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# An Unusual Presentation of Galactosemia in the Newborn: Liver Failure and Hyperammonemia

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## Abstract

Galactosemia is an autosomal recessive inherited disease of the galactose metabolism developing depending on galactose-1-phosphate uridyl transferase deficiency. In this report, a newborn galactosemia case with abnormal presentation has been presented. Hepatic and renal functions of the infants diagnosed with ammonia increase in newborn or early infancy period should be revised rapidly and the treatment should be started immediately.

**Keywords:** Newborn; Galactosemia; Liver failure

## Introduction

Galactosemia is an autosomal recessive inherited disease of the galactose metabolism developing depending on galactose-1-phosphate uridyl transferase deficiency. Classic galactosemia is a disease characterized by vomiting, diarrhea, convulsions, anemia, prolonged jaundice, growth retardation, hepatomegaly, cataracts and mental retardation, food intolerance, hypoglycemia, hepatosplenomegaly, hepatocellular insufficiency, renal tubular dysfunction, hypotonia and sepsis [1-6] depending on the toxic accumulation of galactose metabolites as a result of homozygous or heterozygous mutation in galactose-1-phosphate uridyl transferase (GALT) gene [1-3].

Although hepatomegaly in newborns with galactosemia is not a frequent finding, hepatic failure and hyperammonemia have not been reported in the literature. Some authors have reported that hepatic failure may develop in patients with galactosemia in infancy or childhood period [7]. In this study, the features of the case defined in the newborn period and diagnosed with hepatic failure have been presented.

## Case Presentation

Thirty-two-day-old male patient applied because of vomiting, absence of suckling and fever and was admitted for examination because of the increase of the amount of vomiting and fever. The patient was born with spontaneous vaginal route on time as the second alive from the second pregnancy of the 22-year-old mother. There was no kinship between the mother (22 years) and the father (29 years), the mother had a follow-up and uneventful pregnancy, and without abortion and exitus. There was no family history of inherited metabolic diseases and child death. The family has a healthy 2-year-old girl. Vomiting existing since birth was usually in small quantities immediately after intake, but the frequency and quantity increased from one day before the application to the hospital. For last 2 days, fever was included to the complaints. In monitoring the patient admitted to the State Hospital with such complaints, convulsive movements that cannot be described fully were observed. As identifying the glucose 20 mg/dL, meningitis, sepsis and hypoglycemia have been pre-diagnosed. On physical examination, the weight was 3300 g (50th percentile), the height was 49 cm (50th percentile), and the head circumference was 36 cm (50th percentile). Of the apathetic patient with poor general condition, the sclera was icteric sclera, pupils were isochoric IR: IR: +/+; and the skin was pale and icteric. The respiratory system examination was normal except for subcostal retractions. In cardiovascular system, the findings except for a 2/6 systolic murmur in mesocardiac focus were normal. Physical examination revealed hepatomegaly (liver palpable 3 cm below the costal margin). However it was detected that reflex of moro, sucking, catching were weak, and muscle strength and tonus were found to have decreased. Other findings of physical examination were normal.

In laboratory examinations, the hemotologic (Table 1), biochemical (Table 2) and cerebrospinal fluid (CSF) examination (Table 3) findings were shown in tables.

Breeding was not found in the CSF culture. HBsAg, Anti HBS, anti-HCV and anti-HIV were negative. In the light of these clinical and laboratory findings, the patient was diagnosed

with galactosemia as a result of tandem mass examination. GALT mutation report was determined as homozygous N314D/N314D.

Although the treatment was applied for the liver insufficiency and hyperammonemia, clinic picture became bad very fast. It was occurred cardiopulmoner arrest.

**Table 1.** Hematologic findings.

| **Hemoglobine (g/dl)** | **8.8** |
|---|---|
| MCV (fl) | 101 |
| Platelet ($mm^3$) | 323000 |
| Leucocyte ($mm^3$) | 20200 |
| Erythrocyte ($mm^3$) | 2.6 |
| Hct (%) | 27% |
| MCH (pg) | 32 |
| MCHCH (g/dL) | 32 |
| PT (sec) | 46 |
| PTT (sec) | 178 |
| INR | 5.4 |
| Fibrinogen | 102 |
| D dimer | 10.2 |

**Table 2.** Biochemical findings.

| **BUN (mg/dl)** | **24** |
|---|---|
| Creatinine (mg/dl) | 0.2 |
| Na (meq/L) | 130 |
| K (meq/L) | 6.3 |
| Cl (mmol/L) | 105 |
| Ca (mg/dl) | 7.2 |
| AST (U/L) | 644 |
| ALT (U/L) | 605 |
| Urea (mg/dl) | 52 |
| Total bil. | 14.9 |
| Direct bil. | 12.9 |
| CRP (mg/dl) | 5 |
| Lactate | 7.8 |
| Ammonia | 700 |

**Table 3.** Cerebrospinal fluid findings.

| **Glucose** | **12** |
|---|---|
| Protein (mg/dl) | 80 |
| Cl (meq/L) | 166 |
| SBS (mg) | 80 |
| Cell | + |

## Discussion and Conclusion

The main source of galactose is lactose which is the main carbohydrate of the infant diet. Lactose is used as an energy source by being converted to glucose in liver cells. Galactosemia is an autosomal recessive inherited metabolic disease emerging as a result of galactose-1-phosphate uridyl transferase (GALT) enzyme in where galactose is metabolized (1,2,3). Its frequency ranges between 1/50000 and 1/60000 and has higher frequency (1/23775) like the other autosomal recessive inherited metabolic diseases in Turkey [8].

Galactose-1-phosphate accumulated especially in the liver, kidneys and the brain and is very toxic. There may be a wide variety of mutations and consequently, clinical findings and complications vary [9]. Symptoms in patients start after the intake of lactose. Vomiting, failure to gain weight, diarrhea, lethargy and other symptoms may occur about a week [1,10]. Vomiting in the case existing from the birth have been reported to usually increase after sucking in parallel with the literature [1,10]. Cataract was also detected in the first admission of the patient. In galactosemia, direct hyperbilirubinemia, hyperammonemia, hepatocellular damage and cirrhosis may develop related to the liver [2,4]. In our case, INR was high, AST and ALT have increased; urea, total bilirubin and lactate have increased and it is obvious that these findings indicate hepatocellular damage in the liver. Thus, phototherapy was applied first due to hyperbilirubinemia and in accordance with recommendations, N-acetyl cysteine, ursedeoxycholic acid, lactulose were began to be applied to the patient. Due to ammonia being >700, sodium benzoate was began. Due to the continuation of the resistance acidosis in blood gas monitor of the patient, peritoneal dialysis was opened. Reductant substance in the urine was detected positive.

Renal tubular dysfunctions in galactosemia have also been reported [2,11]. In our case, because of the presence of acidosis in blood gas and failure to respond to the treatment, the failure of the regression of edema and renal failure, peritoneal dialysis was applied.

In galactosemia, erythrocyte GALT enzyme activity is absent or is very low. Blood galactose and erythrocyte galactose-1-phosphate levels are quite high. In such cases, lethal sepsis development risk and galactosemia complication depending on long-term diet is high [12]. The reason of the frequent sepsis in galactosemia is due to galactose or its metabolites to inhibit the antibacterial activity of leukocytes [13]. The patient with sepsis must be subjected to a serious examination. Lumbar puncture must be opened in patients and CSF must be examined. Normal CSF findings in some patients do not indicate the absence of meningitis. This situation can rather result from the suppression the immune system. Thus, culture should be taken [14,15]. In our case, abundant cells were detected in CSF direct examination, sultamicillin and cefotaxime was applied to the patient pre-diagnosed with meningitis and sepsis. With the detection of Cedecea lapagei

in the later blood culture result, cefotaxime was stopped and meropenem (due to its sensitivity) was begun.

More than 40 mutations have been identified so far in p13 region of the chromosome 9 in which the synthesis of the GALT enzyme is known to have been encoded [2]. There are three basic forms of GALT deficiency; the first is the classic galactosemia, the second is the clinical galactosemia and the third is the biochemical galactosemia. Classical genotype is typified by Q188R/Q188R, clinical genotype is typified by S135L/S135L and the biochemical genotype is typified by N314D/Q188R [3]. In the genetic evaluation of our patient, GALT mutation report was determined as the homozygous N314D/N314D and previously established diagnosis of galactosemia by tandem mass screening was revealed genetically.

As a result, in this study, a newborn galactosemia case with abnormal presentation has been presented. As the significant ammonia increase and renal failure in patients with galactosemia in newborns are not frequent in the early stages, this case has been presented in the literature. Hepatic and renal functions of the infants diagnosed with ammonia increase in newborn or early infancy period should be revised rapidly and the treatment should be started immediately. Otherwise, mortality will be inevitable in the baby.

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