Reviewer’s report

Title: West Nile Virus Encephalitis: Neurological Manifestations and Prospective Longitudinal Outcomes

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Reviewer: Koray Ergunay

Reviewer’s report:

The authors report the results of a study on the neurological outcome West Nile virus (WNV) encephalitis; evaluated prospectively in a group of 55 individuals. The study is well-planned with clear criteria for inclusion and parameters for follow-up. Although the data lack neuroimaging and common laboratory test results, the clinical evaluations were performed and interpreted meticulously despite having been performed in various institutions. However, there are several issues that require attention.

Major Points:

- The main problem with this report is that the study was originally planned as a placebo-controlled clinical trial to assess the therapeutic utility of passive immunotherapy in WNV. Within this context, all enrolled subjects were initially assigned to two WNV immunoglobulin preparations or the placebo group. The authors provide only demographic information from subjects from each group (Table 1) and state that no significant difference in clinical evaluation could be demonstrated among groups (page 13). In this kind of a prospective evaluation of clinical outcome, it is not possible to ignore the fact that some of the subjects did receive specific immunoglobulin as a means of therapy and some did not. One cannot help but wonder if there had been any differences in mortality rates, secondary infections, any side effects that can attributed to the hyperimmune globulins administered, the contents and dosage of the preparations, etc. Thus, it can be misleading to combine the clinical data from all cohorts, leaving out the therapy as a parameter. Moreover, it is explained in the manuscript (page 7) that "... the results related to the therapeutic interventions are in preparation", suggesting that some variations, either in outcome or the severity of the symptoms were observed. The authors need to provide at least some data and statistical comparisons among the groups or, even better, combine all data in a single manuscript.

- The laboratory diagnosis of WNV is not clear. Which assays were employed for the detection of IgM (capture or standard assays? which brand?). Is IgG investigated in all subjects? Have both serum and CSF were available for testing? Has intrathecal synthesis of specific antibodies been noted? Have positive results in serum samples been confirmed by virus neutralization? Which PCR assay was used for viral RNA detection? The definition of a confirmed case must also be provided.
Minor Points:
- (Abstract line 4,12 and 14) some grammar and syntax errors were observed in the abstract.
- The conclusion section in the abstract does not provide clear statements as conclusions, but include comparison of initial and late neurologic deficits or findings. These should be moved to the results section and conclusions should be rewritten.
- (Page 14): "Neurologic outcome(s)" has been used as both a main and a subtitle, which is confusing.
- (Table 3 ve 4): These tables include all capital letters, which is hard to read. The term "Polio" should be either explained as a footnote or be replaced with asymmetric limb paresis or weakness.

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