Reviewer's report

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

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Reviewer: Fabienne Brilot

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Charalampos et al report the case of a patient affected by dystonia and slowly progressive basal ganglia necrosis associated with detection of NMDAR antibodies and exclusion of Leigh disease.

This case report shows novel findings as this clinical phenotype has not been described to be associated with NMDAR antibody.

Major Compulsory Revisions

The authors have tested for several known neuronal antigens, such as AMPAR, GABAR, Lgl1, Caspr2, and they only could detect NMDAR antibody. However, this dominant basal ganglia syndrome is atypical of NMDAR encephalitis, and is more reminiscent of Dopamine-2 receptor antibody-associated dystonia/parkinsonism (Dale et al, 2012, Brain). Have the authors considered this possibility and tried to detect these novel antibodies?

What do the authors mean by weaker staining in CSF? As NMDAR antibodies are usually detected in CSF and serum, these results merit deeper analysis. When was the patient tested? Do the authors have access to serial serum for testing? Please, see my point on the issue of pathogenicity. The role of NMDAR antibody in this patient would be strengthened by serial serum testing in this progressive disease.

The authors wrote that the IVIg treatment has reduced the level of NMDAR antibody beyond detection, but no apparent clinical effects has been witnessed. The timeline of testing is unclear. Was the second antibody testing performed two months after the start of IVIG treatment?

The issue of pathogenicity is difficult to assess in this case. The clinical course in this patient was slowly progressive. This is unusual in antibody-associated disorders which are usually acute or subacute and respond to immune therapy. NMDAR antibodies have been detected at one time-point quite late in the disease process with CSF levels weaker than in serum, and treatment with IVIG has not produced improvement in clinical phenotype (although it is likely that the striatum has been too extensively damaged to allow repair). Furthermore, the imaging shows clear necrosis and cell death. This is uncommon in NMDAR antibody-associated disorders which normally have normal or reversible imaging. In terms of pathogenic mechanisms, NMDAR antibodies have not been associated with cytotoxic damages yet (Bien, Brain 2012), but with reversible
changes of localization of the receptor (Hughes, J neurosc 2010). What would be
the pathogenic mechanism behind the pronounced striatal necrosis, this issue
should be discussed.

Level of interest: An article of importance in its field

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