Case Report

Glycogen Storage Disorder

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ABSTRACT

Glycogen Storage Disease (**GSD**, also called **Glycogenosis** and **Dextrinosis**) is the result of defects in the processing of glycogen synthesis or breakdown within muscles, liver, and other cell types. Patients usually present with low blood sugar, enlarged liver, slow growth, muscle cramps, seizures and anemia. Von Gierke disease is the most common type of glycogen storage disorder. Von Gierke[1] described the first patient with GSD type I in 1929 under the name hepatonephromegalia glycogenica. In 1952, Cori and Cori [2] demonstrated that glucose-6-phosphatase (G6Pase) deficiency was a cause of GSD type I. Other types are Pompe, Forbes, Cori, Hers and Anderson types.GSD type 5 McArdle disease affects skeletal muscles [3].

Key Words: Glycogen storage disease, Liver, Hypoglycaemia

INTRODUCTION

Glycogen storage disorders are inherited enzyme defects that cause glycogen to be improperly stored in the body. In the United States, they are estimated to occur in 1 per 20,000-25,000 births. Overall, according to a study in British Columbia[4], approximately 2.3 children per 100 000 births (1 in 43,000) have some form of glycogen storage disease. A Dutch study estimated it to be 1 in 40,000[5].

Symptomatic therapy is very important, in type 1 and 3 preventing hypoglycemia is the target. In type 2 GSD DNA recombinant alglucosidase alfa has been found effective. Gene therapy is an effective mode of treatment but not yet available.

Prognosis depends upon the type of GSD. Complications that might occur are renal failure, malignant alteration of hepatic adenomas, progressive cardiorespiratory insufficiency and rhabdomyolysis.

CASE PRESENTATION

Four years old male child was referred to Paediatrics Unit 2, Civil Hospital due to fever, growth retardation and muscle weakness. He was born to a 25 years old healthy woman after a smooth and uneventful pregnancy at 39 weeks gestational age. He had low grade fever, intermittent in character and partly relieved by medicines. He was not gaining weight since 1 year of age and didn't walk or run like children of his age and got tired easily. He was admitted a year back in a local hospital and received blood transfusion twice for being anemic. Hemoglobin was stated to be 3 in old CBC reports. He was fully vaccinated.

On examination he weighed 4.8kg, height, hypoactive, with abdominal distension. Respiratory rate was 38/min, heart rate 128/min, axillary temperature 37.5c, liver was palpable 3cm below costal margin and spleen was 4cm palpable below the costal margin. Subcutaneous fat was lost with loose axillary and gluteal folds.

The Labs showed Hb 6.7 g/dl, MCV 75.9, TLC 6100/cmm with normal differential count, Platelets 76000/cmm. Urine DR and chest Xray were found to be normal. RBS was 88mg/dl. Metabolic profile was all normal except low calcium levels of 7.8mg/dl. Ultrasound abdomen showed mild parenchymal changes in liver. Hb Electrophoresis showed 97.1% HbA1 and other normal patterns of Hemoglobin excluding thallessemia. All culture results were negative.Liver biopsy revelaed multiple tiny fragments of liver tissue showing effacement of normal architecture by large cells with abundant cytoplasm containing glycogen as demonstrated on special stains, on immunohistochemistry the cells showed positivity with cytokeratin CAM 5.2 and negative for CD 68.

He was transfused with blood to maintain hemoglobin around 10, antipyretics were given for fever and regular monitoring of RBS was done with advice about feeding.

DISCUSSION

There is incomplete degradation of glycogen due to deficiency of various enzymes which breakdown glycogen at various levels of its metabolism. Severe hypoglycemia stimulates epinephrine secretion, which activates lipoprotein lipase and the release of free fatty acids. These fatty acids are transported to the liver, where they are used for triglyceride synthesis and are exported as very-low-density lipoprotein (VLDL), which is elevated in these patients. The lipid abnormalities include hypercholesterolemia (decreased high-density lipoprotein [HDL] cholesterol and increased low-density lipoprotein [LDL] cholesterol), Recent evidence suggests that sera from patients with glycogen-storage disease Ia are able to more efficiently promote scavenger receptor class B type I–mediated cellular cholesterol efflux and that an increased antioxidant effect of these sera is directly related to the increased urate concentration.[6]. However, a recent report suggests that affected individuals may sustain an

increase in carotid artery intimal thickness and arterial dysfunction.[7]

The cause of severe anemia in the absence of renal function compromise in children with glycogen-storage disease it has remained unclear. Some have recently proposed that hepcidin production by hepatic adenomas plays central in patients with glycogen-storage disease. Hepcidin is a peptide hormone that is also a key regulator of the egress of cellular iron; in excess, it may interfere with intestinal iron transport as well as iron release from macrophages.

- Long-term consequences of glycogen storage include the following:
  - Hepatic adenomas
  - Hepatocellular carcinoma
  - Progressive renal insufficiency
  - Hyperuricemic nephrocalcinosis
  - Hyperlipidemic xanthomas
  - Short stature
  - Hypoglycemic brain damage

Blood glucose levels, glucose tolerance test, glucagon tolerance test, LFTs, anion gap, Glycogen content and CPK levels along with electromyography and muscle biopsy are diagnostic aids. Liver biopsy is the confirmatory test.

Management is mainly by maintaining satisfactory blood glucose levels and preventing lactic acidosis. Evidence suggests better control of hypoglycemia in persons with GSD type I and III and an extended duration of euglycemia and better metabolic control for patients[8]. Allopurinol, Cholesterol lowering agents and ACE inhibitors have some role. Currently, efforts are underway in animal models to develop gene therapy in patients with both forms of glycogen-storage disease type I. Type 1 GSD requires nocturnal intragastric feedings of glucose and frequent snacks. Additionally, for patients with GSD type I, the future may bring in adeno associated virus vector – mediated gene experimental therapy, which may result in curative therapy, as is possible in patients with GSD type II[9].

Weekly administration of granulocyte colony–stimulating factor (GCSF), in addition to prophylactic PO iron and prompt treatment of intercurrent infections, is critical in patients with glycogen-storage disease type Ib. in 2006, Roe and Mochel reported a clinical benefit with anaplerotic diet therapy in an adult-onset GSD type II patient with skeletal muscle weakness[10]. Liver transplantation is an option in severe cases.

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