Ten Cases of Hepatic Sinuses Obstruction Syndrome Caused by Sedum Uizoon

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Abstract

Hepatic sinuses obstruction syndrome (HSOS) also known as hepatic venule syndrome, refers to the injury of central lobe and sub-lobular vein of hepatic lobule, resulting in intrahepatic posterior sinus portal hypertension caused by lumen stenosis or occlusion. Currently the pathogenesis is not clear. It may be related to the drug, immunity and inflammation of the liver vein endothelial cells. The clinical manifestations are hepatomegaly, right upper abdominal pain, jaundice and ascites, with a high risk of mortality and poor prognosis for characteristics.

Introduction

In western countries, HSOS is often related with complications after hematopoietic stem cell transplantation, while majoritly taking sedum uizoon containing pyrrolizidine alkaloid in China [1-4]. In China, sedum uizoon is regarded as a good herbal medicine, which has the main function of invigorating the circulation of blood to treat trauma. However, several articles reported that sedum uizoon has the hepatotoxicity component, pyrrolizidine alkaloids which could induce some special disease [5,6]. The mechanism of liver damage induced by plants has not been illuminated, only a hypothesis of “conflict of plant versus animal or plant-animal interaction” seems more acceptable [7]. The defence system of many plants are used to produce compounds such as alkaloids and polypeptides against the animals that intake them (Figure 1). Such animals are also self-protected by efflux transporters in the gut and detoxification of the liver, herbivore counter mechanism to plant chemical defenses, and multidrug resistance associated protein isoform [8]. The underlying mechanism is the destruction of visceral endothelial cells and the late hepatic venous distal obstruction [9]. After intakeing of the plants, pyrrolizidine alkaloids (PAs), the major toxic components are absorbed and converted to highly reactive alkylating pyrroles that cause liver cell necrosis, biliary hyperplasia, fibrosis, and hepatocytomegaly [8].

Patients and Methods

General information

Patients with HSOS according to international diagnostic criteria associated with Tusanqi from December 2014 to July 2017 in Shandong Provincial Qianfoshan Hospital, Jinan China, were included and clinical features were collected. Ten consecutive patients were included in the study. Ten patients (age 42-79 years, five men, five women) were recruit. Ten patients have both the history using of Chinese herbal medicine before the onset of the disease, of which five had taken Tusanqi-a health care product as its Chinese name. In this study, three Tusanqi herbal preparations were provided as herbal wine, power in capsule and herbal rhizome. The time of taking medication varies from twenty days to one year. All ten patients were excluded from autoimmune, viral, genetic and metabolic diseases, denying history of liver disease before disease attack. After a detailed inquiry of the medical history, 2 of the 10 cases had a history of heavy drinking.

Clinical features and physical examination

The first clinical symptoms of 10 patients were abdominal distension, anorexia, jaundice and hepatic hypodynamic. The incidences of abdominal distension, anorexia, jaundice, hypodynamic were 80.0% (8/10), 50.0% (5/10), 20.0% (2/10), (5/10), 50.0%, respectively. A few patients have nausea, vomiting, chest tightness, edema of lower extremities, ascites and jaundice. The first clinical symptoms of 10 patients were abdominal distension, anorexia, jaundice and hepatic hypodynamic. The incidences of abdominal distension, anorexia, jaundice, hypodynamic were 80.0% (8/10), 50.0% (5/10), 20.0% (2/10), (5/10), 50.0%, respectively. A few patients have nausea, vomiting, chest tightness, edema of lower extremities, ascites and jaundice.

Keywords: Hepatic sinuses; Obstruction syndrome; Sedum uizoon; Prognosis

Abbreviations: TBIL: Total Bilirubin; PTA: Activated Partial Thromboplastin Time; ALT: Alanine Aminotransferase; AST: Aspartate Transaminase; Y: Death; N: Survive; TIPS: Trans-Jugular Intrahepatic Portosystemic Shunt; MELD: Model For End-Stage Liver Disease

Figure 1: HSOS short term survival rate and combined disease.

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extremity and other symptoms. Physical examination gives priority to hepatomegaly, ascites and jaundice. Twenty percent of patients have hepatic encephalopathy, liver failure and even multiple organ failure in the late stage of the disease. The physical examination mainly includes hepatomegaly (6/10, 60.0%), jaundice (5/10, 50.0%) and ascites (9/10, 90.0%). There are a few cases of hepatic encephalopathy (1/10, 10.0%) and lower limb edema (1/10, 10.0%).

**Laboratory examinations**

We tested blood samples of 10 patients, including the index of liver function and renal function, blood ammonia, blood glucose, tumor markers, five hepatitis B, autoimmune antibodies and autoimmunity liver antibody. The liver function and coagulation function of the 10 patients have been displayed in the Table 1. Blood samples of 3 patients were tested for autoantibodies and autoantibodies against liver diseases. The detection results of 1 patient were: ds-DNA positive, AMA-M3 antibody weak positive. Blood samples from 9 patients were determined for plasma ammonia, as the result of that was that the levels of plasma ammonia were completely elevated. CA-125 variously went up in six patients detecting tumor markers. All blood samples were negative for hepatitis B virus surface antigen. Renal insufficiency was detected in the blood samples of four patients, having a sharp deterioration in one.

**Imaging data**

Imaging investigations including echocardiography, computed tomography (CT), magnetic resonance imaging (MRI), inferior vena cavaography and the hepatic venography were performed selectively to detect the lesions of liver, ascites and rule out liver cancer, Budd-Chiari syndrome, etc. ascites, cholecystolithiasis or cholecystitis, disperse patchy hepatic enhancement were found in all the patients. Blood flow was visible in the hepatic vein and inferior vena cava although these vessels were found to be narrow in the four patients due to hepatomegaly. Three cases were found to complicate with bilateral pleural effusion.

**Pathematology**

The liver tissue was basically normal, presenting multiple slices of necrosis; the remaining hepatic cells were edematous degeneration. A small amount of acute and chronic inflammatory cells infiltrated, as shown in the liver biopsy specimen obtained from one patient.

**Treatment and prognosis**

Ten patients were given liver protectant, diuresis, low molecular weight heparin, anti-inflammatory, improvement of coagulation function and other symptomatic support treatment. Trans-jugular intrahepatic portosystemic shunt (TIPS) had been used to decompress the portal circulation, and relieve ascites in six patients with hepatic SOS, but Course of disease had been shown to worsen and did not improve the outcome. Four patients with hepatic SOS improved the condition after treatment. One case developed multiple organ failure, one case has occurred to be hepatic encephalopathy. The remaining patients were discharged from the hospital because of their families’ abandonment.

**Discussion**

Ten patients with HSOS were collected. Their history of Tusanqi use and laboratory indicators are shown in Table 1. According to the characteristics of the patient’s medical history and the laboratory examination, we can conclude that there is no gender difference in the incidence of HSOS caused by tusanqi. Age of onset is concentrated in middle and old age. The onset time of the disease may be related to the dose of the drug and medication frequency. The time of the disease depends on the dosage and frequency of the medicine. Laboratory examination suggested that HSOS patients have liver dysfunction with different degrees and abnormal coagulation function. To study the relationship between the laboratory indicators and the prognosis of the disease, we used the MELD score as a criterion for judging the prognosis of the disease. The study showed that the prognosis of the disease was poor when the MELD score exceeded 30 points. We made a line diagram use which the onset time taking tusanqi as X axis, TBIL, PTA, ALT, AST, MELD scores respectively as Y1, Y2, Y3, Y4, Y5. From the chart we found that the increase of bilirubin, ALT, and AST levels was significantly associated with poor prognosis. We summed up the factors affecting the poor prognosis of HSOS, such as Table 2.

The factors associated with the severity of the disease were listed in Table 3. Common combined diseases in HSOS progress include hepatic encephalopathy, peritonitis, hepatorenal syndrome and liver failure. The final stage of HSOS is often characterized by shock, multiple organ dysfunctions. TIPS is an operative way to depress portal pressure and reduce intractable ascites, which does not improve the prognosis of the disease. MELD score was no significant reduction in HSOS patient with TIPS compared ones without TIPS. We can get it from the Table 4 that the severity of the disease is not related to hepatic encephalopathy and peritonitis. Shock and hepatic encephalopathy may be caused as a complication after TIPS, which has caused a low correlation with the severity of the disease. In contrast, MELD scores are closely related to multiple organ dysfunction, hepatorenal syndrome and liver failure. The survival rate of the HSOS patients with more than 30 points was low, while more than 1 years in two patients with the lowest score, which could basically reflect the prognosis of the disease (Table 4).

| S. No. | Gender | Age | Onset time | TBIL (umol/L) | PTA (s) | ALT (U/L) | AST (U/L) | MELD | Death |
|-------|--------|-----|------------|--------------|--------|----------|----------|------|-------|
| 1     | F      | 44  | 3 months  | 16.1         | 67.3   | 78.2     | 92       | 14.188| Y     |
| 2     | M      | 79  | 20 days   | 53.2         | 41.4   | 5.7      | 23.9     | 15.046| Y     |
| 3     | F      | 43  | -          | 40.1         | 39.8   | 17.1     | 30.3     | 13.769| N     |
| 4     | F      | 79  | 11 months | 51.4         | 65.7   | 12.6     | 27.3     | 10.319| N     |
| 5     | F      | 55  | 2 months  | 40.7         | 57.1   | 159.8    | 131.5    | 30.912| Y     |
| 6     | M      | 65  | 2 months  | 38.9         | -      | 698.7    | 551.7    | 11.5016| N     |
| 7     | M      | 68  | -          | 96           | 49.4   | 63.8     | 119.1    | 12.1204| N     |
| 8     | F      | 65  | 1 month   | 42           | 65.3   | 28.3     | 39.2     | 11.9469| N     |
| 9     | F      | 70  | 50 days   | 45.8         | 54.4   | 54.9     | 117.4    | 13.353| Y     |
| 10    | M      | 60  | -          | 790          | 66.7   | 181      | 136      | 33.5715| N     |

TBIL: Total Bilirubin; PTA: Activated Partial Thromboplastin Time; ALT: Alanine Aminotransferase; AST: Aspartate Transaminase; Y: Death; N: Survive; MELD: Model For End-Stage Liver Disease

Table 1: Clinical features and prognosis of patients with HSOS.
Conclusion

At present, the incidence of HSOS is constantly increasing. The diagnosis depends on classical triad of weight gain, jaundice and painful hepatomegaly [9]. When clinical and imaging data are not sufficient diagnosis of the disease depends mostly on liver histopathology [10]. HSOS is associated with considerable mortality because of the severity of the disease and ineffectiveness of treatment [10]. The main clinical manifestations of the patients were abdominal distension, anorexia, jaundice, hypodynamic. There is no exactly effective treatment for HSOS. TIPS does not improve the survival and prognosis of the patients. Considering the high mortality of severe HSOS, liver transplantation is the only way to save a patient’s life, but it is also not conclusive [11]. HSOS as cause of liver graft dysfunction after liver transplantation is rare but has a poor prognosis [12]. Therefore, early diagnosis and treatment of HSOS are very important, especially early identification of disease. So, it’s important to identify the disease for early diagnosis and treatment. It is necessary to obtain accurate information about patients’ use of herbal remedies, and to ensure that they realize about their potential hepatotoxicities.

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