Rhabdomyolysis with different etiologies in childhood

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Abstract

AIM
To investigate different etiologies and management of the rhabdomyolysis in children.

METHODS
Eight pediatric rhabdomyolysis cases who applied to the Dokuz Eylül University Faculty of Medicine Department of Pediatric Nephrology with different etiologies between January 2004 and January 2012 were evaluated in terms of age, gender, admission symptoms, physical examination findings, factors provoking rhabdomyolysis, number of rhabdomyolysis attacks, laboratory results, family history and the final diagnosis received after the treatment.

RESULTS
Average diagnosis ages of eight cases were 129 (24-192) ± 75.5 mo and five of them were girls. All of them had applied with the complaint of muscle pain, calf pain, and dark color urination. Infection (pneumonia) and excessive physical activity were the most important provocative factors and excessive licorice consumption was observed in one case. In 5 cases, acute kidney injury was determined and two cases needed hemodialysis. As a result of the further examinations; the cases had received diagnoses of rhabdomyolysis associated with mycoplasma pneumoniae, sepsis associated rhabdomyolysis, licorice-induced hypokalemic rhabdomyolysis, carnitine palmitoyltransferase II deficiency, very long-chain acyl-CoA dehydrogenase deficiency, congenital muscular dystrophy and idiopathic paroxysmal rhabdomyolysis (Meyer-Betz syndrome).

CONCLUSION
It is important to distinguish the sporadic and recurrent
rhabdomyolysis cases from each other. Recurrent rhabdo-
myolysis cases should follow up more regardful and attentive.

Key words: Rhabdomyolysis; Children; Etiology; Acute
kidney injury; Treatment; Hemodialysis

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Core tip: This is a retrospective study to evaluate rha-
bdomyolysis in childhood. Rhabdomyolysis could be caused
by a number of reasons, which could be classified as
sporadic and hereditary/recurrent. The initial point that is
to attract attention in this manuscript is the importance of
the rhabdomyolysis type (recurrent/sporadic). Even though
rhabdomyolysis is not routinely involved in textbooks
concerning neuromuscular diseases, it is an integral part
of these diseases. It should be taken into consideration
in the first diagnosis and clinical follow-up of patients. It
is possible to encounter with a rhabdomyolysis attack in
every case. But its treatment is different from that of a
primary disease.

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INTRODUCTION

Rhabdomyolysis is a pathological condition that occurs
as a result of musculoskeletal damage. Substances such as creatine kinase (CK), myoglobin, aspartate
aminotransferase, alanine aminotransferase, and potas-
sium pass from cells into circulation as a result of this damage[1]. Among them, particularly myoglobin is
substantially toxic for kidneys and causes acute kidney
injury (AKI)[2]. The syndrome generally presents with the
triad muscle pain, weakness and dark urin[3] Nearly half of
patients with rhabdomyolysis have these symptoms[4].
For the clinician, suspicion starts with increase of creatine
kinase level. This suspicion is verified by measuring
serum or urine myoglobin level[4]. Rhabdomyolysis can result from a wide range of disorders. While 80% of the
cause of rhabdomyolysis in adults is trauma and drugs,
it is infections and congenital disorders in children[4,5]. If
rhabdomyolysis is recurrent, it is recommended to carry
out some further examinations (muscle biopsy, metabolic
and genetic tests). Early diagnosis is crucial to prevent
AKI. Prevention is important in patients with inherited
forms[6]. The purpose of this article is to present eight
pediatric cases with rhabdomyolysis diagnosis depending
upon different etiologies.

MATERIALS AND METHODS

The study consisted of eight patients with rhabdomyolysis.

Medical files of cases, who were referred to Pediatric
Nephrology of Medicine Faculty of Dokuz Eylul University,
were retrospectively examined between the years of 2004
and 2012. The following parameters were recorded as
age, gender, presenting symptoms, provocative factors,
attacks number, positive physical examination findings,
background and family history, laboratory results on
admission, management, and final diagnosis. All cases
were inquired at the admission time in terms of drug
usage, infections, excessive physical activity, alcohol usage
and herbal treatments. Family history was evaluated in
terms of the individuals diagnosed with rhabdomyolysis
in his/her family and neuromuscular diseases. In terms
of etiology; further examinations were performed other
than basic laboratory evaluation especially for the cases
with recurrent rhabdomyolysis attacks. These consisted of
serologic screening (Hepatitis, TORCH, EBV, Mycoplasma,
Trichinella) in terms of infection parameters, bleeding
profile and sepsis screenings, toxic screening, thyroid
function test, ANA and ENA panels, lactic acid, ammonia,
pyruvic acid levels, organic acid profile, acylcarnitine, total
and free carnitine levels, metabolic screening (in terms
of glucose and fat metabolism defects), electrography
and echocardiography, electromyography (EMG), muscle
biopsy and genetic studies. SPSS 18.0 - software package
program was used to conduct statistical analysis.

RESULTS

Average diagnosis ages of eight cases, five of them being
female, in the patient series was 129 (24-192 mo) ±
75.5. Examining the admission symptoms; all the patients
in older age group had specified muscle pain, myalgia,
calf pain, fatigue, and dark urination complaints. In two
younger cases (case 1 and 7); dark color urination finding
was the most remarkable finding. Cases 4 and 5 were
also presented with muscle weakness. Additionally, first,
second and seventh cases had cough and fever and third
case had vomiting complaints. Examining the factors
provoking rhabdomyolysis attack; infection (pneumonia)
in three cases (case 1, 2, 7), excessive physical activity
in three cases (case 4, 5, 8), both infection and excessive
physical activity in one case (case 6), and excessive
licorice consumption in one case (case 3) were observed.
Assessing their physical examination findings on ad-
mision; three patients had fever over 38 degrees and
bilateral crepitation in their pulmonary examination (case
1, 2, 7). Muscle strength loss was determined in upper
and lower extremities in 2 cases (case 4, 5). Findings
of volume loss were present in the third case but blood
pressure was normal and the physical examinations of
sixth and eighth cases were normal except for their muscle
sensitivities. In the evaluation of personal backgrounds;
case 7 was followed for epilepsy due to microcephaly.
In cases 4, 5, 6 and 8, recurrent rhabdomyolysis attack was
present. Also hemodialysis (HD) treatment was applied
to case 6 at a different center due to a rhabdomyolysis
attack 10 mo ago. Parents of cases 4, 5 and 6 were
relatives. Cases 4 and 5 were siblings. In 4 of the cases;
rhabdomyolysis attack was seen for the first time (case 1, 2, 3, 7), but it was the seventh rhabdomyolysis attack for the forth case, sixth rhabdomyolysis attack for the fifth and sixth cases and third rhabdomyolysis attack of the eighth case. Table 1 illustrates general characteristics of the patients. In line with rhabdomyolysis; CK values of all the patients was > 1000 U/L, and their blood and urine myoglobin levels were additionally high. In none of the patients; hypoglycemia and cardiac enzyme increase were observed. In five cases, AKI was present (case 1, 2, 3, 4, 7). Table 2 illustrates laboratory results at the time of admission.

Hydration, alkalinization, electrolyte replacement if needed, antibiotics treatment and allopurinol were applied to all the patients. HD was applied to cases three and four. Examining in terms of etiology; the patients were diagnosed with rhabdomyolysis associated with mycoplasma pneumoniae, sepsis associated rhabdomyolysis, licorice-induced hypokalemic rhabdomyolysis, carnitine palmitoyltransferase II deficiency, very long-chain acyl-CoA dehydrogenase deficiency, congenital muscular dystrophy and idiopathic paroxysmal rhabdomyolysis (Meyer-Betz syndrome) (Table 3).

### DISCUSSION

Rhabdomyolysis is a clinical result that may appear in numerous situations. In this article, eight cases with developed rhabdomyolysis related to different etiologies were assessed. Rhabdomyolysis is diagnosed when serum CK level exceeds 1000 U/L in case of absence of myocardial infarction.[5]

Some studies accept that serum myoglobin level of > 300 ng/mL and urine myoglobin level of > 10 ng/mL are diagnostic.[6]

Presence of myoglobin in serum and its infiltration to urine turns the color of urine into red. While hemolysis occurs in urine sticks, it is typical not to observe erythrocyte in microscopy.[7] Compared to CK, myoglobin is eliminated more quickly and if there is no myoglobinuria at high CK level, the diagnosis of rhabdomyolysis is not excluded.[8] CK levels of all the patients was > 1000 and their concurrent blood and urine myoglobin levels were over the reference values. All of them had red or brown urine findings and no erythrocyte was observed in microscopy. Common symptoms include myalgia, muscle tenderness, and weakness. While numerous patients experience lower-leg pain, some patients may have nonspecific symptoms such as fever, fatigue, vomiting, and nausea.[8] All the patients had applied with the above-mentioned common symptoms. Only the diagnosis of the 24-mo-old first and seventh cases was established with the red urine and laboratory values.

AKI is the most significant complication of rhabdomyolysis. It is defined as creatinine level above 97 percentile with respect to age and gender.[9] Previous studies identified that rhabdomyolysis-related AKI was 17%-35% in adults and 42%-50% in children.[6,7,9] If AKI is also comorbid in the cases with CK level above 100000 U/L, mortality rates reach up to 80%.[10] In five of the cases in this series, AKI was determined at the time of admission.

We stated that infections were more critical in etiology of rhabdomyolysis in children compared to adults. Several causes of infection may be associated with rhabdomyolysis. Viral infections are responsible for one
third of the cases\textsuperscript{[5,10]} (Many infections are associated with rhabdomyolysis. While influenza takes place on the top among viral infection agents, Epstein-Barr virus (EBV), cytomegalovirus (CMV), and human immunodeficiency virus (HIV) are the other causes\textsuperscript{[10]}. Although the pathophysiology is not presently clear, bacterial infections have also been associated with rhabdomyolysis. In a review in which 60 cases were reported, Legionella spp, Francisella spp, Streptococcus spp, Salmonella spp, and Staphylococcus aureus were determined as the most frequent factors\textsuperscript{[11]}. Rhabdomyolysis was also reported with Enterococcus species, Pseudomonas aeruginosa\textsuperscript{[12]}, Neisseria meningitidis\textsuperscript{[13]}, Escheria coli\textsuperscript{[14]}, and Haemophilus influenzae\textsuperscript{[15]}. Mycoplasma pneumoniae\textsuperscript{[16]}, leptospirosis\textsuperscript{[17]}, and Coxiella burnetii (Q fever)\textsuperscript{[18]}. In this case series; two cases (case 1, 2) had infection-associated rhabdomyolysis. Case 1 had applied with cough and high fever complaints and anemia (Hb 8.6 g/dL) reticulocytosis (8.5%), leukocytosis (17500) and acute renal insufficiency (BUN 36, creatinine 2, 3) were found in the laboratory examinations. Blood gas and urine analysis were normal. Concurrently AST, ALT, LDH, CPK and uric acid values were also found high. Empirical antibiotics treatment (IV clarithromycin), hydration and alkalinization were started to be given. Hemolysis findings were found in the peripheral smear which was examined due to anemia, and direct combs test was found as + 2 positive. In the tests sent in terms of the infection agents; mycoplasma pneumoniae IgM was positive. The outcome was rapidly favorable, and she did not experience another attack. The family history was negative for the rhabdomyolysis. Mycoplasma pneumonia infection may lead to multiple organ involvement as well as it may be asymptomatic. 25% of the patients develop extrapulmonary complications (cardiovascular, gastrointestinal, hematologic, and central nervous system). These complications may occur before, during, and after the infection. Sometimes, they appear with autoimmune events without pulmonary findings\textsuperscript{[19]}. Formation of cold agglutinin which is observed in 10% of the patients also occur with this infection agent and is responsible for antibody-induced hemolysis\textsuperscript{[20]}. It has not been understood exactly yet why rhabdomyolysis develops during mycoplasma infections, however direct invasion of muscles by the organism or muscular damage resulting from immune reactions are considered as responsible\textsuperscript{[16]}. Although it is rare, rhabdomyolysis-induced AKI or glomerulonephritis, interstitial nephritis and nephrotic syndrome may develop with this infection\textsuperscript{[20,21]}.

Renal biopsy was not administered to patient due to high renal function tests and no indication of glomerulonephritis.

| Table 2  Laboratory results of patients on admission  |
|-----------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Case No. | Hb  | WBC  | Plt  | Glu  | BUN  | Creat | CPK    | AST    | ALT    | LDH    | Uric acid | Na     | K     | Cl     | Ca     | P  | Urine  |
|          | g/dL | /mm\(^3\) | /mm\(^3\) | mg/dL | mg/dL | mg/dL | U/L    | IU/L   | IU/L   | U/L    | mg/dL | mmol/L | mmol/L | mg/dL | mg/dL | myog. | myog. |
| 1        | 8.6  | 17.5  | 225  | 86   | 36   | 2.3   | 1158   | 451    | 3903   | 1227   | 6.1   | 139    | 4.2    | 110   | 8.6   | 4.5   | 193   | 155  |
| 2        | 12.9 | 6.5   | 93   | 102  | 65   | 4.7   | 12976  | 788    | 215    | 933    | 6.8   | 149    | 4.8    | 114   | 7.8   | 8.3   | 679   | 274  |
| 3        | 15.2 | 20.6  | 307  | 95   | 150  | 3.7   | 8379   | 780    | 250    | 1100   | 10    | 125    | 2.2    | 65    | 8.2   | 8.8   | 1370  | 3740 |
| 4        | 12.6 | 3.6   | 163  | 90   | 57   | 7     | 42670  | 998    | 249    | 1303   | 2.6   | 136    | 3.9    | 107   | 8.7   | 4.3   | 1200  | 1200 |
| 5        | 13.2 | 10.6  | 213  | 75   | 12   | 0.5   | 3012   | 210    | 664    | 1466   | 3.5   | 141    | 4.9    | 104   | 9.9   | 4.3   | 1200  | 1200 |
| 6        | 12.4 | 17.5  | 127  | 119  | 10   | 0.7   | 25983  | 338    | 87    | 1797   | 5     | 136    | 3.9    | 105   | 9.4   | 3.5   | 1200  | 1200 |
| 7        | 9.3  | 9.6   | 146  | 85   | 38   | 1.1   | 31119  | 683    | 235    | 1853   | 6.9   | 144    | 2.9    | 115   | 8.4   | 3.7   | 767   | 800  |
| 8        | 14.2 | 18.6  | 352  | 90   | 125  | 0.8   | 51228  | 1108   | 341    | 2381   | 2.3   | 135    | 3.7    | 107   | 10.1  | 3.6   | 800   | 1200 |

Hb: Hemoglobin; WBC: White blood cell; Plt: Platelet; Glu: Glucose in urine; CPK: Creatine phosphokinase; BUN: Blood urea nitrogen; AST: Aspartate aminotransferase; LDH: Lactate dehydrogenase; ALT: Alanine aminotransferase.

| Table 3  Management and final diagnosis of patients  |
|-----------|---------|---------|
| Case | Management | Renal replacement therapy | Final diagnosis |
| 1    | Antibiotic treatment, hydration, alkalinization | No | Rhabdomyolysis associated with Mycoplasma pneumoniae pneumonia |
| 2    | Antibiotic treatment, hydration, alkalinization, fresh frozen plasma | No | Sepsis, pneumonias, rhabdomyolysis |
| 3    | Hydration, alkalinization, antiemetic, hemodialysis | Yes, HD | Licorice-induced hypokalemic rhabdomyolysis |
| 4    | Hydration, alkalinization, hemodiaylisis | Yes, HD | Rhabdomyolysis with carmine palmitoyltransferase II deficiency |
| 5    | Hydration, alkalinization | No | Rhabdomyolysis with carmine palmitoyltransferase II deficiency |
| 6    | Hydration, alkalinization | No | Rhabdomyolysis with very long-chain acyl-CoA dehydrogenase deficiency |
| 7    | Hydration, alkalinization | No | Rhabdomyolysis due to congenital muscular dystrophy |
| 8    | Hydration, alkalinization | No | Idiopathic paroxysmal rhabdomyolysis *Meyer- Betz Syndrome |

HD: Hemodialysis.
to normal complement levels, absence of nephrotic syndrome, and existence of an AKI that does not require dialysis. Diagnosis of the patient was supported with positive serum mycoplasma IgM titration, antibody-induced hemolysis, and rapid response to anti-mycoplasma antibiotic treatment. Second case was a 84-mo-old girl. While she was being followed up for pneumonia; sepsis chart (thrombocytopenia, hypotension, bradycardia and disseminated intravascular coagulation) was developed. Then, diagnosis of rhabdomyolysis was made due to acute renal insufficiency and high CK, LDH, AST, ALT values. The patient had recovered without the need of appropriate antibiotherapy, hydration and alkalinization treatments and renal replacement treatment. Rhabdomyolysis attack of this patient did not repeat, and her family history was also negative. Sepsis-associated rhabdomyolysis was reported in numerous case reports[22-25]. In this case, we could not show any specific agent in the blood culture that may cause sepsis. Also no causative agent was reported in some studies about sepsis and rhabdomyolysis[26]. But specific causes such as blood pressure, electrolyte abnormalities, tissue hypoperfusion, hyperthermia, hypoxia, dehydration, and acidosis are known to induce rhabdomyolysis in any patient with a critical condition[27]. However, sepsis-associated microorganisms were identified in very few original studies. Even though these studies reported that bacterial sepsis-induced rhabdomyolysis can develop with numerous types of microorganisms, Betrosian et al[11] stated that it may occur mostly with gram positive organisms and Kumar et al[27] indicated that they may develop mostly with gram negative organisms[22,28].

Drugs, toxins and foods are other important causative factors for rhabdomyolysis. There are many drugs associated with development of rhabdomyolysis[29]. Drugs cause rhabdomyolysis due to direct or indirect muscle damage. Toxin poisoning related rhabdomyolysis has been reported by using honeybees[29], rattlesnakes[30], and brown recluse spider bites[31]. Carbon monoxide poisoning is another reason[32]. All the patients were examined during the anamnesis in terms of drug and toxin exposure and there were no patients with positive findings. Foods may also be a triggering factor. The most remarkable example about this issue is consumption of licorice root which may lead to hyperaldosteronism, hypokalemia, and rhabdomyolysis[33-35]. Third case was a 16-year-old male patient with chronic heavy cola consumption-associated rhabdomyolysis and AKI that were reported previously by Kasap et al[32]. Due to the laboratory results that are concordant to hypokalemia, metabolic alkalosis, acute kidney insufficiency; diagnosis of hypokalemia associated metabolic alkalosis was made.

It was then learned from the history of patient that he/she was drinking about 1 lt of cola every day for 2-3 years. A substance was suspected causing the aldosterone effect with low serum plasma renin activity, normal aldosterone, and existence of hypokalemia. Licorice root in the cola consumed by the patient daily was emphasized. The patient was diagnosed with hypokalemic rhabdomyolysis induced by the use of licorice root. HD was applied because of volume load and oliguria developing when the patient was treated with intravenous fluid therapy. Acute tubular damage was determined in the renal biopsy performed in order to exclude the underlying chronic renal disease.

Hereditary diseases, most of which are metabolic diseases, develop another group that cause rhabdomyolysis. It should be especially considered in the cases with positive rhabdomyolysis in the family history and with recurrent rhabdomyolysis attacks[36]. Some individuals tend to have muscle damages especially after exercise. This low exercise tolerance is tried to be explained by CK-MM gene polymorphism and angiotensin-converting enzyme (ACE) polymorphism. C49T and C3788A genotypes of myosin light chain kinase cause CK level increased in response to exercise[37]. When 114 asymptomatic patients varying between ages of 3 and 70 and with incidental CK level increase were evaluated; 18% metabolic or neuromuscular diseases were determined.

The most frequent diagnoses were carnitine palmitoyltransferase deficiency and malignant hyperthermia[37]. Carnitine palmitoyltransferase deficiency was the most frequently observed disease in 36-patient series of idiopathic rhabdomyolysis[38].

Long chain fatty acids (LCFA) are the major source of energy for muscles in case of prolonged exercise. These fatty acids which cannot passively pass into mitochondria move inside actively via carnitine palmitoyltransferase pathway in the outer membrane of mitochondria. This pathway consists of enzymes of carnitine palmitoyltransferase I located in the outer membrane and carnitine palmitoyltransferase II located in the inner membrane.

Autosomal recessive carnitine palmitoyltransferase I deficiency is the most frequent disorder in LCFA metabolism[39]. Clinic of rhabdomyolysis accompanying this condition is considerably variable. CK levels are normal or slightly high between attacks of rhabdomyolysis induced by this enzyme deficiency, increase between attacks, and muscle pains occurring after exercise start as from the childhood[40].

Enzyme analysis and mutation scanning should be performed for the diagnosis. Forth case in this article was an 11-year-old girl and we have learnt that she had complaints of not walking for a long distance, generalized muscle weakness from time to time, muscle cramps and dark colored urination problems from her early childhood ages. Her parents were relatives and her two brothers also had similar complaints. One of these brothers was the case five in our patient group. In CPT 2 gene; homozygote mutation was determined for SI13L. Genetic analysis was planned for his brother and possible CPT II deficiency was accepted.

Case six was a 16-year-old female patient who had applied with sixth rhabdomyolysis attack and was within acyl-CoA dehydrogenase (ACAD) family and taken the diagnosis of very long chain acyl-CoA dehydrogenase
(VLCAD) deficiency. Very long chain acyl-CoA dehydrogenase deficiency is an autosomal recessive disorder progressing with inability for beta oxidation of fatty acids in the mitochondria. Its three phenotypes that are associated with different mutations were identified. The first one is the most critical phenotype starting in newborn period and having high mortality progressing with hypertrophic cardiomyopathy and hypoketotic hypoglycemia. The second one is observed during infancy period. There is no cardiomyopathy. Hypoketotic or nonketotic hypoglycemia develops. Rhabdomyolysis occurring in case of hunger or after exercise in preadolescence period, like in our patient, exists in the muscle type with late onset[41]. In the fibroblast culture of the case; very long chain acyl-CoA dehydrogenase activity was 4.3 nmol/min per milligram protein (controls: 5.1-21.7) (n = 28) and heterozygote carrier was found. Case seven was a patient who was followed up due to epilepsy, microcephaly and hypotonia and who had been diagnosed with infection-induced rhabdomyolysis. Myopathic findings were found in the electromyography and dystrophic changes were specified in the muscle biopsy. Visual examination and hearing test of the patient were normal. Congenital muscular dystrophies are a disease group which is clinically and genetically heterogeneous and is evident with early-onset and progressive muscle weakness. It has numerous genetic types that have been defined till now[42]. Thus, it was decided to conduct a genetic study on the patient in order to determine the sub type.

Despite all the further examinations; it cannot be possible to find the reason of recurrent rhabdomyolysis in some patients and idiopathic recurrent rhabdomyolysis is known as “Meyer Betz Syndrome”. In fact, this is an exclusion diagnosis. Case eight was reported by Kasap et al[43] previously. The patient was applied with rhabdomyolysis finding that was induced by excessive physical activity at the first attack and after two months, he had applied again with a moderate CK increase. Metabolic screening of the patient (blood acylcarnitine analysis, total and free serum carnitine levels, and blood lactic acid level were normal, or tests conducted in terms of fatty acid oxidation defect-) was normal. EMG was normal. Ischemic effort test was applied in order to exclude McArdle’s disease. Blood lactate and ammonia levels examined before and after exercise were above the normal. This picture is not expected in McArdle disease. Thus, muscle biopsy was applied to the patient and no glycogen deposit was observed.

If rhabdomyolysis is suspected in terms of the history and laboratory independently from underlying etiology, aggressive fluid treatment should be immediately started with isotonic saline[8]. Electrolyte abnormalities should be closely monitored and treated[8]. After urine output was observed, the urine may be alkalinized with sodium bicarbonate. Many authors suggest a high hydration value, like 200 mL/h, until CK level decreases below 1000 U/L. Of course, this should be performed in a more controlled manner in pediatric cases. The indications for HD were severe hyperkalemia and prolonged oligo-anuric renal failure[44]. Two patients in this series were applied with HD treatment because of prolonged oligoanuric phase and hypertension in case three and high creatinine level and also hypertension in case four.

As a consequence; although the rhabdomyolysis picture is basically presented to us together with the same clinical and laboratory results, clarification of the etiology should be the primary factor. Especially it is very important to distinguish the sporadic and hereditary cases from each other. It should be considered that the primary organ to be rescued in the acute period is the kidney and aggressive fluid therapy, alkalinization and when needed, HD should be taken into consideration.

COMMENTS

Background
Rhabdomyolysis could be caused by a number of reasons, which could be classified as sporadic and hereditary/recurrent. All of the diseases causing rhabdomyolysis lead formation of cell membrane damage, hypoxia and lytic enzymes such as phospholipase A2, and decrease of energy source ATP as a result of cell's exposure to mechanical stress. Final outcome is disruption of intracellular ion balance, Ca concentration occurring within cell, hyperactivity in Ca-dependent proteolytic enzymes, and formation of oxidative free radicals. In the next periods, on the other hand, cell death occurs as a result of free radicals and proteases. It was intended to convey clinical and laboratory outcomes of rhabdomyolysis to reader and to identify extreme conditions within the scope of basic information. In this study, the authors evaluated clinical differences and etiologies of rhabdomyolysis in childhood.

Research frontiers
Rhabdomyolysis is an important clinical process in childhood. Clinicians must be keep in mind that sporadic and recurrent cases have different clinical properties.

Innovations and breakthroughs
Rhabdomyolysis is an important clinical situation. Clinician must be investigate it carefully. Unless a convenient treatment is performed, it will result in an acute kidney injury.

Terminology
Although the rhabdomyolysis picture is basically presented to us together with the same clinical and laboratory results, clarification of the etiology should be the primary factor. Especially it is very important to distinguish the sporadic and hereditary cases from each other. To concisely and accurately describe, define or explain the specific, unique terms that are not familiar to majority of the readers, but are essential for the readers to understand the article. AKI: Acute kidney injury; ACAD: Acyl-CoA dehydrogenase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; SM: Blood myoglobin levels; BUN: Blood urea nitrogen; Ca: calcium; CPT II: Carnitinepalmitoyltransferase fera II enzyme; Ch: Chlor; CMV: Cytomegalovirus; Creat: Creatinine; CK: Creatinine kinase; EMG: Electromyography; EBV: Epstein-Barr virus; FDA: Food and Drug Administration; HD: Hemodialysis; Hb: Hemoglobin; HIV: Human immuno deficiency virus; K: Potassium; LDH: Lactate dehydrogenase; LCFA: Long-chain fatty acids; Na: Sodium; P: Phosphorus; PRA: Plasma renin activity; Pt: Platelet; UM: Urine myoglobin levels; VLCAD: Very long chain acyl-coA dehydrogenase; WBC: White blood cell.

Peer-review
The manuscript is a series of 8 case-reports occurring in children. I would thank the authors for these clinical cases that remembers us that rhabdomyolysis also occurs in children and that the etiologies are quite different from adults.
Alaygut D et al. Rhabdomyolysis in childhood

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