Type 1 diabetes presenting initially as type 2 diabetes which remitted with lifestyle change: a case report

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Abstract

We present a case of type 1 diabetes (T1DM) in a middle-aged Caucasian woman who initially presented with phenotypic characteristics of type 2 diabetes (T2DM) and whose type 2 phenotype contributed to accelerated progression of T1DM. This case illustrates the challenges in making a clinical diagnosis of T1DM in patients who also have phenotypic features of T2DM. Recognising such presentations is important in order to make the correct diagnosis and potentially to offer immunotherapy-based interventions while beta cell function is still relatively well preserved.

Introduction

Diabetes mellitus is a metabolic disorder characterized by chronic elevation in blood glucose levels due to abnormalities in insulin secretion, action or both.[1] Type 1 diabetes (T1DM) is caused by the autoimmune destruction of beta cells, which leads to persistent hyperglycaemia.[2] Type 2 diabetes (T2DM) is secondary to insulin resistance and relative insulin deficiency.[3] Predisposing factors for type 2 are common and include obesity, family history, ethnicity and drug treatments.[3]

Case history

A 41-year-old Caucasian female presented to her GP in May 2023 with a 3–4-month history of polyuria, polydipsia and fatigue. Gestational diabetes was diagnosed in her two pregnancies in 2013 and 2017 based on oral glucose tolerance tests: in 2013 her FBG was 4.5 mmol and 2-hour glucose 6.4 mmol and in 2017 her FBG was 5.1 mmol and 2-hour glucose 7.7 mmol. She was subsequently noted to have a normal HbA_{1c} post-pregnancy in 2019. She was previously told that she had high blood pressure but was not on any treatment. There was no family history of diabetes or autoimmune disorders, and she did not smoke.

Investigations done by her GP showed a HbA_{1c} level of 101 mmol/mol. She had no ketones in her urine. She was commenced on metformin 500 mg twice daily with a provisional diagnosis of T2DM and was referred to secondary care for advice.

By the time she was first seen in clinic in September 2023, her weight had reduced by 16 kg since her initial presentation (following lifestyle changes), and she weighed 82.3 kg with a body mass index (BMI) of 29.5 kg/m^2. The osmotic symptoms with which she had presented to her GP in May 2023 had resolved and her HbA_{1c} had improved to 31 mmol/mol. Given her atypical presentation, testing for antibodies associated with T1DM was requested and she was found to be positive for anti-GAD, IA2 and ZnT8 antibodies. C-peptide levels done at the same time were within the normal range (Table 1).

Results

Table 1. The patient's blood test results on 20/9/2023

Test	Result	Reference range
Anti-glutamic acid decarboxylase antibody	>2000.0 U/mL	0.0 - 10.9
Anti-tyrosine phosphatase-like IA2 antibody	>4000.0 U/mL	0.0 - 7.4
Zinc transporter 8 islet autoantibody	208.6 U/mL	0.0 - 9.9
C-peptide	874 pmol/L	350-1800 pmol/L.
Glucose (random plasma)	5.4 mmol/L	Less than 11.1 mmol/mol

Management

Based on her antibody positivity, a diagnosis of T1DM was made. As her blood sugar levels were stable, she remained under diabetic specialist nurse follow-up, with regular monitoring. She did not require insulin for the first year following her diagnosis of T1DM.

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In October 2024 she presented with recurrence of her symptoms. She was unable to control her glucose levels despite continuing and intensifying diet and lifestyle changes. A repeat blood test showed that her HbA_{1c} had increased to 75 mmol/mol. In view of her underlying diagnosis of T1DM, she was started on basal insulin, with small bolus doses for her main meal. Her glycaemic control improved after commencing insulin, with her CGM uploads showing 89% of her blood sugars within Time in Range, 0% Time Below Range and a coefficient of variation of 20.2%.

Discussion

This case illustrates the challenges in diagnosing T1DM based on phenotypic characteristics alone. High BMI, absence of ketones and a history of hypertension may have led to the initial diagnosis in this case. With rising levels of obesity, many patients with T1DM may present with features suggestive of T2DM. It is accepted that the presence of two or more antibodies associated with β-cell destruction can be used to make a diagnosis of T1DM.[2,4] Incidental single positive antibodies are seen in up to 5.9% of people without diabetes.[5]

Challenges in differentiating between T1DM and T2DM at presentation have been described previously. A study in the UK of 1,048 newly diagnosed people with diabetes aged 18-50 identified age and BMI as the best discriminators between T1DM and T2DM, although these had poor sensitivity.[6] As was evident in this case, checking antibodies for T1DM can help make a definitive diagnosis where there are overlapping phenotypic features. Research has shown that insulin resistance contributes to more rapid progression of T1DM and that improving insulin resistance delays the presentation of hyperglycaemic T1DM.[7-10] In this case, obesity-induced insulin resistance appears to have accelerated her symptomatic presentation. Subsequent weight loss and lifestyle changes improved what appeared to be stage 3B T1DM to an HbA_{1c} compatible with stage 1 T1DM.[11]

T1DM has been classified into three stages depending on the presence of antibodies, dysglycaemia and symptoms of hyperglycaemia (Table 2).[4]

C-peptide testing would usually be reserved for later in the course of T1DM, but in this case the test was accidentally sent at the time of the diagnostic testing and helped to confirm the level of beta cell function at that time, along with implying that the previous dysglycaemia was not predominantly due to beta cell failure.

Table 2. Classification of T1DM stages

Stage 1 T1DM	Presence of two or more diabetes-related auto-antibodies in an individual without dysglycaemia or symptoms
Stage 2 T1DM	Individuals have abnormal glucose levels i.e. impaired glucose tolerance on an oral glucose tolerance test and / or impaired fasting glycaemia. However, they do not meet the diagnostic criteria for diabetes.
Stage 3 T1DM	Individuals meet the diagnostic criteria for diabetes. Additional sub-classifications or stages are likely to be adopted for this stage (Stage 3a [asymptomatic] or Stage 3b [symptomatic][12]

The rate at which T1DM progresses to insulin dependence is variable and is affected by several factors including age, genetics and the autoimmune profile. A faster rate of progression of T1DM from presymptomatic to symptomatic is associated with young age: studies have shown that children with diagnosis of T1DM progress more rapidly, and adults progress more slowly.[13] In addition, individuals with higher autoantibody titres and positivity for multiple autoantibodies are likely to experience more rapid progression to hyperglycaemic T1DM.[14]

T2DM is being seen more commonly in young adults. In May 2024 Diabetes UK reported that there was a significant increase in diagnosis of T2DM in young adults. The number of people under 40 diagnosed with T2DM in the UK increased by almost 40% between 2016–17 and 2022–23.[15] This trend has been observed in recent epidemiological studies globally.[16] Risk factors associated with this trend include increasing obesity and sedentary lifestyle.[17] T2DM is now more common than T1DM in young adults.[18] There is, therefore, a risk of misclassification of diabetes type and the associated risk of consequent inappropriate treatment.

Guidelines from NICE in 2022 and from the American Diabetes Association in 2025 highlight the importance of recognising T1DM across all age groups and not relying on age and BMI alone to exclude T1DM.[19,13] In order to reduce the risk of misclassification of diabetes type, these guidelines recommend early consideration of antibody testing and measurement of C-peptide levels.

It can be expected that similar cases to the one described here will be seen in clinical practice as a consequence of the increase in population risk factors for T2DM. Making a definitive diagnosis is important: there are opportunities to intervene early and to prevent or delay the presentation of T1DM. Emerging immunotherapies such as teplizumab, an anti-CD3 antibody, have shown promise in delaying progression to symptomatic T1DM.[20] The American Food and Drug Administration (FDA) has approved teplizumab treatment to delay progression of T1DM to stage 3 in adults and paediatric patients aged 8 years and above.[21] In the UK teplizumab is being reviewed by the Medicines and Healthcare products Regulatory Agency (MHRA).[21] This emerging therapeutic intervention with immunotherapy has encouraged research programmes internationally and in the UK. The UK T1D Research Consortium is running trials for treatment (STRIDE - currently on hold), monitoring (ADDRESS2) and screening (T1DRA, INNOVA and ELSA studies).[22]

Conclusion

We present a case in which the phenotypic features of T2DM were associated with an earlier presentation of underlying T1DM. The 'type 2' element of the diabetes reversed following lifestyle changes, but with time, the T1DM progressed to become symptomatic. These phenotypic features are common in the community and could lead to misdiagnosis, and to inappropriate management and follow-up. Therefore, it is important to consider appropriate antibody testing for T1DM.

Key messages

- The diagnosis of type 1 diabetes can be made using two or more relevant antibodies
- The distinction of type 1 and type 2 diabetes can be difficult
- Features seen in type 2 diabetes contribute to the clinical presentation of type 1 diabetes

In the future it is possible that identifying T1DM earlier in its progression, as a result of these presentations, may offer an opportunity for immune-based therapeutic interventions.

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