Induction of long-term glycemic control in a type 2 diabetic patient for 11 years by intensive lifestyle intervention

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1 | INTRODUCTION

Patients with type 2 diabetes will eventually need antidiabetic drugs or even insulin to control blood glucose with the failure of islet function. We report a case of type 2 diabetes who has kept blood sugar levels under control for 11 years only by diet and exercise therapy.

With the progressive decline of islet function, patients with type 2 diabetes mellitus (T2DM) will usually need antidiabetic drugs or even insulin to control blood glucose eventually. Here, we report a case of type 2 diabetes who managed to control blood sugar well for 11 years only by strict dietary and exercise measures.

2 | CASE PRESENTATION

The patient is a 58-year-old female who found her blood sugar went high about 13 years ago in regular medical examination. The fasting blood glucose (FBG) of venous plasma was 7.6 mmol/L then, but further examinations were not performed. She was only told to make some lifestyle intervention. After one year, the patient came back for a visit, and the venous plasma glucose was reexamined. The FBG went higher to 9.8 mmol/L without symptoms like polyuria, polydipsia, or loss of weight. The patient had no past history of other diseases and family history of diabetes.

Physical examination: height 155 cm, weight 68 kg, body mass index (BMI) 28.3 kg/m². Blood pressure and body temperature were normal. No central obesity, moon face, or acromegaly was found in this patient. The physical examinations in cardiac, respiratory, and abdomen were negative. FBG was reexamined twice, and the levels were 9.66 mmol/L and 9.06 mmol/L. 2-hour postprandial blood glucose (PBG2h) was 18.88 mmol/L, glycosylated hemoglobin A1c (HbA1c) was 6.13%. Blood tests revealed no positive results. Islet function was detailed in Table 1. Although the patient did not have the typical symptoms of diabetes such as polydipsia, polyuria, polyphagia, and weight loss, the fasting blood glucose of venous plasma was greater than 7 mmol/L at different times. According to the diabetes diagnostic criteria of WHO in 1999, diabetes can be diagnosed.

Individualized diet was prescribed according to height, weight, labor intensity, and eating habits of the patient.
Total calorie: 1100 kcal; carbohydrate: 180 g (GI < 70); cooking oil: no more than 30 g per day; fish, meat, and eggs: less than 125 g in total; fruits: 200 g at most; milk: less than 250 mL. Take exercises one hour after each meal every day as long as the patient can bear. The exercise is divided into three times, total time of 60 minutes or distance of 5-6 kilometers is appropriate for a day. No drugs of antihyperglycemia or diet pills were administered. The patient strictly followed the diet and exercise therapy. The following changes in weight, blood glucose, and islet function are detailed in Table 1.

The patient in this case was an obese female who had a BMI of 28.3 kg/m² (obesity was defined as BMI ≥ 28 kg/m² in China). The FBG was 9.66 mmol/L while PBG2h was 18.88 mmol/L. The intravenous glucose tolerance test (IVGTT) showed the baseline of insulin secretion was 86.68 pmol/L, and peak level of insulin secretion was 155.8 pmol/L (P/B = 1.797). The patient was treated only with intensive lifestyle intervention and she had lost 8 kilos within a month and a half’s time. FBG and PBG2h went back to normal, with the first-phase insulin secretion improved, too (P/B = 3.299). The patient's weight declined to 56 kg after 1 year with the FBG of 5.43 mmol/L and HbA1c of 5.37%. In the next year, P/B was increased to 6.506. After three years of treatment, the indexes were 55.5 kg (weight), 5.57 mmol/L (FBG), and 7.684 (P/B). The patient followed up regularly and in the 11th year of her treatment, the weight was 56 kg, FBG was 5.8 mmol/L, HbA1c was 6.4% and P/B was 13.263. HOMA-IR decreased obviously from 5.47 before treatment to 1.29 recently. HOMA-β went from 7.29 to 33.76 within a month and a half's time after the adjustment of insulin resistance and remained above the level ever since. The natural course of T2DM was therefore altered with the improvement of insulin resistance and the dysfunction of β cell.

3 | DISCUSSION

Insulin resistance and β cell dysfunction are undoubtedly the core pathophysiological changes during the natural course of T2DM. If the progress of T2DM can be reversed, it must be accompanied with the obvious improvement or even the disappearance of insulin resistance and the β-cell function backing to normal. Insulin resistance appears in the early stage of T2DM and will persist, and the level of insulin increases compensatory at prediabetes period and early-stage diabetestes, but will fall eventually with the progress of the disease. UKPDS shows that β-cell function had already fallen to 50% of normoglycemia at the time the diagnosis of diabetes is confirmed,1 and no matter what strategies we take or how perfect the control of blood glucose is, β-cell function will decline at the speed of 4%-5%. And in that case, very little function will be preserved in 10 years. We will eventually need antidiabetic drugs or even insulin to control the blood glucose.

But is this how things are going actually? Cerasi et al reported in 1997 that newly diagnosed patients who did not respond to diet intervention had achieved improvement in insulin resistance and β-cell function after receiving continuous subcutaneous insulin injection for 2 weeks.2 They therefore altered the course of their T2DM and maintained excellent control of blood glucose for 59 months only through diet intervention. It had also been revealed by Li Yanbing et al that the remission rate of 138 newly diagnosed T2DM patients
with blood glucose higher than 11.1 mmol/L were 72.6%, 67%, 47.1%, and 42.3% in the third, sixth, twelfth, and fourteenth month, respectively.\(^3\) At the same time, the blood glucose remission was considered related to the improvement of β-cell function, especially the recovery of first-phase insulin secretion. Weng Jianping et al compared the effects of continuous subcutaneous insulin injection (CSII), multiple daily injection (MDI), and antidiabetic drugs on β-cell function and diabetes mellitus remission rate through a multi-center, parallel controlled study.\(^4\) The result demonstrated that CSII and MDI could reach the targets of glycemic control in a shorter period of time. The remission rates after 1 year were 51.1% for CSII, 44.9% for MDI, and 26.7% for antidiabetic agents. The HOMA-β and acute insulin response also improved after the intensive therapy of insulin injection. A meta-analysis including 899 patients showed that the β-cell function and insulin resistance had been remarkably improved and the remission rate of diabetes mellitus was elevated.\(^5\)

In addition to insulin use in the early years postdiagnosis, Steven S reported that a very low-calorie diet (VLCD) can also restore blood sugar to normal in some T2DM patients.\(^6\) In the study, T2DM patients followed a VLCD for 8 weeks without any medication. Their weight fell and remained stable over 6 months. Twelve of 30 participants achieved fasting plasma glucose lower than 7 mmol/L associated with return of first-phase insulin response. It should be noted that some subtypes of maturity-onset diabetes mellitus of the young (MODY), such as MODY2 and MODY10, can also control blood glucose only by diet and exercise. MODY is a special type of diabetes mellitus with β-cell dysfunction caused by single gene mutation. The characteristics of MODY include: onset in young, a pattern of autosomal dominant inheritance, β-cell dysfunction, no evidence of autoimmunity, or insulin resistance. Patients with MODY2 usually have a slight increase in FBG at birth (5.3-7.8 mmol/L), and PBG2h is usually normal. The FBG and PBG2h of this patient were significantly increased, which did not conform to the characteristics of MODY2. MODY10 is caused by INS gene mutation, which usually leads to neonatal diabetes. INS gene mutation can lead to insulin precursor synthesis dysfunction and β-cell apoptosis, so insulin secretion is persistent low. Other subtypes of MODY may be associated with other manifestations, such as dyslipidemia (MODY1), renal Fancony syndrome (MODY3), pancreatic exocrine dysfunction (MODY4, MODY8), non-diabetic nephropathy, or renal dysplasia (MODY5), and are sensitive to sulfonylureas or require insulin therapy. Type 2 diabetes mellitus is a heterogeneous disease with polygenic inheritance. At present, PPARG, KCNJ11, CDKAL1, CDKN2A/B, ide-kif11-HHEX, IGF2BP2, SLC30A8, HNF1B, dusp9, zfand3, FTO, and TCF7L2 are closely related to type 2 diabetes.\(^7\) Multiple weak genes and environmental factors lead to the occurrence of disease. MODY is a single gene mutation diabetes mellitus, but its pathogenic gene polymorphism will also have a certain impact on the genetic susceptibility of type 2 diabetes. What genetic factors are involved in the process of long-term remission of our patient? I think gene testing provides us with the possibility to make clear the above problems.

For this patient, the most significant factor of the alteration was weight loss with no rebound from our point of view. T2DM is a condition mainly caused by excess reversible fat accumulation in the liver and pancreas. In the early years postdiagnosis, removal of excess fat from these organs via substantial weight loss can normalize hepatic insulin responsiveness and recover β-cell of acute insulin secretion, possibly by redifferentiation.\(^8\) The redifferentiation of dedifferentiated β cell into mature β cell due to reduced metabolic stress generated from weight loss was fundamental to the recovery of β-cell function.\(^9\) And the improvement of insulin resistance also attributed to weight loss.\(^10\)

## 4 CONCLUSION

T2DM is generally regarded as an irreversible chronic disease. However, this case and recent studies suggest that it can be reversed, and the mechanism needs more clinical and basic research to elucidate.

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## CONFLICT OF INTEREST

The authors declare that they have no competing interests.

## ETHICS APPROVAL

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## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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