Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.0504-22
Intern Med 62: 923-928, 2023
http://internmed.jp

【 CASE REPORT 】

Relapsing Anti-MOG Antibody-associated Disease following COVID-19 Vaccination: A Rare Case Report and Review of the Literature

Hiroto Nakano[1], Kazuyoshi Yamaguchi[1], Naoyuki Hama[1], Yasuko Matsumoto[1], Moeko Shinohara[2] and Hisashi Ide[3]

Abstract:
Anti-myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an autoimmune demyelinating disorder that mainly occurs post-infection or post-vaccination. MOGAD after inoculation with coronavirus disease 2019 (COVID-19) vaccines is rare, and we herein report a rare case of a patient with MOGAD after vaccination using the Pfizer-BioNTech COVID-19 vaccine (BNT162b2, Pfizer Japan, Tokyo). Our report highlights the fact that MOGAD following inoculation with COVID-19 vaccine may show clinical relapse during reduction of the oral steroid dose, and continuous treatments with immunological agents is needed to prevent disease recurrence.

Key words: MOG, anti-MOG antibody-associated disease, SARS-CoV-2, vaccination, steroid

(Intern Med 62: 923-928, 2023)
(DOI: 10.2169/internalmedicine.0504-22)

Introduction

Anti-myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an autoimmune demyelinating disorder that predominantly involves the optic nerve and spinal cord (1). MOGAD has been previously identified in patients with multiple sclerosis (MS), neuromyelitis optica spectrum disorder and pediatric patients with acute disseminated encephalomyelitis (ADEM) (1, 2). MOGAD mainly occurs post-infection or post-vaccination (2). Several cases of MOGAD after severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infections have been reported, and 23 cases of MOGAD after inoculation with several types of SARS-CoV-2 vaccines were reported in May 2022 (1, 3-6).

We herein report a case of relapsing MOGAD following vaccination with an mRNA-based coronavirus disease 2019 (COVID-19) vaccine (BNT162b2, Pfizer Japan, Tokyo) and review the clinical features of MOGAD in COVID-19 vaccine recipients.

Case Report

A healthy 23-year-old woman presented with vertigo, vomiting, and headache from the 33rd day after receiving the second dose of the BNT162b2 vaccine (Figure A). On the 35th day after vaccination, she presented with vertigo, vomiting, and mild headache on a physical examination after walking into the hospital. Neurological findings were unremarkable, and no abnormalities were observed on either otorhinolaryngological examinations or endoscopic examinations of the upper gastrointestinal tract in the outpatient department.

Brain magnetic resonance imaging (MRI) on the 57th day after vaccination revealed mild hyperintensity around the fourth ventricle on fluid-attenuated inversion recovery (FLAIR) imaging (Figure B). She was unable to walk independently due to severe vertigo on the 58th day after vaccination. Therefore, she was admitted to a hospital in a bedridden state on the 77th day after vaccination.

On admission to the previous hospital, the hyperintense

[1]Department of Neurology, Ishikawa Prefectural Central Hospital, Japan, [2]Department of Neurology, Kaga Medical Center, Japan and [3]Department of Neurosurgery, Kaga Medical Center, Japan
Received: June 15, 2022; Accepted: November 20, 2022; Advance Publication by J-STAGE: December 28, 2022
Correspondence to Dr. Hiroto Nakano, neuro-nakano@med.kanazawa-u.ac.jp

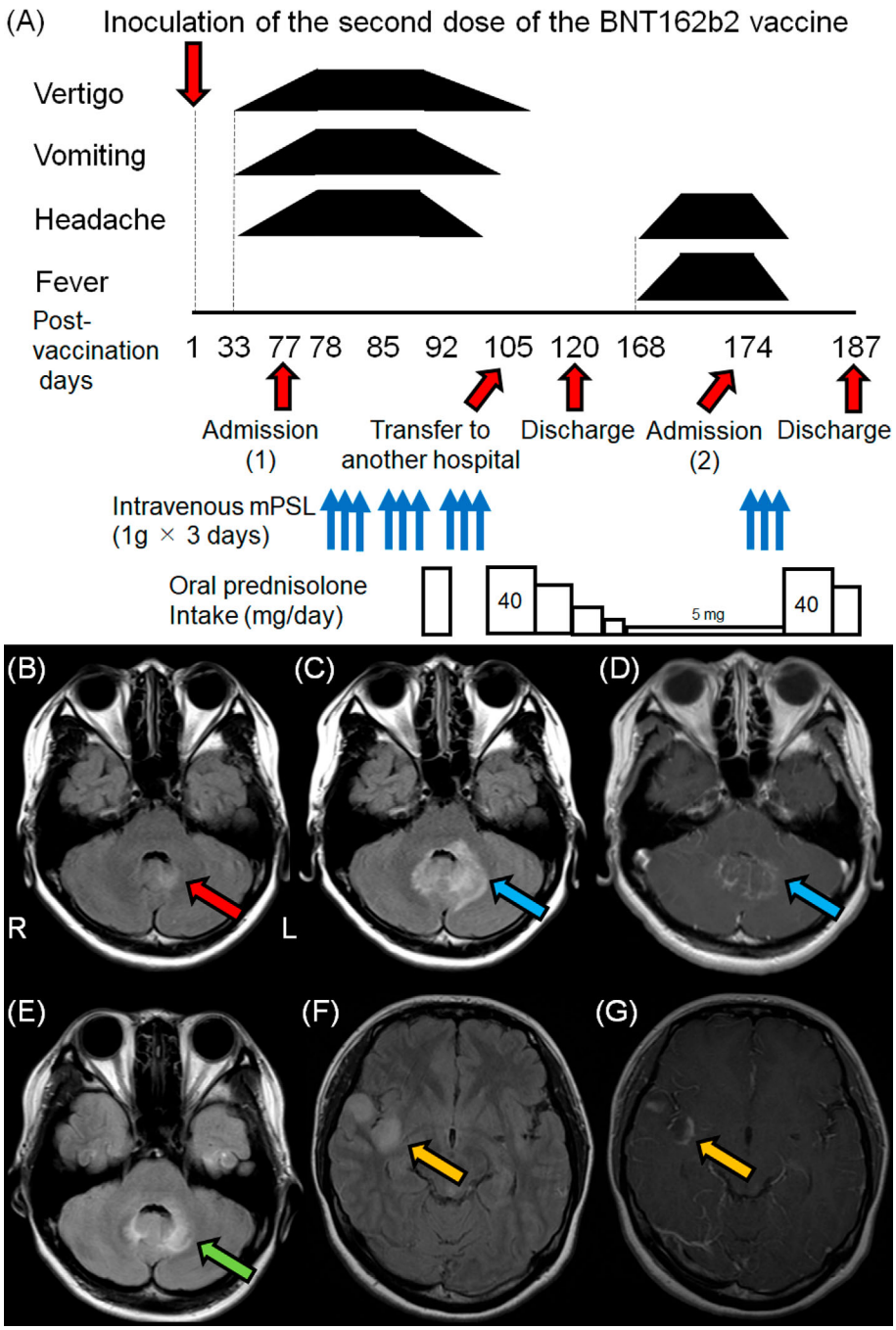

Figure. **Clinical course and magnetic resonance imaging (MRI) findings of our patient. (A) A healthy 23-year-old woman presented with vertigo, vomiting, and headache from the 33rd day after receiving the second dose of the BNT162b2 vaccine. Her neurological symptoms progressively worsened. After admission, she was treated with 3 courses of intravenous methylprednisolone (IV mPSL) from the 78th day after vaccination, followed by oral prednisolone intake. Her neurological symptoms improved gradually. She was transferred to another hospital for rehabilitation on the 105th day after vaccination. On the 168th day after vaccination, she presented with a fever and headache with relapse lesions on brain MRI. Additional IV mPSL improved her neurological symptoms. (B) Brain MRI on the 57th day after vaccination: fluid-attenuated inversion recovery (FLAIR) image. (C, D) Brain MRI on the 77th day after vaccination: C, FLAIR image; D, T1-gadolinium enhancement image. (E) Brain MRI on the 89th day after vaccination: FLAIR image. (F, G) Brain MRI on the 173th day after vaccination: F, FLAIR image; G, T1-gadolinium enhancement image. mPSL: methylprednisolone**

lesions around the fourth ventricle deteriorated on FLAIR imaging with T1-gadolinium enhancement (Figure C, D). MRI revealed no abnormalities in the optic nerves or supratentorial regions. The patient was subsequently transferred to our hospital on the same day. On admission to our hospital, SARS-CoV-2 reverse transcription-polymerase chain reaction

(RT-PCR) using a nasopharyngeal swab was negative. Her body temperature was 36.9°C, pulse rate was 87 bpm, and blood pressure was 94/63 mmHg. She was bedridden and experienced severe vertigo, vomiting, and headache.

A neurological examination revealed bilateral horizontal nystagmus without eye movement disorders. Dysarthria and facial palsy were not observed; additionally, muscle weakness, sensory disturbance, and abnormal deep tendon reflexes were not observed in any extremity. The patient showed mild ataxia in the finger-nose test. Blood tests on admission revealed no abnormalities in C-reactive protein, erythrocyte sedimentation rate, angiotensin-converting enzyme, T-SPOT, TB test for tuberculosis, tumor markers, soluble interleukin-2 receptor, anti-nuclear antibodies, or anti-aquaporin-4 antibodies. On admission, a cerebrospinal fluid (CSF) analysis demonstrated predominantly monomorphonuclear pleocytosis (48 cells/μL) with elevated protein levels (44 mg/dL) in the presence of oligoclonal bands (OCBs). The IgG index (0.42) and myelin basic protein levels (44.9 pg/mL) were normal. On admission, no malignant lesions were observed on chest radiography or abdominal computed tomography; similarly, bacterial cultures of both blood and CSF specimens and CSF cytology were negative. Spine MRI on admission also showed no abnormal signals in the whole spinal cord.

Based on the clinical course and the findings of both the CSF analysis and MRI, she was diagnosed with acute inflammatory encephalitis, and intravenous methylprednisolone (IV mPSL) (1 g) was administered for 3 days from the 78th day after vaccination. After 2 courses of IV mPSL therapy, oral prednisolone (PSL 40 mg/day; 1 mg/kg/day) was administered from the 88th day after vaccination. Her neurological symptoms gradually improved, and she was gradually able to walk with the aid of walking equipment. Hyperintense lesions on FLAIR imaging were reduced with no gadolinium enhancement on the 89th day after vaccination (Figure E). To improve her residual symptoms, the third course of IV mPSL therapy was administered from the 92nd day after vaccination. On the 98th day after vaccination, serological tests confirmed the presence of anti-MOG antibodies in a live cell-based assay with titers of more than 1:16, using anti-IgG1 Fc as the secondary antibody; therefore, she was diagnosed with MOGAD.

After the third course of IV mPSL therapy, she was able to walk independently with no neurological symptoms except for mild vertigo. On the 105th day after vaccination, the patient was transferred to another hospital for rehabilitation. She was discharged from that hospital on the 120th day after vaccination. The oral PSL dose was gradually reduced (10 mg/2 weeks), and 5 mg PSL was administered from the 167th day after vaccination.

On the 168th day after vaccination, she presented with a fever and headache, with negative results on SARS-CoV-2 RT-PCR. A neurological examination on the 173rd day after vaccination revealed clear consciousness, and the patient did not demonstrate any symptoms of vertigo, ataxia, or dysarthria. No muscle weakness, sensation disturbance, or abnormalities in the deep tendon reflexes of the four extremities were observed. Brain MRI on the same day revealed multiple hyperintense lesions on the right side of the insular cortex and temporal pole with T1-gadolinium enhancement (Figure F, G). On the 174th day after vaccination, she was admitted to our hospital and received 1 course of IV mPSL therapy, which improved her symptoms. Oral PSL intake (40 mg/day) was initiated on the 177th day after vaccination. The oral PSL dose was reduced to 30 mg/day from the 184 th day after vaccination. She was discharged from our hospital on the 187th day after vaccination with no neurological symptoms and continued oral PSL intake to prevent relapse.

Discussion

Our patient presented with severe vertigo, vomiting, and headache on the 33rd day after receiving the second dose of the BNT162b2 vaccine. Immunological treatments with IV mPSL and oral PSL intake improved her neurological symptoms; however, relapse lesions were observed on brain MRI following a fever and headache. Additional IV mPSL therapy improved her neurological symptoms, and the oral PSL dose was gradually decreased in the outpatient department. Based on the Brighton case definition for ADEM, the clinical features of our patient did not constitute clinical certainty of ADEM because of the presence of anti-MOG antibodies in the serum (7).

Our patient showed several unique characteristics in her clinical course. First, neurological symptoms appeared on the 33rd day after vaccination. Previous reports found that neurological symptoms of MOGAD after vaccination manifested after a mean of 25.8 days (8). Second, brain MRI revealed a hyperintense lesion around the fourth ventricle, adjacent to the insular cortex and temporal pole during the relapse times. Although a few cases of MOGAD showing cerebellar peduncle and cerebellar vermis lesions have been previously reported, cerebellar lesions are rare in patients with MOGAD (9). The present case suggests that the clinical features of MOGAD in COVID-19 vaccine recipients differ from those of typical MOGAD types.

MOGAD is a relatively new spectrum of autoimmune disorders involving antibodies against MOG, which is expressed on the outer surface of myelin in the central nervous system (CNS) (2). Because of the demyelinating pathomechanisms in the CNS caused by anti-MOG antibodies, the clinical features of MOGAD are similar to those of MS and ADEM, with only serological anti-MOG antibodies distinguishing them (2).

Twenty-three patients with MOGAD following COVID-19 vaccination were reported on May 2022 (1, 3, 5, 6). The clinical features of MOGAD in the COVID-19 vaccine recipients are presented in Table. Twenty-four patients, including the present study patient (12 men, 12 women), showed neurological symptoms 3-33 days after COVID-19 vaccination (Table). Three different COVID-19 vaccines (AZD1222:

Table. Summary of the Clinical Features of Anti-myelin Oligodendrocyte Glycoprotein Antibody-associated Disease in Coronavirus Disease 2019 Vaccine Recipients.

Patient (y.o./ sex)	Past history	Vaccine types	Onset	Neurological symptoms	MRI findings	CSF cell count/ protein (cells/μL, mg/dL)	OCBs	Treatments	Prognosis
43/M[1]	Asthma	AZD1222	7 days after 1st vaccination	Paraplegia, urinary retention, hypoesthesia up to Th5	Cerebral white matter, spinal cord (no enhancement)	43/40.6	(+)	IV mPSL	Recovery
59/M[1]	(-)	AZD1222	14 days after 1st vaccination	Gait disturbance, paresthesia, urinary & rectal dysfunction	Spinal cord (no enhancement)	110/N.D.	(-)	IV mPSL, PE	Recovery
43/F[3]	Migraine	AZD1222	9 days after 1st vaccination	Headache, paraplegia, urinary retention	Spinal cord, cerebral white matter & cortex, brain stem, cerebellar peduncle, pulvinar thalamic nuclei	545/135	(-)	IV mPSL, oral PSL, tocilizumab, PE	Recovery & relapse
29/F[5]	N.D.	AZD1222	11 days after 1st vaccination	Visual deficit, headache	Optic nerve (with enhancement)	0/18	(-)	IV mPSL, oral PSL, PE	Recovery
44/M[5]	N.D.	AZD1222	7 days after 1st vaccination	Urinary retention, tetraparesis, diplopia, hiccups, vomiting	Spinal cord	130/38	N.D.	IV mPSL, oral PSL, PE	Recovery
39/M[5]	N.D.	AZD1222	14 days after 1st vaccination	Visual deficit, eye pain	Optic nerve (with enhancement)	N.D.	N.D.	IV mPSL, oral PSL	Recovery
54/M[5]	N.D.	AZD1222	14 days after 1st vaccination	Visual deficit	Pons	N.D.	N.D.	IV mPSL, oral PSL	Recovery
35/F[5]	N.D.	AZD1222	9 days after 1st vaccination	Paraplegia, confusion	Conus, pons, cerebellar peduncle, basal ganglia, centrum semiovale, midbrain, thalamic nuclei	58/47	N.D.	IV mPSL, oral PSL	Recovery
45/F[5]	N.D.	AZD1222	21 days after 1st vaccination	Visual deficit, left limb spasticity	Optic nerve (with enhancement)	2/52	(+)	IV mPSL, oral PSL, PE	Recovery
33/F[5]	N.D.	AZD1222	14 days after 1st vaccination	Sensory disturbance, vomiting	Cerebrum	105/28	N.D.	IV mPSL, oral PSL	Recovery
36/M[5]	N.D.	AZD1222	32 days after 2nd vaccination	Sensory disturbance (thoracic level), paraplegia, urinary retention	Pons, spinal cord, trigeminal nerve	720/144	N.D.	IV mPSL, PE	Recovery
40/M[5]	N.D.	AZD1222	10 days after 1st vaccination	Visual deficit, urinary retention	Spinal cord, pons, thalamic nuclei, frontal cerebral cortex	8/32	(+)	IV mPSL, oral PSL, MMF	Recovery
45/M[5]	N.D.	AZD1222	10 days after 1st vaccination	Paraplegia, urinary retention	Brain stem, spinal cord	44/91	N.D.	IV mPSL, oral PSL, PE, MMF	Recovery
58/M[5]	N.D.	AZD1222	14 days after 1st vaccination	Hemiparesis, urinary retention, sensory disturbance (Th8 level)	Cerebrum, spinal cord	N.D.	N.D.	IV mPSL, oral PSL	Recovery
28/F[5]	N.D.	AZD1222	14 days after 1st vaccination	Tetraparesis, urinary & rectal dysfunction	Cerebrum, spinal cord	N.D.	N.D.	IV mPSL, oral PSL, PE	Partial recovery
32/M[5]	N.D.	AZD1222	21 days after 1st vaccination	Paraplegia, urinary retention	Spinal cord	N.D.	N.D.	IV mPSL, oral PSL	Recovery
38/F[5]	N.D.	AZD1222	7 days after 1st vaccination	Confusion, headache, paraplegia, urinary retention	Spinal cord, pons, cerebellar peduncle	N.D.	N.D.	IV mPSL, oral PSL, IVIg	Partial recovery
43/F[5]	Migraine	AZD1222	9 days after 1st vaccination	Tetraparesis, coma, urinary retention, meningism	Cerebellar peduncle, spinal cord, brain stem, cerebrum, thalamic nuclei	545/135	(-)	IV mPSL, oral PSL, tocilizumab, PE	Partial recovery
67/M[5]	Hypertension, BPH	AZD1222 (1st, 2nd) BNT162b2 (3rd)	10 days after 3rd vaccination	Visual deficit, headache, eye pain	Optic nerve (with enhancement)	6/51	(-)	IV mPSL, oral PSL	Recovery
68/F[1]	Hypertension, IPMN	mRNA-1273	14 days after 2nd vaccination	Paresthesia on her right V2 & V3 areas	Cerebellar peduncle	0/32	(+)	IV mPSL	Recovery
38/M[6]	(-)	mRNA-1273	3 days after 1st vaccination	Blurred vision, paresthesia (lower limbs), urinary retention, paraplegia	Optic nerve, spinal cord (with enhancement)	215/52	(-)	IV mPSL, oral PSL, PE	Partial recovery
54/F[5]	N.D.	BNT162b2	12 days after 2nd vaccination	Somnolence, urinary retention, facial paralysis, abducens nerve palsy	Basal ganglia, midbrain, cerebral white matter	23/31	N.D.	IV mPSL, PE	Recovery
39/F[6]	Sleep apnea, diabetes type 2	BNT162b2	7 days after 1st vaccination	Dizziness, paraplegia, numbness up to the mid-thoracic region, diplopia, vertigo	Posterior midbrain, spinal cord (with enhancement)	21/53	(+)	IV mPSL	Recovery & relapse
Our case 23/F	(-)	BNT162b2	33 days after 2nd vaccination	Vertigo, vomiting, headache, horizontal nystagmus	Cerebellar peduncle, cerebellar vermis (with enhancement)	48/44	(+)	IV mPSL, oral PSL	Recovery & relapse

y.o.: years old, MRI: magnetic resonance imaging, CSF: cerebrospinal fluid, OCBs: oligoclonal bands, M: male, F: female, IV mPSL: intravenous methylprednisolone, PE: plasma exchange, PSL: prednisolone, BPH: benign prostatic hyperplasia, MMF: mycophenolate mofetil, IVIg: intravenous immunoglobulin, IPMN: intraductal papillary mucinous neoplasm, N.D.: not described

18, BNT162b2:3, mRNA-1273:2, and AZD1222 and BNT 162b2:1) were used (Table). MOGAD appeared after several COVID-19 vaccinations as follows: post-1st vaccination in 19, post-2nd vaccination in 4, and post-3rd vaccination in 1; Table). Various neurological symptoms (paraplegia, hemiparesis, tetraparesis, urinary and rectal dysfunction, sensory disturbance, visual deficits, eye pain, diplopia, confusion, hiccups, meningism, myalgia, somnolence, facial palsy, abducens nerve palsy, headache, vertigo, vomiting, and horizontal nystagmus) have been reported (Table). MRI revealed abnormal lesions in the cerebral white matter and cortex, spinal cord, brain stem, thalamic nuclei, optic nerve, conus, basal ganglia, centrum semiovale, cerebellar vermis, and cerebellar peduncle (Table). Fifteen patients presented with pleocytosis, and 11 patients showed elevated protein levels in the CSF (Table). OCBs were observed in six patients (Table). All patients received immunological therapies (steroids, plasma exchange, tocilizumab, mycophenolate mofetil, and intravenous immunoglobulin) and showed treatment-responsive recovery (Table). During follow-up, three patients demonstrated relapsing symptoms. One of these three patients who had not received consolidation therapy presented with relapsing symptoms after intravenous methylprednisolone treatment, while the other two showed clinical recurrence during tapering of the steroid dose (3, 6). All patients showed good responses to additional immunological treatments. MOGAD has been known to show a high relapse frequency of ≥50% among MOGAD patients (10). However, in the present study, only 3 of the 24 patients with MOGAD following COVID-19 vaccination (12.5%) show recurrence in the clinical course. This may be a unique clinical feature of MOGAD in COVID-19 vaccine recipients.

Several neurological complications, such as Guillain-Barré syndrome and acute transverse myelitis, as we previously reported, have been reported in COVID-19 vaccine recipients (11). Similarly, post-vaccination encephalitis has been reported with a low incidence of approximately 0.1 to 0.2 per 100,000 (12). Although the precise mechanisms underlying the development of autoimmune diseases, including MOGAD, following COVID-19 vaccination remain unclear, activation of abnormal immune systems leading to the release of chemical cytokines may be associated with the pathogenesis of post-vaccination encephalitis (12).

Among the COVID-19 vaccines, the AZD1222 vaccine, an adenovirus-based viral vector vaccine, is associated with a higher risk of developing post-vaccination encephalitis than the BNT162b2 vaccine, an mRNA vaccine (13). In fact, 19 of the 24 patients with MOGAD following COVID-19 vaccinations (79.2%) had been inoculated with AZD1222 vaccines, as shown in Table. Furthermore, 17 of those 19 patients (89.5%) showed neurological symptoms after the first vaccination. Adenovirus-based viral vector vaccines induce the development of pathogenic immune complexes and accelerate the synthesis and release of chemical cytokines (5, 14). Conversely, mRNA vaccines, including the BNT 162b2 vaccine, activate the B-cell immune system, leading to antibody production (5, 14). We speculate that both adenovirus-based viral vector vaccines and mRNA vaccines activate abnormal immune systems, leading to the development of pathogenic antibodies. Furthermore, booster vaccination for mRNA vaccines is needed to induce antibody production, and adenovirus-based viral vector vaccines have a stronger potential to activate the development of pathogenic antibodies than mRNA vaccines.

In conclusion, we reported a rare case of MOGAD after vaccination with the BNT162b2 vaccine. This report highlights the fact that inoculation with the COVID-19 vaccine may lead to the development of MOGAD. While a good response to steroid treatment has been observed, we should be alert for instances of relapse.

The authors state that they have no Conflict of Interest (COI).

References

1. Matsumoto Y, Ohyama A, Kubota T, et al. MOG antibody-associated disorders following SARS-CoV-2 vaccination: a case report and literature review. Front Neurol **1**: 845755, 2022.
2. Salama S, Khan M, Pardo S, Izbudak I, Levy M. MOG antibody-associated encephalomyelitis/encephalitis. Mult Scler **11**: 1427-1433, 2019.
3. Escolà JK, Deuschl C, Junker A, et al. MOG antibody-associated encephalomyelitis mimicking bacterial meningomyelitis following ChAdOx1 nCoV-19 vaccination: a case report. Ther Adv Neurol Disord **15**: 17562864211070684, 2022.
4. Ide T, Kawanami T, Eriguchi M, Hara H. SARS-CoV-2-related myelin oligodendrocyte glycoprotein antibody-associated disease: a case report and literature review. Intern Med **61**: 1253-1258, 2022.
5. Jarius S, Bieber N, Haas J, Wildemann B. MOG encephalomyelitis after vaccination against severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2): case report and comprehensive review of the literature. J Neurol **23**: 1-15, 2022.
6. Morena J, Gyang TV. Myelin oligodendrocyte glycoprotein antibody-associated disease and transverse myelitis probably associated with SARS-CoV-2 mRNA vaccines: two case reports. Neurohospitalist **12**: 536-540, 2022.
7. Sejvar JJ, Kohl KS, Bilynsky R, et al. Encephalitis, myelitis, and acute disseminated encephalomyelitis (ADEM): case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine **25**: 5771-5792, 2007.
8. Kumar N, Graven K, Joseph NI, et al. Case report: postvaccination anti-myelin oligodendrocyte glycoprotein neuromyelitis optica spectrum disorder: a case report and literature review of postvaccination demyelination. Int J MS Care **22**: 85-90, 2020.
9. Fujimori J, Nakashima I. Cerebellar lesions in a patient with anti-myelin oligodendrocyte glycoprotein antibody-associated encephalitis. Clin Exp Neuroimmunol **10**: 264-266, 2019.
10. Li Y, Liu X, Wang J, Pan C, Tang Z. Clinical features and imaging findings of myelin oligodendrocyte glycoprotein-IgG-associated disorder (MOGAD). Front Aging Neurosci **14**: 850743, 2022.
11. Nakano H, Yamaguchi K, Kawabata K, Asakawa M, Matsumoto Y. Acute transverse myelitis after BNT162b2 vaccination against COVID-19: report of a fatal case and review of the literature. J Neurol Sci **434**: 120102, 2021.
12. Gao JJ, Tseng HP, Lin CL, Hsu RF, Lee MH, Liu CH. Acute encephalitis after COVID-19 vaccination: a case report and literature review. Hum Vaccin Immunother **14**: 2082206, 2022.
13. Zuhorn F, Graf T, Klingebiel R, Schäbitz WR, Rogalewski A.

Postvaccinal encephalitis after ChAdOx1 nCov-19. Ann Neurol **90**: 506-511, 2021.

14. Li M, Wang H, Tian L, et al. COVID-19 vaccine development: milestones, lessons and prospects. Signal Transduct Target Ther **7**: 146, 2022.