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Case Report

An Insulin Resistance Case Report: Uncontrolled Hyperglycaemia in Type 1 Diabetic Patient Post COVID-19 Infection

Yousef Almehrzi*, Majdi Al Najjar, Mohammed Alnuaimi

Department of Endocrinology, Zayed Military Hospital, Abu Dhabi, UAE

ABSTRACT

COVID-19, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in late December 2019 in Wuhan, China, and has spread to become a pandemic with over 100 million confirmed cases and still growing. The infectious nature and hence, high hospitalization rates and intensive care admissions are resulting in high mortality rates. Alarmingly, COVID-19 infection and virus-induced respiratory dysfunction poses a serious threat to patients with chronic illnesses such as diabetes, Asthma, COPD and obesity. COVID-19 patients with diabetes show higher complication and mortality rate than patients without diabetes. Transient non-severe increased insulin requirement in patients hospitalized for medical conditions such as sepsis or myocardial infarction is a well-known phenomenon. However, extremely high-dose insulin requirement remains a very rarely reported entity, but this showed up in COVID-19 positive cases. Here, we report the case of transitory moderate increase in insulin requirement in a type 1 diabetic (T1D) patient who was previously well controlled in the absences of any medical conditions known to be a causative factor. We collected the data and compared total insulin daily requirement against pre-meal glycemia and blood gas results to reflect insulin resistance and multiple DKA events related to trials of multiple oral hypoglycemic agents and GLP1 analogue as potential target for intervention in addition to insulin therapy and low carb diet.

Keywords: Covid 19; Type 1 diabetes; Insulin resistance; GLP1; Metformin; Pioglitazone; Insulin; Risk factors; Low carb diet

INTRODUCTION

Here, we report a case of uncontrolled hyperglycemia reflecting insulin resistance occurred following *SARS-CoV-2* infection in a 24-year-old female with normal BMI of 24, who previously had T1D. She was presented at our emergency department with diabetic ketoacidosis (DKA), C-peptide level: 0.5 $\mu g\,l^{-1,}$ Blood glucose concentration: 30.6 $mmol\,l^{-1}$ (552 $mg\,dl^{-1}$), Hemoglobin A1C: 7.4%. The patient tested positive for COVID-19 infection and managed conservatively. The patient developed uncontrolled hyperglycemia requiring increased doses of insulin for 2 months then returned to usual doses gradually. The patient was investigated for a possible cause for insulin resistance and no causative factor was found. We attempted to manage the hyperglycemia insulin and low carb diet. We used metformin, pioglitazone and liraglutide as potential intervention for insulin resistance but the patient developed DKA and medication was stopped.

CASE PRESENTATION

24 years female, T1D treated with subcutaneous insulin pump, well controlled (HbA1 c 7.4%) was admitted to isolation ward due to positive COVID-19. She developed fever of 38°C, sore throat, loss of appetite, generalized fatigability, and dry cough on the first 2 days of infection. The patient did not receive any medication or steroids as management for Covid-19 which lasted 10 days, during which she developed multiple DKA episodes. The multiple DKA episodes were treated according to international approved protocol but the insulin requirement was also higher than expected, ranging from 3 to 4 units/h of IV insulin infusion pump.

The pre meal glycaemia: The fasting blood sugar, PH, and total insulin daily dose were correlated against time over the admission period until the resolution of hyperglycemia as shown in Figure 1. The patient's total daily dose before COVID-19 infection was 28 units/day, her requirement increased to 55 to 94 units/day as MDI, insulin glargine u300 (20 units) and insulin apart (24 units) TDS on average at the time of discharge.

The patient had euglycemia DKA after initiation of treatment by metformin and beta-oh-butyric acid was extremely elevated at 2354mcg/l (normal range up to 270) to confirms DKA and

***Corresponding to:** Yousef Almehrzi, Department of Endocrinology, Zayed Military Hospital, Alkahleej Alarabi st, Al Rawdh, Abu Dhabi, UAE, Tel: +97124055000; E-mail: sayhi2me2@gmail.com

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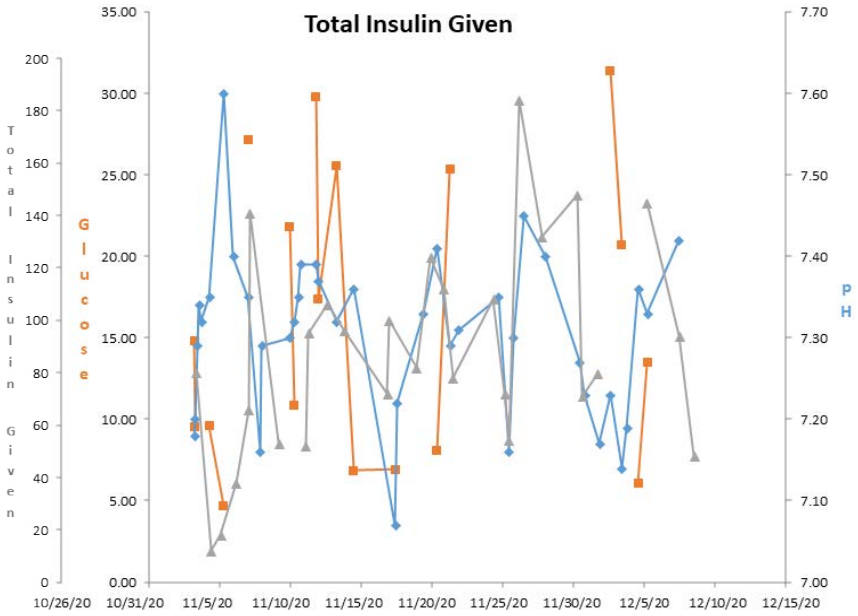

Figure 1: Total daily insulin vs glucose vs PH during admission, reflecting insulin resistance.

metformin was stopped. Similar scenario accrued with pioglitazone and liraglutide. The Possible causes of insulin resistance were investigated to rule out secondary causes of DKA, normal thyroid function test, normal cortisol, 24 h urine cortisol and ACTH and normal dexamethasone suppression test, no sepsis or UTI and normal CRP. Insulin auto antibodies are weakly positive at 0.8 u/ml (normal range <0.4) [1]. The patient weight was stable at 60kg and BMI was 24 with no family history of type 2 diabetes, and her diabetes duration is of 15 years without micro-complications [2].

The patient was discharged on low carb (40g per meal) diet and total insulin dose of 92 units as insulin Glargine u300 20 units and 24 units of insulin apart TDS to keep the blood glucose in target below 200. The period of uncontrolled hyperglycemia and increased insulin resistance lasted 10 weeks and eventually over time the insulin dose was reduced gradually every two weeks in outpatient clinic as glycaemia improved overtime.

DISCUSSION

Insulin resistance has also been described in T1D and may be a potential target for intervention in addition to insulin therapy [1]. The role of metformin in aid to ongoing intensive insulin therapy in T1D has been evaluated in several randomized trials [3,4]. Several other anti-diabetic drugs have been investigated for their add-on role including thiazolidinediones, DPP4 inhibitors, GLP-1 analogs, α-glucosidase inhibitors, SGLT2 inhibitors and dual SGLT1-SGLT2 inhibitors [5].

In this case, we tried metformin, pioglitazone and liraglutide with no reduction on required total daily dose and observed increase risk of DKA. We noticed the difference between infused insulin and subcutaneous insulin as sliding scale (given by nurse); total daily requirement was less by 30% when given IV. A low glucose diet (40g) was tried successfully with glucose range within 100-200 and lower doses of insulin required before each meal to keep the glucose in target range. The diet helped in preventing further DKAs, but it was not tolerated by the patient for long time.

Our report findings cannot fully establish connection between COVID-19 and the development of insulin resistance in this patient after excluding all possible causes of insulin resistance, we suggest that SARS-CoV-2 infection, might negatively affect pancreatic function, perhaps through direct cytolytic effects of the virus on β-cells or through the effects on insulin receptor or its degradation [3,6].

CONCLUSION

Health practitioners should be aware of the possibility of insulin-resistance in diabetic patients as a complication in patients infected with *SARS-CoV-2*.

Insulin remains the mainstay of treatment approach in diabetic patients with insulin resistance as a complication of COVID-19 infection. The optimal management of hyperglycemia of diabetic patients infected with *SARS-CoV-2* is very important [7] and has not been defined yet.

Given the situation of this case, more research into *SARS-CoV-2* entry receptors, including angiotensin-converting enzyme 2, which are expressed on pancreatic β-cells is required to explain this phenomenon.

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Statement of Ethics: The patient has given her written informed consent.

The study protocol was approved by the Abu Dhabi Region Ethics and Research Committee/ Zayed Military Hospital with reference no 2021.3 dated 28/02/2021.

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