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Acid maltase deficiency--Pompe's disease

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Case Report

Acid Maltase Deficiency — Pompe's Disease

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Abstract

Mutation in genes encoding for proteins involved in glycogen synthesis, degradation or regulation results in various inborn errors of glycogen metabolism. The disorders that result in abnormal storage of glycogen are known as glycogen storage diseases (GSD).We report a rare and interesting case of a young boy who presented with generalized weakness and reduced muscle bulk since childhood. He was diagnosed to have acid maltase deficiency, also known as Pompe's disease, one of the rare types of glycogen storage disease. The case is presented here in the form of a case study, including a review of the pertinent literature on the subject. This case has the potential to be the first reported case of such a disease from Pakistan (to the best of our knowledge).

Keywords: Glycogen Storage disease Type II, Pompe's disease, Acid Maltase deficiency.

Introduction

Pompe's disease, which is also known as acid maltase deficiency, is a glycogen storage disease type II. It is an autosomal recessive lysosomal storage disorder characterized by acid alpha-glucosidase deficiency. This deficiency results from mutations in the encoding gene (GAA). Acid alpha-glucosidase is an enzyme required to hydrolyze lysosomal glycogen to glucose. Glycogen is the stored form of glucose and serves as a buffer for glucose needs. It is composed of long polymers of a 1-4 linked glucose, interrupted by a 1-6 linked branch point every four to ten residues.

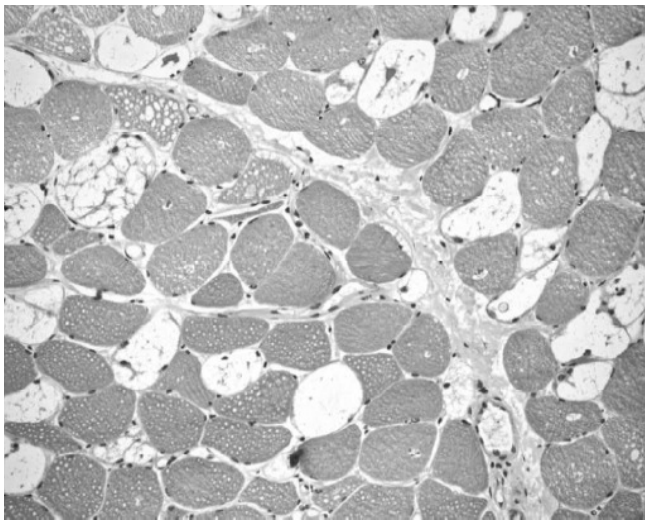
The clinical manifestations are characterized by progressive skeletal muscle weakness affecting motor and respiratory functions and is typical for both adult and infantile forms of Glycogen storage disease type II (GSD II).[1]

Overall disease frequency was reported as 1 in 40,000 in one study with an incidence of 1 in 38,000 for infantile GSD II and 1 in 57,000 for adult GSD II.[2,3]

Case Report

An 18 years old boy presented to the out-clinic in March 2005 with weight loss and progressively increasing weakness for the past eleven years. He further complained to experience episodes of feeling of suffocation and palpitations on exertion. His family history was significant, with known similar illnesses in his uncles, aunties and cousins. All of them died at ages between 20 and 25 years. His family history was positive for diabetes mellitus. He also gave history of consanguineous marriages in the family.

On examination his blood pressure was 110/80mmHg, heart rate was110 per minute regular and respiratory rate was 22 breaths per minute. His weight and height were 36.7 kilogram and 165 centimeters, respectively. His Body Mass Index (BMI) was 13.5. On general examination he was pale, thin looking with uniformly decreased muscle mass, however, he was oriented to time,



Figure=1: On H&E multiple bundles of skeletal muscle fibers are seen exhibiting extensive vacuolization.

place and person. His recent and remote memory was also intact. His jugular venous pressure was raised but there was no pedal oedema. His abdominal, respiratory and cardiovascular examinations were unremarkable except a loud second heart sound was heard at the cardiac apex. On musculoskeletal examination the muscle bulk was significantly reduced all over the body, although the power, tone and deep tendon reflexes were normal. Investigations revealed normal complete blood count, serum creatinine, serum electrolytes, calcium, phosphorous and alkaline phosphatase. His serum aminotransferase levels were mildly raised and serum aldolase level was elevated to 25.4 U/L (0.1-7.6), creatine-phospho-kinase (CPK) level was also raised at 1179 IU/L (males17-176) and lactate dehydrogenase

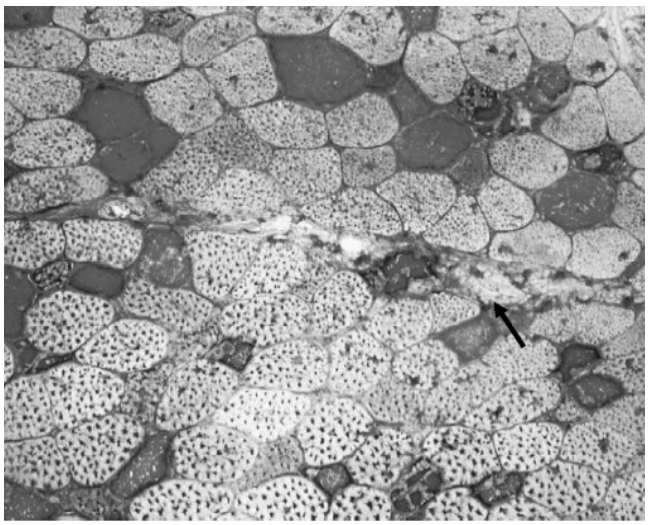


Figure-2: On GOMORI trichrome mild increase in fibrosis is noticed and special stains for glycogen (PAS) are strongly positive.

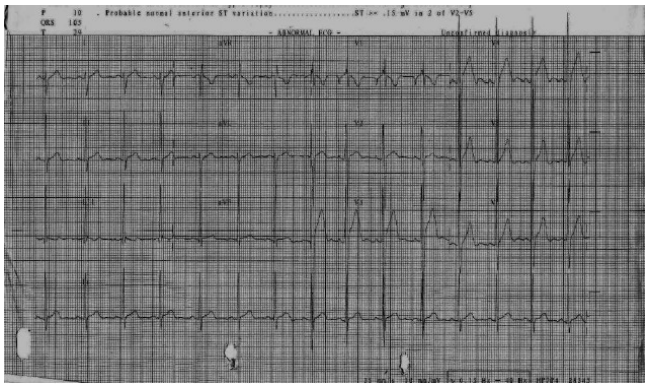


Figure-3:Electrocardiogram showing large voltage left Ventricular QRS complexes.

level (LDH) was 1205 IU/L (males153-548). The random blood sugar, thyroid function tests and serum albumin were normal. His electrocardiogram showed left ventricular hypertrophy by voltage criteria, as shown in Figure-3, however echocardiogram revealed normal left ventricular systolic functions with no significant left ventricular hypertrophy. The Chest X-Ray was normal except showing scoliotic deformity of dorsal spine, whereas X-Ray of the hands revealed bone age of 18 years but there was no evidence of rickets. In order to rule out muscular dystrophy, EMG/NC (electromyography/nerve conduction) study was done, which showed diffuse irritable myopathic process consistent with muscle dystrophy. Muscle biopsy was suggested. The muscle biopsy was taken from the left biceps and the findings were consistent with Glycogen storage disease type II (Figure-1,2)

Discussion

Pompe's disease is an autosomal recessive disorder characterized by deficiency of acid alpha-glucosidase resulting in intra-lysosomal accumulation of glycogen and leading to progressive muscle dysfunction. The natural history of infantile-onset Pompe disease is characterized by Hypertrophic cardiomyopathy and profound generalized weakness presenting in the first few months of life, with rapid progression and death usually occurring by one year of age. Late-onset Pompe's disease is characterized by onset of symptoms after one year of age, less severe or absence of cardiac involvement and slower progression, with symptoms primarily related to progressive dysfunction of skeletal muscles and respiratory muscle involvement.[4] Our patient had a late onset disease as he presented at the age of 18 years with an 11 years history of progressive skeletal muscle weakness, however there was no significant respiratory muscle involvement. Recent clinical trials of enzyme replacement therapy have begun to allow greater opportunity for potential improvement in motor status, function, and survival than ever before, with hopes of moving toward maximizing physical

function for individuals with Pompe's disease. Children generally live longer, with some achieving independent sitting, creeping, and walking-milestones typically never achieved in the untreated natural history of the disorder.[4]

Electrocardiogram (ECG) abnormalities are universal in infantile Pompe's disease. Hallmarks of this disease include a shortened PR interval, an increased QT dispersion (QTd), and large left ventricular (LV) voltages, as seen in Figure-3.[5]

Our patient had increased left ventricular voltage on electrocardiography; however his echocardiogram did not show evidence of left ventricular hypertrophy. Adult-onset glycogen storage disease type II (GSD II) is a progressive disabling myopathy. At present there is no treatment of proven clinical efficacy. Enzyme replacement therapy may in the future provide benefit but it will be costly and is not yet freely available.[6] There is some data which supports that a high-protein diet may be helpful in adult-onset disease.[7,8]

In both childhood and adult cases that progress to respiratory failure, mechanical ventilation is usually necessary. Noninvasive ventilation during sleep may improve nighttime hypoxaemia and daytime hypercapnia in some adult-onset patients.[9]

Conclusion

Pompe's disease is an extremely rare, inherited disorder of glycogen metabolism. It causes progressive muscle weakness leading to death either because of respiratory or cardiac muscle involvement. We report the first case (to the best of our knowledge) of late onset glycogen storage disease type II from Pakistan.

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