

CASE REPORTS

Hypoglycaemic Brain Injury: A Case Report

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Abstract:

Neurological features of severe hypoglycemia range from reversible focal deficits to irreversible coma or death. Diffusion weighted MRI of brain image is a useful tool in evaluating profound hypoglycemic brain injuries. We report a case of 27 year old male who died from brain injuries following an episode of prolonged hypoglycemia. We here discuss the neuropathological and diffusion-MRI changes of hypoglycemic brain injuries and its prognostic importance.

Keywords: Hypoglycemia, Brain Injuries, Diffusion Magnetic Resonance Imaging, Cerebral Cortical Necrosis, Prognosis.

Introduction:

Hypoglycemic brain injury presents with diverse neurological manifestation ranging from reversible brain injury to profound brain damage resulting in death. Out of many radiological sequence of Magnetic Resonance Imaging of brain, Diffusion weighted image is a unique brain image for diagnosing hypoglycemia as well as differentiating it from hypoxic brain injury and also to predict outcome depending on the severity of brain damage. We here report a case of profound hypoglycemic brain injury as evidenced by neuroradiological findings.

Case Report:

A young boy of 17 year old, was admitted in the Intensive Care Unit (ICU) of Square Hospital LTD through Emergency on 5th April of 2012 after being transferred from another hospital with the complaints of decreased level of consciousness for 12 hours, fever and shortness of breath for the same duration and history of multiple drug ingestion 24 hours prior to admission. He was a known case of Yaba and Intravenous drug abuser for last 8 months. According to his parents he took multiple drugs,

used by his mother (which included gliclazide, metformin and antihypertensive) for deliberate self harm following a familial conflict one day before admission. Apart from drug abuse he had no known medical illness. He was an A- level student and was the only child of his parents.

On arrival, the patient's physical exam was unremarkable except for his neurological examination. His Glasgow Coma Scale was 7 (E1 V1 M5), his pupils were constricted, round, and non reactive to light and there were no corneal reflexes and Doll's eye reflexes were present. There was decreased tone throughout all four extremities. Neck rigidity and Kernig's sign were negative. Blood pressure was 120/80 mmHg, pulse 75 beats/min, respiratory rate 20 breaths/min, and temperature 102F. The blood glucose was found to be 1.6 mmol/L, which lead to immediate administration of 10% glucose with a bolus followed by continuous infusion. On Baseline Arterial Blood Gas analysis report his arterial pH was 7.402, PaO₂ 51.3 mmHg, PaCO₂ 30.1 mmHg, base excess-0.9 mmol/L, and oxygen saturation 88.7%. He was intubated and mechanical ventilation commenced. S. Electrolytes

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were normal. Other blood chemistry results (including Calcium, SGOT, SGPT, Albumin, ALP, Trop I, Gamma GT, PT, aPTT, S. Creatinine, Blood Urea) were unremarkable except for Magnesium (1.2 reference range 1.7- 2.4 mg/dl, CK-MB (68 U/L ref <16), CPK (587 U/L, reference range: 55-170 for male). His Hb% was 14.1 g/dl and total count of WBC was 25.7 K/mL, neutrophil count 92.7%. Toxicology screening was negative for opiate, amphetamine, barbiturates but benzodiazepine was at upper limit of the normal. Blood and Urine, sputum culture revealed no growth. Viral screening including Hepatitis B, C, HIV, and Herpes were negative. Computed tomography scans showed no findings of acute cerebrovascular injury except for diffuse cerebral and brainstem edema. MRI brain revealed on day 2 showed hyper-intense lesions along the cortices of both cerebral hemispheres signifying restricted diffusion on DW1, while on FSET2 and T2 FLAIR images of the same areas also showed hyperintensities. Similar signal intensities were noted in the right basal ganglia and both thalami with resultant mass effect causing mild ventricular effacement including lateral and 4th ventricle. Adjacent sulcal effacement, mild

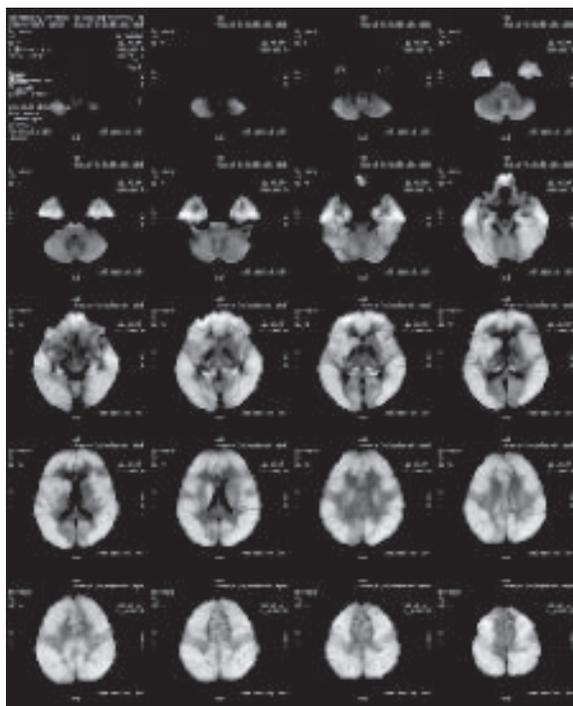


Fig.-1:

cerebellar tonsillar herniation and compression over brain stem were also noted. On T2 flair image hyperintensities are noted along the frontoparietal subarachnoid space on both sides, may be due to supplemental oxygen. He was put on intravenous acyclovir empirically as a case of Acute Viral Encephalitis and intravenous broad spectrum antibiotic to cover possible sepsis. He was also treated with intravenous Mannitol to treat brain edema. Despite intensive medical treatment in ICU, the patient's neurological condition failed to improve. The patient died of cardio- respiratory failure on day 11. Postmortem examination was not followed.

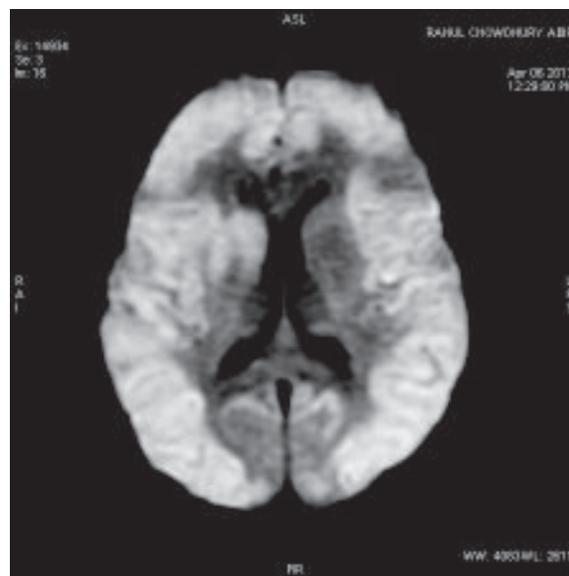


Fig.-2:

Discussion and literature review:

Hypoglycemia is the sudden decrease in serum glucose level <50 mg/dL, and the organ systems that manifest the signs and symptoms are the central and autonomic nervous system.¹ Diverse neurologic manifestations of hypoglycemia have been reported frequently. These neurologic symptoms range from reversible focal neurologic deficits, profound memory loss, transient motor deficits, to permanent dysfunction, persistent vegetative state or death in 2-4%¹⁻³. Hypoglycemia can be induced by overuse of insulin or oral hypoglycemic agents, undiagnosed insulinoma, or other medical diseases such as sepsis, or renal, or hepatic failure¹.

Among different brain image sequences Diffusion weighted image (DWI) of Magnetic Resonance Image of brain is a special technique that can measure the alteration of the diffusion of water within the extracellular space and between intracellular and extracellular spaces. These diffusion alterations are encountered not only in acute ischaemia but also in hypoglycemia itself¹. The commonly affected sites in severe hypoglycemia are Cerebral cortex, Hippocampus, and Basal Ganglia as demonstrated in Neuropathological studies; however, the cerebellum and brain stem are usually spared. High-intensity signals are also noted in numerous different locations of the brain like the internal capsules, pons, splenium of the corpus callosum, corona radiata, and cortex of the frontal or parietal or occipital lobe in Diffusion weighted image of patients with acute hypoglycemia^{1,2,4}.

The pathogenesis of hypoglycemic brain injury still remains unclear. Some proposed pathogenesis for diffusion restriction in hypoglycemic encephalopathy includes the following: 1) energy failure, 2) excitotoxic edema, and 3) asymmetric cerebral blood flow. Neurochemical changes are induced by hypoglycemia. Glucose deprivation leads to arrest of protein synthesis in many regions, incomplete energy failure and loss of ion homeostasis, cellular calcium influx, and intracellular alkalosis. Consequently, neuroactive amino acid (aspartate) release into the extracellular space occurs and results in selective neuronal necrosis, predominantly in the cerebral cortex, caudoputamen, and hippocampus¹. However, protein synthesis in the cerebellum, brain stem, and hypothalamus remains unaffected because of the greater activity of the glucose transport mechanisms. Excitotoxic edema is a cytotoxic form due to increased extracellular glutamate. The presence of glutamate leads to calcium and sodium entry into the cell and induces apoptosis. In contrast to cytotoxic edema, excitotoxic edema does not imply neuronal damage, because glutamate induces edema of glial cells and myelinic sheaths might protect axons from intracellular edema and irreversible damage. In addition, glutamate reuptake systems are not impaired in hypoglycemia. When

hypoperfusion complicates hypoglycemia, the brain is not exposed to an equal fall in perfusion. Due to the focal loss of autoregulation, the frontal and parietal lobe areas have grossly decreased cerebral flow, whereas the cerebellum and brain stem show almost no fall in local cerebral blood flow^{1,5-9}.

Hypoglycemia constitutes a unique metabolic brain insult. Hypoglycemic effects on the brain are derived mostly from animal studies. Although infarction and hypoglycemia exhibit similar findings on Diffusion weighted image, profound differences are revealed by the neurochemical analyses. Cellular redox system are reduced in ischemia but are oxidized in hypoglycemia, brain pH is decreased in ischemia due to the formation of lactic acid, it is increased in hypoglycemia due to the formation of ammonia from deamination of amino acids, the absence of lactic acid, and the consumption of metabolic acid. In hypoglycemia, adenosine triphosphate levels are still more than one-third of normal but less than 5% in ischemia¹⁰. Energy failure is considerably less severe in hypoglycaemia than in ischemia as production of lactic acid during hypoglycaemia is not possible due to glucose deficiency^{4,5,6,10}. If prevailing symmetric superficial laminar necrosis of the cerebral cortex is demonstrable, then hypoglycemic brain damage is more likely, while symmetric superficial laminar necrosis after ischemia is less often seen⁴. Furthermore, hypoglycemia is generalized but not dependent on vascular territories, resulting in a distribution of lesions that does not follow any vascular territory⁴.

Post-cardiac arrest encephalopathy share similar findings with hypoglycaemic encephalopathies. Two major differences between hypoglycemic and ischemic encephalopathies have been proposed in one study: (1) serial MR images showed minor hemorrhages in the localized lesions of ischemic encephalopathy but not of hypoglycemic encephalopathy, possibly from tissue acidosis leading to alterations of cerebrovascular permeability and (2) symmetrical thalamic lesions of abnormal intensity on CT and MR images exist in post-cardiac arrest encephalopathy but seem absent in hypoglycemic encephalopathy¹¹.

Diffusion restricted image of MRI of brain is also valuable in predicting outcome. Several literature reports that reversibility of hyper-intense lesion in diffusion-MRI indicates the good prognosis², whereas involvement of the basal ganglia and diffuse and extensive injury predicts a poor neurologic outcome in patients with hypoglycemic injuries^{2, 11, 13}. MR imaging in our patients showed involvement showed hyper-intense lesions along the cortices of both cerebral hemisphere signifying restricted diffusion on DW1, while on FSET2 and T2 FLAIR images the same areas also show hyperintensities. Similar signal intensities are noted in the right basal ganglia and both thalami. Resultant mass effect is causing mild ventricular effacement including lateral and 4th ventricle. Adjacent sulcal effacement, mild cerebellar tonsillar herniation and compression over brain stem are also noted. On T2 flair image hyperintensities are noted along the frontoparietal subarachnoid space on both sides, may be due to supplemental oxygen. Our patient had involvement of the cortex, and all cortical lesions were located in the frontal and parietal lobes. The MR imaging findings of our patient were in accord with the proposed mechanisms.

Conclusion:

In hypoglycemic brain injuries neurological deficits and radiologic images are variable. Diffusion weighted image of MRI of brain is a neuroimaging technique that can not only diagnose a case of hypoglycemia but also predicts the outcome and differentiate it from hypoxic brain injury by the characteristic findings of hypoglycemic brain injury. So in case of a suspected hypoglycemic brain injury a Diffusion weighted image of MRI of brain should be requested to see the severity of brain damage as well as to exclude hypoxic ischemic encephalopathy and also to predict outcome.

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