Reviewer’s report

Title: Progressive striatal necrosis associated with anti-NMDA receptor antibodies

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Reviewer: Maarten Titulaer

Reviewer’s report:

Dear editor,

In this case-report, Tzoulis et al. describe a case of anti-NMDA-receptor encephalitis with an insidious, mono-symptomatic disease course (dystonia), with specific, progressive MRI abnormalities, unfortunately with chronic disabilities. The case report is well written, the clinical information is detailed and the discussion focused and convincing. There are some minor issues that need to be addressed regarding the comparison with an earlier report, the position within the large amount of patients published with anti-NMDA-receptor encephalitis and some more details on the MRIs.

The information is of value to both neurologists, especially those interested in movement disorders, and pediatricians/pediatric neurologists.

Major Compulsory Revisions: none

Minor Essential Revisions:

1. First sentence of “conclusion of the abstract”, halfway in “Background” (“... has not been reported”) and last sentence of “Background”: The authors are too outspoken in declaring the case being unique and first report. Although there are differences, there is overlap with the case published by Rubio-Agusti (Movement Disorders 2010, reference 4 of this manuscript). Both started asymmetrically with pure dystonia and both had serious headaches. That case was miraculously identified very quickly and treated with immunotherapy. An early MRI did not show abnormalities in that case, but one can speculate what would have happened if it had remained untreated for multiple years. It would be nice to compare the case in this manuscript with the previously published one.

2. In line with comment 1 in “Minor Essential Revisions”, I don’t think this rare case is a direct expansion of the clinical spectrum. To use sentences like “expansion of the clinical spectrum” more robust data are necessary. I would recommend rephrasing the first part of the sentence. Also, it will be important that this will be a rare manifestation of anti-NMDA-receptor encephalitis as in the largest cohort present only 1% of 577 patients had a mono-symptomatic course.

3. Case report, 3rd paragraph: The information about the MRIs is useful, but I would like to see some additional details:

a. How long after disease onset the first MRI was done? This will also allow the
authors to compare it with the normal MRI published by Rubio-Agusti.

b. The authors refer to the cavitations on T1 sequences; when was this noted, only on later MRIs or already on one of the earlier MRIs?

c. Case report, last paragraph: the authors mention that after treatment “.. MRI findings are stable..”. Did the ADC remain low, even though time passed and though the patient was treated? Or did they not perform diffusion weighted imaging (DWI) that scan? If it did change, this needs to be added; if not this should be added to the 3rd paragraph of the discussion where the treatment effect (stabilization) is discussed.

d. In the legend of Figure 1 and 2, the authors should mention if the scans were all pre-immunotherapy.

e. In the last sentence of the conclusion, the authors state testing should be included in all with “chronic movement disorders with striatal lesions.” Do the authors mean all lesions or specific lesions, like T2-attenuated ones only?

4. Case presentation, 5th paragraph: The authors describe the positive staining of serum and CSF of their patient with the Euroimmun kit and state “with weaker staining in the latter.” As the authors do not provide dilutions used this is not informative. According to the Euroimmune site, dilutions of 1:10 and undiluted are advised, respectively. Research laboratories mostly advise 1:40 and 1:2. Whichever dilution is used, the ratio (serum:CSF) is between 10 and 20, while the IgG ratio between serum and CSF normally is around 400. To assess this properly, serial dilutions would be necessary, which are outside the scope of this manuscript. Therefore, I would recommend deleting “.. with weaker staining in the later.”

5. Discussion, 4th paragraph: the authors state that “Anti-NMDA-receptor antibodies are rare and false positive occurrence has not been reported.” Although I agree this is rare and has not been reported in CSF, it has been reported in serum of two cases in Creutzfeldt-Jakob disease (Mackay, J Neurology 2012). This has not been replicated by others. I would recommend adapting this to “Anti-NMDA-receptor antibodies are rare and false positive occurrence in both serum and CSF has not been reported.”

Discretionary Revisions

1. Halfway “Background”, the authors state that “MRI of the brain may show non-specific T2 hyperintense lesions..”. Non-specific is a very vague term and in many patients with anti-NMDAR encephalitis the lesions might not be specific for that disease, but are located congruently with the clinical symptoms. The authors might consider rephrasing this word. Sequential MRIs as presented here have not been described previously, but isolated basal ganglia involvement is not unique.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests