Hepatic myelopathy associated with advanced liver cirrhosis

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A 41-year-old man was admitted to our institution with inertia of both lower extremities and walking instability. The patient had been diagnosed with chronic hepatitis B (hepa B) for 10 years, including hepa B virus associated cirrhosis within the last 4 years. The patient had also suffered hepatic encephalopathy within the last 6 months, which resolved following treatment. A month before the current admission, the patient experienced difficulty in moving both lower extremities, which gradually worsened until medical attention was sought. The patient's ability to walk was significantly impaired, with a markedly altered gait and swinging of the upper-body, especially when walking with his eyes closed. The patient reported no numbness or tightness of the lower extremities; furthermore, there was no urinary or fecal incontinence.

Physical examination showed the patient had normal levels of consciousness, a spastic gait as described above, and numerous indictors of underlying liver disease including hepatic facies, yellowing of the sclera, palmar erythema and spider angioma, although Kayser-Fleischer rings were absent. Heart and lung function was assessed and found to be normal. The abdomen was distended, the liver was not palpable, and splenomegaly was noted. There was no shifting dullness. Examination of all the limbs revealed no evidence of myotrophy, and the muscular power and tension of the muscles in the upper extremities was normal. Examination of the lower limbs revealed muscle rigidity with normal muscle power. The patellar reflex was present in both lower limbs; similarly, the Babinski reflex was also normal. Deep and light touch sensations were normal.

Laboratory blood tests revealed the following results: white blood cell count = 3.1×10^9/L; red blood cell count = 2.85×10^{12}/L; hemoglobin concentration = 98 g/L; platelet count = 40×10^9/L. Laboratory testing of liver function yielded the following results: alanine aminotransferase activity = 44 IU/L; aspartate aminotransferase activity = 83 IU/L; γ-glutamyl transpeptidase activity = 69 IU/L; the concentration of serum total bilirubin = 57.1 μmol/L, serum albumin = 27.2 g/L, and blood ammonia = 130 μmol/L. The alpha-fetoprotein levels were normal. The patient was positive for hepa B virus surface antigen (HBsAg), and possessed anti hepa B e antigen and anti hepa B c antibodies.

Abdominal ultrasound examination revealed changes that were characteristic of liver cirrhosis, the portal vein was widened, and there was embolization in the portal vein. Splenomegaly was also observed. Examination of the upper digestive tract with a barium meal revealed esophageal vein varicosis. A CT examination of the cranium was clear and no lesions were detected; the thoracic and lumbar spine MRI examinations were normal. Electroencephalogram revealed only borderline changes in the brain activity state. No examination of the cerebrospinal fluid was performed as the patient refused to consent to this procedure. Following our extensive examination, the clinical diagnosis was made of hepa B virus-related cirrhosis and hepatic myelopathy. Treatment was provided to protect liver function, decrease blood ammonia levels, and protect nerve cells for 2 months; the patient was then discharged. There was some evidence of remission in the symptoms of lower limb inertia and walking instability during the treatment period.

Hepatic myelopathy is a chronic and progressive syndrome associated with the loss of myelin in the dorsal or lateral corticospinal tracts of the spinal cord, which is a rare complication of cirrhosis of the liver, accounting for approximately 2.5% of patients with cirrhosis. The pathogenesis of hepatic myelopathy is poorly understood, although it may be related to vitamin B deficiency; its characteristics in comparison to other forms of severe liver cirrhosis include enhanced portosystemic shunting, increased ammonia levels, hypoproteinemia, and malnutrition.[1] The onset of hepatic myelopathy is insidious and occurs slowly, and is more common in patients with portosystemic shunts that have been created surgically, or have occurred spontaneously. As the onset of hepatic myelopathy is often latent, the main clinical feature is spastic paraparesis of the double lower extremities. At first, the symptoms may be asymmetrical, but will invariably progress to affect both legs and increase in severity. Increased tone and hyperreflexia are the most common clinical findings, and the upper extremities are minimally affected, if at all. Plantar responses are usually extensor,

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but flexor responses have also been described. Sensorial involvement or sphincteric impairment is uncommon, and few individuals will present with muscular atrophy. Interestingly, almost 90% of the reported cases are in men. After several months of progression, the disease plateaus, leaving most patients dependent on assistance, or confined to a wheelchair. As described above in the case report, and consistent with the reviewed literature, the symptoms shown by the patient in the current case are typical of hepatic myelopathy, specifically spastic paraparesis during the course of liver cirrhosis, which is progressive and permanent. Furthermore, the patients gender and age is also consistent with the population that is most affected by hepatic myelopathy, that is, 30 to 60-year-old male patients.

Most patients with hepatic myelopathy have a history of hepatic encephalopathy, which was also found in this case report. The link between hepatic myelopathy and encephalopathy is supported by the following observations: 1) they are both associated with portosystemic shunting; 2) analogies between cerebral and spinal MRI abnormalities in patients with cirrhosis; and 3) the high prevalence of motor impairment in encephalopathic patients. However, spinal cord symptoms are not parallel to the fluctuating symptoms of encephalopathy. Furthermore, encephalopathy is characterized as a temporary episode which frequently recurs, while myelopathy has the characteristics of a slowly and progressive clinical development that does not resolve.[2] Despite these parallels, while the development of myelopathy usually occurs after hepatic encephalopathy, it may also occur before encephalopathy, or be independent of it. This suggests that there may not necessarily be a correlation between the occurrence of hepatic myelopathy and encephalopathy.

Hepatic myelopathy remains a difficult diagnosis to make in the clinical setting, and is usually made only after the exclusion of other causes of spastic paraparesis and partial transverse myelopathy. An accurate history, along with appropriate imaging and neurological testing is crucial. Hepatic myelopathy can be diagnosed based on the following criteria: symptoms of liver disease, portosystemic anastomosis or the formation of an extensive portosystemic collateral circulation, and the progressive development of lower limb spastic paraplegia or quadriplegia, with no accompanying sensory disturbances or sphincter disorders, and with no obvious muscular atrophy. Furthermore, cerebrospinal fluid test is normal, and EEG shows diffuse abnormalities. Abnormal liver function and sustained elevated blood ammonia are also important to diagnose this disease. However, the blood ammonia levels are not parallel to the severity of the nervous system damage. It is necessary to make the further differential diagnoses of multiple sclerosis, hereditary spastic paraplegia, amyotrophic lateral sclerosis or space occupying lesions of the spinal cord, amongst others, when patients present with progressive incomplete spastic paralysis.

Hepatic myelopathy is almost ineffective to many therapeutic strategies that are effective in hepatic encephalopathy by reducing ammonia production and absorption. It has been shown that a liver transplant can fully reverse the effects of hepatic myelopathy in patients with early-stage disease, whereas it had little effect in patients with more advanced stages.[3] These findings indicate that the early stage of the disease only involves demyelination of the spinal cord, but that axonal loss occurs at the advanced stage. Thus, early and accurate diagnosis of hepatic myelopathy and a subsequent transplantation is important to prevent disease progression.[4] However, early diagnosis remains a challenge, and the notable shortage of donor livers limits the option of transplantation. As such, a comprehensive set of measures has been recommended in the treatment of hepatic myelopathy. This includes limiting the intake of protein in the diet, protecting liver function and lowering blood ammonia, as well as large doses of B group vitamins. This should be accompanied with medication to prevent damage to nerve cells and microcirculation improving agents, such as the traditional Chinese medicine, Salvia. Hepatic myelopathy itself is rarely a life-threatening condition, although it has a negative impact on the patient's quality of life. The prognosis of patients with hepatic myelopathy is more closely determined by the severity of their underlying liver disease. It is generally believed that the cause of death in patients with hepatic myelopathy will be associated with hepatic encephalopathy or other hepatic and neurological complications.[5]

In summary, hepatic myelopathy is a serious complication of liver cirrhosis, associated with portal hypertension and portosystemic shunting. While hepatic encephalopathy is commonly diagnosed in this patient group, the diagnosis for hepatic myelopathy is complex, and is often missed or misdiagnosed. Problems in diagnosis are associated with coexisting hepatic encephalopathy, which may also present with movement disorders. Therefore, it is important to gain a better understanding of the pathogenesis of hepatic myelopathy in order to improve early detection and diagnosis, as well as treatment strategies to treat the primary liver disease and the myelopathy. Through this knowledge, it may become possible to prevent

the development of the disease, or provide treatment that can relieve the symptoms and slow down disease progression.

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