Case Report

Isolated hepatomegaly became Her's – a case report

Abstract

Glycogen storage diseases (GSDs) are a group of inherited metabolic disorders caused by mutations in one of the several enzymes involved in glycogen synthesis or breakdown. GSD VI is caused by mutations of PYGL gene encoding hepatic glycogen phosphorylase on chromosome 14q22.1, which has a major role in glycogen metabolism. We report a case of 2year old girl child presented with complaints of slowly progressive abdominal distention of one year duration. Abdominal examination revealed hepatomegaly (liver span 9cm). Lab investigations revealed mild anemia, hypertriglyceridemia and normal liver function. Liver biopsy showed marked elevation of glycogen content in liver with structurally normal glycogen which was consistent with GSD. Sanger sequencing done to identify the subtype of GSD showed PYGL gene mutation, pathogenic variant of type-VIGSD. In the case of isolated hepatomegaly, a glycogen storage disease must be considered in the differential diagnosis and Sanger sequencing must be done for confirmation and prognostication.

Keywords: hepatomegaly, Her's disease, glycogen storage disorder, PYGL mutation

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Introduction

Glycogen storage diseases (GSDs) are a group of inherited metabolic disorders caused by mutations in one of the several enzymes involved in glycogen synthesis or breakdown[1]. GSDs are divided into two groups: those with hepatic involvement, which causes hypoglycemia, and those with neuromuscular illness and paralysis, which causes paralysis.[1] There are over 12 types and they are classified based on the enzyme deficiency and the affected tissue.

GSD VI or Her's disease is caused by mutations of PYGL gene encoding hepatic glycogen phosphorylase on chromosome 14q22.1, which has a major role in glycogen metabolism.[2] It has an incidence of 1 in 60,000-80,000 live births and rarer than other GSDs.[3] Hepatomegaly, Short stature, raised transaminases, ketotic hypoglycemia, hyperlipedemia, low pre-albuumin level are the common clinical manifestations.[2] It is usually a mild disease, that begin from infancy or childhood. Most of them became asymptomatic with a sequalae of hepatic fibrosis but hardly a few may develop cirrhosis and cardiomyopathy.[2] Here we report a child who presented with abdominal distension and diagnosis was made through liver biopsy and mutation studies.

Case report

2 years old girl, first born to non-consanguineous parents, who had a smooth transition at birth and developmentally normal child presented with complaints of slowly progressive abdominal distention of one year duration. No history of vomiting, recurrent respiratory infections, seizures, muscle weakness, gait abnormalities, jaundice. On examination she has pallor but no clubbing, edema, cyanosis, or significant lymphadenopathy. Her anthropometry (weight- 11kg; Height- 87cm; Wt x Ht- 2 to-1 Zscore; OFC-48cm) was adequate for age. She had a respiratory rate of 26/min, Heart rate – 96/minute, SpO_2 – 98% at room air, BP- 100/60mm Hg, CRT<2 seconds. Head to toe examination was normal. Abdominal examination revealed there was distention, soft, hepatomegaly (liver span 9cm) non-tender, smooth surface, soft in consistency, regular margin. spleen was not palpable. Other systemic examination was unremarkable. Differential diagnosis considered –Chronic liver disease –Metabolic, chronic viral hepatitis and storage disorders. Laboratory investigation showed normal Liver function test (SGOT-48U/L, SGPT-30U/L, ALP-237U/L, total protein-6.3g/dl, S.albumin-3.9g/dl), hemogram showed mild anemia (Hb-9.9g/dl,TLC-10110cells/cu.mm) and peripheral smear study was normal, deranged lipid profile (Total cholesterol: 191mg/dl, Triglycerides: 641mg/dl, HDL: 18mg/dl, LDL: 108mg/dl). Renal function, thyroid profile, ammonia, lactate, fasting blood glucose, urine ketones, inflammatory markers (CRP,ESR) were within normal limits. Ophthalmological screening had no evidence of cataract/ cherry red spots. TB workup and hepatitis viral markers were negative. To rule out storage disease, Liver biopsy was performed which showed pale, enlarged hepatocytes with thickened borders containing glycogen, focal porto-portal bridging and spotty necrosis noted which suggestive of Glycogen storage disease (Figure 1). Sanger sequencing was done to identify the subtype of GSD which showed PYGL gene mutation, pathogenic variant (c.1620+1 G>C) of type-VI GSD (Figure 2).

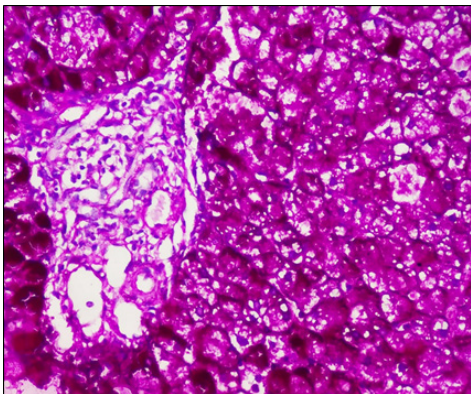
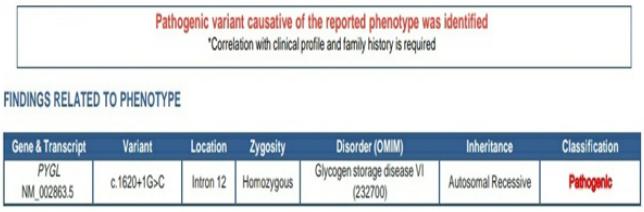


Figure 1 Enlarged hepatocytes loaded with glycogen, PAS, X 40.



Pathogenic variant causative of the reported phenotype was identified
*Correlation with clinical profile and family history is required

FINDINGS RELATED TO PHENOTYPE

Gene & Transcript	Variant	Location	Zygosity	Disorder (OMIM)	Inheritance	Classification
PYGL NM_002863.5	c.1620+1G>C	Intron 12	Homozygous	Glycogen storage disease VI (232700)	Autosomal Recessive	Pathogenic

Figure 2 Sanger sequencing.

Discussion

Glycogen storage disease type VI (formerly known as Her's disease) is an rare autosomal recessive disease.[4] PYGL is the only gene known to be associated with GSD VI.[4,5] First reported case in 1959.[6] Children with GSD-VI show signs of growth retardation,hepatomegaly,[6] failure to thrive in most of the cases.5% of these children can have mild hypoglycemia, as opposed to the more severe variant of GSDs.[7] But our child had hepatomegaly with normal weight and height, without hypoglycemia. Heart and muscle are usually normal in children with Her's disease. Development also will be normal in all children[7]. Development assessment and 2D Echocardiography of our child also was normal.

Roscher et al., reported that 86-90% of children with GSD VI will have elevated transaminases, Butour child had normal transaminases.[8] Hypertriglyceridemia and hypercholesterolemia in 67 and 76% of GSD VI children in Canada.Our child also had hypertriglyceridemia. Liver biopsy reveals hepatic fibrosis but not cirrhosis.[2] It can be confused with GSD III and IX[2]. Despite the presence of significant hepatomegaly, the patient is essentially asymptomatic in the absence of hypoglycemia.[3] Marked elevation of glycogen content in liver with structurally normal glycogen is consistent with GSD VI.[9] Our child also had enlarged hepatocytes containing glycogen. Genetic studies and mutation analysis not only help to confirm the diagnosis and also in prognostication, genetic counselling and prenatal diagnosis. There are around 40 different mutations reported world-wide. The mutation analysis of our study revealed PYGL gene mutation, a pathogenic variant GSD-VI that is hardly reported.

Uncooked starch and refined starch remain the mainstay of treatment. The Prognosis is usually good[7]. Around 90% will not have improvement in hepatomegaly.[7] Adenoma and carcinoma may develop for a few children with GSD VI[7]. Hence frequent follow up is recommended.

Conclusion

Glycogen storage disorder must be considered in the differential diagnosis for a clinical presentation of isolated hepatomegaly. Mutation analyses are required to confirm the subtype of GSDs and also for prognostication.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's mother has given her consent for their daughter's clinical information to be reported in the journal. The patient's mother understand that their daughter's name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Since it is a case report, Ethics committee has not been taken.

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Conflicts of interest

There is no conflicts of interest.

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References

1. Chen Margaret A, Weinstein David A. Glycogen Storage Diseases: Diagnosis, Treatment and Outcome. 2016;45–72.
2. Labrador E, Weinstein DA. Glycogen Storage Disease Type VI. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews. Seattle (WA): University of Washington, Seattle; 2009.
3. Zhan Q, Lv Z, Tang Q, et al. Glycogen storage disease type VI with a novel PYGL mutation: Two case reports and literature review. *Medicine (Baltimore)*. 2021;100(16):e25520.
4. Chang S, Rosenberg MJ, Morton H, et al. Identification of a mutation in liver glycogen phosphorylase in glycogen storage disease type VI. *Hum Mol Genet*. 1998;7:865–70.
5. Wilson LH, Cho JH, Estrella A, et al. Liver Glycogen Phosphorylase Deficiency Leads to Profibrogenic Phenotype in a Murine Model of Glycogen Storage Disease Type VI. *Hepatol Commun*. 2019;3(11):1544–1555.
6. Hers HG. Enzymatic studies of hepatic fragments; application to the classification of glycogenoses. *Revue internationaled'hepatologie*. 1959;9:35–55.
7. Jagadisan B, Ranganath P. Glycogen storage disease type VI with a novel mutation in PYGL gene. *Indian Pediatr*. 2017;54(9):775–776.
8. Roscher A, Patel J, Hewson S, et al. The natural history of glycogen storage disease types VI and IX: long–term outcome from the largest metabolic center in Canada. *Molec Genet Metab*. 2014;113:171–176.
9. Kishnani PS, Goldstein J, Austin SL, et al. Diagnosis and management of glycogen storage diseases type VI and IX: a clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2019; 21:772–789.