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When Type 1 Diabetes Breaks The Rules: A Rare Hyperosmolar Hyperglycemic State Presentation

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Abstract:
Hyperosmolar Hyperglycaemic State (HHS) is a medical emergency with a high mortality rate. It occurs less often than diabetic ketoacidosis (DKA) and mainly affects individuals with pre-existing or new type 2 diabetes mellitus. Although it increasingly impacts adults, it is uncommon in type 1 diabetes patients due to the underlying mechanisms of insulin deficiency.
In this rare setting of a type 1 diabetes mellitus patient with pure Hyperosmolar Hyperglycaemic State (HHS) presentation, we try to present and discuss potential risk factors, diagnostic challenges, and underlying pathophysiology to achieve better outcomes and decrease further morbidity and mortality
Delayed recognition may increase morbidity and mortality. Emergency physicians and internists should be aware of Hyperosmolar Hyperglycaemic State HHS to make an early diagnosis for appropriate management, as it can be complicated in adult patients with T1 diabetes mellitus.
Patient concerns: The patient was admitted due to GI symptoms and severe dehydration associated with severe hyperglycemia and hyperosmolarity without significant acidosis.
Diagnoses: On the basis of clinical manifestations and history with laboratory results, she was diagnosed with Hyperglycaemic State (HHS).
Interventions: Treatment was started with intravenous fluid and regular insulin.
Outcomes: She was discharged without any complications related to Hyperglycaemic State (HHS) and adjusted her insulin therapy.

Keywords: Adult, hyperosmolar hyperglycaemic state, diabetes mellitus, diabetic ketoacidosis, anti-glutamic acid decarboxylase antibody, Insulin Autoantibodies, Islet Antigen-2 Autoantibodies, Zinc Transporter 8 Autoantibodies, Islet Cell Cytoplasmic Autoantibodies

Introduction:

Diabetes mellitus is a group of metabolic disorders of carbohydrate metabolism caused by either a lack of insulin secretion, impaired insulin action, or both.
Type 1 diabetes mellitus is a prevalent chronic illness globally, characterized by the immune system attacking β cells, typically resulting in complete insulin deficiency. (1)
In 2025, 513,000 new cases of type 1 diabetes mellitus are expected worldwide. Approximately 43.3% of new type 1 diabetes mellitus cases worldwide are expected in people under 20. (2)
Saudi Arabia ranks among the top ten countries globally for type 1 diabetes mellitus, with approximately 237,000 patients expected by 2025. (2)
Prevalence varies by region and countries, influenced by age, sex, genetics, and environmental triggers. (2)
The global rise in type 1 diabetes mellitus cases is accompanied by an increase in related morbidity and mortality rates, including diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS).
Patients with type 1 diabetes mellitus frequently present with diabetic ketoacidosis (DKA) due to the underlying disease mechanisms.(1)
Distinguishing diabetic ketoacidosis (DKA) from hyperosmolar hyperglycemic state (HHS) can be challenging, since both have similar presentations and clinical features.

Hyperosmolar hyperglycemic state (HHS) is characterized by very high blood sugar levels (≥600 mg/dL), significant hyperosmolarity (serum osmolality >300 mOsm/kg or total serum osmolality >320 mOsm/kg), with no significant acidosis, β-hydroxybutyrate levels below 3.0 mmol/L or urine ketones less than 2+, and a blood pH of ≥7.3 with bicarbonate levels of ≥15 mmol/L.
We present a rare case of hyperosmolar hyperglycemic state (HHS) in a middle-aged woman with Long-standing type 1 diabetes mellitus, followed by a discussion on the importance of identifying causes and contributing factors that may lead to the development of hyperglycemic state and severe hyperosmolarity (HHS) in type 1 diabetes mellitus (T1DM) patients.

Case Presentation

A fifty-nine-year-old Saudi female with long-standing type1 diabetes mellitus since age 23, lifelong dependence on insulin, presented with a one-day history of gradually worsening nausea and severe hyperglycemia (859 mg/dL ≈ 47.7 mmol/L).
She experienced four episodes of vomiting gastric contents, along with dehydration symptoms in the form of dry mouth, reduced urine output, fatigue, weakness, and dizziness. She also noted reduced oral intake over the last two days.
She had a history of poorly controlled type 1 diabetes, with a recent hemoglobin A1c of 12.5%. Her disease course was complicated by poor adherence to insulin therapy and irregular outpatient follow-up with another hospital. She experienced Recurrent diabetic ketoacidosis about 2–3 times annually, with the last episode occurring a month ago and required admission. Following discharge, her insulin therapy was intensified to a basal-bolus regimen: a total of 20 units per day of insulin degludec with a total of 18 units of insulin aspart before meals.
The laboratory investigation confirmed type 1 diabetes mellitus, including an Elevated HBA1C of 12.5%, undatable C-peptide below 0.03 ng/mL, a serum blood glucose of 859 mg/dL (approximately 47.7 mmol/L), and elevated zinc transporter 8 antibodies at 482 U/mL. Islet cell antibodies (ICA) and glutamic acid decarboxylase antibodies (GAD65) were within normal ranges. This pattern is typical in long-standing cases.
The patient had established microvascular complications of diabetes mellitus, including diabetic neuropathy, nephropathy, and retinopathy, and was followed by ophthalmology at her primary hospital.
Her other significant past medical history also included essential hypertension and non-obstructive coronary artery disease. She had severe rheumatic mitral stenosis and was on warfarin as part of her ongoing treatment and potential balloon mitral valvuloplasty.
Her medication regimen consisted of bisoprolol, furosemide, valsartan, amlodipine, and rosuvastatin.
She had a history of multiple diabetic ketoacidosis (DKA) episodes, with several prior hospitalizations, some of which involved ICU admission.
There is no history of non-prescribed medications or illicit drugs, and she denied smoking.
During the exam, she was alert and oriented, without distress. However, clinical features of dehydration were evident, including dry mouth, lips, and skin.
Her vital signs included a blood pressure of 105/59 mmHg, a heart rate of 102 bpm, a respiratory rate of 18 breaths per minute, oxygen saturation at 96% on room air, and a normal temperature.
The cardiac and chest exam revealed a low-pitched mid-diastolic murmur at the apex, with no jugular venous distention, and clear vesicular breathing.
The abdomen was soft, lax, and non-tender, with no guarding or organomegaly.
No signs of skin or soft tissue infection, lipodystrophy, or lipohypertrophy observed.
The neurological exam was unremarkable, and no signs of infection were detected.
Electrocardiography showed sinus tachycardia with no corrected QT interval prolongation.
Given the absence of an obvious precipitating factor, further investigations were performed to exclude common triggers of Hyperosmolar Hyperglycaemic State (HHS), including myocardial infarction, sepsis, and pancreatitis. The results were unremarkable.
A computed tomography scan of the head demonstrated no acute intracranial abnormalities.

Based on the patient's clinical presentation and laboratory findings,and in accordance with the American Diabetes Association (ADA) criteria (1) a diagnosis of Hyperosmolar Hyperglycaemic State (HHS) was established .Initial venous blood gas analysis demonstrated mild metabolic acidosis with a pH of 7.30, pCO_2 of 40.4 mmHg, and bicarbonate of 18.9 mmol/L. The anion gap was elevated at 22.1, serum lactate was 2.3 mmol/L, measured serum osmolality was 324 mOsm/kg H_2O, and urine ketones were detected at +1 (Table 1).

Her glucometer was unreadable ("high" on arrival. Blood samples were sent for laboratory testing. She received 10 units of short-acting IV insulin and 2 liters of 0.9% saline.

The patient was admitted under the endocrinology department as a case of hyperosmolar hyperglycemic state, attributed to inadequate insulin and dehydration.

She was transferred to the high dependency unit (HDU) for close monitoring of her cardiac status and fluid management .Following confirmation of the diagnosis, treatment was initiated according to institutional HHS protocol and ADA recommendations. Her management involved careful rehydration using intravenous fluids, insulin infusion, and regular electrolyte monitoring and replacement. Laboratory investigations were performed every 2–4 hours.

Investigations (Table 1):

Parameter	Result	Reference / Comment
WBC	6.36 ×10⁹/L	Normal
Hemoglobin	13.2 g/dL	Normal
Platelets	353 ×10⁹/L	Normal
INR	3.94	Therapeutic as on warfarin
Sodium (Na)	127 mmol/L	pseudohyponatremia
Potassium (K)	5.1 mmol/L	normal
Creatinine	1.23 mg/dL	Elevated (baseline 0.6)
BUN	26 mg/dL	Elevated
pH (VBG)	7.30	Mild acidemia
pCO_2 (VBG)	40 mmHg	Normal
Bicarbonate (HCO_3) (VBG)	18.9 mmol/L	Mild metabolic acidosis
Lactate	2.3 mmol/L	Slightly elevated
Glucose serum	859 mg/dl ≈ (47.7 mmol/L).	Sever hyperglycemia
Serum Osmolality	324 mOsm/kg	Elevated (HHS range)
Troponin	Negative	No myocardial injury
BNP	431 pg/mL	Elevated, likely cardiac baseline
Total Bilirubin	2.0 mg/dL	Mildly elevated
Direct Bilirubin	0.9 mg/dL	Mildly elevated
Islet cell abs (ICA)	<1:10 Titer	Normal
Glutamic Acid Decarboxylase Abs (GAD65)	<10.0 IU/ml	Normal
Zinc transporter 8 abs.	482	High

Fifteen hours after admission, the patient's metabolic acidosis had resolved, serum osmolality had decreased to below 300 mOsm/kg, and adequate urine output was maintained. She was subsequently transitioned from intravenous insulin infusion to a subcutaneous basal-bolus regimen comprising 20 international units of insulin glargine at bedtime and 15 international units of insulin aspart before meals. At discharge, the patient was educated about Diabetes self-management, including insulin adherence and Identification and avoidance of risk factors and causes of diabetic ketoacidosis and hyperosmolar hyperglycemic state. She also received counseling regarding sick-day management and the importance of appropriate vaccination.

In addition, the patient was instructed on regular blood glucose monitoring, individualized nutritional planning, and adherence to scheduled follow-up appointments. Ongoing surveillance was recommended, including periodic assessment of glycated hemoglobin (HbA1c), renal function, and urine albumin-to-creatinine ratio.
The importance of routine screening for diabetes-related complications was emphasized, including regular ophthalmologic and foot examinations. Continued follow-up for the early detection and management of both microvascular and macrovascular complications of diabetes mellitus was advised.

the patient was lost to follow-up after discharge, 8 months after her presentation the patient was electively admitted for a valvular replacement surgery and during hospitalization her condition deteriorated due to cardiogenic and septic shock, which ultimately led to her death.

Discussion:
Hyperosmolar hyperglycemic state (HHS) is a life-threatening acute metabolic complication that is most commonly linked to type 2 diabetes mellitus (T2DM), although it can also occur in individuals with type 1 diabetes mellitus (T1DM). Similar to diabetic ketoacidosis (DKA), HHS remains a significant contributor to diabetes-related morbidity and mortality (3).
We report a rare case of HHS in a middle-aged woman with type 1 diabetes mellitus , who presented with severe hyperglycaemia and clinical evidence of dehydration without significant ketoacidosis. The patient's history of poor adherence to insulin therapy and inadequate insulin dosing likely played a central role in the development of HHS. A plausible pathophysiological explanation is that residual circulating insulin activity was sufficient to suppress significant ketogenesis but inadequate to prevent severe hyperglycaemia, osmotic diuresis, and progressive hyperosmolality.
Although uncommon, similar cases have been described in the literature.
David Simmons reported a rare HHS case in an adult with type 1 diabetes. The report included a picture related to mixed medication overdose, involving benzodiazepines, tricyclic antidepressants, and/or opioids, and their relation to counter-regulatory hormones (CRHs). (4)
Jun Kido reported a first presentation of an adolescent patient presenting with severe hyperglycemia and hyperosmolarity, but without significant ketosis. Further assessment and laboratory results led to a diagnosis of type 1 diabetes mellitus (5).
In another report, Kene Ebuka described a 14-year-old patient who presented with severe dehydration, CNS manifestations combined with marked hyperglycemia, hyperosmolarity, and hypernatremia. The initial diagnosis was type 1 diabetes mellitus complicated by hyperosmolar hyperglycemic state (HHS).(6)

Limitations
This case presented several diagnostic challenges. First, the patient's presentation included overlapping features of hyperosmolar hyperglycemic state (HHS) and diabetic ketoacidosis (DKA). Mild metabolic acidosis, together with an elevated anion gap, initially raised the possibility of a mixed DKA–HHS presentation. Additionally, acute kidney injury and mild hyperlactatemia may have contributed to the observed acid–base disturbances, further complicating the diagnostic evaluation.
A further limitation was the unavailability of serum β-hydroxybutyrate measurement at our institution, which limited definitive assessment of the degree of ketosis. To address this limitation, urine ketone testing was repeated on three separate occasions and consistently demonstrated only minimal ketonuria, supporting the absence of significant ketoacidosis.
Another challenge was establishing a definitive diagnosis of type 1 diabetes mellitus (T1DM). The patient had received care at multiple healthcare institutions, resulting in variations in insulin regimens and incomplete longitudinal clinical data. Furthermore, diabetes-related autoantibodies such as islet cell antibodies (ICA) and glutamic acid decarboxylase 65 (GAD65) antibodies may become undetectable in individuals with long-standing T1DM. Nevertheless, the diagnosis of T1DM was supported by the clinical presentation, the absence of features suggestive of type 2 diabetes mellitus or significant insulin resistance, low C-peptide levels, marked hyperglycemia, and strongly positive zinc transporter 8 (ZnT8) antibodies.

Finally, long-term assessment of treatment outcomes was limited because the patient was lost to follow-up after discharge, 8 months after her presentation the patient was electively admitted for a valvular replacement surgery and during hospitalization her condition deteriorated due to cardiogenic and septic shock, which ultimately led to her death.

Clinical Message and Conclusion

This case highlights that hyperosmolar hyperglycemic state (HHS), although rare, should be recognized as a potential acute hyperglycemic emergency in patients with long-standing type 1 diabetes mellitus (T1DM). Clinicians should maintain a high index of suspicion for HHS in patients presenting with severe hyperglycemia, dehydration, and hyperosmolality, even in the absence of significant ketoacidosis.

Careful clinical assessment is essential for distinguishing HHS from diabetic ketoacidosis and mixed hyperglycemic crises, as early diagnosis and appropriate management are crucial for reducing diabetes-related morbidity and mortality.

This case also emphasizes the importance of comprehensive evaluation of the patient's diabetes type, treatment regimen, adherence to insulin therapy, previous hospitalizations, and diabetes-related complications. Identifying precipitating factors and contributors to severe hyperglycemia and hyperosmolality, particularly inadequate insulin replacement and poor treatment adherence, is essential for preventing recurrence and improving long-term outcomes in patients with T1DM.

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