

## Answering Reviewers

**Name of Journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 41105

Title: Ductopenia and cirrhosis in a 32-year-old woman with progressive familial intrahepatic cholestasis type 3: A case report

Youwen Tan, Hailei Ji, Zhonghua Lu, Guohong Ge, Li Sun, Xinbei Zhou, Jianhui

Sheng, Yuhua Gong

### **Dear Editors and Reviewers:**

Thank you very much for your comments regarding our manuscript. We have carefully revised the manuscripts per your suggestion.

Reviewer #1: The authors described a rare case of progressive familial intrahepatic cholestasis type 3, by confirming a mutation in the ABCB4 gene encoding multidrug resistance protein 3. Interesting case presentation addressing a rare topic. I think it should be published in the present form.

**A:** Thanks for your very kindly comments.

Reviewer #2: interesting case reminding a rare cause of cholestasis

**A:** Thanks for your review and recommendation.

Reviewer #3: In this manuscript, authors reported a case of PFIC3 in a 32-year-old woman based on clinical symptoms, pathological findings, and gene mutation detection. It is an interesting case suggesting important differential diagnosis in a patient with recurrent cholestasis. I would like to indicate some minor comments. 1. Since the clinical features of PFIC3 overlap with many other forms of liver disease in childhood, definitive diagnosis may be problematic or delayed. In addition, impaired copper secretion and copper

accumulation can be seen in all chronic cholestatic disorders. In this case report, liver histology showed copper-associated protein sinking in hepatocyte cytoplasm (Figure 1C). Therefore, please describe the findings for differential diagnosis with Wilson disease (WD) in this case, such as serum ceruloplasmin, serum and 24-hour urinary copper level, and liver histology etc. In addition, it would be better to comments about differential diagnosis or overlapping with WD in young patients with recurrent cholestasis and/or cirrhosis in 'Discussion'. 2. Please correct the errors in English.

A:1. Wilson disease (WD) may mimic non-Wilsonian liver disease. The diagnosis of WD should be based on clinical and pathologic parameters as well as genetic testing. Liver biopsy often demonstrates glycogenated nuclei and hepatic steatosis. Typically, there is little or no accumulation of copper. In this patient, WD was finally ruled out because the serum copper level was 90  $\mu\text{g/dL}$  (80–155  $\mu\text{g/dL}$ ), the serum ceruloplasmin level was 210  $\text{mg/L}$  (200–500  $\text{mg/L}$ ), the amount of 24-h urinary copper excretion was 64  $\mu\text{g/dL}$  (<100  $\mu\text{g/dL}$ ), no Kayser-Fleischer (K-F) rings were observed, and genetic testing revealed no *ATP7B* mutation

Copper overload in liver disease is not necessarily synonymous with WD, though this is the most commonly known disorder. Other less common disorders of copper overload include idiopathic copper toxicosis, Indian childhood cirrhosis, and endemic Tyrolean infantile cirrhosis. These generally have more diffuse and intense copper deposition, mainly on orcein stain, usually in a cirrhotic liver.

Copper accumulation may also be seen in primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), secondary sclerosing cholangitis, biliary atresia, prolonged extrahepatic biliary obstruction, and in the livers of some normal neonates. The differential diagnosis of these cholestatic liver diseases depends on the corresponding immunological antibody detection and imaging examination.

We have added these in the discussion section.

2. The revised manuscript has been edited and proofread again by a medical editing company .

Reviewer #4: It is an interesting case study. The authors analyzed every aspect of it by the most appropriate way.

A: Thanks for your review and recommendation.

Sincerely.

Youwen Tan, MD,

Department of Hepatology, The Third Hospital of Zhenjiang Affiliated  
Jiangsu University (No.300,Daijiamen,Runzhou Distinct,Zhenjiang 212003),  
Zhenjiang, China

Tel: +86-13914567088;

Fax: +86-511-88970796;

E-mail: [tyw915@sina.com](mailto:tyw915@sina.com)