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CASE REPORT

Parkinson's mimicker in Acute and Chronic Hepatic Encephalopathy

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ABSTRACT

Hepatic encephalopathy (HE) is a neuropsychiatric spectrum mainly caused by cirrhosis, portosystemic shunt, or portal hypertension. It may also mimic the presentation of Parkinson's disease, which can make clinical diagnosis a challenge. A 42-year-old man with underlying chronic hepatitis C with liver cirrhosis was initially admitted for chronic lower back pain. During admission, he appeared drowsy but was able to answer questions appropriately albeit with delayed and slow speech. He had bradykinesia without stigmata of chronic liver disease. Differentials at the time were hypoactive delirium and Parkinson's disease. Blood results were normal. Magnetic resonance imaging (MRI) of the brain showed bilateral symmetrical hyperintensities at the inferior temporal lobes, medial thalamus, cingulate gyri, head of caudate nuclei, posterior limbs of internal capsules and insula on fluid-attenuated inversion recovery (FLAIR) sequence. On the T1 weighted imaging (T1WI) sequence, bilateral symmetrical hyperintensities were seen at globus pallidi, cerebral peduncles and periaqueductal regions extending to superior cerebellar peduncles. Based on imaging, a diagnosis of acute chronic hepatic encephalopathy was made. The patient was treated conservatively in the ward and was discharged with persistent Parkinsonism. In patients with neurological abnormalities where hepatic encephalopathy

(HE) is least expected due to subtle symptoms, MRI could play an important role in eliciting the underlying cause, and extent of disease and for prognostication.

INTRODUCTION

Hepatic encephalopathy (HE) is a neuropsychiatric spectrum, mainly caused by cirrhosis, portosystemic shunt, or portal hypertension (Nizamani et al., 2018). It is associated with poor survival and a high recurrence rate without prompt initiation of adequate treatment (Vilstrup et al., 2014). Magnetic resonance imaging (MRI) can detect the extent of brain parenchymal injury and correlation to the patient's clinical status is the utmost importance (Nizamani et al., 2018). Herein we report a case of a 42-year-old man with underlying hepatitis C, with atypical presentation of Parkinsonism in a classic MRI imaging findings of acute on chronic hepatic encephalopathy.

CASE PRESENTATION

A 42-year-old man with underlying chronic hepatitis C with Child-Pugh A liver cirrhosis was admitted with an initial presentation of chronic lower back pain. He appeared drowsy and slow to respond, but was able to answer questions coherently. The neurological examination noted bradykinesia with no neurological deficit depicted. There were no stigmata of chronic liver disease either. No preceding history of fever or any notable neurological symptoms such as seizure, hemiparesis or behavioural changes. Social history revealed that the patient did not work in the mining industry. Vital signs, liver enzymes and hepatitis C virus (HCV) RNA tests were all normal. Magnetic resonance imaging (MRI) of the brain showed bilateral symmetrical hyperintense signal seen at inferior temporal lobes, medial thalamus, cingulate gyri, head of caudate nuclei, posterior limb of internal capsules and insula (Figures 1 and 2). These findings are typical in acute on chronic hepatic encephalopathy. There was no abnormal signal intensity involving the substantia nigra and red nuclei to suggest Parkinson's disease. The patient was treated conservatively with syrup lactulose in the ward and subsequently discharged well with persistent Parkinsonism.

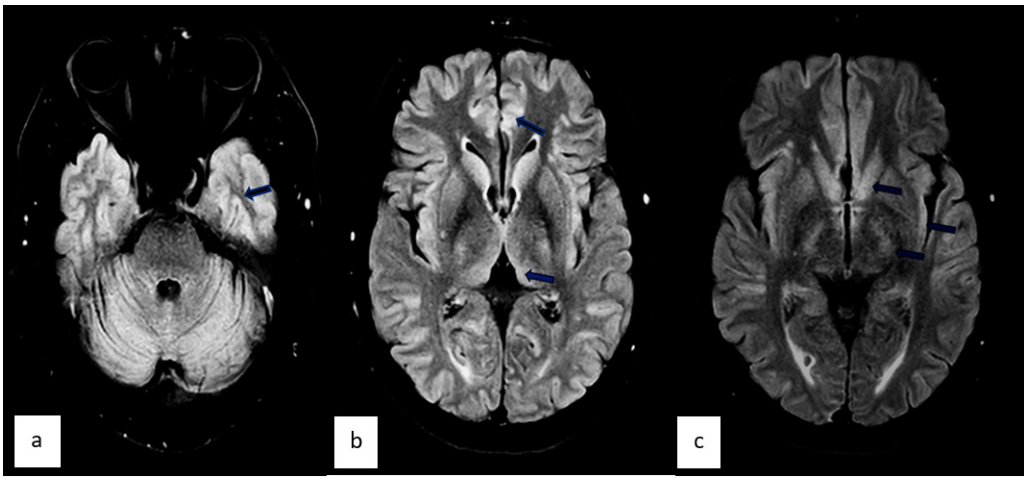

Figure 1 Axial FLAIR (a, b, and c) shows bilateral symmetrical hyperintensities at inferior temporal lobes, medial thalamus, cingulate gyri, caudate head, posterior limb of internal capsules and insula

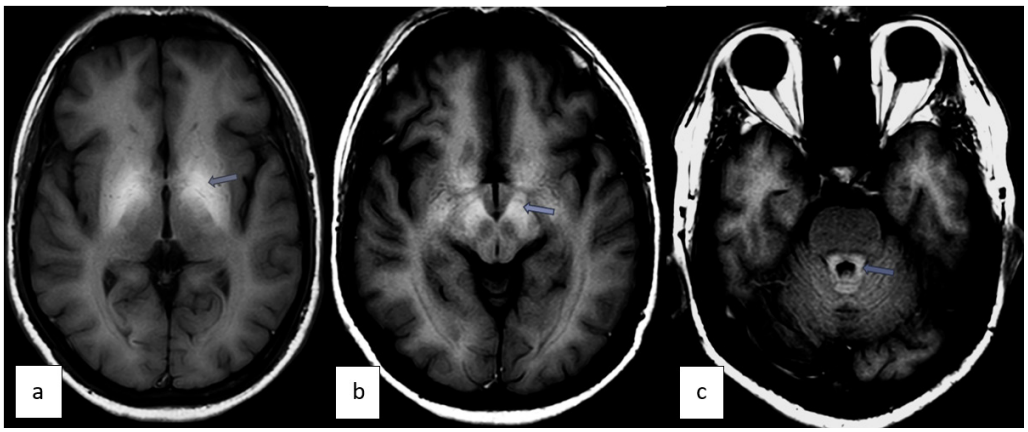

Figure 2 Axial T1W (a, b, and c) displays bilateral symmetrical hyperintensities at globus pallidus, cerebral peduncles and periaqueductal region extending to superior cerebellar peduncles

DISCUSSION

Hepatic encephalopathy (HE) is a neuropsychiatric spectrum, mainly caused by cirrhosis, portosystemic shunt, or portal hypertension (Nizamani et al., 2018). It is associated with poor survival and a high recurrence rate unless the underlying cause is successfully treated (Vilstrup et al., 2014). In a middle-aged patient with a rapid onset of symmetric Parkinsonism, hepato-cerebral Parkinsonism should be suspected (Noone et al., 2008). In the literature, the reported prevalence rate ranges from as low as 3.5 – 4.2% to as high as 21.6% (Burkhard et al., 2003; Tryc et al., 2013; Kang et al., 2011). Global hypokinesia and gait impairment are early Parkinsonian symptoms in cirrhosis, whereas dementia and resting tremors are uncommon symptoms (Noone et al., 2008).

Excess manganese within the brain is believed to be the cause of T1 weighted image (T1WI) hyperintensity on magnetic resonance imaging (MRI), which can be seen affecting bilateral globus pallidi and substantia nigra, which explains Parkinsonian manifestation (Noone et al., 2008; Rovira et al., 2008; McPhail et al., 2012). It coincided with autopsied brain tissue, where it affects the post-synaptic dopamine D2 binding sites, associated with high levels of manganese (Spahr et al., 1996).

Although the diagnosis of hepatic encephalopathy is almost always clinical, we can however appreciate the affected brain areas, in which different areas of distribution can be seen in acute and chronic hepatic encephalopathy. MRI is an important modality in aiding the diagnosis of hepatic encephalopathy. Fluid attenuated inversion recovery (FLAIR) sequence is sensitive to detect hyperintense white matter lesions which is a combination of reversible oedema and irreversible neuronal damage. This can be seen along the hemispheric corticospinal tract and subcortical hemispheric white matter (Rovira et al., 2008). Meanwhile, on diffusion-weighted imaging (DWI) sequence increased diffusion can be seen at hemispheric white matter, which suggests interstitial brain oedema (Rovira et al., 2008).

On magnetic resonance spectroscopy (MRS), an increased glutamine/glutamate signal is seen, caused by osmolar adaptation of intra-astrocytic accumulation of glutamine (Rovira et al., 2008). Diffuse cortical lesion involving the cingulate gyrus and insula cortex, with sparing occipital and perirolandic cortices is highly specific to hepatic encephalopathy, which may be explained by susceptibility towards hyperammonemic-hyperglutaminergic encephalopathy (Nizamani et al., 2018; Reis et al., 2020). Other sites involved include thalami, midbrain, and periventricular areas (Reis et al., 2020).

However, it is important to take note that any other hyperammonemic cause of encephalopathy also yields similar findings on MRI (Reis et al., 2020). Differences in frequency and imaging findings on MRI between acute HE and chronic HE were summarized, as shown in Table 1.

Table 1 Comparison of acute and chronic hepatic encephalopathy

Types of hepatic encephalopathy	Chronic hepatic encephalopathy	Acute hepatic encephalopathy
Frequency	Common	Rare
Aetiology	Chronic severe liver disease (cirrhosis)	Varies – hyperammonemia, infections, drug toxicities, parenteral nutrition
Imaging findings	T1WI hyperintensities involving: • Globus pallidus • Substantia nigra	FLAIR/DWI hyperintensities involving: • Mainly insula and cingulate gyri • Spares perirolandic and occipital regions • May involve basal ganglia, thalami, and periventricular regions MRS may show glutamate-glutamine peak
Cause of imaging findings	Attributed to manganese deposits	Hyperammonemia

Source: Rovira et al., 2008; McPhail et al., 2012; Spahr et al., 1996; Osborn et al., 2018

Manganese and ammonia are two of many compounds that are metabolized by the liver (Rovira et al., 2008). They may enter the brain and induce disturbances in neurological function (Rovira et al., 2008). It is widely accepted that ammonia is the main cause of hepatic encephalopathy, where it is deposited into astrocytes and causes brain oedema (McPhail et al., 2012). In turn, they will be converted into glutamine which causes neurological disturbance (McPhail et al., 2012). Manganese was already considered neurotoxic 150 years ago when industrial workers exposed to black oxide manganese developed unsteady gait and muscle weakness (Rovira et al., 2008). In this case, they typically exhibit extrapyramidal symptoms such as hypokinesia, rigidity and tremors (Rovira et al., 2008).

In cases of cirrhosis and portosystemic shunts, plasma manganese levels are increased and then transported to the brain, causing neuronal loss in basal ganglia structures and reactive gliosis (Rovira et al., 2008). At the toxic level, it affects mitochondria where it catalyzes dopamine oxidation mainly in globus pallidus, extending to substantia nigra (which has a high concentration of neuromelanin) (Goldman, 2014; Ratner & Feldman, 2005).

Acute disseminated encephalomyelitis (ADEM) is also a possible diagnosis for this patient, but it is rare in hepatitis virus infection (Lazibat & Brinar, 2013). While it can cause encephalopathy in the affected patients, their imaging features are very different as their distributions are asymmetric and may involve both subcortical and deep white matter and grey matter, like thalamus and basal ganglia in particular (Lazibat & Brinar, 2013).

Currently, the first choice treatment for HE is by administrating nonabsorbable disaccharides which is lactulose (Vilstrup et al., 2014). Rifamixin may also be given together with lactulose to reduce the risk of HE recurrence in a patient (Vilstrup et al., 2014). There are many other medical treatments available as mentioned by Vilstrup et al., however, it is not the main focus of this article. It was also reported that these symptoms are reversible once the patient is treated with portosystemic shunting or liver transplant (Noone et al., 2008), and only done if medical treatments are exhausted (Vilstrup et al., 2014). Some of the patients, however, may show good responses from taking Levodopa (Burkhard et al., 2003).

CONCLUSION

Hepatic encephalopathy is a sequelae of a failing liver, due to excessive unmetabolized plasma manganese and ammonia. In patients with neurological abnormalities where hepatic encephalopathy is least expected due to subtle symptoms, MRI could play an important role in eliciting the underlying cause and extent of disease and for prognostication.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in publishing this article.

CONSENTS

Written consent was obtained from the patient to publish this case report. A copy of the written consent is available for review by the Chief Editor.

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