Reviewer’s report

Title: Application of the 2016 diagnostic approach for autoimmune encephalitis from Lancet Neurology to Chinese patients

Version: 1 Date: 04 Sep 2017

Reviewer: Maarten Titulaer

Reviewer’s report:

Dear editor,

In this revised manuscript, Li and co-authors discuss the usefulness of the diagnostic flowchart of the recent position paper on autoimmune encephalitis (AIE) in Lancet Neurology 2016. The authors have improved the manuscript considerably, but there are still some serious concerns about important issues mentioned below. I have described them in a point-by-point fashion.

1. Methods:

a) The authors explain why they want to keep positive predictive value (PPV) and negative predictive value (NPV). The authors have added some cases in the negative group, thereby directly altering PPV and NPV, even without changing anything in the criteria. This is one of the reasons the use of PPV and NPV is simply not allowed in this type of study, and I disagree to their wish to keep it in the manuscript.

b) The number of non-autoimmune cases is still low despite the increase, and this should be mentioned in the weaknesses of the study (discussion, with respect to specificity of items).

c) The authors suggest using of the whole flow chart, and not just one item. However, in the order of the results and discussion this is not shown. Similarly, the use of the flow chart is shown in an additional figure online, and not as one of the main figures. Consider to reorder some of the results and discussion to show that you do consider the whole flowchart and not just the items one by one.

2. Abstract: "At the early disease stage … lead to exclusion .."; this is too strong. It did not lead to a likely diagnosis at this stage, but the conclusion was still made after antibody testing. Exclusion would mean these would be missed all the way. Please rephrase.

3. Methods: it is unclear what was used in this study as the reference for diagnosis. The authors mention cell-based assays, but do not mention whether diagnosis was made in serum or CSF samples. This is for example important as NMDAR antibodies can return falsely positive in serum sampling only. This could be an explanation why the number of symptoms in the patients
with anti-NMDAR encephalitis was less than in the other published cohorts. For example 30% had 4 or more symptoms within 4 weeks, compared to for example >80% in the cohort by Titulaer et al. The authors should discuss this as the number of symptoms affect the chance of being included as probable anti-NMDAR encephalitis.

4. Discussion, page 12: "only 16 of the 54 pAE (+) cases reach 'probable autoimmune' level". I do not understand this calculation: 11 dALE and 16 pr NMDAR would lead to 27. This would mean 27/54 patients are treated before antibody status is known, and probably the most severe cases. Maybe I have understood this part incorrectly, but please enlighten me.

5. Discussion: please reorder and shorten the discussion to tell first what is most important.

6. Twelve PNS cases: how were these selected? 2/12 had no tumors.

Are the methods appropriate and well described? 
If not, please specify what is required in your comments to the authors.

Unable to assess

Does the work include the necessary controls? 
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown? 
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