

January 20, 2022

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 73608\_Auto\_Edited.doc).



**Title:** Primary hepatic angiosarcoma manifested as hepatic sinusoidal obstruction syndrome: A case report

**Author:** Jiaxing Tian, Min Li, Jiangquan Liao, Wenke Liu, Xiaolin Tong

**Name of Journal:** World Journal of Gastrointestinal Oncology

**ESPS Manuscript NO:** 73608

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

#### **The first review's composition comment on the manuscript and my answer**

Discussion is too long conclusion too long and you can not suggest this statement from one case report

Answer: Yes, I agree with your comment and make the corresponding modification about the part of discussion.

#### **The second review's composition comment on the manuscript and my answer**

This report presents a case of primary hepatic angiosarcoma and it is claimed that it manifested as hepatic sinusoidal obstruction syndrome (SOS). It is unclear on what criteria the suspicion of SOS was based. To the best of my knowledge, acute SOS typically presents with abdominal pain and swelling, sudden weight gain due to fluid accumulation and signs of portal hypertension (ascites, edema, varices). Liver histology demonstrates obstruction of sinusoids in central areas (and not dilation as reported in this case) with hepatocyte necrosis and hemorrhage. The clinical syndrome is similar to Budd Chiari syndrome (hepatic vein thrombosis), but the obstruction is due to narrowing and occlusion of sinusoids and small hepatic venules. The case presented in this manuscript had a weight loss and not a weight gain with abdominal swelling, and there were no signs of portal hypertension. Therefore, except for abdominal pain, the typical clinical signs of acute SOS were not present. Answer: This meta-analysis focused on diabetic gastroparesis that were gastric emptying

Answer: Yes, I agree with your comment that the clinical syndrome is similar to Budd Chiari syndrome. The history of herbal medicine intake makes this diagnosis more difficult. In China, hepatic sinusoidal obstruction syndrome is often associated with the oral intake of plants that contain pyrrolidine alkaloids. Our case met the "Nanjing criteria" for the diagnosis of hepatic sinusoidal obstruction syndrome except that the herbal medicine that the patient had ingested in its common form does not contain pyrrolidine alkaloid. The patient presented with abdominal distension, jaundice, ascites, and hepatomegaly, in conjunction with the evidence on enhanced computed tomography; in addition, Budd-Chiari syndrome was ruled out because there were no communicating branches between the narrowed hepatic veins. Communicating branches between the narrowed hepatic veins are seen in Budd Chiari syndrome and are a critical feature that distinguishes Budd Chiari syndrome from other similar conditions

## The third review's composition comment on the manuscript and my answer

Rare case of PHA reported by authors is interesting. Some of the comments are follows:

1. Rephrasing of sentences of physical findings are required at two places -one in the abstract and other in the main body of the case report under heading --Physical examination upon admission "Physical examination was significant for the right and left upper quadrant for pain and tenderness. Percussion elicited pain over the liver area." It may phrased as "both the liver and spleen were enlarged and liver was tender on percussion"

Answer: Yes, we agree with your comment and make the corresponding modification about this part.

2.What was the differential diagnosis at admission? based on clinical presentation and CT scan?

Answer: The clinical syndrome is similar to Budd Chiari syndrome. The history of herbal medicine intake makes this diagnosis more difficult. In China, hepatic sinusoidal obstruction syndrome is often associated with the oral intake of plants that contain pyrrolidine alkaloids. Our case met the "Nanjing criteria" for the diagnosis of hepatic sinusoidal obstruction syndrome except that the herbal medicine that the patient had ingested in its common form does not contain pyrrolidine alkaloid. Communicating branches between the narrowed hepatic veins are seen in Budd Chiari syndrome and are a critical feature that distinguishes Budd Chiari syndrome from other similar conditions

3. Why was Trans jugular biopsy planned ?

Answer: The patient's condition progressed rapidly. Thus, the diagnosis was questionable. A liver biopsy was necessary to establish a definitive diagnosis. However, because the platelet count of the patient continued to decline and coagulation disorders and jaundice could not be controlled, a percutaneous liver biopsy was not performed, as it is associated with an increased risk of bleeding. There is evidence that transjugular liver biopsy is a highly efficacious, well-tolerated, and safe procedure. It can be safely performed multiple times in the same patient or in critically ill, severely coagulopathic patients and does not significantly increase the rate of complications while maintaining an extremely favourable diagnostic yield

4.Figure 5 may be deleted and be put in the text as there are too many figures.

Answer: Yes, we agree with your comment and make the corresponding modification about this part

5. Indications of Trans jugular liver biopsy in cases of hepatosplenomegaly may be added in discussion

Answer: Yes, we agree with your comment and add some words about Trans jugular liver biopsy in this revision

6. Grammar needs correction

Answer: Yes, we agree the reviewers' opinion and make the corresponding modification

Fushuang Ha, Hua Liu, Tao Han, Dezhao Song, The Third Central Clinical College of Tianjin Medical University, Tianjin 300170, China

Fushuang Ha, Hua Liu, Tao Han, Dezhao Song, Tianjin Key Laboratory of Extracorporeal Life Support for Critical Diseases, Tianjin 300170, China

Fushuang Ha, Hua Liu, Tao Han, Dezhao Song, Artificial Cell Engineering Technology Research Center, Tianjin 300170, China

Fushuang Ha, Hua Liu, Tao Han, Dezhao Song, Tianjin Institute of Hepatobiliary Disease, Tianjin, China

Tao Han, Tianjin Union Medical Center, Naikai University Affiliated Hospital, Tianjin 300121, China

Answer: Yes, I agree with your comment that the clinical syndrome is similar to Budd Chiari syndrome. The history of herbal medicine intake makes this diagnosis more difficult. In China, hepatic sinusoidal obstruction syndrome is often associated with the oral intake of plants that contain pyrrolidine alkaloids. Our case met the "Nanjing criteria" for the diagnosis of hepatic sinusoidal obstruction syndrome except that the herbal medicine that the patient had ingested in its common form does not contain pyrrolidine alkaloid. The patient presented with abdominal distension, jaundice, ascites, and hepatomegaly, in conjunction with the evidence on enhanced computed tomography; in addition, Budd-Chiari syndrome was ruled out because there were no communicating branches between the narrowed hepatic veins. Communicating branches between the narrowed hepatic veins are seen in Budd Chiari syndrome and are a critical feature that distinguishes Budd Chiari syndrome from other similar conditions

