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Hepatic Encephalopathy Mimicking Creutzfeldt-Jakob Disease on Laboratory, Physiological, and Imaging Evaluations

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Female, 84-year-old
Final Diagnosis: Hepatic encephalopathy
Symptoms: Cognitive impairment
Medication: —
Clinical Procedure: —
Specialty: Neurology

Objective: Unusual clinical course

Background: Creutzfeldt-Jakob disease (CJD) is an irreversible, neurodegenerative, prion disease presenting with cognitive, behavioral, and motor dysfunction. The clinical presentations or laboratory findings of treatable autoimmune and metabolic processes may mimic those of CJD. Hepatic encephalopathy (HE) is a complication of severe hepatic failure that is characterized by neuropsychiatric manifestations. A case of HE whose laboratory, physiological, and imaging results were similar to that of Creutzfeldt-Jakob disease (CJD) in the process of treatment for HE is presented.

Case Report: An 84-year-old woman with hepatic encephalopathy (HE) was admitted to our hospital because of acute consciousness disturbance. She had chronic hepatitis type C, liver cirrhosis, and hepatocellular carcinoma, and had had an episode of HE once. Her severe consciousness disturbance did not improve after treatment for concurrent hyperammonemia, unlike in her previous episode. Diffusion-weighted brain magnetic resonance imaging (MRI) showed widespread hyperintensity of the whole cortex. Her electroencephalogram showed periodic sharp wave complexes (PSWCs). Both total t-tau and 14-3-3 proteins were detected in her cerebrospinal fluid. According to these clinical data, CJD was highly suspected. However, the consciousness disturbance was alleviated by the tenth day of admission, and her general condition was markedly improved, which supported the initial diagnosis of HE.

Conclusions: The present results suggest that treatable disorders, such as HE, should be considered before making a final diagnosis of a fatal disease such as CJD, since the spectrum of diseases that CJD mimics is vast. We should also aggressively treat patients with severe conditions from which recovery is possible.

Keywords: Creutzfeldt-Jakob Disease, Sporadic • Diffusion Magnetic Resonance Imaging • Hepatic Encephalopathy

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Background

Creutzfeldt-Jakob disease (CJD) is an irreversible, neurodegenerative, prion disease presenting with cognitive, behavioral, and motor dysfunction. Treatable autoimmune and metabolic processes may mimic CJD in their clinical presentation or examination findings. Hepatic encephalopathy (HE) is a complication of severe hepatic failure that is characterized by neuropsychiatric manifestations. A case of HE whose laboratory, physiological, and imaging results were similar to that of CJD in the process of treatment for HE, is presented.

Case Report

An 84-year-old Japanese woman was admitted to our hospital because of progressive severe consciousness disturbance which had progressed from somnolence to coma over 3 days. Her mental state was normal before consciousness disturbance, and she was able to handle her daily life without any physical support. She had neither myoclonus nor convulsions. Her past history included chronic hepatitis type C, liver cirrhosis, and hepatocellular carcinoma. She had continued multimodal therapy for these diseases. On laboratory examinations on admission, hyperammonemia was noted (296 μg/dL). She was diagnosed as having HE and was immediately administered the branched chain amino acid arginine and lactulose. Although the serum ammonia level decreased rapidly, her consciousness level did not improve from coma. As a differential diagnosis for conscious disturbance, including status epilepticus, central nerve system infection, metabolic diseases, or psychiatric diseases, further examinations were performed. Serum anti-nuclear, anti-SS-A/SS-B, myeloperoxidase-antineutrophil cytoplasmic antibodies were all negative, and serum thyroid hormone and glucose levels were normal. The cerebrospinal fluid (CSF) was almost normal except for the positive results for both total tau (>2200 pg/mL) and 14-3-3 (>500 μg/mL) proteins.

Diffusion-weighted imaging (DWI) of brain magnetic resonance imaging (MRI) showed diffuse hyperintensity in the cortices (especially the insular and parietal areas) and bilateral thalami (**Figure 1A**). On the electroencephalogram (EEG), periodic sharp wave complexes (PSWCs) were noted (**Figure 1B**), whereas there were neither triphasic waves characteristic of HE nor spike-and-wave complexes. Based on these findings, a clinical diagnosis of CJD was also suspected. However, her consciousness began to improve gradually from the tenth hospital day, the hyperintensities on brain MRI (DWI) decreased, and the EEG was normalized (without PSWCs). When she was discharged, her consciousness level had become almost alert, and she was able to walk without any supports.

Discussion

This was a characteristic case of HE that presented with a progressive continuous consciousness disturbance with unique MRI, EEG, and CSF findings.

HE is a common complication of liver cirrhosis with various neuropsychiatric abnormalities. Various drugs and management strategies are available [1,2]. The major characteristic MRI finding of HE is reported to be hyperintensities on T1-weighted imaging at the globus pallidus bilaterally [3]. In some cases of HE, DWI showed hyperintensities in cortical regions, as in the present case [4,5]. Muir et al presented such a case of HE and discussed the differential diagnosis of HE and CJD [6].

In the present case, it appeared that another disease had occurred concomitantly or in succession because the patient's consciousness disturbance continued despite the decreasing serum ammonia level. Based on the MRI findings and other additional examinations, such as positive total tau and 14-3-3 proteins in CSF and PSWCs on EEG, CJD was suspected. As diagnostic markers for CJD, the sensitivity and specificity of total tau in CSF, 14-3-3 protein in CSF, and PSWCs on EEG were 87%, 90%, 64% and 67%, 40%, 91% each in diagnosing CJD [7,8]. The sensitivity and specificity of each study are not high; however, if positive findings are detected at the same time in these multiple examinations, the diagnosis is more likely to be CJD. Therefore, we should consider CJD as a differential diagnosis.

CJD is a disease that shows rapidly progressive dementia. However, there are many other diseases presenting with similar clinical conditions, and they should be distinguished from CJD [9,10]. In the process of the differential diagnosis of CJD, there are many diseases to consider or exclude. In the previous reports, HE was one of them, although in only a few [11-13]. In some cases, the difficulty in differential diagnosis has been discussed. For example, cases that were finally diagnosed as CJD after being initially regarded as HE have been reported [14], as well as a case of concomitant HE and CJD [15].

Nevertheless, this is the first reported case of HE in which the results of investigations were similar to those of CJD, not only the MRI findings, but also the CSF and EEG findings. Because the spectrum of CJD mimics is wide, careful attention to the differential diagnosis is required. As Chitravas et al stated, we also emphasize that, in patients with rapidly progressive dementia, treatable disorders should be considered and excluded before diagnosing CJD [16]. We should also remember that HE is included as one of the diseases that should be differentiated from CJD. When we encounter such a patient whose clinical condition or findings on investigations are similar to those of CJD, it is important to continue careful clinical observation without relying too much on the results of the examinations.

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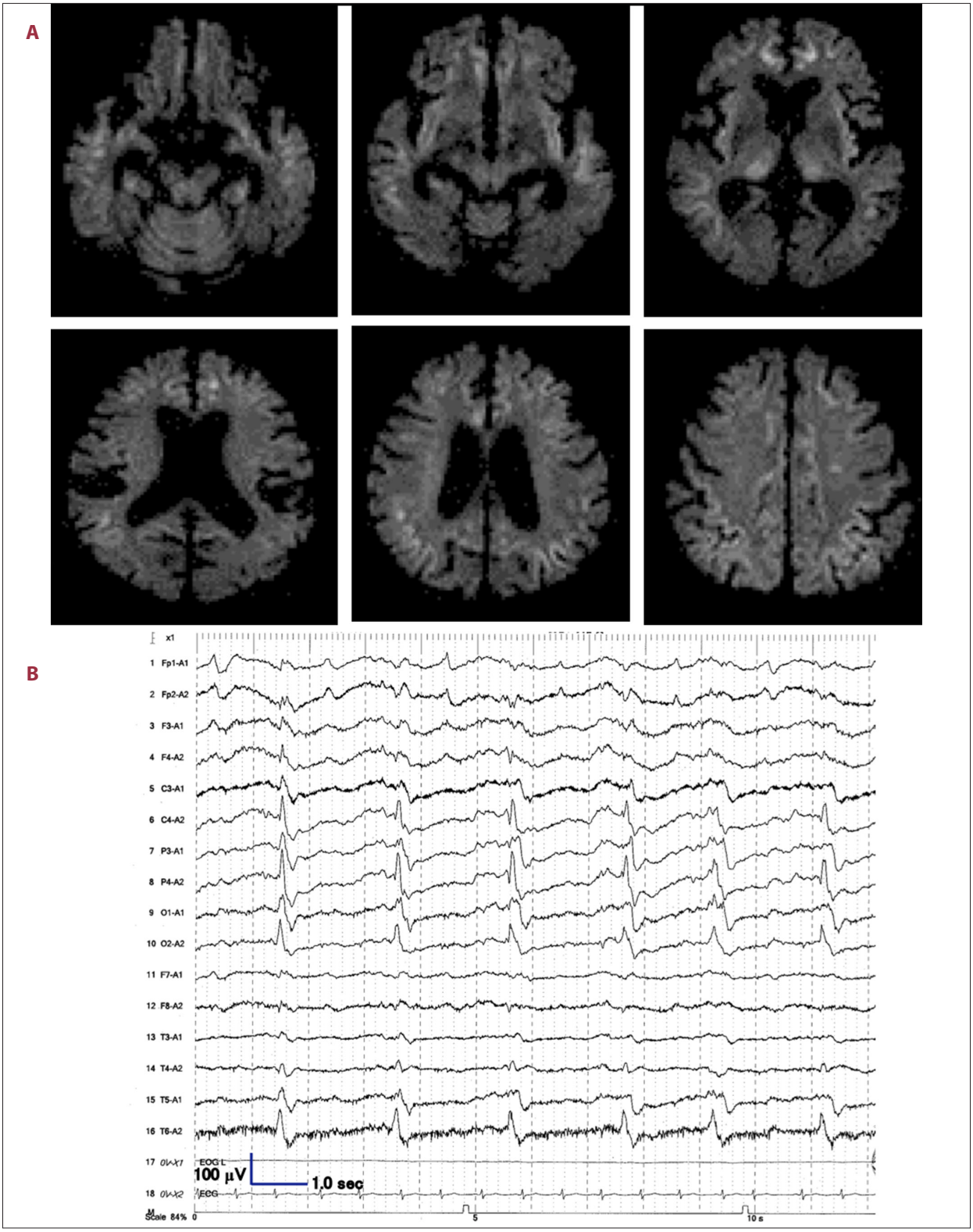

Figure 1. (**A**) Diffusion-weighted imaging of brain magnetic resonance imaging (MRI) at the time of the patient's worst clinical condition. Diffuse hyperintensity lesions are seen in the cortices of bilateral frontal, parietal, and insular areas and in bilateral thalami. (**B**) Periodic sharp wave complexes (PSWCs) are noted on the electro-encephalogram. This was recorded at almost the same time as the MRI in A above.

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Conclusions

HE and CJD may overlap partially in their clinical findings such as laboratory, physiological, and imaging study, even though they are originally different diseases. Even a patient who presents with severe HE may be cured with rapid diagnosis and optimal treatment. We should remember the possibility of recovery in several diseases that seem to be severe and irreversible before making a diagnosis of a fatal disease such as CJD.

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Conflict of Interest

None declared.

Declaration of Figures Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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