□ CASE REPORT □

Treatment for Restless Legs Syndrome Secondary to Chronic Liver Disease: A Case Report

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Abstract

We report a patient with restless legs syndrome (RLS) and chronic liver disease (CLD), whose RLS symptoms fluctuated in correlation with serum ammonia level. RLS in this patient seemed to be secondary to CLD because palliative medications for the liver dysfunction showed an additional effect on RLS symptoms that were partially controlled by levodopa. CLD should be born in mind as one of the factors to cause RLS symptoms; the therapeutic mechanism of RLS enhanced by palliative medications for CLD is discussed.

Key words: restless legs syndrome, chronic liver disease, branched-chain amino acid, lactulose, levodopa

(Intern Med 51: 933-934, 2012)

(DOI: 10.2169/internalmedicine.51.6853)

Introduction

Although more than 60% of patients with chronic liver disease (CLD) appear to have restless legs syndrome (RLS) symptoms (1), its etiology and appropriate therapeutics remain unclear. We encountered a patient with RLS accompanied by CLD, in whom RLS symptoms were successfully controlled with levodopa and its effect was enhanced by palliative medications for liver dysfunction.

Case Report

A 73-year-old man with a 20-year history of liver cirrhosis due to hepatitis C came to our clinic with a complaint of nocturnal foot discomfort. This symptom urged him to walk around in the bedroom at night, which made his leg discomfort less intolerable. As a result, his sleep had been severely interrupted. In the clinical examination, his cognitive function including orientation and memory was normal for his age, and neither parkinsonism nor other neurological deficits were observed. The routine electroencephalogram on resting awake showed organized 8-9 Hz activity without concomitant slow waves. Polysomnography (PSG) with a video-recording revealed periodic leg movements during sleep index (PLMSI) of 32.2, and PLMS with arousal index (PLMSAI) of 8.9. These symptoms and findings confirmed

the diagnosis of RLS. Low-dose loading of levodopa initially reduced the intensity of the uncomfortable sensation and frequency of voluntary leg movements at night (Fig. 1, arrows). These symptoms, however, sometimes deteriorated, showing a general correlation with serum ammonia (NH₃) elevation. Addition of lactulose (Fig. 1, black arrowhead), intensification of branched-chain amino acids (BCAAs) administration (Fig. 1, white arrowheads) or dietary protein restriction more dramatically reduced his nocturnal symptoms. This regime was initially introduced by liver specialists, with an aim towards stabilizing serum NH₃ level and maintaining liver function, not intending to control RLS. RLS symptoms of the patient were maintained under good control by the combination of levodopa and palliative medications for liver dysfunction. This improvement was confirmed by repeated PSG (PLMSI and PLMSAI decreased from 32.2 to 27.9 and from 8.9 to 0, respectively before and after treatment).

Discussion

Although it is well known that the basic strategy to treat secondary RLS is to control the primary illness properly, the therapeutics remain unclear about RLS secondary to CLD. In the present case, the combination of lactulose, BCAAs, dietary protein restriction and levodopa decreased the intensity of discomfort as well as the frequency of both voluntary

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Received for publication November 1, 2011; Accepted for publication January 11, 2012
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Figure 1. Clinical course and response to treatment. PSG: polysomnography, BCAAs: branched-chain amino acids, DI: drip infusion, PO: per oral. *Subjective 11-ranked scale; 10: maximally uncomfortable, 0: no uncomfortable sensation.

and involuntary leg movements. This subjective improvement was confirmed by repeated PSG.

The mechanism of palliative hepatic treatment on RLS is unclear. Dysfunction in the dopaminergic system has been considered to play a central role in cases of idiopathic RLS (2), while the number of D_2 receptors within the striatum was reported to decrease in cases of hepatic encephalopathy (3). These findings suggest that there might also be additional dopaminergic dysfunction even in patients with RLS secondary to CLD associated with elevated NH_3 . This speculation is supported by the fact that normalization of the serum NH_3 level in combination with levodopa generally correlated with RLS symptoms, and an elevated NH_3 level seemed to be a major contributing factor in worsening RLS. In this process, intake of replenished BCAAs result in modulating imbalance in neurotransmitters and catecholaminergic metabolism by competitively inhibiting aromatic amino acids to pass through the blood brain barrier (4), which may involve the dopaminergic system. In addition, BCAAs also contribute to NH_3 detoxication through the citric acid cycle. These therapeutic mechanisms seemed to work together effectively in the present case, since intensive replenishment of BCAAs by drip infusion prevented RLS worsening even in the period of NH_3 fluctuation. Why RLS alone occurred in our case without any consciousness disturbance or cognitive impairment was not fully explained, however, regional difference in dopamine D_2 receptor density or

binding capacity might be a possible factor (5).

CLD should be born in mind as one of the factors to cause RLS symptoms and the future accumulation of RLS patients with liver dysfunction will be warranted for clarifying the pathophysiology and effective treatment strategy.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

We thank Dr. Fuminori Segawa for his helpful discussion.

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