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Vaka Sunumu

A Case of Classical Galactosemia Presenting with Indirect Hyperbilirubinemia and Long QT Syndrome in the Early Neonatal Period

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A Case of Classical Galactosemia Presenting with Indirect Hyperbilirubinemia and Long QT Syndrome in the Early Neonatal Period

Classical galactosemia is a life-threatening metabolic disease caused by an autosomal recessive inherited defect of galactose metabolism. Newborns with classical galactosemia are unable to metabolize galactose-1-phosphate. Infants with galactosemia may develop symptoms such as vomiting, liver problems, and jaundice in the first days of life if they are fed with formula that contains lactose or breast milk. In classical galactosemia generally direct hyperbilirubinemia is the prominent feature. However the disease may onset with indirect hyperbilirubinemia at its early stage. The long QT syndrome is a disorder of myocardial repolarization characterized by a prolonged QT interval on the electrocardiogram. This syndrome is associated with an increased risk of sudden infant death. We report here a case of classical galactosemia presenting with severe indirect hyperbilirubinemia and long QT syndrome during early neonatal period.

Keywords: *Hyperbilirubinemia, long QT syndrome, galactosemia*

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Erken Neonatal Dönemde Direkt Hiperbilirübinemi ve Uzun QT Sendromu ile Ortaya Çıkan Klasik Galaktozemi Vakası

Klasik galaktozemi galaktoz metabolizmasındaki otozomal resesif bir kalıtsal bir bozukluğun neden olduğu yaşamı tehdit eden bir metabolik hastalıktır. Klasik galaktozemili bebeklerde galaktoz-1-fosfat metabolize edilemez. Galaktozemili bebeklerde yaşamın ilk günlerinde laktoz içeren mama veya anne sütüyle beslenmeyi takiben kusma, karaciğer sorunları ve sarılık gelişebilir. Klasik galaktozemide genellikle direk hiperbilirübinemi ön plandadır. Bununla birlikte hastalık erken dönemde indirek hiperbilirübinemi ile de ortaya çıkabilir. Uzun QT sendromu elektrokardiyogramda uzun QT mesafesi ile karakterize bir myokard repolarizasyon bozukluğudur. Bu sendromda ani bebek ölümü riski yüksektir. Bu makalede erken neonatal dönemde ciddi indirek hiperbilirubinemi ve uzun QT sendromu ile ortaya çıkan klasik galaktozemili bir yenidoğan vaka sunuldu.

Anahtar kelimeler: *Hiperbiliübinemi, uzun QT sendromu, galaktozemi*

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INTRODUCTION

Galactosemia is an autosomal recessive disorder of carbohydrate metabolism, which was firstly described in a patient in 1935 by Mason and Turner [(1)]. The incidence is approximately 1 case per 40,000-60,000 people in western countries, but it's relatively prevalent (1/23.775) in Turkish population [(2)]. Newborns with classical galactosemia are unable to metabolize galactose-1-phosphate. The accumulation of galactose-1-phosphate results in injury on kidney, liver, brain and eyes. Affected newborns are usually normal at birth and show clinical signs in the first weeks of life after ingestion of galactose.

Long QT syndrome is an inherited disorder that causes sudden cardiac death. Perinatal manifestations are rare, but early diagnosis and treatment is necessary to prevent sudden infant death syndrome [(3)]. Here is a case of a neonatal classical galactosemia presenting with severe indirect hyperbilirubinemia and long QT syndrome.

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CASE

A male baby weighing 3100 g was born at 38 weeks to a 34-year-old gravida 3, para 1 mother. He was discharged home in good health after 24 h of follow-up in maternal & baby unit. At the 60th hour of her life, the patient was presented to outpatient clinic with jaundice. There was no hepatosplenomegaly and muscle tone was normal. Total and direct bilirubin levels were 23.1 mg/dl and 0.7 mg/dL, respectively. Reticulocyte count was 8.6 percent.The patient's blood type was 0 Rh positive, and he was negative for the direct and indirect antibody testing. Total serum bilirubin levels of the patient did not decrease despite intensive phototherapy and he underwent a double volume exchange transfusion. The patient was discharged home 48 h after exchange transfusion. Five days later, he was readmitted to neonatal intensive care unit with fever (38,5°C), vomiting, dehydration and jaundice. His weight was 2650 g (14.5% weight loss). Physical exam was notable for decreased muscle tone, jaundice, and hepatomegaly. Laboratory evaluations revealed increased levels of blood urea nitrogen (BUN 116 mg/dL), creatinine (1.7 mg/dL), sodium (151 mEq/L), and total/direct bilirubin 15.7/8.9 mg/dL. C-reactive protein concentration was high (31 mg/dL). After blood culture results were obtained, intravenous antibiotic (ampicillin and cefotaxime) treatment was started.

At follow-up, bradycardia developed; the patient's cardiac rate and blood pressure were 76/min and 84/56 mmHg, respectively. Electrocardiographic examinations detected long QT syndrome (cQT: 0.55 sec) (Figure 1). *Escherichia coli (E. coli)* was identified in blood culture. Further investigation showed positive reducing substance in the urine. The chromatographic examination of urine revealed that the reducing substance was galactose. Galactose-1-phosphate uridyl transferase (GALT) activity was normal, reflecting donor blood. Galactose-1-phosphate content of the infant's red blood cells after exchange transfusion was 238 μg per g Hb (normal range 5 to 29 μg per g Hb), which was consistent with galactosemia. Low GALT activity in red cells (2.3 U/dL; normal value: 21.2 U/dL) confirmed the diagnosis of classical galactosemia. There was no history of consanguineous marriage.

Lactose containing formula was changed on the 12th day of life to lactose free (LF) diet, and enteral intake improved immediately. Genetic testing indicated a compound heterozygote genotype for two of the most common alleles for GALT deficiency, Q188R and K285N. Ophthalmologic exam was negative for cataract. Galactose-restricted diet improved the clinical signs of the patient rapidly. Long QT syndrome did not repeat after LF diet.

He was discharged on the 28th day of life while on enteral feeding. At 24th month of the follow up, he was well with normal anthropometric measurements, there was no cataract on slit lamp examination and he was developmentally normal for his age.

DISCUSSION

In classical galactosemia, presenting symptoms such as vomiting, hypoglycemia, jaundice, hepatomegaly, sepsis, hepatocellular dysfunction, diarrhoea, renal

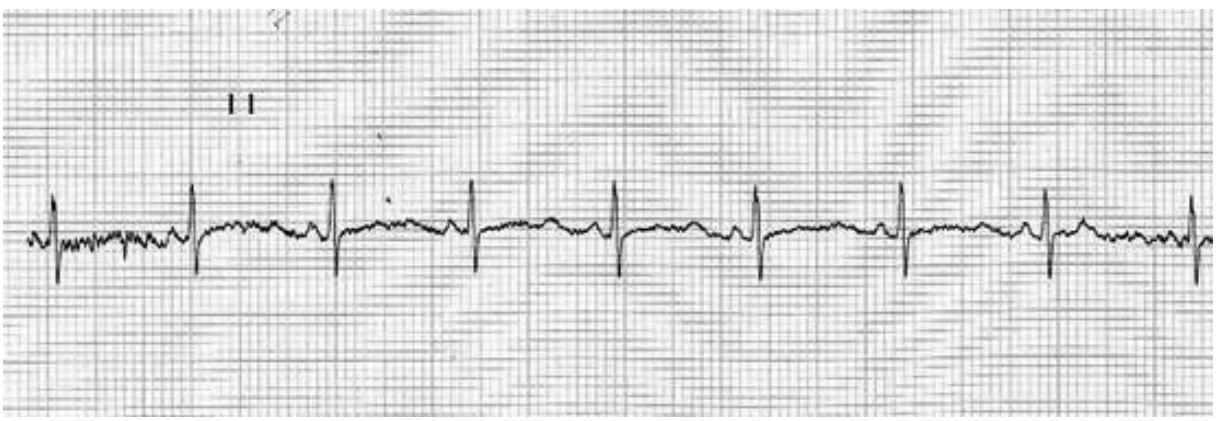

Figure 1.

tubular dysfunction, and cataract are caused by accumulation of the metabolites galactitol and galactose-1-phosphate [4]. Jaundice associated with galactosemia is often due to direct hyperbilirubinemia. However, our patient showed indirect hyperbilirubinemia in the first 72 h of life.Woo et al. [5] reported a newborn with galactosemia and severe indirect hyperbilirubinemia in early infancy. Indirect hyperbilirubinemia may result in hemolysis after galactose-1-phosphate accumulation in red cells. Another proposed mechanism is the involvement of galactose-1-phosphate in the phosphorylation cycle in which ATP is dephosphorylated to metabolites that have no energy-generating capability, and resulting with early erythrocyte death [6].

Newborns with galactosemia are at increased risk for E. coli sepsis. Besides, the onset of sepsis often precedes its diagnosis [2]. Strong consideration should therefore be given for early antibiotic therapy in infants with suspected galactosemia in spite of the absence of clinical signs or symptoms of sepsis [4]. E. coli sepsis increased the suspicion for galactosemia in our patient and the diagnosis was confirmed in further investigations.

Long QT syndrome is a cardiac repolarization disorder with idiopathic, iatrogenic, and congenital etiologies. The characteristic electrocardiographic findings are long cQT interval relative to patient's age, T wave abnormalities, and torsade de pointes-type ventricular tachyarrhythmias and bradyarrhythmias. Iatrogenic form is more often related to drugs and electrolyte imbalances [3]. Galactosemia-induced long QT syndrome has not been reported in the in the literature before. Our patient presented with early severe indirect hyperbilirubinemia and bradyarrhythmia (long QT syndrome).The mechanism of toxicity is unclear, but inhibition of cardiac repolarization is still possible by galactose-1-phosphate or other toxic metabolites that accumulate in galactosemia. As there is no reliable data on this issue, we only speculate that the association of galactosemia and long QT syndrome may be a mere coincidence, or one of them is an etiologic factor for the other.

Q188R is the most common mutation among Turkish patients with classical galactosemia as well as for all Caucasian populations [7]. A compound heterozygote genotype for two of the most common alleles for GALT deficiency, Q188R and K285N were detected in our patient.

Classical galactosemia is a life-threatening metabolic disease, which can affect different tissues. Our case showed that the imbalance of galactose and its metabolites might also induce long QT syndrome in galactosemia. Further reports will clarify the underlying pathogenesis.

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