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: 17 Nov 2018

Reviewer: Olga Gursky

Reviewer's report:

This case study describes a patient with liver involvement who is a carrier of a novel mutation in the apolipoprotein A-I gene, CTG to CGG, leading to an amyloidogenic apoA-I variant, Leu60Pro. A similar protein variant has been previously reported in ref. 13, although the clinical phenotype was different. The clinical and genetic information is somewhat limited; e.g., it is not clear whether symptoms such as hypogonadism were caused by the apoA-I mutation, or whether or not the mutation occurred in this patient de novo or was inherited. Still, the paper is well written and represents a publishable unit.

The authors may want to address several points prior to publication.

1. Bottom of page 5, Line 58 and beyond: "…the main acceptor of high-density lipoprotein…” and the rest of this sentence is confusing and needs re-writing. ApoA-I is not an acceptor of HDL but its main structural and functional protein. Further, ref. 5 cites pre-beta apoA-I; this lipid-poor form contains little if any cholesterol. ApoA-I in the form of mature HDL mediates plasma transport of cholesterol (not "cholesterol trafficking" in general). HDL remove cholesterol from peripheral cells; how exactly does this action relate to hypogonadism and infertility? Please clarify.

2. Page 9 bottom line 58: "the clinical presentation provides a complex model of interactions between the produced amyloid fibrils and the involved tissues." Not sure if fibrils are biologically active species that cause pathology.

Minor points:
3. Bottom of page 5, line 48 ""its clinical spectrum may be heterogeneous" Unclear what "it" refers to; please specify.

4. p. 8 line 46 "case report" has no hyphen; "for the first time" insert "the".
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?
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Not relevant to this manuscript

Quality of written English
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