J Compr Ped. 2015 November; 6(4): e28020. doi: 10.17795/compreped-28020

Published online 2015 November 29. **Case Report**

Severe Symptomatic Hypophosphatemia With Thrombocytopenia in a Child With Diabetic Ketoacidosis

Vinod Prabhu Ganapathy,[1] Vijay Anand Palaniswamy,[2] Pratibha Vinod,[3] Lakshmi Narayanan,[4] Tanushree Sahoo,[5] and Rashmi Ranjan Das[6,*]

[1]Department of Pediatrics, Jupiter Medical Center, Dubai, UAE
[2]Department of Critical Care, G Kuppuswamy Naidu Memorial Hospital, Coimbatore, Tamilnadu, India
[3]Department of Pediatrics, iCARE Clinics, Dubai, UAE
[4]Department of Pediatrics, G Kuppuswamy Naidu Memorial Hospital, Coimbatore, Tamilnadu, India
[5]Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), New Delhi, India
[6]Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), Bhubaneswar, India

*Corresponding author: Rashmi Ranjan Das, Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), Bhubaneswar, India. Tel: +91-6742476301, Fax: +91-6742476001, E-mail: rrdas05@gmail.com

Received 2015 February 19; **Revised** 2015 July 4; **Accepted** 2015 November 15.

Abstract

Introduction: Although asymptomatic hypophosphatemia is a common finding in diabetic ketoacidosis (DKA), severe symptomatic hypophosphatemia is an uncommon complication.

Case Presentation: We report a 16-year-old female child with DKA, who developed thrombocytopenia, rhabdomyolysis, muscle weakness, and acute renal failure due to severe hypophosphatemia. She was managed with intravenous fluids, insulin infusion, phosphate therapy, and dialysis. After two weeks of hospitalization, the patient was discharged home with no squeal.

Conclusions: In critically ill patients, the symptoms of hypophosphatemia may not be apparent, but clinicians should be vigilant about this complication during therapy. In cases of severe symptoms (e.g., cardiopulmonary distress, anemia and thrombocytopenia, or rhabdomyolysis), phosphate therapy under close surveillance is warranted.

Keywords: Child, Diabetes Mellitus Type 1, Phosphates, Fluid Therapy, Diabetic Complications

1. Introduction

Asymptomatic hypophosphatemia is a common finding during diabetic ketoacidosis (DKA), and may rarely manifest clinically (1). Although osmotic dieresis in DKA leads to increased urinary phosphorus excretion, hyperphosphatemia is a more common phenomenon in DKA as compared to hypophosphatemia. A combination of factors is responsible for hypophosphatemia, such as fluid resuscitation, insulin therapy, and correction of acidosis, resulting in intracellular shifting of phosphate (1). The most common manifestation of hypophosphatemia during DKA is muscle weakness that may lead to cardiorespiratory failure, encephalopathy, acute renal failure, seizure, and rhabdomyolysis in severe cases (2-8). In this report, we describe a 16-year-old female with type 1 diabetes mellitus, who developed severe symptomatic hypophosphatemia with DKA and was successfully managed. The development of thrombocytopenia in the index case, in addition to other complications, needs attention.

2. Case Presentation

A 16-year-old girl presented to the emergency department with complaints of vomiting, shortness of breath, and unresponsiveness for one day. There was no current history of fever, cough, coryzae, diarrhea, skin rash, bleeding manifestations, or abnormal movement. She had had a febrile illness six months prior to this hospitalization, during which she was found to have high blood glucose levels. She was started on some indigenous local medication after which she remained stable, and the medication was discontinued without any further investigations. There was no history of polyuria, polydipsia, or weight loss. There existed no family history of diabetes mellitus, hypertension, heart disease, or endocrine disorders. On examination, she was afebrile, with a heart rate of 160 beats/min, shallow respiration, feeble peripheral pulses but well-palpable central pulses, SPO2 of 90% on room air, capillary refilling time of > 3 seconds, and blood pressure of 126/82 mmHg. She looked pale without any cyanosis, clubbing, edema, lymphadenopathy, jaundice, or skin rash. The patient's Glasgow coma scale score was 3/15, and her pupils were 4 mm, equal in size, and sluggishly reactive to light. Her deep tendon reflexes were brisk in all four limbs, and plantar reflexes were bilaterally extensor. Her weight was 38 kg (< 3rd centile), and height was 152 cm (5th - 10th centile). She had attained

Table 1. Serial Changes in Laboratory Parameters During Hospitalization

Parameter	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
pH	6.7	7.1	7.3	7.37	7.4		
Urine ketones	4+	4+	3+	3+	2+	1+	NA
Serum urea (mg/dL)	52	86	88	49	89	68	32
Serum creatinine (mg/dL)	1.2	2.1	2.7	4.2	3.1	2.3	1.0
Serum phosphate (mg/dL)	0.8	1.2	2.4	4.5	4.7	3.8	
Platelet count (lakh/cumm)	2.12	0.5	0.57	0.74	0.83	2.48	
Creatinine phosphokinase (IU/L)		2813			355		

Abbreviation: NA, not available.

menarche at 13 years of age. The remainder of the systemic examination was normal. Her blood glucose was very high (629 mg/dL), with glycosuria and ketonuria. Arterial blood gases (ABGs) showed severe metabolic acidosis (pH = 6.73, bicarbonate = 3.2 mEq/L), and there were deranged renal function tests (urea = 52 mg/dL, creatinine = 1.2 mg/dL). Computerized tomography (CT) scan of the brain revealed diffuse cerebral edema. She was admitted to the ICU, mechanically ventilated, and put on anticerebral edema therapy (sedation, analgesia, mannitol, and phenytoin). Normal saline boluses were given for compensated shock, and 8.5% dehydration correction was planned over 48 hours in view of severe acidosis. Regular insulin infusion was initiated at 0.1 U/kg/h after 3 hours of initiation of intravenous fluid. The patient's blood glucose values, ABGs, urinary ketones, and vital parameters were monitored serially during the course of management (Table 1). Her glycosylated hemoglobin (HbA1c) level was high (14.7 gm/dL), indicating longstanding diabetes. The blood glucose level began to decrease with improvement of the acidosis, but her kidney function began to deteriorate. Her phosphorus level was 0.8 mg/dl at admission before initiating insulin infusion, and her serum creatinine phosphokinase (CPK) level was found to be very high (2813 U/L). Therefore, the possibility of severe symptomatic hypophosphatemia with rhabdomyolysis was considered (but surprisingly, there was no myoglobinuria), and phosphate replacement in the form of sodium phosphate was given. She developed oliguria along with increased urea and creatinine, for which sustained low efficiency dialysis (SLED) was initiated. After four sessions of SLED, renal function and urine output began to improve. The patient's platelet count and CPK level were normalized by day seven of her ICU stay. She was given mechanical ventilation for five days. Subsequently, she was extubated, oral feeding was initiated, and intravenous insulin infusion was converted to subcutaneous insulin. She was finally discharged home in a healthy condition after two weeks of hospitalization, and was advised to follow up.

3. Discussion

One of the most common complications requiring hospitalization in patients with diabetes mellitus is diabetic ketoacidosis (DKA). The clinical picture of severe hypophosphatemia can mimic that of an associated underlying illness, which may lead to disastrous consequences in sick children. Common manifestations of severe hypophosphatemia include malaise, gastro-intestinal discomfort (nausea, vomiting), myopathic symptoms (muscle weakness, rhabdomyolysis), neurologic symptoms (numbness, irritability, convulsion), cardiorespiratory symptoms (cardiomyopathy, respiratory failure), and hemolytic anemia (2-8). Severe hypophosphatemia may sometimes appear even before the initiation of therapy (1). Phosphate replacement in asymptomatic DKA is not presently recommended, based on the results of randomized clinical trials that have failed to show any benefit (9). However, in patients with cardiorespiratory compromise, symptomatic anemia, or a very low phosphate level (< 1 mg/dL), parenteral replacement of phosphate should be considered (9). For a few reasons, extra caution should be taken when initiating phosphate therapy (1). First, phosphate is mainly an intracellular ion (< 1% present in the plasma); therefore, serum levels may not indicate actual total-body phosphate stores, making the response unpredictable. This is especially true in patients with underlying renal insufficiency, in whom hyperphosphatemia could easily develop. Second, hypocalcemia may develop as a consequence of hyperphosphatemia, which may result in a fall in blood pressure, metastatic calcification, and kidney damage. Third, as most of the preparations also contain potassium salts, hyperkalemia may occur in patients with compromised renal function. For those reasons, the levels of these electrolytes (phosphorous, calcium, and potassium) must be carefully monitored during phosphate-repletion therapy in DKA (1). In a review of the literature, we could find three published cases of severe symptomatic hypophosphatemia in the pediatric population (Table 2) (5-7). The manifestations described were seizure, severe acute renal failure, and rhabdomyolysis without myoglobinuria. All three of these cases survived with timely treatment. We could not find any published report of hypophosphatemia causing thrombocytopenia in DKA. Possible explanations are as follows: first, ADP, which contains two phosphate molecules, is a constituent of blood platelets and is secreted from platelet granules to stimulate platelet aggregation for blood clotting. In hypophosphatemia, the platelets may be dysfunctional. Second, phosphate is necessary for cellular metabolism and nucleic acid (DNA/RNA) synthesis. In hypophosphatemia, platelet survival may be decreased because of faulty cellular metabolism.

Table 2. Cases of Symptomatic Hypophosphatemia Complicating DKA in a Pediatric Population

Author	Year	Country	Reference Number	Age, y	Gender	Type of Diabetes	Clinical Presentation	Serum Phosphate level (mg/dL)	Outcome
de Oliveira Iglesias et al.	2009	Brazil	(5)	1	Male	Type 1	Seizure due to hypophosphatemia	1.2	Survived
Al-Matrafi et al.	2009	Canada	(6)	12	Female	Type 1	Severe acute renal failure	0.9	Survived
Kutlu et al.	2011	Turkey	(7)	11	Male	Type 1	Rhabdomyolysis without detectable myoglobulinuria	0.53	Survived

Our case highlights the fact that although the clinical picture of hypophosphatemia may not be apparent in sick patients, clinicians should be vigilant about this complication during therapy. Phosphate therapy under close surveillance is warranted in any patient who develops symptoms of severe hypophosphatemia in the form of cardiopulmonary distress, anemia and thrombocytopenia, or rhabdomyolysis.

Footnote

Authors' Contribution: Study concept and design: Vinod Prabhu Ganapathy, Rashmi Ranjan Das; Acquisition of data: Vinod Prabhu Ganapathy, Vijay Anand Palaniswamy, Pratibha Vinod, Lakshmi Narayanan; Analysis and interpretation of data: Vinod Prabhu Ganapathy, Rashmi Ranjan Das, Tanushree Sahoo; Drafting of the manuscript: Tanushree Sahoo, Lakshmi Narayanan, Vinod Prabhu Ganapathy; Critical revision of the manuscript for important intellectual content: Rashmi Ranjan Das; Statistical analysis: N/A; Administrative, technical, and material support: Vijay Anand Palaniswamy; Study supervision: Vinod Prabhu Ganapathy, Vijay Anand Palaniswamy, Pratibha Vinod, Lakshmi Narayanan

References

1. Ditzel J, Lervang HH. Disturbance of inorganic phosphate metabolism in diabetes mellitus: clinical manifestations of phosphorus-depletion syndrome during recovery from diabetic ketoacidosis. *Diabetes Metab Syndr Obes.* 2010;**3**:319–24. doi: 10.2147/DMSOTT.S13476. [PubMed: 21437101]
2. Murakami T, Yoshida M, Funazo T, Matsuda Y, Matsuo K, Nambu T, et al. Prolonged disturbance of consciousness caused by severe hypophosphatemia: A report of two cases. *Intern Med.* 2014;**53**(19):2227–32. [PubMed: 25274235]
3. Osuka A, Matsuoka T, Idoguchi K. Is this the worst outcome of metabolic syndrome? Hypophosphatemia and resulting cardiac arrest during the treatment of diabetic ketoacidosis with hypertriglyceridemia. *Intern Med.* 2009;**48**(16):1391–5. [PubMed: 19687585]
4. Megarbane B, Guerrier G, Blancher A, Meas T, Guillausseau PJ, Baud FJ. A possible hypophosphatemia-induced, life-threatening encephalopathy in diabetic ketoacidosis: a case report. *Am J Med Sci.* 2007;**333**(6):384–6. doi: 10.1097/MAJ.0b013e318065adc4. [PubMed: 17570993]
5. de Oliveira Iglesias SB, Pons Leite H, de Carvalho WB. Hypophosphatemia-induced seizure in a child with diabetic ketoacidosis. *Pediatr Emerg Care.* 2009;**25**(12):859–61. doi: 10.1097/PEC.0b013e3181c399f6. [PubMed: 20016359]
6. Al-Matrafi J, Vethamuthu J, Feber J. Severe acute renal failure in a patient with diabetic ketoacidosis. *Saudi J Kidney Dis Transpl.* 2009;**20**(5):831–4. [PubMed: 19736483]
7. Kutlu AO, Kara C, Cetinkaya S. Rhabdomyolysis without detectable myoglobulinuria due to severe hypophosphatemia in diabetic ketoacidosis. *Pediatr Emerg Care.* 2011;**27**(6):537–8. doi: 10.1097/PEC.0b013e31821dc68a. [PubMed: 21642790]
8. Liu PY, Jeng CY. Severe hypophosphatemia in a patient with diabetic ketoacidosis and acute respiratory failure. *J Chin Med Assoc.* 2004;**67**(7):355–9. [PubMed: 15510933]
9. Keller U, Berger W. Prevention of hypophosphatemia by phosphate infusion during treatment of diabetic ketoacidosis and hyperosmolar coma. *Diabetes.* 1980;**29**(2):87–95. [PubMed: 6766411]