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LETTER TO THE EDITOR

Short-term changes in pancreatic α-cell function after the onset of fulminant type 1 diabetes

A 25-year-old unconscious woman was transferred to Center Hospital, National Center for Global Health and Medicine, Tokyo, Japan. She had ketonuria with blood glucose levels, arterial pH, and HCO_3^- levels of 843 mg/dL, 6.94 and 3.0 mmol/L, respectively, indicating diabetic ketoacidosis. Her glycated hemoglobin, serum C-peptide, and 24-h urinary C-peptide excretion levels were 6.4%, 0.28 ng/mL and 2.4 μ/day, respectively. Her islet autoantibodies were negative. She was finally diagnosed with fulminant type 1 diabetes. Pancreatic α- and β-cell functions were evaluated using the arginine stimulation test (AST). Basal insulin was changed from a subcutaneous injection to a continuous intravenous injection 24 h before the AST, and was stopped 1 h before the AST. A total of 30 g of arginine was intravenously administered over a 30-min period, and blood samples were collected before and at 15, 30, 60, 90 and 120 min after arginine loading[1]. The serum C-peptide response was almost diminished, and the plasma glucagon response measured using radioimmunoassay (Sceti Medical Labo, Tokyo, Japan) increased to a peak of 415 pg/mL (Figure 1a). Her blood glucose levels fluctuated between 40 and 500 mg/dL after 6 months. Her glycated hemoglobin level increased to 8.6%, and she was readmitted to our hospital. In the repeat AST, although glucose elevation was similar to that at diabetes onset, the serum C-peptide response was completely absent. Interestingly, the peak plasma glucagon level decreased from 415 to 295 pg/mL, plasma glucagon response during the first 15 min diminished from 292 to −10 pg/mL and the incremental area under the curve decreased from 13.0×10^3 to 8.1×10^3 pg/mL/min (Figure 1a,b). Plasma glucagon levels were also measured using sandwich enzyme-linked immunosorbent assay (Mercodia AB, Uppsala, Sweden), and the curve of plasma glucagon was similar to that obtained using radioimmunoassay. AST was carried out after

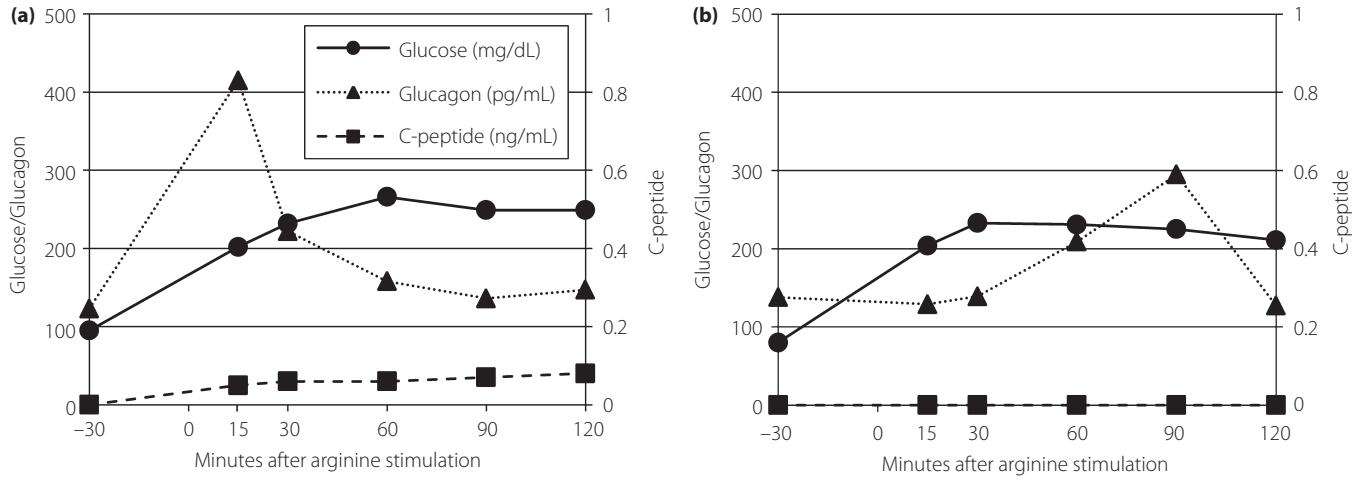

Figure 1 | Glucose, C-peptide and glucagon responses to arginine stimulation in a patient with fulminant type 1 diabetes. Thirty grams of arginine was intravenously administered over 30 min, and the levels of plasma glucose, serum C-peptide, and plasma glucagon were measured before and 15, 30, 60, 90, and 120 min after arginine loading[1] at the (a) onset of fulminant type 1 diabetes and (b) 6 months later.

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achieving glycemic control without any hypoglycemia (<70 mg/dL), as confirmed by continuous glucose monitoring at diabetes onset and 6 months later.

Fulminant type 1 diabetes has recently been reported as a novel subtype of type 1 diabetes, and is characterized by a remarkably abrupt disease onset and rapidly depleted insulin secretion[2]. To our knowledge, this is the first case report describing changes in plasma glucagon response to AST in a patient with fulminant type 1 diabetes. According to a previous report, glucagon responses to AST in patients with type 1 diabetes are positively correlated with diabetes duration, which is contrary to our present result[1]. In another study, the areas of α- and β-cells morphologically decreased in patients with fulminant type 1 diabetes compared with those in patients with acute-onset type 1 diabetes[3]. Rodent autoimmune diabetes models have revealed a substantial loss of alpha cells and impaired glucagon response to hypoglycemia.[4] We have considered that the loss of alpha cells is correlated with the early-phase attenuation of glucagon response and appears to be delayed in the present case.

In conclusion, we report the short-term changes in the plasma glucagon response to AST in a patient with fulminant type 1 diabetes. Further research with multiple participants is desirable to confirm the pancreatic endocrinological functions in patients with fulminant type 1 diabetes.

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DISCLOSURE

The authors declare no conflict of interest.

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