Acute stroke-like presentation of acquired hepatocerebral degeneration

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Abstract

Neurological manifestations in liver diseases have been well-described. Parkinsonism developing in cirrhotic patients is a unique clinical, neuroradiological, and biological entity. The symptoms are often insidious in onset and occur after liver disease has made its presentation. Acute dysarthria as the presenting manifestation of cirrhosis is rare. Here we report three cases where liver disease made an unusual presentation as acute dysarthria. In all cases the abruptness of the onset prompted the treating physicians to make a diagnosis of stroke. The computed tomography (CT) scans of all these patients did not show any evidence of stroke. This was followed by magnetic resonance imaging (MRI) which showed the characteristic symmetric high-signal intensities in globus pallidus and substantia nigra in T1-weighted images, a reflection of increased tissue concentrations of manganese that helped in making a retrospective diagnosis of liver disease, confirmed later by altered serum albumin to globulin ratios and altered liver echo texture in ultra sonogram.

Key Words

AHCD, MRI, pallidal hyperintensities, stroke

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Ann Indian Acad Neurol 2014;17:204-6

Case Report

Case report 1

A 42-year-old school teacher presented with a history of acute onset of dysarthria while he was addressing the class. He had no other symptoms and had been asymptomatic until the day of presentation. At the time of examination he was conscious, well-oriented, had dysarthria but no other cranial nerve abnormalities. His higher mental functions were normal and he had no neurological deficits. There was no KF ring or hepatosplenomegaly. Because of the acute presentation, stroke was suspected and a CT scan was ordered which turned out to be normal. An MRI taken later revealed bilateral symmetric hyperintense signals in the basal ganglia, especially globus pallidus [Figure 1] and substantia nigra [Figure 2] in T1-weighted image with normal T2 image. Diffusion-weighted images did not show diffusion restriction. Liver function tests revealed A/G reversal. A/G ratio was 0.85. Liver enzymes were at normal levels. Serum electrolytes and blood routine were normal. Serological tests were negative for hepatitis B, C and, HIV. Serum copper, ceruloplasmin, iron, ferritin, transferrin and TIBC were within normal limits. An ultra sonogram of abdomen showed features of cirrhosis. The etiology of his liver disease could not be identified.

Access this article online	
Quick Response Code:	Website: www.annalsofian.org
	DOI: 10.4103/0972-2327.132631

Case report 2

A 45-year-old man presented with dysarthria and ataxia, which were noticed in the morning, on waking up from sleep. He did not have any other symptom referable to other cranial nerve dysfunction, limb weakness, sensory symptoms, or involuntary movements. His higher mental functions were normal. The patient had a mask-like facies. He had mild rigidity in all four limbs and impaired tandem walking. The typical presentation in the early hours of the day with normal CT brain, prompted the physician to make a diagnosis of stroke. MRI brain showed the symmetric T1 hyperintense lesions in globus pallidus without restriction in diffusion-weighted images. MR spectroscopy showed the characteristic glutamine-glutamate signal peak. Shrunken liver in ultrasonogram and abnormal liver function tests in the form of A/G reversal confirmed the diagnosis of cirrhosis. He underwent an esophago-duodeno gastroscopy which revealed esophageal varices and fundal gastropathy. A work-up for Wilson's disease drew negative results. His viral markers were negative as well. A specific cause for cirrhosis could not be found in spite of extensive investigations.

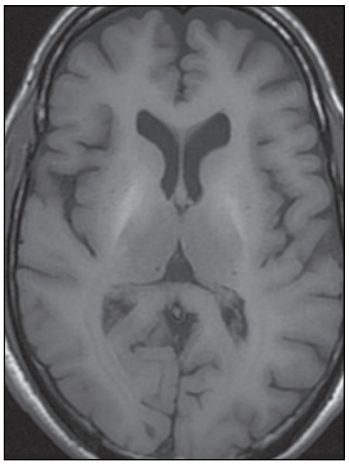

Figure 1: T1-weighted brain MRI showing symmetric hyperintensities in globus pallidus

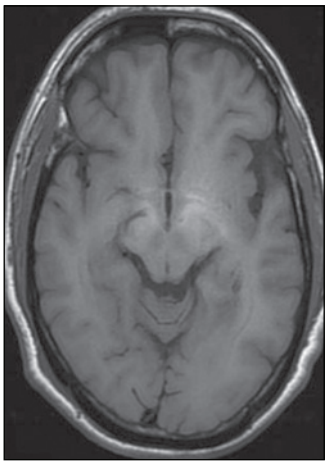

Figure 2: T1-weighted brain MRI showing hyperintensities in substantia nigra

Case report 3

A 45-year-old male woke up in the morning to find that his speech was slurred. He was hypertensive and was on treatment with 5 mg of amlodipine. He had no weakness, numbness, or signs of incoordination. His BP at presentation was 146/100 mmHg. He had dysarthria but otherwise his neurological examination was normal. An MRI was ordered which showed the bilaterally symmetric T1 hyperintensities in globus pallidus and substantia nigra. Liver function tests were deranged showing albumin- globulin reversal. Diagnosis of cirrhosis was confirmed by an abdominal ultra sonogram which showed coarse echo texture with shrunken liver. He had no documented liver disease previously. As in the other cases the serologic tests for viral markers and Wilson's disease were negative in this case as well.

Table 1: Differential diagnosis of basal ganglia signal changes

Conditions causing T1 hyperintensities in basal ganglia	Conditions causing T2 hyperintensities in basal ganglia
Total parental nutrition	Carbon monoxide poisoning
Non-ketotic hyperglycemia	Acute hyperammonemia
Neurofibromatosis Type I	Wilson's Disease
Hypoxic ischemic encephalopathy	Osmotic myelinolysis
Industrial Mn toxicity	Hypogycemia
Early Kernicterus	Wernicke's encephalopathy
Wilson's Disease	NBIA
MSA-P	Cocaine poisoning
	Neurofibromatosis Type I

Discussion

Patients with chronic liver diseases frequently experience neurological problems the most common of which is hepatic encephalopathy. A proportion of patients with chronic liver disease develop acquired hepatocerebral degeneration (AHCD), a chronic progressive neurological syndrome characterized by Parkinsonism, ataxia, dementia and other movement disorders. Although this entity has been recognized as early as 1914, the exact prevalence still remains largely uncertain. In a large retrospective study ~1% of patients with cirrhosis was found to have AHCD and was found to be related to portal-systemic shunts.[1] The term acquired hepatocerebral degeneration was introduced in 1965 by Victor *et al.,* to distinguish the clinical manifestation in chronic liver disease from the genetic form, Wilson's disease.

The pathophysiology of the more common neurological manifestation of liver disease, hepatic encephalopathy, is better understood. Various abnormalities ranging from structural alteration of astrocytes to that of neurotransmitters and accumulation of toxic metabolites have been postulated. Astrocyte is the most vulnerable cell to liver failure. Astrocytes undergo swelling in acute liver failure which results in a rise in intracranial pressure. On the other hand, in chronic liver failure they undergo a characteristic change known as Alzheimer's type II astrocytosis which can cause altered expression of several key proteins and enzymes.[2]

The exact pathophysiology of AHCD is less well understood. Pallidal hyperintensities on T1-weighted MR imaging seen in patients with chronic liver disease correlate with the presence of extra-pyramidal symptoms and is thought to be a consequence of manganese deposition secondary to portal-systemic shunting. Elevated manganese levels found in patients with cirrhosis due to portal-systemic shunting accumulates preferentially in globus pallidus, substantia nigra pars reticulata, and to some extent in striatum. Manganese preferentially produces pallidal degeneration, loss of dopamine-binding sites, while sparing the nigrostriatal system to some extent, in contrast to Parkinson disease, which preferentially damages dopaminergic neurons in the substantia nigra pars compacta.

A characteristic MRI picture with bilaterally symmetric hyperintensities in globus pallidus and substantia nigra is seen in 71-92% of patients with cirrhosis.[3] Pallidal hyperintensity correlates with blood manganese levels and is thought to be due to deposition of manganese in these structures. A similar picture can be seen in some other conditions as well. Table 1 lists conditions which come under the differential diagnosis of this neuroimage.

Most cases of AHCD are diagnosed in patients with overt liver disease.[3,4] Review of literature describes AHCD as a chronic process occurring in patients with documented liver disease who have had repeated episodes of hepatic encephalopathy. In a case report by Noone *et al.,* two patients who presented with slowly progressive Parkinsonism were subsequently diagnosed to have cirrhosis based on subtle abnormalities in liver function tests and MRI findings.[5] In all reports of Parkinsonism in liver disease, except one, Parkinsonism was slowly progressive. In a case report by Pendlebury *et al.,* a similar stroke-like presentation with dysarthria, dysphagia and difficulty in walking was reported in a 17-year-old boy who was subsequently diagnosed to have Wilson's disease.[6]

We report three cases of cirrhosis that made a stroke-like presentation before the diagnosis of liver disease was made. In all cases the presentation was marked by the acute occurrence of dysarthria with the striking absence of other neurological deficits. The diagnosis of cirrhosis would have been missed had it not been for the typical MRI picture. All three patients had identical MRI pictures and almost similar clinical presentations. Reversal of A/G ratio consistently seen in all the three patients could prove to be an important clue toward the diagnosis of AHCD in these patients. None of them had any reported evidence of hepatic encephalopathy. All our patients showed good response to treatment with dopa agonists which conforms to the findings in literature that AHCD is a reversible phenomenon.

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How to cite this article: Smita B, Gafoor VA, Saifudheen K, Jose J. Acute stroke-like presentation of acquired hepatocerebral degeneration. Ann Indian Acad Neurol 2014;17:204-6.
Received: 17-03-13, **Revised:** 02-10-13, **Accepted:** 14-10-13

Source of Support: Nil, **Conflict of Interest:** Nil