Author’s response to reviews

Title: TRMA syndrome with a severe phenotype, cerebral infarction, and novel compound heterozygous SLC19A2 mutation: a case report

Authors:

Xin Li (Lixin@scmc.com.cn)
Qing Cheng (2011513541@qq.com)
Yu Ding (Dingyu@scmc.com.cn)
Qun Li (15221272316@163.com)
Ruen Yao (yaoruen@scmc.com.cn)
Jian Wang (wangjian@scmc.com.cn)
Xiumin Wang (wangxiumin@scmc.com.cn)

Version: 1 Date: 17 Jun 2019

Author’s response to reviews:

Jun/17/2019

Diana L. Cousminer, PhD
Editor-in-Chief
BMC Pediatrics

Dear Prof. Cousminer and Reviewers:

Thank you for your letter and for the reviewers’ comments concerning our manuscript (ID: BPED-D-19-00266). Those comments are all very important for revising and improving our paper. We have studied comments carefully and have made the correction. The revised portion in revised version is marked in red. The responses to the reviewer’s comments are as flowing:
Responds to the reviewer’s comments:

Reviewer 1:

1. Response to comment: (1. This study has documented two novel mutations such as c.405dupA (p.Ala136Serfs*3) and c.903delG (p.Trp301Cysfs*13) in compound heterozygous state in the TRMA patient. Further, authors have stated that c.405dupA mutation has been inherited from father and c.903delG mutation has been inherited from mother. But, it is not correctly presented in the Figure 2 and it looks like the chromatograms of father and mother are switched over. Authors can check for this and correct it.)

Response: Thank for your insight comments. We have checked the two mutations and it was identified that the patient's father carried c.903delG mutation (heterozygous) in the SLC19A2 gene, and the patient's mother carried c.405dupA mutation (heterozygous).

Then, We have revised the manuscript (page 6, line 26) and figure 2 and in the revised version.

2. Response to comment: (2. Authors can include the data reg the status of these mutations from the healthy volunteers (atleast 50) of same ethnic group if available.)

Response: Thanks. The two frameshift variants in our study does not exist in the current the genome Aggregation Database (gnomAD) which include at least 8,624 exome sequencing data of Eastern Asian populations and our in-house sequencing database which include more than 500 exome sequencing data of Chinese Han healthy control population. Thus, it is quite unnecessary to Sanger sequencing 50 healthy volunteers as an evidence for the population frequency of these variants. We also have added the part in the revised version. (page 6, line 20)

3. Response to comment: (In the discussion, authors have mentioned that there are only 40 mutations in SLC19A2 have been reported from TRMA patients. According the HGMD database, 45 mutations are documented in the SLC19A2 gene from TRMA patients. Thus, the authors can include this update in the revised manuscript by citing HGMD database.)

Response: Thanks. We have revised the part in revised version (page 9, line 17).

4. Response to comment: (Secondly, it is written as 'Most of these mutations are nonsense mutations', in the line no. 18, Page no. 10. This is not true……It sholud be corrected as 'Most of these mutations are missense/nonsense mutations'.)

Response: We are glad to accept your suggestions and we have revised the part( page 9 ,line 19).
Reviewer 2:

1. Response to comment: (1. Were other, e.g. infectious causes of cerebral infarction in this patient excluded? Please, describe this in Clinical data section.)

Response: Thanks. He had no symptoms of infection in the period of cerebral infarction at the age of nine months and we have added the part in the revised version (page 3, line 20).

Responds to the Editor's comments:

We have revised the paper according to the comments and addressed each of the points individually.

Special thanks to you for your good comments.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. We appreciate for Editors/Reviewers’ warm work earnestly and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Yours sincerely,

Xiumin Wang

Department of Endocrinology and Metabolism, Shanghai Children's Medical Center, Shanghai Jiaotong University School of Medicine, Shanghai 200127, China.

1678 Dongfang Road, Pudong New Area, Shanghai 200127, China.

Tel.: +86 21 38626161;

Fax: +86 21 58393915.

E-mail: wangxiumin@scmc.com.cn