An Obese Patient with Slowly Progressive Type 1 Diabetes Diagnosed by Ketoacidosis

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Abstract

The patient was a 69-year-old woman with a family history of type 2 diabetes. Her body mass index was 31.5. She was diagnosed as type 2 diabetes 32 years previously, and treated with insulin for 8 years. She had no episode of weight loss. She was hospitalized with diabetic ketoacidosis for the first time. Her GAD antibodies were not detected. However, ICA antibodies and insulin antibodies were positively detected. She was diagnosed with type 1 diabetes. Interestingly, her diabetes state was controlled to the same level after recovery from ketoacidosis.

Key words: slowly progressive insulin dependent diabetes mellitus, diabetic ketoacidosis, obesity

(Inter Med 49: 393-395, 2010)

(DOI: 10.2169/internalmedicine.49.2843)

Introduction

Autoimmune type 1 diabetic patients can be categorized in at least two clinical subtypes: acute onset type 1 diabetes (1) and slowly progressive type 1 (insulin-dependent) diabetes (SPIDDM) (2). SPIDDM is a disease in which diabetes mellitus, after an initial non-insulin dependent stage, progresses to an insulin-dependent state as a result of a gradual decrease in insulin secretion and the presence islet cells (3). It is prevalent and found in 10% of phenotypic type 2 diabetic patients (4).

Case Report

A 69-year-old woman was admitted to our hospital due to repetitive vomiting and loss of appetite. She had mental retardation without deafness since childhood and lived in a care facility. She had a family history of type 2 diabetes. When she was 37 years old, she was diagnosed with type 2 diabetes and she was prescribed diet and anti-diabetic oral agents. At the age of 61, she was diagnosed with cholecysti-

tis and underwent abdominal operation. Her HbA_{1c} level was around 9.0% before the operation. Oral agents (glibenclamide: 7.5 mg/day) were stopped to change to insulin therapy. Subcutaneous insulin injection was undertaken with rapid-acting insulin lispro (7 units before breakfast, 7 units before lunch, 6 units before supper) and intermediate-acting insulin lispro (10 units at bedtime) per day. After the operation, her glycemic control was around 8.0% of HbA_{1c}. During the 30 years, she had no episode of diabetic ketosis. Usually, she had a good appetite and was regularly given her meals and insulin injection by the staff in the care facility. Two days before admission, she refused her meals and at that time, insulin injection was not performed. Just before admission, she had repeated vomiting several times.

Physical examination on admission showed that her height was 139 cm and body weight was 60.8 kg (corresponding to a BMI of 31.5 kg/m²). She had no weight loss prior to admission. Her blood pressure was 120/55 mmHg, heart rate was 64 bpm and body temperature was 36.6°C, respectively. Her consciousness was I-3 for Japan coma scale. Physical examination for chest and abdomen was normal. Her deep tendon reflex was normal. Neither pathologi-

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Received for publication September 2, 2009; Accepted for publication November 4, 2009

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Table 1. Laboratory Data on Admission

WBC	4490 / μ L	TP	7.0 g/dL
RBC	375×10^4 / μ L	ALB	3.6 g/dL
Hemoglobin	11.4 g/dL	BUN	15.6 mg/dL
Hematocrit	33.4 %	Cre	0.70 mg/dL
Platelets	17.4×10^4 / μ L	UA	5.3 mg/dL
Urinalysis		T-Bil	0.9 mg/dL
Protein	(-)	GOT	36 IU/L
Blood	(-)	GPT	27 IU/L
Glucose	(4+)	ALP	336 IU/L
Keton Body	(2+)	LDH	268 IU/L
		γ GTP	41 IU/L
		AMY	82 IU/L
Blood gas analysis Room air, supine		Na	135 mEq/L
pH	7.227	K	4.8 mEq/L
pCO ₂	45.2 mmHg	Cl	97 mEq/L
pO ₂	72.7 mmHg	CRP	0.50 mg/dL
HCO ₃ ⁻	18.4 mmol/L	Plasma Glucose	405 mg/dL
Base Excess	-9.1 mmol/L	HbA1c	8.1 %
SaO ₂	91.7 %		

Table 2. Laboratory Data Related on Endocrine Gland Functions

On admission	
Fasting serum C-peptide	0.1 ng/mL
GAD antibodies	< 1.3 U/mL
Cytoplasmic islet cell antibodies	(+)
IA-2 autoantibodies	< 0.4 U/mL
Three months after admission	
Glucagon test	
Serum C-peptide levels:	
Pre-injection	0.1 ng/mL
6 min after injection	0.1 ng/mL

GAD: glutamic acid decarboxylase

cal reflex nor paralysis was observed.

Laboratory data are shown in Table 1. Plasma glucose and HbA_{1c} levels on admission were 405 mg/dL and 8.1%, respectively. Arterial blood gas analysis and marked elevation of ketone bodies indicated ketoacidosis. Ultrasonography revealed no abnormalities in her pancreas. No thyroid specific antibodies were positively detected. Her serum C-peptide level was 0.1 ng/mL. Serum levels of glutamic acid decarboxylase (GAD) antibodies, IA-2 antibodies were detected by radioimmunoassay (BML Inc, Tokyo, Japan). Islet cell antibodies (ICA) were detected by indirect immunofluorescence assay using type O human pancreas tissue (BML Inc, Tokyo, Japan). GAD and IA-2 were within normal limits. However, ICA-IgG was detected positively (15.0 JDF units) (Table 2). She was diagnosed as having type 1 diabetes mellitus. After treatment for ketoacidosis her gastrointestinal symptoms disappeared and her appetite recovered. Three months after admission, a glucagon test was performed. Serum C-peptide levels before and 6 minutes after injection of 1 mg glucagon were 0.1 ng/mL, and 0.1 ng/mL, respectively. Interestingly, after recovery from ketoacidosis, her diabetes state was controlled at the same level as before

the incident, so that no change in treatment was necessary.

Discussion

SPIDDM occurs generally in adulthood and progresses to the insulin-dependent stage within several years. Anti-GAD antibody is characteristically high in titer and persists for a long time (5). SPIDDM is characterized by a better preserved residual beta-cell function (6). Consequently, it is often misclassified as type 2 diabetes (7). It is noteworthy that SPIDDM can also occur in obese patients. Obese type 2-like diabetic patients with islet antibodies show progressive beta-cell failure (8).

The present patient was obese and had a family history of type 2 diabetes, therefore she was treated for type 2 diabetes for a period of 30 years. One day, she was angry and refused her meals a couple of times. At that time, she did not take insulin injection. That might be one reason that led to the state of ketoacidosis. Diabetic ketoacidosis is most likely to occur in type 1 diabetic patients rather than type 2 diabetic patients (9). Since her anti-GAD antibody was consistently negative it has been previously difficult to diagnose her as type 1 diabetes.

Suzuki et al (10) reported a case of an elderly patient with a long history of type 2 diabetes who was diagnosed as type 1 diabetes mellitus. They pointed out the possibility that late onset type 1 diabetes can be superimposed on top of type 2 diabetes and they proposed the term, "type 1 on type 2 diabetes". However, it is not clear that the present patient is also a case of "type 1 on type 2 diabetes", because she was not proved as negative for ICA at the onset of type 2 diabetes.

Interestingly, the degree of insulin dependency (i.e. the dose of insulin for glycemic control) showed no difference before and after the episode of ketoacidosis. It has been reported that when only ICAs or only GADs are detected in SPIDDM, severe beta-cell dysfunction tends to occur long after the initial diagnosis (4). On the other hand, the pres-

ence of at least two islet antibodies (ICAs, GADs, and IA-2 As) at the point of diagnosis indicates that severe deterioration in beta-cell function would usually occur within 5 years (4). A 12-year prospective study (11) showed that multiple islet antibodies or GAD alone at diagnosis of diabetes predict future complete beta-cell failure. The fasting plasma C-peptide level was undetectable in the patients with two or three islet antibodies within 5 years. The C-peptide in the patients with only GAD was undetectable within 12 years. Whereas, in patients with only ICA or IA-2, the C-

peptide was still detectable after 12 years (11). We hypothesize that this situation is because the present patient was positive for only one autoimmune antibody (ICA) and therefore her beta-cell function may have been well preserved.

In general, the examination of GAD antibodies is used for the screening of type 1 diabetes in Japan. The present case emphasizes the importance of checking all available autoimmune antibodies in the diagnosis of the slowly progressive type 1 (insulin-dependent) diabetes in patients.

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