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CASE REPORT OPEN ACCESS

TYPE 1 DIABETES MELLITUS PRESENTING AS DISTAL RENAL TUBULAR ACIDOSIS (RTA TYPE 1)

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Abstract

Background: Type 1 Diabetes Mellitus (DM) is an autoimmune process which causes destruction of b-cells and absolute insulin deficiency. This insulin deficiency prone patient to hyperglycemia and resultant early micro-vascular and macro-vascular complications. Macro-vascular complication seen early in diabetes are CAD, CVA and PAD. In micro-vascular complications, we have retinopathy, neuropathy and nephropathy. In diabetic nephropathy, usually glomerular injury is widely described in literature but little is known about the tubular changes. We report a case which has tubular damage in the form of distal tubular damage causing renal tubular acidosis. Patient has classical bilateral nephrocalcinosis, normal anion gap acidosis and persistently low HCO3. This entity in type 1 DM is not reported in literature. **Case :** Patient S, 42 yr Male with Type 1 DM for 15 years on Inj. Insulin mixtard presented to emergency with swelling of bilateral lower limb associated with pain/tingling and numbness for 3 months. **Conclusion:** In a patient with type 1 DM, acidosis can occur due to causes other than DKA and workup should be done if acidosis persists even after treatment.

Abbreviations: DM(diabetes mellitus), HCO3(bicarbonate), RTA(renal tubular acidosis), CAD(coronary artery disease), CVA(cerebrovascular accident), PAD(peripheral artery disease).DKA(diabetic ketoacidosis)

INTRODUCTION

Type 1 Diabetes Mellitus (DM) is usually an auto-immune[1] process in which there is an immunological destruction of beta(β) cell which causes absolute insulin deficiency. In absence of insulin deficiency, there is lactic acidosis which is a high anion gap metabolic acidosis. Patient with type 1DM generally presents with DKA (Diabetic keto-Acidosis) in which acidosis is due to high ketones in body. We present a case which has normal anion gap acidosis in type 1 DM with uncontrolled hyperglycemia. Distal RTA commonly occur in condition like amyloidosis, Sjogren syndrome, SLE (Systemic Lupus Erythematosus) and Sickle cell diseases. Distal RTA presents as nephrocalcinosis, normal anion gap with hyperchloremic acidosis which occurs due to inability of distal convoluted tubule to produce hydrogen(H+) ions[2]. This in turn, leads to loss of H+ ions and subsequently loss of potassium(K) in the body causing hypokalemia and alkaline urine. This alkaline in urine causes precipitation of calcium stones in urine and patient presents as asymptomatic/ symptomatic nephrolithiasis.

CASE REPORT

Patient S, 42yr Male with Type 1 DM for 15 years on Inj. Insulin mixtard presented to emergency with swelling of bilateral lower limb associated with pain/tingling and numbness for 3 months. Swelling in bilateral lower limb was gradual, extending up to ankle. No history of pain abdomen, nausea, vomiting, chest pain, shortness of breath, syncope, palpitation, sweating, burning micturition or decreased urine output. No history of Hypertension, Tuberculosis, Asthma in past. Family history was

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also not significant. Patient left Inj. Insulin for the past 3 days due to unavailability. Patient was admitted and investigations were sent. Investigations at admissions were (Table 1):

TABLE 1

Date	**24/01/2019**	**28/01/2019**
Hemoglobin	7.49g/dl	
Total Leucocyte Count	11340/mm3	
Differential Leucocyte count	N89L5M5	
Platelets	146 lakh/mm3	
Hematocrit	23.7	
Blood Urea	81mg/dl	22mg/dl
Serum creatinine	1.96mg/dl	0.96mg/dl
Serum sodium	124mEq/l	137mEq/L
Serum K	5.5mEq/L	3.2mEq/L
Serum Chloride	98mEq/L	106mEq/L
Serum Calcium	7.6mg/dl	7.7mg/dl
Serum Phosphorus	3.9mg/dl	3.4mg/dl
Total bilirubin	0.46mg/dl	
Direct bilirubin	0.12mg/dl	
SGPT	15U/L	
SGOT	36U/L	
ALP	168U/L	
Total Protein	5.3gm/dl	
Albumin	3.2gm/dl	
Globulin	2.1gm/dl	
pH	7.32	
HCO3	11.1mEq/L	
Anion gap	11mEq/L	
RBS	High	
HbA1C	12.7	
Urine R/M	Glucose ++, protein + and ketones absent	

Patient was managed on the line of DKA with Intravenous fluids and insulin as the patient had very low bicarbonate (HCO3) and high dextrose. During 2-day course, patient ABG showed persistent low HCO3 in spite of blood sugar being controlled, so cause of persistent acidosis other than DKA was sought, urine pH was advised which came out to be 6.0.

Patient was evaluated for causes of low HCO3 with high urinary pH. USG (ultrasound) abdomen was suggestive of multiple hyperechoic calculi seen in upper pole with largest measuring 7.8mm in the right kidney. Left kidney size normal with multiple hyperechoic calculi in lower pole and posterior pole longest 9mm. Ophthalmology evaluation suggested bilateral moderate Non Proliferative Diabetic Retinopathy (NPDR). Patient repeat investigations were (Table 2):

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TABLE 2			
Date	**28/01/2019**	**30/01/2019**	**04/02/2019**
Urine pH	6.0	6.0	6.0
Urine R/M	Glucose-nil, protein-nil, ketone-nil	Protein +,glucose-nil	Proteins +, glucose - nil
pH	7.29	7.41	
HCO3	15.6mEq/L,	18.8	
Anion Gap	9mEq/L	5mEq/L	
iPTH	14.9(11-79)		

Patient had kidney stones despite serum calcium to be low. iPTH was advised due to low calcium which also lies in the lower range, ruling out secondary hyperparathyroidism. We searched literature for the same and most common cause for this presentation was distal RTA.

DISCUSSION

Type 1 DM is a chronic autoimmune disease beginning with genetic susceptibility and progressing to autoimmunity leading to destruction of β-cells. Autoantibodies against the pancreatic islet, islet cell antibodies (ICA) and Glutamic acid decarboxylase (GAD) are detected in childhood in these patient[3]. It is usually a disease of childhood/ young. According to 2009 census, 6666 of 3.4 million youth were diagnosed with type 1 diabetes for a prevalence of 1.93 per 1000. The highest prevalence of T1D was 2.55 per 1000 among white youth and the lowest was 0.35 per 1000 in American Indian youth[4].

Distal RTA is a syndrome of systemic hyperchloremic acidosis with alkaline urine pH, hypocitraturia and hypercalciuria due to reduced secretion of H+ ions by the cells of the collecting tubules[5,6]. Metabolic acidosis in distal RTA contributes as a predisposing factor to recurrent nephrolithiasis and bone loss[6]. Patients with distal RTA are unable to lower urine pH normally in the presence of systemic metabolic acidosis regardless of its severity[7].

15-30% of subjects with type 1 DM have autoimmune thyroid disease, 4–9% have celiac disease, and 0.5% have Addison's disease [3]. Distal RTA is also multifactorial, it can develop as a consequence of autoantibodies, most commonly in Sjögren's syndrome and systemic lupus erythematosus(SLE). There are various case reports which has linked distal RTA with autoimmunity and destruction of collecting ducts[8]. There are only few case reports with patients of type 1 DM developing distal RTA, in which one patient having due to autoimmune and other patient is having Sjogren syndrome[9-10] and no cause could be found in some other[11].

Our patient had all features of distal RTA in the form of nephrocalcinosis, acidic urine, low bicarbonate, metabolic acidosis which persisted even after correction of blood sugar. He had proteinuria and slightly deranged creatinine, also had retinopathy which favours nephropathy. But destruction of glomeruli alone cannot explain the development of distal RTA in our patient. Various studies previously had already shown that diabetic patients have interstitial and tubular injury along with glomerular injury[12-14].

Additional investigations in the form of kidney biopsy would be required for further confirmation of the cause of destruction of collecting ducts Tubular damage.

Distal RTA improved with alkali therapy and it also prevent the formation of renal stones. Our patient already has developed renal stones, still alkali therapy will prevent the progression of stones. We thus present a case which was unusual

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in T1D as every type 1DM doesn't have acidosis due to DKA. Also, patients with hypokalaemia and nephrocalcinosis, we should rule out causes and extensive investigations are required for confirmation of diagnosis. Further research is required in this field.

CONCLUSION

Type 1 DM patients are prone for autoimmune diseases but we should think beyond autoimmunity in type 1 DM as they may develop disease which may be complications of DM per se. Acidosis in type 1 DM is not always due to DKA and we should search for other causes of persistent acidosis.

We have taken a written consent from the patient for the publication of this case report. There is no conflict of interest between the authors. This research has not received any specific grant from any funding agency in public, commercial or not-for-profit sector.

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