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: 16 Nov 2018

Reviewer: Kazuchika Nishitsuji

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In the present study, Moutafi et al. identified a previously unknown amyloidogenic mutation in apolipoprotein A1 (apoA1). The mutation is quite interesting, because the patient demonstrated apoA1 amyloid deposition in the liver without renal involvement and polyneuropathy, and hypogonadism possibly due to testicular amyloid deposition. However, because of the patient's refusal of biopsy, the authors failed to confirm testicular deposition of amyloid fibrils. Overall, the case reported here is very interesting, and the manuscript will contribute to the research of both AApoA1 amyloidosis and HDL formation or stability.

1. Histological and/or immunohistochemical data and images preferably need to be included.

2. Which apoA1 fragment was accumulated or deposited in the patient liver? In most of AApoA1 amyloidosis, apoA1 fragments, not the full-length apoA1, reportedly deposit as amyloid fibrils in tissues/organisms, and the cleavage of apoA1 sometimes may be critical for amyloid formation by destabilizing apoA1.

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.

Unable to assess

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

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Please indicate the quality of language in the manuscript:  
Acceptable

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