Journal of Clinical and Translational Research
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A case of drug-induced parkinsonism and tardive akathisia with e1143g polymerase γ mutation-innocent bystander or a culprit?

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Ref.: Ms. No. JCTRes-D-21-00006
Coincidental POLG mutation found in a case of drug-induced Parkinsonism
Journal of Clinical and Translational Research

Dear Dr. Idiculla,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Apr 24, 2021.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Editor:
1) Please polish the language in compliance with the journal requirements regarding academic level English (see https://www.jctres.com/en/author-guidelines/). Please do not take this task lightly. We encourage the authors to involve a native speaker. Manuscripts written in substandard English cannot be published.

Reviewer #1: Thank you for allowing me to review this manuscript.
Though suggested as a benign variant E1143G, this report indicated that the mutation may enhance or worsen the disease process as seen in few studies in the past. The authors have done a good job at compiling the literature review and this paper can add value to current literature. The case report is well explained and the discussion is kept short and to the point.
Here are a few suggestions I would like the authors to add-
1. Changing the title to something that indicates the mutation is a silent culprit can be more appropriate, as this indicates the objective of the paper.
2. The explanation and analysis of his sensory exam findings need to be indicated as a part of his diagnosis.
3. Location of E1143G on the POLG gene as some studies have indicated this can be an added reason for its benign nature.
4. Mention the common POLG variants with which E1143G mutation can or has been found to co-occur with.
5. Conclude with indicating the need for requiring future studies focussing on this particular variant is required to further understand the particular mutation.
Overall, good job.

Reviewer #2: Very well written case report with literature review. Content and novelty of the case report is unique. Fascinating to read about POLG mutation and it's association with parkinsonism. No grammatical errors. Few suggested changes
Page 1 line 10: Present at any time.
Page 2 line 10: Present at any time.

Authors' response

Thank you very much for reviewing our manuscript and providing your valuable comments. We have tried our best to address all the reviewer comments.

Editor:
1) Please polish the language in compliance with the journal requirements regarding academic

level English (see https://www.jctres.com/en/author-guidelines/). Please do not take this task lightly. We encourage the authors to involve a native speaker. Manuscripts written in substandard English cannot be published.
We have reviewed and made necessary changes in language in compliance with the journal requirements.

Reviewer #1: Thank you for allowing me to review this manuscript.
Though suggested as a benign variant E1143G, this report indicated that the mutation may enhance or worsen the disease process as seen in few studies in the past. The authors have done a good job at compiling the literature review and this paper can add value to current literature. The case report is well explained, and the discussion is kept short and to the point.
Here are a few suggestions I would like the authors to add-
1. Changing the title to something that indicates the mutation is a silent culprit can be more appropriate, as this indicates the objective of the paper.

We have changed the title to- A case of drug-induced Parkinsonism and Tardive Akathisia with E1143G POLG mutation- Innocent bystander or Culprit?

2. The explanation and analysis of his sensory exam findings need to be indicated as a part of his diagnosis.

This has been updated in the revised manuscript- and peripheral neuropathy, most likely due to poor diabetic control.

3. Location of E1143G on the POLG gene as some studies have indicated this can be an added reason for its benign nature.

This has been added to the revised manuscript- The mutation is rendered benign due to its occurrence outside the identified pathogenic cluster [19].

4. Mention the common POLG variants with which E1143G mutation can or has been found to co-occur with.

This has been added to the revised manuscript- The commonly encountered pathogenic POLG variants include A467T, W748S, G848S, and T251I-P587L [20]. Studies have shown that the co-occurrence of E1143G with other POLG variants may aggravate the disease's occurrence and clinical severity. Horvath et al. reported five patients with E1143G mutation, of which two individuals had compound mutations- A467T/E1143G and S433C/E1143G [21]. Chan et al. investigated the biochemical consequences of POLG proteins with E1143G polymorphism. They described that the occurrence of W748S in cis with E1143 mutation could modulate the former's phenotypic effects [22].

5. Conclude with indicating the need for requiring future studies focusing on this particular variant is required to further understand the particular mutation.

This has been updated in the revised manuscript- The pathogenicity of E1143G is debatable, and future studies involving this particular variant may help understand the pathological consequences when it occurs as a single or compound mutations.

Overall, good job.

Reviewer #2: Very well written case report with literature review. Content and novelty of the case report is unique. Fascinating to read about POLG mutation and its association with parkinsonism. No grammatical errors. Few suggested changes
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2nd Editorial manager
30-Mar-2021

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A case of drug-induced Parkinsonism and Tardive Akathisia with E1143G POLG mutation- Innocent bystander or Culprit?
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Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: