Case Report

Permanent neonatal diabetes mellitus

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ABSTRACT

Neonatal diabetes is a rare disease usually diagnosed before the age of six months. It can be transient or permanent. We report a case of permanent neonatal diabetes that was diagnosed based on clinical presentation and course of the disease. (Rawal Med J 2011;36:328-329).

Key words

Neonatal diabetes mellitus, gene testing, sulfonylurea.

INTRODUCTION

Neonatal diabetes mellitus (NDM) is a rare and heterogeneous disorder that occurs in the first 6 months of life with an incidence of 1 in 300,000-400,000 live births.\(^1\) Two types are described, transient and permanent, based on length of insulin dependency. Transient NDM, as the name indicates, resolves by a median of 12 weeks and is associated with specific genes, while permanent NDM is a life-long disease with a monogenic etiology.\(^2,3\) It is a result of pancreatic inability to produce sufficient amounts of insulin. Most patients have intrauterine growth retardation, poor weight gain and severe dehydration with or without ketoacidosis.

CASE PRESENTATION

Our patient is a three year old female, who was delivered vaginally at 36 weeks with a birth weight of 2.12kg. She was born to consanguineous parents who had another two sisters and one brother who are healthy. Pregnancy was uneventful and family history was positive for diabetes in maternal grandfather and grandmother. At the age of 21 days, the baby presented with two days history of vomiting and poor feeding. She was severely dehydrated. Her initial CBC was normal but then she developed leucopenia (WBC 2.6). Her initial glucose level was 1335 mg/dl with blood urea nitrogen (BUN) of 73 mg/dl, creatinine of 1.5 mg/dl and potassium of 6 mmol/l. Blood gases showed severe metabolic acidosis with \(\text{PH} < 7\) and \(\text{HCO}_3^-\) was 2 mmol/l. Urine ketones were negative but urine sugar was 4+. She was treated as neonatal diabetic ketoacidosis with insulin infusion, sodium bicarbonate, hydration and antibiotics.
Few days later, all her results were normal and she was started on NPH insulin at dose of 0.3 unit/kg. Brain ultrasound, chest x-ray and abdominal ultrasound were normal while brain CT scan showed ischemic infarction in periventricular area. TORCH screens and thyroid function tests were normal, but c-peptide and insulin level were low. Islet cell antibodies were not done. Hearing and ophthalmic assessments were normal.

For genetics study, we sent blood samples of both parents and the baby to the molecular genetics laboratory in Royal Devon and Exeter NHS Foundation Trust in UK. At present, the patient is on NPH insulin 3 units three times daily and her blood sugar is stable between 135-150 mg/dl. She is developmentally delayed as she can not walk or talk till now. Just one month ago, she got another sister who presented with diabetes ketoacidosis and was diagnosed as NDM.

**DISCUSSION**

NDM is defined as persistent hyperglycemia which occurs in the first few months of life and diagnosed before the age of 6 months,\(^1\) which is considered as the cut off between nonautoimmune and type one diabetes.\(^4\) It is a rare disorder.\(^5\)\(^-\)\(^7\) There are two types of neonatal diabetes. First is transient NDM that usually disappears in weeks or months and needs insulin in only first 3 months of life.\(^4\) It should be differentiated from other causes of transient hyperglycemia like septicemia and central nervous system disorders.\(^6\) Some of these infants have recurrence of type one diabetes in late childhood.\(^7\) Second is permanent NDM, which was the case in our patient, and constitutes about 50% of NDM.\(^1\)\(^,\)\(^7\) Most patients have intrauterine growth retardation, as in our patient whose birth weight was 2.12 kg, which could be related to intrauterine insulin deficiency.\(^1\)\(^,\)\(^3\)\(^,\)\(^8\)\(^,\)\(^9\)

Other presenting symptoms of NDM like severe dehydration, acidosis, vomiting and weight loss occur,\(^1\)\(^,\)\(^2\)\(^,\)\(^5\)\(^,\)\(^8\) as seen in our patient. Ketonuria and ketoacidosis may occur in NDM\(^1\)\(^,\)\(^6\) but were not seen in our patient. Insulin level and c-peptide level are usually low in patients with permanent NDM which was the case here which may indicate total failure of B-cell. Islets cell antibodies, which are seen in patients with type one diabetes, are typically negative in NDM.\(^6\) Unfortunately, this test was not
done for our patient. Other associated problems like hypothyroidism, cataract and deafness which can occur in these patients\(^6\) were not seen in our patient.

Gene mutations that are related to ATP-sensitive potassium channel (KATP) are the primary cause of permanent NDM.\(^1\) Pancreatic agenesis or hypoplasia and complete glucokinase deficiency are rare causes.\(^8\) Most common gene mutation is KCNJ11 that encodes Kir6.21 which accounts for 40%-64% of cases.\(^2,3\) Forty percent of permanent NDM has unknown gene causes.\(^9\)

Neurological features like epilepsy and developmental delay are associated with Kir6.2 mutation.\(^3,7\) This syndrome is known as DEND syndrome (developmental delay, epilepsy, neonatal diabetes).\(^7\) Our patient had developmental delay as she can not talk, walk or stand till now, but no seizures or dysmorphic features were noted. Her brain showed ischemic insult. This syndrome was referred to as intermediate DEND syndrome.\(^7\)

Patients on sulfonylurea drugs have good glycemic control as it restores insulin secretion.\(^2,3,9,10\) However, insulin is the mainstay of therapy. Prognosis is usually good unless it is associated with developmentally delay or episodes of hypoglycemia. In conclusion, NDM should be considered in any patient with neonatal hyperglycemia. Many patient could achieve good glucose control when insulin injections were replaced by oral sulfonylurea drugs.

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