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STEROID-INDUCED DIABETIC KETOACIDOSIS WITH HYPERNATREMIC DEHYDRATION AND HYPOKALEMIA IN BIOPSY-PROVEN MINIMAL CHANGE DISEASE: A DIAGNOSTIC AND THERAPEUTIC CHALLENGE

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) is typically associated with absolute or relative insulin deficiency; however, glucocorticoids can precipitate hyperglycemic crises even in individuals without previously diagnosed diabetes. Patients receiving corticosteroid therapy for nephrotic syndromes such as minimal change disease (MCD) may develop metabolic instability due to enhanced gluconeogenesis, insulin resistance, and accelerated lipid oxidation. Concomitant electrolyte disturbances such as hypernatremia and hypokalemia in the setting of steroid-associated DKA are uncommon and may complicate metabolic management.

Case Presentation: A 50Kg/42-year-old woman with biopsy-proven minimal change disease receiving oral corticosteroid therapy presented with progressive fatigue, dizziness, dysphagia, and difficulty ambulating for three days. On admission she appeared drowsy and dehydrated with tachycardia. Capillary blood glucose ranged between 505–579 mg/dL. Laboratory investigations revealed serum sodium of 158.6 mEq/L, potassium 2.7 mEq/L, chloride 121.8 mEq/L, ketonuria (2+), and glucosuria (3+). Arterial blood gas analysis showed a pH of 7.24 with bicarbonate of 9 mmol/L and high anion-gap metabolic acidosis consistent with diabetic ketoacidosis. Ultrasonography demonstrated a collapsed inferior vena cava suggestive of significant intravascular volume depletion. Inflammatory markers were not elevated and renal function remained preserved.

Management: The patient was treated with intravenous fluid resuscitation using isotonic saline followed by gradual free-water replacement. Hypokalemia was corrected with intravenous potassium supplementation prior to initiation of insulin therapy. Continuous insulin infusion was initiated using a weight-based dosing protocol (approximately 0.5 units/kg/day) with close monitoring of blood glucose levels. Electrolytes and arterial blood gases were monitored serially. Dyselectrolytemia and metabolic acidosis improved progressively over the following 24 hours. Corticosteroid therapy was subsequently stopped after receiving 1mg/kg/day for 3 weeks. Patient received IV Hydrocortisone 100mg twice daily for 3 days and there was gradual improvement sensorium, Hemodynamic parameters and metabolic profile. Patient was restarted with oral steoids after 24hours urine protein showed 2.4gms/day. Corticosteroid therapy was subsequently tapered under nephrology supervision, with improvement in sensorium, hemodynamic parameters, and metabolic profile.

Conclusion: This report describes an uncommon presentation of steroid-associated diabetic ketoacidosis occurring in a patient with minimal change disease and accompanied by hypernatremic dehydration and hypokalemia. The coexistence of nephrotic syndrome, corticosteroid exposure, and intravascular volume depletion can create a complex metabolic environment requiring careful correction of fluid deficits and electrolyte imbalance. Early identification of steroid-related dysglycemia and vigilant metabolic monitoring are essential to ensure safe management in patients receiving corticosteroid therapy.

KEYWORDS: Diabetic Ketoacidosis; Hypernatremia; Hypokalemia; Minimal Change Disease; Glucocorticoids; Prednisolone; Steroid-Induced Diabetes; Nephrotic Syndrome; Dyselectrolytemia; Critical Care.

INTRODUCTION

Diabetic ketoacidosis (DKA) is an acute endocrine emergency characterized by relative or absolute insulin deficiency, hyperglycemia, ketoauria, and high anion-gap metabolic acidosis. Although it is classically associated with type 1 diabetes mellitus, DKA may also occur secondary to medications or hormonal influences, particularly glucocorticoids. Corticosteroids are well known to induce hyperglycemia through increased hepatic gluconeogenesis, peripheral insulin resistance, and enhanced lipolysis. Episodes of metabolic decompensation, including DKA, have been reported even in individuals without previously diagnosed diabetes when corticosteroid therapy is administered for inflammatory or renal disorders. These observations highlight the importance of careful metabolic monitoring during corticosteroid therapy [1].

Minimal change disease (MCD) is a common cause of nephrotic syndrome 10-20% of adults and is frequently treated with prolonged corticosteroid therapy as first-line management. Patients receiving on steroids develop impaired glucose tolerance, newly detected diabetes, or metabolic decompensation related to steroid exposure. The coexistence of MCD with newly detected diabetes has been documented, suggesting a predisposition toward glycemic instability in this population [2]. Hyperosmolar hyperglycemic states have also been reported in patients receiving steroid therapy for MCD, demonstrating the potential for significant metabolic disturbances even in the absence of previously diagnosed diabetes [3]. These findings highlight the complex metabolic consequences of corticosteroid therapy in patients with proteinuric renal disease.

Although steroid-associated hyperglycemia is relatively common, steroid-precipitated DKA remains an uncommon clinical entity and may present with marked biochemical abnormalities. Reports have described abrupt onset of metabolic acidosis with ketonemia following continued corticosteroid exposure, suggesting a direct role of glucocorticoids in promoting lipolysis, hepatic gluconeogenesis, and insulin resistance [4]. In individuals with renal disease, these metabolic changes may be further influenced by alterations in intravascular volume, catabolic stress, and disrupted metabolic homeostasis.

The coexistence of nephrotic syndrome and evolving diabetes further complicates glycemic management. Slowly progressive autoimmune diabetes following steroid-sensitive nephrotic syndrome has been described, suggesting that immune modulation, persistent proteinuria, and corticosteroid exposure together may contribute to metabolic dysregulation [5]. Electrolyte abnormalities are frequently encountered in DKA, with hypokalemia representing an important complication requiring early recognition and correction. Significant potassium depletion has been associated with adverse neurological outcomes, including rare complications such as central pontine myelinolysis, highlighting the importance of careful potassium replacement before and during insulin therapy [6].

Given these interacting mechanisms, the development of steroid-associated DKA in a patient with biopsy-proven minimal change disease presents diagnostic and therapeutic challenges. Coexisting dyselectrolytemia and hypernatremic dehydration may further complicate metabolic management, particularly when intravascular volume depletion and metabolic acidosis coexist. This report describes an uncommon clinical presentation emphasizing the importance of early recognition, careful metabolic stabilization, and appropriate adjustment of corticosteroid therapy in patients with nephrotic syndrome.

Case Presentation

A 42-year-old woman was brought to the emergency department with complaints of progressive reduction in activity and generalized fatigue for two days. She became bed-bound three days prior to admission and required assistance for standing and passing urine on the day of presentation. She also reported dizziness for three days and throat discomfort for one week, associated with difficulty swallowing over the preceding two days. There was no history of vomiting, seizures, behavioral changes, trauma, or loss of consciousness.

She had a known diagnosis of biopsy-proven minimal change disease made two months earlier and had been receiving oral corticosteroid therapy (Wysolone 30 mg twice daily). She also had recently detected steroid-associated diabetes mellitus along with hypothyroidism, systemic hypertension, and dyslipidemia. Her medications included Telmisartan, Amlodipine, Thyronorm, Atorvastatin, calcium supplementation, diuretics, and corticosteroids under nephrology supervision.

On arrival, the patient appeared dehydrated and drowsy but remained arousable and was able to follow simple commands. Initial vital signs showed a pulse rate of 123 beats per minute, temperature of 100.1°F, respiratory rate of 32 breaths per minute, and oxygen saturation of 97% while receiving oxygen through a non-rebreathing mask. Blood pressure was initially not recordable but was subsequently measured as 120/90 mmHg. Capillary blood glucose values ranged between 505 and 579 mg/dL.

General examination revealed dry mucous membranes and reduced skin turgor. Cardiovascular examination demonstrated tachycardia without murmurs. Respiratory examination was unremarkable. Neurological examination revealed no focal deficits, and the Glasgow Coma Scale score was 13/15. Ultrasonography demonstrated a collapsed inferior vena cava, suggestive of significant intravascular volume depletion. Electrocardiography showed sinus tachycardia without ischemic changes.

Laboratory investigations revealed notable metabolic abnormalities. Serum sodium was elevated at 158.6 mEq/L, potassium was 2.7 mEq/L, chloride was 121.8 mEq/L, and bicarbonate was reduced. Urine ketones were positive (2+), and urine glucose was 3+, Serum ketones was positive. Arterial blood gas analysis demonstrated a pH of 7.24, pCO_2 of 21 mmHg, bicarbonate of 9 mmol/L, and an elevated anion gap consistent with high anion-gap metabolic acidosis in keeping with diabetic ketoacidosis. A repeat arterial blood gas analysis following initial stabilization showed improvement with pH 7.45 and bicarbonate 12.1 mmol/L. Renal function tests remained within normal limits (creatinine 0.4–0.5 mg/dL), and liver function tests were normal. Inflammatory markers including C-reactive protein and procalcitonin were not elevated.

The patient was admitted to the intensive care unit for further management. Initial treatment consisted of intravenous fluid resuscitation with isotonic saline followed by appropriate fluid adjustment. Intravenous potassium supplementation was administered to correct hypokalemia before initiating insulin therapy. Continuous insulin infusion was started with careful titration based on serial glucose measurements. Electrolytes, arterial blood gases, and capillary glucose levels were monitored closely during treatment. Over the next 24 hours,

potassium levels improved to 3.6 mEq/L, serum sodium levels gradually normalized. And metabolic acidosis was corrected PH-7.42 and serum HCO_3 - 23.
The corticosteroid dose was subsequently stopped after receiving 1mg/kg/dg for 3 weeks . In was started at 100mg IV BD X 3 lap and there was gradual improventin, the patient's sensorium improved and hemodynamic parameters stabilized. Patient was re-started with oral steroids after 24hrs urine protein slowed 2.4 gms/day. Other chronic medications were continued. With ongoing therapy, the patient's sensorium improved and hemodynamic parameters stabilized. Urine output progressively returned to an adequate level. Resolution of ketonemia and improvement in biochemical parameters were observed during the hospital course.
Overall, the clinical presentation—characterized by hyperglycemia, ketonemia, high anion-gap metabolic acidosis, hypokalemia, and hypernatremic dehydration occurring in the context of corticosteroid therapy for minimal change disease—was consistent with steroid-associated diabetic ketoacidosis accompanied by dyselectrolytemia.

DISCUSSION

This case illustrates the diagnostic and therapeutic complexity of managing steroid-associated diabetic ketoacidosis in a patient with biopsy-proven minimal change disease (MCD), further complicated by hypokalemia and hypernatremic dehydration. Hypernatremia in the setting of DKA is relatively uncommon, as most patients present with normal or low sodium concentrations due to dilutional effects of hyperglycemia. However, the coexistence of DKA with hyperosmolar states can lead to substantial free-water loss, resulting in elevated serum sodium levels. Similar patterns have been described in pediatric hyperglycemic crises reported by Shima et al., where combined metabolic disturbances produced marked hypernatremia and dehydration [7]. The findings in our patient, including sodium levels above 158 mEq/L and a collapsed inferior vena cava on ultrasonography, suggest significant intravascular volume depletion consistent with these observations.
Although traditionally regarded as a podocyte-specific disorder, MCD is increasingly recognized as a condition associated with broader immune-metabolic alterations, including dysregulated T-cell signaling and cytokine activity. Such mechanisms may influence glucocorticoid responsiveness and metabolic homeostasis. Maas et al. proposed that MCD represents more than a purely structural podocyte disorder and may involve systemic immunologic factors capable of affecting hormonal and metabolic pathways [8]. These mechanisms may contribute to the development of steroid-associated hyperglycemia and ketoacidosis observed in susceptible individuals.
Steroid-associated DKA has been reported in several clinical contexts. Cavataio et al. described cases in which corticosteroid therapy precipitated ketoacidosis in individuals without previously diagnosed diabetes, highlighting the capacity of glucocorticoids to induce hyperglycemia, enhance lipolysis, and increase hepatic ketogenesis beyond the compensatory capacity of endogenous insulin secretion [9]. Subsequent analyses have reinforced these findings, suggesting that corticosteroid exposure can lead to rapid metabolic decompensation, particularly when therapy is prolonged or when underlying metabolic susceptibility exists [10]. In the present case, the patient had no prior documented diabetes before initiation of corticosteroid therapy for MCD and later developed metabolic features consistent with diabetic ketoacidosis requiring insulin infusion.
Recent endocrinology reports have also documented cases of steroid-associated DKA accompanied by notable biochemical abnormalities. Azmat et al. described a comparable case in which corticosteroid exposure resulted in ketoacidosis associated with significant potassium depletion requiring careful electrolyte correction [11]. Hypokalemia in DKA typically results from osmotic diuresis, secondary hyperaldosteronism, intracellular potassium shifts during treatment of acidosis, and mineralocorticoid effects of glucocorticoids. These mechanisms correspond with the potassium level observed in our patient (2.7 mEq/L) and emphasize the importance of correcting potassium deficits before initiating insulin therapy.
The need for cautious corticosteroid use in individuals with diabetes or impaired glucose tolerance has been highlighted in clinical practice guidelines. Singh et al. emphasized that patients receiving corticosteroids should undergo regular glucose monitoring, and insulin therapy should be initiated promptly when significant hyperglycemia develops [12]. The coexistence of nephrotic syndrome, corticosteroid exposure, and evolving hyperglycemia in our patient underscores the importance of careful metabolic monitoring during steroid therapy.
Evidence from pediatric nephrology literature also supports the association between corticosteroid therapy in MCD and metabolic complications. Verma et al. reported that children receiving corticosteroid treatment for minimal change nephrotic syndrome frequently develop adverse metabolic effects including disturbances in glucose regulation and electrolyte imbalance [14]. Although the study population differs from the adult case presented here, the underlying pathophysiological mechanisms remain relevant across age groups.
Steroid-associated metabolic crises have also been reported following localized corticosteroid administration. Pabani et al. documented diabetic ketoacidosis occurring after intra-articular steroid injection in a patient with type 1 diabetes mellitus, demonstrating that even limited corticosteroid exposure may trigger metabolic instability in susceptible individuals [15]. Collectively, these reports highlight the unpredictable metabolic consequences of glucocorticoid therapy and emphasize the importance of early recognition and timely management.
In the present case, the coexistence of minimal change disease, corticosteroid therapy, hypernatremic dehydration, and potassium depletion produced a complex metabolic presentation. The progression from steroid-related hyperglycemia to diabetic ketoacidosis accompanied by dyselectrolytemia reflects the interaction between renal

disease, metabolic stress, and glucocorticoid-induced insulin resistance. Clinical improvement following fluid resuscitation, potassium supplementation, and insulin therapy is consistent with established principles of DKA management. This case therefore highlights the importance of careful metabolic monitoring and early intervention in patients receiving corticosteroids for renal or autoimmune conditions.

CONCLUSION

This case describes an uncommon presentation of steroid-associated diabetic ketoacidosis occurring in a patient with biopsy-proven minimal change disease and accompanied by hypernatremic dehydration and hypokalemia. The coexistence of nephrotic syndrome, corticosteroid therapy, and intravascular volume depletion created a complex metabolic environment requiring careful correction of fluid deficits, electrolyte imbalance, and metabolic acidosis.

The report emphasizes the importance of routine metabolic monitoring in patients receiving corticosteroid therapy, particularly those with underlying renal or immune-mediated disorders. Early recognition of steroid-associated dysglycemia, timely potassium replacement prior to insulin administration, and appropriate fluid management are critical components of safe treatment. Awareness of these metabolic complications may facilitate prompt intervention and reduce morbidity in patients receiving corticosteroid therapy.

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