Acute and Chronic Magnetic Resonance Imaging (MRI) Head Scan Changes in Adult Hyperammonemic Encephalopathy: A Case Report

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Abstract

Hyperammonemic encephalopathy is a type of an acute toxic-metabolic encephalopathy resulting from elevated plasma ammonia levels. Increased ammonia may be due to a variety of etiologies, at times leading to acute and chronic brain changes. Acute and chronic clinical and radiographic changes are well documented in the pediatric population, however, there is a paucity of reports pertaining to chronic changes in the adult population. In some adult patients, complete resolution of acute changes or mild cerebral atrophy has been reported differing from the pediatric population where significant chronic changes including neurologic devastation have been documented. Furthermore, hyperammonemia in adults is often attributed to hepatic disorders or typically thought of triggers such as use of Depakote, whose absence may at times be associated with late detection. We present a patient with acute hyperammonemic encephalopathy secondary to newly diagnosed Ornithine Transcarbamylase (OTC) deficiency followed over a 3-year period with persistent cognitive dysfunction and significant Magnetic Resonance Imaging (MRI) of the head abnormalities. Hyperammonemic encephalopathy should be confirmed by serologic testing, however, in the event, that brain imaging is obtained prior to this, certain features of MRI of head should raise one’s suspicion and prompt early diagnosis and management. This case will emphasize the need for prompt diagnosis, identification of the causes and treatment of acute hyperammonemic encephalopathy especially in the absence of commonly implicated causes, to mitigate further brain injury as well as hopefully avoiding a recurrence.

Case Presentation

A 39-year-old man with no notable past medical history was admitted with altered mental status. His brother had died at 14 years of age following a confusion episode of an unclear etiology, while his sister was in good health. At the time of admission, he was married with two healthy sons and worked full-time as an operations manager with no limitations. Two weeks prior to admission, following a sick contact, he developed a sore throat, and cough. Initially not responding to cefuroxime, the fever and sore throat resolved with dexamethasone with clindamycin, however, four days prior to admission, he became progressively tired, spending long hours in bed, “fuzzyheaded”, confused with word finding difficulty and poor memory of recent events. At the local emergency room, he was found to be sleepy with paucity of movements prior to becoming unresponsive with no focal weakness. Initial work up including, a complete blood count (CBC), comprehensive metabolic panel (CMP), toxicology, urinalysis showed elevated platelets 54110×9/L, ammonia 249 umol/L, relatively normal liver function tests alkaline phosphatase 59 U/L, aspartate transaminase (AST) 17 U/L, alanine transaminase (ALT) 41 U/L, AST/ALT ratio 0.4, albumin 4.3 g/dl, total bilirubin 0.7 mg/dl, and slightly elevated prothrombin time 14.4 seconds and international normalized ratio (INR) 1.4. A head CT scan showed effacement of the sulci, without
The patient improved gradually to the point of carrying out activities of daily living, however, not to the pre-illness state. There was no pre-illness intelligent quotient but the patient could resume his prior employment. The patient had serial MRI head scans that demonstrated acute changes with interval development of diffuse cortical atrophy (Figures 1B-E).

**Discussion**

Acute toxic-metabolic encephalopathy is an acute condition of global cerebral dysfunction in the absence of primary structural brain disease [1]. There are several causes of encephalopathy including elevated plasma ammonia levels. All forms of acute toxic-metabolic encephalopathy interfere with the function of the ascending reticular activating system and/or its projections to the cerebral cortex, leading to impairment of arousal and/or awareness [2]. Most toxic metabolic encephalopathies are reversible, making their prompt recognition and treatment important, however, certain metabolic encephalopathies, such as sustained hypoglycemia, thiamine deficiency (Wernicke's encephalopathy), may be associated with permanent structural brain damage [3].

Elevated ammonia levels can result from impaired endogenous hepatic detoxification (such as liver dysfunction, inborn urea cycle disorders and urea cycle suppressors like antiepileptic medications) or increased production of ammonia (such as overgrowth of urease-producing bacteria in the intestine or urinary tract). Most often in the adult population, liver dysfunction is implicated, however, as previously published other etiologies need to be considered especially in the absence of liver disease [4,5]. Prior publications show that ammonium ions penetrate the brain, reacting with astroglia-specific enzyme, glutamine synthetase to form glutamine whose osmotic action appears to be responsible for brain edema, intracranial hypertension, and cerebral hypoperfusion, particularly affecting the cingulate gyrus and insular cortex seen on MRI head scans, however permanent impairment, can occur [9,10]. It is therefore crucial to diagnose encephalopathy and its etiologies for optimal management and prevent acute and long term organ injuries [11]. The presentation of hyperammonemic states varies and is often nonspecific with clinical presentation including nausea, vomiting, protein intolerance, behavior changes, lethargy, ataxia, seizures, and coma typically presenting and precipitated by catabolic stress, infections, dehydration, protein load, surgery, childbirth, and gastrointestinal bleeding.

To identify hyperammonemic states one must test for ammonia levels. In our patient, checking and following ammonia levels was vital for proper treatment. Whereas ammonia is easily checked in patients with typical etiologies such as liver disease or use of certain medications, it’s vital that health care providers consider checking ammonia in unexplained encephalopathic patients. In situations where brain imaging studies may have been obtained first, one has to be able to recognize patterns suggestive of hyperammonemic encephalopathy. In our patient, the initial head CT scan imaged showed sulcal effacement, raising concerns for increased intracranial pressure. MRI scans of the patient’s head later showed cortical signal abnormalities (restricted diffusion) maximal in the cingulated gyrus and insular cortex (Figure 1A) features previously reported [9,10] in hyperammonemia related encephalopathy. Recognition of such patterns should prompt health care providers to consider hyperammonemonic encephalopathy and pursue prompt appropriate.
testing and management. Elevated ammonia levels in encephalopathic patients should prompt timely intervention to enhance its clearance w/wo decreasing production while identifying the causative factor to help with long term management and avoiding a recurrence. A systematic evaluation including consideration of genetic etiologies in the adult population has been previously published [4]. Particular attention should be paid to the history of previous episodes and to factors that might predispose to elevated ammonia or a family history of similar symptoms. In our patient, the encephalopathy of unclear etiology preceding his brother’s death, and the preceding infectious process in the patient were concerning. Further testing later showed features consistent with OTC, a not so uncommon disorder seen in adults [10]. Long-term complications in pediatric patient including learning disabilities with and without focal neurologic deficits as well as imaging evidence of acute or chronic ischemic cerebral damage which may be generalized, regional, or focal have been reported in hyperammonemic encephalopathies [10,12]. In the adult population, little is known about the long-term effects in adults with previous reports showing complete resolution of cortical lesions seen on MRI brain scans [6], while other cases noted mild atrophy in the cingulate gyrus and/or insular cortex [9]. Our patient responded to the appropriate management although never returned to his baseline. Follow-up patient MRI headscons (Figure 1B-E) showed diffuse cortical and subcortical gliotic and atrophic changes associated with CSF ventricular and extracerebral space enlargement. Extrapolation of Evan’s ratio of baseline to MRI head scans obtained at 21 months showed an increase from 0.21 to 0.42. It’s believed that the chronic changes are secondary to the extent of injury seen in the acute stage of hyperammonemic encephalopathy. These changes may likely correspond to the clinical deficits seen.

**Conclusion**

In conclusion, in patients of any age with altered consciousness, coma, or seizures with no clear anatomic or toxicologic cause, one should consider obtaining plasma ammonia levels. Elevated ammonia without evidence of hepatic failure or typically implicated etiologies should prompt more detailed work up including genetic etiologies. The authors encourage checking for ammonia levels in unexplained encephalopathy, in addition to recognizing brain imaging patterns previously reported in patients with hyperammonemnic encephalopathy to enable prompt diagnosis and management to help mitigate potential subsequent morbidity and mortality.

**References**