ENDOCRINOLOGY RESEARCH AND PRACTICE

SOCIETY OF ENDOCRINOLOGY AND METABOLISM OF TÜRKİYE

Autoimmune Gestational Diabetes, An Uncommon Cause of Type 1 Diabetes: A Case Report

CASE REPORT
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ABSTRACT

Less than 10% of gestational diabetes mellitus (GDM) cases are type 1 diabetes mellitus (T1DM), and the pre-diabetic stage of T1DM may be missed in women diagnosed with GDM during pregnancy. We present a patient who was diagnosed with GDM at 24 weeks gestation but who was diagnosed with T1DM after presenting with diabetic ketoacidosis in the early postpartum period. In presenting this case, we aim to remind and raise awareness of the risk of developing postpartum T1DM in patients with lean GDM who have no signs of insulin resistance, are aged <30 years, have no family history of type 2 diabetes mellitus, and require insulin therapy.

Keywords: Diabetic ketoacidosis, gestational diabetes, islet autoimmunity

Introduction

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of varying degrees that is first recognized during pregnancy. Gestational diabetes mellitus occurs in the second half of pregnancy and usually resolves after childbirth but is associated with an increased risk of developing diabetes later in life.[1] Gestational diabetes mellitus can occur in 2 ways: non-autoimmune (90%) due to the triggering of insulin resistance mechanisms, and less commonly autoimmune (10%).[2,3] Epidemiological data show that carbohydrate intolerance is associated with beta cell autoimmunity in 5%-10% of GDM cases.[4,5] These women are more likely to develop type 1 diabetes mellitus (T1DM) and/or latent adult autoimmune diabetes after pregnancy.[6] The potential predictive role of autoantibodies in GDM patients for the development of postpartum T1DM has been investigated in several studies. Most of these studies have confirmed the predictive role of islet cell antibody (ICA) and glutamic acid decarboxylase antibody (GADA) positivity, particularly in the presence of 2 or more autoantibodies.[7-9]

In this case, we present a patient who was diagnosed with GDM at 24 weeks gestation. She was diagnosed with type 1 diabetes after experiencing diabetic ketoacidosis (DKA) in the early postpartum period. Less than 10% of GDM cases are T1DM, and the pre-diabetic stage of T1DM may be missed in women diagnosed with GDM during pregnancy. Our aim in presenting this case is to remind and raise awareness of the risk of developing postpartum T1DM, especially in pregnancies with GDM that do not have typical risk factors for type 2 diabetes (T2DM). Written informed consent was obtained from the patient who agreed to take part in the study.

Case Presentation

A 19-year-old female patient, 1 month post partum, presented with left breast swelling and redness. An abscess was suspected, and drainage was performed. She presented to the emergency department with shortness of breath, nausea, and vomiting 1 day after the procedure. On physical examination, she was confused, tachypneic, and tachycardic with Kussmaul breathing. Vital signs in the emergency department were: temperature 36.7°C, blood pressure 138/81 mm Hg, pulse 140/min, and saturation 97%. Laboratory investigations revealed serum glucose 396 mg/dL;, HbA1c 8.5%, blood gas pH 6.93, HCO_3 6 mmol/L, and +2 ketones in the urine. The patient was diagnosed with DKA and admitted to the intensive care unit, where she received fluid resuscitation, sodium bicarbonate, and intravenous insulin therapy. Analysis of the patient's medical history revealed that her pre-pregnancy body mass index (BMI) was 22.3 kg/m^2, and there was no known

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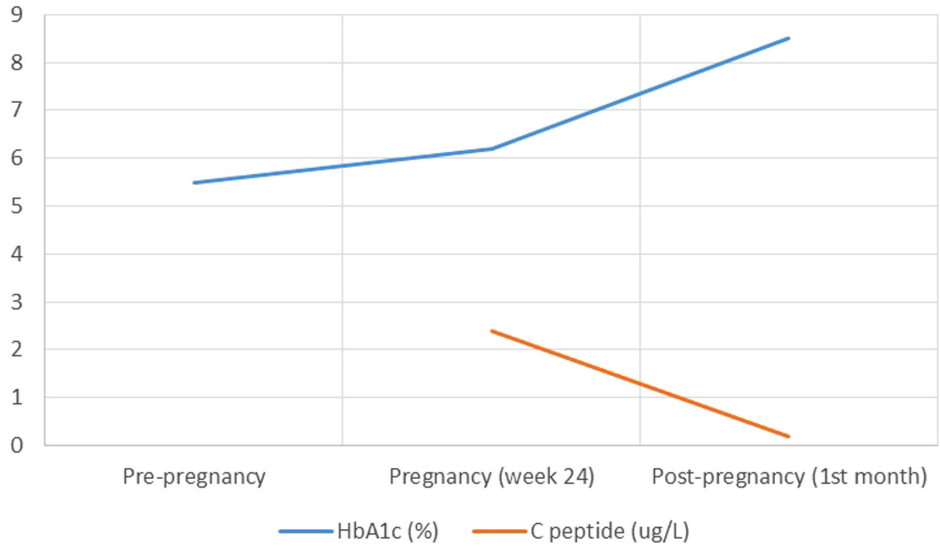

Figure 1. Pre- and post-diagnosis changes in patient HbA1c and C-peptide levels.

history of diabetes mellitus. In addition, the patient had no family history of diabetes. At 24 weeks gestation, the center following the patient performed a 75 g oral glucose tolerance test (OGTT) and was diagnosed with GDM. At that time, HbA1c was 6.2%, and the fasting C-peptide was 2.4 µg/L. The gestational hyperglycemia could not be controlled by diet, and intensive insulin treatment was started, including insulin detemir and insulin aspart. Initial glycemic control was achieved with 0.6 IU/kg/day of insulin, but insulin requirements increased to 1.2 IU/kg/day during the delivery. The baby weighed 2685 g and was born by cesarean section at 37 weeks gestation. The patient discontinued treatment spontaneously after delivery. On admission to our clinic, intensive insulin treatment was resumed after the resolution of the DKA. Fasting serum C-peptide, GADA, insulin autoantibodies (IAA), and ICA were measured to determine the diabetes type. The C-peptide level was 0.2 µg/L, and the GADA was positive at 24.58 IU/mL (reference range <17 IU/mL), but the ICA and IAA were negative. Changes in the patient's HbA1c and C-peptide levels during pregnancy, pre-pregnancy, and at the time of diagnosis are shown in Figure 1. All of these findings were consistent with T1DM. Metabolic control of the patient was achieved with intensive insulin treatment (0.56 IU/kg/day). Routine follow-up is ongoing in our endocrinology clinic.

MAIN POINTS

- The cause of hyperglycemia in pregnancy varies throughout patients. GDM, or gestational diabetes mellitus, may occasionally be mistaken for type 1 diabetes mellitus (T1DM).
- When screening for GDM, it is important to consider the risk of autoimmune GDM in individuals who are under the age of 30, have no family history of type 2 diabetes mellitus, are of low or normal weight, and require insulin treatment during GDM.
- Beta-cell autoantibody levels during pregnancy may be beneficial in the prediction of T1DM in high-risk pregnant women.

Discussion

In this article, we present our case in which GDM was diagnosed during pregnancy, and T1DM was diagnosed after the onset of DKA in the early postpartum period.

Gestational diabetes mellitus is routinely screened in every pregnant woman because of its adverse effects on the mother, the fetus, and the course of the pregnancy. Therefore, all pregnant women, whether at risk or not, are screened with a 1- or 2-step OGTT at 24-28 weeks' gestation according to the American Diabetes Association criteria. Pregnant women at high risk of T2DM (older age, high BMI, family history of T2DM) are screened with standard diabetes screening tests at the first antenatal visit.[1] However, these screening tests can sometimes misdiagnose pregnant women at the prediabetic T1DM stage with GDM.[2] Our case was a woman at low risk of non-autoimmune GDM, and therefore, GDM was diagnosed with a one-step test at 24 weeks. However, it should be remembered that autoimmune GDM may be responsible for about 10% of GDM cases,[10] as in our case. We believe that it should not be forgotten that diagnosis by OGTT alone may miss cases of autoimmune GDM, especially in pregnant women who do not have T2DM risk factors.

In fact, relative immune tolerance develops during pregnancy to prevent the maternal immune response against the semi-allograft fetus.[3] However, in the serum of women with GDM, variable levels of autoimmune serological markers against pancreatic beta cells have been found.[6-8] The pathogenesis of autoimmune GDM has been attributed to mechanisms such as fetal antigen exposure and the presence of the HLA DQ8/DR3/DR4 haplotype.[9] A study in Finland, where the incidence of T1DM is high, found that ICA, GADA, and insulinoma-related-2 autoantibodies (IA-2A) were significantly higher in pregnancies with GDM than in those with normal glucose tolerance (NGT) (12.5%, 5.9%, and 4.7%, respectively), excluding IAA (1%).[7] In Sardinia, where the prevalence of T1DM is high and obesity low, almost 40% of GDM patients were found to be positive for at least 1 pancreatic autoantibody.[11] However, the presence of autoantibodies in GDM outside of these populations suggests that different mechanistic effects may play a role in the etiology of GDM. McEvoy et al[12]

found higher IAA positivity in pregnancies with GDM, 5.6% vs. 0.9%, and ICA positivity, 31.3% vs. 8.0%, compared with those with NGT. Nilsson et al[13] reported 6% positivity for at least 1 autoantibody (ICA, GAD, or IA-2A) in women with GDM. During 8 years of follow-up, 50% of the autoantibody-positive women developed T1DM, while 21% had impaired glucose tolerance. Among the women who developed T1DM (all GADA-positive), this occurred within 6 months of delivery in 41% of cases and within 1 year in 50% of cases. These findings highlight the importance of screening for autoantibodies during and after pregnancy to ensure that T1DM is detected at an early stage. As our case was admitted to our clinic after pregnancy, autoantibody levels could not be measured before pregnancy. However, we were able to measure our case's autoantibodies at her presentation 1 month after delivery, and accordingly, GADA was found to be positive, ICA and IAA were negative, and T1DM was diagnosed.

Several observational studies have shown that hyperglycemia is the main determinant of pregnancy outcomes and that there is no significant difference in maternal–fetal outcomes between women with and without autoimmunity.[2,4] Therefore, universal screening of all patients with GDM for the presence of beta-cell antibodies is not recommended.[10] Instead, a more rational approach would be to identify pregnant women who are at high risk of developing this autoimmune form of GDM and to monitor their autoantibody levels, as they are at risk of developing T1DM in the postpartum period. Accordingly, risk factors are defined as young age (<30 years), low/normal body weight, need for insulin therapy during GDM, and the presence of concomitant autoimmune thyroid disease (ATD).[8,11] In our case, she was 19 years old, of normal weight, and required insulin treatment during her pregnancy. However, there was no concomitant ATD. Therefore, we believe that if autoimmunity had been detected in our case by monitoring islet autoantibody levels during pregnancy, the risk of T1DM could have been determined with close follow-up after birth, and the development of DKA could have been prevented. In addition, in light of our case, we would like to draw attention to the fact that women with GDM should be screened for glucose intolerance in the fourth to sixth week after delivery because of the high risk of developing diabetes after pregnancy.[1,14]

Consequently, T1DM may be missed in some pregnant women diagnosed with GDM, but universal screening in all cases of GDM is difficult in practice. A more rational approach would be to select high-risk cases during pregnancy and measure beta-cell antibodies (especially GADA) in these cases. This would allow appropriate management of cases at risk of developing postpartum T1DM.

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in the study.

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