OBSERVATIONS

Diabetic Ketoacidosis: the Usual Villain or a Scapegoat?

A novel cause of severe metabolic acidosis in type 1 diabetes

We describe a case of severe metabolic acidosis in type 1 diabetes far exceeding the accompanying diabetic ketoacidosis (DKA), highlighting pitfalls to management of DKA by protocol alone. A 19-year-old woman with type 1 diabetes since age 4 years presented with 1 day of drowsiness. While her parents believed diabetes control was satisfactory (21 units insulin glargine nocturnally and 4–6 units insulin lispro premeals), this was not supported by the reported A1C level of 11%.

She was afebrile with blood pressure 110/65 mmHg, pulse rate 100 bpm, and central venous pressure 3 mmHg. Neurological examination revealed neither lateralizing signs nor meningism.

Biochemistry demonstrated severe metabolic acidosis disproportionate to DKA (pH 6.7 [range 7.35–7.45], bicarbonate 2.3 mmol/l [24–30], glucose 23 mmol/l [3–7.8], and β-hydroxybutyrate 3.2 mmol/l [<0.6]). Metabolic acidosis persisted (pH 7.0, bicarbonate 2.4 mmol/l, glucose 8 mmol/l, and β-hydrobutyrate 2.6 mmol/l) despite insulin infusion. Biochemistry excluded liver failure, thyroid dysfunction, lactatemia, hypoadrenalism, pancreatitis, and renal tubular acidosis. Serum creatinine kinase was 495 units/l (0–110). Drug screen excluded salicylate, amphetamines, cannabinoid, ethanol, and methanol use.

Both calculated serum osmolar gap (37 mmol/l) and anion gap (24 mmol/l) were elevated, with a calculated Δ/Δ of 0.5. Metabolic acidosis appeared to be more severe than expected from ketoacidosis alone, confirmed by moderate β-hydroxybutyrate elevation with change not parallelling clinical improvement.

Continuous venovenous hemodiafiltration was begun because of persisting acidemia, with prompt improvement in acidosis within 2 hours (pH 7.4, bicarbonate 17 mmol/l). A specific drug screen retrospectively confirmed ketamine use, which was denied by the patient.

Ketamine comes in two forms: liquid (injected or added for smoking) and powder (smoked, snorted, or dissolved in drinks). Differentiation between ketamine and phencyclidine is difficult because both are analogs of arylhexylamines. In Australia, ketamine abuse is more common than phencyclidine abuse, with prevalence approaching 60% among ecstasy users (1).

Ketamine is an *N*-methyl-D-aspartate receptor antagonist that reduces excitatory neurotransmission resulting in disassociative anasthesia. Effects are dose dependent, ranging from relaxation ("K-land") at 40–100 mg to near-death experiences ("K-hole") at doses >500 mg. Spiked drinks usually contain 100–400 mg.

Rhabdomyolysis is an uncommon complication of DKA (prevalence 17–42%) (2). Patients with higher serum sodium, creatinine, and osmolarity were at highest risk. Ketamine may cause acidosis and rhabdomyolysis in severe intoxication. Ketamine is a major danger in the "rave" scene (3), compounding the complications of ketoacidosis. Although our patient denied ketamine use, mild rhabdomyolysis was congruent with ketamine toxicity. Drink spiking was possible. Severe metabolic acidosis with ketamine intoxication without rhabdomyolysis is reported (4). Another possibility is urinary bicarbonate loss secondary to ketamine-induced urinary excretion of large amount of β-hydroxybutyrate (5). Urinary bicarbonate was not measured.

Intoxication by designer drugs (intentionally consumed or via spiked drinks) should be considered in younger patients despite an absent drug history. A strong index of suspicion should be maintained especially when there are inconsistencies in history (e.g., high A1C level but good diabetes control reported).

While DKA should be promptly treated, management should not be limited to insulin infusion protocols. Identification and treatment of concurrent acidosis is lifesaving; substance abuse must now be considered, especially in younger people.

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