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Letter to the Editor

Post-SARS-CoV-2 vaccination neurology

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We read with interest the review article by Mohseni Afshar *et al.* about the neurological side effects of SARS-CoV-2 vaccinations ^[1]. It was found that neurological side effects to SARS-CoV-2 vaccines include seizures, re-activation of the varicella-zoster virus, stroke, Guillain-Barre syndrome (GBS), Bell's palsy, transverse myelitis, and acute disseminated encephalomyelitis (ADEM)^[1]. It was concluded that an acute SARS-CoV-2 infection needs to be ruled out before classifying a neurological manifestation as a vaccination related side effect and that the benefits of vaccination outweigh the risks of the vaccination^[1]. The study is appealing but raises concerns that warrant further discussion.

The main limitation of the review is that only a small section of the potential neurological side effects of SARS-CoV-2 vaccinations was discussed ^[1]. The spectrum of neurological side effects to SARS-CoV-2 vaccinations is much broader than presented. Undisputed central nervous system (CNS) side effects of SARS-CoV-2 vaccination were apoplexy of the pituitary gland, which mainly occurs in patients with a pre-existing pituitary adenoma ^[2], acute, hemorrhagic, encephalomyelitis (AHEM) ^[3], immune encephalitis ^[4], multifocal, necrotising encephalitis ^[5], limbic encephalitis ^[6], rhombencephalitis ^[7], opsoclonus myoclonus syndrome ^[8], giant cell arteritis ^[6], meningitis, status epilepticus, cytotoxic lesions of the corpus callosum, MOG encephalomyelitis, Bickerstaff encephalitis, Tolosa-Hunt syndrome, and reversible, cerebral vasoconstriction syndrome ^[9], Among the SARS-CoV-2 vaccine adverse reactions affecting the peripheral nervous system (PNS) not mentioned in the review were trigeminal neuralgia [100noda], plexitis (Parsonage Turner syndrome (PTS)) ^[11], new onset myasthenia ^[12], rhabdomyolysis ^[13], and myositis or dermatomyositis ^[6].

A further limitation of the review is that neurological symptoms have been mixed up with neurological diagnoses. Although they may overlap, they should be distinguished from each other as clearly as possible. For example, seizures are a neurological symptom. They may appear with or without structural lesions on cerebral imaging. Therefore, patients with venous sinus thrombosis (VST), stroke, encephalitis, meningitis, that manifest with seizures, should be delineated from those without a plausible explanation. The term "seizures" should be replaced by epilepsy.

Another limitation is that the term "encephalopathy" was not defined. We should know if the authors mean cerebral manifestations due to infection, intoxication, or vaccination in the absence of any structural lesion on CNS imaging. Surprisingly, seizures can be a feature of encephalopathy ^[1]. Why were new onset seizures not generally classified as encephalopathy?

We disagree with the classification of reactivation of herpes zoster virus as a neurological side effect of SARS-CoV-2 vaccinations ^[1]. Although SARS-CoV-2 vaccinations can reduce the immune-competence, precipitating superinfections, reinfection with H. zoster not necessarily manifests in the nervous system but rather on the skin. Only if the vaccination triggers, H zoster encephalitis or zoster neuralgia, it should be classified as a neurological complication of a SARS-CoV-2 vaccination.

Another limitation is that not all complications to SARS-CoV-2 vaccines that secondarily damage the nervous system were mentioned. In addition to vaccine-induced immune thrombotic thrombocytopenia (VITT), SARS-CoV-2 vaccinations can cause myocarditis / pericarditis, which may be secondarily complicated by cardio-embolic, ischemic stroke ^[14]. Embolic stroke in these patients may derive from intra-cardiac thrombus formation due to concomitant heart failure.

Overall, the study carries obvious limitations that require re-evaluation and discussion. Clarifying these weaknesses would strengthen the conclusions and could improve the study. The spectrum of neurological side effects to SARS-CoV-2 vaccines of any type is broader than usually believed.

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