

Dear Dr. Wang,

We thank you for your encouragement and advice. We would like to resubmit the manuscript entitled “Relationship of familial cytochrome P450 4V2 gene mutation with liver cirrhosis: Case report and literature review” (Manuscript 78270, Case Report) for your further consideration as an original research article for publication in *World Journal of Clinical Cases*.

We also thank the reviewers for their constructive comments and suggestions. We have revised the manuscript accordingly, and provided point-by-point responses below. All amendments are indicated by red font in the revised manuscript. In addition, we have carefully checked every sentence in the revision to eliminate errors in language use, and this revision was proofread by two native English-speaking biologists from *Medjaden*, a professional publication services company. We think that this manuscript is easily understandable and the language usage is appropriate. We have enclosed a language certificate from the *Medjaden*.

If I can be of any assistance regarding the process of this manuscript please contact me. I look forward to hearing from you soon.

Sincerely,

Yi-Huai He.

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Responses to the Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: This is an interesting case, but I have a few comments: 1) In Core tip “CYP4V2 functions in hepatic lipid metabolism and inflammatory responses. “ – there is no verb in the sentence;

Response: We appreciate this advice. In this sentence, “functions” is a verb. Some other medical examples: “The heart functions as a pump.” “The circulatory system functions in the delivery of oxygen.” (Page 5, line 8)

2) “The specific history of a patient and liver biopsy results can help to identify common liver diseases, such as autoimmune liver disease, drug-induced liver damage, and non-alcoholic fatty liver disease.” - it should be added that the results of laboratory tests are also an important basis in the differential diagnosis of liver diseases;

Response: We appreciate this advice. Laboratory test results are indeed an important basis for the differential diagnosis of liver disease, and we added this to the text. (Page 6, line 3)

3) “Cryptic cirrhosis (CC) can persist after systematic clinical, laboratory, and pathological examinations of liver disease with unknown etiology.” - the sentence should be revised because it implies that examinations does not (and should not!) cure cryptic cirrhosis;

Response: We appreciate this advice. We believe this sentence was inappropriate, and after careful consideration, we chose to delete it.

4) tables should be numbered as they are mentioned in the article;

Response: We appreciate this advice. We checked that the numbering of the Tables in was consistent with the order in which they were mentioned.

5) “with positive dullness” – may be «positive test for shifting dullness” since dullness (liver, spleen) is always present in the abdomen, but unlike ascites, they do not shift when the position of the body changes;

Response: We appreciate this advice. We revised this text to “was positive for shifting dullness”. (Page 9, line 7)

6) Case description is too long, it should be shortened

Response: We appreciate this advice. We reduced the length of the Case Presentation section.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This case shows a link between the CYP4V2 mutation and liver cirrhosis, although a causal association, which most certainly exists here, cannot be established. A liver biopsy might have been helpful, but the patient refused, as the authors have already acknowledged. I have no other pertinent criticism to add. The writing is precise and well-organized, and the English is excellent. I believe it to be a case worth publishing.

Response: Thank you for these helpful and complementary comments.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: The case and the family history is very interesting. The analysis of the underlying mutation is correct. However, even if I am not a native speaker, I think the written presentation should be considerably improved.

E.g. Page 6: Hemochromatosis is the most common GLD, but there are more than 600 other kinds of confirmed GLDs, such as hepatolenticular degeneration, hereditary hemochromatosis, glycogen storage disease, α 1-antitrypsin deficiency, hereditary hyperbilirubinemia, Dubin-Johnson syndrome, Rotor syndrome, hereditary hyperbilirubinemias, and congenital liver fibrosis [7]

Response: We appreciate this advice. Our original statement was inaccurate, and we modified this text as follows: “At present, there are more than 600 kinds of GLD, including and primary hemochromatosis, hepatolenticular degeneration, hereditary hemochromatosis, glycogen storage disease, α 1-antitrypsin deficiency, hereditary hyperbilirubinemia, Dubin-Johnson syndrome, Rotor syndrome, hereditary hyperbilirubinemias, and congenital liver fibrosis.” (Page 6, line 21 - Page 7, line 3)

Page 8: following treatment for liver preservation and with a diuretic. What does that mean?

Response: We are sorry for the confusion. We changed this text as follows: “... these symptoms resolved after administration of a liver protectant and a diuretic to reduce swelling”. (Page 8, line 10 - 11)

Page 9: The thyroid function tests indicated a decreasing level of T3, and an increasing level of thyroid stimulating hormone (TSH), gradually leading to hypothyroidism. This is difficult to understand.

Response: We appreciate this advice. We changed this text as follows: “...an increasing level of TSH, indicating progression from subclinical hypothyroidism to clinical hypothyroidism.” (Page 8, line 12 - 13)

Page 10: Color Doppler ultrasonography of the thyroid showed bilateral glioceles. What is that glioceles?

Response: We're sorry this was not clear. We changed this text as follows: “Color Doppler ultrasonography of the thyroid showed bilateral thyroid cysts.”. (Page 9, line 20)

Page 10: Please explain Li Fanta Test Discussion: The interpretation of the results seems to be correct.

Response: We're sorry we this was not clear. We changed this to "Rivalta test", a test of the plasma mucin. (Page 9, line 14)

However, the text of the "Discussion" section must be shortened.

Response: We appreciate this advice. We reduced the length of this section as suggested.

4 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A).

Response: We have carefully checked every sentence in the revised text with the assistance of two native English-speaking biologists from *Madjaden*, a publication services company. We believe this manuscript is easily understandable and the language usage is appropriate. Please see the language certification from the company.

Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

Once this step is completed, the manuscript will be quickly accepted and published online. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly.

The basic rules on abbreviations are provided here:

(1) Title: Abbreviations are not permitted. Please spell out any abbreviation in the title.

(2) Running title: Abbreviations are permitted. Also, please shorten the running title to no more than 6 words.

(3) Abstract: Abbreviations must be defined upon first appearance in the Abstract. Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*).

(4) Key Words: Abbreviations must be defined upon first appearance in the Key Words.

(5) Core Tip: Abbreviations must be defined upon first appearance in the Core Tip. Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*)

(6) Main Text: Abbreviations must be defined upon first appearance in the Main Text. Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*)

(7) Article Highlights: Abbreviations must be defined upon first appearance in the Article Highlights. Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*)

(8) Figures: Abbreviations are not allowed in the Figure title. For the Figure Legend text, abbreviations are allowed but must be defined upon first appearance in the text.

Example 1: A: Hepatocellular carcinoma (HCC) biopsy sample; B: HCC-adjacent tissue sample. For any abbreviation that appears in the Figure itself but is not included in the Figure Legend textual description, it will be defined (separated by semicolons) at the end of the figure legend. Example 2: BMI: Body mass index; US: Ultrasound.

(9) Tables: Abbreviations are not allowed in the Table title. For the Table itself, please verify all abbreviations used in tables are defined (separated by semicolons) directly underneath the table. Example 1: BMI: Body mass index; US: Ultrasound.

6 EDITORIAL OFFICE’S COMMENTS

Authors must revise the manuscript according to the Editorial Office’s comments and suggestions, which are listed below:

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Response: Thanks for your comments.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author’s intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the

reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is ‘original’, the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content. Please upload the approved grant application form(s) or funding agency copy of any approval document(s). Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Response: Thank you for your advice. We have formatted the manuscript accordingly.