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CASE REPORT

Transition of blood glucose level in a patient with pregnancy-associated fulminant type 1 diabetes mellitus

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ABSTRACT

We report on the transition in blood glucose levels before and after the onset of fulminant type 1 diabetes mellitus in a perinatal woman. In week 38 of pregnancy, before which the patient had normal glucose tolerance, idiopathic acute pancreatitis was diagnosed. Five days thereafter, she became hypoglycemic, so we closely monitored her blood glucose levels. A total of 13 days later, she was hyperglycemic with a blood glucose level >16.0 mmol/L and glycated hemoglobin of 6.4%. Her fasting serum C-peptide reactivity level was 3.6 ng/mL on the 5th day, and 0.2 ng/mL on the 18th day. Multiple insulin injection therapy was administered since the 18th day; after that, ketoacidosis did not occur. The patient was diagnosed with fulminant type 1 diabetes mellitus based on hyperglycemia without high glycated hemoglobin levels and sudden onset insulin-dependent diabetes. Monitoring glucose levels in the case of idiopathic acute pancreatitis during pregnancy and prompt initiation of insulin therapy are important.

INTRODUCTION

Fulminant type 1 diabetes mellitus is defined as a sudden onset of insulin-deficient severe hyperglycemia and the consequent development of ketoacidosis within 1 week thereof[1,2]. Its pathogenesis is hypothesized to be associated with immunological dysfunction[3]. Owing to an immune tolerance that occurs perinatally, incidental fulminant type 1 diabetes mellitus is diagnosed quite frequently during that period[4]. Prompt diagnosis and treatment of fulminant type 1 diabetes mellitus are paramount, as any delay thereof is liable to adversely affect prognosis.

Any delay in diagnosing fulminant type 1 diabetes mellitus during pregnancy has the potential to cause both fetal and maternal death[4]. Thus, in the event that a pregnant patient develops digestive problems, particularly acute pancreatitis and/or an upper respiratory infection, monitoring blood glucose levels might help physicians to rule out fulminant type 1 diabetes mellitus or even to diagnose it early enough to avoid such feared complications.

We report as follows a case of fulminant type 1 diabetes mellitus whose onset in the perinatal period first manifested in idiopathic acute pancreatitis, and blood glucose monitoring had started before hyperglycemia had been observed.

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CASE REPORT

A 42-year-old Japanese woman in the 38th week of pregnancy was referred to the emergency department of Uji Tokushukai Medical Center (Uji, Japan) with a chief complaint of severe upper abdominal pain. Her obstetric history included two previous uncomplicated pregnancies. She had undergone a 75-g oral glucose tolerance test at week 13 of the current pregnancy, which was normal.

On presentation, the patient's vital signs and physical findings were as follows: body temperature, 37.3°C; pulse rate, 108 b.p.m.; blood pressure, 115/87 mmHg; respiratory rate, 19/min; and Glasgow Coma Scale score of 15. She was 151-cm tall and weighed 73 kg. Abdominal ultrasonography showed no apparent fetal abnormalities; the estimated fetal weight was 3,038 g. The abdominal examination was unremarkable, aside from tenderness in the upper quadrants, with normal bowel sounds. The laboratory findings were significant for an elevated serum C-reactive protein 2.91 mg/dL, serum total amylase 180 U/L and serum pancreatic amylase 160 U/L. Her blood glucose level was within normal limits at 4.3 mmol/L. Urinalysis was negative for glucose. Abdominal computed tomography was contraindicated in light

of her pregnancy. She was diagnosed clinically with acute pancreatitis and thus admitted to the hospital.

On the 2nd day of admission, because the patient's serum total amylase was further elevated at 213 U/L and her C-reactive protein was elevated at 4.40 mg/dL, she underwent an emergency cesarean section owing to increased risk to the fetus. At the time of birth, the infant had no apparent abnormalities. On the 4th day, the patient underwent an abdominal computed tomography scan that showed edematous enlargement of the pancreatic body and stranding of the surrounding fat, thereby corroborating the clinical diagnosis of acute pancreatitis. Then, on the morning of the 5th day of hospitalization, she reported chills and rigors. Her blood glucose was measured at 1.9 mmol/L; however, the cause of hypoglycemia was not yet certain.

Thereafter, preprandial blood glucose levels were closely monitored. On the 5th day, the fasting serum C-peptide reactivity (CPR) level was 3.6 ng/mL, and the blood glucose level was 6.7 mmol/L. On the 6th day, serum amylase level decreased to 171 U/L and C-reactive protein decreased to 3.1 mg/dL, and the measured blood glucose level before lunch was 8.6 mmol/L. Because the acute pancreatitis improved, meals were restarted on the 8th day. She took 1,600 kcal a day. Because her high blood glucose level continued (Figure 1), she was examined by a diabetologist on the 17th day. Thereupon diagnosed with a new onset of diabetes mellitus, the patient was started on multiple insulin injection on the 18th day. Her fasting serum total ketone body level increased slightly to 339 μmol/L on the 15th day, but did not meet the criteria for either ketosis or ketoacidosis. Her glycated hemoglobin level was 6.4% on the 13th day. The fasting serum CPR level had been elevated at 3.6 ng/mL on the 5th day, yet decreased to 0.9 ng/mL on the 7th day, and even further to 0.2 ng/mL on the 18th day. Anti-glutamic acid decarboxylase antibody was positive at 89.9 U/mL, although anti-islet antigen-2 antibody was negative. On the 22nd day, the patient was discharged from the hospital. At the discharge, the subcutaneous injection of 6 U, 6 U and 6 U of insulin aspart were prescribed before breakfast, lunch and dinner, respectively, and 6 U insulin glargine was prescribed before dinner. For half a year after

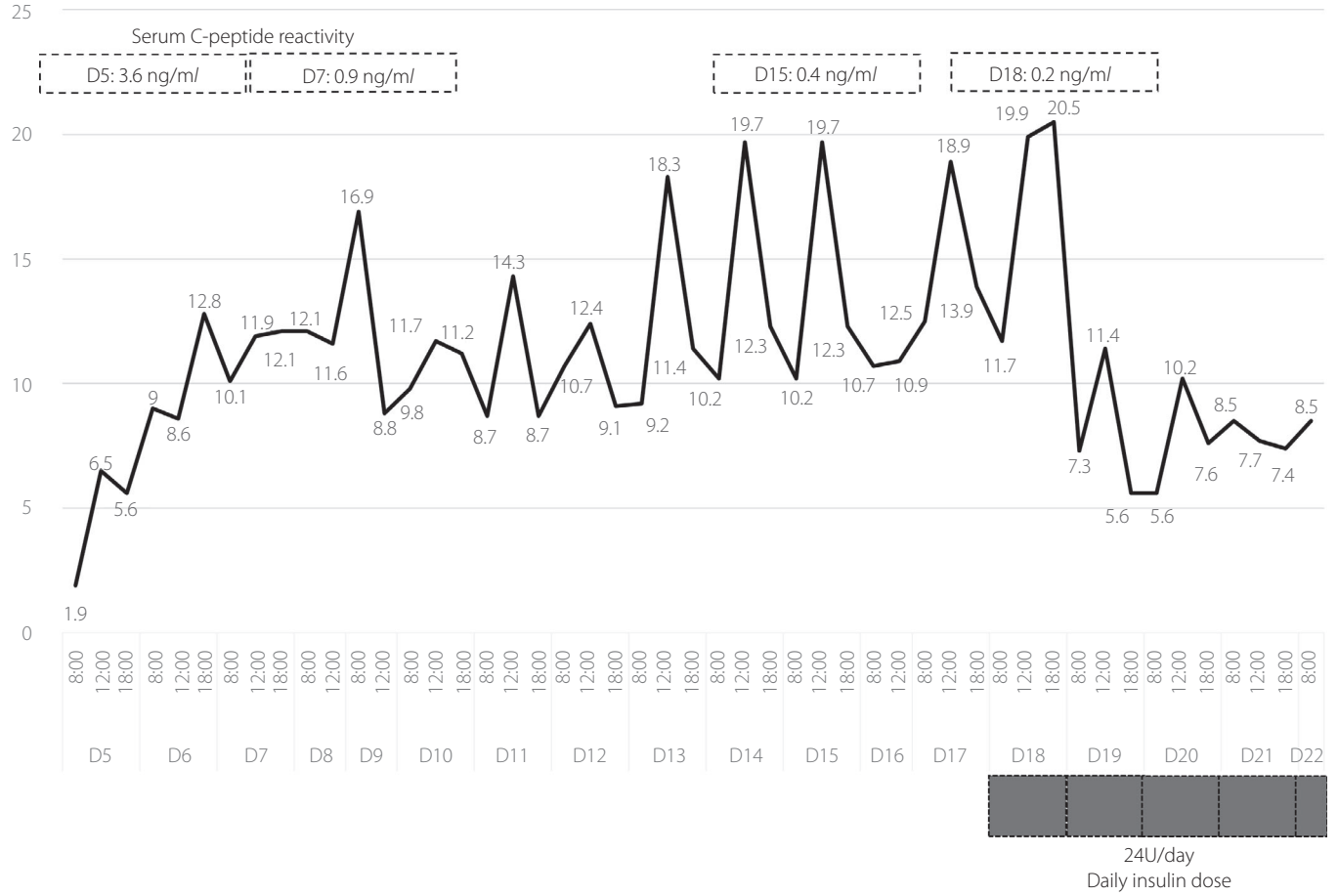

Figure 1 | The time course of blood glucose (mmol/L). The transition in blood glucose levels by blood glucose meters during hospitalization. D5, day 5; U, units.

discharge, the patient was prescribed almost the same amount of insulin.

The glucagon stimulation test was carried out 1 month after discharge, and showed that the serum CPR level was 0.1 ng/mL before loading and 0.2 ng/mL at 6 min after loading, then impairment of endogenous insulin secretion was confirmed. Anti-glutamic acid decarboxylase antibody was positive at 30.4 U/mL at 6 months after the discharge. Subsequent testing was positive for human leucocyte antigens DRB1*04:05, DQB1*04:01 and DRB1*13:02, DQB1*06:04. The former has been reported to be the most frequent haplotype in patients with fulminant type 1 diabetes mellitus[1]. On the 7th day of admission, she felt a sore throat and cough, and was suspected of having a viral upper respiratory infection. The viral antibody titers of the patient were examined in paired sera on the 15th and 80th day, but the virus antibody titers, including cytomegalovirus, Herpes simplex virus, Epstein–Barr virus and coxsackievirus A4–6, B1–6, were all negative. In addition, the acute pancreatitis preceded the symptom of viral upper respiratory infection by >1 week, and therefore there was no clear relationship between incident diabetes and virus infection in this case.

DISCUSSION

This is the first study to report how fasting and preprandial blood glucose levels change before and after the onset of pregnancy-associated fulminant type 1 diabetes mellitus. This patient's fulminant type 1 diabetes mellitus was diagnosed based on the following findings: the pre-prandial blood glucose level had surpassed 16.0 mmol/L after the 13th day, whereas her glycated hemoglobin level was <8.3%. The serum CPR was <0.3 ng/mL on the 18th day, having been in an insulin-dependent state for approximately 10 days after the appearance of hyperglycemia. Prompt insulin therapy helped her to avoid diabetic ketoacidosis, whereas severe ketosis and ketoacidosis are usually observed in patients with fulminant type 1 diabetes mellitus within a week after the appearance of hyperglycemic symptoms[1]. The monitoring of preprandial blood glucose, as well as fasting blood glucose, helped us to make the diagnosis as early as possible, thereupon to administer proper insulin therapy, and thus to prevent the feared complication of ketosis or ketoacidosis.

In conclusion, judging from our observations of the time course of rising blood glucose levels at the onset of pregnancy-associated fulminant type 1 diabetes mellitus, we strongly recommend that treating physicians closely monitor blood glucose levels during treatment for idiopathic acute pancreatitis in pregnancy, which might lead to an early diagnosis of fulminant type 1 diabetes mellitus and thereby reduce the risk of a poor prognosis for the mother and fetus alike.

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DISCLOSURE

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