Die Glykogenose Typ II : Morbus Pompe

Thomas Hundsberger, Ursula Hohl & Kai Michael Rösler

Abstract:
Glycogen storage disease type II (Pompe disease) is a rare autosomal recessive disorder due to mutations in the acid alpha-glucosidase (GAA) gene. The disease defining genetic alteration can be found at several nucleotides as more than 200 different mutations has been reported so far. Some of these mutations lead to a complete loss of function of the GAA whereas others only reduce enzyme activity to various degrees. Deficient GAA activity leads to harmful lysosomal glycogen storage and disruption of various cell types. Depending on the degree of residual enzyme activity symptoms of the disease evolve in infancy, childhood or adulthood. As a rule loss of enzyme function or low residual activity is associated with a severe phenotype and early onset disease. Glycogenosis type II is a multisystem disorder with a broad clinical spectrum. Muscle weakness and respiratory failure are the most important clinical symptoms in adults. In infants symptoms due to cardiomyopathy, arrhythmia and heart failure are most prominent and life threatening. Glycogen accumulation has also been detected in the brain, brainstem and anterior horn cells. Soon after birth first symptoms occur with a fast disease progression leading to death after 6-12 month in untreated patients (“classic form”). Infants with signs of generalized myopathy (floppy infant) and cardiomyopathy should be screened for Pompe´s disease as early enzyme replacement therapy (ERT) with recombinant human GAA (rhGAA) can prevent a lethal outcome. If the enzyme activity of GAA is more than 1% children and adults have a more benign phenotype consisting of muscle weakness and ventilatory problems. In children developmental motor milestones are usually delayed or not reached (i.e. walking). Adults are affected by proximal myopathy and diaphragmal insufficiency (“late-onset form”). Diagnosis is based on the clinical suspicion of a proximal myopathy, a muscle biopsy showing intracellular glycogen accumulation and the biochemical measurement of GAA activity in lymphocytes, dried blood spots assays, skin fibroblast or muscle. The diagnosis should be confirmed by genetic testing at least for the most common IVS1 splice site mutation. ERT with rhGAA (Myozyme®) for this disease is worldwide available since 2006. For infants and children this therapy is well established despite high costs and the need for frequent intravenous infusions every other week in a dosage of 20 mg/kg body weight. Reconstitution of measurable cardiomyopathy clearly improves survival and enhances quality of life compared with untreated children with a life expectancy of less than one year. The timing, duration and benefit of ERT in adults is still an open question. Due
to the few published studies, reflecting the rarity of the disease, muscle strength and ventilator function improves under ERT. Early therapy seems to prevent disease progression. Unfortunately, there is no predictive marker for the beneficial effect of ERT therapy in Pompe patients. Nevertheless, a randomized controlled phase III trial of 90 “late-onset” patients showed significant effects on the vital capacity and walk distances. Keeping the high costs of therapy in mind and knowing the wide spectrum of clinical presentation the indication for ERT in “late-onset” patients must be considered on an individual basis. This decision depends on the degree of muscle weakness, impairment of daily life activities and especially the presence of diaphragmal insufficiency. If respiratory insufficiency occurs it has to be treated by lifetime invasive or non-invasive ventilation. Of note, diaphragmal weakness can rapidly deteriorate triggered by respiratory infection or elective intubation with prolonged weaning. This review is meant to raise more attention and to describe the latest insights in glycogen storage disease type II.

**keywords**
Morbus Pompe, glycogen storage disease type II, enzyme replacement therapy, recombinant human acid alpha-glucosidase

**type**
journal paper(review (Deutsch)

**date of publishing**
26-2-2010

**journal title**
Schweizer Archiv für Neurologie und Psychiatrie (161/2)

**pages**
55-59