

Type 1 diabetes mellitus presenting with diabetic ketoacidosis (DKA) in a neonate

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Abstract

Neonatal diabetes mellitus (NDM) is a rare manifestation with an incidence of one affected individual among 400000 live births. NDM can be divided into Transient (TNDM) and Permanent (PNDM) types. A significant overlap occurs between both groups, to an extent that TNDM cannot be distinguished from PNDM based solely on clinical features. Diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality in children with type 1 diabetes mellitus (T1DM). DKA at diagnosis is more common in young children near the age of five years. Neonatal DKA is a rare occurrence causing it to be missed in the differential diagnosis of neonatal illness and results delay in appropriate management and increase in morbidity and mortality rate.

Keywords: Neonate diabetes mellitus, Diabetic Ketoacidosis, Pakistan.

Introduction

Diabetes mellitus (DM) is a diverse group of metabolic diseases that has no age restriction to manifest. Neonatal diabetes mellitus is a very rare entity with an incidence of 1/90,000 to 1/210,000 live births approximately and usually affects children in their first 6 months of life.^{1,2} It can be divided into Transient (TNDM) and Permanent (PNDM) types. In instances of TNDM, infants develop diabetes in the first few weeks of life however, they go into remission a few months later, with a possibility of relapsing into a permanent diabetic state usually around their adolescence or adulthood.³ Its most common clinical presentation includes dehydration, hyperglycaemia, sometimes accompanied by mild ketonaemia or ketonuria.⁴

Diabetic ketoacidosis (DKA) is the leading cause of morbidity and mortality in children with type 1 diabetes mellitus (T1DM). DKA at diagnosis is more common in young children near the age of five years.⁵ DKA cases

are usually encountered frequently as an acute illness in the paediatric emergency room. Neonatal DKA is a rare occurrence causing it to be missed in the differential diagnosis of neonatal illness and results delay in appropriate management and increase in morbidity and mortality rate. The risk of DKA in established T1DM is 1-10% per patient per annum.^{6,7} The risk increases gradually in children with poor metabolic control or previous episodes of DKA, young age, children with psychiatric and eating disorders, low socioeconomic status and low parental education and those with stressful lifestyles.^{8,9}

Mortality rates from DKA in national population based studies are relatively constant at 0.15% in the USA.¹⁰ Regions with poorly developed medical facilities have higher incidence of DKA associated mortalities prior to receiving any form of treatment.¹¹

Case Report

We report the case of a 26 days old boy, who presented to Emergency department of Aga Khan University Hospital in February, 2014, with the complaints of fever for 2-days accompanied with respiratory distress since morning. He was born healthy at full term following an uncomplicated pregnancy and was the second child of consanguineous marriage. Upon inquiry of the patient's family history, it was revealed that one of the siblings had passed away at 4 months of age from myocarditis; no medical records were available for it. A family history of DM was also present from the paternal side.

Physical examination revealed an irritable, drowsy, and dehydrated neonate. Vitals recorded at the time of admission were as follow; heart rate of 165 beats/min, respiratory rate of 62 breaths/min, oxygen saturation of 94% on room air, body temperature was 37.1°C (axillary), and blood pressure of 90/35 mmHg. Systemic examination was unremarkable. Bed side glucose check displayed "High" on the glucometer. Suspecting severe sepsis, blood workup and urine detailed report was sent, results of which were:

Random Glucose: 1299 mg/dL, (Normal range: 80-

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160mg/dl)

Blood Urea Nitrogen: 74mg/dl, (Normal range: 6-20mg/dl)

Creatinine: 1.7mg/dl, (Normal range: 0.3-0.7mg/dl)

Sodium: 148 mmol/L, (Normal range: 136-145mmol/L)

Potassium: 7.7 mmol/L, (Normal range: 3.5-5.1mmol/L)

Chloride: 111 mmol/L, (Normal range: 98-107mmol/L)

Bicarbonate: 6.3mmol/l, (Normal range: 20-31mmol/L)

Calcium: 9.2 mg/dL, (Normal range: 8.6-10.2mg/dl)

Arterial blood gas analysis, pH: 7.19 (7.25-7.45), HCO₃: 6.6 mEq/L (19.24), and pCO₂: 17.2 mmHg (27.40); pO₂:90.6 mmHg (54.95). O₂ sat: 93.4%

Urine dip stick: Glucose: +4, Ketones: Large,

Detailed urinalysis revealed: glucose: 28mmol/l, ketones: 15mmol/l

Complete blood count, Hb : 8.7mg/dl (13.5-19.5), Hct : 27.8% (44.64), TLC : 21.4 10E⁹/L (10.26), N : 40 (37-57), L : 60 (25-35), Plt : 482 (150-400).

On the basis of hyperglycaemia, severe metabolic acidosis and ketonuria, a provisional diagnosis of DKA was established and appropriate management was initiated. Patient was kept NPO with intravenous hydration (0.9% NaCl with KCL 20meq/l +KPo₄ 20meq/l) and insulin infusion (0.3units/Hr) was started. Broad spectrum antibiotics i.e. injection Cefotaxime, Amikacin and Cloxacillin were given). Strict fluid input and output charting was kept with hourly monitoring of blood glucose levels, and 4 hourly electrolyte measurements.

Patient was then shifted to the neonatal intensive care unit for further management.

Discussion

Diabetic ketoacidosis (DKA) is caused by a decrease in the levels of circulating insulin, with associated increases in counter regulatory hormones (glucagon, catecholamine, cortisol, and growth hormone).³ Hyperglycaemia and acidosis subsequently result in osmotic diuresis, dehydration, and an obligate loss of electrolytes. The biochemical criteria for the diagnosis of DKA are hyperglycaemia (blood glucose 11 mmol/l or 200 mg/dl) with a venous pH 7.3 and bicarbonate of 15 mmol/l or less. It is associated with glycosuria, ketonuria, and ketonaemia.¹² DKA is generally categorised by the severity of the acidosis; which varies from mild (venous pH 7.30, serum bicarbonate 15 mmol/l), to moderate (pH

7.2, bicarbonate 10mmol/l), to severe (pH 7.1, bicarbonate 5mmol/l).

The aetiology of NDM still remains unclear, and its pathogenesis differs from that of insulin dependent diabetes mellitus in children. Permanent neonatal diabetes although less common does not go into remission.¹³ It accounts for nearly half of the NDM cases globally.¹⁴ To date, no specific clinical features have been identified that may help differentiate PNDM from TNDM.¹⁴ In a study by Metz et al, intrauterine growth retardation (IUGR) showed decreased association with PNDM when compared to TNDM.¹¹ However, severe IUGR has been reported in some instances of PNDM associated with pancreatic agenesis.¹⁵ There are case reports presenting with NDM secondary to gene mutation but their long term outcome was not predictable.¹⁶

During the neonatal period, the prognosis is linked to the severity of the disease, the degree of dehydration and acidosis, as well the time taken to diagnose the disease and initiate its management.

Conclusion

Neonatal Diabetes is a very rare disease and DKA in neonatal age group is very unlikely and may mimic sepsis, so the emergency physician should keep DKA as a differential diagnosis in their mind for all newborns who present with shortness of breath, vomiting, and dehydration to initiate early management and to prevent life threatening complication of DKA.

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References

1. Iafusco D, Massa O, Pasquino B, Colombo C, Iughetti L, Bizzarri C, et al. Minimal incidence of neonatal/infancy onset diabetes in Italy is 1: 90,000 live births. *Acta diabetologica*. 2012; 49:405-8.
2. Slingerland AS, Shields BM, Flanagan SE, Bruining GJ, Noordam K, Gach A, et al. Referral rates for diagnostic testing support an incidence of permanent neonatal diabetes in three European countries of at least 1 in 260,000 live births. *Diabetologia*. 2009; 52:1683-5.
3. American Diabetes A. 2. Classification and diagnosis of diabetes. *Diabetes Care*. 2015; Suppl 1:S8-S16.
4. Abaci A, Razi CH, Ozdemir O, Hizli S, Kislal F, Argas PI, et al. Neonatal diabetes mellitus accompanied by diabetic ketoacidosis and mimicking neonatal sepsis: a case report. *J Clin Res Pediatr Endocrinol*. 2010; 2:131-3.
5. Dunger DB, Sperling MA, Acerini CL, Bohn DJ, Daneman D, Danne TPA, et al. European Society for Paediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society consensus statement on diabetic ketoacidosis in children and adolescents. *Pediatrics*.

- 2004; 113:e133-e40.
6. Smith CP, Firth D, Bennett S, Howard C, Chisholm P. Ketoacidosis occurring in newly diagnosed and established diabetic children. *Acta Paediatrica*. 1998; 87:537-41.
 7. Rosilio M, Cotton J-BT, Wieliczko M-C, Gendrault Bnd, Carel J-C, Couvaras O, et al. Factors associated with glycemic control: a cross-sectional nationwide study in 2,579 French children with type 1 diabetes. *Diabetes Care*. 1998; 21:1146-53.
 8. Gruber N, Reichman B, Lerner-Geva L, Pinhas-Hamiel O. Increased risk of severe diabetic ketoacidosis among Jewish ultra-orthodox children. *Actadiab*. 2015; 52:365-71.
 9. Keenan HT, Foster CM, Bratton SL. Social factors associated with prolonged hospitalization among diabetic children. *Pediatrics*. 2002; 109:40-4.
 10. Dunger DB, Sperling MA, Acerini CL, Bohn DJ, Daneman D, Danne TP, et al. ESPE/LWPES consensus statement on diabetic ketoacidosis in children and adolescents. *Arch Dis Child*. 2004; 89:188-94.
 11. Edge JA, Ford-Adams ME, Dunger DB. Causes of death in children with insulin dependent diabetes 1990-1996. *Arch Dis Child*. 1999; 81:318-23.
 12. Hattersley A, Bruining J, Shield J, Njolstad P, Donaghue K. ISPAD Clinical Practice Consensus Guidelines 2006-2007 The diagnosis and management of monogenic diabetes in children. *Pediatric Diab*. 2006; 7:352-60.
 13. Polak M, Shield J. Neonatal and very-early-onset diabetes mellitus. *Semin Neonatol*. 2004; 9:59-65.
 14. Polak M, Cave H. Neonatal diabetes mellitus: a disease linked to multiple mechanisms. *Orphanet J Rare Dis*. 2007;2:12.
 15. Giannattasio A, Pintaudi M, Mancardi MM, Battaglia FM, Veneselli E, Lorini R, et al. Neonatal diabetes mellitus due to pancreatic agenesis and pervasive developmental disorder. *Ital J Pediatr*. 2009; 35:23.
 16. Fredrick F, Sawe H, Muze K, Mally D, Majaliwa E. A seven weeks old baby with diabetic ketoacidosis: a case report. *Clin Case Rep*. 2015; 4:147-50.
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