Healthy Pregnancy and Birth during Unusually Long-Lasting Remission of Type-1 Diabetes: Case Report

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Abstract

The 26-year-old woman was diagnosed with type 1 diabetes in 2014. The diagnosis was confirmed while there was a slight increase in blood glucose and HbA1c levels using oral glucose tolerance test, determination of insulin levels and GADA testing. This was followed by a 2-year period with complete remissions and partial remissions of 2-8 U daily basal insulin glargine. Thereafter, the patient became pregnant. The minimal basal insulin used to date has been switched to human rapid-acting and NPH insulins five times daily, which had to be increased to 11 times the initial dose in the third trimester of pregnancy. After a successful spontaneous birth of a healthy baby girl, our patient wished to return to one-tenth of the maximum insulin dose that was used during pregnancy, to once daily insulin glargine. After three months, her blood glucose levels began to rise, with oral glucose challenge test showing a marked increase in blood glucose and a drastic reduction in C-peptide levels. This was when we switched to multiple daily insulin administration using glargine basal- and glulisine analogue insulins. Later, glargine was switched to insulin degludec, and with a 30-33 U total daily insulin dose and CGM for the past two years, the patient was in a satisfactory metabolic state.

Keywords

Type-1 Diabetes; Long Term Remission; Pregnancy During Remission; Basisinsulin Treatment; Multiple Daily Insulin

Abbreviations

CGM: Continuous Glucose Monitoring; GADA: GAD Antibody; MDI: Multiple Daily (Insulin) Injection; OGTT: Oral Glucose Tolerance Test; TIDM: Type-1 Diabetes Mellitus

Introduction

The remission of type 1 diabetes (T1D) has been a widely studied topic primarily in children and adolescents for nearly 4 decades. This “honeymoon” period of remission is a phase in which insulin requirements are reduced to a minimal level (usually below 0.2 U/kg body weight) for a few weeks up to 2-3 years and in a very small proportion of cases this remission can be complete over a shorter or longer period, meaning that normal metabolism is
maintained without insulin administration (HbA1c ≤6%) [1,2].

The older the patient is at the time of the diagnosis with T1D, the greater the likelihood and duration of the remission: the smallest in infancy [3], greater in adolescents, and even greater in those over 20 years of age. Gender differences have also been shown: women are less likely to be in remission than men [4]. Another important consideration for remission is the metabolic situation at the time of diagnosis. Lower HbA1c levels mean there is a greater potential for remission, higher baseline C-peptide levels may provide a longer duration of remission, and the initial insulin treatment also plays an important role: intensive insulin treatment increases the duration of remission [5].

The honeymoon period may be due to the course of autoimmune beta-cell damage varied with remissions/relapses [6]. Particular attention should also be paid to the precise classification of diabetes in young people with mild diabetes mellitus, the practical implementation of which we refer to the 2017 publication in Diabetologia Hungarica [7].

The interesting feature of our present case report is the pregnancy during the remission period of 3 years and the extreme insulin requirement during the pregnancy, which was followed by the continuation of remission.

**Case report**

The maternal uncle of the woman born in 1988 has been diabetic since he was 1 year old. In May 2014, she had a screening test measuring 7.6 mmol/l blood glucose with 6.3% HbA1c. The result of the oral glucose tolerance test (OGTT) performed at this time is shown in Table-1 along with two other measurements. The patient had normal body structure and a body mass index of 21.6kg/m². For classification purposes and to estimate the dynamics of beta cell damage, GADA, blood glucose and insulin/C-peptide tests were performed on fasting and OGTT samples (Table-1).

When the patient first visited our specialty clinic in 2014, we started dietary treatment with basal insulin based on the data, initially consisting of 2 IU insulin glargine in the evening. Subsequently, the patient discontinued insulin administration several times for several weeks. The dose of glargine was then increased in a multisteps process to 8 IU (0.13 IU/kg body weight).

The patient became pregnant at the end of June

| Table-1: The classification of diabetes and the studies conducted to assess disease course |
|-----------------------------------------------|--------|--------|--------|
|  | May-14  | Apr-15 | Sep-17 |
| GADA IU/ml  | 87 | 71 | 69 |
| Blood glucose mmol/l  | 6.9 | 7.8 | 8.8 |
| Insulin mU/l 0 min  | 5.5 | NA | NA |
| C-peptide ng/ml  | 1.15 | 1.38 | 0.48 |
| Blood glucose mmol/l  | 13.4 | 12.2 | 19.2 |
| Insulin mU/l 60 min  | 20.6 | NA | NA |
| C-peptide ng/ml  | NA | 2.40 | 0.95 |
| Blood glucose mmol/l  | 12.6 | 12.3 | 22.0 |
| Insulin mU/l 120 min  | 28.9 | NA | NA |
| C-peptide ng/ml  | NA | 2.29 | 1.01 |

The gradual loss of capacity for insulin secretion due to gradual progression of beta-cell dysfunction and beta-cell death can be observed.
2016 and treatment was changed to multiple daily insulin doses (MDI) after one month using twice NPH and three times rapid-acting human insulin. Insulin requirements increased steadily during pregnancy and eventually exceeded 11 times the pre-pregnancy level (Fig-1). The patient subsequently gave birth to a healthy girl with a weight of 3800 grams with vaginal delivery at the 38th week of gestation. Her insulin requirements decreased sharply during the last 3 weeks of pregnancy and for 3 months following delivery it reached about 9 IU with once daily insulin glargine, which was her minimal requirement before pregnancy. We then resumed MDI using once daily glargine and then early in 2019 using insulin degludec as basal insulin accompanied by three times daily mealtime insulin glulisine. Her daily insulin requirements stabilized at around 30-33 IU. Her HbA1c values were predominantly within the range of 6-7% (Fig-2). From the end of 2016, she switched from blood glucose self-monitoring at finger sites to the use of the FreeStyle Libre sensor, which greatly helped her to continue her normal lifestyle (Fig-3 and Fig-4).

Fig-1: Changes in insulin demand during pregnancy and after delivery

Fig-2: HbA1c levels during the past 5 years
Case Report

Discussion

Beta-cell dysfunction (indicated by the loss of the early phase of insulin secretion) and beta-cell necrosis (indicated by the gradual decrease in global insulin secretion capacity) occur partially during the autoimmune process leading to T1DM. With the fluctuating course of the above, the clinical picture is further affected by the degree of insulin requirement, which is determined by insulin sensitivity (an important factor is body mass index) and contrainsulin hormones (during pregnancy).

Women are less likely to be in remission than men with respect to T1DM, and although the conditions for remission have been studied extensively, especially in children, the occurrence of a healthy pregnancy during remission and subsequent remission is unknown. The peculiarity of our case is that during the 3-year remission that could be described as complete for several times over several weeks, the

Fig-3: CGM curves 1 year after labour, in 2018.

Fig-4: CGM curves in August 2019.
patient became pregnant and the pregnancy insulin requirement has increased 11-fold compared to the pre-pregnancy levels. However, after birth it returned to pre-pregnancy levels. It should be noted that in our case, the patient received only basal insulin during the pre- and post-pregnancy remission phase. We did not use MDI until 3 months after delivery, at the increase in insulin requirement, i.e. after the end of the remission. With this therapy, the patient had an excellent metabolic status for 2 years and could have a good quality of life.

References


