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Increased fasting and stimulated c- peptide levels after the diagnosis of type 1 diabetes: a case report

Gonca Incemehmet Tamer[1]*, Ozge Telci Caklili[2], Ilkay Kartal[1] and Hasan Huseyin Mutlu[3]

[1]Endocrinology and Metabolism, Istanbul Medeniyet University Goztepe Training and Research Hospital, Turkey

[2]Internal Medicine Department, Istanbul Medeniyet University Goztepe Training and Research Hospital, Turkey

[3]Family Medicine Department, Istanbul Medeniyet University Goztepe Training and Research Hospital, Turkey

Abstract

Context: Recently a few studies showing α-cell ability to differentiate into insulin–producing β-cells after prolonged duration of diabetes and reconstruction of new insulin–producing cells in the absence of autoimmunity in mice with completely ablated β-cells were reported. Here, we present a patient with type 1 diabetes and increased fasting and mixed-meal stimulated C-peptide levels 10 years after the diagnosis.

Case description: A female patient with type 1 diabetes for 10 years was referred to our endocrinology clinic for hypoglycemia attacks. Her fasting glucose, HbA1C, fasting and mixed-meal stimulated C-peptide levels were measured three years ago and recently. Fasting and mixed-meal stimulated C-peptide levels were found to be increased compared to the levels of three years ago (<0.01 ng/mL vs. 0.06 ng/mL and <0.01 ng/mL vs 0.28 ng/mL respectively).

Conclusion: It is possible that β-cell function may increase in type 1 diabetes, a decade after the diagnosis as observed in our patient. .

Introduction

Type 1 diabetes (T1D) is a disease with absolute insulin deficiency and it has high short and long term complication rates along with high mortality rate. The decrease in β-cell function in type 1 diabetic patients varies from patient to patient [1]. Increased endogenous insulin production in patients with type 1 diabetes can improve glycemic control and decrease the complication and mortality rates.

Although destruction of beta cells is believed to be permanent, in recent studies beta cells including insulin were observed in pancreatic autopsy samples obtained from patients with T1D and increased C-peptide secretion after meal stimulus were reported [1,2]. Herein, we present a case with increased fasting and mixed-meal stimulated C-peptide levels, 10 years after the diagnosis of T1D.

Case report

A 20 year-old woman was admitted to our endocrinology outpatient clinic with the complaints of vertigo and sweating. She stated she had a hypoglycemia attack recently and her glucose level was 50 mg/dL with glucometer at home when her complaints began. She decreased total dose of daily insulin she used by herself because of the hypoglycemic attacks. She had no weight gain or loss. She is not a smoker and does not consume alcohol. She was diagnosed with T1D 10 years ago. There was no family history of diabetes. Her physical examination was normal. Her anti-glutamic acid decarboxylase (GAD)-antibody was positive at the time of diagnosis and still is. Her metabolic parameters from 2012 are presented in table 1.Her fasting glucose level was found measured with the hexokinase method and her HbA1c level was 10,5% (91 mmol/mol) measured via high performance liquid chromatography (Tosoh G7 and 2.2, Tokyo, Japan) (Table 1) . The C-peptide level was measured via direct electrochemiluminescence immunoassay using mouse monoclonal anti-C- peptide antibody (Immulite 2000,Siemens, Germany). We performed a mixed-meal tolerance test (MMTT) to the patient after an overnight fasting of ≥ 12 hours without administering her usual morning insulin treatment. After fasting blood glucose, C-peptide, and HbA1c levels were measured, a mixed meal containing 33 g of carbohydrate, 15 g of protein, and 6 g of fat (240 kcal total) [2] was eaten in less than 10 minutes, and C-peptide level was measured 90 minutes after the mixed-meal. Parameters were confirmed with repetitive measurements.

Total daily insulin dose, fasting glucose and HbA1c level of the patient was decreased and her fasting and mixed-meal stimulated C-peptide levels were increased compared to her levels 3 years ago. Her current laboratory parameters and those in 2012 are shown in Table 1.

Discussion

It is accepted that T1D is a disease with absolute insulin deficiency. However recent studies have shown endogen insulin secretion is still present in some patients with T1D even in patients with long disease duration [2-4]. In these studies, it was not clear whether β-cell function was ongoing since the disease begun, or if it has increased or decreased. To our knowledge this case may be the first case in literature with fasting and mixed-meal stimulated C-peptide levels increased compared to the levels three years ago.

Correspondence to: Gonca Incemehmet Tamer, Istanbul Medeniyet University Goztepe Training and Research Hospital, Endocrinology and Metabolism, Fahrettin Kerim Gokay Street, Kadikoy, Turkey, Tel: +90 (216) 5709195; Fax: +90 (216) 5709191; E-mail: hgtamer@yahoo.com

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Table 1. Differences in patient's laboratory parameters.

Metabolic parameters	Year 2012	Year 2014	Reference range
Fasting blood glucose (mg/dL)	168	114	70 -106
Hb A1c % (mmol/mol)	13,1 (119)	10,5 (91)	4 -6 (20-42)
Fasting c-peptide level (ng/mL)	< 0,01	0,06	0.90-7.10
MMTT stimulated C-peptide (ng/mL)	< 0,01	0,28	0.90-7.10
Total daily insulin dose per kilogram	1.5U/kg	0,14 U/kg	-
TSH (uIU/mL)	2,3	2,1	0,27 - 4,2
Free T4 (ng/dL)	1,1	0,98	0,61 - 1,12
08:00 am cortisole level (uU/mL)	19	17,8	6,7 -22,6

Based on a murine model Thorel *et al.* [5] showed that in β-cell-depleted mice, α-cells could differentiate into β-cells after prolonged duration of diabetes. Similarly, Chera *et al.* [6] observed that pancreas reconstituted new insulin–producing cells in the absence of autoimmunity in mice with completely ablated β-cells. They also reported that glucagon-producing α-cells could begin to produce insulin via a process of reprogramming (transdifferentiation) without proliferation and posited that these phenomena might be translatable to humans, because efficient β-cell regeneration had been determined in children with type 1 diabetes or after pancreatectomy [6]. Also, glucagon/insulin bihormonal human cells were observed following epigenetic manipulation *ex vivo* [7], and in diabetic patients [8]. Moreover, Zhou et al reported that aciner cells were capable of conversion into β-cells *invivo* when administered an adenovirus cocktail of some transcription factors [9].

Insulin producing β-cells in patients with long duration of type 1 diabetes have been reported in histological studies since 1965 [10]. These findings can explain the increase in β-cell function in our case 10 years after the diagnosis.

The source of the increasing β-cell function observed in our case, is not clear, however there might be multiple reasons. β-cell proliferation and redifferentiation and/or dedifferentiation of α-cells, δ cells and aciner cells into β-cells may have led to increase of β-cell function.

In conclusion, the physiology behind this phenomenon as in our case and how the function of β-cells in patients with type 1 diabetes can be enhanced remains a question, but discovery of the mechanisms behind this can increase long-term survival and may reduce the incidence of macrovascular and microvascular complications in type 1 diabetes.

Patient consent

Informed consent has been obtained from the patient (or patient's guardian) for publication of the case report and accompanying images.

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