HYPERNATREMIA IN DIABETIC KETOACIDOSIS: A RARE METABOLIC DERANGEMENT REQUIRING A CAUTIONARY APPROACH IN FLUID RESUSCITATION

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INTRODUCTION

Type 1 diabetes mellitus (T1DM) is an autoimmune disorder leading to the destruction of insulin producing pancreatic beta cells, resulting in elevated blood sugar levels [1]. Polyuria, polydipsia and weight loss are the key presenting symptoms [2]. A systematic review and meta-analysis reported the global T1DM prevalence of 9.5%, with an incidence of 15 per 100,000 people[3]. Diabetic ketoacidosis (DKA) is a grievous complication of diabetes mellitus caused by insufficient insulin, resulting in elevated blood glucose, ketonemia and acidosis. The overall DKA prevalence across 13 countries over 13 years was 29.9%, with a 3.5% prevalence in Nepal. [4,5].

The most common risk factors leading to DKA include missed insulin doses and infections, while other factors like stress-inducing events or the initial onset of diabetes can also trigger DKA. The clinical manifestations of DKA encompass a range of symptoms, including nausea, severe vomiting, dehydration, polyuria, polydipsia, abdominal pain or discomfort, presence of acetone breath odor, Kussmaul breathing, overall profound fatigue with altered consciousness, disorientation, confusion or occasionally coma when the condition is severe [6]. Typical diagnosing criteria for DKA include blood glucose greater than 250 mg/dl, arterial pH less than 7.3, serum bicarbonate less than 15 mEq/l, and the presence of ketonemia or ketonuria [7].

Immediate intervention is crucial that includes restoring the circulatory volume, correcting electrolyte abnormalities, insulin therapy and addressing the underlying cause [8]. Failure to promptly treat DKA can result in the breakdown of compensatory mechanisms and cause electrolyte abnormalities like hyponatremia, hyperkalemia and ultimately lead to life threatening complications including cerebral edema, acute respiratory distress syndrome, and sepsis. Nursing management for a patient with Diabetic Ketoacidosis (DKA) involves a comprehensive approach that involves monitoring vital signs, blood sugar levels, and electrolytes, administering fluids, assessing renal function and mental status, monitoring intake output, checking for signs of infection, assessing lung sound; educating the patient on insulin injection techniques, medication compliance, promoting lifestyle changes like smoking cessation and diabetic diet[9].

In DKA, dilutional hyponatremia is common due to rising glucose level that creates osmolar gradient causing water to shift from cells into the intravascular space. However, on rare occasion, hypernatremia is found that happens when there's a deficit of water intake and excessive loss of free water, which outweighs electrolyte loss through various factors[10]. This report emphasizes the significance of a fluid management strategy for DKA patients, even when encountering the unusual occurrence of hypernatremia.

CASE DESCRIPTION

A 33 years old male with a past medical history of Type-I Diabetes Mellitus (T1DM) presented to the

Emergency department of Tribhuvan University Teaching Hospital with the complaint of altered sensorium and shortness of breath. The family stated that the patient had been experiencing polyuria, polydipsia, nausea, generalized malaise, weight loss and his symptoms worsened over the past four days to the point that he could not get out of the bed. He was under basal-bolus insulin regimen (Glargine 10 units subcutaneously at bedtime and Regular insulin 8 units each before breakfast, before lunch and before dinner) for T1DM since 3 years. However, he had not been adhering to his insulin treatment since 1 week due to lipodystrophy. He was born healthy at term following an uncomplicated pregnancy and was the first child of a non-consanguineous marriage. There was no history of T1DM or significant chronic illness in family. He used to consume alcohol occasionally but does not smoke. His socioeconomic history were noncontributory.

During first encounter in Emergency room his vital signs reflected tachycardia (138 beats/minute), tachypnea (30 breaths/minute) with Kussmaul breathing, hypotension (Blood Pressure: 70/40 mm of Hg), peripheral oxygen saturation of 96% in room air. On neurological examination, patient was confused with Glasgow Coma Scale (GCS) of 14/15 (E4M6V4). The general findings revealed patient to be mildly dehydrated, pale, underweight with Body Mass Index 16.4 kg/ m2. Lipodystrophy was present in bilateral thigh. Abdominal and cardiovascular examination were unremarkable.

Various laboratory studies were carried out on the basis of history and physical examination. Electrocardiography displayed normal sinus rhythm. Arterial blood gas (ABG) analysis revealed partially compensated metabolic acidosis with low pH of 6.719, low partial pressure of carbon dioxide (pCO2) level of 9.3 mmHg, low bicarbonate (HCO3) level of 1.2 mmol/L, partial pressure of oxygen (pO2) of 161.7 mmHg, elevated lactate level of 3.7 mmol/L and high anion gap of 33.7 mmol/L. Initial lab investigations showed elevated random blood glucose level (RBS) at 655 mg/dl, normal serum sodium level of 143 mEq/L, normal serum potassium level of 3.7 mEq/L, leukocytosis with White Blood Cells (WBC) 24,400 cells/mm^3 and markedly elevated glycosylated hemoglobin level (HbA1c) of 19.4%. All other biochemical and hematological parameters were unremarkable. Routine urine examination indicated that the urine was acidic, containing glucose and acetone positive.

Based on hyperglycemia, metabolic acidosis, and ketonuria a diagnosis of Diabetic Ketoacidosis (DKA) was made and management was initiated. The patient was resuscitated with 1000 ml of Ringer lactate and concomitantly started with Injection Noradrenaline at 0.1 mcg/kg/min, Injection Regular insulin 12 units Intravenously (IV) stat, Injection Sodium bicarbonate 100 mEq IV stat, Injection Tramadol 50 mg IV stat, Injection Ondansetron 4 mg IV stat, and subsequently shifted to Intensive Care Unit (ICU) for further evaluation and management.

In ICU, a comprehensive treatment plan was initiated for the patient which included fluid resuscitation, maintaining blood pressure and blood glucose levels, correcting acidosis and electrolyte. For fluid resuscitation and electrolyte correction, an intravenous infusion of potassium chloride (KCl) 20 mEq was added to every alternate pint of 0.9% Normal Saline (NS) solution and administered at a rate of 250 ml per hour. Regular insulin infusion started according to protocol to maintain blood sugar level at 150-200 mg/dL. Dosage of injection Nor-adrenaline was titrated to maintain blood pressure with mean arterial pressure of 65 mm of hg. To correct acidosis, intravenous sodium bicarbonate 100 mEq was administered three times per day, with additional doses as needed if pH was < 7. Injection Piperacillin and Tazobactam 4.5 gm IV stat and four times a day, Injection Paracetamol 1gm IV thrice a day and Injection thiamine 200 mg IV twice a day were started.

Monitoring Blood Sugar, vital signs monitoring, intake-output charting, neurological assessment was done hourly; ABG analysis were performed 2 hourly and serum electrolytes every 4 hourly until the patient was stable. Electrolytes repeated after four hours, revealed an increase of sodium level from 143 mEq/L to 148 mEq/L and to 158 mEq/L in next 4 hours. Because of hypernatremia, his fluid therapy was switched from 0.9% normal saline to 0.45% NS and $\frac{1}{2}$ DNS (5% Dextrose & 0.45% Sodium Chloride).

Table 1: Serial laboratory investigations

Parameters	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Da
Na+ (mEq/L)	143	158	158	151	149	143	140	136	13
K+ (mEq/L)	3.7	3.1	3.3	3.5	3.7	3.7	3.7	4.1	3.6
Blood Glucose (mg/dl)	655	255	210	172	155	129 Fasting (FBS)	125 FBS	85 FBS	96
pH	6.719	7.322	7.408	7.404	7.421	7.438	-	-	-
Bicarbonate (mmol/L)	7.2	7.9	19.4	20.6	19.7	26.1	-	-	-
pCO2 (mmHg)	9.3	15.1	30.5	32.6	30.0	38.2	-	-	-
Lactate (mmol/L)	3.7	1.1	2.4	1.2	1.2	1.1	-	-	-
WBC (cells/mm^3)	24,400	19,800	12,800	9,200	5,800	5,500	5,800	5,800	-

Changing laboratory investigation values over time are summarized in Table 1. C-reactive protein and procalcitonin level was elevated at 73.63 mg/L (reference range: 0-6 mg/L) and 0.82 ng/mL (reference range: $<$ 0.07 ng/Ml) respectively. Blood, urine and sputum culture were sterile. Serum cortisol level measured at 8:00 A.M. was within normal range. Computed Tomography (CT) Scan of head, X-ray chest, ultrasonography of abdomen were unremarkable. Ophthalmology consultation was done which showed no changes in retina.

The dose of Nor-adrenaline was gradually tapered and discontinued on 5th day, sodium level returned to normal range on 6th day of admission. Concurrently, after 5th day of admission, patient was kept on basal-bolus insulin regimen with Insulin Glargine (14 units subcutaneously (SC) at bedtime) and Regular insulin; 8 units subcutaneously before breakfast, before lunch and before dinner.

Witnessing improving level of consciousness, gradual reduction in blood glucose level, correction of acidosis and electrolytes, the patient was transferred to the medical ward on 6th day of admission and discharged on 9th day of admission with basal-bolus insulin regimen (Glargine 20 units subcutaneously at bedtime and Regular insulin 8 units subcutaneously before breakfast, lunch and dinner). During discharge, patient was counseled regarding his disease condition & its complications, and measures of prevention which includes self-monitoring of glucose level, correct insulin injection techniques, avoiding alcohol, following diabetic diet. Patient was advised to follow up in Endocrine OPD in 7 days.

DISCUSSION

We report a 33 years old male who presented with severe Diabetic ketoacidosis (DKA) which was complicated by hypernatremia. DKA is a serious and preventable acute complication of diabetes mellitus that occurs due to a relative or absolute deficiency of insulin, resulting in reduced glucose uptake and utilization by cells and excessive lipolysis, which in turn triggers the uncontrolled production of ketone bodies, ultimately resulting in state of acidosis [11]. DKA predominantly occurs in individuals with T1DM, accounting for approximately 82.6% of cases [12]. The median age of patients with DKA was 35 years with males constituting the majority at 62% [13]. In line with these statistics, our patient was a 33-year-old male and had history of T1DM.

Several studies have identified poor adherence to insulin therapy and infections as the most common precipitating factors for DKA in T1DM patients [14–16]. Multiple socioeconomic and behavioral factors also play the important role. Our patient had not been adhering to his insulin treatment for a week due to lipodystrophy resulting from incorrect insulin injection technique. Additionally, his low socioeconomic status had hindered access to a glucometer for glucose monitoring at home.

In the study conducted by Shahid et al., the predominant clinical symptom reported was nausea and vomiting (57.7%), followed by pain in abdomen (42.2%), dehydration (42.2%), polyuria/polydipsia (28.1%), altered sensorium (25.3%), weakness (16.9%), hypotension (14%), kussmaul breathing (14%) [16]. Our patient also presented with similar symptoms from which provisional diagnosis of DKA was made which was later confirmed by biochemical examination.

According to American Diabetic Association 2009, the severity of DKA is classified as mild, moderate, or severe as follows: mild DKA, pH (7.25-7.3) and HCO3 (15-18) mmol/L or anion gap > 10; moderate DKA, pH 7.0–7.24 and HCO3 (10-<15 mmol/L) or anion gap > 12; severe DKA, pH < 7.0 and HCO3 < 10 mmol/L or anion gap > 12 with presence of ketones in urine and blood. In the study conducted by Chukwuma et al., the mean HbA1c in known T1DM was 12.4 ± 3.3 %[17]. In several studies, leukocytosis in DKA has been associated with various factors, including infection, insulin deficiency, dehydration, and the secretion of stress hormones. Additionally, a high WBC count has been linked to increased blood acidity [18]. DKA, even in the absence of bacterial infection, can lead to increased levels of C-reactive protein and procalcitonin. Therefore, it is crucial to determine whether the elevation is because of bacterial infection or due to DKA itself [19,20]. In our case, low pH level of 6.719, low bicarbonate level of 1.2mmol/L, high anion gap of 33.7 mmol/L, positive urine ketone was present indicating severe DKA. HbA1c was markedly elevated in our case; this discrepancy may be due to poor medication compliance for long time. Although the values of WBC, pro-calcitonin and c-reactive protein values were elevated, blood, urine and sputum cultures were sterile.

In DKA, we expect to find normal or low serum sodium as rising glucose level creates osmolar gradient causing water to shift from cells into the intravascular space. This initial shift of water leads to a decrease concentration of sodium in the blood. Hypernatremia in DKA results from excessive water loss relative to sodium and potassium due to glycosuria-induced osmotic diuresis which leads to inadequate water replacement which was present in our case as well [10].

80.8% of patients with severe DKA required ICU care and close monitoring. Blood glucose, neurological assessment, vitals, and urine routine examination should be monitored on hourly basis; and serum electrolytes every 2 hourly and initial ABG monitoring, followed by as-needed precipitating events [12,21].

Management of hypernatremia in DKA constitutes of infusing 0.9% NS at the rate of 150-250 ml/hour during the first hour, to maintain effective plasma osmolality. However, in patients with hypernatremia and DKA, relatively low sodium containing fluids such as $\frac{1}{2}$ NS is more appropriate. Once blood glucose declines to 200 mg/dL, $\frac{1}{2}$ DNS is administered to maintain blood glucose concentration at 150-200 mg/dl. If the serum potassium level falls below 3.3 mEq/L during the treatment of DKA, it is necessary to halt insulin administration and provide intravenous potassium supplementation. In cases where the serum potassium is within the range of 3.3 to 5.3 mmol/L, it is standard practice to include modest amounts of potassium (20–30 mEq/L) in the intravenous fluids. Insulin is typically administered via IV infusion beginning with 0.1 unit/kg bolus of regular insulin, followed by a continuous infusion at the rate of 0.1 unit/kg/h and later on adjusted as per need. Subcutaneous insulin should be started when DKA has resolved and the patient is able to tolerate oral feeding. In severe DKA, the infusion of 100 mEq of bicarbonate in 400 mL of sterile water mixed with 20 mEq potassium chloride over 2 hours, and repeating the infusion until the pH is greater than 7.0 is recommended[8,22]. Likewise, similar treatment regimen was applied in our case along with Injection Noradrenaline infusion, Injection Piperacillin and Tazobactam, Injection Paracetamol and Injection thiamine as part of a comprehensive approach to patient care.

The length of stay in the ICU in severe DKA was 0–8 days[23]. Mortality rate ranges from 2 to 5% in industrialized nations and 6 to 24% in underdeveloped countries[24]. In our case, patient was discharged on 9^{th} day of admission after successful clinical outcome.

CONCLUSION

In conclusion, this case report highlights the uncommon occurrence of hypernatremia in the DKA in a patient with T1DM. DKA is a severe metabolic complication of diabetes, often triggered by factors like non-adherence to insulin therapy and infection. The patient's presented with typical DKA symptoms and diagnosis was

made based on history, examination and laboratory parameters. The emergence of hypernatremia, though rare, underscores the complexity in managing DKA which typically results from a deficit in water intake and excessive loss of free water during glycosuria-induced osmotic diuresis. It emphasizes the significance of early recognition, prompt intervention, and close monitoring to ensure effective treatment and desired outcome. In this patient, meticulous fluid administration, insulin infusions and electrolyte correction and acidosis correction led to a good clinical outcome.

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Conflict of interests

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Author contribution

SG and UC reviewed the literature; drafted and edited the manuscript.

Ethical approval

Our institution does not require ethical approval for reporting individual cases.

Consent statement

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Guarantor

Sushmita Ghimire is the guarantor of this report.

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