Response to reviewers and editors

Title: Multi-systemic smooth muscle dysfunction syndrome with seizures in a Chinese child: a case report and literature review

Manuscript NO: 60505

We gratefully thank the editor and all reviewers for their time spend making their constructive remarks and useful suggestions, which has significantly raised the quality of the manuscript and enabled us to improve the manuscript. Each suggested revision and comment, brought forward by the reviewers was accurately incorporated and considered. Below the comments of the reviewers are response point by point and the revisions are indicated.

Reviewer #1（number ID: 01436649）：

General comments:
In this manuscript authors described a 7-year-old and eight-month-old girl who experienced seizures which are related to pathology of ACTA2 gene mutation. Paper was well prepared and written.
1. Comment: Laboratory examinations have to be better described.
Reply: We gratefully appreciate for your comment. According to your opinion, we have further improved the laboratory examination of patients. We added the results of blood analysis, procalcitonin, serum C-reactive protein and fecal occult blood test, as well as ECG and chest X-ray examination. The specific amendments are in the revised manuscript. Thank you again for your valuable comments.

Laboratory examinations

Blood analysis revealed leukocytosis 8.58 × 10^9/L with the neutrophils as the major cells (68%). The hematocrit and platelet count were normal. The level of procalcitonin increased slightly (1.42ng/mL). Serum C-reactive protein was 33.84mg/L (normal range < 8mg/L). The stool occult blood test was positive. The electrocardiogram showed sinus rhythm and axis deviation to the right. Chest X-ray showed thickened texture in both lungs, together with patchy blurred shadows and enlarged heart shadow. There was obvious protruding in pulmonary artery segment, plump edge of right heart, and left heart margin beyond the midline of clavicle. For the liver and renal function determination, cardiac enzymes, electrolytes, blood glucose and organic acid, no abnormality was found. The score based on the Wechsler Intelligence Scale was 75.

2. Comment: Please describe why patient got treatment which was described and cite treatment in literature for patients with this mutation.
Reply: Thank you for your comments. The question you raised is also a problem that we pay close attention to, and it is also very important and meaningful to refer to treatment plan of other patients. However, MSMDS, as a disease caused by gene mutation, has no specific treatment plan in the world at present. Our treatment is mainly based on the clinical manifestations of patients and given symptomatic treatment. Of course, we use these drugs after weighing the advantages and disadvantages through various references. Here we add references of our treatment with corresponding drugs. The following are our specific modifications and references. We hope our treatment can provide some feasible ideas.

TREATMENT

To date, there is no standardized treatment plan for the treatment of MSMDS. For the children with MSMDS, we checked the conventional treatment plans for related symptoms. After screening, we made the following treatment plans to alleviate the children's conditions. Sildenafil was utilized to decrease the pulmonary hypertension[3]. Fructose diphosphate sodium was used to nourish the cardiac muscles[4]. Oral administration of sodium valproate was given to for the treatment of epilepsy[5].

[3] Bhogal S, Khraisha O, Al Madani M, Treece J, Baumrucker SJ, Paul TK. Sildenafil for Pulmonary Arterial Hypertension. Am J Ther 2019;26:e520-e526. [PMID: 30946047 DOI: 10.1097/MJT.0000000000000766]
[4] Bai, Yantao, Quanbao Shi, and L. I. Yan. "Clinical Study of Fructose Sodium Diphosphate in the Treatment of Acute Myocardial Infarction." China Pharmacy 28.8 (2017): 1076-1079.
[5] Nevitt SJ, Marson AG, Weston J, Tudur Smith C. Sodium valproate versus phenytoin monotherapy for epilepsy: an individual participant data review. Cochrane Database Syst Rev 2018;8:CD001769. [PMID:30091458 DOI: 10.1002/14651858.CD001769.pub4]

Reviewer #2（number ID: 03815241）：

Comment:
Nevertheless, I read the article, referred to a heterozygous mutation (c.536G>A)

identified in the ACTA2 gene, resulting in generation of p.R179H and a diagnosis of a MSMDS in this 7-year-old and eight-month-old girl carefully. As authors stated the coexistence of seizures with this syndrome is very rare. The manuscript is well-written, and authors investigated for mutations the ACTA 2 gene which demonstrated a new mutation responsible for seizures. The language is without errors.

Reply: Thank you very much for your comments. It is a great honor to get your recognition of our work. As you said, the case of MSMDS with epilepsy is very rare, so we write this case report in the hope of making more people know about it. Thanks again for your valuable comments.

Science editor and Company editor-in-chief

General comments:

1 Scientific quality: The manuscript is a case report of two children experienced seizures which are related to pathology of ACTA2 gene mutation. The topic is within the scope of the WJCC. (1) Classification: Grade A; (2) Summary of the Peer-Review Report: this is an overall well written case report. Lab exams and treatments should be described in greater details in revision. (3) Format: There are 2 figures and 2 tables; (4) References: A total of 20 references are cited, with 3 references published in the last 3 years; (5) Self-cited references: There is no self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript) and remove all other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade A. A translation certificate from XinDa Translation was issued. 3 Academic norms and rules: No academic misconduct was found in the Google/Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The topic has not previously been published in the WJCC.

1. Comment: Core-Tip Audio and Copyright License Agreement and Conflict of Interest Disclosure Form are missing.

Reply: Thank you very much for your comments. Due to our mistake, some materials were not uploaded. We have uploaded Core-Tip Audio and Copyright License Agreement and Conflict of Interest Disclosure Form as required. We are very sorry for our carelessness.

2. Comment: Figure legends should be written per journal standard. 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.
Reply: Thank you very much for your comments. We have reviewed the latest journal standards and edited the original pictures of Figures 1 and 2 in PowerPoint as required, ensuring that each image, each arrow and each text can be reworked by the editor. Figure 1 and Figure 2 have been uploaded. If there is anything wrong, please inform us in time. Thanks again for your comments.

3. Comment: Manuscript format should be updated per journal standard.
Reply: Thank you very much for your comments. We've looked at the format of the latest articles in the journal. We added the running title, and put the footnotes part of the article after the references according to the format. The format of references is also revised according to the latest standards of the journal. At the same time, we have supplemented the patient's personal and family history according to the standard format of the journal. Thank you again for your comments.

4. Comment: Author provided a Chinese to English translation certificate. We require an English editing certificate from a professional editing company, please refer to https://www.wjgnet.com/bpg/gerinfo/240, as there are typos in the manuscript , e.g. page 1"Afliated".
Reply: Thank you very much for your comments. I'm very sorry that we didn't provide the correct materials before. We have got the English editing qualification certificate from the translation company and have uploaded it. At the same time, we checked the words and sentences of the article and corrected the problems you mentioned. I hope our amendment can be approved by you.Thank you again for your comments.

5. Comment: The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).
Reply: Thank you very much for your comments. We have revised the title to "multi systematic smooth muscle dysfuction syndrome with traits in a Chinese child: a case report and literature review". Thank you again for your comments.

We look forward to hearing from you regarding our submission. We would be glad to respond to any further questions and comments that you may have.