

# ACQUIRED HEPATOCEREBRAL DEGENERATION IN HEPATITIS C INFECTION

Nasir Khokhar, Arsalan Ahmad and Muhammad Mansoor Butt

## ABSTRACT

Patients with chronic liver disease (CLD) often have neurological sequelae, of which hepatic encephalopathy is the most frequent and reversible. Rare irreversible complications of CLD are acquired (non Wilsonian) hepatocerebral degeneration (AHCD) and hepatic myelopathy (HM). To our knowledge, AHCD has rarely been reported in patients with hepatitis C virus (HCV) infection. We report a patient with HCV infection who developed AHCD and resulted in serious complications.

**KEY WORDS:** *Hepatitis C. hepatocerebral. Chronic liver disease. Degeneration.*

---

## INTRODUCTION

Acquired hepatocerebral degeneration (AHCD) is a rare irreversible complication of chronic liver disease (CLD)<sup>1</sup> and was first described by Van Woerkom in 1914<sup>2</sup> and Victor and coworkers in 1965<sup>3</sup> They attributed it to prolonged exposure to metabolic toxins that cause encephalopathy. Dementia, dysarthria, cerebellar dysfunction, movement disorders, myoclonus, rigidity, dystonia, myelopathy, hyperreflexia, and extensor plantar responses have all been reported.<sup>4</sup> Recent neuro-radiological imaging studies, mainly MRI, have shown hyper intense signals in the pallidum, putamen, mesencephalon internal capsule, lentiform nucleus and cerebral peduncles on T1 weighted images.<sup>5</sup> Lewis et al. also reported extensive white matter disease on T2 weighted MRI images.<sup>1</sup>

Extrahepatic manifestations of chronic hepatitis C virus (HCV) infection can be varied.<sup>6</sup> Central nervous system involvement in patients with HCV infection has only rarely been reported.<sup>7</sup> Peripheral neuropathy,<sup>8</sup> stroke and progressive encephalomyelitis with rigidity<sup>9</sup> have been reported rarely and HCV RNA has been detected in brain tissue.<sup>10</sup> Some of these conditions have been associated with cryoglobulinemia and anticardiolipin antibodies.<sup>6,7</sup> While AHCD and other neuropsychiatric symptoms have been seen in CLD, cases of AHCD with HCV infection have, to our knowledge, not been reported. We report a patient of HCV infection who developed AHCD, and had no evidence of Wilson's disease.

## CASE REPORT

The patient was a 37-year-old male who presented with a two-week history of fever, generalized aches and pains, and mild weakness of the left upper and lower limbs. He had a short history of diabetes mellitus, and was recently diagnosed with

Department of Medicine, Division of Gastroenterology and Neurology, Shifa International Hospital / College of Medicine, Islamabad.

**Correspondence:** Dr. Nasir Khokher, Shifa International Hospital, Sector H-8/4, Islamabad 44000, Pakistan. E-mail: drnkhokhar@yahoo.com

Received April 12, 2004; accepted November 10, 2004.

HCV infection and was strongly positive for HCV by PCR. His pulse was 110 per minute at the time of admission, and temperature was 101 degrees Fahrenheit. Serum creatinine was 1.1 and blood glucose was 216 mg/dl. Total bilirubin was 2.23 mg/dl, AST was 100 U/L, ALT was 58 U/L and alkaline phosphatase was 120 U/L. Childs-Pugh class was B.

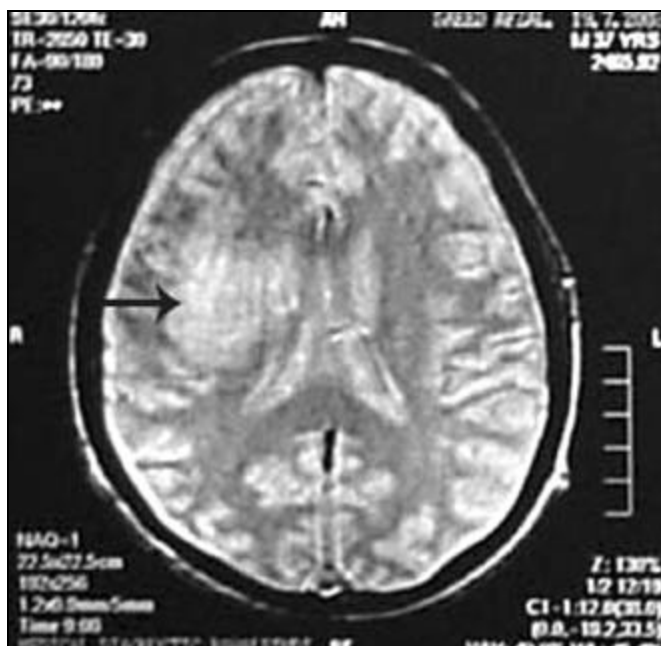
On the first day of admission, he had a focal onset (left arm), generalized seizure. After the seizure, he was unable to move his left arm and leg. On CNS examination, he was alert, replied to simple questions and carried out commands. Extraocular movements were full. Pupils measured 4mm and were equal, circular and active. He had a mild left lower facial weakness, moderate weakness of left upper limb (MRC scale 3/5) and mild weakness of left leg (MRC scale 4/5). Deep tendon reflexes were diminished in the left arm and leg. Plantar responses were extensor on the left and flexor on the right. He had no neck rigidity. A CT scan of the head showed no infarct, hemorrhage or space-occupying lesion. An ultrasound of the abdomen showed coarse echo texture of the liver. EEG showed normal background rhythm and no epileptiform activity. A chest X-ray had no significant findings.

An MRI of the brain showed high signal intensity areas in the lentiform nucleus and basal ganglia on T1 weighted images (Figure-1), a mild low signal intensity area in the right frontoparietal area and a high signal intensity area in the frontoparietal white matter on the right side on T2 weighted images (Figure-2), reported as microvascular angiopathy and possible deposition of copper and manganese, with regional cerebritis.

Serum ceruloplasmin level was 23 mg/dl (normal 20 - 60 mg/dl). A slit lamp examination showed no Keyser-Fleischer ring. Anti-nuclear antibody was negative. The symptoms and signs supported by the laboratory and radiological evidence led to a diagnosis of acquired hepatocerebral degeneration, secondary to hepatitis C infection. He was given phenytoin 30mg orally daily, prednisolone 30 mg daily orally, a low copper diet and physiotherapy. He had no further seizures, his weakness improved and he was discharged but did not report for follow-up.



**Figure 1** T1 AHCD coronals showing high signal intensity areas in the lentiform nucleus and basal ganglia.



**Figure 2** T2 AHCD Axial showing high signal intensity area in the frontoparietal white matter.

## DISCUSSION

In addition to hepatic disease, there are important extrahepatic manifestations of HCV infection. Most of these syndromes are associated with autoimmune or lymphoproliferative states, and may be related to the possibility that HCV is able to replicate in lymphoid cells.<sup>6</sup> Cryoglobulins have been found in upto half of patients with HCV infections and the cryoprecipitates usually contain large

amounts of HCV antigens and antibodies. However, only a small fraction of affected persons (10-15%) have symptomatic disease.<sup>6</sup>

Central nervous system involvement in patients with HCV infection has been reported in a 31-year-old woman who developed cerebral ischemia.<sup>7</sup> Presence of viral RNA in nerve tissues has been demonstrated with nested RT-PCR technique in patients with HCV infection with peripheral neuropathy in the absence of mixed cryoglobulinemia.<sup>8</sup>

Although AHCD was first described in 1914<sup>2</sup>, subsequent details were published later<sup>3</sup> and foci of destruction of nerve cells, in addition to widespread transformation of astrocytes were noted.<sup>2</sup> Clinical manifestations have ranged from tremors, twitching, unsteady gait and paralysis to EEG abnormalities.<sup>2</sup> Blood ammonia level has been found to be elevated.<sup>2</sup> Extensive white matter disease with high signals on T2 weighted MRI have also been reported.<sup>1</sup>

Our patient showed clinical and MRI findings similar to those reported earlier in AHCD patients. There was no evidence of copper overload in this case and he suffered from CLD due to HCV. In conclusion, AHCD may be a rare manifestation of hepatitis C virus infection. Hence, AHCD needs to be considered if patients with HCV infection develop neurological features.

## REFERENCES

1. Lewis MB, Mac Quillan G, Bamford JM, Howdle PD. Delayed myelopathic presentation of the acquired hepatocerebral degeneration syndrome. *Neurology* 2000;**54**:1011.
2. Victor M, Ropper AH. Acquired metabolic disorders of the nervous system. In: Victor M, Ropper AH (edi). New York: McGraw Hill, 2001; 1195-96.
3. Victor M, Adams RD, Cole M, The acquired (non Wilsonian) type of chronic hepatocerebral degeneration. *Medicine* 1965;**44**: 345.
4. Lockwoodr AH. Hepatic encephalopathy and other neurological disorders associated with gastrointestinal disease. In: Aminoff MJ, (edi). *Neurology and general medicine: the neurological aspects of medical disorders*. New York: Churchill Livingstone 1989; 22-30.
5. Bozluolcay M, Pelin Z, Denktas. Neuroimaging aspects of chronic acquired hepatocerebral degeneration in a case report. *Neurological Sciences (Turkish)* 2001.
6. Lauer GM, Walker BD. Hepatitis C virus infection. *N Engl J Med* 2001;**345**:41-52.
7. Younes S, Chebel S, Boukhris S, Frih-Ayed M. Central nervous system involvement in patients with hepatitis C infection. *Rev Neurol* 2002;**158**:1202-4.
8. De Martino L, Sampaolo S, Tucci C, Ambrosone L, Budillon A, Migliaresi S, et al. Viral RNA in nerve tissues of patients with hepatitis C infection and peripheral neuropathy. *Muscle Nerve* 2003;**27**:102-4.
9. Gazulla Abio J, Benavente Aguilar I, Capablo Liesa JL. Progressive encephalomyelitis with rigidity: clinical and electrophysiological aspects. *Neurologia* 2001;**16**:85-8.
10. Bolay H, Soylemezoglu F, Nurlu G, Tuncer S, Varii K. PCR detected hepatitis C virus genome in the brain of a case with progressive encephalomyelitis with rigidity. *Clin Neurol Neurosurg* 1996;**98**:305-8.

.....★.....