Reviewer’s report

Title: Immune Mediated Pediatric Encephalitis – Need for Comprehensive Evaluation and Consensus Guidelines

Version: 0 Date: 09 Sep 2019

Reviewer: Ming Lim

Reviewer's report:

In this manuscript, Shekunov and colleagues report four cases of suspected negative autoimmune encephalitis seen in their tertiary hospital. They describe the neuropsychiatric symptoms of these four cases, as well as the treatments and response to them. The authors emphasize in the discussion why these cases are relevant. Overall, the paper is well written and appropriately discussed. As very little is known on antibody negative autoimmune encephalitis in children, this subject matter is calling out for publication.

The key aspect that requires attention from the authors is the reporting the neuroinflammatory aspect of the data.

* Firstly, there needs to be a more systematic reporting of the range of neuronal surface antibody testing for the 4 cases. For the international readership of the journal, it will be important for the authors to detail what is tested on the Mayo panel, contemporary to the time-point of testing. In essence, a more exhaustive (within reason) evaluation really needs to be demonstrated before any confidence can be ascribed to the "antibody negative" label.

* CSF intrathecal bands (or any other patterns) should be reported and specifically detailed as negative. A family history of autoimmunity could be additionally informative.

* Finally, careful attention needs to be given to delineating when to suspect AE (predominantly clinical) and what the final diagnosis as proposed (currently widely adopted) by Graus and colleagues. The authors could summarise that in their table.

As it stands, the cases not fulfilling the Graus criteria and not convincingly responding to immunotherapy precludes any conclusion being made about an immune aetiology.

There are some other aspects that could be clarified and detailed: -
Introduction P3 L11/12: Is the prevalence referring to adults or children? In case there are not data regarding prevalence in children, this could be mentioned, as the paper is about autoimmune encephalitis in pediatric population.

Case 1: The authors refer that the psychiatrist concluded a diagnosis of "functional communication disorder". But then they explain that the patient continued having monthly IVIG. Was the diagnosis of Functional communication disorder finally ruled out? If not, did he receive any kind of therapy/treatment for this diagnosis? When was the diagnosis changed to autoimmune encephalitis, and based on what?

Case 2: It is mentioned that the psychiatrist assessed the patient and "there was no evidence of mood or anxiety disorder, or catatonia". However, in the next paragraph the authors report "A five day course of 1 gram per day IV methylprednisolone and IVIG for suspected autoimmune encephalitis were initiated, with lorazepam to assist with sleep and anxiety". Did she present anxiety but did not meet criteria for a disorder? If so, why did she have some lorazepam for anxiety? Lorazepam might have been prescribed for the insomnia and helped at the same time for some mild anxious symptoms, but the 2 previous statements are confusing and some clarification might be interesting to the reader.

Case 3: she was prescribed risperidone when assessed in an outside facility. Was it prescribed due to suspected psychosis? Or to manage aggression or behavior?

Case 3: After 5 months she was hospitalized for medical evaluation. Was there any reason for this referral? Was it because she did not improve or respond to the antipsychotic, or were there new (neurological?) symptoms? If so, which ones?

Case 4: When did he start aripiprazole? The authors explained "Mental status changes beginning six months prior". Was the aripiprazole prescribed due to these symptoms or did he present mood symptoms previously? It is not clear enough.
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.

No

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:

Acceptable

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