

Successful Secundigravida in Fulminant Type 1 Diabetes Mellitus: A Case Report

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1. Abstract

1.1. Purpose: To present a woman with successful secundigravida after being diagnosed fulminant type 1 diabetes mellitus.

1.2. Method: A descriptive case report of a single patient.

1.3. Results: A healthy baby girl was delivered by Caesarean section. A 33-year-old woman, at 34 weeks and five days of her first pregnancy, was admitted to our hospital with severe nausea, vomiting, diarrhea and stomach ache. She was subsequently diagnosed as FT1DM based on significantly high blood sugar, normal HbA1c, positive ketones, absolute deficiency in insulin secretion and no diabetic autoantibodies. Induction of labour was performed due to stillbirth, blood glucose was well controlled with long-term insulin therapy and no diabetes-related complications have been identified to date. After five years, the patient recently has a successful secundigravida by naturally conception and delivery.

1.4. Conclusions: Despite FT1DM is a rare disease. Herein, this case was successful second pregnancy and delivery five years after the diagnosis of FT1DM, with the aim of obtaining widespread attention to FT1DM patients, providing the patients with more consulting on their pregnancy suggestion which might get adverse outcomes reduce

2. Introduction

As a result of the vast majority of the destruction of pancreatic beta-cells shortly, Fulminant type 1 diabetes mellitus (FT1DM) is infrequent and distinguished though the advancement of hyper-

lycemia and diabetic ketoacidosis (DKA) [1]. The mechanism of FT1DM is unknown and may be related to the pregnancy, autoimmunity, hereditary susceptibility, and viral infection. Herein, we reported a case of FT1DM infected by Coxsackievirus type B1 infection during the first pregnancy causing intrauterine stillbirth, who had successful secundigravida five years later. This is the first case report of a woman who had successful secundigravida and delivery after being diagnosed with FT1DM.

3. Case History

A 33-year-old female patient, G1P0 (G: gestation, P: parturition) denied a family history of diabetes. No abnormalities were found in her medical examination during her pregnancy. She had undergone a 75-g oral glucose tolerance test at the 28th week of gestation, which was normal. On Aug 15, 2016, 34 weeks and five days of gestation, she developed nausea, vomiting, stomach ache and diarrhea for about half a day, without seeking any medical help. One hour later, the patient's symptoms deteriorated and she suffered from dyspnea. She was taken to a general hospital but with undiagnosed. Thereafter, she was transferred to the emergency department of our hospital. On admission, laboratory results showed that fingertip blood glucose was high (≥ 33.3 mM), urine ketone and glucose both were 4+, blood pH was 7.1. Other statistics were shown in (Table 1). Vital signs: temperature, 37.5°C; pulse rate, 110 beats per minute; respiratory rate, 28 breaths minute; and blood pressure, 150/90 mmHg. Examination revealed fetal bradycardia. The patient was diagnosed with DKA and intrauterine

stillbirth. And was immediately given effective fluid infusion, intravenous insulin, anti-infection to maintain vital signs. Multi-disciplinary treatment (obstetrics, endocrinology and anesthesiology departments) was conducted immediately, and the patient was transferred to the ICU after induction of labour. In the ICU, her blood glucose fluctuated greatly (4.5-27.5 mM), with continuous intravenous insulin infusion. A week later, she was transferred to the endocrinology department, her fingertip blood glucose ranged from 5.3 to 22.6 mM, and ketone was negative with insulin pump. The laboratory examination results are reported in (Table 1). Acute pancreatitis was excluded by abdominal CT scan. From Aug 23, daily multiple injections of insulin aspart (Novonordisk, Denmark) and insulin lantus (Sanofi, France) were administered, instead of insulin pump. After 14 days of treatment, she recovered and was discharged from the hospital. During the five years, many C-peptide releasing tests confirmed that fasting C-peptide was

<0.01ng/mL, and postprandial 2h C-peptide was also <0.01ng/mL the fluctuation of glucose ranged from 4.0 to 20 mM, and no diabetes-related complications occurred. Her menstruation stopped in May 2021, she found she was pregnant and HbA1c 6.5%. Doppler ultrasonography suggested visible fetal heartbeat and intrauterine live fetus at the beginning of September (Figure 1A). On Dec 15, four-dimensional color ultrasound indicated that the gestational week of the fetus was 22 weeks, and the gestational week was 22 and 5 days according to the last menstruation. The size of the fetus by color Doppler ultrasound was consistent with the actual gestational week (Figure 1B). On Mar 25, 2022, she gave birth to a baby girl with a weight of 3200g. Other parameters are shown in (Table 1). The Apgar score was 10 points in the first minute, 10 points in the fifth minute and 10 points in the tenth minute. The blood insulin dosage and glucose levels before conception, the period of conception and after delivery in the second pregnancy are shown in (Figure 2).

Table 1: The laboratory examination results in the first and second pregnancy

	Aug 15, 2016 (first pregnancy)	Aug 22, 2016 (first pregnancy)	Mar 25, 2022 (second pregnancy)
RBC (4.3-5.8 ¹² /L)	4.1*10 ¹² /L	5.3*10 ¹² /L	4.1*10 ¹² /L
WBC(3.5-9.5*10 ⁹ /L)	13.8*10 ⁹ /L	4.8*10 ⁹ /L	5.2*10 ⁹ /L
HB(130-175G/L)	108	95	108
NEUT	12.0*10 ⁹ /L	2.21*10 ⁹ /L	2.41*10 ⁹ /L
PLT(100-300*10 ⁹ /L)	224*10 ⁹ /L	98*10 ⁹ /L	115*10 ⁹ /L
Hcrp(0-10mg/dl)	55	8.5	11
ESR(0~20mm/h)	95	8	9
Coxsackievirus B1	positive	NA	NA
ALT (9-50U/L)	56	51	45
AST (15-40U/L)	85	53	32
TP (65-85g/L)	68.5	55	61.5
K+ (3.5-5.5mmol/L)	5.24	3.8	4.2
Na+ (135-145mmol/L)	140.2	135.3	132.2
Cl- (99-110mmol/L)	100.7	89.4	95.7
Ca2+ (2.10-2.55mmol/L)	2.05	2.17	2.2
Amylase (20-52U/L)	57.6	30.2	12.6
Lipase(5.6-35U/L)	32.3	27.4	24.3
Crea(58-110umol/L)	88	56	56
glucose(3.9-6.1)mmol/L	34.95	6.8	5.7
Blood Ketone	positive	Negative	Negative
Fasting C-peptide (0.78-1.89ng/mL)	<0.01	<0.01	<0.01
2h C -peptide (0.78-1.89ng/mL)	<0.01	<0.01	<0.01
HbA1c (3.6-6.1%)	6.70%	6.70%	6.50%
ICA	Negative	NA	Negative
IAA	Negative	NA	Negative
GADA	Negative	NA	Negative
pH (7.35-7.45)	7.02	7.41	NA
pO2 (95-115mmHg)	105.5	110	NA

pCO ₂ (31-44mmHg)	24.9	35	NA
Urine glucose	4+	2+	—
Urine ketone	3+	—	—
Urine Protein	—	—	—

RBC: Red blood cells; WBC: White blood cells; HB: Hemoglobin; NEUT: neutrophilia; hCRP: hypersensitive C-reactive protein; ESR: erythrocyte sedimentation rate; AST: aspartate aminotransferase; ALT: alanine aminotransferase; TP: Total protein; Crea: creatinine; GADA: glutamic acid decarboxylase antibody; IAA: insulin autoantibody; ICA: islet cell autoantibody; HbA1c: glycated hemoglobin; pH: potential of hydrogen; pO₂: partial pressure of oxygen; pCO₂: partial pressure of carbon dioxide; .NA: Not Applicable.

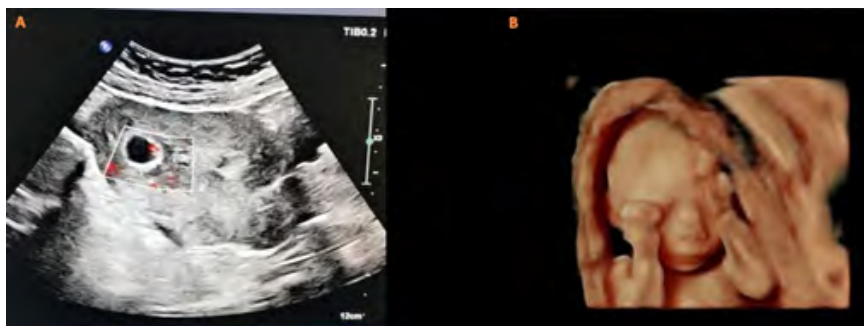


Figure 1: The fetus in different trimester.

Figure 1A: visible fetal heartbeat and intrauterine live fetus on Sep 1.

Figure 1B: four-dimensional color ultrasound suggested biparietal diameter was 53.2mm, head circumference was 196mm, abdominal circumference was 170mm, femoral length was 37.7mm, transverse diameter of cerebellum was 21.9mm On Dec 15.

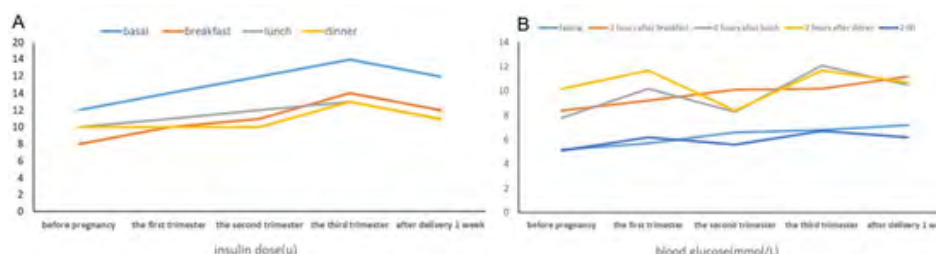


Figure 2: The insulin dose and fluctuation of the blood glucose in the second pregnancy.

Figure 2A: the insulin dose in the second pregnancy.

Figure 2B : the fluctuation of the blood glucose in the second pregnancy.

4. Discussion

Fulminant type 1 diabetes mellitus (FT1DM) was first reported in 2000 by Imagawa et al [1]. The majority of confirmed cases of FT1DM occurred in East Asia, especially in Japan. In Japan, FT1DM accounts for approximately 15-20% of the ketosis-onset or ketoacidosis-onset T1DM, and most T1DM during or after pregnancy were diagnosed as FT1DM [2]. In South Korea, FT1DM accounted for 7.1% from new confirmed T1DM cases [3]. In China, The prevalence of FT1DM was 4.5% which data based from a single center [4]. In addition, a literature analysis had showed that 18% of FT1DM were related to pregnancy [5]. However, cases were sporadic in other countries. More than 90% patients with FT1DM are adults, and the incidence rate between men and women is similar [2]. The criteria for definite diagnosis of FT1DM was published by the committee of the Japan diabetes society, which were: (1) occurrence of diabetic ketosis or ketoacidosis shortly (approximately one week) after the onset of hyperglycemic symptoms (elevation of urinary and/or serum ketone bodies

at first visit), (2) plasma glucose level ≥ 16.0 mmol/L and HbA1c level $< 8.5\%$ at first visit, and (3) urinary C-peptide excretion < 10 $\mu\text{g}/\text{day}$ or fasting serum C-peptide level < 0.10 nmol/L and < 0.17 nmol/L after intravenous glucagon (or after meal) load at onset [6]. The etiology and mechanism of FT1DM was uncertain, which may possibly associate with genetic susceptibility, viral infection, pregnancy and autoimmunity [7]. It is not known why FT1DM is associated with pregnancy, but as we all known that immune system is changed during pregnancy [8]. Most T1DM during pregnancy is FT1DM, which maybe correlated with the changes of immune environment [2]. Viral infection and human leukocyte antigen were also related to FT1DM [9]. Coxsackie B1 belongs to the family of enteroviruses (EVs). Epidemiological studies have confirmed a close association between EVs and T1DM because of the EVs significant destruction upon β -cells, which leads to T1DM [10,11]. The exact pathogenesis by which EVs could cause T1DM remain unknown. HLA-DR and DQ genes were significantly correlated with the FT1DM in pregnancy [12], unfortunately, the above genes were not tested.

In this case, the patient had abdominal symptoms and serum amylase above the upper laboratory limit, the increased serum pancreatic enzyme levels disappeared after the treatment of DKA, and acute pancreatitis was excluded by abdominal CT scan. It is reported that 50% of cases with FT1DM during pregnancy had abdominal symptoms and higher serum lipase and/or amylase levels [1]. Pancreatic specimens taken by biopsy showed cellular infiltration both to endocrine and exocrine pancreas in patients who died 1–5 days after the FT1DM, respectively [13].

Diabetes-related autoantibodies are seldom positive in FT1DM, and only 4.8% of FT1DM cases were positive for GADA, while others were negative [14]. GADA, ICA, IAA were negative in this case. However, other autoantibodies, such as IA2, Zinc transporters, were not tested.

After the diagnosis of FT1DM, the patient became insulin-dependent, without any oral antidiabetic drugs. FT1DM decreases the chance of spontaneous pregnancy. The reason why includes the diabetic autonomic neuropathy which affecting the reproductive system; renal insufficiency which leading to an increase in prolactin affecting ovulation and some psychological factors, et al. Compared to typical T1DM, there is no data support on fertility reduction.

In this case, the patient was diagnosed with FT1DM in her first pregnancy, the patients were treated according to the therapeutic principle of ketoacidosis. As the prognosis of FT1DM in pregnancy is worse than that the classic T1DM, the character of FT1DM were rapid progress, critical clinical symptoms, usually associated with multiple organ dysfunction such as exocrine, liver and kidney dysfunction, and poor prognosis. We found laboratory evidence of Coxsackie B1 virus infection. Symptoms are non-specific with virus in the early-phase, and may be easily confused with the symptoms caused by diabetes ketoacidosis. Hyperglycemia, dehydration, severe acidosis, electrolyte metabolism disorder, hypoxia, infection, et al were blamed for stillbirth. The patient had a systematic education on FT1DM to make her have enough knowledge of the disease. Her regular outpatient follow-up for five years without complications which may lay a good foundation for the patient's second pregnancy and delivery.

T1DM complicated approximately 0.3-0.5% of pregnancies [15]. With no contraception in the past five years, the patient conceived again in May 2021. No Pregnancy-complications, such as gestational hypertension, fetal macrosomia, and neonatal hypoglycemia were attributing to periodically antenatal care and blood glucose management throughout the re-pregnancy. In summary, FT1DM is a rare disease. Herein, we reported a case of successful second pregnancy and delivery five years after the diagnosis of FT1DM, with the aim of obtaining widespread attention to FT1DM patients, providing the patients with more consulting on their pregnancy suggestion which might get adverse outcomes reduced. This report aiming to display the case which and how FT1DM patient was

promoted the chances of pregnancy and successfully delivered.

5. Ethics Statement

The research on human participants did not require ethical review and approval in line with the local legislation and institutional requirements. We obtained written informed consent from the patient at the time of the clinical investigation for the figure and data in this article.

6. Author Contribution

All the authors have contributed significantly. WS collected the clinical data. GJ summarized the relevant literature. YD and WP wrote the manuscript. PD revised the manuscript. All authors agreed to submit this version.

7. Declaration of Interest

The authors declare that they have no interests or personal relationships that could have appeared to influence on this case report.

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