-up scan was performed after ten days to assess progression in disease

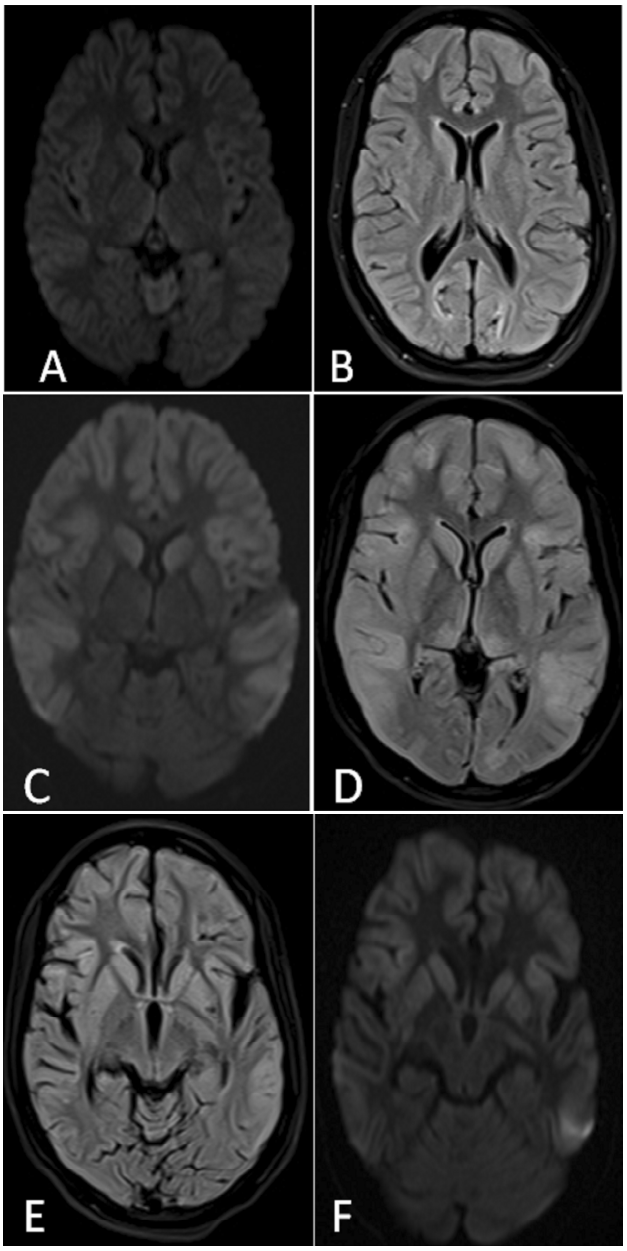


Fig. 10: *An 18-year-old female presented with a status epilepticus. The MRI scan demonstrates mild diffusion restriction along the cortical and sub cortical regions of bilateral cerebral hemispheres on diffusion weighted image (A) and subtle hyperintense signal in periventricular white matter in peritrigonal areas in corresponding FLAIR image (B). Follow-up scan after ten days for assessment of progression in disease and treatment effect. The MRI reveal bilateral symmetrical areas of altered signal intensities seen involving bilateral basal ganglia, inferomedial aspects of bilateral thalami, bilateral frontal, temporal and parietal lobes. There is mild swelling of underlying cortical grey and subcortical white matter that appear hyperintense on axial FLAIR image (C) and show restriction on the diffusion-weighted image (D). Follow-up scan after twenty days for progression of disease and treatment effect where MRI demonstrates bilateral symmetrical abnormal high signals on axial FLAIR image (E) involving caudate nucleus, putamina and cortical gyri showing restriction on the diffusion-weighted image (F). These MRI findings are showings further deterioration in the patient condition.*

and treatment effect. The repeat MRI revealed bilateral symmetrical areas of altered signal intensities involving bilateral basal ganglia, inferomedial aspects of bilateral thalami, bilateral frontal, temporal and parietal lobes. There was mild swelling of underlying cortical grey and subcortical white matter that appeared hyperintense on axial FLAIR image (Fig. 10C) and showed restriction on the diffusion-weighted image (Fig. 10D). The patient continued with the same treatment. The following follow-up scan was done after twenty days to evaluate the disease status, where MRI demonstrated bilateral symmetrical abnormal high signals on FLAIR image (Fig. 10E) involving caudate nucleus, putamina and cortical gyri showed restriction on the diffusion-weighted image (Fig. 10F). These MRI findings corroborate the clinical deterioration in the patient's condition. This case of severe grade HII highlighted the importance of MRI in diagnosis and follow-up for such patients.

Case 11

A 35-year-old male bought to the hospital with the complaints of seizures, cerebrovascular accident, and unconsciousness for one day. The MRI scan demonstrated acute ischemic changes. FLAIR image revealed high signal intensities in both hippocampi (Fig. 11A) and bilateral subcortical white matter showed restricted diffusion (Fig. 11B). This was an another case of severe grade HII.

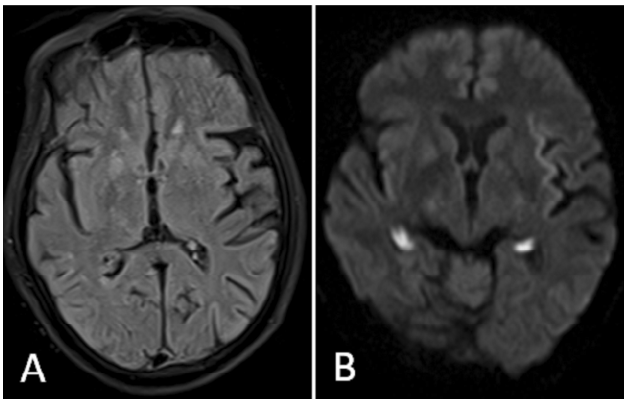


Fig. 11: *A 35-year-old male bought to the hospital with complaints of seizure, cerebrovascular accident, and unconsciousness for one day. The MRI scan demonstrates acute ischemic changes, which are (A) Axial FLAIR image reveals high signal intensities bilateral hippocampi, bilateral subcortical white matter show restricted diffusion on the diffusion-weighted image (B).*

Case 12

In older patients, diffusion-weighted MRI is the earliest modality to detect or evaluate the injury within a few hours after the insult. Here we discuss a case of a 44-year-old

male who had respiratory failure following oesophageal perforation. The patient was treated with emergent medical stabilisation and sent for an MRI scan for further evaluation. MRI scan showed restriction diffusion along the frontal, temporal-parietal and occipital cortices and the hippocampi bilaterally. Extensive bilateral hemispheric cortical oedema more in the occipital lobes was seen on the – attenuated inversion – recovery (FLAIR) image (Fig. 12A and B). The diagnosis was made as severe grade HII.

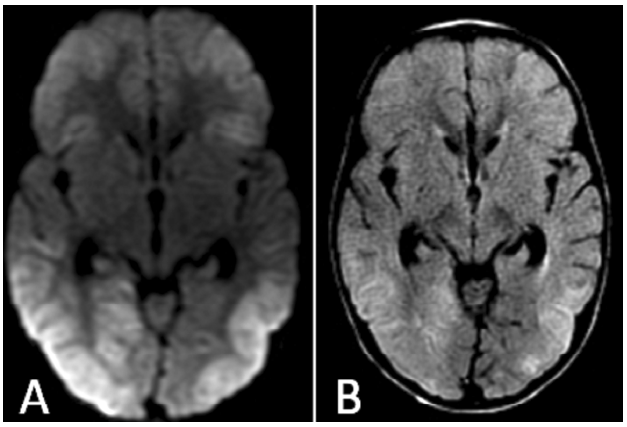


Fig. 12: *A 44-year-old male had respiratory failure following oesophageal perforation. He underwent an MRI scan: (A) diffusion-weighted image shows high signal intensity areas along the frontal, temporal-parietal and occipital cortices, and the hippocampi bilaterally. Extensive bilateral hemispheric cortical oedema more in the occipital lobes is seen on the axial fluid-attenuated inversion – recovery (FLAIR) image (B).*

Treatment

The prognosis of HIE is very challenging because of the decisions to withdraw life-supporting therapies which define its prognosis. Therapeutic hypothermia stands to be very effective in limiting the neurological damage. After the asphyxial event or brain injury, the outcome of resuscitated patients is improved by providing mild-to-moderate hypothermia (temperature 32° to 34° C) in staring hours. Treatment has to start as soon as possible after stabilising the patient and maintaining a low temperature for 48 hours. The suggested protocol is to maintain a goal temperature of 32° to 34° C for 12 or 24 hours, followed by gradual rewarming (0.25° C/hour). The most common advantage of therapeutic hypothermia is reduced intracranial pressure which also reduces the seizure frequency. Therapeutic hypothermia causes shivering, so sedation (and potentially neuromuscular blockade) may be required to facilitate cooling. All our patients were managed using therapeutic hypothermia and anti-epileptics as and when required. Some of the adverse effects of therapeutic hypothermia were also noted in some of the cases like impaired coagulation, arrhythmia, hyperglycaemia, hypovolaemia, hypomagnesaemia, hypophosphataemia, hypokalaemia and increased risk of infection. Supportive and symptomatic treatment was administered as per the patient status and underlying disease profile. In our case series the mortality was zero; however, morbidity in the form of permanent residual neurological deficit and requirement of lifelong drug support remained high.

References

1. Barkovich AJ, Baranski K, Vigneron D *et al*. Proton MR spectroscopy for the evaluation of brain injury in asphyxiated, term neonates. *AJNR Am J Neuroradiol* 1999; 20: 1399-1405.
2. Grant PE, Yu D. Acute injury to the immature brain with hypoxia with or without hypoperfusion. *Radiol Clin North Am* 2006; 44: 63-77, viii.
3. Christophe C, Fonteyne C, Ziereisen F *et al*. Value of MR imaging of the brain in children with hypoxic coma. *AJNR Am J Neuroradiol* 2002; 23: 716-23.
4. Vannucci RC, Perlman JM. Interventions for perinatal hypoxic-ischemic encephalopathy. *Pediatrics* 1997; 100: 1004-14.
5. Biagas K. Hypoxic-ischemic brain injury: advancements in understanding of mechanisms and potential avenues for therapy. *Curr Opin Pediatr* 1999; 11: 223-8.
6. Barkovich AJ. MR and CT evaluation of profound neonatal and infantile asphyxia. *AJNR Am J Neuroradiol* 1992; 13: 959-72.
7. Arbela´ez A, Castillo M, Mukherji S. Diffusionweighted MR imaging of global cerebral anoxia. *AJNR Am J Neuroradiol* 1999; 20: 999-1007.