VOLUME - 14, ISSUE - 08, AUGUST - 2025 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Paediatrics

CONGENITAL HYPERINSULINEMIC HYPOGLYEMIA – A RARE CASE REPORT

Dr. Vishaka Shankar	3rd Year Post Graduate, Department Of Paediatrics, Sri Devaraj Urs Medical College, Tamaka, Kolar – 563101
Dr. Karthik S.	Assistant Professor, Department Of Paediatrics, Sri Devaraj Urs Medical College, Tamaka, Kolar – 563101.
Dr. C. Srikanth.	Associate professor, Department of Paediatrics, Sri Devaraj Urs Medical College, Tamaka, Kolar – 563101.
Dr. Krishnappa J.	Professor, Department Of Paediatrics, Sri Devaraj Urs Medical College, Tamaka, Kolar –563101.

KEYWORDS :

INTRODUCTION:

Congenital hyperinsulinism (CHI) has an estimated incidence of 1/50,000 live births and is the most common cause of severe and persistent hypoglycaemia (hyperinsulinemic hypoglycaemia, HH) in the neonatal, infancy and childhood periods. Early diagnosis and treatment positively influence the prognosis, preventing permanent brain damage. Most commonly, CHI is the consequence of loss-of-function (LOF) mutations in the ABCC8 (SUR1) and KCNJ11 (Kir6.2) genes located on chromosome 11p15.1, which encode the adenosine triphosphate (ATP)-sensitive potassium channel (K_{ATP}) of pancreatic cells. Mutations of other genes involved in the regulation of insulin secretion are rarely identified: GCK, GLUD1, HADH, SLC16A1, HNF4A, HNF1A, UCP2, HK1 and PGM1.[1] Hyperinsulinemic hypoglycaemia (HH) is the leading cause of prolonged and persistent hypoketotic hypoglycaemia in neonates. Insulin secretion occurs excessively and uncontrollably, even in the presence of low plasma glucose concentrations in the affected neonates. Hypoglycaemia can present on a wide spectrum, from asymptomatic to life-threatening apnea or status epilepticus. Due to the crucial role of glucose as the primary source of energy for the neonatal brain and the absence of ketone bodies as an alternative energy source in HH, persistent and severe hypoglycaemia can result in irreversible cerebral damage and long-term neurological sequelae, including developmental delay, cerebral palsy, and epilepsy in infants.[2]

Case Report:

A single live term male baby was extracted by LSCS with birth weight of 4.02 kg. Baby cried immediately after birth. Baby was shifted to NICU in view of respiratory distress. At admission to NICU baby was active and plethoric with tachypnea of 66cpm and saturation being 94% on 2 liters oxygen support via nasal prongs. Systemic examination done revealed Respiratory system - Mild bilateral subcostal retractions with Downe's score of 3. Baby was started on IV fluids and other supportive management. GRBS was low in view of which GIR 6 was started. In view of persistent respiratory distress baby was connected to HFNC support. In view of persistent hypoglycemic episodes GIR was increased, Inj Hydrocortisone was started. Critical samples sent revealed RBS of 20mg/dl. In view of persistent hypoglycemic episodes, Pediatric Endocrinologist opinion was taken, and Injection Octreotide was started. Baby was regularly monitored. As distress was resolving HFNC was weaned off to oxygen support via nasal prongs. In view of further hypoglycemic episodes, Octreotide dose was increased and GIR was continued. Baby had further hypoglycemic episodes in view of which Pediatric Endocrinologist opinion was taken, and Tab Diazoxide was started. As baby was maintaining GRBS, IV fluid was tapered accordingly. Molecular Genetic Investigation sent revealed that variation lies in the ABC Transmembrane domain of the ABCC8 protein. Pediatric endocrinologist opinion was taken, and Inj Octreotide was made subcutaneous, and Tab Sirolimus was started. DBF was continued, mother was counseled regarding feeding practices and Octreotide and Sirolimus administration. Baby was hemodynamically stable, tolerating feeds well with no further hypoglycemic episodes. Hence baby was discharged with advice to continue Inj Octreotide SC, Tab Sirolimus and Pre and Post feed GRBS monitoring. Regular follow-ups were advised.

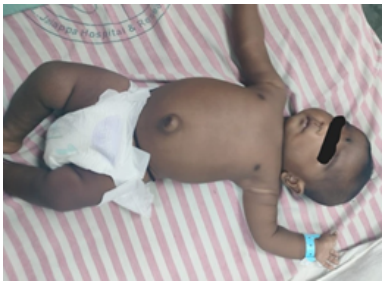

Fig 1. Day 10 of life

Result:

S. No	Genomic position	Gene (Strand)	c.DNA Position	Amino acid change	Location
1	Chr11:17395665 G>A	*ABCC8* (-)	c.4252 C>T (ENST00000389817.8)	p.Arg1418Cys	Exon 35

Fig 2. Molecular genetic test result

DISCUSSION:

Neonatal Hypoglycaemia and Hyperinsulinism: Neonatal hypoglycaemia is a common but potentially life-threatening condition, which, if untreated, can lead to neurological sequelae. In this case, the baby's recurrent episodes of hypoglycaemia and failure to respond to standard interventions (e.g., increasing the glucose infusion rate or GIR) suggested a possible congenital hyperinsulinism. This condition is characterized by the unregulated secretion of insulin from pancreatic β-cells, leading to excessive glucose uptake and hypoglycaemia.

Given the severity and persistence of the hypoglycaemic episodes, the decision to initiate Octreotide, a somatostatin analog, was appropriate. Octreotide inhibits insulin release by binding to somatostatin receptors on β-cells, thus helping to manage hyperinsulinism. The addition of Diazoxide, which works by opening K_ATP channels to inhibit insulin secretion, was a step forward as well, highlighting the multifaceted

approach required in the management of congenital hyperinsulinism.

Genetic Investigation And Molecular Basis: The pivotal finding in this case was the genetic investigation that revealed a mutation in the ABCC8 gene. This gene encodes the sulfonylurea receptor 1 (SUR1), a critical component of the K_ATP channel in pancreatic β-cells. Variants in this gene are associated with congenital hyperinsulinism, which can present in the neonatal period with severe, refractory hypoglycaemia. ABCC8 mutations are among the most common causes of persistent neonatal hypoglycaemia and are often treated with Diazoxide, Octreotide, or, in severe cases, pancreatectomy.

The discovery of the ABCC8 gene mutation in this case confirms the diagnosis of congenital hyperinsulinism due to ABCC8-related dysfunction. This underscores the importance of genetic testing in the diagnosis and management of neonatal hypoglycaemia, particularly in cases where the clinical course is not responding to conventional treatment.

Management and Treatment Plan: The treatment strategy for this neonate was comprehensive and involved multiple specialists. The paediatric endocrinologist's opinion was crucial in optimizing the management plan, starting with IV fluids to correct hypoglycaemia and later transitioning to oral therapies like Sirolimus, which inhibits mTOR signalling and has been shown to improve glucose metabolism in congenital hyperinsulinism.

The use of Octreotide and Sirolimus represents an evolving therapeutic approach in hyperinsulinism management. It highlights the need for personalized care based on the specific genetic mutations identified, which directly impact the pharmacological treatment regimen.

Regular monitoring of blood glucose levels (pre- and post-feeding) was essential in ensuring the baby's condition stabilized, with appropriate adjustments made to fluid therapy and medication as necessary. Continued long-term management of blood glucose levels remains crucial.

Follow-up and Prognosis: The prognosis for neonates with ABCC8-related hyperinsulinism is generally favourable with proper treatment and follow-up, especially when managed with medications such as Octreotide and Sirolimus. Early intervention and regular follow-ups help prevent neurodevelopmental sequelae often associated with untreated hypoglycaemia.

The importance of family counselling regarding the management of Octreotide injections and Sirolimus administration is critical to ensure compliance and proper home care. Regular follow-up visits will help monitor the baby's glucose levels, growth, and development to ensure a favourable outcome.

CONCLUSION:

The baby was discharged with advice to continue Inj Octreotide SC, Tab Sirolimus and Pre and Post feed GRBS monitoring. Regular follow-ups were advised. Parents were counselled regarding need for regular evaluation of the child for neurodevelopmental retardation and various neurological disorders, including epilepsy and microcephaly in the long-term. The baby having a severe form of the disease (based on maximal diazoxide dose) and early presentation (<7 days following birth) being associated with abnormal neurodevelopment. Therefore, the need for monitoring neurological development closely was explained. The baby having mutation of ABCC8 protein and hence likely to have diffuse hyper functioning islets throughout the pancreas and probable need for subtotal pancreatectomy (leaving approximately 5% residual pancreas) to reduce hypoglycaemia in the future was explained to the parents. The child is currently on Inj Octreotide SC, Tab Sirolimus and Pre and Post feed GRBS monitoring and is under regular follow-ups in Paediatric OPD at RLJH, Kolar.

This case emphasizes the critical role of early genetic testing in diagnosing congenital hyperinsulinism, particularly in neonates with refractory hypoglycaemia. The combination of Octreotide, Diazoxide, and Sirolimus offers a promising approach to managing this complex condition. Continued follow-up will be essential to ensure the baby remains free from further hypoglycaemic episodes and to assess long-term growth and development.

REFERENCES:

1. Demirbilek H, Hussain K. Congenital hyperinsulinism: diagnosis and treatment update. Journal of clinical research in pediatric endocrinology. 2017 Dec;9(Suppl 2):69.
2. Estebanez MS, Worth C, Banerjee I. Congenital Hyperinsulinism–Notes for the General Pediatrician. Indian Pediatrics. 2024 Jun;61(6):578-84.
3. Butnariu LI, Bizim DA, Păduraru G, Păduraru L, Moisă ŞM, Popa S, et.al. Congenital Hyperinsulinism Caused by Mutations in ABCC8 Gene Associated with Early-Onset Neonatal Hypoglycemia: Genetic Heterogeneity Correlated with Phenotypic Variability. International Journal of Molecular Sciences. 2024 May 19;25(10):5533.
4. Tiberi V, Cherubini V, Iannilli A, Gasparini F, Marino M. Adjustment of octreotide dose given via insulin pump based on continuous glucose monitoring (CGM) in a child with congenital hyperinsulinism. Journal of Pediatric Endocrinology and Metabolism. 2023 Aug 28;36(8):803-7.
5. Bezirganoglu H, Okur N, Celik K, Tas FF, Ozbek MN. Evaluation and management of neonatal onset hyperinsulinemic hypoglycemia: a single neonatal center experience. The Journal of Maternal-Fetal & Neonatal Medicine. 2023 Dec 15;36(2):2272014.
6. Panigrahy N, Chirla DK, Bagga N, Gunda RK, Sukhija B, Reddy L. Sirolimus in infants with congenital hyperinsulinism (CHI)—a single-centre experience. European Journal of Pediatrics. 2022 Jan 1:1-6.
7. Karlekar MP, Sarathi V, Arya S, Flanagan SE, Patil V, Lila A, et.al. Octreotide-LAR is a Useful Alternative for the Management of Diazoxide-Responsive Congenital Hyperinsulinism. Hormone and Metabolic Research. 2021 Nov;53(11):723-9.
8. Salomon-Estebanez M, Yau D, Dunne MJ, Worth C, Birch S, Walewski JL, et.al. Efficacy of dose-titrated glucagon infusions in the management of congenital hyperinsulinism: A case series. Frontiers in Endocrinology. 2020 Sep 3;11:441.