Reviewer’s report

Title: New Genetic Variant in the SERPINC1 gene: Hereditary Antithrombin Deficiency Case Report, Familial Thrombosis, and Considerations on Genetic Counseling.

Version: 1 Date: 10 Feb 2020

Reviewer: Stavroulla Xenofontos

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Manuscript number: MGTC-D-19-00607R1

The case report is of interest to the field of thrombosis and thrombophilia as it addresses a rare but serious risk factor in the context of current efforts using in silico tools to characterize the functional significance of variants identified by DNA sequencing. The evaluation of the data is scientifically sound and carried out in accordance with international practices. The case report is therefore worthy of publication, making a useful contribution to the subject matter. The following corrections must however be made to allow easier reading by peers.

The authors are kindly requested to proceed with the following corrections:

1) Glycosylation throughout the document is spelt in different ways, correct as follows: "glycosylation".

2) "y.o" - should be written in full throughout the document, "years old".

3) Spell out the full name of SERPINC1 in the abstract once and include in the abbreviations list.

4) Line 1- title- add the word "Gene" after "SERPINC1".

5) Line 28 - add the word "the" before "SERPINC1".

6) Line 31 - add the letter "A" at start of sentence "New genetic variant c.662G\gt;C."

7) Line 36 - add the letter "a" before the word "hematologist"

8) Line 37 - change sentence as follows: "Based on all …..the p.W221S variant as a variant of unknown…”

9) Line 53 - delete the word "the" in front of the word "most".

10) Line 54 - add the word "the" in front of the word "affected".
11) Line 55 - replace "4-5" with the following "the fourth to fifth".
12) Line 58 - replace the first word of the sentence "This" with the word "Thus".
13) Line 61 - correct as follows: "…lead to AT type I deficiency. Many of the known…"
14) Line 62 - add the word "to" before the words "AT type II…"
15) Line 79 - correct spelling of word "panning" to "planning".
16) Line 82 - a clarification of what is meant by "no specific findings were made" is deemed necessary for better understanding of clinical evaluation of the patient.
17) Line 83 - the colorimetric method used for AT quantification should be described.
18) Line 85 - further details of the sequencing methodology: Sequencing kit, sequencer, data analysis software would provide support to the methods used as this section is somewhat disproportionate to the in silico analyses details.
19) Line 85 - add reference/source for the "originally designed oligo-primers" mentioned.
20) Lines 91 & 92 - references should be moved to the end of the sentences.
21) Line 95 - sentence should begin with "In the proband…"
22) Line 96 - the name of the calorimetric test and number of repetitive experiments should be stated. Were these repeated experiments a standard procedure or were any factors in doubt?
23) Line 96 - the second sentence should start as follows "A new genetic variant.."
24) Line 97 - add "the" before "proband".
25) Line 98 - add "the" before "symptomatic".
26) Line 99 - add "the" before "healthy sister".
27) Line 100 - add "the" before "literature"
28) Line 100 - add "the" before "1000 Genomes".
29) Line 103 - add "the" before "predictive value".
30) Line 103 - delete the word "have" before the word "proceeded".
31) Line 105 - add "the" before "glycosylation".
32) Line 108 - add "the" before "mutated".
33) Line 128 - add "the" before "219-221".
34) Line 134 - add "the" and delete "a" before "bloodstream".
35) Line 134 - add "the" before "heterozygous" and delete "of mutation".
36) Line 136 - replace the word "of" with the word "with" before "type 1 AT deficiency".
37) Line 139 - add the letter "a" before "hematologist".
38) Line 141 - add "the" before "American College of Chest Physicians".
39) Line 143 - add the letter "A" before "Recent".
40) Line 144 - replace the word "claim" with "claims".
41) Line 147 - add "the" before "general population".
42) Line 152 - add "they" before "do not discuss it in the review".
43) Line 155 - add "the" before "SERPINC1 gene" both at the beginning and end of line 155.
44) Line 157 - add "the" before "Chinese".
45) Line 158 - add the letter "s" to the word "population" so as to read "populations".
46) Line 161 - add the letter "a" before the word "limited".
47) Line 166 - add "the" before "canonical".
48) Line 166 - replace "won't" with "will not".
49) Line 168 - replace the word "high" with any of the words "stringent/strict/rigorous" since these terms are more appropriate when referring to requirements/criteria.
50) Line 168 - add the letter "a" before 'Genetic variant...".
51) Line 170 - add "the" before "one hand" so as to read "On the other hand".
52) Line 176 - add "the" before "literature".
53) Line 176 - add the letter "a" before "patient".
54) Line 180 - add "the" before "asymptomatic".

55) Line 182 - replace "due to" with "expected from".

56) Line 189 - add "the" before "mutated".

57) Line 190 - add "the" before "mutated".

58) Line 192 - add "The" before "combination".

59) Should add a figure showing a sequence electropherogram to illustrate the heterozygous mutation (with 5-10 bases upstream and downstream of the mutation) for documentation and traceability of the results and to be in line with all other data reported.

**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

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