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Diabetes Remission in a Young Diabetic Patient with Non-Alcoholic Liver Disease

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Abstract

We present the case of a 24-year-old newly diagnosed type 2 diabetic person with NAFLD and hyperlipidaemia. Intensive glucose management and weight loss normalized HbA1c and liver function tests. This report illustrates the impact of a comprehensive diabetes management inducing diabetes remission and reversion of NAFLD.

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Introduction

Diabetes represents a worldwide health problem associated with a number of chronic complications, augmenting the risk for premature morbidity and mortality [1]. NAFLD frequently present in obese and in type 2 diabetics with insulin resistance increases the risk for progression to non-alcoholic steatohepatitis, fibrosis, cirrhosis and mortality from cardiovascular complications [2-3].

Current diabetes guidelines emphasize multifactorial management and an individualized approach [4-5]. It has pointed to the occurrence of diabetes remission with weight loss and metabolic control [6]. We present a case of a diabetic patient with NAFLD in whom HbA1c levels remained < 6.5 % (48.0 mmol/mol) after cessation of antihyperglycemic medication throughout 24 months of observation, consistent with diabetes remission criteria [6].

Case Presentation

A 24-year-old male without family history of diabetes was brought into an emergency room suffering from hyperglycemia. During the previous two years the patient gained weight, had familial dyslipidemia, which was treated with statins. He was sedentary, did not smoke, neither drink alcoholic beverages. One week before admission, the patient presented polyuria, polydipsia, blurred vision and his blood glucose concentration was 613 mg/dL. He was seen in another facility, where intravenous saline solutions and rapid human insulin were administered. Following this, he was referred to our hospital for further assessment and treatment. On admission to the hospital, the patient was conscious, his blood pressure was 120/80 mmHg, BMI was 32.5 kg/m2. Abdominal ultrasound revealed hepatomegaly and steatosis. There was no evidence of infection, cardiovascular or respiratory complications.

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Diagnostic Assessment

Blood glucose concentration was 216 mg/dL (reference 80–100), glycosilated hemoglobin A1c (%HbA1c) 7.3% (56 mmol/mol), alanine amino transferase (ALT) 179 U/L (reference 0-55), aspartate amino trasnferase (AST) 173 U/L (reference 0-34), HOMA IR 13.4, (normal range < 2.5), C-peptide 3.6 ng/dL (reference 1.1-4.4), glutamate carboxilase-65 (GADA-65) < 5.0 units (normal range <5.0). The hemogram, cortisol, thyroid stimulating hormone, renal function tests, uric acid and electrolyts were normal. Serology for infectious hepatitis was negative, urinalysis showed glucosuria and there was vitamin D deficiency. Abdominal ultrasound revealed hepatomegaly and steatosis.

Treatment

In the hospital, he received intravenous saline solutions and basal-bolus insulin regimen with glargine 28 U once a day and glulisin 8 U before meals. Normoglycemia was promptly reached. Upon discharged, 24 hours later, the patient maintained normal glucose levels. The patient continued to take atorvastatin, received vitamin D and was immunized. Diabetes training, including an intensive lifestyle modification plan, was provided.

Outcome and follow-up

After one month, while the patient maintained normoglycemia, insulin therapy was switched to dulaglutide 1.5 mg per week, empagliflozine 25 mg and metformin 1000 mg daily. This treatment was maintained for 18 months, at the end of that time, all drugs were withdrawal including the lipid lowering therapy. Regular visits to the clinic ensured compliance with lifestyle modification. Twelve months after the initial visit, the abdominal ultrasound did not reveal abnormalities. HOMA IR at baseline was 13.4 and at the end of the observation period it was 6.2. Changes in body weight, BMI, lipid profile, liver function tests, and HbA1c values are presented in Table 1.

Table 1: Baseline and follow up of clinical tests.

	Baseline	1	12	24	31	38	48	Range
Weight (Kg)	78.0	71.0	60.0	69.0	NA	67.8	70.85	44.5-63.0
Body mass index (Kg/m^2	32.5	29.5	25,0	28,7	NA	28.2	29.5	18.5-24.9
Glycemia mg/dL (mmol/L)	266 (14.8)	94 (5.22)	102 (5.66)	105 (5.83)	104 (5.77)	106 (5.88)	104 (5.77)	80-100 (4.44-5.55)
HbA1c% (mmol/mol)	7.3 (56)	6.1 (43)	5.0 (31)	5.4 (36)	5.7 (39)	5.7 (39)	5.4 (36)	< 6.5 (<48)
Total Cholesterol mg/dL (mmol/L)	147 (3.80)	114 (2.95)	192 (4.97)	154 (3.98)	185 (4.78)	193 (4.99)	212 (5.48)	< 200 (<5.17)
HDL cholesterol (mg/dL)	20 (0.52)	24 (0.62)	27 (0.70)	33 (0.85)	30 (0.78)	32 (0.83)	30 (0.78)	> 40 (>1.03)
LDL cholesterol (mg/dL)	112 (2.9)	62 (1.60)	123 (3.18)	83 (2.15)	115 (2.97)	112 (2.90)	125 (3.23)	< 100 (< 2.59)
Triglycerides mg/dL (mmol/L)	205 (2.31)	143 (1.61)	205 (2.31)	189 (2.13)	201 (2.27)	247 (2.79)	284 (3.21)	< 150 (< 1.69)
ALT (units/L)	179	67	47	23	36	29	24	0 - 55
AST (units/L)	173	42	38	27	32	32	25	0 - 34

NA: data not available (this visit was done virtualy during the pandemia

Discussion

We present the case of a newly diagnosed diabetic patient with NAFLD whose intensive glucose control and marked weight loss had a disease-modifying effect leading to diabetes remission [6]. The absence of GAD-65 autoantibodies and ketosis rule-out autoimmune diabetes [5-6]. It is unlikely that the patient had MODY as there was no family history of diabetes. Furthermore, the patient had insulin resistance, hypertriglyceridemia, abnormal liver enzyme concentration and liver steatosis. Insulin resistance, a key factor associated with some type 2 diabetes subtypes, increases the risk of progression to steatohepatitis, fibrosis and cirrhosis [2-3]. NAFLD and diabetes are associated with risk of mortality from cardiovascular complications and predicts mortality in acute myocardial infraction, even in patients without known cardiovascular risk factors [2-3]. Therefore, in these patients intensive treatment is warranted to control glucose concentrations and other risk factors aiming to avoid chronic complications [4-5]. In severe insulin resistance obese patients, fat accumulation in the liver and pancreas leads to increased hepatic glucose production and accelerate cell mass loss with reduction of insulin production and secretion [7]. Reversibility of fat accumulation in the liver and pancreas has been associated with improved insulin sensitivity and β cell response, improving glucose control [7]. In our patient an intensive insulin treatment for one month, followed by a combined therapy with GPL-1 RA, metformin, SGLT-2inhibitor and weight management reduced plasma glucose and HbA1c levels. These results were seen shortly after initiation of diabetes management and remained within normal range for a prolonged period of time (Table 1). Our findings are consistent with diabetes remission, which has been defined as a return of HbA1c to < 6.5% (48.0 mmol/mol) for at least 6 months in the absence of glucose-lowering medication [6]. In patients with type 2 diabetes, the remission of diabetes was documented after bariatric surgery, very low calorie diet and insulin treatment [6]. These results have been associated with the improvement of β cell function, particularly the restoration of first-phase insulin secretion [6].

While there is no established pharmacotherapy for NALFD, current recommendations emphasize that lifestyle change and concurrent weight loss in obese individuals are beneficial [8]. Moreover, some studies have assessed the effectiveness with pioglitazone, GLP-1 RAs, and SGLT2 inhibitors in patients with NAFLD [8]. For example, empagliflozine had a major effect on hepatic fat and ALT levels in patients with type 2 diabetes and NAFLD [9]. Furthermore, dulaglutide a weekly injectable GLP-1 RA, indicated for diabetes control also reduces liver fat content [10]. Thus, in addition to their normoglycemic effects the newer antidiabetic agents can help improve liver steatosis favoring diabetes remission [9-10]. In our case, the relative contribution of pharmacologic versus lifestyle modification and weight loss to diabetes remission was difficult to

ascertain. However, as it is stated in current guidelines, both non-pharmacologic approaches and pharmacologic are necessary for an adequate diabetes management [5]. Lastly, despite the fact that the patient lost weight, reduced insulin resistance and improved glucose control, the triglyceride and LDL cholesterol concentrations remained elevated. This can be atributed to a familial dyslipidemia trait present in this patient. Therfore, it would be recommended to re-start lipid lowering therapy.

In conclusion, despite the fact that the follow-up of this patient was done during the COVID pandemic which represented a limitation, it was possible to establish an early and intensive management of diabetes, allowing the patient to lose weight, to improv glucose control, and to reduce insulin resistance,. All of which lead to a complete remission of diabetes. Moreover, the resolution of steatolsis was also observed, suggesting that reversion of NAFLD paralleled the improvements in glucose metabolism.

- Learning PointsType 2 diabetes mellitus and non-alcoholic liver disease often co-exist.
- Insulin resistance increases the risk for progression to non-alcoholic liver disease and for the developing cardiovascular disease.
- Lifestyle modification associated with weight loss improve glucose control and reverts NAFLD.
- Diabetes remission can be achieve with intensive and early glycemic management in an out-patient diabetic clinic.

Contributors

All authors made individual contributions to authorship reviewed and approved the final draft. JGJM: conducted the clinical evaluation and follow-up therapeutic management of the patient. MVB: performed the nutritional evaluation and set-up the dietary plan. She also was involved in diabetes education.

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