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Round-1

RESPONSES TO REVIEWER COMMENTS

Reviewer #1

The authors present the case report of an uncommon association between IgA nephropathy and acute hepatic failure. The manuscript is written in a clear and concise manner.

Authors' Response: We thank the Reviewer for the positive comments.

It would be interesting to have more information on the results of the tomography scan (whether there were radiological signs of chronic hepatopathy and portal hypertension) and of the endoscopy (for any findings suggestive of primary sclerosing cholangitis).

Authors' Response: We thank the Reviewer for the excellent suggestion. We have added computed tomography and endoscopic retrograde cholangiopancreatography findings according to the reviewer's comments. (Page 7, 8)

Since the histopathological study of the liver was unable to unequivocally confirm autoimmune hepatitis as the primary cause of the liver failure, it would be also interesting to know if other causes of acute liver failure were excluded (such as copper, ceruloplasmin and iron metabolism studies).

Authors' Response: We agree with the Reviewer and have included the copper and iron metabolism studies in Table 2 in the revised manuscript, according to the reviewer's suggestion.

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Reviewer #2

In this manuscript, authors reported a case of IgA nephropathy concurrent with autoimmune hepatitis which led to acute liver failure requiring liver transplantation. The case seems to be interesting because IgA nephropathy in patients with autoimmune hepatitis has been rarely reported. However, there are some concerns in this report. The reviewer's comments are described as follows.

1. In this report, the temporal association between IgA nephropathy and autoimmune hepatitis remained unclear. Subclinical IgA nephropathy is relatively common in Asian populations. When abnormalities of urine test and liver function test occurred, respectively, and which occurred first are critical points.

Authors' Response: We thank the Reviewer for raising this critical issue. We have mentioned that liver function test results were normal at the time of kidney biopsy in revised manuscript.

2. There were no findings suggesting autoimmune mechanisms of IgA nephropathy rather than impaired IgA clearance in liver disease in this case. Detection of circulating autoantibody against galactose-deficient IgA1 should be useful to explain the autoimmune mechanisms.

Authors' Response: We appreciate the reviewer's excellent suggestion. However, we did not perform the test for circulating antibody to galactose-deficient IgA1. Serum levels of Gd-IgA1 and IgG autoantibodies specific for the Gd-IgA1 have been recently reported to specific markers of primary IgA nephropathy. Furthermore, Gd-IgA1-specific monoclonal antibody, KM-55, has been recently reported to specifically stain glomerular deposits in primary IgA nephropathy. However, recent study showed Gd-IgA staining was present not only in primary IgAN, but also in biopsies with secondary IgAN (Cassol CA, et al., NDT, 2019). Moreover, there were no differences between secondary and primary IgAN in plasma Gd-IgA1 levels and

plasma IgA1-IgG complex levels. (Wang M, et al., KI reports, 2020). Therefore, we think that staining for Gd-IgA may be not specific enough to distinguish between primary and secondary form of IgAN.

3. Authors diagnosed autoimmune hepatitis based on the revised scoring system of the International Autoimmune Hepatitis Group and the score was 16. However, the patient had hepatitis B antigen as described in laboratory data. The score for positive hepatitis virus is -3 but not +3. Therefore, the score 16 appears to be wrong. In addition, Including IgA nephropathy as "other autoimmune disorder" is generally uncommon. This case could not be considered definitive as autoimmune hepatitis based on the scoring system.

Authors' Response: We apologize if our interpretation of hepatitis B serologic test was not clear. Our patient was positive for hepatitis B surface antibody and negative for hepatitis B surface antigen and anti-HBc antibody. We rewrote this sentence.

An epidemiologic study with autoimmune hepatitis showed extrahepatic manifestation such as thyroiditis, arthritis and inflammatory bowel disease were common (8~28%). Glomerulonephritis was also seen in 5 patients (1%) (Werner M et al., Scand J Gastroenterol. 2008). However, it is not yet established which type of glomerulonephritis is usually accompanied by autoimmune hepatitis. Our study may add to the list of concomitant autoimmune disorders of autoimmune hepatitis.

4. In renal histology, were there any complement depositions? In addition, were there any glomerular chronic lesions such as segmental or global sclerosis?

Authors' Response: We appreciate the reviewer's suggestion. We have added kidney histopathologic description and figure in the revised manuscript.

5. Acute kidney injury was probably caused by hepato-renal syndrome but not IgA

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nephropathy. Authors should clearly explain the pathogenesis of kidney injury at each timing.

Authors' Response: We thank the reviewer for the helpful comments. To respond to the reviewer's concern, we have added the explanation about cause of AKI, in the revised manuscript.

We appreciate the effort that will be undertaken to review this manuscript and look forward to your reply. We hope that our manuscript is now suitable for publication in World Journal of Clinical Cases.

August 5th, 2020

Sincerely yours,

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Round-2

Reviewer #1

Authors have addressed most of the reviewer's concerns. However, regarding the comments #3, including IgA nephropathy in International autoimmune hepatitis group (IAIHG) scoring system as an autoimmune disease appears to be inappropriate. IAIHG scoring system was revised in 2008. Now, the simplified scoring system has been more popular and does not need complicated information. The reviewer recommends replacing the original scoring in the manuscript with revised, simplified scoring. The results should not be changed.

Authors' Response: We rewrote a sentence in the revised manuscript, according to the reviewer's suggestion.

Reviewer #2

The case reported by the authors is of scientific interest, and the revised manuscript is clear, well-written and informative. We recommend it for publication.