CASE REPORT

Acquired hepatocerebral degeneration

Pushendra Nath Renjen,¹ Laxmi Khanna,¹ Ruchi Rastogi,² Nadeem Israr Khan¹¹Department of Neurology, Indraprastha Apollo Hospital, New Delhi, India²Department of Radiology, Indraprastha Apollo Hospital, New Delhi, India**Correspondence to**
Professor Pushendra
Nath Renjen,
pnrenjen@hotmail.com**SUMMARY**

Acquired (non-Wilsonian) hepatocerebral degeneration is a rare irreversible neurological syndrome that occurs in patients with chronic liver disease associated with multiple metabolic insults. Van Woerkom was the first to describe acquired hepatocerebral degeneration in 1914 followed by the landmark article by Victor *et al* in 1965. Multiple bouts of hepatic coma are the only known risk factors that trigger this devastating neurodegenerative disease with features suggesting toxic exposure to the brain. Clinically and pathologically the disorder is similar to Wilson's disease although subtle differences in immunostaining of glial fibrillar acidic protein have been documented. Acquired hepatocerebral degeneration occurs in 0.8–2% of patients with cirrhosis. As acquired hepatocerebral degeneration is relatively rare, we are reporting one such case from our hospital in a 50-year-old male patient who had long-standing portal systemic shunt and presented with progressive cognitive decline, bradykinesia, tremors and bilateral extrapyramidal signs.

BACKGROUND

Acquired hepatocerebral degeneration is a rare irreversible neurological syndrome, which is rarely encountered by a neurologist in clinical practice. Though it is commonly confused with hepatocerebral degeneration owing to Wilson's disease, it is important to differentiate them so as to determine the plan of treatment. Liver transplantation has been found to be very effective in stopping the progression of neurological damage, and at times gradual improvement of neurological function in such cases.

CASE PRESENTATION

A 50-year-old man was admitted in September 2012 for progressive walking difficulty, stiffness and recurrent falls of 6 months duration. He had a history of chronic liver disease diagnosed 3 years ago. An infectious aetiology for the liver disease was not established and viral markers were negative. He did not consume alcohol in the past. No familial hepatic or neurological diseases were reported. In 2009, he was evaluated for cirrhosis and portal hypertension. Upper gastrointestinal endoscopy detected grade 4 giant fundal varices, which were resected. Postoperatively, he had episodes of somnolence and confusion lasting for 24 h for which the family members were administering frequent enemas and bowel wash at home. In March 2012, he developed a stiff gait with recurrent falls in the night while getting up to pass urine. In June 2012, he developed speaking and swallowing difficulty with emotional incontinence. He also had signs of encephalopathy (confusion

and asterix) both reversed by medical therapy. In July 2012, he was presented with sleep disorders, tremor, motor slowness and memory disturbance not reversed by medical therapy for hepatic encephalopathy. In September 2012, he was admitted with slowness of psychomotor activity, speaking difficulty, progressive swallowing difficulty, impaired memory and inability to walk.

Physical examination revealed a middle-aged man with significant clubbing. He was not jaundiced. There was no pedal oedema or other stigmata of chronic liver disease like palmar erythema, telangiectasia and dilated veins over the abdomen or ascites. There was no hepatosplenomegaly. At the time of examination liver failure was grade B 7 of the Child Pugh classification. The neurological examination showed emotional incontinence, hypomimia, dysarthria, bradykinesia and mild bilateral hand tremor. He had increased tone in all four limbs with exaggerated deep tendon reflexes and extensor plantars. Neuropsychological examination showed a remarkable impairment of information processing (attention, vigilance, psychomotor speed, intelligence) and impairment of memory. On slit-lamp examination there was no Kayser-Fleischer ring and ophthalmological examination was normal.

INVESTIGATIONS

An EEG disclosed diffuse slow activity in the θ range. There were no triphasic waves. Cerebral MRI showed bilateral symmetrical pallidal hyperintensities on T1 images (arrows) and hyperintense signal on T2 images (figure 1). There were symmetrical areas of signal alteration in bilateral deep cerebellar white matter and brachium pontis, seen as hypointense on T1-weighted (T1-W) (arrows) and hyperintense on both T2-weighted (T2-W) and fluid-attenuated inversion recovery sequences (figure 2). Laboratory studies revealed normal haematocrit, platelet count ($148\,000/\text{mm}^3$), prothrombin time 16.8/10.4 (International Normalised Ratio (INR) 1.6), normal liver function tests except for albumin globulin reversal (serum total bilirubin of 1.2 mg/dL (0.1–1.0 mg/dL), direct bilirubin 0.6 mg/dL (0–0.4 mg/dL), serum glutamic oxaloacetic transaminase (SGOT) 53 U/L (10–40 U/L), serum glutamic pyruvate transaminase (SGPT) 35 U/L (10–55 U/L), alkaline phosphatase 171 U/L (20–70 U/L), gamma-glutamyl transpeptidase (GGTP) 30 IU/L (11–51 IU/L), serum protein 6.2 g/dL (6–8.5 g/dL), albumin 2.7 g/dL (4–5 g/dL) /globulin 3.5 g/dL (2.5–3.5 g/dL). Normal serum ceruloplasmin 21.1 mg/dL (25–50 mg/dL), serum copper was 110 $\mu\text{g/L}$ (70–155 $\mu\text{g/L}$) and serum ammonia was 159.0 $\mu\text{mol/L}$ (9–33 $\mu\text{mol/L}$). His ultrasound scan of the abdomen showed a small echogenic liver with splenomegaly.

To cite: Renjen PN, Khanna L, Rastogi R, *et al*. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-009387

Figure 1 (A) Axial non-contrast T1-weighted image showing bilateral symmetrical pallidal hyperintensities (arrows). (B) Corresponding areas are showing hyperintense signal on T2-weighted sequence (arrows).

OUTCOME AND FOLLOW-UP

The patient underwent liver transplantation within 2 weeks of admission and postoperatively he showed a steady improvement in cognitive functions. He was discharged in a stable condition with improvement in speech, bradykinesia and reduction in the intensity of tremor.

DISCUSSION

Liver diseases give rise to variable degrees of neurological impairment ranging from hepatic encephalopathy caused by the toxic effects of ammonia on the brain to a chronic progressive encephalopathy called acquired hepatocerebral degeneration characterised by Parkinsonism, cognitive decline and movement disorders.^{1 2} The disease appears after one or more episodes of hepatic coma or it begins insidiously following a decline in hepatic function.^{1 2} The pathogenesis of the disease is not known but diversion of portal blood in to the systemic circulation appears to underlie the condition.² The disease is common in patients with large porto systemic shunts and usually does not respond to therapy for hepatic encephalopathy.^{2 3} The neuropsychiatric changes include apathy, psychomotor retardation, memory failure and deficits in attention and concentration suggestive of a subcortical dementia.² In the case reports by Stracciari *et al*² there were significant impairment in visuospatial attention and motor sequencing. The movement disorders include severe bradykinesia, rigidity, postural instability, postural

tremor and orobuccolingual dyskinesias.² Acquired hepatocerebral degeneration may be associated with myelopathy and spastic paraplegia.² A neurotoxic substance from the portal circulation bypasses hepatic metabolism and enters in to the systemic circulation traversing the blood–brain barrier.² Manganese is one such potential neurotoxin that could accumulate in the mitochondria of the globus pallidum damaging the glial cells and disrupting their energy metabolism.² The neuropathological changes observed in non-Wilsonian hepatocerebral degeneration include diffuse astrocytic hyperplasia, microcavitation and zonal necrosis of the deeper parts of the cerebral cortex and the lenticular nuclei with loss of nerve cells in the cerebral cortex, putamen, thalamus, cerebellar cortex and dentate nuclei.^{2 3} Polymicrocavitation of the cortex and adjacent internal capsule along with loss of axons in the corticospinal tracts of the spinal cord occur.^{2 3} MRI of the brain shows lesions in the lenticular nuclei and midline cerebellum.^{3–5}

Our patient presented with cognitive decline, spasticity and extrapyramidal signs. Wilson's disease was unlikely in this 50-year-old man who had no Kayser-Fleischer rings, normal serum copper and ceruloplasmin levels. MRI changes have been reported in cases of acute hepatic encephalopathy; however, such cases respond to medical therapy.⁶ It is difficult to differentiate between neurological symptoms owing to hyperammonaemia which occurs in the case of hepatic encephalopathy or owing to acquired hepatocerebral degeneration, as pathogenesis

Figure 2 Axial non-contrast T1-weighted (A), T2-weighted (B) and fluid-attenuated inversion recovery (FLAIR) sequences (C) at corresponding cross-sectional levels obtained a day after admission demonstrating symmetrical areas of signal alteration in bilateral deep cerebellar white matter and brachium pontis seen hypointense on T1-W (white arrows) and hyperintense on both T2W and FLAIR sequences.

of both these entities is complex and not fully understood.⁷ Our patient despite having high levels of ammonia did not respond to medical management for hepatic encephalopathy and there was no consciousness impairment, both features are present in hepatic encephalopathy. Furthermore, the clinical presentation and radiological findings could not solely be attributed owing to hepatic encephalopathy. In our patient MRI of the brain showed characteristic bilateral symmetrical pallidal hyperintensities with signal alteration in bilateral deep cerebellar white matter and brachium pontis (figures 1 and 2). Both the clinical and neuro-radiological abnormalities are reversed by liver transplantation.^{2–5} Neurological improvement following liver transplantation occurs gradually over the course of 1 month to 1 year.^{2 3 5} The duration of the response following transplantation is not known but favourable outcomes in excess of 6 years following transplantation have been documented.^{2 3}

Learning points

- ▶ All cases of hepatocerebral degeneration are not owing to Wilson's disease; other causes should be looked for.
- ▶ MRI findings described in the above case are pathognomonic hepatocerebral degeneration, and should be looked for in every case of recurrent hepatic encephalopathy.
- ▶ Patient with non-Wilsonian hepatocerebral degeneration do fairly well after liver transplantation.
- ▶ Early liver transplantation is very effective in stopping progression of neurological symptoms, and at times may lead to gradual improvement of such symptoms to a certain extent.

Contributors All the authors have been involved in the conception, drafting of the article and the final version of the draft has been approved.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Stracciari A, Guarino M, Pazzaglia P, *et al.* Acquired hepatocerebral degeneration: full recovery after liver transplantation. *J Neurol Neurosurg Psychiatry* 2001;70:136–7.
- 2 Ferrara J, Jankovic J. Acquired hepatocerebral degeneration. *J Neurol* 2009;256:320–32.
- 3 Powell EE, Pender MP, Chalk JB, *et al.* Improvement in chronic hepatocerebral degeneration following liver transplantation. *Gastroenterology* 1990;98:1079–82.
- 4 Wijds EF, Weisner RH. Acquired (non-Wilsonian) hepatocerebral degeneration: complex management decisions. *Liver Transpl* 2003;9:993–4.
- 5 Lee J, Lacomis D, Comu S, *et al.* Acquired hepatocerebral degeneration: MR and pathologic findings. *AJNR Am J Neuroradiol* 1998;19:485–7.
- 6 Jong MC, Yoon HK, Sook YR. Acute hepatic encephalopathy presenting as cortical laminar necrosis: case report. *Korean J Radiol* 2013;14:324–8.
- 7 Romeiro FG, Américo MF, Yamashiro FS, *et al.* Acquired hepatocerebral degeneration and hepatic encephalopathy: correlations and variety of clinical presentations in overt and subclinical liver disease. *Arq Neuropsiquiatr* 2011;69:496–501.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow