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Starvation Ketoacidosis as a Cause of Unexplained Metabolic Acidosis in the Perioperative Period

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Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 24
Final Diagnosis: Starvation ketoacidosis
Symptoms: None
Medication: —
Clinical Procedure: Lumbar laminectomy
Specialty: Orthopedics and Traumatology

Objective: Unusual clinical course





Background: Besides providing anesthesia for surgery, the anesthesiologist's role is to optimize the patient for surgery and for post-surgical recovery. This involves timely identification and treatment of medical comorbidities and abnormal laboratory values that could complicate the patient's perioperative course. There are several potential causes of anion and non-anion gap metabolic acidosis in surgical patients, most of which could profoundly affect a patient's surgical outcome. Thus, the presence of an acute acid-base disturbance requires a thorough workup, the results of which will influence the patient's anesthetic management.

Case Report: An otherwise-healthy 24-year-old female presented for elective spine surgery and was found to have metabolic acidosis, hypotension, and polyuria intraoperatively. Common causes of acute metabolic acidosis were investigated and systematically ruled out, including lactic acidosis, diabetic ketoacidosis, drug-induced ketoacidosis, ingestion of toxic alcohols (e.g., methanol, ethylene glycol), uremia, and acute renal failure. Laboratory workup was remarkable only for elevated serum and urinary ketone levels, believed to be secondary to starvation ketoacidosis. Due to the patient's unexplained acid-base disturbance, she was kept intubated postoperatively to allow for further workup and management.

Conclusions: Starvation ketoacidosis is not widely recognized as a perioperative entity, and it is not well described in the medical literature. Lack of anesthesiologist awareness about this disorder may complicate the differential diagnosis for acute intraoperative metabolic acidosis and lead to a prolonged postoperative stay and an increase in hospital costs. The short- and long-term implications of perioperative ketoacidosis are not well defined and require further investigation.

MeSH Keywords: Acidosis • Fasting • Ketosis

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/900002>

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Background

As the concept of Perioperative Surgical Home becomes an increasingly important part of the way we practice anesthesiology in the United States, the perioperative physician needs to play a progressively more important role in the coordination of patient care. The Perioperative Surgical Home is a care model that has been driven by a desire for more patient-centered care combined with changes in United States healthcare reimbursement and increased anticipated demand for healthcare services [1]. Problems that may lead to delay or cancellation of surgical cases or lead to prolonged postoperative care and increased hospital costs must be triaged appropriately in order to improve patient satisfaction and decrease hospital operating costs.

We describe the case of a young female who was in her usual state of health prior to diagnosis of a lumbar giant cell tumor requiring laminectomy. Due to a significant metabolic aberrance secondary to ketoacidosis diagnosed intraoperatively as well as intraoperative hypotension requiring vasopressor support, she was kept intubated and transferred to the critical care unit postoperatively. Her workup did not reveal any significant underlying disorder, although her metabolic acidosis complicated her perioperative care and led to an unnecessarily prolonged hospital admission.

Case Report

A 24-year-old, 64 kg, American Society of Anesthesiologists (ASA) Physical status I female with no prior medical history was admitted through the emergency department (ED) with new-onset lower back pain and numbness and tingling in her lower extremities bilaterally. A computed tomography (CT) scan of her lumbar and thoracic spine revealed a primary bone neoplasm affecting the lumbar spine with paraspinous and extradural extension, necessitating surgical biopsy and possible lumbar laminectomy. Her physical examination and vital signs were within normal limits. A paraneoplastic workup, including measurement of serum liver function tests, vitamin D level, parathyroid hormone level, thyroid-stimulating hormone, free T4, free T3, erythrocyte sedimentation rate, and C-reactive protein, was unremarkable. Preoperative blood glucose level was 69 mg/dL.

In the ED, prior to transfer to the operating room, 1 L of normal saline (NS) was administered. The patient underwent anesthetic induction with 50 mg of lidocaine, 100 mg of propofol, 100 µg of fentanyl, and 35 mg of rocuronium, followed by uneventful oral endotracheal intubation. She became hypotensive shortly thereafter with mean arterial pressures (MAPs) in the mid to low 50's. A radial arterial line was placed, and a

baseline arterial blood gas (ABG) revealed a metabolic acidosis with a pH of 7.3, PCO₂ 39.9, base deficit 6, and bicarbonate 19.6 mEq/L. Her hemoglobin was 11.9 g/dL and glucose 55 mg/dL. An additional crystalloid bolus of 1.5 L of PlasmaLyte was given, as well as 25 g of dextrose for hypoglycemia. A repeat ABG revealed a pH of 7.29, base deficit 8, bicarbonate 18.6 mEq/L, glucose 154 mg/dL, and lactic acid 0.6 mmol/L. Ketonemia was confirmed from a venous blood sample.

Throughout the biopsy phase of the procedure, the patient continued to experience arterial hypotension, requiring frequent administration of phenylephrine and norepinephrine doses despite minimal blood loss. The biopsy results indicated a giant cell tumor, and the surgical team proceeded with a lumbar laminectomy. Total intravenous anesthesia was used to facilitate intraoperative nerve monitoring. This consisted of propofol at 75–100 µg/kg/min, remifentanyl at 0.05–0.2 µg/kg/min, and dexmedetomidine at 0.1–0.2 µg/kg/hr. Metabolic acidosis and hypotension persisted with a pH <7.3, requiring the administration of 50 mEq of sodium bicarbonate towards the end of surgery. Her intraoperative course was also significant for polyuria with an average urine output of 5 mL/kg/hr. Hypotension was believed to be a result of polyuria leading to intravascular hypovolemia. Thus, it was treated with goal-directed fluid therapy (total of 4 L of crystalloid and 1 L of 5% albumin) and the temporary use of a vasopressor infusion (norepinephrine 0.02–0.05 µg/kg/min). Fluid administration enabled the norepinephrine infusion to be discontinued throughout the course of the case. The patient's serum lactic acid level remained grossly normal, indicating adequate systemic perfusion. Furthermore, the patient remained normoglycemic after the initial dose of dextrose was administered. The total case length (from beginning to end of anesthesia) was approximately 8 hours, while total operating time was approximately 6 hours. Throughout the intraoperative course, the highest recorded blood glucose level was 144 mg/dL.

Given her metabolic derangement and hemodynamic instability, the anesthesiologists managing the patient decided to transport the patient to the surgical intensive care unit (SICU) while she was still intubated and sedated for further metabolic workup prior to extubation. This was remarkable for a normal serum uric acid level, serum lactate level, electrolyte levels, serum osmolality, and osmolal gap. Laboratory workup was remarkable only for elevated serum and urinary ketones. After completing this workup, the patient was extubated later that evening and continued to do well at follow-up with no further complications. She was questioned about her diet and fasting prior to surgery and did not report an abnormal diet. She reported fasting for the recommended period of at least 8 hours prior to her scheduled surgery time.

Discussion

Identification and management of perioperative ketonemia are sparsely described in the medical literature. Ohkawa et al. examined the incidence of ketonemia in the perioperative period [2]. This observational study reported an incidence of ketonemia of approximately 5%, although it did not affect the perioperative management or time to extubation. Furthermore, intraoperative ketonemia as described in this observational study did not cause a significant change in pH.

The most common cause of ketoacidosis is diabetic ketoacidosis due to inadequate treatment of diabetes mellitus or acute infection triggering uncontrolled hyperglycemia. Other common causes are fasting ketosis and alcoholic ketoacidosis, which usually occurs in malnourished patients with chronic alcoholism who have a history of binge drinking. Non-diabetic patients could develop significant acidosis due to elevated serum lactate level, methanol or ethylene glycol poisoning, uremic acidosis, strict dieting (fruitarianism, Atkins diet), extreme exertion, or malnutrition with extremely poor intake [3].

In clinical practice, fasting is seldom suspected to be the cause of significant metabolic acidosis. In an otherwise-healthy individual, mild ketosis generally develops after a 12- to 14-hour fast although pH usually remains above 7.3 [4]. However, when combined with physiologic stress or when there is a large glucose requirement, starvation may cause a severe acid-base disturbances [5]. This exaggerated response to fasting has been described in pregnant patients, in the elderly, and in young infants [3,6,7]. We could not identify any cases in the literature in young, otherwise-healthy subjects. Similarly, we could not identify specific demographic risk factors that would increase the likelihood of this complication in otherwise-healthy patients.

The patient described above was evaluated for several potential causes of perioperative anion gap metabolic acidosis including diabetic ketoacidosis, alcoholic ketoacidosis, starvation ketoacidosis, drug-induced ketoacidosis, ingestion of toxic alcohols (e.g., methanol, ethylene glycol), lactic acidosis, uremia, and acute renal failure [8]. Calculation of the osmolar gap may be used to help differentiate between these different types of high anion gap acidosis. The osmolar gap was calculated to be normal for our patient, which, together with her normal mental status preoperatively and negative patient history, makes drug-induced causes unlikely. Diabetic ketoacidosis was high on our differential diagnosis, especially given the finding of polyuria and suspected osmotic diuresis. However, the patient's blood glucose levels both preoperatively and intraoperatively and the absence of a prior history of diabetes made this diagnosis less likely. A grossly normal BUN/creatinine ruled out established renal failure, and serum lactate levels were normal, which ruled out the diagnosis of lactic acidosis. Serum

uric acid levels combined with a grossly normal electrolyte profile also made tumor lysis syndrome unlikely.

Further post-surgical review of systems with the patient was remarkable only for a decreased appetite lasting approximately 1 month. She did not report a change in diet or any associated weight loss. She denied a history of smoking, alcohol, or drug use and denied using any health supplements. Thus, the diagnosis of starvation ketoacidosis was made based on the exclusion of other causes, assisted by laboratory workup revealing an elevated anion gap with elevated ketone levels in the urine and blood.

Adverse effects of acute metabolic acidosis primarily include decreased cardiac output, arterial dilatation with hypotension, altered oxygen delivery, decreased ATP production, predisposition to arrhythmias, and impairment of the immune response [9]. Metabolic acidoses resulting from different organic and inorganic acids are associated with different outcomes, with some forms of metabolic acidosis (such as lactic acidosis) being associated with worse outcomes than others [10]. Despite some convincing experimental data, no clinical trial has established the level at which pH becomes deleterious for hemodynamics, and no clinical trials have looked specifically at hemodynamic derangements from ketoacidosis [11].

Independent of the hemodynamic implications, acidosis is often seen as a reflection of poor organ perfusion or poor myocardial function; and an acidosis seen on ABG or negative base excess may prompt additional intravenous fluid administration, the use of blood products, escalation of inotropic support, and initiation or prolongation of ventilatory support [12].

Conclusions

This case is unique on account of the severity of ketoacidosis in the setting of acute starvation and the absence of other diagnosed comorbidities. It illustrates the importance of recognizing starvation ketonemia as a perioperative entity, especially in patients who have been fasted for prolonged periods of time prior to surgery. It is routine to ask patients about the time of their last meal prior to surgery in order to assess their risk of aspiration during anesthetic induction or emergence. While surgical plans are often altered by an inappropriately fasted patient, prolonged fasting is not considered harmful and it is often actively encouraged. At minimum, one must consider preoperative measurement of serum glucose levels in such patients as well as measurement of serum ketones in a patient presenting with an unexplained metabolic acidosis. This may help to avoid an unnecessary workup and a prolonged postoperative course. Further prospective research needs to be performed to evaluate the frequency of starvation ketoacidosis

in different patient populations and whether it is associated with adverse short- and long-term postoperative outcomes.

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Statement

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Conflict of interest statement

The above authors have no conflicts of interest to report.