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Neurologic Side Effect after Injection of SARS-CoV-2 mRNA-1273 Vaccine (Modern a COVID-19 Vaccine): A Case Report

Su Jeong Shin*, You Ho Mun and Jung Ho Kim

Department of Emergency Medicine, Yeungnam University College of Medicine, Daegu, Republic of Korea

Abstract

In late December 2020, vaccination for the coronavirus disease 2019 (COVID-19) started among the personnel of the United States Forces Korea and related units, including the medical team. Because its usage was approved based on emergency circumstances, sufficient research on the possible side effects has not been conducted yet. We experienced an unusual neurologic side effect after injection of the SARS-CoV-2 mRNA-1273 vaccine. A 32-year-old U.S Army male soldier with headache, blurred vision, and cramping chest pain after second-dose injection visited the emergency room. Subsequently, left-sided weakness developed during the observation. Imaging of the cervical lesion for the diagnosis of acute intracranial disease was performed but revealed no definite disease. While under close observation, the patient's symptoms progressed to nearly hemiplegic but then improved gradually in an ascending and peripheral-to-center manner with only supportive care. We report this case as the first unilateral neurologic side effect of the SARS-CoV-2 mRNA-1273 vaccine.

Keywords: Side effect • Modern a vaccine • COVID-19

Introduction

Recently, the successful development of a Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) vaccines against the Coronavirus Disease 2019 (COVID-19) pandemic has been reported in a timely manner [1]. among the several available vaccines, the SARS-CoV-2 mRNA-1273 vaccine has been shown to have appropriate efficacy and safety standards. The mRNA-1273 vaccine has an encapsulated mRNA encoding the full-length of the modified SARS-CoV-2 spike glycoprotein trimer. The most common side effects noted in the clinical trials were headache, fatigue, myalgia, chills, and injection-site pain. Although rare, more severe systemic symptoms have occurred after the second injection [2]. Nevertheless mRNA-1273 and BNT162b2 have been granted the first Emergency Use Authorization (EUA) in the US. There are still unidentified problems including long-lasting protective effect and coverage of candidates regardless of comorbidity or age, immune status, etc [3]. Recently, preferential vaccination of the United States Forces Korea and related personnel using the Modern a (mRNA-1273) COVID-19 vaccination commenced. Among those vaccinated, there was a case of unusual side effects after the second dose. As the patient visited the hospital promptly, we were able to observe every course of symptom change. To the best of our knowledge, this is the first reported neurologic complaint after the injection of the Modern a COVID-19 vaccine.

Case Description

A 32-year-old male U.S Army soldier visited the emergency department of a university hospital on February 3, 2021. He complained of the abrupt onset of headaches with blurred vision and cramping chest pain right after receiving the second dose of the Modern a vaccine to his left upper arm. He had a history of allergic reactions to sulfur drugs, penicillin, amoxicillin, and coconut. However, there was no evidence of typical allergic reactions, such as itching sensation or redness, dyspnea, and edema. His vital signs at triage were within the normal range. Approximately two months earlier, he underwent a liver biopsy due to an abnormal liver function test at another hospital and has been taking ursodeoxycholic acid. He also underwent incision and drainage of his left elbow due to abscess formation following an insect bite in August 2020.

An initial Electro Cardio Gram (ECG) showed no definite ST abnormality with a regular atrial rhythm. The serologic test revealed no definite abnormal cell count or electrolyte imbalance, except for a slight elevation of total bilirubin level (1.6 mg/dL) and aspartate aminotransferase/alanine aminotransferase (101/294 IU/L).

He visited the hospital within 15 minutes of the injection. A left-side hemiparesis developed during observation, while the patient was waiting for the result of the primary evaluation. According to his description, weakness worsened after the visit, and the upper extremity was weaker than the lower extremity. On initial physical examination, pendular nystagmus and bidirectional gaze-evoked nystagmus were observed. For differential diagnosis and to rule out any disease of the central nervous system, brain Computed Tomography (CT) scans including angiography and brain Magnetic Resonance Imaging (MRI) were performed. The scans did not show any definite sign of neurologic diseases, such as hemorrhage, infarction, or other space-occupying lesions (Figure 1).

Corresponding Author: Su Jeong Shin, Department of Emergency Medicine, Yeungnam University College of Medicine, Daegu, Republic of Korea; E-mail: zezec@naver.com

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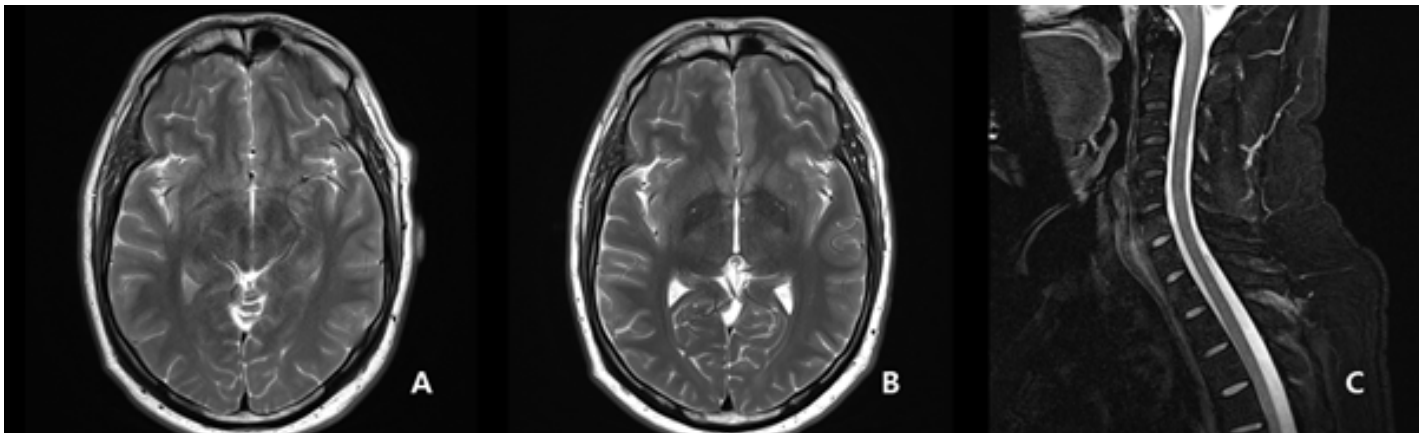

Figure 1. A) No abnormal findings on the MRI performed on the day of visit; B) Additional MRI performed on the 5th day of the visit showed no abnormalities; C) No abnormal findings were found on cervical spine MRI on the 2nd day of visit.

Ophthalmologic consultation was conducted for visual disturbances. Mono-ocular diplopia was confirmed. The patient's visual acuity was significantly impaired in the right eye. No other specific structural or functional abnormalities were found. The ophthalmologists recommended assessing for other intracranial or systemic conditions that evoke headaches and dizziness.

Neurologic examination revealed that the deep tendon reflex was normal to hyperactive on the affected side, and the Hoffman sign was positive. Therefore, cervical spine MRI and nerve conduction tests were performed successively during the neurology consultation. Meanwhile, supportive care was provided to the patient and close observation for any changes to his condition was maintained.

On hospital day 2, the patient's left leg weakness improved. However, his visual disturbance accompanied by headaches persisted. Pendular nystagmus was consistently observed. The neurological deficit in his left arm was constant. Arm elevation was nearly impossible but elbow flexion (motor grade 2/5) and hand grasp (motor grade 3/5) power were preserved. Sensory impairment was also accompanied by an inability to feel touch sensation distal to his left elbow.

On hospital day 3, the power in his lower limb recovered, and the patient was able to walk by himself. On hospital day 4, the power in his right elbow flexion and hand grasp became worse (motor grade 1/5 but his shoulder elevation power improved (motor grade 3/5). Electro Myo Graphy (EMG) and Nerve Conduction Velocity (NCV) were performed, and the results were non-specific. On hospital day 5, the patient's headaches improved and he did not require more analgesics. However, his diplopia remained. The results of the patient's neurologic examination showed no significant difference, and a follow-up MRI revealed non-specific results. Cerebrospinal fluid analysis was also considered. We decided to postpone tapping because there was no sign of meningeal irritation or abnormal lesion on the enhanced brain MRI. On hospital day 7, neurological examination of the patient revealed slow but steady recovery. He was discharged, and clinical observation while he was on steroid therapy was recommended.

After 5 days, the power in the patient's upper arm improved substantially (shoulder abduction 4/5, finger flexion abduction and flexion 4+/5, elbow flexion 3/5 elbow extension 5-/5). However, the Hoffmann sign and DTR hyperactivity remained.

Results and Discussion

The SARS-CoV-2 mRNA-1273 vaccine is currently one of the approved mRNA vaccines for the prevention of COVID-19 [4]. Unlike typical vaccines; mRNA vaccines do not contain weakened or inactivated bacteria or a live virus. Instead, a piece of mRNA transcribing "spike protein" is included in the vaccine formulation that subsequently guides the host's immune system to produce antibodies against the virus.

Vaccines made with mRNA are a promising therapeutic method that has been actively studied recently because of their advantages, including safety, no potential risk of infection, and efficacy. Various modifications have enabled mRNA to be more stable and highly translatable [5]. Numerous clinical trials in several types of cancer and infectious disease, such as Human Immunodeficiency Virus (HIV), rabies, Zika virus, and influenza, have been conducted [5,6]. Despite its hypothetical safety, human phase 1 clinical trials for the mRNA rabies vaccine (CV7201) reported a case of vaccine-induced Bell's palsy. This unexpected serious adverse reaction occurred 7 days after a second dose of the vaccine [7]. Several other clinical studies testing mRNA vaccines on various diseases have also reported adverse events (Table 1) [8-12]. In the case of the SARS-CoV-2 mRNA vaccine, BNT162b2 (Pfizer-BioNTech), several episodes of serious adverse events have been reported, mostly related to the allergic response to Poly Ethylene Glycol (PEG) and PEG derivatives [13,14]. In 4 out of 21 reported cases of anaphylaxis after the first injection of the Pfizer-BioNTech COVID-19 vaccine, there was no history of allergy [15].

Table 1. Sample Size determination table.

Vaccine type	Target antigen	Injection route	Vaccination cycle	Phase of trial	Number of participants	Side effect
Autologous dendritic cells transfected	PSA[a]	intravenous	3	1	16	Flulike symptoms, injection site erythema, transient elevation of antinuclear Ab titers and rheumatoid factor
Personalized RNA mutanome vaccine	TAA[b]	Percutaneously into inguinal lymph nodes	8~20	1	13	No serious adverse event outgrowth of B2Mdeficient tumour cells
LNP-formulated,	H10N8 HA[c]	intramuscular	1	1	31	injection site pain, myalgia, headache, fatigue, and chills/ common-cold-like symptoms No serious adverse event
modified mRNA-based						

alphavirus replicon vaccine	CMV proteins gB, pp65 and IE1	Intramuscular or subcutaneous	3	1	40	injection site pain, tenderness, erythema or swelling myalgia, fatigue, malaise, headache low hemoglobin, low white cell count, hemoglobinuria, proteinuria, glucosuria
alphavirus replicon vaccine	HIV-1 subtype C gag	Subcutaneous	3		144	Epigastric discomfort(attributed to pregnancy), elevated liver function tests and hyperglycemia, severe hypertension, HIV infection Infectious hepatitis A or E, severe fatigue, severe headache Recurrence of Bell's palsy

Note: [a]Prostate-specific antigen in prostate cancer.
[b]Tumour-associated self-antigen in NY-ESO-1- and/or tyrosinase-positive melanoma.
[C]Hemagglutinin.

Initially, we thought that the patient experienced a simple allergic reaction to vaccination. However, there were no typical allergic signs, such as redness, itching, or shortness of breath. As time progressed, he complained of unilateral weakness and we had to differentiate the space-occupying lesion of the central nervous system. We were also concerned if the patient had an acute onset of various demyelination diseases such as multiple sclerosis or acute disseminated encephalomyelitis, or an abnormal systemic infection, such as HIV, progressive multifocal leukoencephalopathy, and Lyme disease, or even neuroborreliosis, although that was less likely. However, the result from the patient's serologic and brain imaging tests were all negative.

Therefore, Guillain–Barre Syndrome (GBS) was considered based on the acute-onset sensorimotor neuropathy. This condition usually occurs after vaccination and is self-limiting. However, the patient's course did not show an ascending feature and was not symmetrical. Even though symptoms subsided naturally, the rate of changes was too fast for GBS, even without regarding the preserved respiratory function. Cerebrospinal fluid analysis was not performed because his condition showed rapid improvement and electrophysiological studies revealed normal results.

Peripheral nerve disease could not explain the results of his neurologic examination or the EMG/NCV test. Focusing on the patient's upper arm symptoms, brachial plexopathy or myelopathy could be considered. However, issues with his peripheral nerves seemed unrelated to other systemic symptoms, including diplopia.

Conclusion

In the end, a definitive diagnosis of his condition was not confirmed. However, there have been several reports of peripheral neuropathy related to mRNA vaccines. Due to the peculiarity of the COVID-19 situation, sufficient data regarding the safety of mRNA vaccines cannot be obtained. As vaccine commercialization continues, unexpected adverse events with diverse symptoms may appear. Although the pathophysiology of the neurologic side effects of mRNA vaccines has not been investigated sufficiently, it is probable that the neurologic side effects may be related to past injury of neighboring tissues and is likely self-limiting.

Disclosure

The authors have no potential conflicts of interest to disclose.

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