Author’s response to reviews

Title: An Immunocompetent Patient with a Nonsense Mutation in NHEJ1 Gene

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Response to Reviewers’ comments:
Reviewer 1

1. Lines 14-41: it is not clear if clinical data shown were measured when the patient's age was 1 year, before or after this age. It must be stated because the "Case Presentation" section starts describing the patient when she was 3.5 years old and this is misleading. In Table 1 also, the age of the patient at the time the analyses were performed must be specified.
   Author: The clinical presentations started at the age of one year with jaundice (Page 4, Case Presentation, Line 5). Whole exome sequencing was done at the age of 3.5 years. immunophenotyping test was were performed at the age of 2.5 years (Page 4, Case Presentation, Lines 16-17).

2. Lines 33-36: it is stated that the stop-gain mutation described in this manuscript would lead to a protein lacking about one-third of its C-terminal. It would be appropriate to perform a western blot to confirm this fact in an incontrovertible manner, comparing the protein produced in the patient with appropriate healthy and pathological controls.
   Author: Although Western Blot could help us confirm this fact, it was not done for lack of resources. We believe the results of the sequencing and bioinformatics analysis (CADD score: 37) provide sufficient evidence to support the pathogenicity of this nonsense mutation.
3. TREC and KREC expression analysis from peripheral blood could be usefully added to this study to provide more information regarding the actual functionality of lymphocytes.
Author: Unfortunately, these tests were not available at our center.

4. Table 1: some values should be commented more extensively in the text, especially the WBC count showing leukopenia, the low level of CD19+ and the very high level of CD56+ cells and how can this framework be compatible with an immunocompetent phenotype as described in the paper's title? Absolute cell values should be written in the table and not only their percentages. How is DHR calculated? Is it a percentage? If so, how is possible to have 180? If not, why the reference value is a percentage whereas the patient's value is a number?
Author: The reason for the high titer CD56+ cells is not clear for the authors as well. We think that it might be a novel presentation and phenotype. (Page 7, Discussion and conclusion, Lines 12-15).
Table 1 values were updated to include Absolute cell values.
DHR was calculated based on mean fluorescent intensity. Values more than 50 were considered normal. Table 1 was updated.

5. It should be stated in the manuscript if there are special precautions (and/or drugs) taken to preserve patient's health (like a sort of low bacterial or germ-free environment) or if she lives a normal life.
Author: She lives a normal life without any special precautions. (Page 5, Case Presentation, Line 15)

Reviewer 2

1. Background, line 20: Please rephrase the sentence "One of the products of this process is DSB". DSB occur during V(D)J recombination, but it cannot be said that they represent the products of this process
Author: The sentence was changed to “One of the consequences of this process is DSB”

2. Background, line 20: "One of the products of this process is DSB [3]". Reference 3 is not the original source of these data, please use a more appropriate reference
Author: The Reference was updated.

3. Case presentation, page 2, Line 31. Please introduce the abbreviation CMV with the corresponding full label of the virus
Author: OK

4. Case presentation, page 2, line 41. Please comment shortly on the values that are out of range in Table 1. and the possible causes/effects (CD8+ (%),CD19+ (%),CD14+ (%),CD56+ (NK cells), CD20+ (B cells marker), Plt (103/mm3), IgA (g/L))
Author: We think that out of range values are new phenotype (Page 7, Discussion and conclusion, Lines 12-15)

5. Case presentation, page 2, line 57. Please add more methodological details on the WES methods here
Author: Further Information was added. (Case Presentation Lines:25-29)

6. Discussion and Conclusion, page 1, line 37: please rephrase "…variety of endogenously and exogenously..." to "…variety of endogenous and exogenous..."
7. Discussion and Conclusion, page 2, line 33: please rephrase "This mutation would lead to a protein..." to "This mutation would lead to the production of a protein..."
Author: OK

8. Discussion and Conclusion, page 4, line 15: please rephrase "…initially diagnosed with AIHA, which responded..." to "…initially diagnosed with AIHA, but responded..."
Author: OK

9. The abbreviation list is incomplete, please add all the terms used in the manuscript
Author: The abbreviation list was updated.

10. Table 1. Please add the Reference Values for CD45+ (%)
Author: CD45+ is a marker for differentiating WBC from RBC and does not have normal range.