

Euglycemic ketoacidosis as a cause of a metabolic acidosis in the Intensive Care Unit

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Abstract

Euglycaemic ketoacidosis is a rare endocrine emergency, which can have disastrous consequences if left undiagnosed. We present the case of a 57 year old man with type 2 diabetes who developed ketoacidosis (DKA) following a myocardial infarction, despite being normoglycaemic, following discontinuation of his insulin infusion in an intensive care setting. The case highlights the importance of capillary ketone body testing in this scenario as well as the dangers of an over reliance on blood glucose values in the diagnosis of ketoacidosis. The notion that DKA can occur in both type 1 and type 2 diabetes is reaffirmed and the value of adequate insulin therapy in euglycaemic ketoacidosis is emphasized.

Keywords

Euglycaemic diabetic ketoacidosis, ketone bodies

Key Learning points

- Diabetic ketoacidosis can present in both type I and type II diabetes.
- The presence of normoglycaemia does not exclude the diagnosis of diabetic ketoacidosis in an unwell diabetic patient.
- Blood ketone testing is a vital diagnostic tool, particularly in anuric patients in whom euglycaemic diabetic ketoacidosis is suspected.

Case Report

A 57 year old South Asian man was transferred to the Intensive Care Unit (ICU) from the cardiac catheterization lab following balloon dilation of a new ostial Left Main Stem (LMS) occlusion resulting in non-ST elevation myocardial infarction (NSTEMI). His past medical history included hypertension, hypercholesterolaemia, ischaemic heart disease and type 2 diabetes mellitus complicated by end-stage renal failure for which he received haemodialysis three times a week. His diabetes was usually poorly controlled with biphasic insulin (Human Mixtard 30/70 - 25 units twice daily), in addition to his regular cardiac medication.

His extensive cardiac history consisted of three previous NSTEMIs, one 3-vessel coronary artery bypass graft operation and previous drug eluting stent deployment in the left anterior descending artery and LMS.

On admission to ICU he was unsedated, spontaneously ventilating on 2L of oxygen and required noradrenaline to support his blood pressure. An arterial blood gas showed a mixed respiratory and metabolic acidosis: pH 7.20 pCO₂ 6.94 kPa pO₂ 13.27

kPa HCO₃⁻ 18.8 mmol/L BE -6.9 mmol/L lactate 1.39 mmol/L glucose 11.1 mmol/L (200 mg/dL).

Continuous venovenous haemofiltration was commenced uneventfully and continued throughout his ICU stay.

Clinically he improved, with his noradrenaline requirements being weaned and his gas exchange normalising on minimal respiratory support.

Throughout the first 24 hours he was treated with a variable rate intravenous insulin infusion (VRIII) and regular arterial blood gases were taken as per ICU protocol. His blood glucose levels remained between 3.7 -11.1 mmol/L (67-200mg/dL). His VRIII was discontinued 27 hours after admission to the ICU with no substantial rise in glucose concentrations (See graph 1). He was then restarted on his usual home insulin regimen.

Despite the clinical improvement, he remained profoundly acidotic with a deteriorating base excess. With a normal blood lactate, and the absence of a history suggestive of methanol, salicylate or ethylene glycol ingestion that could account for the high anion gap metabolic acidosis, a diagnosis of ketoacidosis was considered. Due to anuria, routine urine ketone analysis was not possible and we instead relied upon

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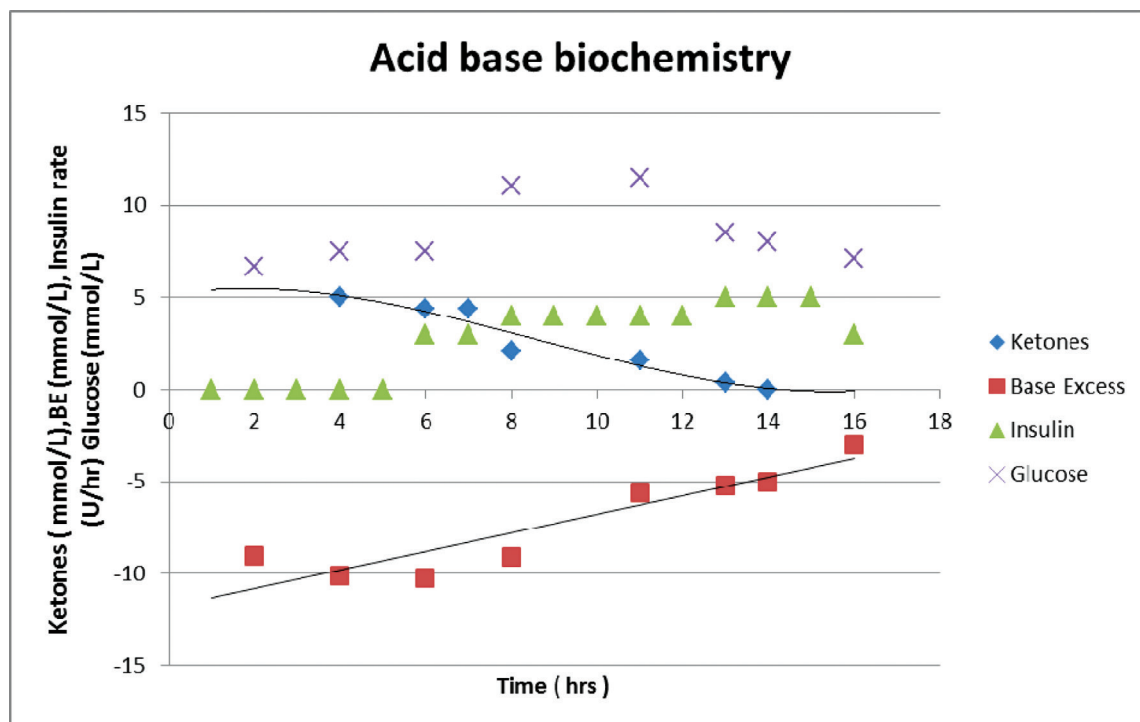


Figure 1.

direct serum ketone testing for the diagnosis. Serum β hydroxybutyrate levels were elevated (5.0 mmol/L, ref range <0.3 mmol/L) despite a serum glucose of 7.5 mmol/L (135 mg/dL). He was diagnosed with euglycaemic ketoacidosis.

To switch off endogenous ketone production, he was started on a basal insulin infusion of 3-4 units/hr whilst simultaneously administering a carbohydrate infusion peripherally to maintain euglycaemia. Within 10 hours, blood ketone levels were undetectable, and the base excess had returned to near normal levels (Figure 1). His condition continued to improve and he was discharged to the renal ward 36 hours after the intravenous insulin regimen had been restarted.

Discussion

Diabetic ketoacidosis (DKA) was first described in 1886, and is one of the most serious acute metabolic complications of diabetes with historical mortality rates of virtually 100% prior to the discovery of insulin in 1922. Despite medical advances in diabetes care, it remains a life threatening condition with a UK mortality rate of approximately 2%.¹ Complications of DKA and its management include fluid imbalance, electrolyte disturbances, acute respiratory distress syndrome, cerebral oedema and thromboembolism. Consequently, a prompt diagnosis is vital in order to initiate the correct management for this treatable condition.

Characteristically, ketoacidosis presents with hyperglycaemia, ketosis and a metabolic acidosis. Reliance on blood glucose however, can be misleading. A 16 year prospective study² found that out of the 722 cases of DKA, 43 cases (6%)

presented with an initial blood glucose of less than 16.7 mmol/L. In the same study, 8 cases (1.1%) presented with a blood glucose concentration of less than 10 mmol/L.

Earlier, Munro *et al*³ described 211 cases of DKA, 37 (18%) of which presented with a plasma glucose concentration of less than 16.7 mmol/L, calling this syndrome "euglycaemic diabetic ketoacidosis".

Diabetic ketoacidosis is a well known complication of type 1 diabetes, but not exclusively manifested in this diabetic subset. A study⁴ evaluating 138 consecutive DKA admissions at a large academic centre, identified 30 (21.7%) patients with Type 2 diabetes.

Likewise, *euglycaemic* diabetic ketoacidosis is predominantly, but not exclusively associated with type 1 diabetes. To our knowledge there has only been one reported case of this rare form of DKA in a patient with type 2 diabetes.⁵

Although there is general consensus on the pathophysiology of DKA presenting with hyperglycaemia, the underlying pathogenesis of euglycaemic DKA is less well understood.

Burge *et al*⁶ suggests that fasting may predispose patients to euglycaemic ketoacidosis during periods of insulin deficiency due to raised plasma concentrations of catecholamines and glucagon, promoting lipolysis. Indeed in the only previous reported case of a patient with type 2 diabetes and euglycaemic DKA, the patient concerned had a preceding reduced oral intake.

Contributing factors to our patient's euglycaemic state may have been a reduced carbohydrate intake during his ICU stay, the recommencement of his

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regular insulin coupled with a constant glucose clearance via his continuous haemofiltration.⁷

Our patient presented a practical diagnostic challenge by virtue of his anuria preventing routine urine ketone analysis. Although conventional urine ketone testing provides a readily available fast and affordable test to estimate body ketone levels, it presents some limitations. Firstly, it only offers a semi-quantitative estimate of ketone levels, and is prone to error in the presence of certain drugs. Furthermore, urine ketone analysis measures the presence of acetoacetate, whereas the predominant ketone present in ketoacidosis is β hydroxybutyrate (BHB), which can now be readily measured using capillary ketone analysis strips. Capillary testing also offers a better measure of response to therapy as urine ketone analysis can remain positive once ketosis has resolved due to BHB oxidation. Recent guidelines from the Joint British Diabetes Societies recommend capillary blood ketone testing to monitor response to insulin therapy in diabetic

ketoacidosis.⁸ Our patient's anuria can be viewed as serendipitous since it forced us to utilize capillary blood ketone testing.

Conclusion

This case highlights the importance of capillary ketone testing in the diagnosis of diabetic ketoacidosis, and reminds us that DKA is not confined to patients with type 1 diabetes. Over reliance on a hyperglycaemic state to diagnose ketoacidosis can result in a dangerous, but treatable diagnosis being missed. We concur with previous authors who have described euglycaemic ketoacidosis and advise frequent capillary ketone testing in all critically ill patients with diabetes.

Conflict of Interest

All authors have no conflict of interest to declare. No extraneous funding was obtained. All authors contributed significantly to study design, implementation or writing.

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