Reviewer’s report

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

Version: 5 Date: 15 February 2015

Reviewer: Michele Roberts

Which of the following best describes what type of case report this is?: Other

Successful diagnostic technique for genetically heterogeneous syndrome – demonstrates the utility of application of genome-wide homozygosity mapping in identifying the causative mutation in three siblings with Joubert syndrome, which is known to be genetically heterogeneous.

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

I found this report to be very interesting, and convincingly presented. The language needs a little work, but the report was understandable as is. In reading the manuscript, I did some stylistic editing with track changes (I do this
professionally). I am happy to share my edited version with the authors (attached).

“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.

The term “hypoplasia of the cerebellar vermis” is usually clearer than “cerebellar vermis hypoplasia”.

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?

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? 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.

Perhaps the space constraints of a case report limit the detail of the Materials and Methods section, but the details seemed a bit sparse. This is what I was referring to in answer to the question about missing information, but I don’t believe that it is deficient.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Declaration of competing interests:

I declare that I have no competing interests.