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Autoimmune Encephalitis as an Adverse Event of COVID-19 Vaccination

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Dear Editor,

Neurological complications in coronavirus disease 2019 (COVID-19) patients have been reported previously, such as from a retrospective multicenter study of 64 patients with confirmed COVID-19 from 11 hospitals reviewing neurological manifestations and brain magnetic resonance imaging (MRI).[1] Here we describe a very rare case of autoimmune encephalitis following a COVID-19 vaccination.

A 35-year-old female visited an emergency room presenting with dysarthria and abnormal movements. She had received her first dose of the ChAdOx1 nCoV-19 vaccine 5 days previously. She reported a mild fever and headache 1 day after the vaccination, and on the following day her movements were slower when riding on indoor bike. Additionally, she used to enjoy dancing every evening when singers were on the television, but she was not able to dance anymore. Symptoms of dysarthria, extreme anxiety, and reduced voluntary movements had also developed. Her symptoms progressively worsened, so she was no longer able to communicate 3 days after the vaccination. On examination, she had mild fever (37.5°C) and sinus tachycardia (110/min). Her arousal was intact, but she had severe rigidity in all of her extremities, catatonia, motor aphasia, jaw-opening dystonia, hypophonia, and drooling (Supplementary Video 1 in the online-only Data Supplement). There was no pathological reflex. Although she had intellectual disability of a 7-year-old child level since she was a child since elementary-school level, she had not previously experienced any problems with her gait, activities of daily living, or speech.

Brain MRI showed mild swelling of the right hippocampus without abnormal enhancement in contrast-enhanced fluid-attenuated inversion recovery (FLAIR) and T1-weighted images (Fig. 1). Chronic encephalomalacia in both frontoparietal lobes was also observed, which was assumed to be a cause of her pre-existing intellectual disability. Electroencephalography revealed diffuse beta wave activity, with intermittent generalized delta waves. Bacterial or fungal infections were excluded based on the cerebrospinal fluid (CSF) profile (Supplementary Table 1 in the online-only Data Supplement). We administered simultaneous intravenous methylprednisolone and immunoglobulin for 5 days based on suspicion of vaccination-induced autoimmune encephalitis. Intravenous acyclovir was also administered since viral encephalitis could not be excluded. After 1 week her catatonia, rigidity, and drooling had improved, and she could walk for a short distance without assistance. Her score on the modified Rankin Scale improved from 5 to 3. However, she still had significant rigidity and could barely communicate (Supplementary Video 2 in the online-only Data Supplement).

Reverse transcriptase polymerase chain reaction (RT-PCR) assays for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus in samples taken from her upper and lower respiratory tracts were negative. The results for the following autoimmune encephalitis antibodies were also all negative: serum paraneoplastic antibodies, anti-myelin oligodendrocyte (MOG) antibody, serum and CSF synaptic antibodies, serum antiganglioside anti-

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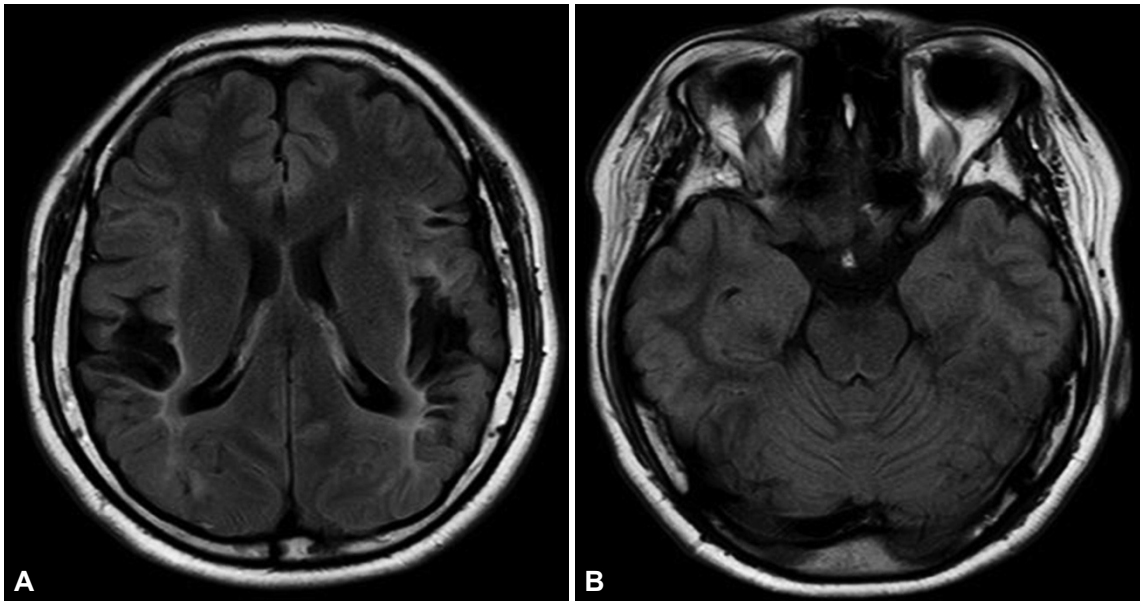

Fig. 1. Brain magnetic resonance imaging of the patient. The contrast-enhanced fluid-attenuated inversion recovery images show chronic encephalomalacia in bilateral frontoparietal lobes (A) and mild swelling in the right hippocampus (B).

bodies, and CSF oligoclonal band. Infection laboratory findings including for culturing and PCR were also all negative. She was not tested for antibodies against the SARS-CoV-2 virus. To explore the possibility of hidden cancer, chest and abdomen computed tomography as well as torso fluorodeoxyglucose positron-emission tomography were performed, but these findings were also normal. Follow-up cranial MRI performed 4 weeks after symptom onset showed no significant changes. We eventually started the patient on weekly rituximab, and she is monitored for further improvement.

The present case presented with autoimmune encephalitis after receiving the ChAdOx1 nCoV-19 vaccine. However, laboratory test results, including for autoimmune encephalitis antibodies, did not support the etiology.

Cases of autoimmune encephalitis secondary to COVID-19 infection have been reported previously.[2,3] Neurological symptoms in COVID-19 are attributed to interleukin-6, an important factor in the cytokine storm, or the presence of autoreactive antibodies targeting the central nervous system. Indeed, there are even cases of postinfectious encephalitis associated with anti-N-methyl-D-aspartate receptor (NMDAR) antibodies and anti-MOG antibodies in COVID-19 patients.[3,4]

Similarly, neurological complications following vaccination have also been well recognized. In particular, previous reports have shown that anti-NMDAR encephalitis can be associated with H1N1 influenza, tetanus, diphtheria, pertussis, and poliomyelitis vaccines.[5] Regarding the ChAdOx1 nCoV-19 vaccine, there have been cases of thrombotic thrombocytopenia and acute transverse myelitis as rare serious adverse events, which may be caused by the replication-deficient chimpanzee adenovirus adjuvant that the vaccine contains.[6,7]

We hypothesize that this rare clinical condition developed in our patient due to autoimmune activation by the ChAdOx1 nCoV-19 vaccine. This case report demonstrates that rare serious adverse events still have to be considered when administering COVID-19 vaccinations.

Supplementary Video Legend

Video 1. The patient initially presented with severe rigidity, catatonia, and jaw-opening dystonia.

Video 2. After intravenous high-dose steroid and immunoglobulin treatment, her catatonia, rigidity, and drooling improved partially. She could walk for a short distance without assistance, and her score on the modified Rankin Scale improved from 5 to 3.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2022.18.1.114.

Ethics Statement

The study was approved by Chungbuk National University Hospital's Institutional Review Board (2021-05-006-001). The patient provided informed consent to publish the manuscript and supplementary videos.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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