Case Report

Fulminant Type I Diabetes: The First Case Report in Thailand

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Type 1 diabetes is classified as either autoimmune (type IA) or idiopathic (type IB) diabetes. Fulminant type 1 diabetes is a recently-discovered subtype of idiopathic type 1 diabetes. It is defined as diabetes with complete abrupt onset of β cell destruction and progression to hyperglycemia and ketoacidosis within a short period of time, but with a near-normal HbA1c level. The patients often have flu-like or abdominal symptoms at onset and elevated levels of pancreatic exocrine enzymes. Their diabetes-related autoantibodies are usually negative. In the present report, the authors present a case of fulminant type 1 diabetes in a 43-year-old Thai woman who presented with sudden onset of flu-like symptoms and abdominal pain. Findings on admission included a high blood glucose level and ketoacidosis, but a prediabetes range of HbA1c level. Autoantibodies to glutamic acid decarboxylase (GAD) were negative. This subtype of type 1 diabetes was first identified in 2000 and there have been case reports from Japan, Korea, the Philippines and the Netherlands. Nonetheless, no case had been reported in Thailand until the present study. Here the authors report the first case of fulminant type 1 diabetes in Bangkok, Thailand.

Keywords: *Fulminant type 1 diabetes, Diabetic ketoacidosis*

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Fulminant type 1 diabetes was first reported by Imagawa et al in 2000[1] and was defined as a rapid process involving complete beta cell destruction and progression of hyperglycemia and ketoacidosis within a short period, accompanied by a normal or near-normal HbA1c level at onset. Some evidence has suggested that viral infection and genetics are associated with the development of fulminant type 1 diabetes. According to Imagawa et al, fulminant diabetes accounted for 15-20% of Japanese type 1 diabetes with ketosis or ketoacidosis at onset[2] while in Korea, the prevalence of the newly-diagnosed type 1 diabetes was 7.1%[3]. Cho et al reported on 7 Korean adult patients with fulminant type 1 diabetes[3] and one Korean child with fulminant type 1 diabetes with peripheral neuropathy[4]. In 2007-2008 there were a few reported cases in China with and without genotypic analysis[5]. There had been no case reported in Thailand before the present study. Here the authors report a case of fulminant type 1 diabetes from Rajavithi Hospital, Bangkok, Thailand.

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Case Report

A 43-year-old Thai woman living in Bangkok, Thailand visited the hospital on November 5, 2010, presenting with fever and epigastric pain over 2 days. Physical examination revealed tenderness at the epigastrim, and laboratory data showed blood glucose 103 mg/dl, urine ketone negative, serum bicarbonate 21 mEq/L, serum amylase 211 IU/L and urine amylase 1,393 IU/L. She was diagnosed as having acute pancreatitis and was given a pain reliever. However, 3 days later on November 8, 2010 she developed thirst, general malaise, nausea, vomiting, fever and epigastric pain. She revisited the emergency department where severe hyperglycemia was found. Her physical examination showed a height of 165 cms and a weight of 61 kgs, with a body mass index of 22.5 kg/m^2. On admission, the patient was conscious and dehydrated. Her vital signs consisted of a blood pressure of 120/70 mmHg, pulse rate of 110/minute, respiration rate of 26/minute, body temperature of 37.2°C, and she had mild tenderness at the epigastrim. On admission, blood glucose was 399 mg/dl whereas HbA1c was

6.2%. Her arterial blood gas analysis revealed a pH of 7.163, serum level of bicarbonate was 10 mEq/L and serum ketone was 4.4 mmol/L (< 0.6 mmol/L), reflecting severe ketoacidosis. Complete blood count was as follows: white blood cell count (WBC 8,200 cell/uL, n 83%, L 13%, Eo 3%), platelets 469,000 cell/uL, Hct 41.2%, Hb13.5 g/dl, serum level of amylase was 70 IU/l. Blood chemistry showed that plasma potassium (4.9 mEq/L), AST, ALT, blood urea nitrogen, and creatinine were normal. Abdominal ultrasound showed no remarkable findings in the pancreas on admission. Chest x-ray and electro-cardiogram were normal. Based on these findings, this patient was diagnosed as having type 1 diabetes and diabetic ketoacidosis, and she was admitted for treatment for diabetic ketoacidosis. She was treated with intravenous infusions of saline and insulin and eventually was switched to intensive insulin therapy four times a day. After metabolic derangement was corrected, insulin secretion was evaluated. The fasting serum C-peptide concentration was < 0.01 ng/ml, reflecting absolute beta cell loss, but no C-peptide level was obtained following intravenous administration of 1 mg glucagon. Diabetes-related autoantibodies including glutamic acid decarboxylase (GAD) antibody and islet cell antibody were negative (Table 1).

Virological examinations of Epstein-Barr, Rubella virus, cytomegalovirus, and herpes simplex virus were not done. The abrupt onset of severe insulin deficiency, low HbA1c and lack of antibodies to islet antigens were compatible with symptoms of fulminant type 1 diabetes. Since then, the patient has been monitored for almost one year. She has been treated with an insulin dose of 0.8 unit/kg/day. The HbA1c level, which was near normal at the time of diagnosis, has been increased to 8.1%. Fig. 1 illustrates the changes in fasting glucose, HbA1c and insulin dosage in one year after diagnosis.

Final diagnosis Fulminant type 1 diabetes.

Table 1. Laboratory test

Complete Blood Count	
White blood count (cell/uL)	8,200
Neutrophils (%)	83
Lymphocyte (%)	13
Monocyte (%)	-
Eosinophil (%)	3
Hemoglobin (g/dl)	13.5
Hematocrit (%)	41.2
Platelets (cell/uL)	469,000
Blood chemistry	
Random blood glucose (mg/dl)	399
Creatinine (mg/dl)	0.9
Sodium (mEq/L)	127
Potassium (mEq/L)	4.9
Chloride (mEq/L)	93
Bicarbonate (mEq/L)	10
Calcium (mg/dl)	8.3
Phosphate (mg/dl)	2.6
AST (U/L)	45
ALT (U/L)	30
Amylase (U/L)	66
Ketone (< 0.6 mmol/L)	4.4
Urine analysis	
Urine specific gravity	1.020
pH	6
Glucose	3+
Ketone	2+
RBC	0-1
WBC	0-1
Amylase (28-100 U/L)	66
Endocrine laboratory value	
Thyrotropin (TSH mIU/L)	0.877
Free thyroxine (fT4 microg/dl)	1.31
Free triiodothyroinine (fT3 pg/dl)	1.80
C-peptide (ng/ml)	< 0.01
Anti-GAD	Negative
Anti-IA2	Negative

Discussion

Type 1 diabetes is an insulin-deficient status and is classified into two subtypes depending on the etiology. Type 1A is the immune-mediated type and type 1B is idiopathic diabetes. Recently, fulminant type 1 diabetes has been identified as a new subtype of idiopathic diabetes[6]. The precise mechanism of beta-cell destruction in patients with this subtype of diabetes is not known. The possibility of an association with a viral infection cannot be excluded because of preceding symptoms of infection[7]. Although fulminant type 1 diabetes has been clinically recognized, its etiology still remains obscure. The evidence accumulated to date suggests that both the viral infection itself and the subsequent immune reaction are likely to cause β-cell destruction and finally, fulminant type 1 diabetes[8]. In a nationwide survey, fulminant diabetes accounted for 20% of Japanese type 1 diabetes with ketosis or ketoacidosis at the onset and > 90% of these patients were adults[2]. Most patients who have this disease are Japanese, and few cases have been reported outside of Japan[9]. There are case reports from Korea, the Philippine and the Netherlands, although it is rarely reported in Caucasians. Occurrences in ethnicities other

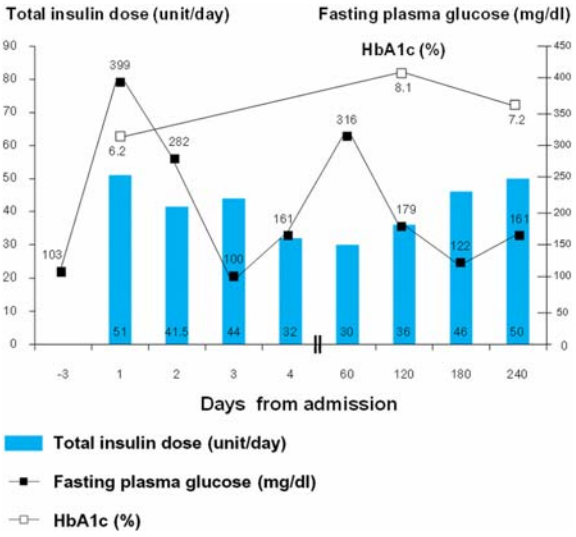

Fig. 1 Changes in Fasting glucose, HbA1c and insulin dosage in one year after diagnosis

than Japanese are rare, reflecting possible immunogenetic differences. There are two possible hypotheses regarding the different incidences between Japanese and Caucasians. One is that fulminant type 1 diabetes is specific to Asian ethnicities and the other is that the high incidence of type 1A diabetes covers up the presence of fulminant type 1 diabetes in the Caucasian population. The clinical characteristics of this subtype are: 1) remarkably abrupt onset of the disease, 2) very short duration, usually less than a week, of diabetic symptoms, 3) the presence of acidosis at diagnosis, 4) negative findings for islet-related autoantibodies such as islet-cell antibodies (ICA), anti-glutamic acid decarboxylase antibodies (GADAb), insulinoma-associated antigen 2 (IA-2) antibodies, 5) no C-peptide secretion, 6) elevated serum pancreatic enzyme levels, 7) frequent flu-like symptoms around the time of disease onset, 8) association with pregnancy, and 9) strong association with HLA-DR4-DQ 4 haplotype[10].

The present case satisfied all the recommended clinical criteria previously reported as well as Imagawa's criteria. In 71.2% of patients with fulminant type 1 diabetes, flu-like symptoms can be observed[2]. Patients with fulminant type 1 diabetes more frequently have flu-like symptoms and abdominal symptoms[8]. This type of diabetes is most likely an adult-onset disease, and there have been few cases in children. There is some evidence that the onset is related to environmental factors and the specific HLA subtype has been suggested. Japanese patients with fulminant diabetes usually have DR4-DQ4, while classic type 1 diabetes patients have DR9-DQ3[10]. Although this is the first case of an adult patient with fulminant diabetes reported among Thais, it is possible that it has not yet been fully recognized in Thailand and actually may be more common than initially thought.

Potential conflicts of interest

None.

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โรคเบาหวานชนิดที่ 1 ขั้นรุนแรง: รายงานการศึกษาผู้ป่วยครั้งแรกในประเทศไทย

นวพร นภาทิวาอำนวย, ทองคำ สุนทรเทพวรากุล, ชัยชาญ ดีโรจนวงศ์, วีระศักดิ์ ศรินนภากร, สถิต นิรมิตรมหาปัญญา

ผู้ป่วยหญิงคู่อายุ 43 ปี มีอาการไข้ ปวดท้อง 2 วัน ตรวจระดับน้ำตาลได้ 103 มิลลิกรัมต่อเดซิลิตร 3 วัน ต่อมายังมีไข้ ปวดท้อง คลื่นไส้ อาเจียน หอบ ตรวจระดับน้ำตาลได้ 399 มิลลิกรัมต่อเดซิลิตร ร่วมกับภาวะคีโตซีส โดยที่ระดับของค่าน้ำตาลเฉลี่ยสะสมยังไม่ได้เป็นเบาหวาน antiGAD และ anti IA2 ให้ผลลบจึงวินิจฉัยว่าเป็นโรคเบาหวานชนิดที่ 1 ชนิดรุนแรงที่มาด้วยอาการภาวะน้ำตาลในเลือดสูงชนิดที่มีภาวะคีโตซีส