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Potential Conflicts of Interest

Nothing to report.

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Cerebro-Spinal-Fluid Cytokine Profiles Do Not Reliably Delineate Encephalopathy and Inflammation in Neuro-COVID

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To the Editor:

We read with interest the article by Espindola et al about cerebrospinal fluid (CSF) cytokine-profiles in three groups of patients with neuro-COVID (group-1: refractory headache, group-2: encephalopathy, group-3: inflammatory syndrome).[1] Group-3 had elevated IL-2, IL-4, IL-6, IL-10, IL-12, CXCL8, and CXCL10, whereas group-2 had elevated IL-6, CXCL8, and active TGF-β1.[1] The study is appealing but raises comments.

First, it is important to know how the CSF cytokine-profiles of the three groups compared with those in the serum. This is of particular concern because it was not mentioned in how many patients the blood–brain-barrier (BBB) was disrupted versus intact, and in how many patients lumbar puncture was traumatic. For example, the CSF erythrocyte count could be mentioned to determine the degree to which CSF cytokine-profiles were contaminated by serum cytokine-profiles.

Second, the inclusion/exclusion criteria were not unequivocal. One inclusion criterion for group-2 was "convulsions" and for group-3 "focal abnormalities on EEG". We are interested to know if focal EEG activity refers to seizure activity and if so how were patients chosen between group-2 and group-3 to avoid overlaps between these two groups.

Third, it would be interesting to know if reproducibility of the results was tested, particularly if any patient of group-2 or group-3 underwent repeated CSF investigations and if the cytokine-profile remained unchanged between follow-up investigations. Knowing how many group-2 subjects developed pleocytosis over time is essential as it is conceivable that the cytokine-profile depends on the disease stage and changed over time. Since there was sequential onset of headache, encephalopathy, and inflammation, 2, 3, and 4d after onset of COVID-19, it is conceivable that the pathophysiology is the same in all three groups and that the findings in the CSF at different times represent different stages of the same pathology.

Finally, it would be interesting to know how refractory headache was defined, and if the cause of refractory headache, in particular possible venous sinus thrombosis, was determined. We are interested to know if NMO-antibodies were present in the patient with NMO.

Discussing these points could strengthen the conclusions of this elegant study.

Potential Conflicts of Interest

The authors declare no conflicts of interest.

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