

Hypoglycaemia associated with anorexia nervosa

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Summary: A 41 year old woman with severe emaciation due to longstanding anorexia nervosa presented with recurrent hypoglycaemia. During an episode of hypoglycaemia, serum insulin and C peptide were undetectable and plasma β hydroxybutyrate, free fatty acids and lactate were inappropriately low. Response to intravenous glucagon was poor. Muscle enzymes were grossly elevated until she gained weight. Hypoglycaemia was abolished by weight gain.

Introduction

Although hypoglycaemia has been previously reported in patients with anorexia nervosa,^{1,2} the pathophysiology and biochemical events leading to hypoglycaemia have not been previously investigated. We describe a patient with anorexia nervosa who presented in an emaciated state with recurrent hypoglycaemia which gave us an opportunity to investigate this condition.

Case report

A 41 year old woman with anorexia nervosa (weight loss, amenorrhoea and fear of putting on weight), for 24 years was admitted in hypoglycaemic coma which responded promptly to intravenous dextrose. She had not had a convulsion and there was no history of trauma or muscle injury. She had suffered recurrent hypoglycaemic episodes with symptoms of neuroglycopenia, sweating and palpitations for over 10 years and had been treated for hypoglycaemic coma in hospital on one occasion. She had learnt to prevent these episodes by eating small 'snacks' approximately every 2 hours. Her estimated daily energy intake was 660 KCal. Typical 'snacks' consisted of one of the following – 5 g bread; 2 g cheese and a grape; 3–4 lettuce leaves; 1 slice of tomato with 1 prawn; 20 ml Clinifed (20 KCal) or 20 ml of Ensure (20 KCal). She also ingested 25 to 30 tablets of various proprietary vitamins and mineral supplements and in addition received Parenterovite 2 ml and vitamin B12, 250 μ g intramuscularly every 2 weeks. She had abused laxatives in the past but they were now ineffective. She denied self-induced vomiting. She had refused hospital care and psychiatric follow-up.

On examination she was emaciated, weighing 23 kg with a height of 162 cm. Systemic examination was unremarkable, apart from generalized muscle weakness.

Investigations: Plasma glucose 1.1 mmol/l; plasma creatinine: 33 μ mol/l (normal range 60–120); plasma urea 9.2 mmol/l; plasma sodium 129 mmol/l; plasma potassium 3.7 mmol/l; plasma calcium 2.19 mmol/l; plasma magnesium 0.91 mmol/l; total plasma protein 61 g/l; plasma albumin 39 g/l; serum creatine kinase (CK) 2580 U/l – 3.5% of serum CK was CK-MB; serum HBD 463 U/l (normal 50–150); serum aspartate transaminase 226 U/l (5–40); serum alkaline phosphatase 94 U/l (35–150); plasma bilirubin 6 μ mol/l (5–17); plasma urate 0.09 mmol/l (0.1–0.40); muscle enzymes remained elevated for 3 weeks after admission until the patient gained weight and hypoglycaemia stopped. Electrocardiogram (ECG) – low voltage, otherwise normal.

The patient continued having hypoglycaemic episodes in hospital on fasting for more than 4 hours and the following investigations were carried out whilst the patient was hypoglycaemic – plasma glucose 0.4 mmol/l; serum insulin < 3 mU/l (< 20 pmol/l); serum C-peptide < 77 pmol/l; serum cortisol 1251 nmol/l; serum growth hormone 114 mU/l (0–10); serum insulin like growth factor I (IGF-1) 0.05 mU/l (0.3–1.2); plasma β hydroxybutyrate 60 μ mol/l (inappropriately low for hypoglycaemia with hypoinsulinaemia); plasma free fatty acids: 60 μ mol/l (100–600); plasma lactate: 0.98 mmol/l (0.63–2.4). Following an intravenous injection of glucagon 1 mg, plasma glucose rose from 0.4 mmol to only 1.4 mmol/l.

On weight gain in hospital to 27 kg, hypoglycaemia became less frequent and was abolished at 29 kg. A liver biopsy carried out when she weighed 27 kg, showed adequate glycogen stores and was otherwise normal. She agreed to maintain a body weight of at least 27 kg.

Discussion

Investigation of our patient during an episode of hypoglycaemia revealed that she was depleted of energy stores, with low serum concentrations of lactate, free fatty acids and β hydroxybutyrate. Lack of substrate for gluconeogenesis precluded recovery from hypoglycaemia. Furthermore, glucagon administration resulted in a small and inadequate rise in blood glucose. The patient's ability to recover from hypoglycaemia improved on weight gain and replenishment of liver glycogen stores.

Anorexia nervosa is associated with considerable increased mortality; some of the deaths may be unrecognized hypoglycaemia.³ Suicide is a common mode of death although sudden death has been described⁴ and is most likely to be attributed to cardiac arrhythmias or cardiac failure.⁵

Smith concluded, from an analysis of 8 cases of hypoglycaemia associated with anorexia nervosa, published in the literature between 1982 and 1988, that hypoglycaemia is a serious risk factor when body weight falls below 30 kg.⁶ In men it may occur at higher total body weight.⁷ Hypoglycaemia has been suggested as a cause of death in one patient with anorexia, although the patient also had pulmonary oedema and was uraemic.² Hypoglycaemia has not been implicated in the death of hunger strikers but it is not uncommon in children with severe malnutrition.⁸ Increased metabolic demands such as those created by infection may precipitate hypoglycaemic coma in anorectic patients, sometimes with fatal results.⁶ This possibility should be borne in mind since infection is the immediate cause of death in some 35% of all cases.⁹

Most of the other biochemical abnormalities seen in our patient have been previously described, including a low plasma creatinine.¹⁰ The undetectable serum insulin and C-peptide rule out an

insulinoma or self-administration of insulin. The elevated serum cortisol and growth hormone rule out a primary endocrine cause for her hypoglycaemia. It is noteworthy that the elevated serum growth hormone is unable to cause a rise in serum IGF-1 (sometimes known as somatomedin C), probably because of starvation, in which condition it is invariably low except when protein intake is maintained.¹¹ The low plasma β -hydroxybutyrate and free fatty acid levels in the presence of severe hypoglycaemia and greatly reduced plasma insulin and C-peptide levels indicate a virtually complete absence of any mobilizable fat with a result that glucose becomes the only fuel – not only for the brain but for all other tissues. This may account for both the severity and resistance to treatment of hypoglycaemia occurring under these conditions. Hypoglycaemia occurred even after replenishment of liver glycogen stores (much less frequently than previously), indicating that mobilizable fat was still absent.

It is of interest that our patient's muscle enzymes were elevated at presentation indicating muscle breakdown which persisted until she gained weight. Muscle weakness associated with a modest elevation in creatine kinase has been previously reported in 4 patients with anorexia although the degree of elevation of the serum CK was considerably less than that in our patient.¹²

We conclude that hypoglycaemia may occur in patients with anorexia nervosa who are severely emaciated. Recovery from hypoglycaemia may be impaired because of substrate depletion. Glucagon may be ineffective in treating hypoglycaemia in these patients. It is therefore imperative that these patients are admitted to hospital so that (a) intravenous glucose can be promptly administered during hypoglycaemia and (b) energy stores can be restored and body weight increased as quickly as possible.

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