A considerable percentage of patients have neurological symptoms both during and after the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Nearly 30% of COVID-19 patients have neurologic sequelae that affect the central nervous system (CNS) and the peripheral nervous system (PNS). Movement disorders associated with current or past COVID-19 infection or COVID immunization have been documented in many studies. In these two systematic reviews, the authors examined the literature on chorea, a hyperkinetic movement disorder, after COVID-19 infection or COVID vaccination.

Chorea (a term derived from the Ancient Greek that means dance) is a hyperkinetic movement disorder with multiple causes or etiologies. According to the Committee on Classification of the World Federation of Neurology, chorea is a state of excessive, spontaneous movements that are irregularly timed, nonrepetitive, randomly distributed, and abrupt. In many conditions, chorea is generalized, involving the entire body; however, this movement disorder can be strikingly asymmetric or even unilateral. It interferes with speech, swallowing, posture, and gait, disappearing in sleep. There are numerous different etiologies for chorea, including acquired and hereditary ones. Infectious agents, endocrine, metabolic, immunological, paraneoplastic, autoimmune, vascular, toxic, drug-induced, and idiopathic are examples of acquired etiologies.

Interestingly, in 2021, Yapici-Eser et al. utilized a computational methodology to detect mimicry between human proteins and SARS-CoV-2 proteins and classified these interactions

according to the molecular pathways of neuropsychiatric symptoms associated with COVID-19. They found that SARS-CoV-2 proteins mimic 49 proteins linked with Huntington's disease (also known as Huntington's Chorea), the prototypic autosomal dominantly inherited chorea that typically presents with involuntary movements, impaired coordination, cognitive disorders (memory loss and attention deficits), and psychiatric issues (depression, irritability, psychosis, and anxiety). (Yapici-Eser et al. Neuropsychiatric Symptoms of COVID-19 Explained by SARS-CoV-2 Proteins' Mimicry of Human Protein. Front Hum Neurosci 2021; 15: 656313.)
https://www.frontiersin.org/journals/human-neuroscience/articles/10.3389/fnhum.2021.656313/full

The first systematic review

In the first paper, the authors from Romania systematically reviewed LitCOVID, the World Health Organization database on COVID-19, and MedRxiv up to March 2023. They identified 16 articles reporting 22 cases of chorea, 14 associated with SARS-CoV-2 infection, and eight associated with a recent COVID vaccination. In the cases with chorea following SARS-CoV-2 infection, the number of males equaled the number of females (50%), but in the COVID vaccination group, there was a male predominance (87.5%).

In patients infected with SARS-CoV-2, chorea occurred in both vaccinated (21%) and unvaccinated (22%) individuals. 57% did not report vaccination status. Chorea was concomitant with COVID-19 in 50% of cases; it developed within 15-30 days after the onset of COVID-19 in 21% of cases and within 3 months in 7% of cases. The chorea onset was sudden and acute in 57% of cases, whereas 21% had progressive chorea with gradual worsening. Other associated movement disorders like hemiballismus were rare. Cerebrospinal fluid (CSF) samples were taken from six cases. Of these, 50% had normal CSF findings, 33% had increased lymphocyte counts, and 33% had proteinorachia.

Magnetic resonance imaging (MRI) was performed in all cases, and 36% (including one patient with ketoacidosis) had lesions of the basal ganglia. One case presented multiple focal enhancing lesions in the cortical and subcortical regions and the cerebellum, suggesting an autoimmune-mediated process such as acute disseminated encephalomyelitis (ADEM). The coexistence of small vessel disease was reported in 14% of cases.

https://discovermednews.com/wp-content/uploads/2025/02/cureus-0015-00000041327-i01.mp4

Video: Generalized chorea albeit left hemibody predominant. From Grimm BG et al. New-onset chorea post-COVID-19 infection: A case report. Cureus 2023: 15(7): e41327

In patients with chorea associated with COVID-19 vaccination, chorea developed within 2 weeks after vaccine administration. In 25% of cases, chorea was detected after the second dose of the mRNA Pfizer-BioNTech vaccine, in 13% after the second Moderna booster, in 38% after the first dose of ChAdOx1 nCoV-19, and in 25% after the first dose of the inactivated virus vaccine BBIBP-CorV (Sinopharm). Most cases presented unilateral chorea, frequently associated with hemiballismus or other movement disorders (e.g., dystonia, myoclonus, parkinsonism). Additional neurological findings were rare.

CSF samples were taken from six patients, and all had abnormal findings. 83% had proteinorachia, and 17% had oligoclonal bands, markers that indicate an intrathecal immune-mediated process.

Neuroimaging was performed in all cases. 88% showed no lesions or abnormal signals in the basal ganglia. MRI showed an acute thalamic lacunar infarction in one patient (12.5%), and multiple white matter lesions in another young patient. Two patients (25%) presented with cerebral small vessel disease. Two patients underwent fluorodeoxyglucose (FDG)-positron emission tomography (PET) and in one case, it showed increased metabolism in the right putamen, and in another, the findings were normal. One patient underwent single photon emission computed tomography (SPECT), which showed asymmetrically reduced perfusion in the left thalamus.

Antibodies to voltage-gated potassium channel (VGKC) and glutamic acid decarboxylase (GAD) were reported in both groups. However, according to the authors, their significance is unclear, as chorea is a rare manifestation of these antineuronal antibody syndromes.

The second systematic review

In the second systematic review, the authors from the Philippines analyzed the literature on movement disorders that developed after COVID-19 vaccination. This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The research included case series and case reports on patients who

developed hyperkinetic and hypokinetic movement disorders following any COVID-19 vaccine. Inclusion criteria were detailed descriptions of the neurologic symptoms, vaccine received, symptom onset, cranial imaging, treatment, outcome, and possible mechanism of vaccine-related adverse events. There were no restrictions in terms of age, sex, or ethnicity of the population. Studies on patients with prior or ongoing COVID-19 infection or preexisting movement disorders were excluded.

The authors noted that approximately 40 cases of hemichorea and hemiballismus were attributed to COVID-19 vaccination according to a pharmacovigilance database, but, they identified ten published cases. The details of other cases are unknown. They also emphasized that a literature search revealed very few patients with movement disorders related to other vaccinations, like a 30-year-old woman with opsoclonus-myoclonus syndrome that developed after rubella vaccination. Molecular mimicry and cross-reactivity between cerebral and viral antigens were the proposed pathomechanisms.

Results

Eight articles contained 10 patients who met the inclusion criteria. Of these, 4 received the Pfizer BioNTech COVID-19 vaccine, 2 received the AZD1222 vaccine, 2 received the BBIBP-CorV (Sinopharm) vaccine, 1 received the ChAdOx1 nCoV-19 vaccine, and 1 received the Moderna Biotech vaccine. Chorea occurred as early as 12 hours after the COVID vaccination. Most patients (7/10) experienced symptoms after receiving their first dose, and three patients after receiving the second dose of the vaccine. The majority were males (80%), and the median age was 64.5 years.

Importantly, in most cases (70%), hemichorea was the predominant movement disorder after COVID-19 vaccination. The remaining three patients had generalized chorea with myoclonus, cervical dystonia, akathisia, and hemiballismus. These movement disorders have also been reported in pharmacovigilance reports.

Neuroimaging was mostly unremarkable. One of the reported cases had vaccine-induced thrombocytopenia resulting in an ischemic infarct in the thalamus. Another case had voltage-gated potassium channel (VGKC) and glutamic acid decarboxylase (GAD) antibodies, possibly explaining movement disorder as an autoimmune disorder.

Since an autoimmune reaction following vaccination was the proposed pathophysiology for movement disorders associated with COVID vaccination, methylprednisolone, and

intravenous immunoglobulin therapy showed good results in most cases (7/10). In one case report, tetrabenazine was used but was eventually discontinued due to the absence of any effect, after which the patient was switched to methylprednisolone therapy. Clonazepam and botulinum toxin for dystonia and hemichorea, haloperidol for hemichorea, and ropinirole for generalized chorea were other therapeutic options.

Conclusion

Although approximately 40 cases of hemichorea and hemiballismus attributed to COVID-19 vaccination are registered in a pharmacovigilance database, this systematic review identified only 10 cases of vaccine-related movement disorders, suggesting a lack of documentation on movement disorders related to COVID vaccination.

Importantly, according to these systematic reviews, unilateral chorea was the most common movement disorder following the COVID vaccination. Although most authors suggested an autoimmune reaction, the pathogenesis of chorea following the COVID vaccination is unclear.

Unilateral chorea is classically related to a contralateral structural lesion, e.g., of the putamen or the subthalamic nucleus. According to previous studies, the vast majority of asymmetric or hemichorea cases are acquired, such as, but not limited to, Sydenham's and other autoimmune diseases, polycythemia vera, *chorea gravidarum*, and hyperglycemic hemichorea/hemiballism, rather than with genetic, degenerative, or congenital causes. Autoimmune causes of chorea have been recognized when antibodies to basal ganglia were identified in Sydenham disease. (Cincotta M, Walker RH. One Side of the Story; Clues to Etiology in Patients with Asymmetric Chorea. Tremor and Other Hyperkinetic Movements. 2022; 12(1): 3, pp. 1–14). https://doi.org/10.5334/tohm.675

On the other hand, chorea in patients with SARS-CoV-2 infection may be caused by direct damage related to infection (as suspected with other pathogens), infection-related complications, or an autoimmune response. According to the first systematic review, MRI showed lesions of the basal ganglia in 36% of chorea cases following the SARS-CoV-2 infection (including one patient with ketoacidosis).

In addition, both, severe SARS-CoV-2 infection and COVID vaccination may trigger ADEM and lead to basal ganglia lesions and subsequent generalized chorea. https://discovermednews.com/acute-disseminated-encephalomyelitis-after-sarscov2-infection

-or-vaccination/ Also, in both groups chorea may indicate potentially severe complications like thromboembolism.

The authors concluded that the lack of standardized reporting of individual cases of movement disorders associated with COVID-19 infection or vaccination and the quality and extent of information in the included reports limit the results.

These articles were published in the International Journal of Infectious Diseases and Journal of Movement Disorders.

Journal References

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