Reviewer’s report

Title: Comprehensive chromosomal aberrations in a case of a patient with TCF3-HLF-positive BCP-ALL

Version: 0 Date: 29 Jan 2020

Reviewer: Xiaowei Chen

Reviewer's report:

This case report presents a rare BCP-ALL case with TCF3-HLF fusion combined with additional chromosomal variations. The case itself holds clinical significance, providing insights to the understanding and possible treatment of the disease.

In the current version of the manuscript, the relationship between TCF3-HLF and the additional variations are not illustrated thoroughly. Perhaps a different journal would be more appropriate for the article. Still, there are a few points whose revision could increase the value and clarity of the publication for the reader:

1. Page 4, line 53: A reference backing up the incidence percentage would be nice.

2. Page 4, line 69-70: Perhaps a rephrase to "No central nervous system involvement was observed" would be better, as the original statement may mislead the readers to think there was, at that time, some undiscovered central nervous system involvement.

3. Page 4, line 70-74: Results of the FISH tests demonstrating a lack of chromosomal aberrations (both at initial treatment and relapse), if available, should be provided. Also, as is shown in figure 2a, the deletion of 13q12.2-q21.1 would be possible to be observed in a karyotype examination, would it not? Therefore, the statement "the karyotype was normal" seems questionable, and may need a brief explanation.

4. Page 5, line 80: "Clinic", the capitalization doesn't seem to be necessary.

5. Page 5, line 85: Do you mean that the myelogram presented 75% blasts? Perhaps a rephrase is needed.

6. Page 5, line 91-98: What is the percentage of blasts in which the 13q deletion, the PAX5 and NOTCH1 variations took place, respectively? Are they limited to the same cell population with the presence of TCF3-HLF fusion?

7. Following point 6. Readers would be interested in the relationship of these genetic variations, and may raise questions such as: Do they always occur in the same subgroups of cells in this patient? Does one type of the variations make the cell more prone to other variations? At what stage did the fusion/deletion/duplication take place,
simultaneously or not? A short discussion of the above aspects would be interesting for the reader, even if these questions cannot be answered definitively.

8. Page 6, line 102: A reference backing up the poor prognosis would be nice. Or maybe line 105-106 could be moved here to avoid repetition.

9. Page 7, line 131-136: In this patient, is the RB1 deletion restricted to the blasts? Are there any abnormalities concerning chromosome 13, or RB1, in the patient's pedigree? As the loss of 13q is of great significance to not only this work but to the field as well, a deeper discussion of the possible mechanisms lying behind would be beneficial.

10. Relating to the discussion part of the article: The manuscript presents a thorough review of each of the genetic anomalies in the patients. However, readers would be more interested in the situation where all these anomalies lie in one patient. A discussion of the relationship of these genetic variations is highly recommended. What is their relationship? How did they act interactively to cause this patient's situation?

11. The figures have poor resolution. If improved, it will greatly satisfy the readers.

12. Fig 1b: Type I of the fusion is difficult to understand. Where did EX16 go? Which part is the "insertion" composed of? Perhaps it would be easier to understand with more thorough figure legends.

13. Fig 2: A brief annotation/legend will help a lot for better understanding of this figure.

**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

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