Reviewer's report

Title: A de novo ANK1 mutation associated to hereditary spherocytosis: a case report

Version: 1 Date: 19 Oct 2018

Reviewer: Anirban Das

Reviewer's report:

I congratulate the authors on their report of use of Sanger sequencing to diagnose HS. However, I would suggest that the authors address the following issues:

1. Line 25: It would be better if the statement that HS has 'few clinical manifestations' be changed suitably to highlight the unique manifestations of HS in the neonate and infant

2. OFT is well known to be fallacious in HS. Did the authors perform EMA binding as recommended in the recent BCSH guidelines?

3. It is well known that in infants, the diagnosis of HS is difficult. The neonatal HS ratio is often useful to guide the diagnostic algorithm. In the index infant, the ratio was >0.36, which points towards a diagnosis of HS. It will be more clinically relevant if the authors discuss the unique clinical and laboratory manifestations, including the diagnostic challenges of HS, specific to the neonatal period and infancy.

4. Sequencing is useful in difficult hemolytic anemias after a complete diagnostic workup has failed to yield a diagnosis. I think that in the index case, there was an opportunity to diagnose by conventional methods. Even if not possible at 3-4 months, often the diagnosis becomes quite evident as the infant grows a bit older. As sequencing, though useful, is not easily available to all, the authors may chose to be prudent and highlight that a wait-and-watch approach may also be appropriate, especially in resource-limited settings and sequencing may be useful only if the conventional algorithm does not yield a diagnosis once the child is 8-10 months old.

5. The authors stress on the absence of family history; however, this is a well-known phenomenon in many countries. A contributary family history is more likely in the Western population, but is often infrequent in many studies in the East. The authors may chose to mention this.
6. The triad of HS is rarely found in infants. Transfusion requirement in infancy is not predictive of severity of disease in later life, as there is often a component of hypoproliferation, which requires transfusions and sometimes even EPO to restrict transfusions, in addition to folic acid. It would be interesting to know the subsequent clinical course in this child and the authors may seek to highlight this. This would provide a more practical and educational clinical perspective. The word limit can be managed by omitting several repetitions.

7. Lines 80 and 128: Please change from "liver-splenomegaly' to the more conventionally used terminology, 'Hepatosplenomegaly.'

8. Line 35: Please omit the term 'first report' and just mention that this is a novel mutation.

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.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published
Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal.