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CASE REPORT

Not all ketosis is type 1 – remember Flatbush

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Abstract

A 35-year-old otherwise healthy gentleman from Togo, was referred as a 'walk-in' to our clinic with polyuria and polydipsia, and a glycated haemoglobin (Hba1c) of 119 mmol/mol (13.1%). The patient also noted 5kg weight loss over a short span of time. He had a significant family history of Type 2 Diabetes Mellitus (T2DM). Initial blood tests revealed a blood glucose of 22.84 mmol/L, with positive ketones (1.2 mmol/L). Urinalysis showed glycosuria (1000 mg/dL) but was negative for nitrites and white cells. Renal, liver and thyroid function tests were all within normal limits. He had mild metabolic acidosis.

Key words: Atypical diabetes; Autoantibodies; Diabetic ketoacidosis; Ketosis-prone diabetes

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Introduction

Ketone-prone diabetes (KPD) or Flatbush diabetes is becoming increasingly recognised. This heterogenous type of diabetes is more commonly seen in male patients with a high Body Mass Index (BMI), with a family history of Type 2 Diabetes Mellitus (T2DM). Patients commonly present with ketosis and after an initial period of insulin therapy, may attain euglycaemia on diet or oral hypoglycaemic agents. Increased awareness improves timely diagnosis and management. We present a case of a middle-aged gentleman, with a presumed diagnosis of Type 1 Diabetes Mellitus (T1DM) at presentation and who was eventually rendered normoglycaemic on a single oral hypoglycaemic agent.

Case report

A 35-year-old otherwise healthy gentleman from Togo, was referred as a 'walk-in' to our clinic with new-onset diabetes and a glycated haemoglobin (Hba1c) of 119 mmol/mol (13.1%). He initially presented to his general practitioner with polyuria and polydipsia, and 5 kg of weight loss. He denied any change in bowel habits and had no recent illness or infections. He had a Body Mass Index (BMI) of 28 kg/m^2, and the rest of the examination was unremarkable. Both parents had Type 2 Diabetes Mellitus (T2DM) diagnosed in their 50 s. He worked as a shop assistant, drank alcohol socially, and was a life-long non-smoker.

Initial blood tests revealed a blood glucose of 22.84 mmol/L, with positive ketones (1.2 mmol/L). Urinalysis showed glycosuria (1000 mg/dL) but was negative for nitrites and white cells. Renal, liver and thyroid function tests were all within normal limits. He had mild metabolic acidosis as shown in Table 1. A markedly elevated blood glucose level in association with ketoacidosis strongly suggested a diagnosis of Type 1 Diabetes Mellitus (T1DM).

The patient was admitted to the diabetes ward and treated with a fixed-rate insulin infusion as per diabetic ketoacidosis (DKA) protocol. There was a fairly rapid improvement in both hyperglycaemia and ketonaemia within a few hours. Anti-glutamic acid (GAD), anti-insulinoma antigen 2 antibodies (IA2) and anti-insulin antibodies were all negative. The next day, the patient was discharged on a basal bolus regime of glargine and aspart after review by the inpatient diabetes team.

When the patient was reviewed by the diabetic specialist nurses, his glucose levels continued to improve with incremental insulin dose reductions and eventual complete cessation. As he continued to show borderline hyperglycaemia, he was given low-dose metformin (500 mg daily) to maintain near normal glycaemia and his Hba1c normalised after 6 months.

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Table 1. Initial investigations

	On admission	Reference range
Glucose		22.84
Creatinine (umol/L)	48	59–104
Urea (mmol/L)	5.4	1.7–8.3
Sodium (mmol/L)	130	135–145
Potassium (mmol/L)	4.07	3.5–5.1
Glycated haemoglobin (Hba1c, mmol/mol)	119	28–46
Venous blood gases		
pH	7.34	7.35–7.45
Partial pressure of carbon dioxide (pCO_2, kPa)	5.5	5.1–5.6
Partial pressure of oxygen (pO_2, kPa)	6.2	10.5–13.5
Lactate (mmol/L)	1.3	<2
HCO_3^- (mEq/L)	23.6	18–22
Chest X-Ray	Normal	
Electrocardiogram (ECG)	Normal sinus rhythm at 95 bpm	

A rapid response to insulin, and negative testing for type 1 autoimmunity, in a young gentleman of African origin, suggested a diagnosis of ketosis-prone/Flatbush diabetes was most likely. He continues with regular clinic reviews and is adequately controlled on low-dose metformin.

Discussion

KPD is an evolving, heterogenous syndrome which shares characteristics with both T1DM and T2DM (Lebovitz and Banerji, 2018). It mimics T1DM in both clinical and biochemical presentation (Colloby, 2014), yet is similar to T2DM with regards to beta cell dysfunction and long-term management. Its prevalence is highest in African-American and Hispanic populations (20–50%) (Bavuma et al, 2019; Sjoholm, 2019). Most commonly, KPD affects overweight, middle-aged men, with a family history of diabetes. Its aetiology and pathogenesis are still undetermined, but some studies suggest glucose desensitisation and pancreatic beta cell toxicity secondary to elevated glucose levels, leading to ketosis (Umpierrez et al, 2006; Lebovitz and Banerji, 2018). There are four subtypes, depending on preserved (β+) or absent (β–) beta cell reserve and presence (A+) or absence (A–) of autoantibodies, all measured around 3 months following presentation. Unlike T1DM, patients have normal C-peptide levels, and negative anti islet tyrosine phosphatase 2 (IA-2), anti-glutamic acid decarboxylase (GAD) and islet cell antibodies.

Patients often present with markedly elevated glucose levels and ketoacidosis. This classically follows a period of polyuria and polydipsia, with associated weight loss. In the acute phase, patients should be managed with intravenous insulin and fluids to help achieve normoglycaemia and improve acid-base balance. Any triggering factors such as infections should be managed accordingly.

Most patients with KPD will respond very well to a short period of insulin treatment and can often continue on diet or oral anti-diabetic medications alone. Sodium glucose co-transporters 2 (SGLT-2) should be avoided in view of an increased risk of ketosis. In > 70% of patients, anti-diabetic agents could be discontinued after a few months (Bavuma et al, 2019).

Learning points

- The aetiology of ketone-prone diabetes remains unknown. Further studies may help future therapies.
- A diagnosis of ketosis-prone diabetes should always be borne in mind in patients of African ethnicity presenting with new-onset diabetes and ketosis.
- Misdiagnosing patients with KPD as T1DM can lead to unnecessary treatment with long-term insulin therapy, with all its implications (e.g., hypoglycaemia, occupational impact).
- Hyperglycaemia in patients with KPD is often rapidly responsive to insulin treatment with quick conversion to oral hypoglycaemic agents or diet alone.
- Subtyping patients with KPD according to the Aβ classification may be useful in predicting response to long-term insulin (β– subgroups) or oral agents (β+ subgroups).

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Availability of data and materials

All the data of this study are included in this article.

Author contributions

SC, AM and DC made substantial contributions to the conception and design, acquisition of data, analysis and interpretation of data. SC, AM and DC drafted the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics approval and consent to participate

The patient provided signed consent for publication of this case report.

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Conflict of interest

The authors declare no conflict of interest.

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