Reviewer’s report

Title: Extensive myelitis revealing anti-NMDA receptor encephalitis

Version: 1 Date: 9 November 2013

Reviewer: Harald Prüss

Reviewer’s report:

- Major Compulsory Revisions

Outteryck et al. report an interesting case of a 65-year-old woman with progressive brain and spinal cord disease, clinically improving after immunotherapy with steroids, plasma exchange and rituximab. Low titer NMDAR antibodies were found in CSF and serum.

The authors partly discuss the possibility that the patient primarily had (AQP4-) seronegative NMO. The clinical findings (LETM, ON, diverse brain changes, periventricular Gd enhancement, response to immunotherapy) are indeed highly suggestive of NMO, consequently the authors assumed this diagnosis initially. In contrast, the symptoms are quite far away from the spectrum of NMDAR encephalitis in the published ~800 cases. Even in the somewhat related case cited in ref. #5, widespread infiltrations of macrophages, neutrophils, T- and B-lymphocytes were noted in a biopsy specimen and further serum autoantibodies were found, altogether suggesting diseases mechanism far beyond NMDAR antibodies.

In addition, a number of studies now report the presence of NMDAR antibodies in the context of diverse neurological disorders – in some of which the antibody response is thought to be secondary to massive brain damage (such as in herpes encephalitis). It seems very possible here that the rather low NMDAR antibody titers in the present case reflect such secondary responses. Of course, nobody could anticipate how broad the spectrum of NMDAR encephalitis might become in future years, but in my opinion it is more likely that the present findings are part of a different disease rather than being at the very end of the NMDAR-E spectrum.

Taken together, the diagnosis of NMDAR encephalitis seems not sufficiently supported by the clinical case and the title is therefore misleading. In my opinion, when critically discussing the above mentioned points, the case is still interesting for clinicians as it suggests that positive NMDAR antibodies help to identify an immunotherapy-responsive CNS autoimmune disease, irrespective of the presence of further (unknown) pathogenic antibodies and T-cells. Thus, I recommend focusing the story on this point and re-phrasing the text accordingly.

- Minor Essential Revisions
+ Resolution of the MR images (in particular A, B, D) is very poor (at least in the version sent out for review), so it is hard to follow what is described in the manuscript. Please provide high resolution images.

+ Whenever the authors mention ‘ventricular enhancement’ the probably mean ‘periventricular’?

+ Were the NMDAR antibodies of the IgG isotype?

+ Was an autopsy performed?

+ The title could potentially be changed to “Extensive myelitis associated with NMDAR antibodies”.

- Discretionary Revisions

None

**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.