Management of autoimmune diabetes for two years without insulin treatment: a case report

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Abstract

We describe here a case of dietary and metformin intervention, achieving and maintaining normoglycaemia beyond two years from autoimmune diabetes diagnosis, without exogenous insulin. The case, a 53 year old white male, was initially diagnosed with typical type 2 diabetes, presenting with elevated fasting glucose and HbA_{1c} combined with excess weight (BMI 28). Metformin and dietary advice were very successful with good weight loss and subsequent HbA_{1c} near normal. However, eighteen months later, a routine HbA_{1c} test at 83 mmol/l (9.7%) suggested reversion to an autoimmune diabetes, confirmed by autoantibody test, and therefore considered type 1 diabetic and referred to a specialist clinic to begin insulin therapy. In the period between taking the sample and receiving the antibody results, the patient had begun home blood glucose monitoring and revising his carbohydrate intake downwards to achieve serum glucose targets. On the basis of this management, the patient refused insulin therapy and has maintained normoglycaemia for a period in excess of two years. The dietary regimen is reported as easy to manage, satisfying and represents less of a lifestyle impact and cost than would be the case for good glycemic control with insulin therapy. It seems likely that this approach could prove beneficial for many other newly diagnosed adult diabetics.

Introduction

Type 1 diabetes (T1D) is regarded as an irreversible condition resulting from an absolute deficiency of insulin production associated with β-cell loss through the action of autoantibodies. An immediate introduction of insulin therapy is common.[14] In many cases, a period where insulin treatment can be greatly reduced or even temporarily ceased develops, called the honeymoon period.[1] In essence, T1D is often described as a progression from the preclinical phase of autoimmune initiation leading to progressive β-cell loss, to the onset of clinical disease, transient remission to established disease and subsequent complications.[1,2,6,14]

Although insulin therapy is generally begun at diagnosis, it is clear that β-cell loss is not complete at this stage, and recent determination is that, even under long term insulin therapy, endogenous insulin production continues.[20] However, a subset of T1D generally do not require insulin at diagnosis and may be diagnosed with latent autoimmune diabetes of the adult where autoimmune markers are present (LADA).[21] Clearly there is scope for an initial type 2 diabetes (T2D) diagnosis in these cases, subsequently needing revision to T1D as autoimmunity becomes more apparent.[13] The American Diabetes Association does not recognise this classification, but does recognise difficulty in

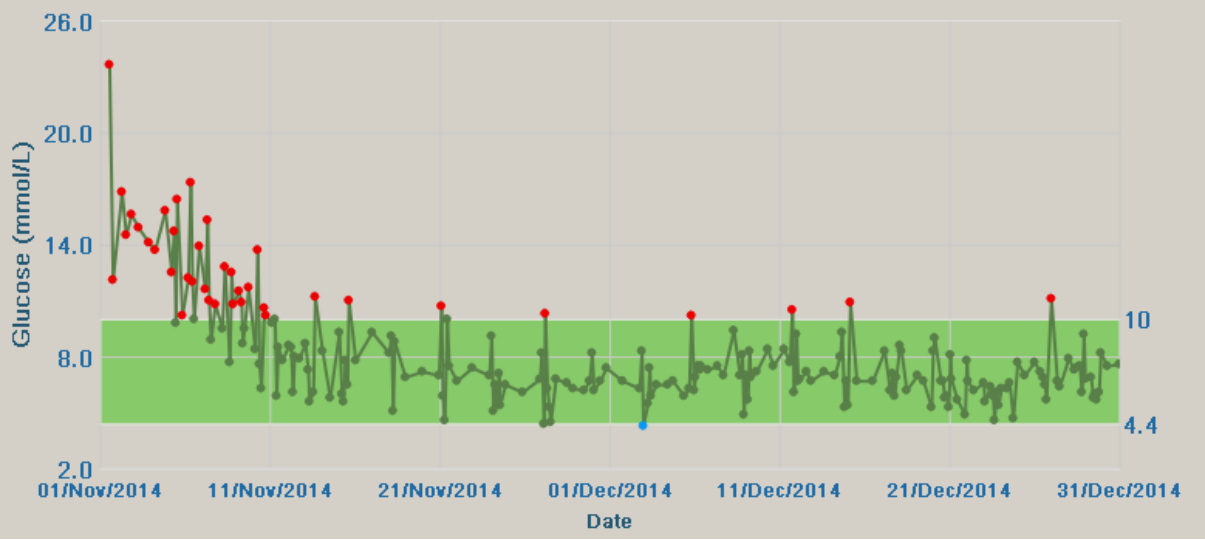

Figure 1 Rapid normalisation of serum glucose, both pre and post prandial, by reducing the carbohydrate component of the diet in the period between drawing the sample and receiving the autoantibody test results.

Table 1 Markers commonly associated with diabetes. TRG/HDL above 3.5 is a marker for insulin resistance[15] and cardiac event risk, raised liver enzyme combined with normal bilirubin, excess weight and no evidence of other pathologies is a marker for NAFLD.[9]

Date	HbA_{1c} ≤40 mmol/mol	TRG/HDL <3.5	Liver function	BMI ≤25	Notes
Dec 1990		4.01	Raised GGT/ALT/AST		Bilirubin normal
Nov 1998		6.43	Raised GGT/ALT/AST		Ins = 74pmol/L Bilirubin/thyroid normal
Feb 2013	58	4.08	Raised GGT/ALT/AST	28	
Nov 2013	37	1.42	Normal	26	
Apr 2014	45	1.62			
Oct 2014	83	3.78*			*Non-fasting test
Dec 2014	49		Normal		GAD (unrecordably high)
Feb 2015	38	1.70	Normal	25	IA2, ICA – at top of measurable range
Jun 2015	40	2.62*	Normal		*Non-fasting test
Sep 2015	38				
Mar 2016	38		Normal		Ins = 66pmol/L (20-80)
Jul 2016	37			24.5	
Sep 2016	38		Normal	24.8	
Dec 2016	40	1.94	Normal		

some cases in correctly distinguishing between types 1 and 2. T1D is defined as hyperglycaemia combined with the presence of one or more autoimmune markers.[2]

Case report

In early 2013 the patient, a white male 53 years of age, was diagnosed diabetic following a routine screening test, based on fasting glucose of 10.8 mmol/L and HbA_{1c} of 58 mmol/mol. Mild overweight, especially abdominal, mild hypertension, mild dyslipidaemia and elevated liver function panel (Table 1) indicated the onset of T2D. Metformin 500mg twice daily and 10kg weight loss were indicated. Advice on weight loss was primarily calorie control (particularly between-meal calories, as the patient self-reported a tendency to snack in the evenings on biscuits). Snacks were recommended to be reduced and cheese or almonds suggested as options. The patient was highly motivated and within nine months HbA_{1c} test showed a pleasing result at 37 mmol/mol and BMI of 26 (Table 1).

However, a year later a routine HbA_{1c} of 83 mmol/mol occurred, associated with unexplained weight loss and fatigue. By this time, the BMI target was very close to achievement. Anti-GAD tests were ordered on the assumption it was likely the patient had resolved to a Type 1 diabetic pattern. The result was unrecordably high autoantibodies and the patient was referred to a specialist diabetes clinic to begin insulin therapy.

In the interim, the patient had begun using a home glucose meter with nearly immediate resolution of blood glucose from the 15-23 mmol/L range to sub-10 postprandial tests (Figure 1). This was achieved by an immediate drastic reduction of bulk dietary carbohydrates, primarily experimenting with reducing carbohydrate intake to achieve acceptable postprandial glucose levels. A food diary indicated sub 100g carbohydrate per day, and more stringent dietary intervention from January 2015 suggests <75g/day is being achieved.

The patient attended two clinic visits, but expressed reluctance to begin insulin therapy while home blood glucose testing indicated dietary interventions were working. At this time, HbA_{1c} had already reverted to 49 mmol/mol and by the second visit, 3 months later, was down to 38 mmol/mol. Further autoantibody tests indicated both IA2 and ICA at the top of the measurable range. A fasting insulin test returned 66pmol/L.

The patient reports the new diet is completely satisfying, tasty and easy to manage other than when faced with commercial food offerings eaten away from home. In particular, airline and hospital "diabetes" choices are completely incompatible with a low carbohydrate diet. The patient reports completely removing wheat flour products (such as breads, cake/biscuits, pasta, couscous), potato, rice, maize and other obvious high starch products (including gluten free options such as quinoa and buckwheat). The dietary bulk provided by these foods is largely replaced with salad and vegetable as

appropriate. High carbohydrate vegetables (such as carrots, pumpkin, green peas) are not eliminated, but are eaten in moderation.

Quarterly HbA_{1c} tests have remained at ≤40 mmol/mol (5.8%) for two years on this diet. The patient has felt confident to reduce the frequency of home blood glucose testing to one day per week of pre/post prandial testing for one or two meals on that day plus occasional testing following introduction of new food items.

Discussion

Quality of life is a key component of self-management of diabetes.[3] The degree of glycemic control evidenced in this case, while at the upper end of commonly accepted normal, is far better than even the more stringent targets commonly applied with T1D and insulin therapy (HbA_{1c} <48mmol/mol, 6.5%)[4]. However, to achieve these stringent targets requires considerable blood glucose monitoring throughout the day, and sometimes at night, as well as calculating insulin type and quantity relative to carbohydrate intake and exercise. Optimal control by this means requires continuous glucose monitoring and automated insulin injection. This represents significant change to quality of life and cost.[6]

As an alternative, strict adherence to a very low carbohydrate diet seems a relatively lesser influence on quality of life and cost. The low carbohydrate diet is not particularly expensive and combined with savings on monitoring and insulin costs, plus the need for more stringent medical oversight, could well be a cheaper option. It has not been stigmatising, it is not extreme or difficult to maintain, and appears to be producing good results over at least two years. This is a considerable difference to the maxim "People with type 1 diabetes can inject the insulin they lack as appropriate for the carbohydrate load and their activity level".[11]

In addition to maintaining normoglycaemia, elevated liver function panel also resolved to normal (Table 1). NAFLD is strongly associated with insulin resistance and dyslipidaemia.[9] The change in the TRG/HDL ratio is suggestive of resolving insulin resistance.[15] Both appear to be associated with the weight loss and long term weight maintenance in a reduced carbohydrate diet. This bears a resemblance to another case, but in T2D with renal dysfunction.[18]

Undoubtedly a degree of self-control and motivation is required,[17] but giving clear guidelines to patients and implications of those options in regards to lifestyle impact, cost and long term health prognosis, it is quite likely that many patients will choose the dietary management option. Even intensive conventional (insulin) diabetes management does not reduce HbA_{1c} sufficiently to remove ongoing risk of further complications of diabetes.[23] Good glucose control is also required to prevent glucotoxicity causing further β-cell destruction and thus possibly maintain remaining endogenous insulin production.[7]

It is possible that the simple classification of types 1 and 2 diabetes are insufficiently refined for clinical treatment decisions, the suggestions of "double diabetes" and LADA[8,13,21] indicating possibly different clinical recommendations. The relatively high fasting insulin value in this case suggests hyperinsulinaemia rather than an absolute lack of insulin generally assumed in T1D, and therefore more suggestive of T2D. However, the presence of autoantibodies, at high titre, confirms current diagnostic criteria for autoimmune diabetes (T1D).

Perhaps a low carbohydrate diet is an alternate to insulin therapy as a means of "sparing" the β-cells, thus allowing the natural increase in β-cell proliferation at onset of clinical T1D to maintain a degree of insulin production.[24] This harks back to the pre-insulin era when carbohydrate restriction was a well-known therapy option,[19] and the role of intensive carbohydrate restriction may prove more widely appropriate.[5,10,12,16,22]

Conclusion

Maintenance of endogenous insulin production is the goal of early stage intervention following T1D diagnosis. It would appear that carbohydrate restriction is a viable alternative to exogenous insulin. It is easily implemented at minimal cost and has a relatively small effect on lifestyle.

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