CASE REPORT

Nocturnal reactive hypoglycaemia well treated subjectively and objectively with voglibose

Hiroyuki Koyama, Hideomi Ohguchi, Takashi Yagi, Kenro Imaeda

Gastroenterology and Metabolism, Nagoya City University Graduate School of Medical Sciences, Aichi, Japan

Correspondence to

Dr Hiroyuki Koyama, hk0515@kuhp.kyoto-u.ac.jp

Accepted 21 September 2017

SUMMARY

Clinicians sometimes encounter difficulty in diagnosing hypoglycaemia. Here, we present a case report of a 53-year-old woman with recurrent nocturnal hypoglycaemia. A continuous glucose monitoring system (CGMS) revealed postprandial hyperglycaemia and subsequent hypoglycaemia, and an oral glucose tolerance test showed an impaired glycaemic and delayed hyperinsulinaemic pattern. On the basis of these clinical findings, we diagnosed her unexplained hypoglycaemia as reactive hypoglycaemia. CGMS showed a sharp contrast of diurnal variation in blood glucose levels including hypoglycaemia between before and after treatment with an alpha-glucosidase inhibitor, voglibose. Her hypoglycaemic attacks disappeared.

attacks, and she purchased a kit for self-monitoring of blood glucose at home on her own. Indeed, her blood glucose levels measured at the times when she felt ill were always in the range of 50 to 70 mg/dL.

She had not been suspected of having diabetes mellitus in the past, and she had no family history of diabetes mellitus. She was routinely prescribed famotidine, ethyl loflazepate, brotizolam, Hochuekkito (a Japanese herbal medicine) and ascorbic acid by a local clinic. She had a balanced diet and had not ingested excessive carbohydrates, which stimulate insulin secretion. She had no history of alcohol consumption. Her height and body weight were 150 cm and 50 kg, respectively (with no recent remarkable change) and her body mass index was 22 kg/m². She had not undergone any abdominal surgery.

BACKGROUND

Hypoglycaemia is common in patients with diabetes taking insulin or oral medications.¹ However, it is not uncommon in people without diabetes, in whom clinicians sometimes encounter difficulty with diagnosis.

Reactive hypoglycaemia (postprandial hypoglycaemia) is defined as documented hypoglycaemia (generally defined as below 70 mg/dL) and resultant symptoms that usually occur within 2–4 hours after eating. This is different from hypoglycaemia that occurs while fasting. The symptoms of reactive hypoglycaemia are quite diverse including hunger, sweating, palpitations and drowsiness.² This disorder is occasionally seen in patients with other clinical conditions such as hyperthyroidism,³ impaired glucose tolerance and the early stages of diabetes mellitus.²

Here, we report a 53-year-old woman with recurrent hypoglycaemia. We were successful in diagnosing her unexplained nocturnal hypoglycaemia as reactive hypoglycaemia on the basis of clinical findings. This case presentation may provide some suggestions and help in the differential diagnosis of hypoglycaemia.

INVESTIGATIONS

Physical and neurological findings revealed no overt abnormalities. Laboratory test results were as follows: fasting plasma glucose, glycated haemoglobin and glycosylated albumin level were 80 mg/dL, 39 mmol/mol in International Federation of Clinical Chemistry units (5.7% in National Glycohaemoglobin Standardization Program units) and 14.4%, respectively. Serum levels of immunoreactive insulin and C-peptide after overnight fasting were 4.1 µU/mL (normal 1.1–9.0 µU/mL) and 1.42 ng/mL (normal 0.61–2.09 ng/mL), respectively. Neither anti-insulin nor anti-insulin receptor antibodies were detected. Liver enzymes and renal function tests were all within normal limits. Serum levels of pituitary, adrenal and thyroid hormones were also near normal ranges. Especially an early-morning cortisol level was checked several times, for which all results showed normal. An abdominal MRI showed a cystic lesion in the uncinate process of the pancreas, which had been discovered previously but remained unchanged. A brain MRI showed no significant abnormality.

Next, we measured diurnal variation in blood glucose using a continuous glucose monitoring system (CGMS) (iPro2, Medtronic, Northridge, California, USA). As shown by the solid line in figure 1, the blood glucose level rapidly increased after each meal and dropped into the hypoglycaemic range (below 70 mg/dL) from 23:00. The glucose level was still low in the morning, however, overnight fasting did not exacerbate her hypoglycaemia.

CASE PRESENTATION

A 53-year-old Japanese woman was admitted to our hospital. She frequently experienced sweating and hunger, which gradually disappeared after taking some chocolates or candy. These symptoms occurred only at midnight or so, not in the morning or at noontime. In searching the internet, she suspected that her symptoms were hypoglycaemic

CrossMark

To cite: Koyama H, Ohguchi H, Yagi T, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-220295

Figure 1 Diurnal variation in blood glucose levels measured by a continuous glucose monitoring system (CGMS) before (-) and after (...) voglibose treatment.

Subsequently, we performed a 75 g oral glucose tolerance test (OGTT). The results are shown in figure 2. The baseline glucose level was 88 mg/dL, and increased to 208 mg/dL at 60 min, which met one of the criteria for diabetes mellitus. Likewise, her insulin concentration was 4.4 μ U/mL at baseline and rose to 90.9 μ U/mL after 60 min. The high concentration of insulin released following hyperglycaemia was observed until 180 min. A hypoglycaemic condition was not documented by the test, and naturally, she did not feel a hypoglycaemic attack. With the aid of these useful diagnostic tools, we conclusively diagnosed her unexplained nocturnal hypoglycaemia as postprandial reactive hypoglycaemia.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of nocturnal hypoglycaemia includes hepatic failure, renal failure, adrenal insufficiency, growth hormone deficiency, drug-induced hypoglycaemia, insulin autoimmune syndrome and insulinoma.

TREATMENT

We started voglibose administration at 0.6 mg/day because we expected that voglibose slows the absorption of carbohydrates, which had an increased chance of preventing her postprandial hyperglycaemia and subsequent hypoglycaemia. After that, surprisingly, her hypoglycaemic episodes became much less frequent. Another CGMS monitoring test revealed that postprandial hyperglycaemia and nocturnal hypoglycaemia were dramatically ameliorated (figure 1).

OUTCOME AND FOLLOW-UP

She sometimes complained of loose stools, which were probably a side effect of the voglibose, but she consented to continue the treatment and was discharged in remission.

DISCUSSION

We experienced a patient who suffered from recurrent hypoglycaemia without any history of diabetes and, thus, any prescriptions for antidiabetic agents and were able to reach a diagnosis of reactive hypoglycaemia. Her hypoglycaemic symptoms became pronounced only after supper, not after breakfast or lunch, which is a red herring in differentiating the cause. Two diagnostic tools were decisive in our successful diagnosis—CGMS and OGTT.

Figure 2 Results of a 75 g OGTT. The plasma glucose (-) and serum IRI levels (...) were measured. IRI, immunoreactive insulin; OGTT, oral glucose tolerance test.

CGMS is a very effective tools for determining diurnal variation in glucose levels, and therefore can help detect postprandial hyperglycaemia, glucose excursions and silent hypoglycaemia occurring at odd times. The patient's hypoglycaemia was documented as occurring past midnight, as the patient had reported; nevertheless, the glucose level returned to normal in the morning. In other words, her blood glucose level did not drop after a long fast. Equally, postprandial hyperglycaemia was seen in her CGMS record. This phenotype is consistent with reactive hypoglycaemia. Suzuki *et al* also used CGMS in diagnosis, but these investigators observed changes in the continuous glucose levels only during OGTT, not diurnal variations.⁴

OGTT is universally used to diagnose diabetes and impaired glucose tolerance and evaluate insulin resistance and beta cell function. We did not observe hypoglycaemia in this patient's OGTT results, but we might have caught hypoglycaemia if we had tracked the glucose level for a longer time. However, the patient's OGTT pattern showed hyperglycaemia and subsequently insulin levels that were quite high. Tamura *et al* reached a correct diagnosis in a very elderly patient suffering from severe hypoglycaemia with the help of OGTT.⁵

Several treatments for reactive hypoglycaemia have been reported. Alpha-glucosidase inhibitors are oral antidiabetic drugs widely used to improve postprandial hyperglycaemia to delay the absorption and digestion of dietary polysaccharides by inhibiting carbohydrate digestive enzymes such as maltase and sucrase. This mechanism acts very favourably for the amelioration of reactive hypoglycaemia.⁶ In the present patient, the agents markedly improved both the patient's postprandial hyperglycaemia and reactive hypoglycaemia, which were observed visually in the CGMS results. Other treatment options are low carbohydrate diets⁷ and pioglitazone.⁸

Learning points

- ▶ Reactive hypoglycaemia can present as a form of nocturnal hypoglycaemia.
- ▶ Continuous glucose monitoring system (CGMS) and oral glucose tolerance test are useful tools for diagnosing reactive hypoglycaemia.
- ▶ CGMS also serves as an evaluation of treatment for reactive hypoglycaemia.

To summarise, we successfully diagnosed a patient who experienced recurrent nocturnal hypoglycaemia as reactive hypoglycaemia and effectively treated the patient with voglibose. We recommend that performance of CGMS and OGTT are considered in patients with hypoglycaemia of unknown aetiology to reveal otherwise hidden reactive hypoglycaemia.

Contributors HK has charge of the patient's history taking, attachment and detachment of CGMS and drafting the article. HO and TY have charge of the arrangement of the examinations including MRI/OGTT/CGMS and collecting and interpreting the data (OGTT, CGMS). KI is the head of our department. We gather everyone together and argue about the patient to achieve a correct diagnosis. He also had final approval of the article to be published.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Marrett E, Radican L, Davies MJ, *et al.* Assessment of severity and frequency of self-reported hypoglycemia on quality of life in patients with type 2 diabetes treated with oral antihyperglycemic agents: a survey study. *BMC Res Notes* 2011;4:251.
- 2 Hofeldt FD. Reactive hypoglycemia. *Endocrinol Metab Clin North Am* 1989;18:185–201.
- 3 Kabadi UM, Eisenstein AB. Glucose intolerance in hyperthyroidism: role of glucagon. *J Clin Endocrinol Metab* 1980;50:392–6.
- 4 Suzuki K, Katsura D, Sagara M, *et al.* Postprandial reactive hypoglycemia treated with a low-dose alpha-glucosidase Inhibitor: voglibose may suppress oxidative stress and prevent endothelial dysfunction. *Intern Med* 2016;55:949–53.
- 5 Tamura Y, Araki A, Chiba Y, *et al.* Postprandial reactive hypoglycemia in an oldest-old patient effectively treated with low-dose acarbose. *Endocr J* 2006;53:767–71.
- 6 Peter S. Acarbose and idiopathic reactive hypoglycemia. *Horm Res* 2003;60:166–7.
- 7 Hirose S, Iwahashi Y, Seo A, *et al.* Concurrent therapy with a low-carbohydrate diet and miglitol remarkably improved the postprandial blood glucose and insulin levels in a patient with reactive hypoglycemia due to late dumping syndrome. *Intern Med* 2016;55:1137–42.
- 8 Arai K, Ota K, Suehiro T, *et al.* Pioglitazone prevents reactive hypoglycemia in impaired glucose tolerance. *Diabetes Res Clin Pract* 2005;69:305–8.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow