Steroid-induced diabetic ketoacidosis - case report

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) is an acute complication of diabetes, a severe metabolic disorder that requires urgent treatment. The aim of this article is to present a case of steroid-induced diabetes with complications.

Case presentation: A young 25-year-old man without any co-morbid, presented to the emergency department with fever, vomiting, coughing, and buttock pain which started 3 days before. On the right gluteus, there was a hematoma approx. 10 × 5 cm with fluctuation. The patient had hyperglycemia (9.1 mmol/l), associated with high anion-gap metabolic acidosis, acute kidney injury (AKI), grossly elevated muscle enzymes, hyperkalemia, hyperphosphatemia, hypoalbuminemia, hypocalcemia and hypomagnesemia, and deranged liver function tests. The urine dipstick was grossly cola-colored and biochemically was positive for glucose, ketones, and proteins. Abscess drainage was performed, and *Streptococcus pyogenes* was isolated on culture and sensitivity. The patient was treated for DKA, complicated by an AKI and infection. Diabetes is confirmed based on glycosylated hemoglobin.

Conclusion: The risk of ketoacidosis and hyperglycemia should be considered in the course of steroid therapy, even without a diagnosis of diabetes, in patients who abuse steroids or have risk factors for diabetes and obesity.

Keywords: Diabetic ketoacidosis, steroids, case report, diabetes mellitus, infection, glycosylated hemoglobin, acute kidney injury.

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Background

Diabetic ketoacidosis (DKA) is a common and most severe acute complication of diabetes mellitus (DM), with a high morbidity rate followed by hyperketonemia, hyperglycemia, and metabolic acidosis [1,2]. DKA is a severe metabolic disorder that refers to extremely unregulated diabetes followed by a lack of insulin (absolute or relative) that requires urgent treatment [2].

It is commonly precipitated by an acutely stressful event such as the development of infection leading to overt sepsis, organ infarction, burns, pregnancy, or intake of drugs that affect carbohydrate metabolism such as corticosteroids. The presence of these stressful conditions incites the release of counter-regulatory hormones such as glucagon, catecholamines, and growth hormone. These hormones induce the mobilization of energy stores of fat, glycogen, and protein. The net effect of this is the production of glucose. As a result of absent or deficient insulin release, DKA present with the following metabolic derangements: profound hyperglycemia, hyperketonemia, and metabolic acidosis. The production of ketones outweighs its excretion by the kidneys. This results in further reduction of systemic insulin, and elevated concentrations of glucagon, cortisol, growth hormone, and catecholamine. In peripheral tissues, such as the liver, lipolysis occurs to free fatty acids, resulting in the further production of excess ketones causing ketosis and metabolic acidosis. Symptoms of DKA usually develop within 24 hours. Gastrointestinal symptoms such as nausea and vomiting are very prominent. When the renal threshold is reached, profound hyperglycemia leads to glucosuria. This is accompanied by dehydration causing volume depletion and reactive tachycardia. As a result of volume depletion, hypotension may occur. Classically, these patients present with Kussmaul's respiration and a fruity odor due to metabolic acidosis and ketosis respectively. Patients should be investigated for the presence of an underlying infection. Finally, neurological symptoms such as decreasing sensorium when present warrant emergent care [1,2]. The blood glucose cut-offs for 11 mmol/l and higher are suspicious for impaired glucose metabolism and DM as well. DKA may also be the first manifestation of diabetes.

The aim of this article is to present a case of steroid-induced diabetes, complicated by acute kidney injury (AKI), infection, and rhabdomyolysis.

Case Presentation

A young 25-year-old man with no positive familiar anamnesis and comorbidities presented to the emergency department (ED) with fever, vomiting, coughing, and buttock pain in the last 3 days. On further probing, the patient admitted to using anabolic steroids on occasion during his physical training and the ketogenic diet.

His vital signs were: blood pressure 115/80 mmHg, pulse 115/minutes, temperature 39.3°C, RR 24/minutes, O2 Sat 99%, electrocardiogram (ECG) with high T voltage in precordial leads. His abdominal, cardiopulmonary, and neurologically exams were unremarkable. Over the right gluteal region, there was a single hematoma approx. 10 × 5 cm with fluctuation.

His laboratory values were: Serum glucose 9.1 mmol/l (3.0-7.8), Na 140 mmol/l (135-145), K 6.7 mmol/l (3.2-4.5), Cl 98 mmol/l (100-110), bicarbonates 17 mmol/l (22-33), Anion Gap 24 mmol/l (4-13), urea 14.0 mmol/l (3.0-8.0), creatinine 218 µmol/l (70-120), Ca 1.9 mmol/l (2.2-2.6), corrected Ca 2.1 mmol/l (2.3-2.7), phosphate 2.7 mmol/l (0.7-1.4), Mg 0.44 mmol/l (0.7-1.0), protein 43 g/l (62-83), albumin 22 g/l (33-47), globulin 20 g/l (25-45), ALP 99 U/l (40-110), ALT 126 U/l (<45), AST 675 U/l (<40), LDH 2470 U/l (110-250), GGT 15 U/l (<50) CK 9000 U/l (39-308).

Blood arterial gases were: pH 7.2 (7.35-7.45), pO2 85 mmHg (80-110), pCO2 30 mmHg (35-50), BE-11 (-3-+3), HCO3 16 mmol/l (22-27), SpO2 99%.

The urine dip-stick was grossly cola-colored and biochemically was positive for glucose, ketones, and proteins.

The chest X-ray and abdomen US were done with unremarkable findings.

The abscess was diagnosed by physical examination, drained surgically in the ED, and the aspirated pus was sent for cultures. The *Streptococcus pyogenes* was isolated.

The patient was admitted to the intensive care unit (ICU) and was treated for infection, AKI, and DKA with a standardized protocol. He was treated with 0.9% saline, insulin, 5% glucose solution, sodium bicarbonate 7.5% solution, proton pump inhibitor, analgesic, hepatoprotective therapy, and antibiotics according to antibiogram (levofloxacin, amoxicillin with clavulanic acid).

His clinical course was complicated by rhabdomyolysis and AKI which required dialysis. His hemoglobin A1c (HbA1c) was elevated at 9% (reference range: 4.5%-6.0%). He was treated for 3 days in the ICU where dialysis was performed, after which was transferred to the endocrinology department. All cultures (blood, urine, source-pus) were negative and laboratory values at discharge were normal, except for liver function test (LFTs) which remained elevated for a month. Moreover, DM was confirmed by elevated HbA1c and this was understood as the first presentation of DM, manifesting as DKA. It was deduced that the patient was receiving injectable (I/M) steroids in the gluteal region so it was steroid-induced diabetes. After the resolution of the DKA, the patient was switched over from I/V soluble insulin to the subcutaneous basal-bolus insulin regime. On the subsequent follow-ups, insulin was replaced with oral metformin.

Discussion

Although DM is not uncommon in patients on high-dose steroid treatment, DKA is distinctly rare. Only a few patients have been reported, and DKA was mild, so none required insulin. No case of steroid-induced DKA in a patient with type 2 DM has been reported in the literature, and there are a few cases that described steroid-induced DM. This is a presentation of a young patient whose desire for looking good was rewarded with a disease, to be treated, maybe for the rest of his life. It is unusual to find steroid-induced DKA as a presentation of DM, as the glucose level usually does not go high enough to produce symptoms typical of DM. Possible causes of euglycemic ketoacidosis are recent insulin use, reduced caloric intake, higher alcohol consumption, chronic liver disease, glycogen storage disorders, as well as pregnancy [3]. The problem of normoglycemia can mislead clinicians into making a diagnosis and thus delay the start of therapy for this emergency [3]. Sodium-glucose cotransporter-2 (SGLT2) inhibitors are relatively new drugs approved for diabetes, but they increase the risk for DKA, particularly in patients with type 1 diabetes and those with certain high-risk conditions. In some cases, blood glucose levels are normal or only mildly elevated (euglycemic ketoacidosis), which can delay the diagnosis. Check ketones in patients taking SGLT2 inhibitors with symptoms or precipitating factors for ketoacidosis regardless of blood glucose levels [4]. The American Food and Drug Administration. (FDA) and European Medicines Agency warn about the possible atypical presentation of DKA with SGLT2 inhibitors and suggest interrupting SGLT2 inhibitors and monitoring ketosis in patients scheduled for surgery or hospitalized [4].

The patient's laboratory results revealed, a high anion gap metabolic acidosis, AKI, and hyperkalemia. Additionally, there was marked hyperphosphatemia, grossly elevated muscle enzymes, along with high serum LDH and AST levels. This pattern is commonly associated with rhabdomyolysis [5,6]. Glucose level was slightly high, bicarbonates were low and the anion gap was almost double, so the diagnosis of euglycemic DKA and rhabdomyolysis, with new-onset DM was made [3,5], which can be seen in steroid users. There has been a link between diabetic emergencies and rhabdomyolysis [7-9] which has a high mortality rate. This link is not well known, and that is why there is a potential to miss out on the diagnosis of rhabdomyolysis, in the presence of DKA [9]. The pathophysiological mechanism leading to rhabdomyolysis in DKA remains unknown as yet. From the literature, it is evident that those patients who develop rhabdomyolysis,

have very high glucose levels and a high osmolality on admission [10]. Also, rhabdomyolysis commonly occurs as a consequence of trauma to skeletal muscles, and very rarely it is secondary to DKA [11].

The rhabdomyolysis in our patient could have occurred as a complication of steroid injections in the buttock area in the form of either pyomyositis/necrotizing fasciitis or compartment syndrome. Muscle cell lysis leads to the release of potassium, phosphate, myoglobin, several muscle enzymes creatine kinase (CK), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and other cellular components. The released phosphate combines with magnesium and calcium ions to form complexes and leading to hypocalcemia and hypomagnesemia. Hypocalcemia is followed by hyperphosphatemia, but in acidosis, a low phosphate would be expected.

AKI was predominantly a complication of rhabdomyolysis in our patient and could have well been a complication of possible shock or sepsis (lactate should have been high in such a case, but it was in the reference range) [7,9]. That LDH is quite high suggesting a massive cell death of myocytes and erythrocytes. The presence of blood in urine analysis may have been myoglobin rather than hemoglobin (darker color indicates the severity of rhabdomyolysis). Confirmation with specific urine myoglobin was advisable. However, myoglobin is rapidly excreted, and negative urine myoglobin does not exclude the diagnosis. Renal failure may ensue due to dehydration, sepsis, hyperosmolality, and due to the toxic effects of myoglobin.

AKI looks prerenal but with those liver function blood tests it could also be hepatorenal. Renal lesions can range from microscopic hematuria to glomerulonephritis and AKI. Acute renal failure predicts a poor outcome, and the causes are numerous: immune complex and vasculitic glomerulonephritis, renal infarction, hemodynamic impairment due to heart failure, severe sepsis, or after cardiac surgery, and antibiotic toxicity [12].

To avoid missing cases of steroid-induced DM, and ultimately DKA, both fasting and postprandial blood glucose values should be monitored [13]. DKA may occur in the absence of any other triggering factor, and even in patients with well-controlled DM [14]. Parenteral glucocorticoid therapy can precipitate DKA in patients with DM, and the risk for DKA is high when pro-inflammatory cytokines are high according to Mondal et al. [15] New findings suggest that serum IL-6 levels at admission have the best predictive potential for DKA [15].

What certainly remains uncertain is whether the DKA was caused by steroids or whether the precipitating factor was an infection, [16] caused probably by poor steroid-injection technique into the muscle.

Conclusion

This is a case report of steroid-induced DM, which had presented as DKA, complicated by AKI and infection. This association represents an additional threat to renal function and warrants its close follow-up. The risk of ketoacidosis and hyperglycemia should be considered in the course of steroid therapy, even without a diagnosis of diabetes. It can occur especially in patients who have risk factors for DM including obesity and long-term use of steroids, but also in the young population, who abuse steroids for different reasons. Early identification of DKA in such a scenario can prevent further morbidity and mortality.

What is new?

Steroid-induced DM first presented as DKA, complicated by AKI and infection. Only a few patients have been reported as it is unusual to find steroid-induced DKA as an onset of DM.

Acknowledgments

Not applicable.

List of Abbreviations

DKA	Diabetic ketoacidosis
DM	diabetes mellitus
AKI	acute kidney injury
ED	emergency department
ECG	electrocardiogram
ICU	intensive care unit
LFT	liver function test
SGLT2	Sodium-glucose cotransporter-2
FDA	Food and Drug Administration
CK	creatine kinase
LDH	lactate dehydrogenase
AST	aspartate aminotransferase

Conflict of interest

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Consent for publication

Not needed since there was no patient identity in the article.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	Patient (gender, age)	25-year-old male
2	Final diagnosis	DKA
3	Symptoms	Infection, vomiting, fever
4	Medications	Saline solutions, antibiotics, insulin, sodium bicarbonate, glucose
5	Clinical procedure	/
6	Specialty	Internal medicine