

## Letter to the Editor



# Post COVID-19 Vaccination Encephalitis as a Cause of Subacute Progressive Dementia: A Case Report and Literature Review

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**Received:** Mar 22, 2023  
**Revised:** Apr 21, 2023  
**Accepted:** Apr 26, 2023  
**Published online:** Apr 30, 2023

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### Conflict of Interest

The authors have no financial conflicts of interest.

### Author Contributions

Conceptualization: Jung HS, Hong YJ;  
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The coronavirus disease 2019 (COVID-19) pandemic has caused more than 500 million infected cases, causing a new public health crisis.<sup>1</sup> Many people are vaccinated against COVID-19 to prevent infection and bring an end to the pandemic. However, various complications have been reported.<sup>1,2</sup> Autoimmune encephalitis is a progressive encephalopathy that can develop rapidly (usually in less than 6 weeks) caused by brain inflammation.<sup>3</sup> In this case report, we present a rare case of a 59-year-old woman who visited an outpatient clinic because of subacute onset cognitive decline. She was diagnosed with post COVID-19 vaccination encephalitis. We observed 1-year cognitive outcomes and neuroimaging changes of the patient. Clinical, neuroimaging, and cerebrospinal fluid (CSF) findings of the patient are described below.

A 59-year-old woman visited our outpatient clinic due to subacute cognitive impairments and abnormal behaviors for 3 weeks. She had diabetes mellitus, hypertension, hyperlipidemia, and hypothyroidism on stable medications. She had received the second COVID-19 vaccination (BNT162b2, BioNTech and Pfizer). She suffered from generalized weakness and mild frontal headache without any other symptoms such as nausea or fever. At one month after the vaccination, she showed memory impairments and disorientation and started to get lost in familiar places. Her younger sister reported that the patient had inappropriate self-talking and aggressive behaviors. These symptoms were progressive for a few weeks. However, they had become stationary before the admission. On admission, physical examination and vital signs were normal. On neuropsychological tests, the Mini-Mental State Examination (MMSE) score was 13 (7 years of education) and the clinical dementia rating (CDR) score was 2, suggesting moderate to severe dementia. She showed cognitive impairments in naming, verbal and visual memory encoding, visuospatial, and frontal executive functions (**Table 1**). Brain magnetic resonance (MR) imaging revealed high signal intensities in left anterior & medial temporal lobe in fluid attenuated inversion recovery imaging with gyral enhancements in T1-weighted contrast enhancement (**Fig. 1**). MR angiography showed no large vessel stenosis. On CSF examination, total protein was slightly increased to 47.3 mg/dL, while other findings (1 WBC/mm<sup>3</sup>, 0 RBC/mm<sup>3</sup>) were normal. CSF cytology, antibodies for autoimmune encephalitis, infection markers (including viral markers), and serologic paraneoplastic antibodies were unremarkable. An electroencephalography also showed normal findings. Considering her stable course and refusal to an intravenous steroid therapy, the patient received conservative treatment without any immunosuppressive agents. Her symptoms were stable during admission.

**Table 1.** Patient’s cognitive trajectories using neuropsychological tests

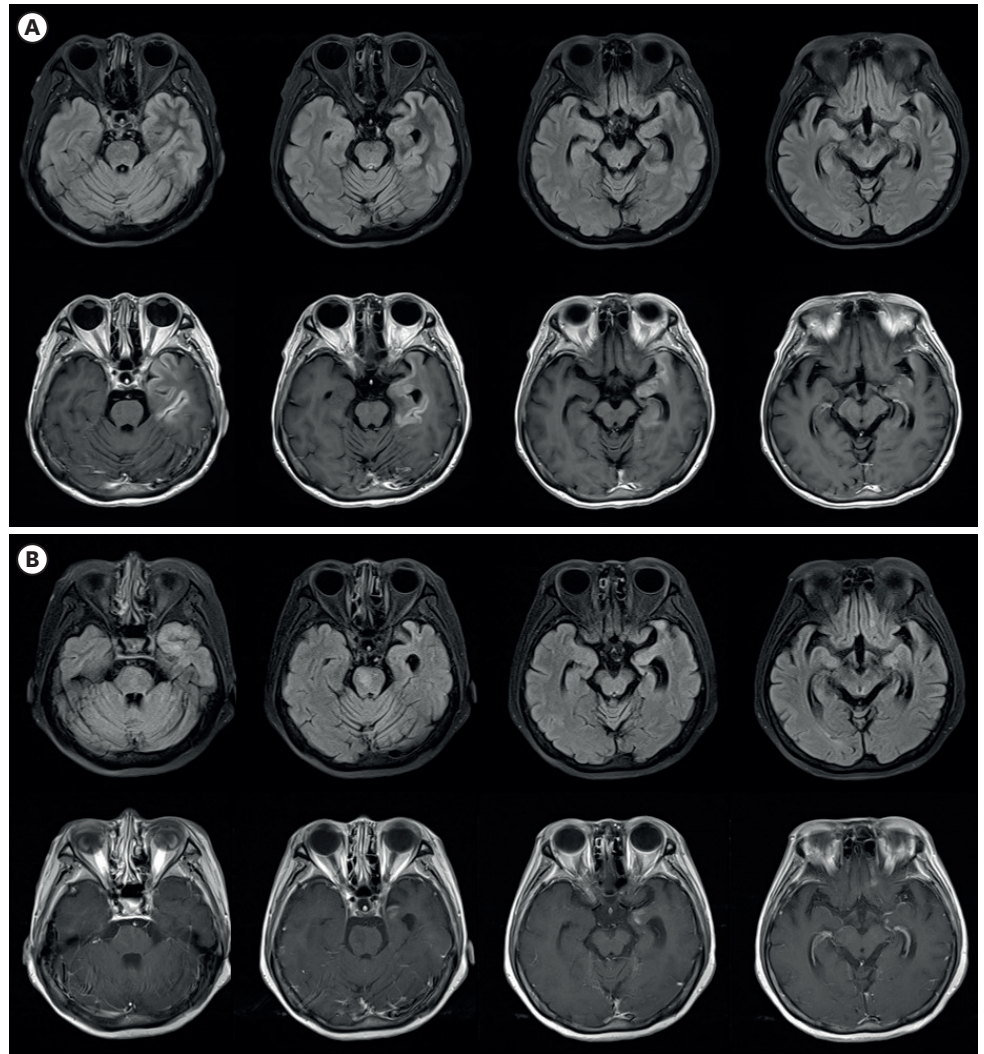
Variables	2021.11.18	2022.3.4	2023.1.11
K-MMSE	13	14	17
CDR (SB)	2 (10)	1 (6)	1 (6)
K-IADL	2.1	0.6	0.8
Geriatric depression scale	7/15	0/15	10/15
Digit span forward (percentile)	19.79	6.72	6.72
K-BNT	0.01	0.01	0.01
RCFT, copy	0.01	0.10	0.01
SVLT, immediate recall	0.01	0.01	0.02
SVLT, delayed recall	0.07	0.15	0.15
SVLT, recognition	2.76	0.06	5.03
RCFT, immediate recall	1.87	4.99	2.07
RCFT, delayed recall	0.35	2.44	0.68
RCFT, recognition	1.13	0.08	5.39
COWAT, phonemic	0.19	0.35	0.24
Stroop, color reading	Uncheckable	0.01	Uncheckable

K-MMSE: Korean version of the Mini-Mental State Examination, CDR: clinical dementia rating, SB: sum of boxes, K-IADL: Korean version of instrumental activities of daily living, K-BNT: Korean version of Boston naming test, RCFT: Rey complex figure test, SVLT: Seoul verbal learning test, COWAT: controlled oral word association test.

Her cognitive function was improved to mild to moderate dementia (MMSE 14, CDR 1 [sum of boxes: 6]) at 3 months after discharge (**Table 1**). According to her sister, she could perform everyday housework independently without any help and go out to meet other people just before re-admission due to a pontine infarction after 16 months. At the re-admission, left temporal lesions disappeared and became atrophic (**Fig. 1**).

Our patient visited a hospital due to cognitive decline. She was diagnosed as encephalitis. On laboratory tests, there was no positive result in autoimmune antibody markers or plausible provoking event/signs suggesting central nervous system (CNS) infection. Thus, we assumed that her encephalitis might be induced by COVID-19 vaccination. Our case fulfilled the criteria for possible autoimmune encephalitis suggested by Graus et al.<sup>3</sup> Autoimmune encephalitis might be associated with antibodies against neuronal cell surface or synaptic proteins. It can develop with symptoms resembling infectious encephalitis. It can also show neurological and psychiatric manifestations without fever or CSF pleocytosis.<sup>3</sup> After vaccination, antigens are recognized as potential pathogens and activate circulating immune cells. Peripheral proinflammatory cytokines expressed after vaccination are important because they might partly cause neuroinflammatory reactions by microglial activation.<sup>4</sup> These processes exhibit cognitive impairments of autoimmune encephalitis.<sup>4</sup> The incidence of post-vaccination encephalitis associated with Pfizer-BioNTech mRNA vaccine has been reported to be 2 per 10 million doses of vaccinations. Complications due to such encephalitis are very rare.<sup>4</sup> The Pfizer vaccine is based on mRNA. Although there are a variety of CNS symptoms, cognitive impairments are easily underdiagnosed due to its non-specificity.<sup>1,2,4,5</sup> Our case report has a few limitations in that we cannot prove a cause-and-effect relationships between the vaccine and encephalitis. Because vaccination-induced encephalitis is considered a reversible cause of dementia, her remnant cognitive declines after 1 year should be re-evaluated further due to a possibility of underlying neurodegenerative disorders.

In summary, we report a rare case of vaccination induced encephalitis in a patient presented with dementia. Thus, we should carefully examine and undergo history takings for elderly patients with cognitive impairments to exclude reversible causes. Clinicians should consider autoimmune encephalitis as a possible diagnosis when assessing post-vaccination neurologic symptoms and subacute dementia.



**Fig. 1.** Brain magnetic resonance images of the patient. (A) Left temporal high signal intensities (upper, fluid attenuated inversion recovery) and gyral enhancements (lower, T1-weighted contrast enhancement) at initial admission. (B) Disappearance of the left temporal lesion after one year.

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