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Case Report

Hypoglycaemic coma due to adrenal failure in a chronic haemodialysis patient

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Abstract

A 62-year-old man, receiving chronic haemodialysis and suffering from alcoholic liver cirrhosis and chronic pancreatitis, presented with hypoglycaemic coma. Plasma cortisol was undetectable (<5.5 nmol/L) with suppressed adrenocorticotropic hormone (ACTH), which established a diagnosis of adrenal failure due to ACTH deficiency. Twenty-five milligrams of oral hydrocortisone eradicated hypoglycaemia. Presentation of adrenal failure in this patient was atypical because he was hypertensive, serum electrolytes including sodium were normal and anaemia was unremarkable, which were all due to end-stage renal disease and its treatment with haemodialysis. As far as we are aware, this is the first case report of hypoglycaemic coma due to adrenal failure in a chronic haemodialysis patient.

Keywords: adrenal failure; haemodialysis; hypoglycaemia

Background

Adrenal failure is a potentially fatal disorder, and the prevalence of primary and secondary adrenal failure is 93–140 and 150–280 per million, respectively [1]. Because symptoms of adrenal failure such as anorexia, nausea, vomiting, weight loss and fatigue are rather non-specific, they may well be mistaken as those occurring from other disorders in patients suffering from severe co-morbidities. We encountered a rare case of a chronic haemodialysis patient with type 2 diabetes, alcoholic cirrhosis and pancreatitis, presenting as hypoglycaemic coma due to severe adrenal failure caused by ACTH deficiency.

Case report

A 62-year-old man was admitted in emergency in the early morning because he could not be awakened.

His type 2 diabetes had been treated with insulin for 18 years. He had started haemodialysis for diabetic nephropathy 3 years previously and had been receiving regular haemodialysis three times a week. He also suffered from hypertension, alcoholic cirrhosis and chronic pancreatitis. During the last 15 months, with progressive appetite loss and fatigue, HbA_{1c} had become lower with smaller amounts of insulin. Seven weeks previously, he had experienced hypoglycaemia and was treated with intravenous (iv) glucose. Insulin dosing was 4 U NovoRapid® twice a day at that time, which had been stopped since then.

Upon arrival, the level of consciousness was Glasgow coma scale 14 (E4V4M6) without focal neurological deficit. He appeared malnourished (body mass index 16 kg/m^2) without skin pigmentation. His body temperature was 33.1°C (on a warm June day), blood pressure (BP) 146/78 mm Hg, pulse rate 66/min, respiration rate 14/min, arterial pH 7.383 and O_2 saturation 100% (with room air). The general laboratory data (Table 1) were compatible with the known morbidities of chronic renal failure, liver cirrhosis and chronic pancreatitis, except for hypoglycaemia and a lowered HbA_{1c} for a patient with diabetes. Ten grams of glucose was administered iv and, 30 min later, capillary blood glucose (BG) was 5.7 mmol/L, and he was fully conscious. However, he again became drowsy 1 h later when the BG was 2.8 mmol/L. He was admitted for further evaluation.

Factitious, alcoholic and drug-induced hypoglycaemia were excluded by history. This was securely confirmed by information from his wife. The computerized tomography scan revealed no tumour in the abdomen. Cortisol was undetectable with a very low ACTH level (Table 1), which established a diagnosis of adrenal failure due to ACTH deficiency. Plasma renin activity and aldosterone level were within the normal range. Mild secondary hypogonadism and hyperprolactinaemia were also present (Table 1). The magnetic resonance imaging revealed no hypothalamic or pituitary abnormality, and serum antipituitary antibody [2] was negative. He was receiving 5 mg of amlodipine, and BP was 132 ± 16/67 ± 9 mm Hg (mean ± SD, n = 17) during Days 1–8.

Upon diagnosing adrenal failure, 25 mg of oral hydrocortisone (10 mg, 10 mg and 5 mg after each meal, respectively) was started on Day 9, which promptly restored appetite and well-being. BP was 151 ± 18/83 ±

Table 1. Laboratory data

A. General data			
Total protein	61 g/L	Urea nitrogen	4.1 mmol/L
Albumin	34 g/L	Creatinine	428 μmol/L
AST	27 IU/L	Sodium	137 mmol/L
ALT	10 IU/L	Potassium	3.7 mmol/L
Alkaline phosphatase	313 IU/L	Chloride	102 mmol/L
LDH	138 U/L	Calcium	2.2 mmol/L
γ-GTP	25 U/L	Blood count[a]	
Amylase	53 IU/L	Leukocyte	2.51×10^9/L
Total cholesterol	2.43 mmol/L	Red cell	3.65×10^{12}/L
Triglycerides	1.13 mmol/L	Haemoglobin	6.83 mmol/L
C-reactive protein	21 mg/L	Haematocrit	31.9%
Plasma glucose	2.1 mmol/L	Platelet	30×10^9/L
HbA_{1c}	4.4%		
B. Endocrine data[b]			
Cortisol	<5.5 nmol/L (110–505)	Prolactin	2138 pmol/L (155–555)
ACTH	0.95 pmol/L (1.58–13.9)	Growth hormone	1.40 μg/L (<1.7)
Thyroid stimulating hormone	4.63 mIU/L (0.27–4.2)	Antidiuretic hormone	1.7 pmol/L (0.28–3.23)
Free triiodothyronine	0.035 pmol/L (0.039–0.076)	Insulin	15.1 pmol/L (12.7–84.5)
Free thyroxine	17.0 pmol/L (12.9–23.2)	C-peptide	0.46 nmol/L (0.20–0.70)
Luteinizing hormone	5.13 IU/L (0.79–5.72)	Plasma renin activity	2.1 μg/L/h (0.3–5.4)
Follicle stimulating hormone	2.49 IU/L (2.00–8.30)	Aldosterone	0.13 nmol/L (0.10–0.67)
Free testosterone	8.68 pmol/L (18.9–58.5)		

AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; GTP, glutamyl transpeptidase.
[a]The patient was receiving 7500 U Epogen® per week.
[b]Cortisol and ACTH were determined before breakfast on Day 2; other endocrine data were obtained at 1000 h on Day 7 when capillary blood glucose was 6.2 mmol/L; cortisol was undetectable by radioimmunoassay (Immunotech®) with the detection limit being 5.5 nmol/L. The reference range for the endocrine data is indicated in the parentheses.

14 mm Hg (n = 15) during Days 9–16 with 5 mg of amlodipine, which was modestly higher than the values recorded before the treatment with hydrocortisone (P = 0.005 for systolic BP and P <0.001 for diastolic BP, Mann–Whitney U-test). Hypoglycaemia did not recur, and insulin was resumed on Day 11, because BG (mean ± SD from the premeal and the midnight values) for the preceding 2 days was 11.8 ± 2.2 mmol/L (n = 7) with 1800 kcal diet.

Discussion

In this patient, adrenal failure was due to ACTH deficiency, not due to Addison's disease, hence there was no skin pigmentation. Loss of appetite, general fatigue, malnutrition and previous hypoglycaemic events had been considered to be due alcoholic binge 'drinking', liver cirrhosis, chronic pancreatitis, renal failure or a combination thereof. Anaemia was not marked because he had been appropriately treated with erythropoietin. Above all, he was receiving an antihypertensive agent, amlodipine and hypertensive. This is very unusual for patients with severe adrenal failure [1,3].

As far as we are aware, adrenal crisis or hypoglycaemic coma due to adrenal failure has not been reported in chronic haemodialysis patients. Toth and Lee [4] analysed 36 patients with uraemic hypoglycaemia in the literature and identified 19 haemodialysis patients. Adrenal dysfunction was not identified as a cause of hypoglycaemia in any of them. Actually, it was not ruled out in eight [4]. The number of dialysis patients is estimated to be 1.5 million and >90% of them are receiving haemodialysis [5]. The prevalence of primary and secondary adrenal failure is 93–140 and 150–280 per million, respectively [1]. Therefore, occurrence of adrenal failure in haemodialysis patients would be relatively rare.

Adrenal failure was finally very severe in our case. Upon admission, cortisol production must have been virtually absent because plasma cortisol was undetectable despite the cortisol metabolism is depressed in haemodialysis patients [6]. However, the patient presented with only hypoglycaemic coma and mild hypothermia, but not with circulatory collapse or electrolyte abnormalities. We consider haemodialysis had protected him from adrenal crisis because the circulating volume and electrolytes were maintained by haemodialysis. Because the glucose concentration of the dialysis solution was 8.3 mmol/L, hypoglycaemia, if any, might have been relieved to some extent during each haemodialysis session.

Adrenal crisis develops not only in patients with Addison's disease but also in patients with ACTH deficiency [1,3,7], and hyponatraemia is not rare in the latter group [8]. This is in part due to the fact that cortisol concentration in plasma is 1000-fold higher than that of aldosterone, and cortisol elicits its effects not only through the glucocorticoid receptor but also through the mineralocorticoid receptor [9]. Because cortisol is a tonic inhibitor of antidiuretic hormone (ADH), ADH excess is often present in adrenal insufficiency [8], which also contributes to hyponatraemia in adrenal failure. Haemodialysis most likely protects the patients with either primary or secondary adrenal failure against volume depletion and hyponatraemia.

In summary, adrenal failure should be suspected in chronic haemodialysis patients with hypoglycaemia even if other salient features of adrenal failure are absent.

Conflict of interest statement. None declared.

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