



# Cortical Reflex Myoclonus in a Patient with Hyperammonemic Encephalopathy

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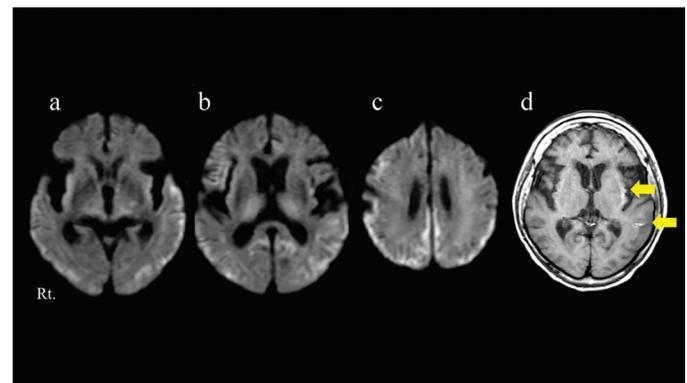
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An 82-year-old woman with burned-out non-alcoholic steatohepatitis (NASH) developed hepatic encephalopathy two months prior to admitting to us. Subsequently, the patient developed focal impaired seizures and was administered levetiracetam. After treatment with lactulose and molecular chain amino acids, her seizures began to decline, and her ammonia levels decreased from 790  $\mu\text{g}/\text{dl}$  to 29  $\mu\text{g}/\text{dl}$  (reference range: 30-86  $\mu\text{g}/\text{dl}$ ). Additionally, a rapid cognitive decline was not observed. Three weeks prior to admitting to us, the patient noticed blood in her stools; her stool tested positive for occult blood (immunoassay). During that time, the iron-deficiency anemia progressed and the ammonia levels increased to 180  $\mu\text{g}/\text{dl}$ , without worsening of the neurological symptoms. Gastrointestinal endoscopy was not performed owing to the patient's condition. She continued to notice blood in her stools, without any further progression of anemia or increase in ammonia levels. Four days before admitting to us, she experienced involuntary movements in her face and upper extremities, which were distinguishable from convulsions and had occurred without an increase in ammonia levels (79  $\mu\text{g}/\text{dl}$ ).

The patient was admitted to our facility owing to the worsening of the involuntary movements and disturbances in consciousness. At the time of admission, the Glasgow Coma Scale score was 6 (E1V1M4). The patient exhibited roving eye movements and myoclonus of the face and extremities. These episodes lasted for only a few seconds and were triggered by mild stimulation. The intervals between the involuntary movements were irregular. There were no signs of asterix, muscle rigidity, or tremors. Brain magnetic resonance imaging (MRI) revealed hyperintensities in both cortices, including in the insula, cingulate gyrus, and thalamus, on diffusion-weighted images (DWI) (Figure 1 a-c) and reduced diffusion on the apparent diffusion coefficient (ADC) map. No hyperintensity areas were observed in the occipital lobe or perirolandic cortex. Certain parts

of the cortex demonstrated increased T1 signal intensities, indicating of laminar necrosis (Figure 1 d). No hyperintensity was observed in the globus pallidus on T1-weighted images. Laboratory test results revealed an increase in ammonia levels (646  $\mu\text{g}/\text{dl}$ ), a significant increase in blood urea nitrogen, and persistent anemia. There were no episodes of hypoxia or hypoglycemia. Electroencephalography could not be performed and short-latency somatosensory evoked potential could not be measured due to the lack of equipment at our facility. Laboratory test results revealed a low platelet count due to severe liver cirrhosis. Thus, a lumbar puncture was not performed considering the associated bleeding risk. Abdominal computed tomography revealed no significant findings. The patient was



**FIG. 1.** (a, b, c). Magnetic resonance imaging of the brain revealed hyperintensities in both cortices, including in the insula, cingulate gyrus, and thalamus, on diffusion-weighted images and reduced diffusion on the apparent diffusion coefficient map. d. Certain parts of the cortex demonstrated increased T1 signal intensities, which were indicative of laminar necrosis.



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diagnosed with hyperammonemic encephalopathy and received intensive care. However, she passed away the following day.

Hyperammonemic encephalopathy affects regions, including the insular cortex, cingulate gyrus, and thalamus, exhibiting high signal intensity on DWI and low signal intensity on ADC, which signifies an acute injury.<sup>1</sup> In one study, high signal intensity in the insula cortex and cingulate gyrus was observed in all the patients.<sup>2</sup> Another study<sup>3</sup> reported that hyperintense areas in these regions were characteristic of hyperammonemic encephalopathy and that the occipital lobe and perirolandic cortex were more likely to appear normal. This is consistent with the findings in our patient. Furthermore, the observed laminar necrosis was likely a result of the toxic effects of ammonia.<sup>4</sup> We hypothesized that the myoclonus in our patient was a cortical reflex myoclonus,<sup>5</sup> originating from these cortical lesions. Furthermore, the involuntary movements seen before the increase in ammonia levels might have indicated the onset of hyperammonemic encephalopathy, even though they were different from asterixis or myoclonus. The patient's background, rapid deterioration, and lack of sufficient facilities limited our examination of the patient. Furthermore, the possibility of Creutzfeldt-Jakob disease or autoimmune or viral encephalitis could not be ruled out because the cerebrospinal fluid could not be analyzed. However, we believed that the MRI was useful in assessing the etiology of the patient's disease based on a limited physical examination and the patient's symptoms.

Our patient experienced two episodes of hyperammonemic encephalopathy. The initial episode was due to burned-out NASH, and the second episode was triggered by the acute exacerbation of NASH with chronic gastrointestinal bleeding. When patients present with involuntary movements, prompt treatment is crucial after identifying the cause of hyperammonemia.

**Informed Consent:** Written informed consent was obtained from the patient.

**Authorship Contributions:** Concept- F.E.; Design- F.E., M.T., S.T.; Supervision- H.M.; Materials- F.E., S.T.; Data Collection or Processing- F.E., M.T., S.T.; Analysis or Interpretation- F.E., M.T., S.T.; Literature Search- F.E., M.T., H.M.; Writing- F.E.; Critical Review- M.T., S.T., H.M.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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