

Pompe Disease: A Case with Cardiomyopathy and Hypotonia

Inva Gjeta¹, D.Sala², I. Bakalli³, R. Lluka⁴, E. Celaj⁵, E.Kola⁶

Pediatric Intensive Care Unit- University Hospital Center of Tirana "Mother Teresa"- Albania

Abstract: Pompe disease also known as Glycogen Storage Disease type II, Acid Maltase Deficiency, and Glycogenosis type II is a rare autosomal recessive disease caused by the deficiency of acid α -glucosidase (GAA) [1]. The absence, or almost complete absence, of GAA in Pompe disease leads to the accumulation of high levels of glycogen in various tissues, particularly cardiac and skeletal muscle, as well as respiratory muscles, leading to generalized myopathy, cardiomyopathy and respiratory failure. Through this article we aim to increase the awareness in the medical community as an early treatment of this disease could enhance quality and longevity of patients' life. We will discuss the most severe form of the Pompe disease the classic infantile form, the cardiovascular involvement in Pompe disease and how important it is to test children with hypertrophic cardiomyopathy for this disease as well. Further we will present our own experience with a case with Cardiomyopathy and Hypotonic presented at University Medical Center of Tirana "Mother Teresa".

Keywords: Pompe Disease, Glycogen Storage Disease Type II, Acid Alfa-Glucosidase, Hypertrophic Cardiomyopathy, Left Ventricular Hypertrophy

1. Introduction

Pompe disease also known as glycogen storage disease type II, is a rare and progressive disorder caused by the deficiency of the enzyme acid α -glucosidase [1]. It is a glycogen disorder with a defect in lysosomal metabolism identified in 1932 [2]. The accumulation of glycogen in certain organs and tissues, muscles, especially in the heart, skeletal muscles, liver, and nervous system impair their ability to function normally [3].

Pompe is a rare disease with an incidence of 1: 40,000 births in the USA. The incidence depends on geographical position and ethnicity. In the Caucasian population, the frequency is estimated at 1: 100,000 for the infantile form and for the late form 1: 60,000. In South China / Taiwan is estimated at 1: 50,000 and in the African-American population is estimated at 1: 14,000 [4].

Based on the age of the presented disease, the organ being affected, the degree of progression and the significance degree Pompe disease is often divided in two subtypes: classic infantile form and late on-set forms [6].

Classic infantile form (4-8 month of age) is the most severe Pompe form [7]. Patients with this form are unable to hold up their heads, very weak arms and legs muscles, unable to do basic tasks for their age. They show respiratory insufficiency, cardiac insufficiency, hypotonia, fatigue in nutrition and not significant weight growth. Without treatment, classic infantile patients usually die before 12 months of age due to heart failure and respiratory weakness [8].

Late on-set forms (non-classic infantile form and late-onset) shown at patient greater than one year of age through to adulthood is the result of a partial deficiency of GAA. Muscle weakness progressing slowly over the years to respiratory weakness and death from respiratory failure.

A diagnosis of Pompe disease can be confirmed by screening for the common genetic testing GAA, measuring the level of GAA enzyme activity in a blood sample, assessment of GGA in lymphocytes, muscle biopsy and fibroblasts cultures.

Residual activity of the enzyme correlates with the severity of the disease, less than 1% of the enzyme normal activity are seen in the infantile form of the disease and more than 40% of the enzyme normal activity on the late on-set forms [7]. It was noticed that the disease progress in a variable way in children that have a certain level of GGA enzyme activity [8].

The introduction of enzyme replacement therapy (ERT) in 2006 is a major therapeutic advance. ERT with acid α -glucosidase is approved in the United States for all age affected by Pompe disease [9].

Treatments improve cardiac functions, the quality and longevity of patients' life.

2. Case history

A male infant four month old was admitted to Pediatric Intensive Care Unit with a 10 days history of cough, difficulty breathing and feeding.

An objective examination observed respiratory distress, pale skin, tachypnea without cyanosis, moderate hepatomegaly and systolic murmur at left intercostal on auscultation and bronchial rhonchi in the lungs.

A cardiac echo identified a left ventricle hypertrophy, a left ventricle hypokinesis and a left ventricle dilatation with FS (shortened fraction 23%) (Fig 1).

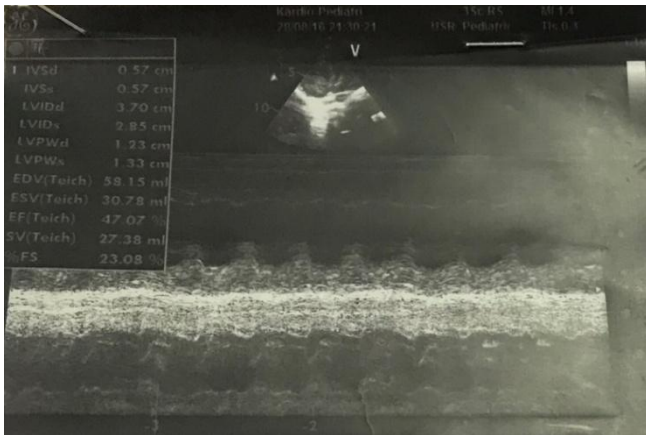


Figure 1: Patient's Cardiac Echography

Chest x-ray showed evidence of cardiomegaly (Fig 2).

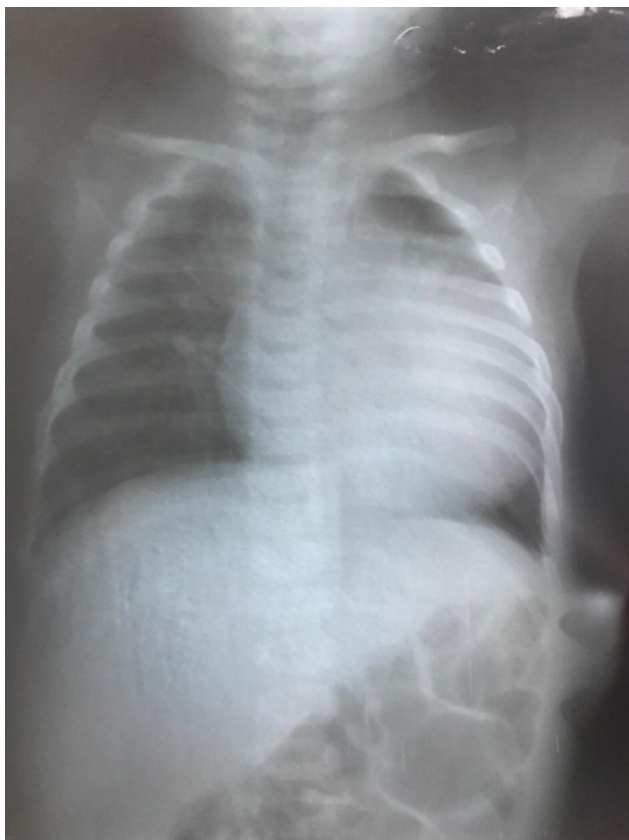


Figure 2: Patient's Chest Radiography

The laboratory analysis showed kinase creatinine level of 317U/l (normal range 0-170 U/l) that was increased moderately, aspartate transaminases level 248 U/l (normal range 0-35U/l), alanine transaminase level 155U/l (normal range 0-45 U / l), the lacto- dehydrogenase level 882 U/l (normal range 125-220 U/l) and lack of l-Carnitine was excluded.

Initially, the child was treated as an idiopathic form of hypertrophic cardiomyopathy with ACE -inhibitors, diuretics and inotrope positive. However no clinical improvements were noted.

After two weeks of hospitalization, an objective examination identified a progressive hypotonia, emphasized later that was not reflected on the initial examinations.

These results raised the suspicion of a secondary form of hypertrophic cardiomyopathy as a result of a metabolic Pompe disease.

The team conducted the GGA enzymatic activity test on the skin fibroblast culture that resulted with low values 0.02 nmol/mg protein/min (normal range 0.29-6.23). These results confirmed on the Pompe disease.

3. Discussion

The most common clinical signs of the Pompe disease, infantile form are cardiomyopathy, progressive hypotonia, respiratory distress and difficulty in nourishing, gastritis, myopathy, no weight gain, poor or missing reflexes, macroglossia and malnutrition [10].

The clinical presence of Pompe disease varies from the classic infantile form that progressive fast and it is life threatening to the slow progressive of the late on-set form [11].

In our case relevant clinical signs were respiratory distress, difficulty with feeding, needs for oxygen therapy later and cardiac insufficiency due to hypertrophic cardiomyopathy.

Because of the rare frequency and the extensive clinical and variable presentations the Pompe disease diagnosis is often delayed, difficult and misdiagnosed.

This case aims to highlight the variable and progressive clinical spectrum of this disease, enhancing health professionals' knowledge and the proper interpretation of clinical data in our daily practice.

Different studies have shown that the classic form of infantile-onset Pompe disease begins within a few months of birth. Infants with this disorder typically experience muscle weakness/myopathy, poor muscle tone/hypotonia, an enlarged liver/hepatomegaly) and heart defects[11], [3].

Infants may also fail to gain weight and grow at the expected rate (failure to thrive) and have breathing problems [3], [4].

If untreated, this form of Pompe disease leads to death from heart failure in the first year of life [6].

4. Conclusions

In a child with hypertrophic cardiomyopathy associated with a late progressive hypotonia and moderate persistent creatinine kinase level, differential diagnosis of the secondary form of cardiomyopathy in the field of metabolic disorders Pompe should be highly considered.

Early diagnosis and initiation of replacement enzyme therapy prior to installing signs of cardiac insufficiency can improve the quality of life and increase life expectancy.

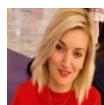
References

- [1] Alpha-Glucosidase deficiency in generalized glycogen storage disease (Pompe's disease). HERS HG Biochem J. 1963 Jan; 86():11-6.
- [2] Pompe JC. Over idiopatische hypertrophie van het hart. Ned Tijdschr Geneesk 1932;76:304-11.
- [3] A Lim-Jeong, Li Lishu, et al. Pompe disease: from pathophysiology to therapy and back again. Front Aging Neurosci. 2014;6:177. Published online 2014 Jul 23. Prepublished online 2014 Jul 3.
- [4] Leslie N, and Bailey L. Pompe Disease. Synonyms: Acid Alpha-Glucosidase Deficiency, Acid Maltase Deficiency, GAA Deficiency, Glycogen Storage Disease Type II (GSD II), Glycogenosis Type II. August 31, 2007; Last update: May 11 2017. Leslie N, Bailey L. In: Adam MP, Ardinger
- [5] HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. GeneReviews® [Internet] @. Seattle (WA): Pompe disease. University of Washington, Seattle; 1993-2018. 2007 Aug 31 [updated 2017 May 11]. [PubMed]
- [6] Slonim AE, Bulone L, Ritz S, Goldberg T, Chen A, Martiniuk F. Identification of two subtypes of infantile maltase deficiency. J Pediatr. 2000 Aug; 137(2):283-85. [PubMed].
- [7] Di Rocco M, Buzzi D, and Tarò. Glycogen storage disease type II: Clinical overview. Acta Myol. 2007 Jul; 26(1): 42-44.
- [8] Understanding Pompe disease. From diagnosis to action 2008 Genzyme Corporation.
- [9] Enzyme replacement for lysosomal diseases. Brady RO, Annu Rev Med. 2006; 57():283-96.
- [10] Abha D, Kaushik AY, Ganesh NS. Pompe Disease: A Rare Disease of Glycogen Storage. Indian Journal of Pharmacy Practice. 2013;6(2):6-12.
- [11] Kishnani PS, Steiner RD, et al. Pompe disease diagnosis and management guideline. Genet Med. 2006 May; 8(5): 267-288.



Prof. Elmira Kola, Division Chief of Pediatric Intensive Care Unit, University Medical Hospital of Tirana "Mother Teresa", Albania

Author Profile



Inva Gjeta, Pediatrician Division of Pediatric Intensive Care Unit, University Hospital Center of Tirana "Mother Teresa", Albania



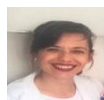
Durim Sala, Pediatrician Division of Pediatric Intensive Care Unit, University Hospital Center of Tirana "Mother Teresa", Albania



Prof. Assoc. Ilirjana Bakalli, Pediatrician Division of Pediatric Intensive Care Unit, University Hospital Center of Tirana "Mother Teresa", Albania



Robert Lluka, PhD, Pediatrician Division of Pediatric Intensive Care Unit, University Hospital Center of Tirana "Mother Teresa", Albania



Ermela Celaj, Pediatrician Division of Pediatric Intensive Care Unit, University Hospital Center of Tirana "Mother Teresa", Albania