Journal of Medical Case Reports and Reviews

Received 13 Jan 2021 | Revised 18 Jan 2021 | Accepted 17 Mar 2021 | Published Online 22 Mar 2021

JMCRR 04 (03), 834-835 (2021) ISSN (O) 2589-8655 | (P) 2589-8647

JMCRR

CSF CYTOKINE PROFILES NOT NECESSARILY DISCRIMINATE NEURO-COVID SUBGROUPS

Finsterer J, MD, PhD [1] and Scorza FA, MD [2]

[1] Klinik Landstrasse, Messerli Institute, Vienna, Austria

[2] Disciplina de Neurociência. Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM). São Paulo, Brasil.
scorza@unifesp.br, carlascorza.nexp@gmail.com, tel. 0055 11 5576-4000, ORCID: 0000-0002-0694-8674 (SFA), ORCID SCA: 0000-0001-7810-4748

Key words: SARS-CoV-2, COVID-19, neuro-COVID, complications, brain, encephalitis

Corresponding author: **Finsterer J, MD, PhD**

Postfach 20 1180 Vienna, Austria,Tel. +43-1-71165-72085,Fax. +43-1-71165E-mail: fifigs1@yahoo.de

Letter to the Editor

With interest we read the article by Espindola et al. about cerebrospinal fluid (CSF) cytokine profiles of 48 patients with neuro-COVID (refractory headache (n=12, group-1), encephalopathy (n=22, group-2), inflammatory syndrome (n=14, group-3)) [1]. It was concluded that 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]. We have the following comments and concerns.

The main shortcoming is that the CSF cytokine-profile was not compared to that of the serum in all patients. Since no information was provided in how many patients the blood-brain-barrier (BBB) was disrupted respectively intact, and since it was not reported in how many patients lumbar puncture was traumatic or non-traumatic and the CSF erythrocyte count was not considered, it remains unclear to which degree the serum cytokine profile influenced the CSF cytokine profile.

A further shortcoming is that inclusion/exclusion criteria are not unequivocal. We should know if patients in group-2 and group-3 needed to fulfil all clinical criteria or only some. This is crucial as these criteria allow overlaps between the two groups. For example, an inclusion criterion in group-2 was “convulsions” and in group-3 “focal abnormalities on EEG”. We should know if focal activity includes seizure activity or not.

Another shortcoming is that reproducibility of the results was not tested. We should know if any patient in groups-2 or group-3 underwent repeated CSF investigations and if the cytokine profile remained unchanged during follow-up. How many of group-2 developed pleocytosis during the course? Since cytokine-profile may depend on the disease stage it is conceivable that it changed over time. Since there was sequential onset of headache, encephalopathy, and inflammation (2, 3, respectively 4d after onset of COVID-19), it is conceivable that the pathophysiology is the same in all three groups and in fact different pathology represents different stages of the same disease.

A further shortcoming is that normal CSF cell count does not exclude encephalitis/meningitis. There are several examples of viral meningitis showing normal routine CSF but virus nucleic acid or virus proteins within the CSF [2]. Thus, the delineation between the two groups could be artificial and there may be overlaps. We should know how refractory headache was classified, the cause of refractory headache, and if venous sinus thrombosis was excluded.

Overall, limitations of the study question the results. The points raised above should be met before drawing final conclusions.

COI: The authors declare no conflicts of interest

Funding: No funding was received

Author contribution: JF: design, literature search, discussion, first draft, critical comments

Informed consent: was obtained

Ethics approval: The study was approved by the institutional review board

Data availability: not applicable

Consent to participate: not applicable

Consent for publication: not applicable

References:

1 Espíndola OM, Gomes YCP, Brandão CO, Torres RC, Siqueira M, Soares CN, Lima MASD, Leite ACCB, Venturotti CO, Carvalho AJC, Torezani G, Araujo AQC, Silva MTT. Inflammatory cytokine patterns associated with neurological diseases in COVID-19. Ann Neurol. 2021 Feb 6. doi: 10.1002/ana.26041.

2 Kadambari S, Braccio S, Ribeiro S, Allen DJ, Pebody R, Brown D, Cunney R, Sharland M, Ladhani S. Enterovirus and parechovirus meningitis in infants younger than 90 days old in the UK and Republic of Ireland: a British Paediatric Surveillance Unit study. Arch Dis Child. 2019 Jun;104(6):552-557. doi: 10.1136/archdischild-2018-315643.