Hepatic glycogenosis in a patient with poorly controlled type 1 diabetes mellitus

Hye Young Jin, M.D., Dae-Young Kang, M.D.*, and Jin-Ho Choi, M.D.

Division of Pediatric Endocrinology and Metabolism, Department of Pediatrics, Asan Medical Center Children’s Hospital, University of Ulsan College of Medicine, Seoul, Korea
Department of Pathology†, Chungnam National University Hospital, College of Medicine, Chungnam National University, Daejeon, Korea

= Abstract =

Hepatomegaly and liver dysfunction might develop in patients with diabetes mellitus due to glycogen deposition or nonalcoholic steatohepatitis. We experienced a case of hepatic glycogenosis in a patient with type 1 diabetes mellitus who presented with recurrent hypoglycemia, suggesting impairment of glycogenolysis and gluconeogenesis. A 10-year-old girl with a 4-year history of type 1 diabetes mellitus was admitted because of recurrent hypoglycemia and abdominal pain in the right upper quadrant. She had Cushingoid features and hepatomegaly that extended 6 cm below the right costal margin. Laboratory data and radiologic examination revealed elevated liver enzyme levels due to fatty liver. Periodic acid-Schiff (PAS) staining revealed intense glycogen deposition in the cytoplasm of the hepatocytes and PAS reactivity was lost with diastase treatment. At 2 months after administration of glucagon injection and uncooked cornstarch between meals and at bedtime, the hypoglycemic episodes and liver dysfunction improved. It is important to distinguish hepatic glycogenosis from steatohepatitis, because it is possible to prevent excessive hepatic glycogen storage in hepatic glycogenosis cases by strictly controlling blood glucose level and by glucagon administration. To prevent severe hypoglycemic symptoms accompanied by hepatic glycogenosis, we suggest that uncooked cornstarch, which is effective in maintaining blood glucose level, can also be administered. (Korean J Pediatr 2009;52:1279-1282)

Key Words: Starch, Glucagon, Hypoglycemia, Diabetes mellitus, Type 1

Introduction

Hepatomegaly and hepatic dysfunction in patients with diabetes mellitus can be caused by excessive hepatic glycogen deposition or nonalcoholic steatohepatitis (NASH). The frequency of hepatic glycogenosis in patients with type 1 diabetes mellitus is relatively rare in children who undergo insulin therapy. The clinical features of hepatic glycogenosis in type 1 diabetes mellitus are hepatomegaly, hypoglycemia, elevated transaminase, hyperlipidemia and ketosis1). It is important to distinguish between hepatic glycogenosis and NASH, because hepatic glycogenosis can be reversed by strict blood glucose control and glucagon injection, whereas for the latter this is not possible. Moreover, NASH is a progressive disease that may lead to fibrosis or cirrhosis of the liver, while hepatic glycogenosis is not known to cause fibrosis or cirrhosis1, 2). We experienced a case of hepatic glycogenosis in a girl with poorly controlled type 1 diabetes mellitus who presented with recurrent hypoglycemia and hepatomegaly, which suggested impaired glycogenolysis and gluconeogenesis.

Case report

A 10-year-old girl, who was diagnosed with type 1 diabetes mellitus at 6 years of age, was admitted because of recurrent hypoglycemia and right upper quadrant pain. She had been treated with a conventional insulin regimen consisting of combinations of intermediate- and rapid-acting insulin preparations. However, hyperglycemia and hypoglycemia occurred alternately during daytime as well as nighttime due to poor compliance and irregular insulin
Fig. 1. Histological findings of liver biopsy. (A) Periodic acid–Schiff (PAS) staining reveals intense reaction in the cytoplasm of hepatocytes (PAS without diastase, ×200). (B) PAS staining after diastase treatment demonstrates complete absence of the reaction (D–PAS stain, ×200).

Discussion

Long-standing hyperglycemia, overinsulization, glucose given to control hypoglycemia, and increased concentrations of the counterregulatory hormones are the risk factors for hepatic glycogenosis in patients with type 1 diabetes mellitus by their concerted actions on the glycogen phosphorylase and synthase enzymes. In 1930, noticeable hepatomegaly due to excessive hepatic glycogen accumulation and hepatic dysfunction in patients with poorly controlled type 1 diabetes mellitus was identified and referred to as Mauriac syndrome. So far, three cases of Mauriac syndrome have been reported in the literature in Korea. A typical Mauriac syndrome presents pro-
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found growth retardation in addition to poorly controlled diabetes, hepatic dysfunction. However, our case is not associated with dwarfism and delayed bone age, which is different from typical Mauriac syndrome. Hepatic glycogenosis in patient with uncontrolled diabetes occurs as a result of passive flux of glucose into hepatocyte. Glucose is converted into glucose-6-phosphate by glucokinase. Then glucose-6-phosphate is converted into glycogen by glycogen synthase. Glycogen synthase exist in an inactive (phosphorylated) and active (dephosphorylated) form. The conversion of inactive form into active form is controlled by phosphatase. Long-term hyperglycemia, irregular insulin injection and large doses of glucose administered to correct the recurrent hypoglycemia result in increased phosphatase concentration, which lead to glycogen synthesis and accumulation\(^4\). Decreased glycogenolysis is also a cause of hepatic glycogenosis. Phosphorylase kinase activate glycogen phosphorylase, which is associated with glycogenolysis. However, prolonged hyperglycemia leads to inactivation of phosphorylase kinase\(^5\). Hepatic glycogenosis can also occur as one of the early manifestations in type 1 diabetes mellitus\(^1^1\). In adults with type 1 diabetes mellitus, two cases of hepatic glycogenosis have been reported in Korea\(^1^0,1^2\). However, this is the first case of hepatic glycogenosis in a child with type 1 diabetes mellitus in Korea. Hepatic glycogenosis in type 1 diabetes mellitus is a benign disease with little chance of progression to fibrosis or cirrhosis, and readily treatable by improvement of glycemic control in a few weeks to months. Minimum dosage of insulin and glucagon injection is required for regression of hepatomegaly and better metabolic control\(^5\). To prevent severe hypoglycemic symptoms accompanied by hepatic glycogenosis, uncooked cornstarch can be used and was effective in maintaining blood glucose concentrations. Uncooked cornstarch has been studied extensively in glycogen storage disease and diabetes mellitus. There have been several reports that used uncooked cornstarch as a bedtime snack to prevent nocturnal hypoglycemia in patients with type 1 diabetes mellitus\(^1^3-1^5\). When hypoglycemia becomes prolonged, the use of glucagon will reduce the amount of glucose administered, and perhaps reduce the amount of glycogen stored in the liver\(^5\). It is unusual to use multiple glucagons injections per day. However, glucagon injections were inevitable because of severe hypoglycemic symptoms including mental change and seizures. In this case, recurrent hypoglycemic symp-
References