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【 CASE REPORT 】

Miller Fisher Syndrome Following Vaccination against SARS-CoV-2

Makoto Yamakawa[1], Keiichi Nakahara[1], Toshihito Nakanishi[2], Toshiya Nomura[1] and Mitsuharu Ueda[1]

Abstract:
After BNT162b2 messenger ribonucleic acid (mRNA) coronavirus disease 2019 (COVID-19) vaccination, a 30-year-old man developed bilateral lateral gaze palsy, diplopia, absent tendon reflexes, and ataxic gait. Serum anti-GQ1b and anti-GT1a immunoglobulin G (IgG) antibodies were strongly positive. Based on those findings, he was diagnosed with Miller Fisher syndrome (MFS). Intravenous immunoglobulin therapy was administered, and his symptoms fully recovered within approximately 3 months. To the best of our knowledge, this is the first report to describe the development of MFS after COVID-19 mRNA vaccination.

Key words: Miller Fisher syndrome, vaccine, COVID-19, SARS-CoV-2, adverse event

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic has necessitated large-scale global vaccination campaigns to control the spread of this infection under emergency use authorization. Although the the risks and benefits of vaccination should be considered for the individual, we still do not fully understand the risk of neurologic disorders after COVID-19 vaccine administration. We herein report the case of a patient who developed Miller Fisher syndrome (MFS) after BNT162b2 messenger ribonucleic acid (mRNA) COVID-19 vaccination. To the best of our knowledge, this is the first report to describe the development of MFS after mRNA COVID-19 vaccination.

Case Report

A 30-year-old healthy Japanese man received a second dose of tozinameran (BNT162b2 mRNA COVID-19 vaccine). He reported fever and cough during the first week after the vaccination. On day 7 post-vaccination, he experienced diplopia, dizziness, and difficulty walking. The patient was admitted to our hospital on day 8. A neurological examination revealed multidirectional diplopia, while his eye movement was full and smooth and tandem gait was impossible. A laboratory analysis revealed normal findings. All other clinical findings associated with the cranial, motor, and sensory nerves, as well as reflexes, were normal. Cerebrospinal fluid (CSF) and nerve conduction studies were normal on admission. Respiratory function tests, chest radiography, and contrast-enhanced magnetic resonance imaging of the brain and spine showed normal findings. On day 11, the patient developed bilateral lateral gaze palsy and ataxic gait (Figure). The biceps and patella tendon reflexes were absent, whereas the Achilles reflex was present. Serum anti-GQ1b and anti-GT1a immunoglobulin G (IgG) antibodies were strongly positive. Based on those findings, he was diagnosed with MFS. On day 12, intravenous immunoglobulin (IVIg) therapy (400 mg/kg/day for 5 days) was administered. His symptoms fully recovered by day 105.

Discussion

To date, Guillain-Barré syndrome (GBS), a rare but serious autoimmune neurological disorder affecting the peripheral nervous system (PNS), has been reported in several cases after mRNA COVID-19 vaccination (1-5). In the pre-

[1]Department of Neurology, Graduate School of Medical Sciences, Kumamoto University, Japan and [2]Department of Neurology, Kumamoto Kinoh Hospital, Japan
Received for publication October 17, 2021; Accepted for publication November 28, 2021
Correspondence to Dr. Keiichi Nakahara, k1nakahara@kuh.kumamoto-u.ac.jp

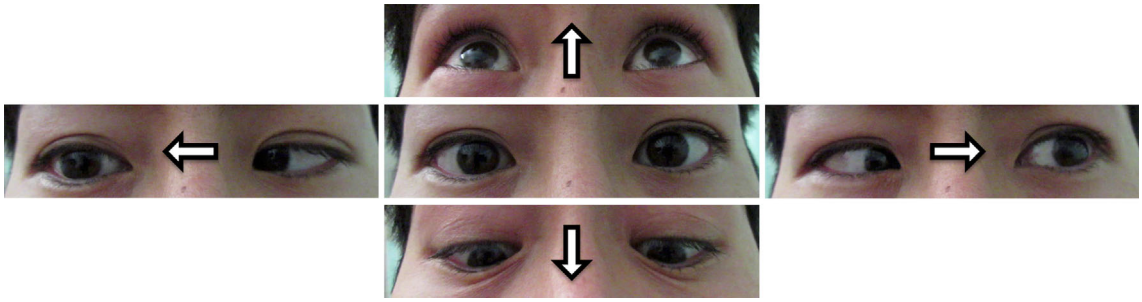

Figure. **Limitation of extraocular movements. Bilateral lateral gaze palsy was observed after mRNA COVID-19 vaccination.**

Table. **Cases with Miller Fisher Syndrome and Guillain-Barré Syndrome after mRNA COVID-19 Vaccination without Infection and Other Vaccination.**

Diagnosis	Country	Age (years)/ Sex	Vaccine type	Number of dose	Days from inoculation to onset	Neurological symptoms	CSF cells (/μL)/ Protein (mg/dL)	Anti-ganglioside antibody	NC study	Treatment	Outcome	Reference
MFS	Japan	30/M	BNT162b2	Second	7	Bilateral lateral gaze palsy, areflexia, and ataxic gait	1/30.8	GQ1b GT1a	Normal	IVIg	Recovered	Present case
GBS	Qatar	73/M	BNT162b2	Second	16	Muscle weakness, areflexia	Normal/80	N.D.	Absent H reflexes	IVIg	Recovered	2
GBS	US	82/F	BNT162b2	First	14	Muscle weakness, sensory loss, areflexia	4/88	N.D.	N.D.	IVIg	Improved	1
GBS	US	86/F	BNT162b2	First	1	Muscle weakness, areflexia	2/162	N.D.	N.D.	IVIg	Recovered	3
GBS	US	65/M	BNT162b2	First	2	Bilateral facial palsy, muscle weakness, sensory loss, areflexia	1/107	N.D.	AIDP	IVIg	Improved	5
GBS	Mexico	31/M	BNT162b2	First	11	Muscle weakness, areflexia	Not performed	N.D.	AIDP	IVIg	Improved	4
GBS	Mexico	67/F	BNT162b2	First	4	Muscle weakness, areflexia, respiratory failure	22/30	N.D.	AMAN	IVIg	Dead	4

MFS: Miller Fisher syndrome, GBS: Guillain-Barré syndrome, N.D.: not detected, AIDP: acute inflammatory demyelinating polyneuropathy, AMAN: acute motor axonal neuropathy, CSF: cerebrospinal fluid

sent case, a typical clinical presentation of MFS, which is a variant form of GBS, with serum anti-GQ1b IgG antibody positivity was observed after mRNA COVID-19 vaccination. MFS is characterised by the clinical triad of ophthalmoplegia, ataxia, and areflexia (6), with a higher incidence in Asian countries than in Western countries (7). It is usually preceded by viral or diarrhoeal illness and is strongly associated with serum anti-GQ1b IgG antibodies (8). The prognosis of MFS is usually good, with a median time to full recovery of 1 month for ataxia and 3 months for ophthalmoplegia (7). The present patient exhibited the clinical triad of MFS accompanied with serum anti-GQ1b IgG antibody positivity. He was treated with IVIg therapy and fully recovered in approximately 3 months.

A score of 5 on the Naranjo adverse drug reaction probability scale (9) suggested an association between the

mRNA COVID-19 vaccination and MFS, which was supported by the absence of any other trigger of MFS. Furthermore, the interval between the vaccination and the onset of neurological symptoms was 7 days. Most cases of GBS after mRNA COVID-19 vaccination, as well as that of GBS after influenza vaccination, occurred within 2 weeks of vaccination (10) (Table). In several reports, mRNA COVID-19 vaccination was not associated with GBS (4, 11, 12). Whereas, adverse events were more commonly reported among the mRNA COVID-19 vaccination group (13). The spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is provided in the mRNA vaccine, binds to sialic acids linked to host cell surface gangliosides (14). This affinity of spike proteins for gangliosides may lead to the development of GBS. Although it remains unclear how mRNA COVID-19 vaccination induced MFS in this case, mRNA COVID-19 vaccination could be associated with MFS.

In conclusion, mRNA COVID-19 vaccination may rarely induce MFS.

Written informed consent was obtained by the patient for use and publication of the facial photographs.

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

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