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A Case of Glycogen Storage Disease: A Case Report and Review of Literature

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Abstract: Glycogen is the principal storage form of glucose in muscle and liver. Enzyme deficiencies lead to glycogen accumulation in liver, skeletal muscle, and heart. There are eleven subtypes of disease that are commonly included under the group of glycogen storage diseases. Here we report a case of glycogen storage disease in 7 year old male child.
Keywords: Glycogen storage disease, Enzyme deficiency

INTRODUCTION

Glycogen storage diseases (GSD) are inborn errors of metabolism caused by various enzymes deficiencies which regulate the synthesis and degradation of glycogen [1]. Glycogen is a principal storage molecule of glucose in our body which is stored in muscle and liver tissue mainly [2]. The clinical manifestations of these diseases are due to hypoglycemia and excessive accumulation of glycogen in different organs [3]. Depending on the type of enzyme deficiency and tissues affected, glycogen storage diseases are classified into subtypes [4].

CASE REPORT

A 7 year old male child presented to the pediatrics outpatient department with complaints of easy fatigability and abdominal distension for past 6 months. He had dysmorphic facial features.

Fig. 1: Seven year old male with dysmorphic face

There was no history of jaundice, convulsions or significant family history. He had normal language and psychomotor development. On clinical examination, non-tender hepatomegaly was palpated 2 cm below the right costal margin.

Complete hemogram revealed anaemia (hemoglobin - 6.1gm/dl) with normal total leucocyte and platelet counts. Coagulation profile was within normal limits. Serology for hepatitis B was negative. Liver function tests revealed total bilirubin of 0.3 mg/dl, total protein of 7.5 g/dl with albumin 4.7 g/dl, alkaline phosphate 65 IU/L, SGOT 70 IU/L, SGPT 60 IU/L. Hypoglycemia with a serum glucose level of 31 mg/dl was detected.

No abnormality was observed in ECG and chest radiograph. Ultrasonography of the abdomen confirmed marked hepatomegaly with mild coarse echotexture of liver. Spleen and kidneys were of normal size, shape and echotexture. Liver biopsy showed effaced liver architexture with regenerating nodules.

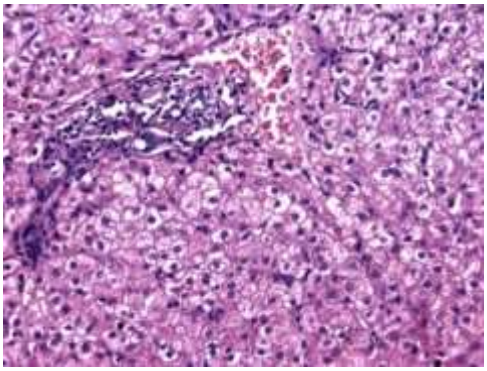

Fig. 2: Photomicrograph showing effaced architecture (H&E, 200X)

The hepatocytes contained eosinophillic PAS positive material.

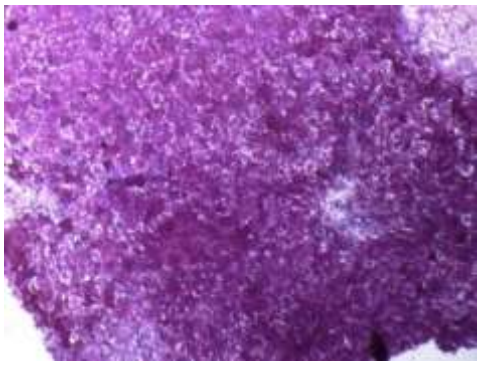

Fig. 3: Photomicrograph showing eosinophillic PAS positive material in hepatocytes (H&E, 100X)

These features were compatible with glycogen storage disease with early changes of cirrhosis. Due to lack of facilities for enzymatic studies in our hospital, it was rather difficult to precisely categorize our patient into subtype of GSD.

DISCUSSION

Liver and muscle store glucose in our body in the form of glycogen [2]. Various enzymes are involved in metabolism of glycogen to release glucose from these tissues. Due to the specific enzyme deficiency, glycogen remains accumulated in liver, skeletal muscle, and heart and interferes with the normal functions of these organs. Based on the type of enzyme deficiency and tissues affected, Glycogen storage diseases (GSD) are classified into subtypes [5]. Some of them are discussed below.

Von Gierke disease (GSDI)

Glucose-6-phosphatase (G6Pase) breaks down the glucose-6-phosphate (G6P) and releases a phosphate group and glucose molecule in the blood stream. This enzyme is present in liver and kidney but is absent in muscle. Glucose-6-phosphatase is an enzyme located on endoplasmic reticulum within the cell, deficiency of which GSDI [5].

The gene encoding G6Pase (G6PC) is located on chromosome 17q21 [5, 6] and gene encoding the G6P transporter (G6PT) is located on Chromosome 11q23 [5, 7]. Depending on type and site of mutation in gene, GSDI is divided into three subtypes- Ia, Ib and Ic. The major types are Ia and Ib [8, 9]

Principal manifestations of this disease are hepatomegaly, hypoglycemia, lactic acidosis, hyperuricemia and hypertriglyceridemia [5, 10]. Liver and kidney functions tests, biochemical tests for estimating serum levels of sugar, lipid, uric acid and lactic acid are required to support the diagnosis. Radiological imaging especially ultrasound abdomen is used to evaluate liver span and renal size. Histological confirmation of glycogen accumulation in hepatocytes in liver biopsy is diagnostic along with estimation of functional levels of Glucose-6-phosphatase [11].

Acid maltase deficiency or Pompe disease (GSD II)

GSDII is an autosomal recessive disorder due to deficiency of lysosomal α-glucosidase (acid maltase) enzyme. Here, Glycogen accumulates in the lysosome of tissues especially muscle and heart. It causes progressive muscle weakness and affects various body tissues, particularly heart, skeletal muscles and nervous system [5].

Depending on the onset of disease, it is divided into infantile and late onsent forms [12]. Infantile form is characterized by cardiomyopathy, cardiomegaly, hypotonia, generalized muscle weakness and respiratory difficulties. In late onsent form juvenile and adult-onset) is characterized by proximal muscle weakness and respiratory insufficiency; cardiac involvement is absent. Biochemical tests reveal increased serum creatine kinase levels. Organ involvements are identified on chest X-ray and echocardiogram [13].

Cori or Forbes disease (GSD III)

This autosomal recessive disorder is due to deficiency of amylo-1,6-glucosidase enzyme which is debranching enzyme. This debranching enzyme defect leads to excess glycogen accumulation in the liver and muscles. Chromosome 1p21 contains the gene for this enzyme [5]. It is characterized by variable liver, cardiac muscle, and skeletal muscle involvement [14]. There are four subtypes of GSD type III on the basis of differences in tissue expression of the deficient enzyme. i.e., IIIa, IIIb, IIIc and IIIc [15].

Clinical manifestations include ketotic hypoglycemia, hepatomegaly, hyperlipidemia, elevated hepatic transaminases, Hepatomegaly, firm and enlarged liver in infancy and early childhood. Cardiomyopathy appears in childhood GSDIII. Lliver manifestations become less prominent in adolescence and adulthood. Hepatic cirrhosis and adenomas are observed in fewer patients. Marked Hypertrophic cardiomyopathy is seen in GSDIIIa patients. GSD III may be indistinguishable from GSD I in infancy, differential diagnosis can be done to differentiate between them. Management includes liver ultrasound examination, Baseline electrocardiogram and echocardiogram and Medical genetics consultation [14].

Andersen disease (GSDIV)

Andersen disease or GSDIV occurs due to deficiency of glycogen branching enzyme, amylo-1,4-1,6 transglucosidase. This disease is also known by various different names such as Polyglucosan body

disease, or amylopectinosis. It is an autosomal recessive disorder [5]. This leads to accumulation of amylopectin-like compact fewer branched glycogen molecules in liver [16]. The gene responsible for causing GSDIV is GBE1 [17].

Its sub types include Fatal perinatal neuromuscular subtype, Congenital neuromuscular subtype, Classic (progressive) hepatic subtype, Non-progressive hepatic subtype, Childhood neuromuscular subtype. Clinical manifestations vary according to different subtypes with variable ages of onset, severity, and clinical features. Hepatomegaly, liver dysfunction, progressive liver cirrhosis are seen in Classic (progressive) hepatic subtype. Failure to thrive, hepatomegaly, liver dysfunction, progressive liver cirrhosis. Clinical menifestations of non-progressive hepatic subtype includes liver dysfunction, myopathy, and hypotonia in childhood. Diagnosis is done by confirming glycogen branching enzyme (GBE) deficiency in liver, muscle, or skin fibroblasts. Diagnosis can also be done by the identification of biallelic mutations in GBE1 [17].

McArdel disease (GSD V)

It is an autosomal recessive disorder that occurs due to muscle phosphorylase deficiency. Glycogen phosphorylase breaks down the glycogen and produces glucose-1-phosphate which is further converted into glucose-6-phosphate by the enzyme phosphoglucomutase. Three isoforms of glycogen phosphorylase are identified in different tissues: brain/heart, muscle, and liver. Due to deficiency of myophosphorylase, glycogen accumulates in muscles (GSDV). Gene PYGM for this enzyme is identified on chromosome 11q13 [5].

It is characterized by exercise intolerance manifested by rapid fatigue, myalgia, and cramps in exercising muscles. It diagnosed by clinical findings, cycle test and laboratory findings such as increased resting serum creatine kinase activity and no change in plasma lactate concentration). Confirmation of the diagnosis is done by molecular genetic testing of PYGM [18].

Hers disease (GSD VI)

Glycogen storage disease type VI (GSDVI) is also known as Hers disease. It is an autosomal recessive disorder due to the liver glycogen phosphorylase enzyme deficiency. Gene for this enzyme (PYGL) is located on 14q21 [5].

Patients present with hepatomegaly, growth retardation, ketotic hypoglycemia. Diagnosis can be done by the assay of hepatic glycogen phosphorylase enzyme activity, but molecular genetic testing of PYGL the preferred method of diagnosis [19].

Traui's disease (GSD VII)

GSDVII is also known as phosphofructokinase (PFK) deficiency and Traui's disease [5]. Mutations in the PFKM gene cause GSDVII [20]. Deficiency of the M subunit (PFKM) of this enzyme impairs the ability of erythrocytes and rhabdomyocytes to use carbohydrates for energy [21].

It is characterized clinically by exercise intolerance, muscle cramping, exertional myopathy, and compensated hemolysis. Myoglobinuria may also occur [22].

PhK Deficiency (GSD IX)

Glycogen storage disease type IX is caused by deficiency of Phosphorylase Kinase (PHK) enzyme. Based on clinical presentation and mode of inheritance, GSD IX has been classified into six subtypes that include X-linked liver glycogenosis (GSD IXa), combined liver and muscle PHK deficiency (GSD IXb), autosomal liver PHK deficiency (GSD IXc), X-linked muscle glycogenosis (GSD IXd), autosomal muscle PHK deficiency (GSD IXe) and [6] heart PHK deficiency (GSD IXf) [5].

Liver PhK deficiency is characterized by hepatomegaly, growth retardation, and often fasting ketosis and hypoglycemia. Muscle PhK deficiency is rarer that is characterized by exercise intolerance, myalgia, muscle cramps, myoglobinuria, and progressive muscle weakness. Diagnosis is done byon clinical findings and confirmed by assay of PhK activity [24].

CONCLUSION

Glycogen storage diseases must be a part of differential diagnoses in young children presenting with hepatomegaly for early diagnosis, treatment and prevention of complications.

REFERENCES

1. Raghavan VA; Glucose-6-phosphatase deficiency. Medscape. Available from http://emedicine.medscape.com/article/119184-overview
2. Glycogen Metabolism. Available from http://themedicalbiochemistrypage.org/glycogen.php
3. Chen YT, Kishnani PS, Koeberl D; Glycogen storage diseases. Available from http://ommbid.mhmedical.com/content.aspx?bookid=971&sectionid=62672129&jumpsectionID=62672143
4. Hicks J, Wartchow EP, Mierau G; Glycogen storage diseases: a brief review and update on clinical features, genetic abnormalities, pathologic features, and treatment.

Ultrastructural Pathology, 2011; 35(5): 183-196.
5. Gholami S, Sadr-Nabavi A; Genetic and glycogen storage disease. Zahedan J Res Med Sci., 2013; 15(10): 7-11.
6. Matern D1, Seydewitz HH, Bali D, Lang C, Chen YT; Glycogen storage disease type I: Diagnosis and phenotype/genotype correlation. Eur J Pediatr., 2002; 161(Suppl 1): S10-9.
7. Bahreyni-Toossi MT, Fardid R, Rezaee A, Sadr-nabavi A, Rafatpanah H, Bolbolian M; Expression of apoptotic genes can distinguish radiation workers from normal population. Int J Low Radiat., 2011; 8(5/6): 388-399.
8. Chen YT; Glycogen storage diseases. In Scriver CR, Beaudet AL, Sly WS, Valle D, Vogelstein B editors; The metabolic and molecular bases of inherited disease. 8th edition, NY: McGraw-Hill, New York, 2001:1521-1551
9. Chen YT; Glycogen storage disease and other inherited disorders of carbohydrate metabolism. In Kasper DL, Braunwald E, Fauci A, Hauser S, Jameson J editors; Harrison's Principles of Internal Medicine. 16th edition, NY: McGraw-Hill, New York, 2004.
10. Chou JY, Matern D, Mansfield BC, Chen YT; Type I glycogen storage diseases: disorders of the glucose-6- phosphatase complex. Curr Mol Med., 2002; 2(2): 121-143.
11. Bali DS, Chen YT, Goldstein JL; Glycogen storage disease type I. Gene Reviews. Available from http://www.ncbi.nlm.nih.gov/books/NBK1312/
12. Type II Glycogen Storage Disease. Available from http://www.agsdus.org/html/typeiigsd.html
13. Leslie N, Tinkle BT; Glycogen Storage Disease Type II (Pompe Disease). Gene reviews. Available from http://www.ncbi.nlm.nih.gov/books/NBK1261/
14. Dagli A, Sentner CP, Weinstein DA; Glycogen Storage Disease Type III. Available from http://www.ncbi.nlm.nih.gov/books/NBK26372/
15. Endo Y, Horinishi A, Vorgerd M, Aoyama Y, Ebara T, Murase T *et al.*; Molecular analysis of the AGL gene: heterogeneity of mutations in patients with glycogen storage disease type III from Germany, Canada, Afghanistan, Iran, and Turkey. J Hum Genet., 2006; 51(11): 958–963.
16. Talente GM, Coleman RA, Alter C, Baker L, Brown BI, Cannon RA *et al.*; Glycogen storage disease in adults. Ann Int Med., 1994; 120(3): 218-226.
17. Magoulas PL, MS, El-Hattab AW; Glycogen storage disease type IV. Gene reviews. Available from http://www.ncbi.nlm.nih.gov/books/NBK115333/
18. Martín MA, Lucía A, Arenas J, Andreu AL; Glycogen storage disease type V. Available from http://www.ncbi.nlm.nih.gov/books/NBK1344/
19. Aditi I Dagli, MD and David A Weinstein; Glycogen Storage Disease Type VI. Gene Reviews. Availavle from http://www.ncbi.nlm.nih.gov/books/NBK5941/
20. Glycogen storage disease type VII. Available from http://ghr.nlm.nih.gov/condition/glycogen-storage-disease-type-vii
21. Phosphofructokinase deficiency. Available from http://en.wikipedia.org/wiki/Phosphofructokinase_deficiency
22. Muscle phosphofructokinase deficiency. Available from http://www.omim.org/entry/232800
23. Goldstein J, Austin S, Kishnani P, Bali D; Phosphorylase kinase deficiency. Gene reviews. Available from http://www.ncbi.nlm.nih.gov/books/NBK55061/