Severe DKA at presentation in young people - is it always type 1 diabetes?

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Introduction

Diabetes mellitus is caused by deficient insulin secretion, resistance to the action of insulin, or both.[1] It usually manifests as type 1 diabetes (T1DM) and type 2 diabetes (T2DM). While both types lead to high glucose levels, the pathogenesis, diagnosis and management of these conditions differ greatly. T1DM, an autoimmune disorder, involves the destruction of beta cells in the pancreas, resulting in a complete lack of insulin. T2DM is characterised by the body's reduced sensitivity to insulin and a gradual decrease in insulin production.[2]

Identifying the specific type of diabetes is essential for effective disease management. T1DM typically manifests during childhood or adolescence and is characterised by a sudden onset of symptoms such as excessive thirst, frequent urination and unexplained weight loss. Diabetic ketoacidosis (DKA) is a significant risk for those with T1DM, as it can be fatal. T2DM typically has a more gradual onset in adults, and can be asymptomatic for an extended period. Diagnosis is confirmed by measuring increased levels of glycosylated hemoglobin (HbA_{1c}) and fasting or random plasma glucose levels, with the need for repeat testing if a person is asymptomatic.[3] Given the increasing prevalence of T2DM in children and young people, it is essential to distinguish and diagnose diabetes effectively in this age group, ensuring that T1DM is not overlooked and T2DM is accurately identified, in order to optimise risk management.

There are significant differences in the treatment approaches for the two types of diabetes. Individuals with T1DM must administer lifelong insulin therapy. Treatment for T2DM typically begins with implementing lifestyle modifications such as dietary adjustments and physical activity, with options in oral and injectable medications tailored to risk factors, and, if necessary, insulin therapy.

We present two distinct cases of severe DKA and newly diagnosed diabetes, emphasising the intricacies associated with differentiating between T1DM and T2DM in young adults who present acutely in severe DKA.

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Case 1

Patient information: A 19-year-old male of Somali origin with obesity (BMI 40 kg/m^2) and a history of immune thrombocytopenia presented after three days of vomiting. He reported two weeks of lethargy, polyuria and polydipsia. There was a family history of T2DM (his father).

Clinical findings: He was found to be tachycardic with deep, laboured breathing indicative of Kussmaul respiration on presentation to the emergency department (ED). Dehydration and mild epigastric tenderness were observed but the rest of the abdominal examination and systemic examinations were unremarkable. Obesity and the presence of acanthosis nigricans were noted.

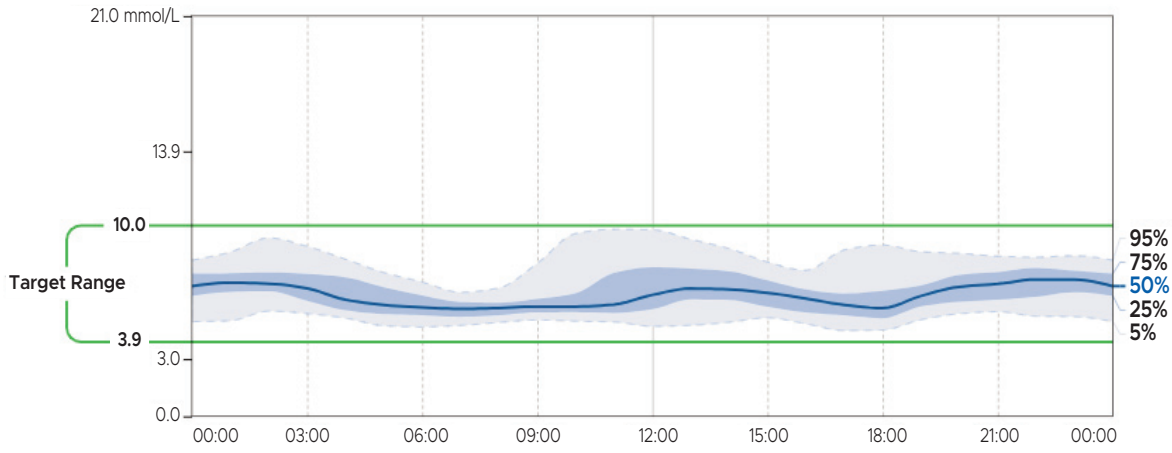
Timeline: A two-week history of polyuria, polydipsia and progressive fatigue was elicited. In the three days prior to presentation at the ED, he reported multiple episodes of vomiting daily.

Diagnostic assessment: The patient was found to have leukocytosis and near-normal CRP levels. Venous blood gas (VBG) measurement revealed a pH of 7.061, high ketones (>6mmol/L) and a blood glucose of 38 mmol/L, confirming the diagnosis of diabetic ketoacidosis (DKA). His initial HbA_{1c} 9.7%, and a diabetes autoantibody profile was sent during admission.

Therapeutic intervention: Since the patient had severe acidosis, he received ITU care with IV fluids and insulin according to the DKA protocol. He continued to need high insulin doses even after DKA resolution. He was discharged on Humulin I and Novorapid, with virtual follow-up for diabetes management using a continuous glucose monitor (CGM).

Follow-up: The autoantibody screen was negative for all four screened autoantibodies: GAD, ZnT8, IA-2 and islet cell. Along with symptomatic improvement his insulin requirement dropped significantly from 96 units/day initially to 64 units/day three months post-discharge, aided by dietary changes and weight loss. CGM showed excellent time-in-range, glucose management indicator (GMI) 6.1% and low glucose variability of 18.2% (Figure 1). C-peptide levels will be checked three years post diagnosis.

Figure 1. Freestyle Libre tracing in Case 1, highlighting low glucose variability and high time in target glucose range on reducing SC insulin doses during outpatient follow-up



Average glucose - 6.5mmol/L
Glucose Management Indicator (GMI) - 6.1% or 42 mmol/mol
Glucose Variability Defined as a percent coefficient or variation (%CV); target ≤36% - 18.2%

Case 2

Patient information: The patient was a 35-year-old white British male with obesity (BMI 39.5 kg/m^2) and a family history of pre-diabetes (his mother). His alcohol intake was excessive: he reported 40-50 units weekly, and he was a current smoker of 10-15 cigarettes per day. He presented with a four-day history of vomiting, epigastric pain, polyuria and lethargy.

Clinical findings: He was clinically dehydrated with documented polyuria and polydipsia. He had mild tenderness in the epigastric region upon examination, with normal bowel sounds and no guarding.

Timeline: The initial onset of symptoms was four days prior to admission, although he described a one-year history of indigestion associated with acid reflux. He took no regular medication prior to hospital admission in February 2024.

Diagnostic assessment: Blood tests on admission revealed raised infection markers and acute kidney injury (AKI), but a septic screen (CT-AP and chest X-ray) found no evidence of infection. Elevated blood glucose (21.4mmol/L), ketonemia (6.0mmol/L), and metabolic acidosis (pH 7.04, HCO3 7.8mmol/L) on VBG met the criteria for severe DKA, requiring high dependency unit (HDU) management. His amylase level was checked given his epigastric pain but was found to be normal at 69 U/L). His HbA_{1c} was 9.4% and a diabetes autoantibody profile was requested.

Therapeutic intervention: The patient was treated for DKA and AKI, with IV insulin and IV fluids. He was discharged from hospital after a five-day admission on insulin therapy (Humulin I and Novorapid) and metformin, and was given lifestyle and dietary advice.

Follow-up: The diabetes autoantibody profile was negative. He achieved weight loss with dietary interventions and insulin doses were reduced. Five months post admission he continues on Humulin I 20 units twice daily and 10 units Novorapid with meals, with excellent glycaemia results; his most recent HbA_{1c} level was 6.2% (44mmol/mol).

Discussion

We describe the first clinical presentation of diabetes in two young males admitted to the hospital with severe DKA. In both cases, high BMI (obesity), and a family history of T2DM were elicited. However, one was of Somali origin, the other White British. In both, there were negative diabetes autoantibodies at presentation, and following DKA management insulin requirements decreased over a period of months, with low glycaemic variability, high time-in-range and near-normal HbA_{1c} levels.

DKA, historically considered a hallmark of T1DM, is now more frequently recognised in those with T2DM, with its incidence reaching up to 24% of all DKA episodes in the UK.[4] DKA incidence in T2DM is higher in patients of non-White ethnicity.[5] Clinicians should suspect T2DM in patients presenting with DKA if risk factors such as obesity and family history are present. In T2DM, DKA results from relative insulin deficiency, due to persistent 'glucose toxicity' from hyperglycaemia and stressors, triggering lipolysis and ultimately DKA. While there may not always be a specific trigger, infections and poor compliance with glucose-lowering therapy are the most common precipitating factors for DKA in both T1DM and T2DM.[5] The recognised concept of ketosis-prone diabetes (KPD) aligns with this mechanism. KPD was first described in the 1960s, and as a result of incorporating features of both T1DM and T2DM this entity has a variety of terminologies, including type 1b, idiopathic type1 diabetes, Flatbush diabetes, type 1.5 diabetes mellitus, latent autoimmune diabetes in adults (LADA), and ketosis-prone type 2 diabetes.[6] LADA is immunologically similar to T1DM, with

Key messages

- DKA is increasing recognised in individuals with type 2 diabetes, almost one quarter of episodes of DKA in the UK
- Obesity, family history of T2DM and lack of diabetes autoantibodies can guide towards classification of diabetes type.
- The emergence of non-insulin based therapies with significant metabolic benefits, necessitates the need for correct diagnosis as early as possible.

the presence of autoantibodies.[7] KPD is predominantly reported in non-White populations and is frequently associated with overweight and obesity.[8] Classification of KPD according to antibody status (A+/-) and beta cell function (B+/-) utilising C-peptide levels can guide prognosis and ongoing treatment. A-B+ KPD patients may phenotypically have T2DM but present in DKA.[5] Following DKA resolution insulin therapy can often be withdrawn, with excellent blood glucose levels maintained on oral agents.[6]

The Exeter calculator is a diagnostic tool to aid determination of the probable diabetes type, particularly MODY, and to distinguish the likelihood of T1DM or T2DM. There is the caveat that this was developed for the white British population.[9] Using this tool, the probability of T1DM is just 16% in case 1, and 1% in case 2. Autoantibodies (islet cell, anti-ZnT8, anti-GAD and anti-IA2) and C-peptide levels, along with clinical features, are key diagnostic tools for identifying diabetes type. C-peptide levels reflect the functional status of pancreatic beta cells. During the early 'honeymoon phase' of T1DM, with residual pancreatic function, C-peptide levels may appear near normal; therefore, it is ideal to check them three years post-diagnosis.[10] They have not yet been assessed in the patient cases described.

Evidence of beta cell function enables physicians to treat with non-insulin-based therapies, such as GLP-1 agonists. These offer weight loss benefits, particularly in patients with obesity. This is a crucial modifiable risk factor in these young individuals to optimise cardiovascular risk, with the potential for diabetes remission.

Conflict of interest None to declare.
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