Reviewer’s report

Title: A new genetic variant of hereditary Apolipoprotein A-I amyloidosis: a case-report followed by discussion of diagnostic challenges and therapeutic options

Version: 0 Date: 03 Dec 2018

Reviewer: Giorgio Cavigiolio

Reviewer's report:

This is a case report presenting a previously unknown amyloidogenic single point mutation in apolipoprotein A-I. The case is clearly and thoroughly reported and the manuscript is well written with interesting discussion points.

The paper can be considered for publication upon addressing the following points:

1) The authors should provide more technical details of the Immuno EM measurements, e.g. Name and description of the antibody used for the detection of apoA-I and of the other antibodies tested with negative results.

2) From the Immuno EM data, is there any extra information regarding the nature of the apoA-I deposits available? It would be very important to better identify the apoA-I peptide that produces the amyloid deposits. In particular, is it full length apoA-I or a fragment of it? N-terminal fragment?

3) To better illustrate the single amino acid mutation identified in the apoA-I sequence of this patient, it is suggested to add a figure in which the N-terminal amino acid sequence of apoA-I (e.g. 1-80) is shown and the mutated residue clearly indicated. Even this simple graphic illustration would improve the understanding of the case at the molecular level. To put it in the context of the current knowledge, ideally, the other known amyloidogenic mutations involving the first 80 amino acids of apoA-I could be also marked in the same figure.

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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