

A case report of hyperosmolar hyperglycemic state in a 7-year-old child

An unusual presentation of first appearance of type 1 diabetes mellitus

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Abstract

Rationale: A hyperosmolar hyperglycemic state (HHS) is a rare presentation of a hyperglycemic crisis in children with diabetes mellitus. As this condition can be fatal and has high morbidity, early recognition and proper management are necessary for a better outcome. Here, we report a rare case of HHS as the first presentation of type 1 diabetes mellitus (T1DM) in a 7-year-old girl.

Patient concerns: The patient was admitted due to polyuria and weight loss in the past few days. The initial blood glucose level was 1167mg/dL.

Diagnoses: On the basis of clinical manifestations and laboratory results, she was diagnosed with T1DM and HHS.

Interventions: Treatment was started with intravenous fluid and regular insulin.

Outcomes: She was discharged without any complications related to HHS and is being followed up in the outpatient clinic with split insulin therapy.

Lessons: As the incidence of T1DM is increasing, emergency physicians and pediatricians should be aware of HHS to make an early diagnosis for appropriate management, as it can be complicated in young children with T1DM.

Abbreviations: anti-GAD antibody = anti-glutamic acid decarboxylase antibody, BMI = body mass index, DKA = diabetic ketoacidosis, ECF = extracellular fluid, HHS = hyperosmolar hyperglycemic state, T1DM = type 1 diabetes mellitus, TSH = thyroid-stimulating hormone.

Keywords: child, diabetes mellitus type 1, hyperglycemic hyperosmolar nonketotic coma

1. Introduction

Type 1 diabetes mellitus (T1DM) is characterized by low or no endogenously produced insulin due to autoimmune destruction of pancreatic beta-cells. The incidence of T1DM in children and adolescents <15 years old has increased worldwide.^[1,2] The incidence varies greatly among countries, with the highest incidence in Finland, and a very low incidence in Asia.^[1] However, countries with a traditionally low incidence of T1DM have shown a tendency for a rapid increase in children and adolescents.^[3] One

study showed a 2.33-fold increase in the incidence of T1DM in Korea during 1995 to 2000 and 2012 to 2014.^[4]

As T1DM is increasing significantly, diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are emerging as a life-threatening hyperglycemic crisis. The prevalence of DKA among children <15 years of age with T1DM in the EURODIAB study was 33%.^[5] However, the incidence of DKA with new-onset T1DM is 15% to 67% depending on the country and geographical region.^[6] Most cases of HHS are seen in elderly patients with type 2 diabetes, and HHS is extremely uncommon as the first presentation of T1DM.^[7,8] It is not easy to distinguish DKA and HHS from a patient's history because of their similar characteristic features. However, there are definite differences between their diagnostic criteria. HHS presents as severe hyperglycemia, hyper-osmolality, with no evidence of severe ketosis or acidosis. Although HHS is a rare presentation of childhood diabetes, the importance of proper management cannot be emphasized enough due to the high mortality rate.^[9]

Here, we report a rare case of HHS as the first presentation of T1DM in a 7-year-old child, which is younger than previous reports,^[10] and discuss the importance of early identification of hyperglycemic crisis in severely dehydrated children.

2. Case description

A 7-year-old girl visited the emergency department with severe polyuria. She had a 3-day history of frequent urination (3–4 times every hour), polydipsia, and lethargy. Although she drank more beverage than usual, she felt excessive thirst and lost weight from 22 to 19.6 kg in 7 days. She had recently moved to a new house

Editor: Yoshifumi Saisho.

Our case report has received review exemption by Hallym University Sacred Heart Hospital Institutional Review Board.

The authors report no conflicts of interest.

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Medicine (2017) 96:25(e7369)

Received: 7 April 2017 / Received in final form: 2 June 2017 / Accepted: 6 June 2017

<http://dx.doi.org/10.1097/MD.0000000000007369>

Table 1
Laboratory results of the case.

	References	Unit	Initial	6h	12h
Venous pH	7.35~7.45	pH	7.34	7.40	7.41
Venous pCO ₂	35.0~45.0	mmHg	36.6	35.8	37.1
Venous base excess	-3.0 to 3.0	mEq/L	-6.0	-2.5	-1.2
Venous bicarbonate	23.0~29.0	mEq/L	19.9	22.5	23.7
Serum glucose		mg/dL	1167	660	323
Serum sodium	135~145	mmol/L	123	141	144
BUN	5.0~18.0	mg/dL	19.7	28.4	33.9
Creatinine	0.40~0.60	mg/dL	1.03	1.05	0.87
Serum osmolality	275~295	mOsm/kg	350	ND	320
Urine ketone body	negative		++	Negative	ND

BUN=blood urea nitrogen, ND=not done.

and was having a hard time fitting in at the new school. She was previously healthy with no past admissions or serious illness. She had no change of eating habits and lifestyle recently. No history or family history of endocrine disease including diabetes mellitus was reported. At admission, her height was 127.4 cm (50th–75th percentile), weight was 19.6 kg (5th–10th percentile), and body mass index (BMI) was 12.08 kg/m² (<first percentile). Her temperature was 37.2°C, heart rate was 88 beats/min, respiratory rate was 18 beats/min, blood pressure was 100/60 mm Hg, and pulse oximetry was 100% on room air. Her mental status was alert, sensation was intact, and motor strength was quite good considering her condition. However, she looked cachectic and lethargic. Her glucose level was too high to check with a capillary blood glucose meter, so a blood test was performed and rehydration therapy with intravenous fluid (isotonic saline 10 mL/kg loading dose for 1 hour) was started immediately (Table 1). Initial biochemistry results demonstrated severe hyperglycemia (1167 mg/dL), hyperosmolality of 350 mOsm/kg (effective osmolality 311 mOsm/kg), mild acidosis (venous pH 7.34), hyponatremia (sodium 123 mmol/L; corrected for blood glucose: 140 mmol/L), severe glycosuria, and mild ketonuria.

On the basis of the laboratory results, intensive intravenous fluid and regular insulin were administered and laboratory examinations were performed every 2 hours to check and modulate electrolyte changes. Serum glucose level decreased approximately 60 mg/dL/h and normalized to 115 mg/dL 17 hours after treatment started, which led a gradual decrease in serum osmolality (Fig. 1). No evidence of acidosis or severe ketosis confirmed the diagnosis of HHS. A neurological examination and brain computed tomography scan were performed to check for complications of HHS, but no cerebral edema was found.

The laboratory results that confirmed the diagnosis of T1DM were as follows: glycosylated hemoglobin (HbA1c), 15.6% (reference, <5.6%); C-peptide, 0.12 ng/mL (reference, 1.10–4.40 ng/mL); anti-GAD antibody, 2.4 U/mL (reference, ≤9.0 U/mL); anti-insulin antibody, 4.9% (reference, ≤7.0%); anti-islet cell antibody, negative; and 24-hour urine c-peptide, 4.5 μg/day (reference, 17.2–181.0 μg/day). All parameters of other hormone group were within normal range; triiodothyronine, 86.23 ng/dL (reference, 80.00–200.00 ng/dL); free thyroxine, 1.40 ng/dL (reference, 0.70–2.00 ng/dL); thyroid-stimulating hormone (TSH), 2.78 μIU/mL (reference, 0.5–4.5 μIU/mL); anti-thyroglobulin, 25.30 IU/mL (reference, ≤115.00 IU/mL); anti-microsome, 5.19 IU/mL (reference, ≤34.0 IU/mL); anti-TSH receptor 0.40 IU/L (reference, ≤1.75 IU/L).

After a 13-day hospital stay that included blood glucose control and T1DM education, she was discharged without any symptoms. Anthropometric measurements at discharge were height, 127.0 cm (50th–75th percentile); weight, 24.0 kg (25th–50th percentile); and BMI, 14.88 (29th percentile). She is being followed-up in the outpatient clinic regularly with split insulin therapy (Neutral protamine Hagedorn and regular insulins) and self-glucose monitoring. At recent visits (4 months after discharge), her HbA1c level was 7.1%, and she was maintaining blood glucose within the target range.

3. Discussion

A rise in the incidence of T1DM has been observed globally in recent decades.^[1,6] Approximately 86,000 children <15 years old are estimated to develop T1DM annually worldwide.^[11] In Asia, particularly Korea, the incidence of T1DM was very low compared with other continents and nations (approximately 1.36 per 100,000 person-years in 1995–2000).^[12] However, 1 study reported a significant increase of 3.19 per 100,000 person-years in 2012 to 2014,^[4] which means Korea will not remain a diabetes-safe country in a few years.

DKA and HHS are the most serious acute hyperglycemic emergencies among DM complications. Hyperglycemia in a patient with DKA results from increased hepatic and renal glucose production and impaired peripheral glucose utilization leading to osmotic diuresis and electrolyte imbalance. Ketonemia and metabolic acidosis are the consequences of increased lipolysis

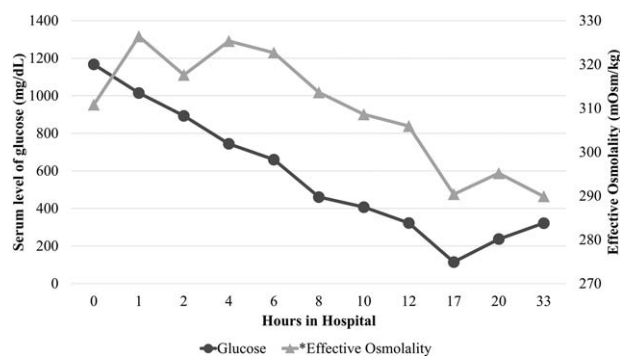


Figure 1. Changes in serum glucose level and effective osmolality during treatment are shown. Effective osmolality was elevated to 326 mOsm/kg, but decreased gradually and normalized 17 h after hydration was started. *Effective osmolality = 2[measured Na (mEq/L)] + glucose (mg/dL)/18.

and ketoacid production.^[13] Different from DKA, HHS commonly occurs after a prolonged and gradual increase in polyuria and polydipsia, resulting in profound dehydration, with fluid losses estimated to be twice those of DKA. This is accompanied by severe electrolyte loss, also greater than that observed in DKA because of the longer duration of osmotic diuresis.^[8] Hypovolemia eventually occurs due to continued osmotic diuresis, which leads to a progressive decline in glomerular filtration rate and worsening hyperglycemia.^[9]

HHS is a rare presentation in T1DM, particularly in children, which bears a high degree of morbidity and mortality. Mortality due to HHS has been reported as high as 50% to 60%, and a recent cohort study reported 30-day mortality of 16%.^[14] HHS was first described as an extreme elevation in serum glucose concentration and hyper-osmolality without significant ketosis or acidosis. HHS usually causes greater morbidity and mortality than DKA, depending on the severity of dehydration, hyper-osmolality, and patient age.^[9] As a result of insulin deficiency and increasing levels of counter-regulatory hormones, increased gluconeogenesis and conversion of glycogen to glucose create blood hyperglycemia.^[9] In a hyperglycemic state, the glycosuria uses a large volume of water and electrolytes are lost by urination, leading to a hyperosmolar condition. Thus, osmolality is useful as an indicator of HHS severity and for monitoring the rate of change with treatment in the hyperosmolar state.^[15] If osmolality cannot be measured frequently, it should be calculated using a formula.^[16]

The classic presentation of HHS in children is an obese adolescent with type 2 diabetes. However, recent studies have reported a few cases of HHS in T1DM or HHS in nonobese patients.^[7,8,17] One study reported 71 patients with HHS from 2001 to 2008; 49 were obese adolescents as a classic presentation of HHS. However, the remaining patients were not obese and younger than those in the obese group. Although T1DM was predominant in nonobese survivors, T2DM was overwhelmingly present in the obese group.^[8]

Some differences exist in the treatment of DKA and HHS; however, intensive fluid hydration is important as initial management for both conditions. Hydration by isotonic solution is recommended at 10 to 20 mL/kg/h during the first hour. Initial hydration usually decreases the glucose concentration by reducing counter-regulatory hormones and improving renal perfusion. During this process, plasma sodium levels should be monitored to prevent cerebral edema or central pontine myelinolysis as a complication given the rapid correction in blood osmolality. Serum sodium level can change on the basis of the pre-existing high glucose level and therefore needs to be corrected to reflect the actual situation in the body. Increased extracellular fluid (ECF) osmolality in hyperglycemic states forces water to move to the ECF, which decreases serum sodium in proportion to dilution of the ECF. This mechanism is called translational hyponatremia and returns to normal when glucose drops (Fig. 2). Fluid deficits should be corrected gradually over 48 hours, aiming for 12% to 15% correction with a goal of promoting a gradual decline in serum sodium and osmolality. Serum osmolality in our case was maintained at a similar level for several hours and then decreased gradually (Fig. 1).

After initial hydration therapy is completed, intravenous rapid insulin should be administered to decrease the glucose level and resolve the metabolic acidosis. Insulin should be started after the initial fluid expansion to avoid the risks of severe hypokalemia and an excessive decrease in serum osmolality.^[18] The management strategy may differ with insulin infusion rates of 0.1 unit/kg/h in patients with DKA and 0.05 unit/kg/h in those with HHS.^[18]

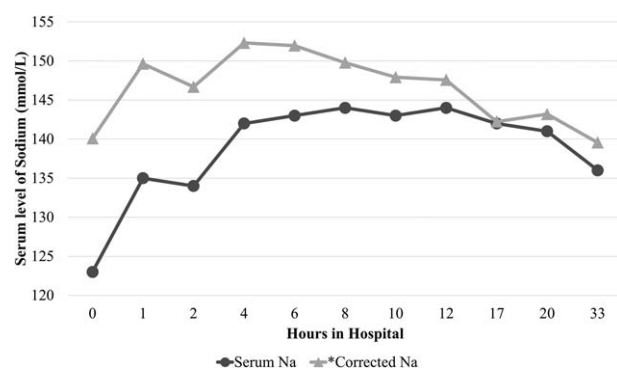


Figure 2. Serum sodium and corrected sodium levels during treatment are shown. Initial serum sodium level was low at 123 mmol/L, but the corrected sodium level was in the normal range at 140 mmol/L. Sodium level was normalized after serum glucose level was lowered. *Corrected Na = Na + (Glucose - 100) × 0.016.

Although our patient started with insulin infused at 0.1 unit/kg/h as for DKA, we lowered the insulin rate after diagnosing HHS considering no evidence of severe acidosis and the rapidly improved mild ketonuria.

HHS can cause serious complications, such as brain edema and rhabdomyolysis.^[19] Although cerebral edema is rarely seen in these cases except in children or in patients with pure HHS,^[20] a neurological examination and radiological study should be considered, as the condition can be fatal. Severe dehydration and hyperviscosity of the blood increase the risk of thromboembolism in patients with HHS. Rhabdomyolysis, acute renal failure, and malignant hyperthermia are other reported complications and warrant monitoring of renal function and creatine kinase levels.^[18]

The limitation of this case was that the reason of the sudden onset of T1DM was obscure. The gene study including human leukocyte antigen (HLA) typing was not performed due to the high cost. She recently had some social stress, but this is hard to prove. Therefore, further genetic evaluation might be needed especially in nonautoimmune T1DM. Nevertheless, our case is valuable, as we experienced that nonobese children with T1DM can present with HHS at a young age. Therefore, emergency physicians and pediatricians should be aware of HHS and to make an accurate diagnosis of the hyperglycemic crisis, which could be complicated in children with T1DM.

Acknowledgment

The authors thank the patient for permitting us to report this case.

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