A Rare Case of Neonatal Hyperinsulinemic Hypoglycemia

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BACKGROUND

Hyperinsulinemic Hypoglycemia refers to low plasma glucose levels in the presence of inappropriate insulin secretion by pancreatic β cells. Congenital Hyperinsulinism is one of the most common cause of nonketotic prolonged severe hypoglycemia in neonates. This is a rare condition affecting 1 in 50,000 live births.[1]

We report a case of severe Hyperinsulinemic Hypoglycemia in a neonate.

CASE PRESENTATION

A 1 day old full term male infant, delivered by Caesarean section presented with severe hypoglycemia few hours after birth. His birth weight was 3.6kg, APGAR score was 8 and 9 at 1 and 5 minutes. He was born to non-consanguineous parents. Mother did not have a history of gestational diabetes mellitus or intake of any medications during pregnancy.

General physical examination was unremarkable except for tachypneoa for which he was closely monitored.

Glycemic monitoring revealed persistent hypoglycemia with a recording of plasma glucose 43 mg/dl (2.3 mmol/L), 14 mg/dl (0.7 mmol/L). Simultaneous Cortisol and GH levels were 690 nmol/l (171- 536), >10ng/ml respectively and Urine ketones negative. Serum TSH was : 8.53 mIU/ml (1-39), Free T4: 2.32 ng/dl (0.93-1.7). Serum insulin was inappropriately elevated 16 mIU/L with a corresponding plasma glucose 39mg/dl and Insulin-Glucose ratio 0.41 (<0.25). Post Glucagon challenge the plasma glucose rose by > 30 mg/dl (1.6 mmol/L).

18 F- DOPA PET/CT confirmed diffuse enhancement in pancreas with higher intensity at head and neck region.

Genetic investigation revealed two heterozygous mutations (*Asp854Asn* and *Arg1394cys*) in the *ABCC8* gene.

DISCUSSION

Hyperinsulinemic hypoglycaemia (HH) in neonates, formerly described as Congenital Hyperinsulinism is characterised by persistently elevated insulin secretion resulting in severe persistent hypoglycaemia.[1, 2] Already known etiology include inactivating mutations of the K-ATP channel genes (ABCC8 and KCNJ11), HNF4A, HNF1A, HADH, and UCP2 or activating mutations of GLUD1, GCK, and SLC16A1.[4]

Mutations of ABCC8 and KCNJ11 are likely the main causes of K-ATP-HH as seen in our patient. The most widely accepted treatment is initial Glucose infusion as first line to normalise glycaemic level , Octreotide as second line in order to reduce the high Glucose infusion rate (GIR) and Diazoxide (K-ATP channel agonist) as a definitive medical line of management when diagnosis is confirmed.[3, 4]

We successfully discontinued Diazoxide therapy in our patient at age 3 although not much information regarding this is available in literature . A recent study (2018) reports discontinuation of Diazoxide at a median age of 6.8 years in 5 children with Diazoxide- responsive probands HNF1A- and HNF4A .[5]

INVESTIGATIONS

INVESTIGATIONS	WEEK 1	WEEK 2
Random Plasma Glucose	43 mg/dL 14 mg/dL	39mg/dL
Serum Cortisol	690 (171-536)	
Serum GH	>10ng/ml	
Urine Ketones	Negative	
Post glucagon -glucose	30mg/dL (1.6mmol/L)	
Serum TSH	8.53mIU/ml (1-39)	
Free T4	2.32 ng/dL (0.93-1.7)	
Serum Insulin		16mIU
Insulin-Glucose Ratio		0.41
PET scan (18 F DOPA PET)		Pancreas showed diffuse enhancement with higher intensity in head and neck region.
Genetic testing		Two heterozygous mutations (Asp854Asn and Arg1394cys) in the ABCC8 gene

MANAGEMENT

Glucose infusion was initiated at 12-15mg/kg/min. Oral feeds with Dextrose fortified breast milk was also initiated. The baby responded well to treatment and infusion was tapered and stopped on Day 4.

Hypoglycemia recurred (11mg/dL (0.6mmol/L) necessitating glucose Infusion at a higher rate. Octreotide (Somatostatin analogue) subcutaneously was initiated at 15 mcg/kg/day to maintain euglycemia until Diazoxide was available. Commenced on Diazoxide 10 mg/kg/day (up to 30 mg/kg/day) with which he maintained euglycemia and successfully weaned off glucose infusion.

He demonstrated appropriate response to Diazoxide and was discharged without any neurological deficit.

On follow up, patient developed hypertrichosis and the dose was reduced. Currently the patient is 4 years old, off Diazoxide and is doing well.

CONCLUSION

This case highlights the importance of prompt diagnosis of persistent hypoglycaemia in neonates (HH) and prevention of complications such as neurodevelopmental deficits.

Majority of the affected newborns require high intravenous glucose to maintain euglycemia[1, 2] until definitive medical management with Diazoxide is started.

The diagnosis and treatment of this rare condition (1 in 50,000 births) have made tremendous progress over the years where genetic markers may help predicting spontaneously reversible hypoglycaemia and avoid irreversible surgeries.

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