1. Introduction

Glycogen storage disease Ia (GSD Ia) is an autosomal recessive inborn error of carbohydrate metabolism that is caused by a deficiency of the enzyme glucose-6-phosphatase, leading to disturbed glycogenolysis and gluconeogenesis. Patients with GSD Ia are dependent on supplementary exogenous sources of glucose and suffer severe fasting hypoglycemia, lactic acidosis, hyperuricemia, and hyperlipidemia. The primary objective in treatment is to prevent hypoglycemia either by frequent meals, consumption of uncooked cornstarch, continuous gastric drip feeding, or glucose infusion.1 GSD Ia presenting as neonatal hypoglycemia is uncommon, as most GSD Ia patients are diagnosed at a median age of 3–6 months.2 Here, we describe a case of neonatal GSD Ia. The diagnosis was confirmed by gene analysis.

2. Brief report

A 33-year-old woman gave birth vaginally to a male infant at 38 4/7 weeks gestational age, with a birth weight of 3100 g and good Apgar scores. There was no family history of liver or metabolic disease. At age 3 days, the infant was admitted to hospital because of pneumonia. During his hospitalization, he was found to have hypoglycemia and prominent hepatomegaly, liver palpable at 4 cm below the right costal margin, but no splenomegaly. Biochemical tests on Day 7 showed a moderate increase in alanine amino transferase 87 IU/L, aspartate amino transferase 233 IU/L, and fasting hypoglycemia 1.8 mM, (neonatal hypoglycemia defined as glucose <2.6 mM). Biochemical tests on Day 14 showed worsening transaminase levels with alanine amino transferase 216 U/L, and aspartate amino transferase 561 IU/L. On Day 16, he was referred to our hospital for further investigations.

On the day of admission, his physical examination showed hepatomegaly with liver palpable at 3.5 cm below the right costal margin and mild wasting of his limbs. His coagulation function was normal. After admission, he had prefeeding glucose levels <2.6 mM on four occasions, which quickly returned to normal after feeding. His fasting blood analyses revealed hypoglycemia, lactic acidosis, and hypertriglyceridemia. On Day 19, before feeding, his glucose level was 1.8 mmol/L, and functional tests showed the absence of a glycemic response and an aggravation of lactic acidosis after injection of glucagon. His thyroid function and insulin/glucose ratio were normal with glucose level at 1.8 mM. On Day 20, his urine was tested for galactosemia. Due to the hypertriglyceridemia, he was fed every 2 hours with a special formula that was galactose-free and contained medium chain triglycerides (MCTs), pending urine results. On Day 20, his blood was sent for genetic testing. His urine test ruled out galactosemia. His fasting blood glucose level was maintained within normal range, lactate and triglycerides levels decreased gradually, and liver function tests also improved substantially by Day 25 (Table 1). Gene analysis revealed a homozygous mutation in exon 1 (c.202 G > A, p.G68 R, CM980780, PMID:9700613), which was first reported in 1998.3 His parents refused genetic testing. He was transitioned from MCT formula to regular formula and the parents were taught how to feed him and monitor his glucose before he was discharged home.

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3. Discussion

Hypoglycemia is a life-threatening problem in patients with GSD Ia. More commonly, patients present at around age 3 months with a protruding abdomen due to marked hepatomegaly. Our patient was diagnosed during the neonatal period, and neonatal GSD has only been reported occasionally.

Unlike long chain triglycerides, MCTs are not incorporated into chylomicrons, and the released medium-chain fatty acids enter mitochondria without the carnitine system that is essential for long-chain fatty acids to pass through the mitochondrial membrane. Patients with GSD Ia do not require special formula, although Nagasaka et al found that MCT milk helped lower blood triglyceride levels and raise HDL cholesterol levels in GSD Ia patients. Before we ruled out galactosemia in our patient with hypertriglyceridemia, we fed a special galactose-free, MCT formula. After we fed him every 2 hours, his glucose levels were maintained in the normal range, and the hypertriglyceridemia and lactic acidosis gradually improved.

The human glucose-6-phosphatase gene was isolated by Lei et al, and has been localized to chromosome 17 at 17q21. It includes five exons and codes for a highly hydrophobic protein of 357 amino acids containing nine transmembrane helices. More than 85 mutations (Human Gene Mutation Database; http://www.hgmd.cf.ac.uk) have been identified. The diagnosis in our patient was confirmed by gene analysis. Hufton and Wharton also suggested that in the neonatal period, any unexplained metabolic acidosis, hypoglycemia, hepatomegaly, or hyperlipidemia merits the consideration of GSD in the differential diagnosis. Complete sequencing of the GSD Ia genes allows diagnosis in nearly all patients with evocative clinical and biochemical signs of GSD Ia, thereby eliminating the need for a liver biopsy.

Conflicts of interest

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