

A case of persistent neonatal hyperinsulinaemic hypoglycaemia (nesidioblastosis)

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Introduction

Transient neonatal hypoglycaemia due to hyperinsulinism is seen commonly in infants of diabetic mothers, infants with erythroblastosis fetalis and in those with Wiedemann-Beckwith syndrome¹. Persistent hyperinsulinaemic hypoglycaemia is rarer in neonate although it assumes increasing importance during first year of life to become the most common cause of severe hypoglycaemia in this age group². The high incidence of mental retardation in survivors may be related to delayed diagnosis and to extreme difficulty experienced in controlling hypoglycaemia².

Case report

A male infant, the first product of a non-consanguineous marriage, was born at term by spontaneous vaginal delivery at the Kalutara General Hospital in September 2001. The birth weight was 2.6 kg. There was no history of maternal diabetes mellitus. On the second postnatal day, the baby did not suck well, had a high-pitched cry and developed seizures. Subsequently, he developed acute respiratory distress and septicaemia and was transferred to the intensive care unit of the Lady Ridgeway Hospital for further management. He did not require ventilation and was transferred to a medical unit after initial stabilization.

The baby was jittery and continued to have frequent subtle and multifocal clonic seizures. His blood sugar was noted to be persistently below 2mmol per litre with both glucometer and laboratory assessment while on dextrose infusions (10%, 12%, 15%) and boluses. Ultrasound scan of the abdomen showed a hypertrophied and enlarged pancreas but no evidence of a tumour. Computerized Tomography showed no abnormality. Insulin level was 92 μ IU/ml, more than three times the upper normal limit (5-27 μ IU/ml).

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A provisional diagnosis of nesidioblastosis was made and a distal pancreatectomy carried out in October 2001. The histology (Figure 1) confirmed our diagnosis. As distal pancreatectomy did not help to stabilize blood sugar levels, most of the remaining pancreas was removed to achieve 95% pancreatectomy. The blood sugar level remained within normal range but there were subtle seizures for a few more days. Post-operative ultrasound scan of the brain revealed mild dilatation and deformity of the frontal lobe of the left lateral ventricle due to an area of ischaemia with associated atrophy.

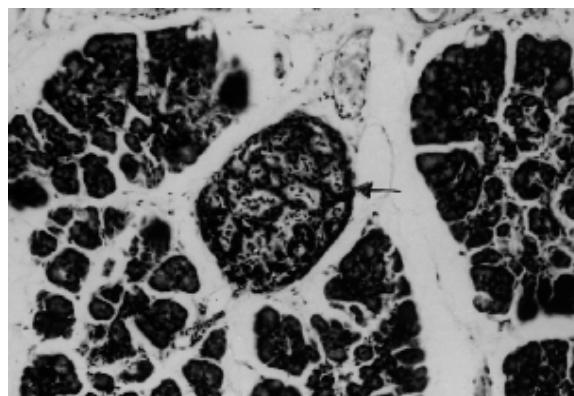


Figure 1. *Haematoxylin eosin stain; magnification 1 × 400; hyperplasia of islet cells seen in the centre.*

2 weeks after surgery, serum insulin level was 4.5 μ IU/ml, below the normal range (5-27 μ IU/ml). After surgery the dextrose infusions were tailed off and oral dextrose was given for a few days. Following the stoppage of dextrose, blood sugar levels remained in the normal range. The baby was discharged home with necessary instructions to the mother. He was last reviewed six months after surgery and was normoglycaemic, free of convulsions and thriving well with normal development.

Discussion

Nesidioblastosis is a term first used by Laidlaw in 1938 to indicate the formation of isolated endocrine cells and islets from pancreatic duct cells³. Brown

and Young first reported the association of nesidioblastosis with severe infantile hypoglycaemia⁴. Persistent hyperinsulinism in infancy, whilst most commonly associated with diffuse abnormality of β -cell regulation, is also occasionally associated with focal disease such as isolated islet adenoma⁵. In the past, the term nesidioblastosis was applied to the non-focal type of disorder⁵. More recently, the term has fallen into disfavour because the pattern is entirely nonspecific and can be found in the pancreas of newborn infants⁶. Today, the term 'nesidioblastosis' has been superseded by terms such as 'persistent neonatal hyperinsulinaemic hypoglycaemia' and 'persistent hyperinsulinaemic hypoglycaemia of infancy'⁶.

Most cases are sporadic; however, familial forms appear to be inherited in an autosomal recessive manner⁷. There was no parental consanguinity in our patient. The primary feature of hyperinsulinism is recurrent episodes of symptomatic hypoglycaemia⁵. In severe cases hypoglycaemia occurs soon after or even despite feedings⁵. Signs and symptoms in neonates and young infants usually include seizures⁵. Frequent subtle and multifocal clonic seizures were present in our patient.

Inappropriately raised insulin levels for blood glucose concentration and requirement of high glucose infusion rates to maintain blood glucose level support a diagnosis of hyperinsulinism¹. In our patient insulin level was 92 μ IU/ml (> three times upper normal limit) whereas blood sugar was very low in spite of dextrose infusions (10%,12%,15%) and boluses.

The immediate priority in treatment is to increase blood glucose concentrations to prevent convulsions and brain damage¹. Treatment modalities include high glucose infusion rates, use of medications and surgical intervention. Diazoxide is the drug of first choice in hyperinsulinism as the large proportion of patients who respond do so fully and can be maintained on drug by mouth for many years⁵. Octreotide, a long-acting somatostatin analogue, is useful in short-term management of hypoglycaemia but due to problems with tachyphylaxis, has been effective as a chronic treatment in only a limited number of infants with severe hyperinsulinism⁸. Although conservative management of persistent hyperinsulinaemic hypoglycaemia of infancy (PHHI) is very laborious for the family and the physician, it is recommended as long as euglycaemia is accomplished with these drugs⁹. Unfortunately these

drugs are not available in Sri Lanka. It must be stressed that early pancreatectomy should be performed in those with inadequate maintenance of euglycaemia, prolonged course of medical therapy being feasible only in selected cases¹⁰. Surgical treatment includes subtotal to near total pancreatectomy with splenic preservation¹⁰. Complications from this procedure have been few, most commonly those associated with decreased insulin production (diabetes) at puberty requiring insulin¹¹. Exocrine pancreatic deficiency requiring replacement therapy has also been reported. Other important short-term complication is inadequacy of resection, which may respond to oral nifedipine or surgery¹². Various types of intractable seizures and neurological sequelae have been reported¹³. Partial pancreatic regrowth has been evident at reoperation¹⁴.

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