Author's response to reviews

Title:A homozygous AHI1 (Abelson Helper Integration site 1) gene mutation (p.Thr304AsnfsX6) in a consanguineous Moroccan family with Joubert Syndrome: a case report

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Version:6Date:21 September 2015

Author's response to reviews: see over
Dear Editor

Please find attached the revised version of our manuscript entitled ” A homozygous AHI1 (Abelson Helper Integration site 1) gene mutation (p.Thr304AsnfsX6) in a Moroccan consanguineous family with Joubert Syndrome: a case report”.

We would like to thank the referee for the helpful comments. Please find below point-by-point responses to all comments.

We hope that you will find the paper now suitable for publication.

Sincerely.

Dr. L. BAALA

1) Referee comment :
“JSRD” often stands for “Joubert syndrome and related disorders” (without the “and”, “Joubert-syndrome-related disorders” should be hyphenated, although the first hyphen frequently is omitted). In your manuscript, your use of “JSRD” includes individuals who meet the specific diagnostic criteria of having a molar-tooth sign, hypotonia, and developmental delay, as well as those with related disorders including those with ocular, renal, or hepatic findings, hence “Joubert syndrome and related disorders” may be a better descriptor.

Our response :
Thank you for this comment. As suggested, we kept “Joubert syndrome and related disorders” in the manuscript.

2) Referee comment :
- The term “hypoplasia of the cerebellar vermis” is usually clearer than “cerebellar vermis hypoplasia”.

Our response :
- “cerebellar vermis hypoplasia”.was replaced by “hypoplasia of the cerebellar vermis” As suggested.

3) Referee comment :
- One important point that you make re Joubert syndrome is that it is a genetically heterogeneous syndrome in which mutations in different genes cause different clinical presentations. Valente et al. (2006) found “AHI1 mutations are a frequent cause of JS with
retinal involvement or other CNS abnormalities, or both” (consistent with your report), and in addition, “No correlate was evident between the type of mutation (truncating, missense, or splicing) or the exon involved and the phenotypes observed.” Do you think this latter observation is worth mentioning?

Our response:
We added the sentence in the discussion paragraph.

4) Referee comment:
- In the Discussion section, you state: “…renal ultrasound in our three patients did not reveal any abnormalities.” Was there any other assessment of renal function?

Our response:
After examination of all clinical and biological exams, Dr. S. Chafai Elalaoui who was charged of clinical investigation confirmed that Urea and creatinine measured in blood were normal. We added this information in the article.

5) Referee comment:
Also in the Discussion section, you state: “The same finding was observed in the Spanish and Dutch patients…” but it is not clear to me which finding you are referring to.

Our response:
The finding that we are referring to is the absence of renal disease which was observed in our patients, and also was found in the Spanish and Dutch patients.
We have changed the stylistic form of this paragraph.