—Case Reports—

A Neonate with Severe Acidosis Caused by Diabetic Ketoacidosis Associated with Maternal Fulminant Type 1 Diabetes

Kenta Igami[1,2], Yoshio Shima[3], Sakae Kumasaka[1], Haruka Iwata[1], Naoyuki Ikari[1] and Toshiaki Shimizu[2]

[1]Department of Pediatrics, Japanese Red Cross Tokyo Katsushika Perinatal Center, Tokyo, Japan
[2]Department of Pediatrics, Juntendo University Faculty of Medicine, Tokyo, Japan
[3]Department of Neonatal Medicine, Nippon Medical School Musashi Kosugi Hospital, Kanagawa, Japan

Fulminant type 1 diabetes mellitus (fulminant T1DM) can progress rapidly to diabetic ketoacidosis (DKA). It can develop in pregnant women with no prior history of diabetes, and such cases are associated with severe perinatal consequences. We report the detailed clinical course of a neonate born from a mother with DKA caused by fulminant T1DM. The male neonate weighed 3,024 grams and was born at 36 weeks of gestation. The patient's mother had an uneventful pregnancy until she visited the hospital on the day of delivery with headache, nausea, and decreased fetal movement. The APGAR score of the neonate was 8/8, but he was transferred to our hospital for further evaluation because umbilical cord blood gas analysis showed unexplained acidosis (pH = 6.92). We were later informed that the mother was diagnosed as having DKA due to fulminant T1DM after the neonate was born. On admission, laboratory testing of the neonate revealed hypoglycemia, hyperinsulinemia, and hyperkalemia, all of which were induced by the mother's metabolic condition. Intravenous glucose supplementation resolved the neonate's metabolic derangement, and he was discharged on day 10. He showed no neurological abnormalities, but magnetic resonance imaging showed lesions indicating hypoglycemic encephalopathy. Maternal fulminant T1DM and DKA should be considered in neonates with severe metabolic acidosis. Even a neonate who is asymptomatic at birth may rapidly develop severe disease.
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Key words: acidosis, diabetes mellitus, diabetic ketoacidosis, hypoglycemia, neonate

Introduction

Fulminant type 1 diabetes mellitus (fulminant T1DM) is a subtype of T1DM characterized by abrupt onset and absence of diabetes-related antibodies[1]. Patients with fulminant T1DM often develop diabetic ketoacidosis (DKA) with severe metabolic acidosis and electrolyte imbalance[2]. Furthermore, fulminant T1DM and accompanying DKA may develop during pregnancy, which can harm the mother and fetus. Several studies have reported high fetal mortality, and one study found that over half of such cases resulted in stillbirth[3–5]. However, these reports primarily focused on mothers, and the clinical course of neonates who survived this perinatal complication has not been carefully described. We describe the clinical course of a neonate born to a mother who developed DKA during delivery, primarily focusing on the child's metabolic condition.

Case

A male neonate weighing 3,024 g (85.3 percentile) was born at 36 weeks of gestation to a 38-year-old Japanese woman (gravida 8, para 2). The child was delivered by emergency cesarean section because of non-reassuring fetal status. The APGAR score was 8 at 1 minute and 8 at 5 minutes. The mother had no medical or family history of diabetes. A 75-gram oral glucose tolerance test was con-

Correspondence to Yoshio Shima, MD, PhD, Department of Neonatal Medicine, Nippon Medical School Musashi Kosugi Hospital, 1–383 Kosugi-cho, Nakahara-ku, Kawasaki, Kanagawa 211–8533, Japan
E-mail: shima-p@nms.ac.jp
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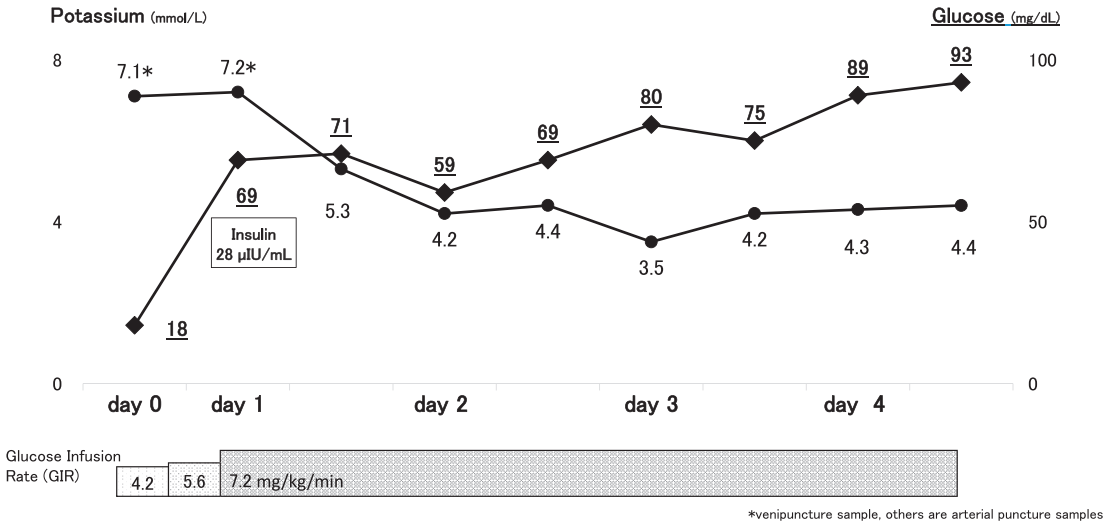

Fig. 1 Clinical course

The patient presented with marked hypoglycemia and hyperkalemia. Glucose infusion was started at 4.2 mg/kg/minute and then increased to 7.2 mg/kg/minute. The insulin level was 28 μIU/mL at a glucose level of 69 mg/dL. Hyperkalemia was resolved by glucose supplementation and did not require insulin administration.

ducted at 32 weeks 2 days because the baby was slightly large for gestational age, but the test result was normal. She had a preoperative workup at 36 weeks 2 days for a scheduled Cesarean section: serum glucose was 145 mg/dL and urine dipstick was 2+ for glycosuria, but she had no polyuria or polydipsia. Three days later, she visited the hospital with nausea, headache, and decreased fetal movement on the day of delivery. Emergency operative delivery was indicated because of the non-reassuring fetal status on fetal heart rate monitoring and the maternal clinical symptoms. The neonate started breathing promptly and had good muscle tonus; however, unexplained acidosis (pH=6.92 on umbilical arterial blood gas analysis) was noted and he was transferred to our neonatal intensive care unit for further evaluation. On admission, laboratory tests revealed hyperkalemia (potassium: 7.1 mmol/L, venipuncture sample) and hypoglycemia (glucose: 18 mg/dL). Hyperkalemia was treated with intravenous calcium and sodium bicarbonate. Glucose infusion was initiated at 4.2 mg/kg/min, and the infusion rate was increased to 7.2 mg/kg/min. A blood test performed shortly after glucose infusion showed an insulin level of 28 μIU/mL and a glucose level of 69 mg/dL (**Fig. 1**). A few hours after his arrival we were informed that his mother had been diagnosed as having DKA due to fulminant T1DM after delivery. The laboratory findings for the mother were serum glucose 307 mg/dL, HbA1c (NGSP) 5.7%, serum C-peptide 0.23 ng/mL, acetoacetic acid 1,868 μmol/L, 3-hydroxybutyric acid 8,109 μmol/L, sodium 130 mEq/L, and potassium 5.0 mEq/L. She was categorized as having "moderate DKA" on the basis of the diagnostic criteria of the American Diabetes Association[6]. In contrast, the child's laboratory test results showed elevated serum insulin associated with hypoglycemia and hyperkalemia. He developed tachypnea 1 hour after birth and was started on a high-flow nasal cannula (pH 7.24, CO_2: 56.5 mm Hg, HCO_3^-: 24 mmol/L, BE: −5 mmol/L). However, he required further respiratory support and was switched to nasal directional positive airway pressure (DPAP) 6 hours later (pH 7.07 CO_2: 87.1 mm Hg, HCO_3^-: 25.2 mmol/L, BE: −8 mmol/L). Labored breathing persisted, and he was intubated 15 hours after birth (pH 7.22, CO_2: 58.9 mm Hg, HCO_3^-: 23.8 mmol/L, BE: −5 mmol/L). His cardiorespiratory status improved by metabolic correction with adequate intravenous glucose supplementation, and he was successfully weaned from all intensive care at age 7 days. There was no recurrent hypoglycemia and he was discharged on day 10. Magnetic resonance imaging (MRI) on day 26 showed areas of slightly increased signal in the occipital cerebral cortex on a T2-weighted image, indicating hypoglycemic encephalopathy (**Fig. 2**). He remains stable, without neurological sequelae, and is scheduled for careful developmental follow-up.

Written informed consent for publication was obtained from the parents.

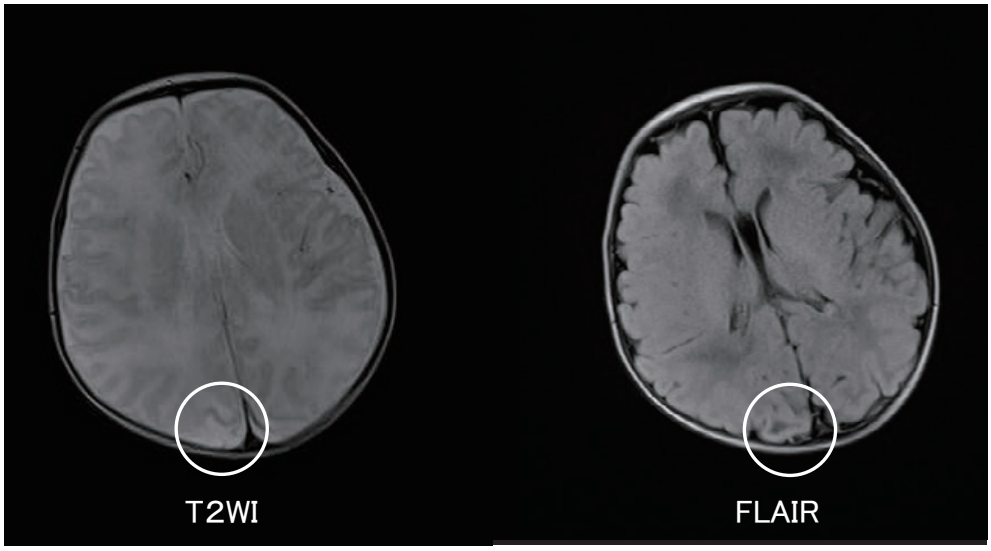

Fig. 2 Brain MRI
Brain MRI taken on day 26 showed areas of increased signal on T2WI and FLAIR, affecting the occipital cerebral cortex, which indicated hypoglycemic encephalopathy.
MRI: magnetic resonance imaging, T2WI: T2-weighted image, FLAIR: fluid-attenuated inversion recovery

Discussion

T1DM is caused by insulin deficiency after destruction of pancreatic beta cells[1]. Fulminant T1DM is a subtype of T1 DM characterized by rapid onset and can develop in pregnant women without a previous history of diabetes[4]. Consistent with previous findings, the mother of our patient had an uneventful pregnancy but unexpectedly developed DKA due to fulminant T1DM after an emergency cesarean section. Viral infection is a possible trigger[1,4,5]; however, no such episode was observed in the present case. This suggests that pediatricians may need to initiate management without any information on this maternal comorbidity, especially when DKA due to fulminant T1DM occurs around childbirth, as in this case. DKA is associated with maternal hemodynamic instability, which often results in decreased uterine blood flow[7]. However, our patient's postnatal cardiopulmonary adaptation was satisfactory, with Apgar scores of 8/8 at 1/5 minutes, respectively. Therefore, we concluded that the neonate's marked metabolic acidosis (pH 6.9 in the umbilical artery sample) was induced by transplacental transfer of ketoacidosis, not by asphyxia. Contrary to classic clinical manifestations of DKA (hyperglycemia, insulin deficiency, and hypokalemia), our patient presented with hypoglycemia, hyperinsulinemia, and hyperkalemia. Hypoglycemia is a common metabolic complication of neonates born to mothers with diabetes[8–10]. The underlying mechanism is that fetal insulin secretion induced by maternal hyperglycemia causes a rapid fall in neonatal glucose levels after delivery[8–10]. Regarding the cause of hyperkalemia, glucose depletion and extracellular acidosis may have prevented intracellular potassium transfer despite excess insulin secretion. Hyperosmolarity caused by DKA may also have contributed to hyperkalemia[11]. This patient's brain MRI findings were compatible with hypoglycemic encephalopathy. Neonatal hypoglycemia is associated with neurological symptoms such as developmental delay, seizure, and visual impairment, but the association between the severity of clinical manifestations and MRI findings is unclear[12]. Our patient has not developed any neurological sequelae, but careful follow-up is scheduled.

Fulminant T1DM is a critical condition for both the mother and neonate. A study in China of the clinical course of 12 patients found that 4 of 8 cases resulted in fetal death[3]. A similar study of data from 22 pregnant Japanese women with fulminant T1DM reported that 12 of 22 cases resulted in stillbirth (67%)[4]. Of the 6 cases in which the neonates survived, 5 neonates were delivered by cesarean section[4]. Previous reports showed that prompt cesarean section improves outcomes for both the neonate and mother. Although diagnosis of DKA/fulminant T1DM is challenging, we were able to initiate intensive care for the unexplained acidosis immediately after the emergency cesarean section, which led to a favorable neonatal outcome.

In conclusion, maternal DKA caused by fulminant T1 DM should be considered in the differential diagnosis

when evaluating a neonate with unexplained metabolic acidosis. A neonate can be in critical condition after birth if metabolic disorders are not treated rapidly.

Conflict of Interest: The authors declare no conflict of interest.

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