Reviewer's report

Title: Novel likely pathogenic variants in TMEM126A identified in non-syndromic autosomal recessive optic atrophy: two case reports

Version: 0 Date: 11 Mar 2019

Reviewer: Reviewer 2

Reviewer's report:

"PEER REVIEWER ASSESSMENTS:

RELEVANCE - Does this case report make a contribution to medical knowledge, have educational value, or highlight the need for a change in clinical practice or diagnostic/prognostic approaches?
Yes, this report contributes to medical knowledge

CASE DESCRIPTION - Are the details of the case sufficiently well described to understand the patient's symptoms and course of treatment?
No - there are minor issues

DIAGNOSIS/INTERPRETATION - Based on the facts presented, are the diagnosis, interpretation, and course of treatment medically sound?
Yes, the work described is medically sound

DISCUSSION OF THE CASE - Does the discussion appropriately analyse the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Has an adequate literature review pertinent to the case been included?
Yes, the case is discussed fully in the context of the literature

OVERALL MANUSCRIPT POTENTIAL - Could an appropriately REVISED version of this work represent a technically sound contribution?
Probably - with minor revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: This was an interesting case report.

REQUESTED REVISIONS:
The manuscript contains too many figures (n=6). The results of the molecular genetic analysis and the pedigrees could be merged. Also, clinical data should be presented in one figure, which
will provide more concise information. There is no need to show all the sequence chromatograms. Just the one showing the mutation is sufficient.

Line 37 A diagnostic gene panel revealed a splice donor variant (c.86+2T>C) in the TMEM126A gene
It would better for clarity to add that the mutation was found in a homozygous state
39 aberrant transcript lacking exon 2, presumably representing a functional null allele.

Line 105 visual acuity testing,
Which charts were used for visual acuity testing?

Line 124 variants were called (VarScan 2.4.2, CeGaT extended version) with a minimum variant allele frequency of 5%
Why the 5% threshold?

41 early childhood. A missense variant (p.S36L)
I would recommend to describe the mutation at protein level using HGVS guidelines, i.e. with ()

Line 147 Please add to the methods which OCT device was used.

Line 160 The girl was diagnosed with poor vision and achromatopsia in early childhood.
Was she misdiagnosed? This should be noted for clarity to avoid readers thinking that she had two different ocular traits.

Line 205 TMEM126A was proposed as the genetic defect underlying non-syndromic autosomal-recessive optic atrophy (arOA)
Abbreviation orOA has been introduced already in the Introduction.

Line 239 needed to confirm the exact pathogenic mechanisms that cause autosomal-recessive non-syndromic

The same comment as above.

Line 210 the current manuscript, we provide additional evidence for the implication of biallelic TMEM126A mutations in arOA, as we diagnosed two additional cases
Avoid using additional twice in the same sentence."
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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:

Acceptable

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