

Life-threatening hypernatremia in a 22-year-old man with concurrent diabetic ketoacidosis and hyperosmolar hyperglycemic state

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ABSTRACT

In diabetic ketoacidosis (DKA), hyponatremia is commonly observed due to hyperglycemia-induced water shift and osmotic diuresis. Thus, hypernatremia is rare and indicative of severe free water loss. We describe here a case of DKA with life-threatening hypernatremia. A 22-year-old type 1 diabetic male was admitted after experiencing polyuria and polydipsia, followed by nausea, vomiting, and lethargy for 2 weeks. On admission, plasma glucose was 1230 mg/dL and plasma sodium was 158 mEq/L. The patient developed acute kidney injury, lactic acidosis, and ketosis. Despite fluid resuscitation, sodium level continued to rise to 180 mEq/L. Tachycardia persisted and shock liver developed. After free water-deficit calculation, the patient was given more boluses of isotonic fluid in addition to 0.45% NaCl. Tachycardia began to improve, and hypernatremia and hyperglycemia were safely reduced. This case demonstrated how tedious volume evaluation and resuscitation helped the patient fully recover despite extreme hypernatremia, lethargy, and multiorgan failure.

Key words: Acute kidney injury, Diabetic ketoacidosis, Hyperglycemic hyperosmolar state, Hypernatremia, Shock liver

Diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS) are two extremes in the spectrum of acute hyperglycemic complications. DKA represents the triad of hyperglycemia, metabolic acidosis, and ketosis while HHS is defined by severe hyperglycemia and hyperosmolality without significant ketoacidosis [1]. One study showed that the prevalence of DKA in all hyperglycemic crisis admissions was 62.6%, while HHS and overlapping DKA/HHS were 22.9% and 14.5%, respectively [2]. In type 1 diabetes with DKA, hyponatremia prevalence is significant compared to hypernatremia. Onyiriuka confirmed this prevalence, with hyponatremia occurring in 25.5% of cases and hypernatremia only occurring in 2.1% [3].

Treatment modalities for DKA/HHS include insulin therapy, fluid therapy, electrolyte repletion, and addressing underlying medical illnesses [1]. Although there have been well-developed diagnostic criteria and treatment protocols for these conditions, DKA and HHS are still important sources of morbidity and mortality among diabetic patients [1]. During the treatment course for patients with hyperglycemic crises, neurologic status must be closely monitored to prevent overcorrection of hypertonicity which can lead to cerebral edema [4,5]. Conversely, a rapid increase of serum sodium levels in the first few hours of resuscitation in DKA places patients at risk for osmotic demyelination syndrome [4,6].

CASE REPORT

A 22-year-old man was diagnosed with type 1 diabetes mellitus 15 months before admission. He did not regularly follow-up with a primary care doctor or comply with insulin injection due to disease denial. The patient lost 10 kg body weight and experienced symptoms of polyuria, polydipsia, nausea, and vomiting over a period of 2 weeks. These symptoms culminated with progressive lethargy 2 days before admission. The patient's family reported on admission that he did not take insulin for 1–2 weeks and often consumed fast food and soft drinks. He experienced no fever or symptoms indicative of infection.

On admission, the patient was poorly interactive and irritable with dry mucous membrane, heart rate of 136 bpm, and blood pressure of 126/93 mmHg. Initial blood tests revealed severe hyperglycemia of 1230 mg/dL, HbA1c of 13.2%, and hypernatremia of 158 with corrected Na of 176 mEq/L. The metabolic panel showed creatinine of 1.9 mg/dL and high anion gap (AG) acidosis with high ketone and lactate levels (HCO₃ of 18 mmol/L, venous pH of 7.18, AG of 35 mEq/L, lactate of 6.4 mmol/L, and beta-OH butyrate of 6.81 mmol/L).

The patient was diagnosed with DKA/HHS and we promptly began aggressive intravenous fluid (IVF) resuscitation associated with an insulin drip and potassium supplementation per DKA protocol. He was treated in the intensive care unit with vital

signs, mental status, and metabolic panels closely observed. The patient received 3 L of isotonic fluid (NaCl 0.9%) during the first 3 h to address severe hypovolemia. As corrected sodium levels were already high, IVF was switched to hypotonic fluid (NaCl 0.45%) for the rest of the day. After 24 h, however, the patient's tachycardia persisted at 140/min while his blood pressure remained in a normotensive range. Hyponatremia worsened and peaked at 180 mEq/L with corrected Na of 186 mEq/L, as shown in Fig. 1.

The water-deficit equation showed a total loss of 10 L. It was decided to administer more boluses of isotonic IVF in addition to continuing his regimen of hypotonic IVF. The patient received a total of 8.5 L of isotonic fluid, 8 L of hypotonic fluid, and 9.5 L of free water over 6 days. Table 1 details the patient's tachycardia normalizing to the 90s over a 3-day period. Sodium levels were safely reduced with a correction rate ranging from 4 to 18 mEq/L per 24 h. The patient's acute kidney injury (AKI) resolved alongside plasma sodium normalization and he returned to baseline mental status.

Severe hypovolemia led to a notable increase in transaminase levels from a normal range in day 1 to peaked aspartate aminotransferase/alanine transaminase (AST/ALT) of 2071/729 U/L in day 2. Fig. 2 indicates that hyperbilirubinemia developed later than transaminitis with a lag of 1 day but was more protracted. Viral hepatitis serologies were negative. An

abdomen ultrasound did not reveal any liver abnormalities or biliary obstruction. Liver function tests responded well to fluid resuscitation with AST/ALT lowered to 25/99 U/L before discharge. His bilirubin levels also normalized after 5 days.

The patient was successfully transitioned to the basal-bolus insulin regimen and discharged after symptoms resolved. He remained well and continued his insulin regimen. Following 3 month's discharge, his A1C decreased to 6.9% and his AST/ALT, bilirubin, creatinine, and sodium levels were in the normal range.

DISCUSSION

Following the literature review, we found <20 cases reported with hyponatremia and DKA. In one report, an Asian patient had high carbohydrate intake before DKA presentation accounting for significant hyponatremia [7]. This intake was explained by the fact that DKA patients often become parched and resort to soft drink consumption. Unfortunately, these beverages contain significant glucose and NaHCO₃ content. Conditions were inadvertently worsened due to high glucose and sodium intake resulting in severe hyperosmolality. Our patient reported frequent and excessive consumption of fast food and soda.

According to McDonnell *et al.*, high-carbohydrate drink ingestion may precipitate more severe presentation of type 1 diabetes mellitus. Another report reported five patients with newly diagnosed diabetes mellitus. A 5–12 L of soft drinks was consumed before admission and required intensive therapy. These drinks contain an average of 40 g of sugar and 15–120 mg of sodium per 370 mL [8]. Similar cases were also reported by Vanelli and Viswanathan *et al.* [9,10]. In addition to frequent soft drink ingestion, our patient was insulin non-compliant. This is a classic precipitating factor of DKA.

The sudden rapid increase in transaminitis and bilirubin levels in the patient was consistent with ischemic hepatitis or "shock liver." This condition is characterized by a sudden increase of AST/ALT to more than 20 times the upper limit than normal, then decreases to near-normal levels within a week after cellular anoxia resolution. While decreased cellular perfusion was documented in all 10 cases of shock liver, Rawson only found four cases with systemic hypotension.

Our case also had normal blood pressure throughout his hospital course. Similar to our case, this author also noticed a

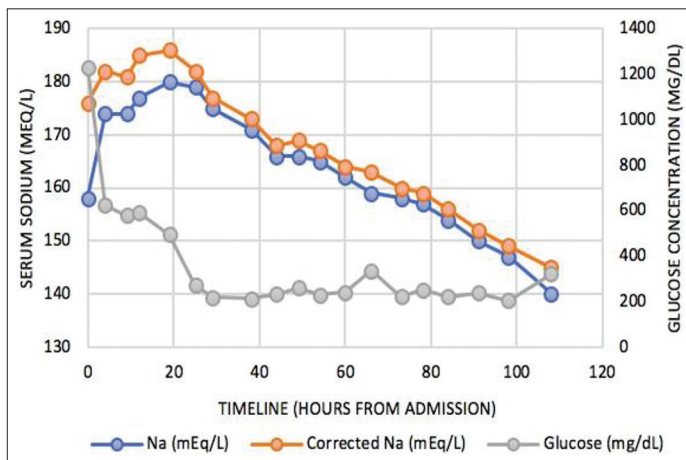


Figure 1: Sodium and glucose levels

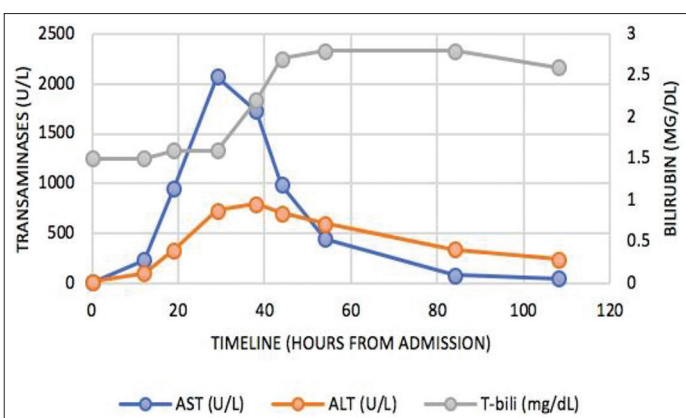


Figure 2: Transaminases and bilirubin level

Table 1: Vital signs and laboratory response to the treatment

Time (h)	0 h	12 h	24 h	48 h	156 h
Heart rate	136	138	142	109	93
Blood pressure (mmHg)	128/93	138/94	139/81	135/84	130/72
Glucose (mg/dL)	1230	591	271	261	320
Corrected (Na)*	176	185	182	169	142
Plasma tonicity**	384	386	373	347	293
Creatinine (mg/dL)	1.9	1.7	1.7	1.0	0.7
AST (U/L)	12	238	2071	449	43
ALT (U/L)	18	99	729	597	129
Total bilirubin (mg/dL)	1.5	1.5	1.6	2.7	0.5

*Corrected (Na) = Measured (Na)+1.6×(glucose (mg/dL)–100)/100. **Plasma tonicity = 2 (Na)+glucose (mg/dL)/18. AST: Aspartate aminotransferase, ALT: Alanine transaminase

transient rise in serum bilirubin which followed transaminase elevations by 24–48 h [11]. For striking increases in AST levels exceeding 1000 IU/L, the most common causes are ischemic hepatitis, acute drug/toxin-induced liver injury, and acute viral hepatitis [12]. Thorough evaluation in our case ruled out other causes. As liver function tests normalized following fluid resuscitation, this also proved that hypoperfusion was the culprit for initial deranged liver function tests.

The patient's hyperglycemia associated with tachycardia to 140/min suggested a severe hypovolemic state. His altered sensorium, shock liver, and AKI are manifestations of multiorgan failure due to hypovolemic shock. The patient received 1L of NaCl per hour during the first 3 h and 0.45% NaCl afterward per the DKA protocol. Fluid repletion typically corrects the estimated volume deficits within 1 day [1]. In our case, patient's tachycardia remained despite intensive fluid resuscitation which raised concerns of the inadequately corrected hypovolemic state. He was reevaluated, and the water-deficit equation showed a total loss of 10 L. With added isotonic boluses, tachycardia resolved with improved AKI. The patient's shock liver also resolved, and he recovered without any sequelae. Hence, fluid replacement in DKA is challenging and requires meticulous and thorough consideration. As in our case, a healthy patient's heart can compensate for hypovolemia by increasing its rate. Normal blood pressure may lead to an underestimation of the underlying volume deficit. Our patient's heart rate was a valuable sign to assess the severity of volume depletion and monitor treatment effectiveness.

The type of fluid used must also be considered. With hyponatremia of 180 mEq/L and severe volume depletion, the isotonic fluid should be prioritized while carefully observing plasma sodium change. In cases where hyponatremia developed over several days, sodium correction should not exceed 0.5 mEq/L per hour and not over 8–10 mEq/L over 24 h [13]. Correcting hyponatremia associated with hyperglycemia, however, requires a different algorithm with plasma tonicity guidance, due to complex interplay between the primary effect of extracellular glucose increase and secondary effects of hyperglycemia on solute and water balances [4,14].

Effective hypertonicity is vital as the body can sense and regulate not only sodium or glucose separately but also in total as tonicity [15]. As cerebral edema can occur while rapidly correcting hypertonicity, it is advised that the decrease in plasma tonicity should not exceed 3 mosmol/kg/h. Hyponatremia may be also permitted to prevent a drastic drop in plasma tonicity while correcting hyperglycemia [4]. In a case report by Arya *et al.*, a 4-year-old girl with DKA had serum sodium increase from 158 mEq/L to 189 mEq/L after standard treatment initiation [16]. Accordingly, patients with severe hyperglycemia and normal/high serum sodium levels on presentation are prone to severe hyponatremia during the treatment course [4].

CONCLUSION

Treatment of severe hyponatremia in DKA/HHS patients is challenging and requires a meticulous calculation to determine correct fluid types and dosage amounts. Treatment success

requires both isotonic fluid use to restore intravascular volume and correcting plasma sodium levels at a safe rate. Tachycardia can be utilized as a sensitive indicator for assessing and monitoring fluid resuscitation effects.

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