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Case Report

Myasthenia Gravis Exacerbation Following COVID-19 Vaccine: A Case Report

Thoybah Yousif Ibrahim Gabralla,[1] Hayat Abdoallah Ahmed Bashir,[2] Omaima Abdalla Hajahmed Mohamed.[3]

Abstract

Background: Vaccination remains the mainstay of strategy for prevention of Coronavirus Disease-2019 (COVID-19). AZD1222 (AstraZeneca vaccine) was distributed in Sudan by the COVID-19 Vaccines Global Access facility in March 2021. It was added to the emergency use list by the WHO in mid-February 2021. However, vaccine safety among patients with autoimmune diseases, such as myasthenia gravis (MG), is yet to be established. MG is a relatively rare illness that could result in life-threatening complications. Myasthenic crisis is considered the most serious complication of MG that can lead to death due to aspiration and respiratory failure. **The case:** We report the case of a 37-year-old Sudanese female who presented to the emergency room with an exacerbation of her normally well-controlled MG following her second dose of AZD1222 vaccination. She continued to deteriorate and was admitted to the intensive care unit, where she was intubated and placed on a mechanical ventilator. The low-income setting was a major barrier in obtaining intravenous immunoglobulin until the patient died. Our study aims to present an MG case with features of MG exacerbation following administration of a second dose of AZD1222. **Conclusion:** Little is known about the effect of different COVID-19 vaccines on subgroups of patients with autoimmune diseases like MG. In our case, an exacerbation of MG may have been precipitated by the COVID-19 AstraZeneca vaccine. Therefore, more efforts and experimental studies may be needed, with closer vigilance in MG patients.

Key Words: Myasthenia gravis; COVID-19; Vaccine; Case report (Source: MeSH-NLM).

Introduction

To date, the Coronavirus disease-2019 (COVID-19) pandemic has resulted in millions of deaths worldwide. As of December 2021, the World Health Organization (WHO) reported 280,119,931 confirmed cases of COVID-19 and 5,403,662 COVID-19-related deaths.[1] While COVID-19 continues to be a major cause of deaths in Sudan, the COVID-19 Vaccines Global Access (COVAX) facility distributed more than 800,000 doses of AstraZeneca vaccine (AZD1222) in Sudan in March 2021.[2] According to the WHO, AZD1222 is a novel recombinant replication-deficient chimpanzee adenovirus carrying a gene encoding the S protein antigen of SARS-CoV-2.3 It is synthesized by SK Bioscience Co. Ltd (SK Bio) in the Republic of Korea.[3]

AZD1222 was added to the emergency use list by WHO in mid-February 2021.[4] Five Clinical trials in UK, Brazil, and South Africa, which included 23,745 participants, were conducted to assess its safety. The vaccine was well tolerated with minor side effects such as injection site inflammation, headache, nausea, fever+/-chills, muscles and joint pain, and fatigue.[3] Thrombosis and thrombocytopenia were uncommon, but serious side effects were reported in few cases after administration of AZD1222.[5] However, vaccine safety among patients with autoimmune diseases, such as myasthenia gravis (MG), is yet to be established and needs further studies. MG is a relatively rare illness with a worldwide prevalence rate of 12 per 100,000 population.[6] The principal underlying pathology is the destruction of the postsynaptic membrane at the neuromuscular junction by autoantibodies, mostly anti-acetylcholine receptor antibodies (Anti-AChR). It manifests clinically as fatigable weakness of ocular, bulbar, proximal extremities, neck, and respiratory muscles. Common exacerbating factors are physical exertion, high temperature, drugs, emotional stress, surgical procedures, infections, menses, or pregnancy.[7] MG exacerbation can present with a progressive pattern over a few days or up to one month. It should be considered as a potential

Highlights:

- COVID-19 is a relatively new pandemic that was first reported in Wuhan, China in 2019.
- COVID-19 vaccines were created to curb the spread of the disease.
- The effects of COVID-19 vaccines on pre-existing diseases such as Myasthenia gravis patients is still questionable.
- By sharing this case, we aim to elucidate the effects of the AstraZeneca COVID-19 vaccine on a Myasthenia gravis patient.

[1] House officer. Al-Shuhada Hospital, Khartoum, Sudan.

[2] Fifth-year Medical Student. University of Khartoum, Khartoum, Sudan.

[3] Medical officer at Alribat teatching hospital- Emergency department- Khartoum, Sudan.

About the Author: *Thoybah Yousif Ibrahim Gabralla is currently a house officer in the second shift (obstetric and gynecology) Al-Shuhada Hospital . She is also a recipient of Amlodac bonafide certification for doctors (2018) (Participation at country level medical excellence program).*

Correspondence:
Thoybah Yousif Ibrahim Gabralla
Address: F3X3+HH8, Kabol, Afghanistan
Email: Thoibona@hotmail.com

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imminent crisis. The main features of myasthenic crisis are weakness in respiratory and oro-pharyngeal muscles, which can deteriorate in a short period of time and be complicated by aspiration and respiratory failure. Plasma exchange (PLEX), Immunoadsorption (IA) and Intravenous Immunoglobulin (IVIG) are the first-line treatments for myasthenic crisis. It is also proven that cortisone has a positive effect when used as add-on therapy with PLEX/IA and IVIG.[8]

Our study aims to present a myasthenia gravis case with features of MG exacerbation following the administration of a second dose of AZD1222.

The Case

A 37-year-old Sudanese female with known MG since 2011 had been maintained on pyridostigmine (60 mg tablet once daily), and reported compliance to treatment. She received a first dose of the COVID-19 AstraZeneca vaccine, followed by a second dose a month later. She reported experiencing mild generalized weakness after the first dose that did not significantly limit her daily activities, and she did not seek any medical help at that time. After receiving the second dose, she had been experiencing severe generalized body weakness that increased overtime and inability to walk for about one month, for which she was on sick leave from her work. This was the presenting complaint at the emergency room (ER), along with a complaint of shortness of breath for one day. Dyspnea was not associated with fever or cough. Examination of other organ systems was non-significant. She had been missing her menstruation during this exacerbation. Her last MG exacerbation was about 10 years ago and had been treated accordingly. Thereafter, her disease was well controlled. Her last visit to the ER was about 4 years ago, where she had severe anemia that necessitated blood transfusion. There was no hypertension, diabetes mellitus, asthma, or any other diagnosed comorbidity. Moreover, there was no history of recent surgical procedures or administration of any drugs other than pyridostigmine. On examination, the patient was not cyanosed, pale or jaundiced. Vitals were as follows: pulse rate of 95 beats per minute, blood pressure of 175/125 mmHg, and respiratory rate of 24 breaths per minute. The patient's temperature was within normal range and the Glasgow coma scale was 6/15. Chest was clear on auscultation with the trachea being central. The abdomen was soft, with no tenderness, superficial masses, or organomegaly. After almost half an hour from the presentation, the patient developed cardiopulmonary arrest. Cardiopulmonary resuscitation was initiated immediately and was revived with the return of spontaneous circulation. She was intubated and ventilation was assisted with an Ambu® bag.

Thereafter, she started to breathe spontaneously. A few hours later, the patient developed respiratory arrest again and was assisted with an Ambu bag for about 6 hours until she was admitted to the intensive care unit (ICU), where a mechanical ventilator was utilized. Laboratory results were significant for hyperglycemia (470 mg/dL) at the time of presentation. Complete Blood Count was within normal ranges and a malaria blood test, which was done as per routine in Sudan, was negative. Computerized tomography of the chest was performed, and it revealed no evidence of COVID-19. Management at the ER started with rehydration and IV methylprednisolone 1g, followed by IV hydrocortisone 200mg. IVIG was requested, but could not be obtained, and fourteen days after admission, the patient died due to circulatory collapse. We obtained an informed consent for publication from the patient representatives due to the patient's death.

Discussion

We reported a case of MG exacerbation after a second dose of AZD1222. Present findings are consistent with the findings from another case that reported an exacerbation of MG after a second dose of the Moderna COVID-19 vaccine. The symptoms of exacerbation were dysphagia, non-specific joints pain, on and off fevers with chills, and fatigue.[9] In a recent case report, the patient developed fatal MG crisis after receiving AZD1222, but exacerbation occurred after the first dose.[10] Single-center case series investigated 22 MG patients and reported that 90.9% of patients had no exacerbation of symptoms four weeks after receiving vaccines (all of them received inactivated vaccines), and only 9.1% (n=2, one received an inactivated vaccine and the other received a recombinant vaccine) reported mild symptoms like neck and limb weakness.[11] In a study concerning neurological complications after the first dose of COVID-19 vaccines, AZD1222 was associated with an increased risk of hospitalization and death among MG patients. This increased risk was significantly associated with the age group of 50 years or below.[12] In a cohort study that evaluated 80 MG patients, where most of them received the BNT162b2 (Pfizer) vaccine, five patients received the Moderna vaccine, while three received AZD1222, the results showed that only four patients experienced myasthenic exacerbation. These four patients experienced MG exacerbation after the second dose of the BNT162b2 (Pfizer) vaccine.[13]

It is worth noting that almost all of the aforementioned vaccines that led to worsening of symptoms, including AZD1222, used genetic material to encode for specific proteins in order to activate the immune system. On the contrary, the administration of whole virus vaccines (inactivated vaccine) to 21 MG patients in a single-center case series did not lead to a worsening of symptoms, except in one patient who experienced mild symptoms. It could be that the difference depends on the type of vaccine itself. Although it has not been elucidated how COVID-19 vaccine provokes autoimmunity, several theories have been proposed. The molecular mimicry theory explains how the genetic material of a virus could provoke autoimmunity due to the cross-reactivity of antibodies produced against proteins encoded by viral genetic material with the proteins located at the post-synaptic membrane.[14]

MG can be classified according to etiology into Congenital Myasthenic Syndromes, Transient Neonatal due to maternal anti-

AChR antibodies, Drug-Induced, or Acquired Autoimmune.[7] A new MG diagnosis was reported in a patient who experienced slurred speech after receiving the BNT162b2 vaccine.[15] Additionally, other two individuals were newly diagnosed with MG following a second dose of the same vaccine.[16]

We noticed that the exacerbation, in most cases, occurred after the second dose instead of the first. MG patients have defective lymphocytes[17] which may respond to the vaccines in a different way. Sensitization may have occurred following the first dose, and since the second dose was administered after their lymphocytes already developed immunologic memory, a cytokine storm could have been stimulated.[18] This is still a hypothesis as it is yet to be proven in preclinical studies and in a clinical setting.

Infections are a well-known trigger of MG exacerbation.[7] Likewise, the COVID-19 infection is reported to cause an exacerbation of symptoms in MG patients and causes symptoms such as dysphagia, weakness, and respiratory failure.[19] Outcomes can include: ICU admission, mechanical ventilation, and death.[20] Nevertheless, a single-center study that assessed 83 MG patients with COVID-19 infection reported a favorable clinical outcome in 79 patients.[21] We can conclude that MG outcome in relation with COVID-19 infection is still controversial. This may raise questions about whether the vaccines' benefits outweigh the risks in MG patients or not. However, we believe that MG patients should be informed about the benefits and risks of COVID-19 vaccination.

The management of exacerbations involves steroids and IVIG.[19] Our patient was on steroids at the ICU, and IVIG was requested, but due to the high cost of this medication, it is not easily accessible in Sudan, and it was not possible to obtain it prior to her death. The use of immunosuppressive therapy is controversial. Some studies suggest that the use of immunosuppression can lead MG patients to a more severe course of COVID-19 disease,[22] while others suggest that MG patients infected with COVID-19 may need increasing immunosuppressive doses but should be stopped if sepsis occurs.[23]

Although the safety profile of AZD1222 is generally reassuring, people with severe underlying diseases were excluded from trials.[3] This report highlights the potential risks of vaccine use in individuals with pre-existing illnesses such as MG, in which its safety is unknown.

Conclusion

In summary, we reported a case of MG exacerbation following a second dose of AZD1222. The course of illness started with shortness of breath and generalized weakness, which deteriorated to respiratory arrest and necessitated ICU admission, followed by a fatal outcome. Little is known about the effect of different COVID-19 vaccines on subgroups of patients with autoimmune diseases such as MG. Therefore, more efforts and experimental studies may be needed, and closer vigilance in MG patients is recommended.

Summary – Accelerating Translation

العنوان: تفاقم الوضع الصحي لمريض الوهن العضلي الوبيل بعد تلقي لقاح مرض فيروس كورونا المستجد ٢٠١٩: تقرير حالة

ملخص:

تهدف الدراسة الى عرض حالة لمريضة مصابة بالوهن العضلي الوبيل اظهرت أعراض تفاقم مرض الوهن العضلي الوبيل بعد تلقي الجرعة الثانية من *AZD1222* لقاح مرض فيروس كورونا المستجد ٢٠١٩. تتوفر قليل من المعلومات عن تأثير لقاحات مرض فيروس كورونا المستجد ٢٠١٩ المختلفة على المرضى المصابين بأمراض المناعة الذاتية مثل مرض الوهن العضلي الوبيل .

بالرغم من أن درجة سلامة اللقاح مطمئنة الا أن المرضى المصابين بأمراض المناعة الذاتية استبعدوا من التجارب السريري، بالتالي هنالك حاجة ملحة للمزيد من الدراسات مع متابعة يقظة و لصيقة لمرضى الوهن العضلي الوبيل.

حاليا لا توجد معلومات عن الطريقة التي يقوم بها لقاح مرض كورونا المستجد ٢٠١٩ بتحفيز المناعة الذاتية لكن توجد نظريات عديدة, أشهرها نظرية التمويه او المحاكاة الجزيئية يمكنها تفسير كيف المواد الجينية للفيروس يمكنها تحفيز المناعة الذاتية. يوجد خلاف حول هل فائدة اللقاح بالنسبة لمرضى الوهن العضلي الوبيل أكبر من المخاطر التي يمكن أن يتعرضوا لها بعد تلقي اللقاح أم لا, وبالتالي يجب مناقشة فوائد و أضرار اللقاح مع مريض الوهن العضلي الوبيل.

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