CASE REPORT

Navigating the Complexity of Hyper-insulinemic Hypoglycaemia: Insights and Strategies

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Abstract

Neonatal hyperinsulinemic hypoglycaemia (NHH) is a complex metabolic disorder characterized by dysregulated insulin secretion leading to persistent hypoglycaemia. We present a detailed case report of a 34-weeks male neonate with low birth weight (LBW) and intrauterine growth restriction (IUGR) who exhibited recurrent asymptomatic hypoglycaemia despite conventional treatment measures. Through a systematic diagnostic approach and targeted therapy, we successfully managed the patient's condition, ultimately achieving normoglycemia and favourable clinical outcomes.

Keywords: Neonatal Hyper-insulinemic Hypoglycaemia, Neonatal Hypoglycaemia, Diazoxide, Octreotide

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Introduction

Neonatal hypoglycaemia is a common metabolic disorder affecting up to 15% of newborns, with various etiologies ranging from transient to persistent forms. Among these, neonatal hyperinsulinemic hypoglycaemia (NHH) stands out due to its unique pathophysiology and clinical challenges. NHH is characterized by excessive insulin secretion leading to persistent hypoglycemia, which, if left untreated, can result in serious neurologic sequelae. Despite advances in neonatal care, the diagnosis and management of NHH remains complex, requiring a multidisciplinary approach for optimal outcomes.

Case Presentation

A 34-weeks male neonate weighing 1.34 kg was delivered via spontaneous vaginal delivery to a 26-year-old primigravida mother with an uneventful antenatal history, except for the diagnosis of IUGR on routine ultrasound scans. The infant required immediate resuscitation at birth due to respiratory distress (RD) and was subsequently admitted to the Neonatal Intensive Care Unit (NICU) for further management. Upon admission, the infant was started on continuous positive airway pressure (CPAP) and intravenous fluids (D10%) to support respiratory function and maintain adequate hydration and blood sugar level.

Within two hours of life, the respiratory distress resolved, and CPAP was discontinued. However, during routine blood glucose monitoring, the neonate was found to have asymptomatic hypoglycaemia with a blood sugar level (BSL) of 35 mg/dL. A bolus of D10% was administered, but despite this, the patient continued to experience recurrent hypoglycaemic episodes. Glucose infusion rate (GIR) was gradually increased up to 11 mg/kg/min to maintain

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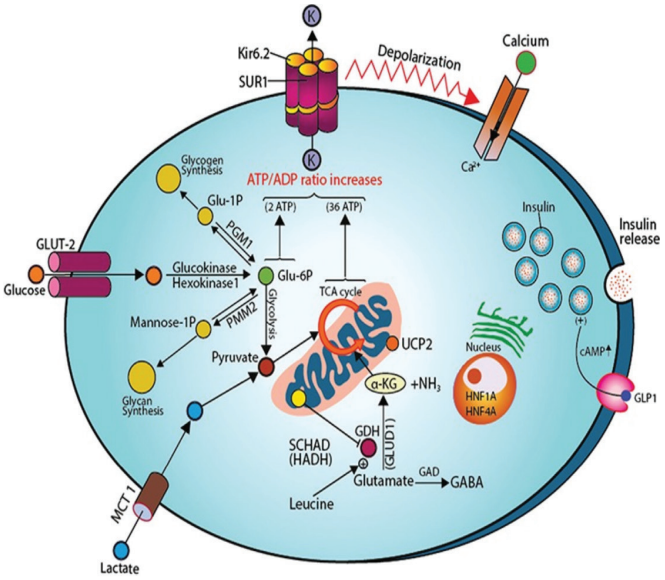

Figure 1: Regulation of insulin release from beta cells and sites of gene mutations involved in genetic etiology of hyperinsulinemic hypoglycemia.

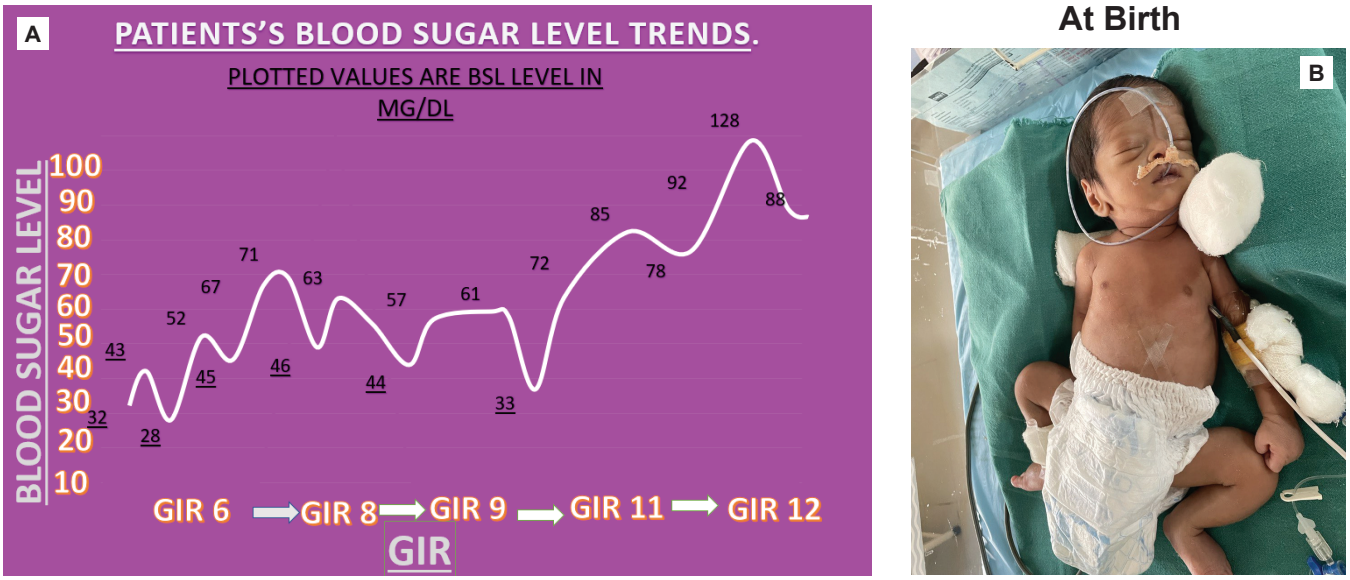

Figure 2: (A) Graphical representation of Blood sugar level of patient. **(B)** Patient in Neonatal Intensive Care Unit (NICU).

normoglycemia, but attempts to taper GIR resulted in recurrent hypoglycaemia.

Given the persistent hypoglycaemia despite high GIR, critical samples were obtained at a BSL of 33 mg/dL for further evaluation. Serum insulin and c-peptide levels were found to be elevated (2.49 mU/L and 2.48 ng/mL, respectively), suggestive of hyper-insulinemic hypoglycaemia. Additionally, serum ammonia levels were elevated at 113 mcg/dL, indicating a potential metabolic disturbance. Urine ketones were absent, ruling out ketotic hypoglycaemia.

Based on the diagnostic findings, the patient was initiated on subcutaneous injections of octreotide (25 mcg/dose) administered four times daily. With octreotide therapy, blood sugar levels stabilized, allowing for a gradual tapering of GIR. Subsequently, the patient was transitioned to an oral regimen of diazoxide, a potassium channel opener known to inhibit insulin secretion. With diazoxide therapy, the patient maintained stable blood sugar levels without experiencing further hypoglycaemic episodes.

During the hospital course, the patient's parents were extensively counselled on the nature of the condition, treatment modalities, and the importance of vigilant glucose monitoring. Additionally, they received training on administering medications and recognizing signs of hypoglycaemia. Upon achieving stable glycaemic control, the patient was discharged home with close outpatient follow-up.

Table 1: Test results of Serum Insulin, Serum Ammonia, C-peptide, and Urine Ketones.

TESTS	RESULTS	
SERUM INSULIN	24.9 µU/L	2.0 to23 µU/L
SERUM AMMONIA	113 µ/dl	(<45 µ/dl)
C PEPTIDE	3.8 ng/mL	(0.929 to 3.7)
URINE KETONES	**ABSENT**	

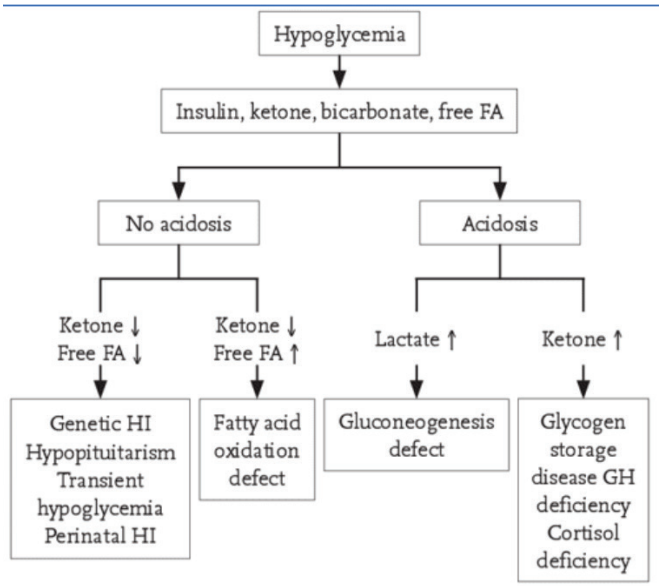

Figure 3: Diagnostic approach in Non-transient Hypoglycaemia.

Discussion

Neonatal hyper-insulinemic hypoglycaemia (NHH) is a heterogeneous disorder characterized by dysregulated insulin secretion, leading to persistent hypoglycaemia in the neonatal period. The underlying pathophysiology of NHH involves various genetic, metabolic, and environmental factors contributing to aberrant insulin production and secretion.

The clinical presentation of NHH can vary widely, ranging from asymptomatic hypoglycaemia to severe

neurologic manifestations such as seizures, lethargy, and poor feeding. In many cases, the diagnosis of NHH is challenging, requiring a systematic approach that includes biochemical, hormonal, and imaging studies to elucidate the underlying etiology.

Biochemical evaluation plays a crucial role in confirming the diagnosis of NHH. Elevated serum insulin and c-peptide levels in the setting of hypoglycaemia are indicative of inappropriate insulin secretion and support the diagnosis of hyperinsulinemic hypoglycaemia. Additional laboratory tests, such as serum ammonia and urine ketones, help differentiate between different forms of hypoglycaemia and guide therapeutic interventions.

Management of NHH involves a combination of medical, nutritional, and surgical strategies aimed at maintaining euglycemia while minimizing the risk of neurologic injury. Initial treatment consists of providing exogenous glucose to counteract hypoglycaemia and prevent neurologic sequelae. In cases refractory to glucose therapy, pharmacologic agents such as diazoxide, octreotide, and glucagon may be used to suppress insulin secretion and promote glycaemic stability.

In our case, the patient exhibited persistent hypoglycaemia refractory to glucose therapy, prompting further evaluation for NHH. Elevated serum insulin and c-peptide levels confirmed the diagnosis, leading to the initiation of octreotide therapy followed by diazoxide maintenance. The successful management of the patient's condition highlights the importance of early recognition and targeted therapy in achieving favourable outcomes.

Conclusion

This elaborated case report provides a comprehensive overview of the clinical presentation, diagnosis, and management of neonatal hyperinsulinemic hypoglycaemia, highlighting the complexities involved in its evaluation and treatment.

Neonatal hyper-insulinemic hypoglycaemia (NHH) is a challenging metabolic disorder characterized by dysregulated insulin secretion and persistent hypoglycaemia in the neonatal period. Early recognition and prompt intervention are essential to prevent neurologic sequelae and ensure optimal long-term outcomes. A multidisciplinary approach involving neonatologists, endocrinologists, and geneticists is crucial for the accurate diagnosis and management of NHH. Long-term follow-up is necessary to monitor for recurrence, assess developmental milestones, and provide on-going support to affected families.

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