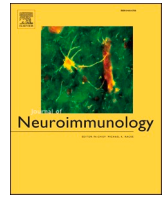




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Review Article

A systematic review of cases of CNS demyelination following COVID-19 vaccination

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ABSTRACT

Background: Since the emergency use approval of different types of COVID-19 vaccines, several safety concerns have been raised regarding its early and delayed impact on the nervous system.

Objective: This study aims to systematically review the reported cases of CNS demyelination in association with COVID-19 vaccination, which has not been performed, to our knowledge.

Methods: A systematic review was performed by screening published articles and preprints of cases of CNS demyelination in association with COVID-19 vaccines in PubMed, SCOPUS, EMBASE, Google Scholar, Ovid and medRxiv databases, until September 30, 2021. This study followed PRISMA guidelines. Descriptive findings of reported cases were reviewed and stratified by demographic and clinical findings, diagnostic work-up, management, and overall outcome.

Results: A total of 32 cases were identified, with female predominance (68.8%) and median age of 44 years. Eleven cases were reported after Pfizer vaccine, 8 following AstraZeneca vaccine, 6 following Moderna, 5 following Sinovac/ Sinopharm vaccines, and one following each of Sputnik and Johnson&Johnson vaccines. The majority of cases (71.8%) occurred after the first dose of the vaccine, with neurological symptoms manifesting after a median of 9 days. The most common reported presentations were transverse myelitis (12/32) and MS-like pictures (first diagnosis or a relapse) in another 12/32 cases, followed by ADEM-like (5/32), and NMOSD-like (3/32) presentations. History of a previous immune-mediated disease was reported in 17/32 (53.1%) cases. The mRNA-based vaccines resulted in the greatest number of demyelinating syndromes (17/32), followed by viral vector vaccines (10/32), and inactivated vaccines (5/32). Most MS-like episodes (9/12) were triggered by mRNA-based vaccines, while TM occurred following both viral vector and mRNA-based vaccines. Management included high dose methylprednisolone, PLEX, IVIg, or a combination of those, with a favorable outcome in the majority of case; marked/complete improvement (25/32) or stabilized/ partial recovery in the remaining cases. **Conclusion:** This systematic review identified few cases of CNS demyelination following all types of approved COVID-19 vaccines so far. Clinical presentation was heterogenous, mainly following the first dose, however, half of the reported cases had a history of immune-mediated disease. Favorable outcome was observed in most cases. We suggest long-term post-marketing surveillance for these cases, to assess for causality, and ensure the safety of COVID-19 vaccines.

1. Introduction

Coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), had a devastating impact on public health, global economy, and social life worldwide. In response, there has been an unprecedented effort for the rapid development of vaccines, as the most effective tool in reducing

morbidity and mortality (World Health Organisation, 2021).

Despite the challenges related to the development of the vaccine, an emergency use approval has been granted for COVID-19 vaccines by the end of 2020, by different regulatory authorities around the world before the completion of conventional phases of clinical trials.

Currently, there are four types of vaccines against COVID-19; whole virus (live attenuated, inactivated), nucleic acid (mRNA, DNA), viral

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