CASE REPORT

Diabetic Ketoacidosis with Lower-than-anticipated Glucose Levels, and Recalcitrant Metabolic Acidosis Requiring Rescue Hemodialysis in a Patient of COVID-19 Infection

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Abstract

Coronavirus disease-2019 (COVID-19) has stood out as a disease of great medical interest, influencing disease evolution, and severity of diabetes mellitus. The intersection of COVID-19 infection and diabetes mellitus has unmasked inflammation and critical metabolic disturbances. We deliberate the case of a young woman, with type 2 diabetes mellitus, who was hospitalized for COVID-19 infection. Work-up revealed diabetic ketoacidosis (DKA) with lower-than-anticipated glucose levels, and acute metabolic acidosis. Refractoriness of metabolic acidosis to standard treatment required hemodialysis as a salvage therapy.

Keywords: COVID-19 infection, Diabetic ketoacidosis with lower-than-anticipated glucose levels, Hemodialysis, Refractory metabolic acidosis.

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Introduction

Diabetes mellitus increases the risk of complications as well as mortality following COVID-19 infection. Tropism of severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) for beta cells damages them leading to impaired insulin secretion.[1] The resultant COVID-19 infection is characterized by inflammation and suppressed immunity. As we stand at the cross-roads of diabetes mellitus and COVID-19 infection, we are faced with challenging complications of the old illness as well as the new virus.

Case Description

A 45-year-old woman with a body mass index of 23 kg/m^2 and a medical history of type 2 diabetes mellitus presented to the emergency room (ER) with a 3-days history of vomiting with generalized weakness, and fever since a day. Medications consisted of Metformin, Pioglitazone, Glimepiride, and Canagliflozin. On arrival to the ER, she was tachycardic at 130 beats/minute, blood pressure of 130/80 mm Hg, saturating at 100% on 4-L oxygen (nasal cannula) with a respiratory rate of 22 breaths/minute. Finger-stick blood glucose in the ER was 186 mg/dL. Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) ribonucleic acid polymerase chain reaction test was positive. She was transferred to the COVID-19 ICU for further management. She was tachypneic and appeared lethargic. She was able to communicate in complete sentences. High anion gap metabolic acidosis, finger-stick glucose levels <250 mg/dL, urine ketones at 4+ and a medication history of sodium–glucose co-transporter-2 (SGLT2i) was managed as DKA with lower-than-anticipated glucose levels with intravenous fluids, and short-acting insulin infusion. All oral hypoglycemic medications were discontinued. Intravenous sodium bicarbonate (Table 1) did not affect her metabolic acidosis (Fig. 1) requiring hemodialysis twice as a rescue therapy. Also, estimated glomerular filtration rate (eGFR) was 94 mL/min/1.73 m^2. Hypokalemia, hypophosphatemia, and hypomagnesemia were managed with appropriate supplements. Intravenous methylprednisolone and subcutaneous low molecular weight heparin were administered for the COVID-19 pneumonia. Figure 2 displays her finger-stick blood glucose trends. Glycosylated hemoglobin was 12.1%.

Stabilized, she was discharged a fortnight later with continuation of subcutaneous short and long-acting insulin. At 3 months of follow-up, her blood glucose levels are under control.

Disussion

This was a patient with type 2 diabetes mellitus on Metformin and an SGLT2i. Both these medications predispose to acidosis. Metformin[2] and Pioglitazone upregulate angiotensin-converting enzyme-2 receptors (ACE2Rs),[3] the portal of entry for SARS CoV-2. Low pH favors entry of SARS CoV2 into the cells, with subsequent viral replication.[4] Virus–host interaction in the pancreas leads to destruction with consequent reduced function of the beta cells. The COVID-19 infection stimulates cytokines and hence the production of stress hormones. The resultant increased inflammation increases

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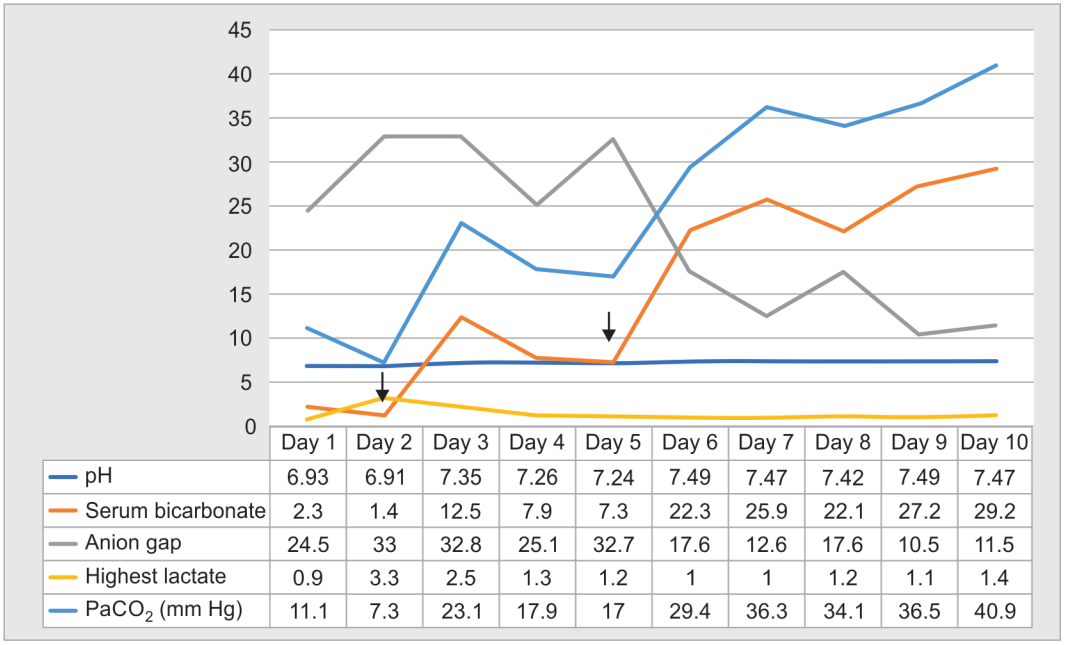
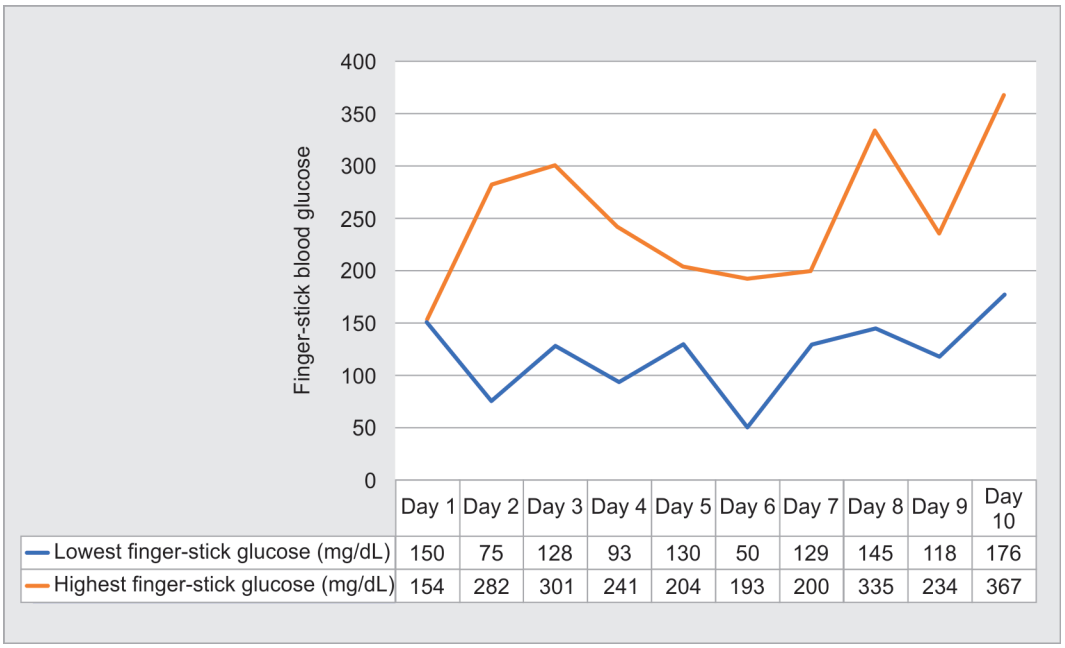
Table 1: Intravenous fluids to closure of anion gap

ICU day	*Day 1*	*Day 2*	*Day 3*	*Day 4*	*Day 5*	*Day 6*	*Day 7*	*Day 8*	*Day 9*	*Day 10*
Intravenous fluids (mL/24 hr)	7,280	5,762	5,033	4,531	4,595	4,492	2,982	4,797	3,670	5,400
Sodium bicarbonate (8.4% conc.) (mL/24 hr)	196	680	90	—	100	—	—	—	—	—
Anion gap (mEq/L)	24.5	33	32.8	25.1	32.7	17.6	12.6	17.6	10.5	11.5



	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
pH	6.93	6.91	7.35	7.26	7.24	7.49	7.47	7.42	7.49	7.47
Serum bicarbonate	2.3	1.4	12.5	7.9	7.3	22.3	25.9	22.1	27.2	29.2
Anion gap	24.5	33	32.8	25.1	32.7	17.6	12.6	17.6	10.5	11.5
Highest lactate	0.9	3.3	2.5	1.3	1.2	1	1	1.2	1.1	1.4
$PaCO_2$ (mm Hg)	11.1	7.3	23.1	17.9	17	29.4	36.3	34.1	36.5	40.9

Fig. 1: Acid-base trajectory during ICU stay (arrow = hemodialysis)



	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
Lowest finger-stick glucose (mg/dL)	150	75	128	93	130	50	129	145	118	176
Highest finger-stick glucose (mg/dL)	154	282	301	241	204	193	200	335	234	367

Fig. 2: Finger-stick blood glucose levels (mg/dL)

expression of ACE2R.[5] A possible mechanism for development of DKA. Studies show that following COVID-19 infection, glycemic irregularity is prognostic factor for diabetic patients. Hyperglycemia stimulates the production and release of cytokines. Insulin requirements have reportedly increased following SARS infection.[6] Severe metabolic complications of diabetes have also been

reported.[7,8] Breakdown of fats generating ketosis and ketoacidosis has been reported following COVID-19 infection.[7] Metformin and SGLT2i need to be discontinued following COVID-19 infection in view of their intrinsic risk of lactic acidosis, and DKA with lower-than-anticipated glucose levels.[9]

This patient had a suboptimal glycemic control but of note, there was no history of DKA in the past. Management consisted of insulin infusion and intravenous fluids, the basis of treatment of DKA. Bicarbonate therapy is controversial and is generally avoided if pH is more than 7.1. It may prevent the need for dialysis.[10] The evolution of the patient's course is notable for persistence of metabolic acidosis with several doses of bicarbonate failing to raise her pH requiring dialysis. There was neither an evidence of acute kidney injury nor a history of chronic kidney disease. Metabolic parameters improved transiently only to destabilize over the next 48 hours, re-requiring hemodialysis. Acidosis reversed after hemodialysis without any complications of cerebral edema.

Potential influencers of hypokalemia were intravenous insulin infusion, renal potassium wasting as a result of COVID-19 infection,[11] and downregulation of ACE2R by SARS CoV-2 with resultant reduced degradation of angiotensin II increased aldosterone secretion leading to urinary potassium loss.

Temporal course of acid–base disturbances, correlates of renal replacement therapy instituted for the intractable metabolic acidosis (Fig. 1), and time to closure of anion gap (Fig. 2) raise a question whether the intersection of COVID-19 infection and diabetes mellitus have an additive or an augmenting effect.

Conclusion

Clinical complexity determines the treatment strategy of patients with DKA. Hemodialysis should be offered as a life-saving intervention early in the course of therapy if metabolic acidosis persists despite an adequate fluid resuscitation and insulin therapy.

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