November 15, 2021

Trieste, Italy

Mr. Jin-Lei Wang

Company Editor-in-Chief

Baishideng Publishing Group, Inc.

7041 Koll Center Parkway

Suite 160

Pleasanton, California 94566

USA

Dear Mr. Wang,

Thank you very much for considering our Case Report – *Diagnosis of Acute Intermittent Porphyria in a renal transplant patient* -- for publication in the World Journal of Transplantation. Below you will find our comments and revisions according to the suggestions of the Reviewers.

Reviewer 1 (ID number 00006486):

Regarding the comment Language Quality: Grade B (Minor language polishing), the manuscript was written in English by two native English speakers. We have reread the manuscript with strict attention to grammar, spelling and meaning, and we have sought language that needs polishing.

We added the following sentence to the first paragraph of the Discussion: *Although Lazareth et al have reported improved AIP outcomes following renal transplantation (), the hepatic origin of the disease may present a risk of acute attack in case of post-transplant complications, medications, infection or reduced carbohydrate intake.*

The spectrophotometric technique was used to measure urinary porphobilinogen and the other porphyrins, and we have included this information in the paragraph Final Diagnosis.

We agree with the Referee that it would be very interesting to know the precise location and type of mutation within the PBGD gene. We have included in the text in the Treatment section the method used to search for the mutation (gene sequencing and PCR), and we hope to find the expertise to sequence the entire gene. Also we will discuss with the Genetics department the possibility to sequence the PEPT2 gene as well. Unfortunately, the patient has no family members available for study.

The nephrectomy specimen, in addition to the small renal carcinoma, revealed chronic tubulointerstitial lesions and nephroangiosclerosis. According to Pallet et al (Reference number 7), in a large cohort of patients with porphyria-associated kidney disease, kidney biopsies revealed "diffuse glomerulosclerosis and chronic interstitial changes", and thus it is conceivable that the AIP was responsible for the renal insufficiency. On the other hand, these findings are very common and nonspecific in nephropathy patients, and may not accurately reflect the etiology of the renal disease. We have included this information and caveat in the second paragraph of the Discussion.

We thank the Referee for the information regarding hyperinsulinemia. We have clarified this in the Discussion.

We added the enzyme protoporphyrinogen oxidase to Figure 1 and we corrected the misspelling of ferrochelatase.

Reviewer 2 (ID number 00503026):

We have removed the specific dates from the case descriptions in the text, as requested.

Mr. Wang commented that the manuscript met the basic publishing requirements of the *World Journal of Gastroenterology.* A small error – this Case Report is destined for the *World Journal of Transplantation*, to remind those colleagues that rarely see AIP that this disease should be included in the differential diagnosis of abdominal pain in transplanted patients.

Regarding the comment of the Science Editior, we have revised Table 1.

Reviewer 3 (ID number 05190615):

This is the first report of new onset AIP symptomatology in a renal transplant patient. which provides new knowledge supplement for emergency doctors:an older subject with a common presentation of an uncommon disease. In patients with postoperative abdominal pain, we exclude common causes such as intestinal obstruction, and suspicion of AIP is also necessary.In short, this is a very rare and meaningful case.

Thanks for your comments.

We hope the modifications to the text satisfy the suggestions of the Reviewers. Please advise us if we can be of further assistance.

Sincerely,

Cristina Sirch, M.D.