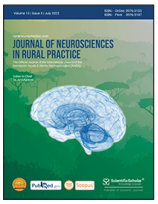
ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

https://ruralneuropractice.com

Journal of Neurosciences in Rural Practice



Case Series

Chronic liver disease and hepatic encephalopathy patients with new-onset focal motor status epilepticus: Indicates herpetic encephalitis

Roshan Koul[1], Navin M. Kumar[2], Darakshan Naheed[1], Shiv K. Sarin[2]

Department of [1]Neurology and [2]Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India.

ABSTRACT

Seizures are not common in cases with chronic liver disease. Overall seizures have been reported in 20–30% of cases in chronic liver disease associated with hepatic encephalopathy. We report two cases of chronic liver disease patients who presented with new-onset refractory focal status epilepticus (SE). Both patients had encephalitis and seizures which responded only when acyclovir was added to the treatment with antiepileptic medication. Herpes encephalitis should be considered as a possible diagnosis in new-onset focal seizures or focal SE in patients with chronic liver disease with or without hepatic encephalopathy, pending further investigations.

Keywords: Chronic liver disease, Focal seizures, Encephalitis, Magnetic resonance imaging, Positron emission tomography computed tomography

INTRODUCTION

Convulsive status epilepticus (SE) is a neurological emergency that requires urgent management to avoid mortality and morbidity.[1] Convulsive SE may be generalized or focal (partial). An urgent three-pronged management approach is recommended in the form of stabilizing patients' vitals, controlling seizures, and diagnosing the etiology of the underlying disease process.[2] Central nervous system (CNS) infection, autoimmune disease, a structural lesion or malignancy, vascular etiology, demyelinating disorders, CNS autoimmune disease, or a toxic/metabolic condition are possible etiologies.[3] With convulsive SE in patients with chronic liver disease and hepatic encephalopathy, one would expect the liver disease to be the cause of seizures, but if there are focal seizures or SE, another etiology, particularly herpes simplex encephalitis (HSE), should be considered until workup for an alternative etiology is completed. Herpes encephalitis patients usually present with focal seizures, altered mental state, and focal neurological deficits. Mortality of 7% is seen in herpetic encephalitis if early diagnosed and treated as compared to 70% if not treated.[4] Herpes encephalitis as underlying etiology in two patients with chronic liver disease, who presented with focal SE is reported in this article. Permanent sequelae and mortality rates can be reduced if patients with chronic liver disease, presenting with refractory new-onset SE, are treated for HSE with appropriate antiviral medication.

CASE SERIES

Case 1

A 50-year-old male, known case of chronic liver disease (ethanol related), with jaundice, ascites, portal hypertension, and esophageal varices, presented with abnormal movements of the left foot and leg of 3-day duration [Table 1]. He was admitted to the institute of liver and biliary sciences in January 2020. Over the next 3 days, there was spread of these movements to the left upper limb and occasionally to the left angle of mouth. These focal seizures occurred every 5 min and continued non-stop in awake and sleep state. Following these movements, the patient experienced weakness of the foot. There was no loss of awareness, unconsciousness, or tonic–clonic movements of the rest of the body. There was no involvement of speech. There was no history of fever, trauma, or recent alcohol intake before hospital admission. His neurological examination was essentially normal other than exaggerated deep tendon reflexes in the left upper and lower limbs with the left plantar extensor. Electroencephalograph (EEG) revealed mild slowing on the right side. Brain magnetic resonance imaging (MRI) revealed altered signal intensity in bilateral insular cortex and medial temporal lobes, right more than left [Figure 1]. Positron emission tomography (PET) and computerized tomography (CT) showed increased fluorodeoxyglucose uptake in the right mid and

***Corresponding author:** Roshan Koul, Department of Neurology, Institute of Liver and Biliary Sciences, New Delhi, India.
koulroshan@gmail.com

Received: 15 June 2021 **Accepted:** 15 October 2021 **EPub Ahead of Print:** 02 November 2022 **Published:** 16 December 2022 **DOI:** 10.25259/JNRP-2021-6-30 (1812)

Table 1: Summary of the two cases with chronic liver disease and focal seizures.

S. No.	Age (Y)	Sex (M/F)	Clinical presentation	EEG	MRI	PET-CT	Cerebrospinal fluid	Management	Outcome
1	50	M	Chronic liver disease (CLD), ethanol, focal seizures (epilepsia partialis continua)	Focal slowing	Involvement of bilateral insular cortex and medial temporal lobes, right more than left	Increased FDG uptake in right posterior cingulate gyrus, para hippocampus	Normal for routine Negative herpes virus DNA, negative autoimmune panel	Treatment of CLD, levetiracetam, lacosamide, acyclovir	Seizure free, off medications
2	61	M	CLD, liver transplant, left focal status epilepticus	Focal electrical status epilepticus	Right medial temporal lobe involvement	Not done	Refused	Treatment of CLD, levetiracetam, lacosamide, acyclovir	Seizure free, off medications

Y: Year, M: Male, EEG: Electroencephalograph, MRI: Magnetic resonance imaging, PET: Positron emission tomography, CT: Computerized tomography, FDG: Fluorodeoxyglucose, DNA: Deoxyribose nucleic acid

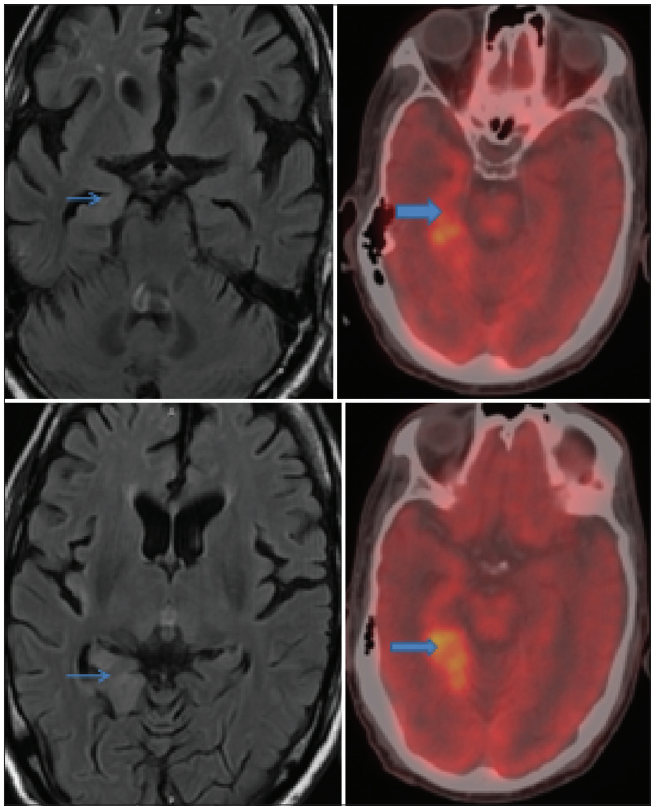


Figure 1: Magnetic resonance imaging (MRI) and positron emission tomography computed tomography (PET-CT) brain show T2-weighted fluid-attenuated inversion recovery sequence axial view hyperintensities involving right temporal gyrus (MRI – small arrow, PET-CT – thick arrow).

posterior cingulate and right precuneus gyri extending along up to right parahippocampal gyrus in the medial temporal lobe [Figure 1]. MRI and PET changes were suggestive of encephalitis. Cerebrospinal fluid (CSF) examination revealed no white cells, proteins and sugar were normal, and herpes simplex DNA was not detected on polymerase chain reaction (PCR). Other CSF parameters for autoimmune encephalitis such as N-methyl-D-aspartate antibody and voltage-gated potassium antibodies were negative.

At the time of admission, the patient was started on levetiracetam 500 mg every 8 h and the dose was increased to 1 g twice a day, as there was no control of seizures, lacosamide was added at 100 mg twice a day after 3 days of levetiracetam. The addition of lacosamide did not control the focal seizures. Acyclovir was added in the treatment in view of imaging results (MRI/PET/CT) in dose of 500 mg intravenous, every 8 h beginning on the 4th day of hospitalization. After 3 days of acyclovir treatment, there was complete control of focal seizures. Acyclovir was given for 3 weeks. Over the next 9 months, there was no recurrence of seizures. The patient continued levetiracetam 500 mg every 8 h and lacosamide 100 mg twice a day. On follow-up after 1 year, the patient had stopped antiepileptic medications of his own.

Case 2

A 61-year-old male with a history of ethanol-related chronic liver disease and subsequent living-donor liver transplant presented with fever, left-sided focal seizures involving face, and left upper and lower limbs [Table 1]. He presented to emergency room (ER) with continuous focal seizures (focal status epilepticus) involving left face and left upper and lower limbs which lasted 1 h, with associated impairment of awareness. A routine 20 min EEG in ER revealed right-sided continuously occurring spike and sharp wave discharges (electrical status epilepticus) [Figure 2]. IV midazolam 5 mg and levetiracetam, 1 g were given in ER. Seizures stopped after 30 min. He was started on maintenance levetiracetam 1 g every 12 h. After initial loading medications, infrequent brief focal seizures continued to occur over the next 48 h. Injection lacosamide 100 mg twice/day was added to the

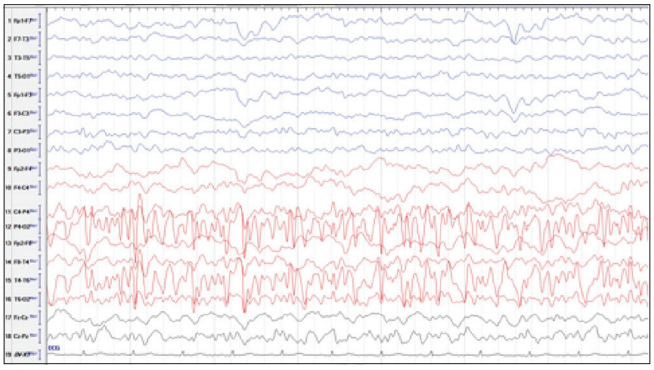


Figure 2: Initial electroencephalograph shows high amplitude spike and sharp discharges from the right temporal leads.

treatment regimen. Occasional brief focal seizures persisted even after the additional supplemental lacosamide. A follow-up EEG obtained after 4 days of treatment showed lateralized periodic discharges. During his hospital stay, the family also noted patient's memory and behavioral problems. The patient had lost orientation to space, was forgetful, and naming relatives wrongly. There was inappropriate laughter. Neurological examination was normal. MRI of the brain revealed hyperintense changes in the right medial temporal lobe suggestive of HSE. The patient was started on intravenous acyclovir 500 mg every 8 h and was given for 3 weeks. A CSF examination was refused by the family. After 4 days of acyclovir therapy, the patient's behavior and memory improved and he became seizure free, as well. He was discharged after approximately 4 weeks of hospitalization. At the 3-month follow-up, the patient was seizure free on levetiracetam 500 mg every 8 h and lacosamide 100 mg 2 times a day. He had no neurological deficit. EEG examination this time was normal. This patient had focal SE due to encephalitis in a setting of liver transplant patient on immunosuppressive therapy.

DISCUSSION

Seizures are seen in 20–30% of patients with chronic liver disease and particularly when in hepatic encephalopathy.[5,6] The most common seizures are focal and subtle seizures.[5] Seizures are typically seen in these patients when admitted in intensive care unit for the management of acute encephalopathy.[5] Hepatic encephalopathy itself with elevated ammonia, hyponatremia, cerebrovascular accidents (bleed/occlusion), malignancies, infections, and combination of factors are the most common causes for the seizures in liver disease patients.[5,6] Both Case 1 and Case 2 had ethanol-related chronic liver disease and presented with focal SE. EEG in one patient had only focal slowing while the second case had continuous spike and sharp discharges from the right side [Figure 2]. The use of continuous video EEG monitoring would have provided increased possibility for detecting epileptiform activity in first case. After initial management of the SE, MRI revealed focal brain changes consistent with herpes encephalitis in Case 1 [Figure 1]. PET and CT in this case revealed areas of increased uptake of radioactive drug in the corresponding MRI brain scan [Figure 1]. PET and CT scan was not done in the second patient as MRI brain was typical of HSE. HSE and autoimmune encephalitis may have a similar clinical presentation. The two are differentiated on further investigations such as CSF, MRI, and PET/CT scan. In both Cases 1 and 2, seizures responded completely after addition of acyclovir in the treatment. Both patients made a complete recovery. The diagnosis of HSE was made on clinical features, EEG, and radiological findings according to the consensus statement of the international encephalitis consortium.[7] CSF study was not supportive. In HSE, the CSF examination usually shows lymphocytic pleocytosis and positive herpes simplex DNA on PCR. PCR test is highly sensitive (94%) and specific (98%) for diagnosis of HSE. However, the test can be negative if sampled early or late (<3 and >14 days).[8] The CSF study was negative in Case 1 and the second patient refused CSF examination. However, typical CSF findings are not necessary to make a diagnosis if other criteria such as clinical features, brain imaging, and EEG are supportive of the diagnosis.[7,9,10] The EEG in the second patient and imaging features in both cases were typical for the diagnosis of HSE.[7] The EEG is abnormal in almost all cases of HSE and may reveal focal abnormalities such as slowing, spikes, lateralized, or multifocal epileptiform discharges involving the frontotemporal leads; however, none of these findings are specific for HSE.[3] The two patients, Case 1 and Case 2, had routine 20 min EEG. A continuous video EEG monitoring would have been preferable. HSE alone can present with new onset seizures in a normal person.[11] There are several reports describing HSE as the cause for focal seizures.[3,11-13] Commonly medial aspect of temporal lobes, orbital surface of frontal lobes, insular cortex, or cingulate gyrus are involved in HSE and MRI shows usually hyperintense (bright) T2 and FLAIR lesions in these areas.[7,11] This was seen in both patients.

A high proportion of patients died due to encephalitis in the pre-acyclovir era.[14] Morbidity and mortality rates decreased dramatically after antiviral acyclovir treatments were instituted.[3] If a possible diagnosis of HSE is not considered and treated early, the consequences could be post-encephalitic neurological sequelae, chronic seizures, or death. Mortality of 7% is seen in herpetic encephalitis if early diagnosed and treated as compared to 70% if not treated.[4]

CONCLUSION

In the two cases reported new-onset, persistent, and focal seizures/SE resolved with addition of acyclovir in the therapy, in a setting of chronic liver disease. Antiepileptic medications alone were not effective in stopping seizures. HSE should

be included in the differential diagnoses in such cases, early acyclovir started till additional workup for alternative causes of seizures other than HSE is found.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Trinka E. Types of status epilepticus: Definitions and classification. In: Drislane F, Kaplan P, editors. Status Epilepticus. Current Clinical Neurology. Cham: Springer; 2018.
2. Brophy GM, Bell R, Claassen J, Alldredge B, Bleck TP, Glauser T, *et al*. Guidelines for the evaluation and management of status epilepticus. Neurocrit Care 2012;17:3-23.
3. Sellner J, Trinka E. Seizures and epilepsy in herpes simplex virus encephalitis: Current concepts and future directions of pathogenesis and management. J Neurol 2012;259:2019-30.
4. Patoulias D, Gavriiloglou G, Kontotasios K, Tzakri M, Keryttopoulos P, Koutras C. HSV-1 encephalitis: High index of clinical suspicion, prompt diagnosis, and early therapeutic intervention are the triptych of success report of two cases and comprehensive review of the literature. Case Rep Med 2017;2017:5320839.
5. Koul R, Ramalingam A, Kumar S, Dhamija RM, Pamecha V, Sarin SK. Role of EEG in predicting outcome of hepatic encephalopathy patients. Neurodiagn J 2020;60:272-88.
6. Prabhakar S, Bhatia R. Management of agitation and convulsions in hepatic encephalopathy. Indian J Gastroenterol 2003;22:S54-8.
7. Venkaesan A, Tunkel AR, Bloch KC, Lauring AS, Sejvar J, Bitnun A, *et al*. Case definitions, diagnostic algorithms and priorities in encephalitis: Consensus statement of the international encephalitis consortium. Clin Infect Dis 2013;57:1114-28.
8. Davies NWS, Brown LJ, Gonde J, Irish D, Robinson RO, Swan AV, *et al*. Factors influencing PCR detection of viruses in cerebrospinal fluid of patients with suspected CNS infections. J Neurol Neurosurg Psychiatry 2005;76:82-7.
9. Jakob NJ, Lenhard T, Schnitzler P, Rohde S, Ringleb PA, Steiner T, *et al*. Herpes simplex virus encephalitis despite normal cell count in the cerebrospinal fluid. Crit Care Med 2012;40:1304-8.
10. Weil AA, Glaser CA, Amad Z, Forghani B. Patients with suspected herpes simplex encephalitis: Rethinking an initial negative polymerase chain reaction result. Clin Infect Dis 2002;34:1154-7.
11. Chaudhuri A, Kennedy PG. Diagnosis and treatment of viral encephalitis. Postgrad Med J 2002;78:575-83.
12. Costello DJ, Kilbride RD, Cole AJ. Cryptogenic new onset refractory status epilepticus (NORSE) in adults infectious or not? J Neurol Sci 2009;277:26-31.
13. Verma R, Raut TP, Giri P, Praharaj HN. New onset refractory status epilepticus (NORSE) as the heralding manifestation of herpes simplex encephalitis. BMJ Case Rep 2013;2013:bcr2013009466.
14. Whitley RJ, Alford CA, Hirsch MS, Schooley RT, Luby JP, Aoki FY, *et al*. Vidarabine versus acyclovir therapy in herpes simplex encephalitis. N Engl J Med 1986;314:144-9.

How to cite this article: Koul R, Kumar NM, Naheed D, Sarin SK. Chronic liver disease and hepatic encephalopathy patients with new-onset focal motor status epilepticus: Indicates herpetic encephalitis. J Neurosci Rural Pract 2022;13:764-7.