CLINICAL NOTE

Acquired chronic hepatocerebral degeneration due to cirrhosis from non-alcoholic steatohepatitis

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ABSTRACT

Introduction and objective: acquired chronic hepatocerebral degeneration, acquired hepatolenticular degeneration or pseudo-Wilson is an infrequent disorder with a hepatic origin. Cases in the literature are scarce and it is frequently confused with hepatic encephalopathy and Wilson's disease. The aim of this essay is to report a patient suffering from this disorder due to cirrhosis from non-alcoholic steatohepatitis.

Case report: we present a 54-year-old man diagnosed from cirrhosis grade B9 of the Child Pugh classification. He progressively developed a picture with bradykinesia, mild postural and action tremor and spatial and temporal disorientation. Further studies demonstrated an increase of the values of hepatic transaminases and a hiperintensity in the basal nuclei in the cerebral magnetic resonance imaging. Clinical and radiological data established the diagnosis of hepatocerebral degeneration.

Conclusions: acquired chronic hepatocerebral degeneration is a disorder rarely reported in the literature that it is usually confused with other diseases. We alert about the need of having this diagnosis into account with patients developing neurological symptoms after hepatic disease.

Key words: Acquired hepatolenticular degeneration. Hepatic encephalopathy. Acquired chronic hepatocerebral degeneration. Wilson's disease.

INTRODUCTION

Acquired chronic hepatocerebral degeneration (AHD), acquired hepatolenticular degeneration, or pseudo-Wilson is an infrequent neurological disorder provoked by a hepatic disorder that is usually mistaken for hepatic encephalopathy and Wilson's disease. It was initially de-

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scribed in 1914 by van Woerkom (1), although Victor et al. (2) reported a complete anatomopathological description in 1965 in an attempt to clearly differentiate it from Wilson's disease. Neuropathological findings included patchy cortical laminar neuronal loss, neuronal drop-out in the cerebellum and basal ganglia, proliferation of Alzheimer type II glia, and cytoplasmic glycogen granules in basal ganglia (3,4).

AHD has been described in patients suffering from severe liver disease because of several reasons, especially in those with surgically or spontaneously induced portosystemic shunts. Other causes include hepatic parenchymal diseases such as cirrhosis, chronic and acute hepatitis, and hemochromatosis, or cholestatic diseases such as primary sclerosing cholangitis and primary biliary cirrhosis. However, similar cases to AHD have been described in patients without a history of liver disease (5). These case reports are scarce in the literature, many aspects of the disease are still unclear, and patients respond poorly to conventional therapy. We report the case of a patient suffering from this disorder due to cirrhosis from non-alcoholic steatohepatitis.

CASE REPORT

We report the case of a 54-year-old man with a history of type-2 diabetes mellitus and obesity, diagnosed with cirrhosis grade B9 in the Child Pugh classification (MELD score of 19) with portal hypertension (splenomegaly, collateral circulation, and esophageal varices) seven years ago. The results of hepatic investigations including no alcohol consumption, viral serologies,

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copper and iron studies, immunological studies and alpha-1-antitrypsin were normal. Liver biopsy showed micronodular cirrhosis and parenchymal hepatic cells with clear cytoplasm, hepatocyte balloon degeneration with Mallory bodies, macrovesicular fat, megamitochondria, and absence of hemosiderin deposits. These biopsy findings and the clinical picture of the patient allowed to establish a diagnosis of non-alcoholic steatohepatitis.

He progressively developed a two-month picture with bradykinesia, mild postural and action tremor, and spatial and temporal disorientation. These symptoms did not improve with lactulose and paramomycin therapy.

The patient scored 29/30 and 10/10 on Folstein's Mini-Mental Status Examination and the Clock Drawing Test, respectively. Neurological examination revealed dysarthria, bradykinesia, mild action and postural tremor focalized on the left side of his body without flapping tremor, cog-wheel rigidity, and slow alternating movements in his left upper extremity. Laboratory tests revealed the following values: thrombocytopenia 105,000 platelets/dl, prothrombin activity 57%, glutamic-pyruvic transaminase (GPT) 36 U/l, glutamic-oxaloacetic transaminase (GOT) 52 U/l, bilirubin 8.1 mg/dl, alkaline phosphatase 85 U/l, gamma-glutamyl transpeptidase (GGT) 77U/l, albumin 3.3 g/100 ml, glucose 130 mg/100 ml, and lactate dehydrogenase 494 U/l. The results of other laboratory investigations, including thyrotropin (TSH), vitamin B12, and folic acid were all normal. His electroencephalogram showed a general slowing of brain waves (6 cycles per second) without asymmetries or paroxysmal activity. Cerebral tomography showed leukoariosis and T1- and T2-weighted magnetic resonance imaging (MRI) displayed symmetric high-intensity signal lesions in the basal nuclei and cerebral peduncles (Fig. 1). Clinical and radiological data established the diagnosis of hepatocerebral degeneration. The patient was treated with lactulose and paramomycin with initial improvement, which was followed by gradual neurological worsening over the next months. The patient was scheduled for liver transplantation, which was considered the best therapeutic option due to the lack of effectiveness of conventional treatments.

DISCUSSION

Although the pathogenesis of AHD has not been well elucidated, studies have indicated that this disease is associated with multiple metabolic insults, such as ammonia, aromatic amino acids, or manganese, associated with an abnormal susceptibility of certain brain areas to hypoperfusion (3,6-9). The toxic effects of manganese might be a major determinant. It has been proved that manganese is cleared by the hepatobiliary system, and whole blood and cerebrospinal fluid manganese concentrations are several fold above the reference range in some patients with AHD, so that deposition of manganese in the brain is postulated that may induce diffuse degeneration in the cerebral parenchyma. Other theories

Fig. 1. An axial T1-weighted magnetic resonance imaging usually shows a hyperintense signal in basal nuclei.

Hiperintensidad en los núcleos basales en una secuencia de resonancia magnética potenciada en T1.

relate AHD to the same osmotic mechanisms at work in central pontine/extrapontine myelinolysis because the radiologic picture may be similar to cases of central pontine/extrapontine myelinolysis (10).

Clinical symptoms are variable: psychiatric complaints such as apathy, lethargy, excessive somnolence or secondary dementia (11-13), movement disorders such as chorea, focal dystonia, postural tremor, myoclonus (8) or parkinsonism (6), cerebellar symptoms such as ataxia or dysarthria (14,15), or mielopathy –transverse myelitis (16-21)–. The most common symptoms are cognitive impairment, movement disorders or both. Most frequent movement disorders include tremor and chorea (3).

T1-weighted MRI usually shows a hyperintense signal in the basal nuclei (3,6,7), and fronto-parietal lobe and cerebellar atrophy is shown frequently. There seems to be a correlation between the intensity and extension of T1-weighted MRI hyperintensity areas and liver disease severity (22,23). However, this correlation seems not to exist between hyperintensity areas and neurological symptoms (23-26). Although the origin of this radiological hyperintensity is still unclear, recent studies performed by spectroscopy have demonstrated that this lesion is reversible and may show metabolic changes such as a deposition of paramagnetic substances not detoxified

by the liver because of porto-caval shunt or hepatic dysfunction (26).

Some patients showing increased signal intensity in the bilateral dentate nuclei on T2-weighted sequences have also been reported, making the condition indistinguishable from Wilson's disease. The clinical symptoms, neuropathological features, and MRI appearance of AHD are rather uniform and similar to those seen in Wilson's disease. Discrimination depends on the following aspects: age at onset (AHD usually starts after severe liver disease), copper metabolism (out of balance only in Wilson's disease), and Kayser-Fleischer ring (characterizing Wilson's disease but not always present, and absent in AHD). Differences between Wilson's disease and AHD are shown in table I.

Table I. Differential diagnosis between AHD and Wilson's disease

	<i>Wilson's disease</i>	<i>AHD</i>
Etiology	Autosomal-recessive inheritance	Acquired
Age of initiation	Usually < 30 years old	Different age (it usually starts after a severe liver disease)
Copper metabolism	Ceruloplasmin < 200 g/L Contents of copper in liver > 250 µg/g dry weight tissue Contents of copper in urine > 100 µg/24 h	Normal
Kayser-Fleischer ring	Characterizing Wilson's disease although not always present	Absent

Moreover, the disease also differs from the more acute and transient episodes of hepatic encephalopathy: the neurological symptoms of hepatic encephalopathy disappear when the disease is relieved, and there is no organic damage in hepatic encephalopathy. However, individuals with AHD usually experience several episodes of hepatic encephalopathy before brain damage when typical AHD symptoms develop gradually (Table II).

Some patients respond to lactulose diet (3) or branched chain amino acid therapy (27), apart from symptomatic therapies for parkinsonism, including levodopa (6). It has also been reported that an endovascular occlusion of a porto-systemic shunt is temporarily effective. Liver transplantation in selected cases may be curative (6-8,27) but some studies reported a worsening after an initial period of some months of improvement (28,29). A complete resolution of neurological manifestations as well as of MRI findings in the basal nuclei has been described after liver transplantation (19,30,31), although this improvement has not been observed in all cases (13). In addition, we should not forget about the neurotoxic effects of calcineurin inhibitors (cyclosporine and tacrolimus),

Table II. Differential diagnosis between AHD and acute hepatic encephalopathy

	<i>Acute hepatic encephalopathy</i>	<i>AHD</i>
Response to conventional therapy	Yes	No
Organic damage	No	Yes

which are used for immunosuppression in liver transplantation.

AHD is a disorder rarely reported in the literature, but more and more diagnosed by clinical and radiological findings. We alert about the need of having this diagnosis into account with patients with cirrhosis who do not respond to conventional therapy for hepatic encephalopathy.

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