Reviewer’s report

Title: Homozygous NOTCH3 p.R587C mutation in Chinese Patients with CADASIL: a case report

Version: 0 Date: 26 Nov 2019

Reviewer: Michele Ragno

Reviewer's report:

Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.
Please overwrite this text when adding your comments to the authors.

The authors described the clinical and MRI features of two CADASIL brothers with the same homozygous c.1759C>T (p.R587C) missense mutation in exon 11 of the NOTCH3 gene. The authors underlined that their two CADASIL brothers with homozygous mutation showed clinical manifestations similar to those previously reported in heterozygous patients with the same mutation. On this basis, the authors hypothesized that vascular risk factors and/or environmental factors may contribute to the phenotypic variation of CADASIL.

This study is of interest, as it collected clinical and MRI data on relatively rare CADASIL cases caused by homozygous NOTCH3 mutations.
I suggest that the authors might acknowledge in their discussion that additional unknown genetic factors might contribute to phenotypical heterogeneity of CADASIL.
Moreover, I would strongly suggest that the manuscript should be revised carefully with the aid of by a native English speaker, as it contains are several mistakes. Two instances are reported below.
1) abstract, line 14, "partial temporal lobes" should be changed to "anterior temporal lobes".
2) page 8, lines 1-2, the sentence "we demonstrate that clinical presentations in our patients with homozygous NOTCH3 c.1759C>T (p.R587C) mutation are resemble to patients with heterozygous the same mutation described before" should be rephrased.
3) page 8,lines 2-3-4, the sentence "The phenotype of CADASIL could be modified by other vascular risk factors or environmental factors, and results in phenotypic variation of CADASIL in the same genetic background" should be deleted.

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'

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/](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