

Neonatal diabetes mellitus - A Case Report

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Vol. 14, No. 1 (2010-01 - 2010-06)

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Abstract

Neonatal diabetes mellitus is a rare form of insulin dependent diabetes mellitus that presents within the first month of life, lasting for at least two weeks and requiring insulin therapy. We report such a case admitted in our hospital.

Key Words: Insulin, neonatal diabetes mellitus

Accepted August 31 2009

Introduction

Neonatal diabetes mellitus is a rare form of insulin de-pendent diabetes mellitus(1DDM) with an incidence of 1/400,000 that presents within the first four weeks of life persisting for at least two weeks and requiring insulin treatment[1,2]. The outcome is highly variable, may be either permanent or transient with or without subsequent recurrences based mainly on clinical course and duration of insulin dependency. [3]. Recently, various genetic defects like chromosome 6 uniparental disomy and KJN11 gene mutations have been associated with Neonatal diabetes mellitus. We report one such rare case admitted in our hospital.

Case report:

This term female neonate was the third child of consan-guineously wed parents. The previous two siblings had expired immediately after birth. The mother was 30 years old and the pregnancy was complicated by severe oligo-hydramnios. She was delivered at term by LSCS. Birth weight of the child was 1.5 kg (< 10th centile), the length was 42 cm (10-25th centile) and head circumference was 30 cm. The physical examination was normal.

On the 10th day of hospitalization, she had hyperglycemia (> 600mg/dl) without ketonuria and the neonate was put on insulin infusion due to persistently high blood glucose values. Once the child accepted mother's milk the infusion was stopped and regular insulin was started subcutaneously. Investigations showed hemoglobin 7.4gm%, total leukocyte count of 7,500/mm³, Serum Urea 21mg/dl, Sepsis screen, skeletal survey, stool for fat globules, and TORCH Screening did not reveal any abnormality. Her insulin value was 2.0 mic IU/ml (normal value-2.1-30.8) and the C peptide value was 0.2 ng/ml. (normal values 1.1-3.2 ng/ml) and the tests for islet cell antibodies were negative. CT Scan showed a normal pancreas. The sugar levels were quite erratic and was not controlled with 6th hourly regular insulin and the Hb1AC value was 10.8. Then the child was put on twice daily intermediate insulin regimen and top up regular insulin was added to maintain the sugar levels. There were phases of hyperglycemia with intermittent episodes of hypoglycemia. Gradually the hyperglycemia improved with proper titration of the feeds. Child showed consistent weight gain and was feeding well. The child was discharged with twice daily insulin regimen and on full feeds. On follow up visit at three months of age the child is still on insulin regimen with a consistent weight gain and feeding well without any further complications.

Discussion:

Neonatal diabetes mellitus, an uncommon cause of hyperglycemia in the newborn period, presents within the first four weeks of life and persists for more than two weeks. It can be transient, transient with recurrence at 7-20 yrs old and permanent neonatal diabetes mellitus. Intrauterine growth retardation, failure to thrive, fever, dehydration,

hyperglycemia, acidosis with or without ketonuria are the clinical features of the disease. Insulin secreted by the fetal pancreas has a significant role in growth and metabolism of the fetus during the later half of gestation. Intrauterine deficiency of insulin may be the cause for intrauterine growth restriction [4]. Our patient was term baby with intrauterine growth restriction with low levels of insulin and C-peptide and negative for Islet cell antibody.

Etiology of neonatal diabetes mellitus is unclear and its pathogenesis differs from insulin dependent diabetes in children due to its highly variable course. Presence of islet cell antibodies has not been reported in neonatal diabetes mellitus [5].

Neonatal diabetes mellitus seem to form a distinct entity of inborn pancreatic malfunction. First phase of insulin release during the intravenous glucose tolerance test is a sensitive index of the beta cell reserve. If there is a decreased first phase of the insulin response, this is a good predictor of later development of diabetes mellitus [6]. Most children with transient neonatal diabetes mellitus in remission have no evidence of beta cell dysfunction or insulin resistance in the fasting state [7].

Transient neonatal diabetes mellitus typically lasts for weeks or months requiring insulin therapy [8,9]. Although they often have a permanent remission, they need to be closely followed as diabetes can recur. Several hypotheses concerning its etiology have been postulated, such as pancreatic immaturity, paternal uniparental isodisomy of chromosome 6 and the existence of a gene located in 6q22-23 chromosome region subjected to imprinting and exclusively of paternal expression [10].

The cause of the beta cell destruction in permanent cases is not yet known. Permanent neonatal diabetes mellitus is uncommon and usually due to a pancreatic dysgenesis often associated with other malformation [11]. Giralt et al described permanent diabetes of a neonate with hypothyroidism, bilateral sensorineural deafness and bilateral congenital cataract [12]. Kentrup et al described a case of NDM with hypergalactosemia [13]. Milenkovic et al reported macroglossia, umbilical hernia, onychomycosis and inguinal hernia with transient neonatal diabetes mellitus [14].

The prognosis is different in transient and permanent forms and it is difficult to distinguish these forms at onset. Recently, mutations in KCNJ11 gene, which encodes the Kir6.2 subunit, and mutations in ABCC8, which encodes the SUR1 subunit, of the pancreatic ATP-sensitive potassium channels (KATP) have been implicated in the genesis of permanent neonatal diabetes mellitus [15].

Various congenital syndromes like leprechaunism, IPEX syndrome, Wolcott-Rallison and Mitochondrial disorders should be considered when evaluating a neonate or young infant with Permanent neonatal diabetes mellitus. In addition to neonatal diabetes, affected neonates can have neurological features like developmental delay and epilepsy, known as Developmental delay epilepsy and neo-natal diabetes (DEND) syndrome. These conditions were excluded in our patient.

Insulin therapy, high calorie diet, periodic follow-up, and parent's education and training are the main stay of the management. Various regimens, from continuous infusion, periodic regular insulin to once daily isophane insulin have been tried. However, most pediatricians face numerous difficulties in managing young infants with NDM like route of administration, type of insulin, frequency, coordinated feeding, long term complications and psychosocial issues. We too encountered few difficulties in management of our case. We started with regular insulin, but it was difficult to synchronize feeding with insulin administration, especially during night time. We finally managed to stabilize blood sugar levels with combination of intermediate and regular insulin with strict regulation of feeds by counseling the mother to provide regular and timely spaced feeding, especially during night hours. Though, insulin administration by infusion pump can be an alternate method as suggested by various other teams, the major disadvantage is that it needs more stringent supervision under specialist care and home management might be difficult for parents with poor socioeconomic and low education level. Various oral hypoglycemic agents, like Sulphonylurea and Glibenclamide, have been considered as an alternative to insulin injections in permanent neonatal diabetes mellitus, especially in those with Kir 6.2 mutations, because these agents can still be able to close ATP insensitive KATP channels.[16,17]. However, the experience with oral hypoglycemic agents is still very limited and further studies warranted in pediatric population to assess their role in the management of neonatal diabetes mellitus. The Parent's education and training needs special attention before discharging the patient because chances of an episode of severe hypoglycemia leading to permanent long term neuro-developmental sequelae are much higher in young infants due to their lack in ability to communicate with the caregiver. Neonatal diabetes mellitus should be considered in the diagnosis of hyperglycemic a small for date infants. The prognosis is different in transient and permanent forms and it is difficult to distinguish these forms at onset. So monitoring of insulin dose and blood sugar and proper follow up is mandatory in these children.

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