Diagnosis of type 1 diabetes mellitus in adulthood – a case report

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A Caucasian woman, 55 years of age, was referred to a general practitioner (GP) after an optometry assessment revealed possible signs of diabetes. Her blood glucose, measured at a community pharmacy, was found to be 28.5 mmol/L. The patient was generally healthy and not on any regular medications. She had a hereditary solitary kidney but renal function had always been normal. On specific questioning, she reported a short history of polyuria and polydipsia. There was also history of intermittent epigastric and right upper quadrant abdominal pain over several years and, more recently, these pains were associated with meal times and so she had decreased her food intake. There was no unintended weight loss. An abdominal ultrasound, performed 2 months prior to investigate these symptoms, had revealed no biliary pathology. Routine blood tests collected at that time revealed a fasting glucose level of 6.3 mmol/L. An oral glucose tolerance test had not been performed. There was no family history of diabetes.

At presentation, examination findings were normal. Blood pressure was 120/80 mmHg and heart rate was 80 beats per minute. Abdominal examination was unremarkable. She weighed 57 kg and was 158 cm tall (body mass index of 22.8 kg/m^2). Clinically, there were no signs of dehydration. Neurological examination revealed decreased vibration sensation only in her first metatarsophalangeal joints bilaterally. Urinary ketones were negative, but glucose was moderately positive on urine dipstick analysis. Random blood glucose was 26.3 mmol/L, but blood ketones were not available.

A diagnosis of diabetes mellitus was considered and the patient was sent for urgent investigations including fasting blood glucose, electrolytes, liver, kidney and thyroid function tests, and a coeliac disease screen in case gluten intolerance was causing her abdominal pains with meals. The patient was asked to return within the next 24 hours for results of the initial tests. Fasting glucose was 15.6 mmol/L and HbA1c was 10.3% (89 mmol/mol). Thyroxine (T4) was mildly elevated at 20.9 pmol/L but thyroxine stimulating hormone (TSH) was within the normal range. Albumin:creatinine ratio, measured on a spot urine sample, was 14.5 mg/mmol, which is indicative of microalbuminuria. There were no previous assays to use as a comparison. The coeliac disease screen was negative.

On the basis of these initial results, the patient was advised to commence insulin treatment. She was reluctant to accept this, despite attempts to explain the importance of glycaemic control, the need to avert diabetic ketoacidosis and the likelihood of substantial symptom relief from the control of her hyperglycaemia. The patient decided to adopt a strict 'raw' diet and observe its effect on her blood glucose levels. Given the rapid onset of hyperglycaemia in this case, further testing for autoimmune pathology was indicated. Within the week, the results returned with strongly positive glutamic acid decarboxylase (GAD) antibodies, insulinoma antigen-2 (IA2) antibodies and islet cell antibodies, confirming a diagnosis of type 1 diabetes mellitus.

Despite this, the patient could not accept the need for insulin treatment. Against medical advice, she managed to keep her blood glucose levels remarkably well controlled initially with a low-carbohydrate diet. Despite being advised that dietary modifications alone would be unsustainable to manage her blood glucose levels while ensuring adequate nourishment, she resolved to continue a low-carbohydrate

diet for a further week. A postprandial serum assay revealed reduced serum C-peptide levels, confirming depletion of endogenous insulin.

Further education regarding the absolute insulin depletion in type I diabetes was still met with refusal to consume a more feasible, balanced diet and commence insulin therapy.

The patient returned 1 week later complaining of worsening visual acuity, particularly with long distance sight, intense hunger and a concern about the effects it would have on her driving. At this stage she began to accept her condition and the medical and nutritional management required, permitting the necessary treatment and allied health professionals to be involved in her care. She remains defiant, however, over the need to use insulin.

Discussion

Type 1 diabetes mellitus results from a T-cell-mediated destruction of pancreatic beta islet cells, resulting in rapid progression to absolute insulin deficiency. Of patients newly diagnosed with type 1 diabetes, 80% are positive for GAD or IA2 antibodies,[1] whereas 20% are antibody negative at the time of diagnosis.[2] The risk of developing diabetes over a 10-year period, on the basis of positive GAD and IA2 antibody tests, is three times greater with a family history of type 1 diabetes in a first-degree relative.[2] This patient had no family history of type 1 diabetes or of any autoimmune disease.

The incidence of anti-islet cell autoantibodies is 31% in type 1 diabetes, 6% in non-type 1 diabetes and 8–9% in unaffected first-degree relatives of people with type 1 diabetes. This is in contrast to type 1a diabetes, also called latent autoimmune diabetes of adulthood (LADA), where there is a more insidious progression of hyperglycaemia due to insulin resistance.[2] The development of GAD antibodies in adulthood is associated with type 1 diabetes, but also occurs in adults developing type 1a diabetes.[3] Interestingly, the BABY-DIAB study,[4] TEEN-DIAB study[5] and the Diabetes Autoimmunity Study in the Young (DAISY)[6] have shown that in children these anti-islet cell antibodies can first appear in early life and are predictive of the development of type 1 diabetes later in life. These antibodies are also present in 1% of individuals without diabetes, although usually at low titre.[7]

This case highlights an important diagnostic point, that types 1 or 1a diabetes should be considered in adult patients who present with particularly rapid-onset hyperglycaemia. In this case, there was no evidence of other associated autoimmune conditions. Coeliac disease is known to occur in up to 10% of patients with type 1 diabetes,[8] and there is a strong association between type 1 diabetes and autoimmune thyroiditis.[9] Although there have been numerous immunological markers identified in types 1 and 1a diabetes,[10] the commercially used assays that are acceptably sensitive and specific for the condition are the anti-GAD and anti-IA2 antibodies.[2] Early detection of autoimmune diabetes mellitus in adults ensures appropriate treatment of the condition and early establishment of euglycaemia,[11] which supports a legacy effect of blood glucose control,[12] and reduction in the risk of complications such as diabetic nephropathy and retinopathy.

Although it is possible to predict the development of type 1 diabetes through human leukocyte antigen (HLA) genetic predisposition and the appearance of islet cell autoantibodies,[13,14] none of the treatments trialled to date have been able to arrest the progressive loss of insulin secretion resulting from destruction of beta islet cells.[15] Further research has enabled identification of another major islet autoantigen, zinc transporter-8 (ZnT8), which is associated with beta islet cell secretory granules. Antibodies against ZnT8 are found in about 70% of patients with type 1 diabetes and may predict the development of the disorder, thereby providing an opportunity to treat patients before the onset of autoimmune beta cell destruction.[16]

It is also pertinent to consider the psychological effects of such a diagnosis in adulthood. Significant changes across all areas of life are generally required and the condition has the potential to affect work and family life. As with other chronic disease diagnoses, patients would be expected to experience the usual stages of bereavement, and GPs play a pivotal role in supporting these patients to overcome the grief of the diagnosis. Beyond accurate and timely diagnosis of the condition, education and instilling confidence in the adult patient newly diagnosed with type 1 diabetes is critical to the patient's ability to self-manage. Indeed, there is a need not only for counselling and support from the GP, but also the consideration of additional counselling from allied health professionals such as psychologists for optimal support and patient outcomes.

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