Peer Review File

Article Information: https://dx.doi.org/10.21037/acr-23-46

Reviewer A

The authors report rare cases of aminoacylase 1-deficiency. The clinical courses and syndrome are clearly described.

1. The authors should describe the method how genetic mutation was identified. Did they perform only Sanger Sequencing or did they do whole exome sequencing of other panel sequencing? This method should be clearly stated.
   Reply: **Agreed. The methods for mutation analysis were described and added into the manuscript. For diagnostic testing in proband, the NGS targeted sequencing was performed. For predicative testing in other family members, the Sanger sequencing was used.**
   See: Page 6, lines 132 -137

2. The family includes familial hypercholesterolemia cases. Do the affected patients have any pathogenic variants in the FH genes? This information should also be provided.
   Reply: **Agreed. The genetic testing of the proband's father was performed. Targeted sequencing revealed only ε4/ε4 isoform in the *APOE* gene, no other pathogenic variants were found. This paragraph was added into to manuscript.**
   See: Page 7 lines 167 - 171

3. Line 134 here should be there?
   Reply: **Agreed. The mistype was fixed.**
   See: Page 7, line 145

4. Line 135 should be 'two brothers' homozygous variant for the familial c1057C>T ACY1
   Reply: **Agreed. The sentence was rewritten to be clearer.**
   See: Page 7, line 147

Reviewer B

1. The manuscript should be extensively rewritten to use precise scientific/correct genetic language and terminology. Genetic disorders listed must correspond to genes mentioned. Recommend carefully proofreading.
   Reply: **Agreed. The manuscript has been double-checked and correct terminology was used. DACY1 was replaced by ACY1D, italic for gene symbols were used.**
   See: The tracked changes in the manuscript.

2. Information is disorganized would focus on the actual inborn error of metabolism and biochemical findings and use of more objective terms even in neuropsychology aspects.
   Reply: **Agreed. The more detailed information was provided and added into the manuscript. Especially, the biochemical findings were discussed in more detail.** See: Page 5, lines 121 - 126; page 9, lines 222 - 225
   The more objective and precise terms were used describing the psychological findings in patients. The "opinion ability" was replaced by more correct "perceptual ability". See: Tracked changes in the manuscript.

3. Both phenotype and variant has been already reported, might need additional detailed literature review to contribute to the current medical literature.
   Reply: **There are no more recent publications on ACY1D than mentioned in our references. To our knowledge, there are only 15 patients reported in the literature.**
   See: Page 9, lines 215-221