ISSN: 2577-2996

PROGRESS IN MEDICAL SCIENCES, 2024
VOL 8, NO. 2, PAGE 1 – 3
Doi: doi.org/10.47363/PMS/2024(8)202

CASE REPORT

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Peritoneal Dialysis in Neonatal Diabetes Presenting With Severe Dka: A Case Report

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ABSTRACT

Introduction: Neonatal diabetes is a rare genetic disease characterized by severe, persistent hyperglycemia requiring treatment. It commonly occurs between the neonatal period and infancy, and rarely between 6 months and 1 year. presentation happens before 6 months of age. The mode of presentation can vary widely, ranging from simple incidental hyperglycemia to full on dehydration and diabetic ketoacidosis (DKA). Patients with neonatal diabetes are responding very well to insulin therapy and rarely showed insulin resistance .In our case the patient did not respond to high doses of intravenous insulin reaching 0.5 iu/kg/hr and required peritoneal dialysis.

Case Report: We report the case of a 7 month old Omani male, born to non-consanguineous young parents,who is clinically and biochemically healthy , previously investigated for stress related hyperglycemia and all his investigations was normal , presented to the private clinic with high grade fever, reduced activity and poor oral intake of and found to have Diabetic ketoacidosis and subsequently referred to Royal hospital as an emergency case for further management .on arrival to Emergency room the patient appeared tachypneic, with subcostal and suprasternal recession and grunting in keeping with Kussmaul breathing with SMBG 38 mmol /dl and severe Metabolic acidosis (pH 6.9, bicarbonate 3.7 mEq/L, lactate 3.2, sodium 152, potassium 5.7.Management of DKA initiated as per protocol in ER , but the patient did not respond and He subsequently developed respiratory and cardiovascular compromise warranting admission to pediatric intensive care unit (PICU). As such, he was intubated and started on adrenaline 0.05 mcg/kg/min. Blood gas continued to show persistent metabolic acidosis PH 6.9 and HCO3 4mEq/L, not responding to fluid and insulin dose increasing from 0.1 unit /kg/hr reaching 0.7 IU /kg/hr (which consider to be a high dose with a dextrose fluid of 20% to avoid rapid drop in Blood glucose), After 12 HRS of resistant to DKA measures, peritoneal dialysis initiated. After starting peritoneal dialysis the acidosis improved and insulin dose weaned to gradually reached 0.1 iu /kg/hr .He was also initially started on Ceftriaxone, later kept on tazocin, vancomycin, and tamiflu for continuous spikes of fever.

Result: After three days we are able to stop peritoneal dialysis and the baby out of DKA with normal fine and motor function. He was then shifted to the high dependency unit for further care and was transferred to the ward under the endocrine team. All cultures, including blood, urine cultures came as no growth and subsequently antibiotics stopped and the baby was able to take orally well and started on subcutaneous insulin. Genetic test confirmed a heterozygous for a likely pathogenic INS missense variant (Monoallelic pathogenic variants in INS cause permanent neonatal diabetes.

Conclusion: Neonatal Diabetes Mellitus is a rare disease and requires urgent medical intervention. Intravenous insulin infusion is the standard of care in infants with hyperglycemia & amp; DKA. Peritoneal dialysis is previously not reported in literature to manage DKA in neonatal diabetes. In this particular case of severe and resistance to IV insulin Diabetic ketoacidosis, was successfully managed with peritoneal dialysis.

ARTICLE HISTORY

Received March 18, 2024
Accepted March 20, 2024
Published April 04, 2024

KEYWORDS

Neonatal Diabetes, Peritoneal Dialysis, Genetic Test, Intravenous Insulin Infusion, DKA

Abbreviations

DKA: Diabetic Ketoacidosis

PICU: Pediatric Intensive Care Unit

SMBG: Self-Monitoring Blood Glucose

HRS: Hours

ER: Emergency Room

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Introduction

Neonatal diabetes is a rare genetic disease characterized by severe, persistent hyperglycemia requiring treatment. It commonly occurs between the neonatal period and infancy, and rarely between 6 months and 1 year [1]. Diabetic ketoacidosis is an uncommon presentation of neonatal diabetes, and if presented it responds well to insulin therapy. Hence, we are presenting a baby with severe DKA who is refractory to insulin therapy and requires peritoneal dialysis to restore his metabolic status.

Case History

Five months old Omani male, born to a non-consanguineous parent, primigravida mother with a birth weight of 2.4 kg, was investigated at a local hospital at the age of two months for hyperglycemia with the impression of stress induced hyperglycemia, as blood test showed Negative Anti-GAD & Anti-Islet Cell with C-peptide of 335 pmol/L, insulin level 62 pmol/L, and HbA1C 6.2%. At five months of life he presented to the emergency room at Royal Hospital with a high grade fever, reduced activity, and poor oral intake for 1 week duration. At emergency, he was grunting with kussmal breathing, but his BP was maintained. Investigations showed BG > 38 mmol/dl, and blood gas showed severe metabolic acidosis and unrecordable HCO3 with normal lactate (Table 1).

Table 1: Blood Gas and Electrolytes

Time	At ER	At 2 hours	At 4 hours	At 8 hours	Peritoneal Dialysis - 4 hours	Peritoneal Dialysis - 8 hours
RBS	>38	>38	>38	36		
pH	< 6.8	6.85	6.88	6.8	7.2	7.34
HCO3	Unrecordable	4	2	2	8	15
Cl	122	122	123	122		
Lactate	1.2	3.2	1.8	1.8		
Na	152	152	158	152		
K	4.3	5.7	5.1	5.1		
Urea	16				7.5	
Creatinine	105				43	
Insulin Infusion	0.1 IU/kg/hr	0.2 IU/kg/hr	0.4 IU/kg/hr	0.8 IU/kg/hr		

The baby was diagnosed with newly onset diabetes with severe DKA in which treatment with IV fluid and insulin infusion at a rate of 0.1 IU/kg/hr was initiated, and the baby was admitted to the pediatric Intensive Care Unit (PICU). On arrival at the PICU, the patient appeared tachypneic, with subcostal and suprasternal recession and grunting in keeping with kussmaul breathing. He subsequently developed respiratory and cardiovascular compromise, warranting intubation. The baby is not responding to DKA measures, and his acidosis is refractory, reaching an infusion of insulin at 1 IU/kg/hr. The infant had also developed an acute kidney injury with very high triglyceride levels. He was continued on DKA measures, HCO3 administration at a small dose started, and peritoneal dialysis (PD) was initiated. After 8 hrs of starting PD, all parameters including blood gas, glucose and bicarbonate levels improved. The baby remained intubated for five days and covered with vancomycin and then tazocin as he remained febrile. On day 2 of PD, metabolic acidosis resolved and bicarbonate was normalized. An MRI was requested and showed an acute ischemic infarct of the medial aspect of the cerebellum extending to the left side of the vermis. In which a neurologist reviewed the case and there was no neurological sequelae. He was then shifted to the high dependency unit for further care and was admitted to the inpatient ward under the endocrine team. Genetic panel for neonatal DM showed a heterogeneous pathogenic INS missense variant (Table 2). During the OPD follow up the baby was doing well on the MDI insulin regimen with normal growth and development.

Table 2: Genetic Test Results -consistent with a genetic diagnosis of neonatal diabetes, subtype INS

Gene	Zygosity	Inheritance	HGVS description	Location: GRCh37 (hg19)	Classification
INS	Heterozygous	Not Known	NM_001185098.1: c.128G>A p.(Cys43Tyr)	Chr11:g.2182074C>T	Likely Pathogenic

Discussion

Neonatal DM can either be temporary, permanent, or part of a syndrome. The cause is oftentimes attributed to an underlying monogenic defect if the presentation happens before 6 months of age. That is a specific mutation encoding proteins that take part in the

normal functioning or synthesis of pancreatic beta cells. In Oman, there was 24 cases of neonatal diabetes, non were presented with DKA and the most common cause is a homogeneous GCK gene mutation, which are all treated and responded to insulin [2]. Internationally, the most common mutation is in KCNJ II and ABCC8, which can be treated with oral sulfonylurea and account for almost 40% [3]. ND is due to the insulin gene (INS), and it is considered to be the third cause of neonatal diabetes worldwide [4]. Mutation due to INS with the variant identified (see table 2) is the first case identified in Oman; however, mutation in INS with Cys43 has been identified in one patient with neonatal diabetes before and reported to have a de novo mutation [5]. INS mutations are heterozygous, affecting preproinsulin, and transmitted in an autosomal dominant manner. Usually, patients with INS mutations respond well to insulin therapy [6].

The mode of presentation can vary widely, ranging from simple incidental hyperglycemia to full on dehydration and diabetic ketoacidosis (DKA). Although this has been scarcely studied in infancy, the likelihood of presenting with DKA has been seen to increase with age [7]. A study conducted at the University of Chicago showed that 66.2% of patients with neonatal monogenic diabetes presented with DKA [3]. Another study revealed that DKA was found in almost 80% of patients with mutations of KCNJ11/ABCC8, and none in children with over-expression of 6q24 [8]. While it is important to recognize early signs of neonatal diabetes mellitus, it is also mandatory to manage DKA properly to prevent complications. Our patient presented with severe DKA, which was refractory to a supra-physiological dose of insulin reaching 1 IU/kg/hr, and indeed the baby developed an acute ischemic insult to the brain due to persistent acidosis. Furthermore, our patient responded well to peritoneal dialysis along with an insulin infusion at a dose of 0.8 IU/kg/hr. This is the first case of neonatal diabetes presenting with severe DKA and treated with peritoneal dialysis, and this may be explained by the genetic test, which showed the variant in our patient has not been reported in the genome AD database (139,528 individual) (PM2_Moderate).

Conclusion

Neonatal diabetes mellitus is a rare disease and requires urgent medical intervention. Management with intravenous insulin infusion and intravenous fluid is the standard of care for infants with DKA. Close monitoring is also needed in all cases. In this particular case of neonatal diabetes presented with severe DKA refractory to a high dose of intravenous insulin infusion, peritoneal dialysis should be considered as a modality of treatment to avoid complications.

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