Journal of Neonatal Research and Pediatrics Care

Chembio Publishers
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Case Report *Volume 1; Issue 1*

A Preterm Infant with Galactosemia Presenting with Severe Growth Retardation and Klebsiella Urinary Tract Infection

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Received Date: May 28, 2018; **Published Date:** June 06, 2018

Abstract

Galactosemia is an uncommon diagnosis in preterm infants with intrauterine growth retardation. We are reporting an infant presenting with severe intrauterine growth retardation, Klebsiella pneumoniae urinary tract infection, and galactosemia. There was no clear etiology for intrauterine growth retardation except for a maternal history of smoking. The infant had normal blood glucose measurements during the hospital stay. After a positive state screening report for galactosemia, the infant was switched to soy formula. Klebsiella pneumoniae urinary tract infection (UTI) was treated with 7 days of gentamicin. The infant had a normal neurological examination and eye exam did not reveal any cataracts. A multi-disciplinary team will provide follow up after discharge from the hospital. The growth and development will be closely monitored.

Keywords: Galactosemia; Infants; Retardation; Klebsiella; Urinary tract infection

Abbreviations: UTI: Urinary Tract Infection; GALT: Galactose-1-Phosphate Uridyl Transferase; UDP: Uridine Diphosphate; GALE: Galactose 4-Epimerase; GALK: Galactokinase

Case Presentation

A 36 week and 3-day gestation, female, Caucasian infant was born by cesarean delivery after a failed induction of labor. The prenatal examinations were suggestive of severe intrauterine growth retardation. Mom is 28-year-old G1P0, hepatitis B surface antigen negative, hepatitis C anti-bodies negative, rubella immune. She is a known smoker and her urine drug screen was positive for cannabinoids. The prenatal course was unremarkable except for the intrauterine fetal growth retardation and there was no evidence of any uterine abnormality. The infant weighed 1304 g (below the 1st percentile). The Apgar score was 8 at one minute and 9 at 5 minutes. The infant did not require any resuscitation in the delivery room. The length was 39.4 cm (below the 1st percentile) and the head circumference was 28 cm (below the 1st percentile).

Initial exam was unremarkable; there were no petechiae+ or other skin lesions noted. There was no hepatosplenomegaly. The infant had normal tone and normal activity with positive Moro reflex. Maternal breast milk feedings were introduced soon after birth as per feeding protocol. The patient initially tolerated small volume of feeds. She required supplemental hyper-alimentation for 3 days. The infant maintained blood glucose in the normal range throughout the stay in the

Citation: Des Bharti and Katherine Anne Wood Silva. A Preterm Infant with Galactosemia Presenting with Severe Growth Retardation and Klebsiella Urinary Tract Infection. J Neo Res Pedia Care 2018, 1(1): 180003.

neonatal intensive care unit. Total serum IgM was in the normal range and the urine was negative for cytomegalovirus. The infant had physiological hyperbilirubinemia with the highest bilirubin of 9.2mg/dl. She received phototherapy for 3 days. The highest direct bilirubin recorded was 2.1 on day 8 of life. Her liver enzymes, including aspartate aminotransferase and alanine aminotransferase, were normal; her abdominal ultrasound was unremarkable. The gallbladder was mildly distended without gallstones or biliary sludge. The infant was given Ursodial 10 mg/kg twice daily for 5 days until the direct bilirubin was reported as less than 2.0mg/dl. The urine culture on day 8 of life was reported negative. Alpha-1-antitrypsin level, thyroid studies, reticulocyte count, haptoglobin level, and a peripheral blood smear were all reported normal.

On day 11 of life, her newborn screen was reported positive for galactosemia and this was confirmed with a second newborn screen. Further studies reported normal transaminases, low Galac-1-Phos Uridyl transferase enzyme activity (4.1, normal range 14.7-25.4 U/g*), and two separate mutations in the GALT gene, one common GALT mutation and the Duarte (D) variant mutation consistent with DG Variant Galactosemia. The infant was immediately transitioned to soy formula (isomil). On day 14 of life, the catheterized urine sample was reported positive for Klebsiella pneumoniae 30,000-50,000 CFUs, resistant to ampicillin but sensitive to gentamicin. Repeat urine culture on day of life 16 was positive for Klebsiella pneumoniae greater than 100,000 CFUs. She was treated with 7 days of Gentamycin and a follow-up urine culture on day 20 of life was reported negative. Renal ultrasound showed grade 1 hydronephrosis with a normal voiding cystourethrogram. Head sonogram was reported normal. She was discharged home on soy formula with recommendations to schedule a follow-up with the pediatric nephrologists, ophthalmologist, geneticist, and general pediatrician.

Discussion

Galactosemia is one of the 69 genetic diseases tested for in the State of Tennessee newborn screen. It follows an autosomal recessive inheritance pattern and is the disease process that occurs with deficiencies in the following proteins: Galactose-1-phosphate uridyl transferase (GALT), Uridine diphosphate (UDP) galactose 4-epimerase (GALE), or Galactokinase (GALK) deficiency [1]. Classic galactosemia, the most common and severe type, is a complete deficiency in the GALT protein [2]. In classic disease, the GALT enzyme activity is less than 5% of the control levels. Our index patient had the Duarte variant galactosemia that usually results in about 25% GALT protein function. Due to the higher percentage of protein function, the disease process can be less severe than classic disease [3].

Classic symptoms of galactosemia include persistent or worsening jaundice, vomiting, hepatomegaly, failure to thrive, poor feeding, lethargy, diarrhea, and sepsis. There is no case of galactosemia reported in literature which presented with severe intrauterine growth retardation and Klebsiella pneumoniae urinary tract infection without the common characteristics of hepatomegaly, bleeding disorder, vomiting, diarrhea, failure to thrive, hypoglycemia, coagulopathy, cataracts, hemolysis or renal tubular acidosis [4]. The index patient had physiological hyperbilirubinemia and mild elevation of direct bilirubin. Liver functions were in normal range. Although most infants with galactosemia manifest some form of cataracts prior to 2 weeks of age, this infant had a normal ophthalmologic exam prior to discharge at 26 days of life. For unknown reasons, *E. Coli* is the most common bacterial etiology for sepsis in infants with galactosemia [5]. It is suggested that neonates with galactosemia experience an inhibition of neutrophil function in the presence of galactose, predisposing them to higher rates of sepsis [6].

The onset of the disease may be subtle, and as the illness progresses, it can be associated with developmental delay, cataracts, and hepatosplenomegaly. Untreated patients with classic galactosemia may develop mental retardation, developmental delay, speech delay, and possible cirrhosis [7]. Long-term outcome studies have revealed that several treated patients may develop growth and developmental delays, speech disorders, neurological deficit and relatively lower intelligent quotient. Incidence of ovarian failure is reported in affected females although majority of them are able to achieve normal pregnancy [8,9,10]. The body makes small amounts of galactose despite a galactose free diet and therefore, patients can have neuropsychological sequelae despite proper treatment. The studies attempting to decrease the amount of indigenously produced galactose do not show much promise [11].

There is currently no consensus on whether infants with Duarte variant galactosemia, like the index patient, benefit from galactose restriction in the first year of life. These patients have an average of 25% GALT function, some have more, and some have less. Pediatricians are encouraged to work with families when deciding whether to restrict dietary galactose and to what degree. If galactose is restricted during infancy, then a galactose challenge should occur at age one to see if the infant has sufficient GALT activity to initiate dietary galactose

intake. If erythrocyte galactose-1-phosphate level is within the normal range (<1.0 mg/dL) then it is assumed that the infant has sufficient GALT activity and will not experience the effects of unprocessed galactose. This approach is controversial, as the sequelae of inadequate GALT function can be devastating, and many parents do not want to take that risk [11].

Conclusion

We are reporting an unusual case of an infant with severe intrauterine growth retardation who was diagnosed with galactosemia and had associated Klebsiella pneumoniae urinary tract infection. An early diagnosis and introduction of soy formula was able to avert the potential complications associated with galactosemia. No hepatosplenomegaly was noted, liver functions were in normal range, eye exam was negative for any evidence of cataract. This infant will require follow-up by multi-disciplinary medical team after discharge from the hospital.

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