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Review on Pompe Disease

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Abstract: *Pompe disease, also known as glycogen storage disease type II, is a rare genetic disorder caused by the deficiency of the enzyme acid alpha-glucosidase. This enzyme is essential for breaking down glycogen, a stored form of glucose, into glucose that the body can use for energy. In individuals with Pompe disease, the lack of this enzyme leads to the accumulation of glycogen in various tissues, particularly in the heart, skeletal muscles, and liver.The disease can manifest in different forms, primarily categorized into infantile-onset and late-onset types. Infantile-onset Pompe disease typically presents within the first few months of life, characterized by severe muscle weakness, respiratory difficulties, and heart enlargement (cardiomyopathy). If left untreated, it can lead to significant morbidity and mortality within the first year of life. Late-onset Pompe disease, which can occur from childhood to adulthood, tends to have a milder course, with symptoms including progressive muscle weakness and respiratory issues, but typically without the severe cardiac involvement seen in the infantile form.Diagnosis of Pompe disease is usually confirmed through enzyme assay testing and genetic testing to identify mutations in the GAA gene responsible for the enzyme deficiency. Treatment options include enzyme replacement therapy (ERT) with alglucosidase alfa, which can help improve muscle function and overall health in affected individuals. Early diagnosis and intervention are crucial for better outcomes in managing Pompe disease. Pompe disease is a serious genetic condition that affects glycogen metabolism, leading to significant health challenges, particularly in muscle and heart function, but can be managed with appropriate treatment strategies.*

Keywords*:* Pompe disease; GSD-II; GAA deficiency; Lysosomal disorder; Infantile-onset; Late-onset; Enzyme replacement therapy; Alglucosidase alfa; Gene therapy; AAV vectors; CRISPR; Glycogen accumulation; Muscle weakness; Cardiomyopathy; New treatments

I. INTRODUCTION

(GAA) enzyme, due to recessive mutations in the GAA gene, which leads to accumulation of lysosomal glycogen Pompe disease, also known as glycogen storage disease type II (GSD II) or acid maltase deficiency (AMD), is a genetic disorder caused by a defciency of the acid alpha-glucosidase. [1] P ompe disease is a rare autosomal recessive disorder caused by a deficiency of the lysosomal enzyme that degrades glycogen, acid -glucosidase (GAA). Glycogenosis type II (GSDII), or Pompe disease, is a rare autosomal recessive disease caused by a deficiency of the enzyme solely responsible for glycogen degradation within lysosomes: acid maltase or acid alpha-glucosidase (GAA). Over time, the progressive accumulation of glycogen alters cellular architecture, causing a loss of function and eventually necrosis. Although it has long been considered a disease that mainly affects striated muscular tissue with a disproportionate involvement of respiratory muscles, GSDII is multisystemic: glycogen accumulatesin all tissues and organs, particularly in the skeletal muscle, central nervous system, heart and brain (the latter are almost exclusively affected by the early-onset form of the disease), causing not only a reduction in motor function and important respiratory deficits, the main cause of death in patients with Pompe disease, but also arrhythmias, dysphagia, incontinence, gastrointestinal symptoms, several other problems.[2,3,4] Pompe disease, also known as glycogenosis type II, glycogen storage disease type II, or acid maltase deficiency is an autosomal recessive inherited disorder, which is progressively debilitating. In a

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considerable number of children, death occurs by cardiac and respiratory failure. A significant number of adult patients suffer from respiratory failure, too. This rare disorder has an estimated prevalence of 1 in 40,000. [5,6] Pompe disease is a rare autosomal recessive metabolic disorder, whereby mutations in the GAA gene lead to partial or total absence of the lysosomal enzyme acid α-glucosidase. The disease presents as a spectrum of phenotypes, ranging from a rapidly fatal phenotype in infants [7]

II. TYPES OF POMPE DISEASE

CLINICAL PHENOTYPES

1. Infantile Pompe Disease

seen in infants at diagnosis and may also be identified prenatally. Infantile-onset Pompe disease presents during the first few months of life with symptoms of hypotonia, generalized muscle weakness and hypertrophic cardiomyopathy. There is a high mortality rate by one year of age if untreated[8,9]. The dysfunctional left ventricle may be dilated as well as hypertrophied, and there can be underlying myocardial fibrosis detected by cardiac magnetic resonance imaging.[10] . Hypertrophy, predominantly affecting the left ventricular posterior wall and interventricular septum, is typically

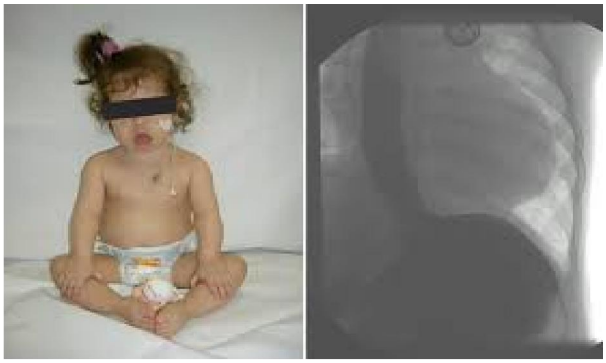

Figure 1

2. Late-Onset Pompe Disease

late-onset Pompe disease (LOPD) is often used to describe all patients with Pompe disease who do not have a typical infantile (cardiomyopathy) presentation.[11] The majority of patients with LOPD present with weakness beginning when they are adults, although the history of symptoms in some patients can be traced back to childhood and in some circumstances to less than one year of age.[12] . There have been estimates that the prevalence of late-onset Pompe disease is ~1:57,000, while for the infantile form it is ~1:138,000, but no studies have been performed in Canada.[13]

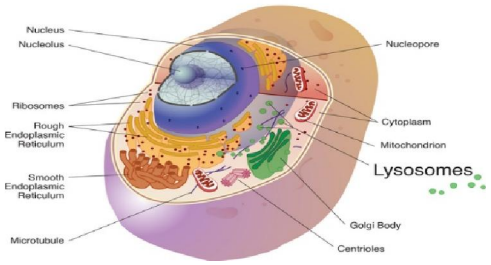

Figure 2

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3. Enzyme Replacement Therapy

ERT in Infants.

A breakthrough in treating LSDs came with the serendipitous discovery of the lysosomal enzyme secretion–reuptake pathway: Neufeld and colleagues demonstrated that cultured fibroblasts from patients with two different lysosomal storage disorders, Hunter and Hurler's disease, were able to correct each other [14,15]. Subsequent studies showed that secreted lysosomal enzymes can enter the endocytic pathway and reach lysosomes via the cation-independent-M6P receptors (CIMPR) on the cell surface [16]

Gene Therapy Strategies.

Initial studies using adeno- (Ad), adeno-associated viruses (AAV), and retroviruses demonstrated the feasibility of gene therapy for Pompe disease [17,18]. Systemic correction of muscle pathology in KO mice was achieved by hepatic targeting of a modified Ad-virus encoding human GAA [19]. However, it is important to note that such reactions have been controlled during clinical trial using Bcell depletion by the drug rituximab to reduce reactivity to both the AAV capsid and to the GAA transgene [20]. Researchers at Duke University developed such a strategy to enhance and potentially replace ERT. Systemic injection of a modified AAV8 vector containing liver-specific promoter (AAV2/8-LSPhGAA) induced immune tolerance to rhGAA and improved the efficacy of ERT in KO mice when administered at a low dosage of viral particles [21]. Preclinical studies have demonstrated that the secreted GAA is taken up by cardiac and skeletal muscles leading to glycogen reduction and improved muscle function [22,23]. A more recent preclinical study sought to optimize the liver-directed strategy by testing genetically engineered GAA transgenes (that were codon optimized and contained small deletions within the progene and modified secretion signals) for their ability to be expressed by hepatocytes and produce the highly secretable GAA protein [24]. Modification of a splice site using NHEJ has been done successfully to correct disease pathology in mdx mice, the animal model for Duchenne's muscular dystrophy [25,26]

III. PATHOGENESIS OF MUSCLE DAMAGE

The loss of muscle structure and muscle force have long been attributed to the progressive enlargement of glycogen-filled lysosomes in the intermyofibrillar space followed by lysosomal rupture, accumulation of cytoplasmic glycogen, and displacement of the myofibrils [43,44]. In retrospect, this view seems overly simplistic and inadequate because it does not take into consideration any of the secondary events that may occur as a result of accumulation of unmetabolized substrates in the lysosomes. Recently, it became abundantly clear that a number of pathogenic mechanisms, such as autophagy, calcium homeostasis, oxidative stress, and mitochondrial abnormalities, all contribute to tissue damage in Pompe disease as well as in other LSD

The morphological evidence for abnormal autophagy in muscle biopsies from adult Pompe disease patients was first reported by Dr. Engel [45]. However, this pathology and its contribution to the pathogenesis of the disease have largely been ignored. Later on, in preclinical trials, poor skeletal muscle response to ERT was, at least in part, linked to the presence of large areas of autophagic accumulation (autophagic buildup) reminiscent of those described by Engel in adult Pompe patients [46]. The extent of this pathology became clear when single muscle fibers were immunostained for LAMP1 (a marker for lysosomes) and LC3; the core of the fibers contained large areas composed of numerous autophagosomes, clustered late endosomes and lysosomes with broken borders, and autofluorescent material, as well as other cellular debris of unknown origin. In addition, the area is filled with undigested autophagic substrates, such as p62/SQSTM1 and potentially toxic ubiquitinated protein aggregates [47,48]. The presence of large pools of autophagic debris in skeletal muscle and the impact of this pathology on therapy warrant the classification of Pompe disease into a group of disorders known as autophagic myopathies [49]. Furthermore, it has been shown that the autophagic build-up affects the trafficking and delivery of the recombinant enzyme to the lysosome [50,51]. Thus, in Pompe disease, a profoundly disordered intracellular recycling system appears to be an important contributor to muscle weakness and incomplete response to treatment.

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IV. EPIDERMIOLOGY

The traditional estimate of incidence is around 1/40,000 overall [52,53], with about 3/4 of the cases as LOPD and 1/4 as IOPD. Incidence can vary widely among different ethnic groups and has historically been based on retrospective data from carrier frequencies. The populations that appear to be at higher risk include people of African American, Taiwanese, Dutch, and Israeli descent. However, now that newborn screening protocols are being put in place, we are getting more definitive incidence frequencies. Newborn screening (NBS) from California showed a birth prevalence of 1/25,200 [54]. NBS in Illinois, Pennsylvania, and Missouri have shown incidences of 1/23,596, 1/16,095, and 1/10,152 respectively [55,56]. Analysis of NBS data in Japan showed an overall incidence of ~ 1/37,000 from 2013 to 2020 [57]. Studies from Taiwan have shown birth prevalence rates of 574 Curry Treat Options Neurol (2022) 24:573–588 1/26,466 or 1/20,114 for LOPD and 1/67,047 for IOPD [57,58]. Overall, the incidences from these newer studies for Pompe disease are higher than the previously estimated 1/40,000 as above. For IOPD specifcally, the data has been quite variable. The screening data from Japan, California, Pennsylvania, and Illinois has shown IOPD incidence ranging from around 1/200,000 to 1/300,000 [59,60]. However, the incidence rates seen in Taiwan and Missouri are much higher at 1/67,047 and 1/46,700 respectively [61,62]. Further data collected with newborn screening in different parts of the world will be key in gaining a better understanding of the epidemiology of this disease. The new data does raise an interesting conundrum. If the incidence is indeed so much higher, it approximates the incidence of relatively more common neuromuscular disorders such as facioscapulohumeral muscular dystrophy (FSHD) (1 in 15,000) [63] and myotonic dystrophy (DM1) (1 in 8000) [64]. The prevalence of Pompe disease in the Neuromuscular Clinics or the Muscular Dystrophy Association (MDA) clinics is nowhere close to those of FSHD or DM1, which begs the question whether these patients with Pompe disease are misdiagnosed as other musculoskeletal disorders or whether not all mutations have the same penetrance and may not manifest disease

V. DIAGNOSIS OF POMPE DISEASE

Infantile-onset Pompe disease is usually recognized because of the unique and acute constellation of findings. However, precious time can be lost between onset of symptoms and consideration of a diagnosis of Pompe disease. Most infants survive only a few months beyond their diagnosis[,37]Because the disease progresses so rapidly, it is imperative that pediatricians and pediatric specialists become aware of possible signs and symptoms of Pompe disease and how to establish a differential diagnosis so that these infants can receive available therapy as soon as possible

Although the laboratory findings described here are important in establishing a differential diagnosis, GAA assay in muscle or skin fibroblasts remains the gold standard because it can render a definitive diagnosis of Pompe disease. Several diagnostic procedures that do not require tissue biopsy are in development, including measuring glucose oligosaccharides or the total concentration of GAA protein (precursor and mature forms) in urine, plasma, or blood spots.[38-40]

1. Blood Chemistry

Blood tests in infants and children should include a serum CK examination as an early step to determine whether more invasive testing is warranted, because CK elevation is a sensitive although very nonspecific marker for Pompe disease. The greatest elevation is usually found in infantileonset patients (as high as 2000 UI/L). Approximately 95% of late-onset patients have an elevated CK32; however, some adults with Pompe disease may have CK levels within the normal reference range. Serum enzymes such as aspartate aminotransferase, alanine aminotransferase, or lactate dehydrogenase may be elevated and may reflect enzymes released from muscle.[41]

2. Electromyography

Electromyography generally reveals a myopathic pattern in all patients with Pompe disease, although some muscles may appear normal in late-onset patients. Other common findings may include pseudomyotonic discharges (myotonic discharges without clinical myotonia), fibrillation potentials, positive sharp waves, and excess electrical irritability. Conduction times for motor and sensory nerves are usually normal.[42,]

3. Chest Imaging Studies

In many cases, a chest radiograph showing massive cardiomegaly provides the first clue that an infant may have Pompe disease. Beyond that, both echocardiography and electrocardiography are important tools in establishing a differential

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diagnosis of Pompe disease in infants and in determining the degree of cardiac involvement. Late-onset patients rarely ever display hypertrophy of the heart.

In infantile-onset patients, echocardiography may reveal thickening of both ventricles or the intraventricular septum or left ventricular outflow tract obstruction, whereas electrocardiography typically shows a shortening of the PR interval as well as very tall and broad QRS complexes. Late-onset patients (adult-onset presentation) have normal patterns.[43]

VI. TREATMENT OF POMPE DISEASE

1. Treatment of Cardiomyopathy

Cardiomyopathy in patients with Pompe disease should be treated cautiously and by a pediatric cardiologist who has experience with the disease. Each patient's care must be individualized and based on the stage of disease, because inappropriate use of the standard drugs used to treat cardiomyopathy can be very detrimental. Infants with Pompe disease in the earlier phases of the disease generally present with severe ventricular hypertrophy with or without left ventricular outflow tract obstruction. Left ventricular systolic function is normal or even hyperdynamic. Such patients anecdotally may benefit from the use of beta blockers if they have significant outflow tract obstruction. In this situation, the use of digoxin, other inotropes, diuretics, and afterload-reducing agents such as angiotensin converting enzyme inhibitors may exacerbate the left ventricular outflow tract obstruction. These agents, however, are generally used in the later phases of the disease, when the ventricle becomes dilated with poor systolic function.

2. Dietary Therapy

A high-protein, low-carbohydrate diet or, alternatively, a diet rich in L-alanine has shown benefit in some but not all patients with late-onset Pompe disease.4-6 Controlled studies of this treatment have not been performed. Patients who are extremely weak—especially infants—may require tube feeding. The early initiation of tube feeding in infants can greatly improve nutritional status as well as prevent aspiration of food.

3. Physical Therapy

Early intervention by occupational, physical, and speech therapists with experience in Pompe disease is paramount for infants with Pompe disease. Late-onset patients with lost mobility because of weakened muscles may benefit from a customized exercise or physical therapy program. Intervention is designed to optimize and preserve motor functions and functional independence and prevent or minimize secondary complications of the disease.

VII. CONCULSION

Overall, these preliminary results in infants suggest that the earlier enzyme replacement therapy is begun, the better the response. Other factors that could also affect outcome include stage of disease, genotype or presence of modifying genes or both, extent of muscle damage at start of therapy, and the immunologic status of the patient. The suggestion that early treatment in infantile-onset Pompe disease might be most beneficial, in addition to the fact that symptoms and diagnosis are made only months before death, raises the possibility that newborn screening may be valuable if the treatments are proven efficacious.

With enzyme replacement therapy likely to be available in the near future and other disease-specific therapies such as gene therapy in development, recognition and medical management of Pompe disease has assumed new importance. Thus, pediatricians and pediatric specialists need to be alert to the signs and symptoms of this life-threatening disease so that patients can be recognized early and treated as soon as possible.

REFERENCES

[1]. van der Ploeg AT, Reuser AJ. Pompe's disease. Lancet. 2008;372(9646):1342–53

[2]. Hirschhorn R, Reuser AJJ. Glycogen storage disease type II: acid -glucosidase (acid maltase) deficiency. In: Scriver C, Beaudet A, Sly W, Valle D, editors. The metabolic and molecular bases of inherited disease. 8th ed. New York: McGraw-Hill; 2001. p. 3389-420.

[3]. Kishnani PS, Berger KI, Carter GT, Case LE (2017) Late-onset Pompe disease presentation, diagnosis, and management. In: A CME monograph

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[4]. Wokke JHJ, Escolar DM, Pestronk A, Jaffe KM, Carter GT, van den Berg L, Florence JM, Mayhew J et al (2008) Clinical features of late-onset pompe disease: a prospective cohort study. Muscle Nerve.38(4):1236–1245.

[5]. Chan J, Desai AK, Kazi ZB, Corey K, Austin S, Hobson-Webb LD, Case LE, Jones HN et al (2017) The emerging phenotype of late-onset Pompe disease: a systematic literature review. Mol Genet Metab. 120(3):163–172.

[6]. Martiniuk F, Chen A, Mack A, et al. Carrier frequency for glycogen storage disease type II in New York and estimates of affected individuals born with the disease. Am J Med Genet 1998;79(1): 69–72.

[7]. Hirschhorn R, Huie ML. Frequency of mutations for glycogen storage disease type II in different populations: the delta525T and deltaexon 18 mutations are not generally ‘‘common’’ in white populations. J Med Genet 1999;36(1):85–6.

[8]. Kishnani PS, Howell RR. Pompe disease in infants and children. J Pediatr. 2004;144(Suppl 5):S35-43.

[9]. Kishnani PS, Hwu WL, Mandel H, Nicolino M, Yong F, Corzo D. A retrospective, multinational, multicenter study on the natural history of infantile-onset Pompe disease. J Pediatr. 2006;148(5): 671-6.

[10]. Barker PC, Pasquali SK, Darty S, Ing RJ, Li JS, Kim RJ, et al. Use of cardiac magnetic resonance imaging to evaluate cardiac structure, function and fibrosis in children with infantile Pompe disease on enzyme replacement therapy. Mol Genet Metab. 2010; 101(4):332-7

[11]. . Hamdan MA, El-Zoabi BA, Begam MA, Mirghani HM, Almalik MH. Antenatal diagnosis of Pompe disease by fetal echocardiography: impact on outcome after early initiation of enzyme replacement therapy. J Inherit Metab Dis. 2010;33(Suppl 3):S333-9.

[12]. Hagemans ML, Winkel LP, Hop WC, Reuser AJ, van Doorn PA, van der Ploeg AT. Disease severity in children and adults with Pompe disease related to age and disease duration. Neurology. 2005; 64(12):2139-41.

[13]. Hagemans ML, Winkel LP, van Doorn PA, Hop WJ, Loonen MC, Reuser AJ, et al. Clinical manifestation and natural course of late-onset Pompe’s disease in 54 Dutch patients. Brain. 2005; 128(Pt 3):671-7.

[14]. Ausems MG, Verbiest J, Hermans MP, Kroos MA, Beemer FA, Wokke JH, et al. Frequency of glycogen storage disease type II in The Netherlands: implications for diagnosis and genetic counselling. Eur J Hum Genet. 1999;7(6):713-6.

[15]. ratantoni JC, Hall CW, Neufeld EF. Hurler and Hunter syndromes: mutual correction of the defect in cultured fibroblasts. Science 1968;162(3853):570–572

[16]. Neufeld EF. From serendipity to therapy. Annu Rev Biochem 2011;80:1–15

[17]. Dahms NM, Lobel P, Kornfeld S. Mannose 6-phosphate receptors and lysosomal enzyme targeting. J Biol Chem. 1989;264(21): 12115–12118

[18]. Zaretsky JZ, Candotti F, Boerkoel C, et al. Retroviral transfer of acid alpha-glucosidase cDNA to enzyme-deficient myoblasts results in phenotypic spread of the genotypic correction by both secretion and fusion. Hum Gene Ther 1997;8(13):1555–1563.

[19]. . Pauly DF, Johns DC, Matelis LA, Lawrence JH, Byrne BJ, Kessler PD. Complete correction of acid alpha-glucosidase deficiency in Pompe disease fibroblasts in vitro, and lysosomally targeted expression in neonatal rat cardiac and skeletal muscle. Gene Ther 1998;5(4):473–480.

[20]. Amalfitano A, McVie-Wylie AJ, Hu H, et al. Systemic correction of the muscle disorder glycogen storage disease type II after hepatic targeting of a modified adenovirus vector encoding human acid-alpha-glucosidase. Proc Natl Acad Sci U S A 1999;96(16): 8861–8866.

[21]. Fraites TJ, Jr, Schleissing MR, Shanely RA, et al. Correction of the enzymatic and functional deficits in a model of Pompe disease using adeno-associated virus vectors. Mol Ther 2002;5(5 Pt 1): 571–578

[22]. Amalfitano A, McVie-Wylie AJ, Hu H, et al. Systemic correction of the muscle disorder glycogen storage disease type II after hepatic targeting of a modified adenovirus vector encoding human acid-alpha-glucosidase. Proc Natl Acad Sci U S A 1999;96(16): 8861–8866.

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[23]. Corti M, Elder M, Falk D, et al. B-cell depletion is protective against anti-AAV capsid immune response: a human subject case study. Mol Ther Methods Clin Dev 2014;1

[24]. Sun B, Kulis MD, Young SP, et al. Immunomodulatory gene therapy prevents antibody formation and lethal hypersensitivity reactions in murine pompe disease. Mol Ther 2010;18(2):353–360.

[25]. Bond JE, Kishnani PS, Koeberl DD. Immunomodulatory, liver depot gene therapy for Pompe disease. Cell Immunol 2017.

[26]. Puzzo F, Colella P, Biferi MG, et al. Rescue of Pompe disease in mice by AAV-mediated liver delivery of secretable acid alphaglucosidase. Sci Transl Med. 2017;9(418).

[27]. Long C, Amoasii L, Mireault AA, et al. Postnatal genome editing partially restores dystrophin expression in a mouse model of muscular dystrophy. Science 2016;351(6271):400–403.

[28]. Bengtsson NE, Hall JK, Odom GL, et al. Muscle-specific CRISPR/Cas9 dystrophin gene editing ameliorates pathophysiology in a mouse model for Duchenne muscular dystrophy. Nat Commun 2017;8:14454

[29]. Hirschhorn R, Reuser AJJ. Glycogen storage disease type II; acid -glucosidase (acid maltase) deficiency. In: Scriver CR, Beaudet AL, Sly W, Valle D, eds. The metabolic and molecular bases of inherited disease. 8th ed. New York: McGraw-Hill, 2001:3389 –3420.

[30]. Van den Hout H, Reuser AJ, Vulto AG, Loonen MC, Cromme-Dijkhuis A, Van der Ploeg AT. Recombinant human alpha-glucosidase from rabbit milk in Pompe patients. Lancet 2000;356:397–398.

[31]. Klinge L, Straub V, Neudorf U, et al. Safety and efficacy of recombinant acid alpha-glucosidase (rhGAA) in patients with classical infantile Pompe disease: results of a phase II clinical trial. Neuromusc Disord 2005;15:24 –31.

[32]. Kuo WL, Hirschhorn R, Huie ML, Hirschhorn K. Localization and ordering of acid alpha-glucosidase (GAA) and thymidine kinase (TK1) by fluorescence in situ hybridization. Hum Genet 1996;97(3):404–406.

[33]. Tsuburaya RS, Monma K, Oya Y, et al. Acid phosphatase-positive globular inclusions is a good diagnostic marker for two patients with adult-onset Pompe disease lacking disease specific pathology. Neuromuscul Disord 2012;22(5):389–393.

[34]. Feeney EJ, Austin S, Chien YH, et al. The value of muscle biopsies in Pompe disease: identifying lipofuscin inclusions in juvenile- and adult-onset patients. Acta Neuropathologica Communications 2014;2(1):2–17.

[35]. Burton BK, Kronn DF, Hwu WL, Kishnani PS, Pompe Disease Newborn Screening Working G. The Initial Evaluation of Patients After Positive Newborn Screening: Recommended Algorithms Leading to a Confirmed Diagnosis of Pompe Disease. Pediatrics 2017;140(Suppl 1):S14-S23.

[36]. Griffin JL. Infantile acid maltase deficiency. I. Muscle fiber destruction after lysosomal rupture4. Virchows Arch Cell Pathol Mol Pathol 1984;45(1):23–36

[37]. Chan J, Desai AK, Kazi ZB, et al. The emerging phenotype of late-onset Pompe disease: A systematic literature review. Mol Genet Metab 2017;120(3):163–172.

[38]. Thurberg BL, Lynch MC, Vaccaro C, et al. Characterization of pre- and post-treatment pathology after enzyme replacement therapy for pompe disease. Lab Investig 2006;86(12):1208–1220.

[39]. Lieberman AP, Puertollano R, Raben N, Slaugenhaupt S, Walkley SU, Ballabio A. Autophagy in lysosomal storage disorders. Autophagy 2012;8(5):719–730.

[40]. Cori GT. [Enzymes and glycogen structure in glycogenosis]. Osterreichische Zeitschrift fur Kinderheilkunde und Kinderfursorge 1954;10(1–2):38–42

[41]. Hers HG. Alpha-glucosidase deficiency in generalize glycogen storage disease (Pompe's disease). Biochem J 1963;86:11

[42]. in JL. Infantile acid maltase deficiency. I. Muscle fiber destruction after lysosomal rupture4. Virchows Arch Cell Pathol Mol Pathol 1984;45(1):23–36