

Case Report

COVID-19 Vaccine-Induced Rhabdomyolysis in a 53-Year-Old Woman

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Abstract

Introduction

COVID-19-induced rhabdomyolysis is a common complication in COVID-19 infection. However, only a handful of cases have been reported showing links between COVID-19 vaccine and rhabdomyolysis.

Case Presentation

We present the case of a 53-year-old woman, who recently received COVID-19 vaccine and presented to the hospital with progressive extremity weakness. Common reasons for rhabdomyolysis were ruled out as possibility and the patient was found to have rhabdomyolysis induced from COVID-19 vaccine.

Conclusion

Even though COVID-19 vaccine-induced rhabdomyolysis is rare, it should be considered in the differential diagnosis with patients presenting with neuromuscular complaints and a recent COVID-19 vaccine.

Keywords

adverse drug reaction; COVID-19 vaccine; rhabdomyolysis; statin

Introduction

COVID-19 infection has been linked to causing rhabdomyolysis; however, COVID-19 vaccine has been linked to only a few cases of rhabdomyolysis. Rhabdomyolysis is typically characterized by breakdown of skeletal muscles which causes release of intracellular components to the rest of the body, including an increase in enzymes like creatinine kinase. Rhabdomyolysis has been known to cause severe electrolyte abnormalities and acute renal failure, which can be fatal.¹ Potential etiologies of rhabdomyolysis have been studied extensively. This case presentation addresses an adverse effect in a 53-year-old woman who developed rhabdomyolysis after receiving the COVID-19 vaccine. The most common etiologies pertaining to rhabdomyolysis were ruled out, leaving the most likely diagnosis of latent COVID-19 vaccine-induced rhabdomyolysis.

Case Presentation

A 53-year-old woman initially presented to the hospital after 3 weeks of progressive proximal extremity weakness. The patient reported bilateral proximal upper and lower extremities pain, which started with the left lower extremity and progressed to the right lower extremity. One week later, the patient reported right upper extremity pain followed by left extremity pain. She noted a decrease in exercise capacity, from 30 minutes on the treadmill to 10-15 minutes. She denied prior similar symptoms. The pain was described as muscle soreness from a workout that occurred predominantly with movement. Neck and lower back pain were endorsed but the patient attributed these findings to a sedentary job. The patient received the second dose of COVID-19 vaccine (Pfizer-BioNTech COVID-19 Vaccine), in early 2021, with both vaccines given in the left arm. Adverse effects

reported from the vaccine included nausea and vomiting that resolved after 2 weeks. Presentation of symptoms occurred about 45 days after the second dose. The patient denied fever, chills, headache, recent trauma, shortness of breath, recent upper respiratory infections, gastrointestinal infections, pain in extremities, chest pain, rashes, recent travels, camping, new diet/foods (honey), medication changes, family history or cancers personally or in family.

The patient had a past medical history of diabetes mellitus and dyslipidemia. Medications included atorvastatin 80 mg which was decreased to 40 mg, due to left extremity soreness, about 45 days after the second dose, and metformin 500 mg. Of note, the patient had been on atorvastatin for over 3 years. Surgical history included ectopic pregnancy status post laparoscopy. She had no known drug allergies. The patient reported she consumed alcoholic beverages on occasion but denied smoking or recreational drug use. Physical exam showed the patient had bilateral proximal weakness in the upper and lower extremities, which was specifically pronounced bilaterally in the thighs. She was also noted to have pronounced tenderness on passive and active movements of bilateral upper and lower extremities.

Initial labs included creatine kinase of 7800 U/L initially, which trended down during hospitalization (**Table 1**). Other labs included, aspartate aminotransferase 241 U/L, alanine aminotransferase 384 U/L, total bilirubin 1.2 mg/dL, white blood cell (WBC) count $10.4 \times 10^9/L$, thyroid-stimulating hormone 7.18 uIU/mL with free T4 1.15 ng/dL, creatine kinase MB 292.3 U/L, HbA1c 6.3%, rheumatoid factor less than 10 IU/mL, cytoplasmic anti-neutrophil cytoplasmic antibody less than 0.2 IU/mL, and anti-smooth muscle antibody of 14 units. Cerebrospinal fluid (CSF) analysis was obtained, which showed colorless fluid with CSF protein of 24.7 mg/dL, CSF WBC $0 \times 10^9/L$, CSF RBC 1, CSF glucose 66 mg/dL. The CSF results were not consistent with Guillain-Barré syndrome.

Imaging consisted of chest x-ray which demonstrated no abnormalities. A magnetic resonance image without contrast of cervical spine/lumbar spine/extremities demonstrated mild degenerative changes in the discs throughout the region with mild diffuse annular disc bulging and spondylosis at C5-6 and C6-7.

Lumbar region findings included mild degenerative changes in discs, otherwise, with no other acute abnormality. Extremities were noted to have no significant abnormality.

A right thigh skeletal muscle biopsy was ordered, which was consistent with necrotizing myopathy, without specific diagnostic features and without features of chronic myopathic disorder. HLA class I immunohistochemistry was negative which provided support for nonimmune myopathy.

Atorvastatin was discontinued on day 1 of hospitalization. The patient received aggressive intravenous hydration consisting of normal saline at 150 cc/hr, increased to 200 cc/hr on day 2 of hospitalization, and sustained at 200 cc/hr until day 41. Kidney function was monitored throughout the hospitalization and remained within normal limits. Strict intake and output were documented along with volume status evaluation. The patient also received prednisone from day 1 to day 42 of hospitalization (30-40 mg PO daily) due to suspicion of an autoimmune process. She was also given intravenous immunoglobulin from day 37 to day 42 and was monitored for possible improvement in creatine kinase. The patient symptomatically improved throughout the hospitalization and was discharged home on Day 43 with close follow-up.

Discussion

Rhabdomyolysis is defined as a breakdown of skeletal muscle tissue. It has a typical clinical presentation of myalgia, generalized weakness, and darkened red to brown urine, with creatine kinase value 5 times above the upper limit of normal. In the setting of COVID-19, we first had to rule out other possible causes.

Possible etiologies for rhabdomyolysis can be grouped into traumatic vs nontraumatic.² Traumatic being crushed or direct injury. As our patient did not experience any type of trauma and symptoms of generalized weakness and myalgia started before exercising, trauma-related rhabdomyolysis was ruled out. Nontraumatic etiologies include seizures, tic disorders, overexertion, intoxication (cocaine, heroin, alcohol, carbon monoxide, phencyclidine), skeletal muscle ischemia, infection, adverse drug reactions (neuroleptics, statins), malig-

Table 1. Trend of Creatine Kinase Throughout Hospitalization

Hospitalization days	Creatine kinase (U/L)
1-7	>7800
8	5960
9	5721
10	4155
11	4525
12	4122
13	3979
14	3479
15	3651
16	3933
17	3143
18	2960
19	2847
20	3189
21	3094
22	3604
23	3690
24	3855
25	4444
26	4242
27	4147
28	4261
29	4001
30	3874
31	3632
32	3836
33	4240
34	3897
35	3928
36	4234
37	3672
38	3174
39	3116
40	3661
41	3189
42	3714

nant hyperthermia, inflammatory myopathies (poly/dermatomyositis), sickle cell disease, and genetic/metabolic disorders.³ Based on our patient's history, we limited our differential to infection and adverse drug reactions.

There are few published cases of similar symptoms with COVID-19 vaccine.^{4,5} Unlike prior similar cases, our patient demonstrated a delayed adverse effect, approximately 5 weeks after injection of the second vaccine dose. This could be attributed to the efficacy of the second dose of vaccine with age, cellular, and humoral immune responses as contributing factors, with studies demonstrating peak IgA/IgG approximately 5 weeks.⁶

Confounding Statin Use

According to the Paricalcitol Capsule Benefits in Renal Failure–Induced Cardiac Morbidity (PRIMO) study,⁷ median onset of symptoms was 1 month following initiation of statin therapy. Our patient had been taking atorvastatin 80 mg for over 3 years, recently decreased to 40 mg in the spring of 2021. With this in mind, we can rule out statin-induced myopathy. Statins were discontinued on day one of hospitalization. Of note, statin-associated muscle symptoms clinical index (SAMSCI) scoring cannot be used in this case, as the patient was not re-challenged. Furthermore, biopsy results in statin-induced myopathy would be consistent with nonspecific finding that includes necrosis, degeneration, regeneration of fibers and phagocytic infiltration,⁸ whereas the muscle biopsy obtained in this patient showed necrotizing myopathy without specifically diagnostic features and no diagnostically significant ultrastructural pathological features by electron microscopy.

Rhabdomyolysis secondary to vaccines has been previously described with the influenza vaccine.^{9,10} These cases displayed similar histopathological features⁹ on biopsy as our patient: a small number of lymphocytes, almost exclusively associated with necrotic and regenerating myofibers; minimal inflammation, with negative HLA Class I immunohistochemistry, supporting a non-immune (non-inflammatory) myopathy.

Non-inflammatory myofiber necrosis (or regeneration) has many potential causes, including, but not limited to toxin (eg, statin induced), electrolyte abnormalities, errors of metabolism, fever, flu infection, post-infectious, ischemic, or dystrophic.

As a diagnosis of exclusion, the remaining factor was the proximity in timing to her second vaccine dose. Though rare, we must entertain

the possibility of a vaccine-induced rhabdomyolysis.

Pathogenesis: Rhabdomyolysis From Infection

The mechanism is not clear; however, the current suggested pathogenesis is viral invasion of skeletal muscle tissue with direct damage from cytokines.¹¹ From MERS-CoV in 2005, there were cases of reported viral particles found in skeletal muscle. Both MERS and COVID-19 use angiotensin converting enzyme II (ACE2) receptors for cell invasion. ACE2 receptors are found in several organs, including muscles. Thus, it was suggested that COVID-19 shares a similar route of invasion leading to rhabdomyolysis.

The pathway of vaccine-related rhabdomyolysis is unclear, but it may follow a similar path to rhabdomyolysis related to COVID-19 infection. The patient was vaccinated with the Pfizer-BioNTech COVID-19 vaccine. An mRNA vaccine that causes muscle cells to produce the spike protein and induce a primary response and antibodies. These spike proteins attach to ACE2 receptors similar to the actual virus. Our proposed mechanism is therefore similar to that of a COVID-19 infection. Spike proteins are produced with the vaccine, followed by cellular invasion via ACE2 receptors and direct cytokine damage, from the subsequent inflammatory response.

Conclusion

Though rare and requiring more study, vaccine-induced rhabdomyolysis should be on the differential diagnosis list when patients present with neuromuscular complaints. Proper surveillance should therefore include questions regarding recent vaccines as well as recent infections when eliciting a history of present illness.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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