Pompe's Glycogen Storage Disease

Synonyms: glycogen storage disease type II; acid maltase deficiency

Pompe's disease is a glycogen storage disorder. Deficiency of the lysosomal enzyme alpha-1,4-glucosidase (acid maltase) leads to the accumulation of glycogen in many tissues:

- The clinical spectrum is continuous and broad and three major forms are recognised: infantile, juvenile and adult-onset.\(^1\)
- In the infantile form, accumulation of glycogen in cardiac muscle leads to cardiac failure.
- Accumulation may also occur in the liver, which results in hepatomegaly and elevation of hepatic enzymes.
- Glycogen accumulation in muscle and peripheral nerves causes hypotonia and weakness.
- Glycogen deposition in blood vessels may result in intracranial aneurysms.

Epidemiology

- The overall prevalence has been estimated at 1 in 40,000, with 1 in 138,000 for the infantile form and 1 in 57,000 for the adult form.\(^2\)
- Pompe's disease has an estimated frequency of 1 in 40,000 in African-American, 1 in 50,000 in Chinese, 1 in 40,000 in Dutch, and 1 in 146,000 in Australian populations.\(^3\)
- Infantile and adult forms are inherited as autosomal recessive conditions. The gene has been traced to chromosome 17.\(^4\)

Presentation

- Presentation later in life is associated with a less severe form of disease.
- There is a continuous spectrum between the classic infantile and adult forms.
- The infantile form presents in the first six months of life (typically at between 4-8 weeks) with weakness, hypotonia, respiratory distress, feeding difficulties and heart failure.
- The juvenile form presents later in childhood with delayed motor development, muscle weakness and hypotonia.
- The adult form usually presents as skeletal and respiratory muscle weakness. The typical age of presentation is 20-40 years. There may be limb-girdle weakness and weakness of respiratory muscles.\(^5\)

Signs

Infantile form:
- Cardiomegaly and congestive heart failure.
- Generalised hypotonia, absent or reduced reflexes.
- Enlarged tongue, enlarged liver.
- Reflexes may be depressed or absent because of glycogen accumulation in spinal motor neurons.
- Alertness may be impaired.

Adult form:
- Weakness may affect only specific muscle groups, eg upper arms, and may be asymmetrical.
- Limb-girdle weakness is common and respiratory muscle involvement may be prominent.\(^6\)

Differential diagnosis

- Other glycogen storage disorders.
- Muscular dystrophy: Duchenne muscular dystrophy (or less severe muscular dystrophies for older-onset disease).

Investigations

- Serum creatine kinase and aspartate aminotransferase are elevated.\(^7\)
- Definitive diagnosis is made by the measurement of acid alpha-glucosidase activity in cultured skin fibroblasts or peripheral blood lymphocytes.\(^8\)
- Intracranial aneurysms may be shown on angiography or magnetic resonance angiography.
- Echocardiogram to assess heart size and degree of left ventricular hypertrophy.
- ECG: short PR interval and elevated QRS complexes in the infantile form.
Electromyography (EMG) shows a myopathic pattern and also often shows pseudomyotonic discharges, fibrillation potentials and positive waves.[1]

Muscle biopsy for the evaluation of differential diagnosis of muscle weakness.

Management

Enzyme replacement therapy:
- Enzyme replacement therapy has been shown to be very effective and substantially improves the prospects for patients.[8]
- Alglucosidase alfa (Myozyme®), an enzyme produced by recombinant DNA technology, is licensed for long-term replacement therapy in Pompe’s disease. [8] Myozyme® is available by referral to an expert centre.[9]
- Paediatric centres in England: Addenbrooke’s (Cambridge), Birmingham Children’s Hospital, Great Ormond Street Hospital, Willink (Royal Manchester Children’s Hospital).
- Alglucosidase alfa therapy has been shown to improve cardiac and skeletal muscle function.[10, 11] Therapy has been shown to achieve significant reductions in the risk of death and invasive ventilation among treated patients.[1]

Complications

- In the infantile form, cardiomegaly and congestive heart failure lead to death.
- Cardiomegaly with progressive obstruction to left ventricular outflow is a major cause of mortality.
- Aspiration pneumonia: weakness of ventilatory muscles increases the risk of pneumonia.
- The adult form manifests with dystrophy and respiratory muscle weakness.
- In the adult form, intracranial aneurysms present the greatest complication.
- Liver failure may occur.

Prognosis

- Without enzyme replacement therapy, the infantile form is usually fatal, with most deaths occurring within one year of birth.[14]
- Later clinical onset usually corresponds with more benign symptoms and disease course.
- The adult form is not necessarily fatal, but complications, such as rupture of an aneurysm or respiratory failure, may cause significant morbidity and mortality.

Further reading & references

1. Ibrahim J et al; Genetics of Glycogen-Storage Disease Type II (Pompe Disease), Medscape, Jul 2011
4. Glycogen Storage Disease II, Online Mendelian Inheritance in Man (OMIM).
9. Pompe Pages; Association for Glycogen Storage Disease UK.

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