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Letter to the Editor

The spectrum of neurological complications of SARS-CoV-2 vaccination is broader than is generally assumed

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We read with interest the review article by Castillo *et al.* about the neurological complications of SARS-CoV-2 vaccinations^[1]. Neurological complications of SARS-CoV-2 vaccinations described in the literature include cerebrovascular disease, demyelinating disorder of the central nervous system (CNS), epilepsy, meningitis/encephalitis, headache, mono- or polyradiculitis, plexitis, myasthenia and myositis^[1]. It was concluded that a causal relation between SARS-CoV-2 vaccinations and post-vaccination neurological disorder cannot be established and that their frequency cannot be reliably calculated. The study is appealing but raises concerns that warrant further discussion.

We disagree with the notion that a causal link between SARS-CoV-2 vaccinations and neurological compromise cannot be established. On the contrary, there is ample evidence that COVID vaccinations can cause neurological complications.

A further limitation of the review is that neurological symptoms were mixed up with neurological diagnoses. Although they can overlap, they should be delineated as clearly as possible. For example, headache can be a symptom of venous sinus thrombosis (VST), intracerebral bleeding (ICB), meningitis, encephalitis, subarachnoid bleeding (SAB), vasculitis, or reversible, cerebral vasoconstriction syndrome (RCVS), but it may also occur isolated in the absence of a structural or functional cerebral lesion. Therefore, cases with headache should be split up into those with and without a structural or functional lesions on cerebral imaging. Likewise, seizures are a neurological symptom. They may occur with or without structural lesions on cerebral imaging. Therefore, patients with 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”.

It is not comprehensible why radiculopathy was delineated from Guillain-Barre syndrome (GBS)^[1]. GBS is a subtype of radiculopathy unless the authors mean with the term radiculopathy a mononeuropathy as compared to GBS, which is a polyradiculopathy. This issue should be clarified.

It is not comprehensible why herpes zoster was listed as a neurological complication of a SARS-CoV-2 vaccination^[1]. H. zoster is an infectious disease with or without affection of the nervous system. We should know how many of the listed patients manifested with neurological manifestations and how many without.

It is not comprehensible why Bell's palsy was delineated from “cranial nerve involvement”^[1]. Bell's palsy means affection of the VIIth cranial nerve. Therefore, these two entities should be evaluated together.

It is not comprehensible why “headache” was not classified as central nervous system (CNS) disease but categorised as “other”^[1].

An increasingly recognised adverse reaction of SARS-CoV-2 vaccines, not mentioned in the review, is small fiber neuropathy (SFN)^[2]. SFN is characterised by affection of C- or A-delta fibers and manifests with focal, regional, or generalised pain, sensory disturbances, and autonomic abnormalities^[3]. In a series of three patients, dizziness, balance problems, brain fog, palpitations, dysphagia, flushing, sleep problems, fatigue, pre-syncope, hair loss, chest pain, dyspnea, paresthesias, irregular menstrual cycle, muscle weakness, diarrhoea, and hives were reported^[2].

A further neurological complication of SARS-CoV-2 vaccinations not discussed is apoplexy of the pituitary gland^[4]. Apoplexy of the pituitary gland particularly occurs in patients with a pre-existing adenoma of the pituitary gland.

Another neurological complication of SARS-CoV-2 vaccinations not discussed in the review is opsoclonus myoclonus syndrome^[5].

It should be clarified that encephalitis as a complication of SARS-CoV-2 vaccinations is an immune encephalitis, which can also manifest as limbic encephalitis, rhombencephalitis, or cerebellitis.

There is no mention of complications to SARS-CoV-2 vaccines that secondarily damage the nervous system. In case a SARS-CoV-2 vaccination is complicated by vaccine-induced immune thrombotic thrombocytopenia (VITT), venous sinus thrombosis (VST) may ensue [6]. Recent data suggest that up to 40% of patients with VITT induced VST die from these complications [6]. In case SARS-CoV-2 vaccinations cause myocarditis / pericarditis, cardio-embolic, ischemic stroke may ensue.

Overall, the review carries obvious limitations that require re-evaluation and discussion. Clarifying these weaknesses would strengthen the conclusions and could improve the study. There is a definite causal relation between SARS-CoV-2 vaccinations and post-vaccination neurological compromise. The spectrum of these neurological side effects is broader than anticipated.

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