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EDİTÖRE MEKTUP / LETTER TO THE EDITOR

A novel mutation in congenital glucose galactose malabsorption syndrome

Konjenital glukoz galaktoz malabsorbsiyonu sendromunda yeni bir mutasyon

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To the Editor,

Congenital glucose-galactose malabsorption (CGGM) is a rare metabolic disease characterized by life treating osmotic diarrhea and dehydration as early as in the first days of life. It is inherited by autosomal recessive trait and is due to mutations within the *SLC5A1* gene that provides instructions for producing a Na+/glucose cotransporter 1 (SGLT1) protein[1-4]. More than 40 mutations related to the CGGM have previously been reported[3]. Here, we report a newborn baby admitted to hospital for severe dehydration and persistent diarrhea diagnosed as glucose-galactose malabsorption syndrome with a novel mutation.

The male infant was admitted to our hospital for intractable diarrhea on the 22nd day of life. He was the product of uneventful pregnancy and his birth weight was 3000 g. On the second day of life he was admitted to a hospital for 15 times per day diarrhea and fever. He was severely dehydrated. He was rehydrated and lactose free formula was started. However diarrhea persisted and he was referred to our hospital. His parents were consanguineous and he was the first child of the parents (Figure 1). He was 3050 g, his mucosa was dry and turgor was decreased. The other physical findings were normal. In laboratory tests, Na: 140 mEq/L, BUN 32 mg/dl, creatinine 1,62 mg/dL. He was hydrated and as he had urinary tract infection, antibiotherapy was started. Parenteral nutrition was started and diarrhea stopped. Diarrhea started again when enteral feeding was started with lactose free formula. Fecal pH was acidic. Nephrocalcinosis was present in both kidneys. Diarrhea with enteral feeding suggested a malabsorption disorder. As he had diarrhea with breast milk and lactose free formula, fructose based formula (Glutamin 19) was started. He had no diarrhea and CGGM was diagnosed. His weight gain was satisfactory after the new formula and he was discharged on 36th day of life, his weight was 3500 g. Genetic analysis of the patient was performed by Sanger technique (3130XL Genetic Analyzer, Applied Biosystem) and a homozygote for p.A239D (c.716C>A) mutation in *SLC5A1* gene was identified which is a new mutation. The mutation was also confirmed in the parents whom were carriers for the same mutation. He is now 13 months old and weight is 8750 g (10-25 p), length is 72 cm (10-25 p). Informed consent was gained from the parents.

Congenital glucose-galactose malabsorption is caused by a defect in glucose and galactose transport across the intestinal lining. Lactose in breast milk is broken down into glucose and galactose by the lactase enzyme. The protein product of SGLT1 moves the glucose and galactose from the lumen of the small intestine to intestinal enterocytes. Mutations in *SLC5A1* gene leads the accumulation of glucose and galactose that result in osmotic diarrhea[1-4].

Neonatal onset diarrhea resulting severe dehydration, hypernatremia and metabolic acidosis

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are typical findings in CGGM. Dramatic improvement of diarrhea only after elimination of glucose and galactose using fructose based formula is characteristics and diagnostic. Reducing substances are positive in stool and small bowel biopsy is normal[4-9]. Measuring the concentration of hydrogen in breath, oral glucose tolerance test and glucose, galactose and fructose absorption by jejunal perfusion are not performed in daily practice[10]. Many clinically related mutations in *SLC5A1* gene have been previously reported (http://www.hgmd.org/). Molecular diagnosis becomes a must and a mutation status must be confirmed[3], however diagnosis mostly depends on clinical improvement with withdrawal of glucose and galactose from diet. The whole coding regions and exon-intron boundary regions of *SLC5A1* gene have been sequenced in this patient as he was the first child of consanguineous parents. His diagnosis was confirmed by an identified novel homozygote p.A239D(c.716C>A) mutation.

Hypernatremia, gangrenous ischemia of extremities due to severe dehydration, growth retardation, hypercalcemia, nephrocalcinosis, nephrolithiasis and renal tubular acidosis have been reported in patients with CGGM[9-10]. We have detected bilateral nephrocalcinosis in the present patient.

Prognosis is good in patients diagnosed in the early days of life. Fructose based feeding is recommended in newborn and infancy period. In the weaning period, patients should be kept away from apple, pear, carrot, green bean and zucchini; meat and egg may be added to their meals[6]. Tolerance to carbohydrates tends to improve following the first year of life[12]. Patients may tolerate small amount of glucose later in life[6,12].

We here report a CGGM with a new mutation in a Turkish newborn baby. CGGM is a very rare malabsorption syndrome. If lactose free diet fails to cease diarrhea in a newborn, glucose-galactose malabsorption syndrome should be in mind and glucose-galactose free fructose based formula should be started. Parents should be informed about molecular genetic testing of *SLC5A1* gene for genetic counseling and prenatal diagnosis.

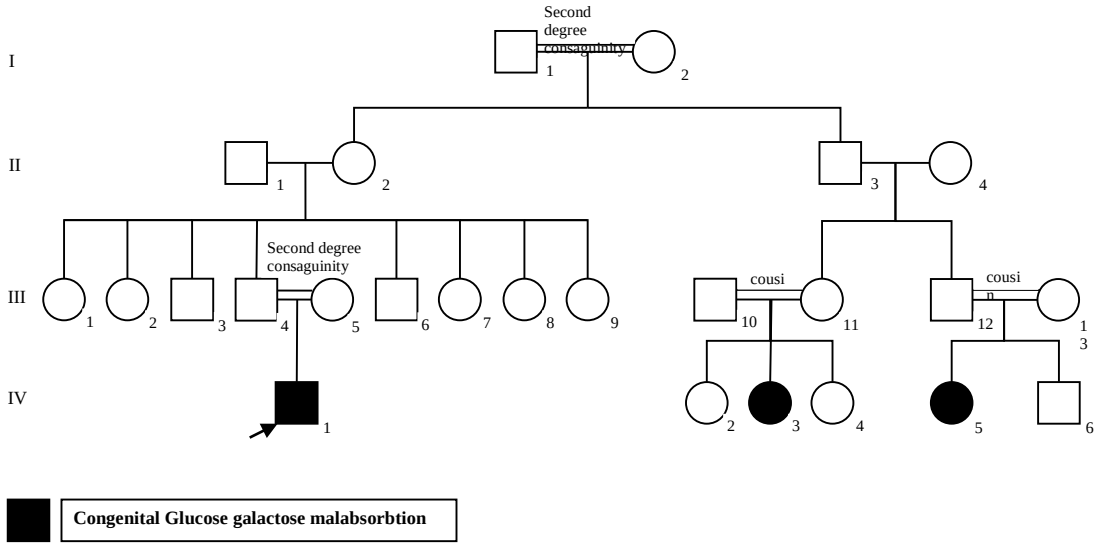

Figure 1. Pedigree of the family.

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