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Case Report

Persistent Hyperinsulinemic Hypoglycemia Of Infancy: A Case Report

BHAKHRI B K, ARYA S, DEBATA P K, CHELLANI H

ABSTRACT

Hypoglycaemia in newborns is usually a transient metabolic event. Hyperinsulinaemic hypoglycaemia is an important cause of nonketotic hypoglycaemia and it is characterized by macrosomia and hypoglycaemia with potential short and long term complications, if not properly managed with available medical and surgical options. We are presenting a neonate with this condition, who was managed in our unit and who underwent pancreactomy to control hypoglycaemia.

Key Words: Hypoglycaemia, Infant, insulin

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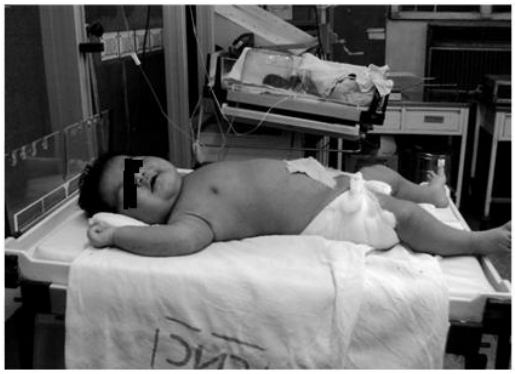
Introduction

Hypoglycaemia in newborns is usually a transient metabolic event. It is considered to be persistent when >6-8 mg/kg/min of dextrose infusion is required for more than 7 days of life to keep the blood sugar level above 40-50 mg%[1]. Various disorders at different steps of glucose metabolism can give rise to this condition. Hyperinsulinaemic hypoglycaemia is an important cause of nonketotic hypoglycaemia and it is characterized by macrosomia and hypoglycaemia with potential short and long term complications, if not properly managed with available medical and surgical options. We are presenting a neonate with this condition, who was managed in our unit and who underwent pancreactomy to control hypoglycaemia.

Case Report

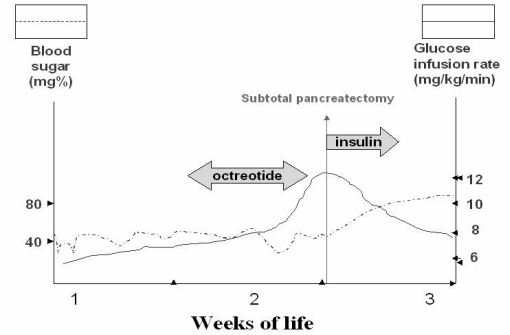
This term neonate was male baby who was born to nondiabetic nonconsanguinously related parents, with one live issue and one first trimester spontaneous abortion. The baby was delivered by LSCS in view of the large size of the baby, with out any evidence of perinatal asphyxia. At birth, the baby was haemodynamically stable and had weight of 6.26 kgs (>97th centile), length of 62 cm (>97th centile) and a head circumference of 39 cm (>97th centile). There was no organomegaly, dysmorphism or gross malformation [Table/Fig 1].



[Table/Fig 1]: Photograph of newborn showing macrosomia

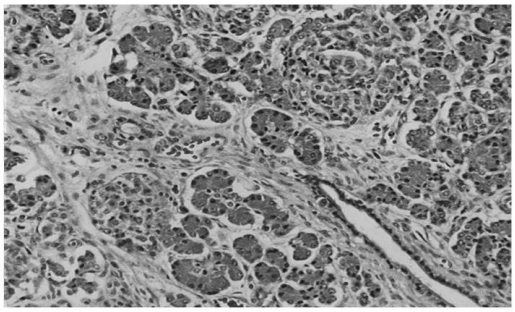
The baby started having tachypnoea at 6 hrs of life, with documented hypoglycaemia while on entral feeds and was therefore started on

parenteral dextrose therapy. Starting from glucose infusion rate (GIR) of 6 mg/kg/min and on regular blood sugar monitoring. His glucose requirement went on increasing for the first 2 weeks of life, reaching a maximum of upto 14 mg/kg/min [Table/Fig 2]. He was intermittently symptomatic, including one episode of multifocal seizure at the time of documented hypoglycaemia.



[Table/Fig 2] : Relation between blood sugar levels and glucose infusion requirement during hospital stay

His investigations revealed haemoglobin- 17 g%, PCV~ 50% and TLC- 9000/cmm. His serum electrolytes were normal, with normal renal functions. His serum calcium was 10.8 mg% and serum magnesium was 2 meq/l. His blood lactate was 1.2 mmol/l (normal range - 0.5-1.3 mmol/l). There were no reducing substances or ketones in the urine examination. His serum insulin was 64.6 µl/ml (normal<8 µl/ml) at the time of documented hypoglycaemia and his serum basal cortisol was 40.1 µgm/ml. Imaging did not reveal any focal lesion in pancrease. In the view of persistent hypoglycaemia in spite of a GIR of 14 mg/kg/min, he was started on hydrocortisone 10 mg/kg/24 hrs, but with no desirable effects on blood sugar levels over 24 hours. On administering octreotide (20µg/kg/24 hrs), the blood sugar levels rose and remained above 40 mg%, allowing a reduction in GIR to 8 mg/kg/min. However, there were downward fluctuations in blood sugar levels again, thus requiring the GIR to be increased upto 10mg/kg/min. In view of the clinical course and laboratory findings, the patient was diagnosed as a case of persistent hyperinsulinaemic hypoglycaemia and was advised subtotal pancreatectmy, that he underwent during the third week of life. The diagnosis was confirmed by gross and histopathology [Table/Fig 3] with tiny nodules of abnormal β cells scattered throughout the pancrease. Supplemental insulin was given for the first 3 postoperative days; subsequently, the baby was euglycaemic on feeds. At 3 months of age, the baby was well on feeds and anthropometric measures, though above normal, were found to be approaching normalcy.



[Table/Fig 3]: Histopathology of pancrease showing abnormal cells scattered in groups suggestive of diffuse PHHI

Discussion

Persistent hyperinsulinaemic hypoglycaemia of infancy (PHHI) is a major cause of persistent nonketotic hypoglycaemia in the neonatal period. The incidence of the disease ranges from 1 in 50,000 live births in sporadic cases to 1 in 2,500 live births[2] in certain communities with familial predisposition.

This genetic defect is identifiable in up to half of the patients and is a functional defect in the SUR1 and the Kir6.2 genes which are located on the 11p chromosome, resulting in insulin hypersecretion [3]. On histopathological examination, the abnormal β cells were found to be present in the pancreas, either locally or in the diffuse form. Other rare disorders with hyperinsulinism are the Beckwith Wiedman syndrome and insulinoma.

About 2/3rd of the affected patients present in the neonatal period with relatively poor response to conservative therapy. The clinical features are in the form of macrosomia, jitteriness, seizures, coma and documented hypoglycaemia, requiring a dextrose infusion rate persistently above 10

mg/kg/min to maintain the blood sugar level at 40-50 mg%.

Investigations show that there were high insulin levels (>10 µg/dl with increased C- peptide secretion) during episode of documented hypoglycaemia. Plasma free fatty acids were decreased and there was an inappropriate (>40 mg %) glycaemic response to glucagon. The list of intermediary metabolites and hormones to be measured at the point of hypoglycaemia is given in [Table/Fig 4]. Imaging has a negligible role in the diffuse disease. Apart from high parenteral dextrose infusion, other options in the therapeutic armamentarium [Table/Fig 5] are oral drugs – diazoxide, nifedipine, and chlorthiazide and parenteral drugs such as octreotide and glucagon, with responses varying from 30-60% in various studies [1]. Surgical therapy i.e. total and subtotal pancreatectomy is indicated in those with focal disease in imaging, or in those with high dose dextrose infusion dependency, despite taking maximum doses of drugs available. Post operatively, euglycaemia is achieved in approximately 27% of the patients and IDDM is seen in 27% of the patients after a mean follow up of 11 years, the other concern being exocrine pancreatic deficiencies [4]. Overall, about half of the patients develop long-term neurological morbidities with mental retardation in 44% of the patients and epilepsy in 25% of the patients and hence require a close follow up for physical and psychomotor development [5],[6].

[Table/Fig 4]: Intermediary metabolites and hormones to be measured at the point of hypoglycemia

Blood	Urine
Glucose Lactate/pyrutate Ketone bodies Free fatty acids Amino acids Ammonia Total/free carnitineAcyl-carnitine profile Insulin/C peptide Cortisol/growth hormone	Ketones Reducing substances Organic acids

[Table/Fig 5]: Drugs used in the medical management of hyperinsulinism

Drug	Mechanism of action	Dose	Side effects
Diazoxide	Opens KATP channels, increases adrenaline secretion, gluconeogenesis	5-20 mg/kg/day orally 8 hourly	Fluid retention (hypertrichosis, hyperuricaemia, facial changes, hypotension
Chlorothiazide	activating non-KATP channels	7-10 mg/kg/day in 2 divided doses	Hyponatraemia, hypokalaemia
Nifedipine	Calcium channel antagonist	0.25-2.5mg/kg/day orally 8 hourly	Hypotension
Octreotide	Activates G protein coupled rectifier K channel	5-20 µg/kg/day intravenous or subcutaneous	Suppression of growth hormone, TSH, ACTH. Steatorrhea, cholelithiasis
Glucagon	Increased glycogenolysis/gluconeogenesis	1-10 µg/kg/hour intravenous infusion, 1 mg bolus dose intramuscular or intravenous	Nausea, vomiting, increases growth hormone concentrations, increases myocardial contractility, decreases gastric acid/pancreatic enzymes

References

[1] A Aynsley, K Hussain, J Hall, J M Saudubray. Practical management of hyperinsulinism in infancy. Arch Dis Child Fetal Neonatal Ed 2000;82: F98-F107.

[2] Ruth M Shepherd, Karen E Cosgrove, Rachel E O'Brian, Phillipa D Barnes. Hyperinsulinism of infancy : Towards an understanding of unregulated insulin release. Arch Dis Child Fetal Neonatal Ed 2000;82: F87-F97.

[3] C Sempoux, Yues Guiot, Karin Dahan, Pierre Moulin. The focal form of PHHI. Diabetes 2003; 52: 784-94.

[4] G Leibowitz, B Glaser, A A Higazi, M Salameh. PHHI in clinical remission: High incidence of beta cell dysfunction at long term follow up. J Clin Endo Metab 1995; 80(2): 386-391.

[5] T Meissner, U Wendel, Peter Burgard, S Schaetzle. Long term follow up of 114 patients with congenital hyperinsulinism. Eu J Endo 2003; 149: 43-51.

[6] F Menni, P Lonlay, C Sevin, G Touati. Neurologic outcomes of 90 neonates and infants with PHHI. Paediatrics 2001;107(3):476-79.