The First Vietnamese Patient with Fulminant Type 1 Diabetes Mellitus

Hee Jin Kim, Ho-Su Kim, Jong Ryeal Hahm, Jung Hwa Jung, Soo Kyoung Kim, Sang Min Lee, Sungsu Kim, Soon Il Chung and Tae Sik Jung

Abstract

A 23-year-old pregnant woman had a stillbirth at 30 weeks gestation due to abrupt diabetic ketoacidosis. The patient had a normal HbA1c, severe hyperglycemia, negative islet cell autoantibodies, and very low insulin secretion capacity. The viral markers associated with fulminant type 1 diabetes were negative. The patient’s human leukocyte antigen genotypes were DRB1*04:06 and DQB1*03:01/05:02, not common subtypes for fulminant type 1 diabetes. This is the first Vietnamese patient with fulminant type 1 diabetes mellitus.

Key words: diabetes mellitus, fulminant type 1 diabetes, human leukocyte antigen, pregnancy


Introduction

Fulminant type 1 diabetes (FTD) has been defined as a new subtype of type 1 diabetes in which pancreatic islet cell failure rapidly leads to hyperglycemia and ketoacidosis (1). While FTD is frequently reported in far eastern Asia, patients from other areas or ethnic groups are very rare (2-4). Certain human leukocyte antigens (HLA) and viral infections have been proposed as potential mechanisms underlying disease development. FTD can occur during pregnancy or delivery and has an extremely poor prognosis for the fetus.

Here, we report a case of FTD associated with pregnancy in a Vietnamese woman.

Case Report

A previously healthy 23-year-old Vietnamese woman presented at our hospital in week 30 of gestation with abdominal pain. She had not felt fetal movement accompanying the symptoms of thirst and polyuria since the previous day. The patient did not present with nausea, vomiting, or flu-like symptoms. She had been born in Vietnam and immigrated to Korea when she married a Korean man 3 years prior. The patient delivered a healthy boy 2 years prior and had no family history of diabetes. The patient underwent a 50-gram oral glucose tolerance test at 25 weeks of pregnancy and the 1 hour plasma glucose level was 128 mg/dL.

Upon arrival at our hospital, the patient appeared acutely ill and distressed, but had a normal mental status. Vital signs were as follows: blood pressure 125/65 mmHg, pulse 104 beats/min, respiratory rate 20 breaths/min, and body temperature 37.0°C. The patient’s height and weight were 165.9 cm and 54.5 kg, respectively. There was no fetal heartbeat detected and the fetus was delivered stillborn. Her laboratory data were as follows: arterial pH, 7.09; serum bicarbonate, 4 mmol/L; ketone bodies, 3+; anion gap, 14.8 mmol/L; white blood cell counts, 20,310/mm^3; glucose, 629 mg/dL; HbA1c, 5.4% (used National Glycohemoglobin Standardization Program (NGSP) value); osmolarity, 297 mOsm/kg; sodium, 131.6 mmol/L; potassium, 5.4 mmol/L; total cholesterol, 152 mg/dL; high-density lipoprotein, 76 mg/dL; triglyceride, 82 mg/dL; low-density lipoprotein, 76 mg/dL; serum amylase, 106 U/L (normal range, 29-110); and lipase, 50.88 U/L (normal range, 14-60). Serum C-peptide (0.1 ng/mL) and 24 hours urine C-peptide (2.67 μg) levels were extremely low. The autoantibodies against glutamic acid decarboxylase, insulin, and islet cells were all negative. Thyroid function was within normal ranges and thyroid autoantibodies were not detected. A fundus exam showed no evidence of diabetic retinopathy. We diagnosed this patient with FTD.
by short duration of symptoms, diabetes ketoacidosis despite normal HbA1c level, low level of insulin secretion, and negative anti-islet autoantibodies.

The patient was treated for diabetic ketoacidosis with intravenous insulin and saline hydration. The patient’s HLA genotypes were DRB1*04:04 and DQB1*03:01/05:02. Serum cytomegalovirus IgM was and IgG were negative and reactive (165.1 arbitrary unit/mL), respectively. Serum Epstein-Barr virus (EBV) viral capsid antigen IgM and IgG were negative (0.19 arbitrary unit/mL) and positive (1.69 arbitrary unit/mL), respectively. Serum EBV early antigen IgM, IgG, and nuclear antigen IgG were all negative. Both serum herpes simplex virus IgM and IgG were negative. Serum coxsackie virus B3 and B4 IgG titer was 1:4 and 1:32 at baseline and 1:4 and 1:64 after 4-weeks follow-up, respectively. Coxsackie viral infection can be suspected if coxsackie virus IgG titers increased more than 4-fold between acute and convalescent phase. Therefore, we did not find any susceptible viral infection associated with FTD. The patient was treated with premix insulin twice a day (total 0.8 unit/kg/day).

**Discussion**

This patient had typical clinical features of FTD and presented with acute onset hyperglycemic ketoacidosis, normal HbA1c, low C-peptide levels, negative islet-cell related autoantibodies, and concurrence with pregnancy. Although the patient had normal pancreatic enzymes levels and did not have previous flu-like or gastrointestinal symptoms, these were minor additional findings for diagnosis (1).

FTD accounts for up to 20% of type 1 diabetes in Japan (2). In Korea, the prevalence of FTD is 7.1% among all patients newly diagnosed with type 1 diabetes and 30.4% among patients with adult-onset diabetes (5). Interestingly, FTD is frequently observed in far eastern Asia; however, Caucasian FTD is very rare (4). Other Asian patients excluding Japanese, Korean, and Chinese patients are also rare (6,7), and a Vietnamese case has not been previously reported.

Certain class II HLAs are known to increase susceptibility to this disease. Imagawa et al. (8) examined serological types of class II HLA in 182 patients with FTD in Japan. They reported that the DR4-DQ4 haplotype occurred in 41.8% (76/182) of patients and showed the highest allele frequency. Kawabata et al. (9) reported that homozygosity for DRB1*04:05-DQB1*04:01 was much higher in FTD (12.5%, odds ratio 11.2) than in the acute-onset (8.3%, odds ratio 7.1) and slowly progressive (7.1%, odds ratio 6.0) subtypes. Zheng et al. (10) found that the most frequent haplotype was DQA1*03-DQB1*03:03 (18.4%) and the second was DQA1*01:02-DQB1*06:01 (15.8%) in Chinese populations.

Shimizu et al. (11) analyzed 34 FTD cases associated with pregnancy and reported that the most frequent haplotype was DRB1*09:01-DQB1*03:03 (41.2%) and the secondary was DRB1*04:05-DQB1*04:01 (14.7%). The HLA class II genotype of our patient was DRB1*04:04 and DQB1*03:01/05:02, which has been rarely reported in FTD patients (8). These data indicate that the patient did not have an immunogenetic predisposition to FTD.

Certain viral infections may trigger the destruction of beta cells in susceptible individuals. In fact, there have been many case reports in which the occurrence of FTD has been associated with evidence of several viral infections such as coxsackie virus, echovirus, human herpes virus 6, herpes simplex virus, mumps virus, and influenza (12, 13). In our case, however, the patient did not show any suspicious symptoms of antecedent viral infection. In addition, there was no significant elevation in viral antibody titers.

The development of FTD is often associated with pregnancy or delivery. It usually develops after 20 weeks of gestation or just after delivery, with an extremely poor prognosis for the fetus. In a nationwide Japanese survey, 13 out of 14 women who developed type 1 diabetes mellitus during pregnancy or within 2 weeks of delivery appeared to have FTD mellitus (2). Shimizu et al. (11) reported that fetal demise occurred in 12 out of 18 patients (67%) who developed FTD during pregnancy. Additionally, cases of fetal death showed more severe acidosis than patients with live-born infants. In diabetic ketoacidosis, maternal hypovolemia and/or maternal acidemia decreases uteroplacental blood flow and leads to fetal demise. Because the clinical course of FTD is much faster and leads to more severe deterioration than general type 1 diabetes, fetal mortality is much more likely.

This is the first case report of FTD in a Vietnamese patient. We did not find any susceptible viral markers associated with FTD. The patient did not have a susceptible HLA genotype. The patient developed FTD during the third trimester of pregnancy and induced a stillbirth.

The authors state that they have no Conflict of Interest (COI).

**References**

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