LETTER TO THE EDITOR

Neurological Adverse Events Associated with COVID-19 Vaccination

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Dear Editor,

We read the article by Chakor et al. on post-COVID-19 encephaloradiculoneuropathy.¹ This study demonstrates that COVID-19 can trigger neurological complications and has emphasized the importance of recognition of neurological complications among COVID-19 patients. Nonetheless, no mention is made of neurological adverse events after COVID-19 vaccination. Vaccination is undoubtedly a key to controlling many infections and avoiding spreading infections. It also dramatically decreases severe infection and death. Therefore, shortly after the onset of the pandemic, global research efforts have focused on the development of vaccines against COVID-19 and fortunately, the efforts have borne fruits in a relatively short time. Currently, four main types of vaccines are in use: viral vector, protein subunit, inactivated, and mRNA-based. Undoubtedly, all of them could play a significant role in reducing the spread of the virus. But concurrently, they can cause adverse reactions in different organ systems including nervous system. Neurological complications may be mild or severe. The mild adverse effects are much more common and transient and have been observed after the administration of all kinds of COVID-19 vaccines. These symptoms usually go away within a few days and include fever/chills, headache, muscle and joint pain, or injection-site reactions. Some vaccinated people may experience severe neurological adverse events. These complications are rare and may be life-threatening or organimpairing. Some of the severe effects are functional neurological disorder, cerebral venous thrombosis, encephalopathy, Bell's palsy, and Guillain–Barré syndrome.²

Now, it is hard to determine a direct or indirect causal relationship between the neurological complications and COVID-19 vaccination. Nonetheless, several theories have been proposed to address the pathogenic mechanisms behind the neurological disorders in COVID-19-vaccinated individuals. Molecular mimicry, direct neurotoxicity, and abnormal immune responses are three major theories that explain the mechanisms of neurological complications following COVID-19 vaccination.^{2,3}

A possible relationship between the COVID-19 vaccine production technologies and the appearance of neurological symptoms is another point of focus. For instance, the Oxford-AstraZeneca as a viral vector vaccine has great potential for induction of thrombosis with thrombocytopenia syndrome in different sites of the body, including cerebral venous sinus. The *interaction* of the cationic *platelet factor 4 with* anionic-free DNA Department of Immunology, Tehran University of Medical Sciences, Tehran, Iran

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in the vaccine *may* generate platelet-activating antibodies. These antibodies can activate platelets causing platelet activation and consumption, which in turn can lead to hypercoagulability and thromboembolic complications.⁴

Another important aspect is vaccine-related adverse events in people who suffer from neurological disorders like multiple sclerosis (MS). In this scenario, some essential questions regarding vaccination included the ability of the vaccine to aggravate the underlying disorder and its role in the initiation and/or progression of new neuromuscular diseases. Vaccination is essential for these patients because they are at increased risk for severe COVID-19. Conversely, the use of the immunosuppressive drug in MS patients may attenuate their immune responses to vaccine antigens. Consequently, the timing of the vaccine is crucial for providing a balanced immune response in these patients. The timing of COVID-19 vaccination before starting the treatment or near the end of a treatment cycle seems to have a beneficial effect (maximizing the immune response) in MS patients who take certain disease-modifying therapies.⁵

CONCLUSION

Neurological adverse effects following COVID-19 vaccination are uncommon but can lead to significant mortality or morbidity when they occur. A causal relationship between COVID-19 vaccination and these adverse events is controversial. Therefore, more studies are needed to clarify whether such associations are plausible.

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