Ketoacidosis and normal glucose tolerance

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A 29-year-old Caucasian woman presented to hospital after 48 hours of anorexia, vomiting and epigastric pain. Three days prior to admission she terminated a one-week episode of heavy alcohol intake, during which time she had barely eaten. She had a long history of heavy alcohol intake, associated with elevated serum transaminases, and had been admitted with alcohol withdrawal seizures one year previously. There was no history of insulin-dependent diabetes mellitus and no preceding symptoms of polyuria or polydipsia. Her only medication was the oral contraceptive. On examination she was distressed, but alert and orientated. Pulse was 120 beats/min, respiratory rate 26 breaths/min, blood pressure 140/85 mmHg; mild epigastric tenderness was elicited but bowel sounds were normal. There were no stigmata of chronic liver disease, though her liver was palpable 3 cm below the right costal margin.

Plasma biochemistry showed sodium 124 mmol/l, potassium 6.6 mmol/l, bicarbonate 7 mmol/l, urea 12.7 mmol/l, creatinine 167 mmol/l, glucose 18.3 mmol/l, amylase 386 IU/l (normal range <200 IU/l), γ -glutamyl transferase 220 IU/l (<30 IU/l), arterial hydrogen ion 73 nmol/l, pO₂ 16.1 kPa, pCO₂ 2.2 kPa, plasma ketones 4 mmol/l (Ketostix), urinary ketones not detected (Acetest).

Diabetic ketoacidosis was diagnosed and she was treated with intravenous insulin and 0.9% saline. Blood glucose normalised with resolution of symptoms in four hours and 5% dextrose was introduced. Within 24 hours, intravenous fluids and insulin were discontinued, normal diet was resumed and subcutaneous insulin commenced. After three days, subcutaneous insulin was discontinued because of recurrent hypoglycaemia. Blood glucose remained normal on a sugar-free diet. A 75 g oral glucose tolerance test (OGTT) showed normal glucose tolerance (table) and she was discharged from hospital on a normal diet.

She remained free of glycosuria and did not develop osmotic symptoms of diabetes despite a normal diet and continuing alcohol excess. Eighteen months following discharge her serum transaminase and γ -glutamyl transferase concentrations were persistently elevated; an OGTT was repeated, and the results showed impaired glucose tolerance (table). The insulin and C-peptide responses to the glucose load were completely normal and her plasma was negative for islet cell antibodies.

Table Results of glucose tolerance tests in 1994 and 1996

Time	1994 Glucose (mmol/l)	1996		
		Glucose (mmol/l)	Insulin (mU/l)	C-peptide (mU/l)
0	5.1	4.3	8.2	0.62
1 h	7.2	9.7	30	3.39
2 h	7.2	9.6	38.5	4.62

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Questions

- 1 What is the diagnosis?
- 2 Was the acute management appropriate?
- 3 Why did the Acetest give a negative result?
- 4 Explain the results of the 1996 OGTT

Answers

QUESTION 1

Alcoholic ketoacidosis. Although this woman was treated as a case of diabetic ketoacidosis, the lack of antecedent symptoms of diabetes, the history of alcohol abuse culminating in an acute episode of vomiting and epigastric pain, together with her rapid metabolic recovery and subsequent normal insulin secretion make the diagnosis of alcoholic ketoacidosis more likely. Alcoholic ketoacidosis is rarely reported in the UK,^{1,2} but is thought to be responsible for 20% of cases of ketoacidosis in the US.³ It typically occurs in chronic abusers of alcohol, who develop vomiting due to alcohol poisoning, gastritis or pancreatitis, following a period of binge drinking (box 1). Poor carbohydrate intake leads to rapid depletion of hepatic glycogen stores and resultant suppression of insulin secretion. A combination of dehydration, alcohol withdrawal and acute illness lead to activation of the sympathetic nervous system and the secretion of gluconeogenic hormones such as adrenaline, cortisol and glucagon (box 2). The resultant hormonal milieu produces overwhelming lipolysis and the generation of ketoacidosis. Metabolism of alcohol alters the hepatic redox state which inhibits gluconeogenesis, predisposing to hypoglycaemia, and shifting ketone body metabolism such that β -hydroxybutyrate is produced at the expense of acetoacetate. It is unusual for alcoholic ketoacidosis to present with hyperglycaemia.¹ In the clinical context of no prodromal osmotic symptoms, rapid resolution of the metabolic abnormalities with treatment, and lack of subsequent need for insulin, consideration should be given to the role of alcohol in the differential diagnosis of ketoacidosis.

QUESTION 2

The treatment of alcoholic ketoacidosis, with intravenous saline and dextrose, is similar to that of diabetic ketoacidosis, and in those rare cases which present with hyperglycaemia, insulin therapy, as used in this case, is also appropriate. Recognition of alcoholic ketoacidosis is important, however, in order to avoid unnecessary treatment with insulin. In two recent reports of alcoholic ketoacidosis, subcutaneous insulin therapy was continued for several months after discharge from hospital,^{4,5} and one patient suffered recurrent hypoglycaemic episodes prior to discontinuation of insulin.⁴

- 1 Thompson CJ, Johnston DJ, Baylis PH, Anderson J. Alcoholic ketoacidosis: an underdiagnosed condition. *BMJ* 1986; **292**: 463–5.
- 2 McMahon AJ, Green ST, Sandler M, Hillis WS. Alcoholic ketoacidosis: a case report. *Scott Med J* 1987; **32**: 183–4.
- 3 Cooperman MT, Davidoff F, Spark R, Pakotta J. Clinical studies of alcoholic ketoacidosis. *Diabetes* 1974; **23**: 433–9.

Alcoholic ketoacidosis: clinical features

- history of chronic alcohol abuse
- recent alcoholic binge producing prolonged vomiting
- no preceding osmotic symptoms of diabetes
- rapid resolution with intravenous fluids
- normal glucose tolerance

Box 1

Alcoholic ketoacidosis: laboratory features

- blood glucose low/normal, rarely high
- moderate/severe ketoacidosis
- suppressed insulin concentrations
- elevated glucagon, cortisol, catecholamines
- Acetest negative for ketonuria
- Ketostix strongly positive for ketonaemia

Box 2

QUESTION 3

Acetest is only sensitive to the presence of acetoacetate, and as it is principally β -hydroxybutyrate rather than acetoacetate which is generated in alcoholic ketoacidosis, Acetest may therefore give a negative reading, despite marked ketoacidosis. The use of Ketostix, which detects increased plasma concentrations of β -hydroxybutyrate, is necessary to diagnose this syndrome (box 2). One clue to the presence of increased plasma ketone concentrations in patients with severe acidosis but negative Acetest results, is inappropriate elevation of plasma creatinine concentration; ketone bodies cross-react in some assays for creatinine, giving spurious elevations of plasma creatinine in ketotic patients.

QUESTION 4

The impaired glucose tolerance response despite normal insulin and C-peptide responses suggests a degree of insulin resistance, which is common in patients with alcoholic liver disease.

Final diagnosis

Alcoholic ketoacidosis.

Keywords: ketoacidosis, alcohol, diabetes

- 4 Simpson D, Cundy T. Alcoholic ketoacidosis mimicking diabetic ketoacidosis. *NZ Med J* 1992; **69**: 38–9.
- 5 Hart SP, Frier BM. Alcoholic ketoacidosis associated with hyperglycaemia – a diagnostic dilemma. *Pract Diabetes* 1996; **13**: 131–2.