



# Severe rhabdomyolysis secondary to COVID-19 mRNA vaccine in a teenager

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## Abstract

**Background** Rhabdomyolysis, the breakdown of skeletal muscles following an insult or injury, has been established as a possible complication of SARS-CoV-2 infection. Despite being highly effective in preventing COVID-19-related morbidity and mortality, several cases of COVID-19 mRNA vaccination-induced rhabdomyolysis have been identified. We provide the second description of a pediatric case of severe rhabdomyolysis presenting after COVID-19 mRNA vaccination.

**Case: diagnosis/treatment** A 16-year-old male reported to the emergency department with a 2-day history of bilateral upper extremity myalgias and dark urine 2 days after his first dose of COVID-19 vaccine (Pfizer-BioNtech). The initial blood work showed an elevated creatinine kinase (CK) of 141,300 units/L and a normal creatinine of 69  $\mu\text{mol/L}$ . The urinalysis was suggestive of myoglobinuria, with the microscopy revealing blood but no red blood cells. Rhabdomyolysis was diagnosed, and the patient was admitted for intravenous hydration, alkalinization of urine, and monitoring of kidney function. CK levels declined with supportive care, while his kidney function remained normal, and no electrolyte abnormalities developed. The patient was discharged 5 days after admission as his symptoms resolved.

**Conclusion** While vaccination is the safest and most effective way to prevent morbidity from COVID-19, clinicians should be aware that rhabdomyolysis could be a rare but treatable adverse event of COVID-19 mRNA vaccination. With early recognition and diagnosis and supportive management, rhabdomyolysis has an excellent prognosis.

**Keywords** Rhabdomyolysis · mRNA vaccine · COVID-19 · Nephrology · Adverse event · Immunization

## Introduction

Rhabdomyolysis is the breakdown of skeletal muscles following an insult or injury, with common causes that include trauma, excessive exercise, immobility, drug or alcohol use, medications, or neuroleptic malignant syndrome [1]. Further, rhabdomyolysis has been established as a complication of SARS-CoV-2 infection [2]. Despite being highly effective in preventing COVID-19-related morbidity and mortality [3], several cases of COVID-19 mRNA vaccination-induced rhabdomyolysis were identified on a comprehensive

MEDLINE and Embase literature review [4–12]. These previously reported cases have exhibited a wide range of clinical features with little consistency between patients, although the prognoses have generally been favorable [4–12]. There has been one previously reported case in the pediatric population [12]. We describe a rare presentation of a patient with severe rhabdomyolysis secondary to COVID-19 mRNA vaccination, and the second case reported in a pediatric patient.

## Case presentation

A 16-year-old male presented to the emergency department with a 2-day history of severe bilateral upper extremity myalgia and a 1-day history of dark urine. Several hours prior to the onset of symptoms, he received his first dose of COVID-19 mRNA vaccine (Pfizer-BioNtech). The initial symptoms appeared overnight, presenting with severe bilateral upper extremity myalgia causing nocturnal wakening.

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Over the next day, his upper body muscle pain worsened, limiting his ability to perform normal daily activities such as carrying a school bag. He also noticed progressive darkening of his urine, prompting his presentation to the emergency department.

In the emergency department, he was afebrile, hemodynamically stable, and reported 10/10 muscle pain in both upper extremities. He appeared well and was cooperative. On exam, he had a limited range of motion of his upper extremities secondary to muscle pain. There was no visible rash, no sign of injury, and the neurological exam was within normal limits. The remainder of his physical exam was unremarkable. The initial blood work revealed an elevated creatinine kinase (CK) of 141,300 U/L and a creatinine of 69  $\mu\text{mol/L}$ . The cardiovascular screening, including electrocardiogram and serum troponin, yielded no abnormal results, and myocarditis was ruled out. Similarly, ultrasound of the abdomen and pelvis was performed and was within normal limits; specifically, the right kidney measured 10.5 cm, and the left kidney measured 10.2 cm, with normal parenchyma, good cortico-medullary differentiation, and no hydronephrosis. The urinalysis was positive for blood on dipstick with the absence of red blood cells on microscopy, suggestive of myoglobinuria. He was diagnosed with rhabdomyolysis and was admitted for intravenous hydration, sodium bicarbonate infusion, and monitoring of kidney function.

His medical history included long-standing asthma treated with inhaled salbutamol and seasonal allergies treated with over-the-counter cetirizine; he was taking no other medications. There was no recent history of trauma, crush injury, new medications, or previous adverse reactions to vaccines or other medications. He denied recent exercise, weightlifting, fever, or any other infectious symptoms. Notably, the patient had been infected with SARS-CoV-2 four months prior to the vaccination, which resolved following mild symptoms. The patient had no contributory family history.

The patient was admitted for a total of 5 days, and his symptoms resolved rapidly. His CK peaked at 147,600 U/L within 16 h of admission and returned to normal levels within 13 days, his kidney function remained normal, and no electrolyte abnormalities developed. On the 14-day follow-up, he remained asymptomatic and creatinine remained at a baseline of 78  $\mu\text{mol/L}$ . His physical exam was unremarkable, he reported no upper extremity myalgia, and his urine appeared normal. A medical genetics consult was initiated to investigate potential metabolic causes of acute-onset rhabdomyolysis. All subsequent investigations, including fatty acid oxidation defects (i.e., carnitine palmitoyltransferase II deficiency), glycogen storage diseases (i.e., type V and type IX), purine metabolism disorders, and mitochondrial disorders of the respiratory chain, had unremarkable findings. On the 3-month follow-up, it was noted that his creatinine was

slightly elevated at 80  $\mu\text{mol/L}$ . Glomerular filtration rate was 139 ml/m (per 1.73  $\text{m}^2$ ). His bloodwork and urinalysis were normal; he had a normal blood pressure and was back to all normal activities with no muscle pain.

## Discussion

We describe a case of rhabdomyolysis following COVID-19 vaccination in a previously healthy 16-year-old male that resolved with no lasting sequelae after supportive care. There have been a small number of case reports of rhabdomyolysis secondary to COVID-19 mRNA vaccination, with this being the second description in a pediatric patient. The previous pediatric case was that of a 16-year-old girl who presented with myalgia and weakness [12]. She had presented previously with similar symptoms following other immunologic stimuli such as the Gardasil vaccine [12]. Her symptoms also resolved following IV hydration and alkaline diuresis [12]. As global vaccination efforts against COVID-19 continue, it is important to document potential adverse events associated with vaccination, particularly in patients with preexisting COVID-19 infection, as these patients were excluded from early vaccine trials.

Mack et al. (2021) were the first team to report rhabdomyolysis that was presumed to be secondary to mRNA vaccination [4]. They described an 80-year-old diabetic man who presented with myalgia, nausea, and vomiting 2 days after his second Moderna COVID-19 vaccination [4]. His symptoms resolved following a 1-day course of supportive care. A similar case was later described by Elias et al. [7]. The case most analogous to ours was reported by Nassar et al. (2021), in which a healthy 21-year-old man with asthma presented with muscle pain and swelling in his lower back 1 day after vaccination with the Pfizer mRNA vaccine [9]. After the diagnosis of rhabdomyolysis was made, he was admitted for 5 days and made a full recovery with IV fluids and supportive care [9]. Faissner et al. described a case of rhabdomyolysis in a healthy 28-year-old female with a 4-week course that required IV methylprednisolone [5]. Rhabdomyolysis secondary to vaccination has also been described in a patient with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis [8] and in a patient with a ryanodine receptor 1 (*RYR1*) gene mutation [10]. One complex case presented with myocarditis, pulmonary hemorrhage, myositis, and rhabdomyolysis [11]. Finally, one fatal case of rhabdomyolysis following vaccination was reported, with the patient having many preexisting comorbidities [6]. The patient's preexisting heart failure with preserved ejection fraction prevented aggressive fluid therapy, leading to disease progression and death [6]. The previously reported cases of rhabdomyolysis secondary to COVID-19 mRNA

**Table 1** Comparison of our case presentation with the other nine published case reports about rhabdomyolysis secondary to COVID-19 mRNA vaccination

Case	Age	Sex	Presentation	PMHx	Treatment	Outcome
Puccio 2022 (this report)	16	Male	Presented 2 days following 1st Pfizer dose with upper extremity pain and limited range of motion	Asthma, seasonal allergies, and previous COVID-19 infection	IV fluids	Patient recovered without sequelae over 5-day admission with supportive care
Ajmera 2021 [6]	85	Female	Presented one day following 2nd Moderna dose with weakness, cramps, darkening urine, and loss of appetite	Rheumatoid arthritis, hyperlipidemia, asthma, previous cerebrovascular accident	IV bicarbonate-rich fluids, glucocorticoids, and ICU supportive care	Could not provide aggressive hydration due to heart failure, cardiac arrest in ICU, terminal extubation, and death
Al-Raspi 2022 [12]	37	Male	Presented 12 days after his first dose of Pfizer with back pain, limb swelling, paresthesia, and shortness of breath	None noted	Hydration, IV bicarbonate, antimicrobial coverage, IVIG, and methylprednisolone	Hospitalized for 16 days and discharged home on a tapering dose of oral prednisolone for 6 weeks
Elias 2021 [7]	81	Male	Presented 3 days after 1st dose of Pfizer with generalized weakness resulting in a fall	Ischemic heart disease with left bundle branch block, cerebrovascular disease, and idiopathic pulmonary fibrosis	IV fluids	CK and myoglobin returned to baseline, acute kidney injury resolved
Faïssner 2022 [5]	28	Female	Presented 5 days following 1st Moderna dose with lower extremity myalgia and weakness	Healthy	High-volume IV fluids, urine alkalization, and IV methylprednisolone	Four weeks after onset, CK returned to normal and symptoms resolved entirely
Hakroush 2021 [8]	79	Female	Presented 2 weeks after 2nd dose of Pfizer with weakness and upper thigh pain, diagnosed with ANCA-associated vasculitis leading to rhabdomyolysis	Hypertension and degenerative disk disease	IV fluids, IV methylprednisolone, and oral prednisone	Rhabdomyolysis ceased and kidney function normalized
Katz 2022 [11]	16	Female	Presented 1 week after her second Pfizer vaccine with myalgia, weakness, and dark urine	Previous reactions to immunologic stimuli secondary to heterozygous pathogenic variant in the <i>DYSF</i> gene encoding dysferlin	High-volume IV fluids and urine alkalization	Discharged in 10 days following resolution of symptoms and normalization of CK
Mack 2021 [4]	80	Male	Presented 2 days following 2nd Moderna dose with myalgia, nausea, and vomiting	T2DM and previous COVID-19 infection	IV fluids	Did not develop acute kidney injury or electrolyte abnormalities and symptoms resolved with supportive care
Nassar 2021 [9]	21	Male	Presented 1 day following 1st Pfizer dose with pain and swelling in the back	Asthma	IV fluids and morphine	Maintained normal kidney function and electrolyte levels, discharged 5 days after admission with resolved symptoms
Salter 2022 [10]	30	Female	Presented 8 days following 2nd Moderna dose with myalgia, weakness, and difficulty ambulating	Ryanodine receptor 1 ( <i>RyR1</i> ) gene mutation, five previous rhabdomyolysis since age 10 (usually triggered by viral infection), schizoaffective disorder, latent tuberculosis, polycystic ovarian syndrome, iron deficiency anemia, and obstructive sleep apnea	IV fluids and oral dantrolene	Improved clinically over 7 days with CK normalizing by day 10 of admission (18 post vaccination)

CK, creatinine kinase; T2DM, type 2 diabetes mellitus

vaccination are summarized in Table 1. The true rate of rhabdomyolysis secondary to COVID-19 mRNA vaccination could be much higher than these limited case reports would suggest, as it has been reported 228 times with 16 deaths, as per a query in the Vaccine Adverse Event Reporting System (VAERS) on June 22, 2022.

The mechanism of a rhabdomyolysis event after mRNA COVID-19 vaccination is not known. There have been previous reports of rhabdomyolysis following viral vector COVID-19 vaccinations [13, 14] and influenza vaccinations [15]. It is thus plausible that this is a rare nonspecific reaction to any vaccination and not unique to mRNA or COVID-19 vaccines. Previous reports have speculated that the mechanism of some instances of rhabdomyolysis could be viral invasion of myocytes or exaggerated immunological reactions, analogous to cytokine storm [4]. The latter could be supported by the significantly more potent immune response following mRNA vaccination when compared to traditional vaccines [4]. However, as there are very few similarities in the patient characteristics of the reported cases, it is challenging to suggest risk factors without a further study. Notably, myalgia near the injection site is among the most common side effects following mRNA vaccination [16]. While the underlying pathophysiology of this muscle pain has not been identified, nonspecific inflammatory response and trauma have been speculated to be possible mechanisms [16]. It is plausible that rhabdomyolysis represents the extreme end of the spectrum of muscle injury following vaccination.

## Conclusion

We provide the second description of a pediatric case of rhabdomyolysis presenting after COVID-19 mRNA vaccination. Vaccination is the safest and most effective way to prevent morbidity from COVID-19. Clinicians should be aware that rhabdomyolysis could be a rare but treatable adverse event of COVID-19 mRNA vaccination. With early recognition and diagnosis and supportive management, rhabdomyolysis has an excellent prognosis, as is demonstrated in the majority of reported cases.

**Author contribution** Aidan Pucchio participated in project conception, performed the literature search, drafted the initial manuscript, and reviewed and revised the manuscript. Maya Heled Akiva, Helena Evangelidou, Jesse Papenburg, and Marina I Salvadori participated in project conception, patient management, and data collection, supported in manuscript writing, and reviewed and revised the manuscript. All the authors approved the final version of the manuscript as submitted and agreed to be accountable for all aspects of the work.

**Code availability** Not applicable.

## Declarations

**Ethics approval** As this is a single patient case report, no institutional ethics approval was required.

**Consent to participate** Verbal informed consent was obtained from both the patient and his parents.

**Competing interests** The authors declare no competing interests.

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