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Persistent acidosis at presentation in a patient with type 1 diabetes: Concomitant diagnosis of type 1 distal renal tubular acidosis

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ABSTRACT

We present a rare case of a 7-year-old boy who was diagnosed with type 1 diabetes mellitus and type 1 distal renal tubular acidosis concomitantly. The proband presented with history of polyuria, polydipsia and lethargy. He was found to be severely dehydrated. Initial pH value was 7.025 with bicarbonate level of 5.3 mmol/L, and serum glucose of 23 mmol/L. Despite adequate rehydration and insulin therapy (0.1 U/kg/hr), he continued to have persistent metabolic acidosis with normal bicarbonate. Other causes for acidosis were thought off, and with further inquiry, the parents revealed that the father and two other siblings are treated for renal tubular acidosis. Our patient had urine pH of 8, serum potassium 2.9 - 3.7 (3.5 - 5.4 mmol/L), chloride 110 - 116 (98 - 110 mmol/L). The diagnosis of type 1 renal tubular acidosis was made, and the acidosis was corrected with oral sodium bicarbonate and potassium chloride. The patient was discharged on subcutaneous multiple daily insulin injections.

Keywords: Distal Renal Acidosis; Type 1 Diabetes; Persistent; Childhood

1. INTRODUCTION

The incidence of diabetic ketoacidosis (DKA) among newly diagnosed children with type 1 diabetes remains high even in countries with highly developed medical care system. Dehydration, hyperglycemia and acidosis consistent with DKA is present in up to 67% of diabetic children at presentation [1].

In most countries, treatment of DKA follows standard protocols. Restoring circulatory volume will improve tissue perfusion and renal function. The administration of insulin will stop further ketogenesis and regenerate bicarbonate leading to the restoration of acidosis [2].

We present a case of a child who had persistent metabolic acidosis in spite of adequate hydration and appropriate insulin therapy.

2. CASE REPORT

Abdulrahman, a 7-year-old previously healthy boy, presented to the emergency department with 5-days history of polyuria, polydipsia and decreased appetite. Two days before admission, he developed shortness of breath and was noted by the parents to be lethargic.

On initial physical examination, he was found to be severely dehydrated and obviously small for his age. (–3.8 SDS for weight and –2.6 SDS for height). Blood pressure was 100/63 mmHg, HR 100/m, he was hyperventilating (RR 45/m), and oxygen saturation of 100% in room air.

Family history was negative for diabetes, and the patient was not on any medications.

Laboratory investigations revealed initial venous gas pH of 6.9, bicarbonate of 6.0 mmol/L (N = 22 - 30) and base excess of –25.6. Serum glucose was 40.2 (N = 3.9 - 6.1 mmol/L), creatinine 80 (N = 44 - 71 μmol/L), urea 5 (N = 2.5 - 6 mmol/L), sodium 128 (N = 135 - 148 mmol/L) potassium 3.7 (N = 3.7 - 6 mmol/L), and chloride 109 (N = 102 - 112 mmol/L).His urine showed +4 glucose and +2 ketones.

The diagnosis of severe diabetic ketoacidosis was made, and the patient was admitted to the intensive care unit. He was resuscitated with 0.9% normal saline (NS), and subsequently with intravenous insulin infusion 0.1 U/kg/hr. He continued to be drowsy; mannitol 0.5 g/kg was given. Computer tomography scan was normal.

His level of consciousness and hydration status improved, however, his acid-base alternation persisted for 5 days (**Figure 1**). Urine analysis showed pH of 8, +4 glucose and negative for ketones and anion gap was 13.5 repeat-

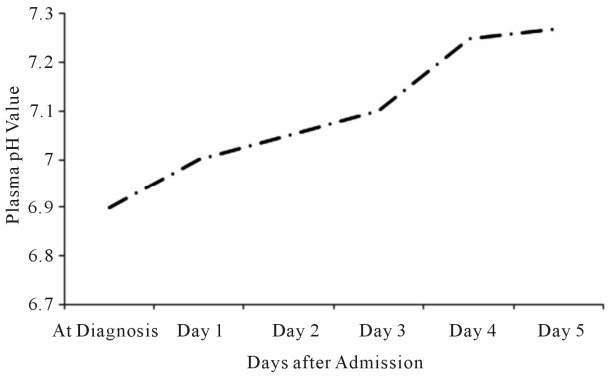

Figure 1. Plasma pH values after admission. Four days after admission, pH continues to be low. The pH value continues to be low (acidosis) 5 days after treatment, despite absence of ketone in the urine.

edly, leading to the suspicion of another etiology for the acidosis other than his diabetes.

Further inquiry revealed that the father who is short (−4.7 SDS), and 2 siblings have a form of persistent acidosis, which turned out to be distal (type 1) renal tubular acidosis, with mental sub-normality and short stature (both below –3.3 SDS).

Repeat urine and serum analysis on day 5 are shown in **Table 1**.

Renal ultrasound showed mild degree of right hydronephrosis, but no nephrocalcinosis.

A diagnosis of concomitant renal tubular acidosis (type 1) made, based on the results of the investigations and the family history and he was commenced on potassium and bicarbonate replacement. The acidosis was resolved, and he was discharged in stable general condition.

On last follow-up, 11 months after diagnosis, he continue to be is on multiple daily insulin injection of short and long acting analogues, bicarbonate and potassium supplements. However, his latest biochemical analysis showed HbA1c of 10.1% (4.1% - 6.2%), sodium 139 mmol/L, potassium 4mmol/L bicarbonate 15 mmol/L (he is non-compliant with the treatment), and chloride 110 mmol/L.

3. DISCUSSION

We describe the first case of type 1 diabetes associated with type 1 distal renal tubular acidosis (dRTA) in pediatric age group. We could find three previous case reports of dRTA occurring in patients with T1DM in the literature: one as part of multiple autoimmune diseases [3], a second associated with Sjorgen's syndrome [4] and the third only with T1DM in a 25-yr-old female [5].

Distal RTA is a clinical syndrome identified by a normal anion gap hyperchloremic metabolic acidosis secondary to a selective defect in distal renal acidification. It is characterized by inappropriately high urine pH, hypokalemia and reduced net acid excretion [6]. Primary hereditary forms of dRTA have predominantly seen as autosomal dominant traits [6-8], although an autosomal recessive form has been described with or without associated sensorineural deafness [9].

The incidence of DKA among newly diagnosed patients remains high (11% - 67%) even among nations with the most highly developed medical system. The primary etiology of acidemia in patients with DKA is ketoacidosis, with contribution of lactic acidosis and renal dysfunction [10]. In most countries, treatment of DKA follows standard protocols of intravenous fluids and insulin infusion. After initial 0.9% NaCl bolus, maintenance should is continued with 0.45% NaCl to decrease the risk of hyperchloremic metabolic acidosis by the prolonged use of 0.9% normal saline. After metabolism during recovery phase, bicarbonate is regenerated and aids the restoration of acidosis. In more than 50% of adults and pediatric patients, hyperchloremia develops 4 hours after therapy [11]. It was suggested to be contributed by renal excretion of ketone preferentially over chloride anion and volume replacement with saline.

The mean time to achieve pH > 7.3 and bicarbonate > 15 is 10 - 14 hours [12]. In DKA, bicarbonate levels recover more slowly than pH value. Our patient had persistent acidosis for more than 5 days. Rosenbloom [13] defines persistent acidosis as bicarbonate < 10 mmol/L after 8 - 10 hours after treatment. He considers, as many other do [14-16] inadequate insulin dose, inaccurate preparation as the main factors. Renal impairment secondary to severe dehydration can lead to acute tubular necrosis leading to acidosis (2 - 6 DKA). Our patient had normal renal function, and the insulin preparation and dose (0.1 U/kg/hr) was appropriate. Infections were also ruled out. Urine analysis of our patient showed pH value

Table 1. Serum and urine biochemistry on Day 6, after the family history of dRTA was revealed. Acidosis was persistent with negative urine ketones. Urine and serum biochemistry on day 5: Persistent acidosis, with alkaline urine and hypokalemia and normal anion gap consistent with renal tubular acidosis.

	Osmolality mmol/L	pH	HCO_3 mmol/L	K mmol/L	Cl mmol/L	Phosphate mmol/L	Ca/Cr Ratio	AG
Serum (Normal)	278 (275 - 300)	7.28 (7.35 - 7.45)	17 (22 - 30)	3.4 (3.5 - 4.5)	117 (98 - 110)	0.65 (1.05 - 1.8)	-	12.4 (6 - 16)
Urine (Normal)	289 (500 - 800)	8	-	46	56	10.1	1.79 (0.08 - 0.57)	-

of >7 on 2 occasions, in the face of metabolic acidosis, mild hypokalemia and hyperchloremia. The father's height SDS is −3.6, the 18-year-old brother's height SDS is –4 with low IQ and nephrocalcinosis, and the 15-year-old sister's height SDS is –2.8. Based on the family history, the urinary pH and the normal anion gap, the diagnosis of dRTA concomitant with type 1 diabetes was made. He responded to bicarbonate and potassium supplements, however, he is (as is his siblings) non-compliant with his medications. He continued to have persistent mild degree of acidosis (bicarbonate of 12 - 14.2) and high HbA1c (10.2). His ultrasound, one year after diagnosis, continue to show no signs of nephrocalcinosis.

In addition to describing the first case of concomitant diagnosis of dRTA and type 1 diabetes in children, this rare case emphasizes the importance to document the presence or absence of ketones in diabetic patients presenting with acidosis, especially if persisting despite aggressive treatment. Not all acidosis is ketoacidosis in T1DM.

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