An Atypical Presentation Of McArdle’s Disease With Congenital Arthrogyriposis

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Introduction: McArdle's disease - glycogen storage disease type V (GSD-5) is a rare autosomal recessive disorder, caused by the deficiency of muscle myophosphorylase enzyme. Enzyme deficiency leads to defective degradation of glycogen causing fatigue, pain, increase in creatine kinase levels, rhabdomyolysis, myoglobinuria, and renal failure under intense exercise and stress conditions. Patients have mutations in both alleles of the PYGM gene which encodes myophosphorylase, the skeletal muscle isoform of glycogen phosphorylase. Myophosphorylase initiates the breakdown of muscle glycogen by removing α-1,4 linked glycosyl units from the outer branches of glycogen, which leads to the liberation of glucose-1-phosphate.
Glucose-1-phosphate is normally converted to glucose-6 phosphate, which subsequently undergoes glycolysis, resulting in pyruvate production. Muscle pyruvate can be converted to lactate in anaerobic conditions, which is then released to the blood. Most of the pyruvate crosses the mitochondrial membrane, where it is converted to acetyl coenzyme A (acetyl-CoA) and further metabolized in the citric acid cycle.

GSD V patients have absent myophosphorylase activity and are unable to mobilize muscle glycogen stores during exercise. However, they can take up glucose from the blood, which is converted to glucose-6 phosphate and metabolized via the intact glycolytic pathway.

People with GSDV typically experience fatigue, muscle pain, and cramps during the first few minutes of exercise (exercise intolerance). Exercise such as weight lifting or jogging usually triggers these symptoms in affected individuals.
The discomfort is generally alleviated with rest. If individuals rest after brief exercise and wait for their pain to go away, they can usually resume exercising with little or no discomfort (a characteristic phenomenon known as "second wind").

Arthrogryposis Multiplex Congenita (AMK); present at birth, characterized multiple congenital joint contractures, due to soft tissue contractures in two or more joints, it is defined as non-progressive limitation of movement. Arthrogryposis Multiplex Congenita has a multifactorial etiology. Absence or scarcity of fetal movements and genetic defects are most frequently blamed. It mainly involves the extremities.

Case Presentation: The girl who is now 2 years old, at the age of 4 months presented to our clinic with joint stiffness in all extremities and an increase in CK levels. Her joint stiffness is marked in the neck and hip. In her perinatal history, intrauterine movements were diminished. Although her intellectual ability is compatible with her age, motor developmental milestones were late. During infancy, CK levels of 2500 IU/L were observed. After the start of the walking ability, a ‘second wind phenomenon’ was described which is a specific clinical description of McArdle’s Disease.

Whole Exome Sequencing was held and a homozygous mutation of c.1A>g (p.Met1?) in the PYGM gene was detected and reported as a pathogenic variant.
The patient was given vitamin B6 (1x250 mg), creatine monohydrate (100 mg/kg/day, 3 doses), ramipril 1 time a day, gradually increasing the dose to 1x2.5 mg. With the supportive treatment applied to the patient, muscle enzymes (CK, Troponon T, CK-MB, AST) started to decrease. Followup and treatment of the patient for arthrogryposis multiplex congenita was planned in the Department of Physical Therapy and Orthopedics.

**Conclusion:** McArdle’s disease (GSD-5) is a specific type of glycogen storage disorder with a specific clinical picture. Arthrogryposis can be seen in some types of glycogen storage disorders, like type-4 and type-7, but not mentioned in McArdle’s disease before. Here we present a girl with arthrogryposis and McArdle’s disease with a novel PYGM mutation. With this case, we aimed to add a new clinical feature to McArdle’s disease. If the patient has arthrogosis multiplex congenita finding and muscle enzymes are high; it is an important clue for metabolic myopathies.