Pompe disease: A comprehensive guide to genetics, management, and future therapies.

Rania Khan*

Department of Metabolic Medicine, University Hospital of Wales, UK

Introduction

Pompe disease, also known as glycogen storage disease type II, is a rare, inherited metabolic disorder caused by a deficiency in the enzyme acid alpha-glucosidase (GAA). This enzyme is essential for breaking down glycogen, a stored form of sugar used for energy, into glucose. The deficiency in GAA leads to the accumulation of glycogen in various tissues, particularly in the muscles, which can cause a range of symptoms and complications [1].

Pompe disease was first described by Dutch pathologist Dr. Joannes Cassianus Pompe in 1932. He observed an infant who had died of a severe form of muscle disease and noted the excessive accumulation of glycogen in the heart muscle. This discovery led to the identification of the condition as a distinct glycogen storage disease. Over the years, further research has expanded our understanding of the disease, its genetic basis, and potential treatments [2].

Pompe disease is inherited in an autosomal recessive manner, meaning that an individual must inherit two defective copies of the GAA gene, one from each parent, to develop the disease. The GAA gene is located on chromosome 17, and mutations in this gene result in reduced or absent activity of the acid alpha-glucosidase enzyme. To date, more than 300 different mutations in the GAA gene have been identified, leading to varying levels of enzyme activity and, consequently, a wide spectrum of disease severity [3].

Pompe disease is classified into three main types based on the age of onset and the severity of symptoms: Infantile-Onset Pompe Disease (IOPD): This is the most severe form, usually presenting within the first few months of life. Infants with IOPD often exhibit symptoms such as profound muscle weakness (hypotonia), enlarged heart (cardiomegaly), breathing difficulties, and failure to thrive. Without treatment, the disease typically leads to death from cardiorespiratory failure within the first year of life [4].

Late-Onset Pompe Disease (LOPD): This form can present at any age, from childhood to adulthood, and is characterized by a slower progression of symptoms. Individuals with LOPD may experience progressive muscle weakness, particularly in the respiratory and skeletal muscles, leading to difficulties in mobility and respiratory function. Unlike IOPD, cardiac involvement is less common in LOPD [5].

Non-Classical Infantile-Onset Pompe Disease: This intermediate form presents in infancy but with a less severe progression compared to IOPD. Symptoms may include muscle weakness and respiratory issues, but heart involvement is less prominent than in IOPD [6].

The diagnosis of Pompe disease involves a combination of clinical evaluation, laboratory tests, and genetic testing. Key diagnostic steps include: Enzyme Activity Assay: Measuring the activity of the acid alpha-glucosidase enzyme in blood, muscle, or skin cells can confirm the diagnosis. Low or absent enzyme activity is indicative of Pompe disease [7].

Genetic Testing: DNA analysis can identify mutations in the GAA gene, providing a definitive diagnosis and helping to distinguish between different forms of the disease. Muscle Biopsy: In some cases, a muscle biopsy may be performed to examine glycogen accumulation in muscle tissues [8].

The primary treatment for Pompe disease is enzyme replacement therapy (ERT), which involves the intravenous administration of recombinant human acid alpha-glucosidase (rhGAA). ERT has been shown to improve survival, reduce cardiac hypertrophy, and enhance motor and respiratory function, particularly in individuals with IOPD. However, the response to ERT can vary, and it may not completely halt disease progression, especially in cases of LOPD [9].

Supportive therapies are also important in managing Pompe disease and may include: Physical Therapy: To maintain muscle strength and mobility, and to prevent contractures and skeletal deformities. Respiratory Support: Non-invasive ventilation or, in severe cases, mechanical ventilation to manage respiratory insufficiency. Nutritional Support: Ensuring adequate nutrition and addressing feeding difficulties, particularly in infants. Cardiac Care: Regular monitoring and management of cardiac function, especially in those with IOPD [10].

Conclusion

Pompe disease is a complex and multifaceted disorder with significant variability in clinical presentation and progression. Advances in genetic and therapeutic research continue to offer hope for better management and improved quality of life for those affected by this rare disease.

***Correspondence to:** Rania Khan, Department of Metabolic Medicine, University Hospital of Wales, UK. E-mail: khanr12@uhw.uk.in

Received*:** 29-Dec-2023, Manuscript No. JNNR-24-137403; ***Editor assigned: 2-Jan-2024, Pre QC No. JNNR-24-137403(PQ); ***Reviewed*:** 16-Jan-2024, QC No. JNNR-24-137403; ***Revised:*** 22-Jan-2024, Manuscript No. JNNR-24-137403(R); ***Published:*** 29-Jan-2024, DOI: 10.35841/aajnnr-9.1.190

Citation: *Khan R. Pompe disease: A comprehensive guide to genetics, management, and future therapies. J Neurol Neurorehab Res.2024;9(1):190*

References

1. Taverna S, Cammarata G, Colomba P, et al. Pompe disease: pathogenesis, molecular genetics and diagnosis. Aging (Albany NY). 2020;12(15):15856.
2. Meena NK, Raben N. Pompe disease: new developments in an old lysosomal storage disorder. Biomolecules. 2020;10(9):1339.
3. Unnisa Z, Yoon JK, Schindler JW, et al. Gene therapy developments for Pompe disease. Biomedicines. 2022;10(2):302.
4. Davison JE. Advances in diagnosis and management of Pompe disease. J Mother Child. 2020;24(2):3-8.
5. Keutzer JM. Establishing Pompe disease newborn screening: the role of industry. Int J Neonatal Screen. 2020;6(3):55.
6. Leon-Astudillo C, Trivedi PD, Sun RC, et al. Current avenues of gene therapy in Pompe disease. Curr Opin Neurol. 2023;36(5):464-73.
7. Borie-Guichot M, Tran ML, Génisson Y, et al. Pharmacological chaperone therapy for Pompe disease. Molecules. 2021;26(23):7223.
8. Huang W, Zhang Y, Zhou R. Induced pluripotent stem cell for modeling Pompe disease. Front Cardiovasc Med. 2022;9:1061384.
9. Díaz-Manera J, Walter G, Straub V. Skeletal muscle magnetic resonance imaging in Pompe disease. Muscle Nerve. 2021;63(5):640-50.
10. Schoser B, Laforet P. Therapeutic thoroughfares for adults living with Pompe disease. Curr Opin Neurol. 2022;35(5):645-50.

Citation: *Khan R. Pompe disease: A comprehensive guide to genetics, management, and future therapies. J Neurol Neurorehab Res.2024;9(1):190*