Euglycaemic diabetic ketoacidosis

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INTRODUCTION

Diabetic ketoacidosis (DKA) is an acute metabolic emergency. DKA is classically defined as the triad of hyperglycaemia, acidosis and ketosis. However, this case series demonstrates that this biochemical triad is not always present.

DISCUSSION

DKA is caused by insulin deficiency, either relative or absolute (Alberti, 1989). The biochemical triad is what many medical students and junior doctors have learnt and are familiar with. However, inexperienced doctors may discard the possibility of DKA when confronted with a normal or near-normal blood glucose, resulting in the delay of life-saving treatment.

Despite major advances in the understanding of the pathophysiology and treatment of DKA over the past two decades, its morbidity and mortality remains significant. The mortality rate for ketoacidosis ranges from 2 to 5% in developed countries and 6 to 24% in developing countries (Lebovitz, 1995). Complications include myocardial, bowel and brain infarctions, fluid overload, cerebral oedema and acute respiratory distress syndrome. In a UK review of deaths in diabetic patients aged less than 50 years, the major contributory factors in deaths from DKA were errors by patients, primary health-care staff and hospital staff (Tunbridge, 1981).

Munro et al (1973) reported a series of 211 episodes of DKA in which 37 were euglycaemic (defined as blood glucose of 16.7 mmol/litre or less with a plasma bicarbonate of 10 mmol/litre or less). Jenkins et al (1993) reported a similar study of 722 episodes of DKA and found that in 6% of patients, the initial blood glucose was less than 16.7 mmol/litre and plasma bicarbonate was less than 15 mmol/litre. The clinical features of these patients suggested that the relatively low blood glucose levels were a result of persistent vomiting and reduced carbohydrate intake, together with continuation of insulin treatment.

CASE REPORT 1

A 74-year-old woman with insulin-dependent diabetes was admitted to the medical high dependency unit with a 2-day history of increasing nausea and confusion. On examination she was afebrile, dehydrated and confused. Systemic examination was unremarkable. Capillary blood glucose by self-monitoring strip was 10.6 mmol/litre and urinalysis demonstrated 3+ ketones and 3+ glucose. Biochemical examination revealed plasma glucose 11.9 mmol/litre, sodium 127 mmol/litre, potassium 5.1 mmol/litre, urea 13.9 mmol/litre and creatinine 87 mmol/litre. Arterial blood gas analysis showed pH 7.30, partial pressure of carbon dioxide = 4.4 kPa, partial pressure of oxygen = 9.0 kPa, bicarbonate = 15.3 mmol/litre, base excess -9.2 mmol/litre and oxygen saturation 97%. She was treated with intravenous dextrose-saline and low dose insulin infusion. She made a good recovery and was well within 48 hours of presentation.

CASE REPORT 2

A 52-year-old man with insulin-dependent diabetes and chronic renal failure presented with a 1-day history of vomiting and lethargy. On admission to the medical high dependency unit, he was disorientated, dehydrated and pyrexial. Physical examination was unremarkable. Laboratory plasma glucose was 5.6 mmol/litre (capillary blood glucose by self-monitoring strip was 13.4 mmol/litre). Biochemical analysis revealed sodium 123 mmol/litre, potassium 6.2 mmol/litre, urea 18.4 mmol/litre and creatinine 616 mmol/litre. Arterial blood gas analysis showed pH 7.19, partial pressure of carbon dioxide = 5.4 kPa, partial pressure of oxygen = 10.2 kPa, bicarbonate = 12.4 mmol/litre, base excess -10.0 mmol/litre and oxygen saturation 95%. Urinalysis demonstrated 3+ ketones, 2+ glucose and 1+ protein. Treatment was commenced with intravenous saline and low dose insulin infusion. Within 36 hours of admission, his usual insulin regimen was recommenced.

CASE REPORT 3

A 27-year-old woman at 32 weeks gestation was admitted to the antenatal ward with a 24-hour history of flu-like illness, sputum production, fever and vomiting. She had impaired glucose tolerance secondary to pancreatic debridement as a result of gallstone-induced pancreatitis 6 years previously and had developed gestational diabetes requiring insulin. Capillary blood glucose by self-monitoring strip on admission was 4.7 mmol/litre and she had 1+ ketones in the urine. Over the next 36 hours she became increasingly dyspnoeic with a respiratory rate of 40 breaths per minute and was admitted to the intensive care unit. A chest infection was diagnosed and intravenous antibiotics were commenced. Other investigations showed plasma glucose 11.1 mmol/litre, sodium 133 mmol/litre, potassium 5.5 mmol/litre, urea 1.7 mmol/litre and creatinine 103 mmol/litre. Arterial blood gas analysis demonstrated pH 7.10, partial pressure of carbon dioxide = 1.36 kPa, partial pressure of oxygen = 37.5 kPa, bicarbonate = 3.1 mmol/litre and base excess -24.3 mmol/litre. The anion gap was 24.4 mmol/litre. Blood urea and lactate levels were normal and there was no history of drug ingestion. Excessive plasma levels of hydroxybutyrate were confirmed by an aqueous enzymatic assay and an electrochemical ketone detector. Urine analysis with a reagent strip demonstrated high levels of acetoacetate. Treatment was commenced with 5% dextrose with potassium, normal saline and low dose insulin infusion. Sputum culture demonstrated *Streptococcus pneumoniae* as the causative organism. She had 20 days of intravenous insulin.

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Insulin prevents gluconeogenesis and facilitates cellular utilization of the available glucose, preventing the development of hyperglycaemia (Munro et al, 1973). Since diabetic patients are able to self-monitor capillary blood glucose levels, they can manage intercurrent illness by increasing their insulin dose. This dose may be sufficient to prevent hyperglycaemia but insufficient to prevent lipolysis and ketosis.

Euglycaemic DKA can occur in pregnancy. DKA affects only 1–3% of pregnancies complicated by diabetes but can result in significant morbidity and mortality for both mother and fetus (Ramin, 1999). Pregnancy predisposes to ketoacidosis. Factors include accelerated starvation, dehydration secondary to emesis, lowered buffering capacity because of the respiratory alkalosis of pregnancy, increased production of insulin antagonists (human placental lactogen, cortisol and prolactin) and stress such as infections (Chauhan and Perry, 1995). In the third case, it is possible that significant hyperglycaemia did not develop because of the vomiting-induced reduction in carbohydrate intake, continuous uptake of glucose by the fetus and the presence of sufficient exogenous insulin to prevent hepatic glycogenolysis. A further factor may have been the inability to produce sufficient glucagon as a result of her previous partial pancreatectomy.

CONCLUSION

These cases highlight one end of the spectrum of biochemical abnormalities found in DKA. There is no universally accepted biochemical definition of DKA and diagnosis is proposed in patients presenting with positive serum ketones, arterial pH ≤7.30 and/or a serum bicarbonate ≤15 mmol/litre (Lebovitz, 1995). Plasma ketone assays are possible but bedside measurement of capillary blood 3-hydroxybutyrate concentration has been used successfully to manage DKA (McBride et al, 1991; Wiggam et al, 1997). Therefore, in diabetic patients who are unwell, the emphasis should be on urine or blood testing for ketones and arterial blood gas analysis to exclude DKA. HM

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IN THE PUBLIC'S VIEW...

Slips and axes

What a difference an s makes. The sub-title to the *Observer*'s article about the Biobank project (27 July 2003) described it as '...a radical long-term plan to conquer disease'. Not diseases, but disease. Journalist Jo Revill was realistic: knowing and being able to do something are not the same; and the project will be fantastically expensive. We may learn an immense amount about genetics within populations, but risk holding back numerous other less fashionable research projects that have more immediate promise of improving health. There is also the risk of industry 'gene fishing' to patent potential treatments.

But a sub-editor made the Freudian slip and, whatever their or our subconscious desire, while genetics may enable better control or treatment of some diseases, it will never enable us to conquer disease. The sub-editor is not alone. When the Human Genome Project unveiled its success Bill Clinton expressed the banal hope that cancer would soon be something only read about in history books. It is surprisingly easy to overlook that disease and death are part of life, but they are inescapable.

There's a lot of money to be made while we refuse to give in gracefully. Hamamatsu Photonics is a Japanese company that is advertising their new PET scanner in *Nature* under the banner 'Photonics for a society unburdened by cancer deaths'. Their website (www.hamamatsu.com) is even more optimistic, its first page containing gloom and doom statements about recent upsurges in cancer. These mean nothing unless placed in context, which Hamamatu carefully avoid.

By the end of their extremely detailed website, they seem to be suggesting that their PET scanners (if not now, then sometime in the future) will enable detection of the early stages of heart disease and dementia. Their advert tells us they are developing 'new screening methods that will enable patients with a strong possibility [sic] of having cancer or other disease conditions to be identified more efficiently, in order to make an infrastructure where a greater number of patients can be tested and diagnosed by fewer physicians'. They are explicitly working towards 'A society in which no one dies of cancer and no one falls into the black depths of dementia'. The begged questions left by these statements would fill a number of pages.

Speaking of context, during this silly season the press made much of a survey of doctors revealing that 83% wanted to retire at 60 and that 79% had felt 'stressed' at work. This was conflated with the sad story of a 'perfectionist' GP who committed suicide. Without knowing how many solicitors, bus drivers and judges also want to retire at 60 and feel stressed at work, and without telling us the overall suicide rates in GPs and whether they've changed with perceived stress in the job, these are figures useful only for grinding axes. HM

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