Acute disseminated encephalomyelitis (ADEM) is a demyelinating disease of the central nervous system (CNS) with acute onset, rapid progression, and multifocal neurological deficits. Acute hemorrhagic leukoencephalitis (AHLE) is a hemorrhagic and more severe variant of ADEM, which may result in coma and death. In this review article, the researchers from Romania analyzed the medical literature on ADEM or AHLE cases that developed after acute infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or COVID-19 vaccination. The authors also presented a case of ADEM that developed after COVID-19 vaccination from their clinical practice.

Infections caused by diverse pathogens can lead to ADEM, particularly those caused by herpes simplex virus, influenza, Epstein–Barr virus, cytomegalovirus, and measles. In addition, postvaccinal ADEM has been reported following immunization against influenza, varicella, measles, mumps, rabies, hepatitis B, diphtheria, and tetanus. Similarly, neuro-immunological adverse events have been reported following the COVID-19 vaccination. A recent review article discussed the association between *de novo* onset or relapse of neuromyelitis optica spectrum disorder (NMOSD), a rare chronic, relapsing, demyelinating, autoantibody-mediated disease of the central nervous system, and SARS-CoV-2 infection or COVID-19 vaccination.
https://discovermednews.com/the-association-between-sars-cov-2-infection-or-anti-sars-cov-2-vaccination-and-neuromyelitis-optica-spectrum-disorder/

About the study

In this systematic review of medical publications from the PubMed database, published

between January 1, 2020, and November 30, 2022, the authors selected articles on ADEM and AHLE cases that developed after severe SARS-CoV-2 infection or COVID-19 vaccination.

The inclusion criteria were as follows: the patients were older than 18 years, had a confirmed diagnosis of ADEM after acute COVID-19 or COVID-19 vaccination, and had undergone a brain and spine magnetic resonance imaging (MRI) scan.

The following data were analyzed from the selected publications: age, gender, type of vaccine, results of reverse transcription-polymerase chain reaction (RT-PCR) test for SARS-CoV-2, latency between the onset of neurological symptoms and SARS-CoV-2 infection/ COVID-19 vaccination, brain and spine MRI scans, cerebrospinal fluid (CSF) examination, other laboratory tests, treatment, and outcome.

Results

This review included 24 publications with 74 cases of acute disseminated encephalomyelitis (ADEM) and 13 patients of acute hemorrhagic leukoencephalitis (AHLE), a hemorrhagic and more severe variant of ADEM, that developed after severe SARS-CoV-2 infection or COVID-19 vaccination.

Of 74 patients with ADEM, 45 developed ADEM after acute COVID-19 infection and 29 after COVID-19 vaccination. Of these 45 individuals with postinfectious ADEM, four patients had a positive RT-PCR test of CSF for SARS-CoV-2.

According to the authors, more than 170 patients who developed ADEM following COVID-19 vaccination were reported to the EudraVigilance database of the European Medicine Agency before the end of March 2022. Of these 170 patients with postvaccinal ADEM, 91 were vaccinated with the BioNTech Pfizer vaccine, 46 with the AstraZeneca vaccine, 27 with the Moderna vaccine, and 8 with the Johnson & Johnson vaccine.

The average time between acute SARS-CoV-2 infection and the onset of ADEM was 19.5 days, and between COVID-19 vaccination and the onset of ADEM was 12.3 days.

Most patients (88%) were treated with corticosteroid therapy alone or with other treatments, including intravenous immunoglobulins (32%), plasmapheresis (18%), and rituximab (5%).

A case of ADEM that developed after COVID-19 vaccination from the clinical practice of the study's authors

A 33-year-old, previously healthy, man was admitted to the neurology clinic. He had no prior medical conditions or family history of autoimmune diseases.

His symptoms started 14 days after his first Johnson & Johnson vaccine. Three days before admission, he experienced fever, headache, nausea, vomiting, decreased muscle strength (mainly in the legs), paresthesias, and urinary retention. Neurologic examination showed spastic tetraparesis, with grade 4+/5 in the upper limbs and grade 4/5 in the lower limbs, hyperreflexia in the lower limbs, bilateral Babinski sign, and acute urinary retention.

Sagittal spinal cord MRI. Longitudinally extensive lesion at the level of the cervical spinal cord. From the original paper of Stoian, A. et al. Vaccines 2023, 11, 1225.

The rt-PCR swab test for SARS-CoV-2 was negative. The tests for a panel of neurotropic viruses (*cytomegalovirus*, *Epstein–Barr* virus, human immunodeficiency virus 1 and 2,

herpes simplex viruses 1 and 2, *hepatitis* B and C, *varicella-zoster* virus, and *rubella*) were negative, as well as the tests for *Treponema pallidum*, *Borrelia burgdorferi,* and toxoplasmosis. The blood tests for endocrinopathies and autoimmune diseases (neuromyelitis optica, antinuclear antibodies, anti-myelin oligodendrocyte antibodies, and autoimmune panel for encephalitis) were also negative.

The CSF examination demonstrated a glucose concentration of 93 mg/dL, protein concentration of 469 mg/dL, and pleocytosis of 650/μL. The majority of CSF cells (95%) were lymphocytes, but the cells were not indicative of lymphoma.

The brain MRI scan showed multiple T2/FLAIR hyperintense, poorly demarcated lesions without contrast enhancement, localized in the white matter of the right frontal and parietal lobes, left occipital lobe, left basal ganglia, pons, and right cerebellar peduncle.

The patient was diagnosed with postvaccinal ADEM and treated with corticosteroids. A control brain MRI scan demonstrated reduced demyelinating lesions. No new lesions were detected 40 days after the initial MRI scan.

Conclusion

This review provided valuable insights into articles describing cases of acute disseminated encephalomyelitis (ADEM) and acute hemorrhagic leukoencephalitis (AHLE) that developed after severe SARS-CoV-2 infection or COVID-19 vaccination, their diagnosis, and treatment.

Although causation cannot be proven, cases with a short latency (from SARS-CoV-2 infection, 19.5 days, and from COVID-19 vaccination, 12.3 days) are less likely to be coincidental. The authors concluded that reported cases of ADEM or AHLE after acute SARS-CoV-2 infection or COVID-19 vaccination require further research in a larger population.

The article was published in Vaccines.

Journal Reference

Stoian, A. et al. The Occurrence of Acute Disseminated Encephalomyelitis in SARS-CoV-2 Infection/Vaccination: Our Experience and a Systematic Review of the Literature. Vaccines

2023, *11*, 1225. (Open Access) https://doi.org/10.3390/vaccines11071225