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Treatment of Parkinsonism Secondary to Chronic Liver Disease with Amantadine Sulfate: A Case Report

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Introduction

Parkinsonism is a clinical syndrome with rest tremor, rigidity, bradykinesia, and postural instability as its main features. Parkinsonism has a rapid or subacute course onset. Rest tremor is mild or absent, akinesia, rigidity, and if early gait disturbance with loss of balance should be considered secondary causes of parkinsonism (1). Many metabolic disorders may result in parkinsonism, including liver failure, thyroid disease, renal failure, calcium disorders of iron metabolism, electrolyte imbalance; mitochondrial, infectious, and autoimmune diseases; paraneoplastic disorders, toxins, and drugs (1).

There is no definitive treatment of parkinsonism symptoms resulting from liver failure. However, liver transplantation has been reported to improve parkinsonism symptoms (1). Herein, we present the treatment protocol offered to a patient with parkinsonism secondary to chronic liver disease.

Case Report

A 61-year-old right-handed male patient with a history of cirrhosis presented with walking disturbance. He complained of difficulty walking and tremors. His spouse reported that he was partially dependent on her for activities of daily living, such as dressing and ambulation. On neurological examination, the patient was conscious and oriented but with slowed cognitive speed. His Mini-Mental Status Exam (MMSE) score was 23/30. He displayed flexed body posture when standing and while walking. The motor examination showed slightly increased muscle tone, which was more prominent in his right arm, without any strength reduction. No pathologic reflexes were noted. His tremor was mainly postural between the frequencies of 4-6 Hz, which affect distal parts of the upper extremities, and was more prominent on the right side of the body. Some pertinent laboratory test results were as follows: aspartate aminotransferase (AST): 46 u/L (reference range: 5 - 40), AST/alanine aminotransferase ratio 1.09, ammonia 90 mcmol/L (reference range: 9 - 33), manganese 25.30 nmol/L (normal value < 15). The serologic markers of viral hepatitis were negative. The endoscopic examination showed grade 1-2 esophageal varices. Following brain magnetic resonance imaging (Figure 1) and electroencephalography (Figure 2), our patient was diagnosed with parkinsonism secondary to chronic liver disease.
On admission, the patient was using lactulose and L-Ornithine-L-Aspartate for ammonia level reduction, which was previously prescribed by a gastroenterologist. We additionally prescribed amantadine (100 mg twice daily) to either control his parkinsonism symptoms or delay neuronal loss. One month later, he became more aware than before and could walk 2 or 3 times daily for at least 30 minutes without assistance from his wife.

**Discussion**

This case represents the first attempt to treat the extrapyramidal symptoms of hepatic encephalopathy (HE) with amantadine, a weak NMDA receptor antagonist. It should be mentioned that the drug was well-tolerated and no adverse effects were noted. Several studies have reported a benefit in using L-Dopa, pramipexole (2), or liver transplantation (3) for HE, but amantadine is considered safer and easier to use. The side effects of amantadine include nausea, constipation, drowsiness, pedal edema, livedo reticularis, anxiety, and depression (4). These symptoms resolve in two to three weeks after drug discontinuation.

Acquired (non-Wilsonian) hepatocerebral degeneration (AHCD) is a chronic progressive neurological syndrome, which may be caused by repeated episodes of liver failure or chronic liver cirrhosis and is characterized by parkinsonism, ataxia, and other movement disorders (5). AHCD is an exceptional type of HE accompanied by organic damage, especially in the basal ganglia. The disease develops gradually, and the symptoms become progressively worse. Recent evidence suggests that manganese plays a crucial role in the pathogenesis of AHCD (6).

Magnetic resonance imaging abnormalities associated with AHCD mainly consist of signal hyperintensity on T1-weighted images in the internal pallidum. The signal hyperintensity may also be seen in the putamen, caudate nucleus, capsula interna, mesencephalon, and cerebellum; it is believed to reflect local manganese accumulation (7).

In summary, amantadine sulfate may be an alternative treatment for parkinsonism in patients with liver cirrhosis. Randomized controlled trials will be required to establish its efficacy.
**Figure 1.** Coronal and axial T1-weighted magnetic resonance images of the brain in a patient with chronic liver failure and parkinsonism. The bilateral and symmetric high T1 signal intensity changes involving the globus pallidus can be seen.

![Figure 1](image)

**Figure 2.** Frontal intermittent rhythmic delta activity supports the diagnosis of toxic or metabolic encephalopathy.

![Figure 2](image)

All authors have no conflicts of interest to disclose.