Reviewer’s report

Title: Clinical, Neuroimaging, Biochemical, and Genetic Features in Six Chinese Patients with Adrenomyeloneuropathy

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Reviewer: Saadet Andrews

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Reviewer comments

Title: Clinical, Neuroimaging, Biochemical, and Genetic Features in Cases of Chinese Patients with Adrenomyeloneuropathy

Journal: BMC Neurology

Manuscript number: NURL-D-18-00841R2

Manuscript type: Research article

Authors: Li et al.

Li et al report 6 adult X-ALD patients with the phenotypes of Addison's disease, AMN and progression to cerebral X-ALD in adulthood. They genotyped 5 of those patients and reported biochemical and neuroimaging results. They also identified a novel variant in one of the patients.

This study is a small case series reporting 6 X-ALD patients with adult presentations. The information that the authors have reported, has been known for many years. The study did not report anything new. There are some grammatic errors that makes difficult to understand what the authors report.

There are following questions, which should be answered:

1. Manuscript is too long for the dataset. There are too many details for routine investigations such as MRI, NCV, electrophysiology.

2. The message of the manuscript is not clearly written what the study team trying to give.

3. This manuscript is more suitable in the format of Case Report, instead of a Research Article.
4. It is not clear, if the study team had all those AMN/X-ALD patients and reviewed their charts retrospectively, or enrolled cases to investigate for X-ALD/AMN.

5. Why do investigators say that AMN is the most common adult form of X-ALD, if the majority of the patients have Addison disease in their cohort?

6. Study team reports 6 patients, but genetic test results of 5 patients. What is the information for genetic test result for the patient 3?

7. What are the targeted and specific treatment options for AMN patients that the diagnosis will change the outcome of the disease?

8. For the patient 6 with cerebral form of the disease, how did study group manage this patient? How quick was the disease progression? Did they look into bone marrow transplantation option for the cerebral form of the disease?

9. What was the Loes score of patient 6?

10. What do authors try to say with the following? "It is noteworthy that the psychiatric symptoms of patient 6 were significantly aggravated after divorce." Do they think that psychiatric problems are the result of the divorce, not the other way around?

11. Was is reported in the literature that stress can initiate cerebral disease? The references are related to head trauma and does not support what the authors wrote in the following sentence: "This suggested that the development of cerebral AMN might be triggered or aggravated by environmental factors (i.e., trauma, mental stimulation, etc)27-29.

12. The following sentence should be re-written, as the neurologist would not neglect the results, rather would not have sufficient knowledge to interpret the result: "Nevertheless, it's likely that this percentage were underestimated, which may be attributed to part of neurologists who tend to neglect the diagnostic tests on AMN as adrenal function is normal24."

13. Five patients with skin pigmentation in childhood, were they treated or investigated for adrenal insufficiency? If not did they have any symptoms?
14. Please summarize clinical characteristics of patients in table 1 which are listed in results under the subheading of "Clinical Characteristics". This will remove the duplicate information and shorten the manuscript.

15. Please add the reference ranges for VLCFA in the table 2, first row in brackets instead of having those underneath of the table.

16. There are grammar and language issues that should be corrected. Some of those are listed below:
   a. Please read through the manuscript to correct some language issues.
   b. Change "cured" to "followed"
   c. Change "conditions" to "inclusion criteria"
   d. Change "strangely" to "interestingly"
   e. Change "speculate" to "think"

**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.

No

**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:

Not suitable for publication unless extensively edited

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