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Letter to the Editor

Acute transverse myelitis after BNT162b2 vaccination against COVID-19: Report of a fatal case and review of the literature

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Dear Editor,

The coronavirus disease 2019 (COVID-19) pandemic, originating from Wuhan City in China, has been a serious global concern (1). One of the cornerstones of ending the COVID-19 pandemic is vaccination. However, several vaccination-related neurological complications have been reported (2). There was an unexpectedly high incidence of acute transverse myelitis (ATM) as a neurological complication following COVID-19 infection (approximately 1.2–3.2%) (3,4), and 11 cases of ATM after inoculation of several types of COVID-19 vaccines had been reported by October 7, 2021 (5–7). Herein, we describe a case of ATM with a fatal prognosis following vaccination with an mRNA-based COVID-19 vaccine (BNT162b2, Pfizer) and review the clinical features of ATM in COVID-19 vaccine recipients.

An 85-year-old man presented with vertigo and vomiting one day after receiving the second dose of the BNT162b2 vaccine (Fig. 1A). At admission, the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) reverse transcription-polymerase chain reaction (RT-PCR) test using nasopharyngeal swabs was negative. He did not present with fever or other symptoms suggestive of infection. Neurological examination revealed rotatory nystagmus on the right side in the absence of weakness and sensory disturbance in the lower limbs. Blood tests showed no hematologic abnormalities. Thoracic CT findings were unremarkable. The vertigo and vomiting improved gradually, and the patient was discharged from the hospital on the 3rd day after vaccination. Subsequently, he presented with progressive gait disturbance and urinary retention, and he was admitted to the hospital because of gait disturbance on the 15th post-vaccination day. He had no fever or other symptoms suggestive of infection. The SARS-CoV-2 RT-PCR test was negative. Neurological examination showed proximal-dominant weakness and distal-dominant hypoesthesia in the lower extremities bilaterally. Hematological examinations and thoracic CT revealed no abnormalities. Brain CT and MRI were unremarkable, however, on the 16th day after vaccination, thoracic MRI revealed a longitudinal hyperintense lesion from the Th3–5 vertebral levels on T2-weighted imaging (Fig. 1B and C). On the 25th day after vaccination, the patient was referred to our hospital. Routine physical examination and RT-PCR for COVID-19 were normal. He was bedridden and neurological examination revealed that he was disoriented, with right-dominant paraplegia. He also had hypoesthesia in both lower limbs and hyporeflexia in both his upper and lower limbs, without an extensor plantar response. His consciousness immediately improved the following day. Blood tests revealed elevated levels of HbA1c (6.9%) and C-reactive protein (CRP) (3.26 mg/dL). Serologic tests confirmed the absence of anti-aquaporin (AQP)-4 antibodies. Cerebrospinal fluid (CSF) analysis demonstrated predominantly monomorphonuclear pleocytosis (11 cells/μL), with elevated protein levels (120 mg/dL) and the absence of oligoclonal bands. The IgG index (0.67) and myelin basic protein (MBP) level (58.1 pg/mL) were normal. Bacterial cultures and CSF cytology results were unremarkable. The patient was diagnosed with ATM, and intravenous methylprednisolone (0.5 g) for three days, followed by oral prednisolone (40 mg/day), was administered from the 30th day after vaccination. However, the patient's neurological symptoms did not improve. A second course of intravenous methylprednisolone (0.5 g) for three days from the 42nd day after vaccination still did not resolve his neurological symptoms. On the 52nd day after vaccination, he presented with fever and oxygen desaturation. Blood tests revealed pancytopenia with an elevated CRP level (15.72 mg/dL). Chest radiography revealed bilateral pneumonia. Treatment with intravenous sulbactam/ampicillin (6 g/day) did not improve the patient's condition, and on the 58th day after vaccination, he died. His family declined a postmortem examination.

Our patient presented with progressive paraplegia, hypoesthesia in both lower limbs, and urinary retention following a two-day history of vertigo and vomiting after receiving the second dose of the BNT162b2 vaccine. Based on the Brighton case definition for myelitis, our patient was diagnosed with myelitis with level 2 diagnostic certainty (8). Treatment with continuous steroid therapy did not improve his neurological symptoms. Subsequently, he died of a poor general condition.

An increasing number of people are having the opportunity to get access to COVID-19 vaccines, and several neurological manifestations have been reported in COVID-19 vaccine recipients (2). Among the cases

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; ATM, acute transverse myelitis; RT-PCR, reverse transcription-polymerase chain reaction; CRP, C-reactive protein; AQP, aquaporin; CSF, cerebrospinal fluid; MBP, myelin basic protein.

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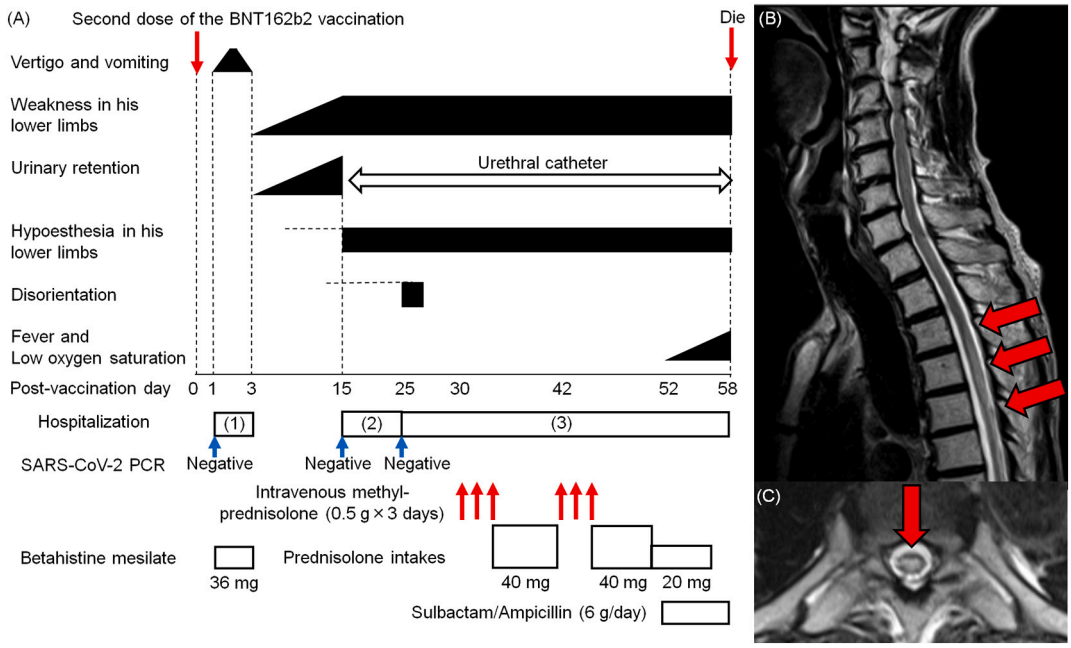

Fig. 1. Clinical course and MRI findings of our patient. (A) An 85-year-old man presented with vertigo and vomiting one day after receiving the second dose of the Pfizer-BioNTech coronavirus disease 2019 vaccine (BNT162b2). On the 3rd day after vaccination, the patient's symptoms improved. However, he presented with progressive paraplegia, hypoesthesia in the lower limbs bilaterally, and urinary retention, which prompted referral to our hospital. He was diagnosed with acute transverse myelitis. A three-day course of intravenous methylprednisolone (0.5 g) was initiated. However, the patient's neurological symptoms did not improve. Subsequently, he developed bilateral pneumonia. Treatment with sulbactam/ampicillin (6 g/day) did not resolve his condition. On the 58th day after vaccination, he died. (B, C) Thoracic MRI demonstrates a longitudinal hyperintense lesion at the Th3–5 vertebral levels (red arrow) (B: sagittal image, C: axial image at the Th4 vertebral level).

of severe neurological complications following COVID-19 vaccination, 11 of ATM had been reported by October 7, 2021 (5–7). We have shown the clinical features of ATM after COVID-19 vaccination (Table 1). The remarkable difference between the previously reported cases and ours was the prognosis after treatment. Both our patient and the previously reported patients were treated with immunological therapies (Table 1). The previously reported patients had recovery of neurological symptoms after treatment; however, our patient did not respond to treatment, and he died 58 days after receiving the second dose of the BNT162b2 vaccine (Table 1). The BNT162b2 vaccine is a lipid-nanoparticle-formulated mRNA vaccine against SARS-CoV-2 (9). Once administered, the mRNA is translated into SARS-CoV-2 spike proteins, which are expressed on the surface of host cells. The transient expression of spike antigens induces the production of antibodies against SARS-CoV-2 (9). Although the precise pathophysiologic mechanisms of the neurological complications following BNT162b2 vaccination remain uncertain, an abnormal immune-mediated inflammation has been implicated (10). This study highlights that ATM after COVID-19 vaccination may be refractory to conventional steroid therapy, and that ATM in COVID-19 vaccine recipients could have a poor prognosis.

Author agreement

All authors read and approved the final version of the manuscript. They warrant that the article is the author's original work, has not received prior publication, and is not under consideration for publication elsewhere.

Disclosure statement

We confirmed that there is no financial/personal interest or belief that could affect objectivity.

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Availability of data and material

Anonymized data and material regarding this case report not included in the manuscript are available on request to the corresponding author by any qualified investigator.

Author's contributions

HN, KY, KK, MA, and YM performed the clinical and bedside studies. HN wrote the initial draft of the paper and all authors contributed to its preparation. The final version was read and approved by all authors.

Ethics approval

This work was approved by the ethic committee in Ishikawa prefectural central hospital.

Consent to participate

Informed concent was obtained from his family.

Consent for publication

Informed concent was obtained from his family.

Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

Table 1
Summary of the clinical features of acute transverse myelitis in coronavirus disease 2019 vaccine recipients.

Patient (y.o./ sex)	Past history	Vaccine types	Onset	Neurological symptoms	MRI findings	Treatments	Prognosis
36/M[5)]	(−)	AZD1222	8 days after first vaccination	abnormal sensations in bilateral lower limbs, impaired vibration up to sternum	C6–7 (mild enhancement)	IV mPSL (1 g × 5 days), oral mPSL (16 mg/day, 12 hourly)	recovery
45/M[5)]	dermatitis	AZD1222	11 days after first vaccination	acute flaccid tetraparesis, thoracic back pain, urinary retention	C3-Th2 (no enhancement)	IV mPSL (1 g × 5 days), oral PSL (100 mg/day)	recovery
44/F[5)]	(−)	AZD1222	4 days after first vaccination	bilateral plantar feet paresthesia, hypoesthesia in her lower back	C6–7, Th2–3 (partial enhancement)	IV mPSL (1 g × 5 days), oral mPSL (1 mg/kg/day)	recovery
40/F[5)]	RRMS	AZD1222	2 weeks after first vaccination	binocular blindness, back pain, lower-limb weakness and numbness	C4–5, C7-Th1, Th7–10 (no information about enhancement)	IV mPSL (2 g × 2 days), plasma exchange	recovery
58/M[5)]	diabetes mellitus, pulmonary sarcoidosis	AZD1222	7 days after first vaccination	hyperesthesia below Th7, urinary retention, lower-limb numbness	Th2–10 (partial enhancement)	IV mPSL (1 g × 5 days), oral PSL (60 mg/day), plasma exchange	recovery
41/M[5)]	diabetes mellitus	AZD1222	2 weeks after first vaccination	paresthesia below Th4, lower-limb weakness and clumsiness, loss of joint position and vibration	Th1–6 (no information about enhancement)	IV mPSL (1 g × 5 days), oral PSL (1 mg/kg/day)	recovery
67/F[5)]	coronary artery disease, CKD, colon rupture	mRNA-1273	1 day after vaccination	weakness in four limbs	C1–3 (partial enhancement)	IV methylprednisolone sodium succinate (1 g × 3 days), plasma exchange	recovery
76/F[6)]	hypertention	mRNA-1273	4 days after vaccination	unsteadiness and abnormal sensations in four limbs	C2–5 (partial enhancement)	IV mPSL (1 g × 5 days), oral PSL (60 mg/day)	recovery
44/F[5)]	(−)	Ad26. COV2·S	10 days after vaccination	nausia, urinary retention, back pain, lower-limb numbness and weakness	C2–3 (no information about enhancement)	mPSL, plasma exchange	recovery
78/F[5)]	hypertension, diabetes mellitus, breast cancer	CoronaVAC	3 weeks after second vaccination	tetraparesis, paresthesia in bilateral upper limbs, urinary retention	C1-Th3 (no information about enhancement)	IV mPSL (1 g × 4 days), plasma exchange	recovery
38/M[7)]	(−)	BNT162b2	2 days after first vaccination	pain and weaknes in his lower limbs, headache	Th5–6 (no information about enhancement)	N.D.	N.D.
Our patient 85/M	hypertension, diabetes mellitus, interstitial pneumonia	BNT162b2	1 day after second vaccination	paraplegia, hypoesthesia in bilateral lower limbs, urinary retention	Th3–5 (no enhancement)	IV mPSL (0.5 g × 3 days, 2 courses), oral PSL (40 mg/day)	die

y.o., years old; M, male; F, female; RRMS, relapsing remitting multiple sclerosis; CKD, chronic kidney disease; IV, intravenous; mPSL, methylprednisolone; PSL, prednisolone; N.D., not described.

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