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Research letters

Hyperglycaemic hyperosmolar syndrome in a 5-year-old girl with newly diagnosed type 2 diabetes mellitus

Introduction

Hyperglycaemic hyperosmolar syndrome (HHS) is a life-threatening condition characterized by non-ketotic, non-acidotic severe hyperglycaemia, with high serum osmolality and altered consciousness or seizures [1,2]. The pathogenesis of HHS results from disturbances in glucose metabolism and fluid balance [3]. It arises when there is a critical deficit of insulin activity leading to a reduction of glucose utilization and severe hyperglycaemia [4]. Given the absence of lipolysis and ketogenesis in HHS, acidosis is not considered a typical finding.

Known precipitating factors for HHS include infections and other coexisting diseases, medication or substance abuse, poor compliance and undiagnosed diabetes mellitus [5]. Indeed, HHS is often seen in adults with type 2 diabetes mellitus (T2DM) and, due to the increased prevalence of obesity and T2DM in paediatric populations over the past three decades, the incidence of HHS in this age group has also been increasing [4].

The present report describes the case of a 5-year-old girl who presented with HHS and was also found to have T2DM. To the best of our knowledge, this is the youngest child with T2DM found to present with HHS.

Case report

This 5-year-old Sudanese girl arrived at our paediatric emergency department (ED) for a complaint of decreased activity and headache followed by drowsiness lasting for 1 day. She was a known case of morbid obesity and panhypopituitarism secondary to surgical resection of a craniopharyngioma and radiotherapy at the age of 3.5 years. She subsequently developed diabetes insipidus, hypothyroidism and glucocorticoid deficiency, and was maintained on a regimen of steroids (8.5 mg/m^2/day), levothyroxine and desmopressin. Although her fluid intake and output were well balanced, the patient continued to gain weight over time due to impaired satiety and uncontrolled caloric intakes.

Two months prior to her ED presentation, the patient had normal electrolyte and FT4 concentrations, but her HbA1c was 6.5% (48 mmol/mol). An oral glucose tolerance test (OGTT), along with daily multiple glucose monitoring were ordered, but the child's parents missed the follow-up appointment and showed up 2 months later with a normal OGTT report from another hospital, but no follow-up HbA1c or blood glucose readings.

Upon arriving at the ED, the patient was found to be in a state of moderate-to-severe dehydration. She had severe acanthosis nigricans, and her body mass index (BMI) standard deviation score (SDS) was +3.4. The initial laboratory results revealed severe hyperglycaemia, increased osmolality and mild acidosis with no ketonaemia (Table 1), which were consistent with HHS. Her HbA1c was 9.8% (84 mmol/mol), and computed tomography (CT) of the brain showed no signs of oedema or intracranial haemorrhage, and a normally sited ventriculoperitoneal shunt.

The patient was treated with two intravenous boluses of normal saline followed by subcutaneous insulin boluses, while urine output and serum Na and glucose levels were monitored. The patient's dehydration and hyperglycaemia gradually improved after the first 12 h of treatment. She was then maintained on a basal–bolus regimen of insulin glargine and lispro at a total daily dose of 0.8 units/kg/day, and was discharged home with the same hormone replacement therapy for hypopituitarism plus long-acting and short-acting insulin.

Her blood glucose readings on post-hospitalization follow-up after 1 month ranged from the 80s to low 100s of mg/dL with no episodes of hypoglycaemia. HbA1c levels fell to 7.9% (63 mmol/mol), and her anti-glutamic acid decarboxylase (GAD), anti-insulin and anti-islet antigen 2 (IA2) antibodies all came back negative, whereas insulin and C-peptide levels were high at 205 (normal range: 1.9–16.1) mIU/L and 2.8 (normal range: 0.37–1.47) nmol/L, respectively, with concomitant serum glucose at 7 mmol/L.

The patient's most recent HbA1c, measured 1 year after admission, was 5.7% (39 mmol/mol) while on the same basal–bolus insulin regimen, but with a lower total daily dose of 0.6 units/kg/day.

Table 1
Patient's laboratory results at the time of presentation at emergency.

Laboratory test	Results	Normal range
Corrected sodium	169 mmol/L	136–145
Potassium	4.9 mmol/L	3.6–5.1
Chloride	119 mmol/L	101–111
Bicarbonate	21 mmol/L	22–32
Creatinine	100 μmol/L	44–88
Urea	12.3 mmol/L	2.9–7.1
Random glucose	65.6 mmol/L	3.9–10
Calculated serum osmolality	440 mOsm/kg	
HbA1c	9.8%	4.4–6.4
Arterial blood gas		
pH	7.32	7.35–7.45
pCO_2	44 mmHg	35–45
pO_2	74.5 mmHg	80–100
HCO_3	22.1 mmol/L	22–26
Base excess	−3.9 mmol/L	−2–2
Lactate	2.6 mmol/L	0.5–2.2
Urine dipstick		
Specific gravity	1.010	1.016–1.022
Glucose	56 (4+)	≤3
Ketones	Negative	≤0.5

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Discussion

Our present report is of the youngest child, to the best of our knowledge, to be newly diagnosed with T2DM and presenting with HHS. Although the incidence of HHS in children is increasing, it is still considerably less frequent than diabetic ketoacidosis (DKA) [1]. Fourtner et al. [6] reported that 3.7% of adolescents with T2DM also presented with HHS. Rosenbloom [4] compared 26 cases of HHS reported during 1966–2000 with 65 reported and six unreported cases during 2001–2008, and found that all patients in the more recent group were aged > 9 years, with a male-to-female ratio of 3.5:1, and 75% of them were obese, whereas 73% of patients in the earlier reports were < 9 years of age and showed an equal gender distribution, with no reported cases of obesity [4].

Underlying infection represents the most common precipitating cause of HHS [7]. However, delayed diagnosis of new-onset T2DM with an insidious presentation could lead to the development of HHS as well, as in the case of our present patient, whose clinical presentation was similar to those of previously reported cases of children with HHS [4,7], except that she is one of the youngest so far and the index of suspicion was too low for such a diagnosis. Yafi and Collins [8] reported a case of Texan toddler with T2DM, but no HHS. This was thought to be the youngest child ever diagnosed with T2DM, although other causes of diabetes were not ruled out by the necessary genetic tests.

Most current case reports of HHS in T2DM are of adolescent patients, although other atypical presentations of HHS had been previously reported. Tsai et al. [9] reported on an obese 15-year-old African American boy newly diagnosed with T2DM who presented with HHS, but with a mixed picture of DKA, whereas Moued et al. [5] reported on a 7-year-old boy who presented with HHS with newly diagnosed type 1 diabetes mellitus complicated by hypernatraemic dehydration.

As an increasing prevalence of T2DM in children and adolescents of all ethnicities has recently been reported around the world [10], regular screening for diabetes in patients with risk factors, regardless the age, should be reemphasized to avoid diagnostic delays and to minimize the risk of life-threatening complications like HHS.

Conclusion

T2DM should be anticipated in children of any age as long as they show the typical phenotype and risk factors. Delaying the diagnosis could lead to more serious, and sometimes life-threatening, complications.

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Disclosure of interest

The authors declare that they have no competing interest.

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GLP-1 agonist associated acute kidney injury: A case report and review

Introduction

Glucagon-like-peptides (GLP)-1 agonists have gained popularity over the last decade and are being increasingly used in the management of obese diabetes type-2 patients, owing to their much desired weight loss benefits in addition to effective glycemic control. However, since the FDA approval of Byetta® (exenatide) in 2005, there have been cases of acute kidney injury (AKI) reported to the agency [1] and 11 such published cases [2–8], leading to FDA's revision of the drug label in 2008, to highlight that Byetta should not be used in patients with severe renal impairment or end stage renal disease.

All these cases of AKI have occurred in patients taking Byetta®, which needs twice daily dosing. However, in 2012, a new extended release (ER) preparation of exenatide, requiring once weekly dosing (Bydureon) was approved by the FDA. Ours is the first case of acute kidney injury (AKI) caused by the extended release formulation in a patient who had normal baseline renal function before commencing the drug. The patient had a distinctive clinical presentation that included a peculiar skin rash appearing just before the kidney injury and improvement with treatment of the same. Also included are the detailed renal biopsy report as the only two published biopsy reports of exenatide induced AKI, have