BRAIN MRI FINDINGS IN ACUTE HYPERAMMONEMIC ENCEPHALOPATHY SECONDARY TO ISCHEMIC HEPATITIS: CASE REPORT AND REVIEW OF THE LITERATURE

Ana-Maria Vladila[1], Dan-Andrei Mitrea[1], Sanda Nica[1,2], Gabriela Mihailescu[1,2], Ioan Buraga[1,2]

[1]Neurology Department, ''Colentina'' Clinical Hospital, Bucharest, Romania
[2]''Carol Davila'' University of Medicine and Pharmacy, Bucharest, Romania

ABSTRACT

Acute encephalopathy is frequently seen in Neurology and Internal Medicine Departments, it makes for a wide spectrum of neuropsychiatric abnormalities, but its brain magnetic resonance imaging appearance in the adult population is not well recognised.

We present the case of an acute hyperammonemic encephalopathy in the setting of ischemic hepatitis secondary to global heart failure and its MRI findings with a review of the literature.

Keywords: acute hepatic encephalopathy, hyperammonemia, ischemic hepatitits, insular cortex, FLAIR hypersignal, restriction of diffusion

INTRODUCTION

Hepatic encephalopathy comprises a wide spectrum of neurological and psychiatric symptoms and signs which are potentially reversible if rapidly recognised and hepatic injury treated. (1,2,8)

Acute hyperammonemic encephalopathy refers to the association of encephalopathy, hyperammonemia and impaired synthetic function (INR>1.5), secondary to acute liver injury in a patient with no previous hepatic disease. It has significant morbidity and a high mortality rate unless promptly treated. (7)

Magnetic resonance imaging (MRI) of chronic acquired hepatocerebral degeneration is well characterised in the literature and consists of symmetrical T1 hypersignal within the basal ganglia, especially the putamen and globus pallidus and atrophy; those subsequent to severe acute encephalopathy include cerebral edema and herniation; in contrast, lesions found in the early stages are underrecognized, especially in the adult population. (1,2)

CASE REPORT

We report the case of a 63 years old female patient referred from the Infectious Diseases Department for confusion, followed by slurred speech and psychomotor agitation with a sudden onset and progressive course over several hours.

She had been admitted 48 hours previous to her neurological deterioration with the suspicion of viral hepatitis, having altered general status, malaise, right upper quadrant pain and moderate hepatic cytolysis syndrome.

Her medical history consisted of multiple cardiovascular risk factors including arterial hypertension, obesity and cardiac ischemic disease with a documented left branch bundle block and multiple

Author for correspondence:
Ana-Maria Vladila, "Colentina'' Clinical Hospital, 19-21 Stefan cel Mare Road, Bucharest, Romania
E-mail: anamariavladila@yahoo.ro

heart failure decompensation episodes with no cardiologic evaluation in the past year.

The blood laboratory tests performed in the Infectious Diseases Department excluded a viral etiology of the hepatitis, but her liver enzymes values increased dramatically (100-fold N).

The neurological examination revealed disorientation, mild deficit of attention and working memory, dysarthria and right side brisk deep tendon reflexes; the remaining of the clinical exam was consistent with a class III NYHA heart failure decompensation, the patient having dyspnea on minimal exertion, mild oedema in her inferior limbs and painful hepatomegaly.

Brain computed tomography (CT) scan didn't reveal any heterodense lesions. (Fig. 1)

CT was followed by brain MRI which showed bilateral asymmetrical (right > left) abnormal FLAIR hypersignal in the insular cortex and minimal hypersignal in the right subinsular area, with restriction of diffusion (DWI). (Fig. 2)

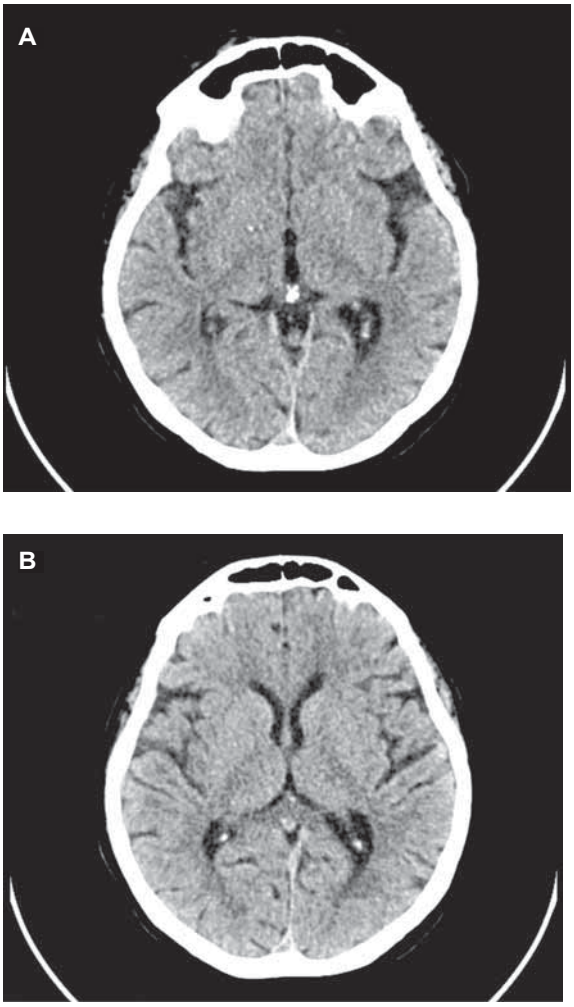

FIGURE 1. *A, B – Brain CT scan, transverse section at la the level of the insula and basal ganglia showing no heterodense lesions, cortical atrophy*

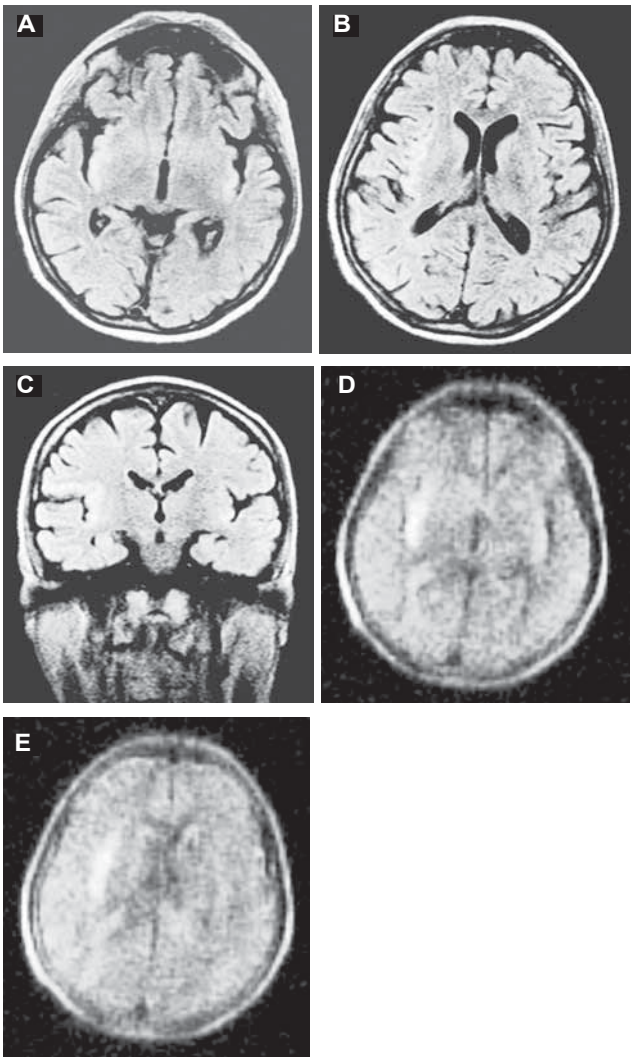

FIGURE 2. *Brain MRI with FLAIR (sections A-C) and DWI (sections D, E), at the level of the insula and basal ganglia showing asymmetrical abnormal hypersignal in the insular cortex (sections A, C) and mild hypersignal in the right subinsular area (section B) with restriction of diffusion (sections D, E); cortical atrophy*

Lumbar tap (LP) was performed with cerebrospinal fluid (CSF) analysis, results being within normal range.

Doppler examination of the cervical and cerebral vessels showed minimal atheromatosis of the carotid artery bilaterally.

Blood laboratory tests confirmed the cardiac decompensation and acute liver failure: NT-proBNP=10056 ng/l (N 0-125 ng/l), AST=590 U/l (N 9-37 U/l), ALT=980 U/l (N 9-52 U/l), INR=1.6, (N 0.90-1.15), LDH=1392 U/l (N 313-618 U/l); plasma ammonia level of 78 umol/l (N 0-34 umol/l) and cardiac enzymes within normal range.

Transthoracic cardiac ultrasound revealed a hypokinetic anterior wall and interventricular septum, a corrected ejection fraction of 20% and dilated non-compressible inferior vena cava; abdominal

ultrasound showed hepatomegaly and dilated suprahepatic and splenic veins consistent with right cardiac insufficiency.

The clinical setting corroborated with the paraclinical exams were indicative for an ischemic etiology of the hepatitis with acute liver failure and hyperammoniemia, secondary to global heart failure; the neurological deficits and MRI lesions were interpreted as type A, grade I hyperammonemic encephalopathy.

The patient was transferred to the Cardiology Department where she received specific treatment for cardiac insufficiency and hepatic adjuvants, with good outcome, being discharged three weeks after with no residual neurological deficits, minimal exertional dyspnea and mild hepatic cytolysis.

DISCUSSIONS

The majority of cases published in the literature implicating lesions in early hepatic encephalopathy were described in children with metabolic disorders; recently, several clinical series in the adult population were also published, but these lesions remain underrecognized or in many cases are misinterpreted as secondary to hypoxic – ischemic pathology.

Arnold et al (4) and U-King-Im (1) described cases of diffuse cortical necrosis on FLAIR sequences with restriction of diffusion, predominantly implicating the insular cortex, and the latter a series of cases implicating symmetrical lesions in the cingular and insular cortices.

Rosario et al (2) also described lesions in the same cortical areas but present only as restriction on DWI while Mckinney et al (5) and Takanashi (3) also pointed to abnormalities implicating the brainstem, thalamus, basal ganglia and diffuse cortical matter; the majority of cases were in the context of hyperammonemia secondary to acute liver failure in critically ill patients in the Intensive Care Unit (ICU), but other etiologies were also reported: sepsis, portosystemic shunting, post-marrow or lung transplantation, multiple myeloma, hypothyroidism or drugs (valproic acid, acetaminophen, chemotherapy). (1-3)

Our case refers to the same pathology, the etiology of the acute liver failure being secondary to ischemic hepatitis in the setting of global heart failure in a patient with cardiac ischemic disease.

Acute liver failure attributed to ischemic hepatitis in the context of heart dysfunction has a better prognosis than liver dysfunction seen in critically ill patients or to ones seen in cirrhosis, also known as acute-on-chronic lesions. (7,8)

Symptoms usually subside 7-10 days after the hepatic hypoxic event and hepatic cytolysis in 10-14 days if proper treatment is issued and if patients don't require vasopresor and treatment in ICU. (7)

Ammonia is a by-product of protein metabolism and it is excreted primarily by the liver, but also the skeletal muscles, urinary tract and cerebral tissue.

In cases of liver failure, an increased quantity of ammonia crosses the brain blood barrier through passive diffusion and ion channels; it is metabolised to glutamine and glutamate within the astrocites, but the process implies a great consumption of ATP. Subsequently, there is a increase of cellular osmolarity with intracellular water retention and eventual astrocite loss; hyperammonemia also affects the modulation of GABA and NMDA receptors. (1,2,9)

All the changes induced at the cerebral tissue level translate into cytokine pathway activation, leading to lactate levels elevation and loss of cerebral flow autoregulation with secondary brain edema and in severe cases herniation syndromes. (9)

Data published so far supports the idea that brain lesion extension depends on a predisposing susceptibility to metabolic injury and also to severity and duration of hyperammonemia; subtle changes on MRI are observed at levels of ammonia of 50-60 umol/l, while extensive ones at levels of at least to 4-5 times the upper normal value. In addition, the insular and cingular cortices are primarily affected but to this point the mechanism involved is still under investigation. (1-4)

Our patient had an ammonia level of 78 umol/l and bilateral asymmetric abnormal high signal on MRI in the insular cortex.

In less severe cases, the data is in favor of potential reversibility of the brain lesions if proper treatment is started rapidly; in more severe cases with more profound lesion extension, in surviving patients, despite treatment, the follow-up imaging studies revealed cortical atrophy in the affected areas. (6)

CONCLUSIONS

Brain MRI findings in early stages of hyperammonemic encephalopathy are not well documented in the adult population. It is important that, in the proper setting, a pattern of bilateral, usually symmetrical hypersignal in FLAIR sequence with restriction of diffusion or only restriction on DWI at the level of the insular and cingulate cortex, point

both the radiologist and the clinician towards hyperammonemic encephalopathy.

Of note, lesions can extend to the thalamus, brainstem, basal ganglia and more diffusely to the cortex.

The condition has a wide spectrum of neuropsychiatric abnormalities and multiple etiologies to consider; it is a potentially deadly but treatable condition.

REFERENCES

1. **U-King-Im J.M., Yu E., Bartlett E., Soobrah R., Kucharczyk W.** Acute hyperammonemic encephalopathy in adults: imaging findings. *AJNR Am J Neuroradiol.* 2011; 32(2):413-418
2. **Rosario M., Mcmahon K., Finelli P.F.,** Diffusion-Weighted Imaging in Acute Hyperammonemic Encephalopathy, *Neurohospitalist.* 2013 Jul; 3(3): 125-130
3. **Takanashi J. et al,** Brain MR imaging in acute hyperammonemic encephalopathy arising from late-onset ornithine transcarbamylase deficiency. *AJNR Am J Neuroradiol* 2003*;* 24:390-93
4. **Arnold S.M. et al,** Acute hepatic encephalopathy with diffuse cortical lesions*. Neuroradiology* 2001*;* 43:551-54
5. **McKinney A.M., Lohman B.D., Sarikaya B., et al.** Acute hepatic encephalopathy: diffusion-weighted and fluid-attenuated inversion recovery findings, and correlation with plasma ammonia level and clinical outcome. *AJNR Am J Neuroradiol.* 2010; 31(8):1471-1479
6. **Capizzano A.A., Sanchez A., Moritani T., Yager J.** Hyperammonemic encephalopathy: Time course of MRI diffusion changes. *Neurology* 2012; 78(8):600–601
7. **Lawrence S. Friedman,** Ischemic hepatitis, hepatic infarction, and ischemic cholangiopathy, www.uptodate.com
8. **Peter Ferenci,** Hepatic encephalopathy in adults: Clinical manifestations and diagnosis, www.uptodate.com
9. **Peter Ferenci,** Hepatic encephalopathy: Pathogenesis, www.uptodate.com