Author’s response to reviews

Title: Mucopolysaccharidosis III B and Mild Skeletal Anomalies: coexistence of NAGLU and CYP26B1 missense variations in the same patient in a Chinese family

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Author’s response to reviews:

Dear Allan,

Many thanks for giving us an opportunity to revise our manuscript. We appreciate your and the reviewers’ kind and constructive comments on our manuscript entitled “Mucopolysaccharidosis III B and Mild Skeletal Anomalies: Coexistence of NAGLU and CYP26B1 missense variations in the same patient in a Chinese family”. (ID: MGTC-D-17-00335).

We have revised the manuscript carefully according to your suggestions, and the revised texts were all marked in red. The comments replied point-by-point were as follows:

To reviewer Shunji Tomatsu

1. Specify how many cases were reported with concurrent mutant in two genes?

Reply : Through literature review (search through PubMed and Medline, and the keywords include “two pathogenic genes” or “two mutant genes”), we did not find any report describing a combination of the two mutated genes in a patient. To our best knowledge, this report might be the first one introducing one patient having concurrent pathogenic mutations in two genes
respectively. That means a patient has two hereditary diseases or syndromes (Conclusions section of abstract, line 1 to 4, page 2).

2. Specify which sign and symptom in this case is from MPS IIIB and CYP26B1 mutation.

Reply: In this case, epilepsy, sleep disturbance, repeated respiratory infection, navel hernia and inguinal hernia mainly resulted from the NAGLU mutation (MPS IIIB). Facial asymmetry, skull deformity, bilateral ventricle enlargement and asymmetry of brain structure were probably caused by the CYP26B1 variant. Kyphosis in this patient might be related to both mutated genes. We made a summary of the symptoms and signs of this case in the part “Discussion and conclusions section” (Discussion and conclusions section, paragraph 5).

3. Patients with MPS IIIB have clinical presentation at around 3 years old. Do the authors think all neurological signs and symptoms come from MPS IIIB in such an early stage?

Reply: We considered that not all neurological signs and symptoms were caused by MPS IIIB (the NAGLU mutation), facial asymmetry, skull deformity, bilateral ventricle enlargement and asymmetry of brain structure were mainly related to mutations of CYP26B1. Developmental delay, sleep disturbance and epilepsy were probably related to NAGLU mutations, that is MPS IIIB, although they had not been reported in such an early stage previously (Discussion and conclusions section, line 15 to 18, page 5; Discussion and conclusions section, line 7 to 9, page 6; Discussion and conclusions section, paragraph 5).

We appreciate your and reviewers’ comments again. Looking forward to hearing from you soon.
Thank you and best regards.

Yours sincerely

Yuwu Jiang, MD. PhD.

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