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Rhabdomyolysis following Oxford/AstraZeneca COVID-19 vaccination; two case reports from Iran

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ABSTRACT

Defined as the destruction of the skeletal muscle wall and the release of cellular contents into the bloodstream, rhabdomyolysis has been reported as a complication for some forms of vaccines. On the other hand, the COVID-19 pandemic has led to the extensive production and use of several vaccines against SARS-CoV-2, meanwhile, the side effects of these vaccines are gradually being reported. Up to now, few cases of rhabdomyolysis due to COVID-19 vaccination have been reported in the studies. The present study intended to report two cases of rhabdomyolysis due to vaccination with Oxford/AstraZeneca COVID-19 vaccines. The patients were two men aged 70 and 75 years old who presented to a healthcare facility with weakness, myalgia, nausea, and vomiting for about ten days after receiving their first dose of the Oxford/AstraZeneca COVID-19 vaccine. Patients had elevated levels of creatine phosphokinase (CPK), which were 5540 IU/L and 18760 IU/L in patients, respectively.

Implication for health policy/practice/research/medical education:
Vaccination is currently considered the only available option for terminating the COVID-19 pandemic. However, the potential side effects of the available vaccines against COVID-19 can be concerning. The present study intended to report the incidence of two cases of rhabdomyolysis following vaccination with Oxford/AstraZeneca COVID-19 vaccines.

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Introduction

Rhabdomyolysis results from the disruption of the cellular membranes of the muscle cells with the subsequent release of intracellular contents into the bloodstream. This disorder may eventually lead to volume depletion, metabolic and electrolyte disturbances, and acute kidney failure (1). Several causes have been found for this disorder including; immobility, trauma, strenuous activity, seizure, some drugs like statins, and various toxins such as alcohol and cocaine (2,3). Moreover, several cases of virus-induced rhabdomyolysis due to the influenza A virus and some coronaviruses (4-6), including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (7), have been reported.

According to growing evidence, extensive vaccination is the only available option for terminating the COVID-19 pandemic. Therefore, the side effects of these vaccines are gradually being more and more reported. Up to now, two cases of rhabdomyolysis due to vaccination with the Pfizer/BioNTech (8) and Oxford/AstraZeneca vaccines (9) for COVID-19 have been reported in the studies. The present study intended to report two other cases of rhabdomyolysis due to vaccination with Oxford/AstraZeneca COVID-19 vaccines.

Case Series

Case 1

The first patient was a 70-year-old man without any considerable medical history who presented to the emergency department with severe nausea and four episodes of vomiting during the past three days. The patient stated that he was not able to get out of bed quickly in the morning due to generalized weakness. No other symptoms were reported. Moreover, the patient

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Case Series

had received his first shot of the Oxford/AstraZeneca COVID-19 vaccine ten days before and denied any recent trip or direct contact with the COVID-19 patients. In addition, he did not take any medications, including over-the-counter drugs, and did not have a history of alcohol or tobacco use. No history of recent exercise or trauma was reported as well.

At the time of the admission, the patient's vital signs were stable and as follows; blood pressure was 110/60 mm Hg, heart rate was 86 beats per minute, respiratory rate was 19 per minute, the temperature was 37°C, while O_2 saturation was 96% at ambient air. Moreover, there was no abnormal finding in the physical examination.

The related laboratory test results at the time of admission are listed in Table 1. Moreover, no urinary red blood cells (RBCs) or RBC casts were reported. Furthermore, polymerase chain reaction (PCR) for COVID-19 was negative.

On the other hand, the patient had paroxysmal supraventricular tachycardia in electrocardiography (ECG) that was converted to sinus rhythm using adenosine. Moreover, the troponin levels were low in the follow-up tests. Likewise, the patient had normal ejection fraction (EF) in echocardiography, and no regional wall motion abnormality was reported. Finally, ischemic causes were excluded based on the cardiology consult.

The patient was hydrated using intravenous therapy, including crystalloids and normal saline, and his urine output was maintained in the normal range. Moreover, during hospitalization for one week, the levels of serum creatinine, creatine phosphokinase (CPK), aspartate transaminase (AST), and alanine transaminase (ALT) reached 1.6 mg/dL, 370 IU/L, 48 U/L, and 42 U/L from the bases as reported in Table 1, respectively. Additionally, the patient did not need dialysis during his hospitalization.

Case 2

The second patient was a 75-year-old man who presented to the emergency department with weakness, inability to walk, nausea, vomiting, dark urine, and decreased urinary volume. The patient had received his first shot of the Oxford/AstraZeneca COVID-19 vaccine 10 days before the hospital admission. In his past medical history, diabetes mellitus, hypertension, ischemic heart disease, and chronic kidney disease (serum creatinine; 1.8 mg/dL) were reported. Moreover, he had a peripheral vascular disease and had undergone surgery for the placement of an avascular graft in his left lower extremity about six months ago.

At the time of the admission, the patient's vital signs were stable and was as follows; blood pressure was 105/75 mmHg, heart rate was 95 beats per minute, respiratory rate was 21 per minute, the temperature was 37°C, and O_2 saturation was 90% at ambient air. Moreover, there was

Table 1. Laboratory test results of case 1

	At the time of admission	At the time of discharge	Reference range
WBC (per µL)	6.4	7.8	4-10
Hb (g/dL)	14.4	12.8	14-18
Platelet (per µL)	169	135	150-450
Sodium (mEq/L)	128	137	136-145
Potassium (mmol/L)	5	4.7	3.5-5.1
CPK (IU/L)	5540	370	30-200
LDH (IU/L)	1240	440	100-480
BUN (mg/dL)	51	32	8.4-25.7
Creatinine (mg/dL)	2.42	1.6	0.86-1.4
Calcium (mg/dL)	8.06	8.00	8.8-10.2
Phosphorus (mg/dL)	3.55	3.2	2-6-4.5
Albumin (g/dL)	3.3	3.6	3.9-4.9
Magnesium (mEq/L)	2.05	1.8	1.8-2.6
AST (SGOT, U/L)	300	48	10-40
ALT (SGPT, U/L)	140	42	10-41
ALP (IU/L)	240	239	100-270
CRP (mg/L)	25	6	0-6
ESR (mm/h)	24	15	0-12
PTT (s)	30	34	28-40
PT (s)	13.2	12.9	10-12
INR	1.32	1.29	1-1.2
D-dimer (ng/mL)	960	700	0-500
Troponin (ng/mL)	1098	86	0-50

WBC; White blood cell, Hb; Hemoglobin, CPK; Creatine phosphokinase, LDH; Lactate dehydrogenase, BUN; Blood urea nitrogen, AST; Aspartate aminotransferase, ALT; Alanine aminotransferase, ALP; Alkaline phosphatase, CRP; C- reactive protein, ESR; Erythrocyte sedimentation rate, PTT; Partial thromboplastin time, PT; Prothrombin time, INR; International normalized ratio.

no abnormal finding in the physical examination except for the weakness of proximal muscles.

The related laboratory test results at the time of admission are listed in Table 2. No urinary RBC or RBC casts were reported too. Moreover, the patient underwent PCR testing for COVID-19 which was negative.

Despite the initial hydration, the patient's urinary output was not enough, and he became anuric within two days after admission. Likewise, electrolyte disturbances, including hyperkalemia and hyperphosphatemia, which were resistant to medical treatment were developed. Eventually, hemodialysis was started for the patient. He underwent seven sessions of hemodialysis every 2-3 days. In addition, hydration was continued during, however the patient remained oliguric. Finally, the renal function was not recovered, and the patient underwent a catheter placement for permanent dialysis.

Discussion

Rhabdomyolysis is a potentially life-threatening disorder that is caused by the disruption of the membranes of the skeletal muscle cells and subsequent release of the intracellular contents into the circulation, leading to increased blood levels of CPK, LDH, aldolase, potassium, and phosphate. This disorder can result from extensive causes, such as trauma, toxins, and infection. Moreover, the related manifestations range from merely elevated enzyme levels and electrolyte disturbance to a life-threatening disease leading to AKI (10).

It has been shown that viral infection can lead to rhabdomyolysis. For example, some cases of rhabdomyolysis following infection with influenza or coronaviruses, including the SARS-CoV-2, as the causative agent of the recent COVID-19 pandemic, have been reported (4-7). Moreover, reports have shown that rhabdomyolysis can be a rare side effect of vaccines, such as the recombinant vaccine against herpes zoster virus (11) and influenza vaccine (6,12). However, the underlying mechanism of post-vaccination rhabdomyolysis is not fully illustrated yet. It can be an excessive immune response to the vaccine's components (11).

Following the global spread of COVID-19, related morbidity and mortality, and the lack of effective antiviral treatments, the need for the development of vaccines to terminate the pandemic was highlighted (13). Several attempts have been made so far to develop highly effective and safe vaccines for COVID-19, and many types of vaccines, including mRNA vaccines, have been produced to stimulate the immune system of the human body against SARS-CoV-2 (13). However, some cases of myositis leading to rhabdomyolysis have been reported due to vaccination with mRNA (9) including an 80-year-old male patient who developed myalgia and vomiting

Table 2. Laboratory test results of case 2

	At the time of admission	At the time of discharge	Reference range
WBC (per µL)	14.6	6.5	4-10
Hb (g/dL)	8.1	9.7	14-18
Platelet (per µL)	184	120	150-450
Sodium (mEq/L)	149	146	136-145
Potassium (mmol/L)	5.6	4.2	3.5-5.1
CPK (IU/L)	18760	69	30-200
LDH (IU/L)	2204	650	100-480
BUN (mg/dL)	41	25	8.4-25.7
Creatinine (mg/dL)	4.1	2.1	0.86-1.4
Calcium (mg/dL)	7.5	7.8	8.8-10.2
Phosphorus (mg/dL)	5.9	4.1	2-6-4.5
Albumin (g/dL)	3.00	3.2	3.9-4.9
Magnesium (mEq/L)	2.01	1.9	1.8-2.6
AST (SGOT, U/L)	407	41	10-40
ALT (SGPT, U/L)	486	15	10-41
ALP (IU/L)	464	340	100-270
CRP (mg/L)	20	13	0-6
ESR (mm/h)	85	13	0-12
PTT (s)	46	33	28-40
PT (s)	13.7	15	10-12
INR	1.37	1.5	1-1.2
D-dimer (ng/mL)	3594	1600	0-500
Troponin (ng/mL)	93	51	0-50

WBC; White blood cell, Hb; Hemoglobin, CPK; Creatine phosphokinase, LDH; Lactate dehydrogenase, BUN; Blood urea nitrogen, AST; Aspartate aminotransferase, ALT; Alanine aminotransferase, ALP; Alkaline phosphatase, CRP; C- reactive protein, ESR; Erythrocyte sedimentation rate, PTT; Partial thromboplastin time, PT; Prothrombin time, INR; International normalized ratio.

following his second shot of the Moderna COVID-19 vaccine.

The patient had a CPK level of 6546 IU/L (normal range; 30-200 IU/L) and received Intravenous fluids during his hospitalization. Finally, his renal function recovered and he was discharged in stable condition (9). The next case was a 21-year-old man who presented with myalgia and dark urine and had received his first shot of the Pfizer/BioNTech COVID-19 vaccine recently. This patient had a CPK level of 22000 IU/L (normal range; 20-190 IU/L) and was discharged following five days of fluid therapy without any remaining renal dysfunction (8). In addition, the present study reported two cases of rhabdomyolysis in 70 and 75-year-old male patients following vaccination with the first dose of the Oxford/AstraZeneca COVID-19 vaccine.

Conclusion

Following the global spread of COVID-19 and the development of vaccines as the only feasible way for pandemic termination, several side effects have been reported for the COVID-19 vaccines. Publication of these reports can increase the awareness of clinicians, which may lead to on-time diagnosis and treatment.

Authors' contribution

Conceptualization: Marzieh Hashemi.
Data curation: Ghazaleh Sajadi.
Formal analysis: Marzieh Hashemi.
Investigation: Marzieh Hashemi and Ghazaleh Sajadi.
Methodology: Marzieh Hashemi.
Resources: Marzieh Hashemi and Samaneh Pourajam.
Supervision: Marzieh Hashemi.
Validation: Marzieh Hashemi, Ghazaleh Sajadi, and Samaneh Pourajam.
Visualization: Ghazaleh Sajadi and Samaneh Pourajam.
Writing–original draft: Ghazaleh Sajadi.
Writing–review and editing: Ghazaleh Sajadi.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical considerations

The present case series followed the principles of the Declaration of Helsinki by the World Medical Association and the patients gave written informed consent for their data to be published in the form of a case report. Moreover, the present study was approved by the Ethics Committee of the Isfahan University of Medical Sciences with the ethics number of IR.ARI.MUI.REC.1401.175. Ethical issues, including plagiarism, data fabrication, and double publication, have been completely observed in this study.

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