Journal of Pharmacy Technology
2022, Vol. 38(4) 247–250

DOI: 10.1177/87551225221093944
journals.sagepub.com/home/pmt
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A Possible Case of COVID-19 Booster Vaccine–Associated Rhabdomyolysis and Acute Kidney Injury

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Abstract

Background: Nearly 10 billion doses of the various messenger ribonucleic acid (mRNA) and viral vector vaccines against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) have been administered worldwide. Adverse drug reactions (ADRs) have been overwhelmingly mild to moderate in nature. Rare side effects have included myocarditis/pericarditis, *thrombosis with thrombocytopenia syndrome (TTS)*, Guillain-Barré Syndrome (GBS), and death. However, vaccine-related ADR data are still being collected using a variety of reporting systems. **Purpose:** We will describe a case of suspected mRNA coronavirus disease 2019 (COVID-19) booster–related rhabdomyolysis in a woman who developed signs and symptoms 10 days after administration of the vaccine dose. With a Naranjo ADR probability score of 4, the vaccine was deemed to be a possible cause of our patient's rhabdomyolysis. **Methods:** A search of the VAERS (Vaccine Adverse Event Reporting System) mined in November 2021 revealed 386 reported cases of COVID-19 vaccine–related rhabdomyolysis. However, system limitations make the utility of the information problematic. **Conclusions:** It is vitally important that clinicians, scientists, and patients are aware of rhabdomyolysis as a potential side effect of vaccination. Suspected vaccine-related ADRs should be promptly and accurately reported via VAERS or other surveillance systems to support the ongoing effort to ensure vaccine safety.

Keywords

vaccines, booster, COVID-19, rhabdomyolysis, acute kidney injury

Introduction

On September 27, 2021, the Food and Drug Administration (FDA) issued an emergency use authorization for the Pfizer-BioNTech coronavirus disease 2019 (COVID-19) vaccine as a single booster dose for high-risk individuals who received the primary immunization series at least 6 months previously. On October 21, 2021, eligibility for booster doses was extended to the Moderna and Johnson & Johnson vaccines. Additional doses of the messenger ribonucleic acid (mRNA) COVID-19 vaccines have not been associated with any unexpected safety signals and adverse reactions have tended to be mild to moderate and short-lived.[1]

Severe rhabdomyolysis is an uncommon yet serious clinical syndrome that encompasses myoglobinuria, acute kidney injury (AKI), and a creatine kinase (CK) value greater than 1000 U/L.[2] The development of rhabdomyolysis results from skeletal muscle injury and the release of intracellular myoglobin. The accumulation of myoglobin in the renal tubules results in obstruction, direct renal damage, and precipitates AKI. The causes of rhabdomyolysis are many and include crush injuries, infection, excessive physical exertion, immobilization, venoms, and certain medications.[3] Effective treatment involves early recognition and aggressive fluid resuscitation along with elimination of the likely cause(s).

A possible case of Pfizer-BioNTech COVID-19 vaccine-associated rhabdomyolysis will be described in an elderly woman who developed signs and symptoms 10 days following administration of the dose. The patient has provided her written consent for her case to be discussed.

Case Report

The patient is a 69-year-old woman with a past medical history of type 2 diabetes mellitus, morbid obesity, coronary

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artery disease, mood disorder, hypertension, hyperlipidemia, hypothyroidism, chronic pain, osteoarthritis, pedal edema, asthma, and a remote history of breast cancer in remission. Two years prior to her presentation, she was prescribed rosuvastatin for hyperlipidemia and plaque stabilization. She had no history of lab abnormalities or intolerance with statin use. The patient was also taking furosemide, metformin, and losartan. At the time of presentation, her medical conditions were stable. On October 3, 2021, she received a mRNA COVID-19 mRNA booster dose (Pfizer-BioNTech, Comirnaty) as part of her health care maintenance. The next day, she noticed that her urine was dark brown and frothy. She was experiencing frequent nighttime awakenings to urinate with urgency. She reported groin pain that only occurred with urination. She denied any dysuria, flank pain, fevers, or chills. She denied dyspnea, chest pain, or myalgias. She had been eating and drinking normally and denied any type of trauma. On October 11, 2021, 8 days following her booster, she had standard bloodwork drawn in preparation for her upcoming appointment with her primary care physician (PCP). Her results revealed a serum creatinine of 1.77 mg/dL (baseline of 0.8 mg/dL). She was called by her endocrinologist and asked to hold her furosemide and metformin due to the increase in serum creatinine. She became concerned and reported to her PCP on October 13, 2021, to discuss her lab work. Bloodwork was repeated on the day of this visit, which revealed an AKI with a serum creatinine of 2.51 mg/dL. The patient was advised by her PCP to report to the emergency department (ED) for further evaluation and treatment.

Upon presentation to the ED on October 13, 2021, her creatinine was further elevated to 2.73 mg/dL, her CK was found to be 8394 U/L (N: 25-190 U/L), and her liver enzymes were elevated with an aspartate aminotransferase (AST) of 235 U/L (N: 8-45 U/L) and an alanine aminotransferase (ALT) of 211 U/L (N: 8-22 U/L). She was subsequently admitted to the hospital with the diagnosis of AKI and transaminitis in the setting of rhabdomyolysis due to unknown etiology. The patient denied any seizure history, strenuous activity, trauma, viral illness, or myalgias. She was euthyroid upon presentation. She did report a positive family history of polymyositis rheumatica.

Her metformin, furosemide, and losartan were held due to her AKI, and her rosuvastatin was held due to her transaminitis and rhabdomyolysis. The patient was started on a normal saline (NS) infusion at 300 mL per hour and an ultrasound was ordered of the right upper quadrant and the kidneys. She was also encouraged to continue oral hydration.

The NS infusion was later changed to lactated ringers with potassium at 200 mL per hour along with continued oral hydration. During the course of her admission, the serum creatinine, CK, and transaminitis improved with fluid resuscitation and holding medication that could worsen renal and hepatic function.

Rhabdomyolysis was determined to be the cause of her AKI. A renal ultrasound was negative for any anatomic cause. Common plasma cell disorders that can cause AKI were investigated and serum protein electrophoresis and urine electrophoresis were ordered prior to discharge and were found to be negative. A peripheral blood smear to assess for signs of multiple myeloma showed microcytic, normochromic anemia with mild anisopoikilocytosis with no definitive blasts identified.

This patient's transaminitis was also investigated. A right upper quadrant ultrasound showed no abnormality in the liver or biliary tree.

Rheumatology was consulted during her hospitalization due to a family history of polymyositis and lack of a clear etiology for the elevated CK. Recommendations included continued current management of rhabdomyolysis, obtaining an aldolase level to assess muscle breakdown and consideration of inflammatory myositis should her rhabdomyolysis not improve. Aldolase was elevated to 18.2 U/L (N: ≤8.1 U/L) confirming muscle damage and breakdown.

Further workup for rhabdomyolysis was conducted. Glucose-6-phosphate dehydrogenase was unremarkable. Epstein Barr virus Immunoglobulin M antibody was negative. The patient was also tested for the COVID-19 virus with polymerase chain reaction (PCR) upon admission on October 13, 2021, and was found to be negative.

The patient continued to improve with supportive care through intravenous and oral hydration. On October 19, 2021, she was deemed stable for discharge with a CK level of 855 U/L and a serum creatinine of 2.04 mg/dL. A discharge clinic follow-up appointment on October 20, 2021, revealed continued improvement of the CK and serum creatinine to 467 U/L and 2.02 mg/dL, respectively. Her transaminitis had resolved by that time and further testing was not required.

The patient was seen by rheumatology on December 2, 2021, and recommended no further workup for myositis with resolution of the elevated CK. The patient was seen in nephrology clinic on December 16, 2021, with continued improvement. Eleven weeks following the booster dose, her serum creatinine (1.16 mg/dL) had nearly returned to her baseline of 0.8 mg/dL.

Discussion

Worldwide, more than 10 billion doses of the mRNA and viral vector COVID-19 vaccines have been administered to date.[4] Despite the large number of doses given, the adverse effects associated with their use have been generally mild to moderate and transient.[1] Likewise, adverse effects following booster doses have generally mimicked those resulting from the primary series of doses.[1]

Rhabdomyolysis is a serious condition that results from extensive muscle damage and the release of myoglobin,

which can lead to an AKI if left untreated. Rhabdomyolysis has many causes, including trauma, infection, toxins, medication, and even COVID-19.[3,5] Management generally involves vigorous fluid resuscitation, seeking and eliminating the cause and avoidance of nephrotoxic agents.[3,5] Whether the COVID-19 vaccine can cause rhabdomyolysis is indeterminate. Interestingly, a search mined in November 2021 of the VAERS (Vaccine Adverse Event Reporting System) database found 386 cases of COVID-19 vaccine–related rhabdomyolysis (United States, its territories, and unknown). Given the limitations of this reporting system (eg, self-reports, incomplete patient data, inability to evaluate causation), the reliability and utility of the information is questionable. However, a PubMed (November 2021) search using the keywords "rhabdomyolysis" and "vaccine" yielded the first published case report and literature review on the topic. A 21-year-old man developed symptoms of pain and swelling in his lower back 1 day following an initial dose of the Pfizer-BioNTech COVID-19 vaccine.[6] His admission creatine phosphokinase (CPK) was approximately 22 000 U/L, and his liver function tests were elevated. Renal function was normal. An extensive workup revealed no obvious cause for the rhabdomyolysis. Following fluid resuscitation, his CPK and transaminase levels improved.[6]

Since that case, there have been more reported cases of a possible link between the Pfizer-BioNTech COVID-19 vaccine and rhabdomyolysis. A 37-year-old man with no significant past medical history developed myocarditis, pulmonary hemorrhage, AKI, thrombocytopenia, and extensive myositis with rhabdomyolysis 12 days after administration of the Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine.[7] The patient presented to the ED with acute left arm pain, swelling, and paresthesias as well as sudden-onset severe dyspnea and excessive sweating. During the hospital stay, the patient rapidly declined despite aggressive measures. Given an unremarkable workup and the proximity of the Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine administration, a generalized vaccine immune mediated process was suspected.[7] Following intravenous methylprednisolone, the patient improved dramatically and was weaned from oxygen on hospital day 7.[7]

This association has not been reported solely with the Pfizer-BioNTech COVID-19 vaccine as there was a case of rhabdomyolysis described in New Jersey, United States, following administration of the Ad26.COV2.S COVID-19 vaccine.[8] A 19-year-old male patient noted myalgia, muscle weakness, and darkened urine 2 days following his Ad26.COV2.S (Johnson & Johnson) COVID-19 vaccination. Laboratory evaluation revealed an increased CK of 15 638 U/L (peak of 44 180 U/L) and a urinalysis was positive for blood consistent with rhabdomyolysis. Further examination in the hospital stay excluded an autoimmune etiology, and strenuous physical activity were ruled out during the hospitalization. Following aggressive oral and parenteral hydration as an outpatient, his CK returned to normal within 2 weeks.[8] A previously heathy 28-year-old woman presented with muscle pain and lower limb muscle weakness 5 days following the administration of the mRNA SARS-CoV-2 (Moderna) vaccine.[9] The workup showed an elevated CK (17 959 U/L) with marked left leg subcutaneous edema. The patient also developed fasciitis which completely resolved with intravenous methylprednisolone.[9]

Our patient was admitted with an AKI, transaminitis, and rhabdomyolysis. It is likely that the rhabdomyolysis contributed to the kidney insult and hepatic dysfunction.[5] However, an extensive diagnostic workup revealed no specific cause for her symptoms or biochemical abnormalities. She had restarted her statin about 2 years prior to this presentation and had no previous intolerance to this medication. She has also restarted her metformin about 7 months prior to her presentation with no side effects. She did not have any symptoms of COVID-19 infection or other viral illness, and her COVID-19 PCR was negative. The temporal relationship between the administration of the booster dose of the COVID-19 vaccine and symptom onset supports the most credible explanation for the findings. With a Naranjo adverse drug reaction (ADR) probability score of 4, the vaccine was deemed to be a possible cause of our patient's rhabdomyolysis.[10]

Clinicians need to be aware that the COVID-19 vaccine could be a cause of rhabdomyolysis. It is plausible that this adverse effect could occur during the primary series of injections as well as following booster doses. Patient complaints of muscle pain and/or weakness and dark urine should alert the clinician of the possibility of rhabdomyolysis. A thorough history can help establish a temporal relationship to symptom onset and support a diagnosis of vaccine-induced muscle damage when all other etiologies have been excluded. Patients and clinicians alike should report possible vaccine-related adverse effects to the vaccine-related adverse event monitoring system (VAERS) to ensure ongoing surveillance efforts.

Author Contributions

CDP saw the patient in the hospital. KU and DA saw this patient in clinic. KU and CDP performed the literature search. All authors took part in drafting and editing the manuscript. All authors approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Consent for Publication

The patient provided written informed consent to publish the details contained within this case report.

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