CASE REPORT

Minimal Hepatic Encephalopathy Diagnosis by Magnetic Resonance Spectroscopy. A Case Report

Cristian Scheau[1,2], Anca Ioana Bădărău[1], Andreea Elena Gherguş[2], Gelu Adrian Popa[2], Ioana Gabriela Lupescu[2]

1) Department of Physiology I, Carol Davila University of Medicine and Pharmacy;
2) Department of Radiology and Medical Imaging, Fundeni Clinical Institute, Bucharest, Romania

Address for correspondence:
Scheau Cristian, MD
Department of Radiology and Medical Imaging, Fundeni Clinical Institute
258 Fundeni Ave., II
22328 Bucharest, Romania
cristianscheau@gmail.com

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ABSTRACT

Minimal Hepatic Encephalopathy (MHE) is a potentially reversible spectrum of neuro-psychiatric alterations in patients with acute or chronic liver disease, in the presence of a normal neurological examination. Studies demonstrated that early diagnosis and treatment of this complication increases the quality of life of the patients and leads to an overall better liver disease management. Currently, a practical method of diagnosing MHE is through psychological tests, with modest accuracy. A highly sensible and specific non-invasive method of diagnosis is Magnetic Resonance Spectroscopy (MRS) which identifies the key neuro-biochemical profile of hepatic encephalopathy. In selected cases of equivocal psychological test results, MRS is justified and adequate according to the authors' opinion.

Key words: Minimal Hepatic Encephalopathy – Magnetic Resonance Spectroscopy – Neuropsychological test

INTRODUCTION

Minimal Hepatic Encephalopathy (MHE) is a neuro-psychiatrical disorder characterized by altered cognitive or psychomotor functions despite a normal neurological examination. Minimal hepatic encephalopaty requires the presence of an impaired liver function, and can predict the onset of clinical hepatic encephalopathy (HE). The impact of MHE is increasingly debated as it has been shown that patients who suffer from this complication have altered daily functionality and possibly a lowered quality of life. Also, if diagnosed and treated, patients show an improvement in the Child-Turcotte-Pugh score. The patient we are presenting shows clinical psychiatric symptoms which could suggest the diagnosis of MHE, but the psychological tests employed (PSE-Syndrome Test), currently the only commonly-accepted diagnostic procedure, are inconclusive in the context of the poor education and tuition of the patient. Magnetic Resonance Spectroscopy (MRS) certifies the diagnosis, as it identifies highly-specific neuro-biochemical findings of MHE. We support this diagnostic procedure, of significant specificity and sensibility, in selected cases.

CASE PRESENTATION

A 59-year-old patient with no prior hospital admissions presented to the medical emergency department accompanied by his family for the deterioration of his neuro-psychological status. The man had a long history of alcohol abuse, 30 pack year smoking history, but no other known pathology. The family's concern was that the modified behavior of the patient, with slight attention deficit and somewhat slow reactions, may have been the onset symptoms of a stroke.

Clinical evaluation by the doctor on-call demonstrated typical dermatological signs of long-term alcohol consumption (such as rosacea, seborrheic dermatitis, spider angiomata), gynecomastia, Dupuytren's contracture, as well as bilateral symmetrical hand tremor. Consultation with the neurologist on call certified that the tremor was of essential type, most likely in the alcoholism context. The neurologist excluded flapping tremor, so the diagnosis of overt hepatic encephalopathy was dismissed. Nevertheless, the patient did present a shortened attention span as well as a slight lack of awareness.

The patient was submitted to a basic biochemical profile, as well as an abdominal ultrasound. The biological investigation

(Table I) together with abdominal ultrasound (no ascites) allowed the classification of the patient as Child-Pugh A or B, depending on the presence of HE [1].

Closer attention was therefore paid to the neuro-psychiatric evaluation, and the patient was submitted to a PSE-Syndrome test [2]. The test is composed of four tests, one of them in two parts (Fig 1). The patient's scores versus an average normal individual are listed in Table II. It is obvious that the results of the tests are far worse than expected, and furthermore, one of the tests is completed incorrectly.

The clinician in charge of the patient decided that a central nervous system evaluation could be useful, and because he predicted that a computed tomography might be inconclusive (as the clinical changes were subtle and the patient had a normal clinical neurological exam), he opted for a Magnetic Resonance Imaging (MRI) procedure.

The MRI examination (Fig. 2) showed no acute vascular events, a mild cerebral atrophy, small calcifications in the basal nuclei bilaterally [3]. Also, more specific, the T1-weighted images showed symmetrical bilateral hyperintensities in the globus pallidus, which was an expected finding in the patient's context [4].

At this moment, for supplementary diagnostic information a MRS examination was performed (Fig. 3). In this case, single voxel spectroscopy (SVS) was employed on a 1.5T MRI unit, using the following parameters: short TE (30 ms), 8 cc voxel size (2x2x2 cm), parieto-occipital white matter placement.

The spectrum acquired showed decreased values of myo-inositol and choline as well as increased values of the glutamine-glutamate-gamma amino butyric acid. As these changes are highly specific to HE (virtually sustaining no differential diagnosis, MRS wise), the diagnosis of MHE was established. This explained the psychiatric symptoms different from acute inebriation, in the absence of any concurring pathology. Clinical (or overt) HE was dismissed from the beginning, as the patient did not present confusion, dysarthria, flapping tremor or disorientation.

Table I. Biochemical profile of the patient on admission.

Parameter analyzed	Result	Reference interval / measurement unit
Serum albumin	3.2	3.5 – 5.2 g/dL
ALT	20.00	0 – 45 U/L
AST	48.00	0 – 35 U/L
Conjugated bilirubin	1.20	0.0 – 0.4 mg/dL
Unconjugated bilirubin	0.70	0.00 – 1.20 mg/dL
Total bilirubin	1.90	0.3 – 1.2 mg/dL
Total cholesterol	86.00	100 – 200 mg/dL
Creatinine	0.70	0.60 – 1.30 mg/dL
Alkaline phosphatase	154.00	42 – 128 U/L
Gamma-GT	65.00	7 – 55 U/L
Glucose	81.70	74 –106 U/L
Fibrinogen	158.70	200 – 400 mg/dL
INR	1.51	0.9 – 1.27
Prothrombin time %	45.40	70 – 120 %
Prothrombin time sec	15.90	10.4 – 14.3 sec

Table II. The PSE-Syndrome Test score of our patient compared to a normal reference individual.

PSE-Syndrome test components	Patient's time	Reference time
Serial dotting	3 min 48 sec	29 sec
Line tracing	7 min 20 sec	1 min 15 sec
Number connection - A	1 min 2 sec	33 sec
Number connection - B	2 min 3 sec	43 sec
Digit symbol	5 min 40 sec	6 min 40 sec

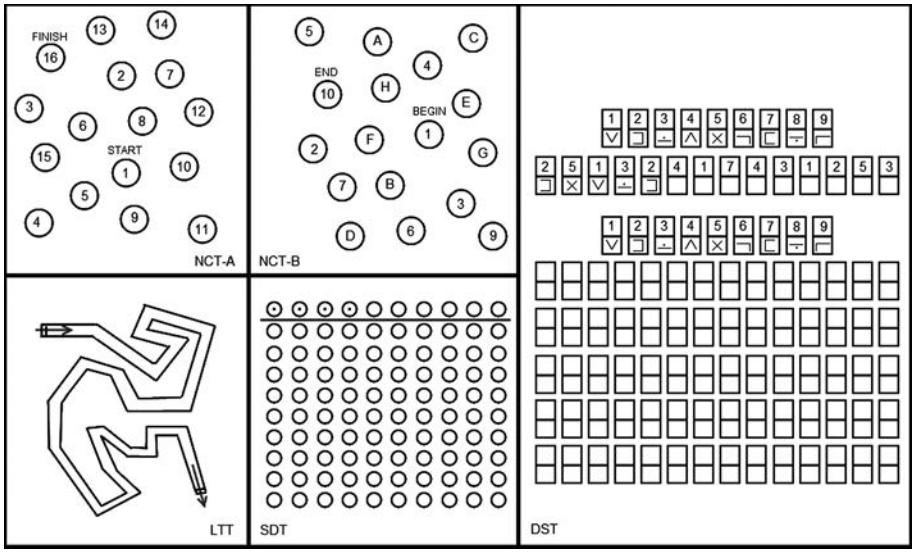

Fig. 1. Schematic representation of the PSE syndrome test. NCT - Number Connection Test – the patient must connect circles which hold increasing numbers, or alternate increasing numbers/letters, LTT - Line Tracing Test – the patient must follow the trail from start to finish, SDT - Serial Dotting Test – the patient must fill a dot inside every circle of a 10x10 grid, and DST - Digit Symbol Test – the patient is given a cypher of digit-symbol correspondence and has to follow the code throughout a series of random digits.

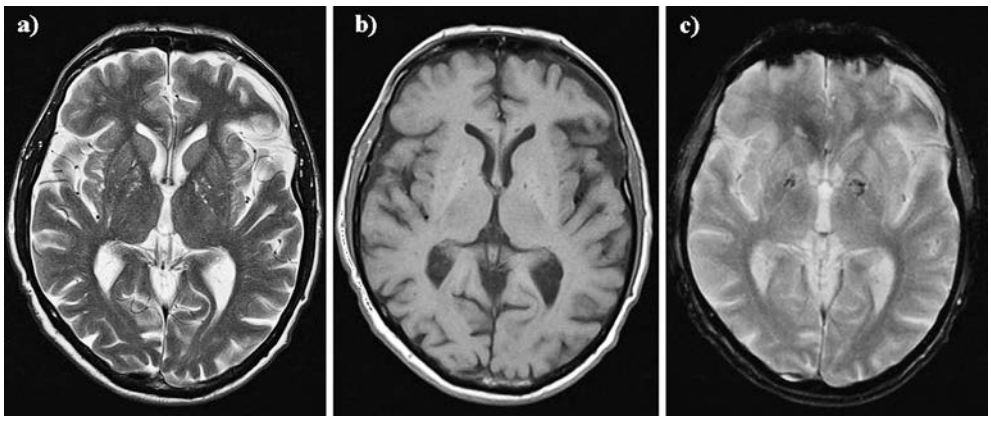

Fig. 2. Cerebral MRI examination of the patient: images performed in an axial (bicommisural) plane, through the lateral ventricles: a) T2 spin-echo weighted image, b) T1 spin echo weighted image, c) Gradient echo (T2*) image.

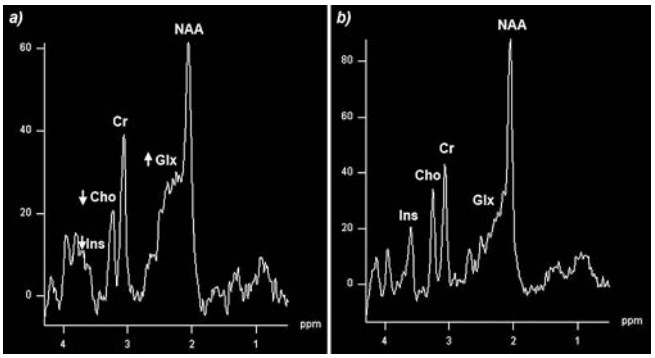

Fig. 3. Magnetic Resonance Spectroscopy (MRS) evaluation of the patient (a) versus a normal reference patient (b) using the same parameters and scanning protocol. Note the decreased values of myo-inositol (mI) and choline (Cho), and elevated glutamate-glutamine-gamma amino butyric acid complex (Glx) as compared to a normal spectrum.

DISCUSSION

Hepatic encephalopathy is a spectrum of neurological and psychiatric deficits determined by an acute or chronic liver failure. The key role appears to be played by ammonia, as increased values in the plasma determine a stimulation of the conversion of glutamate to glutamine in the astrocyte cells [5, 6]. Secondarily, accumulation of glutamine represents an osmotic stress leading to cell swelling and clinical signs (Fig. 4).

Minimal hepatic encephalopathy is considered the mildest form of HE with no clinical neurological symptoms, just a slight cognitive impairment.

The psychological test employed was not useful in our case. The PSE-Syndrome Test is the most commonly used instrument in the diagnosis of MHE. Although not internationally validated as a standard method, it is used successfully in the majority of cases to raise the suspicion of MHE. Nevertheless, it is an interactive examination where the patient must cooperate, understand the requests and fulfill a series of tasks as demanded by the examiner. In our case, the patient failed to understand and successfully complete the questionnaire, thus rendering the test inconclusive. The last resort method was to seek specific cerebral metabolites alterations through MRS.

Magnetic Resonance Spectroscopy does not bear special requirements other than the software and hardware capabilities of the machine. Patient positioning, antenna, environment are no different from a routine cerebral examination.

Voxel placement in the parieto-occipital white matter is, in our experience, optimal in HE assessment as it best objectifies the metabolite imbalances [7].

The findings in our patient were conclusive with HE. On the morphological sequences we noted basal ganglia hyperintensities on the T1-weighed images (most likely manganese deposits). MR spectrum showed a decrease of myo-inositol as well as choline, and an increase of the glutamate-glutamine-gamma amino-butyric acid complex (Fig. 5). Because of the adjoining frequencies of these three molecules, current clinical MR machines cannot delineate them individually, appearing as a complex, or a mixture of three neighboring peaks [8].

The importance of establishing this diagnosis is evident. First, MRI eliminated any suspicion of concurring central nervous system disease, and at the same time, MRS successfully confirmed the diagnosis of MHE. Therefore, the patient was classified in the Child-Pugh class A. Second, the latest practice guidelines state the correct algorithm for treatment and monitoring of cirrhotic patients [9]. If the diagnosis of MHE is established, the patient is initiated on lactulose and probiotics. Otherwise the recommendation is to retest the patient in 6 months. In other words, if omitted, the patient may be forced to cope with MHE until re-evaluated.

CONCLUSION

The diagnosis of minimal hepatic encephalopathy is necessary because of the possibility to elude further complications (overt hepatic encephalopathy). Also, initiating the treatment of MHE may improve the quality of life of these patients. Further improvements of the diagnostic procedure of MHE are needed, as the psychological tests may be inconclusive in a variety of cases, as presented in this paper. Magnetic Resonance Spectroscopy can be a successful tool in these situations, as it provides objective data and combined with its non-invasiveness, might be of future interest as a diagnostic standard.

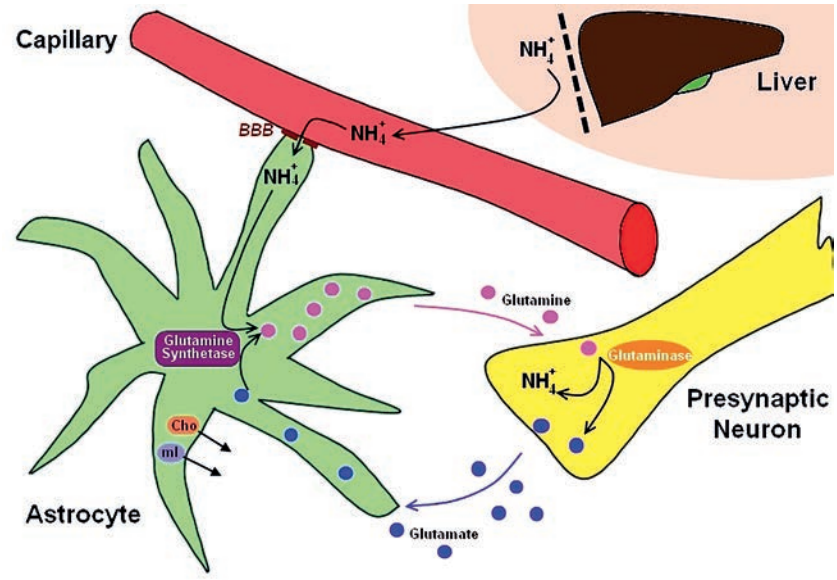

Fig. 4. Physiopathology of hepatic encephalopathy. Excessive ammonia crosses the blood-brain-barrier (BBB) and participates in increased glutamate to glutamine conversion. Choline (Cho) and myo-inositol (mI) are released from the astrocytes to compensate the high osmotic pressure [5, 6].

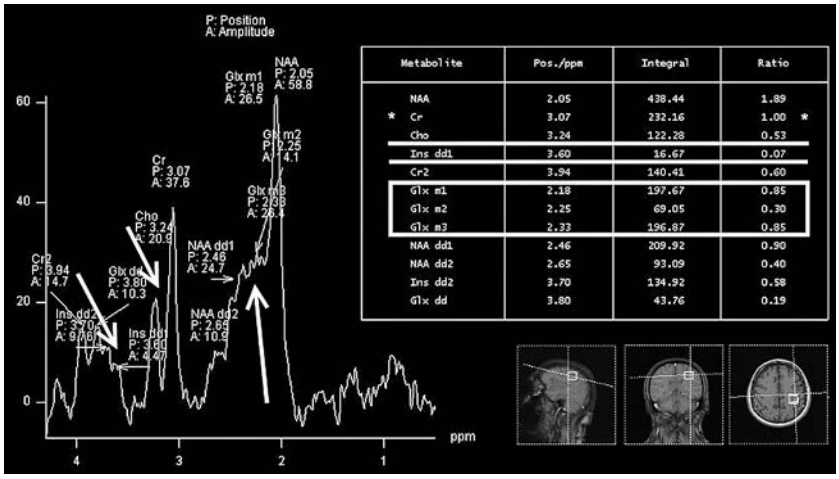

Fig. 5. Original raw MRS acquisition. Spectrum and reference table (with three dimensional localizer displayed). Note the decreased choline (Cho), very low values of myo-inositol (Ins), increased glutamate-glutamine-gamma amino butyric acid complex - peak (Glx m1, m2, m3). Values in the table are referenced to creatine (Cr, *). Corroborated with the clinical status of the patient, the final diagnosis is that of minimal hepatic encephalopathy.

Conflicts of interest: None to declare.

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