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Case Report

Acute Hyperammonemic Encephalopathy: A Reversible Encephalopathy

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ABSTRACT

Acute hyperammonemic encephalopathy is a rare toxic encephalopathy caused by accumulated plasma ammonia. A few literatures are reported about MRI findings of acute hyperammonemic encephalopathy. It is different form of the well known chronic hepatic encephalopathy. The clinical symptom and MRI findings of acute hyperammonemic encephalopathy can be reversible with appropriate treatment. Acute hyperammonemic encephalopathy involves cingulate cortex, diffuse cerebral cortices, insula, bilateral thalami on diffusion-weighted imaging (DWI), and fluid-attenuated inversion-recovery. Acute hyperammonemic encephalopathy might mimic hypoxic-ischemic encephalopathy because of their similar sites involvement. We are reporting a case of acute hyper-ammonemic encephalopathy. MRI of present case report showed restricted diffusion at the cingulate cortex, cerebral cortices, insula, and bilateral dorsomedial thalami on diffusion weighted imaging. The patient was treated successfully and discharged. In this report, we present characteristic features of DWI in acute hyperammonemic encephalopathy.

Keywords: Acute hyperammonemic encephalopathy, Hepatic encephalopathy, Magnetic Resonance Imaging (MRI), Diffusion Weighted Imaging (DWI).

INTRODUCTION

Acute hyperammonemic encephalopathy results from hyperammonemia associated with acute liver failure. Acute hyperammonemic encephalopathy can cause sudden altered mentation or even abrupt progression to a state of coma. Because acute hepatic encephalopathy is a clinical diagnosis, imaging studies were rarely performed until recently. There is a specific pattern of imaging findings on acute hyperammonemic encephalopathy. According to recent studies, the most commonly involved sites of acute hyperammonemic encephalopathy are insula, diffuse cerebral cortex, cingulated cortices, and bilateral thalami. [1,2] Additional sites involved are sub cortical white matter, basal ganglia, and brainstem. However, these are not common sites of involvement. Our patient had classic changes of acute hyperammonemic encephalopathy on diffusion weighted imaging on MRI. MRI findings can give clues for diagnosis of acute hyperammonemic encephalopathy. [2,3] Acute hyperammonemic encephalopathy can mimic hypoxic-ischemic encephalopathy (HIE) because both involve diffuse cerebral cortex and bilateral thalami. [4] However in the setting of acute elevation of ammonia levels, one

should consider possibility of acute hyperammonemic encephalopathy.

CASE REPORT

A 50-year-old male patient brought by relatives with history of unconsciousness. The patient was a chronic alcoholic for many years. On admission, the patient was vitally stable with saturation level of oxygen (SpO_2) of 96%. Clinically patient was unconscious, no response to deep pain with depressed deep tendon reflexes, and obviously normal cranial nerves. Plantar response was not elicitable. There was no obvious neck stiffness (meningeal signs). Cardiovascular system, respiratory system and per abdominal examination were unremarkable. Laboratory testing showed serum ammonia level of 316 µmol/L (normal range: 23-90µmol/L). Haemoglobin, total WBC count, platelet count were within range. Liver function tests [AST-42 I/U and ALT-27 I/U, total bilirubin 1.1 mg prothrombin time] were normal. Other biochemical parameters including random blood sugar, kidney function tests and electrolytes were within normal limits. Urine examination was unremarkable. Chest radiogram and ECG were normal. Fundoscopic examination was normal. CSF study was normal. MRI Brain was performed. On fluid attenuated inversion-recovery (FLAIR) images, there was no significant abnormality. But diffusion-weighted imaging (DWI) showed symmetrical bilateral increased signal intensities at the insula, cingulated cortex, and bilateral dorso-medial thalami. Apparent diffusion coefficient (ADC) maps confirmed reduced diffusion. [Figure 1] The patient's hyperammonemia was treated with conservative management. On 3rd day patient became fully conscious and on 8th day patient was discharged from the hospital in conscious and ambulatory state.

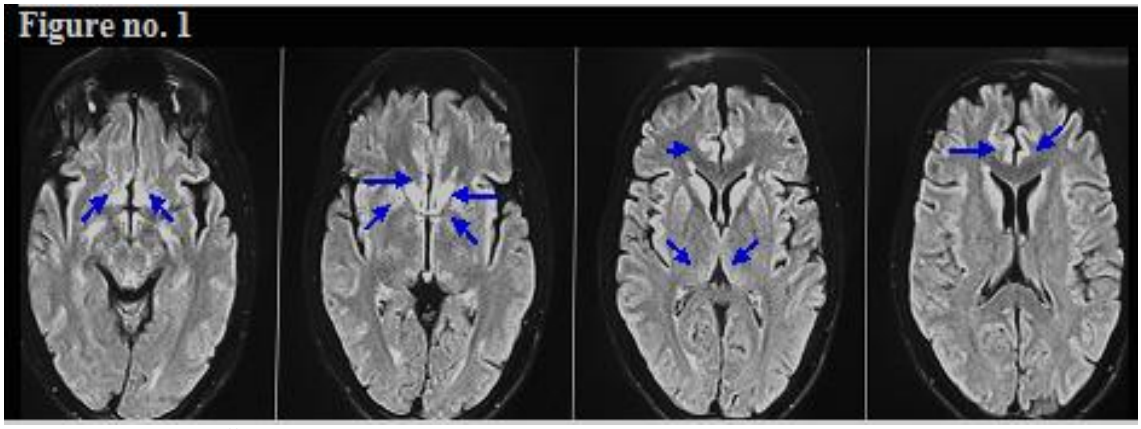

Figure 1: MRI brain on diffusion-weighted imaging (DWI) showed symmetrical bilateral increased signal intensities at the insula, cingulated cortex, bilateral dorso-medial thalami. Apparent diffusion coefficient (ADC) maps confirmed reduced diffusion

DISCUSSION

Symptoms of acute hyperammonemic encephalopathy includes sudden onset of drowsiness and seizures. Untreated hyperammonemia can lead to permanent and irreversible brain injury, therefore, early diagnosis and prompt treatment of hyperammonemia is crucial to prevent long-term sequelae and to avoid fatal complications such as brain oedema, herniation, and even death. [1,2,5] Our patient was diagnosed and treated in appropriate time and made a full recovery without any long-term sequale. Ammonia is produced in gastrointestinal tract as a by-product of protein digestion and bacterial metabolism. It is metabolised in the liver to urea through urea cycle. [2] When the metabolic capacity of liver is overwhelmed, elimination depends on kidneys, skeletal muscle, and even brain. In the brain, ammonia affects the excitatory glutaminergic N-methyl-D-aspartate receptors and gamma-amino

butyric acid receptors. This pathway makes subsequent cell swelling and even apoptosis. [1,2,6] The most common cause of hyperammonemic encephalopathy is acute liver failure. Other aetiologies are porto-systemic shunt surgery, drugs (valproic acid, narcotics), urinary tract infection with urease-producing organism, uretero-sigmoidostomy, parenteral nutrition, bone marrow transplantation, solid organ transplantation, severe exertion, septic shock and inborn errors of metabolism. [2,3,7] The clinical presentation of hyperammonemic encephalopathy can be varied and includes irritability, agitation, drowsiness, coma and occasionally paradoxical seizures. There is a good correlation between fall in serum ammonia level and clinical improvement. MRI findings of chronic liver disease show bilateral hyper intensities of the globus pallidus, subthalamic region and midbrain on T1-weighted images. [1,2] Radiological findings of acute hyperammonemic encephalopathy are less well reported. [1,2,4] U-King-Im *et al* reported 4 adult patients with acute hyperammonemic encephalopathy with restricted diffusion involving insula, cingulate cortex and diffuse cerebral cortex. [2] Arnold *et al* also reported a case of diffuse cortical necrosis secondary to hyperammonemia. [8] In present case report MRI showed restricted diffusion at diffuse cerebral cortices, insula and the cingulate cortex. It is unclear why the insula and cingulate cortex are particularly susceptible to toxic effects of ammonia. [1] Choi *et al* reported severe case of cortical laminar necrosis after hyperammonemic encephalopathy. [4] Involvement of brain regions other than the insula or cingulate cortex, diffuse cerebral cortices are more variable. Other areas are deep gray matter such as bilateral thalami, basal ganglia, subcortical white matter, periventricular white matter, and brainstem. McKinney *et al* found that, thalamic involvement was present in 85% of 20 patients on FLAIR and in 70% of 20 patients on DWI. [3] They reported that thalamic involvement was very common. Rosario *et al* and McKinney *et al* reported that, the involved regions were thalami on DWI. [1,3] Dorsomedial thalami lesions are also known as predominant site of Koraskoff's syndrome. Koraskoff's syndrome results from conditions of malnutrition and vitamin deficiency (thiamine) due to chronic alcoholism. Chronic alcoholic patients have a tendency to hyperammonemia due to repeated liver damage. It is suggested that lesions of dorsomedial thalami in Koraskoff's syndrome might be associated with patient's previous subclinical hyperammonemic encephalopathy. [6] According to McKinney *et al* the plasma ammonia level correlate with clinical outcome. It was suggested that MRI features only moderately correlated with clinical outcome. [3] Early vague clinical manifestations of hyperammonemia such as anorexia, lethargy, disorientation can be seen with lower plasma ammonia levels of 60µmol/L. Early MR imaging changes can be seen at such lower levels. U-King-Im *et al* reported a patient with ammonia levels of 55µmol/L (normal range: 0-34µmol/L), the patient in that case had extensive MR imaging changes and made an excellent recovery without significant neurologic deficit with proper treatment. [2,9] Our patient was treated with I.V fluids, rifaximin for gut sterilization, and lactulose and made full recovery. Acute hyperammonemic encephalopathy can cause severe long term sequelae, such as intellectual disability or even death. However, if aggressive treatment is instituted, cortical changes in hyperammonemic encephalopathy can be potentially reversible. [1,2,5] Acute hyperammonemic encephalopathy may be misinterpreted as hypoxic-ischemic encephalopathy (HIE) due to their similar involving sites. Hypoxic-ischemic encephalopathy involves diffuse cerebral cortex and thalamus. Arnold *et al* regarded

acute hyperammonemic encephalopathy as HIE initially. However, with combination of plasma ammonia level and absence of hypoxic event, they made early diagnosis of acute hyperammonemic encephalopathy**.** [8] It is very important to make differential diagnosis, because acute hyperammonemic encephalopathy is reversible. However, in contrast to acute hyperammonemic encephalopathy, HIE is irreversible. Knowing predominantly involving sites of HIE and considering patient's medical history, laboratory findings can make precise diagnosis of acute hyperammonemic encephalopathy. At present, the pharmacologic treatment of choice in patients with hyperammonemic encephalopathy is the administration of non-absorbable disaccharides (lactulose or more recently lactitol). [10] Rifaximin, a non-absorbable rifamycin derivate, exhibits wide in vitro and in vivo antimicrobial activity against both aerobic and anaerobic gram-positive and gram-negative microorganisms. [11,12] Furthermore, unlike other rifamycins, rifaximin is practically unabsorbed by the gut, thereby allowing the antibiotic to reach high concentrations in the intestinal tract and to remain in the faeces in its active form. [13] Patient in present case report had typical neuro-imaging findings of HE and was managed conservatively and responded well with near total recovery.

CONCLUSIONS

Present case report revealed reversible aetiology of metabolic encephalopathy in chronic alcoholic patient. It is important to make early diagnosis of acute hyperammonemic encephalopathy as well as differential diagnosis; because acute hyperammonemic encephalopathy is a reversible if diagnosed and managed early otherwise it is fatal condition. There are four main predominant sites involved in acute hyperammonemic encephalopathy: insula, cingulate cortex, diffuse cerebral cortex, and dorsomedial bilateral thalami.

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