DILEMMA IN DIAGNOSING A CASE OF GALACTOKINASE DEFICIENCY WITH AN UNUSUAL PRESENTATION: A CASE REPORT

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ABSTRACT

An infant with metabolic disorder can have vague presentations like repeated chest infections, feeding intolerance and failure to thrive. This may lead to a diagnostic dilemma.

Detailed clinical history together with biochemical investigations are must to reach a diagnosis. Galactokinase Deficiency (GKD) has a varied presentation with some features like microcephaly, juvenile cataracts and failure to thrive. We encountered a case of GKD in an infant in which there was an absence of cataracts. Raised Immunoreactive Trypsinogen (IRT) in Newborn Screening was strongly suggestive of Cystic Fibrosis (CF), however Genetic Analysis revealeda heterozygous missense variation in EXON4 of the GALK1 GENE, confirming the diagnosis of GKD. Hence, this case highlights the importance of considering different metabolic disorders as differential diagnoses of one another even in absence of a typical feature of a particular disorder.

KEYWORDS

Cystic fibrosis, Galactokinase, GALK1 Gene, Immunoreactive Trypsinogen

INTRODUCTION

Inborn errors of metabolism are disorders that have non specific symptoms at presentation including lethargy, poor feeding, recurrent chest infections and vomiting. Newborns especially full term with these symptoms with no other risk factors should be kept under strong suspicion after sepsis has been ruled out. Therefore, biochemical tests along with genetic evaluation is a must to rule out pathologies which can produce similar clinical features.[1] Galactokinase deficiency (GKD), a mild type of Galactosemia is an autosomal recessive disorder that presents with early onset of juvenile bilateral cataract and failure to thrive if not treated can lead to mental retardation in later life. [2] Infants with GKD typically present with feeding intolerance as soon as the breast milk feeding is started followed by jaundice, abnormal liver function tests, coagulation disorder and hepatomegaly due to hepatocellular damage. *Escherichia coli* sepsis is a life-threatening complication in every case. Early onset of juvenile cataract is a common presentation of GKD.[3]

CASE REPORT

A 10 weeks old male child presented to the pediatric OPD with symptoms of fever, cough, fast breathing and feed intolerance. On examination the child had bilateral crepitations, wheeze over the chest and hepatomegaly of 4cm below right costal margin along the mid clavicular line. Thus Liver Function Tests and Ultrasonography Abdomen were conducted which came back normal. Chest Xray revealed pneumonia for which he was treated for a total of 10 days with intravenous antibiotics in the Neonatal Intensive Care Unit (NICU) after which he was discharged. However the baby still continued to have repeated chest infections and an inability to feed when examined at the ages of 12 and 14 weeks respectively. On both occasions, sepsis screening was negative and blood culture was sterile. CT chest done during this period showed aspiration pneumonia which was treated appropriately. Echo heart showed peri membranous Ventricular Septal Defect (VSD) (2.6mm) and Atrial Septal Defect / Patent Foramen Ovale (PFO) both left to right shunt with mild Mitral regurgitation with normal Pulmonary Artery pressure. Stool examination showed presence of reducing substance and abundant fat globules therefore his feeding was switched to lactogen free formula milk.

The child was born to non-consanguineous parents with an uneventful pregnancy via Emergency Lower Segment Cesarean Section (LSCS) for Oligohydramnios, at 40 weeks of gestation. Postnatally the baby was admitted in NICU and managed for Transient Tachypnea of Newborn. He was formula fed along with breastfeeding due to inadequacy of breast milk. At 4 weeks of life, he was admitted for multiple episodes of non bilious non projectile vomiting. For this, he was admitted, investigated further and sepsis was ruled out. Ophthalmological examination done routinely ruled out cataracts. Baby was discharged after improvement.

With all of this in mind, a clinical suspicion of a metabolic disorder was made. Essential Newborn Metabolic Screening was done. Result revealed elevated Immunoreactive Trypsinogen (IRT) which was suggestive of Cystic Fibrosis. The baby was discharged with vitamins and pancreatic enzyme supplements. Parents were counselled accordingly and the baby was kept on close follow up.

At the age of 6 months the baby again presented with fever and shortness of breath and multiple episodes of loose, greasy, mustard colored foul-smelling stool.

During this visit, genetic analysis was done which revealed a heterozygous missense variation in EXON 4 of the GALK1 GENE confirming the diagnosis of GKD. Ophthalmic examination revealed no cataracts.

Once the diagnosis was confirmed, the parents were counseled and educated about the condition of their baby. They were advised regarding a strict galactose free diet (mainly to avoid dairy products) for the baby throughout his life. The baby is currently on a monthly follow up regimen. Currently the baby is hemodynamically stable, tolerates feed and is gaining weight.

DISCUSSION

Newborn screening tests may be suggestive but not conclusive for diagnosing a particular disorder. In this case of a term neonate who presented with repeated chest infections and failure to thrive had raised immunoreactive trypsinogen (IRT) which is usually suggestive of cystic fibrosis (CF). There have been different investigation strategies implemented worldwide for CF but the approach varies from immunoreactive trypsinogen (IRT), cystic fibrosis transmembrane receptor (CFTR) mutation analysis or both.[4] Raised IRT alone cannot be conclusive for CF, IRT/IRT/DNA is more sensitive than IRT/IRT alone.[5]

In case of GKD, feeding intolerance can cause failure to thrive, recurrent vomiting, leading to aspiration pneumonia, hence multiple hospital admissions. Previous studies have shown that GKD classically presents as neonatal illness in 79.8% of cases where, elevated liver enzymes in 70.3%, bleeding diathesis in 42.5% , encephalopathy in 29.0% , clinical signs of infection in 27.4%, cataract in 25.8% and hypoglycemia in 25.1%.[6] However, absence of these typical features doesn't necessarily rule out GKD. Unusually a child with galactosemia can present with cataract at late childhood too.[7]

Term infants without perinatal complications presenting with feeding intolerance, repeated chest infections and failure to thrive should be investigated with scrutiny and managed as early as possible. Monitoring and management of complications including neuro developmental delay, cataracts and growth retardation is more imperative for the quality of life of these infants.

CONCLUSION

Inborn errors of metabolism have vague clinical presentations. Therefore, strong suspicion with consummate laboratory investigation aids in its early diagnosis and management. Regular follow up, dietary regulations and timely interventions is a must to eliminate complications as much as possible.

PATIENT CONSENT

Informed written consent has been taken from the parents of the child.

CONFLICTS OF INTEREST

None

REFERENCES

1. Burton BK. Inborn errors of metabolism in infancy: a guide to diagnosis. Pediatics.1998 Dec; 102 (6) E69 .doi :10.1542/ peds.102.6.e69. PMID:9832597
2. Hennermann, J.B., Schadewaldt, P., Vetter, B. et al. Features and outcome of galactokinase deficiency in children diagnosed by newborn screening. J Inherit Metab Dis 34, 399–407 (2011). https://doi.org/10.1007/s10545-010-9270-8
3. Adam M.P,Ardinger H , Berry G.T. , Pagon R. A. et al., Classic galactosemia and clinical variant galactosemia. In:eds. GeneReviews® [Internet]. Seattle: University of Washington; 1993–2016.
4. Sinclair G,McMahon V, Schellenberg A, Nelson TN,Chilvers M, Vallance H. Performance of a Three-tier (IRT-DNA-IRT) Cystic Fibrosis Screening Algorithm in British Columbia.Int J Neonatal Screen. 2020Jun 2;6(2):46. doi :10.3390/ijns6020046. PMID: 33073036 ;PMCID :PMC7423010.
5. Sontag MK, Lee R, Wright D, Freedenberg D,Sagel SF. Improving the Sensitivity and Positive Predictive Value in a Cystic Fibrosis Newborn Screening Program Using a Repeat Immunoreactive Trypsinogen and Genetic Analysis .J Prediatr.2016 Aug ; 175:150-158.el.doi: 10.1016/j.jpeds.2016.03.046.Epub 2016 Apr 27. PMID27131402.
6. A.M.,Bosch, Haskovic, M., M.E., Rubio-Gozalbo, et al. The natural history of classic galactosemia: lessons from the GalNet registry. Orphanet J Rare Dis 14, 86 (2019). https://doi.org/10.1186/s 13023-019-1047-z
7. Jennifer J. MacKenzie, Sarah M. Simpson, Yi NingJ.Strube E194-E196 (August 01,2019). Atypical late presentation of galactosemia VOLUME 54, ISSUE4 https://doi.org/10.1016/j.jcjo.2018.10.004