Case Report

Classic Galactosemia: A Rare Cause of Neonatal Jaundice in Infants - A Case Report

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Abstract

Classic galactosemia is a rare inborn error of galactose metabolism which is caused by a deficiency of an enzyme known as galactose-1-phosphate uridyl transferase (GALT). A 4-month-old male infant presented with yellowish discolouration of the skin and eyes (jaundice) and clay-coloured stools. On examination, the baby has normal development and no signs of chronic liver disease. Blood tests and ultrasound show raised bilirubin and liver enzymes, but no structural abnormality or biliary atresia. However, urine sugar chromatography detected galactose and lactose, and a direct enzyme assay confirmed a deficiency of galactose-1-phosphate uridyl transferase. The patient was treated with a galactosemia-based diet, non-lactose milk, and vitamin supplements and showed improvement. The patient is currently on follow-up for monitoring

Keywords: Classic galactosemia, neonatal jaundice, GALT deficiency, dietary modification, inborn errors of metabolism

Introduction

Classic galactosemia is a rare inborn error of galactose metabolism which is caused by a deficiency of an enzyme known as galactose-1-phosphate uridyl transferase (GALT).[1] It is an autosomal recessive disorder with an estimated occurrence of 1/60,000 newborns.[2]

Milk sugar contains two crucial components: glucose and galactose.[3] If breastfeeding or formula milk containing lactose is continued, infants with GALT shortage may develop any or all of the non-specific symptoms such as poor feeding; weight loss; convulsions; irritability; lethargy; vomiting; or jaundice. Hepatomegaly, ascites, aminoaciduria, or hypoglycemia are the important signs in these patients.[4,5] Early detection of signs and symptoms and prompt dietary limitation of galactose can stop the onset of complications like cataracts, premature ovarian failure, the decline in bone mineral density, and mental retardation.[5] Once complications start to develop, it becomes a potentially fatal condition for infants.[6]

It is challenging for medical professionals to make a differential diagnosis of classic galactosemia due to its rarity and non-specific clinical symptoms, including jaundice, lethargy, and poor feeding.[4] Its diagnosis is confirmed by urinalysis for reducing chemicals and ketones, urine chromatography for galactose, measurement of GALT activity in RBC, and blood culture for bacterial infection (E. coli sepsis). However, neonatal screening for galactosemia using a heel-prick test and perinatal diagnosis by direct enzyme analysis of amniocytes or chorionic villi are both considered to be very effective for early diagnosis and good prognosis of the disease.[5]

This case report follows the CARE 2013 guidelines.[7] It describes a very rare presentation of jaundice in infants that finally results in the diagnosis of classic galactosemia. This case report aims to increase awareness of this rare disease and emphasize the significance of its early detection by newborn screening, which can improve outcomes and disease progression.

Case Presentation

The 4-Month-old male infant resident of Rawalpindi presented in OPD on with the complaint of yellowish discolouration of skin and eyes since 1 month of age. Jaundice was insidious in onset, slow in progression, and was associated with Clay-colored stools (off & on) and dark-coloured urine. There was no history of abdominal distension, swelling of any part of the body, vomiting, pruritis, petechiae, bruises, or constipation. Furthermore, there was no history of fever, lethargy, reluctance to feed, fits, cough, breathing difficulty, orthopnea, paroxysmal nocturnal dyspnea, or loss of consciousness. The patient had not received any treatment for this illness before admission. He is a full-term infant with uncomplicated delivery. There is no significant antenatal, natal, or postnatal history. Baby exclusively breastfed till 3 months of age and is now on formula feeding for one month. Caloric intake at present is 400 kcal/day. He was vaccinated according to the EPI schedule till now, BCG scar is positive. His developmental history is normal as he started holding his neck at 3.5 months (Gross motor), grasping rattle at 3.5 months (Fine motor), and smiling in response to face and voice at 2 months of age (Communication skills).

On general physical examination, he was an icteric child with no facial dysmorphism, no peripheral

stigmata of chronic liver disease, no corneal opacity, and no evidence of petechiae, bruises, or pruritic marks. Vitals were as follows heart rate 110/min, temperature 98.6 ^{0}F, blood pressure 90/60mmHg, respiratory rate 38/min, blood sugar (random) 85mg/dl.

He has normal anthropometry measures such as a head circumference of 41 cm (25th centile), length of 64.8cm (50th centile), and Weight of 5.5 kg (5th centile).

There was a distended abdomen with no prominent veins, scar marks, and pulsations. The liver was palpable 5cm below the costal margin (firm and regular margins) with a total span of 10.5cm, spleen and bilateral kidneys were not palpable. There were no signs of free fluid in the abdomen. Respiratory, CNS, and CVS examinations were not remarkable.

On basis of the causes of yellowish discolouration of eyes in infants, we made the differential diagnosis of cholestasis secondary to biliary atresia, progressive familial intrahepatic cholestasis, or idiopathic neonatal hepatitis. Moreover, we suspected inborn errors of metabolism (Galactosemia), storage disorder (Glycogen storage disease), and TORCH infections.

Several investigations were done to have a definitive diagnosis. Complete blood count (CBC) showed low Hemoglobin (Hb), raised TLCs, and raised PLTs. Total and direct bilirubin was raised. Renal function tests (RFTs) and serum electrolytes were slightly deranged. Random blood sugar (BSR) was normal. Liver function tests (LFTs) were deranged, with raised bilirubin, and alanine transaminase (ALT), but alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) were normal **(Table-I).**

Table-I Laboratory Investigations

INVESTIGATION	RESULT	REFERENCE VALUE	INTERPRETATION
Hemoglobin (Hb)	9.8 g/dl	12 – 16 g/l	Low
TLCs	13.6*10^3/µL	4 – 11 *10^3/µL	High
PLTs	616*10^3/µL	150 – 450 *10^3/µL	High
Total Bilirubin	11 mg/dl	Up to 1.2 mg/dl	High
Direct Bilirubin	9.1 mg/dl	-	High
Indirect Bilirubin	1.1 mg/dl	-	Slightly raised
ALT	102.4 U/L	Up to 43 U/L	High
ALP	549.2 U/L	Up to 705 U/L in Children	Normal
GGT	Normal	-	Normal
PT / APTT	Normal	-	Normal

Serum Albumin	4.8 g/dl	3.4 – 5.4 g/dl	Normal
BSR	86 mg/dl	Up to 100 mg/dl	Normal
Serum sodium	147 mEq/L	135- 145 mEq/L	Slightly Raised
Serum Potassium	4.9 mEq/L	3-5 mEq/L	Normal
Serum Chloride	111 mEq/L	95-108 mEq/L	Slightly Raised
Serum Urea	15 mg/dl	15 – 50 mg/dl	Normal
Serum Creatinine	0.3 mg/dl	0.7 – 1.2 mg/dl	Low

X-ray was done to identify any underlying lung pathology, but this was normal too. Ultrasound abdomen showed hepatomegaly with no structural abnormality, and no evidence of biliary atresia was found on the HIDA scan (FIGURE-1). Moreover, Arterial blood gases, LDH, uric acid, TORCH titer, thyroid profile, eye evaluation, and echocardiography were unremarkable.

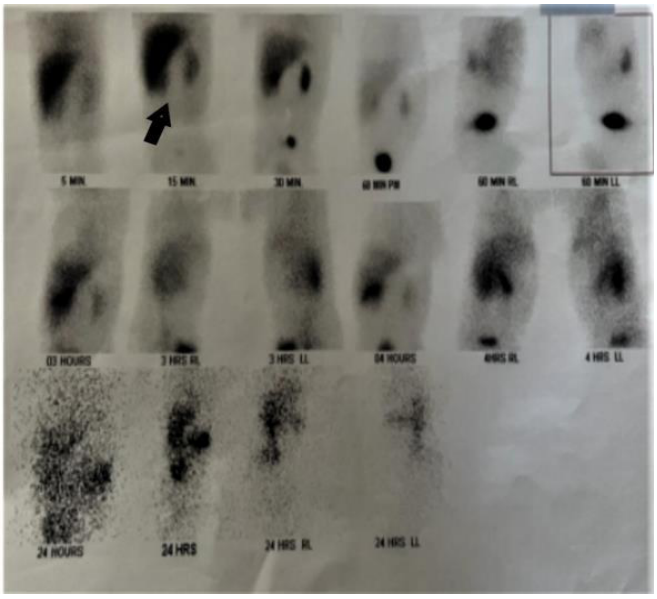

FIGURE 1 HIDA SCAN

HIDA scan is negative for biliary atresia, meaning the bile ducts are not obstructed or narrowed. Arrow showing the prompt filling of the gallbladder with a radioactive tracer and the normal flow of bile through the liver and bile ducts.

Galactose and lactose were detected in urine sugar chromatography. Based on the findings of urine sugar chromatography, we suspect it as a case of galactosemia (TABLE-2). Direct enzyme assay (GALT) on erythrocytes was done to confirm the diagnosis which showed a deficiency of galactose-1-phosphate uridyl transferase (5.9 umol/m/g Hb).

Table-II Urine Chromatography Report.

Urine sugars	Result
Lactose	Detected
Galactose	Detected
Sucrose	Not Detected
Glucose	Not Detected
Fructose	Not Detected
Xylose	Not Detected

Galactosemia-based diet chart and non-lactose milk were introduced as management. Moreover, the patient was given multiple vitamins for dietary insufficiency (Vitamin A 10,000 IU/day, vitamin E 200 IU/day, vitamin D 5000IU/day, vitamin K 5mg/day, syrup B complex 5ml/day). The patient showed remarkable improvement on this dietary modification and currently is on follow-up with continuous monitoring of anthropometric measures, compliance with dietary modifications, liver function tests, renal function tests with urine indices, eye evaluation, developmental assessment, and neurological evaluation.

Discussion

Classic galactosemia is a rare autosomal recessive disorder characterized by a deficiency of galactose-1-phosphate uridyl transferase (GALT). Symptoms present earlier with severe jaundice, hepatomegaly, failure to thrive and vomiting[2], and later with cataracts and E. coli sepsis.[8] In our case report, a 4-month-old male child was brought to the Pediatric Department of Benazir Bhutto Hospital, Rawalpindi, with a history of severe jaundice associated with dark urine, clay-colored stools, and hepatomegaly without splenomegaly. All these symptoms were non-specific. Confirmation of diagnosis was made through urine sugar chromatography and GALT enzyme assay, which revealed a deficiency.

Cataracts have been reported in 14-30% of galactosemia patients, and increased indirect bilirubin is a frequent early finding.[8,9] Signs and symptoms usually resolve with lactose- and galactose-free diet within a month of onset of diarrhea.[9] Early diagnosis through neonatal screening, such as urine chromatography and GALT enzyme assays, is essential to avoid the serious complication of psychomotor retardation associated with toxic galactose levels, liver damage and long-term neurological deficits.[10]

Classic galactosemia is relatively frequent in Pakistan compared to its rarity globally. A study conducted in Pakistan identified 22 cases of galactosemia among 239 patients evaluated for suspected inherited metabolic disorders.[11] However, in Rawalpindi, no case studies have been reported to date, highlighting its rarity in the region. Other similar cases reported in the

literature have presented with atypical symptoms, such as irritability, hypotonia, and recurrent bacterial infections. For instance, one case in Lithuania presented with severe renal tubular acidosis and jaundice during the initial assessment.[9] The Galactosemia Network (GalNet) stresses the necessity of lifelong dietary restriction of galactose and lactose, combined with vigilant observation of developmental milestones and metabolic health, to minimize long-term risks. Universal newborn screening currently remains the best strategy for early diagnosis and good prognosis.[12]

Conclusion

Galactosemia patients present with non-specific clinical symptoms, including jaundice, lethargy, and poor feeding. Early detection of signs and symptoms and prompt dietary limitation of galactose can stop the onset of complications like cataracts, premature ovarian failure, the decline in bone mineral density, and mental retardation. Once complications start to develop, it becomes a potentially fatal condition for infants.

References

1. Coelho AI, Rubio-Gozalbo & ME, Vicente JB, Rivera I. Sweet and sour: an update on classic galactosemia. Wiley Online Libr [Internet]. 2017 May 1 [cited 2022 Oct 23];40(3):325–42. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1007/s10545-017-0029-3

2. Lewis V, Welch F, Cherry F, … EF-TJ of the, 1995 undefined. Galactosemia: clinical features, diagnosis and management. A case report. europepmc.org [Internet]. [cited 2022 Oct 23]; Available from: https://europepmc.org/article/med/7642981

3. Sasaoka N, Imamura H, Iscience AK-, 2018 undefined. A trace amount of galactose, a major component of milk sugar, allows maturation of glycoproteins during sugar starvation. Elsevier [Internet]. [cited 2022 Oct 23]; Available from: https://www.sciencedirect.com/science/article/pii/S2589004218302256

4. Kavehmanesh Z, … MT-TA of, 2020 undefined. A case of classic galactosemia manifesting as neonatal early and profound indirect hyperbilirubinemia. ncbi.nlm.nih.gov [Internet]. [cited 2022 Oct 23]; Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7536454/

5. Saleem U, Author C, Ahmad B. PREVALENCE, EPIDEMIOLOGY AND CLINICAL STUDY OF GALACTOSEMIA. J App Pharm. 2012;01(04):524–30.

6. Demirbas D, Coelho A, Rubio-Gozalbo M, Metabolism GB-, 2018 undefined. Hereditary galactosemia. Elsevier [Internet]. [cited 2022 Oct 23]; Available from: https://www.sciencedirect.com/science/article/pii/S0026049518300337

7. Riley DS, Barber MS, Kienle GS, Aronson JK, Von Schoen-Angerer T, Tugwell P, et al. CARE guidelines for case reports: explanation and elaboration document. Elsevier [Internet]. 2017 [cited 2022 Oct 23];89:218–35. Available from: https://www.sciencedirect.com/science/article/pii/S0895435617300379

8. Woo HC, Phornphutkul C, Laptook AR. Early and severe indirect hyperbilirubinemia as a manifestation of galactosemia. J Perinatol. 2010 Apr;30(4):295–7.

9. Rokaitė R, Traberg R, Dž enkaitis M, Kuč inskienė R, Labanauskas L. Two Lithuanian Cases of Classical Galactosemia with a Literature Review: A Novel GALT Gene Mutation Identified. Medicina (Kaunas) [Internet]. 2020 Nov 1 [cited 2022 Oct 23];56(11):1–7. Available from: https://pubmed.ncbi.nlm.nih.gov/33113773/

10. Olivera J, Elcarte R, Erice B, … PO-AE, 1986 undefined. Galactosemia of early diagnosis with psychomotor retardation. europepmc.org [Internet]. [cited 2022 Oct 23]; Available from: https://europepmc.org/article/med/3800174

11. Perspective on newborn screening (NBS) [Internet]. eCommons@AKU. Available from: https://ecommons.aku.edu/cgi/viewcontent.cgi?article=2389&context=pakistan_fhs_mc_pathol_microbiol [Accessed 2025 Jan 28].

12. Welling L, Bernstein LE, Berry GT, Burlina AB, Eyskens F, Gautschi M, et al. International clinical guideline for the management of classical galactosemia: diagnosis, treatment, and follow-up. J Inherit Metab Dis [Internet]. 2017 Mar 1 [cited 2022 Oct 23];40(2):171–6. Available from: https://onlinelibrary.wiley.com/doi/full/10.1007/s10545-016-9990-5