A Novel Frameshift Mutation of the ALDOB Gene in a Korean Girl Presenting with Recurrent Hepatitis Diagnosed as Hereditary Fructose Intolerance

Hae-Won Choi*, Yeoun Joo Lee*, Seak Hee Oh*, Kyung Mo Kim*, Jeong-Min Ryu*, Beom Hee Lee*,† Gu-Hwan Kim†, and Han-Wook Yoo*,†

*Department of Pediatrics and †Medical Genetics Clinic and Laboratory, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Hereditary fructose intolerance is an autosomal recessive disorder that is caused by a deficiency in fructose-1-phosphate aldolase (Aldolase B). Children can present with hypoglycemia, jaundice, elevated liver enzymes and hepatomegaly after intake of dietary fructose. Long-term intake of fructose in undiagnosed patients can result in hepatic failure or renal failure. We experienced a case of hereditary fructose intolerance presenting as recurrent hepatitis-like episodes. Detailed evaluation of her dietary habits revealed her avoidance of sweetened foods and fruits. Genetic analysis of ALDOB revealed that she is a homozygote for a novel frameshifting mutation c[758_759insT]+[758_759insT] (p.[val253fsX24]+[val253fsX24]). This report is the first of a Korean patient diagnosed with hereditary fructose intolerance using only molecular testing without undergoing intravenous fructose tolerance test or enzyme assay. (Gut Liver 2012;6:126-128)

Key Words: Fructose intolerance; Aldolase B; Hepatitis; Hypoglycemia; Gene

INTRODUCTION

Hereditary fructose intolerance (HFI, OMIM# 229600) is an autosomal recessive disorder, caused by a deficiency in fructose-1-phosphate aldolase (Aldolase B) which exists in the liver, kidney, and intestines.1 Deficiency of this enzyme causes an accumulation of fructose-1-phosphate after fructose intake, which results in toxic symptoms like vomiting, hypoglycemia, jaundice, elevated liver enzymes and hepatomegaly.2 HFI was diagnosed traditionally by biochemical tests such as intravenous fructose tolerance test or enzyme assay through liver or small intestine biopsy.3 Here we report a 2-year-old girl with HFI manifesting recurrent hepatitis-like episodes, which was diagnosed by the ALDOB gene analysis.

CASE REPORT

A 2-year-old girl was admitted for the evaluation of recurrent episodes of aminotransferase elevation. At 6 month of age, she was first diagnosed with hepatitis at another hospital after developing fever, vomiting, and diarrhea. She showed hepatomegaly which was palpable by four finger breadth below the costal margin. Laboratory findings revealed elevated aspartate aminotransferase (AST) of 2,017 IU/L and alanine aminotransferase (ALT) of 1,242 IU/L with prothrombin time prolongation. No definite cause was found and liver enzymes were normalized after supportive care. She experienced similar episodes of aminotransferase elevation at 15-month-old and 23-month-old of age when she had symptoms of upper respiratory infections, each revealing AST of 240 IU/L, ALT of 260 IU/L and, AST of 457 IU/L, ALT of 530 IU/L. When she was admitted to our hospital at 2 years of age, her height was 115.7 cm (25th to 50th percentile), and body weight was 12.9 kg (25th to 50th percentile). Blood pressure was 116/77 mm Hg, heart rate 136/min, respiratory rate 32/min, and body temperature was 36°C and there was no abnormal findings on physical examination. She had no siblings and no family history of liver disease or genetic disease. Blood hemoglobin was 11.8 g/dL, white blood cell count 6,200/mm³ (neutrophils 28%, lymphocytes 54%, monocytes 14%, and eosinophils 2%), platelet count 397,000/mm³, total protein 7.0 g/dL, albumin 4.0 g/dL, AST 88 IU/L, ALT 68 IU/L, total bilirubin 0.4 mg/dL, direct bilirubin 0.1 mg/dL, gamma-glutamyltranspeptidase 23 IU/L, alkaline phospha-
Deficiency of fructose-1-phosphate aldolase (aldolase B) causes accumulation of fructose-1-phosphate in the liver, kidney, small intestines, which leads to symptoms like abdominal bloating, vomiting and elevated liver enzymes. Deficiency of this enzyme also causes inhibition of other enzymes such as fructose-1,6-bisphosphate aldolase and fructokinase, resulting in impaired glycogenolysis and gluconeogenesis which can lead to fatal hypoglycemia. Chronic ingestion of fructose of sucrose results in failure to thrive and repeated episodes of hypoglycemia eventually leads to fatal hepatic or renal failure. Our patient presented with typical features of HFI such as vomiting, elevated liver enzymes, and hepatomegaly. Other symptoms of HFI include lethargy, convulsions, proximal tubular dysfunction which our patient didn’t present. However, these manifestations can also be found in other metabolic liver diseases including galactosemia.