59180-Figures.ppt

59180-Tables.docx”

(1) 59180-Answering Reviewers

(3) 59180-Conflict-of-Interest Disclosure Form

(4) 59180-Copyright License Agreement

(6) 59180-Signed Informed Consent Form(s) or Document(s)

(9) 59180-Image File

(10) 59180-Table File

(11) 59180-CARE Checklist–2016

(12) 59180-Supplementary Material

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors:

The ms brings a novel and interesting observation in the ultra-rare disease of GSD1a - the "bull eye" appearance has not been described previously. This has a potential to improve dg of the HCA in this setting. The ms is very well and meticulously written. Methods are appropriately described. Several major aspect would need to be addressed for the ms to have broader implications:

Comment 1. - much more general clinical data on the both cases could be provided (genotype, phenotype, therapy,...) to better understand and support the findings clinically;

Reply to comment 1: Thanks for your comment. The following information has been added for each case:

Patient 1: body mass index equal to 29 Kg/m^2, good metabolic control on cornstarch since the age of 1 year and had been operated 10 years before of partial hepatectomy for an HCA in the left lobe.

and

Patient 2: body mass index equal to 20 Kg/m^2, good metabolic control on cornstarch and later protein supplement started at the age of 19 months and gastrostomy tube at the age of 4 years before high school.

Comment 2 - it would be also good to put the findings in a broader perspective - how many MR were performed at the center in this same group of patients (GSD1a) and what was the proportion of such findings? How many had HCA? How many HCC? Were any other particular clinical characteristics related to this finding? were any longitudinal results available, what happened with this MR appearance over time?

Reply to comment 2: Thanks for your comment. We have reviewed our database of GSD1 patients and we identified 24 patients with glycogenosis type 1 who had been imaged with MRI for focal liver lesions, including some MRI exams with extracellular agents, others with eovist and finally some exams with no contrast. In agreement with your suggestion, we have added the following text: "At our hospital – which is a tertiary referral center for GSD –24 patients with glycogenosis type 1 have been imaged with MRI for focal liver lesions.". We agree that a more comprehensive analysis of this dataset – including assessment of MRI in the whole cohort and evaluation of longitudinal follow-up – is interesting; however, it is important to perform an adequately designed retrospective study, to carefully analyze all MRI exams and to retrieve all the MRI images. Therefore we have added this at the end of the manuscript "Further studies are needed to confirm this hypothesis, investigate the possible underlying pathological mechanisms and assess whether the different radiological features may predict evolution into hepatocellular carcinoma; therefore, we plan to further analyze our GSD1 cohort with this purpose."

Comment 3 - in addition to HCA, also HCC are not very rare in GSD1a. the HCC and relation between HCA and HCC is only briefly addressed in the ms. Is there any prognostic value of this finding with regard the progression to HCC?

Reply to comment 3: Thanks for your comment. We agree that evolution into HCC is very important in GSD patients. Therefore, in agreement with your suggestion, we have added the following text in our manuscript "In a series of 32 GSD patients with HCAs, evolution of HCAs into hepatocellular carcinoma has been reported in about 12.5% of cases in a median interval

time from the diagnosis of HCA to the diagnosis of hepatocellular carcinoma of 6.7 years [8].". As regards the prognostic value of our finding with regard to the progression to HCC, we don't have a clear answer as none of the two patients had HCC. By analyzing a recent article, we saw that changes in number and size could be helpful for assessing evolution into HCC and, therefore we have added the following text "In this series recently published by Jang HJ et al [8], the radiological changes of HCAs in the 4 patients that developed hepatocellular carcinoma included an increase either in the number or size of HCA in two patients and an increase in both size and number in the remaining two patients.". We agree that it could be also important to assess whether the new finding may have a role in regard to progression to HCC and this is why we have added this at the end of the manuscript "Further studies are needed to confirm this hypothesis, investigate the possible underlying pathological mechanisms and assess whether the different radiological features may predict evolution into hepatocellular carcinoma; therefore, we plan to further analyze our GSD1 cohort with this purpose."

(1) ***Science editor:*** 1

Scientific quality: The manuscript describes a case report of the "bull's eye" appearance of hepatocellular adenomas in patients with glycogen storage disease. The topic is within the scope of the WJG.

(1) Classification: Grade B;

(2) Summary of the Peer-Review Report: The authors reported a novel and interesting observation in the ultra-rare disease of GSD1a. This has a potential to improve dg of the HCA in this setting. The manuscript is very well and meticulously written. Methods are appropriately described. However, some questions raised by the reviewers should be answered; and

(3) Format: There are 2 figures. A total of 17 references are cited, including 2 references published in the last 3 years. There are no self-citations.

2 Language evaluation: Classification: Grade A.

3 Academic norms and rules: The authors provided the signed Copyright License Agreement. The authors should provide the Conflict-of-Interest Disclosure Form. The CARE Checklist–2016 lacks of the page number. Written informed consent was waived. No academic misconduct was found in the CrossCheck detection and Bing search.

Authors reply: We added the **Conflict-of-Interest statement**

4 Supplementary comments: This is an invited manuscript. The topic has not previously been published in the WJG.

5 Issues raised:

(1) The authors' information should be added in the first page;

Authors reply to issue 1: We added authors' information in the first page

(2) The "Author Contributions" section is missing. Please provide the author contributions;

Authors reply to issue 2: We added Author Contributions" section

(3) The authors did not provide original pictures. 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; however, we are sending it as Audio-core-tip as there is no dedicated section for upload.

Authors reply to issue 3: We have added a power point with the original figures so that these can be reprocessed by the editor;

(4) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

Authors reply to issue 4: We added the PMID and DOI numbers and we listed all the authors in the reference list.

(5) The cited references should be superscript;

Authors reply to issue 5: We modified the cited references in the text accordingly.

(6) The "Case Presentation" section was not written according to the Guidelines for Manuscript Preparation. Please re-write the "Case Presentation" section, and add the "FINAL DIAGNOSIS", "TREATMENT", and "OUTCOME AND FOLLOW-UP" sections to the main text, according to the Guidelines and Requirements for Manuscript Revision.

Authors reply to issue 6: We modified the sections in order to comply with the Guidelines for Manuscript Preparation.

6 Re-Review: Required.

7 Recommendation: Conditional acceptance.