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A Rare Case of Elevated Osmolar Gap in Diabetic Ketoacidosis/Hyperosmolar Hyperglycaemic State in the Absence of Concomitant Toxic Alcohol Ingestion

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ABSTRACT

The serum osmolar gap, defined as the difference between measured osmolality and calculated osmolarity, is a convenient method to screen for toxins in serum. In normal circumstances, the difference between the two is 6–10 mol/kg. Typical contributors to serum osmolarity are sodium bicarbonate, sodium chloride, glucose and urea. An elevated gap, defined as a difference >10 mol/kg, can occur if a sufficient quantity of an additional solute other than those mentioned above is present in the serum or there are inaccuracies in sodium measurement secondary to hyperlipidaemia and hyperproteinaemia. An elevated serum osmolar gap should thus prompt clinicians to check for toxic alcohol levels. Treatment with fomepizole should not be delayed if suspicion is high. Isolated diabetic ketoacidosis can occasionally present with an elevated osmolar gap in the absence of concomitant alcohol ingestion. This finding is attributed to the production of acetone and glycerol.

We describe the case of a 62-year-old man presenting with diabetic ketoacidosis/hyperosmolar hyperglycaemic state and an elevated osmolar gap in the absence of toxic alcohol ingestion.

KEYWORDS

Diabetic ketoacidosis, hyperglycaemic hyperosmolar state, osmolar gap, absence of toxic alcohol ingestion

LEARNING POINTS

- The osmolar gap is the difference between the measured and the calculated serum osmolarity and should be calculated in all patients presenting with elevated serum osmolarity; if elevated, toxic alcohol ingestion should be considered and prophylactic treatment with fomepizole immediately administered if the index of suspicion is high.
- Although toxic alcohol ingestion is one of the common causes of an elevated osmolar gap, hyperlipidaemia, hyperproteinaemia and less occasionally lactic acidosis and ketoacidosis have also been implicated.
- In the setting of ketoacidosis, the osmolar gap can be elevated in the absence of toxic alcohol ingestion, is attributed to increased production of acetone and glycerol, and is responsive to treatment with insulin and intravenous fluids.

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INTRODUCTION

Diabetic ketoacidosis is a metabolic state of insulin deficiency where the breakdown of fatty acids leads to the formation of ketone bodies, causing acidosis [1]. Prompt management is essential to prevent cerebral oedema and arrhythmia complications.

The hyperosmolar hyperglycaemic state is a life-threatening condition characterized by elevated serum glucose and elevated serum osmolarity with minimal or absent ketosis [2].

Commonly implicated solutes for an increased osmolar gap include ethanol, isopropanol, diethyl ether, ethylene glycol, methanol, propylene glycol, mannitol, sorbitol and glycine. Although the prevalence of an elevated osmolar gap in diabetic ketoacidosis is not clearly known, a few cases have been reported [3, 4]. Diabetic ketoacidosis is an uncommon cause of an elevated serum osmolar gap and should be considered when evaluating these patients.

CASE DESCRIPTION

A 62-year-old man with a past medical history of insulin-dependent diabetes mellitus and dyslipidaemia presented to the emergency department with acute onset, diffuse, non-radiating abdominal pain associated with multiple episodes of non-bloody and non-bilious emesis, which had started 1 day previously. He endorsed shortness of breath at rest but denied any orthopnoea, paroxysmal nocturnal dyspnoea, pedal oedema, fevers or diarrhoea.

He reported being non-compliant with his medications and took his last insulin dose 1 week previously. He also admitted to not watching his diet and eating lots of sweets in the past week. He denied any alcohol use or ingestion of toxic substances.

On presentation, the patient's temperature was 37°C, heart rate was 130/min, respiratory rate was 24 deep breaths per min, blood pressure was 100/60 mmHg, and SpO2 was 99% on room air.

The patient appeared to be in moderate distress on physical examination due to tachypnoea and abdominal pain. He was alert and oriented times three. The abdominal examination was significant for generalized guarding but no rigidity or tenderness. Cardiovascular, respiratory, and extremities examination was non-significant.

Laboratory tests revealed serum glucose 1163 mg/dl, bicarbonate 3 mg/dl, sodium 127, potassium 8.0, chloride 84 and anion gap 40. Trace acetone was noted. Renal injury with creatinine 6.09 and BUN 92 was noted (unknown baseline). An arterial blood gas analysis showed pH 6.9, pCO2 14, and bicarbonate 4.2. Measured serum osmolarity was 412 mOsm/kg, while calculated osmolarity was 351 mOsm/kg (serum osmolarity corrected for elevated BUN was 326). Therefore, an osmolar gap of 61 was noted. A lipid panel (TTG 346 mg/dl) and total body protein (7.5 g/dl) were within normal limits. Urine analysis was significant for acidic urine with pH 5.0, increased specific gravity 1.020 with glucosuria and ketonuria, but an absence of crystals on microscopy.

The blood alcohol level for ethanol was <10, while analysis for other toxic alcohols such as methanol, propylene glycol, ethylene glycol, isopropanol, diethyl ether and propylene glycol was sent out to another laboratory facility. Blood salicylate and acetaminophen levels within normal limits.

The patient was given a bolus of intravenous regular insulin and a 100 mEq push of sodium bicarbonate and then started on an insulin and bicarbonate drip with aggressive intravenous fluid hydration. Subsequently, serum chemistries were measured every 4 hours; the osmolar gap sequentially reduced to 26 to 20 to 8 with simultaneous improvement in acidosis and renal function.

After being on the insulin drip for 16 hours, the patient was bridged with long-acting insulin and started on this home regime.

Levels of other toxic alcohols were within normal limits, reported 3 days after the patient's presentation.

DISCUSSION

Diabetic ketoacidosis is associated with low insulin and high glucagon levels, which activate hormone-sensitive lipase, breaking down triglycerides to long-chain fatty acids and glycerol. The fatty acids then undergo beta-oxidation producing ketone bodies. Although acetone is electrochemically inactive and does not contribute to the anion gap, it imparts osmolality with glycerol [5]. Hence an osmolar gap in diabetic ketoacidosis can be attributed to the elevated serum acetone and glycerol levels.

Toxic alcohol ingestion can be associated with fatal outcomes like blindness with methanol, renal failure with ethylene glycol, respiratory depression with ethanol, circulatory collapse with isopropanol, and sepsis-like syndrome with propylene glycol poisoning [6].

Given the deadly outcomes associated with these alcohol toxicities, when in doubt, intravenous fomepizole should be administered prophylactically without waiting for the results for the alcohol levels as many laboratories around the country are not equipped to test for these substances and hence the samples need to be sent out to a different facility which could lead to a significant delay in diagnosis.

Our patient denied toxic alcohol ingestion, which was later confirmed with his wife. As his medical condition improved and the suspicion for toxic ingestion was low, fomepizole was not administered. A toxicology screen reported 3 days later was negative for any toxic alcohol ingestion.

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CONCLUSION

This case adds to a limited number of cases of diabetic ketoacidosis with an elevated osmolality gap and highlights the importance of considering diabetic ketoacidosis in the differential diagnosis in addition to the causes listed above.

REFERENCES

1. Misra S, Oliver NS. Diabetic ketoacidosis in adults. *BMJ* 2015;**351**:h5660. doi:10.1136/bmj.h5660
2. Stoner GD. Hyperosmolar hyperglycemic state. *Am Fam Physician* 2017;**96**(11):729–736.
3. Davidson DF. Excess osmolal gap in diabetic ketoacidosis explained. *Clin Chem* 1992;**38**(5):755–757.
4. Bhagat CI, Garcia-Webb P, Beilby JP, Hackett PL. Unexplained osmolal gap in diabetic ketoacidosis (not due to acetone). *Clin Chem* 1990;**36**(2):403–404.
5. Al-Darzi W, Chaaban S, Abu Sayf A, Tirgari S, Uduman J. Gaps in osmolal gap: a case of mistaken osmolal gap in a patient with diabetic ketoacidosis. *Am J Respir Crit Care Med* 2017;**195**:B57.
6. Zar T, Graeber C, Perazella MA. Recognition, treatment, and prevention of propylene glycol toxicity. *Semin Dial* 2007;**20**(3):217–219. doi:10.1111/j.1525-139X.2007.00280.x