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Case Report

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Rhabdomyolysis Following SARS-CoV-2 Infection in Children: A Case Report and Systematic Review

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ABSTRACT

Rhabdomyolysis is a syndrome that causes various complications due to the release of substances from muscle cells, often associated with preceding infectious diseases. We report the case of a 7-year-old Korean boy with recent severe acute respiratory syndrome coronavirus 2 infection, presenting with fever, chills, and generalized body aches, diagnosed as rhabdomyolysis. Additionally, we conducted a systematic review with the aim of delineating the disease spectrum, treatment, and outcomes. We identified seven reports that met the inclusion criteria. Among the cases, 5 had fever, with creatine kinase levels ranging from 3,717 and 274,664 IU/L. Two individuals received treatment in intensive care unit, 2 underwent renal replacement therapy, and 1 case has deceased. For children with coronavirus disease 2019 infection and muscle pain, a thorough examination of urine color and an assessment of muscle enzymes through blood tests can help diagnose and treat rhabdomyolysis, a condition that might otherwise be overlooked.

Keywords: Rhabdomyolysis; Myositis; COVID-19; SARS-CoV-2

INTRODUCTION

Rhabdomyolysis is a syndrome characterized by complications arising from the release of substances such as myoglobin from muscle cells into the bloodstream, along with muscle enzymes such as creatine kinase (CK), due to damage to skeletal muscles.[1] The condition can be triggered by various factors, including drugs, trauma, excessive exercise, prolonged immobility, and rarely, infections.[2]

In this report, we describe a case of rhabdomyolysis induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a Korean boy and aims to conduct a systematic review of cases involving rhabdomyolysis with a preceding history of coronavirus disease 2019 (COVID-19).

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CASE

A 7-year-old Korean boy, with history of attention-deficit/hyperactivity disorder (ADHD), presented to the emergency department with a 3-day history of fever (39.1°C), chills, and generalized body aches. Symptomatic treatment, including antipyretic drugs every 4 hours, was administered. He also reported a 2-day history of cough, sputum prior to admission. On admission, the patient developed severe myalgia, most prominently on the inner side of the thighs, hindering his walking ability. Although urine color was normal, urine volume decreased. He had no known history of liver, kidney, or muscle disorders, and denied recent immobility, trauma, seizures, or new medications. The patient was not on medications, including those for ADHD.

In the emergency department, initial vital signs were as follows: blood pressure, 101/62 mmHg, heart rate 100 beats/min, respiratory rate 22 breaths/min, body temperature 38.24°C, and oxygen saturation of 100% on room air. Physical examination demonstrated signs of dehydration, throat injection, mild palatine tonsillar hypertrophy, both tympanic membranes were intact, clear breath sounds without crackle or wheezing, and mild generalized muscle tenderness on palpation. The lower limb tenderness, especially in the proximal end, was evident. Muscle strength was grades II-III (lower motor), with increased muscle tension. Sensory was intact in lower limbs and trunk, and pathological reflex was negative. The patient's height was 127 cm (78 percentile); weight, 28 kg (78 percentile); and body mass index, 17.4 kg/m^2 (70 percentile).

Initial laboratory evaluation showed a hemoglobin level of 14.4 g/dL, white blood cell counts of 7.34×10^3/μL, platelets of 214×10^3/μL, blood urea nitrogen level of 10.7 mg/dL, creatinine level of 0.29 mg/dL, C-reactive protein level of 0.94 mg/dL and erythrocyte sedimentation rate of 11 mm/hour. Elevated CK had a peak of 124 ng/mL. Lab test results were significant for CK-MB of 124 ng/mL, myoglobin of 4,958 ng/mL and lactate dehydrogenase (LDH) of 1,113 IU/L and creatinine phosphokinase of 10,232 IU/L. Electrolytes were within normal range. Liver function test indicated elevated aspartate aminotransferase at 269 IU/L and alanine aminotransferase at 41 IU/L. Antistreptolysin O screen was normal.

The patient reported recent exposure to his mother with confirmed COVID-19 in the week preceding his illness. SARS-CoV-2 real-time polymerase chain reaction testing was positive. Urinalysis showed yellow urine, specific gravity 1.019, blood 3+, protein 2+, 0–4 red blood cells (per high power field), and no casts. Urine myoglobin was negative. The rest of the lab test results were unremarkable.

Following administration of isotonic intravenous fluids, urine output was restored, and myalgia improved. Moreover, his muscle power gradually restored to grade V (lower motor). On the second day of admission, serum CK-MB elevated to 288 ng/mL, creatine phosphokinase (CPK) exceeded17,210.0 IU/L and LDH was 1,113 IU/L. Urinalysis showed yellow urine, specific gravity 1.003, blood 2+, and negative protein. Five days later, urinalysis was normal, and serum CPK was 3,717 IU/L, LDH was 2,542 IU/L, and CK-MB was 30 ng/mL.

After 6 days of hospitalization, the patient was discharged as his clinical and laboratory symptoms had improved.

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DISCUSSION

We conducted a comprehensive search on PubMed for clinical reports on rhabdomyolysis associated with SARS-CoV-2 from January 2020 to August 10, 2022. Using "rhabdomyolysis" as a MeSH search term AND "coronavirus" OR "COVID-19" OR "SARS-CoV-2" in all search fields, we searched titles, abstracts, and full-length texts in English to identify eligible articles. Adult-onset cases (defined as aged >18 years), duplicate entries, and nonclinical publications were excluded. We adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for extracting and organizing relevant data, including age, sex, month, and year of onset, interval since infection, geographic site of report, comorbidities, signs and symptoms, treatment regimen, and outcome.

We identified seven reports meeting the inclusion criteria (**Fig. 1**).[3-9] Among 8 cases of rhabdomyolysis including our case, 6 were males,[3,5,6,8,9] and 4 had underlying comorbidities (**Table 1**).[5,6,8] Cases were reported across a diverse geographic distribution, with 3 patients in the U.S.,[5,6,8] 2 in Europe,[7,9] 1 in the Middle East,[3] 1 in Africa,[4] and 1 in South Korea. Five

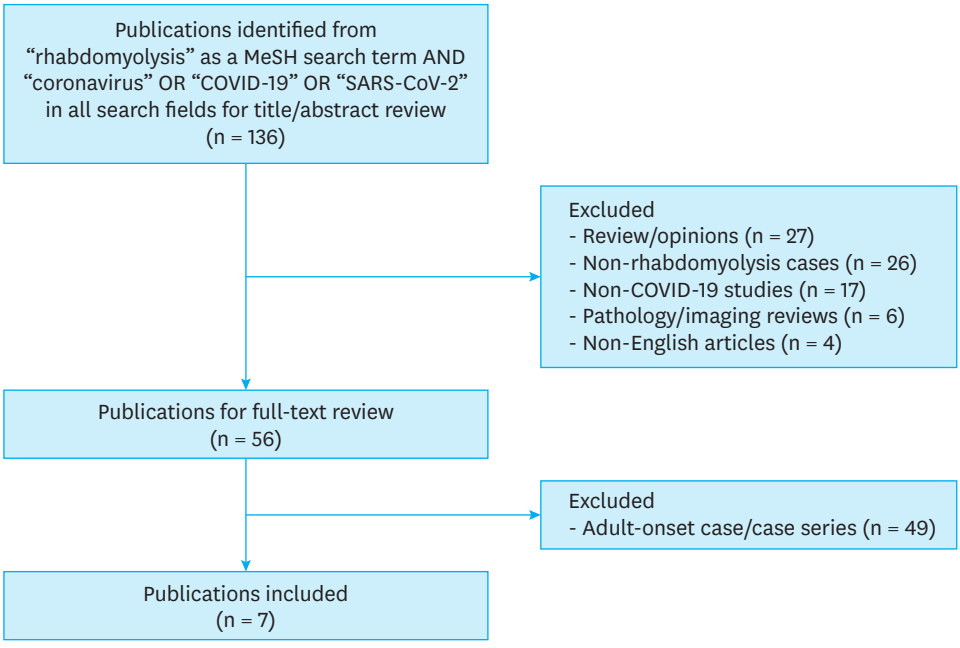

Fig. 1. Results of literature search and identification of studies according to the Preferred Reporting Items of Systematic Reviews and Meta-Analyses guidelines.
Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 1. Systematic review on rhabdomyolysis following SARS-CoV-2 infection

Case	Age	Sex	Country	Month/Year	Race	PMHx	Fever	CK (highest)	Hospitalization	Events	Outcome
Tram et al.[9]	15 yr	Boy	Belgium	Mar 2020	Unknown	None	None	21,876	9 days	ICU care	Improved
Samies et al.[8]	16 yr	Boy	U.S.	Jul 2020	African	Obesity, T2DM	Intermittent	274,664	14 days	Hemodialysis	Improved
Kontou et al.[7]	10 yr	Girl	Greece	Nov 2021	Unknown	None	Intermittent	13,147	Not reported	None	Improved
Gilpin et al.[6]	16 yr	Boy	U.S.	Oct 2020	Unknown	Asthma	None	116,640	7 days	None	Improved
Gefen et al.[5]	16 yr	Boy	U.S.	May 2020	Unknown	ASD, obesity	Febrile	108,059	12 days	None	Improved
Cassim et al.[4]	12 yr	Girl	South Africa	Jul 2021	African	None	None	>22,000	16 days	ICU, RRT	Improved
Anwar et al.[3]	16 yr	Boy	Oman	Sep 2020	Arabic	None	Febrile	Not reported	3 days	Not reported	Death
Present case	7 yr	Boy	South Korea	May 2022	Asian	ADHD	Febrile	3,717	days	None	Improved

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; CK, creatine kinase; ICU, intensive care unit; T2DM, type 2 diabetes mellitus; ASD, autism spectrum disorder; RRT, renal replacement therapy; ADHD, attention deficit hyperactivity disorder.

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patients exhibited fever, and CK levels ranged between 3,717 and 274,664 IU/L. Two patients received intensive care unit treatment,[4,9] 2 underwent renal replacement,[4,8] and all but 1 case survived the course.[3]

Rhabdomyolysis can lead to various complications, ranging from mild to severe, as a large amount of intramuscular substances leak into the bloodstream after muscle damage due to various causes. While this case is rare, it was attributed to COVID-19. For children infected with COVID-19 experiencing muscle pain, a meticulous examination of change in urine color and an evaluation of muscle enzymes levels in blood tests may facilitate the diagnosis and treatment of potentially overlooked rhabdomyolysis.

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요약

횡문근융해증(rhabdomyolysis) 근육세포의 파괴에 따라 근세포 내 물질이 세포 외부액과 혈액으로 방출되어 증상이 나타나며, 주로 외상, 근효소 결핍, 감염, 전해질 불균형, 약물, 내분비 질환 등에 의해 유발될 수 있다. 본 연구에서는 SARS-CoV-2 감염이 확인된 7세 남아에서 나타난 횡문근융해증 사례를 보고하고자 한다. 또한, 질병 스펙트럼, 치료 및 결과를 확인하기 위한 체계적인 문헌 고찰을 수행하였다. 검색 결과, 코로나19 감염 후 7건의 횡문근융해증 보고 사례를 확인하였다. 그 중 5건은 발열이 있었으며 크레아틴 키나제(creatine phosphokinase, CK)는 3,717에서 274,664 IU/L 범위에 속하였다. 두 명은 중환자실에서 치료를 받았으며 두 명은 신장 대체 요법을 받았으며 한 명을 제외하고 모두 생존하였다. 코로나19 감염 후 횡문근융해증이 나타날 수 있으며, 근육 통증을 호소하는 소아에서의 소변 색상의 철저한 검사 및 혈액 검사를 통한 근육 효소의 평가가 진단과 치료에 도움이 될 수 있다.