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Seven-Digit Creatine Kinase in Acute Rhabdomyolysis in a Child

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Abstract

Rhabdomyolysis is an acute life-threatening condition that can occur in childhood secondary to many causes. The authors report the case of a 3-year-old male child who presented with acute rhabdomyolysis. The peak plasma creatine kinase level was extremely high. The 2 main causes of rhabdomyolysis in childhood are viral myositis and trauma, which can sometimes lead to acute renal failure. The highest creatine kinase levels reported in the literature so far was a 6-digit level in 2014 case report. In this study, the authors report the case of a 7-digit creatine kinase level in a child secondary to viral myositis who did not require renal dialysis.

Keywords

rhabdomyolysis, child

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Rhabdomyolysis is a potentially life-threatening syndrome characterized by the breakdown of muscle fibers.[1,2] There are a variety of causes that can lead to this syndrome, including infection, trauma, exercise, drug reaction, metabolic disorders, and status epilepticus.[1,3] The muscle breakdown is clinically manifested as muscle aches, muscle weakness, and tea-colored urine, the classical findings in rhabdomyolysis.[1,4] Elevation in the level of plasma creatine kinase is the most sensitive laboratory finding related to muscle injury.[1] The most common complication is acute renal injury and failure. Some patients may even require renal transplant.[2] Seven percent of acute kidney injury in the United States is attributed to rhabdomyolysis.[5] The authors report a case of a 3-year-old male who presented with acute rhabdomyolysis that resulted in an extremely high 7-digit creatine kinase level (1 778 856 IU/L).

Case Report

A 3-year-old male, known to have isolated speech delay, presented to the emergency department with severe body aches and inability to walk. Few days prior to his presentation, the child started to have flu-like symptoms in the form of rhinorrhea and low-grade fever. This was followed by irritableness, hypoactivity, and inability to move his legs and arms. He was seen in a private hospital where computed tomography of the brain and a lumber puncture were done that showed no abnormalities. In the next day, his condition continued to worsen. He developed difficulty in swallowing and dark-colored urine, so he was transferred to our institution. Upon physical examination, the patient had generalized muscle weakness with absent deep tendon reflexes. The laboratory tests showed elevated creatine kinase level (1 778 856 U/L; normal range 20-200 U/L), elevated serum transaminases (serum glutamic-pyruvic transaminase [SGPT] = 1857 U/L [normal range 0-50 U/l], serum glutamic-oxaloacetic transaminase [SGOT] = 8626 U/L [normal range 0-50 U/L]), and creatinine 0.72 mg/dL (0.3-0.7 mg/dL). The child started on intravenous hydration and received 1 dose of intravenous immunoglobulin. On the second day, the creatine kinase and serum transaminase levels improved, with creatinine reaching 0.94 mg/dL, the highest level reached. The creatine kinase and serum transaminase levels continued to improve gradually over the following days, with slow improvement in the clinical condition. He had better swallowing and less muscle aches. Figure 1 shows the decline in the creatine kinase level during hospitalization. He received another 2 doses

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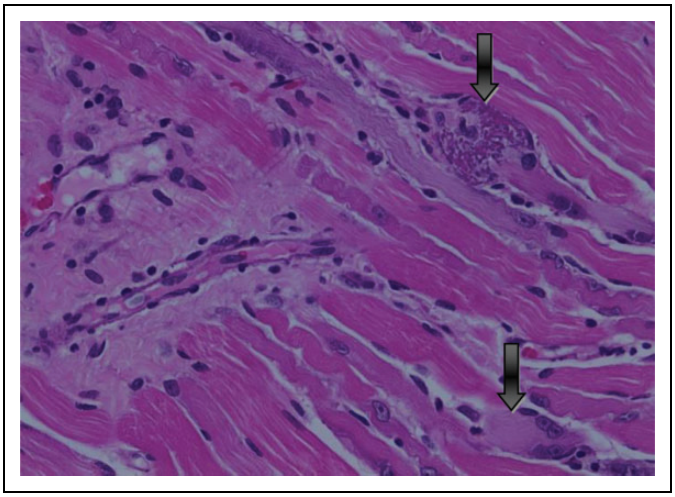

Figure 1. Decline in the creatine kinase levels during and after hospitalization.

of intravenous immunoglobulin on days 13 and 14 of admission. Electromyography showed myogenic aspect of weakness. Muscle biopsy showed endomysial inflammatory infiltrates, mostly composed of CD8 and CD4 lymphocytes; myofibers necrosis mostly ventral portion of myofibers; residual granular microcalcifications; and terminal complement complex deposits that outline necrotic myofibers, all features compatible with necrotic myopathy and early rhabdomyolysis (Figure 2). Echocardiography was normal.

Upon discharge, the child had mild muscle aches, was able to sit, and move his arms and feet. He had persistent weakness in the lower limbs, but was unable to walk, with a follow-up examination 1 month after discharge, revealing that the child was able to walk normally with positive deep tendon reflex. Two months after discharge, the creatine kinase level dropped to 193 IU/L. (Figure 1)

Discussion

Rhabdomyolysis results from skeletal muscle breakdown due to various causes. Viral myositis, trauma, and inherited disorders are the most common causes in the pediatric age group.[2,5] Table 1 shows the differential diagnosis of pediatric rhabdomyolysis. The breakdown releases the normal cell contents into the bloodstream, including creatine kinase, myoglobin, phosphorus, and potassium.

Rhabdomyolysis is suspected clinically when muscle aches, muscle weakness, and tea-colored urine are present. The diagnosis is based on the high creatine kinase level, which is the most sensitive marker.[2] Although there is no established cutoff levels, a concentration 5 to 10 times higher than the upper limit of normal reference range (ie, 500-1000 U/L) is commonly used.[2,6] Other laboratory indicators include serum and urine myoglobin concentrations that may be useful but not essential for the diagnosis.[2]

The most common complication of rhabdomyolysis is kidney damage.[1,2] In recent large pediatric studies reported by Mannix et al[7] and Wu et al,[8] it was shown that the rate of acute renal failure in the pediatric patients with rhabdomyolysis ranged from 5% to 8.7%. The risk factors that predispose a patient with rhabdomyolysis for developing acute renal injury are creatine kinase level concentration more than 5000 U/L,[2] creatine kinase value upon admission, and slower decline in the serum creatine kinase level.[9] Other factors include high myoglobin level,[1] persistent or abrupt increase in the potassium or calcium level, as well as persistent metabolic acidosis.[10] On the other hand, a recent study by Fernandez et al showed that the most reliable predictor of acute renal failure and the need for dialysis is the creatinine level above 1.7, despite the peak creatine kinase.[15] However, the mean peak of creatine kinase in their study was only 43 578 IU/L.[15]

The mainstay for the prevention and treatment of acute kidney injury is early and aggressive volume resuscitation.[2,5] Other management options include alkalization of the urine, forced diuresis with mannitol, and loop diuretics.[2] In severe cases or when the treatment fails, patients can undergo renal replacement therapy.[11,12]

In our case, the child developed extremely high creatine kinase levels that were not reported in the literature.

A thorough literature review was done searching for high creatine kinase levels in patients with acute rhabdomyolysis. In 2014, a case report described a pediatric patient with McArdle disease who developed rhabdomyolysis with a high 6-digit creatine kinase level reaching 500 000 IU/L, and the patient didn't require dialysis.[2] Our patient's levels are more than triple their values. In 1985, 2 pediatric cases were reported. In both, the creatine kinase levels reached were 60 000 IU/L. One case required hemodialysis.[13] In 2011, a case report of an adolescent with rhabdomyolysis due to undiagnosed hypothyroidism was reported with a creatine kinase level that reached around 34 000 IU/L, and the patient didn't require dialysis.[4] A research article in 2013 examined the clinical spectrum of patients with rhabdomyolysis presenting to the pediatric emergency department, in which the peak serum level of creatine kinase was 9825.1 $\pm$ 23 079.1 U/L in 37 patients. None of the patients required renal replacement therapy.[10]

Our patient experienced severe rhabdomyolysis as indicated by his extremely high creatine kinase levels. The peak creatine kinase level was upon admission. Despite the severity of rhabdomyolysis, the patient did not develop acute renal injury. The only risk factor for developing acute renal injury that our patient had was a high peak creatine kinase level upon admission. On the other hand, he did not develop metabolic acidosis and had a normal albumin and electrolytes levels throughout his hospitalization. He responded very well to volume resuscitation with rapid decline in the creatine kinase level. He didn't require dialysis. Although he received intravenous immunoglobulin for the fear of Guillain-Barre syndrome or other underlying immune-mediated diseases, neither the creatine kinase level decline nor the clinical status improvement was affected by the intravenous immunoglobulin administration. The sharp decline in the creatine kinase level was noticed after aggressive intravenous hydration. There are no clues in the family history

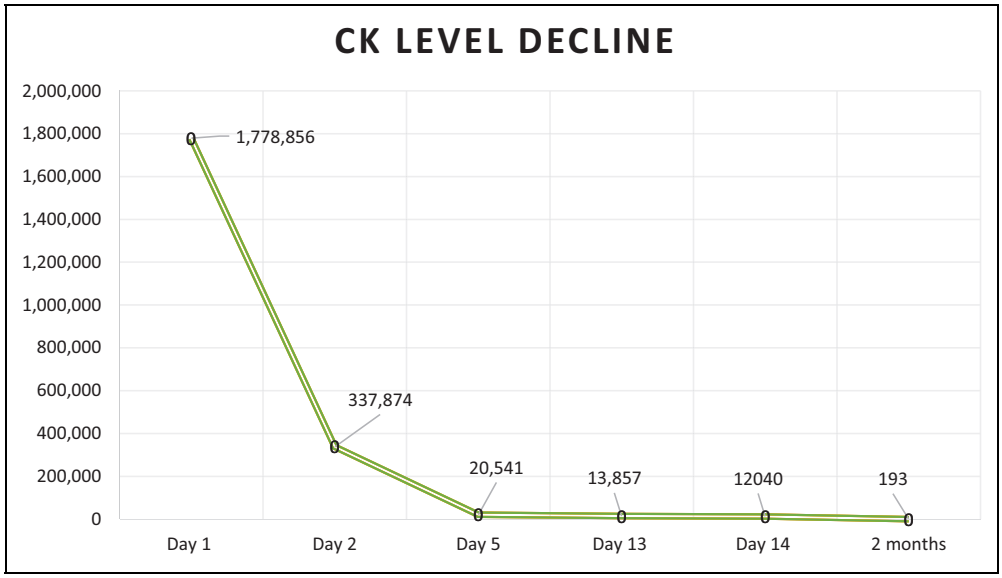

Figure 2. The arrows showed the degenerated myofibers.

Table 1. Differential Diagnosis of Acute Rhabdomyolysis in the Pediatric Age Group.

Causes	Examples
Infection	Most common cause of those younger than 10 years of age
	Viral causes are leading causes (viral myositis)
Trauma	Leading causes in teenagers
	Asphyxia, burns, nonaccidental abuse, strenuous exercise
Genetic or metabolic diseases	Glycogen phosphorylase deficiency type 5 (McArdle disease)
	Phosphofructokinase deficiency
	Mitochondrial disease
	Connective tissue diseases (dermatomyositis, systemic lupus erythematosus [SLE])
	Muscular dystrophy
Neurological diseases	Guillain-Barre syndrome
Drugs	Ethanol, amphetamines, antihistamines, salicylates
Malignant hyperthermia	
Cold exposure	
Dehydration	

or the patient's personal history that may suggest an underlying inherited metabolic, muscular, or genetic disease. The child has an isolated speech delay. He had adequate development in other fields. He had no chronic illnesses and did not take any chronic medications. The metabolic workup (plasma amino acids, urine organic acids) was negative. The muscle biopsy did not show any specific finding. So the cause was attributed to inflammatory myositis, probably viral in origin.

However, this could be the first presentation of lipin-1 mutation that causes recurrent rhabdomyolysis in children. Lipin-1 gene encodes the muscle-specific phosphatidic acid phosphatase, a key enzyme in triglyceride and membrane phospholipid biosynthesis.[14] The episodes of rhabdomyolysis are mostly triggered by intercurrent infections and fever and to a lesser extent by fasting or exercise.[14] The prognosis of lipin-1 deficiency is poor, with up to one-third of patients dying during an episode of rhabdomyolysis.[14] In about 60% of patients with recurrent rhabdomyolysis, no identifiable cause can be found.

Author Contributions

NB and SM drafted and revised the article. MR supervised and approved it.

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Ethical Approval

The institutional review board for Human Research at Makassed General Hospital approved this work.

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