Ketosis Prone Type 2 Diabetes: A Case Report

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Abstract

This case demonstrates a rare presentation of 28-year-old Omani woman, who was admitted with features suggestive of diabetic ketoacidosis and was discharged on basal-bolus insulin therapy. However, Anti-GAD and islet-cell antibodies were negative and her C-peptide was normal. Subsequent to her discharge, she experienced recurrent hypoglycaemic episodes, necessitating a reduced insulin dosage, and her physician ultimately discontinued insulin therapy and initiated treatment with metformin. Her glycosylated haemoglobin was well controlled. This case sheds light on the topic of ketosis-prone type 2 diabetes (KPT2D) and highlights the complex clinical subtleties, epidemiological viewpoints and ongoing research that make up KPT2D. Giving important information on its unique pathophysiology and treatment strategies, the study emphasises the need for tailored therapies, which advances our understanding of diabetes mellitus throughout time.

Keywords: Diabetes Mellitus, Ketosis-Prone, Type I, Sudden-Onset, Autoimmune, Oman.

Introduction

Type 1 diabetes mellitus (type 1 DM) results from an autoimmune attack on pancreatic beta cells, mainly affecting the young and requiring a lifelong treatment with insulin therapy. Conversely, type 2 diabetes mellitus (type 2 DM) involves insulin resistance and inadequate production and is typically seen in older adults with symptoms developing gradually. Latent autoimmune diabetes in adults (LADA) combines attributes of type 1 and type 2, emerging in adulthood and often initially being managed without insulin. Maturity-onset diabetes of the young (MODY) includes rare monogenic variations influenced by genetic mutations, usually identified at a younger age and treated through diverse approaches.[1] Within these, ketosis-prone type 2 diabetes (KPT2D), known as "Flatbush diabetes", marks a distinctive presence in sub-Saharan Africa and among individuals of African descent. This variant mirrors features of both type 1 and type 2 diabetes, showing sporadic insulin needs during spontaneous ketotic episodes.[1] Ketosis-Prone Type 2 Diabetes Mellitus (KPT2DM) is a form of diabetes that presents with an acute episode of diabetic ketoacidosis (DKA), but in individuals who exhibit features of Type 2 diabetes, such as obesity, insulin resistance, and the ability to discontinue insulin therapy after initial treatment. Unlike Type 1 diabetes, where patients are insulin-dependent for life, people with KPT2DM may regain sufficient beta-cell function to manage their diabetes with oral medications or diet alone. However, they remain at risk for future metabolic decompensation and episodes of DKA.[2]

This disease challenges conventional diabetes care, as demonstrated by the experiences of the current case of a 28-year-old Omani woman. Her story takes an unexpected turn as she initially presented with features suggestive of diabetes ketoacidosis (DKA), but her diagnosis later changed. To the best of our knowledge, this is the first case reported in Oman.

Case Report

A 28-year-old Omani woman, para 2, last child birth was three years ago, was admitted with diabetes ketoacidosis (DKA), characterised by symptoms of polyuria and polydipsia, a blood sugar level of 32 mmol/L, significantly elevated urine ketones (3+), a pH of 7.2 and an HCO_3 level of 14 mmol/l. Examination revealed a body mass index of 39.6 kg/m^2 and the presence of acanthosis nigricans. Her blood pressure was 125/75 mmHg and her heart rate was 75 beats per minute, temperature was 37.5 C. Vital signs and systemic examination were normal. Laboratory investigations revealed normal complete blood count, renal function test, thyroid function test and chest X ray. The patient received treatment in accordance with the DKA protocol. She received IV fluid, IV insulin and potassium. After 5 days, she was discharged on insulin glargine 22 units and insulin lispro 8 units three times a day, to a total of 46 units (0.4 units/kg). Interestingly, anti-GAD-65 and anti-Islet cell antibodies were negative. Her C-peptide level was 502 pmol/L (normal) and her LDL cholesterol was 3.1 mmol/l (reference: less than 2.6 mmol/l). Subsequent to her discharge, she experienced recurrent hypoglycaemic episodes ranging from 3.0 to 3.9 mmol/l, which were aborted by the consumption of sugary drinks. The frequent hypoglycaemic episodes necessitated a reduced insulin dosage and her physician ultimately discontinued insulin therapy and initiated treatment with metformin. A few months later, the patient discontinued metformin by herself and remained euglycaemic. Her most recent HgbA1c measurement was 6.6% (it was 12% at baseline). Of note, the patient had history of gestational diabetes mellitus (GDM) in the last pregnancy three years ago and was treated with diet only. Moreover, there was no family history of diabetes mellitus. After a thorough investigation, a diagnosis of rare type of diabetes was reached: ketosis-prone type 2 diabetes (KPT2D).

Discussion

KPT2D is a distinct subset of the diabetes spectrum that mostly affects people of African origin.[2] Given the frequency of KPT2D in African and African American groups, as well as in African-Caribbeans suffering from diabetic ketoacidosis, a thorough understanding of its clinical implications is crucial.[3]

According to International Diabetes Federation projections, the incidence of diabetes is expected to rise significantly in Africa, accounting for a 100% increase between 2010 and 2030. It is projected that KPT2D will account for over half of all African American diabetics who are diagnosed with ketoacidosis.[4] Epidemiological assessments are made more difficult by the lack of accurate prevalence data and the nosological difficulties in differentiating KPT2D from type 1 and type 2 diabetes.[5]

Sjöholm Å et al.[1] discussed five cases of KPT2D. The first case involved a 45-year-old man from Congo, with a BMI of 29.5 kg/m^2, who presented with classic catabolic symptoms. His blood investigations revealed an A1c of 14.2%, urine ketone 4+ and negative autoantibodies. He required an initial insulin dose of 82 U/d. However, following the patient's discharge, there was a notable and rapid reduction in insulin requirements. Additionally, the patient reported frequent occurrences of hypoglycaemia, leading to the discontinuation of insulin and the initiation of sitagliptin. Upon follow-up, the patient exhibited excellent glycaemic control. In the second case, a 34-year-old woman from Somalia, with a BMI of 29.8 kg/m^2, an initial A1C of 11.4%, with ketosis, required very high dose of insulin therapy (186 U/d). Substantial progress was noted in the follow-up, with a remarkable reduction in A1C of (5.5%) and a reduced insulin requirement to 18 U/d. The third case involved a 22-year-old man from Sierra Leone, with a BMI of 26.7 kg/m^2, who presented with catabolic symptoms and severe ketosis. His initial A1C was 16.0% and autoantibodies were negative. He was started on insulin therapy at a dose of 0.44 U/kg. However, his insulin requirement reduced substantially during follow up and ultimately stopped and replaced with metformin and sitagliptin. The fourth and fifth cases showed almost similar presentation with high blood glucose and ketosis. The fourth case was a 36-year-old man from Somalia, diagnosed with Ketosis prone Diabetes and an initial A1C of 9.2%, The follow-up showed an A1C of 5.8%, leading to the discontinuation of insulin and initiation of saxagliptin and dapagliflozin. The fifth case involved a 29-year-old man from Somalia, with an initial A1C of 9.7%. Initially he was started on 26 U/d of insulin, but the follow-up demonstrated an A1C of 6.2% and the insulin was discontinued.

Middle-age, a positive family history and dysmetabolic features are clinical factors shared by KPT2D patients that are consistent with T2D characteristics.[6] However, the disease's abrupt onset, which is frequently accompanied by extreme hyperglycaemia and ketosis, mimics several features of T1D, leading

to diagnostic challenges.[7] When autoantibody studies provide negative findings, it can be confusing and lead to an incorrect diagnosis.[8]

Unlike T1D, current research reveals that impaired ketone oxidation rather than enhanced ketogenesis is the cause of ketosis in KPT2D, suggesting underlying defects in mitochondrial substrate metabolism.[9] Additionally, post-discharge remission in KPT2D patients, which is characterised by a significant decrease in insulin requirements, suggests a reversible β-cell malfunction brought on by glucotoxicity.[10] Lipotoxicity does not seem to play a role in the pathophysiology of KPT2D, in contrast to T2D. However, it is still unknown how long-term ketonemia affects β-cell activity. Moreover, peripheral insulin resistance has been reported, adding even more complexity to the clinical picture, particularly in skeletal muscle.[11]

Treatment paradigms for KPT2D have changed, with current approaches including medications such as sitagliptin and metformin.[12] Limited information on the best drugs to choose highlights the need for more studies. The use of oral anti-diabetic medication post-insulin treatment and a strong C-peptide response to stimulation, which suggests the possibility of continued β-cell activity, are predictors of extended remission.[13] The risk of DKA recurrence in KPT2DM patients is a significant concern, and limited evidence in the literature indicates that this risk is influenced by several factors, including metabolic stress (such as infection or trauma), non-adherence to treatment, insulin deficiency, and ethnicity. One study found that Hispanic patients had greater beta-cell functional reserve and were less likely to require long-term insulin therapy.[14] Therefore, educating patients on the importance of adhering to their treatment plan and regularly monitoring blood glucose levels is crucial for the effective long-term management of KPT2DM.

Conclusion

As the case report shows, KPT2D is still a clinical conundrum, with complicated aspects of diagnosis and treatment. The need for ongoing studies is highlighted by the complicated pathophysiology characterised by reversible β-cell malfunction and different clinical characteristics. A thorough understanding of KPT2D is essential in the dynamic field of diabetes care to develop methods that effectively treat diabetes mellitus.

Disclosure

The authors declared no conflicts of interest. Informed consent was obtained from the patient.

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