症　例

Extreme hyperglycemia and diabetic ketoacidosis occurring in a patient on chronic dialysis

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Abstract

Diabetic ketoacidosis (DKA) is a complication that is rarely reported in patients on chronic dialysis. Herein, we describe the case of a patient on chronic hemodialysis who presented to us with acute onset diabetic ketoacidosis. A 50-year-old man with insulin-dependent diabetes mellitus, who was on hemodialysis for 2 years, presented to us with altered consciousness. Laboratory data revealed the following results: blood sugar, 110.1 mmol/L (1984 mg/dL); serum sodium, 107 mmol/L; β-hydroxybutyric acid, 1991 μM; pH, 7.048. A diagnosis of diabetic ketoacidosis was made, and insulin therapy and hemodialysis were initiated, following which his parameters including blood glucose, and serum potassium and sodium improved. High osmotic dehydration was not observed in our patient owing to his renal dysfunction. The patient's consciousness normalized following the correction of hyperglycemia and DKA. This case report highlights the importance of early diagnosis of DKA, and prompt initiation of insulin therapy and hemodialysis in patients on chronic dialysis. Therefore, in patients with end stage renal disease, the blood glucose correction should be followed by the restoration of sodium and osmolality, guided by corrected sodium concentration and effective osmolality, and by the appropriate adjustment of insulin and dialysis.

Key words: End-stage renal disease, diabetic ketoacidosis, hyperglycemia.

Introduction

Diabetic ketoacidosis is a common medical emergency in patients with diabetes mellitus, and its appropriate diagnosis and treatment are important in ensuring good outcomes. DKA is a complication that is rarely reported in patients on chronic dialysis.

DKA is considered a condition of hyperglycemia, hyperketonemia, and acidosis owing to a significant decrease or deficiency in insulin, or an excess of insulin counter-regulatory hormone. DKA occasionally occurs in patients with insulin-dependent diabetes mellitus (IDDM) within 24 hours.[1] The pathophysiology of DKA is different in patients with preserved renal function compared to those with end stage renal disease. There is limited literature on this topic, with the difference being highlighted by just 4 case reports and two review articles.[2-6] Herein, we describe the successful treatment of a patient on chronic hemodialysis who presented to us with DKA.

Case report

A 50-year-old man was admitted to our hospital with altered consciousness. He was diagnosed with IDDM at the age of 33 years, and had an episode of diabetic ketoacidosis at 48 years. He had been on hemodialysis for the last 2 years. He self-injected his insulin in doses of 25 units/day of human insulin and 10 units/day of insulin glargine. His glycoalbumin level (50.4%) was high, possibly owing to irregular eating habits and missed insulin doses. He had modest residual renal function, and was anuric.

At admission he was found to have the following physical findings: poorly responsive to pain stimulus; Glasgow coma scale, 8 (eye opening response, 2; best verbal response, 2; and best motor response, 4); body temperature, 36.7°C; heart rate, 55/min; blood pressure, 154/56 mmHg; respiratory rate, 13/minute without Kussmaul breathing; height, 161 cm; body weight, 61.3 kg (body weight at the end of his last dialysis, 57.6 kg; dry weight, 57.5 kg); mild upper and lower limb edema; and normal findings for head and neck, chest, and abdomen. He did not have abdominal pain, nausea, or diarrhea. His electrocardiogram identified sinus rhythm with no evidence of any segment depression. X-ray and computed tomography (CT) scan ruled out cardiomegaly (cardiothoracic ratio, 49%) and pneumonia. His laboratory findings at admission were as follows: significant hyperglycemia (serum glucose, 110.1 mmol [1984 mg/dL]); acidosis (pH, 7.048; bicarbonate, 11.3 mmol/L); hyperketonemia (β-hydroxybutyric acid, 199.1 mmol/L); hyponatremia (serum sodium, 107 mmol/L), and hyperkalemia (serum potassium, 6.6 mmol/L). There were no bacterial isolates found on his blood and urine cultures. Based on these findings, we made a diagnosis of DKA, with hyponatremia and hyperkalemia (Table 1).

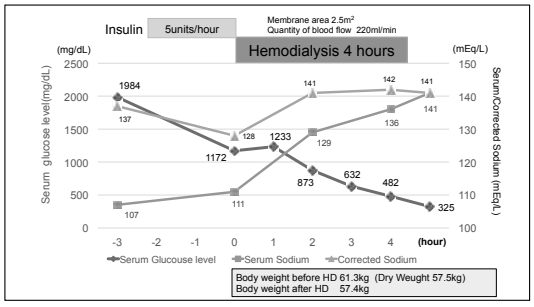
The patient was placed on continuous insulin injection therapy, followed by hemodialysis. Ten units of insulin were infused intravenously for 2 hours, following a single subcutaneous injection of 5 units. Following insulin treatment, his blood glucose level dropped to 65.1 mmol/L (1172 mg/dL) prior to dialysis. Hemodialysis (dialysate: sodium, 140 mmol/L; potassium, 2.0 mmol/L; glucose,

Table 1. Laboratory data at admission

Hematology:		Blood chemistry:		Ketones fraction:	
WBC (cells/ μL)	13900	BUN (mg/dL)	56	AA (μmol/L)	830
RBC (cells/ μL)	299×10^4	Cr (mg/dL)	9.93	BHA (mmol/L)	199.1
Hb (g/dL)	9.2	UA (mg/dL)	6.5	TKB (μmol/L)	2821
Hct (%)	28.8	TC (mg/dL)	122		
Pl (cells/ μL)	16.9×10^4	TG (mg/dL)	168		
Serology:		SAP (IU/L)	631	Blood gas analysis:	
CRP (mg/dL)	0.03	GGT (IU/L)	24	pH	7.048
Blood chemistry:		AST (IU/L)	19	pO^2 (mmHg)	47.7
Glu (mmol/L)	110.1	ALT (IU/L)	11	pCO^2 (mmHg)	42.1
Na^+ (mmol/L)	107	LDH (IU/L)	336	HCO^{3-} (mmol/L)	11.4
K^+ (mmol/L)	6.6	CK (IU/L)	206	BE (mmol/L)	-18.7
Cl^- (mmol/L)	78	ChE (IU/L)	147	AG (mEq/L)	17.6
Ca^{2+} (mmol/L)	8.0	TP (g/dL)	6.0		
PO^{4-} (mmol/L)	9.0	Alb (g/dL)	4.0		

WBC, white blood cells; RBC, red blood cells; Hb, hemoglobin; Hct, hematocrit; Pl, platelets; CRP, C-reactive protein; Glu, glucose; Na+, sodium; K+, potassium; Cl-, chloride; Ca2+, calcium; PO4-, phosphate; BUN, blood urea nitrogen; Cr, creatinine; UA, uric acid; TC, total cholesterol; TG, Triglycerides; SAP, Alkaline Phosphatase; GGT, γ-glutamyl transpeptidase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, Lactate dehydrogenase; CK, creatine kinase; ChE, cholinesterase; TP, total protein; Alb, albumin; AA, acetoacetic acid; BHA, β-hydroxybutyric acid; TKB, total ketone bodies; pO2, partial pressure of oxygen; pCO2, partial pressure of carbon dioxide; HCO3-, BE, base excess; AG, anion gap.

Figure 1. Changes in serum glucose, serum sodium, and corrected serum sodium levels during the treatment period.



8.3 mmol/L; and bicarbonate, 25.0 mEq/L) was performed for 4 hours (membrane area, 2.5 m^2; and flow rate, 220 mL/min). At the end of dialysis, there was a further drop in blood glucose to 26.8 mmol/L (482 mg/dL). The combination of insulin therapy and hemodialysis also resulted in improvement in serum sodium to 136 mmol/L (Figure 1). Similarly, his serum potassium reduced from 6.6 mmol/L to 3.4 mmol/L. He was started on insulin glargine on day 4, and by day 5, he was restarted on subcutaneous insulin injections. His consciousness improved by the second day of his admission. There was no evidence of cerebral edema on CT scans performed on day 1 and day 3. He did not have any features of osmotic dehydration, possibly owing to his renal dysfunction. At the time of his discharge from hospital, his glycoalbumin levels decreased from 50.4% to 30.7%.

Discussion

DKA is a metabolic disorder characterized by very low levels of insulin activity, leading to reduced glucose utilization and increased ipolysis, finally resulting in hyperglycemia and free-fatty acidosis. It is known to occur in patients with IDDM, secondary to discontinuation of insulin injections, infections, severe systemic disease, cerebrovascular disorders, and cardiovascular disorders. Although DKA is a common medical emergency among patients with diabetes mellitus, it is extremely rare in patients on hemodialysis. This is owing to the correction of acidosis, and the clearance of β-hydroxybutyric acid during dialysis. Further, the regular monitoring of blood

glucose and specialist consultations during the dialysis sessions contribute towards preventing DKA. In our patient, DKA was induced by low compliance with diabetic control secondary to a general disinterest in life, irregular diet, and irregular insulin dosing, in addition to insulin deficiency. Clinical assessment excluded infection, severe systemic disease, cerebrovascular disorder, and cardiovascular disorder as contributory factors for DKA.

Patients with preserved renal function and DKA present with polyuria, hyperhidrosis, dehydration, and weight loss secondary to osmotic diuresis. On the other hand, patients with end stage renal disease (including those on hemodialysis) present with oliguria or anuria. Further, since the renal function is impaired, there is an absence or reduction in the correction of acidosis and excretion of ketones, and consequently, an absence of dehydration. Therefore, the treatment of DKA in patients with renal failure should include blood purification therapy in addition to insulin injections. Immediate institution of insulin infusion should be the first priority, regardless of the status of dialysis. At a dose of 0.1 units/kg/h, insulin improves both ketonemia and hyperglycemia.[7] Patients who are hyperglycemic prior to dialysis are known to demonstrate a gradual decrease in their blood glucose levels with the onset of dialysis. This is owing to glucose diffusion into the dialysate. We used a dialysate that contained sodium (140 mmol/L), potassium (2 mmol/L), glucose (8.3 mmol/L), and bicarbonate (25 mmol/L), and found that over the 4 hours of dialysis, the blood glucose and electrolyte levels approached the dialysate levels. There are no specific recommendations for initiating dialysis in patients with DKA and end stage renal disease.

In patients with DKA and end stage renal disease, hyponatremia and hyperosmolar dehydration are uncommon, as opposed to patients with preserved renal function. Patients with oliguria and anuria do not develop body fluid and electrolyte depletion. Therefore, sodium and potassium continue to be stored in the body, and hyperosmotic diuresis does not occur. In these patients, there is a fall of 2.4 mmol/L in serum sodium level for every 5.5 mmol/L (100 mg/dL) increase in serum glucose level. Therefore, corrected sodium levels are to be calculated as given by the following formula: measured serum sodium + ([Serum glucose – 100]/100) x 2.4).[8] In our patient, although the serum sodium appeared to have sharply improved from 107 mmol/L to 136 mmol/L over 4 hours, on applying the formula for correction, the sodium levels before and after 4 hours of treatment were 137 mmol/L and 142 mmol/L, respectively (Figure 1). Body fluid correction should be based on corrected sodium levels in all patients, irrespective of the need for dialysis.[9]

Effective osmolality may be calculated using the following equation:

Effective osmolality (mmol/kg H_2O) = 2 × (serum Na [mmol/L] + serum K [mmol/L]) + serum glucose (mg/dL)/18.[8]

In our patient, the effective osmolality was found to be high (337.4 mmol/kg H_2O). The osmolality decreased to 305.5 mmol/kg H_2O over 4 hours, implying that the rate of reduction of effective osmolality was 4.65

mmol/kg/h. Current guidelines recommend a rate of 3 mmol/kg/h for lowering osmolality.[4] However, Gupta et al reported that mental obtundation did not develop when osmolality was rapidly decreased at a rate of 14.5 mmol/kg/h. Rapid sodium correction is known to cause brain edema. However, this is not the case when dilutional hyponatremia results from an intracellular to extracellular shift in water, in patients on dialysis.[8] Subhash et al described that 11 out of 12 patients on chronic dialysis, who presented with hyperglycemia and DKA, returned to normal consciousness following successful insulin therapy.[10] The level of hyperglycemia as well as the rapidity of onset of hypertonicity may contribute to mental impairment.[10] Therefore, in patients with end stage renal disease, blood glucose correction should be followed by the restoration of sodium and osmolality. This process should be guided by corrected sodium concentration and effective osmolality, and by the appropriate adjustment of insulin and dialysis.

In conclusion, hyperosmolar dehydration is uncommon in patients on chronic dialysis who develop DKA. Hyperglycemia and body fluid abnormalities in DKA should be adjusted with insulin and dialysis, based on corrected sodium concentration and effective osmolality.

Conflict of Interest: There are no conflicts of interest to declare.

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