**INTRODUCTION:**

Biallelic mutations in LPIN1 are an important cause of severe recurrent rhabdomyolysis. Fulminant hyperkalaemia unresponsive to known pharmacological therapies is a common complication. Despite known roles in lipid metabolism, inflammation and oxidative stress, the mechanism is unclear. We report a series of patients presenting to regional hospitals under 5 years of age with hyperkalaemia resulting in death.

**Case 1:**

This 4yo boy woke with a sore knee, then complained of sore elbow and tongue, with a history of minimal intake the previous evening. Background of episodes of sore joints and funny smelling/dark urine. Elevated AST (9000/L), ALT (284U/L), LDH were noted during a previous episode which normalised (GP suspected transient hepatitis, and AST>ALT did not trigger the addition of a CK level). Rapid deterioration occurred in the afternoon, with hyperkalaemic arrest occurring within minutes of arrival at the emergency department. Resuscitation was unsuccessful. On the advice of a metabolic specialist, a creatine kinase (CK) level (10,1000/L) and then LPIN1 sequencing were added retrospectively.

**Case 2:**

A 2yo girl had 2 episodes of severe rhabdomyolysis, both triggered by adenovirus and rhinovirus-positive respiratory tract infections. She initially presented lethargic, floppy and diaphoretic, with a 24 hour history of thigh pain and fever, and a few hours of reluctance to walk. CK was 22,000/L, with mild acidosis, glucose 13.3mmol/L and ketones 2.2mmol/L. CK peaked at 500,000/L around 36 hours later. Maximum K+ was 5.3mmol/L (haemolysed sample) and she required supplementation as it dropped to 2.9mmol/L when the CK peaked.

The second episode was similar, with late presentation after 2 days of illness, CK was 500,000/L and peaked at 660,000/L. Potassium was again low, requiring supplementation, and BIPAP respiratory support was given. Myopathy was prolonged but recovery appeared complete.

Genetic testing sent after the first episode confirmed LPIN1 mutations. At least one febrile illness was subsequently managed proactively and CK peaked at 36/L.

At 4 yrs she presented with sore throat and legs, and reportedly slightly lethargic the day prior. BSL was 4.4mmol/L, treated with glucocortic. CK of 1,214/U/L was recorded with K+4.0mmol/L. 10% glucogel was given. 10% K+ was given and urine myoglobin became positive. CK peaked at 536U/L.

**DISCUSSION:**

LPIN1 mutations are a significant cause of rhabdomyolysis in young children. Fatal episodes due to fulminant hyperkalaemia can occur in both undiagnosed and diagnosed children, even with aggressive management. While hyperkalaemia can complicate rhabdomyolysis of any cause, the reported death rate in LPIN1 mutations is around 30% whereas deaths are almost unheard of in other causes such as fatty acid oxidation defects.

As demonstrated here, hyperkalaemia may occur early in an episode, despite CK being at relatively low levels. In case 1, the AST recorded in a previous episode suggests a higher CK level than was reached in the fatal episode, similarly demonstrated in case 2. The mechanism for this is unknown, but LPIN1 is believed to have roles in phospholipid biosynthesis, lipid metabolism, inflammation, and oxidative stress.

Prodromes of less than 24 hours to three days were reported, with vomiting, other mild infective symptoms or fasting being present in all children. Causative organisms were not identified. Diagnosis is challenging in sudden deaths. Paediatric and emergency physicians may not be aware of rare disorders such as LPIN1. CK and/or urine myoglobin samples may not be taken prior to death, and peri- and post-mortem results may be confounded by haemolysis, cardiopulmonary resuscitation and post-mortem changes.

**CONCLUSION:**

Specialist input is warranted in sudden unexpected childhood death, to consider specific case circumstances and guide investigations to enable identification of rare disorders such as LPIN1. Appropriate pre- and peri-mortem biochemical investigations including CK, urine myoglobin, amino acids and organic acids can yield vital diagnostic information and guide genetic testing.

**References:**