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Steroid-Induced Hyperosmolar Hyperglycemic Syndrome in a Young Patient Without Diabetes After Treating Him for Minimal Change Disease—Case Report

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ABSTRACT

Hyperosmolar hyperglycemic syndrome (HHS) is a common complication of diabetes mellitus. The episodes of HHS have been reported in patients with no prior history of diabetes. However, these incidents have rarely been reported in the literature. The present study reports the case of hyperosmolar hyperglycemic syndrome in a patient without diabetes history after being prescribed high-dose steroid therapy. This case highlights the importance of regularly monitoring blood glucose levels in patients prescribed supraphysiological doses of steroids. The present study presents a 29-year-old male patient with no previous history of diabetes who presented with HHS, manifested by a decreased level of consciousness, lethargy, and history of polyuria. Laboratory work revealed significantly high serum glucose and high serum osmolality, with no ketones. Two weeks prior to the presentation, the patient was started on 1 mg/kg of oral prednisolone for his new diagnosis of minimal change disease with a nephrotic syndrome picture. The management of HHS included aggressive fluid intake and insulin therapy, and the steroid was tapered quickly. Hyperglycemia resolved completely with normalization of his HbA1c after the complete stoppage of steroids and he did not require to continue lifelong insulin. The present study highlights the importance of assessing the risk of hyperglycemia, screening, and regular glucose monitoring in patients prescribed supraphysiological doses of steroids, even if no prior history of diabetes has been recorded.

JEL Classification: Nephrology.

1 | Introduction

Hyperosmolar hyperglycemic state (HHS) is a potentially fatal complication usually associated with diabetes mellitus. However, HHS has also been reported in patients with no diabetes history [1]. Notably, 20% of HHS patients may not have previously been diagnosed with diabetes [2]. Individuals with insulin-dependent diabetes have a higher risk of developing HHS [3].

The infection is the predominant precipitating factor, contributing to 40%–60% of reported cases of HHS. Pneumonia is the prevailing ailment, constituting as much as 60% of reported cases, while urinary tract infections account for less than 16% of cases [2–4]. Diabetes medication nonadherence ranks as the second most prevalent cause, contributing to 21% of cases [5]. Additionally, significant is the decreased water consumption in older people and those with chronic ailments [6]. Nevertheless, the HHS remains a rare incidence in individuals who do not

Summary

- Hyperosmolar hyperglycemic syndrome (HHS) can develop in patients who have no history of diabetes but are receiving high-dose steroid therapy.
- This case underscores the critical need for rigorous blood glucose monitoring and risk assessment when prescribing supraphysiological doses of steroids to prevent serious complications such as HHS.
- Early recognition and management are essential for resolution and recovery.

have a prior history of diabetes. The present study reports the incidence of HHS in a patient with no prior history of diabetes and on high-dose steroid therapy. The case report highlights the importance of monitoring blood glucose levels in patients using supraphysiological doses of steroids.

2 | Case Report

2.1 | Patient Information

A 29-year-old male presented to the emergency department with bilateral lower limb edema on November 17, 2022. The patient reported foamy urine and facial and scrotal swelling for several days, with poor oral intake and decreased urine output. The vitals were recorded on admission and are described in Table 1.

2.2 | Previous Medical History

The patient had been recently diagnosed with idiopathic diabetes insipidus (DI) in another hospital (we lack accurate information), and an endocrinological investigation did not reveal any significant causative factor. The patient was prescribed 10 μg of internasal desmopressin daily and instructed by his endocrinologist to not drink more than 1.6 L of water a day although the patient reported that he was not strictly complaint on this. According to the patient. He has an intact thirst for which he drinks water of more than 1.6 L in some days. The patient had no prior history of any systemic disease, including diabetes mellitus or hypertension.

The chest exam revealed bi-basal crackles with stony dullness. Abdominal Examination revealed marked ascites with abdominal distension. However, no signs of bowel obstruction were observed. The lower extremities showed pretibial pitting edema of grade III-IV with no signs of infections or deep venous thrombosis. The cardiac exam was unremarkable. A genital exam revealed scrotal edema with no erythema or tenderness. Chest radiography revealed bilateral pleural effusion. The electrocardiogram (ECG) showed normal sinus rhythm. Both kidneys were of normal size with normal cortical echogenicity and maintained cortical medullary differentiation.

The laboratory findings revealed nephrotic syndrome; 24-h urine protein was 7 g/24 h, total cholesterol was 13.58 mmol/L (normal: < 5.2 mmol/L), and the serum albumin levels were observed as 10 g/L (normal: 35–52 g/L). On admission, the random blood glucose and hemoglobin A1C (HbA1c) were 5.5 mmol/L (normal: 4.11–5.89 mmol/L) and 5.1%, respectively. The blood urea nitrogen and serum creatinine were 6.5 mmol/L (normal: 2.76–8.07 mmol/L) and 74 μmol/L (normal: 59–104 μmol/L), respectively, and serum sodium ranges 125–140 mmol/L (normal: 135–145 mmol/L). Note, his measure body weight was 87 kg. Autoimmune screening ruled out the presence of any autoimmunity with negative antinuclear antibody, negative double-stranded DNA, negative antineutrophilic cytoplasmic antibody (ANCA), and normal complement levels. Screening for hepatitis B, hepatitis C, and human immunodeficiency virus (HIV) were negative. Renal biopsy showed diffuse foot process effacements with negative immunofluorescence consistent with the diagnosis of minimal change disease.

TABLE 1 | The patient characteristics recorded at the time of admission.

Age	29
Sex	Male
Smoking history	Negative
Systolic blood pressure	119 mmHg
Diastolic blood pressure	78 mmHg
Pulse	76 beats/min
Body temperature	36.2°C
Oxygen saturation	99%
Body weight	80 kg

Conservative therapy, including a low salt diet, renin–angiotensin inhibitor, and diuresis with intravenous (IV) diuretics, were initiated immediately after admission. Five days post-admission and following a biopsy, the patient was prescribed 1 mg/kg daily (total of 80 mg once daily) prednisolone for minimal change disease, along with proton pump inhibitor, *Pneumocystis pneumonia* (PCP) prophylaxis, and calcium and vitamin D. The patient responded positively to diuresis and steroid therapy with an improvement in edema. The patient was discharged.

2.3 | Clinical Findings and Diagnostic Assessment

The patient 3 weeks later presented to the emergency department after 3 weeks with decreased consciousness and lethargy, Also, he reported a history of polyuria which started a week earlier than his presentation to the emergency department. The patient was admitted to the critical care unit and intubated. Brain CT-scan showed no abnormality. Based on laboratory findings, the patient was diagnosed with HHS (Table 2).

2.4 | Therapeutic Intervention

The patient was managed for HHS and severe hypernatremia with free water through the nasogastric tube at a rate of 100 mL/h, intravenous isotonic fluids boluses, continuous

intravenous insulin infusion at a rate of 0.1 unit/kg/h, and his desmopressin switched to intravenous form at 2 μg twice daily. Also, the prednisolone dose was reduced immediately and tapered very quickly from 80 mg to 40 mg during hospitalization. The level of consciousness improved after the blood sugar and serum osmolarity returned to normal ranges over 4 days. The patient was in complete remission for minimal change disease with 24-h protein levels of < 200 mg/day. The complete recovery was achieved after 1 week of admission, and the patient was discharged. The patient was prescribed maintenance therapy comprising of prednisolone 40 mg/day to be tapered quickly till stopped completely and insulin glargine 10 units every night.

TABLE 2 | Laboratory findings upon HHS presentation.

Blood glucose level	> 60 mmol/L (3.9–5.6 mmol/L)
Serum sodium levels	170 mmol/L (136–145 mmol/L)
Measured serum osmolarity	394 mOsmol/kg (275–300 mOsmol/kg)
Calculated serum osmolality	409 mOsmol/kg
Hemoglobin A1c	8.2% (5.7%–6.4%)
Serum pH	7.385 (7.35–7.45)
Serum urea	21 mmol/L (2.76–8.07 mmol/L)
Serum creatinine	120 μmol/L (62–106 μmol/L)
Serum bicarbonate	31 mmol/L (21–28 mmol/L)
Urine dipstick test	Negative for ketones
Potassium	4.91 mmol/L (3.6–5.2 mmol/L)
Calcium	2.24 mmol/L (2.25–2.62 mmol/L)
Serum albumin level	3.5 g/dL (3.5–5.5 g/dL)
Chloride	82.9 mmol/L (96–106 mmol/L)
Creatinine	64 μmol/L (88–150 μmol/L)

The clinical timeline and the patient recovery are shown in Figure 1, and Figure 2, respectively.

2.5 | Patient Follow-Up and Outcomes

Follow-ups at 1, 2, and 3 months post-discharge showed HbA1c levels of 7.6%, 5.9%, and 5.8%, respectively. Prednisolone was tapered till stopped completely 2 months post-discharge. The patient reported hypoglycemic episodes on the third follow-up visit where he was not on any steroid and was, therefore, taken off insulin. Owing to the patient's age and speedy recovery, no immunosuppressive regime was prescribed after discontinuing steroid therapy. The patient remained asymptomatic under complete remission with no immunosuppression and without insulin or medication for blood sugar control. The patient reported feeling much better clinically after stopping the steroid completely, and his blood glucose has returned to normal without needing insulin.

3 | Discussion

The current study presents the case of a rare occurrence of steroid-induced HHS in a 29-year-old male patient with no prior history of diabetes mellitus. The patient was administered with 1 mg/kg daily dose of prednisolone. The steroids have been known to increase the risk of hyperglycemia [7]; however, the reports of HHS are rare. Several causes have been linked to the risk of HHS, the most notable being diabetes and infection. However, in the present case, no history of diabetes or infection was present, and he has no other obvious risk factor for HHS [8].

Steroids, when administered in dosages exceeding the body's physiological capacity, display remarkable therapeutic efficacy in treating various illnesses [9–11]. These medications entail certain hazards and adverse reactions that warrant careful consideration. The most frequent adverse event is hyperglycemia without a prior diagnosis of diabetes. Hyperglycemia affected

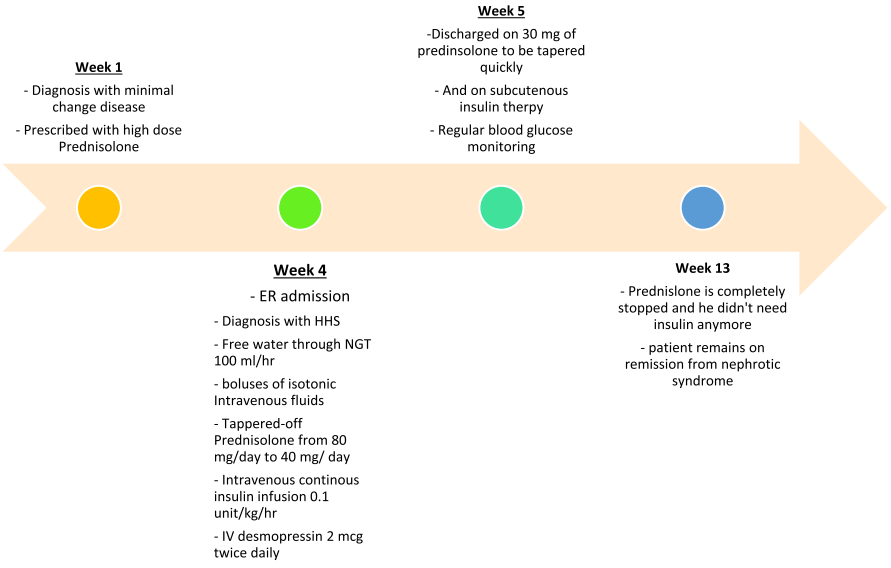

FIGURE 1 | The patient timeline.

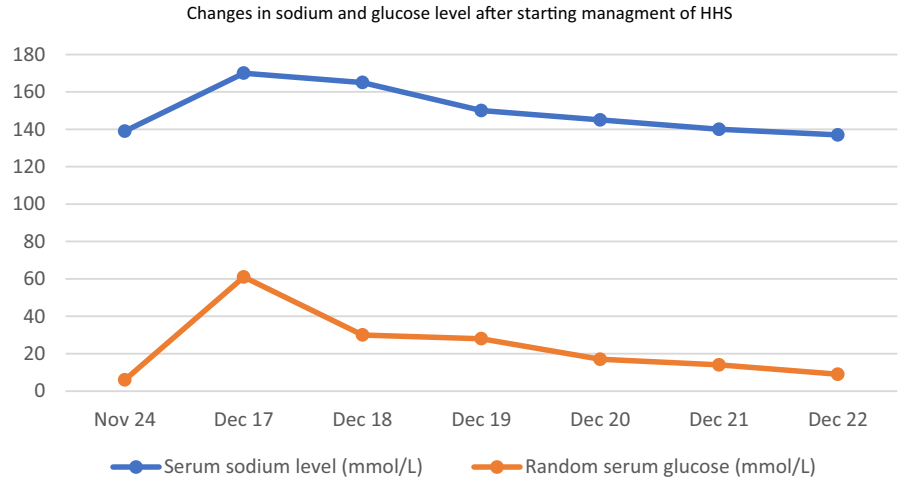

FIGURE 2 | The patient recovery after starting management of HHS.

32.3% of patients undergoing steroid medication, with 18.6% of those patients developing steroid-linked diabetes (GID) [12 13].

The pathophysiology of steroids in inducing hyperglycemia has been well understood. The steroids interfere with the insulin-signaling cascade in skeletal muscle and liver. This reduces glucose uptake and glycogen synthesis, increasing skeletal muscle breakdown and hepatic glucose production. Additionally, steroids induce whole-body lipolysis, impairing glucose metabolism and inducing hepatic steatosis and dyslipidemia [12]. However, the pathophysiology underlying the induction of hyperosmolarity is poorly understood. The hyperosmolar state results from serum water loss without the sodium loss [13]. In the present case, due to the patient's underlying diabetes insipidus, the patient was more susceptible to water loss, which made him more likely to have hyperosmolarity and develop HHS.

The risk of HHS in patients undergoing steroid therapy, including prednisolone, is very low and has only been reported rarely. Previously, HHS was reported in a lupus nephritis patient administered with high-dose steroid therapy (methylprednisolone at a daily dose of 750 mg for 3 days, followed by prednisolone at a daily dose of 60 mg). The seizure presented as the first complication of HSS in the patient [12]. In another case study, a patient diagnosed with Wegener's granulomatosis was administered a 500 mg/day dosage of methylprednisolone for 3 days, followed by oral prednisolone at 1.03 mg/kg/day developed HHS [14]. The present case study reports the occurrence of HHS in a patient with minimal change disease.

Considering the transient nature of steroid use and that they predominantly induce insulin resistance postprandially, it is advisable to establish the diagnosis based on glycemia measurement of 200 mg/dL or higher throughout the day. This stands in opposition to the application of fasting glycemia or glycosylated hemoglobin (HbA1c) [15]. A correlation has been identified between the initiation of hyperglycemia and the subsequent complications that manifest following hospitalization: an elevated risk of nosocomial infections, an extended duration of hospitalization, a heightened susceptibility to hyperosmolar nonketotic syndrome or diabetic ketoacidosis, and a high mortality rate [6 18]. A 10% escalation in the mortality risk has been identified in correlation with each 18 mg/dL rise in blood glucose [6]. Current guidelines indicate that mean glycemia levels between 140 and 180 mg/dL are satisfactory for care during hospitalization [16]. The type, dosage, and route of administration of the steroid all have an impact on how carbohydrates are metabolized. When prednisone or methylprednisolone is administered in the morning in a single dose, maximal hyperglycemia is often detected before or during dinner. Nevertheless, the patient's fasting blood glucose measurement might yield normal results.

Conversely, the administration of dexamethasone or multiple doses of methylprednisolone results in the manifestation of hyperglycemia in a consistent fashion over the entire day. Hence, to maintain a balanced approach encompassing the prevention of hyperglycemia, the dosing regimen must be sufficiently flexible to accommodate the specific steroid type and delivery method employed while also providing sufficient foresight regarding potential dosage adjustments [6]. Nevertheless, regular monitoring of blood glucose levels and serum electrolytes is necessary to diagnose the life-threatening emergency of HHS in patients administered with high doses of steroids, even in those that have no prior history of diabetes.

4 | Strengths and Limitations

The current study highlights the importance of regular glucose monitoring and serum electrolyte monitoring in patients prescribed drugs that can alter carbohydrate metabolism, especially high-dose steroid therapy. The report includes the patient's detailed clinical and therapeutic history, presentation to the emergency department, diagnosis of HHS, and management. The patient was followed up for 2–3 months. The study shows the tapering-off steroidal regime should be slowly managed. However, the study lacks the optimal blood glucose level range (s) that must be maintained in such patients during the follow-up period after the patient is discharged on 80 mg of prednisolone. These levels can help in early diagnosis and management of HHS and thus prevent any serious complications in the patients prescribed with supraphysiological doses of steroids.

5 | Conclusion

This paper describes a rare case of hyperosmolar state (HHS) in a patient who did not have a history of diabetes but who was treated with steroids. In the past, prednisolone-treated patients have occasionally experienced hyperglycemia; however, HHS has not been frequently observed. In the current instance, the patient's preexisting diabetes insipidus rendered him more prone to water loss, which increased his risk of hyperosmolarity and HHS. The current case study emphasizes how crucial it is to routinely check serum electrolyte levels and blood sugar levels in patients getting high-dose steroid medication, even if they have never had diabetes before. And also assessing any underlying conditions that could put the patient at risk.

The steroid therapy can alter carbohydrate metabolism and thus increase the risk of HHS. Due to the distinct genetic makeup and lifestyle of the Saudi population, there are presently no regional guidelines for the appropriate dosage of glucocorticoids for the treatment of glomerulonephritis. The development of glomerulonephritis management guidelines tailored to the Saudi population is a priority for nephrologists.

Author Contributions

Rehab B. Albakr: conceptualization, data curation, formal analysis, methodology, resources, writing – original draft, writing – review and editing.

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Consent

Written informed consent in Arabic (the patient's language) was acquired from the patient, and the patient consented to publish all images, clinical data, and other data included in the manuscript. (Attached in the submission documents).

Conflicts of Interest

The author declares no conflicts of interest.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Patient Perspective

The patient showed optimal signs of recovery during the second and third monthly visits and was satisfied with the management and overall therapeutic outcome.

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