A Rare Case of Acquired Hepatocerebral Degeneration in Cirrhosis

Rohan Ramesh Badave, Anita Basavaraj
Department of Medicine, Byramjee Jeejeebhoy Government Medical College, Pune, Maharashtra, India

Abstract
Hepatic encephalopathy is the most common neurologic complication of cirrhosis of the liver, while acquired hepatocerebral degeneration (AHD) is an underestimated neurologic manifestation. It is characterized by parkinsonism, ataxia, and neuropsychiatric symptoms. It is an underdiagnosed cause of psychomotor retardation in patients with chronic parenchymal liver disease with portosystemic shunting. Manganese deposition in the basal ganglia has been proposed as a mechanism for AHD. Here, we report a case of AHD in a patient with chronic parenchymal liver disease who responded to dopamine agonist.

Keywords: Hepatocerebral degeneration, manganese, parkinsonism

INTRODUCTION
The condition acquired hepatocerebral degeneration (AHD) was first described by Van Woerkem in 1914.[1] Victor et al.[2] in their landmark study reported clinical and pathological features of AHD. It is a neurological complication, characterized by apathy, tremors, psychomotor retardation, and attention deficit. It differs from Wilson disease in underlying pathogenesis. It is proposed that failure of detoxification by liver and presence of portosystemic shunts predisposes to manganese deposition in the basal ganglia leading to AHD.[3] It gets manifested in 0.8%–2% of patients with cirrhosis. It has overlapping features with hepatic encephalopathy, but its management differs. As AHD is a relatively rare and underdiagnosed condition, we report one such case from our hospital, a 32-year-old man with a history of significant alcohol intake presented with extrapyramidal signs and progressive psychomotor retardation.

CASE REPORT
A middle-aged man had altered sensorium of 4-week duration. He was remaining quiet and drowsy throughout the day. He had intermittent melena for 15 days. He had been diagnosed to have chronic parenchymal liver disease 3 months back. He had a history of alcohol intake – 120 ml of wine per day for the past 7 years. There was no significant familial history of hepatic or neurological diseases. On examination, he was afibrile, icteric with a pulse rate of 78/min in sinus rhythm, and blood pressure was 120/80 mmHg. On systemic examination, he was stuporous with hypertonia and exaggerated deep tendon reflexes in all four limbs. Plantar reflexes were bilateral flexors. Other system examinations were within normal limits, except for mild splenomegaly.

On evaluation, he was found to have thrombocytopenia (1.3 lakh/cumm), deranged liver function tests (total bilirubin – 1.3 mg/dl; serum aspartate aminotransferase – 162 IU/l; serum alanine aminotransferase – 59 IU/l; total protein – 6.2 g/dl; albumin – 2.5 g/dl; and globulin – 3.7 g/dl), raised erythrocyte sedimentation rate, and prolonged prothrombin time-international normalized ratio. His Child–Pugh status was class B (score of 7) and model for end-stage liver disease score was 14. Ultrasound of the abdomen showed features suggestive of chronic parenchymal liver disease with portal hypertension. Portal vein diameter was 13 mm. Serum ammonia level was raised – 135 mcg/dl (30–86 mcg/dl). Viral markers for hepatitis B and hepatitis C were negative. Upper gastrointestinal endoscopy was suggestive of two...
columns of grade I varices and portal hypertensive gastropathy. Electroencephalogram [Figure 1] showed triphasic waves on a background of slow waves, suggestive of grade II hepatic encephalopathy. He was started on antihepatic coma measures including syrup lactulose, syrup rifaximin, Ryle’s tube feeding, and thiamine supplementation along with other supportive care. Patient’s sensorium improved, but did not completely recover. Cerebrospinal fluid analysis was normal. Once he became conscious and ambulatory, his further clinical examination on day 6 revealed mask-like face, monotonous speech, and short shuffling gait. It was associated with decreased arm swing while walking. Cranial magnetic resonance imaging (MRI) [Figure 2] revealed increased signal intensity of globus pallidus and subthalamic nucleus bilaterally on T1-weighted images similar to hepatolenticular degeneration (Wilson disease). T2-weighted images showed hyperintensities in periventricular white matter (lateral ventricle). His serum ceruloplasmin levels (38 mg/dl) and 24-h urinary copper levels (16 mcg) were normal. A slit-lamp examination found no Kayser–Fleischer ring. Considering the possibility of AHD, he was started on dopamine agonist tablet pramipexole (0.25 mg 1/2-1/2-1/2) and tablet syndopa ([100 + 25 mg] 1/2-1/2-1/2). He improved subsequently during further hospital course. He was advised to refrain from alcohol and counseled for liver transplantation. He was prescribed medications including tablet pramipexole (0.25 mg 1/2-1/2-1/2) and tablet syndopa ([100 + 25 mg] 1/2-1/2-1/2) for further 3 months. On follow-up, we found that he had recovered well and could take care of himself.

Thus, we had a patient with a clinical profile and investigations suggestive of hepatic encephalopathy (which recovered partially) with AHD causing parkinsonism in the background of chronic liver disease with portal hypertension (ethanol related).

**DISCUSSION**

Hepatic encephalopathy is the most common neurological complication of advanced liver disease. With advanced disease, detoxification function of liver gets impaired. Portosystemic shunts transport these toxic substances to cerebral circulation. Underlying pathogenesis of AHD is deposition of toxic substances at basal ganglia. AHD is a relatively rare neurological condition found in cirrhosis. AHD is characterized by extrapyramidal signs and neuropsychiatric symptoms. The neuropsychiatric manifestations include apathy, psychomotor retardation, memory failure, and deficits in attention. As in our case, the patient had apathy, psychomotor retardation with extrapyramidal signs. Burkhard et al. reported 11 patients of AHD which manifested predominantly as parkinsonism with cirrhosis, seen over a period of 1 year. In this study, all 11 patients were from a hepatic transplantation unit.

In AHD, deposition of manganese at basal ganglia has been attributed for clinical manifestations. Optimal excretory function of the liver is required for clearance of manganese from body fluids. Advanced liver dysfunction with patent portosystemic shunts leads to transport and deposition of manganese at basal ganglia. As a result, selective neuronal dysfunction (especially in the basal ganglia, brainstem, cerebral cortex, and surrounding white matter) occurs. It affects presynaptic dopamine transporters and postsynaptic dopamine receptors, causing extrapyramidal symptoms. Being a paramagnetic substance, deposited manganese presents with T1 shortening. Without neurological symptoms, a patient with cirrhosis can have pallidal hyperintensities on T1-weighted images. The presence of hyperintensities at substantia nigra or subthalamic nucleus on T1-weighted images is a specific marker on MRI of parkinsonism symptoms. In our patient, T1-weighted hyperintensities were seen at globus pallidus and subthalamic nucleus.

Dopamine agonists have shown a variable response in patients with AHD. Treatment modalities such as embolization of portosystemic shunting and liver transplantation have been reported with significant improvement in the symptoms. In our case, the patient improved dramatically with dopamine agonist.

In case of chronic parenchymal liver disease presenting with neurological complications, not improving with antihepatic coma measures and with characteristic manifestations, AHD...
should be suspected. As reported in the literature, it responds
to dopamine agonist, embolization of portosystemic shunting,
and liver transplantation.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Van Woerkem W. Hepatic cirrhosis with alteration in nerve centers
evolving in subjects of middle age. New Iconography of the Salpetriere
[Article in French]. Clin Mal Systeme Nerveux 1914;7:41-5.
2. Victor M, Adams RD, Cole M. The acquired (non-Wilsonian) type
of chronic hepatocerebral degeneration. Medicine (Baltimore)
1965;44:345-96.
3. Burkhard PR, Delavelle J, Du Pasquier R, Spahr L. Chronic parkinsonism
associated with cirrhosis: A distinct subset of acquired hepatocerebral
degeneration. Arch Neurol 2003;60:521-8.
4. Layrargues GP. Movement dysfunction and hepatic encephalopathy.
Metab Brain Dis 2001;16:27-35.
5. Stracciari A, Guarino M, Pazzaglia P, Marchesini G, Pisi P. Acquired
hepatocerebral degeneration: Full recovery after liver transplantation.
J Neurol Neurosurg Psychiatry 2001;70:136-7.
6. Ferrara J, Jankovic J. Acquired hepatocerebral degeneration. J Neurol
2009;256:320-32.
7. Folte W, Wiltfang J, Schindler CG, Unterberg K, Finkenstaedt M,
Niedmann PD, et al. Bright basal ganglia in T1-weighted magnetic
resonance images are frequent in patients with portal vein thrombosis
without liver cirrhosis and not suggestive of hepatic encephalopathy.
J Hepatol 1998;29:443-9.
8. Lee J, Lacomis D, Comu S, Jacobsohn J, Kanal E. Acquired
hepatocerebral degeneration: MR and pathologic findings. AJNR Am J
Neuroradiol 1998;19:485-7.
9. da Rocha AJ, Braga FT, da Silva CJ, Maia AC Jr., Mouro GS,
Gagliardi RJ. Reversal of parkinsonism and portosystemic
encephalopathy following embolization of a congenital intrahepatic
venous shunt: Brain MR imaging and 1H spectroscopic findings. AJNR
Am J Neuroradiol 2004;25:1247-50.
10. Shulman LM, Minagar A, Weiner WJ. Reversal of parkinsonism
following liver transplantation. Neurology 2003;60:519.