

Case Report

## The Life-Threatening Case of Rhabdomyolysis Caused by A LIPIN1 Deficiency

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### Abstract

Rhabdomyolysis is a serious condition caused by damage to the skeletal muscle [1,2], which release a large volume of toxic intracellular contents into the bloodstream. Rhabdomyolysis has many etiologies in children, sometimes leads to life-threatening crises.

Lipin-1 deficiency is considered now as a major cause of severe recurrent rhabdomyolysis in early childhood [1,2]. It is inherited as Autosomal recessive and cause recurrent attacks of rhabdomyolysis associated with muscle pain, weakness and followed by excretion of myoglobin in the urine.

### Objective

To present a case of severe recurrent rhabdomyolysis caused by LIPIN 1 deficiency, in a patient was admitted to the pediatric department.

### Case

A 1-year-old boy, presented with floppiness and inability to walk after 1 day of upper respiratory tract infection, he had dark urine. Physical examination showed a floppy child with diminished deep tendon reflexes. The blood test revealed high CPK up to 100.000 u/l. There was a family history of children who passed away with the same symptom. Considering the previous findings, we did genetic test showed LIPIN 1 deficiency, which is a major cause of Autosomal recessive rhabdomyolysis. Our patient had until now 2 crises resolved by aggressive hydration without complications, his CPK level between the crises remained elevated.

### Conclusion

LIPIN 1 deficiency is a cause of Autosomal recessive recurrent myoglobinuria also known as familial paroxysmal paralytic myoglobinuria. It is characterized by recurrent attacks of Rhabdomyolysis associated with muscle pain, weakness and followed by excretion of myoglobin in the urine. The attacks need early recognition and aggressive treatment to prevent the complication [3,4].

**Keywords:** Myoglobinuria; Familial Paroxysmal Paralytic Myoglobinuria; Autosomal Recessive Recurrent Myoglobinuria; Rhabdomyolysis

### Introduction

Rhabdomyolysis is a serious condition, caused by damage to the skeletal muscle that releases a large volume of toxic intracellular contents into the bloodstream [1,2]. The main hereditary causes of severe recurrent rhabdomyolysis in children are Fatty acid oxidation disorders and lipin-1 deficiency. Lipin-1 deficiency is an autosomal recessive disorder, caused by mutations in LIPIN1 gene that leads to crises of severe rhabdomyolysis and myoglobinuria in young children [5,6]. In this case, we described an episode of a severe Rhabdomyolysis caused by LIPIN 1 deficiency, with a family history of death after Rhabdomyolysis crises, the patient was admitted to the pediatric ward in the hospital.

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## Case Report

Our patient was 1-year-old healthy boy, he presented with a history of mild fever and running nose for 1 day, next day he became floppy and unable to walk as before, he was crying when letting him support himself, his mother noticed that his urine became darker, no other symptoms.

Past medical history was unremarkable.

Birth History: Born at term, NVD, anti-natal and postnatal history was unremarkable.

Vaccinated up to date.

### Family History

Parent's consanguinity is cousins, the patient was the second child in the family, and elder brother had same complain and passed away at age of 30 months. In the family of his uncle, there was a history of children who died in early childhood.

Origin of the family: Arab.

Vital signs on admission:

Tem: 36c, BP:95/56 mmHg, PR:150/min, RR:35/min, Spo2:99% in room air.

Weight: 11.6kg, Length77cm, H.C: 46.5 CM.

Physical Examination: The general condition was well, no respiratory distress, he was crying when we touched him or tried to move his legs.

Chest: good air entry bilateral.

Heart: regular rhythm, normal heart sounds.

Abdomen: soft, no organomegaly.

CNS: intact, deep tendon reflexes were weak.

Investigations:

CBC: normal, CRP: negative, Urea electrolyte/ normal,

Amonia/ 46 umol/L,

Lactic acid/ 1.4 mmol/L,

CPK:183180 u/L,

LDH: 11344 u/L,

Urine analysis: myoglobin positive,

ECG: normal.

Leucine/ Isoleucine: 494.79 (60-265 mmol/l)

Acylcarnitine profile: 1.04 (0.04-0.9mmol/L)

Metabolic screen in urine: negative

Genetic study: An apparently homozygous variant in LIPIN1 gene, NM-001261428.1:c1417>T (PArg473\*), inheritance is autosomal recessive.

The treatment was supportive by intravenous fluid with sodium bicarbonate, and monitoring vital signs, electrolyte, heart rhythm.

After 5 days CPK started to decrease, and on discharge after 7 days CPK was 1265 U/L.

On discharge, he started to sit-down, and to walk comfortably with support without crying.

Now the child is 3 years old, he had 2 episodes of myoglobinuria needed admission and treatment, between the episodes the child is completely normal and CPK level between 650-750 u/l.

## Discussion

Lipin-1 deficiency caused by mutations in the LPIN1 gene is considered now a major cause of severe recurrent rhabdomyolysis in early childhood [1,2], it leads to death in up to one-third of patients [5], in our case, there is a family history of death during the crises(elder brother).

Lipin 1 is an important enzyme in the pathway of triglyceride and phospholipid biosynthesis; also it acts as a transcriptional protein that regulates cellular lipid metabolism [7]. Reviewing the patient who had LIPIN1 deficiency showed elevated levels of lysophosphatidate, phosphatidate, and lysophospholipids muscle tissue. In a normal situation, any disturbance in phosphatidate levels may lead to inappropriate modulation of signaling cascades, oxidative processes, cAMP degradation [8] that destroys the cell muscle.

Diseases associated with LIPIN1deficiency include Acute Recurrent Myoglobinuria, Autosomal Recessive and Genetic Myoglobinuria and familial paroxysmal paralytic myoglobinuria. The crises are spontaneous or triggered by febrile illness, exercises or fasting [9].

The symptoms including hyporeflexia, muscle weakness, and areflexia.

Treatment of the crises is symptomatic with aggressive hydration, high energy intake from carbohydrates and monitoring for hyperkalemia and cardiac arrhythmias, there is a general agreement of the importance of early detection of the episodes [5,9].

In our case, after we diagnosed a Lipin 1 deficiency which is an autosomal recessive disease, it was easy to predict the crises in the family and to start the aggressive treatment early that helped to avoid the complications.

Now our patient is 3 years old, and had two crises: First one came at age of 1 year after signs of upper respiratory tract infection, and the second one came at age of two years without predisposing factors. The treatment for both crises was with hydration and sodium bicarbonate. Both episodes resolved without any complication, and CK level between crises remained mildly elevated.

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## Summary

Lipin 1 deficiency is the main cause of life-threatening Rhabdomyolysis crises [1,2]. The most important factor in treatment is the early recognition of the episodes, aggressive hydration, sodium bicarbonate, and monitoring for hyperkalemia, and cardiac arrhythmia [3,10,4].

The diagnosis of lipin-1 deficiency is confirmed by genetic testing.

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