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Letter to the Editor

## **Generalised non-epileptic myoclonus shortly after vaccination in an asymptomatic SARS-CoV-2 positive: Who's to blame?**

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We read with interest the article by Ben Mohamed *et al.* on a 60 years-old male with non-epileptic myoclonus status described as the initial and only manifestation of a SARS-CoV-2 infection<sup>[1]</sup>. The etiological classification of myoclonus yielded only negative results despite extensive blood tests, electroencephalography (EEG), magnetic resonance imaging (MRI), and cerebrospinal fluid (CSF) examinations<sup>[1]</sup>. The patient benefited from dexamethasone, clonazepam, and levetiracetam and gradually recovered<sup>[1]</sup>. The study is excellent, but has limitations that are cause for concerns and should be discussed.

The main limitation of the study is that myoclonus occurred shortly after SARS-CoV-2 vaccination, but the vaccine was not considered responsible for myoclonus and debated since the index patient was also SARS-CoV-2 positive in RT-PCR<sup>[1]</sup>. At least the opsoclonus myoclonus syndrome was reported as complication not only in SARS-CoV-2 infected<sup>[2]</sup>, but also in SARS-CoV-2 vaccinees<sup>[3]</sup>.

We disagree with the statement that myoclonus was the only and first manifestation of SARS-CoV-2 infection<sup>[1]</sup>. In addition to myoclonus, the patient has been described as having downward gaze paralysis, tremor, dysarthria, gait disturbance, and diarrhoea<sup>[1]</sup>. This discrepancy should be resolved and the time course of these clinical manifestations should be clearly presented.

We also disagree with the notion that “neurological manifestations involving the central nervous system are sparse, ranging from headaches, drowsiness, and neurovascular attacks to seizures and encephalitis”<sup>[1]</sup>. Central nervous system (CNS) complications of SARS-CoV-2 infections are common and include in addition to headache, drowsiness, neurovascular attacks, seizures, and encephalitis, cerebellitis, acute disseminated encephalomyelitis (ADEM), acute, hemorrhagic, necrotising encephalitis (AHNE), pontine myelinolysis, cerebral vasculitis including giant cell arteritis, ventriculitis, hypophysitis, intracerebral bleeding, demyelinating disorders (multiple sclerosis, neuromyelitis optica (NMO) spectrum disorders, myelin-oligodendrocyte glycoprotein (MOG) associated disease), increased intra-cerebral pressure (pseudotumour cerebri), reversible, cerebral vasoconstriction syndrome (RCVS), Wernicke encephalopathy, and transverse myelitis (neuro-COVID)<sup>[4]</sup>.

Discussion of CNS abnormalities due to SARS-CoV-2 infection should also include psychiatric disorders that have been reported in SARS-CoV-2 infected, such as delirium, isolated hallucinations, mania, akinetic mutism, psychosis, eating disorders, autism spectrum disorders, altered mental state, anxiety, sleep disorders, and depression<sup>[4]</sup>.

Another limitation of the study is that the cerebral MRI was performed without contrast medium. Because infectious or immune encephalitis can present with normal cerebrospinal fluid (CSF) findings either early or throughout the disease course, the use of contrast medium is critical, since enhancing cerebral lesions may be the only abnormal instrumental finding in such patients.

Another limitation is that the current medication that the patient was regularly taking was not provided. Knowing the medication is critical to assessing whether any of them might have a triggering effect.

Since non-epileptic myoclonus can also originate from the skeletal muscle, it is crucial that myopathy, myositis, and rhabdomyolysis are ruled out. Therefore, we should know if creatine-kinase, lactate-dehydrogenase, myoglobin, aldolase were increased, if needle electromyography showed abnormalities suggestive of myopathy or myositis, and if muscle contrast-enhanced MRI showed edema, inflammation, or atrophy.

Overall, the interesting study has limitations that call the results and their interpretation into question. Addressing these issues would strengthen the conclusions and could improve the status of the study. Generalised non-epileptic myoclonus shortly after a SARS-CoV-2 vaccination in an asymptomatic SARS-CoV-2 positive is from vaccination rather than infection.

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