RESPONSES TO REVIEWERS' COMMENTS

Dear Editor,

We are truly grateful for your letter and the reviewer's insightful comments on our manuscript titled "CYP17A1 Mutation Causes Severe Pseudohermaphroditism: a Case Report and Literature Review" (Ms. No.??). We have made careful revisions on the manuscript according to the reviewers' comments and would like to re-submit it for your consideration. All changes are highlighted in yellow color in the revised manuscript. Point-by-point responses to all the comments are listed below this letter. We hope that the revised version of the manuscript is now acceptable for publication in your journal. Thank you again for your time and consideration.

We look forward to hearing from you at your earliest convenience.

Yours Sincerely,

Xingjian Zhou

First of all, we would like to express our sincere gratitude to the reviewers and editor for their constructive and positive comments.

Replies to Reviewer 1

1. In the introduction of the case you should add data on the prevalence and incidence of this disorder.

   Re: Thank you for this helpful comment. We have revised the manuscript according to your advice.

2. In the presentation of the case you refer to the fact that the patient was also diagnosed with multiple myeloid lipoma and at no time have you made reference to this pathology throughout the manuscript except in the introduction. They should correlate this pathology with the syndrome they describe and whether or not it may have associated effects. In my opinion, this could be an important bias and they should make reference to it in the text.

   Re: Thank you for this careful suggestion. Adrenal myelolipoma is a rare benign neoplasm of the adrenal gland, and it is composed of elements of adipose tissue and extramedullary hematopoiesis. If the tumor is large, it may compress the blood vessels and nerves of the kidney, resulting in symptoms such as hypertension, dysuria, lumbar and abdominal pain. However, if the tumor is small, it usually does not cause any trouble to the patient (Endocrine 2018; 59(1):7-15). In this case, we mainly attributed the symptoms of hypertension and hypokalemia to 17α-hydroxylase deficiency, for adrenal myelolipoma, we only observed and

followed up without treatment. And after the therapy of dexamethasone, the blood pressure and potassium of the patient returned to normal, besides, the electrolytes (serum potassium levels 4.6 mmol/L) and blood pressure (130/75mmHg) of the patient were still normal in the re-examination one year later. Hence, in our opinion, the syndrome we describe in this case may not be related to adrenal myelolipoma.

Reference:

Decmann Á, Perge P, Tóth M, Igaz P: Adrenal myelolipoma: a comprehensive review. Endocrine 2018, 59(1):7-15.

3. The attached images are of a male and a female, which does not refer to your real patient, please remove the one that does not correspond and keep and/or add photos of your patient.

Re: Thank you for this careful comment. Patients with 17α-hydroxylase deficiency [genetic males (46, XY)] commonly present with female external genitalia (European journal of endocrinology 2021; 185(5):729-741). In this case, the karyotype of this patient was 46XY. Pelvic MRI showed no obvious cryptorchidism and uterine accessory tissues were observed. Therefore, although the patient has female external genitalia, he is biologically male. The attached images are correct.

Reference:

Sun M, Mueller JW, Gilligan LC, Taylor AE, Shaheen F, Noczyńska A, T'Sjoen G, Denvir L, Shenoy S, Fulton P et al: The broad phenotypic spectrum of 17α-hydroxylase/17,20-lyase (CYP17A1) deficiency: a case series. European journal of endocrinology 2021, 185(5):729-741.

4. You should add the duration of the treatment applied to your patient and what has been the follow-up.

   Re: Thank you for this careful comment. The patient needs hormone therapy for life. One year after therapy, the electrolytes (serum potassium levels 4.6 mmol/L) and blood pressure (130/75mmHg) of the patient were normal after re-examination. We have revised the manuscript according to your advice.

Replies to Reviewer 2

1. This is a rare clinical manifestation of 17-hydroxylase deficiency. Only about 200 cases have been reported thus far. Genetic investigation (Fig. 3) revealed homozygous mutations in the CYP17A1 gene (NM 000102.3:c.81C>A(p.Tyr27*)). Hormone replacement therapy and antihypertensive therapy should be initiated immediately upon diagnosis. Meanwhile, patients' psychological well-being should be continuously examined. This, I believe, is an excellent announcement that contributes to world literature.

   Re: Thank you for this kind comments.

Replies to Office's Comments

(1) Science editor:

1. Can the author supplement the literature in recent years as a reference？.

   Re: Thank you for this kind comments. We have revised the manuscript according to your advice.

2. Pseudohermaphroditis does not seem to be reflected in the case.

   Re: Thank you for this kind comments. In this case, the patient's vulva was a female infantile vulva (as shown in Fig.1 c and d), however, his karyotype is 46, XY. And we found no female gonadal tissue in the examination. Therefore, we can consider this patient as male pseudohermaphroditism

3. Whether the author can explain the relevant differential diagnosis ideas and whether there are relevant exclusion tests.

   Re: Thank you for this kind comments. We have revised the manuscript according to your advice.

(2) Company editor-in-chief:

1. I have reviewed the Peer-Review Report, the 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. However, the quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by

a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: https://www.wjgnet.com/bpg/gerinfo/240. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, “Figure 1Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...”. The author(s) must provide the Signed Informed Consent Form(s) or Document(s) of treatment. 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.

Re: Thank you for this kind reminding. We will attach the English Language Certificate and the Signed Informed Consent Form(s) or Document(s) of treatment.