Possible Cefcapene Pivoxil- or Clarithromycin-Induced Severe Hyperglycemia in a Patient With Type 2 Diabetes: A Case Report

Yoji Miyoshi

Abstract

There are various reasons for the deterioration of glycemic control observed in patients with diabetes, one of which is drug-induced hyperglycemia. Antibiotics, especially the fluoroquinolones, have been reported to be associated with glucose disturbances. However, induction of hyperglycemia by cepham or macrolide antibiotics has rarely, if ever, been reported. Here, we report the case of possible antibiotics-induced severe hyperglycemia in a patient with type 2 diabetes. A 67-year-old Japanese diabetic man, who was not using oral hypoglycemic agents or insulin but whose condition was controlled with diet and exercise, presented at an otolaryngology clinic with nasal discharge and rhinorrhea. His glycosylated hemoglobin (HbA1c) level had been stable at 6.6-7.2% for several years. He was diagnosed with acute sinusitis and given an oral cepham antibiotic, cefcapene pivoxil, for 1 week. His otolaryngeal symptoms were slight and disappeared soon. Thereafter, therapy was switched to a macrolide antibiotic, clarithromycin, for 3 weeks. Twenty-five days after the initiation of antibiotic therapy, severe hyperglycemia was pointed out; his random serum glucose and HbA1c levels were 29.4 mmol/L and 10.6%, respectively. The patient required insulin and oral hypoglycemic agent therapy. The Naranjo probability scale suggests that the relationship between the administration of cefcapene pivoxil or clarithromycin and the patient’s severe hyperglycemia might be possible. To the best of our knowledge, there has been no previous report of a deterioration in glycemic control in a patient with diabetes administered a cepham (cefcapene pivoxil) or macrolide (clarithromycin) antibiotic. Considering the global prescription of cepham and macrolide antibiotics, awareness of the fact that some patients are at high risk for impaired glucose tolerance is important when prescribing antibiotics. Further studies are warranted to determine the incidence rate of hyperglycemia among patients with diabetes who are administered cepham and macrolide antibiotics.

Keywords: Cefcapene pivoxil; Clarithromycin; Drug-induced hyperglycemia; Type 2 diabetes

Introduction

Various factors can cause the sudden deterioration of glycemic control in patients with diabetes, one of which is drug-induced hyperglycemia [1]. Antibiotics, especially the fluoroquinolones, have been reported to be associated with alterations in glycemic control among patients with diabetes as well as those without diabetes [2-5]. However, cepham or macrolide antibiotics have rarely, if ever, been reported to induce hyperglycemia.

We herein report the case of a patient with diabetes who developed severe hyperglycemia following treatment with a cepham antibiotic, cefcapene pivoxil hydrochloride (CFPN-PI), and a macrolide antibiotic, clarithromycin (CAM), for acute sinusitis.

Case Report

The patient was a 67-year-old Japanese man with diabetes and hypertension (height, 172 cm; weight, 66 kg). He also had a history of coronary artery disease as he had suffered a myocardial infarction and undergone percutaneous coronary intervention 5 years previously. His medications included enalapril maleate 2.5 mg/day (an ACE inhibitor), ticlopidine hydrochloride 100 mg twice daily (an antiagulant), and rebamipide 100 mg twice daily (a stomachic). His cardiac function was stable and he had not felt any cardiac symptoms for several years. Although he had diabetes, he had never taken any medications for diabetes, but instead had controlled his condition with diet and exercise. Over the past several years, his random serum glucose levels were between 5.83 and 9.66 mmol/L, and his glycosylated hemoglobin (HbA1c, NGSP) level had been stable at 6.6-7.2% (Fig. 1).

In December 2010, the patient presented at an otolar-
Otorhinolaryngology clinic with symptoms of nasal discharge and rhinorrhea. He was diagnosed with acute sinusitis and administered oral CFPN-PI on December 20, 2010. Although his otolaryngeal symptoms were slight and disappeared a few days after taking CFPN-PI, he was switched to CAM on December 27, 2010, when he experienced a sudden onset of thirst and pollakiuria. Eighteen days later (on January 14, 2011), he was diagnosed with hyperglycemia and referred to our endocrinology clinic for an evaluation of the sudden deterioration in serum glucose levels. At this point, his random serum glucose level was 29.4 mmol/L and his HbA1c level was 10.6%. Other laboratory findings were as follows: blood urea nitrogen, 4.2 mmol/L (reference, 2.9 - 7.1); serum creatinine, 73.3 μmol/L (reference, 54.0 - 92.0); plasma beta-hydroxybutyric acid, 97 μmol/L (reference, < 76); random serum C-peptide, 0.80 nmol/L. An anti-glutamic acid decarboxylase antibody test was negative. His serum C-reactive protein (CRP) level and white blood cell (WBC) count were less than 0.48 nmol/L (reference, < 2.86) and 4.63 × 10⁹/L (reference, 3.3 - 9.0), respectively. Although the patient’s sinusitis symptoms had disappeared a few days after the initiation of antibiotic therapy, his serum glucose readings ranged from 22.2 to 27.8 mmol/L. Thus, the patient required insulin and oral hypoglycemic agents (Fig. 1).

**Discussion**

It is common to encounter cases of deterioration of glycemic control among patients with type 2 diabetes. Although CFPN-PI or CAM might be considered a possible cause, the other factors also should be taken into consideration. Various factors affect glycemic control, including deteriorations in the living environment of the surrounding area, other diseases, physical stress induced by infection [6, 7], and drugs [1].

In our case, no changes in the patient’s living environment had occurred at that point in time. He had no pertinent history of alcohol or tobacco use. He drank Japanese tea, but not sweet beverages, eliminating the possibility of soft-drink ketosis. Extensive investigations confirmed that no diseases of the liver, pancreas, or gastrointestinal system were present (data not shown). The stress by infection is a known cause of hyperglycemia [6, 7]. However, the patient’s otolaryngeal symptoms were slight, and they improved rapidly a few days...
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and macrolide antibiotics. In addition, further evaluation is warranted to determine the incidence rate of hyperglycemia among patients with diabetes who are administered cephem antibiotic treatments. To the best of our knowledge, there has been no previous report of a deterioration in glycemic control in a patient with diabetes administered a cephem (CFPN-PI) or macrolide (CAM) antibiotic. Whether the initiation of antibiotic therapy itself or other factors precipitated the severe hyperglycemia is unknown. Further studies are needed to establish the mechanisms for precipitation of hyperglycemia in patients treated with antibiotics.

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Competing Interests

The author declares that he has no competing interests.

Abbreviations

HbA1c: glycosylated hemoglobin; CFPN-PI: cefcapene pivoxil hydrochloride; CAM: clarithromycin; ACE: angiotensin-converting enzyme; CRP: C-reactive protein; WBC: white blood cell.

References

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