CLINICAL AND EXPERIMENTAL VACCINE RESEARCH

Clin Exp Vaccine Res 2021;10:293-297
https://doi.org/10.7774/cevr.2021.10.3.293
pISSN 2287-3651 • eISSN 2287-366X

A case of acute encephalopathy and non-ST segment elevation myocardial infarction following mRNA-1273 vaccination: possible adverse effect?

Sabrina Yesmin Barsha[1], Miah Md. Akiful Haque[2], Md Utba Rashid[3], Mohammad Lutfor Rahman[4], Mohammad Ali Hossain[1], Sanjana Zaman[5], Elias Bhuiyan[6], Rahima Sultana[7], Mosharop Hossian[8], Mohammad Hayatun Nabi[2], Mohammad Delwer Hossain Hawlader[2]

[1]Ibn Sina Medical College Hospital, Kallyanpur, Dhaka; [2]Department of Public Health, North South University, Dhaka; [3]International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka; [4]Institute of Statistical Research and Training (ISRT), University of Dhaka, Dhaka; [5]Department of Public Health, Daffodil International University, Dhaka; [6]Bangladesh Medical College and Hospital, Dhaka; [7]Dhaka Dental College, Dhaka; [8]Public Health Professional Development Initiative (PPDI), Dhaka, Bangladesh

Received: August 15, 2021
Accepted: September 5, 2021

Corresponding author: Miah Md. Akiful Haque, MPH
Department of Public Health, North South University, Dhaka 1229, Bangladesh
Tel: +880-2-55668200, Fax: +880-2-55668202
E-mail: miah.haque@northsouth.edu

No potential conflict of interest relevant to this article was reported.

A 77-year-old man with a past medical history of type 2 diabetes mellitus, peripheral neuropathy, and chronic obstructive pulmonary disease was admitted to the intensive care unit of Bangladesh Medical College Hospital with acute encephalopathy and non-ST segment elevation myocardial infarction (NSTEMI). The patient was on antidiabetic medicine along with H_2 blocker and multivitamins for his existing diseases. The patient's attendant reported that the patient had received his first dose of the Moderna coronavirus disease 2019 (COVID-19) vaccine just 2 days ago. Physical examination revealed that he had a Glasgow Coma Scale of 8/15; a pulse of 106 beats/min; a respiratory rate of 30 breaths/min; oxygen saturation of 80% on room air, which became with 10 L of oxygen and blood pressure of 90/60 mm Hg at the time of admission. During the hospital stay, the patient was treated conservatively with intravenous antibiotics and other necessary medication. Although we have observed the onset of encephalopathy and NSTEMI following COVID vaccination for this patient, we, as healthcare professionals, cannot directly attribute the cause of the complications to the Moderna vaccine without further epidemiological studies with large samples.

Keywords: Non-ST elevated myocardial infarction, Encephalopathy, COVID-19, Bangladesh, Moderna vaccine, Case report

Introduction

Globally, as of 13th August 2021, there have been 205,338,159 confirmed cases of coronavirus disease 2019 (COVID-19) infection, including 4,333,094 deaths according to the World Health Organization COVID-19 dashboard [1]. Several new vaccines have been invented within a short time to combat this exceptionally challenging public health issue. It was the first instance in medical history to develop vaccines with extraordinary speed [2]. Following the invention of COVID-19 vaccines, worldwide, 4.66 billion doses have been administered already [3]. Even though the mass vaccination coverage program is fully operational, it is also essential to ensure the safe implementation of these vaccines to restrain the effect of the virus as soon as possible.

Among the all-approved vaccines available to use, the inactivated Moderna mRNA-1273 COVID-19 vaccine is one of the most effective. It was approved by the US Food and Drug Administration on 18th December 2020 for emergency use based on concrete phase III trial data [4]. The Directorate General of Drug Administration, Bangladesh, approved the vaccine for emergency use on 29th June 2021 [5]. Although it is

considered one of the safest COVID-19 vaccines, the complaints of post-vaccine complications also increase with more people being administered the vaccine. The most common complications following uptake of the inactivated COVID-19 vaccines are mild pain at the injection site, fatigue, headache, muscle pain, joint pain, chills, and fever [6]. Along with these, several adverse complications, including shingles, myocardial infarction, and acute encephalopathy, were also observed among people who took the Moderna vaccine [7-9]. While directly jumping to firm conclusions regarding the side effects of COVID-19 vaccines would be severely harmful to the mass vaccination coverage program, it is necessary, as we wait for solid clinical evidence, to carefully observe the immediate onset of severe disorders after vaccination.

Herein we present a case of acute encephalopathy and non-ST segment elevation myocardial infarction (NSTEMI) in a 77-year-old male patient to create an awareness among our clinicians to better manage these adverse conditions following the post-vaccination complications induced by the Moderna vaccine.

Case Report

A 77-year-old man with a medical history of type 2 diabetes mellitus (DM), peripheral neuropathy, and chronic obstructive pulmonary disease was admitted to the intensive care unit (ICU) of Bangladesh Medical College Hospital with complaints of high-grade fever and unconsciousness. The patient was first brought into the emergency department and eventually shifted to the ICU based on the patient's condition. The attendant reported that the patient received his first dose of the Moderna vaccine just 2 days ago, and he was stable before vaccination. However, after 12 hours of vaccination, he developed fever, went unconscious after 36 hours, and was admitted to this hospital 48 hours after the vaccine.

On examination, the patient was found febrile and unconscious with a Glasgow Coma Scale of 8/15 where the score for eye-opening, motor response, and verbal response were 3, 3, and 2, respectively. His pulse rate was 106 beats/min, and his respiratory rate was 30 breaths/min. At the time of admission, the duty doctor found his blood pressure 90/60 mm Hg. The patient's initial oxygen saturation recorded 80% on room air, which became 97% with 10 L of oxygen. No meningeal irritation or focal neurological deficits were noted. Plantar flexion was found. Notably, on admission, a chest X-ray was unremarkable, and COVID-19 was negative by reverse transcription-polymerase chain reaction test. The patient had no known neurological or psychiatric history except mild peripheral neuropathy due to DM. Besides, he had never used tobacco, alcohol, or any other harmful substances in his lifetime. As a regular medication, he was taking antidiabetic medicine along with H_2 blocker and multivitamins.

Several laboratory tests were conducted on the first day of admission. The results were significant for erythrocyte sedimentation rate (ESR) of 80 mm in 1st hour, hemoglobin 8.20 g/dL, white blood cell 35.93×10^9/L, neutrophil 33%, lymphocyte 61%, platelets 75.00×10^9/L, C-reactive protein (CRP) 101.5 mg/L, random blood sugar 8.3 mmol/L, blood urea 73.2 mg/dL, serum creatinine 1.19 mg/dL, serum albumin 34.9 gm/L, lactate dehydrogenase 399 U/L, and troponin I 860.1 ng/L. The electrocardiogram report showed transient ST elevation with T wave inversion in the lead III (v1 and aVL) and ST depression in leads I and II (v4, v5, v6, and aVL) (Fig. 1).

On the second day, arterial blood gas (ABG) and thyroid-stimulating hormone (TSH) tests were performed, and the results were ABG (PH, 7.22; PCO_2 [partial pressure of carbon dioxide], 64.3 mm Hg; PO_2 [partial pressure of oxygen], 122 mm Hg) and TSH 0.34 μIU/mL. A non-contrast computed tomography scan of the brain revealed mild cerebello-cerebral atrophy of the brain (Fig. 1). Lipase 332.9 U/L, calcium 7.62 mg/dL, D-dimer 8,782 ng/mL, and prothrombin time 14.90 seconds were found on the third day of hospital admission.

However, after being admitted into ICU, the consciousness level improved almost 24 hours later, and the fever subsided 36 hours later. Then, another 30 hours later, the doctor shifted the patient to the critical care unit (CCU) due to cardiac abnormalities. In the CCU, patient was found to have upper abdominal tenderness.

Noticeably, on the 5th day of admission, the patient's high-sensitivity troponin I was reduced to 144.6 ng/L along with his D-dimer (7,989 ng/mL). The Doppler echocardiogram report showed mild tricuspid regurgitation with mild pulmonary hypertension, impaired diastolic function with suitable left ventricular systolic function (left ventricular ejection fraction: 61% at rest). All the above investigations indicated that the patient was diagnosed with acute encephalopathy, NSTEMI, and acute pancreatitis (AP). During the hospital stay, he was treated conservatively with injection methylprednisolone, injection enoxaparin, intravenous (IV) antibiotic, and other supportive treatment. Finally, he was discharged after satisfactory improvement on the 10th day of hospital admis-

 https://doi.org/10.7774/cevr.2021.10.3.293

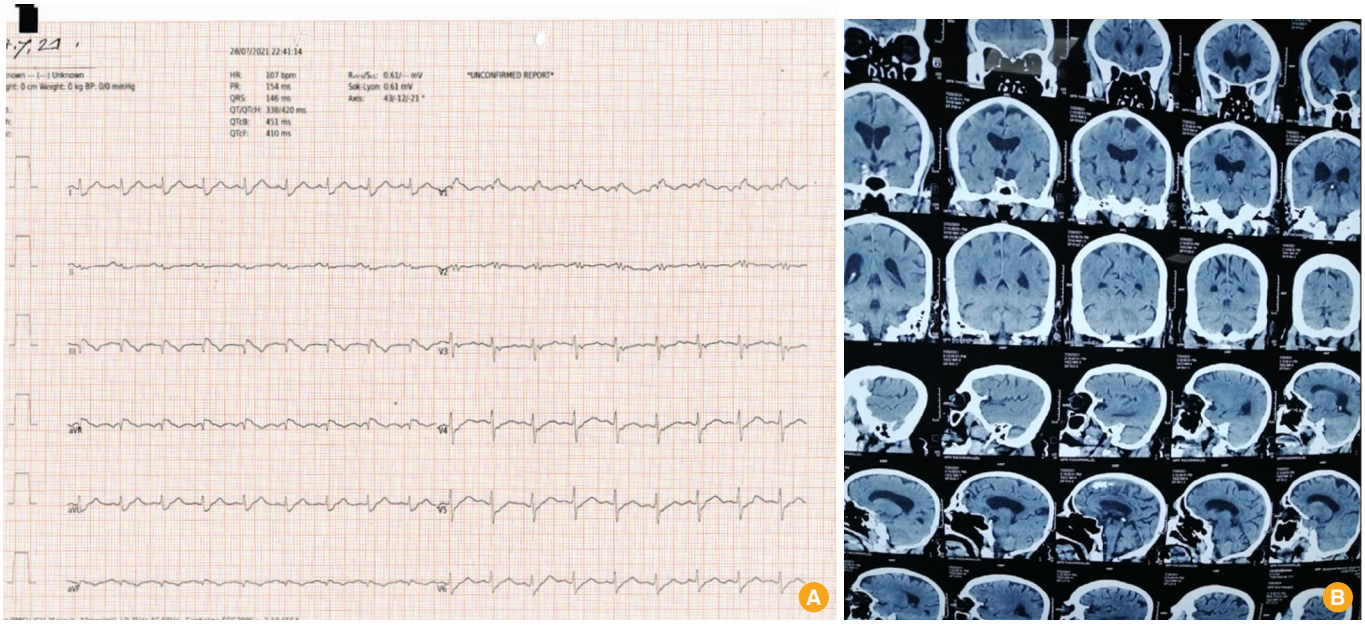

Fig. 1. Electrocardiogram report (A) and computed tomography scan of the brain (B). We obtained written informed consent for the publication of these reports from the patient's relative.

sion. On discharge, his vitals were pulse 78 beat/min, blood pressure 110/70 mm Hg, and SPO_2 (blood oxygen saturation) 95% with 4 L of oxygen.

Discussion

The patient's unconsciousness occurred within 36 hours of vaccination and consciousness level improved almost 24 hours of starting conservative therapy. The patient did not have any prior history of neurological or psychiatric events except mild peripheral neuropathy due to DM. This acute onset of unconsciousness in the absence of any metabolic abnormalities is therefore unlikely to be a typical image of fever-related disorientation in the elderly, rather could be a brain dysfunction. However, a variety of different factors can cause acute encephalopathy as well as unconsciousness. Nonetheless, unconsciousness has been reported in the aftermath of vaccines in the past [10].

Although the Moderna COVID-19 vaccine is not a protein vaccine, it does contain the antigen S-2P [11]. The severe acute respiratory syndrome coronavirus 2 glycoprotein is included in this antigen. As a result, it can be mentioned that the creation of the spike protein by cells that translate the mRNA initiates the same immune response as a COVID-19 infestation, increased inflammatory signals, culminating in these neurotropic consequences [7]. Notably, our patient meets this criterion due to high CRP, ESR, and D-dimer levels within days following symptoms began and 2 days from the first immunization.

Additionally, we observed a crucial confounder, in this case, is the patient's AP. Further, Wernicke encephalopathy, which occurs during the restoration step of AP [12], might be a possibility in this case. This patient was febrile with upper abdominal pain and costovertebral discomfort consistent with a severe AP. Of note, he was given IV antibiotic (meropenem) and other supportive treatments during his stay in the ICU to treat the AP.

According to the Centers for Disease Control and Prevention (CDC), persons 75 years or older account for 33% or more myocardial infarction events [13]. This indicates that the COVID-19 vaccine not necessarily causes myocardial infarctions, but it may significantly increase the heart's workload [9].

The Moderna trial's initial findings indicated that 92% of participants stated discomfort at the injection site, 70% expressed exhaustion, 15.5% reported a rise in their body temperature, 19.8% reported armpit swelling or soreness, and 23% experienced nausea and vomiting. Of the study subjects, 24.8% (7,520) were 65 years or older [14]. While Moderna deemed these adverse effects modest, they may be substantial for older persons, particularly those with established comorbidities. In Norway, there was worry that the Pfizer vaccination was connected with an increased risk of death in older persons,

with a questionable rumor about 23 deaths, and a study into these deaths revealed that some of the side effects listed above might have contributed to the ends of "frail patients" [15]. As per the CDC, more than 1,100 deaths have been reported following the COVID-19 immunization, with no evidence of a relationship to the vaccination [16]. However, none of these cases have been published, restricting our capacity to comprehend the circumstances underlying these fatalities.

It's reasonable to assume that older persons with several comorbidities may be overwhelmed by the possible adverse effects of COVID-19 vaccines. In the situation detailed here, the stress associated with receiving the COVID-19 immunization may have resulted in myocardial infarction in the older adult with a background of type 2 DM and concomitant peripheral neuropathy. Our patient presented to the emergency department 48 hours after getting the vaccine, likely too soon for any listed adverse effects.

We describe an abrupt encephalopathy and NSTEMI following Moderna COVID-19 immunization in a patient with no neurological or psychiatric background. We acknowledge that attributing pathology to the vaccine is impossible in a single case report or case series. Even large-scale examinations of probable adverse events, such as those conducted via the government-issued Suspected Adverse Event Reporting Form, can only reveal connections, not causation. Nonetheless, we hope that these findings raise awareness about the likelihood of a Moderna COVID-19 vaccine-related adverse event and encourage others to report similar cases if they occur.

ORCID

Sabrina Yesmin Barsha *https://orcid.org/0000-0002-5304-1151*
Miah Md. Akiful Haque *https://orcid.org/0000-0001-9134-6653*
Md Utba Rashid *https://orcid.org/0000-0002-2530-9982*
Mohammad Lutfor Rahman
https://orcid.org/0000-0001-9100-0476
Mohammad Ali Hossain *https://orcid.org/0000-0002-2153-5667*
Sanjana Zaman *https://orcid.org/0000-0002-8856-2352*
Elias Bhuiyan *https://orcid.org/0000-0002-6885-2782*
Rahima Sultana *https://orcid.org/0000-0002-6618-1954*
Mosharop Hossian *https://orcid.org/0000-0001-9584-7076*
Mohammad Hayatun Nabi
https://orcid.org/0000-0001-9816-2080
Mohammad Delwer Hossain Hawlader
https://orcid.org/0000-0002-1443-6257

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