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Acute disseminated encephalomyelitis (ADEM) can develop after acute SARS-CoV-2 infection or COVID-19 vaccination | 1

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 post-vaccinal ADEM from their clinical practice.

Infections caused by diverse pathogens can lead to ADEM, particularly those caused by herpes simplex, influenza, Epstein-Barr virus, cytomegalovirus, and measles. In addition, postvaccinal ADEM was described following influenza, varicella, measles, mumps, rabies, hepatitis B, diphtheria, and tetanus immunization.

Following the COVID-19 vaccination, various adverse events have been reported, including neurological. 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/> Additionally, several case reports described ADEM that developed 1 to 14 days following COVID-19 vaccination, especially after the first dose of the vaccine.





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About the study

In this systematic review of the medical publications from the PubMed database published between 1 January 2020 and 30 November 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 infection/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 ADEM and 13 patients with AHLE. Out of 74 patients with ADEM, 45 developed ADEM after acute COVID-19 infection and 29 after COVID-19 vaccination. In the postinfectious ADEM group of 45 individuals, CSF from four patients tested positive for SARS-CoV-2 on reverse transcription polymerase chain reaction (rt-PCR) test.

The authors emphasized that more than 170 patients who developed ADEM following vaccination were reported to the EudraVigilance database of the European Medicine Agency until the end of March 2022. Of these 170 postvaccinal ADEM patients, 91 received BioNTech Pfizer vaccines, 46 AstraZeneca vaccines, 27 Moderna vaccines, and 8 Johnson & Johnson vaccines.

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

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

The authors presented a case of postvaccinal ADEM from their clinical practice

A 33-year-old, previously healthy, man was admitted to the neurology clinic. He had no prior

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medical conditions or family history of autoimmune diseases.

His symptoms started 14 days after his first Johnson & Johnson vaccine. Three days before the admission, he experienced fever, headache, nausea, vomiting, decreased muscle strength (mainly in the legs), paresthesias, and urinary retention. The 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, rubella, and hepatitis) were negative, as well as the tests for *Treponema pallidum*, *Borrelia burgdorferi*,



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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 showed a glucose concentration of 93 mg/dL, protein concentration of 469 mg/dL, and pleocytosis of 650/ μ L. 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 diagnosing and treating of acute disseminated encephalomyelitis that developed after SARS-CoV-2 infection or COVID-19 vaccination.

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>