Reviewer’s report

Title: Identification of novel L2HGDH mutation in a large consanguineous Pakistani family - a case report.

Version: 0 Date: 20 Mar 2017

Reviewer: Faïza Fakhfakh

Reviewer's report:

Comments to the Authors:

Title: Identification of rare L2HGDH mutation in a large consanguineous Pakistani family and update of previous mutations.

Manuscript number: MGTC-D-16-00247

Manuscript type: Research article

Authors: Muhammad Ikram Ullah, Abdul Nasir, Arsalan Ahmad, Gaurav Vijay Harlalka, Wasim Ahmad, Muhammad Jawad Hassan, Emma L. Baple, Andrew H. Crosby, Barry A. Chioza

General points:

1- This manuscript should be reported as case report and shortened up according to journals requirements for case report.

2- The title should be modified: « and update of previous mutation » should be removed and « rare L2HGDH mutation » could be replaced by « novel L2HGDH mutation »

Following points need improvements and clarification:

Methods:

No details were provided about primers used and the PCR amplification program to allow others to replicate the work. A description or a reference should be added.
Results:

1- The paragraph in Molecular Analysis from "The variant alters ..........to score of 1 " should be included in part "computational analysis".

2- Scores obtained for mutation with each prediction program should be precised

3- Is not necessary to indicate References related to standard prediction programs (PROEVAN, Polyphen 2 and Mutation Taster) in results as they already indicated in methods

4- A sequence alignment of L2HGDH protein from different species should be added using the Clustal W program.

5- Table 1, and 2 and related sentence « previously reported mutation in exon 2…… ;tables 1 and 2 respectively » in last paragraph of Molecular Analysis should be in discussion.

6- MRI changes should be indicated by orrows

Discussion:

1- Sentence in line 185 "although additional phenotypic characteristics ....... our patients" should be placed after sentence in line 187 "MRI showed the persistent........leukodystrophy"

2- Sentence in line 203/204 is not clear; authors should give exemple of modifier factors which could have an effect on the phenotypic variation and should indicate references related to this point.

3- References related to the paragraph from line 205 to line 208; should be added.

4- The paragraph from line 211 to line 215 is not clear and should be reformulated.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that i have no competing interests 'below

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons
CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal