Original Research Paper

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Paediatrics

CLASSICAL GALACTOSEMIA

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ABSTRACT Galactosemia is an autosomal recessive disorder caused by deficient or absent activities of one of the three enzymes involved in the galactose metabolic pathway. The predominant form is classic type galactosemia caused by severe reduction or absence of the galactose-1-phosphate uridyl transferase (GALT) enzyme. We report on a case of classical galactosemia in which the diagnosis was masked by the presence of non-specific clinical symptoms suggesting lactose intolerance. This case exemplifies the problems faced in reaching a correct diagnosis in patients with metabolic diseases demonstrating the importance of tandem mass spectrometry in correctly identifying galactosemia which may be lifesaving as treatment simply involves instituting a galactose free diet throughout life.

KEYWORDS : Galactosemia, Lactose Intolerance, Galactose-1-phosphate Uridyl Transferase (galt)

INTRODUCTION

Classical galactosemia is an inherited recessive disorder of galactose metabolism caused by deficiency of the enzyme galactose-1-phosphate uridyl transferase (GALT) [1-4]. As with other metabolic disorder, the clinical presentation of galactosemia is often nonspecific and may mimic other diseases. It is not uncommon that patients with metabolic disorders are not correctly recognized and that there is a mild delay between onset of clinical manifestations and diagnosis. In this communication, we present a case of classical galactosemia illustrating the problems faced in achieving a correct diagnosis when clinical manifestations were non-specific and non-indicative of a particular disorder

CASE REPORT

A 16-day old male infant born to second degree consanguineous parents was admitted to the pediatric ward of our hospital with a history of jaundice since birth and abdominal swelling for a few days. Baby was passing high colored urine and clay colored stools and had recurrent vomiting. He had been feeding well on breast milk until a few days earlier when he started tiring during feeds but without sweating or cyanosis. No bleeding tendencies or rashes were reported

Physical examination revealed a gross distended abdomen and superficial prominent venous pattern was visible. The weight was 3.25 kg, length was 50 cm, and occipitofrontal circumference was 32.8 cm. ophthalmic examination did not show any cataracts. There was mild hepatomegaly and no splenomegaly. Biochemical investigations showed normal blood cell and reticulocyte counts. Liver function tests showed aspartate and alanine transaminase of 387 U/L and 136 U/L, respectively (normal range: 15–45 U/L). The total serum bilirubin was 6.2 mg/dL. The serum alkaline phosphatase was 641 IU/L (range: 20–250 IU/L),serum GGT 94 (range3-22). The coagulation profile revealed a prothrombin time of 18s (normal range 10– 15s), activated partial thromboplastin time of 58s (normal range 31–54s), and an international normalized ratio of 1.58. A hypothesis for lactose intolerance was made on the basis of recurrent vomiting. The child was putoff from breast feeding and shifted to a low-protein, lactose-free, hydrolysate formula for 10 days, until the age of 26 days. He made progressive clinical improvement and recovered completely from the biochemical abnormalities. He was kept on lactose free diet and discharged from the hospital.

At the age of 1.5 months, standard formula feeding was re-introduced along with intermittent breast feeding. The child was also given supplementary oral lactase enzyme to aid in the lactose absorption. To our surprise, he was again admitted to our hospital at age of 3 months and presented with jaundice and recurrent vomiting. The child looked lethargic and emaciated. There was hepatomegaly (liver was 5 cm below right costal margin with a span of 10.5 cm) and splenomegaly (4 cm under left costal margin). The total serum bilirubin was found to be 8 mg/dl. The aspartate and alanine transaminase levels were 230 U/L and 155 U/L (normal range: 15–45 U/L), respectively, while serum alkaline phosphatase was 527 IU/L (range: 20– 250 IU/L). The prothrombin time was 14s and activated partial thromboplastin time was 37s with an international normalized ratio of 1.05. Virology study for congenital infections – toxoplasmosis, rubella, cytomegalovirus and herpes simplex virus (TORCH screen) was negative.

In view of cholestasis, galactosemia was suspected and the child was evaluated for same.sample came positive for galactosemia on tandem mass spectrometry.

The child was managed with appropriate supportive and nutritional care along with stoppage of breast feeding whilst soya-milk formula was started. His general condition progressively improved and he was discharged from the hospital after 14 days on appropriate dietary advice and multivitamin supplementation. At 5 months of follow-up, the infant is passing normal colored stools and is anicteric and gaining weight, although at a slower pace.

DISCUSSION

We present a case of a neonate with a nonspecific presentation of vomiting, failure to thrive, lethargy, and prolonged jaundice, abdominal distension. This case emphasizes the importance of thinking to rare metabolic disorders in the differential diagnosis of patients presenting with relatively non-specific symptoms.

On the basis of a large number of biochemical and clinical observations, it is evident that galactosemia can manifest in a variety of clinical pictures[6].

Milk and dairy products contain lactose, the major dietary source of galactose. The metabolism of galactose produces fuel for cellular metabolism through its conversion to glucose-1-phosphate . Galactose also plays an important role in the formation of galactosides, which include glycoproteins, glycolipids, and glycosaminoglycans. Galactosemia denotes the elevated level of galactose in the blood and is found in 3 distinct inborn errors of galactose metabolism in 1 of the following enzymes: galactose-1-phosphate uridyl transferase, galactokinase, and uridine diphosphate galactose-4-epimerase. The term galactosemia, although adequate for the deficiencies in any of these disorders, generally designates the transferase deficiency.Two forms of the deficiency exist: infants with complete or near complete deficiency of the enzyme (classic galactosemia) and those with partial transferase deficiency. Classic galactosemia is a serious disease with onset of symptoms typically by the second half of the 1st wk of life. The incidence is predicted to be 1 in 60,000 live births. The newborn infant receives high amounts of lactose (up to 40% in breast milk and certain formulas), which consists of equal parts of glucose and galactose. Without the transferase enzyme, the infant is unable to metabolize galactose-1-phosphate, the accumulation of which results in injury to kidney, liver, and brain. This injury may begin prenatally in the affected fetus by transplacental galactose derived from the diet of the heterozygous mother or by endogenous production of galactose in the fetus.

CLINICAL MANIFESTATIONS

The diagnosis of uridyl transferase deficiency should be considered in newborn or young infants with any of the following features: jaundice, hepatomegaly, vomiting, hypoglycemia, seizures, lethargy, irritability,

feeding difficulties, poor weight gain or failure to regain birth weight, aminoaciduria, nuclear cataracts, vitreous hemorrhage, hepatic failure, liver cirrhosis, ascites, splenomegaly, or intellectual disability.Symptoms are milder and improve when milk is temporarily withdrawn and replaced by intravenous or lactose-free nutrition. Patients with galactosemia are at increased risk for *Escherichia coli* neonatal sepsis; the onset of sepsis often precedes the diagnosis of galactosemia. Pseudotumor cerebri can occur and cause a bulging fontanel. Death from liver and kidney failure and sepsis may follow within days. When the diagnosis is not made at birth, damage to the liver (cirrhosis) and brain (intellectual disability) becomes increasingly severe and irreversible.

Partial transferase deficiency is generally asymptomatic. It is more frequent than classic galactosemia and is diagnosed in newborn screening because of moderately elevated blood galactose and/or low transferase activity. Galactosemia should be considered for the newborn or young infant who is not thriving or who has any of the preceding findings. Light and electron microscopy of hepatic tissue reveals fatty infiltration, the formation of pseudoacini, and eventual macronodular cirrhosis. These changes are consistent with a metabolic disease but do not indicate the precise enzymatic defect(8).

DIAGNOSIS

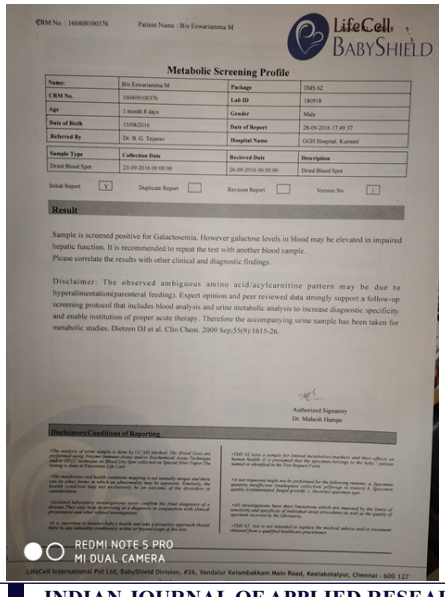
The preliminary diagnosis of galactosemia is made by demonstrating a reducing substance in several urine specimens collected while the patient is receiving human milk, cow's milk, or any other formula containing lactose. Direct enzyme assay using erythrocytes establishes the diagnosis. One needs to confirm that the patient did not receive a blood transfusion before the collection of the blood sample, as a diagnosis could be missed. A novel method utilizes nonradioactive UV and high-performance liquid chromatography to accurately detect levels of galactose-1-phosphate uridyl transferase in erythrocytes(8)

TREATMENT AND PROGNOSIS

Because of newborn screening for galactosemia, patients are being identified and treated early. Various non–lactose-containing milk substitutes are available (casein hydrolysates, soybean-based formula). Elimination of galactose from the diet along with adequate calcium supplementation reverses growth failure and renal and hepatic dysfunction. Cataracts regress, and most patients have no impairment of vision. Early diagnosis and treatment have improved the prognosis of galactosemia; however, on long-term follow-up, patients still manifestovarian failure with primary or secondary amenorrhea, decreased bone mineral density, developmental delay, and learning disabilities that increase in severity with age(8).

CONCLUSION

Every newborn with unexplained clinical manifestations like vomiting, diarrhea, weight loss, lethargy, hypotonia, jaundice, hepatomegaly, E. coli sepsis, cataracts, bleeding tendencies and liver failure should be suspected of having an inborn error of metabolism since a substantial number of these diseases respond well to treatment but may otherwise be fatal.


CRM No. : 160409100376 Patient Name : B/o Eswariamma M

LifeCell BABYSHIELD

Metabolic Screening Profile

Name:	B/o Eswariamma M	Package	TMS 62
CRM No.	160409100376	Lab ID	1805/8
Age	1 month 8 days	Gender	Male
Date of Birth	15/08/2016	Date of Report	28-09-2016 17:49:37
Referred By	Dr. B. G. Tejaswi	Hospital Name	GGH Hospital, Kurnool

Sample Type	Collection Date	Recieved Date	Description
Dried Blood Spot	23-09-2016 00:00:00	26-09-2016 00:00:00	Dried Blood Spot

Initial Report [Y] Duplicate Report [ ] Revision Report [ ] Version No. [1]

Result

Sample is screened positive for Galactosemia. However galactose levels in blood may be elevated in impaired hepatic function. It is recommended to repeat the test with another blood sample.
Please correlate the results with other clinical and diagnostic findings.

Disclaimer: The observed ambiguous amino acid/acylcarnitine pattern may be due to hyperalimentation(parenteral feeding). Expert opinion and peer reviewed data strongly support a follow-up screening protocol that includes blood analysis and urine metabolic analysis to increase diagnostic specificity and enable institution of proper acute therapy. Therefore the accompanying urine sample has been taken for metabolic studies. Dietzen DJ et al. Clin Chem. 2009 Sep;55(9):1615-26.

Authorized Signatory
Dr. Mahesh Hampe

Disclaimers/Conditions of Reporting

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