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Journal Pre-proof

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PII: S2589-5559(22)00131-8

DOI: https://doi.org/10.1016/j.jhepr.2022.100559

Reference: JHEPR 100559

To appear in: *JHEP Reports*

Received Date: 4 August 2022

Accepted Date: 9 August 2022

Please cite this article as: Weiss N, Thabut D, Ammonia rises again from the ashes!, *JHEP Reports* (2022), doi: https://doi.org/10.1016/j.jhepr.2022.100559.

Ammonia rises again from the ashes!

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Word count: 479
Figure: 1
References: 10

Disclosures: the authors have nothing to disclosure.
Authors contribution: Nicolas Weiss and Dominique Thabut wrote this manuscript and reviewed it critically
Financial support: none

Sir,

We read with great interest the study by Hadjihambi et al. (1) showing impaired oxygen concentration in the brain of an animal model of cirrhosis, which was probably mediated by hyperammonemia. The authors suggest that this brain hypoxia could participate to the pathogenesis of hepatic encephalopathy (HE) that is still matter of debate (2).

With respect to this, we would like to report our clinical experience of a 35-year-old woman who was admitted in ICU for coma (Glasgow coma scale at 3), variceal bleeding and shock, revealing decompensated alcoholic cirrhosis. Control of bleeding was rapidly obtained by vasoactive drugs and banding. She displayed hyperammonemia at 106 μmol/L. Neurological examination was unremarkable; especially, it showed no focal sign and EEG showed diffuse slowering without any epileptic discharge. Coma was rapidly resolutive with symptomatic ICU measures and lactulose through the nasogastric tube. Surprisingly, brain MRI revealed a diffuse cortical hypersignal (Figure 1A). The patient was discharged at day 15 with mild neurological impairment, short-span memory loss and attention complaints. She stopped alcohol and was monitored regularly in our outpatient clinics. Control brain MRI performed 3 months after ICU discharge showed partial disappearance (Figure 1B) and the one performed at 6 months the total disappearance of cortical hypersignals (Figure 1C). Currently, cirrhosis is recompensated and all cognitive complaints have disappeared.

Diffuse cortical hypersignals on T2-weighted or FLAIR-weighted sequences are classically observed on brain MRI in a limited number of circumstances almost all associated with hypoxemia: cardiac arrest, severe hypoglycemia, status epilepticus or mitochondrial disease (3). Rarely those abnormalities are observed in Creutzfeld-Jakob disease. Very similar abnormalities have been described in some case reports in HE, but their pathogenesis was unclear (4). We hypothesize that cortical hypersignals on brain MRI in HE are related to decreased cortical oxygenation, mediated by hyperammonemia as described by Hadjihambi et al. (1), potentially compromising brain energy metabolism as previously shown by us and others (5,6). We would like here to outline that brain lesions were reversible in our case with a strict control of ammonemia, together with control of the bleeding and symptomatic ICU management.

The reversibility of HE is debated after liver transplantation, even if neuropsychological sequalae don't mimic perfectly HE symptoms (7). The combination of long periods of hyperammonemia before transplantation and a second hit constituted of hypovolemia inherent of the liver transplantation procedure, especially while the anhepatic phase, could be responsible for altered brain oxygenation. Hence, a strict control of ammonia levels before transplantation could be an appealing strategy to avoid neurological sequalae (8).

Finally, hyperammonemia and its consequences in terms of prognosis have been completely revisited lately, and this in acute and outpatient settings (9,10). Going back to basis, we have here another building block in the construction, evidencing this time the interest of a strict ammonia control in clinical situations favoring hypoxia, which are very frequent in patients with decompensated cirrhosis.

Figure legend:

Brain MRI
A, MRI imaging in ICU showing diffuse cortical hypersignals on both FLAIR and diffusion weighted sequences. T2* weighted sequence was normal ; B, Partial disappearance of the cortical hypersignals at 3 months ; C, Total disappearance of the cortical hypersignals at 6 months.
Abbreviations: FLAIR, fluid attenuated inversion recovery ; ICU, intensive care unit.

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