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Transient Decrease of Insulin Secretion after COVID-19 Infection in a Patient with Hyperosmolar Hyperglycemic Syndrome

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Abstract A 52-year-old male was transported to a local medical facility due to unconsciousness and involuntary movement. His past history included only hypertension. He consumed over 2 L of soft drink per day. His body mass index was 34. As he had hyperosmolar hyperglycemic syndrome and COVID-19 infection, he was transferred to our department. On arrival, he was in a coma and pre-shock state. He was therefore intubated. Initially, his blood C-peptide level was low, and he showed hyperglycemia with ketosis. Whole body computed tomography (CT) showed pneumonia. He was diagnosed with hyperosmolar hyperglycemic syndrome with ketosis, COVID-19 infection, convulsion, hemoconcentration, liver dysfunction, rhabdomyolysis, pancreatitis, renal failure and hypernatremia. He was admitted to the intensive care unit, where he was successfully treated. His blood C-peptide returned to the normal range (2.2 ng/mL) on day 20, and he returned to the local medical facility on day 21. This is the first report of transient decrease in insulin secretion after COVID-19 infection in a patient with a combination hyperosmolar hyperglycemic syndrome and ketosis. Further prospective studies are needed to clarify the characteristics of the insulin secretion function following COVID-19 infection.

Keywords: *COVID-19, soft drink, hyperglycemic hyperosmolar syndrome, c-peptide*

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1. Introduction

The increased consumption of soft drinks is associated with the onset of metabolic diseases, such as obesity, metabolic syndrome (MetS), type 2 diabetes mellites (DM2), hypertension, dyslipidemias, stroke, and cardiovascular diseases [1,2,3,4]. There is increasing awareness about the impact of obesity and DM2 on COVID-19, including increased risk of infection, post-infection complications, and mortality [5,6]. Furthermore, oral glucose tolerance tests and the C-peptide release test demonstrate a decrease in glucose-stimulated C-peptide secretory capacity and an increase in HbA1c in COVID-19 patients [7]. COVID-19 virus spike protein and virus RNA, coronavirus-like particles were detected in the autophagolysosomes of pancreatic acinar cells of a patient with COVID-19 [7]. Accordingly, it is considered that COVID-19 can directly or indirectly damage the islet function in the pancreas [7,8] While previous reports have demonstrated that COVID-19 caused permanent impairment of the islet function, no studies have reported the recovery of the islet function after COVID-19 infection [8,9,10]. We herein report the case of a patient with soft drink syndrome followed by a hyperglycemic hyperosmolar state with ketosis induced by a transient decrease of insulin secretion after COVID-19 infection.

2. Case Report

A 52-year-old male was transported to a local medical facility due to unconsciousness and involuntary movement. His past history included only hypertension, which was treated with amlodipine (10 mg), losartan (100 mg) and celiprolol (400 mg). Glucose intolerance had not been pointed out in a medical checkup. He had smoked 20 cigarettes per day for 22 years and consumed over 2 L of soft drink per day. His height was 171 cm, and his weight was 95 kg, corresponding to a body mass index of 34. He was diagnosed with hyperosmolar hyperglycemic syndrome (glucose, 637 mg/dL) and polymerase chain reaction test was positive for COVID-19. He was therefore transferred to our department. On arrival, his vital signs were as follows: Glasgow Coma Scale, E1V1M5; blood pressure, 120/80 mmHg; heart rate, 120 beats per minute; and respiratory rate, 26 breaths per minute. A physical examination revealed no particular findings other than obesity. He was intubated due to unconsciousness. The results of an arterial blood gas analysis under 100% oxygen were as follows:

pH, 7.418; $PaCO_2$, 45.7 mmHg; PaO_2, 64.9 mmHg; HCO_3^-, 29.0 mmol/L; and lactate, 3.7 mmol/L. The patient's other blood test results are shown in Table 1. Initially, his blood level of C-peptide was below the normal range, suggesting decreased insulin excretion [11]; he also showed hyperglycemia with ketosis. Electrocardiography showed sinus tachycardia. Whole body computed tomography (CT) showed pneumonia (Figure 1) and swelling of the liver.

Table 1.

variables	level
white blood cell count	17,500 /μL
hemoglobin	19.5 g/dL
platelet	35.7×10^4/μL
total protein	6.7 g/dL
albumin	3.5 g/dL
aspartate aminotransferase	72 U/L
alanine aminotransferase	45 U/L
amylase	899 U/L
creatinine phosphokinase	3668 U/L
glucose	523 mg/dL
HbA_1C	15.50%
blood urea nitrogen	73.8 mg/dL
creatinine	3.57 mg/dL
sodium	162 mEq/L
potassium	4.5 mEq/L
C-reactive protein	1.61 mg/dL
prothrombin time international normalized ratio	1.04
activated partial thromboplastin time	22.3 seconds
D-dimer	6.0 μg/mL
total ketone body	3570 (<130)μmol/L
acetoacetate	1089 (<55)μmol/L
β-hydroxybutyric acid	2481 (<85)μmol/L
C-peptide	0.9 (1.5-3.5) ng/mL
anti glutamic acid decarboxylase antibody	5.0> U/mL

( ), normal range.

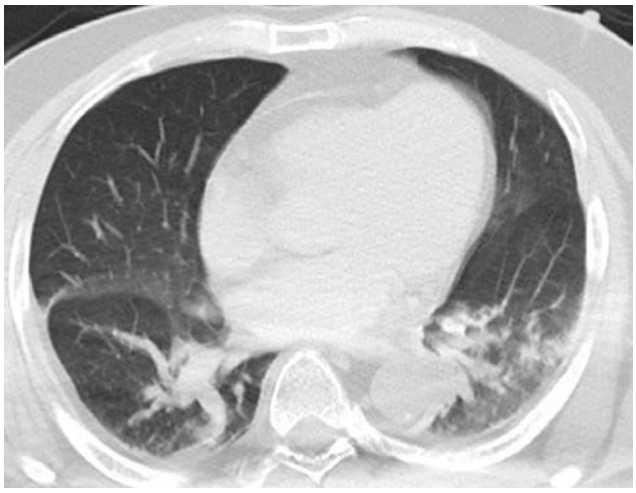

Figure 1. Chest computed tomography (CT) on arrival CT showed mild consolidation in the dorsal region of the bilateral lungs

He was diagnosed with hyperosmolar hyperglycemic syndrome with ketosis, COVID-19 infection, convulsion, hemoconcentration, liver dysfunction, rhabdomyolysis, pancreatitis, renal failure and hypernatremia. The patient was therefore admitted to the intensive care unit. The time course of the infusion volume, PaO_2/FiO_2 (P/F) ratio, and contents of antibiotics are shown in Figure 2. The time course of his blood levels of glucose, sodium and potassium, and the speed of continuous infusion of insulin are shown in Figure 3.

An infusion volume of over 10,000 ml per day was initially required to maintain urinary flow. The PaO2/FiO2 ratio (P/F ratio) initially deteriorated; thus, tazobactam/piperacillin (TAZ/PIPC) was switched to the combination of meropenem (MEPM), vancomycin (VCM), and micafungin (MCFG). After switching antibiotics, the P/F ratio gradually improved and the patient was extubated on day 8.

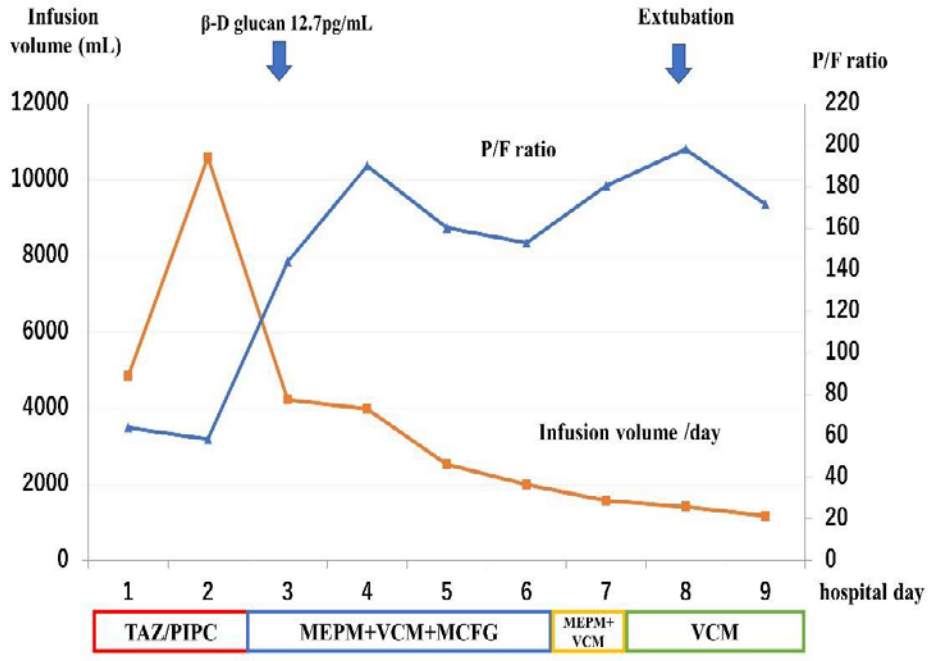

Figure 2. Time course of the infusion volume, P/F ration and antibiotics

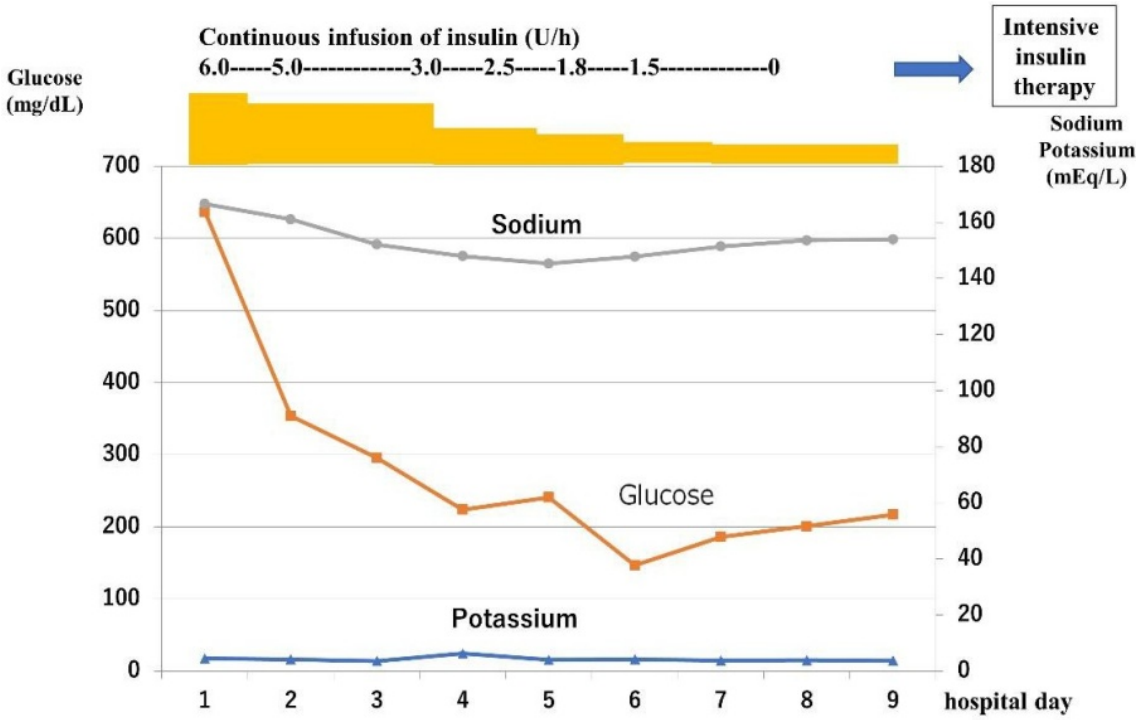

Figure 3. Time course of the blood levels of glucose, sodium and potassium, and the speed of the continuous infusion of insulin (P/F, PaO2/FiO2; TAZ, Tazobactam; PIPC, piperacillin; MEPM, Meropenem; VCM, vancomycin; MCFG, micafungin.)

The speed of the continuous infusion of regular insulin gradually decreased and infusion was ceased on day 9. Insulin therapy was then switched to intermittent subcutaneous injection of insulin, dependent on the blood level of glucose on the same day.

An infusion volume of over 10,000 ml per day was initially required to maintain the urinary flow. The P/F ratio initially deteriorated; thus, tazobactam/piperacillin (TAZ/PIPC) was switched to a combination of meropenem (MEPM), vancomycin (VCM), and micafungin (MCFG) on day 3. After this switch, the P/F ratio gradually and improved the patient was extubated on day 8. The speed of continuous infusion of regular insulin was gradually decreased and infusion was ceased on day 9. Insulin therapy was then switched to intermittent subcutaneous injection of insulin dependent on the blood level of glucose on the same day. Sputum cultures on day 1 later showed Staphylococcus aureus and Streptococcus agalactiae. Blood cultures on day 1 later showed Streptococcus equinus and Propionibacterium avidum ssp granulosum. Blood cultures on day 3 later showed Methicillin-Resistant Staphylococcus epidermidis and Staphylococcus aureus. Later, tests for β-D glucan were negative. Based on these results, the antibiotic therapy was deescalated to VCM only until day16 based on the results of drug sensitivity testing. On day 9, he showed upper extremity-dominant muscle weakness corresponding to grade 3 on a manual muscle test with decreased tendon reflexes induced by disuse atrophy, critical illness neuromyopathy and/or Guillain-Barré Syndrome. His respiratory function improved and supplemental oxygen could be withdrawn on day 11. His muscle weakness smoothly improved with rehabilitation, and he was able to stand and feed himself on day 16. His blood level of C-peptide returned to the normal range (2.4 ng/mL) on day 20. He returned to the local medical facility for further rehabilitation on day 21.

3. Discussion

This is the first report describing a transient decrease of insulin secretion after COVID-19 infection in a patient with the combination of hyperosmolar hyperglycemic syndrome and ketosis.

A previous report showed that a patient with soft drink syndrome maintained insulin secretion and showed increased insulin resistance in target organs. 4 Another report showed that a patient with hyperosmolar hyperglycemic syndrome maintained insulin secretion and showed increased insulin resistance in target organs [12]. Although a previous study expressed the opposite opinion, COVID-19 infection could reduce insulin secretion [13]. Patients with decreased C-peptide levels can develop severe hyperosmolar hyperglycemic syndrome and/or ketosis [12,14]. Accordingly, the hypothesized pathophysiological mechanism of the present case is as follows. The patient had a high glucose level due to increased insulin resistance because of his excessive caloric intake. This was followed by the complication of ketosis, which was induced by decreased insulin secretion induced by COVID-19 infection, resulting in the severely illness of the patient in the present case.

4. Conclusion

This is the first report of transient decrease in insulin secretion after COVID-19 infection in a patient with a combination hyperosmolar hyperglycemic syndrome and ketosis. Further prospective studies are needed to clarify the characteristics of the insulin secretion function following COVID-19 infection.

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