

Dear Editor,

We would like to thank *World Journal of Clinical Cases* for giving us the opportunity to revise our manuscript entitled "A novel *ATL1* mutation in a Chinese HSP family: A case report and review of literature" (Manuscript Number: 46157), and the reviewers for their thoughtful comments on our previous manuscript. We have revised the manuscript according to their comments, which we hope will meet with approval.

We have submitted the manuscript to Editage for language editing. For easy reference, revised parts in the revised manuscript are highlighted in yellow. The point-by-point responses to the reviewer's concerns are indicated below.

Reviewer#1:

Q1: Grammar and style should have a revision.

Thank you for this suggestion. We have carefully checked the manuscript and corrected them.

Besides, we have sent the manuscript for language editing.

Q2: Some of the references are inadequate, and some new, more recent, should be added.

Thanks for reviewer's good suggestion. We have reviewed the relevant studies by searching the keywords 'atlastin-1 (*ATL1*) gene', 'hereditary spastic paraplegia', 'SPG3A' in the PubMed and Human Gene Mutation Database again. The newly added references include reference 8-12 and reference 33-34.

Q3: Technical errors in the text of the manuscript - for an example, writing number and unit, spacing, introducing abbreviations.

Thanks for reviewer's advice. We have corrected them in the revised manuscript.

Q4: The title should be changed - delete the last part of it "and review of literature", because it is something that is assumed.

Thanks for your good suggestion. We have deleted it in our revised manuscript.

Q5: Last part of the Abstract should be deleted starting from the last sentence in Core tip part "In addition..." until the end.

Thank you for your good suggestion. We have deleted it in the abstract in the revised manuscript.

Q6: Technical representation of the results should be improved.

Thanks for good advice. As suggested, the results part has been improved in our revised manuscript.

Reviewer#2:

Q1: "Laboratory examinations" chapter should be written more extensively.

Thanks for your good suggestion. The laboratory examinations have been described in more detail. We have added the urine routine test, stool routine test, renal function test, serum creatase, serum electrolyte, plasma ammonia, and serum lactic acid level in the revised manuscript.

Q2: There is no description or reference on the gene panel test used for the mutation detection. It is important to indicate genes included in the panel.

Thanks for reviewer's good advice. The gene panel included 72 known pathogenic genes associated with HSP. We have added the description of gene panel in the "Laboratory examinations". Furthermore, the detailed gene list was shown in supplementary Table S1.

Q3: It is recommended to add more citations into the review as it is stated in the title of the manuscript, e.g. Willkomm L Heredia R Hoffmann K Wang H Voit T et. al. Homozygous mutation in *Atlastin* GTPase 1 causes recessive hereditary spastic paraplegia // *Journal of Human Genetics*. 2016 vol: 61 (6) pp: 571-573.

Thanks for reviewer's good suggestion. As suggested, we have carefully searched the related articles in PubMed and Human Gene Mutation Database again. Reference 8-12 and reference 33-34 were newly added. We also reanalyzed the *ATL1* pathogenic mutation types in discussion and table 2.

Q4: Despite the overall good language of the manuscript it is recommended to perform final "polishing" of English text by a native speaker or proof-reading company.

Thanks for reviewer's advice. We have sent our manuscript to Editage for language editing.

Reviewer#3:

Q1: I consider the manuscript very interesting and could be publish

Thanks for reviewer's good comment.

Reviewer#4:

Q1: To make this case study more useful for the specialist clinicians in this area authors might consider discussing potential reasons explaining the fact that the same mutation results in the exhibition of different clinical manifestations in different members of the family.

Thank you for your good advice. We have searched the relevant articles why the same mutation lead to different phenotypes in PubMed. We added "The intra-family variable penetrance may result from environmental modifiers as well as regulatory variants [33]. Furthermore, sex and mutation types are of great importance in modifying the penetrance in HSP [34]. In our SPG3A family, regulatory variants, gender differences and environmental factors may be the underlying contributors to of different phenotypes." in page 9 to discuss the potential reasons.

Thanks and Best regards!

Yours sincerely,

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