Author’s response to reviews

Title: Hb Knossos (HBB: c.82G>T), β-globin CD 5 (-CT) (HBB: c.17_18delCT) and δ-globin CD 59 (-A) (HBD: c.179delA) mutations in a Syrian patient with β-thalassemia intermedia

Authors:
Faten Moassas (ascientific1@aec.org.sy)
Mohamad Nweder (ascientific2@aec.org.sy)
Hossam Murad (ascientific@aec.org.sy)

Version: 2 Date: 19 Dec 2018

Author’s response to reviews:

Dear Sir,

Thank you for your kind interest and your fast reply. Your remarks are justified and to the point and we appreciate so much your suggestions to improve the manuscript. We would like to adjust our manuscript to satisfy your request:

Sincerely Yours,
Hossam MURAD

Editor Comments:

In addition to the referee comments, please address the following editorial points:

We note that family members of the child reported in your case report also underwent genetic testing. Please add details of consent for these individuals, including if written or verbal, to the Declarations section.

The response:
We have modified the Consent for publication as editor request.

Reviewer 1

The manuscript describes a rare and interesting case of hemoglobinopathies which is worthy of publication. However, some points can be improved to make it more suitable to the reader.

1- The title could be a bit more concise: "Hb Knossos (HBB:c.82G-T), β-globin CD 5 (-CT) (HBB:c.17_18delCT) and δ-globin CD 59 (-A) (HBD:c.179delA) mutations in a Syrian patient with β-thalassemia intermedia".

The response:
We have modified the title of the manuscript as request.

2- In addition to this nomenclature, the one recommended by the HGVS should be mentioned at least once in the text.

The response:
We have done the request

3- In both the Abstract and the Background, it should be clarified what is thalassemia intermedia and what are its most frequent causes.

The response:
We have added the request in both the Abstract and the Background

4- In Case Presentation, both in the Abstract and in the text, it would be important to include the patient's age and clinical presentation, as well as his history of blood transfusions (never? Once? Sometimes? Under what circumstances?).
The response:
We have added the request information to the abstract and the text

5- The concomitant presence of deletional α-thalassemia should be excluded and this should be mentioned in both the Abstract and the text.

The response:
We have added the request phrase in the Abstract and the text

6- At the end of the Conclusions, in the Abstract, the authors declare that "different δ-thalassemia gene mutation must be screened to avoid the misdiagnosis of β-thalassemia disease". On what basis should this be done? Please complete this sentence.

The response:
We have modified the statement as request.

7- In line 55 of page 2 (Background), the authors declare that "Hb A2 increased more than 3.2% in a typical ...". The cut-off value depends on the method used, please make this clear.

The response:
We have modified the phrase.

8- In line 8 of page 3 (Background), the statement "However, homozygous δβ-thalassemia may give ... with mild anemia" requires a specific reference or should be excluded.

The response:
We have added the specific reference for this statement.
9- In Case Presentation (page 3), there is no reference to Table 1. Hematological data could be summarized as they are detailed in this table.

The response:
We have summarized the Hematological data and we have added the table 1 as reference to these data.

10- The methods could also be summarized, provided it has the proper references. Sequences of the primers, for example, if not original, can only be indicated by references.

The response:
We have summarized the methods section.

11- Please inform about the investigation of deletional α-thalassemia.

The response:
We have done the request.

12- Discussions and Conclusions may also be more concise.

The response:
We have summarized the discussions and conclusions as much as possible.

13- Figure 1 is unnecessary.

The response:
We have removed the figure 1 as request.

14- References are Ok but need standardization.

The response:
We have checked all references.

15- English can be improved.

The response:
We have revised all the manuscript and we have improved the English language as much as possible.

Reviewer 2

1- The authors repeatedly refer to the "Xmn-1 locus". This is a SNP that should be described according to the gene and nucleotide change, specifically HBG2:c.-211C>T.

The response:
We have added the specific nomenclature of the polymorphism as request.

2- Page 3, lines 38-55: This can be omitted from this section since all of this data is contained in Table 1.

The response:
We have summarized the Hematological data.

3- Page 5, line 26: RFLP not RFPL

The response:
We have corrected the error.

4- Page 5, line 39: The correct HGVS nomenclature is HBB:c.82G>T, p.Ala28Ser (not Ala27Ser).

HGVS counts the ATG initiation codon as codon 1, whereas the traditional hemoglobinopathy nomenclature begins with the first amino acid.

The response:
We have corrected the error.

5- Page 7, line 23: The danger is failing to detect beta-thalassemia carriers, as opposed to misdiagnosing beta-thalassemia carriers.

The response:
We have modified the phrase.

6- Should include their most recent study of beta-thalassemia mutations in Syria (Hematology 2018; 23:697-704).

The response:
We have added the request reference to the manuscript.