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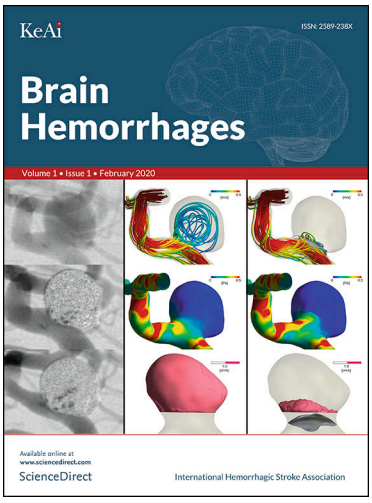

SARS-CoV-2 may underlie NMDA-related autoimmune encephalitis and venous sinus thrombosis

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S e encephalitis and venous sinus thrombosis

Shor title: diagnosing SFN

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With interest we read the article by Khan et al. about an 18 years-old, previously healthy male who experienced venous sinus thrombosis (VST) without recovery of intermittent headache since three months under anticoagulation [1]. Additionally, he developed fever, nausea, and vomiting, followed by mood & behavioural changes, impaired consciousness, dystonia, opisthotonus, and recurrent tonic clonic seizures [1]. Further work-up revealed mild pleocytosis and antibodies against the N-methyl D-aspartate receptor (NMDA-R) in the cerebrospinal fluid (CSF) [1]. Glucocorticoids were ineffective but incomplete recovery could be achieved with plasmapheresis [1]. The study is appealing but raises concerns that require further discussion.

The main limitation of the study is that the patient was not tested for SARS-CoV-2. The manuscript had been submitted during the SARS-CoV-2 pandemic, which is why it is essential that SARS-CoV-2 infection is ruled out as the cause of VST. Additionally, we need to know if the patient had received an anti-SARS-CoV-2 vaccination shortly before the occurrence of VST or of encephalitis. VST is a known complication of anti-SARS-CoV-2 vaccination [2]. There is even increasing evidence that SARS-CoV-2 can trigger the development of NMDA-related autoimmune encephalitis [3]. There are also cases that developed NMDA-R related autoimmune encephalitis following application of an anti-SARS-CoV-2 vaccination [4].

A further limitation of the study is that the results of electroencephalography (EEG) was not provided. Knowing the EEG results is crucial to eventually identify the location of autoimmune encephalitis. The patient should have also received EEG-video monitoring to assess whether oro-facial dyskinesias and opisthotonus were not dystonia but in fact focal or generalised seizures.

Missing is the fluor-deoxy-glucose positron emission tomography (PDG-PET), which has been shown a valuable tool to document encephalitis even in the absence of an enhancing lesion on cerebral magnetic resonance imaging (MRI) [5].

It should be explained why the patient received 1.5g levetiracetam thrice daily. We should know if the patient was obese, eventually justifying a daily dosage of 4.5g/d.

Overall, the study carries obvious limitations that require re-evaluation and discussion. Clarifying these weaknesses would strengthen the conclusions and could improve the study. In times of COVID-19, SARS-CoV-2 infection or recent SARS-CoV-2 vaccination must be ruled out as the cause of autoimmune encephalitis and of VST.

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1 Naveed Ullah Khan NU, Hassan M; Jan Z, Mobeen H, Munawar Z, Hussain N, Badshah M. A rare case of anti-NMDA receptor encephalitis with CVST. Brain Hemorrhages 2022;3:128-130.

2 Finsterer J. SARS-CoV-2 vaccination associated venous sinus thrombosis in three patients. J Appl Biomed. 2022 Oct;20(3):83-86. doi: 10.32725/jab.2022.011.

3 Nabizadeh F, Balabandian M, Sodeifian F, Rezaei N, Rostami MR, Naser Moghadasi A. Autoimmune encephalitis associated with COVID-19: A systematic review. Mult Scler Relat Disord. 2022 Jun;62:103795. doi: 10.1016/j.msard.2022.103795.

4 Flannery P, Yang I, Keyvani M, Sakoulas G. Acute Psychosis Due to Anti-N-Methyl D-Aspartate Receptor Encephalitis Following COVID-19 Vaccination: A Case Report. Front Neurol. 2021 Nov 4;12:764197. doi: 10.3389/fneur.2021.764197.

5 Shen R, Shen D, Zhou Q, Zhang M, Chen S. Antibody-mediated autoimmune encephalitis evaluated by ^{18}F-DPA714 PET/MRI. Brain Behav Immun Health. 2022 Oct 13;26:100535. doi: 10.1016/j.bbih.2022.100535.