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Case Report

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Hypophosphatemia, A Silent Killer in Diabetic Ketoacidosis Patients

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ABSTRACT

Diabetic ketoacidosis is a serious complication of diabetes that occurs when your body produces high levels of blood acids called ketone. Without enough insulin, your body begins to break down fat as fuel. This process produces a buildup of acids in the bloodstream called ketones, eventually leading to diabetic ketoacidosis if untreated. Although hypophosphatemia is common in DKA, it is rarely very severe leading to the complications. Hypophosphatemia leading to rhabdomyolysis in DKA has been reported by various authors with or without significant renal failure requiring renal replacement therapy [1].

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Introduction

Phosphate Depletion of intracellular phosphate occurs in DKA and phosphate is lost as a result of osmotic diuresis. Plasma phosphate levels fall after starting treatment and this is exacerbated by insulin, which promotes entry of phosphate into cells. Decreased intracellular ATP levels impair cellular functions that depend on energy-rich phosphate compounds, and a decrease in 2, 3-diphosphoglycerate (DPG) level increases the affinity of hemoglobin for oxygen and reduces oxygen release in tissues. Many organ systems can be affected [2].

Case Report A 14 year old girl, has past history of knee ligaments repair and eye ligaments fixation due to Ptosis, presented with one week history of polyuria and polydipsia and at ER high blood sugar, Ketonuria +2 and severe metabolic acidosis ABG at presentation: Ph 6.83 Co2 21 Hco3 4.4 Na 150 K 3.3 in severe dehydration given usual fluid therapy as severe DKA case, GCS 8/15, blood pressure was 90/50 with weak peripheral pulsations then developed Hypotension 70/40 and absent peripheral pulsations then the patient treated as a shocked DKA patient CVC inserted to allow more fluid therapy, and given Inotropes (Noradrenaline 0.1 mic and Dobutamine 15 mic) Then the patient developed Bradycardia 50 bpm and Bradypnea then the patient intubated and put on Mechanical Ventilation to secure the airway, treated by Ceftriaxone, Vancomycin, IVF deficit 100%, Insulin infusion, Given empirical Saline 3% after suspected a cerebral oedema case without satisfying results, then given empirical phosphate solution (Glycofos) then the GCS improved to 12/15. After six hours the patient became Oliguric then became anuric. After nephrology consultation, after assess the patientwith severe metabolic acidosis with anuria state decided to put the patient on haemodialysis after given a urine sample to examine after suspect change in colour (became more darker and suspect rhabdomyolysis which confirmed after examination of urine) Ultrasonography revealed an increase renal echogenicity and echocardiography revealed a uremic Cardiomyopathy, EF 50%. After regular haemodialysis for 3 consecutive days the metabolic acidosis improved and ABG became PH 7.38 Co2 28 Hco3 16 K 3 NA 134 Mixed Venous 45% The patient extubated successfully and stopped IV fluids and change to subcutaneous insulin therapy, the patient now GCS 15/15 without any neurological deficit and after consecutives days of haemodialysis the patients passed a clear urine with improved creatinine and urea levels. Laboratory finding:

NB: Myoglobin in Urine.: 77.1 high (N :upto 5)

	30/8	31/8	1/9	2/9	3/9
HB	15	12	10		9.2
WBCS	23	6.7	9.1		10.2
PLT	385	139	130		91
ALBUMIN	5.7	3.8	3.3	2.7	2.5
Creat	0.8	3.6	5.5	5.7	6.8
Urea	22	84	93	94	107
Phosphorus		1	1	3.7	4.2
Calcium	8.7		9	9.8	7
Prothrombin Activity		100%	90%	64%	
INR		1	1	1.2	
HbA1C					12.3
TSH					0.52
FT4					0.62

Discussion

The patient described here presented with DKA as the initial presentation of T1DM. However, her clinical course was complicated by RM with anuric renal failure. The possible cause attributed for her RM was severe hypophosphatemia. The cause of RM can be multiple, ranging from viral etiologies to mechanical trauma and various metabolic causes. Rhabdomyolysis(RM) is a syndrome characterized by injury to skeletal muscle fibers with disruption and release of toxic metabolites into circulation. It is characterized by triad of muscle weakness, myalgia and dark urine and is associated with increased creative kinase (CK) and lactate dehydrogenase (LDH).since our resources were limited to do the complete workup to find out the cause of RM, we believed that it might be due to severe hypophosphatemia considering the fact that after correcting serum phosphate, patient's clinical features gradually subsided and she eventually improved.

Although hypophosphatemia is common in DKA, it is rarely very severe leading to the complications. Prolonged profound ketoacidosis with insulin infusion in the initial rehydration phase can lead to severe hypophosphatemia, mainly due to intracellular shifting of the phosphate. Additionally, prolonged acidosis can lead to decreased proximal tubular phosphate reabsorption which further leads to increased excretion of phosphate resulting in severe hypophosphatemia. The mechanism leading to RM in DKA is unclear. Other factors that play role in the development of RM are depletion of potassium and phosphate. Phosphate is one of the constituents of adenosine triphosphate (ATP) and in case of severe hypophosphatemia, there is ATP depletion which leads to cellular injury and then rhabdomyolysis.7 Acute Kidney Injury (AKI) is a dreadful complication of rhabdomyolysis and is reported in 15-30% of rhabdomyolysis patient. AKI is believed to be triggered by myoglobin as a toxin causing renal dysfunction . Hypophosphatemia leading to rhabdomyolysis in DKA has been reported by various authors with or without significant renal failure requiring renal replacement therapy [3, 4].

Phosphate replacement in DKA is still controversial with no clear cut guideline. We supplemented our patient with iv phosphate As a result, serum phosphate gradually increased and rhabdomyolysis subsequently decreased. General management of rhabdomyolysis includes fluid resuscitation and prevention of ARF.1 Accordingly, we increased the fluid and, to prevent ARF, urinary alkalinization , but our case was anuric so hemodialysis was our choice for treatment of rhabdomyolysis [5].

Conclusion

Severe hypophosphatemia combined with phosphate depletion (i.e., when not solely due to intracellular phosphate translocation) is uncommon, but can have severe consequences.

Manifestations depend on the severity and chronicity of the phosphate depletion; patients usually do not have symptoms until plasma phosphate is <1 mg/dL (0.32 mmol/L).

1. Severe hypophosphatemia can occur during treatment of DKA; however, symptoms are uncommon because the hypophosphatemia usually is acute and there typically is no antecedent chronic phosphate deficiency.

2. Inical manifestations of hypophosphatemia are largely due to intracellular phosphate depletion. Decreased intracellular ATP levels impair cellular functions that depend on energy-richphosphate compounds, and a decrease in 2,3-diphosphoglycerate (DPG) level increases the affinity of hemoglobin for oxygen and reduces oxygen release in tissues [6]. Many organ systems can be affected. Manifestations include:

- Metabolic encephalopathy (irritability, paresthesias, confusion, seizures, coma); impaired myocardial contractility and respiratory failure due to weakness of the diaphragm; muscle dysfunction with proximal myopathy, dysphagia and ileus; rare hematologic effects include hemolysis, decreased phagocytosis and granulocyte chemotaxis, defective clot retraction, and thrombocytopenia. Acute hypophosphatemia in a patient with preexisting severe phosphate depletion can lead to rhabdomyolysis [7, 8].
- Severe hypophosphatemia associated with any of the above symptoms should be treated [9, 10].

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