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Case Report

Seizure Disorder Exacerbated by Hepatic Encephalopathy: A Case Report

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Abstract

BACKGROUND: Hepatic encephalopathy is a serious complication of cirrhosis that presents with a variety of neuropsychiatric abnormalities, including disorientation, asterixis, and coma. Seizures are an uncommon and potentially dangerous complication of hepatic encephalopathy. We present a unique case of a 42-year-old female with a history of well-controlled seizure disorder suddenly become refractory to anticonvulsant therapy following the development of hepatic encephalopathy secondary to liver decompensation.

CASE PRESENTATION: A 42-year-old female presented to our hospital following a seizure accompanied by loss of consciousness, urinary incontinence, and the prolonged postictal state. She reports her seizures were initially well-controlled with Levetiracetam 500 mg twice a day but recently began experiencing seizures every other day despite up-titration of Levetiracetam to 1500 mg twice a day over a few weeks. On arrival, her serum ammonia level was 116 µmol/L. CT brain was negative while CT liver was consistent with cirrhotic morphology. An electroencephalogram revealed irregular, diffuse, delta/theta slowing consistent with mild to moderate encephalopathy. The patient was started on lactulose 40mg and Rifaximin 550 mg twice a day. Her symptoms of disorientation and lethargy resolved over 3 days.

CONCLUSION: Though uncommon, hepatic encephalopathy should be considered in patients presenting with convulsions, especially if there is a known history of liver disease. Until the underlying liver issues are addressed, patients may not respond to traditional anti-convulsant therapy for their seizures.

Introduction

Around 30 to 45% of patients with cirrhosis develop hepatic encephalopathy (HE), and this development has been associated with a poor prognosis [1]. HE is a serious complication of cirrhosis and portosystemic shunts that presents with a spectrum of neuropsychiatric abnormalities, ranging from disorientation to coma, that can greatly debilitate patients' lives. Abnormal motor symptoms such as irregular tremor and asterixis are also frequently associated with the disorder [2], [3], [4], [5]. Seizures are uncommon yet potentially dangerous complications of HE [3], [6], [7].

Case Presentation

A 42-year-old female with a history of cirrhosis secondary to chronic hepatitis B virus infection was brought to our emergency department following a seizure accompanied by loss of consciousness and urinary incontinence. She reports a history of seizures that began 5 months prior when she was admitted to a different hospital for HBV cirrhosis and abdominal pain. During that hospital stay, the patient was given Tramadol, which she attributes the onset of her seizures too. The seizures were initially controlled with Levetiracetam 500 mg twice a day; however patient states that seizures have increased in frequency to every other day over the past few weeks despite up-titration of Levetiracetam to 1500 mg twice a day. Her other medications at the

time include Tenofovir 300 mg daily for her HBV infection and propranolol 10 mg twice a day and pantoprazole 20 mg daily for portosystemic varices seen on prior CT imaging. She also reports intermittent lower extremity oedema which she takes Furosemide 20 mg daily. She usually does not go to the ED when she has a seizure. However, she presented to our ED because her seizures have increased in frequency and been accompanied by prolonged post-ictal states. Per discussion with family, the patient had had increasingly slower mentation since the initial admission 5 months ago. Patient reports feeling more lethargic and "off" for the past few weeks.

Vitals on admission were a blood pressure of 139/97, the pulse of 93 beats/minute, and SpO_2 of 99% on room air. On clinical exam, the patient was somnolent and slow to answer questions. She was alert and oriented to person and place but not time. Scleral icterus, asterixis, and mild upper abdominal pain were present. There were diminished vibration and position sense in the lower extremities bilaterally. There was no ascites or oedema. Heart sounds were normal, and the lungs were clear to auscultation.

Laboratory studies showed a white blood cell count of 4500/mm^3, haemoglobin of 12.1 g/dL, hematocrit of 37.9%, and platelets of 112000/mm^3. Electrolytes were normal. Other labs include: total protein of 7.3 mg/dL, total bilirubin of 3.8 mg/dL, albumin of 2.6 g/dL, aspartate aminotransferase of 98IU/L, alanine aminotransferase of 71IU/L, alkaline phosphatase of 275IU/L, and ammonia of 116μmol/L (reference range 9 μmol/L-33 μmol/L). Prothrombin time was 20.6 seconds, and INR was 1.79. CT brain was without evidence of acute bleed or mass effect while CT liver was consistent with hepatic cirrhotic morphology. An electroencephalogram revealed findings consistent with mild to moderate encephalopathy (Figure 1). The patient denied the prior history of hepatic encephalopathy.

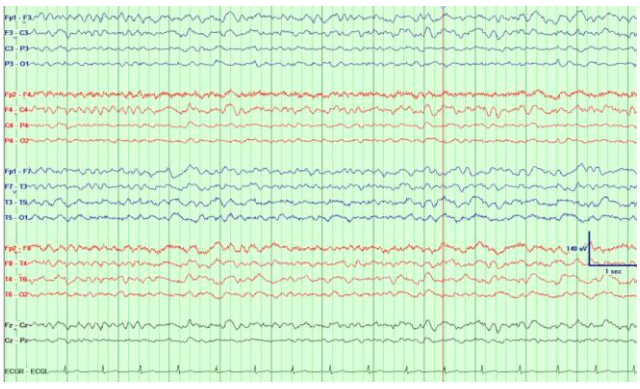

Figure 1: Electroencephalogram showing irregular, diffuse, delta/theta slowing consistent with mild to moderate encephalopathy

Based on the laboratory, imaging, and clinical findings, her altered mental status and seizures refractory to anticonvulsant therapy were attributed to hepatic encephalopathy secondary to liver decompensation from HBV cirrhosis. The patient was started on lactulose 40 mg twice a day, titrated to 2-3 bowel movements daily and Rifaximin 550 mg twice a day. Over 3 days, her mental status improved, she was no longer lethargic, and her scleral icterus and asterixis resolved. She was discharged on the fourth hospital day with her home medication and lactulose for further management of her hepatic encephalopathy. She has not experienced another seizure on 3 months follow up and continues to do well.

Discussion

Hepatic encephalopathy (HE) is a reversible consequence of advanced liver disease and/or portosystemic shunting characterised by impaired neurologic function including altered mental status, asterixis, and possible coma [2], [3], [4], [5]. The frequency of seizures in HE remains uncertain. One study found that up to one-third of their patients with HE developed seizures; however, this was largely in more advanced disease stages [8]. Other authors suggest seizures are an uncommon event [3], [6], [7]. Ficker et al. reviewed EEG tracings in patients with HE and found that when epileptiform abnormalities were present, they were associated with a poorer prognosis [6].

The pathophysiology of HE is multifactorial and complex, including changes in ammonia (NH_3) levels, inflammatory cytokines, and amino acids [2], [4], [7]. The most widely understood mechanism involves the hepatic metabolism of NH_3. The 2 primary metabolic pathways by which ammonia is handled is through the urea cycle and glutamine synthase (produces glutamine from glutamate) [4]. In patients with cirrhosis, there is hepatocellular dysfunction and portosystemic shunting, resulting in increased levels of ammonia through the systemic circulation. Astrocytes in the brain convert NH_3 and glutamate to glutamine. Hyperammonemia results in increased glutamine production and accumulation in astrocytes creating an osmotic gradient that promotes astrocytic swelling [2], [4], [7]. Elevated glutamine levels also result in the generation of reactive oxygen species through a process of hydrolysis in mitochondria, which contributes to the neuronal dysfunction in hepatic encephalopathy. A milieu of inflammatory cytokines augment the neurotoxic effects of ammonia by enhancing the diffusion of ammonia across the blood-brain barrier in addition to exerting their neurotoxic effects [4].

EEG recordings have been useful in identifying the underlying aetiology of altered mental status in patients with liver cirrhosis. A few reports

detail the use of EEG recordings to discern hepatic encephalopathy from conditions such as nonconvulsive status epilepticus (NCSE), which can be hidden within a diagnosis of HE yet requires a different course of medical management [9], [10], [11]. While other cases of status epilepticus secondary to HE have been reported [3], [12], [13], our case demonstrates a patient who initially had a history of seizures well-controlled with anti-convulsants, and no prior history of HE, suddenly become refractory to her medication. Her decompensated liver state aggravated her neurological issues, which prompted further medical management of her condition beyond regular anti-convulsant therapy. The addition of lactuolose and Rifaximin produced a clinically significant resolution of symptoms in our patient. Therefore, although rare, it is important to appreciate HE as an exacerbating factor in convulsive patients because the therapeutic management of these patients may change. Furthermore, certain anti-epileptic drugs, such as benzodiazepines, can potentially worsen HE, so it is imperative that a diagnosis of HE is not overlooked in convulsive patients [2], [3].

In conclusion, seizures are an uncommon and potentially serious complication in patients with hepatic encephalopathy. EEG recordings may be useful in ruling out other etiologies of altered mental status in patients with a history of liver disease presenting with convulsions. Patients experiencing seizures secondary to HE may not respond to traditional anti-convulsant therapy, and therefore, the underlying liver problems must be addressed.

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