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CASE REPORT

Status epilepticus as a complication after COVID-19 mRNA-1273 vaccine: A case report

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Abstract

BACKGROUND

We present a rare case of status epilepticus in a 56-year-old man which arose as a complication after vaccination with the coronavirus disease 2019 (COVID-19) mRNA-1273 vaccine. The patient's history included well-compensated secondary epilepsy. The root cause of the situation was a fever which had developed as a side effect of the vaccination.

CASE SUMMARY

A 56-year-old man received the first dose of mRNA-1273 vaccine against the severe acute respiratory syndrome-coronavirus-2. The vaccine was administered intramuscularly (100 mg, 0.5 mL). The next morning the man was found to be suffering from fever and headaches while at the same time experiencing general weakness. He lost consciousness suddenly and experienced generalized clonic seizures which turned into status epilepticus. When the Emergency Medical Service arrived the patient was unconscious with spontaneous breathing and generalized clonic seizures. It was necessary to administer diazepam repeatedly. It was also necessary to administer high doses of levetiracetam and temporary propofol. The status epilepticus was brought under control approximately 90 min after the patient's transport to the Emergency Department. A follow-up electroencephalogram no longer revealed abnormal indications of epileptic fit. The patient was temporarily hospitalized in the Intensive Care Unit and after seven days care was discharged without any further apparent effects.

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CONCLUSION

There is currently no specific treatment against COVID-19. Therefore, the benefits of COVID-19 vaccine protection outweigh the risks.

Key Words: SARS-CoV-2; COVID-19; mRNA vaccine; Complication of vaccination; Status epilepticus; Case report

Core Tip: Coronavirus disease 2019 (COVID-19) is a severe viral infection caused by the severe acute respiratory syndrome-coronavirus-2. There is no specific antiviral therapy for the COVID-19 infection but several vaccines have been developed. The safety of currently used mRNA vaccines has been confirmed by extensive research studies and common side effects are observed. However, there is no described case of status epilepticus as a complication after vaccination. In our case of such, involving a patient with epilepsy, the cause was likely a fever and an immune reaction as a side effect after the mRNA COVID-19 vaccine.

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INTRODUCTION

It was the last quarter of 2019 when a high number of cases of severe respiratory illness, mainly affecting the lower respiratory tract and lungs, occurred in Wuhan, China. The epidemiological investigation connected the first cases to the Huanan Seafood Market in Wuhan, China[1]. The disease rapidly spread from China to populated countries worldwide. A new β-coronavirus, designated 2019-nCoV and subsequently named severe acute respiratory syndrome (SARS)-coronavirus-2 (CoV-2), was identified as the causative agent. Most coronaviruses cause slight, common respiratory illness[2]. However, highly pathogenic coronaviruses, which can cause severe diseases such as the Middle Eastern respiratory syndrome or SARS, have long been recognized. The dominant source of SARS-CoV-2 is the person infected. Most of the virus is excreted in the initial phase of the disease during episodes of coughing and sneezing.

The disease manifests itself mainly in respiratory symptoms. However, it is possible to observe the effects of the virus on individual organs and systems. The most common symptoms are fever, cough, shortness of breath, myalgia, and arthralgia. Further symptoms include overall weakness, intensified tiredness, diarrhea, fatigue, sore throat, anosmia, ageusia, chest pain, hemoptysis, rhinorrhea, nausea, vomiting, skin rash, impaired consciousness, and seizures[3-5]. Laboratory examinations of patients with a moderate or severe course of the disease have shown elevations of C-reactive protein, interleukin-6 protein, lactate dehydrogenase, creatine kinase and ferritin. The number of leukocytes range mostly in the normal or lower level. Where differential blood count is concerned lymphocytopenia is more frequently observed [6]. In regards to imaging it is advisable to perform a chest X-ray or computed tomography (CT) scan. This can reveal the typical image of viral pneumonia.

Although dexamethasone and remdesivir appear to be promising medical therapies, there are currently no definite or specific treatments available. The mainstay of treatment today remains focused on supportive therapies. There are presently over 150 vaccines under investigation[7]. The most widely applied and effective of these are mRNA vaccines. An effectiveness rate of 95% has been noted upon completion of the coronavirus disease 2019 (COVID-19) vaccination cycle[8,9].

CASE PRESENTATION

Chief complaints

The emergency medical service (EMS) was called to examine an unconscious 56-year-old man who was experiencing generalized seizures.

History of present illness

The patient received the first dose of the mRNA-1273 SARS-CoV-2 vaccine one day before he began to experience difficulties. The vaccine was administered intramuscularly (0.5 mL containing 100 mg). The following morning the patient developed a fever, headache and overall weakness prompting the initial call to EMS for help.

History of past illness

The patient was under treatment for arterial hypertension. In 2012 he had suffered a cerebrovascular incident with residual spastic paresis of the right upper limb. In 2018 he had been hospitalized with a traumatic subarachnoid hemorrhage at the right frontal region. He was under treatment for secondary epilepsy and taking 1000 mg of valproate in the morning and 500 mg in the evening. There was no record of an epileptic seizure within the last 2 years.

Personal and family history

Personal history of the patient was otherwise unremarkable. Family history of the patient also proved unremarkable.

Physical examination

When EMS arrived the patient was unconscious with Glasgow coma score (GCS) of 1-1-1, spontaneous breathing and generalized clonic seizures. His respiration rate was 12 breaths per minute. Blood oxygen saturation was 87% in room air. His heart rate was 120 beats per minute and blood pressure was 170/95 mmHg. Blood glucose was 6.2 mmol/L and lactate was 9.7 mmol/L. Body temperature was 38.6 °C, indicating fever. After critical care was provided by EMS and the patient was transported to the Emergency Department The consciousness disorder remained with GCS of 2-1-5. The patient ventilated spontaneously and was able to keep his airways clear on his own while using an oxygen mask (flow rate of 6 L/min). The oxygen saturation in hemoglobin was 96%–98% and his circulatory system was stable. A few minutes after hospitalization the convulsive activity developed again. This was solved by emergent administration of anticonvulsants.

Laboratory examinations

The laboratory examination findings are summarized in Table 1. The values stated are from the first examination conducted upon arrival at the Emergency Department, during the hospitalization period and on the day of discharge.

Imaging examinations

Brain CT scan showed no intracranial hemorrhage, cerebral edema, or any new focal infections or processes. The only changes observed were the frontal-temporo-parietal changes caused by the previous cerebrovascular accident. Electroencephalogram (commonly known as EEG) conducted 3 h after the problems first occurred yielded normal findings. The majority of time the non-REM I stage of sleep was observed in the readings.

FINAL DIAGNOSIS

Status epilepticus of a patient with well-compensated secondary epilepsy. The cause was most likely an immune reaction and fever after receiving the mRNA COVID-19 vaccine.

TREATMENT

When the EMS first arrived, the patient was given an oxygen mask. Two intravenous entries were also made to deliver two doses of 10 mg (20 mg in total) of diazepam but

Table 1 Laboratory results

Laboratory marker	On admission	Day 2	On dismission	Normal range	Unit
Red blood cell count	4.08	3.8	4.0	4.0-5.8	$\times 10^{12}$/L
Hemoglobin	131.0	124.0	125.0	135.0-175.0	g/L
White blood cell count	6.8	5.2	4.6	4.0-10.0	$\times 10^{9}$/L
Platelets	163	136	204	150-400	$\times 10^{9}$/L
C-reactive protein	13.0	NT	8.0	0.3-10.0	mg/L
Total bilirubin	0.8	NT	0.4	0.1-1.2	mg/dL
Aspartate aminotransferase	25.0	NT	20.0	0.1-50.0	IU/L
Alanine aminotransferase	27.0	NT	17.0	0.1-40.0	IU/L
Glucose	6.8	NT	5.5	3.6-5.6	mm/L
Urea	18.3	16.5	11.0	7.0-30.0	mg/dL
Creatinine	0.95	0.83	0.81	0.7-1.2	mg/dL
Sodium	142	144	142	136-144	mm/L
Potassium	3.8	3.8	3.9	3.8-5.2	mm/L
Chloride	108	110	108	98-109	mm/L
Lactate	9.7	NT	NT	0.5-1.0	mm/L

NT: Not tested.

to no effect. This being the case, a short-term infusion of saline with 4000 mg levetiracetam was administered in moderate intervals. Afterwards, the convulsions subsided. The patient remained unconscious and his breathing was spontaneous. The oxygen mask provided oxygen therapy such that his saturation was sufficient and circulatory system stable. To address the fever 1000 mg of paracetamol was administered intravenously.

During transport of the patient to the hospital by ambulance, generalized clonic seizures reappeared. Boluses of 50 mg propofol were repeatedly administered intravenously with good results. In total the patient was given 150 mg of propofol.

Shortly after admittance to the Emergency Department of the hospital convulsion activity began again. As a result another dose of 2000 mg levetiracetam was administered intravenously. After some time 400 mg lacosamide was also administered intravenously. A short-term infusion of 100 mg thiamine was further administered. After some time the patient's disordered consciousness adjusted and he regained conscious. His response to verbal stimuli was slow but he was making active attempts to communicate. There was no recurrence of seizures.

After the CT scan and EEG examination the patient was admitted to the Intensive Care Unit (ICU) for follow-up treatment. In the ICU the patient experienced no complications. His regular dose of valproate was adjusted to account for the input level being lower (near the borderline level).

OUTCOME AND FOLLOW-UP

On the 3rd day of hospitalization the patient was moved from the ICU to a regular room. At this time his consciousness was stable and he was communicating normally. From the neurological point of view only the former deficiency (from after the previous cerebrovascular accident) was present (*i.e.* the right upper limb paresis). On the 7th day the patient was discharged. Since then no repeated epilepsy seizure has occurred (according to self-report during the in-person follow-up).

DISCUSSION

The new mRNA-1273 SARS-CoV-2 vaccine has been properly tested per international standards and norms. After administrating it to 15210 people the main side effects reported have been pain in the place of application and headache. After receiving the second dose of vaccine, however, the side effects of fever, increased tiredness, muscle and joint pain and chills have been the most frequently reported. Hypersensitivity reactions have been described in 1.5% of vaccinated people. Only two deaths have been reported after receiving the vaccine. Neither had any connection to the vaccine application (one was a cardiopulmonary arrest and the other was a suicide)[9]. Status epilepticus of a treated epileptic as a complication of fever that developed after the Moderna mRNA vaccine application has not been described yet.

Approximately 13% of patients with epilepsy have a history of experiencing febrile convulsions. Some studies point to a common genetic basis for febrile convulsions and some epileptic seizures[10]. Here we find a link between the fever and the development of status epilepticus in a patient in this case report.

Generalized status epilepticus must be considered an urgent and life-threatening condition. The seizures might be related to apnea and cyanosis states. Metabolic acidosis may also develop but in most cases it is automatically corrected in the context of proper control of the seizure. Most patients can breathe properly during the fit unless there is another reason for airway obstruction[11]. Therefore, oxygen should only be given in a case of a significant hypo-saturation. In a case of prolonged apneic pauses providing supportive ventilation is also necessary.

After securing vital life functions the most frequent first-line treatment of adults in the first 10 min of the seizure is a 10 mg intravenous dose of diazepam. The administration can be repeated up to a total dose of 30 mg of diazepam. Abroad it is more likely that an intravenous dose of 2–4 mg lorazepam be used. It is also alternatively recommended to administer 10 mg midazolam intramuscularly. However, the intramuscular application is not considered a very suitable choice in cases of ongoing convulsion activity. When vascular entry cannot be assured a dose of diazepam (0.2–0.5 mg/kg, up to 20 mg in total) per rectum or internasal administration of midazolam[12] is recommended.

If the seizure is persistent the second-line treatment, after approximately 20 min, is phenytoin administered as an intravenous dose of 20 mg/kg. According to Lowenstein *et al*[13] 60% of status epilepticus cases ceased upon phenytoin administration after the previous administration of diazepam. To prompt a faster effect it is possible to first administrate benzodiazepines. Then, instead of phenytoin, valproic acid is recommended at 20-30 mg/kg and administered at a maximum rate of 100 mg per minute or levetiracetam at 60 mg/kg administered as an extended intravenous infusion.

If status epilepticus lasts longer than 30 min it is advisable to administer propofol at an initial intravenous dose of 2 mg/kg when tracheal intubation is provided. Thereafter, it is delivered as a continuous intravenous dose of 2–5 mg/kg per hour. If the status epilepticus persists even further (mostly longer than 90 min), it is necessary to administer phenobarbital at an initial intravenous dose of 5 mg/kg with continuance based upon the patient's response; the dosage is usually in the range of 1–5 mg/kg per hour. The medication should also include thiamine in the total dosage up to 500 mg and ideally in a glucose infusion solution to prevent the depletion of available thiamine stores and an acute Wernicke encephalopathy[14] with prolonged status epilepticus.

CONCLUSION

COVID-19 is a severe viral infection caused by SARS-CoV-2. There has been no significant breakthrough in the treatment of the disease. Therefore, vaccination seems to be the main protection strategy against it. The safety of vaccines in current use has been confirmed by extensive research. The side effects of the vaccine which have been observed are mainly the same for any other viral disease vaccine.

Those side effects are mostly local reactions, increased tiredness, subfebrile state, headaches, and muscle and joint pain. The benefits of COVID-19 vaccine protection far outweigh the risks of an allergic reaction and/or other side effects of the vaccine.

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