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LETTER TO EDITOR

Rule out alternative entities before diagnosing post-COVID-19 psychosis

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Dear editor,

We have read with interest the article by Wong and George reporting the case of a 54-year-old man with psychosis that developed 55 days after the diagnosis of COVID-19.[1] For respiratory insufficiency due to COVID-19, the patient required assisted ventilation for 2 days and high-dose steroid therapy. Thirty-two days after discharge, he was re-admitted because of aggressive behaviour and new-onset psychosis since 3 days. Under anti-psychotic treatment, he made an incomplete recovery within 8 days of hospitalisation. The study is appealing but raises concerns that warrant further discussion.

We disagree with the authors' notion that psychosis was triggered by SARS-CoV-2 infection in their patient.[1] The patient had received high-dose dexamethasone therapy from 6 January 2021 to 23 February 2021 for moderate SARS-CoV-2 infection requiring assisted ventilation (nasal prongs, high-flow performance devices). Because steroids are well known for their pro-psychotic effect,[2] it is more likely that steroids but not SARS-CoV-2 infection were the cause. A further argument against SARS-CoV-2 infection as a cause of psychosis is the long latency (55 days) between the onsets of COVID-19 and psychosis.

A limitation of the study is that no tests for cytokines or chemokines were conducted using cerebrospinal fluid (CSF) samples. The cytokine and chemokine levels are commonly elevated in patients with COVID-19 with central nervous system involvement but normal central nervous system imaging or routine CSF investigation findings.[3]

The study does not provide information about the drugs the patient received for COVID-19. It is essential to know whether any of them, in combination with steroids, could have contributed to the development of psychosis.

A further limitation is that there is no information about the magnetic resonance imaging modalities applied. Whether frontal lacunar stroke was acute or subacute must be clarified. It is also unclear whether the lesions were hyperintense on diffusion-weighted imaging and whether the susceptibility-weighted imaging sequences were indicative of micro-bleeds. Furthermore, the study does not explain bilateral frontal lacunar stroke: It is unclear whether it was due to arterial hypertension or hyperlipidaemia, whether there was a genetic component and whether the blood pressure and lipid level were well controlled.

Another limitation of the study is that electroencephalography was not recorded. In patients with new-onset psychosis, non-convulsive status epilepticus needs to be ruled out.

Since the patient had generalised headache at the onset of COVID-19 and an elevated D-dimer level, it is crucial that venous sinus thrombosis is ruled out by magnetic resonance venography.

The study does not describe whether the patient received antibiotics and virostatics during the second hospitalisation in the psychiatric department and whether there were any indications for an infection.

Further, the CSF was not investigated for antibodies associated with autoimmune encephalitis. Cerebral magnetic resonance imaging findings can be normal in patients with autoimmune encephalitis, while CSF test findings can be normal in patients with autoimmune encephalitis. Ruling out immune encephalitis and infectious encephalitis is crucial in patients with COVID-19, as both complications have been reported to occur in these patients.

In general, the study carries apparent limitations that require re-evaluation and discussion. Clarifying these weaknesses could strengthen the conclusions and improve the study. Before attribution of post-COVID-19 psychosis to SARS-CoV-2 infection, alternative aetiologies, such as steroid therapy, immune encephalitis, multisystem inflammatory syndrome in adults, non-convulsive status epilepticus and viral or autoimmune encephalitis, need to be adequately ruled out.

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JF: Study design, literature search, discussion, initial manuscript drafting, provision of critical comments and final approval

Conflicts of interest
None.

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