

# Rare Presentations of Ketoacidosis: Diabetic Ketoalkalosis and Ketoacidosis Secondary to Fasting and Muscular Dystrophy

Mads Vandsted Svart,<sup>1</sup> Thomas Schmidt Voss,<sup>1</sup> Michael Bayat,<sup>2</sup> Lene Ring Madsen,<sup>1</sup> Lone Thing Andersen,<sup>3</sup> Per Løgstrup Poulsen,<sup>1</sup> and Niels Møller<sup>1</sup>

**D**iabetic ketoacidosis (DKA), a hallmark of type 1 diabetes, is the result of uncontrolled production of ketone bodies (3-hydroxybuturate and acetoacetic acid), leading to a lowering of blood pH (1). Ketogenesis in the liver is triggered by low levels of insulin and high levels of glucagon. In addition, other stress hormones (epinephrine, growth hormone, and cortisol), together with lack of insulin, accelerate lipolysis in peripheral tissues and lead to increased amounts of free fatty acids (FFAs) in the blood. FFAs are the most important precursor for ketone body formation. This process takes place in the mitochondria (1). In general, ketoacidosis presents in patients with type 1 diabetes and is characterized by a high anion gap metabolic acidosis, which is usually compensated by hyperventilation and pulmonary loss of carbon dioxide. Below we report six unusual presentations of ketoacidosis.

## Presentation 1

A 42-year-old man with known alcohol abuse and type 1 diabetes resulting from pancreatitis was brought to the hospital with vomiting, coughing, and general weakness. Before hospitalization, he had not taken any alkaline medicine or diuretics. His status at arrival and his blood test results are shown in Table 1. He had high 3-hydroxybutyrate (3-OHB), low potassium, and an anion gap >12 mEq/L. His condition was further complicated by pneumonia. He

was moved to the intensive care unit (ICU), where treatment with antibiotics, insulin, glucose, and potassium was initiated, and he recovered.

## Presentation 2

A 28-year-old woman with type 1 diabetes was hospitalized. She had multiple complications, including nephropathy, retinopathy, peripheral neuropathy, gastroparesis treated with gastric electric stimulation (GES), and impaired urinary bladder function. On admission, she had symptoms of urinary tract infection (UTI) and reported having undergone eye surgery with local anesthesia the day before. She reported abdominal discomfort and vomiting. Blood test results (Table 1) showed hyperglycemia, high 3-OHB, pH of 7.47 indicating alkalosis, and low levels of bicarbonate compensated by hyperventilation. She was treated with insulin, glucose, and potassium and recovered fully.

## Presentation 3

A 38-year-old woman with type 1 diabetes, nephropathy, incipient retinopathy, and gastroparesis treated with GES was hospitalized with lower stomach pain, signs of a UTI, and vomiting. She had a metabolic alkalosis and high 3-OHB (Table 1). Serum chloride was not measured. The infection and DKA were successfully treated with antibiotics, insulin, glucose, and potassium.

## Presentation 4

A healthy 50-year-old man was brought to the hospital with nau-

<sup>1</sup>Medical Department MEA, Aarhus University Hospital, Aarhus, Denmark

<sup>2</sup>Medical Department, Vendsyssel Hospital, Hjørring, Denmark

<sup>3</sup>Department of Nuclear Medicine & PET, Aarhus University Hospital, Aarhus, Denmark

Corresponding author: Mads Svart, mvsv@clin.au.dk

DOI: 10.2337/diaclin.33.1.37

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**TABLE 1. Blood Test Results and Vital Parameters in Three Patients With Diabetic Ketoacidosis (Cases 1–3), One Patient After a 7-Day Fast (Case 4), and Two Patients With Muscular Dystrophy (Cases 5 and 6)**

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Plasma glucose (mmol/L)	39	25.5	7.2	7.8	8.6	8.5
Arterial pH (normal range 7.37–7.45)	7.47	7.47	7.49	7.21	7.18	7.03
S-bicarbonate (mmol/L; normal range 22.5–26.9)	42.3	19.7	29.9	11.6	9.6	8.0
Base excess (mmol/L; normal range –3.0 to 2.0)	20	–7.2	7.1	–19.4	–21.3	–24.7
3-Hydroxybuturate (mmol/L; normal range < 0.3)	7.8	4.7	3.6	7.8	5.1	4.1
Plasma chloride (mmol/L; normal range 98–106)	51	101	—	98	102	115
Anion gap (mEq/L; normal range 3–12)	27.7	21.3	—	28.4	17.4	57.7
Potassium (mmol/L; normal range 3.5–4.6)	2.3	3.3	3.7	4.2	2.2	3.4
Creatinine ( $\mu$ mol/L; normal range 60–105)	130	158	167	119	39	80
Carbon dioxide (kPa; normal range 4.7–6)	8.45	3.1	5.4	2.9	2.5	3.2
Lactate (mmol/L; normal range 0.5–2.5)	2.3	2.6	1.3	2.5	0.7	1.7
Blood pressure (mmHg)	112/60	150/80	107/62	117/81	91/66	90/52
Heart rate (bpm; normal range 60–90)	82	70	104	93	71	81
Respiratory rate (breaths/min; normal range 14–18)	12	12	20	30	14	12
Temperature ( $^{\circ}$ C; normal range 36.4–37.1)	37.4	36.7	39.9	37.0	36.6	36.8

sea and abdominal pain. He had no history of alcohol abuse, diabetes, or use of prescription medications. In an attempt to lose weight, he had been fasting for 7 days, only allowing himself water. He reported dizziness and had noticed tachypnoea. His status on arrival and blood test results can be seen in Table 1. A metabolic acidosis partly compensated by hyperventilation was present with elevated blood 3-OHB and an anion gap >12 mEq/L. He was treated with insulin and intravenous glucose. He recov-

ered, and subsequent testing failed to show any signs of diabetes.

**Presentation 5**

A 65-year-old woman with limb girdle muscular dystrophy with permanent respiratory support at home but no history of diabetes was hospitalized with diarrhea and vomiting. She was moved directly to the ICU because of a low systolic pressure of 91 mmHg and a pH of 7.18 (Table 1). She had metabolic acidosis with elevated levels of 3-OHB and normal lactate. She was treated with insulin,

glucose, potassium, and bicarbonate and recovered.

**Presentation 6**

A 47-year-old man with Duchenne muscular dystrophy and permanent respiratory support at home but no history of diabetes was hospitalized with pneumonia. After some days of treatment with antibiotics, his condition worsened. He needed increased respiratory support; his blood pressure dropped to 90/52 mmHg; and he had a pH to 7.03. He had metabolic acidosis with elevated levels of

3-OHB and normal lactate. He was treated with insulin, glucose, and potassium and recovered.

### Questions

1. Is it possible to have ketoacidosis with an alkali pH?
2. How can fasting affect ketone body production and pH?
3. Are patients with muscular dystrophy more vulnerable to ketoacidosis even without having diabetes?

### Commentary

In this report, we describe six cases of unusual ketoacidosis—three presented as ketoalkalosis in patients with type 1 diabetes and three depicting ketoacidosis secondary to fasting or muscular dystrophy in patients without diabetes. All patients had high levels of 3-OHB and a high anion gap.

Ketoalkalosis (also called “masked DKA” or “alkaline ketoacidosis”) refers to cases of ketoacidosis in which the acidosis is overridden by a coexisting alkalosis (2,3). A number of factors participate in the alkaline masking of the ketoacidosis. Common features are vomiting and activation of the renin-angiotensin-aldosterone system because of hypovolemia leading to loss of hydrogen and chloride ions (3). All three patients with type 1 diabetes (Cases 1–3) had nausea and vomiting and two of them had severe GES-treated gastroparesis.

With regard to Case 4, the patient had been fasting for ~1 week and presented with frank ketoacidosis partially compensated by hyperventilation. Ketoacidosis precipitated by fasting has been reported in previous case reports, in particular during pregnancy (4). Metabolically, fasting

resembles ketoacidosis in terms of low levels of insulin and high levels of stress hormones, FFAs, and ketone bodies (5,6). In this case, there was no history of excessive alcohol use, so alcoholic ketoacidosis appears unlikely (7). Theoretically, a nondiabetic patient with ketoacidosis and adequate insulin secretion could be treated solely with glucose, which would stimulate endogenous insulin secretion. However, in this case, the patient’s diabetes status was unknown on admission.

In Cases 5 and 6, ketoacidosis most likely resulted from a combination of infection and muscular dystrophy. Ongoing diarrhea episodes may lead to excessive amounts of bicarbonate being lost to the lumen of the bowel, resulting in an increased anion gap and hampering respiratory compensation of the acidosis. In addition, patients with muscular dystrophy have small muscle glycogen stores and therefore are prone to hypoglycemia. Low insulin and high stress hormone levels, together with reduced clearance of ketone bodies in muscle, may accelerate ketogenesis. Ketoacidosis in patients with muscular dystrophy, in particular Duchenne muscular dystrophy, has been reported in rare cases (8,9). As with the patient in Case 4, we treated the patient in Case 6 with both insulin and glucose, although glucose alone likely would have been as effective.

### Clinical Pearls

- It is important to keep in mind that even insulin production in people without diabetes can become insufficient, resulting in ketoacidosis.

- Patients with muscular dystrophy are more vulnerable to stress-induced ketoacidosis.
- People with type 1 diabetes can present with ketoacidosis masked as alkalosis but still requiring ketoacidosis treatment.

### Duality of Interest

No potential conflicts of interest relevant to this article were reported.

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