Endocrinology, Diabetes & Metabolism CASE REPORTS

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ID: 18-0131; March 2019
DOI: 10.1530/EDM-18-0131

Hyperglycemic hyperosmolar state in an adolescent with type 1 diabetes mellitus

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Summary

Hyperglycemic hyperosmolar state (HHS) and diabetic ketoacidosis (DKA) are the most severe acute complications of diabetes mellitus (DM). HHS is characterized by severe hyperglycemia and hyperosmolality without significant ketosis and acidosis. A 14-year-old Japanese boy presented at the emergency room with lethargy, polyuria and polydipsia. He belonged to a baseball club team and habitually drank sugar-rich beverages daily. Three weeks earlier, he suffered from lassitude and developed polyuria and polydipsia 1 week later. He had been drinking more sugar-rich isotonic sports drinks (approximately 1000–1500 mL/day) than usual (approximately 500 mL/day). He presented with HHS (hyperglycemia (1010 mg/dL, HbA1c 12.3%) and mild hyperosmolality (313 mOsm/kg)) without acidosis (pH 7.360), severe ketosis (589 μmol/L) and ketonuria. He presented HHS in type 1 diabetes mellitus (T1DM) with elevated glutamate decarboxylase antibody and islet antigen 2 antibody. Consuming beverages with high sugar concentrations caused hyperglycemia and further exacerbates thirst, resulting in further beverage consumption. Although he recovered from HHS following intensive transfusion and insulin treatment, he was significantly sensitive to insulin therapy. Even the appropriate amount of insulin may result in dramatically decreasing blood sugar levels in patients with T1DM. We should therefore suspect T1DM in patients with HHS but not those with obesity. Moreover, age, clinical history and body type are helpful for identifying T1DM and HHS. Specifically, drinking an excess of beverages rich in sugars represents a risk of HHS in juvenile/adolescent T1DM patients.

Learning points:

- Hyperglycemic hyperosmolar state (HHS) is characterized by severe hyperglycemia and hyperosmolality without significant ketosis and acidosis.
- The discrimination between HHS of type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) in initial presentation is difficult.
- Pediatrician should suspect T1DM in patients with HHS but not obesity.
- Age, clinical history and body type are helpful for identifying T1DM and HHS.
- Children with T1DM are very sensitive to insulin treatment, and even appropriate amount of insulin may result in dramatically decreasing blood sugar levels.

Background

Hyperglycemic hyperosmolar state (HHS) and diabetic ketoacidosis (DKA) are the most severe acute complications of diabetes mellitus (DM). HHS is characterized by severe hyperglycemia and hyperosmolality without significant ketosis and acidosis. HHS has been frequently reported in adult patients with type 2 DM (T2DM), but other than at

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academic meetings, no pediatric cases with HHS have been reported in Japanese patients with type 1 DM (T1DM). Although HHS and DKA share some clinical appearances, they are distinct clinical entities causing different complications and requiring different treatments. Here, we report on a 14-year-old Japanese boy with HHS and T1DM and discuss the causes of this condition.

Case presentation

A 14-year-old Japanese boy presented at the emergency room with lethargy, polyuria and polydipsia. He had been healthy without a personal or family history of medical problems. He belonged to a baseball club team and had habitually drank sugar-rich beverages daily. Three weeks earlier he suffered from lassitude and developed polyuria and polydipsia 1 week later. He had been drinking more sugar-rich isotonic sports drinks (approximately 1000–1500 mL/day) than usual (approximately 500 mL/day). His weight decreased from 57 to 51.8 kg in the past month. At admission, his height, weight and BMI were 172 cm, 51.8 kg and 17.5 kg/m^2 (Z score: –0.74, https://zscore.research.chop.edu/index.php), respectively. His body temperature was 37.2°C; heart rate, 81 beats/min; respiratory rate, 12 breaths/min; blood pressure, 129/73 mmHg; and pulse oximetry, 98% in room air. He appeared obtunded and developed significant dehydration with decreased skin turgor, he had dried mucous membranes, a capillary refill time >2 s and a cardiothoracic ratio of 32% on a chest radiograph.

Investigation

He presented with HHS (hyperglycemia (56.1 mmol/L, HbA1c 12.3%) and mild hyperosmolality (313 mOsm/kg)) without acidosis (pH 7.360), severe ketosis (589 µmol/L) and ketonuria (Tables 1 and 2). He did not present acanthosis nigricans or skin tags. His abdominal ultrasonography demonstrated non-fatty liver disease. He was suspected of presenting HHS with T2DM.

Treatment

Intensive transfusion with 0.9% saline was administered, and his blood glucose levels decreased to 47.3 mmol/L. Moreover, 5 U (0.1 U/kg) intravenous insulin was administered; infusions commenced at a rate of 0.06 U/(kg·h). Two hours after hospitalization, insulin infusions were decreased to 0.01 U/(kg·h) (Fig. 1). Twenty-four hours after hospitalization, the patient started oral intake and subcutaneous regular insulin treatment (6 U at every meal) while undergoing continuous insulin treatment of 0.01 U/(kg·h). The continuous insulin infusion ended 6 days after hospitalization.

Table 1 Arterial blood and urine data before and after treatment in a patient with T1DM who developed HHS.

	Initial presentation	14 h
pH	7.36	7.39
pCO_2 (mmHg)	42.0	44.0
Bicarbonate (mM)	23.7	26.6
Base excess (mM)	–1.8	1.2
Lactate (mM)	1.0	0.7
Serum sodium (mEq/L)	136.5	137
Serum potassium (mEq/L)	4.9	4.1
Serum chloride (mEq/L)	87	105
Serum glucose (mg/dL)	1010	201
Serum BUN (mg/dL)	23	15
Serum creatinine (mg/dL)	0.63	0.62
Plasma osmolality (mOsm/L)	313	284
Urine glucose	3+	–
Urine ketone body	–	–

Outcome and follow-up

The patient, as well as his parents, learnt about intensive insulin therapy and carbohydrate counting. His brain magnetic resonance imaging and nerve conduction velocity examinations demonstrated no abnormal findings. The retinal condition evaluation by the ophthalmologist concluded that his retinal condition was normal. His blood glucose levels were controlled

Table 2 Specific laboratory data for T1DM.

Parameters	Values	Reference range
HbA1c (%)	12.3	4.6–6.2
IRI (µU/mL)	3.99	1.84–12.2
C-peptide (ng/mL)	0.58	0.61–2.09
Total ketone bodies (µmol/L)	589	0–130
Acetoacetic acid (µmol/L)	198	0–55
Beta-hydoroxybutyric acid (µmol/L)	341	0–85
GAD antibodies (U/mL)	32.1	0–4.9
IA-2 antibodies (U/mL)	19.0	0–0.39
TPO antibodies (U/mL)	14.0	0–15.9
TSH-R antibodies (U/mL)	<1.0	0–0.9
Tg antibodies (U/mL)	≦10	0–27
HLA-DNA DQB1	03:01:01 03:03:02	

GAD, glutamate decarboxylase; HHS, hyperglycemic hyperosmolar state; HLA, human leukocyte antigen; IA-2, islet antigen 2; IRI, immunoreactive insulin; T1DM, type 1 diabetes mellitus; Tg, thyroglobulin; TPO, thyroid peroxidase; TSH-R, thyroid-stimulating hormone receptor.

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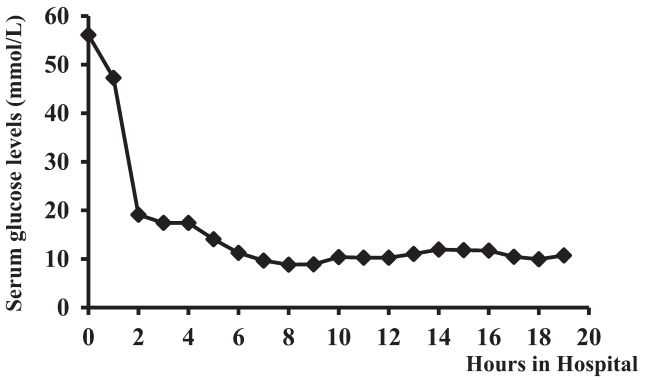

Figure 1
Patient blood glucose levels after hospitalization in a patient with T1DM who developed HHS.

by intensive insulin therapy and carbohydrate counting (32–38 U/day). He was discharged without neurological disorders 14 days after hospitalization. He was diagnosed with T1DM, detected by elevated blood glutamate decarboxylase (GAD) and islet antigen 2 (IA-2) antibodies (Table 2). We obtained the informed consent for a case report from him and his mother.

Discussion

We present a case of T1DM developing into HHS. Although the patient was initially suspected of HHS in T2DM because of his elevated blood glucose and HbA1c levels, he was diagnosed with T1DM owing to detection of elevated autoantibody in T1DM.

Autoantibodies to GAD and IA-2 have an important role in the clinical classification of diabetes (1), prediction of the need for insulin treatment (2), identification of individuals at risk of developing T1DM (3) and as endpoints in observational studies (4). The sensitivity and specificity of these autoantibodies when detected in the individuals with T1DM and in healthy individuals have been found to slightly differ across laboratories, and according to the assay method used (e.g., radioimmunoassay vs ELISA) (5, 6). We measured these autoantibodies using the ELISA method. In the Diabetes Antibody Standardization Program (DASP) 2005 (6), the median sensitivity and specificity of GAD antibody using an ELISA were 89% (N=8, interquartile range 85–92%) and 98% (N=8, interquartile range 96–99%), respectively. The median sensitivity and specificity of IA-2 antibody using ELISA were 65% (n=6, interquartile range 62–67%) and 99% (n=6, interquartile range 98.8–99.2%). Moreover, Törn *et al*. (2008) (5) reported that the sensitivity and specificity for the combination of GAD and IA-2 antibody was 67 and 100% respectively, and the sensitivity and specificity for the GAD or IA-2 antibody was 98 and 99% respectively. Therefore, in this case in which the patient presented with both GAD and IA-2 antibodies, he had unequivocally developed T1DM.

HHS can cause thrombosis, brain infarction, electrolyte abnormality, electrolyte abnormality and damage to multiple organs. The mortality rate of HHS is 5–20%, higher than that of DKA (7), so early detection and intervention is critical. According to the Clinical Practice Consensus Guidelines 2014 (8), this case met five of the six clinical criteria for HHS. While HHS is common in elderly patients with T2DM, it is rare in children with T1DM. Kershaw *et al*. (2009) reported only 2.5% of 121 children with DM presented with HHS, and only two developed both DKA and HHS (9). Moreover, McDonnell *et al*. (2005) reported that 5% (5/100) of patients with DKA developed HHS (10). Almost 1–5% of children with T1DM are likely to develop HHS, and all five patients developing HHS had consumed large volumes of soft drinks (4–8 L/day) in the 5 days prior to admission. Soft drinks commonly contain approximately 50–70 g sugar per 500 mL. Because blood insulin levels in patients with T1DM are significantly lower than that in those with T2DM, cellular glucose uptake is lower in T1DM than in T2DM. Consuming beverages with high sugar concentrations causes hyperglycemia and further exacerbates thirst, resulting in further beverage consumption.

The time between the onset of T1DM to HHS in our patient was longer than in previously described cases. He had developed symptoms related to diabetes 3 weeks before the time of his initial visiting; however, his blood HbA1c was already elevated to 12.3. We presumed that a relatively severe hyperglycemic state lasted several weeks before his initial visit and his insulin secretion ability was likely just about maintained. Although differences in race and environment may influence outcomes, we hypothesize that relatively stable insulin secretion capacity with mild ketosis, combined with the intake of moderate amounts of beverages, contributed to the slow development of HHS in our case. Soft drink ketosis is a famous glucose metabolic disorder similar to that in this case. Soft-drink ketosis is characterized by acute-onset ketosis induced by excessive ingestion of sugar-containing soft drinks in obese T2DM patients (11).

Rosenbloom (2010) reported that 74% of T1DM patients with HHS had BMI <25, and 90% of T2DM patients with HHS had BMI ≥25 (12). We should therefore suspect T1DM in patients with HHS but not obesity. Treatment for HHS in children requires extracellular fluid

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administration to alleviate dehydration and increase renal blood flow. Moreover, insulin treatment is essential for HHS with ketosis or ketoacidosis. We should carefully administer insulin to children with T1DM as they are especially sensitive to insulin treatment, and even the appropriate amount of insulin may result in dramatically decreasing blood sugar levels, as in our case.

In conclusion, we experienced an adolescent case of HHS from excessive beverage consumption, in which the patient was first suspected of having T2DM but had in fact already developed T1DM. The discrimination between HHS of T1DM and T2DM during initial presentation is difficult. Age, clinical history and body type are helpful in identifying T1DM and HHS. Specifically, drinking an excess of beverages rich in sugars in lean boys and girls represents a risk of HHS in T1DM patients.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding
This work did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

Patient consent
We obtained the informed consent for a case report from him and his mother.

Author contribution statement
W S and K J designed the case report and wrote the manuscript. W S, K J, O M, N K and M T collected and analyzed data. All authors read and approved the final manuscript.

Acknowledgements
The authors would like to thank Dr Keiko Ono (Department of Endocrinology and Metabolism, National Hospital Organization Kumamoto Medical Center) for assistance and advice in the diagnosis and treatment of this case. They thank all staff members in the Department of Pediatrics, National Hospital Organization Kumamoto Medical Center, for their help in clinical practice.

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Received in final form 8 February 2019
Accepted 13 February 2019