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Case Report

A Case of Inflammatory Demyelinating Disease of the Central Nervous System Presenting with Clinical Manifestation of Multiple Sclerosis Following SARS-CoV-2 mRNA Vaccination

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Summary

A 57-year-old woman presented with abnormal sensations and muscle weakness in the left upper and lower limbs and difficulty in walking four days after coronavirus disease 2019 (COVID-19) vaccination. The patient had deep sensation deficits and increased tendon reflexes in the left upper and lower limbs. Her head and cervical spinal cord magnetic resonance imaging showed a ring-shaped contrast-enhancing lesion. Cerebrospinal fluid examination showed a mildly elevated cell count, myelin basic protein, and IgG index, and positive oligoclonal bands. The patient was diagnosed as inflammatory demyelinating diseases of the central nervous system (IDDCNS) due to vaccination and was treated with pulse steroids. Her symptoms improved to a greater degree compared to previously reported cases of IDDCNS after COVID-19 vaccination. The disease course of this case was monophasic, but was more similar to multiple sclerosis than to acute disseminated encephalomyelitis (ADEM) according to their diagnostic criteria. Careful long-term observation is necessary because vaccination, as in this case, may lead to relapses in multiple sclerosis (MS) patients who have not received disease-modifying drugs.

Key Words: Inflammatory demyelinating diseases of the central nervous system, Multiple sclerosis, Acute disseminated encephalomyelitis, COVID-19 vaccination, SARS-CoV-2

Introduction

Coronavirus disease 2019 (COVID-19), which was first identified in Wuhan, China at the end of 2019, developed into a global epidemic. COVID-19 vaccination was initiated as a measure to prevent infection. Subsequently, adverse reactions were often experienced after COVID-19 vaccination. The most common adverse reactions are fever, general malaise, and myalgia. As of January 2, 2022, a total of 33 cases of multiple sclerosis after COVID-19 vaccination had been reported: 12 after Pfizer-BioMTech, 11 after Takeda-Moderna, and 0

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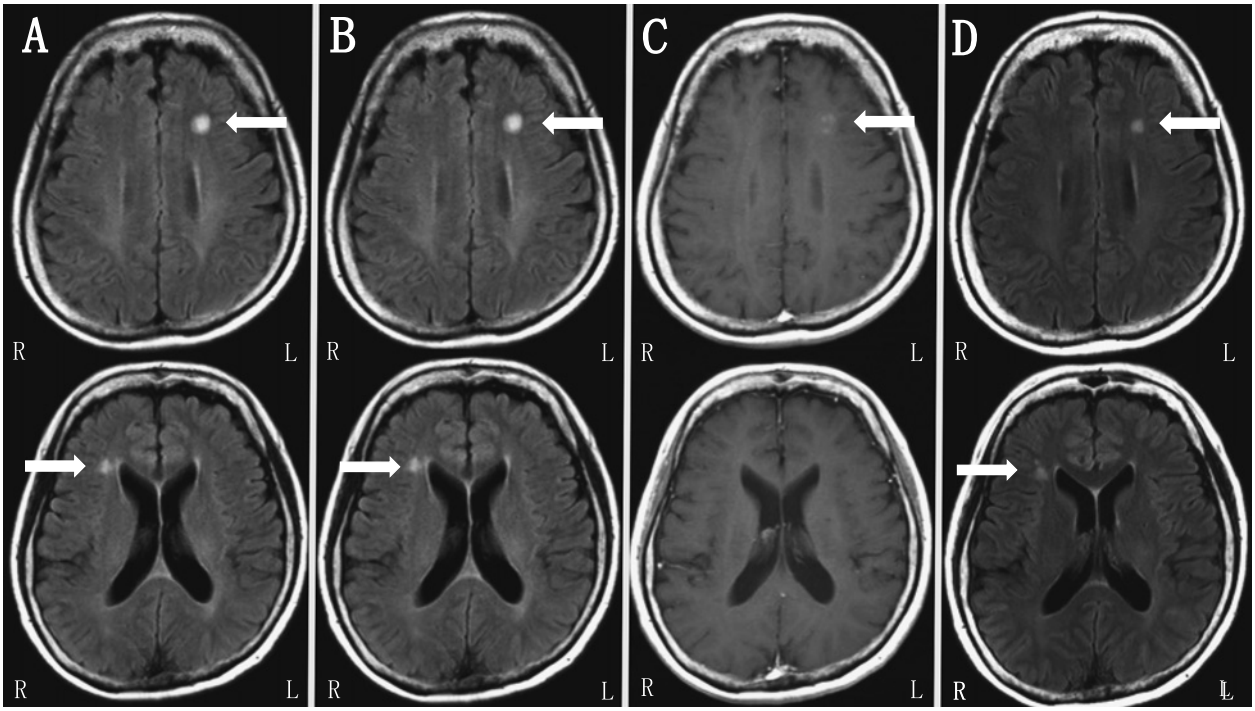

Figure 1 Brain MRI findings (axial view).
Fluid-attenuated inversion recovery (FLAIR) hyperintensity involving the left frontal white matter and right periventricular white matter on day 13 from symptom onset **(A)**. On day 21 after symptom onset, there was no significant change on FLAIR **(B)**. Left frontal white matter lesion exhibited mild gadolinium enhancement **(C)**. FLAIR on day 146 after symptom onset **(D)**.

after AstraZeneca[1]. We encountered a case of inflammatory demyelinating diseases of the central nervous system (IDDCNS)[2] after COVID-19 vaccination and report the main points of differentiation and comparison with previously reported cases after COVID-19 vaccination.

Clinical Summary

A 57-year-old woman was admitted to the hospital with complaints of weakness of the left upper and lower limbs, difficulty in walking, and numbness from the left shoulder to the fingertips; she received the first dose of Cominati® (BNT162b2, Pfizer) in August 2022. Four days later, she became aware of her difficulty in using the left upper and lower limbs and numbness in the left upper limb (day 1 of onset). The symptoms worsened, and the patient visited our hospital on day 13 of onset. Her temperature was 36.7°C, blood pressure was 106/78 mmHg, and pulse rate was 66 bpm. Her neurological examination showed clear consciousness, no Lhermitte's sign, and no Uhthoff's sign. There were no abnormalities in the cranial nerve examination. Manual muscle testing (MMT) showed MMT grade 3 in the distal and proximal muscles of the left upper limb and MMT grade 4 in the proximal muscles of the lower limb, with a grip strength of 23 kg on the right side and 8 kg on the left side. There were increased tendon reflexes in both upper and lower limbs and negative Babinski's sign. There was numbness in the left upper limb beyond the shoulder joint and deep sensory disturbance in the left upper and lower limbs, whereas the tactile and thermal sensations were normal. There was no motor incoordination, but the Romberg test was positive. There was no bladder or rectal disorder.

Brain magnetic resonance imaging (MRI) showed high-signal areas on Fluid-attenuated Inversion Recovery (FLAIR) images near the anterior horn of the right ventricle and in the left frontal subcortex (Fig. 1 A), while contrast-enhanced MRI showed contrast enhancement of the left frontal lesion (Fig. 1 B, C). Cervical MRI showed a T2 high-signal area at the level of C4 (Fig. 2 A-C) and contrast-enhanced cervical MRI showed mild contrast uptake (Fig. 2 D-G).

Upon hospitalization, the cerebrospinal fluid (CSF) showed opening pressure of 150 mmH_2O, cell count of

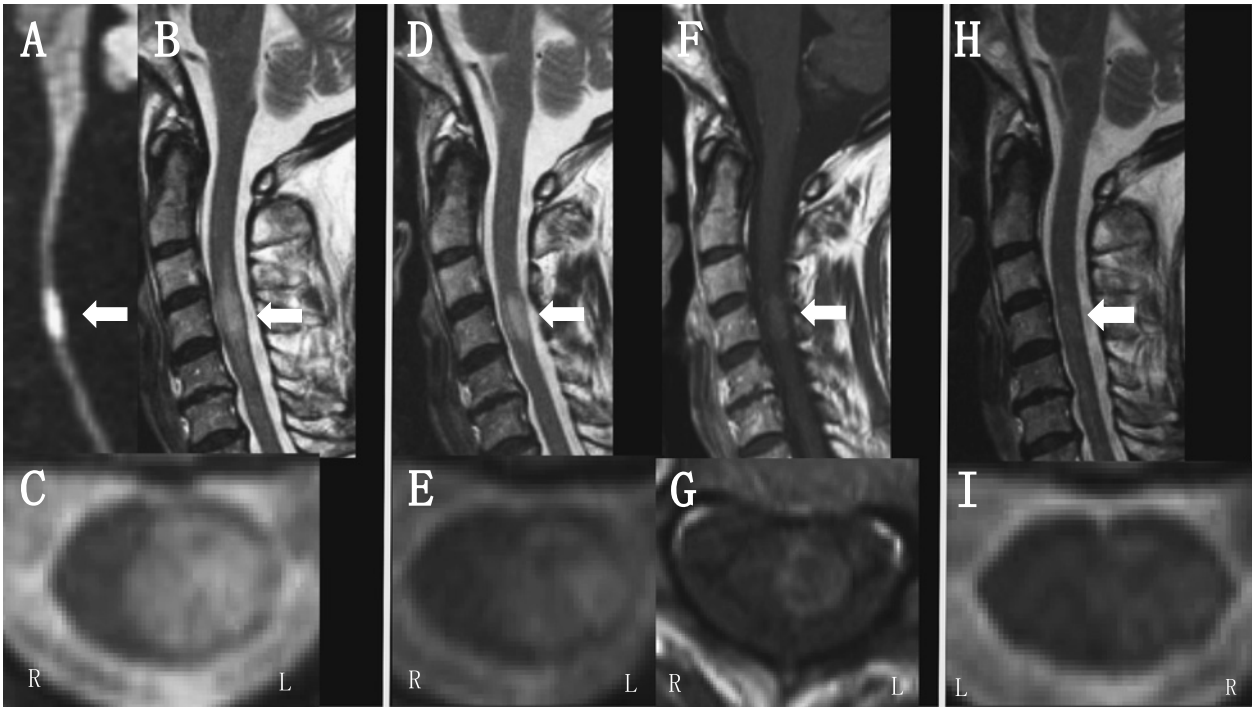

Figure 2 Cervical spine MRI findings.
On day 20 after symptom onset, MRI with diffusion-weighted image (DWI) (**A:** sagittal view) and T2 weighted image (**B:** sagittal view, **C:** axial view) was performed. On day 21 from symptom onset, T2-weighted image (**D:** sagittal view, **E:** axial view) and post contrast T1-weighted image (**F:** sagittal view, **G:** axial view) were analyzed. On day 146 from the onset of symptoms, T2 weighted image was evaluated (**H:** sagittal view, **I:** axial view).

8/μL (predominant mononuclear cells), protein level of 29.4 mg/dL, glucose level of 56.0 mg/dL, CSF/serum sugar ratio of 0.58, IgG index of 1.71, IL-6 level of 5.3 pg/mL, IL-10 level of < 2 pg/mL, myelin basic protein (MBP) of 176 pg/mL (reference range, < 102), and positive oligoclonal IgG band (OCB). Herpes simplex virus, varicella-zoster virus IgM (EIA), cytomegalovirus IgM (CLIA), general bacterial culture, and acid-fungus culture were negative. The cytology result was class I. Antigen test for SARS-CoV-2 and PCR test of pharyngeal swab fluid were negative. Serum anti-nuclear antibody, anti-GM1 antibody (ELISA), anti-GQ1b antibody (ELISA), anti-AQP4 antibody (ELISA), and anti-myelin-oligodendrocyte glycoprotein (MOG) antibody (CBA) were negative. SARS-CoV-2 anti-spike protein IgG antibody (ECILA) was 3.6 AU/mL (reference range: < 1.0 AU/mL). She had a history of cervical cancer surgery in her 30s, but her CEA, CA19-9, CA125, AFP, CA125, and CYFRA levels were within the normal range.

Based on the post-hospitalization course (Fig. 3) and laboratory findings, a diagnosis of IDDCNS due to vaccination was made. The overall disability scale EDSS (Expanded Disability Status Scale) was 6.0. Referring to the diagnostic criteria for autoimmune encephalitis[3] and the revised McDonald diagnostic criteria[4], this case was diagnosed as multiple sclerosis (MS). Two courses of 1000 mg/day of intravenous methylprednisolone (IVMP) were administered for 3 days from day 20 of symptom onset. The muscle weakness improved and the patient was able to walk unassisted. She was discharged home on day 31 of symptom onset. Brain MRI was performed on day 146 of symptom onset (Fig. 1 D). Cervical MRI on day 153 of symptom onset (Fig. 2 H, I) showed no new lesions. On examination performed on day 470 of symptom onset, only mildly residual numbness was present at the finger tips. No disease-modifying drugs were used.

Discussion

On day 4 after COVID-19 vaccination, the patient presented with CNS symptoms, acute course, multiple cerebral and cervical spinal cord lesions with contrast enhancement on MRI, elevated MBP, and positive OCB in CSF. Negative findings of serum anti-AQP4

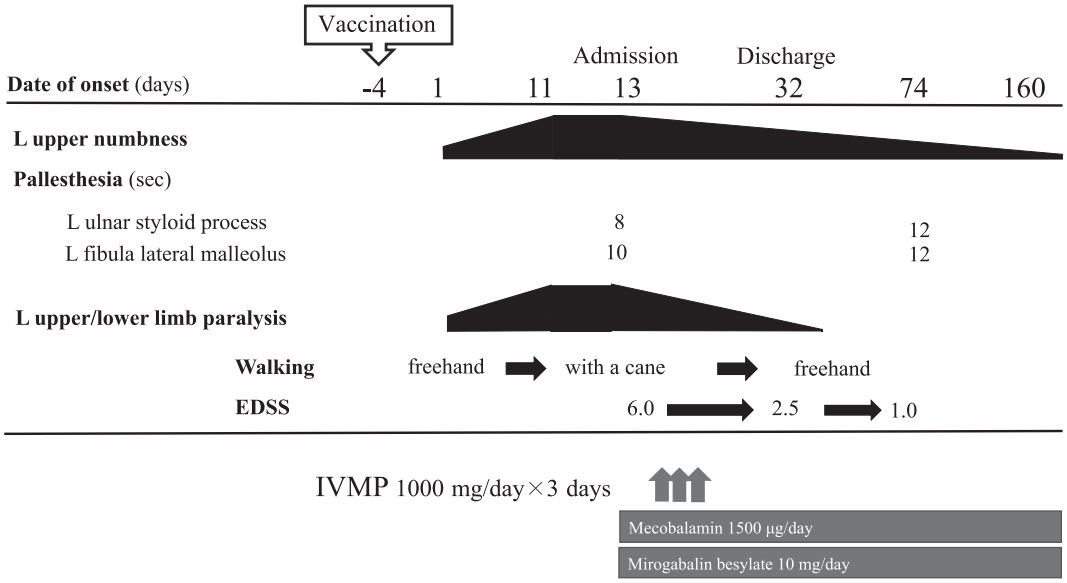

Figure 3 Clinical course
EDSS, expanded disability status scale; IVMP, intravenous pulsed methylprednisolone; L, left.

and MOG antibodies ruled out the diagnoses of neuromyelitis optica spectrum disorder (NMOSD) and MOG antibody-associated disease. Furthermore, infectious myelitis, neoplastic lesions, vitamin deficiency, and other diseases were ruled out. COVID-19 vaccine-related CNS adverse reactions include cerebral venous sinus thrombosis (14.47%), IDDCNS (transverse myelitis, ADEM, MS, and NMOSD) (9.30%), encephalopathy/encephalitis (3.10%), and others (4.13%)[5]. The present case was diagnosed as IDDCNS that developed after COVID-19 vaccination.

This case fulfilled the 2017 revised McDonald diagnostic criteria[4] for MS, with spatial multiplicity, contrast-enhancing and non-contrast-enhancing lesions on a single MRI, and temporal multiplicity. However, we considered it necessary to exclude ADEM. A diagnosis of definite ADEM is made if the following five criteria are met: 1) multifocal, clinical CNS disorder, probably due to inflammatory demyelination, 2) encephalopathy that is difficult to explain by fever, 3) and abnormal brain MRI findings, including large diffuse, and poorly demarcated lesions (> 1-2 cm), mainly in the white matter of the brain. Rarely, T1 low-signal areas are seen in the white matter, 4) no new clinical symptoms or MRI findings 3 months after onset, and 5) other possible causes have been excluded.

In the acute phase of ADEM, CSF shows mild to moderate hypercellularity with mononuclear cell predominance in 30-85% of cases and mildly increased protein in 25-70% of cases, but may be normal. The MBP level is elevated, reflecting demyelination. However, OCB positivity is less common in ADEM than in MS (0-30%), and even when positive, it is transient. MRI is characterized by T2-weighted and FLAIR images showing a 5 mm to 5 cm high-signal area with indistinct borders extending from the subcortical white matter to the deep white matter in the cerebrum, with multiple asymptomatic areas. The contrast enhancement effect of gadolinium in the acute phase is variable[5]. Lesions may be present in the grey matter, including the cortex, thalamus, and basal ganglia, as well as in the cerebellum, brainstem, spinal cord, and optic nerves. However, these areas are rarely affected alone and are usually accompanied by cerebral lesions. In the present case, contrast-enhanced MRI showed ring or open ring lesions in the cerebrum and spinal cord, with imaging findings similar to MS. With regard to ADEM, the diagnostic criteria for definite ADEM were not met, as criteria numbers two and three were not fulfilled.

In a previous report[6], an association between vaccination and onset of MS was observed for hepatitis B vaccine, varicella virus vaccine, mumps virus vaccine, measles virus vaccine, and rubella virus vaccine. On the other hand, there are reports of no change in the risk of MS relapse with vaccination[7,8]. The present case

Table 1 Cases of first-onset and relapsed multiple sclerosis (MS) after COVID-19 vaccination

Author	Age/ Gender	Past medical and family history	COVID-19 infection	Name of vaccine	Vaccine type	Number of doses	Vaccination to onset time	CNS demyelination	Clinical features	Laboratory data	CSF	MRI	Treatment	Outcome
Sriwastava S, et al. [5]	UNK	RRMS	UNK	UNK	UNK	1st	UNK	MS relapse	UNK	UNK	UNK	UNK	IVMP	Improved
Havla J, et al. [9]	28/F	MS family history	Negative	Pfizer-BioMTech	mRNA	1st	6 days	MS	L abdominal neuropathic pain, sensory impairment below the Th6 level, and L leg paresis	SARS-CoV-2 IgG: 50.8 U/mL (37 days after vaccination)	OCB (+)	Th6, multiple (> 20) Brain	IVMP 2nd cycle, and PE	Partial improvement
Mathew T, et al. [10]	24/F	MS	NA	AstraZeneca	Viral vector	2nd	7 days	MS	Paresthesia of L upper and lower limbs, and positive Lhermitte's phenomena	NA	NA	Brain and spinal cord	IVMP and oral steroids	Marked recovery
Watad A, et al. [11]	45/F	Hypothyroidism	Negative	Pfizer-BioMTech	mRNA	1st	7 days	MS	L leg weakness, disequilibrium, and distal numbness of lower limbs	Normal	OCB (+)	Multiple PV white matter	IVMP	Marked recovery
Etemadifar M, et al. [12]	34/F	RRMS	Negative	Gam-COVID-Vac	Viral vector	1st	3 days	MS relapse	Fatigue, myalgia, generalized weakness, which progressed to severe R hemiplegia and ataxia	Normal	Not done	PV, juxtacortical, brainstem, and cerebellar peduncle lesions	IVMP	Marked recovery

Table 1 Cases of first-onset and relapsed multiple sclerosis (MS) after COVID-19 vaccination (continued)

Author	Age/ Gender	Past medical and family history	COVID-19 infection	Name of vaccine	Vaccine type	Number of doses	Vaccination to onset time	CNS demyelination	Clinical features	Laboratory data	CSF	MRI	Treatment	Outcome
Maniscalco GT, et al. [13]	26/F	RRMS	NA	Pfizer-BioMTech	mRNA	1st	2 days	MS relapse	Paresthesia in L arm and weakness in L upper and lower limbs	Normal	NA	Frontal and temporal cortices	IVMP	Complete recovery
Khayat-Khoei M, et al. [14]	Pt. 1, 35/F	RRMS	Negative	Takeda-Moderna	mRNA	2nd	21 days	MS relapse	R arm dysmetria and impaired balance/gait	Negative	Not done	R cerebellum	IVMP	Complete recovery
	Pt. 2, 26/F	None	Negative	Takeda-Moderna	mRNA	2nd	14 days	MS	Blurred vision and pain of L eye	Negative	Elevated cell count and IgG index	PV, subcortical, posterior fossa, and spinal cord lesions	IVMP	Complete recovery
	Pt. 3, 24/F	RRMS	NA	Pfizer-BioMTech	mRNA	2nd	1 days	MS relapse	Vision change and pain in L eye	Positive serum SARS-CoV-2 spike antibody	Not done	Brain lesions without any optic abnormalities	IVMP	Complete recovery
	Pt. 4, 33/M	None	NA	Pfizer-BioMTech	mRNA	2nd	1 days	MS	Unilateral painless blurring of vision	Negative	OCB (+) and elevated IgG index	Multiple white matter lesions	IVMP	Complete recovery
	Pt. 5, 44/F	RRMS	NA	Takeda-Moderna	mRNA	2nd	6 days	MS relapse	Numbness and R-sided weakness	NA	Not done	Brain	IVMP	Complete recovery

Table 1 Cases of first-onset and relapsed multiple sclerosis (MS) after COVID-19 vaccination (continued)

Author	Age/ Gender	Past medical and family history	COVID-19 infection	Name of vaccine	Vaccine type	Number of doses	Vaccination to onset time	CNS demyelination	Clinical features	Laboratory data	CSF	MRI	Treatment	Outcome
	Pt. 6, 48/F	CIS	NA	Pfizer-BioMTech	mRNA	1st	15 days	MS	Pain with R eye movement, worsened Lhermitte's, and balance/ gait difficulty	NA	Not done	White matter lesions	Oral steroids	Marked recovery
Seyed Ahadi M, et al. [15]	42/F	RRMS	NA	Sinopharm vaccine	inactivated	1st	2 days	MS relapse	Paraparesis without paresthesia	Normal	Not done	Brain and cervical	IVMP	Improved recovery
Nistri R, et al. [16]	Pt. 1, 45/M	RRMS	UNK	AstraZeneca	Viral vector	1st	21 days	MS relapse	Dysesthesia in both legs	UNK	UNK	Temporal gyri and spinal cord lesion at Th3 level	IVMP	UNK
	Pt. 2, 48/F	None	UNK	AstraZeneca	Viral vector	1st	8 days	MS	Visual acuity deficit in her R eye	UNK	UNK	Corpus callosum and multiple white matter lesions	IVMP	Marked recovery of the visual deficit
	Pt. 3, 54/F	RRMS	UNK	AstraZeneca	Viral vector	1st	3 days	MS relapse	Hypoesthesia below the T6 level	UNK	UNK	Thoracic spinal cord	IVMP	Complete recovery
	Pt. 4, 66/F	None	UNK	AstraZeneca	Viral vector	1st	7 days	MS	Visual disturbance and postural instability on the R limbs	UNK	OCB (+)	Multiple white matter lesions	IVMP	Partial recovery
	Pt. 5, 42/F	RRMS	UNK	Takeda-Moderna	mRNA	1st	14 days	MS relapse	Slight weakness of the L upper limb	UNK	UNK	Multiple lesions	UNK	UNK

Table 1 Cases of first-onset and relapsed multiple sclerosis (MS) after COVID-19 vaccination (continued)

Author	Age/ Gender	Past medical and family history	COVID-19 infection	Name of vaccine	Vaccine type	Number of doses	Vaccination to onset time	CNS demyelination	Clinical features	Laboratory data	CSF	MRI	Treatment	Outcome
	Pt. 6, 57/F	RRMS	UNK	Takeda-Moderna	mRNA	2nd	14 days	MS relapse	Motor deficit in both legs	UNK	UNK	Pontine lesion	IVMP	Partial recovery
	Pt. 7, 49/F	RRMS	UNK	Pfizer-BioMTech	mRNA	1st	5 days	MS relapse	Numbness on the L hand and L-side of head	UNK	UNK	Brain and spine	IVMP	Almost complete recovery
	Pt. 8, 39/M	RRMS	UNK	Pfizer-BioMTech	mRNA	1st	10 days	MS relapse	Paraesthesia on L leg	UNK	UNK	L parietal lobe and PV white matter	Oral steroids	Partial recovery
	Pt. 9, 39/F	None	UNK	Pfizer-BioMTech	mRNA	1st	3 days	MS	Dysesthesia on R hand and foot	UNK	UNK	Mesencephalon	IVMP	Good recovery
	Pt. 10, 60/F	RRMS	UNK	Pfizer-BioMTech	mRNA	1st	2 days	MS relapse	Fatigue and numbness in both legs	UNK	UNK	L PV white matter	UNK	UNK
	Pt. 11, 30/F	RRMS	UNK	Pfizer-BioMTech	mRNA	2nd	20 days	MS relapse	Language disturbance	UNK	UNK	R corona radiata and L centrum semiovale	UNK	UNK
	Pt. 12, 58/F	None	UNK	Pfizer-BioMTech	mRNA	1st	3 days	MS	Headache, balance disturbances, urinary incontinence, difficulties in walking, and dysphagia	UNK	UNK	L frontal lobe	IVMP	UNK
	Pt. 13, 34/F	RRMS	UNK	Pfizer-BioMTech	mRNA	2nd	4 days	MS relapse	Neck pain and hypoesthesia on R arm	UNK	UNK	R posterior PV, L PV white matter, and spinal cord	UNK	UNK

Table 1 Cases of first-onset and relapsed multiple sclerosis (MS) after COVID-19 vaccination (continued)

Author	Age/ Gender	Past medical and family history	COVID-19 infection	Name of vaccine	Vaccine type	Number of doses	Vaccination to onset time	CNS demyelination	Clinical features	Laboratory data	CSF	MRI	Treatment	Outcome
	Pt. 14, 35/F	RRMS	UNK	Pfizer-BioMTech	mRNA	2nd	1 days	MS relapse	Paraesthesia on the L side of the body	UNK	UNK	L temporal lobe and L centrum semiovale	UNK	UNK
	Pt. 15, 54/M	RRMS	UNK	Pfizer-BioMTech	mRNA	1st	7 days	MS relapse	R hemiparesis	UNK	UNK	L PV white matter	IVMP	Full recovery
	Pt. 16, 37/M	RRMS	UNK	Pfizer-BioMTech	mRNA	2nd	10 days	MS relapse	Weakness on R limbs	UNK	UNK	L fronto-parietal white matter	IVMP	Partial recovery
Fragoso YD, et al. [17]	Pt. 1, 22/F	RRMS	UNK	Takeda-Moderna	mRNA	UNK	7 days	MS relapse	Facial paralysis, hemiparesis, and ataxia	UNK	UNK	UNK	IVMP	Not yet recovery
	Pt. 2, 2/F	RRMS	UNK	Takeda-Moderna	mRNA	UNK	10 days	MS relapse	Loss of vision and papillitis in the L eye	UNK	UNK	L eye	IVMP	Partial recovery
	Pt. 3, 35/M	SPMS	UNK	Takeda-Moderna	mRNA	UNK	7 days	MS relapse	Worsening of disability, could not walk, and severe weakness of both legs	UNK	UNK	UNK	MP pulse, oral PSL, and IVIg	Not yet recovery
	Pt. 4, 30/F	RRMS	UNK	Takeda-Moderna	mRNA	UNK	25 days	MS relapse	R hemiparesis	UNK	UNK	Spinal cord (Th2)	IVMP	Recovered
	Pt. 5, 42/F	RRMS	UNK	Takeda-Moderna	mRNA	UNK	15 days	MS relapse	Rapidly progressive weakness in both arms (grade III at its worst)	UNK	UNK	Brainstem	IVMP	Recovered

Table 1 Cases of first-onset and relapsed multiple sclerosis (MS) after COVID-19 vaccination (continued)

Author	Age/ Gender	Past medical and family history	COVID-19 infection	Name of vaccine	Vaccine type	Number of doses	Vaccination to onset time	CNS demyelination	Clinical features	Laboratory data	CSF	MRI	Treatment	Outcome
	Pt. 6, 35/M	RRMS	UNK	Takeda-Moderna	mRNA	UNK	20 days	MS relapse	Incoordination of R arm and hand	UNK	UNK	Brain	IVMP	Not yet recovery
	Pt. 7, 51/M	PPMS	UNK	Takeda-Moderna	mRNA	UNK	25 days	MS relapse	Motor and sensory deficits in R leg and foot	UNK	UNK	Cervical spinal cord	None	Not yet recovery
	Pt. 8, 32/F	RRMS	UNK	Takeda-Moderna	mRNA	UNK	7 days	MS relapse	Loss of vision in the L eye	UNK	UNK	UNK	IVMP	Not yet recovery
Fujimori J, et al. [18]	40/F	Peripheral facial nerve palsy	UNK	Pfizer-BioMTech	mRNA	2nd	14 days	MS relapse	Numbness and sensory disturbance in the R hand and shoulder	UNK	Elevated cell count, IgG index, Myelin basic protein and IL-6 level, OCB (+)	PV and subcortical white matter lesions, Spinal cord (C5/6)	IVMP	Recovered
Toljan K, et al. [19]	Pt.1, 29/F	Migraine	UNK	Pfizer-BioMTech	mRNA	1st	1 day	MS	Weakness and numbness in L leg, paresthesia in R arm	UNK	Elevated cell count and IgG index, OCB (+)	PV and juxtacortical white matter lesions	IVMP	Recovered
	Pt.2, 37/M	None	UNK	Pfizer-BioMTech	mRNA	1st	3 days	MS	L hand paresthesia	Negative	UNK	PV lesions, Spinal cord (C3/4)	Oral steroids	UNK

Table 1 Cases of first-onset and relapsed multiple sclerosis (MS) after COVID-19 vaccination (continued)

Author	Age/ Gender	Past medical and family history	COVID-19 infection	Name of vaccine	Vaccine type	Number of doses	Vaccination to onset time	CNS demyelination	Clinical features	Laboratory data	CSF	MRI	Treatment	Outcome
	Pt.3, 43/F	UNK	UNK	Pfizer-BioMTech	mRNA	2nd	35 days	MS	Weakness in R arm, numbness in R periorbital and palatal	UNK	OCB (+)	Temporal and callosal PV lesions, trigeminal nerve	IVMP	Recovered
	Pt.4, 41/M	None	UNK	Takeda-Moderna	mRNA	2nd	30 days	MS	Bilateral foot numbness	Negative	Elevated cell count and IgG index, OCB (+)	PV and juxtacortical lesions, Cervical and thoracic spinal cord	IVMP, oral steroids, and PE	Recovered
	Pt.5, 46/F	Optic neuritis	UNK	Takeda-Moderna	mRNA	1st	UNK	MS	R leg numbness	Negative	Elevated cell count and IgG index, OCB (+)	PV and juxtacortical lesions, Cervical and thoracic spinal cord	IVMP	UNK
Our case	57/F	MS	Negative	Pfizer-BioMTech	mRNA	1st	4 days	MS	Weakness of the L upper and lower limbs, difficulty in walking, and numbness from the L shoulder to the fingertips	SARS-CoV-2 anti-spike protein IgG: 3.6 U/mL (93 days after vaccination)	Mild elevated cell count, OCB (+), Elevated IgG index	Anterior horn of the R ventricle and in the L frontal subcortex, spinal cord lesion at the level of C4	IVMP	Marked recovery

Abbreviations: CIS, clinically isolated syndrome; COVID-19, coronavirus disease 2019; CNS, central nervous system; CSF, cerebral spinal fluid; IVIg, intravenous immunoglobulin; IVMP, intravenous methylprednisolone pulse therapy; L, left; MRI, magnetic resonance imaging; MS, multiple sclerosis; NA, not available; OCB (+), oligoclonal band IgG positive; PE, plasma pheresis; PPMS, primary progressive MS; PV, periventricular; RRMS, relapsing-remitting MS; R, right; SPMS, secondary progressive MS; UNK, unknown.

was compared with previously reported cases of first-onset and relapsed MS after vaccination[9-19] (Table 1). New-onset MS developed after vaccination in ten cases. Of these, seven cases developed after the first vaccination and three cases developed after the second vaccination. The time to onset ranged from 3 to 15 days in 7 cases with onset after the first vaccination and from 1 to 14 days in 3 cases with onset after the second vaccination. Three cases were positive for OCBs. All patients had received steroids, including IVMP. Six of the nine cases with documented results had marked symptomatic improvement. On the other hand, 26 cases of MS relapsed due to vaccination. Of these, 11 cases of MS occurred in 19 first-time vaccinators and 8 cases of MS relapses after the second vaccination. The time to onset ranged from 2 to 21 days in first-time vaccination cases and from 1 to 21 days in second-time vaccination cases. Steroids, including pulse steroids, were used in 31 cases with known treatment. Of the 29 cases with a known outcome, complete recovery or marked improvement was observed in 15, insufficient recovery in 10, and non-recovery in 4, with a high proportion of steroid-effective cases. Although MS after COVID-19 vaccination often has a relatively mild disease, some patients may develop severe symptoms[20]. The present case is the first onset of MS after vaccination. The time to onset was 4 days, and the positive OCB were like those in previous cases. She was treated with IVMP and had a relatively severe disease with EDSS 6.0 at the onset, but her disease course was good.

Following injection of the vaccine, the produced proteins or inactivated viruses that cross the blood-brain barrier (similar to SARS-CoV-2) cause molecular mimicry in the CNS, leading to inflammation. In addition, the production of S-protein by vector-based and mRNA vaccines causes activation of innate and adaptive immunity. In MS, immune cells identify vaccine-related antigens, invoking other immune cells, including T-cells, plasma cells, neutrophils, and macrophages. Thereafter, they generate inflammatory cytokines that lead to cytokine storms, demyelination, and neuronal degeneration[21].

In conclusion, a patient with IDDCNS resembling MS developed after COVID-19 vaccination and underwent IVMP with a good outcome. However, careful long-term observation is necessary because vaccination, as in this case, may lead to future relapses in MS patients who have not received disease-modifying drugs.

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