Reviewer's report

Title: Clinical, radiographic characteristics and immunomodulating changes in neuromyelitis optica with extensive brain lesions

Version: 1 Date: 6 November 2012

Reviewer: Jun-ichi Kira

Reviewer's report:

Comments to the authors:

The authors characterized the clinical and neuroimaging features of neuromyelitis optica (NMO) patients with and without extensive brain lesions (EBLs) on MRI. I have the following concerns.

1. In the Introduction, the authors should cite the report of Matsushita et al. (Multiple Sclerosis 15: 834-847, 2009), which presented the neuroimaging characteristics of a series of NMO patients with EBLs.

2. Based on the Wingerchuk criteria, anti-AQP4 antibody-seronegative NMO patients must not have brain lesions that meet the Paty criteria. Accordingly, inclusion of seronegative NMO patients in the present series inevitably decreased the frequency of brain MRI lesions and brain symptoms in the NEBLs group. Therefore, the authors should delete these cases from the current comparison.

3. The authors should describe the clinical course of NMO patients. For example, according to Table 2, diffuse lesions comprised 43.75% of EBLs and no mass effect was seen in 81.25% of EBLs. However, there is no evidence or data indicating whether those lesions developed acutely or chronically.

4. Did all EBLs develop acutely? According to Table 1, 37.5% of EBLs were asymptomatic. It is therefore possible that these asymptomatic EBLs developed chronically. The clinical course of the asymptomatic EBLs should be clearly mentioned, and the authors should explain the reasons why they were asymptomatic.

5. ADEM-like lesions do not appear like those presented in Figure 2. These lesions are actually diffuse subcortical and deep white matter lesions, and not scattered perivascular lesions. The author’s naming is misleading and should be corrected.

6. Tumefactive-like lesions and PRES-like lesions are not clearly differentiated, except with respect to their location; therefore, these two categories should be combined.

7. Two cases with unclassified EBLs could be included in the tumefactive/PRES-like group. However, classifying EBLs into acute EBLs and
chronic diffuse EBLs would be simpler and easier to understand. The author’s original classification scheme is much too complex.

8. In Table 2, it should be stated whether acute or chronic EBLs were subjected to DWI examination.

9. The authors should indicate how many days elapsed after the start of relapses when CRP and ESR were examined (it is also better to indicate mean ± SD).

10. Was there any significant correlation between CRP and ESR levels in the present patients?

11. Why did ADEM-like lesions lack gadolinium enhancement? Is it possible that these diffuse lesions might be chronically produced?

12. Doi et al. (Ref. 31) also studied CRP levels in NMO. The authors should cite their findings in the Discussion section.

13. The authors should describe any systemic complications that potentially contributed to the elevation of CRP and ESR levels in NMO patients, such as upper respiratory tract infection, pneumonia, or lower urinary tract infection.

14. The authors stated that CRP and ESR levels were not different between anti-AQP4 antibody-seropositive and -seronegative NMO patients, excluding influence of EBLs. However, they did not describe any data along with this statement. Corresponding data should be presented in the text.

15. Was there any statistically significant difference in EDSS scores between NMO patients with and without EBLs during the follow-up period?

16. The Discussion section is too long, and should be more concise. There are many typos and the English is not sufficiently clear.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I have no competing interests.