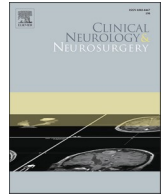




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Response to Letter to the Editor on the article “Acute disseminated encephalomyelitis after SARS-CoV-2 vaccination”

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We were pleased to receive the correspondence from colleagues in relation to our publication in *Clinical Neurology and Neurosurgery* that described a patient who developed a severe neuroinflammatory disorder of the CNS shortly after being vaccinated for SARS-CoV-2 [1].

The patient – a 56-year-old lady – developed left sided hemi-ataxic gait and ipsilateral dysmetria associated with mild weakness of the upper limb (scale for the assessment and rating of ataxia [SARA] score: 7) two weeks after receiving the first dose of the Pfizer-BioNTech COVID-19 vaccine. Brain MRI demonstrated an area of hypersignal on T2-weighted and fluid attenuated inversion recovery (FLAIR) sequences involving the left cerebellar peduncle, without contrast enhancement, together with new supratentorial areas of hyperintensity, the largest in the left centrum semiovale [1]. Intriguingly, the patient had a previous history of post-infectious rhombencephalitis 5 years before, which recovered completely without any relapses. After comprehensive immunological and microbiological investigations, we concluded that the most likely diagnosis of the CNS disorder ensuing after vaccination was that of an acute disseminated encephalomyelitis (ADEM)-like disorder, although we acknowledged that several atypical findings were present, notably the absence of encephalopathy [1]. Dr. Finsterer commented on the following points [2]:

- (1) He stated that MRI findings were not in agreement with the clinical presentation. This is not correct. Lesions involving the cerebellar peduncles are associated with clinical signs (e.g. limb ataxia) ipsilateral to the lesion [3], as in the presented case. Weakness is not a common complaint in cerebellar patients but a mild degree of weakness and hypotonia are possible [4]. In our report, we highlighted in both the text and the diagram that the main symptoms were hemi-ataxia and dysmetria [1], which are perfectly compatible with the lesion apparent on brain MRI.
- (2) Dr. Finsterer also stated that ADEM requires per definition the presence of myelitis. This is not correct. The diagnosis of ADEM requires a single polyfocal CNS event and presumed inflammatory demyelination [5], but the presence of myelitis is not mandatory for the diagnosis.

- (3) Dr. Finsterer also considered the hypothesis that the brain lesions “were old and originated from the recurrent herpetic infections during previous years”. This is not correct.

In the report we explicitly stated that the patient suffered from “recurrent episodes of cutaneous herpes zoster” [1]. How is it possible that cutaneous herpes zoster triggered brain demyelinating lesions? There is no evidence of such possibility in the literature.

- (4) In addition, he stated that a discussion of previous cases of ADEM after SARS-CoV-2 vaccination was missing. This is not correct. In the paper, we discussed previous cases of ADEM after SARS-CoV-2 vaccines reported to the Vaccine Adverse Event Reporting System (VAERS), and also a recently reported case of ADEM described after SARS-CoV-2 [1]. The other case mentioned by Dr. Finsterer was not present at the time of writing of our report.
- (5) Finally, we would like to point out that in our report we acknowledged the possibility of alternative diagnoses as the cause of the patient’s symptoms (in particular multiple sclerosis, neuromyelitis spectrum disorders, Bickerstaff brainstem encephalitis, and autoimmune encephalitis), and the use of terms such as “neuroinflammatory disorder of the CNS” or “ADEM-like syndrome” is emblematic of an effort to highlight the atypical aspects of the case and, after considering its presentation and clinical evolution (monophasic disease after vaccination), we are still convinced of the diagnosis made. This report should not – by any means – discourage from SARS-CoV-2 vaccination. As we also underlined in the paper, a temporal association with vaccination does not imply causation, and the experience so far is that SARS-CoV-2 vaccination is safe and should be encouraged [1]. Conversely, it is now well-established that COVID-19 can cause neurological disorders with much higher frequency, including anosmia [6], stroke [7,8], Guillain-Barré syndrome [9], and encephalopathy [10].

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Data access, responsibility, and analysis

The Corresponding Author had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflicts of interest

None reported.

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