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CASE REPORT

A seven weeks old baby with diabetic ketoacidosis: a case report

Francis Fredrick[1,2], Hendry Sawe[3,4], Kandi Muze[1], Deogratius Mally[3] & Edna Majaliwa[1]

[1]Department of Paediatrics, Muhimbili National Hospital (MNH), Dar es Salaam, Tanzania
[2]Department of Paediatrics and Child Health, School of Medicine, Muhimbili University of Health and Allied Sciences (MUHAS), Dar es Salaam, Tanzania
[3]Department of Emergency Medicine, Muhimbili National Hospital, Dar es Salaam, Tanzania
[4]Department of Emergency Medicine, School of Medicine, Muhimbili University of Health and Allied Sciences (MUHAS), Dar es Salaam, Tanzania

Correspondence
Francis Fredrick, Department of Paediatrics and Child Health, School of Medicine, MUHAS, PO Box 65001 Dar es Salaam, Tanzania. Tel: +255 718 630160; Fax: 255 022 2150473; E-mail: fredrick.francis78@gmail.com

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Key clinical message

Diabetes mellitus is rare during infancy, however, it should be suspected in infants presenting with features consistent with sepsis and hyperglycemia. This is crucial in initiating the treatment of diabetes ketoacidosis which if delayed may result in significant morbidity and death.

Keywords

Neonatal diabetes mellitus, diabetic ketoacidosis, Tanzania.

Background

Neonatal diabetes mellitus (NDM) is a rare endocrinological disorder, which affects children in the first 6 months of life, with estimated incidence of 1/90,000 to 1/210,000 live births [1, 2]. Two forms of this condition have been identified, transient and permanent neonatal diabetes mellitus (TNDM and PNDM). TNDM is a genetically mediated disorder of insulin production that remits in the postnatal period and is commonly associated with intrauterine growth retardation, it accounts for 50–60% of the cases of neonatal diabetes [3]. PNDM, a less common form that results from abnormal pancreatic development, increased apoptosis, and necrosis with cellular dysfunction and causing lifelong insulin dependency [4]. Patients develop inadequate insulin production necessitating exogenous insulin therapy, which if not well balanced results in several complications including diabetic ketoacidosis. We report the case of 7 weeks old boy with diabetic ketoacidosis that required 10 days of intensive care management.

Case Report

A 7-week-old baby was referred to the emergency department (ED) of Muhimbili National Hospital (MNH), Dar es Salaam because of presumed severe pneumonia and septicemia. He presented at the ED with history of fever and difficulty in breathing for 3 days, fever was of high grade with no report of convulsion. Difficulty in breathing was noted concurrently with fever and was not accompanied by cough, however, it was noted to cause difficulty in breastfeeding.

The child was reported to have received vaccination with DPT-HB-Hib, PCV13 rotarix and polio vaccine 4 days prior to onset of above mentioned symptoms. Nothing remarkable was noted during prenatal period, the baby was delivered by spontaneous vaginal delivery with birth weight of 3.5 kg, cried immediately and was breastfed within 1 h of delivery. No family history of diabetes was given.

On presentation at ED the child weighed 5.5 kg, was unconscious responding to pain, febrile (38.1°C) pulse

rate was 170 beats/min, respiratory rate was 49 breaths/min, extremities were warm, and some pallor was noted with no jaundice. Cardiovascular examination revealed normal heart sounds with no murmur, respiratory examination revealed vesicular breath sounds with no added sounds, and abdominal examination revealed normal findings.

Capillary random blood glucose at admission showed high blood glucose (>33 mmol/L). Venous blood gas analysis revealed pH of 6.8, pCO_2 8 mmHg, pO_2 67 mmHg, sodium 154 mmol/L, potassium 3.2 mmol/L, and HCO_3 1.4 mmol/L. Dipstick urinalysis showed glucose 3+, ketone 2+, nitrate+, protein negative, and bilirubin+. Malaria rapid diagnostic test was positive. The final ED diagnoses were neonatal diabetes mellitus with diabetic ketoacidosis, septicemia, and severe malaria. The child was catheterized, given ceftriaxone 600 mg IV stat, artesunate 12 mg IV stat, and normal saline 100 mL for 1 h, then 50 mL hourly for 2 h (Table 1). Soluble insulin 1.0 unit stat was given followed by soluble insulin infusion at o.5 U/h infusion (Table 1).

Venous blood gas (VBG) and/or arterial blood gases (ABG) were monitored every two hours (Table 2), and 4 h after starting treatment, ABG showed pH 6.8, pCO_2 12.8 mmHg, pO_2 67.8 mmHg, sodium 159 mmol/L, potassium 3.4 mmol/L, and HCO_3 2.3 mmol/L. Eight hours later, VBG was pH 7.0, pCO_2 24.5 mmHg, sodium 166 mmol/L, potassium 3.4 mmol/L, and HCO_3 5.9 mmol/L.

After 13 h in ED, the patient was admitted to acute pediatric care unit (APCU) and was noted to be lethargic with respiratory rate of 72/min, lower chest wall in-drawing, pulse rate of 144/min, and tender hepatomegaly. His capillary random blood glucose was 27.1 mmol/L and no ketones was found in the urine. Full blood count revealed WBC of 17.9 K/L, neutrophil 10 K/L (56.8%), monocytes 1.8 K/L, Hb 8.7 g/dL, MCV 85.6 fL, MCH 28.8 pg, and platelet 502 K/L. Serum creatinine was 65.9 umol/L and albumin 30 g/dL. Blood culture had no growth after 72 h of incubation. Thyroid-stimulating hormone was 2.3 μIU/mL (1.7–9.1) and free thyroxin was 1.2 ng/dL (0.9–2.6) all within normal range. Glycated hemoglobin was elevated at 7.7%, and screening for HIV, HBV, HCV, toxoplasmosis, and rubella were performed as part of provider-initiated testing and counseling for HIV and to exclude other viral infections, these were all negative.

In the ward, the patient was given ceftriaxone 500 mg (daily for 10 days), artesunate 12 mg at 12 h and 24 h after initial injection at ED and thereafter daily for 3 days, and 500 mL of normal saline for 24 h. In the ward, soluble insulin 1 IU (calculated as 0.1 U/kg every 1 h) was given subcutaneously every 2 h for 24 h, as there were no facilities for continuous insulin infusion pump. The baby regained consciousness after 12 h of admission in the APCU, was afebrile and able to breast feed. Random blood glucose ranged from 6 to 22.8 mmol/L. Insulin therapy was changed to 2 IU of soluble insulin before breakfast, before lunch, and subsequently changed to 2 IU of Glargine (Lantus) insulin before dinner for 24 h. Two days later, the baby was kept on Glargine insulin 2 IU daily. Urinalysis had no ketones after 24 h of stay in APCU.

The patient was given daily single lantus insulin injection after 24 h of APCU stay and his capillary random blood glucose was ranging between 3.1 and 10.2 mmol/L. Forty eight hours of stay in APCU full blood picture showed WBC 18.3 K/uL, neutrophils 7.56 K/uL, monocytes 4.55 K/uL, and Hb of 6.6 g/dL consistent with severe anemia. Serum creatinine was 28.6 umol/L sodium 141 mmol/L and potassium 4.1 mmol/L. The baby was

Table 1. Fluid and insulin administration and monitoring of random blood glucose.

Time	8.45 pm	9.45 pm	10.45 pm	11.45 pm	12.45 am	01.45 am	02.45 am	03.45 am
RBG	High	24.1	24.6	24.9	21	18.4	14.7	10.8
Fluid (mL)	100	50	50	50	25	25	25	12.5
Insulin (IU)	1	0.5	0.5	0.5	0.5	0.5	0.5	0.5

Table 2. Blood gas monitoring at ED.

Time	7.05 pm (ABG)	9.45 pm (ABG)	11.45 pm (VBG)	04.00 am (VBG)	06.00 am (VBG)	08.15 am (VBG)
pH	6.857	6.870	6.914	7.033	7.057	7.132
pCO_2	8	12.8	11.9	20.3	24.5	11
pO_2	67.1	67.8	20.7	26.0		13.4
HCO_3	1.4	2.3		5.2	5.9	7.1
Na+	154	159	163	167	166	163
K+	3.27	3.42	5.29	3.67	3.4	3.3
Cl−	92	124	137	135	132	124

given 60 mL of packed red blood cells in view of rapid decline of hemoglobin level. The baby was discharged from APCU to general pediatric ward after 10 days, and was then discharged home after 3 days in the ward, with well-controlled blood glucose ranging from 4.8 to 6.8 mmol/L.

Blood specimens were sent to University of Exeter, United Kingdom and genetic testing was performed and sequence analysis of the ABCC8, KCNJ11, and INS genes did not detect a pathogenic mutation, we are currently awaiting further genetic analysis for potential mutations. The patient is still being followed monthly in our pediatric diabetic clinic and has been doing generally well, however, he has been presenting with hypoglycemic episodes and we have advised his parents to monitor his blood glucose regularly.

Discussion

Neonatal diabetes mellitus is a rare metabolic disorder diagnosed within the first 6 months of life and presents with low birth weight, dehydration, hyperglycemia, or diabetic ketoacidosis [5]. Previous studies reported no clear-cut clinical features that may predict whether a neonate with diabetes without any abnormal morphology will present with permanent or transient diabetes mellitus [3].

Our patient presented at the age of 7 weeks with hyperglycemia and features consistent with severe malaria and neonatal sepsis [6]. Neonatal severe infection may present with hyperglycemia resulting from stress and a raise in epinephrine and cortisol, decreased insulin release and impaired glucose utilization [7]. Therefore, hyperglycemia with ketoacidosis may easily be missed if it is solely attributed to infections. Our patient had severe malaria as depicted by positive rapid diagnostic test, however, blood culture test had no growth after 72 h, the clinical picture presented highlights the mimicry between DKA and severe infections. Similar clinical presentation has been described in patients with NDM. Bappal et al. [8] in study conducted among patients with NDM in Oman reported fever, lethargy and poor feeding, polyuria, diarrhea and dehydration, and tachypnea to be the most common presenting symptoms. High index of suspicion is of clinical importance in identifying neonates with NDM. Capillary random blood glucose is an important bedside test in evaluating neonates suspected to have sepsis that may commonly present with hypoglycemia, but may also present with hyperglycemia [9].

Recommended treatment of patients with NDM according to International society for pediatric and Adolescent diabetes (ISPAD) is insulin, sulfonylurea is an useful alternative treatment for patients with KCNJ11 and ABCC8 gene mutations for which it has been reported to have good response [10]. Our patient had diabetic ketoacidosis characterized by hyperglycemia, glycosuria, ketonuria, and metabolic acidosis and was managed with intravenous fluids and soluble insulin. Soluble insulin was substituted with long-acting insulin and the patient attained glycemic control. Intravenous soluble insulin infusion which was used in our patient has been reported to provide satisfactory blood glucose level particularly in the initial management of patients with NDM with hyperglycemia [11]. Erratic blood glucose levels have been described with intravenous insulin infusion therapy [12, 13].

Establishing the chronic insulin therapy is usually a challenge for both health care providers and parents, once the patient is discharged. This was noted in our patient, therefore intensive glucose monitoring at home is important in management of NDM as hypoglycemic attacks are usually accompanied with psychological issues to parents [14].

The most commonly identified genetic mutations with NDM involve ZAC, HYMAI, KCNJ11, ABCC8, and INS genes. None of the later three gene mutations (ABCC8, KCNJ11, and INS) which were sequenced for in our patient were identified. This genetic finding has a bearing to the management of our child as both patients with TNDM and PNDM with activating mutations of KCNJ11 and ABCC8 may be amenable to treatment with sulphonylureas, which stimulate endogenous insulin secretion [7, 10, 14–16]. Therefore, our patient continues to be managed with daily long-acting subcutaneous insulin injections.

Long-term outcome of NDM patients is variable and may be influenced by the form of NDM. Transient forms of NDM tend to remit for years with later recurrences. Mühlendahl et al. [17] described 13 patients who had transient NDM who attained remission and recurred later with median duration in remission of 13 years. This being the case, it is difficult to predict the long-term outcome of our patient although the overall prognosis is influenced by glycaemic control [7, 16].

In conclusion, diabetic ketoacidosis in neonate is a rare, but life-threatening complication of NDM that requires a high degree of suspicion especially in neonates with coexistent infection.

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Conflict of Interest

None declared.

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