【 CASE REPORT 】

# Repeated Hypoglycemic Episodes with Postprandial Hyperinsulinemia after the Recovery from Acute Weight Loss Revealed by Continuous Glucose Monitoring and the Oral Glucose Tolerance Test

Seizaburo Masuda [1], Masanori Murakami [1], Ryotaro Bouchi [1], Isao Minami [1],
Koshi Hashimoto [1,2], Takanobu Yoshimoto [1] and Yoshihiro Ogawa [1]

**Abstract:**

We herein report a case of a 20-year-old woman who experienced hypoglycemia in parallel with acute weight loss confirmed by continuous glucose motoring (CGM). When she recovered from the acute weight loss, CGM revealed nocturnal and postprandial hypoglycemia. Six months were required to resolve the hypoglycemia and hyperinsulinemia after the recovery of her weight. Our case suggests that the adaption of insulin secretion to the rapid loss of weight and to the recovery of weight may require a long period of time, leading to the excessive secretion of insulin relative to the glucose level and repeated hypoglycemic episodes with postprandial hyperinsulinemia.

**Key words:** weight loss, hypoglycemia, CGM

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## Introduction

Recently, the phenomenon of underweight young women has been recognized as a serious social issue in Japan. The Japanese Ministry of Heath, Labour and Welfare reported that 21% of women were underweight (BMI <18.5 kg/m$^2$), and the incidence of eating disorders have been growing closer to that of Western countries (1). It is well known that young women experience symptoms of hypoglycemia when their body weight rapidly decreases (2). As episodes of severe hypoglycemia are reported in patients with anoxia nervosa (3-5), weight loss may be implicated in hypoglycemia in such young women. However, there are few reports on the detailed clinical course of patients with hypoglycemia due to acute weight loss.

We herein report a 20-year-old woman who experienced hypoglycemia in parallel with acute weight loss confirmed by a continuous glucose motoring (CGM) and the 75-g oral glucose tolerance test (OGTT).

## Case Report

A 20-year-old woman presented with complaints of fatigue, loss of appetite, and loss of body weight. She had no remarkable medical history and no family history of diabetes mellitus. At 19 years of age, she had a loss of appetite due to hot weather and lost 15 kg in 1 month, going from 60.0 kg to 45.0 kg in September 2015, without any abnormal diet changes. Although her loss of appetite gradually improved, she still complained of general fatigue, headache, and palpitation and visited a primary care doctor. Her plasma glucose level was 60 mg/dL, and she was admitted to our hospital for the further examination of her hypoglycemia in February 2016.

On admission, her height and weight were 155.5 cm and 51.3 kg (BMI: 21.2 kg/m$^2$). Her weight change is shown in Fig. 1. In September 2015, she lost 15 kg of body weight in
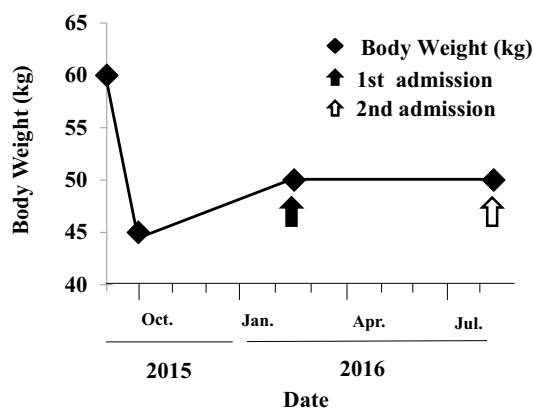
**Figure 1.** The course of body weight from July 2015 to August 2016.



Area under the curve of serum IRI (0-180 min): 15,348 (µU/mL·min)



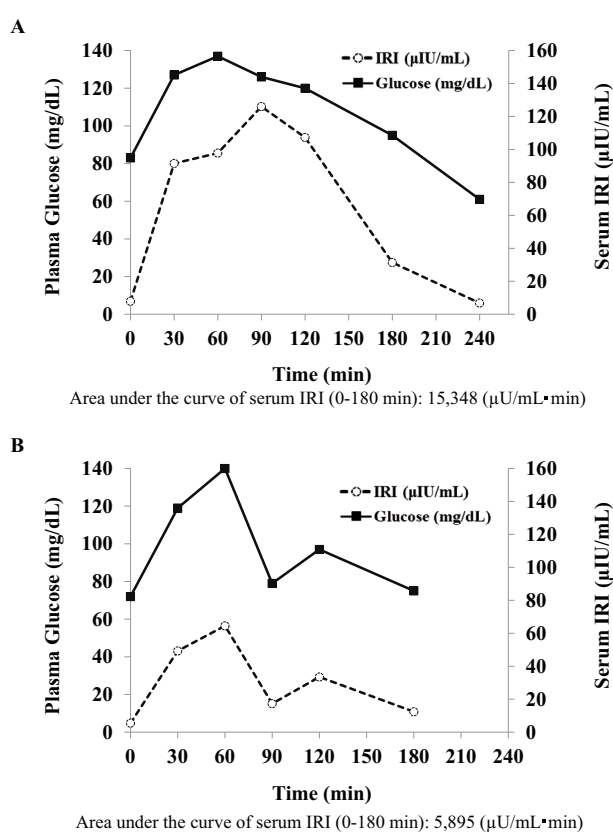Area under the curve of serum IRI (0-180 min): 5,895 (µU/mL·min)

**Figure 2.** A: A 75-g gram oral glucose tolerance test given at the first admission. The plasma glucose (■) and serum IRI (○) concentrations were measured at 0, 30, 60, 90, 120, 180 and 240 minutes after glucose load. The area under the curve of IRI (AUC) from 0 to 180 minutes was calculated. B: A 75-g gram oral glucose tolerance test given at the second admission. The plasma glucose (■) and serum IRI (○) concentrations were measured at 0, 30, 60, 90, 120 and 180 minutes after glucose load. The area under the curve of IRI (AUC) from 0 to 180 minutes was calculated.

**Table.  Laboratory Data on the First Admission.**

| Complete Blood count | |
|---|---|
| White blood cell | 5,600 /µL |
| Total lymphocyte | 1,064 /µL |
| Red blood cell | $439 \times 10^4$ /µL |
| Hemoglobin | 13.9 g/dL |
| Hematocrit | 37.2 % |
| Platelet | $21.8 \times 10^4$ /µL |
| Bloood Chemistry | |
| Total protein | 7.2 g/dL |
| Albumin | 4.7 g/dL |
| Sodium | 139 mEq/L |
| Potassium | 3.9 mEq/L |
| Chlorine | 102 mEq/L |
| Triglycerides | 50 mg/dL |
| HDL-Chol | 63 mg/dL |
| LDL-Chol | 92 mg/dL |
| Glucose | 67 mg/dL |
| HbA1c(NGSP) | 4 % |
| Endocrinological data | |
| IRI | 4 µU/mL |
| Insulin antibody | <0.4 U/mL |
| IRG | 115 pg/mL |
| GH | 3.58 ng/mL |
| IGF-1 | 295 ng/mL |
| Adrenaline | 0.02 pg/mL |
| Noradrenaline | 0.17 pg/mL |
| Dopamine | 0.02 pg/mL |
| ACTH | 13.6 pg/mL |
| Cortisol | 10.5 µg/dL |
| TSH | 1.67 µIU/mL |
| FT3 | 2.82 pg/mL |
| FT4 | 1 ng/dL |

HDL-Chol: high density lipoprotein cholesterol, LDL-Chol: low density lipoprotein, HbA1c: hemoglobin A1c, IRI: immunoreactive insulin, IRG: immunoreactive glucagon, GH: growth hormone, IGF-1: insulin-like growth factor 1, ACTH: adrenocorticotropic hormone, TSH: thyroid stimulating hormone, FT3: free triiodothyronine, FT4: free thyroxine

1 month from an initial weight of 60 kg. She gradually gained some weight back and reached 50 kg by February 2016. Laboratory data, including hormone levels after overnight fasting, are shown in Table. Her baseline plasma glu-

cose level was 67 mg/dL, and her immunoreactive insulin (IRI) level was 6.8 µIU/mL. All serum levels of pituitary and adrenal hormones were within normal ranges. The plasma glucose level was 61 mg/dL and serum IRI level 6.8 µIU/mL after 240 minutes in the 75-g OGTT which was performed after she recovered adequate dietary intake (Fig. 2A). Continuous glucose monitoring (CGM) revealed both nocturnal and postprandial hypoglycemia reaching 725 minutes per day (Fig. 3A). Abdominal computed tomography showed no remarkable findings, so obvious organic disease causing hypoglycemia was denied. Since her hemoglobin A1c was within the normal range and the 75-g OGTT showed normal glucose tolerance, reactive hypoglycemia induced by prediabetes or mild diabetes mellitus was denied.
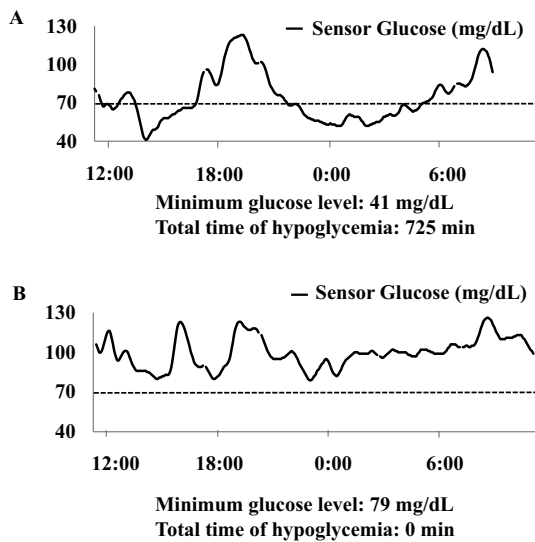
**Figure 3.** The result of continuous glucose monitoring system at the first (A) and second admission (B). The minimum glucose level and total time of hypoglycemia are shown.

Anorexia nervosa was also denied because she did not meet the DSM-5 diagnostic criteria. In this case, hypoglycemia developed with an acute weight loss, and her hypoglycemia continued through Feburuary 2016, although her weight had recovered from its minimum level in October 2015. We therefore suspected that her hypoglycemia was related to her history of acute weight loss. Nutrition education was introduced to prevent further unnecessary weight loss. After she was discharged, she maintained her weight with an improved appetite, and no hypoglycemic episodes were observed for six months.

For the purpose of reassessing her glycemic profile, she was again admitted to our hospital in August 2016. Her weight was 51.2 kg. No hypoglycemia was observed during either the day or night in the CGM analysis (Fig. 3B). In addition, the area under the curve (AUC) of IRI during the 75-g OGTT was decreased at the second admission (5,895 μIU/mL·min) (Fig. 2B) compared with the first admission (15,348 μIU/mL·min) (Fig. 2A) with equivalent AUC values for glucose during the OGTT (Fig. 2A and B), suggesting the improvement of hyperinsulinemia relative to the glucose level.

## Discussion

We encountered a young woman with repeated hypoglycemic episodes with postprandial hyperinsulinemia that occurred immediately after acute weight loss. Given that both the acute weight loss and her symptoms, such as general fatigue, appeared simultaneously, hypoglycemia was suspected to have developed at that time. The symptoms persisted for several months after the recovery of her weight loss (on the first admission, Fig. 1), so nutrition guidance was introduced in order to help her maintain an appropriate body weight. Ultimately, a further several months passed until her hypo-

glycemia was resolved (on the second admission, Fig. 1). Because insulinoma and other endocrine disorders were incompatible with our case, we considered her acute weight loss to be the principal cause of hypoglycemia. Our case showed an inappropriate post-glucose-load secretion of insulin (relatively high level of insulin compared with the glucose levels at the second admission; Fig. 2A). However, the postprandial insulin level returned to the appropriate level by the second admission (Fig. 2B).

### Relationship between weight loss and hyperinsulinemia

Several studies have described a change in the glucose metabolism after weight loss in non-diabetic obese patients, according to the OGTT findings; the plasma insulin level has been shown to be reduced significantly following bariatric surgery (6) and very-low-calorie dietary intervention (VLCD) (7). However, the present patient's BMI before the weight loss was normal. The clinical course of our case suggests that a delay in the normalization of insulin secretion after eating may have contributed to the repeated episodes of postprandial hypoglycemia, and differences in the insulin secretion in response to acute weight loss may exist between our case and obese patients following bariatric surgery or VLCD.

Another possible mechanism underlying hyperinsulinemia is altered incretin secretion from the gut after acute weight loss. Significantly elevated postprandial glucose-dependent insulinotropic polypeptide (GIP) levels have been reported in the 75-g OGTT in an anorectic patient with severe hypoglycemia who recovered from weight loss (8). Therefore, changes in the GIP secretion in response to food intake may have been associated with hypoglycemia in our patient, although we were unable to examine the GIP levels.

### Postprandial and nocturnal hypoglycemia revealed by CGM and OGTT data

Of note, the patient's circadian variation in glucose and response of insulin to the glucose load were able to be followed up in detail using both the CGM and OGTT data. The CGM data at the first admission clearly showed the existence of nocturnal hypoglycemia (Fig. 3A), which clearly improved at the second admission (Fig. 3B). The insulin secretion after glucose load was also decreased in the 75-g OGTT at the second admission (Fig. 2B). Given that the disappearance of hypoglycemia lagged several months behind her weight regain, recovery from hypoglycemia due to acute weight loss might take a rather long time (more than half a year in the present case). It has been reported that a rapid change in eating behavior induced postprandial hypoglycemia (reactive hypoglycemia) in a case of anorexia nervosa (9); however, it is difficult to attribute the pathogenesis of nocturnal hypoglycemia to a reduction in food intake in the present case. The existence of postprandial and nocturnal hypoglycemia after the recovery of acute weight loss is a unique characteristic of our case, and the mechanisms by

which hyperinsulinemia relative to the glucose level occurs concomitantly with acute weight loss and why hypoglycemia persists even after patients regain their weight should be explored in future studies.

One limitation associated with this case warrants mention. Neither glucose nor insulin levels were available in the early phase of her acute weight loss. But hypoglycemia might have appeared in that phase because she experienced symptoms of hypoglycemia in parallel with her acute weight loss.

In conclusion, the findings in the present case suggest that insulin secretion may take a long time to adapt to the rapid loss of weight and to the recovery of weight, leading to the excessive secretion of insulin relative to the glucose level and repeated hypoglycemic episodes with postprandial hyperinsulinemia.

**The authors state that they have no Conflict of Interest (COI).**

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