A RARE METABOLIC DISORDER: POMPE'S DISEASE

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ABSTRACT: Pompe disease is an autosomal recessive metabolic disorder caused by the buildup of a sugar called glycogen in the body's cells.[1,2] It is caused by an accumulation of glycogen in the lysosome due to deficiency or absence of the enzyme acid alpha-glucosidase (GAA). The enzyme GAA is used to breakdown glycogen into a simpler sugar, glucose.[3] It is characterised by progressive weakness in the muscles used for mobility and breathing. In infants with Pompe disease, the heart muscles are often severely affected as well.[4,7] The cells of the heart and skeletal muscles are affected the most.It is caused by a mutation in a gene (Acid alpha-glucosidase: also known as acid maltase) on long arm of chromosome 17 at 17q25.2-q25.3.. Without treatment the disease is particularly lethal in infants and young children.[8]

KEYWORDS: Pompe disease, acid alpha glucosidase, hypotonia, myozyme.

HOW TO CITE THIS ARTICLE: Nazeer Ahmed Jeergal, Rizwan-u-zama, Naushad Ali Malagi. "A Rare Metabolic Disorder: Pompe's Disease". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 88, November 02; Page: 15376-15378, DOI: 10.14260/jemds/2015/2190.

INTRODUCTION: The disease is named after Joannes Cassianus Pompe, who characterized it in 1932. Pompe disease affects roughly 1 in 100,000 people.[9,10] It has been reported in almost all ethnic populations. As with all cases of autosomal recessive inheritance, children have a 1 in 4 chance of inheriting the disorder when both parents carry the defective gene, and although both parents carry one copy of the defective gene, they are usually not affected by the disorder.[11,12] The severity of symptoms, age at which symptoms begin, and rates of disease progression are related to the degree of alpha-glucosidase deficiency. Prognosis depends on the age of onset on symptoms with a better prognosis being associated with later onset disease.[13]

CASE REPORT: A 4 years old female child born out of second degree consanguiness marraige presented to pediatric opd with progressive lower limb weakness. The child had developmental delay with hypotonia from 6 months of life. In the neonatal period, child presented with repeated respiratory tract infections.

On examination: Upper limbs no hypotonia or contractures; Lower limbs hypotonia was present with involvement of proximal skeletal muscles of the limbs, slight contracture of knee and ankle contracture present. On per abdomen examination hepatomegaly. 4cms below the costal margin was present. Other vitals were within the normal limits. Chest x-ray showed cardiomegaly and Echo revealed cardiomyopathy.

Financial or Other, Competing Interest: None.
Submission 01-10-2015, Peer Review 03-10-2015,
Acceptance 20-10-2015, Published 02-11-2015.
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DOI:10.14260/jemds/2015/2190.

INVESTIGATIONS:

- Serum CPK = 664 microns/ litre (Ref: 25-200 microns/litre)
- Serum LDH = 2550 microns/ litre (Ref: 235-470 microns/litre)
- Alpha- 1,4 glucosidase activity: Ratio = 0.17 (Normal >0.2)
- With Acarbose = 2.6 (Ref: 12.68)
- Without Acarbose = 15.6 (Ref: 25.37-228.6)
- Muscle biopsy = Vacuolar myopathy
- Chest X-Ray = Cardiomegaly
- ECHO-Cardiography = Infiltrative Cardiomyopathy & Left ventricular dysfunction.

PROBABLE CLINICAL DIAGNOSIS: In the view of hypotonia of limbs, developmental delay and cardiomyopathy - Infantile Variant of Pompes disease was considered.

DISCUSSION: Pompe disease, also known as glycogen storage disease type II, is an inherited disorder whose primary symptom is progressive weakness in the muscles used for mobility and breathing.[14,17]

Two forms have been described[18,19]:

1. Classic form (Infantile form): It is a severe generalized myopathy and cardiomyopathy. Most commonly affected muscles are cardiac and respiratory muscles along with proximal skeletal muscles of limb. Patients have cardiomegaly, hepatomegaly, and are diffusely hypotonic and weak. Serum CPK levels are greatly elevated. A muscle biopsy of specimen reveals vacuolar myopathy with abnormal lysosomal activities.
2. Late onset form (Juvenile form): It is a much milder myopathy without cardiac or hepatic enlargement.

It may not become clinically expressed until later childhood or early adult life but may be symptomatic as myopathic weakness and hypotonia even in early infancy. Serum CPK levels are greatly elevated and muscle biopsy findings are diagnostic. The diagnosis is confirmed by estimation of acid maltase activity in muscle or liver biopsy.

The usual initial investigations include chest X ray, electrocardiogram and echocardiography. Typical findings are those of an enlarged heart with non-specific conduction defects. Biochemical investigations include serum creatine kinase(typically increased 10 fold) with lesser elevations of the serum aldolase, aspartate transaminase, alanine transaminase and lactic dehydrogenase. Diagnosis is made by estimating the acid alpha glucosidase activity in either skin biopsy (Fibroblasts), muscle biopsy (Muscle cells) or in white blood cells.[20]

In 2006, the FDA approved an enzyme replacement therapy called Myozyme (Alglucosidase alfa, rhGAA), for people with Pompe disease. Myozyme has been shown to decrease heart size, maintain normal heart function, and improve muscle tone and strength in people with the infantile-onset form of the disease.21 The FDA has approved Myozyme for administration by intravenous infusion of the solution. Myozyme treatment clearly prolongs ventilator-free survival and overall survival. The treatment is not without side effects which include fever, flushing, skin rash, increased heart rate and even shock; these conditions, however, are usually manageable.[22,23] Another factor affecting the treatment response is generation of antibodies against the infused enzyme, which is particularly severe in Pompe infants who have complete deficiency of the acid alpha-glucosidase. Immune tolerance therapy to eliminate these antibodies has improved the treatment outcome.[24]

A new treatment option for this disease is called Lumizyme. Lumizyme and Myozyme have the same generic ingredient (Alglucosidase Alfa) and manufacturer (Genzyme Corporation). The difference between these two products is in the manufacturing process.[25] Cardiac and respiratory complications are treated symptomatically. Physical and occupational therapy may be beneficial for some patients. Alterations in diet may provide temporary improvement but will not alter the course of the disease.

The prognosis for individuals with Pompe disease varies according to the onset and severity of symptoms.[26] Babies born with the infantile-onset form of Pompe disease typically die within the first year of life, though enzyme replacement therapy can now prolong that lifespan. Unfortunately, this disease will greatly curtail the lifespan of those affected. Most people with Pompe disease will die from lung failure. Genetic counseling can provide families with information regarding risk in future pregnancies.

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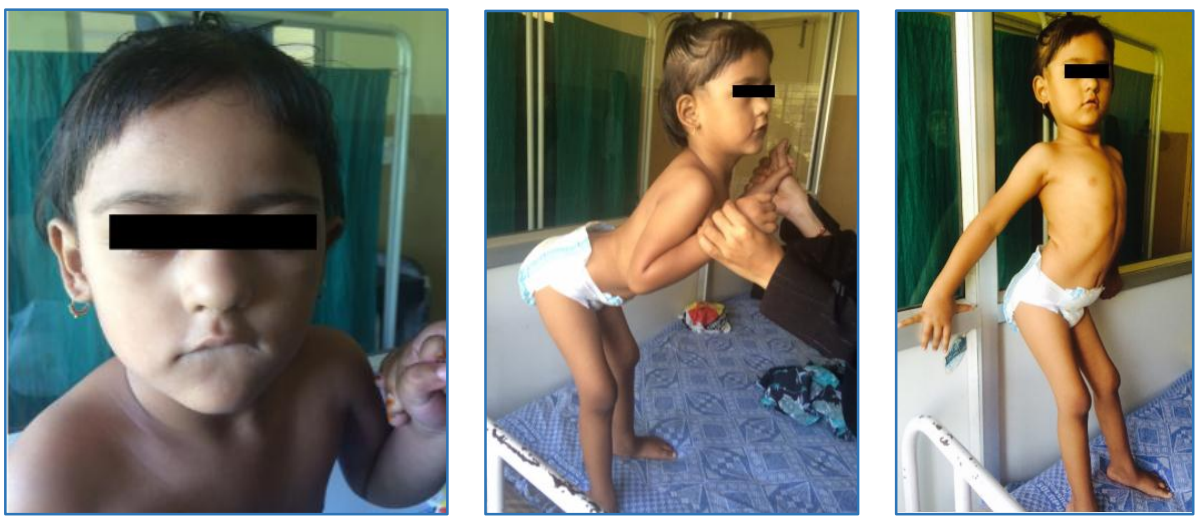

Facial Hypotonia Lower limbs hypotonia Involvement of proximal skeletal muscles of the limbs, Slight contracture of knee and ankle contracture