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LETTER TO THE EDITOR

"Preserved" glucagon secretion in fulminant type 1 diabetes

We have read with interest the recent article by Takahashi *et al.*[1] showing the changes in pancreatic α-cell function of a patient with fulminant type 1 diabetes. The pancreatic α- and β-cell functions were assessed by the arginine stimulation test. Thus far, no study has reported the time-course of changes in glucagon secretion in a patient with fulminant type 1 diabetes.

In recent-onset fulminant type 1 diabetes, α-cell mass should be decreased according to a previous study that reported α-cells, as well as β-cells, were morphologically damaged[2]. Takahashi *et al.* suggested the loss of α-cells in one case of fulminant type 1 diabetes. However, in our study participants with fulminant type 1 diabetes whose diabetes duration was >4 years, no defect in glucagon secretion was observed (Figure 1). A physiological stimulus (mixed-meal) test tended to show rather excessive glucagon levels in the type 1A and fulminant type 1 diabetes patients compared with those of the healthy controls. Comparing among type 1 diabetes patients, the α-cell secretory capacity of fulminant type 1 diabetes seems marginally smaller than that of type 1A diabetes, but it can be said that certain amounts of α-cells do exist. α-Cells might be resistant to cytokine-induced apoptosis, which is postulated to be a mechanism of β-cell destruction in fulminant type 1 diabetes[3].

Type 1 diabetes is characterized by the selective loss of insulin-producing β-cells, which severely disturbs glucose homeostasis. It is also associated with dysfunction of the component of the α-cells, which can exacerbate hyperglycemia as a result of paradoxical hyperglucagonemia or lead to severe hypoglycemia as a consequence of impaired counterregulation. In accordance with this concept, we have previously showed that arginine-stimulated glucagon secretion is closely associated with the degree of glucose fluctuation in patients with type 1 diabetes whose endogenous insulin was completely depleted[4]. This research indicates that, independent of the lack of insulin secretion, the aberrant secretion of glucagon might contribute to glycemic variability.

Thus, α-cell behavior in fulminant type 1 diabetes needs to be urgently clarified when considering improving glycemic control in fulminant type 1 diabetes characterized by complete deficiency of insulin. Long-term longitudinal studies investigating α-cell function and its changes over time are required in the future.

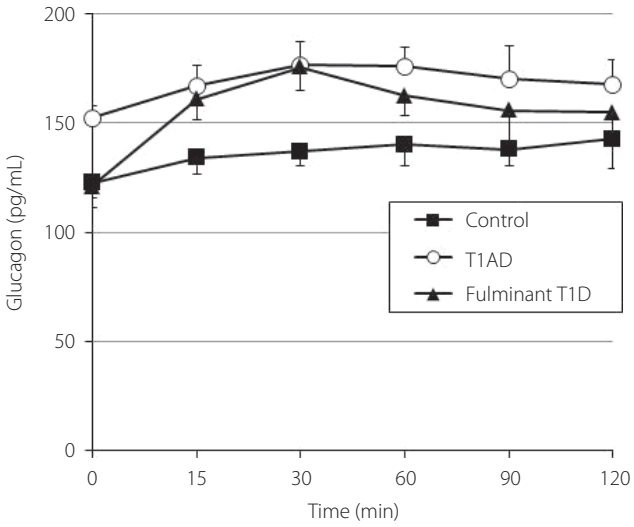

Figure 1 | Mixed-meal tolerance tests were carried out after an overnight fast. A liquid formula meal was used (Sanet-SAR; Sanwa Kagaku Kenkyusho, Nagoya, Japan; 6 kcal/kg bodyweight). Plasma glucagon was measured using a C-terminal-specific radioimmunoassay (Sceti Medical Labo, Tokyo, Japan). Meal-stimulated serum C-peptide levels were undetectable (<0.003 nmol/L) by a highly sensitive immunoradiometric assay kit (Roche, Basel, Switzerland) in all enrolled patients. Healthy control participants (■; n = 3, mean age 35.3 ± 6.1 years), type 1A diabetes patients (○; n = 6, mean age 57.7 ± 17.5 years, range 32–78 years, diabetes duration 14.2 ± 11.0 years, range 2–27 years) and fulminant type 1 diabetes patients (▲; n = 3, mean age 66.0 ± 13.0 years, range 51–73 years, diabetes duration 9.3 ± 5.5 years, range 4–15 years). Graphical data are presented as the mean ± standard error of the mean. The protocol for this research project has been approved by the ethics committee of the Osaka Medical College (approval No. 1274), and informed consent was obtained from all participants.

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DISCLOSURE

The authors declare no conflict of interest.

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