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A discussion of new-onset extrapyramidal syndrome without tremor and neuroimaging signs of encephalopathy following hepatic cirrhosis

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ABSTRACT

Liver cirrhosis can cause neurological, extrapyramidal-type disorders, such as stiffness, bradykinesia, tremor, confusion, depression. Cirrhotic extrapyramidal syndrome can worsen clinically, leading to encephalopathy, which in the most severe cases leads to coma. Brain MRI is able to highlight the extrapyramidal signs, through the presence of hyperintensity areas at the basal ganglia. In addition, extrapyramidal symptoms appear already in the metabolic compensation phase. We describe the case of a 50-year-old male, suffering from new-onset extrapyramidal syndrome, secondary to alcoholic hepatic cirrhosis, diagnosed seven years before. The case is singular for some features: the late-onset of the extrapyramidal syndrome, the absence of tremor, and especially the lack of neuroimaging findings such as MRI hyperintense areas along the basal ganglia.

We hypothesize a mechanism of metabolic compensation, which would be responsible for the late appearance of the extrapyramidal syndrome and the lack of signs of encephalopathy in brain MRI.

The lack of tremor is less clear, because it is a constant symptom of extrapyramidal pathology, and it is unusual that it is lacking as a symptom, after so many years.

1. Introduction

Extrapyramidal syndrome is frequently associated with hepatic encephalopathy (HE). HE can be secondary to liver cirrhosis and B virus infection. The brain MRI shows bilateral and symmetric high T1 signal-intensity in the basal ganglia, particularly in the globus pallidus.

Chronic liver disease often causes neurological manifestations, including HE and hepatic myelopathy (HM). HE is the most common complication of liver disease and is characterized by neuropsychiatric disorders [1]. These include cognitive symptoms, such as confusion, anxiety, depression, decreased concentration and memory until coma, in severe cases, and neuromuscular symptoms, such as flapping tremor, ataxia, hyperreflexia (or hyporeflexia). HE can be present in about 28% of patients with liver cirrhosis, and can be alleviated by lowering the blood ammonia levels [1]. Another syndrome is acquired hepatocerebral degeneration (AHD), a progressive, irreversible neurological syndrome caused by decompensated liver disease, and characterized by abnormal movements, dysarthria, rigidity, tremor, ataxia, and impairment of cognitive functions. AHD is a rare syndrome, about 0.8–2% of cirrhotic patients [2]. The more relevant risk factors are portosystemic shunts both for HE and AHD. In this study we describe the case of a 50-year-old male, suffering from alcoholic hepatic cirrhosis, presenting an unusual new-onset extrapiramidal syndrome, with no neuroimaging signs of encephalopathy.

2. Case report

A 50-year-old male, suffering from alcoholic hepatic cirrhosis was admitted to our observation about a year ago. Seven years after the diagnosis of cirrhosis, he reported the sudden appearance of a symptomatology characterized by mild confusion, rigidity, bradykinesia. Tremor was absent. The symptoms were episodic, the duration was several hours and the frequency was one to two days per month.

The neurological examination showed slightly ataxic gait, muscle hypertonia extrapiramidal-type of upper and lower limbs, bradykinesia. The answers to the examiner's questions were slow.

Laboratory tests, including serum electrolytes and serum glucose, as well as renal function tests were normal, except low proteins values 4,8 g/dL (normal values from 6,4 to 8,3 g/dL).

Hepatic examinations were the following: aspartate aminotransferase (AST) 31,0 IU/L (normal values from 0 to 40 IU/L), alanine transaminase (ALT) 55.5 IU/L (normal values from 0 to 40 IU/L), total bilirubin 16.5 μmol/L (normal values from 0 to 17.1 IU/L). Blood ammonia was 142,5 mmol/L (normal values from 0 to 47 mmol/L). Hepatitis B virus antibodies were negative. There was no ascites. An electroencephalogram showed diffuse theta slow waves. Brain MRI

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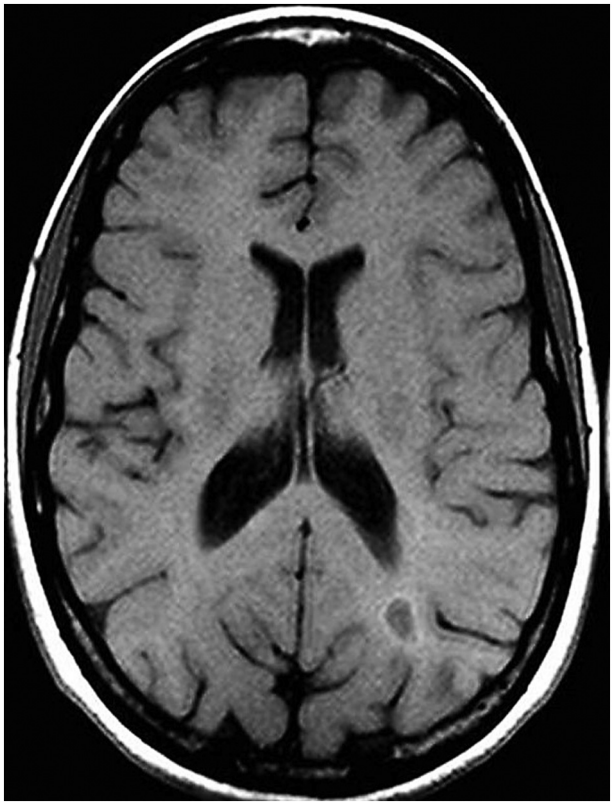

Fig. 1. Axial T1 weighted brain MRI resulting normal.

revealed normal results, especially about the basal ganglia (Fig. 1). The patient was given 30 ml thrice daily lactulose and he was advised of hospital admission. He reported an improvement in general conditions while neurological symptoms did not change.

3. Discussion

HE is caused by ammonia accumulation in the blood, concentrating in the brain.

Brain MRI T2 hyperintensity on T2-weighted images is a common finding in HE patients. The lesions are located on the cortex or on the white matter, and may be related to the increased ammonia concentration in basal ganglia. Manganese accumulation also may contribute to the onset of extrapyramidal symptoms in liver cirrhosis [3].

The white matter abnormalities resulting in the bilateral globus pallidus hyperintensity on MRI T1-weighted images are related to the extrapyramidal symptoms, and ammonia is probably implicated in their development [4].

Studies have been conducted on presence of extrapiramidal symptoms in liver cirrhotic patients. Ashour et al. (2017) observed 98 viral liver cirrhotic patients and found clinical extrapyramidal manifestations in 57 patients (59.4%) with predominant akinetic rigid syndrome (ARS) (87.7%). Bradykinesia and axial features were the most frequent signs (89.5% and 70.2%, respectively). 38.6% of patients had postural tremors, whereas only 3.5% had rest tremors. Gait and postural abnormalities were detected in 38.6% and 36.8% respectively. Parkinsonism-like symptoms were associated with advanced hepatic cirrhosis [5]. Miletic et al., 2014 described the case of a patient with subacute onset of bilateral, asymmetric, hypokinetic-rigid syndrome and ataxia as initial presentation of liver cirrhosis. Manganese toxicity had major role in epatoencephalopathy appearance. Brain regions containing manganese deposits are globus pallidum (GP) and substantia nigra (SN). Characteristic MRI findings of bilateral, symmetrical hyperintensities of GP and SN on T1-weighted sequences supported the extrapiramidal signs. Low-dose levodopa was administered, but failed to provide beneficial effects [6]. Company et al., 2010 affirm that the long-term evolution of cirrhotic patients with extrapyramidal signs has not yet been studied. They investigated the influence of extrapyramidal signs on the prognosis, evolution, and quality of life of 46 patients with liver cirrhosis [7].

Cognitive impairment was measured with psychometric tests, while extrapyramidal signs were evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS). Health-related quality of life was measured using the SF-36 scale and the Chronic Liver Disease Questionnaire (CLDQ). Results were the following: 11 of the 46 patients developed hepatic encephalopathy (HE) during the follow-up. The presence of extrapyramidal signs was the unique factor that predicted HE and patients with basal higher score in the part 3 of the UPDRS developed HE more frequently. In the 18 re-evaluated patients, there was an increase in the score of the UPDRS. Patients with extrapyramidal signs persisted with worse scores in several items of the SF-36 scale and the CLDQ [8]. So, the presence of extrapyramidal signs in patients with liver cirrhosis predicts the development of HE and a bad influence on quality of life.

Extrapyramidal symptoms belong to the most prominent features of episodic hepatic encephalopathy, and usually decrease upon ammonia-lowering therapy. Rapidly progressing parkinsonian symptoms, which are unresponsive to treatment of hepatic encephalopathy, indicate cirrhosis-related Parkinsonism [9]. Cirrhosis-related Parkinsonism is very frequent. It seems that pre- and postsynaptic alterations of striatal dopaminergic neurotransmission could be a possible cause of cirrhosis-related Parkinsonism as revealed by the limited effects of dopaminergic therapy [10].

Considerations on the case described: a 50-year-old male, manifested seven years after the diagnosis of hepatic cirrhosis, an extrapyramidal syndrome. Talking points: literature does not report cases of new-onset extrapyramidal syndrome in cirrhotic patients. This eventuality could be explained by a good metabolic compensation, which would be responsible for the late -onset of neurological symptoms. Second point: the absence of tremor, typical of extrapyramidal syndrome, whether resting or intentional. It is an unusual event, because the tremor is caused by alterations of the cerebral structures responsible for muscle tone and movement, the basal ganglia. The absence of tremor is not clear. It could be due to a presumed mechanism of compensation. Third, the normality of neuroimaging examinations, showing no signs of basal ganglia compromission, such as hyperintensity areas along the globus pallidus and substantia nigra, bilaterally. We can hypothesize a mechanism of metabolic compensation, which would be responsible for both the late-onset of the extrapyramidal syndrome and the lack of signs of encephalopathy at brain MRI.

The lack of tremor is less clear, because it is a constant symptom of extrapyramidal pathology, and it is unusual that it is lacking as a symptom, after so many years.

4. Conclusions

The case described appears singular for the new-onset extrapyramidal syndrome, without clinical signs of tremor and encephalopathy at neuroimaging. We believe in the hypothesis of metabolic compensation that is responsible for the partial form of extrapyramidal disease, which lacks tremor, and especially MRI signs, characteristic of hepatic encephalopathy.

Patient consent

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Conflicts of interest

There is no conflict of interest.

Authorship

Authors attest that they meet the current ICMJE criteria for Authorship.

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